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ABSTRACT SUPPLEMENT

ACR Convergence 2020

November 5–9, 2020

Virtual

American College of Rheumatology
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Table of Contents

Monday, November 9

9:00 AM - 11:00 AM
Poster Session D
(#1527-1947)

10:00 AM – 1:00 PM; 3:00 – 6:00 PM
Oral Abstract Sessions
(#1948–1952) Cytokines & Cell Trafficking
(#1953–1957) Genetics, Genomics & Proteomics
(#1958–1962) Health Services Research
(#1963–1967) Measures & Measurement of Healthcare Quality
(#1968–1972) Osteoarthritis & Joint Biology – Basic Science
(#1973–1977) Osteoporosis & Metabolic Bone Disease
(#1978–1982) Patient Outcomes, Preferences, & Attitudes II: Engagement, Perceptions, & Quality of Life
(#1983–1987) Pediatric Rheumatology – Clinical II: Outcomes & Care Delivery
(#1988–1992) Pediatric Rheumatology – Clinical III: Systemic Autoimmune Disease
(#1993–1997) RA – Treatments I: Maximizing Health in RA
(#1998–2002) RA – Treatments II: Potential Harms & Adverse Events
(#2003–2007) RA – Treatments III: Predictors of Treatment Response
(#2008–2012) RA – Treatments IV: New Therapies & Strategies
(#2013–2017) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II
(#2018–2022) Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes III: Imaging in SpA
(#2023–2027) Spondyloarthritis Including Psoriatic Arthritis – Treatment II: Emerging Therapies
(#2028–2032) Spondyloarthritis Including Psoriatic Arthritis – Treatment III: Axial Spondyloarthritis
(#2033–2037) Systemic Sclerosis & Related Disorders – Clinical I: Stratification Strategies for Clinical Trials
(#2038–2042) Systemic Sclerosis & Related Disorders – Clinical II: Lessons Learned from Clinical Trials & Cohorts
(#2043–2047) T Cell Biology & Targets in Autoimmune & Inflammatory Disease
(#2048–2052) Vasculitis – ANCA-Associated

Late-Breaking Abstracts
Monday, November 9

9:00 - 11:00 AM
Poster Session D
(#L01–L05) Late-Breaking Posters

11:30 AM - 1:00 PM
Late-Breaking Oral Session
(#L06–L11) Late-Breaking Abstracts

Patient Perspectives
Sunday, November 8

12:00 - 1:00 PM
Patient Perspectives
(#PP09–PP12) Patient Perspectives

Monday, November 9

9:00 AM - 11:00 AM
Poster Session D
(#PP01–PP08) Patient Perspectives Poster Session

Arthritis & Rheumatology
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DOI 10.1002/art.41538

American College of Rheumatology
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Abstract Number: 0001

Management of Rheumatic Diseases During COVID-19: A National Veterans Affairs Survey of Rheumatologists

Jasvinder Singh[1], John Richards[2], Elizabeth Chang[3], Amy Joseph[4] and Bernard Ng[5], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, [3]PVAHCS, Phoenix, AZ, [4]Washington University / St. Louis VA, Saint Louis, MO, [5]VA Puget Sound HCS, Seattle, WA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Rheumatic Disease
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: To assess the experience, views and opinions of rheumatology providers at Veterans Affairs (VA) facilities about rheumatic disease healthcare issues during the COVID-19 pandemic.

Methods: We used the Qualtrics™ survey to perform an anonymized cross-sectional survey of all VA rheumatology providers, who were members of the VA Rheumatology Consortium, a volunteer organization of VA rheumatologists. Non-responders received reminders to complete the survey from April 16 to May 18, 2020. We assessed provider experience, views and opinions about various COVID-19 issues and resilience.

Results: Of the 153 eligible VA rheumatologists, 103 (67%) completed the survey. Potential participants were slightly older (16% vs. 11% were ≥65 yrs) and more likely to be male compared to the survey responders (45% vs. 38%).

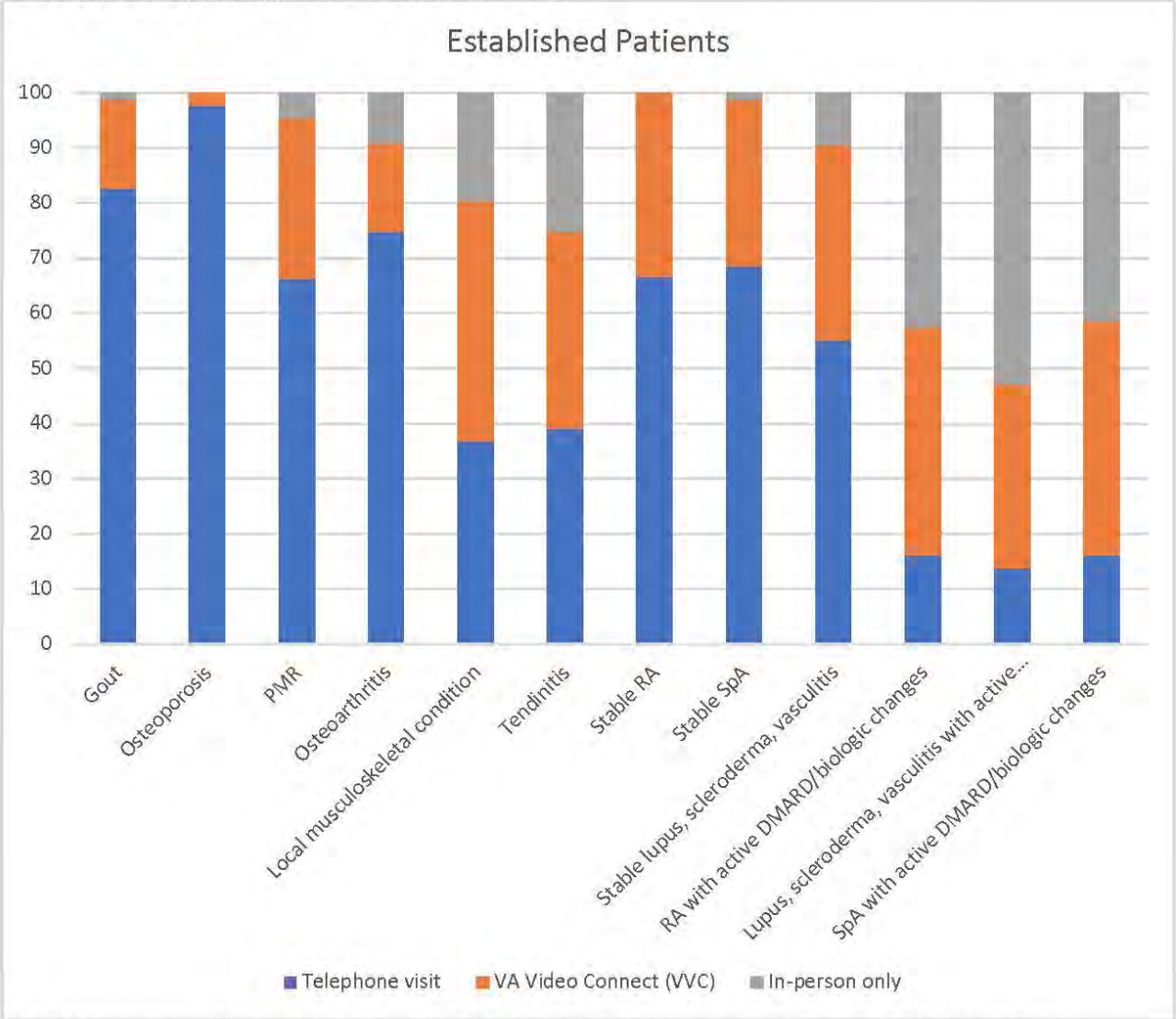
Established patients. Most/majority of rheumatologists considered that the following conditions were appropriate for telephone follow-up visits: gout, osteoporosis, polymyalgia rheumatica, sTable rheumatoid arthritis, sTable spondyloarthritis, and osteoarthritis (**Figure 1**). One-third or more rheumatologists considered it appropriate to have a video based VA video connect (VVC) visit for local musculoskeletal conditions, tendinitis, rheumatoid arthritis with active medication (DMARD/biologic) changes and patients with sTable lupus, scleroderma or vasculitis; 53% preferred an in-person for people with lupus, scleroderma, vasculitis with immunosuppressive or glucocorticoid dose changes (**Figure 1**).

Most/majority of the responders were somewhat or very comforTable with technology for providing healthcare to established patients during COVID-19 pandemic using: (1) telephone, 87%; (2) VA video connect (VVC), 64%; and (3) in-person visits, 54% (**Figure 2**). A smaller proportion were comforTable with technology providing healthcare to new clinic patients (**Figure 2**).

High provider resilience was independently associated with significantly higher odds ratio (OR) of more comfort with technology for telephone (OR, 3.1 (95% CI, 1.1-9.7)) and VVC visits for new patients (OR, 4.7 (95% CI, 1.4-15.7)), with no difference for in-person visits (OR, 1.8 (95% CI, 0.7-5.0)).

Live vaccine. Most responders would not hold hydroxychloroquine (95%) or sulfasalazine for a live COVID-19 vaccine (74%). A majority would hold methotrexate or leflunomide (66%) and glucocorticoids of 20 mg/day or higher (52%)

Figure 1. Provider preferred clinic follow-up appointment modality for established patients due to COVID-19, by the type of rheumatic disease



Y-axis represent the percent of all valid non-missing responses. The number of missing responses for each condition varied n=16 to n=18

Figure 1. Provider preferred clinic follow-up appointment modality for established patients due to COVID-19, by the type of rheumatic disease Figure 1 legend. Y-axis represent the percent of all valid non-missing responses. The number of missing responses for each condition varied n=16 to n=18. VA telehealth includes 3 modalities: (1) telephone care; (2) a video-based VA video connect (VVC) visit with the healthcare provider, usually with the patient at home; and (3) clinical video telehealth (CVT) visits with a facilitator, usually with a facilitator (nurse, technician, primary care provider) assisting patient examination at a healthcare facility close to patient's home. Due to limited relevance of CVT facilitator during the COVID-19 pandemic, choices offered were telephone care, video-based VVC or in-person visit

for 2 weeks or less (**Figure 3**); and would hold non-TNF biologics (76%), anti TNF-biologics (85%), Janus-kinase inhibitors (78%), anti IL-17/23 biologics (82%), belimumab (77%)immunosuppressive drugs such as azathioprine (64%), for 3-8 weeks (**Figure 3**).

Killed vaccine. A majority of responders (50% or higher) would not withhold these drugs for a killed COVID-19 vaccine; another 25% would hold them off for < 2 weeks (**Figure 3**).

Figure 2. Provider comfort with technology in providing care to new or established patients using each of the modality during COVID-19 pandemic

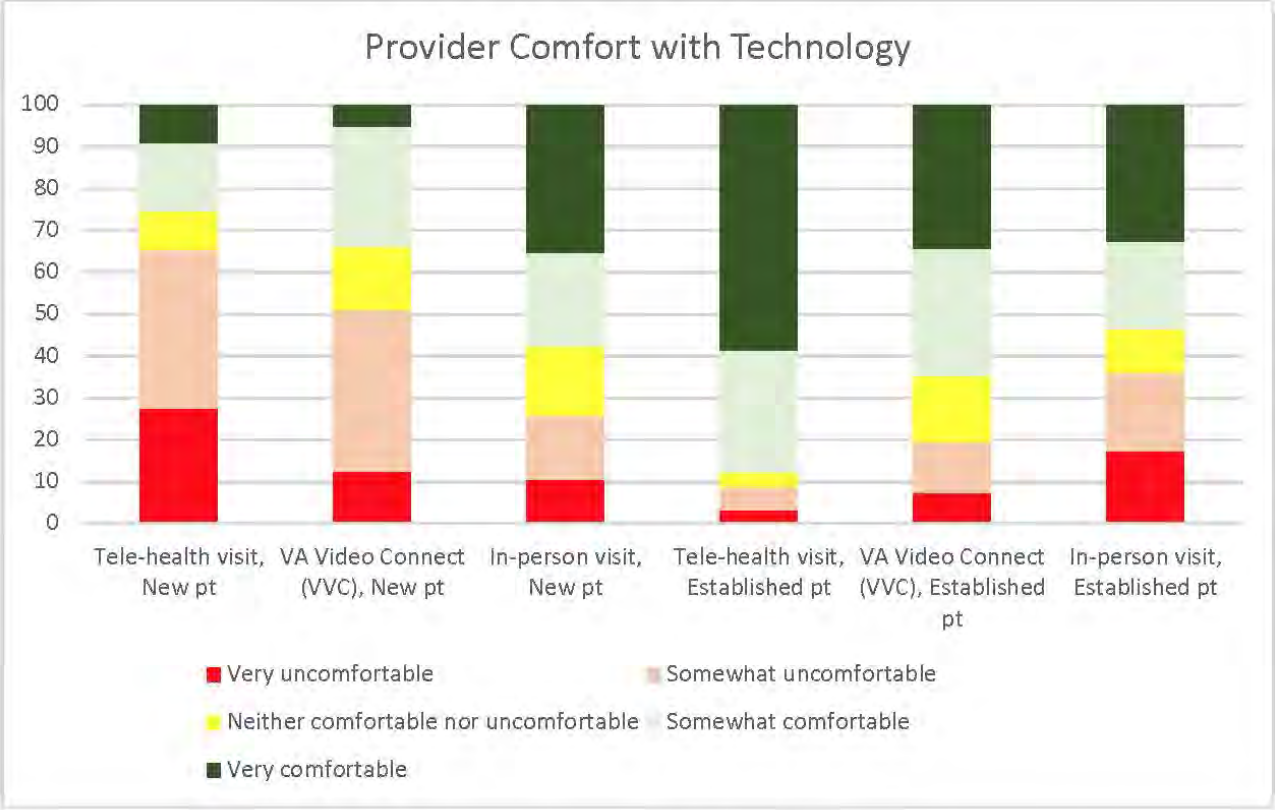


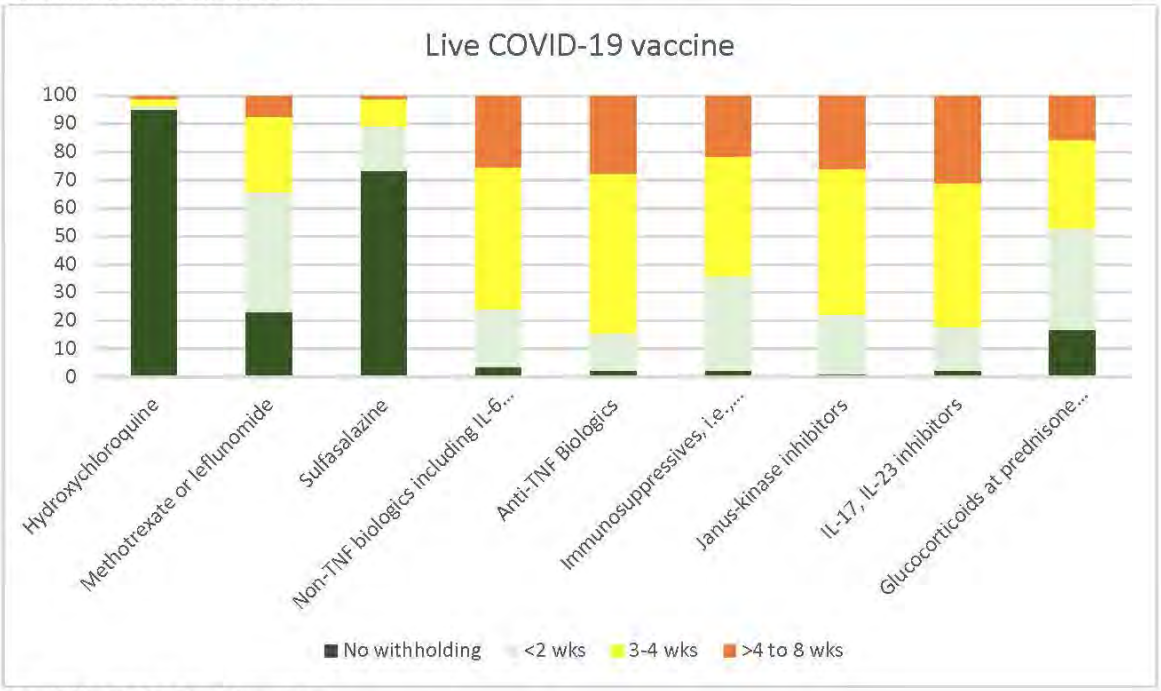
Figure Legend: The Y-axis represent the percent of all valid non-missing responses

Figure 2. Provider comfort with technology in providing care to new or established patients using each of the modality during COVID-19 pandemic Figure Legend: The Y-axis represent the percent of all valid non-missing responses

Conclusion: A better understanding of COVID-19 rheumatic disease healthcare issues using a health-system approach can inform improve the care of Veterans with rheumatic disease and their providers.

Figure 3. Provider opinion on period of withholding of treatments for rheumatic diseases for administering a potential COVID-19 live (3A) or killed (3B) vaccine

3A. Live COVID-19 vaccine



3B. Killed COVID-19 vaccine

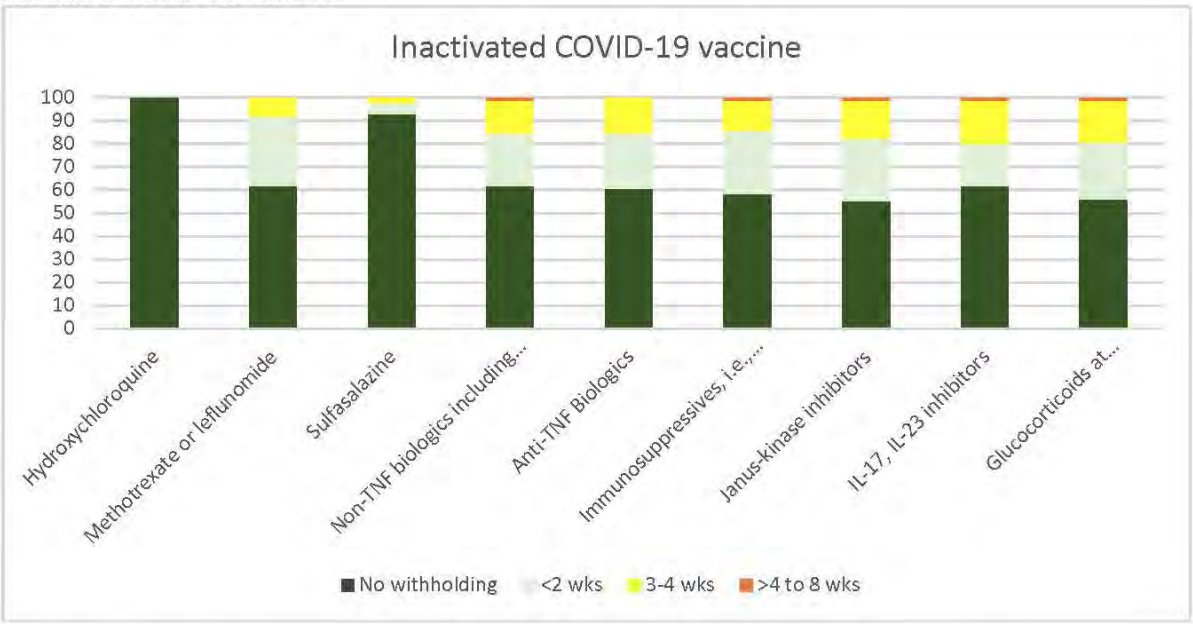


Figure Legend: The Y-axis represent the percent of all valid non-missing responses

Figure 3. Provider opinion on period of withholding of treatments for rheumatic diseases for administering a potential COVID-19 live (3A) or killed (3B) vaccine Figure Legend: The Y-axis represent the percent of all valid non-missing responses

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Disclosure: J. Singh, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of

Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **J. Richards**, None; **E. Chang**, None; **A. Joseph**, None; **B. Ng**, None.

Abstract Number: 0002

Hydroxychloroquine and Chloroquine and Hospitalizations for Viral Infection in the Pre-COVID-19 Era

Cristiano Moura[1], Marina Machado[1], Celline Almeida-Brasil[1], Jeffrey R Curtis[2], Kevin Winthrop[3], Michal Abrahamowicz[1] and Sasha Bernatsky[4], [1]McGill University, Montreal, Canada, [2]Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, [3]Oregon Health & Science University, Portland, OR, [4]The Research Institute of the McGill University Health Centre, Montreal, ON, Canada

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Rheumatic Disease

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Chloroquine (CQ) and hydroxychloroquine (HCQ) have been shown to have antiviral properties and were considered as potential therapeutic options amid the COVID-19 pandemic. The purpose of the current study is to evaluate the risk of hospitalization for viral infections among patients previously exposed (or not) to HCQ/CQ in the pre-COVID-19 era.

Table 1 - Baseline characteristics of RA and SLE patients with outpatient viral infection, Marketscan 2011-2018.

Characteristic	RA/SLE cohort (n= 54,561)
Underlying condition	
SLE	9286 (17.0)
RA	45275 (83.0)
Female sex, N (%)	43668 (80.0)
Mean age (standard deviation), years	57.4 (13.9)
Comorbidities	
Diabetes	10416 (19.1)
Hypertension	29941 (54.9)
COPD/asthma	14611 (26.8)
Cardiovascular disease	7586 (13.9)
Congestive heart failure	3171 (5.81)
Renal disease	3767 (6.90)
Cerebrovascular disease	4632 (8.49)
Cancer	2185 (4.00)
Recent medications[2], N (%)	
Hydroxychloroquine/chloroquine	12473 (22.9)
Methotrexate	14446 (26.5)
Mycophenolate	791 (1.45)
Azathioprine	921 (1.69)
Other synthetic DMARDs[3]	4314 (7.91)
Biologics	12152 (22.3)
NSAIDs	11744 (21.5)
Corticosteroids	12923(23.7)

[1] Any time before the first episode of infection

[2] 90 days before the outpatient/emergency room diagnosis of viral respiratory infection, except for NSAIDS for which a 14-day time window was applied.

[3] Includes cyclophosphamide, sulfasalazine, and leflunomide

Table 2 – Multivariate Poisson analyses of hospitalized viral infection in RA/SLE patients

Model 1: Model without interaction			Model 2: Interaction between HCQ/CQ and underlying condition		
Variables	*RR**	*95% CI*	*Variables*	*RR*	*95% CI*
			HCQ/CQ vs non-HCQ/CQ in RA	0.86	0.66-1.13
HCQ/CQ*	0.89	0.70-1.12	HCQ/CQ vs non-HCQ/CQ in SLE	0.94	0.60-1.48
			SLE pts vs RA pts non treated	1.16	0.82-1.65
SLE	1.20	0.90-1.58	SLE pts vs RA pts treated	1.26	0.83-1.94
Female sex	0.93	0.75-1.15	Female sex	0.93	0.75-1.15
Age	**1.04**	**1.03-1.05**	**Age**	**1.04**	**1.03-1.05**
Comorbidities	**1.86**	**1.41-2.45**	**Comorbidities**	**1.86**	**1.41-2.45**
Methotrexate	0.95	0.77-1.18	MTX	0.95	0.77-1.18
Mycophenolate	**2.54**	**1.51-4.28**	**MMF**	**2.54**	**1.51-4.26**
Azathioprine	**1.90**	**1.12-3.22**	**Azathioprine**	**1.89**	**1.12-3.20**
Other DMARDs	1.17	0.86-1.59	DMARDs	1.17	0.86-1.59
Corticosteroids	**1.57**	**1.29-1.91**	**Corticosteroids**	**1.57**	**1.29-1.91**
Biologic	1.10	0.87-1.37	Biologic	1.09	0.87-1.37
NSAID	0.88	0.69-1.12	NSAID	0.88	0.69-1.12
Emergency room	3.06	2.46-3.82	Emergency room	3.06	2.46-3.82

*RR=risk ratio; all drug exposures were at the time of initial outpatient

Methods: We studied adult rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) individuals identified in the MarketScan database with an outpatient diagnosis (including emergency room, ER) of viral pneumonia or other viral acute respiratory infections. We required patients to be covered in the medical/pharmacy plan at least one year before time zero (date of outpatient infection). The main exposure was recent use of HCQ/CQ in the 90 days prior to time zero. We defined the outcome as hospitalization for viral infection within the 30 days after time zero. We used multivariate Poisson regression models with a robust error variance to estimate hospitalization in relationship to exposure to these drugs. Our models included demographic variables (age, sex), setting in which viral infection was initially identified (ER or other), underlying condition (RA or SLE), comorbidities, and use of other medications (modeled in the same way as the main exposure): methotrexate (MTX), mycophenolate (MMF), azathioprine, other DMARDs (cyclophosphamide, sulfasalazine, and leflunomide), corticosteroids, biologics, and NSAIDs. Analysis were combined for RA and SLE patients, but interaction terms were included to allow for the effect of HCQ to differ in the two conditions.

Results: We identified 63,971 episodes of outpatient infections among 54,561 RA/SLE patients. Baseline characteristics are presented in Table 1. Individuals were mostly women (80%), with average age of 57.4 years (standard deviation, SD 13.9). During the 30-day period following outpatient infection, we found 480 occurrences of hospitalization for viral respiratory infections. In adjusted multivariate analyses, we were unable to detect a clear difference in the risk of hospitalized viral infection when comparing recent versus non-recent use of HCQ/CQ in the past 90 days before the initial outpatient viral infection (adjusted RR: 0.89, 95% CI: 0.70–1.12; Table 2). In the same model, we found that comorbidity, ER presentation, older age, and MMF, azathioprine, and corticosteroids were all significantly associated with hospitalized viral infection.

Conclusion: While we saw no clear effect of HCQ/CQ, comorbidity, ER presentation, older age, and MMF, azathioprine, and corticosteroids were all significantly associated with hospitalized viral infection in RA and SLE.

Baseline characteristics of RA and SLE patients with outpatient viral infection, Marketscan 2011-2018.

Multivariate Poisson analyses of hospitalized viral infection in RA/SLE patients

Disclosure: C. Moura, None; **M. Machado**, None; **C. Almeida-Brasil**, None; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **K. Winthrop**, Pfizer, 2, 5, UCB, 2, 5, Abbvie, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Roche, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 5; **M. Abrahamowicz**, None; **S. Bernatsky**, None.

Abstract Number: 0003

Assessing Cytokine Profiles and COVID Serology in Patients on Immunosuppression to Guide Care Recommendations

Quinn Pritchett[1], Rebecca Overbury[1], Dorota Lebiedz-Odrobina[1], Julie Thomas[1], Tawnie Braaten[2], Stacey Clardy[1], Marc Elgort[3], Emily Spivak[1], Patricia Slev[3], Lisa Peterson[3] and Tracy Frech[4], [1]University of Utah, Salt Lake City, UT, [2]University of Utah, Salt Lake City, [3]ARUP, Salt Lake City, UT, [4]University of Utah and Salt Lake Veterans Affair Medical Center, Salt Lake City, UT

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Rheumatic Disease

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The COVID-19 pandemic is especially terrifying for patients on immunosuppression for autoimmune disease. With the exception of social isolation, experts do not have clear guidelines for these patients due to the concern that stopping medications may increase risk of autoimmune disease flares and pro-inflammatory cytokine/chemokine response. These same inflammatory molecules are thought to be responsible for virus-induced immunopathological events and death in COVID-19. The purpose of this project is to establish guidelines for management of immunosuppression in autoimmune disease patients and collect pilot data to develop strategies at the healthcare system level to address barriers and facilitators in the treatment of high-risk populations.

Methods: Participants were consented prior to blood collection for routine toxicity monitoring (IRB #00131823). Patients verified their autoimmune diagnosis; current immunosuppression medication list; and whether they believe they currently have or had symptoms of COVID-19. They were asked if they had previous COVID PCR testing and those results. A cytokine panel developed by ARUP (Test #0051394) assessed the concentrations of interleukin (IL)-2 receptor (IL-2r), soluble, TH1 cytokines (interferon (IFN)-γ, IL-2, IL-12); TH2 (IL-4, IL-5, IL-10, IL13); Monokines (tumor necrosis factor (TNF)-α, IL1β, IL6, IL8) and IL-17. COVID-19 IgG serologic testing developed by ARUP for research purposes was performed. We summarized demographics and clinical outcomes of interest using median and range for distribute skew continuous variable; we reported counts for categorical variables.

Results: Thirty-nine patients with autoimmune disease on immunosuppressive/immunomodulatory therapy were enrolled between April 18 and May 21, 2020. The clinical features of these patients shown in Table 1. The median age of participants was 45 years within the range of 23 to 76 years. Most participants were white (n=27, 69%), females (n=35, 90%) and had a diagnosis of systemic sclerosis (n=27, 69%). Half of these patients were on hydroxychloroquine (n=20, 51%). One patient reported current COVID symptoms and five patients were previously symptomatic for COVID-19 infection. One patient that obtained COVID PCR testing while symptomatic was positive. There was minimal elevations in cytokine profiles including, IL-2r (n=2), IL-10 (n=1), and IL-6 (n=1). Serology testing of The Utah COVID cases by testing day are described in Figure 1. Only one patient of the five reporting previous symptoms was positive for COVID IgG. This subject had rheumatoid arthritis (RA) and was on Enbrel. She reported diarrhea and a

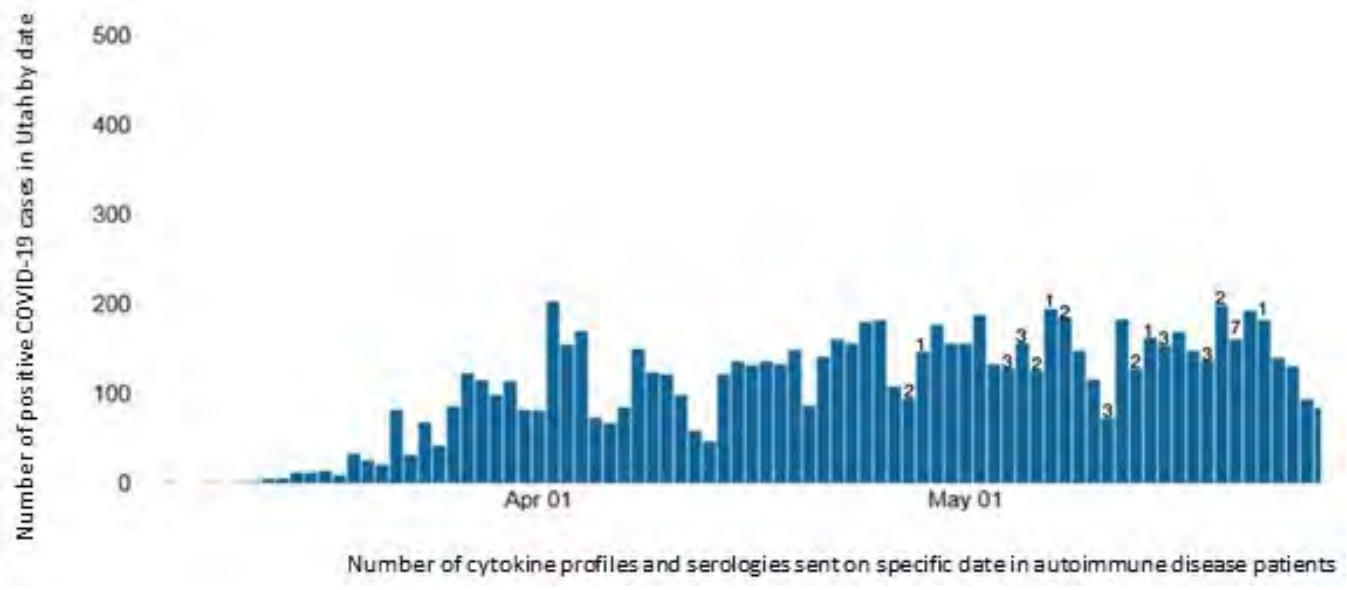
Variable	Total (N=39)
Age at baseline (yr):	
• Median	45
• Range	23-76
Gender: Female	35
Male	4
Race	
American Indian/Alaskan Native	2
Asian	3
Black or African American	1
• Native Hawaiian or Other Pacific Islander	1
• Other	4
• Unknown or Not Reported	1
White	27
Diagnosis	
• Systemic Sclerosis	18
• SLE	4
• MCTD	4
• RA	6
ILD	1
• Chronic inflammatory demyelinating polyneuropathy (CIDP)	1
• Ankylosing Spondylitis	1
• UCTD	1
• Myositis	1
• Sjogren's	1
• Adult Onset Stills	1
Immunosuppression	
• Methotrexate	4
• Hydroxychloroquine	20
• Chloroquine	0
• IVIG	0
• Rituximab	1
• Imuran	1
• Anakinra	1
• Enbrel	2
• Leflunomide	0
• Prednisone	3
• Amlodipine	1
• Azathioprine	1
• Mycophenolate	6

Variable	Total (N=39)
Self-Reported COVID 19 Symptoms	5
Confirmed COVID 19 PCR Positive	1
Cytokine Profile Elevation	
IL-2 receptor	2
TH1	
• INF-γ	0
• IL-12	0
• IL-2	0
TH2	
• IL-4	0
• IL-10	1
• IL-5	0
• IL-13	0
Monokines	
• IL-1 β	0
• IL-6	1
• IL-8	0
• TNF-α	0
COVID 19 Serology IgG Positive	1

Clinical Features of Autoimmune Disease Patients Tested in Utah During COVID Pandemic

low-grade fever for one day, a mild cough s mild, and loss of taste and smell for five days. All other subjects had negative COVID IgG response.

Conclusion: In this cohort of 39 autoimmune disease patients that presented for routine laboratory monitoring during the COVID pandemic, there were minimal elevations in serum cytokines suggesting that their inflammation was



COVID cases during study period

well controlled. The single COVID positive patient had mild symptoms on immunosuppression. Cytokine profiles and COVID serology testing can possible guide rheumatologists' recommendations regarding immunosuppression.

Disclosure: Q. Pritchett, None; **R. Overbury**, None; **D. Lebiedz-Odrobina**, None; **J. Thomas**, None; **T. Braaten**, None; **S. Clardy**, None; **M. Elgort**, None; **E. Spivak**, None; **P. Slev**, None; **L. Peterson**, None; **T. Frech**, None.

Abstract Number: 0004

The Impact of the COVID-19 Pandemic on Patients with Chronic Rheumatic Diseases: A Study in 15 Arab Countries

Nelly Ziade[1], Lina El Kibbi[2], Ihsane Hmamouchi[3], Nizar Abdulateef[4], Hussein Halabi[5], Wafa Hamdi[6], Fatemah Abutiban[7], Manal el Rakawi[8], Mervat Eissa[9] and Basel Masri[10], [1]Saint-Joseph University, Beirut, Lebanon, Beirut, Lebanon, [2]Specialized Medical Center, Riyadh, Saudi Arabia, Riyadh, Saudi Arabia, [3]Temara Hospital, Laboratory of Biostatistics, Clinical Research and Epidemiology (LBRCE), Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco, Rabat, Morocco, [4]Rheumatology Unit, Department of Medicine, College of Medicine, University of Baghdad, Iraq, Baghdad, Iraq, [5]King Faisal Specialist Hospital and Research Center, Jeddah, Saudi Arabia, Jeddah, Saudi Arabia, [6]Department of Rheumatology, Kassab Institute of orthopedics, UR17SP04, Faculty of Medicine of Tunis, Tunis El Manar University, Tunisia, Tunis, Tunisia, [7]Rheumatology Unit, Department of Medicine, Jaber Alahmed Alsabah hospital, State of Kuwait, Jahra, Kuwait, [8]Departement of Rheumatology, Douera Hospital, Faculty of Medicine, Saad Dahlab, Blida, Algeria, Blida, Algeria, [9]Rheumatology Department, Cairo University, Cairo, Egypt, Cairo, Egypt, [10]Jordan Hospital, Amman, Jordan, Amman, Jordan

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Rheumatic Disease

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the impact of the Coronavirus Disease 2019 pandemic (COVID-19) on the access to rheumatology care for patients with chronic rheumatic diseases in the Arab countries.

	All participants	
Number	2163	
Age, mean (SD)	40.0 (11.9)	
Females n (%)	1564	(72.3)
Occupation n (%)		
- **Full-time employed**	631	(29.2)
- **Part-time employed**	178	(8.2)
- **Self-employed**	187	(8.6)
- **At home**	1105	(51.1)
Countries n (%)		
- **Iraq**	539	(24.9)
- **KSA**	480	(22.2)
- **Egypt**	283	(13.1)
- **Morocco**	155	(7.2)
- **Algeria**	137	(6.3)
- **Kuwait**	117	(5.4)
- **Lebanon**	91	(4.2)
- **Jordan**	78	(3.6)
- **Tunisia**	60	(2.8)
- **UAE**	34	(1.6)
- **Syria**	12	(0.6)
- **Libya**	11	(0.5)
- **Palestine**	11	(0.5)
- **Oman**	10	(0.5)
- **Qatar**	6	(0.3)
- **Other**	28	(1.3)
Regions n (%)		
- **Levant**	731	(33.8)
- **Gulf**	671	(31.0)
- **North Africa**	649	(30.0)

Table 1. Characteristics of the 2163 participants in the survey

Methods: A web-based cross-sectional survey was designed by the Arab Adult Arthritis Awareness group (AAAA) consisting of 16 rheumatologists representing countries from the Arab League of Associations for Rheumatology (ArLAR) and was validated by the ArLAR scientific committee. The survey was disseminated through social media and patients' associations' channels between May 8 and May 22, 2020. The steering committee developed recommendations to improve the care of patients with chronic rheumatic diseases during the COVID-19 pandemic.

Results: A total of 2163 patients were included in the analysis; 72% were females; their mean age was 40 years (SD 11.9). The Levant, the Gulf, and North Africa contributed almost equally to the sample (Table 1). The COVID-19 pandemic had a significant negative impact on rheumatology visits in 82% of cases, including 27% where it had been impossible to contact the rheumatologist. The negative impact was also significant on the access to hydroxychloroquine (HCQ) (47% of cases), and on chronic medication persistency (partial or complete discontinuation in 28%) (Table 2). The negative impact on rheumatology visits was associated with the female gender, the country of residence, the medication non-persistency, the isolation due to COVID-19, and the impact on mental health (Table 3). The pandemic had an impact on mental health in 73% of the participants (minor in 48%, major in 25%). The impact on mental health was associated with the country of residence, the rheumatology visits, the medication non-persistency, the decreased access to HCQ, the personal infection with SARS-CoV-2, the isolation due to COVID-19 and the negative impact on income. Sixty-one patients (2.8%) stated that they had COVID-19, 5% said that a close contact was infected, and 47% were in isolation because of COVID-19. When asked about their attitude towards telemedicine, 98.8% said that they would accept a teleconsultation (50% through the internet and 48.8% through a telephone contact).

Impact of COVID-19 pandemic	Type of impact	N	%
Impact on rheumatology visit	Not affected	371	17.2
	I can see my rheumatologist only in emergencies	511	23.6
	I can only have a remote contact with my rheumatologist	625	28.9
	It is impossible to see my rheumatologist	578	26.7
Impact on access to Hydroxychloroquine (HCQ)	No impact	872	52.8
	Shortage of HCQ	297	18
	Difficulty to access HCQ	481	29.2
Impact on persistency on chronic medication	No impact	1495	69.1
	I stopped all medication because of the fear of infection	98	4.5
	I stopped some medication because of the fear of infection	177	8.2
	I stopped some medication because of drug shortage	317	14.7
Impact on mental health	No impact	511	23.6
	Minor effect	1044	48.3
	Major effect	540	25.0
Impact on income	Not affected	821	38.0
	Slightly affected	657	30.4
	Significantly affected	589	27.2
Personal infection with SARS-Cov-2	Yes	61	2.8
Contact infection with SARS-Cov-2	Yes	106	4.9%
Personal isolation due to COVID-19	Yes	1009	46.6%

Table 2. Impact of COVID-19 pandemic on patients with chronic rheumatic diseases

	OR*	95% CI		p-value
Female Gender	1.53	1.12	2.09	0.008
Region				
North Africa	1			<0.001
Levant	1.66	1.13	2.43	
Gulf	0.77	0.51	1.18	
Medication non persistence	3.90	2.08	7.30	<0.001
Isolation due to COVID-19	1.57	1.17	2.13	0.003
Mental impact of COVID-19	1.49	1.07	2.07	0.018
Accepting a teleconsultation	0.27	0.08	0.93	0.006

* After adjusting on: HCQ difficulty, Mask, Precautions, Personal COVID infection, Contact COVID infection, Impact on income, Impact on mental health

Table 3. Factors associated with a negative impact of the COVID-19 pandemic on the patient's visit to the rheumatologist

Conclusion: The current study highlights the deleterious consequences of the COVID-19 pandemic on the continuity of rheumatology care, the persistence on chronic medication, and the patients' mental health, all key predictors of disease prognosis. Therefore, an action plan, including establishing a telemedicine platform, securing drug availability, and promoting medication persistence through the appropriate communication channels, is strongly recommended.

Disclosure: N. Ziade, None; **L. El Kibbi**, None; **I. Hmamouchi**, None; **N. Abdulateef**, None; **H. Halabi**, None; **W. Hamdi**, None; **F. Abutiban**, None; **M. el Rakawi**, None; **M. Eissa**, None; **B. Masri**, None.

Abstract Number: 0005

Geographical Variations in COVID-19 Perceptions and Patient Management: A National Survey of Rheumatologists

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Rheumatic Disease

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate the perceptions and behaviors of rheumatologists in the United States (US) regarding the risk of COVID-19 for their autoimmune patients and the subsequent management of immunosuppressive and anti-inflammatory medications.

Methods: We administered an online survey to a convenience sample of rheumatologists in the US from 4/8/20-5/4/20 via social media and group emails. Survey respondents provided demographic information such as, age, gender, state of practice, and practice type. We asked questions about what they perceived their rheumatic patients COVID-19 risk to be, and furthermore what their management of immunosuppressive (steroids, biologics) and non-steroidal anti-inflammatory (NSAID) medications has been during the pandemic. Descriptive analyses were performed.

Results: 271 respondents completed the survey nationally. 48% of respondents either agreed or strongly agreed with the statement "Patients with rheumatic diseases are at a *higher risk* of COVID-19 irrespective of their immunosuppressive medications".(Figure 1) 50% disagreed or strongly disagreed with the statement "The pandemic has led you to reduce the use/dosage/frequency of biologics", while 56% agreed or strongly agreed with the statement "The pandemic has led you to reduce the use/dosage/frequency of steroids". A third of respondents indicated that at least 10% of their patients had self-discontinued or reduced at least one immunosuppressive medication to mitigate their risk of COVID-19. Responses to these questions as well as to questions regarding NSAID prescription patterns were significantly different in the Northeast region of US compared to other regions.(Figure 2)

Conclusion: In this national sample of rheumatologists, there are variations regarding perceptions of patients' risk of COVID-19, and how to manage medications such as NSAIDs, biologics and steroids during the pandemic. These variations are more pronounced in geographical areas where COVID-19 disease burden was higher. Limitations include difficultly to obtain a survey response rate; this was an online survey advertised through social media and email campaigns, so we cannot estimate how many rheumatologists had the opportunity to participate. Of those who the survey reached, the rheumatologists who chose to respond may reflect a respondent bias.

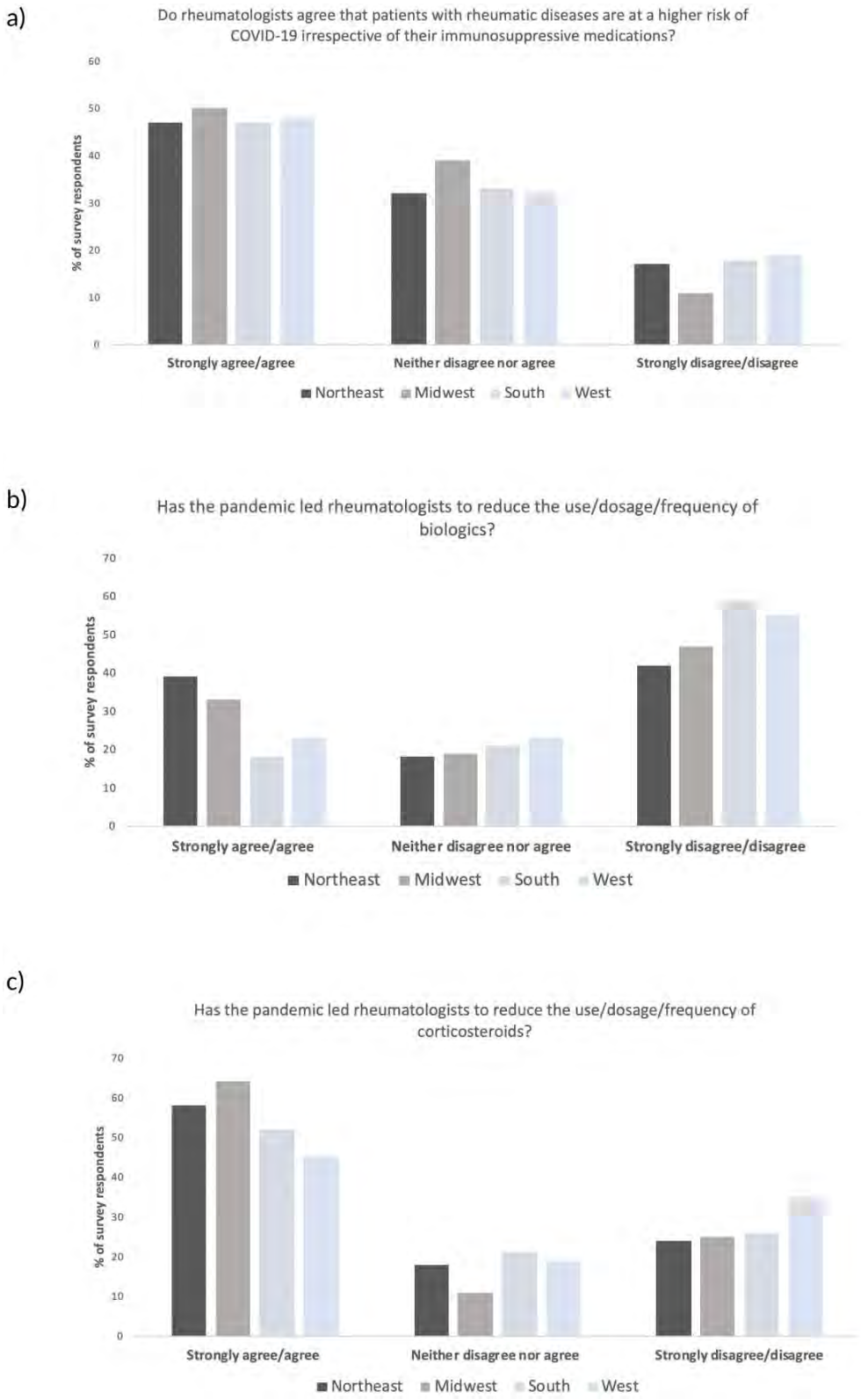

Figure 1. 1a) Responses to whether rheumatologists think their patients are at higher risk for COVID-19 1a) Responses to whether rheumatologists are altering biologic regimes during the pandemic 1c) Responses to whether rheumatologists are altering corticosteroid regimes during the pandemic

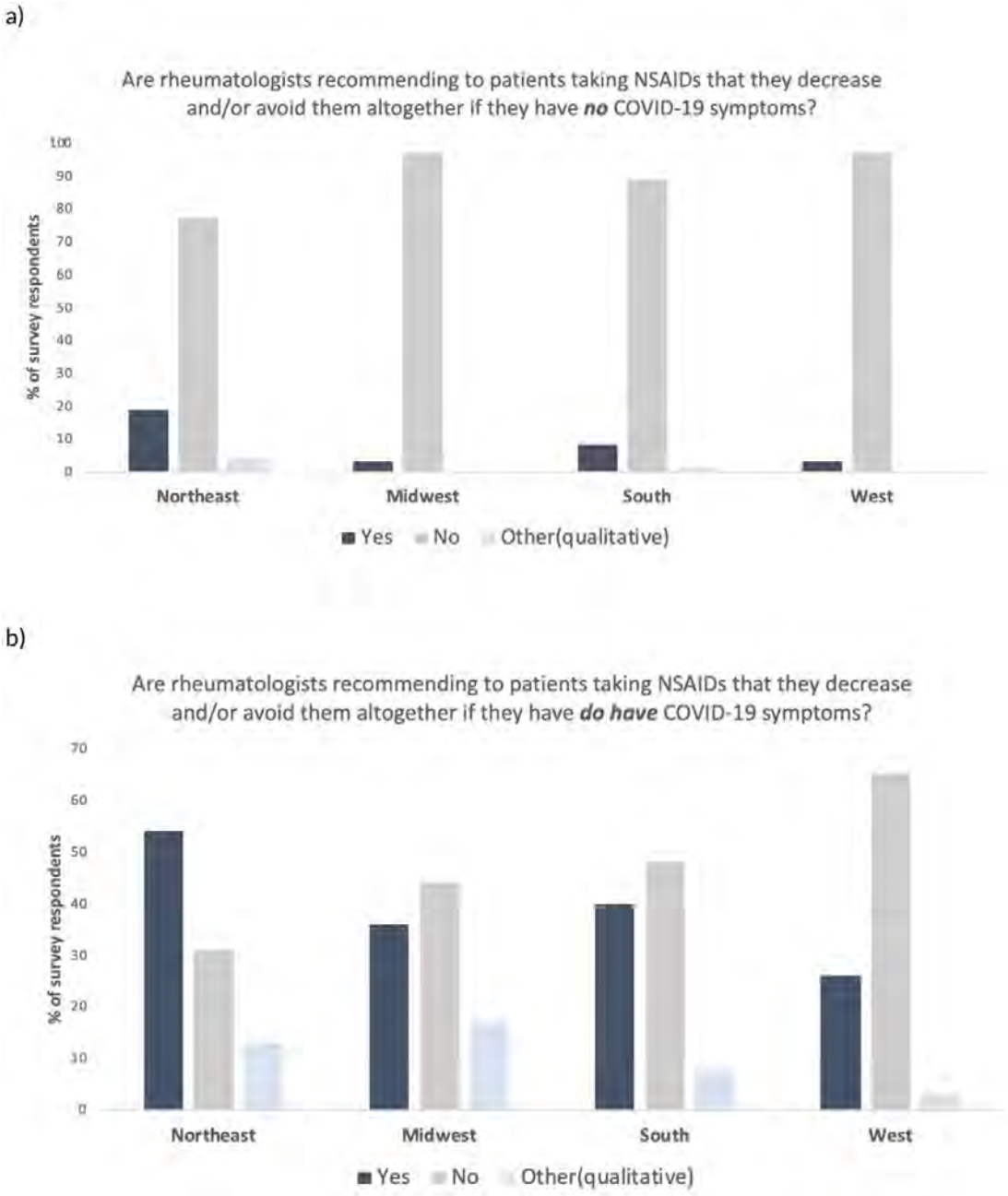

Figure 2: 2a) Responses to whether rheumatologists are recommending patients with no COVID-19 symptoms to decrease or avoid NSAIDs. 2b) Responses to whether rheumatologists are recommending patients with COVID-19 symptoms to decrease or avoid NSAIDs

Disclosure: B. Mehta, None; **D. Jannat-Khah**, Astrazeneca, 1, Cytodyn, 1, Walgreens Boots Alliance, 1; **C. Mancuso**, None; **A. Bass**, None; **C. Moezinia**, None; **A. Gibofsky**, None; **S. Goodman**, Pfizer, 1, Novartis, 1, UCB, 1, regenosine, 1, 2, Horizon, 1; **S. Ibrahim**, None.

Abstract Number: 0006

Race/ethnicity Is Associated with Poor Health Outcomes Amongst Rheumatic Disease Patients Diagnosed with COVID-19 in the US: Data from the COVID-19 Global Rheumatology Alliance Physician-Reported Registry

Milena Gianfrancesco[1], Liza Leykina[2], Zara Izadi[3], Carly Harrison[4], Suleman Bhana[5], Wendy Costello[6], Rebecca Grainger[7], Jonathan Hausmann[8], Jean Liew[9], Emily Sirotich[10], Paul Sufka[11], Zachary Wallace[12], Gabriela Schmajuk[13], Pedro M Machado[14], Philip Robinson[15] and Jinoos Yazdany[16], [1]University of California, San Francisco, San Francisco, CA, [2]UCSF, San Francisco, [3]University of California San Francisco, San Francisco, CA, [4]Lupus Chat, NA, [5]Crystal Run Health, Middletown, [6]Irish Children's Arthritis Network, Tipperary, Ireland, [7]University of Otago, Wellington, New Zealand, [8]Boston Children's Hospital / Beth Israel Deaconess Medical Center, Cambridge, MA, [9]University of Washington, Seattle, WA, [10]McMaster University, Hamilton, ON, Canada, [11]Healthpartners, St Paul, [12]Massachusetts General Hospital, Newton, MA, [13]University of California, San Francisco, Atherton, CA, [14]University College London, London, United Kingdom, [15]University of Queensland, Herston, Queensland, Australia, [16]UCSF, San Francisco, CA

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Rheumatic Disease

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Individuals with rheumatic disease, particularly those on immunosuppressive medications, have a higher risk of developing severe infections. However, whether these patients experience more severe outcomes of COVID-19 is unknown, as is whether outcomes vary by race/ethnicity as has been demonstrated in the general United States (US) population. The aim of this study was to examine the association between race/ethnicity and COVID-19 hospitalization, ventilation status, and mortality in people with rheumatic disease using data from the largest case series to date.

Methods: Patients with rheumatic disease and COVID-19 from the COVID-19 Global Rheumatology Alliance physician registry from March 24, 2020 to May 22, 2020 were included. The analysis was limited to patients in the US. Race/ethnicity was defined as white, black, Latinx and other. COVID-19 outcomes included hospitalization status (yes/no), requirement for ventilatory support (not hospitalized/no supplementary oxygen; supplementary oxygen or non-invasive ventilation; invasive ventilation/ECMO), and death (yes/no). Multivariable logistic regression was used to estimate odds ratios (ORs) and 95% confidence intervals (CIs) of hospitalization; ordinal logistic regression was used to estimate ORs and 95% CIs of ventilatory support; and Poisson models were used to estimate ORs and 95% CIs of mortality. All models were controlled for age, sex, smoking status, rheumatic disease diagnosis (RA, SLE, PsA, AS or other spondyloarthritis, other), comorbidities (hypertension/cardiovascular disease, lung disease, diabetes, and chronic renal insufficiency/end stage renal disease), rheumatic disease medications taken prior to infection (conventional synthetic DMARD (csDMARD) monotherapy; biologic and targeted small molecule DMARD monotherapy (b/tsDMARD); csDMARD + b/tsDMARD combination therapy), NSAID use, prednisone-equivalent glucocorticoid use, and rheumatic disease activity (remission/low vs. moderate/high).

Results: A total of 694 patients were included. Disease characteristics and outcomes by race/ethnicity are shown in Table 1. In multivariable models, racial/ethnic minorities were more likely to experience poor outcomes, including hospitalization and requirement for ventilatory support, compared to white patients (Table 2). Black and Latinx patients had 2.70 and 1.98 higher odds of being hospitalized compared to white patients, respectively ($P< 0.01$, $P=0.01$).

Table 1. Rheumatic Disease Characteristics and COVID-19 Outcomes by Race/Ethnicity (N=694)

	White N=339	Black N=161	Latinx N=128	Mixed/Other Race N=66
Female	246 (73)	134 (83)	105 (82)	51 (77)
Age > 65 years	87 (26)	35 (22)	28 (22)	10 (15)
Rheumatic Disease				
RA	130 (38)	54 (34)	53 (41)	23 (35)
SLE	32 (9)	57 (35)	28 (22)	7 (11)
Psoriatic Arthritis	51 (15)	4 (2)	8 (6)	8 (12)
Axial Spondyloarthritis	27 (8)	2 (1)	5 (4)	5 (8)
Vasculitis	23 (7)	3 (2)	11 (9)	5 (8)
Other	76 (22)	41 (25)	23 (18)	18 (27)
Hypertension/Cardiovascular	122 (36)	101 (63)	50 (39)	18 (27)
Lung Disease	67 (20)	47 (29)	32 (25)	13 (20)
Diabetes	43 (13)	35 (22)	38 (30)	11 (17)
Renal	17 (5)	20 (12)	9 (7)	4 (6)
Ever Smoker	87 (27)	38 (24)	21 (28)	13 (22)
Medication Pre-COVID-19				
No DMARD	61 (18)	27 (17)	24 (19)	14 (21)
csDMARD Only	114 (34)	86 (53)	49 (38)	25 (38)
b/tsDMARD Only	86 (25)	17 (11)	19 (15)	9 (14)
csDMARD + b/tsDMARD	78 (23)	31 (19)	36 (28)	18 (27)
NSAID	74 (24)	33 (22)	34 (29)	14 (24)
Prednisone-Equivalent Glucocorticoids				
None	254 (76)	102 (64)	71 (57)	49 (77)
1-9 mg/day	46 (14)	42 (26)	32 (26)	5 (8)
≥10 mg/day	34 (10)	15 (9)	22 (18)	10 (16)
Rheumatic Disease Activity				
Remission or Low	260 (81)	110 (74)	80 (64)	43 (69)
Moderate or High	63 (20)	38 (26)	45 (36)	19 (31)
Route of COVID-19 Transmission				
Transportation/travel	34 (10)	5 (3)	3 (2)	3 (5)
High-risk living environment	109 (32)	58 (36)	54 (42)	26 (39)
High-risk work environment	60 (18)	21 (13)	16 (13)	11 (17)
COVID-19 Complications				
Acute Respiratory Distress Syndrome (ARDS)	15 (4)	23 (14)	19 (15)	8 (12)
Sepsis	11 (3)	14 (9)	11 (9)	4 (6)
Hospitalization	91 (31)	82 (57)	54 (47)	23 (40)
Ventilation Status				
Not Hospitalized/No Supplemental Oxygen	227 (82)	77 (60)	70 (67)	37 (73)
Supplemental Oxygen/Non-Invasive Ventilation	28 (10)	25 (19)	15 (14)	9 (18)
Invasive Ventilation/ECMO	13 (5)	23 (18)	17 (16)	5 (10)
Unknown	9 (3)	4 (3)	2 (2)	0 (0)
Death	20 (6)	10 (6)	13 (10)	3 (5)

N, column %; csDMARD = conventional synthetic DMARD; b/tsDMARD = biologic and targeted small molecule DMARD

Table 2. Association between race/ethnicity and COVID-19 outcomes*

	Hospitalization N=599	Ventilation N=540	Death N=681
Race/Ethnicity			
White	*Ref*	*Ref*	*Ref*
Black	2.70 (1.66, 4.42), *P*<0.01	3.10 (1.77, 5.41), *P*<0.01	1.10 (0.49, 2.50), *P*=0.81
Latinx	1.98 (1.17, 3.33), *P*=0.01	2.97 (1.63, 5.41), *P*<0.01	1.78 (0.84, 3.78), *P*=0.13
Other/Mixed Race	1.79 (0.93, 3.44), *P*=0.08	2.34 (1.11, 4.95), *P*=0.03	1.22 (0.35, 4.26) *P*=0.76

*Models adjusted for sex, age greater than 65, rheumatic disease, comorbidities, ever smoking, medication prior to COVID-19, NSAID use, glucocorticoid use, and disease activity; sample size varies due to missing data on outcomes

Black and Latinx patients also had a three-fold increased odds of requiring ventilatory support compared to white patients ($P < 0.01$). No differences in mortality based on race/ethnicity were found.

Conclusion: Similar to findings in the general US population, we found that racial/ethnic minority patients with rheumatic disease had increased odds of hospitalization and invasive ventilation in the rheumatic disease population even after adjustment for disease and comorbidities. These results further illustrate health disparities related to COVID-19 and suggest that attention should be drawn to addressing the needs of vulnerable populations during public health emergencies.

Disclaimer: The views expressed here are those of the authors and participating members of the COVID-19 Global Rheumatology Alliance, and do not necessarily represent the views of the American College of Rheumatology (ACR), or National Institutes of Health (NIH).

Disclosure: M. Gianfrancesco, None; **L. Leykina**, None; **Z. Izadi**, None; **C. Harrison**, None; **S. Bhana**, Novartis, 9; **W. Costello**, None; **R. Grainger**, Pfizer Australia, 9, Cornerstones, 9, Janssen New Zealand, 9, Janssen Australia, 9, Novartis, 9; **J. Hausmann**, Novartis, 5; **J. Liew**, None; **E. Sirotich**, Canadian Arthritis Patient Alliance, 9; **P. Sufka**, Wiley Publishing, 5; **Z. Wallace**, Bristol-Myers Squibb, 2; **G. Schmajuk**, None; **P. Machado**, Abbvie, 5, 8, Eli Lilly, 5, Novartis, 5, 8, UCB, 5, 8, Pfizer, 8; **P. Robinson**, Novartis, 2, 5, 8, UCB, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 5, Pfizer, 5, Abbvie, 5, 8, BMS, 9; **J. Yazdany**, Eli Lilly, 5, Astra Zeneca, 5.

Abstract Number: 0007

Antimalarial Drug Shortages During the COVID-19 Pandemic: Results from the Global Rheumatology Alliance Patient Experience Survey

Emily Sirotich[1], Kevin Kennedy[2], Salman Surangiwala[3], Teresa Semalulu[1], Maggie Larche[1], Jean Liew[4], Zachary Wallace[5], Philip Robinson[6], Rebecca Grainger[7], Jeffrey Sparks[8], Julia Simard[9], Jinoos Yazdany[10], Monique Gore-Massy[11], Richard Howard[12], Mitchell Levine[2] and Jonathan Hausmann[13], [1]McMaster University, Hamilton, ON, Canada, [2]McMaster University, Hamilton, Canada, [3]Queen's School of Medicine, Kingston, Canada, [4]University of Washington, Seattle, WA, [5]Massachusetts General Hospital, Newton, MA, [6]University of Queensland, Herston, Queensland, Australia, [7]University of Otago, Wellington, New Zealand, [8]Division of Rheumatology, Inflammation, and Immunity; Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [9]Stanford Medicine, Stanford, CA, [10]UCSF, San Francisco, CA, [11]Lupus Foundation of America, Brooklyn, NY, [12]Spondylitis Association of America, Van Nuys, CA, [13]Boston Children's Hospital / Beth Israel Deaconess Medical Center, Cambridge, MA

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Rheumatic Disease

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Early in the COVID-19 pandemic, hydroxychloroquine and chloroquine were empirically promoted and used for treatment and prevention of SARS-CoV-2 infection. The repurposing of these drugs before robust efficacy data were available led to potentially harmful shortages for people with rheumatic diseases. The aims of this study were to assess (1) whether the use of antimalarials in patients with rheumatic disease was associated with a lower risk of COVID-19 infection, and (2) the prevalence and impact of drug shortages during the COVID-19 pandemic.

	All Patients (n = 9393)	Patients on antimalarials (n = 3872)	Patients not on antimarials (n = 5521)
	N (%)	N (%)	N (%)
Gender			
Female	8453 (90)	3711 (95.8)	4742 (85.9)
Male	908 (9.7)	153 (4)	755 (13.7)
Non-binary	9 (0.1)	1 (0)	8 (0.1)
Prefer not to answer	23 (0.2)	7 (0.2)	16 (0.3)
Age			
18-35	2130 (22.7)	1049 (27.1)	1081 (19.6)
36-50	3548 (37.8)	1532 (39.6)	2016 (36.5)
50-65	2933 (31.2)	1064 (27.5)	1869 (33.9)
65+	782 (8.3)	227 (5.9)	555 (10.1)
WHO Region			
Region of the Americas	6164 (65.6)	2945 (76.1)	3219 (58.3)
European Region	2725 (29)	710 (18.3)	2015 (36.5)
Western Pacific Region	258 (2.7)	95 (2.5)	163 (3)
Eastern Mediterranean Region	140 (1.5)	60 (1.5)	80 (1.4)
African Region	84 (0.9)	48 (1.2)	36 (0.7)
South-East Asia Region	22 (0.2)	14 (0.4)	8 (0.1)
Race/Ethnicity			
White	6334 (67.4)	2412 (62.3)	3922 (71)
Latin American	1576 (16.8)	734 (19)	842 (15.3)
Black	198 (2.1)	124 (3.2)	74 (1.3)
Asian	190 (2)	104 (2.7)	86 (1.6)
Native American / Aboriginal / First Nations	42 (0.4)	20 (0.5)	22 (0.4)
Other	1053 (11.2)	478 (12.3)	575 (10.4)
Medications			
csDMARDs	6657 (70.9)	3872 (100)	2785 (50.4)
Steroids	3264 (34.7)	1526 (39.4)	1738 (31.5)
Biologic DMARDs	2896 (30.8)	616 (15.9)	2280 (41.3)
tsDMARDs	299 (3.2)	75 (1.9)	224 (4.1)
Other	155 (1.7)	47 (1.2)	108 (2)
Rheumatic disease diagnosis			
Systemic lupus erythematosus	3651 (38.9)	2958 (76.4)	693 (12.6)
Rheumatoid arthritis	3626 (38.6)	1328 (34.3)	2298 (41.6)
Sjogren's syndrome	1290 (13.7)	781 (20.2)	509 (9.2)
Ankylosing spondylitis	1006 (10.7)	58 (1.5)	948 (17.2)
Psoriatic arthritis	673 (7.2)	77 (2)	596 (10.8)
Anti-phospholipid antibody syndrome	497 (5.3)	327 (8.4)	170 (3.1)
Inflammatory myopathy	425 (4.5)	129 (3.3)	296 (5.4)
Mixed connective tissue disease	422 (4.5)	292 (7.5)	130 (2.4)
Other inflammatory arthritis	390 (4.2)	159 (4.1)	231 (4.2)
Inflammatory eye disease (uveitis, scleritis, etc.)	317 (3.4)	102 (2.6)	215 (3.9)
Other	1921 (20.5)	521 (13.3)	1400 (25.4)
Comorbidities			
Pain Syndromes	2176 (23.2)	1022 (26.4)	1154 (20.9)
Hypertension	2142 (22.8)	820 (21.2)	1322 (23.9)
Pulmonary	2010 (21.4)	857 (22.1)	1153 (20.9)
Immunologic	1005 (10.7)	475 (12.3)	530 (9.6)
Obesity	664 (7.1)	269 (6.9)	395 (7.2)
Other	2834 (30.2)	1166 (30)	1668 (30.2)
COVID-19 status			
With COVID-19	519 (5.5)	260 (6.7)	259 (4.7)
Without COVID-19	8874 (94.5)	3612 (93.3)	5262 (95.3)

Table 1. Demographic and clinical characteristics of adults according to use of antimalarials in the C19-GRA Patient Experience Survey (n=9393). Participants may have more than one condition and take more than one type of medication. csDMARD medications included: antimalarials (hydroxychloroquine, chloroquine), azathioprine, cyclophosphamide, cyclosporine, leflunomide, methotrexate, mycophenolate mofetil/mycophenolic acid, sulfasalazine, tacrolimus. bDMARD included: abatacept, belimumab, CD-20 inhibitors, IL-1 inhibitors, IL-6 inhibitors, IL-12/IL-23 inhibitors, IL-17 inhibitors, and anti-TNF. tsDMARD included: Janus Kinase inhibitors. Other included: IVIG, apremilast, thalidomide. bDMARD, biologic DMARD; csDMARD, conventional synthetic DMARD; tsDMARD targeted synthetic DMARD, DMARD, disease-modifying antirheumatic drug..

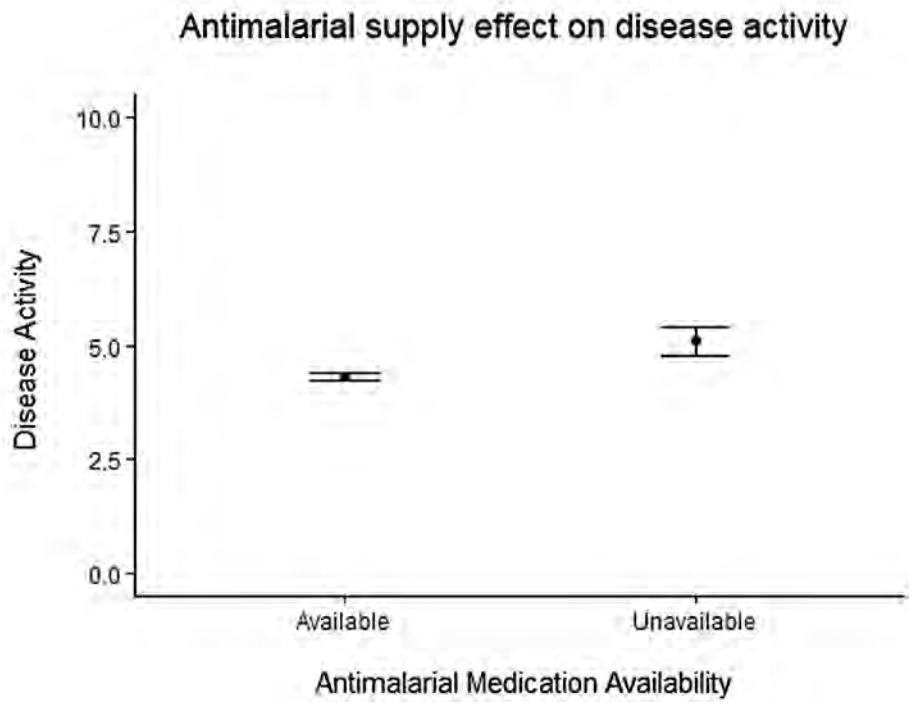

Figure 1. Antimalarial supply effect on disease activity in rheumatic disease patients.

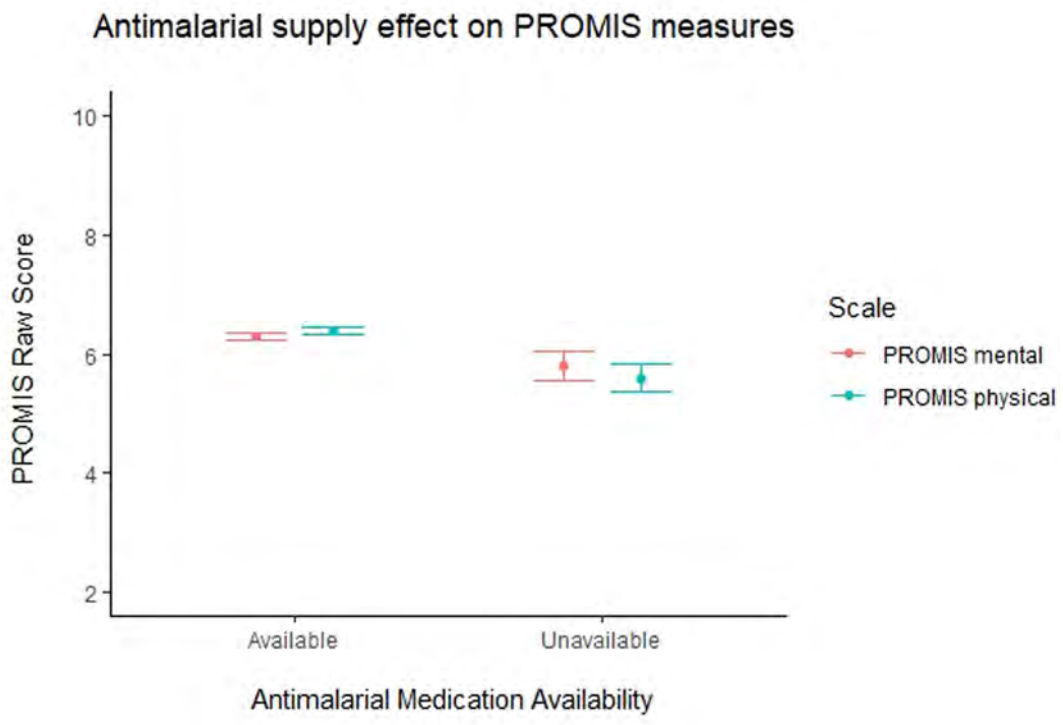

Figure 2. Antimalarial supply effect on PROMIS measures in rheumatic disease patients.

Methods: The COVID-19 Global Rheumatology Alliance (C19-GRA) Patient Experience Survey was distributed online through patient support organizations and on social media. Patients with rheumatic diseases (or the parents of pediatric patients) anonymously entered data including their rheumatic disease diagnosis, medications, COVID-19 status, and disease outcomes. Impact of drug shortages was evaluated for the effect on patient disease activity,

mental health and physical health states by comparing mean values with two-sided independent t-tests to identify significant differences.

Results: From 9,393 respondents (mean age 46.1 (SD 12.8) years, 90.0% female), 3,872 (41.2%) were taking antimalarials (Table 1). Of these, 230 (6.2%) were unable to continue taking antimalarials because of a lack of supply at their pharmacy. 21.4% of patients in South-East Asia and 26.7% in African regions reported an inadequate supply of antimalarials in pharmacies, in contrast to 6.8% of patients in the Americas and 2.1% in European regions.

There were similar rates of COVID-19 infection among patients on antimalarials as compared to patients not on these drugs (6.7% vs. 4.7%). A total of 28 patients (10.8%) with COVID-19 who were taking antimalarials were hospitalized. Of 519 patients diagnosed with COVID-19, 68 (13.1%) indicated they were prescribed antimalarials as a treatment for their COVID-19 infection.

Patients who were unable to obtain antimalarials from their pharmacies compared to those who did not experience medication shortages experienced higher levels of rheumatic disease activity ($5.1 > 4.3$, $t(244) = 4.44$, $p < 0.001$) (Figure 1) and poorer mental ($5.8 < 6.3$, $t(252) = 3.82$, $p < 0.001$) and physical health ($5.6 < 6.4$, $t(254) = 5.97$, $p < 0.001$) (Figure 2).

Conclusion: Patients in African and South-East Asian regions reported greater difficulty obtaining antimalarial drugs to treat their rheumatic disease in contrast to patients in the Americas and European regions. Patients who experienced antimalarial drug shortages reported worse mental and physical health outcomes than those able to obtain their medications. Antimalarials did not protect patients with rheumatic disease from COVID-19 or from hospitalization as a result of COVID-19. The unintended harmful consequences of repurposing antimalarials, without adequate evidence for benefit, highlights the importance of maintaining scientific rigor even in the context of a pandemic. Regional disparities of access to medications should be addressed to ensure all people, particularly those living in developing countries, receive fair and equiTable access to these essential medications.

Disclaimer: The views expressed here are those of the authors and participating members of the COVID-19 Global Rheumatology Alliance and do not necessarily represent the views of the American College of Rheumatology, the European League Against Rheumatism (EULAR), or any other organization.

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Abstract Number: 0008

COVID-19 Infection Among Patients with Rheumatic Disease on Biologic & Targeted Therapies: A Systematic Review

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Rheumatic Disease
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Information about the outcomes of patients with rheumatic disease with SARS-CoV-2 infection is scarce. Patients with rheumatic disease on immunosuppressive medications might represent a population at increased risk of SARS-CoV-2 infection or serious infection. Interestingly, few studies have suggested protective role of these drugs for COVID-19. We thus conducted a systematic review of studies reporting outcome of COVID-19 infection among patients with rheumatic diseases on biologic & targeted therapies.

Methods: We systematically searched PubMed/Medline and Scopus from January 1, 2020 to June 1, 2020 to identify studies that reported outcome of COVID-19 among patients with rheumatic disease. Demographic information, use of biologic (anti-TNF, IL-1, IL-6, IL-17, IL-12/IL-23, B cell, or T cell) or targeted therapy (Janus kinase inhibitor) were extracted from studies. The outcome measured was hospitalization, ICU admission, and death. Based on the clinical symptoms and need for hospitalization and ICU care, patients were grouped into severe (increased risk of respiratory failure or life-threatening complications) or non-severe.

Results: Our systematic review included eight observational cohort studies which comprised of 6095 patients with rheumatic disease. Of these, 123 patients (2%) were positive or highly suspicious for COVID-19 infection based on clinical features. The most common rheumatic diseases were rheumatoid arthritis (28%) and psoriatic arthritis (7%). The proportion of COVID-19 patients on biologics across all studies was 68%. The most common biologic agent was anti-TNF agents (31%). The percentage of users of JAK inhibitors was 6%. Among those with SARS-COV2 infection, 91 patients (73%) were not hospitalized. Among those hospitalized, 13 patients (11% of total) required ICU admission and 4 patients died (3.2% of total).

Conclusion: In this systematic review, the incidence of COVID-19 infection was low in patients with rheumatic disease. The majority had a mild clinical course and case fatality was low. However, larger cohort studies are necessary to examine outcomes of COVID-19 among biologic and non-biologic users. Furthermore, factors such as disease severity index and duration of biologic & targeted therapy use need to be considered in future studies.

Disclosure: A. Sood, None; **A. Galestanian**, None; **V. Murthy**, None; **E. Gonzalez**, None; **M. Raji**, None.

Abstract Number: 0009

Prevalence of Hydroxychloroquine and Chloroquine Side Effects in Rheumatology Patients: A Retrospective Survey of 115 Cases

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SESSION INFORMATION

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Session Title: Epidemiology & Public Health Poster I: COVID-19 & Rheumatic Disease

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Session Time: 9:00AM–11:00AM

Background/Purpose: Antimalarial drugs (ADs), including chloroquine (CQ) and hydroxychloroquine (HCQ), have anti-inflammatory, immunomodulatory, antiparasitic, anti-thrombotic, and antiviral properties. Their indications in rheumatology have been known for many years, especially in systemic lupus erythematosus, Sjogren's syndrome, or rheumatoid arthritis. Their recent use in treatment protocols for COVID-19 has been the subject of controversy for a number of reasons, including their potential side effects (SEs). The purpose of this study is to determine the

Table 1. Characteristics of the population.

Characteristics	Total n = 115	HCQ group n = 82	CQ group n = 33	p value
Age (years), mean (extremes)	47 (16 – 82)	45 (16 – 80)	51 (22 – 82)	0,067
Female (%)	111 (96.5%)	80 (97.5%)	31 (93.9%)	
Cumulative duration (years), mean (standard deviation)	2.5 (5.4)	3.5 (3.9)	6.9 (7.5)	0,002
Cumulative dose (g), mean (standard deviation)	432.8 (470.5)	422.5 (473.5)	458.5 (469.4)	0,713
n patients with cumulative duration of ADs > 5 years	35	22	13	
n patients with cumulative duration of ADs > 10 years	14	5	9	
ADs indication				
SLE	36	24	12	0,458
RA	35	20	15	0,026
Primary SjS	21	19	2	0,042
Secondary SjS[a]	13	6	7	
MCTD	17	15	2	
Others[b]	6	4	2	

ADs : Antimalarial Drugs ; CQ : Chloroquine ; HCQ : Hydroxychloroquine
SLE : Systemic Lupus Erythematosus ; RA : Rheumatoid Arthritis ; SjS : Sjogren's syndrome ; MCTD : Mixed Connective Tissue Diseases
[a] Secondary causes: RA (13 cases), Rhupus (1 case)
[b] Chondrocalcinosis, n = 1 ; Dermatomyositis, n = 1 ; Psoriatic arthritis, n = 1 ; Sarcoidosis, n = 1 ; Rhupus, n = 1 ; Peripheral Spondyloarthritis, n = 1

Table 2. Characteristics of the side effects observed in the 45 patients.

Characteristics	Total n = 45	HCQ group n = 30	CQ group n = 15	p value
Number of side effects (% among total)	45/115 (39.1)	30/82 (36.6)	15/33 (45.5)	0,451
Type				
Subjective (reported by the patient) (%)	13	9 (30)	4 (26.7)	
Objective (noted by the physician or test) (%)	32	21 (70)	11 (73.3)	0,816
Mean time until onset in years (extremes)	2.56 (0 – 15.3)	2.28 (0 – 15.3)	3.11 (0.01 – 13)	0,427
Number of SEs according to time until onset				
< 7 days	5	4[a]	1[b]	
Between 7 days and < 3 months	7	4[c]	3[d]	
≥ 3 months	33	22	11	0,670
SE, mean time until onset (y = years, d = days)				
Ophthalmic	25	18	7	
Loss of visual acuity	2	2 (1.95 y)	0	
Maculopathy	19 (2.90 y)	13 (2.28 y)	6 (4.25 y)	
Modification of the cornea (edema, deposits)	1	1 (0.26 y)	0	
Retinopathy	2	2 (2.97 y)	0	
Accommodation disorders	1	0	1 (3 y)	
Cutaneous	14	6	8	
Alopecia	1	1 (0.17 y)	0	
Skin rash	4	2 (5 d)	2 (15 d)	
Pruritus	2	1 (1 d)	1 (12 d)	
Drug-induced hypersensitivity syndrome	1	1 (6 d)	0	
Lyell syndrome	1	0	1 (3 d)	
Hyperpigmentation	5	1 (5.92 y)	4 (3.82 y)	
Gastrointestinal	2	2	0	
Abdominal pain	1	1 (36 d)	0	
Dyspepsia	1	1 (60 d)	0	
Cardiovascular	1	1	0	
Palpitations	1	1 (59 d)	0	
Hepatic	1	1	0	
Transaminases > 3x normal	1	1 (2.49 y)	0	
Neuromuscular	1	1	0	
Peripheral neuropathy	1	1 (2.09 y)	0	
Neurosensory	1	1	0	
Tinnitus	1	1 (2.30 y)	0	
Side effects management				
Definitive cessation	41	27	14	
Dose reduction	2	2[e]	0	
Temporary cessation	1	1[f]	1[g]	
Number of patients still under ADs (%)	70/115 (60.9)	52/82 (63.4)	18/33 (54.5)	

ADs : Antimalarial Drugs ; CQ : Chloroquine ; HCQ : Hydroxychloroquine

[a] Skin rash (n = 2), Pruritus (n = 1), Drug-induced hypersensitivity syndrome (n = 1)

[b] Lyell syndrome (n = 1)

[c] Abdominal pain (n = 1), Dyspepsia (n = 1), Palpitations (n = 1), Alopecia (n = 1)

[d] Skin rash (n = 2), Pruritus (n = 1)

[e] Transaminases > 3x normal (n = 1), Dyspepsia (n = 1)

[f] Abdominal pain (n = 1)

[g] Hyperpigmentation (n = 1)

Table 3. Number of side effects leading to definitive cessation of antimalarial drugs.

Side effects	Total (%) n = 42	HCQ group n = 27	CQ group n = 15
Ophthalmic	24 (57.1)	17	7
Loss of visual acuity	2	2	-
Maculopathy	18	12	6
Modification of the cornea (edema, deposits)	1	1	-
Retinopathy	2	2	-
Accommodation disorders	1	-	1
Cutaneous	14 (33.3)	6	8
Alopecia	1	1	-
Skin rash	4	2	2
Pruritus	2	1	1
Drug-induced hypersensitivity syndrome	1	1	-
Lyell syndrome	1	-	1
Hyperpigmentation	5	1	4
Gastrointestinal	1 (2.4)	1	-
Abdominal pain	1	1	-
Dyspepsia	0	0	-
Cardiovascular	1 (2.4)	1	-
Palpitations	1	1	-
Hepatic	0 (0)	0	-
Transaminases > 3x normal	0	0	-
Neuromuscular	1 (2.4)	1	-
Peripheral neuropathy	1	1	-
Neurosensory	1 (2.4)	1	-
Tinnitus	1	1	-

ADs : Antimalarial Drugs ; CQ : Chloroquine ; HCQ : Hydroxychloroquine
0 : reported side effect, not leading to drug cessation
- : not reported

Table 3. Number of side effects leading to definitive cessation of antimalarial drugs.

prevalence of SEs, and to study the association between their characteristics and the type of ADs in a rheumatologic population.

Methods: We conducted a retrospective study on medical records of patients hospitalized then followed up in the Department of Rheumatology of the University Hospital of Ibn Rochd, between January 2010 and April 2020, who were treated with CQ or HCQ. The SEs were recorded from a pre-established exploitation sheet. Drug causality was assessed using the World Health Organization Uppsala Medical Center (WHO-UMC) system for standardized case causality assessment. SEs were included if they pertained to the categories of "Certain", "Probable/Likely", or "Possible"; and they were excluded if they pertained to the categories of “Unlikely”, “Conditional/Unclassified”, and “Unassessable/Unclassifiable”. The prevalence of SEs is estimated with a confidence interval of 95%, and the study of the factors associated with SEs is performed with univariate analysis with a significance threshold of $p < 0.05$.

Results: 115 patients received ADs, of which 96% were females, with a mean age of 47 (16 – 82). The indications for ADs were systemic lupus erythematosus (31%), rheumatoid arthritis (30%), and primary Sjogren’s syndrome (18%). The overall prevalence of SEs is 39% (30% – 48%). The specific prevalence of SEs is 37% (26% – 47%) under HCQ, and 45% (28% – 63%) under CQ. 57% of the SEs are ophthalmic, 33% are cutaneous, and 2.2% are cardiovascular.

36% of SEs resulted in the definitive cessation of ADs, 24% under HCQ and 12% under QC. Maculopathy was the main reason for definitive cessation of ADs (43%). The average duration of treatment is significantly different ($p < 0.01$) with HCQ (3.5 years) versus CQ (7 years). There was no significant association between the categories of SEs and the type of ADs.

Conclusion: n our study, almost two fifths of the patients under ADs presented SEs, with a higher prevalence in the CQ group than in the HCQ group. In addition, prolonged use of ADs is mainly limited by the risk of maculopathy, which is the most frequent cause of definitive cessation. However, the administration of short-course ADs with high doses, as in COVID-19, is likely to modify the prevalence of ADs, compared to those found in rheumatology practice.

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Abstract Number: 0010

Antirheumatic Disease Therapies in Patients with COVID-19: A Systematic Review and Meta-analysis

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SESSION INFORMATION

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Session Type: Poster Session A

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Background/Purpose: Antirheumatic disease therapies have been used to treat coronavirus disease 2019 (COVID-19) and its complications. There has been particular interest in the antimalarial agent hydroxychloroquine (HCQ) and in agents that inhibit interleukin-1 (IL1) or interleukin-6 (IL-6). We conducted a systematic review and meta-analysis to describe the current evidence.

Methods: A search of published and preprint databases in all languages was performed on 3/19/2020 and updated on 05/07/2020. Included studies described one or more relevant clinical outcomes in five or more people who were infected with SARS-CoV-2 and were treated with antirheumatic disease therapy. Pairs of reviewers screened articles and extracted data. The risk of bias was assessed using the Newcastle-Ottawa Scale for cohort studies and the Risk of Bias 2.0 tool for randomized controlled trials (RCTs). A meta-analysis of effect sizes using random-effects models was performed when possible.

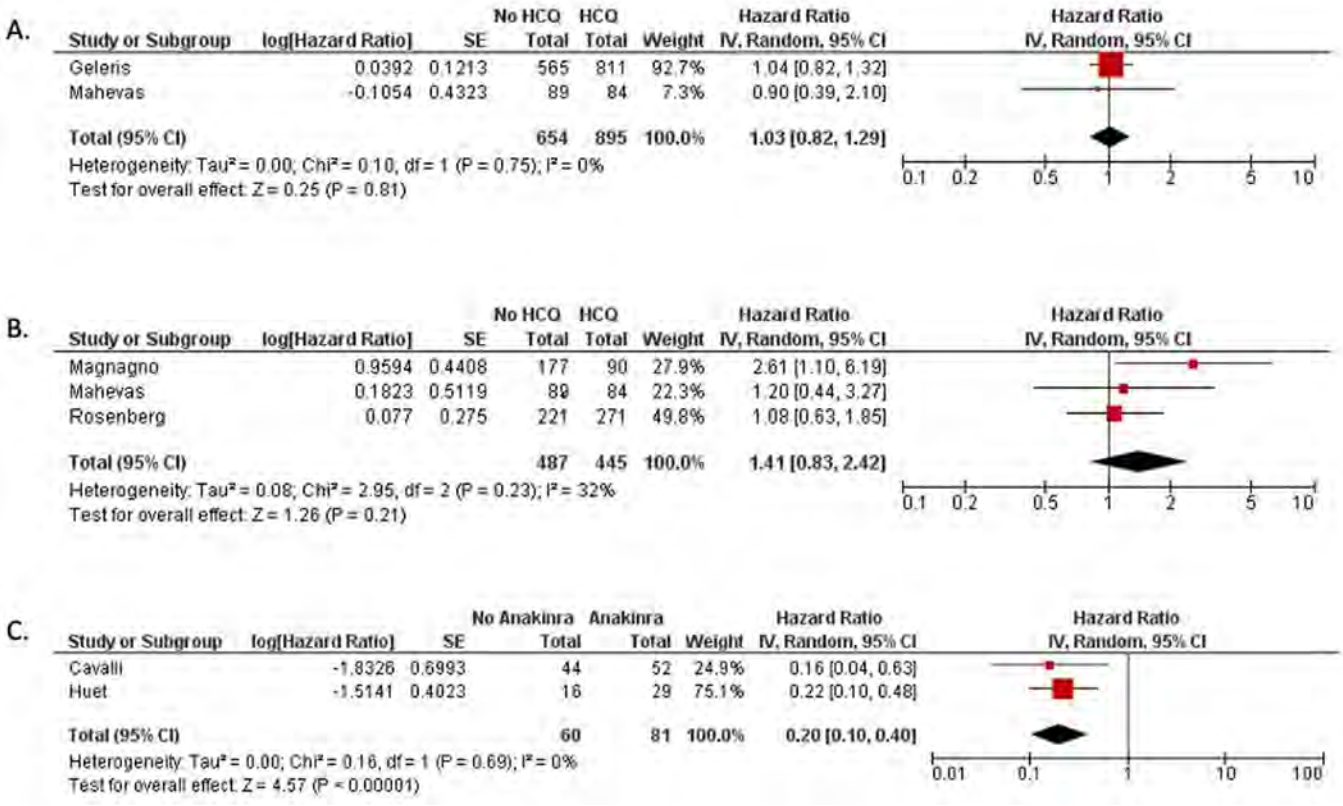

Figure 1A Meta-analysis of two observational studies investigating hydroxychloroquine and the composite outcome of death or intubation among patients hospitalized with COVID-19 Figure 1B: Meta-analysis of three observational studies investigating hydroxychloroquine and mortality among patients hospitalized with COVID-19 Figure 1C: Meta-analysis of two observational studies investigating anakinra and mortality among patients hospitalized with COVID-19.

Results: The searches identified 3,935 articles, of which 275 were included for full text review. After full text exclusion, 45 studies were included in qualitative review (4 randomized controlled trials, 29 cohort studies, and 12 case series) and six studies were included in meta-analyses (4 cohort studies of HCQ, 2 cohort studies of anakinra). All studies evaluated hospitalized patients and 29 out of 45 had been published in a peer-reviewed journal. In a meta-analysis of three cohort studies with a low risk of bias, hydroxychloroquine use was not significantly associated with mortality (pooled hazard ratio (HR) 1.41, 95% confidence interval (CI) 0.83-2.42) (Figure 1A, Figure 1B, Table 1). In a meta-analysis of two cohort studies with some/high risk of bias, anakinra use was associated with lower mortality (pooled HR 0.2, 95% CI 0.1-0.4) (Figure 1C). A meta-analysis could not be performed on interleukin-6 inhibitor studies, which were frequently conflicting and had some/high risk of bias (Table 2). Studies that assessed glucocorticoids, intravenous immunoglobulin, and baricitinib also had conflicting results and the majority had a high risk of bias.

Conclusion: In this systematic review and meta-analysis, hydroxychloroquine use was not associated with benefit or harm with regard to COVID-19 mortality. The IL-1 inhibitor anakinra was associated with lower mortality, but this should be interpreted with caution given substantial risks of bias. Evidence supporting the effect of other antirheumatic disease therapies in COVID-19 is currently inconclusive, though randomized controlled trials are ongoing.

TABLE 1: Included studies investigating antimalarial therapies and COVID-19 (n = 14)

Author (citation)	Design (n)	Outcome and Inference	Bias Assessment*	Direction of Effect†
Hydroxychloroquine				
Mortality				
Rosenberg	Cohort (1,438)	No significant difference in mortality (adjusted HR 1.08, CI 0.63-1.85)	Low	QS
Magagnoli	Cohort (368)	Increased mortality in HCQ group (adjusted HR 2.6, CI 1.1-6.2)	Low	QS
Mahevas	Cohort (173)	No difference in overall survival at 21 days (weighted HR 1.2, CI 0.4-3.3) or survival without transfer to intensive care unit (weighted HR 0.9, CI, 0.4 - 2.1)	Low	QS
Yu	Cohort (568)	Lower mortality in HCQ group among those critically ill (adjusted HR 0.33, CI 0.17-0.64)	High	+
Ashraf	Case Series (100)	Higher rate of survival in HCQ group (OR 61.9, CI 9.0 - 424.7)	High	NA
Mathian	Case Series (17)	2 out of 14 hospitalized patients taking HCQ died	High	NA
Composite of Intubation and Death				
Mahevas	Cohort (173)	No difference in the combined outcome of ICU care or death (HR 0.9, CI 0.4-2.1)	Low	QS
Geleris	Cohort (1,376)	No difference in the combined outcome of IMV or death (HR 1.04, CI 0.82-1.32)	Low	QS
Escalation of Care (ICU transfer, intubation and mechanical ventilation)				
Magagnoli	Cohort (368)	No difference in IMV (adjusted HR 1.43, CI 0.53-3.79)	Low	-
Mathian	Case Series (17)	Out of 17 patients taking HCQ, 14 admitted to hospital and 7 to the ICU	High	NA
Hospital or ICU Discharge				
Mahevas	Cohort (173)	No difference in discharge (RR 1.0, CI 0.9-1.3) at 21 days	Low	NA
Clinical Improvement				
Tang	RCT (150)	No difference in symptom resolution at 28 days (60% vs 67% SoC, p = 0.97)	High	+
Chen	RCT (62)	Shorter recovery for fever (2.2 days vs 3.2 days, p < 0.001) & cough (2.0 days vs 3.1 days, p = 0.002)	High	+
Mahevas	Cohort (173)	No difference oxygen weaning at 21 days (RR 1.1, CI 0.9-1.3)	Low	+
Gautret	Case Series (80)	81% with "favorable outcome" and only 15% required oxygen	High	NA
SARS-CoV-2 Clearance				
Tang	RCT (150)	No difference in viral clearance at 28 days (85% vs 81% SoC, p = 0.34)	High	+
Mallat	Cohort (34)	Longer duration of SARS-CoV-2 test positivity in HCQ (17 days vs 10 days SoC, p = 0.023)	Some	-
Gautret	Cohort (42)	Higher rate of viral clearance at 6 days (70% vs 13% SoC at other hospitals, p = 0.001)	High	+
Molina	Case Series (11)	Viral load persistent 6 days after treatment in 8/10 patients	High	NA
Million	Case Series (1,061)	Persistent SARS-CoV-2 test positivity at 10 days in 47 patients	High	NA
Gautret	Case Series (80)	74 out of 80 patients had viral clearance at 8 days	High	NA

* Bias assessment using the Newcastle-Ottawa Scale for cohort studies and the Risk of Bias 2.0 tool for randomized controlled trials; case series assumed to be high risk by default
†Direction of effect quantified using the Cochrane vote counting method for data syntheses. Studies eligible for quantitative synthesis and case series were excluded
Abbreviations: Hazard ratio (HR); 95% confidence interval (CI); quantitative synthesis (QS); hydroxychloroquine (HCQ); intensive care unit (ICU); randomized controlled trial (RCT); risk ratio (RR); standard of care (SoC); severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2); odds ratio (OR); chloroquine (CQ); invasive mechanical ventilation (IMV); not applicable (NA)

TABLE 2: Included studies investigating interleukin-1 and interleukin-6 inhibitors and COVID-19 (n = 3 studies for anakinra, n = 7 studies for tocilizumab, 1 study for siltuximab)

Author (citation)	Design (n)	Outcomes and Inference	Bias Assessment*	Direction of Effect†
Anakinra				
Mortality				
Huet	Cohort (96)	Anakinra associated with lower rate of death (HR 0.3, CI 0.1-0.7)	Some	QS
Cavalli	Cohort (52)	Anakinra high dose 5mg/kg BID associated with lower mortality at 21 days (HR 0.2, CI 0.04-0.63)	High	QS
Composite of Intubation and Death				
Huet	Cohort (96)	Anakinra associated with lower rate of composite IMV/death (HR 0.2, CI 0.1-0.5)	Some	+
Escalation of Care (ICU transfer, intubation and mechanical ventilation)				
Huet	Cohort (96)	Anakinra associated with lower rate of invasive mechanical ventilation (HR 0.2, CI 0.1-0.8)	Some	+
Cavalli	Cohort (52)	No difference with high dose and IMV free survival at 21 days (HR 0.5, CI 0.2-1.3)	High	+
Clinical Improvement				
Aouba	Case Series (9)	9 out of 9 patients treated with anakinra improved	High	NA
Interleukin-6 Inhibitors				
Mortality				
Roumier	Cohort (59)	No difference in mortality in TCZ group (17.2% vs 18.7% SoC p=0.837)	Some	+
Quartuccio	Cohort (111)	Higher mortality in TCZ group (9.5% vs 0% SoC)	High	-
Klopfenstein	Cohort (45)	Numerically lower mortality in TCZ group (25% vs 48% historical SoC, p = 0.07)	High	+
Sciascia	Case Series (63)	Mortality of 11% at day 14; increased survival with early TCZ (HR 2.2, CI 1.3-6.7)	High	NA
Luo	Case Series (15)	Death in 3/15 (20%) treated with TCZ at 1 week of follow up	High	NA
Alattar	Case Series (25)	Death in 3/25 (12%) treated with TCZ at day 14	High	NA
Gritti	Case Series (21)	IMV or death in 5/21 treated with siltuximab (24%)	High	NA
Composite of Intubation and Death				
Klopfenstein	Cohort (45)	Lower death / ICU admission in TCZ group (25% vs 72% historical SoC, p = 0.002)	High	+
Escalation of Care (ICU transfer, intubation and mechanical ventilation)				
Roumier	Cohort (59)	Lower rate of IMV in TCZ group (adjusted OR 0.42, CI 0.2-0.9).	Some	+
Klopfenstein	Cohort (45)	Lower rate of IMV in TCZ group (0% vs 32% historical SoC, p = 0.006)	High	+
Hospital or ICU Discharge				
Klopfenstein	Cohort (45)	No difference in hospital discharge rate with TCZ (55% vs. 44% historical SoC, p = 0.453)	High	+
Alattar	Case Series (25)	Discharge after improvement from ICU at day 14 in 9/25 (36%) treated with TCZ	High	NA
Clinical Improvement				
Quartuccio	Cohort (111)	Lower rate of "complete" recovery in TCZ group (21% vs. 100% SoC)	High	-
Sciascia	Case Series (63)	P/F ratio improved (152+/-53 day 0; 284+/-116 day 7; 302+/-126 day 14, p < 0.05)	High	NA
Gritti	Case Series (21)	Improvement in 7/21 treated with siltuximab (33%)	High	NA
Xu	Case Series (21)	Improved oxygenation in 15/20 (75%) and discharge in 21/21 (100%) treated with TCZ	High	NA

* Bias assessment using the Newcastle-Ottawa Scale; case series assumed to be high risk by default
†Direction of effect quantified using the Cochrane vote counting method for data synthesis. Studies eligible for quantitative synthesis and case series were excluded
Abbreviations: Hazard ratio (HR); confidence interval (CI); tocilizumab (TCZ); odds ratio (OR); invasive mechanical ventilation (IMV); intensive care unit (ICU); standard of care (SoC); arterial partial pressure oxygen to fractional inspiration ratio (P/F); not applicable (NA)

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Abstract Number: 0011

Patients Receiving Cytokine Inhibitors Have Low Prevalence of SARS-CoV-2 Infection

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SESSION INFORMATION
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Background/Purpose: Therapeutic interventions for Immune-mediated inflammatory diseases (IMIDs) target cytokines, such as TNF-a, IL-6, IL-17 and IL-23, which are involved in the physiological and pathological host response elicited by SARS-CoV-2 [1]. We therefore questioned whether IMID patients receiving cytokine inhibitors might be at lower risk for SARS-CoV-2 infection and measured the development of anti-SARS-CoV-2 IgG responses [2] in IMID patients treated with cytokine inhibitors and respective controls during the outbreak of COVID-19 in Europe.

Methods: IMID patients with sTable (> 3 months) treatment with cytokine inhibitors (TNFi, IL-6i, JAKi, IL-17i, IL-23i, IL-12/23i; N=534) were analyzed. As controls, (i) IMID patients receiving no cytokine inhibitors (N=259), healthy control subjects unrelated to health care (NHC, N=971) and health care professionals involved in the treatment of these patients (HC, N=285) were recruited. Respiratory and other infectious symptoms as well as social behavior during the outbreak of COVID-19 in Europe between February 1st to April 30th 2020 were recorded for a period of 12 weeks. To test for exposure to SARS-CoV-2 we used an S1 domain-based antibody ELISA for the initial testing (commercial enzyme–linked immunosorbent assay from Euroimmun (Lübeck, Germany)). A cut-off of ≥0.8 (OD450nm) was considered as positive. Relative risks (RR) of seropositivity in study groups using the NHC group as the reference and adjusting for age, sex and sampling-date using a Poisson regression model with robust sandwich standard errors weres estimated. Adjustment for sampling date was achieved using the cumulative confirmed COVID-19 case-counts in the region where the study was conducted.

Results: Positive anti-SARS-CoV-2 IgG was observed in 22 of 971 NHC with a prevalence (95%CI) of 2.27% (1.42% to 3.43%), 12 of 285 HC with a prevalence of 4.21% (2.18% to 7.25%), 8 of 259 IMID patients without cytokine blockade with a prevalence of 3.09% (1.33% to 6.09%) and 4 of 534 IMID patients under cytokine blockade with a prevalence of 0.75% (0.20% to 1.92%) (Fig. 1B). After age-, sex- and sampling date adjustment, the prevalence of anti-SARS-CoV-2 IgG was significantly lower (RR: 0.32, 95%CI: 0.11 to 0.99, p=0.048) in IMID patients receiving cytokine inhibitors compared to NHC. In contrast, IMID patients receiving no cytokine inhibitors had similar (RR: 1.21, 95%CI: 0.50 to 2.90, p=0.676) prevalence of anti-SARS-CoV-2 IgG. Standardized Pearson's residuals of the expected frequencies for self-reported contact with individuals having a respiratory tract infection, workplace attendance and travel to risk areas were similar in IMID patients with and without cytokine inhibitors (Fig. 1C).

Conclusion: Patients with IMIDs receiving cytokine inhibitors are not at enhanced but rather at lower risk for SARS-CoV-2 infection compared to the general community and IMID patients not receiving such drugs. These data support a pathogenic role of cytokines, targeted by treatment of IMIDs, in COVID-19 and clearly speaks against stopping cytokine inhibitor treatment in patients with IMIDs during the current SARS-CoV-2 pandemic.

[1] Schett et al. Nat Rev Immunol. 2020
[2] Okba et al. medRxiv; https://doi.org/10.1101/2020.03.18.20038059

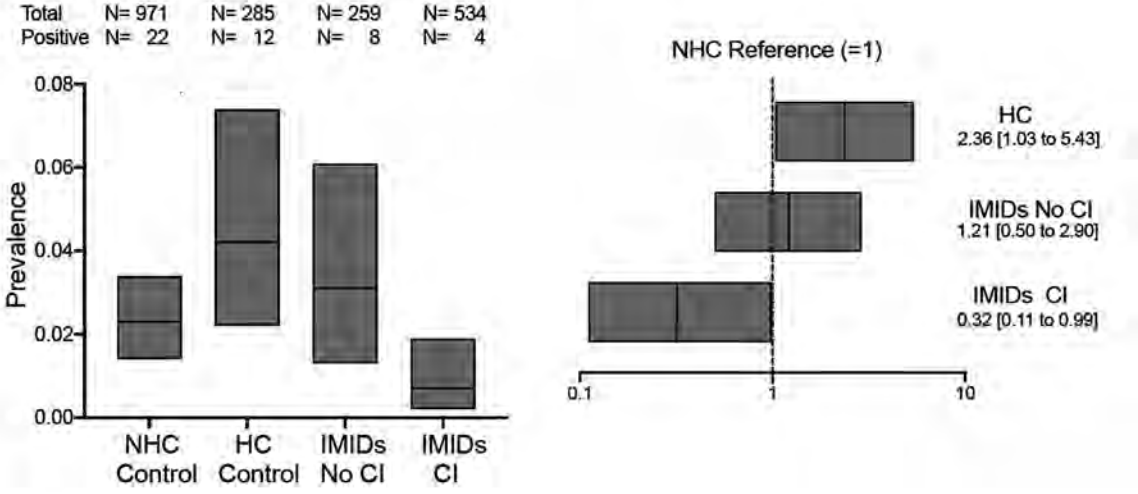
(a) Characteristics of the patients with IMIDs and controls. (b) left side: Prevalence and 95% confidence intervals of a positive anti-SARS-CoV-2 IgG antibody test recognizing the S1 domain of the spike protein in non-health care (NHC) controls, health care (HC) controls and IMIDs with and without cytokine inhibitors (CI); right side: risk ratios and 95% confidence intervals of anti-SARS-CoV-2 IgG antibody positivity in health care (HC) controls and IMIDs with and without cytokine inhibitors (CI) with NHC controls as reference; (c) Standardized Pearson's residuals showing deviation from the expected frequencies for exposure risk variables (contact with persons with respiratory infections, presence at workplace outside home, travel to risk areas) of IMID patient groups and control groups.

a.

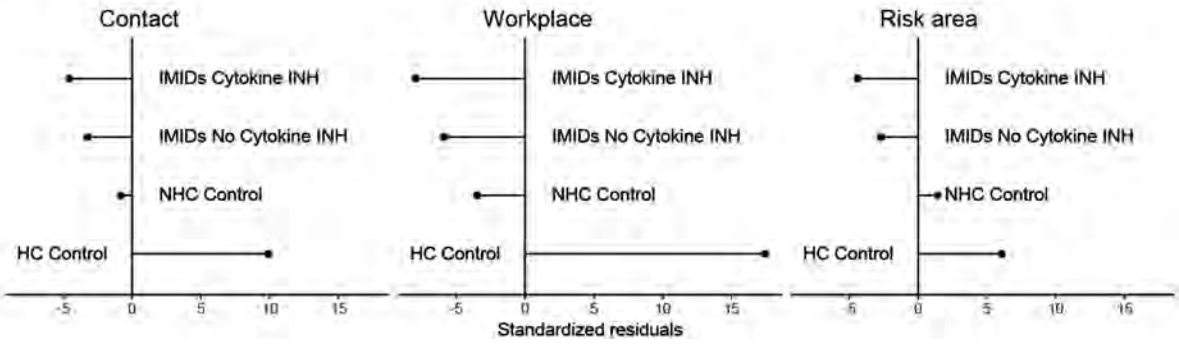
	Non-Healthcare Control N=971	Healthcare Control N=285	IMIDs Cytokine INH N=534	IMIDs Standard Care N=259
Demographic Characteristics				
Age, mean±SD, years	43.2±14.3	40.3±12.7	48.9±15.7	55.3±16.1
Females, N (%)	274 (28.2)	189 (66.3)	285 (53.4)	152 (58.7)
BMI, mean±SD	26.5±6.0	23.6±4.4	26.4±5.8	26.4±4.5
Smoking, N (%)	181 (18.6)	35 (12.3)	94 (17.6)	40 (15.4)
Diabetes, N (%)	59 (6.1)	12 (4.2)	42 (7.9)	14 (5.4)
Hypertension, N (%)	117 (12.0)	8 (2.8)	145 (27.2)	75 (29.0)
Chronic lung disease, N (%)	67 (6.9)	7 (2.5)	46 (8.6)	16 (6.2)
Type of IMID				
SpA, N	0	0	117 (21.9)	34 (13.1)
RA, N	0	0	130 (24.3)	106 (40.9)
IBD, N	0	0	176 (33.0)	14 (5.4)
Psoriasis, N	0	0	63 (11.8)	28 (10.8)
Other*, N	0	0	48 (9.0)	77 (29.7)
Cytokine Inhibitors				
TNF Inhibitors, N (%)	0	0	227 (42.5)	0
IL-6 Inhibitors, N (%)	0	0	44 (8.2)	0
IL-23 Inhibitors, N (%)	0	0	85 (15.9)	0
IL-17 Inhibitors, N (%)	0	0	51 (9.6)	0
JAK Inhibitors, N (%)	0	0	39 (7.3)	0
Others*, N (%)	0	0	88 (16.5)	0

BMI, body mass index; IBD, inflammatory bowel disease; IL, interleukin; IMID, immune-mediated inflammatory diseases; INH, inhibitor; JAK, Janus kinase; RA, rheumatoid arthritis; SpA, spondyloarthritis; TNF, tumor necrosis factor; *systemic lupus erythematosus, primary Sjogren's syndrome, systemic sclerosis, polymyositis, IgG4-related disease, sarcoidosis, juvenile idiopathic arthritis, adult onset Still's disease, periodic fever syndromes, Behcet's disease, autoimmune hepatitis, giant cell arteritis, takayasu arteritis, granulomatosis with polyangiitis, polymyalgia rheumatica. †abatacept, anakinra, apremilast, belimumab, canakinumab, etrolizumab, mepolizumab, rituximab, vedolizumab

b.



c.



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Experiences of Patients with Rheumatic Diseases in the US During the Early Months of the COVID-19 Pandemic

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SESSION INFORMATION
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Background/Purpose: Patients with rheumatic diseases such as RA and lupus have increased risk of infection and are treated with medications that may increase this risk yet are also hypothesized to help treat COVID-19. We expanded upon our previously published work on the early few weeks of the COVID-19 pandemic[1] to the early few months to better understand how patients have been impacted.

Methods: Participants were enrolled in FORWARD, The National Databank for Rheumatic Diseases, a longitudinal registry of patients with rheumatic diseases. Participants with active email were invited to answer 5 COVID-19 surveys sent every 2 weeks from March 25 through June 2, 2020. Participants were asked about new symptoms, COVID-19 testing, changes in their rheumatology care, safety measures, social contact, economic impact, and more. Responses were linked to each participant's most recently completed semiannual questionnaire for demographics, diagnosis, patient-reported outcome measures, and medication use. Student's t tests, X^2 tests, and logistic regression were used to assess significance ($p< 0.05$) as appropriate. Two of the authors (YS and TAS) independently read and open coded optional free text comments using a grounded theory approach and organized them into themes.

Results: total of 7217 participants were invited, and 2000 (28%) responded to one or more COVID-19 questionnaires. RA was the most frequent diagnosis (63%). Geographic distribution was diverse, with respondents representing all 50 states. Respondents and non-respondents had slight demographic differences, and respondents had lower disease

	Respondents n=2000	Nonrespondents n=5216	p
Demographics			
Age, mean (SD), years	64.9 (11.3)	63.8 (12.9)	<0.01
Female, %	85.0	83.8	0.21
White, %	93.0	89.7	<0.001
Education, mean (SD), years	15.3 (2.1)	14.7 (2.3)	<0.001
Married, %	69.3	67.0	0.07
Rural, %	22.6	27.0	<0.001
History of smoking, %	37.9	41.6	<0.01
BMI, mean (SD), kg/m2	28.4 (7.6)	29.4 (7.9)	<0.001
US Geographic Distribution, %			
Northeast	16.6	18.1	<0.001
Midwest	33.9	33.1	
South	24.7	27.9	
West	21.4	16.7	
PROMs, mean(SD)			
Pain, 0-10	3.4 (2.6)	3.9 (2.8)	<0.001
Global Severity, 0-10	3.3 (2.4)	3.8 (2.6)	<0.001
Fatigue, 0-10	3.8 (2.9)	4.4 (3.1)	<0.001
HAQ-II, 0-3	0.78 (0.60)	0.94 (0.69)	<0.001
PAS-II, 0-10	3.1 (2.1)	3.6 (2.3)	<0.001
Primary Diagnosis, %			
Rheumatoid arthritis	64.0	62.6	<0.01
Osteoarthritis	14.5	15.1	
Systemic lupus erythematosus	5.0	5.2	
Psoriatic arthritis	3.9	2.5	
Fibromyalgia	4.3	5.7	
Ankylosing spondylitis	1.5	1.2	
Other	6.8	7.7	
Medications, %			
Conventional DMARD	50.0	45.0	<0.001
Biologic DMARD	40.9	35.5	<0.001
JAK inhibitor	6.0	5.0	0.13
Corticosteroid	20.0	18.0	<0.01
NSAID	38.9	34.5	<0.01

Table 1. Characteristics of participants who were emailed the COVID-19 supplemental questionnaire by response status.

activity (Table 1). More than half (59%) of respondents experienced one or more changes in their rheumatology care due to COVID-19. Patients with higher disease activity or who met COVID-19 screening criteria were significantly more likely to experience a change in care (Table 2). Nearly all (99%) respondents reported taking safety measures to reduce risk, 6% received COVID-19 testing, 0.8% tested or were presumed positive, and 16% reported a negative economic impact. Qualitative analysis of the free text comments from 762 respondents revealed 5 key themes: emotions in response to the pandemic, perceptions of risk from immunosuppressive medications, protective measures to reduce risk, disruptions in accessing medications, and limited access to COVID-19 testing (Table 3).

Conclusion: In the first few months of the COVID-19 pandemic in the US, most patients with rheumatic diseases had important changes to their healthcare, with many changing medical appointments, altering medications with and without professional consultation, and unable to access prescriptions. Those with higher disease activity and those who met CDC priority testing criteria were significantly more likely to experience changes in their rheumatology care

Change in Care[a]	All (n=2000) %	Disease Activity[b] Low (n=1384) %	High (n=616) %	Screening Criteria[c] No (n=1220) %	Yes (n=780) %
Canceled or postponed appointments	30.6	**28.0**	**36.7**	**26.7**	**36.8**
Switched to teleconference appointments	30.1	**26.2**	**39.0**	**26.6**	**35.6**
Could not reach the rheumatology office	2.5	2.2	3.2	**2.0**	**3.3**
Could not obtain my medications	4.2	**3.5**	**5.8**	**3.3**	**5.6**
Physician changed the dose of patient's medication(s)	4.7	3.9	6.3	**3.4**	**6.5**
Physician added or removed medication(s)	7.0	6.0	9.3	**5.7**	**9.0**
Patient changed the dose of medication(s)	4.3	4.0	5.2	**3.1**	**6.3**
Patient added or removed medication(s)	7.0	**6.1**	**9.1**	**4.4**	**11.2**
Other	7.8	7.6	8.3	**5.7**	**11.0**
No change	40.6	**45.1**	**30.5**	**45.7**	**32.6**

[a]Statistically significant differences (after controlling for demographics and medications) are shown in bold.

[b]Disease activity was defined by PAS-II (PAS-II≤3.7 low, PAS-II>3.7 high)

[c]Based on April 27, 2020 CDC COVID-19 testing priorities (healthcare wokers, workers in congregate living settings, first responders, residents in long-term care facilities with 1 or more symptoms; people with cough or shortness of breath; people with 2 or more other symptoms of COVID-19)

Table 2. Changes in rheumatology care during the COVID-19 pandemic reported March through May 2020.

even after controlling for demographic and medication differences. The relatively low rate of positive COVID-19 tests may be due to reporting bias and future follow up will be necessary to identify changes in care for COVID-19-positive patients.

References

1. Michaud K et al. Experiences of Patients with Rheumatic Diseases in the US During Early Days of the COVID-19 Pandemic. ACR Open Rheumatol. 2020.

Themes	Subthemes
Emotions in response to COVID-19 related experiences	Anxiety/nervousness/worry/fear
	Motivated to take actions to reduce personal risk of COVID-19 infection
	Not worried about COVID-19
	Uncertainty about whether symptoms are due to COVID-19
	Frustration over difficulties accessing medications, treatment, or testing
	Anger/despair over how the crisis has been managed by local or national leaders
	Sadness/grief from being separated from/mourning the loss of family, friends, and others
	Gratitude for economic stability or the ability to limit personal exposure to COVID-19
	Hope
	Desire to help others by not using limited testing resources or by helping those in need
	Managing negative emotions/stress
Perceptions of risk	Increased risk due to age, chronic conditions, or potential exposure to infected people
	Increased risk due to taking immunosuppressive medications
	Personal limit for acceptable/unacceptable risk
	Doubts about the seriousness of the risks of COVID-19
Protective measures to reduce risk of COVID-19 infection	Self-isolation/social distancing
	Cancelling medical appointments that can be postponed
	Working from home
	Cancelling travel plans
	Wearing masks or gloves when in close contact with others
Impacts on healthcare, health, and well-being	Stopping arthritis medications to lessen risk of COVID-19
	Reduced access to medications (including hydroxychloroquine and tocilizumab)
	Reducing medication dose/frequency to make it last longer
	Medical consultations cancelled/switched to telephone or video consultations
	Cancellation/postponement of procedures/services that must be conducted in person
	Reduction in physical activity
	Loss of health care coverage
	Lost employment/income
	Exposure to COVID-19 among essential workers
Access to COVID-19 testing	Limited testing available for those with symptoms or exposure to COVID-19
	Long wait times for test results
	Interest in antibody testing

Table 3. Themes and subthemes identified from COVID-19 questionnaire optional free response comments.

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Abstract Number: 0013

Colchicine to Weather the Storm in Hospitalized Patients with COVID-19

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SESSION INFORMATION
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Background/Purpose: Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome–coronavirus-2 (SARS-CoV-2) infection, is a global pandemic causing havoc. There is a knowledge gap regarding the use of use of immunomodulation and anti-inflammatories in patients with COVID-19 and the optimal treatment is yet to be defined. The repurposing of colchicine for the treatment of COVID-19 has been suggested based in its immunomodulatory, anti-inflammatory, and anti-viral properties.

Methods: single-center propensity score matched cohort study, including all consecutive COVID-19 patients, with confirmed SARS-CoV-2 infection admitted to community teaching hospital between March 1, 2020 and May 12, 2020 was performed. Patients were stratified according to the receipt of colchicine. The primary endpoint was defined as all-cause in-hospital death within 28-day follow-up.

Results: In total, 50 patients were included in the 1:1 matched cohort study. The mean age of the total study population was 58.3 years (range: 26 – 90 years), and 24% (n=12) were female. The most prevalent chronic comorbidities included hypertension (54%; n=27), diabetes (40%; n=20), obesity (46%, n=23), and chronic pulmonary disease (16%; n=8). At the end of the 28 day follow-up, patients receiving colchicine were approximately 2 times more likely to be discharged from the hospital (odds ratio, 2.11; 95% confidence interval, 0.63 – 7.1; p=0.225) and when comparing mortality, there were 3 deaths (12%) in patients receiving colchicine versus 10 deaths (40%) in the groups receiving standard of care (odds ratio, 0.21; 95% confidence interval, 0.05 – 0.87; p=0.032).

Conclusion: To our knowledge, this is the first cohort report using colchicine for the treatment of COVID-19. Treatment with colchicine led to a higher rate of discharge from the hospital and was associated with a decrease in mortality in patients with severe COVID-19. These observations warrant further investigation in large colchicine controlled clinical trials.

Disclosure: L. Brunetti, CSL Behring, 2, Astellas Pharma, 2, Horizon Blue Cross Blue Shield of New Jersey, 5; **O. Diawara**, None; **A. Tsai**, None; **B. Firestein**, None; **R. Nahass**, None; **G. Poiani**, None; **N. Schlesinger**, Johnson and Johnson, 5, Horizon, 5, IFM, 5, Pfizer, 2, AMGEN, 2.

Abstract Number: 0014

Does the Type of Rheumatic Disease or Biologic Treatment Increase the Risk of Developing Severe COVID-19?

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SESSION INFORMATION

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Background/Purpose: Patients with inflammatory rheumatic diseases (IRD) have an increased risk for infection related to immunosuppression secondary to their disease, treatment and comorbidities. Nonetheless recent studies

Table 1. Risk for hospital admission in adult patients with IRD compared with patients with no IRD

	Patients in HAC (n)	Admitted to hospital due to COVID 19			
		n	Rate (%)	RR†	95% (CI)
No IRD patients	475,183	2,375	0.49%	1	
IRD patients	4,592	48	1.04%	2.09	(1.57-2.78) *
RA	1,708	17	0.99%	1.99	(1.24-3.2) *
PsA	515	7	1.35%	2.72	(1.3-5.68) *
SpA	862	1	0.11%	0.23	(0.03-1.65)
SS	175	5	2.85%	5.72	(2.41-13.57) *
SLE	254	4	1.57%	3.15	(1.19-8.34) *
Vasculitis	165	4	2.42%	4.85	(1.84-12.78) *
IIM	88	0	0%	-	
PMR	474	8	1.68%	3.38	(1.7-6.72) *

† Comparisons were made between patients without IRD and each IRD subtype.
HAC= hospital's area of care, IIM=idiopathic inflammatory myopathy, PsA=psoriatic arthritis, PMR=polymyalgia rheumatica, RA=rheumatoid arthritis, RD= rheumatic disease, SLE=systemic lupus erythematosus, SpA=spondyloarthritis, SS= Sjögren's Syndrome.

Table 2. Risk for hospitalization in adult IRD patients on bDMARDs and JAK inhibitors compared with IRD patients with classic or no DMARD

	Total patients	Admitted to hospital			
		n	Rate (%)	RR†	CI (95%)
IRD patients without biologics/JAK inhibitors	3684	33	0.89%	1	
Rituximab	71	8	11.26%	12.58	(6.03-26.25) *
TNF inhibitors	604	6	0.99%	1.11	(0.47-2.64)
Abatacept	40	1	2.5%	2.79	(0.39-19.91)
Tocilizumab	72	0	0%	-	-
JAK inhibitors	17	0	0%	-	-

† comparisons were made between IRD patients without biologics/JAK inhibitors and each treatment group.

don't support a higher risk for SARS-CoV-2 infection (COVID19) or a more severe disease in the patients. Analysis of individual risk factors among IRD related to their disease group and treatment is necessary.

The aim of this study is to assess the risk for hospital admission due to COVID 19 in adult patients with different IRDs and targeted immunosuppressive treatments.

Methods: Patients with confirmed COVID19 that were hospitalized in Ramón y Cajal University Hospital between February the 1st and May the 22nd 2020 were included. Confirmed infection was established by positive nasopharyngeal swab for SARS-CoV-2 or characteristic bilateral infiltrates on chest radiograph/computerized tomography. We identified among hospitalised patients those diagnosed with IRD followed in the Rheumatology department. Demographic and clinical data were collected, and risk for hospital admission was compared between patients with and without IRD. Individual risks according to specific IRD and treatments were analysed.

Results: A total of 2423 patients (0.5% of the population in hospital's area of care) were hospitalized due to COVID19 during the study period and 48 of them had a previous diagnosis of IRD (1.04% of all IRD patients). Median age was 62 years (range 19 to 88), and 62.8% were female. Risk for hospital admission was significantly higher in patients with IRD older than 65 years, with arterial hypertension, diabetes and/or interstitial lung disease related to IRD (data not shown).

Rates and relative risk ratios for infection and hospital admission regarding IRD and immunosuppressive treatments are represented in Tables 1 and 2. There was no difference in hospital admission rates among patients on bDMARDs with or without methotrexate.

Conclusion:

- Patients with IRD had a higher risk for hospital admission due to severe COVID 19. Sjögren syndrome and systemic vasculitis had the highest risk for hospitalization among IRD patients.
- We found a higher risk for hospitalization in patients treated with rituximab, but not in patients with anti-TNF drugs or other biologic treatment.

Disclosure: F. López-Gutierrez, None; **A. García-Fernández**, None; **J. Loarce-Martos**, None; **L. Calvo-Sanz**, None; **I. Del Bosque-Granero**, None; **V. Garcia**, None; **B. Blanco-Cáceres**, None; **C. Pijoan-Moratalla**, None; **L. Villalobos-Sánchez**, None; **J. Bachiller-Corral**, None; **M. Vázquez**, None.

Abstract Number: 0015

COVID -19 Lung Inflammation – What Have We Learnt so Far ?

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Background/Purpose: The SARS CoV-2 pandemic has inspired new interest in understanding the fundamental pathology of pneumonia and Acute Respiratory Distress Syndrome (ARDS). SARS CoV-2 in humans is associated with a broad spectrum of clinical respiratory syndromes, ranging from mild upper airway symptoms to progressive life

Table 1: Baseline Cohort characteristics
*Comorbidities of Interest have been selected. SFR is categorised by American European consensus

Total	500
Male	300(60%)
Female	200(40%)
Age, mean (SD)	69.39(17.41)
median (min-max)	73(16-100)
<40	43(8.6%)
40 – 70	178(35.6%)
70 – 80	121(24.2%)
>80	158(31.6%)
Ethnicity, Caucasian	436(87.2%)
Asian	31(6.2%)
African	21(4.2%)
Unknown	12(2.4%)
Comorbidities, None	49 (9.8%)
<2	218(43.6%)
>2	280(56%)
DM	128(26%)
Hypertension	186(37%)
Cardiovascular disease	178(36%)
Cerebrovascular disease	44(9%)
Respiratory disease	148(30%)
Other	281(56%)
Respiratory rate >24	272(54.4%)
Heart rate >100	174(34.8%)
Temp	256(51.2%)
SFR, mean	371
SFR <235	56(11%) (ARDS)
SFR <315	181(36.7%) (Acute lung injury)
SFR >315	311(63.2%)
Symptoms, Cough	295(59%)
SOB	294(58.8%)
Sore throat	33(6.6%)
GI	89(17.8%)
Fever	248(49.6%)
Lethargy	52(10.4%)
Falls	64(12.8%)
Myalgia	20(4%)
Confusion	47(9.4%)
Alive	307 (61.4%)
Dead	193(38.6%)

threatening pneumonia. A proportion of patients develop ARDS. Although evidence is emerging on risk factors, not much is known about the morphologic and molecular changes in the lungs of patients with Covid-19. Radiographically, peripheral ground glass opacities on CXR and CT scan fulfil the criteria for ARDS but are still not well characterized. What seems consistent is that ARDS and critical illness appear to develop most commonly between 1–2 weeks after the onset of symptoms. Some Covid-19 patients are at increased risk of developing respiratory failure

Table 2: Baseline Clinical parameters of the Cohort

CRP, mean (SD)	114.19(91.26)
median	95.5(1-544)
Lymphocyte, mean (SD)	1.37(4.56)
median (min-max)	0.82(0-55)
Neutrophil, mean (SD)	6.9
median (min-max)	5.64
NL Ratio, mean (SD)	11.64(14.72)
median (min-max)	6.77(.060-112.75)
Urea,mean	9.66(7.7)
median (min-max)	7.5(1-70)
Creatinine,mean	114 .75(107.7)
median (min-max)	88.0(21-1013)
CXR Not done	28(5.6%)
1	140(28%)
2	317(63.4)
3	15(3%)
CT Scan Not done	397(79.4%)
Covid	103(20.6%)
Blood cultures, Gram positive	34(6.8%)
Gram negative	10(2.0%)
No growth	218(43.6)
Not done	238(47.6%)
Oxygen requirement	348(69.6%)
CPAP	56(11.2%)
Mechanical ventilation	64(12.8%)
Length of stay, mean	8.43(9.88)
median (min-max)	5 (0-60)

*CXR 1= Mild/Indeterminate, 2= Moderate, 3 = Severe(as per UK radiology guidelines)

Table 3: Baseline predictors for Mortality

	B	SE (B)	Wald	Sig	Unadjusted OR(95% CI)	Adjusted OR	95% CI	
Comorbidities>2(ref1)	.755	.251	9.018	.003	2.76(1.9-4)	2.128	1.300	3.483
SFR	-.005	.001	25.592	.000	.994(.992-.996)	.995	.993	.997
CRP	.009	.001	34.801	.000	1.008(1.005-1.01)	1.009	1.006	1.011
Creatinine	.002	.001	3.407	.065	1.003(1.001-1.005)	1.002	1.000	1.005
Age	.050	.009	28.671	.000	1.05(1.04-1.07)	1.051	1.032	1.071
Constant	-3.703	.833	19.741	.000		.025		

Variable(s) entered on step 1: Gender, Comorbidities >2, SFR, NLR, CPAP, CRP, Creatinine, Age, Total LOS
Ref1: comorbidities <2
Model(x^2) =162.36, p<.001*; NagelkerkeR^2=40.2% (model could explain 40% of variance in Mortality outcome)

which appears to be driven by hyper-inflammation, resembling cytokine storm syndrome (CSS). There are currently no approved pharmacological treatments; however several trials are on going at present. The lack of reliable clinical

and serological predictors for deterioration is making it harder to triage and manage these patients appropriately. This study aimed at identifying potential predictors for outcomes, using baseline clinical parameters.

Methods: or this study, demographics, clinical and laboratory data, imaging and outcomes were collected for 592 patients with COVID 19 between February 20th and May 7th 2020 from a single centre in Essex, United Kingdom. 500 were included in final analysis. We used multivariable logistic regression models to identify risk factors.

Results: Refer to Tables 1&2. Mean age of the cohort was 69.4, 300(60%) were males. Majority were Caucasians, 436 (87%) and our cohort comprised of patients over 70, 290(58%). Most patients had 2 or more comorbidities 280(56%). Most common were hypertension 186(37 %), Cardiovascular disease 178(36 %) and Diabetes 128 (26 %). Cough was the common presentation 295(59%) followed by dyspnoea 294(58.8%) and fever 248(50 %.). Mean CRP was very high at baseline 111, neutrophil-lymphocyte ratio was 11.64 and baseline mean creatinine was 114. 44(8.8 %) had secondary bacterial infection.

The mean SpO 2/FIO 2 ratio (SFR) was 371 and 56 (11%) of patients fell into ARDS criteria and 181(36.7%) had acute lung injury. 66.4% had significant CXR findings including bilateral ground glass opacities and consolidation. 348(69.6%) required Oxygen, 56(11.2%) required CPAP and 64(12.8%) needed mechanical ventilation.

Of the 500, 193(38.6%) died and mean length of stay was 8.43 days. Baseline predictors for mortality were: comorbidities >2 OR 2.13(95% CI 1.30 – 3.48), CRP OR 1.01(95% CI 1.01 – 1.01), Creatinine OR 1.00 (95% CI 1.00 – 1.01), Age OR 1.05(95% CI 1.03 – 1.07). SFR had a trend towards increase mortality OR 0.99 (95% CI 0.99 – 0.10)

Conclusion: In this single centre study, older patients, comorbidities, baseline CRP and creatinine were risk factors for worse outcomes. Real-time consistent monitoring of SFR and inflammatory markers are essential in monitoring disease course, allowing for early intervention to improve patient outcomes.

Disclosure: S. Gokaraju, None; **M. Darda**, None; **V. Warrier**, None; **I. Duta**, None; **F. Hayes**, None; **Y. Ahmed**, None; **G. Koduri**, None.

Abstract Number: 0016

Differential Characteristics in Inflammatory Rheumatologic Patients with Severe and Mild COVID-19 Infection

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SESSION INFORMATION

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Background/Purpose: SARS COV 2 pandemic has been an issue which has challenged the health care systems around the world. Rheumatology has been involved in two ways: on the one hand, due to the use, in its treatment, of specific agents usually indicated in rheumatologic conditions and, on the other hand, the fear that our patients could be at higher risk due to the use of immunosuppressive agents.

The main objective of our study was to analyze which features were associated with a serious course of the infection in a cohort of inflammatory rheumatologic patients and COVID-19 infection.

Methods: All patients with rheumatologic inflammatory conditions and COVID infection (confirmed by PCR of nasopharyngeal swab or serology) followed at three university referral centers from Basque Country were identified. Severe course was defined as those who required hospital admission or die. Comparisons of those with serious and non-serious disease course were performed using standard tests.

Results: Among 97 rheumatologic patients with COVID-19 infection, 37 (38%) presented with a severe course, 29 (29.9%) were admitted to hospital, 2 (2%) transferred to an intensive care unit and 12 (12.4%) died. Comparisons between those with severe and non-severe course can be seen in 'Table 1'. Multivariate analysis of those variables found to be significant in the univariate analyses showed that only glucocorticoid (GC) use [0R 95%CI: 9.4 (2.3-39.0)] was associated with a severe course. Similar analyses also showed that death was associated with elder age, obesity and GC use.

Table 1

	Severe	Non-severe	p
Age, mean (±SD)	66.9±13.9	58.0±17.0	0.006
Sex (%female)	64.9	61.7	0.830
Obesity (%)	18.9	5	0.040
Heart disease (%)	29.7	15.0	0.120
HBP (%)	54.1	51.7	0.837
Lung disease (%)	35.1	20.0	0.151
Diabetes mellitus (%)	16.2	11.7	0.551
scDMARD (%)	62.2	55.0	0.531
Targeted therapies (%)	18.9	25	0.620
GCs (%)	70.3	33.3	0.001
CRP mg/L, mean (±SD)	217.7±341.8	87.3±122.4	0.040
Ferritin mg(dl, mean (±SD)	676.5±718.5	945.6±1416.2	0.603
LDH mg/dl, mean (±SD)	296.6±152.1	275.8±94.4	0.592
D dimer mg/dl, mean (±SD)	1067.4±1207.6	1249.7±1134.9	0.684
Lymphocytes, mean (±SD)	813.4±575.8	1541.7±1134.9	0.008

Conclusion: A severe course of COVID infection was observed in almost forty patients. GC were associated with either bad outcome and death whereas elder age and obesity were also associated with fatal outcome.

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Abstract Number: 0017

Impact of COVID19 on Missed/Cancelled Rheumatology Office Visits and Parenteral Immunosuppressive Medications

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Background/Purpose: The global COVID19 pandemic has had a major impact on healthcare. The effect on rheumatology patients and providers is unclear, as is the role of telemedicine service to meet unique challenges posed by the pandemic.

Methods: Using the Columbus data warehouse of the AARA rheumatologist network, we examined calendar trends in the frequency of kept vs. missed/cancelled office visits and intravenous (IV) infusions of immunomodulatory medications (e.g. abatacept, golimumab, infliximab, tocilizumab) from January to May, 2020. We compared results by primary diagnosis, driving distance from physician office, and socieoeconomic status(SES), proxied by the Area

	Office Visits			Infusions		
	Missed/Cancelled	Kept	P value	Missed/Cancelled	Kept	P value
Patients, n	23,420	88,337	-	429	4,652	-
Providers, n	94	92	-	47	63	-
Patient weeks, n	27,650	206,985		589	18,114	
Age, years	59.8 (16.9)	60.1 (15.4)	0.0005	62.0 (17.2)	63.1 (14.1)	0.07
Female Sex	78.0	77.1	<0.0001	73.7	77.9	0.05
U.S. Region			<0.0001			<0.0001
Central	9.2	6.3		10.4	13.6	
Northeastern	8.5	6.3		7.8	2.1	
Southern	70.2	72.4		73.2	65.4	
Western	12.1	15.1		8.7	18.9	
Driving Distance from Provider Office or Infusion Center, miles	19.8 (86.9)	17.5 (74.2)	<0.0001	37.9 (162)	22.1 (98.5)	0.0002
Area Deprivation Index group, quintile			<0.0001			<0.0001
1-20 (highest SES)	18.6	20.5		17.7	19.5	
21-40	24.6	24.6		31.1	27.7	
41-60	20.9	21.2		18.8	23.4	
61-80	17.6	17.4		18.8	15.9	
81-100 (lowest SES)	14.4	13.3		10.6	10.8	
Missing	3.9	3.0		3.1	2.8	

Data shown as n(%) or mean +- standard deviation (SD); SES = socioeconomic status

Table Partial List of Factors Associated with Missed/Cancelled vs. Kept Office Visits and Infusions Associated with the Temporal Evolution of the COVID19 Outbreak

Deprivation Index (ADI). Descriptive statistics and multivariable logistic regression were used to identify factors associated with missed/cancelled visits, controlling for clustering (visits within patients), with results as odds ratios (OR) with 95% confidence intervals(95%CI).

Results: Before March 15th (i.e. Pre-COVID), mean weekly visit volume overall was 17,203 visits/week among 121,843 unique rheumatology patients, which decreased minimally (3.1%) Post-COVID. Among return patient visits (mean 10,678/week, dropping 9.1% Post-COVID), 100% pre-COVID were in-person visits, but dropped to 70.3%, and were supplemented by 29.7% telemedicine visits. In addition to the decline in office visit volume and the transition to telemedicine visits, the frequency of missed/cancelled in-person appointments Post-COVID also increased. It peaked during week 12 (March 23-28) in which 15.2% of all appointments were missed/cancelled overall, 17.9% for in-person visits vs. 5.1% for infusions ($p< 0.0001$).

Univariate characteristics of patients keeping vs. missing visits and infusions is shown (Table). After adjustment, and referent to week 1 (Jan 5-11), the OR (95% CI) for cancellations associated with the pandemic at its peak was 1.30 (1.27, 1.34). Compared to follow-up visits for rheumatoid arthritis, new patient visits and return patient visits for osteoarthritis and osteoporosis were associated with a greater likelihood of missed/cancelled office visits, with corresponding OR (95% CI) of 1.59 (1.51, 1.67), 1.34 (1.31, 1.37) and 1.75 (1.71, 1.80), respectively. Patients with lower SES had a 5-20% higher likelihood to miss/cancel office visits compared to those in the highest SES quintile. Multivariable-adjusted factors also associated with missing/cancelled office visits included greater driving distance to the rheumatologist office, female sex, smoking, comorbidities (e.g. anxiety, asthma, back pain, diabetes, fibromyalgia, GERD, sleep disorder); and region.

Conclusion: The impact of COVID19 on both rheumatology practice visit volume and immunomodulatory treatments has been substantial. Telemedicine and other technology-focused tools for remote digital patient data capture and monitoring are essential to optimize rheumatology care and outcomes.

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Abstract Number: 0018

PROMIS-29 and Health Related Quality of Life in Rheumatology Outpatients During the COVID-19 Pandemic in New York City

Gregory Vitone[1], Marianna Frey[2], Candace Feldman[3], Lindsay Lally[2], Anne Bass[4], Jane Salmon[2], Mary Crow[2], Michael Lockshin[5], Vivian Bykerk[2], Medha Barbhaiya[5] and Lisa Mandl[2], [1]Hospital for Special Surgery, New York, [2]Hospital for Special Surgery, New York, NY, [3]Brigham and Women's Hospital, Boston, MA, [4]Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, [5]Hospital for Special Surgery, Barbara Volcker Center for Women and Rheumatic Diseases, New York, NY

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Epidemiology & Public Health Poster I: COVID-19 & Rheumatic Disease

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Baseline Characteristics of Rheumatology Outpatients in New York City During the COVID-19 Pandemic, Overall and Stratified by Self-Report Rheumatic Disease			
	SRD± (N=4147)	Non-SRD (N=2437)	p-values
DEMOGRAPHICS			
Age (Mean, SD)	57.5 (15.5)	63.2 (15.0)	<0.0001
Female (N, %)	3282 (79%)	1736 (71%)	0.0005
Ethnicity (N, %) Not Hispanic or Latino	3888 (88%)	2211 (91%)	0.004
Race (N, %) White	3401 (82%)	2108 (86%)	<0.0001
BMI (Mean, SD)	26.7 (6.2)	26.7 (5.7)	0.2
Obesity (N,%)	977 (25%)	575 (24%)	0.88
Employed (N,%)	2281 (55%)	1228 (50%)	0.0003
Ever Smoker (N,%)	1303 (31%)	779 (32%)	0.66
Education level • High School or less • Any Amount of College • Graduate or Professional	202 (5%) 2062 (40%) 1877 (45%)	95 (4%) 1132 (46%) 1208 (49%)	0.002
Income (N, %) • <$100,000 • Unknown/ Not reported	1183 (29%) 768 (18%)	594 (24%) 497 (20%)	0.0006
COVID-19 STATUS			
Confirmed Close Contact with COVID-19 (N, %)	918 (22%)	487 (20%)	0.04
Expression of COVID-19-like symptoms *(since January 1st, for more than 4 days)*	1758 (42%)	894 (37%)	<0.0001
% time homebound due to social isolation • >95% of time	3054 (74%)	1701 (70%)	0.0008
± Patients seen by a rheumatologist and with self-reported RA, Lupus, Psoriatic Arthritis, Spondyloarthritis, Scleroderma, Vasculitis, Myositis, Undifferentiated Connective Tissue Disease, Mixed Connective Tissue Disease, Sjogren's Syndrome, Polymyalgia Rheumatica, and Juvenile Idiopathic Arthritis			

Table 2. PROMIS-29 Domains Measured in Outpatient Rheumatology Patients During the COVID-19 Pandemic			
	SRD± (N=4147)	Non- SRD (N=2437)	p-values
PROMIS T-Scores (Median, [Range])			
Pain Interference	55.2 [41.6, 75.6]	52.4 [41.6, 75.6]	<0.0001
Depression	51.2 [41.0, 79.3]	48.9 [41.0, 79.3]	<0.0001
Fatigue	51.0 [33.7, 75.8]	48.6 [33.7, 75.8]	<0.0001
Anxiety	57.8 [40.3, 81.4]	56.0 [40.3, 81.4]	<0.0001
Sleep Disturbance	52.7 [32.0, 69.1]	51.7 [32.0, 69.1]	<0.0001

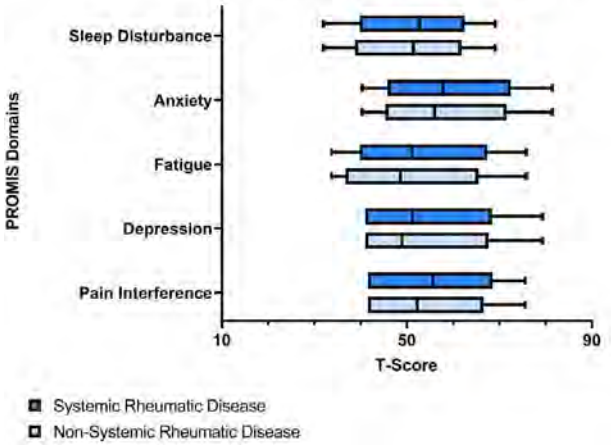
Higher scores=worse outcomes; 50=population mean

± Patients seen by a rheumatologist and with self-reported RA, Lupus, Psoriatic Arthritis, Spondyloarthritis, Scleroderma, Vasculitis, Myositis, Undifferentiated Connective Tissue Disease, Mixed Connective Tissue Disease, Sjogren's Syndrome, Polymyalgia Rheumatica, and Juvenile Idiopathic Arthritis

Background/Purpose: Little is known about the general health and wellbeing of patients with systemic rheumatic diseases (SRD) during the COVID pandemic. We sought to compare health related quality of life in patients with and without SRD during the height of the COVID-19 pandemic in New York City.

Methods: We emailed a secure web-based survey to 26,045 patients aged ≥18 years who were evaluated at least once by a rheumatologist during the two years prior to April 1, 2020 at a tertiary care academic center in New York City. Patients were invited to complete the survey by email or phone between April 24, 2020 and May 26, 2020. Information collected included self-reported COVID-19 diagnosis, potential COIVD-19 symptoms, rheumatic disease diagnosis, and sociodemographic factors. Respondents completed 5 domains from the PROMIS-29 (depression, anxiety, sleep disturbance, fatigue, pain interference). PROMIS-29 results were transformed to T-scores, with 50 being the mean for the US population, and a difference of 5 points considered to be clinically meaningful. Wilcoxon

Figure. The Effects of the COVID-19 Pandemic on Patients with Systemic and Non-Systemic Rheumatic Diseases as Measured by the PROMIS-29



rank-sum, Fischer's exact or chi-square tests were used, as appropriate, to compare demographics and PROMIS-29 scores in patients who reported having an SRD vs. those who did not.

Results: 6,584/26,045 (25.3%) respondents completed the PROMIS-29, and 4,147/6584 (62.9%) self-reported having an SRD. Most common SRDs included RA (N=1081, 26%), Psoriatic Arthritis/Spondyloarthritis (N=521,12.6%) and SLE (N=310, 7.5%). Patients with SRD were younger, less likely to be white and more likely to be Hispanic/Latino. Patients self-reporting an SRD were statistically significantly more likely to have had a confirmed close contact with a person with COVID-19 (22% vs. 20%; p=0.04), and spend > 95% of their time homebound (74% vs. 70%; p=0.0008). Those SRD patients who reported COVID-19 symptoms were more likely to exhibit their COVID-19 like symptoms for > 4 days compared to those without an SRD (42% vs. 37%; P< 0.0001) **(Table 1).** Across the five measured PROMIS-29 domains, patients with an SRD had worse scores than the population mean, and statistically significantly worse scores compared to those without SRD; however these differences were not clinically meaningful **(Table 2 and Figure 1).**

Conclusion: During the COVID-19 pandemic, patients with SRDs reported statistically significantly worse pain interference, depression, fatigue, and anxiety than the mean of the US population and those without SRD; however, these differences were not clinically meaningful. Patients with SRD were more likely to have had a confirmed close contact with someone with COVID-19, COVID-19 like symptoms for > 4 days, and were more likely to spend >95% of their time homebound compared to those without SRD. These data suggest that while patients with and without SRD had similar mental and physical health domains during the pandemic, SRD patients' quality of life may be differentially impacted by COVID-19, due to longer disease course, increased social exposure to COVID-19 cases, and greater social isolation. Further study is needed to evaluate whether COVID-19 continues to differentially impact the life of patients with SRD as the pandemic progresses.

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Abstract Number: 0019

Lasting COVID-19 Impacts on US Rheumatology Practices

Lynn Price[1], Gianna Melendez[1] and Phil Pouliot[1], [1]spherix global insights, Exton, PA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Epidemiology & Public Health Poster I: COVID-19 & Rheumatic Disease
Session Type: Poster Session A
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Background/Purpose: In late 2019, a novel, highly contagious coronavirus (COVID-19), was discovered in China and quickly spread throughout the world, equating to arguably the largest and most impactful modern-day world-wide pandemic. By March of 2020, the virus had fully spread to the US, forcing all but essential-working individuals to practice self-isolation in their homes, businesses to temporarily close their doors, and widespread social, economic, and medical impacts.

Methods: An independent market analytics firm collaborated with US specialists (n=257), including rheumatologists (n=50) from June 5 to 8, 2020 in order to gain insights on the impact of COVID-19 on their practice. Data collected included physician demographics, greatest impacts to date, attitudinal survey responses, and projected lasting change. Data has been collected on a rolling basis weekly, biweekly, or monthly since March 20, 2020.

Results: As of early June 2020, 36% of rheumatology practices have fully re-opened with appropriate social distancing pre-cautions in place; however, while improving, the majority continue to report high negative impacts of the COVID-19 crisis on their practice, with 70% agreeing that the COVID-19 experience will have a lasting impact on how they operate their practice. Half or more of rheumatologists report the areas of high impact include use of telemedicine, the financial health of their practice, the number of patient visits, and patient-outreach regarding COVID-19.

Specifically, while the use of telemedicine has grown week over week despite lifting the social distancing/stay at home requirements, overall in-person patient visits remain down 65% compared to pre-COVID levels. Furthermore, rheumatologists do not anticipate their use of telemedicine to cease once the crisis has abated, as 72% agree telemedicine will continue and estimate that 26% of their weekly patient engagements will be conducted virtually once the COVID-19 crisis is over. Although this new treatment modality has increased in popularity, rheumatologists largely remain unsatisfied and unclear exactly how they will be compensated or reimbursed for this type of care.

Other long-term projected practice impacts include rheumatologists' use of PPE, attendance of medical conferences, and interaction with pharmaceutical industry representatives. Of note, just one-fifth (or less) of rheumatologists project that their use of specific brands for rheumatologic conditions, their in-office administration of drugs, and the stocking of product inventory will be vastly different than pre-COVID.

Conclusion: While rheumatologists largely anticipate that their use of products and stocking/administration of specific products for rheumatologic conditions will largely revert to pre-COVID-19 levels, other aspects of how they manage their practice will likely undergo permanent changes. Specifically, elements of their profession that can be done virtually in the future likely will maintain some element of change once the crisis has fully abated—with emphasis and consideration to the use of telemedicine, the way physicians interact with industry, and conference attendance.

Disclosure: L. Price, None; **G. Melendez**, None; **P. Pouliot**, None.

Abstract Number: 0020

Characteristics of Rheumatology Outpatients with Suspected or Confirmed COVID-19 During the Pandemic in New York City

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SESSION INFORMATION

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Session Title: Epidemiology & Public Health Poster I: COVID-19 & Rheumatic Disease

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Session Time: 9:00AM–11:00AM

Background/Purpose: The incidence and disease severity of COVID-19 in rheumatic disease patients, who may be at higher risk due to underlying immune dysregulation and use of immunomodulatory medications, remains poorly understood. We evaluated the characteristics of rheumatology outpatients with suspected or confirmed COVID-19 in New York City during the pandemic "surge".

Methods: We emailed a secure web-based survey to 26,045 patients ≥18 years old evaluated at least once by a rheumatologist between April 1, 2018-April 21, 2020 at a tertiary care academic center in New York City. Patients were invited to complete the survey by email or phone between April 24, 2020 and May 26, 2020. Information collected included potential COVID-19 exposures, symptoms, and diagnoses, rheumatic and general medical history, and medication use. COVID-19 was suspected if patients were diagnosed by a healthcare worker or was confirmed if they reported a positive nasopharyngeal PCR test. T-tests, Fischer exact tests or chi-squares were used as appropriate to compare characteristics in patients with suspected/confirmed COVID-19 compared to those without, and in the subgroup of suspected/confirmed COVID-19 patients whose presentation was severe enough to require emergency room (ER) visit or hospitalization.

Results: Of the 7,057/26,045 (27.1%) who responded to our survey, 430/7,057 (6.1%) reported suspected/confirmed COVID-19. Mean age of patients with suspected/confirmed COVID-19 was lower than those without COVID-19 (53.6 [14.6] years vs. 60.0[15.6] years). There was a higher prevalence of Hispanic ethnicity, obesity, and current smoking or vaping in patients with suspected/confirmed COVID-19, as well as asthma, cancer, fibromyalgia and hypertension **(Table 1).** Although not significant, suspected/confirmed COVID-19 patients had a higher prevalence of SLE. Patients with COVID-19 had higher use of hydroxychloroquine, abatacept and belimumab in the preceding 6 months, and were more likely to have had a close contact with a person with COVID-19 **(Table 2).** In the subgroup with suspected/confirmed COVID-19, 79/430 (18.4%) presented to the ER or were hospitalized; age, race, ethnicity, education, income, BMI and smoking status were similar compared to those who did not **(Table 3).** However, ER/hospitalized patients were more likely to report SLE or Fibromyalgia and to use anti-malarials and conventional DMARDs**.** No difference in COVID-19 exposure status from close contact with an affected individual (p 0.24) or time spent at home (p 0.61) was noted in those who went to ER/hospitalized.

Conclusion: During the peak of the COVID-19 pandemic, 6.1% of rheumatology patients surveyed at a large, specialty hospital in NYC reported suspected/confirmed COVID-19, of whom 18.4% went to the ER or were hospitalized. This is likely a conservative estimate as those ill from COVID-19 may not have responded to our survey. Our findings provide insight into potential characteristics associated with the incidence and disease severity of COVID-19 in rheumatic disease patients in a COVID-19 "hot spot" during the pandemic.

Table 1. Characteristics of 7,057 Rheumatology Outpatients from a Tertiary Academic Center in New York City During the COVID-19 Pandemic, Overall and by COVID-19 Status			
	Survey Respondents without COVID-19 (N=6,627)	**Suspected or Confirmed COVID-19 (N=430)**	**p-value**
Sociodemographic Factors			
Age (mean (SD)	60.0(15.6)	53.6 (14.6)	<0.001
% Female	5048 (76.2%)	345 (80.2%)	0.055
Race*			0.073
Black	305 (4.6%)	27 (6.3%)	
White	5668 (85.5%)	360 (83.7%)	
Asian/Indian Subcontinent	276 (4.2%)	13 (3.0%)	
Other/Prefer not to answer/Missing	364 (5.5%)	28 (6.5%)	
Ethnicity*			<0.001
Hispanic/Latino	437 (6.6%)	53 (12.3%)	
Not Hispanic or Latino	5798 (87.5%)	357 (83.0%)	
Unknown/Prefer not to answer/Missing	392 (5.9%)	20 (4.6%)	
BMI**			0.017
Underweight <18	129 (1.9%)	12 (2.8%)	
Average Weight18-25	2843 (42.9%)	183 (42.6%)	
Overweight 25-29.9	2034 (30.7%)	107 (24.9%)	
Obesity class 1: 30-34.9	946 (14.3%)	66 (15.3%)	
Obesity class 2: 35.0	607 (9.2%)	55 (12.8%)	
Missing	68 (1.0%)	7 (1.6%)	
Smoking Status (cigarette smoking or vaping)			0.028
Current	169 (2.6%)	18 (4.2%)	
Former	1894 (28.6%)	104 (24.2%)	
Never	4274 (64.5%)	287 (66.7%)	
Missing	290 (4.4%)	21 (4.9%)	
Medical History			
• RA or inflammatory arthritis	1957 (29.5%)	123 (28.6%)	0.68
• SLE	583 (8.8%)	49 (11.4%)	0.068
• Psoriatic Arthritis/Spondyloarthritis	789 (11.9%)	54 (12.6%)	0.69
• Scleroderma/Vasculitis/Myositis	312 (4.7%)	25 (5.8%)	0.30
• Osteoarthritis	1532 (23.1%)	90 (20.9%)	0.30
• Asthma	1036 (15.6%)	111 (25.8%)	<0.001
• Cancer	943 (14.2%)	44 (10.2%)	0.021
• Chronic Kidney Disease	148 (2.2%)	7 (1.6%)	0.41
• Diabetes	353 (5.3%)	29 (6.7%)	0.21
• Fibromyalgia	503 (7.6%)	55 (12.8%)	<0.001
• Myocardial Infarction	114 (1.7%)	10 (2.3%)	0.35
• Hypertension	1904 (28.7%)	96 (22.3%)	0.004
• Lung Disease	234 (3.5%)	14 (3.3%)	0.76
• Obesity	728 (11.0%)	54 (12.6%)	0.31

*Self-reported race/ethnicity from survey used when available, otherwise obtained from self-report in medical chart
**BMI recorded at most recent medical visit
P-value threshold of <0.05 considered to be significant

Table 2. Medication Use and COVID-19 Exposure Status in 7,057 Rheumatology Outpatients from a Tertiary Academic Center in New York City During the COVID-19 Pandemic, Overall and by COVID-19 Status			
	Survey Respondents without COVID-19 (N=6,627)	**Suspected or Confirmed COVID-19 (N=430)**	**p-value**
Medication History			
Anti-malarials (Hydroxychloroquine (HCQ)/Chloroquine)	1244 (18.8%)	119 (27.7%)	<0.001
JAK inhibitors (Tofacitinib, Baricitinib, Updicitinib)	106 (1.6%)	10 (2.3%)	0.25
Apremilast	54 (0.8%)	4 (0.9%)	0.80
Biologics	1029 (15.5%)	64 (14.9%)	0.72
• Abatacept	73 (1.1%)	0 (0.0%)	0.029
• Belimumab	44 (0.7%)	10 (2.3%)	<0.001
• TNF-inhibitors (Infliximab, Etanercept, Adalimumab, Golimumab,Certolizumab)	628 (9.5%)	36 (8.4%)	0.45
• IL-6 inhibitors	85 (1.3%)	3 (0.7%)	0.29
• IL-1 inhibitors	9 (0.1%)	1 (0.2%)	0.61
• IL-12/23 inhibitors (Ustekinumab Guselkumab)	20 (0.3%)	1 (0.2%)	0.80
• IL-17 inhibitors(Secukinumab Ixekizumab)	99 (1.5%)	5 (1.2%)	0.58
• Cyclophosphamide	9 (0.1%)	0 (0.0%)	0.44
• Rituxan	116 (1.8%)	10 (2.3%)	0.38
Conventional DMARDs (Leflunomide, Mycophenolate, Methotrexate, Sulfasalazine, Azathioprine)	1229 (18.5%)	70 (16.3%)	0.24
Tacrolimus or Cyclosporine	56 (0.8%)	5 (1.2%)	0.49
COVID-Exposure Status			
Close Contact with someone with COVID-19	1230 (18.6%)	270 (62.8%)	<0.001
Percent of 24-hour day spent at home			0.007
>95% of time	4768 (71.9%)	318 (74.0%)	
76-95% of time	1422 (21.5%)	71 (16.5%)	
50-75% of time	278 (4.2%)	30 (7.0%)	
< 50% of time	159 (2.4%)	11 (2.6%)	
P-value threshold of <0.05 considered to be significant			

Table 3. Characteristics of 430 Rheumatology Outpatients with Suspected/Confirmed COVID-19 in New York City by Disease Severity			
	No ER or hospitalization (N=351)	**ER visit or Hospital Admission (N=79)**	**p-value**
Sociodemographic Factors			
Age (mean (SD)	53.4(14.5)	54.2 (15.1)	0.67
% Female	283 (80.6%)	62 (78.5%)	0.67
Race*			
Black	20 (5.7%)	7 (8.9%)	0.76
White	296 (84.3%)	64 (81.0%)	
Asian/Indian Subcontinent	11 (3.1%)	2 (2.5%)	
Other/Prefer not to answer/Missing	22 (6.3%)	6 (7.6%)	
Ethnicity*			0.058
Hispanic/Latino	40 (11.4%)	13 (16.5%)	
Not Hispanic or Latino	297 (84.6%)	60 (75.9%)	
Unknown/Prefer not to answer/Missing	14 (4%)	6 (7.6%)	
BMI in Categories			0.13
Underweight <18	10 (2.8%)	2 (2.5%)	
Average weight 18-24.9	159 (45.3%)	24 (30.4%)	
Overweight 25-29.9	85 (24.2%)	22 (27.8%)	
Obesity class 1: 30-34.9	50 (14.2%)	16 (20.3%)	
Obesity class 2: 35+	41 (11.7%)	14 (17.7%)	
missing	6 (1.7%)	1 (1.3%)	
Smoking status (cigarette smoking or vaping)			0.069
Current	18 (5.1%)	0 (0.0%)	
Former	81 (23.1%)	23 (29.1%)	
Never	238 (67.8%)	49 (62.0%)	
Medical History			
RA or inflammatory arthritis	98 (27.9%)	25 (31.6%)	0.51
SLE	32 (9.1%)	17 (21.5%)	0.002
Psoriatic Arthritis/Spondyloarthritis	48 (13.7%)	6 (7.6%)	0.14
Scleroderma/Vasculitis/Myositis	21 (6.0%)	4 (5.1%)	0.75
Osteoarthritis	73 (20.8%)	17 (21.5%)	0.89
Asthma	87 (24.8%)	24 (30.4%)	0.30
Cancer	38 (10.8%)	6 (7.6%)	0.39
Chronic Kidney Disease	5 (1.4%)	2 (2.5%)	0.48
Diabetes	22 (6.3%)	7 (8.9%)	0.41
Fibromyalgia	38 (10.8%)	17 (21.5%)	0.010
Hypertension	77 (21.9%)	19 (24.1%)	0.68
Medication History			
Anti-Malarials	88 (25.1%)	31 (39.2%)	0.011
JAK inhibitors	8 (2.3%)	2 (2.5%)	0.89
Apremilast	4 (1.1%)	0 (0.0%)	0.34
Biologics	54 (15.4%)	10 (12.7%)	0.54
• Belimumab	6 (1.7%)	4 (5.1%)	0.074
• TNF-inhibitors)	33 (9.4%)	3 (3.8%)	0.10
• IL-6 inhibitors	3 (0.9%)	0 (0.0%)	0.41
• IL-1 inhibitors	1 (0.3%)	0 (0.0%)	0.63
• IL-12/23 inhibitors	1 (0.3%)	0 (0.0%)	0.63
• IL-17 inhibitors	4 (1.1%)	1 (1.3%)	0.92
• Cyclophosphamide	0 (0.0%)	0 (0.0%)	
• Rituxan	8 (2.3%)	2 (2.5%)	0.89
• Conventional DMARDS	45 (12.8%)	25 (31.6%)	<0.001
• Tacrolimus/Cyclosporine)	5 (1.4%)	0 (0.0%)	0.29
*Self-reported race/ethnicity from survey used when available, otherwise obtained from self-report in medical chart **BMI recorded at most recent medical visit			

Disclosure: M. Barbhaiya, None; **G. Vitone**, None; **M. Frey**, None; **D. Jannat-Khah**, Astrazeneca, 1, Cytodyn, 1, Walgreens Boots Alliance, 1; **C. Feldman**, Biogen, 8, Voyager Therapeutics, 5, Merck, 5; **L. Lally**, None; **A. Bass**, None; **J. Salmon**, UCB, 1, 2, BMS, 1, 2, Abbott, 1, Pfizer, 1, Johnson & Johnson, 1, Lilly, 1, Merck, 1, Regeneron, 1; **M. Crow**, Bristol Myers Squibb, 5, Gilead, 5, Lilly, 5, Principia, 5; **M. Lockshin**, None; **V. Bykerk**, Amgen, 1, BMS, 1,

Gilead, 1, Sanofi-Genzyme/Regeneron, 1, Scipher, 1, Pfizer, 1, UCB, 1, NIH, 1; **L. Mandl**, Annals of Internal Medicine, 9, UpToDate, 7, Regeneron, 2.

Abstract Number: 0021

Prioritizing Patient Safety While Maintaining Study Integrity During COVID-19: Lupus Intervention Fatigue Trial Modifications and Lessons Learned

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: The coronavirus disease 2019 (COVID-19) global pandemic has drastically impacted the health system and the research community. Many research institutions and funding agencies recommended a moratorium on conducting in-person research and study enrollment until protocol changes to protect patient safety were implemented and approved. We turned the guidance provided by the Institutional Review Board (IRB) into actionable items without compromising the integrity of the primary, secondary, and exploratory outcomes of the study. The purpose of this project is to detail the modifications made to the Lupus Intervention Fatigue Trial (LIFT) and to summarize the lessons learned to meet the varied challenges created by the highly transmissible virus.

Methods: The research team evaluated current study protocols to determine which components required modification. The research team determined that the following protocols required modifications: 1) the intervention that included four individual coaching sessions and 2) four, two-hour, in-person assessments, including a physician exam, blood draws, and urine samples along with online patient-reported outcomes (PROs) at a University Medical Center Research Unit. The team made modifications that would allow for all interventions and assessments to be safely conducted remotely without compromising the integrity of the study aims.

Results: The intervention components were revised immediately to convert all individual coaching sessions to remote sessions. Next, we reviewed all study assessments and modifications were made to electronically consent participants, provide links for completion of online PROs, and perform telemedicine visits for the physician assessment. Collection of safety labs presented the biggest challenge since this required an in-person visit at a laboratory and we elected to delay this up to one month after the physician assessment, or used standard of care test results if they were done within a month of the physician assessment. We also offered the option of not doing the lab tests. With these modifications, we were able to complete all follow-up visits and no patients dropped out of the study. We were not able to collect the protocol extra blood for future research testing and some patients could not measure their vital signs at home.

Conclusion: The LIFT study was severely impacted by COVID-19. We provide insight into how our study protocol was modified without compromising the integrity of the primary, secondary, and exploratory outcomes of the study. The modifications utilized by the LIFT study and lessons learned while revising the LIFT protocols resulted in efficiencies that will be included in a revised protocol and will foster additional ideas to overcome the challenges in areas where we missed data collection and may serve as a useful example for other behavioral interventions to adapt their research studies given COVID-19 restrictions.

Disclosure: D. Kinnett-Hopkins, None; **L. Ehrlich-Jones**, Zimmer Biomet, 8; **H. Milaeger**, None; **A. Kenney**, None; **L. Rosiles**, None; **R. Ramsey-Goldman**, None.

Abstract Number: 0022

Association Between Changes in Pain Sensitization and Changes in Disease Activity After 12 Weeks of Disease Modifying Anti-Rheumatic Drug Therapy in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1: Changes in quantitative sensory testing measurements after 12 weeks of DMARD treatment

Quantitative sensory testing measure[1]	Mean score at baseline (SD)	Mean score at 12-weeks (SD)	Mean change in score (SD)	p-value[2]
Peripheral pain sensitization				
Wrist PPT[3]	3.62 (1.88)	4.06 (2.04)	0.44 (1.49)	<.0001
Knee PPT[3]	5.31 (2.81)	5.74 (2.87)	0.43 (1.75)	0.0002
Central pain sensitization				
Trapezius PPT[3]	2.89 (1.58)	3.26 (1.74)	0.37 (1.09)	<.0001
Thumbnail PPT[3]	3.62 (1.88)	4.06 (2.04)	0.44 (1.49)	<.0001
Pain facilitation				
Arm TS	12.78 (14.52)	14.09 (16.75)	1.31 (16.82)	0.2391
Wrist TS	13.21 (14.38)	14.02 (17.19)	0.81 (18.44)	0.5037
Pain inhibition				
CPM	1.41 (0.34)	1.37 (0.43)	-0.04 (0.51)	0.2802

[1] Sample size for each measure: wrist PPT N = 236; knee PPT N = 232; trapezius PPT N = 236; thumbnail PPT N = 236; arm TS N = 230; wrist TS N = 231; CPM = 230

[2] P-value is for pairwise t-test comparing mean score at baseline and at 12-weeks.

[3] Units of PPT in kgf

PPT, Pressure pain threshold; TS, Temporal summation; CPM, Conditioned pain modulation

Table 2: Correlations between changes in pain sensitization and changes in disease activity

Indicator of pain sensitization[1]	Δ DAS28-CRP[5]	(95% CI)
Peripheral pain sensitization		
Δ PPT[2] Wrist	**-0.29**	**(-0.41, -0.15)**
Δ PPT[2] Knee	**-0.31**	**(-0.43, -0.18)**
Central pain sensitization		
Δ PPT[2] Trapezius	**-0.18**	**(-0.31, -0.04)**
Δ PPT[2] Thumb	**-0.20**	**(-0.33, -0.06)**
Pain facilitation		
Δ TS[3] Arm	0.04	(-0.10, 0.18)
Δ TS[3] Wrist	0.08	(-0.07, 0.22)
Pain inhibition		
Δ CPM[4]	0.03	(-0.11, 0.17)

[1] Sample size for each measure: wrist PPT N = 194; knee PPT N = 191; trapezius PPT N = 194; thumbnail PPT N = 194; arm TS N = 189; wrist TS N = 190; CPM = 190
[2] Pressure pain threshold in kpf/s. [3] Temporal summation. [4] Conditioned pain modulation. [5] Disease activity score in 28 joints using C-reactive protein.
Correlations are Pearson's correlations reported with 95% confidence intervals
Significant correlations are bolded

Background/Purpose: Patients with rheumatoid arthritis (RA) have abnormalities in central nervous system regulation of pain, leading to enhanced pain sensitivity at joint sites (peripheral sensitization) and in a widespread distribution (central sensitization). Pain sensitization is important because it is associated with elevations in composite disease activity measures and patient-reported pain. It is unknown whether treatment with disease modifying anti-rheumatic drug (DMARD) therapy can modify pain sensitization. The objective of this study was 1) to examine changes in pain sensitization in RA following 12 weeks of DMARD therapy and 2) to determine the association between changes in pain sensitization and changes in disease activity.

Methods: This study included 236 participants with active RA who were changing DMARD therapy per standard of care. Participants underwent quantitative sensory testing (QST) to assess pressure pain thresholds (PPTs) at the wrist and knee to assess peripheral sensitization and PPTs at the trapezius and thumbnail to assess central sensitization.

Temporal summation (TS) was assessed as a specific measure of central sensitization involving pain facilitation, and conditioned pain modulation (CPM) was measured to assess pain inhibition. Disease activity was assessed using the disease activity score in 28 joints using C-reactive protein (DAS28-CRP). Differences in QST measures between baseline and 12-weeks after DMARD initiation were assessed using paired t-tests. Associations between changes in QST measures and changes in DAS28-CRP and its components were assessed with Pearson's correlation coefficients.

Results: PPTs increased (reflecting lower pain sensitivity) from baseline to follow-up; however, changes were small (ΔPPT wrist = 0.44 kpf/s, p = < 0.0001; ΔPPT knee = 0.43 kpf/s, p = 0.0002; ΔPPT trapezius = 0.37 kpf/s, p = < 0.0001; ΔPPT thumb = 0.44 kpf/s, p=< 0.0001) (Table 1). TS and CPM did not change significantly from baseline to follow-up. Negative correlations between changes in PPTs and changes in DAS28-CRP were strongest at joint sites (wrist r = -0.29, 95% confidence interval (CI) = -0.41 to -0.15; knee r = -0.31, 95% CI = -0.43 to -0.18) and weaker at non-joint sites (trapezius r = -0.18, 95% CI = -0.31 to -0.04; thumb r = -0.20, 95% CI = -0.33 to -0.06) (Table 2). Changes in TS or CPM were not significantly correlated with changes in DAS28-CRP.

Conclusion: All PPTs increased with DMARD treatment reflecting decreasing pain sensitivity. Correlations with DAS28-CRP were strongest with measures of peripheral sensitization. This is consistent with the idea that peripheral sensitization is driven by joint inflammation. However, changes in PPTs were small in magnitude. Treatment with DMARDs alone may not be sufficient to address pain sensitization in RA.

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Abstract Number: 0023

Hypophosphatasia May Be Misdiagnosed as Fibromyalgia: A Single Center Experience

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Hypophosphatasia (HPP) is a rare disease characterized by incomplete or defective bone mineralization due to a mutation in the alkaline phosphatase gene (ALPL). Given the heterogeneity of gene mutation, phenotypes, and mode of inheritance, the disease has several presentations, including femoral and stress fractures, tooth loss, muscle weakness, chondrocalcinosis, nephrolithiasis, chronic pain, and osteoarthropathy, and chronic pain syndromes similar to fibromyalgia (FM). HPP diagnosis is marked by consistently low levels of alkaline phosphatase (ALP), elevated levels of inorganic phosphate, pyridoxal-5'- phosphate, a breakdown product of vitamin B6, phosphoethanolamine, and genetic testing. Although this patient population is prone to fractures and osteoporosis, the use of bisphosphonates is contraindicated due to worsening bone demineralization disease. There are very few

Table 1: Characteristics of patients with Fibromyalgia and consistently low ALP

	Normal ALP n (%)	ALP ≤25 on at least 2 occasions n (%)	ALP ≤ 35 on at least 3 occasions n (%)
Total number of patients	246 (80)	12 (4)	57 (19)
Age (mean)	51	56	53
Male	40 (16)	2 (17)	10 (18)
Female	206 (83)	10 (83)	47 (82)
Normal Bone Density	11 (4)	2 (16)	2 (4)
Osteopenia	18 (7)	1 (8)	6 (11)
Osteoporosis	5 (2)	1 (8)	7 (12)
History of fractures	88 (35)	7 (58)	23 (40)

Table 1: Characteristics of patients with Fibromyalgia and consistently low ALP

case reports showing patients diagnosed with hypophosphatasia were initially misdiagnosed with fibromyalgia however there are no larger studies done on the subject. Our objective was to determine the prevalence of hypophosphatasia in a population of patients diagnosed with fibromyalgia

Methods: We performed a retrospective chart review of all patients 18 years or older at a single academic center diagnosed with FM based on ICD 10 Code "Fibromyalgia**"** M79.7 and at least one ALP level ≤ 35 were reviewed. Number of consecutively low ALP levels were noted. Gender, age, history of fragility fracture, bone mineral density screening, complete blood counts and medications were reviewed. For patients who have undergone HPP evaluation, genetic testing, and vitamin B6 levels were noted.

Results: Out of 305 patients diagnosed with fibromyalgia and at least one low ALP level, 57 (19%) had at least 3 consecutively low measurements of ALP ≤ 35 while 12 (4%) of patients had at least 2 consecutively low measurements of ALP ≤25. Mean age was 52 (range 18-94), 41% of patients were female, and 59% were male. Of the patients with at least 3 consecutively low ALP ≤ 35, 23 (40%) had a history of fractures. Fifteen patients had bone density scans: 2 (4%) had normal results, 6(11%) had osteopenia, and 7 (12%) patients had osteoporosis. No patients had Vitamin B6 levels checked. None of the patients had previous genetic testing for HPP. Of the patients with consistently low ALP levels, 16 (28%) were taking bisphosphonates.

Conclusion: Up to 19% of FM patients in our population were found to have consistently low levels of ALP and high suspicion for undiagnosed underlying HPP. None of the patients had Vitamin B6 level checked or genetic testing done which suggests the diagnosis was not suspected despite the similarity of clinical symptoms and low ALP levels. It is increasingly important to diagnose these patients with HPP given treatment availability and to avoid bisphosphonate use to prevent worsening bone fragility. Furthermore, our data supports screening for this condition as a part of the initial workup of FM.Table 1: Characteristics of patients with Fibromyalgia and consistently low ALP

Disclosure: P. Injean, None; **S. Lee**, None; **C. Downey**, None.

Abstract Number: 0024

An International Delphi Consensus on Non-pharmacological Interventions for Fibromyalgia

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SESSION INFORMATION

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Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia (FM) impacts directly on health and quality of life (QoL) of patients and associates with a large health economic burden. Non-pharmacological interventions are recommended as first-line treatment for FM[1]. However, there are no evidence-based recommendation for which intervention(s) to offer to patients with different manifestations of FM as core and adjunctive treatments. The aim of this Delphi exercise was to prioritise non-pharmacological treatments for FM based on the results of our meta-analysis[2].

Methods: A three-stage Delphi exercise was designed. Panel members were selected from the author list of EULAR, American Pain Society and Canadian FM guidelines and local clinicians with expertise in FM. In the first round Delphi survey, participants were asked to select interventions that they thought should be offered to people with FM, and then rate these interventions as either core or adjunctive treatments separately for pain, fatigue, sleep and depression. They were provided a summary of current research evidence from our recent meta-analysis to support their decision-making. Items receiving more than 70% votes were accepted, those receiving less than 30% were rejected and those obtaining between 30-70% were recirculated in the following rounds.

Results: Seventeen of 48 invitees agreed to participate and completed the 3 rounds of the survey. There were 7 rheumatologists, 2 physiotherapists, 1 pain specialist,1 psychologist, 1 nurse and 5 other professionals. This Delphi exercise identified 14 non-pharmacological interventions for pain, 11 for fatigue, 12 for sleep and 11 for depression that were considered potentially accessible and beneficial for the four common manifestations of FM (Table 1). Aerobic exercise, education, sleep hygiene and cognitive behavioural therapy were supported as core treatments for all manifestations. Other interventions, including music, periods of relaxation/enjoyment during the day, use of hot baths and local heat, achieved consensus as adjunctive treatments for certain outcomes (Table 2).

Interventions	Pain	Fatigue	Sleep	Depression
Aerobic exercise	94*	94*	88*	94*
Education	94*	94*	88*	76*
Sleep hygiene	94**	100**	100**	76**
Cognitive behavioural therapy	94*	88*	88*	88*
Stress management	94**	88**	94**	88**
Mind-body exercise	94*	88*	76*	82*
Clear understanding of the crucial role of stress	94**	NR	94**	94**
Strengthening exercise	88*	71*	NR	NR
Periods of relaxation/enjoyment during the day	88**	NR	76**	76**
Goal setting	82**	76**	NR	71**
Hot bath and local heat	82**	NR	71**	NR
Mindfulness	82*	76*	76**	71*
Pacing	82**	76**	82***	NR
Flexibility exercise	71*	NR	NR	NR
Music	NR	NR	76**	NR
Determination to "build well-being/Happiness	NR	NR	NR	71*

NR: not recommended

All values are percentages. Number of asterix (*) shows in which round the intervention was accepted.

Table 1. Accepted non-pharmacological interventions and percentage of agreement for pain, fatigue, sleep and depression

Interventions	Pain	Fatigue	Sleep	Depression
Aerobic exercise	**88**	**94**	**80**	**56**
Education	**88**	**88**	**93**	**85**
Sleep hygiene	**81**	**94**	**94**	**85**
Cognitive behavioural therapy	**75**	**53**	**60**	**80**
Mind-body exercise	**75**	**88**	**54**	50
Strengthening exercise	**73**	**83**	NR	NR
Flexibility exercise	**58**	NR	NR	NR
Goal setting	**57**	**77**	NR	**75**
Mindfulness	50	46	45	**58**
Stress management	50	**60**	**56**	**73**
Pacing	43	**92**	**73**	NR
Periods of relaxation/enjoyment during the day	40	NR	23	23
Hot bath and local heat	14	NR	8	NR
Clear understanding of the crucial role of stress	44	NR	**56**	**56**
Determination to "build well-being/Happiness	NR	NR	NR	50
Music	NR	NR	0	NR

NR: not recommended

All values are percentages. Text in bold shows interventions recommended as core and non-bold text as adjunctive interventions. For example, aerobic exercise was voted as core by 88% of the panel members for pain and 94% for fatigue.

Table 2. The classification of accepted non-pharmacological interventions as core or adjunctive for pain, fatigue, sleep and depression

Conclusion: This Delphi exercise provides an up-to-date consensus of expert practitioners and researchers on core and adjunctive non-pharmacological treatments for four manifestations of FM, specifically pain, fatigue, sleep and depression. This information will inform the development of a complex non-pharmacological treatment package for FM which will subsequently be tested in clinical research.

1. Macfarlane, G.J., et al., EULAR revised recommendations for the management of fibromyalgia. Annals of the rheumatic diseases, 2017. 76(2): p. 318-328.

2. Kundakci B, Kaur J, Goh S, Hall M, Doherty M, Zhang W, Abhishek A. The Efficacy of Non-Pharmacological Interventions for Fibromyalgia: A Systematic Review with Meta-Analysis [abstract]. Arthritis Rheumatol. 2019; 71 (suppl 10). https://acrabstracts.org/abstract/the-efficacy-of-non-pharmacological-interventions-for-fibromyalgia-a-systematic-review-with-meta-analysis/. Accessed May 27, 2020.

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Abstract Number: 0025

Clinical and Psychological Assessment of Rheumatoid Arthritis Patients with Fibromyalgia: A Real World Study

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Table1 Demographic Characteristics of RA patients with FM *vs.* those without FM

Feature	RA (n=160)	RA-FM (n=42)	P-value
Age, years	64 (56, 71)	62.5 (56, 71.5)	0.779
Disease duration, years	9 (4, 17.8)	11.5 (2, 21)	0.617
Sex			0.567
Male, n(%)	33 (20.6%)	7 (16.7%)	
Female, n(%)	127 (79.4%)	35 (83.3%)	
Smoking, n(%)	144/160 (90.0%)	37/42 (88.1%)	0.939
Education			0.584
Primary, n(%)	26 (16.3%)	9 (21.4%)	
Junior, n(%)	47 (29.4%)	11 (26.2%)	
Senior, n(%)	41 (25.6%)	14 (33.3%)	
Higher education, n(%)	46 (28.8%)	8 (19.0%)	
Race			0.755
Han, n(%)	152 (95.0%)	41 (97.6%)	
others, n(%)	8 (5.0%)	1 (2.4%)	
Marital status			0.536
married, n(%)	155 (84.9%)	42 (100.0%)	
unmarried, n(%)	5 (3.1%)	0 (0%)	
Occupation			0.792
employed, n(%)	16 (10.0%)	2 (4.8%)	
retired, n(%)	113 (70.7%)	30 (71.4%)	
other, n(%)	31 (19.4%)	10 (23.8%)	

Table2 Clinical and immunological characteristics of RA patients with FM *vs.* those without FM

Feature	RA (n=160)	RA-FM (n=42)	P-value
DAS28	4.4±1.4	6.0±1.2	**0.011**
TJC	4.5 (1, 8)	16.5 (10, 24)	**P <0.001**
SJC	1 (0, 3.8)	2 (0.8, 4)	0.47
Morning stiffness, min	15 (0, 60)	25 (3.8, 99)	0.062
CRP, mg/dL	14.9 (4.1, 36.1)	27.9 (3.0, 54.7)	0.152
ESR, mm/h	43.5 (17, 70.8)	50.5 (16.8, 76.5)	0.518

DAS28: disease activity score in 28 joints; TJC: tender joint counts; SJC: swollen joint counts; ESR: erythrocyte sedimentation rate; CRP: C-reactive protein;

Table3 Quality of life and functional status of RA patients with FM *vs.* those without FM

Feature	RA (n=160)	RA-FM (n=42)	P-value
HAQ	0.66 (0.2, 0.9)	1.24 (0.26, 1.5)	**P<0.001**
VAS, cm	3 (2, 5)	5 (3, 7)	**0.01**
SF-36	58.22 (47.26, 73.17)	28.63 (19.8, 39.97)	**P<0.001**

HAQ: health assessment questionnaire; VAS: visual analogue score;

Table4 Psychological and fatigue characteristics of RA patients with FM *vs.* those without FM

Feature	RA (n=160)	RA-FM (n=42)	P-value
Anxiety	4 (1, 7)	10 (7.75, 12.25)	**P<0.001**
Depressed	6 (3, 8)	12 (9.75, 15)	**P<0.001**
Fatigue, n%	81/160 (50.6%)	37/42 (88.1%)	**P<0.001**
Fatigue VAS(0-10)	3.6 (1, 4.7)	5.6 (4.6, 5.9)	**P<0.001**

Hospital Anxiety and Depression Scale, HADS.

Background/Purpose: To assess the clinical features and psychological status of the rheumatoid arthritis(RA) patients with fibromyalgia(FM) in a real-world observational setting.

Methods: Between December 2018 to April 2019, 202 patients with RA were enrolled from the inpatients in Rheumatology and Immunology Department in Peking University People's Hospital. All the patients were evaluated whether incorporating FM translation using the 1990 ACR-FM classification criteria. Disease activity, functional and psychological status were accessed by Disease Activity Score in 28 joints (DAS-28), Short Form-36 survey (SF-36), Health Assessment Questionnaire(HAQ), Hospital Anxiety and Depression Scale (HADS) and 0-10 visual analogue scale (VAS).

Results: Among the 202 RA patients, 42(20.8%) were concomitant with FM. Compared to those patients without FM, RA patients with FM (RA-FM patients) had higher DAS-28 score (6.0 *vs.* 4.4, *p*=0.011) and much more 28-tender joint counts (TJC) (16.5 *vs.* 4.5, *P*< 0.001). RA-FM patients had worse HAQ (1.24 *vs.* 0.66, *P*< 0.001) and lower SF-36 (28.6 *vs.*58.2, *P*< 0.001). Fatigue is more common in RA-FM patients (88.1% *vs.* 50.6%, P< 0.001). RA-FM patients also had higher anxiety (10 *vs.* 4, *P*< 0.001) and depression scores (12 *vs.* 6, *P*< 0.001). ESR, CRP, morning stiffness time and 28-swollen joint counts (SJC) showed no difference between these two groups.

Conclusion: From these real world data, fibromyalgia is more common than generally regard in RA patients. RA patients with FM result in higher disease activity, worse functional and psychological status. RA patients with FM also have poorer quality of life. DAS-28 scores may be overestimated in RA patients with FM. In RA patient that does not reach remission, the possibility of fibromyalgia should be considered.

Disclosure: T. Liu, None; **C. Gao**, None; **L. Chen**, None.

Abstract Number: 0026

A Modified Version of the 2016 ACR Fibromyalgia Criteria Cognitive Items Results in Stronger Correlation Between Subjective and Objective Measures of Cognitive Impairment

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

Background/Purpose: In a previous study, we showed that the subjective item assessing cognitive impairment (SSS-Cog) for fibromyalgia (FM) did not correlate with objective cognitive measures. In the current study we describe two modifications designed to enhance this correlation: extending the current SSS-cog scale from 0-3 to 1-5, and a new questionnaire that specifically targets cognitive impairments associated with FM.

Methods: Sixty-two FM patients underwent a computerized cognitive assessment battery. FM symptoms were assessed on the Fibromyalgia Impact Questionnaire (FIQ); the Widespread Pain Index (WPI); the Symptom Severity Scale (SSS), the new SSS-Cog scale ranging from 1 to5, the Beck Depression Inventory (BDI) and the new cognitive questionnaire developed by the authors.

Results: ignificant correlations were found between the new SSS-Cog scale, the global cognitive score and all indices [Global Score r= -. 532, p= .00; Indices: Memory r= -.305, p= .01; Executive function r = -.514, p= .00; Attention r = -.471, p= .00; Processing Speed r = -.468, p= .00; Motor Skills r= -.495, p= .00]. Significant correlations were found between the questionnaire items developed by the authors and the global cognitive score and all indices except the memory index [Global Score r= -. 522, p= .00; Indices: Memory r= -.163, p= .212; Executive function r= -.477, p= .00; Attention r= -.439, p= .00; Processing Speed r= -.496, p= .00; Motor Skills r= -.532, p= .00].

Conclusion: Given the simplicity of the extending scale, we suggest incorporating this modification into the American College of Rheumatology (ACR) FM diagnostic criteria.

Disclosure: V. Aloush, None; **C. Yaalon**, None; **S. Raev**, None; **N. Sobol**, None; **J. Ablin**, None; **R. Shorer**, None; **O. Elkana**, None.

Abstract Number: 0027

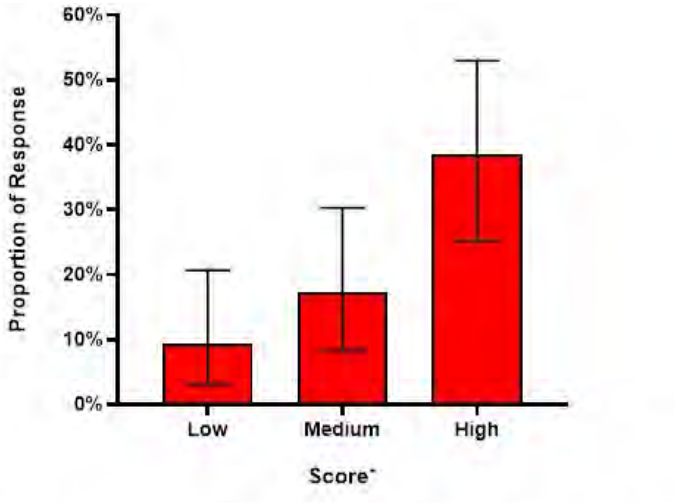
CYP2D6 Genotype and Reduced Codeine Analgesic Effect in Real-World Clinical Practice

Daniel Carranza Leon[1], Alyson Dickson[2], Andrea Gaedigk[3], C. Michael Stein[2] and Cecilia Chung[2], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville, [3]University of Missouri, Kansas City

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Codeine, a widely prescribed analgesic, is an inactive pro-drug that is metabolized to morphine, the active drug, by cytochrome P450 2D6 (CYP2D6), a highly polymorphic enzyme. However, the impact of CYP2D6 metabolizer status on pain control in patients receiving codeine in real-world clinical practice is still poorly defined. We examined the hypotheses that among patients prescribed codeine (1) CYP2D6 poor and intermediate metabolizers have poorer pain control than normal or ultrarapid metabolizers; and (2) a response score combining clinical data with CYP2D6 phenotype is associated with pain response in real-world clinical practice.

Methods: We studied 157 patients with a baseline pain score higher than 4 (0-10 scale) who received codeine and had complete clinical data using a DNA biobank linked with electronic health records (EHRs). The primary outcome was pain response, defined as pain score of 4 or lower while receiving codeine. Clinical variables were collected from



*Score Group	Standardized Score Range	Observed Proportion (95% CI)
Low	0.0-55.6	9.4 (3.1-20.7)
Medium	55.7-73.3	17.3 (8.2-30.3)
High	73.4-100.0	38.4 (25.3-53.0)

EHRs and a propensity score developed to adjust for potential confounders. Patients were classified as poor (PM), intermediate (IM), normal (NM), or ultrarapid CYP2D6 metabolizers (UM) based on *CYP2D6* genotyping. To discriminate between patients who responded and who did not respond to codeine, we built a score that included clinical variables and CYP2D6 phenotype.

Results: There were 69 PM or IMs and 88 NM or UMs. Among the PM and IMs, the response rate was 14% (10 out of 69), compared to 27% among the NM or UM metabolizers (24 out of 88), p=0.08. After propensity score adjustment, the odds ratio of achieving a pain score of 4 or lower was 0.35 (95% CI: 0.14-0.84, p=0.02) among PM or IMs. The response rate was 38.5% (95% CI=25.3-53.0%) among patients in the high, 17.3% (95% CI: 8.2-30.3%) in the intermediate, and 9.4% (95% CI: 3.1-20.7%) in the low response score groups, respectively (p=0.001) (Figure).

Conclusion: The analgesic effect of codeine was lower among PM and IMs than in NM and UMs. A score based on CYP2D6 phenotype and clinical variables improved the discrimination between analgesic response and non-response to codeine in real-world clinical practice.

Disclosure: D. Carranza Leon, None; **A. Dickson**, None; **A. Gaedigk**, None; **C. Stein**, None; **C. Chung**, None.

Abstract Number: 0028

Pain in the Time of Corona: Impact of COVID 19 Outbreak on Fibromyalgia Patients

Valerie Aloush[1], Avital Gurfinkel[2], Noam Shachar[3], Jacob Ablin[1] and Odelia Elkana[4], [1]Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, [2]Academic College TelAviv- Jaffa, Tel Aviv, Israel, [3]Acamedic College Tel Aviv- Jaffa, Tel Aviv, Israel, [4]Academic College Tel Aviv Jaffa, Tel Aviv, Israel

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Fibromyalgia & Other Clinical Pain Syndromes Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Fibromyalgia is a chronic pain disorder, characterized by abnormal pain processing in the central nervous system. Acute or chronic stress may trigger or aggravate symptoms. We aimed to evaluate the physical and mental health of fibromyalgia (FMS) patients during the COVID 19 outbreak, and to identify related protective and risk factors.

Methods: An online survey was published via social media dedicated to fibromyalgia patients (FMS associations) in May 2020, following two months of lockdown and social distancing due to the COVID 19 outbreak. The survey included questionnaires regarding demographic and socio-economic characteristics, access to medical services, anxiety, depression, life approach, coping strategies and perception of social support. Fibromyalgia severity was assessed using the widespread pain index (WPI) and symptoms severity scale (SSS), insomnia severity index (ISI) and patient global assessment

Results: A total of 262 fibromyalgia patients were recruited of which 233 (90% women, median age 46.1 years) completed the entire study questionnaire and thus were included in the analysis. During the lockdown, 43% of patients stopped contact with their treating physician and 98% were forced to discontinue complementary - alternative treatments. On the other hand, all patients undergoing psychotherapy continued online follow-up. Among the 41% of responders who had been treated with medical cannabis, 30% were forced to discontinue treatment due to

logistic difficulties and this was associated with significantly higher scores of WPI/SSS compared with patients who continued cannabis treatment (p=0.024). Higher levels of anxiety and depression were significantly correlated with higher levels of pain, sleep disorders and subjective perception of deterioration (p=0.00). Higher scores of social support and positive life approach were correlated with less anxiety and depression (p< 0.01), lower levels of pain (p< 0.05) and less sleep disturbances (p< 0.01). Avoidant coping style such as denial and behavioral disengagement was strongly associated to higher levels of pain, sleep disturbances, anxiety, depression and subjective perception of worsening (p< 0.01).

Conclusion: The current study documented high levels of anxiety, depression, sleep disturbances and pain among fibromyalgia patients during the COVID-19 outbreak, with a large proportion of patients reporting a worsening of symptoms during this period. While general stress associated with the pandemic is an obvious possible culprit for this course, additional factors such as difficulty in accessing medical and complementary treatments, as well as specific medications such as medical cannabis, may play a central role. Protective factors such as social support and a positive life approach appear to be particularly important.

Disclosure: V. Aloush, None; **A. Gurfinkel**, None; **N. Shachar**, None; **J. Ablin**, None; **O. Elkana**, None.

Abstract Number: 0029

Urine Proteomic Classifiers Predict Renal Histological Activity and Chronicity Indices and May Predict Treatment Response in Lupus Nephritis

Emma Weeding[1], Andrea Fava[1], Jill Buyon[2], H. Michael Belmont[3], Peter Izmirly[4], Robert Clancy[5], Jose Monroy-Trujillo[6], Derek Fine[6], William Apruzzese[7], Harald Mischak[8] and Michelle Petri[9], [1]Johns Hopkins University, Baltimore, MD, [2]Department of Medicine, NYU School of Medicine, New York, NY, [3]NYU School of Medicine, New York, NY, [4]Department of Medicine, New York University School of Medicine, New York, NY, [5]New York University School of Medicine, New York, NY, [6]Johns Hopkins University, Baltimore, [7]., Boston, [8]Multiple Institutions, Glasgow, United Kingdom, [9]Johns Hopkins University School of Medicine, Baltimore

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Current management of lupus nephritis (LN) is guided by histopathological features on kidney biopsy and measurement of proteinuria. Urine proteomics is a non-invasive source of novel biomarkers which may better reflect the complex dynamic immunobiology of LN in real time. Two composite measures include CKD273, which can predict the risk of progression of chronic kidney disease in the general population, and LN120, which was designed to diagnose LN. Both are multidimensional urine proteomic classifiers consisting of 273 or 120 peptides, respectively, with major components including collagen fragments, abundant blood-derived proteins, and proteins involved in inflammation. We investigated the ability of these classifiers to predict traditional biopsy features and disease response in LN.

Methods: A total of 31 adults with biopsy-proven LN were included in this study. All participants met the SLICC and 2019 EULAR/ACR Classification Criteria for SLE based on a spot urine protein-to-creatinine ratio of >0.5 and class III, IV, and/or V LN on renal biopsy. Urine samples were collected at week 0 (at the time of renal biopsy) and week 12 and then subjected to peptidome analysis using a capillary electrophoresis-mass spectrometry (CE-MS) platform.

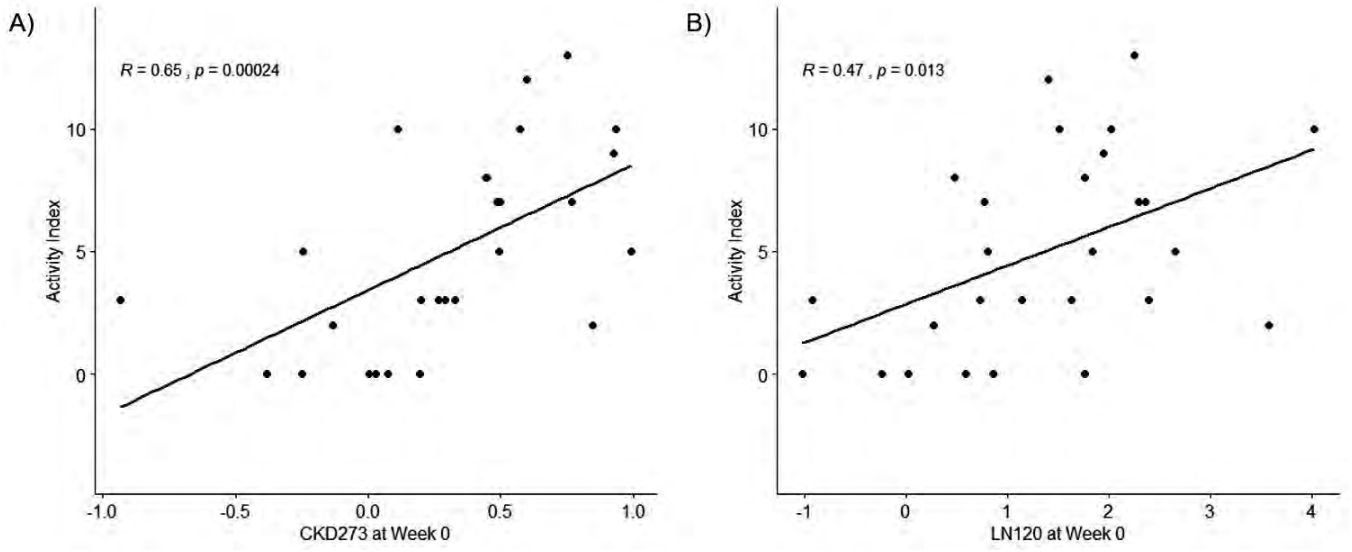


Figure 1. A) Correlation between CKD273 and activity index on renal biopsy at week 0. B) Analogous correlation between LN120 and activity index at week 0. R = Spearman's rank correlation coefficient.

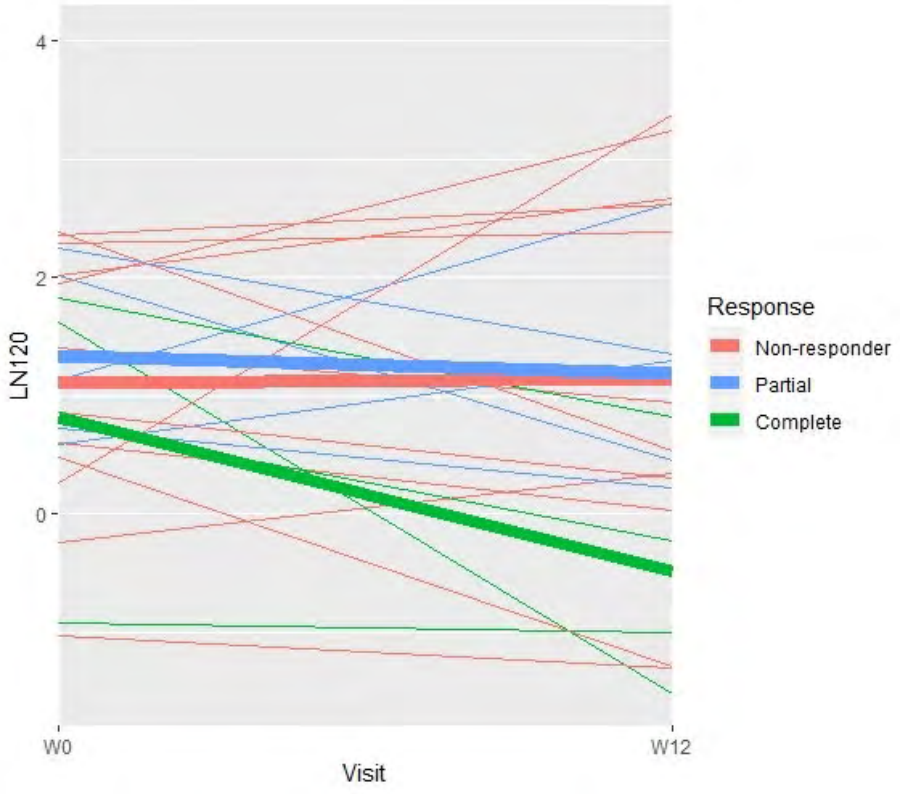


Figure 2. Change in LN120 from week 0 (W0) to week 12 (W12) by response group. Thin lines represent individual participants, and thicker lines represent the average LN120 per response group. Only individuals with urine peptidome data from both time points were included in this Figure (4 complete responders, 5 partial responders, and 12 non-responders).

This peptidome data was used to calculate CKD273 and LN120 classifiers at each time point. LN response status was determined at week 52 based on proteinuria, creatinine, and prednisone dosage (no more than 10 mg daily). Spearman's rank correlation and t-tests were used to compare proteomic classifiers with renal biopsy characteristics and response.

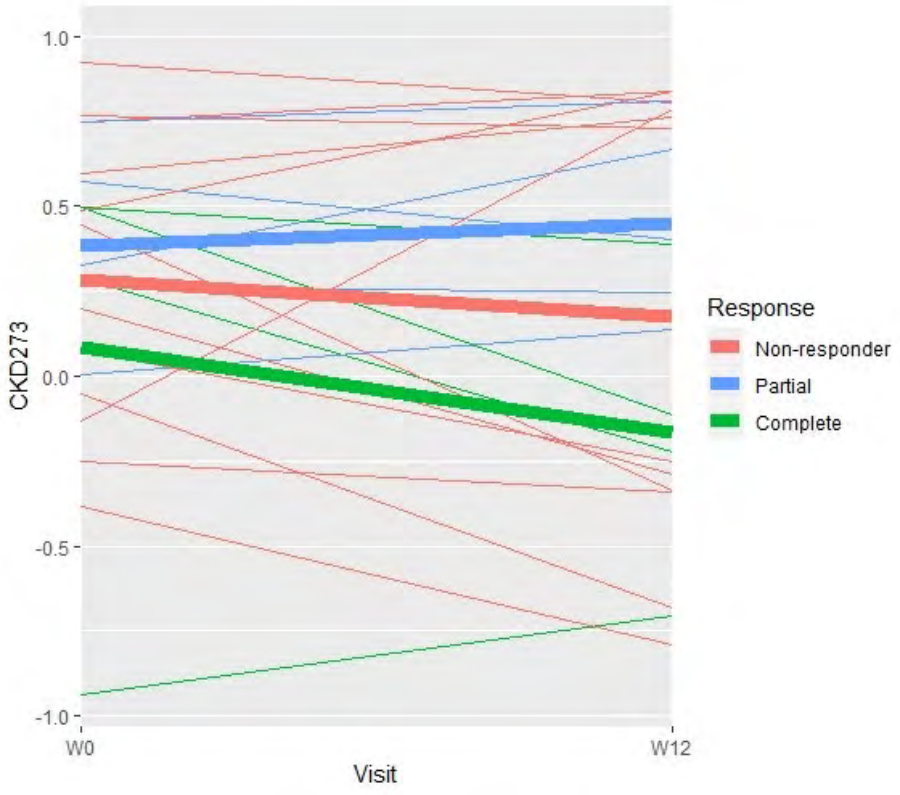


Figure 3. Change in CKD273 from week 0 (W0) to week 12 (W12) by response group. Thin lines represent individual participants, and thicker lines represent the average CKD273 per response group. Only individuals with urine peptidome data from both time points were included in this Figure (4 complete responders, 5 partial responders, and 12 non-responders).

Results: At week 0, both CKD273 and LN120, but not proteinuria, exhibited a moderate to strong correlation with histological activity index on renal biopsy (**Figure 1**; $\rho = 0.65$ with $p = 0.00024$ for CKD273; $\rho = 0.47$ with $p = 0.013$ for LN120). CKD273 also correlated with chronicity index ($\rho = 0.54$, $p = 0.0037$). Neither classifier significantly correlated with lupus nephritis ISN class. With respect to response, CKD273 and LN120 were not significantly different between groups at week 0. However, a reduction in LN120 was observed in 100% of complete responders, 60% of partial responders, and 50% of non-responders at week 12 (**Figure 2**). The magnitude of this change in LN120 in complete responders versus non-responders did not reach statistical significance ($p = 0.13$), though this is potentially because of the small number of responders with CE-MS data available at both time points ($n = 4$). CKD273 did not significantly change with time in any response group (**Figure 3**).

Conclusion: This work provides proof of concept that urine proteomic classifiers can noninvasively predict histological activity and chronicity in LN. Complete responders, but not partial responders or non-responders, exhibited an impressive numerical decrease in LN120 by week 12, suggesting that proteomic scores may track with and predict a durable treatment response. Larger studies are needed to validate these findings.

Disclosure: E. Weeding, None; **A. Fava**, None; **J. Buyon**, None; **H. Belmont**, Exagen, 5; **P. Izmirly**, GSK, 5; **R. Clancy**, None; **J. Monroy-Trujillo**, None; **D. Fine**, GSK, 5; **W. Apruzzese**, None; **H. Mischak**, Mosaiques Diagnostics, 9; **M. Petri**, AbbVie, 5, Amgen, 5, AstraZeneca, 2, 5, BMS, 5, Decision Resources, 5, GSK, 2, 5, INOVA, 5, IQVIA, 5, Janssen, 5, Eli Lilly, 2, 5, Merck EMD Serono, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5, Exagen, 2.

Abstract Number: 0030

Distinct DNA Methylation Patterns of Rheumatoid Arthritis Peripheral Blood and Synovial Tissue T Cells

Rizi Ai[1], Gary Firestein[2], David Boyle[3] and Wei Wang[4], [1]University of California San Diego, San Diego, CA, [2]University of California, San Diego, La Jolla, CA, [3]UCSD, La Jolla, CA, [4]UCSD, La Jolla

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: To understand the epigenetic patterns of T cells accumulated in rheumatoid arthritis (RA) synovium, we characterized DNA methylation of CD3+ T cells in peripheral blood and synovial tissue in RA and osteoarthritis (OA) patients.

Methods: Genomic DNA of CD3+ T cells was isolated from RA (synovial tissue: n = 8, with 3 matched peripheral blood) and matched OA (5 matched synovial tissue and peripheral blood) patients after separating peripheral blood cells using antibodies and magnetic beads. Methylation was measured using the Illumina Infinium Methylation EPIC Kit chip. Differentially methylated loci (DMLs) were identified using Welch's *t*-test and mapped to gene promoter regions to define differentially methylated genes (DMGs). Principal component analysis (PCA) and hierarchical clustering were used to represent the relationship among each group. To compare enriched biological pathways, pathway analysis was applied using Reactome and MSigDB.

Results: PCA results showed that methylation differences in T cells primarily distinguished based on location (blood vs. synovium PCA1 95%) compared with by disease (RA vs OA), mainly with more diversity in synovial T cells (peripheral blood CD3+ cells were clustered within PC3 0.35%) (Figure 1). By comparing DNA methylation differences

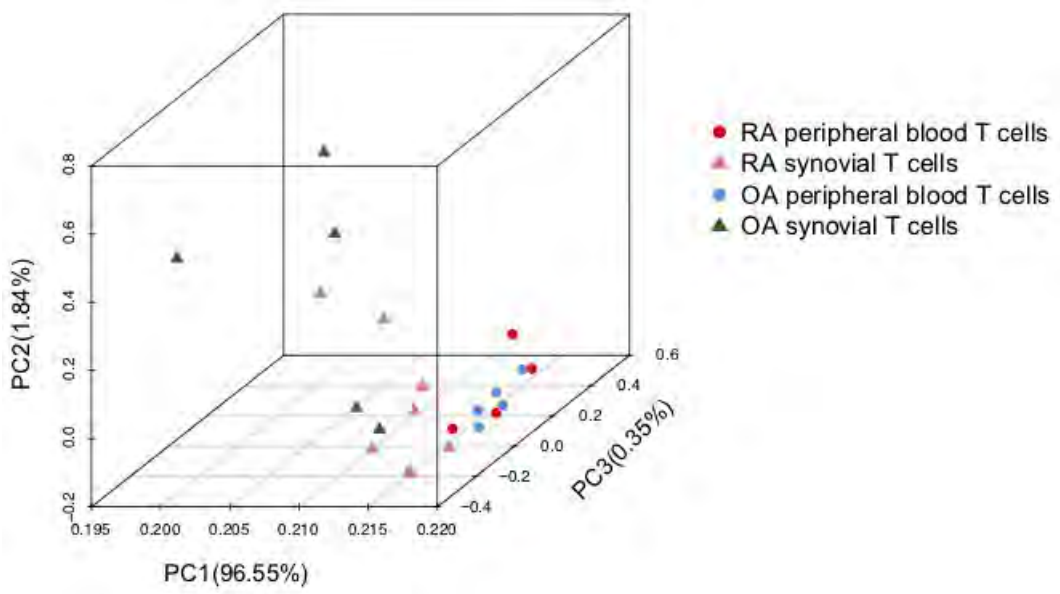


Figure 1. PCA plot shows the segregation of samples are more distinguishable between T cell location (peripheral blood and synovium) than disease. The greatest differences were observed between RA synovial and peripheral blood T cells.

and DMGs of CD3+ T cells between peripheral blood and synovial tissue, we found 4615 and 832, respectively, for RA but only 164 DMLs and 36 DMGs for OA (q value < 0.05). Therefore, significant blood/synovium methylation differences were mainly identified in RA. By comparing RA and OA to each other, we found 1120 DMLs (p value < 0.05) in 363 DMGs in blood CD3+ T cells and 4104 DMLs (p value < 0.01) in 870 DMGs in synovial CD3+ T cells, respectively. Differentially modified pathways were significantly enriched between RA blood and synovial T cells, especially in genes related to complement, integrin cell surface interactions and the P53 pathway. Only a small number of significantly different pathways were observed between RA and OA peripheral blood. Three significantly enriched pathways between RA and OA in synovial T cells show that the main differences are related to metabolic pathways. Although 870 DMGs were identified between RA and OA in synovial T cells using p value < 0.01, most do not fall into pathways, possibly due to the small sample size. No significant pathways distinguished OA peripheral blood CD3+ T cells compared to OA synovium as only 36 DMGs were identified.

Conclusion: The patterns of DNA methylation in RA show disease and location specific differences in immune pathways including cell contact interactions (compliment and integrins) and survival. The RA joint-specific signatures could be due to selective accumulation of T cell populations, epigenetic modification *in situ*, or expansion of differentially marked adaptive immune cells. Identifying epigenetic patterns could provide clues to site and event specific targeTable T cells in the RA.

Disclosure: R. Ai, None; **G. Firestein**, Eli Lilly, 2; **D. Boyle**, None; **W. Wang**, None.

Abstract Number: 0031

Metabolomics Profiling Predicts Outcome of Tocilizumab in Rheumatoid Arthritis

Jessica Murillo-Saich[1], Cesar Diaz-Torne[2], M. Angeles Ortiz[2], Roxana Coras[1], Arthur Kavanaugh[3], Hector Corominas[2], Silvia Vidal[2] and Monica Guma[4], [1]University of California San Diego, La Jolla, CA, [2]Institut Rec. Hospital de la Santa Creu I Sant Pau., Barcelona, Spain, [3]Division of Rheumatology, Allergy, & Immunology, University of California San Diego Medical School, San Diego, CA, [4]Division of Rheumatology, University of California San Diego, Department of Medicine, Autonomous University of Barcelona, La Jolla, CA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Metabolomics may provide information about the activity and severity of specific diseases and potentially help discriminate between diseases. Choosing the right biological therapy earlier in the course of rheumatoid arthritis (RA) could help to reach the goal of remission. We hypothesized that characterization of patients' metabolic profiles, utilizing high resolution ^{1}H-nuclear magnetic resonance (NMR), may predict response to tocilizumab therapy prior to treatment in patients with RA.

Methods: 41 patients meeting the 2010 ACR/EULAR classification criteria had initiated treatment with 8 mg/kg of tocilizumab every 4 weeks following usual clinical practice were included in the study. Clinical outcomes were determined at baseline and at 6 months after treatment. Using EULAR response criteria, patients were categorized as responders (good response) or non-responders (moderate response and no response) . Blood was collected at baseline and at 6 months after tocilizumab therapy. A 600 MHz Bruker Avance III spectrometer ^{1}H-NMR was used to acquire NMR spectra of serum samples. Software Chenomx NMR suite 8.5 professional was used for metabolite

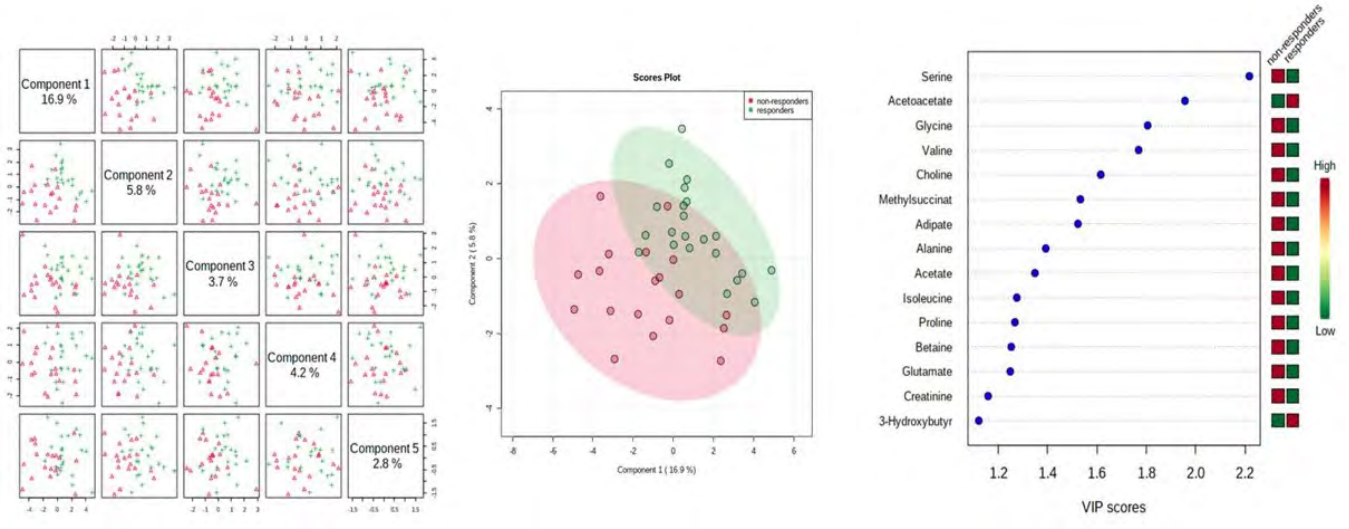


Figure 1. PLS-DA (explaining 16.9% of the total variance) confirmed that metabolites profiles differ among groups. A total of 15 metabolites had VIP scores >1.

identification and quantification. Significantly metabolites were identified and the relationship between metabolites and clinical outcome was studied. SPSS and MetaboAnalyis 4.0 KEGG 2019 were used for statistical and pathway analysis.

Results: 41 patients (average age 53 , standard deviation (SD) 11) were analyzed. The patients had an initial DAS-28CRP of 5.7±1.1. Multivariate statistical analysis of the ^{1}H-NMR baseline spectra successfully discriminated between RA patients classified as tocilizumab responders (n = 22) and non-responders (n = 19), at baseline and 6 months after tocilizumab treatment. A two sample t-test produced p-values of less than 0.05 for seven metabolites which were increased significantly at baseline in responders: 3-hydroxybutyrate, Isobutyrate, Lysine, O-phosphocholine, Phenylalanine, Tryptophan, and Tyrosine. Several metabolites varied their levels following treatement with tocilizumab in both responders and non responders. Of interest, acetoacetate and acetone significantly decreased in non-responders at 6 months of treatment. A PLS-DA (explaining 16.9% of the total variance) confirmed that metabolites profiles differ among groups, although a certain overlap existed (Figure 1). A total of 15 metabolites had VIP scores >1. Individual metabolites yielded area under the curve (AUC) values lower than 70%, indicating relatively poor specificity and sensitivity. A multivariate diagnostic model, showed that concentrations of hydroxybutyrate, leucine, tryptophan, and alanine, improved the sensitivity and specificity of the diagnosis with an AUC of 92.7%. Using this biomarker model, 85% of the patients were correctly classified.

Conclusion: The clear relationship between blood profiles and patient response to tocilizumab therapy suggests that the application of ^{1}H-NMR profiling is a promising clinical tool for RA therapy optimization. More metabolic profiles studies are needed to determine if metabolic profiling can predict response to other biological therapies in RA patients**.**

Disclosure: J. Murillo-Saich, None; **C. Diaz-Torne**, None; **M. Ortiz**, None; **R. Coras**, None; **A. Kavanaugh**, AbbVie, 2, 9, Amgen, 2, 9, AstraZeneca, 2, 9, Bristol-Myers Squibb, 2, 9, Celgene, 2, 9, Janssen, 2, 9, Pfizer, 2, 9, Roche, 2, 9, UCB, 2, 9; **H. Corominas**, None; **S. Vidal**, None; **M. Guma**, None.

Abstract Number: 0032

A Prospective, Multicenter, Clinical Performance Evaluation Study for an in-vitro Diagnostics Medical Device (PREDYSTIC® Infliximab RA) for Prediction of Infliximab Responsiveness in the Treatment of Rheumatoid Arthritis

Miklos Sebeszta[1], Katalin Tauberne Jakab[1], Tamas Ponyi[1], Gyula Poor[2], Zsolt Hollo[1], Laszlo Szilagyi[1], **Emese Kiss**[2] and Gabor Zahuczky[3], [1]Egis Pharmaceuticals, Budapest, Hungary, [2]ORFI, Budapest, Hungary, [3]UD Genomed, Debrecen, Hungary

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Approximately 30-40% of RA patients fail to respond to first biological therapy. Predicting the patient's responsiveness to the first biological therapy is still an unmet need in the clinical setting. In the case of non-responder (NR) patients it leads to unnecessary exposure, delay of adequate therapy, disease progression and therapy cost increase. By identifying those bio-naive RA patients who are likely responders (Rs) or NRs to infliximab (both intravenous and subcutaneous) treatment, a predictive in vitro testing would have a significant effect on the administration of TNF-α inhibitor therapy, on the real life implementation of effective personalized therapy.

The purpose of this in vitro diagnostic medical device performance evaluation study was to demonstrate that – gene expression profiles of a selected gene set as genomic biomarkers (i.e. the IVD medical device) and a proprietary algorithm for data analysis – predict month 6 therapeutic response to infliximab, discriminate between Rs and NRs. Rs were defined if they reached DAS target value DAS28≤3.2 at 6 month (M6).

Methods: Two hundred twenty bio-naive RA patients were enrolled with moderate-high activity RA (DAS28-CRP >3.2), who have responded inadequately to DMARDs (including methotrexate), after they have been assigned to infliximab treatment. All patients received commercially available infliximab, procured according to SmPC, local guidelines and regulations in this non-interventional clinical study. The clinical response was evaluated according to the change from baseline in disease activity at M6. Clinical characteristics (RA duration, smoke, steroid treatment) and serological parameters (RF, ACPA, aCVM) were collected. A 3rd visit was scheduled around week 22 (M6) and change of DAS28-CRP value from the baseline has been evaluated. Gene expression profiling was performed from blood samples taken at month 0 (M0) – just before the first infliximab infusion. Global gene expression profiling was performed to identify differentially expressing genes using RNA sequencing.

Results: A total of 250 genes were identified by a combination of differential gene expression analyses, feature elimination techniques and various machine learning modelling methods of which 44 genes showed significant differences between NR and good Rs groups The expression of the reduced gene set was confirmed and further analyzed

Modell building_ID	Accuracy	Sensitivity	Specificity	Modell Verification	Accuracy	Sensitivity	Specificity
00232	100.00	100.00	100.00	00232	88	88.89	87.50
00249	98.82	96.55	100.00	00249	84	77.78	87.50
00270	98.82	96.55	100.00	00270	88	77.78	93.75

using reverse-transcription and quantitative real-time PCR. Interim analysis identified associations between gene expression and clinical response/ non-response to infliximab therapy.

Table: Three models containing gene expression + clinical data sets illustrates some statistical characteristics

Conclusion: This set of genes and selected clinical parameters are predictive markers for infliximab specific response in RA patients. The complete results of the ongoing clinical validation in an independent patient cohort (n=56) is expected in September 2020. This novel in vitro diagnostic test method, for the prediction of infliximab treatment responsiveness before treatment initiation of RA patients, is a tool to personalize infliximab therapy.

Disclosure: M. Sebeszta, None; **K. Tauberne Jakab**, None; **T. Ponyi**, None; **G. Poor**, None; **Z. Hollo**, None; **L. Szilagyi**, None; **E. Kiss**, None; **G. Zahuczky**, None.

Abstract Number: 0033

Pre-pregnancy Long Non-coding RNA Expression Signatures Among Women with Rheumatoid Arthritis Who Improve or Worsen During Pregnancy

Matthew Wright[1], Mette Kiel Smed[2], J Lee Nelson[3], Jørn Olsen[4], Merete Hetland[5], Vibeke Zoffmann[2] and Damini Jawaheer[6], [1]UCSF Children's Hospital Oakland Research Institute, Oakland, CA, [2]The Juliane Marie Center, Copenhagen, Denmark, [3]Fred Hutchinson Cancer Res Ctr and U of WA, Seattle, WA, [4]Aarhus University Hospital, Aarhus, Denmark, [5]The DANBIO Registry, Rigshospitalet, Glostrup, Denmark, [6]UCSF Benioff Children's Hospital Oakland Research Institute, Oakland, CA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Pregnancy is known to have disease-modifying effects on rheumatoid arthritis (RA). A role for long non-coding (lnc) RNAs in the improvement or worsening of RA during pregnancy has not previously been investigated. We have examined lncRNAs signatures associated with RA before and during pregnancy, when the disease improves or worsens, and their co-expression with protein coding genes.

Methods: Data and samples collected at pre-pregnancy (T0) and 3rd trimester (T3) from women with RA (n=21) and healthy women (n=14) enrolled in our prospective pregnancy cohort were included in this analysis. Disease activity was assessed using the Clinical Disease Activity Index (CDAI). Total RNA from whole blood were sequenced (RNA-seq). Following mapping of RNA-seq reads (HISAT2) and transcript assembly (StringTie), lnc and coding RNA transcripts were quantified (featureCounts) and normalized. At each time-point, RA-associated expression signatures were identified using differential expression analysis (edgeR), comparing each RA group (subsequently improved or worsened during pregnancy) to healthy women (significance threshold: $q < 0.05$ and fold-change≥ 2). lnc and coding RNAs were examined for co-expression. Functional analysis was performed using Cytoscape.

Results: Of the 21 women with RA,15 improved by T3 ($RA_{improved}$), while 6 worsened ($RA_{worsened}$). At T0, 311 lncRNAs (99 known, 212 novel) were differentially expressed (DE) between $RA_{improved}$ and healthy women. Of these, 48 were co-expressed ($r > 0.95$) with 264 protein-coding genes, many of which were also DE ($RA_{improved}$ vs healthy at T0). Several had been previously associated with RA (e.g. *FCGR2A, IL1R1, IL1R2, IL6R, S100A6* and *TLR4*). The co-expressed

genes were enriched in gene ontology (GO) terms leukocyte activation ($q=1.2x10^{-15}$), immune response ($q= 1.4x10^{-14}$) and neutrophil activation ($q= 2.4x10^{-14}$). At T3, when RA improved, 287 of the 311 lncRNAs (92%) in the T0 RA signature were no longer DE between $RA_{improved}$ and healthy women. Among the $RA_{worsened}$ women, a very different RA lncRNA signature was identified at T0, although disease activity was similar in both RA groups at baseline (p=0.9): 81 lncRNAs (26 known, 55 novel) were DE ($RA_{worsened}$ vs healthy), of which only 23 overlapped with the RA lncRNA signature of $RA_{improved}$ women at T0. Many of these lncRNAs (n=57) were co-expressed with protein-coding genes, most of which were not DE. At T3, when RA worsened, only 41 of the 81 (51%) lncRNAs DE at T0 lost their differential expression, and an additional 34 became newly DE.

Conclusion: In our dataset, there was little overlap in pre-pregnancy RA-associated lncRNA expression signatures between women with RA who improved during pregnancy and those who worsened. Further, many of the lnc and coding RNAs DE at T0 in the improved group were co-expressed, and were no longer DE at T3 when RA improved. We speculate that those lncRNAs could have a role in regulating expression of the coding RNAs during pregnancy, contributing to RA improvement.

Disclosure: M. Wright, None; **M. Kiel Smed**, None; **J. Nelson**, Chimerocyte, Inc., 1, 4, 6; **J. Olsen**, None; **M. Hetland**, Bristol-Myers Squibb Company, 2, AbbVie, 2, Roche, 2, Novartis, 2, Merck, 2, 5, Biogen, 2, 5, Pfizer, 2, 5, Eli Lilly, 5, Orion Pharma, 5, Celltrion, 5, Samsung Bioepis, 5; **V. Zoffmann**, None; **D. Jawaheer**, None.

Abstract Number: 0034

Gene Expression Signatures in C-Reactive Protein High and Low Rheumatoid Arthritis

Adam Cornish[1], **Kristin Wipfler**[1] and Kaleb Michaud[2], [1]FORWARD, The National Databank for Rheumatic Diseases, Omaha, NE, [2]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Transcriptome profiling has expanded our ability to identify biomarkers and therapeutic targets and better understand disease progression in a wide variety of conditions. Serum C-reactive protein (CRP) is a marker of inflammation and is widely used to assess disease activity in RA. The aim of this study was to identify differentially expressed genes in CRP high and low patients with RA.

Methods: Whole blood samples were collected from participants in the Arthritis Internet Registry and FORWARD, The National Databank for Rheumatic Diseases. The biosamples are associated with demographic and clinical data from comprehensive biannual questionnaires. RNA was extracted and sequenced for 60 participants with RA (30 with high inflammatory levels and 30 with low inflammatory levels, assessed using blood concentrations of CRP). Version 1.2.3 of the bcbio pipeline was used to perform alignments (hisat2), read data qc (qualimap, fastqc), and transcript quantification (salmon). For differential expression analysis, DESeq2 was used in conjunction with the bcbioRNAseq R package. Student's t tests and X^2 tests were performed to assess significant demographic and clinical differences between the high and low disease activity cohorts.

	CRP-low (CRP<0.1 mg/dL) n=25	CRP-high (CRP>0.8 mg/dL) n=27	p
Demographics			
Age, mean (SD), years	59.6 (11.4)	55.5 (14.1)	0.26
Female, %	88.0	88.9	0.92
White, %	96.0	85.2	0.19
Education, mean (SD), years	14.4 (3.1)	14.6 (2.7)	0.81
Married, %	64.0	59.3	0.73
History of smoking, %	56.0	44.4	0.41
BMI, mean (SD), kg/m2	26.1 (5.2)	30.5 (6.9)	**0.01**
Disease Activity Measures, mean(SD)			
Pain, 0-10	2.9 (2.8)	4.1 (2.4)	0.09
Global Severity, 0-10	3.1 (2.7)	4.0 (2.1)	0.17
Fatigue, 0-10	3.8 (3.5)	4.7 (2.8)	0.3
HAQ-II, 0-3	0.7 (0.5)	1.1 (0.7)	**0.02**
PAS-II, 0-10	2.7 (2.2)	3.9 (2.0)	**0.04**
Biomarkers, %			
RF positive	96.0	89.0	0.34
anti-CCP positive	100.0	100.0	1
Medications, %			
Conventional DMARD	72.0	92.6	0.05
Biologic DMARD	68.0	48.1	0.15
TNF inhibitor	64.0	44.4	0.16
Corticosteroid	44.0	44.4	0.97
NSAID	52.0	48.1	0.78

Table 1. Demographic and clinical characteristics of high and low disease activity groups. Bold p values indicate statistical significance.

Results: After restricting the dataset to samples from participants with an associated comprehensive questionnaire fewer than 90 days from the date of sample collection, the high disease activity (CRP >0.8 mg/dL; CRP-high) cohort included 27 participants and the low disease activity (CRP< 0.1 mg/dL; CRP-low) cohort included 25 participants. There were no statistically significant differences in demographics or medications between the two groups, with the exception of BMI, which was higher in the CRP-high group. As expected, the CRP-high group had significantly higher scores on measures of disease activity. All participants in both groups were RF and/or anti-CCP positive (Table 1). Differential Gene Expression analysis with an alpha of 0.01 revealed 32 genes dysregulated between the CRP-high and CRP-low groups. Clustering with Ward's method using these genes as input generated two distinct clusters: one included 30 samples (5 CRP-high, 25 CRP-low) and the other exclusively contained CRP-high samples (22).

Conclusion: NoTable gene signatures resulted in two distinct clusters each comprised almost exclusively of the high and low disease activity groups. Significantly differentially expressed genes identified in this study include several that have previously been implicated in RA and other autoimmune diseases (KLRC1, RAP1GAP, IFI27, LY6E, ISG15, PIM2) as well as several genes not clearly associated with RA, including a group of genes related to cell signaling by receptor tyrosine kinases (EFNA1, SHC2, RHBDF1). RHBDF1, which encodes a catalytically inactive rhomboid protein, may be of particular interest due to its regulatory relationship with ADAM17, a key regulator of TNF that has been implicated in the development and progression of several autoimmune diseases, including RA.

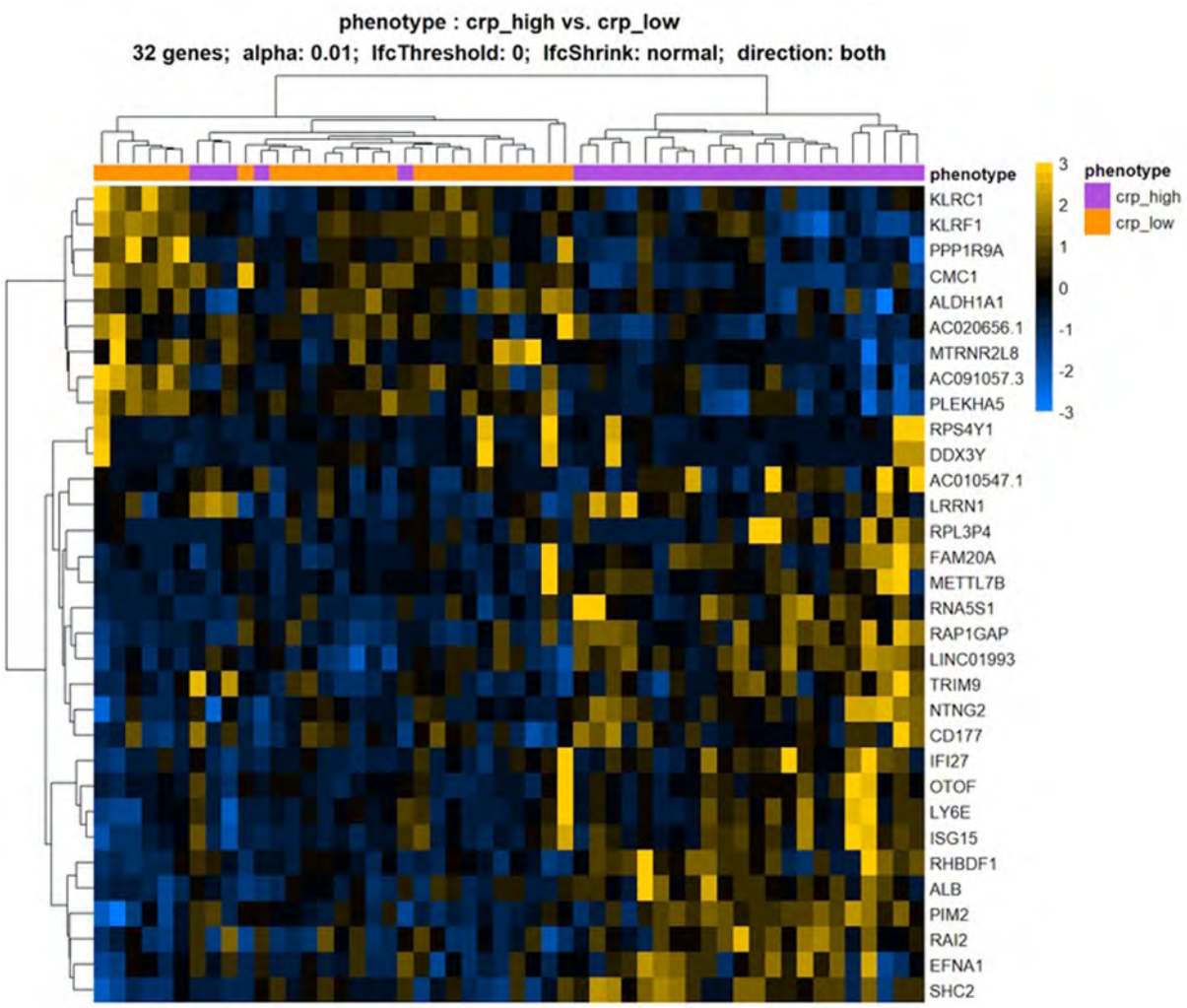


Figure 1. Heat map of dysregulated genes labeled by disease activity (CRP high vs low) and grouped using hierarchical clustering.

Disclosure: A. Cornish, None; **K. Wipfler**, None; **K. Michaud**, Rheumatology Research Foundation, 2.

Abstract Number: 0035

Distinct Biological Pathways in Both Blood and Kidney Further Define Molecular Profiles Across Diverse Nephritides

Loqmane Seridi[1], Matteo Cesaroni[1], Qingxuan Song[2], Ashley Orillion[1], Frédéric Baribaud[1], Tatiana Ort[1], Sheng Gao[2], Tomas Parker[3], James Chevalier[3], Dan Levine[3], **Alan Perlman**[3] and Jarrat Jordan[1], [1]Janssen Research & Development, LLC, Spring House, PA, [2]Janssen Research & Development, LLC, Spring House, PA, USA, Spring House, PA, [3]The Rogosin Institute, New York Presbyterian Hospital-Weill Medical College of Cornell University New York, NY, USA., New York, NY

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Approximately 40% of SLE patients will develop Lupus Nephritis (LN), of which 10-30 % will progress to end-stage renal disease. To further understand LN pathogenesis, we conducted transcriptomic profiling of blood and kidney biopsy samples from LN patients, healthy control (HC), and from four other nephritides.

Methods: Blood and kidney biopsies from healthy subjects (n=28 and 20 respectively), LN (26,21), Diabetic Nephropathy (DN; 10,6), Hypertensive kidney disease (HT;8,3), Minimal change disease (MC; 7,4), and Membranous nephropathy (MB; 4,4) were collected under informed consent. Gene expression profiling was conducted using RNA-Sequencing (RNASeq). Genes differently expressed between any two conditions (FDR < 0.05) were identified and clustered into co-expressed signatures.

Results: We detected 5 and 6 gene signatures in blood and kidney, respectively. The signatures were enriched in distinct biological pathways, including "Interferon Signaling," "Natural killer cell-mediated cytotoxicity (NK_CMC)," and "Aquaporin-mediated transport (AMT)." When compared to HC, Gene Set Variation Analysis (GSVA) showed an increase of "Interferon Signaling" expression in LN (p = 2.8E-6) and DN (p= 0.0038) blood and in LN (p=8.7E-8), DN (p=3.8E-4), HT (p=0.018) and MB (p=0.018) kidney. In LN and HT blood, we observed a decreased enrichment of the NK_CMC signature (p =1E-13, p=6.3E-3). A bimodal enrichment was observed in DN and MC blood, and ~40% of those patients showed an expression level comparable to that of the LN population. Also, the NK_CMC signature was upregulated in LN (P=0.011) and DN (P=0.016) kidney. Finally, the AMT signature was downregulated in kidney in all indications compared to healthy (p< 0.05).

Conclusion: Co-expression clustering of dysregulated genes unveiled signatures enriched in distinct biological pathways in both blood and kidney of nephritides. IFN signature upregulation in blood was specific to LN and DN, with a more prominent signal observed in LN. The IFN signature was upregulated in the kidney in all indications except MC. An NK-mediated cytotoxicity gene signature was down-regulation in the blood of LN and HT and upregulated in the kidney of LN and DN, suggesting a possible role of NK mediated cytotoxicity in LN and DN pathogenesis. A signature enriched in aquaporin-mediated transport genes was downregulated in the kidney and might reflect kidney damage. Although this analysis was adequately powered for LN, trends observed in other indications require further validation with larger cohorts.

Disclosure: L. Seridi, Janssen Research & Development, LLC, 1, 3; **M. Cesaroni**, Janssen Research & Development, LLC, 1, 3; **Q. Song**, Janssen Research & Development, LLC, Spring House, PA, USA, 3; **A. Orillion**, Janssen Research & Development, LLC, 1, 3; **F. Baribaud**, Janssen Research & Development, LLC, 1, 3; **T. Ort**, Janssen Research & Development, LLC, 1, 3; **S. Gao**, Johnson & Johnson, 3; **T. Parker**, None; **J. Chevalier**, None; **D. Levine**, None; **A. Perlman**, None; **J. Jordan**, Janssen Research & Development, LLC, 1, 3.

Abstract Number: 0036

Molecular Phenotyping of Late-Stage Knee Osteoarthritis Synovium Through Total RNA-Sequencing

Anusha Ratneswaran[1], Chiara Pastrello[1], Pratibha Potla[2], Osvaldo Espin-Garcia[2], Starlee Lively[2], Anthony Perruccio[3], Raj Rampersaud[2], Rajiv Gandhi[2] and Mohit Kapoor[4], [1]University Health Network, Toronto, ON, Canada, [2]Krembil RI, Toronto, Canada, [3]Krembil Research Institute, UHN; University of Toronto, Toronto, ON, Canada, [4]Krembil RI, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Knee Osteoarthritis (OA) is a painful, disabling condition and molecular mechanisms underlying this disease are poorly understood. In recent years, OA is increasingly viewed as a disease with differing phenotypes which may contribute to its pathogenesis. Characterizing these phenotypes could play an integral role in the development of appropriate therapies. The synovium is a key driver of pathological changes in OA and to date there are few studies examining total RNA sequencing in synovial tissue. This study uses total RNA sequencing to profile the synovium of patients with advanced radiographic knee OA, and elucidates whether these patients have differing endogenous molecular phenotypes.

Methods: Total RNA sequencing was performed on synovium samples from 50 end-stage knee OA patients (KL 3/4). After filtering, 19,857 genes were expressed in synovium. Genes with a mean, and variance greater than 30 across samples were kept for further downstream analysis (4267). To objectively identify number of distinct clusters within the patient cohort, mean silhouette width was plotted, and peaked at 3; indicating this was the optimal cluster number. Genes differentially expressed between clusters were used for pathway analysis. Identified pathways with a q-value less than 0.01 and a gene-ratio higher than 0.05 were retained and annotated to pathways. Interactions among genes were collected using Integrated Integrations Database (University of Toronto), and networks were constructed. Pearson correlation was calculated in each cluster for long-noncoding (lnc) and circular (circ) RNA from differentially expressed genes between clusters. Only correlations with absolute rho greater than 0.95 (lncRNA) or 0.85 (circRNA) were retained and used to construct Protein-Protein Interaction networks.

Results: Unbiased gene clustering indicated 3 clusters of patients distinguished by endogenous molecular differences. These groups do not demonstrate significant differences in measured clinical or anthropometric characteristics including sex, BMI, blood pressure, cholesterol, synovial inflammation, and patient reported pain. The clusters share signaling pathways such as EGFR1, innate and adaptive immune system. Differentially regulated pathways include: signaling by receptor tyrosine kinase, cytokine signaling, and TCR (cluster 2 vs 1) as well as neutrophil degranulation, skeletal muscle, EMT regulation, apoptosis, membrane trafficking, vesicle mediated transport, toll-like receptor signaling and hemostasis (cluster 3 vs 2). We have identified several lnc and circRNA that interact with genes in each distinct pathway and have defined their associated clusters and their positive or negative gene interactions.

Conclusion: Overall, we have observed that endogenous molecular signatures derived from synovium of end-stage OA patients cluster into 3 groups. Pronounced differences in gene expression between clusters indicate both shared and distinct actively transcribed pathways. Identified lnc and circRNA contribute to unique molecular mechanisms differentially expressed between clusters. These differences in endogenous molecular mechanisms may play a role in heterogenous disease development.

Disclosure: A. Ratneswaran, None; **C. Pastrello**, None; **P. Potla**, None; **O. Espin-Garcia**, None; **S. Lively**, None; **A. Perruccio**, None; **R. Rampersaud**, None; **R. Gandhi**, None; **M. Kapoor**, None.

Abstract Number: 0037

Lipoprotein-associated Phospholipase A2: A New Biomarker for Lymphoma Development in Sjögren's Syndrome

Adrianos Nezos[1], Eleni Kotsifaki[1], Charalampos Skarlis[2], Konstantinos Markakis[1], Haralampos Moutsopoulos[3], Michael Koutsilieris[1], Clio Mavragani[1] and Anna Psarrou[1], [1]National & Kapodistrian University of Athens, Athens, Greece, [2]National &Kapodistrian University of Athens, Athens, Greece, [3]National & Kapodistrian University of Athens/ Academy of Athens, Athens, Greece

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: B-cell non-Hodgkin's lymphoma (B-NHL) is one of the major complications of primary Sjögren's syndrome (SS). Chronic inflammation and macrophages in SS minor salivary glands have been previously suggested as significant predictors for lymphoma development among SS patients. Extracellular lipoprotein-associated phospholipase A2 (Lp-PLA2) -a product of tissue macrophages- is found in the circulation associated with lipoproteins and has been previously involved in cardiovascular, autoimmune and malignant diseases, including lymphoma.

The purpose of the current study was to investigate the role of Lp-PLA2 as a potential biomarker for the development of B-NHL in the setting of primary SS.

Methods: Lp-PLA2 activity in serum samples collected from 50 primary SS patients with no lymphoma (SS-nL), 9 primary SS patients with lymphoma (SS-L) and 42 healthy controls (HC) was determined by detection of [^{3}H]PAF degradation products by liquid scintillation counter (Cohort 1). Additionally, sera from an independent cohort of 50 SS-nL, 30 SS-L and 32 HC were tested for Lp-PLA2 activity using a commercially available ELISA kit (Cohort 2). Lp-PLA2 mRNA and protein expression in minor salivary gland (MSG) tissue samples from SS-nL, SS-L patients included in the 2 cohorts and sicca controls (SC) were analyzed by real-Time PCR, western blot and immunohistochemistry.

Results: Serum Lp-PLA2 activity was significantly increased in SS-L compared to both SS-nL and HC in the two independent cohorts included in the study [mean±SD (nmol/min/ml): 62.0±13.4 vs 47.6±14.4 vs 50.7±16.6, p-values: 0.003 and 0.04, respectively (Cohort 1) and 19.0±4.7 vs 15.3±3.2 vs 14.5±3.0, p-values: 0.0005 and 0.0001, respectively (Cohort 2)]. Lp-PLA2 expression in MSG tissues was also increased in SS-L compared to SS-nL and SC at both mRNA and protein level. No significant difference in either serum Lp-PLA2 activity or MSG tissue expression was observed between SS-nL and HC.

Conclusion: Lp-PLA2 serum activity and MSG tissue mRNA/protein expression could serve as a novel biomarker for B-cell lymphoproliferation in the setting of SS.

Disclosure: A. Nezos, None; **E. Kotsifaki**, None; **C. Skarlis**, None; **K. Markakis**, None; **H. Moutsopoulos**, None; **M. Koutsilieris**, None; **C. Mavragani**, None; **A. Psarrou**, None.

Abstract Number: 0038

Protein Biomarkers May Differentiate Responders and Non-Responders to Adalimumab, a Tumour Necrosis Factor Inhibitor, in Ankylosing Spondylitis Patients - The Bioefficacy SpA Study

Ana Fernandes[1], Atlas Mashayekhi Sardoo[2], Miguel Bernardes[3], Patrícia Pinto[4], Helena Santos[5], João Lagoas Gomes[6], José Tavares-Costa[7], José A. P. da Silva[8], João Madruga-Dias[9], Alexandra Bernardo[10], Jean-Charles Gaillard[11], Lúcia Domingues[12], Sara Maia[12], Jean Armengaud[11], Jaime C. Branco[13], Ana Varela Coelho[14] and Fernando Pimentel-Santos[15], [1]1.Instituto de Tecnologia Química e Biológica, Universidade NOVA de Lisboa; 2.Universidade de Trás-os-Montes e Alto Douro, Vila Real, Portugal, Oeiras, Portugal, [2]3. CEDOC, NOVA Medical School, Faculdade de Ciências Médicas da Universidade NOVA de Lisboa, Lisboa, Portugal, Lisbon, Portugal, [3]4.Centro Hospitalar de S. João (Rheumatology Department) , Porto, Portugal, Porto, Portugal, [4]5. Centro Hospitalar de Vila Nova de Gaia/Espinho (Rheumatology Department), Vila Nova de Gaia, Portugal, Vila Nova de Gaia, Portugal, [5]6.Instituto Português de Reumatologia (Rheumatology Department), Lisboa, Portugal, Lisboa, Portugal, [6]7.Hospital Egas Moniz (CHLO) (Rheumatology Department), Lisboa, Portugal, Lisboa, Portugal, [7]8.Unidade Local de Saúde do Alto Minho (Rheumatology Department), Ponte de Lima, Portugal, Ponte de Lima, Portugal, [8]9.Centro Hospitalar e Universitário Coimbra (Rheumatology Department), Coimbra, Portugal, Coimbra, Portugal, [9]10.Centro Hospital Médio Tejo (Rheumatology Department), Torres Novas, Portugal, Dublin, Ireland, [10]5.Centro Hospitalar de Vila Nova de Gaia/Espinho (Rheumatology Department), Vila Nova de Gaia, Portugal, Vila Nova de Gaia, Portugal, [11]11.Centre d énergie atomique (Laboratoire Innovations technologiques pour la Détection et le Diagnostic (Li2D), Service de Pharmacologie et Immunoanalyse (SPI)), Avignon, France, Avignon, France, [12]3.CEDOC, NOVA Medical School. Faculdade de Ciências Médicas da Universidade NOVA de Lisboa, Lisboa, Portugal, Lisboa, Portugal, [13]3.CEDOC, NOVA Medical School, Faculdade de Ciências Médicas da Universidade NOVA de Lisboa, Lisboa, Portugal; 7.Hospital Egas Moniz (CHLO) (Rheumatology Department), Lisboa, Portugal, Lisboa, Portugal, [14]1.Instituto de Tecnologia Química e Biológica, Universidade NOVA de Lisboa, Oeiras, Portugal, Oeiras, Portugal, [15]3.CEDOC, NOVA Medical School, Faculdade de Ciências Médicas da Universidade NOVA de Lisboa, Lisboa, Portugal; 7.Hospital Egas Moniz (CHLO) (Rheumatology Department), Lisboa, Portugal, Lisbon, Portugal

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial Spondyloarthritis (AS) is amongst the most common forms of inflammatory arthritis. Widely used in the treatment of axSpA, adalimumab is an engineered antibody holding only human peptide sequences with high affinity and specificity to soluble and transmembrane TNFα, blocking its interaction with receptors p55 and p75. However, the response to TNFi is heterogeneous and might be linked with some side effects. A priori identification of patients more propense to respond to TNFi is critical in clinical practice.

Methods: The proteomic analysis involved 33 patients with AS from the Bioefficacy SpA Study, of which 19 responders and 14 non-responders after 14 weeks treatment with adalimumab, according to ASAS20 criteria. Serum samples were collected at baseline, 3-5 days, 2 weeks and 14 weeks after treatment. The experimental workflow combined immunoaffinity depletion of the high-abundant serum proteins, tryptic digestion of the proteins extracted from the depleted serum, HPLC separation of tryptic peptides, MS/MS based identification and MS quantification of the detected proteins. Uni- and multivariate statistical analysis of the differentially abundant proteins was used to select the more sensitive and specific serum biomarkers related with therapeutic response. Protein function association network analysis of differential proteins was performed with STRINGdb.

Results: LC-MS/MS method allowed the identification of 333 proteins with at least 2 non-ambiguous peptides. A set of new putative biomarkers was identified with 8 proteins displaying differences between R and NR ($p < 0.05$) at

baseline. Of these, 3 proteins were highly linked with a good clinical response, while the other 5 proteins were strongly related with a non-response to adalimumab therapy at W14. This set of proteins was confirmed to be predictive of the type of response to treatment with an area under the Receiver Operating Characteristics (ROC) curve of 1. Additionally, our analysis showed that the pathways dysregulated in both groups were relatively similar.

Conclusion: Proteomic approaches constitute a very promising strategy to the identification of biomarkers to predict a therapeutic response. These results provide evidence that a panel of biomarker proteins might be identified even before the beginning of treatment which is of utmost importance for clinical practice.

Disclosure: A. Fernandes, None; **A. Mashayekhi Sardoo**, None; **M. Bernardes**, None; **P. Pinto**, None; **H. Santos**, None; **J. Lagoas Gomes**, None; **J. Tavares-Costa**, None; **J. da Silva**, MyFibromyalgia®, a webcompany delivering services to patients with Fibromyalgia, 9; **J. Madruga-Dias**, None; **A. Bernardo**, None; **J. Gaillard**, None; **L. Domingues**, None; **S. Maia**, None; **J. Armengaud**, None; **J. Branco**, None; **A. Varela Coelho**, None; **F. Pimentel-Santos**, None.

Abstract Number: 0039

Identification of a Regulatory Pathway Governing Expression of *TRAF1* via a JIA-associated Non-coding Variant

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

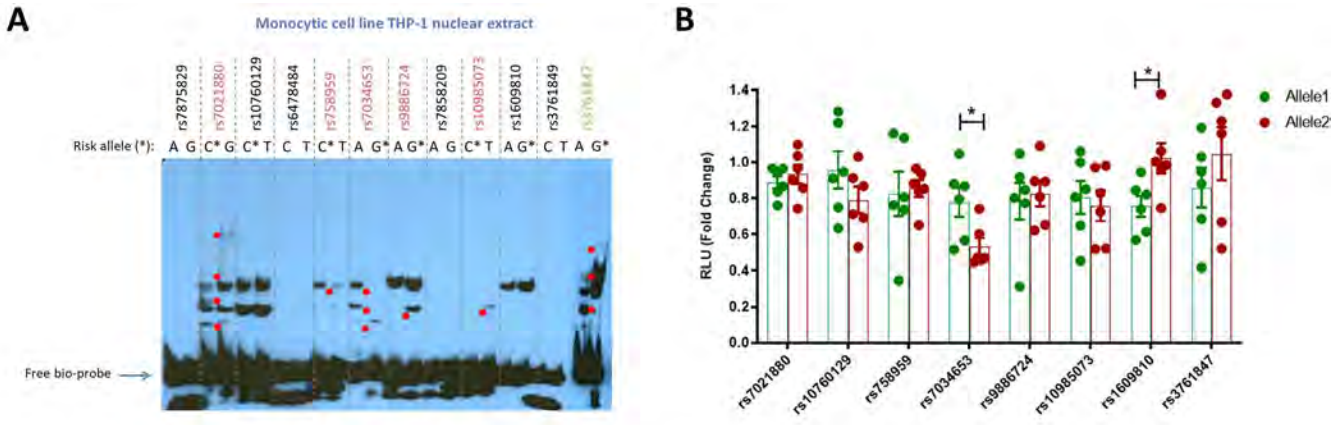

Figure 1 EMSA and luciferase reporter assay for candidate fSNPs from SNP-seq screening. (A) EMSA for 12 SNPs candidates. Allele-specific gel shift/binding are shown as red dots.(*n* = 3 independent biological replicates with similar results). (B) Luciferase reporter assay showing relative luciferase activity in human THP-1 cells between the non-risk (green) and risk (red) alleles of 8 candidate fSNPs. (mean ± s.d., *n* = 3 biological replicates, *t* test with two tails without correction for multiple hypothesis testing, * shows p<0.05).

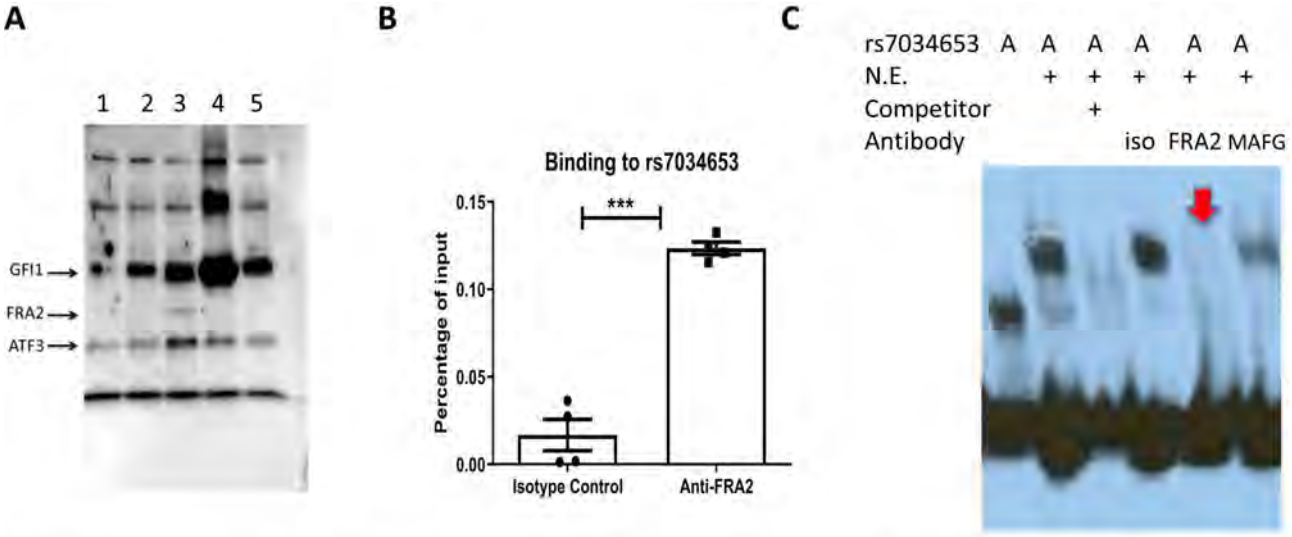

Figure 2 FRA2 binding to rs7034653 validation. (A) oligo pulldown western blot assay. 1: rs1609810-G; 2: rs1609810 –G with non-biotinylated competitor (30x); 3: rs7034653-A; 4: rs7034653-A with non-biotinylated competitor (30x) ;5: control SNP rs3768056-A. FRA2 binds specifically to rs7034653-A, control antibodies GFI1 and ATF3 bind to all five samples. (*n* = 3 independent biological replicates with similar results). (B) CHIP-qPCR shows FRA2 binding to rs7034653 in human THP-1 cells (mean ± s.d., *n* = 2 biological replicates, *t* test with two tails without correction for multiple hypothesis testing, *** shows p<0.0001). (C) EMSA supershift assay shows specific binding of rs7034653-A to FRA2. The addition of antibody to FRA2 in the oligo/nuclear extract (THP-1) mixture caused the disappearance of shift band (arrow), whereas isotype control antibody and antibody to MAFG did not.

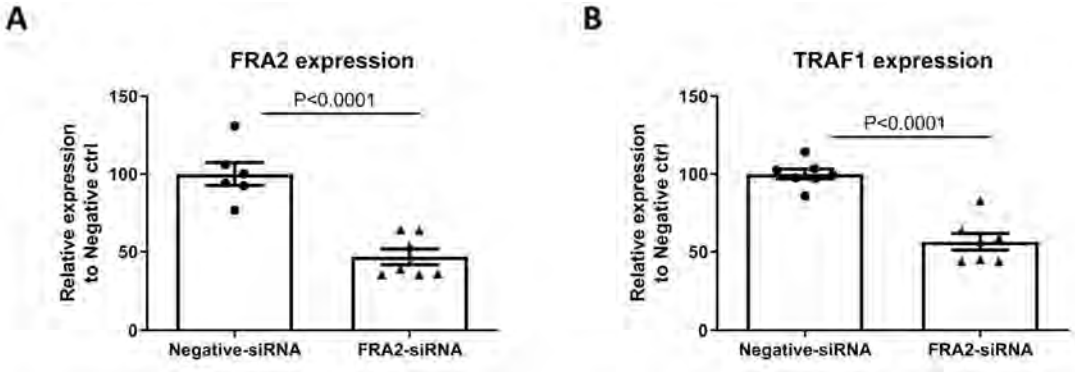

Figure 3 RT-qPCR mRNA gene expression for gene FRA2 and TRAF1 after FRA2 siRNA knockdown in THP-1 cells. (A) FRA2 mRNA expression relative to negative siRNA treated control (mean ± s.d., *n* = 2 biological replicates, *t* test with two tails without correction for multiple hypothesis testing, p<0.0001). (B) TRAF1 mRNA expression relative to negative siRNA treated control (mean ± s.d., *n* = 2 biological replicates, *t* test with two tails without correction for multiple hypothesis testing, p<0.0001).

Background/Purpose: Over the past decade, genome-wide association studies (GWAS) have identified TRAF1/C5 locus as a risk locus for rheumatoid diseases including RA and JIA(Plenge, Seielstad et al. 2007, Behrens, Finkel et al. 2008), and TRAF1 negatively regulates Toll-like receptor signaling(Abdul-Sater, Edilova et al. 2017). However, the exact risk variant within that locus and its underlying mechanism regulating TRAF1 expression are still not known. We aim to identify non-coding variant in TRAF1/C5 locus governing the expression of TRAF1 gene and its regulatory pathway.

Methods: Single-nucleotide polymorphisms (SNPs) in linkage disequilibrium (LD) with the most disease-associated SNP in TRAF1/C5 locus from immunochip data (5 thousand JIA patients and 14 thousand health controls) were high-throughput screened by SNP-seq(Li, Martinez-Bonet et al. 2018). Top candidates' regulatory function were further validated by electrophoretic mobility shift assay (EMSA) and luciferase reporter assay. Then the transcriptional factor that might bind to the functional variant after validation was tested by CHIP-qPCR, oligo pulldown assay as well as supershift assay. Finally, the association between this transcriptional factor and TRAF1 gene expression was analyzed by RNAi knockdown experiment.

Results: After screening by SNP-seq, EMSA, and luciferase reporter assay, rs7034653 was found to be the best functional non-coding variant in TRAF1/C5 locus that is associated with JIA. EMSA shows that protein from monocyte nuclear extract has a preferential binding to protective allele A than the risk allele G of rs7034653, and that binding preference likely regulates higher gene expression as shown by luciferase reporter assay, which is consistent of existing eQTL data that shows higher expression of TRAF1 in protective allele A than risk allele G in human monocytes. Furthermore, this variant is found to be able to bind to AP1 transcriptional factor FRA2. Suppressed expression of FRA2 by RNAi leads to lower expression of TRAF1 after LPS stimulation in the THP-1 monocytic cell line.

Conclusion: Non-coding variant rs7034653 in TRAF1/C5 locus likely regulates TRAF1 gene expression in monocytes through binding to transcriptional factor FRA2.

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Abstract Number: 0040

Whole Blood RNA Expression in Clinically Suspected Arthralgia Patients Shows a Potential Value in Prediction of Inflammatory Arthritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Genetics, Genomics & Proteomics Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA)-patients have differently expressed genes involved in cytokine/chemokine-mediated immunity compared to healthy controls, which are changed years before RA-diagnosis. It is unclear, if immunity genes differ between patients with clinically suspect arthralgia (CSA), the phase that precedes IA-development, that do and do not develop clinically evident inflammatory arthritis (IA), which was investigated in this study with whole blood RNA expression.

Methods: Between April 2012-March 2015, 234 patients were consecutively included in the Leiden CSA-cohort. Follow-up ended when patients developed clinically apparent IA (determined at physical examination), or else after 2-years. RNA expression in whole blood, at the moment of inclusion, was determined for 135 genes of the innate and adaptive immune system by dual color Reverse-Transcription Multiplex Ligation-dependent Probe Amplification (dcRT-MLPA) profiling. Cox proportional hazard models were used to associate time-to-event with gene expression

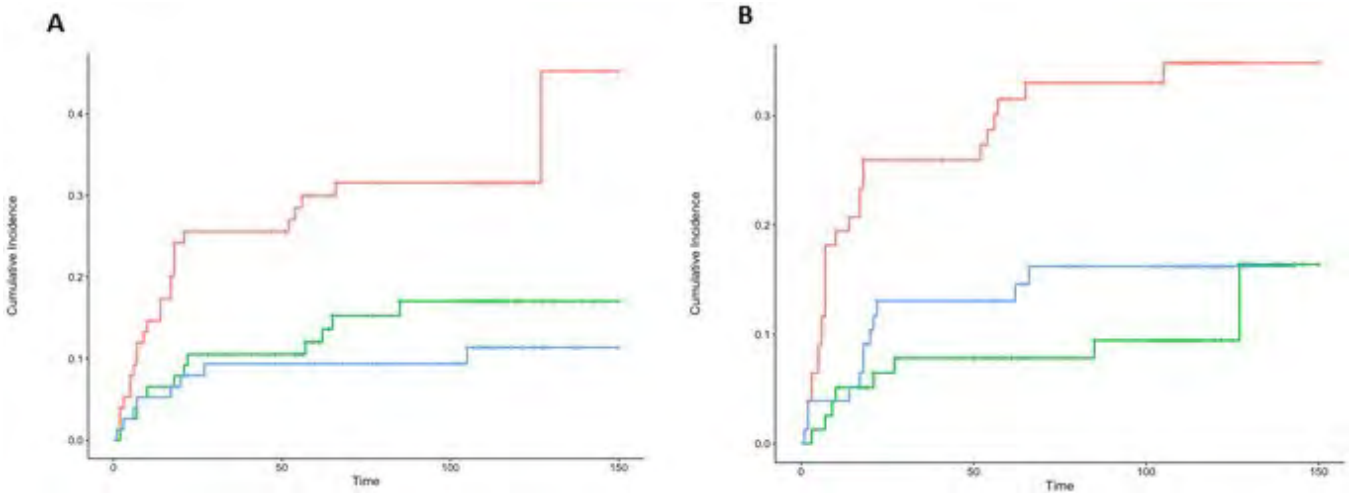

Figure 1. Association between RNA expression divided in tertiles of IGF-1 (A) and IL7R (B), and development of inflammatory arthritis

level at inclusion, while adjusting for age, gender, and assay plate. The false discovery rate was used to correct for multiple testing. Genes with significantly different expression were subsequently studied for reproducibility by qPCR, and mutual independence in their association with IA-development. Resulting mutually independent genes were further investigated for their added predictive value over known risk factors, CRP, ACPA, and subclinical joint inflammation.

Results: 20% of CSA-patients developed IA after mean 3.6 months (IQR:1.6-10.7) follow-up. After correction for multiple testing, six genes were significantly associated with IA-development, namely IFN-G, PHEX, IGF-1, IL7R, CD19, or CCR7 (ordered by significance). For all six genes, a lower expression at inclusion was associated with an increased risk of IA-development. IFN-G was only weakly expressed in peripheral blood, hampering the technical reproducibility between MLPA and qPCR results, and was excluded for further analyses. PHEX and IGF-1 were highly correlated (R^2 0.97) and only IGF-1, but not PHEX, was included in further analyses. Of the remaining significant genes (IGF-1, IL7R, CD19, CCR7), an independent association with IA-development was observed for IGF-1 and IL7R, but not for CD19 or CCR7. qPCR data of IL7R correlated with MLPA results ($p< 0.001$), confirming the robustness of the transcriptomic outcome. Lastly, when analysing IGF-1 and IL7R with known clinical predictors, both IGF-1 and IL7R remained independently associated with progression to IA.

Conclusion: IGF-1 and IL-7R were differentially expressed between CSA-patients that did or did not progress to IA, which was independent of known predictors. This also supports T cell mediation in the phase of arthralgia, before progression to IA.

Disclosure: E. Niemantsverdriet, None; **E. van den Akker**, None; **D. Boeters**, None; **S. van den Eeden**, None; **A. Geluk**, None; **A. van der Helm - van Mil**, None.

Abstract Number: 0041

Association of the *RPA3-UMAD1* Locus with Interstitial Lung Diseases Complicated with Rheumatoid Arthritis in Japanese

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

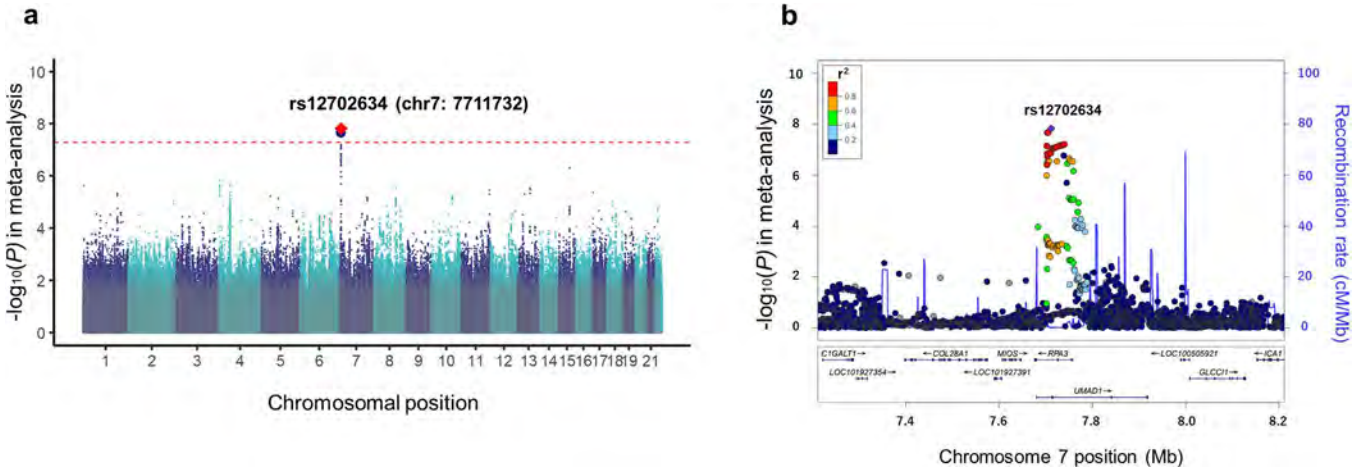
Session Title: Genetics, Genomics & Proteomics Poster

Session Type: Poster Session A

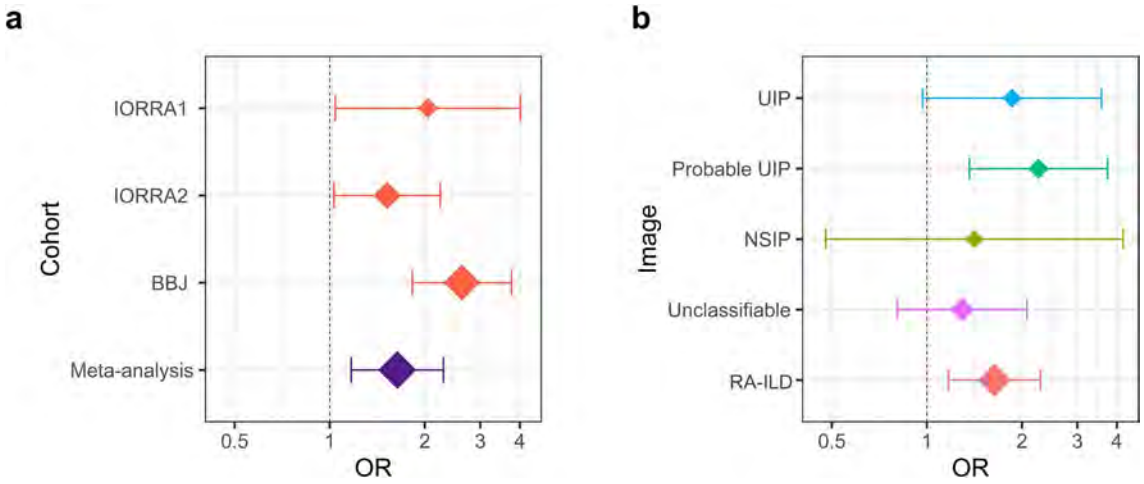
Session Time: 9:00AM–11:00AM

Background/Purpose: The genetic background of rheumatoid arthritis-interstitial lung disease (RA-ILD) has been evaluated in Europeans, but little knowledge has been obtained in non-Europeans. In particular, The *MUC5B* promoter variant (rs35705950) has been noted as a common risk variant with large effect on both IPF and RA-ILD in Europeans. However, the frequency of the variant varies heterogeneously among ancestral populations. While its minor allele frequency (MAF) was common in Europeans (= 0.107 in 1000 Genomes Project Phase 3; 1KGP3), it was as low as 0.008 in east Asians. This observation implies that genetic underpinning of RA-ILD is heterogeneous among populations, and identification of additional risk variants other than *MUC5B* in east Asians should be warranted. Furthermore, previous studies assessed RA-ILD risk of the mutations in specific genes implicated with risk of pulmonary fibrosis through candidate gene approaches. There have been no studies that investigated genome-wide risk of RA-ILD. This study aimed to elucidate genome-wide risk of RA-ILD in non-Europeans.

Methods: This study enrolled 1,117 and 3,899 individuals affected with rheumatoid arthritis (RA) from Institute of Rheumatology Rheumatoid Arthritis (IORRA) and BioBank Japan (BBJ), respectively. IORRA is a RA cohort which was established in 2000 at Tokyo Women's Medical University, Japan. In the IORRA cohort, we extracted the RA subjects who had normal CT scans and chest CT image of each subject was reviewed by an experienced physician, and



Association results of the GWAS meta-analysis for the three datasets.



The odds ratio and the 95% confidence interval of rs12702634-C in each dataset and CT image pattern.

Table1 Genome-wide significant variant associated with RA-ILD

SNP	Chr	Position(bp)	Positional candidate gene(s)	eGene	Alleles		Cohort	No. subjects		REF allele frequency		OR(95%CI)	P
					REF	ALT		Case	Control	Case	Control		
rs12702634	7	7711732	RPA3 UMAD1	RPA3	C	G	IORRA1	60	176	0.17	0.11	2.05 [1.04-4.02]	3.80E-02
							IORRA2	195	681	0.11	0.08	1.52 [1.03-2.24]	3.40E-02
							BBJ	103	3693	0.19	0.08	2.62 [1.83-3.77]	1.74E-07
							Meta-analysis	358	4550	0.14	0.08	2.04 [1.59-2.60]	1.50E-08

Genome-wide significant variant associated with RA-ILD.

findings were confirmed based on the concordance with those by the radiologist's report. BBJ is a hospital-based cohort with multi-omics data from genotype to multitude phenotype. The status of RA or ILD in the BBJ cohort was examined through interviews and reviews of medical records. GWAS genotyping and imputation were conducted for all the subjects. After the quality control, we performed a GWAS meta-analysis of the IORRA cohort and the BBJ cohort, which included 358 RA-ILD cases and 4,550 RA subjects without ILD. We then conducted the stratified analysis of the effect of the GWAS risk allele in each computerized tomography (CT) image pattern.

Results: We identified one novel RA-ILD risk locus at 7p21 that satisfied the genome-wide significance threshold (rs12702634, odds ratio [OR] = 2.04, 95% confidence interval [95%CI] = 1.59-2.60, P = 1.5×10-8). Subsequent stratified analysis based on the CT image patterns demonstrated that the effect size of the RA-ILD risk allele (rs12702634-C) was large with the UIP pattern (OR = 1.86, 95%CI = 0.97-3.58, P = 0.062) and the probable UIP pattern (OR = 2.26, 95%CI = 1.36-3.73, P = 0.0015). The RA-ILD risk variant of rs12702634 was located in the intron region of *RPA3* and *UMAD1* and within the enhancer histone marks in several immune cells. The GTEx data showed that the rs12702634-C risk allele increased *RPA3* expression levels in various tissues including lung.

Conclusion: We revealed one novel genetic association with RA-ILD in Japanese. The RA-ILD risk of the identified variant at *RPA3-UMAD1* was relatively high in the CT image patterns related to fibrosis. Our study should contribute to the elucidation of the complicated etiology of RA-ILD.

Disclosure: Y. Shirai, None; **S. Honda**, None; **K. Ikari**, None; **M. Kanai**, None; **Y. Takeda**, None; **Y. Kamatani**, None; **T. Morisaki**, None; **E. Tanaka**, Abbvie, 1, Asahi Kasei Pharma, 1, Chugai Pharmaceutical Co., Ltd., 1, Eisai Pharmaceutical, 1, Janssen Pharmaceutical K.K., 1, Pfizer, 1, Takeda Pharmaceutical, 1, Astellas Pharmaceutical, 1, Ayumi

Pharmaceutical, 1, Eli Lilly Japan K.K., 1, GlaxoSmithKline K.K, 1, Kyowa Pharma Chemical CO., LTD, 1, Mochida Pharmaceutical CO., LTD, 1, Teijin Pharma Ltd., 1; **A. Kumanogoh**, None; **M. Harigai**, AbbVie Japan GK, 1, 2, Asahi Kasei Corp., 1, Astellas Pharma Inc., 1, Ayumi Pharmaceutical Co. Ltd., 1, 2, Bristol Myers Squibb Co., Ltd, 1, 2, 3, Chugai Pharmaceutical Co. Ltd., 1, 2, Daiichi-Sankyo, Inc., 1, Eisai Pharmaceutical, 1, 2, Nippon Kayaku Co. Ltd., 1, Mitsubishi Tanabe Pharma Co., 1, Taisho Pharmaceutical Co. Ltd., 1, Takeda Pharmaceutical Co. Ltd., 1, 2, Eli Lilly Japan K.K, 1, Pfizer Japan Inc, 1, AbbVie, 1; **Y. Okada**, None.

Abstract Number: 0042

Racial and Ethnic Differences in a Multiple Biochemical Measure of Rheumatoid Arthritis Disease Activity

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Although management of RA has improved greatly over the past two decades with the advent of novel therapeutics, racial/ethnic and socioeconomic disparities persist. Traditional RA disease activity measures, including the Clinical Disease Activity Index (CDAI) and DAS28-ESR, are influenced by provider and patient subjectivity which may impact racial/ethnic differences observed in prior studies. A multiple-biochemical measure of disease activity (MBDA) score, a composite of 12 serum biomarkers, was designed to be a more objective measure of RA disease activity. This study examined racial and ethnic differences in MBDA scores within a diverse cohort of RA patients.

Methods: Data are derived from the University of California, San Francisco RA Cohort, a longitudinal observational cohort, in which disease activity was measured as part of routine clinical care and MBDA was obtained at the time of each clinical encounter. All participants were from a safety-net hospital thereby reducing variations in income and insurance. Participants with ≥1 MBDA measure and self-reported race/ethnicity were included. Multivariable linear regression evaluated the association between race/ethnicity groups and mean MBDA score, adjusting for age at enrollment, sex, smoking history, RA symptom duration at enrollment, number of study visits, ACPA status, mean BMI, mean conventional DMARD (cDMARD) use, mean biologic DMARD (bDMARD) use and mean prednisone use. Missing data elements were estimated using multiple imputation with chained equations (MICE). Sensitivity analyses substituted CDAI and DAS28-ESR for the MBDA in multivariable linear regression models.

Results: There were 267 subjects, 86% female, mean age 52.7±13.3, and the majority were Hispanic (n=137, 51%) followed by Asian (n=91, 34%). Participants were followed an average 8.4±3.4 years and had moderate disease activity by all three measures (Table 1). After adjustment, Hispanic participants had the highest mean MBDA score (40.6), compared with White participants (33.0) (p=0.032). Black (36.2) participants had the second highest mean MBDA followed by Asian participants (36.0), although neither were significantly different from White participants (Table 2). The trends observed in the sensitivity analyses were similar to those in the primary analysis.

Table 1. Baseline demographics and clinical characteristics of the RA cohort categorized by race/ethnicity. (n=267).

	Hispanic (n = 137)	Asian (n = 91)	Black (n = 24)	White (n = 15)
Demographics				
Age years	50.5 ± 14.4	56.4 ± 11.2	54.0 ± 11.6	48.0 ± 13.5
Male sex	15 (11%)	12 (13%)	6 (25%)	4 (27 %)
Ever smoker	33 (28%)	17 (23%)	9 (47%)	8 (57%)
BMI, kg/m^2	30.1 ± 6.5	25.4 ± 4.3	31.5 ± 6.4	31.6 ± 8.0
Number of study visits	21.0 ± 13.5	20.9 ± 12.6	16.9 ± 10.9	17.3 ± 13.1
Years in study	8.3 ± 3.8	8.8 ± 2.9	8.7 ± 3.0	7.9± 3.0
RA characteristics				
RA symptom duration, years	6.7± 7.8	7.3± 7.9	5.7 ± 6.7	5.7± 6.9
ACPA positivity	105 (77%)	82 (90%)	17 (71%)	10 (67%)
RF positivity	118 (86%)	80 (88%)	20 (83%)	11 (73%)
Medications				
cDMARD use, ever	135 (99%)	89 (98%)	21 (88%)	15 (100%)
cDMARD use, proportion of visits	0.8 ± 0.3	0.8 ± 0.3	0.7 ± 0.3	0.8 ± 0.2
bDMARD use, ever	86 (63%)	46 (51%)	8 (33%)	10 (67%)
bDMARD use, proportion of visits	0.3 ± 0.3	0.3 ± 0.4	0.2 ± 0.3	0.5 ± 0.4
Prednisone use ever	129 (94%)	80 (88%)	21 (88%)	8 (53%)
Mean prednisone dose	4.5 ± 3.3	3.4 ± 2.6	4.4 ± 4.2	2.1 ± 2.5
Disease Activity Measures*				
Mean MBDA	41.2 ± 12.7	35.0 ± 14.2	38.0 ± 14.7	30.6 ± 12.7
Mean CDAI	17.5 ± 9.3	13.6 ± 7.4	15.1 ± 9.9	12.6 ± 8.7
Mean DAS28-ESR	4.4 ± 1.4	4.1 ± 1.3	3.9 ± 1.3	3.3 ± 1.2

-Continuous variables are reported as mean ± SD and categorical variables as n (% of column total).
-Abbreviations: ACPA = anti-cyclic citrullinated protein antibodies; CDAI = clinical disease activity index, DAS28 = 28-joint disease activity score, cDMARD = Conventional disease modifying anti-rheumatic drug (includes methotrexate, sulfasalazine, hydroxychloroquine, leflunomide); bDMARD = Biologic DMARD (includes tocilizumab, etanercept, certolizumab, adalimumab, anakinra, abatacept, infliximab, rituximab, golimumab). MBDA- multiple biomarker disease activity.
CI = 95% confidence interval
*Disease activity measures calculated as the overall mean disease activity score of each participant's mean disease activity scores. MBDA score range 0-100 (Disease activity ranges: low<30, medium 30-44, high >44); DAS28-ESR range 2-10 (Disease activity ranges: low ≤3.2, moderate >3.2-5.1, high >5.1); CDAI range 0-76 (disease activity ranges: low ≤10, moderate 10.1-22, high >22.1).
-Values are missing for the following variables: smoking: n = 41; BMI: n = 60; symptom duration: n = 23, DAS: n = 2, CDAI: n = 1.

Conclusion: In a diverse observational RA cohort, Hispanic participants had the highest mean MBDA score, which was significantly higher than that of White participants after adjustment in the multivariable model. Black and Asian participants also had higher disease activity scores than White participants, although these differences did not reach statistical significance. Regardless of the method of assessment, racial/ethnic differences in disease activity are observed in RA. MBDA scores appear to add no additional information beyond standard, ACR-endorsed measures of disease activity in this analysis. Further studies focusing on early access to care, mitigating language barriers and addressing racial disparities should be done to enable improvement of disease outcomes across minority racial/ethnic groups.

Table 2. RA disease activity score predictions by race/ethnicity after adjustment in multivariable linear regression (n=267). Data presented for the primary model (MBDA score) as well sensitivity analyses with DAS28-ESR and CDAI.

Race/Ethnicity	MBDA (95%CI)	DAS28ESR (95%CI)	CDAI (95%CI)
Hispanic	40.6 (26.4-39.5)*	4.3 (4.1-4.5)*	16.9 (15.5-18.3)
Asian	36.0 (38.4-42.7)	4.3 (4.0-4.5)*	14.5 (12.7-16.3)
Black	36.2 (31.1-41.4)	3.7 (3.2-4.3)	14.2 (10.8-17.5)
White	33.0 (23.4-39.5)	3.4 (2.7-4.1)	14.2 (9.9-18.5)

-Controlled for age at enrollment, sex, smoking history, RA symptom duration at enrollment, number of study visits, anti-cyclic citrullinated peptide status, body mass index, cDMARD use (proportion of visits using), bDMARD use (proportion of visits using) and mean prednisone use. Missing data elements were estimated using multiple imputation with chained equations (MICE).

* indicates p-value <0.05 in the multivariable linear regression using White race as the reference group.

-Abbreviations: CDAI = clinical disease activity index, DAS28 = 28-joint disease activity score, cDMARD = Conventional disease modifying anti-rheumatic drug (includes methotrexate, sulfasalazine, hydroxychloroquine, leflunomide); bDMARD = Biologic DMARD (includes tocilizumab, etanercept, certolizumab, adalimumab, anakinra, abatacept, infliximab, rituximab, golimumab). MBDA- multiple biomarker disease activity.

Disclosure: R. Baker, None; **J. Graf**, None; **L. Trupin**, None; **S. Goglin**, None; **P. Katz**, None; **J. Barton**, None; **J. Liew**, None; **K. Wysham**, None.

Abstract Number: 0043

Geographical Disparity in Rheumatoid Arthritis Disease Burden Independent of Race/Ethnicity

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Healthcare Disparities in Rheumatology Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: In the US, health care systems vary, as does cost sharing and access to various RA therapies. However, the burden of RA – a systemic disorder – is often a confounder in management decisions. Whether the burden of RA disease is homogeneous in various regions of the US, and independent of race/ethnicity and/or health care coverage, is unknown.

Methods: US Rheumatology practices from the Northeast, South, and West regions enrolled RA outpatients. Socio-demographics, RA disease status, activity and therapies, and comorbidities were collected, and rheumatic comorbidity disease index (RDCI) was calculated. Primary insurance coverage type (Private, Medicare, Medicaid) was documented, and copay for office visits and medications stratified. Univariable pairwise differences between regions was conducted using Tukey post-hoc corrected analysis of variance for continuous variables, Bonferroni-adjusted

	Total		Northeast			South			West		
	Obs	Statistic	Obs	Statistic	Different	Obs	Statistic	Different	Obs	Statistic	Different
Age (years)	402	61.9 (14.0)	176	61.9 (12.1)	—	149	61.0 (15.7)	—	77	63.4 (14.4)	—
Female [N(%)]*	392	327 (83.4%)	174	153 (87.9%)	—	143	114 (79.7%)	—	75	60 (80.0%)	—
Race [N(%)]†					S,W			NE,W			S,NE
Black		80 (20.1%)		60 (34.1%)			20 (13.4%)			4 (5.2%)	
Hispanic		50 (12.4%)		18 (10.2%)			14 (9.4%)			18 (23.4%)	
White		218 (54.2%)		90 (51.1%)			90 (60.4%)			38 (49.4%)	
Primary Insurance [N(%)]†					W			—			NE
Private		112 (27.9%)		63 (35.8%)			30 (20.1%)			19 (24.7%)	
Medicare		142 (35.3%)		59 (33.5%)			44 (29.5%)			39 (50.7%)	
Medicaid		19 (4.7%)		17 (8.7%)			2 (1.3%)			0	
Other		16 (4.0%)		8 (4.6%)			7 (4.7%)			1 (1.3%)	
Co-pay Office Visit [N(%)]†					S,W			NE,W			S,NE
<$10		181 (45.0%)		88 (50.0%)			54 (36.2%)			39 (50.7%)	
$10-25		57 (14.2%)		30 (17.1%)			18 (12.1%)			9 (11.7%)	
$25-50		81 (20.2%)		35 (19.9%)			41 (27.5%)			5 (6.5%)	
$50+		36 (9.0%)		5 (2.8%)			21 (14.1%)			10 (13.0%)	
Co-pay Medications [N(%)]†					S,W			NE			NE
<$10		128 (31.8%)		69 (39.2%)			34 (22.8%)			25 (32.5%)	
$10-25		45 (11.2%)		10 (5.7%)			24 (16.1%)			11 (14.3%)	
$25-50		91 (22.6%)		49 (27.8%)			35 (23.5%)			7 (9.1%)	
$50+		51 (12.7%)		24 (13.6%)			17 (11.4%)			10 (13.0%)	
Smoking History [N(%)]†					—			—			—
Never		142 (35.3%)		82 (46.6%)			35 (23.5%)			25 (32.5%)	
Prior Smoker		58 (14.4%)		26 (14.8%)			24 (16.1%)			8 (10.4%)	
Current Smoker		10 (2.5%)		4 (2.3%)			5 (3.4%)			1 (1.3%)	
Duration (years)	233	13.2 (10.8)	123	11.8 (9.2)	—	104	14.9 (12.1)	—	6	11.5 (13.7)	—
Rheumatoid Factor Titer	169	71.6 (146.5)	81	72.6 (111.3)	—	74	74.7 (186.6)	—	14	49.2 (70.5)	—
Anti-CCP Titer	155	64.2 (112.1)	79	58.9 (109.9)	—	62	66.9 (110.4)	—	14	82.1 (136.7)	—
Sedimentation Rate (mm/hr)	328	21.6 (24.2)	153	26.4 (25.2)	S,W	118	18.0 (20.0)	NE	57	16.2 (27.1)	NE
C-Reactive Protein	308	7.9 (18.9)	153	9.8 (24.9)	—	98	6.7 (10.5)	—	57	5.0 (8.4)	—
Nodules [N(%)]*	286	47 (16.4%)	141	17 (12.1%)	—	134	27 (20.1%)	—	11	3 (27.3%)	—
Prior Predisone Use [N(%)]*	349	148 (42.4%)	153	74 (48.4%)	W	124	53 (42.7%)	—	72	21 (29.2%)	NE
Prior Methotrexate Use [N(%)]*	349	235 (67.3%)	153	118 (77.1%)	W	124	84 (67.7%)	W	72	33 (45.8%)	NE,S
Rheumatic Disease Comorbidity Index	355	1.3 (1.5)	167	1.2 (1.4)	S	120	1.7 (1.7)	NE	68	1.1 (1.4)	—
RAPID3 [0-10]	312	3.7 (2.3)	125	3.5 (2.1)	—	120	3.7 (2.4)	—	67	4.1 (2.3)	—
CDAI [0-76]	296	14.4 (14.1)	144	10.5 (9.8)	S	94	22.5 (17.9)	NE,W	58	11.1 (10.7)	S
DAS28-ESR [0-10]	275	3.3 (1.6)	150	3.0 (1.4)	S	93	3.7 (1.7)	NE	32	3.2 (1.8)	—
DAS28-CRP [0-10]	280	2.8 (1.4)	150	2.5 (1.1)	S	74	3.6 (1.5)	NE,W	56	2.3 (1.3)	S

*N(%) and Bonferroni-corrected logistic regression between groups reported.

†N(%) and Bonferroni-corrected Chi-square between groups reported. Otherwise, Mean (SD) and Tukey-post-hoc ANOVA between groups reported.

NE: Corrected P-value compared to Northest Sites P<0.05; **S**: Corrected P-value compared to South Sites P<0.05; **W**:Corrected P-value compared to West Sites P<0.05

Table. Clinical Characteristics of RA patients in US Geographic Regions

Chi-square for categorical variables, and Bonferroni-adjusted logistic regression for dichotomous variables. Multivariable regression models were estimated to investigate disparities in RDCI between insurance variables as well as race while controlling for region.

Results: 402 RA patients were enrolled from 10 outpatient practices (Table). A predominantly Caucasian, female population, with established disease, most received government sponsored primary insurance (40% vs 27.9%). Copay for office visits and medications were < $10 in 45% and 31.8% of observations, respectively, and more prevalent in the Northeast/West subsets than in the South. Office copays > $25 were more frequent in South patients, while more often in Northeast patients for medications. Tobacco use was similar in all subsets. Disease activity scores inclusive of physician/laboratory core measures were higher for South than Northeast patients. RDCI was higher in the South group, 1.7 [1.7], compared to both other subsets and the cohort mean 1.3[1.5]. Hispanics had significantly less RDCI than Blacks (RDCI -0.78, 95% CI [-1.35, -0.21], P=0.008) and Whites (RDCI -0.68, 95% CI [-1.18, -0.17], P=0.009), independent of region. RDCI was significantly lower for privately insured than Medicare (RDCI -0.78, 95% CI [-0.41, -1.15], P< 0.001) and Medicaid (RDCI -0.83, 95% CI [-0.13, -1.54], P=0.020), independent of region. [Figure 1]. However, RDCI was significantly higher for office visit copays < $10 than $25-50 (RDCI +0.61, 95% CI [0.16, 1.06], P=0.008) and $50+ (RDCI +0.89, 95% CI [0.17, 1.62], P=0.016), as well as for medication copays both < $10 (RDCI

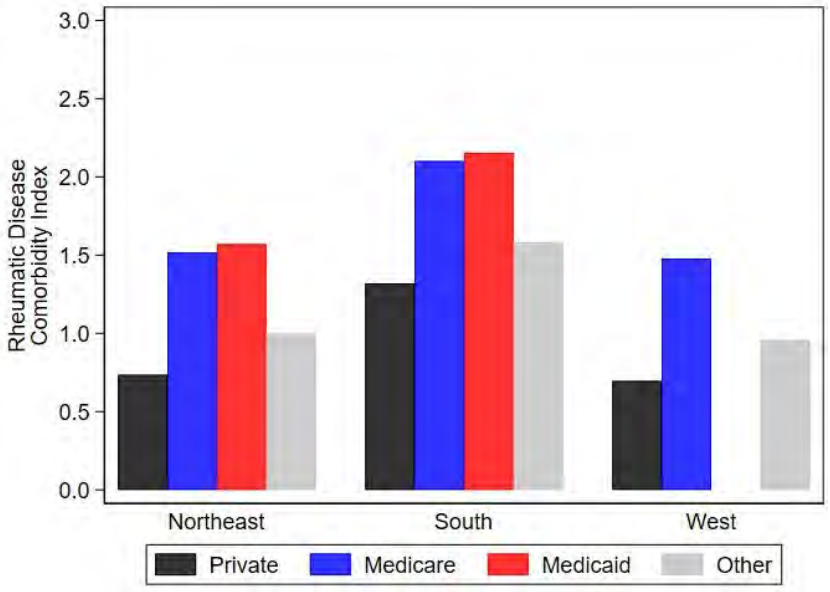

Figure 1. Rheumatic Disease Comorbidity Index by Region and Insurance Type

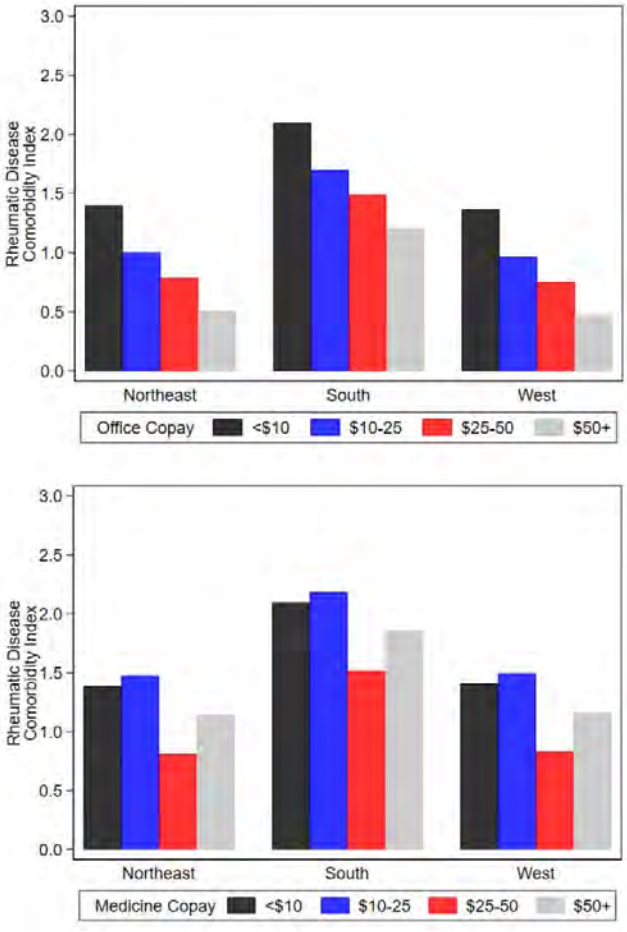

Figure 2. Rheumatic Disease Comorbidity Index by Region and Office and Medication Co-pay

+0.58, 95% CI [0.12, 1.03], P=0.013) and $10-25 (RDCI +0.67, 95% CI [0.03, 1.31], P=0.041) compared to $25-50, both independent of region. [Figure 2].

Conclusion: While RA disease burden was evident in patients receiving care in Southern practices, it was independent of race/ethnicity. Government health care rather than private insurance plans covered complicated RA patients, regardless of site of care. Cost sharing may further complicate access to optimum care. Application of this analysis to a larger dataset that includes additional US regions, expanded insurance parameters and potential founders such as socioeconomic status, is needed.

Disclosure: G. Kerr, Novartis, 1, BMS, 1, 2, Gilead, 1, Regeneron, 1, Janssen, 1; **C. Swearingen**, None; **M. Pedra-Nobre**, None; **D. Wollaston**, None; **S. Najmey**, None; **C. Lawrence-Elliott**, None; **T. Lawrence Ford**, None; **S. Dowell**, Horizon Pharma, 8, Bristol Myers Squbb, 2, Pfizer, 2; **H. North**, None; **R. Dore**, AbbVie, 2, 5, Amgen, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly and Co, 2, 5, Gilead Sciences, Inc., 2, 5, GlaxoSmithKline, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Radius, 2, 5, Regeneron, 2, 5, Sanofi, 2, 5, UCB, 2, 5, Exagen, 8; **S. Dolatabadi**, None; **T. Ramanujam**, None; **A. Winkler**, Abbvie, 8, Amgen, 8, Janssen, 8, Lilly, 8, Pfizer, 8, Sanofi Genzyme, 8, Novartis, 5, 8, Crescendo, 8; **S. Kennedy**, None; **I. Jileaeva**, None; **A. Richardson**, None; **J. Kaine**, None; **G. Wright**, Exagen, 5, 8, AbbVie, 5, 8, Amgen, 5, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly and Company, 5, 8, Myriad Autoimmune, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Regeneron Pharmaceuticals, Inc., 5, 8, Sanofi Genzyme, 5, 8, UCB, 5, 8.

Abstract Number: 0044

Characterization of Racial Disparities in Rheumatoid Arthritis Treatment Choice and Location of Care

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Racial disparities in access to care and treatment regimens exist but remain poorly characterized in the rheumatoid arthritis (RA) patient population. Previous studies using the Ethnic Minority RA Consortium (EMRAC) have demonstrated non-Caucasian RA patients have a lower frequency of biologic use versus Caucasian patients despite controlling for comparable disease activity and access to treatment. Here we explore longitudinal racial disparities in rheumatoid arthritis treatment and emergency department (ED) use in a single tertiary academic center.

Methods: Structured de-identified data from 2010-2018 of patients who had at least two diagnoses of RA from a rheumatology outpatient encounter and at least one DMARD script during the follow-up period were extracted from the electronic health record of a single tertiary care center. Follow-up was measured from each patient's first visit to each patient's last visit within the 2010-2018 timeframe. Patient demographics were measured at the baseline visit, with medication use and comorbidities measured at baseline or at any point during follow-up. The average number of outpatient visits and ED visits per year (limited to ED visits within the health system) during follow-up were also measured. Differences in patient characteristics and visits were compared in patients who were black versus white based on standard t-test and χ^2 analysis.

Characteristic	Black or African American (n=639)	White (n=991)	Comparing Black and White Patients
Age, mean (SD), years	57.05 (14.67)	54.25 (14.21)	P=0.0002
Female (%)	87.32	77.90	
BMI, mean (SD)	31.02 (7.62)	27.99 (6.55)	P<0.0001
Smoking Status (% Former or Current)	40.85	33.20	P=0.0017
Diabetes (%)	201 (31.46%)	101 (10.19%)	P<0.0001
Cardiovascular Disease (%)	456 (71.36%)	446 (45.01%)	P<0.0001
Medications			
Prednisone	507 (79.34%)	685 (69.12%)	P<0.0001
Biological DMARD	428 (66.98%)	737 (74.27%)	P=0.0013
Conventional DMARD	618 (96.71%)	927 (93.54%)	P=0.0049
Tofacitinib	35 (5.48%)	56 (5.65%)	P=0.88
Median Duration of Follow-Up [IQR]	8.44 [6.26-8.89]	8.02 [5.21-8.83]	P=0.0004
Median Number of ED Visits Per Patient Per Year [IQR]	0.24 [0.00-0.79]	0.00 [0.00-0.00]	P<0.0001
Median Number of Outpatient Office Visits Per Patient Per Year [IQR]	5.76 [3.32-9.53]	3.93 [2.44-6.37]	P<0.0001
Median Number of Outpatient Rheumatology Office Visits Per Patient Per Year [IQR]	2.15 [1.23-3.02]	1.82 [1.08-2.69]	P<0.0001

Comparison of Patient Characteristics

Results: A total of 1831 patients with rheumatoid arthritis were identified from 2010-2018. Baseline demographics were measured at each patient's first visit and include mean [SD] age, 55.05 [14.47] years; 1499 [81.87%] female; and 991 [54.12%] white. Average [SD] duration of follow-up for all patients was 6.97 [2.28] years. Comparing black (n=639) and white (n=991) patient demographics, significant findings include that black patients were more likely to be older, have higher BMI, former or current smoking status, and have higher rates of diabetes and cardiovascular disease ($p< 0.0001$). Prednisone and csDMARD use were significantly more frequent in black patients compared to white patients (79.3% vs 69.1% $p< 0.0001$; 96.7% vs 93.5%, $p=0.005$, respectively). Biologic use was significantly more common among white patients compared to black patients (white 74.3%, black 67.0% $p=0.001$). In terms of site of care delivery, black patients had significantly more ED visits, with a median 0.24 ED visits per patient per year versus 0.00 for white patients. A summary of the findings are shown in Table 1.

Conclusion: Patients who were black were less likely to receive a biologic and more likely to use glucocorticoids. ED visit use was higher in black patients, which could be related to higher rates of comorbidities, although differences in geographic location could also influence whether patients visited an ED or saw non-rheumatology providers within or outside the health system. Further studies identifying drivers of racial disparities in access to care and outcomes are needed.

Disclosure: E. He, Roivant Sciences, 5, Synovium, 4; **E. Cornblath**, Synovium, 5; **P. Yalamanchi**, Roivant Sciences, 5, Synovium, 4; **A. Ogdie**, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1; **J. Baker**, None; **M. George**, Bristol-Myers Squibb, 2.

Abstract Number: 0045

Healthcare Practitioner Confidence Assessing Rashes in Patients of Skin of Color with Lupus

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Medical education can promote bias that disproportionately affects patients of color. Patients of color with lupus are especially vulnerable as they often carry a greater disease burden, yet studies show that individuals with darker skin tones are underrepresented in medical educational materials. Given this disparity, we surveyed practitioners' confidence assessing rashes in patients with lupus and skin of color (SOC) and identified factors that may influence confidence.

Methods: We designed a survey to collect demographic information and measure providers' confidence assessing any rash and rashes in patients with lupus and varied skin tones. We invited providers in the Greater St. Louis Area to participate, distributing surveys in person and via Qualtrics. For our primary outcome, we compared Likert scores for providers' confidence assessing rashes in patients with lupus and SOC with least square means and pairwise differences. To identify variables that correlate with practitioners' confidence, we created univariate linear models and multivariate generalized linear models using Spearman's rank correlation coefficients and backward selection. We set statistical significance at $p< 0.05$ for all analyses.

Results: In total, 132 providers participated (Table 1). The mean confidence level diagnosing any rash was significantly higher than diagnosing lupus rashes, including in patients with fair skin and SOC ($p=0.03$; 0.049; < 0.0001). The mean confidence diagnosing lupus rashes in patients with fair skin was also significantly higher than confidence diagnosing lupus rashes in patients with SOC ($p=0.0090$). Mean confidence levels for each specialty were collected (Table 2). Univariate analysis found that provider specialty, years in practice, extent of training, experience in diagnosing, and frequency of treating white or African American patients correlated with confidence level diagnosing lupus rashes in patients of color. However, in the final multivariate model, only practitioners' self-reported experience level diagnosing rashes in patients with lupus and SOC correlated with their confidence doing the same ($p=< 0.001$). Lastly, 92% of participants indicated interest in education about lupus rashes and 93% wanted to learn about rashes in patients of color.

Conclusion: Healthcare providers are less confident evaluating lupus-related rashes in SOC compared to fair skin, representing a disparity between provider confidence and the patient population lupus traditionally affects. While our univariate model demonstrated correlations among confidence in diagnosing rashes in patients with lupus and SOC and several factors, the multivariate model revealed a relationship between confidence and experience alone. Based upon the principle of collinearity, we believe specialty, years in practice, extent of training, and frequency of treating

Table 1 – Characteristics of Participants at Baseline

Characteristic	Dermatologist (N=24)	Rheumatologist (N=33)	Internist (N=57)	Other[1] (N=18)
Provider Role				
NP/PA	0	9	2	1
Resident or Fellow	4	3	37	3
Attending Physician	19	20	17	11
Other	1	1	1	3
How many years in practice (years)[2]				
0 to 5	10	17	42	3
6 to 10	1	5	5	2
11 to 15	4	0	0	0
16 to 20	0	2	1	5
21+	8	9	9	8
Practice Environment (mark all that apply)				
Private Practice	11	13	5	10
Academic Center	12	14	48	7
VA Hospital	4	2	12	1
Other	0	5	1	3
Urban	13	21	50	10
Suburban	15	13	11	10
Rural	2	6	3	0
Inpatient only	0	0	2	2
Outpatient only	12	21	8	12
Both	12	12	47	4
Participants identifying as Hispanic, Latino, or of Spanish Origin				
	1	2	3	0
Practitioner Race[3]				
Asian	3	7	17	2
Black or African American	2	0	1	2
White	19	24	38	13
Other	0	2	0	1
American Indian or Alaskan Native	0	0	0	0
Native Hawaiian or other Pacific Islander	0	0	0	0
Ranked following race or ethnicity of patient as most often seen in practice				
Black or African American	1	9	30	6
White	23	24	25	11

1 Those that elected to fill in OTHER include Family Medicine (5), Med-Peds (1), Orthopedics (1), Surgery (1)
2 One participant identified as Dermatology left this answer blank
3 One participant identified as Internal Medicine left this answer blank
NP = Nurse practitioner, PA = Physician assistant

Characteristics of Participants at Baseline

different ethnicities may all contribute to provider experience level. Training is unique as it can be modified immediately. Over 90% of participants were interested in education on this topic. Future educational interventions may help practitioners improve their confidence when diagnosing rashes in lupus patients with SOC.

Table 2 - Distribution of provider characteristics regarding extent of training, experience in diagnosing, and confidence diagnosing rashes as a function of provider specialty training

Characteristic	Dermatologist (N=24)	Rheumatologist (N=33)	Internist (N=57)	Other[2] (N=18)
Non-white providers (%)	20%	27%	32%	27%
Extent of training involving (mean)[1]				
Any rash	4.00	2.85	2.80	2.83
Lupus rash	3.96	2.81	2.57	2.59
Lupus rash – fair skin	3.88	2.67	2.61	2.33
Lupus rash – skin of color	3.71	2.42	2.00	2.00
Experience in diagnosing (mean)[1]				
Any rash	3.96	2.76	2.68	2.82
Lupus rash	3.65	2.70	2.14	2.29
Lupus rash – fair skin	3.52	2.70	2.14	2.06
Lupus rash – skin of color	3.26	2.46	1.79	1.88
Confidence in diagnosing (mean)[1]				
Any rash	3.57	2.42	2.36	2.53
Lupus rash	3.48	2.52	1.95	2.12
Lupus rash – fair skin	3.48	2.52	2.02	2.00
Lupus rash – skin of color	3.26	2.24	1.68	1.82
Mean confidence in diagnosing based on specialty following multivariate analysis				
Any rash	Dermatology > Internist > Rheumatology			
Lupus rash	Dermatology > Rheumatology > Internist			
Lupus rash – fair skin	Dermatology > Rheumatology > Internist			
Lupus rash – skin of color	No correlation based on specialty after multivariate analysis			

1 Assigned 1 ('None'), 2 ('Very Little'), 3 ('Moderate'), and 4 ('A lot') for each provider survey response; the mean for each specialty group is recorded rounded to the nearest hundredth.
2 Those that elected to fill in OTHER include Family Medicine (5), Med-Peds (1), Orthopedics (1), Gen Surgery (1).

Distribution of provider characteristics regarding extent of training, experience in diagnosing, and confidence diagnosing rashes as a function of provider specialty training

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Abstract Number: 0046

Socioeconomic Disparities in Functional Status Among RA Patients: A Longitudinal Analysis Using RISE Data

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

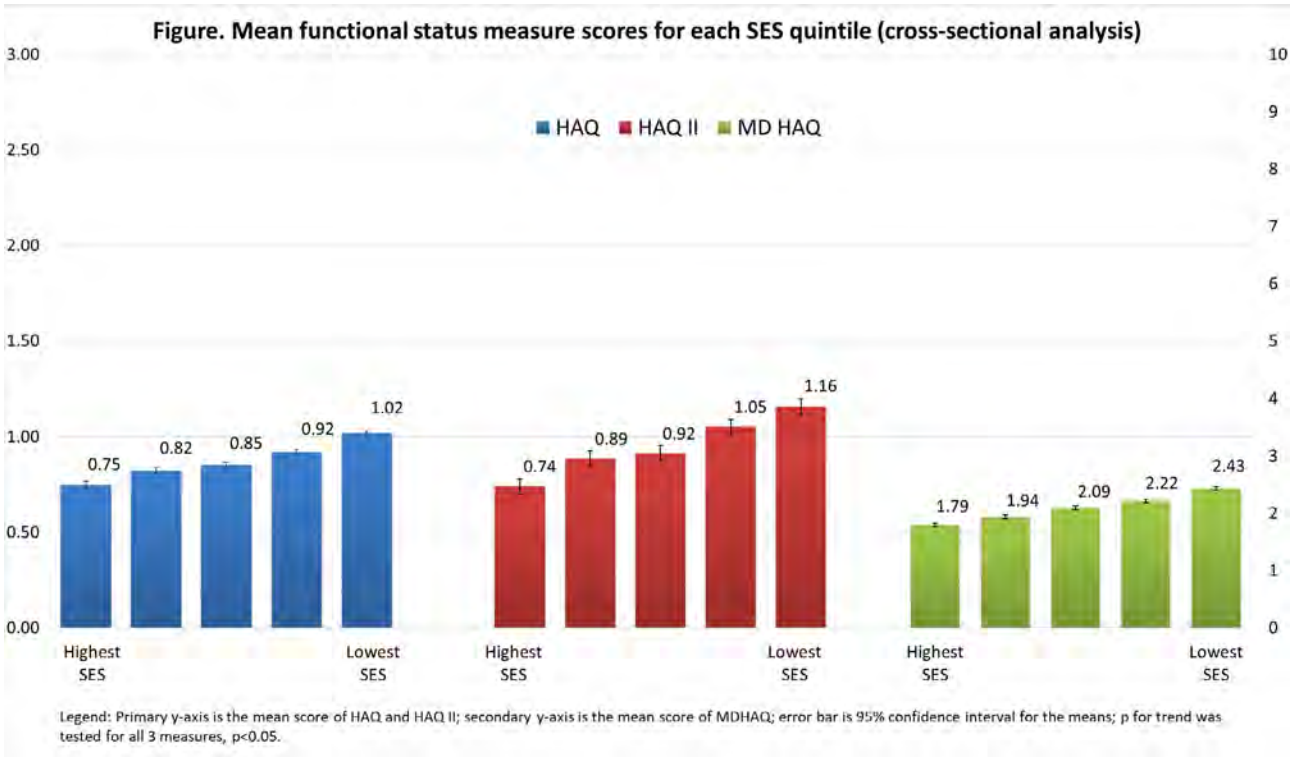
Background/Purpose: Prior studies have shown that RA outcomes, including disease activity, erosions, and disability, are worse among patients with low socioeconomic status (SES). However, few studies have examined the relation-

Table 1. Demographics of patients in cross-sectional analysis and MDHAQ longitudinal analysis

	RA patients with any FSAM score recorded N=83,965		RA patients with at ≥ 1 MDHAQ score recorded in 2 consecutive calendar years N=24,846	
	N	%	N	%
Female	64649	77.0	19134	77.01
Age, mean (SD)	63.4 (13.7)		63.8 (13.2)	
Race/Ethnicity				
White	60037	71.5	17985	72.4
Hispanic	4304	5.1	992	4.0
African American	6900	8.2	2250	9.0
Asian	1106	1.3	394	1.6
Other/Mixed	4996	6.0	1464	5.9
Unknown/Declined	6622	7.9	1761	7.1
Insurance				
Private	22584	26.9	7477	30.1
Medicare	24698	29.4	8798	35.4
Any Medicaid	2051	2.4	388	1.6
Other	1763	2.1	474	1.9
Unknown	32869	39.2	7709	31.0
Area Deprivation Index				
Highest SES quintile (ADI score 1-18)	16718	19.9	4916	19.8
2nd Quintile (ADI score 19-34)	16424	19.5	4963	20.0
3rd Quintile (ADI score 35-51)	16845	20.1	4995	20.1
4th Quintile (ADI score 52-71)	17351	20.7	5013	20.2
Lowest SES quintile (ADI score 72-100)	16627	19.8	4959	19.9
Geographic division				
New England	953	1.1	203	0.8
Mid-Atlantic	9068	10.8	1397	5.6
East North Central	10486	12.5	2076	8.4
West North Central	7972	9.5	2730	11.0
South Atlantic	32715	39.0	10971	44.2
East South Central	11688	13.9	3900	15.7
West South Central	2843	3.4	1317	5.3
Mountain	3719	4.4	1382	5.6
Pacific	4521	5.4	870	3.5
Functional status measures documented				
HAQ	20500	24.4	-	-
HAQ II	6525	7.8	-	-
MDHAQ	56940	67.8	-	-

ship between RA functional outcomes and SES at the national level. We used the ACR's Rheumatology Informatics System for Effectiveness (RISE) registry to investigate the relationship between individual SES and functional status (FS) among individuals with RA across U.S. rheumatology practices.

Methods: Data derived from RISE, a national EHR-enabled registry that passively collects data on all patients seen by participating rheumatology practices. As of 2018, RISE held validated data from 1,113 providers in 226 practices,



representing about 32% of the U.S. clinical rheumatology workforce. Patients included in this study were ≥18 years old, had ≥ 2 visits with RA codes ≥ 30 days apart, and ≥ 1 FS measure (MDHAQ, HAQII, or HAQ) in 2016-2018. As a proxy for SES, we used the Area Deprivation Index (ADI) score, a 9-digit ZIP-code-based indicator of neighborhood socioeconomic disadvantage (range 1-100, higher score = lower SES).

We investigated cross-sectional and longitudinal relationships between FS and SES. In a cross-sectional analysis, we calculated the mean FS scores for each quintile of SES. We used only the most recent FS measure for patients with ≥ 1 score recorded during a calendar year. In a longitudinal analysis, patients with ≥2 of the same FS measure, at least 12 months apart, were categorized as worsening (Y/N) based on the minimal clinically important difference for each tool. We used multi-level logistic regression to assess the association of worsening FS for each quintile of SES, accounting for age, sex, race, baseline FS score, and clustering by practice.

Results: 83,965 patients from 109 practices were included (characteristics in Table). MDHAQ was the most commonly reported FS measure (67.8% of patients), followed by HAQ (24.4%) and HAQII (7.8%). Overall, mean (SD) FS scores for these measures were 2.1 (2.0), 0.89 (0.58), 0.9 (0.6), respectively.

In the cross-sectional analysis, mean FS score was worse at lower SES levels, regardless of the measure used (p-trend< 0.05, see Figure). Among 24,846 RA patients included in the longitudinal analysis with MDHAQ scores, the proportion of patients with a worsening score increased modestly as lower SES levels, even after adjustment (p< 0.05): in the highest SES quintile, 12.7% (95% CI 8.9%-16.5%) patients worsened; in the lowest SES quintile, 16.6% (95% CI 12.1%-21.1%) worsened. The same trend was observed for patients with HAQ and HAQII.

Conclusion: We found evidence of significant disparities in FS across SES in this national cohort of individuals with RA, with worse functional status across each successive lower quintile of SES. In addition, FS declined more rapidly over time in those with lower SES. Future research is needed to identify the source of these disparities, which exist in spite of access to rheumatologic care for all patients in the cohort.

Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

Disclosure: J. Li, None; **G. Schmajuk**, None; **M. Evans**, None; **Z. Izadi**, None; **P. Katz**, None; **A. Ogdie**, AbbVie, 5, Amgen, 2, 5, BMS, 1, Celgene, 1, Corrona, 1, Janssen, 1, Eli Lilly, 1, Novartis, 2, 5, Pfizer, 2, 5, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 2, Rheumatology Research Foundation, 2, National Psoriasis Foundation, 2; **L. Suter**, None; **J. Yazdany**, Eli Lilly, 5, Astra Zeneca, 5.

Abstract Number: 0047

Administrative Barriers to Enrollment of Ethnic Minorities in Clinical Research of Rheumatic/Immune-Mediated Diseases

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Inclusion of ethnic minority subsets in clinical research remains subpar despite mandates for increased participation. Lack of trust, cultural sensitivity and bias, stereotyping, health literacy are all acknowledged barriers that are active areas of rehabilitation [4, 5]. Ethnic minority patients are often cared for by ethnic minority physicians, and despite their limited health coverage, target academic institutions to receive care[1, 2].Therefore, academic institutions with ethnic minority clienteles and physicians are the prime targets for recruitment of non-Caucasians in clinical trials. However, whether administrative operations at ethnic minority institutions can facilitate this process, and in timely fashion, is unknown. We examined the time intervals for approval of administrative procedures for clinical research at a predominantly ethnic minority academic institution.

Objective: To assess time intervals for the administrative approval procedures for clinical research at a predominantly ethnic minority institution.

Methods: At a single historically Black academic institution (HBCU), we examined the time points for multiple clinical trials between submission and responses to institutional review board review, and contract negotiations. The agreed contractual numbers for each study and their unit reimbursement were also obtained. Time to approval of each stage was documented, including the final approval in relation to study initiation.

Results: The average time for IRB approval across 8 clinical trials was 3.75 months, ~ 6 weeks longer than other local academic institutions (1.5-3m). The most frequent reason for delay was multiple, repetitive queries, which could have been avoided by systematic review processes. Additionally, contract approval for 4 funded clinical trials was 8.5 months, resulting in the inability to recruit patients before study closure, with potential loss of institutional funds ($10, 226/patient).

Conclusion: At a single HBCU academic site, there was a consistent, prolonged interval for each step of approval of clinical research. Although it is unknown if enrollment would have met targets, these results suggest a significant lost opportunity for inclusion of ethnic minority subsets in clinical trials. Further, the potential loss of revenue to the insti-

tution due to these inefficiencies, cannot be ignored. Measures to improve the process must therefore be an integral requirement of the overall process for increased ethnic minority involvement in clinical research.

Disclosure: B. Banbury, None; **S. Dowell**, Horizon Pharma, 8, Bristol Myers Squbb, 2, Pfizer, 2; **G. Kerr**, Novartis, 1, BMS, 1, 2, Gilead, 1, Regeneron, 1, Janssen, 1; **M. Quinones**, Pfizer, 2, Ampel, 2, Biogen, 2, Sanofi Genzyme, 8; **G. Okoye**, Pfizer, 2, Unilever, 5; **I. Jileaeva**, None.

Abstract Number: 0048

Determinants of Participation in Clinical Trials Among Patients with Lupus in the United States

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patient and family participation in research is critical to improving health outcomes, and identifying factors that contribute to participation or lack of participation in clinical trials is a necessary first step. There is limited data regarding why patients with lupus choose to participate in clinical trials. Research in other conditions has identified factors including age, race/ethnicity, gender, presence of co-morbidities, and disease severity. The primary objective of this study was to examine whether age, race/ethnicity, sex, or greater disease organ involvement are associated with *previous* clinical trial participation in patients with lupus.

Methods: Data were collected by The Lupus and Allied Diseases Association, the Lupus Foundation of America, and the Lupus Research Alliance for their Externally-led Patient-Focused Drug Development (PFDD) Initiative. From this dataset, we examined the influence of age, sex, race/ethnicity, and organ involvement on clinical trial participation. Data was available for 2,100 individuals with lupus or their parents/legal guardians for children. Participants completed a 46-question survey (in English or Spanish) electronically or on paper, which was distributed online or at lupus events. Logistic regression was used to test a model including demographic and disease characteristics; it was expanded to include duration of illness, number of medications, number of comorbidities, and number of other autoimmune diseases.

Results: Survey participants' characteristics are summarized in Table 1. More than 50% of respondents had not participated in a clinical trial. Univariate analysis suggests that race/ethnicity, age of symptom onset, illness duration, lupus type, and history of organ transplant were associated with trial participation. The expanded model indicated that African Americans (OR=1.71) and Hispanics (OR=1.42) were more likely to participate than whites, respondents reporting longer illness duration were more likely to participate (OR=1.52), and respondents with a greater number of medications (OR=1.13) and other self-reported autoimmune diseases (OR=1.07) were more likely to participate in a clinical trial (Table 2).

Conclusion: Several medical (i.e., illness duration, number of medications and comorbid autoimmune disorder) and demographic (i.e., race/ethnicity) factors appear to be important determinants of participation in clinical trials. Compared to previous studies, these data suggest that African American and Hispanic individuals are willing to

Characteristics	% Non-participants (N=1906)	% Participants (N=314)	P-value
Demographical			
Female	96.54	96.82	0.8018
Race			
American Indian or Alaska Native	0.58	0.64	0.7049
Asian	3.67	4.14	0.6858
Black or African American	13.64	18.79	0.0160
Hispanic or Latino	11.75	12.74	0.6168
Native Hawaiian or Other Pacific Islander	0.94	0.32	0.5033
White	66.00	58.28	0.0079
Other	3.41	5.10	0.1400
Age			0.1160
Under 18 years	1.57	1.91	
18-29 years	13.33	8.92	
30-39 years	20.41	17.20	
40-49 years	23.71	25.80	
50-59 years	22.93	27.71	
60 years or older	18.05	18.47	
Age at onset of symptoms			0.0004
Under 18 years	22.06	31.53	
18-29 years	34.19	30.25	
30-39 years	20.33	23.25	
40-49 years	14.71	9.87	
50-59 years	6.30	4.46	
60 years or older	2.42	0.64	
Duration of illness			<.0001
Less than 2 years	15.75	5.10	
2-5 years	24.62	12.10	
6-10 years	23.20	21.02	
11-20 years	20.21	32.48	
More than 20 years	16.22	29.30	
Disease			
Type of lupus			0.0576
Cutaneous (subacute)	3.01	1.60	
Cutaneous (discoid)	3.48	3.19	
Drug-induced	0.32	0	
SLE without nephritis	73.18	68.69	
SLE with nephritis	20.01	26.52	
On dialysis	4.13	2.30	0.5479
Received organ transplant	3.65	9.20	0.0268
Lupus impacted sleep cycle	85.86	83.07	0.2550
Factor influencing treatment choice			
Delay or prevent symptoms	15.98	13.66	0.4207
Improve symptoms	51.35	51.91	0.8871
Increase life expectancy	12.16	10.93	0.6315
Slow organ damage	16.53	16.94	0.8903
Other	3.02	2.73	0.8303
Most negatively impactful symptoms*			
Joint and muscle pain or swelling	71.98 (1.74±0.79)	71.66 (1.78±0.76)	0.9048
Fatigue	70.57 (1.79±0.79)	66.60 (1.81±0.80)	0.1512
Stomach or bowel problems	15.27 (2.25±0.75)	14.65 (2.26±0.74)	0.7774
Sun sensitivity	13.27 (2.33±0.78)	15.29 (2.25±0.81)	0.3344
Increased susceptibility to infections	13.38 (2.11±0.78)	14.33 (2.06±0.86)	0.6474
Reduced physical strength	13.22 (2.23±0.77)	11.46 (2.31±0.67)	0.3907

*The mean of the ranking of most negatively impactful symptoms (1, 2, 3) ± the standard deviation is shown in parentheses.

Table 1. Demographic and disease characteristics of clinical trial non-participants vs. participants

participate in clinical trials, but perhaps only trials that are related to their chronic condition, or this finding may be due to underrepresentation in this sample. Future research studies with larger samples of diverse participants are recommended.

Parameter	Estimate	Standard Error	Odds Ratio	95% Confidence Limits	P-value
Intercept	-3.12	0.53			<.0001
Age (ordinal)	-0.05	0.06	0.96	0.85 - 1.07	0.43
Female	0.01	0.36	1.01	0.50 - 2.04	0.97
Race (ref white)					0.04
Asian	0.32	0.34	1.38	0.71 - 2.68	0.35
Black	0.53	0.18	1.71	1.21 - 2.41	0.00
Hispanic	0.35	0.20	1.42	0.96 - 2.11	0.08
Hawaiian	-0.87	1.04	0.42	0.05 - 3.20	0.40
Indian	0.22	0.80	1.25	0.26 - 5.98	0.78
Others	0.46	0.30	1.58	0.88 - 2.83	0.13
Involvement (ref skin and joint)					0.13
Beyond skin and joints	0.28	0.17	1.32	0.95 - 1.86	0.10
Involving organs	0.27	0.16	1.31	0.97 - 1.78	0.08
Duration of illness	0.41	0.06	1.52	1.35 - 1.70	<.0001
Quality of Life worst	-0.10	0.07	0.91	0.79 - 1.05	0.19
Number of Medications	0.12	0.05	1.13	1.03 - 1.24	0.01
Number of Comorbidities	0.03	0.04	1.03	0.94 - 1.12	0.54
Number of autoimmune diseases	0.07	0.04	1.07	0.99 - 1.16	0.10

Table 2. Multivariate logistic regression model showing effect of different variables (e.g., age (on ordinal scale), gender, race) on clinical trial participation

Disclosure: O. Harry, Lupus Research Alliance, 2; **C. Langefeld**, Lupus Research Alliance, 2; **M. Marion**, Lupus Research Alliance, 2; **T. Younts**, None; **L. Crosby**, Lupus Research Alliance, 2; **M. Vitolins**, None; **A. Modi**, Lupus Research Alliance, 2.

Abstract Number: 0049

Disparities in Patient Portal Use Among Patients with Rheumatic and Musculoskeletal Diseases in a Large Academic Medical Center

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Many aspects of rheumatic and musculoskeletal disease (RMD) management require a high level of patient agency and open avenues for patient-provider contact. In the era of COVID-19 and social distancing the shift to virtual care has become essential for the continued care of our patients. More so than ever before, patient portal and health technology use has become crucial in the care of patients with RMDs around the country.

Many studies have shown positive effects on outcomes and satisfaction when patients are more engaged in their care through digital technology use. However, several studies have shown that low health literacy, lower educational

Table 1. Adjusted Odds Ratios of MyChart Activation by Patient Characteristics

Covariates	*aOR (95% CI)* Complete Cases* (N=4756)
Visit date, 120 days (~4 months) more recent	**1.22 (1.16, 1.28)**
Number of visits (vs 3 or more)	
1 or 2 (ref)	1.00
3 or more	**1.35 (1.13, 1.60)**
Age group (vs Baby Boomers)	
17-24 years (Gen Z)	**5.39 (2.67, 10.9)**
25-39 years (Millennials)	**2.86 (2.22, 3.69)**
40-54 years (Gen X)	**1.72 (1.42, 2.08)**
55-74 years (Baby Boomers)	1.00
75 years and older (Silent Gen)	0.80 (0.62, 1.03)
Sex (vs Females)	
Females (ref)	1.00
Males	**0.61 (0.51, 0.71)**
Race/Ethnicity (vs White/Caucasian)	
White/Caucasian (ref)	1.00
Black/African American	**0.39 (0.33, 0.47)**
Hispanic/Latino	0.86 (0.56, 1.31)
Other Race	**0.44 (0.27, 0.70)**
Asian	1.04 (0.52, 2.09)
AI/AN or NH/PI	1.09 (0.44, 2.70)
Primary Language (vs English)	
English (ref)	1.00
Spanish	**0.31 (0.20, 0.48)**
Other	0.46 (0.21, 1.01)
County of residence (vs NC Urban)	
NC Urban (ref)	1.00
NC Suburban	**1.22 (1.00, 1.49)**
NC Rural	**0.78 (0.65, 0.93)**
Insurance	
Medicare (ref)	1.00
Commercial	**1.77 (1.41, 2.23)**
Uninsured	0.85 (0.67, 1.08)
Medicaid	**0.64 (0.49, 0.83)**
State	**2.67 (1.76, 4.05)**
Military	**2.20 (1.19, 4.10)**
Median income‡	
<$25,000	**0.62 (0.42, 0.90)**
$25,000 - <$50,000 (ref)	1.00
$50,000 - <$75,000	**1.89 (1.53, 2.33)**
$75,000 - <$100,000	**3.61 (1.74, 7.47)**

American Indian/Alaska Native (AI/AN), Native Hawaiian/Pacific Islander (NH/PI)
*North Carolina (NC) residents with no missing data (complete cases)
‡Based on available 2017 income data by zip code
aOR>1 indicates higher odds of being a MyChart user; aOR<1 indicates lower odds of being a MyChart user

Table 1

attainment, residence in a rural area, being of minority race/ethnicity, and older age are associated with lower rates of technology ownership and use.

To date there have been limited studies examining inequities in health technology use among patients with RMDs. Our goal is to identify characteristics of technology users versus non-users from a group of patients in a large hospital-based rheumatology clinic.

Methods: Epic (electronic medical record, EMR) data was queried to identify established patients of the University of North Carolina Hospitals adult rheumatology clinic between November 1, 2017 through November 30, 2019. Demographic and clinical data were collected and used to compare patients who have activated Epic's patient portal (MyChart) to patients who have not activated MyChart. MyChart use was modeled using logistic regression and adjusted odds ratios and confidence intervals were estimated.

Results: We identified 5287 established patients who were seen at our clinic during the study period. The mean age was 54.4 years and 73.6% were female. Fifty-one percent of established patients identified as white/Caucasian and 26.6% as black/African American. Eighty-nine percent identified English as their primary language. Patients were evenly split between urban, suburban, and rural residences. Two-thirds had a median adjusted gross income between $25,000 - < $50,000. Thirty-six percent had Medicare and 25.4% had commercial insurance.

Using data from complete cases among North Carolina residents (n=4756), we found that younger age, suburban residence, commercial/state/military insurance, and median income $50,000 or greater were associated with significantly higher odds of MyChart activation.

Characteristics significantly associated with lower odds of MyChart use were male gender, black/African American or "other" race, Spanish as primary language, rural residence, Medicaid as primary payor, and median annual income < $25,000.

Conclusion: These results support the findings of previous studies that show that residence in a rural area, being of minority race/ethnicity, and older age are associated with lower rates of health technology use. We also noted that lower median income, having Medicaid as primary insurance, and non-English primary language are associated with lower odds of patient portal activation. We hope that by studying factors associated with lower EMR use we can identify at-risk populations who may benefit from targeted interventions to close the gap in health technology use among patients with RMDs.

Disclosure: E. Sun, None; **C. Alvarez**, None; **L. Callahan**, Gilead, 5; **S. Sheikh**, Pfizer, 2, GSK, 5.

Abstract Number: 0050

Demographic Disparities in the Medically Underserved Populations of Southern California: A Rheumatology Cohort of Cytokine Release Syndrome Patients Due to COVID-19

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Healthcare Disparities in Rheumatology Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1: Demographic characteristics of patients with CoV-CRS referred to the rheumatology consult service.

	University Medical Center		County Medical Center		Total	
	N	%	N	%	N	%
Age						
18-30	3	4.7%	1	1.2%	4	2.7%
31-40	5	7.8%	5	5.8%	10	6.7%
41-50	10	15.6%	8	9.3%	18	12.0%
51-60	14	21.9%	20	23.3%	34	22.7%
61-70	15	23.4%	24	27.9%	39	26.0%
71-80	10	15.6%	24	27.9%	34	22.7%
81-90	7	10.9%	3	3.5%	10	6.7%
91-100	0	0.0%	0	0.0%	0	0.0%
101+	0	0.0%	1	1.2%	1	0.7%
Total	64	100.0%	86	100.0%	150	100.0%
Sex						
Female	27	42.2%	14	16.3%	41	27.3%
Male	37	57.8%	72	83.7%	109	72.7%
Ethnicity						
White, Non-Hispanic	17	26.6%	27	31.4%	44	29.3%
Asian	21	32.8%	3	3.5%	24	16.0%
Black	8	12.5%	6	7.0%	14	9.3%
Hispanic	16	25.0%	49	57.0%	65	43.3%
Others	2	3.1%	1	1.2%	3	2.0%
Insurance						
Public	28	44%	74	86.0%	102	68.0%
Private	36	56%	9	10.5%	45	30.0%
None			3	3.5%	3	2.0%
Incarcerated	0	0	35	40.7%	35	23.3%
Healthcare Facility Residents	23	35.9%	5	5.8%	28	18.7%
Total Deaths	16	25.4%	15	17.4%	31	20.8%

Demographic characteristics of patients with CoV-CRS referred to the rheumatology consult service

Table 2: Demographic characteristics of zip codes with the highest number of patients referred for CoV-CRS

Zip Code	92324	92553	92571	92551	92501	92555	91710	San Bernardino	Riverside
Number of Patients	13[a]	11	7	7	5	5	30[b]		
Ethnicity									
· Hispanic	6	11	5	2	5	2	8		
· Black	0		1	2		0	1		
· Asian	2		1	2		0	1		
· White, non-Hispanic	1			1		2	20		
· Other									
Sex:									
· Male	6	9	5	4	5	4	30		
· Female	3	2	2	3	0	1	0		
Insurance:									
· Public	3	10	5	4	5	4	30	41.8%	40.6%
· Private	6	1	2	3	0	1	0	56%	58.2%
· None								9.4%	10%
Outcome									
· Deceased	7	2	1	0	1	3	4		
· Discharged	5	8	6	7	4	2	18		
· Current Inpatient	1	1					8		
Zip Code Demographic(%)[c]									
· Hispanic	68.7	66.3	74.5	62.2	55.1	47.6		52.8	48.4
· Black	6.5	16.3	11.9	17.8	6.3	22.3		7.9	6.1
· Asian	4.7	4.8	5.4	5.8	5.9	8.3		6.8	6.2
· White, non-Hispanic	18.3	10.3	31.3	12.2	29.1	18.2		29.2	35.9
Poverty Rate (%)[c,d]	14.9	20.8	18.1	17.5	17.4	8.4		17.30%	14.70%
								California Poverty Rate 12%	

[a] 7 from Healthcare facility including skilled nursing facilities
[b] 29 inmates
[c] Reference: https://data.census.gov/cedsci/
[d] Poverty Rate refers to the percentage of people living below the poverty threshold set by the government

Demographic characteristics of zip codes with the highest number of patients referred for CoV-CRS

Background/Purpose: The severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has led to the present coronavirus disease (COVID-19) pandemic. Multiple epidemiologic reports across the country show that COVID-19 disproportionately affects minorities.

San Bernardino and Riverside counties comprise two of the geographically largest and ethnically diverse counties in California and in the United States. Much of its population is indigent and relies on public health services.

A rheumatology-driven protocol was developed in March 2020 for the management of patients with cytokine release syndrome due to COVID-19 (CoV-CRS) at a university-based and a county hospital. This study analyzes the demographic disparities among this patient population.

Methods: 150 patients were included in this retrospective chart review study with data collected between March 15-May 30, 2020. Hospital-based electronic medical records were utilized to collect information on patients referred to the rheumatology consult service for the evaluation of CoV-CRS. Demographic data, including age, sex, ethnicity, and postal zip code entered on hospital admission was collected. Co-morbidities, medications used and various laboratory data, including CBC with differential, ferritin, fibrinogen, complete metabolic profile, autoantibody profiles were included. Hospital-based and county-reported data were utilized to determine general populations affected by COVID-19. Descriptive statistics were used for analysis.

Results: 71.3% (107/115) of patients were within the 51-80 year-old age group (mean age 61.7 years). Males comprised 72.7% of the cohort. Hispanics represented the majority of this population (43.3%), followed by White non-Hispanics (29.3%), Asians (16%) and Blacks (9.3%). Public insurance was used in 68%, and private insurance in 30%. Thirty-five patients (23.3%) were incarcerated at the time of hospitalization; while 28 (18.7%) were from various healthcare facilities including skilled nursing facilities.

Patients came from a total of 53 postal zip codes, but 52% resided in 7 zip codes: 91710 (30); 92553 (11); 92324 (13, including 7 from one healthcare facility); 92551 (7); 92571 (7); 92501(5); 92555 (5). Census data shows that the population at these zip codes are predominantly Hispanic (47.6-74.5%). Four of these zip codes are represented by 18.4-41.5% greater poverty rates compared to their respective counties. Of 31 patients who died in our cohort, 18 (58%) were residents of these zip codes.

Of note, 29/30 patients located at zip code 91710 were incarcerated at a local state prison for men. Twenty (69%) were white non-Hispanic; 7 (24.1%) were Hispanic; 1 (3.4%) Asian and 1 (3.4%) Black. There was a total of 10 Covid-19 related deaths in the California prison system, 4 of which were part of this cohort.

Conclusion: A higher percentage of patients affected with CoV-CRS in this rheumatology-managed cohort from Southern California were largely male, of Hispanic ethnicity, used public insurance, living in an area with higher poverty rate, or were incarcerated or residents at a healthcare facility. More than half of deaths in the cohort were observed in this particular population.

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Abstract Number: 0051

COVID-Related Distress and Mental Health in Adult Rheumatology Patients During the COVID-19 Pandemic

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SESSION INFORMATION
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Session Type: Poster Session A
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Background/Purpose: The novel coronavirus disease 2019 (COVID-19) pandemic has significantly affected all aspects of society, especially in the epicenters of New York City (NYC) and the Bronx. The Bronx patient population is characterized by a high percentage of individuals from racial/ethnic minorities and low socioeconomic status. Black and Hispanic individuals have been disproportionately affected by COVID morbidity and mortality, with the Bronx accounting for the highest number of cases per capita in NYC. Low-income Bronx residents also may have been more susceptible to financial losses brought on by the pandemic. With the added concern of increased risk of infection and poorer outcomes in rheumatology patients, Bronx rheumatology patients may be particularly susceptible to emotional suffering during the COVID-19 pandemic. We sought to investigate the burden of mental health symptoms on rheumatology patients and the association with COVID-related distress from the Bronx following the peak of the outbreak.

Methods: A registry was created of Montefiore Medical Center (MMC) rheumatology patients consisting of 1,692 adult and pediatric patients. Patients were contacted over email or phone to consent and participate in a survey on the impact of the COVID-19 pandemic. Participants completed surveys by email or phone. To assess stress we used the Perceived Stress Scale (PSS), to assess depression symptoms we used the Patient Health Questionnaire 8-item depression screen (PHQ-8), and to assess anxiety we used the Generalized Anxiety Disorder-7 item screen (GAD-7). The PSS, GAD and PHQ-8 are all scales (0-40, 0-21, 0-27, respectively) and can be categorized as mild, moderate, severe. Participants were asked to rate their distress related to the COVID pandemic over the last 30 days on a scale from 0-10 (0 no distress, 10 extreme distress). Spearman rank correlations were used to determine whether COVID-related distress scores were correlated to mental health scales.

Results: Of the 361 survey participants , 202 (56%) had complete data on mental health scales. Among those with complete data, 123 (56%) had at least mild symptoms of depression, 36 (16%) had moderate, 27 (12%) had severe, with median score 5 (IQR 2, 11); 106 (48%) had at least mild symptoms of anxiety, 31 (14%) had moderate, 20 (9%) had severe, median score 4 (IQR 1,9). Based on the Perceived Stress Scale, 182 (83%) had moderate stress, and 32 (15%) had severe stress, median score 21 (IQR 18-24) . The median level of COVID-related distress was 6 (IQR 3,8). All mental health scales were moderately correlated with the COVID-related distress scale; PSS (rho 0.6, $p< 0.0001$), PHQ-8 (rho 0.5, $p< 0.0001$), GAD-7 (rho 0.7, $p< 0.0001$).

Conclusion: Surveyed rheumatology patients reported high levels of COVID-related distress and perceived stress. COVID-related distress levels correlated with levels of anxiety, depression, and overall perceived stress. These results underscore the importance of addressing mental health symptoms in rheumatology patients during the pandemic.

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Abstract Number: 0052

Loneliness and Social Isolation Are Important Social Determinants Among Patients from Minority Communities with Rheumatic Diseases

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Session Time: 9:00AM–11:00AM

Background/Purpose: Loneliness and social isolation have detrimental effects on health and are associated with risk of an earlier death, depression and poor self-rated health. Few studies have investigated the prevalence of these social determinants among patients with rheumatic conditions and none have focused on minority communities. We therefore set about to determine the prevalence and pervasiveness of loneliness and social isolation among African American and Latinx communities.

Methods: This is an ongoing community based participatory research conducted by physicians from the University of Rochester Medical Center (URMC) in conjunction with members of the Rochester community. The study aims to survey a 1,000 patients and conduct 5 focus group meetings, from the African American and Latinx communities seen at the URMC Center and two community health centers. The *Campaign to End Loneliness Measurement Tool*, a short and academically rigorous took with a simple scoring method was used to assessed loneliness. Scores range from 0-12 with higher scores representing more pronounced loneliness. The *Lubben social network scale -6* was used to calculate the presence and extent of social isolation; scores range between 0 and 30, with a lower score indicating less social engagement. The questionnaires also gathered information on age, gender, zip code, presence of chronic medical conditions, disease duration and the number of hospitalizations.

Results: To date, 367 surveys have been provided of which 154 surveys have been returned. Of these, 110 had complete data for analysis and comprised of 78 females and 32 males with a mean age of 50.2 years. A total of 40

	Patients with no chronic medical conditions (n=40)	Patients with rheumatic disease (n=48)	p-value	Patients with other chronic diseases (22)
Loneliness score (Campaign to End Loneliness)	2.6	3.5	0.01	5.7
Social isolation score (Lubben-6)	18.3	14.4	0.40	12.6
Female: male	24: 16	38:10		16:6
Mean age (median)	43.3 (38.5)	54.4 (55)		54.3 (56)
Disease duration (<5 vs. >5 years)	N/A	10:38		8: 14
Hospitalizations	8	12		10

Table shows scores for loneliness and social isolation among patients with chronic medical conditions compared to those with no chronic medical conditions along with demographics for all groups

respondents, comprised of 24 females with a mean age of 43.3 years reported no arthritis or chronic medical conditions. Another 48 patients, with 34 females and a mean age of 54.4 years, noted arthritis or other rheumatic conditions. There were an additional 22 patients who disclosed other chronic medical conditions (heart disease, diabetes and mental health). The mean loneliness score for patients with arthritis was 3.5 with 8 patients having total scores of 8 or higher and compared with a mean score of 2.6 (p=0.01) among those without chronic medical conditions with only 2 patients in this group noted to have a score of 8 or above. The mean Lubben score for the arthritis cohort was 14.4 compared with 18.30 (p=0.4) for those without chronic medical conditions. Most patients with chronic disease had >5 years disease duration. Hospitalization rates were surprisingly similar between the groups (see Table).

Two focus group meetings have been completed and included 28 subjects (21 females and 7 males). Preliminary quantitative analysis revealed an emphasis of family in relation to loneliness and the relevance of spirituality with regards to overcoming social isolation. The role of race and not fitting in to the "white society" was highlighted as a contributor to loneliness and social isolation.

Conclusion: Loneliness and social isolation are common and more pronounced in members of minority communities with rheumatic diseases. Efforts to measure these social determinants and develop methods to address them are important steps in implementing strategies to overcome healthcare disparities.

Disclosure: A. Anandarajah, None; **N. Shelton**, None; **L. Yi**, None; **M. Graham**, None; **E. Papa**, None; **R. Carter**, None.

Abstract Number: 0053

¿Comprende? Assessing the Readability of Freely Available Spanish-Language Online Patient Education Materials for Rheumatologic Diseases

Carleigh Zahn[1], Bharat Kumar[1] and Cindy Puga[2], [1]University of Iowa Hospitals and Clinics, Iowa City, IA, [2]Carver College of Medicine, Iowa City

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Spanish is the second most popular language in the United States and third most commonly spoken language internationally. Despite the high prevalence of Spanish and the increasing recognition that language barriers and low health literacy contribute to healthcare disparities, there is little information about Spanish-language patient education materials (PEMs) regarding rheumatologic diseases. In this investigation, we systematically examine and appraise the accuracy and readability of Spanish-language online PEMs using validated measures.

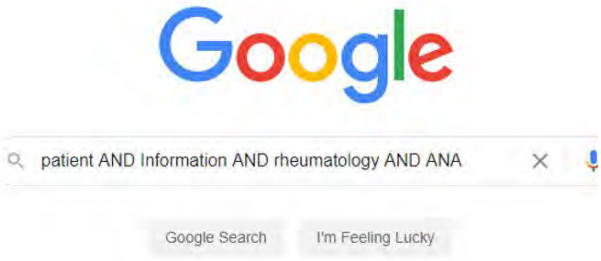
Methods: Three investigators compiled a set of common rheumatologic terms in both Spanish and English (Table 1). Two investigators independently conducted a search to identify Spanish-language PEMs using a Boolean search strategy (Figure 2) and compared results for consistency. The Spanish-language PEMs resulting from this search were then reviewed for medical accuracy by two investigators. Spanish spelling, grammatical, and syntactical errors were noted by a native Spanish speaker. The PEMs were further evaluated for readability based on (1) Fry Graph calculations, (2) the Fernandez-Huerta modification of the Flesch Reading Ease Score, and (3) the Flesch-Kincaid Grade Level.

Table 1

Rheumatology	Antinuclear antibodies	Lupus	Sjogren	RS3PE	Rheumatic Fever
Arthritis	Rheumatoid Factor	Rheumatoid	Sicca	CRMO	Lyme Disease
Arthropathy	Citrullinated peptide	Felty	Keratoconjunctivitis	CAPS	HIV
Arthralgia	Westergren	Caplan	Polychondritis	FMF	Human Immunodeficiency Virus
Joint pain	Erythrocyte Sedimentation Rate	Spondyloarthropathy	Behcet	HIDS	AIDS
Joint swelling	C-Reactive Protein	Spondyloarthritis	Adamantiades	PFAPA	Acquired Immunodeficiency Syndrome
Rheumatism	Vasculitis	Ankylosing Spondylitis	Gout	TRAPS	Hepatitis
Rheumatica	Arteritis	Psoriasis	Pseudogout	Periodic Fever Syndrome	HCV
Rheumatic	Capillaritis	Psoriatic	Calcium pyrophosphate	Autoinflammatory	HBV
Myositis	Polyangiitis	Osteoarthritis	Basic calcium	Juvenile Idiopathic Arthritis	Tuberculosis
Myopathy	Antiphospholipid	Lumbar stenosis	Crystalline arthropathy	Still's Disease	Parvovirus
Tendinitis	Inflammation	Spinal stenosis	Crystal arthropathy	Kawasaki	Measles
Bursitis	Inflammatory	Diffuse Idiopathic Skeletal Hyperostosis	Crystal arthritis	Giant cell arteritis	Mumps
Tendinopathy	Inflamed	DISH	Crystalline arthritis	Takayasu	Rubella
	Immunity	Lumbago	Fibromyalgia	Osteoporosis	Ehlers-Danlos
	Immune	Spondylolysis	Amplified Musculoskeletal	Osteonecrosis	Crohn Disease
	Anti-neutrophil cytoplasmic antibodies	Spondylolisthesis	Hypermobility	Osteopenia	Ulcerative Colitis
	ANCA	Spondylosis	Scleroderma	Paget's Disease	Celiac Disease
	HLA-B27	Degenerative disk disease	Systemic Sclerosis	Osteitis Deformans	
	Enthesitis	Degenerative joint disease	CREST	Granulomatosis with Polyangiitis	
	Dermatomyositis	Sarcoidosis	CRST	Wegener	
	Polymyositis		Raynaud	Henoch Schonlein	
				IgA Nephropathy	
				IgG4-related disease	

107 terms were searched in both English and in Spanish (Table lists English only)

Logistics of the search:



- Term A: (Patient OR Caregiver) AND
- Term B: (Information OR Resources) AND
- Term C: (Bold terms from first column of Appendix A) AND
- Term D: (Other terms from Appendix A)

- Searching in both Spanish and English
  - Results in Spanish

Demonstration of the Boolean Search Strategy independently conducted by two investigators

Results: The investigators identified 134 Spanish-language PEMs from 14 sources for the 107 terms utilized. Major medical inaccuracies were noted in only 3% of cases (4/134). However, 53.7% had at least one spelling or grammatical error (72/134) and 7.4% (10/134) had more than three spelling or grammatical errors. The Grade Level was determined to be >15 ('College' Level) in 94% of PEMs (126/134), per Fry Graph calculations. Similarly, The Flesch-Kincaid Grade Level was 17.3 (SD=2.3) and Flesch readability score was 5.4 (SD=0.6), signifying "very confusing" text.

Conclusion: Freely available rheumatologic Spanish-language PEMs do not meet accepted standards for patient education. While the majority of Spanish-language PEMs were considered medically accurate, the vast majority of Spanish-language PEMs greatly exceeded the recommended maximum 5th grade reading level. Based on these data, we advocate for the development and dissemination of new Spanish-language PEMs that prioritize both accuracy and readability.

Disclosure: C. Zahn, None; **B. Kumar**, None; **C. Puga**, None.

Abstract Number: 0054

"Is It Spiritual?" Complexities of Understanding Health-Seeking Behaviour in Patients with Chronic Autoimmune Rheumatic Diseases in Sub-Saharan Africa

Maame-Boatemaa Amissah-Arthur[1], Anna Gyaban-Mensah[2], Vincent Boima[1], Ernerst Yorke[1], Dzifa Dey[1], Delali Fiagbe[3], Vincent Ganu[2], Kelvin Acquaye[4] and Christopher Mate-Kole[5], [1]UGMS, Korle Bu Teaching Hospital, Accra, Greater Accra, Ghana, [2]Korle Bu Teaching Hospital, Accra, Greater Accra, Ghana, [3]UGMS, Accra, Greater Accra, Ghana, [4]Univesity of Ghana, Accra, Greater Accra, Ghana, [5]University of Ghana, Accra, Greater Accra, Ghana

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Challenges exist in the management of autoimmune inflammatory rheumatic diseases (AIRDs) in low and middle income countries due to factors, such as poverty and under-resourced healthcare infrastructure. Patient-dependent factors, determined by societal, religious and cultural practices are also contributory factors. We examined the impact of knowledge and perception, socio-economic and cultural factors on health-seeking behaviour and access to healthcare in Ghanaian patients with AIRDs, specifically assessing the factors that contribute to delay in receiving care from formal medical and specialist rheumatology services.

Methods: A cross-sectional study using an explanatory sequential mixed methods design. Structured questionnaires and standardised research instruments assessing demographics, health seeking patterns and contemporary and alternative medicine use were used to obtain quantitative data. Twenty individuals were further divided into two groups; ten for in-depth interviews and ten focus group discussions. Association between the socio-demographic variables, knowledge and perception; predictors of knowledge and access to health care; and duration of symptoms and delay in diagnosis were analysed.

Results: 110 patients enrolled (45.4% RA; 36.4% SLE; 14.5% MCTD, 3.6% SSc). 86.4% were female and the mean age was 36.8 years (SD=14.6 years). The median duration from onset of symptoms until diagnosis was 18 months (IQR = 43.94) across all disease groups. The maximum duration of *seeking help for the first time from onset of*

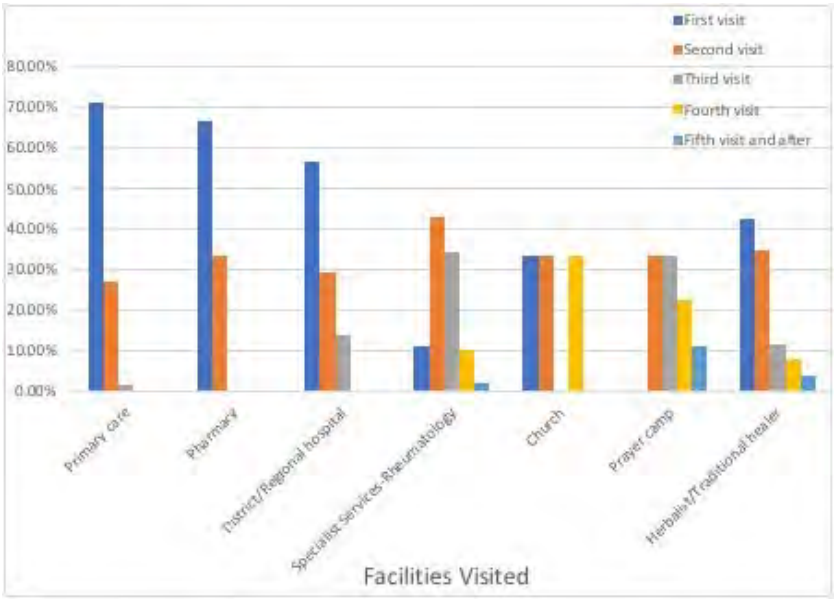


Figure 1. Distribution and order of facilities visited by attendance

Characteristics N (%)	Total	Non-specialist Facilities	Specialist facilities	Non-medical facilities	p-value*
Age Category	110				.593
29 years and below	45	38 (84.4)	4 (8.9)	3 (6.7)	
30 to 45 years	37	30 (81.1)	4 (10.8)	3 (8.1)	
Above 45 years	28	21 (75.0)	2 (7.1)	5 (17.9)	
Gender	110				.068
Male	15	10 (66.7)	1 (6.7)	4 (26.7)	
Female	95	79 (83.2)	9 (9.5)	7 (7.4)	
Marital Status	110				.747
Married/ co-Habiting	48	37 (77.1)	5 (10.4)	6 (12.5)	
Single/Never Married	53	45 (84.9)	4 (7.5)	4 (7.5)	
Divorced/ Separated	4	3 (75.0)	0	1 (25.0)	
Widow/Widower	5	4 (80.0)	1 (20.0)	0	
Religion	110				.632
Christianity	99	81 (81.8)	9 (9.1)	9 (9.1)	
Islam	11	8 (72.7)	1 (9.1)	2 (18.2)	
Educational Level	110				.497
JHS and Below	21	19 (90.5)	1 (4.8)	1 (4.8)	
Senior High/ O'/A' Level	36	29 (80.6)	2 (5.6)	5 (13.9)	
Tertiary	53	41 (77.4)	7 (13.2)	5 (9.4)	
Occupation	109				.399
Employed	56	43 (76.0)	6 (10.7)	7 (12.5)	
Unemployed	53	46 (86.8)	3 (5.7)	4 (7.5)	
Reason for first facility visited					.001
Previous patient	12	11 (91.7)	1 (8.3)	0	
Due to symptoms	35	30 (85.7)	4 (11.4)	1 (2.9)	
Recommendation	15	6 (40.0)	3 (20.0)	6 (40.0)	
Proximity	22	21 (95.5)	0	1 (4.5)	
Patient works at the facility	4	4 (100.0)	0	0	
Needed to be treated	19	15 (78.9)	1 (5.3)	3 (15.8)	

Table 1. Analyses of Association between socio-demographic characteristics of participants and first facility visited

symptoms was 204 months, minimum of 2 weeks, and a median of 0.23 months (IQR= 3) [i.e. 1 week]. The median duration *from seeking help at the first facility to obtaining a final diagnosis* was 12 months (IQR = 33). The first facilities visited were pharmacies, non-specialist medical centres, churches and traditional healers, which were determined by multiple factors [X^2 (12, N = 107) = 32.29, p = .001]. Twenty-one participants (19.6%) had knowledge of their disease prior to diagnosis and causality was attributed to spiritual, lifestyle and biological factors. Education predicted having prior knowledge [OR = 2.6 (95% CI = .66 - 10.12), p< .021]. Unemployment increased the odds of seeking help after

Main themes	Sub-themes	Quotations
Knowledge and perception about condition	Biological	I know it is about our immune system (*FGD; Participant 2, female)*
	Lifestyle	Lack of exercise and if you don't eat well *(FGD; Participant 10, female)*
	Spiritual	When the symptoms started I did not understand, the way the sickness is, you will think maybe someone is causing it. *(FGD; Participant 5, female)*
Care seeking: Personal actions of relief	Rest or sleep	I sleep because of the pain *(IDI; Participant 4, female)*
	Visit health professionals	I go to the pharmacy *(FGD; Participant 2, female)*
	Self-medication	I use first aid *(IDI; Participant 10, female)*
Care seeking: Desperate actions for permanent treatment	Healer shopping	I visited several private hospitals which were of no help so my husband took me to a prayer camp. After, I visited Esukuma Government Hospital and they gave me drugs based on the symptoms I talked about but it wasn't working so I decided to try herbal centres which were of no help too. After, I went to Apam Hospital and they referred me to Korle Bu. *(IDI; Participant 6, female)*
	Search for information	I read about it in pamphlets, and online but sometimes the things you see are scary. We also have a WhatsApp group where we can ask questions and the doctors help us there. *(FGD; Participant 10, female)*
Effects of condition: Social Reactions	Relationships	I want to quit because of my condition. He does not treat me the way he is supposed to treat me. When he is supposed to help me he doesn't. When I ask for something he gets angry… *(IDI; Participant 6, female)*
	Education	"When I was sick I wasn't able to go to school; I was always at home feeling weak. I wasn't able to write exams. It has affected me" *(FGD; Participant 4, female)*
	Child bearing	"Yes, I am 32 and I have not given birth, that will push men away, maybe they will want a child." *(FGD; Participant 5, female)*
	Non-disclosure	Ooohh! Noo! If you don't know, you don't know. That's how it is. I am not that type of person who prefers to keep things, because if I tell you, there's nothing that you can do to it. So if you know, you know. If you don't know, that's all *(IDI; Participant 9, female)*
Effects of condition: Negative Feelings	Anxiety	Like sometimes when you want to do something, even when you work and you feel tired then it seems like you are feeling the sickness again, then you are in pain. Then it comes to mind, is it (illness) coming back. So I have to relax. *(IDI; Participant 5, female)*
	Pessimism	There are periods when I get very emotional. It is like the world is coming to an end. But you start getting guilty within yourself. It goes on and off. *(FGD; Participant 2, female)*
Coping strategies	Spiritual	It hasn't been long since this happened, but it's like God has given me the courage……Since I have God I have a future. *(FGD; Participant 5, female)*
	Significant others	My family have been so supportive I couldn't have done it without them *(FGD; Participant 2, female)*
	Knowledge of diagnosis	Knowing about it has helped me manage it well *(IDI; Participant 9, female)*

Table 2. Main themes, Sub-themes and quotations from thematic analysis

a month compared to those who were employed [Odds ratio = 2.60 (95% CI = 1.14 - 5.90), p = .02]. Forty (36.4%) participants utilised complementary and alternative treatment options. Thematic analysis of transcripts resulted in five key themes: *knowledge and perceptions of AIRDs, care-seeking behaviour, social reactions and stigma, negative feelings and coping strategies*.

Conclusion: Our study, the first of its kind to report health-seeking behaviour among Ghanaian patients with AIRDs, observed poor understanding of disease and recognised a multiple health-seeking medical culture which is significant among Ghanaian patients with a heavy reliance on religious, spiritual and traditional beliefs. Access to healthcare is determined by locality, availability and affordability of formal health facilities and alternative centres. These factors are associated with significant diagnostic and therapeutic delays, which can consequently lead to unfavourable clinical outcomes.

Disclosure: M. Amissah-Arthur, None; **A. Gyaban-Mensah**, None; **V. Boima**, None; **E. Yorke**, None; **D. Dey**, None; **D. Fiagbe**, None; **V. Ganu**, None; **K. Acquaye**, None; **C. Mate-Kole**, None.

Abstract Number: 0055

Racial and Sex-based Disparities in Health Care Utilization: Eye Inflammation as a Paradigm

Krati Chauhan[1] and James Rosenbaum[2], [1]Southern Illinois University - School of Medicine, Springfield, IL, [2]Oregon Health & Science University, Portland, OR

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Healthcare Disparities in Rheumatology Poster

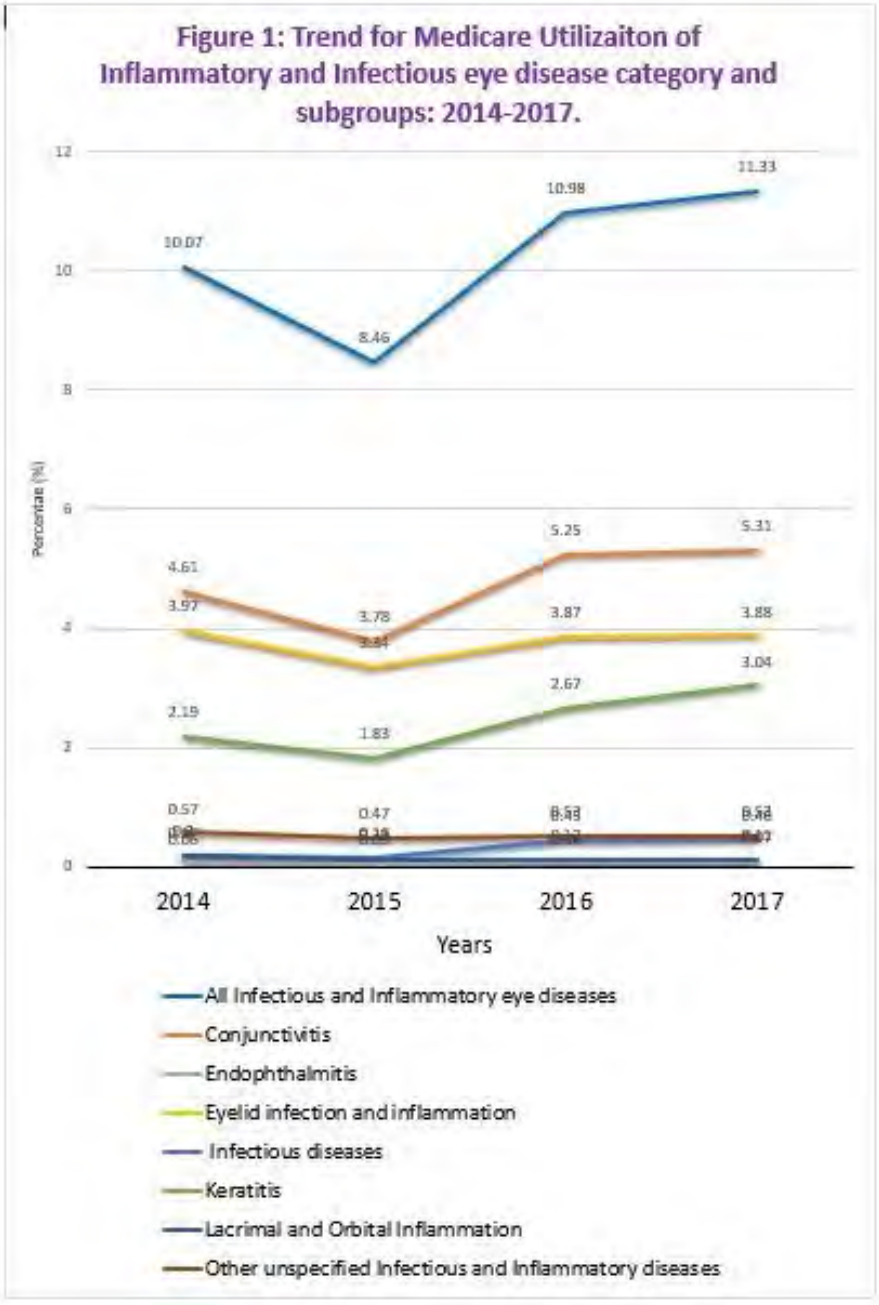


Figure 1. Trend for Medicare Utilizaiton of Inflammatory and Infectious eye disease category and subgroups: 2014-2017.

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

Background/Purpose: Disparities in health care utilization based on sex, race, education, or income affect outcomes in rheumatologic care. We have used ocular inflammatory and infectious disease, which complicates many rheumatic diseases, to study some of these disparities. These eye conditions, significantly increase disease burden, especially in people greater than 65 years of age and disproportionately affect females and racial minorities. However, there is lack of national level data in the US regarding influence of age, sex and race on utilization of medical care for inflammatory and infectious eye disease in people > 65 years. We have conducted an epidemiologic study using the Medicare database to analyze these trends and the influence of age, sex and race.

Methods: We have used Medicare data available through National Vision and Eye Health Surveillance System (VEHSS). Medicare data are collected from research identifiable files obtained through the Center for Medicare and Medicaid Services (CMS) and include all fee for service beneficiaries.

VEHSS uses ICD-10 codes to identify ocular disorders and organizes them into two level categorization, which are category and subgroup. Each code is categorized in one subgroup and multiple subgroups are combined to form a

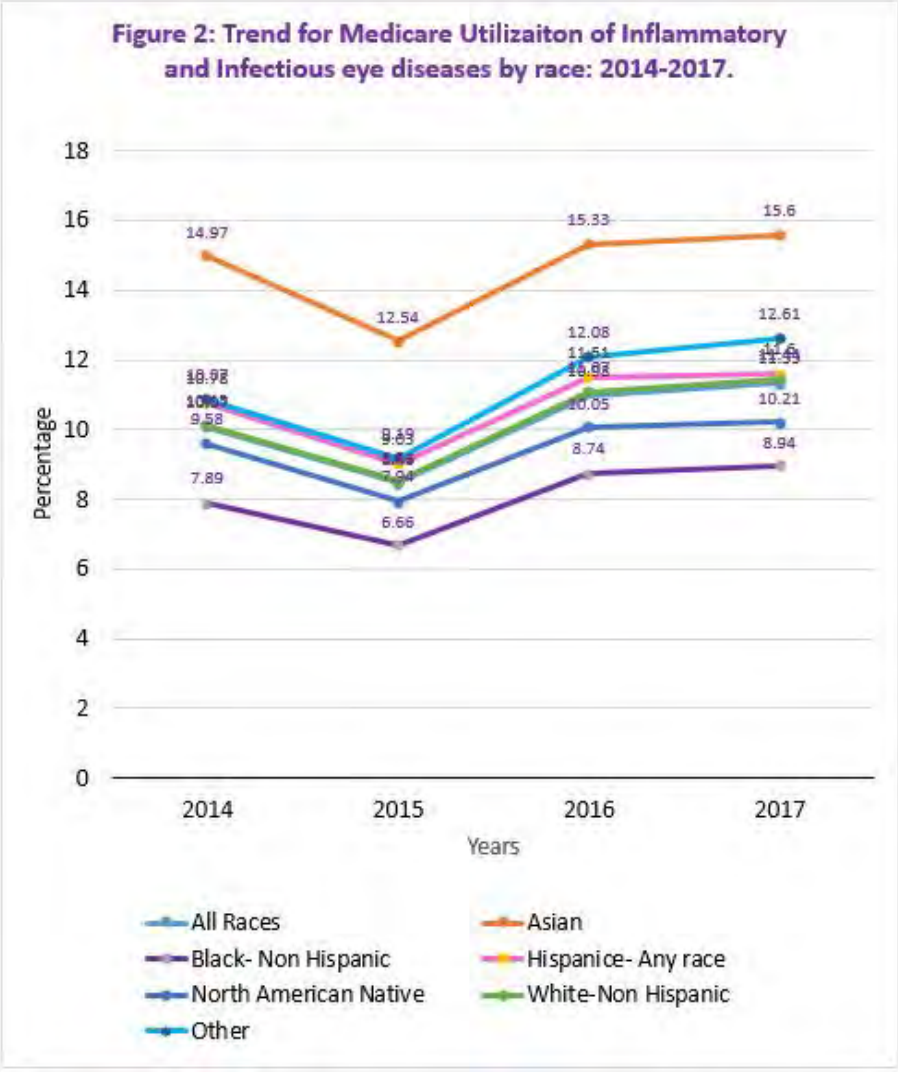


Figure 2 Trend for Medicare Utilizaiton of Inflammatory and Infectious eye diseases by race: 2014-2017.

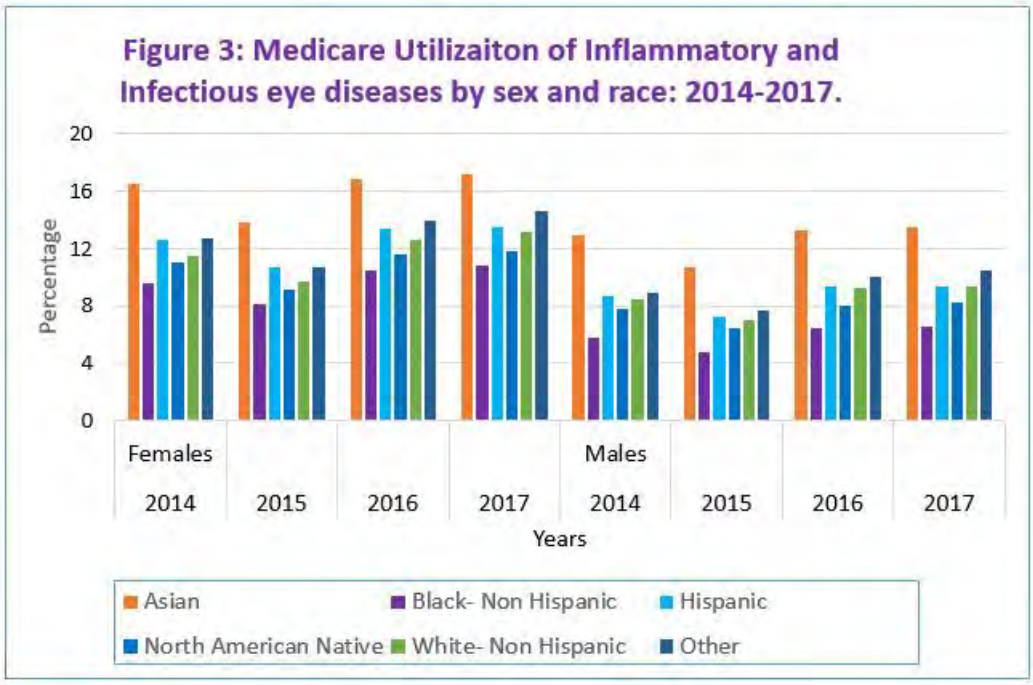


Figure 3. Medicare Utilization of Inflammatory and Infectious eye diseases by sex and race: 2014-2017.

category. Inflammatory and infectious eye disease category includes subgroups of ocular inflammatory conditions, lacrimal system and orbital inflammation, keratitis, conjunctivitis, eyelid inflammation and infection and endophthalmitis.

Utilization for the inflammatory and infectious eye disease caterogory, is stratified by age, sex and race. We have measured trends of utilization for the category and for the individual subgroups for the years 2014-2017. We have identified the effect of stratification on utilization; by race, sex, age alone; combining race and sex; age and sex; and the combination of race, sex and age.

Results: There were 29,971,000, 30,027,208, 30,423,400 and 30,238,300 million Medicare beneficiaries enrolled for the years 2014 to 2017 respectively. There was a decrease in utilization for inflammatory and infectious eye diseases category and subgroups from the year, 2014 to 2015 followed by a steady increase from 2015-2017 (Figure 1). This trend remains, when utilization is stratified by sex, race and age.

Asians and Hispanics have higher utilization for the inflammatory and infectious eye diseases category, and for the individual subgroups, for both males and females (Figure 2). This higher utilization remains, when further stratified by age.

Females have higher utilization across all races. This holds true when utilization is stratified by race; an Asian female has higher utilization than an Asian male (Figure 3). And remains steady when we further stratify by age groups. An Asian female of age group: 65-84 has higher utilization than an Asian male of the same age group; for all the years of the study 2014 to 2017.

Conclusion: Females, Asians and Hispanics have higher Medicare utilization for inflammatory and infectious eye diseases. These results may be due to higher disease prevalence or service utilization in these subgropus. Racial and sex-based disparitiies should be considered when making health care policy decisions

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Disclosure: K. Chauhan, None; **J. Rosenbaum**, Gilead, 1, Eli Lilly, 1, Abbvie, 5, UCB Pharma, 5, Roche, 1, Santen, 1, Corvus, 1, Celldex, 1, Horizon, 1, Novartis, 1, Eyevensys, 5, Janssen, 5, UpToDate, 7.

Abstract Number: 0056

Role of Socioeconomic and Cultural Factors in Racial Disparities in Disease Severity and Health Status of Patients with Axial Spondyloarthritis

Leila Muhieddine[1], Shakaib Hayat[2], Katja Reuter[3], Charles Thomas[4] and Marina Magrey[5], [1]Case Western Reserve University- Metrohealth Medical Center, Cleveland, OH, [2]Case Western Reserve University-Metrohealth Medical Center, Cleveland, OH, [3]University of Southern California, Keck School of Medicine, Los Angeles, CA, [4]Case Western Reserve University, School of Medicine, Cleveland, OH, [5]Case Western Reserve University School of Medicine, Cleveland, OH

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Healthcare Disparities in Rheumatology Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To confront the persistent racial and ethnic disparities in health outcomes in the United States, it is imperative to study cultural and socioeconomic differences as potential contributors of worse disease severity among Black patients with AxSpA. In this two-phase, cross-sectional survey study, we aimed to identify differences in cultural, socioeconomic factors, and education levels among the Black and White patients with AxSpA in the United States.

Methods: The first phase consisted of qualitative research to develop a questionnaire. A focus group including Black patients with AxSpA was convened at an urban medical center to investigate participants' knowledge about SpA symptoms, disease course, and barriers to management of the disease. The focus group was audio-recorded, transcribed, and the feedback obtained was tabulated for trends. The survey content was generated using feedback from the focus group. Phase two of the study involved the distribution of the survey in person in a single rheumatology practice and nationwide electronically via social media (Facebook) and search engine marketing (Google search pages). The survey assessed respondent's demographics, understanding of their disease, educational level, income level, employment status, information about medication use including biologic use, availability of primary and specialty care, shared decision-making, cultural and family influences, and trust of the medical system. Categorical variables were analyzed with Fischer's Exact Test and ordinal variables with the Kruskal-Wallis Test. All tests were two-sided, with $p< 0.05$ considered significant.

Results: A total of 120 surveys were completed (62.5% web-based, 37.5% in person). The total was was composed of 65% White participants with a mean age 51.9 ± 13.0 years, 25% Black participants with a mean age 56.3 ± 11.1 years, and 10% other. The mean BASDAI, BASFI, and ASAS HI among the two groups were not different as shown

	Blacks	Whites	P Value
BASDAI (mean ± SD)	6.5 ± 2.7	6.6 ± 2.3	0.90
BASFI (mean ± SD)	5.9 ± 2.8	6.4 ± 2.5	0.52
ASAS-HI (mean ± SD)	9.4 ± 4.3	10.8 ± 4.3	0.15

Table 1. Disease Activity, Function and Health Status between Black and White participants.

	Blacks	Whites	P Value
Male (%)	79.3%	39.7%	**<0.001**
Post-Secondary Education (%)	25.9%	51.4%	**0.02**
Employed (%)	24.1%	45.5%	**0.04**
Reported Salary >30,000	16.7%	32.1%	0.12
Self-Identified Unhealthy Diet	46.7%	41.0%	0.65
Utilize Home Remedies (%)	23.3%	51.3%	**0.001**
Other Medications (Non-Biologic) (%)	80%	88.9%	0.34
Fear of Side Effects (%)	30%	62.3%	**0.005**
Utilize Biologics (%)	28.6%	31.5%	0.81
Insurance Coverage for Medications (%)	17%	26.9%	0.37
Established Care with Primary Care (%)	96.7%	94.9%	1.00
Established Care with Rheumatology (%)	80%	79.5%	1.00
Fear of Health Care System (%)	69.0%	73.1%	0.81
Fear of Rheumatologist (%)	73.3%	81.0%	0.43
Looks Forward to Seeing Physician (%)	73.3%	73.2%	1.00
Misses Appointments Frequently (%)	13.3%	10.3%	0.34
Difficulty Scheduling Appointments (%)	23.3%	29.5%	0.63
Wait for Appointments >2 months (%)	50%	43.5%	0.66
Delay in Diagnosis (%)	37.9%	50.9%	0.28
Shared Decision Making (%)	86.7%	85.9%	1.00
Other Illness (%)	70%	71.8%	1.00

Table. 2 Socioeconomic, cultural and other factors between Black and White participants.

in Table 1. Black patients were less likely to have a post-secondary education (25.93% vs. 51.35%, P=.0256), be employed (24.14% vs. 45.45% p=.0491), use home remedies (23.33% vs. 51.32 p=.0079), and be fearful of medication side effects (30.00% vs. 62.34% p= .0046). Black participants were more likely to be male (79.31% vs. 39.74% p= .0004). There was no significant difference in other survey questions among the two groups as shown in Table 2.

Conclusion: While this study demonstrated a difference in three areas among Black and White patients with AxSpA (i.e., cultural beliefs, education, employment), we did not find significant differences in terms of diagnostic delays, access to physicians, rapport with physicians, access to medication, income, disease activity, function, and health status. Interventions to address the AxSpA health disparity gap can build on these findings.

Disclosure: L. Muhieddine, None; **S. Hayat**, None; **K. Reuter**, None; **C. Thomas**, None; **M. Magrey**, Novartis, 5, Eli Lilly, 5, AbbVie, 2, UCB, 2, Amgen, 2, Pfizer, 5, Janssen, 5.

Abstract Number: 0057

Increased Susceptibility to Measles in Patients from Central America and Mexico in a U.S. Rheumatology Clinic

Alice Fike[1], Abhimanyu Amarnani[2], Yanira Ruiz-Perdomo[3], Sarfaraz Hasni[3], Michael Ward[3] and James Katz[4], [1]NIAMS, Bethesda, MD, [2]SUNY Downstate Health Sciences University, Brooklyn, NY, [3]National Institutes of Health, Bethesda, MD, [4]NIH NIAMS, Bethesda, MD

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Healthcare Disparities in Rheumatology Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Infections in patients with rheumatic disease are a leading cause of morbidity and mortality. Preventive measures such as immunizations can reduce the burden of infections. In 2019 the United States experienced a surge in measles infections with significant outbreaks totaling more than 1,000 cases. Most of these

	Immune* (n= 221)	Non-immune (n=45)	p-value
Age, mean, SD	45.3 ± 9.2	44.6 ± 9.1	0.46
Gender, %, n			0.37
Female	190 (85.9%)	41 (91.1%)	
Disease, %, (n)			0.54
Rheumatoid Arthritis	69 (31.2%)	16 (35.5%)	
Systemic Lupus Erythematosus	111 (50.2%)	18 (40.0%)	
Seronegative Spondyloarthropathy	10 (4.5%)	4 (8.8%)	
Mixed Connective Tissue Disease	7 (3.1%)	1 (2.2%)	
Sjogren's Syndrome	4 (1.8%)	0	
Systemic Sclerosis	4 (1.8%)	2 (4.4%)	
Other	16 (7.2%)	4 (8.8%)	
Ethnicity, %, n			0.98
Hispanic or Latino	148 (66.9%)	30 (66.6%)	
Not Hispanic or Latino	72 (32.5%)	15 (33.3%)	
Chose Not to Answer	1 (0.04%)	0	
Race, %, n			0.57
Black/African American	39 (17.6%)	5 (11.1%)	
White	103 (46.6%)	20 (44.4%)	
Asian	13 (5.8%)	4 (8.8%)	
Multiracial/Other	66 (29.8%)	16 (35.5%)	
Region of Birth, %, n			0.25
USA	35 (15.9%)	9 (20.0%)	
Mexico and Central America	111 (50.5%)	29 (64.4%)	
Asia	14 (6.4%)	3 (6.7%)	
South America and Caribbean	44 (20.0%)	3 (6.7%)	
Africa and Middle East	14 (6.4%)	1 (2.2%)	
Europe	2 (0.9%)	0	

*Immune as defined as rubeola IgG > 30 AU/mL.

Table 1. Demographics of Patients Tested for Measles Immune Status

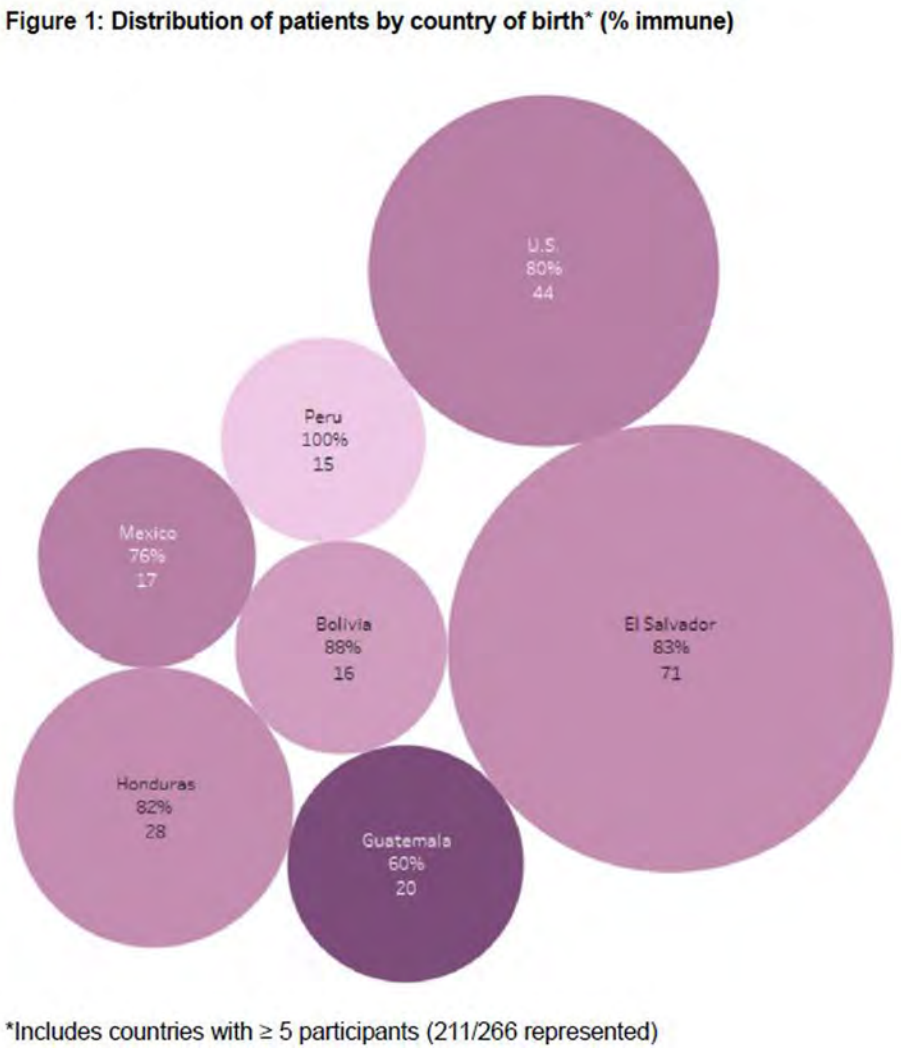


Figure 1. Distribution of patients by country of birth* (% immune)

outbreaks were associated with communities opposed to vaccination for varying reasons. With increased outbreaks, little attention has been given to communities at increased risk for measles secondary to limited access to care. Current guidelines for infectious disease screening prior to immune modulating therapy do not discuss measles. The Centers for Disease Control defines measles immunity as a positive titer, or evidence of two MMR vaccines, or birth prior to 1957. Seroprevalence studies of Central American countries have shown less than optimal rates of immunity to measles. We describe measles immune status in our cohort of majority underserved, Hispanic, non-U.S. born patients with rheumatic diseases.

Methods: Cross-sectional with a convenience sample of 266 patients born after 1957 who were seen in a rheumatology clinic from May 2019 to February 2020. All patients were participants in a rheumatic disease natural history study. Titer for anti-rubeola IgG was requested for each patient with their routine clinical lab draw. Immunization records were requested from primary care providers for patients whose titers were negative or equivocal. Demographic information including age, sex, place of birth, rheumatic disease diagnosis, and willingness to be vaccinated at a future visit were collected. To compare immune and non-immune groups, t tests and chi square tests were used on demographic variables where appropriate.

Results: The cohort was comprised of 86.8% women, 66.9% Hispanic ethnicity, and 52.6% from Central America or Mexico. Forty-five patients (17%) had negative or equivocal titers (Table 1), and none had records documenting prior

measles immunization. Patients born in Central America or Mexico (64.4%, n=29) were more likely to be non-immune (p=0.04) than patients born elsewhere (35.6%, n=16) . Nineteen of the 45 non-immune patients (42%) were potentially eligible to receive a live vaccine. Each of these patients indicated willingness to receive the MMR vaccine at a future visit. Patients from Guatemala had the highest percentage of non-immune titers, while those from Peru had the lowest percentage non-immune titers (Figure 1).

Conclusion: Our study demonstrates susceptibility to measles in our cohort with those from Central America or Mexico more likely to be non-immune. We highlight an underserved immigrant community affected by rheumatic diseases at increased risk for morbidity and mortality related to measles outbreaks. Evidence of measles susceptibility in our cohort coupled with the finding that 42% of our non-immune patients were eligible to receive live vaccines highlights an unmet need to evaluate measles immunity in rheumatology patients prior to immune-modulating therapy particularly in underserved populations. Clinicians can avoid missed opportunities to reduce infection risk in these at-risk communities by integrating immunizations into daily practice.

Disclosure: A. Fike, None; **A. Amarnani**, None; **Y. Ruiz-Perdomo**, None; **S. Hasni**, None; **M. Ward**, None; **J. Katz**, None.

Abstract Number: 0058

Drug Retention and Discontinuation of Biological DMARDs and Novel Small Molecules: Data from the Singapore National Biologics Registry

Li Wearn Koh[1], Man Hua Aw[2], Preeti Dhanasekaran[3], Rosa Lim Mui San[1], Stephanie Wong[4], Xanthe Chua[5], Wei Joo Choy[1], Manjari Lahiri[6] and Siaw Ing Yeo[2], [1]Tan Tock Seng Hospital, Singapore, Singapore, [2]Singapore General Hospital, Singapore, Singapore, [3]National University of Singapore, Singapore, Singapore, [4]Clinical Research and Innovation Office, Tan Tock Seng Hospital Singapore, Singapore, Singapore, [5]Tan Tock Seng Hospital, Singapore, Singapore, Singapore, [6]National University Hospital, Singapore, Singapore

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: To describe drug retention rate and reasons for discontinuation of biological disease modifying anti-rheumatic drugs (bDMARD) and novel small molecules in patients from the Singapore National Biologics Register (SNBR).

Methods: The SNBR is a prospective cohort started in 2016 in collaboration between the Rheumatology departments of National University Hospital, Tan Tock Seng Hospital and Singapore General Hospital to collect data about the epidemiology, disease activity, adverse effects and the development of comorbidities in patients treated with biologics and small molecules in patients with rheumatoid arthritis (RA) and spondyloarthropathy (SpA).

Patients with physician-diagnosed RA and SpA (axial (AS), peripheral and psoriatic arthropathy (PsA)) who were newly started on a bDMARD or small molecule, were recruited into this multi-centre, inception cohort. Data was collected via face-to face, telephone consultations and review of medical records at baseline, 6, 12, 18 and 24 months. Kaplan-Meier analysis for survival on drug by clinical diagnosis, income, educational level and financial assistance was performed.

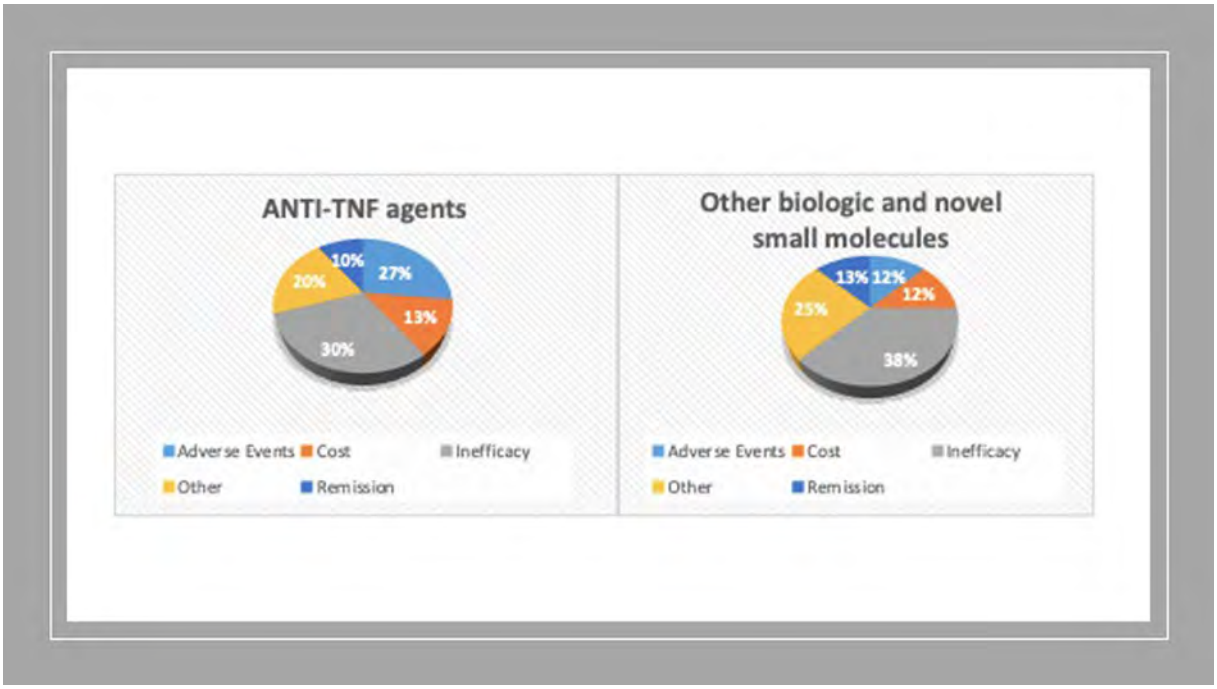


Figure 1. Reasons for discontinuation of biologic/novel small molecules

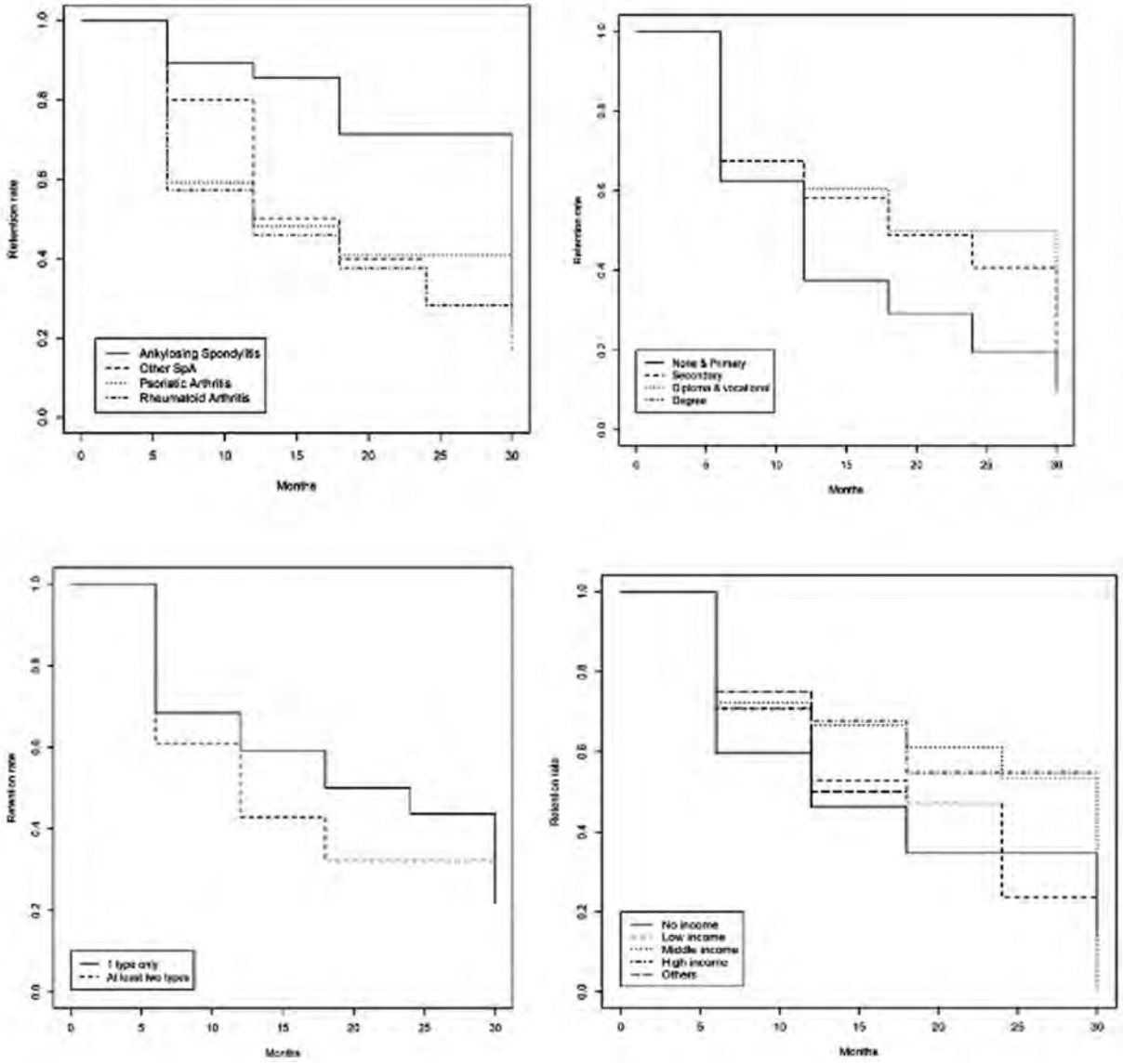
Results: 126 patients had completed 2-years follow-up and were included in our analysis. 67.5% were female and 32.5% were male. 118 were initiated on bDMARDS and 8 on small molecules at the baseline visit (48.4% RA, 22.2% AS, 21.4% PsA and 7.9% other SpA). Baseline disease activity scores (mean) of DAS28-ESR in RA was 4.95 (SD 4.64-5.26) and in PsA was 3.97 (SD 3.55-4.39) while the mean BASDAI in AS was 4.38 (SD 3.56 -5.21) and in other SpA 5.59 (SD 4.1-7.08). At the end of 24 months, Kaplan-Meier estimated retention rate of the original bDMARD/ small molecule was 41.1% (SD 33.0% -51.1%).

Reasons for discontinuation of these treatments are demonstrated in Figure 1. The commonest reason for discontinuation was inefficacy of the treatment (30% in patients on anti-TNF agents and 38% on other biologics and novel small molecules respectively).

The survival on drug was higher in patients with axial spondyloarthropathy (AS) compared to those with peripheral SpA, PsA and RA (Figure 2). Educational level, funding source and income group did not significantly influence retention rate of these medications.

Conclusion: In our cohort at the end of a 2 year follow up, fewer than half of our patients on high cost bDMARDs/ small molecules remained on their original bDMARD/small molecule. The retention rate of these medications was influenced by clinical diagnosis and inefficacy of the treatment was the main reason for discontinuation.Figure 1: Reasons for discontinuation of biologic/novel small molecules

Kaplan-Meier estimated drug retention rate by (clockwise from top left): underlying diagnosis (logrank p 0.0183), education (logrank p 0.1031), income group (logrank 0.2748) and financial assistance (logrank p 0.211).



Disclosure: L. Koh, DKSH, 9, Astellas Pharma, 8; **M. Aw**, None; **P. Dhanasekaran**, None; **R. Lim Mui San**, None; **S. Wong**, None; **X. Chua**, None; **W. Choy**, None; **M. Lahiri**, Pfizer, 5, 8, Gilead, 5, Sanofi, 9; **S. Yeo**, DKSH, 9.

Abstract Number: 0059

EHR-Supported Staff Protocol Improves Smoking Cessation in a Diverse Rheumatology Clinic: Results of Quit Connect Dissemination Project

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Smoking is a key risk factor for rheumatologic conditions such as rheumatoid arthritis and lupus that disproportionately impacts disadvantaged patients and predicts worse outcomes. Both smoking and rheumatic diseases increase risk for cardiovascular disease, yet rheumatology clinics address cessation in fewer than 10% of visits and offer referrals to free state-run tobacco quit lines (TQLs) in < 1% of visits. TQLs are proven to increase cessation 4-fold through free coaching and nicotine replacement.

Quit Connect supports rheumatology staff medical assistants or nurses with electronic health record (EHR) tools to *Ask* smokers about 30-day readiness to quit or cut back, *Advise* cessation support, and *Connect* ready patients via EHR orders to receive a TQL call (Figure 1). *Quit Connect* increased TQL referrals 26-fold in our prior study, and required < 90 seconds. We disseminated *Quit Connect* to the Grady Rheumatology Clinic, a public clinic in Atlanta, GA to test generalizability and increase TQL and smoking cessation class referrals.

Methods: We engaged medical assistants, nurses, clinic administrators, and rheumatologists to tailor *Quit Connect* implementation in a focus group. One-hour training offered cessation evidence and practice with talking points and EHR tools (Figure 2). Adults in the rheumatology clinic with current tobacco use were targeted. EHR tags captured process steps for when a patient was *Asked* about smoking/quit readiness, *Advised* regarding TQL and cessation class, or *Connected* via referral to TQL or cessation class. We compared performance before and after active implementation of the protocol, and we report 3 month midpoint data. Chi-square tests and unadjusted odds ratios compared findings months 1 to 3.

Results: At baseline, 83% of patients were Black, 40% were uninsured, and 52% received Medicare/Medicaid. During the 3 months of *Quit Connect* implementation, among 780 visits, 16% were smokers (Table 1). Among smokers, rates of triage staff asking readiness to quit increased from 13% in month 1 to 51% in month 3 (OR 8.6), compared to 0% before the project. Among smokers who were asked (n=30), 76% said that they were ready to quit or cut back in the next 30 days. Among those ready (n=23), 82% were offered referral to the TQL or class. Among those offered (n=19), 63% accepted the e-referral to the TQL and 68% accepted a referral to the class (p=0.99) compared to zero referred before *Quit Connect* implementation.

Conclusion: In a low resource rheumatology clinic with a majority of Black patients with limited insurance, many were ready to quit but had not been offered support. Within three months, *Quit Connect* dramatically increased referrals to a tobacco quit line and cessation class. This process is easily integrated into the EHR, engages staff, and leverages

Figure 1. Quit Connect trains medical assistants and nurses to ASK smokers about readiness to quit, ADVISE cessation, and CONNECT patients to cessation resources such as a tobacco quit line or cessation class in under 90 seconds during clinic rooming.

Figure 2. Quit Connect implementation steps and timeline. Participants included study team, clinic manager, nurses, medical assistants and rheumatologists. Participants were engaged with a focus group and then trained with evidence-based information regarding effects of smoking on rheumatologic disease and how to connect patients to TQL or a cessation class using EHR referrals. Staff received monthly audit feedback regarding process of ASK, ADVISE, CONNECT to smoking cessation resources.

Table 1. Quit Connect process steps before and after implementation

	Before n=2674 visits/yr.		Month 1 n=289		Month 2 n=300		Month 3 n=191		Unadjusted OR Month 3 vs Month 1	Total n=780 visits	
Tobacco Assessed at Triage	NA	NA	248	85.8%	251	83.7%	138	72.3%		637	81.7%
Current Smoking	535	20%	48	16.6%	46	15.3%	29	15.2%		123	15.8%
Ready to Quit Asked (of current smokers)	0	0%	6	12.5%	9	19.6%	15	51.7%	OR 8.6	30	24.4%
Ready to Quit (Current smokers)	0	0%	4	66.7%	9	100.0%	10	66.7%		23	76.7%
Offered E-Referral or Class (If ready to quit)	NA		2	50.0%	9	100.0%	8	80.0%	OR 4.0	19	82.6%
Accepted Tobacco Quit Line E-Referral (Among offered)	NA		1	50.0%	5	55.6%	6	75.0%	OR 3.0	12	63.2%
Accepted Class (Among offered)	NA		0	0.0%	7	77.8%	6	75.0%		13	68.4%

Table 1. Quit Connect process steps before and after implementation

free, state-run resources for rheumatology patients. Monthly audit feedback will continue to encourage this brief intervention for rheumatology patients who smoke. Short and long-term outcomes will be evaluated including TQL reports of cessation attempts and patient outcomes. Future studies seek to scale out and disseminate *Quit Connect* in other populations and health systems.

Disclosure: J. Brandt, None; **S. Lim**, None; **E. Ramly**, None; **M. Messina**, None; **C. Bartels**, Independent Grants for Learning and Change (Pfizer), 2.

Abstract Number: 0060

ANCA-associated Vasculitis in Caucasian and Hispanics of the Inland Empire of Southern California

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Healthcare Disparities in Rheumatology Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) is often studied in the Caucasian population with few studies looking at the disease in other races. Disease presentation and treatment implications of autoimmune conditions vary by ethnicity, as seen in systemic lupus erythematous. A 2014 study of the Chicago area compared AAV in Hispanic and Caucasian patients and found increased disease severity, as defined by the Birmingham Vasculitis Activity Score (BVAS) and the Vasculitis Disease Index (VDI), with greater renal involvement in Hispanics. We performed a similar study examining the differences in AAV in the Hispanic and Caucasian populations living in the Inland Empire region of Southern California.

Methods: A retrospective study was conducted on data extracted from the Loma Linda University Medical Center and the Riverside University Health System's Electronic Medical Record, using ICD 9 and ICD 10 CM codes pertaining to vasculitis. Data span the dates of January 1, 2003 to December 31, 2019. Vasculitis cases were classified using the Diagnostic and Classification of the Systemic Vasculitis (DCVAS). Data extracted from the electronic charts include demographics, ICU admission due to vasculitis flare, presence of chronic kidney disease or end stage renal disease (ESRD), BVAS on presentation and VDI as detailed on recent clinic visit. We calculated odds ratios for the categorical data and ran Independent sample T-test for the continuous data with alpha equal to 0.05 for statistical significance.

Results: 129 charts were included in the analysis with 66 Hispanics and 63 Caucasians (see Table 1). 72 cases of Granulomatosis Polyangiitis (GPA), 47 cases of Microscopic Polyangiitis (MPA) and 10 cases of Eosinophilic Granulomatosis Polyangiitis (EGPA) were identified. Hispanics had a 49% increase in odds of being admitted to the ICU secondary to vasculitis when compared to Caucasians [OR 1.49 (95% CI 0.72, 3.07)]. Hispanics were noted to have more flares with a maximum recorded number of flares for a single patient to be 15 compared to 7 for a Caucasian patient. They also had a 71% increase in odds of having kidney disease in comparison to Caucasians [OR 1.71 (95% CI 0.85, 3.43)]. Of the patients with kidney disease, Hispanics had a 95% increase in odds of having ESRD when compared to Caucasians [OR 1.95 (95% CI 0.68, 5.55)]. See Table 2. The BVAS and VDI averages between Hispanics and Caucasians were comparable at 8.53 ± 7.3 vs 7.69 ± 6.3 and 2.32 ± 2.0 vs 2.2 ± 1.5, respectively (p = 0.49; p =

Table 1. Observed Attributes of Hispanic and Caucasian patients with ANCA-associated Vasculitis.

	Total N = 129	Hispanic N = 66	Caucasian N = 63
Male	42 (32.6%)	18 (27.3%)	24 (38%)
Female	87 (67.4%)	48 (72.7%)	39 (61.9%)
GPA	72 (55.8%)	31 (47%)	41 (65.1%)
MPA	47 (36.4%)	31 (47%)	16 (25.4%)
EGPA	10 (7.8%)	4 (6.1%)	6 (9.5%)
# of deaths	16 (12.4)	6 (9.1%)	10 (15.9%)
Chronic Kidney Disease	62 (48.1%)	36 (54.5%)	26 (41.3%)
ESRD	39 (62.9%)	25 (69.4%)	14 (53.8%)
Renal transplant	13 (21.0%)	10 (27.8%)	3 (11.5%)
ICU admission	47 (36.4%)	27 (40.9%)	20 (31.7%)
Maximum recorded # of vasculitis flares for one patient	15	15	7

Table 1. Observed Attributes of Hispanic and Caucasian patients with ANCA-associated Vasculitis.

Table 2. Odds Ratio for Ethnicity

	OR (Hispanic/Caucasian)	95% CI
ICU Admission	1.49	0.72 – 3.07
Chronic Kidney Disease	1.71	0.85 – 3.43
ESRD	1.95	0.68 – 5.55
Renal Transplant	2.95	0.72 – 12.0

Table 2. Odds Ratio for Ethnicity

Table 3. Independent Sample T-test of BVAS and VDI.

	P-value	Ethnicity	N	Mean	Std. Deviation
BVAS	0.49	Hispanic	62	8.53	7.3
		Caucasian	61	7.69	6.3
VDI	0.70	Hispanic	62	2.32	2.0
		Caucasian	61	2.20	1.5

Table 3. Independent Sample T-test of BVAS and VDI.

0.70). See Table 3. Although we observed differences in disease severity proportions between Hispanics and Caucasians, the measures of association were not statistically significant.

Conclusion: Like the Chicago study, we saw greater incidences of renal disease and increased severity in Hispanics compared to Caucasians, as defined by increased rates of ICU admissions and vasculitis flares, despite analogous average BVAS and VDI scores. Our data shows that conventionally used disease activity scores may not convey the seriousness of renal or pulmonary vasculitis in Hispanic populations. Clinicians treating Hispanic patients with AAV should have a high index of suspicion for more severe disease in this patient population when compared to Caucasians.

Disclosure: S. Lee, None; **P. Injean**, None; **P. Tran**, None; **D. Panikkath**, None; **C. Downey**, None.

Abstract Number: 0061

Rheumatologists' Attitudes Toward Palliative Care and Medical Assistance in Dying

Alexandra Saltman[1], Caroline McGuinty[2], Gursimran Chandhoke[3], Simon Oczkowski[4], Heather McDonald-Blumer[1], Ebru Kaya[5] and Kirsten Wentlandt[6], [1]University Health Network and Sinai Health System, University of Toronto Faculty of Medicine, Toronto, ON, Canada, [2]Ottawa Heart Institute and University of Ottawa, Ottawa, ON, Canada, [3]Lakeridge Health, Oshawa, ON, Canada, [4]Juravinski Hospital and McMaster University, Hamilton, ON, Canada, [5]University Health Network,, University of Toronto Faculty of Medicine, Toronto, ON, Canada, [6]University Health Network, University of Toronto Faculty of Medicine, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Healthcare Disparities in Rheumatology Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite major advances in the treatment of systemic rheumatic diseases, a population remains—including those with systemic vasculitis, inflammatory myositis and systemic sclerosis—who suffer from life-limiting disease. Typically, these patients have little access to palliative care services, and there is a paucity of data on this potential care gap. This study aims to define the referral practices of Canadian Rheumatologists to pal-

liative care services and to explore rheumatologists' attitudes toward palliative care and medical assistance in dying (MAiD).

Methods: All rheumatologists who are members of the Canadian Rheumatology Association were invited to complete an online questionnaire using *Survey Gizmo*. Responses were received anonymously by the online survey program, aggregated and analyzed using descriptive statistics.

Results: 37 (19%) of rheumatologists completed the survey. 22 (60%) self-identified as academic physicians. The majority were general rheumatologists (n=30, 83%), caring primarily for adult patients (n=33, 89%). 68% reported exposure to elements of palliative care during medical training, covering pain management (n=23, 77%), management of other physical symptoms (n=21, 70%), end-of-life planning (n=19, 63%) or communication skills (n=21, 70%).

Rheumatologists categorized up to 50% of their inpatients and up to 10% of their outpatients as having advanced rheumatologic disease with significant functional limitation or low estimated 1-year survival. 44% (n=16) reported access to palliative care unit or hospice services for their patients, and 36% (n=13) were aware of local palliative home care services. 54% (n=19) had never referred a patient to palliative care services. For those who had, they did so most often for uncontrolled symptoms and prognosis less than 1 year (n=22, 66%), or for terminally ill inpatients who required assistance with discharge planning (n=24, 60%). 14% (n=5) reported feeling "very comforTable" identifying patients with life-limiting rheumatic conditions that might benefit from a palliative care approach to care, and 22% (n=5) were "very comforTable" discussing such an approach with their patients. 42% indicated they were "not very comforTable" (n=10, 28%), or "not at all comforTable" (n=5, 14%) engaging in advance care planning conversations with their patients.

While 33% (n=12) of rheumatologists had been approached by a patient requesting MAiD, a large number rated their knowledge of eligibility criteria (n=17, 47%) and of the assessment and approval process (n=19, 53%) as "poor".

Conclusion: This study is the first to describe self-reported referral practices of rheumatologists to palliative care services, and to identify attitudes of these physicians towards palliative care consultation. The results expose gaps in knowledge of, and comfort with, palliative care services for patients with life-limiting rheumatic diseases, as well as barriers to accessing these services for patients with non-cancer illnesses. Further work is needed to engage rheumatologists about the role that palliative care teams can play in providing higher quality care to patients with advanced systemic rheumatic illnesses toward the end of life.

Disclosure: A. Saltman, None; **C. McGuinty**, None; **G. Chandhoke**, None; **S. Oczkowski**, None; **H. McDonald-Blumer**, None; **E. Kaya**, None; **K. Wentlandt**, None.

Abstract Number: 0062

The Role of PGLYRP1 in the Pathogenesis of Lyme Disease

Akash Gupta[1], Gunjan Arora[1], Connor Rosen[2], Yongguo Cao[1], Jiri Cerny[3], Carmen Booth[4], Noah Palm[2], Aaron Ring[2] and Erol Fikrig[1], [1]Section of Infectious Diseases, Department of Internal Medicine, Yale University School of Medicine, New Haven, CT, [2]Department of Immunobiology, Yale University School of Medicine, New Haven, CT, [3]Faculty of Tropical AgriSciences, Czech University of Life Sciences in Prague, Prague, Czech Republic, [4]Department of Comparative Medicine, Yale University School of Medicine, New Haven, CT

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Lyme Disease is caused by the spirochete *Borrelia Burgdorferi (Bb).* The infection often begins in the skin, following a tick bite, and spreads to the joints, heart, and other tissues. The pathogenesis of Lyme disease is multifactorial, involving both pathogen-derived factors that influence dissemination, and host factors that are responsible for the inflammation and modulation of infection. PGLYRP1, a member of the peptidoglycan recognition proteins, is a host immune factor associated with the innate immune response. PGLYRP1 has been linked to pro-inflammatory processes in many chronic inflammatory diseases. The goal of this study is to understand the function of PGLYRP1 in Lyme Borreliosis.

Methods: Flow cytometry and ELISA were used to characterize the ability of *Bb* to recognize PGLYRP1. Wild type (WT) and PGLYRP1 knockout (KO) BALB/C mice, 6-8 weeks old, were infected subcutaneously with $1x10^6$ spirochetes. Pathogen burden was measured by qPCR in heart, joint, and skin tissues in WT and KO mice at 25 days post infection. Blood samples were collected in both groups of mice to determine antibody titers against *Bb*. Serum cytokine profile was assessed, using a mouse chemokine/cytokine array. Histopathology was used to evaluate the severity of inflammation in both heart and joint tissues.

Results: In vitro assays showed a concentration-dependent interaction between *Bb* and PGLYRP1. Infected KO mice had significantly higher pathogen burden in hearts and joints, but no difference in skin samples compared to WT mice. There was a significant reduction in *Bb* specific IgG titers in sera obtained from infected KO mice. Similar to overall IgG, levels of IgG1, IgG2a, IgG2b, and IgG3 against Bb were significantly lower in PGLYRP1 infected KO mice than in WT. NoTable increases in pro-inflammatory cytokines IFN-y, CXCL-9, and CXCL-10 were observed in infected KO mice. There was no significant difference in arthritis and carditis severity in WT and KO mice.

Conclusion: These studies suggest that PGLYRP1 plays a role in the host modulation of *Bb* in the systemic phase of infection and immune response. This leads to a better understanding of the pathogenesis of Lyme Disease.

Disclosure: A. Gupta, None; **G. Arora**, None; **C. Rosen**, None; **Y. Cao**, None; **J. Cerny**, None; **C. Booth**, None; **N. Palm**, None; **A. Ring**, None; **E. Fikrig**, None.

Abstract Number: 0063

Novel Repurposed Drugs Against Joint Inflammation Reveal Potential Use for Gout Treatment: An *In Silico*, *In Vitro* and Clinical Study

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

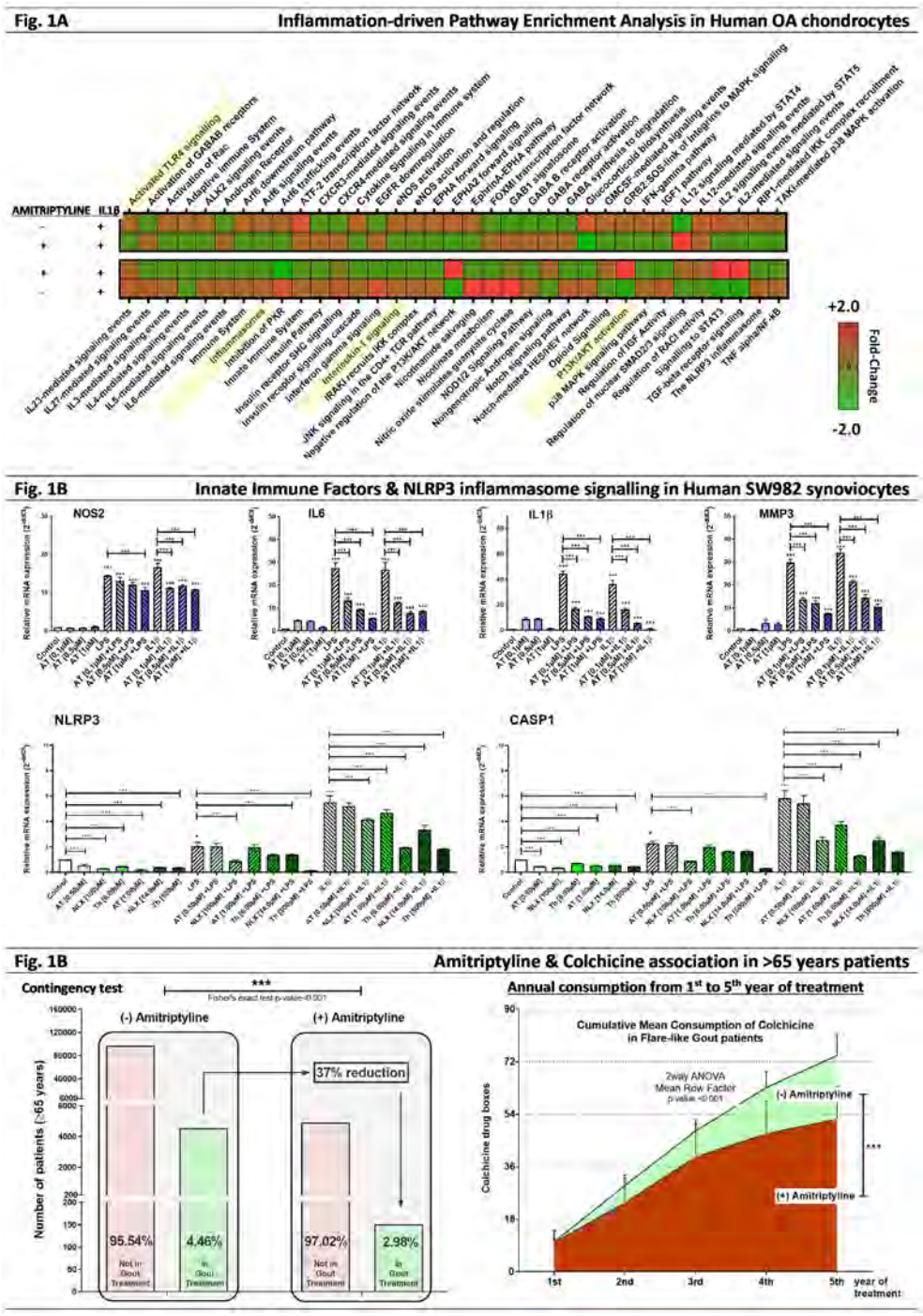

Figure 1. Amitriptyline blocked the proteome of IL1R–mediated innate immune response factors Fig. 1A.- Inflammatory-driven Pathway Enrichment Analysis of proteins quantified (SWATH) on primary human OA chondrocytes co-treated 24h with AT [1μM] and IL1β [0.1ng/ml]. Fig. 1B.- Blocking effects of amitriptyline (AT), naloxone (NLX) and thalidomide (Th) were evaluated on TLR4 (LPS [100ng/ml]) & IL1R (IL1β [0.1ng/ml])– activated human SW982 synoviocytes. Innate immune factors (NOS2, IL6, IL1β and MMP3) and NLRP3 inflammasome signalling were analysed by RT-PCR. Fig. 1C.- Contingency test comparing the number of patients requiring colchicine in both amitriptyline and non-amitriptyline consumers against the whole population (>65 years). Cumulative mean consumption of colchicine drug boxes in colchicine gout-patients who suffered of flare-like episodes, namely those who consumed >18 colchicine boxes in at least a single year. Statistics: SWATH data were filtered by FDR 1% and at least a p-value <0,05. Data of three independent experiments was used and "Control" was used to normalise RT-PCR. Clinical data was obtained from the healthcare area of EOXI Santiago de Compostela (Spain) that covers a 400.000 citizen area. Contingency test was analysed by Fisher's exact test. Cumulative mean tests were analysed by 2-way ANOVA Row factor, and other data was by one-way ANOVA. Tukey post-test was used, and results were expressed as the mean ± standard error of the mean (SEM) with the significance NEJM system (*p<0,05; **p<0,01; ***p<0,001). Abbreviations: Toll like receptor 4 (TLR4), interleukin 1 receptor (IL1R), amitriptyline (AT), naloxone (NLX) and thalidomide (Th), human OA chondrocytes (hOC), lipopolysaccharide (LPS), interleukin 1 beta (IL1β), interleukin 6 (IL6),

Background/Purpose: Joint inflammation is a common feature across multiple rheumatic diseases. To deal with the induction of innate immune factors, targeting therapeutic targets such as TLR4 and IL1R is required. We have recently reported the use of amitriptyline (AT), thalidomide (Th), and naloxone (NLX) to block TLR4 & IL1R-mediated innate immune responses in OA cartilage. Now we explore their use in synovia and gout inflammation.

Methods: The ethics committee approved (CAEIG 2016/258) the use of human samples and aggregated and dissociated clinical data from 440.000 citizens.

The activity and expression of TLR4, IL1R, and NLRP3 signaling pathways were determined by docking analysis (Autodocks-Vina), MTT cell viability assay, RT-PCR, and Western Blot, ELISA or MALDI-TOFF in human OA chondrocytes and synoviocytes (SW982 cell line). Statistics were performed using GraphPad Prism 9.0.

Results: The docking of AT, Th, and NLX towards TLR4 was confirmed by *in silico* binding affinity analysis. In human synoviocytes, the use of therapeutic doses of AT [0.1-1μM], NLX [1.4-100μM], and Th [3-500μM]) prevented the induction of several factors including NOS2, IL6, IL1B and MMP9 at the mRNA and protein level (up to -97%). The inhibition of the NLRP3 inflammasome pathway, which is linked to both synovitis and gout-associated inflammation, was verified by RT-PCR & MALDI-TOFF in OA chondrocytes and synoviocytes. Considering this link, we requested access to clinical data and found that amitriptyline consumers are less prone to require colchicine drug for gout treatment.

Conclusion: Amitriptyline, naloxone, and thalidomide prevent the induction of TLR4 & IL1R-mediated innate immune factors in OA chondrocytes and synoviocytes. Moreover, amitriptyline consumption reduced the dose of colchicine needed for gout treatment.

Considering that these drugs are being used in other indications, their repurpose might be a novel tool to manage inflammation across diverse rheumatic diseases.

Disclosure: E. Franco-Trepat, None; **A. Alonso-Pérez**, None; **M. Guillán-Fresco**, None; **M. López-Fagundez**, None; **A. Pazos-Pérez**, None; **A. Lois Iglesias**, None; **S. Bravo**, None; **A. Jorge-Mora**, None; **J. Gómez-Reino**, None; **R. Gómez**, None.

Abstract Number: 0064

Neutrophil Extracellular Traps Are Sufficient to Activate the Alternative Pathway of Complement

Rebecca Schriefer[1], Michelle Elvington[2], Priyan Weerappuli[3] and **Alfred Kim**[4], [1]Washington University School of Medicine, Saint Louis, MO, [2]Kypha, Inc., Saint Louis, MO, [3]University of Michigan, Ann Arbor, MI, [4]Washington University School of Medicine, St. Louis, MO

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) replies on complement activation to drive many of the pathophysiologic features of disease. We and others have noted that SLE patients have constitutive activation of the complement component C3 (1). Elevated C3 activation products such as C3(H_2O) suggest that the alternative pathway is preferentially used to drive this process. Importantly, the production of C3(H_2O) is also critical for the com-

plosome, the intracellular C3 activation pathway that confers functional changes in numerous cells types (2). Furthermore, prior work has shown that stimulated neutrophils can drive C3 activation, which in turn further activates neutrophils (3). As NETs are a key feature of SLE pathophysiology, we hypothesized that neutrophil extracellular traps (NETs) promote alternative pathway activation, producing C3(H_2O) which is in turn used to drive intracellular C3 activation.

Methods: To independently assess whether NETs can activate C3, we leveraged a recently developed acellular mimic of NETs, DNA-histone mesostructures (DHMs), that possess the ultrastructural and functional properties of NETs (4). Purified human native C3 and C2-depleted human serum (Complement Technologies, Tyler, Tx, USA) were added to DHMs or DNA-histone-free DHMs (control). C3(H_2O), factor Bb, C3a, C5a, and C5b-C9 were assessed using ELISA. Isolated human neutrophils were obtained from consented healthy controls and activated by either DHM-induced C3(H_2O) or phorbol myristate acetate (PMA), some in the presence of DNAse to digest NETs. Cell lysates were examined by western blot for intracellular C3 activation products (goat anti-human C3 polyclonal antibody, Complement Technologies). Images of neutrophils were obtained using a Zeiss LSM 880 Confocal with AiryScan.

Results: DHMs drove the rapid (< 5 minutes) and nearly complete (>90%) activation of native C3 into C3(H_2O), suggesting a contact mechanism promotes early C3 activation. When C2-depleted was added to DHMs, products of alternative (Bb) and common pathway (C3a, C3a, C5b-9) were observed. When DHM-induced C3(H_2O) was added to primary neutrophils, it was readily taken up both unstimulated and PHA-activated neutrophils as observed by AiryScan confocal microscopy. Interestingly, only PHA-activated neutrophils were able to generate intracellular C3a and C3b products. Finally, using DNase-treated PHA-activated neutrophils to digest NETs, only the addition of DHM-induced C3(H_2O), and not native C3, induced C3 uptake, further supporting the role of NETs in C3 activation.

Conclusion: We found that NETs are sufficient to activate the alternative pathway of complement. The C3(H_2O) generated through this process was internalized by neutrophils, but only activated neutrophils were capable of intracellular C3 activation. Given the high NET load in SLE, we suspect that this may be the etiology for constitutive C3 activation observed in SLE patients.

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Disclosure: R. Schriefer, None; **M. Elvington**, Kypha, Inc., 3; **P. Weerappuli**, None; **A. Kim**, Exagen Diagnostics, Inc., 5, 8, GlaxoSmithKline, 2, 5, 8, Alexion Pharmaceuticals, 5, Annexon Biosciences, 5, JPMorgan Chase & Co., 5.

Abstract Number: 0065

The Energy-dependent Hierarchy of Immune Functions in Human Monocytes

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: At sites of inflammation, monocytes carry out specific immunological functions while facing challenging bioenergetic restrictions. Here, we investigated the potential of human monocytes to adapt under conditions of reduced energy supply by gradually inhibiting oxidative phosphorylation (OXPHOS) under glucose free conditions.

Methods: We modelled this reduced energy supply with myxothiazol, an inhibitor of mitochondrial respiration, at 0, 2 and 4 pmol/10^6 cells to decrease mitochondrial ATP production for 0%, 25% and 66% under glucose free conditions. For the three energy levels, we assessed (i) phagocytosis of FITC-labelled *E.coli* using flow cytometry, (i) production of reactive oxygen species (ROS) through NADPH oxidase (NOX) as determined by VAS2870-sensitive OCR using a Clark-type electrode, (iii) ATP generation and steady state level using a Clark-type electrode and luminometric assessment (iv) expression of surface activation markers CD16, CD80, CD11b, HLA-DR and (v) production of the inflammatory cytokines IL-1β, IL-6 and TNF-α using flow cytometry in peripheral blood-derived human monocytes with and without LPS-stimulation.

Results: As a prerequisite for our study, we demonstrate that human monocytes survived strong inhibition of mitochondrial respiration without any sign of apoptosis as determined by flow cytometry. As a result of the inhibition of OXPHOS, we demonstrate a reduction of VAS2870-sensitive OCR (ROS production through NOX), ATPase-dependent OCR and ATP steady-state levels. Focusing on immune function, we observed that phagocytosis and the production of IL-6 were the least sensitive to reduced energy supply while surface expression of CD11b, HLA-DR, production of TNF-α and IL-1β were most affected by inhibition of OXPHOS.

Conclusion: Our data demonstrate an energy-dependent hierarchy of immune functions in monocytes, which may represent a potential therapeutic target in monocyte-mediated inflammatory diseases.

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Abstract Number: 0066

AMP Deaminase 2 Is Expressed on the Surface of Human Immune Cells as a Novel Regulator of Extracellular Adenosine Metabolism

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Adenosine and its nucleotides represent crucial immunomodulators in the extracellular environment. ATP and ADP are released from stressed cells in states of inflammation, whereas adenosine serves as a key anti-inflammatory mediator. The ectonucleotidases CD39 and CD73 are responsible for the sequential catabolism of ATP to adenosine via AMP, thereby promoting an anti-inflammatory milieu induced by the "adenosine halo". Great importance has been attributed to these enzymes in the pathogenesis of autoimmune diseases such as rheumatoid arthritis (RA) and as targets in cancer therapy. AMPD2 mediates AMP deamination to IMP, thus constituting an ambiguous mediator both enhancing the degradation of inflammatory ATP and reducing the formation of protective adenosine. Here, we postulate that this pathway is also present on the cell surface of immune cells and modified under inflammatory conditions. Therefore, we analysed surface AMPD2 expression and its modulation on distinct cell lines and primary immune cells.

Methods: Firstly, AMPD2 surface expression was verified by immunoprecipitation from membrane fractions isolated from cell lines (HEK293 and HMEC1) and CD14+ monocytes analysed by western blot and mass spectrometry. In addition, surface biotinylation of the aforementioned cells was performed. Also, AMPD2 surface expression was evaluated by flow cytometry, analysing both cell lines (HEK293, HMEC1, THP1, and Jurkat) and primary human immune cells from healthy donors and patients with RA. Secondly, co-expression of surface AMPD2, CD39 and CD73 on PBMCs was analysed by flow cytometry directly after isolation as well as after a 24h culture period. Moreover, surface expression was assessed after immunostimulation and Golgi transport inhibition.

Results: AMPD2 surface expression was confirmed by western blot and mass spectrometry of (i) precipitated AMPD2 from membrane fractions and (ii) biotinylated surface molecules in HEK293 and HMEC1 as well as CD14+ monocytes. Surface expression was reduced after AMPD2 knockdown in HEK293. Flow cytometric analysis further verified AMPD2 surface expression and revealed a significant decrease after Golgi transport inhibition ($p< 0.01$). TLR stimulation strongly enhanced the surface expression of AMPD2 and CD39 on monocytes ($p< 0.05$), whereas dexamethasone at high therapeutic doses inversely affected AMPD2 surface expression on lymphocytes and monocytes ($p< 0.01$). Analysis of AMPD2 surface expression on PBMCs from RA patients revealed higher expression levels compared to sex- and age-matched healthy controls ($p< 0.05$).

Conclusion: We demonstrate AMPD2 surface expression on immune cells for the first time. Hence, we reveal a novel regulator of the extracellular ATP-adenosine balance that is differentially expressed in RA patients compared to healthy controls. The extracellular conversion of AMP into IMP may constitute a shunt-like mechanism adding to the CD39-CD73 system controlling immunomodulation.

Disclosure: L. Ehlers, None; **A. Kuppe**, None; **M. Kirchner**, None; **A. Damerau**, None; **C. Strehl**, None; **F. Buttgereit**, AbbVie, 8, Eli Lilly, 8, Pfizer, 8, Roche, 8; **T. Gaber**, None.

Abstract Number: 0067

Functionally Mature CD1c$^+$ Dendritic Cells Contribute to Synovial Inflammation in Rheumatoid Arthritis via STAT3

Mary Canavan[1], Viviana Marzaioli[1], Vipul Bhargava[2], Sunil Nagpal[3], Phil Gallagher[4], Conor Hurson[5], Ronan Mullan[6], Douglas Veale[7] and Ursula Fearon[1], [1]Molecular Rheumatology, Trinity College Dublin, Dublin, Dublin, Ireland, [2]Janssen Research & Development, Springhouse, PA, [3]Janssen Research & Development, Collegeville, PA, [4]St Vincents University Hospital, UCD, Dublin, Ireland, [5]St Vincents University Hospital, UCD, Dublin, Dublin, Ireland, [6]Adelaide and Meath Hospital, Dublin, Dublin, Ireland, [7]EULAR Centre for Arthritis and Rheumatic Diseases, St Vincents University Hospital, UCD, Dublin, Dublin, Ireland

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Myeloid Dendritic Cells (DC) are potent antigen presenting cells that can be subdivided into CD141$^+$ and CD1c$^+$ DC. We have previously reported an unacknowledged role of CD141$^+$DC in the RA synovium. However, the identification and function of CD1c$^+$ DC in the RA synovium has yet to be fully elucidated. Therefore our aim was to investigate if CD1c$^+$DC reside in the RA synovium and ascertain if they represent a unique population, distinct from peripheral blood CD1c$^+$DC.

Methods: Synovial tissue (ST) biopsies and synovial fluid mononuclear cells (SFMC) were obtained via arthroscopy and healthy control (HC) ST was obtained during ACL surgery. Synovial biopsies were enzymatically and mechanically dissociated to yield a single cell suspension. SFMC and peripheral blood mononuclear cells (PBMC) in addition to synovial tissue digests were stained with a panel of fluorochrome conjugated antibodies and single cell analysis was performed by multicolour flow cytometry. CD1c$^+$DC were sorted from RA SF and peripheral blood (PB) and RNA-sequencing was performed. Principal Component Analysis (PCA), Enriched pathway analysis, heatmaps and hierarchical clustering were identified using the DeSeq2 R package and Ingenuity® Pathway Analysis (IPA). For functional experiments CD1c$^+$DC were magnetically sorted from RA SFMC and RA PBMC and phagocytosis was assessed using flow cytometry. Finally allogeneic T cell cocultures were performed with SF and PB CD1c$^+$DC in the presence or absence of the STAT3 inhibitor Stattic.

Results: CD1c$^+$DC are significantly decreased in RA PB compared to HC PB ($p< 0.01$) and express significantly higher levels of the chemokine receptors CCR7 ($p< 0.05$) and CXCR3 ($p=0.08$) compared to HC DC - suggestive of DC migration to the synovium. In support of this hypothesis, CD1c$^+$DC were identified in RA ST by multicolour flow cytometry and were significantly increased in RA ST compared to RA PB ($p< 0.01$). RA ST CD1c$^+$DC express significantly higher expression of the DC activation marker CD80 compared to RA PB ($p< 0.01$) or HC ST ($p< 0.05$). CD1c$^+$DC are also enriched in RA synovial fluid compared to RA PB ($p< 0.05$), express significantly higher levels of the maturation markers CD80,CD83,CD40,PD-L1 and BTLA (all $p< 0.05$) and are less phagocytic compared to matched PB. RNA-sequencing and PCA analysis revealed distinct transcriptional variation between synovial and PB CD1c$^+$DC. Moreover, IPA analysis revealed an enrichment in the STAT3 pathway in synovial DC. Synovial CD1c$^+$DC induce proinflammatory cytokines (TNFα, GMCSF, IFNγ) from CD4$^+$ T-cells in allogeneic cocultures, and effect which is abrogated in the presence of a STAT3 inhibitor.

Conclusion: CD1c$^+$DC are present in the RA synovium in a mature state, have distinct tissue specific characteristics and mediate their T cell stimulatory capabilities via STAT3.

Disclosure: M. Canavan, None; **V. Marzaioli**, None; **V. Bhargava**, None; **S. Nagpal**, None; **P. Gallagher**, None; **C. Hurson**, None; **R. Mullan**, None; **D. Veale**, AbbVie, 2, Health Beacon, 1, Janssen, 2, 8, Pfizer, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5; **U. Fearon**, None.

Abstract Number: 0068

Single Cell RNA-seq to Characterize Monocyte Subtypes in the Autoinflammatory Interferonopathy, SAVI and the Inflammasomopathy, NOMID

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Innate Immunity Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

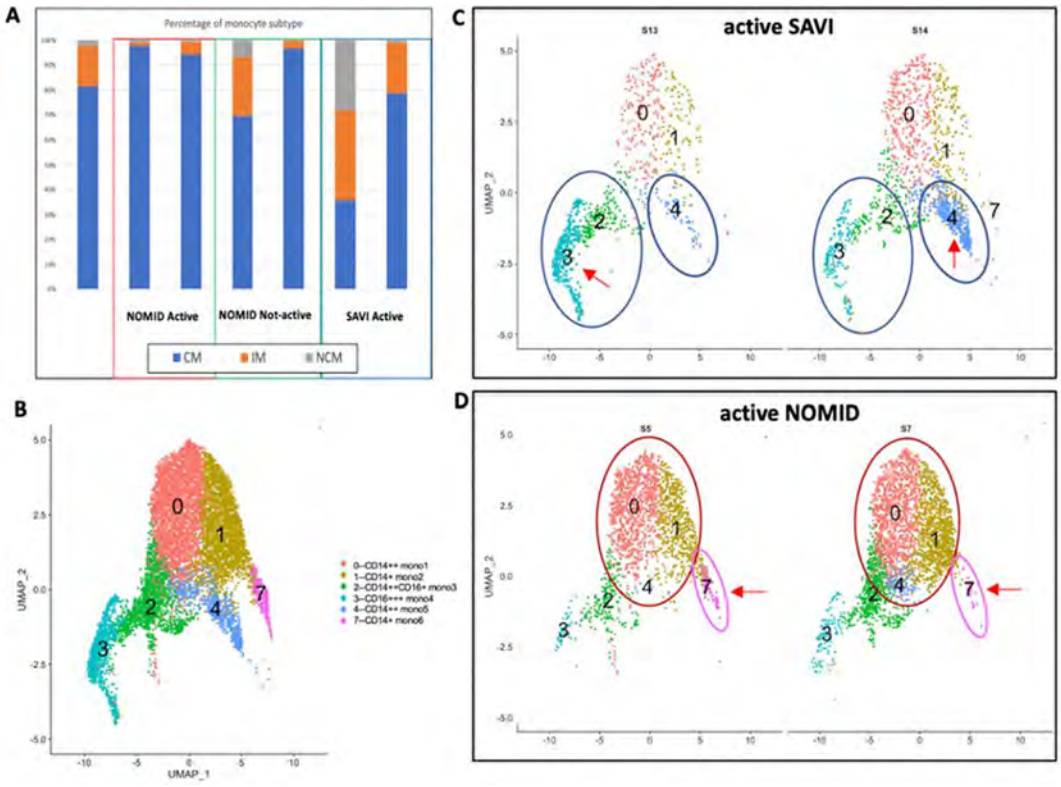

Figure 1. A. Each cell is annotated to be a classical (CM), intermediate (IM) or non-classical monocyte (NCM) by SingleR using MonacoImmuneData reference. Expansion of IM and NCM populations in one SAVI patient S13 and expansion of CM populations in mostly active NOMID patients and a patient who has been treated for 3 months with anakinra were quantified. B. Six monocyte subsets were identified by a shared nearest neighbor (SNN) modularity optimization- based clustering algorithm using Seurat. C, D. In active SAVI CD16+ mono3 (2), mono4 (3) and CD14+ mono5 (4) subsets were expanded, while in active NOMID expansion of CD14+ subsets mono1 (0), mono2 (1) and mono6 (7) were seen.

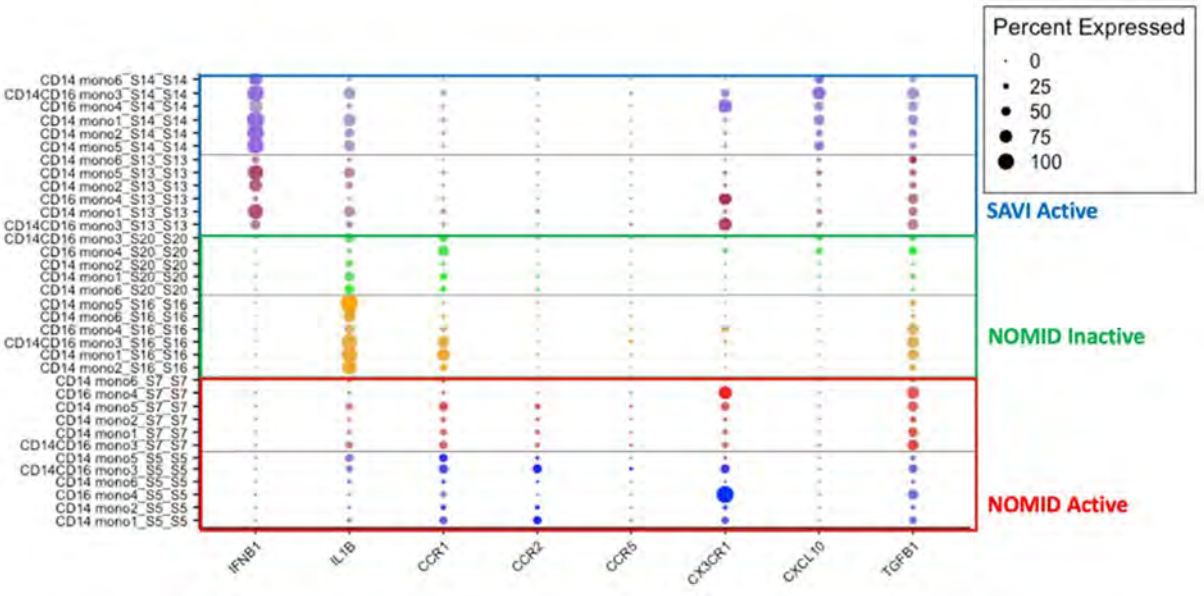

Figure 2. Selected gene expression patterns in SAVI and NOMID monocytes. In SAVI, active patients' monocytes have strong IFNB1 and moderate IL1B expression. CD16+ monocytes from active SAVI and NOMID pts. express CX3CR1 transcripts. NOMID patients do not express IFNB1. In inactive NOMID patients' monocytes express more IL1B but lower CCR2 transcript levels than in clinically active NOMID patients.

Background/Purpose: Monocytes are pivotal producers of key inflammatory cytokines that drive autoinflammatory diseases. In SAVI, constitutive STING activation causes chronic activation with increased type-I IFN response gene expression in whole blood, and in NOMID, constitutive activation of the NLRP3 inflammasome leads to IL-1β mediated chronic inflammation. The effects of the respective activation of STING or the NLRP3 inflammasome on monocyte activation and differentiation are poorly understood. We used single cell RNA sequencing (scRNAseq) to profile purified monocytes from 2 SAVI and 3 NOMID patients.

Methods: Monocytes were positively selected from peripheral blood using CD14+ MicroBeads (Miltenyi). Transcription profiles from bead-purified monocytes from 2 SAVI and 3 NOMID patients (pts) enrolled in an IRB approved protocol (NCT02974595) were generated; 3000 monocytes were prepared for scRNAseq using Chromium™ Single Cell 3' v2 Reagent Kit (10x genomics) and were sequenced (NextSeq®, Illumina) targeting 60,000 reads/cell. Files were demultiplexed and aligned to the GRCh38 transcriptome reference using Cell Ranger. Gene-barcode-matrices that passed quality control were analyzed individually and integrated; monocyte subsets were identified by a shared nearest neighbor (SNN) modularity optimization-based clustering algorithm (Seurat). Cell subsets were annotated based on cell-type specific marker expression. Each cell is also annotated as a classical (CM), intermediate (IM) or non-classical (NCM) monocyte (SingleR using MonacoImmuneData reference).

Results: Gene expression of *CD14* and *FCGR3A*/CD16 transcripts and SNN modularity optimization-based clustering algorithms identified 6 monocyte subsets for all samples (active SAVI (n=2), active NOMID (n=2) and inactive NOMID (n=2)) (Fig.1 A, B). In SAVI pts, CD16+ NCM and CD14+CD16+ IM are expanded. Interestingly, in SAVI all monocyte subsets strongly express IFNB1 with less IL1B expression. CX3CR1 is high in CD16 NCM subsets. In contrast, in NOMID pts, CD14+ CM subpopulations are expanded. NOMID monocytes do not express IFNB1 and IL1B expression was stronger in CD14+ CM from the 2 inactive than active NOMID pts. Comparing active and inactive NOMID, the percentage of CD14+ cells decreases as well as their CCR2 expression but not CCR1 expression. Furthermore, CX3CR1 expression drops in CD16+ NCM in inactive NOMID (Fig. 2).

Conclusion: In the active, NLRP3-inflammasome mediated disease, NOMID, classical monocytes (CM) subsets are expanded while in the Type-1 interferonopathy, SAVI, CD16+ NCM are expanded. The distinct expression of *IFNB1*

transcripts in SAVI only and the chemokine receptor modulation in active (SAVI and NOMID) and inactive (NOMID) disease, suggest disease-specific activation dependent monocyte subset heterogeneity in chronic autoinflammatory diseases. Gene expression profiling is ongoing and may contribute to the characterization of the monocyte diversity in NOMID and SAVI that propagates chronic inflammation and tissue damage.

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Abstract Number: 0069

Identification of CD13 as a Potential Cause for SARS-CoV-2-triggered Hyperinflammation and Thrombosis

Eliza Pei-Suen Tsou[1], Gautam Sule[1], Mikel Gurrea Rubio[2], M. Asif Amin[1], Yu Zuo[1], Jason Knight[1], Yogendra Kanthi[3] and David Fox[1], [1]Division of Rheumatology, University of Michigan, Ann Arbor, MI, [2]Division of Rheumatology, University of Michigan, Canton, MI, [3]Division of Cardiovascular Medicine, Ann Arbor

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The ectopeptidase CD13, which is highly expressed on stromal and myeloid cells in joints, lung and other tissues, is a known receptor for many coronaviruses. Its soluble form (sCD13) is a powerful pro-inflammatory mediator with strong chemotactic, angiogenic and arthritogenic properties. Neutrophil extracellular traps (NETs) are known to trigger formation of thrombi in antiphospholipid syndrome (APS), and likely also in other inflammatory and rheumatologic conditions. Recently NET-associated markers have been shown to correlate with disease severity in COVID-19 patients. Moreover, sera from COVID-19 patients trigger healthy neutrophils to undergo NETosis. We hypothesized that CD13 is also a receptor for SARS-CoV-2, and that both the cell membrane-anchored and soluble forms of CD13 trigger aggressive inflammatory responses in SARS-CoV-2 infection, including NETosis.

Methods: Serum samples from healthy volunteers (n=53) and hospitalized COVID-19 patients (n=172) were used in this study. The levels of sCD13, citrullinated histone H3 (Cit-H3), and MPO-DNA complexes were measured by ELISA. NETosis was measured by SYTOX Green and NET-associated elastase activity. GraphPad Prism v8 was used for statistical analysis. The Mann-Whitney test or Kruskal-Wallis test was used to compare groups. Correlation was tested by Spearman's correlation coefficient. Statistical significance was defined as $p< 0.05$.

Results: Significant elevation of sCD13 was observed in COVID-19 patients as compared with healthy subjects (960 ± 81.2 vs. 94.7 ± 37.6 ng/ml, mean ± SEM, $p< 0.0001$), with the highest levels observed in patients who required mechanical ventilation. sCD13 levels were two-fold higher in African American compared to Caucasian patients ($p=0.02$). In addition, sCD13 positively correlated with inflammation-indicative markers, including ferritin ($r=0.252$, $p=0.002$) and lactate dehydrogenase ($r=0.374$, $p< 0.0001$), as well as NETosis-related markers, such as Cit-H3 ($r=0.243$, $p=0.001$) and MPO-DNA ($r=0.242$, $p=0.001$). Both sCD13 and anti-CD13 monoclonal antibodies induced robust NETosis in control neutrophils *in vitro*.

Conclusion: Although not yet identified as a cell surface receptor for cell entry of the novel coronavirus SARS-CoV-2, CD13—which is much more widely expressed than ACE2—could play several unique roles in viral pathogenesis. These data identify CD13 and a cell surface receptor for sCD13 as potential triggers for COVID-19-associated NETosis, vascular stress and thromboembolic complications. The powerful pro-inflammatory effects of sCD13 may account for an important component of the unusual hyperinflammatory complications of this viral infection. Receptors for sCD13, one of which we have recently identified as the bradykinin 1 receptor (B1R) could become therapeutic targets in patients with severe COVID-19.

Disclosure: E. Tsou, None; **G. Sule**, None; **M. Gurrea Rubio**, None; **M. Amin**, None; **Y. Zuo**, None; **J. Knight**, None; **Y. Kanthi**, None; **D. Fox**, None.

Abstract Number: 0070

Neutrophils Transiting Through Megakaryocytes During Emperipolesis Exhibit Distinct Fates and Acquire the Capacity to Guide Other Neutrophils via MK Trails

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Megakaryocytes (MKs) can contribute directly to experimental arthritis via pro-inflammatory microparticles containing IL-1 (Cunin et al. *Journal of Clinical Investigation*, 2017). MKs also interact with immune cells via emperipolesis (EP), a novel cell-in-cell interaction whereby neutrophils pass through MKs before egressing without apparent harm to either cell. EP is common in bone marrow, but its cell biology and implications for MKs and neutrophils are unknown.

Methods: We compared the frequency of EP between healthy mice and different inflammatory models (K/BxN serum transfer arthritis, LPS injection, cecal ligation and puncture). We developed an *in vitro* model of EP by culturing bone marrow MKs with neutrophils and quantitated the time course using live cell spinning disk microscopy. We used transmission electron microscopy and immunofluorescence microscopy to explore intermediate stages of EP.

Results: P frequency increased 2-3-fold in inflammatory arthritis, after administration of LPS, and after cecal ligation and puncture (a model of polymicrobial sepsis). EP bifurcated into fast and slow events, with approximately 40% of

neutrophils transiting through MKs in less than 10 minutes whereas 35% persisted for 50 minutes or more. Slow EP was often associated with direct physical contact between neutrophils and the MK nucleus. Electron microscopy revealed that most neutrophils within MKs were encased by a phagosome-like compartment, termed the "emperisome". However, some neutrophils could be observed only exiting the emperisome to enter the MK cytoplasm, where we could observe physical association with the endoplasmic reticulum or the demarcation membrane system (the MK's platelet membrane reserve). These observations suggest the existence of different forms of EP. Intriguingly, we observed that neutrophils pull long tubes consisting of CD41+ MK membrane ("MK trails") during their egress from MKs. MK trails express markers for immune cell attachment and rolling. Post-EP neutrophils deposited fragments of these trails on endothelial cells during migration *in vitro*, marking paths then preferentially visited by other neutrophils.

Conclusion: EP increases markedly during inflammation, including inflammatory arthritis. We identified fast and slow modes of EP, as well as distinct intracellular areas of neutrophil localization within MKs, suggesting that EP can serve multiple functions. EP results in the generation of novel MK trails that are deposited by neutrophils on endothelial cells, suggesting a new mechanism by which EP enables coordination of neutrophil behavior and thereby an organized and efficient inflammatory response.

Disclosure: F. Huang, None; **P. Cunin**, None; **F. Radtke**, None; **R. Grieshaber-Bouyer**, None; **R. Darbousset**, None; **P. Nigrovic**, Novartis, 2, 5, BMS, 2, 5, Pfizer, 2, 5, Sobi, 5, Miach Orthopedics, 5, Simcere, 5, XBiotech, 5, Quench Bio, 5, Siglion, 5, Cerecor, 5, UpToDate, 7, American Academy of Pediatrics, 7, CARRA, 9.

Abstract Number: 0071

Significant Enrichment of Transcriptionally Distinct CD206+CD163+ Macrophage Population in Rheumatoid Arthritis Synovial Tissue

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Innate Immunity Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Synovial tissue macrophages are an exquisitely plastic pool of innate cells that play a key role in RA disease progression. However, the precise nature, diversity and function of macrophage subsets within the inflamed joint remains unexplored.

Methods: Single cell analysis of Rheumatoid Arthritis, Psoriatic Arthritis, Osteoarthritis and healthy control synovial tissue biopsies and synovial fluid mononuclear cells was performed using advanced flow cytometry with the following panel (CD40, CD45, CD64, CD68, CD163, CD206, CD253, CCR4, CCR7, CXCR1, CXCR3). CD206+CD163+ and CD206-CD163- macrophages were sorted from RA synovial tissue by FACSAria sorter for subsequent RNAseq, FLIM analysis and autologous T-cell co-culture experiments.

Results: RA synovial tissue and fluid macrophages display markers typical of both M1 (CD40+CD253+) and M2 (CD206+CD163+) macrophages with a spectrum of macrophage activation states identified in RA synovial tissue that don't fully conform to the classic M1/M2 framework. Within this spectrum, significant enrichment of a dominant CD206+CD163+ macrophage-subtype is present in synovial tissue versus fluid ($p< 0.05$). CD206+CD163+ synovial tissue macrophages express significantly more CD40 compared to synovial fluid ($p< 0.0003$), positively correlate with disease activity ($r=0.6$, $p< 0.01$), with baseline levels predicting response to therapy ($p< 0.05$). Moreover, CD206+CD163+CD40+ macrophages are enriched in RA synovial tissue compared to PsA and OA pathotypes ($p< 0.05$) and display distinct chemokine receptor expression patterns. While the CD206+CD163+ macrophage subset is present in healthy synovial tissue, expression of CD40 is completely absent in the healthy synovium ($p< 0.05$). RNA-seq analysis indicates that the CD206+CD163+ population is transcriptionally distinct from synovial tissue CD206-CD163-, synovial fluid CD206+CD163+, and pure RA monocyte-derived M1/M2 macrophages, with unique tissue-resident gene signatures (TREM2+, FOLR2+, LYVE1+ C1QA+, TIMD4+, CD48-, CCR2-). Moreover, differing metabolic demands between CD206+CD163+ and CD206-CD163- subsets was demonstrated by RNAseq and FLIM analysis. Finally, CD206+CD163+ macrophages have the capacity to induce autologous T-cell responses and spontaneously secrete high levels of pro-inflammatory cytokines, thus further contributing to the local inflammatory response.

Conclusion: This data identifies enrichment of a previously undescribed dysfunctional dominant and transcriptionally distinct macrophage subtype in RA synovial-tissue.

Disclosure: M. Hanlon, None; **M. Canavan**, None; **Q. Song**, Janssen Research & Development, LLC, Spring House, PA, USA, 3; **C. Low**, None; **P. Gallagher**, None; **R. Mullan**, None; **C. Hurson**, None; **S. Nagpal**, None; **D. Veale**, AbbVie, 2, Health Beacon, 1, Janssen, 2, 8, Pfizer, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5; **U. Fearon**, None.

Abstract Number: 0072

Characterizing Heterogeneity of Synovial Macrophages in Rheumatoid Arthritis Patients

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SESSION INFORMATION
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Session Title: Innate Immunity Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Macrophages in the synovial lining of the joint are critical players in the pathogenesis of rheumatoid arthritis (RA). While they are potent producers of inflammatory molecules, there is also evidence that macrophage play a role in the resolution of inflammation. A better understanding of macrophage heterogeneity in humans could help pinpoint pathways and potential therapeutic targets for treating RA that are specific to particular subpopulations.

Methods: We obtained synovial tissue samples from the wrist joints of patients with active RA through minimally invasive ultrasound-guided synovial biopsy. Tissue was processed into single-cell suspension and enriched for CD45+ immune cells by Fluorescence Activated Cell Sorting (FACS). Next, droplet-based single cell RNA-sequencing (scR-

NA-seq) was performed using the 10X Genomics instrument. The sequenced reads were aligned and mapped to genes using CellRanger pipeline, followed by R package.

Results: We previously used single-cell RNA-sequencing to report the presence of 4 distinct subpopulations of mouse synovial macrophages. Based on their distinct transcriptional profiles, we characterize these populations as synovial lining, interstitial, antigen presenting, and infiltrating. Here, we examined the single cell expression profiles of RA synovial biopsy samples to investigate whether humans exhibit similar disposition of synovial macrophage heterogeneity as observed in mice. Using integrative gene module scoring of top 10 orthologous markers, the labels of 4 mouse subpopulations were projected onto human macrophages. Large variations in the composition of macrophage subppopulations was observed among patients. Strikingly, patients with higher proportions of synovial lining and interstitial macrophage subpopulations are significantly associated with lower clinical severity of RA, which is consistent with their anti-inflammatory phenotypes observed in mice. We also compared the 4 mouse subpopulations against an independent dataset generated by Accelerating Medicines Partnership (AMP) Consortium, where synovial myeloid cells from patients with RA or osteoarthritis (OA) were profiled. We observed the enrichment of synovial lining expression signatures in OA, which is generally associated with lower levels of inflammation. In contrast, signatures of antigen presenting and infiltrating subsets are enriched in the RA patients with high immune cell infiltration, supporting the expansion of these subsets by recruitment of circulating monocytes.

Conclusion: We were able to characterize human synovial macrophage heterogeneity by translating our findings from subpopulations in mice. Further investigation of the activation of these macrophages in the inflamed joint may lead to the development of therapies to target the pathogenic function of specific subpopulations in RA.

Disclosure: S. Chen, None; **Y. Wang**, None; **A. Montgomery**, None; **S. Dominguez**, None; **C. Cuda**, None; **G. Gadhvi**, None; **H. Perlman**, None; **D. Winter**, None.

Abstract Number: 0073

A Cross-Species Map of Neutrophil Inflammatory Responses

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

Background/Purpose: Neutrophils are important mediators of immune defense as well as key protagonists in immune-mediated disease. How these cells adapt differently to sterile and septic inflammatory conditions may offer opportunities to target neutrophils without disarming immune defense.

Methods: Here, we applied an in-depth, cross-species and cross-condition analysis of publicly available RNA sequencing data from 286 neutrophil populations from 26 different datasets. Condition-variance versus species-variance was calculated on a per-gene basis. Similarities and differences between conditions were examined by KEGG pathways, gene ontology (GO), and principal component analysis (PCA). The regulatory activity of transcription factors was predicted using ENCODE and ChEA3 libraries.

Results: 87% of human genes could be assigned one-to-one murine orthologs with high confidence according to ENSEMBL version 100. The overall transcriptional landscape of healthy human and murine neutrophils exhibited strong correlation (Pearson's R = 0.66; $P < 2.2 \times 10^{-16}$). By PCA, human blood neutrophils resembled murine blood neutrophils more than neutrophils from murine bone marrow, spleen and liver.

Within orthologous genes that exhibited a high dynamic range, 48% varied more between species than between experimental conditions. These genes were enriched for GO terms including cell-cell adhesion and metabolism. By contrast, 52% displayed higher variance between experimental conditions, reflecting conserved transcriptional responses in human and murine neutrophils. Condition-variant genes were associated with immune function and degranulation. A query of the GWAS catalog for SNPs associated with these genes identified association with immune-mediated conditions including allergy, psoriasis, rheumatoid arthritis and systemic lupus erythematosus.

We then compared different disease states. Neutrophils from aortic aneurysms, PAPA syndrome, influenza vaccination and CD200R-knockout mice exhibited few differences from healthy controls. By contrast, systemic juvenile idiopathic arthritis blood neutrophils differed from healthy human blood neutrophils by more than 300 genes. We identified a 151-gene transcriptomic inflammatory response program conserved across a broad range of conditions and between humans and mice, including elevation of *NFKBIA*, *TNFAIP3*, *SOCS3*, *IL1B* and *CCL2*. Transcription factor enrichment analysis implicated NFKB1, RELA, STAT1 and JUN as key drivers ($P < 1 \times 10^{-6}$), consistent with strong enrichment for the GO terms associated with NFkB activation and cytokine response.

Conclusion: Through a comparison of neutrophils across species and conditions, we identified substantially conserved transcriptomic responses between human and murine neutrophils. We define a conserved neutrophil inflammatory response program preserved across species and conditions. These findings provide new insight into the selection of potential targets for therapeutic manipulation of the contribution of neutrophils to sterile inflammatory diseases.

Disclosure: F. Radtke, None; **F. Huang**, None; **P. Nigrovic**, Novartis, 2, 5, BMS, 2, 5, Pfizer, 2, 5, Sobi, 5, Miach Orthopedics, 5, Simcere, 5, XBiotech, 5, Quench Bio, 5, Siglion, 5, Cerecor, 5, UpToDate, 7, American Academy of Pediatrics, 7, CARRA, 9; **R. Grieshaber-Bouyer**, None.

Abstract Number: 0074

The Intracellular DNA Sensor STING Protects Against Bone Loss Through Regulation of Type I Interferons

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Innate Immunity Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The intracellular DNA sensor Stimulator of Interferon Genes (STING) is essential for detection of viral and bacterial pathogen DNA. As with other pathways in the innate immune system, hyperactivation of the STING pathway is associated with autoinflammatory and autoimmune diseases. Activation of STING promotes anti-viral responses through production of type I interferons, including IFNβ. A pleiotropic cytokine, IFNβ is a potent stimulus of the innate immune system and has also been shown to inhibit the formation of osteoclasts. We therefore sought to determine whether the STING pathway impacts bone homeostasis and osteoclastogenesis.

Methods: Osteoclast formation assays were performed using RANKL-stimulated bone marrow progenitors from STING deficient (KO) mice and myeloid-specific STING KOs. The immortalized myeloid cell line RAW294.7 was engineered to stably overexpress murine STING or an empty vector control. RANKL was used to stimulate osteoclast precursors to form osteoclast-like cells *in vitro*. Secreted IFNβ was monitored using ELISA. IFNβ activity was inhibited using an IFNaR1 blocking antibody (Biolegend). Trabecular and cortical bone parameters were determined in femurs from aging (6, 13, and 15 months) STING whole body KO mice and littermate controls using microCT. Ovariectomies in myeloid-specific-STING KOs ($STING^{flox/flox}$ $LysM^{+/-}$, hereafter referred to $STING^{LysM}$ KO) and littermate controls ($STING^{flox/flox}$ $LysM^{-/-}$), were performed in young female mice and bone parameters were evaluated by microCT 8 weeks after surgery.

Results: Osteoclast differentiation assays demonstrate that young STING KO bone marrow progenitors develop into osteoclasts faster than littermate controls. This phenotype of increased osteoclast formation is sustained in progenitors from aged (6 month old) STING KO mice. The $STING^{LysM}$ KO precursor cells recapitulate the osteoclast formation phenotype of STING KO cells *in vitro*. A reciprocal effect is observed in RANKL-stimulated RAW294.7 cells overexpressing STING, where fewer osteoclast-like cells are generated compared to RAW294.7 cells containing an empty vector. STING overexpressing RAW294.7 cells produce more IFNβ than empty vector controls, and blocking IFNaR1 downstream of IFNβ limited osteoclast formation in STING over expressing RAW294.7 cells. To determine the role of STING for bone turnover *in vivo*, microCT was used to characterize bone in aging cohorts of STING KO mice. Consistent with these *in vitro* observations, STING KO mice lose trabecular bone faster than wildtype (WT) littermate controls. Myeloid STING is sufficient for enhanced bone turnover, as ovariectomized $STING^{LysM}$ KO mice exhibit a larger decrease in trabecular bone compared to littermate controls.

Conclusion: Our results are the first to implicate any of the cytosolic DNA sensors in the maintenance of bone. We demonstrate thatincreased STING activity limits osteoclast formation, an effect which is mediated at least in part by IFNβ. Moreover, loss of STING activity results in accelerated bone loss. These data suggest that STING activation plays an important role inthe protection from bone loss in the settings of viral infection and inflammation in inflammatory rheumatic diseases.

Disclosure: S. MacLauchlan, None; **C. Manning**, None; **S. Chen**, None; **K. Fitzgerald**, None; **S. Sharma**, None; **E. Gravallese**, New England Journal of Medicine, 3, UpToDate, 7, Co-editor of the textbook Rheumatology, 7.

Abstract Number: 0075

$CD209^{+}/CD14^{+}$ Dendritic Cells Characterization in Rheumatoid versus Psoriasis Arthritis Patients

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

Background/Purpose: Dendritic cells (DCs) are a heterogeneous population of professional antigen-presenting cells which are at the interface between innate and adaptive immunity. There are different DCs subsets, classified according to their tissue location and their functions. A specific subset of DCs is known to derive from monocyte and has a key role in inflammation and infection. This study aimed to identify and characterize a specific subset of DC $CD209^+$/$CD14^+$ and evaluate their characteristics in the periphery of patients with inflammatory arthritic (IA). In addition, it aimed to evaluate the enrichment and activation of these cells at the site of inflammation, the join of rheumatoid (RA) and psoriatic arthritic (PsA) patients.

Methods: Peripheral blood and synovial fluid mononuclear cells (PBMC and SFMC) were isolated by Ficoll density gradient from healthy subject (HC), RA and PsA patients. Single cell synovial tissue suspension from RA and PsA patients was obtained by enzymatic digestion. PBMC, SFMC and synovial tissue cell suspensions were analysed by flow cytometry to identify the $CD209^+$/$CD14^+$ DC subset and its frequency. Expression of chemokines receptors (CCR6, CCR7, CXCR3, CXCR4 and CXCR5) and activation markers (CD40 and CD80) on the surface of the $CD209^+$/$CD14^+$ DC subset were also evaluated by flow cytometry.

Results: We identified, for the first time, the $CD209^+$/$CD14^+$ DC population in PBMC of RA and PsA patients and HC, with no significant differences among the groups. Interestingly, we observed that this population was enriched in SFMC of RA and PsA patients, with a further increased frequency demonstrated in the synovial tissue cell suspensions. This was paralleled by a more mature phenotype of the DC subset at the site inflammation compared to periphery, with a significant increase in CD40 ($p< 0.01$) in PsA patients and CD40 and CD80 in RA patient ($p< 0.01$). In addition, SPICE analysis identified a differential expression and co-expression of chemokine receptors at the periphery of RA and PsA patients, when compared to the HC, suggests that DCs in the periphery are already activated to migratory to sites of inflammation in IA. We further observed a unique profile of chemokines receptors in single cell analysis of synovial tissue cell suspension demonstrating increased expression of both and CXCR3 ($p< 0.01$) and CXCR5 ($p< 0.001$) in RA and PsA.

Conclusion: We identify for the first time a monocyte-derived DC population characterised as $CD209^+$/$CD14^+$ in the periphery of RA and PsA patients. This population was enriched at the site of inflammation and displayed a unique chemokine receptor profile and activation markers, suggesting these cells are already activated in the periphery of IA patients, and are recruited and further activated into the joint of IA patients.

Disclosure: V. Marzaioli, None; **A. Floudas**, None; **M. Canavan**, None; **S. Wade**, None; **K. Murray**, None; **R. Mullan**, None; **C. Hurson**, None; **D. Veale**, AbbVie, 2, Health Beacon, 1, Janssen, 2, 8, Pfizer, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5; **U. Fearon**, None.

Abstract Number: 0076

The Role of Interferon Kappa in Psoriasis

Mehrnaz Gharaee-Kermani[1], Shannon Estadt[2], Sonya Wolf-Fortune[1], Jianhua Liu[1], Tamra Reed[3], Johann Gudjonsson[4] and J. Michelle Kahlenberg[5], [1]University of Michigan, Ann Arbor, MI, [2]University of Michigan, Ypsilanti, MI, [3]University of Michigan, Ann Arbor, [4]University of Michigan, Ann ArborUniversity of Michigan, [5]Division of Rheumatology, University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Friday, November 6, 2020
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriasis is a common, chronic inflammatory autoimmune skin diseases characterized by hyperproliferation and abnormal differentiation of keratinocytes and infiltration of inflammatory cells. Early infiltration of plasmacytoid dendritic cells and detection of an interferon (IFN) signature occurs in many psoriasis lesions. Recently, we described keratinocyte production of interferon kappa (IFNk) as an important source of type I IFN production in the epidermis. We thus wanted to explore the role of IFNk in psoriasis.

Methods: We used the well-characterized imiquimod (IMQ) psoriasis model for these studies. 10-week old male and female wild type (WT) and mice transgenic for *Ifnk* (TG) expressed under the K14 promoter (thus inducing expression only in the epidermis) and mice deficient for *Ifnk* (KO) were used. Psoriasis was induced by topical application of IMQ on both ears for 8 consecutive days (n=6-10 mice per each group. Control mice received Vaseline (n=10 mice per each group). Animals were monitored daily for ear thickness, lesion severity, and body weight and photo were taken daily. On day nine, mice were euthanized, and disease severity were compared among all groups via RT-qPCR, immunohistochemistry, and flow cytometry.

Results: For all evaluations, untreated mice did not show any sign of inflammation or disease. While all IMQ treated mice exhibited psoriasis lesions in both ears after 8 days of treatment, development of splenomegaly, ear thickness, cutaneous lesion size and spleen weight were significantly higher in TG mice ($p < .001$) vs. WT for both male and female mice. The spleen size and ear thickness were significantly smaller in KO mice compared to WT ($p < .01$). Interestingly, the difference was more exaggerated in TG female vs. male mice. H&E staining revealed higher number of inflammatory cell infiltrates in IMQ treated TG vs. WT and fewer inflammatory infiltrates in KO mice. IL-17 and CD8 co-staining of ear tissues revealed greater number of CD8 and IL-17 double-positive cells in IMQ treated TG > WT >KO mice in both male and female groups. Gene expression for type I IFNs, the IFN-regulated gene *Mx1*, *Stat3,* and inflammatory cytokines, *Il1b*, *Il17*, *Tnfa*, *Il6, Il12* and *Il23* were significantly higher in IMQ treated TG >WT >KO ($p < 0.05$ for all genes tested). While both TG and WT mice demonstrated influx of monocytes by flow cytometry, KO mice did not exhibit a detectible increase after IMQ treatment. No difference in plasmacytoid dendritic cell recruitment was noted between groups.

Conclusion: Overexpression of *Ifnk* in the epidermis results in increased disease severity after topical application of IMQ, whereas deletion of *Ifnk* attenuated disease. Although, overexpression of *Ifnk* alone in the skin does not trigger skin inflammation, our data suggests that epidermal type I IFNs may trigger may act as a rheostat for psoriasis inflammatory responses, driving more inflammatory cells in the skin and promoting a heightened inflammatory and IL-17-oriented response. Together, these data suggest that overproduction of type I IFNs may impact psoriasis development and there may be a role of targeting IFNs in early disease. Further studies will need to elucidate the specific mechanisms that may be at play, especially in human skin.

Disclosure: M. Gharaee-Kermani, None; **S. Estadt**, None; **S. Wolf-Fortune**, None; **J. Liu**, None; **T. Reed**, None; **J. Gudjonsson**, Celgene, 2; **J. Kahlenberg**, AstraZeneca, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 5, Avion Pharma, 5, Celgene, 2.

Abstract Number: 0077

Mimickers of Immunoglobulin G4-Related Disease

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Immunoglobulin G4-related disease (IgG4-RD) is a fibro inflammatory condition of unclear etiology. This rare condition can affect any organ system and has protean manifestations mimicking many other diseases. As the knowledge regarding this condition has increased among providers, there has been a tendency to over diagnose IgG4-RD. Therefore, the primary aim of this retrospective study is to identify common mimickers of IgG4-RD in an United States cohort.

Methods: The study design is a retrospective chart review**.** All patients referred to the IgG4 clinic at Emory University with specific diagnosis of IgG4-RD from August 2013- February 2020 were reviewed and categorized into mimickers versus IgG4-RD. The diagnosis of IgG4-RD and mimickers were made with clinicopathological correlation. Emory University Institutional Review Board approved this study.

Results: From August 2013- February 2020, a total of 198 patients were referred to the Emory IgG4- RD clinic. As outlined in Table 1, 85 or 43% were noted be mimickers of IgG4-RD. We classified the mimickers into infection (2%), neoplastic disease (21%), autoimmune disease (31%), and other (46%). Based on the IgG-RD classification criteria, 93% of these cases met exclusion criteria and only 7% met inclusion criteria, which had mean scores of 3 and ranged from 0-10 (greater than 20 meets criteria).

The neoplastic category included lymphoma (28%), plasma cell dyscrasia (17%), and histiocytosis (Rosai Dorfman, Langerhans's, Erdheim Chester Disease) (17%). Noteworthy, 75% of the neoplastic diagnoses were made when repeat biopsy was performed either due to clinical suspicion or lack of response to treatment.

Categories	Number of Cases	Serum IgG4 mg/dL* Mean (Range)	Average Serum IgG mg/dL*
Infection	2	70 (51-89	1129
Neoplasia	18	105 (8- 4090)	1411
Autoimmune Disease	26	41 (6-136)	1158
Other	39	88 (5-308)	1255
Total Mimickers	85	76 (5-4090)	1246

*Normal Reference Values:
Serum IgG levels: 610-1,616 mg/dL
Serum IgG4 levels: 1-123 mg/d

Table 1. Categories of Mimickers

CATEGORIES	SUBCATEGORIES	NUMBER OF CASES
NEOPLASIAS	Lymphoma	5
	Histiocytosis	3
	Plasma Cell Dyscrasia	3
	Meningioma	2
	Head and Neck Cancer	1
	Myelodysplastic syndrome causing Kikuchi lymphadenitis	1
	Pancreatic Cancer	1
	Castleman's Disease	1
	Sarcoma	1
	TOTAL	19
AUTOIMMUNE DISEASE		
	Sjogren's Syndrome	6
	Inflammatory arthritis	5
	ANCA Associated Vasculitis	4
	Undifferentiated connective tissue disease	3
	Sarcoidosis	2
	Systemic Lupus Erythematosus	2
	Isolated aortitis	2
	Idiopathic Retroperitoneal Fibrosis	1
	Inflammatory myositis	1
	TOTAL	26
INFECTION		
	Bacterial infection	1
	Fungal (Mucormycosis)	1
	TOTAL	2
OTHER		
	Idiopathic / recurrent pancreatitis	15
	Fibromyalgia	4
	Lymphadenopathy	3
	Sclerosing mesenteritis	3
	Primary Sclerosing Cholangitis	2
	Inflammatory Pseudotumor	2
	Biliary stenosis of unclear etiology	1
	Crohn's Disease	1
	Arteriovenous Malformation	1
	Yellow Nail Syndrome	1
	Chronic inflammatory demyelinating polyneuropathy	1
	Osteoarthritis	1
	Benign Parotid Mass	1
	Unclear soft tissue swelling of neck	1
	IgA Nephropathy	1
	TOTAL	39

Table 2. Subcategories of Mimickers

Sjogren's syndrome was the predominant condition mistaken by IgG4-RD in the autoimmune category. We included cases that could not be proven to be IgG4-RD or any other specific diagnosis in the other category. Interestingly, in that category 60% had a GI manifestation, with half of those cases being recurrent pancreatitis as shown in Table 4.

The average serum IgG4 level across all mimickers was normal, but the levels ranged from 5-4,060 mg/dL (normal range 1-123 mg/dL). We identified 20 cases with elevated serum IgG4. Based on the IgG-RD classification criteria, these patients met exclusion criteria with 9 cases meeting pathologic criteria, 7 radiologic, 2 serologic, and 2 disease specific exclusions. Of note, 8 of these 20 cases had neoplastic disease and 4 cases had recurrent pancreatitis.

Conclusion: This study highlights that almost half of the patients referred for diagnosis of IgG4-RD actually were found to have a mimic of the disease. GI manifestations, particularly recurrent pancreatitis, were among the most

common referred diagnosis in our center. It should be emphasized that serum IgG4 levels are not diagnostic for the disease and can be elevated in other conditions. A tissue biopsy is indicated in majority of cases with atypical clinical presentation and repeating the biopsy is indicated if the patient's course is not typical for IgG4-RD. Also, a lymph node biopsy is not considered diagnostic. By identifying these mimickers, we hope to emphasize the necessity of considering these conditions while evaluating patients with IgG4-RD.

Disclosure: M. Ahmad, None; **R. Spandorfer**, None; **A. Khosroshahi**, None.

Abstract Number: 0078

Retrospective Analysis of Clinical Characteristics and Classification Criteria Performance in a Single Center Cohort of 114 Patients Diagnosed with IgG4-Related Disease

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Immunoglobulin G4 Related Disease (IgG4-RD) is a fibroinflammatory condition that can involve almost any organ system. Diagnosis is made based on correlation of clinical, pathological and laboratory data. The 2019 American College of Rheumatology (ACR) / European League Against Rheumatism (EULAR) classification criteria for IgG4-RD were recently published to provide unified classification criteria in clinical research. The purpose of this study was to characterize demographics, disease attributes and treatments of patients referred to our specialized IgG4-RD clinic. We evaluated the performance of the new classification criteria on this cohort to understand its correlation to diagnosis.

Methods: This was a retrospective chart review of patients referred to the IgG4-RD clinic at Emory University Hospital from August 2013 through September 2020. Data collected include disease manifestations, histopathology, serological markers, and treatments used. Patients were categorized based on the clinician's decision for diagnosis as: 1) definite, if they had typical clinical findings supported by histopathology or serology and diagnosed as IgG4-RD; 2) probable, if the diagnosis of IgG4-RD was still considered but could not be proven; 3) mimickers, if the patient was diagnosed as not having IgG4-RD. An ACR/EULAR classification criteria score was calculated to compare performance in these categories. The Emory University Institutional Review Board approved this study.

Results: A total of 198 patients referred to the Emory IgG4-RD clinic were evaluated. 84 (42%) were mimickers. Of the remaining 114, 58 (51%) were defined as definite and 56 (49%) as probable cases of IgG4-RD by treating clinicians. Patient demographics are shown in Table 1. Our cohort has the most representation of black patients with IgG4-RD in the published literature.

The most common organ systems affected are displayed in Figure 1. Pancreas was the most common at 37% of patients. Nearly half of patients had a less common (i.e. < 10% of patients) organ system involved. 61% of patients had multi-organ disease. Serology and treatments are shown in Table 2.

	Definite IgG4-RD (*n*=58)	Probable IgG4-RD (*n*=56)
Age	59 ± 14	56 ± 16
Gender		
Male	34 (59%)	24 (43%)
Female	24 (41%)	32 (57%)
Race/Ethnicity		
White/Caucasian	32 (55%)	28 (50%)
Black/African American	20 (34%)	23 (41%)
Asian/ South Asian	5 (9%)	3 (5%)
Hispanic	1 (2%)	1 (2%)
Native Hawaiian	0 (0%)	1 (2%)
History of asthma	7 (12%)	3 (5%)
History of seasonal or food allergy	6 (10%)	2 (4%)

Table 1. Demographics of patients with definite or probable IgG4-RD.

	Definite IgG4-RD (*n*=58)	Probable IgG4-RD (*n*=56)
Elevated Serum IgG4 level	42 (74%)	10 (18%)
Elevated IgG4/IgG Ratio (>20%)	19 (33%)	4 (7%)
Elevated Serum IgE level	23 (40%)	8 (14%)
Hypocomplementemia	6 (10%)	1 (2%)
ANA (> 1:40)	6 (10%)	4 (7%)
Rheumatoid Factor +	3 (5%)	6 (11%)
Treatment with Glucocorticoids	50 (86%)	50 (89%)
Treatment with Rituximab	34 (59%)	22 (39%)
Remission Rate	34 (59%)	30 (54%)

Table 2. Serology and treatment factors of patients with definite or probable IgG4-RD.

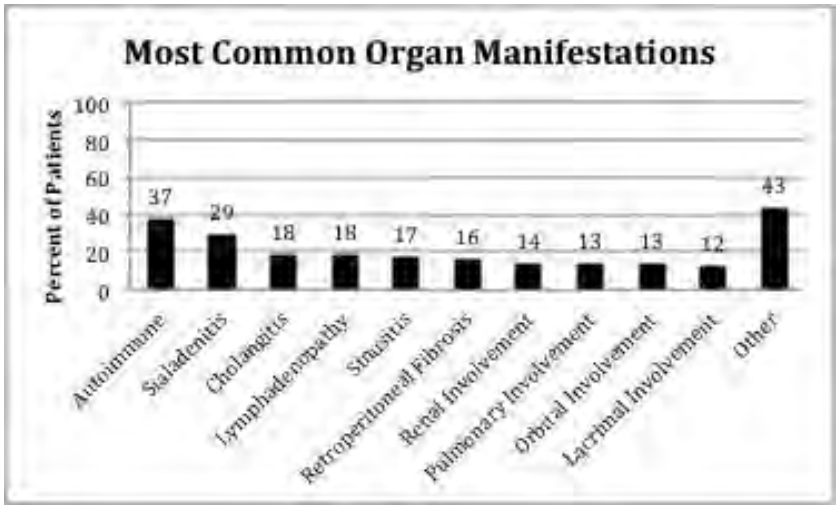

Figure 1. Organ system involvement in all definite and probable IgG4-RD cases expressed as a percentage of all patients

84% of patients with definite diagnosis were considered IgG4-RD based on classification criteria (i.e. score ≥ 20) with average score of 29 (range 4 -56). 9% in the probable category passed this threshold with an average score of 8 (range 0 – 31). None of the mimickers was classified as IgG4-RD based on classification criteria.

Conclusion: This study highlights that clinicians encounter many challenges in making a definitive diagnosis of IgG4-RD. In our cohort, 49% of patients fell into the category of probable diagnosis due to a lack of sufficient evidence to exclude or prove this condition. Patients with probable disease were treated similarly to those with definite disease and had similar rates of remission.

This is also the first study to evaluate the performance of ACR/EULAR IgG4-RD Classification Criteria in a single-center cohort. Patients with clinicopathological diagnosis of definite IgG4-RD largely met the scoring cutoff for diagnosis and mimickers did not, leaving the probable cases in a grey zone.

Disclosure: R. Spandorfer, None; **M. Ahmad**, None; **A. Khosroshahi**, None.

Abstract Number: 0079

Analysis of COVID-19 and Rheumatology Twitter Activity During the Pandemic Months

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Twitter is a popular social media platform that is widely used to publish information and exchange ideas. There are over 300 million active monthly users on Twitter with about 500 million tweets sent daily. Therefore, Twitter is a unique tool with the ability to distribute ideas and information rapidly and widely to a large audience. Social media platforms including Twitter are an important source of health information nowadays, especially during the COVID-19 pandemic. Rheumatology providers and patients are likely to utilize Twitter to send and receive information related to COVID-19. In this study, we aim to analyze COVID-19 and rheumatology Twitter activity during the pandemic months.

Methods: The advanced search function on Twitter was used to retrieve tweets (English language only) with both hashtags #COVID19 and #Rheumatology from 12/31/2019-06/10/2020. Tweets were categorized by author and content. Tweet authors were categorized into: 1. Professional organization/patient advocate groups, 2.Academic institutions, 3.Medical journals/websites/network, 4.Patients, 5.Rheumatologists, 6.Other physicians, 7.Other providers, 8.Pharmaceutical companies, 9.Others. Tweets contents were categorized into: 1.COVID19 global rheumatology alliance/EULAR COVID19 database, 2.Hydroxychloroquine (HCQ) use for COVID19, 3.HCQ shortage, 4.Biologics use for COVID19, 5.Providers guidance, 6.Patients guidance, 7.COVID19 risk in rheumatology patients, 8.Webinars/learning opportunities, 9.Miscellaneous: telemedicine, COVID19 pathophysiology, conversational, publications, patient care challenges, and legislation.

Results: The first tweet with both hashtags was sent on March 4th. A total of 511 tweets were sent during the study period. Twenty-six percent of tweets were by professional organizations (136/511), 25% by rheumatologists (128/511), 17% by medical journals/websites/networks (91/511), and 14% by others (71/511). Tweets by other physicians and patients were 6% (31/511) and 3% (18/511) respectively. Tweets in the miscellaneous category were 28%, followed by provider guidance category (14%), patient guidance (13%), tweets related to COVID19 global rheumatol-

ogy alliance/EULAR database (13%), webinars/learning opportunities (12%), HCQ use for COVID19 (6%), COVID19 risk in rheumatology patients (5%), HCQ shortage (4%), and biologics use for COVID19 (4%). The number of tweets was highest in April (220) followed by March (152) and May (115). The trend for certain topics appeared to change by month. HCQ shortage represented 0.9% of topics in May, 8% in April, and 3% in March. The topic of HCQ use for COVID19 was 13% in March, 3% in April with no tweets with this topic in May.

Conclusion: Twitter is an excellent tool for disseminating ideas and information that can be helpful for both providers and patients. This can be more pronounced during the COVID19 pandemic where there is a strong shift toward the online exchange of information. It is very encouraging to see that the number of professional organizations and rheumatologists using this tool is significant which can help spread credible information to rheumatology patients.

Disclosure: M. Mohameden, None; **A. H.Ali**, None.

Abstract Number: 0080

Understanding Ankylosing Spondylitis -

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatology is underrepresented in the medical training of students in Germany. [1] Tools and methods are needed to inspire young students for specialist training as a rheumatologist.

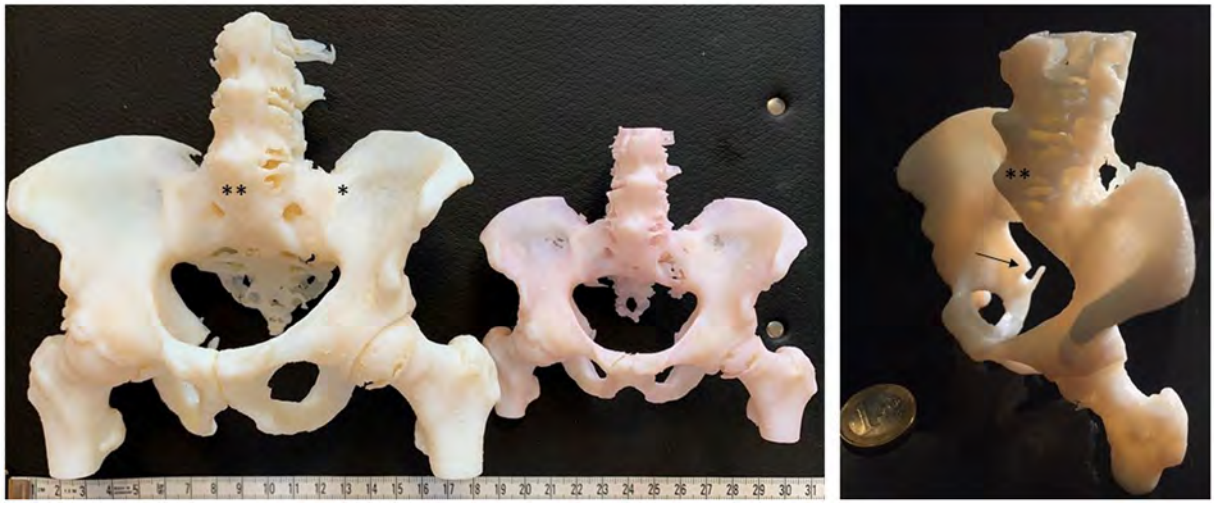

Figure 1. shows 3D prototypes of the pelvis and lumbar spine. * marks SI ankylosis ** ankylosis of the spine; the arrow marks large enthesiophytes at the tuber ischiadicum

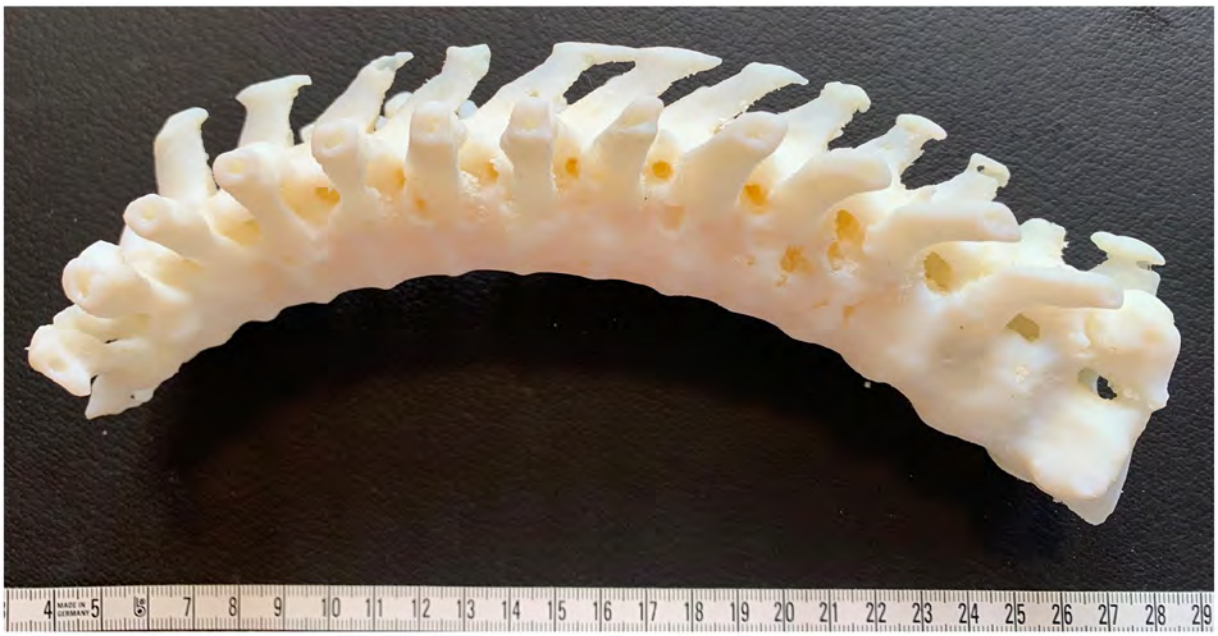

Figure 2. Displays the print out of the spine, including ankylosing syndesmophytes as well as partially merged processi spinosi

3D printing as a rapid prototyping technology is a suiTable method to display bone pathologies vividly and realistically. Recently we could show the usage of 3D printed models of peripheral joints of patients with rheumatic diseases for patient education.[2] However the feasibility to 3D print pathologies from rheumatic disease affecting the axial skeleton and their possible application field in rheumatology training for students has not been assessed yet.

Methods: Routinely acquired computed tomography data (2mm layer thickness) from the pelvic and spine from two patients with longstanding ankylosing spondylitis were used.Both data sets were segmented (surface rendering Osirix Lite) and converted to an STL surface model (Osirix Lite). After post processing, these models were 3D printed with the polyjet polymer technique (Objet30, Stratasys).[2]

Results: This approach allowed the prototyping of the pelvis and thoracic spine illustrating typical pathologies such as ankylosing syndesmophytes of the spine, enthesiophytes of various enthesial sites as well as ankylosing SI joints in great detail. Images of the pelvis with lumbar spine as well as the thoracic spine are displayed in Figure 1 and 2. We were able to produce different sizes of these models. Sizes are displayed in Figure 1. Printing time was 24 hours with material costs of about 300 Euro for the largest prototype.

These models are now used in the multimodal teaching concept “Rheuma begreifen” (Understanding Rheumatism) at the the Skills Lab of the University Erlangen-Nuremberg.

Instructions for usage are given, an evaluation and interim examination are currently performed

Conclusion: Bone pathologies caused by spondylitis ankylosans can be presented and haptically understood by 3D printed models. This can supplement rheumatological teaching and also patient education in the future.

References:

1. Riemekasten, G., et al., [Rheumatology - Integration into student training (RISA) : Current structure of clinical rheumatology in German universities (RISA III)]. Z Rheumatol, 2016. 75(5): p. 493-501.

2. Kleyer, A., et al., Development of three-dimensional prints of arthritic joints for supporting patients' awareness to structural damage. Arthritis research & therapy, 2017. 19(1): p. 34.

Disclosure: A. Kleyer, Lilly, 8, Novartis, 8, BMS, 8, Sanofi, 8, Gilead, 8; **M. Pachowsky**, None; **L. Schuster**, None; **L. Valor-Mendez**, None; **G. Schett**, None; **A. Hueber**, Abbvie, 5, 8, BMS, 8, Gilead, 5, GSK, 5, 8, Janssen, 5, 8, Roche/Chugai, 5, Lilly, 2, 5, 8, Novartis, 2, 5, 8; **D. Simon**, Novartis, 8, Lilly, 5, 8, Janssen, 8, AbbVie, 5.

Abstract Number: 0081

Prevalence of Systemic Autoimmune Diseases in Polycystic Ovary Syndrome

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Polycystic ovary syndrome (PCOS) is characterized by hormonal abnormality, chronic anovulation, hyperandrogenism, and obesity. Due to the hormonal imbalance, we hypothesize that patients with PCOS may tend to develop inflammatory and immune disorders. To test this hypothesis, we sought to examine the frequency of systemic autoimmune diseases in PCOS.

Methods: A retrospective chart review of patients in a single center between January 2004 and February 2020 was conducted after approval by the Institutional Review Board. There were two groups consisting of PCOS patients aged 18 and older and age- and BMI-matched patients without PCOS in a ratio of 1:2. Exclusion criteria were endometrial or ovarian cancer. Electronic medical records (EMRs) were searched for individual rheumatic and systemic autoimmune diseases using ICD-9 and ICD-10 codes and for laboratory data. A comparison between PCOS and non-PCOS subjects was made in relevant parameters followed by a subgroup analysis between these groups based on weight categories: obese (BMI >=30), overweight (BMI 25-30), and nonobese (BMI< 25). Fisher Exact, Chi-square, Wilcoxon rank sum and Kruskal Wallis tests were used for statistical analysis.

Results: There were a total of 2,262 patients including 754 PCOS and 1,508 non-PCOS as control. The study population included 12.8% nonobese, 22.6% overweight, and 64.7% obese females with median age of 30.0 years and median BMI of 33.1. The rheumatic disorders and relevant laboratory data were compared between the two groups and are summarized (Tables 1 and 2). Our study showed that the frequency of RA was 2.25% in PCOS group and 1.26% in control (p=0.0747). The prevalence of RA in PCOS group more than doubled that (1%) in the general population, suggesting PCOS patients may tend to develop seropositive/seronegative inflammatory arthritis. There was no significant difference in positive RF (0.27% VS 0.33%, p=1.0) or CCP (0.27% VS 0.07%, p=0.26) between groups. Our study also showed that compared with non-PCOS group, both SSc (0.0% VS 0.04%, p=0.0369) and UCTD (0.0% VS 0.53%, p=0.0123) were more prevalent in PCOS patients. Interestingly, PCOS patients were more likely to have ANA (11.41% VS 7.56%, p=0.0024) and ESR tested (19.10% VS 13.13%, p=0.0002) compared to controls. However, there was no significant difference in the positivity rate of ANA and other serologic markers between the two groups even with subgroup analysis of weight categories. PCOS patients had significantly higher frequency of OA than non-PCOS patients (5.44% VS 2.92%, p=0.0030).

Table 1. Comparison of serologic markers between patients with polycystic ovary syndrome (PCOS) and those without

N=2262	Presence of Polycystic Ovary Syndrome			
	No (N=1508)	Yes (N=754)	OR (95% CI)	P-Value
ANA, n (%)				
Not Checked	1394 (92.44)	668 (88.59)	1.574 (1.172 – 2.114)	0.0024
Checked	114 (7.56)	86 (11.41)		
ANA, n (%)				
Not Checked	1394 (92.44)	668 (88.59)	1.196 (0.780 – 1.833) *	0.4125*
Negative	55 (3.65)	51 (6.76)		
Positive	59 (3.91)	35 (4.64)		
dsDNA, n (%)				
Not Checked	1451 (96.22)	717 (95.09)	1.314 (0.860 – 2.006)	0.2054
Checked	57 (3.78)	37 (4.91)		
dsDNA, n (%)				
Not Checked	1451 (96.22)	717 (95.09)	1.000 (0.250 – 4.001) *	1.0000*
Negative	51 (3.38)	34 (4.51)		
Positive	6 (0.40)	3 (0.40)		
SSA, n (%)				
Not Checked	1453 (96.35)	726 (96.29)	1.019 (0.641 – 1.620)	0.9370
Checked	55 (3.65)	28 (3.71)		
SSA, n (%)				
Not Checked	1453 (96.35)	726 (96.29)	0.570 (0.118 – 2.752) *	0.7263*
Negative	48 (3.18)	26 (3.45)		
Positive	7 (0.46)	2 (0.27)		
SSB, n (%)				
Not Checked	1453 (96.35)	726 (96.29)	1.019 (0.641 – 1.620)	0.9370
Checked	55 (3.65)	28 (3.71)		
SSB, n (%)				
Not Checked	1453 (96.35)	726 (96.29)	0.666 (0.069 – 6.416) *	1.0000*
Negative	52 (3.45)	27 (3.58)		
Positive	3 (0.20)	1 (0.13)		
RNP, n (%)				
Not Checked	1453 (96.35)	722 (95.76)	1.171 (0.751 – 1.827)	0.4866
Checked	55 (3.65)	32 (4.24)		
RNP, n (%)				
Not Checked	1453 (96.35)	722 (95.76)	0.221 (0.028 – 1.749) *	0.1796*
Negative	46 (3.05)	31 (4.11)		
Positive	9 (0.60)	1 (0.13)		
Smith, n (%)				
Not Checked	1454 (96.42)	721 (95.62)	1.232 (0.792 – 1.918)	0.3535
Checked	54 (3.58)	33 (4.38)		
Smith, n (%)				
Not Checked	1454 (96.42)	721 (95.62)	N/A	0.3082*
Negative	50 (3.32)	33 (4.38)		
Positive	4 (0.27)	0 (0.0)		
SCI-70, n (%)				
Not Checked	1503 (99.67)	747 (99.07)	2.817 (0.891 – 8.905)	0.1194
Checked	5 (0.33)	7 (0.93)		
SCI-70, n (%)				
Not Checked	1503 (99.67)	747 (99.07)	N/A	0.3333*
Negative	5 (0.33)	6 (0.80)		
Positive	0 (0.0)	1 (0.13)		
Centromere, n (%)				
Not Checked	1502 (99.60)	749 (99.34)	1.671 (0.508 – 5.493)	0.5221
Checked	6 (0.40)	5 (0.66)		
Centromere, n (%)				
Not Checked	1502 (99.60)	749 (99.34)	2.001 (0.125 – 32.04) *	1.0000*
Negative	5 (0.33)	4 (0.53)		
Positive	1 (0.07)	1 (0.13)		
RF, n (%)				
Not Checked	1408 (93.37)	697 (92.44)	1.151 (0.821 – 1.614)	0.4128
Checked	100 (6.63)	57 (7.56)		
RF, n (%)				
Not Checked	1408 (93.37)	697 (92.44)	0.800 (0.155 – 4.130) *	1.0000*
Negative	95 (6.30)	55 (7.29)		
Positive	5 (0.33)	2 (0.27)		
CCP, n (%)				
Not Checked	1454 (96.42)	723 (995.89)	1.155 (0.736 – 1.812)	0.5317
Checked	54 (3.58)	31 (4.11)		
CCP, n (%)				
Not Checked	1454 (96.42)	723 (95.89)	4.008 (0.363 – 44.27) *	0.2592*
Negative	53 (3.51)	29 (3.85)		
Positive	1 (0.07)	2 (0.27)		
ESR, n (%)				
Not Checked	1310 (86.87)	610 (80.90)	1.562 (1.235 – 1.976)	0.0002
Checked	198 (13.13)	144 (19.10)		
ESR, Median (IQR)	16.0 (20.0)	14.5 (23.0)		0.6768
CRP, n (%)				
Not Checked	1324 (87.80)	662 (87.80)	1.000 (0.766 – 1.306)	1.0000
Checked	184 (12.20)	92 (12.20)		
CRP, Median (IQR)	1.2 (3.9)	1.2 (5.6)		0.8035

*Statistical comparison of percentage of positives between patients with PCOS and patients without.

Table 2. Comparison of rheumatologic diseases between patients with polycystic ovary syndrome (PCOS) and those without PCOS

N=2262	Presence of Polycystic Ovary Syndrome			
	No (N=1508)	Yes (N=754)	OR (95% CI)	P-Value
Systemic autoimmune disease, n (%)				
RA, n (%)				
No	1489 (98.74)	737 (97.75)	1.808 (0.934 – 3.498)	0.0747
Yes	19 (1.26)	17 (2.25)		
SLE, n (%)				
No	1479 (98.08)	740 (98.14)	0.965 (0.507 – 1.837)	0.9133
Yes	29 (1.92)	14 (1.86)		
Sjogren's syndrome, n (%)				
No	1498 (99.34)	751 (99.60)	0.598 (0.164 – 2.181)	0.5626
Yes	10 (0.66)	3 (0.40)		
SSc, n (%)				
No	1508 (100.0)	751 (99.60)	N/A	0.0369
Yes	0 (0.0)	3 (0.40)		
UCTD, n (%)				
No	1508 (100.0)	50 (99.47)	N/A	0.0123
Yes	0 (0.0)	4 (0.53)		
Noninflammatory disease, n (%)				
OA, n (%)				
No	1464 (97.08)	713 (94.56)	1.913 (1.239 – 2.955)	0.0030
Yes	44 (2.92)	41 (5.44)		

Conclusion: For the first time**,** our study suggests that PCOS patients may have higher frequency of systemic autoimmune diseases (seropositive/seronegative RA, SSc, and UCTD). The study is limited due to the inherent weakness of a retrospective study and search methodology using ICD codes. Future multicenter study with a larger sample size would be needed to validate the significance of our findings.

RA=Rheumatoid Arthritis; SLE=Systemic Lupus Erythematosus; UCTD=Undifferentiated Connective Tissue Disease; SSc=Systemic Sclerosis; OA=Osteoarthritis

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Disclosure: S. Sharmeen, None; **H. Nomani**, None; **E. Taub**, None; **Q. Yao**, None.

Abstract Number: 0082

Diffuse Sclerosing Osteomyelitis of the Jaw: An Underdiagnosed Disease in Maxillofacial Surgery Department

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing
Session Type: Poster Session A
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Background/Purpose: Diffuse sclerosing osteomyelitis of the jaw is a rare and under-recognized disease. Many authors include this diagnosis in the spectrum of aseptic osteitis sometimes associated with the SAPHO syndrome.

Differential diagnosis with infectious osteomyelitis is difficult, therefore the final diagnosis might be delayed by several years. Although considered as an auto-inflammatory disorder, patients can primarily be addressed to maxillofacial surgeons and not to the rheumatologist.

In this work, we describe a cohort of patients addressed to the maxillofacial surgery department for a spontaneous osteomyelitis of the jaw in order to identify characteristics that can help the surgeon to suspect this disease, make an earlier diagnosis and appropriate management.

Methods: We extracted patient records coded either "Osteomyelitis" or "Inflammatory conditions of jaws"(International Classification of Diseases) then selected the cases of spontaneous osteomyelitis of the mandible. Patients included had clinical and radiographic osteomyelitis for at least 3 months. Exclusion criteria were history of local radiotherapy, osteonecrosis and post-surgical infections. The final diagnosis was based on clinical and radiological outcomes at least one year after the first symptoms.

Results: Of the 960 records extracted, 24 patients met the inclusions criteria: 16 were classified as aseptic, 5 as infectious osteomyelitis and no definite diagnosis could finally be made for 3 of them. Aseptic osteomyelitis mainly affected women (10 out of 16) in their forties (median of 40.5 years) presenting with painful swelling of the mandible since several months (median of 8 months). Two patients presented an associated palmoplantar pustulosis leading to the diagnosis of SAPHO syndrome. Initial radiological examinations showed early osteolytic lesions (50%) progressing to medullary sclerosis, solid periosteal appositions and bone hypertrophy (90%).

Eleven out of 36 biopsies remained sterile but the others were positive for commensal germs of the oral flora (69%).

Interestingly, out of 8 patients who had a bone scintigraphy, 4 had other osteitis localizations allowing the diagnosis to be integrated into a SAPHO syndrome or chronic multifocal recurrent osteitis (CMRO).

Over 80% of patients received iterative antibiotic cures with inefficiency or recurrence of the pathology in all of them. Mandibular decortication was followed by 100% of recurrence. Among the 16 patients, 12 were finally treated with NSAIDs effectively on relapses, and 2 were cured with anti-TNF alpha.

Conclusion: Aseptic osteomyelitis remains rare but patients might be addressed directly to maxillofacial surgeons for management. It must be differentiated as early as possible from infectious osteomyelitis by its clinical and radiological characteristics. Germs of the oral flora can be found in the biopsy but might be only contamination. Most of patients of our series underwent multiple antibiotics cures and even surgery. We recommend that rheumatologist should be included as soon as possible to perform a clinical examination for extra-mandibular involvement to integrate aseptic osteomyelitis of the jaw into a SAPHO syndrome or CMRO and discuss NSAIDs or biologics.

Disclosure: P. Preuss, None; **H. Bertin**, None; **P. Corre**, None; **B. Le Goff**, None.

Abstract Number: 0083

Chronic Nonbacterial Osteomyelitis Is Associated with HLA-B*27

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SESSION INFORMATION
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Background/Purpose: Chronic nonbacterial osteomyelitis (CNO) is an auto-inflammatory condition primarily affecting children with an estimated prevalence of 1 per 10^5 - 10^6. It is characterized by relapsing episodes of localised bone inflammation. Extraosseous manifestations, including psoriasis, Crohn's disease and enthesitis-related arthritis, frequently occur in patients and relatives. However, no increased frequency of HLA class I alleles associated with these diseases, such as HLA-B*27 and HLA-C*06, has been shown in patients with CNO. The aim of this study was to determine the frequency of HLA class I alleles in and Irish cohort of patients with CNO compared to Irish population frequencies.

Methods: 43 Irish children and adolescents currently attending paediatric rheumatology services with CNO were recruited. Whole exome sequencing was performed on blood using Agilent SureSelect XT Human All Exon V6 kits and Illumina HiSeq 3000 with 150bp paired-end reads. Reads were aligned to the hg19 reference genome using BWA software, duplicates removed using Picard tools and GATK software used to realign indels and call variants. HLA alleles were predicted from whole exome sequencing results using Optitype software through the Nextflow nf-core/hlatyping pipeline (version 1.1.5). Comparison was made with previously published Irish HLA allele frequencies. Statistical analysis was performed in RStudio (version 1.1.456).

Results: Whole exome sequencing and HLA allele prediction was performed on 43 patients, 40 unrelated and 3 siblings. All were ethnically Irish with a female:male ratio of 2.9:1, 88% had multifocal disease and 51% required a second-line agent for treatment. Psoriasis was present in 18.6% of patients a further 18.6% of $1^{st}/2^{nd}$ degree relatives. HLA class I prediction was successful in all patients. HLA-B*27:05 was present in 17.5% of patients compared to 6% of the Irish population (OR 3.28, 95%CI 1.18 – 7.8, p=0.011). Patients carrying HLA-B*27:05 allele did not have more frequent co-morbidity with HLA-B*27 associated diseases than the overall cohort. HLA-C*06:02 was present in 27.5% of patients compared to 17.5% (OR 1.96, 95% CI p=0.13). Patients carrying HLA-C*06:02 were not significantly associated with a personal or family history of psoriasis. All other alleles were found at frequencies close to the Irish population frequency.

Conclusion: There is a statistically significant association between the Irish CNO population and HLA-B*27:05 allele known to be associated with inflammatory diseases such as enthesitis-related arthritis. Results need to be replicated in a larger cohort for further stratification to be possible.

Disclosure: D. O'Leary, None; **O. Killeen**, None; **A. Wilson**, None.

Abstract Number: 0084

Clinical Characteristics of Patients with Rheumatism of Juvenile Onset and Adult Onset in the BIOBADAGUAY Cohort

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing

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Session Time: 9:00AM–11:00AM

	Adult onset rheumatism	Juvenile onset rheumatism
n, %F	698, 74.1%	68, 64.7%
Age of diagnosis	52.2 ± 13.6	10.5 ± 4.3
Disease duration	13.1 ± 8.7	18.5 ± 11.2
Diagnosis		
Rheumatoid Arthritis	495 (70.9%)	15 (22.1%)
Ankylosing espondylitis	88 (12.6%)	8 (11.8%)
Psoriatic arthritis	55 (7.9%)	2 (2.9%)
Undifferenciated SpA	12 (1.7%)	0
Systemic lupus erythematosus	9 (1.3%)	1 (1.5%)
Juvenile idiopathic arthritis	1 (0.1%)	38 (55.9%)
Enteropathic arthritis	7 (1.0%)	0
Polymyositis/Dermatomyositis	5 (0.7%)	0
Vasculitis	5 (0.7%)	0
Uveitis without rheumatic disease	3 (0.4%)	0
Non-radiographic axial SpA	3 (0.4%)	0
Still disease	3 (0.4%)	0
Juvenile undifferentiated SpA	2 (0.3%)	2 (2.9%)
Undifferentiated connective tissue disease	2 (0.3%)	0
Scleroderma	2 (0.3%)	0
Eosinophilic fasciitis	2 (0.3%)	0
Sarcoidosis	1 (0.1%)	1 (1.5%)
Juvenile SpA	1 (0.1%)	1 (1.5%)
Reactive Arthritis	1 (0.1%)	0
Primary Sjogren's syndrome	1 (0.1%)	0
Disease activity		
DAS28*	5.1 ± 1.1	5.4 ± 1.2
BASDAI**	5.9 ± 2.0	6.6 ± 1.9
Comorbidities§		
High comorbidity	11 (1.6%)	0
Low comorbidity	37 (5.3%)	0
No comorbidity	650 (93.1%)	68 (100%)

Background/Purpose: The Paraguayan-Uruguayan cohort of patients with rheumatic inflammatory diseases (BIOBADAGUAY), collect clinical and epidemiological information on adults and children patients receiving biological therapies (BT). The obtained data enable to describe with comparative purposes the cohort of patients, considering the age of symptom onset (i.e. juvenile or adult)

Methods: BIOBADAGUAY cohort includes 18 centers (9 in Uruguay and 9 in Paraguay). The descriptive analysis was made in two phases. First, we have selected the adult population on BT and second, we have separated it in two groups according onset of disease considering the age when diagnosis of rheumatic disease was made. Clinical features of both populations were described in a second phase

Results: A total of 766 adult patients was included, in which 91,1% had adult-onset, and 8.9% had juvenile-onset rheumatic disease. Female predominance was observed in both adult-onset and juvenile-onset groups (74.1% vs 64.7%, respectively). Mean disease duration was 18.5 ± 11.2 years for juvenile-onset rheumatic disease and 13.1 ± 8.7 years for adult-onset rheumatic disease. Disease activity was similar for both rheumatoid arthritis and spondylarthritis in the two groups. All of juvenile-onset rheumatic disease patiets, did not have a comorbidity when starting a BT. Mean body mass index was 24.9 ± 4.5 for juvenile-onset rheumatic disease and 27.9 ± 6.0 for adult-onset rheumatic disease. Table 1 describes main clinical and epidemiological characteristics of analyzed populations.

Conclusion: Patients with juvenile-onset rheumatic disease present with particular characteristics (disease duration, comorbidities and mean body mass index) that differentiate them from adult-onset rheumatic disease patients. This should be taken into consideration when assessing and follow-up is being made on each patient

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Abstract Number: 0085

Classifications of Inflammatory Myopathies: Differentially Expressed Membrane-Bound Complement Regulators Allow Specific Patterns of Membrane Attack Complex Deposition

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Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a group of heterogeneous disorders that typically present with proximal muscle weakness. According to the classification criteria, IMs are classified into five categories: polymyositis (PM); non-specific myositis (NSM); dermatomyositis (DM); necrotizing autoimmune myopathy (NAM); and sporadic inclusion body myositis (IBM), with further subgrouping by autoantibodies that are specific or non-specific to myositis. There is a need to develop optimal diagnostic and classification criteria with more reliable and reproducible markers of pathological and serological evidence for all subgroups of IIM.

Methods: Following ethical approval, paraffin- and frozen sections from muscle biopsies of patients meeting inclusion criteria and controls (patients with no diagnostic abnormalities on muscle biopsy) were obtained. The sections were stained with hematoxylin and eosin (H&E), membrane attack complex (MAC) C5b–9, and major histocompatibility complex (MHC) class I for CD59, CD55, and CD46. A blinded examination was then achieved by randomly mixing the specimen numbers.

Results: CD46, CD55, and CD59 were differentially expressed in endomysial capillaries and myofibers. Whereas CD59 was expressed in endomysial capillaries as well as myofibers, CD46 expressed in capillaries only, and CD55 expression was prominent in myofibers and only equivocal in capillaries. MAC C5b-9 pathological expression correlated with significant reduction of expression of membrane-bound complement regulators.

In DM, MAC C5b-9 deposition is present mainly in perifascicular endomysial capillaries with corresponding clear downregulation of CD59 and CD46, mainly in perifascicular areas. This and earlier findings suggest that much of the ischemic/inflammatory effect in DM is complement-mediated and related to classical pathway complement activation on capillary endothelium that is not protected by membrane-bound complement regulators. This early event in the process of injury occurs prior to inflammatory cell infiltrate.

In PM, MAC C5b-9 deposition in the general group of PM is in necrotic myofibers; however, there was clear but less pronounced staining in capillaries with weaker downregulation of membrane-bound regulatory proteins.

Conclusion: Complement activation should be determined in each subgroup of IIM

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Geographic Distribution of Eosinophilic Fasciitis Cases in Massachusetts and Associated Environmental Triggers

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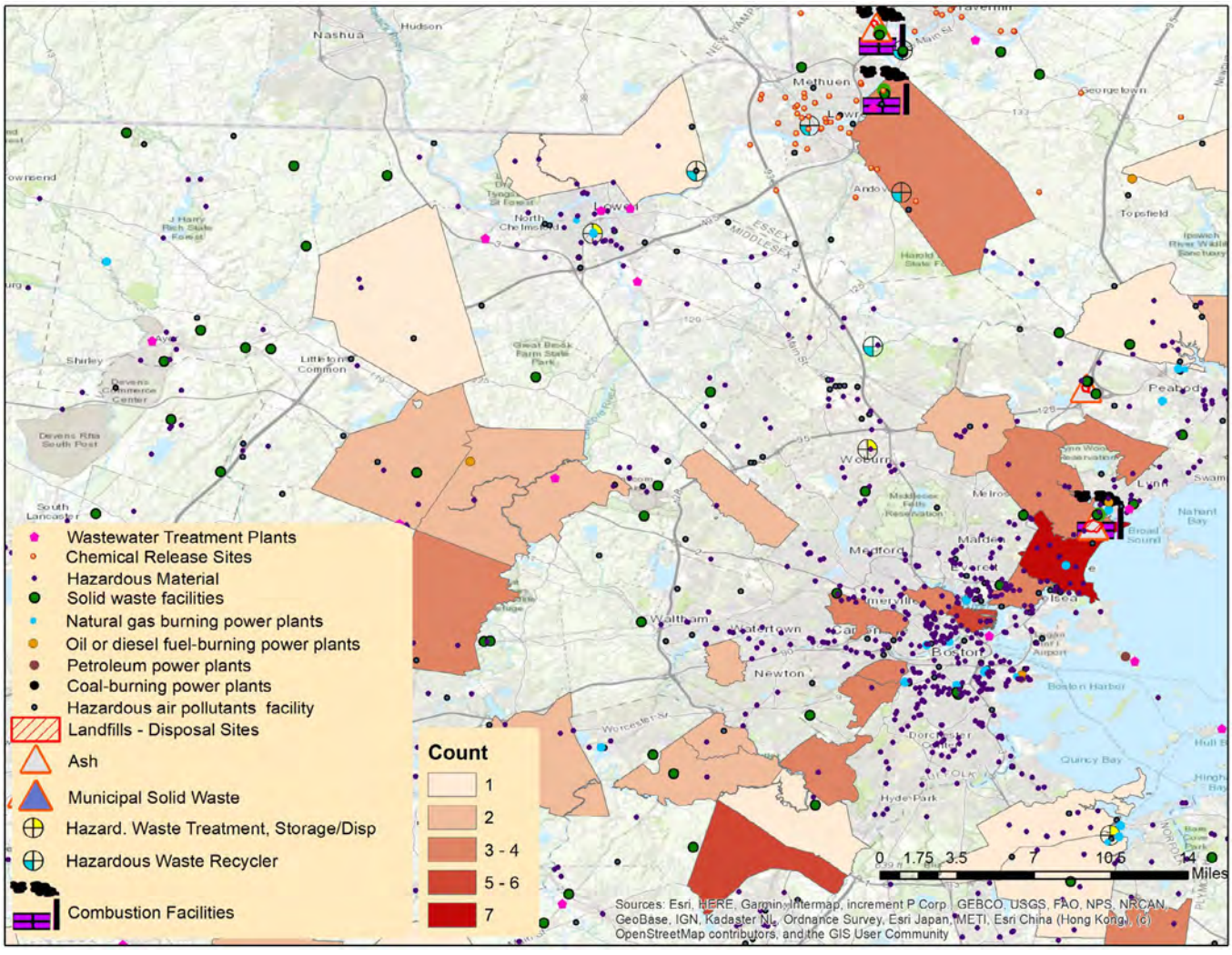

Figure 1 Locations of industries and waste sites in relation to EF case-counts

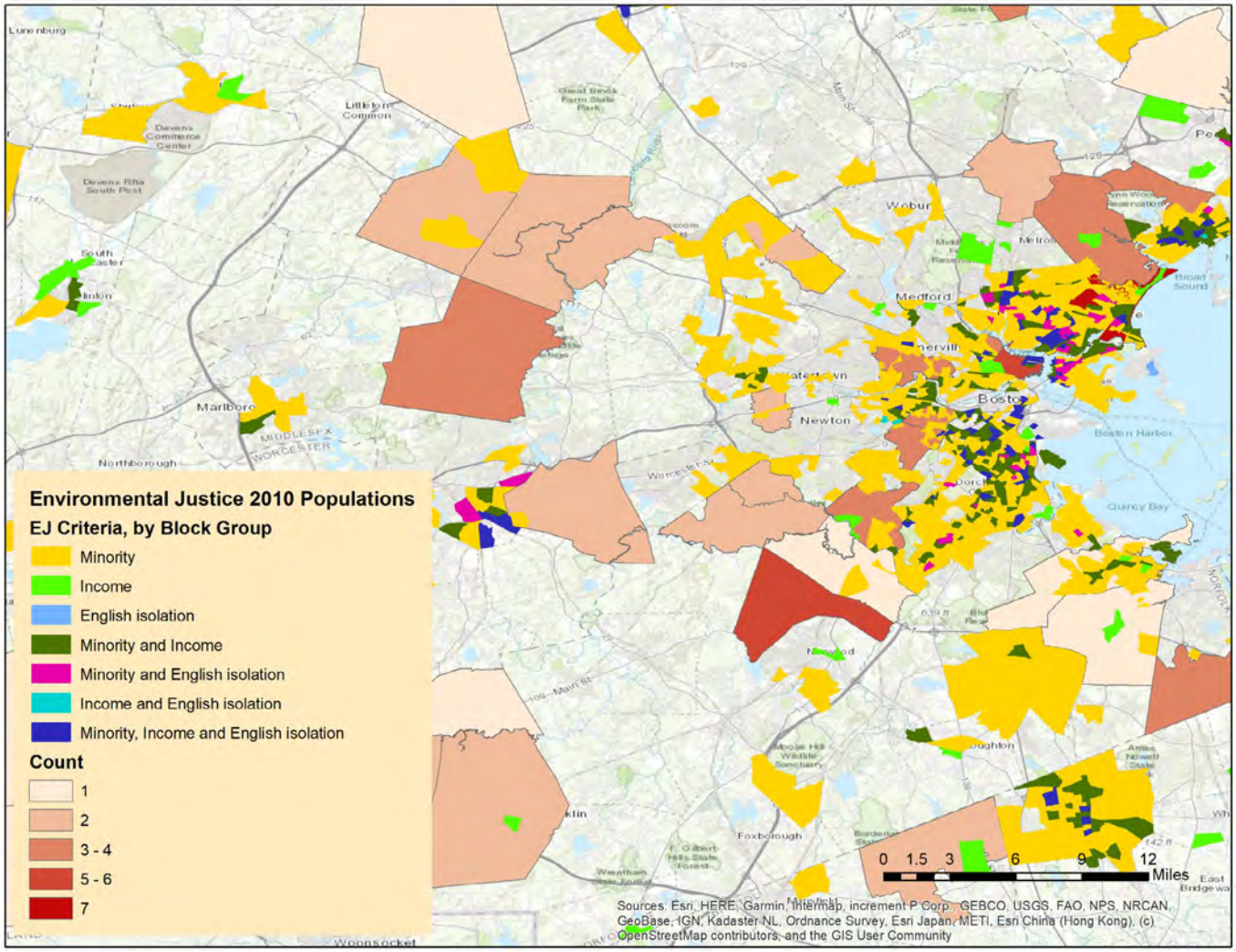

Figure 2. Social justice index and geographic distribution of EF cases

Background/Purpose: Eosinophilic fasciitis (EF) is a rare fibrosing disorder of the fascia characterized by induration progressing proximally along the upper and lower extremities. Given the potential impact on joint mobility, EF can be associated with a high degree of morbidity and have a major impact on quality of life. To date, the etiologic trigger leading to disease onset remains unknown. Assessment of high incidence geographic clusters may be a crucial initial step to cause identification. ArcGIS is a geospatial processing program used to create and analyze geographic distributions and has recently been utilized to determine high incidence clusters for several cancers and autoimmune diseases. The purpose of this study is to determine the geographic distribution of eosinophilic fasciitis (EF) cases in Massachusetts and evaluate for possible environmental triggers.

Methods: The Research Patient Data Registry, which combines medical records from two large, academic tertiary care centers in Boston, was utilized to identify 294 potential cases of EF. Eighty-one of these were confirmed by board certified dermatologists or rheumatologists and were included in the study. Demographic and geographic data was extracted. EF cases were mapped by zip code using ArcMap 10.7.1. These maps were then compared to environmental exposure maps including those for industry and toxic waste sites, as well as to social justice maps.

Results: Elevated case counts of EF were observed in specific geographic regions in Massachusetts, including Revere, Charlestown, Westwood, North Andover, and Saugus. These regions were in proximity to landfills, chemical release sites, ash pollution, and combustion facilities (Figure 1). Based on social justice maps, EF cases were found

to be more prevalent among low-income and minority communities (Figure 2). Review of medical records revealed that a high proportion of EF cases were smokers (49%) compared to the general population (~21% smokers). Of the patients with EF who underwent evaluation (n=40), 25% demonstrated a monoclonal gammopathy. Additionally, 26% of patients have a recorded past medical history of at least one more autoimmune disease in addition to EF.

Conclusion: To our knowledge, this is the first study to date assessing the geographic distribution of EF. The regional clustering of EF cases in proximity to ash, landfills, chemical release sites, and combustion facilities illustrates the potential contribution of environmental pollutants to the development of EF. Additional investigation using larger cohorts of patients with EF is warranted.

Disclosure: B. Kassamali, None; **A. Muntyanu**, None; **R. Vleugels**, None; **A. LaChance**, None.

Abstract Number: 0087

Hemophagocytic Syndrome. Clinical Characteristics and Prognostic Factors of a Series of 30 Clinical Cases

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Background/Purpose: Hemophagocytic syndrome (HPS) is classified into primary and secondary. The secondary form is mainly associated with hematological malignancies (HN) such as lymphomas, and autoimmune diseases (AI) such as Systemic Lupus Erythematosus. The mortality rate varies between 20% and 90%. Underlying malignancies, thrombocytopenia, age, hyperferrhythmia and prolonged prothrombin time are considered an adverse prognostic factor. The present work aims to obtain clinical and laboratory findings that can guide us to an early etiological diagnosis and treatment.

Methods: This is a retrospective observational study, which was approved by the hospital's ethics committee. Any patient who met the diagnostic criteria for LHH proposed by Henter JI. or who presented hemophagocytic cells (HC) in bone marrow (BM) biopsy were included. We describe and identify clinical, laboratory findings and underlying disorder differences between HPS subgroups; and between patients who survived and did not survive to HPS at a tertiary hospital between 2005 and 2019. Continuous variables are described with the mean or median according to the degree of normality, and qualitative variables are shown with the absolute value and percentage. Kruskal Wallis, Fisher test and Mann-Whitney U test were used for the bivariate analysis.

Results: Thirty patients were found **(Table 1)**. The coincidence of an infectious disease with HPS was observed in 8 [AI: 5 cases (2 cytomegalovirus, 2 probably viral respiratory infections and 1 bacterial infection) and HM: 3 cases (2 Epstein Barr virus and 1 bacterial infection)]. In 2 patients with acute leukemia, allogeneic transplantation was related as a possible trigger of HPS; and in one patient with myelodysplastic syndrome it was related to the appearance of

Table 1: Etiologies and underlying disorders during admission of patients with Hemophagocytic Syndrome				
Etiological subgroups	n	Debut of etiology	Infectious trigger	Mortality
Autoimmune diseases	n = 10	n = 6	n = 5	n = 1
Systemic Lupus Erythematosus	5	3	3	1
Adult Still's Disease	3	2	1	0
Rheumatoid arthritis	1	0	1	0
IgG4 Sclerosing Disease	1	1	0	0
Hematological Malignancies Diseases	n = 12	n=4	n = 3	n = 8*
Non-Hodgkin's Lymphoma	3	0	0	1
Myelodysplastic syndrome	3	1	1	2
Acute leukemia	3	1	1	3
Lymphoma extranodal NK cell	1	1	1	1
Multiple Myeloma	1	0	0	0
Probably lymphoproliferative disease	1	1	0	1
Infectious diseases	n = 2	n = 2	n = 2	n = 1
Pneumocystis jirovencii in patient with HIV	1	1	1	1
Gastroenteritis by Campylobacter jejuni	1	1	1	0
Malignant Solid tumor disease	n = 1	n = 0	n = 0	n = 0
Glioblastoma multiforme in treatment with temozolomide	1	0	0	0
HPS without defined etiology	n = 5	5	0	3

HIV: Human immunodeficiency Virus, NK: Natural Killer, *p = 0.029

graft-versus-host disease. Age at diagnosis of HPS was lower in the AI subgroup [40 (26.5 - 56.3); p 0.001]. The HM subgroup presented more severe cytopenias [platelets 4500 (650 - 15 750; p 0.009), leukocytes 2050 (20 - 728; p 0.0001) and neutrophils 0 (0 - 280; p 0.002)] **(Table 2)**. Overall intra-hospital mortality was 43.3%, being higher in the HM subgroup [8 patients (66.7%); p 0.029]. The group of patients who did not survive had a longer time of prolongation of the INR compared to those who survived [2.1 (1.2 - 3.7) versus 1.5 (1.1 - 1.6); p 0.028] and an older age at diagnosis of HPS compared to the group who survived [68 years (58.2 - 74.5) versus 40 years (34 - 57); p 0.043] **(Table 3)**.

Conclusion: The HM subgroup had higher mortality, and more and more severe cytopenias. The AI subgroup showed higher transaminase elevation and better prognosis. The non-survivor group had a longer time of prolongation of the INR and an older age at the time of the diagnosis of HPS compared to the survivor group.

Table 2: Epidemiological characteristics, clinical manifestation, underlying disorders and mortality of each subgroup of HPS

	Total		AI		HM		Infection		MST	HPS without defined etiology		P<0,05
n	30		10		12		2		1	5		
Age (x ± s)	55.5	±18.3	40	26.5-56.3	68	57.5-73.8	45.5	30-61	78	71	53.5-73.5	0.006
Gender, man	14	46.7%	3	30%	9	75%	1	50%	1	0	0%	0.013
Gender, women	16	53.3%	7	70%	3	25%	1	50%	0	5	100%	
Splenomegaly	16	53.3%	5	50%	8	66.7%	2	100%	0	1	20%	0.216
Hepatomegaly	10	33.3%	4	40%	4	33.3%	2	100%	0	0	0%	0.138
Global hospital stay**	35.5	20-60.8	30,5	9.5-53.3	61.5	29.3-93.3	23	16-30	28	23	16.5-59	0.191
Hospital stay previous to the diagnosis**	16.5	8.5-29.8	10	5-16.5	26	10-39	14	11-17	13	36	11.5-50	0.191
Mortality	13	43.3%	1	10%	8	66.7%	1	50%	0	3	60%	0.029
Hb (g/dL)	7.1	6.4-7.9	7.2	6.6-8.4	6.5	5.9-7.3	7.5	7.3-7.8	8.6	7.1	6.5-11.7	0.120
Pt (x10⁹/L)	13 500	5 000-52 500	31 650	11 000-100 250	4 500	650-15 750	9 500	9 000-10 000	5 000	87 000	26 500-186 000	0.009
Leu (x10⁹/L)	1 250	2 383-153	1 985	1 350-3 382	185	20 – 728	2 050	1 010-3 090	480	4 370	2 975-5 640	0.0001
Neu (x10⁹/L)	615	0-1 550	948	633-1 808	0	0-280	1160	0 - 2 320	230	3 090	1 280-4 040	0.002
Fib (mg/dL) (n=24)	171	111-358	212	90-450	167	114-354	214	214	117	195	105-261	0.940
Fer (ng/mL) (n=28)	15 330	5 434-38 284	14 263	4 254-14 263	16 796	8 287 - 56 969	10 346	9 755-10 938	#	6 689	2 914-26 748	0.410
Tg (mmol/L)	341	226-438	412	234-572	321	234-404	373	274-471	149	337	119-540	0.594
AST (U/L)	139	78-406	457	289-1 140	106	71-193	79	23-134	54	111	57-485	0.026
ALT (U/L)	162	46-388	432	174-599	109	54-263	133	32-234	88	41	28-287	0.054
INR (n=29)	1.5	1.1-1.9	1.5	1.1-1.8	1.7	1.3-2.1	1.2	1.1-1.4	1.9	1.3	1.2-3.7	0.615
T.P. (n=29)	4.8	±,1.04	5.0	4.5-5.8	4.3	3.9-4.5	5.5	5.4-5.6	3.1	5.2	4.8-6.7	0.003

Hb: hemoglobin; Pt: platelets; Leu: leukocytes; Neu: neutrophils; Fib: fibrinogen; Fer: ferritin; Tg: triglycerides; AST: aspartate aminotransferase; ALT: alanine aminotransferase; INR: INR

Table 3: Characteristics and differences between survivor and non-survivor groups

	Total		Non-survivor		survivor		p<0,05
n	30		13		17		
Age	55,5	±18,3	68	58,2-74,5	40	34-57	0,043
Women	16	53,3%	7	61,5%	9	47,1%	1,00
Comorbidities (≥2)	5	16,7%	2	15,4%	3	17,6%	1,000
Hospital stay	35,5	20-60,8	29	15,5-39	13	8-17	0,563
Splenomegaly	16	53,3%	7	53,8%	9	52,9%	1,000
Hepatomegaly	10	33,3%	5	38,5%	5	29,4%	0,705
Hb (g/dL)	7,1	6,4-7,9	710%	6,2-7,8	7,1	6,6-7,8	0,094
Pt (x10^9/L)	13 500	5 000-52 500	16 000	11 000-44 000	12 000	5 000-99 000	0,281
Pt ≤ 100 000	25	83,3%	13	100%	12	70,6%	0,052
Leu (x10^9/L)	1 250	238-3 153	1 300	150-3 940	1 400	200-3 340	0,457
Neu (x10^9/L)	615	0-1 550	1 290	20-3 300	650	0-1 400	0,805
Fb (mg/dL) (n=24)	171	111-358	167,00	106-253	169,00	103-451	0,796
Fer (ng/mL) (n=28)	15 330	5 434-38 284	29 063	5 728-74 604	13 225	8 287-28 729	0,108
Tg (mmol/L)	341	226-438	254,00	184-382	471,00	341-604	0,053
GOT (U/L)	139	77,5-406,3	133,00	101-513	179,00	101-512,5	0,483
GPT (U/L)	162	46-389	109,00	41-333	199,00	99-298	0,198
INR (n=29)	1,5	1,1-1,9	2,1	1,2-3,7	1,5	1,1-1,6	0,028

Disclosure: C. Egües Dubuc, None; **J. Calvo-Alén**, None; **A. de Diego Sola**, None; **E. Cabrera-Miranda**, None; **N. Alcorta**, None; **L. Lopez Dominguez**, None; **O. Maiz**, None; **E. Uriarte Isacelaya**, None; **J. Cancio Fanlo**, None; **J. Valero Jaimes**, Novartis, 1; **J. Belzunegui**, Novartis, 1.

Abstract Number: 0088

The Spectrum of Hemophagocytic Lymphohistiocytosis: Autoimmunity vs. Malignancy

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Background/Purpose: Macrophage activation syndrome (MAS), a life-threatening condition resulting from aberrant immune activation, is a form of hemophagocytic lymphohistiocytosis (HLH) that develops in patients with an underlying rheumatologic disease, classically juvenile idiopathic arthritis. Patients may or may not have an established rheumatologic diagnosis at the onset of MAS, making the identification of an underlying trigger challenging. Moreover, the commonly used diagnostic tools, such as the H-score, were developed from an adult population with a paucity of autoimmune disease. We aim to identify clinical features that may distinguish MAS cases from malignancy-associated HLH.

	MAS	Malignancy-associated HLH	p-value
Patient Characterestics			
Total number of patients (n)	18	16	
Underlying disease process - SLE (n)	8 (44%)		
Underlying disease process - AOSD (n)	6 (33%)		
Underlying disease process - other rheumatologic condition (n)	4 (22%)		
DLBCL (n)		8 (50%)	
Other hematologic malignancy (n)		8 (50%)	
Hospital Course			
Days in hospital, mean	17.5 (13.1)	36.1 (13.5)	<0.001
Vasopressor requirement (n)	8 (47%)	5 (31%)	0.35
Intubation (n)	7 (39%)	5 (31%)	0.64
Transfusion (RBC or platelet) (n)	10 (56%)	16 (100%)	0.002
Death (n)	4 (22%)	7 (44%)	0.18
Repeat episode of MAS at any point (n)	0 (0%)	2 (25%)	0.043
Treatment			
Pulse corticosteroids (defined as methylprednisolone 1000mg x3 days) (n)	14 (78%)	2 (12%)	<0.001
Cumulative dose of corticosteroids over hospitalization in mg equivalents of methylprednisolone, mean (SD)	3981.7 (3410.6)	2468.9 (3042.1)	0.19
Cyclophosphamide (n)	2 (11%)	8 (50%)	0.013
Mycophenolate mofetil (n)	1 (6%)	0 (0%)	0.34
Etoposide/dexamethasone protocol (n)	0 (0%)	7 (44%)	0.002
IVIG (n)	4 (22%)	0 (0%)	0.045
Anakinra (n)	6 (33%)	0 (0%)	0.011

Table 1. hospital course and outcomes of MAS vs. malignancy-associated HLH (n=number of patients; MAS=macrophage activation syndrome; HLH=hemophagocytic lymphohistiocytosis; SLE=systemic lupus erythematosus; AOSD=adult onset Still's disease; DLBCL=diffuse large B-cell lymphoma).

Methods: We identified adult HLH patients using ICD9/10 coding for HLH at an academic center from 2004 to 2020. A diagnosis of HLH required fulfillment of the 2004 HLH diagnostic criteria and/or clinical diagnosis by an expert. We included HLH cases that were secondary to either a rheumatologic disease (MAS) or a hematologic malignancy. MAS cases were compared to malignancy-associated HLH using STATA®.

Results: Of the 162 patients identified, 34 fulfilled inclusion criteria: 18 patients with MAS and 16 patients with hematologic malignancy-associated HLH. As expected, rheumatologic patients were younger (39.7 years vs. 62.3 years, $p< 0.001$) and more likely to be female (78% vs. 44%, $p=0.042$). MAS patients were less likely to have hepatomegaly (0% vs. 25%, $p< 0.024$), and developed milder cytopenias (Neutrophils: 3.7 vs. 1.2 K/μL, $p=0.012$; hemoglobin: 9.1 vs. 7.2 g/dL, $p=0.004$, platelets: 59.7vs. 30.9 K/μL, $p=0.005$) than malignancy-associated HLH patients. Soluble IL-2 receptor serum concentration was higher in malignancy patients but the difference did not reach statistical significance (5797.5 vs. 81786.4 pg/mL, $p=0.11$). MAS and HLH patients did not differ in the initial need for ICU levels of care but those with malignancy had a more prolonged hospital stay and a non-statistically significant increased mortality (Table 1). MAS patients were exclusively treated with immunosuppressives including pulse corticosteroids, while HLH patients were treated with chemotherapy or etoposide-based protocols.

Conclusion: MAS patients had overall better outcomes including shorter hospital stays than malignancy-associated HLH patients. While there were numerically fewer deaths in the MAS versus the malignancy-associated HLH cohort, one in five patients died from MAS during their initial hospitalization. Some noTable differences in disease characteristics between the two groups include organomegaly and severity of cytopenias, which could be helpful in differentiating malignancy from rheumatologic etiologies of hemophagocytic syndromes.Table 1: hospital course and outcomes of MAS vs. malignancy-associated HLH (n=number of patients; MAS=macrophage activation syndrome; HLH=hemophagocytic lymphohistiocytosis; SLE=systemic lupus erythematosus; AOSD=adult onset Still's disease; DLBCL=diffuse large B-cell lymphoma).

Disclosure: S. Good, None; **S. Wade**, None; **V. Kyttaris**, GlaxoSmithKline, 5, Exagen Diagnostics, 2, 5.

Abstract Number: 0089

The Risk Factors of Recurrence in Relapsing Polychondritis; A Study of 41 Cases

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SESSION INFORMATION

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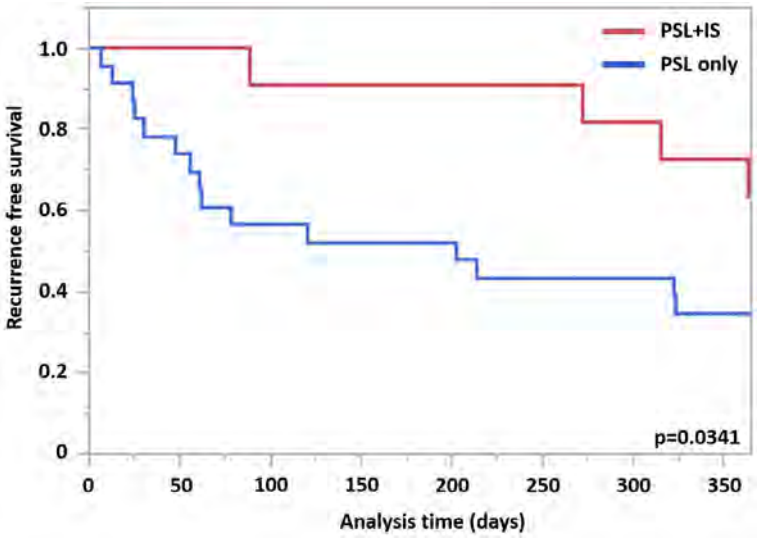
Background/Purpose: Relapsing polychondritis (RP) is a rare disease which causes inflammation in systemic cartilages. Although glucocorticoids (GC) and immunosuppressive drugs (IS) have been used, the recurrence rate remains high. It has been reported that tracheobronchial lesion is a poor prognostic factor, however, other risk factors have not been sufficiently investigated. We conducted a retrospective study on risk factors for recurrence.

Methods: We selected patients who had been diagnosed as RP according to Damiani's or Michet's criteria and treated at Kyoto University Hospital between 2001 and 2020. We excluded the patients with observation period less than one year and patients who had been taking oral GC for the treatment of other diseases at the time of the diagnosis of RP. Recurrence was defined as 1) aggravation of any symptoms or 2) worsening of the laboratory data that led to intensified treatments.

Results: Forty-one patients were extracted. The mean age at onset was 50±18 years, and the rate of women was 58.5%. The duration of observation was 6.6±5.8 years and the time from onset to diagnosis was 433±903 days. Of the 41 patients, 30 underwent recurrences (73.2%). The number of recurrences was 73 in total and 2.4 per person in



Recurrence free survival rate between prednisolone only therapy and prednisolone combinded with Immunosuppressant.

average. The median time to the initial recurrence was 202 days. The median dose of prednisolone (PSL) at the first relapse was 10 mg.

The patients were divided into recurrence and non-recurrence groups. In the recurrence group, the patients with tracheobronchial lesion as an initial symptom were more frequent (p=0.0108), and the activity index (RPDAI) (p=0.0178), serum CRP (p=0.0030) and IgG (p=0.0347) levels at the time of onset were higher than in non-recurrence group.

We next compared initial PSL monotherapy group (n=23) with initial PSL plus IS group (n=11) and found that the latter group showed significantly higher recurrence free survival rate at 1 year after initial treatment (p=0.0341, Figure 1).

Conclusion: We found tracheobronchial lesion, high RPDAI, high serum CRP and IgG as risk factors for recurrence. It was suggested that initial combination of PSL with IS could prolong recurrence-free period.

Disclosure: T. Yoshida, None; **H. Yoshifuji**, None; **M. Shirakashi**, None; **K. Kitagori**, GlaxoSmithKline, 2; **S. Akizuki**, None; **R. Nakashima**, None; **K. Murakami**, None; **M. Hashimoto**, None; **M. Tanaka**, UCB Japan Co., Ltd., 1, 2, AbbVie GK, 1, Asahi Kasei Pharma Corp., 1, 2, Astellas Pharma Inc., 1, Ayumi Pharmaceutical Corp., 1, 2, Bristol-Myers Squibb, 1, Chugai Pharmaceutical Co., Ltd., 1, 2, Eisai Co., Ltd., 1, Eli Lilly Japan K.K., 1, Pfizer Inc., 1, Janssen Pharmaceutical K.K., 1, Mitsubishi Tanabe Pharma Corp., 1, 2, Novartis Pharma K.K., 1, Taisho Pharma Co., Ltd., 1; **K. Ohmura**, Sanofi, 2, 8, Tanabe-Mitsubishi, 2, Chugai, 2, Astellas, 2, Eisai, 2, Abbvie, 2, 8.

Abstract Number: 0090

110 Patients with Monoclonal Gammopathy of Undetermined Significance (MGUS) in a Rheumatology Disease Unit: Fracture, Neuropathy, and Pernicious Anemia Are Clues to Recognition

Michael Lovy[1] and Andrew Dulalia[1], [1]Desert Oasis Healthcare, Palm Springs, CA

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Background/Purpose: Monoclonal gammopathy of undetermined significance (MGUS) has been associated with osteoporosis, neuropathy, pernicious anemia, and low vitamin B12, and may precede multiple myeloma and lymphoplasmacytic disorders. The purpose of this study is to determine the characteristics of a group of MGUS patients diagnosed in an outpatient rheumatology disease unit.

Methods: A retrospective chart review was conducted of patients found to have MGUS, including history and physical, laboratory and x-ray studies. Patients were excluded if they had a preexisting lymphoproliferative disorder, if myeloma was subsequently diagnosed, or a repeat immunofixation did not show a paraprotein.

Results: There were 39 males and 71 females, ranging in age from 31 to 101 (mean 77 years). The reasons for referral included subacute fracture of spine or pelvis-59, osteoporosis evaluation-11, inflammatory arthritis-16, degenerative and crystal induced arthritis-20, neuropathy-1, and abnormal laboratory result-3. Preexisting conditions included: history of solid tumor-29, previous major osteoporotic fracture-63, hepatitis C-4,, RA-7, SLE-3, Sjogren's-2, ulcerative colitis-3, thyroid disease-17, myasthenia gravis-1, and primary biliary cirrhosis-1. Neuropathy defined by

a sensory loss above the ankle was found in 66 patients. Paraprotein was identified by serum immunofixation in 93 patients: IgG 68 %, IgM 18%, IgA-14% with 56 % lambda and 44% kappa chains. Serum protein electrophoresis failed to show M-spike in 20 of these patients. Light chains only were found among the remaining 17 patients; 3 kappa and 14 lambda. Urine immunofixation was positive in 32 out of 77 tested. Among the neuropathy patients,14 had IgM, 37 IgG, 4 IgA paraprotein, 8 lambda only and 3 kappa only light chains. Pernicious anemia was diagnosed in 15 patients based on low vitamin B12 levels and the presence of either intrinsic factor or anti-parietal cell antibody. 79 of the 110 patients had either osteoporotic fracture, neuropathy, or PA. Upon follow up one lupus patient was subsequently diagnosed with plasmablastic lymphoma and the one patient referred for neuropathy was diagnosed with follicular lymphoma

Conclusion: Rheumatologists will most likely encounter MGUS among patients evaluated for osteoporosis. Neuropathy, pernicious anemia, and previous fracture should prompt investigation with immunofixation as a screening test. If a MGUS is found and work up for myeloma is negative, studies for lymphoproliferative disorder should be considered in at risk patients.

Disclosure: M. Lovy, None; **A. Dulalia**, None.

Abstract Number: 0091

Helicobacter Pylori Infection, Autoimmune Disease and Paraproteinemia Influence the Presentation of a Cohort of 150 Pernicious Anemia Patients Diagnosed in a Rheumatology Clinic

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Background/Purpose: The most familiar presentation of pernicious anemia is an elderly Northern European woman with hematologic and neurologic manifestations. More recently the influence of Helicobacter pylori (H. pylori), autoimmune polyendocrine syndromes (APS) and paraproteinemia on the development of pernicious anemia has been recognized. The purpose of this study is to document the spectrum of pernicious anemia as manifest in a cohort of pernicious anemia patients diagnosed in a rheumatology clinic.

Methods: A retrospective chart review of the history and physical, laboratory and x-ray studies was conducted among patients diagnosed with pernicious anemia over a 10 year period. Pernicious anemia was diagnosed on the basis of a low vitamin B12 level and either intrinsic factor or anti-parietal cell antibodies.

Results: A total of 150 patients, 106 females and 44 males ranging in age from 32-101 years (mean 71.8) were diagnosed with pernicious anemia. Referral was based on acute fracture of the spine or pelvis-41,RA-30, arthritis-30, osteoporosis-16, pain-15, autoimmune disease-9, SLE-7, psoriasis-2. There was a history of major osteoporotic fracture in 54, heartburn-73, past peptic ulcer disease-16, lower esophageal ring-3, thyroid disease-42, type 1 diabetes-13, and vitiligo-2. 12 patients were on proton pump inhibitors and 5 were on H-2 antagonists. The mean BMI was 27.3. 101 patients had a sensory deficit at the level of the ankle, including 38 with findings of a glove and stocking sensory loss. Only 25 patients were anemic with 2 patients having a MCV >100 fL and 5 with a low serum iron. Folic

acid was < 8 ng/mL in 19 patients with a predominance of intrinsic factor over anti-parietal cell antibody present (p=0.039). Vitamin D levels were < 12 ng/mL in 13. H. pylori was diagnosed on the basis of a positive urea breath test in 21 patients at the time of initial evaluation (Group 1). Paraproteinemia was identified with serum immunofixation in 19 (Group 2). Autoimmune disease diagnosis (Group 3) included RA-32, SS-a or SS-b positive Sjogren's 9, SLE -3, psoriatic arthritis-4, CREST-2, spondyloarthropathy-2,inflammatory bowel disease-2, anti-PLA2R+ glomerulonephritis-1. Patients with thyroid disease-42 constituted Group 4, with the remaining 51 in Group 5. Mean age of the groups was 65.8, 77, 66, 71.3, and 71.7 respectively. There was a statistically significant increase of autoimmune disease present in H. pylori + Group 1 compared to the remaining 129 patients without H. pylori (p=0.0295). No other statistically significant differences were noted between Groups 1-5 or between intrinsic factor and anti-parietal cell antibody positive patients.

Conclusion: Pernicious anemia is most likely to be found among rheumatology patients with fracture, primary Sjogren's ,thyroid disease, vitiligo and other features of APS as well as in patients with paraproteinemia. Patients with autoimmune disease and those with H. pylori infection present with pernicious anemia at a younger age. The statistically significant correlation among pernicious anemia patients between H. pylori infection and underlying autoimmune disease supports the hypothesis that H. pylori can act as a trigger of an autoimmune response in a genetically predisposed host.

Disclosure: M. Lovy, None; **N. Aguirre Vega**, None; **C. Escobar**, None.

Abstract Number: 0092

Diagnosis of Behçet's Disease: Comparison of Two Sets of Classification Criteria. Application in 111 Patients of a Well-defined Population

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SESSION INFORMATION

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Background/Purpose: Behçet's disease (BD) is a systemic, chronic, relapsing vasculitis with no pathognomonic diagnostic test. The most widely used classification criteria are those of the International Study Group (ISG) for BD. These criteria were repeatedly found to have low sensitivity. Therefore, the International Criteria for Behçet's Disease (ICBD) were published in 2014.

Objectives: To compare the ISG with ICBD diagnostic criteria for BD.

Methods: The study included all consecutive 111 patients diagnosed with definitive or possible BD by expert rheumatologists. They were diagnosed at a well-defined population in Northern Spain between 1980 and 2019. The ISG and ICBD diagnostic criteria for BD were applied to and compared among all patients.

TABLE 1

	Expert diagnosis (N=111)	ISG criteria (N=65)	ICBD criteria (N=86)
Age, mean (SD)	36.7 (13.2)	36 (12.8)	36.7 (13)
Gender, men/women, N (%)	49/62 (44.1/55.8)	29/36 (44.6/55.4)	38/48 (44.2/55.8)
Oral aphthosis	110 (99)	65 (100)	85 (100)
- Recurrent (3 times/year)	91 (87.2)	61 (93.8)	74 (86)
Genital aphthosis	59 (53.1)	42 (64.6)	56 (65.1)
Skin manifestations	76 (68.4)	56 (86.15)	71 (70.9)
- Pseudofolliculitis/ Erythema nodosum	51 (67.1)/ 27 (35.5)	38 (58.5)/ 21 (32.3)	42 (68.8)/ 22 (36.1)
Ocular lesions	39 (35.1)	32 (49.2)	39 (45.3)
- Anterior/ Posterior/ Panuveitis	17 (43.6);12 (30.8)/ 0	16 (50)/ 8(25)/ 7 (21.9)	17 (45.6); 0; 12 (30.8)
- Retinal vasculitis	4 (10.3)	1 (3.1)	4 (10.6)
Joint manifestations	76 (68.5)	43 (66.1)	58 (67.4)
- Arthralgias / Arthritis	69 (92.8)/ 45 (60)	39 (90.7)/ 24 (55.8)	52 (89.6)/ 33 (56.9)
Neurological manifestations	20 (18)	11 (16.9)	16 (18.6)
- Peripheral / Central	11 (55)/ 14 (70)	7 (63.6)/ 7 (63.6)	12 (75)/ 10 (62.5)
Vascular manifestations	9 (8.6)	7 (10.8)	10 (11.6)
- Arterial/ Vein thrombosis/ Phlebitis	0/ 5 (55)/ 1 (11.1)	0/ 4 (57.1)/ 1 (14.3)	1 (12.5)/ 5 (62.5)/0
Gastrointestinal features	4 (4.5)	4 (6.1)	4 (4.6)
Pathergy test positive (available data; %)	6 (28; 21.4)	4 (19; 21)	4 (25, 16)
HLA B51 positive (available data; %)	38 (86; 44.2)	19 (47; 40.4)	28 (63; 44.4)

Results: We studied 111 patients (62 Women/49 Men), mean age 36.8±13.2 years. BD was diagnosed in 65 (58.5%) by ISGBD criteria and in 86 (77.5%) by ICBD criteria. No significant differences were observed between both criteria ($p < 0.001$). The overall concordance was fair (Kappa 0.3; $p< 0.001$). Sensitivity was 58.6% for ICBD criteria and 80.2% for ISG. (TABLE-1)

Conclusion: ICBD criteria exhibit higher sensitivity than ISG criteria. Thus, the application of these new criteria can achieve a more correct and earlier diagnosis of BD.

Disclosure: D. Martinez-Lopez, Lilly, 2; **A. Herrero Morant**, None; **C. Alvarez-Reguera**, None; **L. Sanchez-Bilbao**, None; **I. Gonzalez-Mazon**, None; **J. Martín-Varillas**, None; **G. Suarez-Amorin**, None; **P. Setien-Preciados**, None; **C. Mata-Arnaiz**, None; **M. González-Gay**, None; **R. Blanco**, None.

Abstract Number: 0093

Review of Gastrointestinal Manifestations of Kohlmeier-Degos Disease

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SESSION INFORMATION
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Background/Purpose: Kohlmeier-Degos disease is a rare obliterative vasculopathy that can present in a benign cutaneous form or with potentially malignant systemic involvement. While the benign form is restricted to cutaneous lesions, the malignant form involves visceral organs and may occur with or, rarely, without cutaneous lesions. In systemic cases, central nervous system, renal, respiratory, cardiac, and gastrointestinal manifestations have all been noted, in addition to other organs. Of these, the gastrointestinal tract is most commonly involved and mortality of systemic Kohlmeier-Degos is often related to bowel perforations. Given this, further characterization of this disease's gastrointestinal manifestations is essential to increasing awareness and recognition of this life-threatening entity.

Methods: Published case reports of gastrointestinal Kohlmeier-Degos disease were compiled by searching EBSCO*host* database. Case reports included are all those in which patients were diagnosed with Kohlmeier-Degos disease and reported at least one gastrointestinal symptom. Demographics, presentations, imaging, complications, and treatments were evaluated for approximately 40 cases. Novel pathophysiology of the gastrointestinal aspect of this disease was also elucidated.

Results: The average age of gastrointestinal Kohlmeier-Degos occurring in adults was 43, with a slight predilection for females. Infantile disease is present but rare. Bowel perforations occurred in roughly 40% of cases. Most perforations occurred in the small intestine, specifically the jejunum. Repeat perforations are possible, although not well documented due to the high risk of fatality. Various gastrointestinal visualization methods and treatments were employed across all cases. Pathology of the disease in the gastrointestinal tract is characterized as a purely arteriopathic and extravascular sclerosing process confined to the subserosal fat. Enhanced interferon alpha expression is likely involved in the obliterative arteriopathic process. Under the influence of a type I interferon microenvironment, there is an initial influx of monocytes into the intima. They undergo transdifferentiation into procollagen-producing cells with myofibroblastic properties, producing excessive collagen and hyaluronic acid that eventuates into the acellular plug that defines the final obliterative arterial lesion. A similar procollagen phenotype reminiscent of the scleroderma phenotype is encountered in the fibroblasts within the zone of serosal fibrosis; the fibroblasts express smooth muscle actin and show a noticeable absence of CD34 staining.

Conclusion: Gastrointestinal Kohlmeier-Degos remains a rare and elusive entity, but patterns can be seen in existing published cases. All gastrointestinal cases were preceded by characteristic skin lesions and the presence or histology of these cutaneous lesions often aided diagnosis. All cases of bowel perforation were preceded by at least one gastrointestinal symptom. Although underutilized, laparoscopy proves to be the most specific visualization and diagnostic technique. Presently, the combination of eculizumab and treprostinil is the most effective treatment option.

Disclosure: S. Sattler, None; **L. Shapiro**, Actelion, 5; **C. Magro**, None.

Abstract Number: 0094

Validation Study of Proposed Diagnostic Criteria for Sympathetic Joint Effusion

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Background/Purpose: Sympathetic joint effusion (SJE) is a rarely diagnosed rheumatologic entity characterized by painful yet non-inflammatory range synovial effusion. The condition was originally described in 1978 as a reactive joint effusion associated with adjacent pathology. Literature on the subject has remained scarce due to lack of clinician familiarity and diagnostic criteria, and remains markedly underdiagnosed.[1-3] A delay in diagnosis can lead to significant healthcare expenditure, unnecessary treatment and poor outcome.[1] A validated diagnostic criteria (Figure 1) would improve diagnostic certainty for clinicians and aid future studies and treatment.

Methods: Retrospective chart review was performed on diagnostic arthrocentesis with synovial fluid analysis between 1/31/2010 – 2/1/2019. Those with synovial fluid White Blood Cell (WBC) counts (< 2000 cells/mm3), with com-

Figure 1. Proposed Diagnostic Criteria for SJE

Definite SJE = Clinical features + Synovial Fluid features + Adjacent Pathological Process **Probable SJE = Clinical features + Synovial Fluid features**		
Clinical features (fulfill all 4 below):	**Synovial fluid analysis features (fulfill all 3 below):**	**Adjacent pathological process in same limb:**
1) Monoarticular (1 joint) 2) Joint or bursa effusion with evidence of inflammation on exam (Erythema, Pain, and/or Warmth) 3) Subacute onset of joint effusion (typically >24 hours and <1 month) 4) No history of concurrent osteoarthritis, recent direct trauma, or fracture.	1) Normal (<200 WBC/mm3) or non-inflammatory (<2,000 WBC/mm3) range 2) Culture negative for microbial growth 3) No intracellular crystals	Contiguous area, adjacent to, or in close anatomical proximity (either superficial or deep, proximal or distal) to the joint effusion. Includes, but not limited to, infection, DVT, soft tissue fluid collection, nearby trauma, recent orthopedic surgery, loosening of joint prosthesis, and ECMO catheter cannulation, e.g., knee SJE/SSE may be seen with foot infection.

Figure 1. Proposed Diagnostic Criteria for SJE

Table 1. Patients' Demographic and Clinical Features by Original Description

Clinical Feature	SJE (N=125)	Non-SJE (N=215)
Gender		
Male	81 (64.8%)	123 (57.2%)
Female	44 (35.2%)	92 (42.7%)
Age (years)		
Mean (STD)	57.5 (16.8)	58.6 (15.6)
Median (range)	59.0 (18-99)	58.5 (23-96)
Interquartile Range	47-67	48-68
WBC Count		
Median (range)	82.5 (0-2000)	291.5 (1-2000)
Interquartile Range	35-194	106-759.5
Joint Site		
Interphalangeal (finger) joint	1 (0.8%)	0
Wrist Joint	0	1 (0.5%)
Elbow Joint	7 (5.6%)	14 (6.5%)
Shoulder Joint	6 (4.8%)	9 (4.3%)
Lumbar Spine (disc)	0	1 (0.5%)
Hip Joint	6 (4.8%)	21 (9.8)
Knee Joint	93 (75.1%)	157 (72.9%)
Ankle joint	9 (7.2%)	12 (5.6%)
Metatarsal Joint	2 (1.6%)	0

Table 1. Patients' Demographic and Clinical Features

plete crystal and culture studies were included. A total of 1095 synovial fluid analyses were initially evaluated, with 340 having negative crystal and culture studies.

Results: Using the original SJE description, 125 cases were determined to have SJE with the remaining 215 cases as negative controls. The annualized incidence was 1.268%. Some of the adjacent pathologies found were infections (cellulitis, abscess), vascular manipulation (AV fistula, ECMO, line placement), and DVT.

Table 2. Independent and Joint Effects of Diagnostic Features for SJE Clinical Diagnosis

Independent Effects	N	(Raw) Odds Ratio (95% CI)	p-value
Effusion: Yes vs. No	324	4.37 (1.65, 11.55)	0.001
Erythema: Yes vs. No	300	4.00 (2.19, 7.29)	<0.0001
Warmth: Yes vs. No	293	1.63 (0.99, 2.67)	0.057
Pain/Tenderness: Yes vs. No	330	1.92 (0.74, 4.94)	0.20
WBC Count: <200 vs. ≥200 cells/mm3	340	4.61 (2.84, 7.48)	<0.0001
Adjusted/Joint Effects	**N**	**Adjusted Odds Ratio (95% CI)**	**p-value**
Effusion: Yes vs. No	297	4.69 (1.60, 13.75)	0.005
Erythema: Yes vs. No		4.92 (2.50, 9.71)	<0.0001
WBC Count: <200 vs. ≥200 cells/mm3		5.71 (3.24, 10.04)	<0.0001

Table 2. Independent and Combined Effects of Diagnostic Features for SJE Clinical Diagnosis

The sensitivity of monoarticular involvement was 38.1% while specificity was 75.8%. Eight of the SJE patients based on original description with adjacent pathology had complained of >1 joint involved. 65.7% of SJE cases presented with symptoms for greater than 1 day but less than 7, while 14.3% presented after day 7 but within the month. The odds of diagnosis increased 4-fold with erythema (Table 2). On multivariable analysis, erythema and WBC Count < 200 increased the odds of diagnosis 4.9 and 5.7-fold, respectively, after having adjusted for effusion and each other.

With the proposed diagnostic criteria, 59 cases would be considered "Definite" with 58 cases considered "Probable." Comparing cases on original description with intention to treat all "Definite" or "Probable" cases, the sensitivity of our proposed diagnostic criteria is 93.6% with specificity of 96.7% (PPV=94.4%,NPV=96.3%).

Conclusion: To our knowledge, this is the first proposed and validated diagnostic criteria of SJE. The sensitivity and specificity of our criteria are very high, driven by the use of exclusion diagnoses. Strong Odds Ratios for Erythema and WBC Count < 200 indicate the severity of physical symptoms yet minimal synovial inflammation. A weakness of our study is that data was collected retrospectively which is limited by history and exam included in the chart.

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Disclosure: J. Levinson, None; **M. Jurkowski**, None; **J. Kahlon**, None; **H. Youn**, None; **D. Yu**, None; **I. Tan**, None.

Abstract Number: 0095

Systematic Evaluation of Nine Monogenic Autoinflammatory Diseases Reveals Common and Disease-Specific Correlations with Allergy-Associated Features

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Monogenic autoinflammatory diseases (AID) are caused by mutations in innate immune signaling genes. The effect of these mutations on the risk of allergy is unknown. We previously reported results of our preliminary analysis, which indicated that allergy-associated features were rare in AID based on retrospective review [1]. We have now performed a full systematic analysis using a combination of retrospective chart review, standardized questionnaires, and T cell immunophenotyping. This revealed common and disease-specific correlations with allergy-associated clinical and immunologic phenotypes. This study was the first of its kind to investigate the prevalence of allergic features in multiple monogenic AID, and the first to do so within the U.S. population.

Methods: We investigated the prevalence of allergic clinical and immunologic phenotypes in AID caused by pathogenic mutations in *MEFV, TNFRSF1A, MVK, NLRP3, PSTPIP1,* proteasome genes, *STING, TNFAIP3*, and *ADA2*. We used retrospective chart review and questionnaires to assess clinical and laboratory features of patients enrolled on NIH protocol 94-HG-0105 or 17-I-0016. Questionnaires were developed by a panel of clinical allergists, clinical rheumatologists, and survey researchers. Six clinical syndromes were assessed (Table 1). Surveys were administered via the telephone, internet, and in the NIH Clinical Center. Informed consent was obtained from all participants. Comparator data was obtained from the National Center for Health Statistics and Chicago Food Allergy Research Surveys [2-6]. To determine if T helper 2 (Th2)/Th9 cells were expanded in AID, we stimulated peripheral blood mononuclear cells (PBMCs) and analyzed the data with flow cytometry.

Results: Allergic rhinitis, eczema, and eosinophilic gastrointestinal (GI) inflammation were prevalent in multiple AID (Table 1). Asthma was rare in patients with *MEFV* and proteasome mutations but common in patients with *NLRP3* mutations. A trend towards increased food allergy prevalence was seen in patients with *NLRP3*, *TNFAIP3*, and proteasome mutations. Median IgE was reduced in patients with *ADA2* and *MVK* mutations; median absolute eosinophil count (AEC) was reduced in patients with most AID but elevated in patients with *NLRP3* mutations (Figure 1). T helper 2 (Th2) cells were expanded in patients with *NLRP3, TNFRSF1A,* and *MVK* mutations; Th9 cells were expanded in patients with *TNFAIP3* mutations (Figure 2).

Disease (number of subjects)	**Allergic rhinitis**	**Asthma**	**Eczema**	**Food Allergy**	**Multiple food allergies**	**EGID**	**Flare-related urticaria**	**Flare-related angioedema**
General population (n = variable, from public datasets)	7.1%	12.9%	9.2%	9.2%	4.0%	0.0%	N/A	N/A
FMF (n = 94)	22.3%*	4.3%*	7.5%	5.3%	2.1%	0.0%	1.1%	2.1%
CAPS (n = 85)	40.0%*#	25.9%*#	21.2%*	14.1%	9.4%	0.0%	91.8%	3.5%
TRAPS (n = 69)	21.7%*	17.4% #	7.3%	1.5%	1.5%	1.5%*	4.3%	4.3%
HIDS (n = 36)	19.4%*	13.9%	11.1%	5.6%	2.8%	2.8%*	22.2%	5.6%
PAPA (n = 18)	16.7 %	22.2% #	16.7%	11.1%	0.0%	0.0%	5.6%	0.0%
DADA2 (n = 51)	13.7%	11.8%	43.1%*#	5.9%	5.9%	2.0%*	7.8%	5.9%
HA20 (n = 13)	46.2%*	30.8% #	53.9%*#	15.4%	15.4%	7.7%*	7.7%	15.4%
CANDLE (n = 14)	14.3%	0.0%*	35.7%*#	14.3%	14.3%	7.1%*	28.6%	0.0%
SAVI (n = 12)	8.3%	25.0% #	25.0%	0.0%	0.0%	0.0%	8.3%	0.0%

Table 1. Prevalence of atopic features in patients with autoinflammatory disease confirmed by genetic testing, and comparison data in the general population. Column shows prevalence in each population. FMF = Familial Mediterranean Fever; CAPS = Cryopyrin-Associated Periodic Syndrome; TRAPS = Tumor necrosis factor Receptor-Associated Periodic Syndrome (TRAPS); DADA2 = Deficiency of Adenosine Deaminase 2; HIDS = Hyper-IgD Syndrome; PAPA = Pyogenic Arthritis, Pyoderma gangrenosum, and Acne; HA20 = Haploinsufficiency of A20; CANDLE = Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated temperature; SAVI = STING-Associated Vasculopathy with onset in Infancy. *FDR<0.05 vs. general US population. #FDR<0.05 vs. FMF; Benjamini-Hochberg adjusted Fisher t-test.

Figure 1

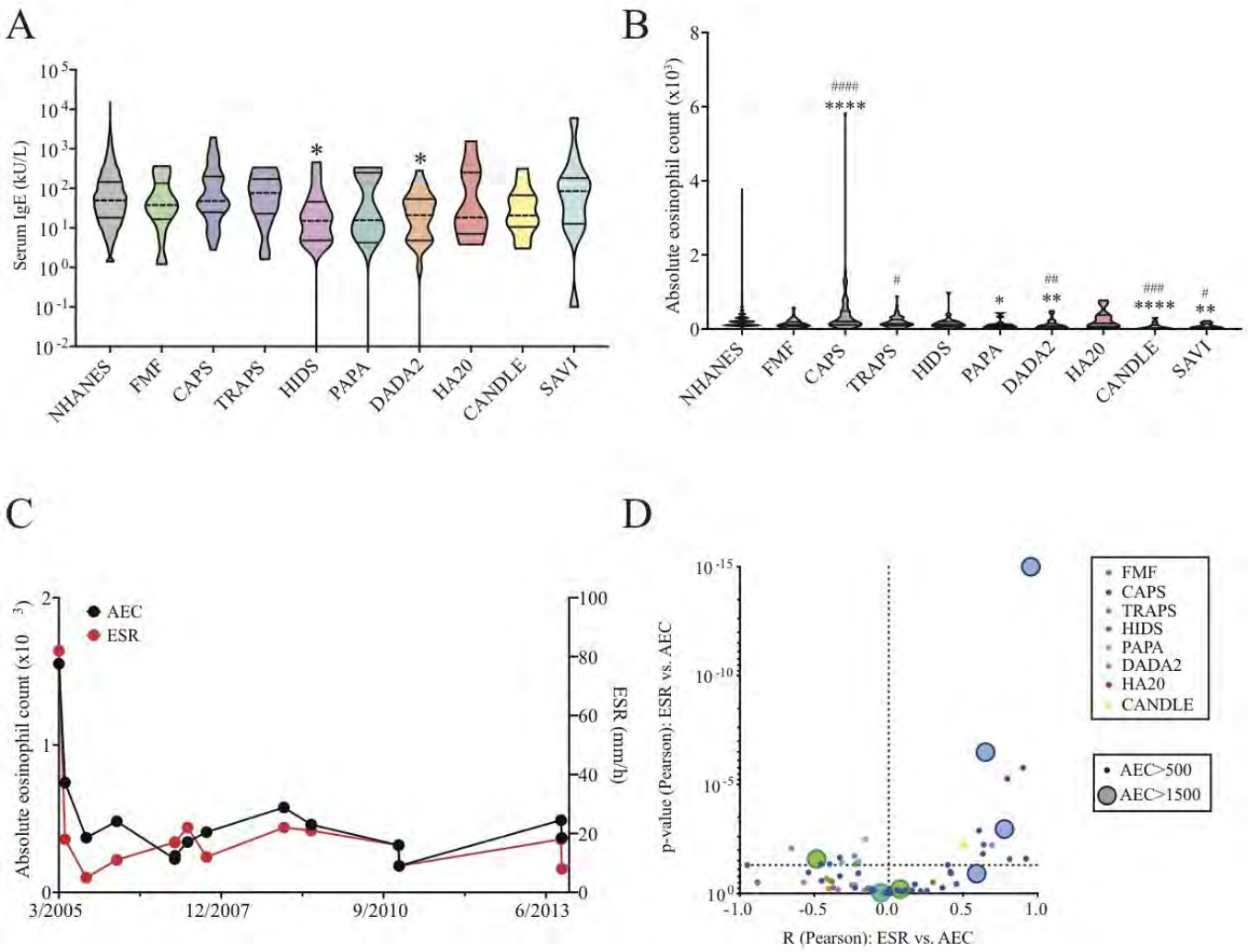

Figure 1. Eosinophilia and absolute eosinophil counts (AEC) in the general US population and in nine monogenic autoinflammatory diseases (AID). Data are shown for the general US population, Familial Mediterranean Fever (FMF); Cryopyrin-Associated Periodic Syndrome (CAPS); TNF-Receptor Associated Periodic Syndrome (TRAPS); Hyper-IgD Syndrome (HIDS); Pyogenic Arthritis, Pyoderma gangrenosum, and Acne (PAPA); Deficiency of ADA2 (DADA2); Haploinsufficiency of A20 (HA20); Chronic Atypical Neutrophilic Dermatosis with Lipodystrophy and Elevated temperature (CANDLE); and STING Associated Vasculopathy with onset in Infancy (SAVI). (A) Violin plot shows serum IgE levels for each population. (B) Violin plot shows serum IgE levels for each population. (C) Representative plots are shown for one CAPS patient with hypereosinophilia: dot plot of AEC and ESR values over a period of 8 years. (D) Volcano plot shows correlation (R, Pearson test) vs. p-value (Pearson test) of AEC vs. erythrocyte sedimentation rate (ESR, mm/h) for each AID patient with eosinophilia (AEC > 500). Colors of dots indicate specific AID (FMF, green; CAPS, dark blue; TRAPS, purple; HIDS, fuchsia; PAPA, teal; DADA2, orange; HA20, red; CANDLE, yellow). Size of dots distinguishes patients with eosinophilia (AEC > 500) from those with hypereosinophilia (AEC > 1500). *p<0.05, **p<0.01, ***p<0.005, ****p<0.001 vs. general US population. #p<0.05, ##p<0.01, ###p<0.005, ###p<0.001 vs. FMF; Benjamini-Hochberg adjusted Mann-Whitney (B).

Conclusion: Allergy-associated clinical and immunological phenotypes are prevalent in many AID, reinforcing a role for innate immunity in allergy pathogenesis. Further investigations are needed to determine the role of allergy-associated factors in AID pathology.

Figure 2

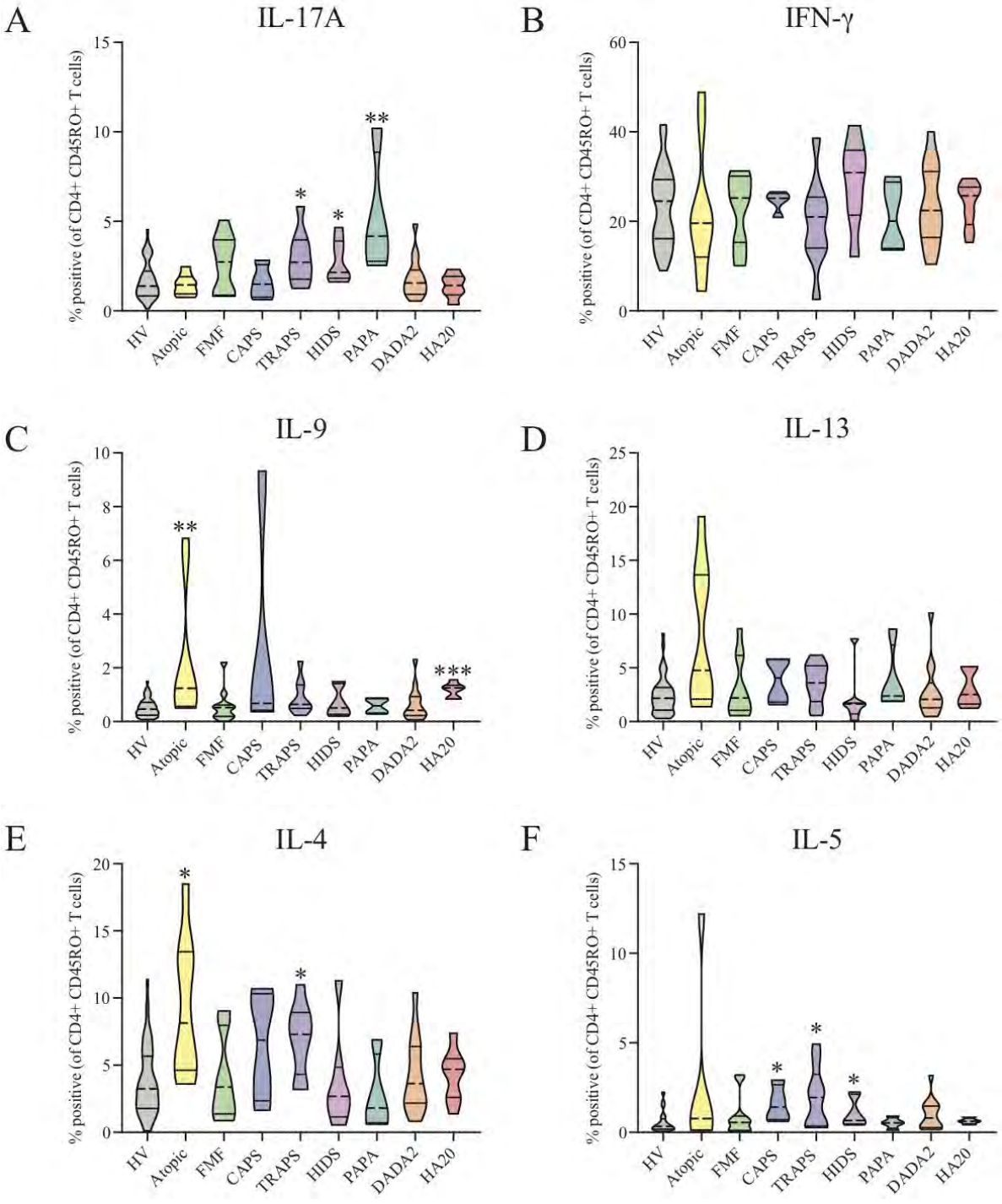

Figure 2. T helper immunophenotypes in seven monogenic autoinflammatory diseases (AID). Data are shown for healthy volunteers (HV); atopic dermatitis patients; Familial Mediterranean Fever (FMF); Cryopyrin-Associated Periodic Syndrome (CAPS); TNF-Receptor Associated Periodic Syndrome (TRAPS); Hyper-IgD Syndrome (HIDS); Pyogenic Arthritis, Pyoderma gangrenosum, and Acne (PAPA); Deficiency of ADA2 (DADA2); and Haploinsufficiency of A20 (HA20). Violin plots show percentage of memory T helper cells (CD3+ CD4+ CD8- CD45RO+) producing IL-17A (A), IFN-gamma (B), IL-9 (C), IL-13 (D), IL-4 (E), and IL-5 (F). *p<0.05, **p<0.01, ***p<0.005, ****p<0.001 vs. HC. #<0.05, ##p<0.01, ###p<0.005, ###p<0.001 vs. FMF; Benjamini-Hochberg adjusted Mann Whitney.

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Abstract Number: 0096

The Bicipital Stress Test: A Maneuver to More Accurately Diagnose Bicipital Tendinitis and Its Referred Pain Patterns

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammation of the bicipital tendon contributes heavily to shoulder joint morbidity. To date, diagnosis of bicipital tendinitis has relied on physical exam findings, particularly Yergason's sign and the Speed's test (ST). These tests have fallen out of fervent use due to their relative insensitivity. In this study, we introduce a novel diagnostic paradigm, the Bicipital Stress Test (BST), with improved sensitivity in comparison to previously standard tests.

Methods: This retrospective cohort study reviewed 151 patients over a six-month period. Patients were included who presented with upper body pain and whose exam demonstrated a positive ST and/or BST. Given a positive test, a treatment paradigm was utilized, and patients were reevaluated at four to six-week intervals for clinical improvement. Statistical analysis determined the sensitivity and specificity of the BST.

Results: The BST identified 248 positive upper extremities versus 71 for the traditional ST test. In every case that the ST test was positive, the BST was also positive.

Conclusion: Physical examination techniques of the upper extremity have been described but are infrequently utilized in clinical practice; this is due to the relative insensitivity of the most well-known tests for bicipital tendinitis, Yergason's sign (43%) and the ST (32%). The BST is a more sensitive test in diagnosing bicipital tendinitis. The clinical validity of the BST is supported by normalization of the physical exam and improvement in symptomatology following

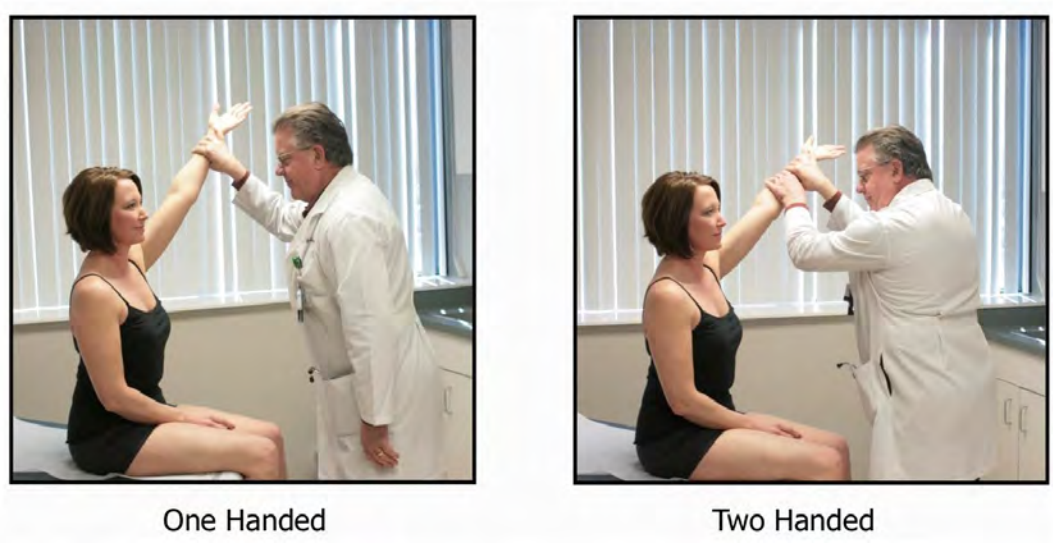

Figure 1. The Bicipital Stress Test. In the BST, the clinician faces the seated patient. The shoulder is forward flexed to 120 degrees, abducted to 30 degrees, and the arm is in the supinated position. The examiner then places direct downward force at the wrist. Inability to maintain position against forceful downward pressure is the key that determines a positive test.

treatment of a positive test. Implementation of the BST yields early detection, accurate diagnosis, and successful treatment of bicipital tendinitis and its referred pain patterns.

Disclosure: M. Thomley, None; **D. Spalding**, None; **A. Preda-Naumescu**, None; **R. Waldrop**, None.

Abstract Number: 0097

Does Testing for SAA Is More Beneficial Than CRP for the Follow-up of Patients with FMF?

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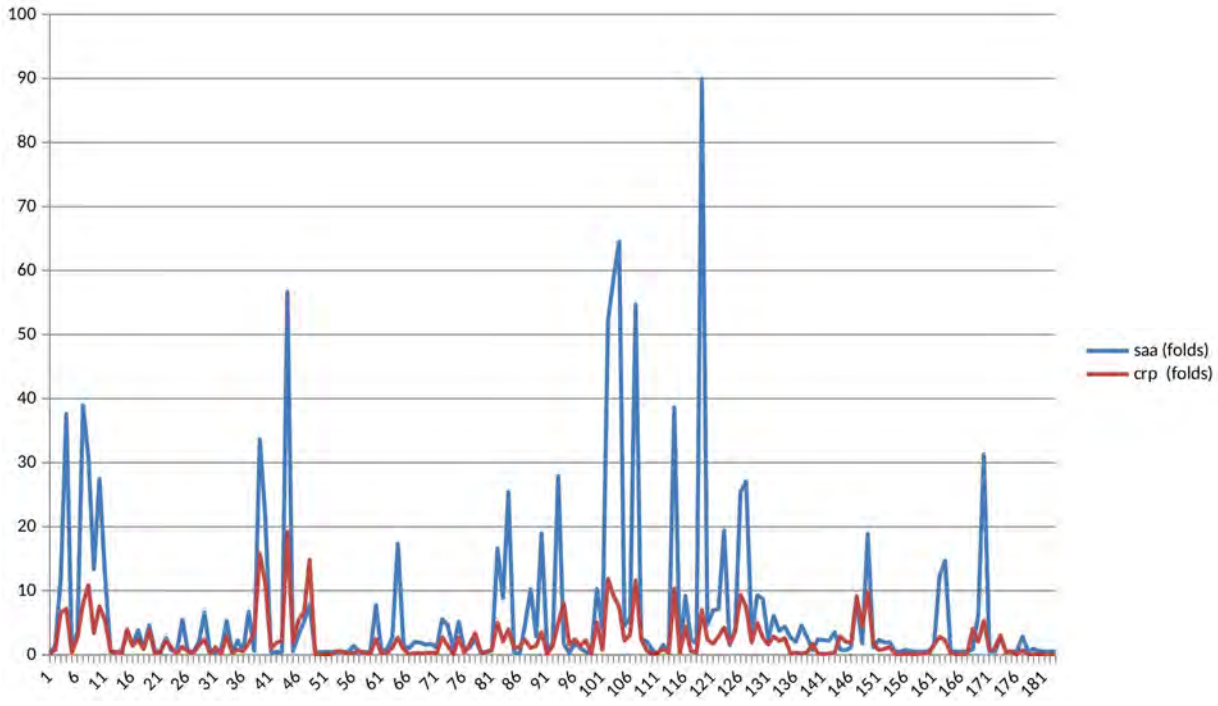
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In order to follow subclinical inflammation and adjust the therapy for an optimal disease control, clinicians seek for readily accessible, affordable and reproducible markers. C reactive protein (CRP) is widely used for this purpose. Some suggest that CRP measures are not conclusive in all cases, especially in initial stages of inflammation. It is suggested that Serum Amyloid A (SAA) may be more reliable and sensitive in predicting an ongoing inflammation.

Methods: In order to evaluate and to compare the sensitivity of SAA and CRP, 153 measurements from 28 patients M694V homozygous mutation and 31 measurements from 15 patients with M694V heterozygous mutation were obtained during a mean follow-up of 1 year. For the analysis, the folds of normal CRP and SAA values were used for correlation. Serum levels of the given markers were measured with nephelometric kits (normal CRP levels < 5 mg/L



The folds of the CRP and SAA in whole M694V homozygous and heterozygous mutant population

and SAA levels < 6,8 mg/L). More than one and half fold increasement of CRP and SAA was defined as an active inflammation.

Results: Except a patient, all patients in whole cohort were on prophylactic colchicine. Among 28 patients with M694V homozygous mutation, a patient with adalimumab, 12 patients with anti-IL-1 regimens. Of 15 patients with M694V heterozygous mutation, 4 were under anti-IL-1 treatment. There was a total of 183 measurements of CRP and SAA from 43 patients. Twenty-three measurements were obtained during the attack period in M694V homozygous group and the remaining 160 measurements were collected in attack free period. Figure demonstrates the correlation between CRP and SAA results ($r=0.745$, $p< 0.001$). Both acute phase reactants were increased in 69 measurements, while in 13 CRP was high but SAA was normal and in 31 SAA was high however CRP was within normal limits. The mean increase in CRP of the whole cohort was 2,37 ± 3,22-fold, whereas mean increase in SAA was 6,77 ± 13,23-fold of the normal.

Conclusion: According to these results, serial testing of SAA does not provide any additional advantages over CRP. Readily accessible and affordable bio-marker CRP seems to be sufficient for follow-up of patients with FMF

Disclosure: M. Oztas, None; **S. Ugurlu**, None; **O. Selvi**, None; **B. Ergezen**, None; **H. Ozdogan**, None.

Abstract Number: 0098

CCL2 and CCR2 in Adult Onset Still's Disease

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Adult onset Still's disease (AOSD) is a rare systemic inflammatory disease characterized by a high spiking fever, evanescent rash, arthralgia, generalized lymphadenopathy, and leukocytosis. The activation of innate immune system is the main pathogenesis of AOSD. Chemokine C-C motif ligand (CCL) 2 and CC chemokine receptor (CCR) 2, a ligand of CCR2, have a chemical attractant activity and migrate monocyte and macrophages to the site of inflammation.

Methods: This study checked the serum levels of CCL2 and CCR2 in patients with AOSD and rheumatoid arthritis (RA), and healthy controls (HC), and analyzed their associations with clinical markers in patients with AOSD.

Results: The levels of CCL2 in serum were significantly increased in patients with AOSD (476.41 ± 689.06 pg/mL) compared in patients with RA (169.15 ± 118.71 pg/mL, $p = 0.007$) and HCs (135.14 ± 71.66 pg/mL, $p = 0.003$). The levels of CCR2 in serum were increased in AOSD patients rather than RA and HC, but it was not statistically significant because the large variation between individuals. The levels of CCL2 in serum was significantly increased in active group (589.49 ± 772.41 pg/mL) than inactive group (157.73 ± 71.02 pg/mL, $p < 0.001$) in patients with AOSD. The levels of CCL2 in serum correlated with systemic score ($r = 0.539$, $p < 0.001$), the counts of leukocyte ($r = 0.316$, $p = 0.041$) and neutrophil ($r = 0.316$, $p = 0.041$), C-reactive protein ($r = 0.321$, $p = 0.044$), ferritin ($r = 0.607$, $p < 0.001$), LDH ($r = 0.597$, $p < 0.001$) and albumin ($r = -0.428$, $p = 0.005$). However, the level of CCR2 in serum was not associated with any clinical markers of disease activity. After disease was resolved, the levels of CCL2 were significantly decreased in patients with AOSD ($p = 0.029$).

Conclusion: Circulating CCL2 was elevated in patients with AOSD and was associated with disease activity, suggesting that CCL2 might take a role in the inflammatory response of AOSD.

Disclosure: J. Jung, None; **J. Kim**, None; **C. Suh**, Celltrion, 5; **H. Kim**, None.

Abstract Number: 0099

Interleukin 6 Concentration in Synovial Fluid of Patients with Different Types of Arthritis

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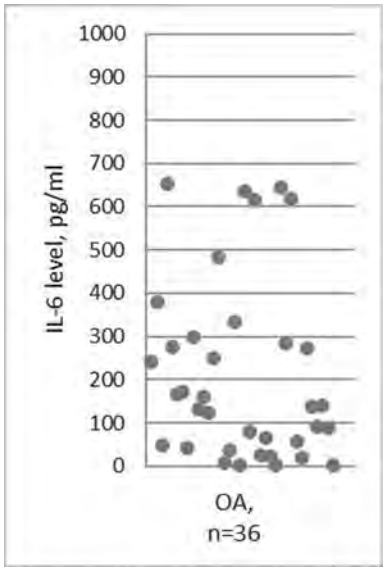
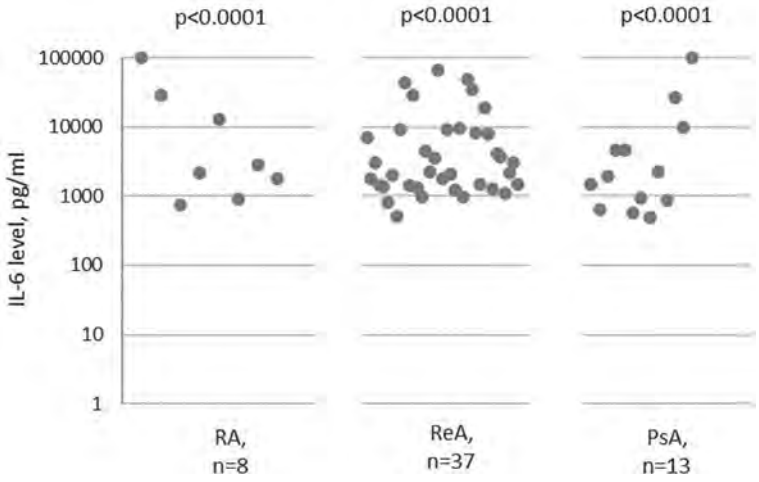
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM



IL-6 concentration in patients with osteoarthritis



IL-6 concentration in patient with inflammatory arthritis

Background/Purpose: Persistent synovitis without known markers such as rheumatoid factor (RF), anti-citrullinated protein antibodies (ACPA) as well as without genetic markers as HLAB27 is not uncommon. It is valuable to determine the presents of chronic inflammation and differentiate with age-related changes, what are especially relevant for middle-aged patients with mono- or oligo- arthritis, when dilemma to start disease modifying drugs for inflammatory disease often is present. Interleukin 6 (IL6) is a pleiotropic pro-inflammatory cytokine, which play significant role in the chronic inflammation and autoimmunity. IL6 concentration in synovial fluid was studied in different types of arthritis. The aim of present study to compare concentration of IL6 in synovial fluid in patients with known type of arthritis.

Methods: Synovial fluid was obtained from one hundred one patients with chronic synovitis, mostly from knee joints. IL6 concentration was determined by immunochemical luminescence method.

Results: The median IL6 concentration in synovial fluid in patients with osteoarthritis (OA) was 138.0 pg/ml (IQR 43.4 to 296.0) without any significant differences in primary and secondary osteoarthritis. In inflammatory arthropathies median IL6 level was 2194.0 pg/ml (IQR 1254.0 to 8625.0). Median IL6 concentration in patients with rheumatoid arthritis (RA) was 2516.5 pg/ml, (IQR 1136.0 to 25058.0). There was not significant differences found between seronegative and seropositive RA groups. In reactive arthritis (ReA) median IL6 level was 2281.0 pg/ml (IQR 1392.0 to 8652.0); psoriatic arthritis (PsA) - 1964.0 pg/ml (IQR 754.0 to 7300.0) and ankylosing spondylitis (AS) - 2776.0 pg/ml (IQR 514.7, 3944.0). In group of 19 patients with negative RF, ACPA and HLAB27 inflammatory arthritis (IA) median IL6 level was 2163.0 pg/ml (IQR 822.0 to 7875.0). The pairwise comparison of diagnosis by Kruskal-Wallis Test show statistically significant difference in OA and RA, OA and ReA, OA and PsA groups, $p< 0.0001$.

Conclusion: IL6 detection in the synovial fluid is useful in arthritis evaluation. The results show that IL6 level over 1000 pg/ml suggest diagnosis of inflammatory arthritis.

Disclosure: A. Bukina, None; **A. Mihailova**, None.

Abstract Number: 0100

Concordance Between the QuantiFERON-TB Gold In-Tube and Tuberculin Test for the Diagnosis of Latent Tuberculosis Infection in Patients with Rheumatic Diseases

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster I: Diagnosis and Testing

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatic diseases (RD) are at higher risk of latent tuberculosis infection (LTBI) reactivation. To detect and treat it before starting treatment, especially with biological therapies, decrease the reactivation risk. Diagnosis is carried out by the tuberculin skin test (TST) or interferon-gamma release assays (IGRAs), IGRAs might be more specific and sensitive. We aim to analyze the concordance between QuantiFERON-TB Gold In-Tube (QTF) and TST for the diagnosis of LTBI in patients with rheumatic diseases.

Methods: A retrospective observational study was conducted including patients diagnosed with RD screened for LTBI with both TST and QTF (2014-2018). Demographical and clinical variables at screening and at follow-up were collected. The concordance between both tests has been estimated as categorical variables using Cohen´s Kappa test, considering "poor" if it is $\leq 0,20$; “low” if $0,20 < k \leq 0,40$, “moderate” if $0,40 < k \leq 0,60$, “substantial” if $0,60 < k \leq 0,80$ and “optimal” if $k > 0,80$.

Table 1. Kappa concordance between QTF and TST.

	TOTAL SAMPLE	PATIENTS WITH GC AT LTBI SCREENING	PATIENTS WITHOUT GC AT LTBI SCREENING
Number of coincidences (p1)	147 (88.02%)	64 (83.12%)	83 (92.22%)
Number of randomly expected coincidences (p_e)	124.1 (74.28%)	62.9 (81.73%)	61.8 (68.62%)
Kappa = p1- p_e /1- p_e	**0,534**	**0,117**	**0.752**
IC 95%	(0.358-0.710)	(-0.154-0.305)	(0.579-0.926)

Results: 167 patients were included (57% women) with a mean age of 52±16 years. 42% of them had systemic autoimmune diseases, 22% spondyloarthropathies and 36% other RD. 2 had history of past active tuberculosis (TB). At the time of screening, 46.11% were treated with GC.

LTBI was diagnosed in 35 patients: 15 had both QTF and TST positive, 16 only QTF positive and 4 only TST positive. 12 from 31 QTF positive patients were treated with GC at the time of screening. 3 from 19 TST positive patients were treated with GC at the time of screening.

After LTBI screening 62 patients received biological treatment, 4 of them had both test positive, 6 only QTF positive and 2 only TST positive. 11 received LTBI treatment according to the hospital protocol (isoniazid for 6 to 9 months). 10 completed treatment, 1 did not because of intolerance and did not receive other treatment. 1 patient with only TST positive was considered a false positive and did not receive treatment. During follow-up no TB reactivation was reported.

23 patients with LBTI received treatment other than biological therapy during follow-up, of them 8 received LBTI treatment. There was no TB reactivation during follow up.

The Kappa concordance between QTF and TST was estimated: moderated in the whole sample, poor in the patients treated with GC at screening, and substantial when the patients treated with GC at screening were excluded. Results are shown in Table 1.

Conclusion: QTF seems to be the most appropriate LTBI screening test in patients with RD treated with GC. Screening and treatment of LTBI in patients with RD treated with or without biological agents was effective in reducing TB reactivation.

Disclosure: C. Pavez Perales, None; **A. Quiles Rocher**, None; **E. Grau Garcia**, None; **M. De la Rubia Navarro**, None; **S. Leal Rodriguez**, None; **R. Gonzalez Mazario**, None; **J. Fragio Gil**, None; **C. Alcañiz Escandell**, None; **J. Ivorra Cortes**, None; **I. Chalmeta Verdejo**, None; **L. Gonzalez Puig**, None; **I. Martinez Cordellat**, None; **R. Negueroles Albuixech**, None; **J. Oller Rodriguez**, None; **F. Ortiz Sanjuan**, None; **E. Vicens Bernabeu**, None; **C. Najera Herranz**, None; **I. Canovas Olmos**, None; **J. Roman Ivorra**, None.

Abstract Number: 0101

Romosozumab After Denosumab Improves Lumbar Spine and Maintains Total Hip Bone Mineral Density in Postmenopausal Women with Low Bone Mass

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Osteoporosis & Metabolic Bone Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Romosozumab, an anti-sclerostin antibody that increases bone formation while decreasing bone resorption, reduces fracture risk within 12 months. Here we evaluate the effects of transitioning from denosumab to romosozumab in treatment-naïve patients.

Methods: This phase 2 trial (NCT00896532) enrolled postmenopausal women with a lumbar spine, total hip, or femoral neck T-score ≤ –2.0 and ≥ –3.5. Patients were randomized to placebo or various doses of romosozumab monthly or every 3 months from baseline to month (M) 24, were rerandomized to 12 months of denosumab 60 mg every 6

Treatment from M0–24: Treatment from M24–36: Treatment from M36–48:	Placebo Placebo Romosozumab 210 mg QM N = 12	Placebo Denosumab 60 mg Q6M Romosozumab 210 mg QM N = 16
Bone Mineral Density, mean % change (95% CI)		
Lumbar spine		
M0–24	2.7 (0.2, 5.1)	−0.8 (−2.8, 1.1)
M24–36	−0.4 (−2.1, 1.4)	5.5 (3.6, 7.4)
M36–48	9.1 (6.1, 12.1)	5.3 (3.2, 7.4)
M24–48	8.9 (5.5, 12.4)	11.5 (8.8, 14.3)
Total hip		
M0–24	−2.2 (−3.6, −0.8)	−1.6 (−2.7, −0.5)
M24–36	−0.3 (−1.4, 0.8)	2.8 (2.1, 3.6)
M36–48	4.6 (2.7, 6.4)	0.9 (−0.1, 1.8)
M24–48	4.7 (2.7, 6.7)	3.8 (2.6, 5.0)
Bone Turnover Marker, median (Q1, Q3)		
P1NP, µg/L		
M0	37.0 (33.8, 41.0)	52.6 (44.9, 59.2)
M24	38.2 (30.0, 55.6)	50.0 (40.0, 56.0)
M36	35.9 (30.3, 55.5)	17.4 (11.2, 21.4)
M39	49.5 (36.3, 79.9)	43.1 (31.6, 55.6)
M48	36.2 (29.2, 48.2)	64.6 (54.2, 72.5)
β-CTX, ng/L		
M0	372.0 (306.0, 415.5)	503.5 (392.5, 635.5)
M24	534.0 (433.5, 692.0)	626.0 (466.0, 833.0)
M36	376.0 (305.0, 533.5)	162.5 (95.5, 268.0)
M39	348.0 (282.0, 438.5)	311.0 (239.0, 385.0)
M48	321.0 (276.5, 407.0)	532.0 (378.0, 661.0)

β-CTX = β-isomer of the C-terminal telopeptide of type I collagen, CI = confidence interval, M = month, P1NP = procollagen type 1 N-terminal propeptide, Q1 = quartile 1, Q3 = quartile 3, QM = monthly, Q6M = every 6 months.

Table

months or placebo (M24–36), and then all were to receive romosozumab 210 mg monthly for 12 months (M36–48). Results for the overall population have been previously published (McClung et al, J Bone Miner Res 2018; Kendler et al, Osteoporos Int 2019). Here we present data from a subset of patients who were randomized to placebo for 24 months, denosumab (n = 16) or placebo (n = 12) for 12 months, and then romosozumab for 12 months.

Results: In patients who were randomized to placebo followed by denosumab, romosozumab treatment for 12 months maintained BMD gained during denosumab treatment at the total hip (mean change from end of denosumab treatment, 0.9%) and further increased BMD gains at the lumbar spine (mean change from end of denosumab treatment, 5.3%) (Table). As expected, P1NP and CTX levels decreased with denosumab. Upon transition to romosozumab (M36–48), P1NP levels initially increased and gradually returned to baseline by M48 while CTX gradually increased to baseline levels.

In patients who transitioned to romosozumab after 36 months of placebo, BMD increased at the lumbar spine and total hip (Table). P1NP levels initially increased with romosozumab and gradually returned to baseline by M48 while median CTX level remained below baseline with romosozumab treatment.

Conclusion: BMD response in the placebo to romosozumab group was similar to that observed in other studies. Transitioning to romosozumab after 12 months of denosumab further improves lumbar spine BMD and maintains total hip BMD.

Disclosure: M. McClung, Amgen Inc., 1, 2, Myovant, 1; **M. Bolognese**, Amgen Inc., 1, 2; **J. Brown**, Mereo Biopharma, 1, Servier, 1, 2, Amgen Inc., 1, 2, Orimed, 1, Janssen, 1; **J. Reginster**, None; **B. Langdahl**, Amgen Inc., 1, 2, 3, Novo Nordisk, 1, UCB, 1, 2, Eli Lilly, 1, Gedeon-Richter, 1, Gilead, 1; **N. Ruiz-Santiago**, Amgen Inc., 1, 2; **Y. Shi**, Amgen Inc., 1, 2; **M. Rojeski**, Amgen Inc., 1, 2; **J. Timoshanko**, UCB Pharma, 1, 2; **C. Libanati**, UCB Pharma, 1, 2; **H. Kassahun**, Amgen Inc., 1, 2; **M. Oates**, Amgen Inc., 1, 2.

Abstract Number: 0102

Bone Health in Patients with Psoriatic Arthritis in the National Swiss Cohort: A Cross-sectional Study

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: There is much controversy surrounding the loss of bone mass in patients with psoriasis arthritis (PsA). We wanted to evaluate the prevalence of osteoporosis (OP) and fracture in patients with PsA in the Swiss Clinical Quality Management (SCQM) cohort, a large national database of patients with inflammatory arthritis; to study different factors influencing bone health and the correlation between disease activity, treatment and occurrence of densitometric osteoporosis or fracture.

Methods: We analyzed all PsA-patients included in the cohort from 2006 to April 2019. We evaluated demographic and clinical data: age, gender, BMI, disease duration, smoking/alcohol habits, patient's and physician's global as-

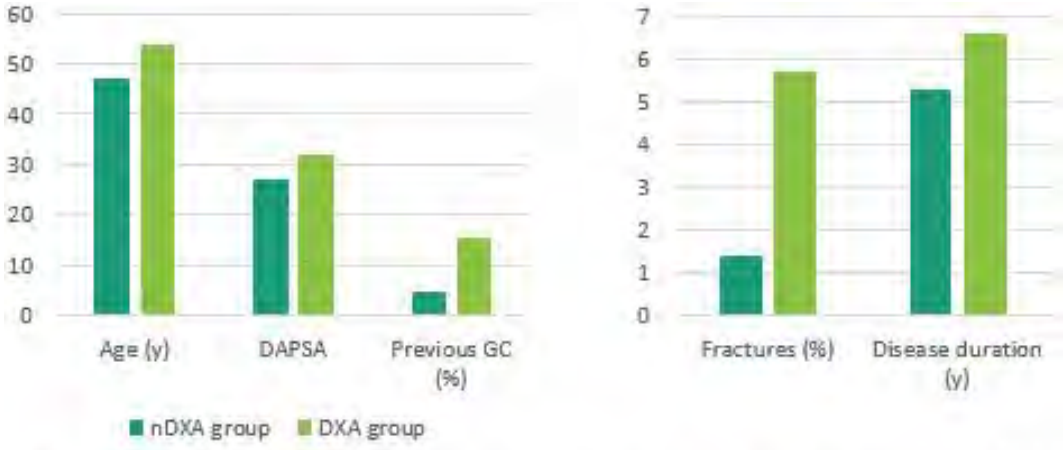

Figure 1: *Significant differences between patients with vs without DXA*

	NO OSTEOPOROSIS N=244	OSTEOPOROSIS N=51	P value
Age (years)	55 ± 9	59 ± 12	0,009*
Female (%)	67,6	68,6	0,89
Disease duration (years)	6,3 ± 8	7,7 ± 9,9	0,339
Body mass index	26,6 ± 5	22,7 ± 4,8	0,0001*
Smoking (%)	19,9	29	0.69
Alcohol consomption(%)	77,2	68,6	0,37
HAQ	0,7 ± 0,5	0,9 ± 0,7	0,03*
PGA	3,8 ± 2,2	4,1 ± 2,5	0,329
ESR (mm/1h)	16,6 ± 16,7	20,8 ± 20,9	0,2
CRP (mg/L)	9,1 ± 12,8	16,9 ± 36,2	0,001*
DAS28-ESR score	3,2 ± 1,4	3,6 ± 1,3	0,08
DAS28-CRP score	3,1 ± 1,2	3,4 ± 0,9	0,04*
DAPSA score	29,6 ± 23,6	37,8 ± 43,5	0,04*
Fracture history (%)	2	3,9	0,4
TNF inhibitors (%)	35,7	25,5	0,16
Prednisone (%)	15,2	13,7	0,069

Table 1: *Characteristics of DXA patient with and without OP. HAQ: health assessment questionnaire; PGA: Physician global assessment; *: significant.*

sessment, joint count, HAQ, medication and inflammatory activity measured by ESR, CRP, DAS 28 and DAPSA score. We compared patients with BMD measurement (DXA) with the group without DXA (nDXA). In DXA group we analyzed patients according to osteoporotic status and did subgroup analysis in premenopausal, menopausal women and men. We used STATA program vs 16, chi2-test, student's t-test and simple and multiple regression models for statistics. Statistical significance was set up at $p < 0.05$.

Results: Of the 2443 patients, 545 had a DXA. The age of scanned patients was 18-84 years. Only 295 BMD data were available for analysis. DXA patients were 6.4 years older (54.2±11,1 vs 47.8±12.4 years, p< 0.001), and were more female (67% vs 43%). Duration of the disease was longer (6.6±8.3 vs 5.3±7.1 y, p< 0.001) in the DXA group. DAS28-CRP and DAS28-ESR were higher in DXA group (3,1 ± 1,2 vs 2,9 ± 1,1, p< 0,04 and 3,2 ± 1,4 vs 3 ± 1,3, p< 0,002, respectively), as was the DAPSA score (32 ± 30 vs 27 ± 20 p< 0.04). Patients in DXA group were more exposed to prednisone and conventional DMARDs (15.4% vs 4.7%, p< 0.001 and 51.7% vs 43%, p< 0.01 respectively). There were more fractures in the DXA- than in nDXA-group (5.7% vs 1.4%, P< 0.001) (Figure 1).

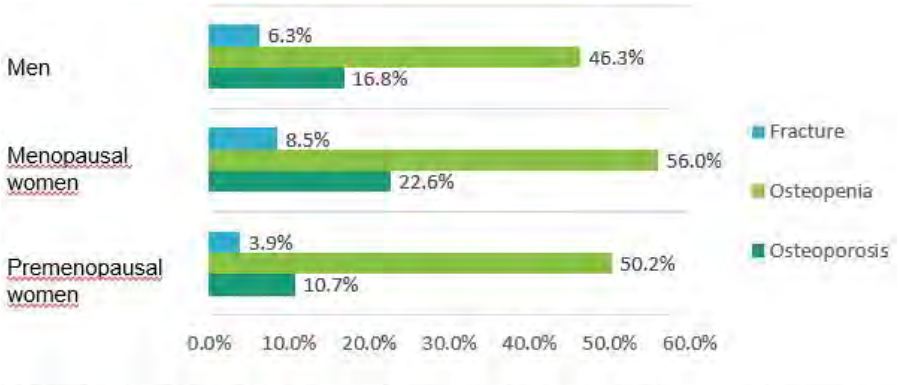

Figure 2: *Prevalence of fractures, osteopenia and osteoporosis in patient subgroups.*

In the DXA group 18.4% patients had OP and 50.2% osteopenia. Patient characteristics are shown in Table 1. We confirmed a positive correlation between femoral and lumbar T-score and BMI, and negative correlation between age and femoral T-score. Disease duration was inversely correlated with femoral, but not lumbar T-score. Interestingly, other variables, including disease activity, showed no correlation with T-score, but OP patients had higher disease activity.

Subgroup analysis (Figure 2) showed higher OP prevalence in postmenopausal women (22,6%) vs in men (16.8%) or premenopausal women (10.7%) in concordance with the fracture rate (8.3% vs 6.3% vs 3.9%). T-score was lower and the disease activity was higher in postmenopausal women compared to the others groups.

Conclusion: Our data suggest that Swiss clinician are aware of risk of poor bone-health in PsA patients and perform DXA in this population even in younger patients and in men. Interestingly, we describe that the patients with OP had higher disease activity and poorer functional status than patients without OP.

Longitudinal studies are needed to evaluate bone quality, fractures, and relationship between bone health in PsA and disease associated factors. They should integrate parameters of bone turnover and use an appropriate control group.

Disclosure: D. Dan, None; **Y. Ibrahimy**, None; **B. Aubry-Rozier**, None; **D. Aeberli**, None.

Abstract Number: 0103

The Association of Methotrexate, Sulfasalazine and Hydroxychloroquine Use with Incident Fractures in Postmenopausal Women with Rheumatoid Arthritis: Findings from the Women's Health Initiative

Rachel Elam[1], Sandeepkumar Gupta[2], Omar Tolaymat[2], Sowmya Vasan[3], Carolyn Crandall[4], Jean Wactawski-Wende[5], Karen Johnson[6] and Laura Carbone[2], [1]Augusta University, Evans, GA, [2]Augusta University, Augusta, GA, [3]WHI, Seattle, WA, [4]UCLA, Los Angeles, CA, [5]University of Buffalo, Buffalo, NY, [6]University of Tennessee Health Sciences Center, Memphis, TN

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: This study was conducted to evaluate the extent to which disease modifying antirheumatic medications (DMARDs) used as part of triple therapy for treatment of rheumatoid arthritis (RA) including methotrexate, sulfasalazine and hydroxychloroquine are associated with incident fractures in postmenopausal women with RA.

Methods: Of the 161,808 postmenopausal women who were enrolled in the Women's Health Initiative (WHI), all who self-reported at baseline a history of RA and had either a DMARD and/or a biologic use or presence of anti-cyclic citrullinated peptide (Anti-CCP) antibody were included as RA patients. There were too few users of standard triple therapy (methotrexate, sulfasalazine and hydroxychloroquine use (n=9)) to determine the association of standard triple therapy use with incident fractures. Therefore, incident fractures in postmenopausal women with RA following use of methotrexate, sulfasalazine and/or hydroxychloroquine alone or as "combination therapy" (methotrexate and sulfasalazine or methotrexate and hydroxychloroquine) were estimated by Cox proportional hazards models using hazard ratios (HR) and 95% confidence intervals (CI) after consideration of potential confounders.

Results: here were 1,201 postmenopausal women with RA enrolled in WHI included in these analyses, of which 74% were Caucasian, 17% were African American and 9% were of other or unknown race/ethnicity. Of the postmenopausal women with RA, 421 (35%) had not used either methotrexate, sulfasalazine or hydroxychloroquine while 519 (43%) had used methotrexate, 83 (7%) sulfasalazine and 363 (30%) hydroxychloroquine at some time during study follow-up. Over a median length of 6.46 years of follow-up, in multivariable adjusted models, no statistically significant association was found between methotrexate (HR 1.1 [95% CI 0.8-1.6]), sulfasalazine (HR 0.6 [95% CI 0.2-1.5]) or hydroxychloroquine use (HR 1.0 [95% CI 0.7-1.5]) and incident fractures or between combination therapy with methotrexate and sulfasalazine or methotrexate and hydroxychloroquine use (HR 0.9 [95% CI 0.5-1.6]) and incident fractures.

Conclusion: In conclusion, use of methotrexate, sulfasalazine or hydroxychloroquine alone or in combination is not associated with incident fractures in postmenopausal women with RA. Postmenopausal women with RA receiving any component of triple therapy should not be expected to have any substantial reduction in fracture risk from use of these medications.

Disclosure: R. Elam, None; **S. Gupta**, None; **O. Tolaymat**, None; **S. Vasan**, None; **C. Crandall**, None; **J. Wactawski-Wende**, None; **K. Johnson**, None; **L. Carbone**, None.

Abstract Number: 0104

Bone Effects of One-year Tofacitinib Treatment in Rheumatoid Arthritis

Attila Hamar[1], Anita Pusztai[2], Edit Végh[1], Ágnes Horváth[1], Katalin Gulyás[1], Szilvia Szamosi[1], Zsófia Pethő[1], Nóra Bodnár[1], Boglárka Soós[1], Monika Czókolyová[1], Sándor Szántó[1], Gabriella Szűcs[1], Harjit Bhattoa[1], Gábor Nagy[1], Gábor Tajti[1], Andrea Domján[1], Katalin Hodosi[1] and **Zoltán Szekanecz**[1], [1]University of Debrecen, Debrecen, Hungary, [2]University of Debrecen Faculty of Medicine, Department of Rheumatology, Debrecen, Hungary

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Oral JAK inhibitor, tofacitinib appeared as a new therapeutic option, beside biological therapies, which has already proven its safety and effectivity in RA, but we lack of knowledge how it affects density of bone

structures and bone turnover markers. The aim of this study was to assess the effects of one-year tofacitinib therapy on bone metabolism in patients with RA.

Methods: Altogether 30 RA patients with active disease were recruited and treated with tofacitinib in this 12-months follow-up study. Mean age of patients were 52.8±10.0 years, duration of rheumatoid arthritis were 7.7±5.0 years. Half of the patients haven't received biological treatment prior tofacitinib therapy, other half of the patients switched to tofacitinib therapy after completing washout. 15 patients received 2x5mg and 15 patients received 2x10mg tofacitinib daily for 12 months. On both arms 2-2 patients have discontinued treatment and excluded from the study. Assessments were performed at baseline, month 6 and 12. Levels of CRP and IgM rheumatoid factor (RF) antibodies were measured by quantitaive nephelometry and levels of anti-CCP, sclerostin, osteocalcin (OC), P1NP were assesed by ELISA. Bone density was assesed by DXA (dual-energy X-ray absorptiometry, Lunar) and pQCT imaging techniques. Levels of DKK-1, OPG, RANKL were measured by multiplex microbead immunoassay (BioLegend LEGENDplex). In addition, disease activity (DAS28), age and disease duration were also measured. Correlations were determined by Spearman's analysis. Univariate and multiple regression analysis using the stepwise method was applied to investigate independent associations between DXA measurements (dependent variables) and laboratory parameters (independent variables).

Results: Tofacitinib significantly reduced DAS28 ($p< 0.001$) and HAQ values ($p=0.001$), also level of CRP ($p< 0.001$) and We ($p=0.014$). With respect to bone biomarkers we have experienced significant increase in levels of OC ($p=0.013$), OPG ($p=0.006$), sclerostin ($p=0.026$) and vitamin-D ($p=0.017$) at month 6, also in levels of OPG and vitamin-D ($p=0.004$, $p=0.003$) at month 12. We have found decrease in levels of CTX at month 6 ($p=0.009$) and 12 ($p=0.003$). When we examined the groups separately, we've found significant increase in levels of P1NP ($p=0.027$, $p=0.005$), OPG ($p=0.005$, $p=0.002$) and vitamin-D ($p=0.001$, $p=0.004$) at month 6 and 12, also in OC at month 6 ($p=0.027$) in Group A (2x5mg). In Group B (2x10mg) we've experienced a significant decrease in levels of phosphate and CTX at month 6 and 12 ($p=0.012$, $p=0.021$, and $p=0.005$, $p=0.007$).

Conclusion: One year tofacitinib treatment effectively stabilized bone density in patients with rheumatoid arthritis, and led to the increase of bone turnover markers, which is beneficial for ossification in long term.

Disclosure: A. Hamar, None; **A. Pusztai**, None; **E. Végh**, None; **Á. Horváth**, None; **K. Gulyás**, None; **S. Szamosi**, None; **Z. Pethő**, None; **N. Bodnár**, None; **B. Soós**, None; **M. Czókolyová**, None; **S. Szántó**, None; **G. Szűcs**, None; **H. Bhattoa**, None; **G. Nagy**, None; **G. Tajti**, None; **A. Domján**, None; **K. Hodosi**, None; **Z. Szekanecz**, Pfizer, 1.

Abstract Number: 0105

Use of Peripheral Quantitative Computed Tomography in the Assessment of Bone Mineral Density in Anti-TNF-treated Rheumatoid Arthritis and Ankylosing Spondylitis Patients

Balázs Juhász[1], Katalin Gulyás[1], Ágnes Horváth[1], Edit Végh[1], Anita Pusztai[2], Ágnes Szentpétery[3], Zsófia Pethő[1], Nóra Bodnár[1], Attila Hamar[1], Levente Bodoki[1], Harjit Bhattoa[1], Éva Szekanecz[1], Katalin Hodosi[1], Andrea Domján[1], Szilvia Szamosi[1], Csaba Horváth[4], Sándor Szántó[1], Gabriella Szűcs[1], Hennie Raterman[5], Oliver FitzGerald[6] and **Zoltán Szekanecz**[1], [1]University of Debrecen, Debrecen, Hungary, [2]University of Debrecen Faculty of Medicine, Department of Rheumatology, Debrecen, Hungary, [3]Uppsala University Hospital, Uppsala, Sweden, [4]Semmelweis University, Budapest, Hungary, [5]Northwest Clinics, Alkmaar, Netherlands, [6]Conway Institute for Biomolecular Research, University College Dublin, Dublin, Ireland

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) have both been associated with generalized and localized bone loss. Inflammatory cytokines like tumor necrosis factor (TNF) have been implicated in bone resorption and, therefore, anti-TNF biologics may improve bone status. There have been very few observational or longitudinal data on the use of peripheral quantitative computed tomography (QCT) for determining changes in bone status in anti-TNF-treated RA and AS patients. Therefore, we assessed volumetric bone mineral density (BMD) by forearm QCT in conjunction with disease activity, dual-energy X-ray absorptiometry (DXA) and bone biomarker parameters in a mixed cohort of RA and AS patients.

Methods: ifty-three consecutive patients including 36 RA patients treated with etanercept (ETN) or certolizumab pegol (CZP) and 17 AS patients treated with ETN were included in a 12-month follow-up study. Volumetric (3-dimensional) and areal (2-dimensional) BMD were determined by peripheral QCT and DXA, respectively. Bone biomarkers, such as calcium, phosphate, PTH, osteocalcin, soluble RANKL, vitamin D3, P1NP, CTX, sclerostin, DKK-1 and cathepsin K (CATHK) were assessed by ELISA. DAS28 and BASDAI served as markers of disease activity in RA and AS, respectively. Determinants of volumetric BMD were investigated by uni- and multivariable regression analyses, as well as RM-ANOVA.

Results: One-year ETN or CZP therapy arrested further progression of bone loss in the radius in RA and AS as determined by peripheral QCT. Volumetric (QCT) and areal (DXA) BMD showed significant, variable correlations with each other ($p< 0.05$). The univariable analysis showed that total QCT BMD after 12 months was inversely determined by disease activity at baseline ($p=0.030$). Cortical BMD was negatively determined by baseline disease activity ($p=0.005$), as well as baseline ($p=0.025$) and 12-month CATHK levels ($p=0.033$). The negative associations of 12-month total ($p=0.030$) and cortical BMD ($p=0.012$) with baseline disease activity was also confirmed by multivariable analysis. The change in QCT trabecular BMD between baseline and 12 months was related to the anti-TNF treatment together with higher baseline vitamin D3 levels (VITD3-0) ($p=0.031$). In addition, TNF inhibition and lower cathepsin K determined cortical BMD changes over the one-year period ($p=0.006$).

Conclusion: QCT may be a suiTable methodology to measure volumetric BMD in various compartments (trabecular and cortical) of the radius. QCT confirmed that biologics may arrest generalized bone loss. Moreover, we identified baseline parameters, such as disease activity, CATHK and possibly VITD3 that may predict the effects of one-year anti-TNF treatment on volumetric BMD changes over time.

Disclosure: B. Juhász, None; **K. Gulyás**, None; **Á. Horváth**, None; **E. Végh**, None; **A. Pusztai**, None; **Á. Szentpétery**, None; **Z. Pethő**, None; **N. Bodnár**, None; **A. Hamar**, None; **L. Bodoki**, None; **H. Bhattoa**, None; **Z. Szekanecz**, None; **K. Hodosi**, None; **A. Domján**, None; **S. Szamosi**, None; **C. Horváth**, None; **S. Szántó**, None; **G. Szűcs**, None; **H. Raterman**, None; **O. FitzGerald**, AbbVie Inc., 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Janssen, 2, 5, Eli Llilly, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **Z. Szekanecz**, Pfizer, 1.

Abstract Number: 0106

A Machine Learning-derived Radiomics Nomogram for Diagnosis of Osteoporosis and Osteopenia

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Osteoporosis & Metabolic Bone Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To discriminate osteoporosis and osteopenia using a quantitative computed tomography (QCT) radiomics signatures and clinical variables.

Methods: This retrospective study enrolled 635 patients with QCT images and clinical characteristics from November 2016 to November 2019. 851 radiomics features extracted from the QCT images of the third lumbar vertebra of each patients. Minimum redundancy and maximum relevance (mRMR) and least absolute shrinkage and selection operator (LASSO) were used for features selection. A radiomic nomogram was constructed based on the radiomics signatures and clinical characteristics for diagnosing osteoporosis and osteopenia. We systematically evaluated the diagnostic performance of the combined radiomics model, clinical model and radiomics model. Moreover, we investigated the value of the radiomics score in normal group and abnormal group.

Results: A total of 6 optimal radiomics features were selected to construct quantitative computed tomography (QCT) based signatures. The individualized nomogram included these features and 3 clinical characteristics (age, alkaline phosphatase, homocysteine) achieved good discrimination performance in both the training cohort (N=414; area under the curve (AUC) 0.96, 95% CI 0.95–0.98) and the validation cohort (N=176; AUC 0.96, 95% CI 0.92–1.00). The alone radiomics score also demonstrated significant differences in osteoporosis and osteopenia ($P < 0.001$).

Conclusion: This study presents a radiomics nomogram that incorporates the radiomics score and clinical risk factors, which can serve as a reliable and powerful tool for discriminating osteoporosis and osteopenia.

Disclosure: Q. Xie, None; **Y. Chen**, None; **Y. Hu**, None; **F. Zeng**, None; **P. Wang**, None; **L. Xu**, None; **J. Wu**, None; **J. Li**, None; **J. Zhu**, None; **M. Xiang**, None; **F. Zeng**, None.

Abstract Number: 0107

Effects of Abaloparatide on Modeling and Remodeling Based Bone Formation

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

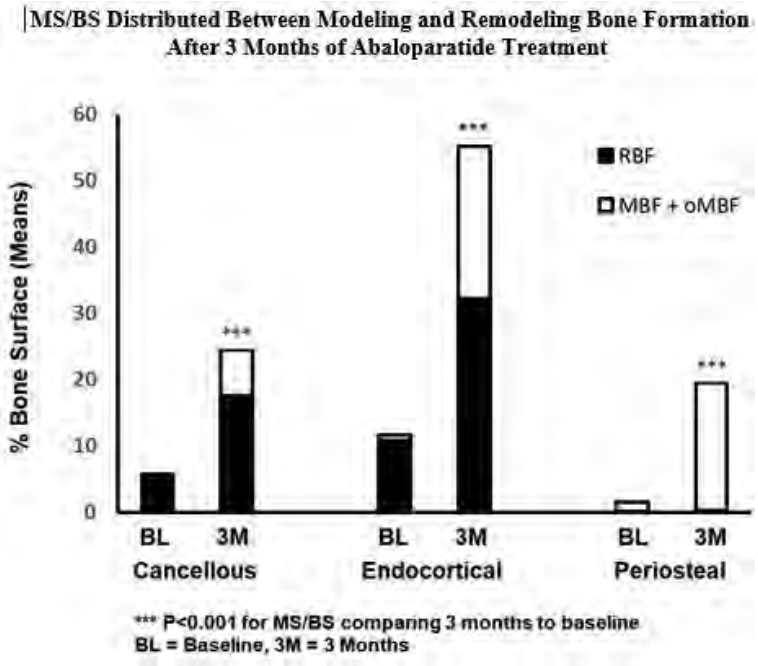
Session Title: Osteoporosis & Metabolic Bone Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate abaloparatide-induced changes in the bone formation indices of mineralizing surface (MS), bone formation rate (BFR) and mineral apposition rate (MAR); and to assess the effect of abaloparatide on 3 types of bone formation: modeling-based formation (MBF), remodeling-based formation (RBF), and overflow MBF (oMBF) in transiliac bone biopsies.

Methods: Twenty-three postmenopausal women with osteoporosis were enrolled at 4 centers in the US; all received open label abaloparatide (80 µg/day SC) for 3 months in this phase 3 study. Subjects were administered double fluorochrome labeling at baseline and prior to biopsy at 3 months. Bone formation indices were evaluated by histomorphometry. Changes at 3 months from baseline were assessed for the indices on cancellous, endocortical, intracortical and periosteal bone envelopes. Sites of bone formation were designated as MBF if the underlying cement line was



Figure

smooth, RBF if scalloped, and oMBF if formed over smooth cement lines adjacent to scalloped reversal lines. Paired t-tests were used to compare the differences of the indices between baseline and 3 months in the 4 bone envelopes.

Results: Bone biopsies were obtained from 19 of the 23 subjects were enrolled in the study; all biopsies were evaluable. After 3 months of abaloparatide treatment, MS/ BS increased significantly from baseline in all of the 4 bone envelopes ($p < 0.001$), BFR/BS increased significantly in cancellous, endocortical and intracortical envelopes ($p < 0.001$); no significant change was observed in MAR in the 4 bone envelopes. Consistent with MS/BS, RBF/BS, MBF/BS and oMBF/BS increased significantly from baseline in the cancellous and endocortical envelopes ($p < 0.001$), as did MBF/BS in the periosteum ($p < 0.001$).

Conclusion: This study provides histomorphometric evidence that abaloparatide has a robust effect on bone formation in postmenopausal women with osteoporosis after 3 months of treatment. Both modeling- and remodeling-based bone formation were stimulated. This study also shows that abaloparatide has a favorable effect on cortical bone by increasing bone formation in endocortical and periosteal envelopes.

Disclosure: D. Dempster, Radius Health, Inc., 1, 2, 3; **H. Zhou**, None; **S. Rao**, None; **C. Recknor**, None; **P. Miller**, Radius Health, Inc., 1, Amgen, 1; **B. Leder**, Amgen Inc., 1, 2, Radius, 1; **M. Annett**, Radius Health, Inc., 1, 2; **M. Ominsky**, Radius Health, Inc., 1, 2; **B. Mitlak**, Radius Health, Inc., 1, 2.

Abstract Number: 0108

The Relationship Between Body Fat Percentage and Bone Mineral Density in Rheumatoid Arthritis Patients

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SESSION INFORMATION
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Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Currently, Dual-Energy X-ray Absorptiometry (DEXA) scans are used to determine fracture risk by calculating Bone Mineral Density (BMD). It is well established that body weight is one of the strongest predictors of bone mass, but there is ongoing controversy as to whether fat mass is a better predictor of bone density. Our research set out to find out whether there is association between body fat percentage and BMD in patients with rheumatoid arthritis stratified by steroid use.

Methods: Data were used from a cohort of rheumatoid arthritis (RA) patients referred for DEXA scan to a District General Hospital between 2004 and 2010. The following were recorded: age, sex, weight, height, body mass index (BMI), BMD at L1-L4, BMD at femoral neck (left and right) and BMD at hip (left and right). Multivariate linear regression was used to identify associations between body fat percentage and BMD at L1, L2, L3, L4, right neck of femur and left neck of femur in RA patient on steroids or not. Data was adjusted for age, sex, weight, height and BMI at scan.

Results: 1,527 patients were used in the study. 79% were female and mean age was 64.3 years (SD 11.6). Mean height was 1.62 m (SD 8.57), mean weight was 71.6 kg (SD 16.4 SD) and mean BMI was 26.8 kg/cm2 (SD 5.2). The

Table 1. The Bone mineral density (BMD) of lumbar spine, hips and femoral necks

Level	Mean BMD (SD)
L1	0.10 (0.19)
L2	1.08 (0.22)
L3	1.16 (0.23)
L4	1.16 (0.24)
Left Femoral Neck	0.85 (0.15)
Left Femur Total	0.90 (0.17)
Right Femoral Neck	0.85 (0.15)
Right Femur Total	0.90 (0.17)

Table 2. The linear relationship between BMD and body fat percentage (age-, sex-, weight, height- and BMI adjusted)

Level	On steroids β (95% CI) (Body Fat Percentage)	Not on steroids β (95% CI) (Body Fat Percentage)
L1	**0.34 (0.20, 0.48)**	0.10 (-0.08, 0.29)
L2	**0.39 (0.24, 0.55)**	0.03 (-0.18, 0.25)
L3	**0.31 (0.14, 0.49)**	0.02 (-0.20, 0.25)
L4	0.13 (-0.05, 0.32)	-0.07 (-0.31, 0.16)
Left Femoral Neck	0.07 (-0.03, 0.18)	-0.00 (-0.14, 0.13)
Left Femur Total	**0.18 (0.05, 0.32)**	0.07 (-0.07, 0.22)
Right Femoral Neck	0.05 (-0.07, 0.17)	-0.06 (-0.20, 0.07)
Right Femur Total	0.11 (-0.02, 0.25)	0.04 (-0.11, 0.20)

results of BMD are presented in **Table 1**. The results of the linear regression analysis of the relationships between fat percentage and BMD at each level are presented in the **Table 2**.

Conclusion: This study identifies that fat percentage is a predictor of the bone density at L1- L3 in RA patients on steroids. This association reflects how steroids affect the bone metabolism in different regions of the skeleton as bone loss is more marked in the trabecular bone (high content in vertebrae) in patients on steroids. The fat distribution may change in patients on steroids who can develop central obesity with the lower limbs spared and even wasted. This altered fat distribution may explain the association of fat percentage and bone density at a lumbar spine level and not at neck or hip level. Our results also suggest that the Fracture Risk Assessment (FRAX) tool underestimates the risk of fracture in patients on steroids as it takes into consideration the bone density at the femoral neck and not at the lumbar spine.We suggest further research in finding better tools for assessing fracture risk in glucocorticoid-induced osteoporosis.

Disclosure: A. Madenidou, None; **M. Bukhari**, Bristol- Myers Squib, 1, UCB celltech, 1, 2, Roche, 1, 2, Abbvie, 1, 2, Merck, 1, 2, Mennarini, 1, 2, Sanofi-aventis, 1, 2, Elli-Lilly, 1, 2, Janseen, 1, Amgen, 1, 2, Novartis, 1, 2.

Abstract Number: 0109

Glucocorticoid-Induced Osteoporosis: Are We Practicing Prevention?

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Descriptive study designed to assess compliance to evidence-based practice guidelines for the prevention of Glucocorticoid-Induced Osteoporosis (GIOP).

Methods: We queried the electronic database of the Department of Veterans Affairs Hospital in New Orleans and collected data on all veterans who filled systemic glucocorticoid (GC) prescriptions during a 2-year study period (January 1, 2016 - December 31, 2017). Data was collected on GC dosage and duration of therapy - with long term GC therapy defined as continuous treatment for ≥3 months (90 days). Data was also collected on demographics, specialty of the ordering prescriber, bone mineral density (BMD) testing, prescriptions for anti-osteoporotic therapy, and prescriptions for Vitamin D and/or Calcium supplementation. The recommendations followed were in accordance with the American College of Rheumatology, American Geriatrics Society, Institute of Medicine, and National Osteoporosis Foundation guidelines.

Results: During our study period, a total of 1,962 separate GC prescriptions were filled. Of those, 1,051 unique patients were identified. A total of 206 patients were prescribed GC for ≥90 days during the study window and they comprised our study population. Patients were predominately male (97%); 51% self-identified as Caucasian, and 46% as African American. A majority (68%) of prescriptions were for less than 10mg prednisolone-equivalent doses. Most prescriptions (63% n=130) were for >7.5mg prednisolone-equivalent doses for greater than 90 days. Primary care providers were the main prescribers of long-term GC (51%, n=105), followed by rheumatologists (24%, n=49). BMD testing was performed in 20% of patients (n=42). Of those tested, 14% (n=6) were found to have osteoporosis and 21% (n=9) had osteopenia. Approximately half of our study population (52%) were prescribed Vitamin D supplementation with 80% prescribed the guideline-recommended dose. Twenty-six percent of patients were prescribed supplemental Calcium, with 44% prescribed the guideline-recommended dose. Fewer than 10% of the patients taking greater than 7.5mg for ≥3 months (and meeting ACR treatment guidelines) were on primary prophylaxis with anti-osteoporotic therapy.

Conclusion: Our findings are overall worsethan previously published data. GIOP remains an under recognized and undertreated condition despite updated evidence-based practice guidelines. Bone mineral density screening rates remain low, as do Calcium/Vitamin D supplementation and primary prophylaxis with anti-osteoporotic therapy.

Disclosure: E. Rife, None; **E. Nkechinyere**, None; **J. Leon de la Rocha**, None.

Abstract Number: 0110

Does Urate Directly Influence Bone Turnover? Randomized Controlled Trial of Inosine Supplementation

Nicola Dalbeth[1], Anne Horne[2], Borislav Mihov[1], Tony Merriman[3], Gregory Gamble[1], Lisa Stamp[4] and Ian Reid[1], [1]University of Auckland, Auckland, New Zealand, [2]The University of Auckland, Auckland, New Zealand, [3]University of Otago, Dunedin, New Zealand, [4]University of Otago Christchurch, Christchurch, New Zealand

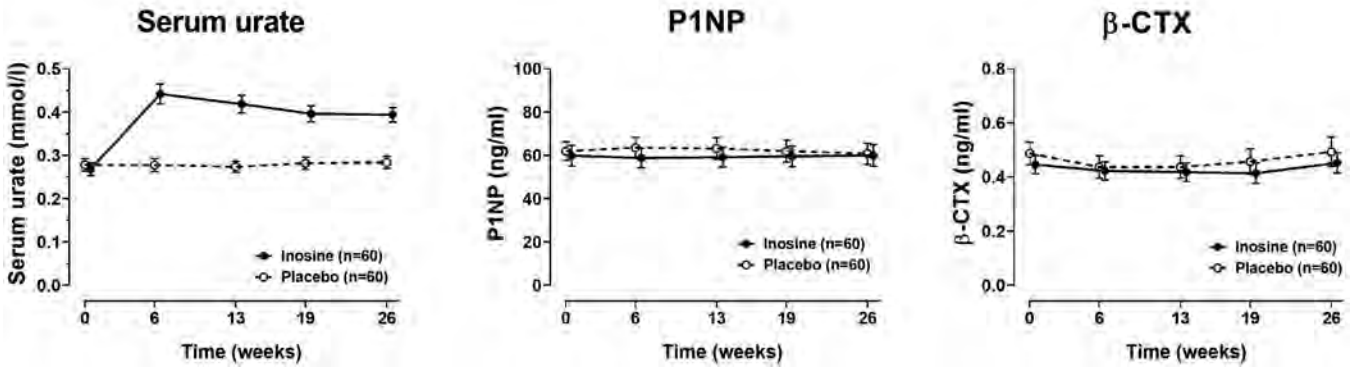
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Observational studies have reported that serum urate positively correlates with bone mineral density (BMD) and that hyperuricaemia is protective for the development of osteoporosis and risk of fragility fractures. In laboratory studies, urate has anabolic effects on bone through differential effects on osteoblast and osteoclast function. However, Mendelian randomization studies do not support a causal role for serum urate in BMD. Inosine is a purine nucleoside that increases serum urate concentrations. The aim of this study was to determine whether moderate hyperuricaemia induced by inosine supplements influences bone turnover markers over a six-month period.

Methods: Six month randomised, double-blind, placebo-controlled trial of 120 post-menopausal female participants. Key exclusion criteria were bone mineral density T-score below -2.5 at the total hip, femoral neck or lumbar spine, previous fragility fracture, bisphosphonate therapy, gout, kidney stones, and urine pH ≤5.0. Participants were randomised 1:1 to either placebo or inosine 500mg twice daily. The co-primary endpoints were change in procollagen type-I N-terminal propeptide (P1NP) and change in β-C-terminal telopeptide of type I collagen (β-CTX). Key secondary endpoints were measures of kidney function, blood pressure and other features of metabolic syndrome. Change in BMD measured by dual-energy x-ray absorptiometry was an exploratory endpoint. Data were analysed on an intention to treat basis, using a mixed models approach to repeated measures.

Results: Administration of inosine supplements led to a significant increase in serum urate over the study period (P< 0.0001 for all follow-up time-points, Figure). At week 26, the mean change in serum urate was +0.13 mmol/L (+2.2mg/dL) in the inosine group and 0.00mmol/L (0mg/dL) in the placebo group. There was no difference in P1NP or β-CTX

Figure. Serum urate, P1NP, and β-CTX over the study period. Data are presented as mean (95% CI).



between groups over the six months (false detection rate protected pairwise comparisons at each time point all P > 0.61 for P1NP and P=0.37 for β-CTX, Figure). No significant treatment by time interaction differences were observed in serum creatinine, systolic or diastolic blood pressure, body mass index, fasting lipids, or HbA1c over the study period (all P >0.13). Consistent with the bone turnover marker results, there were no significant changes in BMD between groups over the six months (P >0.48 for all sites). Adverse events and serious adverse events were similar between the two groups.

Conclusion: Although inosine supplementation leads to sustained increases in serum urate over a six month period, it does not alter markers of bone turnover. These findings do not support the concept that urate has direct biological effects on bone turnover.

Disclosure: N. Dalbeth, AstraZeneca, 1, 2, Abbvie, 1, Arthrosi, 1, Dyve BioSciences, 1, Selecta, 1, Janssen, 1; **A. Horne**, None; **B. Mihov**, None; **T. Merriman**, None; **G. Gamble**, None; **L. Stamp**, None; **I. Reid**, None.

Abstract Number: 0111

Assessment and Treatment of Glucocorticoid-Induced Osteoporosis in a Rheumatology Clinic

Amanda Stefl[1], **Shikha Singla**[2], Jessica Michaud[1], Kama Thomas[2], Lisa Rein[2] and Mary Ellen Csuka[2], [1]Froedtert Hospital, Milwaukee, WI, [2]Medical College of Wisconsin, Milwaukee, WI

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoids (GC) are used as a long-term treatment option for an estimated 1% of the US population. The American College of Rheumatology has maintained guidelines to aid in the prevention and treatment of glucocorticoid-induced osteoporosis (GIOP). These recommendations include optimization of calcium and vitamin D intake and initiation of oral bisphosphonates based on age, fracture risk, and GC dose. The purpose of this study was to evaluate whether patients at the Rheumatology Clinic of Froedtert & the Medical College of Wisconsin's Froedtert Hospital who were prescribed chronic high-dose prednisone (> 7.5mg/day for ≥ 3 months) for a rheumatologic disease underwent a comprehensive assessment for GIOP.

Methods: This was a retrospective quality improvement study of 61 patients aged 40 to 90 years who were prescribed chronic high-dose prednisone by Froedtert Hospital Rheumatology Clinic providers between January 1, 2017 and December 31, 2017. The primary outcome was the percentage of patients who had a comprehensive assessment for GIOP, defined as assessment of calcium, vitamin D, dual-energy x-ray absorptiometry (DXA), and Fracture Risk Assessment Tool (FRAX™). Secondary outcomes included the percentage of patients with osteoporotic and non-osteoporotic fractures during the follow-up period; the percentage of patients starting an osteoporosis medication during the follow-up period; new osteopenia or osteoporosis diagnosis during the follow-up period; assessment of calcium, vitamin D, DXA and FRAX as individual measures; presence of calcium supplementation on the medication list; and appropriate vitamin D treatment.

Results: A comprehensive GIOP assessment including calcium, vitamin D, DXA imaging, and FRAX calculation was completed in 7% of the study population. Approximately 21% of patients had 0 factors assessed, 39% had one fac-

tor assessed, 16% had two factors assessed, and 16% had three factors assessed. The lowest rates were with FRAX calculation at 11% and DXA imaging at 26%. During the follow-up period, 8% of patients developed a new fracture, 8.5% were diagnosed with osteopenia or osteoporosis, and 14.9% were started on a new osteoporosis medication. The statistically significant results within the subgroup analyses included a higher rate of: calcium supplementation on the medication list (79% vs 32%, p=0.004) in patients with baseline diagnosis of osteoporosis; number of individual components of GIOP assessment completed (p=0.049) and DXA (33% vs 0%, p=0.026) in patients ≥ 50 years of age; comprehensive GIOP assessment (25% vs 2%, p=0.022), number of individual components (p=0.003), and FRAX (42% vs 4%, p=0.002) in patients who met with rheumatology clinic pharmacist; and number of individual components (p< 0.001), calcium assessment (77% vs 44%, p=0.016), and vitamin D level assessment (77% vs 41%, p=0.008) in patients taking very high-dose prednisone.

Conclusion: A comprehensive GIOP assessment was not routinely completed when patients were initiated on a high-dose GC. When evaluating the individual components of the assessment, DXA and FRAX were not completed as regularly as calcium and vitamin D assessments.

Disclosure: A. Stefl, None; **S. Singla**, None; **J. Michaud**, None; **K. Thomas**, None; **L. Rein**, None; **M. Csuka**, None.

Abstract Number: 0112

Description of Risk Factors at Baseline and Need of Bone Agent According to Hadji Recommendations in Patients Taking Aromatase Inhibitors as Breast Cancer Therapy

David Montero-Seisdedos[1], Oihane Ibarguengoitia-Barrena[2], Lucía Vega-Álvarez[2], Carmen Lucía García Gomez[2], Itziar Calvo-Zorrilla[3], Juan M. Blanco-Madrigal[2], Maria Esther Ruiz-Lucea[2], María Luz García-Vivar[2], Eva Galindez-Agirregoikoa[2], Ana R. Inchaurbe-Pellejero[2], Olaia Fernandez-Berrizbeitia[2], Clara E. Perez-Velasquez[2], Eduardo Cuende-Quintana[4], Amaia Bilbao-González[3] and Iñaki Torre-Salaberri[3], [1]Basurto University Hospital, Bilbao, Pais Vasco, Spain, [2]Basurto University Hospital, Bilbao, Spain, [3]University Hospital of Basurto, Bilbao, Pais Vasco, Spain, [4]Basurto University Hospital, Madrid, Spain

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: A well-known adverse effect of aromatase inhibitors (AI) in the bone is the loss of mineral density with the consequent increased risk of fracture (fx).

A widely used algorithm for the management of bone agent treatment in patients taking AI is that of Hadji from 2011. Depending on the risk factors and densitometric values, patients would or would not be subsidiaries of receiving such treatment.

Methods: Retrospective cross-sectional study of 200 patients collected in the period between 2014 and 2019 on the monographic consultation of osteoporosis, referred by Medical Oncology to assess the risk of fracture at the start of AI treatment after being diagnosed with breast cancer. BMD and clinical risk factors for fractures are included, based on the 2011 Hadji algorithm, what percentage of patients required treatment with bone agents during follow-up.

Results: The average age of our sample is 64.8 years with a SD of 9.5 and a median of 64.5 (Q1 58 and Q3 72). Regarding the treatment, 56 patients (28%) took Anastrozole, 122 (61%) Letrozole and 22 (11%) Exemestane. The risk factors are: 28 patients (14%) were active smokers and 35 (17.5%) ex-smokers; 11 (5.5%) recognized daily alcohol intake at significant doses. 42 women (21%) had previous fx, of which 15 (35.71%) were on the wrist, 8 (19.05%) vertebral, 2 (4.76%) on the shoulder and 1 (2.38%) on the hip. 44 women (22%) recognized habitual falls and 15 (7.5%) had familiar history of hip fx. There were no patients on chronic steroid treatment and 9 (4.5%) had osteoporosis secondary to a chronic disease. The DXA at the baseline visit showed OP in 64 patients (32%), osteopenia in 108 (54%) and normality in the other 28 (14%). In the blood tests, all women except 1 had normal phospho-calcium levels. Regarding VitD, 13 patients (6.67%) had values < 10 ng/mL, 50 (25.64%) from 10 to 20, 68 (34.87%) from 20 to 30, and the remaining 64 (32.82%) over 30 ng/mL. PTHi levels were high in 15 women (7.69%) and the CTX was elevated in 34 (17.53%). Monitoring data is collected with the following interest: 12 patients (6%) suffer a new fx during AI treatment, 58% vertebral, 25% wrist, and 16% in other locations. 121 women in our sample (60.5%) received treatment for OP according to Hadji's protocol, 92 (76.03%) of them alendronate, 7 (5.79%) risedronate, 18 (14.88%) denosumab, and the remaining 4 (3.3%) zoledronate and ibandronate in equal proportion (1.65%).

Conclusion: 60.5% of the patients in our series required a bone agent based on the Hadji combining risk factors and BMD values. Highlight that only 30% of patients presented osteoporosis values in DXA at the initial assessment and that 21% had previous fractures, the most on the wrist. We consider the systematic assessment of the risk of fracture presented by patients with breast cancer who begin treatment with AI, assessing the need to prescribe bone agents using an algorithm as practical as that of Hadji.

Disclosure: D. Montero-Seisdedos, None; **O. Ibarguengoitia-Barrena**, None; **L. Vega-Álvarez**, None; **C. García Gomez**, None; **I. Calvo-Zorrilla**, None; **J. Blanco-Madrigal**, None; **M. Ruiz-Lucea**, None; **M. García-Vivar**, None; **E. Galindez-Agirregoikoa**, None; **A. Inchaurbe-Pellejero**, None; **O. Fernandez-Berrizbeitia**, None; **C. Perez-Velasquez**, None; **E. Cuende-Quintana**, None; **A. Bilbao-González**, None; **I. Torre-Salaberri**, None.

Abstract Number: 0113

Improving Glucocorticoid-Induced Osteoporosis Screening and Management in Patients with Rheumatic Diseases Using the 2017 ACR Guidelines

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoid-induced osteoporosis (GIOP) is a potentially prevenTable complication in those who are maintained on glucocorticoid (GC) therapy. It is imperative to identify these patients and initiate osteoporosis (OP) therapy to outweigh the potential harm from GC continuation. As per the ACR guidelines, those on ≥2.5mg/day of GC for ≥90 days should have baseline DEXA at initiation of GC therapy as well as repeat screening every 2-3 years if continued on GC. For those on >7.5mg/day of GC, the FRAX score should be increased by 1.15 for major osteoporotic fracture and 1.2 for hip fracture. Those identified as moderate to high risk or on ≥30mg/day of

GC with a cumulative dose of >5gm should be started on OP therapy. We aim to raise awareness of the 2017 ACR guidelines to increase appropriate screening and OP therapy initiation.

Methods: Retrospective chart review of 2,665 patients at 3 outpatient specialty clinics affiliated with the University of South Florida (James A. Haley VA, Tampa General Hospital Health Park, USF Morsani) between April 2018 and November 2019 was performed for baseline data. Included were those age ≥40 on ≥2.5mg for ≥90 days of GC (n=385). Excluded were those age < 40, on < 2.5mg/day of GC, on < 90 days of GC, or whose GC was not prescribed by our rheumatology group. Intervention consisted of educating our providers and having pre-visit chart reviews to identify patients at risk based on the ACR guidelines. Post-intervention, retrospective chart review of 925 patients was performed between November 2019 and April 2020. Of these, 230 patients met inclusion criteria. Chi-square and Student's t test were used for comparisons. Bonferroni correction was used for subgroup comparison. All analyses were conducted using the SAS System.

Results: A total of 385 patients composed the pre-intervention group compared to 230 in the post-intervention. Of these, 55.6% vs 47.0% were females and 44.4% vs 53.0% were males, respectively. Average age between groups was similar (63.9 vs 64.2). New GC prescription was higher in pre-intervention group (177 vs 56, p< 0.001). Rheumatoid arthritis (RA) was the most common disease between groups (39.7% vs 32.6%). Prednisone was the most prescribed steroid (93.5% vs 93.0%) at a frequent dose of >5mg to < 10mg daily (34.2% vs 33.1%).

Pre-intervention, appropriate DEXA was obtained in 56.9% (n=219) which increased to 68.3% (n=157) in the post-intervention group with an absolute difference of 11.4% (p=0.005). Overall screening amongst each condition increased, notably in RA (56.9% vs 61.3%) and vasculitis (58.7% vs 73.0%), but this was not statistically significant. Screening did not increase for those on ≥30mg/day (48.3% vs 48.0%). Appropriate OP treatment increased post-intervention (30.3% vs 48.1%, p=0.002). Modifying the FRAX risk score in pre- and post-intervention groups separately upgraded lower risk scores to higher risk (low: 50 to 45 vs 34 to 32; moderate: 69 to 63 vs 31 to 26; high: 70 to 81 vs 55 to 62).

Conclusion: Implementation of the 2017 ACR GIOP guidelines increased DEXA screening and OP therapy initiation in the post-intervention group by improving the identification of high-risk patients. Abiding by these guidelines will lead to a reduction in further OP complications.

Disclosure: M. Figueroa Sierra, None; **A. Vafa**, None; **S. Cao**, None; **Y. Lu**, None; **H. Bateman**, None; **J. Carter**, None; **Y. Lin**, None; **R. Cuchacovich**, None; **M. Maldonado**, None; **J. Valeriano-Marcet**, None; **G. Montes-Rivera**, None.

Abstract Number: 0114

Incidence of Follow-Up Dual-Energy X-Ray Absorptiometry Scanner Error: A Contributor to Precision Error

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
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Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis is characterized by decreased bone tissue microarchitecture. This leads to reduced bone density and quality and is a significant contributor to morbidity, mortality, and resources. Current guidelines recommend serial BMD measurement with a DXA scan every 1 to 3 years and the latest position paper from International Society for Clinical Densitometry explicitly states the use of the same or cross-calibrated DXA scanners. Interpreting follow-up DXA scan results from different scanners that are not cross-calibrated may lead to erroneous clinical decisions. This retrospective study aims to determine the proportion of patients who had follow-up DXA scans done on different scanners that have not been cross-calibrated and to determine potential risk factors that may contribute to this type of error.

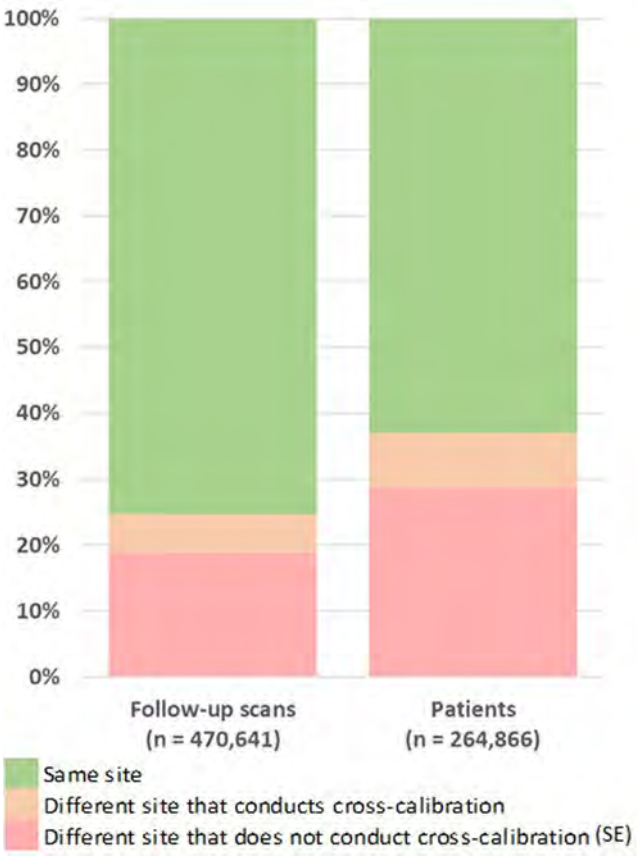
Methods: Service code X128 was used to extract DXA scan records from the Physician Claim Database (PCD) between 1 April 2009 and 31 December 2018, inclusively. Patients at least 18 years of age with at least 2 DXA scans completed during this period were included. Variables for each patient and DXA scan were obtained from the Pharmacy Information Network and PCD using pre-defined pharmaceutical, ICD-9, and ICD-10 codes.

The imaging facility identifier codes of all follow-up scans were compared to that of the immediately preceding scan. A follow-up scan was considered to have a scanner error (SE) if it was performed on different scanner that was not cross-calibrated. Logistic regression model with repeated measurements was used to calculate odds ratios for variables leading to SE.

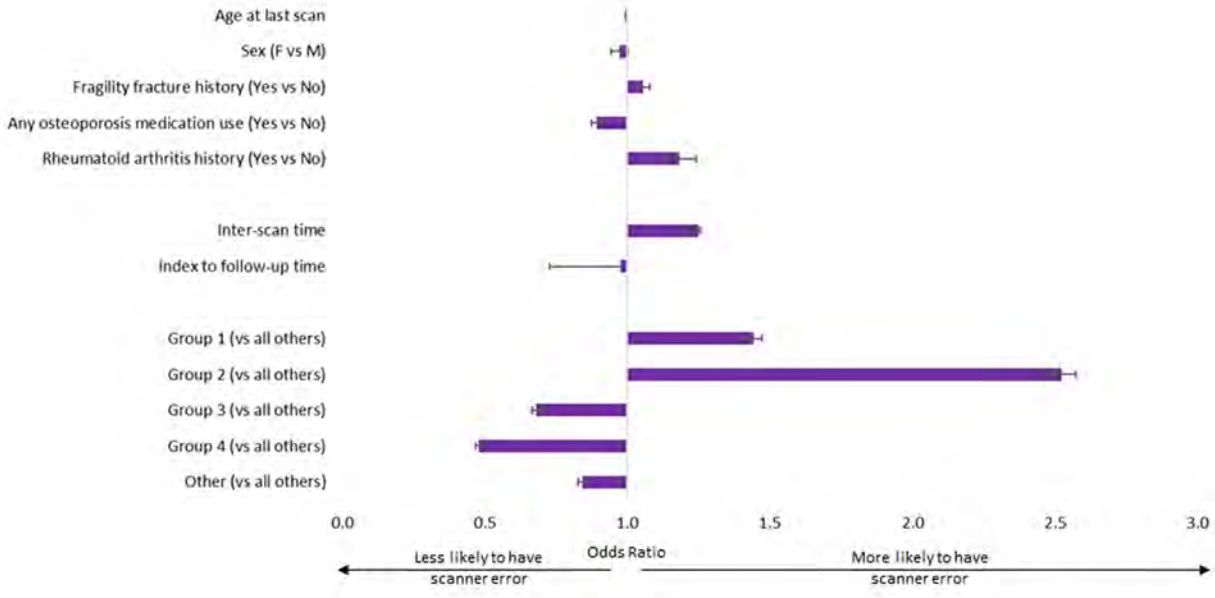
Results: At least 2 DXA scans were done by 264,866 patients for a total of 470,641 follow-up DXA scans. Of the follow-up DXA scans, 116,401 (25%) were done on a different scanner. With consideration of cross-calibrations done between these different scanners, 88,922 (19%) had a SE. Overall, 97,813 patients (37%) had at least one follow-up

Characteristics	n = 264,866 (%)
Age (mean ± stdev, in years)	
Index (First) DXA scan	61.3 ± 10
Last DXA scan	66.3 ± 10
Female	240,654 (90.9%)
Fragility fracture location	
Wrist	28,553 (10.8%)
Humerus	9,258 (3.5%)
Vertebra	8,241 (3.1%)
Hip	7,705 (2.9%)
Osteoporosis medication use	
Alendronate and Risedronate	69,980 (26.4%)
Zoledronic	3,846 (1.5%)
Denosumab	3,356 (1.3%)
Teriparatide	386 (0.1%)
Rheumatoid arthritis	7,195 (2.7%)

Baseline characteristics



Percentage of follow-up DXA scans and patients



Factors associated with scanner error

DXA scan done at a different facility. With cross-calibration considered, 75,928 (29%) of all patients experienced at least one SE.

Factors associated with SE include increasing time between consecutive DXA scans (OR 1.2502, CI 1.2435-1.2569), rheumatoid arthritis (OR 1.1830, CI 1.1277-1.2410), and fragility fractures (OR 1.0564, CI 1.0339-1.0794). Factors associated with less SE include use of osteoporosis medication (OR 0.8922, CI 0.8753-0.9095), increasing follow-up scan year (OR 0.9762, CI 0.7260-0.9798), and older age at time of last DXA scan (OR 0.9942, CI 0.9933-0.9950). Female sex did not significantly affect SE (OR 0.9725, CI 0.9433-1.0026). The imaging facility groups at which follow-up DXA scans were performed was also associated with differing risk of patients experiencing SE.

Conclusion: Proper management of osteoporosis requires interpretation of comparable DXA scans. This study found that a large proportion of follow-up DXA scans were of minimal clinical utility due to use of different DXA scanners that were not cross-calibrated. Using such results pose significant risk to patients and economic cost to the healthcare system. Interventions are needed to decrease this type of DXA scan error.

Disclosure: K. Lee, None; **K. Al Jumaily**, None; **M. Lin**, None; **K. Siminoski**, None; **C. Ye**, None.

Abstract Number: 0115

Improving Osteoporosis Screening in Men at a Resident-run Primary Care Clinic: A Quality Improvement Project

Khiem Vu[1], Chima Ohadugha[1], Kevin Dao[1], Rabih Nayfe[2] and Andrew Mangano[1], [1]Grand Strand Medical Center, Myrtle Beach, SC, [2]Carolina Health Specialists - Rheumatology, Myrtle Beach, SC

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: There are known indications for osteoporosis screening in women. However, osteoporosis also occurs in men and fragility fractures are linked to increased morbidity and mortality. Organizations as the National Osteoporosis Foundation, International Society for Clinical Densitometry, Endocrine Society, American College of Preventive Medicine, American College of Physicians, and American College of Rheumatology recommend that men ≥ 70 years old need universal screening for osteoporosis by dual energy x-ray absorptiometry. However, we have observed this recommendation to be underutilized in our resident clinic. The aim of this quality improvement project was to increase the documentation of osteoporosis screening in males ≥70 years old in our resident clinic (Grand Strand Primary Care) from the baseline 4-month average of 0% to ≥10% during the time period November 2019-May 2020.

Methods: Internal medicine residents were sent an educational email about osteoporosis screening in men ≥70 years old on November 1, 2019. It included the indications for screening in men, specific test to order, suggested diagnosis codes, references from literature, and solicited feedback regarding concerns about the project or clarification. Also, males ≥ 70 years old who were seen in clinic between July 1 and November 1, 2019 had their clinic notes reviewed for whether plans for screening was documented in the chart. Each resident was provided a customized list of patients (who had at least one scheduled follow-up in the next six months) for whom documentation about screening was lacking. Lastly, paper flyers were displayed in the clinic workspace similarly to those of other preventative health/screening recommendations for other medical conditions. On May 1, 2020 (six months later), charts were reviewed to evaluate the documentation rate of osteoporosis screening during the period November 1, 2019-May 1, 2020.

Results: Between July 1 and November 1, 2019, a total of 62 males ≥70 years old were seen in clinic among 26 residents. None of these patients had initial documentation regarding osteoporosis screening. Six months after our interventions (i.e. email sent on November 1, 2020, paper flyers displayed in clinic workroom), results were as follows: 11 patients were lost to follow-up (including one death), and 51 patients were seen at least once but osteoporosis screening was still not documented/discussed.

Conclusion: Our project did not meet the goal screening rate of at least 10% at six months. The results were humbling in that despite osteoporosis screening being recommended in men ≥70 years old by several medical organizations, screening rates remain exceptionally low, if not utilized at all. Although it is difficult to extrapolate our results to a broader scale, the major obstacles to screening most likely are limited life expectancy, prioritization of patients' other comorbidities, cost (i.e. lack of insurance coverage), or the perception that osteoporosis is a disease solely of women. Further discussion must be held to reevaluate whether this universal screening recommendation will still hold in the future, or whether it is rather a highly individualized decision best discussed between patient and physician.

Disclosure: K. Vu, None; **C. Ohadugha**, None; **K. Dao**, None; **R. Nayfe**, None; **A. Mangano**, None.

Abstract Number: 0116

The *in Vitro* 3D Fracture Gap Model: A Tool for Preclinical Testing

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Background/Purpose: Approximately 10% of fractures lead to significant fracture healing disorders. Of note, especially immunosuppressed patients with ongoing inflammation show difficulties in the correct course of fracture healing.

Current research has the focus on small animal models, facing the problem of translation towards the human system. In order to improve the therapy of fracture healing disorders, we have developed a human cell-based *in vitro* model to mimic the initial phase of fracture healing adequately. This model will be used for the development of new therapeutic strategies.

Our aim is to develop an *in vitro* 3D fracture gap model (FG model) which mimics the *in vivo* situation in order to provide a reliable preclinical test system for fracture healing disorders.

Methods: To assemble our FG model, we co-cultivated coagulated peripheral blood and primary human mesenchymal stromal cells (MSCs) mimicking the fracture hematoma (FH model) together with a scaffold-free bone-like construct (SFBC) mimicking the bony part of the fracture gap under hypoxia, to reflect the *in vivo* situation after fracture most adequately. To analyze the impact of the SFBC on the *in vitro* FH model with regard to its osteogenic induction capacity, we cultivated the fracture gap models in medium with or without osteogenic supplements. To analyze the impact of Deferoxamine (DFO, known to foster fracture healing) on the FG model, we treated our FG models with

either 250 µmol DFO or left them untreated. After incubation and subsequent preparation of the fracture hematomas, we evaluated gene expression of osteogenic (*RUNX2*, *SPP1*), angiogenic (*VEGF*, *IL8*), inflammatory markers (*IL6*, *IL8*) and markers for the adaptation towards hypoxia (*LDHA*, *PGK1*) as well as secretion of cytokines/chemokines using quantitative PCR and multiplex suspension assay, respectively.

Results: We found that both the fracture hematoma model and the bone-like construct had close contact during the incubation, allowing the cells to interact with each other through direct cell surface and signal molecules or metabolites. Additionally, we could show that the SFBCs induced the upregulation of osteogenic markers (*RUNX2, SPP1*) within the FH models irrespective of the supplementation of osteogenic supplements. Furthermore, we observed an upregulation of hypoxia-related, angiogenic and osteogenic markers (*RUNX2*, *SPP1*) under the influence of DFO, and the downregulation of inflammatory markers (*IL6*, *IL8*) as compared to the untreated control. The latter was also confirmed on protein level (e.g. IL-6 and IL-8). Within the bone-like constructs, we observed an upregulation of angiogenic markers (RNA-expression of *VEGF*, *IL8*), even more pronounced under the treatment of DFO.

Conclusion: In summary, our findings demonstrate that our established *in vitro* FG model provides all osteogenic cues to induce the initial bone healing process, which could be enhanced by the fracture-healing promoting substance DFO. Therefore, we conclude that our model is indeed able to mimic the human fracture gap situation and is therefore suiTable to study the influence and efficacy of potential therapeutics for the treatment of bone healing disorders in immunosuppressed patients with ongoing inflammation.

Disclosure: M. Pfeiffenberger, None; **A. Damerau**, None; **P. Hoff**, None; **A. Lang**, None; **F. Buttgereit**, AbbVie, 8, Eli Lilly, 8, Pfizer, 8, Roche, 8; **T. Gaber**, None.

Abstract Number: 0117

Development of an *In Vitro* Trabecular Human Bone Model to Recapitulate Features of Glucocorticoid-induced Osteoporosis

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SESSION INFORMATION
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Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The bone matrix consists of inorganic and organic components and a variety of specialized cells such as osteoblasts, osteocytes and osteoclasts. The bone-forming osteoblasts are responsible for the production of organic matrix components; they differentiate later into osteocytes which is accompanied by matrix mineralization. Osteoclasts are multinuclear giant cells, which resorb bone. The healthy bone homeostasis is characterized by a balanced, dynamic and continuous remodeling process. Glucocorticoids (GCs) are commonly used to successfully treat patients with inflammatory rheumatic and other autoimmune diseases. However, long-term treatment with GC can potentially lead to several adverse effects such as the inhibition of osteoblast proliferation and the increase of osteoclastic activity resulting in osteoporosis. Hence, the aim of our project is to i) develop an *in vitro* trabecular human bone model, ii) integrate this bone model into a perfusion system to accelerate mineralization and provide biomechanical stimuli and iii) applying prednisolone to induce osteoporosis. Here we present our initial results describing

the successful differentiation of osteoblasts and osteoclast in a 3D environment, and the accomplished integration of the bone model into a perfusion system.

Methods: In a first step, different cultivation conditions were tested to allow optimal osteogenic or osteoclastic differentiation. To this end, a) human bone marrow derived mesenchymal stromal cells (hMSCs) were treated with osteogenic medium, and b) monocytes (isolated from buffy coats) were differentiated into osteoclasts using following protocol: incubation for 3 days with 25 ng/ml M-CSF followed by an 18-day incubation with M-CSF and 50 ng/ml RANKL. Calcification of hMSCs was evaluated via Alizarin-red staining. Osteoclasts were identified using immunofluorescence staining observing multinucleated (DAPI) giant (ß-Actin) cells with TRAP and Cathespin K activity. Additional gene expression analyses are currently conducted using qRT-PCR and looking for osteoclast-specific genes. In parallel to the monolayer cultures, cells were transferred on β-tricalcium phosphate (βTCP) – a suiTable bony-like scaffold. Furthermore, first experiments in a dynamic bioreactor platform (OSPIN GmH) were conducted to evaluate the influence of shear stress on the cells and model systems.

Results: We have been able to populate the βTCP scaffold with monocytes, which were differentiated into osteoclasts (morphological changes) without any effect on cellular viability as measured by Live/Dead staining. The morphological changes of those osteoclasts such as formation of filopodia could be demonstrated by scanning electron microscopy. In addition, the cultivation of βTCP populated with hMSCs in a perfusion system showed the upregulation of osteogenic marker (*RUNX2, OSX*) on mRNA-level.

Conclusion: These first results of our approach to develop an *in vitro* 3D model for glucocorticoid-induced osteoporosis are promising. Our next step will be the co-cultivation of osteoblasts and osteoclasts under dynamic and optimized cultivation conditions.

Disclosure: A. Lang, None; **K. Diesing**, None; **A. Damerau**, None; **M. Pfeiffenberger**, None; **T. Gaber**, None; **F. Buttgereit**, AbbVie, 8, Eli Lilly, 8, Pfizer, 8, Roche, 8.

Abstract Number: 0118

Indicators of Effectiveness After 6 Years of Follow-up in a Fracture Liaison Service

Antonio Naranjo Hernandez[1], Amparo Molina[2], Cristina Sepúlveda[2], Francisco Rubiño[3], Adrian Quevedo[3] and Soledad Ojeda[3], [1]Hospital Universitario Dr Negrin, Las Palmas, Canarias, Spain, [2]Hospital Universitario de Gran Canaria Dr Negrin, Las Palmas, Spain, [3]Hospital Universitario de Gran Canaria Dr Negrin, Las Palmas

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Data on the effectiveness of FLS in the medium and long term are needed. The objetive of this study was to analyze the indicators of long-term persistence to treatment, refracture and mortality in our Fracture Liaison Service (FLS)

Methods: We review the medical records of patients with an indication of treatment to prevent new fractures (bisphosphonate -BP- or equivalent) whose baseline visit took place between 2012 and 2016. The data included those of the baseline visit (age, sex, type of index fracture, FRAX scale and DXA results) and for the follow-up (death and date,

	(n = 896)
Women, n (%)	742 (83)
Age, mean (SD)	75.6 (10)
Primary fracture site, n (%)	
Femur	300 (33.4)
Forearm	245 (27.3)
Humerus	180 (20.0)
Vertebra	97 (10.8)
Other	74 (8.2)
Previous fragility fracture, n (%)	163 (18.1)
FRAX score, mean (SD)	
Major	15.4 (9)
Hip	7.3 (7)
Previous treatment with bisphosphonates, n (%)	180 (20.1)
Baseline DXA scan*, n (%)	
Normal	40 (5.3)
Low bone mass	306 (40.9)
Osteoporosis	401 (53.7)

Table 1. Baseline characteristics of patients Abbreviations: SD, standard deviation; DXA, dual energy X-ray absorptiometry , *analysed in 747 patients

refracture including revision of spine x-rays - it was considered only the first refracture and, in the case of several fractures the most serious was chosen-, prescribed treatment, persistence of treatment trough electronic prescription on the date of review or death, and MPR or proportion of days covered by treatment).

Results: 896 patients were included, with an average follow-up of 63,6 months (DE 29, range 42-90). Table 1 shows the baseline characteristics.

Follow-up.- The persistence of treatment was assessed in 888 patients; 618 patients (69.6%) were prescribed a treatment at any time, 480 of them (77,9%) with a MPR≥80% at the time of chart review or death (in that case). Therefore, 54% of the analyzed patients persist with the treatment defined as MPR > 80%.

When analyzing patients with prescribed treatment, in 378 cases (61.1%) it was a BP in a sustained manner, in 85 cases (13.7%) a BP was prescribed and subsequently changed to denosumab, while in 151 cases (24,4%) it was initiated and maintained denosumab, and 4 patients other treatments. The MPR > 80% was 75% in patients who started and maintained BP, 79% in those who started BP and switched to denosumab, and 87% in those who had denosumab throughout the analysis period.

138 of 891 pacients (15,4%) had a new fracture, 112 a major fracture (12,5%) and 50 hip fracture (5,6%). Taking the 6-year period, 42% of refractures occurred in the first two years after the index fracture.

In patients without a prescribed treatment, refracture ocurred in 15,1% (major and hip fractures in 12.9% and 8.5%). In patients with a prescribed treatment refractures ocurred in 15,7% (major and hip fractures in 12.5% and 4.3%). Compared to patients without treatment we found a significant lower incidence of hip fracture in patients wit a prescribed treatment (OR 0.49, CI 95% 0.20-0.79) but a similar incidence of major fracture, mean FRAX (15.8 vs 14.4) and age (75.4 vs 76.2).

212 patients (23.6%) died. Compared to those alive, in patients who died we found a higher age (81 vs 74), a higher frequence of hip fracture at baseline (52% vs 27%), a higher hip refracture (9.4% vs 4.4%) and a lower prescription of treatment (56.4% vs 73,6%).

Conclusion: 6 years after the assessment in an FLS, the persistence of treatment with MPR≥80% was 54%. We found an association with prescription of treatment with lower hip refracture.

Disclosure: A. Naranjo Hernandez, None; **A. Molina**, None; **C. Sepúlveda**, None; **F. Rubiño**, None; **A. Quevedo**, None; **S. Ojeda**, None.

Abstract Number: 0119

Fracture Liaison Service at an Academic Center with an Open Health System: 30-month Outcomes

Donna Jose[1], Micah Yu[2], Karina Torralba[3], Christina Downey[4], Justin Dunn[5] and Vinicius Cabido[5], [1]Loma Linda University Medical Center, Ontario, CA, [2]Loma Linda University Medical Center, Loma Linda, CA, [3]Loma Linda University School of Medicine, Redlands, CA, [4]Loma Linda University Medical Center, Redlands, CA, [5]Loma Linda University Medical Center, Loma Linda

SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis causes significant morbidity, mortality and healthcare burden. There continues to be a care gap in osteoporosis recognition, treatment and prevention. Several healthcare systems in the USA and worldwide have implemented a Fracture Liaison Service (FLS) aimed at secondary fracture prevention. Locally, a 2015-2016 study showed that up to 90% of elderly patients admitted to a tertiary academic center were not screened or treated for osteoporosis. An FLS was established fall 2017 to bridge the care gap in our population. The objective of this study is to longitudinally analyze the effectiveness of the FLS during the initial thirty-month period.

Methods: Data from the electronic health record (EHR) were analyzed to identify the number of inpatient FLS consults received between September 2017and February 2020 (30 months). The following metrics were recorded: demographics, anatomic location of fracture, any prior fractures, calcium and Vitamin D supplementation, pharmacotherapy initiation, DXA completion, transition to osteoporosis specialist and transition to any dependent living facilities. Current data was compared to 8-month data. Main target outcome was a 10% improvement in treatment initiation. Prior data noted that at month 8 and 18 transition to outpatient specialist was delayed, and a significant number of patients (25%) had a primary care provider outside of the academic health system. An FLS nurse practitioner (NP),

Descriptor	Result
Number of patients referred (N)	189
Sex	
Female	69.3% (131)
Male	30.7% (58)
Age	
<60	11.6% (22)
61-70	16.4% (31)
71-80	28.6% (54)
81-90	29.1% (55)
>90	14.3% (27)
Anatomic Location of Fracture	
Femoral	38% (72)
Vertebral	16.4% (31)
Had Prior Fracture	43.4% (82)
Primary Care Provider:	
Within academic health system	79.9% (151)
Outside academic health system	20.1% (38)
Never had DXA done pre-Fracture	60.0% (111)
Was not on Ca+, Vit D supplementation	64.8% (118), 52.7% (96)
Never been on Osteoporosis Treatment	79.6% (148)

Table 1. FLS Population at an Academic Medical Center associated with an Open Health System at 30 months Data Collection

Outcome Metric	8 months	30 months	p-value
Number of patients referred	65	124	N/A
Dual-Energy Bone Absorptiometry completed after discharge	17.5% (11)	19.8% (24)	0.697
Transitioned to outpatient osteoporosis specialist	27.4% (17)	32.5% (39)	0.482
Osteoporosis treatment initiation after discharge	18.8% (12)	15.3% (19)	0.548

Table 2. Outcome Metrics of a Fracture Liaison Service at an Academic Health System at 8 months and 30 months Data Collection

who also acted as an FLS coordinator, was hired at 18 months. A Chi-square test of independence was utilized to determine if there were proportional differences between those at the 8-month follow-up compared to those at the 30-month follow-up. Alpha was set equal to 0.05 for statistical significance.

Results: 189 patients were referred to the FLS service since initiation (Table 1). A 5% improvement in outpatient follow up was noted at the 30-month mark (32.5%) compared to the 8-month (27.4%) mark (Table 2). Treatment initiation rates that slightly decreased at the 30-month mark were noted to be largely due to patient refusal. This refusal in treatment initiation was noted to be due to patients' poor understanding of osteoporosis, fracture complications and risk aversion to use of medications. When a comparison was made between the 8-month group with the 30-month

group using the chi-square test, no proportional differences in DEXA completed after discharge, transition to outpatient osteoporosis specialist, or osteoporosis treatment initiation after discharge was seen (Table 2).

Conclusion: The number of patients transitioning to outpatient care has improved since the hiring of a NP/FLS Coordinator, even among patients who had a primary care provider outside of the academic health system. However, this number is not statistically significant. A study to analyze patient perceptions about osteoporosis and treatment risk aversion would be useful. Further education efforts are needed aimed at improving osteoporosis awareness not only among patients but also among Primary Care Providers.

Disclosure: D. Jose, None; **M. Yu**, None; **K. Torralba**, None; **C. Downey**, None; **J. Dunn**, None; **V. Cabido**, None.

Abstract Number: 0120

Risk of Fracture in Patients with Different Glucocorticoid Requiring Diseases

Giovanni Adami[1], Angelo Fassio[2], Alessandro Giollo[2], Luca Idolazzi[2], Ombretta Viapiana[1], Davide Gatti[2] and Maurizio Rossini[2], [1]University of Verona, Verona, Italy, [2]Rheumatology Unit, University of Verona, Verona, Italy

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

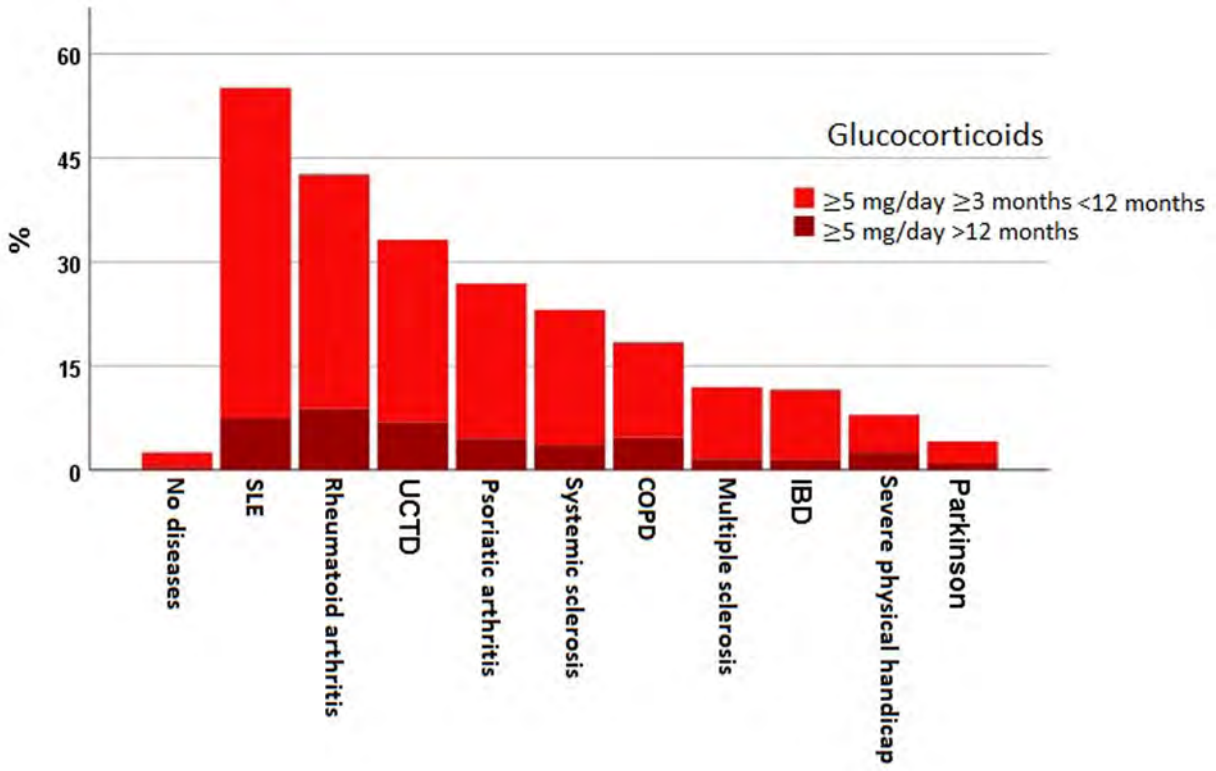

Figure 1. Glucocorticoid use in the cohort under analysis

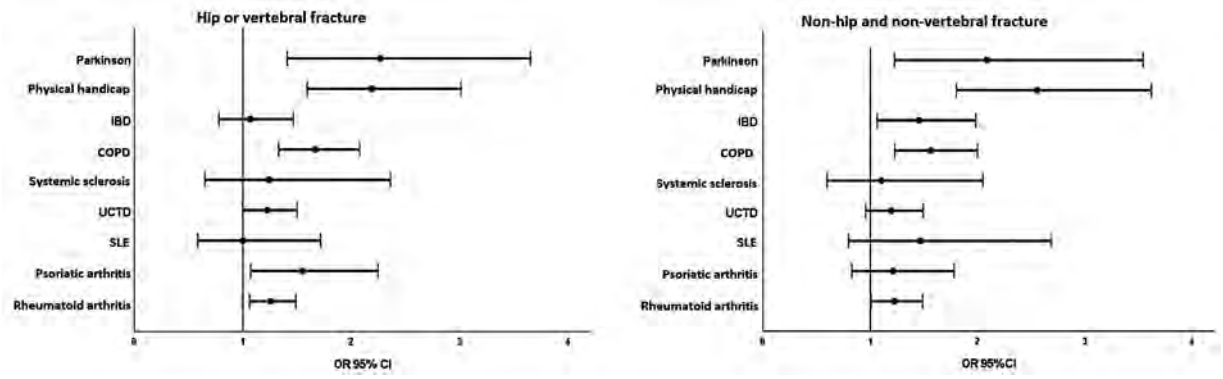

Figure 2. Odd ratios of vertebral and hip fracture and non-vertebral, non-hip fractures in the study population

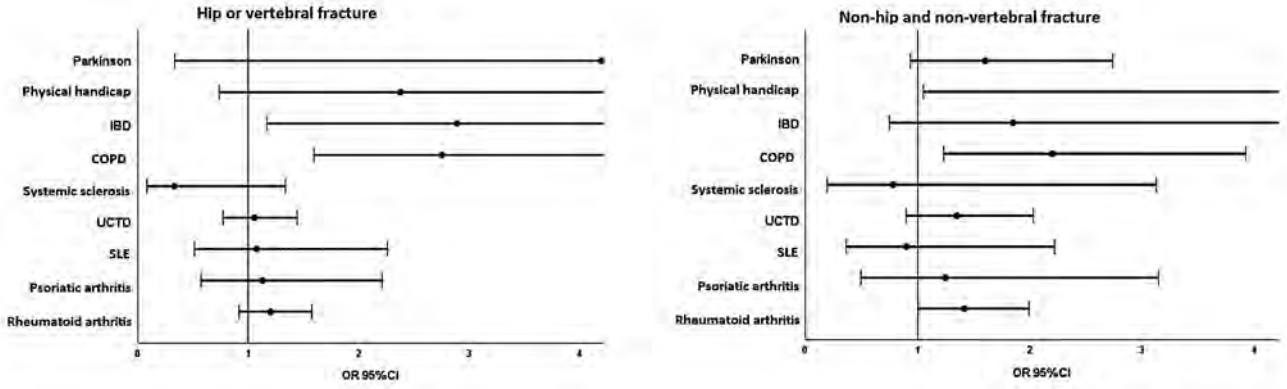

Figure 3. Odd ratios of vertebral and hip fracture and non-vertebral, non-hip fractures in the study population (excluding glucocorticoid users)

Background/Purpose: The aim of the present work is to determine the fracture risk associated with glucocorticoids requiring diseases

Methods: We conducted a retrospective analysis of a nation-wide cohort (DeFRACalc79 database). We collected many clinical variables, including the use of glucocorticoids, the presence of prior hip or vertebral and non-vertebral or non-hip fractures and the presence of comorbidities (rheumatoid arthritis, psoriatic arthritis, undifferentiated connective [UCTD], systemic lupus erythematosus [SLE], systemic sclerosis, chronic obstructive pulmonary disease [COPD], multiple sclerosis, chronic inflammatory bowel diseases [IBD], severe physical handicap, diabetes, Parkinson's and HIV). We generated age and T-score matched groups of patients with and without comorbidities via propensity score matching. After 1:1 matching we analyzed the prevalence of fragility fractures. We performed a sensitivity analysis by eliminating all patients who used glucocorticoids ≥5 mg/day for ≥3 months.

Results: 59950 women aged 65.1 years (SD 11.0), with total-hip T-score of -2.16 (SD 0.94) and lumbar spine T-score of –2.50 (SD 1.15) were included in the analysis. Among 13,546 women with comorbidity 3114 (23.0%) had diabetes; 3008 (22.2%) rheumatoid arthritis; 1910 (14.1%) UCTD; 1614 (11,9%) BPD; 942 (7,0%) IBD; 794 (5,9%) severe motor disability; 703 (5,2%) psoriatic arthritis; 412 (3,0%) Parkinson's. 294 (2,2%) LES; 277 (2,0%) systemic sclerosis; 243 (1,8%) multiple sclerosis and 235 (1,7%) had HIV. **Figure 1** shows the prevalence of glucocorticoid use stratified by disease. Glucocorticoid intake ≥5 mg/day for ≥3 months (after 1:1 matching by age and T-scores) was significantly

associated with vertebral fractures (aOR 1.5 95% CI 1.3-1.7) but not with non-femoral non-vertebral fractures (aOR 1.0 95% CI 0.9-1.2) while intake of ≥5 mg/day for ≥12 months was associated with fractures of all kind (aOR 1.3 95% CI 1.2-1.3 and 1.3 95% CI 1.1-1.8). **Figure 2** and **Figure 3** show the ORs for the presence of vertebral or hip fractures and non-vertebral or non-hip fractures (glucocorticoid users and non-users respectively). Diseases with increased risk of fracture, independently from glucocorticoid intake, were rheumatoid arthritis, COPD and severe physical handicap for non-vertebral and non-hip fractures and COPD and IBD for vertebral or hip fractures.

Conclusion: At a population level, glucocorticoid intake is still common, especially in patients with rheumatic diseases, and is associated with an increased risk of fractures, both vertebral, hip and non-vertebral non-hip fractures. Rheumatoid arthritis, COPD and severe physical handicap were independently associated with an increased risk of non-vertebral and non-hip fractures whereas only COPD and IBD were associated with vertebral or hip fractures.

Disclosure: G. Adami, None; **A. Fassio**, None; **A. Giollo**, None; **L. Idolazzi**, None; **O. Viapiana**, None; **D. Gatti**, None; **M. Rossini**, None.

Abstract Number: 0121

Association of Low Bone Density with Need for Early Revision After Elective Joint Replacement for Osteoarthritis in Postmenopausal Women

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Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Total joint replacement (TJR) is the standard surgical treatment for end-stage hip and knee osteoarthritis (OA). Patient optimization may limit the need for early revision surgeries. Low bone mineral density (BMD) may cause periprosthetic fractures, osteolysis and implant migrations which can affect postoperative outcomes, but the data is limited. There is also no standardized approach to assess bone health prior to TJR. Our primary objective was to study the prevalence of low bone mass and its relationship to early revision arthroplasty.

Methods: We performed a retrospective, case-control, single-center study using Reading Hospital Joint Database. We reviewed charts of postmenopausal women who underwent hip and knee arthroplasty from January, 2013 to December, 2019 and identified patients who underwent *early (within 5 years)* revision arthroplasty for aseptic indications ("cases"). We matched each of the cases to 2 postmenopausal women who did not undergo a revision surgery during the time period ("controls"), matched for age at index surgery (+/- 5 years), timing of initial TJR (+/- 6 months) and type of TJR. We identified patients with BMD testing with DEXA (dual-energy X-ray absorptiometry) within 2 years of the index TJR. We collected data on patient characteristics including age, body mass index (BMI), use of vitamin D and calcium, chronic glucocorticoid (prednisone equivalent of 5 mg/day for > 3 months) and anti-osteoporotic therapy use. Late revision surgeries and infectious indications were excluded.

	TJR for OA with need for early revision arthroplasty (n=25)	* Matched TJR for OA with no revision till date (n=50)
Mean Age (at index surgery), years	69.72	68
Mean BMI (at index surgery), kg/m^2	33.03	35.96
BMI categories		
Obesity (at index surgery)- n (%)	11 (44)	22 (44)
Morbid obesity (at index surgery)- n (%)	5 (20)	16 (32)
Bone density assessment with DEXA - n (%)	10 (40)	31 (60)
Osteoporosis by DEXA- n (%)	1 (10)	4 (12.90)
Osteopenia by DEXA- n (%)	6 (60)	13 (41.94)
Mention of fragility fracture- n (%)	4 (16)	8 (16)
Anti-osteoporotic medication use (in osteoporosis or fragility fractures)- n (%)	3/4 (75)	7/11 (63.63)
Calcium supplementation- n (%)	10 (40)	22 (44)
Vitamin D supplementation- n (%)	13 (52)	34 (68)
Steroid use for > 3 months - n (%)	2 (8)	4 (8)
Diabetes mellitus at index surgery- n (%)	11 (52)	37 (74)
Diabetes on insulin - n (%)	4 (36.36)	10 (27.03)

Table 1: Characteristics of postmenopausal women undergoing early joint revision (n=25) compared to those who did not undergo revision surgery during the study period (n=50)

*Matched by age at index surgery (+/- 5 years), timing of initial TJR (+/- 6 months) and type of TJR

Table 1. Characteristics of postmenopausal women undergoing early joint revision (n=25) compared to those who did not undergo revision surgery during the study period (n=50) *Matched by age at index surgery (+/- 5 years), timing of initial TJR (+/- 6 months) and type of TJR

Results: We identified 25 postmenopausal women with elective TJR for OA who underwent early revision hip (n=11) and knee replacement (n=14) for aseptic indications. The mean age for index TJR was 70 years. The average duration between index and revision surgery was 22 months (12 months for hip and 30 months for knee revision).

Each of the postmenopausal women who underwent early joint revision (n=25) were matched to 2 postmenopausal women who did not undergo early revision surgery (n=50) during the study period (**Table 1**). Forty percent patients in the early revision group had documentation of a screening DEXA compared to 60 % patients in the non-revision group. Among patients who had DEXA, 7/10 (70%) had low bone mass (osteopenia or osteoporosis) in the early revision group compared to 17/31 (55%) in the non-revision group. Of the 4 patients with a history of fragility fracture in the early revision group, 75% underwent revision surgery within the first 2 months of index TJR (two due to periprosthetic fracture and one due to femoral loosening). The use of calcium and vitamin D was identified in 40% and 52% in the early revision group compared to 44% and 68%, respectively, in the non-revision group.

Conclusion: Our study found a lower rate of DEXA screening and a higher prevalence of low bone mass in the early revision group, which may suggest a higher prosthetic failure in patients with low bone mass. We were unable to assess the role of anti-osteoporosis medication on the outcome due to the small sample size. Further studies are needed to explore the impact of osteoporosis and its treatment on postoperative outcomes, particularly in those with a history of a prior fragility fracture.

Disclosure: R. Dhital, None; **P. Nicholas**, None; **G. Emkey**, None; **A. Donato**, None.

Abstract Number: 0122

Osteoporosis Medication Utilization Patterns over Time in the ACR RISE Registry

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

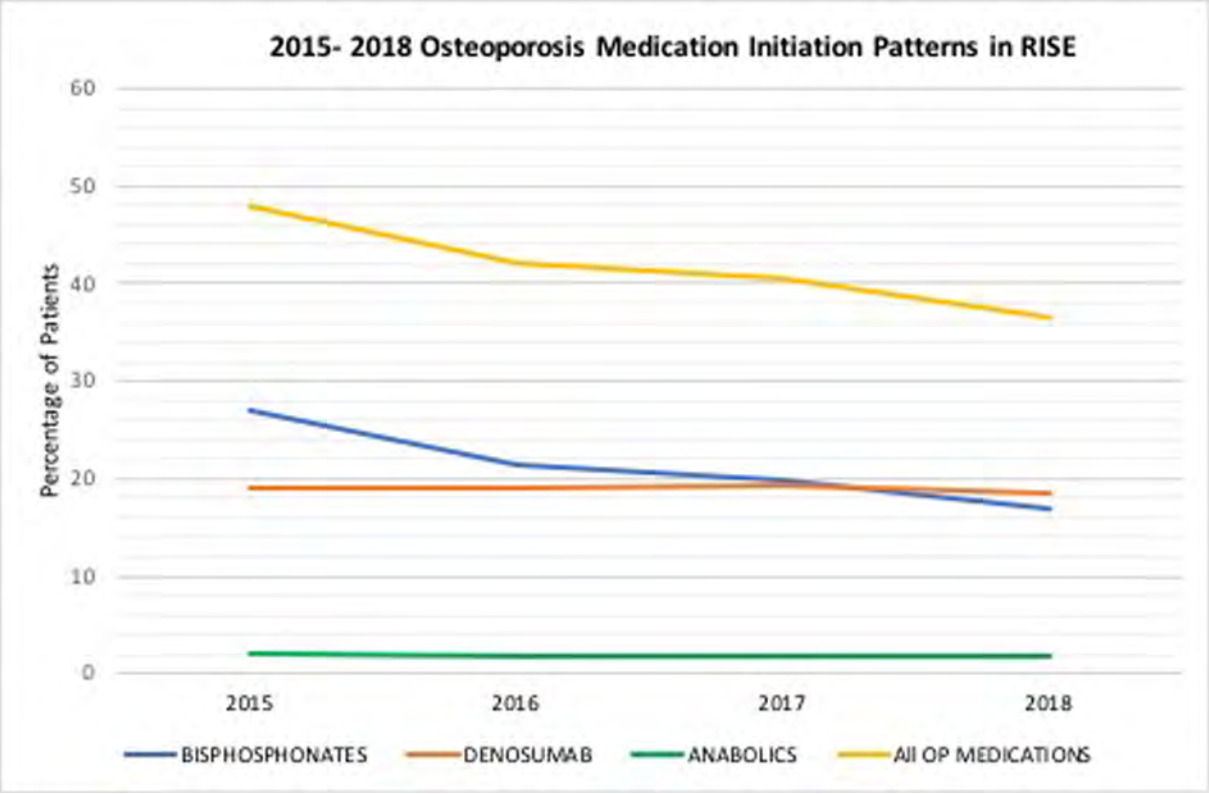
Session Title: Osteoporosis & Metabolic Bone Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Many effective medications are available for osteoporosis treatment. However how rheumatologists use these therapies is not well understood, particularly in patients with concomitant rheumatologic conditions. The objective of this study was to examine the patterns of utilization of osteoporosis medications among rheumatologists reporting to the ACR's Rheumatology Informatics System for Effectiveness registry (RISE).

Methods: RISE is a national registry that passively collects data from real-world rheumatology practices. As of December 2018, RISE held validated data from 715 rheumatology providers in 226 practices, representing ~20% of the U.S. clinical rheumatology workforce. Patients included in this study were ≥18 years old and had osteoporosis based on ≥ 1 diagnosis code for osteoporosis or prescriptions/administrations of osteoporosis medications, each calendar



	Bisphosphonates (n= 70,904)	Denosumab (n= 35,046)	Teriparatide (n= 5,371)
Osteoarthritis	35.6%	35.6%	30.2%
Rheumatoid arthritis	20.7%	14.8%	15.1%
Long term steroid use	8.3%	3.9%	4.6%
Polymyalgia rheumatica	4.7%	2.4%	2.0%
Sjogren's	3.6%	3.0%	3.1%
Ankylosing spondylitis	3.2%	2.8%	3.4%
Systemic Lupus Erythematous	2.7%	2.1%	2.4%
Undifferentiated connective tissue disease	1.4%	1.0%	0.9%
Gout	1.1%	1.2%	0.7%
Scleroderma	0.8%	1.0%	1.2%
Mixed connective tissue disease	0.3%	0.3%	0.4%

year from 2015 to 2018. We identified autoimmune rheumatic disease type using ICD10 codes. We assessed osteoprosis medication use, including bisphosphonates, denosumab, and anabolics in each calendar year from 2015 to 2018, examining both prevalent use (i.e. any use) and separately, new osteoporosis medication initiation (i.e. use in that year, with no prior recorded use in RISE in any previous year).

Results: In 2018, we identified 251,620 eligible patients from 217 practices. Of these, 89.6% were female, 68.4% were white, 4.5% were black, and 7.5% were identified as Hispanic or Latino with an overall mean age of 73.0 +/- 11.3 years. The most common co-morbid autoimmune rheumatic disease in this cohort was RA (11.9%). The underlying rheumatic disease by first line osteoporosis medication choice is presented in the Table. In 2018, a nominally greater proportion (18.5%) of patients initiated denosumab, compared to bisphosphonate therapy (16.9%). Of patients who initiated denosumab in 2018, 34.6% had a prior recorded history of being on bisphosphonate therapy. Conversely, 9.0% of patients that started bisphosphonates in 2018 had a prior recorded history of being on denosumab previously. In patients who had never received any osteoporosis therapy, bisphosphonates remained the most frequently prescribed first-line treatment in 2018. Using the same definition of osteoporosis, compared to prior years, we observed a decline in proportion of registry participants initiating osteoporosis medications in each calendar year, decreasing from 47.9% in 2015 to 42.1% in 2016, 40.5% in 2017, and 36.5% in 2018, despite an increasing number of patients in the registry with osteoporosis (Figure).

Conclusion: Osteoporosis medication initiation in rheumatology practices declined over 2015-2018, however denosumab treatment appears to be gaining popularity. Bisphosphonate therapy remains favored as first line therapy for osteoporosis, but overall denosumab was initiated more frequently in 2018 compared to bisphosphonate therapy or anabolics.

(Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR)

Osteoporosis therapy initiated by U.S. rheumatologists participating in RISE in 2018 by patients' underlying rheumatologic diagnosis.

Disclosure: N. Khullar, None; **L. Chen**, None; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **J. Baker**, None; **H. Yun**, Pfizer, 2; **A. Reimold**, Lilly, 5, Abbvie, 2, Pfizer, 2; **M. Danila**, Pfizer, 2, Horizon, 2, Genentech, 2, Boehringer, 2, Amgen, 5, Sanofi, 5, Novartis, 5.

Abstract Number: 0123

Aromatase Inhibitor-Associated Bone Loss: Screening and Prevention

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Aromatase inhibitors (AI) are frequently used in hormone receptor-positive breast cancer, which encompasses nearly 75% of all breast cancers. By preventing peripheral estrogen production, AIs magnify the effects of estrogen suppression during menopause causing accelerated bone loss at a rate 2-4 times higher than expected. Approximately 1 in 5 women treated with AI therapy will suffer from a fracture, increasing their risk of mortality. AI therapy is also used in men for the treatment of gynecomastia, but there is a lack of data regarding the effects of AIs on bone loss in men.

The American Society of Clinical Oncology recommends obtaining a baseline DXA in postmenopausal breast cancer survivors treated with an AI. Several studies have shown this screening is suboptimal but cost-effective in the U.S. The aim of this study was to assess our adherence to osteoporosis screening in patients on AI therapy and to understand factors that may influence screening.

Methods: In this retrospective cross-sectional study, clinic and hospital medical records were used to identify and analyze subjects on an aromatase inhibitor from January 2015 – January 2020. Descriptive and statistical analyses using Pearson's Chi-Square were used to compare the characteristics of subjects who received DXA screening to those who did not.

Results: We identified 4,340 subjects on AI therapy from 2,248,780 charts available in the medical record system, giving AI therapy a prevalence of 0.19%. Of those, 3,797 (87.4%) were female and 549 (12.6%) were male. A DXA was ordered in 818 (19%) subjects and was not ordered in 3,522 (81%) subjects. Ninety-eight percent of subjects who had a DXA ordered were females [X^2 (1, N=4340)=100.42, $p< 0.01$].

DXA screening was more likely to be ordered in subjects aged 65 years or older with a history of alcohol use [X^2(2, N=4340)=54.94, $p< 0.01$], rheumatoid arthritis [X^2(1, N=4340)=17.45, $p< 0.01$] , hypogonadism [X^2(1, N=4340)=70.60, $p< 0.01$], and fragility fracture [X^2(1, N=4340)=5.32, $p< 0.025$]. Among those who had DXA screening, the above fac-

Demographics	DEXA	No DEXA
Gender		
Male	18 (2%)	533 (15%)
Female	800 (98%)	2989 (85%)
Age (years)		
<45	0	251 (7%)
45-64	322 (39%)	1140 (32%)
65 or older	496 (61%)	2131 (61%)
Ethnicity		
Hispanic	44 (5%)	187 (5%)
African American	30 (4%)	149 (4%)
Asian	8 (1%)	26 (1%)
White	736 (90%)	3122 (89%)

Table 1. Descriptive Analysis of Demographics

OP Risk Factors	DEXA	No DEXA
BMI 18.5 or less	32 (4%)	112 (3%)
Smoking Status		
Current	50 (6%)	249 (7%)
Quit	296 (36%)	1104 (31%)
Passive	1 (0.1%)	13 (0.3%)
Never	431 (53%)	1849 (52%)
Unknown	5 (1%)	40 (1%)
Alcohol Use	415 (51%)	1296 (36.3%)
3 or more drinks/day	7 (1%)	12 (0.3%)
<3 drinks/day	408 (50%)	1284 (36%)
Unknown	403 (49%)	2226 (63%)
Rheumatoid Arthritis	38 (5%)	72 (2%)
Type I Diabetes Mellitus	31 (4%)	146 (4%)
Osteogenesis Imperfecta	0	0
Hyperthyroidism	38 (5%)	128 (4%)
Hypogonadism	17 (2%)	417 (12%)
Chronic Liver Disease	88 (11%)	352 (10%)
Premature Menopause	4 (0.5%)	4 (0.1%)
Chronic Malnutrition	33 (4%)	177 (5%)
History of Fragility Fracture	40 (5%)	115 (3%)
Family History of Hip Fracture	1 (0.1%)	2 (0.05%)

Table 2. Descriptive Analysis of Osteoporosis (OP) Risk Factors

Variable	Pearson's Chi Square	Degrees of Freedom	p-value
Gender	100.42	1	<0.01
Age	2770.19	2	<0.01
Alcohol	54.94	2	<0.01
Rheumatoid Arthritis	17.45	1	<0.01
Hypogonadism	70.60	1	<0.01
History of Fragility Fracture	5.32	1	<0.025
Steroid Use	30.95	1	<0.01
Bisphosphonate Use	7.79	1	<0.01
Vitamin D Use	35.92	1	<0.01
Calcium Use	26.71	1	<0.01

Table 3. Pearson's Chi-Square Report of Statistically Significant Variables

tors were present in 51%, 5%, 2%, and 5%, respectively. Subjects with glucocorticoid [X2(1, N=4340)=30.93, p< 0.01], bisphosphonate [X2(1, N=4340)=7.79, p< 0.01], or vitamin D use [X2(1, N=4340)=35.92, p< 0.01] were also more likely to have DXA screening.

Conclusion: This investigation highlighted that osteoporosis screening for patients on AI therapy is low, despite the current guidelines. The osteoporosis risk factors associated with higher rates of screening were advanced age, alcohol use, rheumatoid arthritis, hypogonadism, and history of a fragility fracture. The rate of DXA screening was similar for patients with low BMI, tobacco use, type I diabetes mellitus, hyperthyroidism, liver disease, premature menopause, chronic malnutrition, and a family history of hip fracture. Males encompass nearly 13% of our population on AI therapy, and future studies are needed to understand the impact of AI treatment on bone health in men. More intense osteoporosis screening is needed for patients on AI therapy, especially for those with additional risk factors, and can be achieved through multidisciplinary collaboration.

Disclosure: M. White, None; **L. Barre**, None.

Abstract Number: 0124

Appropriate Timing of Denosumab Dosing and Subsequent Therapy After Discontinuation: An Academic Medical Center Experience

Hugo Raposo[1], Daniel Lindstrom[1] and Jonathan Cheah[2], [1]University of Massachusetts Medical School, Worcester, MA, [2]University of Massachusetts Medical School, Shrewsbury, MA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Denosumab, a monoclonal antibody that binds to the receptor activator of nuclear factor kappa-B ligand (RANKL) is a popular choice for osteoporosis therapy. However, it has been demonstrated that late

	All n=249	Endocrinology n=175	Rheumatology n=45
Female (n, %)	228 (92)	156 (89)	43 (96)
Age (years) (mean, SD)	75 (10)	75 (11)	77 (8)
Average number of doses of denosumab per individual (median, range)	3 (1-7)	3 (1-7)	2 (1-5)
Total number of doses received			
1 dose (n, %)	60 (24)	38 (22)	12 (27)
2 doses (n, %)	44 (18)	27 (15)	13 (29)
3 doses (n, %)	49 (20)	31 (18)	10 (22)
4 doses (n, %)	40 (16)	29 (17)	7 (16)
5 doses (n, %)	44 (18)	38 (22)	3 (1)
6 doses (n, %)	11 (4)	11 (6)	0 (0)
7 doses (n, %)	1 (0.4)	1 (0.6)	0 (0)
Average time between doses (months) (mean, SD)	6.4 (2.2)	6.3 (2.8)	6.5 (1.5)
Doses administered within 7 months (n, %)	446 (90)	351 (91)	56 (85)
Doses administered at month 8 or 9 (n, %)	21 (4)	13 (4)	5 (8)
Doses administered at month 10-12 (n, %)	11 (2)	6 (2)	5 (8)
Doses administered at >12 months (n, %)	16 (3)	14 (4)	0 (0)
>7 months after the last denosumab dose (n, %)	99 (40)	68 (39)	25 (56)
Patient deceased (n, %)	19 (19)	13 (19)	5 (20)
Transition plan documented (n, %)	7 (7)	4 (6)	3 (12)
No transition plan documented (n, %)	73 (74)	51 (75)	17 (68)

Table 1. Characteristics of Denosumab Prescribing

administration or discontinuation without change to a different osteoporosis therapy, results in a subsequent decline in bone mineral density (BMD) and the development of new vertebral fractures (often multiple). Recent guidance recommends that a repeat dose of denosumab or an alternative osteoporosis therapy is administered no later than 7 months after the prior denosumab dose. Therefore, the aim of the present study was to identify current practices regarding the timing of denosumab administration as well as subsequent treatment of osteoporosis after denosumab discontinuation at an academic medical center.

Methods: Pharmacy records for a single academic medical center were accessed to identify all dispenses of denosumab between October 1, 2017 and March 5, 2020. Individuals between 18 and 100 years of age, who had had at least one dose of denosumab dispensed were included, except for those whose denosumab was prescribed by an Oncologist or Urologist. The electronic medical record was then reviewed for age, specialty of the prescribing physician, total number and dates of denosumab injections. If denosumab was discontinued, it was recorded whether or not an alternative osteoporosis therapy was prescribed. T-tests and chi-squared tests were utilized to assess for any differences between those treated by Endocrinologists and Rheumatologists.

Results: 389 individuals were initially identified of whom 249 (92% female) met inclusion criteria (Table 1). Mean (SD) age was 75 (10) years. In 175 (70%) individuals, denosumab was prescribed by an Endocrinologist, compared to Rheumatology (45 individuals, 18%) and 29 (12%) by other specialties. The median number of doses of denosumab

administered per individual was 3 (range 1-7) with the mean time between doses 6.4 months (SD 2.2 months). 446 (90%) of all subsequent denosumab doses were administered within 7 months. There was no significant difference in the mean time between doses nor the proportion of individuals receiving their denosumab dose within 7 months between Endocrinology and Rheumatology (p=0.5 and 0.09, respectively). For 99 (40%) individuals, greater than 7 months had elapsed since their last denosumab dose. Of those, only 7 (7%) were clearly transitioned to an alternative osteoporosis therapy, most commonly zolendronate (5 individuals).

Conclusion: 90% of denosumab doses were administered within the recommended timeframe of 7 months with no significant difference between Endocrinologists and Rheumatologists. However, where denosumab was discontinued, whether knowingly or not, only 7% were prescribed an alternative osteoporosis therapy. Given this, a considerable number of individuals may be at risk of decline in BMD and incident vertebral fracture. Moving forward, additional work is required to understand the reasons for both late administrations, but more importantly the lack of alternative therapy upon discontinuation before specific interventions can be implemented to address these deficiencies.Table 1: Characteristics of Denosumab Prescribing

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Disclosure: H. Raposo, None; **D. Lindstrom**, None; **J. Cheah**, None.

Abstract Number: 0125

A Resident-Led Interdisciplinary Quality Improvement Initiative to Increase Osteoporosis Screening in an Urban Clinic

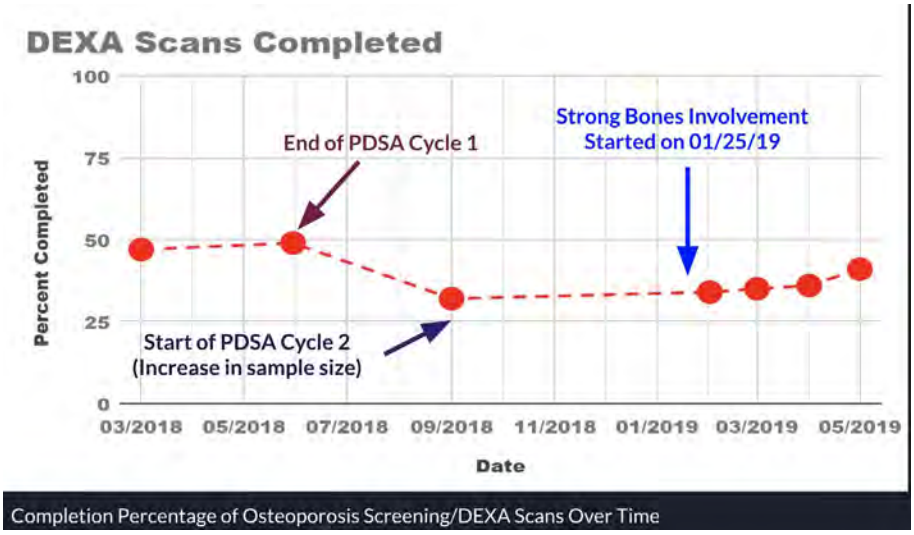
Catherine Teskin[1] and Hiba Sayed[2], [1]Christiana Care, Wilmington, [2]Christiana Care, wilmington, DE

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis is a major cause of morbidity and mortality in the United States. The USPSTF recommends screening all women age 65 and older or younger women with risk factors for osteoporosis.[2] Unfortunately, osteoporosis screening rates remain low nationwide.[3] In our residency clinic, the baseline screening rate for women age 65 and older was 47%. We aimed to increase this rate by 10% over a three month period.

Methods: Our root cause analysis identified provider, patient, and system level barriers to osteoporosis screening. Plan-Do-Study-Act (PSDA) cycle 1 targeted provider knowledge through didactic education and posters in the clinic space. PDSA cycle 2 identified patient barriers. We collaborated with an institutional nurse-led program called “Strong Bones” that has existing initiatives in place to detect and treat osteoporosis. We used a health registry embedded within our electronic medical record to identify patients from our clinic who were eligible for osteoporosis screening. A Strong Bones nurse then reached out to each patient to explain the need for screening and to help navigate barriers. We then tracked the rate of osteoporosis screening between PDSA cycles through the health registry and manually reviewed patient level data during a three month patient outreach period.

Results: After PDSA cycle 1, we saw a slight increase in our screening rate from a baseline of 46% (101/216) to 49% (106/216). During PDSA cycle 2, we identified and chose 138 patients eligible for osteoporosis screening to be contacted. 71 of these patients were called during the outreach period, and 11 scans were completed. Our screening rate



Completion Percentage of Osteoporosis Screening/DEXA Scans Over Time

at the beginning of cycle 2 was 34% (111/322) and increased to 36% (122/338). The most common barrier identified during this period was patient disinterest, though many were unreachable.

Conclusion: Results from PDSA-1 showed that resident education alone increased the number of DEXA scans ordered, but did not substantially increase completed screenings due to patient barriers. Furthermore, relying on "inreach" interventions targeting only the patients present at the office visit missed a large proportion the patient panel. PDSA cycle 2 addressed both of these issues. There was a substantial increase in DEXA completion and we were also able to quantify the barriers our patients faced in the process. Limitations included difficulty in obtaining reliable data. Additionally, ongoing changes to the health registry's patient attribution characteristics led to a lower rate of completed screening even though the total number of screenings increased. Although our intervention led to more patients having their screening completed, it was very time-intensive and would be difficult to sustain moving forward. Next steps consist of identifying ways to decrease system level barriers, such as through streamlined scheduling and same day appointments.

Disclosure: C. Teskin, None; **H. Sayed**, None.

Abstract Number: 0126

Immunophenotyping of Peripheral Blood Highlights an Association of Dysregulated Lymphocytes with Patients with Glucocorticoid-induced Osteonecrosis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Avascular necrosis (AVN) is a musculoskeletal condition that can result in significant pain and compromised quality of life. The diverse etiologies of AVN have been described; glucocorticoid (GC) use is the most common cause for non-traumatic AVN. However, the pathogenesis of GC-induced AVN has yet to be fully elucidated. While a wide range of the immunomodulatory effects of GC has been reported, little is known of the changes in circulating cellular phenotype for patients with GC-induced AVN. This study investigated the linkage between GC-induced AVN and altered immune homeostasis. We hypothesized that GC may differentially affect the phenotype of immune cells in AVN patients, which may serve as a measure for the systemic status of AVN patients.

Methods: Fifty-four AVN patients (47.7 ± 14.5 yr [mean ± SD]; female 26 and male 29) were enrolled for the study. Twenty-nine patients had received GC therapy and 41.3% of GC-induced AVN patients had SLE. The maximum dose of glucocorticoid in the GC-induced AVN group was 56.8 ± 22.5 mg/day. Average cumulative glucocorticoid was 42.8 ± 54.5 g. The non-GC AVN group included twenty-five patients with idiopathic AVN (40.0%), heavy alcohol use (36.0%), osteoarthritis (16.0%), and trauma (8.0%). There were no significant differences in mean age and BMI between the two groups. The GC-induced AVN group had a higher female-to-male ratio. Serum cytokines were measured by multiplex assay. Circulating immune cells were defined by cell surface markers and measured by flow cytometric analysis. Gene expression profiles from macrophages and T cells were also measured and analyzed.

Results: As the composition of innate and adaptive immune cells reflects the systemic status of the host, we measured CD14+ macrophages, myeloid dendritic cells (DCs), plasmacytoid DCs, B cells, and T cells (CD4+ and CD8+ T cells) in blood from the GC-induced AVN and non-GC-induced AVN groups. There was no difference in the number of macrophages, dendritic cells (DCs), pDCs, and B cells between the two groups. There was also no difference in the number of CD4+ T cells between the two groups, but we found the number of CD8+ cells in the GC-induced AVN group to be significantly higher than that of the non-GC AVN group ($p = 0.0252$). To determine if the increased count of CD8+ T cells in the GC-induced AVN group resulted from GC therapy, we also compared the number of CD8+ T cells in the GC-induced AVN group to that of the GC-treated patients who did not have AVN. The number of CD8+ T cells was higher for GC-induced AVN patients ($p = 0.0008$). Accordingly, a CD4/CD8 T cell ratio was significantly lower for this group ($p = 0.0063$). In addition to the cellular phenotype, we also found that serum TNF-α and CXCL10 were significantly higher in the GC-induced AVN group compared to those of the non-GC induced AVN group.

Conclusion: Our findings revealed the status of circulating immune cells in GC-induced AVN patients and found that the subset of lymphocytes significantly increased in the GC-induced AVN group. Our study suggests that lymphocytes in the GC-induced AVN group may escape the immunosuppressive effect of GC, and we believe further study is needed to identify the mechanism of altered immune profiles in GC-induced AVN.

Disclosure: K. Kaneko, None; **H. Chen**, None; **A. Krez**, None; **S. Zeng**, None; **P. Park**, None; **Y. Lee**, None; **T. Fujii**, None; **H. Kim**, None; **S. Mun**, None; **S. Bae**, None; **T. Pannellini**, None; **J. Lane**, None; **D. Hansen**, None; **D. Mintz**, None; **R. Bockman**, None; **E. Stein**, Novartis, 2, Radius, 2; **K. Park-Min**, None.

Abstract Number: 0127

Biochemical Algorithm to Identify Individuals with *ALPL* Variants Between Subjects with Persistent Hypophosphatasaemia

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Osteoporosis & Metabolic Bone Disease Poster

Session Type: Poster Session A

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Background/Purpose: Studies show a long diagnostic delay in Hypophosphatasia (HPP) and the accessibility for the genetic testing is not always possible. Our previous cross-sectional study (Tornero et al. OJRD (2020) 15:51) revealed alkaline phosphatase (ALP) levels < 25 IU/L seemed to be useful to identify individuals with *ALPL* variants

Table 1. Regression logistic models for the detection of genetic *ALPL* variants including ALP, PLP and PEA cut-off levels.

	Biochemical variables	R^2 Nagelkerke	B	Odds Ratio (95% CI:)	p-value	Diagnostic utility measures
Model 1:	ALP<25	0.161	ALP: 1.935 C: -0.325	6.923 (1.81-26.39)	0.005	S: 36.6 E: 92% PPV: 83% NPV: 58%
Model 2:	ALP<25 + PLP>180	0.461	ALP: 1.483 PLP 2.593 C: -1.283	4.407 (0.94-20.5) 13.364 (4.01-44.5)	0.059 0.000 0.001	S: 29% E: 97% PPV: 92% NPV: 56%
Model 3:	ALP<25 + PLP>180 + PEA>35	0.526	ALP: 1.875 PLP: 2.087 PEA: 1.486 C: -1.619	6.521 (1.07-39.6) 8.06 (2.18-29.9) 4.4 (1.03-18.9)	0.042 0.002 0.045 0.000	S: 22% E: 100% PPV: 100% NPV: 55%

Table 1

among subjects with persistent hypophosphatasaemia. These data highlight the importance of establishing a specific biochemical profile and the value of including TNSALP substrates is a matter of interest. First, to confirm our previous results in a one-year follow-up of a longitudinal study. Second, to determine the value of including TNSALP substrates (serum pyridoxal phosphate-PLP-and urinary phosphoetanolamine-PEA) in a specific biochemical profile to detect variants in *ALPL* in individuals with persistent low ALP levels.

Methods: Biochemical parameters of subjects included in a prospective longitudinal study conducted at La Paz Hospital were employed. Subjects were divided into two groups according to their genetics (+ GT or -GTgroup). Substrates were determined at baseline and at one-year visit and ALP levels also at six-months. To confirm the threshold, diagnostic utility measures were calculated at the 3 visits. ROC curves were employed to determine PLP and PEA best cut-off levels. Hierarchical binary logistic regression analysis was used to determine how well the different models fit (Nagelkerke R^2). Finally, diagnostic utility measures for each model were calculated.

Results: Using ALP data from the three visits, Specificity (E) ranged between 84-91%; positive predictive value (PPV), 76-87% and +LR 3-6.1%. The ROC curves revealed cut-off PLP levels with the best combination of S and E for PLP were 180 nmol/L (S: 72%, E:86%) and for PEA, 35 (S:58%, E89%) umol/g creat. The regression model showed an OR (95% IC) for ALP< 25 IU/L, PLP >180 and PEA >35 of 6.52 (1.07-39.6), 8.06 (2.2-29.9) and 4.4 (1.03-18.9). Compared to the model just including ALP, R^2 improved (0.161 to 0.526) when substrates were added (E and PPV:100% and S:22%), especially when PLP was included (Table 1).

Conclusion: This study confirms that ALP levels < 25 IU/L could be useful to identify individuals displaying *ALPL* variants. Additionally, the combination of this threshold with the proposed cut-off levels of its substrates, especially PLP, have shown a very high specificity to detect the disease and could help vigorously in the diagnostic work-up of HPP.

Disclosure: C. Tornero, None; **V. Navarro-Compán**, Novartis Pharma, 1, 5, 8, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, UCB, 5, 8; **J. Tenorio**, None; **S. Garcia-Carazo**, None; **A. Buño**, None; **I. Monjo**, None; **C. Plasencia**, None; **J. Iturzaeta**, None; **P. Lapunzina**, None; **K. Heath**, None; **A. Balsa**, BMS, 9; **P. Aguado**, Alexion Pharmaceuticals, 2, Alexion Pharmaceuticals, 2.

Abstract Number: 0128

Short-Term Monitoring of Denosumab Effect in Breast Cancer Patients Receiving Aromatase Inhibitors Using Radiofrequency Echographic Multi-Spectrometry (REMS) Technology on Femoral Neck

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SESSION INFORMATION

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Background/Purpose: The aim of the study was to carry out a short-term monitoring of the effect of aromatase inhibitors (AI) and Denosumab on bone health in post-menopausal women with breast cancer (BC) with positive estrogen receptor through a bone densitometry performed with Radiofrequency Echographic Multi-Spectrometry (REMS) and Dual-Energy X-ray Absorptiometry (DXA).

Methods: A group of patients (Group A) received AI adjuvant therapy annually and 60 mg Denosumab every 6 months. The other group (Group B) received annual AI therapy only. All patients underwent a femoral neck scan with REMS and DXA before receiving the first AI therapy (T0) and 12 months after (T1). Only REMS scans were repeated after additional 6 months (T2).

The results were analyzed in terms of relative changes in bone mineral density (BMD) compared to the basal value obtained at T0. The analysis of the results was carried out by balancing the two groups by age.

Results: The results of 200 patients were analyzed. As expected, for Group A (assuming Denosumab) an increasing trend in BMD was observed, whereas a decreasing trend in BMD was found for Group B both with REMS and DXA.

The difference between REMS and DXA obtained for patients in each group at each time point was not statistically significant. Instead, the difference between Group A and Group B is statistically significant for DXA (at T1) and REMS (at T1 and T2).

Conclusion: The effect of Denosumab in reducing the risk of fracture in BC patients treated with AIs is well known. The densitometric techniques currently available are not able to monitor BMD in the short term, since the minimum time between two consecutive measurements is at least 1 year [1]. REMS technology, on the other hand, has demonstrated high performance in terms of precision and repeatability of BMD measurement, and the consequent low least significant change (LSC) value [2]: consequently, it might overcome the limit of current densitometric techniques, allowing a repeated exam at 6 months. The results of this study demonstrate the feasibility of short-term follow-up using REMS technology with femoral neck scans.

Disclosure: R. Forcignanò, None; **F. Lombardi**, None; **M. Ciccarese**, None; **E. Quarta**, None; **A. Grimaldi**, None; **L. Quarta**, None; **D. Ciardo**, None; **E. Casciaro**, None; **P. Pisani**, None; **F. Conversano**, None; **M. Muratore**, None; **S. Casciaro**, None.

Abstract Number: 0129

Glucocorticoid-Induced Osteoporosis in Patients with Chronic Inflammatory Rheumatic Diseases: A Multivariate Linear Regression Analysis Identifying Factors Affecting Bone Mineral Density

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
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Session Time: 9:00AM–11:00AM

Table 1: Demographics, glucocorticoid therapy and bone status

Demographics	
Age in years, mean *(±SD)*	62.1 (±13.2)
Female patients, *no. (%)*	819 (75.1)
Past pregnancies, *no. (% of total women)*	665 (81.2)
Menopause, *no. (% of total women)*	717 (87.5)
BMI in kg/m², *mean (±SD)*	27.1 (±5.6)
Glucocorticoid therapy	
Patients with current GC therapy, *no. (%)*	708 (64.9)
≤ 2.5 mg/day, *no. (% of total current GC)*	360 (37.0)
> 2.5 and < 5 mg/day	79 (8.1)
≥ 5 and < 7.5 mg/day	274 (28.2)
≥ 7.5 and < 10 mg/day	105 (10.8)
≥ 10 mg/day	155 (15.9)
Life-time total GC dose in g, *mean (±SD)*	17.8 (±24.6)
Duration of GC therapy in years, *mean (±SD)*	7.8 (±8.5)
Mean GC dose, *(±SD)*	14.8 (±36.4)
Bone Status	
T-score, mean *(±SD)*	
Spine	-0.72 (±1.51)
Normal, *no. (%)*	524 (51.6)
Osteopenia	387 (38.1)
Osteoporosis	104 (10.2)
Left femur neck	-1.12 (±1.09)
Normal	410 (41.5)
Osteopenia	486 (49.1)
Osteoporosis	93 (9.4)
Right femur neck	-1.09 (±1.12)
Normal	409 (41.5)
Osteopenia	471 (47.8)
Osteoporosis	105 (10.8)
Osteoporotic Fractures, *no. (%)*	
Vertebral	67 (6.1)
Non-vertebral	296 (27.1)

Table 2: Disease specific factors

Disease activity	
HAQ, *mean (±SD)*	0.78 (0.80)
S-CRP mg/l [< 5], *median [IQR]*	2.4 [0.8;6.7]
Disease duration (yrs), mean (±SD)	12.0 (±10.6)
Need for professional care, *no. (%)*	464 (42.5)
Rheumatic disease group, *no. (%)*	
Rheumatoid Arthritis	393 (36.0)
Connective tissue diseases	250 (22.9)
Vasculitides	155 (14.2)
Spondyloarthropathies	147 (13.5)
Other	146 (11.4)
Underweight (BMI < 18.5 kg/m²), *no. (%)*	28 (2.6)
Family History, *no. (%)*	
For osteoporosis	218 (20.0)
For osteoporotic fractures	106 (9.7)
Co-medication, *no. (%)*	
Antihyperuricemic drugs	42 (3.8)
Proton pump inhibitors	465 (42.6)
NSAIDs	223 (20.4)
Oral antidiabetics	67 (6.1)
Insuline	58 (5.3)
Estrogens (female pts. only)	19 (2.3)
Antidepressants	73 (6.7)
Concomitant diseases, *no. (%)*	
Renal insufficiency	77 (7.1)
Diabetes	129 (11.8)
Hyperuricaemia/Gout	54 (4.9)
Depression	89 (8.2)
Hyperthyroidism	53 (4.9)

Table 3: Preventive factors for osteoporosis

Treatment of underlying disease		
Biologics, no. (%)	309	(28.2)
TNF-alpha antagonists, no. (% of biol.)	129	(42.4)
IL-6R-Antagonists	41	(13.3)
Rituximab	50	(16.2)
Abatacept	23	(7.4)
IL-1 antagonists	6	(1.9)
IL-17 and IL-12/23 Antagonists	49	(15.9)
csDMARDs	630	(57.7)
tsDMARDs	25	(2.3)
Anti-osteoporotic therapy		
Calcium supplementation	51	(4.7)
Vitamin D supplementation	850	(77.9)
Bisphosphonates	137	(12.6)
Strontium ranelate	1	(0.1)
Teriparatide	4	(0.4)
Denosumab	34	(3.1)
Behavioral		
Sun exposure (>30min/day)	501	(45.9)
Non-smoker / former smoker	900	(82.5)
No Alcohol consumption	474	(43.4)
Regular exercise	486	(44.5)
Laboratory tests, *median [IQR]*		
25-hydroxy vitamin D nmol/l [50 – 150]	79.1	[59.6;95.6]
Vitamin D deficiency, no. (%)	146	(13.4)
S-osteocalcin ng/ml [11 – 46.0]	12.3	[8.1;18.0]
S-BAP µg/l [5.5 – 38.0]	16.7	[12.7;21.6]
S-AP U/l [35 – 130]	65	[54;80]
Gamma-GT U/l [5 – 61]	24.0	[17;42]
Urine Desoxypyridinoline nmol/l [< 64]	42.5	[23;74]

Background/Purpose: Rheumatic diseases are associated with increased systemic bone loss and fracture risk related to chronic inflammation, disease-specific, general and demographic risk factors as well as treatment with glucocorticoids (GC). The purpose of this study was to investigate the prevalence of osteoporosis and fragility fractures in patients with inflammatory rheumatic diseases and to analyze the impact that treatment with GCs, other known risk factors and preventive measures have on bone health in these patients.

Methods: Rh-GIOP is an ongoing prospective observational study collecting and analyzing disease- and bone-related data from patients with chronic rheumatic diseases or psoriasis treated with GCs. In this cross-sectional analysis, we evaluated the initial visit of 1091 patients.

A multivariate linear regression model with known or potentially influential factors adjusted for age and sex was used to identify predictors of BMD as measured by dual-energy X-ray absorptiometry (DXA). Multiple imputation was applied for missing baseline covariate data.

The following T-scores were considered: i) minimum overall T-score, ii) minimum T-score of the lumbar spine and iii) minimum T-score of the femoral neck. P-values lower than 0.05 were considered significant; no adjustment for multiple testing was done.

Table 4: Variables with at least one significant result in one of the 3 models for minimal (min.) T-score at any site, min. T-score at the lumbar spine or min. T-score at the femoral neck in the multivariate linear regression model in all patients. Significant impact factors are highlighted in bold.

	MIN. T-SCORE Reg. coefficient (95%CI)	*p-value*	MIN. LUMBAR T-SCORE Reg. coefficient (95%CI)	*p-value*	MIN. T-SCORE FEMORAL NECK Reg. coefficient (95%CI)	*p-value*
Age at enrollment	**-0.012 (-0.018;-0.006)**	***0.000***	-0.008 (-0.017;0.00)1	*0.069*	**-0.014 (-0.020;-0.008)**	***0.000***
Male sex	**-0.378 (-0.656;-0.100)**	***0.008***	-0.049 (-0.442;0.345)	*0.809*	**-0.382 (-0.656;-0.108)**	***0.006***
Menopause	**-0.430 (-0.686;-0.174)**	***0.001***	**-0.527 (-0.892;-0.162)**	***0.005***	**-0.367 (-0.619;-0.114)**	***0.004***
BMI	**0.067 (0.055;0.079)**	***0.000***	**0.061 (0.044;0.078)**	***0.000***	**0.070 (0.058;0.082)**	***0.000***
Sun exposure (>30min/day)	0.057 (-0.065;0.179)	*0.361*	0.075 (-0.099;0.249)	*0.400*	**0.129 (0.008;0.250)**	***0.037***
Alkaline phosphatase	**-0.006 (-0.009;-0.004)**	***0.000***	**-0.007 (-0.011;-0.003)**	***0.001***	**-0.005 (-0.008;-0.003)**	***0.000***
Gamma-GT	**0.002 (0.000;0.004)**	***0.015***	0.002 (-0.001;0.004)	*0.155*	0.002 (0.000;0.003)	*0.051*
Bisphosphonates	**-0.509 (-0.694;-0.325)**	***0.000***	**-0.600 (-0.868;-0.332)**	***0.000***	**-0.482 (-0.667;-0.297)**	***0.000***
Denosumab	**-0.609 (-0.956;-0.261)**	***0.001***	**-0.523 (-1.020;-0.026)**	***0.039***	**-0.357 (-0.699;-0.014)**	***0.041***
GC current dose	**0.003 (0.001;0.005)**	***0.008***	0.002 (-0.002;0.005)	*0.345*	**0.003 (0.001;0.005)**	***0.010***
GC cumulative dose	0.000 (0.000;0.000)	*0.909*	0.000 (0.000;0.001)	*0.487*	0.000 (0.000;0.000)	*0.779*
NSAIDs	**0.168 (0.019;0.317)**	***0.028***	0.210 (-0.002;0.423)	*0.053*	**0.202 (0.053;0.350)**	***0.008***
Proton pump inhibitors	**-0.187 (-0.313;-0.061)**	***0.004***	**-0.304 (-0.486;-0.121)**	***0.001***	**-0.174 (-0.299;-0.049)**	***0.006***
Hyperthyroidism	0.257 (-0.025;0.539)	*0.074*	0.126 (-0.277;0.529)	*0.540*	**0.351 (0.071;0.632)**	***0.014***
HAQ	-0.093 (-0.189;0.003)	*0.057*	-0.021 (-0.158;0.116)	*0.762*	**-0.132 (-0.227;-0.037)**	***0.007***

Results: In the total cohort of 1091 patients (75% female of which 87.5% were postmenopausal) with a mean age of 62.1 (±13.2) years, the prevalence of osteoporosis by DXA was 21.7%, while fragility fractures have occurred in 31.2% of the study population (6.7% vertebral, 27.7% nonvertebral). Current GC therapy was common (64.9%), with a median daily dose of 5.0mg [0.0;7.5], a mean life-time total GC dose of 17.7g (±24.6), and a mean GC therapy duration of 7.8 years (±8.5). Bisphosphonates were the most commonly used anti-osteoporotic drug (12.6%).

BMD as expressed by min T-Score at all measured sites was predicted by age, sex, menopause and BMI, Bisphosphonate and Denosumab treatment, as well as current GC therapy, proton pump inhibitor intake and use of NSAIDs. Current GC dose showed a positive correlation with BMD. Of measured bone-specific laboratory parameters, alkaline phosphatase levels and Gamma-GT were determinants of BMD. BMD was neither predicted by duration of GC treatment, GC cumulative dose nor by treatment with DMARDs or other factors relating to disease activity. Determinants for BMD varied slightly at the anatomical site with HAQ, hyperthyroidism and sun exposure affecting only femoral T-Score.

Conclusion: This cross-sectional analysis of our cohort study revealed a high prevalence of osteoporosis by DXA and fragility fractures. We identified and corroborated predictive variables of BMD that warrant consideration in the management of patients with rheumatic diseases.

Disclosure: E. Wiebe, None; **D. Freier**, None; **D. Huscher**, None; **S. Hermann**, None; **R. Biesen**, None; **F. Buttgereit**, AbbVie, 8, Eli Lilly, 8, Pfizer, 8, Roche, 8.

Abstract Number: 0130

The Prevalence of Osteoporosis in Individuals with Osteoarthritis: A Systematic Review

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Osteoporosis & Metabolic Bone Disease Poster

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Background/Purpose: There is controversy regarding the relationship between osteoarthritis (OA) and osteoporosis (OP). While OA may be associated with increased bone mineral density (BMD) due to increased weight, evidence exists that the incidence of OP may be increased in patients with OA.

Our purpose was to determine whether the prevalence of OP is increased in patients with OA, compared to age and sex-matched populations.

Methods: We conducted a systematic literature review using the databases PubMed, Embase, Scopus, and Web of Science, including articles that that analysed the frequency, rate, prevalence, incidence, risk, or excess risk of OP in patients with OA compared to age and sex-matched comparison groups (controls). Articles with fewer than 200 participants, and those without controls were excluded. Two reviewers conducted title and abstract screening.

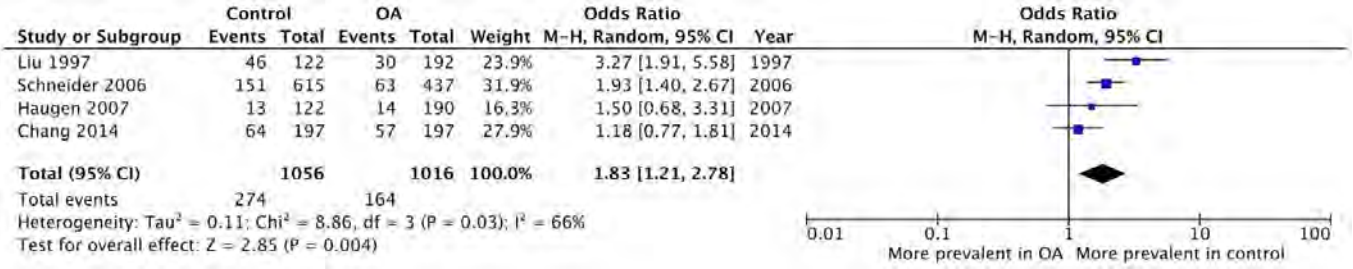

Figure 1. Prevalence of OP in OA vs. control in men and women with BMD measured at any site (lumbar spine, total hip, femoral neck) with confirmed diagnosis of OA at any site (lumbar spine, knee, hand)

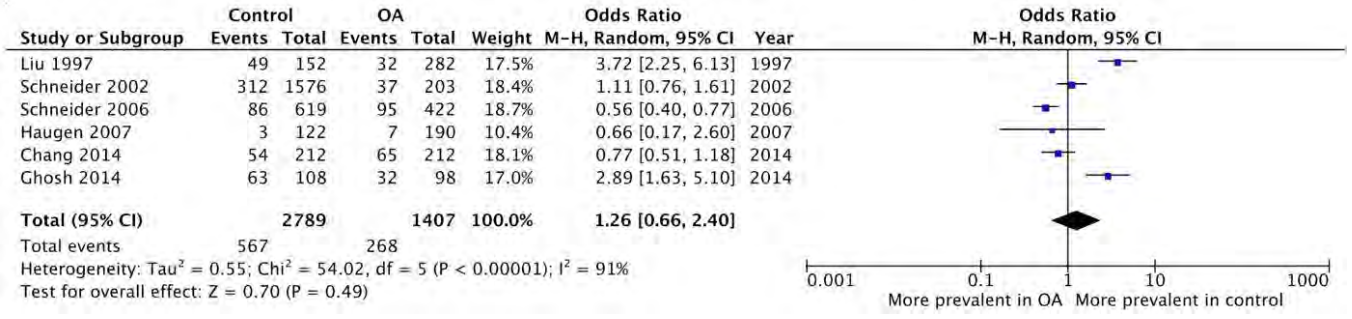

Figure 2. Prevalence of OP in OA vs. control in in men and women with BMD measured at the lumbar spine with OA at any site

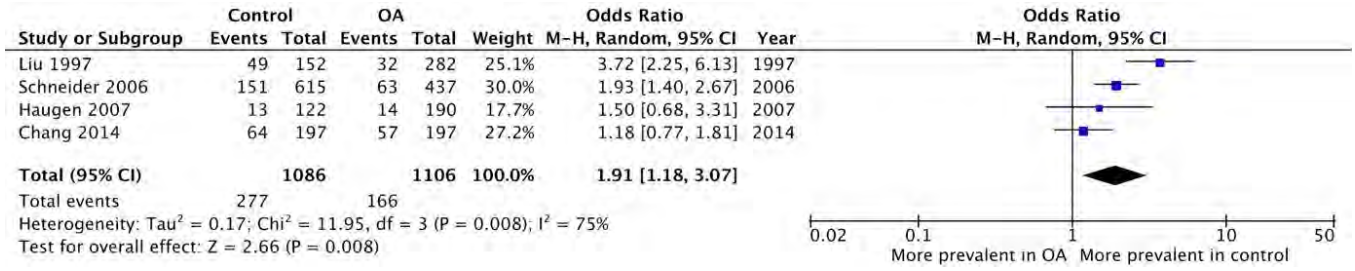

Figure 3. Prevalence of OP in OA vs. control in women with BMD measured at the lumbar spine with OA at any site

Results: Of 2772 unique articles, 49 articles were chosen for full article screening, and 6 articles met the inclusion criteria of our present study. These articles showed that there was no significant difference in prevalence of OP in the OA group compared to the respective control group in both men and women, when BMD was measured at femoral neck, hip or lumbar spine (Figure 1).

Subgroup analysis of both men and women whose BMD was measured at the lumbar spine showed higher prevalence of OP in the control group compared to the OA group (Figure 2). This difference remained significant in the subsequent subgroup analysis of only women whose BMD was measured at the lumbar spine (Figure 3).

Conclusion: Our findings suggest no significant difference in prevalence of OP in subjects with OA compared to those without OA; this suggests that OA may not have protective effects on development of OP. Therefore, diagnosis of OA should not preclude patients from being investigated for OP. OA may present with atrophic features associated with increased frequency of osteoporotic fractures compared to OA with osteophytosis; this distinction may be important to consider for future studies.

Disclosure: T. Varghese, None; **A. Pirshahid**, None; **D. Kim**, None; **Y. Li**, None.

Abstract Number: 0131

Analysis of the Total Body Composition in a Cohort of Patients with Elderly Onset Arthritis

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SESSION INFORMATION
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Background/Purpose: Inflammatory arthritis in the elderly leads to greater comorbidity than that of the young patients, however, there are few data on body composition in this population.

Objective: To analyze the total body composition measured by dual-energy x-ray absorptiometry (DXA) in patients with arthritis in the elderly, its relationship with the activity disease scores and its evolution at 12 months.

Table 1: Total body composition parameters

Variable	RA		PMR		Control
	Baseline	12 months	Baseline	12 months	
Age (years)	74±7		77±5		73±8
Weight (kgs)	73±12	73±12	63±14 +	66±13	73±13
Size (cm)	161±8	159±9	153±8	153±8	161±13
BMI (Kg/cm2)	28±5	29±5	28±5	28±4	28±4
Abdominal perimeter (cm)	101±12	101±12	98±11	99±9	-
BMD total (g/cm2)	1,132±0,137	1,134±0,136	1,038±0,149 +	1,081±0,199	1,124±0,159
Fat mass (g)	29506±8391	29784±8697	28364±8331	32232±6215	28976±7274
Lean mass (gr)	40555±6836	39822±6798*	34459±6361 + ţ	36941±6273	41669±9927
Bone mass (gr)	2129±460	2206±459	2219±420	1928±410	2319±655

*p<0.05 compared to 12 months. + p< 0.05 compared to control group. ţ p<0.05 compared to patients with RA

Method: Prospective observational study of patients with elderly onset arthritis (> 65 years) recruited between January 2013 and December 2014 (ARTIEL cohort). Patients with previous known osteoporosis (OP) and/or antiosteoporotic treatment were excluded. We collected clinical-analytical variables, anthropometric data (weight, height , body mass index (BMI) and abdominal perimeter) and total body composition measures that include fat mass in grams (g), lean mass (g), and bone mineral density (BMD; g/cm2), at baseline (without treatment) and at 12 months. Data was compared with a control group without arthritis. The statistical study was performed using SPSS.

Results: We included 73 patients (37M: 36V), with a mean age of 75±7 years in the study. Most were diagnosed with rheumatoid arthritis (RA; n=43), followed by polymyalgia rheumatica (PMR; n=16) and others (n=14). 31.9% had densitometric OP at baseline and 31.3% at 12 months. When assessing comorbidities: 38.4% were diabetic and 33% were obese (BMI >30 Kg/cm2). Total body composition data is shown in the Table 1.

At the time of inclusion, patients with PMR had less lean mass than the control group, with no significant difference observed between the RA group and the control group. When comparing PMR vs RA, patients with PMR had lower weight, total BMD and lean mass than patients with RA.

When assessing the complete cohort (n=73), no significant changes were observed in the evolution of total body composition at 12 months. However, a significant loss of lean mass was observed in the subpopulation of RA patients at 12 months of follow-up (p=0.017), while patients with PMR showed no change in total body composition.

In the RA group, there was a negative correlation between lean mass and activity scores (DAS28PCR: r=-0.370, p=0.017; DAS28VSG: r=-0.401, p=0.009) at the time of patient inclusion in the study; while fat mass was positively correlated with DAS28VSG (r=0.429, p=0.005) and abdominal circumference (r 0.835; p< 0.001). In the group of patients with PRM, there was a positive correlation between fat mass and abdominal circumference (r=0.900; p< 0.001).

Conclusion: Patients with RA in the elderly present a significant loss of lean mass at 12 months. In addition, lean mass in these patients negatively correlated with disease activity scores, suggesting a relationship between inflammation and the changes in body composition. It should be noted that patients with PMR had a lower lean mass at the time of diagnosis, so we cannot rule out the possibility that they may have lost muscle mass before inclusion in the study.

Disclosure: A. Brandy García, None; **M. Martinez-Morillo**, None; **A. Prior**, None; **R. Serrano**, None; **L. Mateo**, None; **M. Guma**, None; **L. Gifre**, None.

Abstract Number: 0132

Prevalence of Osteoporosis and Fragitlity Fractures Is Not Different Between ACPA Positive Patients Compared to ACPA Negative Patients in a Real World Setting, Despite Longer Disease Duration and Glucocorticoid-Treatment

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Osteoporosis & Metabolic Bone Disease Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with increased systemic bone loss, leading to a high risk for hip, vertebral and non-hip, non-vertebral fractures. Especially ACPA positivity is considered a risk factor for local bone erosions and systemic bone loss.

The purpose of this study was to compare ACPA positive versus ACPA negative RA patients in terms of the prevalence of osteoporosis and fragility fractures and to identify differences in underlying risk factors that influence bone health.

Methods: Rh-GIOP is an ongoing prospective observational study collecting and analyzing disease- and bone-related data from patients with chronic rheumatic diseases or psoriasis treated with glucocorticoids (GC). In this cross-sectional analysis, we performed a matched-pair analysis, matching 114 ACPA positive to 114 ACPA negative RA patients according to age (5-year-steps), sex, and body mass index (BMI, 2-unit-steps). Descriptive analyses were performed, with values displayed as mean ± standard deviation for continuous variables. Non-parametric tests were used at a two-sided significance level of 5% to compare differences in underlying and potential risk factors without adjustment for multiple testing.

Results: At same mean age (63.9 ±10.2 years) and BMI (27.9 ±5.6kg/m^2), the matched groups had a female proportion of 82.5%. APCA positive patients had a significantly longer mean disease duration (13.9 vs 9.9 years, $p< 0.001$), a higher mean cumulative GC-dose (22.3 vs 13.2g, $p< 0.01$) and mean duration of GC therapy (10.1 vs 6.6 years, $p< 0.01$). There was no significant difference in the prevalence of osteoporosis as defined by dual-energy X-ray absorptiometry (DXA) (18.4 vs 20.2%), nor in the prevalence of vertebral (7.0 vs 5.3%) or non-vertebral fractures (31.6 vs 29.8%). C-reactive protein levels as a marker of disease activity were significantly higher in ACPA positive patients (mean: 8.8 vs 4.3mg/l, $p= 0.02$), while mean disease activity score (DAS)28 levels were slightly lower in ACPA positive patients (2.4 vs 2.7, $p= 0.05$). No difference in health assessment questionnaire (HAQ) was found. RA-specific treatments were similar, especially concerning current daily GC-dose (8.6mg vs 7.1mg/day), except for Rituximab and targeted synthetic disease modifying anti-rheumatic drugs (DMARDs) which were more commonly used in ACPA

positive patients (9.6 vs 2.6%, p=0.05) and (5.3 vs 0%, p=0.029), respectively. ACPA positive patients did not differ significantly from ACPA negative patients in specific anti-osteoporotic treatment, nor in the prevalence of comorbidities or concomitant medication. There were no significant differences in bone-specific laboratory parameters.

Conclusion: In a cross-sectional analysis of our cohort, the prevalence of osteoporosis and fragility fractures was similar between ACPA positive and ACPA negative RA patients, despite longer disease duration and GC-treatment in ACPA positive patients. This is remarkable since it implies that ACPA negative patients are at a similar risk for osteoporosis and associated fractures.

Disclosure: E. Wiebe, None; **D. Freier**, None; **D. Huscher**, None; **G. Dallagiacoma**, None; **S. Hermann**, None; **R. Biesen**, None; **G. Burmester**, AbbVie, 5, 8, Pfizer, 5, 8, Gilead Sciences, Inc., 5, 8, Eli Lilly, 5, 8, Novartis, 5, Celgene, 5; **F. Buttgereit**, AbbVie, 8, Eli Lilly, 8, Pfizer, 8, Roche, 8.

Abstract Number: 0133

Pharmacist-Driven Clinic Development for Patients with Incidental Vertebral or Hip Fractures

Julie Ferm[1], Lanh Dang[1] and Gurjit Kaeley[2], [1]UF Health Jacksonville, Jacksonville, FL, [2]University of Florida College of Medicine - Jacksonville, Jacksonville, FL

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Osteoporosis & Metabolic Bone Disease Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Non-traumatic vertebral and hip fractures are detrimental complications of osteoporosis and those with a previous fracture have double the risk of subsequent fractures. The objective of this quality improvement (QI) project was to determine the baseline characteristics that may have contributed to the vertebral or hip fracture and determine if bone health was optimized subsequent to the fracture. Our institution determined the need for a pharmacist-driven clinic to assist patients with incidental vertebral and hip fractures receive appropriate follow-up care to prevent future fractures. This analysis completes the initial analysis that focused on patients who had an outpatient prednisone prescription prior to admission.

Methods: Data was retrospectively collected from the electronic health record for patients aged 45 and older admitted to UF Health Jacksonville for an active vertebral or hip fracture diagnosis between January 1, 2017 and January 31, 2019. Traumatic injuries were excluded. Retrospective chart review could occur dating back to January 2014 for completeness. Data on patient demographics, any medication that may affect bone health (e.g. steroids, calcium and vitamin D products, bisphosphonates, etc.), DXA scans, and pertinent labs were collected.

Results: A total of 287 patients were admitted 296 times between January 1, 2017 and January 31, 2019. Of these, 100 patients were screened and 33 patients were excluded. For the 67 hospitalized patients included in this analysis, 44 (65.7%) had a hip fracture and 23 (34.3%) had a vertebral fracture. A majority, 62.7%, were female with a mean age of 67 years old (range 46-97 years old). A total of 4 patients (6%) had a DXA scan prior to admission and 7 patients (10%) had a DXA scan after admission. No patient analyzed had chronic glucocorticoid dose ≥ 5 mg/day prednisone equivalent for greater than 3 months. A total of 17 patients had prednisone bursts with 23.5% of patients having cumulative burst doses between 10-100 mg, 52.9% patients between 101-500 mg, 5.9% patients between

501-1000 mg, and 17.7% patients > 1000 mg. Patients were also on other medications that may affect bone health with the highest rates of concomitant medication use being proton pump inhibitors 43.3%, antiepileptics 40.3%, serotonergic receptor inhibitors 31.3%, and levothyroxine 16.4%. Only 3% of patients were on a bisphosphonate prior to admission and 3% were newly started after admission. One patient was on denosumab prior to and after admission. Baseline vitamin D deficiency observed in 25.4% of patients.

Conclusion: In this convenience sample of patients with an active non-traumatic vertebral or hip fracture prior to admission, the rate of baseline DXA scan was low (6%) and after admission DXA (10%). The rate of pharmacologic antiresorprtive therapy after admission was 7.5%. The goal in development of this novel pharmacist – driven care pathway and clinic is to create a post-discharge process for patients admitted to the hospital for vertebral or hip fractures to optimize bone health by mitigating modifiable risk factors and increasing appropriate osteoporosis medication prescriptions to reduce the future risk of fractures.

Disclosure: J. Ferm, None; **L. Dang**, None; **G. Kaeley**, Novartis Pharmaceuticals Corporation, 5.

Abstract Number: 0134

The Impact of Exercise on Sleep in People with Rheumatoid Arthritis: A Pilot Randomised Controlled Trial

Sean McKenna[1], Laura Comber[2], Alan Donnelly[3], Alexander Fraser[4], Bente Appel Esbensen[5] and Norelee Kennedy[3], [1]University of Limerick, Mallow, Cork, Ireland, [2]HIQA, Limerick, Limerick, Ireland, [3]University of Limerick, Limerick, Limerick, Ireland, [4]University College Limerick, Limerick, Limerick, Ireland, [5]University of Copenhagen, Glostrup, Hovedstaden, Denmark

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Poor sleep quality and reduced sleep duration are prevalent complaints in people with RA. These in turn may further deteriorate functional ability and reduce exercise levels. Current rheumatology guidelines recommend exercise as a key component in the management of people with RA however, what is lacking is its impact on sleep. Purpose of this pilot randomised controlled trial was to obtain reliable estimates regarding recruitment rates; participant retention; protocol adherence and possible adverse events, in addition to producing estimates of the potential effect sizes of the intervention on changes in outcomes of sleep duration; sleep quality and disturbances; pain; depression; anxiety; functional limitation; disease activity and fatigue.

Methods: Participants were recruited in person at weekly rheumatology clinics at a University Hospital and through self-selected social networking. They were randomised to either a walking based exercise intervention consisting of 28 walking sessions, with 1 per week being supervised by a trained physiotherapist, spread over 8 weeks (2-5 times/week), or a control group who received advice on the benefits of exercise for people with RA. Ethical approval was received. Descriptive statistics and t-tests were used to analyse the data with SPSS v22.

Results: One hundred and one (101) people were identified, with 36 contacting through social networking. Of these, 24 met the eligibility criteria, with 20 being randomised (18% recruitment; 100% female; mean age 57 (SD 7.3 years). Ten exercise participants (100%) and 8 controls (80%) completed final assessments, with both groups being equivalent for all variables at baseline. Exercise participants completed 87.5% of supervised sessions and 93% of unsu-

pervised sessions. No serious adverse events were related to the intervention and through semi-structured interviews the intervention was highly accepTable to exercise participants. Pittsburgh Sleep Quality Index (PSQI) global score showed a significant mean improvement between exercise group -6.6 (SD 3.3) compared to control -0.25 (SD 1.1) (p=0.012); PSQI subcomponent sleep duration showed a significant improvement in mean hours between the exercise group 1.65 (SD 0.39) hours and control 0.56 (SD 0.46) hours (p=0.021); PSQI subcomponent sleep quality indicated those in exercise group improved their sleep quality from fairly bad/poor to fairly good/very good, while those in control reported no change at fairly bad/poor. Global rating of change indicated exercise participants reporting their sleep was minimally/much improved, while control participants reported no change/minimally worse, post intervention.

Conclusion: The walking based exercise intervention designed to improve sleep was feasible, safe and highly accepTable to study participants, with those in the exercise group reporting improvements in sleep duration and sleep quality compared to control group. Adverse events were predominantly mild. This pilot provides a framework for larger intervention studies and based on these findings a fully powered trial of walking as an exercise based intervention is recommended, preceded by focus groups to investigate methods to improve recruitment of males.

Disclosure: S. McKenna, None; **L. Comber**, None; **A. Donnelly**, None; **A. Fraser**, None; **B. Appel Esbensen**, None; **N. Kennedy**, None.

Abstract Number: 0135

Understanding the Rheumatologist-Patient Relationship in Treating Rheumatoid Arthritis

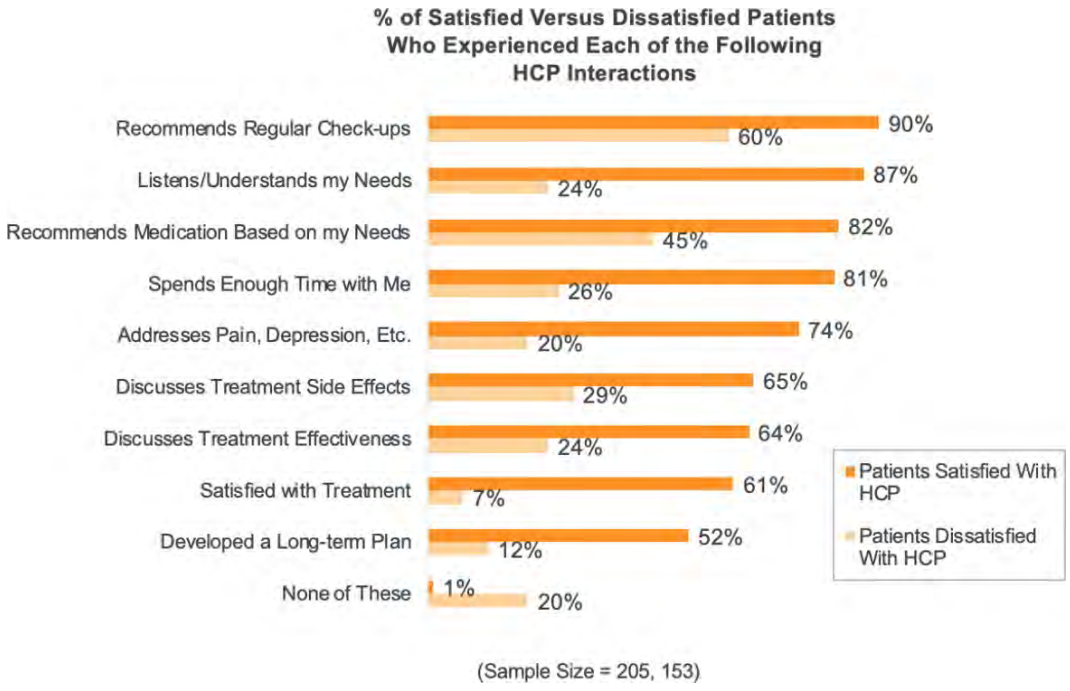
Beth Schneider[1] and Eric Peacock[1], [1]MyHealthTeams, San Francisco, CA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

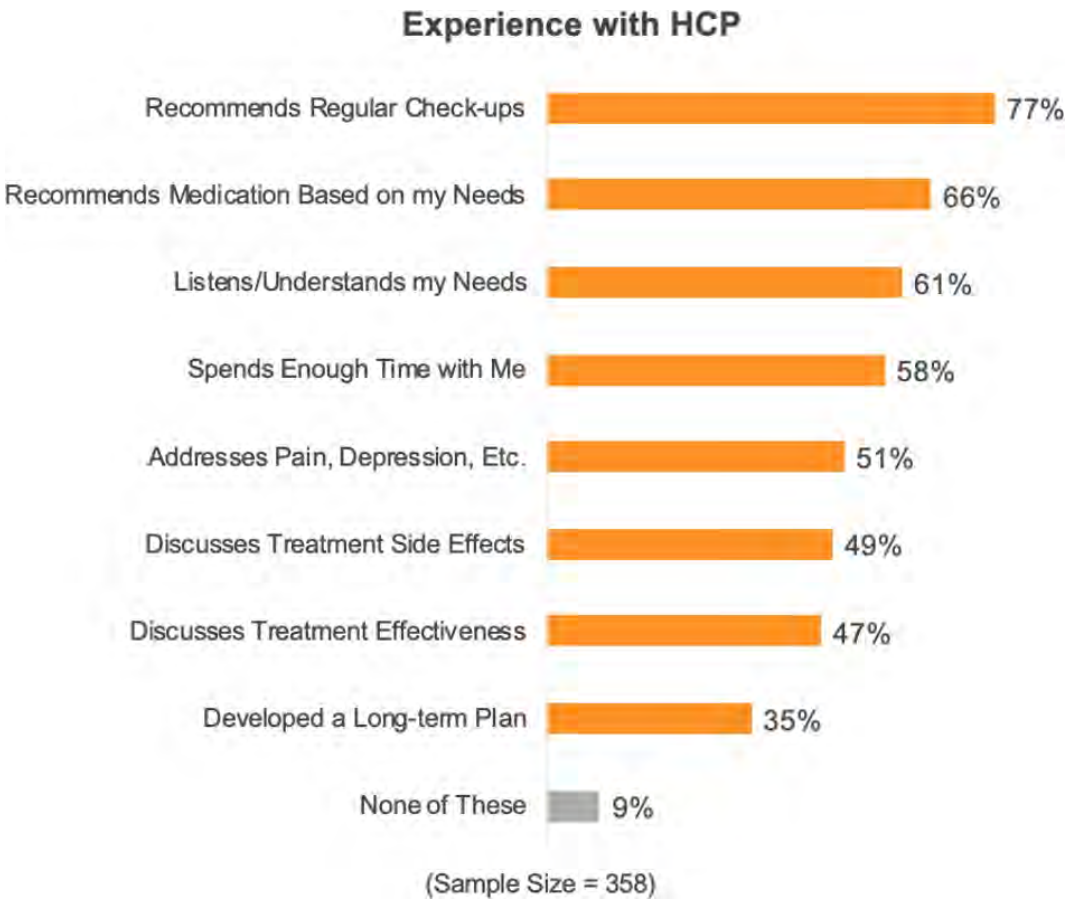
Background/Purpose: Understanding patient satisfaction with their rheumatologist and the drivers of satisfaction is crucial to improving doctor-patient interactions, helping patients get on the right treatment path to help slow progression and improving health outcomes overall.

Methods: In January 2020 an email invitation to an online survey was sent to US members of myRAteam, a social network of over 122,000 members. In total, 374 US members completed the 21-question survey regarding the HCP-patient experience.

Results: Over half of RA patients surveyed are satisfied with their HCP (57%) and 78% feel they are able to have meaningful conversations. The majority feel they're HCP is doing a good job of recommending regular checks-ups (77%) and medications (66%) based on the patient's unique needs. Slightly less than two-thirds feel they're doctor listens to them and truly understands what they are going through (61%) or spends enough time with them (58%). While biggest obstacles to managing RA are pain (80%), relentless fatigue (72%) and depression/anxiety (51%), only 51% of patients feel their HCP addresses these symptoms. Further, only 37% are satisfied with their current treatment and only 49% feel their HCP is adequately discussing potential side effects and 47% treatment efficacy. And only 35% feel their HCP has developed a long-term plan for treating this progressive disease. There is a significant



Experiences with HCPs



Satisfaction with HCP

delta in experiences among those who are satisfied versus dissatisfied with their HCP. 61% of satisfied patients feel their treatment is working versus only 7% who are dissatisfied with their HCP. 87% of satisfied patient feel their HCP listens to and understands them versus 24% of dissatisfied patients. Likewise, 81% of satisfied patients feel their HCP spends enough time with them versus 26% among dissatisfied patients. 74% of satisfied patients feel their doctor addresses symptoms like pain and depression versus 20% of dissatisfied patients.

Conclusion: Understanding the needs of RA patients provides significant opportunities for rheumatologists to better support and educate their patients. This includes offering a stronger recommendation on treatment path based on the patient's specific needs and goals, and specific information on diet/exercise approaches. It also means listening to patient concerns and addressing the mental health aspects of RA including pain, depression and fatigue, and not just disease progression.

Disclosure: B. Schneider, None; **E. Peacock**, None.

Abstract Number: 0136

Filgotinib Significantly Improved Patient-reported Health-related Quality of Life for Patients with Active Rheumatoid Arthritis: A Post Hoc Analysis of SF-36 and HAQ-DI from Phase 3 Studies

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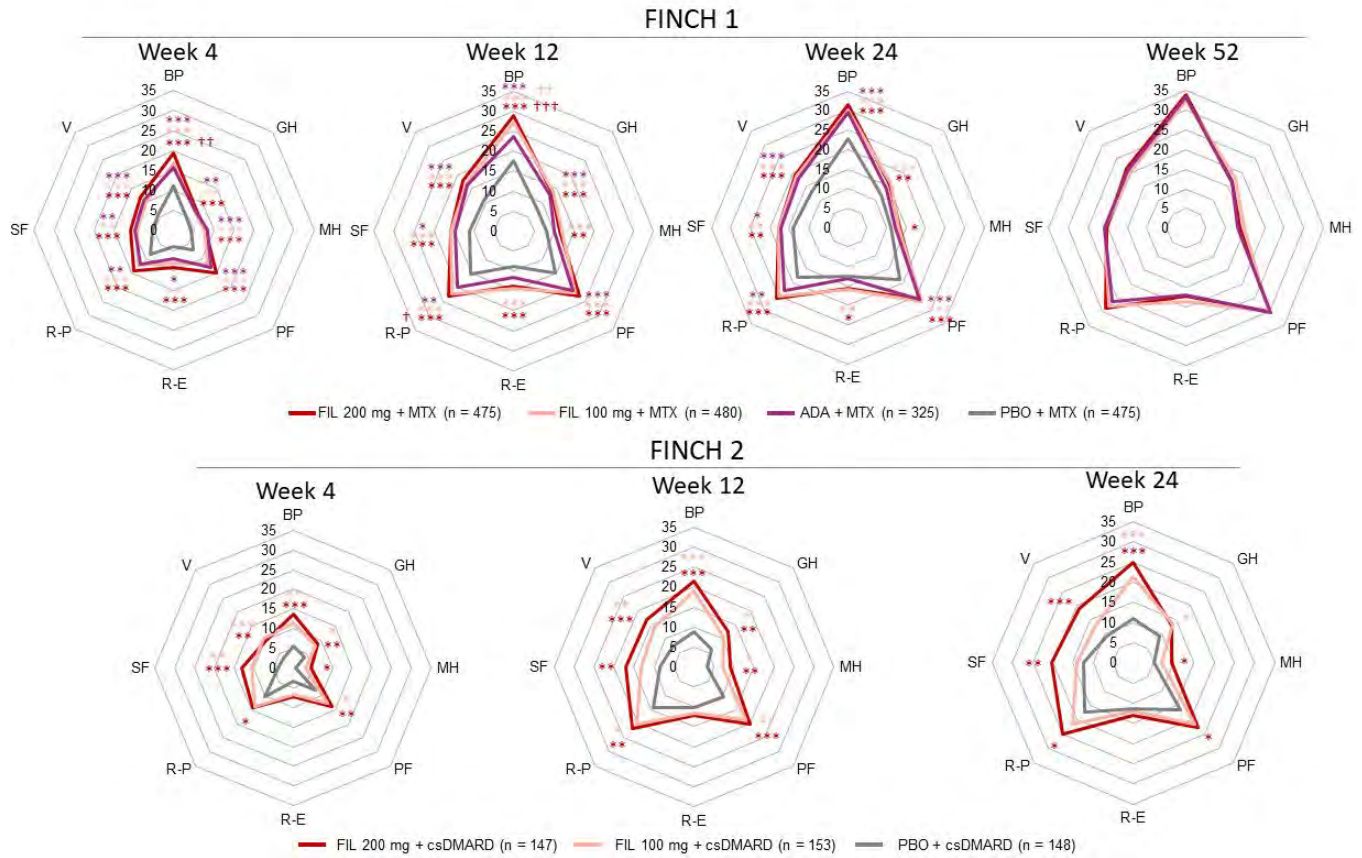
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Reduction in pain and fatigue, maintenance of physical functioning, and improvement in health-related quality of life (HRQoL) are vital aspects of successful treatment for patients (pts) with RA. In phase 3 clinical trials, filgotinib (FIL)—a potent, selective, oral, small molecule Janus kinase 1 inhibitor—improved signs and symptoms of RA when used in combination with MTX in pts with inadequate response to MTX (MTX-IR; FINCH 1 study [F1]), or to a biologic (b)DMARD (bDMARD-IR; FINCH 2 study [F2]).[1,2] This is a post hoc analysis of functional status in both studies, with a focus on patient-reported outcomes using the Short Form-36 (SF-36) and HAQ-Disability Index (HAQ-DI).

Methods: All pts met 2010 ACR/EULAR criteria for RA. F1 pts were randomized 3:3:2:3 to receive once-daily FIL 200 mg, FIL 100 mg, adalimumab (ADA), or placebo (PBO) for up to 52 weeks (W) on a weekly sTable background dose of MTX; at W24, pts receiving PBO were rerandomized 1:1 to FIL 200 or 100 mg. F2 pts were randomized 1:1:1 to receive once-daily FIL 200 mg, FIL 100 mg, or PBO for up to 24W on a sTable background dose of permitted conventional synthetic (cs)DMARD(s). SF-36 was assessed at baseline and by visit on W4, 12, 24, 36, and 52. HAQ-DI was assessed at baseline and by visit on W2, 4, 8, 12, 14, 16, 18, 20, 24, 26, 30, 36, 44, and 52. The proportion of pts achieving HAQ-DI $\leq$0.5 was compared for FIL vs PBO (F1/F2) and FIL vs ADA (F1) using logistic regression with treatment groups and stratification factors in the model. Comparisons of change from baseline in SF-36 domains between FIL vs PBO and FIL vs ADA were conducted using mixed-effects model for repeated measures (MMRM)

Figure 1. LS-mean change from baseline in SF-36 individual domains by visit



including treatment group, visit, treatment group by visit interaction, stratification factors, and baseline value as fixed effects; and subjects as random effect. All analyses were exploratory without multiplicity adjustment, and nominal P values are reported.

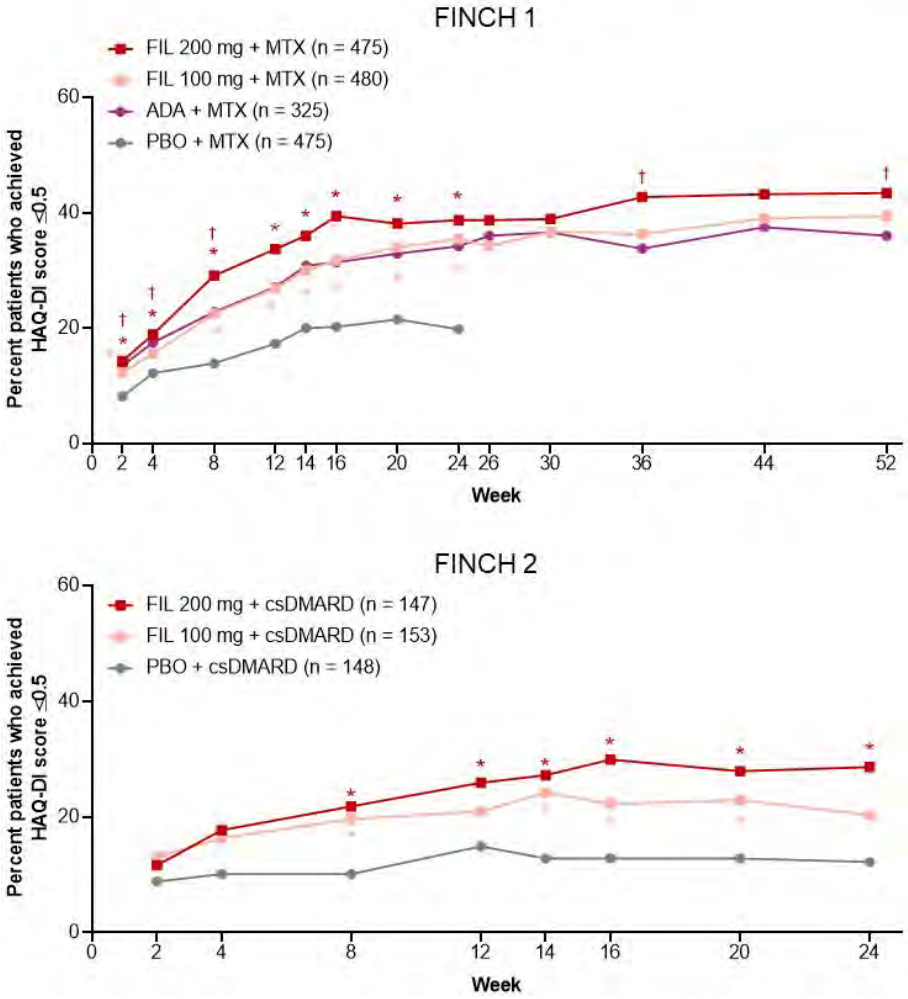
Results: Improvements in SF-36 domains in all FIL arms were observed as early as W4 and were sustained or increased through end of study (Fig 1). Nominally statistically significant improvements across all SF-36 domain scores occurred for pts on FIL 200 mg vs PBO at W4, 12, and 24 in F1, and 7/8 domains at W4 and 12 in F2; substantial improvements were evident particularly for bodily pain, physical functioning, and role-functional (Fig 1). The proportion of pts with HAQ-DI ≤0.5 was nominally statistically significantly higher in each FIL arm vs PBO early in treatment (W2 for F1 and W8 for F2) and for FIL 200 mg vs ADA at W4, 8, 36, and 52 (F1) (Fig 2).

Conclusion: FIL provided rapid and sustained improvements across multiple aspects of pts' HRQoL captured by SF-36 and HAQ-DI when used in combination with csDMARD for treatment of MTX-IR or bDMARD-IR RA. Improvements in physical activities were observed with both HAQ-DI and SF-36. Furthermore, FIL meaningfully reduced HAQ-DI score to near-normal levels in relatively treatment-resistant bDMARD-IR patients, in addition to more MTX-IR pts on FIL 200 mg reaching this state by end of study when compared to pts on ADA. These results suggest that FIL can improve the daily lives of pts with advanced RA.

References

1. Combe et al. Ann Rheum Dis. 2019; 78 (Suppl 2): A77.
2. Genovese et al. JAMA. 2019; 322(4):315–25.

Figure 2. Patients who achieved HAQ-DI score of ≤0.5 by visit



Concentric octagons represent the LS-mean change from baseline in the SF-36 domain score. Comparison with PBO: ***P <0.001, **P <0.01, *P <0.05. Comparison with ADA: †††P <0.001, ††P <0.01. All are nominal P-values (not adjusted for multiplicity) and were from the MMRM including treatment, visit (as categorical), treatment by visit, stratification factors, and baseline value as fixed effects; and subjects as random effect. In FINCH 1, patients on PBO were rerandomized to FIL 200 or 100 mg at week 24. The FINCH 2 study ended at week 24. ADA, adalimumab; BP, bodily pain; csDMARD, conventional synthetic DMARD; FIL, filgotinib; GH, general health; LS, least squares; MH, mental health; MMRM, mixed-effects model for repeated measures; PBO, placebo; PF, physical functioning; R-E, role-emotional; R-P, role-physical; SF, social functioning; SF-36, Short Form-36; V, vitality.

Comparison with PBO: *P <0.05. Comparison with ADA: †P <0.05. All are nominal P-values (not adjusted for multiplicity) and were from logistic regression with treatment groups and stratification factors in the model. A non-responder imputation was used. In FINCH 1, patients on PBO were rerandomized to FIL 200 or 100 mg at week 24. The FINCH 2 study ended at week 24. ADA, adalimumab; csDMARD, conventional synthetic DMARD; FIL, filgotinib; HAQ-DI, HAQ-Disability Index; PBO, placebo.

Disclosure: C. Bingham III, Bristol-Myers Squibb, 2, 5, 8, Genetech, 5, 8, Sanofi, 5, 8, AbbVie, 5, Eli Lilly, 5, Pfizer, 5, Gilead Sciences, Inc., 5, Regeneron, 5; **D. Walker**, Eli Lilly, 5, 8, Pfizer, 5, 8, Novartis, 5, 8, Gilead Sciences, Inc., 5, 8; **P. Nash**, AbbVie, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8; **S. Lee**, Gilead Sciences, Inc., 3; **L. Ye**, Gilead Sciences, Inc.,

1, 3; **H. Hu**, Gilead Sciences, Inc., 1, 3; **J. Khalid**, Galapagos BV, 3; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8.

Abstract Number: 0137

PROMIS-29 Scores Are Significantly Higher in Patients with Rheumatoid Arthritis Who Meet Criteria for Co-morbid Fibromyalgia (FM) Than in Those with Rheumatoid Arthritis and No FM

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The Patient-Reported Outcomes Measurement Information System short form 29 (PROMIS-29)[1] uses computer assisted technology (CAT) to derive patient assessments. High PROMIS-29 scores are seen in patients with rheumatoid arthritis (RA) with high disease activity, but may also reflect co-morbid FM. This problem is seen also in traditional indices used to assess patients with rheumatoid arthritis (RA), including DAS28, CDAI, and RAPID3 (routine assessment of patient index data 3). For example, a patient with no tender or swollen joints, a physician global assessment of 0, ESR of 20 mm/hr, but a patient global assessment of 80/100, would have a DAS28 of 3.2, suggesting moderate disease activity. Therefore, high scores may indicate high disease activity or co-morbid FM (or both) in RA patients.

	All patients (n=159)	FM 2011 positive (n=37)	FM 2011 negative (n=122)	P	FAST3P positive (n=46)	FAST3P negative (n=113)	P
PROMIS29							
Pain interference	58.0 (9.7)	66.3 (6.6)	55.5 (9.1)	<0.0001	66.3(6.7)	54.6 (8.7)	<0.0001
Depression/Sadness	50.9 (11.1)	62.0 (10.1)	47.5 (8.9)	<0.0001	60.0 (11.6)	47.1 (8.4)	<0.0001
Physical Function	42.2 (8.5)	36.0 (5.5)	44.1 (8.3)	<0.0001	35.1 (4.6)	45.0 (8.0)	<0.0001
Ability to Participate	48.0 (10.4)	39.8 (6.9)	50.4 (10.0)	<0.0001	39.6 (6.9)	51.4 (9.6)	<0.0001
Fatigue	52.5 (11.1)	62.6 (8.5)	49.5 (10.0)	<0.0001	62.5 (8.4)	48.5 (9.5)	<0.0001
Anxiety/Fear	52.0 (11.3)	62.7 (9.6)	48.8 (9.7)	<0.0001	60.6 (11.7)	48.5 (9.1)	<0.0001
Sleep disturbance	53.2 (9.4)	60.8 (8.0)	50.9 (8.6)	<0.0001	60.4 (8.7)	50.3 (8.1)	<0.0001
Pain (VNS)	4.7 (2.8)	7.3 (1.7)	3.9 (2.6)	<0.0001	7.4 (1.5)	3.6 (2.4)	<0.0001
RAPID3 (0-30)	11.5 (7.1)	18.7 (4.9)	9.3 (6.1)	<0.0001	19.2 (3.5)	8.4 (5.7)	<0.0001

PROMIS29 and RAPID3 in all patients and patients with and without FM by 2011 and FAST3P criteria. Higher scores indicate more of the concept being measured in PROMIS-29. In MDHAQ higher scores indicate more severe patient impact of the concept being measured.

Methods: All RA patients attending the Rheumatology clinic at Liverpool Hospital complete a MDHAQ at each visit, and were asked to complete a PROMIS-29 questionnaire,[1] and the 2011 modification of the criteria for Fibromyalgia (2011 FM criteria)[3] on paper. Two indices derived from MDHAQ scores RAPID3=0-30: (physical function=0-10 + pain=0-10 + patient global assessment=0-10) assesses clinical status, and FAST3-P (Fibromyalgia Assessment Screening Tool 3 (2/3=FM): pain≥6/10=1 + number of painful joints≥16/48=1 + number of symptoms≥16/60=1) provides a clue to the presence of FM. PROMIS-29 t-scores were obtained from the Assessment Center scoring service (https://www.assessmentcenter.net/ac_scoringservice). Cross sectional analysis of 159 patients with complete data was performed. Descriptive statistics and t-tests were derived using Stata/IC 16.1 (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC.)

Results: Patients had a mean (SD) age of 55.7 (15.2) years, were 67.3% female and had a mean education of 11.6 (4.0) years. 23.3% were found to have co-morbid FM by 2011 FM criteria and 28.9% by FAST3-P criteria. All PROMIS-29 t-scores indicated significantly poorer status in patients with co-morbid FM either by 2011 FM criteria or by FAST3-P criteria (Table). All scores for pain interference, depression/sadness, fatigue, anxiety/fear and sleep disturbance and poorer physical function and ability to participate were more than 0.5 SD from the population mean in the FM positive group, and within 0.5 SD of the population mean in those who did not have positive screening for FM (Table). All MDHAQ variables, including the components of RAPID3 indicated significantly poorer status in patients with co-morbid FM by either criterion (data not shown).

Conclusion: RA patients with comorbid FM by either the 2011 FM criteria or by FAST3-P had significantly higher PROMIS-29 t-scores, than RA patients who did not have FM. Interpretation of these scores in RA patients should consider whether there is coexisting FM in addition to any active inflammatory disease.

1. Cella D.et al (2019) Value in Health, 22(5):537-544.
2. Pincus T et al (2007) Best Pract Res Clin Rheumatol; 21(4):789– 804.
3. Wolfe F et al. (2011) J Rheumatol; 38:1113-22.

Disclosure: K. Gibson, Janssen, 1, UCB, 1, Novartis, 1, Abbvie, 1; **G. Hassett**, Abbvie, 1, Amgen, 1, Janssen, 1; **T. Pincus**, Medical History Services LLC, 9.

Abstract Number: 0138

Alignment and Discordances in Treatment Perceptions and Shared Decision-Making Among RA Patients and Rheumatology Care Teams

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SESSION INFORMATION

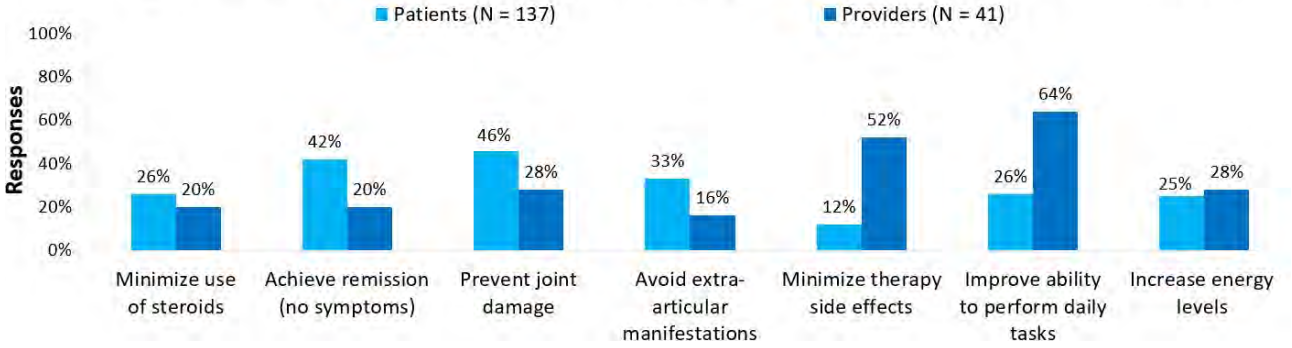
Session Date: Friday, November 6, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Figure 1. Provider and Patient Perspectives on Most Important RA Treatment Goals



Background/Purpose: Evidence-based guidelines for rheumatoid arthritis (RA) call for shared decision-making (SMD) as a method to personalize treatment decisions and achieve treat-to-target goals. We assessed alignment and discordances on treatment and SDM perceptions among RA patients and their rheumatology care teams.

Methods: Between 09/2019 and 06/2020, surveys were administered to RA patients and their health care professional (HCP) teams as part of in-clinic collaborative patient education sessions across 13 US-based rheumatology community practices. On 5-point Likert scales and multi-select questions, patients and HPs rated or indicated their perceptions, preferences, and concerns regarding RA treatment and SDM.

Results: Surveys were completed by 137 patients with RA (81% female, mean age 57 years) and 41 HCPs (52% physicians, 20% nurse practitioners, 4% physician assistants, 24% nurses) who reported 13 mean years of experience in rheumatology. Alignments were found in patients' and HCPs' perceptions of patients' current level of RA control (well or very well controlled: 50% patients vs 58% HCPs) and satisfaction with current therapy (high or very high: 68% patients vs 65% HCPs).

Discordances were found in patients' and HCPs' top goals for RA treatment (Figure 1), which included: prevent joint damage (46% patients, 28% HCPs), achieve remission (42% patients, 20% HCPs), avoid extra-articular manifestations (33% patients, 16% HCPs), improve ability to perform daily tasks (26% patients, 52% HCPs), and minimize therapy side effects (12% patients, 52% HCPs). Discordances were also observed in patients' and HCPs' main concerns about targeted therapy for RA (Figure 2), which included potential side effects (54% patients, 42% HCPs), efficacy (46% patients, 17% HCPs), cost (17% patients, 50% HCPs), and monitoring requirements (6% patients, 33% HCPs).

A high proportion of patients and HCPs reported often or always engaging in multiple components of SDM (Figure 3). However, compared with their patients' responses, HCPs underestimated how often they: explain goals of treat-

Figure 2. Provider and Patient Perspectives on Top Concerns on Targeted Therapies for RA

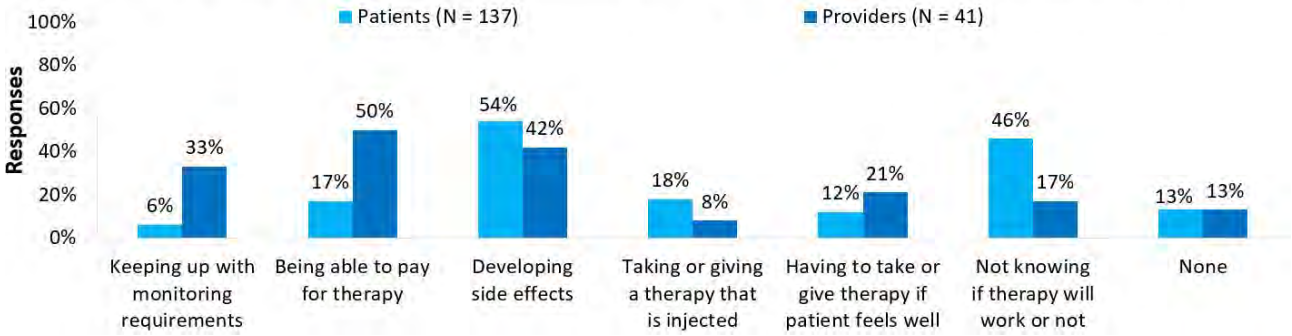
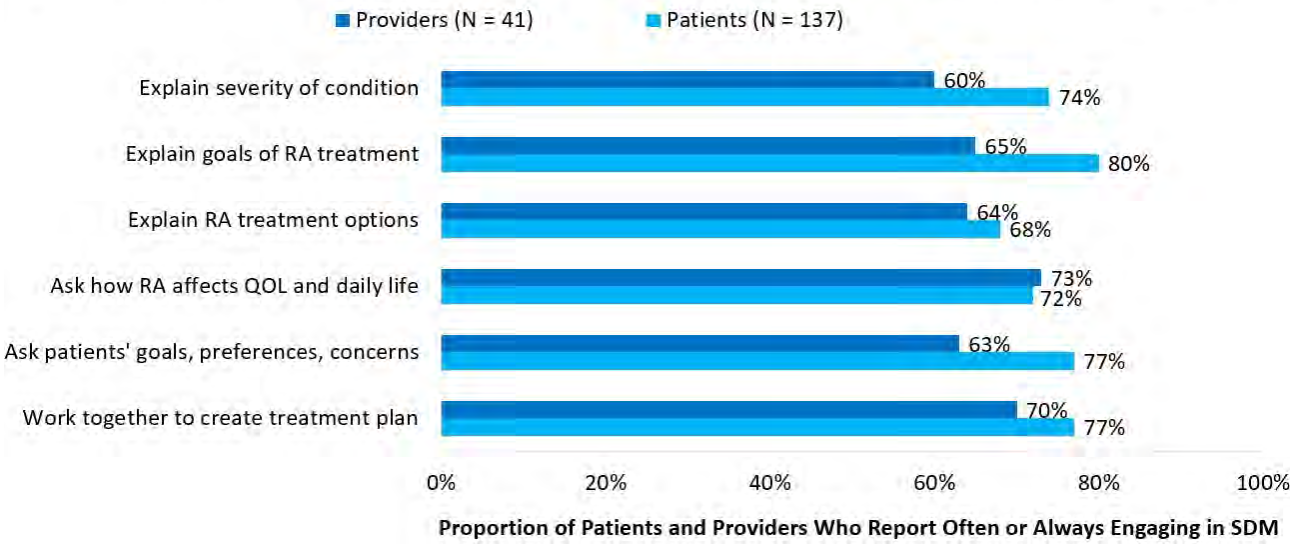


Figure 3. Provider and Patient Perspectives on the Frequency of Shared Decision-Making (SDM)



ment (80% patients; 65% HCPs), explain disease severity to patients (74% patients; 60% HCPs), and ask patients' treatment goals, preferences, and concerns (77% patients; 63% HCPs). When asked about the main barrier to SDM, patients reported not knowing enough about RA and available therapies (46%) while HCPs reported perceived patient resistance to SDM (57%).

Conclusion: Identifying alignments and discordances in perceptions of treatment and SDM can support rheumatology teams in individualizing treatment decisions and patient engagement for optimal RA care.

Disclosure: R. Levin, Exagen, 1, 2, Abbvie, 1, 2, Takeda, 1, Sanofi, 1, Janssen, 1, Pfizer, 1, Myriad, 1, 2, Lilly, 1; **C. Parker**, Amgen, 8, AbbVie, 8; **K. Botsoglou**, None; **J. Shah**, Abbvie, 1, GSK, 1, Horizon Pharma, 1, Janssen, 1; **N. Dayal**, None; **K. Fajardo**, None; **L. Simone**, None; **J. Carter**, None; **T. Sapir**, None.

Abstract Number: 0139

Routine Assessment of Patient Index Data (RAPID) 3 as a Predictor of Weight Reduction in Rheumatology Patients Undergoing Bariatric Surgery

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

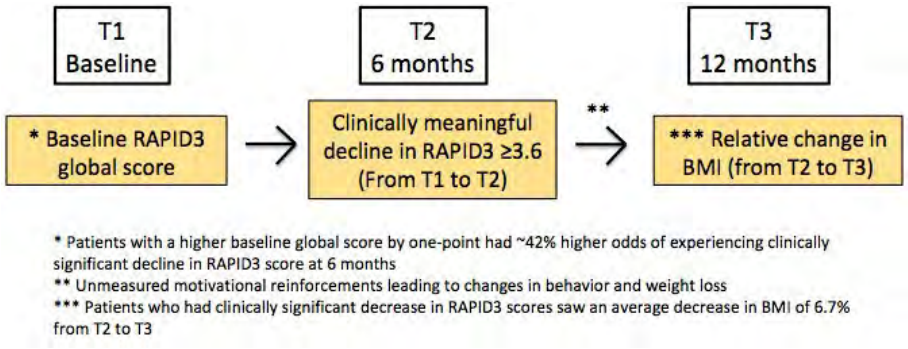
Background/Purpose: Obesity is associated with higher disease activity in many rheumatologic diseases with evidence of improvement following bariatric surgery. Despite the impressive average weight loss values that occur after surgery, 10–30% of patients will have suboptimal weight loss or weight-regain. The RAPID3 on Multidimensional Health Assessment Questionnaire (MDHAQ), is a patient-reported, disease monitoring index with 3 components:

Age at Surgery (mean ± SD) years	49.2 ± 8.9
Women (%)	97
Race (%)	
Caucasian	30.3
African American	48.5
Hispanic	21.2
Education (mean ± SD) years	14.0 ± 2.8
Osteoarthritis (%)	57.6
Fibromyalgia (%)	51.5
Average # of Medical Comorbidities	5.0
Type of Bariatric Surgery (%):	
Laparoscopic surgical gastrectomy	69
Lap band	9
Open surgical gastrectomy	3
Roux-en-Y gastric bypass	15
Unknown	3

Patient Baseline Characteristics Prior to Bariatric Surgery

Variable	T1 baseline/pre-surgical	T2 (6 months post-surgical)	T3 (12 months post surgical)
BMI (mean ± SD)	45.8 ± 7.1	37.6 ± 6.4	37.1 ± 6.6
% Change (decrease) in BMI		17.7	19.3
MDHAQ FN (mean ± SD)	3.4 ± 2.0	2.3 ± 1.5	2.8 ± 1.8
MDHAQ PN (mean ± SD)	6.4 ± 2.7	6.1 ± 2.9	5.8 ± 2.9
MDHAQ GL (mean ± SD)	5.2 ± 3.1	5.0 ± 2.7	5.2 ± 2.7
RAPID3 index (mean ± SD)	15.0 ± 6.4	13.4 ± 6.3	13.8 ± 6.4
Patients with Significant Decline in RAPID3 of at Least 3.6 compared to baseline (%)		30.3	21.4

Changes in BMI and RAPID3 Variables After Bariatric Surgery



Two-Stage Model Showing Longitudinal Relationship Between T1 RAPID 3 Global Score, Clinically Significant Decline in RAPID3 at T2, and Subsequent BMI decline from T2 to T3

Function (FN), Pain (PN), and Global Health (GL). This longitudinal study explored predictors of improvement in RAPID3 and weight loss in rheumatology patients before and after bariatric surgery.

Methods: Rheumatology patients evaluated between 2012-2019 with documented RAPID3 scores were enrolled. Variables collected included demographics, BMI, and MDHAQ components at baseline/pre-surgery (T1), 6 month post-surgery (T2) and 12 month post-surgery (T3). For Model 1, we conducted a univariate binary logistic regression analysis with clinically significant improvement in RAPID3 (defined as decline of ≥3.6) between T1 and T2 as the dependent variable (DV). Predictor variables (PV) tested include age, education, comorbidities, T1 BMI, and TI MDHAQ. For Model 2, we performed a linear regression analysis for % change in BMI between T2 and T3 as the DV, and clinically significant change in RAPID3 index as the PV. Change in BMI of 5% was considered clinically relevant. A P value of ≤0.05 was considered significant on two-tailed tests.

Results: 33 patients were enrolled (97% women). 30.3% were Caucasian, 48.5% African American, and 21.2% Hispanic (Table 1). Mean BMI and RAPID3 Index at T1 were 45.8 and 15.0, respectively. Changes in BMI and RAPID3 at T2 and T3 are shown in Table 2. There were no differences in BMI or RAPID3 by race. T1 RAPID3 GL predicted attainment of a clinically significant improvement in RAPID3 at T2 (OR 1.42, 95% CI 1.02-1.98, p=0.04). T1 BMI or % change in BMI were not predictive of a clinically significant change in RAPID3 at T2. Subjects with clinically significant decreases in RAPID3 scores at T2, saw a 7.5% greater decline in BMI from T2 to T3 compared to those without significant decrease (β 0.075, 95% CI 0.033-0.117, p=0.0015). Nearly 30% decline in % BMI change from T2 to T3 was explained by clinically significant decrease in RAPID3 index (R-Sq 0.29) at T2 (Figure 1).

Conclusion: Higher pre-surgical MDHAQ GL score predicted clinically relevant improvements in RAPID3 index at 6 months post-bariatric surgery. Attaining significant improvement in RAPID3 index at 6 months was further predictive of clinically relevant decline in BMI at 12 months. A plausible mechanism involves reinforcement in patients' behavioral changes as a result of perceptible health improvements. Longitudinal studies with larger numbers of patients will be required to see if improvements in RAPID3 leads to sustained weight loss, and whether this leads to improvement in their underlying rheumatological condition.

Disclosure: J. Byun, None; **M. Jolly**, PFIZER, 2, CELGENE, 7, BI, 7, BMS, 7, AURINIA, 7, EVIDERA, 7, LUCIN, 5; **T. Beck**, None; **S. Hassan**, None.

Abstract Number: 0140

Meaningful Within-Patient Change in WOMAC Domains in Patients with Moderate-To- Severe Osteoarthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

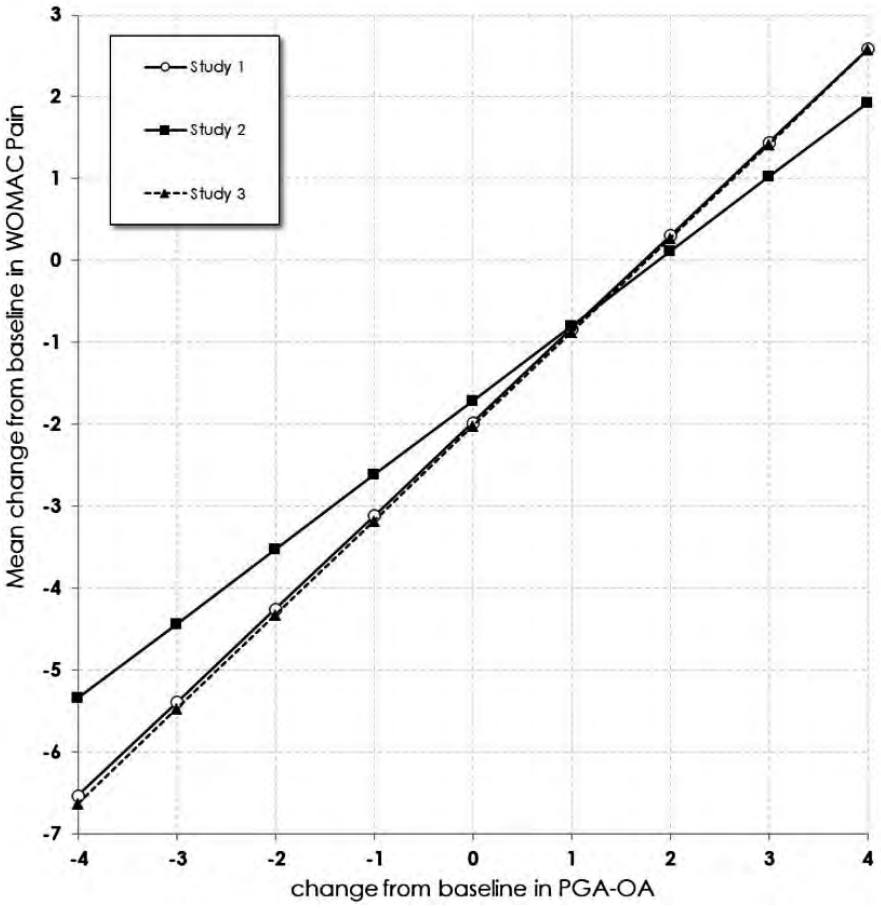
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) is a disease-specific measure of osteoarthritis (OA) symptoms (pain and stiffness) and functional impairment regularly used in clinical trials. To aid interpretation of the clinical meaningfulness of response to treatment, it is important to de-

Figure 1. Change in WOMAC Pain Domain (original units) versus change in PGA-OA in all 3 studies.



PGA-OA, patient's global assessment of osteoarthritis; WOMAC Western Ontario and McMaster Universities Osteoarthritis Index.

Table 1. Meaningful within-patient change by domain and study.

WOMAC domain	Study					
	1		2		3	
	1-category change in PGA-OA	2-category change in PGA-OA	1-category change in PGA-OA	2-category change in PGA-OA	1-category change in PGA-OA	2-category change in PGA-OA
Meaningful Within Patient Change (original units)						
Pain	1.1	2.3	0.9	1.8	1.2	2.3
Physical Function	1.1	2.3	0.9	1.7	1.1	2.3
Stiffness	1.2	2.3	0.8	1.7	1.1	2.3
Total	1.1	2.3	0.9	1.7	1.1	2.2
Meaningful Within Patient Change (%)						
Pain	15.5	31.0	13.5	27.0	15.9	31.9
Physical Function	15.3	30.6	12.5	25.0	15.6	31.3
Stiffness	15.4	30.7	13.2	26.5	16.2	32.5
Total	15.1	30.3	12.9	25.8	15.5	31.0

PGA-OA, patient's global assessment of osteoarthritis; WOMAC Western Ontario and McMaster Universities Osteoarthritis Index.

termine thresholds for WOMAC that would indicate meaningful within-patient change (MWPC), where an individual has experienced a meaningful clinical benefit. Our aim therefore was to define MWPC in WOMAC by examining the relationship between change in WOMAC domains and change in patient global assessment (PGA-OA) as an anchor (as recommended in recent FDA guidance[1]) in patients with moderate-to-severe OA.

Methods: WOMAC numerical rating scale (NRS) 3.1 Index[2] consists of 24 items measuring pain (5 items), stiffness (2 items) and physical function (17 items), assessed using a 0-10 NRS with higher scores indicating worse outcomes. Data were analyzed separately from three Phase 3 clinical trials of tanezumab, a novel treatment intended for the relief of signs and symptoms of moderate-to-severe OA, administered subcutaneously every 8 weeks. Studies 1 (NCT02697773) and 2 (NCT02709486) were 16- and 24-week placebo-controlled trials, respectively; study 3 (NCT02528188) was a 56-week active-controlled trial. Patients with moderate-to-severe OA of the hip or knee completed the WOMAC and PGA-OA at regular time points. A repeated measures model with change in WOMAC domain score as the outcome and change in PGA-OA as the anchor was used to establish MWPC for WOMAC domains.

Results: In the 3 studies there were 688, 844, and 2948 subjects available for analyses, respectively. Analysis showed that a linearity assumption for the relationship between changes in WOMAC domains and changes in PGA-OA was appropriate. Moreover, the relationships between these changes were very close for two trials and similar for the third (**Figure 1)**. The estimated MWPC for the three WOMAC domains were from 0.8 to 1.2 (NRS from 0 to 10) and from 12.5 to 16.2%, depending on study and domain, that corresponded to a 1- category change on PGA-OA (**Table 1**). For a 2-category change those values were from 1.7 to 2.3 and from 25.0 to 32.5%, respectively. Values were similar to and supportive of published results.[3] While the relationship between change in PGA-OA and change in WOMAC was approximately linear, the correspondence between, for example, ratings of 'no change' on the PGA-OA with changes in WOMAC pain may be a manifestation of their measuring similar but distinct concepts.

Conclusion: These results establish MWPCs for WOMAC domains, at the individual patient level, for patients with moderate-to-severe OA of hip or knee. The relationship between change in PGA-OA and change in WOMAC is the focus of ongoing evaluation.

These studies were sponsored by Pfizer and Lilly. Medical writing support was provided by Steven Moore, PhD, of Engage Scientific Solutions and was funded by Pfizer and Lilly.

References

1 FDA Patient-Focused Drug Development Guidance Workshop, 6 Dec 2019.
2 Bellamy N (2008). WOMAC Osteoarthritis Index: user guide IX.
3 Erdogan BD et al (2016). J Rheum 43 (1) 194-202.

Disclosure: P. Conaghan, AbbVie, 1, 2, EMD Serono, 1, Flexion Therapeutics, 1, 2, Galapagos, 1, Gilead, 1, Novartis, 1, 2, Regeneron, 1, Samumed, 1, 2, GlaxoSmithKline, 5, Janssen, 5, Pfizer Inc, 5, Bristol-Myers Squibb, 2, Eli Lilly, 5; **R. Dworkin**, abide, 1, acadia, 1, Analgesic Solutions, 1, Asahi_kasei, 1, Biogen, 1, Centrexion, 1, Clexio, 1, Decibel, 1, Eli Lilly, 1, Glenmark, 1, Hope, 1, Lotus, 1, Mainstay, 1, Merck, 1, Neurana, 1, NeuroBo, 1, Novaremed, 1, Novartis, 1, Pfizer, 1, Regenacy, 1, Sanifit, 1, Scilex, 1, Semnur, 1, Sollis, 1, Vertex, 1, Vizuri, 1; **T. Schnitzer**, Pfizer, 1, 2, Lilly, 1, 2, Regeneron, 1, AstraZeneca, 1; **F. Berenbaum**, Pfizer, 1, Eli Lilly, 1; **A. Bushmakin**, Pfizer Inc, 1, 2; **J. Cappelleri**, Pfizer Inc, 1, 2; **L. Viktrup**, Eli Lilly and Company, 1, 3; **L. Abraham**, Pfizer Inc, 1, 2.

Abstract Number: 0141

Filgotinib Improved Work Productivity and Activity Impairment in Patients with Rheumatoid Arthritis and Inadequate Response to Methotrexate: Results from FINCH-1 Study

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL) is a potent oral selective janus kinase 1 inhibitor which is currently being investigated as an agent to treat rheumatoid arthritis (RA). In the FINCH 1 study (NCT02889796), FIL in combination with methotrexate (MTX) provided a rapid and meaningful clinical response in patients with inadequate response to MTX. Chronic inflammatory diseases such as RA substantially affects a broad range of aspects of the patient's health related quality of life including work participation.[1] The aim of this post-hoc analysis was to evaluate the rate and magnitude of change from baseline and assess the effect of treatment response on work productivity and activity scores in RA patients from the FINCH 1 study.

Methods: Patients with active RA were randomized to receive FIL 200 mg (n=475), FIL 100 mg (n=480), or subcutaneous adalimumab (ADA) 40 mg (n=325), or PBO (n=475) with concomitant MTX treatment in all groups for up to 52 weeks. At week 24, patients receiving PBO were randomized 1:1 to FIL 200 mg or 100 mg. The activity impairment, work productivity impairment, presenteeism, and absenteeism in the past 7 days were evaluated at baseline and then

Table 1. Baseline demographics and mean percentage change from baseline in WPAI scores at each visit.

	FIL 200 + MTX n = 475	FIL 100 + MTX n = 480	ADA 40 + MTX n = 325	PBO + MTX n = 475
Baseline demographics				
Age, mean (SD), years	52 (12.8)	53 (12.6)	53 (12.9)	53 (12.8)
Female, n (%)	379 (79.8)	399 (83.1)	266 (81.8)	391 (82.3)
Duration of RA, years, mean (SD)	7.3 (7.4)	8.5 (8.2)	8.0 (7.4)	7.3 (7.2)
Employed, n (%)	202 (42.8)	198 (41.5)	131 (41.1)	167 (35.6)
WPAI mean percentage change from Baseline (SE)				
Work Productivity Impairment				
Baseline	51.3	50.6	54.3	55.8
Week 4	**-10.2 (2.6)****	-6.4 (2.6)	-8.9 (3.0)	-3.7 (2.8)
Week 12	**-17.6 (2.7)****	**-17.7 (2.6)****	**-16.9 (3.0)***	-10.0 (2.9)
Week 24	**-22.3 (2.7)****	**-21.5 (2.7)****	**-17.9 (3.1)***	-11.4 (3.0)
Week 36	-24.0 (2.7)	-21.2 (2.7)	-22.6 (3.2)	—
Week 52	-27.4 (2.7)	-24.9 (2.7)	-23.3 (3.1)	—
Absenteeism				
Baseline	12.0	9.9	16.0	17.0
Week 4	-1.8 (1.9)	-0.2 (1.9)	-0.7 (2.3)	1.1 (2.1)
Week 12	-1.0 (1.9)	-1.7 (1.8)	-0.5 (2.1)	1.6 (2.0)
Week 24	**-1.7 (1.8)****	**-2.4 (1.9)****	**-0.8 (2.1)***	3.5 (2.1)
Week 36	-0.9 (2.0)	-0.8 (2.0)	-1.2 (2.3)	—
Week 52	-2.0 (1.9)	-0.6 (1.9)	0.0 (2.2)	—
Presenteeism				
Baseline	49.1	48.0	50.8	52.5
Week 4	**-12.2 (2.4)****	-8.0 (2.4)	**-10.1 (2.8)***	-5.0 (2.6)
Week 12	**-19.9 (2.4)****	**-19.1 (2.4)****	**-19.2 (2.8)****	-12.0 (2.6)
Week 24	**-24.4 (2.5)****	**-22.9 (2.4)****	**-20.4 (2.9)***	-14.7 (2.7)
Week 36	-26.3 (2.5)	-24.6 (2.4)	-24.0 (2.9)	—
Week 52	-29.3 (2.4)	-27.6 (2.4)	-26.0 (2.8)	—
Activity Impairment				
Baseline	61.5	60.5	61.3	62.2
Week 4	**-17.8 (1.6)****	**-15.9 (1.6)****	**-15.7 (1.8)****	-10.3 (1.7)
Week 12	**-27.0 (1.7)****	**-25.4 (1.7)****	**-23.4 (1.8)****	-17.6 (1.7)
Week 24	**-31.3 (1.7)****	**-31.0 (1.7)****	**-29.1 (1.9)****	-21.7 (1.8)
Week 36	-33.1 (1.7)	-32.9 (1.7)	-30.4 (1.9)	—
Week 52	-35.7 (1.7)	-35.3 (1.7)	-33.4 (1.9)	—

**p <0.01, *p <0.05 for LS mean of the difference vs PBO. P values were not adjusted for multiplicity.

Decrease in score represents improvement. –, not measured at this time point because in FINCH 1, patients receiving PBO were rerandomized 1:1 to FIL 200 or 100 mg at week 24.

ADA, adalimumab; FIL, filgotinib; MTX, methotrexate; PBO, placebo.

at weeks 4, 12, 24, 36 and 52 on treatment, using the self-administered 6-item Work Productivity and Activity Impairment Questionnaire: Rheumatoid Arthritis (WPAI:RA). (employed patients only) The 4 subscale scores ranged from 0%-100%, with higher scores indicating greater impairment. changes from baseline in WPAI: RA score were analyzed using mixed effect models for repeated measures (MMRM), and missing data were not imputed. All analyses were exploratory without multiplicity adjustment, and nominal P values are reported.

Results: The baseline demographics were relatively consistent across all treatment arms. Patients were (mean ± SD) 35 ± 13 years old, 82% female and 40% employed. Statistically significantly greater improvement in WPAI scores from baseline compared to PBO was reported as early as week 4 with FIL 200 mg, and week 12 with FIL 100 mg for work productivity, presenteeism, and activity (**Table 1**). At 24 weeks, both doses of FIL resulted in 21.5-24.4% improvement in work productivity and presenteeism compared to 11.4-14.7% in PBO. Similarly, both doses of FIL improved activity impairment score by 31% from baseline compared to 21.7% in PBO. Improvement over baseline

persisted throughout treatment until week 52 for both FIL doses. WPAI scores were similar for both FIL doses and ADA throughout the study.

Conclusion: Improvement in overall work productivity, presenteeism, and daily activity was greater with both doses of FIL in combination with MTX compared to PBO + MTX in RA patients who had inadequate response to MTX.

Reference:

1.Kim et al. J Rheumatol. 2017;44(8):1112-1117.

Disclosure: Z. Younossi, Gilead, 5, Terns, 5, Viking, 5, Intercept, 5, Novo Nordisk, 5, Merck, 5, Abbvie, 5, Novartis, 5, BMS, 5, Shionogi, 5, Siemens, 5; **M. Stepanova**, None; **L. Gerber**, None; **S. Lee**, Gilead Sciences, Inc., 3; **H. Hu**, Gilead Sciences, Inc., 1, 3; **T. Hendrikx**, Galapagos, 1, 3; **A. Boonen**, AbbVie, 2, Galapagos, 5, Lilly, 5, Celgene, 2, UC, 5; **D. Walker**, Gilead, 2, 5, Lilly, 5, 8, Pfizer, 5, 8, Novartis, 5, 8; **R. Alten**, Pfizer, 2, 8, Gilead Sciences, Inc., 2, Novartis, 2, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 5, Lilly, 2, 5, UCB, 2, 5; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8.

Abstract Number: 0142

Filgotinib Improved Work Productivity and Activity Impairment in Patients with Rheumatoid Arthritis and Inadequate Response to Biologic DMARDs: Results from the FINCH 2 Study

Zobair Younossi[1], Maria Stepanova[2], Lynn Gerber[1], Susan Lee[3], I-Heng Lee[4], Thijs Hendrikx[5], Annelies Boonen[6], Rieke Alten[7], Bernard Combe[8] and David Walker[9], [1]Betty and Guy Beatty Center for Integrated Research, Inova Health System, Falls Church, VA, [2]Center for Outcomes Research in Liver Disease, Washington, DC, [3]Gilead Sciences, Inc., Foster City, CA, [4]Gilead Sciences, Foster City, CA, [5]Galapagos BV, Leiden, Netherlands, [6]Maastricht University Medical Center, Maastricht, Netherlands, [7]Schlosspark-Klinik, Universitätsmedizin, Berlin, Germany, [8]University of Montpellier, Montpellier, France, [9]Northumbria Healthcare Trust, North Shields, United Kingdom

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL) is a potent oral selective janus kinase 1 inhibitor which is currently being investigated as an agent to treat rheumatoid arthritis (RA). In the FINCH 2 study (NCT02873936), FIL in combination with conventional synthetic (cs)DMARD therapy significantly improved the signs and symptoms of RA in patients with an inadequate response to a biologic (b)DMARD compared with placebo (PBO). Chronic inflammatory diseases such as RA substantially affects a broad range of aspects of patients' health related quality of life, including work participation.[1] The aim of this post-hoc analysis is to evaluate the rate and magnitude of change on work productivity and activity scores from the FINCH 2 study.

Methods: Patients with active RA were randomized to receive FIL 200 mg (n = 147), FIL 100 mg (n = 153), and PBO (n = 148) for 24 weeks. The activity impairment, work productivity impairment, presenteeism, and absenteeism in the past 7 days were evaluated at baseline and at weeks 4, 12 and 52 on treatment, using the self-administered 6-item Work Productivity and Activity Impairment Questionnaire: Rheumatoid Arthritis (WPAI:RA). The WPAI-RA contains

Table 1. Baseline demographics and mean percentage change from baseline in WPAI scores at each visit.

	FIL 200 + csDMARD n = 147	FIL 100 + csDMARD n = 153	PBO + csDMARD n = 148
Baseline demographics			
Age, mean (SD), years	56 (12.5)	55 (12.0)	56 (12.1)
Female, n (%)	120 (81.6)	119 (77.8)	121 (81.8)
Duration of RA, years, mean (SD)	12.6 (9.5)	12.0 (7.7)	12.6 (10.3)
Employed, n (%)	35 (24.0)	54 (35.5)	53 (36.1)
WPAI mean percentage change from Baseline (SE)			
Work Productivity Impairment			
Baseline	52.0	55.8	56.7
Week 4	-21.7 (5.4)**	-10.4 (5.1)	-1.8 (4.8)
Week 12	-24.7 (5.6)**	-16.8 (5.2)*	-4.8 (4.9)
Week 24	-20.6 (5.7)	-21.8 (5.6)	-12.1 (5.5)
Absenteeism			
Baseline	11.3	19.2	10.8
Week 4	-5.1 (4.5)	-0.7 (4.1)	2.9 (3.9)
Week 12	-6.1 (4.6)*	-2.4 (4.2)	3.5 (3.9)
Week 24	-4.9 (5.2)	0.0 (4.9)	4.5 (5.0)
Presenteeism			
Baseline	46.9	51.0	55.7
Week 4	-19.9 (5.0)**	-10.5 (4.7)	-1.3 (4.5)
Week 12	-21.5 (5.1)**	-16.0 (4.8)*	-5.1 (4.5)
Week 24	-18.7 (5.1)	-22.5 (4.9)	-13.6 (4.8)
Activity Impairment			
Baseline	65.6	64.6	65.4
Week 4	-17.2 (2.4)**	-15.1 (2.4)**	-5.8 (2.5)
Week 12	-25.8 (2.6)**	-19.6 (2.5)**	-11.7 (2.6)
Week 24	-31.3 (2.7)**	-25.2 (2.7)**	-16.6 (2.9)

**p <0.01, *p <0.05 for LS mean of the difference vs PBO. P values were not adjusted for multiplicity.

Decrease in score represents improvement.

csDMARD, conventional synthetic disease-modifying antirheumatic agent; FIL, filgotinib; PBO, placebo.

Table 1. Demographics

the activity impairment as a single item score evaluated among all subjects, while work productivity impairment (employed patients only) is absenteeism and presenteeism. The 4 subscale scores ranged from 0%-100%, with higher scores indicating greater impairment. Percentage changes from baseline in WPAI: RA score were analyzed using mixed effect models for repeated measures (MMRM), and missing data were not imputed. All analyses were exploratory without multiplicity adjustment, nominal P values are reported.

Results: Baseline characteristics were similar across all treatment arms. Patients were (mean ± SD) 56 ± 12 years old, 80% female, and 32% employed. Statistically significantly greater improvement in WPAI scores from baseline compared to PBO was reported as early as week 4 with both doses of FIL for work productivity and activity. Similar statistically significant improvement occurred as early as week 4 for presenteeism with FIL 200mg and as early as week 12 for FIL 100mg. (**Table 1**). At 12 weeks, FIL 200mg resulted in 21.5-24.7%% improvement in work productivity and presenteeism compared to 4.8-5.1% in PBO. Both doses of FIL improved activity impairment score by 19.6-25.8% from baseline compared to 11.7% in PBO at week 12 and was maintained through week 24.

Conclusion: Improvement in work productivity, presenteeism and activity was greater with both doses of FIL in combination with csDMARD compared to PBO + csDMARD in RA patients who had inadequate response to bDMARDs.

Reference:

1.Kim et al. J Rheumatol. 2017;44(8):1112-1117.

Disclosure: Z. Younossi, Gilead, 5, Terns, 5, Viking, 5, Intercept, 5, Novo Nordisk, 5, Merck, 5, Abbvie, 5, Novartis, 5, BMS, 5, Shionogi, 5, Siemens, 5; **M. Stepanova**, None; **L. Gerber**, None; **S. Lee**, Gilead Sciences, Inc., 3; **I. Lee**, Gilead Sciences, 1, 2; **T. Hendrikx**, Galapagos, 1, 3; **A. Boonen**, AbbVie, 2, Galapagos, 5, Lilly, 5, Celgene, 2, UC, 5; **R. Alten**, Pfizer, 2, 8, Gilead Sciences, Inc., 2, Novartis, 2, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 5, Lilly, 2, 5, UCB, 2, 5; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **D. Walker**, Gilead, 2, 5, Lilly, 5, 8, Pfizer, 5, 8, Novartis, 5, 8.

Abstract Number: 0143

Filgotinib Improved Work Productivity and Activity Impairment in Patients with Rheumatoid Arthritis Who Are Methotrexate-naïve: Results from the FINCH-3 Study

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL) is a potent oral selective janus kinase 1 inhibitor currently being investigated as an agent to treat rheumatoid arthritis (RA). In the FINCH 3 study (NCT02886728), FIL in combination with methotrexate (MTX), demonstrated rapid and significant improvements in the signs and symptoms of RA vs MTX monotherapy in patients who were MTX-naïve. Chronic inflammatory diseases such as RA substantially affects a broad range of aspects of patient health related quality of life, including work participation.[1] The objective of this post-hoc analysis was to evaluate the rate and magnitude of treatment response on work productivity and activity scores in RA patients from the FINCH 3 study.

Methods: Patients with active RA and MTX-naïve were randomized 2:1:1:2 received FIL 200 mg + MTX, FIL 100 mg + MTX, FIL 200 mg (+ PBO), or MTX (+ PBO) for up to 52 weeks. The activity impairment, work productivity impairment, presenteeism, and absenteeism in the past 7 days were evaluated at baseline and at weeks 4, 12, 24, 36 and 52 on treatment, using the self-administered 6-item Work Productivity and Activity Impairment Questionnaire: Rheumatoid Arthritis (WPAI:RA). The WPAI-RA contains the activity impairment as a single item score evaluated among all subjects, while work productivity impairment (employed patients only) absenteeism and presenteeism. The 4 subscale scores ranged from 0%-100%, with higher scores indicating greater impairment. Percentage changes from baseline in WPAI: RA score were analyzed using mixed effect models for repeated measures (MMRM), and missing data were not imputed. All analyses were exploratory without multiplicity adjustment, and nominal P values are reported.

Table 1. Baseline demographics and mean percentage change from baseline in WPAI scores at each visit.

	FIL 200 + MTX n = 416	FIL 100 + MTX n = 207	FIL 200 n = 210	MTX n = 416
Baseline demographics				
Age, mean (SD), years	53 (13.8)	54 (12.6)	52 (13.9)	53 (13.7)
Female, n (%)	325 (78)	158 (76)	166 (79)	312 (75)
Duration of RA, years, mean (SD)	1.9 (3.6)	2.3 (4.7)	2.6 (6.3)	2.3 (5.5)
Employed, n (%)	174 (42.3)	92 (44.7)	82 (39.6)	171 (41.2)
WPAI mean percentage change from Baseline (SE)				
Work Productivity Impairment				
Baseline	50.8	51.6	54.4	56.1
Week 4	**-19.0 (2.1)****	**-21.8 (3.0)****	**-17.1 (2.8)****	-6.6 (2.2)
Week 12	**-27.6 (2.2)****	**-28.1 (3.1)***	-23.4 (2.9)	-19.5 (2.2)
Week 24	-30.3 (2.1)	-30.5 (3.0)	-24.6 (2.8)	-26.4 (2.2)
Week 36	-31.1 (2.2)	-31.7 (3.1)	-27.8 (3.0)	-28.2 (2.4)
Week 52	-33.4 (2.2)	-31.2 (3.1)	-29.8 (2.9)	-30.3 (2.3)
Absenteeism				
Baseline	12.8	20.1	13.5	15.6
Week 4	-2.9 (2.0)	-0.3 (2.8)	-4.8 (2.7)	-0.2 (2.1)
Week 12	-6.2 (1.8)	-8.3 (2.6)	-2.9 (2.4)	-3.8 (1.8)
Week 24	-6.7 (1.7)	-10.2 (2.3)	-3.6 (2.1)	-9.0 (1.7)
Week 36	-7.4 (1.8)	-9.6 (2.4)	-4.2 (2.3)	-8.6 (1.8)
Week 52	-7.0 (1.8)	-7.9 (2.5)	-4.2 (2.4)	-7.6 (1.9)
Presenteeism				
Baseline	47.3	49.0	52.1	53.6
Week 4	**-19.4 (2.0)****	**-22.3 (2.8)****	**-17.3 (2.6)****	-7.2 (2.1)
Week 12	**-27.2 (2.0)****	**-28.2 (2.8)***	**-25.4 (2.6)***	-19.9 (2.0)
Week 24	-29.8 (1.9)	-32.2 (2.7)	-27.5 (2.5)	-26.8 (2.0)
Week 36	-31.7 (2.0)	-33.0 (2.8)	-28.7 (2.6)	-27.7 (2.1)
Week 52	-33.6 (1.9)	-30.7 (2.7)	-32.2 (2.5)	-30.0 (2.1)
Activity Impairment				
Baseline	60.2	62.8	63.3	64.0
Week 4	**-23.2 (1.3)****	**-17.8 (1.7)***	**-19.7 (1.7)****	-13.5 (1.3)
Week 12	**-32.5 (1.4)****	**-28.1 (1.8)***	**-30.5 (1.8)****	-23.6 (1.3)
Week 24	**-36.4 (1.4)***	-34.6 (1.8)	-32.7 (1.8)	-32.3 (1.4)
Week 36	**-38.7 (1.4)****	-34.7 (1.8)	-35.5 (1.8)	-31.8 (1.4)
Week 52	**-39.9 (1.4)****	-36.4 (1.9)	-38.4 (1.9)	-34.5 (1.4)

**p<0.01, *p <0.05 for LS mean of the difference vs MTX. P values were not adjusted for multiplicity.

Decrease in score represents improvement.

FIL, filgotinib; MTX, methotrexate.

Results: Baseline characteristics were similar across all treatment group. Patients were (mean ± SD) 53 ± 14 years old, 80% female, and 42% employed. Statistically significantly greater improvement in work productivity, presenteeism and activity from baseline was reported as early as week 4 with all FIL treatment group compared to MTX alone (**Table 1**). This improvement over baseline persisted through week 12 for both doses of FIL + MTX and throughout 52 weeks of treatment for FIL 200mg + MTX compared to MTX alone. At week 52, both doses of FIL + MTX resulted in 33.4-39.9% improvement in work productivity, presenteeism, and activity.

Conclusion: FIL monotherapy or with concomitant MTX led to earlier improvements in activity impairment, overall work productivity impairment and presenteeism in RA patients who were naïve to MTX compared to MTX alone.

Reference:

1. Kim et al. J Rheumatol. 2017;44(8):1112-1117.

Disclosure: Z. Younossi, Gilead, 5, Terns, 5, Viking, 5, Intercept, 5, Novo Nordisk, 5, Merck, 5, Abbvie, 5, Novartis, 5, BMS, 5, Shionogi, 5, Siemens, 5; **M. Stepanova**, None; **L. Gerber**, None; **S. Lee**, Gilead Sciences, Inc., 3; **K. Hasegawa**, Gilead Sciences, Inc., 1, 3; **T. Hendrikx**, Galapagos, 1, 3; **A. Boonen**, AbbVie, 2, Galapagos, 5, Lilly, 5, Celgene, 2, UC, 5; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **D. Walker**, Gilead, 2, 5, Lilly, 5, 8, Pfizer, 5, 8, Novartis, 5, 8; **R. Alten**, Pfizer, 2, 8, Gilead Sciences, Inc., 2, Novartis, 2, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 5, Lilly, 2, 5, UCB, 2, 5.

Abstract Number: 0144

Age, Income, Education, and Health Conditions Are Associated with Patient Empowerment Among US Adults with Arthritis, but Race and Geography Are Not

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The purpose of this study is to understand experiences of empowerment in healthcare visits among US adults with arthritis, and key factors associated with discrepancies in empowerment, including sociodemographics and patient-reported health outcomes.

Items by Subdomain	Lead-in and Response Options*	
	During the last 6 months, did you feel that...	*During the last 6 months, how important is it that...*
Patient Information-Seeking	Not at all (1)	Not important at all (1)
You asked for explanations	Somewhat (2)	Slightly important (2)
You asked questions	Quite a bit (3)	Very important (3)
You asked for advice	Very much (4)	Extremely important (4)
Result of Self-Advocacy		
You were able to talk to a professional to answer your questions		
Your choices were respected		
You obtained all the information you wanted		
You got the help you needed		

Note: Respondents rated feeling and importance of each item. Scores are calculated by summing the cross-product of feeling and importance ratings for items within the subdomain. There are three items in the Involvement in Decision subdomains and four items in the Involvement in Interactions, so the possible ranges are 3-48 points and 4-64 points, respectively.

Figure 1. Health Care Empowerment Questionnaire Subdomains

	Mean	SD
Age (years)	60.0	13.9
Time since diagnosis (years)	17.2	13.4
Number of arthritic conditions	2.5	1.6
PROMIS Anxiety T-Score	55.9	9.5
PROMIS Depression T-Score	54.9	9.3
PROMIS Pain Interference T-Score	62.7	7.8
PROMIS Physical Function T-Score	35.2	6.3
Gender	**Number**	**Percent**
Man/Male	955	11.7
Woman/Female	7,225	88.2
Another gender	13	0.2
Race/Ethnicity		
White*	7,093	86.6
Black or African American*	426	5.2
Hispanic or Latino	393	4.8
More than One Race/Ethnicity	141	1.7
Asian*	81	1.0
American Indian or Alaska Native*	37	0.5
Middle Eastern or No. African*	12	0.1
Native Hawaiian or Pacific Islander*	10	0.1
Education level		
Less than high school	76	0.9
High school diploma/GED	814	9.9
Some college (e.g., Associates, technical degree)	2,868	35.0
4-year college degree	2,309	28.2
Graduate degree (e.g., Masters, Doctorate)	2,126	25.9
Household Income		
Less than $15,000	497	7.0
$15,000 to $24,999	733	10.4
$25,000 to $49,999	1,609	22.8
$50,000 to $74,999	1,545	21.9
$75,000 to $99,000	1,164	16.5
$100,000 or more	2,001	28.4
Geographic area		
Urban	6,823	83.3
Rural	1,134	13.8
Arthritis Type (not mutually exclusive)		
Osteoarthritis	5,340	65.2
Rheumatoid Arthritis	4,047	49.4
Fibromyalgia	1,991	24.3
Degenerative disc disease	1,835	22.4
Spinal Stenosis	1,330	16.2
Psoriatic Arthritis	830	10.1
Ankylosing Spondylitis	637	7.8
Sjogren's syndrome	628	7.7
Raynaud's disease	593	7.2
Juvenile Arthritis persistent to adulthood	442	5.4
Gout	382	4.7
Lupus	350	4.3
Ehlers Danlos syndrome	59	0.7

*Non-Hispanic

Table 1. Demographics

Methods: Data were collected through online surveys of a convenience sample of adults with arthritis in the United States from March 2019 to March 2020 through the Arthritis Foundation's LiveYes! INSIGHTS program. The primary outcome, patient empowerment, was measured by two domains of the Health Care Empowerment Questionnaire (HCEQ): Involvement in Decisions (6 items) which we call Patient Information Seeking, and Involvement in Interactions (8 items) which we call Result of Self-Advocacy. Additional patient-reported outcomes were measured using the PROMIS-29® and sociodemographic data were collected. We analyzed surveys in which individuals had seen a

	Patient Information Seeking			Result of Self-Advocacy		
	Correlation Coefficient		p-value	Correlation Coefficient		p-value
Age	-0.054		<0.001	-0.115		<0.001
Time Since Diagnosis	-0.010		0.263	0.166		0.320
Number of Arthritis Conditions	0.047		0.543	-0.602		<0.001
PROMIS Anxiety Score	-0.322		<0.001	-0.987		<0.001
PROMIS Depression Score	-0.407		<0.001	-1.060		<0.001
PROMIS Pain Interference	-0.200		<0.001	-0.850		<0.001
PROMIS Physical Function	-0.263		<0.001	-0.831		<0.001
	Mean	**SD**	**p-value**	**Mean**	**SD**	**p-value**
Gender			0.007			0.006
Men/Male	30.7	11.4		38.5	14.8	
Women/Female	31.7	11.1		39.9	14.5	
Race/Ethnicity			0.522			0.555
White*	31.6	11.1		39.9	14.6	
Black or African American*	32.4	10.6		39.4	14.7	
Hispanic or Latino	31.1	11.0		38.5	14.3	
More than One Race/Ethnicity	33.1	11.9		40.0	15.1	
Asian*	31.0	11.7		39.4	15.7	
American Indian, Alaska Native*	30.8	11.3		36.9	15.2	
Middle Eastern or No. African*	30.3	13.7		36.4	16.5	
Native Hawaiian, Pacific Islander*	30.4	13.7		37.5	15.9	
Education level			<0.001			<0.001
Less than high school	28.1	12.5		34.2	15.4	
High school diploma/GED	29.2	11.4		37.1	14.9	
Some college	30.8	10.9		38.3	14.4	
4-year college degree	31.9	11.1		40.6	14.5	
Graduate degree	33.4	11.0		42.0	14.3	
Household Income			<0.001			<0.001
Less than $15,000	29.7	11.3		35.3	14.6	
$15,000 to $24,999	29.8	10.9		36.9	14.4	
$25,000 to $49,999	30.1	10.9		37.4	14.1	
$50,000 to $74,999	32.1	11.1		40.2	14.5	
$75,000 to $99,000	31.9	10.9		40.5	14.3	
$100,000 or more	33.2	11.2		42.9	14.6	
Geographic Area			0.398			0.018
Urban	31.7	11.1		40.0	14.6	
Rural	31.4	11.1		38.9	14.5	
Arthritis Type (N=2,721)			<0.001			<0.001
Osteoarthritis only (n=1,145)	30.8	11.3		38.1	14.5	
Rheumatoid Arthritis only (n=1,093)	32.6	11.4		42.6	14.9	
OA and RA only (n=483)	31.9	11.0		42.6	14.8	

*Non-Hispanic

Table 2. Bivariate Analyses

doctor in the last 6 months, completed all HCEQ items, and provided key demographics. We tested for association between the dependent variables (Patient Information-Seeking and Result of Self-Advocacy) and independent variables using one-way Analysis of Variance (gender, race, education, income, rurality, arthritis type) or simple linear regression (age, number of arthritic conditions, years since diagnosis, and PROMIS-29 subscales) with the dependent variables (HCEQ scales). P-value < 0.050 was considered statistically significant; between groups, ≥10% differences in means of HCEQ scores were considered meaningful.

Results: 8,193 surveys were analyzed. Lower HCEQ scores for both Patient Information-Seeking and Result of Self-Advocacy were significantly and meaningfully associated with higher age (r^2=0.005, p< 0.001 and r^2=0.012, p< 0.001), lower educational attainment (F(4, 8188) = 29.39, p< 0.001, and F(4, 8188) = 31.47, p< 0.001), and lower income (F(5, 7543) = 21.73, p< 0.001, and F(5, 7543) = 44.55, p< 0.001), Respondents' HCEQ scores did not differ significantly and/or meaningfully based on gender, race, geographic area, time since diagnosis, or number of arthritic conditions (p >0.050). Respondents with Osteoarthritis (OA) only (compared to those with Rheumatoid Arthritis (RA) only or OA and RA only) reported significantly and meaningfully lower Result of Self-Advocacy (F(2, 2718) = 30.97, p< 0.001); their Patient Information-Seeking was significantly but not meaningfully lower (F(2, 2718) = 7.01, p< 0.001). Result of Self-Advocacy had a strong negative correlation with PROMIS subdomains of Anxiety (r^2=0.012, p< 0.001), Depression (r^2=0.022, p< 0.001), Pain Interference (r^2=0.007, p< 0.001), and Physical Function (r^2=0.010, p< 0.001); each of these domains had weak to moderate negative correlation with Patient Information-Seeking.

Conclusion: Results of Self-Advocacy was lower among those who were older, less educated, lower income, more anxious, more depressed, experiencing greater pain, or better physical function. Similar but muted trends were seen for patient information-seeking. The differences between patient information seeking and self-advocacy indicate that while patients may feel comforTable seeking information, they may still have unmet needs.

Disclosure: K. Carluzzo, None; **E. Knight-Zhang**, None; **K. Schifferdecker**, None; **E. Creek**, None; **R. Butcher**, None; **G. Eakin**, None.

Abstract Number: 0145

Treat-to-Target in Rheumatoid Arthritis: Rates of Treatment Changes in Patients Engaged with Care Management Services Compared to Historically Reported National Registry Based Estimates

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Treat-to-target is the foundation of rheumatoid arthritis (RA) management. Prioritizing routine measurement of patient-reported disease activity along with conventional physician, laboratory and imaging assessments is vital to achieving this target. However, in the practice setting, alliance with treat-to-target recommendations is often a challenge. A recent report published in Arthritis Care and Research demonstrates that only 35%-55% of patients change their treatment even when experiencing moderate to high disease activity as measured by either the Routine Assessment of Patient Index Data 3 (RAPID3) or Clinical Disease Activity Index (CDAI) RA assessment tools using data from a national registry. Previous research has indicated that nurse-led care management may improve adherence to treat-to-target recommendations. The purpose of this study is to assess the rate of treatment changes among patients with RA who are actively engaged in a care-management program, monitored using the modified Health Assessment Questionnaire (mHAQ), and results shared with the treating physician compared to historically reported national registry based estimates obtained from a recent study.

Age, years (mean, SD)	52.6 (9.5)
Age, n (%)	
18-39	115 (66.9%)
40-59	41 (23.8%)
60 or more	16 (9.3%)
Gender, n (%)	
Female	132 (76.7%)
Male	40 (23.3%)
Index mHAQ Score (median, IQR)	0.13 (0.00-0.38)
Functional Status*	
Normal	120 (69.8%)
Mild	49 (28.5%)
Moderate	3 (1.7%)
Baseline Therapy	
cDMARD**	102 (59.3%)
bDMARD	12 (7.0%)
Combination	15 (8.7%)
Naïve	43 (25.0%)
Comorbidities	
Depression	30 (17.4%)
Diabetes	22 (12.8%)
COPD	11 (6.4%)
Cancer	7 (4.1%)
Hypertension	11 (6.4%)
Fibromyalgia	13 (7.6%)
Osteoarthritis	13 (7.6%)

* Functional Status - Normal (mHAQ<0.3), Mild (1.3<mHAQ<0.3), Moderate (1.3<mHAQ<1.8), and Severe (mHAQ>1.8)
** cDMARD – Methotrexate, Sulfasalazine, Leflunomide, Hydroxychloroquine
*** bDMARD – Adalimumab, Certolizumab pegol, Etanercept, Golimumab, Infliximab, Abatacept, Rituximab, Sarilumab, Tocilizumab, Baricitinib, Tofacitinib

Table 1. Demographic Characteristics (N=172)

	Patients Experiencing Progressive Functional Losses*	Patients Undergoing Change in Therapy	Change in Therapy (%)
Total	88	60	68.2%
Normal to Mild	49	25	51.0%
Mild to Moderate	32	28	87.5%
Moderate to Severe	7	7	100.0%
	Treatment Naïve (n)	Therapy Initiation (n)	Therapy Initiation (%)
Total	43	18	41.9%
Normal to Mild	30	11	36.7%
Mild to Moderate	13	7	53.8%

*Progressive functional losses defined as transition from normal (mHAQ<0.3), mild (1.3<mHAQ<0.3), moderate (1.3<mHAQ<1.8), and severe (mHAQ>1.8)

Table 2. Rate of Therapy Changes/Initiations

Methods: This is a single arm retrospective study of patients engaged in care management services between 2016 and 2019. Adult patients (≥ 18 years), with RA (by International Classification of Diseases , Tenth Revision codes), and engaged with care-management services for at least 12 months from the index date (date of first mHAQ score) were included in this analysis. Treatment changes associated with progressive functional losses were documented and rates of change were assessed. Progressive functional losses were classified as transitioning from normal (mHAQ<

0.3), mild (0.3< mHAQ< 1.3), moderate (1.3< mHAQ< 1.8), and severe (mHAQ >1.8). Baseline regimens were classified based on utilization of cDMARD (MTX, SSZ, LEF, HCQ) and bDMARD (TNF-α inhibitors, Abatacept, Rituximab, Sarilumab, Tocilizumab, Baricitinib, Tofacitinib). Rates of treatment changes were compared to historically reported national registry based estimates obtained from a recent study.

Results: A total of 172 patients were included in the study, the majority were female (76.7%) and the mean age was 52.6 years (SD = 9.5). Baseline treatment regimens included cDMARD (59.3%), bDMARD (7%), combination (8.7%), and treatment naïve (25%). Depression (17.4%) and diabetes (12.8%) were the most commonly reported comorbidities. The rate of therapy change was 68% among those who were actively engaged and warranted a change in therapy based on progressive loss of functional status. Among the treatment naïve, 42% had initiated therapy during the observation period.

Conclusion: Utilization of patient-reported disease severity measures and shared decision making, in a nurse led care-management program appear to improve adherence to treat-to-target recommendations as compared to standard practice without care-management support. A limitation of this study – and potential value for future research – was the lack of a clinician-driven assessment, such as the CDAI, and its correlation to the findings herein based on patient-driven (mHAQ) assessments.

Disclosure: P. Patel, CVS Health, 1, 3; **A. Krueger**, Accordant, 3; **A. Lipson**, PRAHS, 3; **M. Hamburger**, None; **C. Hunter**, CVS Health, 1, 3, Abbvie, 1.

Abstract Number: 0146

Patients' Perceptions and Expectations Towards the Role of Rheumatologists in the Recommendations of Physical Activity's Practice - A Cross-sectional Study Involving 308 Patients Living with Rheumatoid Arthritis in France

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SESSION INFORMATION
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Background/Purpose: Rheumatologists consider physical activity (PA) to be an important goal in the care for patients with rheumatoid arthritis (RA). However, there are very few studies on patients' perceptions of and expectations on the rheumatologist's role in the advising of PA practice.

The objective of this study was to describe the practice of PA in RA patients, in particular their perception of rheumatologist recommendations to engage in PA.

Methods: An online survey was conducted among French RA patients on Carenity.com, an online patient community. The survey was available from January 17th to February 25th, 2019. To ensure RA diagnosis, only patients who had declared being treated with at least one Disease Modifying Anti-Rheumatic Drug were included in the analysis.

Results: 308 patients participated in the study, 89% women; average age 53 years old (SD: 11.0); average time since RA diagnosis 9 years; 68% of patients were on methotrexate, 37% on biologics and 5% on JAK inhibitors.

97% of patients reported that they were engaged in a PA: domestic activities (77%), active transportation (i.e. walking or cycling) (73%), and sports (36%). However, 74% of patients reported a decrease in their PA level (both frequency and intensity) since their RA diagnosis.

Fatigue (64%), pain (54%) and lack of mobility (38%) were the main barriers to PA practice. Physician advice plays an important role in patients' motivation to engage in PA. In fact, after beneficial effects on mood (69%) and condition (44%), physician's advice (24%) was the third main motivation to engage in PA.

Physicians prescribed physiotherapy for 55% of patients. Despite the important role of doctors in patients' motivation, only 38% of patients were asked about their PA practice by their physician, 34% received advice and 9% were referred to PA sessions by their physician.

Moreover, half of the patients believed their rheumatologist did not know what type of PA to recommend in their case (median: 5.0/10, with 10="Totally agree"); a quarter of patients felt that their rheumatologist had limited knowledge of the impact of PA practice on joints and were not able to answer their questions on PA (third quartile: 5.0/10, with 10= "Totally agree").

When asked about their expectations regarding possible support in the practice of PA, patients spontaneously mentioned personalized advice/information and easier access to sport classes or specialized equipment. Brochures on recommended activities, exercise videos and brochures on the benefits of PA practice were considered useful by 52%, 45% and 42% of patients respectively.

Conclusion: Given that engagement in PA is considered an integral part of RA management, rheumatologists play an essential role in encouraging PA practice, along with other health professionals, including physiotherapists. As the study has shown, communication between physicians and RA patients about PA with personalized and practical information on PA practice should be encouraged.

Disclosure: A. Rat, Sanofi Genzyme, 5; **A. Constantin**, AbbVie Inc., 5, 8, Amgen, 5, 8, Celltrion, 5, Gilead, 5, 8, Eli Lilly and Company, 5, 8, Novartis, 5, 8, Pfizer Inc., 5, 8, UCB, 5, 8, Janssen, 8; **C. Beauvais**, Sanofi Genzyme, 5; **Y. Guillodo**, Sanofi Genzyme, 5; **V. Guay**, Sanofi Genzyme, 5; **E. Pain**, Sanofi Genzyme, 9; **A. Bombezin--Domino**, Sanofi Genzyme, 9; **F. Lévy Weil**, Sanofi Genzyme, 3.

Abstract Number: 0147

The Interpretation of Patient-reported Outcomes in Rheumatoid Arthritis: Do Clinical Trials Adequately Evaluate Meaningful Improvements for Patients?

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

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Background/Purpose: The importance of patient-relevant outcomes, such as pain, fatigue and physical functioning, has been long established in the field of rheumatoid arthritis (RA). Patient-reported outcomes (PROs) questionnaires evaluate these outcomes in RA clinical trials and can differentiate treatments. However, this ability depends on the interpretation of PRO endpoints. Measuring PRO changes that are meaningful to patients can help clinicians optimize the treatment selection and evaluate outcomes within the treat-to-target approach, recommended by ACR. For the incoming RA treatments within the Janus kinase inhibitors (JAKis) class, we aimed to evaluate the available metrics to capture meaningful individual-patient-level change in most common PROs.

Methods: A targeted PubMed literature search was conducted to identify RA clinical trials of JAKis published between 1st Jan 2009 and 1st April 2020 that included a PRO as an outcome. We reviewed relevant publications and conference abstracts to identify values used to interpret PROs. Follow-up literature searches were conducted to determine and critically appraise methods used to derive these values.

Results: Among 101 papers meeting the inclusion criteria, 35 reported the proportion of patients achieving a *minimal* (clinically) important difference [M(C)ID] on Health Assessment Questionnaire Disability Index (HAQ-DI), Pain visual analogue scale (VAS), Patient Global Assessment (PtGA), Short-Form 36 (SF-36), Functional Assessment of Chronic Illness–Fatigue (FACIT-Fatigue), Insomnia Severity Index (ISI), morning stiffness severity and duration. However, the secondary methodological search revealed no evidence supporting the application of these values to interpret individual-patient-level *meaningful* change (Table 1).

Conclusion: Despite common use of PROs MID/MCID thresholds in the RA clinical trials of JAKis, current methods lack evidence of the methodologically robust magnitude of change meaningful to individuals. These findings highlight a need to re-evaluate the patient-relevance of PRO metrics in RA clinical trials, and potentially explore other endpoints, such as the Patient AccepTable Symptom State. The availability of methodologically robust, patient-relevant,

	Values applied to individual patient-level change in RA clinical trials of JAKis		
PRO	**Value applied to individual patient-level change (and reference to source)**	**Sufficient evidence to define individual patient-level change?**	**Methods used to derive value**
HAQ-DI	≥0.22 or ≥0.3 (Wells et al, 1993)	No	Anchor-based, but not an established PRO of the same concept (i.e. physical functioning and disability)
Pain VAS (0-100mm)	≥10mm (ref not identified)	No	Unknown method
PtGA (0-100mm)	≥10mm (ref not identified)	No	Unknown method
SF-36	Component summary scores: ≥2.5, Domain scores: ≥5 (ref not identified)	No	Unknown method
FACIT-Fatigue (0-52)	≥3-4 or 3.56 (Cella et al, 2005)	No	Distribution-based methods only
Insomnia Severity Index (ISI)	≥ 8.4 decrease (Morin et al, 2011)	No	Anchor-based, but not an established PRO of the same concept
Morning stiffness severity (0-10)	≥10mm (Strand et al, 2019)	No	Unknown method
Morning stiffness duration (minutes)	Half a standard deviation (Strand et al, 2019)	No	Distribution-based methods only

Table 1. Values used to interpret individual patient-level change on PROs in RA

clinically-meaningful change thresholds for PROs can help determine most patient-relevant RA therapies.Table 1: Values used to interpret individual patient-level change on PROs in RA

Disclosure: P. Taylor, Eli Lilly, 2, 5, 8, Celgene, 2, 5, 8, AbbVie, 2, 5, 8, Biogen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celltrion, 2, 5, 8, Fresenius, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Janssen, 2, 5, 8, Nordic Pharma, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8, Pfizer, 2, 5, 8, Gilead, 2, 5, 8, Galapagos, 2, 5, 8; **R. Dore**, AbbVie, 2, 5, Amgen, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly and Co, 2, 5, Gilead Sciences, Inc., 2, 5, GlaxoSmithKline, 2, 5, Myriad, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Radius, 2, 5, Regeneron, 2, 5, Sanofi, 2, 5, UCB, 2, 5, Exagen, 8; **K. Williams**, None; **S. Acaster**, None; **J. Antonova**, Gilead Sciences, 1; **M. Genovese**, AbbVie, 2, 5, Eli Lily and Co, 2, 5, EMD Merck Serono, 2, 5, Galapagos, 2, Genentech/Roche, 2, 5, Gilead Sciences, Inc., 1, 2, 3, 5, GSK, 2, 5, Novartis, 2, 5, Pfizer, Inc., 2, Rpharm, 2, 5, Sanofi Genzyme, 2, 5.

Abstract Number: 0148

Perspectives on Treatment Burden for Methotrexate and TNF-inhibitors Among Psoriatic Arthritis and Rheumatoid Arthritis Patients: A Qualitative Study

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Physicians often consider adverse events when choosing therapies for PsA and RA but may give less attention to other ways in which treatments affect the well-being of patients, such as impacts on quality of life, barriers to access, and challenges with taking medications. In a previous study examining the prevalence of side effects to TNF inhibitors (TNFi) and methotrexate (MTX) in FORWARD, The National Databank for Rheumatic Diseases, we found that side effects were wide ranging and differed for PsA and RA and by treatment. The objective of this qualitative study was to consider patients' perspectives on the treatment burdens of MTX and TNFi's, the most commonly used therapies in PsA and RA.

Methods: We conducted semi-structured interviews with 24 patients with RA and 25 patients with PsA from 05/2019-03/2020 who were enrolled in FORWARD with documented use of MTX or TNFi. Participants were asked about their experiences with medications for their disease, specifically MTX and TNFi. Interviews were recorded and transcribed. Transcripts were analyzed using a grounded theory approach and NVivo software (v12.0). We coded concepts related to treatment burden, effectiveness of medications, decision-making, disease course, and impacts on daily life such as social relationships and work. We examined how medication type shaped patient experiences with treatment burdens.

Results: Participants were mostly female (72% in PsA, 88% in RA), all Caucasian, aged 45-85 years, and with disease duration of 4-51 years (Table 1). All participants had used MTX and 82% had used TNFi. We identified 9 types of treatment burdens (Table 2): side effects, managing side effects, psychological, daily functioning, taking medications, accessing medications, economic impact, work, and family planning/breastfeeding. For both patients taking MTX and TNFi, fewer than half of patients reported increased infections/cancer or seeking/receiving further medical atten-

Characteristic	PsA (N= 25)	RA (N=24)
Age, years, range	66.6 (46-80)	66.9 (45-85)
Female	72%	88%
Caucasian	100%	100%
Married	68%	58%
Disease duration, years (range)	27.1 (4-46)	27.2 (12-51)
Current Therapies		
MTX monotherapy	24%	20.8%
TNFi monotherapy	32%	25%
Non-TNFi biologic, no MTX	16%	12.5%
TNFi + MTX	12%	25%
Non-TNFi biologic+ MTX	12%	16.7%
Other or nothing	4%	0%
Previous (discontinued) therapies		
Prior TNFi	68%	72%
non-TNFi biologics	20%	21%
MTX	52%	38%

Table 1. Participant characteristics by diagnosis (mean (range) or %)

Treatment burden	MTX	TNFi
Side effects experienced	- Immunosuppressive effects (infections and cancer) -Nausea, fatigue, hair loss, mouth sores -Liver problems	-Immunosuppressive effects (infections and cancer) -Injection site reactions/allergic reactions -Painful injections
Management of side effects	-Getting medical attention or additional treatment to address side effects -Changing how MTX was taken (formulation, dose, timing) to alleviate side effects -Blood tests and avoiding alcohol to prevent liver damage	-Getting medical attention or additional treatment to address side effects -Dose reduction to reduce infections was only possible for certain TNFis
Psychological	-Worry about side effects -Fear of MTX as a 'cancer drug'	-Worry about side effects -Dread towards injections due to pain/fear of needles
Daily functioning	-Reduced ability to perform usual activities due to nausea/fatigue	—No issues reported—
Taking medications	-Taking MTX could be difficult because it induced nausea	-Self-injections were challenging—sometimes help from someone else was needed -Travel and time needed for infusions -Process of trying/switching biologics is lengthy
Accessing medications	— About one fifth of patients reported issues —	- Coordinating payment for medications (insurance issues, copay assistance) and delivery of medication was complicated -Insurance coverage issues could constrain choice of TNFi or interrupt receipt of effective treatment
Economic impact	— Fewer than one in every twenty patients reported issues —	-Costly and difficult to afford without insurance or copay assistance programs -Inability to pay for medications caused gaps in treatment -Patients preferred not to spend so much money on medication, but felt they had no choice
Work	-Side effects impacted ability to work	-Getting infusions required taking time off work
Family planning/ breastfeeding	-Have to stop MTX for pregnancy or breastfeeding	-Choice of TNFi was influenced by safety for pregnancy or breastfeeding

Table 2. Key Treatment Burdens Discussed by Participants

tion or care to address side effects. A majority of MTX users reported taking steps to manage the negative impacts of nausea, fatigue, mouth sores, or hair loss on quality of life, daily functioning or work. Three-quarters of TNFi users reported challenges with accessing, paying for, or taking medications. Consistent with previous research, discontinuing the use of medication because of lack of effectiveness was more common among participants with PsA than those with RA (data not shown).

Conclusion: Greater awareness of the treatment burdens experienced by patients may help healthcare providers better support patients with any medication-related challenges that they encounter. From the perspective of patients, we found that there are many treatment burdens associated with PsA and RA that are rarely addressed in clinical trials or observational studies.

Disclosure: A. Ogdie, AbbVie, 5, Amgen, 2, 5, BMS, 1, Celgene, 1, Corrona, 1, Janssen, 1, Eli Lilly, 1, Novartis, 2, 5, Pfizer, 2, 5, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 2, Rheumatology Research Foundation, 2, National Psoriasis Foundation, 2; **Y. Shaw**, Amgen Inc., 9; **M. Almonte**, Amgen Inc., 9; **E. Maksabedian**, Amgen Inc., 1, 2; **K. Michaud**, Rheumatology Research Foundation, 2.

Abstract Number: 0149

How STable Are Medication Necessity Beliefs and Safety Concerns in the First Year of RA?

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SESSION INFORMATION

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Background/Purpose: At RA onset, DMARDs are essential to controlling inflammation and preventing disability. In people with established RA, specific beliefs about the necessity of DMARDs and concerns about potential harm influence side effects and adherence. To examine how medication perceptions evolve over time, we evaluated the stability of RA medication beliefs around diagnosis and identified predictors of change 12 months later.

Methods: Data were from Early RA patients enrolled in the Canadian Early Arthritis Cohort (CATCH) March 2017 and January 2020 who completed the Beliefs about Medicines Questionnaire at 0 and 12 months. Necessity and Concerns scales each have 5 statements regarding the need for prescribed medication to control RA and concerns about potential harms of taking them. We used Pearson correlation and multivariable regression to examine associations and predictors of change at 12 months.

Results: The 362 Participants were mostly women (66%), of white racial background (83%), with a mean (SD) age of 56 (15) years, and symptoms of 6 (3) months. Compared with baseline, at 12 months (n=180), mean **Necessity** beliefs were slightly higher (18.1 vs. 18.9;p=.01) and **Concerns** were slightly lower (15.2 vs. 14.3; p< .01).

	Necessity Beliefs Baseline*				Medication Concerns Baseline				Medication Concerns Change at 12 months			
	Model 1 N=312		Model 2 N=312		Model 1 N=312		Model 2 N=312		Model 1 N=143		Model 2 N=136	
	B	95% CI	B	95% CI	B	95% CI	B	95% CI	B	95% CI	B	95% CI
Age (decade)	0.00	-0.35 to 0.34	0.03	-0.31 to 0.37	-0.16	-0.49 to 0.17	-0.03	-0.35 to 0.30	-0.08	-0.59 to 0.44	0.30	-0.20 to 0.78
Women	0.18	-0.82 to 1.17	-0.22	-1.21 to 0.77	0.42	-0.54 to 1.37	0.11	-0.84 to 1.05	0.01	-1.40 to 1.42	0.15	-1.19 to 1.49
Minority	**-1.86**	**-3.17 to -0.54**	**-1.80**	**-3.09 to -0.51**	0.11	-1.16 to 1.37	0.15	-1.08 to 1.37	1.21	-0.72 to 3.15	**1.89**	**0.11 to 3.67**
Education > HS	0.70	-0.31 to 1.70	0.82	-0.16 to 1.79	0.89	-0.07 to 1.86	**1.00**	**0.07 to 1.92**	0.41	-1.01 to 1.83	1.04	-0.31 to 2.39
RDCI	0.06	-0.27 to 0.38	0.01	-0.31 to 0.33	0.11	-0.20 to 0.43	-0.04	-0.34 to 0.27	0.10	-0.36 to 0.56	-0.06	-0.53 to 0.40
CDAI	**0.05**	**0.02 to 0.09**	**0.04**	**0.00 to 0.07**	**0.04**	**0.00 to 0.07**	0.01	-0.02 to 0.05	**0.12**	**0.05 to 0.19**	0.07	-0.01 to 0.15
MTX use	**1.49**	**0.42 to 2.56**	**1.15**	**0.11 to 2.19**	-0.48	-1.50 to 0.55	-0.49	-1.48 to 0.50	1.34	-0.09 to 2.77	**1.56**	**0.16 to 2.96**
PHQ8 depression			0.08	-0.03 to 0.18			**0.15**	**0.05 to 0.25**			**0.33**	**0.05 to 0.60**
Anxiety			0.00	-0.06 to 0.06			**0.08**	**0.02 to 0.13**			**0.12**	**0.03 to 0.22**
Physical function			-0.01	-0.11 to 0.08			-0.05	-0.14 to 0.04			**0.17**	**0.04 to 0.30**
Pain interference			0.06	-0.04 to 0.15			-0.01	-0.10 to 0.08			-0.03	-0.14 to 0.09
Fatigue			**0.09**	**0.02 to 0.15**			-0.05	-0.11 to 0.01			-0.04	-0.15 to 0.06
Sleep			**-0.14**	**-0.20 to -0.07**			-0.03	-0.09 to 0.04			0.01	-0.08 to 0.11
Participation			0.00	-0.08 to 0.07			-0.03	-0.09 to 0.04			**-0.11**	**-0.22 to 0.00**

Table 2. Predictors of medicine beliefs and concerns when starting first medications and change at 12 months in early RA.

	Necessity		Concerns	
	0	12 months	0	12 months
N	362	183	362	183
Age	0.06	0.02	-0.10	-0.09
Sex	-0.01	0.11	0.05	0.05
Education > High School	0.01	-0.15	0.07	0.02
Minority status	**-0.14****	0.10	-0.06	0.10
Rheumatic Disease Comorbidity Index	0.06	0.00	0.04	-0.03
RA Characteristics				
Symptom duration	-0.09	0.01	-0.03	-0.09
CDAI	**0.20****	0.04	**0.11***	**0.27****
Methotrexate Use	**0.16****	0.06	0.04	0.08
Symptoms & Function				
PROMIS Physical function	**-0.22****	-0.12	**-0.23****	-0.11
PROMIS Pain Interference	**0.27****	**0.18***	**0.21****	**0.23****
PHQ 8	**0.23****	**0.15***	**0.32****	**0.38****
PROMIS Anxiety	**0.13***	0.08	**0.29****	**0.36****
PROMIS Fatigue	**0.27****	0.13	**0.18****	**0.31****
PROMIS Sleep disturbance	0.04	**0.20****	**0.18****	**0.26***
PROMIS Participation satisfaction	**-0.21****	**-0.17***	**-0.19****	**-0.28****

Values are Pearson correlation coefficients. *p<0.05; **p<0.01

Table 1. Associations between RA medicine necessity and concern beliefs, individual characteristics, and HRQL at baseline and 12 months in early RA.

At baseline, weak (r< 0.30) associations were evident between **Necessity** beliefs and minority status, CDAI, MTX use, and all HRQL domains except sleep. At 12 months, sleep, depression, and pain were positively though weakly related, and participation was inversely and weakly related to **Necessity** beliefs (Table 1). At baseline, worse CDAI, symptoms, function, and participation were associated with higher **Concerns.** These relationships were somewhat stronger at 12 months, except physical function was no longer associated with **Concerns**.

In multivariable regression, when starting treatment **Necessity** scores were lower in minorities and increased with CDAI, MTX use, and fatigue but decreased as sleep improved (Table 2). No relationships were evident at 12 months. Higher **Concerns** when starting treatment were predicted by higher education, and greater depression and anxiety.

At 12 months, higher **Concerns** were predicted by minority status and MTX use, higher emotional distress, better function and lower participation in social activities.

Conclusion: Our data suggest that in people with early RA, there is an agreement that medicines are generally necessary, but also significant levels of concerns. Further, medication perceptions appear to be reasonably sTable over the first year and are influenced to some degree by some individual characteristics and RA and medication experiences. Findings suggest that specific interventions may be needed to systematically influence medication beliefs and concerns to improve acceptance, tolerance, and long-term adherence.

Disclosure: V. Ta, None; **O. Schieir**, None; **M. Valois**, None; **L. Bessette**, Amgen, 1, 2, 3, BMS, 1, 2, 3, Janssen, 1, 2, 3, UCB, 1, 2, 3, AbbVie, 1, 2, 3, Pfizer, 1, 2, 3, Merck, 1, 2, 3, Celgene, 1, 2, 3, Sanofi, 1, 2, 3, Lilly, 1, 2, 3, Novartis, 1, 2, 3, Gilead, 2, 6, 8; **G. Boire**, Amgen, 1, 2, BMS, 1, 2, 3, Celgene, 1, Merck, 1, 2, Pfizer, 1, 2, 3, Eli Lilly, 1, 2, Janssen, 1, Abbvie, 1, Novartis, 1, Sandoz, 1; **G. Hazlewood**, None; **C. Hitchon**, None; **E. Keystone**, Abbot, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 2, 5, 8, Biotest, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, F. Hoffmann-La Roche Inc., 2, 5, 8, Janssen, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Genentech, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, UCB, 2, 5, 8; **J. Pope**, AbbVie, 2, 5, Amgen, 5, 8, Lilly, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 5, 8, Sandoz, 5, 8, Roche, 2, 5, 8, Pfizer, 5, 8, Novartis, 5, 8, Merck, 2, 5, 8, Janssen, 5, 8, Gilead Sciences, Inc., 2, 5, BMS, 2, 5, 8, Abbott, 5, Actelion, 5, AstraZeneca, 5, Bayer, 5, Boehringer Ingelheim, 5, EICOS, 5, Emerald, 5, GlaxoSmithKline, 5, Medexus, 5, Seattle Genetics, 2; **C. Thorne**, Abbvie, 1, 2, Amgen, 1, 2, Celgene, 1, 2, CaREBiodam, 1, Centocor, 1, Janssen, 1, Lilly, 1, Medexus/Medac, 1, 2, Merck, 1, Novartis, 1, 2, Pfizer, 1, 2, Sanofi, 1; **D. Tin**, None; **N. Andersen**, None; **V. Bykerk**, Amgen, 2, 5, UCB, 5, National Institute of Health, 2, 9, Bristol-Myers Squibb Company, 2, 5, Gilead, 5, Pfizer, 5, Brainstorm Therapeutics, 1, 3; **S. Bartlett**, Pfizer, 1, UCB, 1, Lily, 1, Novartis, 1, Merck, 1, Janssen, 1, Abbvie, 1; **C. (CATCH) Investigators**, Amgen, 2, Pfizer Canada, 2, Medexus Inc., 2, Eli Lilly Canada, 2, Merck Canada, 2, Sandoz Canada, Biopharmaceuticals, 2, Gilead Sciences Canada, 2, Hoffmann-LaRoche, 2, Janssen Biotech, 2, UCB Canada, 2, Bristol-Myers Squibb Canada, 2, Sanofi Genzyme, 2, AbbVie Corporation, 2.

Abstract Number: 0150

The Preparation Experience for Total Knee Arthroplasty of Patients with Osteoarthritis: A Cross-Sectional Survey

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: We previously identified several barriers and facilitators of exercise before total knee arthroplasty (TKA) in a small qualitative study, as well as the existence of patient-reported anxiety in anticipation of TKA. We aim to further explore these domains in a larger group of patients who had TKA within 6 months in order to understand specific patient needs in the design of a pre-habilitation program for TKA.

Methods: We designed a cross-sectional survey deployed online with questions abstracted from the themes that emerged from our previous qualitative study. Patients were > 40 years old from a single center and had a primary

Table 1: Demographic characteristics of individuals surveyed who had total knee arthroplasty (TKA)

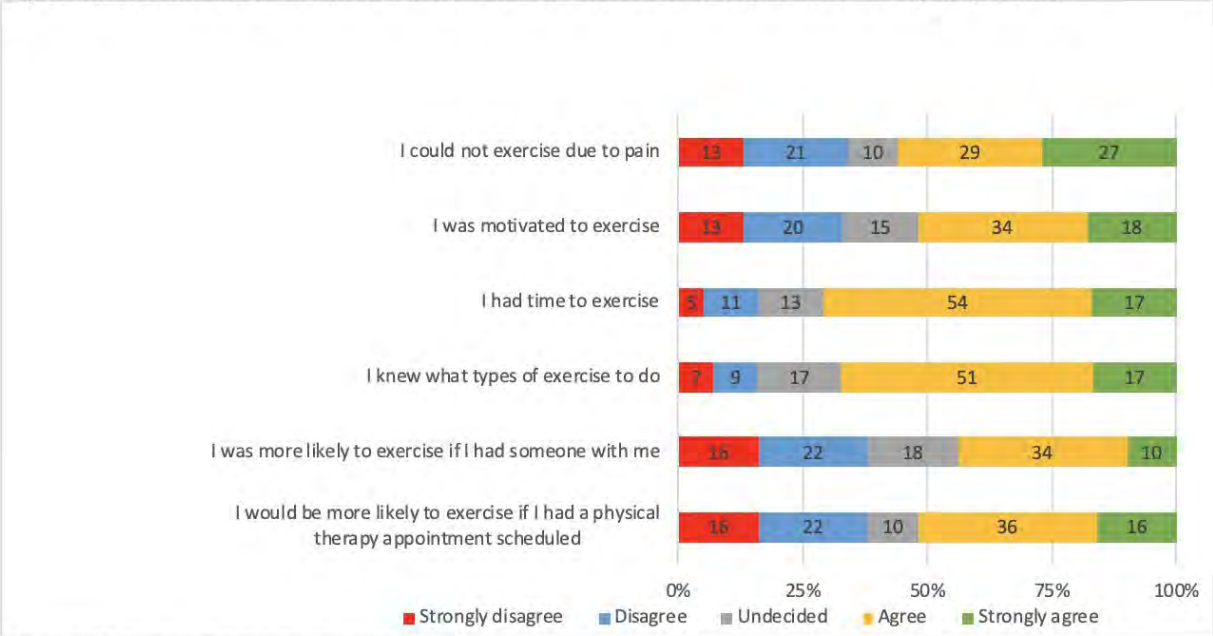
Patient Characteristics	Overall (N = 79) N (%)
Age (yrs)	
50-59	8 (10)
60-69	30 (38)
70-79	33 (42)
80-89	8 (10)
Female	50 (63)
Race/Ethnicity	
White	69 (87)
Black/African-American	6 (8)
Asian/Pacific Islander	1 (1)
Other	2 (3)
Prefer not to answer	1 (1)
Time between TKA and survey	
6-7 months	21 (27)
8-9 months	8 (10)
1 year or more	50 (63)
Physical preparation of patients with OA before TKA*	
Exercised regularly before TKA	45 (58)
Physician provided list of exercises in preparation for TKA	42 (55)
Referred to physical therapy in preparation for TKA	35 (46)
Exercised in preparation for TKA	43 (56)
Attended physical therapy in preparation for TKA	17 (22)

*Missing data from 2 respondents

TKA ≥ 6 months ago. We asked patients about barriers and facilitators to exercise before and after TKA, such as knee pain, knowledge about and motivation to exercise, time to devote to exercise, and peer support. We also examined the prevalence of anxiety in anticipation of TKA and coping mechanisms to alleviate that anxiety.

Results: 79 patients who met the inclusion criteria responded to the survey, age range 50 – 89. 30% had a primary TKA on both knees. 63% (N = 50) were women and 87% (N = 69) were White (**Table 1**). A majority of patients (56%) exercised in preparation for TKA, and 22% attended physical therapy. The most common barriers to exercise before TKA were pain (56%), lack of motivation (33%), lack of time (16%) and lack of knowledge (33%) on how to exercise. The main facilitators to exercise were presence of social support (44%) and scheduled physical therapy appointments (52%) (**Figure 1**). In the 48% of patients (N = 38) who reported anxiety before TKA, 95% sought reassurance from family/friends while 92% asked about the experiences of those who already had TKA (**Table 2**). Only 1 patient sought professional counseling for their anxiety.

Figure 1: Distribution of facilitators and barriers to exercise before total knee arthroplasty (TKA)*



*N = 77. Missing data from 2 respondents.

Table 2: Distribution of coping mechanisms of patients who reported anxiety in anticipation of total knee arthroplasty (TKA)

	Overall (N = 77) N (%)
Reported anxiety in anticipation of TKA*	38 (48)
Coping mechanisms for anxiety**	
Willingness to share concerns with physician	33 (87)
Referred to counseling services	1 (3)
Went to counseling services	0 (0)
Talked to family/friends	36 (95)
Sought others' experiences with TKA	35 (92)
Attended pre-operative education class	37 (97)

* Missing data from 2 respondents

** Answers based on the 38 (48%) patients who reported experiencing anxiety

Conclusion: Knee pain was the major barrier to exercise in preparation for surgery, while social support and physical therapy were the two major facilitators. Anxiety was common and interacting with family, friends or even another person who already had TKA were strategies used to alleviate anxiety in preparation for TKA. Similar leveraging of social support may motivate individuals to engage in physical activity in preparation for TKA.

Disclosure: A. Leung, None; **G. Lui**, None; **S. Goodman**, Pfizer, 1, Novartis, 1, UCB, 1, regenosine, 1, 2, Horizon, 1; **L. Mandl**, Annals of Internal Medicine, 9, UpToDate, 7, Regeneron, 2; **P. Sculco**, EOS imaging, 1, Intellijoint Surgical, 1, Depuy Synthes, 1, Lima Corporate, 1; **M. Figgie**, wishbone, 1, 2, 3, 4, 5, insight, 1, hs2, 1, mekanika, 1, lima, 1, 2; **I. Navarro-Millan**, None.

Abstract Number: 0151

More Than Half of Newly Diagnosed RA Patients Are Not Convinced of the Necessity of RA Medicines: Associations with RA Characteristics, Symptoms, and Function in the Canadian Early Arthritis Cohort (CATCH)

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Although DMARDs are essential for early aggressive control of RA to reduce symptoms and disability, medication adherence is variable. Beliefs about the necessity of medications and safety concerns predict adherence and are modifiable. Little is known about perceptions of RA medications in patients who are newly diagnosed. We examined associations among RA medication necessity beliefs and concerns, sociodemographics, RA characteristics, symptom levels and function in new RA patients around the time of diagnosis and starting medications.

Methods: Baseline data were analyzed from participants in the Canadian Early Arthritis Cohort (CATCH) who enrolled between 2017-2020 and completed the Beliefs about Medicine Questionnaire (BMQ) and PROMIS-29. All met ACR1987 or 2010 ACR/EULAR criteria and had active RA at enrollment. BMQ Necessity (N) and Concerns (C) scores were classified as **high** (≥20) or **low** (< 20) and categorized into: Accepting (↑N ↓C); Ambivalent (↑N↑C); Sceptical (↓N↑C); and 4) Indifferent (↓N↓C). Groups were compared using ANOVA and chi-square tests.

Mean(SD) or N(%)	Accepting	Ambivalent	Skeptical	Indifferent	p-Value
N (%)	113 (31%)	34 (9%)	21 (6%)	196 (54%)	--
Age	57 (15)	57 (14)	56 (12)	55 (15)	0.518
Women	62%	62%	70%	69%	0.605
Minority	12%	24%	10%	20%	0.173
Education > HS	62%	62%	57%	61%	0.862
Currently smoking	**9%$_a$**	**30%$_b$**	**20%$_{a,b}$**	**17%$_{a,b}$**	**0.010**
Former	**47%$_a$**	**39%$_{a,b}$**	**60%$_a$**	**35%$_b$**	
Never	**44%$_a$**	**30%$_{a,b}$**	**20%$_b$**	**49%$_a$**	
Healthy BMI (<25)	**28%$_a$**	**22%$_{a,b}$**	**33%$_{a,b}$**	**41%$_b$**	**0.036**
Overweight (25-30)	**41%$_a$**	**46%$_{a,b}$**	**33%$_{a,b}$**	**28%$_b$**	
Obese (30+)	**31%$_a$**	**32%$_a$**	**33%$_a$**	**32%**	
Tender joint (0-28)	**9 (7)$_a$**	**8 (6)$_{a,b}$**	**8 (6)$_{a,b}$**	**7 (6)$_b$**	**0.032**
Swollen joint (0-28	8 (6)	7 (5)	8 (5)	6 (5)	0.203
CDAI	**27 (13)$_{a,b}$**	**28 (15)$_a$**	**27 (12)$_{a,b}$**	**23 (13)$_b$**	**0.011**
Methotrexate (MTX)	**81%$_a$**	**71%$_{a,b}$**	**71%$_{a,b}$**	**67%$_b$**	**0.057**
Non-MTX DMARDs	54%	59%	57%	54%	0.943
Oral steroids	33%	29%	38%	24%	0.222
Parenteral steroids	35%	32%	29%	30%	0.852

Differing subscripts indicate significantly different values ($p<.05$)

Table 1. Patient characteristics at baseline by profiles.

BMQ Item	Accepting	Ambivalent	Sceptical	Indifferent
Necessity of RA Meds				
My health, at present, depends on my medicines	98%	100%	33%	50%
My life would be impossible without my medicines	90%	97%	14%	20%
Without my medicines, I would become very ill	93%	94%	19%	20%
My health in the future will depend on my medicines	96%	88%	19%	35%
My medicines protect me from becoming worse	97%	97%	57%	62%
Concerns about RA Meds				
Having to take medicines worries me	51%	100%	100%	46%
I sometimes worry about the long term effects of my medicines	71%	97%	100%	69%
My medicines are a mystery to me	20%	77%	86%	14%
My medicines disrupt my life	11%	77%	52%	3%
I sometimes worry about becoming too dependent on my RA medicines	25%	91%	95%	30%

Items were rated Strongly Disagree, Disagree, Neutral, Agree, Strongly Agree

Table 2. Proportions of patients who agreed/strongly agreed with each item.

	Accepting	Ambivalent	Sceptical	Indifferent	p-Value
Patient Global (0-10)	**5.2 (2.7)$_a$**	**6.0 (2.9)$_a$**	**5.8 (2.6)$_a$**	**4.4 (2.6)$_b$**	**0.001**
Pain (0-10)	**5.8 (2.8)$_a$**	**7.0 (2.8)$_b$**	**5.9 (2.8)$_{a,b}$**	**5.2 (2.8)$_a$**	**0.006**
PROMIS-29					
Physical Function	**39 (8)$_a$**	**37 (7)$_a$**	**38 (8)$_a$**	**42 (8)$_b$**	**<0.001**
Depression	**52 (10)$_a$**	**58 (12)$_b$**	**57 (9)$_b$**	**50 (9)$_c$**	**<0.001**
Anxiety	**53 (10)$_a$**	**59 (10)$_b$**	**58 (9)$_b$**	**51 (10)$_a$**	**<0.001**
Fatigue	**56 (10)$_a$**	**58 (10)$_a$**	**55 (12)$_{a,b}$**	**52 (11)$_b$**	**0.002**
Sleep disturbance	53 (9)$_a$	55 (7)$_a$	55 (7)$_a$	53 (9)$_a$	0.508
Social Participation	**42 (10)$_a$**	**41 (10)$_a$**	**41 (8)$_{a,b}$**	**44 (10)$_b$**	**0.055**
Pain Interference	**62 (8)$_a$**	**64 (8)$_a$**	**62 (9)$_{a,b}$**	**59 (9)$_b$**	**<0.001**

Differing subscripts indicate significantly different values ($p<.05$)

Table 3. Physical, emotional, and social function by BMQ attitudinal profiles.

Results: The 362 patients were mostly white (83%) women (66%) with a mean (SD) age of 56 (15), symptom duration of 6 (3) months, and 32% were obese (BMI≥30). More than half (56%) were DMARD-naive or minimally exposed. Mean N and C scores were similar between men and women; 54% were classified as **Indifferent**, 31% **Accepting**, 9% **Ambivalent,** and 6% **Sceptical** (Table 1). As compared to those classified as **Accepting**, more **Indifferent participants** smoked, had a healthy weight, lower TJCs, and trend for lower CDAI (Table 1). Groups were similar by sociodemographics, symptom duration, and DMARD/steroid use, except fewer **Indifferent** patients received MTX.

Most (67-100%) worried about the long-term effects of their medications (Table 2). **Indifferent** patients had statistically and meaningfully lower patient global, depression, anxiety, fatigue and pain interference, and higher function and participation scores (Table 3).

Conclusion: Most new RA patients worried about the long-term safety of their RA medications. Many had low medication necessity beliefs and concerns, and only 31% had high necessity beliefs and low concerns around diagnosis. Lifestyle and lower CDAI, TJCs, symptoms and functional impacts were associated with RA medication indifference. Exploring medication beliefs in newly diagnosed RA patients may help identify information gaps and provide opportunities to address concerns, potentially improving adoption and persistence over time.

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Abstract Number: 0152

Veterans with RA and Gout Identify Their Goals and How They Can Work with Clinicians to Achieve Their Goals

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Understanding patient goals and concerns is essential for aligning treatment decisions with patient preferences and supporting effective patient-clinician partnerships. Yet, little is known about the goals and concerns of people with rheumatoid arthritis (RA) or gout. In this study, we aim to understand the primary goals and concerns expressed by veterans with RA and/or gout and how they envision working in partnership with their clinicians to achieve their goals or allay their concerns.

Methods: Veterans with RA and/or gout (n=283) at a busy rheumatology clinic completed a paper pre-visit survey immediately prior to a clinic visit. The survey included three open-ended questions: (1) What is your #1 concern or goal related to your arthritis?; (2) How can we help you achieve your goals?; and, (3) What steps can you take to help achieve your goals? Data were collected between April and September 2019. We conducted a content analysis of

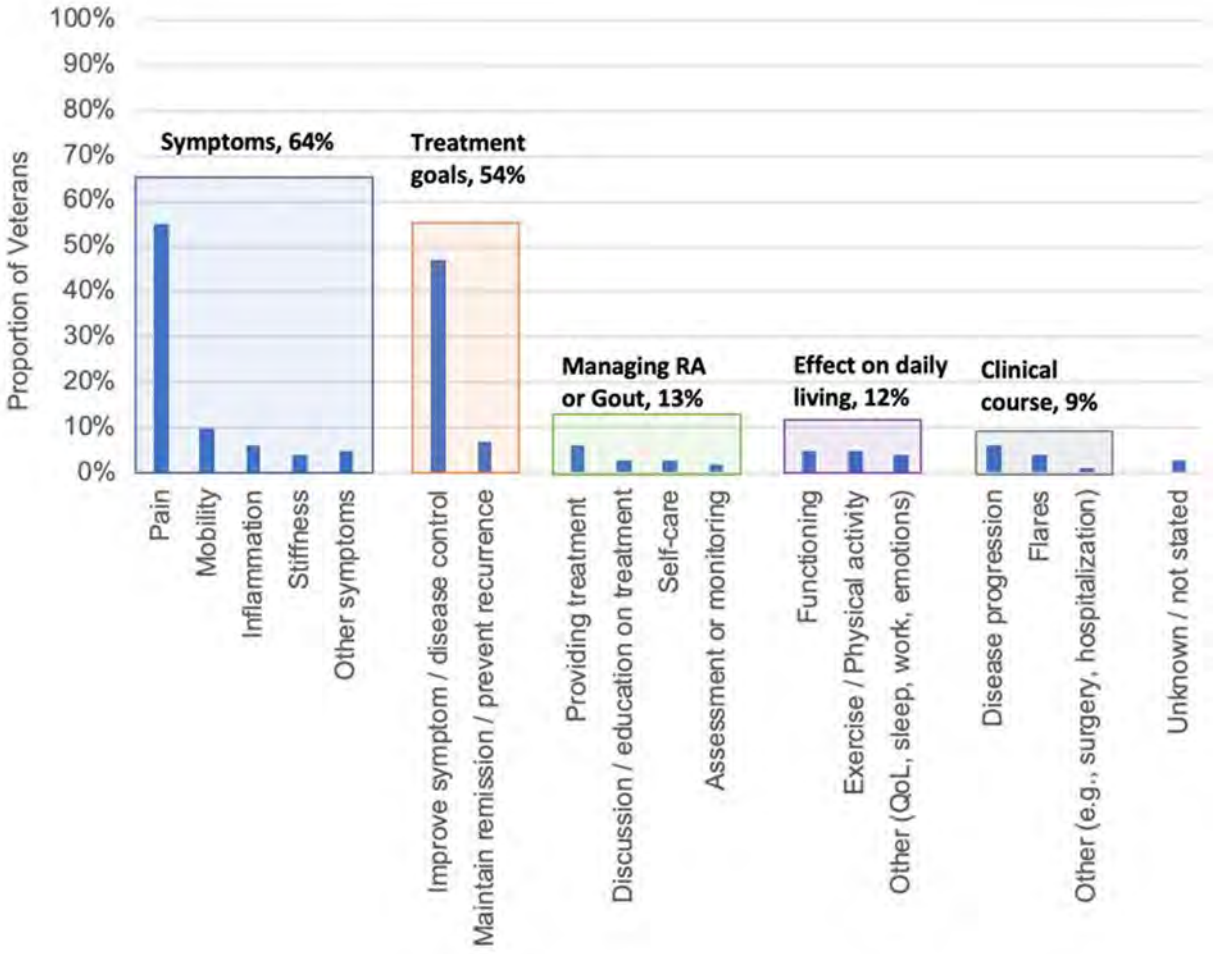

Figure 1. Frequency of Themes and Subthemes of 283 Responses to the Pre-Visit Survey: What is your number one concern or goal related to your arthritis?

patient responses. Codes were developed using grounded theory, with input from rheumatologists and adults with RA. If multiple themes were mentioned in response to any question, the response received multiple codes.

Results: We identified five domains of veteran's goals or concerns, including symptoms (64%), treatment goals (54%), managing RA or gout (13%), effect on daily living (12%), and clinical course of illness (9%). The most common themes in each domain were pain (55%), reducing symptoms or controlling disease (47%), accessing treatment (6%), functioning (5%), and disease progression or damage (6%), respectively (**Figure 1).** Veterans indicated that rheumatologists could help them achieve their goals by providing treatment (37%), discussing or educating around treatment options (18%), or monitoring and assessing disease status (9%) **(Figure 2)**. Veterans felt they (themselves) could achieve their goals through a combination of self-care activities (55%), such as exercising or being physically active (28%) and managing weight or eating a healthy diet (18%), and by following treatment recommendations (35%) **(Figure 2)**.

Conclusion: Veterans with RA and/or gout are largely concerned around improving pain. While they most often report that clinicians and patients can work together to meet goals (e.g., provide treatment/follow treatment recommendations), other important areas include provider education or discussion around treatment options and patient self-care (exercise and diet). Understanding patients' perceptions about their disease and what is most important to them can inform patients and clinicians working together to achieve shared treatment goals.

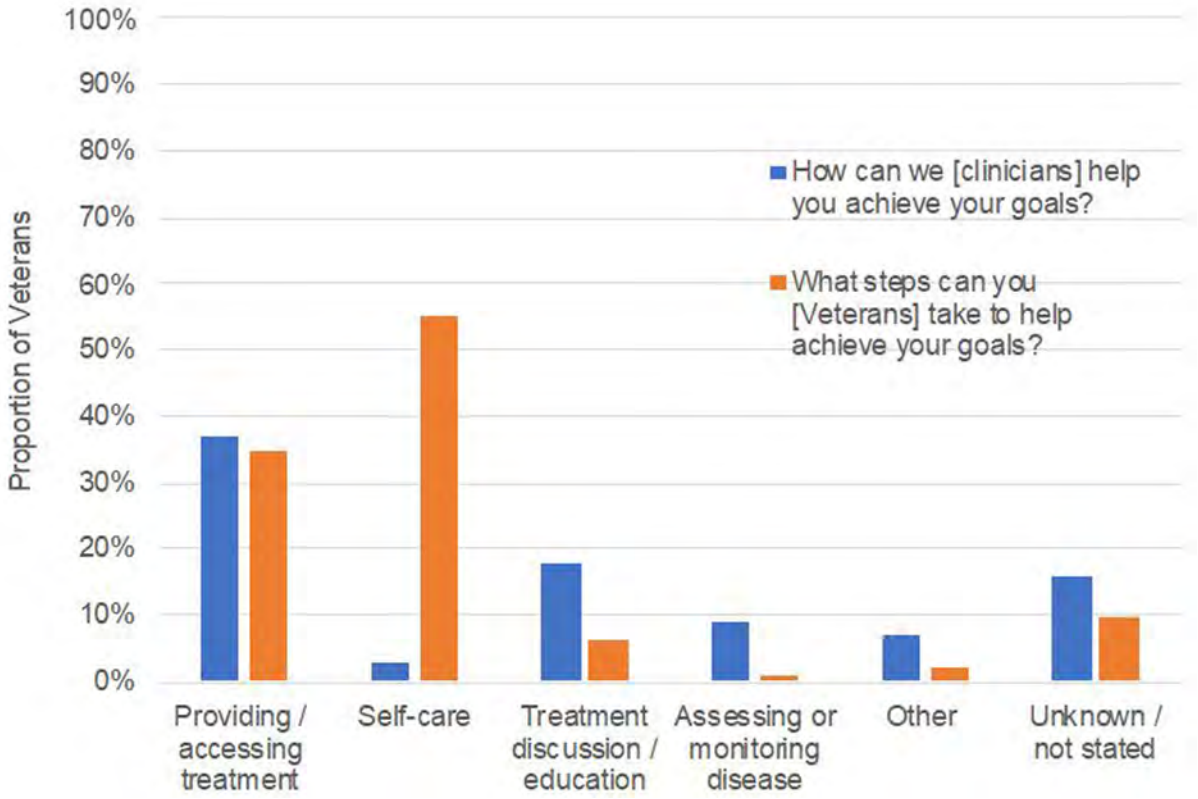

Figure 2. Frequency of Themes and Subthemes of 283 Responses to the Pre-Visit Survey Questions: "How can we help you achieve your goals?" and "What steps can you take to achieve your goals?"

Disclosure: S. Reddy, None; **A. Van Citters**, None; **R. Arora**, None; **K. Shwin**, None; **L. Johnson**, None; **J. Ahmad**, None; **G. Eakin**, None; **E. Nelson**, None; **A. Reimold**, Lilly, 5, Abbvie, 2, Pfizer, 2; **S. Kazi**, ABIM, 1, Regeneron, 1, Sanofi, 1.

Abstract Number: 0153

Counseling on Safe Driving Strategies in Patients with Osteoarthritis and Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
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Background/Purpose: Osteoarthritis (OA) and rheumatoid arthritis (RA) cause functional impairments that impact daily life activities, including automobile driving. Radiographic presence of OA on knee and hip imaging significantly affects braking response time, and use of vehicle adaptations is common in patients with RA. There is little information on the correlation of functional disability scores, particularly the HAQ-DI score, with driving impairment in OA and/or RA patients. Limited studies suggested that an HAQ-DI score ≥ 1 correlated to driving difficulty, but driving

difficulties were also present in those with lower scores. Only three studies from Canada and Europe reported rates of physician counseling on driving difficulties (0-8%) in surveyed patients with RA. Rates of physician counseling on driving safety in OA and/or RA patients in the United States are unknown. Our study aims to address these information gaps by surveying patients with OA and/or RA on functional disability (HAQ-DI), driving habits and limitations, use of vehicle modifications, and whether counseling about driving safety by a healthcare professional has occurred. We hypothesize low rates of physician driving counseling, but suspect that patients with HAQ-DI scores ≥ 1 will have higher rates of counseling and vehicle modifications.

Methods: Participants were recruited and surveyed through the ResearchMatch Network, a national web-based recruitment tool maintained at Vanderbilt University Medical Center. A total of 4,435 patients with OA and/or RA were recruited; 304 (6.9%) respondents met screening criteria (held current US driver's license and were at least 18 years old) and completed the electronic HAQ-DI and study specific survey. Data was dichotomized with HAQ-DI ≥ 1 as a cut point and was analyzed using chi-squared analysis.

Results: Of the 304 completed surveys, 17.1% were male, 82.2% female, and 0.7% other; 65.1% reported OA, 16.8% RA and 18.1% both. The HAQ-DI score was ≥ 1 in 60.5%. Respondents with HAQ-DI ≥ 1 reported driving fewer miles each day that those with HAQ-DI ≤ 1 ($p = 0.001$), and greater level of difficulty with seven areas of driving activities ($p \leq 0.020$ for each activity). Physicians inquired about driving safety in 6.3% and other healthcare providers inquired in 8.6% respondents, with no significant differences based on HAQ-DI scores. Respondents with HAQ-DI ≥ 1 more frequently made the following vehicle modifications: seat supports (26.1% vs 10.8%; $p = 0.001$), extra mirrors (10.9% vs 3.3%; $p = 0.017$), and padded steering wheels (25% vs 5%; $p < 0.001$).

Conclusion: Survey respondents with HAQ-DI ≥ 1 indicated significant disability and impairment with driving related activities and were more likely to report vehicular assistive modifications. Despite this, physician and other healthcare provider rates of driving counseling remain low. Increased physician inquiry into driving safety is needed in patients with OA and RA. An HAQ-DI ≥ 1 could be considered as a screening tool to determine which patients may need more immediate counseling or vehicular modifications.

Disclosure: A. Falls, None; **P. Ricketts**, None; **J. Elliott**, None; **K. Jordan**, None.

Abstract Number: 0154

Treatment Decision Making Among Axial Spondyloarthritis Patients: Real-World Data from the ArthritisPower Registry

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Biologic disease-modifying antirheumatic drug (bDMARD) therapy has been shown to be effective in the treatment of axial spondyloarthritis (axSpA).[1,2] Little is understood about axSpA patients' treatment journey from their own perspective. The purpose of this study was to explore treatment decision-making of axSpA patients and to identify barriers and facilitators to treatment optimization.

Methods: This was an observational, cross-sectional study of participants (pts) in the ArthritisPower registry using a survey developed in partnership with patients and clinicians. Pts aged ≥ 19 years with physician-diagnosed axSpA and access to a computer/smartphone were invited to complete electronic patient-reported outcome measures and an online survey on treatment (tx) decision making. Pts' responses were classified into 2 groups based on whether or not currently on a bDMARD.

Results: 274 pts met inclusion criteria of whom 87.2% were female, 85.4% White, with mean age of 50 years (Table 1). The majority of pts (82.1%) had been diagnosed with axSpA by a rheumatologist. Of all pts, 56.9% (n=156) discussed a tx change at their most recent physician visit, 79.5% of whom researched the treatment change on their own, and 46.2% (n=72) of these pts reported having raised the issue with their clinician themselves. Half (51.3%) of tx

Table 1: Demographic and Clinical Characteristics (N=274)

	All Pts (N=274)	Pts on a bDMARD (n=128)	Pts not on a bDMARD (n=146)	p-value
Age, mean (SD)	49.9 (11.1)	46.9 (10.3)	52.6 (11.1)	<0.01*
Female, n (%)	239 (87.2)	106 (82.8)	133 (91.1)	0.04*
White, n (%)	234 (85.4)	115 (89.8)	119 (81.5)	0.05
College degree or higher, n (%)	125 (45.6)	73 (57.0)	52 (35.6)	<0.01*
Employed (full-time, part-time, self-employed, student), n (%)	134 (48.9)	66 (51.6)	59 (40.4)	0.07
Age first noticed axSpA symptoms, mean (SD)	29.7 (13.2)	26.9 (12.2)	32.2 (13.5)	<0.01*
Age of initial axSpA diagnosis by physician, mean (SD)	40.4 (12.1)	37.9 (12.1)	42.6 (11.8)	<0.01*
First degree relative with axSpA	61 (22.3)	28 (21.9)	33 (22.6)	0.89
Symptoms				
Inflammatory arthritis (other than spine)	186 (67.9)	84 (65.6)	102 (69.9)	0.45
Back or buttock pain that improves with NSAIDs	128 (46.7)	52 (40.6)	76 (52.1)	0.06
HLA-B27 positive blood test	112 (40.9)	64 (50.0)	48 (32.9)	<0.01*
Heel enthesitis	80 (29.2)	36 (28.1)	44 (30.1)	0.72
Elevated C-reactive protein (CRP)	78 (28.5)	40 (31.3)	38 (26.0)	0.34
Sausage finger or toe	44 (16.1)	15 (11.7)	29 (19.9)	0.07
Psoriasis skin rash diagnosed by a doctor	38 (13.9)	21 (16.4)	17 (11.6)	0.26
Uveitis/Irisitis	32 (11.7)	11 (8.6)	21 (14.4)	0.14
Crohn's Disease or ulcerative colitis diagnosed by a doctor	26 (9.5)	12 (9.4)	14 (9.6)	0.95
Self-Rated Health[3]	2.2 (0.9)	2.1 (0.8)	2.3 (0.9)	0.17
BASDAI, mean (SD)[4]	8.3 (2.1)	7.9 (2.0)	8.7 (2.1)	<0.01*
Body Mass Index, mean (SD)[5]	31.8 (8.6)	30.9 (7.8)	32.5 (9.2)	0.12
Current Medications, n (%)				
Biologic DMARD	128 (46.7)	128 (100)	-	-
Conventional Synthetic DMARD (e.g. methotrexate, sulfasalazine)	31 (11.3)	17 (13.3)	14 (9.6)	0.34
Steroid	45 (16.4)	23 (18.0)	22 (15.1)	0.52
Prescription NSAID or other medication	121 (44.2)	59 (46.1)	62 (42.5)	0.55
Corticosteroid, prescription NSAID or other without DMARD	132 (48.2)	-	132 (90.4)	-
Length of current medication regimen				0.41
Up to 6 months, n (%)	61 (26.5)	37 (28.9)	24 (23.5)	
Between 6 months to a year, n (%)	29 (12.6)	18 (14.1)	11 (10.8)	
Greater than a year, n (%)	140 (60.9)	73 (57.0)	67 (65.7)	
Last treatment change[6]				0.27
Up to 6 months, n (%)	110 (40.2)	57 (44.5)	53 (36.3)	
Between 6 months to a year, n (%)	52 (19.0)	25 (19.5)	27 (18.5)	
Greater than a year, n (%)	112 (40.9)	46 (35.9)	66 (45.2)	

* Statistical significance between groups of pts who were on a bDMARD and not on a bDMARD, $p < 0.05$; t tests were performed for continuous variables and chi square tests for categorical variables; p values are nominal in nature and should be interpreted in an exploratory manner
[3] Single-item measure from PROMIS Global; score range from 1 (Poor) to 5 (Excellent)
[4] BASDAI is scored on a 0-10 scale with score ≥4 indicating suboptimal control of disease
[5] n=272 out of 274 since weight was an optional response
[6] Any prescription medication change

Table 2: Treatment Change Behaviors and Rationale among axSpA Patients

	All Pts (n=156)	Pts on a bDMARD (n=77)	Pts not on a bDMARD (n=79)	p-value
What treatment change did your treating provider discuss with you? †				
Starting a new medication	80 (51.3)	34 (44.2)	46 (58.2)	0.08
Switching medications	61 (39.1)	40 (52.0)	21 (26.6)	<0.01*
Increasing the dose of the medication I am currently taking	46 (29.5)	33 (42.9)	13 (16.5)	<0.01*
Stopping a medication	38 (24.4)	15 (19.5)	23 (29.1)	0.16
Other	18 (11.5)	9 (11.7)	9 (11.4)	0.95
Decreasing the dose of the medication I am currently taking	10 (6.4)	4 (5.2)	6 (7.6)	0.54
What treatment change did you make? †				
Starting a new medication	58 (37.2)	28 (36.4)	30 (38.0)	0.84
Switching medications	40 (25.6)	25 (32.5)	15 (19.0)	0.05
Stopping a medication	34 (21.8)	11 (14.3)	23 (29.1)	0.02*
Increasing the dose of the medication I am currently taking	33 (21.2)	23 (29.9)	10 (12.7)	<0.01*
Other	24 (8.8)	9 (7.0)	15 (10.3)	0.34
None, I did not make a treatment change	23 (14.7)	11 (14.3)	12 (15.2)	0.87
Decreasing the dose of the medication I am currently taking	12 (7.7)	5 (6.5)	7 (8.9)	0.58
Why did you agree to the change? †	**All Pts (n=133) n (%)**	**Pts on a bDMARD (n=66)**	**Pts not on a bDMARD (n=67)**	**p-value**
My disease was not being controlled by the treatment I was previously on	73 (54.9)	39 (59.1)	34 (50.8)	0.33
Other (i.e., benefits of medication not worth cost, insurance coverage, disease inactive)	32 (24.1)	12 (18.2)	20 (29.9)	0.09
I experienced side effects with the treatment I was previously on	28 (21.1)	14 (21.2)	14 (20.9)	0.96
My disease was being controlled but I thought it could be better controlled on the new treatment	27 (20.3)	16 (24.2)	11 (16.4)	0.26
The benefits of the medication were not worth the risk of side effects	16 (12.0)	6 (9.1)	10 (14.9)	0.30
Why do you believe a treatment change was not discussed at your last visit? †	**All (n=118) n (%)**	**Pts on a bDMARD (n=51)**	**Pts not on a bDMARD (n=67)**	**p-value**
Other (Doctor does not listen to my concerns; Change in or lack of access; Changing is not an option / not needed; Tests or lack of results; Don't know)	47 (39.8)	17 (13.3)	30 (20.6)	0.11
My provider is happy with my current treatment	42 (35.6)	26 (51.0)	16 (23.9)	<0.01*
I am happy with my current treatment and I have told my provider this	36 (30.5)	23 (45.1)	13 (19.4)	<0.01*
I do not discuss treatment options with my provider	18 (15.3)	1 (2.0)	17 (25.4)	<0.01*

* Statistical significance between groups of pts who were on a bDMARD and not on a bDMARD, $p < 0.05$; t tests were performed for continuous variables and chi square tests for categorical variables; p values are nominal in nature and should be interpreted in an exploratory manner

†Pts could select more than one reason

changes discussed were related to initiation of a new medication, compared with stopping a medication (24.4%) and/or changing its dose (35.9%). The majority of pts (85.3%; n=133) who discussed a change agreed to the tx change and most pts agreeing to a change did so because they felt their disease was not being controlled (54.9%; n=73) or because they thought control could be better on new tx (n=27; 20.3%). Most pts (62.8%) reported agreeing to the suggested tx change by end of clinic visit, while 15.4% needed ≤ 1 week to decide. Pts on a bDMARD were more likely to discuss switching medications (52.0%) or increasing dose (42.9%) vs. non-bDMARD pts (26.6%, p=0.0012; 16.5%, p=0.0003) (Table 2). Among the pts (n=23) who declined a tx change, top reasons were pts not believing there were more efficacious options than their current tx (60.9%) and worries about potential side effects of a new tx (56.5%). For bDMARD pts whose tx change was not discussed at the last visit, pts felt it was because either they or their provider were happy with the current tx (Table 2); bDMARD-treated pts and their clinicians were more likely to report satisfaction with current tx as the reason a tx change was not discussed compared to non-bDMARD pts. Overall, factors that pts on bDMARDs (n=128) considered most important when making tx decisions were preventing other long-term consequences of untreated axSpA (92.2%), preventing damage from axSpA (89.1%), and advice from their doctor (87.5%) (Table 3).

Table 3. Factors* Considered Very Important to axSpA Patients on a bDMARD When Making Decisions about Their Treatment (n=128)

	N	%
Preventing other long-term consequences of untreated axSpA	118	92.2
Preventing damage from axSpA	114	89.1
Advice from my doctor	112	87.5
My doctor's availability to see me or talk to me to deal with problems or questions that come up	91	71.1
How good or bad the disease is making me feel at the time I make a treatment decision	84	65.6
Avoiding surgery	78	60.9
Possible drug interactions	77	60.2
Cost of the treatment	73	57.0
How affordable the treatment is	71	55.5
How easy it is to get the treatment	68	53.1
Wanting to get immediate relief	64	50.0
The newest research	62	48.4
Risk of addiction	56	43.8
Information I have found while doing my own research	54	42.2
Avoiding additional pills	52	40.6
Intuition or 'gut response' when I ask myself if this is the right thing to do	45	35.2
How easy the treatment is to use or do (such as taking a pill versus doing yoga)	41	32.0
Concern that the treatment will only work for a short time and I should save the treatment option for a later date when I feel worse	34	26.6
How often I have to take the treatment (daily versus weekly versus monthly)	30	23.4
How often I will need to get imaging tests (X ray, ultrasound) on this medication	27	21.1
How often I will need to get lab tests on this medication	25	19.5
Avoiding needles or injections	18	14.1
Whether people will judge me for my pain management strategy	11	8.6
Personal recommendations from family or friends	8	6.3
Whether the treatment is a natural remedy	6	4.7
Advertisements	1	0.8

*Not mutually exclusive

Conclusion: Most axSpA patients reported discussing tx changes with their provider at their most recent visit and had done their own research about it beforehand. Prevention of long-term damage and doctor's advice are major factors influencing patient decisions about tx.

References:

[1] Dubash S, et al. Ther Adv Chronic Dis. 2018;9(3):77–87.
[2] Van Der Heijde D, et al. Ann Rheum Dis. 2017;76(6):978–91.

Disclosure: W. Nowell, None; **T. Hunter**, Eli Lilly and Company, 1, 3; **K. Gavigan**, None; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **W. Malatestinic**, Eli Lilly and Company, 1, 2; **R. Bolce**, Eli Lilly and Company, 1, 3; **J. Lisse**, Eli Lilly and Company, 1, 3; **A. Kronbergs**, Eli Lilly and Company, 1, 3; **C. Himelein**, Eli Lilly and Company, 1, 3; **J. Walker**, None; **J. Walsh**, Pfizer, 2, AbbVie, 2, 5, Eli Lilly, 5, UCB, 5, Janssen, 5, Novartis, 5, Amgen, 5.

Abstract Number: 0155

Changes in Patient-Reported Outcome (PRO) Scores for Nausea and Fatigue Following Weekly Methotrexate Dose in a Real-World Sample of RA and PsA Patients in the ArthritisPower Registry

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Methotrexate (MTX) is frequently used in patients with rheumatoid arthritis (RA) or psoriatic arthritis (PsA) because of its beneficial effects in both populations. Despite the well-known benefits of MTX, it is associated with a number of potential side effects. These include nausea and fatigue, are often temporally related to

Figure 1. Nausea PROMIS Score Changes Among Patients Reporting Nausea as a Side Effect of MTX [n=64 observations (32 pairs) among 20 unique pts]

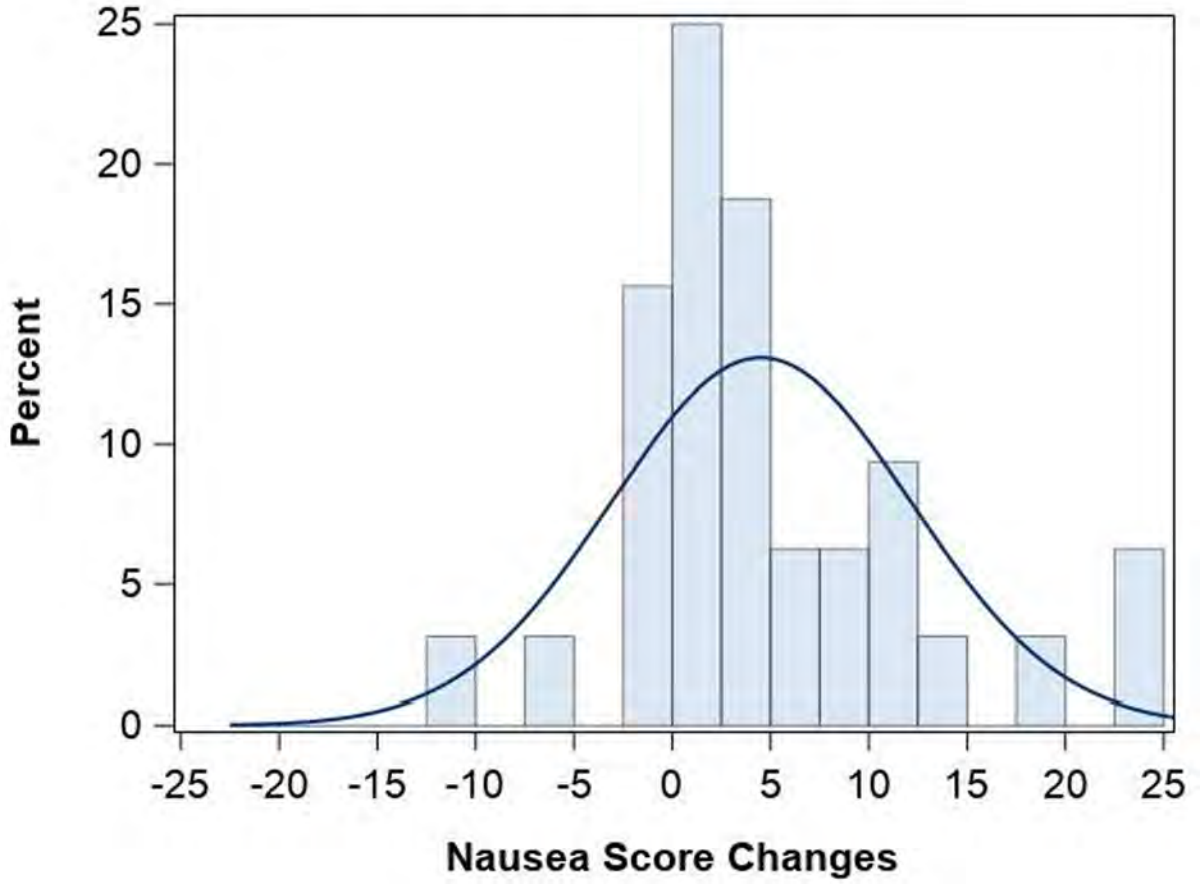
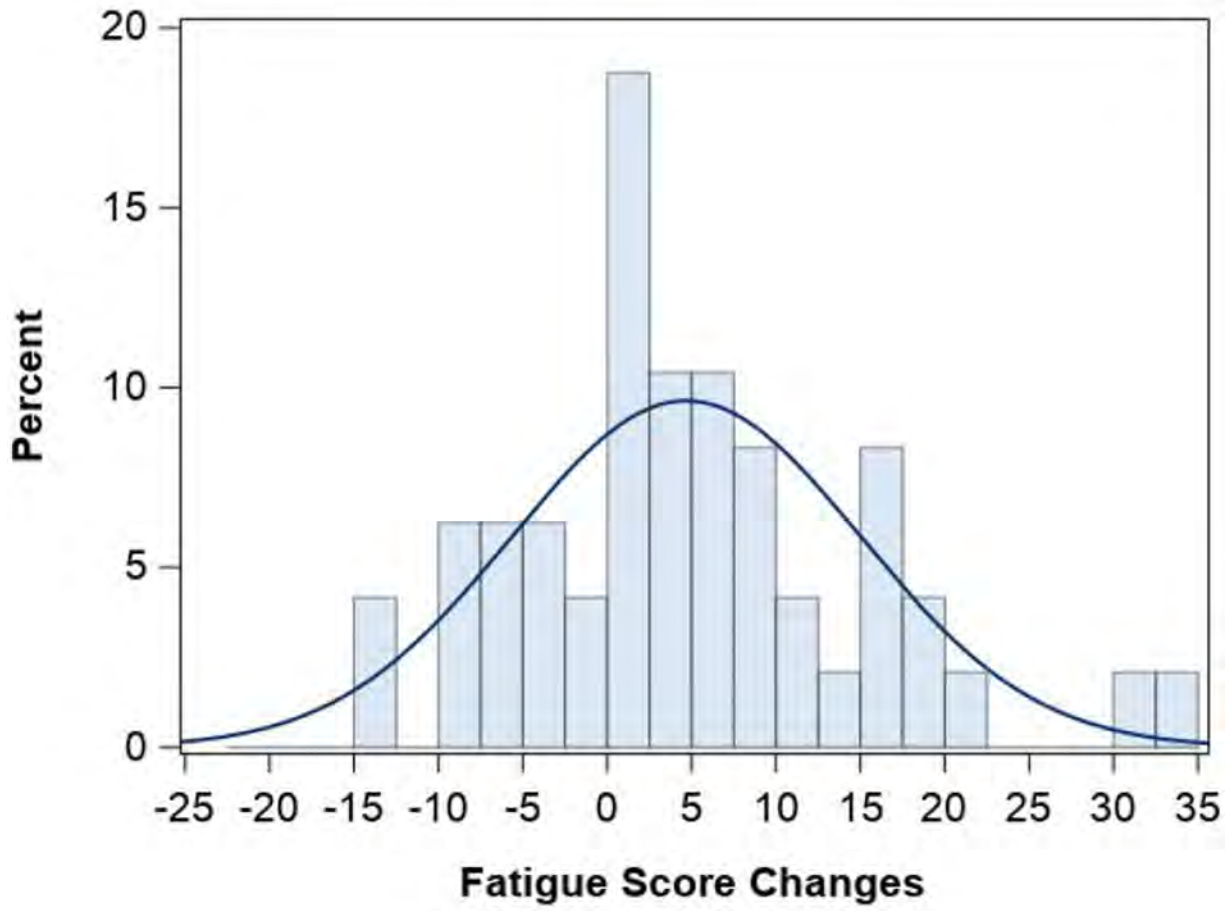


Figure 2. Fatigue PROMIS Score Changes Among Patients Reporting Fatigue as a Side Effect of MTX [n=96 observations (48 pairs) among 28 unique pts]



the timing of weekly MTX administration, and can be severe. The combined patient-reported side effects, along with potential of long term toxicity, may make use of MTX more burdensome. Currently, there is a gap in patient-centered studies that focus on patients' experience of fatigue and nausea relating to oral MTX therapy for the treatment of RA and PsA.

Methods: Adult US patients in the ArthritisPower registry with self-reported RA or PsA taking MTX for less than 10 years were invited to participate in the study via email invitation. Participants (pts) completed a screener and brief online survey. In an ancillary study to the ArthritisPower registry and using a self-controlled case series study design where pts serve as their own control to avoid between-person confounding, pts were asked to complete a set of up to 8 assessments within 6-36 hours ('risk') and 96-144 hours ('control') after taking their oral dose of MTX each week, for up to 4 weeks. Risk and control windows were selected based on the expected temporal relationship between MTX use and peak onset of these symptoms. Assessments included PROMIS short forms for same-day Fatigue, same-day Nausea/Vomiting, and Patient Global. Descriptive statistics were conducted using paired t-tests two-way comparisons. Within-person change in PROMIS scores between the risk (1-2 days after MTX) and control (4-6 days after MTX) windows were analyzed using mixed models for repeated measures, stratified on whether pts reported fatigue or nausea with MTX at baseline. Recruitment for this study is ongoing.

Results: As of December 2019, 91 pts had participated, of whom 76.9% were living with RA and 28.6% with PsA, with mean baseline PROMIS Patient Global score (SD) of 39.5 (7.1). Mean age (SD) was 50.9 (12.0) years, 84.6%

female, 92.3% White, with mean BMI 33.7 (8.8). Mean duration of MTX treatment among current users was 2.1 (2.8) years. Among pts, 41.8% were on a biologic DMARD and 58.2% on non-biologic DMARDs only. Among pts reporting baseline nausea (n=30, 33.0%) where paired within-week measures were observed (n=64 observations among 20 pts), the mean increase in the PROMIS Nausea score was 4.5 units (adjusted p=0.003). Among those reporting MTX-associated fatigue (n=39, 42.9%) as a side effect of MTX on their baseline survey where paired within-week measures were observed (n=96 observations among 28 pts), the mean increase in PROMIS Fatigue was 4.7 (adjusted p=0.004) units. In those pts, the proportion of pts with worsened nausea and fatigue with minimally important difference of >5 units was 40.0% (nausea), and 60.7% (fatigue) [Figures 1 and 2].

Conclusion: People taking MTX to manage RA or PsA commonly experience bothersome side effects, notably fatigue and nausea, that are temporally related to weekly MTX dosing. In this sample, one-third or more of pts were bothered by nausea or fatigue shortly after MTX dosing, many of them with clinically meaningful symptoms.

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Abstract Number: 0156

The Role of Biological Treatment in the Health-Related Quality of Life of Ankylosing Spondylitis Patients' Assessment - Meta-Analysis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Spondyloarthritis (SpA) is a chronic inflammatory rheumatic disease involving the axial skeleton, entheses and peripheral joints, and may occur together with extra-articular manifestations, such as psoriasis, inflammatory bowel disease and uveitis. Patients with SpA are experiencing deterioration or bad quality of life. The most common symptoms are: physical limitations and limitations of motor activity, fatigue and sleep disturbances caused by the disease and inflammatory pain. Due to the young age of patients the sexual disorders, limitations or inability to work or to perform other social roles should be put into considerations.Since the last century in medicine it is considered that the regular quality of life assessment should complement the clinical efficacy assessment of the applied treatment. The efficacy of the biological treatment and its superiority to placebo has been proved in the newest research. There is scarcity of the studies which evaluate the efficacy of biological treatment regarding the quality of life. It is worth paying attention that the patients' satisfaction should be crucial in treatment selection and planning.

The main purpose of this meta-analysis was to evaluate the impact of biological treatment on the quality of life of the patients with ankylosing spondylitis.

Methods: A systematic literature search was performed on PubMed and Web of Science until May 2020 to obtain eligible studies. The used search terms were as follows: ("Quality of Life") OR ("patient-reported outcomes")

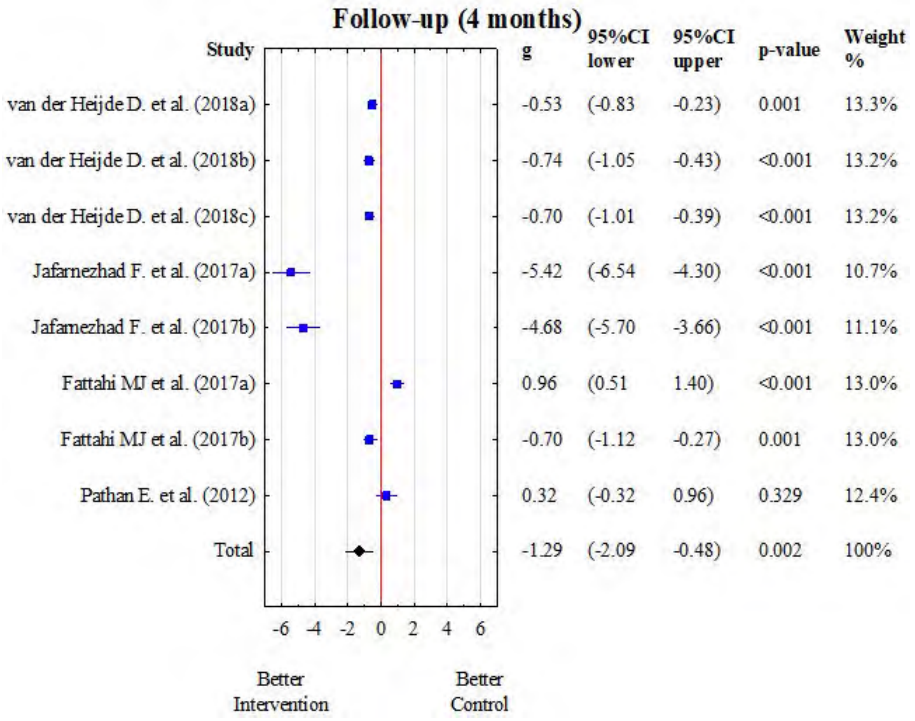

Figure.1 Quality of life in the control and intervention group after 4 months of treatment

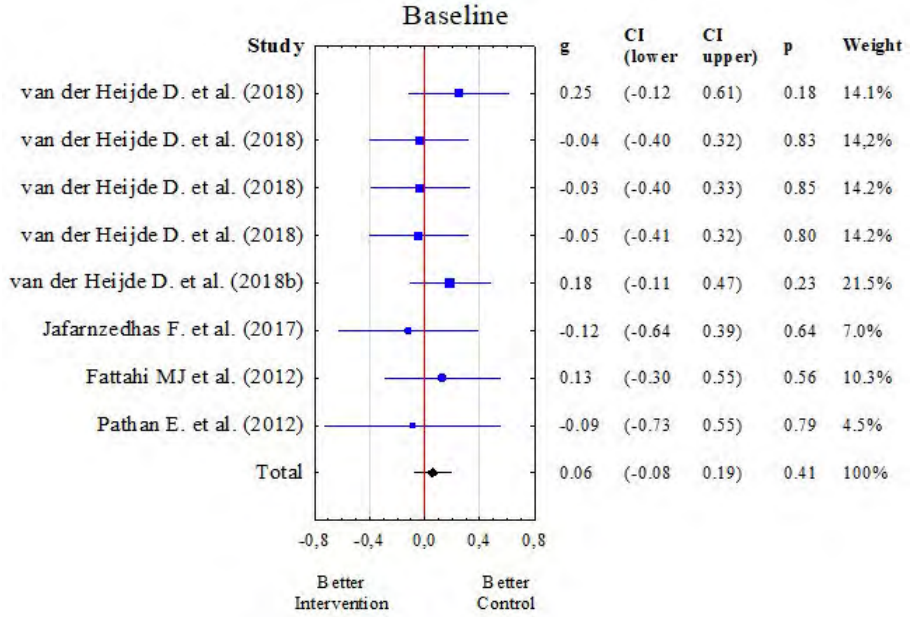

Figure.2 Quality of life in the control and intervention group at the beginning of treatment

OR (“well-being”) OR(“health related quality of life”) AND(“biological treatment ofankylosing spondylitis”) in this meta-analysis.

Results: Twenty-three papers were finally assigned to meta-analysis. Quality of life was evaluated using the questionnaires: SF-36, ASQoLS, FACIT-F: EQ-5D-5L, EQ-5D VAS. The results of the meta-analysis showed thatin baseline

study the quality of life of patients with AsS treated with biological drugs and the control group (placebo) did not differ (Q = 3.32, p = 0.854, I2 = 0.00%). However, after 16 weeks of the study the results were statistically different, and the group treated with biological drugs had better improvement in quality of life. The positive direction of the improvement of functioning was observed within the functional efficiency assessed with questionnaire BASFI.What is more, the significant decrease of CRP in the group with biological treatment was revealed, which confirmed the effectiveness of therapy.

Conclusion: (1) The biological treatment significantly improves the quality of life andfunctional efficiency as well as it decreases the inflammation markers in patients with SpA. (2) There is a need for introduction of the uniform study protocol andthe definition of a standard methodology for research tools in the evaluation of quality of life in patients with SpA in order to comparethe different results in differentscientific teams.

Disclosure: W. Tański, None; **M. Chabowski**, None; **N. Świątoniowska-Lonc**, None; **B. Jankowska-Polańska**, None.

Abstract Number: 0157

Early Arthritis Global Assesment: What Differences Exist Between Patients and Physicians?

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In recent years there is increasing evidence of the relevance of including the assessment of the different aspects of rheumatoid arthritis (RA) from the patient's perspective through patient reported outcomes (PRO). Previous studies showed discrepancies in the disease global disease assessment reported by patients (PtGA) or physicians (PhGA).

Our aim was to evaluate differences between PtGA and PhGA and analyze the variables related to these differences in an early arthritis cohort.

Methods: Cross-sectional study analyzing data from the baseline visit of patients included in the PEARL study *(Princess Early Arthritis Register Longitudinal Study)* in which demographic, laboratory and clinical characteristics including PtGA and PhGA (0-100 mm) are systematically collected.

The main variable was the difference between PtGA and PhGA (ΔGA). The descriptive analysis was performed using the Kruskal-Wallis, Mann-Whitney or Pearson correlation tests as appropriate. Stadistical analysis was perfomed with STATA 14.

A multivariate linear regression model was developed with ΔGA as a dependent variable. All those predictors available at the baseline visit reaching a $p < 0.15$ in the univariate analysis were included in the initial model. The final one

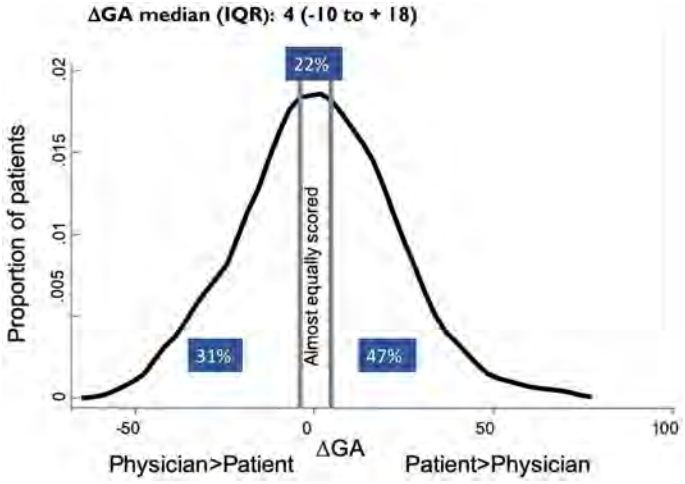

Figure 1. Representation of DGA distribution. DGA: difference between PtGA and PhGA; IQR: interquartile range.

was obtained through the progressive elimination of those variables not showing an improvement in the model as assessed by the adjusted R2 parameter. To categorize the dependent variable, we considered relevant differences between PtGA and PhGA greater than 5 mm.

Results: 530 patients were included, 422 (79.6%) were women with a mean age of 55.3 +/- 16 years, 21.2% current smokers, 54% and 50.4% rheumatoid factor and anti-CCP positive respectively. A 43.3% had moderate activity and 33.6% high, measured by DAS28-VSG.

The median of ΔGA was 4, (interquartile range; -10 to 18; see Figure1). In 22% of the cases patients and physicians scored the same, in 46.5% the patients' scores were higher and physicians' were so in 31.5% of the cases.

The variables that explained DGA after adjusting the multivariate model were pain [β=0.36 (95%CI 0.28 to 0.44)], number of swollen joints [β= -3.19 (95%CI -3.7 to -2.7)] and ESR [β=-0.11 (95%CI -0.2 to -0.03)]. Pain had a greater influence on patients' opinion while the number of swollen joints and ESR were more relevant for physicians. Other variables such as race, marital status, profession, sex, smoking, seropositivity or disease activity were not relevant in the prediction of ΔGA.

Conclusion: In our sample, disagreements between PtGA and PhGA were observed. Patients scored higher based on painful perception and physicians based on objective evidence of inflammation.Figure 1. Representation of DGA distribution. DGA: difference between PtGA and PhGA; IQR: interquartile range.

Disclosure: C. Valero, None; **N. Garcia**, None; **J. Baldivieso**, None; **A. Ortiz**, Lilly, 5, 8, Pfizer, 5, 8, Roche, 9, Sanofi, 9; **S. Rodriguez**, None; **I. González-Álvaro**, Roche, 2, 8, Lilly, 5, 8, Sanofi, 5, Abbvie, 8, MSD, 8.

Abstract Number: 0158

Relationships Between Disease Patterns in RA and Rheumatology Treatment

Kelly O'Neill[1], Kathryne Marks[2], John Davis[3] and Cynthia Crowson[4], [1]Rheumatoid Patient Foundation, Orlando, FL, [2]Rosalind Franklin University of Medicine and Science, North Chicago, IL, [3]Mayo Clinic, Rochester, MN, [4]Mayo Clinic, Rochester, Minnesota, USA, Rochester, MN

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

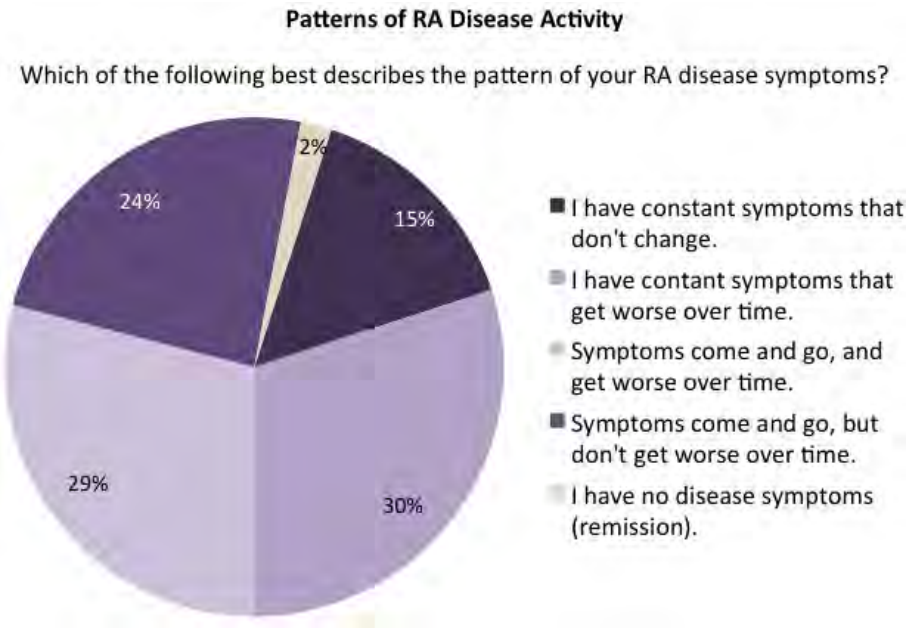

Fig.1 Patterns of RA Disease Activity

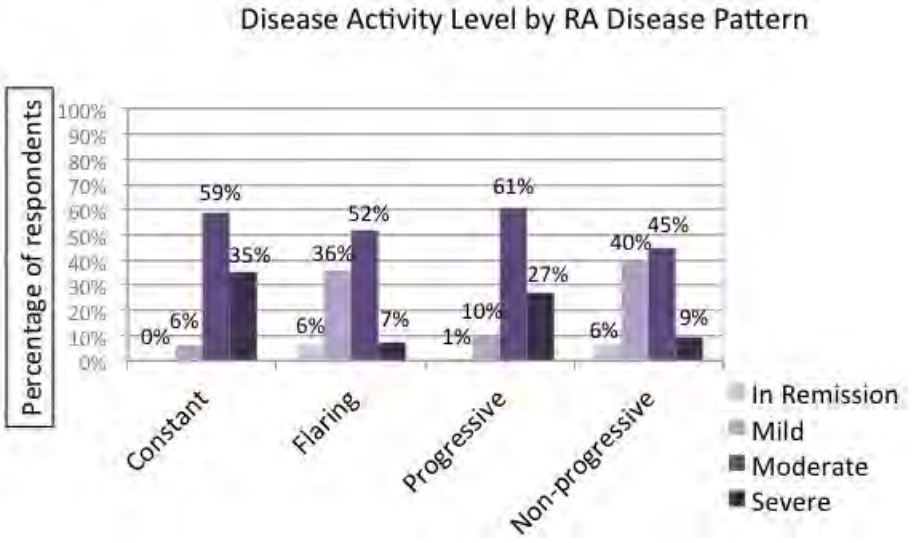

Fig.2 Disease Activity Level by RA Disease Pattern

Background/Purpose: We previously showed rheumatoid arthritis (RA) patients report diversity in disease activity (DA) patterns that may be associated with treatment response. Patients who describe their DA as a flaring or non-progressing pattern are more likely to experience high levels of DA improvement (≥70%). We aimed to better understand the relationship between RA disease activity patterns and rheumatology treatment experiences.

Responses by RA Disease Activity Pattern

	Constant (N=406)	Flaring and Remitting (N=480)	p value
			0.012
Years since diagnosis			
N	405	476	
Mean (SD)	12.0 (10.5)	10.3 (9.7)	
Median	9.0	8.0	
How satisfied are you with your rheumatoid arthritis (RA) treatment?			<0.001
Dissatisfied	98 (24%)	65 (14%)	
I don't have an RA treatment plan	19 (5%)	14 (3%)	
Satisfied	188 (46%)	243 (51%)	
Very dissatisfied	33 (8%)	26 (5%)	
Very satisfied	68 (17%)	132 (28%)	
How would you describe your current RA disease activity?			<0.001
In Remission	1 (0%)	27 (6%)	
Mild	25 (6%)	171 (36%)	
Moderate	238 (59%)	248 (52%)	
Severe	142 (35%)	34 (7%)	
How would you describe your state of health?			<0.001
Missing	0	1	
Fair	162 (40%)	191 (40%)	
Good	95 (23%)	198 (41%)	
Poor	98 (24%)	44 (9%)	
Very good	14 (3%)	31 (6%)	
Very poor	37 (9%)	15 (3%)	

	Non-progressing (N=352)	Progressive (N=534)	p value
Years since diagnosis			<0.001
N	350	531	
Mean (SD)	9.7 (8.9)	12.1 (10.7)	
Median	7.0	9.0	
Years from diagnosis to treatment			0.012
N	346	524	
Mean (SD)	0.4 (2.1)	1.2 (4.3)	
Q1, Q3	0.0, 0.0	0.0, 0.0	
Range	(-12.0-24.0)	(-6.0-40.0)	
Did your healthcare provider ask you what your goals were for RA treatment?			0.008
No	205 (58%)	358 (67%)	
Yes	147 (42%)	176 (33%)	
How would you describe your current RA disease activity?			<0.001
In Remission	22 (6%)	6 (1%)	
Mild	140 (40%)	56 (10%)	
Moderate	158 (45%)	328 (61%)	
Severe	32 (9%)	144 (27%)	
How would you describe your state of health?			<0.001
Missing	0	1	
Fair	108 (31%)	245 (46%)	
Good	164 (47%)	129 (24%)	
Poor	37 (11%)	105 (20%)	
Very good	33 (9%)	12 (2%)	
Very poor	10 (3%)	42 (8%)	

Fig.1 Current RA Disease Activity Level Versus Time to Diagnosis

Methods: An anonymous 28-item questionnaire was developed and pilot-tested by the study team and presented in 2019 on a secure online survey system. Eligible participants were U.S. residents age ≥18 years with a self-reported medical diagnosis of RA. They were asked questions about socio-demographics, RA disease activity, diagnosis and DMARD history, improvement from RA treatment, and RA treatment goals created with their provider. Further, patients were asked which of a list of disease patterns best described their DA (see Figure 1). The patterns were divided into 2 categories: constant vs flaring and remitting and progressive vs non-progressing.

Results: 907 people responded (90% women, 10% men), with a mean age of 58 years and 11.1 years since diagnosis (SD 10.1). Of the 886 people who responded to the disease pattern questions, 46% had constant and 54% were flaring/remitting. Similarly, 60% were progressive and 40% were non-progressing. Longer times from symptom onset to RA diagnosis associated with constant DA patterns (< 6mo 38%, >6mo to < 5yr 46%, >5yr 52%) and progressive DA patterns (< 6mo 50%, >6mo to < 5yr 60%, >5yr 70%).

Moderate-severe levels of DA were more common with constant and progressive patterns (constant 94%, flaring 59%, progressive 88%, non-progressing 54%). Those with constant disease were less likely to say they were in remission (constant 0%, flaring 6%) or have had their doctor say they were in remission (2% and 15%, respectively). Those with progressive disease gave similar responses for being in RA remission (progressive 1%, non-progressing 6%) or diagnosis of remission (6% and 14%, respectively). Those with constant or progressive DA were more likely to say they were in a poor/very poor state of health (constant 33%, flaring 12%, progressive 28%, non-progressing 14%).

Fewer people with constant or progressive disease were satisfied/very satisfied with their rheumatology treatment (constant 63%, flaring 79%, progressive 67%, non-progressing 76%). People with progressive disease were less likely to be asked by their providers about RA treatment goals (progressive 33%, non-progressive 42%). Respondents strongly supported the use of materials to enhance treatment goal discussions with their rheumatology providers.

Conclusion: This survey found previously unreported associations between patterns of RA disease activity and interfaces with rheumatology care including time to initiation of RA treatment, satisfaction with rheumatology care, and occurrence of shared treatment goal discussions as well as higher levels of DA and fewer remissions of disease. Further research should seek greater understanding of the significance of DA patterns in RA treatment and whether patients with more aggressive DA patterns should have adapted treatment recommendations.

Disclosure: K. O'Neill, None; **K. Marks**, None; **J. Davis**, Pfizer, 2, AbbVie, 5, 8, Sanofi-Genzyme, 5, 8; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1.

Abstract Number: 0159

Patient-Reported Data Show the Impact of Time to Diagnosis in RA

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SESSION INFORMATION
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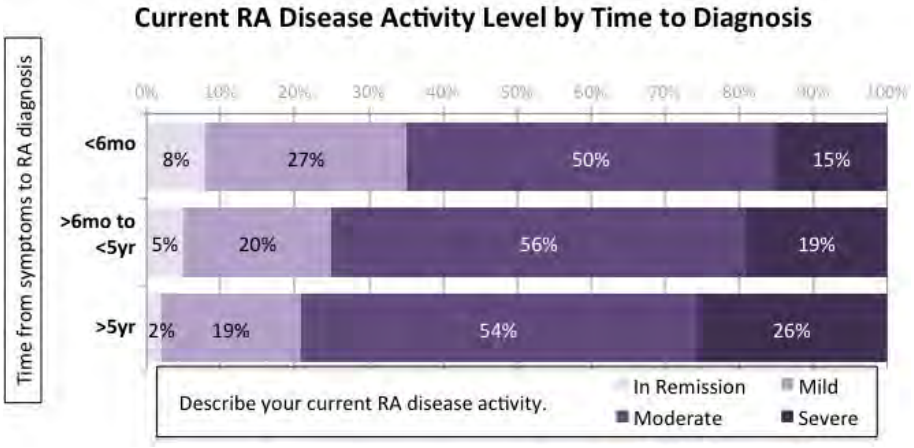

Fig.1 Current RA Disease Activity Level Versus Time to Diagnosis

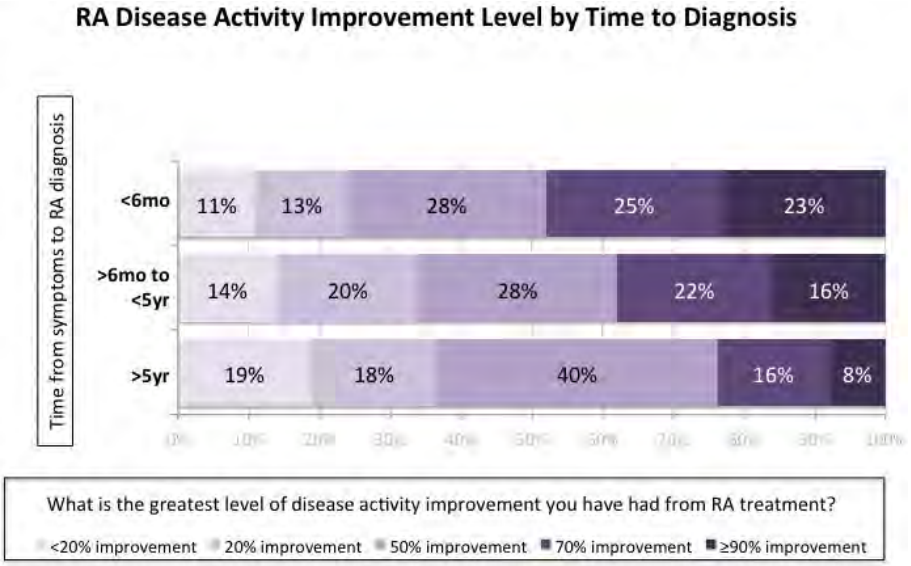

Fig.2 Disease Activity Improvement Level by Time to Diagnosis

Background/Purpose: Time from diagnosis to treatment has been well established to correlate with better outcomes in rheumatoid arthritis (RA). Treatment delays are often associated with worse outcomes and more difficult to treat disease, while early and aggressive treatment leads to better outcomes and increased levels of rheumatoid disease activity (DA) improvement. However time from symptom onset to diagnosis has been less discussed. Building on a collaboration between a non-profit organization and an academic rheumatology center, we aimed to gain greater understanding of the impact of time from symptom onset to diagnosis of RA.

Methods: An anonymous 28-item questionnaire was developed and pilot-tested by the study team and presented in 2019 on a secure online survey system. Eligible participants were U.S. residents age ≥18 years with a self-reported diagnosis of RA by a medical professional. They were asked questions about socio-demographics, RA disease activity, diagnosis and DMARD history, improvement from RA treatment, and RA treatment goals created with their provider. Analyses included descriptive statistics with chi-square and rank sum tests for comparisons.

Responses by Time From Symptom Onset to RA Diagnosis

	<6mo N=268	>6mo to 5yr N-444	>5yr N=194	p value
Years from diagnosis to treatment				0.278
N	263	436	192	
Mean (SD)	0.8 (3.6)	0.6 (2.4)	1.5 (6.0)	
Median	0.0	0.0	0.0	
Q1, Q3	0.0, 0.0	0.0, 0.0	0.0, 0.0	
Range	(-1.0-29.0)	(-12.0-26.0)	(-6.0-40.0)	
How satisfied are you with your rheumatoid arthritis (RA) treatment?				0.077
Dissatisfied	38 (14%)	86 (19%)	38 (20%)	
I don't have an RA treatment plan	9 (3%)	17 (4%)	9 (5%)	
Satisfied	128 (48%)	223 (50%)	82 (42%)	
Very dissatisfied	16 (6%)	25 (6%)	20 (10%)	
Very satisfied	77 (29%)	93 (21%)	45 (23%)	
How would you describe your current RA disease activity?				0.001
In Remission	22 (8%)	24 (5%)	3 (2%)	
Mild	72 (27%)	88 (20%)	36 (19%)	
Moderate	135 (50%)	247 (56%)	104 (54%)	
Severe	39 (15%)	85 (19%)	51 (26%)	
Improvement				<0.001
Less than 20% improvement	29 (11%)	62 (14%)	37 (19%)	
About 20% improvement	36 (13%)	87 (20%)	34 (18%)	
About 50% improvement	74 (28%)	126 (28%)	77 (40%)	
About 70% improvement	68 (25%)	98 (22%)	31 (16%)	
>=90% improvement	61 (23%)	71 (16%)	15 (8%)	
Does your doctor consider you to be in remission from your RA?				0.003
Missing	0	1	0	
No	223 (83%)	402 (91%)	178 (92%)	
Yes	45 (17%)	41 (9%)	16 (8%)	
How would you describe your state of health?				0.128
Fair	104 (39%)	169 (38%)	82 (42%)	
Good	98 (37%)	153 (34%)	53 (27%)	
Poor	33 (12%)	70 (16%)	39 (20%)	
Very good	17 (6%)	30 (7%)	6 (3%)	
Very poor	16 (6%)	22 (5%)	14 (7%)	

Table1. Responses by Time from Symptom Onset to RA Diagnosis

Results: The questionnaire was completed by 907 self-reported RA patients (90% women, 10% men), with a mean (SD) age of 58 years and a mean of 11.1 (10.1) years since diagnosis. According to patient self-reports, 5% were in remission, 22% reported mild DA, 54% moderate DA, and 19% severe DA.

The longer the time to diagnosis, the more likely people were to report moderate to severe DA levels (< 6mo 65%; >6mo-5yr 75%; >5yr 80%). Similarly, people with a shorter time to diagnosis were twice as likely to reach DA improvement levels ≥70% as those with long times to diagnosis (< 6mo 48%; >6mo-5yr 38%; >5yr 24%).

Longer times from symptom onset to diagnosis also associated with longer times between RA diagnosis and eventual treatment. When the time from symptom onset to diagnosis was < 6 months, time from RA diagnosis to treatment was only an additional 0.8 years. However for those whose diagnosis took >5 years, time from RA diagnosis to treatment initiation was an average of an additional 1.5 years.

The longer the time to diagnosis, the less satisfaction and greater dissatisfaction people with RA had with their rheumatology care (satisfied/very satisfied was reported in: < 6mo 76%; >6mo-5yr 71%; >5yr 65%). Additionally, those describing their health as poor/very poor tended to have longer times to diagnosis (< 6mo 18%; >6mo-5yr 21%; >5yr 27%).

Conclusion: This web-based survey found previously unreported associations between time from symptom onset to RA diagnosis and more severe disease activity and lower responses to treatment, independent of time to between RA diagnosis and treatment initiation. Our study is unique in that time to diagnosis and / or to treatment are reported by patients with RA. Further research should seek greater understanding of the significance of early RA diagnosis and investigate ways to decrease times from symptom onset to RA diagnosis.

Disclosure: K. O'Neill, None; **K. Marks**, None; **J. Davis**, Pfizer, 2, AbbVie, 5, 8, Sanofi-Genzyme, 5, 8; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1.

Abstract Number: 0160

Use of PROMIS29 Across Inflammatory Arthritis: Score Distributions and Impact of Contextual Factors

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The Patient-Reported Outcome Measure Information System (PROMIS) includes a set of instruments developed to measure physical, mental and social health. PROMIS measures have been studied in RA but have only recently been used in spondyloarthritis. In this study, we aimed to determine whether there are differences in five PROMIS measures across psoriatic arthritis (PsA), axial spondyloarthritis (axSpA) and rheumatoid arthritis (RA) that would affect differential use in these diseases.

Methods: A cross-sectional study was performed in the Forward database utilizing data from 2019 among patients who had PsA, axSpA or RA and completed at least one PROMIS measure (4-item short forms of PROMIS physical function, fatigue, pain interference, sleep disturbance, and ability to participate in social roles and activities). Score

Table 1. Patient characteristics

	PsA	axSpA	RA
N	180	73	2990
Age (mean, SD)	63.1 (11.1)	59.9 (13.5)	67.1 (11.4)
Sex (%)	70%	66%	84%
Caucasian (%)	95%	93%	91%
College education (%)	57%	49%	50%
Duration (mean, SD)	20.9 (11.3)	25.8 (16.1)	22.8 (12.7)
Comorbidity Index (mean, SD)	2.1 (1.6)	2.4 (1.6)	2.2 (1.7)
Depression	14%	11%	14%
Obese (BMI>30)	50%	36%	35%

Abbreviations: axSpA = axial spondyloarthritis, PsA = psoriatic arthritis, RA = rheumatoid arthritis, SD = standard deviation

Table 1. Patient characteristics

Table 2. Mean scores by disease

		Score Distribution			Health Status***		
		Score	Floor**	Ceiling**	Acceptable	Not Acceptable	
	Instrument*	Mean (SD)	Min Score (% at min)	Max Score (% at max)	Mean (SD)	Mean (SD)	p-value
PsA	Physical function	43.8 (9.2)	22.9 (0.6%)	56.9 (24%)	47.7 (8.3)	38 (7.4)	<0.001
	Fatigue	51.7 (12)	33.7 (17%)	75.8 (6%)	47.8 (11)	57.4 (10.9)	<0.001
	Pain Interference	57.3 (10.2)	41.6 (20%)	75.6 (5%)	52.2 (9.1)	62.9 (8.5)	<0.001
	Sleep disturbance	51.7 (9.7)	32 (4%)	73.3 (5%)	49.1 (8.3)	55.4 (10)	<0.001
	Social satisfaction	50 (9.9)	27.5 (2%)	64.2 (22%)	54.4 (9.3)	43.6 (7)	<0.001
axSpA	Physical function	44.7 (10.5)	22.9 (3%)	56.9 (36%)	49.6 (9.5)	36.8 (6.7)	<0.001
	Fatigue	52.2 (12.4)	33.7 (19%)	75.8 (4%)	48 (12.5)	59.2 (9.2)	<0.001
	Pain Interference	53 (10)	41.6 (39%)	75.6 (0%)	48.2 (8.5)	62.7 (4.3)	0.027
	Sleep disturbance	51.4 (9.2)	32 (7%)	73.3 (3%)	49.5 (9.2)	54.5 (8.7)	0.027
	Social satisfaction	49.9 (10)	27.5 (1%)	64.2 (23%)	53.8 (9.5)	43.6 (7.5)	<0.001
RA	Physical function	42.4 (9.5)	22.9 (3%)	56.9 (21%)	46.4 (8.5)	36.3 (7.5)	<0.001
	Fatigue	52.6 (11.1)	33.7 (12%)	75.8 (4%)	48.4 (9.8)	59.2 (9.8)	<0.001
	Pain Interference	57.1 (9.2)	41.6 (18%)	75.6 (5%)	53 (8.2)	62.6 (7.5)	<0.001
	Sleep disturbance	50.6 (9.1)	32 (5%)	73.3 (2%)	48.1 (8.4)	54.6 (8.7)	<0.001
	Social satisfaction	49 (9.5)	27.5 (3%)	64.2 (18%)	52.8 (8.6)	43 (7.6)	<0.001

*PROMIS scores increase with 'more' of the construct being measured. In other words, the score for physical function increases with better physical function (higher scores are good); likewise, more interference in life activities as a result of pain results in a higher pain interference scores (i.e., higher pain scores are bad).

**Min and max scores are provided as these are not typical scales

***Health status was defined using a question that asked patients "In general, would you say that your health now is: excellent, good, fair, poor." Responses were dichotomized as acceptable (excellent or good) or not acceptable (fair or poor). A student's t-test was used to calculate differences in the mean scores among those with an acceptable health status compared to those with fair or poor health status.

Table 2. Mean scores by disease

Table 3. Standardized differences* by contextual factors

Contextual Factor	Instrument**	PsA	axSpA	RA
Age≥65	Physical Function	-0.33	0.06	-0.12
	Fatigue	-0.35	-0.85	-0.39
	Pain Interference	0.02	-0.16	-0.22
	Sleep Disturbance	-0.35	-0.48	-0.40
	Social satisfaction	-0.02	0.38	0.13
Female Sex	Physical Function	-0.61	-0.64	-0.32
	Fatigue	0.36	0.49	0.30
	Pain Interference	0.93	0.40	0.21
	Sleep Disturbance	0.26	0.14	0.26
	Social satisfaction	-0.59	-0.53	-0.20
Obesity	Physical Function	-0.50	-0.29	-0.55
	Fatigue	0.31	-0.04	0.43
	Pain Interference	0.08	-0.25	0.35
	Sleep Disturbance	0.18	0.08	0.26
	Social satisfaction	-0.36	-0.01	-0.44
Depression	Physical Function	-0.70	-0.39	-0.62
	Fatigue	1.07	0.43	1.12
	Pain Interference	0.30	-0.07	0.68
	Sleep Disturbance	0.40	1.10	0.67
	Social satisfaction	-0.75	-0.37	-1.05

*Standardized difference = (mean in patients with the factor – mean in patients without the factor)/standardized deviation. Standardized differences of greater than an absolute value of >0.10 are considered potentially important. The (-) indicates the direction of the score difference.
**PROMIS scores increase with 'more' of the construct being measured. In other words, the score for physical function increases with better physical function (higher scores are good); likewise, more interference in life activities as a result of pain results in a higher pain interference scores (i.e., higher pain scores are bad).
Abbreviations: axSpA = axial spondyloarthritis, PsA = psoriatic arthritis, RA = rheumatoid arthritis.

Table 3. Standardized differences* by contextual factors

distributions were examined (not shown) and floor and ceiling effects calculated. Differences in mean scores by disease were tested using Kruskal Wallis tests. Differences in scores among patients reporting an accepTable health status (current health status of excellent or good) compared to those rating health status as fair or poor were tested using student's t-tests. Differences in scores by potential contextual factors (age, sex, obesity and depression) were examined using standardized differences. We hypothesized that score distributions, floor and ceiling effects, discrimination between accepTable and not accepTable health status, and the impact of contextual factors on scores would be similar among the three diseases.

Results: In 2019, 3,243 patients completed the PROMIS29: 180 with PsA, 73 with axSpA and 2,990 with RA. Mean age was 63, 60, and 67 for PsA, axSpA, and RA respectively, and generally patients were more likely to be female, Caucasian and have long disease duration (Table 1). 63%, 60%, and 60% respectively rated themselves as having good or excellent health at the time of survey completion. Score distributions were similar across the three diseases. Mean scores for each instrument are shown in Table 2. Patients with PsA reported on average lower physical function compared to RA and axSpA (p=0.04), however there were not significant differences by disease for fatigue, pain interference, sleep disturbance, or social satisfaction (p >0.05). Patients with an accepTable health status had

better scores than those not in an accepTable state, and these differences were statistically significant for all instruments across all three diseases. Finally, contextual factors had an impact on the scores but the association between baseline characteristics and scores differed by disease (Table 3). For example, obese patients had worse physical function in all three diseases but impact on the other four measures was greater in PsA compared to axSpA. Similarly, depression had a significant effect on all scores but was particularly associated with worse fatigue in PsA and RA.

Conclusion: The PROMIS measures tested have similar score distributions and discrimination in PsA, axSpA and RA suggesting that they can be used across inflammatory arthritis. However, contextual factors may have differential influence on the scores in these three diseases.

Disclosure: A. Ogdie, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1; **K. Michaud**, Rheumatology Research Foundation, 2; **M. Hwang**, Novartis, 5, University of Texas Health Science Center at Houston (UTHealth) Center of Clinical and Translational Sciences KL2 program, 2; **S. Pedro**, Forward, The National Databank for Rheumatic Diseases, 3; **P. Katz**, None.

Abstract Number: 0161

Validation of Patient-reported Outcomes (PRO) Lung Questionnaires for Systemic Juvenile Idiopathic Arthritis (SJIA) Patients at Risk for Lung Disease

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Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Juvenile Idiopathic Arthritis (SJIA) involves dysregulation of inflammation and innate immunity, and can cause life-threatening complications including lung disease (LD). However, there are no validated patient-reported outcomes (PRO) that measure SJIA-LD. The primary aims are to validate a lung symptom survey created by Cincinnati Children's Medical Health Center (survey A), and one based on existing Patient-Reported Outcomes Measurement Information System (PROMIS) measures (survey B). We hypothesize that patients with LD have higher scores compared to those without LD.

Methods: Parents or guardians of SJIA patients under 18 years of age, as identified through the CCHMC JIA database and Systemic JIA Foundation, were surveyed via mail or email, and responses stored in Research Electronic Data Capture. LD was divided into three subgroups of patients: interstitial lung disease (ILD) or pulmonary alveolar proteinosis (PAP); asthma; and pulmonary hypertension (PAH), hospital-acquired pneumonia (HAP), or recurrent pneumonia. Total scores were used for survey A. PROMIS survey B are represented by t-scores, defined as standardized scores with a mean of 50 and a standard deviation of 10. Correlation between surveys were made with Pearson coefficient, while between-survey comparisons were done with t-tests, and between-group comparisons with ANOVA. Severity for lung symptoms in survey B were determined by the PROMIS Scores Graph For Profile Domains.

Screening questions

1. Are you a parent of a child with SJIA under 18 years of age? □ Yes □ No
2. Have your child every been diagnosed with ANY lung disease, such as pneumonia, asthma, or interstitial lung disease? □ Yes □ No
   - Yes Check all the types of lung diseases your child has been affected with.
     □ hospital-acquired pneumonia □ asthma □ interstitial lung disease □ pneumonia more than once □ pulmonary hypertension
     □ pulmonary alveolar proteinosis (PAP) □ other
3. Has your child ever been diagnosed or hospitalized with early, subclinical, or occult macrophage activation syndrome (MAS)? □ Yes □ No □ Unsure
4. What SJIA medications has your child PREVIOUSLY been on?
   □ daily oral steroids □ monthly pulse intravenous steroids □ anakinra (Kineret) □ canakinumab (Ilaris) □ tocilizumab (Actemra)
   □ methotrexate □ cyclosporine □ tacrolimus (Astagraf XL, Envarsus XR, Prograf) □ rilonacept (Arcalyst) □ tofacitinib (Xeljanz)
   □ ruxolitinib (Jakafi/ Jakavi) □ baricitinib (Olumiant) □ other
5. What SJIA medications is your child CURRENTLY on?
   □ daily oral steroids □ monthly pulse intravenous steroids □ anakinra (Kineret) □ canakinumab (Ilaris) □ tocilizumab (Actemra)
   □ methotrexate □ cyclosporine □ tacrolimus (Astagraf XL, Envarsus XR, Prograf) □ rilonacept (Arcalyst) □ tofacitinib (Xeljanz)
   □ ruxolitinib (Jakafi/ Jakavi) □ baricitinib (Olumiant) □ other

Survey A*

1. Does your child have a cough lasting more than 2 weeks? □ No (1) □ Yes (2)
2. Does your child have trouble breathing? □ never (1) □ almost never (2) □ often (3) □ almost always (4)
3. Does your child breathe fast? □ never (1) □ almost never (2) □ often (3) □ almost always (4)
4. Does your child get short of breath (winded) at rest or easily? □ never (1) □ almost never (2) □ often (3) □ almost always (4)
5. Does your child have trouble breathing at night or when sleeping? □ never (1) □ almost never (2) □ often (3) □ almost always (4)
6. Does your child's breathing keep them from keeping up with their friends? □ never (1) □ almost never (2) □ often (3) □ almost always (4)
7. If you answered "yes" to any of these, how long has your child had these problems? □ <1 week □ 1-2 weeks □ 2-4 weeks □ >4 weeks

Survey B**

	Question identification
1. In the past 7 days, my child felt scared that he/she might have trouble breathing because of his/her SJIA... □ never (1) □ almost never (2) □ sometimes (3) □ often (4) □ almost always (5)	Pdisabasth10r
2. In the past 7 days, my child's chest felt tight because of his/her SJIA... □ never (1) □ almost never (2) □ sometimes (3) □ often (4) □ almost always (5)	Ppedsa2asth1r
3. In the past 7 days, my child felt wheezy because of his/her SJIA... □ never (1) □ almost never (2) □ sometimes (3) □ often (4) □ almost always (5)	Ppedsa2asth2r
4. In the past 7 days, it was hard for my child to play sports or exercise because of his/her SJIA... □ never (1) □ almost never (2) □ sometimes (3) □ often (4) □ almost always (5)	Ppaqlqasth1r
5. In the past 7 days, it was hard for my child to take a deep breath because of his/her SJIA... □ never (1) □ almost never (2) □ sometimes (3) □ often (4) □ almost always (5)	Ppedsa2asth7r

Figure 1. Patient-reported Outcomes Surveys. *Survey A- Cincinnati Children's Medical Health Center. Point designations in parentheses. Total score ranges (6-22). **Survey B- PROMIS Parent Proxy Item Bank v2.0- Asthma Impact- Short Form 8a. Total scores (5-25) converted to t-scores. Modifications- "asthma" changed to "SJIA," excluded questions Ppedsdiaryasth4r, Ppaqlqasth3r, and Ppedsdiaryasth5r.

Results: Out of 139 participants, 40.3% (n=56) reported at least one LD including 12.9% (n=18) with ILD or PAP; 15.1% (n=21) with asthma; and 15.1% (n=21) with PAH, HAP, or recurrent pneumonia. There was high correlation (r=0.64) between both surveys. In survey A, the < 1 week group (n=21) had a median of 8 (IQR 7-10.5), and >4 weeks (n=51) had a median of 11 (IQR 9-14; p=0.0006). All patients with LD had significantly higher total scores than patients without known LD, with ROC curve showing an area of 0.73. A total score of >6.5 (range 6-22) had moderate sensitivity of 80.4% but poor specificity of 51.8% for identifying LD. However, patients with ILD and PAP had similar scores to those with asthma.

For survey B, patients with LD had significantly higher scores than patients without LD, although the median score was in the normal range. Further evaluation of LD subgroups showed that survey B was only significant for asthma, likely as the survey was based on existing asthma measures. For lung symptom clinical severity t-score thresholds, 95% was normal and 5% was moderate. The questions for survey B were further scrutinized; questions 1, 2, and 5 were significant when comparing no LD vs LD. Question 1 and 2 were significant when comparing no LD and all lung subgroups. The significant range differences between the questions can be helpful in creating future surveys with meaningful change.

Conclusion: While PROs based on lung disease symptoms showed higher scores in children with SJIA and LD, they could not discriminate between asthma and ILD/PAP. This is in agreement with prior work that most patients with

	# of participants *n* (frequency %)
Total	139
No LD	83 (59.7%)
LD	56 (40.3%)
ILD/ PAP	18 (12.9%)
asthma	21 (15.1%)
PAH/ HAP/ >1 pna	21 (15.1%)

Pearson r (survey A vs B)	r= 0.64
95% confidence interval	0.53-0.73
R squared	0.41
p value	<0.0001

Duration groups-survey A	<1 week (n=21)	1-2 weeks (n=8)	2-4 weeks (n=5)	>4 weeks (n=51)
median	8 (IQR 7-10.5)	11.5 (IQR 11-13)	8 (IQR 8-12.5)	11 (IQR 9-14)
range	7-12	9-14	8-13	7-21
mean	8.81 (SD 1.83)	11.75 (SD 1.58)	9.8 (SD 2.49)	11.92 (SD 3.76)
t-test (between <1 week and >4 weeks)= 3.61, *p*=0.0006				

Survey A	No LD (n=83)	LD (n=56)	ILD/PAP (n=18)	asthma (n= 21)	PAP/HAP/>1 pna (n=21)
median	6 (IQR 6-9)	10.5 (IQR 7-13.75)	10.5 (IQR 6-14.25)	11 (IQR 8-14.5)	12 (IQR 6.5-14.5)
range	6-16	6-21	6-21	6-20	6-21
mean	7.8 (SD 2.43)	10.93 (SD 4.24)	11.06 (SD 4.76)	11.52 (SD 3.74)	11.24 (SD 4.83)
Survey B					
median	35.5 (IQR 35.5-41.1)	40.2 (IQR 35.5-47.88)	35.5 (IQR 35.5-51.93)	44.3 (IQR 35.5-49.5)	35.5 (IQR 35.5-50.65)
range	35.5-66.4	35.5-65.1	35.5-61.5	35.5-65.1	35.5-63.3
mean	39.47 (SD 6.63)	42.73 (SD 8.78)	42.23 (SD 9.64)	43.51 (SD 8.6)	42.69 (SD 9.55)

***t*-test**	survey A	survey B
No LD vs LD	*t*= 5.525, *p*<0.0001	*t*= 2.494, *p*<0.0001
No LD vs ILD/PAP	*t*= 4.229, *p*<0.0001	*t*= 1.469, *p*=0.145
No LD vs asthma	*t*= 5.575, *p*<0.0001	*t*= 2.346, *p*=0.0209
No LD vs PAP/HAP/>1 pna	*t*= 4.615, *p*<0.0001	*t*= 1.808, *p*=0.0736

ANOVA- survey B	Q1	Q2	Q3	Q4	Q5
no LD vs LD subgroups					
p value	0.0056	0.0342	0.2317	0.5713	0.2274
no LD vs LD					
p value	0.0007	0.0167	0.1102	0.4387	0.05

PROMIS Scores For Profile Domains- Severity- Survey B		Frequency (%)
t-score ≤ 55 (normal)	132	95%
56-59 (mild)		
60-69 (moderate)	7	5%
≥ 70 (severe)		

***Figure 2*. Descriptive statistical analyses.** *Abbreviations*- LD (lung disease), ILD (interstitial lung disease), PAP (pulmonary alveolar proteinosis), Q (question).

SJIA and LD have mild respiratory symptoms. Future goals would be to identify other patient-reported factors that correlate stronger with LD.

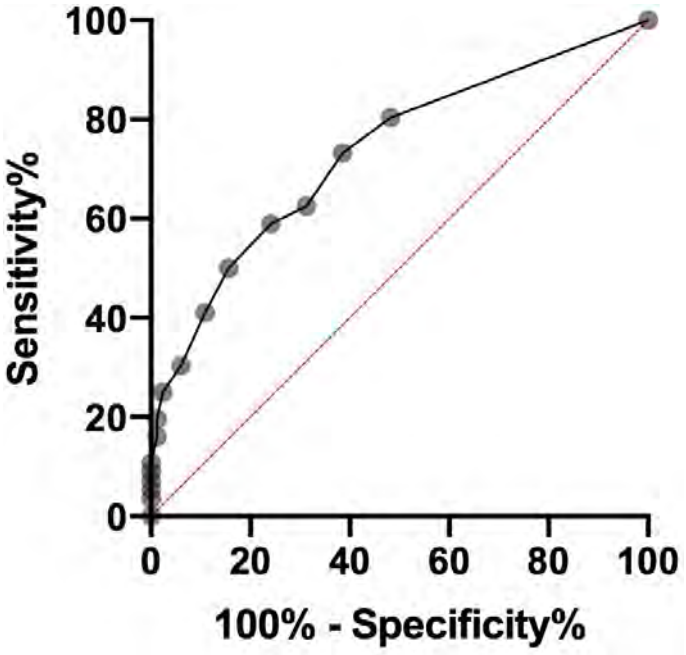


Figure 3. **ROC Curve for Survey A.**

Disclosure: K. Nguyen, None; **C. Towe**, None; **S. Yasin**, None; **A. Grom**, Novartis, 2, 5, SOBI, 2, 5, AB2Bio, 2, 5; **H. Brunner**, Bristol-Myers Squibb, 2, 5, MedImmune, 2, Novartis, 2, 8, Pfizer Inc, 2, 5, AbbVie, 5, AstraZeneca-MedImmune, 5, Bayer, 5, Biocon, 5, Boehringer Ingelheim, 5, Janssen, 5, Eli Lilly, 5, R-Pharm, 5, Roche, 5, 8, Cincinnati Children's Hospital Medical Center, 3, GlaxoSmithKline, 8; **G. Schulert**, Novartis, 5, Sobi, 5.

Abstract Number: 0162

Identifying Sleep Problems in Systemic Juvenile Idiopathic Arthritis (SJIA) Patients with Patient-reported Outcomes (PRO) Questionnaires

Kim Nguyen[1], Christopher Towe[2], Shima Yasin[3], Alexei Grom[4], Hermine I Brunner[5] and Grant Schulert[5], [1]Veterans Affairs Cincinnati, University of Cincinnati Medical Center, Cincinnati, [2]Cincinnati Children's Medical Hospital Center, Cincinnati, [3]Cincinnati Children's Hospital Medical Center, Cincinnati, [4]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [5]PRCSG, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Juvenile Idiopathic Arthritis (SJIA) can cause severe and chronic multisystem involvement. Medical therapies including high-dose corticosteroids can have significant side effects affecting sleep. The primary aims are to validate Patient-Reported Outcomes Measurement Information System (PROMIS) surveys-sleep disturbance (survey A) and sleep impairment (survey B). Our hypothesis is that current steroid drug treatment cause worse sleep.

Screening questions

1. Are you a parent of a child with SJIA under 18 years of age? □ Yes □ No
2. Have your child every been diagnosed with ANY lung disease, such as pneumonia, asthma, or interstitial lung disease? □ Yes □ No
   - Yes Check all the types of lung diseases your child has been affected with.
     □ hospital-acquired pneumonia □ asthma □ interstitial lung disease □ pneumonia more than once □ pulmonary hypertension
     □ pulmonary alveolar proteinosis (PAP) □ other
3. Has your child ever been diagnosed or hospitalized with early, subclinical, or occult macrophage activation syndrome (MAS)? □ Yes □ No □ Unsure
4. What SJIA medications has your child PREVIOUSLY been on?
   □ daily oral steroids □ monthly pulse intravenous steroids □ anakinra (Kineret) □ canakinumab (Ilaris) □ tocilizumab (Actemra)
   □ methotrexate □ cyclosporine □ tacrolimus (Astagraf XL, Envarsus XR, Prograf) □ rilonacept (Arcalyst) □ tofacitinib (Xeljanz)
   □ ruxolitinib (Jakafi/ Jakavi) □ baricitinib (Olumiant) □ other
5. What SJIA medications is your child CURRENTLY on?
   □ daily oral steroids □ monthly pulse intravenous steroids □ anakinra (Kineret) □ canakinumab (Ilaris) □ tocilizumab (Actemra)
   □ methotrexate □ cyclosporine □ tacrolimus (Astagraf XL, Envarsus XR, Prograf) □ rilonacept (Arcalyst) □ tofacitinib (Xeljanz)
   □ ruxolitinib (Jakafi/ Jakavi) □ baricitinib (Olumiant) □ other

Survey A- PROMIS Parent Proxy Item Bank v1.0- Sleep Disturbance- Short Form 4a	Question identification
1. In the past 7 days, my child had difficulty falling asleep... □ never (1) □ almost never (2) □ sometimes (3) □ almost always (4) □ always (5)	sq005p
2. In the past 7 days, my child slept through the night... □ never (5) □ almost never (4) □ sometimes (3) □ almost always (2) □ always (1)	sq020p_r
3. In the past 7 days, my child had a problem with his/her sleep... □ never (1) □ almost never (2) □ sometimes (3) □ almost always (4) □ always (5)	sq041p_r
4. In the past 7 days, my child had trouble sleeping... □ never (1) □ almost never (2) □ sometimes (3) □ almost always (4) □ always (5)	sq042p

Survey B- PROMIS Parent Proxy Item Bank v1.0- Sleep-Related Impairment- Short Form 4	Question identification
1. In the past 7 days, my child was sleepy during the daytime... □ never (1) □ almost never (2) □ sometimes (3) □ almost always (4) □ always (5)	w001p
2. In the past 7 days, my child had a hard time concentrating because he/she was sleepy... □ never (1) □ almost never (2) □ sometimes (3) □ almost always (4) □ always (5)	w011p
3. In the past 7 days, my child had a hard time getting things done because he/she was sleepy... □ never (1) □ almost never (2) □ sometimes (3) □ almost always (4) □ always (5)	w028p
4. In the past 7 days, my child had problems during the day because of poor sleep □ never (1) □ almost never (2) □ sometimes (3) □ almost always (4) □ always (5)	w029p_r

Figure 1. **Survey questions.**

Methods: Patients were identified through the CCHMC JIA database and Systemic JIA Foundation, and included parents or guardians of SJIA patients under 18 years of age at the time of the survey. Survey invitations were mailed or e-mailed, and de-identified data were stored in Research Electronic Data Capture. The two surveys are listed in Figure 1 and include demographic screening questions and past and current drug treatments. In performing descriptive statistical analyses, PROMIS surveys are represented by t-scores, defined as standardized scores with a mean of 50 and a standard deviation (SD) of 10. Between-group comparisons were done with t-tests. Severity of sleep problems were determined by the corresponding PROMIS Scores Graph For Profile Domains (Figure 3).

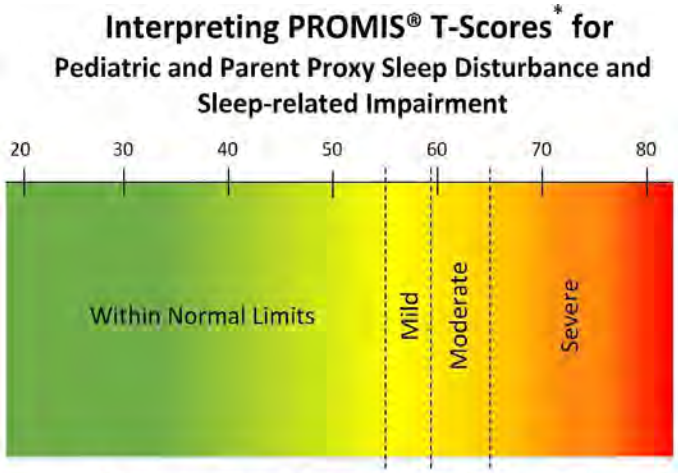
Results: 139 participants were included in the survey. There was reasonable correlation between survey A and B (r=0.5175). For survey A, 51.1% (n=71) of patients reported some level of sleep disturbance; 12.9% were mild, 14.4% were moderate, and 23.8% were severe. For survey B, 53.2% (n=74) of patients reported sleep impairment; 15.8% were mild, 19.4% were moderate, and 18% were severe. For survey A, the steroid treatment group showed a mean of 58.43 (SD 12.01), a median of 57.7 (IQR 47.65-69.4), and a range of 41.4 to 78.9. The no steroid treatment group had a mean of 55.16 (SD 11.72), a median of 54 (IQR 41.4-64.6), and a range of 41.4 to 78.9. T-test treatment group comparison was not significant (p=0.13). In survey B, patients treated with steroids showed a mean of 55.18 (SD 11.79), a median of 51.2 (IQR 46.2-66.13), and a range of 40 to 84.4. The no steroid treatment group had a mean of 54.85 (SD 11.76), a median of 56.1 (IQR 40-63.6), and a range of 40 to 84.4 There was not statistical significance between treatment groups (p=0.88) (Figure 2).

Pearson r (survey A vs B)	r= 0.5175
95% confidence interval	0.38-0.63
p value	<0.0001

PROMIS Scores For Profile Domains- Severity	n	frequency (%)
Sleep Disturbance		
t-score ≤ 55 (normal)	68	48.9%
56-58 (mild)	18	12.9%
59-65 (moderate)	20	14.4%
≥ 66 (severe)	33	23.8%
Sleep-Related Impairment		
t-score ≤ 54 (normal)	65	46.8%
≤ 55-58 (mild)	22	15.8%
59-65 (moderate)	27	19.4%
≥ 66 (severe)	25	18%

Survey A	steroids (n=44)	no steroids (n=95)
median	57.7 (IQR 47.65-69.4)	54 (IQR 41.4-64.6)
range	41.4-78.9	41.4-80.2
mean	58.53 (SD 12.01)	55.16 (SD 11.72)
t-test (*p* value)	*t*= 1.516 (*p*=0.1318)	
Survey B		
median	51.2 (IQR 46.2-66.13)	56.1 (IQR 40-63.6)
range	40-84.4	40-84.4
mean	55.18 (SD 11.79)	54.85 (SD 11.76)
t-test (*p* value)	*t*= 0.1533 (*p*=0.8784)	

Figure 2. **PROMIS Scores For Profile Domains and Descriptive Statistical Analyses.**



Parent proxy	normal	mild	moderate	severe
Sleep disturbance	≤ 55	56-58	59-65	≥ 66
Sleep-Related Impairment	≤ 54	55-58	59-65	≥ 66

Figure 3. PROMIS Scores Graph For Profile Domains

Conclusion: In conclusion, a majority of patient with SJIA have clinically significant sleep disturbance and/or impairment. However, current steroid treatment did not have statistical significance for causing worse sleep. Sleep problems interfere with quality of life and future endeavors include identification of factors that correlate with higher scores.

Disclosure: K. Nguyen, None; **C. Towe**, None; **S. Yasin**, None; **A. Grom**, Novartis, 2, 5, SOBI, 2, 5, AB2Bio, 2, 5; **H. Brunner**, Bristol-Myers Squibb, 2, 5, MedImmune, 2, Novartis, 2, 8, Pfizer Inc, 2, 5, AbbVie, 5, AstraZeneca-MedImmune, 5, Bayer, 5, Biocon, 5, Boehringer Ingelheim, 5, Janssen, 5, Eli Lilly, 5, R-Pharm, 5, Roche, 5, 8, Cincinnati Children's Hospital Medical Center, 3, GlaxoSmithKline, 8; **G. Schulert**, Novartis, 5, Sobi, 5.

Abstract Number: 0163

Cost of Non-Persistence in the Treatment with Subcutaneous Tumor Necrosis Factor-Alpha Inhibitors of Inflammatory Arthritis: A Propensity Score Matching Approach

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Few studies have explored cost consequences of non-persistence in the treatment with Subcutaneous Tumor Necrosis Factor-Alpha Inhibitors (SC-TNFi) in Inflammatory Arthritis (IA; rheumatoid arthritis [RA], psoriatic arthritis [PsA] and ankylosing spondylitis [AS]). Hence, the aim of this study was to estimate the costs associated with non-persistence among biologics-naïve patients treated with SC-TNFi for IA.

Methods: An adult and biologic treatment-naïve population initiating treatment for IA with any available SC-TNFi (adalimumab, etanercept, certolizumab, and golimumab) between May 1, 2010 and December 31, 2017, was identified in the Swedish Health Data Registers. Treatment persistence was derived based on information from filled prescriptions and a grace period of 60 days. Patients not reaching the specified treatment maintenance period (i.e. persistent < 6 months) or with insufficient follow-up data were excluded. Patients were deemed non-persistent if treatment was discontinued or if they switched to another novel synthetic or biologic disease-modifying anti-rheumatic drugs (DMARDs). Costs of non-treatment related Health Care Resource Utilization (HCRU) were captured and compared 12-months before and after the date of non-persistence (i.e. index date). Resources comprised specialized outpatient care, inpatient stays, and medication other than DMARDs. The analysis was conducted on a propensity score matched cohort based on the predicted probability of non-persistence, within two years from treatment initiation; controlling for baseline characteristics collected 12 months before treatment initiation (e.g. age, gender, diagnosis, and level of education). Non-persistent patients (cases) were matched 1:1, without replacement, to persistent patients with at least 12 months additional time on treatment (controls). The number of days on treatment in cases was also used to identify the index date in controls, enabling comparisons across the same time period in relation to treatment initiation.

Results: A total of 9,976 eligible patients initiating SC-TNFi treatment for IA were identified. A PSM cohort was derived with 2,969 cases and an equal number of controls. In this cohort overall, 63% were female, the mean age was

	Persistent patients n = 2,969			Non-persistent patients n = 2,969		
	Mean USD	(SD)	[95% CI*]	Mean USD	(SD)	[95% CI*]
HCRU costs 1 year pre-index†						
Specialized outpatient care	1,745	(1,874)	[1,682, 1,812]	2,257	(1,941)	[2,188, 2,326]
Inpatient care	707	(2,681)	[617, 800]	1,425	(5,512)	[1,238, 1,626]
Non-DMARD medication	511	(3,681)	[423, 658]	544	(958)	[511, 581]
Total	2,963	(5,401)	[2,779, 3,156]	4,227	(6,592)	[3,981, 4,482]
HCRU costs 1 year post-index†						
Specialized outpatient care	1,323	(1,595)	[1,265, 1,383]	2,329	(2,794)	[2,236, 2,438]
Inpatient care	738	(3,336)	[629-867]	2,022	(6,316)	[1,797, 2,264]
Non-DMARD medication	524	(3,927)	[423-636]	612	(1,125)	[544, 695]
Total	2,585	(5,828)	[2,388, 2,825]	4,963	(8,318)	[4,681, 5,254]
Difference in HCRU costs† pre- and post-index						
Specialized outpatient care	-422	(1,818)	[-483, -358]	71	(2,485)	[-20, 164]
Inpatient care	31	(4,001)	[-108, 174]	597	(6,836)	[362, 848]
Non-DMARD medication	13	(1,219)	[-25, 65]	68	(1,884)	[9, 140]
Total	-378	(4,921)	[-548, -197]	736	(8,027)	[439, 1,035]

CI – confidence interval; HCRU – health care resource use; DMARDs – disease,modifying anti-rheumatic drugs; index – index date; SC,TNFi – subcutaneous tumor necrosis factor-α inhibitor; SD – standard deviation; USD – US dollars

** Bootstrapped 95% confidence intervals*

† Costs are presented in 2018 US-dollars.

Table 1. Costs of non-treatment related health care resource utilization 12-months before and after index date in, propensity score matched, persistent and non-persistent patient's treated with SC-TNFi for IA

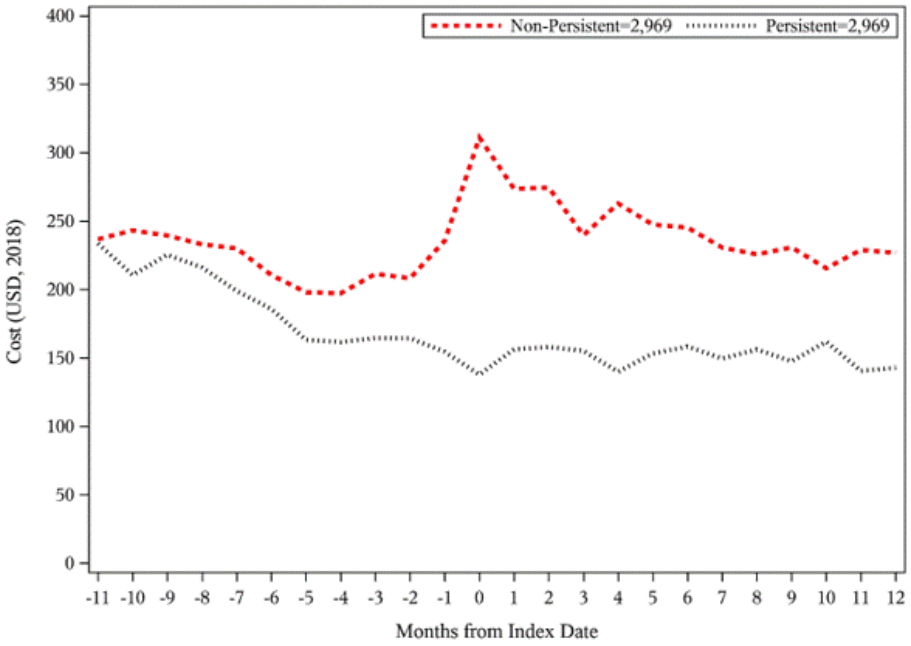

Figure 1. Development of costs for non-treatment related health care resource utilization 12-months before and after index date in, propensity score matched, persistent and non-persistent patient's treated with SC-TNFi for IA

50 years, and 52%, 22%, and 26% were diagnosed with RA, PsA and AS, respectively. While non-persistent patients increased their total non-treatment related cost of HCRU from the 12-month period before to the 12-month period after the index date, persistent patients decreased their costs between the same time periods (Table 1). Figure 1 shows the monthly development of total non-treatment related HCRU costs from 12 months before to 12 months after the index date. Costs were more similar before the index date and the differences increased for non-persistent patients in conjunction with their treatment discontinuation.

Conclusion: Among patients initiating SC-TNFi treatment for IA, non-persistent patients incurred significantly higher non-treatment HCRU costs compared to those who were persistent during the year following index date. This highlights the impact of therapy persistence from an economic point of view, adding further aspects to the clinical perspective.

Disclosure: J. Dalén, Merck & Co., Inc., 9; **K. Luttropp**, Merck & Co., Inc., 9; **T. Olofsson**, Eli Lilly, 9, Merck Sharp & Dohme, 9; **C. Black**, Merck & Co., Inc, 1, 3; **A. Puenpatom**, Merck & Co., Inc., 1, 3.

Abstract Number: 0164

What's in a Name? Patient and Family Perspectives on the Naming of Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The childhood inflammatory disorder systemic juvenile idiopathic arthritis (SJIA) has historically had several names, including Still's disease and systemic juvenile rheumatoid arthritis. While its current name reflects its classification as a subtype of JIA, SJIA is genetically and pathogenically distinct from the other subtypes of JIA. To complicate things further, SJIA and adult onset Still's disease (AOSD) may be the same disorder with different ages of onset. Scant data exists regarding how the name "SJIA" is perceived by patients and families as well as its implications for the patient experience.

Methods: A qualitative study of self-reported online survey of patients with SJIA was developed by the non-profit organizations, the Autoinflammatory Alliance, KAISZ/VAISZ, and SJIA Foundation in English and translated to Dutch. Respondents were recruited by convenience sampling through online social media posts. Respondents were asked if they considered that SJIA adequately described their disease, followed by an open-ended question on what they thought about the name, "Systemic Juvenile Idiopathic Arthritis".

Table 1: Representative patient comments by theme area

Theme areas	Representative comments
1) Insurance reasons	Our insurance company (Tricare) requires "step-wise" therapy. For example: first use steroid, next use MTX and then Humira and after that use Anakinra.
	Other people and insurance see it as just joint pain and nothing else.
2) Gets confused with rheumatoid/osteoarthritis or other forms of JIA	Many people have a misconception about arthritis. They feel that only elderly people are affected by arthritis within their joints.
	People hear "arthritis" and think of the arthritis an old person has, and that isn't an accurate picture of my child.
	When I explain what my daughter has and say the name they only hear "arthritis" and then to proceed to say they know exactly how they feel cause they have arthritis in their finger
3) Other disease features more pronounced than the arthritis	My child is more affected by systemic inflammation and organ involvement than arthritis in her joints (though she has that, as well).
	(we) know that the Systemic subset is made up of so many more symptoms than just inflammation of the joints. I know of patients who are diagnosed with SJIA but have not had inflammation in any joints, therefore arthritis does not cover their experience with this diagnosis
	My daughters main symptoms 3 years after diagnosis are still systemic. Over the years she has had major organ involvement and MAS (needing care in ICU). I find people see the word arthritis and think that's all that's wrong with her
4) Make the name easier to understand to lay people	I would prefer a name that gives laypersons an accurate perception of what is going on inside my child's body.
	We understand it because we live it. But to say it and explain it is difficult for others to understand.
5) The name makes the disease seem less serious than it is	It difficult emotionally to have people not understand why this disease is so dangerous and life altering
	No one understands that it's far more serious than sore joints.
6) Name is difficult to remember/pronounce/ understand	People shut down often with longer names and with arthritis.
	I just know when she was diagnosed five years ago I could not even tell people her disease because I had a hard time remembering SJIA
7) Possibility for subclassification if it has a separate name	I think that this name will be an even bigger issue as discoveries are made about the pathogenesis of this disease and we see indicators of why different subsets of children have differing symptoms. It would be easier to change it now so that subsets could be created later on, if needed."
	I also don't think it should be group together with the other "Juvenile Arthritis" categories. It should be it's own classification with it's own subcategories.
8) Seems to affect only children	By its title one believes it concerns only children. I had my first attack at 4, now 57.. came and went all my life until I was 35 and my disease process came to stay.
9) More similar to period fever syndromes	Since joining the auto inflammatory rare disease but not alone page I have discovered my daughters SJIA presents much more like a periodic fever syndrome than juvenile idiopathic arthritis.

Results: Between 2017 and 2019, there were 72 responses, 54 from parents of children with SJIA and 18 from adults with SJIA. Thirty six (51%) answered that they did not think the name adequately represented the disease, including 61% of adults with SJIA. Responses were grouped into several themes. The most frequent responses were that the name confuses the condition with more common types of arthritis. Several noted this minimizes the disorder as “just

sore joints." Hindrance to appropriate treatment was also noted due to lack of insurance coverage because they had to try and fail treatments for other forms of arthritis. Similarly, many noted that the name does not reflect the most common clinical features of their own disease- "(its) difficult emotionally to have people not understand why this disease is so dangerous and life altering because … Arthritis is only a piece of it". Adult patients with SJIA noted that the name implies it only affects children when they have had life-long symptoms. Finally, several noted the name was too long and complicated to explain to people: "We understand it because we live it, but to say it and explain it is difficult for others to understand".

Several themes also reflected what patients would like to see in a disease name, including: 1) something that is easier to explain to lay people, 2) greater reflection of autoinflammatory disease, rather than a form of JIA, and 3) that there is a wide variety of clinical features, which might benefit from subtypes.

Conclusion: Over half of the SJIA patients and caregivers do not agree with the name. They highlighted many areas where the disease name can negatively impact the perception of their disease. The study is limited by being a convenience sample of parents engaged in social media and may not be representative of the general population of patients with SJIA. However, these responses regarding the limitations of the name and how it could be improved will serve as the basis for a larger and more structured survey, including patients with AOSD, to provide patient and family input on the future classification of SJIA.

Disclosure: M. Correia Marques, This work was supported by a Fred Lovejoy Resident Research and Education Award., 2; **R. Sinha**, None; **K. Durrant**, None; **S. Lapidus**, None; **N. Tennermann**, None; **S. Angevare**, None; **L. Bush**, None; **K. Cupp**, None; **J. Hausmann**, Novartis, 5; **D. Maher**, None; **S. Newton**, None; **M. Ombrello**, None; **P. Reardon**, None; **R. Trachtman**, None; **F. Dedeoglu**, Novartis, 1; **G. Schulert**, Novartis, 5, Sobi, 5.

Abstract Number: 0165

Work Disability and Predictors of Poor Work Outcome in Patients with Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (axSpA) is a chronic inflammatory disease which may lead substantial functional limitation. The disease more commonly affects men in their third decade of life. For patients with chronic disease participation in paid work may be the result of series factors like disease severity, effectiveness of the health care, availability and the type of work. Previously it was reported that ankylosing spondylitis may cause adverse work outcome.

To understand the impact of axSpA on work disability and the factors associated with poor work outcome.

Table. Demographics and diseases related characteristics of study population

Variables	All population (n=219)	No work disability (n=172)	Work disability (n= 47)
Male, n (%)	161 (73.5)	122 (70.9)	39 (83)
Age, years*		41.5 (9.4)	43.1 (12.4)
Ever smoking, n (%)	155 (71.4)	115/171 (67.3)	40/46 (87)
Education duration ≤8 years, n (%)	82/212 (61.3)	53/165 (32.1)	29/47 (61.7)
Disease duration, years	6.7 (8.3)	5.5 (6.3)	10.7 (12.6)
BASDAI*	4.3 (2.4)	4 (2.3)	5.3 (2.6)
BASFI*	3.4 (2.8)	2.9 (2.5)	5.4 (3.0)
ASDAS-CRP*	2.8 (1.2)	2.7 (1.1)	3.3 (1.4)
BASMI*	2.3(2.0)	2 (1.8)	3.5 (2.4)
ASQOL*	9 (5.5)	8 (5.3)	12 (4.9)
Peripheral arthritis, n (%)	81/207 (39.1)	54/163 (33.1)	27/44 (61.4)
Hip arthritis, n (%)	39/205 (19)	26/163 (16)	13/42 (31)
Presence of syndesmophyte, n (%)	92/164 (56.1)	63/125 (50.4)	29/39 (74.4)

* Variables presented as mean (SD).

Methods: A cross-sectional survey was performed among323 patients withaxSpA according to ASAS classification criteriafrom one tertiary center. In total 219 (67.8%) patients were working age at the time study. The others were student, housewife or retired. Demographic, social and disease related characteristics were collected. Characteristic that might be associated with premature work loss were evaluated byunivariable and multivariable logistic regression analysis.

Results: Out of 219 axSpA patients (155 [71%] r-axSpA and 64 nr-axSpA, 69% HLA-B27 positive) who have a work at least once 47 (22%) was either withdrawn from work (n=35) or retired due to disability (n=12) during median (IQR) 12 (12) years symptom duration. Demographic and disease related characteristics of the patients with or without work diasbilitywere summarized in the Table. In univariate analysis gender, smoking, education levels, the presence of peripheral arthritis, BASMI score and radiographically presence of syndesmophyte and hip involvement were found to be associated with poor work outcome. However poor work outcome were similar between r- and nr-axSpA patients. In regression analysis low education level (HR:3.4 [95%CI:1.4-8.6], P=0.007), peripheral arthritis (HR:2.7[95%-CI:1.07-6.8], P=0.035), and ever smoking (HR:4.9 [95%CI :1.3-18.0], P=0.02) were independent predictors of work disability.

Conclusion: Our results suggest that there is still remarkable poor work outcome among axSpA patients and work disability might be similar in r- and nr-axSpA. Patients who are smoker, with low education levels, and peripheral arthritis seem to be at risk for premature work loss.

Disclosure: E. Ediboglu, None; **D. Solmaz**, None; **H. Oz**, None; **G. Kabadayı**, None; **H. Cinaklı**, None; **E. Otman Akat**, None; **M. Ozmen**, None; **S. Akar**, None.

Abstract Number: 0166

Prevalence and Impact of UnaccepTable Symptom State Among Patients with Psoriatic Arthritis: Results from the National Psoriasis Foundation's 2019 Annual Survey

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite many efficacious therapies for PsA, many patients do not achieve remission. Ongoing disease activity leads to many downstream effects including diminished functional ability, reduction in social interaction and in some cases depression. Furthermore, depression may be associated with ongoing symptoms that can be attributed to PsA. The objective of this study was to determine the prevalence of 'unaccepTable' symptom states among patients with PsA and to examine the association with being in an unaccepTable symptom state with depression and impaired social interaction.

Methods: The National Psoriasis Foundation (NPF) surveyed a random, stratified sample of individuals with psoriatic disease in the US from the NPF's constituent database. Patients were active members of the NPF within the past 2 years, age >=18, carried a self-reported diagnosis of psoriasis or PsA and had an active email address or phone number. The presence of accepTable vs unaccepTable level of disease impact of PsA was assessed using the established patient accepTable symptom state for the PsAID-9 (< =4 on a scale of 0-10). Severity of psoriasis was defined by body surface area (BSA, Mild < 3%, Moderate to Severe ≥ 3%) as reported by patients using the Patient Report of Extent of Psoriasis Involvement (PREPI). Linear regression analyses were conducted to compare outcomes of individuals with accepTable level of PsA activity with those who have unaccepTable level of PsA activity while adjusting for severity of PsO. Outcomes of interest were depression and ability to participate in social roles and activities. Depression was assessed by a two-stage assessment process utilizing the PhQ-2 and PhQ-9. The PhQ-2 is utilized in this analysis. Ability to participate in social roles and activities was assessed by the PROMIS Ability to Participate in Social Role and Activities-SF4a. Descriptive statistical analyses were conducted with SPSS Ver 26 and ANOVA and linear regression analyses were conducted in STATA SE Ver 9.

Results: Among 23,340 patients sent a survey, 1,570 individuals completed the survey, including 834 who reported being diagnosed with PsA by a healthcare provider and 801 (96.0%) completed the PSAID. Among individuals who self-reported diagnosis of PsA and completed the PsAID-9, 59.6% reported unaccepTable level of disease activity (PSAID >4) and 40.4% reported accepTable level of disease activity. After adjusting for age, sex, and severity of PsO, statistically significant differences were found between individuals with unaccepTable level of PsA activity and accepTable level of PsA activity for depression [2.56 (SD 2.00) vs 0.08 (SD 1.25, p≤.001] and ability to participate in social roles and activities [mean T-scores 44.56 (SD 6.83) vs 55.46 (SD 6.99), p≤.001].

Conclusion: Not being in a patient accepTable symptom state is common in this US-based population of patients with PsA and is associated with significant decrements in social activity and increase prevalence of depression. Being monitored by a dermatologist or rheumatologist was associated with an increased likelihood of being in a patient accepTable symptom state.

Table 1 – Patient characteristics

	Unacceptable PsA (n)	Acceptable PsA (n)
Age		
18 – 35 years	55.2% (32)	44.8% (26)
36 – 50 years	60.1% (128)	39.9% (85)
51 – 65 years	64.9% (235)	35.1% (127)
Older than 65 years	46.5% (66)	53.5% (76)
BMI		
Normal or Underweight	18.4% (81)	30.5% (94)
Obese or Overweight	81.6% (359)	69.5% (214)
Sex		
Female	67.3% (338)	32.7% (164)
Male	46.6% (138)	53.4% (158)
Psoriasis Severity		
Mild	52.0% (229)	48.0% (211)
Moderate - Severe	70.2% (191)	29.8% (81)
PROMIS Social Activity Score Categories		
Normal (T score > 45)	17.5% (83)	81.2% (259)
Mild Limitation (40-45)	41.8% (198)	16.9% (54)
Moderate Limitation (30-40)	30.8% (146)	1.9% (6)
Severe Limitation (<30)	9.9% (47)	0.0% (0)
PhQ-2 Interpretation (PhQ-2 Score)***		
Depression not likely (0 – 2)	52.3% (248)	90.4% (292)
Depression likely (3 – 6)	47.7% (226)	9.6% (31)
Treatments Used		
Biologic	69.0% (325)	70.2% (226)
Phototherapy	11.0% (52)	10.2% (33)
Topical medication	67.7% (319)	57.5% (185)
Oral therapies	46.1% (217)	35.1% (113)
OTC	48.4% (228)	33.5% (108)
None	3.8% (18)	2.5% (8)
Provider Type***		
Rheumatologist	56.2% (245)	53.5% (160)
Dermatologist	27.3% (119)	38.8% (116)
All other providers	16.5% (72)	7.7% (23)

*** Chi-square test of independence p≤.001

Table 1. Patient characteristics

Table 2. Mean differences in social activity and depression among those in a patient acceptable symptom state compared to those not in PASS.

	Unadjusted (beta-coefficient, 95%CI)	Age-and-sex adjusted (beta-coefficient, 95%CI)	Age, sex, and psoriasis severity adjusted (beta-coefficient, 95%CI)
Social Activity			
Unacceptable vs acceptable	11.38 (10.40 – 12.36)***	11.21 (10.19 – 12.21)***	10.90 (9.82 – 11.98)***
Depression			
Unacceptable vs acceptable	-1.87 (-2.12 – -1.63)***	-1.87 (-2.13 – -1.61)***	-1.76 (-2.03 – -1.49)***

*** p≤.001

Table 2. Mean differences in social activity and depression among those in a patient accepTable symptom state compared to those not in PASS.

Disclosure: A. Ogdie, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1; **G. Gondo**, None; **J. Merola**, AbbVie, 9, Merck, 9, Dermavant, 9, Eli Lilly, 9, Novartis, 9, Janssen, 9, UCB, 9, Samumed, 9, Celgene, 9, Sanofi, 9, Regeneron, 9, GlaxoSmithKline, 9, Sun Pharmaceutical, 9, Almirall, 9, Biogen, 9, Pfizer, 9, Incyte, 9, Aclaris, 9, LEO Pharma, 9; **S. Bell**, None; **A. Gottlieb**, Janssen, 2, 5, Incyte, 2, 5, Novartis, 2, 5, 8, Xbiotech, 2, 9, Boehringer Ingelheim, 2, 5, UCB Pharma, 2, 5, 8, Beiersdorf, 5, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, Sun Pharma, 2, 5, Leo Pharma, 5, Avotres Therapeutics, 5.

Abstract Number: 0167

Rheumatoid Arthritis Patient Phenotypes from a Digital Health Coaching Engagement Program

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
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Session Time: 9:00AM–11:00AM

Background/Purpose: The goal of this study was to examine whether cluster analysis could be used to identify homogeneous subgroups of engagement in RA patients enrolled in a digital health coaching program. The novelty of this approach was our attempt to identify actual user engagement behaviors, as opposed to employing engagement benchmarks derived from a trial protocol. These findings can help clinical staff stratify the RA population for digital health interventions between clinic visits for disease monitoring, self-management, and other efforts.

Methods: A longitudinal, retrospective analysis was conducted in a sample of RA members enrolled in Pack Health digital health coaching program (n = 66). Members reported the primary measures of RA disease severity (RAPID3) and physical and mental health quality of life (PROMIS) upon enrollment. Digital engagement data was measured using the frequency of outbound calls to a health coach, inbound calls from a health coach, the average call length, email open rate, frequency of outgoing patient text messages to a health coach, and incoming member text messages over the initial 12 weeks of the program. An agglomerative hierarchical cluster analysis was performed using Ward's method to link and identify subgroups of members with similar profiles. Dismarilarity between RA members was calculated by the Minkowski distance in nine-dimensional space.

Results: Three clusters were identified with a Minkowski dissimilarity measure greater than 100. Cluster 1 (poor health, highly engaged) consisted of 28 patients with below-average PROMIS mental health (45.15), poor PROMIS physical health (38.70), and moderate to severe RA (RAPID3 4.90). This highly engaged cluster averaged 11.29 connected outbound calls or a 94% call success rate along with the highest volume of total text messages (56.75). Cluster 2 (better health, moderately engaged) consisted of 23 patients with below-average PROMIS mental health (46.50), above-average PROMIS physical health (52.49), and low RA severity (RAPID3 2.61). Cluster 2 averaged 8.48 total calls out of a possible 12 along with 16.3 total text messages. Cluster 3 (poor health, minimally engaged) consisted

Cluster	PROMIS Physical	PROMIS Mental	RAPID3	Inbound Calls	Outbound Calls	Avg Call Length	Inbound Text Messages	Outbound Text Messages	Email Open Rate
1: Poor Health, Highly Engaged	38.70	45.15	4.07	11.29	1.54	11.36	36.25	20.50	63.10%
2: Better Health, Moderately Engaged	46.50	52.49	2.61	7.39	1.09	9.27	13.87	2.43	55.39%
3: Poor Health, Minimally Engaged	32.03	36.35	4.90	3.07	0.53	6.44	12.33	2.87	58.22%

Table1. Cluster Descriptive Statistics

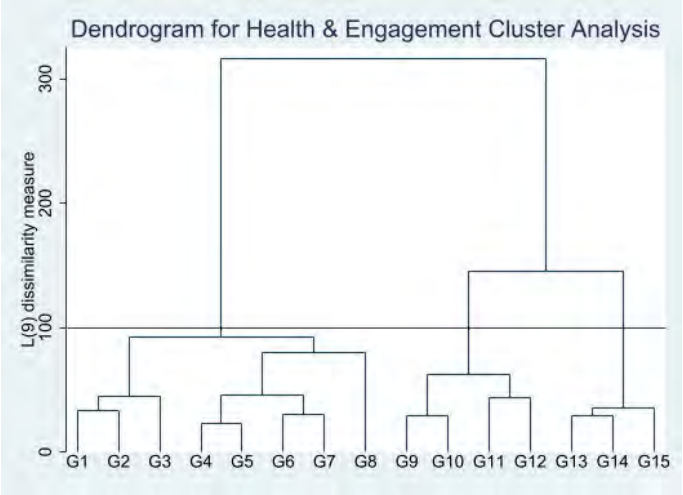

Figure 1. Dendrogram for Hierarchical Cluster Analysis

of 15 members with poor PROMIS mental health (32.05), poor PROMIS physical health (36.35), and high severity RA (RAPID3 4.90). This minimally engaged cluster averaged 3.07 successful calls and 15.2 total text messages. Complete health and engagement cluster data are shown in Table 1.

Conclusion: Results indicated that distinct patterns of engagement exist among RA patients in a digital health coaching program. The demographics and patient attributes identified in each subgroup may be helpful in (a) predicting RA patients' participation and engagement in digital health interventions between clinic visits, and (b) enhancing patient engagement in digital health coaching programs for RA by tailoring treatment to the patient's particular disease severity and engagement phenotype.

Disclosure: J. Patterson, None; **K. Magid**, None; **D. Patel**, None; **M. Allison**, None.

Abstract Number: 0168

Impact of Adalimumab (Humira) Therapy on Ocular Inflammation, Selected Health Care Resource Utilization, and Patient-Reported Outcomes in Patients with Active Non-infectious Intermediate, Posterior, or Panuveitis in Routine Clinical Practice

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA

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Session Time: 9:00AM–11:00AM

Figure 1. Proportion of patients who achieved quiescence and proportion of patients who maintained response (quiescence achieved at prior visit and no flare at current visit) at any visit during the follow-up.

*Quiescence: no new active chorioretinal inflammatory lesions and AC cells and VH grade ≤0.5+ in both eyes.

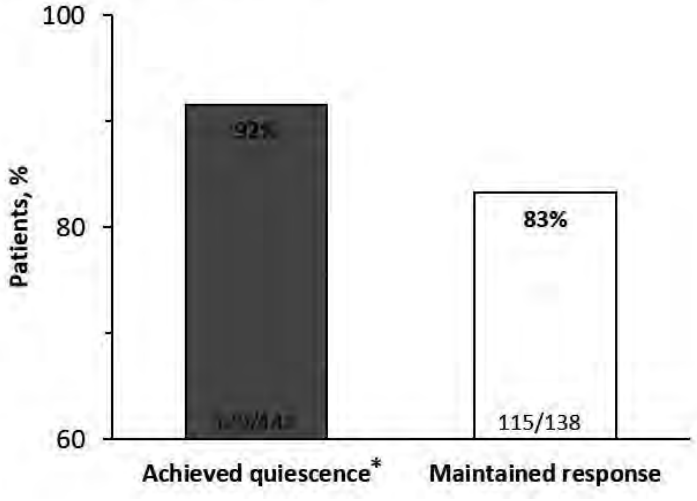
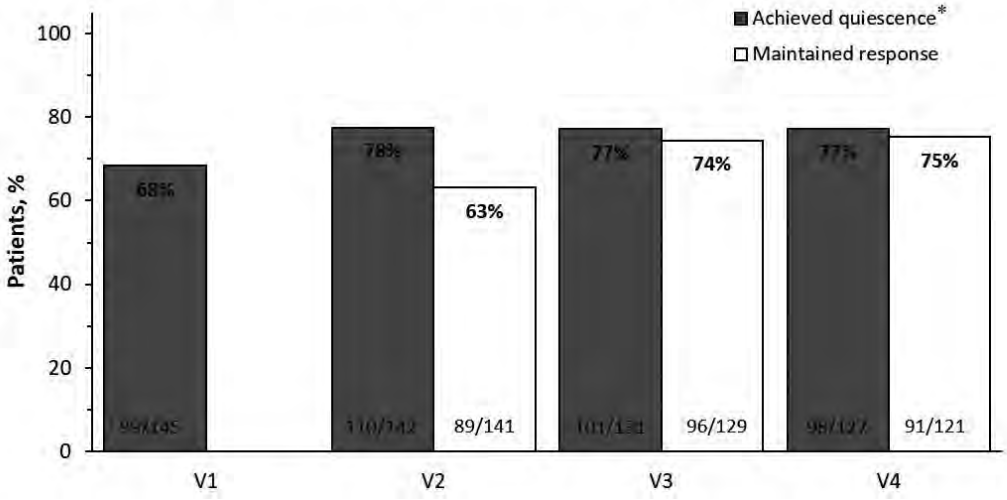


Figure 2. Proportion of patients who achieved quiescence and proportion of patients who maintained response (quiescence achieved at prior visit and no flare at current visit) at separate follow-up visits. Visit schedule included baseline (V0) and 4 follow-up visits over 12 months at 3-month intervals (V1, V2, V3, and V4).

*Quiescence: no new active chorioretinal inflammatory lesions and AC cells and VH grade ≤0.5+ in both eyes.



Background/Purpose: VISUAL clinical trials demonstrated efficacy and safety of adalimumab (ADA) in patients with active and inactive non-infectious, intermediate, posterior, or panuveitis (NIIPPU).[1-3] The purpose of this study (HOPE) was to evaluate disease characteristics and assess real-world effectiveness of ADA, including effects on treatment response (quiescence) and health resource utilization in patients with active NIIPPU.

Methods: HOPE was a post-marketing, prospective, observational study conducted in 15 countries. Included in the study were patients ≥18 years old with active NIIPPU (active, inflammatory, chorioretinal, and/or inflammatory retinal

Table. Demographics and Baseline Characteristics

Variable	Full Analysis Set (N=149)
Age, y	
Mean ± SD	42.3±15.2
Sex, n (%)	
Female	93 (62)
Race, n (%)	
White	120 (81)
Asian	2 (1)
Black or African American	1 (0.7)
Other	26 (17)
Number of flares in the past 12 months	
Mean ± SD	2.2±1.8
Systemic NIPPU-specific therapy,* n (%)	
Any	73 (49)
Prednisone/methylprednisone	60 (40)
Methotrexate	16 (11)
Azathioprine	11 (7)
Cyclosporine-A	4 (3)
Mycophenolate mofetil	4 (3)
Other	6 (4)
Highest daily prednisone or equivalent dose, mg	
Median	48.0
Anatomical localization of uveitis,*† n (%)	
Panuveitis	64 (43)
Intermediate	45 (30)
Posterior	45 (30)
Etiology,* n (%)	
Idiopathic	75 (50)
Behçet syndrome	25 (17)
Vogt-Koyanagi-Harada	13 (9)
Sarcoid	11 (7)
Birdshot choroidopathy	6 (4)
Other	23 (15)

NIIPPU= non-infectious, intermediate, posterior, or panuveitis.
*Multiple entries were possible.
†According to Standardization of Uveitis Nomenclature criteria.

vascular lesion; or anterior chamber [AC] cells grade ≥2+; or vitreous haze [VH] grade ≥2+) despite high-dose corticosteroid therapy. Patient visits included baseline (V0) and follow-up at month 3 (V1), 6 (V2), 9 (V3), and 12 (V4). Patients received ADA per local prescription guidelines and signed informed consent. Excluded were patients with prior ADA treatment, participating in other clinical studies, or unwilling or unable to complete patient-reported questionnaires. Primary endpoint was proportion of patients in quiescence (no new active chorioretinal inflammatory lesions and AC cells and VH grade ≤0.5+ in both eyes) at any of the follow-up visits. Secondary endpoints were proportion of patients in quiescence at each visit; proportion of patients who maintained response (quiescence achieved at prior visit and no flare at current visit); and proportion of patients with flares (new active inflammatory lesions, AC cells grade ≥2+, or VH grade ≥2+ in ≥1 eye) at any visit. Visual function was assessed with National Eye Institute 25-Item Visual Function Questionnaire (VFQ-25). Serious adverse events (SAEs) were recorded at all visits.

Results: Patients in the full analysis set were assessed at V0 (n=149), V1 (n=147), V2 (n=143), V3 (n=133), and V4 (n=127). Of 149 patients, 62% were female, 43% had panuveitis, and 50% had idiopathic etiology; mean age was 42.3 years (**Table**). Quiescence was achieved by 92% of patients, and response was maintained in 83% of patients at any of the follow-up visits (**Figure 1**)**.** Most patients achieved quiescence and maintained response at each visit (**Figure 2**). Flares occurred in 32% of patients at any of the follow-up visits. Proportion of patients with medical visits

for uveitis during the preceding 6 months or since last visit decreased from 89% (132/149) at V0 to 39% (55/142) at V2 and 21% (27/126) at V4. Median change in overall VFQ-25 score from V0 to V2 and V4 was 3.3 (interquartile range [IQR], 0.4–13.4) and 5.1 (IQR, 0.4–15.7), respectively. SAEs were reported for 14 patients (9%).

Conclusion: In patients with active NIIPPU treated in routine clinical practice, ADA showed effectiveness in improving ocular inflammation, achieving quiescence, improving quality of life, and decreasing healthcare resource utilization. No new safety signals were identified.

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Abstract Number: 0169

Patient-Reported Outcomes Differentiate Between Remission and Low Disease Activity in Psoriatic Arthritis

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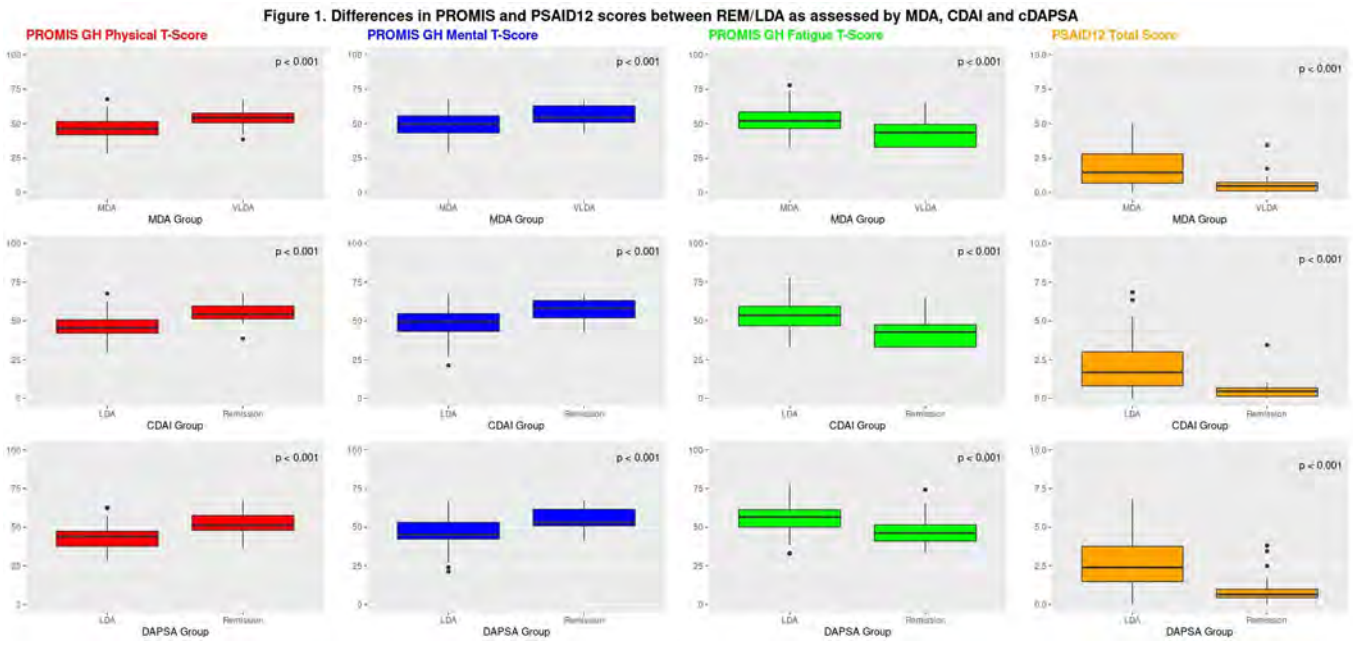
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: For psoriatic arthritis (PsA), several different composite instruments are available to define low disease activity (LDA) and remission (REM) targets for treatment. Patient-reported outcomes (PROs) may also be useful in assessing disease activity and may be more practical than composite indices in some settings. In this study, we examined the ability of PROs to differentiate between states of low disease activity and remission treatment targets (LDA and REM), using composite indices as the reference standards.

Methods: This cross-sectional study was performed with the Psoriatic Arthritis Research Consortium between 2016-2019. PROs included Patient-Reported Outcomes Measurement Information System [PROMIS] instruments, EULAR Psoriatic Arthritis Impact of Disease [PSAID12], and Routine Assessment of Patient Index Data 3 [RAPID3]). Participants (pts) were classified as LDA if they fulfilled composite index criteria for Minimal Disease Activity (MDA), Clinical Disease Activity Index (CDAI)-LDA, or Disease Activity in Psoriatic Arthritis (cDAPSA)-LDA and REM if they fulfilled



composite index criteria for Very Low Disease Activity (VLDA), CDAI-REM, or cDAPSA-REM. PROs were evaluated by determining 1) score differences between pts in LDA vs. REM, 2) correlations with composite indices scores, and 3) percentages of pts in LDA and REM who fulfilled PRO criteria for low disease states (in PROs with previously established low disease state criteria). PROs were compared between groups using t-tests or Wilcoxon rank sum test, depending on their distributions. The categorical versions of RAPID3 and PSAID12 were compared between groups using Chi-Squared test or Fisher's exact test, when appropriate. Correlations were calculated with Spearman's rank correlation. Data was analyzed using R software (Version 3.5; Vienna, Austria).

Results: 227 PsA pts were included (52.2% female, average age 52.7±14 years). Compared to pts in LDA, pts in REM had significantly more favorable PROMIS Physical, PROMIS Mental, PROMIS Fatigue, and PSAID12 scores (Figure

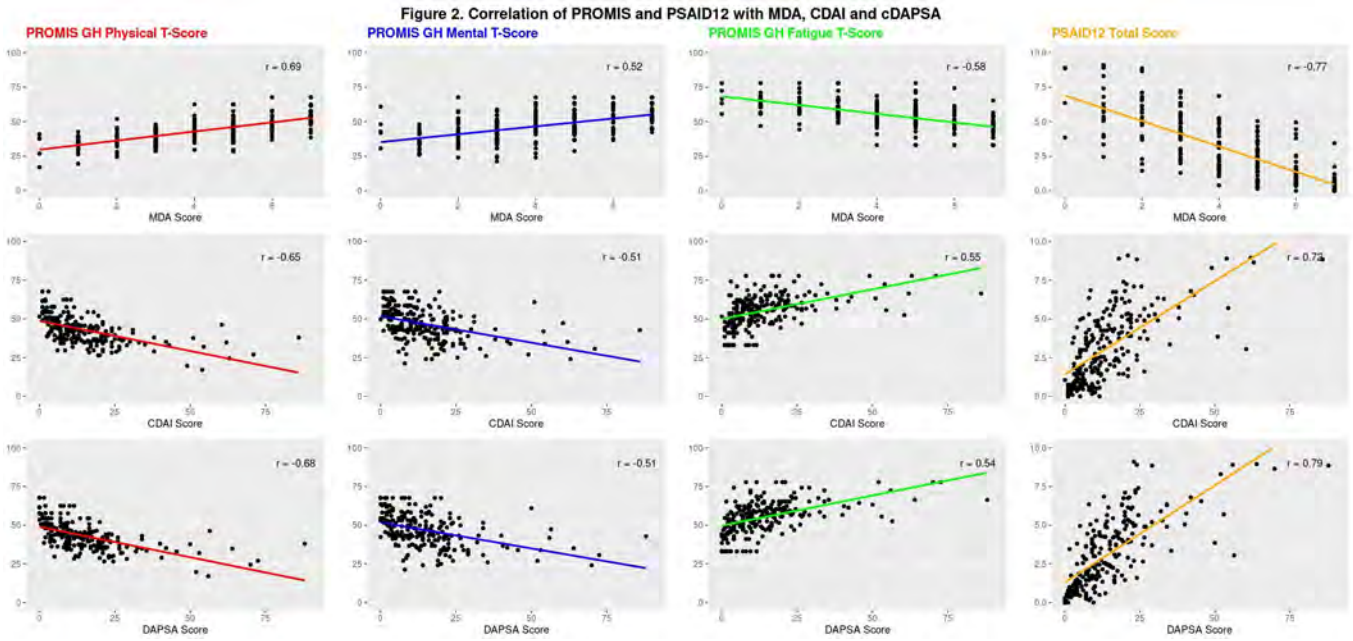


Figure 1. Hierarchical Clustering using complete linkage of Euclidean Distance

Table 1. Comparison of RAPID3 and PSAID12 between composite measures

RAPID3	Total N=100 (%)	MDA N=72 (%)	VLDA N = 28 (%)	p-value
RAPID3 Category				*<0.001*[a]
Near-remission	43 (43.0)	15 (20.8)	28 (100.0)	
Low Severity	21 (21.0)	21 (29.2)	0 (0.0)	
Moderate Severity	32 (32.0)	32 (44.4)	0 (0.0)	
High Severity	4 (4.0)	4 (5.6)	0 (0.0)	
RAPID3	**Total N=107 (%)**	**CDAI LDA N=84 (%)**	**CDAI REM N=23 (%)**	**p-value**
RAPID3 Category				*<0.001*[a]
Near-remission	43 (40.2)	20 (23.8)	23 (100.0)	
Low Severity	25 (23.4)	25 (29.8)	0 (0.00)	
Moderate Severity	35 (32.7)	35 (41.7)	0 (0.00)	
High Severity	4 (3.7)	4 (4.8)	0 (0.00)	
RAPID3	**Total N=134 (%)**	**DAPSA LDA=84 (%)**	**DAPSA REM N=50 (%)**	**p-value**
RAPID3 Category				*<0.001*[b]
Near-remission	43 (32.1)	5 (6.0)	38 (76.0)	
Low Severity	29 (21.6)	18 (21.4)	11 (22.0)	
Moderate Severity	52 (38.8)	51 (60.7)	1 (2.0)	
High Severity	10 (7.5)	10 (11.9)	0 (0.00)	
PSAID12	**Total n=100 (%)**	**MDA n=72 (%)**	**VLDA N=28 (%)**	**p-value**
PSAID12 Category				0.186[a]
Patient acceptable	93 (93.0%)	65 (90.3%)	28 (100%)	
Not Patient acceptable	7 (7.00%)	7 (9.72%)	0 (0.00%)	
PSAID12	**Total n=107 (%)**	**CDAI LDA n=84 (%)**	**CDAI REM N=23 (%)**	**p-value**
PSAID12 Category				0.200[a]
Patient acceptable	98 (91.6%)	75 (89.3%)	23 (100%)	
Not Patient acceptable	9 (8.41%)	9 (10.7%)	0 (0.00%)	
PSAID12	**Total n=134 (%)**	**DAPSA LDA n=84 (%)**	**DAPSA REM N=50 (%)**	**p-value**
PSAID12 Category				*0.001*[b]
Patient acceptable	115 (85.8%)	65 (77.4%)	50 (100%)	
Not Patient acceptable	19 (14.2%)	19 (22.6%)	0 (0.00%)	

p-values: a=Fisher's Exact Test; b=Pearson's chi-square test

PSAID12 patient acceptable state = score ≤4; PSAID12 not patient acceptable state = score >4

1). Correlations were strong between the composite indices and PROMIS GH physical health (r=0.65- 0.69) and between the composite indices and PSAID12 (r=-0.77- 0.79) (Figure 2). RAPID3 Low Severity and Near-Remission were reported by >98% of patients in REM, but only up to 54% of patients in LDA (Table 1). PSAID12 Patient AccepTable State occurred more frequently in pts in DAPSA-REM than pts in DAPSA-LDA (Table 1).

Conclusion: PROMIS and PSAID12 instruments correlated well with composite indices and differentiated between states of LDA vs REM. RAPID3 Near-Remission may be the most rigorous PRO criteria (including only the lowest states of disease activity), while PSAID Patient AccepTable State may identify a broader range of low states of dis-

ease activity. These data contribute to the construct validity of using PROs to measure low states of disease activity that may be considered for additional treatment targets in PsA.

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Abstract Number: 0170

Utilizing Design Thinking to Develop a Decision Aid for Patients with Psoriasis and Psoriatic Arthritis

Marilyn Wan[1], Michele Almonte[2], Joel Gelfand[1] and **Alexis Ogdie**[2], [1]University of Pennsylvania, Philadelphia, [2]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster I: RA, Spondyloarthritis, & OA
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Given the complexity of available treatment recommendations, patients with psoriatic disease would benefit from a process fostering shared decision-making using a patient-centered approach. True shared decision-making is challenging during short visits but patient decision aids (DAs) can assist this. This study aimed to understand patient and clinician needs in the process of starting/switching therapy and use design thinking to develop a patient-centered DA that addresses these needs.

Methods: Design thinking, a method adopted from engineering, first seeks to understand user needs to develop a prototype which is then iteratively revised based on user input. Semi-structured interviews of ten patients and two focus groups with rheumatologists (n=7), dermatologists (including one nurse practitioner) (n=5) and specialty pharmacists (n=2) were conducted to inform the first prototype. Follow-up focus groups with the same healthcare providers and semi-structured interviews with an additional eight patients were conducted to revise the prototype. Interview transcripts were independently coded by two research team members using NVivo12 to elicit pertinent themes. Participants were continually interviewed until saturation of themes was reached where no new themes emerged.

Results: Themes were identified from clinicians and patients (representative quotes in Table 1). Interrater reliability of the two coders surpassed the *a priori* kappa threshold of 0.80 to ensure consistency in coding. Clinicians felt that a DA was most useful for patients initiating or switching therapies and should include basic information about the disease, managing flares, and individual therapies. Clinicians suggested that treatment options should be identified using an algorithm that considers patient characteristics (e.g., comorbidities) and then select 2-3 therapies for patients to learn about. Patients desired a DA that would give them access to all information about therapies including lifestyle alterations from medications, efficacy rates, side effects, insurance coverage, and personal testimonials from other patients. Patients and clinicians noted readability and easy navigation as necessary. Patients desired more detailed information than anticipated by clinicians or would typically be provided in a short encounter. The final decision aid prototype can be found at psoriasisdecisionaid.com.

Theme	Representative Quote
Available treatments for a given circumstance	"I mean, basically it was we discussed whatever all the options and based on my circumstance at that time, which was that I was a young mother with a newborn nursing, I wasn't going to do anything that was systemic because I didn't want to stop nursing and I didn't want to hurt my baby."
Lifestyle	"There were also concerns, like I said, about certain treatments would require me to stop drinking, and it's just because that sort of cuts down on your ability to socialize, that sort of thing."
Novelty	"Well, yeah. I mean, I guess, it's also not knowing really what effects I would have from being on medication like that long-term which isn't something that has been around for a while. Some of the newer medications that I guess there wasn't a whole lot of research on at that time seemed I wasn't sure about."
Side effects	"And I knew, like we had talked about other options like different medications, but the risks associated with them just weren't worth it to me. Like I would rather have the psoriasis that I have than like be on a medication that could maybe cause side-effects like depression or something like that. That just really scared me." "I was willing to try something different because it was, again, if there are long-term effects – if we discover that the biologic drugs do something awful to you for 20 years, I'll be in my 80s by then so that's okay, I'll take it." "I think drug interactions are a key thing."
Risk-benefit Analysis	"I think just making sure everything is in balance. Like I said, I know how badly my psoriasis could be and it's really – it is manageable. So I think just balancing out like, okay, how much do I really hate having these spots versus like what am I really – like what lengths am I willing to go to get rid of them or to have it completely clear. So I just think finding that in between …" "But it was just a question of weighing these different things. Is it time? Have I reached the tipping point, as they would say?"
Efficacy	"I think what's most important is that is that it's effective."
Main concern	"Just because I was in so much pain, I wasn't really mobile, so being able to get up and get exercising again and being more active was important to me." "Also, with the skin lesions, I was also embarrassed. I was self-conscious about it as well." "It always has been the pain, but there's also the sub-issue of the skin lesions on the face. I don't really care about the skin lesions on my legs because nobody really sees those." "…what would be helpful to me as a provider is if I could understand what are the two or three major concerns a patient has that I can address for them"

Figure 2: Circos plot comparing clinical LS subtype to immune-phenotype clustering.

Conclusion: Design thinking was an effective method of creating a comprehensive decision aid; including patients, clinicians and pharmacists was of critical importance in arriving at a final decision aid that serves the needs of all stakeholders. Next steps include testing how the decision impacts treatment decisions and whether it reduces decision conflict.Table 1. Themes identified and representative quotes.

Disclosure: M. Wan, None; **M. Almonte**, Amgen Inc., 9; **J. Gelfand**, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, GlaxoSmithKline, 5, Janssen Biologics, 2, 5, Novartis Corp, 2, 5, Regeneron, 5, UCB, 9, Sanofi, 2, 5, Pfizer Inc, 2, 5, Abbvie, 2, Celgene, 2, Ortho Dermatologics, 2, 9, Eli Lilly and Company, 9, Journal of Investigative Dermatology, 9, Society for Investigative Dermatology, 8, Spirig Pharma, 9; **A. Ogdie**, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1.

Abstract Number: 0171

Interferon Response Gene Expression Differs in Whole Blood, Peripheral Blood Mononuclear Cells, Monocytes, T Cells, B Cells, and NK Cells in Patients with the Autoinflammatory Interferonopathies, CANDLE and SAVI

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The disease progression of patients (pts.) with type-I interferon (IFN)-mediated diseases undergoing treatment with JAK1 and JAK2 inhibitors is monitored in part by measuring the transcription of a 28 IFN response gene (IRG) signature in whole blood with Nanostring technology to calculate a 28-gene IFN score. We sought to determine the differences in 28-gene IFN scores and in the patterns of IRG signatures among peripheral blood mononuclear cells (PBMCs), monocytes, CD4 and CD8 T cells, B cells, NK cells, and neutrophils in the type-I IFN-mediated diseases CANDLE (chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperatures) and SAVI (STING-associated vasculopathy with onset in infancy).

Methods: All patients (pts.) were enrolled into an IRB-approved natural history protocol (NCT02974595). RNA was extracted from pts. and healthy control whole blood, PBMCs, monocytes, CD4 and CD8 T cells, B cells, NK cells, and neutrophils. Transcript counts for 28 IRGs and 4 additional genes were measured with a NanoString instrument and compared to expression in the same cells or tissues in a cohort of healthy controls (HCs).

Results: Both CANDLE (p=0.065) and SAVI pts. (p=0.004) had greater 28-gene standardized IFN scores in whole blood and PBMCs compared to HCs. Significantly higher IFN scores were seen in SAVI PBMCs as compared to SAVI whole blood (p=0.035) while CANDLE PBMC IFN scores were not significantly different compared to CANDLE whole blood. SAVI PBMCs expressed more *IFNA2* and *IFNB1* than PBMCs from CANDLE pts. (p=0.0023; p=0.0012) or HCs (p=0.0097; p=0.0004). One family of SAVI pts. with a novel STING missense variant was found to have elevated IFN scores in their PBMCs while their whole blood IFN scores were not elevated. In cell subsets isolated from PBMCs, CANDLE and SAVI pts. had elevated IFN scores in monocytes and T cells, but the IFN scores in B cells and NK cells were not significantly different from HCs. SAVI pts. had significantly high IFN scores than CANDLE patients in the monocyte (p=0.02) and CD4 T cell (p=0.002) subsets. Within the 28 IRGs of the IFN score, SAVI and CANDLE mono-

cytes had the highest relative expression of *IFIT3* and *LY6E*, respectively. Preliminary studies in neutrophils have also shown that SAVI neutrophils have a greater induction of IRG transcription compared to CANDLE pts.

Conclusion: High expression of type-1 IFNs and IRGs in the PBMCs of SAVI pts. further demonstrate the role of these cells in the amplification of constitutive IFN signaling in this disease. Monocytes make a substantial contribution to the elevated IRG signature in peripheral blood found in both diseases and to a greater extent in SAVI. In addition, pts. with a SAVI phenotype and genotype but a negative IRG signature in whole blood may present an IRG transcription signature when investigating the PBMC fraction.

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Disclosure: J. Mitchell, None; **S. Alehashemi**, None; **B. Marrero**, None; **Y. Huang**, None; **S. Torreggiani**, None; **L. Bichell**, None; **G. Montealegre Sanchez**, None; **R. Goldbach-Mansky**, None; **A. de Jesus**, None.

Abstract Number: 0172

Early Treatment and *IL1RN* Single Nucleotide Polymorphisms Affect Response to Anakinra in Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session A
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Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) represents 10-20% of all chronic arthritis during childhood. The interleukin 1 (IL-1) play a pivotal role in the pathogenesis of the disease. Indeed, several studies confirmed the therapeutic efficacy of anakinra (recombinant IL-1 receptor antagonist) in a significant portion of patients with sJIA, especially in the first phase of disease. The use of anakinra as first-line therapy can benefit from the so-called "window of opportunity", for which the evolution of the disease can be modified preventing the onset of chronic arthritis. Despite a good response to anakinra in a high percentage of patients, there is a subset of non-responders. The early identification of non-responder patients is of primary importance to avoid the progression towards chronic arthritis. Some single nucleotide polymorphisms (SNPs) in *IL1RN* gene have been found associated with sJIA, and recently, a cluster of SNPs in the *IL1RN* non-translated region has been suggested as a possible predictor of non-response to anakinra. The aim of this study was to evaluate the impact of early treatment and genetic variants in *IL1RN* gene on the response to anakinra in sJIA.

Methods: Response to anakinra was considered as clinically inactive disease (CID) at 6 months, without glucocorticoids treatment. Demographic, clinical and laboratory characteristics of 56 patients were analyzed in univariate and

multivariate analysis as predictors of response to treatment. Six SNPs in *IL1RN* gene were genotyped by qPCR or Sanger sequencing. Haplotype mapping was performed with Haploview software and *IL1RN* mRNA expression in whole blood from patients before anakinra initiation was assessed by qPCR.

Results: After 6 months of treatment, 73.2% of patients met the criteria for CID off glucocorticoids. In univariate analysis the variable strongly related with the response was disease duration from onset to anakinra initiation, with an optimal cut-off at 3 months. Patients who started anakinra after 3 months from disease onset had an 8-fold higher risk of non-response at 6 months. We confirmed that the 6 *IL1RN* SNPs were inherited as a common haplotype in our cohort of patients. We found that homozygosity for at least one high expression SNP correlates with higher *IL1RN* mRNA levels and was associated with a 6 fold higher risk of non-response, independently of disease duration.

Conclusion: Our results confirm the important role of early IL-1 inhibition and suggest that genetic *IL1RN* variants predict non-response to therapy with IL-1 blockade in patients with sJIA.

Disclosure: M. Rossi, None; **M. Pardeo**, None; **D. Pires Marafon**, None; **E. Sacco**, None; **C. Passarelli**, None; **C. Bracaglia**, SOBI, 8; **C. Perrone**, None; **A. Tulone**, None; **G. Prencipe**, None; **F. De Benedetti**, Novartis, 2, 8, Novimmune, 2, 9, Sobi, 2, 8, 9, Roche, 2, 8, Pfizer, 2, Sanofi, 2, AbbVie, 8.

Abstract Number: 0173

mTORC1 Signaling Promotes Monocytosis and Arthritis Development in IL-1 Receptor Antagonist-deficient Mice

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) is potentially life-threatening disease characterized by prolonged fever, systemic inflammation and skin rash in addition to joint inflammation. Aberrant activation of the innate immune system driven by interleukin (IL)-1 and IL-6 is thought to be responsible for the initial phase of systemic inflammation. Monocytes propagate the inflammatory process in sJIA and their numbers are greatly increased in patients with active disease. Using mice deficient of IL-1 receptor antagonist (Il1rn$^{-/-}$) to model sJIA, we studied the role of the central metabolic regulator mTORC1 (mechanistic target of rapamycin complex 1) in the development of monocytosis and arthritis.

Methods: We analyzed myeloid cell populations in the bone marrow and peripheral blood of Il1rn$^{-/-}$ mice and wild-type (WT) BALB/c controls (8-10 weeks of age). mTORC1 signaling was quantified by intracellular phospho-flow cytometry. Mice were treated with the recombinant IL1 receptor antagonist anakinra, the mTORC1 inhibitors rapamycin or vehicle control for two weeks to study the impact on monocytosis and arthritis. Monocyte count was analyzed in sJIA patients pre- and post-treatment with anakinra.

Figure 1. Anakinra treatment reversed monocytosis in IL1rn $^{-/-}$ mice

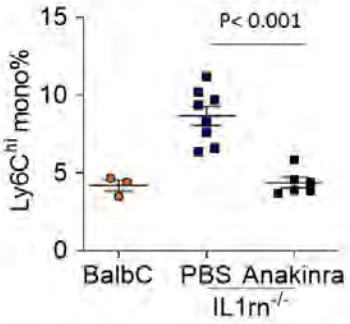


Figure 2. Anakinra treatment reversed monocytosis in sJIA patients (n = 8)

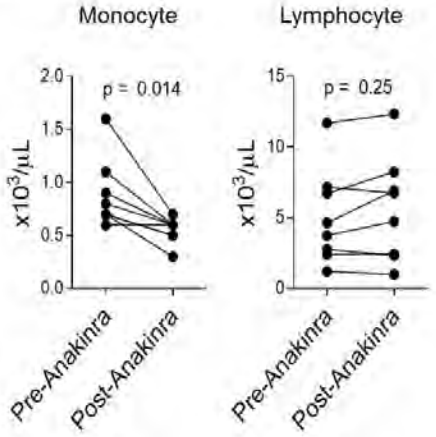
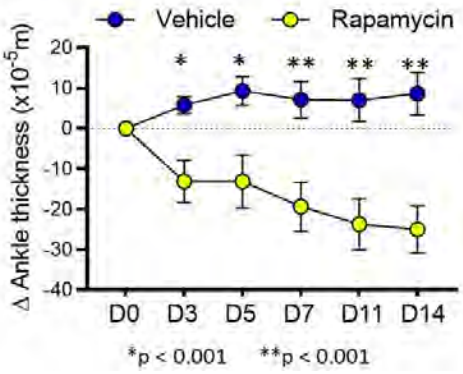


Figure 3. Rapamycin treatment ameliorates arthritis in IL1rn $^{-/-}$ mice



Results: IL1rn$^{-/-}$ mice spontaneously developed severe arthritis by 6–8 weeks of age accompanied by monocytosis in the peripheral blood (Figure 1). Bone marrow cells from IL1rn$^{-/-}$ mice produced a greater number of monocyte-derived macrophages in vitro with or without the addition of macrophage colony stimulating factor. Analysis of hematopoietic stem and progenitor cells by flow cytometry revealed expansion of myeloid progenitors and increased monocyte production in the bone marrow of IL1rn$^{-/-}$ mice. Transcriptomic analysis of IL1rn$^{-/-}$ myeloid progenitors by RNA-sequencing revealed enrichment of genes associated with IL-1 and mTORC1 signaling. Intracellular flow cytometry confirmed increased phosphorylation of the mTORC1 targets S6 and 4E-BP1 in monocytes from IL1rn$^{-/-}$ mice compared to WT controls. Daily treatment of IL1rn$^{-/-}$ mice with anakinra for two weeks reduced circulating monocytes and mTORC1

signaling to levels seen in WT (Figure 1). A similar reduction in monocyte count was observed in sJIA patients after anakinra treatment (Figure 2). Confirming the pathogenic role of mTORC1 activation, rapamycin treatment corrected the monocytosis and reduced the severity of arthritis in $IL1rn^{-/-}$ mice (Figure 3).

Conclusion: mTORC1 activation downstream of IL-1 signaling drives the development of monocytosis and arthritis in $IL1rn^{-/-}$ mice. Inhibition of mTORC1 may be a promising approach for the treatment of sJIA.

Disclosure: Z. Huang, None; **Y. Li**, None; **A. Wactor**, None; **P. Nigrovic**, Novartis, 2, 5, BMS, 2, 5, Pfizer, 2, 5, Sobi, 5, Miach Orthopedics, 5, Simcere, 5, XBiotech, 5, Quench Bio, 5, Siglion, 5, Cerecor, 5, UpToDate, 7, American Academy of Pediatrics, 7, CARRA, 9; **P. Lee**, None.

Abstract Number: 0174

Dense Genotyping of Immunologic Loci Identifies *CXCR4* as a Novel Susceptibility Locus for Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) is a severe, potentially lethal inflammatory condition. It accounts for a disproportionate share of morbidity and mortality among childhood arthritidies. Despite recognition of excessive innate immune activation, specific host or environmental factors that underlie sJIA have eluded detection. Genomic investigations are an important tool for identifying new disease associated genes and pathways, and recent genomic studies of sJIA have yielded important new insights. Here, we examine sJIA with the Immunochip, a single nucleotide polymorphism (SNP) array that generates exceptionally dense genotyping at 186 immunologic loci, many of which are putatively relevant to sJIA.

Methods: Immunochip genotype data were generated in 889 sJIA cases from the International Childhood Arthritis Genetics Consortium and the Juvenile Arthritis Consortium for Immunochip and 16,144 geographically-matched control subjects. All cases fulfilled the ILAR criteria for sJIA. Genotyping/genotype calling were performed according to the manufacturer's protocols. The dataset was subjected to stringent quality control operations (QC) to exclude poor quality samples and markers. The study population was systematically restricted to subjects of northern European ancestry using principal components analysis (PCA). The full dataset was expanded with 1000 Genomes Project (1KG)-based SNP imputation. Haplotypic analysis was performed for novel risk loci and association testing of markers and haplotypes was performed by logistic regression, corrected for sex and ancestry. The effect of sJIA-associated variables on gene expression was examined in paired whole genome (WGS) and RNA sequencing data from lymphoblastoid cell lines (LCL) of 373 European 1KG subjects.

Results: SNP genotyping, imputation and QC produced a panel of 841,043 SNPs in a collection 579 sJIA cases and 12,930 healthy subjects of northern European ancestry (λGC=1.000). Association testing identified a novel, highly-significant susceptibility locus on chromosome 2 that contained *CXCR4*, encoding C-X-C chemokine receptor type 4. The strongest risk factor for sJIA in the study was a 124kb 6-SNP haplotype (case frequency 0.21, control frequency 0.13, p=4.3E-10, OR=1.7 [1.5, 1.9]). Analysis of paired WGS and RNAseq data identified positive correlation between the sJIA risk haplotype and *CXCR4* expression in LCLs (p=4.0E-4). Examination of the risk haplotype in public databases revealed that it 1) intersects with a lymphocyte super-enhancer that regulates *CXCR4*; and 2) engages in 3 distinct chromatin loops with the promoter of *CXCR4* in LCLs.

Conclusion: This study has identified *CXCR4* as a novel risk locus in sJIA. CXCR4 is an immunologically important molecule that is involved immune cell development and migration, particularly that of B lymphocytes. The correlation of the sJIA risk haplotype with increased *CXCR4* expression in LCLs, its intersection with a lymphocyte-specific super-enhancer and its formation of chromatin loops with the *CXCR4* promoter in LCLs may indicate that this haplotype influences sJIA risk through B lymphocytes. Further studies are necessary to systematically evaluate this hypothesis.

Disclosure: E. Shuldiner, None; **E. Remmers**, None; **M. Marion**, Lupus Research Alliance, 2; **M. Sudman**, None; **C. Satorius**, None; **P. Woo**, None; **S. Prahalad**, None; **C. Langefeld**, Lupus Research Alliance, 2; **S. Thompson**, None; **W. Thomson**, None; **M. Ombrello**, None.

Abstract Number: 0175

Identifying Immuno-phenotypes in Juvenile Localized Scleroderma with RNA Sequencing

Christina Schutt[1], Emily Mirizio[2], Kaila Schollaert-Fitch[2], Claudia Salgado[3], Miguel Reyes-Mugica[3] and Kathryn Torok[2], [1]University of Pittsburgh Medical Center, Pittsburgh, PA, [2]University of Pittsburgh, Pittsburgh, PA, [3]University of Pittsburgh Medical Center, Pittsburgh

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Pediatric Rheumatology – Basic Science Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile localized scleroderma (jLS) is an autoimmune disease of the skin and underlying tissue characterized by an early inflammatory infiltrate followed by fibrosis and collagen deposition leading to atrophy. Uncontrolled jLS results in significant disFigurement and functional disability. Our goal was to determine the transcriptome within inflammatory and fibrotic LS tissue vs. healthy controls and identify potential molecular targets using RNA sequencing (RNAseq). Differentially expressed genes (DEGs) identified in jLS patients were compared to histopathological features to determine correlation and were used to cluster LS patients according to common expression pathways.

Methods: RNAseq was performed on paraffin-embedded skin (n=28 jLS, n=10 pediatric healthy) using the Illumina HTS and TrueSeq Access library preparation. Paired-end RNAseq data was aligned using STAR, corrected for batch effect and analyzed for DEGs using DESeq2. Genes were analyzed using DEG cutoffs of log fold change > ±2.0, adjusted p< 0.05, and a false discovery rate (FDR) cutoff of < 0.05 for Reactome and enrichment software (GSEA©). Standardized scoring was developed for inflammation and collagen deposition and was completed between 2 blinded pathologists. Spearman's correlation was used to determine significance between DEGs and histology scoring.

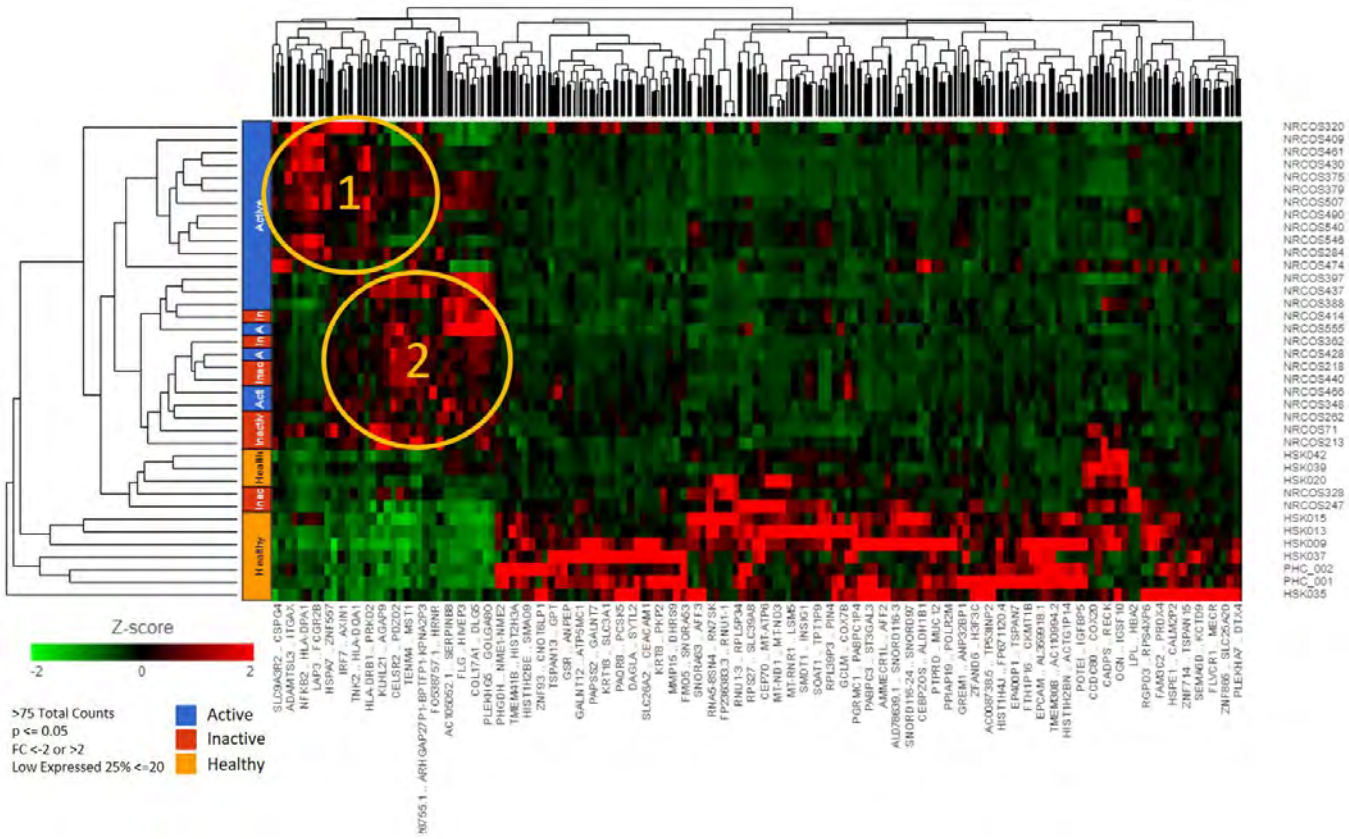

Figure 1. Hierarchical Clustering using complete linkage of Euclidean Distance

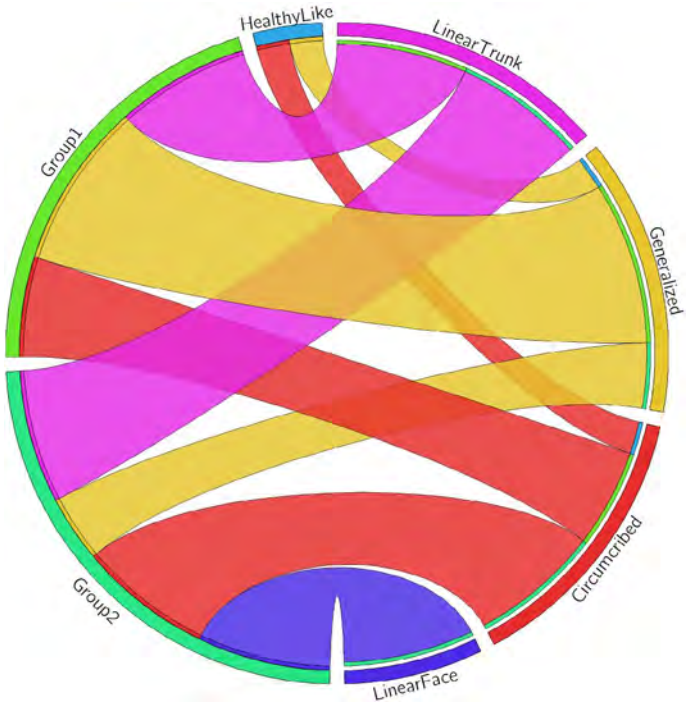

Figure 2. Circos plot comparing clinical LS subtype to immune-phenotype clustering.

Results: We found 589 significant DEGs between jLS vs. pediatric healthy controls with the above cutoffs. Hierarchical clustering using complete linkage of Euclidean distance demonstrated three distinct jLS groupings; Group 1, Group 2 and Healthy-Like (Figure 1). In Group 1, 61 DEGs were identified which associate with interferon gamma signaling, MHC class II antigen presentation, and TCR signaling ($p< 0.01$). Specifically, five are HLA class II genes, HLA-DQA1, HLA-DQB1, HLA-DRB5, HLA-DPA1, and HLA-DRB1 ($p< 0.01$, FC >2, FDR< 0.05). Degree of inflammatory cell infiltrates significantly correlated with HLA-DPB1, HLA-DQA2, HLA-DRA, and STAT1 ($rs > 0.5$, $p< 0.01$). Collagen thickness in upper reticular dermis had a positive correlation with HLA-DQA1 ($rs=0.46$, $p=0.03$). In Group 2, 76 DEGs were identified, which associate with pathways of FGFR1 amplification, collagen formation and keratinization ($p< 0.05$).

Conclusion: The identified groupings of jLS patients showed two distinct genetic signatures, one with upregulated inflammatory-related pathways, which corresponded to inflammatory infiltrate score, and a second group with upregulated fibrosis-related pathways. HLA Class II gene upregulation was observed within the inflammatory group, which has also been described for systemic sclerosis. Interestingly also the immune-phenotype groups did not directly correspond with the patients clinical phenotype. Further investigation into the relationship and functions of these genes in jLS tissue is underway.

Disclosure: C. Schutt, None; **E. Mirizio**, None; **K. Schollaert-Fitch**, None; **C. Salgado**, None; **M. Reyes-Mugica**, None; **K. Torok**, None.

Abstract Number: 0176

Characterization and Molecular Mechanism Underlying NEMO Deleted Exon 5 Autoinflammatory Syndrome (NDAS)

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Pediatric Rheumatology – Basic Science Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The NF-kB essential modulator (NEMO) is a scaffolding protein with a broad immune cell and tissue expression profile. Hypomorphic mutations in *IKBKG* encoding NEMO typically present with immune deficiency. However, we previously showed that the absence of the NEMO C-terminus zinc finger domain (NEMO-ΔCT), encoded by exon 10, leads to impaired negative regulation of the canonical IKK kinase and additional inflammatory

disease phenotypes. Other functional NEMO domains are likely important for the regulation of NF-κB activation and type I IFN induction.

Methods: Patients and healthy controls enrolled in an IRB-approved natural history protocol provided blood and skin samples that were used for genetic and functional analyses. These studies included WGS/WES, minigene cDNA analysis, primary cell line gene reconstitution and knockdown experiments, signal transduction by microscopy, Western blot (WB), and intracellular flow cytometry, transcriptome, cytokine release, co-immunoprecipitation and WB, and in vitro viral infection models.

Results: Here we describe the diagnosis, disease features and molecular mechanism underlying enhanced NF-κB and Interferon induction due to expression of the alternative NEMO isoform lacking the domain encoded by exon 5 (NEMO-Δex5). We demonstrate that the NEMO Deleted exon 5 Autoinflammatory Syndrome (NDAS) is distinct from the immunodeficiency syndrome resulting from loss-of-function *IKBKG* mutations clinically. Dermal fibroblasts from NDAS patients uniquely activate NF-κB in response to TNF, but not TLR3 or RLR stimulation, and type I IFN and antiviral responses are blunted in vitro. By contrast, T cells, monocytes and macrophages expressing NEMO-Δex5 express a strong Type I Interferon and NF-κB transcriptional signature that correlates highly with alternative isoform expression. We utilized these cell specific differences to dissect the roles of TNF and the atypical IKK kinases, TBK1 and IKKε, in altered NEMO-Δex5 signaling and antiviral cell function. NEMO-Δex5 expression in both immune cells and TNF-stimulated dermal fibroblasts specifically protected IKKε from stimulation-induced protein destabilization, promoting type I IFN induction and enhanced antiviral responses in vitro.

Conclusion: NEMO-NDAS represents a distinct disease phenotype with unique cellular gene expression and functional profiles. Ongoing work is directed at understanding the regulation and function of NEMO-Δex5 in host defense and in both monogenic and complex genetic rheumatic diseases.

Disclosure: A. Wessel, None; **Y. Lee**, None; **E. Lee**, None; **J. Xu**, None; **S. Kim**, None; **A. Hsu**, None; **J. Rudenko**, None; **C. Enos**, None; **S. Brooks**, None; **Z. Deng**, None; **B. Lin**, None; **D. Hupalo**, None; **A. Almeida de Jesus**, None; **D. Piotto**, None; **M. Terreri**, None; **V. Dimitriades**, None; **D. Clifton**, None; **S. Holland**, None; **R. Goldbach-Mansky**, None; **R. Siegel**, Novartis, 1, 3; **E. Hanson**, None.

Abstract Number: 0177

Association of Hydroxychloroquine Use with Development of Non-Alcoholic Fatty Liver Disease in Rheumatoid Arthritis

Nicholas Wiemer[1], Rebecca Schorr[2], Mary Chester Wasko[3] and Tarun Sharma[1], [1]Allegheny Health Network, Pittsburgh, PA, [2]Highmark, Pittsburgh, PA, [3]Allegheny Health Network, West Penn Hospital, Pittsburgh, PA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Non-alcoholic fatty liver disease (NAFLD), the most common form of liver disease, refers to a spectrum of conditions which includes non-alcoholic fatty liver (NAFL), non-alcoholic steatohepatitis (NASH), and fibrosis. Progression of NAFL to cirrhosis via inflammatory pathways has been associated with low levels of adiponectin. Hydroxychloroquine (HCQ) is concentrated in the liver, has been shown do increase adiponectin levels,

Table 1: Risk of NAFLD According to HCQ Use

Variable	HCQ Users (n=1285)	Non-HCQ Users (n=4332)	P-value
Age, yrs (± SD)	67 (±12)	69.35 (±12.4)	0.297
Female sex, n (%)	1044 (81.2%)	3234 (74.5%)	0.925
Caucasian, n (%)	1147 (89.3%)	3775 (87.1%)	0.572
Mean BMI, kg/m^2	29 (±7.5)	30.2 (±6.9)	0.282
Alcohol use (%)	496 (38.6%)	1600 (36.9%)	0.438
Duration of RA, mean, yrs (n=95)	6.37(±7.2)	5.02(±5.8)	0.397
Hypertension (n=95) (%)	12/20 (60%)	25/75 (33.33%)	0.0221
Dyslipidemia (n=95) (%)	12/20 (60%)	33/75 (44%)	0.162
Diabetes (n=95) (%)	6/20 (30%)	17/75 (22.67%%)	0.684
Metabolic Syndrome (n=95)	8/20 (40%)	20/75 (26.67%)	0.421
HCQ dose, mean, mg (n =20)	350 (±85.49)	n/a	--
HCQ duration, mean, yrs (n=20)	2.32 (±3.09)	n/a	--
Statin use (n=95) (%)	7/20 (35%)	7/75 (9.33%)	0.0032
MTX use (n=95) (%)	9/20 (45%)	16/75 (21.33%)	0.0743
MTX dose, mean, mg (n=95)	18.61 (±4.17)	15.78 (±4.58)	0.0579
MTX duration, mean, years (n=95)	2.33 (±1.51)	4 (±3.54)	0.657
Transaminitis (n=95) (%)	7/20 (35%)	24/75 (32%)	0.914
Incident NAFLD (%)	5/1285 (0.39%)	19/4332 (0.43%)	0.773
Unadjusted Odds Ratio	0.89 (95% CI: [0.33, 2.38], p=0.81)		
Age, Sex, and Race Adjusted OR	0.76 [0.22, 2.6], p=0.24		

NAFLD=non-alcoholic fatty liver disease, HCQ=hydroxychloroquine, BMI=body mass index, MTX=methotrexate, CI=confidence interval

Table 1. Risk of NAFLD According to HCQ Use

and, per one animal study, shown to improve hepatic steatosis. The role of HCQ in the prevention of NAFLD has not been explored.

Methods: A retrospective review of adult patients with RA (ICD 10 M05 and M06) seen at a tertiary academic rheumatology practice from 12/1/2014 to 5/30/2017 was constructed. Electronic health records (EHR) of patients with any history of liver disease were manually reviewed to confirm eligibility. The primary outcome was incident NAFLD during the observation period. RA diagnoses were confirmed using a previously validated algorithm with greater than 90% accuracy. The diagnosis of NAFLD, according to the American Association for the Study of Liver Disease (AASLD) criteria, was validated by reviewing right upper quadrant ultrasound, abdominal CT imaging, and/or liver biopsy results. History of prior NAFLD, alcohol abuse, alcoholic cirrhosis, infectious hepatitis, hemochromatosis, Wilson disease, alpha-1 antitrypsin deficiency, acetaminophen toxicity were exclusion criteria. Multivariate regression analysis was performed to determine the association between HCQ use and the development of incident NAFLD, after adjusting

for relevant confounders, including demographics (age, sex, body mass index (BMI)), medications (dose and duration of HCQ use, concomitant MTX, and statin use), comorbidities (diabetes, metabolic syndrome, dyslipidemia, hypertension, alcohol use), and laboratory values (AST, ALT).

Results: Our study included 5617 patients with RA, including 1285 HCQ users. 95 patients were found to have history of liver disease in our database (20 in HCQ users and 75 in non-users) and underwent EHR review to screen for incident NAFLD. During the observation period, 5 incident NAFLD events were found in the HCQ users (0.39%) and 19 in the non-users (0.43%). The unadjusted odds ratio (OR) for incident NAFLD was calculated at 0.89 (95% CI 0.33-2.38, p=0.81). When adjusted for age, sex, and race, the OR for incident NAFLD is 0.76 [0.22, 2.6], p= 0.24. Metabolic syndrome, diabetes, hypertension, and MTX use were more prevalent in the HCQ user group. Hypertension and statin use were significantly different between the HCQ group and non- HCQ group.

Conclusion: In this exploratory study, HCQ use was associated with a 24% decrease in incident NAFLD. The higher prevalence of metabolic syndrome and related risk factors in our HCQ user group is unexpected, given the favorable relationship that others and we have described previously. This is the first study to examine the association of HCQ with NAFLD. Given the observational design and small number of events, our findings warrant confirmation in larger studies.Table 1: Risk of NAFLD According to HCQ Use

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Disclosure: N. Wiemer, None; **R. Schorr**, None; **M. Wasko**, None; **T. Sharma**, None.

Abstract Number: 0178

Associations of Multimorbidity with DMARD Initiation and Achieving Target Disease Activity Thresholds in Active Rheumatoid Arthritis: A Cohort Study Using the Rheumatology Informatics System for Effectiveness (RISE) Registry

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Although a treat-to-target strategy is endorsed in rheumatoid arthritis (RA) treatment guidelines, its routine implementation in real-world settings, particularly in the context of multimorbidity, is not well understood. In this study, we examined whether multimorbidity is associated with DMARD initiation and the achievement of target disease activity thresholds in patients with RA using the largest Electronic Health Record-enabled rheumatology registry in the U.S.

Methods: We conducted a retrospective cohort study within the Rheumatology Informatics System for Effectiveness (RISE) registry. We selected patients >18 years of age, with ≥2 encounters for RA based on ICD-10 codes, and who had 2 consecutive visits in moderate or high disease activity (by Clinical Disease Activity Index [CDAI] or Routine Assessment of Patient Index Data 3 [RAPID3]) without treatment changes between visits. For inclusion in analyses assessing treatment response, we additionally required initiation of a new DMARD at or immediately following the

Table 1. Baseline Patient Characteristics by Study Cohort				
	Overall cohorts		Treatment initiation cohorts*	
	RAPID3 (n=15,626)	CDAI (n=5,733)	RAPID3 (n=1,558)	CDAI (n=834)
Demographics				
Age, years	63.6 (13.1)	62.6 (12.7)	59.3 (13.5)	58.9 (12.5)
Female sex, %	80.4	82.2	83.7	82.4
Race, %				
White	68.5	62.8	66.0	57.7
Black	11.3	7.8	11.6	8.9
Other	20.2	29.5	22.5	33.5
Multimorbidity				
# RxRisk categories	10.2 (4.3)	10.0 (4.4)	9.7 (4.3)	9.5 (4.5)
≥5 RxRisk categories, %	89.9	88.3	86.3	84.5
Baseline Medications				
cDMARDs, %	41.2	46.3	52.3	52.9
bDMARDs, %				
TNFi	28.1	29.4	33.1	31.9
Non-TNFi	19.4	22.3	18.9	21.9
tsDMARDs, %	4.6	7.2	5.4	7.2
Oral steroids, %	39.3	41.5	54.7	55.8
DMARDs Newly Initiated				
Any new DMARD, %	23.4	31.1	100	100
cDMARDs, %	7.5	9.4	35.2	31.5
bDMARDS, %				
TNFi	9.9	12.7	45.1	45.6
Non-TNFi	6.9	9.8	32.2	34.5
tsDMARDs, %	3.1	6.8	18.2	22.7
Values mean (SD) unless otherwise indicated * Patients initiating a new DMARD while in moderate or high disease activity with ≥1 visit in the following 365 days				

Table 1. Baseline Patient Characteristics by Study Cohort

Table 2. Association of Multimorbidity with Initiating a New Treatment in Active RA		
	Odds Ratio (95% CI)	P value
RAPID3 cohort (n=15,626)		
Multimorbidity categorical		
0-5 RxRisk categories	1 (referent)	-
6-8 RxRisk categories	0.88 (0.77, 0.99)	0.04
9-11 RxRisk categories	0.99 (0.87, 1.12)	0.85
≥12 RxRisk categories	0.93 (0.82, 1.05)	0.26
Multimorbidity continuous		
Per 1 unit of RxRisk	1.00 (0.99, 1.01)	0.39
CDAI cohort (n=5,733)		
Multimorbidity categorical		
0-5 RxRisk categories	1 (referent)	-
6-8 RxRisk categories	1.04 (0.86, 1.25)	0.69
9-11 RxRisk categories	1.02 (0.85, 1.24)	0.78
≥12 RxRisk categories	1.00 (0.83, 1.20)	0.99
Multimorbidity continuous		
Per 1 unit of RxRisk	1.00 (0.99, 1.02)	0.76
Models adjusted for age, sex, race, U.S. region, insurance status, seropositivity, number of visits, baseline medication use (oral steroids, cDMARDs, and bDMARDs). Continuous and categorical multimorbidity variables tested in separate models.		

Table 2. Association of Multimorbidity with Initiating a New Treatment in Active RA

2nd visit and ≥1 additional visit in the following 365 days. Demographics, seropositivity, disease activity, and medications were obtained from the RISE registry. Multimorbidity was measured using RxRisk, a medication-based index of chronic disease, and modeled both as a continuous variable and categorized into quartiles based on the number of RxRisk categories using all available prior medication data. We used multivariable logistic regression models to assess the independent associations of multimorbidity with 1) the odds of initiating a new DMARD in active RA; and

Table 3. Associations of Multimorbidity with Achieving Treatment Target Following New Treatment Initiation in Active RA		
	Odds Ratio (95% CI)	P value
RAPID3 cohort (n=1,558)		
Multimorbidity categorical		
0-5 RxRisk categories	1 (referent)	-
6-8 RxRisk categories	0.54 (0.36, 0.82)	0.004
9-11 RxRisk categories	0.69 (0.46, 1.01)	0.06
≥12 RxRisk categories	0.48 (0.31, 0.73)	<0.001
Multimorbidity continuous		
Per 1 unit of RxRisk	0.94 (0.91, 0.98)	0.001
CDAI cohort (n=834)		
Multimorbidity categorical		
0-5 RxRisk categories	1 (referent)	-
6-8 RxRisk categories	0.95 (0.58, 1.55)	0.83
9-11 RxRisk categories	0.83 (0.49, 1.39)	0.47
≥12 RxRisk categories	0.55 (0.32, 0.94)	0.03
Multimorbidity continuous		
Per 1 unit of RxRisk	0.94 (0.90, 0.99)	0.01
Models adjusted for age, sex, race, U.S. region, insurance status, seropositivity, number of visits, baseline oral steroid use, # prior cDMARDs, #prior bDMARDs, # prior tsDMARDs, baseline disease activity category, treatment being initiated (cDMARD, TNFi, non-TNFi bDMARD, and tsDMARD). Continuous and categorical multimorbidity variables tested in separate models.		

Table 3. Associations of Multimorbidity with Achieving Treatment Target Following New Treatment Initiation in Active RA

2) among those initiating a new DMARD, the odds of achieving low disease activity or remission. Separate models were constructed for CDAI and RAPID3 cohorts.

Results: We identified 15,626 (RAPID3) and 5,733 (CDAI) patients with active RA, of which 1,558 (RAPID3) and 834 (CDAI) initiated a new DMARD and had ≥1 follow-up visit within 365 days. Patients were middle aged, female and Caucasian predominant, and frequently received medications from ≥5 RxRisk categories (**Table 1**). Multimorbidity was not independently associated with the odds of initiating a new DMARD in the setting of active RA in either the RAPID3 or CDAI cohorts (**Table 2)**. However, among RA patients with active disease initiating a new DMARD, greater multimorbidity burden was associated with a lower likelihood of achieving low disease activity or remission (**Table 3**). Patients with the highest burden of multimorbidity (≥12 RxRisk categories) had approximately half the odds of achieving target RA disease activity (OR=0.48 RAPID3; OR=0.55 CDAI) compared to those with ≤5 RxRisk categories.

Conclusion: After initiating a new therapy for active RA, patients with greater multimorbidity were less likely to achieve target RA disease activity. These findings from a large, real-world registry illustrate the potential impact of multimorbidity on treatment response and indicate that broader management efforts targeted at multimorbidity may be needed to optimize RA disease control in these patients. Comparative effectiveness studies in multimorbid RA patients are needed since the risks and benefits of therapies may differ in this population.

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Abstract Number: 0179

Identification of Multimorbidity Patterns in Rheumatoid Arthritis Through Machine Learning

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic conditions often complicate the disease course of rheumatoid arthritis (RA) and predispose to poor long-term outcomes. The interrelationship of individual chronic conditions and their contribution to

Table 1. Multimorbidity patterns identified through factor analysis within MarketScan

Factor	Eigenvalue	Variance (cumulative)	Representative conditions* (loading)
Females			
RA (n=86,722)			
Cardiopulmonary	7.0	0.47 (0.47)	Heart failure (0.7), arrhythmia (0.6), COPD (0.6)
Mental Health & Pain	2.6	0.17 (0.64)	PTSD/depression (0.7), anxiety (0.7), fibromyalgia (0.6)
Atherosclerosis & Metabolic	1.0	0.07 (0.71)	Hypertension (0.6), hyperlipidemia (0.6), diabetes (0.6)
Non-RA (n=86,722)			
Cardiometabolic	6.8	0.46 (0.46)	Heart failure (0.8), coronary artery disease (0.6), Pulmonary circulation disorder (0.6)
Mental Health & Pain	2.8	0.19 (0.65)	PTSD/Depression (0.7), anxiety (0.7), fibromyalgia (0.6)
Vascular	1.0	0.07 (0.72)	Dementia/Parkinson's (0.6), cerebrovascular disease (0.5), peripheral vascular disease (0.4)
Males			
RA (n=26,703)			
Cardiometabolic	6.5	0.44 (0.44)	Renal disease (0.6), hypertension (0.6), coronary artery disease (0.6)
Mental Health & Pain	2.7	0.18 (0.62)	Anxiety (0.6), PTSD/depression (0.6), headaches (0.5)
Cardiopulmonary	1.1	0.07 (0.69)	COPD (0.6), arrhythmia (0.6), heart failure (0.5)
Mental Health & Substance Abuse	1.1	0.07 (0.76)	Alcohol/drug abuse (0.6), liver disease (0.5), PTSD/depression (0.4)
Non-RA (n=26,703)			
Cardiovascular	7.1	0.50 (0.50)	Heart failure (0.8), coronary artery disease (0.7), arrhythmia (0.7)
Mental Health & Pain	1.9	0.14 (0.64)	Anxiety (0.8), PTSD/depression (0.8), headaches (0.5)
Metabolic	1.0	0.07 (0.71)	Hypertension (0.6), hyperlipidemia (0.6), obesity (0.5)
*For brevity, the three conditions with highest factor loadings are shown			

Table 1. Multimorbidity patterns identified through factor analysis within MarketScan

Table 2. Multimorbidity patterns identified through factor analysis within the Veterans Health Administration.			
Factor	Eigenvalue	Variance (cumulative)	Representative conditions* (loading)
Females			
RA (n=6,774)			
Mental Health & Pain	8.6	0.52 (0.52)	Fibromyalgia (0.6), headache (0.6), back disorder (0.6)
Cardiovascular	2.8	0.17 (0.69)	Heart failure (0.8), valvular heart disease (0.6), arrhythmia (0.6)
Metabolic	1.2	0.07 (0.76)	Diabetes (0.7), hypertension (0.6), hyperlipidemia (0.6)
Non-RA (n=6,774)			
Mental Health & Pain	10.9	0.59 (0.59)	Fibromyalgia (0.7), back disorder (0.7), neuropathy (0.6)
Cardiovascular	2.7	0.15 (0.74)	Heart failure (0.7), headache (0.7), coronary artery/peripheral vascular disease (0.6)
Metabolic	1.2	0.06 (0.80)	Diabetes (0.7), hypertension (0.6), obesity (0.5)
Mental Health & Substance Abuse	1.1	0.06 (0.86)	Alcohol/drug abuse (0.7), PTSD/depression (0.7), bipolar (0.7)
Males			
RA (n=53,616)			
Mental Health & Substance Abuse	8.9	0.48 (0.48)	PTSD/depression (0.7), alcohol/drug abuse (0.7), anxiety (0.7)
Cardiovascular	2.9	0.15 (0.63)	Heart failure (0.7), arrhythmia (0.7), valvular heart disease (0.6)
Chronic Pain	1.3	0.07 (0.70)	Fibromyalgia (0.6), back pain (0.6), headache (0.5)
Metabolic	1.2	0.07 (0.77)	Diabetes (0.7), obesity (0.6), hyperlipidemia (0.5)
Non-RA (n=53,616)			
Chronic Pain	10.7	0.51 (0.51)	Fibromyalgia (0.7), back pain (0.7), headache (0.6)
Cardiovascular	2.9	0.14 (0.65)	Heart failure (0.7), arrythmia (0.7), coronary artery disease (0.7)
Metabolic	1.6	0.07 (0.72)	Diabetes (0.8), hypertension (0.5), obesity (0.5)
Mental Health & Substance Abuse	1.2	0.06 (0.78)	Alcohol/drug abuse (0.7), liver disease (0.7), bipolar disorder (0.5)
Cancer	1.0	0.05 (0.83)	Cancer (0.6), anemia (0.5), diverticular disease (0.4)
*For brevity, the three conditions with highest factor loadings are shown			

Table 2. Multimorbidity patterns identified through factor analysis within the Veterans Health Administration

the overall burden of multimorbidity afflicting patients with RA is not well understood. We aimed to identify patterns of multimorbidity in RA using unsupervised machine learning.

Methods: We constructed RA and age-, sex-, and year-matched (1:1) non-RA cohorts within a large commercial insurance database (MarketScan, 2006-2015) and the Veterans Health Administration (VHA, 2001-2015) using validated administrative algorithms for RA. Chronic conditions (n=44, selected based on relevance to multimorbidity in the general population and RA) were identified using diagnosis codes from outpatient and inpatient encounters. Unsupervised machine learning was conducted separately in both databases and stratified by RA status and sex, to identify patterns of multimorbidity. Tetrachoric correlation coefficients were calculated between pairs of chronic conditions. Factor analysis was performed on this correlation matrix using the principal factor method. Factors with Eigenvalues $^{3}1$ were retained and an orthogonal rotation was executed on the extracted factors. Conditions with a factor loading >0.3 were considered relevant to the extracted factor, and patients were considered to have the multi-

Table 3. Prevalence of multimorbidity patterns in RA and non-RA patients.			
Database / Sex	N (%) with multimorbidity pattern		OR (95% CI)*
	RA	Non-RA	
MarketScan (n=226,850)			
Females (n=173,444)			
Cardiopulmonary	7,317 (8.4)	3,387 (3.9)	2.27 (2.17, 2.36)
Mental Health & Pain	22,148 (25.5)	10,245 (11.8)	2.56 (2.50, 2.63)
Atherosclerosis & Metabolic	21,526 (24.8)	13,427 (15.5)	1.80 (1.76, 1.85)
Males (n=53,406)			
Cardiometabolic	7,832 (29.3)	5,629 (21.1)	1.55 (1.49, 1.62)
Mental Health & Pain	6,085 (22.8)	2,424 (9.1)	2.96 (2.81, 3.11)
Cardiopulmonary	3,105 11.6)	1,624 (6.1)	2.03 (1.91, 2.16)
Mental Health & Substance Abuse	361 (1.4)	193 (0.7)	1.88 (1.58, 2.24)
Veteran's Health Administration (n=120,780)			
Females (n=13,548)			
Mental Health & Pain	3,438 (50.8)	2,191 (32.3)	2.16 (2.01, 2.31)
Cardiovascular	336 (5.0)	201 (3.0)	1.71 (1.43, 2.04)
Metabolic	2,160 (31.9)	1,454 (21.5)	1.71 (1.58, 1.85)
Males (n=107,232)			
Mental Health & Substance Abuse	6,522 (12.2)	5,683 (10.6)	1.17 (1.12, 1.21)
Cardiovascular	3,727 (7.0)	3,047 (5.7)	1.24 (1.18, 1.30)
Chronic Pain	14,036 (26.2)	7,829 (14.6)	2.07 (2.01, 2.14)
Metabolic	24,629 (45.9)	19,544 (36.5)	1.48 (1.44, 1.52)
Patterns are those derived in RA patients; patterns considered present if patients had at least 2 conditions with loading values >0.3. *Conditional odds ratio for multimorbidity pattern among RA vs non-RA, matched on age, sex, and calendar year			

Table 3. Prevalence of multimorbidity patterns in RA and non-RA patients

morbidity pattern specified by that factor if they had at least 2 conditions with factor loadings >0.3 for that factor. The prevalence of the derived multimorbidity patterns was compared between RA and non-RA patients using conditional logistic regression.

Results: We studied 226,850 patients in MarketScan (76% female, mean age 53 [female] and 58 [male] years) and 120,780 patients in the VHA (89% male, mean age 53 [female] and 64 [male] years). In both MarketScan (**Table 1**) and the VHA (**Table 2**), cardiovascular, metabolic, cardiopulmonary, mental health, and pain disorders were the primary patterns of multimorbidity identified in RA and non-RA populations. Similar multimorbidity patterns were also derived separately in men and women. The frequency of each multimorbidity pattern was significantly higher in RA (odds ratios ranging from 1.17 to 2.96), with cardiopulmonary, mental health, and pain disorder related multimorbidity patterns most closely associated with RA (**Table 3**).

Conclusion: Using two independent, large, real-world datasets and unsupervised machine learning, we identified cardiometabolic, cardiopulmonary, and mental health/pain disorders as the predominant patterns of multimorbidity in RA. Patterns of multimorbidity are similar between RA and non-RA populations, suggesting the interrelationships of chronic conditions is similar in RA as in the general population. However, because the prevalence of these overlapping disease processes is significantly higher in RA, it is imperative for clinicians to recognize and address these patterns of multimorbidity to achieve optimal long-term outcomes for patients with RA.

Disclosure: B. England, None; **Y. Yang**, None; **P. Roul**, None; **C. Haas**, None; **L. Najjar**, None; **H. Sayles**, None; **F. Yu**, None; **B. Sauer**, None; **J. Baker**, None; **K. Michaud**, Rheumatology Research Foundation, 2; **F. Xie**, None; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **T. Mikuls**, Horizon Therapeutics, 2.

Abstract Number: 0180

Clinicopathological Characteristics of Lymphoproliferative Disorders in 232 Patients with Rheumatoid Arthritis in Japan

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Lymphoproliferative disorders (LPDs) in patients with rheumatoid arthritis (RA) are one of potentially life-threatening complications. However, the diagnosis of LPDs is complicated by the diversity in clinical, laboratory, and pathological manifestations. As the data on LPDs in RA patients are limited to small-scale studies, we aimed to clarify their clinicopathological characteristics in a large multicenter study.

Methods: We retrospectively reviewed the clinical, laboratory, and pathological data of adult patients with RA who were newly diagnosed as having LPDs between January 2000 and March 2017 in eight tertiary hospitals in Japan. In addition to patients with biopsy-proven LPDs, we included patients clinically diagnosed as having LPD (clinical LPD) without biopsy because of prompt regression of clinical manifestations after withdrawal of immunosuppressive therapy.

Results: Of the 232 patients with LPDs, the median age was 67 years (IQR 60–73 years), and 77.1% were female. At the time of LPD diagnosis, 94.4% of the patients received methotrexate. The development of LPDs was observed from early to long-standing RA, irrespective of disease duration (Table 1). Approximately 60% of patients were in remission or low disease activity status based on the DAS28-CRP with three variables. B symptoms, lymphadenopathy, and extranodal involvement were present in 30.6%, 77.3%, and 50.7% of the patients, respectively (Table 2). Of the 230 patients with available data, 55 (23.9%), 54 (23.5%), 47 (20.4%), and 74 (32.2%) were in the Ann Arbor stages I, II, III, and IV, respectively. Of the 116 patients with extranodal involvement, the most frequently involved sites were the lungs (36 [30.2%]), oropharyngeal mucosa (19 [16.4%]), bone marrow (14 [12.1%]), skin (13 [11.2%]), and gastrointestinal tract (12 [10.3%]). Lymphocytopenia (≤1,000/mm^3) was present in 44.7% of the patients, elevated lactate dehydrogenase (≥230 U/L) in 53.4%, elevated C-reactive protein (≥0.30 mg/dL) in 75.2%, and elevated soluble interleukin-2 receptor (≥500 U/mL) in 82.9%. Biopsy was performed in 195 patients (84.1%). The most common LPD pathological subtype was diffuse large B-cell lymphoma (79 [40.5%]), followed by classic Hodgkin lymphoma (21 [10.8%]), Epstein-Barr virus-positive mucocutaneous ulcer (EBVMCU) (15 [7.7%]), reactive lymphoid hyperplasia (12 [6.2%]), unclassifiable B-cell lymphoma (11 [5.6%]), and follicular lymphoma (10 [5.1%]). The clinical and laboratory characteristics were diverse across the pathological subtypes (Table 3).

Variables	Patients (n=232)
Age	
Median (IQR), yr	67 (60–73)
Range, yr	26–89
Distribution, no./total no. (%)	
20–49 yr	18/232 (7.8)
50–64 yr	77/232 (33.2)
65–79 yr	122/232 (52.6)
≥80 yr	15/232 (6.5)
Female sex, no./total no. (%)	179/232 (77.1)
Duration of RA	
Median (IQR), yr	12.0 (6.0–20.3)
Range, yr	0.1–51.5
Distribution, no./total no. (%)	
0–5.0 yr	49/230 (21.3)
5.1–10.0 yr	48/230 (20.9)
10.1–20.0 yr	74/230 (32.2)
≥20.0 yr	59/230 (25.7)
Rheumatoid factor positivity, no./total no. (%)	174/220 (79.1)
Anti-citrullinated protein antibody positivity, no./total no. (%)	113/137 (82.5)
Median tender joint count (IQR)	0 (0–2)
Median swollen joint count (IQR)	1 (0–3)
Median DAS28-CRP(3) (IQR)	2.9 (2.1–3.9)
Disease activity based on DAS28-CRP(3), no./total no. (%)	
Remission (<2.6)	74/187 (39.6)
Low disease activity (≧2.6 to <3.2)	43/187 (23.0)
Moderate disease activity (≧3.2 to ≦5.1)	57/187 (30.5)
High disease activity (>5.1)	13/187 (7.0)
Current methotrexate use, no./total no. (%)	219/232 (94.4)
Duration of methotrexate use in current users	
Median (IQR), yr	6.5 (3.0–10.1)
Range, yr	0.3–23.0
Current weekly methotrexate dose	
Median (IQR), mg	8.0 (7.6–12.0)
Range, mg	4.0–17.5
Cumulative methotrexate dose	
Median (IQR), mg	2430 (1100–4080)
Range, mg	84–11680
Current oral glucocorticoid use, no./total no. (%)	91/228 (39.9)
Median daily prednisolone dose (IQR), mg	4.5 (2.5–5.0)
Current tacrolimus use, no./total no. (%)	33/230 (13.0)
Current biological DMARD use, no./total no. (%)	55/228 (24.1)

Clinical manifestations of LPDs and laboratory findings in patients with RA

Variables	Patients (n=232)
Clinical manifestations	
B symptoms, no./total no. (%)	71/231 (30.6)
Fever	58/227 (25.6)
Night sweat	17/224 (7.6)
Weight loss	18/221 (8.1)
Involved site, no./total no. (%)	
Nodal alone	113/229 (49.3)
Extranodal alone	52/229 (22.7)
Nodal and extranodal	64/229 (27.9)
Laboratory findings	
White blood cell count	
Median (IQR), /mm^3	6350 (4900–8200)
Distribution, no./total no. (%)	
<4,000/mm^3	23/222 (10.4)
>10,000/mm^3	30/222 (13.5)
Lymphocyte count	
Median (IQR), /mm^3	1080 (650–1510)
Distribution, no./total no. (%)	
<500/mm^3	37/217 (17.1)
500–1,000/mm^3	60/217 (27.6)
1,001–1,500/mm^3	64/217 (29.5)
>1,500/mm^3	56/217 (25.8)
Lactate dehydrogenase	
Median (IQR), U/L	236 (194–316)
Distribution, no./total no. (%)	
<230 U/L	104/223 (45.2)
230–500 U/L	100/223 (44.8)
>500 U/L	19/223 (8.5)
C-reactive protein	
Median (IQR), mg/dL	1.39 (0.30–3.76)
Distribution, no./total no. (%)	
<0.30 mg/dL	56/226 (24.8)
0.30–2.00 mg/dL	75/226 (33.2)
2.01–5.00 mg/dL	50/226 (22.1)
>5.00 mg/dL	45/226 (19.9)
Soluble interleukin-2 receptor	
Median (IQR), U/mL	980 (650–2000)
Distribution, no./total no. (%)	
<500 U/mL	30/175 (17.1)
500–1,000 U/mL	60/175 (34.3)
1,001–2,000 U/mL	42/175 (24.0)
2,001–5,000 U/mL	25/175 (14.3)
>5,000 U/mL	18/175 (10.3)

Demographic and clinical characteristics of RA patients with LPDs

Variables	All (n=232)	DLBCL (n=79)	CHL (n=21)	EBVMCU (n=15)	RLH (n=12)	FL (n=10)	MZL* (n=9)	PTCL and AITL (n=6)	HLL (n=5)	Clinical LPD (n=37)
Clinical Characteristics										
Age (IQR), yr	67 (60–73)	68 (60–73)	63 (59–69)	72 (67–74)	61 (53–69)	63 (56–69)	66 (55–80)	67 (60–70)	64 (58–75)	66 (57–75)
Duration since RA diagnosis (IQR), yr	12.0 (6.0–20.3)	12.5 (6.5–21.8)	14.3 (10.1–21.6)	11.2 (6.5–23.0)	6.2 (1.9–25.0)	12.1 (6.7–18.5)	6.1 (2.8–18.7)	10.1 (2.4–11.9)	7.3 (2.1–21.4)	10.2 (3.9–17.7)
Duration of methotrexate use (IQR), yr	6.3 (2.9–10.2)	6.3 (3.0–10.2)	8.1 (6.5–11.4)	8.2 (3.7–10.3)	1.6 (0.8–7.5)	8.2 (4.9–12.2)	5.9 (1.7–9.1)	4.9 (2.4–8.4)	7.3 (1.7–10.1)	4.9 (2.4–10.3)
DAS28-CRP (3) (IQR)	2.9 (2.1–3.8)	3.0 (2.0–3.8)	3.8 (2.2–4.4)	2.4 (2.1–3.0)	3.7 (2.8–4.6)	2.3 (1.4–3.7)	3.1 (1.7–4.7)	3.0 (2.1–4.1)	2.8 (1.6–6.3)	2.8 (1.9–3.3)
B symptoms, no./total no. (%)	73/232 (31)	21/79 (27)	10/21 (48)	1/15 (7)	3/12 (25)	2/10 (20)	1/9 (11)	3/6 (50)	3/5 (60)	9/37 (24)
Extranodal involvement, no./total no. (%)	116/229 (51)	47/77 (61)	9/21 (43)	15/15 (100)	1/12 (8)	6/10 (60)	7/9 (78)	2/6 (33)	2/5 (40)	10/37 (27)
Laboratory findings										
White blood cell count (IQR), / mm³	6350 (4900–8200)	6250 (4830–8570)	9050 (5800–11600)	6200 (4800–7000)	6250 (5380–8130)	6800 (5150–9450)	6700 (5130–8050)	6960 (4700–7830)	5300 (3500–9360)	5900 (4460–6880)
Lymphocyte count (IQR), / mm³	1080 (650–1510)	1010 (660–1360)	1130 (500–1840)	620 (440–1050)	1190 (1020–1330)	1530 (850–2350)	1590 (570–2190)	1000 (550–1170)	990 (460–1740)	1130 (590–1470)
Lactate dehydrogenase (IQR), U/L	236 (194–316)	272 (207–397)	249 (196–293)	231 (198–285)	192 (182–310)	196 (186–216)	196 (174–216)	228 (188–320)	235 (201–394)	228 (172–272)
C-reactive protein level (IQR), mg/dL	1.39 (0.30–3.76)	1.24 (0.43–3.31)	2.60 (1.05–10.3)	0.90 (0.35–2.07)	2.79 (1.13–3.96)	0.90 (0.08–3.04)	0.57 (0.24–2.57)	4.29 (1.13–11.3)	2.03 (0.37–10.5)	0.69 (0.11–3.15)
Soluble IL-2 receptor (IQR), U/mL	980 (650–2000)	1140 (730–2300)	2240 (980–4690)	770 (520–1870)	870 (590–1510)	1910 (386–4720)	660 (560–990)	1550 (1130–5850)	2640 (NA)	820 (340–1260)
Pathological characteristics										
EBER positivity — no./total no. (%)	74/136 (54)	19/50 (38)	12/17 (71)	15/15 (100)	6/10 (60)	8/10 (80)	1/4 (25)	1/5 (20)	5/5 (100)	NA

Unclassifiable B-cell lymphoma, lymphomatoid granulomatosis, composite lymphoma, polymorphic LPD, extranodal natural killer/T-cell lymphoma, lymphoplasmacytic lymphoma, and other LPDs are excluded from this table because of the small number of patients.

*MZL includes seven patients with extranodal MZL of mucosa-associated lymphoid tissue (MALT lymphoma) and two patients of nodal MZL.

Abbreviation: CHL, classic Hodgkin lymphoma; DLBCL, diffuse large B-cell lymphoma; EBER, Epstein-Barr Virus-encoded small RNA; EBVMCU, Epstein-Barr virus -positive mucocutaneous ulcer; FL, follicular lymphoma; HLL, Hodgkin-like lesion; LPD, lymphoproliferative disorder; MZL, marginal zone lymphoma; NA, not applicable; PTCL, peripheral T-cell lymphoma; RLH, reactive lymphoid hyperplasia.

Clinical characteristics, laboratory findings, and EBV-encoded small RNA (EBER) positivity in each pathological subtype of LPDs in patients with RA

Conclusion: LPDs occurred mainly in patients aged 50 years or older who were receiving methotrexate. Although the clinical manifestations of LPDs vary depending on the pathological subtypes, lymphadenopathy, extranodal mass, and mucocutaneous ulcer should be recognized as possible early signs of LPDs in combination with laboratory abnormalities in patients with RA.

Disclosure: H. Takada, None; **Y. Kaneko**, AbbVie, 1, Astellas, 1, Ayumi, 1, Bristol–Myers Squibb, 1, Chugai, 1, Eisai, 1, Eli Lilly, 1, Hisamitsu, 1, Jansen, 1, Kissei, 1, Kirin, 1, Pfizer, 1, Sanofi, 1, Takeda, 1, Tanabe-Mitsubishi, 1, UCB, 1, Novartis, 1; **K. Nakano**, Mitsubishi-Tanabe, 1, Eisai, 1, Eli Lilly, 1; **M. Tanaka**, UCB Japan Co., Ltd., 1, 2, AbbVie GK, 1, Asahi Kasei Pharma Corp., 1, 2, Astellas Pharma Inc., 1, Ayumi Pharmaceutical Corp., 1, 2, Bristol-Myers Squibb, 1, Chugai Pharmaceutical Co., Ltd., 1, 2, Eisai Co., Ltd., 1, Eli Lilly Japan K.K., 1, Pfizer Inc., 1, Janssen Pharmaceutical K.K., 1, Mitsubishi Tanabe Pharma Corp., 1, 2, Novartis Pharma K.K., 1, Taisho Pharma Co., Ltd., 1; **T. Fujii**, None; **K. Saito**, Eli Lilly Japan K.K, 1; **N. Sugimoto**, None; **S. Sasaki**, None; **S. Saito**, Chugai Pharmaceutical Co. Ltd., 1, Eisai Co.,Ltd., 1, Pfizer Japan Inc., 1, Asahikasei Pharma Corp., 1, Bristol–Myers Squibb, 1, Mitsubishi Tanabe Pharma Co., 1; **R. Saito**, None; **N. Kuramoto**, Eisai Co.,Ltd., 1; **Y. Suzuki**, Chugai Pharmaceutical Co. Ltd., 1, Teijin Pharma Ltd., 1, Asahi Kasei Pharma Co., 1, Eisai Co. Ltd., 1, Ono Pharmaceutical Co., 1, Mitsubishi Tanabe Pharma Co. Ltd., 1, Maruho Co. Ltd., 1, Glaxo Smith Klein K.K., 1, Pfizer Japan Inc., 1; **M. Harigai**, AbbVie Japan GK, 1, 2, Asahi Kasei Corp., 1, Astellas Pharma Inc., 1, Ayumi Pharmaceutical Co. Ltd., 1, 2, Bristol Myers Squibb Co., Ltd, 1, 2, 3, Chugai Pharmaceutical Co. Ltd., 1, 2, Daiichi-Sankyo, Inc., 1, Eisai Pharmaceutical, 1, 2, Nippon Kayaku Co. Ltd., 1, Mitsubishi Tanabe Pharma Co., 1, Taisho Pharmaceutical Co. Ltd., 1, Takeda Pharmaceutical Co. Ltd., 1, 2, Eli Lilly Japan K.K, 1, Pfizer Japan Inc, 1, AbbVie, 1.

Abstract Number: 0181

Methotrexate Use Does Not Increase the Prevalence of Hepatic Steatosis: A Real-World Retrospective Nested Case-Control Study

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: We aimed to determine whether methotrexate (MTX) treatment in patients with rheumatoid arthritis (RA) leads to the development of nonalcoholic fatty liver (NAFL).

Methods: Data were derived from records of all patients with RA who underwent abdominal ultrasonography at Jeonbuk National University Hospital. Patients with ultrasound-proven NAFL were identified, and those without NAFL were matched by age and sex using the propensity score matching method at 1:3 ratio. We also analyzed the Health Insurance Review and Assessment Service-National Patient Samples, a nationwide cohort database, to determine the association between MTX use and NAFL in a large number of patients (n = 24,653).

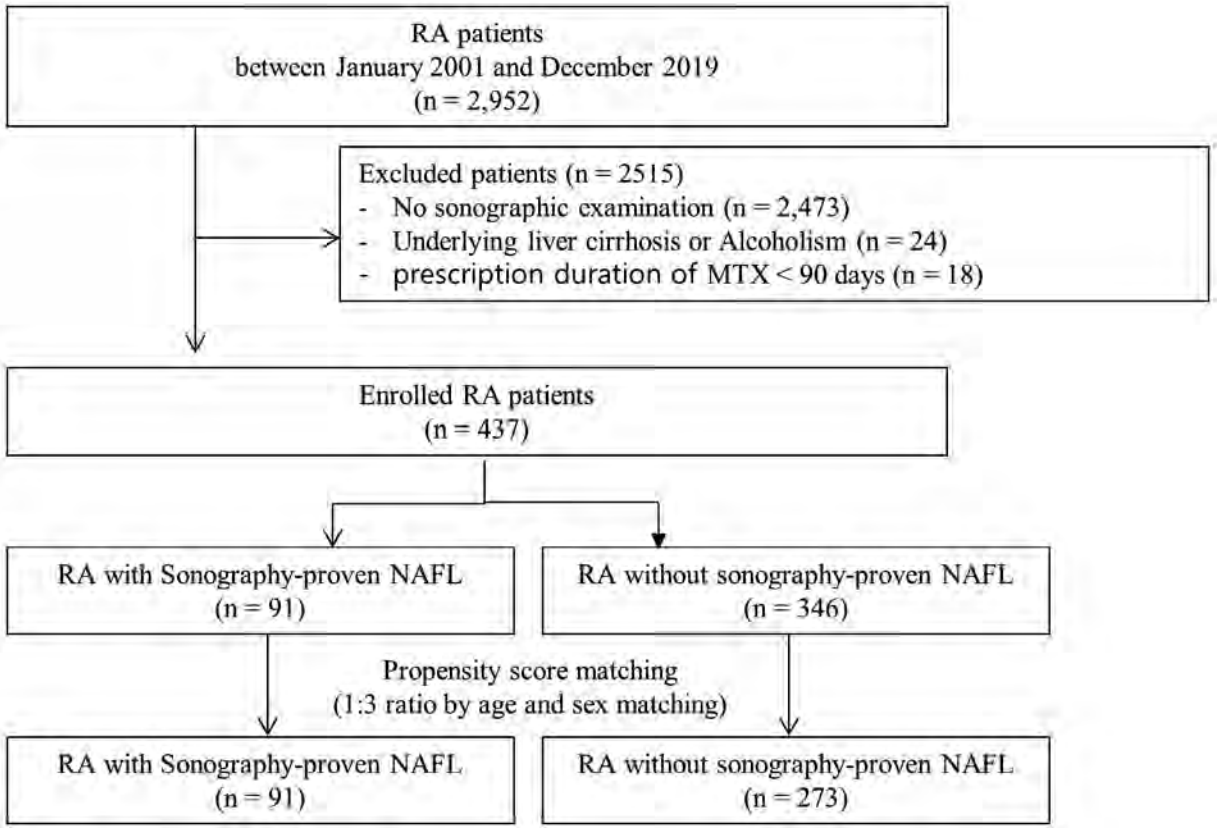

Figure 1. Flow chart of the study design MTX, Methotrexate; NAFL, Non-alcoholic fatty liver; RA, Rheumatoid arthritis

Characteristics	Univariate analysis			Multivariate analysis		
	OR	95% C.I.	*p* value	OR	95% C.I.	*p* value
Age, yrs	0.99	0.97-1.01	0.321			
Female, n (%)	0.71	0.43-1.16	0.174			
Hypertension n, (%)	1.00	0.62-1.61	1.000			
Diabetes, n (%)	1.74	1.01-3.00	0.047	2.03	0.66-6.15	0.213
Dyslipidemia, n (%)	1.81	1.12-2.91	0.015	0.86	0.26-2.79	0.803
BMI, kg/m^2	1.34	1.19-1.50	< 0.001	1.22	1.05-1.41	0.009
HbA1c > 6.5%	1.26	0.45-1.49	0.661			
HDL < 40 mg/dL	2.57	0.65-10.15	0.179			
LDL > 160 mg/dL	2.62	0.66-10.41	0.171			
Total Cholesterol > 200mg/dL	1.91	0.995-3.66	0.052			
Triglyceride cholesterol > 200 mg/dL	6.60	2.52-17.27	< 0.001	4.88	1.13-20.93	0.033
Cumulative dose, $\log_{10}$ (mg)						
MTX	1.33	0.64-2.74	0.443			
Tacrolimus	3.39	0.56-20.66	0.185			
Leflunomide	1.07	0.61-1.87	0.807			
Sulfasalazine	1.71	0.70-4.17	0.237			
Hydroxychloroquine	1.07	0.71-1.61	0.744			
Prednisone equivalent	1.79	1.06-3.02	0.029	1.16	0.86-1.57	0.310

Table 1. Risk factors influencing the development of NAFL among RA patients (n=368) BMI, Body mass index; HbA1c, hemoglobin A1c; HDL, High-density lipoprotein cholesterol; LDL, Low-density lipoprotein cholesterol; MTX, Methotrexate; NAFL, Nonalcoholic fatty liver 95% C.I., 95% Confidence Interval

Results: In the hospital cohort, 92 patients with NAFL did not show significant differences in the cumulative MTX dose when compared with the no-NAFL group (n = 276) (1,908.5 ± 1,757.5 vs. 1,948.6 ± 2,118.8 mg, $p = 0.911$). The prevalence of NAFL was not significantly different across strata of cumulative MTX dose. Multiple logistic analyses identified hypertriglyceridemia (OR, 4.88 [95% CI, 1.13–20.93]) and higher body mass index (OR, 1.22 [95% CI, 1.05–1.41]) as being associated with an increased risk of NAFL. In the nationwide cohort, the MTX exposure rate between the NAFL and no-NAFL groups was not significantly different.

Conclusion: Collectively, no significant association between NAFL development and administration of MTX was detected in this study. Our results suggest that it is more efficient to adjust for individualized risk factors for NAFL prevention rather than discontinuation of MTX in patients with RA.

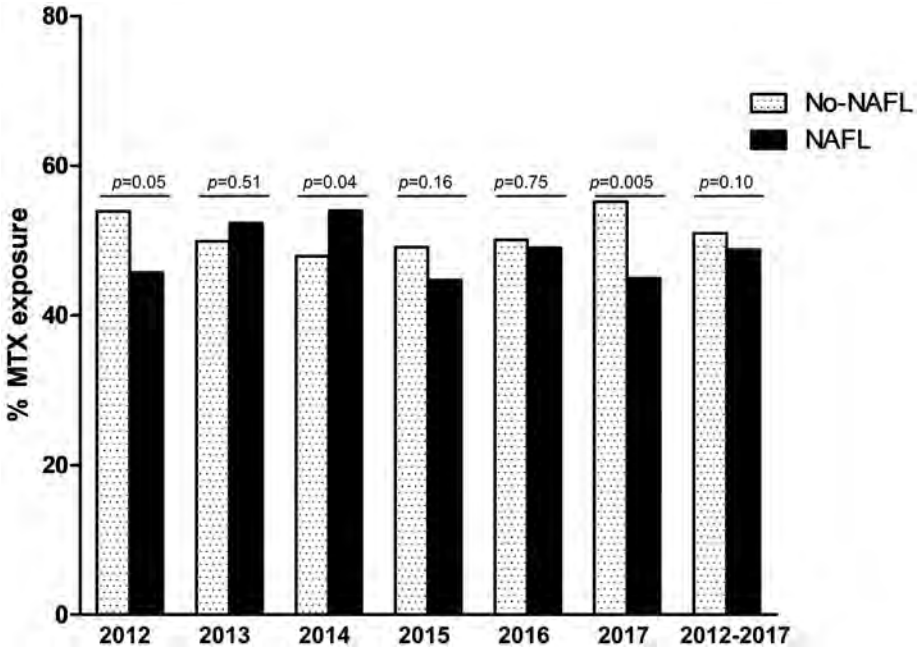

Figure 2. Prescription rate of MTX in RA patients with or without NAFL based on HIRA-NPS data Prescription rate of MTX in RA patients with or without the diagnosis code of NAFL was analyzed and compared using HIRA-NPS data for 6 years, from 2012 to 2017. HIRA-NPS, Health Insurance Review and Assessment Service-National Patient Samples; MTX, Methotrexate; NAFL, Non-alcoholic fatty liver; RA, Rheumatoid arthritis

Disclosure: Y. Choi, None; **C. Lee**, None; **M. Lee**, None; **C. Lee**, None; **S. Park**, None; **W. Yoo**, None.

Abstract Number: 0182

Chronic Kidney Disease Is Underestimated in Patients with Rheumatoid Arthritis – Real World Data Gathered from a Network of Rheumatologists

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patient registries have become a common approach to learn from patient-related data by prospectively including large numbers of individuals into a sample followed over some time. Data quality improves by semi(automated) input of laboratory values or patient input by using apps.

	n	% documented	Mean	SD	Median	25% Q	75% Q
Rheumatoid Arthritis							
Age	4962	100	64.5	14	65	56	76
Female	3655	73.7					
RF positive	2964	59.7					
Symptom duration (years)	4857	97.9	11.3	9.6	9	4	15
DAS 28	4013	80.9	2.7	1.1	2.5	1.9	3.3
SDAI	3456	69.6	6.2	6.8	4.1	1.6	7.9
BSG (mm/h)	4054	81.7	19.2	19.5	15	8	24
CRP (mg/dl)	4065	81.9	0.7	1.7	0.3	0.3	0.5
FFbH	4305	86.8	78.4	22.6	86	67	97
Comorbidities documented	2887	58.2					
GFR analysed	2990	60.3					
Psoriatic Arthritis							
Age	1009	100	58.1	13	58	50	67
Female	576	57.1					
Symptom duration (years)	998	98.9	11	9	9	4	15
DAPSA	330	32.7	8.1	9.1	5.1	2.3	10.6
BSG (mm/h)	560	55.5	15.5	13.7	11	6	20
CRP (mg/dl)	732	72.5	0.5	0.8	0.3	0.3	0.4
FFbH	883	87.5	81.2	20.6	89	69	100
Comorbidities documented	598	59.3					
GFR analysed	599	59.4					
Axial Spondyloarthritis							
Age	1013	100	49.3	13.7	50	39	59
Female	444	43.8					
Age	569	56.2	48.4	13.8	49	38	57
Symptom duration (years)	1011	99.8	12.7	12.1	8	4	19
BASDAI	926	91.4	3.3	2.1	3	1.6	4.6
BASFI	729	72	3.1	2.6	2.6	0.9	4.9
BASMI	288	28.4	1.8	2.4	1	0	3
ASDAS	215	21.2	2.1	0.8	2.1	1.6	2.6
Comorbidities documented	424	41.9					
GFR analysed	524	51.7					

Table 1. Patients' characteristics with different rheumatic diseases (GFR: Glomerular filtration rate; FFbH: Funktionsfragebogen Hannover, range 0-100 (100 normal function), equivalent to Health assessment questionnaire (HAQ-DI) range 3-0)

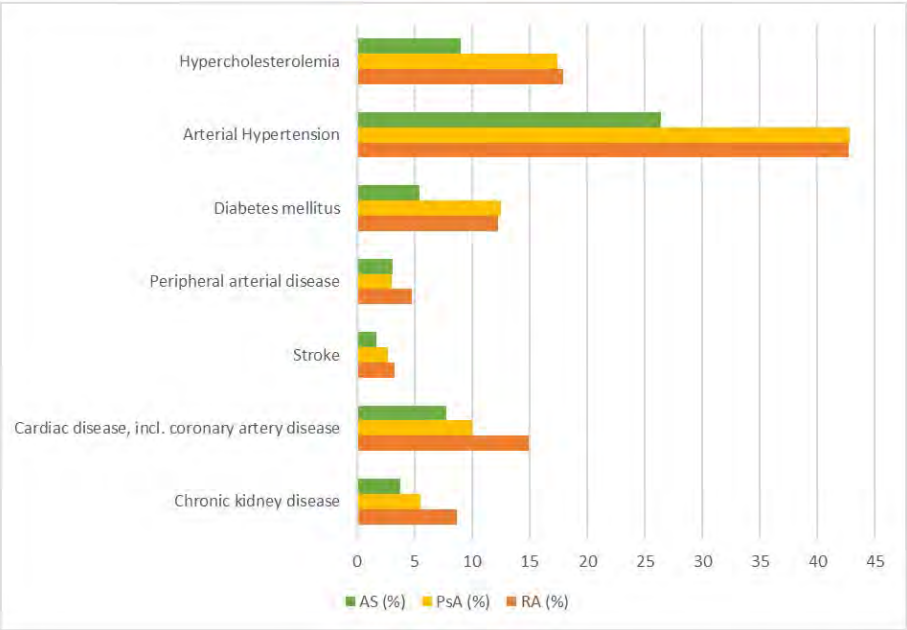

Figure 1. Cardiovascular and renal comorbidities in patients with RA, PsA, and AS as documented by the treating physician.

Chronic kidney disease - G1-5 by glomerular filtration rate (GFR)	RA (n)	RA (%)	PsA (n)	Ps (%)	AS (n)	AS (%)
G 1: Normal (GFR ≥ 90)	1098	36,7	288	48,1	337	64,3
G 2: Mildly decreased (GFR 60-89)	1487	49,7	279	46,6	167	31,9
G 3a: Mildly to moderately decreased (GFR 45-59)	286	9,6	23	3,8	19	3,6
G 3b: Moderately to severely decreased (GFR 30-44)	103	3,4	6	1	1	0,2
G 3 total (GFR 30-59)	389	13	29	4,8	20	3,8
G 4: Severely decreased (GFR 15-29)	14	0,5	2	0,3	0	0
G 5: Kidney failure (GFR <15)	2	0,1	1	0,2	0	0
Total documented	2990	100	599	100	524	100

Table 2. Chronic kidney disease analysed by using the laboratory value “estimated glomerular filtration rate”.

Methods: The RHADAR framework is a network of currently 25 rheumatologists in Germany supplying pseudonymized data for aggregation into a joint database. Every patient, except the patients not consenting, is documented. The growing data input is conducted by physicians, nurses and patients using personal computers, Tablets, and apps. Laboratory values are included (semi)automatically. Comorbidities are documented using the diagnoses in the patients’ records. The database is regularly analysed, lastly after March 31st 2020, using statistical software R and RStudio. (1, 2)

Results: 4962 patients had rheumatoid arthritis (RA), 1009 psoriatic arthritis (PsA), and 1013 axial spondyloarthritis (axSpA). The minimum data set consisted out of age, sex, and symptom duration. Different disease specific scores were present in subsets of patients (Table 1).

Chronic renal disease was documented in 252 (8.7%) RA patients, 33 (5.5%) PsA patients, and 16 (3.8%) of axSpA patients. Further cardiovascular diseases and risk factors are displayed in Figure 1.

Laboratory results regarding estimated renal function (GFR) by the CKD-EPI equation (3) revealed a higher percentage of renal impairment (Table 2) in RA patients, but not in SpA or PsA patients. A grad 3 renal impairment was present in 389 (13 %) RA patients, 29 (4.8 %) PsA patients, and 20 (3.8%) of axSpA patients

Conclusion: Real world data revealed a higher percentage of chronic kidney disease by laboratory values than recognized by the treating physician in RA patients..

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Abstract Number: 0183

Incidence of Malignancies in Japanese Patients with Rheumatoid Arthritis: Data from a Large Japanese National Registry

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients (pts) with RA have an increased risk of some malignancies compared with the general population, and this can vary by region/race.[1,2] Epidemiologic data on the incidence of malignancies in Japanese pts with RA are limited. There are also limited data reporting the impact of biologic (b)DMARDs and targeted synthetic (ts)DMARDs, such as JAK inhibitors, on the incidence of malignancies in Japanese pts with RA. The National Database of Rheumatic Diseases in Japan (NinJa) is one of the largest RA registries in Japan. This study evaluated the incidence of malignancies in Japanese pts with RA using NinJa registry data.

Methods: This retrospective observational study analyzed NinJa registry data for Japanese pts with RA aged ≥ 18 years with ≥ 1 data entry between 2013 (first JAK inhibitor approval for RA in Japan) and 2018. The overall cohort included all pts with RA, and two sub-cohorts were analyzed: pts exposed and unexposed to bDMARDs (exposure defined as ≥ 1 bDMARD reported in the database). Crude incidence rates (IRs) for malignancies (including non-melanoma skin cancer) were calculated as the number of events per 100 pt-years of follow-up (time between start of follow-up and end of the observation period, or withdrawal from the database). The most recent data for incidence of

Table 1. Cross-sectional analysis of the incidence of malignancies[a] in Japanese pts with RA from 2013–2018

	All RA					
	2013 (N=13,423)	2014 (N=15,584)	2015 (N=15,751)	2016 (N=16,107)	2017 (N=15,994)	2018 (N=15,003)
Total follow-up, PY	13,423	14,948	14,916	15,054	14,828	15,003
Number of events, n	140	164	174	168	161	211
Crude IR[b] (95% CI)	1.04 (0.88, 1.23)	1.10 (0.94, 1.28)	1.17 (1.01, 1.35)	1.12 (0.96, 1.30)	1.09 (0.93, 1.27)	1.41 (1.23, 1.61)
SIR[c] (95% CI)	0.96 (0.81, 1.13)	1.00 (0.85, 1.18)	1.01 (0.87, 1.17)	0.95 (0.81, 1.10)	0.90 (0.77, 1.05)	1.15 (1.00, 1.31)
ASR[c] (95% CI)	0.75 (0.59, 0.92)	0.75 (0.61, 0.89)	0.89 (0.68, 1.10)	0.86 (0.67, 1.05)	0.77 (0.60, 0.95)	0.84 (0.71, 0.97)

[a]Including non-melanoma skin cancer; [b]IR was calculated as the number of events per 100 PY of follow-up; [c]Standardized using data from a Japanese general population database of malignancy incidence from 2013–2015, provided by the Center for Cancer Control and Information Services, National Cancer Center, Japan
ASR, age- and sex-adjusted-standardized rate; CI, confidence interval; IR, incidence rate; N, total number of pts evaluated; n, number of events; pts, patients; PY, pt-years; RA, rheumatoid arthritis; SIR, standardized incidence ratio

Table 1

Table 2. Cumulative analysis of the incidence of malignancies[a] in Japanese pts with RA from 2013–2018

	All RA			RA excluding JAK inhibitor-exposed pts		
	All (N=26,607)	Exposed to bDMARDs (N=8,121)	Unexposed to bDMARDs (N=18,486)	All (N=25,930)	Exposed to bDMARDs (N=7,753)	Unexposed to bDMARDs (N=18,177)
Total follow-up, PY	88,172	30,355	57,817	85,242	28,564	56,678
Number of events, n	1,018	301	717	993	283	710
Crude IR[b] (95% CI)	1.15 (1.09, 1.23)	0.99 (0.89, 1.11)	1.24 (1.15, 1.33)	1.16 (1.09, 1.24)	0.99 (0.88, 1.11)	1.25 (1.16, 1.35)
SIR[c] (95% CI)	1.00 (0.94, 1.06)	0.95 (0.85, 1.07)	1.02 (0.94, 1.09)	1.00 (0.94, 1.06)	0.95 (0.84, 1.06)	1.02 (0.95, 1.10)
ASR[c] (95% CI)	0.81 (0.74, 0.88)	0.79 (0.67, 0.91)	0.85 (0.75, 0.94)	0.82 (0.74, 0.89)	0.78 (0.66, 0.91)	0.86 (0.76, 0.95)

[a]Including non-melanoma skin cancer; [b]IR was calculated as the number of events per 100 PY of follow-up; [c]Standardized using data from a Japanese general population database of malignancy incidence from 2013–2015, provided by the Center for Cancer Control and Information Services, National Cancer Center, Japan
ASR, age- and sex-adjusted-standardized rate; bDMARD, biologic disease-modifying antirheumatic drug; CI, confidence interval; IR, incidence rate; JAK, Janus kinase; N, total number of pts evaluated; n, number of events; pts, patients; PY, pt-years; RA, rheumatoid arthritis; SIR, standardized incidence ratio

Table 2

malignancy in the Japanese general population (2013–2015 data from the National Cancer Center, Japan) were used to calculate standardized incidence ratios (SIRs) and age- and sex-adjusted standardized rates (ASRs) for malignancies. Cross-sectional (per calendar year) and cumulative analyses were performed for the overall cohort. Cumulative rates were also calculated for the sub-cohorts, and all cumulative analyses were repeated excluding pts exposed to JAK inhibitors (ie ≥ 1 JAK inhibitor reported in the database).

Results: Data were collected for 26,607 Japanese pts with RA from 2013–2018. In the cross-sectional analysis (Table 1), the SIR and ASR for malignancies in all pts with RA were generally consistent from 2013–2018. In the cumulative analysis (Table 2), the SIR (95% confidence interval [CI]) for malignancies from 2013–2018 was 1.00 (0.94, 1.06) in all pts with RA, and 0.95 (0.85, 1.07) and 1.02 (0.94, 1.09) in pts exposed and unexposed to bDMARDs, respectively. Adjusting for age and sex, the cumulative ASR (95% CI) for malignancies from 2013–2018 was 0.81 (0.74, 0.88) in all pts with RA, and 0.79 (0.67, 0.91) and 0.85 (0.75, 0.94) in pts exposed and unexposed to bDMARDs, respectively (Table 2). In all cohorts, the cumulative SIR and ASR were similar when pts exposed to JAK inhibitors were excluded (Table 2).

Conclusion: The incidence of malignancies in Japanese pts with RA, registered in the NinJa database from 2013–2018, was similar to that in the Japanese general population. The SIR and ASR for malignancies were comparable in pts exposed and unexposed to bDMARDs. In all cohorts, rates did not increase when pts exposed to JAK inhibitors were included.

1. Dougados M et al. Ann Rheum Dis 2014; 73: 62-68.
2. Parikh-Patel A et al. Cancer Causes Control 2009; 20: 1001-1010.

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Abstract Number: 0184

Lymphomas Complicating Rheumatoid Arthritis: Results of a French Multi-Centre Case-Control Study

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with an increased risk of non-Hodgkin B-cell lymphoma (B-cell NHL).

The objectives of this work were:

- To study the characteristics of B-cell NHL complicating RA
- To identify the factors associated with their occurrence.
- To identify single nucleotide polymorphisms (SNP) associated with their occurrence.

Methods: A multi-centre retrolective case-control study was performed in France. Cases were patients with RA fulfilling the ACR-EULAR 2010 criteria, who developed a B-cell NHL after the diagnosis of RA. Cases were reported following a call for observations by the CRI-Imidiate network, registries from the French society of Rheumatology and the ESPOIR cohort. For each case, 2 control patients were drawn at random from patients fulfilling ACR-EULAR 2010 criteria in the ESPOIR cohort; cases and controls were matched on age (age at lymphoma diagnosis for cases and age at the 10-year ESPOIR visit for controls). Patients with associated Sjögren's syndrome were excluded. Cases and controls characteristics were compared for parameters associated with the occurrence of lymphoma. Blood or saliva samples were collected whenever possible for genotyping, looking for 24 SNP of known interest for their association with lymphomas and/or for their implications in B-cell control pathways.

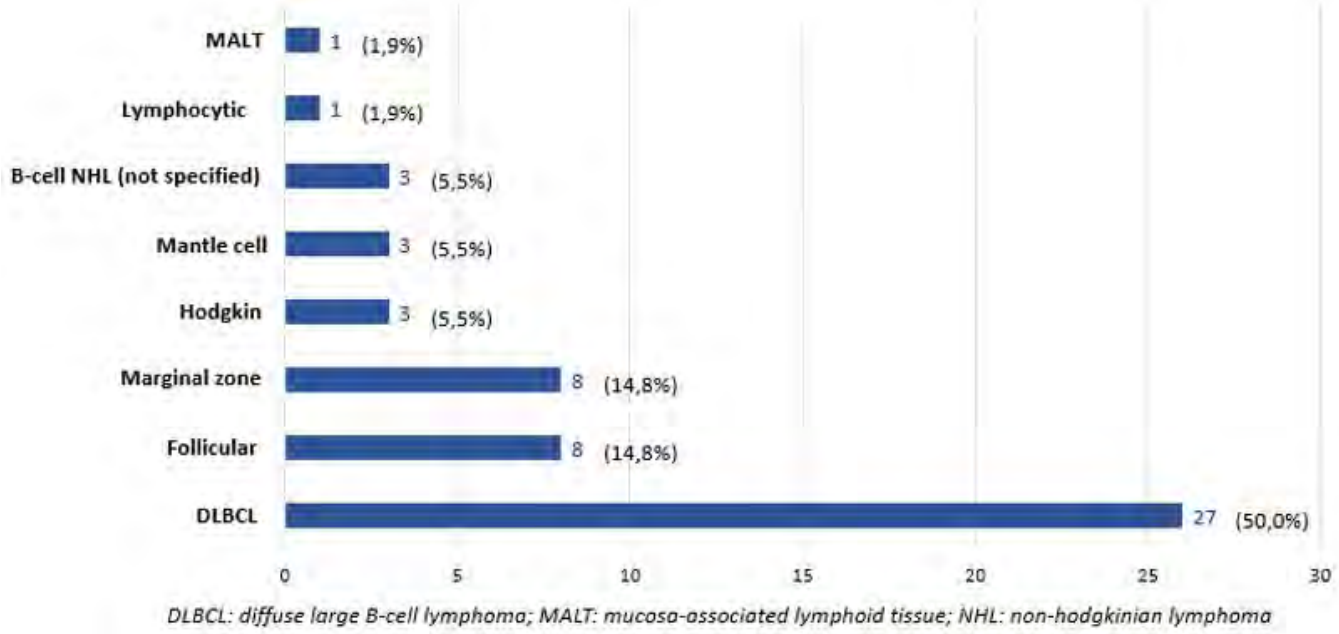

Figure 1. lymphomas histology

Variables	Cases (N=54)	Controls (N=108)	Univariate analysis		Multivariate analysis	
			OR (95%CI)	p-value	OR (95%CI)	p-value
Male gender, N (%)	27 (50.0)	25 (23.2)	**3.3 (1.7-6.7)**	***0.0006***	2.0 (0.7-5.6)	0.18
Positive ACPA, N (%)	49 (90.7)	71 (65.7)	**5.1 (2.0-15.7)**	***0.0006***	3.7 (1.0-18.7)	0.07
Positive RF, N (%)	49 (90.7)	77 (71.3)	**3.9 (1.6-12.2)**	***0.005***	-	-
Positive RF or ACPA, N (%)	49 (90.7)	80 (74.1)	**3.4 (1.3-10.6)**	***0.01***	-	-
Erosions on X-rays, N (%)	44 (81.5)	26 (24.1)	**15.4 (6.9-37.7)**	***< 0.0001***	***9.4 (3.6-27.1)***	***< 0.0001***
DAS28 at B-cell NHL diagnosis/at the 10th year visit*, mean (SD)	4.1 (1.6)	2.6 (1.4)	**2.0 (1.5-2.7)**	***< 0.0001***	***1.8 (1.3-2.7)***	***0.001***

**B-cell NHL diagnosis for cases, 10th year visit for controls*

Table 1. association between RA characteristics and B-cell NHL in univariate and multivariate analysis

Results: A total of 54 cases were included and matched to 108 controls. Lymphomas were mostly diffuse large B-cell lymphomas (n=27, 50.0%) *(Figure 1)*. EBV positivity was found in 4 cases among 27 tested (14.8%). Cases had a mean age of 63.5 years (SD=10.9) and had a mean RA duration of 12.4 years (SD=10.5) at the time of diagnosis of

	Cases (N=54)	Controls (N=108)	OR (95% CI%)	p-value
Glucocorticoids, N (%)	35 (64.8)	78 (72.2)	1.0 (0.5-2.3)	0.93
Methotrexate, N (%)	45 (83.3)	97 (89.8)	1.0 (0.3-3.4)	0.97
Hydroxychloroquine, N (%)	20 (37.0)	19 (17.6)	**3.1 (1.5-6.7)**	**0.002**
Sulfasalazine, N (%)	19 (35.2)	19 (17.6)	**3.1 (1.4-6.6)**	**0.003**
Leflunomide, N (%)	9 (16.7)	22 (20.4)	0.9 (0.4-2.1)	0.81
TNF blockers, N (%)	*21 (38.9)*	*38 (35.2)*	1.1 (0.6-2.2)	0.75
Adalimumab	*7 (13.0)*	*21 (19.4)*	*0.6 (0.2-1.5)*	*0.30*
Certolizumab	*1 (1.9)*	*3 (2.8)*	*0.7 (0.1-5.3)*	*1.00*
Etanercept	*13 (24.1)*	*17 (15.7)*	*1.7 (0.7-3.8)*	*0.19*
Golimumab	*0 (0.0)*	*4 (3.7)*	-	*0.30*
Infliximab	*7 (13.0)*	*25 (23.2)*	*0.6 (0.2-1.3)*	*0.21*
Rituximab, N (%)	*6 (11.1)*	*1 (2.8)*	4.3 (1.0-21.4)	0.06
Abatacept, N (%)	*3 (5.6)*	*5 (4.6)*	1.2 (0.2-5.2)	0.71
Tocilizumab, N (%)	*5 (9.3)*	*4 (3.7)*	2.1 (0.5-9.3)	0.44
Lines of bDMARD, N (%)				0.58
0	*26 (48.2)*	*70 (64.8)*	*reference*	-
1	*12 (22.2)*	*23 (21.3)*	*1.4 (0.6-3.2)*	-
2	*4 (7.4)*	*9 (8.3)*	*1.2 (0.3-4.0)*	-
3	*3 (5.6)*	*3 (2.8)*	*2.7 (0.5-15.4)*	-
4	*2 (3.7)*	*2 (1.8)*	*2.7 (0.3-23.4)*	-
5	*1 (1.9)*	*1 (0.9)*	*2.7 (0.1-69.8)*	-

Table 2: association between RA treatments and B-cell NHL in univariate analysis

lymphoma; there was no significant difference with controls (p=0.47 and p=0.40 respectively). The mean duration of follow-up after the diagnosis of lymphoma was 5.2 years (SD=5.8).

In univariate analysis, factors associated with occurrence of B-cell NHL were: male gender (OR=3.3, 95%CI: 1.7-6.7), positive ACPA (OR=5.1, 95%CI: 2.0-15.7), positive Rheumatoid Factor (RF) (OR=3.9, 95%CI=1.6-12.2), erosions on X-rays (OR=15.4, 95%CI: 6.9-37.7) and DAS28 (OR=2.0, 95%CI: 1.5-2.7). Erosions and DAS28 remained significant in multivariate analysis, and there was a trend for ACPA positivity *(Table 1)*. Methotrexate, TNF-blockers and the number of previous biologics were not associated with the occurrence of B-cell NHL *(Table 2)*. Previous use of hydroxychloroquine and sulfasalazine were more frequent in cases versus controls, which could be linked to a date bias; since the mean year of RA diagnosis was earlier in cases than in controls (1997±10.6 vs 2003±0.7, p< 0.0001), they were more susceptible to have received these drugs than more recent RA.

The exploratory genetic analysis suggested an association of the *BLK* rs2736340 minor allele (encoding for B-cell lymphocyte kinase BLK) with B-cell NHL (OR=1,8, 95%CI: 1.0-3,2, crude p=0.03).

Conclusion: B-cell NHL complicating RA are mostly DLBCL. This study revealed an association between markers of activity (DAS28), severity (erosions) and the risk of B-cell NHL in patients with RA, and suggested the possible

role of B-cell activation (RF, ACPA, *BLK* gene), supporting the paradigm of a continuum between autoimmunity and lymphomagenesis in RA.

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Abstract Number: 0185

Prevalence of Migraine and Neuropathic Pain in Rheumatic Disease

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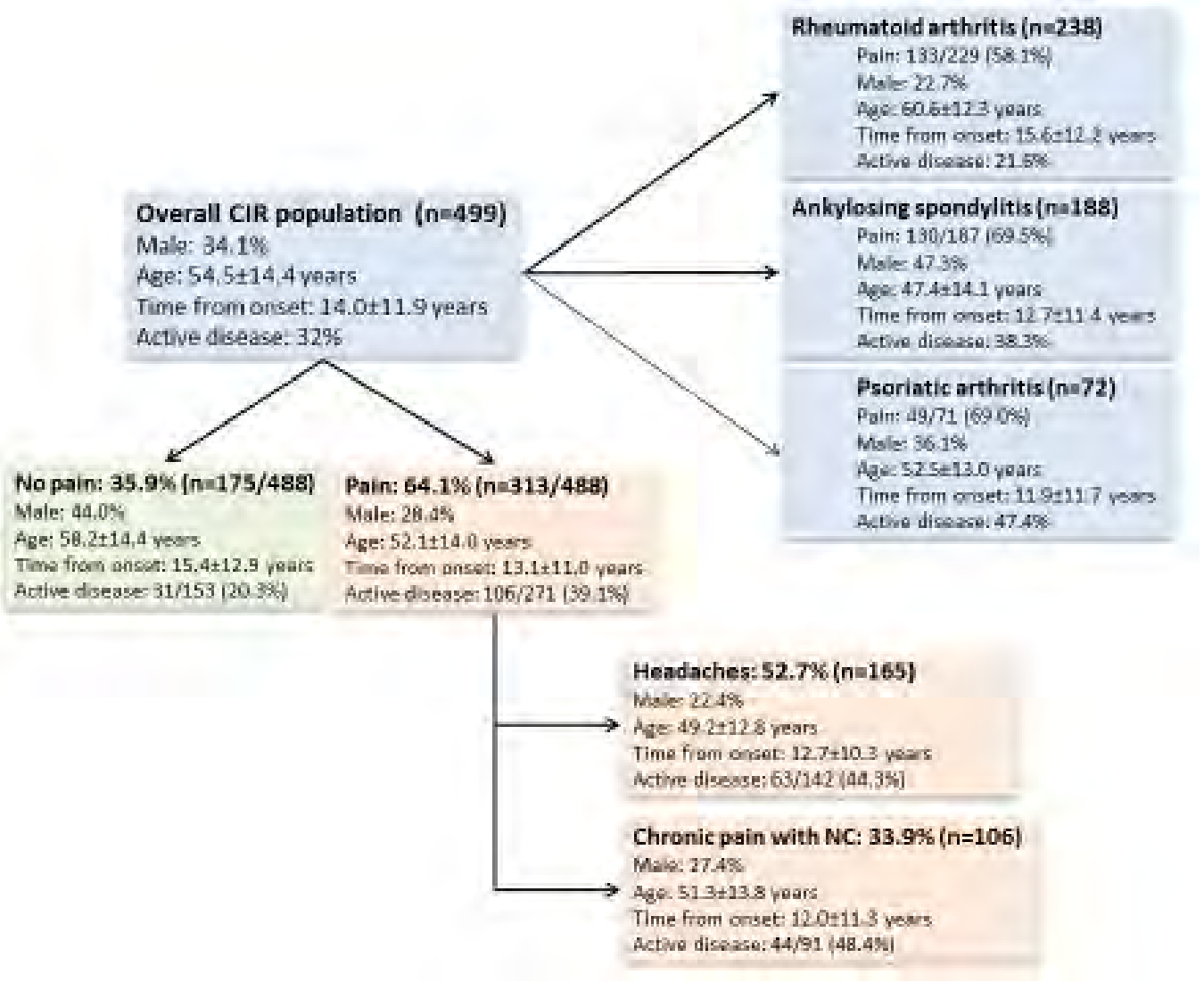
SESSION INFORMATIONSession Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of our study was to assess the prevalence of migraine and neuropathic pain in a sample of patients with chronic inflammatory rheumatism (CIR) routinely followed in Rheumatology and to compare it with that found in the general French population.

Methods: Patients with rheumatoid arthritis (RA), ankylosing spondylitis (AS) and psoriatic arthritis (PsA) were invited to complete a validated self-assessment questionnaire. Migraine was diagnosed according to the IHS migraine diagnostic criteria. Neuropathic pain was retained in case of a total score at 3 or more at DN4-interview questionnaire. Continuous parameters were compared between independent groups (RA/AS/PsA, with/without migraine, with/without neuropathic pain) with the ANOVA or Student *t*-test. Categorical data were compared between groups with the chi-squared test or Fisher's exact test. Binary variables of particular interest, like the presence/absence of migraine or pain, were evaluated with generalized linear models (i.e., logistic regression). Differences between our cohort and the French general population were expressed as ORs, based on the Mantel-Haenszel method.

Results: A total of 499 patients with CIR were included (238 RA, 188 AS and 72 PsA and one patient not classified). We found a prevalence of migraine of 34% (165/484). This prevalence was higher in PsA patients (32/71: 45.1%). Parameters associated with a higher prevalence of migraine were a higher level of anxiety (OR=1.14 [1.05-1.23]), female sex (OR=4.03 [2.24-7.52]), younger age (OR=0.97 [0.95-0.99]), TNF alpha inhibitors treatment (OR=1.91 [1.14-3.23])



Distribution of rheumatic diseases, migraine, and neuropathic pain among study participants.

in the entire population and a high disease activity in AS patients. Systemic inflammation was never significantly associated. Among the 165 patients with migraine, 124 (75.2%) had HIT-6 scores above 55, which indicated that headache had an important impact on these patients.

Chronic pain with neuropathic characteristics was found in 21.5% of 493 patients with CIR. The intensity of pain was moderate (5.0 ± 1.5). Prevalence was significantly higher in the AS group (26.7%) than in the PsA (19.4%) and RA (17.6%) groups (p = 0.02). Active disease (OR = 1.00, 95%CI: 1.00-1.03), and salazopyrine treatment (OR = 1.91. 95%CI: 1.08-12.9) were associated with a higher risk of neuropathic pain.

Compared to the general population, our cohort showed significantly higher rates of migraine (OR = 1.91, 95%CI: 1.57-2.32) and neuropathic pain (OR = 3.71, 95%CI: 2.97-4.62), based on the Mantel-Haenszel method. We observed significant differences in strict and probable migraine rates between the general population and our cohort, when we performed separate analyses, according to gender and age. The higher frequency of neuropathic pain in our sample compared to the general population was more dramatic among younger patients but was not different between the sexes.

Conclusion: We found a high prevalence of migraine and neuropathic pain in our sample of patients with rheumatic disease. It seems therefore important to check the presence of migraine or neuropathic pain in rheumatic disease patients with residual pain despite a clinically well-controlled rheumatic disease.

Disclosure: S. Mathieu, Bristol Myers Squibb, 1, Pfizer, 1, Abbvie, 1, Novartis, 1, Roche and Chugai, 1, Merck Sharp and Dohme, 1; **M. Couderc**, None; **B. Pereira**, None; **J. Dubost**, None; **S. Malochet-Guinamand**, None; **A. Tournadre**, None; **M. Soubrier**, None; **X. Moisset**, Lilly, TBWA, Teva, Novartis, Roche, Biogen, Sanofi-Genzyme, and Merck-Serono, 1.

Abstract Number: 0186

The Number of Associated Comorbidities Can Impact Disease Activity Scores Independently from Objective Measures of Inflammation in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Disease activity scores (DAS) are used as tools to assess persistent inflammation and need for therapeutic escalation in patients with Rheumatoid arthritis (RA). One of the most commonly used disease activity

Table 1. DAS28, Disease Activity Score Components, and Distribution of Comorbidities

Variable	Global	Paraguay (n=182)	Uruguay (n= 193)	p value
DAS28C	5.57 (1.14)	5.41 (1.13)	5.72 (1.14)	0.007
ODAS28	3.03 (0.63)	3.04 (0.58)	3.03 (0.68)	0.75
SDAS28	2.54 (0.77)	2.37 (0.74)	2.70 (0.77)	0
SJC	6.71 (4.74)	6.73 (4.91)	6.70 (4.59)	0.732
TJC	9.26 (6.32)	8.00 (5.90)	10.44 (6.49)	0
ESR	37.75 (25.11)	36.55 (23.25)	38.88 (26.76)	0.588
ptVAS	67.57 (20.19)	64.67 (19.82)	70.31 (20.20)	0.003
CRP	18.65 (27.73)	20.75 (35.49)	16.97 (19.32)	0.511
N of comorbidities				
0	141 (42.5%)	97 (58.1%)	44 (26.7%)	8.04E-11
1	120 (36.1%)	56 (33.5%)	64 (38.8%)	
2+	71 (21.4%)	14 (8.4%)	57 (34.5%)	

DAS28C: disease activity score 28 complete, ODAS28: objective component of DAS28, SDAS28 : subjective component of DAS28, SJC: swollen joint count, TJC: tender joint count, ESR: erithrosedimentation rate, ptVAS: patient global health evaluation by visual analog scale, CRP: C reactive protein.

Table 2. Univariate Analysis of Clinical, serological and demographic variables with subjective components of DAS 28

Number of biologic tx	1.403 (-0.399, 11.205)	0.069	-0.066 (-1.854, 1.721)	0.943	-0.044 (-0.172, 0.26)	0.692
Age	0.01 (-0.157, 0.178)	0.902	0.028 (-0.025, 0.078)	0.317	0.002 (-0.004, 0.0091	0.262
Disease Duration	0.027 (-0.236, 0.291)	0.838	-0.055 (-0.136, 0.025)	0.177	-0.006 (-0.015, 0.004)	0.264
CORTICOID	4.132 (-0.07, 8.334)	0.054	0.534 (-0.76, 1.829)	0.417	0.114 (-0.043, 0.27)	0.153
MTX	-2.887 (-7.502, 1.558)	0.197	-1.951 (-3.334, -0.568)	0.006	-0.22 (-0.387, -0.052)	0.01
HCQ	-2.89 (-7.294, 1.213)	0.173	-2.689 (-2.011, 0.632)	0.306	-0.112 (-0.271, 0.048)	0.17
LEFLU	0.417 (-5.815, 4.453)	0.835	0.516 (-0.721, 1.753)	0.413	0.047 (-0.103, 0.197)	0.537
number of concomitant tx	-0.511 (-2.27, 1.249)	0.59	-0.279 (-0.849, 0.29)	0.335	-0.026 (-0.105, 0.033)	0.304
CRP	0.047 (-0.038, 0.132)	0.279	0.002 (-0.024, 0.029)	0.85	0.001 (-0.002, 0.004)	0.561
Origin PY	-5.719 (-9.702, -1.735)	0.006	-2.474 (-3.683, -1.265)	p	-0.827 (-0.472, -0.181)	p
Male Sex	-2.516 (-8.528, 3.499)	0.411	-0.937 (-2.78, 0.904)	0.318	-0.133 (-0.355, 0.09)	0.242
Age at tx	0.003 (-0.16, 0.157)	0.683	0.043 (-0.005, 0.092)	0.079	0.004 (-0.001, 0.01)	0.141
BMI	0.559 (-0.257, 0.495)	0.748	3.212 (0.088, 0.335)	0.091	0.02 (0.003, 0.038)	0.011
CHARLSON	1.36 (-1.152, 3.872)	0.288	0.075 (-0.697, 0.847)	0.848	0.019 (-0.074, 0.113)	0.682
Comorbidities	4.304 (1.749, 6.859)	0.001	1.123 (0.338, 1.91)	0.005	0.169 (0.074, 0.263)	0.001
CCP neg	3.23 (-7.622, 8.081)	0.854	-0.521 (-1.899, 2.942)	0.672	0.041 (-0.25, 0.331)	0.784
CCP pos	0.465 (-5.525, 6.455)	0.874	0.62 (-1.225, 2.465)	0.509	0.072 (-0.15, 0.295)	0.521
RF neg	0.855 (-11.294, 11.395)	0.992	-0.24 (-3.573, 3.193)	0.891	-0.012 (-0.433, 0.408)	0.954
RF pos	-1.502 (-12.038, 8.914)	0.768	-0.191 (-3.372, 2.99)	0.908	-0.041 (-0.431, 0.348)	0.834
T. mixing	3.112 (-1.995, 8.219)	0.231	1.01 (-0.343, 2.364)	0.203	0.105 (-0.054, 0.324)	0.161
T. Mestrinera	3.024 (-3.9, 9.948)	0.391	2.091 (-0.017, 4.198)	0.052	0.173 (-0.063, 0.43)	0.155
T.Other	-3.685 (-12.687, 5.477)	0.525	2.578 (-0.337, 5.49)	0.083	0.14 (-0.215, 0.494)	0.438
T.Anastemia	0.029 (-9.21 (, 9.275)	0.941	-0.536 (-2.439, 1.368)	0.579	-0.013 (-0.244, 0.218)	0.915
smoker no	-7.153 (-14.475, 0.169)	0.056	-3.174 (-5.417, -0.93)	0.006	-0.373 (-0.642, -0.104)	0.007
smoker yes	-0.251 (-9.68, 9.185)	0.953	-1.218 (-3.864, 1.268)	0.317	-0.068 (-0.393, 0.273)	0.579

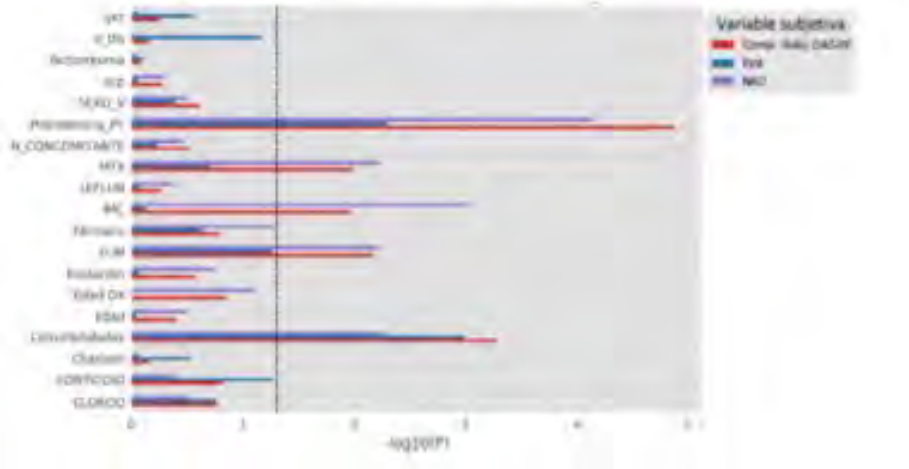
DASDBC disease activity score 28 complete, ODASDB objective component of DAS28 formula SDAS28 subjective component of DAS28, SJC swollen joint count, TJC tender joint count, ESR: erythrosedimentation rate, ptVAS: patient global health Visual analog scale, CRP, C reactive protein

scores is DAS28, which is composed of subjective and objective variables. The subjective component is derived from the patient evaluation of global health by visual analog scale (ptVAS) and the number of tender joints (TJC). Previous studies have reported the impact of comorbidities like fibromyalgia, and depression on TJC ,ptVAS, and DAS, but less is known of how non-pain related comorbidities impact DAS..

Methods: A retrospective, observational study was conducted. Patient data was abstracted from BIOBADAGUAY registry, which prospectively collects data for rheumatologic patients undergoing biologic therapy in Paraguay and Uruguay. Entries for adult patients with RA and complete data for DAS28/TJC/ptVAS scores were used. The DAS28 formula was separated into an objective component (0.28√SJC+ 0.70 ln ESR, called oDAS28) and a subjective component (0,56√TJC + 0,√014 ptVAS, called sDAS28).Descriptive analysis of DAS28, sDAS28, oDAS28 and their individual components, as well as for reported Charlson index comorbidities was done for both populations. Patients were grouped as having 0, 1 or 2+ concomitant comorbidities besides RA. Linear regression analysis was performed

Graphic 1.

Univariate Analysis of Subjective Disease Activity Components and Clinical, demographic and serological variables.



CRP: c reactive protein, treatmeat number (first line or second line) , RF: rhumatoid factor, CCP: cyclic citrulinated peptide, PY: Paraguay, tx: treatment, MTX: metotrexate, Leflu:leflunomide, BMI: body mass index; dx: diagnosis, Charlson: Charlson comorbidity index, HCQ:hidroxychloroquine

to see the impact of different clinical, demographic and serologic variables on the sDAS28 and on ptVAS and TJC independently. Multivariate analysis was used to confirm associations using variables that had reached a p< 0,01 in the univariate analysis.

Results: Significant differences in DAS28 scores were noticed. Patients from Uruguay had significantly higher mean DAS28 scores than Paraguayan patients (5.72 vs. 5.41, p 0.007 respectively), despite having no difference in mean SJC, ESR, or CRP. The difference in DAS28 scores between Uruguay and Paraguay were secondary to differences in the mean ptVAS (70 mm vs. 64 mm respectively, p 0.003) and the TJC (10.4 vs. 8.0 respectively, p 0.00001). Significant differences were also noted in the distribution of number of reported concomitant comorbidities. Paraguayan patients reported a higher number of patients with no concomitant comorbidities (58.1% for Paraguay vs. 26.7% in Uruguay) and a lower number of patients with 2 + comorbidities (8.4 % for Paraguay vs. 34.5% in Uruguay). Linear regression analysis revealed that, despite both TJC and ptVAS being associated with the number of comorbidities, the impact of ptVAS on the sDAS28 was greater. Multivariate analysis confirmed the association of ptVAS with number of comorbidities (p 0.046) , but not for TJC.

Conclusion: The number of Charlson index concomitant comorbidities in Latin-American RA patient can impact their perception of global health and therefore their final DAS28 score. Evaluation of these patients should be personalized. Decisions on therapeutic escalation should take patient characteristics into account and not based solely on DAS28 scores.

Disclosure: M. Zanotti-Cavazzoni, None; **G. Avila**, None.

Abstract Number: 0187

Regional and Widespread Patterns of Non-articular Pain Are Common at RA Diagnosis and Contribute to Poor Outcomes at 12 Months: A Prospective Study of Pain Patterns in Canadians with RA

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Persistent pain can occur in early RA patients, despite improvement in synovitis and may be due to coexisting non-articular pain (NAP). Though NAP is often attributed to fibromyalgia and widespread NAP, regional NAP syndromes may be more common and under-recognized. The purpose of this study is to describe patterns of NAP, predictors of persistent NAP and impact on outcomes in the first year following early RA diagnosis.

Methods: Data were from participants enrolled in the Canadian Early Arthritis Cohort (CATCH) between *2017-2019* who completed 0,6,12-month evaluations with patient-reported outcomes [PROs] and clinical data available. We used the McGill Body Pain Diagram (BPD) to classify patients as experiencing no NAP, regional (RP:1-2 regions) or widespread NAP (WP:3-5 regions). Multinomial regression was used to identify baseline predictors of persistent RP and WP at 12-months. Multi-adjusted GEE with linear and logit links were used to estimate time-varying associations of NAP patterns with outcomes updated at each time point.

Results: Study included 421 participants: 66% were female, with a mean(sd) age 56 (14); 72% were seropositive and 90% were treated with MTX ± csDMARDs as initial therapy. NAP at baseline was common (55%), with majority

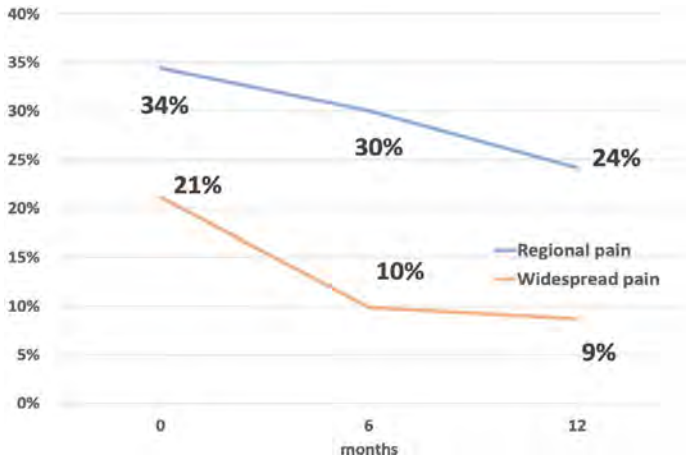

Figure. Point prevalence of regional and widespread NAP at baseline, 6 and 12 months.

NAP Patterns by BPD	Boolean Remission Outcome		SDAI Remission Outcome	
	Age/sex adjusted OR (95% CI)	Fully Adjusted	Age/sex adjusted OR (95% CI)	Fully Adjusted
Regional vs No NAP	**0.34 (0.18, 0.66)**	**0.41 (0.20, 0.83)**	**0.41 (0.23, 0.71)**	**0.55 (0.30, 1.00)**
Widespread vs No NAP	**0.21 (0.07, 0.67)**	**0.27 (0.08, 0.85)**	**0.23 (0.09, 0.61)**	**0.29 (0.11, 0.80)**
Age	NI	1.01 (0.98, 1.04)	NI	1.01 (0.98, 1.03)
Women vs Men	NI	0.76 (0.41, 1.42)	NI	0.69 (0.37, 1.27)
RDCI at baseline	NI	0.91 (0.73, 1.14)	NI	0.90 (0.74, 1.10)
Symptom duration	NI	0.96 (0.86, 1.08)	NI	1.00 (0.90, 1.10)
Seronegative vs ACPA+/RF+	NI	1.15 (0.60, 2.19)	NI	1.43 (0.79, 2.60)
MTX start/use in first 3 months	NI	1.51 (0.73, 3.13)	NI	1.20 (0.64, 2.24)
Oral Steroids use in first 3 months	NI	0.53 (0.25, 1.10)	NI	**0.44 (0.22, 0.87)**

Table. Results of Multi-Adjusted GEE Logistic Regression showing Regional and Widespread NAP is associated with a reduced likelihood of achieving Stringent Remission Targets

(62%) reporting regional NAP. NAP prevalence was 33% at 12 months (Figure). Female sex and baseline depressive symptoms were independent predictors of widespread NAP at 12 months while poorer function and lack of early MTX treatment independently predicted regional NAP, at 12 mos. Regional and widespread NAP were associated with lower likelihood of remission in adjusted models that accounted for changes in NAP and remission over time (Table).

Conclusion: NAP is commonly reported in early RA pts seen in real world settings. Regional NAP was more common than WSP at all time-points, but both NAP patterns were associated with lower odds of achieving remission targets by 12 months. These data support considering the role of NAP when assessing RA treatment efficacy during clinical visits and warrant different treatment approaches to reduce symptoms in RA patients receiving target-based care.

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Abstract Number: 0188

The Risk of Fractures in a Community-based Cohort of Patients with Rheumatoid Arthritis Compared with the Background Population

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

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Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) has been associated with increased risk of osteoporosis and fractures. We have recently presented results on DXA measurements over 10 years in patients with newly diagnosed RA, where women were shown to retain their bone mineral density (BMD) fairly well compared with the reference population whereas men with early RA had reduced BMD in the femoral neck at diagnosis and after 5 years of follow-up [1]. To what extent such patterns have an impact on fracture risk in established RA is an issue of major clinical importance. The aim of this study was to survey the risk of fragility fractures in a community-based sample of patients with RA, compared with controls without RA from the same area.

Methods: A dynamic community-based cohort of patients with RA (n=1928) was investigated. Prevalent cases identified in 1997, and incident cases from 1997-2006 were included. Four controls per patient were matched for age, sex and residential area. Information on fractures in patients and controls during the period 1. July 1997 to 31. December

Table 1. Number of fractures and incidence per 1000 person years for the specific fractures and overall, in RA patients and controls

	Men		Women	
	RA patients	Controls	RA patients	Controls
Hip fracture (n)	43	93	147	465
Hip incidence/1000 PY (95% CI)	6.56 (4.75; 8.84)	3.67 (2.96; 4.50)	8.16 (6.89; 9.59)	6.24 (5.69; 6.84)
Vertebral column fractures (n)	5	12	16	50
Vertebral column incidence/1000 PY (95% CI)	0.75 (0.24; 1.74)	0.46 (0.24; 0.82)	0.85 (0.49; 1.38)	0.65 (0.48; 0.86)
Upper arm fracture (n)	5	11	46	107
Upper arm incidence/1000 PY (95% CI)	0.75 (0.24; 1.75)	0.43 (0.21; 0.77)	2.46 (1.80; 3.28)	1.40 (1.15; 1.69)
Forearm fracture (n)	4	14	27	105
Forearm incidence/1000 PY (95% CI)	0.60 (0.16; 1.53)	0.55 (0.30; 0.92)	1.43 (0.94; 2.08)	1.38 (1.13; 1.67)
Fractures in total (n)	51	119	202	604
Fractures in total incidence/1000 PY (95% CI)	7.86 (5.85; 10.33)	4.73 (3.92; 5.67)	11.6 (10.0; 13.3)	8.29 (7.64; 8.98)

RA: Rheumatoid Arthritis, n: number, PY: person years, CI: Confidence Interval.

Table 2. Risk of fractures in RA patients compared with matched controls

	Men HR (95% CI)	Women HR (95% CI)
Hip	1.68 (1.05; 2.68)	1.41 (1.14; 1.75)
Vertebral column	NA	1.55 (0.85; 2.83)
Upper arm	NA	2.11 (1.43; 3.12)
Forearm	NA	1.10 (0.69; 1.75)
Fractures in total	1.55 (1.03; 2.34)	1.52 (1.27; 1.83)

HR: Hazard Ratio, CI: Confidence Interval.
NA: Not applicable due to <10 events in men with RA

2017 was obtained by linkage to the Swedish National Patient Register and the Cause of Death Register. Fractures of the hip, upper arm, forearm and vertebra were identified based on ICD-9 and ICD-10 diagnostic codes. Patients and controls with identified fractures before study start were excluded. The incidence of fractures was estimated in RA patients and controls, stratified by sex. The relation between RA and the risk of fractures in women and men was assessed using Cox regression models.

Results: Of the patients included, 73 % were women and 73 % were rheumatoid factor positive. The mean age at inclusion in men was 61 years and in women 60 years. Mean duration of disease was 8 years in men and 9 years in women. A total of 51 (9.7%) men and 202 (14.4%) women with RA suffered from at least one of the studied fractures during the study period, compared to 119 (5.6%) male and 604 (10.8%) female controls (Table 1). Men with RA had increased risk of fragility fractures overall (hazard ratio (HR) 1.55, 95% Confidence Interval (CI) 1.03; 2.34) and of fractures in the hip (HR 1.68, 95% CI 1.05; 2.68). Women with RA also had increased risk of fragility fractures overall (HR 1.52, 95% CI 1.27; 1.83), of fractures in the hip (HR 1.41, 95% CI 1.14; 1.75) and in the upper arm (HR 2.11, 95% CI 1.43; 3.12). There was a similar trend in the vertebral column but not in the forearm (Table 2).

Conclusion: In this cohort of patients with RA, the risk of fragility fractures was increased in both men and women compared with controls without RA. For men the results are in line with previous findings of reduced femoral neck BMD in early RA. For women with RA, long term changes in BMD in established disease, or other disease related factors, may be of importance in the assessment of fracture risk.

1. Theander L, Willim M, Nilsson JÅ, et al. Changes in bone mineral density over 10 years in patients with early rheumatoid arthritis. *RMD Open* 2020;6(1):e001142.

Disclosure: L. Theander, None; **J. Nilsson**, None; **M. Willim**, None; **L. Jacobsson**, Abbvie, 1, Eli Lilly, 1, Janssen, 1, Novartis, 1, Pfizer, 1; **C. Turesson**, Roche, 1, 2, Abbvie, 1, Pfizer, 1, Bristol-Myers Squibb, 1, 2.

Abstract Number: 0189

Determining the Relationship Between *Mycobacterium Avium Subspecies Paratuberculosis* Serostatus, Dietary Habits, Medication Regimen, and Joint Pain in Patients with Rheumatoid Arthritis

Chelsea Guan[1], Shazia Majid[2], Sweta Chalise[2], Saleh Naser[2], Robert Sharp[2] and **Shazia Beg**[3], [1]University of Central Florida, Orlando, FL, [2]University of Central Florida, Orlando, [3]University of Central Florida College of Medicine, Orlando

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic, systemic, inflammatory disease that primarily affects synovial tissues. While the exact etiology is unknown, it is hypothesized that RA is caused by a combination of environmental and genetic factors. One possible etiology of RA is *Mycobacterium avium subspecies paratuberculosis* (MAP), a bacterium found in cattle and cow's milk. MAP is known to cause Johne's disease in cattle and has implications in human autoimmune diseases such as type 1 diabetes, Crohn's disease, and recently RA.[1-2] It is unknown if RA patients who are MAP positive have different dietary habits and medication use. This study examines the relationships between MAP serostatus, RA medication use, dietary habits, and perceived levels of joint pain in patients with RA.

Methods: Patients at the UCF Health Clinic with confirmed RA diagnosis according to the ACR classification criteria had blood samples drawn to determine MAP serostatus and were surveyed regarding their dietary habits, perceived levels of joint pain, and RA medication regimen. A total of 69 patients were included in the final analysis. Fisher's exact test was used to explore relationships and p-values < 0.05 were considered statistically significant. All statistical tests were conducted in SPSS 24.0 (IBM Corp. Armonk, NY).

Results: Fisher's exact test revealed a significant association between use of adalimumab and MAP serostatus (p-value for 2-sided test 0.025, p-value for 1-sided test 0.017). There was a significant association between using at least one biologic medication and MAP serostatus (p-value for 2-sided test 0.010, p-value for 1-sided test 0.006). Compared to those that are not on adalimumab, those that are on it have 8.667 times the odds of being MAP+ (95% CI = 1.057-71.077). Compared to those that are on no biologic medications, those that are on at least one biologic medication have 4.680 times the odds of being MAP+ (95% CI = 1.482-14.774). There were no other significant associations between MAP serostatus, medication use, dietary habits, and patient-perceived joint pain. However, 50.7% of patients surveyed (34/67) reported that diet influences their level of joint pain, 25% (17/68) reported that dairy consumption increases their joint pain, and 25.8% (17/66) reported that red meat consumption increases their joint pain.

Conclusion: There is a significant association between adalimumab use and MAP serostatus and using at least one biologic medication and MAP serostatus. Additionally, dietary habits in RA patients may play a role in patient-perceived joint pain.

Disclosure: C. Guan, None; **S. Majid**, None; **S. Chalise**, None; **S. Naser**, None; **R. Sharp**, None; **S. Beg**, None.

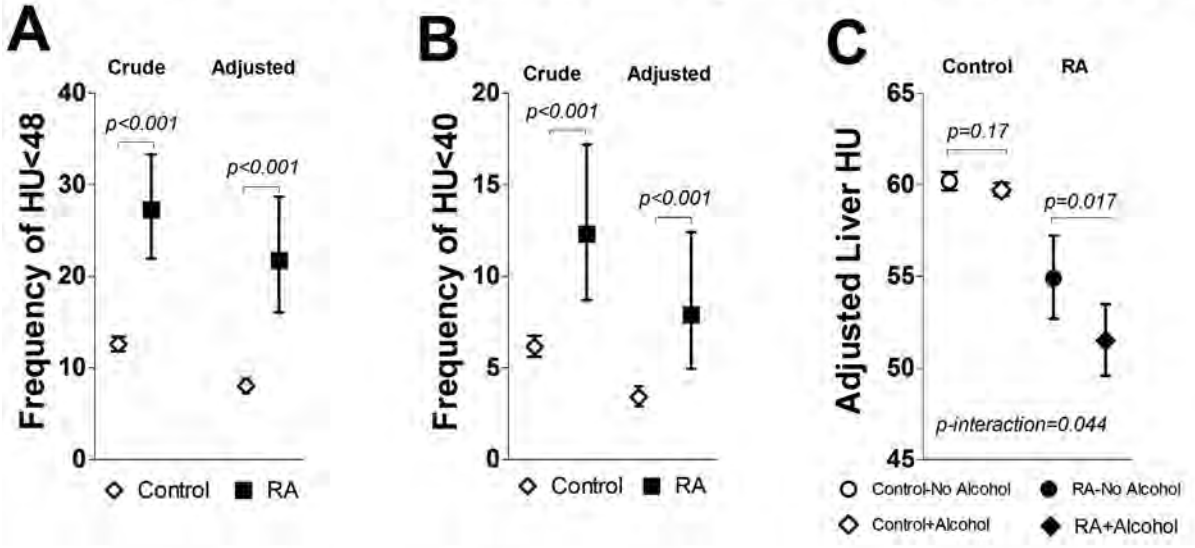
Abstract Number: 0190

Hepatic Steatosis in Rheumatoid Arthritis: Frequency and Disease-Related Contributors

Jun Lee[1], Galina Lagos[2], Joan Bathon[1] and Jon Giles[1], [1]Division of Rheumatology, Columbia University Vagelos College of Physicians and Surgeons, New York, NY, [2]Columbia University Vagelos College of Physicians and Surgeons, New York

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Figure. Measures of Hepatic Steatosis Were More Frequent in RA vs. Control, Particularly Among Current Alcohol Users



Means±95% CIs depicted. Adjusted for age, gender, race, education, BMI, diabetes, smoking, triglycerides, CRP, and IL-6

Background/Purpose: Nonalcoholic fatty liver disease (NAFLD), a spectrum of disorders characterized by the presence of hepatic steatosis, is the most common liver disorder in western countries. Risk factors, such as obesity, hypertension, dyslipidemia, insulin resistance, and elevated inflammatory cytokines, are frequent in RA. However, few prior studies have explored the prevalence and contributors to hepatic steatosis in RA.

Methods: A total of 235 RA patients underwent abdominal computed tomography (CT), with attenuation of hepatic parenchyma (away from hepatic vasculature) measured in Hounsfield units (HU). A cohort of 6615 non-RA controls underwent similar scanning and liver HU assessment. Any steatosis was defined as HU< 48. Moderate/severe hepatic steatosis was defined as HU< 40, a standard that correlates histologically with ≥30% fatty deposition. Generalized linear models were used to compare the prevalence of steatosis between the RA and control groups, adjusted for pertinent confounders, and to assess the associations of RA characteristics and other risk factors with steatosis within the RA group.

Results: Mean hepatic attenuation was 15% lower in the RA group compared with controls (51 vs. 60 HU, respectively; p< 0.001). The prevalence of any steatosis in RA was more than double that of controls (27 vs. 13%, respectively; p< 0.001) and remained significantly higher after adjusting for relevant confounders (adjOR=3.2; p< 0.001) (Fig 1A). The prevalence of moderate/severe steatosis was double that of the controls (12 vs. 6%, respectively; p< 0.001) and also remained significantly higher after adjustment (adjOR=2.5; p< 0.01) (Fig 1B). Alcohol consumption was more strongly linked to steatosis in the RA group compared with the control group (Fig 1C). RA patients with any steatosis had significantly higher CRP levels, on average, compared with RA patients without steatosis (9.3 vs. 4.4 mg/L, respectively; p< 0.001). Rheumatoid factor was more frequent among RA patients with any steatosis (84 vs. 66%, respectively; p=0.01). However, steatosis was not associated with articular disease activity nor current use of corticosteroids, or biologic and non-biologic DMARDs, including methotrexate and leflunomide.

Conclusion: Hepatic steatosis was more frequent in RA compared with controls, even after adjusting for relevant confounders, and was linked with autoimmunity and systemic inflammation. Current use of DMARDs was not associ-

ated with hepatic steatosis. Prospective studies will help elucidate the consequences of increased hepatic steatosis in RA patients and define whether intervention is warranted.

Disclosure: J. Lee, None; **G. Lagos**, None; **J. Bathon**, None; **J. Giles**, Gilead, 5, Eli Lilly, 5, Bristol Myers Squibb, 5, Pfizer, 2.

Abstract Number: 0191

Increased Frequency of Lower Limb Arterial Obstruction in Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Despite a high frequency of cardiovascular disease in rheumatoid arthritis (RA), peripheral arterial disease in RA has received little attention. The objective of the present analysis was to examine the frequency of impaired lower limb arterial function in members of an RA cohort, compared to a control group without RA.

Methods: Patients meeting diagnostic criteria for RA were recruited consecutively from private and public rheumatology practices, from 1996 through 2011. For comparison, we studied participants in the Insulin Resistance and Atherosclerosis Study (IRAS), who were recruited from four clinical centers based on blood glucose tolerance status indicating normal glucose tolerance, impaired glucose tolerance, or diabetes mellitus. The clinical centers were in Los

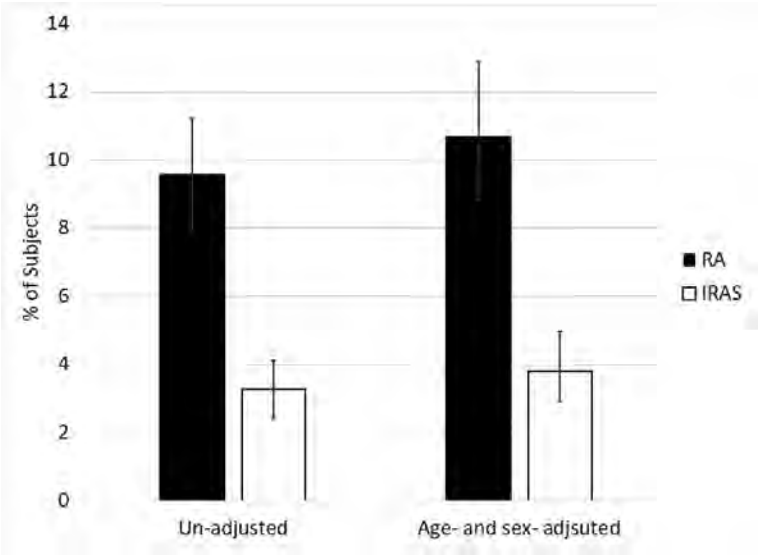

Figure. Unadjusted and adjusted frequency of obstructed ankle brachial index in rheumatoid arthritis and controls. Error bars represent 95% confidence intervals.

Angeles, Oakland, San Antonio and the San Luis valley in Colorado. The ABI was measured using a blood pressure cuff and a doppler ultrasound probe to measure the systolic blood pressure (SBP) in all four extremities. The ABI was calculated for each ankle provided as the ratio of highest SBP in the ankle to the highest SBP in the upper extremities. The ABI was considered obstructed if ≤0.9, normal if >0.9 but ≤1.3, and incompressible if >1.3. Logistic regression was used to compare the frequency of obstruction or incompressibility between RA and controls, adjusting for age, sex, smoking, diabetes mellitus and hypertension.

Results: We recruited 1328 RA patients, of whom 1182 had an ABI measurement. Their mean age was 58 (range 19-91), and 887 (75%) were women. They were compared to 1624 IRAS study participants, whose mean age was 55 (range 39-69), and 905 were women (55%). An obstructed ABI was present in 113 of the RA patients (9.56%), and in 53 of the IRAS participants (3.26%), odds ratio (OR) 3.09, CI 95% 2.18, 4.41, p< 0.0001. Adjusting for age, sex, smoking, diabetes and hypertension, the frequency of obstruction remained higher in the RA group with an OR of 3.74, CI 95% 2.5, 5.59, P < 0.0001. (Figure) An incompressible ABI was present in 183 of the RA patients (15.48%), and in 286 of the IRAS participants (17.6%), OR 0.92, CI 95% 0.75, 1.14. P 0.47. Multivariable adjustment did not alter the odds of incompressibility between the two groups.

Conclusion: Our findings suggesting an increased frequency of peripheral arterial obstruction in RA patients broadens the scope of cardiovascular morbidity in RA. The clinical significance of the increased frequency of peripheral arterial obstruction in RA deserves further study.Figure: Unadjusted and adjusted frequency of obstructed ankle brachial index in rheumatoid arthritis and controls. Error bars represent 95% confidence intervals.

Disclosure: A. Oglah, None; **A. Hussein**, None; **J. Restrepo**, None; **C. Lorenzo**, None; **A. Escalante**, None; **I. Del Rincon**, None.

Abstract Number: 0192

Influence of Inflammatory and Non-inflammatory Rheumatic Disorders on the Clinical and Biological Profile of Adult-onset Diabetes

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Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To compare the profile of adult-onset diabetes in patients with rheumatoid arthritis (RA) or osteoarthritis (OA), two chronic diseases leading to disability differing by their joint and systemic inflammation levels, and identify the disease characteristics associated with insulin resistance and metabolic control.

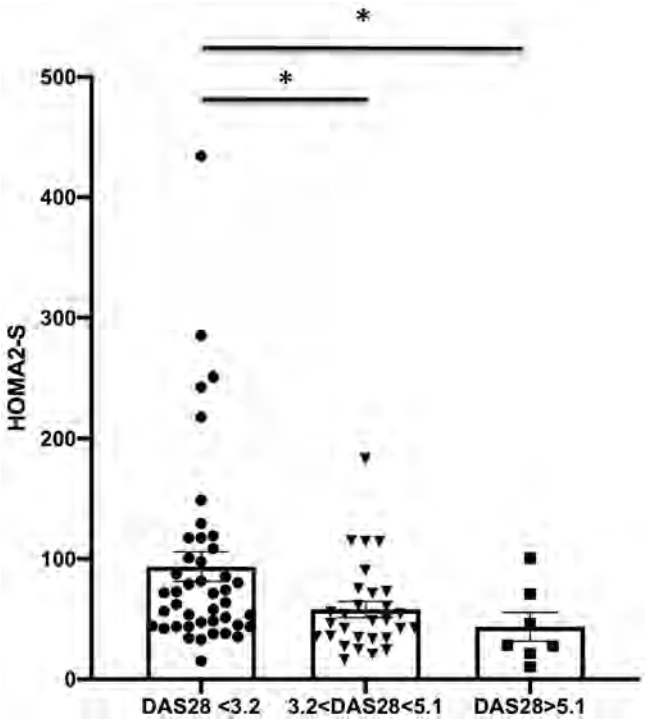


Figure 1. Insulin sensitivity assessed by the HOMA2-S according to the disease activity score (DAS)-28 HOMA2-S was evaluated in these subgroups after excluding patients with Latent Autoimmune Diabetes in Adults and T2D patients treated with insulin. Statistical test: Kruskal-Wallis test with Dunn correction, *p<0.05

Methods: Observational, multicenter, cross-sectional usual-care study, including 7 rheumatology centers. This study included over a 24-month period consecutive patients with type-2 diabetes (T2D) and RA, fulfilling the 2010 ACR / EULAR criteria, and diabetic patients with osteoarthritis (OA). The following data were collected: demographics, disease activity and severity indices, current treatment for RA and diabetes, history and complications of diabetes. A systematic blood test was performed, assessing inflammatory (CRP levels) and metabolic (fasting glycemia and insulin levels, HbA1c) parameters. The HOMA2%B (insulin secretion) and HOMA2%S (tissue insulin sensitivity) indices (HOMA calculator, © Diabetes Trials Unit, University of Oxford) were used to assess insulin resistance.

Results: We included 122 RA patients (74% women, mean age 64±11 years, mean disease duration 15±11 years, 75% with positive ACPA antibodies and 64% with erosive disease). 64% of RA patients were treated with oral corticosteroids < 10 mg/day, 65% received Methotrexate and 53% received targeted biological therapies. We recruited 54 diabetic controls (75% women) with OA (33 knee OA and 21 hip OA), who were significantly older (68.5±11.9 years, p=0.031) and had a significantly higher BMI (31.5±6.3 kg/m2 vs. 27.7±5.5 kg/m2, p< 0.001) than patients with RA.

OA and RA patients had severe T2D with suboptimal metabolic control (mean HbA1c: 7.3%±1.29% and 7.0% ± 1.19%, respectively) and a biological profile of insulin resistance.

Insulin resistance was significantly higher in RA than OA patients after stratification on age and body mass index (HOMA2-S: 69.4±31.6 vs. 98.4±69.2, p=0.002).

The DAS28 negatively correlated with HOMA2-S (r=-0.29, p=0.011) and patients with moderate or high disease activity, had significantly decreased HOMA2-S (Figure 1). In multivariate analysis, HOMA2-S was independently associated with DAS28 (OR: 3.93, 95% CI 1.02-15.06). T2D metabolic control was not related to disease activity and functional impairment, but HbA1c levels were independently associated with bone erosions (OR: 4.43, 95% CI 1.18-16.61). Treatment with low-dose corticosteroids was not associated with decreased insulin sensitivity or increased

HbA1c levels. Treatment with TNF-α inhibitors was associated with increased insulin sensitivity compared to patients not receiving biologics (101.3±58.71 vs. 60.0±32.5, p=0.001).

Conclusion: OA and RA patients with adult-onset diabetes display a clinical profile of severe T2D with suboptimal metabolic control. RA patients displayed a biological profile of insulin resistance associated with joint and systemic inflammatory inflammation. These findings may have therapeutic implications, with the potential targeting of insulin resistance through the treatment of joint and systemic inflammation.

Disclosure: J. Avouac, Bristol Myers Squibb, 2, 5, 8; **M. Elhai**, None; **M. Forien**, None; **J. Sellam**, None; **F. Eymard**, None; **A. Molto**, ABBVIE, 5, BMS, 5, 8, LILLY, 5, NOVARTIS, 5, 8, UCB, 5, 8, GILEAD, 5; **F. Banal**, None; **J. Damiano**, None; **P. Dieude**, None; **E. Larger**, None; **Y. Allanore**, None.

Abstract Number: 0193

Patients with Asthma Have a Higher Risk of Rheumatoid Arthritis: A Systematic Review and Meta-analysis

Nipith Charoenngam[1], Ben Ponvilawan[1], Thanitsara Rittiphairoj[1], Surapa Tornsatitkul[1], Phuuwadith Wattanachayakul[1], Pongprueth Rujirachun[1] and **Patompong Ungprasert**[2], [1]Mahidol University, Bangkok, Thailand, [2]Cleveland Clinic, Cleveland, OH, Cleveland Heights, OH

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Studies have reported the association between asthma and elevated risk of several chronic diseases, such as inflammatory bowel disease, diabetes mellitus and coronary heart disease. Additionally, there are data on the association between asthma and risk of rheumatoid arthritis (RA), although the results from existing studies are largely inconsistent. The current systematic review and meta-analysis was conducted in order to investigate whether patients with asthma have an increased risk of rheumatoid arthritis by identifying all available studies and summarizing their results together.

Methods: Potentially eligible studies were identified from Medline and EMBASE databases from inception to November 2019 using search strategy that comprised of terms for “Asthma” and “Rheumatoid arthritis”. Eligible cohort study must consist of one cohort of patients with asthma and another cohort of individuals without asthma. Then, the study must report relative risk (RR) with 95% confidence intervals (95% CIs) comparing incident RA between the groups. Eligible case-control studies must include cases with RA and controls without RA. Then, the study must explore their history of asthma. Odds ratio (OR) with 95% CIs of the association between RA and prior history of asthma must be reported. Point estimates with standard errors were retrieved from each study and were combined together using the generic inverse variance method of DerSimonian and Laird.

Results: A total of 21,824 articles were identified. After two rounds of independent review by three investigators, 5 cohort studies and 11 case-control studies met the eligibility criteria and were included into the meta-analysis. Patients with asthma had a significantly higher risk of incident RA compared with individuals without asthma with the pooled RR of 1.48 (95% CI, 1.20 – 1.82; I^2 92%).

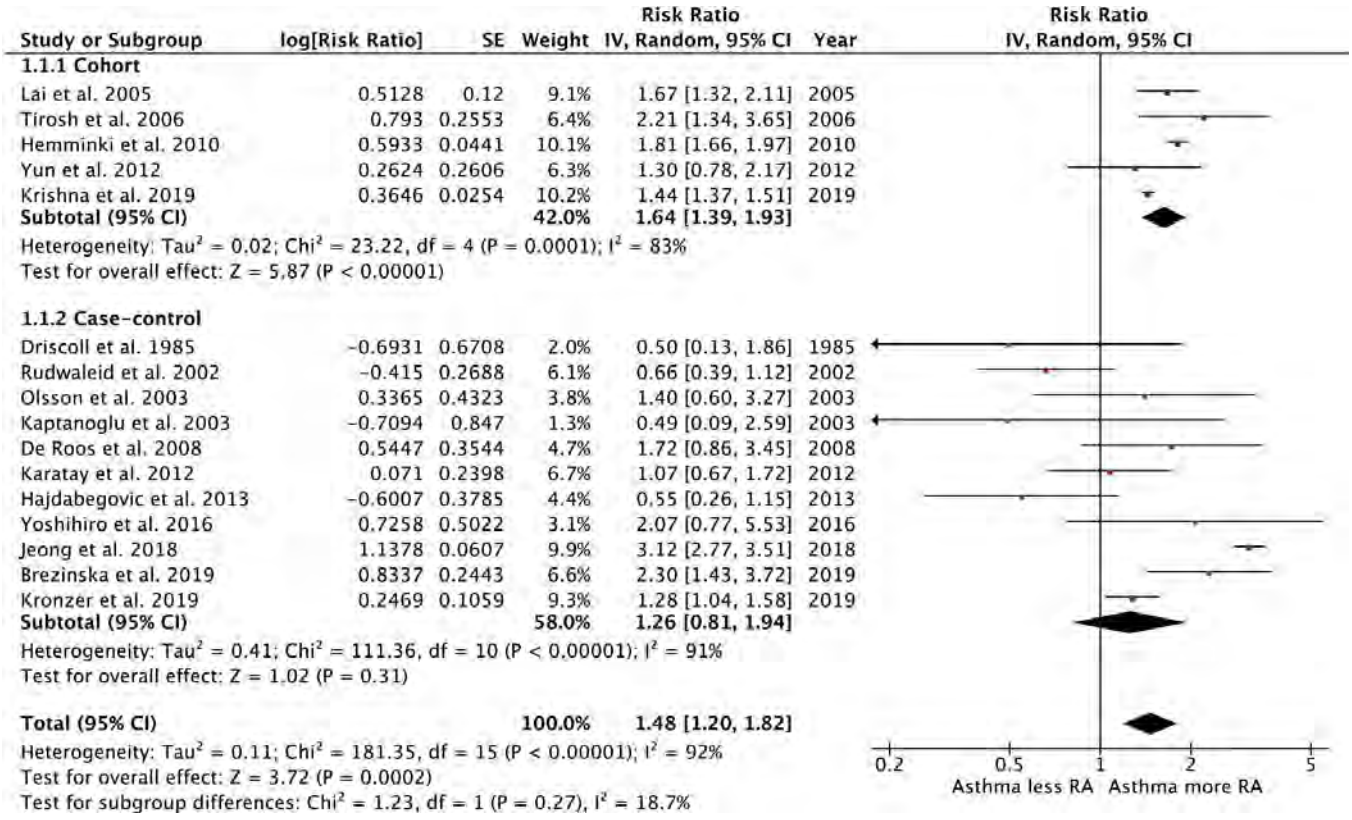


Figure 1. Forest plot of the meta-analysis of risk of RA in individuals with asthma versus individuals without asthma

Conclusion: This systematic review and meta-analysis found a significant association between asthma and a higher risk of incident RA.

Disclosure: N. Charoenngam, None; **B. Ponvilawan**, None; **T. Rittiphairoj**, None; **S. Tornsatitkul**, None; **P. Wattanachayakul**, None; **P. Rujirachun**, None; **P. Ungprasert**, None.

Abstract Number: 0194

Depression Symptoms but Not Clinically Diagnosed Depression Predict Mortality in Rheumatoid Arthritis

Jose Felix Restrepo[1], Inmaculada Del Rincon[1] and Agustin Escalante[1], [1]University of Texas Health Science Center at San Antonio/ Department of Medicine/ Rheumatology, San Antonio, TX

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Depression and depressive symptoms are common but under-recognized in rheumatoid arthritis (RA). Few studies have examined depression symptoms in RA patients compared to clinically diagnosed depression, and their role as mortality predictors. The objectives of the present study were to examine the prevalence

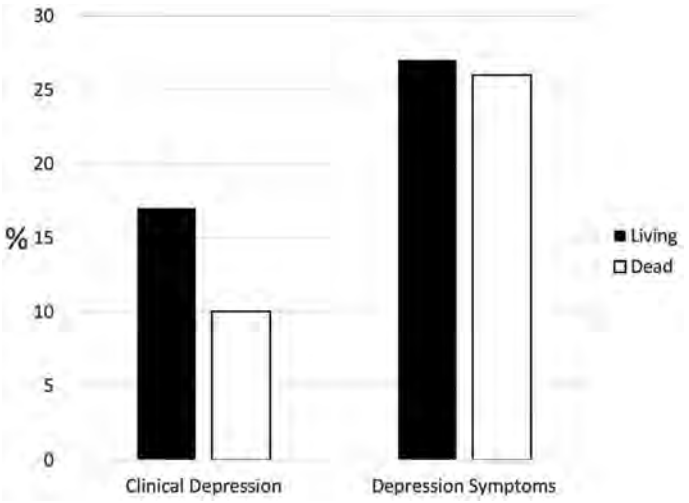


Figure. Significant depression symptoms were more frequent than clinically diagnosed depression in both patients who survived as well as in those who died (P < 0.001)

of depression symptoms compared to clinically diagnosed depression and to examine the association of depression with mortality in RA patients.

Methods: We studied a cohort of RA patients who met the 1987 classification criteria, recruited from 1996 through 2011. All underwent a comprehensive clinical and psychosocial evaluation using standardized instruments. Depressive symptoms were measured with the Center for Epidemiologic Studies Depression Scale (CESD), adjusted for RA (CESD-RA) by eliminating items that may overlap with symptoms of RA. We considered depression as present when the CESD score was ≥ 16. To quantify RA disease activity, we used the DAS28 ESR (DAS28). All deaths were confirmed with a death certificate. Multivariable logistic regression models were fit to examine the combined influence of independent variables on the outcome

Results: We studied 1328 RA patients, 981 of whom were women (74%). A clinical diagnosis of depression was found in the medical records of 220 patients (17%), significantly fewer than the 361 (27%) with significant depression symptoms on the CESD (P < 0.0001). There were 305 deaths during the study period. Of the patients who died, 31 had been diagnosed clinically with depression (10%), but 75 had significant depression symptoms on the CESD (26%). Patients with depression or significant depression symptoms were younger than patients without them, mean age 53 years (95% CI 52, 54) vs. 58 years (95% CI 57, 59), P < 0.0001, and more likely to be women, 82% vs. 69%, OR 1.97, (95% CI 1.48, 2.63), P < 0.0001. Patients with significant depression symptoms had greater disease activity than those without them, mean DAS28ESR 5.1 (95% CI 5.0, 5.3) vs. 4.0 (95% CI 3.9, 4.1), P < 0.001).

Logistic regression analysis adjusted for age and sex revealed that significant depression symptoms predicted all-cause mortality, OR 1.77 (95% CI 1.49, 2.12), P < 0.001, but clinically diagnosed depression did not.

Conclusion: Significant depression symptoms in RA are more frequent than depression diagnosed clinically, suggesting that some patients with depression may go undiagnosed. Depression symptoms predicted mortality in RA patients, while a clinical diagnosis of depression did not. Our findings suggest that strategies to improve the recognition of depression in RA should be studied further.

Disclosure: J. Restrepo, None; **I. Del Rincon**, None; **A. Escalante**, None.

Abstract Number: 0195

Epidemiology and Characteristics of Incident Rheumatoid Arthritis in Persons with and Without HIV

Jennifer Hanberg[1], Kathleen Akgun[2], Liana Fraenkel[3], Evelyn Hsieh[2] and Amy Justice[4], [1]Yale University School of Medicine; West Haven VA, Boston, MA, [2]Yale University School of Medicine; West Haven VA, New Haven, CT, [3]Yale School of Medicine; West Haven VA; Berkshire Medical Center, Lenox, MA, [4]Yale University School of Medicine; Yale School of Public Health; West Haven VA, West Haven, CT

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is the most common chronic inflammatory arthritis, affecting 1-2% of the population. Estimates of the incidence of RA in patients with HIV (PWH) are sparse, as are data regarding the presentation of RA in PWH.

Methods: Patients were selected from the Veterans Aging Cohort Study, a longitudinal cohort of Veterans with HIV and age, sex, race, and site-of-care-matched 1:2 to uninfected Veterans. Between 1997-2017, we searched all International Classification of Diseases (ICD) codes starting from each patient's first entry into the medical record, or in cases of PWH, from the time of diagnosis of HIV. We identified patients with ≥1 outpatient rheumatology clinic ICD code for RA and a positive or negative rheumatoid factor (RF) or anti-CCP antibodies. Charts were reviewed using the 2010 RA Classification Criteria; a score of ≥6 was classified as incident RA if there was no evidence of prior diagnosis, such as listing of RA as past medical history. We recorded conventional and biologic disease-modifying anti-rheumatic drug (DMARD) use, and reasons for changes in therapy during the first contiguous course of therapy (period with no interruption greater than 6 months).

Results: We included 56,250 PWH and 116,944 uninfected persons over 2,384,541 person-years. Of 2,748 patients with an ICD code for RA, 1,030 (37%) had at least one rheumatologist-generated ICD code and 881 (32%) had serology available. "Definite" incident RA was identified in 215 cases, 21 of whom were PWH at the time of RA diagnosis. The crude incidence of RA was 0.33 cases per 10,000 person-years (95% CI, 0.21-0.51) in PWH vs. 1.11 (0.96-1.28) in patients without. The incidence rate ratio of RA in PWH vs. uninfected was 0.29 (95% CI 0.19-0.48, p< 0.0001). Among PWH with incident RA, the median CD4 count closest to diagnosis was 487 cells/mm3 (25th-75th percentile, 367-650), and 81% of patients with recent HIV-1 viral titers available had levels less than 500 copies/mL. Most patients (88%) with incident RA were seropositive. However, high antibody titers were found less frequently in PWH: 5% of PWH had both a high (≥3 times upper limit of normal) anti-CCP titer and a high RF titer, compared to 41% of persons without HIV (Table). DMARDs were prescribed for 71% of PWH with "definite" RA, compared to 94% of uninfected Veterans (p=0.0002). The most commonly used DMARD among PWH was HCQ (57%) while methotrexate was more common in uninfected Veterans (66%). PWH were significantly less likely to be prescribed methotrexate (33% vs. 66%, p=0.004), leflunomide (0% vs. 12%, p=0.01), and biologic or small molecule drugs (10% vs. 32%, p=0.02).

Conclusion: Incident RA was less common in PWH than in matched uninfected persons. PWH with incident RA were less likely to have strongly positive autoantibody profiles than uninfected individuals.

		PWH (n=21)	Uninfected (n=194)	p-value
Serology (N (%))				
	Rheumatoid Factor			0.0002
	High positive	6 (29)	116 (60)	
	Low positive	5 (24)	47 (24)	
	Negative	9 (43)	19 (10)	
	Not tested	1 (5)	12 (6)	
	Anti-CCP			0.01
	High positive	5 (24)	116 (60)	
	Low positive	5 (24)	18 (9)	
	Negative	9 (43)	44 (23)	
	Not tested	2 (10)	16 (8)	
	Overall pattern			0.002
	Both (anti-CCP and RF) high positive	1 (5)	81 (42)	
	One high positive/ One low positive	2 (10)	31 (16)	
	Both low positive	1 (5)	4 (2)	
	One positive/ One negative	11 (52)	43 (22)	
	One positive/ One not nested	2 (10)	22 (11)	
	Seronegative	4 (19)	13 (7)	

Table: Anti-CCP and Rheumatoid Factor Serologies Were More Strongly Positive in Uninfected than in PWH with Incident RA. High positive was defined in accordance with the 2010 RA Classification Criteria as at least 3 times the upper limit of normal per the local laboratory value. Low positive was defined as a result greater than the upper limit of normal but less than 3 times this value, or an unquantified positive result.

Disclosure: J. Hanberg, None; **K. Akgun**, None; **L. Fraenkel**, None; **E. Hsieh**, None; **A. Justice**, None.

Abstract Number: 0196

Objectively-Measured Obstructive Sleep Apnea Is Frequent Among Individuals with Rheumatoid Arthritis

Stephanie Rush[1], Sarah Morsi[2], Jose Pinzón Tirado[2], Laura Trupin[2], Katie Stone[3] and Patricia Katz[4], [1]University of California, San Francisco, San Francisco, CA, [2]UCSF, San Francisco, CA, [3]California Pacific Medical Center Research Institute, San Francisco, CA, [4]University of California, San Francisco, Novato, CA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite frequent reports of sleep problems, accurate information on sleep disturbance in rheumatoid arthritis (RA) is not available. Studies using objective measures of sleep in RA are rare, but are needed to provide greater accuracy than classifications based on self-report. We examined the presence and severity of obstructive sleep apnea (OSA) using a validated home-monitoring device among Individuals with RA.

Methods: Data were from the RA Sleep Study, in which participants were recruited from an academic medical center and a safety-net hospital clinic. They completed in person visits and questionnaires every 6 months over an 18-month period and interviews were conducted in Spanish and English. All have physician-diagnosed RA; current use of a CPAP device was an exclusion criterion. At baseline, participants were provided with a WatchPAT™ device (Itamar Medical, Ltd) to wear for two consecutive nights at home. The WatchPAT™ is a validated diagnostic wrist-worn device which measures multiple channels of data (peripheral arterial tone, oximetry, actigraphy, heart rate and chest motion) with 3 points of contact (wrist, finger, and chest sensor). It yields estimates on a variety of measures, including the apnea-hypopnea index (AHI), reflecting the number of apnea or hypopnea episodes per hour of sleep. AHI was categorized as normal (< 5), mild OSA (5- < 15), moderate OSA (15-< 30), or severe OSA (≥30). The STOP-BANG questionnaire[1], a validated measure of OSA risk was also administered and physician diagnoses of OSA were queried. Potential predictors of the presence and severity of OSA were identified through chi-square test and analysis of variance with post-hoc means comparisons, and included age, sex, race/ethnicity (white non-Hispanic vs.

Table 1. Factors associated with obstructive sleep apnea severity

	AHI (apnea-hypopnea index)				
	Normal 0-5	Mild 5-15	Moderate 15-30	Severe >30	p
N, row percent	6 (10%)	22 (35%)	24 (38%)	11 (17%)	
Age	38.7 ± 5.9	55.7 ± 12.8	62.3 ± 10.0	61.0 ± 10.4	.0001
Female	5 (83.3)	18 (81.8)	18 (75.0)	9 (81.8)	.793
Race/ethnicity					
White, non-Hispanic	2 (33.3)	10 (45.5)	9 (37.5)	3 (27.3)	.512
All other groups	4 (66.7)	12 (54.6)	15 (62.5)	8 (72.7)	
Income below poverty	1 (20.0)	2 (10.0)	5 (23.8)	2 (18.2)	.603
Ever smoked	1 (16.7)	11 (50.0)	12 (50.0)	5 (45.5)	.460
BMI	26.2 ± 3.8	26.7 ± 3.5	28.7 ± 5.6,	33.4 ± 6.1	.003
Obese (BMI≥30)	1 (16.7)	5 (22.7)	9 (37.5)	8 (72.7)	.006
Morbid obesity (BMI≥35)	0 (0)	0 (0)	4 (16.7)	4 (36.4)	.003
Glucocorticoid Use	2 (33.3)	8 (36.4)	6 (25.0)	4 (36.4)	.831
RA Disease Activity Index (RADAI)	3.4 ± 1.8	3.5 ± 1.9	3.7 ± 2.0	3.1 ± 2.2	.858

Note: tabled values are mean ± SD or n (column %), unless specified.

Table 2. Report of physician-diagnosed OSA and risk of OSA from STOP-BANG questionnaire, by Apnea-hypopnea Index (AHI) Category

		AHI (apnea-hypopnea index)			
	Total	Normal (n=6)	Mild (n=22)	Moderate (n=24)	Severe (n=11)
			n (%)		
OSA diagnosed by doctor	9	0 (0)	1 (4.6)	4 (16.7)	4 (36.4)
High risk OSA (STOP-BANG)	13	0 (0)	4 (18.2)	4 (16.7)	5 (45.5)

all others), smoking, low income, BMI, obesity (BMI ≥ 30 kg/m^2), morbid obesity (BMI ≥ 35), glucocorticoid use, and self-reported RA disease activity (Rheumatoid Arthritis Disease Activity Index, RADAI).

Results: Participants (n=63) were 79% female, 38% white non-Hispanic, 16% low income and mean age was 58 ± 13 years. Using AHI, OSA was frequent: 35% had mild OSA, 38% moderate, and 17% severe. Participants with normal AHI were significantly younger, and those with severe OSA had significantly higher BMI (Table 1). Among 13 (21%) participants identified as high risk for OSA in the STOP-BANG questionnaire, 6 (10%) reported a physician's diagnosis of OSA. None of the participants with normal AHI had either a diagnosis of OSA or identified as high risk for OSA. (Table 2).

Conclusion: Some degree of sleep apnea was identified in 90% of this group of individuals with RA, with over half having moderate to severe OSA. Most OSA was unrecognized and would not be identified with current screening measures. OSA is linked to multiple health problems, including cardiovascular disease and fatigue, both of which are common in RA. Results highlight the importance of future objective studies of sleep as well as the importance of considering OSA as a risk factor for poor outcomes in RA.

[1]Chung F et al. Anesthesiology 2008; 108:812-21

Disclosure: S. Rush, None; **S. Morsi**, None; **J. Pinzón Tirado**, None; **L. Trupin**, None; **K. Stone**, None; **P. Katz**, None.

Abstract Number: 0197

The Clinical and Laboratory Features of Seronegative Rheumatoid Arthritis with and Without Malignancy

Misako Higashida-Konishi[1], Keisuke Izumi[2], Satoshi Hama[2], Hiroshi Takei[2], Yutaka Okano[3] and Hisaji Ohshima[2], [1]Department of Connective Tissue Diseases, National Hospital Organization Tokyo Medical Center, Meguro-ku, Tokyo, Japan, [2]Department of Connective Tissue Diseases, National Hospital Organization Tokyo Medical Center, Tokyo, Japan, [3]Department of Connective Tissue Diseases, National Hospital Organization Tokyo Medical Center, Kawasaki, Japan

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Table 1. Types of malignancy and time interval from seronegative RA to malignancy

Sex/Age, years old	Time interval from seronegative RA to malignancy, months	Type of Malignancy
M, 84	-20	Rectal cancer
F, 64	-17	Uterine cancer
M, 82	-6	Ascending colon cancer
M, 69	-5	Small cell lung cancer
F, 80	1	Breast cancer
M, 67	9	Diffuse large B cell lymphoma
F, 58	11	Esophageal cancer
F, 83	18	Pancreatic cancer

F, female; M, Male; RA, rheumatoid arthritis

Table 2. Baseline Characteristic of patients at the diagnosis of seronegative RA

Characteristic	With Malignancy (n = 8)		Without Malignancy (n = 116)		p
Mean age, years	73.4 ± 10.1		66.1 ± 14.8		0.18
Length of follow-up, mean, months	63.1 ± 43.9		68.3 ± 46.5		0.76
Male (%)	62.5		35.3		0.12
Smoking (%)	37.5		17.5		0.16
Diabetes (%)	25.0		17.4		0.60
Hypertension (%)	37.5		49.4		0.52
Hyperlipidemia (%)	57.1		40.3		0.39
Swollen and/or tender joints (%)					
Shoulders	37.5		55.2		0.33
Elbows	50.0		42.2		0.67
Wrists	87.5		80.2		0.61
Finger joints	100.0		96.5		0.59
Hips	12.5		10.3		0.85
Knees	50.0		47.4		0.89
Ankles	25.0		52.6		0.13
Toe joints	25.0		28.5		0.83
Number of large swollen joints, n	**0.6 ± 0.7**		**1.5 ± 1.4**		**0.04***
Number of small swollen joints, n	13.1 ± 5.4		10.0 ± 6.8		0.12
28 swollen joints, n	12.6 ± 6.3		9.4 ± 6.6		0.18
28 tender joints, n	12.8 ± 6.9		11.3 ± 5.8		0.70
Erosion (%)	50		29.3		0.22
Image findings					
Synovitis and tenosynovitis (%)	20.0		27.5		0.72
Only synovitis (%)	40.0		60.0		0.40
Only tenosynovitis (%)	**40.0**		**7.5**		**0.03***
Systemic signs and symptoms (%)					
Fever (≧ 38℃)	0		14.3		0.68
Malaise or fatigue	0		26.7		0.55
Weight loss	0		29.3		0.37
CRP, mg/dL	4.4 ± 3.8		4.3 ± 4.4		0.88
ESR, mm/h					
All patients	47.7 ± 40.3	(n=7)	61.8 ± 36.5	(n=115)	0.20
Male	69.3 ± 42.0	(n=4)	62.7 ± 38.6	(n=41)	0.78
Female	**19.0 ± 7**	(n=3)	**61.3 ± 35.6**	(n=74)	**0.02***
Alb, g/dL	3.8 ± 0.5		3.7 ± 0.6		0.86
IgG, mg/dL	1397.8 ± 871.6		1466.6 ± 435.2		0.36
Fibrinogen, mg/dL	548.5 ± 180.3		625.3 ± 246.9		0.69
LDH, U/L	174.0 ± 35.3		178.4 ± 35.2		0.57
MMP-3, ng/mL					
All patients	**120.8 ± 109.1**	(n=8)	**408.6 ± 564.9**	(n=82)	**0.04***
Male	173.1 ± 108.1	(n=5)	393.8 ± 393.6	(n=30)	0.29
Female	33.7 ± 7.3	(n=3)	417.1 ± 646.9	(n=52)	**0.03***
Hb, mg/dL					
All patients	11.5 ± 2.1	(n=8)	11.9 ± 1.8	(n=116)	0.51
Male	**10.2 ± 1.0**	(n=5)	**12.5 ± 1.6**	(n=41)	**0.005***
Female	**13.7 ± 1.3**	(n=3)	**11.6 ± 1.8**	(n=75)	**0.045***

Alb, albmin; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; IgG, immunoglodulin; LDH, lactate dehydrogenase; MMP-3, matrix metalloproteinase 3; RA, rheumatoid arthritis
*p<0.05

Background/Purpose: Patients with elderly onset rheumatoid arthritis(RA) have been reported to be less positive for RF(rheumatoid factor) and ACPA(anti-cyclic citrullinated peptide antibody), and have a higher risk of malignancy than young onset RA. The aim of this study was to investigate the relationship between seronegative RA and malignancy, and to examine the clinical and laboratory features of those with and without malignancy.

Methods: We retrospectively examined consecutive patients diagnosed with seronegative RA in our hospital from 2007 to 2019. Patients with seronegative RA were negative for both RF and ACPA and met the EULAR/ACR 2010 criteria. The patients who were diagnosed with remitting seronegative symmetrical synovitis with pitting edema syn-

Table 3. Baseline Characteristic of patients at the diagnosis of seronegative RA using a propensity score matching for sex

Characteristic	With Malignancy (n=8)	Without Malignancy (n=8)	p
Mean age, years	73.4 ± 10.1	65.9 ± 12.1	0.23
Male (%)	62.5	62.5	1.0
Number of large swollen joints, n	**0.5 ± 1.93**	**2.1 ± 1.9**	**0.04***
Number of small swollen joints, n	13.1 ± 5.4	8.4 ± 6.3	0.07
Image findings: Only tenosynovitis, n	2	0	0.11
CRP, mg/dL	4.4 ± 3.8	3.9 ± 5.0	0.46
ESR, mm/h	47.7 ± 40.3	52.0 ± 26.3	0.60
Alb, g/dL	3.8 ± 0.5	3.8 ± 0.5	0.92
IgG, mg/dL	1397.8 ± 871.6	2120.2 ± 511.1	0.12
Fibrinogen, mg/dL	548.5 ± 180.3	723.1 ± 264.5	0.43
MMP-3, ng/mL	120.8 ± 127.1	425.8 ± 127.1	0.07
Hb, mg/dL	11.5 ± 2.1	13.2 ± 1.7	0.07

Alb, albmin; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; Hb, hemoglobin; IgG, immunoglodulin; MMP-3, matrix metalloproteinase 3; RA, rheumatoid arthritis
*p<0.05

drome or polymyalgia rheumatica at first and then diagnosed with seronegative RA afterward were included in seronegative RA. The first analysis was performed on the affected joints, C-reactive protein(CRP), erythrocyte sedimentation rate(ESR), hemoglobin(Hb), albmin(Alb), immunoglobulin G(IgG), fibrinogen, lactate dehydrogenase(LDH), matrix metalloproteinase 3(MMP-3), image findings(ultrasound, X-ray, and MRI), and the history of malignancy 2 years before and after the diagnosis with seronegative RA. The affected joints were large joints(shoulders, elbows, hips, knees, and ankles), wrists, finger joints (MCP, and PIP joints), and toe joints (MTP and PIP joints). The secondary analysis was performed on the above evaluations with a propensity score (PS) matching for sex.

Results: In the first analysis, 124 patients with seronegative RA were enrolled. Eight patients had malignancies, and 116 patients did not have malignancy. Table 1 shows the types of malignancy. The median time for the diagnosis of malignancy was 10 months after the diagnosis of RA. Table 2 shows the baseline characteristics at the diagnosis of seronegative RA. The mean ages with and without malignancy were 73.4±10.1 and 66.1±14.8 years old, respectively(p= 0.18). Males were 62.5% and 35.3%(p=0.12). The mean numbers of large swollen joints were 0.6± 0.7, 1.5±1.4(p=0.04). There was no difference in the levels of CRP, ESR, Hb, Alb, IgG, fibrinogen, LDH between seronegative RA with and without malignancy. The levels of MMP-3 were 120.8±109.1 and 408.6±564.9 ng/mL(p=0.04). The patients with only tenosynovitis were 40.0% and 7.5%(p=0.03).

In the secondary analysis with PS, 8 patients with malignancy and 8 patients without malignancy were enrolled(Table 3). The mean numbers of large swollen joints were 0.6± 0.7, 1.5±1.4(p=0.04). The mean levels of MMP-3 were 120.8±127.1 and 425.8±127.1 ng/mL (p=0.07).

Conclusion: In seronegative RA, the patients with malignancy had lower levels of MMP-3 and fewer numbers of large swollen joints at the time of RA diagnosis than those without malignancy. The patients with only tenosynovitis were

more common in the patients with malignancy than in those without malignancy. Furthermore, among seronegative RA patients, it was considered that the patients with lower levels of MMP-3 and fewer numbers of large swollen joints should pay attention especially to the complication of malignancy.

Disclosure: M. Higashida-Konishi, None; **K. Izumi**, Asahi Kasei Pharma, 9, Astellas Pharma, 8, Bristol Myers Squibb, 8, Chugai Pharmaceutical, 8, Eli Lilly Japan, 8, Mitsubishi Tanabe Pharma, 8; **S. Hama**, None; **H. Takei**, None; **Y. Okano**, None; **H. Ohshima**, None.

Abstract Number: 0198

A Prospective Cohort Study of Vehicle Control as a Measure of Driving Performance in Patients with Rheumatoid Arthritis

Kaleb Michaud[1], Jennifer Merickel[1], Yeongjin Gwon[1], Harlan Sayles[1], Haley Kampschnieder[1], Rebecca Hiebert[1], Alison Petro[1], Bryant England[1], Matthew Rizzo[1] and Ted Mikuls[1], [1]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster I: Multimorbidity
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Automobile driving is an instrumental activity of daily living. Owing to symptoms and functional impairment, patients with rheumatoid arthritis (RA) rely disproportionately on driving for the preservation of health, well-being, and quality of life[1]. To date, there have been no rigorously designed prospective studies examining driving performance in patients with RA. This prospective cohort study compared variability in longitudinal (acceleration/braking) and lateral (steering) vehicle acceleration as measures of vehicle control between drivers with RA and healthy controls (HC).

Methods: Patients with RA were recruited from an academic rheumatology practice and were required to have at least one swollen joint and a CDAI score ≥6 to participate. HCs were recruited using advertisements and a pool of

Table 1 – Subject Characteristics

	RA (n = 33)	Healthy Controls (n = 23)
Driving segments, total	166,156	66,382
Age, mean (SD)	57 (14)	62 (13)
Sex, n (%)		
Male	11 (33)	10 (43)
Female	22 (67)	13 (57)
Race/Ethnicity (%)		
Non-Hispanic White	26 (90)	22 (96)
Other	7 (10)	1 (4)
HAQ-II Score, mean (SD)	1.66 (0.51)	-
CDAI Score, mean (SD)	18.1 (8.6)	-
CDAI Category, n (%)		
Low	7 (21)	-
Moderate	15 (45)	
High	11 (33)	

*HAQ-II = Health Assessment Questionnaire-II; CDAI = Clinical Disease Activity Index

Table 2 – Univariate Analysis of Associations with Vehicle Control*

Variable	SD Lateral (Steering) Acceleration		SD Longitudinal (Forward/Braking) Acceleration	
	Estimate	**P-value**	**Estimate**	**P-value**
RA vs. HC	-0.005	0.2558	**-0.013**	**<0.001**
CDAI category Low Moderate High	 Ref. **-0.001** **-0.005**	 — **0.002** **<0.001**	 Ref. **0.001** **0.001**	 — **0.003** **0.019**
Study Period (2 vs. 1)	**0.005**	**<0.001**	0.0002	0.458
Season (Winter vs. Other)	**0.002**	**<0.001**	**-0.001**	**<0.001**
Mean speed (per mph)	**-0.001**	**<0.001**	**-0.0005**	**<0.001**

*Significant associations shown in bold; CDAI = Clinical Disease Activity Index; RA = rheumatoid arthritis; HC = healthy controls; mph = miles per hour

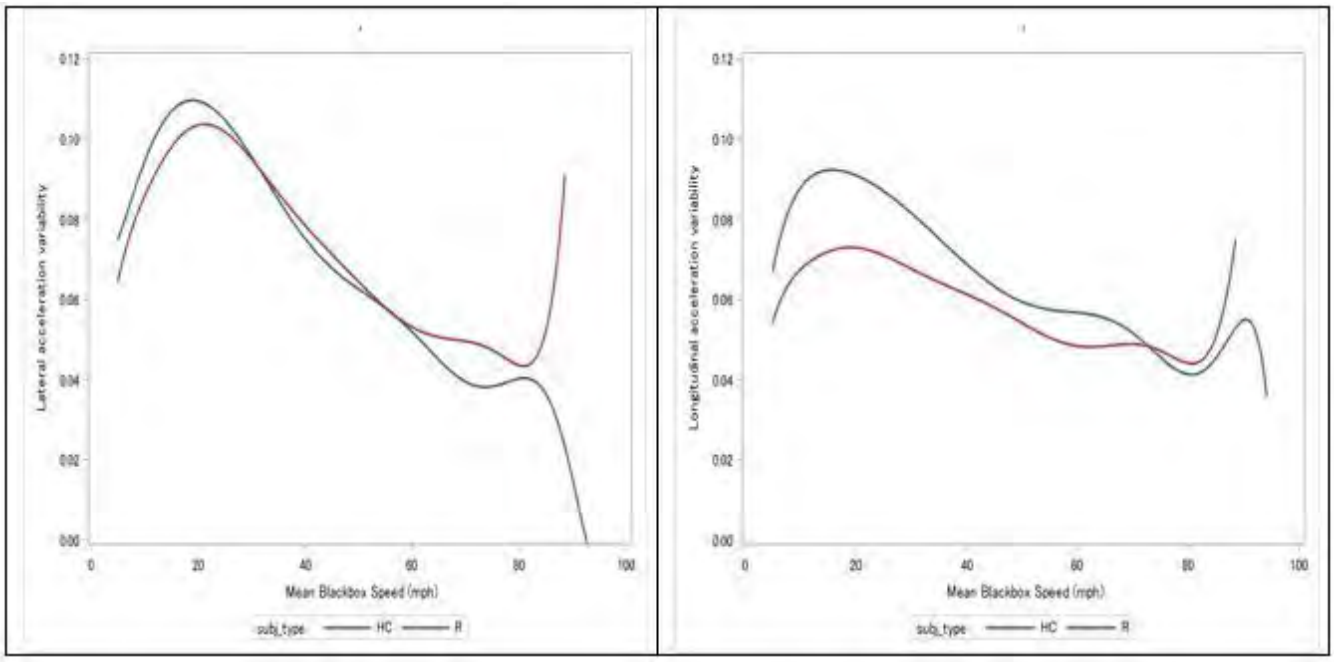


Figure 1. Plot of variability in lateral (left panel) and longitudinal (right panel) acceleration by vehicle speed

local study volunteers. Data collection occurred over 2, 4-week periods (separated by 2 months) of continuous naturalistic driving observation. Driving data were collected using instrumentation installed in participants' own vehicles, collecting video, audio, GPS, speed, acceleration and engine data. Data were aggregated into 45-second segments (from start-to-end) of uninterrupted driving. Segments with >20 seconds of missing data or mean speeds < 5 mph were excluded. Associations of disease status (RA vs. HC) and disease activity (CDAI score, RA only) with acceleration variability (standard deviations, SDs) were examined using mixed-effect linear regression models, accounting for between-patient variability.

Results: Characteristics of RA and HC subjects are shown in **Table 1**. There were 232,538 driving segments (2,906 driving hours) analyzed. Factors associated with variability in longitudinal and lateral acceleration included RA disease status, higher disease activity in RA, study period, season, and mean vehicle speed (**Table 2, Figure 1**). Increases in disease activity between periods 1 and 2 tended to produce more erratic braking/accelerating (increased longitudinal variability; estimate = 0.0004; p = 0.05) without affecting steering.

Conclusion: To our knowledge, this is the first study quantifying naturalistic driving in the real world in patients with RA. These results link RA and heighted arthritis disease activity with aberrant vehicle control. Specifically, increased RA disease activity reduces steering variability while simultaneously increasing erratic/harsh braking and accelerating. These findings support the need for further research to map these observed patterns in vehicle control to metrics of driver risk, and, in turn, to link patterns of real world driving behavior to diagnosis and disease activity.

1. Vrkljan BH et al. Supporting safe driving with arthritis: developing a driving toolkit for clinical practice and consumer use. Am J Occup Ther. 2010;64(2):259-67.

Disclosure: K. Michaud, Rheumatology Research Foundation, 2; **J. Merickel**, None; **Y. Gwon**, None; **H. Sayles**, None; **H. Kampschnieder**, None; **R. Hiebert**, None; **A. Petro**, None; **B. England**, None; **M. Rizzo**, None; **T. Mikuls**, Horizon Therapeutics, 2.

Abstract Number: 0199

A Phase 1, Randomized, Open-label, Parallel Group, Single-dose Study to Compare the Pharmacokinetics and Safety of the Auto-injector and Pre-filled Syringe of CT-P17, a Proposed, Higher Concentration Biosimilar (100 mg/mL) Adalimumab, in Healthy Subjects

Edward C Keystone[1], **Daniel Furst***[2], Jonathan Kay[3], EunJin Choi[4], Antonia Davidson[5], YunJu Bae[4], Darin Brimhall[6], SangJoon Lee[4], SungHyun Kim[4] and DaHye Kwak[4], [1]Mount Sinai Hospital, Toronto, ON, Canada, [2]Department of Medicine, Division of Rheumatology, University of California at Los Angeles, Los Angeles, California, USA, Los Angeles, CA, [3]University of Massachusetts Medical School, Worcester, MA, [4]Celltrion, Inc., Incheon, Republic of Korea, [5]PPD Development, Austin, TX, [6]PPD Development, Las Vegas, NV

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: CT-P17 is a recombinant human monoclonal antibody that was developed as the first biosimilar adalimumab with high concentration (100 mg/mL) and citrate-free formulation. The purpose of this study was to compare the pharmacokinetics (PK), safety, and immunogenicity of the CT-P17 auto-injector (AI) and CT-P17 pre-filled syringe (PFS) after a single subcutaneous (SC) injection of 40 mg (100 mg/mL) in healthy subjects.

Methods: Healthy subjects aged 18 to 55 years (N=193) were randomized in 1:1 (98 subjects in the CT-P17 AI and 95 subjects in the CT-P17 PFS treatment groups) to receive 40 mg of either CT-P17 by AI or PFS. The primary objective of this study was to demonstrate PK similarity in terms of area under the serum concentration-time curve (AUC) from time zero to infinity (AUC0-inf), AUC from time zero to the last quantifiable concentration (AUC0-last), and maximum

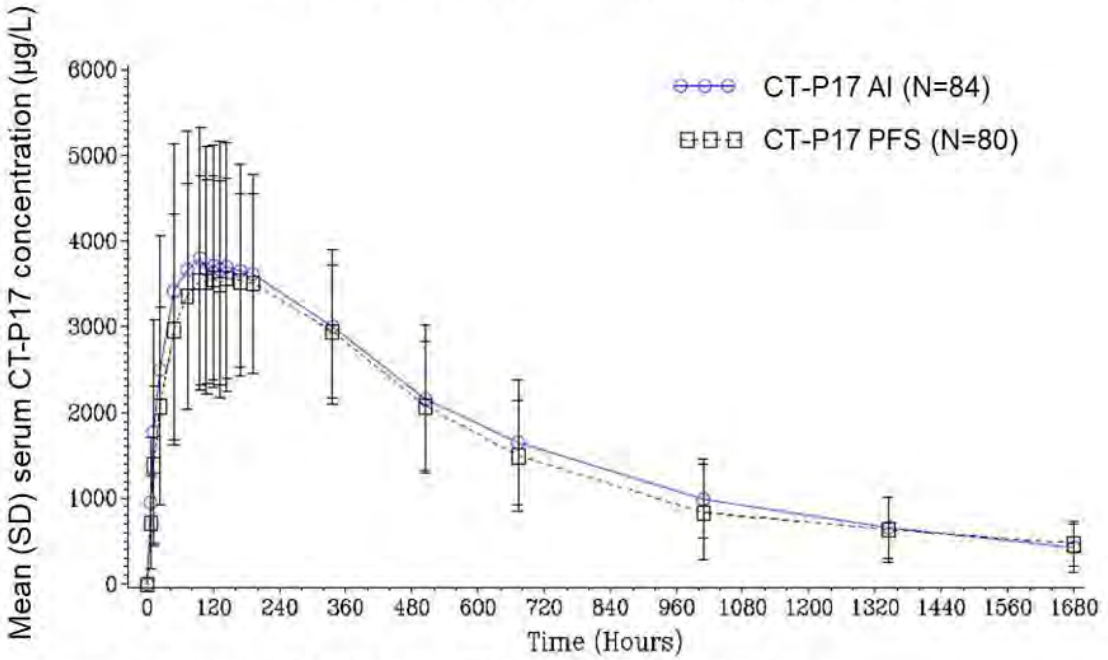
Table 1 Statistical Analysis of the Primary PK Endpoints (Pharmacokinetic Population)

Parameter (units)	Treatment	gLSM	Ratio of gLSMs (90% CI)[a]	P-value[a]
C_{max} (µg/mL)	CT-P17 AI CT-P17 PFS	3.801 3.705	102.60 (94.08–111.90)	0.6244
AUC_{0-inf} (h·µg/mL)	CT-P17 AI CT-P17 PFS	2,606.4 2,514.8	103.64 (93.98–114.29)	0.5459
AUC_{0-last} (h·µg/mL)	CT-P17 AI CT-P17 PFS	2,110.7 2,003.4	105.36 (91.09–121.86)	0.5537

Abbreviations: AI, auto-injector; ANCOVA, analysis of covariance; AUC_{0-inf}, area under the concentration–time curve from time zero to infinity; AUC_{0-last}, area under the concentration–time curve from time zero to the last quantifiable concentration; CI, confidence interval; C_{max}, maximum serum concentration; gLSM, geometric least squares mean; PFS, pre-filled syringe; PK, pharmacokinetic.

[a]Determined by ANCOVA performed with the natural log-transformed PK parameters as the dependent variable, treatment as a fixed effect and stratification factors (sex [male versus female], study center and Day –1 body weight) as covariates.

Figure 1 Mean (± SD) Serum Concentrations of CT-P17 for CT-P17 AI and CT-P17 PFS (Pharmacokinetic Population)



Abbreviations: AI, auto-injector; PFS, pre-filled syringe; PK, pharmacokinetic; SD, standard deviation.

[a]Six and seven subjects in the CT-P17 AI and CT-P17 PFS treatment groups, respectively, were excluded due to absence of ≥1 post-treatment serum concentration above the lower limit of quantification for CT-P17 and ≥3 time points following C_{max}. Three subjects (CT-P17 AI) were excluded due to major protocol deviations (whole volume of study drug was not administered successfully [n=2] and dosing with morphine in a previous clinical study [n=1]).

Figure 1. Trial profile. The SHR0302 8 mg group was added in protocol v2.0 to explore the maximum safe and effective dose according to latest preclinical data. AE, adverse events; INV, investigator; PD, progressive disease; DC, discontinuation.

serum concentration (Cmax) of CT-P17 via AI versus CT-P17 via PFS in healthy subjects. Secondary objectives were to evaluate additional PK parameters, safety and immunogenicity.

Results: Demographics and baseline characteristics were similar between the 2 treatment groups. Following a single SC administration of CT-P17 via AI in healthy subjects, mean peak and total systemic exposure (Cmax, AUC0-inf, and AUC0-last) were equivalent with those of CT-P17 via PFS, since the 90% CIs of the geometric least squares mean

Table 2 Summary of Adverse Events (Safety Population)

	CT-P17 AI (N=93)	CT-P17 PFS (N=87)
Subjects with ≥1 TEAE, n (%)[a]	56 (60.2)	45 (51.7)
Grade 1	44 (47.3)	39 (44.8)
Grade 2	10 (10.8)	6 (6.9)
Grade 3	2 (2.2)[b]	0
Subjects with ≥1 TESAE, n (%)	2 (2.2)[b]	0
Subjects with ≥1 TEAE due to hypersensitivity/allergic reactions, n (%)[c]	3 (3.2)	1 (1.1)
Subjects with ≥1 TEAE due to ISR, n (%)[d]	8 (8.6)	6 (6.9)
Subjects with ≥1 TEAE due to infection, n (%)	10 (10.8)	6 (6.9)
Serious infection	1 (1.1)[e]	0

Abbreviations: AI, auto-injector; ISR, injection site reaction; PFS, pre-filled syringe; SAE, serious adverse event; TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

[a]No subjects experienced TEAEs led to study drug discontinuation or death or TEAEs due to malignancy.
[b]The TESAEs were viral meningitis and rhabdomyolysis; both were grade 3 in intensity and considered related to study drug. Both subjects recovered and completed the study. These were the only grade ≥3 TEAEs reported.
[c]All TEAEs classified as hypersensitivity/allergic reactions were considered study drug-related and were Grade 1–2 in intensity.
[d]All TEAEs classified as ISR were considered study drug-related and were Grade 1 in intensity.
[e]Grade 3 viral meningitis (n=1) reported as a TESAE

ratios were within the predefined equivalence margin of 80% to 125% (Table 1). Median Tmax occurred at 132 hours for both treatment groups. Means of secondary PK parameters (t1/2, λz, CL/F, Vz/F and %AUCextrap) were also comparable between the treatment groups.

Mean serum CT-P17 concentrations observed through 71 days post-dose were comparable between the treatment groups (Figure 1).

Overall, 56 (60.2%) and 45 (51.7%) subjects reported ≥1 treatment-emergent adverse event (TEAE) in the CT-P17 AI and CT-P17 PFS treatment groups, respectively (Table 2). TEAEs considered to be related to study drug were reported by 47 (50.5%) and 38 (43.7%) subjects, respectively. The most frequently reported TEAEs were headache (11 [11.8%] and 8 [9.2%] subjects) and injection site reactions (8 [8.6%] and 6 [6.9%] subjects) in the CT-P17 AI and CT-P17 PFS treatment groups, respectively).

Overall, 91 (97.8%) and 85 (97.7%) subjects in the CT-P17 AI and CT-P17 PFS treatment groups, respectively, had ≥1 positive result post-treatment for anti-drug antibodies (ADA) and 81 (87.1%) and 75 (86.2%) subjects, respectively, had ≥1 positive result post-treatment for neutralizing ADA. ADA titers were similar between the treatment groups. In both treatment groups, higher ADA titers were significantly associated with decreased AUC0-inf and AUC0-last (Fisher's z transformation; p-value <0.0001). Cmax did not correlate significantly with ADA titer.

Conclusion: Mean peak and total exposure were equivalent following administration of high concentration formulation CT-P17 via AI or PFS. Secondary PK parameters and safety, including immunogenicity, were also comparable between the two delivery methods.

Disclosure: E. Keystone, AbbVie, 2, 5, 8, Celltrion, 2, 5, 8, Eli Lilly, 2, 5, 8, Pfizer Inc, 2, 5, 8, Merck, 2, 5, 8, Sandoz, 2, 5, 8, Samsung Bioepsis, 2, 5, 8, Myriad Autoimmune, 2, 5, 8, Purapharm, 2, 5, 8, Janssen, 2, 5, 8, Sanofi-Genzyme, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, F. Hoffman-La Roche Ltd., 2, 5, 8, Genentech, 2, 5, 8, Gilead, 2, 5, 8, UCB, 2, 5, 8; **D. Furst***, Actelion, 1, 2, Amgen, 1, 2, BMS, 1, Corbus, 1, 2, Galapagos, 1, 2, GSK, 1, NIH, 1, Norvatis, 1, 2, Pfizer, 1, 2, Sanofi, 1, Roche/Genentech, 1, Gilead, 1, Horizon, 1, 2, Kadmon, 1, Talaris, 1, 2, CMC Connect (McCann Health Company), 8, Cytori, 5, AbbVie, 5; **J. Kay**, Pfizer Inc., 9, Alvotech Suisse AG, 1, Arena Pharmaceuticals, Inc., 1, Boehringer Ingelheim GmbH, 1, Celltrion Healthcare Co. Ltd., 1, Mylan Inc., 5, Novartis AG, 5, Samsung Bioepis, 5, Sandoz Inc., 5, Gilead Sciences, Inc., 9; **E. Choi**, Celltrion, Inc., 1; **A. Davidson**, None; **Y. Bae**, CELLTRION, Inc., 1; **D. Brimhall**, None; **S. Lee**, Celltrion, Inc., 1; **S. Kim**, Celltrion, Inc., 1; **D. Kwak**, Celltrion, Inc, 1.

Abstract Number: 0200

Predictors of Durable Clinical Response to Tofacitinib 11 Mg Once Daily with or Without Methotrexate in Patients with Rheumatoid Arthritis: Post Hoc Analysis of Data from a Phase 3b/4 Methotrexate Withdrawal Study

Kunihiro Yamaoka[1], Stanley B Cohen[2], Naonobu Sugiyama[3], Harry Shi[4], Jose L Rivas[5], Annette Diehl[4] and Josef Smolen[6], [1]Kitasato University School of Medicine, Sagamihara, Kanagawa, Japan, [2]Metroplex Clinical Research Center, Dallas, TX, [3]Pfizer Japan Inc, Tokyo, Japan, [4]Pfizer Inc, Collegeville, PA, [5]Pfizer SLU, Madrid, Spain, [6]Division of Rheumatology, Department of Medicine III, Medical University of Vienna, Vienna, Austria

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: ORAL Shift, a global Phase 3b/4 non-inferiority study, demonstrated sustained efficacy/safety of tofacitinib modified-release (MR) 11 mg QD following MTX withdrawal in patients (pts) with RA who achieved CDAI low disease activity (LDA) after treatment with tofacitinib + MTX.[1] Here, we assessed predictors of durable clinical response in pts receiving tofacitinib MR 11 mg QD in ORAL Shift.

Methods: ORAL Shift (NCT02831855) enrolled pts aged ≥ 18 years with moderate to severe RA and an inadequate response to MTX. Pts received open-label (OL) tofacitinib MR 11 mg QD + MTX for 24 weeks. Pts achieving LDA (CDAI score ≤ 10) at W24 entered the 24-week double-blind (DB) MTX withdrawal phase and were randomized 1:1 to receive tofacitinib MR 11 mg QD + placebo (PBO) (tofacitinib monotherapy; ie blinded MTX withdrawal) or continue tofacitinib + MTX. In this post hoc analysis of randomized pts, we assessed predictors of durable response (maintenance of response from W24–48) per CDAI LDA and remission criteria (CDAI score ≤ 2.8). All covariates were initially assessed for significance in a univariate logistic regression. Highly correlated covariates were reviewed to assess which would be removed prior to modeling in a multivariable logistic regression. Remaining significant ($p \leq 0.10$) covariates in the univariate regression were selected in the model using a stepwise selection process with $p \leq 0.15$ entry and $p \leq 0.05$ stay criteria. From the final model, estimated odd ratios (ORs) with 95% confidence intervals (CIs) are presented.

Results: In the DB phase of ORAL Shift, durable CDAI LDA and remission rates were: 66.2% and 14.7%, respectively, with tofacitinib + MTX (N=266); and 55.3% and 11.0%, respectively, with tofacitinib + PBO (N=264) (Table). In the

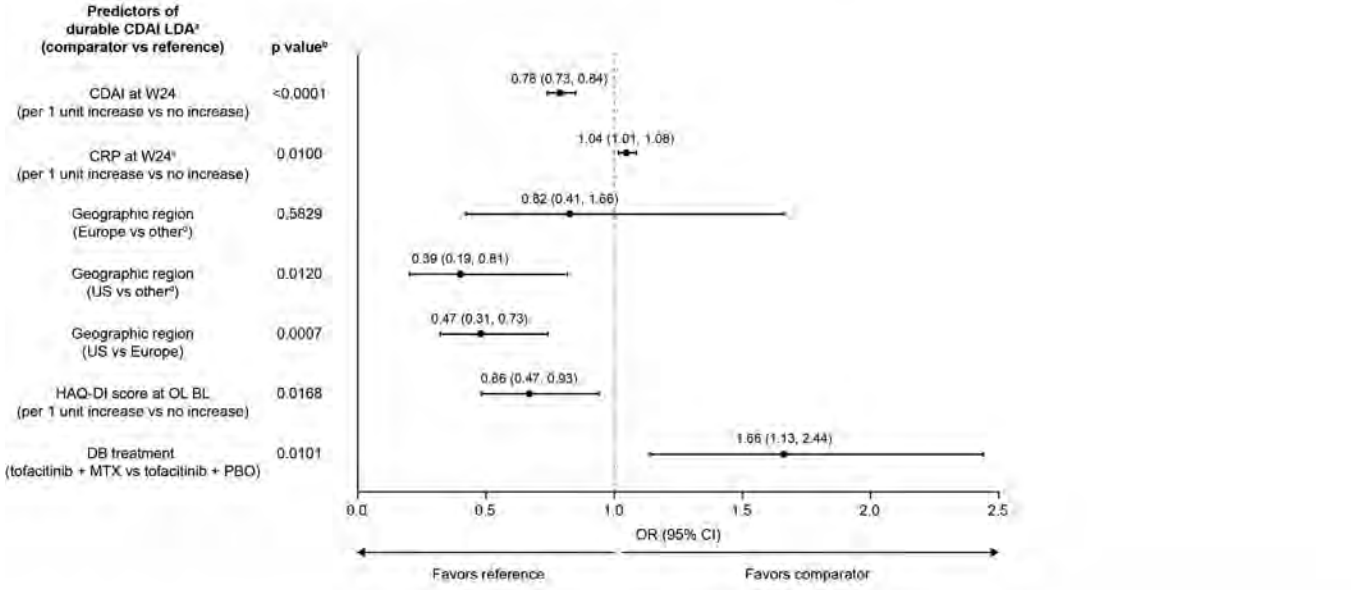
Table. Durable CDAI LDA and remission[a] in pts receiving tofacitinib MR 11 mg QD with MTX or PBO in the DB phase of ORAL Shift

	Tofacitinib + MTX (N=266)	Tofacitinib + PBO (N=264)
Durable CDAI LDA, n (%)	176 (66.2)	146 (55.3)
Durable CDAI remission, n (%)	39 (14.7)	29 (11.0)

[a]Durable CDAI LDA or remission was defined as achievement of LDA (CDAI score ≤10) or remission (CDAI score ≤2.8), respectively, at W24-48

CDAI, Clinical Disease Activity Index; DB, double-blind; LDA, low disease activity; MTX, methotrexate; MR, modified-release; N, number of patients in each group; n, number of patients achieving outcome; PBO, placebo; pts, patients; QD, once daily; W, week

Figure. Multivariable regression results for predictors of durable CDAI LDA[a] in pts receiving tofacitinib MR 11 mg QD with MTX or PBO in the DB phase of ORAL Shift



[a]Durable CDAI LDA was defined as achievement of LDA (CDAI score ≤10) at W24-48; [b]The Wald chi squared test p value for that comparison; [c]Mean CRP levels at W24 (randomization) were 25.6% higher in the tofacitinib + MTX group (mean CRP=5.05 mg/L) vs tofacitinib + PBO group (mean CRP=4.02 mg/L). During the DB phase, CRP stabilized with tofacitinib + MTX but increased with tofacitinib + PBO. The CRP differences between treatment groups may have impacted the CDAI LDA durability outcome; [d]'Other' refers to Australia, Korea, Philippines, Mexico, and South Africa

BL, baseline; CDAI, Clinical Disease Activity Index; CI, confidence interval; CRP, C-reactive protein; DB, double-blind; HAQ DI, Health Assessment Questionnaire-Disability Index; LDA, low disease activity; MR, modified-release; MTX, methotrexate; OL, open-label; OR, odds ratio; PBO, placebo; pts, patients; QD, once daily; US, United States; W, week

multivariable analysis, five pt covariates significantly predicted durable CDAI LDA (Figure; discussed hereafter). Each unit increase in CDAI score at W24 reduced the likelihood of maintaining CDAI LDA by 22.0%. Each unit increase in CRP at W24 increased the likelihood of maintaining CDAI LDA by 4.0%; this may have been due to imbalanced CRP levels at W24 (randomization) between treatment groups (Figure, footnote d). The odds of durable CDAI LDA were 53.0% lower in the US vs Europe and 61.0% lower in the US vs 'other' regions. Each unit increase in baseline (BL)

HAQ-DI score reduced the odds of durable CDAI LDA by 34.0%. Pts receiving tofacitinib + MTX had 66.0% greater odds of durable CDAI LDA vs pts receiving tofacitinib + PBO. CDAI at W24 was the only significant predictor of durable CDAI remission in the multivariable analysis: OR (95% CI) 0.32 (0.24, 0.43); p< 0.0001. Each unit increase in CDAI score at W24 reduced the odds of durable CDAI remission by 68.0%.

Conclusion: This post hoc analysis of data from ORAL Shift found that CDAI and CRP at W24, geographic region, BL HAQ-DI, and treatment could be predictors for durable CDAI LDA. As the findings of this post hoc analysis were limited to pts who achieved CDAI LDA at W24 with tofacitinib MR 11 mg QD + MTX, additional data in the general pt population need to be investigated.

1.Cohen SB et al. Lancet Rheumatol 2019; 1: E23-E34.

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Disclosure: K. Yamaoka, AbbVie, 2, 5, 8, Astellas, 2, 5, 8, Bristol-Myers Squibb, 8, Mitsubishi Tanabe, 2, 5, 8, Pfizer Inc, 2, 5, 8, Takeda, 5, 8, Actelion, 5, 8, Chugai, 2, 5, 8, Eisai, 2, 5, 8, Eli Lilly, 2, 5, 8, GlaxoSmithKline, 5, 8, Janssen, 5, 8, Nippon Shinyaku, 5, 8, Daiichi Sankyo, 2, 8, Teijin Pharma, 2, Merck Sharp & Dohme, 2, 8, Shionogi, 2, Nippon Kayaku, 2, 8, Takeda Industrial Pharma, 2, 8, Asahikasei Pharma Corp, 5, 8, Gilead G. K., 5, 8, Eli Lilly Japan K. K., 5, Japan Tobacco Inc., 5, Actelion Pharmaceuticals Japan, 8, Ono Pharma, 8, Otsuka Pharma, 8, Boehringer Ingelheim Japan, 8, Hisamitsu Pharma Co., 8, Sanofi, 8, AYUMI Pharma Co., 8; **S. Cohen**, AbbVie, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Gilead, 2, 5, Pfizer Inc, 2, 5; **N. Sugiyama**, Pfizer Japan Inc, 1, 3; **H. Shi**, Pfizer Inc, 1, 2; **J. Rivas**, Pfizer Inc, 1, 3; **A. Diehl**, Pfizer Inc, 1, 3; **J. Smolen**, AbbVie, 2, 5, 8, AstraZeneca, 2, 5, 8, Eli Lilly, 2, 5, 8, Celgene, 5, 8, Celltrion, 5, 8, Chugai, 5, 8, Gilead, 5, 8, ILTOO, 5, 8, Janssen, 5, 8, Kabi, 5, 8, Novartis-Sandoz, 5, 8, Pfizer Inc, 5, 8, Samsung, 5, 8, Sanofi, 5, 8.

Abstract Number: 0201

A Multicenter, Randomized, Placebo-controlled, Double-blind Phase 2 Study of SHR0302 versus Placebo in Chinese Subjects with Moderate to Severe Active Rheumatoid Arthritis (RA)

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Proinflammatory cytokine activation of JAK/STAT signal pathway is critical in the pathogenesis and progression of RA. SHR0302, a potent and selective inhibitor of JAK1, demonstrated promising anti-inflammatory effects for RA in both preclinical and phase 1 studies. A multicenter, randomized, placebo-controlled, double-blind phase 2 study was performed to evaluate the efficacy and safety of SHR0302 in Chinese subjects with RA.

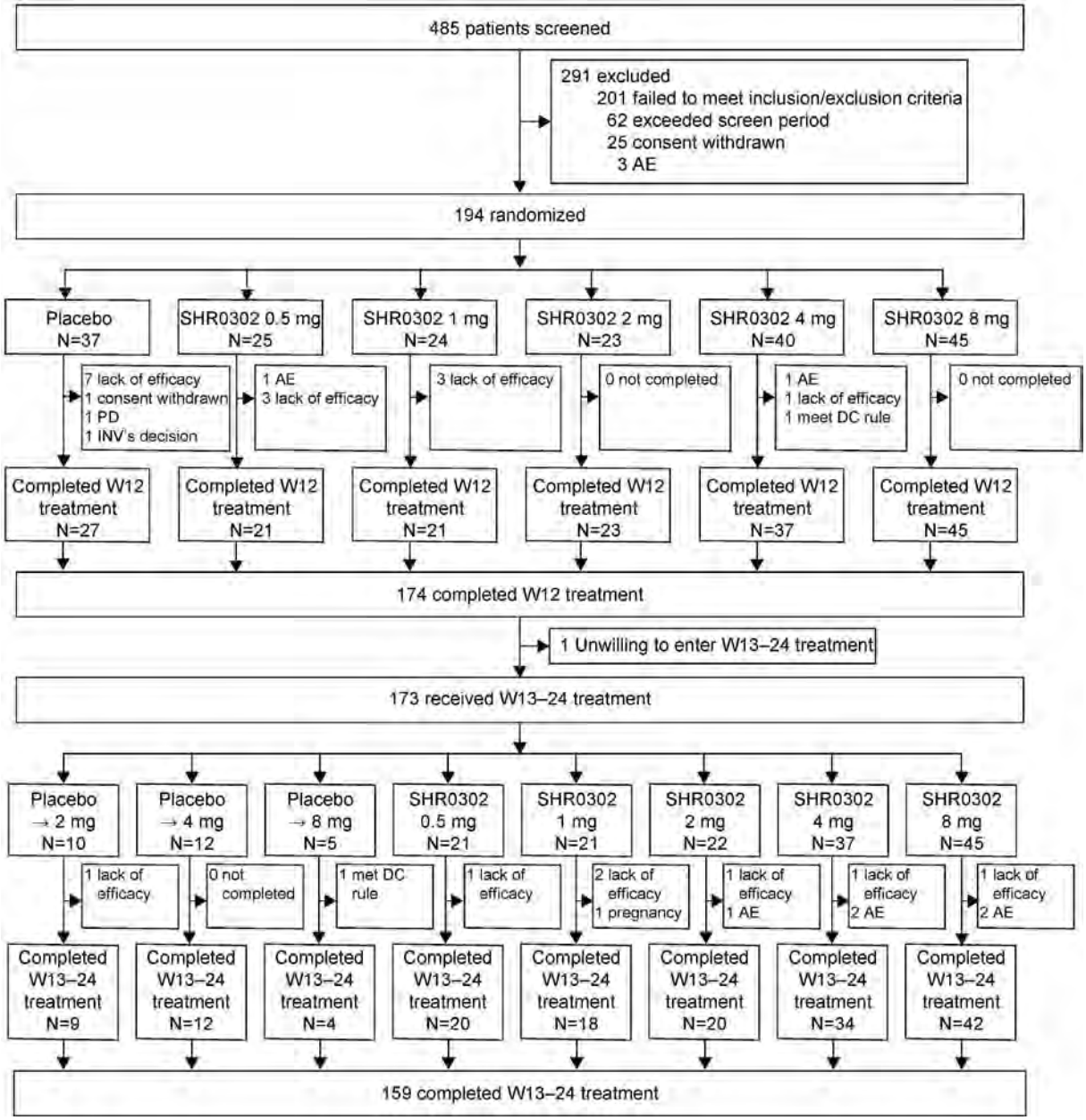

Figure 1. Trial profile. The SHR0302 8 mg group was added in protocol v2.0 to explore the maximum safe and effective dose according to latest preclinical data. AE, adverse events; INV, investigator; PD, progressive disease; DC, discontinuation.

Methods: Eligible subjects were 18–70 years; had a diagnosis of RA according to 2010 ACR/EULAR RA criteria; had moderately to severely active disease defined by ≥6 tender joints, ≥6 swollen joints (out of 68- or 66-joints examined), and ESR > 28 mm/h or CRP > 1.2 times upper limit of normal; were either treatment-naive or inadequately responded or intolerant to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs). Subjects who had prior treatment with JAK inhibitor or biologics were excluded. Eligible subjects were randomized to receive placebo or 0.5, 1, 2, or 4 mg SHR0302 in 1:1:1:1:1 (per protocol v1.1) or to receive placebo, 4 or 8 mg SHR0302 1:1:3 (per protocol v2.0) once daily (oral) for 12 weeks. Afterwards, subjects who initially assigned to placebo were re-assigned to take 2, 4 mg or 8 mg SHR0302 daily for additional 12 weeks, while subjects initially assigned to SHR0302 remained on the same treatment. The primary endpoint was the proportion of subjects who achieved ≥20% improvement according to the American College of Rheumatology response criteria (ACR20) at week 12.

Group	PBO			0.5 mg	1 mg	2 mg	4 mg	8 mg
	PBO + 2 mg	PBO + 4 mg	PBO + 8 mg					
Week 12, N	37			25	24	23	40	45
Week 24, N	10	12	5	21	21	22	37	45
ACR 20								
Week 12	10 (27.0)			11 (44.0)	10 (41.7)	13 (56.5)†	27 (67.5)‡	35 (77.8)‡
Week 24	9 (90.0)	12 (100.0)	4 (80.0)	14 (66.7)	12 (57.1)	16 (72.7)	29 (78.4)	38 (84.4)
ACR 50								
Week 12	1 (2.7)			3 (12.0)	5 (20.8)†	7 (30.4)‡	11 (27.5)‡	17 (37.8)‡
Week 24	5 (50.0)	8 (66.7)	4 (80.0)	8 (38.1)	7 (33.3)	12 (54.5)	15 (40.5)	31 (68.9)
ACR 70								
Week 12	0			1 (4.0)	1 (4.2)	3 (13.0)†	5 (12.5)†	12 (26.7)‡
Week 24	1 (10.0)	6 (50.0)	1 (20.0)	3 (14.3)	3 (14.3)	7 (31.8)	8 (21.6)	22 (48.9)
Changes from baseline in DAS28-3 (CRP), mean (SD)								
Week 12	-0.75 (1.09)			-1.02 (0.91)	-0.80 (1.08)	-1.61 (1.23)	-1.82 (1.34)	-2.07 (1.01)
Week 24,	-1.95 (0.89)	-2.33 (0.91)	-3.02 (0.83)	-1.48 (1.12)	-1.41 (1.16)	-2.29 (1.47)	-2.11 (1.24)	-2.63 (1.03)
DAS28-3 (CRP) <2.6								
Week 12	2 (5.4)			2 (8.0)	1 (4.2)	5 (21.7)	10 (25.0)†	15 (33.3)‡
Week 24	1 (10.0)	2 (16.7)	0	3 (14.3)	1 (4.8)	7 (31.8)	9 (24.3)	23 (51.1)
Changes from baseline in HAQ-DI scores, mean (SD) *:								
Week 12	-0.30 (0.63)			-0.35 (0.37)	-0.24 (0.44)	-0.68 (0.52)†	-0.48 (0.40)†	-0.75 (0.54)‡
Week 24	-0.57 (0.29)	-1.14 (0.68)	-0.72 (0.28)	-0.58 (0.51)	-0.45 (0.56)	-0.89 (0.59)	-0.56 (0.43)	-0.96 (0.64)

Table 1. Efficacy results. †: P< 0.05; ‡: P< 0.01 vs PBO; *: adjusted for baseline HAQ-DI score and previous inadequate response to csDMARDs or not; Data are n (%), unless otherwise specified; PBO, placebo; DAS28-3 (CRP), 3-variable 28-joint Disease Activity Score using C-Reactive Protein; HAQ-DI, Health Assessment Questionnaire Disability Index.

Results: Between Sep 2017 to Oct 2019, 194 eligible subjects were randomized (Figure 1). The ACR20 response rates at week 12 for subjects receiving SHR0302 2 mg (56.5%, p=0.02), 4 mg (67.5%, p< 0.001), and 8 mg (77.8%, p< 0.001) were significantly greater than those of placebo (27.0%). ACR50/70 response rates at week 12 were generally consistent with ACR20 (Table 1). Mean changes from baseline in DAS28-3 (CRP) were numerically greater with the treatment of SHR0302 in comparison with placebo at week 12 (Table 1), and significantly more subjects in 4 mg (25.0%, p=0.02) and 8 mg (33.3%, p=0.002) groups achieved a DAS28-3 (CRP) < 2.6 versus placebo (5.4%) at week 12. SHR0302 2, 4, and 8 mg groups had significantly greater changes from baseline in HAQ-DI scores at week 12 (adjusted mean change: 2 mg, -0.68, p=0.02; 4 mg, -0.48, p=0.048; 8 mg -0.75, p< 0.001) as compared with placebo (-0.30). Above-mentioned improvements were sustained at week 24 (Table 1). The proportion of subjects with any treatment emergent adverse events was higher for SHR0302 (73.9%) vs placebo (62.2%) through week 12, particularly infection (Table 2). A total of four cases of herpes zoster and one case of opportunistic infection (cryptococcal pneumonia) were reported, all in SHR0302 8 mg group. No tuberculosis, malignancy, important cardiovascular events or death were reported. Safety results were presented in Table 2.

Conclusion: SHR0302 showed sustained efficacy in improving signs and symptoms of rheumatoid arthritis in a dose-dependent manner and had a generally accepTable safety profile. Further confirmatory studies with SHR0302 in RA will be planned accordingly.

Week 0–12	PBO			0.5 mg	1 mg	2 mg	4 mg	8 mg	SHR0302
N	37			25	24	23	40	45	157
Any TEAE	23 (62.2)			16 (64.0)	16 (66.7)	16 (69.6)	30 (75.0)	38 (84.4)	116 (73.9)
Serious TEAE	2 (5.4)			2 (8.0)	0	0	3 (7.5)	2 (4.4)	7 (4.5)
AE led to discontinuation	1 (2.7)			1 (4.0)	0	0	1 (2.5)	0	2 (1.3)
AESI									
Infection	6 (16.2)			5 (20.0)	5 (20.8)	7 (30.4)	9 (22.5)	22 (48.9)	48 (30.6)
Herpes zoster	0			0	0	0	0	1 (2.2)	1 (0.6)
MACE	0			0	0	0	0	0	0
VTE	0			0	0	0	0	0	0
Opportunistic infection	0			0	0	0	0	0	0
Week 13–24	**PBO + 2 mg**	**PBO + 4 mg**	**PBO + 8 mg**	**0.5 mg**	**1 mg**	**2 mg**	**4 mg**	**8 mg**	**SHR0302**
N	10	12	5	21	21	22	37	45	173
Any TEAE	6 (60.0)	5 (41.7)	3 (60.0)	15 (71.4)	13 (61.9)	14 (63.6)	23 (62.2)	33 (73.3)	112 (64.7)
Serious TEAE	0	0	1 (20.0)	0	0	0	1 (2.7)	1 (2.2)	3 (1.7)
AE led to discontinuation	0	0	1 (20.0)	0	0	1 (4.5)	2 (5.4)	2 (4.4)	6 (3.5)
AESI									
Infection	4 (40.0)	0	3 (60.0)	6 (28.6)	4 (19.0)	5 (22.7)	7 (18.9)	13 (28.9)	42 (24.3)
Herpes zoster	0	0	0	0	0	0	0	3 (6.7)	3 (1.7)
MACE	0	0	0	0	0	0	0	0	0
VTE	0	0	0	0	0	0	0	0	0
Opportunistic infection	0	0	0	0	0	0	0	1 (2.2)	1 (0.6)

Table 2. Safety profile. Data are n (%), unless otherwise specified. PBO, placebo; TEAE, treatment-emergent adverse event; AESI, adverse event of special interest; MACE, major adverse cardiovascular events; VTE, venous thromboembolism.

Disclosure: X. Zeng, Jiangsu Hengrui Medicine Co., Ltd, 1; **Y. Jiang**, Jiangsu Hengrui Medicine Co., Ltd, 1; **Y. Yang**, Jiangsu Hengrui Medicine Co., Ltd, 1; **H. Li**, Jiangsu Hengrui Medicine Co., Ltd, 1.

Abstract Number: 0202

Safety Profile of Baricitinib for the Treatment of Rheumatoid Arthritis up to 8.4 Years: An Updated Integrated Safety Analysis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Baricitinib (bari) is an oral selective Janus kinase (JAK)1/JAK 2 inhibitor approved for the treatment of moderately to severely active rheumatoid arthritis (RA) in adults. The objective of this study was to update bari's safety profile with data up to 8.4 years of treatment.

Table. Safety summary among patients with RA treated with at least one dose of baricitinib through 1-Sep-2019 (All-Bari-RA analysis set).

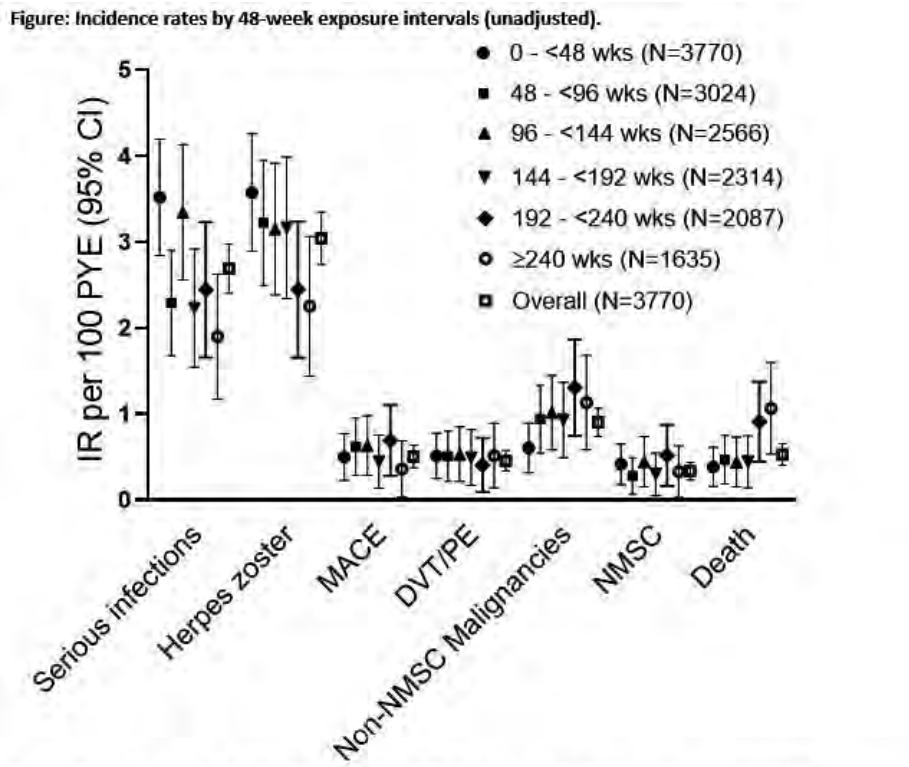
	n/N	IR
Treatment-emergent AE	3391/3770	25.8
Serious AE (including death)	940/3770	7.2
Temporary d/c because of AE	1241/3647	9.5
Permanent d/c because of AE	644/3770	4.8
Death	70/3770	0.5
Serious infection	344/3770	2.7
Opportunistic infection (excluding tuberculosis, including multidermatomal herpes zoster)	61/3770	0.5
Herpes zoster	384/3770	3.0
Tuberculosis	20/3770	0.2
Major adverse cardiovascular events*	63/3251	0.5
DVT	41/3770	0.3
PE	32/3770	0.2
DVT and/or PE	60/3770	0.5
Malignancies excluding NMSC	122/3770	0.9
NMSC	44/3770	0.3
Lymphoma	8/3770	0.06
Gastrointestinal perforation	6/3770	0.04

*positively adjudicated events in studies with adjudication (5 Phase 3 studies and 1 long-term extension study). AE = adverse event; D/C = discontinuation; DVT = deep vein thrombosis; IR = incidence rate; n = number of patients with the event of interest; N = number of patients in the safety analysis set; NMSC = non-melanoma skin cancer; PE = pulmonary embolism.

Methods: Long-term safety of bari was assessed from 9 completed randomized trials (5 Phase 3, 3 Phase 2, 1 Phase 1b) and one ongoing long-term extension (LTE) study. Incidence rates (IR) per 100 patient-years of exposure (PYE) were calculated for all patients treated with ≥1 dose of bari through 1-Sep-2019 (All-Bari-RA analysis set). IRs for deep vein thrombosis (DVT), pulmonary embolism (PE), and DVT and/or PE (DVT/PE) were also calculated for groups of patients while receiving bari 2mg or bari 4mg within All-Bari-RA. Major adverse cardiovascular events (MACE) were adjudicated in 5 Phase 3 studies and the LTE. IRs for serious infections were evaluated by age group (< 65 vs. ≥65) through Week 24 for patients randomized to placebo and bari 4 mg in 7 Phase 2/3 trials (Bari-RA-PC analysis set) as well as within All-BARI-RA. Within All-Bari-RA, events of interest were assessed over time in 48-month intervals. In addition, to account for aging of the cohort, IRs for death and malignancy (excluding non-melanoma skin cancer [NMSC]) were directly standardized to the WHO world population 2000-2025 within each time interval.

Results: A total of 3770 patients received bari for 13,148 PYE, with a median and maximum exposure of 4.2 and 8.4 years, respectively. Overall IRs per 100 PYE for any treatment-emergent adverse event (AE) and serious AE (including death) were 25.8 and 7.2, respectively (Table). Within All Bari-RA, IRs (95% confidence intervals [CI]) for patients while receiving bari 2mg (N=1077) or bari 4mg (N=3400), respectively, were 0.4 (0.2, 0.7) and 0.3 (0.2, 0.4) for DVT, 0.3 (0.1, 0.6) and 0.3 (0.2, 0.4) for PE, and 0.5 (0.2, 0.8) and 0.5 (0.3, 0.6) for DVT/PE. In All-Bari-RA, IRs (95% CI) of serious infections for patients age < 65 and ≥65 were 2.1 (1.9, 2.4) and 4.8 (4.0, 5.7), respectively. In Bari-RA-PC, IRs (95%

Figure: Incidence rates by 48-week exposure intervals (unadjusted).



CI = confidence interval; IR = incidence rate; DVT/PE = deep vein thrombosis and/or pulmonary embolism; MACE = positively adjudicated major adverse cardiovascular events; N = number of patients with any data reported in window; NMSC = non-melanoma skin cancer; PYE = patient-years of exposure; wks = weeks.

CI) of serious infections for placebo (N=1215) and bari 4mg (N=1142) treatment groups, respectively, were 3.1 (1.6, 5.4) and 3.3 (1.8, 5.6) among patients < 65 and 9.9 (4.0, 20.4) and 7.0 (2.6, 15.2) among those ≥65. For MACE, DVT/PE, and NMSC, IRs generally remained sTable over time (Figure). There were no increases in rates of death or non-NMSC malignancy after adjustment for aging of the cohort. Across safety topics, IRs were consistent with previous analyses[1,2].

Conclusion: In this update with 13,148 PYE, bari maintained a safety profile similar to that previously reported,[1,2] with no increase of IRs across safety topics through exposures up to 8.4 years.

References:

1. Smolen JS et al. J Rheumatol. 2019 Jan;46(1):7-18
2. Genovese MC et al. Ann Rheum Dis. 2019 78(supp. 2):A308

Disclosure: K. Winthrop, Pfizer, 2, 5, UCB, 2, 5, Abbvie, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Roche, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 5; **T. Takeuchi**, Astellas Pharma Inc., 2, 5, 8, Daiichi Sankyo Company, Limited, 2, 5, 8, Takeda Pharmaceutical Company Limited, 2, 5, 8, AbbVie GK., 2, 5, 8, Asahi Kasei Pharma Corporation, 2, 5, 8, Mitsubishi Tanabe Pharma Corporation, 2, 5, 8, Eisai Co., Ltd., 2, 5, 8, Nippon Kayaku Co., Ltd., 2, 5, 8, Chugai Pharmaceutical Co., Ltd., 2, 5, 8, Eli Lily Japan K.K, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Pfizer Japan, Inc., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, AYUMI Pharmaceutical Corporation, 2, 5, 8, Novartis Pharma K.K., 2, 5, 8, UCB, 2, 5, 8, Dainippon Sumitomo Co., 2, 5, 8, Shionogi & Co., Ltd., 2, 5, 8; **G. Burmester**, AbbVie, 5, 8, Pfizer, 5, 8, Gilead Sciences, Inc., 5, 8, Eli Lilly, 5, 8, Novartis, 5, Celgene, 5; **P. Durez**, None; **W. Deberdt**, Eli Lilly and Company, 1, 2; **D. Schlichting**, Eli Lilly and Company, 1, 2; **S. Beattie**, Eli Lilly and Company, 1, 2; **D. Mo**, Eli Lilly and Company, 1, 2;

C. Walls, Eli Lilly and Company, 1, 2; **J. Smolen**, Abbvie, 1, 2, Eli Lilly and Company, 1, 2, Janssen, 1, 2, MSD, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, Roche, 1, 2, Amgen, 1, AstraZeneca, 1, Astro, 1, BMS, 1, Celgene, 1, Celltrion, 1, Chugai, 1, Gilead, 1, ILTOO, 1, Medimmune, 1, Samsung, 1, Sanofi, 1, UCB, 1.

Abstract Number: 0203

Safety of Baricitinib in Patients with Rheumatoid Arthritis: Interim Report from All-Case Post-Marketing Study in Clinical Use

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the safety of baricitinib in rheumatoid arthritis (RA) patients in clinical use.

Methods: An all-case post-marketing study of baricitinib, started in September 2017, collects safety and effectiveness for the first 24 weeks of treatment and continues to collect serious adverse events (SAEs) for 3 years. We report patients baseline demographics and adverse events (AEs) for patients completing the 24 weeks case report or discontinued before 24 weeks, as of December 2019.

Results: Data from 1992 patients were collected (females 80%). At dosing, the mean age was 64 years (median: 66 years), ≥65 years 54%; the mean RA duration was 11 years (median: 9 years), baricitinib dose regimen 4 mg 62%, 2 mg 27%, 4 mg → 2 mg 5%, 2 mg → 4 mg 4%, and others 3%. Pre-use of biologic DMARDs was 75% and targeted synthetic DMARDs was 21%; concomitant use of MTX was 55% and corticosteroid was 43%. 73% continued treatment for 24 weeks.

Totally, 536 patients (27%) had AEs. 4 patients died of adenocarcinoma, aspiration pneumonia, bacterial pneumonia, and pulmonary hypertension. The SAEs were 79 patients (4%): pneumonia (9), herpes zoster (5), bacterial pneumonia (4), osteonecrosis (3), anemia (3), aspiration pneumonia (3), fall (3), and femur fracture (3). The major adverse event of special interests were herpes zoster (58), serious infections (29), low hemoglobin or anemia (26), liver dysfunction (68), high lipid or hyperlipidemia (27), cardiovascular event (15), interstitial pneumonia (5), malignancy (7), and venous thromboembolism (2).

Conclusion: No new safety concern has been indicated. Encourage guideline-compliant use of baricitinib, as SAEs, including infections, have been reported.

Disclosure: T. Atsumi, AbbVie Inc., 5, 8, 9, UCB Japan Co.,Ltd., 5, 8, Eisai Co., Ltd., 8, Gilead Sciences, Inc., 5, 8, Bristol Myers Squibb Co., 2, 8, Chugai Pharmaceutical Co., Ltd., 2, 8, 9, Mitsubishi Tanabe Pharma Corporation, 8, 9, Eli Lilly Japan K.K., 2, 5, 8, Astellas Pharma Inc., 8, 9, Pfizer Inc., 2, 8, 9, Daiichi Sankyo Company, Limited, 5, 8, 9; **N. Okamoto**, None; **N. Takahashi**, Eli Lilly and Company, 8; **N. Tamura**, GlaxoSmithKline plc, 2, 8, Eli Lilly Japan K.K., 8, Chugai Pharmaceutical Co.Ltd., 8, Novartis Pharma K.K., 8, AbbVie GK., 8, Eisai Co., Ltd., 8, Mitsubishi Tanabe Pharma Corporation, 8, Janssen Pharmaceutical K.K., 8, Bristol Myers Squibb Co.Ltd., 8; **A. Nakajima**, None; **A. Nakajima**, Eli Lilly, 8; **T. Fujii**, None; **H. Matsuno**, Chugai Pharmaceutical Co., Ltd., 8, Daiichi Sankyo Company, Limited, 8, Mochida Pharmaceutical Co Ltd,, 8, Ayumi Pharmaceutical Co, 8, Nichi-Iko Pharmaceutical Co Ltd, 8; **Y. Takahashi**, Eli Lilly Japan K.K., 3; **F. Inui**, Eli Lilly Japan K.K., 3; **N. Tsujimoto**, Eli Lilly Japan K.K., 3, Eli Lilly and Company, 4; **A. Nishikawa**, Eli Lilly Japan K.K., 3, Eli Lilly and Company, 4; **T. Ishii**, Eli Lilly Japan K.K., 3, Eli Lilly and Company, 4; **T. Takeuchi**, Astellas Pharma Inc., 2, 5, 8, Daiichi Sankyo Company, Limited, 2, 5, 8, Takeda Pharmaceutical Company Limited, 2, 5, 8, AbbVie GK., 2, 5, 8, Asahi Kasei Pharma Corporation, 2, 5, 8, Mitsubishi Tanabe Pharma Corporation, 2, 5, 8, Eisai Co., Ltd., 2, 5, 8, Nippon Kayaku Co., Ltd., 2, 5, 8, Chugai Pharmaceutical Co., Ltd., 2, 5, 8, Eli Lily Japan K.K, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Pfizer Japan, Inc., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, AYUMI Pharmaceutical Corporation, 2, 5, 8, Novartis Pharma K.K., 2, 5, 8, UCB, 2, 5, 8, Dainippon Sumitomo Co., 2, 5, 8, Shionogi & Co., Ltd., 2, 5, 8; **M. Kuwana**, Ono Pharmaceutical, 2, 8, Chugai, 2, 8, Astellas, 8, Mitsubishi Tanabe Pharma Corporation, 2, 8, AbbVie Inc., 8, Eisai Co., Ltd., 8; **M. Takagi**, None.

Abstract Number: 0204

Pharmacokinetics and Safety of CT-P17, a Proposed High Concentration (100 mg/mL) Adalimumab Biosimilar, in Comparison with EU-Approved Adalimumab and US-Licensed Adalimumab; Results of a Phase 1, Randomized, Double-blind, Three-arm, Single-dose Study in Healthy Subjects

KyungSang Yu[1], InJin Jang[1], HyeongSeok Lim[2], JangHee Hong[3], MinGul Kim[4], MinKyu Park[5], Anhye Kim[6], MinSoo Park[7], JaeYong Chung[8], JongLyul Ghim[9], SeungHwan Lee[1], SeokKyu Yoon[2], InSun Kwon[3], Daniel Furst*[10], Edward C Keystone[11], SangJoon Lee[12], SungHyun Kim[12], YunJu Bae[12], JungBin Cha[13], HyeJin Kang[13] and Jonathan Kay[14], [1]Seoul National University College of Medicine and Hospital, Seoul, Republic of Korea, [2]College of Medicine, University of Ulsan, Asan Medical Center, Seoul, Republic of Korea, [3]Chungnam National University Hospital, Daejeon, Republic of Korea, [4]College of Medicine, Jeonbuk National University, Jeonbuk, Republic of Korea, [5]Chungbuk National University Hospital, Cheongju, Republic of Korea, [6]CHA Bundang Medical Center, CHA University, Seongnam, Republic of Korea, [7]Severance Hospital, Yonsei University College of Medicine, Seoul, Republic of Korea, [8]Seoul National University Bundang Hospital, Seongnam, Republic of Korea, [9]Inje University Busan Paik Hospital, Busan, Republic of Korea, [10]Department of Medicine, Division of Rheumatology, University of California at Los Angeles, Los Angeles, California, USA, Los Angeles, CA, [11]Mount Sinai Hospital, Toronto, ON, Canada, [12]Celltrion, Inc., Incheon, Republic of Korea, [13]Celltion, Inc., Incheon, Republic of Korea, [14]University of Massachusetts Medical School, Worcester, MA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

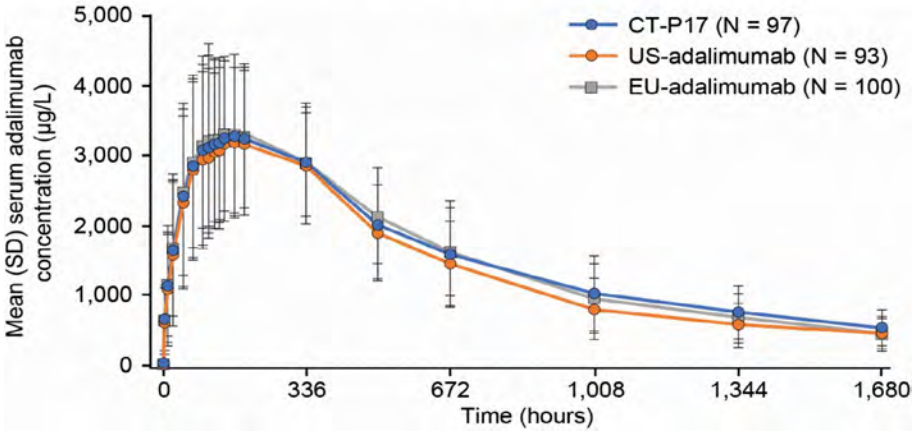
Background/Purpose: CT-P17 was developed as the first biosimilar of the high concentration (100 mg/mL), citrate-free formulation of reference adalimumab. The purpose of this study was to compare the pharmacokinetics (PK), safety, and immunogenicity of CT-P17 to EU-approved adalimumab (EU-adalimumab) and US-licensed adalimumab (US-adalimumab) up to Day 71 after a single subcutaneous (SC) injection of 40 mg (100 mg/mL) of each product in healthy subjects.

Table 1 Primary Pharmacokinetic Endpoints (Pharmacokinetic Population)

Treatment and Comparison	C_{max} (µg/mL) gLSM (n)	AUC_{0-Inf} (h·µg/mL) gLSM (n)	AUC_{0-last} (h·µg/mL) gLSM (n)
CT-P17	3.008 (96)	2,165.0 (80)	1,949.2 (96)
US-adalimumab	2.952 (93)	2,046.5 (86)	1,816.6 (93)
EU-adalimumab	3.006 (98)	2,209.3 (89)	1,933.9 (98)
Ratio (90% CI)*			
CT-P17 vs US-adalimumab	101.89 (95.33–108.89)	105.79 (97.19–115.16)	107.30 (98.29–117.13)
CT-P17 vs EU-adalimumab	100.05 (93.69–106.85)	98.00 (90.06–106.63)	100.79 (92.42–109.92)
US-adalimumab vs EU-adalimumab	98.20 (91.91–104.92)	92.63 (85.29–100.61)	93.93 (86.08–102.50)

Abbreviations: AUC0–inf, area under the concentration–time curve from time zero to infinity; AUC0–last, area under the concentration–time curve from time zero to the last quantifiable concentration; CI, confidence interval; Cmax, maximum serum concentration; EU adalimumab, European Union-approved adalimumab; gLSM, geometric least squares mean; US-adalimumab, United States-licensed adalimumab. *Ratio of geometric least squares mean and 90% CIs for the ratios

Figure 1 Mean (±SD) Serum Concentrations of Adalimumab (Pharmacokinetic Population)



Abbreviations: EU-adalimumab, European Union-approved adalimumab; SD, standard deviation; US-adalimumab, United States-licensed adalimumab.

Methods: 312 healthy subjects aged 19 to 55 years were randomly assigned 1:1:1 to receive either CT-P17, EU-adalimumab or US-adalimumab. The primary objective was to evaluate PK equivalence based on area under the concentration-time curve (AUC) from time zero to infinity (AUC_{0-inf}), AUC from time zero to the last quantifiable concentration (AUC_{0-last}), and maximum serum concentration (C_{max}). Secondary objectives were to assess additional PK parameters, safety, and immunogenicity.

Results: Demographics and baseline characteristics were well balanced among the 3 treatment groups. The 90% confidence intervals (CI) for the geometric least squares mean ratios of each of the primary PK parameters (AUC_{0-inf}, AUC_{0-last}, and C_{max}) were within the predefined equivalence margin of 80% to 125% (Table 1). Secondary PK parame-

Table 2 Summary of TEAEs (Safety Population)

Overall Adverse Events, n (%)	CT-P17 (N=102)	US-adalimumab (N=102)	EU-adalimumab (N=104)
Number of subjects with at least 1:			
TEAE	56 (54.9)	65 (63.7)	60 (57.7)
Study drug-related	45 (44.1)	49 (48.0)	49 (47.1)
TESAE	2 (2.0)	0	1 (1.0)
TEAE leading to study discontinuation	1 (1.0)	0	0
Death	0	0	0
TEAE classified as hypersensitivity/allergic reaction	1 (1.0)	0	1 (1.0)
TEAE classified as injection site reaction	20 (19.6)	16 (15.7)	19 (18.3)
TEAE classified as infection	10 (9.8)	19 (18.6)	13 (12.5)
Study drug-related	9 (8.8)	16 (15.7)	12 (11.5)
TEAE classified as malignancy	0	0	0

Abbreviations: EU-adalimumab = European Union-approved adalimumab; TEAE = treatment-emergent adverse event; TESAE = treatment-emergent serious adverse event; US-adalimumab = United States-licensed adalimumab.

ters (T_{max}, $t_{1/2}$, λ_z, CL/F, V_z/F, and $\%AUC_{extrap}$) were similar among the 3 treatment groups. Mean serum concentrations of adalimumab to Day 71 were comparable among the 3 treatment groups (Figure 1).

The overall safety profile was comparable among the 3 treatment groups (Table 2). The most frequently reported treatment-emergent adverse event (TEAE) was injection site reaction. Overall, most TEAEs were Grade 1 or 2 in intensity. There were 3 treatment-emergent serious adverse events (TESAEs), each of which was assessed as being unrelated to study drug.

Similar numbers of subjects among the 3 treatment groups tested positive for anti-drug antibodies (ADA) and neutralizing ADA (NAb). Overall, 99 (97.1%), 96 (94.1%) and 99 (95.2%) subjects in the CT-P17, US-adalimumab and EU-adalimumab groups, respectively, had ≥1 positive ADA result post-treatment and 79 (77.5%), 85 (83.3%) and 84 (80.8%) subjects in the CT-P17, US-adalimumab and EU-adalimumab groups, respectively, had ≥1 positive NAb result post-treatment. ADA titers were similar across the 3 treatment groups. AUC_{0-inf} and AUC_{0-last} each correlated negatively with ADA titer in all treatment groups (P-value < 0.0001; calculated using Fisher's z transformation). There was no statistically significant correlation of C_{max} with ADA titer.

Conclusion: This study demonstrated PK equivalence of CT-P17 to the high concentration (100 mg/mL), citrate-free formulation of both US- and EU-sourced reference adalimumab in healthy subjects. Safety profiles, including immunogenicity, were comparable among the 3 treatment groups.

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Pharmaceuticals, Inc., 1, Boehringer Ingelheim GmbH, 1, Celltrion Healthcare Co. Ltd., 1, Mylan Inc., 5, Novartis AG, 5, Samsung Bioepis, 5, Sandoz Inc., 5, Gilead Sciences, Inc., 9.

Abstract Number: 0205

Methotrexate Therapy Is Not Associated with an Increased Risk of Liver Fibrosis Assessed by the Fibrosis-4 Index

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Methotrexate (MTX) holds a unique place in the management of rheumatoid arthritis (RA) given its favorable balance between efficacy and safety. However, conflicting data still suggest a potential risk of MTX-induced long-term liver fibrosis. The fibrosis-4 (FIB-4) index was originally proposed as a simple and non-invasive marker of liver fibrosis in HIV/HCV co-infection. In patients with RA, FIB-4 values have been correlated to the amount of histologic liver lesions, suggesting that this index may be a valuable marker to diagnose liver disease in RA patients. Our objective was to estimate the amount of scarring in the liver with the FIB-4 index in RA patients on maintenance therapy with MTX.

Methods: We performed a cross-sectional study including successive RA patients hospitalized in the Rheumatology department of Cochin Hospital for a 12-month period. Data on liver function, disease activity, hepatotoxic and cardiovascular risk factors were systematically collected. The FIB-4 index was calculated according the following formula: (age(years) ×AST(U/L)/platelet (PLT) (109/L) × √ALT(U/L)). Using a lower cutoff value of 1.45, a FIB-4 score < 1.45 had

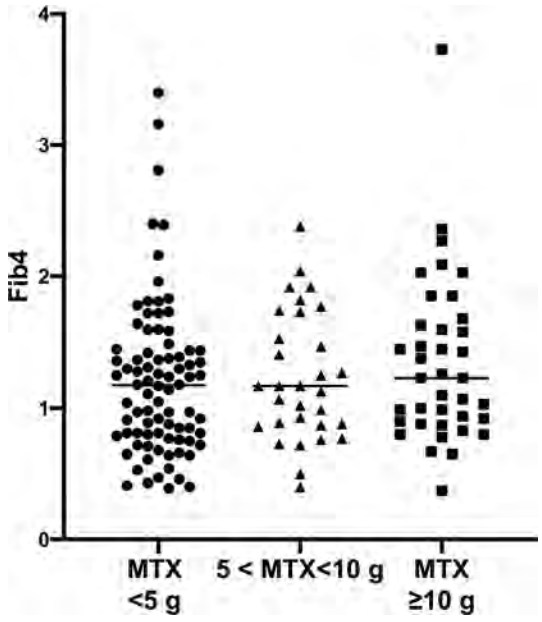

Figure 1. Fibrosis-4 index according to the cumulative dose of methotrexate in patients with rheumatoid arthritis

a negative predictive value of 90% for advanced fibrosis in the patient cohort in which this formula was first validated. In contrast, a FIB-4 >3.25 had a 97% specificity and a positive predictive value of 65% for advanced fibrosis.

Results: We included 170 patients with established RA: 141 (83%) were women, the mean age was 59±12 years and the mean disease duration was 15±11 years. Positive rheumatoid factors and anti-CCP antibodies were detected in 134 patients (79%). 102 patients (60%) were treated with methotrexate, with a mean dose of 10.0±8.4 mg/week, a mean treatment duration of 9.5±10.3 years and a cumulative dose of 5.3±5.1g. 23 patients (13.5%) received conventional synthetic disease modifying anti-rheumatic drugs (csDMARDs) other than MTX, 112 (66%) corticosteroids (99 with a dose < 10 mg/day) and 85 targeted biologic DMARDs (bDMARDs) (50%).

The mean FIB-4 value was 1.24±0.57, with 120 patients (71%) with value < 1.45, 49 (29%) with values ranging from 1.45 to 3.25 and a single patient with FIB-4 >3.25. The FIB-4 was low and not significantly different between patients receiving MTX, patients previously treated with MTX and patients never treated with MTX (median 1.1, 1.25 and 1.18, respectively, p=0.709). This result was not modified after adjustment on treatments with other csDMARDs, corticosteroids, and bDMARDs. No correlation was observed between FIB-4 values and the cumulative dose of MTX (r=0.09, p=0.271). The FIB-4 index was low and similar between patients receiving cumulative MTX doses < 5g, between 5 and 10g and 10g (Figure 1). The cumulative dose of MTX was not significantly higher in patients with a FIB-4 index >1.45 (median cumulative MTX dose 5.5g vs. 3.5g, p=0.302).

No association was detected between the FIB-4 index and parameters of disease activity (DAS28, ESR and CRP levels), the body mass index, traditional cardiovascular risk factors and metabolic syndrome.

Conclusion: RA patients with long-term maintenance MTX therapy have low FIB-4 values suggesting that MTX is not associated with an increased risk of advanced liver fibrosis.

Disclosure: J. Avouac, Bristol Myers Squibb, 2, 5, 8; **R. Degrave**, None; **H. Vergneault**, None; **Y. Allanore**, None.

Abstract Number: 0206

Fifty-Two Week Outcomes of Biologic-Naïve RA Patients Treated with Subcutaneous Abatacept in Japanese Multicenter Investigational Study (ORIGAMI Study)

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SESSION INFORMATION
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Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Table 1. Baseline Demographics and Clinical Characteristics of Patients Treated with ABA

Variables	N=279
Age, years	66.9 ± 12.7
Female	226 (81.0)
Disease Duration <1 / ≥1 to <2 / ≥2 to <3 ≥3 to <5 / ≥5 to <10 / ≥10	 68 (24.4) / 41 (14.7) / 18 (6.5) 28 (10.0) / 43 (15.4) / 81 (29.0)
Comorbidities	224 (80.3)
CRP, mg/dL	1.66 ± 2.25
ESR, mm/h	43.57 ± 28.01
ACPA positive	226 (83.7)
ACPA, U/mL	234.76 ± 359.80
RF positive	197 (73.0)
RF, U/mL	149.74 ± 283.63
MTX use	175 (64.6)
MTX dose, mg/week	4.46 ± 3.76
csDMARD use (except for MTX)	166 (63.1)
Prednisolone use	142 (52.8)
Prednisolone, mg/day	3.58 ± 2.70
SDAI	19.74 ± 5.65
CDAI	18.08 ± 5.10
DAS28-CRP	4.07 ± 0.75
DAS28-ESR	4.74 ± 0.85
J-HAQ (0-3)	1.16 ± 0.74
EQ-5D (0-1)	0.66 ± 0.15
PhGA (0-100 mm)	40.39 ± 14.85
Pain VAS (0-100 mm)	47.39 ± 24.08
Global VAS (0-100 mm)	45.08 ± 23.36

Mean ± standard deviation was shown for continuous variables and n (%) was shown for categorical variables. CRP, c-reactive protein; ESR, erythrocyte sedimentation rate; ACPA, anti-cyclic citrullinated peptide antibody; RF, rheumatoid factor; MTX, methotrexate; CDAI, clinical disease activity index; PhGA, physician's global assessment of disease activity; VAS, visual analog scale.

Table 2. Clinical Outcomes of ABA and csDMARDs at the End of Week 52 (Mean ± SD)

Variables	ABA (N=279)			csDMARDs (N=220)		
SDAI Remission (≤ 3.3)	18.9 % (95%CI: 14.27 to 23.56)			9.9 % (95%CI: 0.00 to 22.33)		
SDAI LDA (≤ 11)	53.3 % (95%CI: 47.39 to 59.12)			41.3 % (95%CI: 20.70 to 61.85)		
Variables	Week 0 (N=279)	Week 52 (N=184)	P-value (vs Week 0)	Week 0 (N=220)	Week 52 (N=174)	P-value (vs Week 0)
SDAI	19.74 ± 5.65	7.18 ± 5.37	< 0.01	19.41 ± 4.80	10.64 ± 6.56	< 0.01
CDAI	18.08 ± 5.10	6.71 ± 5.21	< 0.01	17.97 ± 5.05	10.01 ± 6.37	< 0.01
DAS28-CRP	4.07 ± 0.75	2.36 ± 0.87	< 0.01	4.07 ± 0.65	2.84 ± 0.93	< 0.01
DAS28-ESR	4.74 ± 0.85	3.03 ± 0.98	< 0.01	4.93 ± 0.81	3.81 ± 1.03	< 0.01
J-HAQ (0-3)	1.16 ± 0.74	0.94 ± 0.78	< 0.01	1.24 ± 0.77	1.19 ± 0.81	< 0.01
EQ-5D (0-1)	0.66 ± 0.15	0.75 ± 0.17	< 0.01	0.62 ± 0.13	0.65 ± 0.16	< 0.01

Both groups were adjusted by propensity score matching (sex, age, disease duration, SDAI, J-HAQ, MTX use, history of biologics use, corticosteroid use and comorbidity). 95%CI means 95% Confidence Interval.

Table 3. Safety Information up to Week 52 after ABA Administration

Event	ABA (N=298)	
All AEs, n (%)	151 (50.7)	
All ADRs, n (%)	68 (22.8)	
Death, n (%)	2 (0.7)	
Serious AEs, n (%)	36 (12.1)	
Serious ADRs, n (%)	14 (4.7)	
Event	**Serious AEs**	**Serious ADRs**
Infections, n (%)	7 (2.3)	7 (2.3)
Malignancies, n (%)	9 (3.0)	3 (1.0)
Fractures, n (%)	5 (1.7)	0 (0.0)
Cardiovascular diseases, n (%)	6 (2.0)	2 (0.7)
Interstitial pneumonia, n (%)	0 (0.0)	0 (0.0)
Other, n (%)	12 (4.0)	4 (1.3)

AE, adverse event; ADR, adverse drug reaction.

Background/Purpose: Long-term clinical benefit and patient-reported outcomes (PRO) of subcutaneously-injected abatacept (ABA) in patients with RA in a real-world setting are of therapeutic interest. We conducted a non-interventional, prospective, five-year observational study (ORIGAMI study) to evaluate long-term effectiveness, safety, and PRO of ABA in Japanese patients with RA. We herein report the one-year interim results with the simplified disease activity index (SDAI) remission rate at week 52 as the primary outcome.

Methods: Biologic-naïve patients with RA who showed inadequate responses to conventional synthetic DMARDs (csDMARDs) and had SDAI-moderate disease activity were eligible. A total of 325 patients who started ABA treatment were enrolled at 64 facilities in Japan from June 2016 to October 2018. Clinical outcomes, including SDAI and PRO, were evaluated at weeks 0, 4, 24, and 52. Adverse events (AEs) were assessed during the observational period. Some of the outcomes were compared to those of csDMARDs-treated patients without concomitant biologics therapy and with SDAI-moderate disease activity. These patients were enrolled during the same period in the IORRA registry, which is a prospective, large cohort study for RA in Japan. The propensity score weighting method was used to compare the two groups.

Results: Overall, 279 patients with RA were eligible for effectiveness analyses. The mean age was 66.9 years old and the mean SDAI was 19.7. The proportions of patients with disease durations of < 2, 2 to < 10, and ≥ 10 years were 39.1%, 31.9%, and 29.0%, respectively (Table 1). The proportion of patients with SDAI remission (≤ 3.3) at week 52 was 18.9%. SDAI-low disease activity (LDA, ≤ 11) was achieved in 53.3% of the patients (Table 2). The mean score of SDAI significantly decreased from week 4 and the proportions of LDA at weeks 4, 24, and 52 were 44.6%, 68.6%, and 79.0%, respectively. Similar improvements were observed in other variables such as clinical disease activity index and DAS28-CRP. Treatment with ABA significantly lowered the J-HAQ score. The proportions of patients who achieved HAQ remission (J-HAQ ≤ 0.5) at weeks 4, 24, and 52 were 27.9%, 33.2%, and 36.2%, respectively. These represent a significant increase from 19.4% at baseline. Furthermore, improvement of EuroQol 5 Dimension (EQ-5D) was observed at week 4 and onward. The ABA group showed numerically-higher proportions of patients with SDAI remission and SDAI-LDA, as well as better control of disease activity, J-HAQ score, and EQ-5D score at week 52 than the csDMARDs group (Table 2). The safety of ABA was evaluated in 298 patients. AEs and serious AEs were reported in 151 (50.7%) and 36 (12.4%) patients, respectively. Among patients with serious AEs, malignancy and serious infection were observed in 9 (3.0%) and 7 (2.3%) patients, respectively (Table 3).

Conclusion: ABA significantly improved disease activity, physical disability, and quality of life in as early as 4 weeks of treatment, for up to 52 weeks, in patients with RA in a real-world setting. Moreover, these clinical benefits from ABA, such as improved SDAI and PRO, were apparently better than csDMARDs.

Disclosure: N. Tamura, GlaxoSmithKline plc, 2, 8, Eli Lilly Japan K.K., 8, Chugai Pharmaceutical Co.Ltd., 8, Novartis Pharma K.K., 8, AbbVie GK., 8, Eisai Co., Ltd., 8, Mitsubishi Tanabe Pharma Corporation, 8, Janssen Pharmaceutical K.K., 8, Bristol Myers Squibb Co.Ltd., 8; **E. Tanaka**, Abbvie, 1, Asahi Kasei Pharma, 1, Chugai Pharmaceutical Co., Ltd., 1, Eisai Pharmaceutical, 1, Janssen Pharmaceutical K.K., 1, Pfizer, 1, Takeda Pharmaceutical, 1, Astellas Pharmaceutical, 1, Ayumi Pharmaceutical, 1, Eli Lilly Japan K.K., 1, GlaxoSmithKline K.K, 1, Kyowa Pharma Chemical CO., LTD, 1, Mochida Pharmaceutical CO., LTD, 1, Teijin Pharma Ltd., 1; **E. Inoue**, Bristol-Myers Squibb, 1, Pfizer, 1; **Y. Yoshizawa**, Bristol Myers Squibb K.K., 1, Bristol Myers Squibb, 1; **S. Matsumoto**, Ono Pharmaceutical Co., Ltd., 1; **H. Yamanaka**, Bristol Myers Squibb, 1; **M. Harigai**, AbbVie Japan GK, 1, 2, Asahi Kasei Corp., 1, Astellas Pharma Inc., 1, Ayumi Pharmaceutical Co. Ltd., 1, 2, Bristol Myers Squibb Co., Ltd, 1, 2, 3, Chugai Pharmaceutical Co. Ltd., 1, 2, Daiichi-Sankyo, Inc., 1, Eisai Pharmaceutical, 1, 2, Nippon Kayaku Co. Ltd., 1, Mitsubishi Tanabe Pharma Co., 1, Taisho Pharmaceutical Co. Ltd., 1, Takeda Pharmaceutical Co. Ltd., 1, 2, Eli Lilly Japan K.K, 1, Pfizer Japan Inc, 1, AbbVie, 1.

Abstract Number: 0207

Upadacitinib Monotherapy in Methotrexate-naïve Patients with Rheumatoid Arthritis: Results at 72 Weeks

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SESSION INFORMATION
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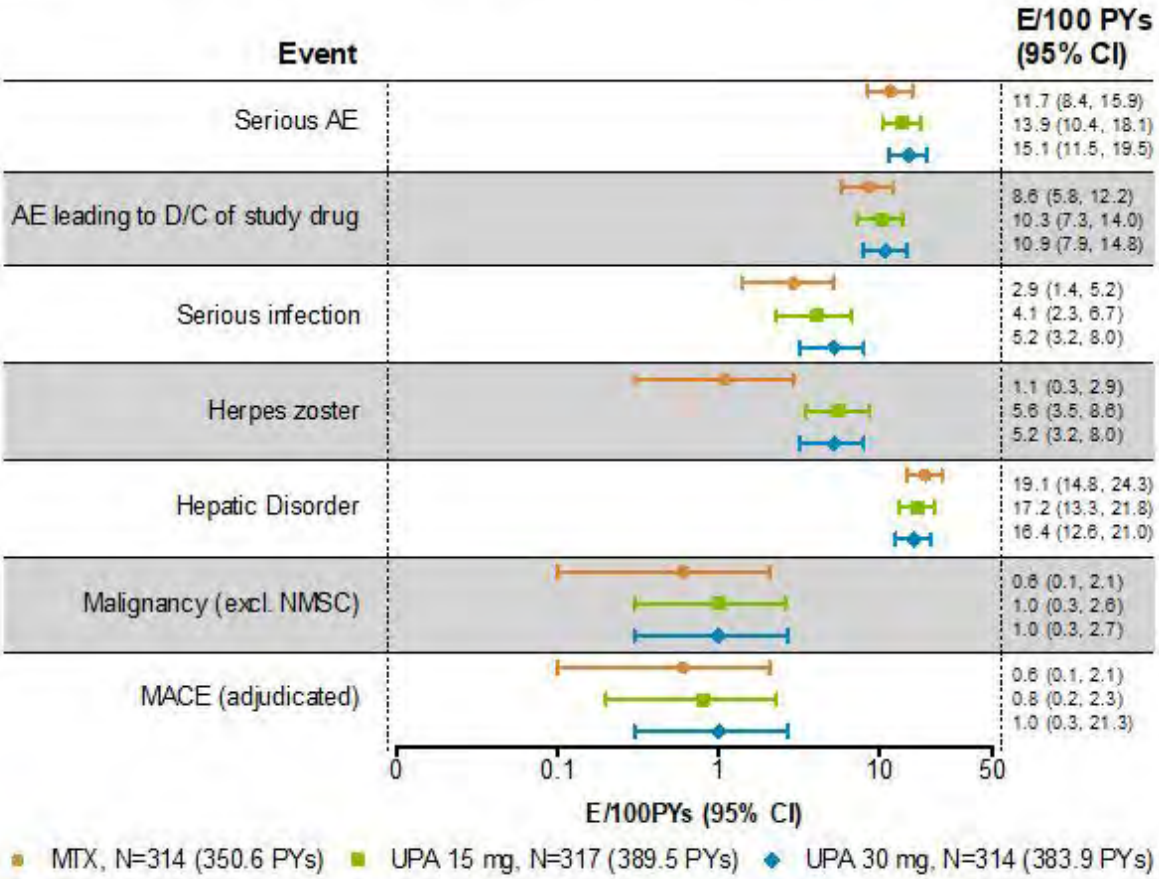
Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib (UPA), an oral JAK inhibitor, demonstrated significant improvements in signs, symptoms, and structural inhibition as monotherapy vs methotrexate (MTX) in a randomized, controlled trial (RCT) of MTX-naive RA patients (pts) through 48 weeks (wks)**.**[1] We present the safety and effectiveness of UPA through 72 wks in an ongoing long-term extension (LTE) of the SELECT-EARLY RCT.

Methods: SELECT-EARLY included 2 study periods: (1) a 48-wk double-blind, active comparator-controlled, with pts randomized to UPA monotherapy 15 or 30 mg once daily or MTX (titrated to 20 mg/wk by Wk8); (2) an LTE, up to 4 years. Pts received open-label treatment once the last pt reached Wk48. Rescue therapy was added (MTX, for UPA groups; UPA, for MTX group) to pts not achieving CDAI remission (≤2.8) at Wk26. Non-responder imputation (NRI) was used for missing data as well as for pts receiving rescue therapy. Treatment-emergent adverse events (TEAEs) are summarized per 100 pt yrs (PY) through the cut-off date of 21 Feb 2019, when all pts had reached Wk72. Data are censored at the time of MTX or UPA addition among rescued patients.

Table. Proportion of Patients at Week 72 (NRI)			
Parameter (%)	MTX Monotherapy	UPA 15 mg QD Monotherapy	UPA 30 mg QD Monotherapy
ACR20/50/70	50/39/26	71***/62***/47***	72***/67***/54***
DAS28(CRP) ≤3.2/<2.6	38/28	63***/52***	69***/61***
CDAI ≤10/≤2.8	42/19	60***/35***	69***/44***
Boolean Remission	13	29***	33***
***, *P* <0.001 for differences between MTX and UPA 15 and UPA 30 mg groups. MTX, methotrexate; UPA, upadacitinib; QD, once daily; ACR, American College of Rheumatology; DAS28(CRP), 28-joint disease activity index based on C-reactive protein; CDAI, clinical disease activity index.			

Figure. Treatment-emergent Adverse Events Through ≥72 Weeks (E/100 PYs, 95% CI).



Results: Of 945 pts randomized and treated, 781 (83%) completed Period 1. Of these, 775 entered the LTE, including 57 rescued pts (MTX, 33; UPA 15 mg, 17; UPA 30 mg, 7). A total of 52 (7%) pts discontinued during the LTE through the cut-off date (primary reasons: AEs [n=16, 2.1%]; consent withdrawal [n=12, 1.5%]; lost to follow-up [n=10, 1.3%]). Cumulative exposures to monotherapy with MTX, UPA 15 mg, and UPA 30 mg were 350.6, 389.5, and 383.9 PYs, respectively. Both UPA 15 mg and 30 mg as monotherapy was associated with continued statistically significant improvements in disease activity measures vs MTX monotherapy observed at Wk 24, and maintained responses through 48 and 72 wks (**Table**). The safety profiles of the UPA 15 and 30 mg groups were comparable for total TEAEs and numerically higher than MTX. Serious TEAEs and TEAEs leading to discontinuation of study drug were comparable across all groups (**Figure**). Most AEs of special interest were comparable across MTX and UPA groups, with the exception of higher rates of herpes zoster, opportunistic infections, and elevated creatine phosphokinase among the UPA groups. Two pts receiving MTX monotherapy experienced

a venous thromboembolic event, with one event reported on UPA 30 mg and none on UPA 15 mg. There were 12 deaths (including 3 non-treatment-emergent) due to varied causes.

Conclusion: Long-term UPA monotherapy was associated with maintained improvements in RA signs and symptoms vs MTX monotherapy through 72 wks, and only a small proportion of pts required MTX addition at Wk26. Through 72 wks of treatment, the safety profile of UPA monotherapy remained consistent with data reported through 48 wks.[1]

References:

1. van Vollenhoven R, *et al*. *Ann Rheum Dis* 2019;78(S):376.
   Original abs: *Ann Rheum Dis.* 2020; 79(S1):330.

Disclosure: R. van Vollenhoven, AbbVie, 2, 5, Bristol-Meyers Squibb, 2, 5, GlaxoSmithKline, 2, 5, Lilly, 2, 5, Pfizer, 2, 5, UCB, 2, 5, 8, AstraZeneca, 5, 8, Biotest, 2, 5, Celgene, 5, Janssen, 5, 8, Roche, 5, Biogen, 5, Galapagos, 5, 8, Gilead, 5, Servier, 5; **T. Takeuchi**, Astellas Pharma Inc., 2, 5, 8, Daiichi Sankyo Company, Limited, 2, 5, 8, Takeda Pharmaceutical Company Limited, 2, 5, 8, AbbVie GK., 2, 5, 8, Asahi Kasei Pharma Corporation, 2, 5, 8, Mitsubishi Tanabe Pharma Corporation, 2, 5, 8, Eisai Co., Ltd., 2, 5, 8, Nippon Kayaku Co., Ltd., 2, 5, 8, Chugai Pharmaceutical Co., Ltd., 2, 5, 8, Eli Lily Japan K.K, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Pfizer Japan, Inc., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, AYUMI Pharmaceutical Corporation, 2, 5, 8, Novartis Pharma K.K., 2, 5, 8, UCB, 2, 5, 8, Dainippon Sumitomo Co., 2, 5, 8, Shionogi & Co., Ltd., 2, 5, 8; **M. Rischmueller**, AbbVie, 2, 5, 8, Amgen, 2, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, Pfizer, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8; **R. Blanco**, AbbVie, 2, 5, 8, MSD, 2, 5, 8, Roche, 2, 5, 8, Pfizer, 5, 8, Bristol-Myers Squibb, 5, 8, Janssen, 5, 8, Eli Lilly, 5, 8, UCB Pharma, 5, 8; **R. Xavier**, AbbVie, 5, 8, Pfizer, 5, 8, Novartis, 5, 8, Janssen, 5, 8, Eli Lilly, 5, 8, Roche, 5, 8, UCB Pharma, 5; **M. Howard**, AbbVie, 1, 3; **A. Friedman**, AbbVie, 1, 2; **Y. Song**, AbbVie, 1, 2; **V. Strand**, AbbVie, 5, Amgen, 5, Celltrion, 5, Janssen, 5, Merck, 5, Novartis, 5, Regeneron, 5, Sanofi, 5, UCB, 5, Genentech/Roche, 5, GSK, 5, Pfizer, 5, Bayer, 5, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, Galapagos, 5, Lilly, 5, Gilead, 5, Samsung, 5, Servier, 5, Setpoint, 5, Arena, 5, AstraZeneca, 5, Horizon, 5, Ichnos, 5, Inmedix, 5, Sandoz, 5.

Abstract Number: 0208

Efficacy and Safety of Filgotinib for Patients with Rheumatoid Arthritis with Inadequate Response to Methotrexate: 52-Week Results

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1: Efficacy outcomes at week 52

Efficacy Outcome	FIL 200 mg (n = 475)	FIL 100 mg (n = 480)	ADA (n = 325)
ACR20/50/70, %[a]	78/62/44	76/59/38	74/59/39
DAS28(CRP) ≤3.2, %[a]	66[+]	59	59
mTSS[b,c]	0.18[+++]	0.45	0.61
HAQ-DI[c,d]	−0.93[+]	−0.85	−0.85
SF-36 PCS[c,d]	12.0	11.5	12.4
FACIT-F[c,d]	11.9	12.2	11.7

[a]Non-responder imputation, [b]Least squares mean change from baseline, [c]Observed case, [d]Mean change from baseline.
[+]nominal p <0.05, [+++]nominal p <0.001 vs ADA
ADA, adalimumab; FACIT-F, Functional Assessment of Chronic Illness Therapy Fatigue; FIL, filgotinib; HAQ-DI, Health Assessment Questionnaire-Disability Index; mTSS, modified van der Heijde TSS; SF-36, 36-Item Short Form Survey.

Table 2. Treatment-emergent AEs of Interest from baseline to W24 and after W24

	PBO-controlled period (Week 0 to 24)				Week 24 to 52				
n (%)	FIL 200 mg (n=475)	FIL 100 mg (n=480)	ADA (n=325)	PBO (n=475)	FIL 200 mg (n= 475)	FIL 100 mg (n=480)	ADA (n=325)	PBO to FIL 200 mg (n=190)	PBO to FIL 100 mg (n=191)
Any TEAE	287 (60.4)	287 (59.8)	186 (57.2)	252 (53.1)	222 (46.7)	224 (46.7)	149 (45.8)	92 (48.4)	97 (50.8)
TE SAE	21 (4.4)	24 (5.0)	14 (4.3)	20 (4.2)	14 (2.9)	17 (3.5)	8 (2.5)	7 (3.7)	8 (4.2)
Infectious AEs	133 (28.0)	128 (26.7)	88 (27.1)	105 (22.1)	107 (22.5)	103 (21.5)	60 (18.5)	45 (23.7)	39 (20.4)
Serious infectious AEs	8 (1.7)	8 (1.7)	8 (2.5)	4 (0.8)	5 (1.1)	5 (1.0)	2 (0.6)	1 (0.5)	2 (1.0)
Herpes zoster	2 (0.4)	2 (0.4)	2 (0.6)	2 (0.4)	5 (1.1)	2 (0.4)	0	2 (1.1)	1 (0.5)
VTE (adjudicated)	1 (0.2)	0	0	2 (0.4)	0	0	1 (0.3)	1 (0.5)	0
MACE (adjudicated)	0	1 (0.2)	1 (0.3)	2 (0.4)	0	1 (0.2)	0	1 (0.5)	1 (0.5)
Malignancy, excluding NMSC	0	1 (0.2)	1 (0.3)	3 (0.6)	2 (0.4)	1 (0.2)	1 (0.3)	0	0
NMSC	0	0	0	0	1 (0.2)	1 (0.2)	0	0	0
Deaths	2 (0.4)	1 (0.2)	0	2 (0.4)	1 (0.2)	0	1 (0.3)	1 (0.5)	1 (0.5)

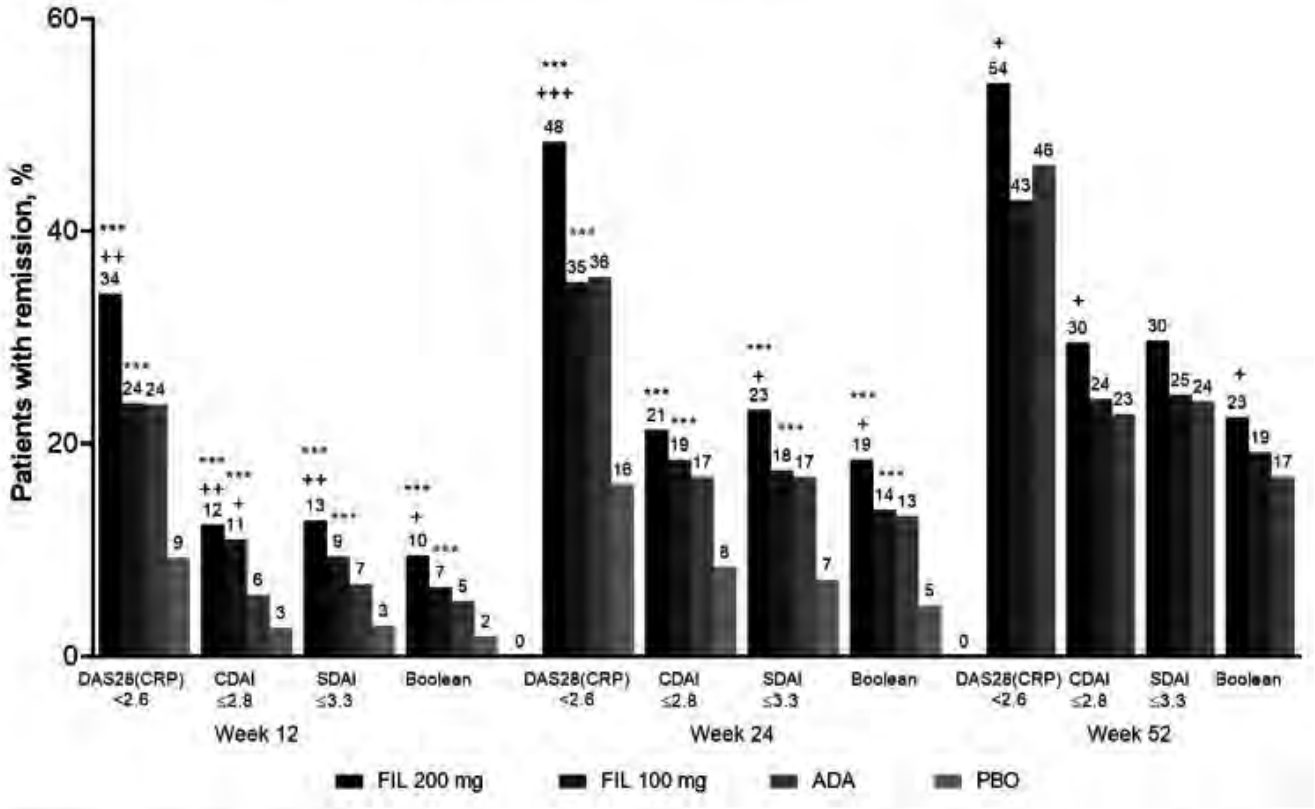
ADA, adalimumab; AE, adverse event; FIL, filgotinib; MACE, major adverse cardiac events; NMSC, nonmelanoma skin cancer; PBO, placebo; SAE, serious AE; TE, treatment-emergent; TEAE, treatment-emergent AE; VTE, venous thromboembolism.

Background/Purpose: Filgotinib (FIL) is an oral, potent, selective Janus kinase 1 (JAK1) inhibitor. FINCH 1 (NCT02889796) assessed FIL efficacy and safety in patients (pts) with rheumatoid arthritis (RA) with an inadequate response to methotrexate (MTX-IR); primary outcome results at week (W)12 and W24 were previously reported.[1] This analysis presents results from the FINCH 1 study through 52 weeks.

Methods: This global, phase 3, double-blind, active- and placebo (PBO)-controlled study randomized MTX-IR pts with active RA on a background of sTable MTX 3:3:2:3 to oral FIL 200 mg or FIL 100 mg once daily, subcutaneous adalimumab (ADA) 40 mg every 2W, or PBO up to W52; pts receiving PBO at W24 were rerandomized to FIL 100 or 200 mg. Efficacy was assessed using clinical, radiographic, and pt-reported outcomes; W52 comparisons were not adjusted for multiplicity, and nominal p-values are reported. Safety endpoints included types and rates of adverse events (AEs) and laboratory abnormalities.

Results: Of 1755 treated pts, 1417 received study drug through W52. The majority (81.8%) were female, mean (standard deviation [SD]) RA duration was 7.8 (7.6) years, and baseline mean (SD) DAS28(CRP) was 5.7 (0.9). FIL ef-

Figure 1. Patients in remission at weeks 12, 24, and 52



***, p vs PBO <0.001, not adjusted for multiplicity except DAS28(CRP) at week 12; +, p vs ADA <0.05; ++, p vs ADA <0.01; +++, p vs ADA <0.001; not adjusted for multiplicity. ADA, adalimumab; FIL, filgotinib; PBO, placebo.
Non-responder imputation. Logistic regression model with treatment groups and stratification factors for treatment comparisons.

ficacy was sustained through W52; 54%, 43%, and 46% of pts receiving FIL 200 and 100 mg and ADA, respectively, had W52 DAS28(CRP) < 2.6 (nominal p for FIL 200 vs ADA = 0.024) (**Figure 1, Table 1**). FIL safety profile through W52 was consistent with W24 data. AEs of interest were infrequent and balanced among treatments (**Table 2**).

Conclusion: Through W52, both FIL 200 and 100 mg showed sustained efficacy based on clinical and pt-reported outcomes and radiographic progression and were well tolerated in MTX-IR pts with RA.

1.Combe et al., Ann Rheum Dis. 2019; 78 (Suppl 2):77–8.

Disclosure: B. Combe, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **A. Kivitz**, Sanofi, 1, 5, 8, Amgen, 1, Gilead, 1, AbbVie, 5, Genzyme, 5, 8, Janssen, 5, Novartis, 8, Regeneron, 5, 8, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 8, Horizon, 8, Merck, 8, Pfizer, 1, 5, 8, Sun Pharma, 5, UCB, 5; **Y. Tanaka**, AbbVie, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 2, 5, 8, Asahi-kasei, 2, 5, 8, Novartis, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Astellas, 2, 5, 8, Chugai, 2, 5, 8, Daiichi-Sankyo, 2, 5, 8, Eisai, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Janssen, 2, 5, 8, Mitsubishi-Tanabe, 2, 5, 8, Pfizer, 2, 5, 8, Takeda, 2, 5, 8, YL Biologics, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer,

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Abstract Number: 0209

Upadacitinib as Monotherapy in Patients with Rheumatoid Arthritis and Prior Inadequate Response to Methotrexate: Results at 84 Weeks

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In the SELECT-MONOTHERAPY trial, upadacitinib (UPA), an oral JAK inhibitor, demonstrated significantly greater efficacy compared to continuing methotrexate (MTX) when used as monotherapy over 14 weeks (wks) in patients (pts) with rheumatoid arthritis (RA) and prior inadequate response to MTX.[1] Here we describe the long-term safety and efficacy of UPA monotherapy in an ongoing long-term extension (LTE) of the SELECT-MONOTHERAPY trial.

Methods: Pts on sTable MTX were randomized to either continue MTX (cMTX, given as blinded study drug) or switch to once-daily (QD) UPA 15 (UPA15) or 30 (UPA30) mg monotherapy for 14 wks. From Wk14, pts could enter a blinded LTE and continue to receive UPA15 or UPA30; pts randomized to cMTX were switched to UPA15 or UPA30 per pre-specified assignment at baseline. Treatment-emergent adverse events (TEAEs) per 100 pt yrs (PYs) of exposure are summarized up to a cut-off data of 5 February 2019, when all pts had reached Wk84. Efficacy outcomes through Wk84 are reported as observed and using non-responder imputation.

Results: Of 648 pts randomized, 598 (92%) completed 14 wks and entered the LTE on blinded UPA. By the cut-off date, 20% in total had discontinued due to the following: AE (6%), consent withdrawal (4%), lost to follow-up

Figure. Treatment-emergent Adverse Events Through ≥84 Weeks (E/100 PYs, 95% CI).

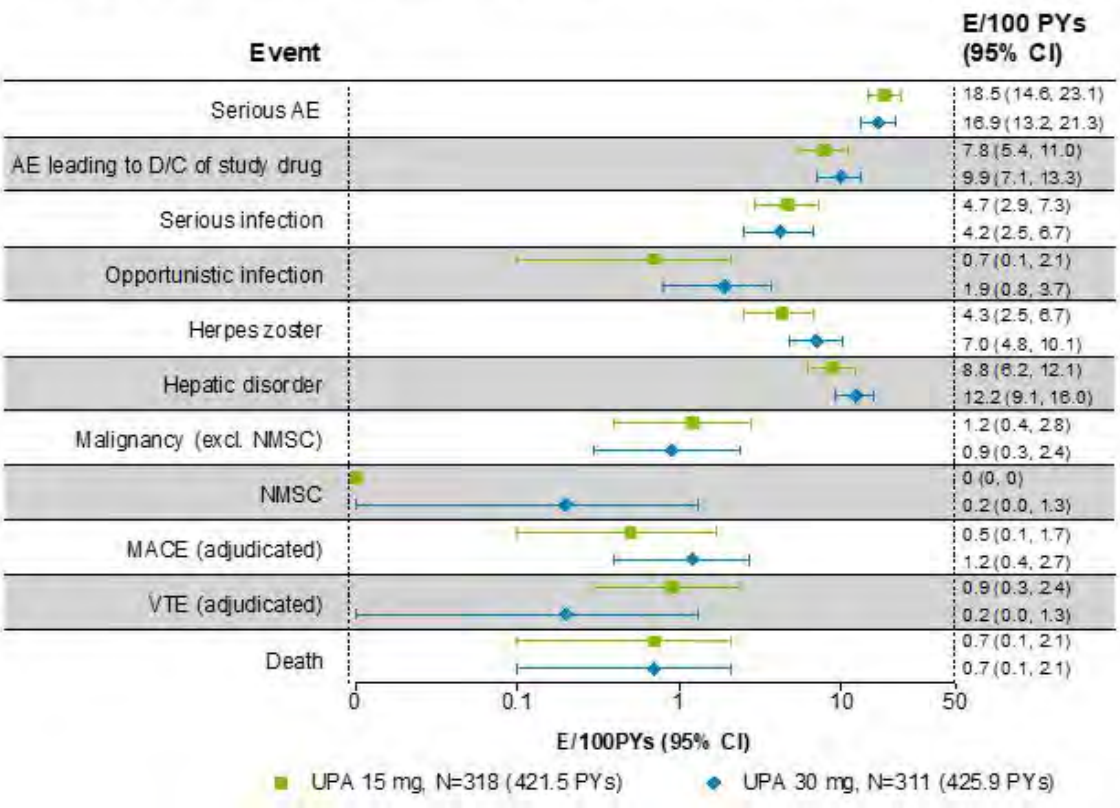

Table. Proportion of Patients at Week 84

Parameter (%)	cMTX→UPA 15 mg n=108		cMTX→UPA 30 mg n=108		UPA 15 mg n=217		UPA 30 mg n=215	
	AO	NRI	AO	NRI	AO	NRI	AO	NRI
ACR20/50/70	86/71/49	67/56/39	90/68/50	66/51/38	88/71/54	65/53/41	96/78/66	74/62/52
DAS28(CRP) ≤3.2/<2.6	80/56	64/44	79/63	62/49	76/60	57/46	85/77	67/61
CDAI ≤10/≤2.8	78/38	62/30	85/29	65/22	74/34	55/25	85/49	67/39
Boolean Remission	27	22	23	18	26	20	41	33

AO, as observed; NRI, non-responder imputation.

(2%), lack of efficacy (1%), or other reasons (7%). Cumulative exposures were 421.5 and 425.9 PYs for UPA15 and UPA30, respectively. The most frequently reported TEAEs were urinary tract infection, creatine phosphokinase (CPK) increase, upper respiratory tract infection, nasopharyngitis, worsening of RA, bronchitis, herpes zoster (HZ), and alanine aminotransferase increase; the most common serious AE was pneumonia. Events of HZ, hepatic disorder, and CPK elevations were higher among pts receiving UPA30, while rates of serious infection and malignancy appeared comparable between doses (**Figure**). Most HZ events involved 1-2 dermatomes, with a single disseminated cutaneous event (UPA30) and none with CNS involvement. Five patients experienced MACE, and there were 5 VTE events (UPA15: 4; UPA30: 1). All MACE and VTE events occurred in pts with underlying risk factors. Pts continuing to receive UPA15 and UPA30 achieved stringent endpoints at Week 84 (**Table**). Pts who switched from cMTX to UPA15 or UPA30 demonstrated comparable efficacy responses to those initially randomized to UPA.

Conclusion: The adverse event profile associated with long-term exposure to UPA15 or 30 as monotherapy was consistent with an integrated analysis of UPA safety across the entire phase 3 program, with no new safety signals identified. Further, UPA15 or 30 monotherapy resulted in continued and sustained improvements in RA signs and symptoms through 84 wks.

References:

1. Smolen, *et al*. *Lancet* 2019;393:2303-11.
Original abs: *Ann Rheum Dis.* 2020; 79(S1):327.

Disclosure: J. Smolen, AbbVie, 2, 5, 8, AstraZeneca, 2, 5, 8, Eli Lilly, 2, 5, 8, Celgene, 5, 8, Celltrion, 5, 8, Chugai, 5, 8, Gilead, 5, 8, ILTOO, 5, 8, Janssen, 5, 8, Kabi, 5, 8, Novartis-Sandoz, 5, 8, Pfizer Inc, 5, 8, Samsung, 5, 8, Sanofi, 5, 8; **P. Emery**, AbbVie, 2, 8, Bristol-Myers Squibb Company, 2, 8, Pfizer, 8, Roche, 2, 8, Celltrion, 8, Eli Lilly, 8, Gilead, 8, Novartis, 2, 8, Samsung, 8; **W. Rigby**, AbbVie, 5, Bristol-Myers Squibb, 5, Genentech, 5, Pfizer, 5; **Y. Tanaka**, AbbVie, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 2, 5, 8, Asahi-kasei, 2, 5, 8, Novartis, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Astellas, 2, 5, 8, Chugai, 2, 5, 8, Daiichi-Sankyo, 2, 5, 8, Eisai, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Janssen, 2, 5, 8, Mitsubishi-Tanabe, 2, 5, 8, Pfizer, 2, 5, 8, Takeda, 2, 5, 8, YL Biologics, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8; **J. Vargas**, AbbVie, 9; **N. Damjanov**, AbbVie, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Richter Gedeon, 5, 8, MSD, 5, 8, Novartis, 5, 8; **M. Jain**, AbbVie, 5, 8, Novartis, 5, 8, Celgene, 5, 8, Medac, 5, 8, Takeda, 5, 8; **Y. Song**, AbbVie, 1, 2; **N. Khan**, AbbVie, 1, 2; **J. Enejosa**, AbbVie, 1, 3; **S. Cohen**, Amgen Inc, 1, 2, AbbVie, 1, 2, Pfizer, 1, 2, Boehringer Ingelheim, 1, 2, Sandoz, 1, 2, Gilead, 2, 5, Eli Lilly, 2, 5.

Abstract Number: 0210

Long-term Safety and Efficacy of Sarilumab over 5 Years in Patients with Rheumatoid Arthritis Refractory to Tumor Necrosis Factor Inhibitors

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Sarilumab is a human IL-6 receptor (IL-6R) inhibitor approved for the treatment of adults with moderate to severely active RA. In the TARGET study (NCT01709578), sarilumab significantly improved signs and symptoms of RA and physical function versus placebo in patients refractory to TNF inhibitors who were receiving background treatment with conventional synthetic DMARDs. Here we report the long-term safety and efficacy of subcutaneous (SC) sarilumab over 5 years in patients who continued treatment in the open-label extension (OLE) study, EXTEND (NCT01146652).

Methods: Patients who received double-blind placebo, sarilumab 150 mg, or sarilumab 200 mg every 2 weeks (q2w) in the 24-week randomized controlled trial TARGET were eligible to receive open-label sarilumab 200 mg q2w during EXTEND, with dose reduction to 150 mg q2w permitted to manage laboratory abnormalities or per investigator's dis-

Table 1. Treatment-emergent adverse events in TARGET and EXTEND, by treatment assignment During TARGET

	Sarilumab 150 mg q2w + DMARD (n=181; 74 PY)	Sarilumab 200 mg q2w[a] + DMARD (n=340; 964 PY)	Any sarilumab dose[b] + DMARD (N=521; 1655 PY)
Summary, number of AEs (AEs/100 PY)[c]			
Any AE	121 (304)	317 (153)	481 (160)
Any SAE	6 (8)	91 (11)	146 (10)
AE leading to discontinuation	14 (19)	66 (7)	132 (8)
AE leading to death[d]	0	4 (0.4)	5 (0.3)
AEs with ≥5 events per 100 PY in any sarilumab dose + DMARD, number of AEs (AEs/100 PY)			
Cumulative total AE observation period, PY	74	964	1655
Neutropenia	34 (46)	102 (11)	254 (15)
Injection site erythema	33 (44)	57 (6)	197 (12)
Nasopharyngitis	12 (16)	69 (7)	131 (8)
Accidental overdose	9 (12)	70 (7)	128 (8)
Urinary tract infection	6 (8)	88 (9)	127 (8)
Pruritus generalized	5 (7)	4 (0.4)	120 (7)
Upper respiratory tract infection	4 (5)	64 (7)	111 (7)
RA	3 (4)	62 (6)	97 (6)
Injection site pruritus	10 (14)	31 (3)	82 (5)
AEs of special interest, number of AEs (AEs/100 PY)			
Infections	59 (79)	571 (59)	956 (58)
Serious infections	2 (3)	41 (4)	64 (4)
Leukopenia	39 (52)	129 (13)	303 (18)
Injection site reactions	48 (65)	120 (12)	367 (22)
Hepatic disorders	11 (15)	91 (9)	145 (9)
Hyperlipidemia	26 (35)	74 (8)	123 (7)
Drug hypersensitivity	15 (20)	63 (6)	105 (6)
Anaphylaxis	0	0	0
Thrombocytopenia	1 (1)	19 (2)	44 (3)
Major adverse cardiac event[e]	0	8 (0.8)	14 (0.8)
Malignancy	1 (1)	6 (0.6)	10 (0.6)
GI ulcerations	1 (1)	2 (0.2)	5 (0.3)
Diverticulitis/potential GI perforations[f]	0	3 (0.3)	4 (0.2)
Lupus-like syndrome	0	1 (0.1)	1 (0.1)
Demyelinating disorders	0	0	0

[a]Including placebo patients from the double-blind phase who switched to sarilumab 200 mg in the OLE; [b]Any dose includes exposure on all sarilumab doses; [c]In summary, rates (AEs/100 PY) were calculated over time to first event; [d]The TEAEs associated with the 5 instances of death were septic shock, acute pulmonary edema, myocardial infarction, pneumonia, and metastatic gallbladder cancer; [e]Includes cardiovascular death, myocardial ischemia, stroke, hospitalization for unstable angina, or hospitalization for transient ischemic attack; [f]Upon medical review, the 4 cases of diverticulitis/potential GI perforation were determined to be colonic abscess (n=1), peritonitis (n=1), and diverticulitis (n=2); AE=adverse event; GI=gastrointestinal; OLE=open-label extension; PY=patient-years; q2w=every 2 weeks; SAE=serious AE; TEAE=treatment emergent AE

Table 1

cretion. Safety outcomes are presented for the EXTEND population for the follow-up from TARGET baseline through EXTEND cut-off date (January 15, 2019). Efficacy assessments included Clinical Disease Activity Index (CDAI) score and the proportion of responders (CDAI ≤10 and ≤2.8) over time.

Table 2. Proportion of responders*

	Assigned TARGET Treatment		
	Placebo + DMARD	Sarilumab 150 mg + DMARD	Sarilumab 200 mg + DMARD
	EXTEND Treatment		
	Sarilumab 200 mg + DMARD (n=156)	Sarilumab 200 mg + DMARD (n=145)	Sarilumab 200 mg + DMARD (n=153)
CDAI ≤2.8, n (%)			
OLE baseline	21 (13)	26 (18)	23 (15)
After 192 weeks' follow-up	17 (11)	28 (19)	28 (18)
CDAI ≤10, n (%)			
OLE baseline	62 (40)	75 (52)	76 (50)
After 192 weeks' follow-up	57 (37)	61 (42)	66 (43)

*Nonresponder imputation; ITT values used as denominators. CDAI= Clinical Disease Activity Index; ITT=intent to treat; OLE=open-label extension

Table 2

Results: Of the 546 patients randomized in TARGET, 454 (83%) entered EXTEND and were treated with open-label sarilumab 200 mg (original placebo group, n=156; sarilumab 150 mg, n=145; sarilumab 200 mg, n=153). At EXTEND baseline, demographic and clinical characteristics were similar between previous treatment groups from TARGET. Overall, 81% of patients in EXTEND were women, mean age was 53 years, and mean RA duration was 12 years. At the time of data cut-off, 199 (36%) patients had discontinued treatment, of whom 100 (18%) had discontinued due to treatment-emergent adverse events (AEs), 27 (5%) due to lack of efficacy, and 68 (13%) due to other reasons. Cumulative exposure to sarilumab through TARGET and EXTEND (n=521) was 1655 patient-years (PY), with 268 (51%) patients having ≥4 years' exposure (Table 1). Overall, there were 160 TEAEs/100 PY, 10 serious AEs/100 PY, 8 AEs/100PY leading to discontinuation, and 0.3/100 PY leading to death (Table 1). The most common AEs were neutropenia (15/100 PY) and injection site erythema (12/100 PY; Table 1). Absolute neutrophil count < 1000 cells/mm^3 (Grade 3–4 neutropenia) was observed in 74 (14%) patients, and normalized on treatment in 65% (48/74) of those patients. Alanine aminotransferase above 3-fold the upper limit of normal was observed in 46 patients (9%) and normalized on treatment in 54% (25/46) of those patients. Infections and serious infections occurred at rates of 58/100 PY and 4/100 PY, respectively. Clinical efficacy was sustained through 5 years of EXTEND (Table 2). At EXTEND Week 240 (n=95), mean ± SD change in CDAI score from TARGET baseline was –31 ± 15.

Conclusion: The safety profile of sarilumab was consistent with results of phase 3 trials, IL-6R inhibition, and SC administration, and no new safety signals were identified over 5 years of follow-up in patients with RA refractory to TNF inhibitors. Clinical efficacy was sustained through 5 years' follow-up.

Disclosure: R. Fleischmann, Pfizer, 2, 5; **K. Maslova**, Sanofi, 1, 3; **H. Leher**, Regeneron, 3, Aurinia Pharmaceuticals, 3, 4; **A. Praestgaard**, Sanofi, 3; **G. Burmester**, AbbVie, 5, 8, Pfizer, 5, 8, Gilead Sciences, Inc., 5, 8, Eli Lilly, 5, 8, Novartis, 5, Celgene, 5.

Abstract Number: 0211

Efficacy and Safety of Upadacitinib in Patients from China, Brazil, and South Korea with Rheumatoid Arthritis Who Have Had Inadequate Response to Conventional Synthetic Disease-modifying Antirheumatic Drugs

Xiaofeng Zeng[1], Dongbao Zhao[2], Sebastiao Radominski[3], Mauro Keiserman[4], Chang Keun Lee[5], Sebastian Meerwein[6], Jeffrey Enejosa[7], Yunxia Sui[7], Mohamed-Eslam Mohamed[7] and Won Park[8], [1]Department of Rheumatology, Peking Union Medical College Hospital (PUMCH), Chinese Academy of Medical Sciences National Clinical Research Center for Dermatologic and Immunologic Diseases (NCRC-DID), Beijing, China (People's Republic), [2]Shanghai Changhai Hospital, Shanghai, China (People's Republic), [3]Universidade Federal do Paraná, Curitiba, Brazil, [4]Pontificial Catholic University, Porto Alegre, Brazil, [5]Asan Medical Center, Seoul, Republic of Korea, [6]Pharmaceutical Development, AbbVie Deutschland GmbH & Co KG, Ludwigshafen, Germany, [7]AbbVie Inc., North Chicago, IL, [8]Inha University, Incheon, Republic of Korea

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: This Phase 3, randomized, double-blind, placebo (PBO)-controlled study assessed the efficacy and safety of upadacitinib (UPA) in combination with csDMARDs in patients with rheumatoid arthritis (RA) from China, Brazil and South Korea who had an inadequate response to csDMARDs (csDMARD-IR).

Table 1. Efficacy endpoints at Week 12

Endpoint[a]	UPA 15 mg QD (n=169)	PBO (n=169)
Primary endpoint		
ACR20, %	71.6***	31.4
Secondary endpoints		
Δ DAS28(CRP)	-2.56***	-0.95
Δ HAQ-DI	-0.62***	-0.18
Δ SF-36 PCS	8.93[c]***	3.36[d]
DAS28(CRP) ≤3.2, %	46.2***	13.6
DAS28(CRP) <2.6, %	29.6***	5.3
CDAI ≤10, %	35.5***	11.2
ACR50, %[b]	40.8***	8.3
ACR70, %[b]	21.3***	3.6
ACR20 at Week 1, %[b]	25.4***	5.9

***p<0.001 versus PBO

[a]NRI for binary endpoints; ANCOVA with multiple imputation for DAS28(CRP) and HAQ-DI; mixed model repeated measures for other continuous endpoints.

[b]Unranked secondary endpoint. [c]n=143 [d]n=149

Methods: Patients were randomized 1:1 to receive UPA 15 mg once daily (QD) or PBO in combination with csDMARDs. The primary endpoint was ACR20 response at Week 12, using non-responder imputation.

Results: 338 patients were randomized, and 310 (91.7%) completed Week 12. At Week 12, statistically significantly more patients receiving UPA vs PBO achieved the primary endpoint of ACR20 (71.6% vs 31.4%, $p< 0.001$). UPA also demonstrated statistically significantly improvements in all ranked secondary endpoints vs PBO at Week 12 (Table 1), including mean change in DAS28(CRP), HAQ-DI, and SF-36 PCS, and patients achieving DAS28(CRP) ≤3.2, DAS28(CRP) < 2.6 and CDAI≤10. Greater responses were also seen with UPA vs PBO for other key secondary endpoints including ACR50 and ACR70. Onset of UPA action was rapid with more patients on UPA achieving ACR20 by Week 1 (25.4% vs 5.9%, $p< 0.001$). The frequency of AEs (61.5% vs 49.1%) and serious AEs (7.1% vs 3.0%) was higher with UPA versus PBO. The frequency of AEs of special interest was generally similar between UPA and PBO, with the exception of herpes zoster (1.8% vs 0.6%), hepatic disorders (9.5% vs 7.1%), neutropenia (3.0% vs 0%), and elevated creatine phosphokinase (1.8% vs 0.6%), which were higher with UPA. One case of breast cancer (on Day 1 of study) and one VTE (pulmonary embolism and deep vein thrombosis in a patient with history of deep vein thrombosis) were reported with UPA treatment.

Conclusion: Efficacy of UPA was demonstrated in this csDMARD-IR population from China, Brazil, and South Korea. The safety of UPA was comparable with the global Phase 3 program.

Reference:

Original abs: *Ann Rheum Dis.* 2020; 79(S1):1016.

Disclosure: X. Zeng, Jiangsu Hengrui Medicine Co., Ltd, 1; **D. Zhao**, None; **S. Radominski**, AbbVie, 5, 8, Celgene, 5, 8, Genentech, 5, 8, Roche, 5, 8, Janssen, 5, 8, Pfizer, 5, 8, UCB, 5, 8; **M. Keiserman**, Pfizer, 5, 9, Abbott, 5, Actelion, 5, Astra Zeneca, 5, 9, Amgen, 5, 9, Roche, 5, 9, Bristol-Myers Squibb, 5, 9, Janssen, 5, Anthera Pharmaceuticals, 9, Biogen Idec Inc, 9, Celltrion, 9, Eli Lilly, 9, Human Genome Sciences, 9, Novartis, 9, Sanofi, 9, UCB, 9; **C. Lee**, None; **S. Meerwein**, AbbVie, 1, 3; **J. Enejosa**, AbbVie, 1, 2; **Y. Sui**, AbbVie Inc, 1; **M. Mohamed**, AbbVie, 1, 3; **W. Park**, Celltrion Healthcare, 5.

Abstract Number: 0212

Long-Term Safety and Effectiveness of Upadacitinib or Adalimumab in Patients with Rheumatoid Arthritis: Results at 72 Weeks

Roy Fleischmann[1], In-Ho Song[2], Jeffrey Enejosa[3], Eduardo Mysler[4], Louis Bessette[5], Patrick Durez[6], Andrew Östör[7], Jerzy Swierkot[8], Yanna Song[9] and Mark Genovese[10], [1]Southwestern Medical Center, Metroplex Clinical Research Center, Dallas, TX, [2]AbbVie Inc., North Chicago, IL, [3]AbbVie Inc., Evanston, IL, [4]Organización Medica de Investigación, Buenos Aires, Argentina, [5]Laval University, Quebec, Canada, [6]Division of Rheumatology, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium, [7]Cabrini Medical Center, Monash University, Malvern, Victoria, Australia, [8]Wroclaw Medical University, Wroclaw, Poland, [9]AbbVie Inc., North Chicago,, IL, [10]Stanford University Medical Center, Palo Alto, CA

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: We report safety/efficacy of upadacitinib (UPA) vs adalimumab (ADA) up to 72 weeks (wks) in patients (pts) with rheumatoid arthritis from the ongoing long-term extension (LTE) of SELECT-COMPARE.

Methods: Pts were randomized to once-daily UPA 15mg, placebo (PBO), or ADA 40mg every other wk. Pts were rescued at Wks 14/18/22 from UPA to ADA, ADA to UPA or PBO to UPA if they met protocol-specified rescue criteria; at Wk26 all remaining patients with CDAI >10 were rescued as above with all remaining PBO pts switched to UPA. Pts continued UPA or ADA in a blinded manner until the last pt completed the Wk48 visit. Completers entered the LTE. Treatment-emergent adverse events (TEAEs)/100PY were summarized up to December 26 2018. Efficacy was analyzed by randomized group. NRI was used for binary endpoints for rescue prior to Wk26.LOCF was used for continuous and binary endpoints for rescue at Wk26.

Results: 1629 pts were randomized (UPA: 1209 [399 non-switched; 159 switched from ADA; 651 from PBO]; ADA: 420 [168 non-switched; 252 switched from UPA]); 1403 entered the LTE. Cumulative exposures were 1396.7 and 515.1 PYs for UPA and ADA, respectively. TEAEs/100PY of any AEs and serious AEs for UPA vs ADA were 266.3 vs 299.4 and 12.7 vs 15.9, respectively. AE of special interest (AESIs)/100PY for UPA vs ADA were 3.7 vs 4.3 for serious infections, 0.9 vs 0.6 for opportunistic infections, 0.7 vs 1.0 for malignancy, 0.4 vs 0.6 for adjudicated MACE, 0.3 vs 1.0 for VTE, and 0.6 vs 1.2 for deaths. The event rates were numerically higher with UPA vs ADA for herpes zoster (3.1 vs 1.2), hepatic disorder (17.3 vs 14.0), and CPK elevation (5.6 vs 2.1). At Wk72, ACR20/50/70 was achieved by 64/51/38% vs 53/38/25% of pts on UPA and ADA ($p< .01/.001/.001$), DAS28-CRP$\leq$3.2/$<$ 2.6 by 49/41% vs 32/26% ($p< .001$), and CDAI$\leq$10/$\leq$2.8 by 46/28% vs 33/17% ($p< .001$), respectively.

Conclusion: UPA continued to demonstrate a safety profile consistent with observations through 48 wks and durable clinical efficacy.[1]

References:

1. Fleischmann R, et al. Annals of the Rheumatic Diseases 2019;78:744-745.
Original abs: *Ann Rheum Dis.* 2020; 79(S1):319.

Disclosure: R. Fleischmann, Pfizer, 2, 5; **I. Song**, AbbVie, 1, 3; **J. Enejosa**, AbbVie, 1, 3; **E. Mysler**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 2, 5; **L. Bessette**, Amgen, 1, 2, 3, BMS, 1, 2, 3, Janssen, 1, 2, 3, UCB, 1, 2, 3, AbbVie, 1, 2, 3, Pfizer, 1, 2, 3, Merck, 1, 2, 3, Celgene, 1, 2, 3, Sanofi, 1, 2, 3, Lilly, 1, 2, 3, Novartis, 1, 2, 3, Gilead, 2, 6, 8; **P. Durez**, None; **A. Östör**, AbbVie, 5, Roche, 5, Janssen, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, Gilead, 5, Paradigm, 5, UCB Pharma, 5, Bristol-Myers Squibb, 5; **J. Swierkot**, AbbVie, 2, 8, Sandoz, 2, 8, Pfizer, 2, 8, Roche, 2, 8, Bristol-Myers Squibb, 2, 8, UCB, 2, 8, MSD, 2, 8, Accord, 2, 8, Janssen, 2, 8; **Y. Song**, AbbVie, 1, 2; **M. Genovese**, Abbvie, 2, 5, Eli Lilly and Company, 2, 5, Galapagos, 2, 5, Gilead Sciences Inc., 2, 5, Pfizer, 2, 5, EMD Merck Serono, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, RPharm, 2, 5, Sanofi-Genzyme, 2, UCB, 5, Amgen, 5.

Abstract Number: 0213

Sustainability of Response to Upadacitinib as Monotherapy or in Combination Among Patients with Rheumatoid Arthritis and Prior Inadequate Response to Conventional Synthetic DMARDs

Arthur Kavanaugh[1], Maya Buch[2], Bernard Combe[3], Louis Bessette[4], In-Ho Song[5], Yanna Song[6], Jessica Suboticki[5] and Peter Nash[7], [1]Division of Rheumatology, Allergy, & Immunology, University of California San Diego Medical School, San Diego, CA, [2]Centre of Musculoskeletal Research, School of Biological Sciences, University of Manchester, Manchester, United Kingdom, [3]University of Montpellier, Montpellier, France, [4]Laval University, Quebec, Canada, [5]AbbVie Inc., North Chicago, IL, [6]AbbVie Inc., North Chicago,, IL, [7]School of Medicine Griffith University, Brisbane, Queensland, Australia

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

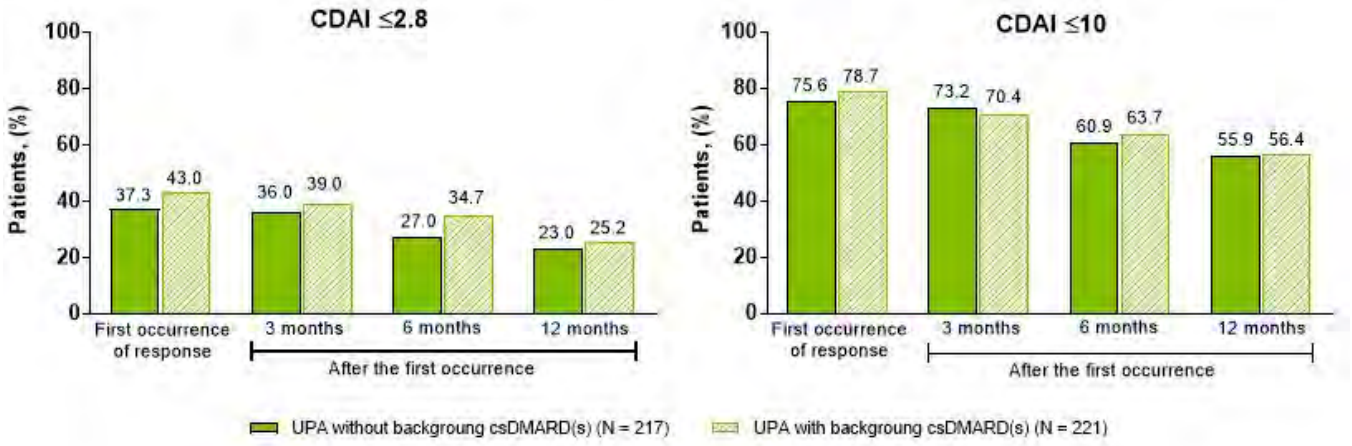
Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To assess long-term sustainability of responses to upadacitinib (UPA), a JAK inhibitor, with or without background csDMARD(s) in patients (pts) with rheumatoid arthritis (RA).

Methods: Data are from two phase 3 trials of UPA in RA pts with roughly similar baseline disease characteristics: SELECT-NEXT enrolled pts with inadequate response (IR) to csDMARD(s) on background sTable csDMARD(s) receiving UPA 15 or 30 mg once daily or placebo for 12 wks; SELECT-MONOTHERAPY enrolled methotrexate (MTX)-IR pts receiving UPA 15 or 30 mg monotherapy or blinded MTX for 14 wks. After 12/14 wks, pts could receive UPA 15 or 30 mg up to 5 years in a blinded long-term extension. This post hoc analysis evaluated clinical remission (REM:CDAI ≤2.8; SDAI ≤3.3), low disease activity (LDA:CDAI≤10; SDAI≤11), and DAS28(CRP) < 2.6/≤3.2 at first occurrence before Wk 84; these were also evaluated at 3, 6, and 12 months after the first occurrence for total number of pts

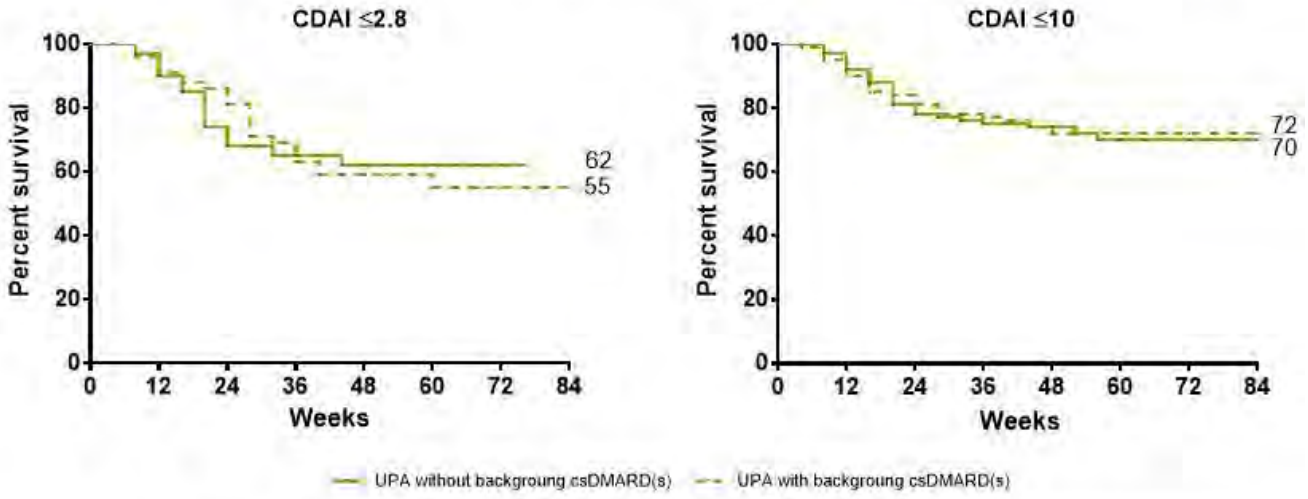
Figure 1. Proportion of patients sustaining CDAI remission or low disease activity at 3, 6, and 12 months after the first occurrence of response among the total randomized population



UPA, upadacitinib; csDMARD, conventional synthetic disease-modifying anti-rheumatic drugs; CDAI, Clinical Disease Activity Index; N, total number of patients randomized to UPA with or without background csDMARD(s).

Data for patients who maintained response through the cut-off (22 March, 2018 for SELECT-NEXT and 25 May, 2019 for SELECT-MONOTHERAPY, when all patients had reached Week 84 visit) were censored. Data are summarized, with no adjustments applied to account for between-study differences. Non-responder imputation was used for missing data.

Figure 2. Kaplan-Meier analysis of time to loss of CDAI remission or low disease activity after the first occurence of response



UPA, upadacitinib; csDMARD(s), conventional synthetic disease-modifying anti-rheumatic drugs; CDAI, Clinical Disease Activity Index; N, number of patients who had achieved CDAI remission or low disease activity.

Results are for patients who had achieved CDAI remission or low disease activity. UPA without backgroung csDMARD(s): CDAI ≤2.8: n = 81;CDAI ≤10: n = 164. UPA with backgroung csDMARD(s): CDAI ≤2.8: n = 95; CDAI ≤10: n = 174.

Data for patients who maintained response through the cut-off (22 March, 2018 for SELECT-NEXT and 25 May, 2019 for SELECT-MONOTHERAPY, when all patients had reached Week 84 visit) were censored. Data are summarized, with no adjustments applied to account for between-study differences. Non-responder imputation was used for missing data. Week 0 indicates the first occurrence of response.

References:

1. EULAR: Smolen JS, et al. Ann Rheum Dis 2017;76:960–977.
2. ACR: Singh et al. Arthritis & Rheumatology Vol. 68, No. 1, January 2016, pp 1–26.
   Original abs: *Ann Rheum Dis.* 2020; 79(S1):323.

randomized to UPA 15 mg. Sustainability was evaluated by Kaplan-Meier for pts who achieved REM/LDA and was defined as time to the earliest date of losing response at two consecutive visits or discontinuation of study drug. Predictive ability of time to clinical REM/LDA was assessed using Harrell's concordance (c)-index (~ 0.5, no ability to predict; closer to1 or -1, perfect prediction). Last follow up dates were 22 March 2018 (SELECT-NEXT) and 25 May, 2019 (SELECT-MONOTHERAPY), when all pts reached the Week 84 visit.

Results: Through Wk 84, CDAI REM/LDA was achieved in 43%/79% of pts receiving UPA 15 mg with background csDMARD(s) (SELECT-NEXT) and 37%/76% without background csDMARD(s) (SELECT-MONOTHERAPY). 35%/25% of pts randomized to UPA 15 mg with background csDMARD(s) and 27%/23% without background csDMARD(s) achieved sustained CDAI REM through 6/12 months after first occurrence. 64%/56% of pts randomized to UPA 15 mg with background csDMARD(s) and 61%/56% without background csDMARD(s) achieved sustained CDAI LDA through 6/12 months after first occurrence (**Figure 1**). Time to initial clinical REM/LDA did not appear to be associated with sustained disease control. The c-indices (95%CI) for CDAI REM in the UPA 15 mg with background csDMARD(s) and without background csDMARD(s) groups were 0.541 (0.47, 0.62) and 0.568 (0.49, 0.65) and LDA were 0.521 (0.46, 0.58) and 0.498 (0.43, 0.56), respectively. Through last follow-up visit, 55% of pts receiving UPA 15 mg with background csDMARD(s) and 62% without background csDMARD(s) remained in CDAI REM while 72% and 70% of pts remained in CDAI LDA, respectively (**Figure 2**). Similar results were observed across other disease activity measures (SDAI REM/LDA and DAS28(CRP) < 2.6/≤3.2).

Conclusion: More than a quarter and more than a half of pts with RA and prior IR to csDMARD(s) receiving UPA with or without background csDMARD therapy achieved sustained clinical REM and LDA, respectively, across disease

activity measures. Sustainability of responses appeared comparable among pts receiving UPA with or without background csDMARDs through up to 84 wks.

Disclosure: A. Kavanaugh, AbbVie, 2, 9, Amgen, 2, 9, AstraZeneca, 2, 9, Bristol-Myers Squibb, 2, 9, Celgene, 2, 9, Janssen, 2, 9, Pfizer, 2, 9, Roche, 2, 9, UCB, 2, 9; **M. Buch**, Pfizer, 2, Roche, 2, UCB, 2, AbbVie, 5, Eli Lilly and Company, 5, Gilead Sciences, Inc., 5, Merck-Serono, 5, Sandoz, 5, Sanofi, 5; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **L. Bessette**, Amgen, 1, 2, 3, BMS, 1, 2, 3, Janssen, 1, 2, 3, UCB, 1, 2, 3, AbbVie, 1, 2, 3, Pfizer, 1, 2, 3, Merck, 1, 2, 3, Celgene, 1, 2, 3, Sanofi, 1, 2, 3, Lilly, 1, 2, 3, Novartis, 1, 2, 3, Gilead, 2, 6, 8; **I. Song**, AbbVie, 1, 3; **Y. Song**, AbbVie, 1, 2; **J. Suboticki**, AbbVie, 1, 3; **P. Nash**, AbbVie, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 0214

Sustainability of Response Between Upadacitinib and Adalimumab Among Patients with Rheumatoid Arthritis and Prior Inadequate Response to Methotrexate

Peter Nash[1], Arthur Kavanaugh[2], Maya Buch[3], Bernard Combe[4], Louis Bessette[5], In-Ho Song[6], Yanna Song[7], Jessica Subotickí[6] and Roy Fleischmann[8], [1]School of Medicine Griffith University, Brisbane, Queensland, Australia, [2]Division of Rheumatology, Allergy, & Immunology, University of California San Diego Medical School, San Diego, CA, [3]Centre of Musculoskeletal Research, School of Biological Sciences, University of Manchester, Manchester, United Kingdom, [4]University of Montpellier, Montpellier, France, [5]Laval University, Quebec, Canada, [6]AbbVie Inc., North Chicago, IL, [7]AbbVie Inc., North Chicago,, IL, [8]Southwestern Medical Center, Metroplex Clinical Research Center, Dallas, TX

SESSION INFORMATION

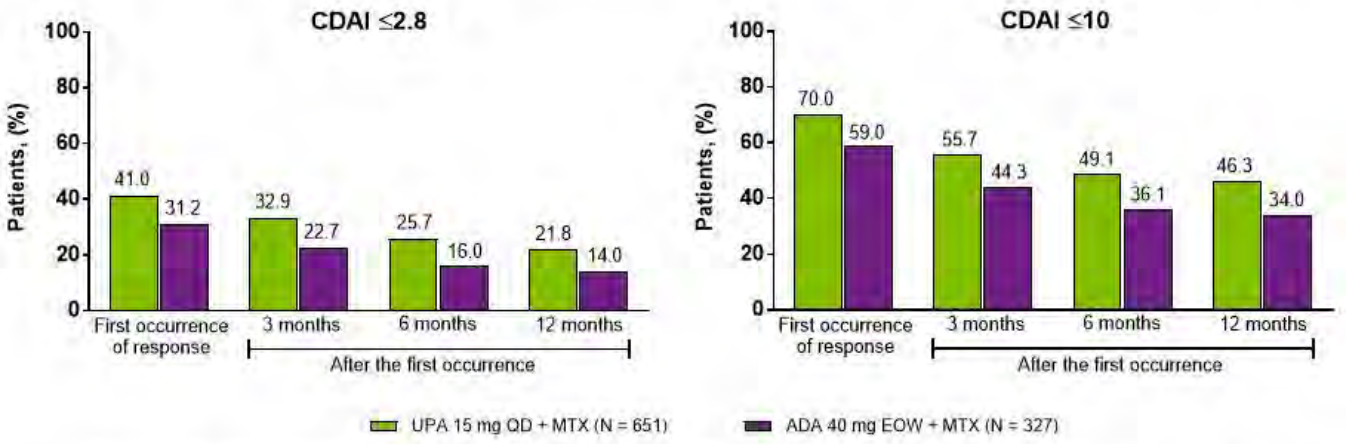
Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

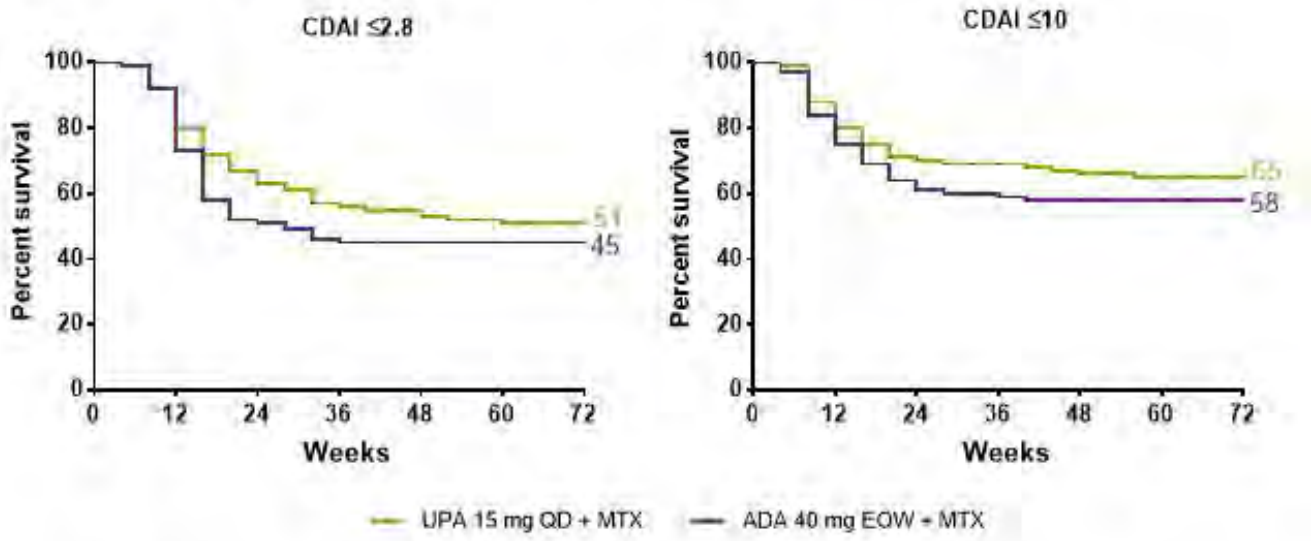
Figure 1. Proportion of patients sustaining CDAI remission or low disease activity at 3, 6, and 12 months after the first occurrence of response among the total randomized population



UPA, upadacitinib; ADA, adalimumab; MTX, methotrexate; QD, once daily; EOW, every other week; CDAI, Clinical Disease Activity Index; N, total number of patients randomized to UPA or ADA.

Data for patients who maintained response through the cut-off (6 July 2018, when all patients had reached Week 72 visit) were censored. Non-responder imputation was used for missing data.

Figure 2. Kaplan-Meier analysis of time to loss of CDAI remission or low disease activity after the first occurrence of response



UPA, upadacitinib; ADA, adalimumab; MTX, methotrexate; QD, once daily; EOW, every other week; CDAI, Clinical Disease Activity Index; N, number of patients who had achieved CDAI remission or low disease activity

Results are for patients who had achieved CDAI remission or low disease activity. UPA 15 mg QD + MTX: CDAI ≤2.8: n = 267; CDAI ≤10: n = 458; ADA 40 mg EOW + MTX: CDAI ≤2.8: n = 102; CDAI ≤10: n = 193.

Data for patients who maintained response through the cut-off (6 July 2018, when all patients had reached Week 72 visit) were censored. Non-responder imputation was used for missing data. Week 0 indicates the first occurrence of response.

References:

1. EULAR: Smolen JS, et al. Ann Rheum Dis 2017;76:960–977.
2. ACR: Singh et al. Arthritis & Rheumatology Vol. 68, No. 1, January 2016, pp 1–26.
   Original abs: *Ann Rheum Dis.* 2020; 79(S1):643.

Background/Purpose: The primary treatment goal for patients(pts) with rheumatoid arthritis(RA) is a state of sustained clinical remission(REM) or low disease activity(LDA).[1,2] W**e** assess long-term sustainability of response to upadacitinib(UPA), a JAK inhibitor, and adalimumab(ADA), both with background methotrexate(MTX), among pts with RA and prior inadequate response to MTX.

Methods: In the phase 3, randomized, placebo(PBO) and active-controlled SELECT-COMPARE trial, pts on sTable background MTX received UPA 15 mg once daily, PBO, or ADA 40mg every other week. Pts not achieving 20% improvements in tender/swollen joint counts(Weeks 14-22) or LDA(CDAI ≤10 at Week 26) were rescued from UPA to ADA or PBO/ADA to UPA; all non-rescued PBO pts were switched to UPA at Week 26. This post hoc analysis evaluated clinical REM(CDAI ≤2.8; SDAI ≤3.3), LDA(CDAI≤10; SDAI≤11), and DAS28(CRP) < 2.6/≤3.2 at first occurrence before Week 72 or prior to treatment switch; additionally, these measures were evaluated at 3, 6, and 12 months after the first occurrence for total number of pts randomized to UPA(n=651) or ADA(n=327). Sustainability of response was evaluated by Kaplan-Meier only for pts who achieved REM/LDA and was defined as time to the earliest date of losing response at two consecutive visits, discontinuation of study drug, or losing response at time of rescue. The predictive ability of time to clinical REM/LDA was assessed using Harrell's concordance (c)-index (for reference, an index ~ 0.5, indicates no ability to predict; an index of 1 or -1 would be a perfect prediction). The date of last follow up was 6 July, 2018, when all pts reached the Week 72 visit.

Results: Through Week 72, a significantly higher proportion of pts receiving UPA + MTX vs ADA + MTX achieved CDAI REM(41% vs 31%, p=.0035) as well as CDAI LDA(70% vs 59%, p=.0007). 26%/22% of pts randomized to UPA + MTX and 16%/14% of pts randomized to ADA + MTX achieved sustained CDAI REM at 6/12 months after the first occurrence. Additionally, 49%/46% of pts randomized to UPA + MTX and 36%/34% of pts randomized to ADA + MTX achieved sustained CDAI LDA at 6/12 months after the first occurrence(**Figure 1**). Time to initial clinical REM/LDA did not appear to be associated with sustained disease control. The c-indices (95% CI) for CDAI REM in the UPA +MTX and ADA + MTX groups were 0.528(0.48, 0.58) and 0.510(0.43, 0.59) and that of LDA were 0.601(0.56, 0.64) and 0.555(0.50, 0.61), respectively. Through last follow-up visit, 51% of UPA + MTX pts and 45% of ADA + MTX pts remained in CDAI REM while 65% of UPA + MTX pts and 58% of ADA + MTX pts remained in CDAI LDA, respectively(**Figure 2**). Similar results were observed across other disease activity measures(SDAI REM/LDA and DAS28(CRP) < 2.6/≤3.2).

Conclusion: A significantly greater proportion of pts with RA and prior inadequate response to MTX receiving UPA + MTX vs ADA + MTX achieved clinical REM or LDA across disease activity measures. REM and LDA were sustained through Week 72 in both treatment arms, with numerically higher proportions retaining response among UPA-treated pts.

Disclosure: P. Nash, AbbVie, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8; **A. Kavanaugh**, AbbVie, 2, 9, Amgen, 2, 9, AstraZeneca, 2, 9, Bristol-Myers Squibb, 2, 9, Celgene, 2, 9, Janssen, 2, 9, Pfizer, 2, 9, Roche, 2, 9, UCB, 2, 9; **M. Buch**, Pfizer, 2, Roche, 2, UCB, 2, AbbVie, 5, Eli Lilly and Company, 5, Gilead Sciences, Inc., 5, Merck-Serono, 5, Sandoz, 5, Sanofi, 5; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **L. Bessette**, Amgen, 1, 2, 3, BMS, 1, 2, 3, Janssen, 1, 2, 3, UCB, 1, 2, 3, AbbVie, 1, 2, 3, Pfizer, 1, 2, 3, Merck, 1, 2, 3, Celgene, 1, 2, 3, Sanofi, 1, 2, 3, Lilly, 1, 2, 3, Novartis, 1, 2, 3, Gilead, 2, 6, 8; **I. Song**, AbbVie, 1, 3; **Y. Song**, AbbVie, 1, 2; **J. Subotickі**, AbbVie, 1, 3; **R. Fleischmann**, Pfizer, 2, 5.

Abstract Number: 0215

Incidence and Risk of Venous Thromboembolic Events Among Patients with Rheumatoid Arthritis Enrolled in the Upadacitinib Clinical Trial Program

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients (pts) with rheumatoid arthritis (RA) are at an increased risk for the development of venous thromboembolism (VTE, including pulmonary embolism [PE] and deep vein thrombosis [DVT]) vs the general

Table. Events of VTE Observed Across Treatment Groups

	UPA 15 mg QD[a] N=2629 (4565.8 PYs)	UPA 30 mg QD[b] N=1204 (2309.7 PYs)	ADA + MTX[c] N=579 (768.6 PYs)	MTX Monotherapy[d] N=314 (456.0 PYs)
Events, n	21	8	4	2
Patients, n	20	7	4	2
PE only	11	1	3	1
DVT only	5	2	1	0
PE + DVT	4	4	0	1

[a]From SELECT-EARLY, -MONOTHERAPY, -NEXT, -COMPARE, and -BEYOND.
[b]From SELECT-EARLY, -MONOTHERAPY, -NEXT, and -BEYOND.
[c]From SELECT-COMPARE.
[d]From SELECT-EARLY.
VTE, venous thromboembolic; PE, pulmonary embolism; DVT, deep vein thrombosis.

Reference:

1. Kim SC, et al. *Arthritis Care Res* 2013;65:1600-7.
   Original abs: *Ann Rheum Dis.* 2020; 79(S1):313.

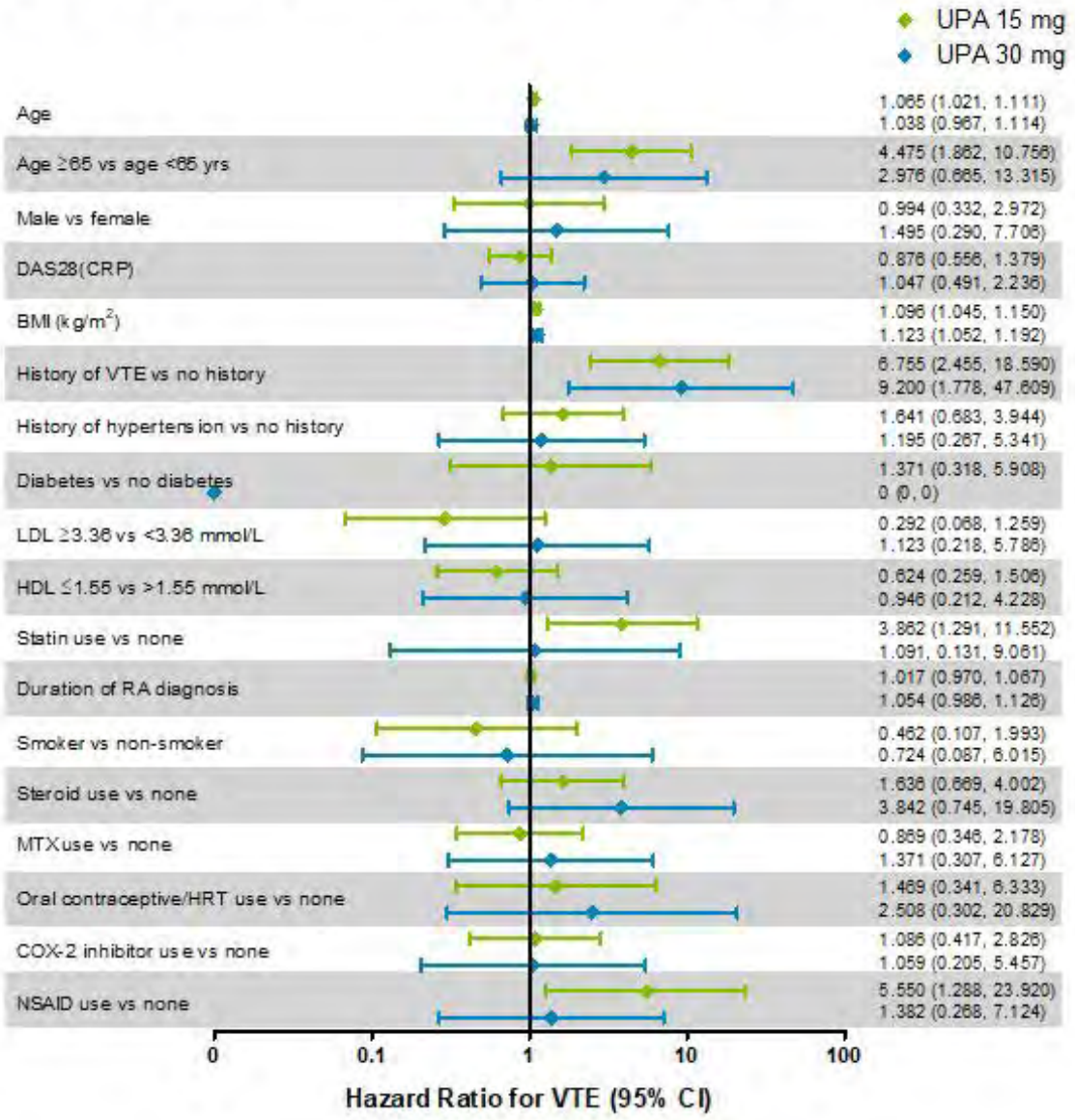
population (~2-fold increase).[1] Beyond RA, additional risk factors have been described, with prior history of VTE and obesity posing particular risk. VTE events have been observed in pts receiving JAK inhibitors, including upadacitinib (UPA). We describe the incidence of VTE in pts with RA receiving UPA relative to active comparators in the phase 3 clinical trial program and to evaluate potential risk factors.

Methods: Adjudicated events of treatment-emergent VTE were determined in pts receiving UPA in an integrated analysis (data cut-off, 30 Jun 2019) of five randomized phase 3 trials (SELECT-EARLY, SELECT-MONOTHERAPY, SELECT-NEXT, SELECT-COMPARE, and SELECT-BEYOND), of which 4 evaluated both the UPA 15 mg and 30 mg QD doses and 1 (SELECT-COMPARE) evaluated only UPA 15. Incidence of VTE was also determined in pts receiving adalimumab (ADA) + methotrexate (MTX) in SELECT-COMPARE and MTX monotherapy in SELECT-EARLY. Events are attributed to treatment received at time of event and are summarized per events/100 patient yrs. VTE risk factors were assessed using univariate Cox regression models.

Results: A total of 35 VTE events were observed across treatment groups. The exposure-adjusted treatment-emergent event rates (E/100 PYs, 95% CI) of VTE were 0.5 (0.3, 0.7) for UPA 15, 0.3 (0.1, 0.7) for UPA 30, 0.5 (0.1, 1.3) for ADA + MTX, and 0.4 (0.1, 1.6) for MTX, with no pattern to event onset across treatments. Events of PE, DVT, or both PE and DVT were reported across treatment groups (**Table**). Pts who experienced VTE, across all treatment groups, on average, were older than pts who did not (62/59/58/61 yrs vs 54/55/54/53 yrs for UPA 15, UPA 30, ADA + MTX, and MTX, respectively). The mean body mass index (BMI) of pts with VTE tended to be higher (34–40 for pts with VTE vs 28-29 kg/m^2 for those without). Across UPA treatment groups, 135/2629 (UPA 15) and 62/1204 (UPA 30) pts had a prior history of VTE; of these pts, 5 (3.7%) and 2 (3.2%) experienced VTE on UPA 15 and UPA 30, respectively. Univariate Cox regression models identified BMI and prior history of VTE as factors associated with VTE in the UPA 15 and 30 mg groups (**Figure**). Age and NSAID use were shown to be associated with VTE risk among pts in the UPA 15 but not 30 mg group.

Conclusion: VTE event rates appeared balanced across UPA doses and active comparator groups in pts with RA. Risk factors for VTE events identified through univariate analyses in pts who received UPA included prior history of VTE and BMI, two factors previously known to be associated with VTE risk. One limitation is the small sample size, limiting the analysis to univariate. Continued follow-up of pts receiving UPA is ongoing to further contextualize the risk of VTE in the clinical trial program.

Figure: VTE Risk Factors in Patients Receiving UPA 15 or 30 mg QD Through Univariate Cox Regression



Disclosure: E. Choy, Abbvie, 2, 8, Amgen, 2, 8, AstraZeneca, 2, 8, Biogen, 2, 8, Bio-Cancer, 2, 8, Boehringer Ingelheim, 2, 8, Bristol-Myers Squibb, 2, 8, Celgene, 2, 8, Chugai Pharma, 2, 8, Eli Lilly, 2, 8, Ferring Pharmaceuticals, 2, 8, GlaxoSmithKline, 2, 8, Janssen, 2, 8, Novartis, 2, 8, Novimmune, 2, 8, ObsEva, 2, 8, Pfizer, 2, 8, R-Pharm, 2, 8, Roche, 2, 8, SynAct Pharma, 2, 8, Tonix, 2, 8, UCB, 2, 8, Synovate, 2, 8, Sanofi, 2, 8, Regeneron, 2, 8, Napp, 2, 8, Hospira, 2, 8, Merck Sharp & Dohme, 2, 8; **I. McInnes**, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **J. Cush**, AbbVie, 2, 5, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb, 2, 5, Genentech, 2, 5, Novartis, 2, 5, Pfizer, 2, Amgen, 5, Boehringer Ingelheim, 5, Gilead, 5, Eli Lilly, 5, UCB, 5; **J. Aelion**, AbbVie, 2, 5, AstraZeneca, 2, Ardea Biosciences, 2, Boehringer Ingelheim, 2, 5, Bristol-Myers Squibb, 2, Celgene, 2, 5, Galapagos, 2, GlaxoSmithKline, 2, Janssen, 2, Eli Lilly, 2, 5, Merck, 2, Mesoblast, 2, Novartis, 2, Novo Nordisk, 2, Pfizer, 2, Roche, 2, Sanofi, 2, Takeda, 2, UCB, 2; **W. Rigby**, AbbVie, 5, Bristol-Myers Squibb, 5, Genentech, 5, Pfizer, 5; **Y. Song**, AbbVie, 1, 2; **S. Meerwein**, AbbVie, 1, 3; **J. Liu**, AbbVie Inc., 1, 2; **N. Khan**, AbbVie, 1, 2; **J. Suboticki**, AbbVie, 1, 3; **A. Cohen**, AbbVie, 5, 8, Apalgon, 5, 8, Aspen, 5, 8, BMS, 5, 8, Pfizer, 5, 8, Bayer, 5, 8, Daiichi Sankyo, 5, 8, Boehringer Ingelheim, 5, 8, Boston Scientific, 5, 8, Janssen, 5, 8, Portola, 5, 8.

Abstract Number: 0216

A Subgroup Analysis of Low Disease Activity and Remission from Phase 3 Study of Filgotinib in Patients with Inadequate Response to Biologic DMARDs

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite effective treatments, many patients (pts) with rheumatoid arthritis (RA) have inadequate responses to biologic DMARDs (bDMARD-IR), highlighting an unmet need. It is unclear whether prior bDMARD use affects efficacy of the oral, selective JAK-1 inhibitor filgotinib (FIL). This analysis explored the clinical response to FIL in bDMARD-IR pts stratified by mode of action (MOA) and number of prior bDMARDs.

Methods: The global, phase 3 FINCH-2 (NCT02873936) study treated 448 bDMARD-IR pts with active RA.[1] Pts were randomized 1:1:1 to once-daily FIL 200 mg, FIL 100 mg, or placebo (PBO) for 24 weeks. Efficacy was assessed by percent of pts achieving low disease activity (LDA) or remission at week (W)24 as measured by CDAI and DAS28(CRP)

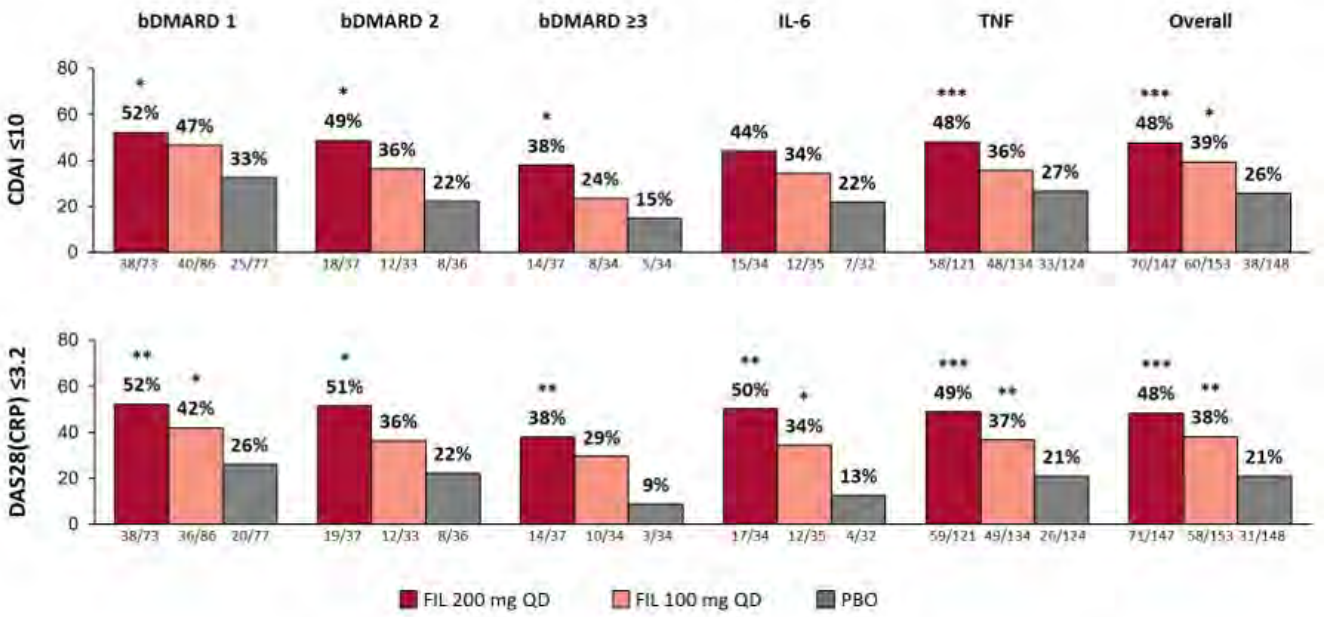
Table. Number and MOA of prior bDMARDs

	FIL 200 mg = 147	n FIL 100 mg n = 153	PBO n = 148	Total N = 448
Prior bDMARDs				
1	73 (49.7)	86 (56.2)	77 (52.0)	236 (52.7)
2	37 (25.2)	33 (21.6)	36 (24.3)	106 (23.7)
≥3	37 (25.2)	34 (22.2)	34 (23.0)	105 (23.4)
LOE ≥1 bDMARD	125 (85.0)	129 (84.3)	126 (85.1)	380 (84.8)
Intolerance ≥1 bDMARD	36 (24.5)	34 (22.2)	32 (21.6)	102 (22.8)
Prior TNFi	121 (82.3)	134 (87.6)	124 (83.8)	379 (84.6)
LOE ≥1 TNFi	97 (66.0)	113 (73.9)	103 (69.6)	313 (69.9)
Intolerance ≥1 TNFi	25 (17.0)	24 (15.7)	24 (16.2)	73 (16.3)
Prior non-TNFi	73 (49.7)	62 (40.5)	75 (50.7)	210 (46.9)
LOE ≥1 non-TNFi	52 (35.4)	43 (28.1)	56 (37.8)	151 (33.7)
Intolerance ≥1 non-TNFi	13 (8.8)	13 (8.5)	11 (7.4)	37 (8.3)
Prior IL-6i	34 (23.1)	35 (22.9)	32 (21.6)	101 (22.5)
LOE ≥1 IL-6i	25 (17.0)	22 (14.4)	21 (14.2)	68 (15.2)
Intolerance ≥1 IL-6i	5 (3.4)	10 (6.5)	5 (3.4)	20 (4.5)

Data presented as n (%).

i, inhibitor; LOE, lack of efficacy.

Figure 1. Low disease activity at week 24



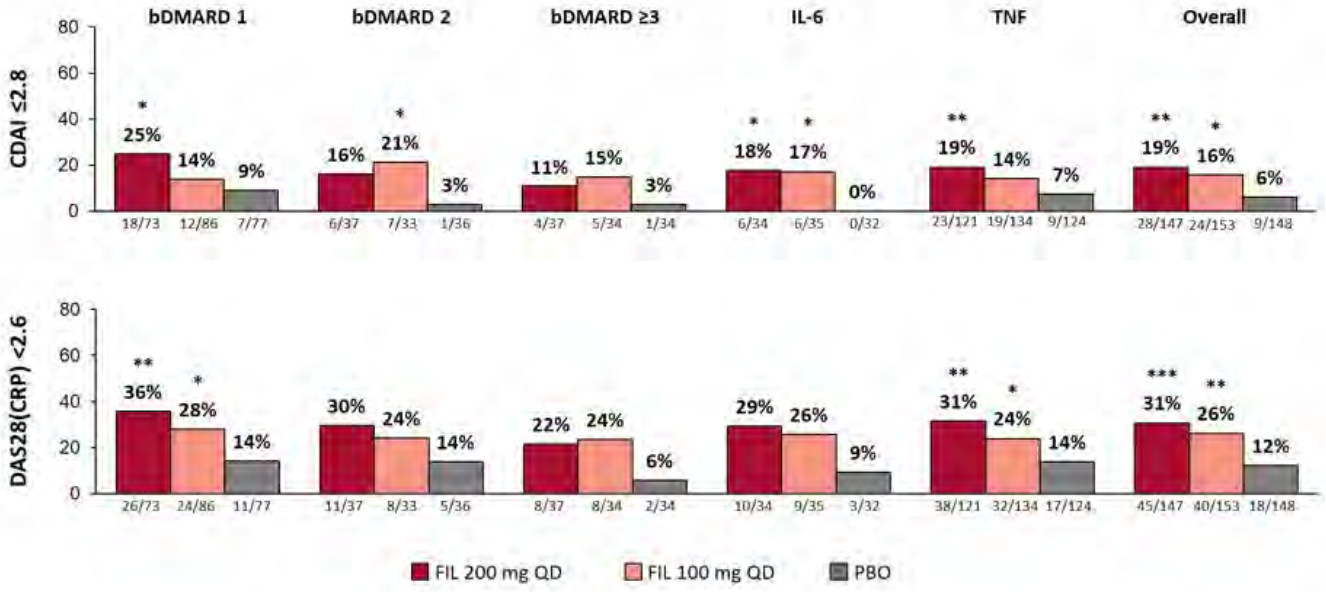
***P<0.001 vs PBO; **P<0.01 vs PBO; *P<0.05 vs PBO bDMARD, biologic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; DAS28(CRP), Disease Activity Score with C-reactive protein; FIL, filgotinib; IL, interleukin; PBO, placebo; QD, once-daily; TNF, tumour necrosis factor.

stratified by number and MOA of prior bDMARDs. Comparisons were not adjusted for multiplicity. Non-responder imputation was used.

Results: In total, 448 bDMARD-IR pts were included, 105 with prior experience with ≥3 bDMARDs (**Table**). At W24, pts receiving FIL were in LDA at a higher proportion vs PBO, irrespective of number of prior bDMARDs or MOA (**Figure 1**). For pts receiving FIL 200 vs PBO, DAS28(CRP) ≤3.2 was achieved at W24 by 52% vs 26%, 51% vs 22%, and 38% vs 9% of pts with 1, 2, or ≥3 prior bDMARDs, respectively, and 49% vs 21% and 50% vs 13% of pts exposed to TNF or IL-6 inhibitors; for all subgroups, rates were significantly higher vs PBO (**Figure 1**). Delta between FIL 200 mg and PBO was maintained irrespective of number or type of prior bDMARDs. At W24, pts receiving FIL achieved remission at numerically higher rates vs PBO (**Figure 2**). For pts receiving FIL 200 mg vs PBO, DAS28(CRP) < 2.6 was achieved at W24 by 36% vs 14%, 30% vs 14%, and 22% vs 6% of pts with 1, 2, and ≥3 prior bDMARDs, respectively, and 31% vs 14% and 29% vs 9% of pts exposed to TNF or IL-6 inhibitors (**Figure 2**). Delta between FIL 200 mg and PBO was maintained irrespective of number or type of prior bDMARDs. Treatment-emergent adverse events across subgroups were consistent with overall study population.

Conclusion: Treatment with FIL vs PBO led to higher rates of LDA and remission in pts with IR to IL-6 or TNF inhibition, or to 1, 2, or ≥3 prior bDMARDs, with a similar safety profile to the overall study population. A significantly higher proportion of pts overall receiving FIL 200 mg vs PBO were in LDA at W24. Improved efficacy of FIL vs PBO in pts who previously failed multiple bDMARDs indicates distinct benefits of selective JAK-1 inhibition with FIL.

Figure 2. Remission at week 24



***P<0.001 vs PBO; **P<0.01 vs PBO; *P<0.05 vs PBO bDMARD, biologic disease-modifying antirheumatic drug; CDAI, Clinical Disease Activity Index; DAS28(CRP), Disease Activity Score with C-reactive protein; FIL, filgotinib; IL, interleukin; PBO, placebo; QD, once-daily; TNF, tumor necrosis factor.

1. Genovese, et al. JAMA 2019;322(4):315–25.

Disclosure: J. Gottenberg, Bristol-Myers Squibb, 2, 8, Pfizer, 2, 5, UCB, 5, 8, Eli Lilly, 2, 8, AbbVie, 2, 8, Roche, 2, 8, Sanofi-Genzyme, 5, 8; **M. Buch**, Pfizer, 2, Roche, 2, UCB, 2, AbbVie, 5, Eli Lilly and Company, 5, Gilead Sciences, Inc., 5, Merck-Serono, 5, Sandoz, 5, Sanofi, 5; **R. Caporali**, AbbVie, Inc., 5, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, 8, Gilead Sciences, Inc., 5, 8, Merck Sharp & Dohme, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8, Galapagos NV, 5, 8, Celgene, 5, 8; **G. Wright**, Exagen, 5, 8, AbbVie, 5, 8, Amgen, 5, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly and Company, 5, 8, Myriad Autoimmune, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Regeneron Pharmaceuticals, Inc., 5, 8, Sanofi Genzyme, 5, 8, UCB, 5, 8; **T. Takeuchi**, Astellas Pharma Inc., 2, 5, 8, Daiichi Sankyo Company, Limited, 2, 5, 8, Takeda Pharmaceutical Company Limited, 2, 5, 8, AbbVie GK., 2, 5, 8, Asahi Kasei Pharma Corporation, 2, 5, 8, Mitsubishi Tanabe Pharma Corporation, 2, 5, 8, Eisai Co., Ltd., 2, 5, 8, Nippon Kayaku Co., Ltd., 2, 5, 8, Chugai Pharmaceutical Co., Ltd., 2, 5, 8, Eli Lily Japan K.K, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Pfizer Japan, Inc., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, AYUMI Pharmaceutical Corporation, 2, 5, 8, Novartis Pharma K.K., 2, 5, 8, UCB, 2, 5, 8, Dainippon Sumitomo Co., 2, 5, 8, Shionogi & Co., Ltd., 2, 5, 8; **K. Kalunian**, AstraZeneca, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, Equillium, 2, 5, Gilead Sciences, Inc., 2, 5, Genentech, 2, 5, ILTOO, 2, 5, Janssen, 2, 5, Lupus Research Alliance, 2, 5, Nektar, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanford Consortium, 2, 5, Vielabio, 2, 5; **A. Pechonkina**, Gilead Sciences, Inc., 1, 3; **Y. Guo**, Gilead Sciences, Inc., 1, 3; **S. Rao**, Gilead Sciences, Inc., 1, 3; **Y. Tan**, Gilead Sciences, Inc., 1, 3; **R. Besuyen**, Galapagos, 1, 3; **M. Genovese**, Abbvie, 2, 5, Eli Lilly and Company, 2, 5, Galapagos, 2, 5, Gilead Sciences Inc., 2, 5, Pfizer, 2, 5, EMD Merck Serono, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, RPharm, 2, 5, Sanofi-Genzyme, 2, UCB, 5, Amgen, 5.

Abstract Number: 0217

Efficacy and Safety of Filgotinib in Methotrexate-Naïve Patients with Rheumatoid Arthritis: 52-Week Results

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL) is an oral, potent, selective JAK 1 inhibitor. FINCH 3 assessed FIL efficacy and safety in methotrexate (MTX)-naïve patients (pts) with rheumatoid arthritis (RA); week (W)24 primary outcome results were previously presented.[1] These analyses report FINCH 3 (NCT02886728) results through W52.

Methods: This global, phase 3, double-blind, active-controlled study randomized MTX-naïve pts with moderately to severely active RA 2:1:1:2 to oral FIL 200 mg once daily + MTX ≤20 mg weekly, FIL 100 mg + MTX, FIL 200 mg monotherapy (mono) + placebo (PBO), or PBO + MTX up to W52. Comparisons at W52 were not adjusted for multiplicity. Safety was assessed from adverse events and laboratory abnormalities.

Results: Of 1249 treated pts, 975 received study drug through W52. FIL efficacy was sustained up to W52. Treatment with FIL + MTX or FIL mono increased proportions of pts achieving ACR20/50/70 and clinical disease remission by DAS28(CRP) < 2.6 (FIL 200 mg + MTX, 53%; FIL mono, 46%), CDAI, SDAI, and Boolean criteria; improved HAQ-DI; and halted radiographic progression vs MTX alone (**Table 1** and **Figure**). Safety was consistent with W24 data (**Table 2**).

Table 1. Efficacy outcomes at week 52

	FIL 200 mg + MTX (n = 416)	FIL 100 mg + MTX (n = 207)	FIL 200 mg (n = 210)	MTX (n = 416)
ACR20, %	75.0***	73.4**	74.8***	61.8
ACR50, %	62.3***	59.4**	61.4**	48.3
ACR70, %	47.8***	40.1*	45.2***	29.8
mTSS[a]	0.21***	0.27*	0.23**	0.74
HAQ-DI[b]	−1.00***	−0.97	−0.95*	−0.88

[a]Least-squares mean change from baseline. [b]Mean change from baseline.

*, p <0.05; **, p <0.01; ***, p <0.001 vs MTX alone; not adjusted for multiplicity.

FIL, filgotinib; mTSS, van der Heijde modified total Sharp score; MTX, methotrexate.

Table 2. Safety outcomes through week 52

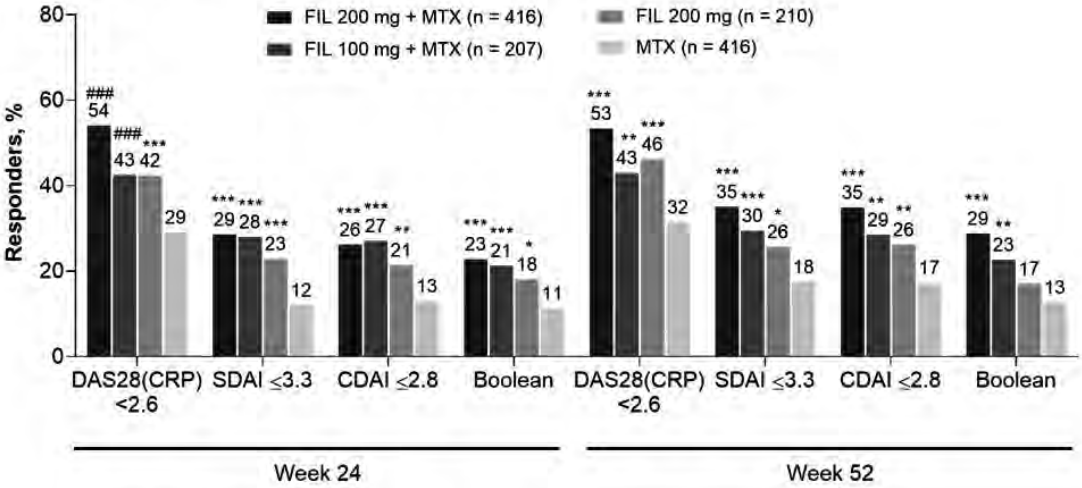
Event, n (%)	FIL 200 mg + MTX (n = 416)	FIL 100 mg + MTX (n = 207)	FIL 200 mg (n = 210)	MTX (n = 416)
All AEs	318 (76.4)	164 (79.2)	143 (68.1)	305 (73.3)
Serious AEs	26 (6.3)	13 (6.3)	17 (8.1)	28 (6.7)
Infection	148 (35.6)	76 (36.7)	75 (35.7)	157 (37.7)
Serious infection	5 (1.2)	3 (1.4)	5 (2.4)	8 (1.9)
Herpes zoster	6 (1.4)	3 (1.4)	4 (1.9)	4 (1.0)
VTE	0	0	0	4 (1.0)
MACE (adjudicated)	4 (1.0)	1 (0.5)	2 (1.0)	2 (0.5)
Malignancy[a]	1 (0.2)	0	0	4 (1.0)
NMSC	2 (0.5)	0	0	1 (0.2)
Death	3 (0.7)[b]	1 (0.5)[c]	0	0

[a]Excluding NMSC.

[b]1 lupus cardiomyopathy, 1 atypical interstitial pneumonia, 1 non–treatment-emergent cardiovascular death. [c]Dissecting cerebral and vertebral aneurysm.

AE, adverse event; FIL, filgotinib; MACE, major adverse cardiovascular event; MTX, methotrexate; NMSC, nonmelanoma skin cancer; VTE, venous thromboembolism.

Figure. Patients in clinical remission at week 52



###, p <0.001 vs MTX alone adjusted for multiplicity.

*, p <0.05; **, p <0.01; ***, p <0.001 vs MTX alone; not adjusted for multiplicity.

CDAI, Clinical Disease Activity Index; DAS28(CRP), Disease Activity Score in 28 joints with Creactive protein; FIL, filgotinib; MTX, methotrexate; SDAI, Simplified Disease Activity Index.

Conclusion: Efficacy of FIL 200 mg + MTX, FIL 100 mg + MTX, and FIL 200 mg mono was sustained through W52, with faster onset[1] and consistently numerically greater efficacy for FIL 200 vs 100 mg. No new safety signals were observed.

1.Westhovens, et al. Ann Rheum Dis. 2019;78(Suppl2):259–60.

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Abstract Number: 0218

Clinical Outcomes of Earlier versus Delayed Treatment of Iraqi Patients with Rheumatoid Arthritis with Etanercept

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The management of patients with early rheumatoid arthritis (RA), defined by the American College of Rheumatology (ACR) guidelines as patients who have had RA disease or symptoms for < 6 months, can improve prognosis and long-term clinical outcomes and reduce joint damage. In the Middle East, available evidence suggests that the management of patients with RA may be suboptimal, indicating a need for guidelines supporting the early use of biologic DMARDs.

Methods: This observational, retrospective study assessed real-world patient data entered in the National Center of Rheumatology database in Iraq from 2012 till 2018. Patients included in the study after they met ACR/EULAR 2010 criteria for Rheumatoid Arthritis with 1 year of follow up after starting their first etanercept therapy. Patients are excluded from the study if previously or currently treated with other biological therapies. Patients were categorized into two separate groups:

- Patients were stratified based on the disease duration before initiation of treatment with etanercept (≤1 year, >1 to ≤4 years, >4 to ≤10 years, >10 to ≤20 years, and >20 years) (group A).
- Patients were stratified based on the mean duration of RA: early and delayed treatment initiation were defined as having a RA diagnosis below or above mean of RA duration, before initiation of treatment with etanercept (group B).

VARIABLES	VALUES (N=979)
TOTALL POPULATION	
WOMEN, N (%)	813 (83)
AGE, YEARS, MEAN ± SD	48.06 ± 12.08
DISEASE DURATION, YEARS, MEAN ± SD	10.08 ± 8.27
PATIENTS STRATIFICATION N (%)	
≤1 YEAR	69 (7.05%)
>1 TO ≤4 YEARS	211 (21.55%)
>4 TO ≤10 YEARS	306 (31.26%)
>10 TO ≤20 YEARS	262 (26.76%)
>20 YEARS	131 (13.38%)
CDAI SCORE, MEAN ± SD	27.65 ± 11.63
DAS28 SCORE, MEAN ± SD	5.68 ± 1.2
METHOTREXATE TREATMENT, N (%)	
YES	535 (54.6%)
NO	444 (45.4%)

Table 1. Summary of baseline characteristics

Results: A total of 979 Iraqi patients with RA (of whom 813 [83%] were female) were included in the analysis, with a mean RA duration at baseline of 10 years and mean Clinical Disease Activity Index (CDAI) and Disease Activity Score 28 (DAS28) scores of 27.65 ± 11.63 and 5.68 ± 1.2, respectively **(Table 1).** Based on the stratified group (A), Patients who had RA symptoms for ≤1 year before etanercept initiation had the greatest CDAI change from baseline (10.9-point) and it was significantly lower in comparison to another stratified group (P=0.01). The change from baseline for >1 to ≤4 years, >4 to ≤10 years, >10 to ≤20 years, and >20 years group were (7.32-, 7.69-, 6.41-, and 6.62- point decrease respectively) [**Figure 1A**]. The mean change in DAS28 score was 1.1- point decrease for patients who had RA symptoms for ≤1 year and >1 to ≤4 years before etanercept initiation, while other patients (>4 to ≤10 years, >10 to ≤20 years, and >20 years groups) showed mean change of (1-, 0.83-, and 0.9- point decrease respectively) [**Figure 1B**]. In group B, at the last follow-up visit, patients with early etanercept initiation (≤10 years) had a higher decrease in CDAI and DAS28 scores from baseline compared with patients with delayed initiation (>10 years) (CDAI 7.9-point and CDAI 6.4-point decrease, respectively) [**Figure 2A**], (DAS28 1.05-point and DAS28 0.88-point decrease, respectively) [**Figure 2B**].

Conclusion: Patients who received earlier etanercept treatment appear to have a better clinical outcome compared with patients with delayed treatment.

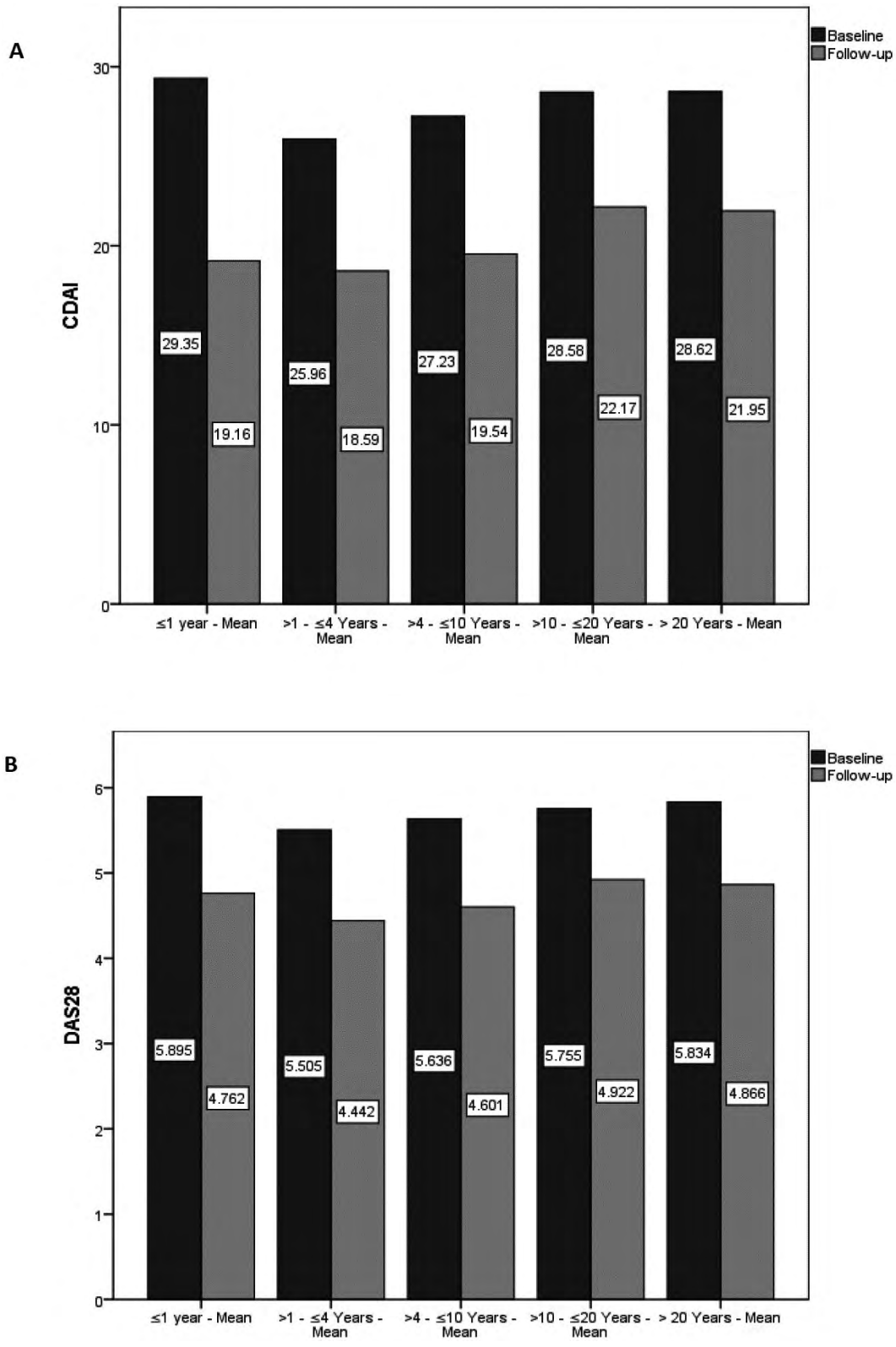

Figure 1. Changes in CDAI (A) and DAS28 (B) scores from baseline in patients stratified by RA duration before initiation of treatment with etanercept

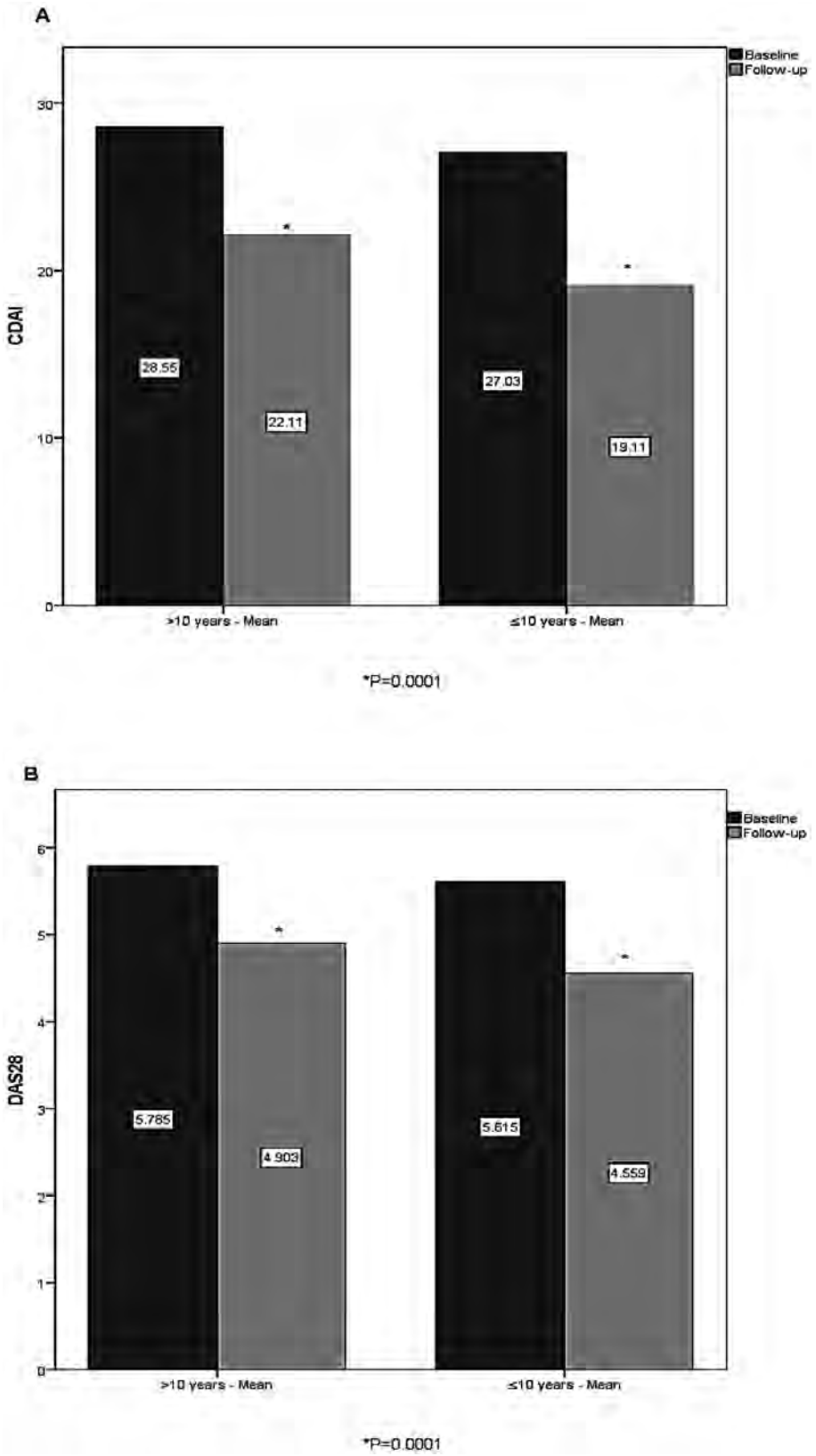

Figure 2. Changes in CDAI (A) and DAS28 (B) scores from baseline in patients with early (≤10 years) versus delayed (>10 years) management with etanercept

Disclosure: N. Abdulateef, None; **F. Gorial**, None; **Y. Humadi**, None; **D. Yasiry**, None; **F. Al Derwibee**, None; **N. Sunna**, Pfizer Inc., 3; **A. AlJabban**, Pfizer Inc., 3.

Abstract Number: 0219

Is It Realistic to Stop Prednisone in Early Rheumatoid Arthritis? A Subanalysis from the BeSt and IMPROVED Studies

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoids are widely used in the treatment of rheumatoid arthritis (RA) patients. It is internationally recommended to taper and stop glucocorticoids as rapidly as clinically feasible, but there are little data regarding this strategy. In two previous clinical trials (BeSt and IMPROVED) patients were treated with methotrexate (MTX) and a temporary course of oral prednisone (60 mg/day, tapered in 7 weeks to 7.5 mg/day). If the treatment target (TT, DAS≤2.4 in BeSt, DAS< 1.6 in IMPROVED) was achieved, prednisone was stopped, but in case of flare it was restarted. We present percentages of successful stopping and looked for potential predictors.

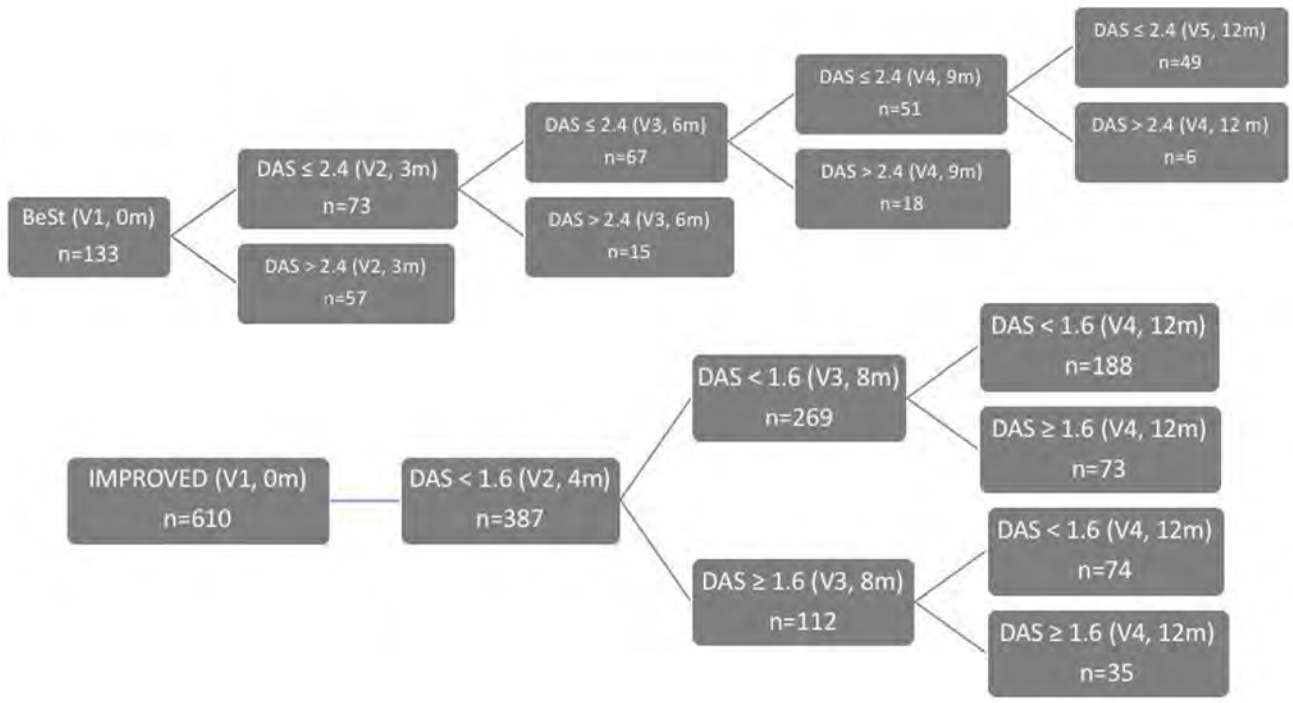

Figure 1. flow chart of the patient selection in BeSt and IMPROVED studies. m (month), DF (drug-free).

Characteristics	BeSt (n=69)		IMPROVED (n=381)	
	Remission (n=51)	No remission (n=18)	Remission (n=269)	No remission (n=112)
Age, mean (SD)	54.32 (11.96)	51.70 (16.20)	52.41 (14.13)	52.39 (13.21)
Female, n (%)	30 (58.82)	14 (77.78)	156 (57.99)	81 (72.32)
Symptom duration (weeks), median (IQR)	25 (16-62)	20 (16-58)	16 (9-29)	17 (8-32)
Erosions, n (%)	37 (72.55)	15 (83.33)	40 (15.15)	21 (19.44)
Fulfill ACR/EULAR2010, n (%)	-	-	207 (78.11)	86 (78.18)
RF positive, n (%)	38 (74.51)	11 (61.11)	152 (58.46)	68 (62.96)
ACPA positive, n (%)	29 (58.00)	11 (61.11)	161 (60.75)	62 (57.01)
bDAS, mean (SD)	4.07 (0.86)	4.30 (0.86)	2.92 (0.82)	3.18 (0.89)
pDAS, mean (SD)	1.37 (0.67)	1.97 (0.35)	0.90 (0.41)	1.15 (0.32)
CRP, median (IQR)	18 (10-44)	13 (3-35)	11 (5-27)	11 (5-29)
bVASGH, median (IQR)	48.66 (24.22)	41.89 (18.71)	47.87 (24.64)	46.96 (21.98)

Table 1. baseline characteristics in the BeSt and IMPROVED studies for patients on and off treatment target after stopping prednisone. RF (Rheumatoid Factor), ACPA (Anti-Citrullinated Protein Antibodies), bDAS (baseline DAS), pDAS (previous visit DAS), CRP (C-Reactive Protein, mg/dl), bVASGH (basal Visual Analogue Score Global Health).

Variables	BeSt (n=69)		IMPROVED (n=387)	
	Univariable	Multivariable (n=68, R^2=0.1641)	Univariable	Multivariable (n=379, R^2=0.2646)
Age	1.02 (0.97-1.06) p=0.463		1.00 (0.98-1.02) p=0.990	
Female	0.41 (0.12-1.42) p=0.158	0.65 (0.16-2.65) p=0.544	**0.53 (0.33-0.85) p=0.009**	**0.57 (0.34-0.94) p=0.029**
Symptom duration	1.00 (0.99-1.01) p=0.897		1.00 (0.99-1.01) p=0.638	
Erosions	0.53 (0.13-2.11) p=0.366		0.74 (0.41-1.33) p=0.311	
ACR/EULAR2010	-	-	1.00 (0.58-1.71) p=0.988	
RF positive	1.86 (0.60-5.80) p=0.285		1.83 (0.52-1.31) p=0.423	
ACPA positive	0.88 (0.29-2.64) p=0.818		1.18 (0.74-1.84) p=0.505	
bDAS	0.73 (0.39-1.39) p=0.341		**0.70 (0.54-0.91) p=0.007**	0.83 (0.61-1.13) p=0.225
pDAS	**0.16 (0.05-0.55) p=0.003**	**0.18 (0.05-0.59) p=0.005**	**0.18 (0.09-0.33) p=0.000**	**0.19 (0.10-0.37) p=0.000**
CRP	1.01 (0.99-1.02) p=0.468		1.00 (0.99-1.01) p=0.970	
bVASGH	1.01 (0.99-1.04) p=0.283		**0.99 (0.98-1.00) p=0.016**	0.99 (0.98-1.00) p=0.198

Table 2. univariable and multivariable analysis of predictors for successful GC stopping (OR 95% CI) in the BeSt and IMPROVED studies. RF (Rheumatoid Factor), ACPA (Anti-Citrullinated Protein Antibodies), bDAS (baseline DAS), pDAS (previous visit DAS), CRP (C-Reactive Protein, mg/dl), ΔDAS (difference between DAS at current visit and DAS at baseline), bVASGH (basal Visual Analogue Score Global Health).

Methods: 508 early RA patients were recruited for the BeSt study, from those 133 patients were randomized into the third arm of treatment (MTX+Sulfasalazin+Prednisone). 610 early RA or undifferentiated arthritis patients were enrolled into the IMPROVED study, all receiving MTX+Prednisone. Disease Activity Score was measured each 3 and 4 months, respectively. Stepwise tapering was slow in BeSt (prednisone tapered only after repeated treatment target achieved, earliest stop at week 35) and more rapid in IMPROVED (prednisone stop as soon as treatment target achieved, earliest at week 16), with a restart in case of flare 3 (BeSt) or 4 months (IMPROVED) after stop, respectively. Percentages still on treatment target after stopping of prednisone were compared in BeSt and IMPROVED. Univariable logistic regression was performed to identify potential predictors of successful stopping. Predictors with $p< 0.2$ were included in multivariable logistic regression analyses.

Results: In the BeSt study, 67/133 (50%) could stop initial prednisone due to sustained low disease activity (Figure 1). After prednisone stop, 51/67 (76%) patients remained on TT, but 18 flared. In the IMPROVED study, 387/610 (63%) patients stopped prednisone because of DAS-remission at 4 months (Figure 1). Of those, 269/387 (70%) remained on TT after stopping prednisone, while 112 flared. Baseline patient and disease characteristics between patients who did or did not flare after prednisone stop in both studies are shown in Table 1. In the BeSt study, DAS at previous visit was an independent predictor for successful secondary stopping of prednisone ($p=0.005$, Table 2). In the IMPROVED multivariable testing showed female gender and lower DAS at previous visit as independent predictors of successful secondary stopping prednisone ($p< 0.03$) Fulfilling the 2010 classification criteria for RA was not associated with the outcome after PRD stop (Table 2).

Conclusion: In these treat-to-target studies, where initial co-treatment with prednisone was stopped after the treatment target was (repeatedly, in BeSt) achieved, a lower DAS at the visit before stopping, was predictive of remaining on treatment target without flare. In IMPROVED, female patients also could more often successfully stop prednisone. Successful stopping of initial co-treatment with prednisone appears to be irrespective of treatment duration and treatment target. The data suggest that in patients with early RA the duration of temporary 'bridging' treatment of prednisone should be individually timed.

Disclosure: R. Dos-Santos, None; **S. Bergstra**, None; **J. Maassen**, None; **T. Huizinga**, Bristol-Myers Squibb Company, 2, 8, Pfizer, 2, 8, Eli Lilly, 2, 8, LUMC, 9; **C. Allaart**, None.

Abstract Number: 0220

Impact of Concomitant Glucocorticoids on the Clinical Efficacy and Safety of Upadacitinib in Patients with Rheumatoid Arthritis: An Ad Hoc Analysis of Data from Three Phase 3 Studies

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Safety in patients receiving UPA or PBO with/without csDMARDs, and with/without GCs

	SELECT-NEXT (through Week 12) All arms with concomitant csDMARDs				SELECT-MONOTHERAPY (through Week 14)				SELECT-EARLY (through Week 24)			
%	PBO +GCs (n=106)	PBO −GCs (n=115)	UPA 15 mg QD +GCs (n=95)	UPA 15 mg QD −GCs (n=126)	MTX +GCs (n=114)	MTX −GCs (n=102)	UPA 15 mg QD +GCs (n=113)	UPA 15 mg QD −GCs (n=104)	MTX +GCs (n=162)	MTX −GCs (n=152)	UPA 15 mg QD +GCs (n=147)	UPA 15 mg QD −GCs (n=170)
AE	48.1	49.6	57.9	57.1	42.1	52.9	48.7	47.1	66.7	66.4	63.3	65.9
Serious AE	1.9	2.6	4.2	4.8	3.5	2.9	4.4	5.8	6.2	2.0	3.4	6.5
AE leading to discontinuation	1.9	4.3	3.2	3.2	3.5	2.0	2.7	4.8	3.7	6.6	4.8	5.3
Deaths[a]	0	0	0	0	0	0	0.9[b]	0	0.6[c]	0	0.7[d]	0.6[e]
AESIs												
Infections	16.0	26.1	29.5	28.6	24.6	28.4	23.0	15.4	32.7	31.6	30.6	34.1
Serious infections	0	0.9	1.1	0	0.9	0	0.9	0	2.5	0	0.7	2.9
Opportunistic infections	0.9	0	0	0	0	1.0	0	0	0	0	0	0.6
HZ	0	0.9	0	0.8	0.9	0	0.9	1.9	0.6	0	2.7	1.8
Malignancies	0	0	0	0	0	1.0	0	1.9	0.6	0	0.7	1.2
MACE (adjudicated)	0	0	0	0	0	0	0.9	0	0.6	0	0.7	0
VTE (adjudicated)	0	0	0	0	0	0	0.9	0	0.6	0	0	0

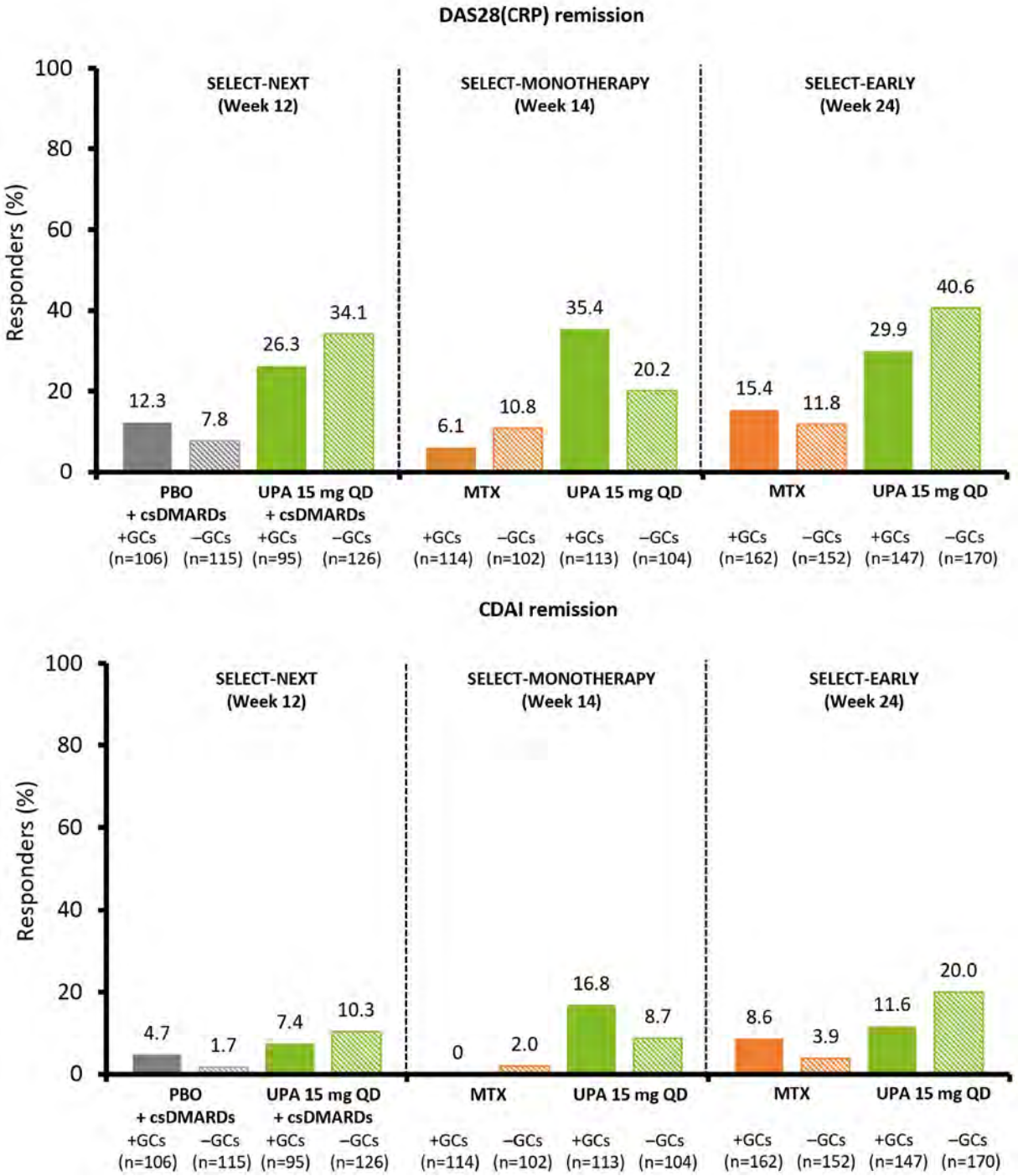
[a]Includes non-treatment-emergent deaths. [b]One death, caused by hemorrhagic stroke due to ruptured aneurysm. [c]One sudden CV death. [d]One CV death. [e]One death, caused by metastatic malignant melanoma. AE, adverse event; AESI, adverse event of special interest; csDMARD, conventional synthetic DMARD; CV, cardiovascular; GC, glucocorticoid; HZ, herpes zoster; MACE, major cardiovascular event; PBO, placebo; QD, once daily; UPA, upadacitinib; VTE, venous thromboembolic event.

Background/Purpose: Glucocorticoid (GC) therapy has strong anti-inflammatory effects and helps slow radiographic progression in RA[1]; however, GCs can be associated with adverse events (AEs) such as infection, especially with long-term use and higher doses. This ad hoc analysis of three Phase 3 studies of upadacitinib (UPA) in RA (SELECT-NEXT, SELECT-MONOTHERAPY, and SELECT-EARLY) aimed to evaluate the impact of baseline GCs on the efficacy and safety of UPA with or without concomitant conventional synthetic DMARDs (csDMARDs).

Methods: Patients with inadequate response to MTX (MTX-IR) receiving UPA 15 mg once daily (QD) or placebo (PBO) + csDMARDs in SELECT-NEXT, and MTX-IR/MTX-naïve patients receiving UPA 15 mg QD monotherapy or MTX monotherapy in SELECT-MONOTHERAPY/SELECT-EARLY, respectively, were included in the analysis. Efficacy outcomes, including measures of remission and low disease activity (LDA) determined by DAS in 28 joints using CRP (DAS28[CRP]; < 2.6/≤3.2) and Clinical Disease Activity Index (CDAI; ≤2.8/≤10), were assessed and stratified by baseline GC use. Patients were permitted to receive oral GCs ≤10 mg/day (prednisone equivalent) at baseline with no adjustment permitted until Week 24/26/48. Safety was reported as number and proportion of patients with AEs. Data were analyzed descriptively with no statistical comparisons between groups or doses.

Results: Of 1,506 patients included in the analysis, 737 (48.9%) were receiving baseline GCs (mean dose 6.2 mg/day). Baseline characteristics were broadly similar across treatment groups; SELECT-EARLY, which enrolled MTX-naïve patients, generally had the shortest duration of RA and higher CRP levels. Across UPA treatment groups, concomitant GCs generally did not influence the proportions of patients achieving remission (**Figure 1**). In SELECT-NEXT, clinical responses with UPA 15 mg in combination with csDMARDs were similar irrespective of concomitant GC use (**Figure 1**). Within SELECT-MONOTHERAPY, responses in patients receiving UPA 15 mg without concomitant csDMARDs or GCs were higher than those in patients receiving MTX alone, but were numerically lower than in those receiving UPA 15 mg with GCs (**Figure 1**). However, this was not observed within SELECT-EARLY, where clinical

Figure 1. Efficacy in patients receiving UPA or PBO with/without csDMARDs, and with/without GCs[a]



[a]Non-responder imputation. CDAI, Clinical Disease Activity Index; csDMARD, conventional synthetic DMARD; DAS28(CRP), Disease Activity Score in 28 joints using CRP; GC, glucocorticoid; PBO, placebo; QD, once daily; UPA, upadacitinib.

responses in patients receiving UPA 15 mg monotherapy without GCs were higher than in those patients receiving UPA 15 mg with GCs for both DAS28(CRP) < 2.6 (40.6% vs 29.9%, respectively) and CDAI ≤2.8 (20.0% vs 11.6%, respectively) (**Figure 1**). A similar trend was observed for LDA. Serious AEs, AEs leading to discontinuation, and AEs

of special interest, including infections (such as herpes zoster), were broadly similar in the UPA groups irrespective of concomitant GC use (**Table 1**).

Conclusion: UPA 15 mg in combination with csDMARDs or as monotherapy was effective in achieving remission and LDA, irrespective of concomitant GC use. Safety of UPA, including incidence of infection, appeared largely unaffected by concomitant GC use.

1.Kirwan JR, et al. Cochrane Database Syst Rev 2007;1:CD006356.

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Abstract Number: 0221

Should We Use BioDMARDS in First Intention in Early Rheumatoid Arthritis? : Results at 5 Years from the ERA Louvain Brussels Cohort

Emilie Sapart[1], Tatiana Sokolova[1], Stéphanie de Montjoye[1], Stéphanie Dierckx[2], Adrien Nzeusseu Toukap[3], Aleksandra Avramovska[1], Laurent Meric de Bellefon[1] and **Patrick Durez**[4], [1]Rheumatology, Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCL) – Institut de Recherche Expérimentale et Clinique (IREC), Brussels, Belgium, [2]Rheumatology, CHU Mont-Godinne, Mont Godinne, Belgium, [3]1Department of Rheumatology, Cliniques Universitaires Saint Luc, 2Institut de recherche expérimentale et clinique (IREC), Brussels, Belgium, [4]Division of Rheumatology, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Early effective treatment has led to major improvements in patients with rheumatoid arthritis (ERA). Low disease activity and remission are achieved earlier and in higher frequency when the initial treatment in rheumatoid arthritis includes a combination of methotrexate (MTX) with a bDMARD compared to MTX alone.

The aim of this study is to retrospectively analyse and compare the benefit of a treatment with methotrexate (MTX) alone or combined with a bDMARD as an induction therapy during 5 years of follow-up in early rheumatoid arthritis (ERA) patients.

Methods: We included ERA patients from the UCLouvain Brussels cohort who met the ACR/EULAR 2010 classification criteria and were naïve to DMARDs. Treatments were initiated based on the decision of a senior rheumatologist. bDMARDs induction therapy was usually limited to 6 or 12 months. We collected patient characteristics at baseline and clinical response was analysed at 6 months, 1 year, 3 years and 5 years.

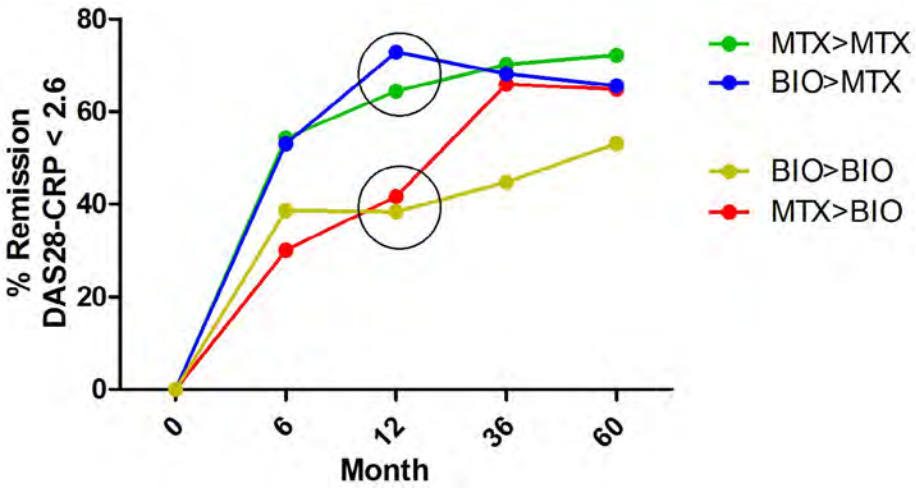


Figure 1. DAS28-CRP remission rate during time in each of the four groups (MTX->MTX (n=134), MTX->BIO (n=103); BIO->MTX (n=95), BIO->BIO (n=59).

Results: Data from 470 eligible ERA patients were collected. The average age of the population is 48.9 years; 70.5% of the patients are women; 27.3% are smokers and 68.8% are positive for anti-citrullinated protein antibody (ACPA). 281 patients (59.8 %) initiated MTX as a monotherapy (MTX group) compared to 189 patients (40.2%) who received a bDMARD (Bio group).

At baseline, the disease activity is the main factor that favors the initiation of bDMARDs (DAS28-CRP 5.2 vs 4.5, p< 0.001) followed by HAQ (1.32 vs 1.15, p=0.009), ACPA positivity (77.8% vs 62.5%, p=0.0006), rheumatoid factor positivity (71.5% vs 60.2%, p=0.0134). Other parameters such as age, gender, smoking habits or baseline erosion were similar between groups.

391 patients were followed up to 5 years. We then divided each of the two groups into two subgroups according to the last treatment they received at 5 years. Figure 1 shows the percentage of DAS28-CRP remission during time in each of the four groups (MTX- >MTX (n=134), MTX- >BIO (n=103); BIO- >MTX (n=95), BIO- >BIO (n=59);

At 12 months, DAS28-CRP response rate was statistically significantly higher in MTX >MTX and BIO >MTX groups compared to the two other groups. As expected, the remission rate was rescued in the group MTX- >Bio after 12 months.

Interestingly, ERA patients initially treated by a bDMARD followed by a MTX maintenance therapy experienced a sTable and sustained rate of remission.

Conclusion: Longterm remission is an achievable goal in ERA followed in daily clinic. Our results suggest that a bDMARD induction therapy followed by MTX maintenance therapy could be a good option in severe case of ERA.

Disclosure: E. Sapart, None; **T. Sokolova**, None; **S. de Montjoye**, None; **S. Dierckx**, None; **A. Nzeusseu Toukap**, AbbVie, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, UCB, 1, 2, Novartis, 1, Celgene Corporation, 1, Pfizer, 1; **A. Avramovska**, None; **L. Meric de Bellefon**, None; **P. Durez**, None.

Abstract Number: 0222

tsDMARD Therapy Is Associated with More Initial Therapy Prolongations Compared to bDMARDs Both in Bionaive and Bioexperienced Patients with Rheumatoid Arthritis

Diederik De Cock[1], Patrick Durez[2], Dirk Elewaut[3], Bernard Lauwerys[4], Rene Westhovens[5] and Patrick Verschueren[6], [1]KU Leuven, Leuven, Belgium, [2]Division of Rheumatology, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium, [3]Ghent University and VIB, Heusden, Belgium, [4]Paediatric Rheumatology International Trials Organisation (PRINTO), Genoa, Italy, [5]University Hospitals Leuven, Belgium, Leuven, Belgium, [6]University Hospital Leuven, Leuven, Belgium

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

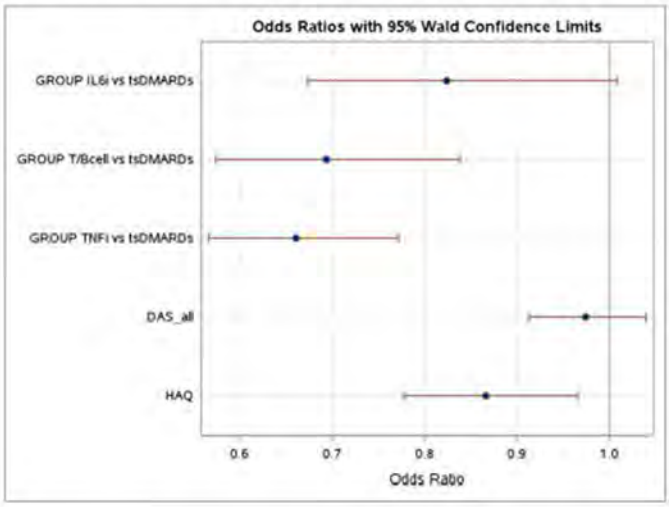
Background/Purpose: The Tool for Administrative Reimbursement Drug Information Sharing (TARDIS) is an electronic platform combining the collection of data from all Belgian patients with Rheumatoid Arthritis (RA) on biologic (b) and targeted synthetic (ts) DMARDs, together with the submission of a request for reimbursement of this medication. Therapy choice after failure of 2 classical synthetic (cs) DMARD is left at the discretion of the treating physician in Belgium. Therapy is prolonged after 3 months for tsDMARDS and after 6 months for bDMARDs if treatment is effective.

Table 1: Baseline characteristics of TARDIS patients

	ALL	TNFi	B/T cell	IL6i	tsDMARDs	p-value
number	6355	2483	1081	969	1822	
Age (years)	57 (49-66)	55 (46-65)	60 (52-68)	58 (49-68)	58 (50-67)	<0.001
Gender (women)	4664, 73%	1816, 73%	779, 72%	700, 72%	1369, 75%	0.207
Weight (kg)	71 (62-82)	70 (62-81)	71 (64-83)	73 (64-84)	71 (61-82)	0.330
Disease duration (years)	6 (2-13)	4 (2-10)	8 (4-16)	6 (2-13)	8 (3-14)	<0.001
HAQ (0-3)	1.5 (1.0-2.0)	1.5 (1.0-2.0)	1.5 (1.0-2.0)	1.5 (1.0-2.0)	1.5 (1.0-2.0)	<0.001
PGA (0-100)	70 (52-80)	70 (50-80)	70 (55-80)	70 (55-80)	70 (50-80)	0.079
CRP (mg/l)	7.1 (2.7-16.8)	6.1 (2.5-14.3)	8.0 (2.9-18.0)	10.0 (3.4-23)	7.0 (2.4-16.0)	<0.001
ESR (mm/h)	20 (9-36)	18 (8-32)	22 (10-38.5)	27 (12-43)	20 (9-35)	<0.001
TJC28	7 (4-12)	7 (4-12)	8 (5-12)	7 (4-12)	7 (4-11)	0.003
SJC28	5 (2-8)	5 (2-8)	5 (3-8)	5 (3-8)	4 (2-8)	<0.001
DAS28	4.79 (4.17	4.72 (4.13-5.40)	4.93 (4.27-5.64)	4.88 (4.28-5.59)	4.72 (4.11-5.43)	<0.001
Bio-Experienced (yes)	3198, 50%	811, 33%	723, 67%	572, 59%	1092, 60%	<0.001
Therapy prolongation (yes)	5046, 79%	1911, 77%	837, 77%	779, 80%	1519, 83%	<0.001

Number given are median, (IQR) or number, proportion. TNFi = tumour necrosis factor inhibitor, ts= targeted synthetic, HAQ= health assessment questionnaire, PGA= Patient Global assessment; CRP= C-reactive protein; ESR= erythrocyte sedimentation rate; TJC= tender joint count; SJC= Swollen joint Count; DAS28 = disease activity score based on the 28joints, Therapy prolongation = patient received same therapy at next visit

Fig1: Multivariate logistic regression predicting prolongation of therapy



Our aim was to investigate which factors are associated with a successful prolongation of therapy in the TARDIS-RA registry.

Methods: The Tool for Administrative Reimbursement Drug Information Sharing (TARDIS) is an electronic platform combining the collection of data from all Belgian patients with Rheumatoid Arthritis (RA) on biologic (b) and targeted synthetic (ts) DMARDs, together with the submission of a request for reimbursement of this medication. Therapy choice after failure of 2 classical synthetic (cs) DMARD is left at the discretion of the treating physician in Belgium. Therapy is prolonged after 3 months for tsDMARDS and after 6 months for bDMARDs if treatment is effective. Our aim was to investigate which factors are associated with a successful prolongation of therapy in the TARDIS-RA registry.

Results: We could include 6355 drug observations in 5471 unique patients. Table 1 describes this population in detail. In univariate logistic regression, prolongation of therapy was associated with lower baseline Patient Global Assessment ($p=0.032$), lower baseline disease activity score ($p=0.036$), lower baseline Health Assessment Questionnaire (HAQ) score ($p=0.003$) and starting at baseline tsDMARD therapy instead of either TNFi ($p< 0.001$), T/B cell ($p< 0.001$) or IL6 inhibition therapy ($p=0.049$) therapy. In multivariate logistic regression, prolongation of therapy remained associated with lower baseline HAQ score ($p=0.022$) and starting at baseline tsDMARD therapy instead of either TNFi ($p< 0.001$) or T/B cell ($p< 0.001$) therapy (Figure 1). Sensitivity analyses in advanced therapy naïve patients confirmed these results, but in advanced therapy experienced patients, baseline HAQ score became statistically insignificant ($p=0.780$).

Conclusion: TsDMARD therapy and lower baseline HAQ scores seem to be associated with more prolongations of therapy, even after adjusting for other confounding factors. However, the absolute difference between groups is small as all therapies show high rates of therapy prolongation, indicating effective initial therapy choices by Belgian rheumatologists.

Disclosure: D. De Cock, None; **P. Durez**, None; **D. Elewaut**, None; **B. Lauwerys**, None; **R. Westhovens**, Celltrion, Inc., 2, 5, Galapagos NV, 2, 5, Gilead Sciences, Inc., 2, 5; **P. Verschueren**, Pfizer, 9.

Abstract Number: 0223

Safety of Low Dose Methotrexate (MTX) and Tuberculosis (TB)

Anna Davidson[1], Alize Gunay[1], Ines Colmegna[2], Diane Lacaille[3], Harold Loewen[4], Michele Meltzer[5], Yewondwossen Tadese[6], Zenebe Yirsaw[6], Sasha Bernatsky[7] and **Carol Hitchon**[4], [1]McGill University, Montreal, QC, Canada, [2]The Research Institute of the McGill University Health Centre, Montreal, Canada, [3]University of British Columbia / Arthritis Research Canada, Richmond, BC, Canada, [4]University of Manitoba, Winnipeg, MB, Canada, [5]Jefferson University, Philadelphia, PA, [6]Addis Ababa University, Addis Ababa, Adis Abeba, Ethiopia, [7]The Research Institute of the McGill University Health Centre, Montreal, ON, Canada

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Increased awareness of the importance of MTX in rheumatic disease is leading to more MTX use in patients from TB-endemic areas. Current management guidelines for rheumatic disease address TB in the context of biologics but not MTX use. We aimed to systematically review the published literature on TB rates with MTX < 30 mg per week.

Methods: We searched CINAHL, Embase, Global, MEDLINE and World of Science databases (Jan 1990 to May 2018) for terms including 'methotrexate' and 'tuberculosis'. We also searched citations from review articles. Titles, abstracts or full manuscripts of the 4707 reports identified were screened independently by 2 reviewers to identify studies reporting TB in patients taking MTX. Study quality was assessed using the McGill Mixed Methods Appraisal Tool (MMAT). Data was extracted on TB incidence (new TB diagnosis vs reactivation of latent TB), and outcomes

Region (Year)	Diagnosis	TB with MTX	TB without MTX	Odds Ratio
Mexico (1999)	Mixed (4 RA)	1/6	5/75	2.76
Japan (2004)	RA	3/47	17/154	0.56
Canada (2009)	RA	29/483	21/1046	3.12
Brazil (2010)	Lupus	2/3	1/57	112
Taiwan _ (2012)	Psoriasis	33/144	464/2341	1.2
Taiwan (2015)	JIA	4/357	4/1026	2.90
South Africa (2017)	RA	0/134	0/18	NA

Case Contro1l Studies

(pulmonary, dissemination, death) and safety of isoniazid, INH. Descriptive summaries are presented on studies providing outcomes in patients taking MTX < 30 mg per week.

Results: After removing duplicates and studies not meeting criteria or providing sufficient information, 31 studies were included (8 cohort, 7 case-control, 1 clinical trial, 15 case reports/case series). Only 27% of articles reported data from low to moderate human development index countries. Studies were of moderate quality. Seven case control studies were heterogeneous but most demonstrated a modest increased risk of TB with MTX (Table). Five cohort studies reported TB incidence rates in rheumatic disease (treated with MTX +/- biologics) ranging from 102-367.9/100,000 patient-years. These rates were generally higher than comparator general population rates. Two cohort studies of MTX in RA (without biologic) reported cumulative TB incidence in Maldova (12 TB cases in 44 RA patients, 27%) and in China (9/114, 7.9%). Other cohort studies generated rates of overt infection (143/100,000 patient years in Spain, higher if co-prescribed with corticosteroids and other immunosuppressants in South Africa), and latent TB rates detection (16/922 RA screened, 1.7%, in Canada). When reported, rates of extra-pulmonary TB were higher than comparator general population rates. One clinical trial (China), 2 cohorts (Japan, USA) and 2 case series (Belgium, USA) evaluated safety of INH and MTX. Isoniazid-related hepatotoxicity and neutropenia were generally more common when taken with MTX, but were usually reversible.

Conclusion: Despite a paucity of high-quality data, this review confirms that TB screening and clinical surveillance are needed in patients from TB-endemic areas who are prescribed MTX, particularly with co-administration of corticosteroids or other immunosuppressants. Isoniazid, if monitored, appears safe and prevents TB reactivation.

Disclosure: A. Davidson, None; **A. Gunay**, None; **I. Colmegna**, None; **D. Lacaille**, None; **H. Loewen**, None; **M. Meltzer**, None; **Y. Tadese**, None; **Z. Yirsaw**, None; **S. Bernatsky**, None; **C. Hitchon**, Pfizer, 1, UCB Canada, 1.

Abstract Number: 0224

Efficacy of Long-term Treatment with Baricitinib 2 Mg in Patients with Active Rheumatoid Arthritis

Alvin Wells[1], Bochao Jia[2], Li Xie[2], Guillermo Valenzuela[3], Edward C Keystone[4], Zhanguo Li[5], Amanda Quebe[2], Kirstin Griffing[2], Susan Otawa[2] and Boulos Haraoui[6], [1]Aurora Rheumatology and Immunotherapy Center, Franklin, [2]Eli Lilly and Company, Indianapolis, IN, [3]Integral Rheumatology & Immunology Specialists, Plantation, FL, [4]Mount Sinai Hospital, Toronto, ON, Canada, [5]Peking University People's Hospital, Xicheng, Beijing, China (People's Republic), [6]Institut de Rhumatologie de Montréal, Montreal, QC, Canada

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The short-term efficacy of baricitinib was demonstrated previously.[1,2] The objectives of this post-hoc analysis were to evaluate long-term efficacy of once-daily baricitinib 2 mg in patients with active rheumatoid arthritis (RA) who were inadequate responders (IR) to conventional synthetic disease-modifying antirheumatic drugs (csDMARD) or biologic DMARDs (bDMARD).

Methods: Data from patients in two 24-week, phase III studies, RA-BUILD (NCT01721057, csDMARD-IR) and RA-BEACON (NCT01721044, bDMARD-IR), and one long-term extension (LTE) study (RA-BEYOND, NCT01885078) were analyzed (120 total weeks); all patients had a diagnosis of adult-onset RA as defined by the American College of

Rheumatology/European League Against Rheumatism 2010 Criteria for the Classification of RA.[3] The main outcomes of this analysis were achievement of low-disease activity (LDA; Simple Disease Activity Index [SDAI] ≤11), clinical remission (SDAI ≤3.3), Health Assessment Questionnaire Disability Index ≤0.5, and safety. Non-responder imputation (NRI) and completer analyses were conducted on the modified intention-to-treat (mITT) population, which included patients who were randomized to baricitinib 2 mg in the RA-BUILD and RA-BEACON studies and who had received ≥1 dose of the study drug after randomization.

Results: A total of 684 patients in RA-BUILD and 527 patients in RA-BEACON were randomized. In RA-BUILD, 229 patients were randomized to baricitinib 2 mg; 180 of whom completed the study and entered RA-BEYOND. In RA-BEACON, 174 patients were randomized to baricitinib 2 mg; 117 of whom completed the study and entered RA-BEYOND. At week 120, based on the mITT population with data up to rescue, 27.5% of csDMARD-IR and 18.4% of bDMARD-IR patients treated with baricitinib 2 mg were in SDAI LDA; 13.1% of csDMARD-IR and 5.2% of bDMARD-IR patients were in SDAI remission (NRI). At week 120, 20.1% of csDMARD-IR and 10.9% of bDMARD-IR patients treated with baricitinib 2 mg met or exceeded the population normative value for physical function (NRI). The completer analysis results are not shown. Rates of adverse events of special interest were consistent with previous reports.

Conclusion: This analysis supports the long-term treatment sustained efficacy and safety of baricitinib 2 mg for up to 120 weeks.

Disclosure: A. Wells, Abbvie, 1, 2, Eli Lilly & Co., 1, 2; **B. Jia**, Eli Lilly and Company, 1, 3; **L. Xie**, Eli Lilly and Company, 1, 3; **G. Valenzuela**, Mallinckrodt, 2, 8, Merck, 5, Lilly, 5, 8, Amgen, 5, 8, Esaote, 5, Sanofi, 5, 8, UCB, 5, 8, Janssen, 5, 8, Horizon, 5, 8, Image Analysis Group, 5, Novartis, 5, 8, Alexion, 5, Celgene, 5, 8, Regeneron, 5, 8, AbbVie, 5, 8, Boehringer Ingelheim, 5, 8, Sandoz, 5, Gilead, 5, Exagen and Global Health Living, 5, Pfizer, 5, 8, Genentech, 5, 8, BMS, 8, Takeda, 8, Centocor, 8, Pharmacia, 8, Radius, 8; **E. Keystone**, AbbVie, 2, 5, 8, Celltrion, 2, 5, 8, Eli Lilly, 2, 5, 8, Pfizer Inc, 2, 5, 8, Merck, 2, 5, 8, Sandoz, 2, 5, 8, Samsung Bioepsis, 2, 5, 8, Myriad Autoimmune, 2, 5, 8, Purapharm, 2, 5, 8, Janssen, 2, 5, 8, Sanofi-Genzyme, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, F. Hoffman-La Roche Ltd., 2, 5, 8, Genentech, 2, 5, 8, Gilead, 2, 5, 8, UCB, 2, 5, 8; **Z. Li**, None; **A. Quebe**, Eli Lilly & Co., 1, 2; **K. Griffing**, Eli Lilly and Company, 1, 3; **S. Otawa**, Eli Lilly and Company, 1, 3; **B. Haraoui**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5.

Abstract Number: 0225

Prevalence and Probability Assessment of Adverse Drug Reactions in Rheumatoid Arthritis Patients Receiving Intravenous Originator Biologics in Saudi Arabia: A Longitudinal Five Years Follow-up Study

Hawazin Alhazzani[1], Reem Tashkandi[1], Lamia Alzamel[1], Haya Almalag[1], Shiekha Alaujan[1], Abdurhman Alarfaj[1], Hussain Alarfaj[1] and Mohammed Omair[1], [1]King Saud University, Riyadh, Saudi Arabia

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Biologics have been advocated by guidelines as effective therapies for rheumatoid arthritis (RA)[1]. Limited longitudinal studies investigated the prevalence and risk factors for developing adverse drug reactions

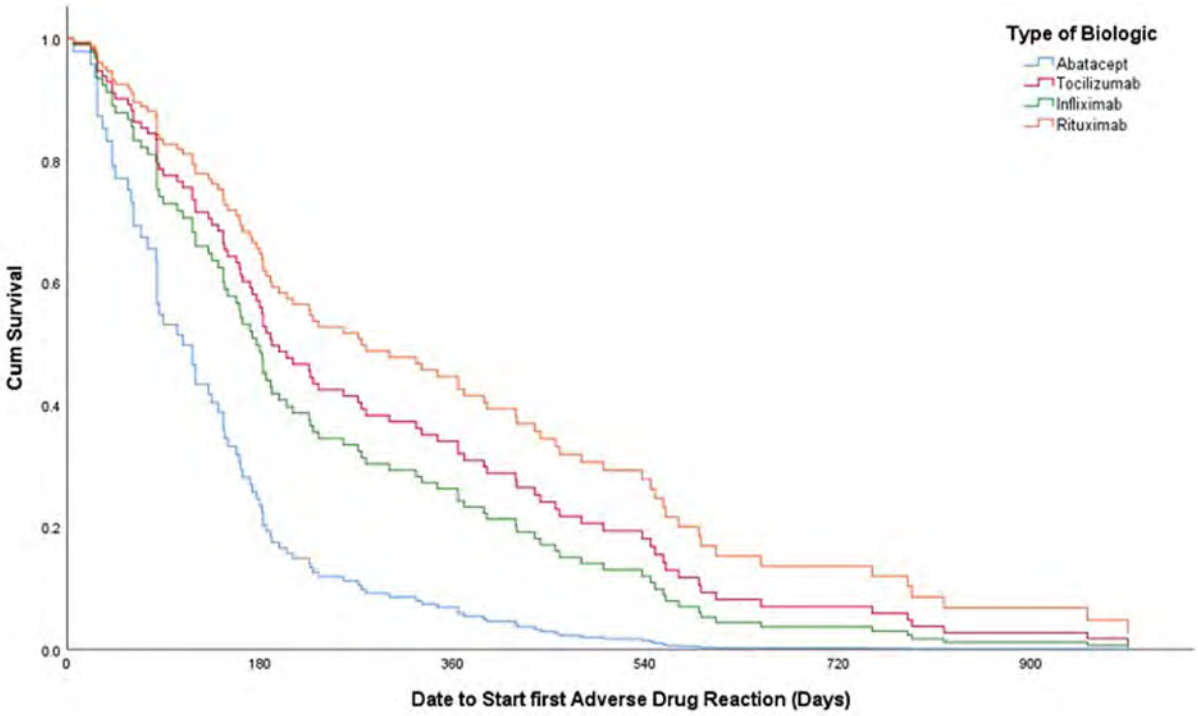


Figure 1. Cox regression and resulting Kaplan Meier graph of different IV originator biologics that shows prediction of having at least one ADR with Naranjo scale ≥1 and its relation to time (days) of experiencing the first ADR

Table 1. Total number of ADRs experienced, with Naranjo scale classification.

Type of ADR	Total Number	Precentage (%)	Naranjo scale classification		
			Possible¥ ADRs	Propable§ ADRs	Definite‡ ADRs
Infections	75	26.6	23	34	18
Skin & Mucous Memebrane	40	14.18	20	13	7
Gastrointestinal	33	11.7	16	9	8
Respiratory Disorders	29	10.28	19	8	2
Hematological	26	9.22	7	14	5
Ophthalmological	9	3.19	6	3	0
Renal Disorders	7	2.48	6	1	0
Rheumatological, Bone & Muscle	7	2.48	4	2	1
Allergy and Infusion Site Reactions	6	2.13	1	3	2
Cardiovascular	5	1.77	3	1	1
Neurological & Psychological	2	0.71	1	1	0
Endocrine	2	0.71	1	1	0
Miscellaneous*	41	14.54	28	12	1

(*) Miscellaneous: Nocturia, hoarseness of voice, fatigue, cough, sleep apnea, sleep disturbance, hypercalcemia, retrograde amnesia, weakness, pain, abortion, dizziness, fever, irregular menstrual cycle, edema, flank pain, breast lump, headache, hyperkalemia, weight gain, iron deficiency, tinnitus, hearing loss, proptosis, dyspnea, varicose veins.

¥ Naranjo scale score from 1 to 4.

§ Naranjo scale score from 5 to 8.

‡ Naranjo scale score of 9 or more.

Table 1. Total number of ADRs experienced, with Naranjo scale classification.

Table 2. Binary logistic regression and corresponding adjusted odds ratio for the prevalence of ADRs in different IV originator biologics

Drug Type	At least 1 ADR with Naranjo scale ≥1			Multiple ADRs		
	Non-adjusted odds ratio	95% CI	*p* value	Non-adjusted odds ratio	95% CI	*p* value
Age (years)	0.973	0.940-1.006	0.109	0.984	0.957-1.011	0.250
Gender Female	1.173	0.348-3.957	0.797	0.948	0.333-2.702	0.921
CCI	0.922	0.696-1.222	0.573	1.157	0.903-1.483	0.249
MTX	1.433	0.592-3.470	0.425	0.923	0.448-1.900	0.828
DMARDs	1.315	0.446-3.884	0.620	2.209	0.928-5.260	0.073
Intravenous biologics						
Abatacept	1.529	0.411-5.967	0.527	3.171	1.059-9.501	0.039*
Tocilizumab	1.046	0.447-2.450	0.917	0.831	0.408-1.689	0.608
Infliximab	3.111	0.381-25.379	0.289	3.055	0.772-12.085	0.112
Rituximab	0.603	0.261-1.389	0.235	0.488	0.237-1.005	0.052
	Adjusted odds ratio	**95% CI**	***p* value**	**Adjusted odds ratio**	**95% CI**	***p* value**
Abatacept¥	1.513	0.386, 5.936	0.553	3.145	1.004, 9.854	0.049*
Tocilizumab¥	1.446	0.511, 4.092	0.487	0.853	0.378, 1.925	0.702
Infliximab¥	2.052	0.213, 19.779	0.534	2.455	0.545, 11.061	0.242
Rituximab¥	0.455	0.163, 1.272	0.133	0.438	0.187, 1.027	0.058

ADR, adverse drug reaction; CI, Confidence Interval; OR, odds ratio; CCI: Charlson comorbidity index; MTX: methotrexate; DMARDs: disease modifying anti-rheumatic drugs

¥ Adjusted to age, gender, Charlson comorbidity, infections, fibromyalgia, proton pump inhibitors and angiotensin converting enzyme inhibitors.

*Significant according to a significance level of 0.05.

Table 2. Binary logistic regression and corresponding adjusted odds ratio for the prevalence of ADRs in different IV originator biologics

(ADRs) in RA patients treated with intravenous (IV) originator biologics[2]. Moreover, none of these studies utilized Naranjo[3] probability assessment for ADRs and compared all IV biologics in one setting.

Methods: A retrospective cohort study of adult RA patients receiving IV abatacept, tocilizumab, infliximab, or rituximab from January 2015 to January 2020 in a tertiary hospital located in Riyadh, Saudi Arabia was conducted. After Naranjo probability assessment [1]of ADRs, data including demographics, comorbidities, and concomitant medications were retrieved and their contribution to ADRs was analysed by logistic regression. Time to develop ADR for each biologic was plotted using Kaplan Meier graph.

Results: A total of 129 eligible patients were included in the study taking tocilizumab, rituximab, abatacept and infliximab (38.76%, 38.76%,13.95% and 8.53%, respectively) with a total of 1963 doses administered over five years. Patients had a mean (±SD) age of 54 (±13) years and were mostly females (87.6%). In addition to biologics used, 72 patients (55.8%) were receiving methotrexate, and 29 (22.5%) were receiving other disease modifying anti-rheumatic drugs (DMARDs). A total of 282 ADRs with Naranjo score≥1 was experienced by 103 patients (79.84%). The most common ADRs were infections (26.6%), skin and mucous membrane disorders (14.18%), and gastrointestinal disorders (11.7%) with predominance of probable ADRs using Naranjo classification (Table 1). Unadjusted odds ratio (OR) and adjusted odds ratio (AOR) for biologics and other factors are available in Table 2. Experiencing multiple ADRs

was significant with abatacept users with an AOR of 3.15 [95% CI: 1.004-9.854, p= 0.049]. The time to experience ADRs was ranging from day zero to three years (Figure 1).

Conclusion: Intravenous biologics use is limited by the prevalence of ADRs globally. Knowledge of different types of ADRs and their expected occurrence aids with clinical decision making and provides a database for future comparison with biosimilars. Although this study had a small number of participants for some IV biologics, the longitudinal nature of study methods provides an insight on the safety profile while managing RA patients.

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Abstract Number: 0226

Similar Efficacy of Sarilumab Monotherapy (MONARCH) vs Sarilumab and Methotrexate Combination Therapy (MOBILITY B) in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Sarilumab, as monotherapy or in combination with conventional synthetic DMARDs like methotrexate (MTX) has demonstrated improvement in symptomatic and functional outcomes in patients (pts) with RA. Comparison of efficacy between monotherapy and combination therapy is important due to suboptimal adherence and persistence to MTX in patients with RA and lack of direct comparison studies. Here, we report the results from a *post hoc* analysis that compared the efficacy of sarilumab monotherapy (MONARCH study; NCT02332590) vs sarilumab and MTX combination therapy (MOBILITY study; NCT01061736).

Methods: MONARCH and MOBILITY were phase III, double-blind randomized controlled studies in pts with RA who showed inadequate responses to or were intolerant to MTX. In MONARCH, pts (enrolled based on 2010 ACR/EULAR criteria) were randomized to receive sarilumab or adalimumab in combination with placebo for 24 weeks. In MOBILITY, pts (enrolled based on 1987 ACR revised classification criteria) were randomized to receive sarilumab or

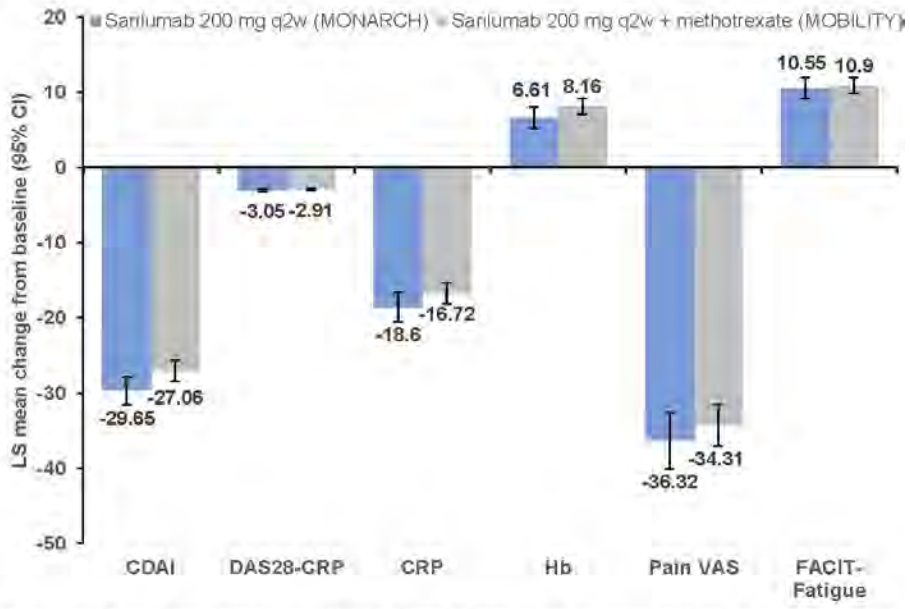
Table 1. Differences in Baseline Characteristics of Patients in the MONARCH and MOBILITY Studies

Parameter	Sarilumab 200 mg q2w (MONARCH; N=184)	Sarilumab 200 mg q2w + MTX (MOBILITY B; N=399)	*P*-Value
Age (years)[a]	50.9 (12.6)	50.8 (11.8)	0.9608
Age group (years)[b], n (%)			
<65	158 (85.9)	348 (87.2)	0.6772
≥65 and <75	25 (13.6)	50 (12.5)	
≥75	1 (0.5)	1 (0.3)	
Sex[b], n (%)			
Male	27 (14.7)	62 (15.5)	0.7873
Female	157 (85.3)	337 (84.5)	
Race[b], n (%)			
Caucasian/White	171 (92.9)	343 (86.0)	0.0007
Black	1 (0.5)	8 (2.0)	
Asian/Oriental	2 (1.1)	33 (8.3)	
Other	10 (5.4)	15 (3.8)	
Ethnicity[b], n (%)			
Hispanic	46 (25.0)	151 (37.8)	0.0023
Non-Hispanic	138 (75.0)	248 (62.2)	
Region[b], n (%)			
Region 1	61 (33.2)	75 (18.8)	<0.0001
Region 2	36 (19.6)	155 (38.9)	
Region 3	87 (47.3)	169 (42.4)	
Weight (kg)[a, c]	72.3 (16.5)	74.7 (19.7)	0.1303
Height (cm)[a, c]	163.3 (9.1)	161.4 (9.0)	0.0203
BMI[a, c]	27.1 (5.6)	28.6 (6.7)	0.0059
BMI group (kg/m^2)[b, c], n (%)			
<25	71 (38.6)	129 (32.4)	0.0123
≥25 and <30	70 (38.0)	127 (31.9)	
≥30	43 (23.4)	142 (35.7)	
Duration of RA since diagnosis (Years)[a]	8.1 (8.1)	8.6 (7.0)	0.5051
RA functional class[b], n (%)			
I	29 (15.8)	42 (10.5)	0.1488
II	125 (67.9)	277 (69.4)	
III	30 (16.3)	80 (20.1)	
IV	0	0	
Rheumatoid factor[a, d], n (%)			
Positive	119 (66.9)	328 (82.6)	<0.0001
Negative	59 (33.2)	69 (17.4)	
Anti CCP antibody[b, d], n (%)			
Positive	134 (75.3)	337 (84.9)	0.0057
Negative	44 (24.7)	60 (15.1)	
Tender joint count (0-68)[a]	28.0 (13.2)	26.5 (14.5)	0.2498
Tender joint count (0-28)[a]	17.0 (6.1)	15.5 (6.6)	0.0102
Swollen joint count (0-66)[a]	18.6 (10.7)	16.8 (9.7)	0.0418
Swollen joint count (0-28)[a]	13.2 (5.7)	11.9 (5.6)	0.0106
CRP (mg/L)[a]	17.4 (21.3)	22.2 (23.8)	0.0188
HAQ-DI (0-3)[a]	1.6 (0.6)	1.7 (0.6)	0.3159
DAS28-CRP (>5.1: high disease activity)[a]	6.0 (0.9)	6.0 (0.9)	0.7433
CDAI[a]	43.6 (12.1)	40.4 (12.3)	0.0033
Pt-GA (mm)	68.0 (17.5)	66.3 (20.8)	0.3007
MD-GA (mm)	66.3 (15.7)	63.5 (17.6)	0.0643
Pain VAS (mm)	71.6 (18.7)	66.6 (21.3)	0.0046

Values are mean (SD) unless indicated otherwise. Region 1 (Western Countries): Austria, Australia, Belgium, Canada, Czech Republic, Finland, Germany, Greece, Hungary, Israel, New Zealand, Norway, Portugal, Spain and USA; Region 2 (South America): Argentina, Brazil, Chile, Colombia, Mexico and Peru; Region 3 (Rest of World): Belarus, Estonia, India, Malaysia, Philippines, Poland, Romania, Russia, South Africa, South Korea, Ukraine, Taiwan and Thailand. [a]*P*-value was obtained using t test for equality of variance. In case equality of variance assumption was not met, Satterthwaite's p-value was provided; [b]*P*-value was obtained using chisquare test. In case expected cell frequency was < 5, Fisher's exact test was used; [c]N=398 for the "sarilumab plus MTX" treatment arm; [d]N=178 for the "sarilumab" treatment arm and N=397 for the "sarilumab plus MTX" treatment arm. Anti CCP, Anti-cyclic citrullinated peptide; BMI, body mass index; CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; DAS28-CRP, 28-joint Disease Activity using C reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; MD-GA, physician's global assessment of disease activity; MTX, methotrexate; N, number of patients assessed; Pt-GA, patients global assessment of disease activity; q2w, every 2 weeks; RA, rheumatoid arthritis; SD, standard deviation

placebo in combination with weekly MTX for 52 weeks. The primary objective of this analysis was to compare the efficacy of sarilumab (200 mg q2w) as monotherapy and in combination with MTX, at Week 24. The endpoints were mean change from baseline in Clinical Disease Activity Index (CDAI), 28-joint Disease Activity using CRP (DAS28-CRP), CRP, hemoglobin (Hb), pain visual analogue scale (VAS) and Functional Assessment of Chronic Illness Therapy

Figure 1. Adjusted Comparisons of Efficacy Between Sarilumab Monotherapy vs Sarilumab and Methotrexate Combination Therapy Using MMRM[a]



All values are LS mean change from baseline (95% CI) at Week 24. Patients with non-missing endpoint values were considered.
[a]MMRM assuming an unstructured covariance structure. Ethnicity, region, baseline BMI Group, rheumatoid factor, anti CCP antibody, SJC at baseline, CDAI at baseline, CRP at baseline, endpoint value at baseline, sarilumab group, visit and sarilumab group-by-visit interaction were used as covariates in this model.

Anti CCP, Anti-cyclic citrullinated peptide; CDAI, Clinical Disease Activity Index; CI, confidence interval; CRP, C-reactive protein; DAS28-CRP, 28-joint Disease Activity using C reactive protein; FACIT, Functional Assessment of Chronic Illness Therapy; Hb, hemoglobin; LS, least square; MMRM, Mixed-effect model repeated measure; q2w, every 2 weeks; SJC, swollen joint count; VAS, visual analogue scale.

(FACIT)-Fatigue. For unadjusted comparisons of efficacy between monotherapy and combination therapy treatment arms, mean change from baseline (95% confidence interval [CI]) at Week 24 in end points was compared between the treatment arms. For adjusted comparisons, continuous change from baseline in endpoints were set as dependent variables and pt baseline characteristics that differed significantly ($P< 0.05$) between the two trials were set as covariates in mixed-effect model repeated measure (MMRM) models; least square (LS) mean change from baseline (95% CI) at Week 24 in end points was compared between the treatment arms.

Results: This analysis included 184 pts from the sarilumab monotherapy arm (MONARCH) and 399 pts from the sarilumab plus MTX treatment arm (MOBILITY). Among the baseline characteristics of pts in these two trials, differences ($P< 0.05$) were observed in ethnicity, region, body mass index group, rheumatoid factor, anti-citrullinated peptide antibodies, swollen joint count, CRP, and clinical disease activity index between the treatment arms (**Table 1**). After adjusting for these differences in MMRM, LS mean change from baseline at Week 24 for all assessments was similar between the treatment arms with overlapping confidence intervals (**Figure 1**). Results of unadjusted comparisons were similar to adjusted comparisons (data not shown). The safety profile of sarilumab was previously reported.

Conclusion: Findings from this *post hoc* analysis of combined data demonstrated that the efficacy of sarilumab as monotherapy was similar to its efficacy as a combination therapy with MTX. These data support previous observations that interleukin (IL)-6R blockade with or without concomitant conventional synthetic DMARDs have similar efficacy.

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Abstract Number: 0227

Real Life Severe Infections in Patients with Rheumatoid Arthritis on Treatment with Biological Therapy and JAK Inhibitors

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Infections are one of the main complications among patients with rheumatoid arthritis (RA) with immunosuppressive treatment. The differences between treatments and the influence of other factors is unclear.

The objective of this study was to evaluate the frequency and factors associated with serious infections in patients with RA treated with biological therapy (BT) and JAK inhibitors (JAKi) and the differences between treatments.

Methods: Descriptive and retrospective study (January 2015-May 2020) of patients with RA treated with BT (TNFi, non-TNFi) and JAKi (tofacitinib, bariticinib) in a single center. RA diagnosis was performed according to ACR classification criteria. Severe infection was considered a life-threatening infection or one that required hospitalization and intravenous treatment. Epidemiological variables, clinical characteristics, Charlson comorbidity index, type of BT or JAKi and concomitant treatment were collected. For the analysis frequencies and percentages are used in qualitative variables, and mean ± SD in the quantitative ones. Statistical analysis was performed with IBM SPSS v 23.

Results: We registered 246 patients (85% women) mean aged 56±13.5 years. RF was positive in 87%, anti-CCP in 75.6% and 15.4% presented extra-articular manifestations (nodulosis 8.9%, intersticial lung disease 5.3%, other 1.2%). At the start of the study 149 patients (60.6%) were with TNFi, 79 (32.1%) non-TNFi and 18 (7.3%) with JAKi. Conventional synthetic DMARDs (csDMARDs) were used in 84.1% of cases (methotrexate 71%, leflunomide 21.3%, other 7.7%).

During the study, 165 patients (67.1%) continued with the same treatment and in 81 (32.9%) it was changed at least once. Four patients discontinued the treatment. At the end of the study, 119 patients (49.2%) were with TNFi, 79 (32.6%) non-TNFi and 44 (18.2%) with JAKi.

TABLE 1. CHARACTERISTICS OF PATIENTS WITH INFECTION VS. WITHOUT INFECTION

	INFECTION		
	YES n:23	**NO** n:223	**p**
FEMALE, n (%)	19 (82.6)	190 (85.2)	0.759
AGE years, (mean±SD)	60.2 ± 13	55.6 ± 13.4	0.116
AGE ≥ 65 n (%)	10 (43.5)	63 (28.3)	0.151
RF +, n (%)	21 (91.3)	193 (86.5)	0.748
ANTI-CCP +, n (%)	17 (73.9)	169 (75.8)	0.803
INTERSTICIAL LUNG DISEASE, n (%)	1 (25)	12 (35.3)	0.708
ALCOHOL, n (%)	2 (8.7)	18 (8.1)	1.00
SMOKER, n (%)	6 (26.1)	59 (26.5)	0.731
COPD, n (%)	6 (26.1)	23 (10.3)	**0.038***
DM, n (%)	7 (30.4)	19 (8.6)	**0.005***
SEVERE LIVER DISEASE, n (%)	2 (8.7)	1 (0.4)	**0.024***
CEREBROVASCULAR ACCIDENT, n (%)	2 (8.7)	2 (0.9)	**0.045***
RENAL INSUFFICIENCY, n (%)	2 (8.7)	3 (1.4)	0.071
PERIPHERAL VASCULAR DISEASE, n (%)	8 (34.8)	24 (10.8)	**0.004***
CHARLSON INDEX (mean±SD)	1.83 ± 2	0.67 ± 1.2	**<0.001***
TNFi, n (%) **NON-TNFi** n (%) **JAKi**, n (%)	12 (52.2) 7 (30.4) 4 (17.4)	107 (48.8) 72 (32.9) 40 (18.3)	
csDMARDs, n (%)	18 (78.3)	151 (67.7)	0.353
GLUCOCORTICOIDS, n (%)	14 (60.9)	111 (49.8)	0.383

Severe infection was developed in 23 (9.3%) patients (respiratory 11, sepsis 4, cellulitis 4, urinary 3, osteomyelitis 1). Two patients had severe infection and herpes zoster and 3 developed a second infection. Twelve patients were with TNFi (52.2%), 7 non- TNFi (30.4%) and 4 JAKi (17.4%).**Table 1**

The inflammatory activity of RA was mild at the time of infection (DAS28: 2.6±1.1). The median time until infection was: TNFi 21.65 [7-60.8] months, non- TNFi 20.09 [17-37.7] and JAKi 28.19 [15.1-28.7]. The Charlson index, chronic obstructive pulmonary disease (COPD), diabetes mellitus (DM), severe liver disease, cerebrovascular accidents and peripheral vascular disease were statistically significantly associated with infection. The infection developed in 60.9% and 78.3% of patients who were on concomitant treatment with corticoid and csDMARD respectively. **Table 1**

Conclusion: In our study, 9.3% of patients with RA treated with BT or JAKi developed severe infection during 4.5 years of follow-up. Comorbidity, especially DM, increased the risk of presenting this complication. Concomitant treatment with corticoid and csDMARDs was not statistically significantly associated with infection.

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Abstract Number: 0228

Impact of Upadacitinib or Adalimumab as Initial Therapy on the Achievement of 48-Week Treatment Goals in Patients with Rheumatoid Arthritis and Inadequate Response to Methotrexate: Post Hoc Analysis of a Phase 3 Study

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

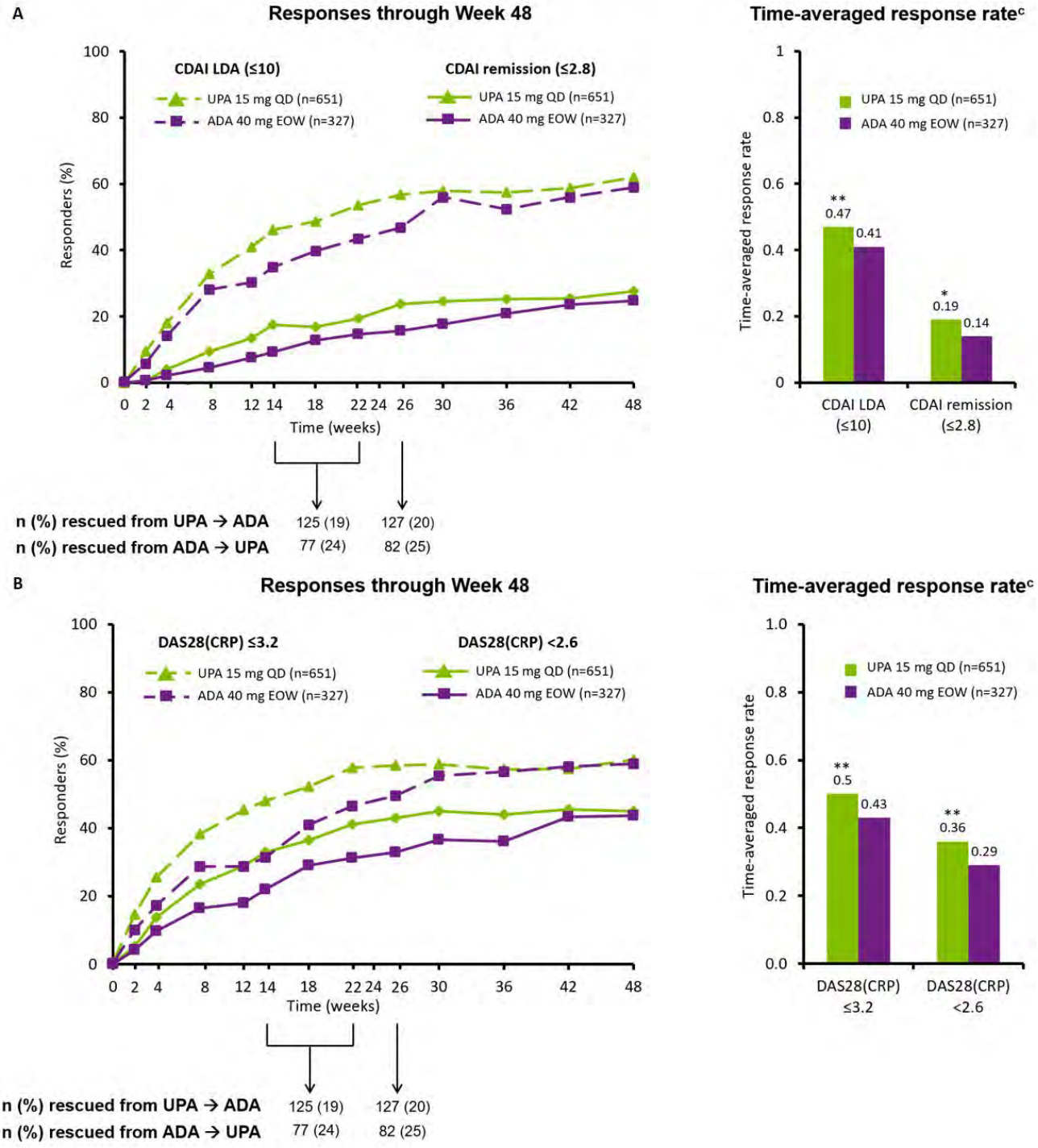
Session Time: 9:00AM–11:00AM

Background/Purpose: In the randomized, double-blinded, Phase 3 SELECT-COMPARE study, upadacitinib (UPA) + MTX demonstrated greater clinical and functional responses vs adalimumab (ADA) + MTX in patients with RA and inadequate response to MTX.[1,2] In SELECT-COMPARE, patients with an insufficient response to their initial therapy were switched from UPA to ADA (and vice versa) according to treat-to-target (T2T) principles. To assess the effectiveness of such a strategy, we analyzed 1-year treatment outcomes in SELECT-COMPARE according to initial randomization group, regardless of whether or not patients subsequently switched therapy.

Methods: Patients initially randomized to UPA 15 mg once daily (QD) or ADA 40 mg every other week (EOW; both + MTX) for up to 48 weeks in SELECT-COMPARE were included in the analysis. As per the protocol-directed rescue strategy, patients experiencing < 20% improvement in tender or swollen joint counts at Week 14, 18, or 22, or Clinical Disease Activity Index (CDAI) >10 at Week 26, were switched from UPA to ADA or ADA to UPA in a blinded fashion. Efficacy outcomes included CDAI remission (≤2.8) and low disease activity (LDA; ≤10), DAS of 28 joints using CRP (DAS28[CRP]) < 2.6 and ≤3.2, and a composite of "deep response" (CDAI remission, HAQ-Disability Index < 0.5, and pain score < 20). Data are presented and attributed to initial randomized group (UPA or ADA) regardless of any subsequent switch in therapy. Time-averaged response rates were calculated as area under the curve of response rate standardized by 48 weeks. The proportions of patients who maintained Week 26 responses through 6 months of follow-up are also reported.

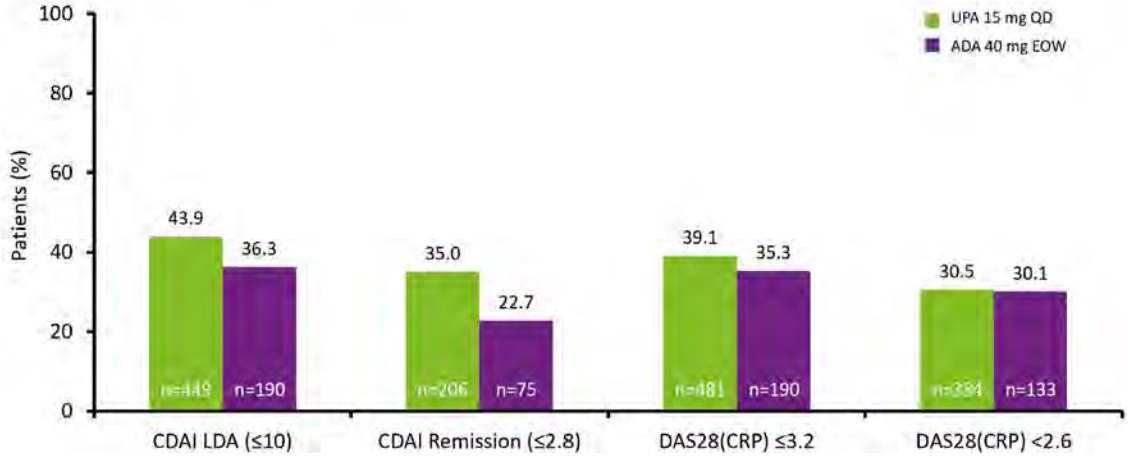
Results: This analysis included 651 patients initially randomized to UPA (of whom 245 switched to ADA) and 327 patients initially randomized to ADA (of whom 157 switched to UPA). Baseline characteristics including age, sex, and BMI were generally well balanced between randomized groups. At Week 48, similar proportions of patients initially randomized to UPA or ADA therapy achieved CDAI remission/LDA (27.6%/61.9% vs 24.8%/59.0%) and DAS28(CRP) < 2.6/≤3.2 (45.0%/60.2% vs 43.7%/59.0%) (**Figure 1**). However, a small but significantly greater proportion of patients achieved a deep response with initial UPA vs initial ADA therapy (17.8% vs 12.8%; p< 0.05). In addition, time-averaged response rates over 48 weeks were higher for initial UPA vs initial ADA therapy across efficacy outcomes (**Figure 1**). Similar trends were observed for other outcomes. Additionally, similar proportions of patients

Figure 1. Achievement of CDAI (A) and DAS28(CRP) (B) responses corresponding with time-averaged response rates over 48 weeks by initial therapy with UPA or ADA in SELECT-COMPARE[a,b]



**p<0.01,*p<0.05 vs ADA. [a]Non-responder imputation. [b]Blinded rescue from UPA to ADA or ADA to UPA was permitted at Weeks 14, 18, and 22 for <20% improvement in TJC/SJC and at Week 26 for CDAI <10. Data are presented and attributed to original randomized group (UPA or ADA) regardless of any subsequent switch in therapy. [c]Calculated as area under the curve of response rate standardized by length of study (48 weeks). ADA, adalimumab; CDAI, Clinical Disease Activity Index; DAS28(CRP), DAS of 28 joints using CRP; EOW, every other week; QD, once daily; SJC, swollen joint count; TJC, tender joint count; UPA, upadacitinib

Figure 2. Proportion of patients maintaining Week 26 CDAI and DAS28(CRP) responses during 6-month follow-up by initial therapy with UPA or ADA in SELECT-COMPARE[a–c]



[a]As observed. [b]Blinded rescue from UPA to ADA or ADA to UPA was permitted at Weeks 14, 18, and 22 for patients with <20% improvement in TJC or SJC and at Week 26 for patients with a CDAI <10. Data are presented and attributed to original randomized group (UPA or ADA) regardless of any subsequent switch in therapy. [c]Maintaining response defined as never losing response at any visit during ~6 months (22–26 weeks) follow up after first achieving response before or at Week 26. ADA, adalimumab; CDAI, Clinical Disease Activity Index; DAS28(CRP), DAS of 28 joints using CRP; EOW, every other week; QD, once daily; SJC, swollen joint count; TJC, tender joint count; UPA, upadacitinib

maintained Week 26 responses with initial UPA vs initial ADA therapy based on CDAI remission/LDA and DAS28(CRP) < 2.6/≤3.2 during 6-month follow-up (**Figure 2**).

Conclusion: Using a stringent T2T approach to RA management, rates of LDA or remission at 1 year were similar, regardless of whether patients were initially randomized to UPA or ADA. However, initial UPA therapy led to more frequent deep responses and higher time-averaged response rates vs initial ADA therapy.

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2. Fleischmann R, et al. Ann Rheum Dis 2019;78:1454–62.

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Abstract Number: 0229

Integrated Safety of Filgotinib in Patients with Moderately or Severely Active Rheumatoid Arthritis Receiving Treatment for up to 5.5 Years

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The oral, selective Janus kinase-1 inhibitor filgotinib (FIL) significantly improved RA signs and symptoms in patients (pts) with MTX-naïve and MTX- and biologic-refractory RA.[1–5] In 52-week (W) active controlled trials, FIL safety was comparable to adalimumab and MTX.[1,2] Updated integrated analysis of FIL safety is needed.

Methods: Data were integrated from 3 phase 3 (FINCH 1–3; NCT02889796, NCT02873936, NCT02886728), 2 phase 2 (DARWIN 1, 2; NCT01668641, NCT01894516), and 2 long-term extension (DARWIN 3, NCT02065700; FINCH 4, NCT03025308) trials including up to 5.5 years (y) FIL exposure. Pts were ≥18 y with active RA per ACR criteria. DARWIN 3 and FINCH 4 data through April 26, 2019, and Sept 16, 2019, respectively, were included; other trials are complete. Placebo (PBO)-controlled analysis set included pts from 4 PBO-controlled trials receiving FIL 200 or 100 mg once-daily (QD) or PBO for 12W. Long-term as treated analysis set included all available data for pts receiving ≥1 dose FIL 200 or 100 mg QD from 7 trials, including after treatment conversion. Incidence (n [%]) and exposure-adjusted incidence rates (EAIR) per 100 pt-years exposure (PYE) of treatment-emergent adverse events (TEAEs; onset after first dose and no later than either 30 days after last dose or new drug first dose date –1 day) and TEAEs of special interest (AESIs) are presented. EAIR and 95% confidence intervals were estimated with Poisson models with treatment

Table 1. Summary of exposure

	PBO-controlled			Long-term (as treated)		
	FIL 200 mg	FIL 100 mg	PBO	FIL 200 mg	FIL 100 mg	Total FIL
N	777	788	781	2267	1647	3691
Total PYE	179.8	181.6	178.4	4047.7	2032.9	6080.7
Treatment duration, years, mean ± SD	0.4 ± 0.07	0.4 ± 0.08	0.4 ± 0.12	1.8 ± 1.18	1.2 ± 0.74	1.6 ± 1.07
Exposed to study drug ≥12 weeks, n (%)	748 (96.3)	754 (95.7)	649 (83.1)	2165 (95.5)	1547 (93.9)	3540 (95.9)
Exposed to study drug ≥52 weeks, n (%)	NA	NA	NA	1731 (76.4)	1001 (60.8)	2740 (74.2)
Exposed to study drug ≥108 weeks, n (%)	NA	NA	NA	600 (26.5)	213 (12.9)	826 (22.4)
Exposed to study drug ≥156 weeks, n (%)	NA	NA	NA	308 (13.6)	10 (0.6)	322 (8.7)

The PBO-controlled analysis set only included data up to 12 weeks.
FIL, filgotinib; NA, not applicable; PBO, placebo; PYE, patient-years exposure; SD, standard deviation.

Table 1. Summary of exposure

Table 2. Overall summary of treatment-emergent adverse events

	PBO-controlled			Long-term (as treated)		
	FIL 200 mg N = 777 PYE = 179.8	FIL 100 mg N = 788 PYE = 181.6	PBO N = 781 PYE = 178.4	FIL 200 mg N = 2267 PYE = 4047.7	FIL 100 mg N = 1647 PYE = 2032.9	Total FIL N = 3691 PYE = 6080.7
TEAE	354 (45.6)	323 (41.0)	316 (40.5)	1771 (78.1)	1140 (69.2)	2848 (77.2)
EAIR (95% CI)	195.4 (173.7, 219.8)	176.3 (156.0, 199.2)	175.9 (155.5, 198.9)	40.4 (38.3, 42.7)	64.2 (58.9, 69.9)	41.1 (39.2, 43.0)
TEAE Grade ≥3[a]	31 (4.0)	30 (3.8)	27 (3.5)	309 (13.6)	206 (12.5)	514 (13.9)
EAIR (95% CI)	12.0 (7.4, 19.5)	11.5 (7.0, 18.7)	10.6 (6.4, 17.5)	6.4 (5.6, 7.4)	7.6 (5.3, 10.8)	6.5 (5.8, 7.4)
TE SAE	21 (2.7)	25 (3.2)	17 (2.2)	254 (11.2)	166 (10.1)	418 (11.3)
EAIR (95% CI)	10.9 (6.7, 17.8)	12.8 (8.1, 20.4)	8.9 (5.2, 15.2)	6.1 (5.4, 7.0)	7.5 (5.6, 10.1)	6.2 (5.5, 7.0)
TEAE leading to premature discontinuation	15 (1.9)	11 (1.4)	15 (1.9)	239 (10.5)	93 (5.6)	332 (9.0)
EAIR (95% CI)	8.7 (4.9, 15.3)	6.3 (3.3, 12.0)	8.8 (5.0, 15.4)	6.0 (5.3, 6.9)	6.8 (5.4, 8.6)	5.9 (5.3, 6.6)
TEAE leading to temporary interruption	58 (7.5)	55 (7.0)	46 (5.9)	576 (25.4)	364 (22.1)	935 (25.3)
EAIR (95% CI)	27.3 (19.7, 37.8)	25.6 (18.3, 35.6)	21.9 (15.4, 31.1)	12.5 (11.3, 13.8)	14.8 (11.9, 18.5)	12.2 (11.2, 13.4)
TEAE leading to death[b]	1 (0.1)	1 (0.1)	1 (0.1)	16 (0.7)	6 (0.4)	22 (0.6)
EAIR (95% CI)	0.6 (0.1, 3.9)	0.6 (0.1, 3.9)	0.6 (0.1, 4.0)	0.4 (0.2, 0.6)	0.3 (0.1, 0.7)	0.4 (0.2, 0.5)
All deaths[b,c]	1 (0.1)	1 (0.1)	2 (0.3)	19 (0.8)	6 (0.4)	25 (0.7)
EAIR (95% CI)[d]	0.6 (0.1, 3.9)	0.5 (0.1, 3.9)	1.1 (0.3, 4.5)	0.5 (0.3, 0.7)	0.3 (0.1, 0.7)	0.4 (0.3, 0.6)

Data are n (%) unless otherwise indicated. EAIR are per 100 PYE.
[a]Grade ≥3 TEAEs were determined by the investigator to be severe, life-threatening, or fatal
[b]EAIR and 95% CI were estimated using Poisson models with treatment as covariate and an offset of natural log of exposure.
[c]Including non-TE deaths.
[d]For the PBO-controlled analysis set, FIL 200 mg PYE = 180.3, FIL 100 mg PYE = 181.9, and PBO PYE = 178.8.
CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; PBO, placebo; PYE, patient-years exposure; SAE, serious adverse event; TE, treatment-emergent; TEAE, treatment-emergent adverse event.

Table 2. Overall summary of treatment-emergent adverse events

and study covariates and natural log of exposure offset, unless otherwise specified for infrequent events. Positively adjudicated major adverse cardiovascular events (MACE) and venous thromboembolisms (VTE) were included.

Results: In long-term as treated set, 74.2% of pts received FIL for ≥52W (**Table 1**). In 12W PBO-controlled set, rates of TEAEs, TEAEs Grade ≥3, serious AEs (SAEs), and TEAEs leading to discontinuation or death were comparable for both FIL doses vs PBO (**Table 2**). EAIR for TEAEs were lower with FIL 200 vs 100 mg in as treated set but comparable between doses for TEAEs Grade ≥3, SAEs, and TEAEs leading to discontinuation or death. All and serious infection incidences were numerically higher for FIL vs PBO in the PBO-controlled set; herpes zoster occurred in 0.1%/0.3%/0.3% receiving FIL 200 mg/100 mg/PBO (**Table 3**). In as treated set, EAIR of all and serious infections were numerically higher for FIL 100 vs 200 mg, and herpes zoster EAIR was numerically higher for FIL 200 vs 100 mg. In PBO-controlled set, 0/3/2 cases of MACE occurred with FIL 200 mg/100 mg/PBO. In as treated set, MACE EAIR were comparable for FIL doses. No VTE occurred in 12W PBO-controlled set. In as treated set, VTE EAIR were 0.2 and 0.0/100 PYE for FIL 200 and 100 mg, respectively. Malignancies were uncommon and comparable for FIL doses.

Conclusion: FIL was well tolerated; no consistent dose dependent effect was observed for AESIs. VTE and other AESIs were infrequent. No new safety signals were identified with FIL dosing up to 5.5 y.

Table 3. Treatment-emergent adverse events of special interest

	PBO-controlled			Long-term (as treated)		
	FIL 200 mg N = 777 PYE = 179.8	FIL 100 mg N = 788 PYE = 181.6	PBO N = 781 PYE = 178.4	FIL 200 mg N = 2267 PYE = 4047.7	FIL 100 mg N = 1647 PYE = 2032.9	Total FIL N = 3691 PYE = 6080.7
Infectious AEs	139 (17.9)	123 (15.6)	104 (13.3)	1074 (47.4)	648 (39.3)	1697 (46.0)
EAIR (95% CI)	76.9 (63.7, 92.9)	67.3 (55.2, 82.1)	58.0 (47.0, 71.7)	24.8 (23.1, 26.5)	34.4 (30.4, 38.8)	24.6 (23.2, 26.1)
Serious infectious AEs	8 (1.0)	7 (0.9)	5 (0.6)	67 (3.0)	51 (3.1)	118 (3.2)
EAIR (95% CI)	3.9 (1.6, 9.1)	3.3 (1.4, 8.2)	2.4 (0.9, 6.7)	1.6 (1.2, 2.1)	3.1 (2.1, 4.5)	1.8 (1.4, 2.2)
Active TB	0	0	0	0	3 (0.2)	3 (<0.1)
EAIR (95% CI)	0.0 (0.0, 2.1)[a]	0.0 (0.0, 2.0)[a]	0.0 (0.0, 2.1)[a]	NA	0.1 (0.0, 0.5)[b]	0.0 (0.0, 0.2)[b]
Opportunistic infections	0	0	0	5 (0.2)	4 (0.2)	9 (0.2)
EAIR (95% CI)	0.0 (0.0, 2.1)[a]	0.0 (0.0, 2.0)[a]	0.0 (0.0, 2.1)[a]	0.1 (0.1, 0.3)[b]	0.2 (0.1, 0.5)[b]	0.1 (0.1, 0.3)[b]
Herpes zoster	1 (0.1)	2 (0.3)	2 (0.3)	74 (3.3)	23 (1.4)	97 (2.6)
EAIR (95% CI)	0.6 (0.1, 3.9)[b]	1.1 (0.3, 4.4)[b]	1.1 (0.3, 4.5)[b]	1.8 (1.4, 2.3)	1.1 (0.8, 1.7)[b]	1.6 (1.3, 2.0)
MACE	0	3 (0.4)	2 (0.3)	19 (0.8)	13 (0.8)	32 (0.9)
EAIR (95% CI)	0.0 (0.0, 2.1)[a]	1.7 (0.3, 4.8)[a]	1.1 (0.1, 4.0)[a]	0.4 (0.2, 0.7)	0.6 (0.4, 1.1)[b]	0.5 (0.3, 0.7)
VTE	0	0	0	8 (0.4)	1 (<0.1)	9 (0.2)
EAIR (95% CI)	NA	NA	NA	0.2 (0.1, 0.4)[b]	0.0 (0.0, 0.3)[b]	0.1 (0.1, 0.3)[b]
Malignancy excluding NMSC	0	1 (0.1)	1 (0.1)	22 (1.0)	11 (0.7)	33 (0.9)
EAIR (95% CI)	0.0 (0.0, 2.1)[a]	0.6 (0.0, 3.1)[a]	0.6 (0.0, 3.1)[a]	0.6 (0.4, 0.9)	0.5 (0.3, 1.0)[b]	0.5 (0.4, 0.8)
NMSC	0	0	0	9 (0.4)	3 (0.2)	12 (0.3)
EAIR (95% CI)	0.0 (0.0, 2.1)[a]	0.0 (0.0, 2.0)[a]	0.0 (0.0, 2.1)[a]	0.2 (0.1, 0.4)[b]	0.1 (0.0, 0.5)[b]	0.2 (0.1, 0.3)[b]
Gastrointestinal perforations	0	0	0	3 (0.1)	0	3 (<0.1)
EAIR (95% CI)	0.0 (0.0, 2.1)[a]	0.0 (0.0, 2.0)[a]	0.0 (0.0, 2.1)[a]	0.1 (0.0, 0.2)[b]	NA	0.0 (0.0, 0.2)[b]

Data are n (%) unless otherwise indicated. EAIR are per 100 PYE.
[a]EAIR and 95% CI estimated using exact Poisson method.
[b]EAIR and 95% CI estimated using Poisson models with treatment as covariate and an offset of natural log of exposure.
AE, adverse event; CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; MACE, major adverse cardiovascular event; NA, not applicable; NMSC, nonmelanoma skin cancer; PBO, placebo; PYE, patient-years exposure; TB, tuberculosis; VTE, venous thromboembolism.

Table 3. Treatment-emergent adverse events of special interest

References

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3. Combe. *Ann Rheum Dis* 2019;78(suppl 2):A77.
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Abstract Number: 0230

Effect of Dose Escalation of Subcutaneous Tocilizumab on Disease Activity in Patients with Rheumatoid Arthritis in a Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Baseline Demographics and Clinical Characteristics Among Patients Who Did Not Achieve LDA at Week 12 in the COMP-ACT, SUMMACTA and BREVACTA Trials

	COMP-ACT* All Patients (N = 328)	SUMMACTA North American Patients† (n = 71)	SUMMACTA All Patients (N = 285)	BREVACTA All Patients (N = 196)
Female, n (%)	270 (82.3)	62 (87.3)	257 (90.2)	170 (86.7)
Age, mean, years	56.9	56.4	53.9	52.7
North America, n (%)	328 (100.0)	71 (100.0)	71 (24.9)	28 (14.3)
Weight, kg	75.9	76.8	70.1	68.1
DAS28 at baseline, mean	6.7	7.1	6.9	6.8
CDAI at baseline, mean	43.9	46.6	42.6	42.7
SDAI at baseline, mean	45.0	48.7	44.9	44.7
DAS28 at week 12, mean	4.8	4.6	4.4‡	4.6
CDAI at week 12, mean	28.6	26.7	23.1	21.9‡
SDAI at week 12, mean	29.0	26.7	23.1	22.4

CDAI, Clinical Disease Activity Index; DAS28, Disease Activity in 28 Joints; LDA, low disease activity; SDAI, Simple Disease Activity Index.
*All patients in the COMP-ACT trial were from the United States.
†North American patients included those from the United States and Canada.
‡$P < 0.0001$ vs COMP-ACT.

Table 2. Comparison of Clinical Response After Dose Escalation or Continuation of the Same Dose Between Patients Who Did Not Achieve LDA at Week 12 in the COMP-ACT, SUMMACTA and BREVACTA Trials

	COMP-ACT*,† All Patients (N = 328)	SUMMACTA North American Patients‡ (n = 71)	SUMMACTA All Patients (N = 285)	BREVACTA All Patients (N = 196)
DAS28 remission (< 2.6) at week 16, n (%)	38 (11.6)	6 (8.5)	30 (10.5)	18 (9.2)
Adjusted odds ratio (95% CI)	Reference	6.27 (1.91 to 20.66)	3.51 (2.12 to 5.82)	3.01 (1.76 to 5.23)
P value	Reference	0.0025	< 0.0001	< 0.0001
DAS28 LDA (≤ 3.2) at week 16, n (%)	81 (24.7)	14 (19.7)	68 (23.9)	35 (17.9)
Adjusted odds ratio (95% CI)	Reference	3.83 (1.65 to 8.90)	3.04 (2.03 to 4.55)	2.74 (1.76 to 4.27)
P value	Reference	0.0018	< 0.0001	< 0.0001
DAS28 remission (< 2.6) at week 20, n (%)	66 (20.1)	5 (7.0)	39 (13.7)	29 (14.8)
Adjusted odds ratio (95% CI)	Reference	6.01 (1.92 to 18.82)	3.40 (2.12 to 5.44)	2.66 (1.58 to 4.46)
P value	Reference	0.0021	< 0.0001	0.0002
DAS28 LDA (≤ 3.2) at week 20, n (%)	116 (35.4)	13 (18.3)	76 (26.7)	52 (26.5)
Adjusted odds ratio (95% CI)	Reference	3.59 (1.64 to 7.85)	2.92 (2.01 to 4.26)	2.48 (1.63 to 3.76)
P value	Reference	0.0014	< 0.0001	< 0.0001
DAS28 remission (< 2.6) at week 24, n (%)	66 (20.1)	7 (9.9)	44 (15.4)	36 (18.4)
Adjusted odds ratio (95% CI)	Reference	5.76 (1.92 to 17.32)	3.29 (2.11 to 5.12)	2.35 (1.44 to 3.84)
P value	Reference	0.0018	< 0.0001	0.0006
DAS28 LDA (≤ 3.2) at week 24, n (%)	122 (37.2)	17 (23.9)	90 (31.6)	60 (30.6)
Adjusted odds ratio (95% CI)	Reference	3.36 (1.61 to 7.00)	2.81 (1.97 to 4.01)	2.24 (1.50 to 3.33)
P value	Reference	0.0012	< 0.0001	< 0.0001
CDAI remission at week 24 (≤ 2.8), n (%)	12 (3.7)	2 (2.8)	13 (4.6)	11 (5.6)
Adjusted odds ratio (95% CI)	Reference	4.50 (1.32 to 15.32)	2.93 (1.37 to 6.27)	1.45 (0.69 to 3.05)
P value	Reference	0.0161	0.0056	0.3325
CDAI LDA (≤ 10) at week 24, n (%)	80 (24.4)	11 (15.5)	81 (28.4)	66 (33.7)
Adjusted odds ratio (95% CI)	Reference	4.19 (1.88 to 9.35)	2.35 (1.63 to 3.39)	1.32 (0.88 to 1.97)
P value	Reference	0.0005	< 0.0001	0.1825
SDAI remission (≤ 3.3) at week 24, n (%)	16 (4.9)	2 (2.8)	15 (5.3)	11 (5.6)
Adjusted odds ratio (95% CI)	Reference	5.23 (1.44 to 19.01)	3.23 (1.54 to 6.76)	1.64 (0.81 to 3.30)
P value	Reference	0.0120	0.0019	0.1670
SDAI LDA (≤ 11) at week 24, n (%)	89 (27.1)	11 (15.5)	91 (31.9)	72 (36.7)
Adjusted odds ratio (95% CI)	Reference	4.68 (2.20 to 9.99)	2.20 (1.56 to 3.11)	1.47 (0.99 to 2.17)
P value	Reference	< 0.0001	< 0.0001	0.0540

CDAI, Clinical Disease Activity Index; DAS28, Disease Activity in 28 Joints; LDA, low disease activity; SDAI, Simple Disease Activity Index.

*Dose escalation from TCZ-SC q2w to qw at week 12 in COMP-ACT. Logistic regression model included protocol, week, week × week, age, sex, baseline weight group (< 80 kg, 80-100 kg), baseline DAS28, DAS28 at week 12 and interactions of protocol with baseline weight group, protocol with DAS28 at baseline, protocol with week and protocol with DAS28 at week 12.

†All patients in the COMP-ACT trial were from the United States.

‡North American patients included those from the United States and Canada.

Background/Purpose: In patients with rheumatoid arthritis (RA), subcutaneous tocilizumab (TCZ-SC) is administered every 2 weeks (q2w) or every week (qw), based on the patient's weight and clinical response. This study evaluated the effects on disease activity at week 24 when the dosing schedule of TCZ-SC was escalated from q2w to qw in patients who did not achieve low disease activity (LDA; Disease Activity Score in 28 Joints [DAS28] > 3.2) at week 12 in COMP-ACT compared with patients who did not achieve LDA and did not escalate dosing in SUMMACTA and BREVACTA.

Methods: US patients in COMP-ACT who weighed < 100 kg at baseline and who received TCZ-SC 162 mg q2w + methotrexate escalated to qw if they did not achieve LDA at week 12. In the primary analysis, DAS28 remission (< 2.6) and LDA (≤ 3.2), Clinical Disease Activity Index (CDAI) remission (≤ 2.8) and LDA (≤ 10) and Simple Disease Activity Index (SDAI) remission (≤ 3.3) and LDA (≤ 11) at week 24 were compared between patients who switched from q2w to qw and North American patients in SUMMACTA who initiated TCZ qw + conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and continued a qw dose (baseline body weight < 100 kg and DAS28 > 3.2 at week 12). A secondary analysis compared COMP-ACT patients who escalated from q2w to qw with all SUMMACTA patients who continued a qw dose and all patients in BREVACTA who initiated a TCZ-SC q2w dose + csDMARDs and continued a q2w dose (baseline body weight < 100 kg and DAS28 > 3.2 at week 12). DAS28 was standardized to DAS28-ESR, and comparisons were calculated using a mixed model with repeated-measures logistic regression, including the following covariates: CDAI, SDAI and/or DAS28 at the reference visit (week 12), as well as study baseline values of CDAI, SDAI and/or DAS28, baseline age, sex, tumor necrosis factor inhibitor use prior to the study (yes or no) and weight category.

Results: A total of 328 US patients in COMP-ACT did not achieve LDA at week 12 and escalated from q2w to qw TCZ-SC. In SUMMACTA, 285 patients did not achieve LDA at week 12 and continued TCZ-SC qw, of whom 71 were from North America. Baseline demographic and clinical characteristics were comparable between patients in COMP-ACT and North American patients in SUMMACTA (**Table 1**). A significantly higher proportion of patients in COMP-ACT achieved DAS28, CDAI and SDAI remission and LDA 12 weeks after TCZ dose escalation (week 24) than North American SUMMACTA patients (**Table 2**). In the secondary analysis, similar results were seen when the proportion of patients who achieved DAS28 remission and LDA was compared at week 24 between patients in COMP-ACT and patients from all geographic regions who did not escalate dosing in SUMMACTA and BREVACTA (N = 196) (**Table 2**). Comparable clinical responses were seen with CDAI and SDAI when the COMP-ACT patients and patients from all geographic regions in SUMMACTA were analyzed.

Conclusion: US patients with RA who did not achieve LDA and escalated from q2w to qw TCZ-SC at week 12 in COMP-ACT had better outcomes at week 24 than North American patients who did not achieve LDA and continued qw dosing in SUMMACTA. These results provide evidence that escalation from q2w to qw has more effect than would be expected without dose change for patients who do not achieve LDA by week 12.

Disclosure: N. Singer, Genentech/Roche, 1; **S. Mohan**, Genentech, Inc., 1, 2; **J. Yourish**, Genentech, Inc., 1, 2; **J. Han**, Genentech, Inc., 1, 2; **M. Edwardes**, Everest Clinical Research, 1; **M. Michalska**, Genentech, Inc., 1, 2.

Abstract Number: 0231

Treatment Patterns of Biologic/Targeted Synthetic DMARDs for the Management of Rheumatoid Arthritis in Australia: An Analysis of the OPAL Dataset

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In Australia the cost of biological/targeted synthetic DMARDs (b/tsDMARDs) for treatment of RA is subsidized if the patient has documented high levels of clinical/laboratory disease activity and has not responded to a pre-specified combination of conventional synthetic DMARDs, including methotrexate. Once eligible for subsidy the clinician can then prescribe the b/tsDMARD deemed most clinically appropriate until the desired level of disease control has been reached, with the available options being adalimumab, etanercept, certolizumab pegol, golimumab, infliximab, abatacept, tocilizumab, rituximab, tofacitinib, baricitinib and upadacitinib. The aim of this analysis was to explore b/tsDMARD treatment patterns and clinical priorities when managing RA in real-world rheumatology practice

Methods: Deidentified clinical data were sourced from the OPAL dataset, which is collected in a custom-built electronic medical record at the time of the consultation[1] by 110 rheumatologists in Australia. Prescribing patterns for patients >18 years with RA treated with a b/tsDMARD between Jan 2010-Dec 2014 and Jan 2015-Dec 2019 were included in the analysis. The software program Tableau® was used to display data on medication initiation and cessation dates, and reasons for starting and stopping b/tsDMARDs, which is recorded at the time of the decision.

Results: At Dec 2019, there were 46,412 patients with RA in the dataset and 27% were prescribed b/tsDMARDs. Between 2010-2014, 63% of patients were prescribed a TNF inhibitor (TNFi), and 16%, 15% and 5% prescribed tocilizumab, abatacept and rituximab, respectively. Between 2015-2019, 46% of patients were prescribed a TNFi, followed by JAK inhibitors (JAKi) (28%), tocilizumab, abatacept, and rituximab (12%, 11% and 3%, respectively). TNFi cycling was frequently observed during 2010-2014 with 58% of patients receiving a TNFi in 1st line switching to another TNFi in 2nd line, which reduced to 40% between 2015-2019; however, TNFi cycling was still frequently observed despite the first TNFi being stopped due to lack of efficacy. From 2015, 33% of patients switched from a TNFi in 1st line to a JAKi, and 57% switched from a JAKi in 1st line to a TNFi. 20% of patients receiving a JAKi in 1st line switched to another JAKi, which increased to 31% between Jan 2019-Dec 2019, citing lack of efficacy, AEs and better alternative.

Conclusion: Real-world treatment patterns for b/tsDMARDs are increasingly complex as more drugs with different modes of action (MOA) become available. There is a trend for earlier introduction of drugs with different MOA; however, TNFi cycling is still frequently observed despite evidence supporting increased persistence after switching MOA. Outcomes of JAKi cycling are uncertain and require further investigation.

References:

[1]Littlejohn GO, Tymms KE, Smith T, Griffiths HT. Using big data from real-world Australian rheumatology encounters to enhance clinical care and research. Clin Exp Rheum Nov 2019.

Disclosure: H. Cooley, Novartis, 5, UCB, 8, Janssen, 9; **T. Smith**, OPAL Rheumatology, 9; **P. Youssef**, Gilead, 2; **K. Tymms**, None; **D. Mathers**, None; **S. Ciciriello**, Gilead, 8; **H. Griffiths**, Janssen, 5, Novartis, 5, Roche, 5, UCB, 5; **C. OSullivan**, Janssen, 3, OPAL Rheumatology, 9; **G. Littlejohn**, MSD, 5, AbbVie, 5, Roche, 5, BMS, 5, Janssen, 5, Pfizer, 5, Seqirus, 5.

Abstract Number: 0232

Safety and Effectiveness of Tocilizumab in Patients with Renal Insufficiency in the Non-interventional Study ICHIBAN

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: RA increases a patient's systemic inflammatory burden, which has been associated with development of chronic kidney disease (CKD), especially in patients with comorbid hypertension, diabetes, or cardiovascular events[1,2]. Propensity-matched real-world cohorts show that treatment of RA with biologic therapies lowers the risk of glomerular filtration rate decline[1]. In the ICHIBAN study, tocilizumab (TCZ) was effective and well tolerated in clinical practice in Germany over up to 2 years[3]. Here, we present a post-hoc analysis of ICHIBAN patients with baseline renal insufficiency (RI; assessed as comorbidity by the study physician).

Methods: ICHIBAN was a prospective, multi-center, non-interventional study (NCT01194401; ML22928) that included adults with active, moderate-to-severe RA who received TCZ according to the local label in Germany. Safety was analysed in all patients who received one dose of TCZ (SAF). Effectiveness outcomes (SAF patients with no prior TCZ analyzed) included DAS28-ESR, CDAI, HAQ, and patient-reported outcomes (PROs) assessed via visual analogue scales (VAS; 0=best; 100=worst).

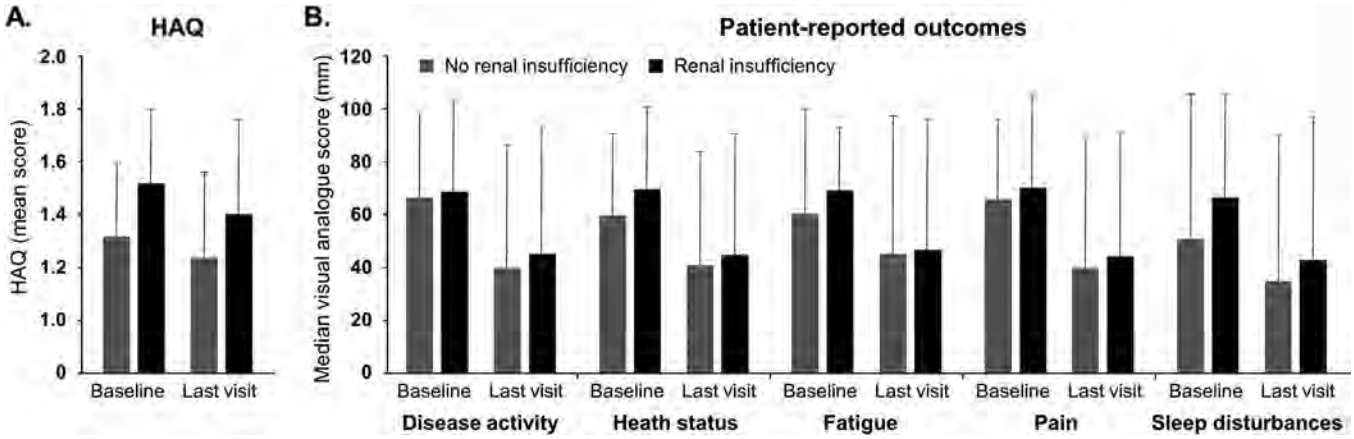

Figure 1. HAQ and patient-reported outcomes (PRO) at baseline and last visit in patient with and without renal insuffciency. A) Mean HAQ score and B) PROs accoring to the visual analogue scale, median mm. Error is presented in standard deviation for HAQ score and interquartile range for PROs. In case of discontinuation of tocilizumab treatment, the last available value was taken and carried forward (last observation carried forward, LOCF). Only patients with data at baseline and last visit under tocilizumab (or LOCF). 9 patients with missing renal status were not analyzed.

	Patients with renal insufficiency	Patients without renal insufficiency
N	90	3068
Female sex, % (n)	68.9 (62)	75.0 (2300)
Age (Mean ± SD) [years]	67.9 ± 10.1	55.1 ± 13.0
Duration of RA (median) [years]	8.0	7.0
BMI (Mean ± SD) [kg/m²]	27.5 ± 4.6	26.9 ± 5.3
Pre-treatment, % (n)		
Biologics naïve	33.3 (30)	30.0 (919)
Anti-TNF	61.1 (55)	66.7 (2045)
Co-medication, % (n)		
Conventional synthetic DMARDs	33.3 (30)	51.3 (1575)
No conventional synthetic DMARDs	66.7 (60)	48.6 (1490)
Glucocorticoids	85.6 (77)	80.6 (2472)
No Glucocorticoids	14.4 (13)	19.4 (594)
Dosage (Mean ± SD)		
GC [mg/day]	8.3 ± 8.5	7.4 ± 14.8
MTX, oral ([mg/week]	12.7 ± 3.9	14.9 ± 9.3
MTX, parenteral [mg/week]	13.3 ± 2.9	16.8 ± 4.6
Comorbidities, % (n)	100.0 (90)	71.3 (2187)
Depression	16.7 (15)	7.2 (221)
Diabetes mellitus	35.6 (32)	9.2 (282)
Coronary heart disease	22.2 (20)	3.9 (120)
Arterial hypertension	81.1 (73)	35.7 (1095)
Osteoporosis	41.1 (37)	16.5 (505)

DMARDs: disease modifying anti-rheumatic drugs; SD: Standard deviation. 9 patients with missing renal status were not analyzed.

Table 2. Effectiveness after two years of observation

Results: Of the 3164 patients in the SAF, 90 (2.84 %) had RI at baseline. These patients were on average 12.8 years older; had a higher frequency of additional comorbidities, such as diabetes, hypertension and coronary heart disease (**Table 1**); and generally worse baseline physical functioning and PROs (especially sleep disturbances) (**Table 2**) than those without RI.

The mean treatment duration was similar patients with and without RI. At baseline, patients with RI less frequently received csDMARDS (**Table 1**), and slightly more frequently glucocorticoids (GCs; 85.4 vs 81.4%) than patients without RI. At last visit however, both groups showed identical proportions of GC therapy (74.4 vs 74.4%).

Importantly, TCZ treatment led to similar improvements in DAS28-ESR, CDAI, HAQ and PROs regardless of RI (**Table 2; Figure 1**).

The rates of adverse events (AEs) and serious AEs per 100 patient years were higher in patients with RI than in those without (169.3 vs 106.8, and 53.6 vs 23.1, respectively). The rate of infections was similar in both groups (23.3 vs 21.1) while the rate of serious infections was higher in patients with RI (11.3 vs 3.7). The rate of gastrointestinal perforations per 100 patient years was 1.9 in patients with RI and 0.2 in those without. The rate of treatment discontinuations due to AE was similar in both groups (9.4 vs 9.2).

		Patients with renal insufficiency	Patients without renal insufficiency
N		82	2814
DAS28-ESR (Mean ± SD)	Baseline (BL)	5.4 ± 1.3	5.2 ± 1.4
	Last Visit	3.4 ± 1.6	3.0 ± 1.7
	Change from BL	-2.0 ± 1.8	-2.2 ± 1.7
< 2.6, % (n)	Last Visit	35.1 (27)	45.9 (1172)
≥ 2.6 ≤ 3.2, % (n)	Last Visit	13.0 (10)	12.0 (305)
CDAI (Mean ± SD)	BL	27.8 ± 14.0	27.7 ± 13.1
	Last Visit	15.5 ± 14.1	14.1 ± 13.0
	Change from BL	-12.3 ± 13.1	-13.5 ± 13.9
≤ 2.8, % (n)	Last Visit	12.9 (9)	16.3 (408)
> 2.8 ≤ 10, % (n)	Last Visit	35.7 (25)	33.3 (833)
HAQ [%] (Mean ± SD)	BL	1.8 ± 0.7	1.3 ± 0.7
	Last Visit	1.5 ± 0.9	1.1 ± 0.8
	Change from BL	-0.3 ± 0.6	-0.2 ± 0.5
Improvement ≥ 0.3, % (n)	Last Visit	37.7 (23)	34.0 (810)
Functional remission (≤ 0.5), % (n)	BL	6.6 (4)	17.3 (411)
	Last Visit	13.1 (8)	30.9 (735)
Visual Analogue Scale (VAS) [mm]			
Disease activity; Median (IQR)	BL	68.5 (35.0)	66.0 (32.0)
	Last Visit	45.0 (48.0)	40.0 (46.0)
Health status; Median (IQR)	BL	69.5 (31.5)	60.0 (31.0)
	Last Visit	45.0 (46.0)	41.0 (43.0)
Exhaustion/Tiredness; Median (IQR)	BL	69.0 (24.0)	60.0 (40.0)
	Last Visit	46.5 (49.5)	45.0 (52.0)
Strength of pain; Median (IQR)	BL	70.5 (34.5)	66.0 (33.0)
	Last Visit	44.5 (46.5)	40.0 (49.0)
Sleep disturbances; Median (IQR)	BL	66.5 (39.0)	51.0 (55.0)
	Last Visit	43.0 (54.0)	35.0 (55.0)

SD: Standard deviation; IQR: Inter quartile range.
In case of discontinuation of tocilizumab treatment, the last available value was taken and carried forward (last observation carried forward, LOCF). Only patients with data at baseline and last visit under tocilizumab (or LOCF).

Table 1. Baseline characteristics of patient with and without renal insufficiency

Conclusion: In the non-interventional ICHIBAN study, despite worse baseline disease in affected patients, the effectiveness of TCZ was similar in patients with and without RI. GC sparing was even more pronounced in patients with CKD compared with those without. As expected, higher rates of baseline comorbid risk factors, such as diabetes and hypertension, and age-dependent serious infections were observed in patients with RI. However, TCZ discontinuation due to an AE was not increased. Overall, this analysis supports the effectiveness and tolerability of TCZ in patients with RA and RI in real-world clinical practice.

[1]Sumida et al. Kidney Int 2018(93):1207–1216

[2]Kochi et al. J Cardiol 2018(71):277–283

[3]Specker et al. Clin Exp Rheumatol (in press)

Disclosure: C. Specker, AbbVie, 5, 8, Boehringer Ingelheim, 2, 5, Chugai, 2, 5, 8, Lilly, 5, 8, GSK, 2, Novartis, 5, Sobi, 5, UCB, 5, 8, Roche, 2, 8; **M. Aringer**, Boehringer Ingelheim, 1, 2, Roche, 1, 2, Bristol Myers Squibb, 1, 2, Chugai, 1, 2, Sanofi, 1, 2, AbbVie, 1, 2, AstraZeneca, 1, 2, Lilly, 1, 2, MSD, 1, 2, Novartis, 1, Pfizer, 1, UCB, 1; **G. Burmester**, AbbVie, 5, 8, Pfizer, 5, 8, Gilead Sciences, Inc., 5, 8, Eli Lilly, 5, 8, Novartis, 5, Celgene, 5; **J. Gerlach**, Roche, 3; **M. Hofmann**, Chugai, 3; **H. Kellner**, Roche, 2, 5; **F. Moosig**, Roche, 2; **H. Tony**, AbbVie, 5, Astra-Zeneca, 5, BMS, 5, Chugai, 5, Janssen, 5, Lilly, 5, MSD, 5, Novartis, 5, Pfizer, 5, Roche, 5, Sanofi, 5; **G. Fliedner**, Roche, 2.

Abstract Number: 0233

Abatacetp in Spanish Patients with Arthritis Rheumatoid and Interstitial Lung Disease. Multicenter Study of 263 Patients

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

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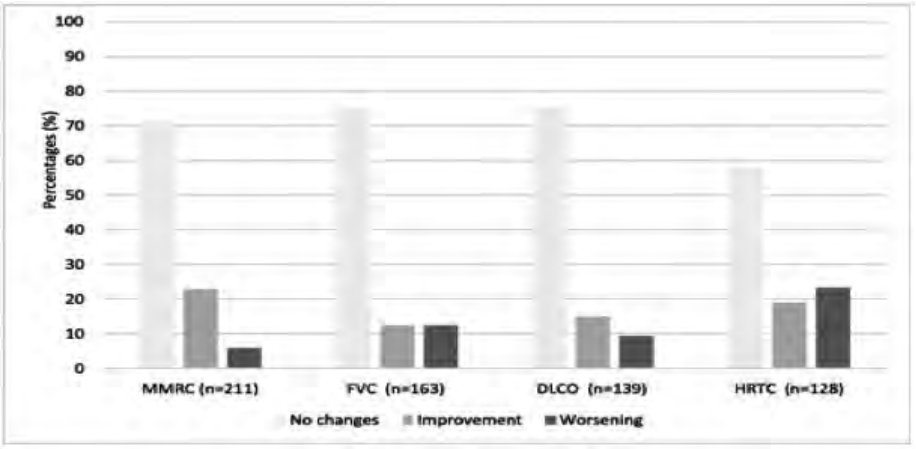
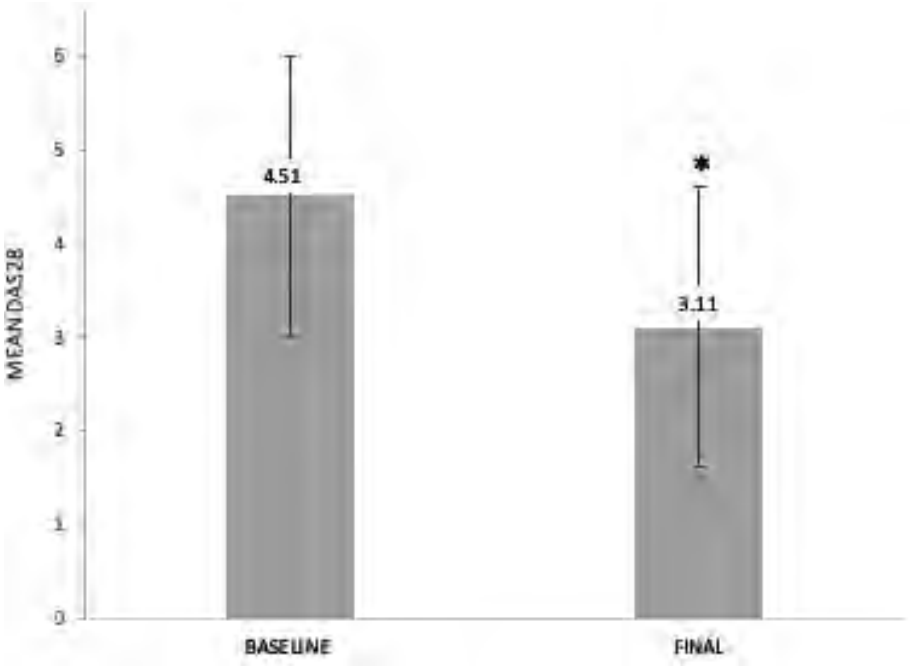
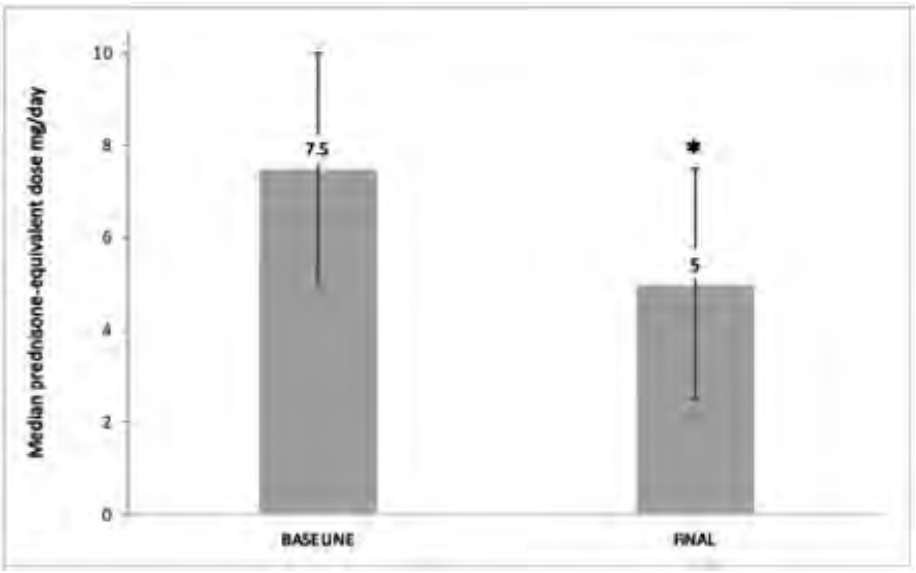
Session Time: 9:00AM–11:00AM







Background/Purpose: To assess the efficacy of abatacept (ABA) in Rheumatoid Arthritis (RA) patients with Interstitial Lung Disease (ILD) (RA-ILD).

Methods: Observational multicenter study of RA-ILD patients treated with at least 1 dose of ABA. ILD was diagnosed by high-resolution computed tomography (HRCT). We analyzed the following variables at baseline (ABA initiation), 12 months, and at the end of the follow-up: **a)** Modified Medical Research Council (MMRC) scale (1-point change), **b)** Forced Vital Capacity (FVC) or Diffusion Lung Capacity for Carbon Monoxide (DLCO) (improvement or *worsening* ≥10%), **c)** HRCT, **d)** $DAS28_{ESR}$, and **e)** corticosteroid sparing effect

Results: We studied 263 RA-ILD patients (150 women/113 men; mean age 64.6±10 years). At baseline, they had a median duration of ILD of 1 [0.25-3.44] years, moderate or severe degree of dyspnea (MMRC grade 2, 3 or 4) (40.3%), FVC (% of the predicted) mean±SD 85.9±21.8%, DLCO (% of the predicted) 65.7±18.3, and $DAS28_{ESR}$: 4.5±1.5. The ILD patterns were: Usual Interstitial Pneumonia (UIP) (40.3%), Non-Specific Interstitial Pneumonia (NSIP) (31.9%), and others (27.8%). ABA was prescribed at standard dose, intravenously (25.5%) or subcutaneously (74.5%). After a median follow-up of 12 [6-36] months the following variables did not show worsening: dyspnea (MMRC) (91.9%); FVC (87.7%); DLCO (90.6%); chest HRCT (76.6%). A significant improvement of $DAS28_{ESR}$ from 4.5±1.5 to 3.1±1.3 at the end of follow-up ($p< 0.001$) and a corticosteroid sparing effect from a median 7.5 [5-10] mg/day to 5 [2.5-7.5] mg/day at the end of follow-up; $p < 0.001$ was also observed. ABA was withdrawn in 62 (23.6%) patients due to adverse events (n=30), articular inefficacy (n=27), ILD worsening (n=3), and other causes (n=2).

Conclusion: ABA may be an effective and safe treatment for patients with RA-ILD.

Disclosure: C. Fernandez-Diaz, None; **S. Castañeda**, Roche, 2; **R. Melero**, None; **F. Ortiz Sanjuan**, None; **A. Juan-Mas**, None; **C. Carrasco Cubero**, None; **R. Almodovar**, None; **S. Rodriguez-Garcia**, None; **C. Aguilera-Cros**, None; **I. Villa**, None; **S. Ordoñez**, None; **E. Raya**, None; **C. Ojeda**, None; **M. Moreno-Ramos**, None; **G. Bonilla**, None; **S. Romero-Yuste**, None; **A. Ruibal-Escribano**, None; **J. Andreu Sanchez**, None; **R. Exposito**, None; **J. Loricera**, None; **N. Mena-Vazquez**, None; **A. Urriticoechea**, None; **C. Peralta**, None; **L. Arboleya**, None; **F. Narváez**, None; **O. Maiz**, None; **J. Fernandez Melon**, None; **P. Vela**, None; **I. Castellvi**, None; **I. Cabezas**, None; **A. Lopez Robles**, None; **P. Carreira Delgado**, None; **J. Blanco-Madrigal**, None; **N. Del-val-del-amo**, None; **E. Salgado**, None; **B. Garcia-magallon**, None; **C. Hidalgo Calleja**, None; **M. Corbeto Lopez**, None; **A. Perez**, None; **S. Castro**, None; **J. De dios**, None; **A. García Valle**, None; **R. Lopez**, None; **A. García Aparicio**, None; **E. Cervantes**, None; **C. Gonzalez**, None; **N. Alvarez-Rivas**, None; **L. Perez**, None; **M. González-Gay**, None; **R. Blanco**, None.

Abstract Number: 0234

Characterization of Serious Infections with Upadacitinib in Patients with Rheumatoid Arthritis

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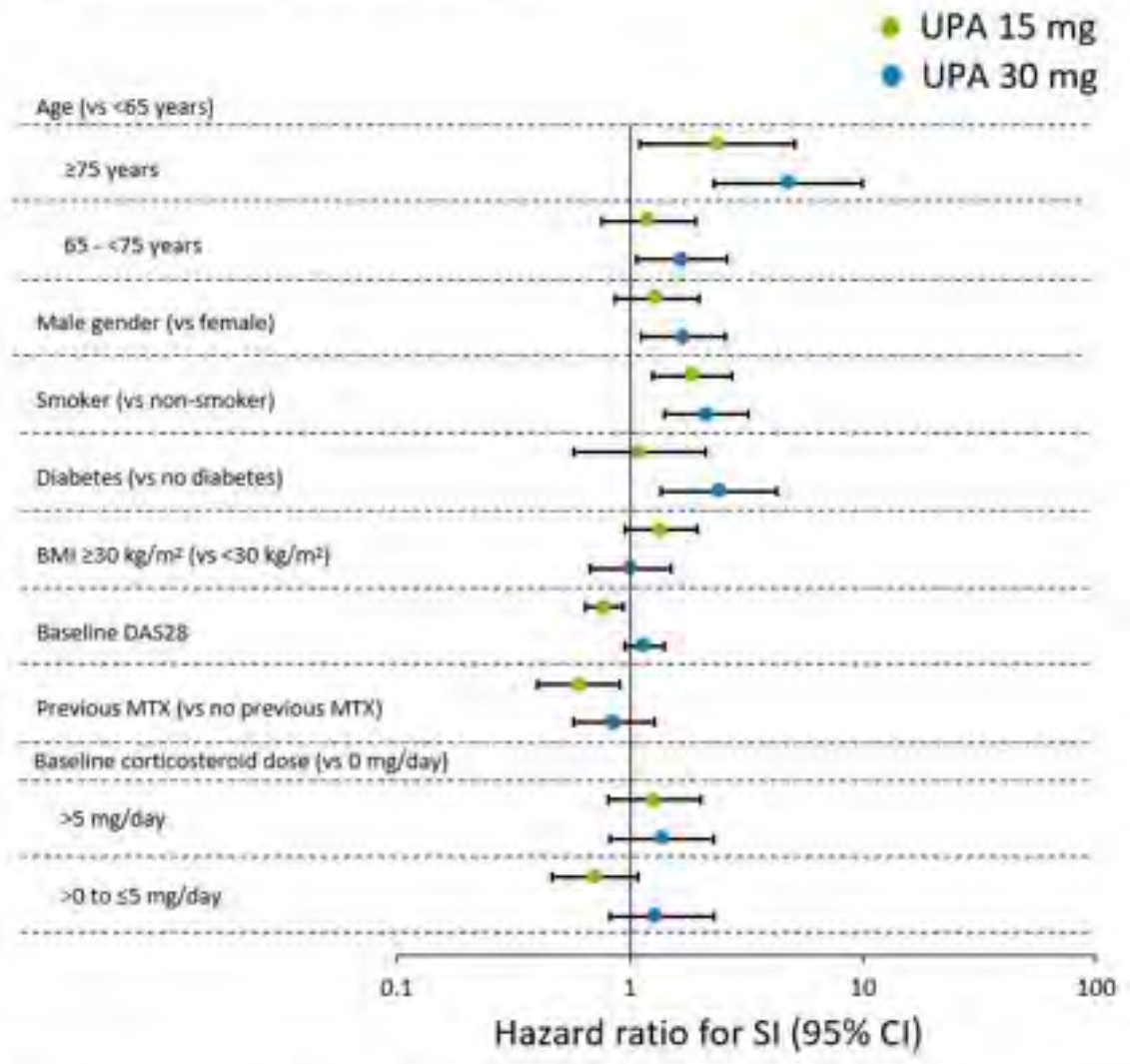
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib (UPA) is a selective and reversible Janus kinase (JAK) inhibitor with an approved dose of 15 mg once daily (QD) for the treatment of rheumatoid arthritis (RA). Patients (pts) receiving JAK inhibitors have been reported to be at increased risk of developing serious infection events (SIE) and opportunistic infections (OI). We evaluate the incidence of SIEs and OIs in pts with RA receiving UPA and active comparators in the Phase 3 SELECT clinical trial program.

Figure. Univariate analysis of SIE risk factors



BMI, body mass index; DAS28, 28-joint disease activity score.

Methods: The exposure-adjusted event rate (EAER) per 100 patient-years (E/100 PY) of SIEs and OIs was determined in pts receiving UPA in five randomized Phase 3 trials (SELECT-EARLY, SELECT-MONOTHERAPY, SELECT-NEXT, SELECT-COMPARE, and SELECT-BEYOND), of which four evaluated both UPA 15 mg and 30 mg QD doses and one (SELECT-COMPARE) evaluated only UPA 15 mg QD. Incidences of SIEs and OIs were also determined in pts receiving adalimumab (ADA) + methotrexate (MTX) in SELECT-COMPARE and MTX monotherapy in SELECT-EARLY. Data were analyzed descriptively, with no statistical comparisons between groups or doses. Risk factors for SIEs were determined using a univariate Cox regression model. The data cut-off was June 30, 2019.

Results: Overall, 2629 pts who received UPA 15 mg, 1204 pts who received UPA 30 mg, 579 pts who received ADA + MTX, and 314 pts who received MTX monotherapy were included in this analysis. The EAERs (E/100 PYs [95% CI]) of SIEs were 3.2 (2.7–3.7) in the UPA 15 mg group, 5.7 (4.8–6.8) in the UPA 30 mg group, 3.9 (2.6–5.6) in pts receiving ADA + MTX, and 3.1 (1.7–5.2) in pts receiving MTX monotherapy. Pneumonia was the most common SIE, with EAERs (E/100 PYs [95% CI]) of 0.7 (0.5–1.0), 1.3 (0.9–1.9), 0.7 (0.2–1.5), and 0.7 (0.1–1.9) in the UPA 15 mg, UPA 30 mg, ADA

+ MTX, and MTX monotherapy groups, respectively. Rates of OIs (including oral candidiasis and disseminated herpes zoster [HZ]) (E/100 PYs [95% CI]) were 0.7 (0.5–1.0), 1.3 (0.9–1.9), 0.4 (0.1–1.1), and 0 (0–0) in the UPA 15 mg, UPA 30 mg, ADA + MTX, and MTX monotherapy groups, respectively. Oral candidiasis was the most frequent OI with EAERs (E/100 PYs [95% CI]) of 0.4 (0.2–0.6) in the UPA 15 mg group, 0.6 (0.3–1.0) in the UPA 30 mg group, 0.4 (0.1–1.1) in the ADA + MTX group, and 0 (0–0) in the MTX monotherapy group. Serious adverse events of HZ were only reported in the UPA groups (0.2 E/100 PYs [95% CI: 0.1–0.3] and 0.6 E/100 PYs [95% CI: 0.4–1.1] in the UPA 15 mg and 30 mg groups, respectively). Overall, there were 3 (4 coded events), 3, 1, and 0 pts who had active tuberculosis events in the UPA 15 mg, UPA 30 mg, ADA + MTX, and MTX monotherapy groups, respectively. Risk factors for SIEs are shown in the Figure. For both UPA doses, age ≥75 years and smoking were noted to have hazard ratios >1.

Conclusion: The incidence rate of SIEs and OIs was higher in the UPA 30 mg group than the UPA 15 mg group. SIEs observed with UPA 15 mg were similar to that seen with ADA although the rates of HZ were higher on UPA. Pts with RA who are ≥75 years old and/or smokers may be at higher risk than other pts with RA for SIEs while receiving UPA.

Reference:

Original abs: *Ann Rheum Dis.* 2020; 79(S1):650.

Disclosure: K. Winthrop, Pfizer, 2, 5, UCB, 2, 5, Abbvie, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Roche, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 5; **L. Calabrese**, AbbVie, 1, 2, GlaxoSmithKline, 1, Bristol-Myers Squibb, 1, Genentech, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Sanofi, 1, Horizon, 1, Crescendo, 1, Gilead, 1; **F. Van den Bosch**, AbbVie, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Gilead, 5, Merck, 5, 8; **K. Yamaoka**, AbbVie, 2, 5, 8, Astellas, 2, 5, 8, Bristol-Myers Squibb, 8, Mitsubishi Tanabe, 2, 5, 8, Pfizer Inc, 2, 5, 8, Takeda, 5, 8, Actelion, 5, 8, Chugai, 2, 5, 8, Eisai, 2, 5, 8, Eli Lilly, 2, 5, 8, GlaxoSmithKline, 5, 8, Janssen, 5, 8, Nippon Shinyaku, 5, 8, Daiichi Sankyo, 2, 8, Teijin Pharma, 2, Merck Sharp & Dohme, 2, 8, Shionogi, 2, Nippon Kayaku, 2, 8, Takeda Industrial Pharma, 2, 8, Asahikasei Pharma Corp, 5, 8, Gilead G. K., 5, 8, Eli Lilly Japan K. K., 5, Japan Tobacco Inc., 5, Actelion Pharmaceuticals Japan, 8, Ono Pharma, 8, Otsuka Pharma, 8, Boehringer Ingelheim Japan, 8, Hisamitsu Pharma Co., 8, Sanofi, 8, AYUMI Pharma Co., 8; **C. Selmi**, Celgene, 1, 2, 3, Janssen, 1, 2, 3, Leo Pharma, 1, Novartis, 1, 2, 3, Pfizer, 1, 2, 3, Roche, 1, 2, Sanofi-Regeneron, 1, 2, Eli Lilly, 1, 2, Bristol-Myers Squibb, 1, 2, UCB Pharma, 1; **Y. Song**, AbbVie, 1, 2; **B. Hendrickson**, AbbVie, 1, 2; **I. Lagunes-Galindo**, AbbVie, 1, 2; **I. McInnes**, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9.

Abstract Number: 0235

Safety and Biological Activity of Rozibafusp Alfa in Subjects with Rheumatoid Arthritis: Final Results of a Phase 1b Randomized, Double-blind, Placebo-Controlled, Multiple Ascending Dose Study

Lubna Abuqayyas[1], Laurence Cheng[1], Kyong Park[1], Marcia Teixeira dos Santos[1], Barbara Sullivan[1], Hui Wang[1], Yanchen Zhou[1], Vishala Chindalore[2], **Stanley Cohen**[3], Alan Kivitz[4], Maximilian Posch[5] and Jane Parnes[1], [1]Amgen Inc., Thousand Oaks, CA, [2]Pinnacle Research Group, Anniston, AL, [3]Metroplex Clinical Research Center, Dallas, TX, [4]Altoona Center for Clinical Research/Altoona Arthritis and Osteoporosis Center, Duncansville, PA, [5]Charité Research Organisation, Berlin, Germany

SESSION INFORMATION

Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

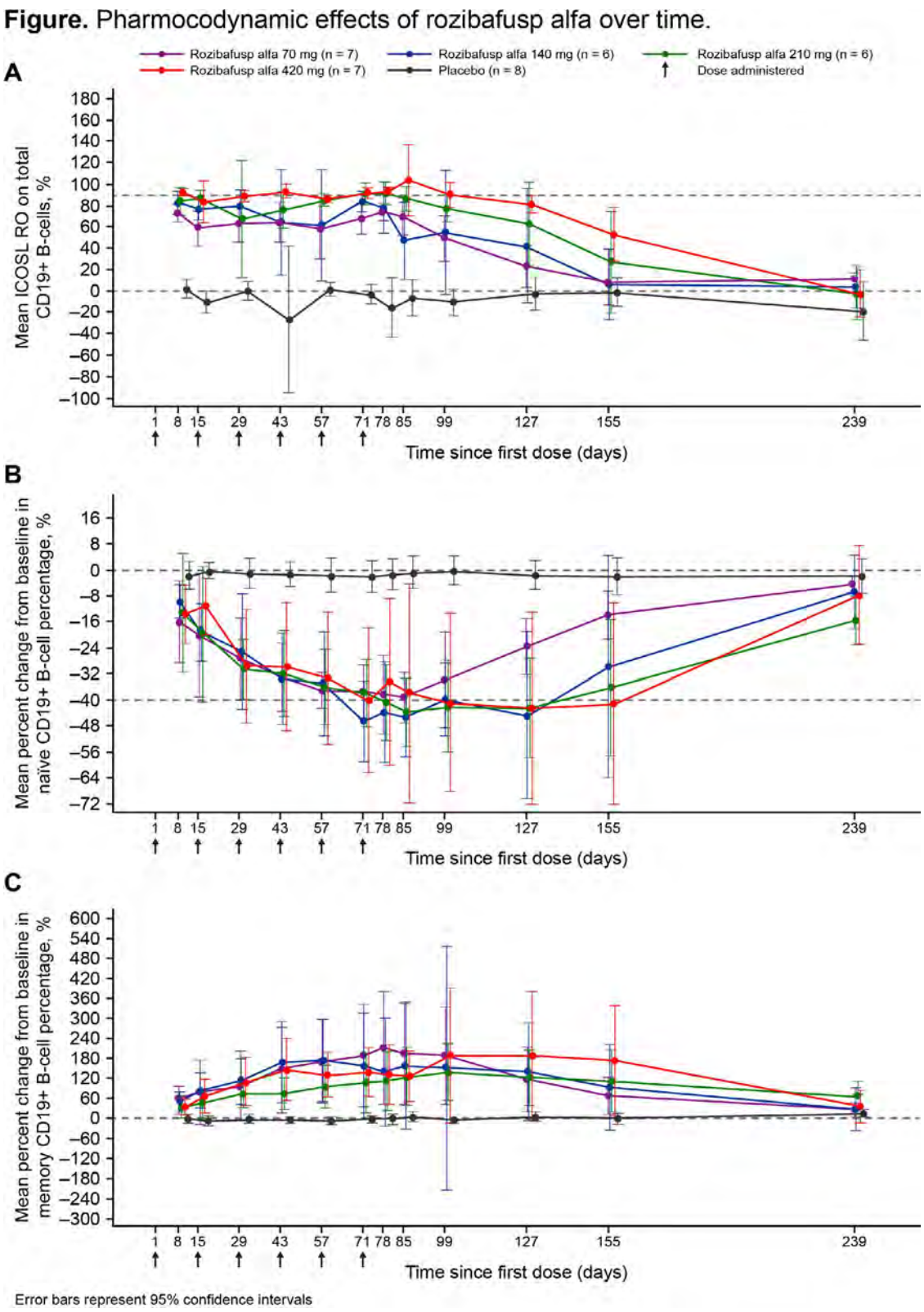


Figure. Pharmacodynamic effects of rozibafusp alfa over time

Background/Purpose: B-cell activating factor (BAFF) and inducible costimulator ligand (ICOSL) are implicated in autoimmune disease pathogenesis, and clinical findings support their utility as drug targets in autoimmune disease (Navarra SV *Lancet* 2011; Cheng LE *Arthritis Rheumatol* 2018). Rozibafusp alfa is a first-in-class bispecific

antibody-peptide conjugate that inhibits BAFF and ICOSL and is currently in phase 2 clinical development for the treatment of SLE. This final analysis of a phase 1b study (NCT03156023) reports the safety, pharmacokinetics (PK), pharmacodynamics (PD), immunogenicity, and effect of rozibafusp alfa on disease control in subjects with RA.

Methods: A total of 34 subjects (age 42–75 years; 82.4% female) with active RA, defined as a disease activity score (DAS28-CRP) >2.6, were randomized 3:1 to receive rozibafusp alfa (N=26, divided into 4 multiple ascending dose cohorts of 70, 140, 210, and 420 mg) or placebo (N=8) subcutaneously every 2 weeks for 10 weeks (6 doses), with 24 weeks of follow-up. All subjects were maintained on a sTable dose of MTX. The primary endpoint was the subject incidence of treatment-emergent adverse events (TEAEs). Additional assessments included serum PK profiles, PD (eg, ICOSL receptor occupancy (RO), changes in peripheral blood B-cells), incidence of anti-rozibafusp alfa antibodies (ADA), and Patient and Physician Global Assessments (PtGA and PhGA) of disease activity.

Results: TEAEs occurred in 96.2% and 87.5% of subjects receiving rozibafusp alfa and placebo, respectively. Two rozibafusp alfa-treated subjects (7.7%) reported serious adverse events; none were considered related to treatment by the study investigator. Rozibafusp alfa demonstrated nonlinear PK and a mean terminal half-life of 4.6–9.5 days, with longer half-lives at higher doses. ICOSL RO on circulating B-cells was dose-related and reversible; >90% mean RO was observed for the 210 and 420 mg dose cohorts (**Figure**). Treatment with rozibafusp alfa reduced the percentage of naïve B-cells and increased the percentage of memory B-cells in all cohorts (**Figure**). Five (20%) subjects developed ADA with no associated AEs, but 1 subject had lower PK and reduced ICOSL RO at day 57. RA disease activity showed greater numerical improvement from baseline in PtGA and PhGA with rozibafusp alfa vs. placebo in the 210 and 420 mg cohorts; maximum score reduction for PtGA and PhGA was achieved after 10 and 6 weeks of rozibafusp alfa treatment, respectively, in both cohorts and persisted through day 183 in the 420 mg cohort.

Conclusion: Multiple ascending doses of rozibafusp alfa were safe and generally well tolerated, with exploratory efficacy results observed in the highest dose cohorts. PK/PD analysis demonstrated nonlinear, target-mediated disposition consistent with cell surface target interaction and PD activity consistent with dual ICOSL/BAFF neutralization. These findings informed the design and dose selection of an ongoing phase 2, randomized, placebo-controlled study to assess the efficacy and safety of rozibafusp alfa in subjects with active SLE and inadequate responses to standard of care therapy.Figure. Pharmacodynamic effects of rozibafusp alfa over time

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Disclosure: L. Abuqayyas, Amgen Inc., 1, 2; **L. Cheng**, Amgen Inc, 1, 2; **K. Park**, Amgen Inc., 1, 3; **M. Teixeira dos Santos**, Amgen Inc., 1, 3; **B. Sullivan**, Amgen Inc, 1, 2, Ultragenyx, 1; **H. Wang**, Amgen Inc., 1, 3; **Y. Zhou**, Amgen Inc., 1, 3; **V. Chindalore**, GlaxoSmithKline, 2, Pfizer, 1, Amgen Inc, 1, Genentech, 1, Novartis, 1, Eli Lilly, 1, Nektar, 1, Boston Pharmaceuticals, 1, AbbVie, 1, Boehringer Ingelheim, 2, EMD Serono, 1, Roche, 1, Merck, 1; **S. Cohen**, Amgen Inc, 1, 2, AbbVie, 1, 2, Pfizer, 1, 2, Boehringer Ingelheim, 1, 2, Sandoz, 1, 2, Gilead, 2, 5, Eli Lilly, 2, 5; **A. Kivitz**, Sanofi, 1, 5, 8, Amgen, 1, Gilead, 1, AbbVie, 5, Genzyme, 5, 8, Janssen, 5, Novartis, 8, Regeneron, 5, 8, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 8, Horizon, 8, Merck, 8, Pfizer, 1, 5, 8, Sun Pharma, 5, UCB, 5; **M. Posch**, None; **J. Parnes**, Amgen Inc., 1, 3.

Abstract Number: 0236

Safety and Usability of Infliximab Administration by Auto-injector (AI) and Pre-filled Syringe (PFS) in Patients with Active Rheumatoid Arthritis (RA): Patient-reported Experience from a Multicenter, Randomized Controlled Pivotal Trial

Rene Westhovens[1], DaeHyun Yoo[2], Piotr Wiland[3], Marek Zawadzki[4], Delina Ivanova[5], Alfredo Berrocal Kasay[6], Elias Chalouhi[7], Eva Balázs[8], SangJoon Lee[9], SungHyun Kim[9], JeeHye Suh[9], NooRi Han[9] and HoJae Lee[9], [1]University Hospitals Leuven, Belgium, Leuven, Belgium, [2]Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [3]Medical Univeristy, Wroclaw, Poland, [4]Medical Univeristy, Dpt of Rheumatology , Wroclaw, Wroclaw, Poland, [5]Diagnostic-Consultative Center Aleksandrovska EOOD, Sofia, Bulgaria, [6]ABK Reuma SRL, LIMA, Peru, [7]Clinica Internacional Sede Lima, Lima, Peru, [8]Dr. Bugyi István Hospital, Szentes, Hungary, [9]Celltrion, Inc., Incheon, Republic of Korea

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The subcutaneous (SC) formulation of CT-P13 received marketing authorization for RA from the EMA by demonstrating non-inferiority compared to CT-P13 intravenous for efficacy in RA patients[1]. CT-P13 SC can provide a clinically meaningful improvement in the quality of life, convenience in treatment and use, as well as enable patients to gain better control over their condition. To provide patients with more comforTable administration

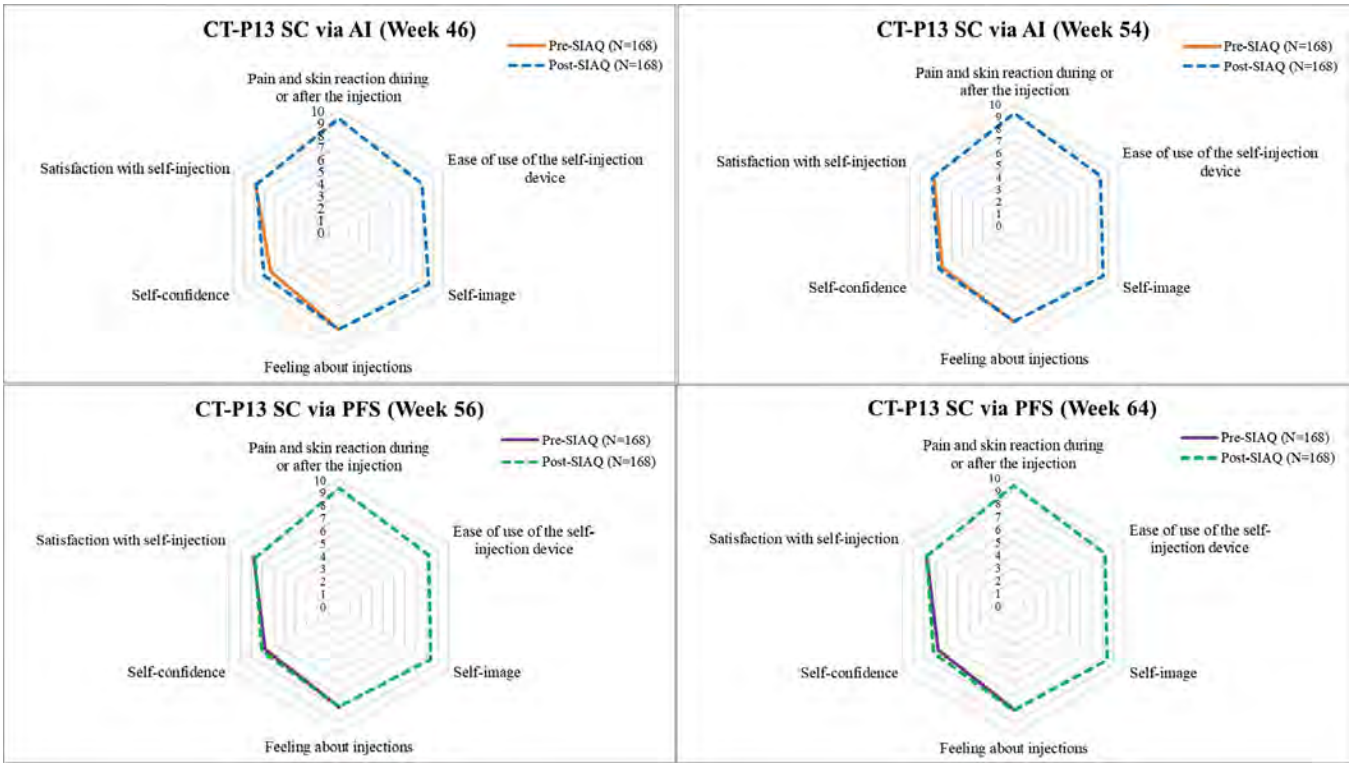

Figure 1. Spidergram of Pre- and Post-Self Injection Assessment Questionnaire

Criteria	Device	Visit	Proportion of patients (%)
Patients with "No" in all items on the Potential Hazard Checklist	AI	Week 46	158/167 (94.6%)
		Week 54	162/165 (98.2%)
	PFS	Week 56	163/164 (99.4%)
		Week 64	158/159 (99.4%)

Note: Percentages were calculated by using the number of patients who self-injected at least one CT-P13 SC via AI or PFS with at least one usability assessment performed and who had hazard-free self-injection assessment as the denominator.

Table 1. Summary of Proportion in Hazard-free Self-Injection

Number of patients, n (%)	**Usability population (N=168)**
Any TEAEs	67 (39.9%)
TEAEs related to the study drug	48 (28.6%)
TEAEs leading to the study drug discontinuation	3 (1.8%)
Localized injection site reaction	1 (0.6%)
Urinary tract infection	1 (0.6%)
Delayed hypersensitivity	1 (0.6%)
Serious TEAEs	1 (0.6%)
Localized injection site reactions	30 (17.9%)
Injection site pain	21 (12.5%)
Injection site erythema	18 (10.7%)
Injection site pruritus	11 (6.5%)
Injection site swelling	10 (6.0%)
Injection site induration	9 (5.4%)
Injection site bruising	3 (1.8%)
Injection site coldness	3 (1.8%)
Injection site irritation	2 (1.2%)
Injection site oedema	2 (1.2%)
Injection site paraesthesia	2 (1.2%)
Injection site haematoma	1 (0.6%)
Injection site ulcer	1 (0.6%)
Injection site urticaria	1 (0.6%)
Scab	1 (0.6%)

Table 2. Summary of Adverse Events during the Usability Assessment

of CT-P13 SC, an AI was developed and this study is to investigate the usability and safety including localized injection site reactions (ISRs) of the AI versus PFS for SC delivery of CT-P13 in RA.

Methods: Usability assessment was conducted as a sub-study of the pivotal CT-P13 SC study in RA patients. Patients self-injected CT-P13 SC every 2 weeks via AI from Weeks 46 to 54 and via PFS from Weeks 56 to 64. The usability of both devices was determined by the observer (healthcare professional) rating of successful, hazard-free self-injection and patient reporting of device experience using the Self-Injection Assessment Questionnaire (SIAQ). Safety, including localized ISRs, was recorded during the usability assessment period.

Results: Patients (N=168) self-injected at least one dose of CT-P13 SC via AI or PFS and had at least one usability assessment performed. The results of usability for CT-P13 SC via AI and PFS were both high (Figure 1), as rated by the patients based on the mean scores ranging from 7.09 to 9.37 for AI and 7.03 to 9.41 for PFS on a scale of 0 (worst experience) to 10 (best experience) for all post SIAQ domains. Following the use of both devices, patients rated their self-confidence higher; 6.47 to 6.97 before using AI, but changed to 7.09 to 7.30 after using AI; 6.73 to 6.84 before

using PFS but changed to 7.03 to 7.20 after using PFS. Except for 11 patients who missed assessment or discontinued from the study, all patients were able to successfully self-administer the injections and completed all instructions from the self-injection assessment checklist for both AI and PFS. The number of patients with the hazard (experiencing a needle stick in the non-critical area) was decreased from 9 patients at Week 46 to 3 patients at Week 54 with AI showing that AI improved in terms of safety by reducing the risk of injury and improper administration. Only 1 patient was with hazard at Weeks 56 and 64, and therefore there was no increase in potential hazard after switching from AI to PFS (Table 1). At least one treatment-emergent adverse event was reported in 67 (39.9%) patients during the usability assessment period. CT-P13 administered by either AI or PFS was generally safe, demonstrating consistency with the known safety profile of infliximab (Table 2).

Conclusion: Infliximab delivered by both AI and PFS was generally well-tolerated and the results demonstrated that there were no differences in usability between AI and PFS. The availability of both AI and PFS will allow patients to select a device based on their own preferences and experiences and will lead to increased adherence during long-term therapy.

References:

1. Westhovens R, et al. Annals of the Rheumatic Diseases 2019;78:1158-1159.

Disclosure: R. Westhovens, Celltrion, Inc., 2, 5, Galapagos NV, 2, 5, Gilead Sciences, Inc., 2, 5; **D. Yoo**, Celltrion, Inc., 1, 2, Celltrion Healthcare, Inc, 1; **P. Wiland**, Celltrion, Inc., 1, Novartis, Pfizer, Abbvie, Gedeon-Richter, Lilly, Roche, Sandoz, 1; **M. Zawadzki**, Celltrion, Inc., 1; **D. Ivanova**, Celltrion, Inc., 1; **A. Berrocal Kasay**, Celltrion, Inc., 1, Pfizer, 1; **E. Chalouhi**, Celltrion, Inc., 1; **E. Balázs**, Celltrion, Inc., 1, Amgen, 1; **S. Lee**, Celltrion, Inc., 1; **S. Kim**, Celltrion, Inc., 1; **J. Suh**, Celltrion, Inc., 1; **N. Han**, Celltrion, Inc., 1; **H. Lee**, Celltrion, Inc., 1.

Abstract Number: 0237

Safety Profile of Upadacitinib up to 3 Years of Exposure in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The safety and efficacy of upadacitinib (UPA), an oral JAK inhibitor, was evaluated in the phase 3 SELECT clinical program, which included 5 randomized, double-blind, controlled trials across a spectrum of rheumatoid arthritis (RA) patients (pts)[1-5]. We describe the long-term integrated safety profile of UPA relative to active comparators in pts with RA treated in the SELECT program up to a cut-off date of 30 June 2019.

Table. Overall TEAEs for UPA and Active Comparators (E/100 PYs [95% CI])				
	MTX n=314 (456.0 PYs)	ADA 40 mg eow n=579 (768.6 PYs)	UPA 15 mg QD n=2629 (4565.8 PYs)	UPA 30 mg QD n=1204 (2309.7 PYs)
Any AE	271.7 (256.8, 287.3)	242.3 (231.4, 253.5)	247.7 (243.2, 252.3)	310.6 (303.5, 317.9)
Any SAE	12.7 (9.7, 16.4)	14.6 (12.0, 17.5)	12.9 (11.9, 14.0)	19.8 (18.0, 21.7)
Any AE leading to discontinuation	7.7 (5.3, 10.7)	8.2 (6.3, 10.5)	6.3 (5.6, 7.1)	10.0 (8.8, 11.4)
Deaths[a]	0.4 (0.1, 1.6)	0.8 (0.3, 1.7)	0.4 (0.2, 0.6)	0.7 (0.4, 1.1)
[a]Deaths included non-treatment emergent deaths: ADA, 1; UPA 15 mg, 3; UPA 30 mg, 3.				

Methods: Treatment-emergent adverse events (TEAEs: AE onset ≥first dose and ≤30 days after last dose) were summarized for the following: methotrexate (MTX, 1 trial, mean exposure 76 wks); adalimumab (ADA, 1 trial, mean exposure 69 wks); pooled UPA 15 mg (5 trials, mean exposure 90 wks); pooled UPA 30 mg (4 trials, mean exposure 100 wks). TEAEs are reported as exposure-adjusted event rates (EAERs; events/100 patient years [E/100PYs]).

Results: 3833 pts received ≥1 dose of UPA 15 mg [n=2629, 4565.8 PYs] or 30 mg [n=1204, 2309.7 PYs] QD, with no option to switch doses. More than half of pts received UPA for ≥96 wks (median: UPA 15, 101.9 wks; UPA 30: 111.7 wks). The EAERs of overall SAEs and AEs leading to discontinuation on UPA 15 mg were comparable to MTX and ADA; rates on UPA 30 mg were numerically higher than UPA 15 mg (**Table**). The most common AEs (≥5 E/100 PYs) reported with UPA 15 mg were upper respiratory tract infection (URTI), nasopharyngitis, urinary tract infection (UTI), bronchitis, increased CPK, and increased ALT. For UPA 30 mg, the most common AEs reported were URTI, UTI, increased CPK, nasopharyngitis, bacterial bronchitis, and herpes zoster (HZ). Overall rates of serious infections and opportunistic infections were comparable between UPA 15 mg, MTX, and ADA groups but were higher on UPA 30 mg (**Figure**). Rates of HZ were higher in both UPA groups (30 mg higher than 15 mg) vs MTX and ADA. The majority of HZ cases were non-serious (96%) and involved a single dermatome (74%). Rates of VTE were comparable across treatment groups (0.3-0.5/100 PYs), as were rates of adjudicated MACE and malignancies (excluding NMSC). Rates of NMSC in UPA 15 mg and ADA were similar, with numerically higher rates on UPA 30 mg. SMR analysis demonstrated that the number of deaths in pts with RA exposed to UPA was not higher than what would be expected for the general population.

Conclusion: Through long-term follow-up, the integrated safety profile of UPA remained consistent with previous analyses, with no new signals identified.

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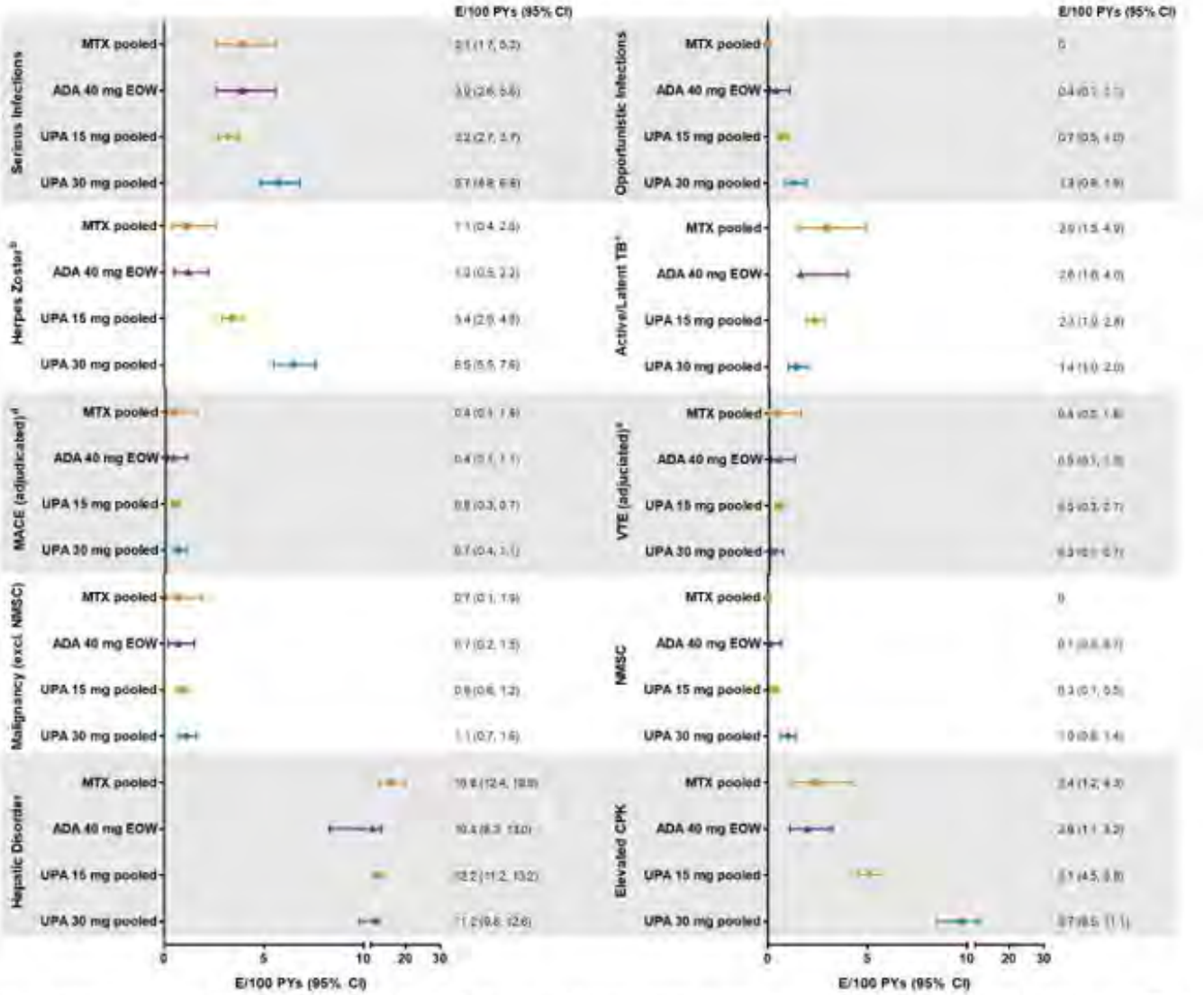
Original abs: *Ann Rheum Dis.* 2020; 79(S1):315.

Figure. Overall AESIs in Patients Treated with Upadacitinib Compared to Active Controls[a]



MTX pooled: N=314, PYs=456.0; ADA 40 mg EOW: N=579, PYs=768.6; UPA 15 mg pooled: N=2629, PYs=4565.8; UPA 30 mg pooled: N=1204, PYs=2309.7

[a]Patients who switched from PBO, ADA, or MTX to UPA were included in the UPA analysis set from the start of UPA, while those who switched from upadacitinib to ADA were included in the ADA dataset from the start of ADA. There was no switch between UPA doses in any study. MTX monotherapy censored at time of rescue to combination therapy (either UPA + MTX or addition of csDMARD).

[b]Most HZ cases were non-serious (95.9%) and single dermatome (74.4%).

[c]There were 6 cases of active TB on UPA (0.1 E/100 PYs) and 1 on ADA.

[d]MACE was defined as CV death, non-fatal MI, and non-fatal stroke.

[e]VTE was defined as deep vein thrombosis and pulmonary embolism

ADA, adalimumab; AE, adverse event; CPK, creatine phosphokinase; CV, cardiovascular; E, events; EOW, every other week; MACE, major adverse cardiovascular event; MI, myocardial infarction; MTX, methotrexate; NMSC, non-melanoma skin cancer; PBO, placebo, PYs, patient-years; QD, once daily; TB tuberculosis; TEAE, treatment-emergent adverse event; UPA, upadacitinib; VTE, venous thromboembolism.

Disclosure: S. Cohen, Amgen Inc, 1, 2, AbbVie, 1, 2, Pfizer, 1, 2, Boehringer Ingelheim, 1, 2, Sandoz, 1, 2, Gilead, 2, 5, Eli Lilly, 2, 5; **R. Van Vollenhoven**, AbbVie, 1, 2, Arthrogen, 1, Bristol-Myers Squibb, 1, 2, GlaxoSmithKline, 1, 2, Lilly, 1, 2, Pfizer, 1, 2, UCB, 1, 2, Astra Zeneca, 1, Biotest, 1, Celgene, 1, Janssen, 1, Medac, 1, Merck & Co, 1, Novartis, 1, Roche, 1; **J. Curtis**, AbbVie, 1, 2, Amgen, 1, 2, Bristol-Myers Squibb, 1, 2, Corrona, 1, 2, Crescendo, 1,

2, Janssen, 1, 2, Pfizer, 1, 2, Sanofi, 1, 2, UCB, 1, 2; **L. Calabrese**, AbbVie, 1, 2, GlaxoSmithKline, 1, Bristol-Myers Squibb, 1, Genentech, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Sanofi, 1, Horizon, 1, Crescendo, 1, Gilead, 1; **C. Zerbini**, Amgen, 1, GlaxoSmithKline, 1, Lilly, 1, Merck & Co, 1, 2, Novartis, 1, Pfizer, 2, 5, Sanofi, 1, 2, Servier, 1, Roche, 1; **Y. Tanaka**, AbbVie, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 2, 5, 8, Asahi-kasei, 2, 5, 8, Novartis, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Astellas, 2, 5, 8, Chugai, 2, 5, 8, Daiichi-Sankyo, 2, 5, 8, Eisai, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Janssen, 2, 5, 8, Mitsubishi-Tanabe, 2, 5, 8, Pfizer, 2, 5, 8, Takeda, 2, 5, 8, YL Biologics, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8; **L. Bessette**, Amgen, 1, 2, 3, BMS, 1, 2, 3, Janssen, 1, 2, 3, UCB, 1, 2, 3, AbbVie, 1, 2, 3, Pfizer, 1, 2, 3, Merck, 1, 2, 3, Celgene, 1, 2, 3, Sanofi, 1, 2, 3, Lilly, 1, 2, 3, Novartis, 1, 2, 3, Gilead, 2, 6, 8; **C. Schlacher**, AbbVie, 1, 2; **T. Shaw**, AbbVie, 1, 2; **J. Liu**, AbbVie Inc., 1, 2; **J. Enejosa**, AbbVie, 1, 2; **Y. Song**, AbbVie, 1, 2; **G. Burmester**, AbbVie, 5, 8, Pfizer, 5, 8, Gilead Sciences, Inc., 5, 8, Eli Lilly, 5, 8, Novartis, 5, Celgene, 5.

Abstract Number: 0238

Gestational Desire and Certolizumab Pegol in Patients with Chronic Inflammatory Rheumatic Disease. Preliminary Results of the GESTAMAD Cohort

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: INTRODUCTION The use of biological therapies during pregnancy has been contraindicated since the beginning of the use of these drugs. In recent years several studies have demonstrated the minimal-to-no transfer of certolizumab pegol (CZP) to the placenta and breast milk, which has allowed its approval for use in pregnancy and breastfeeding if clinically necessary. However, there are no studies evaluating the use of CZP during this period in real life or the characteristics of this subgroup of patients. OBJECTIVE: To describe the profile of women of childbearing age diagnosed with chronic inflammatory rheumatic disease (CIRD): Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) and axial Spondyloarthritis (axSpA), who initiate CZP by gestational desire using the GESTAMAD registry (multicenter study of women with chronic inflammatory rheumatic disease of childbearing age who are initiated on CPZ by gestational desire from the Madrid community).

Methods: Prospective multicenter study that aims to know the characteristics of women of childbearing age diagnosed with CIRD and gestational desire to which CZP is initiated for this reason. The comorbidities of the patients such as hypertension, diabetes and cardiovascular disease were collected. Disease activity was measured by DAS28 using CRP in RA and PsA and BASDAI in axSpA. The present study presents preliminary data from the initial cohort and will be followed prospectively for 24 months to assess the efficacy and safety of the drug during pre-conception, pregnancy and lactation.

Results: A total of 48 patients have been recruited in 6 Madrid hospitals from June 2019 to May 2020. Patients had a mean age of 35.6, (36.3 in RA, 35.2 in PA and 34.9 in SPA). 52.1 percent had RA, 29.2 percent had PA and 18.7

percent had SPA. The mean disease duration for RA, PA and SPA was 9.5, 7.5 and 6.8 years, respectively. 50.0% of women were nulliparous. The abortion rate of patients diagnosed with spondyloarthropathy was 21.8%. 33.3% of the patients had been treated with previous biologicals, with gestational desire/pregnancy being the reason for the change. 78.1 % of the patients had been treated with synthetic disease modifying antirheumatic drugs (DMARD) previously. With regard to disease activity, the mean DAS 28 at the start of treatment was 4.5 in RA and 3.8 in PA and BASDAI 7.0 in axSPA. In RA the highest values of CRP and ESR were found prior to initiation with CZP, but this difference was not statistically significant (p=0.632 and 0.621, respectively). 22.9% of patients had previous comorbidities.

Conclusion: CONCLUSIONS: The mean age of patients with gestational desire in CIRD is high. Women diagnosed with PsA and axSpA have a high rate of previous abortions, upper than 25%. The duration of the disease is equally long at the time of manifesting gestational desire. The use of treatments such as CZP, compatible with pregnancy and lactation would allow a better control of inflammatory joint disease in this period of life, encouraging patients not to postpone their gestational desire.

Disclosure: L. Gonzalez Hombrado, None; **M. Salido Olivares**, None; **M. Ortega de la O**, None; **P. Navarro Alonso**, None; **P. Castro Perez**, None; **A. Castilla**, None; **A. Garcia Martos**, None; **C. Arconada**, None; **A. Aragon Diez**, None; **C. Marin huertas**, None; **E. Andres Esteban**, None.

Abstract Number: 0239

Adjudicated MACE and VTE in the Filgotinib RA Program: Integrated Analysis from Phase 2 and 3 Clinical Trials

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL)—an oral, selective Janus kinase 1 inhibitor (JAKi)—improved RA signs and symptoms in three phase 3 trials. Despite the efficacy of FIL and other JAKi, there are some concerns regarding potential for venous thromboembolism (VTE); major adverse cardiac events (MACE); and elevated platelet levels, which may result from JAK2 inhibition and modulation of thrombopoietin and could be causally related to VTE.

Methods: Patients (pts) meeting 2010 ACR/EULAR criteria for RA who participated in the phase 2 DARWIN 1–2 (D1–2), phase 3 FINCH 1–3 (F1–3), and long-term extension studies (DARWIN 3 [D3] and FINCH 4 [F4]) and received

Table 1. Prevalence of factors associated with cardiovascular risk at baseline in patients receiving FIL 200 mg or FIL 100 mg in pooled phase 3 studies (F1, 2 and 3)

	FIL 200 mg N = 1438 n (%)	FIL 100 mg N = 1031 n (%)
Age		
≥55 years	674 (47)	518 (50)
≥65 years	276 (19)	201 (20)
≥75 years	58 (4)	32 (3)
BMI[a]		
≥25 kg/m^2	881 (61)	638 (62)
≥30 kg/m^2	417 (29)	303 (29)
≥35 kg/m^2	167 (12)	111 (11)
≥40 kg/m^2	62 (4)	46 (4)
Nicotine use		
Former	194 (13)	128 (12)
Current	197 (14)	153 (15)
Concurrent use of oral contraceptive on first dosing date	90 (6)	69 (7)
Concurrent use of statin on first dosing date	138 (10)	122 (12)
Medical history		
Diabetes	158 (11)	108 (10)
Hypertension	480 (33)	353 (34)
Dyslipidemia	214 (15)	175 (17)
CVD	79 (5.5)	39 (3.8)
Ischemic CNS vascular conditions	36 (2.5)	23 (2.2)
Prior DVT/PE event (unadjudicated)	10 (0.7)	7 (0.7)

All data presented as n (%)
[a]Patients may be counted in more than one BMI category.
BMI, body mass index; CNS, central nervous system; CVD, cardiovascular disease; DVT, deep vein thrombosis; FIL, filgotinib; PE, pulmonary embolism.

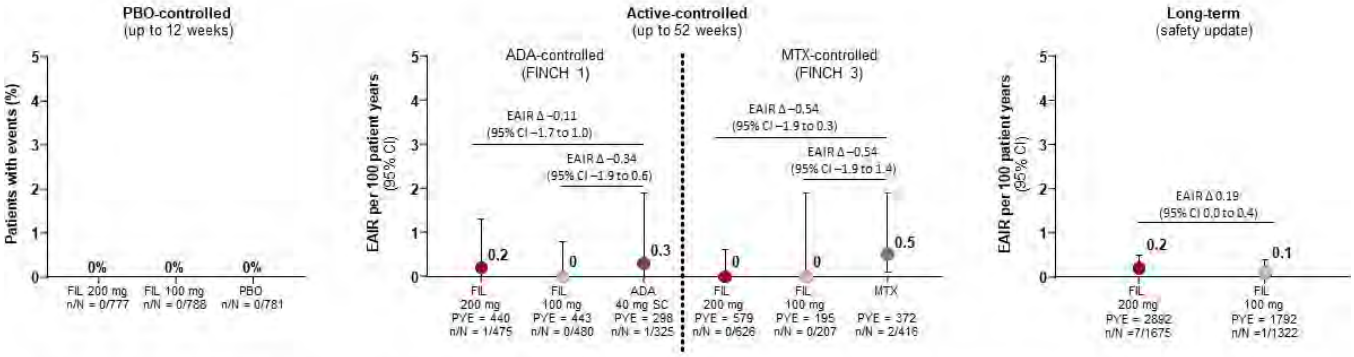
Table 1. Prevalence of factors associated with cardiovascular risk at baseline in patients receiving FIL 200 mg or FIL 100 mg in pooled phase 3 studies (F1, 2 and 3)

FIL 100 mg, FIL 200 mg, adalimumab (ADA), or placebo (PBO) with or without MTX were included. Events were analyzed as-exposed according to treatment received.

The week (W)12 PBO-controlled safety analysis included data from pts who received FIL 100, FIL 200, or PBO for ≤12W (D1–2, F1–2); some PBO-treated pts had additional data through W24 (F1–2). The active-controlled analysis included data from pts who received FIL 100, FIL 200, or ADA with background MTX (F1) and pts who received FIL 100 + MTX, FIL 200 + MTX, FIL 200, or MTX (F3) for ≤52W. The FIL 200 vs FIL 100 analysis included data from pts (D1–3, F1–4) for ≤5.5 years.

Data were analyzed based on whether pts did/did not experience a MACE or VTE event. For active-controlled analysis sets (except MACE in the MTX-controlled analysis set), exposure-adjusted incidence rates (EAIRs) and 95% confidence intervals (CIs) were calculated using the exact Poisson method, and treatment differences were provided with corresponding CIs based on the confidence limits of individual point estimates. For FIL 200 vs FIL 100 analyses and MACE in the MTX-controlled analysis set, EAIRs, difference in EAIRs, and 95% CIs were calculated using Poisson regression with treatment group as a covariate. Suspected MACE (cardiovascular [CV] death, myocardial infarction,

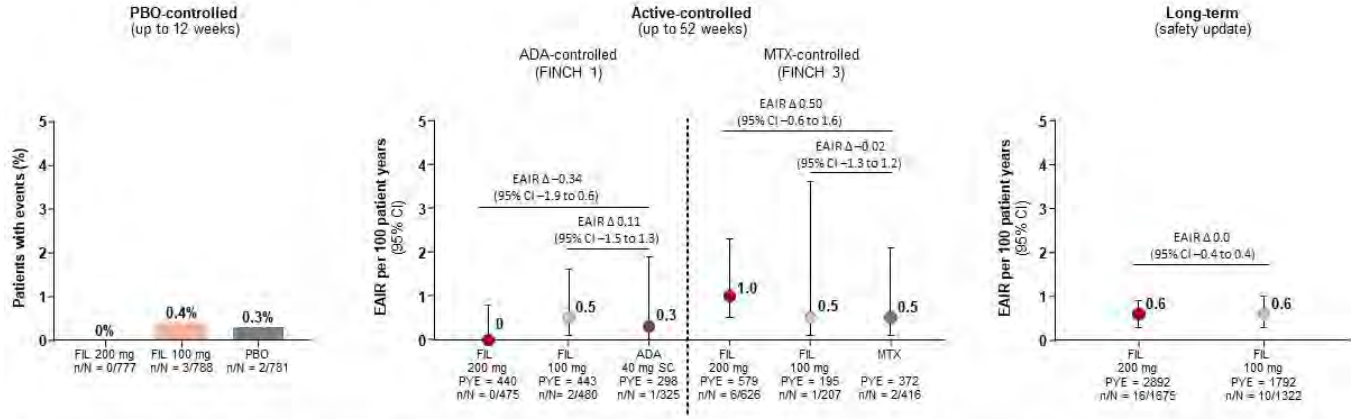
Figure 1. VTE events during the PBO-controlled, active-controlled, and long-term periods



All analyses include all data from the patient's original assigned study treatment but censor data after subjects were rerandomized or assigned to a different treatment; long-term analysis also includes data from patients rerandomized from PBO to FIL.
EAIR for ADA-controlled and MTX-controlled: Exact Poisson method.
EAIR for long-term: Poisson regression with treatment and log exposure as offset.
Two additional events occurred in PBO-treated patients between week 12 and week 24.
Δ, change; ADA, adalimumab; CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; n/N, number of events per total number of patients; PBO, placebo; PYE, patient-years of exposure; SC, subcutaneous; VTE, venous thromboembolism.

Figure 1. VTE events during the PBO-controlled, active-controlled, and long-term periods

Figure 2. MACE during the PBO-controlled, active-controlled, and long-term periods



All analyses include all data from the patient's original assigned study treatment but censor data after subjects were rerandomized or assigned to a different treatment; long-term analysis also includes data from patients rerandomized from PBO to FIL.
EAIR for ADA-controlled: Exact Poisson method.
EAIR for MTX-controlled and long-term: Poisson regression with treatment and log exposure as offset.
One additional event occurred in a PBO-treated patient between week 12 and week 24.
Δ, change; ADA, adalimumab; CI, confidence interval; EAIR, exposure-adjusted incidence rate; FIL, filgotinib; MACE, major adverse cardiovascular event; n/N, number of events per total number of patients; PBO, placebo; PYE, patient-years of exposure; SC, subcutaneous.

Figure 2. MACE during the PBO-controlled, active-controlled, and long-term periods

and stroke) and VTE (deep vein thrombosis and pulmonary embolism) were adjudicated by a blinded independent CV safety endpoint adjudication committee.

Results: CV risk factors were common at baseline (**Table 1**). No VTE occurred in the 12W PBO-controlled safety analysis (**Figure 1**). There were 13 total VTE events. EAIR/100 patient-years of exposure (PYE) were comparable for all treatments (EAIR [n]: FIL 200, 0.2 [7]; FIL 100, 0.1 [1]; ADA, 0.3 [1]; MTX, 0.5 [2]; PBO (up to W24), 0.7 [2]; **Figure**

1). Crude incidence of MACE in the PBO-controlled safety analysis is shown in **Figure 2**. There were 32 MACE events overall. EAIRs were comparable for all treatments (EAIR [n]: FIL 200, 0.6 [16]; FIL 100, 0.6 [10]; ADA, 0.3 [1]; MTX, 0.5 [2]; PBO (up to W24), 1.0 [3]; **Figure 2**). Platelet counts did not increase during the study; at W52, mean platelet counts slightly decreased in all treatment arms.

Conclusion: No safety signal for VTE or MACE was observed in the filgotinib RA program. EAIRs of positively adjudicated VTE and MACE were low and consistent with expectations in patients with RA (EAIR 0.4/100 PYE for VTE and 1.0/100 PYE for MACE).[1,2]

References

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2. Cooksey R et al. Semin Arthritis Rheum. 2018;48:367–73.

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Abstract Number: 0240

Long-term Safety and Efficacy of Sarilumab over 5 Years in Patients with Rheumatoid Arthritis with 1 or >1 Prior Tumor Necrosis Factor Inhibitor Failures

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Treatments Poster I: RA Treatments & Their Safety

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: A proportion of adult patients with RA are refractory to TNF inhibitors (TNFi), and treatment with subsequent biologics may be associated with reduced response. Sarilumab is a human IL-6 receptor inhibitor approved for the treatment of adults with moderate to severely active RA. In the phase 3 TARGET study (NCT01709578), significant improvements in the signs and symptoms of RA and physical function were shown with sarilumab versus placebo in patients refractory to TNFi who were receiving background conventional synthetic DMARDs. Here we investigate the long-term safety and efficacy of subcutaneous sarilumab over 5 years in patients with 1 or >1 TNFi treatment failure prior to their enrollment in TARGET, who continued onto the open-label extension (OLE) study, EXTEND (NCT01146652).

Methods: In the 24-week, randomized, controlled trial TARGET, patients received placebo, sarilumab 150 mg, or sarilumab 200 mg every 2 weeks (q2w), and were eligible to receive open-label sarilumab 200 mg q2w in EXTEND. Dose reduction to 150 mg q2w was permitted per investigator's discretion, or to manage laboratory abnormalities. Safety outcomes are presented for the entire follow-up period from TARGET baseline through EXTEND. Efficacy was assessed using Clinical Disease Activity Index (CDAI) score. Data cut-off date was January 15, 2019.

Table 1. Summary of TEAEs by treatment allocation during TARGET and by TNFi failure status, number of events (events per 100 PY)

	Placebo + DMARD		Sarilumab 150 mg q2w + DMARD		Sarilumab 200 mg q2w + DMARD		All	
Prior TNFi, n	**1**	**>1**	**1**	**>1**	**1**	**>1**	**1**	**>1**
Patients, n	**114**	**42**	**111**	**34**	**114**	**39**	**339**	**115**
PY	**382**	**132**	**361**	**107**	**387**	**133**	**1130**	**372**
Any TEAE	772 (202)	321 (243)	776 (215)	425 (399)	688 (178)	334 (251)	2236 (198)	1080 (291)
Any TE SAE	54 (14)	25 (19)	54 (15)	24 (22)	49 (13)	29 (22)	157 (14)	78 (21)
Any TEAE leading to death	1 (0.3)	2 (2)	1 (0.3)	0	1 (0.3)	0	3 (0.3)	2 (0.5)
TEAE leading to permanent treatment discontinuation	26 (7)	10 (8)	34 (9)	8 (8)	31 (8)	6 (5)	91 (8)	24 (6)

PY=patient-year; q2w=every 2 weeks; TE SAE=treatment-emergent serious adverse event; TEAE=treatment-emergent adverse event; TNFi=TNF inhibitor

Table 1

Table 2. Mean CDAI and proportion of CDAI responders

Treatment allocation in 24-week RCT	Placebo + DMARD (n=156)		Sarilumab 150 mg + DMARD (n=145)		Sarilumab 200 mg + DMARD (n=153)	
TNFi failures	**1**	**>1**	**1**	**>1**	**1**	**>1**
CDAI, mean (SD)						
RCT baseline	43.7 (12.7)	42.5 (10.3)	42.0 (13.0)	44.3 (13.5)	42.1 (13.5)	48.5 (13.0)
Change after 216 weeks' follow-up	−30.9 (17.5)	−32.6 (15.2)	−33.3 (15.8)	−33.1 (12.7)	−30.3 (13.6)	−36.0 (18.1)
CDAI ≤10, n (%)*						
OLE baseline	48 (42)	14 (33)	59 (53)	16 (47)	56 (49)	20 (51)
After 216 weeks' follow-up	24 (21)	10 (24)	29 (26)	7 (21)	29 (25)	8 (21)

*Nonresponder imputation; ITT values used as denominators. CDAI=Clinical Disease Activity Index; ITT=intent to treat; OLE=open-label extension; RCT=randomized controlled trial; TNFi=TNF inhibitor

Table 2

Results: Of the 546 patients randomized in TARGET, 454 (83%) entered EXTEND; of those, 339 had 1 TNFi failure and 115 had >1 TNFi failure. Patients with >1 TNFi failure were older and had a longer duration of RA than patients with 1 TNFi failure (mean ± SD age: 55 ± 13 years vs 52 ± 12 years; RA duration: 14 ± 9 years vs 11 ± 9 years). Kaplan-Meier estimates of the probability of continuation at 5 years were similar between groups: 48% and 54% for patients with >1 and 1 TNFi failure, respectively. By the cut-off date, 36% (199/546) of patients had discontinued treatment during TARGET and EXTEND. In patients with >1 and 1 TNFi failure, there were 291 and 198 treatment-emergent adverse events (AEs) per 100 patient-years (PY), respectively, and 6 and 8 AEs/100 PY leading to discontinuation (Table 1). Clinical efficacy of sarilumab was sustained through 5 years in EXTEND, regardless of initially assigned treatment in TARGET (Table 2).

Conclusion: The long-term safety and efficacy of sarilumab were similar in patients with 1 or >1 prior TNFi failure over 5 years' follow-up. Clinical efficacy could be sustained through 5 years of treatment.

Disclosure: R. Fleischmann, Pfizer, 2, 5; **K. Maslova**, Sanofi, 1, 3; **H. Leher**, Regeneron, 3, Aurinia Pharmaceuticals, 3, 4; **A. Praestgaard**, Sanofi, 3; **G. Burmester**, AbbVie, 5, 8, Pfizer, 5, 8, Gilead Sciences, Inc., 5, 8, Eli Lilly, 5, 8, Novartis, 5, Celgene, 5.

Abstract Number: 0241

A Prospective Analysis of Factors Impacting Medication Adverse Events in Patients with Rheumatoid Arthritis

Elizabeth Salt[1], Amanda Wiggins[1] and Mary Kay Rayens[1], [1]University of Kentucky, Lexington, KY

SESSION INFORMATION

Session Date: Friday, November 6, 2020
Session Title: RA – Treatments Poster I: RA Treatments & Their Safety
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA), a chronic autoimmune disease affecting approximately 1.5 million people in the U.S., is characterized by inflammation of the synovial tissues with the potential for destruction of artic-

Table 1. Demographic and baseline characteristics (N = 143 patients).

	Potential range	Total Sample *Mean* (SD) or *n* (%)
Age		52.0 (10.8)
Gender		
Male		25 (19%)
Female		105 (81%)
Race		
White		123 (91%)
Other		12 (9%)
Years of education		12.9 (2.6)
Trust in provider	0-100	87.4 (9.9)
Disease activity	0-10	2.6 (0.6)
Adverse events		
Yes		68 (48%)
No		75 (52%)

Table 2. Repeated measures models of adverse events with patients nested within providers.

	Adverse events (n = 129)		
	F (*p*)*	Est. *OR* (95% CI for OR)	*p*
Age	<0.1 (.99)	1.00 (0.97 – 1.03)	.99
Gender: Male vs. Female	9.5 (.002)	0.13 (0.03 – 0.47)	.002
Trust in provider	1.5 (.23)	0.98 (0.95 – 1.01)	.23
Disease activity	0.4 (.51)	0.83 (0.46 – 1.47)	.51
Time	9.7 (<.001)		
Baseline		ref	
1-week		0.16 (0.07 – 0.36)	<.001
8-weeks		0.12 (0.04 – 0.34)	<.001
16-weeks		0.13 (0.05 – 0.39)	<.001
24-weeks		0.12 (0.04 -0.41)	<.001

ular cartilage and the juxtaarticular bone. Initiating disease-modifying anti-rheumatic drugs (DMARDs) within three months of diagnosis is currently recommended to prevent the potential effects of untreated synovitis (i.e., joint destruction, loss of joint function, and pain). Patients taking DMARDs commonly experience medication adverse events. The purpose of this study is to report factors predictive of medication adverse events in patients with RA over time.

Methods: We conducted a secondary analysis of a prospective study (baseline, 1 week, 8 weeks, 16 weeks and 24 weeks) in a sample of 143 RA patients at one University health system. Trust in provider was measured with the *Trust in Physician Scale*, an 11-item scale using a 5-point Likert scale (1 = *strongly disagree* – 5 *strongly agree;* Cronbach's α = .87). Disease activity was measured with the *Routine Assessment of Patient Index Data 3* (RAPID3) on three domains: physical function, pain, and patient global assessment on a scale of 0 to 10 (range 0 - 30). The RAPID3 has been significantly correlated with other measures of disease activity. Adverse events and demographic factors were self-reported. We used repeated measures models using last observation carried forward for participants with missing follow-up data.

Results: In the sample of 143 participants, the average age was 52 years (SD=10.8). The majority of participants were female (81%) and White (91%). Disease activity scores were low (mean 2.6; SD=0.6) and trust in the provider scores were high (mean 87.4; SD=9.9; Table 1). Approximately half of the sample experienced an adverse event. For the adverse events model, the only significant predictor in the model was gender. Females compared to males (Odds ratio [OR] = 0.13, 95% confidence interval [CI] for OR: 0.03 – 0.47; p = .002; see Table 2) were more likely to report adverse

events. Time was significantly associated with decreased experiences of adverse events (OR = 0.12-0.16, 95% CI for OR: 0.04 – 0.41; $p < .001$). Trust in the provider and disease activity were not significant predictors.

Conclusion: Females were more likely to report adverse events suggesting either an increased likelihood of experiencing an adverse event or this group is more likely to report the adverse event if it occurs. Identifying this high risk group could facilitate targeted interventions to decrease medication adverse events, and in turn, improving treatment effectiveness.

Disclosure: E. Salt, None; **A. Wiggins**, None; **M. Rayens**, None.

Abstract Number: 0242

Autoantibody Profile and Ethnicity: Risk Factors for Accelerated Development of Lupus Nephritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a multisystem autoimmune disease. African ancestry is associated with an increased risk of Lupus Nephritis (LN). Anti-DNA autoantibodies play a major role in the development of LN and anti-Ro antibodies have also been implicated. McCarty et al suggested that women of African

Crosstabulation of Ab status with the duration to kidney damage regardless of Ethnic group.

Duration groups					
		less than 5	more than 5	Total	
SM, RO, RNP status	Yes	30 (85.7%)	5 (14.3%)	35 (100%)	
	No	26 (53.06%)	23 (46.93%)	49 (100%)	
Total	56	28	84		
Chi-Square Tests					
	Value	df	Asymptotic Significance (2-sided)	Exact Sig. (2-sided)	Exact Sig. (1-sided)
Pearson Chi-Square	9.796[a]	1	.002		
Continuity Correction	8.382	1	.004		
Likelihood Ratio	10.482	1	.001		
Fisher's Exact Test				.002	.001
Linear-by-Linear Association	9.679	1	.002		
N of Valid Cases	84				

Table.1 Crosstabulation of Ab status with the duration to kidney damage regardless of Ethnic group P value= 0.002

Crosstabulation of Ethnic group with Ab status and duration to kidney damage						
Duration groups			Frequency	Percent	Valid Percent	Cumulative Percent
less than 5	Valid	african with positive	20	35.7	35.7	35.7
		african with negative	10	17.9	17.9	53.6
		asian with positive	5	8.9	8.9	62.5
		caucasian with positive	5	8.9	8.9	71.4
		other negatives	16	28.6	28.6	100.0
		Total	56	100.0	100.0	
more than 5	Valid	african with positive	5	17.9	17.9	17.9
		african with negative	6	21.4	21.4	39.3
		other negatives	17	60.7	60.7	100.0
		Total	28	100.0	100.0	
Chi-Square Tests						
	Value	df	Asymptotic Significance (2-sided)			
Pearson Chi-Square	12.034[a]	4	.017			
Likelihood Ratio	15.027	4	.005			
Linear-by-Linear Association	4.694	1	.030			
N of Valid Cases	84					

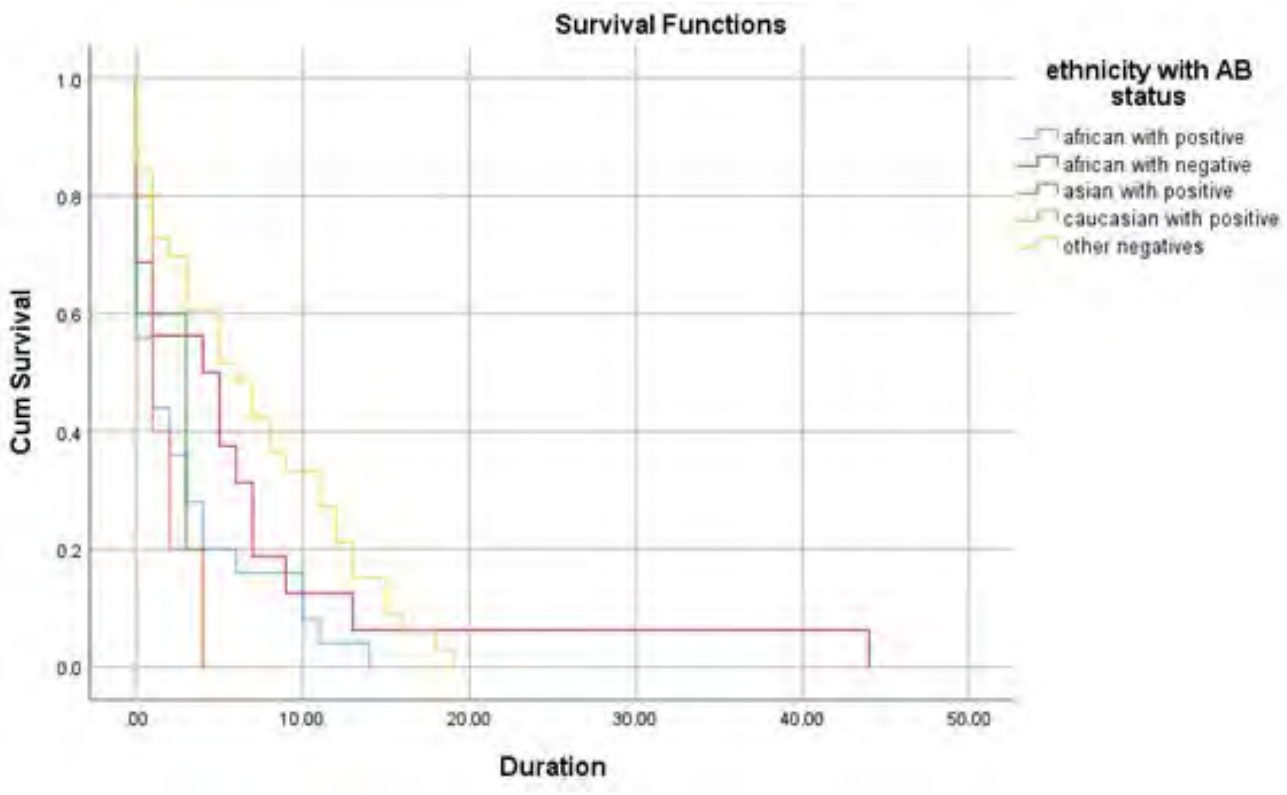
Table.2 Crosstabulation of Ethnic group with Ab status and duration to kidney damage P value= 0.017

ancestry with the unusual autoantibody combination of anti-Sm, Ro & RNP antibodies (AB) were at increased risk of developing LN (1).

Our aim was to determine the correlation between autoantibody profile: Sm, Ro and RNP as a combination in the development of LN in patients with African ancestry. We investigated time to the development of LN from SLE onset.

Methods: A retrospective case-control study was conducted at Guys and St Thomas NHS Trust, London, United Kingdom.

84 patients with confirmed LN meeting the ACR classification criteria for SLE and Nephritis, were included: African (n=41), Caucasian (n=25) and Asian (n=18) ancestry. LN patients with the combination of Sm, Ro and RNP antibodies (Group 1) were compared to LN patients without this autoantibody combination (Group 2). Demographic data, pathology results and laboratory findings were collected.



Graph.1 Kaplan-Meier survival plot

P-values < 0.01 were considered statistically significant. All Anonymized data was analyzed using Statistical Package for Social Sciences (SPSS). Left censorship bias was reduced by use of a database of confirmed LN in our cohort of patients. Research and Development Office approval was obtained for this study.

Results: 84 patients were analyzed, females accounted for 75(89.3%) while males accounted for 9(10.7%), the median range was 44 y.o.

We stratified our population based on their antibody status: Of the 84 (100%) patients, 35 (41.7%) patients had the combination of Sm, Ro & RNP antibodies (Group 1) while the remaining 49 (58.3%) patients did not (Group 2).

In Group 1, regardless of ethnicity, 30 (85.7%) patients developed LN within 5 years or less from the onset of SLE symptoms, while the remaining 5 (14.3%) developed LN after 5 years. In contrast, in Group 2, 26 (53.06%) patients developed LN within 5 years or less while 23 (46.93%) developed LN after 5 years. (P value = 0.002)

Further stratification was based on ethnicity and antibody (AB) status to investigate the time to develop LN from SLE symptom onset: African ancestry with positive AB, African with negative AB, Asian with positive AB, Caucasian with positive AB and Asian & Caucasian with negative Ab. Analysis showed that out of 84 (100%) patients, 20(35.7%) African ethnicity patients with the positive autoantibody combination have developed LN in less than 5 years exceeding the number of those of other ethnic backgrounds. (P value = 0.01).

Conclusion: Patients with the unusual autoantibody combination of Sm, Ro & RNP developed LN significantly earlier than patients who did not have this combination. This autoantibody combination was significantly over represented in the African ancestry patients. Our data suggests that African ancestry patients with this autoantibody combination

are at increased risk of developing LN soon after SLE symptom onset and merit close monitoring for the development of renal disease.

Disclosure: M. Albirdisi, None; **D. d'Cruz**, GlaxoSmithKline, 5, 8; **S. Sangle**, None; **N. Jordan**, None.

Abstract Number: 0243

The Role of Anti-dsDNA Antibodies in Predicting Incident Lupus Nephritis in Newly Diagnosed Lupus

Pooja Kumari[1], Viswanathan Ramakrishnan[2], Jihad Obeid[2], Diane Kamen[3] and Jim Oates[4], [1]The university of Tennesse Health Science center, Memphis, TN, [2]medical university of south carolina, south carolina, [3]Medical University of South Carolina, Charleston, SC, [4]Medical University of South Carolina, Charleston, SC, Charleston, SC

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is a severe manifestation of systemic lupus erythematosus (SLE) that leads to significant morbidity and mortality. Therefore, it is essential to identify biomarkers that predict incident LN in a newly diagnosed SLE patient. Anti-double stranded DNA antibodies (dsDNA) serve as a standard of care disease activity marker in patients with LN. However, the evidence for a predictive role of anti-dsDNA for incident LN is limited. To fill these knowledge gaps, we performed a case-control study to look at the association of anti-dsDNA in newly diagnosed SLE for future incident LN. We determined that the presence of and high titers of anti-dsDNA in newly diagnosed SLE are a significant predictor of future incident LN. Additionally, we found that the presence as well as the titers of anti-dsDNA at the time of SLE diagnosis predict earlier onset of LN. These results provide a roadmap

Baseline characteristics of SLE patients with and without lupus nephritis

Characteristics	SLE with Nephritis (N=300)	SLE without Nephritis (N=94)	p value
Age, median (IQR)	40 (31-52)	42 (33-60)	<0.001
Age at SLE diagnosis, median (IQR)	24 (17-34)	28 (20-41)	<0.001
*Race, N (%)			
African Americans	263 (89)	59 (64)	
Caucasians	24 (8.1)	26 (28)	<0.001
Other	9 (3)	7 (8)	
Females, N (%)	263 (88)	86 (91)	0.09
dsDNA (positive), N (%)	195 (65)	44 (47)	0.002
Age at biopsy mean (SD)	31 (13.8)	NA	
Years of follow up, mean (SD)	4.5 (6.5)	11.6 (10.4)	
Months to first anti-dsDNA, median (IQR) (after SLE onset)	0 (0-2)	1 (0-5)	<0.001

*Race could not be determined for 6 patients

Baseline characteristics of SLE patients with and without lupus nephritis

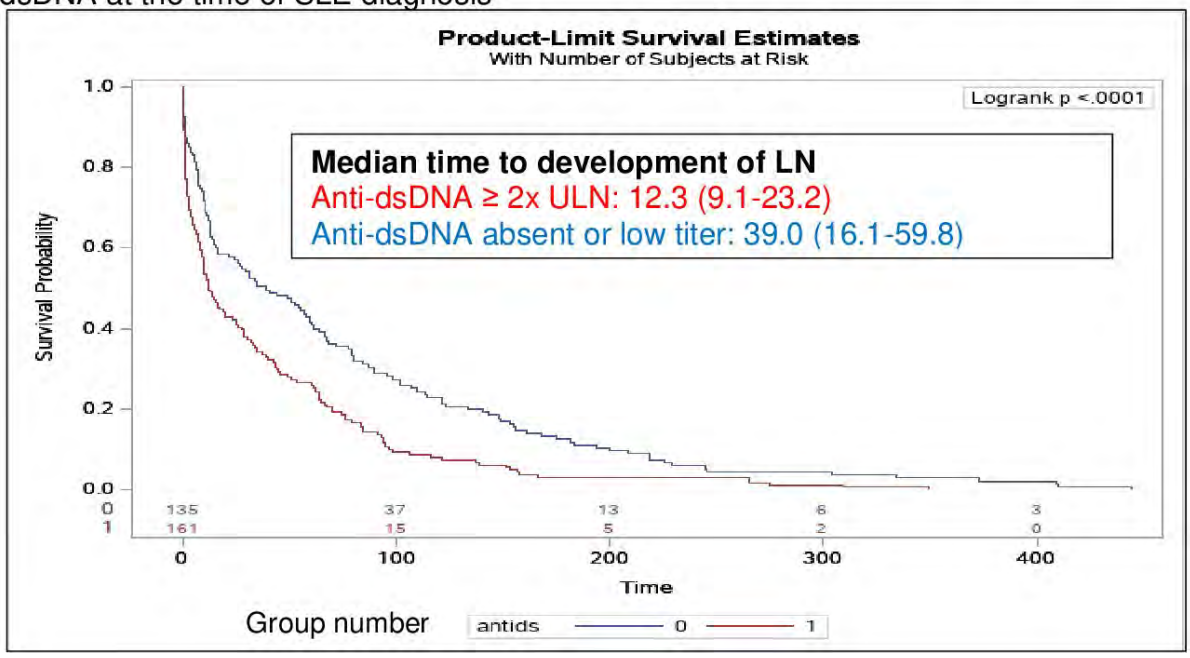
Cox proportional analysis for incident LN by dsDNA titers

Variables	Hazard Ratio	95% Confidence Interval	p value
A. Univariate Cox proportional analysis for the titers of anti-dsDNA			
dsDNA titers	1.112	1.04-1.19	0.001
B. Multivariate Cox proportional analysis for the titers of the anti-dsDNA			
dsDNA titers	1.083	1.02-1.16	0.022
Other race	6.296	2.67-13.8	<.0001
African American	1.363	0.90-2.20	0.177
Age	0.976	0.97-0.99	<.0001
Male	1.320	0.90-1.88	0.133

*Referents: Race (Caucasian), Sex (female), Anti-dsDNA (negative),

Cox proportional analysis for incident LN by dsDNA titers

Kaplan-Meier survival curve for the incident lupus nephritis based on the titers of anti-dsDNA at the time of SLE diagnosis



Kaplan-Meier survival curve for the incident lupus nephritis based on the titers of anti-dsDNA at the time of SLE diagnosis

for the use of anti-dsDNA levels to risk stratify newly diagnosed SLE patients. This stratification could guide disease activity monitoring to diagnose LN at an earlier stage.

Methods: In a prospective, observational case-control study, patients with the diagnosis of SLE were divided into cases (SLE patients with a biopsy proven LN) and controls (without LN). A logistic regression model was utilized to identify the predictive value of the presence of and high titers of anti-dsDNA for future incident LN. A survival analysis was performed to identify the time to new development of LN in relation to the presence of and high titers of anti-dsDNA.

Results: Of 394 SLE patients included in this study, 300 had LN, and 94 did not have LN. In univariate logistic regression analysis, the presence of and high titers of anti-dsDNA were associated with a significantly higher risk for incident LN. In a multivariate logistic regression model, the risk of incident LN was 2-fold with the presence of anti-dsDNA antibodies at the time of SLE diagnosis, adjusting for age, gender and sex (OR 2.1, CI 1.2- 3.4, p 0.005). In comparison to Caucasians the African Americans had a 5-fold risk of developing LN. In a multivariate Cox proportional hazard model, the adjusted risk for the early development of LN was 44% higher in those with anti-dsDNA. The

adjusted risk was about 5-fold for other races in comparison to Caucasian race. By utilizing titers as a continuous variable in the multivariate model, the adjusted risk for early development of LN increased by 8.3% for each doubling of anti-dsDNA. In Kaplan Meier analysis, the median time(month) to development of LN among patients who had a positive anti-dsDNA with new onset SLE was much shorter than patients who did not have anti-dsDNA with new onset SLE (14.4 vs 34.4, p 0.003).Similarly, the median time to incident LN among patients with high anti-dsDNA titers (≥2 times the upper limit of normal) was significantly lower compared to those with lower anti-dsDNA titers (12.3 vs 39.0,$p < 0.001$).

Conclusion: Younger age, African American race, presence of anti-dsDNA and high titers of anti-dsDNA at the time of SLE diagnosis are significant predictors for the incident LN.

Younger age, Hispanic ethnicity, non-Caucasian race, and presence of anti-dsDNA antibody at the time of SLE diagnosis increased the likelihood of a more rapid progression to LN.

Disclosure: P. Kumari, None; **V. Ramakrishnan**, None; **J. Obeid**, None; **D. Kamen**, None; **J. Oates**, None.

Abstract Number: 0244

What Are the Early versus Late Predictors for Systemic Lupus Erythematosus (SLE) Diagnosis?

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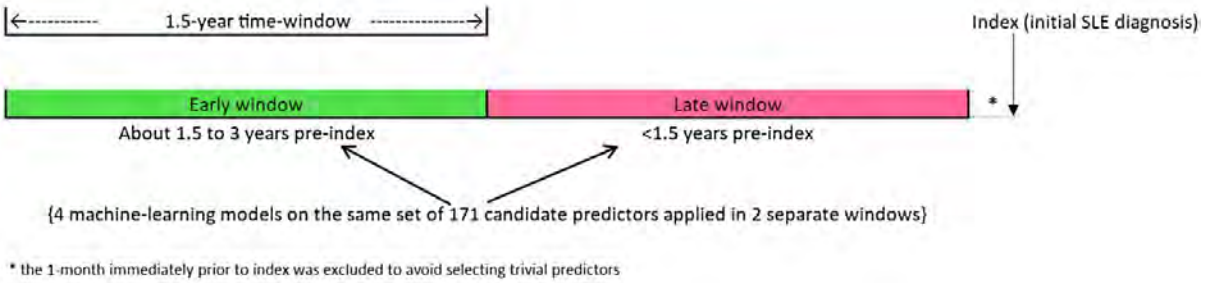
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is clinically heterogenous and its diagnosis is often difficult or delayed. The length of time from symptom onset or from when patients seek care for symptoms to SLE diagnosis has been reported to average 2-3 years. Early recognition and diagnosis provide the chance for timely treatment to minimize organ damage and improve outcomes. We aimed to develop predictive models for SLE diagnosis and to identify differences and overlap between early versus late predictors for SLE.

Methods: A case-control sample was created using the IBM MarketScan® Commercial Claims and Encounters database (2009-2019), which represents data from individuals enrolled in US employer-sponsored insurance health plans. Patients were classified as SLE cases if there were ≥3 outpatient diagnosis records (dx) that spanned at least 60 days, or ≥1 inpatient dx with ≥1 SLE medication records, or ≥1 SLE dx with ≥1 belimumab prescriptions. The first date of SLE dx code or belimumab prescription was designated as the index. Controls were 1:1 matched to each case by age, sex, and latest healthcare visit date (with any diagnosis) within 90 days of the case' index date. All subjects were required to have ≥3 years of pre-index records with the 1.5-3 years and < 1.5 years pre-index periods defined as the early versus late time-window (Figure 1). A set of 171 candidate predictors from existing SLE classification criteria and the literature was observed in both time-windows and used to build 4 machine-learning models for

Figure 1. Illustration of the pre-index early vs late time-windows for the selection of candidate predictors of SLE diagnosis



* the 1-month immediately prior to index was excluded to avoid selecting trivial predictors

	Early Time-window		Late Time-window	
	SLE patients	control	SLE patients	control
Symptoms				
Headache recorded, n (%)	2026 (15)	570 (4)	2472 (18)	572 (4)
Headache, # of times, mean (SD)	2.3 (3.6)	1.9 (2.9)	2.4 (3.9)	1.6 (1.8)
Fatigue recorded, n (%)	479 (3)	92 (1)	1335 (10)	230 (2)
Fatigue, # of times, mean (SD)	2 (2.1)	1.4 (1.5)	2.1 (2)	1.6 (2.5)
Migraine recorded, n (%)	1279 (9)	283 (2)	1553 (11)	309 (2)
Migraine, # of times, mean (SD)	3.1 (5)	1.8 (1.8)	3.3 (5.4)	1.8 (1.7)
Chronic pain recorded, n (%)	4417 (32)	1571 (11)	5373 (39)	1762 (13)
Chronic pain # of times, mean (SD)	5.7 (9.1)	3.9 (6)	6.1 (8.9)	3.8 (5.8)
Myalgia recorded, n (%)	1689 (12)	265 (2)	2655 (19)	260 (2)
Myalgia, # of times, mean (SD)	3.5 (4.9)	4.0 (6.2)	3.6 (5.4)	3.8 (6.7)
Health care utilization				
Rheumatology visits, n (%)	2099 (15)	77 (1)	4235 (31)	88 (1)
Rheumatology visit #times, mean (SD)	3.7 (3.4)	2.5 (1.9)	3.5 (3.3)	2.4 (2.1)
Cardiology visits, n (%)	1888 (14)	476 (3)	2360 (17)	499 (4)
Cardiology visit # times, mean (SD)	2.8 (3.1)	2.1 (2)	2.9 (3.1)	2 (1.9)
Obstetrics and gynecology visits, n (%)	4993 (36)	3610 (26)	5031 (37)	3603 (26)
Obstetrics and gynecology visit # times, mean (SD)	2.8 (3.3)	2.5 (3)	2.8 (3.3)	2.5 (2.9)
Nephrology visits, n (%)	283 (2)	27 (<1)	463 (3)	30 (<1)
Nephrology visit # times, mean (SD)	3.8 (6)	2.3 (1.3)	4.6 (10.3)	2.4 (2.1)
Dermatology visits, n (%)	2826 (21)	1410 (10)	3582 (26)	1522 (11)
Dermatology visit # times, mean (SD)	2.4 (2.9)	1.8 (1.8)	2.4 (2.3)	1.7 (1.4)
Encounter diagnosis for				
Hypertension, n(%)	3919 (28)	1626 (12)	4743 (34)	1789 (13)
Osteoarthritis, n(%)	2811 (20)	677 (5)	3834 (28)	788 (6)
Rheumatoid arthritis, n(%)	977 (7)	32 (<1)	1591 (12)	36 (<1)
Anemia, n(%)	1974 (14)	595 (4)	2780 (20)	651 (5)
Raynaud's, n(%)	325 (2)	16 (<1)	730 (5)	16 (<1)
Alopecia, n(%)	294 (2)	90 (1)	552 (4)	99 (1)
Sjogren's, n(%)	402 (3)	6 (<1)	784 (6)	7 (<1)
Medications				
Opioid, n (%)	3371 (24)	1038 (8)	4230 (31)	1191 (9)
Macrolides, n(%)	4607 (33)	2230 (16)	4888 (35)	2255 (16)
Thyroid therapies, n(%)	2148 (16)	671 (5)	2422 (18)	725 (5)
SSRI/SSNRI Anti-depressants, n(%)	2174 (16)	854 (6)	2870 (21)	1020 (7)
Hydroxychloroquine, n(%)	1467 (11)	13 (<1)	3592 (26)	10 (<1)

Table 1. Descriptions of the study populations, CCAE, 2009-2019 SSRI: Selective Serotonin Reuptake Inhibitors; SSNRI: selective serotonin-norepinephrine reuptake Inhibitors. Early Time-window: from index date- 1127 days to index-580 days; Late Time-window: from index-579 days to ~index-32 days

	Gradient Boosted Trees (GBT)	XGBoost	Random Forest	Regularized (L1) Logistic Regression
Model performance*				
Early time window	AUC 0.82 Accuracy 0.72 Recall 0.82	AUC 0.82 Accuracy 0.73 Recall 0.79	AUC 0.81 Accuracy 0.72 Recall 0.78	AUC 0.81 Accuracy 0.74 Recall 0.74
Late time window	AUC 0.90 Accuracy 0.83 Recall 0.81	AUC 0.90 Accuracy 0.82 Recall 0.81	AUC 0.89 Accuracy 0.82 Recall 0.81	AUC 0.89 Accuracy 0.82 Recall 0.81
Top 10 features (by descending order of feature importance or absolute value of regression coefficient per model)				
Early time window	blood metabolic panel urinalysis opioids myalgia chronic pain macrolides age rheumatoid arthritis benzodiazepines osteoarthritis	age blood metabolic panel macrolides urinalysis chronic pain hypertension rheumatoid arthritis benzodiazepines myalgia headache	blood metabolic panel urinalysis chronic pain opioids benzodiazepines osteoarthritis macrolides rheumatoid arthritis hypertension age	benzodiazepines rheumatoid arthritis cardiology visit pericarditis pulmonary hypertension urinalysis gastroesophageal reflux dermatology visit blood metabolic panel neurology visit
Late time-window	blood metabolic panel myalgia chronic pain urinalysis rheumatoid arthritis dermatosis or dermatitis osteoarthritis opioids anemia macrolides	age blood metabolic panel dermatosis or dermatitis urinalysis hypertension rheumatoid arthritis myalgia Raynaud's syndrome Sjogren's syndrome dermatology visit	blood metabolic panel urinalysis myalgia osteoarthritis chronic pain rheumatoid arthritis dermatosis or dermatitis opioids hypertension anemia	juvenile arthritis systemic vasculitis rheumatoid arthritis autoimmune hepatitis Renal disease, end stage Dermatology visit malignancy, including skin endocarditis Sjogren's syndrome cutaneous lupus

Table 2. Machine learning model results. *AUC: area under the receiver operating characteristic curve; accuracy: weighted arithmetic mean of positive predictive value (PPV) and Inverse PPV (weighted by Bias), where PPV was % true SLE case among those predicted as SLE case; recall: % of true SLE cases that were predicted as SLE case.

each time window: regularized (L1) logistic regression, gradient boosted trees (GBT), XGBoost, and random forest. The models were trained and validated using 5-fold cross-validation in Dataiku DSS 5.0. Model performance was assessed by area under the receiver operating characteristic curve (AUC), accuracy and recall rate.

Results: A total of 13781 incident cases of SLE were identified and matched to the same number of controls. Mean age was 45 (median 47) years, and 87% were female. Table 1 describes the subjects' characteristics: SLE cases had overall higher frequency of health care utilization (HU) than the controls, and generally higher frequency of HU in the late than the early time-window. Based on the same set of 171 candidate features, the top-performing machine learning model in the early and late time-windows was GBT, with AUC 0.82 and 0.90, accuracy 0.72 and 0.83, recall of 0.82 and 0.81, respectively. The other three models performed similarly. Predictors with the highest importance factor included blood metabolic panel, urinalysis, prescriptions for benzodiazepines, opioids and macrolides; and diagnoses of chronic pain, osteoarthritis, rheumatoid arthritis, and hypertension. The top 10 predictors for both windows were very similar (Table 2) though generally higher in frequency of occurrence in the late window (Table 1).

Conclusion: All 4 machine-learning models had good predictive performance, especially using predictors in late time-window. The set of predictors identified in the early window (1.5-3 years pre-index) overlapped substantially with that of the late window (< 1.5 years pre-index), indicating opportunities for earlier diagnosis.

Disclosure: Y. Wang, Janssen R&D, LLC, 1, 2; **K. Lum**, Janssen Data Science, 1, 2; **K. Costenbader**, Glaxo Smith Kline, 5, UpToDate, 7, Lupus Foundation of America, 6, Neutrolis Inc, 5; **G. Wang**, Janssen Data Science, 1, 2; **J. Lofland**, Janssen Market Access, 1; **D. Naessens**, Janssen Market Access, 1, 2; **Y. Zhao**, Janssen Data Science, 1, 2; **K. Davis**, Janssen R&D, LLC, 1, 2; **C. Karyekar**, Janssen Global Services, LLC, 3, Johnson & Johnson, 1, Janssen, 5.

Abstract Number: 0245

Systemic Lupus Erythematosus Phenotype Risk Score Identifies Undiagnosed Cases in a Large Electronic Health Record

April Barnado[1], Robert Carroll[1] and Lee Wheless[1], [1]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogeneous disease with patients often presenting with non-specific symptoms that can cause delays in diagnosis. Phenotype risk scores measure the degree to which a patient's symptoms, as assessed by billing codes, overlap with defined disease criteria. Phenotype risk scores have identified patients with unrecognized Mendelian genetic disorders successfully and may help identify patients earlier with rare diseases. We developed and validated a phenotype risk score for SLE in a large electronic health record (EHR) cohort using billing codes to capture SLE criteria

Methods: We identified 837 SLE cases from a de-identified EHR with over 3 million subjects with decades of follow-up using a previously validated and published algorithm. Subjects were required to have a SLE diagnosis by a rheumatologist. We identified 3,149 age, sex, and race-matched controls with no known autoimmune disease diagnoses. Billing codes that correspond to SLE disease criteria were used in the phenotype risk score (Table 1). The SLE phenotype risk score was the sum of these codes in a given patient weighted by the log inverse prevalence of that code in the entire EHR. Billing codes specifically for SLE (i.e. 710.0 and M32*) were excluded. We compared phenotype risk scores in SLE cases vs. matched controls and evaluated phenotype risk scores in different SLE subgroups. Chart review was conducted on 50 of the controls with the highest SLE phenotype risk scores. We performed logistic regression to estimate the association of SLE case status with phenotype risk score adjusting for demographics. Lastly, we examined phenotype risk scores over time in SLE cases.

Results: SLE cases had a significantly higher SLE phenotype risk score compared to controls (7.2 ± 5.6 vs. 1.7 ± 2.5, $p < 0.001$) (Figure 1). The SLE phenotype risk score was significantly associated with case status after adjusting for age, sex, and race ($p < 0.001$). Of the 50 controls with the highest phenotype risk score, the two controls with the highest score had SLE by ACR SLE and SLICC criteria with an additional 4 patients having incomplete or probable SLE and another 8 having other autoimmune diseases including discoid lupus, Crohn's, and inflammatory arthritis. Comparing subgroups of SLE patients, females and males had similar scores (7.1 ± 5.6 vs. 7.3 ± 5.3, $p = 0.75$). African Americans with SLE had significantly higher scores compared to Caucasians (9.6 ± 6.7 vs. 6.4 ± 5.0, $p < 0.001$). Figure 2 shows trends of SLE phenotype risk scores over time. There was a small cluster of 57 SLE patients who had phenotype risk scores ≥ 50th percentile before their first SLE billing code.

Conclusion: Due to its heterogeneity, SLE can be a difficult disease to diagnose leading to delays in diagnosis and treatment that impact patient morbidity and mortality. We developed a SLE phenotype risk score in a large EHR

Table 1. List of Billing Codes for Systemic Lupus Erythematosus Phenotype Risk Score

Name of Billing Codes*	Weight of Billing Codes**	ICD-9 Codes	ICD-10-CM Codes
Other immunological findings (i.e. positive anti-nuclear antibody)	1.78	279.4, 279.49, 279.8, 279.9, 795.7, 795.79	D89.89, R76.0, R76.8, R76.9
Acquired hemolytic anemia	2.92	283, 283.0, 283.19, 283.9	D59.1, D59.9
Aplastic anemia and pancytopenia	2.16	284, 284.1, 284.19, 284.8, 284.89, 284.9	D60, D60.0, D60.1, D60.8, D60.9, D61.3, D61.81, D61.818, D61.89, D61.9
Anemia of chronic disease	1.90	285.2, 285.21, 285.29	D63.1, D63.8
Coagulation defects	1.56	790.92	D68.4, D68.61, D68.62, D68.8, D68.9
Thrombocytopenia/purpura	1.69	287, 287.2, 287.3, 287.30, 287.31, 287.32, 287.39, 287.4, 287.49, 287.5, 287.8, 287.9	D69, D69.49, D69.2, D69.3, D69.41, D69.49, D69.59, D69.2, D69.3, D69.41, D69.6, D69.8, D69.9
Disorders of white blood cells (i.e. leukopenia)	1.50	288, 288.00, 288.09, 288.4, 288.5, 288.50, 288.51, 288.59, 288.8, 288.9	D70.8, D70.9, D72.810, D72.818, D72.819, D72.89, D72.9, D76.1
Encephalitis, non-infectious	2.95	323.8, 323.81, 323.82, 323.9	G04.81, G04.89, G04.90, G04.91
Pericarditis	2.16	420, 420.0, 420.9, 420.90, 420.91, 420.99, 423.8, 423.9	I30.0, I30.8, I30.9, I31.8, I31.9, I32, M32.12
Pleurisy, pleural effusion	1.51	511, 511.0, 511.8, 511.89, 511.9	J90, J91.8, R09.1
Nephritis	2.15	580*, 581*, 582*, 583*, 587, V13.03	M32.14, M32.15, N00*, N01*, N02*, N03*, N04* N05*, N06*, N08, N15.8, N15.9, N26.9, Z87.441
Renal failure	1.38	584*, 585*,586*, 669.3*, V56*, V45.11, V45.12	N17*, N18*, N19, Z99.2
Abnormal findings on urine examination (i.e. proteinuria)	2.32	791, 791.0, 791.7, 791.9	N06*, R82.8, R82.90, R82.99, R80.0, R80.1, R80.8, R80.9
Rash and other nonspecific skin conditions	1.41	782.1	R21
Disorder of skin and other subcutaneous tissue	1.83	709, 709.8, 709.9, V13.3	L44.8, L44.9, L45, L98.8, L98.9, L99, Z87.2
Alopecia	2.23	704.0, 704.00, 704.8, 704.9	L65.0, L65.8, L65.9, L66.8, L66.9
Symptoms and disorders of the joints	1.35	719.0*, 719.5*, 719.6*, 719.79, 719.8*, 719.9*	M12.0*, M25.4*, M25.6*, M25.8*, M25.9
Pain in joint	0.87	719.4*	M25.5*, M79.64*
Dermatitis due to solar radiation	2.08	692.70, 692.72, 692.74, 692.79, 692.82	L56.8, L56.9, L59.8, L59.9

*These codes most closely aligned with SLE ACR and SLICC disease criteria and were used to create the SLE phenotype risk score. SLE ICD-9 (i.e. 710.0) and ICD-10-CM (i.e. M32.12, M32.14, M32.15) codes were excluded.
**Determined by the prevalence of that particular code in the entire electronic health record.

cohort that identifies missed SLE diagnoses. We propose that phenotype risk scores could serve as a clinical tool, potentially coupled with genetic data, to make earlier and more accurate SLE diagnoses.

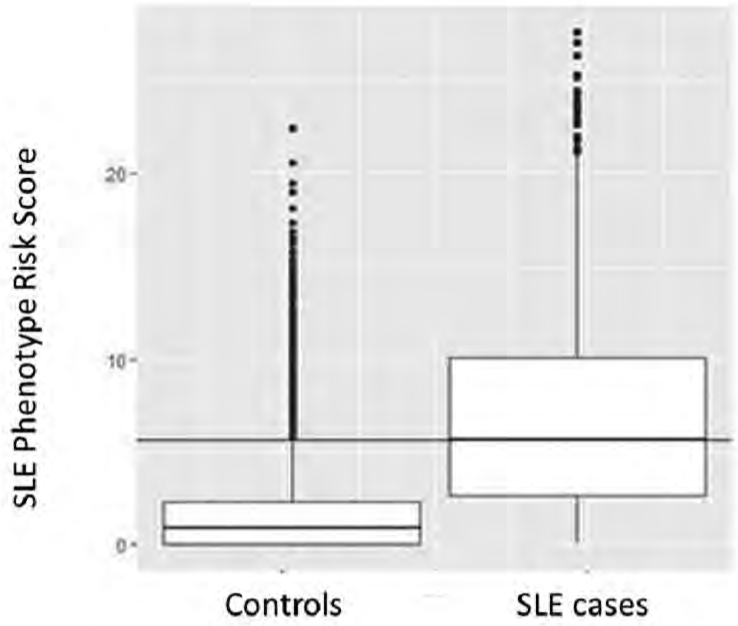


Figure 1. Boxplot of Systemic lupus erythematosus (SLE) phenotype risk scores in SLE cases vs. matched controls. We identified 837 SLE cases, all who had a SLE diagnosis by a rheumatologist. We identified 3,149 age, sex, and race-matched controls with no known autoimmune disease diagnoses. The horizontal line indicates the median SLE phenotype risk score for SLE cases.

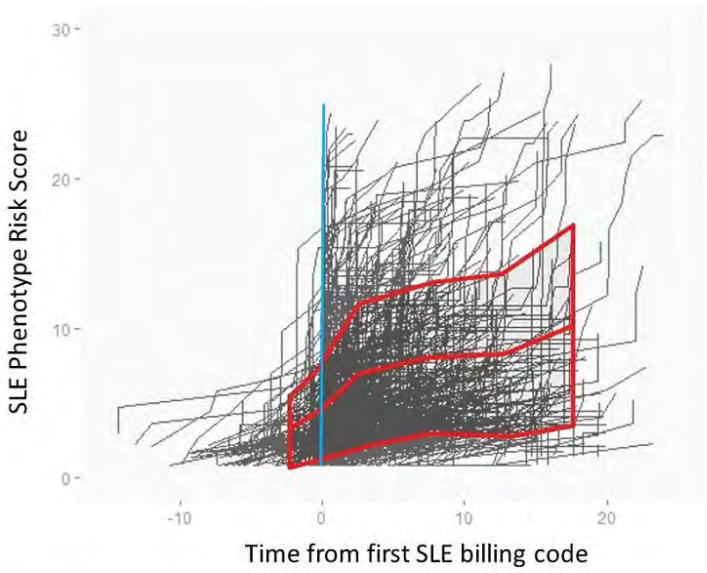


Figure 1. Phenotype risk scores over time. The x axis shows time in years in the electronic health record (EHR). Year 0 designates first SLE code in the EHR and is shown with a vertical blue line. The y axis shows phenotype risk score. The red lines indicate 25th, 50th, and 75th percentiles of the SLE phenotype risk score at each time point.

Disclosure: A. Barnado, Nashville Biosciences, 1; **R. Carroll**, None; **L. Wheless**, None.

Abstract Number: 0246

Extreme Fatigue in Patients with Systemic Lupus Erythematosus and Neuropsychiatric Symptoms

Rory Monahan[1], Rolf Fronczek[1], Jeroen Eikenboom[1], Huub Middelkoop[1], Liesbeth Beaart-van de Voorde[1], Gisela Terwindt[1], Nic van der Wee[1], Thomas Huizinga[1], Margreet Kloppenburg[1] and Margreet Steup-Beekman[1], [1]Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Fatigue is commonly described in chronic illnesses, especially in auto-immune disorders such as systemic lupus erythematosus (SLE). We aim to study the prevalence of fatigue in SLE patients with NP symptoms attributed to major nervous system involvement in SLE and other attributions.

Methods: All patients visiting the tertiary referral center for NPSLE in the LUMC between 2007-2019 with the clinical diagnosis of SLE and age >18 years that signed informed consent were included in this study. Patients underwent a standardized multidisciplinary assessment, including two questionnaires: SF-36 (2007-2019) and multidimensional fatigue index (MFI, 2011-2019). Patients were classified as NPSLE in this study if NP symptoms were attributed to SLE and immunosuppressive or anticoagulant therapy was initiated, otherwise patients were classified as minor/non-NPSLE. The vitality (VT) domain of the SF-36 domain was used to assess fatigue, which generates a score from 0-100, 100 representing the complete absence of fatigue. Patients with a score more than one standard deviation (SD) removed from age-related controls of the Dutch general population were classified as fatigued; patients more than two SD removed were classified as extremely fatigued[1]. The MFI was also assessed, which consists of five sub-domain scores between 0-20, leading to a total score between 0-100, 100 representing the most extreme fatigue. All scores are presented as mean and SD.

	NPSLE *(n = 65)*	**Minor/non-NPSLE** *(n = 167)*
MFI (mean, sd)		
General Fatigue	10.8 (1.8)	11.3 (2.3)
Physical Fatigue	11.4 (2.4)	12.4 (2.2)
Reduced Activity	9.6 (2.9)	10.7 (2.2)
Reduced Motivation	10.7 (2.6)	11.1 (1.9)
Mental Fatigue	9.6 (3.0)	9.9 (2.9)
Total score	51.8 (9.9)	56.2 (9.0)
SF-36 Vitality (mean, sd)	35.9 (20.6)	33.6 (18.6)

Fatigue in patients with NPSLE and minor/non-NPSLE

Results: 373 patients fulfilled the inclusion criteria and SF-36 questionnaires of 335 patients were available (90%). The majority of these patients was female (87%) and 97 were classified as NPSLE (29%). In NPSLE patients, average age was 41 years (SD: 13) and in minor/non-NPSLE the average age was 44 years (SD: 14). The average score of the SF-36 vitality domain was 35 (SD: 21) in NPSLE vs 34 (SD: 19) in minor/non-NPSLE. Overall, 75% of the patients were fatigued and 49% extremely fatigued in NPSLE vs 79% fatigued and 47% extremely fatigued in minor/non-NPSLE.

The MFI questionnaire was available for 230 patients, of which 65 patients were classified as NPSLE (28%). *Table 1* depicts the scores of NPSLE and minor/non-NPSLE patients on the MFI subdomains.

Conclusion: Nearly half of all patients with SLE and NP symptoms are extremely fatigued compared to only 2.5% of the general Dutch population. Extreme fatigue is irrespective of NP attribution to SLE.

1. Aaronson et al. J Clin Epidemiol. 51, No. 11, pp. 1055–1068, 1998

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Abstract Number: 0247

Lupus Low Disease Activity State Achievement Is Important for Reducing Adverse Outcomes in Pregnant Patients with Systemic Lupus Erythematosus

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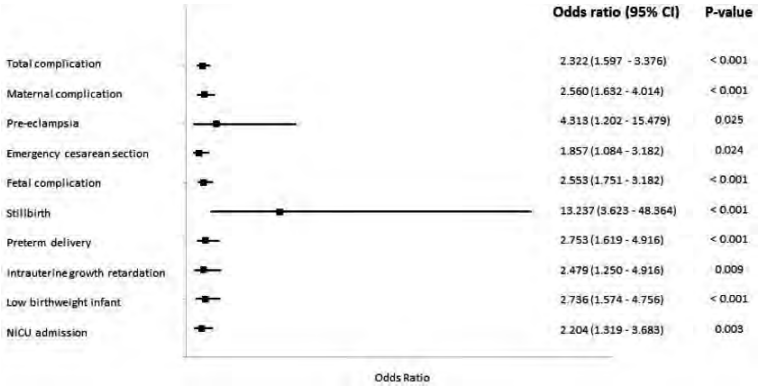
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM



Multivariate analysis of maternal and fetal complications in patients with SLE. Odds ratio (95% confidence interval) of the SLE versus non-SLE population for obstetric outcomes. The odds ratio for obstetric outcomes listed on the left are plotted as dots; lines indicate the 95% confidence intervals (CI). All values were statistically significant ($p < 0.05$).

Variable	SLE (N = 163)	Controls (N = 596)	P-value
Age at diagnosis (years)	26.2 ± 5.7	NA	NA
Maternal age, median (years)	31.9 ± 4.3	31.8 ± 4.1	0.704
Follow-up period (months)	65.8 ± 61.3	NA	NA
Body mass index (kg/m^2)	20.9 ± 3.2	22.3 ± 4.3	0.007*
Comorbidities			
Hypertension, no. (%)	1 (0.6)	15 (2.5)	0.135
Diabetes mellitus, no. (%)	0 (0)	11 (1.8)	0.081
Thyroid disorder, no. (%)	15 (9.2)	65 (10.9)	0.537
Assisted reproductive technology, no. (%)	10 (6.1)	37 (6.2)	0.609
Clinical manifestations			
Oral ulcer, no. (%)	12 (7.4)	NA	NA
Malar rash, no. (%)	31 (19)	NA	NA
Photosensitivity, no. (%)	20 (12.3)	NA	NA
Alopecia, no. (%)	15 (9.2)	NA	NA
Arthritis, no. (%)	34 (20.9)	NA	NA
Nephritis, no. (%)	29 (17.8)	NA	NA
Serositis, no. (%)	2 (1.2)	NA	NA
Laboratory finding			
Leukopenia, no. (%) (<4,000/mm^3)	22 (14)	2 (0)	< 0.001*
Lymphopenia, no. (%) (<1,000/mm^3)	32 (19.6)	27 (0.1)	< 0.001*
Thrombocytopenia, no. (%) (<100,000/mm^3)	19 (11.7)	3 (0)	< 0.001*
Hemoglobin (g/dL)	11.9 ± 1.56	12.1 ± 1.26	0.004*
ESR (mm/h)	24 ± 17.4	23.4 ± 13.4	0.241
Serum creatinine (mg/dL)	0.7 ± 0.15	0.57 ± 0.37	0.969
Immunologic finding			
ANA positivity, no. (%)	162 (99.4)	NA	NA
Anti-ds DNA Ab positivity, no. (%)	56 (34.4)	NA	NA
Anti-Sm Ab positivity, no. (%)	6 (3.7)	NA	NA
APA positivity, no. (%)	30 (18.4)	NA	NA
Low complements (C3 < 90mg/dL or C4 < 10mg/dL), no. (%)	87 (53.4)	NA	NA
Urinalysis			
Proteinuria (mg/day)	660.7 ± 2304.2	53.2 ± 617.9	< 0.001*
Proteinuria >0.5 g/day, no. (%)	22 (13.5)	6 (0)	< 0.001*
SLEDAI-2k, initial	7.20 ± 5.04	NA	NA
SLEPDAI-2k, at pregnancy	3.80 ± 4.57	NA	NA
LLDAS, no. (%)	89 (54.6)	NA	NA
Treatment			
Hydroxychloroquine, no. (%)	110 (67.5)	NA	NA
NSAID, no. (%)	43 (26.4)	14 (0)	< 0.001*
Aspirin, no. (%)	51 (31.3)	3 (0)	< 0.001*
Heparin, no. (%)	15 (9.2)	3 (0)	< 0.001*
Corticosteroid			
Cumulative dose before pregnancy (g prednisone-equivalent)	7.4 ± 12.24	0 (0)	< 0.001*
Total dose 3 months before pregnancy (mg prednisone-equivalent)	230.4 ± 394.7	0 (0)	< 0.001*
Mean dose during pregnancy (mg prednisone-equivalent)	11.2 ± 78.4	0 (0)	< 0.001*
Immunosuppressants no. (%)	45 (27.6)	0 (0)	< 0.001*
Azathioprine, no. (%)	22 (13.5)	0 (0)	< 0.001*
Mycophenolate mofetil, no. (%)	14 (8.6)	0 (0)	< 0.001*
Cyclophosphamide, no. (%)	24 (14.7)	0 (0)	< 0.001*
Cyclosporin, no. (%)	8 (4.9)	0 (0)	< 0.001*
ACE inhibitor or ARB, no. (%)	22 (13.5)	4 (0)	< 0.001*
Vitamin D, no. (%)	60 (36.8)	16 (0)	< 0.001*

General characteristics and treatments of pregnant women with systemic lupus erythematosus

Background/Purpose: This study aimed to examine the frequency and risk factors of complications during pregnancy in women with systemic lupus erythematosus (SLE).

Methods: The medical records of patients with SLE and age-matched controls at Ajou University Hospital were collected. Clinical features and pregnancy complications in women with SLE were compared to those in controls. Multivariate logistic regression analysis was performed to determine the predictors of adverse maternal and fetal outcomes.

Results: We analyzed 163 pregnancies in patients with SLE and 596 pregnancies in the general population; no significant differences regarding demographic characteristics were noted. Lupus patients experienced a higher rate of stillbirth (odds ratio [OR], 13.2), pre-eclampsia (OR, 4.3), preterm labor (OR, 2.6), intrauterine growth retardation (OR, 2.5), admission to neonatal intensive care unit (OR, 2.2) and emergency cesarean section (OR, 1.9) than control group. Multivariate regression analysis revealed that thrombocytopenia, low complement, high proteinuria, high SLE Disease Activity Index (SLEDAI), low Lupus Low Disease Activity State (LLDAS) achievement rate, and high corticosteroid dose were associated with adverse pregnancy outcomes. In the receiver operating characteristic curve analysis, the optimal cut-off value for the cumulative and mean corticosteroid doses were 3,500 mg and 6 mg, respectively.

	Maternal complications					
	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Hemoglobin < 10g/dL	17.7	3.63 – 86.25	< 0.001*	4.38	0.4 – 47.71	0.182
Thrombocytopenia	3.3	1.23 – 8.85	0.024*	2.12	0.46 – 9.61	0.336
C3 < 90mg/dL + C4 < 10mg/dL	4.41	1.9 – 10.26	< 0.001*	1.56	0.48 – 5.03	0.463
Anti dsDNA Ab positivity	2.377	1.12 – 5.03	0.02*	0.86	0.25 – 2.94	0.81
Proteinuria > 0.5g/d	9.82	3.61 – 26.7	< 0.001*	7.25	1.75 – 30.03	0.008*
SLEDAI-2k, at pregnancy > 4	4.61	2.08 – 10.23	< 0.001*	0.7	0.18 – 2.77	0.609
LLDAS	0.09	0.03 – 0.22	< 0.001*	0.18	0.04 – 0.74	0.016*
Cumulative steroid dose after diagnosis > 3500mg	7.81	3.14 – 19.39	< 0.001*	3.99	1.25 – 12.77	0.024*
Mean steroid dose during pregnancy > 6mg/day	6.63	2.95 – 14.89	< 0.001*	1.78	0.53 – 5.94	0.359
History of cyclophosphamide treatment	6.33	2.52 – 15.88	< 0.001*	2.7	0.66 – 11.03	0.176
	Fetal complications					
	Univariate analysis			Multivariate analysis		
	OR	95% CI	P-value	OR	95% CI	P-value
Hemoglobin < 10g/dL	5.91	1.23 – 28.29	0.029*	1.56	0.15 – 16.87	0.71
Thrombocytopenia	7.77	2.16 – 27.89	< 0.001*	18.42	2.09 – 162.63	0.009*
C3 < 90 mg/dL + C4 < 10 mg/dL	4.66	1.93 – 11.24	< 0.001*	4.57	1.46 – 14.33	0.017*
Anti dsDNA Ab positivity	2.53	1.29 – 4.99	0.013*	1	0.36 – 2.784	0.991
Proteinuria > 0.5g/d	3.71	1.37 – 10.09	0.01*	0.94	0.24 – 4.77	0.936
SLEDAI-2k, at pregnancy > 4	9.63	4.06 – 22.8	< 0.001*	2.93	0.75 – 11.5	0.004*
LLDAS	0.14	0.07 – 0.29	< 0.001*	0.21	0.06 – 0.65	0.01*
Mean steroid dose during pregnancy > 6 mg/day	3.59	1.63 – 7.92	0.035*	0.98	0.15 – 1.75	0.281

Potential risk factors of complications in pregnancies with SLE

Conclusion: Pregnant women with SLE have a higher risk of adverse pregnancy outcomes. Pregnancies should be delayed until achieving LLDAS and closely monitored with the lowest possible dose of corticosteroids.

Disclosure: J. Kim, None; **J. Jung**, None; **H. Kim**, None; **C. Suh**, Celltrion, 5.

Abstract Number: 0248

Assessment of Lupus Knowledge Through Creation of the Lupus Knowledge Assessment Test (LKAT)

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
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Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is an inherently complex disease to manage with heterogenous clinical manifestations and complicated medication regimens. The complexity of lupus self-management combined with low health literacy may contribute to poor outcomes. Nationally, over 33% of American adults have low health literacy. The objective of this project was to determine the level of comprehension of SLE specific knowledge amongst patients with SLE and determine whether this was associated with existing validated measures of health literacy and numeracy.

Table 1: Lupus Knowledge Assessment Test (☑ indicates correct answer)

Question	% Correct
(1) My doctor does blood work and urine to check for: ❑ Lupus Activity ❑ Side effects from lupus medications ☑ Both lupus activity and side effects from medication	85%
(2) Plaquenil (hydroxychloroquine) helps prevent lupus flares. ☑ True ❑ False	89%
(3) In lupus patients, fatigue can be caused by which of the following? Check all that apply: ☑ Lupus ☑ Depression ☑ Trouble sleeping (insomnia)	67%
(4) Which of the following UPC lab ratios is **>1000** (mg/g), a sign that may indicate that a patient has active lupus nephritis? ❑ 300 mg/g ❑ 800 mg/g ☑ 2300 mg/g ❑ Not sure	21%

Table 2: Association of Lupus Knowledge Assessment Test, LKAT and Proteinuria Question with Health Literacy and Numeracy Assessments

Health Literacy Measure			LKAT Score mean (sd)	p-value	Nephritis Q	p-value
Self-Reported	Basic Health Literacy Screen (BHLS)	Adequate (n=148)	2.6 (0.9)	0.01*	21% (24/115)	0.09
		Low (n=24)	1.9 (1.1)		0% (0/20)	
	Subjective Numeracy Scale (SNS-3)	Adequate (n=88)	2.7 (0.9)	0.07	26% (18/68)	0.01*
		Low (n=82)	2.4 (0.9)		9% (6/65)	
Objective	Rapid Estimate of Adult Literacy in Medicine (REALM)	Adequate (n=75)	2.7 (0.8)	0.19	30% (25/82)	0.03*
		Low (n=13)	2.4 (0.6)		0% (0/12)	
	Numeracy Understanding in Medicine Instrument, short version (S-NUMI)	Adequate (n=23)	3.1 (0.7)	<0.001	44% (11/25)	0.03*
		Low (n=62)	2.4 (0.8)		20% (13/66)	

Legend:
LKAT = Lupus Knowledge Assessment Test, **average score** from 0-4 (sd)
Nephritis Q = proteinuria question [Question 3 of the LKAT], **%** who answered correctly
BHLS = Basic Health Literacy Screen
SNS3 = Subjective Numeracy Scale 3
REALM = Rapid Estimate of Adult Literacy in Medicine
S-NUMI = Numeracy Understanding in Medicine Instrument, short version

Methods: SLE patients meeting SLICC criteria were recruited from an academic university clinic from March 2019 through January 2020. A four-item questionnaire, the Lupus Knowledge Assessment Test (LKAT, Table 1), was developed and reviewed by six rheumatologists who see patients in a tertiary center lupus clinic. Health literacy was assessed using the self-reported Basic Health Literacy Screen (BHLS) and numeracy by the 3-item Subjective Numeracy Scale (SNS-3). Additionally, we collected objective health literacy assessments in a subset of patients including the Rapid Estimate of Adult Literacy in Medicine (REALM) and the Numeracy Understanding in Medicine Instrument, short form (S-NUMI).

We defined low health literacy as BHLS < 12 and low numeracy as SNS3 ≤ 14. The LKAT and health literacy assessments were administered during routine clinic visits. Additional patient demographics were gathered by survey. Data was analyzed using descriptive statistics.

Results: 225 SLE patients completed the questionnaire, of which 172 had correlating self-reported health literacy assessments and 89 had objective health literacy assessments. 95% of participants were female; 61% were African American. **Table 1** shows the questions comprising the LKAT questionnaire and percentage of correct answers for each question. The majority of patients knew reasons for routine blood and urine monitoring (85%); 67% were able to identify factors contributing to fatigue in SLE. Only 21% were able to answer which urine protein to creatinine (UPC) value was greater than 1000 mg/g correctly (from 300, 800, 2300 mg/g and not sure as choices).

Patients with low health literacy (by BHLS) and low numeracy (by S-NUMI) had lower LKAT scores ($p=0.01$, $p< 0.001$). Those with low health literacy (by REALM) and low numeracy (by SNS3 or S-NUMI) were more likely to miss the proteinuria question ($p \leq 0.03$, **Table 2**).

Conclusion: Patients with lower health literacy and numeracy have less knowledge about SLE, as measured by the LKAT (Lupus Knowledge Assessment Test). Patients had specific deficits recognizing factors contributory to fatigue in SLE and understanding proteinuria; only 21% of patients were able to answer which numerical UPC value is greater than 1000 mg/g correctly. This suggests many patients with low numeracy may have difficulty in functional understanding and interpretation of lab results. Further studies are needed to identify association of decreased lupus knowledge and low health literacy with other health outcomes.

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Abstract Number: 0249

Validation of the SIMPLE Index for Disease Activity of Systemic Lupus Erythematosus in Chinese Patients

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The SIMPLE (SIMple Disease Assessment for People with Lupus Erythematosus) index is a composite numeric tool that captures disease activity from patients' self-assessment with minimal physicians' input. The SIMPLE index consists of 2 components: patient self-reported survey questionnaire (3 items from the lupus symptoms domain from the validated LupusPRO, 10 items from Lupus Impact Tracker [LIT], change in the health status and current glucocorticoids use [and dose]) and two laboratory tests (low complements [C3/C4] and urine protein-creatinine ratio >0.5). The values are put in an equation to derive a number, which is transformed to a 0- to 100-point scale by a formula using weighted scores of the above parameters. The SIMPLE index has been validated in US with good correlation with physicians' assessment of disease activity.

Objective: To validate the SIMPLE index for systemic lupus erythematosus (SLE) disease activity assessment in Chinese patients.

Methods: Adult patients (age ≥18 years) who fulfilled the 2013 SLICC criteria for SLE and were followed in the Rheumatology clinics of Tuen Mun Hospital, Hong Kong were recruited in a cross-sectional study. Participants were invited to complete the SIMPLE questionnaire before seeing doctors on the same day. The two laboratory results were supplemented by research nurses. Physicians, who were blinded to the SIMPLE results, were asked to complete disease activity assessment by the SELENA-SLEDAI and physicians' global assessment (PGA) after consultation. Correlation was made between the SIMPLE score and the SLEDAI/PGA scores by Spearman's rank correlation test. Receiver operating characteristic (ROC) analysis was performed to find the best cut-off SIMPLE score that predicted a clinical SLEDAI score of 1-6 (mild SLE activity) and ≥7 (moderate/severe activity).

Results: 364 SLE patients were studied (94% women; age 45.4±13.4 years; disease duration 13.2±8.0 years). The proportion of patients having a history of neuropsychiatric and renal disease that required immunosuppressive therapies was 9.3% and 56%, respectively. At the time of questionnaire completion, 69 (19%) patients had SLEDAI ≥6 and 192 (53%) had SLEDAI 1-5. The mean SLEDAI was 3.04±2.85 and PGA score was 0.62±0.55. A total of 161 (44%) had SDI score ≥1. The mean SIMPLE index was 26.0±12.9. SIMPLE index correlated significantly with SLEDAI (ρ=0.76; p< 0.001) and PGA score (ρ=0.48; p< 0.001). ROC analysis showed that a SIMPLE index of >27 points best predicted a clinical SLEDAI score of 1-6 (area under the curve [AUC] 0.78[0.73-0.84]; sensitivity 0.75; specificity 0.71), and >36.8 points best predicted a clinical SLEDAI score of ≥7 (AUC 0.87[0.69-1.00]; sensitivity 0.88, specificity 0.85).

Conclusion: SIMPLE shows a good correlation with SELENA-SLEDAI and PGA. It is a simple tool that enables patients to self-report disease activity and communicate with the health care team more efficiently.

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Abstract Number: 0250

Lupus Nephritis and Renal Outcomes in African-Americans: The Accelerating Medicines Partnership Cohort Experience

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The Accelerating Medicines Partnership (AMP) will use multi-omics modalities including single cell RNA sequencing to understand lupus nephritis with the ultimate goal to devise novel and personalized treatment strategies. African-Americans have more lupus nephritis and worse outcomes in terms of end stage renal disease. We report here the clinical findings to date on African-American patients in the AMP cohort.

Methods: We included 118 patients with urine protein-to-creatinine ratio (UPCR) ≥ 1 and biopsy proven class III, IV, V or mixed lupus nephritis at time of enrollment. All patients met revised ACR or SLICC classification criteria. Clinical data were obtained at baseline, 12, 26, and 52 weeks after the renal biopsy. Response status at week 52 was defined as follows. Complete: UPCR ≤ 0.5, normal serum creatinine (sCr) or < 25% increase from baseline if abnormal, and prednisone < 10mg daily; partial: UPCR > 0.5 but ≤ 50% of the baseline value and same sCr and prednisone rules as complete response; no response: UPCR > 50% of baseline value or new abnormal elevation of sCr or ≥ 25% from baseline or prednisone ≥ 10mg daily.

Results: Table 1 shows that African Americans were more likely to have class V lupus nephritis (38% vs 22.5%, p=0.06), were less serologically active (low C3 50% vs 77.5%, p=0.002; anti-dsDNA 63% vs 79%, p=0.006), and were more likely to have elevated serum creatinine (55% vs 30%, p=0.03). Caucasians were older (47 vs 34 years, p=< 0.001) and more likely to be at their first biopsy (64% vs 31%, p=0.04). Table 2 shows the differences based on the first biopsy versus a repeat biopsy. African-Americans were significantly less likely to have a treatment response

	African-American (n=47)	Asian (n=20)	Caucasian (n=11)	Hispanic (n=38)	A-A vs. non A-A p value	A-A vs. Caucasian p value
Female Sex	44 (93.6%)	17 (85%)	10 (90.9%)	35 (92.1%)	*ns*	*ns*
Age (years)	35.1 (10.1)	34.4 (10.2)	46.8 (19.3)	33.6 (10.9)	*ns*	**0.006**
Urine protein/creatinine ratio	3.2 (2.6)	3.3 (2.5)	3.3 (3.0)	3.5 (2.8)	*ns*	*ns*
Abnormal serum creatinine	20 (42.6%)	4 (20%)	2 (18.2%)	10 (27%)	**0.037**	*ns*
Biopsy class						
Membranous	18 (38.3%)	4 (20%)	2 (18.2%)	10 (26.3%)	0.064	*ns*
Mixed	15 (31.9%)	8 (40%)	3 (27.3%)	13 (34.2%)	*ns*	*ns*
Proliferative	14 (29.8%)	8 (40%)	6 (54.5%)	15 (39.5%)	*ns*	*ns*
NIH Chronicity Index	3.5 (2.8)	3.8 (1.9)	1.8 (1.4)	3.2 (2.6)	*ns*	0.09
NIH Activity Index	5.3 (4.2)	7.8 (5.1)	8.0 (4.8)	5.9 (5.1)	*ns*	*ns*
Low C3	22 (50%)	17 (85%)	8 (72.7%)	28 (73.7%)	**0.002**	*ns*
Low C4	25 (56.8%)	10 (50%)	5 (45.5%)	23 (60.5%)	*ns*	*ns*
Anti-dsDNA	29 (63%)	18 (90%)	9 (81.8%)	27 (71.1%)	0.061	*ns*
First biopsy	16 (34%)	4 (20%)	7 (63.6%)	13 (34.2%)	*ns*	0.08
Response						
Complete	9 (19.1%)	5 (25.0%)	6 (54.5%)	11 (28.9%)	*ns*	**0.02**
Partial	10 (21.3%)	7 (35.0%)	1 (9.1%)	7 (18.4%)	*ns*	*ns*
None	28 (59.6%)	8 (40.0%)	4 (36.4%)	20 (52.6%)	*ns*	*ns*

Table 1. Patients characteristics by race / ethnicity. Data are presented as n (%) or mean (SD). Two patients identified as "Other" and are not shown in this Table. P values > 0.1 are indicated as ns.

	Overall (n=118)			First biopsy (n=40)			Repeated biopsy (n=78)		
	African American (n=47)	Non-African American (n=71)	p-value	African American (n=16)	Non-African American (n=24)	p-value	African American (n=31)	Non-African American (n=47)	p-value
Female Sex	44 (93.6%)	63 (88.7%)	*ns*	15 (93.8%)	23 (95.8%)	*ns*	29 (93.5%)	40 (85.1%)	*ns*
Age (years)	35.1 (10.1)	35.8 (13.0)	*ns*	31.3 (9.51)	36.3 (15.3)	*ns*	37.1 (9.99)	35.5 (11.8)	*ns*
Urine protein/creatinine ratio	3.20 (2.55)	3.5 (2.8)	*ns*	2.92 (2.81)	2.99 (2.08)	*ns*	3.34 (2.44)	3.84 (3.13)	*ns*
Abnormal serum creatinine	20 (42.6%)	17 (24.3%)	**0.037**	3 (18.8%)	3 (12.5%)	*ns*	17 (54.8%)	14 (30.4%)	**0.032**
Biopsy class						*ns*			
Membranous	18 (38.3%)	16 (22.5%)	0.064	5 (31.2%)	3 (12.5%)	*ns*	13 (41.9%)	13 (27.7%)	*ns*
Mixed	15 (31.9%)	26 (36.6%)	*ns*	5 (31.2%)	10 (41.7%)	*ns*	10 (32.3%)	16 (34.0%)	*ns*
Proliferative	14 (29.8%)	29 (40.8%)	*ns*	6 (37.5%)	11 (45.8%)	*ns*	8 (25.8%)	18 (38.3%)	*ns*
NIH Chronicity Index	3.5 (2.8)	3.2 (2.3)	*ns*	1.89 (1.96)	1.81 (1.76)	*ns*	4.21 (2.80)	3.87 (2.28)	*ns*
NIH Activity Index	5.3 (4.2)	7.0 (5.1)	*ns*	3.67 (3.12)	7.94 (5.76)	0.052	6.10 (4.53)	6.55 (4.82)	*ns*
Low C3	22 (50%)	55 (77.5%)	**0.002**	7 (50%)	20 (83.3%)	0.061	15 (50%)	35 (74.5%)	**0.028**
Low C4	25 (56.8%)	39 (54.9%)	*ns*	9 (60%)	19 (79.2%)	*ns*	16 (55.2%)	20 (42.6%)	*ns*
Anti-dsDNA	29 (63%)	56 (78.9%)	0.061	10 (66.7%)	21 (87.5%)	*ns*	19 (61.3%)	35 (74.5%)	*ns*
Response status			*ns*			0.018			*ns*
Any response	19 (40.4%)	38 (53.5%)		6 (37.5%)	18 (75%)		13 (41.9%)	20 (42.6%)	
None	28 (59.6%)	33 (46.5%)		10 (62.5%)	6 (25%)		18 (58.1%)	27 (57.4%)	
First biopsy	16 (34%)	24 (33.8%)	*ns*						

Table 2. Comparison of clinicodemographic features between African-American and non African-American patients at first or repeat biopsy. Data are presented as n (%) or mean (SD). P values > 0.1 are indicated as ns.

	Any response vs. no response		Complete vs. non-responders	
African-Americans vs. non African-Americans	OR (95% CI)	p-value	OR (95% CI)	p-value
Model 0: unadjusted	0.2 (0.05, 0.79)	**0.021**	0.14 (0.03, 0.69)	**0.016**
Model 1: adjusted for biopsy class	0.23 (0.06, 0.91)	**0.037**	0.16 (0.03, 0.8)	**0.026**
Model 2: adjusted for activity (n=25)	0.24 (0.04, 1.55)	0.133	0.09 (0.01, 1.11)	0.06
Model 3: adjusted for chronicity (n=25)	0.12 (0.01, 0.94)	**0.044**	0.06 (0.01, 0.75)	**0.029**

Table 3. Multivariable models of response status in African-American and non African-American patients. Only patients at their first biopsy were included.

at the first biopsy. Regardless of first or later biopsy, they were less likely to have low C3. Table 3 shows multi-variate models. African-American patients at their first episode of lupus nephritis were less likely to respond to treatment (37.5% vs 75%, p=0.018) independently of histological features including class, activity and chronicity.

Conclusion: The AMP cohort demonstrates the current unmet clinical need to improve treatment of lupus nephritis in the United States. African-American lupus nephritis is different in terms of ISN class, serologies, first biopsy, and worse in terms of response status even after adjusting for activity and chronicity. Personalized treatments should be developed to improve outcomes in high risk populations such as African-Americans.Table 1. Patients characteristics by race / ethnicity. Data are presented as n (%) or mean (SD). Two patients identified as "Other" and are not shown in this Table. P values > 0.1 are indicated as ns.

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Abstract Number: 0251

Dynamics of Anti-Nuclear Antibodies in a Longitudinal Study of a Large Systemic Lupus Erythematosus Cohort

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations

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Session Time: 9:00AM–11:00AM

Background/Purpose: ANA testing as an approach to diagnosing and classifying SLE, now embedded in the EULAR/ACR Criteria, is more important than ever. Cross-sectional studies indicate that as few as 70% are ANA-positive, although ANA status may change over time. There are limited previous attempts to look at alterations in longitudinal ANA status in newly diagnosed SLE (1). We examined the dynamics of ANA tests in a longitudinal analysis using the SLICC Inception Cohort.

Methods: We evaluated demographic, clinical, and serological data from SLICC patients who fulfilled the 1997 Updated ACR SLE Classification Criteria and were within 15 months of diagnosis at enrolment. We performed two FDA-approved ANA tests: HEp-2 indirect immunofluorescence assay (IFA) and enzyme-linked immunosorbent assay (ELISA) (both from

Table 1. Number of patients with different ANA trajectories using indirect immunofluorescence assay (IFA) and enzyme-linked immunosorbent assay (ELISA)

Trajectory	ANA status at each time point			ANA assay used at each time point			
	Enroll	Year 3	Year 5	IFA only n (%)	ELISA only n (%)	ANA (+) at all three time points on both IFA and ELISA n (%)	ANA (-) at least once on IFA or ELISA n (%)
1	+	+	+	730 (96.2)	658 (86.7)	644 (84.8)	N/A
2	+	+	-	7 (0.9)	30 (4.0)	N/A	32 (4.2)
3	+	-	+	8 (1.1)	25 (3.3)	N/A	27 (3.6)
4	+	-	-	1 (0.1)	20 (2.6)	N/A	20 (2.6)
5	-	+	+	11 (1.4)	8 (1.1)	N/A	13 (1.7)
6	-	+	-	0 (0.0)	7 (0.9)	N/A	8 (1.1)
7	-	-	+	1 (0.1)	1 (0.1)	N/A	3 (0.4)
8	-	-	-	1 (0.1)	10 (1.3)	N/A	12 (1.6)

Abbreviations: ANA, antinuclear antibody; Enroll, enrolment; N/A, not applicable

Inova Diagnostics, San Diego, CA) for each patient at enrolment and follow-up at years 3 and 5, at one central laboratory (Calgary, AB). A positive test was defined as a titer ≥1:80 for IFA and ≥20 units by ELISA. SLE-specific autoantibodies were performed using a commercially available autoantigen array (FIDIS Connective Profile-13, TheraDiag, Paris) in an addressable laser bead immunoassay. Anti-dsDNA positivity and titers were confirmed by chemiluminescent assay (Bio-Flash: Inova Diagnostics). Demographic and clinical characteristics of patients with a negative ANA test at any time point over the 5 years of disease were compared to patients with consistently positive ANA tests.

Results: Overall, 759 patients were included; 88.5% were female and the mean age at diagnosis was 35.2 (SD 13.5) years. There were 8 different ANA trajectories over 5 years; 29 (3.8%) tested negative at least once by ANA IFA and 101 (13.3%) by ELISA (**Table 1**). Compared to patients with a positive ANA at all 3 time points (n=644), those with any negative ANA (either IFA or ELISA, n=115) were diagnosed at an older age (37.9 vs 34.7 years), were more likely to be of white ethnicity (67.8% vs 49.8%), less likely to use steroids at enrolment (60.9% vs 71.0%), less likely to have ever used immunosuppressants/biologics at 5 years (57.4% vs 68.0%) (**Table 2**), and less likely to have other SLE-related antibodies at enrolment and year 5 (**Table 3**). The SLEDAI-2K of patients with a negative ANA (vs those with a persistently positive ANA) was lower (4.2 vs 5.9 at enrolment, 2.0 vs 3.3 at year 5) with less mucocutaneous (28.7% vs 39.0% at enrolment), immunological (38.3% vs 59.5% at enrolment and 31.3% vs 53.4% at year 5), and hematological (3.5% vs 11.8% at enrolment and 2.6% vs 10.1% at year 5) involvement.

Conclusion: Most of the 759 cases (84.8%) in the SLICC inception cohort remained ANA positive on both IFA and ELISA at each time point over the first 5 years of follow-up. The proportion of consistently ANA-positive patients was higher by IFA (96.2%) than ELISA (86.7%). Patients with at least one negative ANA over the first 5 years had features suggestive of milder disease (i.e. lower SLEDAI-2K, less steroid and immunosuppressive use, fewer autoantibodies) compared to patients with persistently positive ANAs, but differences in other disease features, e.g. nephritis and SLICC/ACR Damage Index, were not observed.

Table 2. Comparison of enrolment and year 5 characteristics of ANA (-) patients at least once on indirect immunofluorescence assay or enzyme-linked immunosorbent assay vs. ANA (+) patients at all 3 time points on both assays

	Enrolment			Year 5		
Characteristics	**ANA (-) at least once on IFA or ELISA (n=115)**	**ANA (+) at all three time points on both IFA and ELISA (n=644)**	**Diff. (95%CI)**	**ANA (-) at least once on IFA or ELISA (n=115)**	**ANA (+) at all three time points on both IFA and ELISA (n=644)**	**Diff. (95%CI)**
Mean age of dx (SD), yrs	37.9 (13.5)	34.7 (13.5)	3.1 (0.5, 5.8)			
Mean disease duration (SD), yrs	0.5 (0.3)	0.4 (0.3)	0.04 (-0.03, 0.1)			
Female (%)	102 (88.7)	570 (88.5)	0.2 (-6.1, 6.5)			
White (%)	78 (67.8)	321 (49.8)	18.0 (8.6, 27.4)			
Mean SLICC/ACR Damage, (SD)[1]	0.4 (0.8)	0.3 (0.7)	0.1 (-0.1, 0.2)	0.9 (1.4)	0.8 (1.2)	0.1 (-0.1, 0.4)
Mean Total SLEDAI-2K (SD)	4.2 (4.6)	5.9 (5.6)	-1.7 (-2.8, -0.6)	2.0 (2.9)	3.3 (3.6)	-1.3 (-2.0, -0.6)
Mean Clinical SLEDAI-2K (SD)[2]	3.2 (4.1)	4.1 (4.9)	-0.9 (-1.8, 0.1)	1.2 (2.4)	1.7 (3.0)	-0.6 (-1.2, - 0.003)
Manifestations, (%)[3]						
Neurological	5 (4.4)	18 (2.8)	1.6 (-2.4, 5.5)	0 (0)	7 (1.1)	-1.1 (-1.9, -0.3)[4]
Musculoskeletal	21 (18.3)	124 (19.3)	-1.0 (-8.7, 6.7)	11 (9.6)	48 (7.5)	2.1 (-3.6, 7.9)
Mucocutaneous	33 (28.7)	251 (39.0)	-10.3 (-19.4, -1.2)	16 (13.9)	107 (16.6)	-2.7 (-9.6, 4.2)
Renal	22 (19.1)	148 (23.0)	-3.9 (-11.7, 4)	9 (7.8)	87 (13.5)	-5.7 (-11.3, -0.1)
Serositis	3 (2.6)	31 (4.8)	-2.2 (-5.6, 1.1)	2 (1.7)	2 (0.3)	1.4 (-1, 3.9)
Constitutional	3 (2.6)	27 (4.2)	-1.6 (-4.9, 1.7)	0 (0)	1 (0.2)	-0.2 (-0.5, 0.1)[4]
Immunological	44 (38.3)	383 (59.5)	-21.2 (-30.9, -11.6)	36 (31.3)	344 (53.4)	-22.1 (-31.4, -12.8)
Hematological	4 (3.5)	76 (11.8)	-8.3 (-12.5, -4.1)	3 (2.6)	65 (10.1)	-7.5 (-11.2, -3.8)
Lupus nephritis[5], (%)	32 (27.8)	188 (29.2)	-1.4% (-10.3, 7.5)	37 (32.2)	242 (37.6)	-5.4 (-14.7, 4.9)
Current Medications (%)						
Corticosteroids	70 (60.9)	457 (71.0)	-10.1 (-19.7, -0.5)	59 (51.3)	365 (56.7)	-5.4 (-15.3, 4.5)
Anti-Malarials	80 (69.6)	439 (68.2)	1.4 (-7.7, 10.5)	87 (75.7)	515 (80)	-4.3 (-12.7, 4.1)
Immunosuppressants/ Biologics	39 (33.9)	255 (39.6)	-5.7 (-15.1, 3.8)	55 (47.8)	357 (55.4)	-7.6 (-17.5, 2.3)
Medications Ever Used (%)						
Corticosteroids	85 (73.9)	524 (81.4)	-7.5 (-16, 1.1)	94 (81.7)	565 (87.7)	-6.0 (-13.5, 1.5)
Anti-malarials	88 (76.5)	479 (74.4)	2.1 (-6.3, 10.6)	103 (89.6)	587 (91.1)	-1.6 (-7.6, 4.4)
Immunosuppressants/ Biologics	44 (38.3)	277 (43)	-4.8 (-14.4, 4.9)	66 (57.4)	438 (68.0)	-10.6 (-20.4, -0.9)

Abbreviations: (-) negative; (+) positive; ACR, American College of Rheumatology; ANA, antinuclear antibody; CI, confidence interval; Diff, difference; dx, diagnosis; ELISA, enzyme-linked immunosorbent assay; IFA, indirect immunofluorescence assay; SD, standard deviation; SLEDAI-2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SLICC, Systemic Lupus International Collaborating Clinics; yrs, years.

[1]SDI could only be calculated at enrolment for those patients with disease duration of at least 6 months.

[2]Clinical SLEDAI excluded immunological subscale

[3]Percentages of patients for whom each SLEDAI-2K subscale has a non-zero score.

[4]no patient in the negative group so the variance is likely underestimated

[5] Lupus nephritis was diagnosed by renal biopsy or fulfillment of the renal item on the ACR classification criteria.

Reference

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Table 3. Comparison of enrolment and year 5 autoantibody profile of ANA (-) patients at least once on indirect immunofluorescence assay or enzyme-linked immunosorbent assay vs. ANA (+) patients at all 3 time points on both assays

	Enrolment			Year 5		
Antibodies	ANA (-) at least once on IFA or ELISA (n=115)	ANA (+) at all three time points on both IFA and ELISA (n=644)	Diff. (95%CI)	ANA (-) at least once on IFA or ELISA (n=115)	ANA (+) at all three time points on both IFA and ELISA (n=644)	Diff. (95%CI)
Anti-dsDNA	27 (23.5)	304 (47.2)	-23.7 (-32.4, -15.1)	21 (18.3)	285 (44.3)	-26.0 (-34.0, -18.0)
Anti-Histones	22 (19.1)	263 (40.8)	-21.7 (-29.8, -13.6)	18 (15.7)	191 (29.7)	-14.0 (-21.5, -6.5)
Anti-Ribosomal-P	20 (17.4)	220 (34.2)	-16.8 (-24.6, -8.9)	16 (13.9)	182 (28.3)	-14.3 (-21.6, -7.1)
Anti-Sm	12 (10.4)	187 (29)	-18.6 (-25.2, -12.0)	8 (7.0)	123 (19.1)	-12.1 (-17.7, -6.6)
Anti-U1-RNP	13 (11.3)	237 (36.8)	-25.5 (-32.4, -18.6)	17 (14.8)	199 (30.9)	-16.1 (-23.5, -8.7)
Anti-Ro52/TRIM21	17 (14.8)	300 (46.6)	-31.8 (-39.3, -24.3)	29 (25.2)	293 (45.5)	-20.3 (-29.1, -11.5)
Anti-SS-A/Ro60	22 (19.1)	335 (52)	-32.9 (-41.0, -24.7)	30 (26.1)	328 (50.9)	-24.8 (-33.8, -15.9)
Anti-SS-B/La	10 (8.7)	191 (29.7)	-21.0 (-27.2, -14.7)	12 (10.4)	154 (23.9)	-13.5 (-20.0, -7.0)

Abbreviations: (-) negative; (+) positive; ACR, American College of Rheumatology; ANA, antinuclear antibody; CI, confidence interval; Diff, difference; ELISA, enzyme-linked immunosorbent assay; IFA, indirect immunofluorescence assay; SD, standard deviation

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Abstract Number: 0252

Corticosteroid and Opioid Use Remain High in Systemic Lupus Erythematosus Patients Receiving Biologic Therapy: A Retrospective Claims Database Analysis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is managed by variable combinations of five drug classes: antimalarials, biologics, corticosteroids, non-steroidal anti-inflammatory agents, and immunosuppressants. Opioids are commonly prescribed to SLE patients despite not being effective for the management of long-term musculoskeletal pain.[1] The aim was to describe corticosteroid and opioid use among SLE patients in the United States, and the impact of belimumab initiation on prescribing patterns.

Methods: This retrospective study used MarketScan administrative claims databases to select insured adults, age ≥18, with a diagnosis (International Classification of Diseases (ICD)-9/10 710.0 & M32) of SLE between 1/1/2012 and 5/31/2018 (earliest SLE diagnosis = index date). Patients were followed from index through the earliest of health plan disenrollment or 5/31/2019 (minimum of 12 months). Corticosteroid use was measured in the 12 months following SLE index date. Average daily dose of oral corticosteroids in prednisone equivalents was measured for 12 months after corticosteroid initiation. Opioid use was measured overall, and by strength and length of treatment (chronic use defined as >90 days of supply). Oral corticosteroid and opioid use were compared in the 6 months before and after initiation of belimumab.

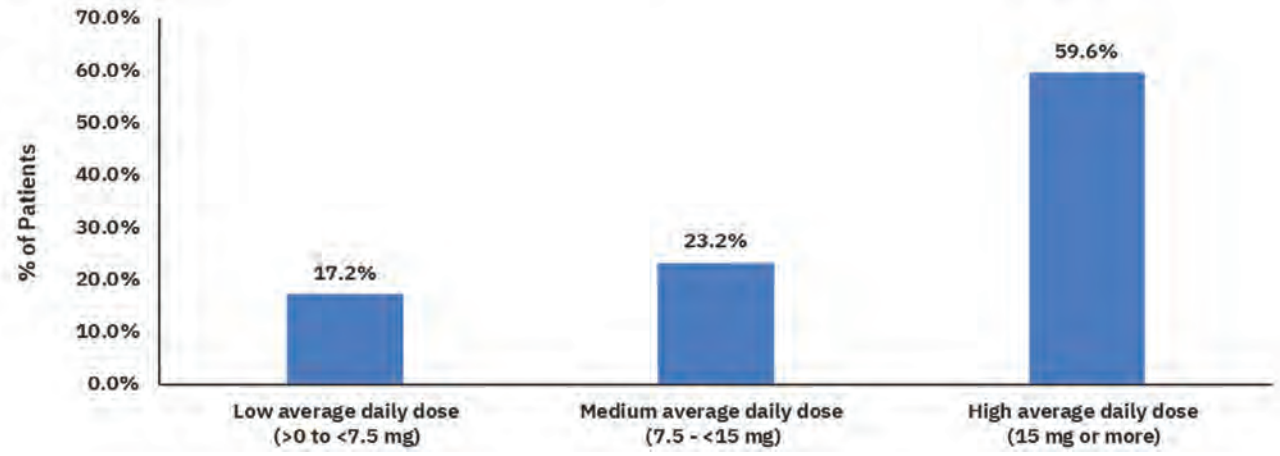
Results: Of 49, 413 SLE patients eligible for analysis, mean [SD] age was 50.1 [14.0] years, 90.2% were female, and average follow-up was 3.6 [1.9] years. 89.8% of patients received any SLE treatment and 68.5% received corticosteroids. The average number of corticosteroid prescriptions was 4.6 [4.1] during 12 months of follow-up. 52.6% of patients had ≥1 claim for an opioid prescription in the 12 months after SLE index and 34.6% were identified as having chronic opioid treatment. Among patients with oral corticosteroid treatment and 12 months of study enrollment post-corticosteroid initiation, the average daily dose for oral corticosteroids was 19.4 [14.2] mg and 59.6% had a high average daily dose of >15 mg (Figure 1). Among 1,710 patients with belimumab treatment and 6 months of study enrollment after the first prescription, use of oral corticosteroids decreased by 9.1% (p=0.001), average daily dose decreased from 14.5 [18.4] mg to 11.9 [18.0] mg (p< 0.001) in the 6 months post initiation as compared to the 6 months prior. However, 48.6% of patients remained on a medium (7.5 mg – < 15 mg) or high dose (≥15 mg). Initiation of belimumab resulted in no change in opioid use (Table 1).

Conclusion: These results suggest that a strikingly high proportion of patients with SLE are treated with corticosteroids to control the disease, and opioid therapy to manage chronic pain. While there was no change in opioid use, corticosteroid use decreased following initiation of belimumab.

Table 1

	Before Belimumab (N = 1,710)		After Belimumab (N = 1,710)		p-Value, pre- vs. post-Belimumab
Patients with an oral steroid prescription (N, %)	**1,242**	**72.6%**	**1,086**	**63.5%**	**0.001**
Number of prescriptions (Mean, SD)	2.3	2.3	2.1	2.3	**<0.001**
Average daily dose (Mean, SD)	14.5	18.4	11.9	18.0	**<0.001**
Low average daily dose (>0 to <7.5 mg; N, %)	210	12.3%	255	14.9%	**0.037**
Medium average daily dose (7.5 - <15 mg; N, %)	389	22.7%	334	19.5%	**0.041**
High average daily dose (15 mg or more; N, %)	643	37.6%	497	29.1%	**<0.001**
Patients with an opioid prescription (N, %)	901	52.7%	861	50.4%	0.341
Weak opioids	356	20.8%	312	18.2%	0.089
Strong opioids	699	40.9%	695	40.6%	0.915
Acute opioid use	538	59.7%	486	56.4%	0.165
Chronic opioid use	363	40.3%	375	43.6%	0.165

Figure 1: Steroid Dosing During the 12 Months Following Initiation of Oral Steroids



Reference

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Disclosure: J. Birt, Eli Lilly and Company, 1, 3; **J. Wu**, Eli Lilly and Company, 1, 3; **K. Griffing**, Eli Lilly and Company, 1, 3; **N. Bello**, Eli Lilly and Company, 1, 3; **N. Princic**, IBM Watson Health, 3; **I. Winer**, None; **C. Lew**, IBM Watson Health, 3; **K. Costenbader**, Glaxo Smith Kline, 5, UpToDate, 7, Lupus Foundation of America, 6, Neutrolis Inc, 5.

Abstract Number: 0253

Serum Albumin as a Predictor of Proteinuria Recovery in Lupus Nephritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Clinical trials and observational studies in lupus nephritis (LN) have shown that proteinuria level at 12 months is the best predictor of long-term renal outcomes (adequate renal function and no dialysis/ transplant), although proteinuria can be a slowly changing parameter with a recovery time often beyond 2 years. Given the high morbidity of LN, an accessible, rapidly responsive biomarker may serve as a useful adjunct to proteinuria in assessing early treatment response.

The aim of this study was to determine if serum albumin can serve as predictor of complete (CPR) and partial proteinuria recovery (PPR) at 6-9 and 18-21 months in LN patients receiving standard treatment.

Methods: We studied all patients followed at the Lupus Clinic from 1990 onwards with baseline and follow-up visits at 6-9 and 18-21 months. Patients were diagnosed with LN based on 24-hour urine proteinuria > 0.5 g/24 hours or a spot urinary protein/creatinine ratio (UPCR) > 0.5 g/g associated with a prednisone start of ≥ 10 mg or a dose escalation of ≥ 5 mg.

CPR was defined as UPCR < 0. 5 g/g. PPR was defined as UPCR < 1.0 g/g (if baseline ≤ 3.0 g/g) or UPCR ≤ 3.0 g/g (if baseline PCR > 3.0 g/g) as defined by Rovin [LUNAR] criteria. We compared this to SLE Disease Activity Index-2000 (SLEDAI-2K) which defines CPR as proteinuria < 0.5g/24 hours and the SLEDAI-2K Responder Index-50 (SLEDAI-2K RI50) which defines PPR as a ≥ 50% decrease in proteinuria from baseline. Complete recovery of serum albumin was defined as ≥ 35 g/L from a baseline of < 30 g/L, with partial recovery defined as ≥ 30 g/L but < 35 g/L from a baseline of < 30 g/L.

Receiver operating characteristic (ROC) curves were generated to test if serum albumin is a predictor of combined proteinuria recovery endpoint (PPR+CPR as defined by Rovin criteria) at 6-9 and 18-21 months. Area under curve (AUC) was analyzed for (a) albumin level at baseline (b) absolute change from baseline to 6-9 and 18-21 months, and (c) percent change between baseline to 6-9 and 18-21 months.

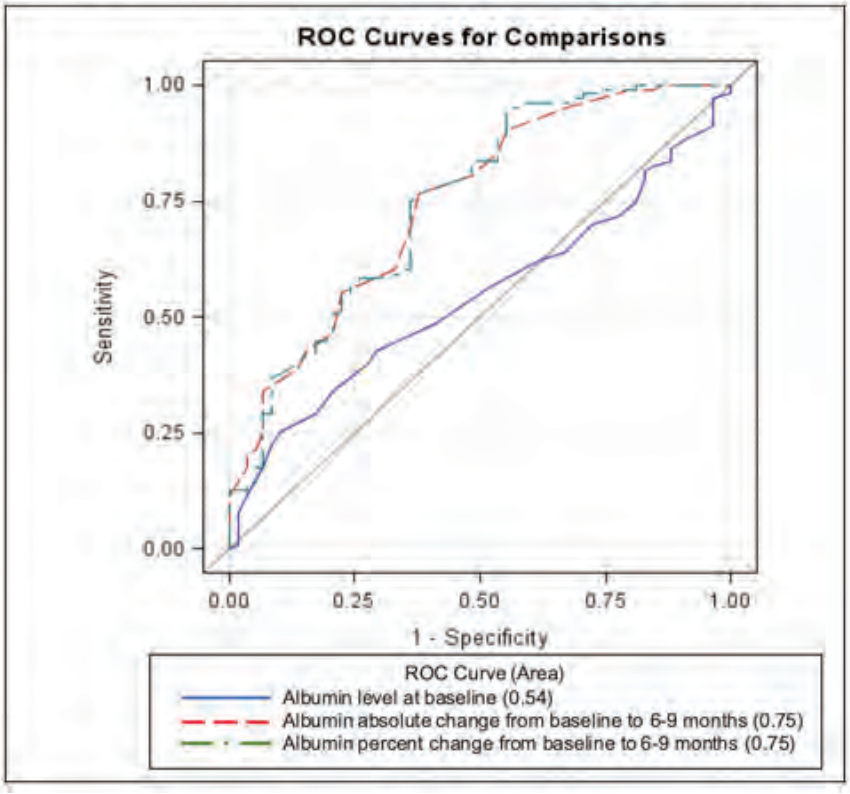
Results: 161 patients with 6-9 month visits (83.9% female) were identified. The mean age and duration of lupus at the start of the study was 34.7 ± 12.6 and 5.2 ± 5.6 years.

At the 6-9 month visit, 22% of patients achieved PPR and 42% of patients achieved CPR (64% combined). Of the 161 patients, 31 (19.3%) had a baseline albumin < 30 g/L. Of the 94 patients with an 18-21 month visit, 17% achieved

Table 1. Percent of patients with proteinuria recovery based on Rovin [LUNAR] and SLEDAI-2K/SLEDAI-2K RI-50 criteria

Definitions of LN recovery	Percent of patients with proteinuria recovery			
	6-9 month visit (n=161)		18-21 month visit (n=94)	
	Rovin [LUNAR]	SLEDAI-2K/ SLEDAI-2K RI-50	Rovin [LUNAR]	SLEDAI-2K/ SLEDAI-2K RI-50
Partial recovery [PPR]	22%	21%	17%	10%
Complete recovery [CPR]	42%	42%	54%	54%
Partial or complete recovery [PPR+CPR]	64%	63%	71%	64%

Figure 1. ROC predicting 6-9 month proteinuria recovery (defined as PPR+CPR by Rovin criteria) using increase of serum albumin from baseline to 6-9 months (n= 161)



PPR and 54% achieved CPR (71% combined). Both Rovin and SLEDAI-2K RI-50 criteria identified similar percentage of responders.

Figure 2. ROC predicting 18-21 month proteinuria recovery (defined as PPR+CPR by Rovin criteria) using increase of serum albumin from baseline to 18-21 months (n= 94)

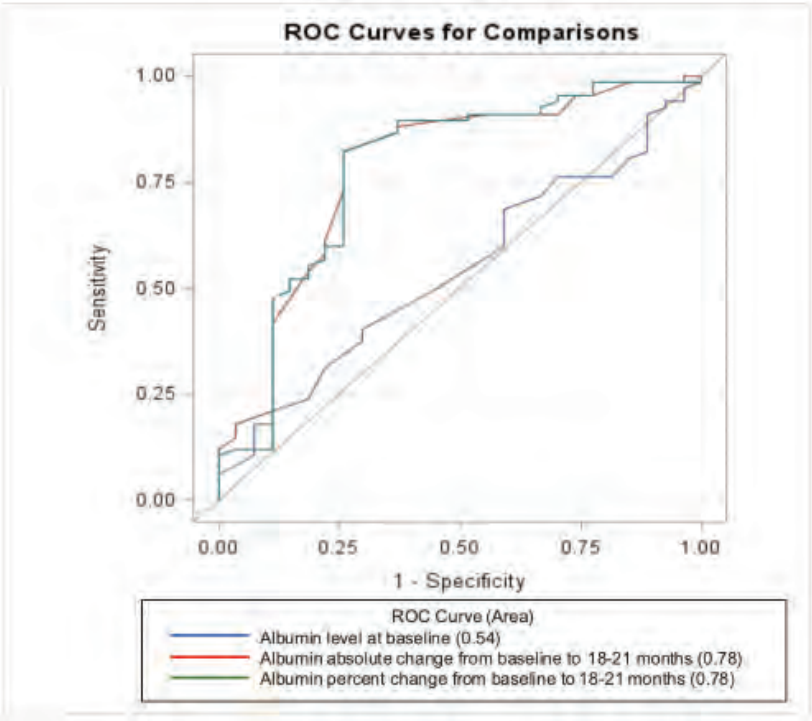


Figure 2. ROC predicting 18-21 month proteinuria recovery (defined as PPR+CPR by Rovin criteria) using increase of serum albumin from baseline to 18-21 months (n= 94)

ROC curves showed serum albumin absolute change (AUC= 0.75) and percent change (AUC=0.75) from baseline to 6-9 months predicted 6-9 month proteinuria recovery. Similarly, serum albumin absolute change (AUC= 0.78) and percent change (AUC=0.78) from baseline to 18-21 months predicted proteinuria recovery at 18-21 months. Serum albumin levels at baseline were not predictive of proteinuria recovery at 6-9 months or 18-21 months (AUC 0.54).

Conclusion: Absolute and percent change in serum albumin from baseline to 6-9 and to 18-21 months is a good predictor of proteinuria recovery. Serum albumin may serve as a readily accessible adjunct to proteinuria in assessing clinical course and treatment response in LN.

Disclosure: T. Tofighi, None; **H. Reich**, None; **J. Su**, None; **Z. Touma**, None.

Abstract Number: 0254

LLDAS (Low Lupus Disease Activity State) and Remission Prevent Damage Accrual in Systemic Lupus Erythematosus (SLE) Patients in a Primarily Mestizo Cohort

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: LLDAS and remission have been proposed as treatment goals for SLE patients. However, their impact on damage prevention in patients from Latin America has been scarcely evaluated. The aim of this study was to determine if achieving LLDAS or remission prevents the occurrence of damage accrual.

Methods: SLE patients from a single center cohort with at least two visits were included. Visits were performed every six months. Remission was defined as a SLEDAI-2k (excluding serology) =0, physician global assessment (PGA)< 0.5, prednisone daily dose≤5 mg/d and immunosuppressive drugs on maintenance dose. LLDAS was defined as a SLEDAI-2k≤4 with no activity in major organ systems, with no new features of lupus disease activity compared to the previous assessment, PGA≤1.0, prednisone daily dose≤7.5 mg/d and immunosuppressive drugs on maintenance dose. Damage accrual was ascertained with the SLICC/ACR damage index (SDI). Univariable and multivariable interval-censored survival regression models were used. Two models were done: 1. Remission vs Not on remission; 2. LLDAS/Remission vs Active. Possible confounders included in the multivariable analyses were gender, age at diagnosis, socioeconomic status, educational level, disease duration, antimalarial use and SDI. Confounders were determined at the same visit than disease activity state but the SDI was assessed at the subsequent visit.

Results: Two hundred and eighty-one patients were included, 260 (92.5%) were female, median age at diagnosis was 34.4 (25^{th}-75^{th} percentile: 27.1-42.4) and a median disease duration at baseline was 7.9 (25^{th}-75^{th} percentile: 3.9-12.8) years. Patients had median of 5 (25^{th}-75^{th} percentile: 2-6) visits and a median follow-up of 3.0 (25^{th}-75^{th} percentile: 1.8-3.5) years. Eighty-three patients (29.5%) increased their SDI during the follow-up. Based on remission, 580 visits (54.6%) were categorized as being on remission, 482 (45.4%) as not on remission. Based on LLDAS, 726 (68.4%) as being on LLDAS and 336 (31.6%) as active. In the analyses of remission, in the multivariable model, being on remission predicted a lower probability of damage (HR=0.586; 95%CI: 0.368-0.933; p=0.024). In the analyses of LLDAS, in the multivariable model, being on LLDAS predicted a lower damage (HR=0.590; 95%CI: 0.358-0.972; p=0.038). These analyses are depicted in Table 1.

	Model 1		Model 2	
Not on remission	Ref.			
Remission	0.586 (0.368-0.933)	0.024		
Active			Ref.	
LLDAS			0.590 (0.358-0.972)	0.038
Age at diagnosis, years	1.009 (0.990-1.028)	0.364	1.012 (0.939-1.032)	0.253
Gender, female	0.626 (0.298-1.313)	0.626	0.662 (0.306-1.436)	0.297
Educational level, years	0.919 (0.824-1.026)	0.131	0.922 (0.826-1.028)	0.143
Socioeconomic status				
Low	Ref.		Ref.	
Medium	0.984 (0.556-1.742)	0.957	0.970 (0.545-1.725)	0.917
High	0.541 (0.199-1.471)	0.229	0.540 (0.199-1.465)	0.226
Disease duration, years	1.048 (1.017 -1.081)	0.004	1.050 (1.017 -1.084)	0.006
Antimalarial use				
Current	Ref.			
Past	0.908 (0.392-2.103)	0.822	0.903 (0.389-2.095)	0.812
Never	0.984 (0.209-4.645)	0.984	0.958 (0.202-4.544)	0.957
SDI	1.073 (0.935-1.230)	0.317	1.080 (0.939-1.032)	0.253

Table 1. Impact of disease activity states on damage accrual. Multivariable models.

Conclusion: LLDAS and Remission predicted less damage accrual. Although Remission is the desirable endpoint on the treatment of lupus, LLDAS also exerts some protective effect and thus could be an alternative endpoint in the management of these patients.

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Abstract Number: 0255

Effect of Removing Haemolytic and Gastrointestinal Activity from the Operational Definition of the Lupus Low Disease Activity State – Implications for Use as a Trial Endpoint

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The Lupus Low Disease Activity State (LLDAS) has recently undergone prospective longitudinal validation in a multinational cohort, demonstrating the association of attaining LLDAS with protection from damage accrual and flare, results that have been replicated in numerous other observational cohorts. Domain 1 of the original LLDAS operational definition captured the absence of significant disease activity by requiring SLEDAI-2K ≤4, the absence of SLEDAI activity in major organs, and also the absence of haemolytic anaemia (HA) and gastrointestinal (GI) activity, manifestations not accounted for in the SLEDAI-2K. The requirement for absence of these infrequent clinical features creates the potential to misclassify patients' LLDAS status, as there is no formal definition of HA and GI activity. This has in turn limited regulatory approval of LLDAS as a clinical trial endpoint. To determine the requirement for capture of HA and GI activity in the LLDAS definition we performed a sensitivity analysis.

Methods: We analysed the prospective LLDAS longitudinal validation dataset. To evaluate whether HA and GI activity were captured by the physician global assessment (PGA) criterion of LLDAS, we compared patients with and without

Table 1 - PGA, stratified by HA and GI activity

	No HA or GI activity	HA &/or GI activity present	p-value
N visits (%)	12,570 (99.21)	100 (0.79)	
PGA, *median [IQR] (range)*	0.4 [0.2, 0.9] (0, 3)	0.7 [0.4, 1.7] (0, 3)	<0.001
PGA>1, *n(%)*	1,939 (15.5%)	34 (34.0%)	<0.001

HA and GI with respect to median PGA and the proportion of patients with PGA >1. The impact on subsequent damage accrual and flare of time-dependent associations of criterion 1 of the LLDAS definition, with and without inclusion of HA and GI activity, were assessed using Cox regression analysis.

Results: Data on 1,707 patients, with 12,689 visits over 2.2 years were analysed. HA and GI activity were recorded in 28 and 73 visits, respectively. The median PGA, and the proportion of patients with PGA >1, were significantly higher in patients with either HA or GI activity (Table 1). Omitting the requirement for absence of HA and GI activity from criterion 1 of the LLDAS definition had no meaningful impact on the protective association with damage accrual in either visit by visit analysis (SLEDAI≤4 ignoring HA&GI: HR 0.55, 95% CI 0.43,0.70, p< 0.001; original definition: 0.55, 95% CI 0.43,0.71, p< 0.001). A similar lack of effect was observed for cumulative time effects of LLDAS (≥50% of time) on reducing damage accrual, and of LLDAS status on disease flare, when the requirement for absence of HA and GI activity was removed.

Conclusion: In data from a large prospective SLE cohort, the PGA adequately captures HA and GI activity. Removing the requirement for 'absence of HA and GI activity' in criterion 1 of the LLDAS definition is without effect on the protective associations of LLDAS attainment. Therefore, the definition of LLDAS does not require specification of HA and GI activity, improving its applicability to datasets where this information is not available and simplifying the use of LLDAS as a clinical trial endpoint. Together with published sensitivity analysis of the SLEDAI-2K and prednisolone dose cut-offs, this completes validation of the LLDAS endpoint.

Disclosure: V. Golder, None; **R. Kandane-Rathnayake**, None; **M. Huq**, None; **W. Louthrenoo**, None; **S. Luo**, None; **Y. Wu**, None; **A. Lateef**, None; **S. Sockalingam**, None; **S. Navarra**, Eli Lilly, 5, 8, Astra-Zeneca, 5, 8, Astellas, 8, Janssen, 5, 8, Novartis, 8, Pfizer, 8, Biogen, 2, 5; **L. Zamora**, None; **L. Hamijoyo**, None; **Y. Katsumata**, None; **M. Harigai**, AbbVie Japan GK, 1, 2, Asahi Kasei Corp., 1, Astellas Pharma Inc., 1, Ayumi Pharmaceutical Co. Ltd., 1, 2, Bristol Myers Squibb Co., Ltd, 1, 2, 3, Chugai Pharmaceutical Co. Ltd., 1, 2, Daiichi-Sankyo, Inc., 1, Eisai Pharmaceutical, 1, 2, Nippon Kayaku Co. Ltd., 1, Mitsubishi Tanabe Pharma Co., 1, Taisho Pharmaceutical Co. Ltd., 1, Takeda Pharmaceutical Co. Ltd., 1, 2, Eli Lilly Japan K.K, 1, Pfizer Japan Inc, 1, AbbVie, 1; **M. Chan**, None; **S. O'Neill**, None; **F. Goldblatt**, None; **C. Lau**, None; **Z. Li**, None; **A. Hoi**, None; **M. Nikpour**, Actelion, 2, 5, 8, GSK, 2, 5, 8, Boehringer Ingelheim, 5; **E. Morand**, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, 5, Merck Serono, 2, 5, Neovacs, 5, Sandoz, 5, Novartis, 8, AbbVie, 5, Amgen, 5, Biogen, 5.

Abstract Number: 0256

Patient Perspective of the Type 1 and 2 SLE Model: A Qualitative Study

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
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Session Time: 9:00AM–11:00AM

Background/Purpose: To better characterize the signs and symptoms of systemic lupus erythematosus (SLE) we have developed a conceptual model to characterize SLE activity into two dimensions: Type 1 SLE consists of inflammatory manifestations like arthritis, nephritis, and rashes; Type 2 SLE includes symptoms of fatigue, myalgia,

mood disturbance, and cognitive dysfunction. The objective of this study was to assess how the Type 1 and 2 conceptual model fits within the disease experience of individuals living with SLE.

Methods: We conducted semi-structured interviews among purposefully selected adult participants meeting SLICC criteria for SLE. High Type 1 symptoms were defined as SLEDAI ≥6, and high Type 2 symptoms were defined as a fibromyalgia severity score ≥12. Participants with a history of high Type 1 and 2 SLE in the prior year were classified as Mixed SLE. All interviews were audio-recorded and transcribed, with subsequent qualitative thematic analysis.

Results: Thirty-seven patients were interviewed (12 with Type 1 SLE, 12 with Type 2 SLE, and 13 with Mixed SLE); 73% were aged ≤55 years, 84% had disease duration ≥5 years, 49% were black or African American, and 35% had a history of nephritis.

Self-Classification: Most patients endorsed some degree of Type 2 symptoms and self-identified as Mixed SLE (n=24), n=8 as Type 2 SLE, and n=5 as Type 1 SLE.

Most Bothersome Symptoms: In every patient sub-group, participants were split on whether Type 1 symptoms (n=16), Type 2 symptoms (n=14), or the combination of both (n=7) were most bothersome. Fatigue, followed by joint pain and rash, were the most bothersome symptoms. The prevalence and severity of these symptoms, as well as their impact on physical and social functioning (fatigue and joint pain) and appearance or self-esteem (rash) made these symptoms most problematic.

Treatment: The type of symptoms the patient wanted to be the focus of therapy was different based on the patient's experience with Type 1 and 2 symptoms: 8/12 Type 1 participants identified Type 1 symptoms, 7/12 Type 2 participants identified Type 2 symptoms, and 7/13 Mixed participants identified both Type 1 & 2 symptoms.

Ignoring Type 2 Symptoms: Participants in all three groups (n=22/31) wanted their rheumatologist to discuss Type 2 symptoms during clinic appointments in order to address their full symptom experience (n=18). Several participants (n=5) stated they would find a new rheumatologist if their Type 2 symptoms were not addressed. Conversely, some participants (n=9) said they accept rheumatologists' emphasis on Type 1 symptoms, primarily because the patient themselves would still bring up their Type 2 symptoms. Three participants felt Type 1 symptoms were more severe and should be addressed first.

Conclusion: The Type 1 and 2 conceptual model appeared to be reflective of most participants' experience, with Type 2 symptoms most frequently reported and both Type 1 and 2 symptoms being bothersome and warranting treatment. Despite their disease classification, almost all participants reported some degree of Type 2 symptoms and most felt discussing and treating these symptoms should be an important component of their lupus care.

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Abstract Number: 0257

Application of Text Mining Methods to Identify Lupus Nephritis from Electronic Health Records

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SESSION INFORMATION
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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
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Background/Purpose: Lupus nephritis (LN) is a frequent complication of SLE and associated with higher morbidity and mortality. Accurate estimates of the prevalence of LN in the population remain limited due to the inability to capture this information through structured data fields such as ICD codes in electronic health records (EHR). We developed a text mining pipeline to extract information on LN and class from clinical notes in the EHR of a large, racially/ethnically diverse university health system.

Methods: Individuals with a single diagnosis code for SLE in the EHR between June 2012 – February 2019 were included. All available clinical notes (including physician ambulatory and hospital progress reports, and biopsy reports)

Table 1. Individuals with a single diagnosis code for SLE from electronic health records of a university health system, June 2012 – February 2019

	N (%) or Mean (SD)
Female	2,425 (87)
Age	46.9 (17.9)
Race	
White	945 (38)
Asian	310 (12)
Black	393 (16)
Other/Mixed Race	560 (22)
Unknown/Declined	300 (12)
Ethnicity	
Non-Hispanic or Non-Latino	2,020 (73)
Hispanic or Latino	526 (19)
Unknown/Declined	236 (8)

Table 2. Comparison of positive and negative annotations of lupus nephritis using text-mining of clinical notes and a published structured data algorithm

	Text-Mining using CLEVER		
Algorithm Using Structured Data*	Negative	Positive	Total
Negative	1,897	631	2,506
Positive	37	217	274
Total	1,934	848	2,782

*Chibnik LB, Massarotti EM, Costenbader KH. Identification and validation of lupus nephritis cases using administrative data. *Lupus* 2010;19(6):741-743.

were extracted and annotated using an open source clinical text-mining tool, the Clinical Event Recognizer (CLEVER). CLEVER is a hybrid information extraction approach that combines rule-based (semantic) and statistical components to annotate and extract information from millions of clinical notes efficiently. A custom-built dictionary that included "lupus nephritis," "class," and various associated terms referring to nephritis was built. Performance of the text-mining tool in identifying LN was assessed by calculating the sensitivity and specificity against a gold-standard subset of SLE patients for whom ACR criteria were assessed through chart review. We also compared our findings to a published algorithm in which LN is identified using structured data only.

Results: We included 2,782 SLE patients; these patients had a total of 614,683 clinical notes. Most patients were female (87%), with a mean age of 46.9 years (± 17.9), and the sample was racially/ethnically diverse (Table 1). A total of 18,354 positive and 9,293 negative mentions of LN were detected using CLEVER. Positive mentions were captured for 848 unique individuals with SLE, indicating that 30% of our SLE population had LN, similar to previously published estimates. When compared to a gold-standard set of chart-reviewed cases (n=152), our text mining tool detected LN with 96% sensitivity and 94% specificity. Compared to a previous algorithm of LN detection based on structured data fields (such as ICD codes) alone, our text-mining pipeline identified 631 additional cases of LN that would have otherwise not been captured (Table 2). Chart review of notes for a random sample of 50 cases from these 631 additional cases indicated that 86% were true positives. Thirty-seven cases that were not tagged by CLEVER, but positive according to the structured data algorithm, were found by chart review to be true negatives, with phrases such as "unclear," "possible," "to be evaluated," or "no evidence." Additionally, of those with LN, CLEVER was able to detect the specific class of LN (I-VI) in 415 (50%) cases.

Conclusion: We developed the first text-mining strategy to extract SLE LN status and class from clinical notes. Additional evaluation on clinical notes from the EHRs of additional institutions is ongoing to examine the generalizability of this algorithm. Further refinement of the pipeline will allow us to determine factors associated with this important disease outcome.

Disclosure: M. Gianfrancesco, None; **S. Tamang**, None; **G. Schmajuk**, None; **J. Yazdany**, Eli Lilly, 5, Astra Zeneca, 5.

Abstract Number: 0258

Using Patient-Reported Outcomes Measures to Classify Patients with Systemic Lupus Erythematous

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SESSION INFORMATION
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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
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Session Time: 9:00AM–11:00AM

Background/Purpose: Because systemic lupus erythematosus (SLE) is a complex and heterogeneous disease, we have developed a conceptual model that divides SLE activity into two dimensions: Type 1 SLE consists of inflamma-

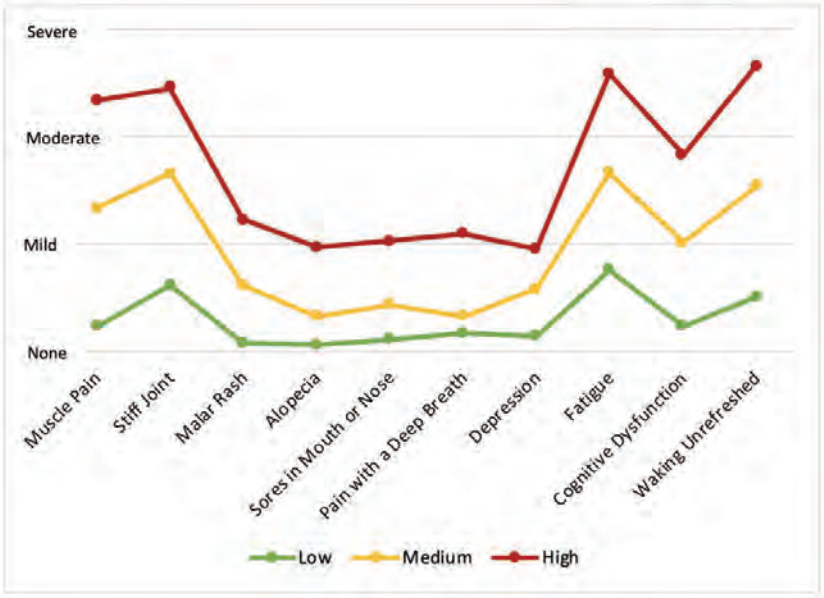

Figure 1. Average patient-reported symptoms by severity class.

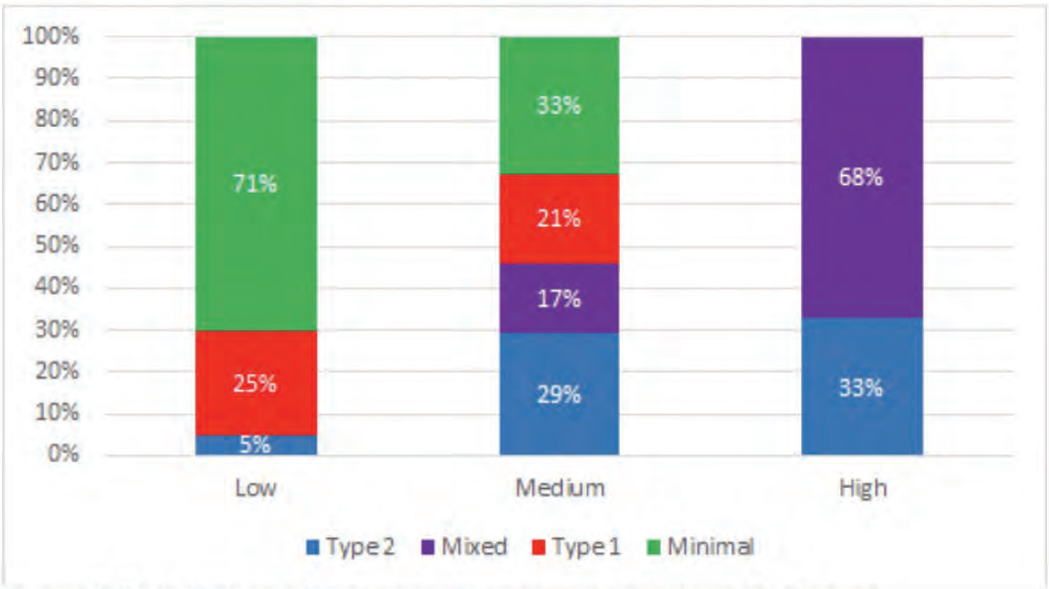

Figure 2. Distribution of Type 1 and 2 groups across severity classes.

tory activity, including arthritis, nephritis, and rashes; Type 2 SLE includes fatigue, myalgia, mood disturbance, and cognitive dysfunction. We theorize that different treatment paradigms may be needed for each dimension because of differences in underlying pathogenesis. In this study, we assessed whether distinct patterns of patient-reported symptoms could provide meaningfully distinguish between Type 1 and Type 2 SLE activity.

Methods: Consecutive SLE patients meeting SLICC criteria in a university lupus clinic registry completed two questionnaires: the Systemic Lupus Activity Questionnaire (SLAQ) and the ACR Fibromyalgia Severity Score (FSS). SLEDAI and physician global assessment (PGA; 0-3) were also recorded. High Type 1 SLE activity was defined as SLEDAI

≥4 (scored without labs), SLEDAI ≥6, active nephritis, or PGA ≥1.5. High Type 2 SLE activity was defined as FSS ≥8. Patients with both high Type 1 and 2 activity were defined as Mixed SLE, and patients with low Type 1 and 2 activity were defined as Minimal SLE.

Latent class analysis (LCA) was used to identify classes of SLE patients based on SLAQ symptoms (muscle pain, stiff joint, malar rash, alopecia, oral or nasal ulcers, chest pain with a deep breath, depression, and a patient global assessment of disease activity) and FSS symptoms (fatigue, cognitive dysfunction, waking unrefreshed, and total areas of widespread pain). Latent classifications were then compared to the clinically defined Type 1 and 2 SLE classification groups to determine if the PRO-derived classes could identify the Type 1/2 disease classifications.

Results: The study included 225 SLE patients. A 3-class solution provided the best fit of the data (entropy >0.90) and classified patients into low (n=85, 38%), medium (n=110, 49%), and high (n=40, 18%) PRO severity classes.

Patients in the low PRO severity class were primarily asymptomatic (Figure 1). While most patients were classified as Minimal SLE, 29% had Type 1 activity, half of whom had active nephritis (Figure 2).

The medium PRO severity class was characterized by mild-moderate fatigue (85%), stiff joints (84%), and waking unrefreshed (70%). Patients in this class were evenly distributed across the *a priori*-defined Type 1 and 2 SLE groups.

The high PRO severity class reported the most severe symptoms, including moderate-severe fatigue (100%), waking unrefreshed (95%), stiff joints (93%), muscle pain (92%), and cognitive dysfunction (65%), as well as high patient-global assessment scores (average: 7.3) and areas of widespread pain (average: 10.4). All patients in this class had active Type 2 SLE, with 33% having inactive and 68% having active Type 1 SLE.

Conclusion: While the LCA was able to classify SLE patients based on the severity of Type 2 SLE activity, this approach was unable to yield a class that was exclusive to Type 1 SLE activity. Ongoing research will explore whether including clinician-reported or laboratory data will better distinguish between these four SLE groups.

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Abstract Number: 0259

Guillain-Barré Syndrome in Systemic Lupus Erythematosus - Results of a Nationwide Analysis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
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Background/Purpose: Guillain-Barré Syndrome (GBS) is a rare autoimmune polyneuropathy well described following viral illness, vaccination, or surgery. Systemic Lupus Erythematosus (SLE) has been associated with several neuropsychiatric syndromes including GBS. This study aims to i) Compare the risk of being hospitalized for GBS in

Table 1. Weighted descriptive characteristics of adult GBS hospitalizations with and without SLE in 2016 and 2017

Hospitalization Characteristics	GBS with SLE (n=130)	GBS without SLE (n=15,975)	P-value
Number of hospitalizations no. (%)	130 (0.8)	15,975 (99.2)	
Females, number (%)	88.5	43.6	<0.001
Age, mean in years	44.7	53.8	0.003
Number (%) hospitalizations by age Age 18-40 years Age 40-60 years Age 60-80 years Age > 80 years	 50 (38.5) 55 (42.3) 25 (19.2) 0 (0)	 3,765 (23.6) 5,520 (34.6) 5,865 (36.7) 825 (5.2)	
Race, Number (%) a) White	70 (56)	10,885 (71.5)	Reference
b) African American	40 (32)	1,360 (8.9)	0.002
c) Hispanic	10 (8)	1,755 (11.5)	0.873
d) Asian or Pacific Islander	5 (4)	560 (3.68)	0.752
e) Native American	0 (0)	85 (0.56)	-
f) Other	0 (0)	580 (3.81)	-

Table 2. Treatment and clinical outcomes of GBS hospitalizations with and without SLE in 2016 and 2017

Variable	GBS with SLE (n=130)	GBS without SLE (n=15,975)	Adjusted odds ratio (AOR)	P value
PLEX, number of patients (%)	35 (26.9%)	1965 (12.3%)	3.06 (1.27-7.35)	0.012*
IVIG, number of patients (%)	15 (11.5)	3,170 (19.8)	0.48 (0.11-2.15)	0.338
			Adjusted mean difference	
LOS, mean days	9.0	11.4	-3.46 (- {6.37-0.54})	0.02*
Total charge, mean USD	140,095	142,977	-1,989 ({-62,285}-58,308)	0.948
In hospital mortality, number (%)	0	215 (1.3%)	-	-

Abbreviations: LOS: Length of stay, C.I: Confidence Interval, PLEX: Plasmapheresis, GBS: Guillain-Barré Syndrome, SLE: Systemic Lupus Erythematosus, USD: United states dollars, *statistically significant

patients with SLE compared to patients without SLE and ii) Compare the characteristics and outcomes of patients primarily admitted for GBS with and without a secondary diagnosis of SLE.

Methods: Data were abstracted from the National Inpatient Sample (NIS) Database. The numbers in the databases are weighted to optimize national estimates. The NIS 2016 and 2017 database was searched for hospitalizations of adult patients with a principal discharge diagnosis of GBS (ICD-10 code G61.0) with and without a concomitant secondary discharge diagnosis of SLE (codes M32, M32.1, M32.10, M32.11, M32.12, M32.13, M32.14, M32.15, M32.19, M32.8, and M32.9). Multivariate logistic regression model was used to calculate the adjusted odds ratio of principal discharge diagnosis of GBS and a secondary diagnosis of SLE. Age, gender and ethnicity distribution, treatment

rates of plasmapheresis and IVIG, outcomes in terms of length of stay (LOS), mortality and total hospital charges were recorded and compared between the two groups. Multivariable logistic and linear regression analyses were used to adjust for confounding variables.

Results: There were over 71 million discharges documented in the combined 2016 and 2017 NIS database. A total of 16,105 hospitalizations were for adults with a principal discharge diagnosis of GBS. Of those, 130 (0.8%) had a secondary diagnosis of SLE and 15,975 (99.2%) did not have a secondary diagnosis of SLE. GBS hospitalizations with a secondary diagnosis of SLE had an adjusted odds ratio (AOR) of 2.06 (95% CI 1.35-3.12, P=0.001) compared to GBS without SLE. Characteristics of GBS patients with and without SLE are displayed in Table 1. The SLE patients were more likely to be female (88.5% vs 43.6%, p< 0.0001) and younger (44.7 vs 53.8, p=0.003). GBS with concomitant SLE was much more common in African American population compared to GBS without SLE (32% vs 8.9%, p 0.002). Total of 2,000 (12.4%) patients received PLEX. GBS with SLE patients were more likely to have received PLEX (26.9% vs 12.3%, AOR: 3.06, 95% CI 1.27-7.35, p=0.012) and had shorter length of stay (9.0 vs 11.4 days, p=0.02) in comparison to GBS patients without SLE. 3,185 (19.8%) patients received IVIG and rates of IVIG treatment were similar between the two groups (11.5% vs 19.8%, AOR: 0.48, 95% CI 0.11-2.15, p=0.338). (Table 2). From all GBS hospitalizations, 215 (1.3%) resulted in inpatient death and all of these occurred in patients without SLE.

Conclusion: Patients with SLE had 2 times the odds of being admitted for GBS compared to non-SLE patients. The inpatient prevalence of GBS in SLE in the United States was 2 cases per 1,000,000 hospitalizations. No mortality was seen in patients with GBS and SLE. Physicians should be aware of this association between SLE and GBS, and should have a high index of suspicion, when SLE patients present with neurologic manifestations suggestive of GBS.

Disclosure: S. Arora, None; **E. Edigin**, None; **A. Manadan**, None.

Abstract Number: 0260

Does Higher Quality of Care in SLE Improve Quality of Life?

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Background/Purpose: Disease activity, damage and quality of life (QOL) are core outcomes in Systemic lupus erythematosus (SLE). ER visits and hospital admissions (non-routine health care utilization, HCU) can be surrogates for higher disease related morbidity. Quality of care (QOC) measured by validated quality measures (QM) is associated with decreased accrual of damage in SLE. We aimed to study the association between high QOC and QOL and non-routine HCU in SLE.

Methods: Data was obtained from 814 participants from Lupus Outcomes Study Sample (LOS), a large observational cohort of individuals with ACR criteria confirmed SLE at University of California, San Francisco. Data on socio-demographics, disease status, medications and healthcare variables were collected through annual interviews beginning in 2003. QOC was available on self-report of 13 QMs. Baseline QOC for this study was measured in Year 10 interviews

Outcome variables	Univariate analysis			Multivariate analysis		
MCID increase in SF 36 domains n (%)			P-value	High QOC	95% CI	P-value
	OR	95% CI		(OR)		
Physical component score (PCS)	1.41	1.05,1.90	0.022	0.981*	0.709, 1.358	0.91
Mental component score (MCS)	1.46	1.09, 1.97	0.012	0.891*	0.643,1.234	0.49
Any ER visit	1.83	1.35,2.47	0.0001	1.073**	0.752, 1.531	0.7
Any hospitalization	1.81	1.33,2.46	0.0002	1.375**	0.945,2.000	0.096

MCID cut off for improvement in PCS: +2.3; MCS: +2.2.

* Multivariate model accounting for baseline disease activity, damage and quality of life, below poverty line and fibromyalgia.

** Multivariate model accounting for demographics, co-morbidities, baseline damage and quality of life, renal involvement, steroid use, disease duration.

Table 1 Relationship between high QOC (at baseline) and (MCID) increase in QOL and non-routine HCU at follow up in Lupus Outcomes Study sample

and follow up QOL and non-routine HCU in Years 11 and 12. We considered a performance on QMs of ≥67% (top quartile) as high QOC. QOL was measured by the Short Form (SF)-36 (Physician Component Summary PCS, mental component summary MCS score). Patient-reported disease activity and damage were measured with the Systemic Lupus Activity Questionnaire (SLAQ) and Brief Index of Lupus Damage (BILD). Chi square and T tests identified co-variates of high QOC at baseline. Univariate and multivariate regression analyses evaluated high QOC at baseline as predictor of minimal clinically important difference (MCID) improvements in SF-36 summary scores, ER visits and hospitalizations at follow up.

Results: Mean age was 53 years, 93% were women. Income below poverty and use of steroids were inversely associated with high QOC while presence of diabetes, lupus nephritis, fibromyalgia, hydroxychloroquine use, a primary care provider, and higher disease activity were directly associated with high QOC. High QOC was associated with worse QOL at baseline (PCS). High QOC at baseline was predictive of MCID based improvements in SF-36 PCS and MCS, and higher non-routine HCU (ER visits and Hospitalizations) at follow up on univariate analyses (Table 1). However, after adjusting for baseline covariates (income below poverty line, disease activity, damage, quality of life, and fibromyalgia), high QOC did not remain an independent predictor of improvement in QOL or non-routine HCU.

Conclusion: High QOC was predictive of subsequent clinically meaningful improvements in QOL. However high QOC did not remain an independent predictor of subsequent QOL or non-routine HCU on adjusting for other baseline covariates, suggesting that the effects may be mediated through one or more of the covariates (such as disease activity).

Disclosure: S. Arora, None; **P. Katz**, None; **J. Yazdany**, Eli Lilly, 1, Astra Zeneca, 1; **J. Block**, None; **E. Yelin**, None; **M. Jolly**, PFIZER, 2, CELGENE, 7, BI, 7, BMS, 7, AURINIA, 7, EVIDERA, 7, LUCIN, 5.

Abstract Number: 0261

Predictors of Future Repeat Renal Biopsies in Patients with Lupus Nephritis and Influence of Repeat Biopsy in Flare Management: A Retrospective Study

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Repeat renal biopsies are considered in patients with Lupus Nephritis (LN) flares or with failure of response to treatment. The influence of repeat renal biopsies on decisions of further management in LN flares

Table 1: Description of Explanatory Variables

Variables	Mean	SD
Gender - Female	84.8%	36.1%
Black	51.5%	50.4%
Hispanic	39.4%	49.2%
Asian	4.5%	21%
White	4.5%	21%
Age at Initial SLE Diagnosis (Years)	33.828	12.766
Nephritis as initial presentation of SLE	51.5%	50.4%
Arthritis as initial presentation of SLE	62.1%	48.9%
Serositis as initial presentation of SLE	22.7%	42.2%
Constitutional symptoms as initial presentation of SLE	12.1%	32.9%
Other symptoms as initial presentation of SLE	40.9%	45.5%
Systolic Blood Pressure at Time of Initial Biopsy (mmHg)	130.774	17.689
Diastolic Blood Pressure (mmHg)	80.667	10.820
Class III LN on Initial Biopsy	19.7%	40.1%
Class IV LN on Initial Biopsy	53.0%	50.0%
Class II LN on Initial Biopsy	10.6%	31.0%
Class V LN on Initial Biopsy	39.4%	49.2%
Number of Glomeruli in Initial Biopsy	16.589	8.446
Activity Index Initial Biopsy	8.650	5.212
Chronicity Index Initial Biopsy	2.620	2.346
Urine Protein Creatinine Ratio (mg/g)	2671.780	2583.590
Hematuria Present at Time of Biopsy	93.5%	24.8%
C4 Level Low at Time of Initial Biopsy	64.5%	48.2%
dsDNA Positive at Time of Initial Biopsy	79%	41%
dsDNA Value at Initial Biopsy (IU/mL)	406.677	394.264
Treatment with MMF	38.5%	49%
Treatment with Cytoxan	24.6%	43.4%
Treatment with Stress Dose Steroids	36.9%	48.6%
Treatment with Prednisone	43.1%	49.9%
Treatment with Imuran	4.6%	21.1%
Treatment with Methotrexate	1.5%	12.4%

Table 1. Description of Explanatory Variables

Table 2: Descriptive Tabulation of Explanatory Variables Used in Logistic Regression Model

Variables	Standard Error	P-Value	Marginal Effect**
Gender – Female*	3.18451	0.02200*	-0.10709
Black	1.57699	0.56600	0.03459
Age at Initial SLE Diagnosis (Years)*	0.00369	0.02970*	-0.00029
Nephritis as initial presentation of SLE	1.80006	0.16480	-0.10704
Systolic Blood Pressure at Time of Initial Biopsy (mmHg)	0.01013	0.47230	-0.00027
Class III LN on Initial Biopsy*	3.97938	0.02980*	-0.96910
Class IV LN on Initial Biopsy	3.08025	0.08020	-0.33087
Number of Glomeruli in Initial Biopsy*	0.00199	0.04210*	-0.00015
Activity Index Initial Biopsy	0.27916	0.12930	0.01557
Chronicity Index Initial Biopsy	0.27886	0.13080	-0.01549
Urine Protein Creatinine Ratio (mg/g)*	0.00023	0.03700*	0.00002
Hematuria Present at Time of Biopsy	1.98342	0.15520	0.10365
C4 Level Low at Time of Initial Biopsy	2.18418	0.12690	-0.12260
Diastolic Blood Pressure (mmHg)	0.01181	0.98550	0.00001
dsDNA Positive at Time of Initial Biopsy	1.98342	0.82140	0.01316
dsDNA Value at Initial Biopsy (IU/mL)	0.00158	0.82130	0.00001
Treatment with MMF	1.30681	0.90670	0.00563

*Statistically Significant
**Average effect of change in the explanatory variables on the change in probability of outcome (repeat renal biopsy)

Table 2. Descriptive Tabulation of Explanatory Variables in Logistic Regression

has been debated. We assessed biochemical, pathological and demographic factors and evaluated their impact on risk of repeat renal biopsies. The role of repeat biopsies in further management of LN flares was also assessed.

Methods: Of the 66 biopsy-proven LN patients identified at two institutions in New York from 2000-2019, 16 were identified to have repeat renal biopsies. LN classes were identified based on the 2003 ISN/RPS Classification and tubulointerstitial pathology was defined by use of NIH LN Activity and Chronicity Indices. A logistic regression model and Wilcoxon signed-rank test were used to analyze the data. P value < 0.05 was deemed to be statistically significant.

Results: Repeat renal biopsies showed that a majority of patients (81%) did not transition between proliferative (class III, IV) and non-proliferative (class II, V) classes of LN. Only 18% of patient's showed a transition from non-proliferative to proliferative class and none of the patient's transitioned from proliferative to non-proliferative class of LN. All patients with a class switch to a proliferative type of LN were seen to have an escalation in immunosuppressive therapy. Escalation of immunosuppressive therapy was seen in 77.7% of patients with LN flares having no class switch between non-proliferative and proliferative. There was a statistically significant progression of chronicity index (mean ± SD) from initial (4.2 ± 2.77) to repeat (7.2 ± 2.58) biopsy, $P = 0.043$.

The logistic regression model had a 96.9% correct prediction, indicating that the model is highly successful in predicting the outcome. The Chi-square probability value was < 0.0005 and McFadden Pseudo R^2 value >0.5, indicating

the model is a good fit. The results indicated that sex, age at SLE diagnosis, quality of first biopsy, urine protein creatinine ratio (UPCR) at time of biopsy or Class III LN on initial biopsy influenced either positively or negatively the probability of a repeat renal biopsy. Females are 10% less likely to have repeat biopsies than their male counterparts, P = 0.022. Patient risk of repeat biopsy increased by 0.29% with every 10 year increase of age at SLE diagnosis, P = 0.029 and reduced with increase in number of glomeruli in initial biopsy, P = 0.042. Identification of Class III LN on initial biopsy decreased risk of repeat by 96.9% when compared to Class II and V (P = 0.03); Class IV LN showed no significant correlation. Higher UPCR at time of biopsy increased the risk of repeat biopsy, P = 0.037.

Conclusion: Demographic, serological and pathological factors can be used to assess likelihood of patients requiring repeat renal biopsies in the future. A majority of patient's did not switch between non-proliferative and proliferative classes of LN on repeat biopsy, however most of these patient's still had an escalation of immunosuppressive therapy. This study shows that there is little relation between repeat renal biopsy findings in LN flares and its use as a tool in determining further management in LN flares

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Disclosure: R. Santana-Flores, None; **A. Ramu**, None; **H. Rajevac**, None; **B. Jim**, None.

Abstract Number: 0262

SLE Pregnancies: C4 as Predictor of Flares and Adverse Pregnancy Outcomes

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Figure 1: comparison of C3 and C4 mean levels between pregnancies with fares *vs* without flares

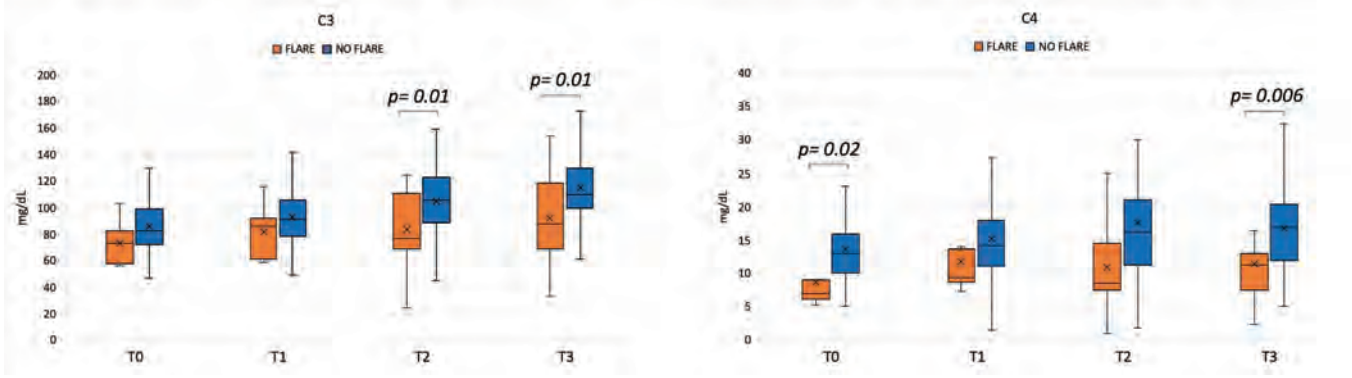

Table 1: C3 and C4 mean levels at T0, T1, T2, T3

C3 (mg/dL)	T0	T1	T2	T3	p T0-T1	p T1-T2	p T2-T3
Flares	73.2 ±16.6	82.2 ± 18.8	83.8 ± 29.2	97.5 ± 37.3	0.04	0.02	0.055
No flares	86.2 ± 20.7	92.9 ± 21.1	105.3 ± 25.4	115.5 ± 25.8	<0.001	<0.001	<0.001
APO	88.7 ± 77.1	97 ± 23.6	98.5 ± 27.1	107.7 ± 36.2	0.4	0.03	0.9
No APO	84.7 ± 19.1	91.4 ± 20.7	104 ± 26	113.8 ± 27.2	<0.001	<0.001	<0.001
C4 (mg/dL)	**T0**	**T1**	**T2**	**T3**	**p T0-T1**	**p T1-T2**	**p T2-T3**
Flares	8.6 ± 4.8	11.8 ± 5.6	10.9 ± 6.33	11.4 ± 6.4	0.01	0.4	0.3
No flares	13.7 ± 5.6	15.1 ± 5.4	17.6 ± 12.4	16.9 ± 6.2	<0.001	0.009	0.4
APO	14.4 ± 8.2	17 ± 7.5	15.9 ± 7.8	14.7 ± 6	0.3	0.3	0.1
No APO	13.2 ± 4.9	14.6 ± 5	17.1 ± 12	16.5 ± 6.5	<0.001	0.01	0.5

Table 2: Frequency of low C3 and low C4 at T0, T1, T2, T3 in pregnancies with and without flare

	Flare	No flare	p
Low C3			
T0	5/7 (71%)	53/121 (44%)	*0.24*
T1	5/9 (56%)	53/122 (43%)	*0.51*
T2	10/11 (91%)	80/121 (66%)	*0.17*
T3	9/11 (82%)	66/109 (61%)	*0.21*
Low C4			
T0	6/7 (86%)	26/122 (21%)	*<0.001*
T1	8/9 (89%)	64/122 (54%)	*0.04*
T2	10/11 (91%)	69/121 (57%)	*0.049*
T3	9/11 (82%)	33/109 (30%)	*0.001*

Background/Purpose: SLE pregnancies have an increased risk of Adverse Pregnancy Outcomes (APO). In clinical practice, low C3 and C4 levels are associated with active disease and, during pregnancy, complement activation products are shown to be associated with APO. Our aim was to analyse C3 and C4 variations during SLE pregnancies, focusing on APO and disease flares.

Methods: Data on SLE pregnancies prospectively-followed by a multidisciplinary team from 1987 to 2017 were analysed. Serum C3 and C4 levels were recorded at preconception visit (T0) and each trimester (T1, T2, T3). Hypocomplementemia was defined according to the normality range calculated in healthy pregnancies by Reggia et al. APO were defined as: early miscarriage (< 10^{th}week), intrauterine fetal death (IFD, >10^{th}week), perinatal death (< 30^{th}day of life), pre-eclampsia (PE), severe preterm birth (< 34^{th}week).

Results: 153 pregnancies in 106 SLE patients were analysed. APO occurred in 25 (16%): 13 early miscarriages, 4 IFD, 3 severe preterm births, 7 PE (hesitated in 2 IFD and 7 live births); 13 flares (2 renal, 4 articular, 6 cutaneous and 1 neurological) were recorded in 11 (7%) pregnancies.

In pregnancies with flares C3 was lower at T2 and T3 as compared with pregnancies without flare while C4 was lower at T0 and T3 (fig 1). There was no difference between pregnancies with and without APO.

Considering the overall pregnancies, C3 progressively increased from T0 to T3, while it remained stable between T2-T3 in the flare group and between T0-T1 and T2-T3 in the APO group (tab1).

In the flare group, C4 increased only between T0-T1 while in the APO group it remained stable throughout pregnancy. Notably, in pregnancies without APO, C4 increased from T0 to T2.

In pregnancies with APO, the variation of C4 levels between T2-T3 trimester was lower than in pregnancies without APO (mean: -2.98 [SD 0.05] vs 0,4 [SD 3.05]; p=0.03).

The frequency of low C4 was higher in pregnancies with flare at T0 and at each trimester as compared with pregnancies without flares (tab2).

Conclusion: Low C4 at pre-conceptional visit seems to predict flares during pregnancy. Lower increase of C4 levels between the 2nd and the 3rdtrimester could predict APO.

Disclosure: F. Crisafulli, None; **L. Andreoli**, None; **M. Filippini**, None; **M. Fredi**, None; **M. Gerardi**, None; **R. Gorla**, None; **M. Lazzaroni**, None; **D. Lini**, None; **C. Nalli**, None; **M. Taglietti**, None; **A. Lojacono**, None; **S. Zatti**, None; **C. Zanardini**, None; **F. Franceschini**, None; **A. Tincani**, None.

Abstract Number: 0263

Factors Associated with Disease Activity Remission and Recurrence in Cutaneous Lupus Erythematosus

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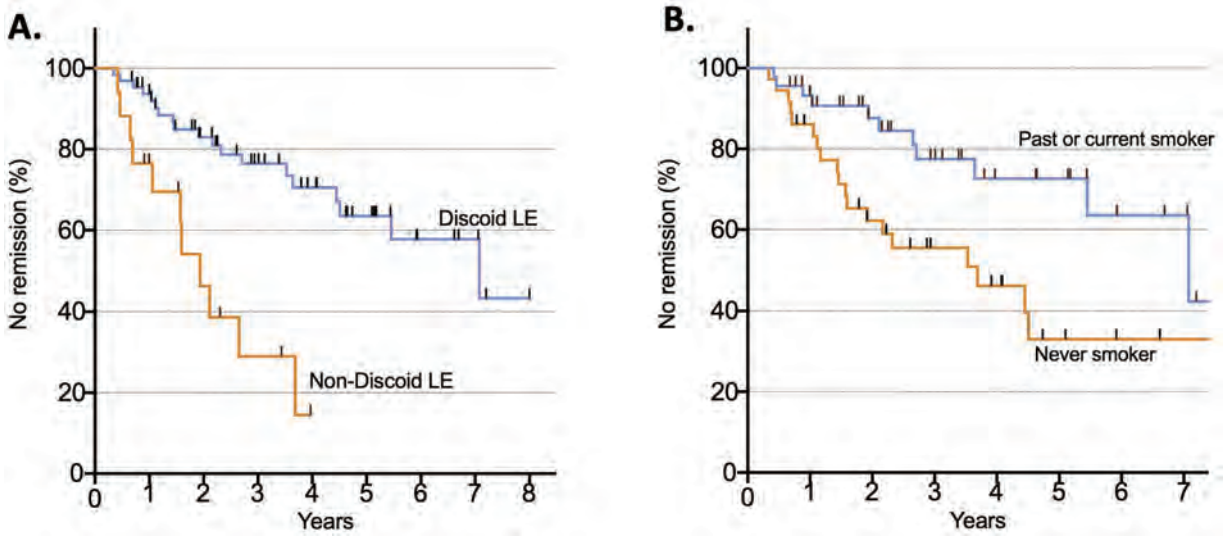
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cutaneous lupus erythematosus (CLE) is a photosensitive skin disorder that can occur with systemic lupus erythematosus. As CLE often fluctuates in disease activity, little is known about the rates of disease remission and recurrence in patients with CLE. In this retrospective study, we assessed the rates of remission and recurrence in a longitudinal cohort study of 97 CLE patients, and identified clinical factors associated with each of these outcomes.

Methods: Inclusion criteria included CLE patients with at least three study visits spanning at least six months. The primary outcomes were remission and recurrence of disease activity. The secondary outcomes were time to remission from the baseline visit, and time to recurrence from documented remission. Disease remission was defined as reaching Cutaneous Lupus Erythematosus Activity and Severity Index activity (CLASI-A) equal to 0. Disease recurrence was defined as having a CLASI-A≥1 after remission. Univariate and multivariable analyses were performed to identify clinical and demographic risk factors associated with disease remission and recurrence. Time to remission and recurrence of activity was calculated by survival curve analyses. Significant variables associated with disease remission based on survival curve analyses were then used to perform a Cox proportional hazards model to identify variables that are predictive of shorter time to remission.

Results: 46 patients (48%) reached remission of CLE activity. Median time to remission was 5.45 years from the initial visit. Patients who achieved remission less likely to have discoid lupus erythematosus (DLE) (OR:0.20 (95% CI: 0.05-0.70), p=0.01) and more likely to have milder baseline disease activity (OR:1.75 (1.30-2.38), p< 0.001). Cox proportional hazards regression model showed that the absence of DLE (HR:4.20 (1.98-8.92) and lifetime non-smoker history (HR:2.57 (1.22-5.43)) were predictors of shorter time to remission (**Figure 1**). 29 patients (63%) of participants experienced disease recurrence within a median of 2.1 years from their remission date. Univariate analyses showed patients with recurrence of CLE activity had a longer disease duration prior to their baseline visit (p=0.002), and were more likely to have DLE (72% v. 29%, p=0.005), but were not significant in the multivariable analyses.



Conclusion: We found that CLE patients with mild baseline disease activity and do not have DLE are more likely to attain disease remission. The presence of discoid lesions and positive smoking history are associated with longer time to remission on standard-of care therapies. These findings can be helpful for clinicians to guide CLE patients on their potential disease course.

Factors associated with remission of disease activity in patients with cutaneous lupus. Patients without discoid rash (A) (HR:4.20 (1.98-8.92) and without a smoking history (HR:2.57 (1.22-5.43) (B) have a significantly shorter time to disease remission.

Disclosure: S. Florez-Pollack, None; **S. Rizvi**, None; **B. Chong**, Viela Bio, 5, Beacon Bioscience, 5, Daavlin Corporation, 2; **L. Hynan**, None.

Abstract Number: 0264

Prevalence and Risk Factors Associated with Isolated Neutropenia in Outpatients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Leukopenia in SLE is defined as leukocyte count below 4,000/mm3 on two or more occasions according to the ACR criteria and may include a combination of lymphopenia and neutropenia or either of these alone. Neutropenia may be mild/moderate or severe and may be associated with increased susceptibility to infection. Our objective was to determine the prevalence and factors associated with isolated neutropenia in outpatients with SLE.

Methods: Retrospective analysis of prospectively collected data. Setting: Patients in our cohort are followed regularly at 2-6 months' intervals according to a standardized research protocol which captures demographic, clinical, laboratory and therapeutic variables along with the major co-morbidities. All data are entered and stored in an electronic database. Neutropenia was defined as absolute neutrophil count (ANC) below 1,500/mm3. Mild/moderate neutropenia was defined as neutropenia ≥ 1000/mm3 and < 1500 /mm3) and severe neutropenia was a neutrophil count < 1000 / mm3. Patients with isolated neutropenia on at least 2 consecutive visits with gap between visits of ≤ 24 months were identified. The baseline characteristics of the patients were compared between patients who experienced isolated neutropenia and those with combined neutropenia and lymphopenia. The percent of infections and the rate of infection in the 2 groups was determined. Mean with standard deviation and median with interquartile ranges were used to describe continuous variables, counts with percentages were use to describe categorical variables, then variables were compared by Student's t-test or Chi-Square test between groups.

Results: Of 2045 patients in the database, 170 (8.3%) were found to have neutropenia on 2 consecutive visits (visit gap ≤24 months) of whom, 30(1.4%) had severe neutropenia and the rest was mild to moderate. Isolated neutropenia was found in 35(1.9%) patients, 29 (82.9%) with mild moderate and 6 (17.1%) with severe neutropenia. Patients with

Table 1. Characteristics of patients with neutropenia.

VARIABLE	VALUE	Isolated Neutropenia	with Lymphopenia	p value
		N=35	N=135	
By neutropenia severity	Severe	6 (17.1%)	24 (17.8%)	0.93
	Mild/Moderate	29 (82.9%)	111 (82.2%)	
Age at index date	Mean ± SD	38.5 ± 12.1	38.7 ± 12.7	0.913
Disease duration in years	Mean ± SD	8.8 ± 8.6	10.4 ± 8.9	0.33
Female Gender	Yes (%)	32 (91.4%)	121 (89.6%)	0.752
Race/Ethnicity	Black	19 (54.3%)	45 (33.3%)	0.135
	Caucasian	11 (31.4%)	64 (47.4%)	
	Chinese	1 (2.9%)	9 (6.7%)	
	Others	4 (11.4%)	17 (12.6%)	
Black ethnicity	Yes (%)	19 (54.3%)	45 (33.3%)	0.023
SLEDAI-2K Score	Mean ± SD	4.0 ± 3.8	5.2 ± 4.5	0.169
low COM or dsDNA+	Yes (%)	23 (65.7%)	91 (67.4%)	0.849
Azathioprine	Yes (%)	3 (8.6%)	37 (27.4%)	0.019
Cyclophophamide	Yes (%)	0 (0.0%)	0 (0.0%)	N/A
Methotrexate	Yes (%)	0 (0.0%)	7 (5.2%)	0.169
Mycophenolate	Yes (%)	7 (20.0%)	21 (15.6%)	0.528
Infection	Yes (%)	3 (8.6%)	12 (8.9%)	0.953
Bacterial infection	Yes (%)	1 (2.9%)	5 (3.7%)	0.809
Viral infection	Yes (%)	2 (5.7%)	6 (4.4%)	0.752

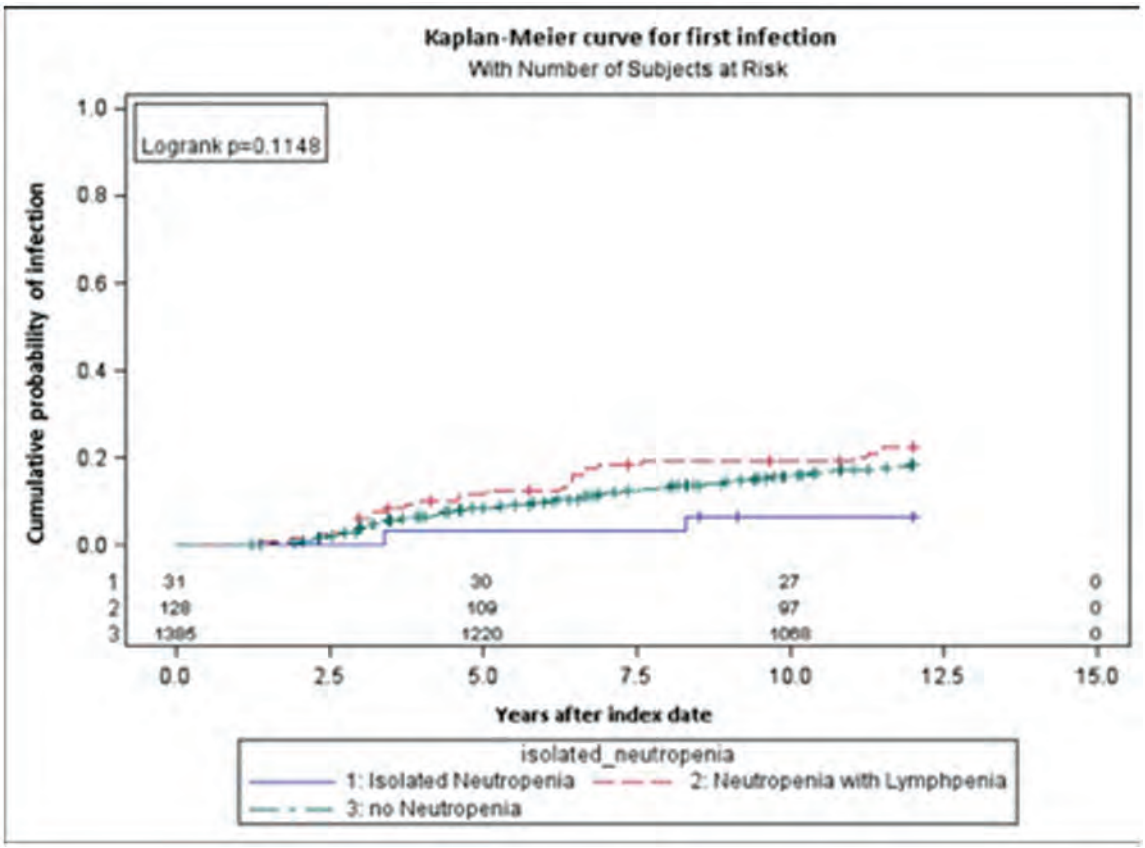

Figure 1. Kaplan Meier curve for first infection.

isolated neutropenia and neutropenia with lymphopenia were similar except for Black ethnicity which was more common in isolated neutropenia and more patients taking azathioprine had neutropenia/lymphopenia (Table 1)

Infections occurred in 17,6% with no neutropenia, 6.5% with isolated neutropenia and 21.9% with neutropenia/lymphopenia**.** Kaplan Meier survival curves showed higher cumulative incidence of infection with no neutropenia and neutropenia/lymphopenia likely due to low numbers (Fig 1)

Conclusion: Isolated neutropenia is not prevalent in SLE patients in general but is more common in Blacks. Risk of infection didn't increase in isolated neutropenia group compared to combined leucopenia and SLE patients without neutropenia.

Disclosure: N. Alhammadi, None; **M. Urowitz**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5.

Abstract Number: 0265

Evaluation of the Lupus Foundation of America-Rapid Evaluation of Activity in Lupus as a Measure of Systemic Lupus Erythematosus (SLE) Disease Activity from the Clinician and the Patient Perspective: Experience from an Italian Cohort

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Multiple indices are available to measure disease activity in SLE patients, but are often considered too complex and time consuming for use in routine clinical practice. The Lupus Foundation of America-Rapid Evaluation of Activity in Lupus (LFA-REAL)[1] is a simplified assessment which provides multiple anchored visual analog scales (range 0–100 mm) for individual symptoms, the sum of individual scores derives an overall disease activity assessment. Moreover, it includes both a clinician- and a patient-reported outcome component for tandem assessments of disease activity. The aim of this study was to analyze the performance of the LFA-REAL as an SLE disease activity measure and to compare it with other clinician- and patient-reported outcome measures in a single-center Italian cohort.

Methods: This is a cross-sectional study that enrolled SLE patients (diagnosed based on 1997 ACR criteria). Disease activity was evaluated using the SELENA-SLEDAI score and organ damage using the SLICC/DI. During the visit, both the clinician and the patient completed the LFA-REAL for the assessment of disease activity. Moreover, each patient completed the following patient reported outcome measures (PROs): SLAQ, SF-36, FACIT-Fatigue, LIT. We evaluated the correlation between clinician LFA-REAL and SELENA-SLEDAI and between patient LFA-REAL and the PROs. ROC curve analysis was applied to compare LFA-REAL with the definition of active disease (SELENA-SLEDAI >4) and low disease activity state (LLDAS)[2].

Results: We enrolled 110 consecutive adult SLE patients (90.9% female, 97.3% Caucasian, mean age 45.06±11.8 years, median disease duration 14 years (IQR 7-21)). Median SELENA-SLEDAI at enrollment was 2 (IQR 0-3). Baseline characteristics of the cohort are summarized in Table 1. The mean clinician total LFA-REAL was 15±27.7 mm, while the mean patient total LFA-REAL was 127.3±114.0 mm; clinician and patient LFA-REAL were significantly correlated ($r= 0.36$, $p< 0.001$). We found a moderate correlation between clinician LFA-REAL and SELENA-SLEDAI ($r=0.31$, $p< 0.001$), while patient LFA-REAL was strongly associated with the SLAQ score ($r= 0.88$, $p< 0.0001$) and with the scores of all other PROs, as reported in Table 2. Clinician LFA-REAL was highly accurate in defining active disease (SELENA-SLEDAI >4) by ROC analysis (area under the curve 0.929). A clinician LFA-REAL of at least 33 mm demonstrated the optimal trade-off of sensitivity (83.33%) and specificity (81.73%) in detecting active disease. Conversely, we found that clinician LFA-REAL performed less well against the definition of LLDAS (area under the curve 0.690).

Table 1. Baseline characteristics of the cohort.

Table 1. Baseline characteristics of the cohort.

N. of patients	110
Mean age (years)	45.1±11.8
Median disease duration (IQR)	14 (7-21)
Median SELENA-SLEDAI (IQR)	2 (0-3)
SLICC-DI>0 (% of patients)	50/110 (45.4%)
Median SLICC-DI among patients with SLICC-DI>0 (IQR)	1 (1-3)
Active lupus arthritis (% of patients)	10/110 (9.1%)
Active muco-cutaneous lupus (% of patients)	4/110 (3.6%)
Active lupus nephritis (% of patients)	4/110 (3.6%)
Active hematologic manifestations (% of patients)	9/110 (8.2%)
Active neuropsychiatric lupus (% of patients)	1/110 (0.9%)
Ongoing GC therapy (% of patients)	50/110 (45.4%)
Mean GC daily dose (mg of prednisone)	1.7±2.7
Ongoing conventional immunosuppressants (% of patients)	42/110 (38.2%)
HCQ therapy (% of patients)	88/110 (80%)
Ongoing biologic DMARDs* (% of patients)	16/110 (14.5%)
Fibromyalgia (% of patients)	14/110 (12.7%)

*Disease Modifying Anti-Rheumatic Drugs

Table 2. Correlation between patient LFA-REAL and PROs.

Table 2. Correlation between patient LFA-REAL and PROs.

SLAQ	r= 0.886 p<0.0001
FACIT-Fatigue	r= -0.817 p< 0.0001
LIT	r= 0.871 p< 0.0001
SF-36 PCS	r= -0.753 p< 0.0001
SF-36 MCS	r= -0.654 p< 0.0001

Conclusion: In our SLE cohort, clinician LFA-REAL demonstrated a good correlation with SELENA-SLEDAI and patient LFA-REAL showed strong correlations with multiple PROs, including the SLAQ score. Therefore, the LFA-REAL may be a valuable simplified screening tool to rapidly identify active patients in routine clinical practice.

[1]Askanase A et al., Lupus Sci Med. 2015. PMID: 25861457; [2] Franklyn K et al., Ann Rheum Dis 2016. PMID 26458737.

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Abstract Number: 0266

The Correlation Between Pregnancy, Disease Activity and Adverse Pregnancy Outcomesin Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) can present with acute disease flares/exacerbations during pregnancy and postpartum period[1]. These flares can cause adverse pregnancy outcomes (APO).

In this study, our pregnant SLE cohort, which was under medical surveillance of both our Rheumatology and Gynecology and Obstetrics departments was analyzed. We intended to determine the effects of pregnancy on disease activity and the correlation between disease flares and adverse pregnancy outcomes.

Methods: 168 pregnancy data involving 136 patients with SLE meeting the ACR criteria were examined. Cumulative clinical, laboratory and serological parameters were described and disease activity and flares were calculated using SLEDAI-2K disease activity index during preconceptional six month period, during all trimesters of pregnancy, and during postpartum six month period. Patients with low lupus disease activity scores (LLDAS) during each of these periods were identified. Fetal/neonatal death, premature birth due to preeclampsia, eclampsia or HELLP syndrome, neonates small for gestational age were determined as adverse pregnancy outcomes. Relationship of APO with disease activity was studied and patients with APO were compared to patients without APO.

Results: Mean SLEDAI-2K scores was 1.3±2.2 (0-16) during preconceptional six month period, 1.3±2.6 (0-16) during conception period, 1.7±3.2 (0-22) during first trimester, 1.4±2.7 (0-16) during second trimester, 1.5±3.3 (0-20) during third trimester and 3.5±5.4 (0-26) during postpartum six month period. Mean postpartum six month period SLEDAI-2K score was higher compared to the mean pregnancy SLEDAI-2K score ($p< 0.05$). LLDAS was sustained in 79% of all pregnancies. 19% of pregnancies resulted in flares. 42% of these flares were severe and 58% were mild or moderate. 49% of severe flares occurred during the postpartum six month period and this percentage was significantly higher compared to each trimester ($p< 0.05$). Most of the flares during pregnancy and postpartum period had mucocutaneous (37%), renal(35%) and hematological(25%) involvement.

APO was observed in 34% of pregnancies (n=57). APO (+) group was characterized by significantly longer disease duration and higher disease activity in all periods compared to APO (-) group (142±70 vs 170±88 months, $p< 0.05$). In APO (-) group, the proportion of patients with severe disease activity during all pregnancy periods and postpartum period was significantly low (%18 vs 35, $p< 0.05$), while the proportion of patients with sustained LLDAS was much higher (%88 vs 70).

Conclusion: Postpartum six-month period appears to have the highest risk for disease flares during SLE pregnancies. Disease activity during pregnancy increases the risk of APO. Patients with sustained LLDAS have significantly lower APO rates. In order to achieve a positive pregnancy outcome and lower maternal morbidity, regular follow up of patients during pregnancy and postpartum period by Rheumatology and Gynecology and Obstetrics Departments is necessary.

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Abstract Number: 0267

Gastrointestinal Disease in SLE: Does It Indicate a Worse Prognosis?

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To describe the GI manifestations of SLE in the RELESSER (Registry of Systemic Lupus Erythematosus Patients of the Spanish Society of Rheumatology) cohort and to determine if those are associated with a more severe disease, damage accrual and a worse prognosis.

Methods: We conducted a nationwide, retrospective, multicenter, cross-sectional cohort study of 3658 SLE patients who fulfill ≥ 4 ACR-97 criteria. Data on demographics, disease characteristics, activity (SELENA-SLEDAI), damage (SLICC/ACR/DI) and therapies were collected. **Table 1** shows the different gastrointestinal manifestations among the RELESSER cohort. Demographic and clinical characteristics were compared between lupus patients with and without GI damage to establish whether GI damage is associated with a more severe disease (**Table 2**). $\chi 2$ tests for categorical variables and Student t-test for continuous variables were used. For non-continuous variables, either Mann-Whitney U test or logarithmic transformation were used (data expressed as median and interquartile range - IQR). Univariate linear and multivariate logistic regression analyses were performed to establish the relation of demographics, different SLE clinical manifestations, damage and GI manifestations.

Table 1. GI manifestations in the RELESSER cohort

	Total (%)
GI damage	**131 (3.7)**
-Mesenteric Insufficiency	6 (0.2)
-Infarction o bowel resection, spleen, liver	101 (2.8)
-Pancreatic Insufficiency	12(0.3)
-Chronic Peritonitis	6 (0.2)
-Stricture or Upper GI Tract Surgery	12 (0.3)
Other GI manifestations	
- Oral ulcers	1603(46.3)
- Splenomegaly	118 (3.4)
- Abdominal serositis	60 (1.7)
- Lupus hepatitis	91 (2.6)
- Protein-losing enteropathy	18 (0.5)
- Gastroduodenal ulcers	128 (3.9)
- Hepatopathy	35 (1.0)
- HCV Infection	48 (1.4)
- Inflammatory bowel disease	7 (0.2)
- Autoimmune hepatitis	6 (0.2)
- Celiac disease	4 (0.1)
- GI solid tumors	11 (0.3)

Results: From 3654 lupus patients, 3.7% developed GI damage (**Table 1**). Patients in this group (group 1) were older (53.1 vs 46 years; p< 0.001), they had longer disease duration (16.4 vs 11.7 years; p=0.001) and were more likely to have vasculitis (14.1% vs 8.7% p=0.056), renal disease (56.1% vs 42.4% p=0.003) and serositis (40.5% vs 28.5% p=0.005) than patients without GI damage (group 2). With regard to treatment, there were statistically significant differences between both groups in terms of glucocorticoids (96.9% vs 88.6% p=0.001), azathioprine (44.2% vs 33.9% p=0.01), mycophenolate mofetil (23.7% vs 14.9% p=0.009) and cyclophosphamide (37.4% vs 21.8% p< 0.001).The use of hydroxychloroquine was more common among SLE patients with no GI manifestations related to damage (83.4% vs 75.2%, p=0.022). Hospitalizations and mortality were significantly higher in group 1 suggesting that having GI damage is linked to a worse prognosis. Moreover, patients in group 1 had higher modified SDI (2; IQR 1-4; p< 0.001) (**Table 2**). After the multivariable analysis, older age, high daily dose of glucocorticoids (≥ 30 mg prednisone) and higher SDI remained significant. Interestingly, even the prevalence of oral ulcers was slightly similar in both groups, the multivariable analysis revealed that the presence of oral ulcers reduced risk of developing damage in 30% of patients (**Table 3**).

Conclusion: Having GI damage is associated with clinical involvement of other target organs in lupus and with a worse prognosis. Patients on high dose of glucocorticoids are at higher risk of developing GI damage which reinforces the strategy of minimizing glucocorticoids. Oral ulcers are common in SLE and seem to be protective from GI damage.

Table 2. Demographics and clinical characteristics. *Modified SLICC/SDI was calculated excluding gastrointestinal damage manifestations

	SLE patients with GI damage (Group 1)	SLE patients without GI damage (Group 2)	P Value
Gender (Women)	122/131 (93.1)	3095/3427 (90.3)	0.363
Age at diagnosis of SLE Mean (SD)	37.0 (17.4)	35.1 (14.6)	0.399
Age at the last intervention; Mean (SD)	53.1 (15.1)	46.6 (14.8)	**<0.001**
Disease duration (years); Mean (SD)	16.4 (8.9)	11.7 (8.3)	**<0.001**
Antiphospholipid syndrome	25/128 (19.5)	465/3400 (13.7)	0.068
Neuropsychiatric disease	35/126 (27.8)	754/3222 (23.4)	0.284
- Organic Brain Syndrome	7/129 (5.4)	96/3385 (2.8)	0.102
- Lupus Headache	8/128 (6.2)	204/3378 (6.0)	0.850
- Craneal Nerve Disorder	16/129 (12.4)	129/3329 (3.9)	**<0.001**
- Seizure	8/131 (6.1)	231/3380 (6.8)	0.861
- Psychosis	1/131 (0.8)	80/3398 (2.4)	0.370
- Visual Disturbance	6/128 (4.7)	129/3366 (3.8)	0.636
- CVA	11/129 (8.5)	186/3405 (5.5)	0.166
Vasculitis	18/128 (14.1)	293/3354 (8.7)	**0.056**
Musculoskeletal disease	97/130 (74.6)	2658/3373 (78.8)	0.275
-Myositis	5/128 (3.9)	126/3365(3.7)	0.813
-Arthritis	95/130 (73.1)	2644/3384 (78.1)	0.195
Renal disease	69/123 (56.1)	1342/3162 (42.4)	**0.003**
-Hematuria	51/120 (42.5)	966/3227 (29.9)	**0.004**
-Pyuria	37/118 (31.4)	690/3159 (21.8)	**0.018**
-Proteinuria>0'5gr/24 h	57/130 (43.8)	1037/3367 (30.8)	**0.003**
-Urinary casts	43/127 (33.9)	677/3260 (20.8)	**<0.001**
Skin disease	100/127 (78.7)	2577/3375 (76.4)	0.595
-New rash	88/127 (69.3)	2226/3394 (65.6)	0.446
-Alopecia	36/126 (28.6)	1222/3372 (36.2)	0.089
-Malar rash	69/131 (52.7)	1863/3392 (54.9)	0.655
-Discoid lupus	25/129 (19.4)	702/3360 (20.9)	0.741
-Oral ulcers	53/129 (41.1)	1550/3335 (46.5)	0.243
Serositis	51/126 (40.5)	953/3339 (28.5)	**0.005**
- Pleurisy	40/127 (31.5)	769/3360 (22.9)	**0.032**
- Pericarditis	32/128 (25.0)	534/3369 (15.9)	**0.010**
Laboratory tests	115/130 (88.5)	3017/3395 (88.9)	0.887
-Increased DNA binding	96/129 (74.4)	2454/3345 (73.4)	0.840
-Low complemente	105/130 (80.8)	2624/3373 (77.8)	0.453
Hematologic disease	88/129 (68.2)	2267/3336 (68.0)	1
-Thrombocytopenia	37/129 (28.7)	755/3283 (23.0)	0.137
-Leukopenia	73/127 (57.5)	2041/3356 (60.8)	0.460
Treatments			
-Antimalarials	97/129 (75.2)	2719/3260 (83.4)	**0.022**
-Glucocorticoids	127/131 (96.9)	2902/3274 (88.6)	**0.001**
-Methotrexate	18/131 (13.7)	548/3255 (16.8)	0.404
-Azathioprine	57/129 (44.2)	1066/3245 (32.9)	**0.010**
-Mycophenolate Mofetilo	31/131 (23.7)	482/3231 (14.9)	**0.009**
-Cyclophosphamide	49/131 (37.4)	710/3250 (21.8)	**<0.001**
-At least one immunosuppressor (IS)	91/131 (69.5)	1729/3230 (53.5)	**<0.001**
- Rituximab	14/131 (10.7)	208/3253 (6.4)	0.068
- Abatacept	0/130 (0)	10/3244 (0.3)	1
- Anti-TNF	2/130 (1.5)	64/3235 (2.0)	0.974
Modified SLICC/SDI Median (IQR)	2 (1-4)	1 (0-2)	**<0.001**
Hospitalizations (any)	93/130 (71.5)	1829/3377 (54.2)	**<0.001**
Number of hospitalizations	3 (1 - 5)	2 (1 - 3)	**<0.001**
Death	23/131 (17.6)	179/3433 (5.2)	**<0.001**

Table 3. Multivariable analysis. Variables independently associated with GI damage

Variables	Odds Ratio	CI 95%	P-value
Age at the last clinic evaluation	1.02	1.01 1.04	**<0.001**
- Glucocorticoids			
- <= 10 mg/d	1.23	0.37 - 4.73	0.751
- 10-30 mg/d	2.61	1.01 - 8.88	**0.074**
- >30-60 mg/d	3.04	1.17 - 10.40	**0.035**
- >60 mg/d	4.14	1.61 - 14.05	**0.008**
Oral ulcers	0.67	0.45 - 0.98	**0.044**
Modified SLICC	1.26	1.16 - 1.36	**<0.001**

Variables originally introduced in the model: age at last assessment (years), duration of SLE (years), serositis activity, APS, renal activity, antimalarial drugs, at least one immunosuppressant, steroids, oral ulcers and modified slicc index.

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Abstract Number: 0268

Impact of Flares on Healthcare Resource Usage and PROs in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION

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Background/Purpose: The effect of flares on healthcare resource usage and patient-reported outcome scores in SLE patients is not well quantified.

To understand how flares impact healthcare resource utilization (HCRU) and patient-reported outcomes amongst an international real-world dataset of SLE patients.

Methods: The Adelphi Real World 2015 Lupus Disease Specific Programme (DSP) is a cross-sectional study of 263 rheumatologists in the US and EU5. Rheumatologists were asked to complete patient record forms (PRFs) for the next 5 prospectively consulting SLE patients; the same patients were asked to complete patient self-completion (PSC) forms describing how SLE affected them. PRFs collected data pertaining to the patient's diagnosis, disease history, current clinical outcomes, treatment and management history. PSCs collected similar data and included patient-reported outcome measures (PROs) to assess humanistic burden. Propensity score matching was used to assess differences in HCRU and health status between SLE patients who had flared (physician defined) in the last 12 months and those who had not. Matching variables were patient ethnicity, time since diagnosis, and severity at diagnosis. Data were extracted from 1134 PRFs, and 635 PSCs. Propensity score matching was carried out on two matched groups of 408 patients.

Results: Demographic data are reported in Table 1. Propensity score matching showed patients who flared in the last 12 months were significantly more likely to have been hospitalized, visited the ER, and had greater total HCP consults in the last 12 months. Significantly greater drug burden lower physician and patient satisfaction, lower EQ-5D score (worse health status), lower FACIT Fatigue score (greater fatigue), and greater overall work impairment (Table 2) were also observed.

Conclusion: The analysis of international real-world data confirmed that SLE patients who flared in the last year represent a greater burden on healthcare resource and demonstrate significantly worse health status, greater fatigue, lower patient and physician satisfaction and greater overall work impairment compared with non-flaring patients. There is a need for more effective treatments in this patient population to reduce patient and healthcare burden.

Table 1 Demographic data

Variable	Flared in last 12 months	Not flared in the last 12 months
Mean age (years)	41.8	42.4
% Female	86.0	87.0
% White/Caucasian	66.2	76.3
Mean years diagnosed	5.9	5.4

Table 2 Propensity score matching results

Outcome variable	Flared mean	Not flared mean	Coefficient	95% CI	p-value
Hospitalized in last 12 months	24.26	7.63	0.17	[0.12 – 0.21]	<0.001
Emergency department visit in last 12 months	20.83	4.19	0.17	[0.12 – 0.21]	<0.001
Number of tests in last 12 months	46.49	38.90	7.59	[3.74 – 11.44]	<0.001
Number of current medications	2.76	2.19	0.57	[0.43 – 0.72]	<0.001
Physician satisfied	64.46	86.63	-0.22	[-0.28 – -0.17]	<0.001
Patient satisfied	69.29	85.09	-0.16	[-0.24 – -0.08]	<0.001
EQ-5D-3L	0.72	0.83	-0.11	[-0.15 – -0.07]	<0.001
FACIT Fatigue	30.06	36.48	-6.42	[-8.5 – -4.3]	<0.001
WPAI overall percentage work impairment	35.98	20.66	15.32	[9.20 – 21.44]	<0.001

Disclosure: Z. Touma, None; **B. Hoskin**, None; **C. Atkinson**, Adelphi Real World, 3; **D. Bell**, None; **J. Pike**, Adelphi Real World, 3; **J. Lofland**, Janssen Market Access, 1; **P. Berry**, Janssen Global Services, LLC, 1, 3; **C. Karyekar**, Janssen Global Services, LLC, 3, Johnson & Johnson, 1, Janssen, 5; **K. Costenbader**, Glaxo Smith Kline, 5, UpToDate, 7, Lupus Foundation of America, 6, Neutrolis Inc, 5.

Abstract Number: 0269

Systemic Lupus Erythematosus with Libman-Sacks Endocarditis Increases Inpatient Mortality

Ehizogie Edigin[1], Precious Eseaton[2], Pius Ojemolon[3] and Augustine Manadan[4], [1]John H Stroger Jr. Hospital of Cook County, Chicago, IL, [2]University of Benin Teaching Hospital, Benin, [3]St. George's University, St. George's, Grenada, [4]Cook County Hospital/Rush University Medical center, Chicago, IL

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Libman-Sacks endocarditis characterized by thrombotic and/or non-infective sterile inflammatory vegetations are common in Systemic Lupus Erythematosus (SLE) and associated with increased morbidity. These vegetations can be complicated with superimposed infective endocarditis, embolic cerebrovascular disease,

severe valvular regurgitation, and need for high-risk valve surgery. The study aims to compare the outcomes of SLE hospitalizations with and without Libman-Sacks endocarditis. The primary outcome was inpatient mortality, while secondary outcomes were hospital length of stay (LOS) and total hospital charges.

Methods: Data were abstracted from the National Inpatient Sample (NIS) 2016 and 2017 Database. This database is the largest collection of inpatient admission data in the USA. It is a nationally representative sample of 20% of hospitalizations from approximately 1,000 hospitals. The numbers in the databases are weighted to optimize national estimates. The NIS was searched for SLE hospitalizations with Libman-Sacks endocarditis ("M32.11") and SLE without endocarditis (remaining M32 ICD-10 codes) as principal or secondary diagnosis. SLE hospitalizations for adult patients (age≥ 18 years) from the above groups were identified. Multivariate logistic and linear regression analysis was used to adjust for confounders for the primary and secondary outcomes respectively. Confounders adjusted for include age, sex, race, median income expected for zip code, Charleston comorbidity index, insurance status, and hospital location/region/teaching status and bed size. STATA software was used to analyze the data.

Results: There were combined 71 million discharges included in the 2016 and 2017 NIS database. 355,740 hospitalizations were for adult patients, who had either a principal or secondary ICD-10 code for SLE. 680 (0.19%) and 355,060 (99.81%) of these hospitalizations were for SLE with and without Libman-Sacks endocarditis respectively. The mean age for SLE with Libman-Sacks endocarditis was 43 vs 52 years without endocarditis (P< 0.001). 7,060 adult SLE hospitalizations (2%) resulted in inpatient mortality. 45 (6.6%) deaths occurred in SLE with Libman-Sacks endocarditis vs 7,015 (2%) without endocarditis (P=0.0001). The adjusted odds ratio (AOR) for inpatient mortality for SLE with Libman-Sacks endocarditis compared to those without endocarditis was 3.64 (95% CI 1.63-8.12, P=0.002). SLE with Libman-Sacks endocarditis hospitalizations had an increase in mean adjusted LOS of 5.22 days (95% CI 1.54-8.90, P=0.005) compared to SLE without endocarditis. Hospitalizations for SLE with Libman-Sacks endocarditis had an increase in mean adjusted total charges by $53,507 compared to SLE without endocarditis (95% CI 10,611-96,404, P=0.015).

Conclusion: Hospitalizations for SLE with Libman-Sacks endocarditis have more than 3 times the risk of in-hospital death compared to those without endocarditis. Hospitalizations for SLE with Libman-Sacks endocarditis have statistically and clinically significant increase in LOS and mean total hospital charges compared to those without endocarditis.

Disclosure: E. Edigin, None; **P. Eseaton**, None; **P. Ojemolon**, None; **A. Manadan**, None.

Abstract Number: 0270

The New EULAR/ ACR 2019 SLE Classification Criteria: Defining Ominosity in SLE

Laura Whittall-Garcia[1], Dafna Gladman[2], Murray Urowitz[3], Jiandong Su[4] and Sindhu Johnson[5], [1]University Health Network, Toronto, ON, Canada, [2]Krembil Research Institute, Toronto Western Hospital, Toronto, ON, Canada, [3]University Health Network, University of Toronto, Toronto, ON, Canada, [4]University of Toronto Lupus Clinic, Centre for Prognosis Studies in Rheumatic Diseases, Toronto Western Hospital, University Health Network, Toronto, ON, Canada, [5]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Figure 1. Histogram distribution of the EULAR/ACR criteria score in our population.

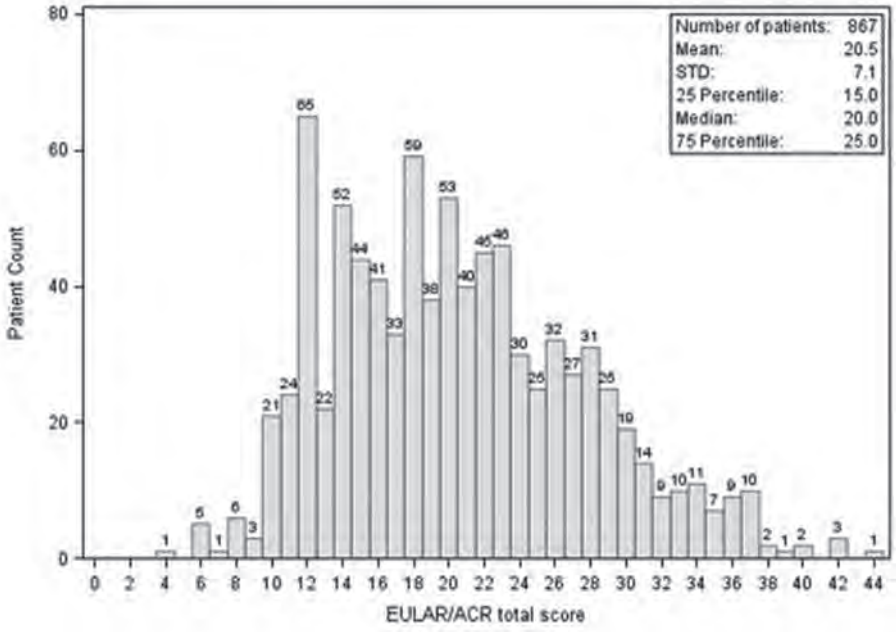
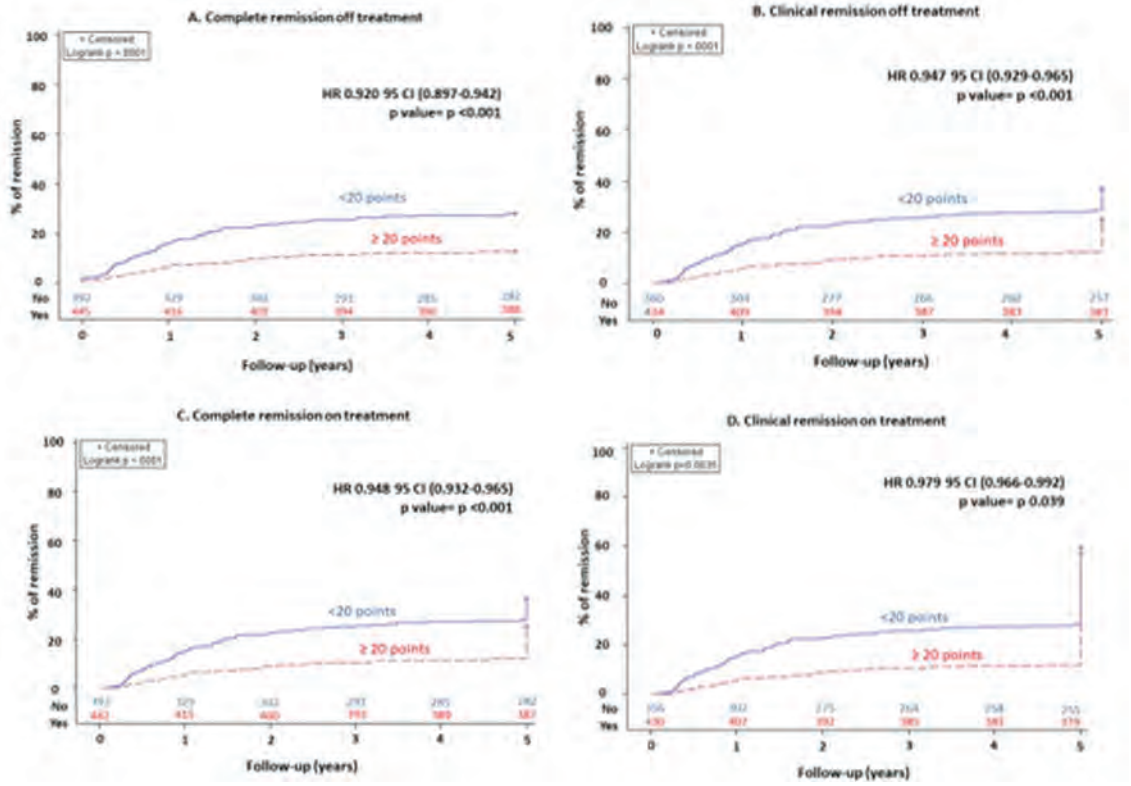


Table 1. Differences in demographic and clinical characteristics at baseline and outcomes between patients with a EULAR/ARC score ≥ 20 vs < 20. Values are expressed as mean ± SD or n (%).

Variables	Score < 20	Score ≥ 20	P value
Baseline characteristics	**N = 415**	**N = 452**	
Race			
Caucasian	316 (76.1)	262 (58.0)	**<0.001**
Black	42 (10.1)	81 (17.9)	**0.002**
Chinese	20 (4.8)	52 (11.5)	**<0.001**
Age (years)	38.1 ± 15.1	34.5 ± 13.1	**<.001**
SLEDAI-2K score	6.3 ± 5.4	12.2 ± 8.9	**<.001**
GC* use	241 (58.1)	374 (82.7)	**<.001**
Immunosuppressive use	83 (20.0)	166 (36.7)	**<.001**
Outcomes			
AMS			
1 year *	4.9 ± 4.5	7.3 ± 4.6	**<.001**
3 years **	4.1 ± 3.7	5.6 ± 3.6	**<.001**
5 years ***	3.7 ± 2.9	5.1 ± 3.2	**<.001**
Flares in first 5 years * **			
No flares	118 (44.2)	92 (30.6)	**<0.001**
1 flare	58 (21.7)	77 (25.6)	0.281
≥2 flares	91 (34.1)	132 (43.9)	**0.017**
Cummulative GC* dose (gr)			
1 year *	3.9 ± 3.3	5.4 ± 3.8	**<.001**
3 years **	9.4 ± 7.3	12.3 ± 8.7	**<.001**
5 years ***	12.5 ± 10.6	16.9 ± 11.4	**<.001**
Immunosuppressive use			
1 year *	86 (23.1)	182 (46.0)	**<.001**
3 years **	103 (32.9)	185 (53.5)	**<.001**
5 years ***	87 (32.6)	170 (56.5)	**<.001**

*There was no significant difference in the antimalarial use between groups.
* N = 372 and 396 in low and high score groups at one year.
** N = 313 and 346 in low and high score groups at three years.
*** N = 267 and 301 in low and high score groups at five years.
* Glucocorticoid.

Figure 2 (A, B, C, D). Remission according to the 4 DORIS definitions. Kaplan-Meier survival curves stratified by EULAR/ACR criteria score of ≥ 20 and < 20. Hazard ratios and 95% confidence intervals of higher score group vs. low score group on the outcome of four types of remissions.



Background/Purpose: SLE is characterized by different patterns of disease activity throughout its course. Overall, a higher disease activity is an important predictor of mortality and damage accrual.

Recently, a new set of classification criteria for SLE using an additive point system has been introduced, the 2019 EULAR/ACR classification criteria (EULAR/ACR) which have proven to be sensitive and specific. Furthermore, these criteria have correlated with SLEDAI and SLAM-R scores at diagnosis. In a different cohort, higher EULAR/ACR scores were associated with higher rates of organ damage.

We aimed to determine the ominosity of the EULAR/ACR by determining their potential predictive role for disease severity in the first 5 years of disease course.

Methods: Inception SLE patients (recruited in the first 12 months after diagnosis) were included.

For each patient a score of the EULAR/ACR was calculated based on the baseline clinical and laboratory information. The baseline information was obtained from the first 2 visits as some of the data and therapies ordered at the first visit were recorded only at the second visit.

To determine the ominosity of the EULAR/ACR, we used outcomes to establish disease severity over the first 5 years after diagnosis including Adjusted mean SLEDAI-2K (AMS), flares, remission and use of immunosuppressive treatment.

Results: A total of 867 inception patients were included, 87.5% were woman, with a mean age of 36.2 years at baseline. Most patients were Caucasians (66.7%), followed by Blacks (14.2%).

The mean disease duration (time between diagnosis and first visit) was 0.2 years, the median time between the first visit and the second visit was 3.3 months.

The median EULAR/ACR score was 20. We used this score as a threshold to compare demographic, clinical characteristics and outcomes between groups. **Fig 1.**

Blacks more frequently presented with a score ≥ 20 compared to Caucasians. At baseline patients with a score ≥ 20 were younger, had higher SLEDAI-2K scores and were more likely to receive immunosuppressive therapy. **Table 1.**

In the first 5 years of disease course, patients with a score ≥ 20 had higher AMS scores. Every increase of 10 points in the score increased the AMS by 2.2 units (Univariate Linear regression, beta = 0.22, p< .0001). Likewise, patients with a higher score were more likely to ever present with a flare and more frequently experienced ≥2 flares. Every 10 points increase in the score increased the risk of a flare by 32% (RR: 1.32 95%CI: 1.173, 1.485, p < .0001) **Table 1**. Looking at specific organ flares this group presented more renal (31.6% vs 12.8%, ≥20 vs < 20, p=< 0.001) and hematologic (8% vs 2.2%, ≥20 vs < 20, p=0.007) flares**.**

In addition, these patients were less likely to achieve remission, **Fig. 2** and had higher requirements for immunosuppressive therapy. **Table 1.**

Conclusion: Overall, EULAR/ACR score ≥20 is an indicator of ominosity in the SLE disease course. SLE patients with a score ≥20 were characterized by higher disease activity throughout the first 5 years after diagnosis. Thus, the new classification criteria could be helpful not only in classifying SLE cases but could also provide prognostic information regarding the disease course in the first 5 years following diagnosis.

Disclosure: L. Whittall-Garcia, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **M. Urowitz**, None; **J. Su**, None; **S. Johnson**, None.

Abstract Number: 0271

External Validation of the Systemic Lupus International Collaborating Clinics Frailty Index (SLICC-FI) as a Predictor of Mortality and Organ Damage Accrual in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Using data from the Systemic Lupus International Collaborating Clinics (SLICC) inception cohort, a frailty index (FI) was recently developed as a measure of susceptibility to adverse health outcomes among individuals with SLE. In this work, higher baseline SLICC-FI values were associated with increased organ damage accrual and mortal-

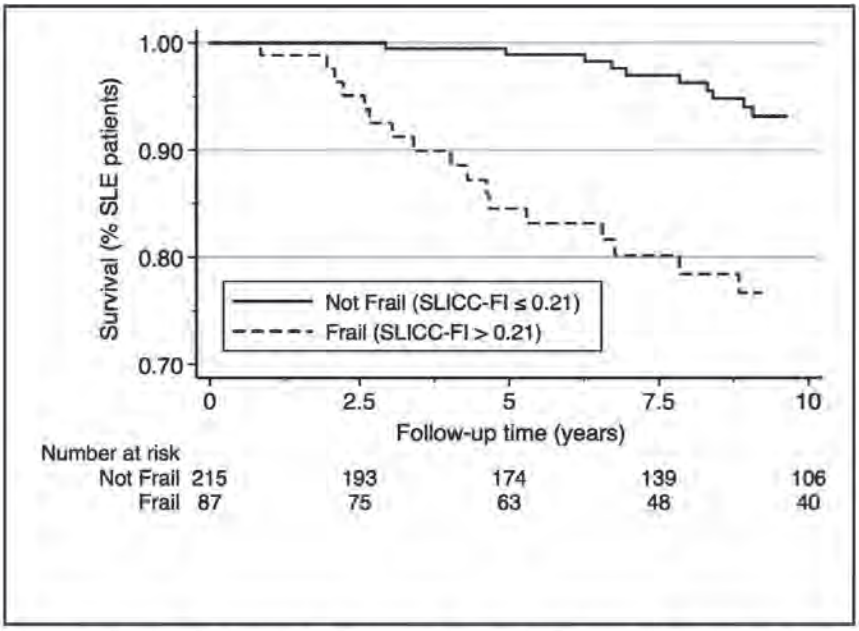

Figure 1. Kaplan-Meier survival curves for the risk of mortality during follow-up among SLE patients, stratified by baseline frailty status. Mortality risk was higher among frail individuals compared to those who were non-frail at baseline (Hazard Ratio 4.01; 95% CI 2.13-7.54).

Table 1. Univariable and multivariable Cox regression models for the association of baseline SLICC-FI values with the risk of mortality during follow-up among patients with SLE.

	Univariable model		**Multivariable model [a]**	
	Hazard Ratio (95% CI)	**p value**	**Hazard Ratio (95% CI)**	**p value**
Main analysis (n=302)				
SLICC-FI (per 0.05 increase)	1.61 (1.34 - 1.94)	<0.001	1.42 (1.14 – 1.78)	0.002
Excluding inception patients [b] (n=168)				
SLICC-FI (per 0.05 increase)	1.52 (1.25 – 1.85)	<0.001	1.31 (1.01 – 1.70)	0.040
Excluding organ damage from the SLICC-FI (n=302)				
Modified SLICC-FI [c] (per 0.05 increase)	1.29 (1.12 – 1.48)	<0.001	1.27 (1.07 – 1.50)	0.006

[a] Models adjusted for the following baseline characteristics: age, sex, corticosteroid use, antimalarial use, immunosuppressive use, education, disease duration, SLICC/ACR damage index (SDI), and cigarette smoking status.

[b] Excludes patients with SLE disease duration < 15 months at study enrolment.

[c] Excludes the 16 health deficits related to organ damage. Baseline SLICC-FI scores re-calculated using the remaining 32 health deficits.

Abbreviations: SLICC = Systemic Lupus International Collaborating Clinics; FI = Frailty Index.

ity risk during follow-up. While promising, these results require external validation. The objective of the current study was to evaluate the properties of the SLICC-FI in a prevalent cohort of individuals with more longstanding SLE.

Methods: This was a secondary analysis of data from a prospective cohort of adult SLE patients at a single academic medical center. All participants met the 1997 revised ACR classification criteria for SLE and were assessed annually for medication use, comorbidities, disease activity (SLEDAI-2K), organ damage [SLICC/ACR Damage Index (SDI)], health-related quality of life [Short-Form 36 (SF-36)], and other measures.

For this analysis, we defined the baseline visit as the first visit at which both SDI and SF-36 data were available. We created an adapted version of the original SLICC-FI by modifying the definitions of individual health deficits based on data availability. Using 48 health deficits, we calculated a baseline SLICC-FI score for each patient. Vital status and SDI score at last follow-up were recorded.

Cox regression was used to estimate the association between baseline SLICC-FI values and mortality risk. Negative binomial regression was used to estimate the association of baseline SLICC-FI values with the rate of change in SDI scores per patient-year of follow-up. Multivariable models adjusted for relevant baseline variables.

Results: The 329 eligible SLE patients (96% of cohort) were mostly female (88%) with mean (SD) age 43.9 (14.4) years and median (IQR) disease duration 3.4 (1.2-13.3) years at baseline. Mean (SD) baseline SLICC-FI score was 0.17 (0.08), with 94 patients (28.6%) classified as frail (SLICC-FI > 0.21).

Table 2. Negative binomial regression models for the association of baseline SLICC-FI scores with the rate of change in the SDI per patient-year of follow-up among patients with SLE.

	Univariable model		Multivariable model [a]	
	IRR (95% CI)	**p value**	**IRR (95% CI)**	**p value**
Main analysis (n=292)				
SLICC-FI (per 0.05 increase)	1.33 (1.23 - 1.45)	<0.001	1.19 (1.09 – 1.31)	<0.001
Excluding inception patients [b] (n=163)				
SLICC-FI (per 0.05 increase)	1.31 (1.21 – 1.43)	<0.001	1.18 (1.07 – 1.29)	<0.001
Excluding organ damage from the SLICC-FI (n=292)				
Modified SLICC-FI [c] (per 0.05 increase)	1.18 (1.10 – 1.26)	<0.001	1.11 (1.04 – 1.19)	0.003

[a] Models adjusted for the following baseline characteristics: age, sex, corticosteroid use, education, disease duration, baseline SDI score, and cigarette smoking status.

[b] Excludes patients with SLE disease duration < 15 months at study enrolment.

[c] Excludes the 16 health deficits related to organ damage. Baseline SLICC-FI scores re-calculated using the remaining 32 health deficits.

Abbreviations: SLICC = Systemic Lupus International Collaborating Clinics; FI = Frailty Index; SDI = SLICC/ACR damage index; IRR = incidence rate ratio.

Forty deaths occurred during mean (SD) follow-up of 10 (5.5) years. Mortality risk was significantly higher among frail individuals (Figure 1). Higher baseline SLICC-FI values (per 0.05 units) were associated with increased mortality risk (Hazard Ratio 1.42; 95% CI 1.14-1.78), after adjusting for age, sex, education, SLE medication use, disease duration, smoking status, and baseline SDI (Table 1).

There were 133 patients with an increase in SDI score during follow-up. Higher baseline SLICC-FI values (per 0.05 units) were associated with increased damage accrual over time (Incidence Rate Ratio 1.19; 95% CI 1.09-1.31), after adjusting for age, sex, corticosteroid use, disease duration, smoking status, and baseline SDI (Table 2).

These associations between baseline SLICC-FI values and adverse health outcomes persisted when inception patients (disease duration < 15 months at enrolment) were excluded, and when items related to organ damage were omitted from the SLICC-FI.

Conclusion: Frailty, measured using the SLICC-FI, predicts organ damage accrual and mortality risk among individuals with established SLE. This external validation study provides additional support for the SLICC-FI as a useful prognostic tool in SLE.

Disclosure: A. Malone, None; **A. Legge**, None; **J. Hanly**, None.

Abstract Number: 0272

Superior Discrimination Between LLDAS and DORIS Remission with Modification of Prednisolone Dose Threshold

Eric Morand[1], Vera Golder[2], Worawit Louthrenoo[3], Shue Fen Luo[4], Yeong-Jian Wu[5], Aisha Lateef[6], Sargunan Sockalingam[7], Sandra Navarra[8], Leonid Zamora[9], Laniyati Hamijoyo[10], Yasuhiro Katsumata[11], Masayoshi Harigai[12], Madelynn Chan[13], Sean O'Neill[14], Fiona Goldblatt[15], Yi-Hsing Chen[16], Yanjie Hao[17], Zhuoli Zhang[17], Jun Kikuchi[18], Tsutomu Takeuchi[19], Chak Sing Lau[20], Zhanguo Li[21], Alberta Hoi[22], Mandana Nikpour[23] and Rangi Kandane-Rathnayake[2], [1]Medicine, School of Clinical Sciences at Monash Health, Monash University, Melbourne, Australia, [2]Monash University, Clayton, Victoria, Australia, [3]Chiang Mai University Hospital, Muang, Thailand, [4]Chang Gung Memorial Hospital-Linkou, Taoyuan, Taipei, Taiwan (Republic of China), [5]Chang Gung Memorial Hospital, Guishan, Taiwan (Republic of China), [6]National University Hospital, Singapore, Singapore, [7]University of Malaya, Kuala Lumpur, Malaysia, [8]University of Santo Tomas, Manila, Philippines, [9]University of Santo Thomas, Manila, Philippines, [10]University of Padjadjaran, Bandung, Indonesia, [11]Tokyo Women's Medical University School of Medicine, Tokyo, Japan, [12]Department of Rheumatology, Tokyo Women's Medical University School of Medicine, Shinjuku-ku, Tokyo, Japan, [13]Tan Tock Seng Hospital, Singapore, Singapore, [14]Sydney University, Sydney, Australia, [15]Royal Adelaide Hospital, Adelaide, Australia, [16]Taichung Veterans General Hospital, Taichung, Taiwan (Republic of China), [17]Peking University First Hospital, Beijing, China (People's Republic), [18]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, [19]Division of Rheumatology, Department of internal Medicine, School of Medicine, Keio University, Tokyo, Japan, [20]Hong Kong University, Hong Kong, Hong Kong, [21]Department of Rheumatology and Immunology, Peking University People's Hospital, Beijing, China (People's Republic), [22]Monash University, Melbourne, Victoria, Australia, [23]The University of Melbourne at St. Vincent's Hospital, Melbourne, Victoria, Australia

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Treat-to-target (T2T) approaches to rheumatic disease require the definition and validation of low disease activity and remission endpoints that should be concentrically more stringent. The Lupus Low Disease

Activity State (LLDAS) has been established as a low-disease activity endpoint for SLE, but multiple possible definitions for remission arise from the Definition of Remission in SLE (DORIS) framework. LLDAS and all remission definitions are associated with improved long term outcomes in terms of damage accrual and flare, but previous analyses suggested that Clinical Remission on Treatment (CROT) allowing 5mg/day prednisolone was insufficiently different from LLDAS (≤7.5 mg/day) to be used separately. Therefore, we examined a more stringent threshold, requiring daily prednisolone < 5mg (CROT< 5), a dose which requires physician and patient to change from standard 5 mg tablets.

Methods: Data from a prospective multinational cohort study of patients with SLE (ACR or SLICC criteria) undertaken in 17 centres between 2013-2017 were used. Time-dependent Cox proportional hazards models were used to compare LLDAS and DORIS definitions of remission in terms of impact on flares (SELENA flare index) and organ damage (SLICC damage index (SDI)). LLDAS and DORIS CROT were defined as described in Golder *et al*, 2019: CROT requires clinical SLEDAI-2K = 0 and physician global assessment (PGA) (0-3) < 0.5; CROT allows prednisolone ≤5 mg/day; whereas CROT< 5 excludes patients taking 5mg/day. LLDAS allows SLEDAI-2K ≤4 with no new/major organ activity, PGA ≤1, and prednisolone ≤7.5 mg.

Results: 18.659 visits of 2,384 patients collected over a mean (SD) 2.26 (1.34) years were analysed. LLDAS was attained in 8,883 (47.6%) visits, CROT in 6,521 (35.0%) and CROT< 5 in 4,373 (23.4%; mean (SD) daily prednisolone 1.16 (1.32) mg)), confirming that lowering the prednisolone threshold resulted in a more stringent remission definition compared to CROT. LLDAS was protective from flare and damage accrual whether assessed visit by visit or cumulatively using a 50% of time exposed threshold. Visit by visit analysis revealed that CROT< 5 was associated with slightly greater protection from future flare (HR (95% CI) 0.48 (0.42,0.54)) than CROT (HR 0.54 (0.49,0.60)). Similarly, future damage risk was slightly less with CROT< 5 (HR 0.60 (0.47,0.78)) than CROT (0.62 (0.50,0.78)). When measured cumulatively using a 50% of time exposed threshold, CROT < 5 was more protective from flare (HR 0.40 (0.35,0.46)) than CROT (0.45 (0.40,0.50)) but not from damage. The effect of cumulative LLDAS on damage accrual overtime remained significant after excluding patients in CROT< 5 (HR 0.74 (0.57,0.96), p=0.022) but not after excluding CROT. Cumulative LLDAS was independently associated with flare excluding either CROT or CROT< 5.

Conclusion: A remission definition requiring a ceiling dose of prednisolone less than 5 mg (CROT< 5) is more stringent than CROT (allowing 5 mg/day) and its effects are independent of LLDAS, while CROT is insufficiently distinct from LLDAS. Confirmation in other cohorts should be undertaken prior to agreeing on a definition of remission for SLE.

Disclosure: E. Morand, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, 5, Merck Serono, 2, 5, Neovacs, 5, Sandoz, 5, Novartis, 8, AbbVie, 5, Amgen, 5, Biogen, 5; **V. Golder**, None; **W. Louthrenoo**, None; **S. Luo**, None; **Y. Wu**, None; **A. Lateef**, None; **S. Sockalingam**, None; **S. Navarra**, Eli Lilly, 5, 8, Astra-Zeneca, 5, 8, Astellas, 8, Janssen, 5, 8, Novartis, 8, Pfizer, 8, Biogen, 2, 5; **L. Zamora**, None; **L. Hamijoyo**, None; **Y. Katsumata**, None; **M. Harigai**, AbbVie Japan GK, 1, 2, Asahi Kasei Corp., 1, Astellas Pharma Inc., 1, Ayumi Pharmaceutical Co. Ltd., 1, 2, Bristol Myers Squibb Co., Ltd, 1, 2, 3, Chugai Pharmaceutical Co. Ltd., 1, 2, Daiichi-Sankyo, Inc., 1, Eisai Pharmaceutical, 1, 2, Nippon Kayaku Co. Ltd., 1, Mitsubishi Tanabe Pharma Co., 1, Taisho Pharmaceutical Co. Ltd., 1, Takeda Pharmaceutical Co. Ltd., 1, 2, Eli Lilly Japan K.K, 1, Pfizer Japan Inc, 1, AbbVie, 1; **M. Chan**, None; **S. O'Neill**, None; **F. Goldblatt**, None; **Y. Chen**, None; **Y. Hao**, None; **Z. Zhang**, None; **J. Kikuchi**, None; **T. Takeuchi**, Astellas Pharma Inc., 2, 5, 8, Daiichi Sankyo Company, Limited, 2, 5, 8, Takeda Pharmaceutical Company Limited, 2, 5, 8, AbbVie GK., 2, 5, 8, Asahi Kasei Pharma Corporation, 2, 5, 8, Mitsubishi Tanabe Pharma Corporation, 2, 5, 8, Eisai Co., Ltd., 2, 5, 8, Nippon Kayaku Co., Ltd., 2, 5, 8, Chugai Pharmaceutical Co., Ltd., 2, 5, 8, Eli Lily Japan K.K, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Pfizer Japan, Inc., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, AYUMI Pharmaceutical Corporation, 2, 5, 8, Novartis Pharma K.K., 2, 5, 8, UCB, 2, 5, 8, Dainippon Sumitomo Co., 2, 5, 8, Shionogi & Co., Ltd., 2, 5, 8; **C. Lau**, None; **Z. Li**, None; **A. Hoi**, None; **M. Nikpour**, Actelion, 2, 5, 8, GSK, 2, 5, 8, Boehringer Ingelheim, 5; **R. Kandane-Rathnayake**, None.

Abstract Number: 0273

Lupus Nephritis Is Associated with a Reduced Prevalence of Fibromyalgia

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with SLE have poor health related quality of life (HRQoL), however the differences in the predominant causes of decreased HRQoL across subgroups of SLE are not known. Features of fibromyalgia including fatigue, widespread pain, depression, sleep and cognitive dysfunction are prevalent in SLE affecting 20-65% of patients and often contribute to disability and poor HRQoL. These aspects of fibromyalgia have not been well described in patients with lupus nephritis (LN). We evaluated self-reported symptoms of fibromyalgia and mood disorders in patients with and without lupus nephritis.

Methods: This was a cross sectional study of SLE patients (ACR 1997 or SLICC 2012 criteria) enrolled in a university registry from June 2018 to November 2019. All patients completed Systemic Lupus Activity Questionnaire (SLAQ), Patient Health Questionnaire-9 (PHQ9), and 2016 ACR Fibromyalgia criteria surveys. Active nephritis was defined as UPC >500mg and/or active urinary sediment excluding other causes. Fibromyalgia was defined as ≥7 widespread pain index (WPI) with ≥5 symptoms severity score (SSS) or ≥4 WPI with ≥9 SSS. Differences across groups were analyzed by Fisher's exact test and ANOVA.

Results: Two hundred and twenty-four patients completed patient-reported outcome measures (93% female, mean age 40 years, 67% Black). In our cohort 11% had active nephritis, 35% had nephritis in remission and 54% had no history of nephritis. Of nephritis patients, 22% had membranous class V, 48% had proliferative or proliferative/mixed LN, 3% class I/II, 5% post-transplant, 6% ESRD on dialysis, and class was unknown in 28%.

Active nephritis patients were younger, more often of Black race, and reported greater social support than non-nephritis patients. There were no differences in sex, disease duration, education, income, disability, insurance, or serologies. The use of plaquenil, anti-depressants, gabapentinoids, muscle relaxers, and narcotics were similar between groups. Active nephritis patients were more often prescribed prednisone (Table 2).

Table 1. Patient demographics and socioeconomic factors of active nephritis, nephritis in remission and non-nephritis SLE patients

	Active Nephritis n=24	Nephritis in Remission n=78	Non-nephritis n=122	p-value
Mean age (SD), years	34.0 (10.6)	38.9 (11.6)	47.1 (14.4)	<0.0001
Mean length of disease (SD), years	12.7 (6.4)	13.2 (8.3)	14.5 (9.7)	0.5
Female	23 (96%)	70 (90%)	117 (95%)	0.3
Black	21 (88%)	51 (65%)	60 (49%)	0.0005
Social support (>2)	18 (75%)	59 (76%)	71 (58%)	0.02
College education (n=215)	12 (55%)	40 (56%)	70 (58%)	0.9
Medicare, Medicaid, uninsured (n=214)	13 (59%)	32 (45%)	55 (45%)	0.5
Income <$15000 (n=200)	8 (36%)	14 (21%)	20 (18%)	0.2
Disability (n=208)	7 (35%)	23 (32%)	49 (42%)	0.3

Table 2. Physician- and patient-reported measures in active nephritis, nephritis in remission and non-nephritis SLE patients

	Active Nephritis	Nephritis in Remission	Non-nephritis	p-value
	n=24	n=78	n=122	
Physician Assessment				
PGA	1.4 (0.7)	0.5 (0.7)	0.5 (0.6)	<0.0001
SLEDAI (n=214)	9.2 (4.8)	2.8 (3.7)	2.5 (2.6)	<0.0001
Patient Reported Measures				
PHQ-9 Depression % (n=190)	4 (19%)	3 (5%)	19 (18%)	0.03
SLAQ				
Patient global activity (range: 0-10) (n=215)	4.7 (2.7)	3.3 (3.0)	4.5 (3.1)	0.02
Lupus flare (n=209)	9 (39%)	15 (21%)	42 (36%)	0.07
Total SLAQ score (n=171)	9.2 (6.0)	8.0 (5.3)	10.5 (7.4)	0.09
Anxiety (n=220)	4 (17%)	9 (12%)	18 (15%)	0.7
ACR Fibromyalgia Criteria				
2016 Fibromyalgia criteria (%) (n=206)	3 (13%)	2 (3%)	24 (21%)	0.001
2011 Fibromyalgia Severity Score (FSS)	6.6 (5.5)	5.3 (4.1)	8.9 (6.0)	<0.0001
WPI (widespread pain index)	3.5 (3.7)	2.3 (2.6)	4.4 (4.2)	0.0003
SSS (symptom severity score)	3.2 (2.7)	3.0 (2.4)	4.4 (2.5)	0.0004
SSS Elements (moderate-severe)				
Fatigue	11 (46%)	32 (41%)	79 (64%)	0.004
Cognitive dysfunction	5 (21%)	11 (14%)	37 (30%)	0.03
Waking unrefreshed	10 (42%)	27 (35%)	65 (53%)	0.04
Laboratory Measures				
	Mean (SD)	Mean (SD)	Mean (SD)	p-value
UPC ratio (n=217)	1655.9 (1153.2)	204.4 (175.4)	98.9 (107.0)	<0.0001
WBC (n=213)	6.1 (2.2)	6.0 (3.0)	5.8 (2.5)	0.9
Platelets (n=213)	235.9 (96.5)	240.5 (76.6)	251.2 (81.3)	0.6
	n (%)	n (%)	n (%)	
Low C3 or C4 (n=218)	9 (38%)	23 (32%)	25 (21%)	0.1
+anti-dsDNA (n=218)	11 (46%)	23 (32%)	31 (26%)	0.1
Medications				
Prednisone use	19 (79%)	39 (50%)	35 (28%)	<0.0001
Plaquenil use	19 (79%)	66 (85%)	98 (80%)	0.7
SNRI use	3 (13%)	8 (10%)	23 (19%)	0.3
SSRI use	3 (13%)	9 (12%)	18 (15%)	0.9
Gabapentin or pregabalin	6 (25%)	15 (19%)	24 (20%)	0.8
Muscle relaxer	1 (4%)	6 (8%)	11 (9%)	0.8
Tramadol	3 (13%)	3 (4%)	6 (5%)	0.3
Opioids	3 (13%)	12 (15%)	11 (9%)	0.4
NSAIDs	1 (4%)	0 (0%)	19 (15%)	0.0001

The prevalence of fibromyalgia was 13% in active nephritis, 3% in nephritis remission and 21% in non-nephritis patients (p=0.001). LN patients had significantly lower fibromyalgia severity, symptom severity, areas of pain, fatigue, cognitive, and sleep dysfunction. Patient-reported disease activity was significantly lower in patients with LN remission. Rates of anxiety and depression were similar across active LN and non-nephritis groups.

Conclusion: Patients with active and inactive LN report less fatigue, fibromyalgia, sleep, and cognitive dysfunction compared to non-nephritis patients. There were differences in demographics as well as greater social support in nephritis patients. Differences in social support could potentially mitigate fatigue and fibromyalgia in nephritis patients. There was no difference in anxiety or depression, suggesting fibromyalgia can occur independently of mood disorders. The drivers of low HRQoL may be distinct across SLE subgroups. Lupus nephritis patients have high rates of disability and poor HRQoL; however, the mechanism underlying these outcomes is nephritis is less likely related to features of fibromyalgia.

Disclosure: J. Rogers, None; **M. Clowse**, UCB, 5, GSK, 2, 5, Astra Zeneca, 5, Pfizer, 2; **L. Criscione-Schreiber**, None; **J. Doss**, None; **R. Sadun**, None; **K. Sun**, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 2, Pfizer, 2.

Abstract Number: 0274

The Rising Incidence of Lupus Nephritis: A Population-Based Study of Four Decades

Mehmet Hocaoglu[1], Shirley-Ann Osei-Onomah[2], Jesse Dabit[3], Rachel Giblon[3], Thomas O'Byrne[3], Fernando C. Fervenza[3], Cynthia Crowson[4] and Ali Duarte-Garcia[3], [1]University of Maryland Medical Center Midtown Campus, Baltimore, MD, [2]Mayo Clinic, Rochester, [3]Mayo Clinic, Rochester, MN, [4]Mayo Clinic, Rochester, Minnesota, USA, Rochester, MN

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Estimating the incidence of lupus nephritis (LN) is important to understand disease burden, particularly since patients with LN have a higher morbidity and mortality than other patients with systemic lupus erythematosus (SLE). Population-based studies that investigate the incidence of LN are lacking, and changes over time remain uncertain. We aimed to estimate the incidence of LN and its secular trends in a well-defined geographic region between 1976 and 2018.

Methods: All patients who had an SLE related diagnostic codes or the following laboratory measures: anti-nuclear antibodies, anti-double stranded DNA, anti-Sm, anti-cardiolipin, anti-beta 2 glycoprotein 1antibodies, complement, coombs and lupus anticoagulant were identified using a population-based research infrastructure. Medical records were thoroughly reviewed from 1976-2018. LN was defined as patients who had either 1) biopsy proven LN in the presence of a positive ANA or ds-DNA antibody, or 2) meeting one of the following SLE criteria: ACR97, SLICC or ACR/EULAR 2019 and developing proteinuria (500 mg in 24hrs urine collection or protein/creatinine ratio > 0.5) that did not have a better explanation. Patients with diabetes or other causes of proteinuria were excluded.

Incident cases were defined as a patient who had been a resident of our geographic region for at least one year prior to meeting the case definition for LN. The incidence date was the earliest date that the patient fulfilled either case definition. LN class data was obtained from biopsy reports. Age- and sex- specific incidence rates were adjusted to the 2010 US white population. The 95% Confidence intervals for incidence rates were calculated by assuming the data follows a Poisson distribution.

Table 1. Demographics and Clinical Characteristics of Incident Lupus Nephritis cohort

Characteristics	Timeframe 1976 to 1988 (N=7)	1989 to 1998 (N=9)	1999 to 2008 (N=13)	2009 to 2018 (N=19)	Total (N=48)
Age, years, mean (SD)	42.0 (15.5)	32.4 (15.1)	37.9 (14.6)	40.7 (19.3)	38.6 (16.7)
Female Sex, n (%)	5 (71)	9 (100)	11 (85)	13 (68)	38 (79)
Race, n (%)					
Asian	0 (0)	2 (25)	5 (38)	4 (21)	11 (23)
Black/African American	0 (0)	0 (0)	0 (0)	3 (16)	3 (6)
Caucasian/White	7 (100)	6 (75)	8 (62)	11 (58)	32 (68)
Other	0 (0)	0 (0)	0 (0)	1 (5)	1 (2)
No information	0	1	0	0	1
Hispanic, n (%)					
No	7 (100)	8 (100)	12 (92)	16 (84)	43 (92)
Yes	0 (0)	0 (0)	1 (8)	3 (16)	4 (8)
Unknown	0	1	0	0	1
LN Class, n (%)					
Class II	0 (0)	0 (0)	1 (8)	1 (5)	2 (4)
Class III	1 (14)	0 (0)	5 (38)	3 (16)	9 (19)
Class IV	3 (43)	2 (22)	4 (31)	7 (37)	16 (35)
Class V	2 (29)	1 (11)	1 (8)	4 (21)	8 (17)
No biopsy	1 (14)	6 (67)	2 (15)	3 (16)	12 (25)

Table 2. Incidence rates of lupus nephritis from 1976 -2018 and by decade.

	Female		Male		Total	
Calendar years	N	Rate* per 100,000 (95CI)	N	Rate* per 100,000 (95CI)	N	Rate** Per 100,000 (95CI)
1976-2018	38	1.3 (0.9, 1.7)	10	0.4 (0.2, 0.7)	48	0.9 (0.6, 1.1)
1976-1988	5	0.7 (0.0, 1.5)	2	0.5 (0.0, 1.3)	7	0.6 (0.1, 1.2)
1989-1998	9	1.5 (0.5, 2.6)	0	0.0 (0.0, 0.0)	9	0.8 (0.2, 1.3)
1999-2008	11	1.4 (0.6, 2.3)	2	0.3 (0.0, 0.6)	13	0.9 (0.4, 1.3)
2009-2018	13	1.6 (0.7, 2.5)	6	0.8 (0.2, 1.5)	19	1.2 (0.7, 1.8)

*Age-adjusted to the US White 2010 population
**Age- and sex- adjusted to the US White 2010 population

Table 3. Age- and sex-specific incidence rates of Lupus Nephritis

	Female		Male		Total	
Age	N	Rate per 100,000 (95CI)	N	Rate per 100,000 (95CI)	N	Rate Per 100,000 (95CI)
0-17	3	0.4	1	0.1	4	0.3
18-29	11	1.9	2	0.4	13	1.2
30-39	10	2.3	1	0.3	11	1.3
40-49	6	1.7	3	0.9	9	1.3
50-59	4	1.4	2	0.7	6	1.1
60-69	1	0.5	0	0.0	1	0.3
70-79	3	2.1	1	0.9	4	1.6
Total	38	1.3* (0.9, 1.7)	10	0.4* (0.2, 0.7)	48	0.9** (0.6, 1.1)

*Age-adjusted to the US White 2010 population
**Age- and sex- adjusted to the US White 2010 population

Results: We identified 48 incident cases between the years 1976 and 2018. As detailed in Table 1, the mean age was 38.6 years (SD15.5), 79% were female and 21% male. The racial distribution was 6% Black, 23% Asian, 68% Caucasian while 8% were Hispanic. There was a decrease in the proportion of Caucasians over the decades.

The overall LN incidence was 0.9 (95%CI: 0.6, 1.1) per 100,000 (Table 2). The incidence rate in females was 1.3 (95%CI: 0.9, 1.7) while in males was 0.4 (95%CI: 0.2, 0.7) per 100,000. Age- and sex- specific incidence peaked at 30-39 years for females and 40-49 for males with rates of 2.3 and 0.9 per 100,000 respectively.

The incidence of LN doubled from 0.6 (95%CI: 0.1, 1.2) in 1976-1988 period to 1.2 (95%CI: 0.7, 1.8) in 2009-2018 period per 100,000 (Table 2).>

For patients who had a biopsy, the LN class distribution was 6% class II, 25% class III, 47% class IV and 22% class V.

Conclusion: Our report provides a population-based estimate on the incidence of LN in the United States previously unavailable. Furthermore, our data shows that the incidence of LN has doubled in the last four decades. Future studies are needed to explain whether these changes are due to increases in racial and ethnic diversity, better detection or environmental influences.

Disclosure: M. Hocaoglu, None; **S. Osei-Onomah**, None; **J. Dabit**, None; **R. Giblon**, None; **T. O'Byrne**, None; **F. Fervenza**, None; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1; **A. Duarte-Garcia**, None.

Abstract Number: 0275

Paradoxical Relationship Between Disease Activity and Satisfaction with Care in Lupus

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Satisfaction with care (SC) is increasingly being used as a surrogate of QOC, with growing emphasis on optimizing SC/patient experience in health care. We previously reported higher disease activity in systemic lupus erythematosus (SLE) to be associated with better SC in a large International study with cross sectional data. However, health care systems differ across regions and countries which could impact SC. Herein, we aimed to study association of disease activity and SC with disease activity (SLEDAI and Treat to Target T2T) at baseline and longitudinally in a single center.

Methods: Baseline (Time 1) data on 147 consenting SLE patients, meeting ACR criteria, were used from the Rush Lupus data repository. Patients completed assessments of demographics, PROs (LupusPROv1.8 and MDHAQ) at routine clinic visits. Other data collected included disease duration, SLE medications, disease activity (SELENA-SLEDAI), Treat to Target category (T2T-Nonoptimal, Low disease activity state -LDAS, Remission on therapy [RONT] and Remission Off therapy [ROFT]), damage (SLICC-SDI/ACR) and other comorbidities. SC was measured using the LupusPRO SC domain items. Univariate and multivariate regression analyses was done, with SC as a dependent variable and demographics, disease activity/duration, comorbidities, and PROs (Lupus-PRO and MDHAQ) as independent variables.

Table 1. Predictors of Satisfaction with Care

Variable	Univariate Analyses			Multivariate analysis, R^2=0.12		
	β	95% CI	*P*	β	95% CI	P
Demographics						
Education	-5.63	12.27 to 1.01	0.1			
Hispanic vs Non-Hispanic	14.01	1.31to 26.7	**0.03**	11.69	-0.70 to 24.08	0.06
Disease features						
Disease duration	0.288	-.35 to 0.93	0.38			
ROFT	-14.06	-25.65 to -2.48	**0.018**	-12.4	-23.7 to -1.03	**0.03**
Comorbidities						
HTN	6.228	-3.7 to 16.2	0.22			
LupusPRO						
LMED	0.126	0.01 to 0.15	0.028			
PRF	0.147	−0.22 to −0.08	0.12			
BI	0.133	0.33 to 0.43	0.1			
SS	0.202	0.05 to 0.35	**0.008**	0.186	0.04 to 0.33	**0.01**
CO	0.107	0.49 to 0.62	0.277			

We developed a conceptual model based on Time 1 data. Longitudinal (Time 2) paired data on T2T and SC were available for 72 patients. We performed univariate linear regression with SC at Time 2 as the dependent and ROFT (Yes/No) T2T Time 1 as the independent variable. P value of ≤0.05 was considered significant.

Results: Mean (SD) age was 43.8 (13.4) years; 90% were female. Median (IQR) SLEDAI was 2(4; 0-14) and SLEDAI was ≥ 4 in 35%. Current prednisone use was observed among 35% patients. T2T category distribution were: Non-Optimal 25%, LDAS 34%, RONT 18% and ROFT 22%. Mean (SD) SC was 86.9±26.8. Total SLEDAI was not correlated with SC.

On univariate analysis, Hispanic ethnicity, and LupusPRO domains of Lupus Medications, and Social Support were directly associated with SC while ROFT (Yes/No) status was inversely associated with SC. On multivariate analysis, LupusPRO-Social Support and ROFT remained independent predictors of SC cross-sectionally (Table 1).

Longitudinal analysis also showed ROFT status at T1 to be a predictor of lower SC at T2 (β -15.56, 95% CI -30.2, -0.92, p 0.038).

Conclusion: SLE Patients in remission off therapy have worse satisfaction with care (as compared to those without ROFT) both at baseline and longitudinally. It is plausible that greater interaction with the care providers or health care system due to either active disease or use of immunosuppressive medications contributes to greater SC among those not in remission off therapy. Satisfaction with care may not be an appropriate surrogate to use for QOC in the context of attainment of disease activity status.

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Abstract Number: 0276

Type 2 SLE Symptoms Persist Despite Type 2 Medication Polypharmacy

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Management of Type 2 SLE (widespread pain, fatigue, depression, sleep distrubance, and cognitive dysfunction) is challenging and often requires multiple medications to ameliorate symptoms. Polypharmacy can increase the risk of drug interactions, side effects, adverse reactions, non-adherence, and lead to greater healthcare costs. Many medications used for Type 2 SLE are associated with QTc interval prolongation. The purpose of this study was to examine symptoms and Type 2 medication polypharmacy.

Methods: This was a cross-sectional study of SLE patients (SLICC 2012 criteria) enrolled in a university registry from May 2018-March 2019. All patients completed the Systemic Lupus Activity Questionnaire (SLAQ), Patient Health

Table 1. Characteristics of SLE patients by Type 2 medication use

	No Type 2 Medications	One Type 2 Medication	Two or More Type 2 Medications	p-value
	n=79	n=39	n=41	
Socioeconomic Factors				
Age n(SD)	38.7 (12.5)	45.0 (13.3)	47.5 (12.6)	0.001
Disease Duration (yrs) (n=148)	12.3 (7.5)	17.2 (8.4)	17.1 (8.8)	0.002
Social Support n(SD)	3.1 (2.0)	3.4 (1.8)	3.0 (2.0)	0.7
Sex, female	74 (93.7%)	38 (97.4%)	40 (97.6%)	0.6
Race				0.14
Black	49 (62.0%)	24 (61.5%)	18 (43.9%)	
White	22 (27.8%)	13 (33.3%)	21 (51.2%)	
Other	8 (10.1%)	2 (5.1%)	2 (4.9%)	
Hispanic (n=158)	8 (10.1%)	0 (0%)	1 (2.4%)	0.048
SLE Manifestations and Disease Activity				
Active nephritis	10 (12.7%)	6 (15.4%)	3 (7.3%)	0.5
Historical nephritis	35 (44.3%)	20 (51.3%)	21 (51.2%)	0.7
Historical arthritis	25 (31.6%)	9 (23.1%)	10 (24.4%)	0.6
Clinical SLEDAI Mean(SD)	1.3 (2.5)	1.7 (2.5)	1.6 (2.3)	0.7
Full SLEDAI Mean (SD)	3.7 (4.3)	4.2 (4.3)	2.5 (3.0)	0.13
QTc Interval Prolonging Type 2 Medications				
QTc Type 2 Meds		23(59%)	35(85.4%)	0.009
Qtc interval prolonging medications: TCA, SNRI, SSR, mirtazapine, tramadol, trazodone				

Questionnaire-9 (PHQ-9), and 2016 ACR Fibromyalgia criteria questionnaires. Type 2 SLE was defined as a polysymptomatic distress (PSD) score ≥8. Type 2 medications included antidepressants (serotonin and norepinephrine reuptake inhibitors (SNRIs), selective serotonin reuptake inhibitors (SSRIs), tricyclic antidepressants (TCAs), mirtazapine, bupropion, muscle relaxers (cyclobenzaprine, baclofen, metaxalone), gabapentinoids (gabapentin, pregabalin), topiramate, zolpidem, trazodone, tramadol, anxiolytics, stimulants, and DHEA. Relationships between clinical variables and medications in different groups were analyzed using ANOVA and Fisher's exact test.

Results: One hundred and fifty-nine patients completed surveys (96% female, 66% Black, 42% Type 2 SLE.) Type 2 medications were prescribed in 50% of patients. Patients on Type 2 medications were older and had longer duration of SLE (Table 1). Multiple Type 2 medication use was more frequent in Type 2 SLE patients than non-Type 2 patients (43% vs 25.7%). The average number of Type 2 medications was 1.9. Of patients taking Type 2 medications, 72% were taking at least one QTc interval prolonging Type 2 medications (mean 1.3 medications).

Despite pharmacologic therapy, 58% of SLE patients had active Type 2 SLE (Table 2). The number of patients with depression and Type 2 SLE activity was greater in those on multiple medications. Moreover, the severity of nearly all Type 2 SLE symptoms including widespread pain, fatigue, depression, forgetfulness and sleep dysfunction was greatest in those on more than one Type 2 medication compared to no Type 2 medications or one Type 2 medication.

Table 2. Type 2 SLE symptoms and Type 2 medication polypharmacy

	No Type 2 Medications	One Type 2 Medication	Two or More Type 2 Medications	p-value
	n=79	n=39	n=41	
Active Type 2 SLE (PSD ≥8)	21 (26.6%)	17 (43.6%)	29(70.7%)	<0.001
2016 ACR Fibromyalgia Criteria				
Fibromyalgia Severity Score	6.0 (4.4)	9.3 (5.9)	13.0 (6.8)	<0.0001
Widespread Pain Index	2.2 (2.4)	3.6 (3.8)	6.4 (4.9)	<0.0001
Symptom Severity Score (SSS)	2.8 (2.2)	4.1 (2.4)	5.2 (2.3)	<0.0001
SSS Elements (moderate-severe)				
Cognitive dysfunction	10 (12.7%)	29 (74.4%)	29 (70.7%)	0.05
Fatigue	29 (36.7%)	22 (56.4%)	30 (73.2%)	0.001
Sleep dysfunction	25 (31.6%)	18 (46.2%)	27 (65.9%)	0.002
PHQ-9				
Depression criteria (n=20)	3 (3.8%)	5 (12.8%)	7 (17.1%)	0.02
Depression severity (PHQ-9 score)	3.9 (3.6)	6.7 (5.3)	8.3 (4.7)	<0.0001
SLAQ (moderate or severe)				
Forgetfulness	8 (10.1%)	32 (82.1%)	25 (61.0%)	0.001

Conclusion: SLE patients have distressing Type 2 symptoms that often require complex pharmacologic interventions. Although the majority of patients with Type 2 SLE activity take therapies aimed at these symptoms, they continue to have a multitude of symptoms. Furthermore, severe symptoms persist despite nearly half of patients taking multiple medications. Several Type 2 medications can prolong the QTc interval, which when combined with other QTc prolonging medications such as hydroxychloroquine, can augment the risk of arrhythmia. The average number of Type 2 SLE medications is similar to the number used for Type 1 SLE, highlighting the difficulty managing Type 2 SLE, the need for targeted Type 2 therapeutics, and the importance of non-pharmacologic management.

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Abstract Number: 0277

Incidence and Time to Classification of Systemic Lupus Erythematosus by Three Different Classification Criteria

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

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Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Classification criteria are standardized definitions required to identify well defined cohorts of patients for research. In practice they are also used as a framework for the diagnosis of diseases with heterogeneous

Table 1. Age- and sex- adjusted incidence rates by different SLE classification criteria from 2000-2018

Table 1. Age- and sex- adjusted incidence rates by different SLE classification criteria from 2000-2018

	1997 ACR		2012 SLICC		2019 EULAR/ACR	
Age	N	Rate Per 100,000	N	Rate Per 100,000	N	Rate Per 100,000
0-17	3	0.4	3	0.4	3	0.4
18-29	11	2.2	16	3.2	16	3.2
30-39	25	6.3	33	8.3	32	8.1
40-49	18	4.8	16	4.3	25	6.7
50-59	13	3.7	19	5.4	20	5.7
60-69	11	4.7	11	4.7	16	6.9
70-79	5	3.5	9	6.3	8	5.6
≥80	5	5.1	7	7.2	7	7.2
Total*	**91**	**3.3 (2.6, 4.0)**	**114**	**4.2 (3.4, 4.9)**	**127**	**4.7 (3.9, 5.5)**

*Age- and sex- adjusted to the US White 2010 population

Table 2. Demographics of SLE by each criteria

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	1997 ACR (N=91)	2012 SLICC (N=114)	2019 EULAR/ACR (N=127)
Age at classification (yrs), mean (SD)	46.4 (17.8)	45.6 (18.2)	46.2 (18.0)
Female Sex, n (%)	71 (78)	93 (82)	100 (79)
Race, n (%)			
Asian	17 (19)	19 (17)	18 (14)
Black/African American	7 (8)	8 (7)	8 (6)
Caucasian/White	66 (72)	86 (75)	99 (79)
Other	1 (1)	1 (1)	1 (1)
Unknown	0	0	1 (1)
Hispanic Ethnicity, n (%)	8 (9)	9 (8)	9 (7)
Time from first disease manifestation to criteria fulfillment (months), median (IQR)	45.3 (2.5, 110)	33.2 (0.43,108.5)	28.47 (0.13, 102.9)

manifestations such as Systemic Lupus Erythematosus (SLE). Recently the 2019 European League Against Rheumatism/American College of Rheumatology classification criteria for SLE was published. The sensitivity and specificity of the 2019 EULAR/ACR criteria are different from the 1997 ACR criteria and the 2012 Systemic Lupus International Collaborating Clinics (SLICC) criteria. The effect on the incidence estimations of the disease using different criteria has not been studied. A reason to develop the new EULAR/ ACR criteria was to classify patients earlier in their disease process; however it has not been proven if this was indeed accomplished. We aimed to 1) estimate the incidence and time-to-classification of SLE using the 1997 ACR, 2012 SLICC and 2019 EULAR/ACR criteria.

Methods: We identified potential incident SLE cases from 2000-2018 in a geographically well-defined population using diagnostic codes for cutaneous and systemic lupus and the following laboratory measures: anti-nuclear antibodies, anti-double stranded DNA, anti-Sm, anticardiolipin, anti-beta 2 glycoprotein 1 antibodies, complement, coombs and lupus anticoagulant. Clinical data included in the 1997 ACR, 2012 SLICC and 2019 EULAR/ACR criteria were abstracted through chart reviews. If a disease manifestation could be better explained by another condition rather than SLE, it was not counted towards the criteria. We defined the time-to-classification based on the first lupus-attributable disease manifestation ever documented in the record to the time meeting criteria by each of the three definitions. Incidence rates were age and/or sex adjusted to the estimated 2010 white population of the US. To compute 95% confidence intervals for incidence rates, it was assumed that the number of incident cases followed a Poisson distribution. Time-to-classification among different criteria was compared using signed rank test.

Results: There were 127 incident cases that met the EULAR/ACR 2019 criteria, corresponding to an adjusted incidence of 4.7 per 100,000 (95% CI, 3.9-5.5). The incidence was higher than that of the 1997 ACR (91 cases; 3.3 per

100,000 [95%CI 2.6 - 4], p=0.015) but similar to 2012 SLICC criteria (114 cases; 4.2 per 100,000 [95%CI, 3.4 - 4.9], p=0.40). (Table 1)

The median time from first disease manifestation to criteria fulfillment was shorter for the EULAR/ACR 2019 criteria (28.47 months) than the 1997 ACR criteria (45.3 months, p< 0.001) and similar to the SLICC 2012 criteria (33.2 months, p=0.89).

The demographic characteristics are detailed in Table 2. Female: male ratio, mean age at classification and the proportion across different races/ethnic groups were similar across the three criteria.

Conclusion: In this population-based study, the incidence of SLE was higher and time to criteria fulfillment sooner by 2019 EULAR/ACR criteria compared to the 1997 ACR but not significantly different than the 2012 SLICC criteria.

Disclosure: A. Duarte-Garcia, None; **M. Hocaoglu**, None; **S. Osei-Onomah**, None; **J. Dabit**, None; **R. Giblon**, None; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1.

Abstract Number: 0278

Trends in Incidence of Cutaneous Lupus Erythematosus from 1976 to 2018: A Population-Based Study

Mehmet Hocaoglu[1], Mark Denis P. Davis[2], Shirley-Ann Osei-Onomah[3], Jesse Dabit[2], Rachel Giblon[2], Thomas O'Byrne[2], Cynthia Crowson[4] and Ali Duarte-Garcia[2], [1]University of Maryland Medical Center Midtown Campus, Baltimore, MD, [2]Mayo Clinic, Rochester, MN, [3]Mayo Clinic, Rochester, [4]Mayo Clinic, Rochester, Minnesota, USA, Rochester, MN

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cutaneous lupus erythematosus (CLE) is a heterogeneous chronic disease with potential for long lasting morbidity. Studies that provide incidence data on the entire spectrum of CLE are needed to better estimate the disease burden. Furthermore, it is unclear whether secular changes in risk factors such as smoking over the decades have had an impact in CLE incidence. We aimed to investigate the incidence of CLE and its secular trends from 1976 to 2018.

Methods: All patients in a geographically well-defined area who received a SLE or CLE diagnostic codes or the following laboratory measures: ANA, anti-double stranded DNA, anti-Sm, complement, and antiphospholipid antibodies underwent a thorough review of clinical notes, pathology and medical photography.

Incident cases were defined based on the criteria by Sontheimer. We categorized CLE as follows: discoid lupus erythematosus (DLE), lupus panniculitis (LP), lupus tumidus (TL), chilblain lupus (CHLE) and subacute cutaneous lupus (SCLE). Those with uncertain diagnosis or subtype were reviewed by a CLE expert dermatologist. The incidence date was when the skin lesion was first described in the medical record. We included both patients with CLE as well as those with systemic lupus erythematosus (SLE) with cutaneous manifestations. We considered chronic CLE in patients who did not have a concurrent (within one year of cutaneous manifestations) or previous diagnosis of SLE.

Table 1. Demographics and Clinical Characteristics of Cutaneous Lupus Erythematosus

Characteristic	Timeframe				
	1976 to 1988 (N=36)	1989 to 1998 (N=49)	1999 to 2008 (N=58)	2009 to 2018 (N=66)	Total (N=209)
Age, years, mean (SD)	45.9 (16.3)	49.3 (19.1)	52.6 (17.1)	51.5 (15.8)	50.3 (17.1)
Female Sex, n (%)	23 (64)	36 (74)	43 (74)	49 (74)	151 (72)
Race, n (%)					
Asian	0 (0)	2 (4)	4 (7)	5 (8)	11 (5)
Black/African American	0 (0)	2 (4)	5 (9)	7 (11)	14 (7)
Caucasian/White	34 (100)	44 (92)	48 (83)	53 (82)	179 (87)
Native American	0 (0)	0 (0)	1 (2)	0 (0.0)	1 (1)
Unknown	2	1	0	1	4
Hispanic, n (%)	1 (3)	0 (0)	2 (3)	3 (16)	3 (2)
Unknown	2	3	0	1	6
CLE Subtype, n (%)					
Subacute Only	3 (8)	12 (25)	16 (28)	18 (27)	49 (23)
Discoid Lupus Erythematosus	32 (89)	35 (71)	30 (52)	35 (53)	132 (63)
Lupus Panniculitis	0 (0)	0 (0)	1 (2)	2 (3)	3 (1)
Chilblain Lupus	0 (0)	1 (2)	2 (3)	4 (6)	7 (3)
Lupus Tumidus	0 (0)	0 (0)	8 (14)	7 (11)	15 (7)
Multiple subtypes	1 (3)	1 (2)	1 (2)	0 (0)	3 (2)

Age and sex specific incidence rates were adjusted to the 2010 US white population. The 95% confidence intervals for incidence rates were computed assuming that the data follows a Poisson distribution.

Results: We identified a cohort of 209 incident CLE cases between 1976 and 2018. Mean age was 50.3 (SD 17.2). 72% were female. The racial make-up was 5% Asian, 7% Black, 87% Caucasian, 1% Native American. 2% percent were Hispanic. The proportion of Caucasians decreased over the years.

Out of 209 patients, 13 (6.2%) had a previous or concurrent diagnosis of SLE by the ACR 97 criteria and 94% were considered chronic CLE.

Table 2. Age- and sex-specific incidence rates for CLE

	Female		Male		Total	
Age	N	Rate per 100,000 (95% CI)	N	Rate per 100,000 (95% CI)	N	Rate Per 100,000 (95% CI)
0-17	2	0.3	1	0.1	3	0.2
18-29	19	3.2	4	0.8	23	2.1
30-39	22	5.1	11	2.8	33	4.0
40-49	31	8.8	12	3.7	43	6.4
50-59	29	9.9	14	5.2	43	7.7
60-69	24	11.8	10	5.6	34	8.9
70-79	12	8.3	6	5.5	18	7.1
>80	12	10.7	0	0.0	12	7.1
Total	151	6.2* (5.2, 7.2)	58	2.7* (2.0, 3.5)	209	4.5** (3.9, 5.2)

*Age-adjusted to the US White 2010 population
**Age- and sex- adjusted to the US White 2010 population

Figure 1. Trends in age-adjusted Cutaneous Lupus Erythematosus incidence over time by Sex (female is solid line and male is dashed line)

The distribution of the CLE subtypes was: 23% SCLE, 63% DLE, 1% LP, 3% CHLE, 7% TL. 1% of the cases had more than one subtype. The proportion of LT, CHLE and LP increased over the decades. (Table 1)

The overall incidence rate of CLE between 1976 and 2018 was 4.5 (95%CI: 3.9, 5.2) per 100,000. Females had a higher incidence than males: 6.2 (95%CI: 5.2, 7.2) and 2.7 (95%CI: 2.0, 3.5) per 100,000, respectively. Age- and sex-specific incidence rates peak at the 60-69 age group in both females and males, 11.8 and 5.6 per 100,000, respectively. (Table 2) There was an increase in CLE incidence during 1985-1995 that was observed in both sexes and posteriorly trended downwards. (Figure 1)

Conclusion: Our data shows that the overall incidence of CLE has remained stable over the decades with a sudden increase in 1985-1995 with posterior return to prior rates. The majority of the CLE cases do not have SLE prior or concurrent to diagnosis. The clinical characteristics of CLE changed with rising proportion of TL, SCLE, CL, LP cas-

es. More studies are needed to investigate whether these changes are due to rising awareness of rare subtypes or changes in environmental or demographic factors.

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Abstract Number: 0279

Pulmonary Involvement in a Single Center Cohort of Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The prevalence of SLE pulmonary involvement varies depending on several factors, including diagnostic methods. In this study, we sought to determine the frequency of involvement with different diagnostic methods in a single-center cohort.

Methods: 300 randomly chosen patients with SLE were included. Chest x-ray (CXR), lung spirometry, carbon monoxide diffusion test (DLCOc), and echocardiography were performed. High-resolution thorax computed tomography (HRCT) was done for a definite diagnosis of interstitial lung disease (ILD) whilst diagram electromyography (EMG), ultrasonography (USG), and magnetic resonance imaging (MR) were utilized to diagnose shrinking lung syndrome (SLS).

Results: 88,3 % of the cohort was female. The mean age and follow-up time were 43 and 11,5 years respectively. Of 300 patients, 16 % had ILD, 6,7 % had pulmonary hypertension (PHT), 3 % had SLS, 0,3 % had pulmonary infarction. At the start of the study, the prevalence of these involvements obtained from the patients' records showed that 4 % had ILD, 5 % PHT, 0,3 % SLS, and 0,3 % pulmonary infarction. The median age, mean duration of disease, and follow-up time were significantly higher and longer in patients with ILD compared to patients without ($p< 0.05$). Forced expiratory volume (FEV1), forced vital capacity (FVC), DLCOc, and total lung capacity (TLC) were significantly lower in patients with ILD and with SLS ($p< 0,001$). Patients with ILD had a significantly higher frequency of arthritis, serositis, Raynaud myositis, and anti-Scl70 positivity. Neuropsychiatric damage, avascular necrosis, diabetes, and malignancy were significantly more frequent in those patients. All patients with suspected SLS has undergone diagram EMG, USG, and MR. Out of 10 suspected cases, in 6 EMG, in 5 USG and in 9 MR was compatible with SLS diagnosis(table 1). 5 patients had 3 of the diagnostic methods positive to diagnose SLS. Patients with SLS had a higher frequency of pleuritis, pericarditis, leukopenia, anti-Ro, and anti-La antibodies. Muscle atrophy and weakness, avascular necrosis were more frequent in this group of patients ($p< 0.05$). There were more patients treated with mycophenolate mofetil (MMF) and cyclophosphamide in the SLS group whilst more with MMF in the ILD group. Significantly higher frequency of patients had stopped using hydroxychloroquine (HCQ) in the ILD group ($p=0,04$).

Table 1. Spirometry, DLCO, diaphragm EMG, diaphragm USG and MR results of patients with Shrinking Lung Syndrome.

Patient/ Age/ Sex	FEV 1 (%)	FVC (%)	DLCO (%)	TLC (%)	USG Movement during deep inspiration (L)	USG Movement during deep inspiration (R)	USG Diaphragm thickness (L)	USG Diaphragm thickness (R)	MR Higher side	MR Height difference	EMG Rest AMP (R)	EMG Rest LAT (R)	EMG Rest AMP (L)	EMG Rest LAT (L)
1/44/F	47	56	45	61	4,70	3,72	4,82	1,23	R	4,92	0,2	7	0,4	6,35
2/57/F	65	73	50	71	4,74	1,98	3,00	1,04	R	6,19	0,3	6,4	0,5	5,75
3/39/F	59	59	44	65	2,59	2,26	2,48	1,84	R	2,87	0,6	7,1	0,8	6,85
4/38/M	63	62	65	66	3,01	2,24	2,84	1,80	R	2,64	0,5	6	0,7	5,6
5/23/F	67	79	53	78	3,06	2,77	2,55	2,19	R	1,67	0,6	6,7	1,2	6,05
6/60/F	62	70	55	64	3,06	2,17	1,59	1,31			0,4	8	0,6	6
7/58/F	71	72	47	54	5,73	4,67	2,09	1,79	R	2,45	0,1	6,15	0,3	6
8/37/F	53	55	65	63	4,17	2,83	3,18	1,97	R	1,73	0,8	4,75	1,2	4,35
9/66/F	70	62	62	62	2,12	4,62	1,62	2,08	L	0,95	0,9	6	0,5	5,2
10/28/F	39	37	45	45	1,59	2,49	1,44	1,63	L	0,78	0,7	5,8	0,5	6,15

Conclusion: Interstitial lung disease is common in patients with SLE and a considerable number of patients have SLS. Spirometry, diffusion tests, and chest x-ray are simple but valuable tools to shape a diagnostic approach for pulmonary involvement in patients with SLE. Diagram MR, USG, and EMG are complementary methods for a definite diagnosis in SLS. Considering the significant difference in prevalence between the start and the end of the study, one of the possibilities is the underrecognition of SLE pulmonary disease due to its being part of a multisystemic presentation. Moreover, the higher usage of immunosuppressives in these patients may support a multisystemic active disease. Although the drug effect is another concern, it is hard to establish a causal relationship due to the study's cross-sectional design. HCQ may have a role in ILD prevention.

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Abstract Number: 0280

Compliance and Validation of Patient Reported Outcome Information Collected from Lupus Patients Using a Mobile Application

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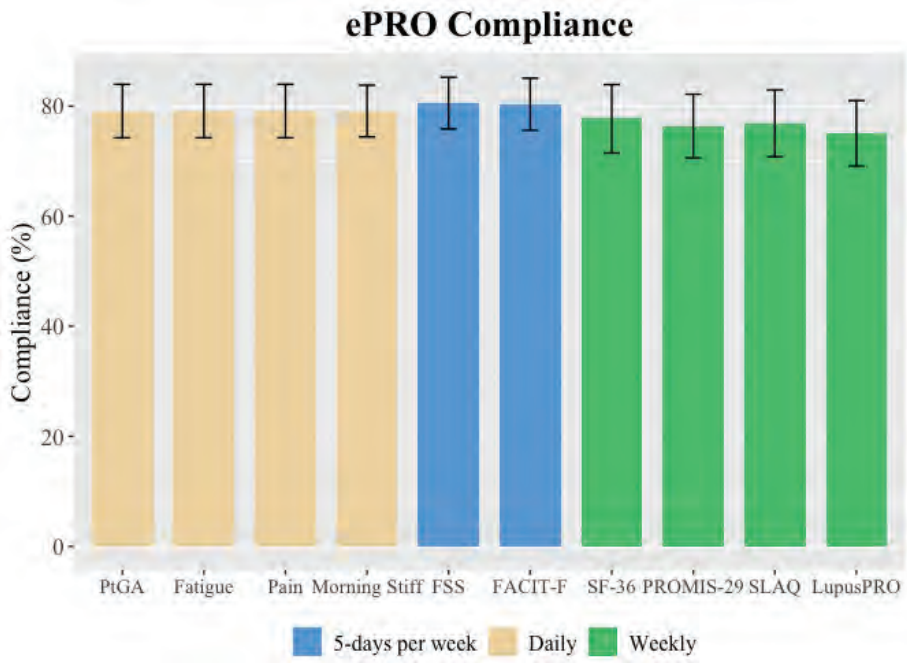
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Patient Reported Outcomes (PROs) can provide critical data in measuring the impact of a disease on an individual as well as the quality of response to treatment. However, PROs are oftentimes recorded intermittently and require patients to recall a period of several weeks or months. As a result, important PRO information may not always be representative of the complete recall period. The development of mobile technology to collect PRO data in an electronic format (ePRO) allows for more frequent assessment in real time and in the person's regular environment. The goal of this study was to assess the compliance and equivalence of a smart phone application (app) in collecting PRO data in individuals SLE.

Methods: A smart phone app was developed that collects ePRO data from various instruments, including the Fatigue Severity Scale (FSS), Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F), Short Form Health Survey (SF-36), Patient Reported Outcome Measurement Information System (PROMIS-29), Systemic Lupus Activity Questionnaire (SLAQ), and LupusPRO. Additionally, the duration of morning stiffness as well as patient global assessment (PtGA), pain and fatigue using a 10 cm visual analog scale were collected. Information was collected as part of a multicenter randomized interventional clinical trial of patients who met ACR criteria for the classification of



Compliance with PRO instruments collected with a mobile app.

Survey	Visit	ICC	Lower 90% CI	Upper 90% CI	P-value
SF-36: General Health	Month 6	0.986	0.9731	0.9928	0
SF-36: Physical Functioning	Month 1	0.9857	0.9754	0.9917	0
SF-36: Physical Functioning	Month 6	0.975	0.9521	0.9871	0
SF-36: Physical Functioning	Month 4	0.9746	0.9533	0.9863	0
SF-36: General Health	Month 1	0.9714	0.9513	0.9833	0
PROMIS-29: Physical Function	Month 4	0.9671	0.9403	0.982	0
SLAQ	Month 6	0.9668	0.9352	0.9831	0
LuPRO: N-HRQOL	Month 2	0.966	0.941	0.9805	0
PROMIS-29: Depression	Month 6	0.9654	0.9226	0.9849	0
PROMIS-29: Pain Interference	Month 6	0.9651	0.9218	0.9848	0
SF-36: Physical Functioning	Day 1	0.9649	0.9419	0.9788	0
Morning Stiffness	Month 3	0.9642	0.9413	0.9782	0
PROMIS-29: Anxiety	Month 6	0.9635	0.9184	0.9841	0
SF-36: Physical Functioning	Month 5	0.9607	0.9274	0.9789	0
SF-36: Bodily Pain	Month 4	0.96	0.9267	0.9783	0

Top 15 intraclass correlation coefficients (ICCs) and respective 90% confidence intervals.

SLE (NCT03098823). ePRO information was collected daily (PtGA, fatigue, pain, morning stiffness), 5-days per week (FSS, FACIT-F), or weekly (SF-36, PROMIS-29, SLAQ, LupusPRO), and biometric data (steps, sleep and location) was recorded daily with the app or a linked smart watch. Additionally, all PRO instruments were completed on seven occasions at the clinical sites utilizing both the app and standard paper forms separated by a distraction. To determine agreement between information collected with the app and the paper-administered PROs, intra-class correlation coefficients (ICCs), paired student's t-tests, and Bland-Altman plots for data collected at each of the seven site visits were evaluated. Compliance, demographic information and Cronbach's alpha as a measure of survey reliability were also assessed.

Results: For the 62 subjects from diverse ancestral backgrounds, compliance with ePRO completion was high for all PRO surveys (>75%; Figure 1). Cronbach's alpha values for each PRO ranged from 0.74 to 0.96 for the ePROs, and 0.70 to 0.96 for the paper versions, suggesting moderate to high inter-survey reliability in measuring the targeted concepts. Of the 168 ICC values computed from each site visit for each survey, 41 were indicative of moderate (0.5 to 0.75), 69 good (0.75 to 0.9) and 55 excellent (>0.90) reliability between measurement methods (Table 1). Bland-Altman plots verified method agreement with 151 of the pairwise comparisons yielding an insignificant difference.

Conclusion: The high rate of compliance in collecting ePROs and the high level of consistency between data collected by paper and electronic methods of administration indicate that the app provides highly reliable information capable of cataloging real-time changes in PROs in SLE patients.

Disclosure: K. Bell, None; **C. Dykas**, None; **H. Rainey**, None; **M. Comberg**, None; **M. Mora**, None; **P. Lipsky**, Horizon Therapeutics, 3.

Abstract Number: 0281

ANCA in SLE: Prevalence and Predictor Factors

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster I: Clinical Manifestations
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Background/Purpose: SLE is a systemic autoimmune disease notable for the ability to affect nearly every tissue, and is associated with a breadth of auto-antibodies. Anti-neutrophilic cytoplasmic antibodies (ANCA) are strongly associated with small-vessel vasculitis, specifically the ANCA-associated vasculitides, but their role in SLE is less clear.

Purpose: To determine whether ANCA are associated with disease features including vasculitis in SLE.

Methods: Patients with 4 or more of the 1971 or 1982 ACR classification criteria, or 3 criteria and a typical biopsy of SLE are registered in the database and are followed longitudinally, with clinical and laboratory information collected at 2-6-month intervals.

SLE patients with at least 2 ANCA tests, between Aug 1979 (when ANCA became locally available) and Nov 2019 were included. Patients with 2 consecutive ANCA (both C and P ANCA) were considered exposed in this study. Controls were patients who never had a positive ANCA. Index date was the time of the second ANCA. Vasculitis was defined by the SLEDAI-2K: ulceration, gangrene, tender finger nodules, periungual infarction, splinter hemorrhages, and biopsy/angiogram. Descriptive statistics were used to show patients' characteristics at ANCA positive or negative in patient groups, Kaplan-Meier survival curves were plotted for outcomes of first vasculitis, Weibull parametric survival regression was applied to evaluate the effects of ANCA positivity on the outcome of vasculitis adjusting other confounding variables.

Results: Of the 1426 patients tested for ANCAs on two occasions, 1091 (77%) had never tested positive, 145 (10%) tested positive twice and 190 (13%) tested positive once. Those that tested positive twice or more included 92 with only p-ANCA, 24 with only c-ANCA, and 29 with both. Median time between first and second ANCA was 12 months. Patients' demographics, clinical measurements, treatments are presented by ANCA subtype in table 1. Patients with either two positive ANCA-C or two positive ANCA-P had lower proportions of steroid treatment compared to 29 patients with both ANCA-C and ANCA-P positive, but were otherwise largely similar to those with both ANCA-C and ANCA-P positivity. Kaplan-Meier survival curves show significantly higher cumulative index of vasculitis in the 145 patients with any ANCA positive compared to none (p=0.0491, Figure 1). Survival regression models revealed that two or more ANCA-P positive (vs. normal ANCA patients) predicted the outcome of vasculitis after adjusting for SLE-

Table 1: Demographics: ANCA positive by subtype versus ANCA negative controls

VARIABLE	VALUE	pure ANCA-C patients	pure ANCA-P patients	both ANCA-C and ANCA-P patients	No ANCA positive
		N=24	N=92	N=29	N=1,091
Age at Index date	Mean ± SD	41.9 ± 15.2	41.3 ± 13.9	38.0 ± 16.2	37.7 ± 13.8
Sex	F	20 (83.3%)	88 (95.7%)	26 (89.7%)	965 (88.5%)
	M	4 (16.7%)	4 (4.3%)	3 (10.3%)	126 (11.5%)
Ethnicity	Black	2 (8.3%)	13 (14.1%)	1 (3.4%)	171 (15.7%)
	Caucasian	16 (66.7%)	65 (70.7%)	18 (62.1%)	663 (60.8%)
	Chinese	1 (4.2%)	8 (8.7%)	4 (13.8%)	113 (10.4%)
	Others	5 (20.8%)	6 (6.5%)	6 (20.7%)	144 (13.2%)
Disease duration at index	Mean ± SD	11.3 ± 12.1	11.5 ± 9.4	9.9 ± 9.8	6.9 ± 7.9
Follow up duration from index date to last visit	Mean ± SD	6.2 ± 7.0	6.9 ± 8.3	7.1 ± 7.4	9.7 ± 7.2
SLEDAI-2K score at index date	Mean ± SD	6.0 ± 5.7	4.7 ± 4.0	5.0 ± 5.6	6.9 ± 6.8
Adjusted Mean SLEDAI within 3 years prior to index	Mean ± SD	5.8 ± 5.1	5.0 ± 4.0	5.9 ± 5.5	7.2 ± 6.6
SLICC score at index date	Mean ± SD	1.2 ± 1.9	1.1 ± 1.4	0.8 ± 1.2	0.5 ± 1.1
Treated with steroids at index *	Yes (%)	11 (45.8%)	54 (58.7%)	25 (86.2%)	722 (66.2%)
Steroid dose (mg/day) at index	Mean ± SD	14.5 ± 10.3	12.0 ± 9.0	13.9 ± 12.4	18.1 ± 16.1
Cumulative steroid dose (gram) within 3 years prior to index	Mean ± SD	20.9 ± 25.8	28.8 ± 39.4	29.2 ± 48.4	13.1 ± 28.5
Treated with antimalarials at index	Yes (%)	13 (54.2%)	43 (46.7%)	15 (51.7%)	613 (56.2%)
Treated with Immunosuppressives at index	Yes (%)	9 (37.5%)	26 (28.3%)	9 (31.0%)	427 (39.1%)

Note that there were no statistical significance differences among the three mutually exclusive ANCA positive groups except the following:
* both ANCA-C and ANCA-P positive patients had statistically higher percentage of patients treated with prednisone, even after Bonferroni multiple comparison adjustment (p = 0.02 and p = 0.005 for ANCA-C and ANCA-p comparing with 29 patients with both ANCA-C and ANCA-P positive).

DAI-2K and prednisone treatment at index date (HR 1.78, 95% CI: 1.15-2.79) in the best fit multivariable model, while two or more ANCA-C positive did not reach significance in the other regression model. Looking into the nature of vasculitis, the proportion of patients with vasculitis within each of the ANCA subgroups were similar (p-ANCA 20.1%, c-ANCA 16.7%, mixed ANCA 20.7%), but only the p-ANCA group was significantly higher than those with no ANCA positivity (12.4%; Table 2) partially due to sample sizes.

Conclusion: In our cohort, approximately 10% of SLE patents have persistent ANCA positivity, predominantly p-ANCA. The presence of p-ANCA was associated with significantly more vasculitis predominantly skin vasculitis.

Figure 1
Years to First Vasculitis Event

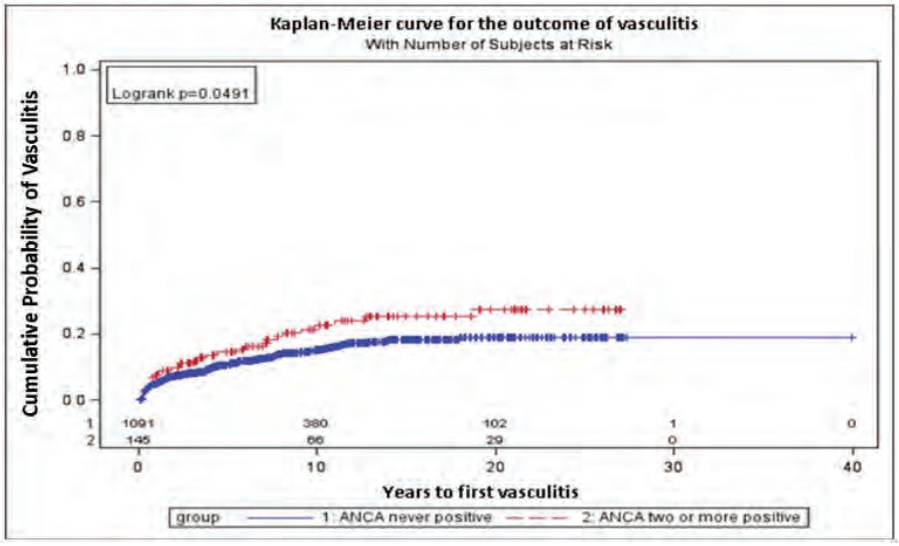

Table 2: Vasculitic Events by Group

Group	Ulceration	Gangrene	Vasculitic skin lesions	Nailfold infarcts	Splinter hemorrhage	Skin or muscle biopsy	Any of previous six items	Percent (any of six items)
92 pure ANCA-P	4	0	13	5	4	0	19	20.6%
24 pure ANCA-C	2	0	3	1	0	0	4	16.7%
29 both ANCA-C and ANCA-P	2	0	3	1	1	0	6	20.7%
1091 No ANCA positive	30	8	93	17	12	5	135	12.4%
Total	38	8	112	24	17	5	164	

Disclosure: R. Mirza, None; **M. Urowitz**, None; **J. Su**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5.

Abstract Number: 0282

Expression of the cGAMP Transporter SLC19A1 Is Altered in Systemic Lupus Erythematosus

Jeong Min Yu[1], Gantsetseg Tumurkhuu[2], Erica Montano[2], Gabriela de los Santos[2], Daniel J Wallace[2], Mariko Ishimori[3] and Caroline Jefferies[1], [1]Cedars-Sinai Medical Center, West Hollywood, CA, [2]Cedars-Sinai Medical Center, Los Angeles, [3]Cedars-Sinai Medical Center, Los Angeles, CA

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Etiology & Pathogenesis Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Inappropriate sensing of nucleic acids leading to enhanced type I interferon (IFN) induction is a hallmark of SLE, contributing to breakdown of immune tolerance and driving pathology. Cytosolic DNA is sensed by cyclic GMP-AMP synthase (cGAS), which synthesizes cyclic GMP-AMP (cGAMP), a potent second messenger that activates STING-dependent type 1 IFN (R Zhou *et al.*, 2019). Recently, the cGAS-STING pathway has been implicated in SLE by the observation that cGAS expression and cGAMP levels were elevated in SLE PBMCs compared to healthy controls (J An *et al.*, 2017). Also, it has emerged that cGAMP can be transported across the cell membrane by SLC19A1, a reduced folate transporter that is found on myeloid cells, leading to direct activation of STING. Interestingly, methotrexate (MTX) is a potent inhibitor of SLC19A1 import of cGAMP in monocytes (RD Luteijn *et al.*, 2019). Here we explore the potential that altered SLC19A1 expression may contribute to increased IFN responses in SLE.

Methods: Peripheral blood samples from SLE patients (meeting ACR classification criteria for SLE) and healthy controls (HC) were collected via a protocol approved by the local institutional review board. Monocytes were isolated from peripheral blood using CD14+ immunomagnetic bead isolation (StemCell Technologies). For gene expression analysis, qPCR analysis was performed using ddCt method, and statistical analyses were performed using GraphPad Prism 5. Four interferon stimulated genes (ISG) RSAD2, IFI44, IFI44L, IFI27 were used to calculate IFN scores, which are associated with increased disease activity in SLE patients (X Feng *et al.*, 2006).

Results: A total of 28 HCs and 89 SLE patients were enrolled in an independent cohort. 95% of the patients were female, with a mean age of 44 (SD ± 13 years). In keeping with cGAS as an ISG, its expression was significantly higher in the peripheral blood of SLE patients compared to HC ($p < 0.0001$) (figure 1a) and correlated positively with IFN score measured in the same samples (figure 1b). Expression of SLC19A1 was also significantly higher ($p=0.0325$) in SLE patient blood compared to HC (figure 1c). In examining the level of expression on patient monocytes compared to those from HC, SLC19A1 was found to be increased on the surface of cells as determined by flow cytometry (data not shown). In assessing how methotrexate (MTX) use altered SLC19A1 at the mRNA level, no difference was seen between those taking MTX (32.9%) and those not. Our preliminary data also indicates that cGAMP and type I IFN can also regulate SLC19A1 expression in whole blood but as to whether there are differences between responses in HC and SLE patient cells is currently been assessed.

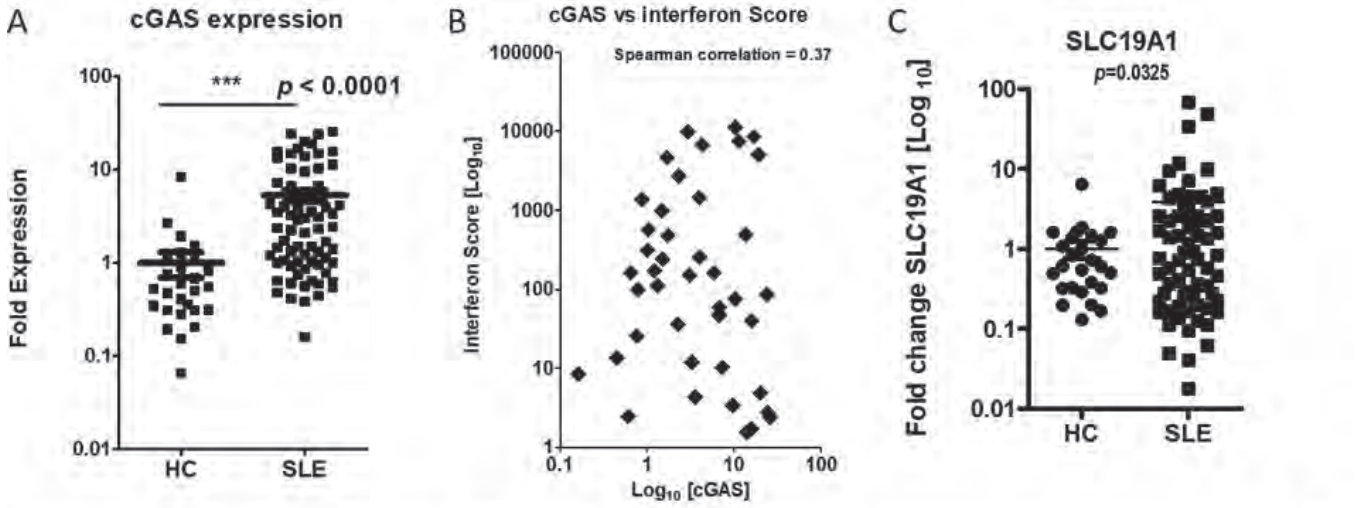

Figure 1: Whole blood from healthy controls (n=28) and SLE patients (n=89) was analyzed for expression of cGAS, ISGs (RSAD2, IFI44, IFI44L, IFI27) and SLC19A1 by qPCR. Between group differences were analyzed by unpaired *t*-test and Spearman's rank correlation used to analyze the correlation between cGAS and IFN score. All statistical analysis was carried out using GraphPad Prism

Conclusion: Increased cGAS expression in SLE patients was consistent with previous reports, in keeping with it being an ISG. Our observation that the cGAMP transporter SLC19A1 is increased is in keeping with the observed elevation of cGAMP levels detected previously in SLE patient serum (J An *et al.*, 2017). This suggests that altered SLC19A1 expression may contribute to enhanced IFNβ expression via direct uptake and activation of STING. Whether enhanced SLC19A1 expression on cells correlates with enhanced cGAMP uptake and STING activation is currently been assessed.

Disclosure: J. Yu, None; **G. Tumurkhuu**, None; **E. Montano**, None; **G. de los Santos**, None; **D. Wallace**, None; **M. Ishimori**, None; **C. Jefferies**, None.

Abstract Number: 0283

Genome-wide DNA Methylation Analysis in Lupus Keratinocytes Identifies Differential Methylation of Genes That Regulate Apoptosis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Cutaneous lupus erythematous (CLE) is a disfiguring manifestation of systemic LE (SLE), and the pathogenesis remains unclear. However, epidermal regulation of skin inflammation and cell death contribute, potentially in a female-biased manner. Differential DNA methylation is important in the organ-specific manifestations of SLE but has not been studied in the skin. Thus, we explored the genome-wide DNA methylation changes in keratinocytes (KC) to investigate the functional relevance in CLE.

Methods: Eight SLE skin biopsy samples were taken from non-sun-exposed, unaffected skin from participants of the Michigan Lupus Cohort as well as age (+/- 6 years), sex, and ethnicity-matched healthy control subjects. Freshly cultured KC (at passage 2) were used to isolate DNA using DNeasy Blood and Tissue Kit. DNA was bisulfite converted for DNA methylation studies using the EZ DNA Methylation Kit. Genome-wide DNA methylation analysis was performed using the Infinium HumanMethylation450 BeadChip Kit. Differentially methylated loci were mapped to genes or gene regions and subject to gene ontology and pathway analysis using the Database for Annotation, Visualization, and Integrated Discovery (DAVID).

Results: We identified 1443 differentially methylated sites with 924 hypomethylated genes and 519 hypermethylated genes in lupus KC compared to controls. Pathway analysis revealed Hippo signaling as the top canonical pathway associated with the DNA methylation profile of primary lupus KCs. TEA Domain Transcription Factor 1 (TEAD1), a key transcription factor in the Hippo pathway, was significantly hypomethylated in lupus compared to control ($\Delta\beta$ =-0.17, P= 4.36 X 10^{-9}). Further, methylation of LATS1/2, which contributes to inactivation of Hippo pathway effector proteins TAZ and YAP, was significantly increased ($\Delta\beta$= 0.11, P= 3.82 X 10^{-4}). YAP and TAZ were both hypermethylated ($\Delta\beta$= 0.11 (P= 1.53 X 10^{-3}) and 0.12 (P= 2.20 X 10^{-4}), respectively), thereby increasing TEAD1 activity.

Conclusion: SLE KCs display methylation changes in the Hippo pathway that may contribute to dysregulated apoptosis, a known feature that contributes to photosensitivity in CLE. Vestigial like family member 3 (VGLL3) has recently been identified as a putative transcription factor and master orchestrator of sex bias in autoimmune diseases, including SLE and CLE. Importantly, studies have shown VGLL3 operates through TEAD1 in other cell types and may be a key upstream regulator in the skin. Overall, these results suggest that differential methylation in KC may underlie dysregulated apoptosis and female bias of CLE.

Disclosure: G. Hile, None; **P. Coit**, None; **C. Zeng**, None; **R. Wasikowski**, None; **A. Tsoi**, None; **A. Billi**, None; **J. Gudjonsson**, Celgene, 2; **A. Sawalha**, None; **J. Kahlenberg**, AstraZeneca, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 5, Avion Pharma, 5, Celgene, 2.

Abstract Number: 0284

Oxidative DNA Damage Accelerates Skin Inflammation in Pristane-induced Lupus Model

Gantsetseg Tumurkhuu[1], Shuang Chen[2], Erica Montano[1], Malcolm Lane[2], Michifumi Yamashita[2], Janet Markman[2], Luz Blanco[3], Mariana Kaplan[4], Kenichi Shimada[2], Timothy Crother[2], Mariko Ishimori[2], Daniel J Wallace[1], Caroline Jefferies[5] and Moshe Arditi[2], [1]Cedars-Sinai Medical Center, Los Angeles, [2]Cedars-Sinai Medical Center, Los Angeles, CA, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Centreville, [4]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, [5]Cedars-Sinai Medical Center, West Hollywood, CA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic inflammatory autoimmune disease in which type I interferons (IFN) play a key role. The IFN response can be triggered when oxidized DNA engages the cytosolic DNA sensing platform cGAS-STING, but the repair mechanisms that modulate this process and govern disease progression are unclear. To gain insight into this biology, we interrogated the role of oxyguanine glycosylase 1 (OGG1), which repairs oxidized guanine 8-Oxo-2′-deoxyguanosine(8-OH-dG), in the pristane-induced mouse model of SLE.

Methods: C57/Bl6 (WT) and Ogg1 KO mice were injected i.p. with 0.5ml of pristane or PBS as control (WT-PBS). In order to observe the effects of Ogg1 deficiency in fully developed SLE, we analyzed the mice 10 months after induction. Histological features of skin and kidney were quantified by an image analysis system. Serum total IgG, IgG subtypes (IgG1 and IgG2a), and autoantibodies (anti-dsDNA and anti-RNP) were measured by ELISA. Gene expression analysis for IFN and ISG genes was performed by RT-PCR using SYBR green.

Immune cell types were analyzed separately for each mouse by standard FACS procedures. Peripheral blood mononuclear cells (PBMCs) were separated from whole blood by density-gradient centrifugation with Ficoll-Paque Plus (GE Healthcare). $CD14^+$ monocytes were purified from fresh PBMCs by positive selection using magnetic $CD14^+$ beads (Miltenyi Biotec) according to the manufacturer's protocol

Results: *Ogg1*$^{-/-}$ mice developed an exacerbated disease profile, characterized by aggravated skin pathology, increased auto-antibodies, higher total IgG, and higher splenic cell number. Neutrophils from pristane-treated *Ogg1*$^{-/-}$ mice exhibited earlier NETosis compared to WT. BMDMs from *Ogg1*$^{-/-}$ mice produced increased basal and cGAMP-driven IFN-β expression, which was diminished by treatment with the STING inhibitor H151, and skin lesions

from pristine-treated *Ogg1*$^{-/-}$ mice had significantly higher expression of type I IFN genes than lesions in WT mice. Finally, expression of *OGG1* was significantly lower in lesioned skin compared with non-lesioned skin in Discoid Lupus patients.

Conclusion: In conclusion, our study clearly supports a crucial role for OGG1 in protecting against IFN production and SLE skin disease.

Disclosure: G. Tumurkhuu, None; **S. Chen**, None; **E. Montano**, None; **M. Lane**, None; **M. Yamashita**, None; **J. Markman**, None; **L. Blanco**, None; **M. Kaplan**, None; **K. Shimada**, None; **T. Crother**, None; **M. Ishimori**, None; **D. Wallace**, None; **C. Jefferies**, None; **M. Arditi**, None.

Abstract Number: 0285

CXCL13 Neutralization Reduces Neuropsychiatric Manifestations in MRL/*lpr* Mice

Michelle Huang[1], Ariel Stock[1] and Chaim Putterman[1], [1]Albert Einstein College of Medicine, Bronx, NY

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Targeted treatments for neuropsychiatric systemic lupus erythematosus (NPSLE) remain challenging to develop due to the unclear pathogenesis of the disease. Our laboratory has previously identified tertiary lymphoid structure (TLS) (a.k.a. ectopic germinal center) formation in the brains of MRL/*lpr* mice, a classic SLE mouse model with neuropsychiatric manifestations. TLS form at sites of chronic inflammation and functionally perform like other lymphoid follicles to create clonotypic immune responses in a localized fashion. This specialized immune response may target self-antigens in autoimmune conditions and perpetuate pathogenesis of disease. CXCL13 is a key chemokine in lymphoid follicle formation and maintenance; in this study, we inhibited CXCL13 in MRL/*lpr* strain and examined the effect of this intervention on TLS formation and the development of neurobehavioral deficits.

Methods: MRL/*lpr* mice share several important similarities with human lupus, including ANA production, widespread immune complex deposition, nephritis, and skin disease. Importantly for this study, this strain also exhibits early onset of cognitive and affective disease similar to that seen in NPSLE patients. Female MRL/*lpr* mice were injected with a CXCL13-neutralizing monoclonal antibody (Vaccinex), an IgG1 isotype control antibody, or PBS intraperitoneally (IP) three times a week for 12 weeks starting at 6-8 weeks of age (n=13-19 per group), or continuously intracerebroventricularly (ICV) with an osmotic pump, over a two-week period starting at 15 weeks of age (n=4-5 per group). Cognitive dysfunction and affective deficits were tested for at the end of treatment using object placement (OP) and object recognition (OR) tasks to evaluate spatial and recognition memory, respectively, and using Porsolt swim test to evaluate depression-like behavior. Anti-DNA antibody titers and serum blood urea nitrogen (BUN) levels were assessed to measure systemic disease progression at the time of the behavioral tests.

Results: MRL/*lpr* mice treated with anti-CXCL13 antibody IP showed significant improvement in spatial memory, recognition memory, and despair-like behavior compared to the two control groups (Figure 1). Mice that received the treatment via ICV pump showed similar results (vs PBS: OP: p=0.059, OR: p=0.090, Porsolt swim: p=0.018; vs isotype control: OP: p=0.029, OR: p=0.19, Porsolt swim: p=0.80). However, antibody titers (indicating systemic disease),

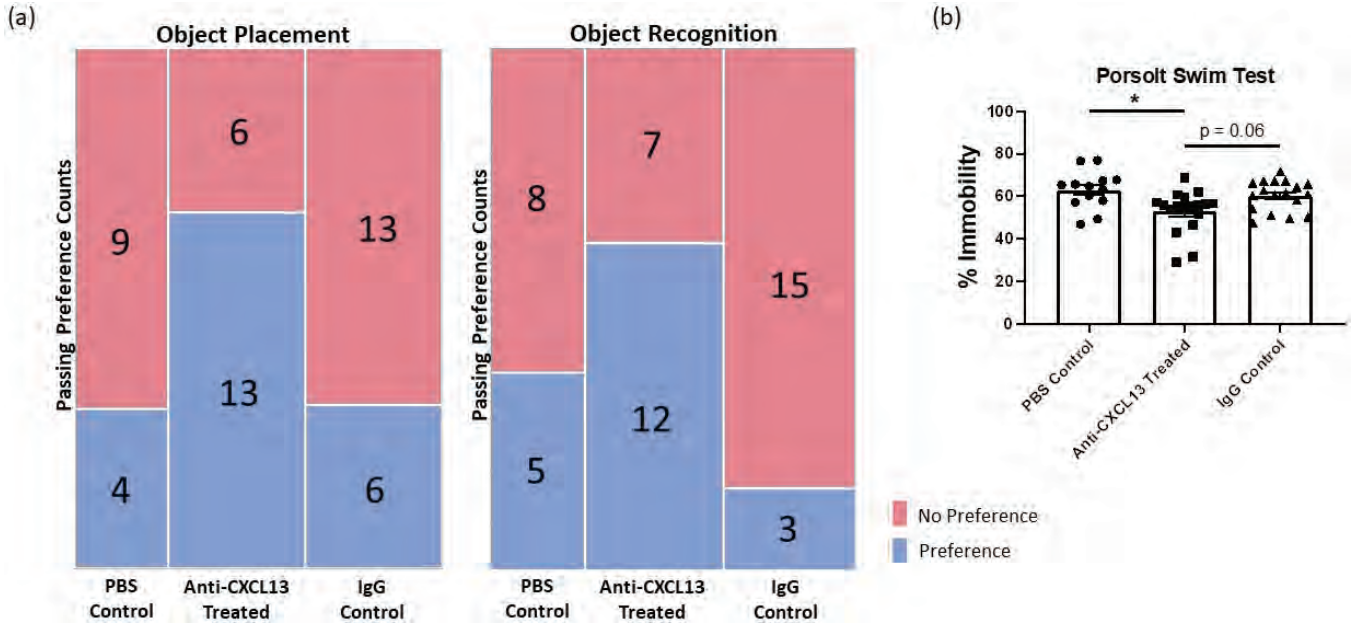

Figure 1. Behavioral Test Results (for IP cohorts). (a) Object placement (OP, left) and object recognition (OR, right) tasks are measured by animals showing over a 55% preference to a novel object. Counts of mice separated into either showing a preference (blue) or no preference (red). Both tasks showed that the treatment group performed significantly better than both the PBS control group (OP: p=0.034; OR: p=0.17) and the IgG control group (OP: p=0.022; OR: 0.0031). (b) Depression-like behavior is measured by percent time spent immobile over the total time in the Porsolt swim test. The treatment group demonstrated significantly less despair-like behavior than both groups (vs PBS: p=0.012; vs IgG: p=0.063; error bars: SEM).

and BUN levels (reflecting renal disease), showed no difference among groups, with any of the two antibody delivery methods. Further analysis of brain histology and cellular infiltration to evaluate for TLS and determine whether germinal center formation was disrupted are ongoing.

Conclusion: Our results suggest that inhibition of TLS formation affects the behavioral phenotype but not systemic or renal disease in the lupus prone MRL/*lpr* strain. Therefore, CXCL13 overexpression contributes to the pathogenesis of murine NPSLE and suggests that neutralizing this chemokine, if it can be done locally and safely, may be a novel therapeutic approach to the treatment of this manifestation.

Disclosure: M. Huang, None; **A. Stock**, None; **C. Putterman**, Equillium, 1, 2.

Abstract Number: 0286

An SLE-linked ITGAM Gene Variant Changes Mac-1 Structure, Signaling, and Surface Expression and Enhances IFNg Production and Antigen Presentation by B Cells

Joseph Blake[1], Alexander Szalai[2], Jeffrey Edberg[3] and James Mobley[3], [1]UAB, Birmingham, [2]University of Alabama at Birmingham, birmingham, AL, [3]UAB, Birmingham, AL

SESSION INFORMATION

Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is a chronic and debilitating disease; in the USA with an estimated incidence of 3-10 per 100,000 people and currently affecting an estimated 300,000 people. The exact pathogenesis of SLE remains unknown, but there is a growing body of evidence that various genetic, hormonal, and environmental factors contribute to its occurrence and severity. Each is thought to modulate the activation and regulation of innate and adaptive immunity in ways that drive autoimmunity, the underlying cause of SLE. The hallmark of autoimmunity in SLE is B cell hyperactivity leading to the generation of autoantibodies, which together drives the deposition of deleterious immune complexes. SLE has strong familial clustering, high heritability, and high concordance rates between monozygotic versus dizygotic twins, suggesting it's a polygenic disease. Among the many different gene variants reportedly associated with SLE risk or severity are single nucleotide polymorphisms (SNPs) in the integrin alpha-M (*ITGAM*) gene, which are present in more than 1/3 of SLE patients. *ITGAM* encodes the protein CD11b, which pairs with CD18 and forms the Mac-1 receptor. Among the *ITGAM* SNPs associated to SLE is SNP rs1143678, encoding a P1146S amino acid substitution in the cytoplasmic tail of CD11b. Mac-1 is widely expressed by myeloid cells, and it is reported that SNP rs1143678 alters myeloid cell functions in ways that could propel SLE. Mac-1 is also expressed on lymphocytes, but comparatively little is known about its role in B cells or whether SNP rs1143678 has any impact on B cell biology. To fill this gap in knowledge we are investigating the impact of *ITGAM* SNP rs1143678 on Epstein-Barr Virus (EBV) transformed B cells from healthy human donors.

Methods: N/A

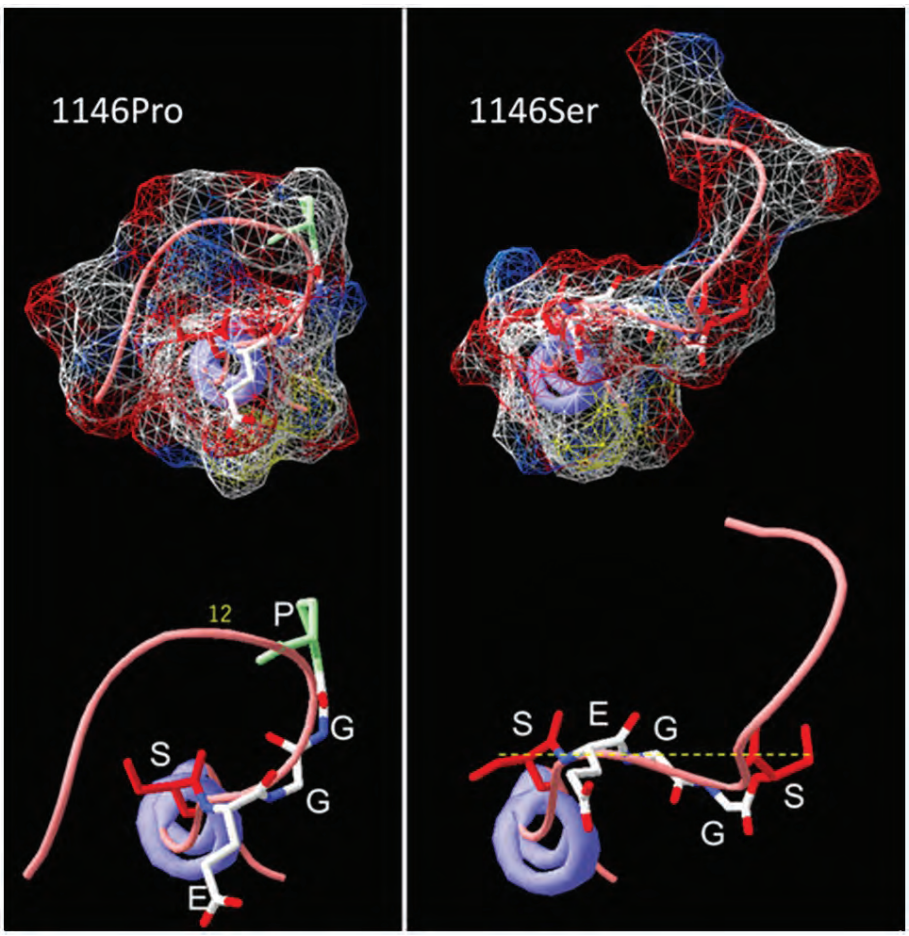

Figure 1. Space filling (top) and ribbon models (bottom) of the cytoplasmic tail of CD11b, viewed from inside the cell looking upwards at the receptor. For individuals carrying the SNP rs1143678 (right) the modelling predicts a 12-angstrom-wide space between the invariant 1142SER and the SNP variant 1146Ser residues (dashed yellow line).

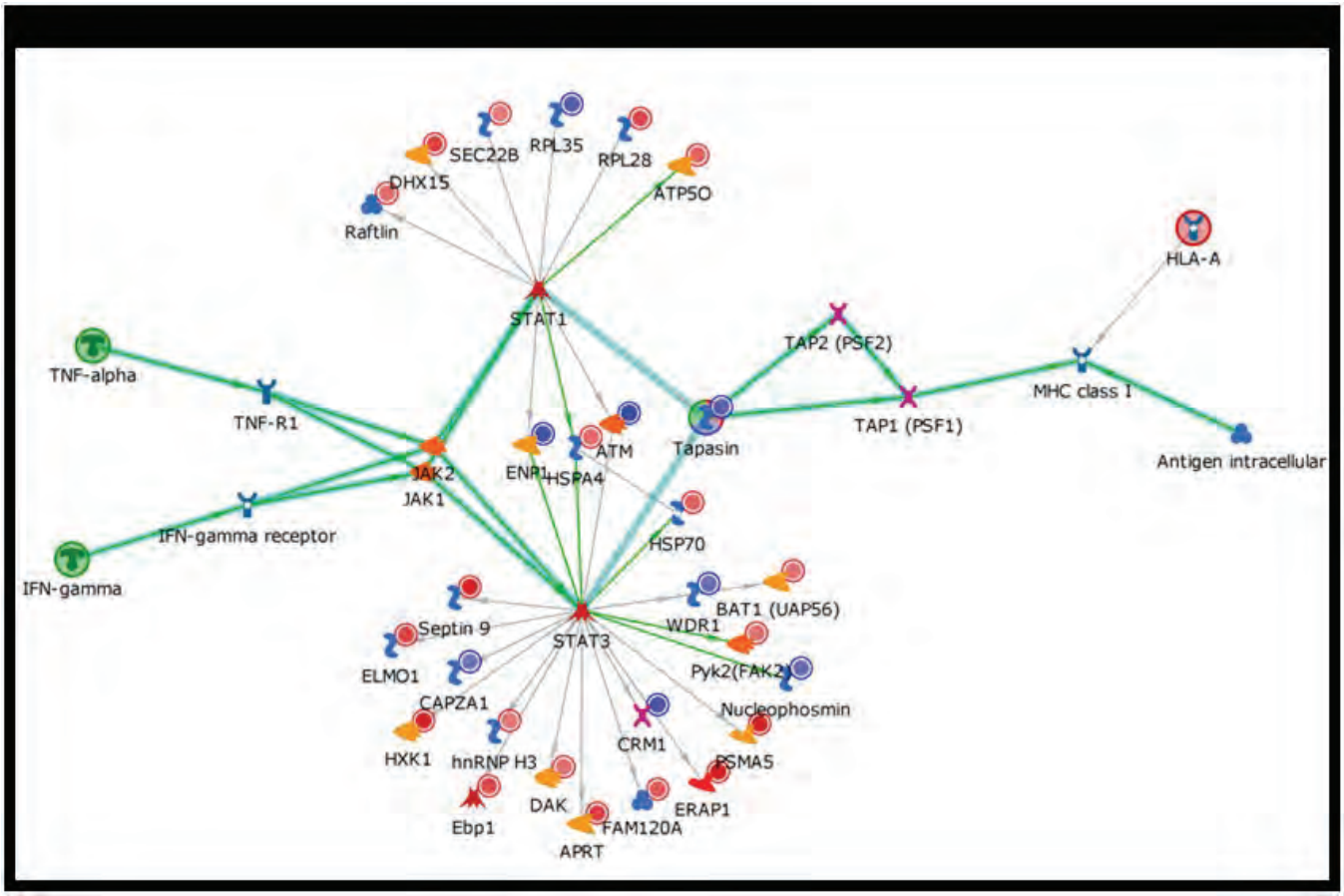

Figure 2. B cells from healthy donors homozygous for the ITGAM SNP rs1143678 or the major allele were transformed with Epstein Bar Virus. The cells were lysed and whole proteome analysis was done by LC MS/MS. Protein expression differences were determined and over-represented pathways in the SNP samples were mapped by Clarivate Analytics pathway analysis software. B-cells expressing the ITGAM SNP rs1143678 had high levels of IFNg induced MHC-1 presentation.

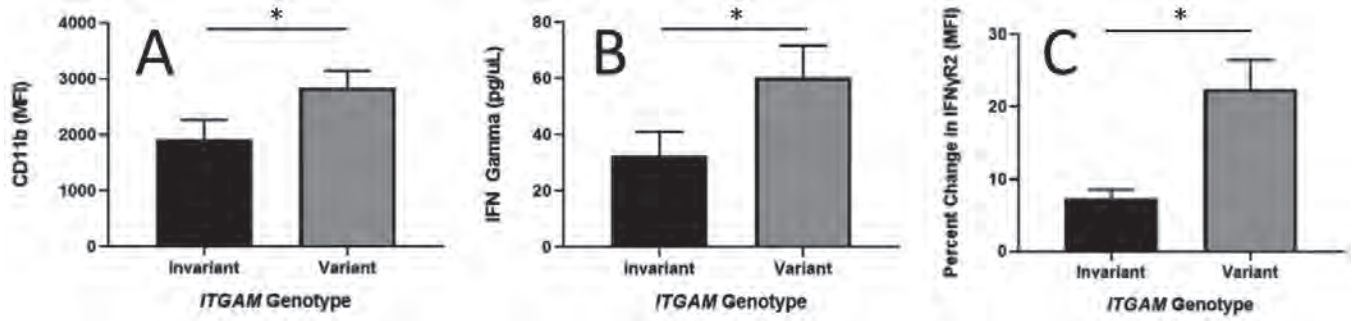

Figure 3. A) B-cells expressing the SLE associated SNP have a higher basal expression of CD11b. B) B-cells expressing the SLE associated SNP spontaneously secrete higher amounts of IFNg. C) Upon stimulation with exogenous IFNg, B-cells expressing the SLE associated SNP increase their surface expression of IFNgR2 to a higher degree than contol. A * indicates $p < 0.05$ by T test.

Results: We report here three of our main findings. First, juxtaposition of the cytoplasmic tails of CD11b and CD18 - and their activation induced separation - are thought to be required for Mac-1-mediated cell signaling. Our *in silico* structural modelling (Fig. 1) predicts that the SLE-associated P1146S substitution significantly changes the conformation of CD11b's cytoplasmic tail. This shape-shift should allow CD11b to accommodate additional or new cytoskeletal/cytoplasmic binding partners, and thereby could influence Mac-1 signaling. Second, phosphorylation of

1142Ser (an invariant residue in CD11b) is thought to be required for Mac-1 signaling, but using *in vitro* kinase assays and Western blots we provide the first direct evidence that the SLE-associated 1146Ser residue is also phosphorylated (data not shown). Third, by mass-spectrometry combined with proteomics and network analyses, we obtained evidence that both IFNγ and antigen presentation pathways are enriched in B cells from donors expressing the *ITGAM* SNP variant (Fig 2). Indeed, compared to B cells from *ITGAM* invariant donors, B-cells from donors carrying the *ITGAM* SNP showed increased expression of CD11b, increased spontaneous secretion of IFNγ, and increased expression of the IFNγR2 receptor following stimulation (Fig 3). This trio of new findings together suggests that the *ITGAM* SNP rs1143678 significantly alters the biology of B cells, which might explain the strong association rs1143678 to SLE.v

Conclusion: N/A

Disclosure: J. Blake, None; **A. Szalai**, None; **J. Edberg**, None; **J. Mobley**, None.

Abstract Number: 0287

RNA Externalized by Neutrophil Extracellular Traps Promotes Inflammatory Pathways in Endothelial Cells

Xinghao Wang[1], Philip Carlucci[2], Jorge Romo-Tena[1], Jose Torres-Ruiz[1], Hong-Wei Sun[1], Markus Hafner[1], Mariana Kaplan[3] and **Luz Blanco**[4], [1]NIAMS, National Institute of Health, Bethesda, [2]New York University School of Medicine, New York, NY, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, [4]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Centreville

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Neutrophil extracellular traps (NETs) are extracellular lattices composed of nucleic material bound to neutrophil granule proteins. NETs may play pathogenic roles in development and severity of autoimmune diseases such as systemic lupus erythematosus (SLE), at least in part, through induction of type I interferon (IFN) responses via externalization of oxidized immunostimulatory DNA. A distinct subset of SLE proinflammatory neutrophils (low density granulocytes; LDGs) displays enhanced ability to form proinflammatory NETs that damage the vasculature. We assessed whether NET-bound RNA can contribute to inflammatory responses in endothelial cells and the pathways that mediate this effect.

Methods: Expression of newly-synthesized RNA was quantified if healthy control and lupus NETs. The ability of endothelial cells to take up NET-bound RNA and downstream induction of type I IFN responses was quantified. RNAs present in NETs were sequenced and specific small RNAs were tested for induction of endothelial type I IFN pathways.

Results: NETs extruded newly-synthesized RNA that was internalized by endothelial cells and this was enhanced when NET nucleic acids were oxidized, particularly in lupus LDG NETs. Internalization of NET-bound RNA by endothelial cells was dependent on endosomal TLRs and the actin cytoskeleton and induced type I IFN stimulated genes (ISGs). This ISG induction was dependent on NET-associated miR-let7b, a small RNA expressed at higher levels in LDG NETs, which acted as a TLR7 agonist.

Conclusion: These results highlight underappreciated roles for small RNAs externalized in NETs in the induction of proinflammatory responses in vascular cells, with implications to lupus vasculopathy.

Disclosure: X. Wang, None; **P. Carlucci**, None; **J. Romo-Tena**, None; **J. Torres-Ruiz**, None; **H. Sun**, None; **M. Hafner**, None; **M. Kaplan**, None; **L. Blanco**, None.

Abstract Number: 0288

Targeted Sequencing Revealed Novel Candidate Genetic Contributions to Lupus Nephritis in a Cohort of Swedish Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is a common debilitating manifestation of Systemic Lupus Erythematosus (SLE). Despite improved understanding of underlying mechanisms driving to LN and early treatment strategies, yet 10% of LN patients progress to end-stage renal disease (ESRD) in 5 years after the onset of LN[1]

Methods: To explore novel genetic associations, we performed a case-case analysis in a quality-controlled dataset of 958 Swedish patients with SLE (337 with LN) and 1030 healthy individuals. We stratified patients based on their histopathologic phenotype as proliferative, pure membranous LN, and ESDR. Mixed phenotypes were excluded. Targeted capture and enrichment was performed using a NimbleGen array, including 1853 genes selected based on their known involvement in systemic inflammatory autoimmune diseases. Variant and gene-level aggregate association testing were performed separately using Plink and SKAT-O respectively[2].

Results: We identified seven candidate loci ($P \leq 1\times 10^{-5}$) associated with proliferative nephritis, five with membranous nephritis, and seven with ESRD. The strongest associations with proliferative nephritis, membranous nephritis, and ESRD corresponded to *chr14q23.3 (*$p=5.58\text{x}10^{-6}$), LTF ($p =1.64\text{x}10^{-6}$), and MERTK($p=9.52\text{x}10^{-6}$), respectively. The gene-based aggregate association, which potentiates the power to detect gene regions with aggregation of functional common and rare variants revealed two additional potentially novel genes, CTF1 ($p= 2.97\text{x}10^{-5}$, FDR=0.03) and FBXL19 ($3.14\text{x}10^{-5}$, FDR=0.03), that were associated with membranous nephritis.

Conclusion: We revealed novel genetic risk loci in association with ESRD and candidate genes in association with membranous nephritis in Swedish SLE patients.

1. Davidson A, Aranow C, Mackay M. Lupus nephritis: challenges and progress. Curr Opin Rheumatol. 2019 Aug.

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Disclosure: S. Yavuz, None; **P. Pucholt**, None; **D. Leonard**, None; **J. Imgenberg-Kreuz**, None; **M. Bianchi**, None; **J. Sandling**, None; **I. Gunnarsson**, None; **S. Sle Network**, None; **L. Ronnblom**, None.

Abstract Number: 0289

Endogenous Interferon-β and Low IL-4R on Transitional B Cells Promotes Lupus Nephritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: We previously showed that B-cell endogenous interferon-beta (IFNβ) at the transitional (Tr) stage correlates with development of anti-Smith (anti-Sm) and renal disease as well as African American (AA) race. We recently identified that down regulation of IL-4 receptor (IL-4R$^-$), a resting B-cell marker, is another phenotype of pathogenic B cells in SLE. This study determined if the Tr B-cell activation phenotype characterized as "IFNβ$^+$IL-4R$^-$" correlated with anti-Sm and can be a useful prognostic marker for autoantibody, renal disease (RD), and histopathologic features of lupus nephritis (LN).

Methods: The expression of IL-4R and interferon beta (IFNβ) in subsets of B cells was analyzed using flow cytometry analysis in 47 patients diagnosed with SLE. Plasma was assayed for IgG anti-Sm/RNP and anti-DNA using a standard ELISA method. Charts of 32 patients among these were reviewed and included in this analysis (30 were female and 21 patients were AA). Serologic manifestations of SLE included anti-DNA, anti-Sm, C3, and C4. Clinical laboratory manifestations of RD included creatinine and urine protein/creatinine ratio. RD classification was diagnosed based on the revised ISN/RPS (2004) criteria (16 patients) and included renal histopathology microscopy findings on light, electron microscopy and immunofluorescence (IF) for deposit of IgM, IgG, IgA, light chain, C1q and C3 (9 patients).

Results: Higher expression of IFNβ and lower expression of IL-4R at the Tr stage correlated with their expansion in naïve B cells and plasma levels of anti-Sm/RNP. Among the 32 patients analyzed 17 (53%) patients were diagnosed with LN. At the time of B cell phenotype analysis, 8 (25%) of patients were positive with anti-DNA, and 20 (62%) of patients were positive with anti-Sm. Multivariate regression analysis indicated a significant positive correlation between the IFNβ$^+$IL-4R$^-$ phenotype with anti-Sm (p=0.0035), anti-DNA (p=0.0234), low C3 (p=0.0360) and high protein creatinine ratio (p=0.0246). RD classification revealed Class II in 5 (29%) patients, Class III or IV in 5 (29%) patients, Class III or IV with Class V in 2 (12) patients and Class V only in 4 (23 %) patients. Direct IF examination of LN biopsies revealed that patients with higher percentage of the Tr B cell IFNβ$^+$IL-4R$^-$ phenotype also exhibited increased deposition of IgM, IgA, and C1q, but not IgG and C3 especially in glomerular mesangium compared to tubular basement membranes and arteries.

Conclusion: These results suggest a sequence for immunopathogenesis in SLE which is initiated as IFNβ$^+$IL-4R$^-$ activated B cells at the earliest Tr stage of development. These B cells are predisposed to undergo tolerance loss, especially to the Sm autoantigen. This is highly correlated with development of renal disease and low C3 consistent with previous studies. Association of the circulating IFNβ$^+$IL-4R$^-$B cell phenotype with immunofluorescence staining for IgM, IgA, C1q, but not IgG or C3 suggest distinct mechanisms of inflammation in the kidney compared to system-

Table 1. Clinical and demographic characteristics

Characteristics	32 patients
Age-year, mean (SD)	40.7 (11.5)
Sex	
Female, N (%)	30 (93.8)
Male, N (%)	2 (6.3)
Race	
African America, N (%)	21 (65.6)
White European, N (%)	11 (34.4)
Labs at time of enrollment	
Anti-DNA (titer) mean (SD)	50.3 (81.8)
Anti-Sm (unit/ml), mean (SD)	72.0(83.5)
C3 (mg/dl), mean (SD)	119.8 (31.7)
C4 (mg/dl), mean (SD)	24.9 (11.5)
Serum creatinine (mg/dl), mean (SD)	0.9 (0.5)
Protein/creatinine ratio, mean (SD)	0.7 (1.0)
% of the IFNβ^{+}IL-4R^{-} subset in transitional B cells, mean (SD)	33.3 (21.6)
Lupus Nephritis class, N (%)	17 (53)
Class II, N (%)	5 (29)
Class III or IV, N (%)	5 (29)
Class III or IV and V, N (%)	2 (12)
Class V only, N (%)	4 (23)
Missing data, N (%)	1 (6)

ic inflammation. Our results suggest that restoration of B cells into the resting status at the Tr stage either through blocking INFβ or the type I IFNR, and/or optimizing IL-4R signaling may prevent or improve RD in SLE.

Disclosure: F. Alduraibi, None; **H. Fatima**, None; **W. Chatham**, None; **H. Hsu**, Lupus Research Alliance Target Identification in Lupus Award, 2; **J. Mountz**, None.

Abstract Number: 0290

Role of Protein Tyrosine Phosphatase 1B (PTP1B) in Endothelial-to-Mesenchymal Transition (EndoMT) Promoted by Inflammation: Implications for SLE

Jorge Romo-Tena[1], José Esparza-López[2], Carmelo Carmona-Rivera[3], Luz Blanco[4], Mariana Kaplan[3] and María de Jesús Ibarra-Sánchez[2], [1]NIAMS, National Institute of Health, Bethesda, [2]INNSZ / UNAM-RAI, Mexico City, Mexico, [3]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, [4]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Centreville

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The endothelial-to-mesenchymal transition (EndoMT) transdifferentiation process can be promoted by several proinflammatory mediators in many pathological conditions. Recently, it was suggested a crucial role of EndoMT in the pathogenesis of vasculopathy in systemic lupus erythematosus (SLE). However, it remains unclear which proinflammatory mediators and signaling pathways promote EndoMT. Phosphatase Tyrosine Protein

1B (PTP1B) regulates signaling pathways of proinflammatory cytokines that are known to be involved in EndoMT. Previous works have shown that type I Interferons (IFNs) are key players in the progression of vascular damage and atherogenesis in SLE, but the role of proinflammatory cytokines such as TNF-α in EndoMT remains to be investigated.

Objective: To elucidate the capacity of TNF-α as EndoMT inducer and the putative role of PTP1B in this process.

Methods: Human aortic endothelial cells (HAEC) and human glomerular microvascular endothelial cells (HGMVEC) were used as model for *in vitro* induction of EndoMT. These endothelial cells (ECs) lines were incubated with human recombinant TNF-α (25 ng/ml) for 2 and 4 days. Expression of specific endothelial markers (eNOS, PECAM-1, VE-cadherin) and mesenchymal (SNAIL1, N-cadherin, α-SMA) markers were analyzed by Western blot (WB). Canonical activation of TNF-α-induced NF-κB pathway in EndoMT was assessed by phosphorylation of p65-Ser536, degradation of IkBa and nuclear translocation of p65 by WB and immunofluorescence (IF), respectively. PTP1B expression changes during EndoMT were evaluated by WB. CRISPR-Cas9 gene editing assay will be performed to generate *PTPN1* knockdown ECs *in vitro* and corroborate its role in EndoMT.

Results: TNF-α induced EndoMT in both HAEC and HGMVEC by downregulation of endothelial markers (eNOS, PECAM-1, VE-cadherin) and upregulation of mesenchymal markers (SNAIL1, N-cadherin, α-SMA). TNF-α induced phosphorylation of NF-κB (p65-Ser 536) and degradation of IkB-α. Nuclear translocation of p65 was observed as early as 5 min after treatment and remained in the nucleus up to 1 h. TNF-α-induced EndoMT provoked an increase in PTP1B levels during the 4 days of EndoMT process. Additionally, PTP1B inhibition by CRISPR-Cas9 system is going to be investigated.

Conclusion: We established a model of TNF-α-induced EndoMT in the HAEC and HGMVEC endothelial cell lines. We observed decreased of endothelial markers and upregulation of mesenchymal markers. Concomitant with these changes of EndoMT markers, we found that PTP1B increases its expression. Furthermore, we found that NF-κB canonical signaling pathway is activated during this process. These findings unveil a putative important pathway in SLE vasculopathy and suggest novel avenues for intervention.

Disclosure: J. Romo-Tena, None; **J. Esparza-López**, None; **C. Carmona-Rivera**, None; **L. Blanco**, None; **M. Kaplan**, None; **M. Ibarra-Sánchez**, None.

Abstract Number: 0291

SLAMF7 and CD38 on NK Cells Represent Potential New Therapeutic Targets for Systemic Lupus Erythematosus

Morgane Humbel[1], Florence Bellanger[2], Craig Fenwick[2], Alice Horisberger[2], Camillo Ribi[2] and Denis Comte[2], [1]CHUV, Lausanne, Vaud, Switzerland, [2]CHUV, Lausanne, Switzerland

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease characterized by the production of autoantibodies. For this reason, anti-B cell therapy seems to be a promising approach. However, B cell depletion with Rituximab, an anti-CD20 monoclonal antibody (mAb), failed to meet the primary endpoint in large

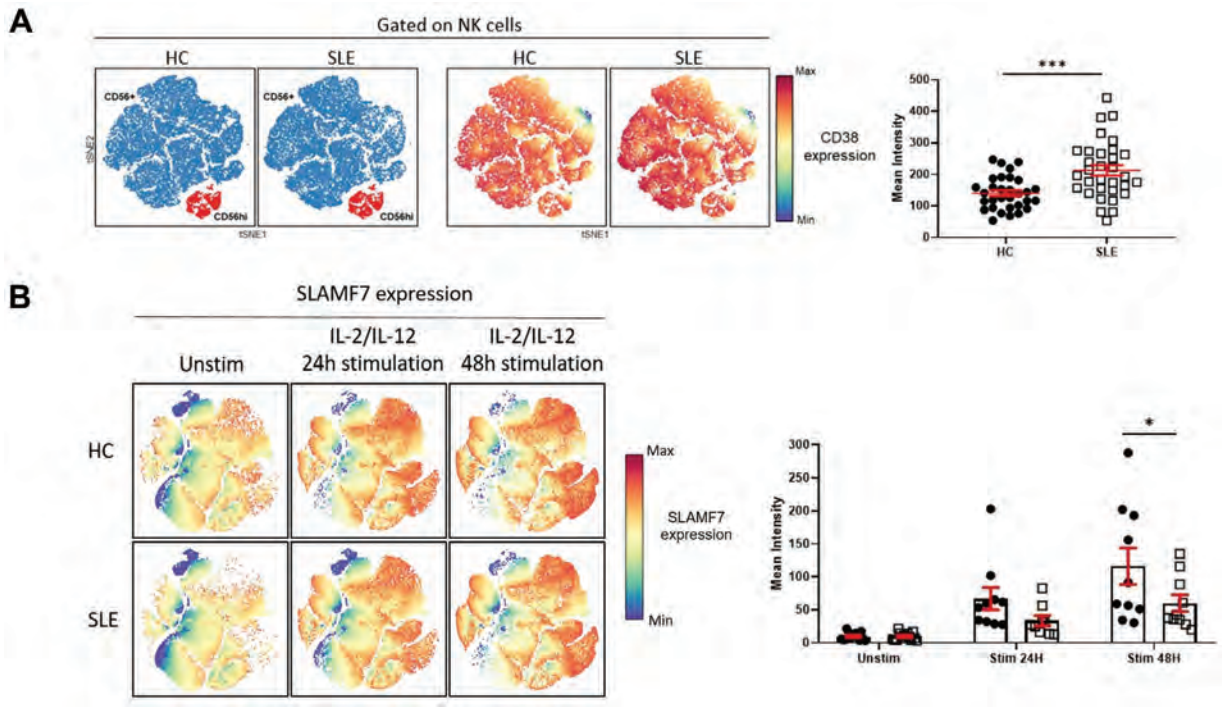

Figure 1. CD38 and SLAMF7 expression is increased on NK cells from SLE patients A. tSNE representation of NK cells distribution and CD38 expression (blue: CD56+; red: CD56hi) in healthy controls (HC) and SLE patients (left panel). Mean intensity of CD38 on total NK cells is significantly increased in SLE patients (right panel, shown as mean±SEM, Welch's t test, $p<0.001$). B. tSNE representation of SLAMF7 expression in NK cells in HC and SLE patients following 24H and 48H cytokine stimulation (left panel). SLE NK cells lack the ability of increasing the expression of SLAMF7 following cytokine stimulation (right panel, shown as mean±SEM, Two way ANOVA, Sidak's multiple comparison, $p<0.05$).

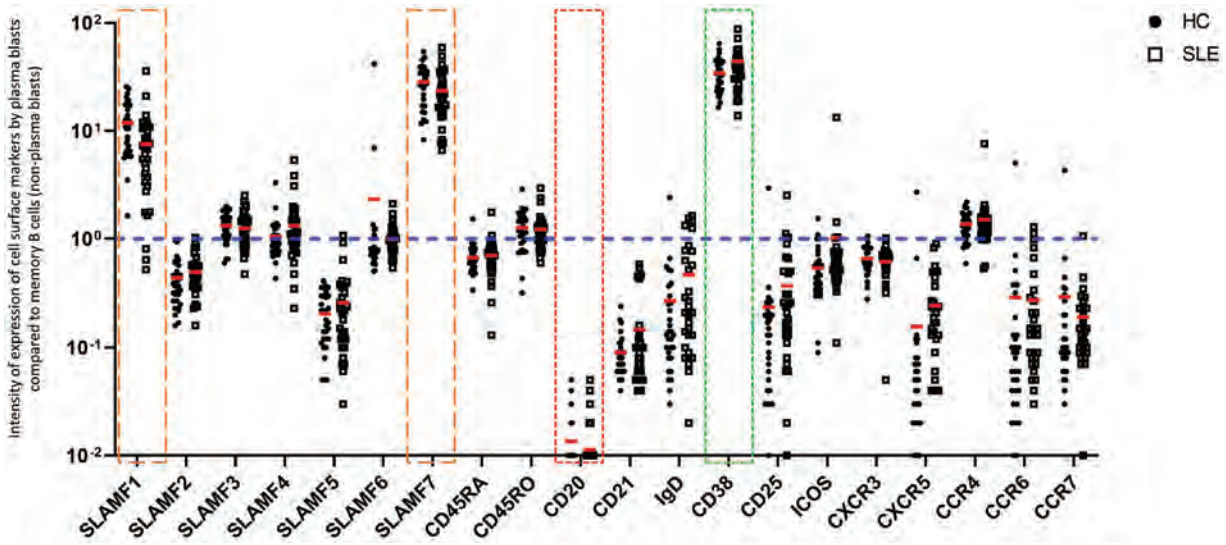

Figure 2. Expression of cell surface markers by plasma blasts from the peripheral blood of SLE patients The intensity of expression of cell surface markers is represented as an expression ratio of circulating plasma blasts (CD19+ CD27+ CD38+ CD20-) on memory B cells (non-plasma blasts) (CD19+ CD27+ CD38-). Accordingly, CD38 represents a positive control (in green) and CD20 represents a negative control (in red). These data show that SLAMF1 and SLAMF7 (in orange) are strongly expressed by plasma blasts compared to other populations of memory B cells. No difference was observed in the expression of these receptors between HC and SLE patients.

clinical trials, possibly because antibody-producing plasma blasts/cells express low levels of CD20. Therefore, strategies that specifically target the depletion of plasma blasts/cells may be effective in treating SLE. Moreover, Natural killer (NK) cells are dysfunctional in patients with SLE, and restoration of NK cell immunity has been shown to promote

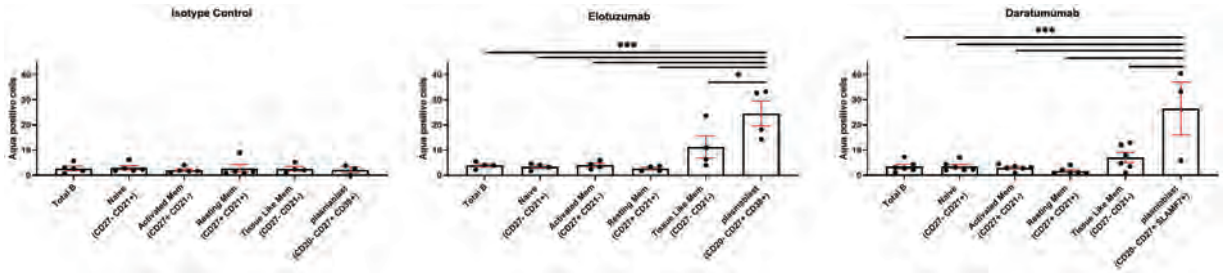

Figure 3. NK stimulation with Elotuzumab and Daratumumab promotes plasmablast killing. The engagement of NK cells with Elotuzumab and Daratumumab predominantly promotes the killing of plasmablasts compared to other B cell subpopulations (One way ANOVA Sidak's multiple comparison, *p<0.05, **p<0.005,***p<0.0001).

the destruction of plasma cells in other diseases such as multiple myeloma. Herein, we hypothesize that alterations in NK cells contribute to the pathophysiology of SLE and the restoration of NK cell immunity may promote the killing of autoantibody-producing plasma blasts/cells.

Methods: The extracellular phenotype of cryopreserved peripheral blood mononuclear cells (PBMC) from 31 SLE patients and 31 gender-, age- and ethnicity-matched healthy controls (HC) was examined by mass cytometry (CyTOF). Functional assays (cytolytic enzyme expression, cytokine production, degranulation, depletion assay) and signaling (calcium influx, phosphoprotein measurements) were examined by flow cytometry. NK cells were pre-treated with anti-SLAMF7 (Elotuzumab) or anti-CD38 (Daratumumab) mAb and were then co-cultured with B cells, to evaluate the killing of plasma blasts by activated NK cells.

Results: Our data shows that SLE NK cells are reduced in number and in function (IFNγ and TNFα production after activation with cytokines). SLE NK cells exhibit phenotypic alterations with respect to HC: (1) SLE NK cells express increased levels of CD38 and (2) fail to upregulate SLAMF7 upon activation with exogenous cytokines (**Figure 1**). In addition, circulating SLE plasma blasts are increased in the peripheral blood compared to HC. Moreover, plasma blasts express very high levels of CD38 and SLAMF7 (**Figure 2**). The engagement of SLAMF7 and CD38 with mAb partially restores the function of SLE NK cells (production of IFNγ and TNFα, degranulation). Furthermore, commercially available mAb directed against SLAMF7 (Elotuzumab) and CD38 (Daratumumab) promote the immunogenicity of NK cells to specifically kill plasma blasts (**Figure 3**).

Conclusion: We showed that SLAMF7 and CD38 are aberrantly expressed or regulated on the surface of NK cells of SLE patients. The engagement of SLAMF7 or CD38 with mAb restores the function of SLE NK cells and promotes the killing of plasma blasts by NK cells. Our data indicates that targeting these receptors may represent future therapeutic options in SLE to eliminate autoantibody-producing cells.

Disclosure: M. Humbel, None; **F. Bellanger**, None; **C. Fenwick**, None; **A. Horisberger**, None; **C. Ribi**, None; **D. Comte**, None.

Abstract Number: 0292

Exhausted pSTAT5-IFNα Signaling Pathways in SLE Patients Are Correlated with Age-associated B Cells and Disease Activity

Samantha Slight-Webb[1], Miles Smith[2], Kevin Thomas[1], Susan Macwana[1], Holden Maecker[3], Paul Utz[4], Judith James[5] and Joel Guthridge[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]Oklahoma Medical Research Foundation, Oklahoma City, [3]Institute for Immunity, Transplantation and Infection, Stanford University School of Medicine, Stanford, CA, [4]Stanford University School of Medicine, Stanford, CA, [5]Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation;Department of Pathology, University of Oklahoma Health Sciences Center;Department of Medicine, University of Oklahoma Health Sciences Center, Edmond, OK

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Etiology & Pathogenesis Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

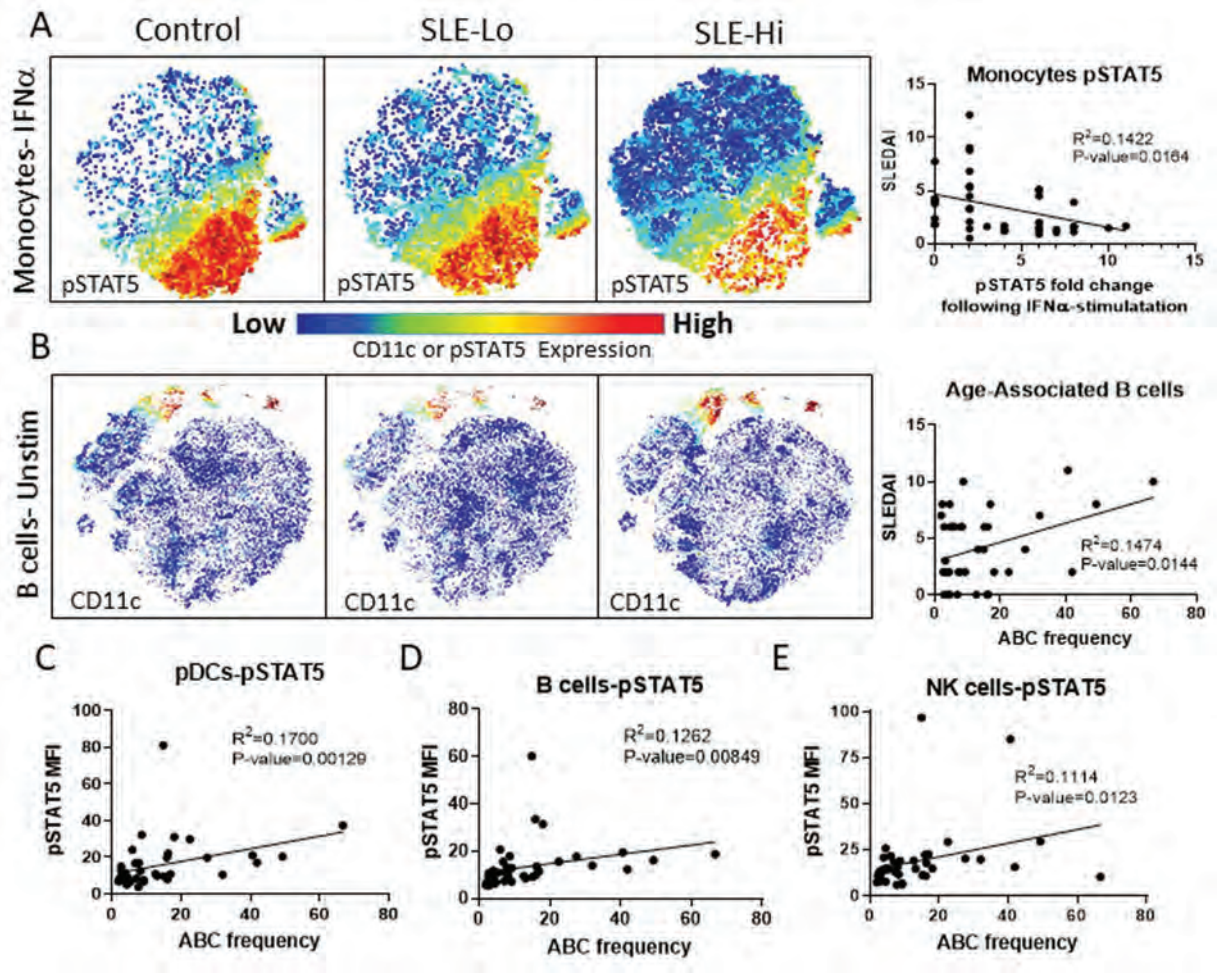

Figure 1. pSTAT5-IFNa signaling pathways are associated with age-associated B cells (ABCs). Whole blood of 58 subjects, either controls or SLE patients with variable disease activity, were used for phenotype analysis by mass cytometry. T-distributed stochastic neighbor embedding (tSNE) was used to visualize and cluster cells that were most similar using 28 surface markers. B cells or monocytes were gating and a second tSNE visualization was rendered to cluster and differentiate B cells or monocytes (A, B). pSTAT5 signaling was strongly reduced in monocytes following IFNa stimulation suggesting exhaustion of this pathway from persistent activation, and this was positively correlated with SLEDAI (A). CD11c+ ABC frequencies were higher in SLE patients, and correlated with lupus disease activity (B). Basal levels of pSTAT5 in pDCs (C), B cells (D), and NK cells (E) were correlated with ABC frequencies.

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease characterized by periods of elevated and suppressed clinical symptoms. Specific cell subsets, such as CD11c+ age-associated B cells (ABCs) have been associated with SLE pathogenesis. While TLR7 and TLR9 are thought to be prerequisites for ABC differentiation, the signaling pathways involved in driving SLE disease activity and ABC generation are still unclear.

Methods: Peripheral whole blood of healthy controls (n=18) and SLE patients with variable disease activity (n=40) were stimulated for 15 minutes with either interferon-α (IFNα), PMA and ionomycin, or Toll-like receptor (TLR) ligands for TLR4, TLR7/8 or TLR9 for phospho-protein analysis. Phenotype and phospho-protein markers were assessed by mass cytometry and cell heterogeneity was analyzed using t-SNE and manual gating. Plasma cytokines were assessed by 37-plex xMAP assays and ELISAs. SELENA-SLEDAI scores were used to correlate phenotype and functional differences with disease activity. All SLE patients met ACR classification criteria.

Results: Basal levels of pSTAT5 in CD4+ (p=0.0094) and CD8+ T cells (p=0.0289), pSTAT1 in B cells (p=0.0246), and cCASP3 in NK cells (p=0.0155) were elevated in SLE patients compared to controls. Following whole blood stimulation, a reduced fold change in pSTAT5 expression following IFNα whole blood stimulation was the primary signaling marker altered in SLE patients with high disease activity (SLEDAI≥4) compared to low disease activity (SLEDAI< 4) (p< 0.05). Most significantly, monocyte pSTAT5 IFNα-induced fold change in expression was negatively correlated with disease activity scores in SLE patients (p=0.0164) (Figure 1A). CD11c+ age-associated B cells had the strongest positive correlation with SLEDAI out of all 45 cell phenotypes assessed (p=0.0144) (Figure 1B), followed closely by HLA-DR+ CD4+ T cells (p=0.0186). A reduced fold change of pSTAT5 IFNα-induced expression in pDCs (p=0.0058), B cells (p=0.0116), and monocytes (p=0.0214) was negatively correlated with ABCs frequencies, while basal levels of pSTAT5 in pDCs, B cells, and NK cells were positively correlated with ABCs (Figure 1C, D, and E). Basal pSTAT1 levels and pSTAT1 IFNα-induced fold changes were not correlated with ABCs. Basal pSTAT5 expression in whole blood was associated with higher plasma levels of BLyS (p=0.02 $x10^8$), TNFα (p=0.02$x10^7$), IL-8 (p=0.01$x10^3$), IL-10 (p=0.00010), IL-6 (p=0.00011), SCF (p=0.0006), IL-22 (p=0.0007), and IL-31 (p=0.0018). ABCs frequencies were also strongly correlated with TNF-β (p=0.0019) plasma levels in SLE.

Conclusion: ABCs are highly correlated with disease activity and exhausted pSTAT5 IFNα-induced signaling in pDCs and other antigen-presenting cells suggesting an important role for this pathway in lupus pathogenesis and ABC differentiation.

Disclosure: S. Slight-Webb, None; **M. Smith**, None; **K. Thomas**, None; **S. Macwana**, None; **H. Maecker**, None; **P. Utz**, None; **J. James**, Progentec Diagnostics, Inc., 9; **J. Guthridge**, None.

Abstract Number: 0293

Contraction of the Stool Taxa *Clostridia* Is Associated with the Development of Clinical Disease Among Anti-Ro+ Mothers of Children with Neonatal Lupus

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-Ro autoantibody production often precedes the development of systemic lupus erythematosus (SLE) or Sjögren's syndrome (SS) by years. Anti-Ro+ mothers of children with manifestations of neonatal lupus such as congenital heart block are a unique cohort at risk for pathologic autoimmunity; many are asymptomatic or have an undifferentiated autoimmune syndrome with vague symptoms (Asym/UAS) and become aware of autoantibodies solely based on identification of disease in the fetus or infant. Over time, a third may progress to established diseases such as SLE or SS (SS/SLE). This study was initiated to investigate the hypothesis that stool microbiome compositional variation and taxa-specific interactions with class II HLA alleles may correlate with transition to SS/SLE.

Methods: The stool microbiome of 125 anti-Ro+ women (Asym/UAS, N=43; SS/SLE, N=82) and 23 healthy controls (HC) were 16S ribosomal RNA sequenced and assigned to taxa (SILVA). At each taxonomic level, the ranks of the centered log ratio transformed relative abundances were compared, adjusting for batch, to test for differences among groups (HC vs. Asym/UAS vs. SS/SLE); false discovery rate (FDR) adjusted p-values were computed. Class II HLA at DRB1 and DQB1 four-digit alleles were assigned by imputation (HIBAG) or sequencing and tested for an interaction between FDR-significant genera and HLA allele (cumulative logit models).

Results: There were reductions in genera and species diversity (Shannon Index) for the SS/SLE patients (g. 2.62±0.53; spp. 2.36±0.43) compared to Asym/UAS (g. 2.74±0.44; spp. 2.53±0.43) and HC (g. 2.77±0.36; spp 2.50±0.52) ($p< 0.05$). There were also differences in the microbial relative abundances among the three groups. Of note, the majority (76.9%) of taxa with significant differences among the three groups were in the class *Clostridia*, which includes the genera *Romboutsia* and *Coprococcus 3*. Specifically, by ranking the conditions by disease severity (HC < Asym/UAS < SS/SLE), there was a reduction in the relative abundance of *Romboutsia* and *Coprococcus 3* (P=2.38E-06 and P=1.58E-3, respectively). Given the overall sample size, HLA allelic frequencies and genus-HLA allele interactions (i.e., differential effect of genus depending on which HLA allele was present) were not significant (FDR P >0.05). However, notable findings include the allele frequencies of the DQB1*0602 allele in Asym/UAS, SS/SLE and HC were 22%, 17% and 10%, respectively (P=0.03). DQB1*0602 taxa by HLA-genus interaction analysis revealed that 70% of the top 20 taxa were contained within *Clostridia*, including *Romboutsia* and the 5 taxa below. Suggestive interactions between taxa within *Clostridia* and DQB1*0602 were *Lachnospiraceae UCG-010* (OR=0.52, P=0.006), *Oscillibacter* (OR=0.57, P=0.01), *Intestinimonas* (OR=0.60, P=0.02) and *Lachnospiraceae_NK4A136* (OR=0.65, P=0.03), and *Anaerotruncus* (OR=0.61, P=0.05).

Conclusion: Given *Clostridia's* critical role in gut homeostasis, including immune functions, reductions in this taxa combined with autoimmune related HLA alleles may serve as harbingers of a shift toward a pathologic gut microbiome that may, in part, explain progression from benign to pathologic autoimmunity and overt SLE and/or SS.

Disclosure: R. Clancy, None; **M. Marion**, Lupus Research Alliance, 2; **P. Izmirly**, GSK, 5; **M. Masson**, None; **H. Ainsworth**, None; **T. Howard**, None; **J. Buyon**, None; **C. Langefeld**, Lupus Research Alliance, 2.

Abstract Number: 0294

Tired T-Cells and Monocytes with Malaise: Investigating the Links Between Cellular Iron Deficiency and Mitochondrial Dysfunction in Systemic Lupus Erythematosus

Chris Wincup[1], Thomas McDonnell[1], George Robinson[2], Filipa Farinha[1], Anna Radziszewska[1] and Anisur Rahman[1], [1]University College London, London, United Kingdom, [2]University College London, Hertford, United Kingdom

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Iron is vital for many physiological processes and is found within respiratory complexes of the mitochondrial electron transport chain, the key site of oxidative phosphorylation ATP energy production.

Previously we demonstrated that patients with SLE are at risk of absolute Iron deficiency, which occurs when stores of iron within the body become deplete. Patients are also at risk of a state of functional iron deficiency, in which there is adequate supplies of iron within the body but there is an inability to mobilise or release iron from stores. At a cellular level, upregulation of the transferrin receptor is consistent with cellular iron deficiency and this has not previously been studied in SLE.

Given that preliminary findings suggest patients are at risk of iron deficiency, this study aimed to identify evidence of cellular iron deficiency and study the impacts on mitochondrial function.

Methods:

1. *Investigating for evidence of cellular iron deficiency and changes in mitochondrial mass in SLE.* Flow cytometry was used to identify cell surface lineage markers of B-cells, T-cells and Monocytes. Cellular transferrin receptor was measured using median fluorescence intensity to quantify cell surface expression of the key iron receptor. Mitochondrial mass was measured using the dye MitoTracker Green.
2. *Studying mitochondrial function in iron deficiency and SLE*. Peripheral blood mononuclear cells (PBMCs) from healthy controls (HCs) and patients with SLE were analysed using Seahorse Respirometry, which measures mitochondrial oxygen consumption rate (a measure of energy metabolism dependent upon oxidative phosphorylation). To assess differences between health, iron deficiency and SLE, 3 groups were assessed; 1. PBMCs derived from HCs; 2. PBMCs from patients with SLE; 3. Healthy PBMCs cultured in iron deficient condition, in which cells were treated with the potent iron chelator, Deferiprone. Following analysis of PBMCs, magnetic bead isolation was used to specifically study monocytes (CD14+) and T-helper cells (CD4+).

Results: Figure 1 highlights that SLE CD4+ T-cells, monocytes and B-cells show increased cell surface transferrin receptor expression compared with HCs thus suggesting these cells are iron deficient.

Figure 2a demonstrates that PBMCs derived from healthy controls grown in iron deficient conditions (with Deferiprone) show both basal and maximal mitochondrial respiration is reduced. PBMCs derived from patients with SLE show similarly reduced respiration at a level comparable to iron deficient healthy cells. Figure 2b shows that monocytes from patients with SLE have reduced basal and maximal respiration when compared with those from HCs whilst Figure 2c shows that T-cells show reduced basal but not maximal respiration.

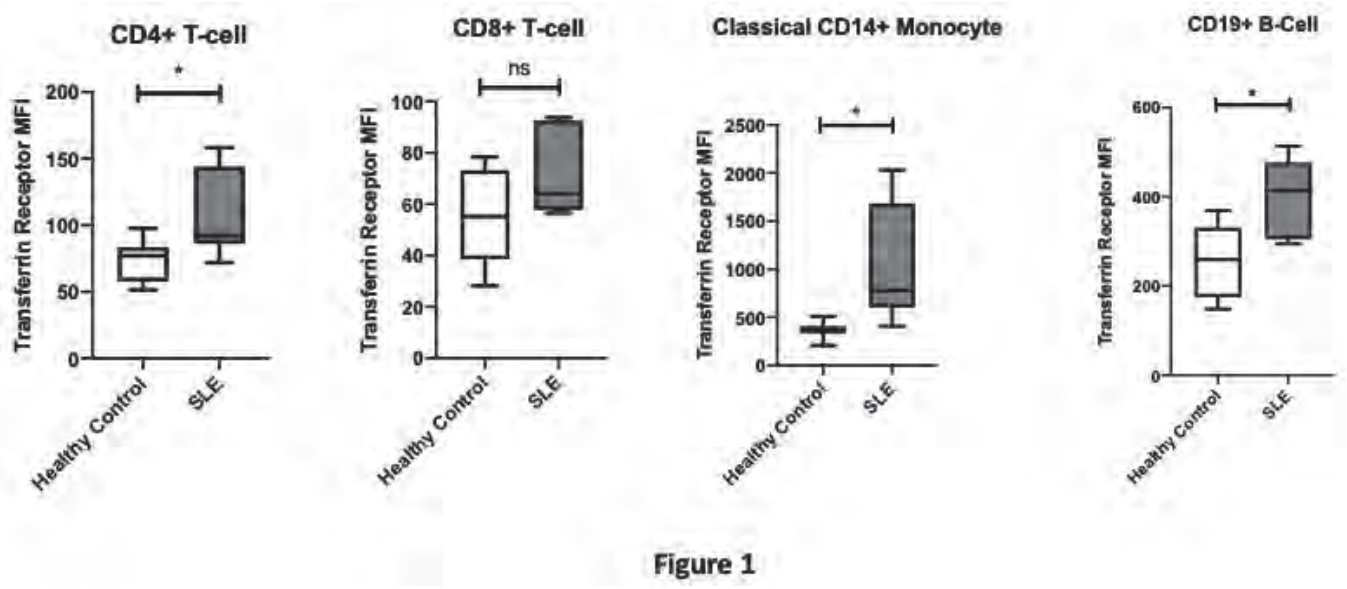

Figure 1. Transferrin Receptor Expression

Figure 3 reveals that both CD4+ and CD8+ T-cells have significantly lower mitochondrial mass when compared with HCs.

Conclusion: These findings suggest that patients with SLE display evidence of cellular iron deficiency in a number of immune cells. In addition, CD4+ T-cells and monocytes derived from SLE patients show reduced mitochondrial

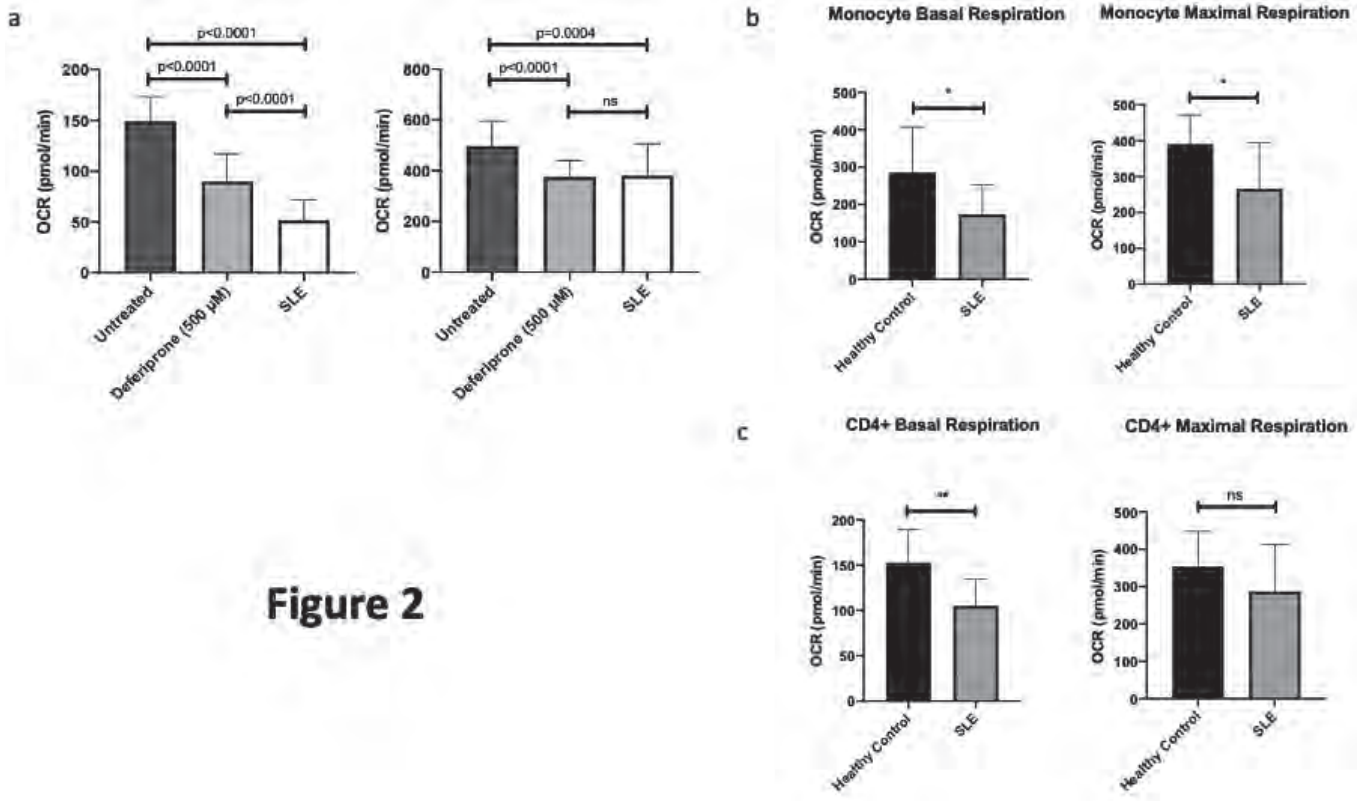

Figure 2. Basal and Maximal Mitochondrial Respiration

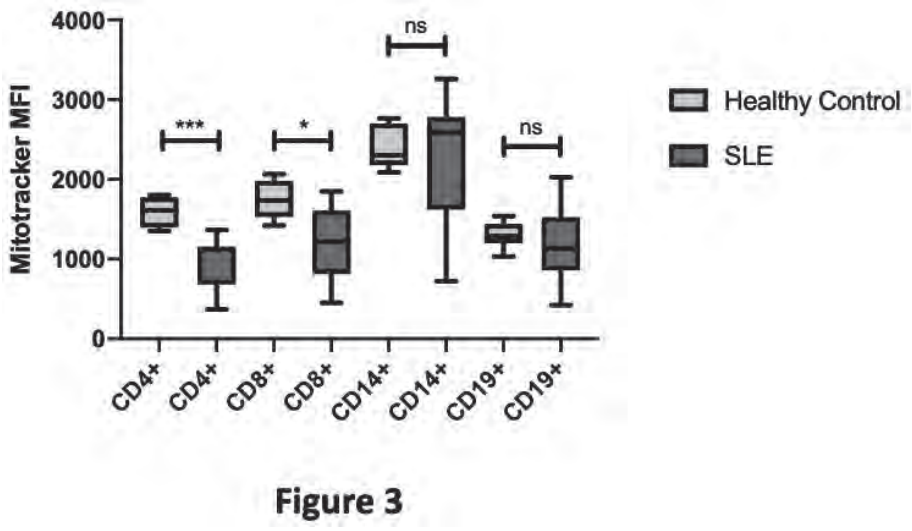

Figure 3. Differences in Mitochondrial Mass between Healthy Controls and SLE

respiration and T-cells from patients with SLE have lower mitochondrial mass, which may be a result of mitochondrial damage due to iron deficiency.

Disclosure: C. Wincup, None; **T. McDonnell**, None; **G. Robinson**, None; **F. Farinha**, None; **A. Radziszewska**, None; **A. Rahman**, None.

Abstract Number: 0295

CCL3L3–null Status May Predispose to Systemic Lupus Erythematosus and Non-scarring Alopecia

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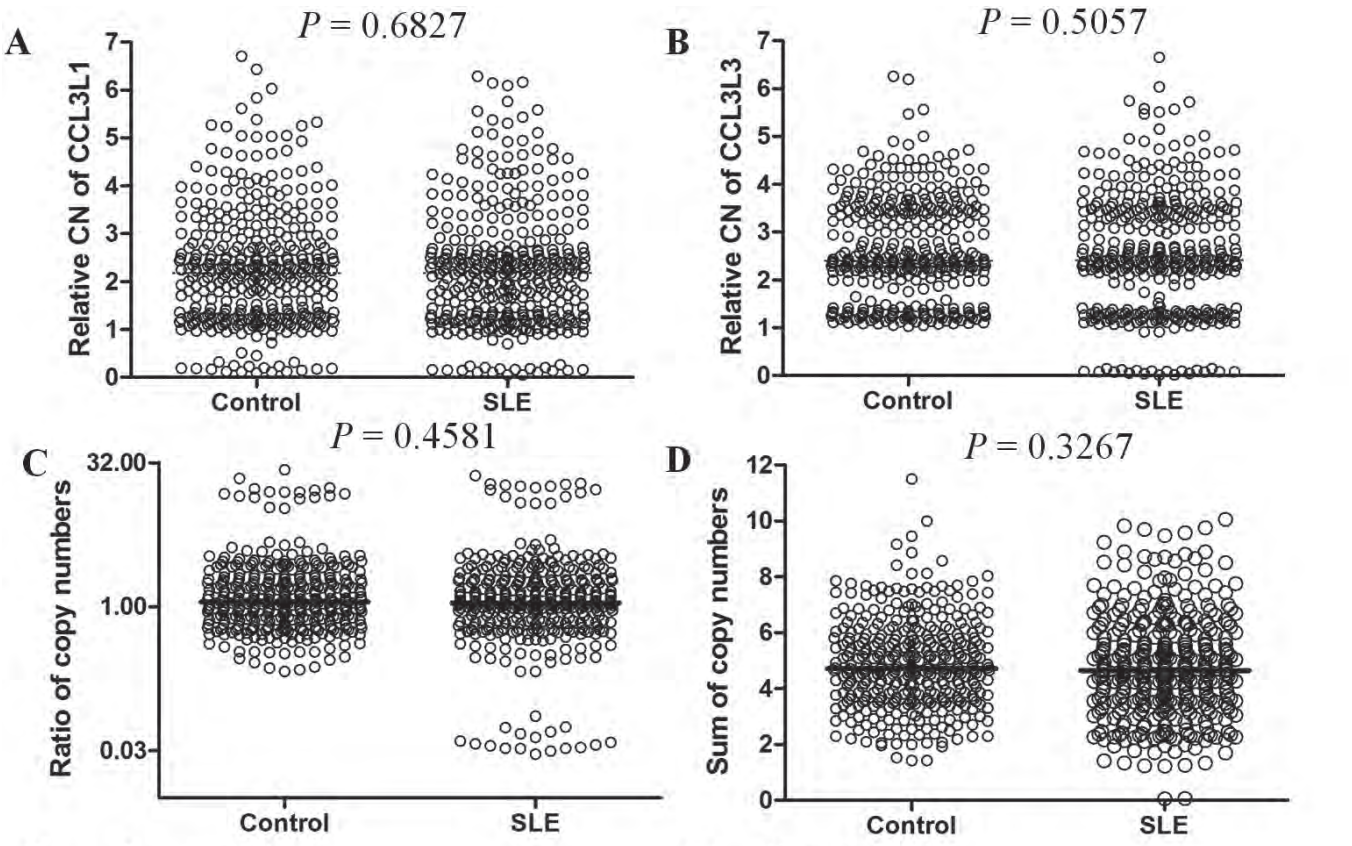
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The correlation between the copy number variation of *CCL3L1* and susceptibility to systemic lupus erythematosus (SLE), rheumatoid arthritis, Kawasaki disease, and HIV infection has been reported. However, the high level of homology (50 – 99%) within the *CCL3L* gene family has raised questions on the previously reported associations.

Methods: A modified real competitive PCR (mrcPCR) assay for the specific detection of *CCL3L1* and *CCL3L3* was developed with consideration of high homology within the *CCL3L* gene family. The *CCL3L1* and *CCL3L3* copy numbers were determined in 373 SLE patients and 358 age- and sex-matched controls by the mrcPCR assay and their associations with SLE or SLE manifestations were analyzed.



E $P = 1.000$

CN of CCL3L1	Control	SLE patients
CN > 0.45	341	356
CCL3L1-null (CN < 0.35)	17	17

F $P < 0.0001$

CN of CCL3L3	Control	SLE patients
CN > 0.8	358	354
CCL3L3-null (CN < 0.2)	0	19

Results: *CCL3L1* or *CCL3L3* copy numbers did not have any significant correlation with the prevalence of SLE. However, the absence of the *CCL3L3* gene or *CCL3L3*-null status was observed only in SLE patients (N = 19, $P < 0.0001$), whereas *CCL3L1*-null status was not significantly associated with SLE ($P = 1.000$). In addition, *CCL3L3*-null status was marginally associated ($P = 0.053$), and lower *CCL3L3* copy status (0 or 1) was significantly associated ($P = 0.013$) with non-scarring alopecia in patients with SLE.

Conclusion: The *CCL3L3*-null status may predispose to SLE, and low *CCL3L3*-copy status was significantly associated with non-scarring alopecia in SLE patients.

Association of CCL3L3-null status with SLE. A. No significant association of CCL3L1 copy number with SLE. B. No significant association of CCL3L3 copy number with SLE. C. No significant association of the copy number ratio of CCL3L3/CCL3L1 with SLE. D. No significant association of the copy number sum of CCL3L3 and CCL3L1 with SLE. Statistical tests for A-D were performed by the Mann-Whitney test. E. No significant association of CCL3L1-null status with SLE (Fisher's exact test) F. Significant association of CCL3L3-null status with SLE (Fisher's exact test).

Disclosure: E. Lee, None; **Y. Kim**, None; **H. Sim**, None; **E. Kang**, None; **Y. Won**, None; **E. Park**, None; **Y. Song**, None; **K. Hong**, None.

Abstract Number: 0296

Investigating the Differences in ANA Specificities Between Asymptomatic and Symptomatic ANA+ Individuals

Carolina Munoz-grajales[1], Stephenie Prokopec[2], Dennisse Bonilla[3], Earl D. Silverman[4], Sindhu Johnson[3], Arthur Bookman[5], Zahi Touma[6], Zareen Ahmad[7], Linda Hiraki[8], Paul Boutros[9], Andrzej Chruscinski[10] and Joan Wither[3], [1]University of Toronto, Toronto, Canada, [2]Ontario Institute for Cancer Research, Toronto, Canada, [3]University of Toronto Lupus Clinic, Centre for Prognosis Studies in Rheumatic Diseases, Toronto Western Hospital, University Health Network, Toronto, ON, Canada, [4]Division of Rheumatology, The Hospital for Sick Children, Translational Medicine, Research Institute, The Hospital for Sick Children, and Department of Paediatrics, University of Toronto., Toronto, ON, Canada, [5]Division of Rheumatology, University Health Network; 8Department of Medicine, University of Toronto; Division of Rheumatology, Toronto, Canada, [6]University of Toronto Lupus Clinic, Centre for Prognosis Studies in Rheumatic Diseases, Toronto Western Hospital, University Health Network; Krembil Research Institute, Toronto, ON, Canada, [7]Department of Medicine, University of Toronto; Division of Rheumatology, Mount Sinai Hospital, Toronto, Canada, [8]Division of Rheumatology, The Hospital for Sick Children; Department of Medicine, University of Toronto, Toronto, Canada, [9]Department of Immunology, University of Toronto; Department of Medical Biophysics, University of Toronto; Department of Pharmacology and Toxicology, University of Toronto; Department of Human Genetics, University of California; Department of Urology, University of California; Eli and Edythe Broad Center of Regenerative Medicine and Stem Cell Research, University of California; Institute for Precision Health, University of California; Jonsson Comprehensive Cancer Centre, University of California, Toronto, Canada, [10]Multi-Organ Transplant Program, University Health Network, Toronto, Canada

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Etiology & Pathogenesis Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Within the Anti-Nuclear Antibody (ANA) associated Systemic Autoimmune Rheumatic Diseases (SARD), such as Systemic Lupus Erythematous (SLE), Sjögren's Syndrome (SS), and Systemic Sclerosis (SSc), changes in the quantity and/or abundance of specific auto-antibodies (auto-Ab) occur as individuals progress towards SARD. However, previous studies have examined only a small number of ANAs. Thus, additional changes in the auto-Ab profile may accompany and predict disease progression that have not yet been appreciated. To address this, we examined the auto-Ab profile for a broad range of auto-antigens (auto-Ag) across 245 ANA^+ asymptomatic and symptomatic individuals.

Methods: A microarray was used to simultaneously measure 144 auto-Ab specificities across six patient groups: ANA^- healthy controls (HC, n=38); ANA^+ (≥1:160 by IF) individuals lacking SARD criteria (ANA^+ NS, n=83); individuals with ≥ 1 SARD criteria but with insufficient evidence for a diagnosis (undifferentiated connective tissue disease; UCTD, n=52); early untreated (except anti-malarial) SARD patients (n=26 SLE, n=30 SS, and n=16 SSc, classified according to the 1997 ACR criteria, 2013 ACR-EULAR criteria, and the 2016 ACR-EULAR criteria, respectively). ANA^+ NS and UCTD patients were followed yearly for up to 4 years, 12 of which demonstrated symptom progression. Eleven specific ANAs were detected using the Bioplex 2200 ANA-Screen and the expression levels of five IFN-α induced genes were measured and summed to generate an IFN5 score.

Results: Following unsupervised hierarchical clustering, IgG but not IgM auto-Ab showed clear patterns by diagnosis (heat map for IgG shown in Figure 1). A subset of ANA^+ NS and UCTD individuals were admixed with SLE and SS patients, which included the majority of progressors. In general, there was a moderate positive correlation between the levels of the auto-Ab detected by Bioplex and the corresponding auto-Ab in the microarray, however, using 2 standard deviations above the mean for ANA^- HC as a cut-off, elevated levels of auto-Ab were seen more frequently in ANA^+ individuals by microarray than by Bioplex. Furthermore, the microarray was able to detect differences in au-

Figure 1

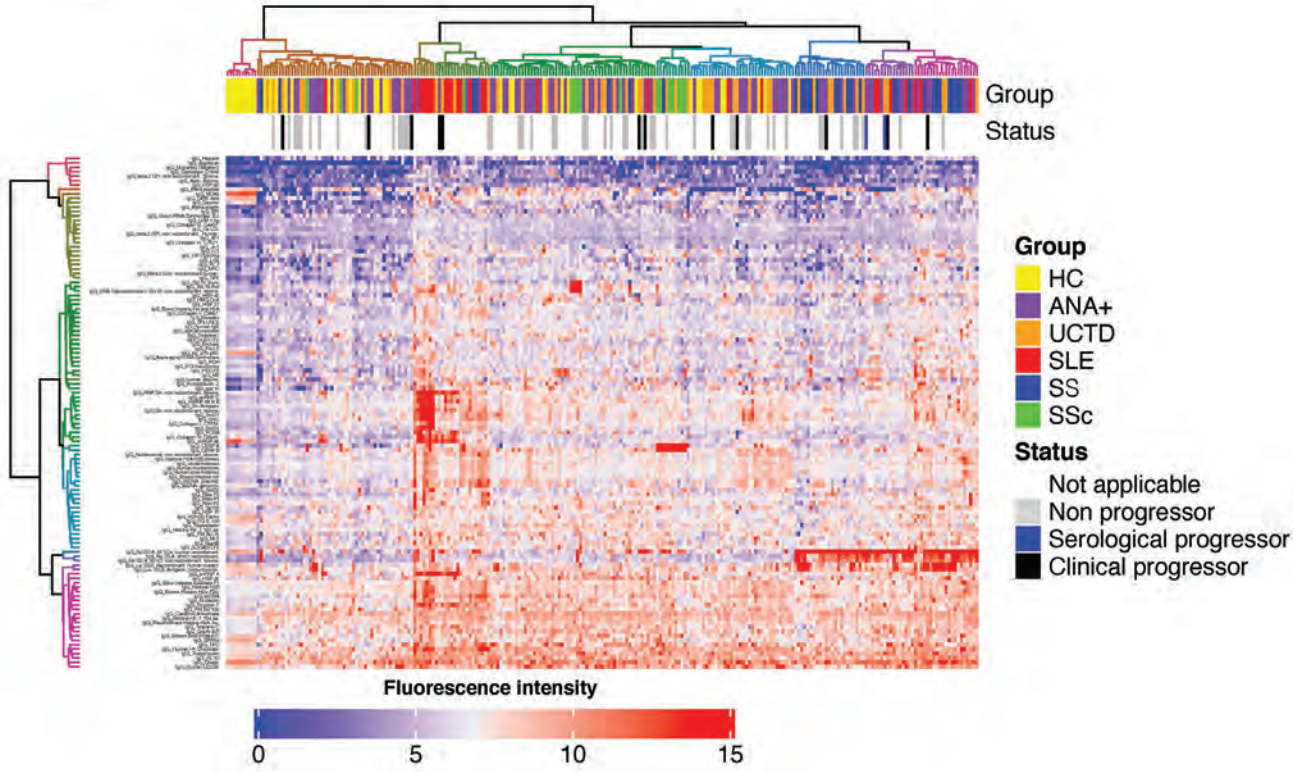


Figure 2

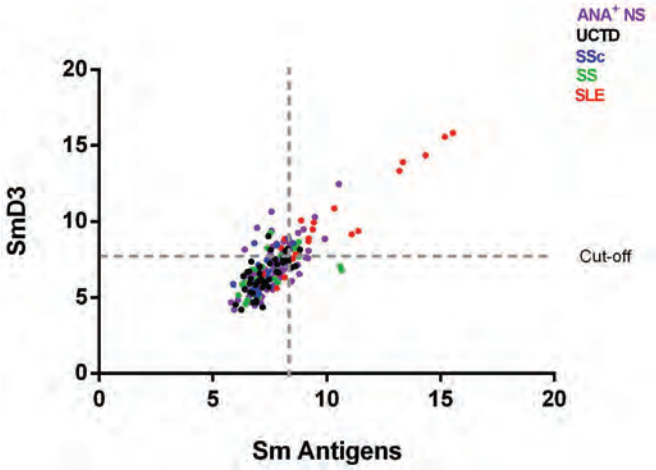


Figure 3

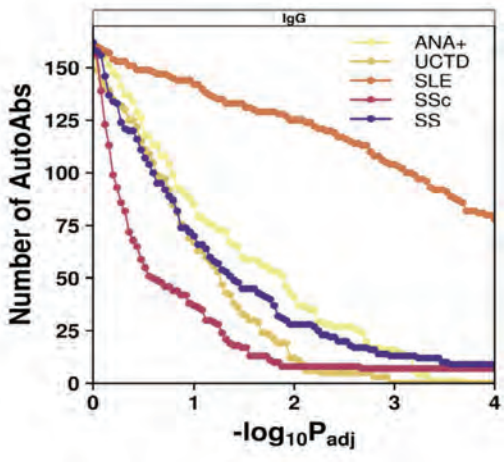


Figure 1. Heat Map of selected antigens following unsupervised clustering. IgG auto-Ab levels in red are high and those in blue are low. Controls are clustered on the left. Note the admixture of asymptomatic ANA+ and UCTD individuals with the early SARD patients, indicating similar auto-Ab profiles. Figure 2. Representative plot showing the levels of auto-Ab (Sm antigen and SmD3 subcomponent in this example) determined by microarray. Note that very high levels are restricted to SLE patients. Figure 3. P-value sensitivity plot examining the number of significantly differentially abundant probes relative to healthy controls, where it can be appreciated that many more IgG auto-Abs are elevated in SLE than in the other ANA+ groups.

to-Ab levels above the upper limit of detection on Bioplex, with very high levels restricted to SARD patients (Figure 2). Many more auto-Ag were recognized by IgG auto-Ab in SLE than in the other ANA$^+$ groups indicating that self-tolerance is significantly more disrupted in SLE (Figure 3). Interestingly, although anti-Ro60 had the strongest correlation with IFN-induced gene expression, only the presence of IgG anti-Ro52 at baseline was associated with progression in ANA$^+$ individuals lacking a SARD diagnosis. Strikingly, the types and levels of auto-Abs remained remarkably stable over time in these individuals regardless of whether they progressed or not.

Conclusion: ANA$^+$ individuals have auto-Ab to many self-antigens that are not being captured by current screening techniques. Measurement of these additional auto-Ab specificities, together with the larger dynamic range of the microarray, may help to identify individuals at high risk of progression.

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Abstract Number: 0297

Towards a Glucocorticoid Exposure Signature in SLE: Effects of Type I Interferon

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoids (GC), utilised in SLE for their broad immunosuppressive actions, predominantly mediate these effects by interaction with the cytoplasmic GC receptor (GR) to modulate gene transcription. Interactions of GC with many pathways in SLE, including the type 1 interferon (IFN) program, are poorly understood, with some evidence that IFN program is GC resistant. Minimising GC exposure is a treatment goal in SLE, however evidence-based treatment guidelines are lacking and no pharmacodynamic measure has been established. We aimed to evaluate GC regulated genes for their potential to be used as biomarkers of GC exposure in SLE.

Methods: A previously described set of 80 GC induced genes (Hu *et al*, Arthritis and Rheumatology, 2018) was measured using Fluidigm Biomark HD in peripheral blood mononuclear cells (PBMC) from patients meeting ACR criteria for SLE. Public data sets GSE49454 and GSE 88884 were accessed; clinical data correlating to GSE88884 were provided by Eli Lily. IFN status was determined using a validated 4 gene signature (IFI44, IFI44L, IFI27, RSAD2). RNAseq was performed on RNA extracted from healthy donor PBMC (n=4) treated with dexamethasone 10^{-7}M (DEX) and/or IFN 1000IU/mL. The HALLMARK_INTERFERON_ALPHA_RESPONSE gene set was extracted from the Broad Institute Molecular Signature Database.

Results: 80 GC-regulated genes were analysed in our cohort (n=18) and GSE49454 (n=62). Five genes (VSIG4, ALOX15B, CD163, AMPH, IL1R2) correlated with daily oral GC dose in both cohorts; these were combined to make a 5-gene GC signature (5GGCS) and this was analysed in GSE88884 (n=1,756). Although a dose-dependent asso-

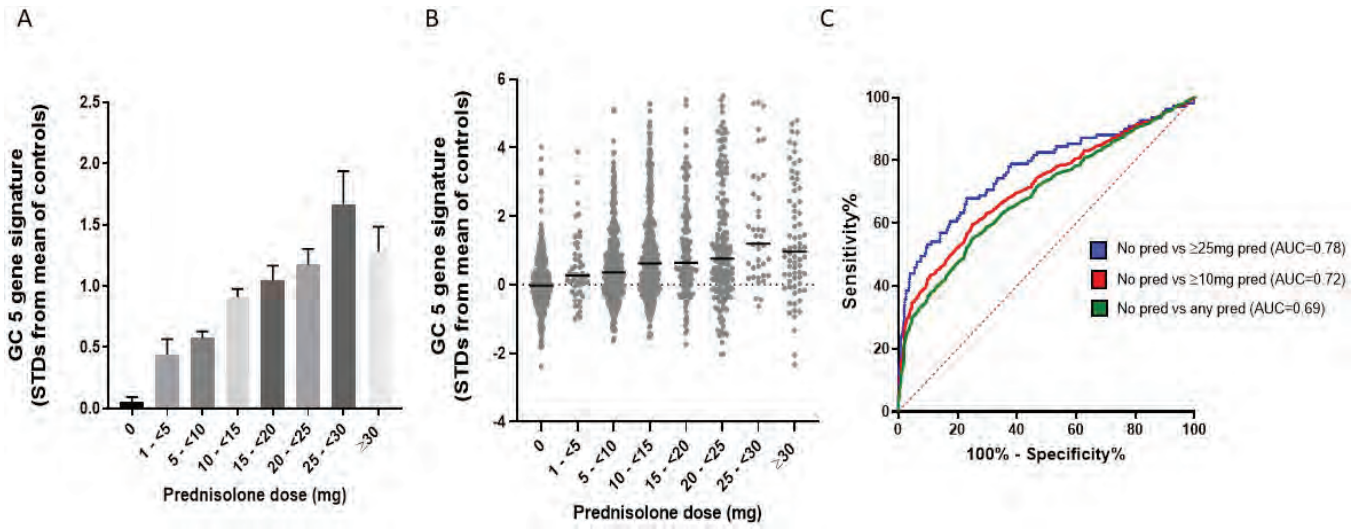

Figure 1. Correlations between 5-gene GC signature and prednisolone (pred) dose in dataset GSE888884. Mean GC signature scores increased with increasing GC dose (A, p for trend <0.0001) but exhibited large interpatient variation (B) and only modest benefit in differentiating patients taking/not taking prednisolone (C).

ciation of 5GGCS expression with GC doses was observed ($p < 0.0001$) (Fig 1A), high interpatient variation (Fig 1B) meant GC signature had only modest ability to distinguish patients taking/not taking GC overall (AUC = 0.69) (Fig 1C). We next examined whether IFN status impacted on GC signatures in SLE. In GSE88884 there was no effect of GC dose on ISG expression. In contrast, we observed a stronger correlation of 5GGCS with GC dose in IFN low patients (R=0.42, p< 0.0001) compared to IFN high patients (R=0.29, p< 0.0001) and IFN low patients had increased 5GGCS expression compared to IFN high patients matched for GC dose ($p < 0.05$), suggesting GC-induced genes are suppressed by IFN. RNAseq on IFN and DEX-treated PBMC confirmed that IFN significantly altered the expression of 29/80 GC-regulated genes, while DEX had minimal impact on ISG expression. We identified 61 genes regulated by DEX but not affected by IFN. Only 9/61 correlated with GC dose in GSE88884. Combined signatures using these genes showed modest ability to distinguish patients taking/not taking GC (AUC=0.63) (Figure 2), with slightly better performance for negatively regulated genes when prednisolone ≥ 25 mg/day (AUC=0.71).

Conclusion: A signature for GC exposure was identified, but interpatient variation and effects of IFN status may limit application in IFN-driven diseases such as SLE. These data confirm insensitivity of IFN-regulated genes to GC, but substantial impact of IFN on GC induced genes, strongly supporting the concept that IFN plays a role in GC resistance in SLE.

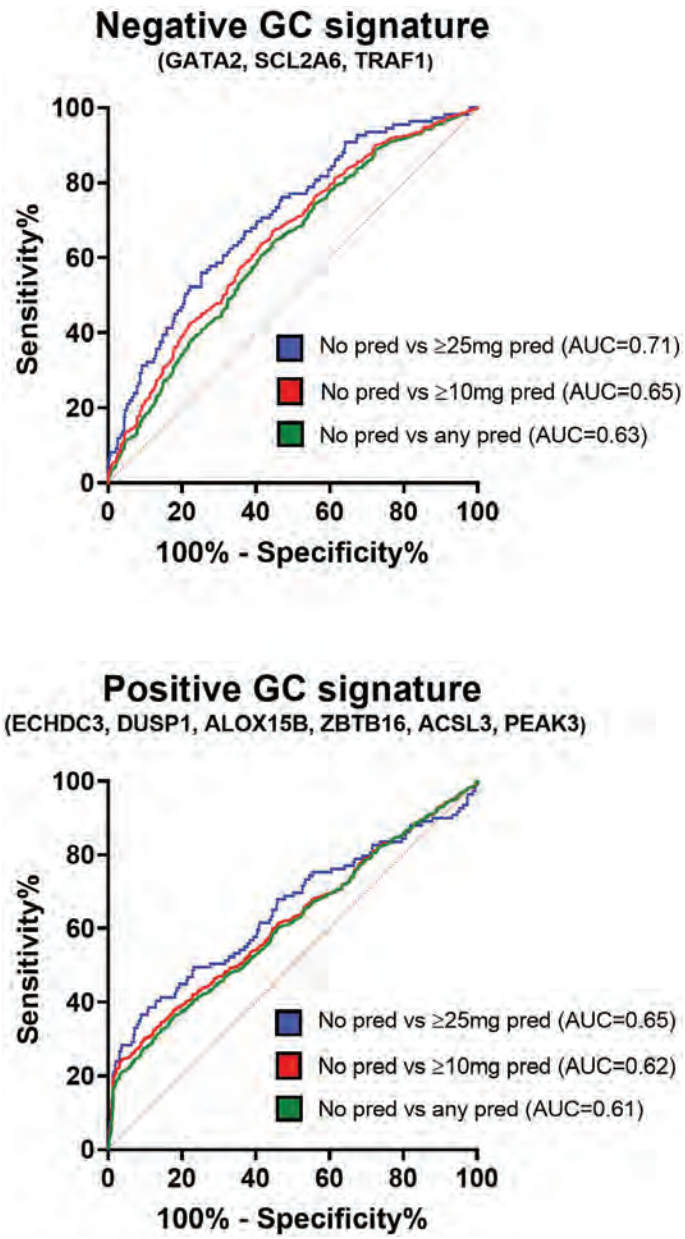

Figure 2. ROC curve analysis for negative and positive GC gene signatures to distinguish patients taking/not taking GC prednisolone (pred).

Disclosure: M. Northcott, None; **L. Gearing**, None; **H. Nim**, None; **C. Nataraja**, None; **S. Jones**, None; **E. Morand**, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, 5, Merck Serono, 2, 5, Neovacs, 5, Sandoz, 5, Novartis, 8, AbbVie, 5, Amgen, 5, Biogen, 5.

Abstract Number: 0298

Local Genetic Ancestry Associations with Clinical Features of Systemic Lupus Erythematosus

Olivia Solomon[1], Cristina Lanata[2], Cameron Adams[1], Joanne Nititham[3], Kim Taylor[3], Sharon Chung[3], Bernardo Pons-Estel[4], Teresa Tusié-Luna[5], Betty Tsao[6], Eric Morand[7], Marta Alarcón-Riquelme[8], Lisa Barcellos[1] and Lindsey Criswell[9], [1]University of California, Berkeley, Berkeley, CA, [2]UCSF, San Francisco, CA, [3]University of California, San Francisco, San Francisco, CA, [4]Centro Regional de Enfermedades Autoinmunes y Reumáticas (GO-CREAR), Rosario, Santa Fe, Argentina, [5]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubiran and Instituto de Investigaciones Biomédicas de la Universidad Nacional Autónoma de Mexico, Mexico City, Mexico, [6]Medical University of South Carolina, Charleston, [7]Medicine, School of Clinical Sciences at Monash Health, Monash University, Melbourne, Australia, [8]Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation;Centro Pfizer-Universidad de Granada-Junta de Andalucía de Genómica e Investigación Oncológica, Granada (GENYO), Granada, Spain, [9]Rosalind Russell/Ephraim P. Engleman Rheumatology Research Center, University of California San Francisco, San Francisco, CA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease with heterogeneous clinical manifestations which are known to vary in severity by race. Health disparities in prognosis and and presentation of SLE place a disproportionate burden on underrepresented populations as non-white populations with SLE are more likely to have features indicative of more severe disease. Prior analyses have shown global ancestry is associated with SLE risk and SLE features such as lupus nephritis; however, it is not yet known if local genetic ancestry is associated with specific SLE manifestations.

Methods: We evaluated local ancestry in multi-ethnic SLE cohorts from the UCSF Lupus Genetics Study and the California Lupus Epidemiology Study (CLUES). Genetic and phenotype data were available for 250 African American, 288 Asian, and 232 Hispanic subjects. All subjects satisfied the American College of Rheumatology criteria for SLE. DNA was extracted from blood or saliva samples and genotyped on the Affymetrix LAT1 World Array, which is designed specifically for diverse ethnic populations. Genotype data were imputed using *IMPUTE4* and phased using *BEAGLEv5.1*. We inferred local ancestry using *RFMix2.0*, which assigns local ancestry proportions to windows of the genome, and analyzed differences in local ancestry within each population. We used a non-parametric test statistic (Montana and Pritchard) to assess the difference in local ancestry between cases and controls at a SNP while adjusting for global ancestry differences. We assessed differences for two key features of SLE including if a subject had been diagnosed with lupus nephritis and age of symptom onset. We conducted tests both genome-wide and for candidate SLE SNPs previously identified to be associated with SLE and lupus nephritis risk.

Results: Although results did not remain significant after adjustment for multiple testing, top results (nominal $p < 0.01$) for differences in African Americans with lupus nephritis showed increased African ancestry at SNPs located in *TTYH2*, which functions in chloride anion channels and may play a role in kidney tumorigenesis. SNPs located in *SGCN,* which encodes a calcium binding protein, showed increased African and Asian ancestry in both African American and Asian subjects with lupus nephritis, respectively. In Hispanic subjects, increased Amerindian ancestry at a SNP previously associated with SLE risk in *DGKQ* was associated with an earlier age of onset.

Conclusion: These results warrant further investigation into local genetic ancestry differences to determine if these differences may contribute to health disparities for admixed patients with SLE.

Disclosure: O. Solomon, None; **C. Lanata**, None; **C. Adams**, None; **J. Nititham**, None; **K. Taylor**, None; **S. Chung**, None; **B. Pons-Estel**, None; **T. Tusié-Luna**, None; **B. Tsao**, None; **E. Morand**, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, 5, Merck Serono, 2, 5, Neovacs, 5, Sandoz, 5, Novartis, 8, AbbVie, 5, Amgen, 5, Biogen, 5; **M. Alarcón-Riquelme**, None; **L. Barcellos**, None; **L. Criswell**, None.

Abstract Number: 0299

The Minor Protective Allele at rs1876453 Is Associated with Increased Age of Onset of Systemic Lupus Erythematosus

Ani Oganesyan[1], Jennifer Kelly[2], Stuart Glenn[2], Adam Adler[2], Adrienne Williams[3], Mary Comeau[4], Julia Ziegler[5], Miranda Marion[5], Marta Alarcón-Riquelme[6], Graciela Alarcón[7], Juan-Manuel Anaya[8], Sang-Cheol Bae[9], Dam Kim[9], Lee Hye-Soon[9], Lindsey Criswell[10], Barry Freedman[11], Gary Gilkeson[12], Joel Guthridge[13], Chaim Jacob[14], Judith James[15], Diane Kamen[16], Joan Merrill[17], Kathy Moser Silvis[18], Timothy Niewold[19], Michelle Petri[20], Rosalind Ramsey-Goldman[21], John Reveille[22], Hal Scofield[23], Anne Stevens[24], Luis Vilá[25], Timothy Vyse[26], Kenneth Kaufman[27], John Harley[28], Carl Langefeld[5], Patrick Gaffney[2], Elizabeth Brown[29], Jeffrey Edberg[7], Robert Kimberly[7], Betty Tsao[12], Daniela Ulgiati[30], Kenneth Jones[31] and Susan Boackle[32], [1]Division of Rheumatology, University of Colorado School of Medicine, Aurora, CO, [2]Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oklahoma City, OK, [3]Department of Biostatistical Sciences and Center for Public Health Genomics Wake Forest School of Medicine, Winston-Salem,, NC, [4]Department of Biostatistical Sciences and Center for Public Health Genomics, Wake Forest School of Medicine; MC Analytics, Winston-Salem, NC, [5]Department of Biostatistical Sciences and Center for Public Health Genomics, Wake Forest School of Medicine, Winston-Salem, NC, [6]Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation;Centro Pfizer-Universidad de Granada-Junta de Andalucía de Genómica e Investigación Oncológica, Granada (GENYO), Granada, Spain, [7]Department of Medicine, University of Alabama at Birmingham, Birmingham, AL, [8]Center for Autoimmune Diseases Research (CREA), Universidad del Rosario, Bogotá, Colombia, [9]Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [10]Rosalind Russell/Ephraim P. Engleman Rheumatology Research Center, University of California San Francisco, San Francisco, CA, [11]Department of Internal Medicine, Wake Forest School of Medicine, Winston-Salem,, NC, [12]Division of Rheumatology, Medical University of South Carolina, Charleston, SC, [13]Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation, Oaklahoma, OK, [14]Department of Medicine, University of Southern California, Los Angeles, CA, [15]Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation;Department of Pathology, University of Oklahoma Health Sciences Center;Department of Medicine, University of Oklahoma Health Sciences Center, Edmond, OK, [16]Medical University of South Carolina, Charleston, SC, [17]Department of Clinical Pharmacology, Oklahoma Medical Research Foundation, Oklahoma City, OK, [18]Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation; Department of Pathology, University of Oklahoma Health Sciences Center, Oklahoma City, OK, [19]Colton Center for Autoimmunity, NYU School of Medicine, New York, NY, [20]Johns Hopkins University School of Medicine, Baltimore, [21]Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, [22]Department of Internal Medicine, University of Texas, Houston, TX, [23]Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation; Department of Medicine, University of Oklahoma Health Sciences Center; US Department of Veterans Affairs Medical Center, Charleston, SD, [24]Janssen Pharmaceuticals, Spring House, PA, [25]Division of Rheumatology, Department of Medicine, University of Puerto Rico Medical Sciences Campus, San Juan, Puerto Rico, [26]Division of Genetics and Molecular Medicine and Immunology, King's College, London, United Kingdom, [27]Cincinnati Children's Hospital Medical Center;US Department of Veterans Affairs Medical Center, Cincinnati, OH, [28]Cincinnati Children's Hospital Medical Center/Univ of Cincinnati College of Medicine, Cincinnati, OH, [29]Department of Pathology, University of Alabama at Birmingham, Birmingham, AL, [30]School of Pathology and Laboratory Medicine, Centre for Genetic Origins of Health and Disease, The University of Western Australia, Crawley, Australia, [31]Harold Hamm Diabetes Center, University of Oklahoma Health Science Center, Oklahoma City, OK, [32]Division of Rheumatology, University of Colorado School of Medicine; Denver Veterans Affairs Medical Center, Aurora, CO

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Etiology & Pathogenesis Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a clinically heterogenous autoimmune disease characterized by autoantibody- and complement-mediated inflammatory damage to multiple organ systems. We previ-

ously showed that the single-nucleotide polymorphism (SNP) rs1876453, located in the first intron of complement receptor 2 (CR2/CD21), is associated with decreased risk of lupus, with a preferential effect on anti-double stranded (ds) DNA antibodies. Since anti-dsDNA antibodies develop prior to clinically apparent disease, we hypothesized that the minor A allele at rs1876453 would delay lupus onset.

Methods: DNA from individuals recruited from multiple sites was processed with institutional review board approval. All patients with SLE met the 1997 American College of Rheumatology revised classification criteria. Age of onset was collected by chart review. Genotyping was performed on the OMRF Illumina iSelect platform. Global ancestry was estimated based on the genotype of ancestry informative markers (AIMs), using principal components analysis and ADMIXMAP, and genetic outliers removed. Final clean data were from European Americans (EA), African Americans (AA; 7.5% Gullahs), Asians (AS; 74.6% Koreans, 16.1% Chinese, 9.3% Japanese and Singaporeans) and Hispanics (HS) enriched for Amerindian–European admixture. Kruskal-Wallis and Mann-Whitney tests were used to detect differences between groups. A p value of < 0.05 was considered significant. Statistics and graphs were generated using GraphPad Prism software.

Results: The median age of lupus onset for subjects with AG or AA at rs1876453 was significantly higher than subjects with GG [median (interquartile range[IQR]) 40 (21) for AA (n=31), 32 (17) for AG (n=488), and 30 (19) for GG (n=5175), $p < 0.0001$]. When stratified based on sex, both females and males with the protective allele had significantly delayed disease onset [median (IQR) 40 (21.75) for AA (n=30), 32 (17) for AG (n=439), and 30 (18) for GG (n=4775) for females, $p = 0.0006$; median (IQR) 37.5 (21) for AA + AG (n=50) and 30 (23.75) for GG (n=400) for males, $p = 0.0083$].

Conclusion: The minor allele at rs1876453 delays lupus onset by 2-10 years. These data provide further support for a protective role for this SNP in lupus pathogenesis and suggest that novel therapies designed to mimic its mechanisms may prevent disease development in at-risk individuals.

Disclosure: A. Oganesyan, None; **J. Kelly**, None; **S. Glenn**, None; **A. Adler**, None; **A. Williams**, None; **M. Comeau**, None; **J. Ziegler**, None; **M. Marion**, None; **M. Alarcón-Riquelme**, None; **G. Alarcón**, None; **J. Anaya**, None; **S. Bae**, None; **D. Kim**, None; **L. Hye-Soon**, None; **L. Criswell**, None; **B. Freedman**, None; **G. Gilkeson**, None; **J. Guthridge**, None; **C. Jacob**, None; **J. James**, Progentec Diagnostics, Inc., 9; **D. Kamen**, None; **J. Merrill**, None; **K. Moser Silvis**, None; **T. Niewold**, None; **M. Petri**, AbbVie, 5, Amgen, 5, AstraZeneca, 2, 5, BMS, 5, Decision Resources, 5, GSK, 2, 5, INOVA, 5, IQVIA, 5, Janssen, 5, Eli Lilly, 2, 5, Merck EMD Serono, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5, Exagen, 2; **R. Ramsey-Goldman**, None; **J. Reveille**, Eli Lilly, 2, UCB, 5, Janssen, 2; **H. Scofield**, None; **A. Stevens**, Janssen Pharmaceuticals, 3; **L. Vilá**, None; **T. Vyse**, None; **K. Kaufman**, None; **J. Harley**, Now Diagnostics, Inc, 1, 6, GSK, 5; **C. Langefeld**, None; **P. Gaffney**, None; **E. Brown**, None; **J. Edberg**, None; **R. Kimberly**, None; **B. Tsao**, None; **D. Ulgiati**, None; **K. Jones**, None; **S. Boackle**, None.

Abstract Number: 0300

Exposure to Topical Antimicrobials Reduces Inflammatory Gene Expression in Cutaneous Lupus Lesional Skin

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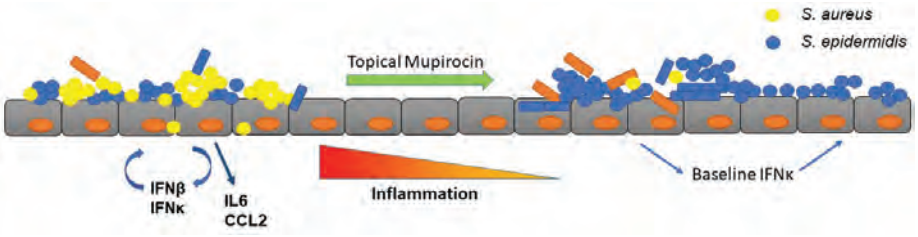
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM



Background/Purpose: Lupus lesional skin has elevated interferon expression, is highly colonized with *Staphylococcus aureus* (50%) and has no FDA-approved treatment options. *S. aureus* is known to induce proinflammatory responses such as cytokine expression and infiltration of immune cells to the affected area. Thus dysbiosis of the cutaneous microbiota could negatively affect the cutaneous immune response. Here we investigated the effect of topical antibiotic on lupus lesional skin to determine whether it affects inflammatory gene expression.

Methods: Adult Systemic Lupus Erythematosus (SLE) patients with skin inflammation (discoid or subacute cutaneous lupus erythematosus lesions) were recruited for this study from the Michigan Lupus cohort. The study was approved by the University of Michigan IRB and all patients gave informed consent. Lesions were swabbed to determine *S. aureus* colonization and then 4 mm skin biopsies were collected from the affected area. Patients were then randomized for either mupirocin treatment or petroleum jelly as the control (3x each). Mupirocin is a topical antibiotic that reduces bacterial load in the treated area. Product was applied to the lesion thrice daily for 7 days followed by repeat swab and biopsy. Biopsies were saved at -80 °C until use. RNA was isolated from the biopsies, checked for quality, and sequenced to determine transcriptomic changes.

Results: Mupirocin treatment results in a greater reduction of differentially-expressed genes (DEGs) (184) when compared to treatment with petroleum jelly (133). Functional enrichment analysis of the differentially regulated genes with each treatment showed that antibiotic treatment resulted in downregulation of genes that were significantly enriched in cytokine pathways including genes such as CCL19, CCL2, CXCL10, FPR1, and PTGS2 and genes such as STAT1, OAS3, SOCS3, ICAM1 and IL6 that are interferon (IFN) regulated. In contrast, downregulated genes post petroleum jelly treatment were enriched in cell communication and extracellular matrix pathways. Importantly, a scatter plot of the data to compare the effects of the two treatments showed that DEGs from the two treatments were almost completely independent with only a few that were DE in both treatments.

Conclusion: Inflammatory signaling can be reduced in lupus lesional skin by reducing Gram-positive bacterial load by topical antibiotic treatment. CCL19 is an interferon regulated gene that mediates ectopic lymphoid aggregates in non-lymphoid tissues. CCL2, a chemokine highly expressed in CLE, and CXCL10 are known to recruit monocytes, memory T cells and dendritic cells to sites of inflammation, resulting in Th1 oriented inflammation in CLE. Thus, modulation of the lesional microbiota may facilitate reduction in inflammation. This may be particularly helpful in patients who are recalcitrant to typical treatment protocols for skin inflammation. Further study of additional patients is underway to confirm this finding.

Graphical representation of lesional skin showing high IFN production that contributes to further inflammation, as well as high S. aureus colonization and low microbial diversity. Mupirocin treatment could reduce the proliferation and density of S. aureus thereby improving microbial diversity as well as reducing inflammation.

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Abstract Number: 0301

Genetic Associations and Polygenic Risk Assessment in Incomplete Lupus Erythematosus

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Etiology & Pathogenesis Poster

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with incomplete lupus erythematosus (ILE) have features of lupus, but have insufficient criteria for SLE classification. Some ILE patients transition to classified SLE, but the majority remain ILE without major organ involvement. ILE presumably shares genetic associations with SLE, while unique ILE variants or reduced genetic load may influence a more mild disease course. This study aims to identify variants associated with ILE through genome-wide association study (GWAS) and compare genetic load of ILE patients, SLE patients, and unaffected individuals.

Methods: ILE was defined as 3 ACR-1997 SLE criteria (ILE^{ACR}) and SLE as ≥4 ACR-1997 criteria by standardized medical record review. The subset of ILE^{ACR} who also did not meet SLE classification by *SLICC* criteria were designated ILE^{SLICC}. Study participants were genotyped on the Infinium Global Screening Array (GSA). After quality control, association testing included 335 ILE^{ACR} patients and 236 controls of diverse ancestry without self-reported lupus manifestations (Table). Principal components were included as logistic regression covariates. For genetic load

Table 1. Demographic Information and Genetic Load for the samples passing quality control for GWAS and genetic load calculations. n/a: not applicable. *p<0.05, **p<0.01, ***p<0.001 vs. control. For ILE vs. SLE comparisons, p>0.05.

Parameter	GWAS		Genetic Load			
	ILE^{ACR} (n=335)	Control (n=236)	ILE^{ACR}	ILE^{SLICC}	SLE	Control
Female, *n* (%)	296 (88.4)	208 (88.1)	159 (86.8)	109 (87.9)	203 (89.8)	134 (86.5)
Ancestry, n						
European American	183	155	183	124	226	155
African American	84	65				
American Indian	7	4				
Asian	8	1				
Hispanic	17	5				
Multiple	34	5				
Other/Unknown	2	1				
Unweighted genetic load, mean (range)	n/a	n/a	631.8*** (92.0)	630.7** (85.0)	632.8*** (104.0)	624.9 (93.0)
Weighted genetic load, mean (range)	n/a	n/a	77.0*** (15.8)	76.7** (11.8)	77.2*** (16.3)	75.9 (13.0)

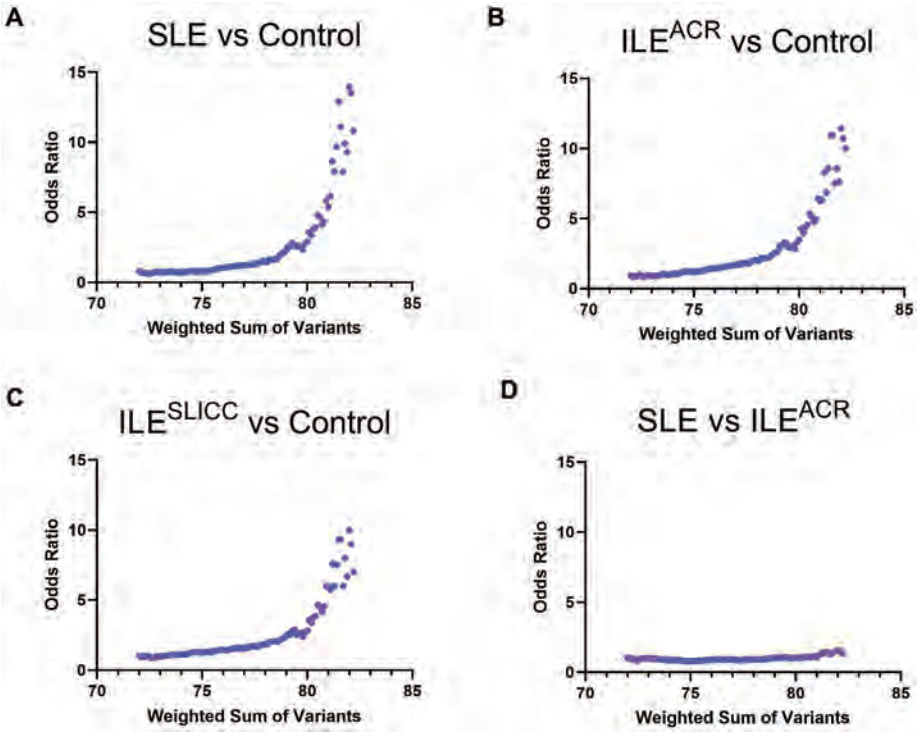

Figure 1. Odds ratio across genetic load range. The odds ratio represents the odds that an individual with a given genetic load (+/-2.0) will have SLE vs control (A), ILE(ACR) vs control (B), ILE(SLICC) vs control (C), or SLE vs ILE(ACR) (D), compared to a baseline comparison group of individuals in the lowest decile for weighted genetic load.

calculations, genotypes were pre-phased and imputed against 1000 Genomes Project haplotypes. Risk alleles that showed association with European SLE in Langefeld, et al (Nat Comm, 2017) (pFDR< 0.05) were identified in unrelated European American (EA) patients with SLE, ILE^{ACR}, ILE^{SLICC}, and controls (Table). Genetic loads were computed for each person as the number of risk alleles (unweighted) and allele sum with each allele weighted by its beta coefficient (weighted).

Results: Through GWAS in the ancestrally diverse population of ILE^{ACR} and controls, 12 variants exceeded the suggestive level of significance ($p < 1 \times 10^{-5}$). Eight were not previously reported in SLE (DPP10-DDX18, LRP1B, HMHB1-YIPF5, PHF14-THSD7A, ABCA1, DMRTA1-LINC01239, LOC105369443-CNTN5, and MIR3649-ADIPOR2), involving genes associated with phospholipid metabolism, asthma, Behçet disease, and cancers. No variants reached genome-wide significance ($p < 5 \times 10^{-8}$) in this small study. EA ILE^{ACR}, ILE^{SLICC}, and SLE patients had significantly greater unweighted and weighted genetic load than controls ($p < 0.001$) ($p < 0.001$) and ($p < 0.01$) (Table), respectively. There was no significant difference between mean genetic load (weighted or unweighted) in ILE and SLE, and weighted genetic load did not significantly differentiate between ILE^{ACR} and SLE in receiver operator characteristics analysis (area under the curve = 0.52). Further, those with a weighted genetic load of 81.0 (+/-2.0) or higher had greater odds of being SLE or ILE vs. healthy control (odds ratios >5.4-6.3), compared to individuals in the lowest weighted genetic load decile (Figure 1-C). However, weighted genetic load did not significantly affect odds of having SLE vs. ILE^{ACR} (Figure 1D).

Conclusion: ILE and SLE patients have similar genetic loads of SLE risk loci, suggesting a similar genetic predisposition between these conditions. Suggestive associations for novel loci are identified in ILE patients which require replication and validation. Phenotypic differences may be influenced by novel ILE variants and gene-environment interaction.

Disclosure: M. Slief, None; **J. Levin**, None; **S. Macwana**, None; **W. DeJager**, None; **R. Bourn**, None; **S. Nath**, None; **M. Munroe**, Progentec Diagnostics, Inc., 2, 9; **T. Aberle**, None; **P. Gaffney**, None; **J. Merrill**, Bristol Myers Squibb, 2, 5, GlaxoSmithKline, 2, 5, AstraZeneca, 5, AbbVie, 5, Amgen, 5, Aurinia, 5, EMD Serono, 5, Remegen, 5, Janssen, 5, Provention, 5, UCB, 5; **J. James**, Progentec Diagnostics, Inc., 9; **J. Guthridge**, None.

Abstract Number: 0302

Longitudinal Study of Acute SLE Flare Reveals Dynamic Changes in Multiple Immune Cell Subsets

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In SLE, periods of relative quiescence are punctuated by flares in disease activity that can lead to extensive tissue damage and morbidity. Existing studies suggest that flare onset is linked to immune cell subsets involved in ANA production, including activated memory T helper cells, plasma cells, and age-associated B

Table 1. There are significant differences between healthy controls and lupus patients in multiple immune cell subsets at baseline; however, many of these populations do not show further differences between flare and inactive patients.

Immune Cell Subsets	Healthy Control (n=16)	Lupus (n=72)	*p value*	Acute Flare (n=47)	Inactive (n=25)	*p value*
B Cells (mean% [standard deviation])						
Total $CD19^+$	8.85 [4.21]	11.85 [11.30]	0.8492	10.95 [9.47]	13.54 [14.20]	0.5314
Naïve (IgD^+CD27^-)	61.91 [10.09]	61.04 [21.60]	0.6619	**56.89 [21.80]**	**69.34 [19.04]**	**0.0162**
Unswitched Memory (IgD^+CD27^+)	**2.47 [1.88]**	**1.51 [1.29]**	**0.0137**	**1.20 [0.92]**	**2.07 [1.71]**	**0.0407**
Switched Memory (IgD^-CD27^+)	5.99 [3.83]	6.74 [7.86]	0.4876	7.33 [8.20]	5.56 [7.17]	0.3506
Activated Total $CD19^+$ ($CD86^+$)	7.88 [6.11]	10.22 [9.59]	0.9623	11.28 [9.44]	8.10 [9.73]	0.0828
Activated Naive ($CD86^+$)	**8.29 [3.62]**	**5.26 [6.43]**	**0.0012**	5.65 [6.65]	4.56 [6.07]	0.2792
Activated Unswitched Memory ($CD86^+$)	**13.11 [9.60]**	**12.22 [17.15]**	**0.0487**	13.16 [17.52]	10.48 [16.65]	0.1333
Activated Switched Memory ($CD86^+$)	25.58 [15.87]	40.63 [26.67]	0.0633	**35.89 [26.56]**	**49.34 [25.09]**	**0.0461**
$Tbet^+$ ABCs ($CD21^-CD11c^+$)	**0.63 [0.78]**	**1.97 [2.00]**	**0.0038**	**2.64 [2.20]**	**1.06 [1.21]**	**0.0004**
Plasma Cells ($CD19^{lo}CD27^{hi}CD38^+CD138^+$)	0.014 [0.013]	0.091 [0.164]	0.1916	0.093 [0.146]	0.087 [0.196]	0.9927
Plasmablasts ($CD19^{lo}CD27^{hi}CD38^+CD138^-$)	0.074 [0.037]	0.285 [0.406]	0.0752	0.273 [0.396]	0.306 [0.430]	0.4747
T Cells (mean% [standard deviation])						
Total $CD4^+$ ($CD3^+CD4^+CD8^-$)	37.54 [11.82]	37.99 [12.72]	0.8768	37.71 [12.36]	38.49 [13.62]	0.6787
T_{fh} ($CD4^+CD45RA^-PD1^{hi}CXCR5^{hi}$)	4.02 [2.24]	4.43 [2.89]	0.6921	4.31 [3.11]	4.64 [2.52]	0.4813
T_h1 ($CCR6^-CXCR3^+$)	0.28 [0.40]	0.36 [0.61]	0.9791	0.34 [0.63]	0.41 [0.60]	0.3230
T_h2 ($CCR6^-CXCR3^-$)	2.20 [1.54]	2.81 [1.81]	0.2847	2.75 [2.00]	2.92 [1.47]	0.4299
T_h17 ($CCR6^+CXCR3^-$)	0.90 [0.84]	1.22 [1.13]	0.5932	1.24 [1.22]	1.19 [0.99]	0.8394
T_{ph} ($CD4^+CD45RA^-PD1^{hi}CXCR5^-$)	**10.25 [6.15]**	**15.86 [8.79]**	**0.0124**	17.28 [9.15]	13.25 [7.60]	0.0559
$T_{ph}1$ ($CCR6^-CXCR3^+$)	0.39 [0.50]	0.57 [1.21]	0.9126	0.65 [1.42]	0.43 [0.68]	0.4968
$T_{ph}2$ ($CCR6^-CXCR3^-$)	**6.06 [3.67]**	**11.17 [7.84]**	**0.0155**	11.86 [7.03]	10.02 [9.07]	0.0865
$T_{ph}17$ ($CCR6^+CXCR3^-$)	3.59 [3.37]	4.84 [3.82]	0.2618	4.91 [3.42]	4.71 [4.49]	0.4805
T_{regs} ($CD3^+CD4^+CD45RA^-CD25^+CD127^-$)	**3.89 [1.35]**	**6.27 [3.98]**	**0.0296**	6.00 [3.99]	6.83 [4.00]	0.4397
Innate Immune Cells (mean% [standard deviation])						
Classical Monocytes ($CD3^-CD20^-CD19^-CD14^{hi}CD16^-$)	**32.71 [8.13]**	**40.04 [15.20]**	**0.0317**	39.18 [16.04]	41.68 [13.64]	0.5673
$CD16^{hi}$ Monocytes ($CD3^-CD20^-CD19^-CD14^{hi}CD16^{hi}$)	**1.25 [0.67]**	**2.94 [2.16]**	**0.0012**	2.97 [2.32]	2.82 [1.81]	0.9304
pDCs ($CD3^-CD20^-CD19^-CD14^-HLA\text{-}DR^+CD123^+CD11c^-$)	0.89 [0.44]	0.74 [0.50]	0.1761	**0.65 [0.50]**	**0.89 [0.48]**	**0.0378**
mDCs ($CD3^-CD20^-CD19^-CD14^-HLA\text{-}DR^+CD123^-CD11c^+$)	1.61 [1.08]	1.73 [1.30]	0.9513	**1.50 [1.33]**	**2.17 [1.16]**	**0.0135**
$CD16^+CD56^+$ NK cells ($CD3^-CD20^-CD19^-CD14^-$)	**34.11 [16.39**	**17.03 [11.88]**	**0.0001**	**14.48 [11.05]**	**21.90 [12.12]**	**0.0139**

cells (ABCs); however, it is largely unknown how these and other immune subsets differ between flare and inactive disease, particularly in the period post-flare.

Methods: Healthy controls (HC, n=16) and acute flare (n=47) or inactive (n=25) SLE patients were recruited, with patients diagnosed based on the 1997 ACR criteria. Flare patients were within 1 month of flare onset (a clinical SLEDAI-2K >0 requiring a change in therapy) while inactive patients had to be inactive for ≥1 year (clinical SLEDAI-2K=0) and on ≤10mg prednisone at recruitment. All patients had blood collected at first visit as well as at 6M and 12M follow-ups. Freshly isolated PBMCs were stained with various fluorochrome-conjugated antibodies to identify immune cell populations by flow cytometry. Statistical significance was determined using Mann-Whitney U tests to compare baseline groups and Wilcoxon matched-pairs signed rank tests to compare baseline and follow-up visits.

Results: SLE patients differed significantly from HC in multiple immune cell subsets at baseline, with higher proportions of ABCs, T peripheral helper (T_{ph}) cells, regulatory T (T_{reg}) cells, and pro-inflammatory monocytes, as well

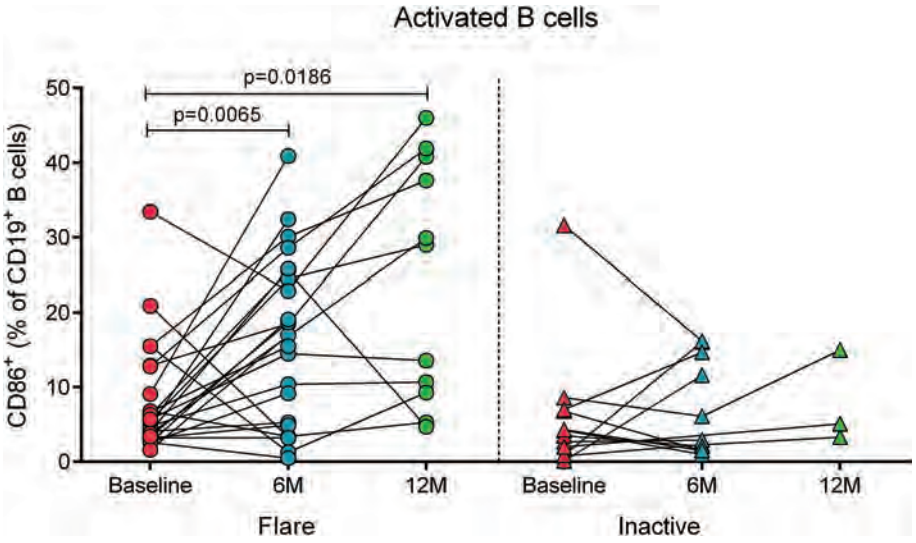

Figure 1. Flare patients show significant increases in the proportions of activated B cells in the blood at 6M and 12M post-flare, while levels remain stable in inactive patients over time.

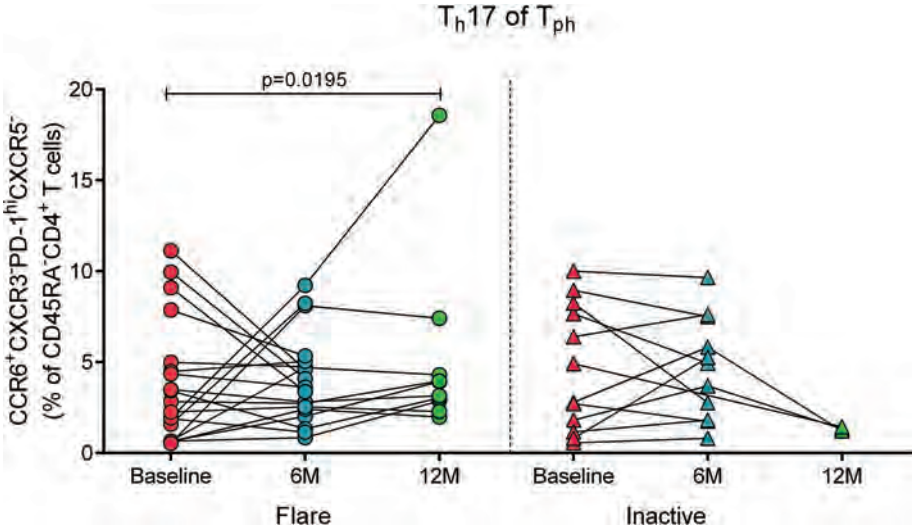

Figure 2. Flare patients show significant increases in the proportions of Tph Th17 cells in the blood at 12M post-flare, while levels remain stable in inactive patients over time.

as a trend to higher plasmablasts (see Table 1). However, stratification of SLE patients into acute flare and inactive groups revealed limited differences between these groups at baseline. While flare patients had significantly higher proportions of ABCs as well as significantly lower proportions of NK cells, pDCs and mDCs as compared to inactive patients, the majority of monocyte, B, T, and antibody-producing cell subsets did not differ between flaring and inactive patients, suggesting that these populations are not enriched in the blood during flare. In contrast, flare patients diverged significantly from inactive patients in multiple immune subsets at 6M and/or 12M following flare treatment, showing significant increases in B cell activation ($p=0.0118$), $CD16^{+}$ monocytes ($p< 0.0001$), transitional B cells ($p=0.0006$), T_{regs} ($p=0.0093$), T_{ph} cells ($p=0.0385$) and $T_{ph}17$ cells ($p=0.0055$). These differences appeared to stem from increases in these populations in flare patients during the post-flare period, while inactive patients remained relatively stable over the same time frame (see Figures 1 and 2 for representative results).

Conclusion: Our results suggest that at the time of acute flare many of the activated immune cell populations that are proposed to participate in flare are absent from the peripheral blood. Instead, differences between flaring and inactive patients become more apparent in the months following flare treatment, as activated immune cells are not recruited into and/or migrate out of inflamed tissues. These findings highlight the importance of longitudinal studies of flare in SLE.

Disclosure: K. Manion, None; **D. Bonilla**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **M. Urowitz**, None; **Z. Touma**, None; **J. Wither**, None.

Abstract Number: 0303

SLE Patients Stratify into Distinct Clusters Based on Their Peripheral Blood Immunologic Phenotype During Acute Flare

Kieran Manion[1], Carolina Munoz-Grajales[2], Michael Kim[3], Kirubel Goliad[4], Dennisse Bonilla[5], Dafna Gladman[1], Murray Urowitz[6], Zahi Touma[7] and Joan Wither[5], [1]Krembil Research Institute, Toronto Western Hospital, Toronto, ON, Canada, [2]University of Toronto-UHN, Toronto, ON, Canada, [3]Krembil Research Insitute, Toronto, ON, Canada, [4]University of Toronto-UHN, Toronto, Canada, [5]University of Toronto Lupus Clinic, Centre for Prognosis Studies in Rheumatic Diseases, Toronto Western Hospital, University Health Network, Toronto, ON, Canada, [6]University Health Network, University of Toronto, Toronto, ON, Canada, [7]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Friday, November 6, 2020
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Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is a chronic autoimmune disease in which periods of quiescence are interspersed with acute flares of disease activity that produce much of the associated tissue and organ damage. Current literature suggests that flares can be induced by multiple environmental triggers and are mediated by pro-inflammatory and ANA-producing immune cell subsets; however, the specific immune response that characterizes acute flare as opposed to disease quiescence in the disease course of an individual with SLE is largely unknown.

Methods: Healthy controls (n=16) and acute flare (n=47) or inactive (n=25) SLE patients were recruited. All SLE patients were diagnosed based on the 1997 ACR criteria. For acute flare, patients had to be within 1 month of flare onset (clinical SLEDAI-2K >0 requiring a change in therapy); inactive patients had to be ≥1 year without flare (clinical SLEDAI-2K=0) and on ≤10mg prednisone. Freshly isolated PBMCs were stained for various immune cell subsets and

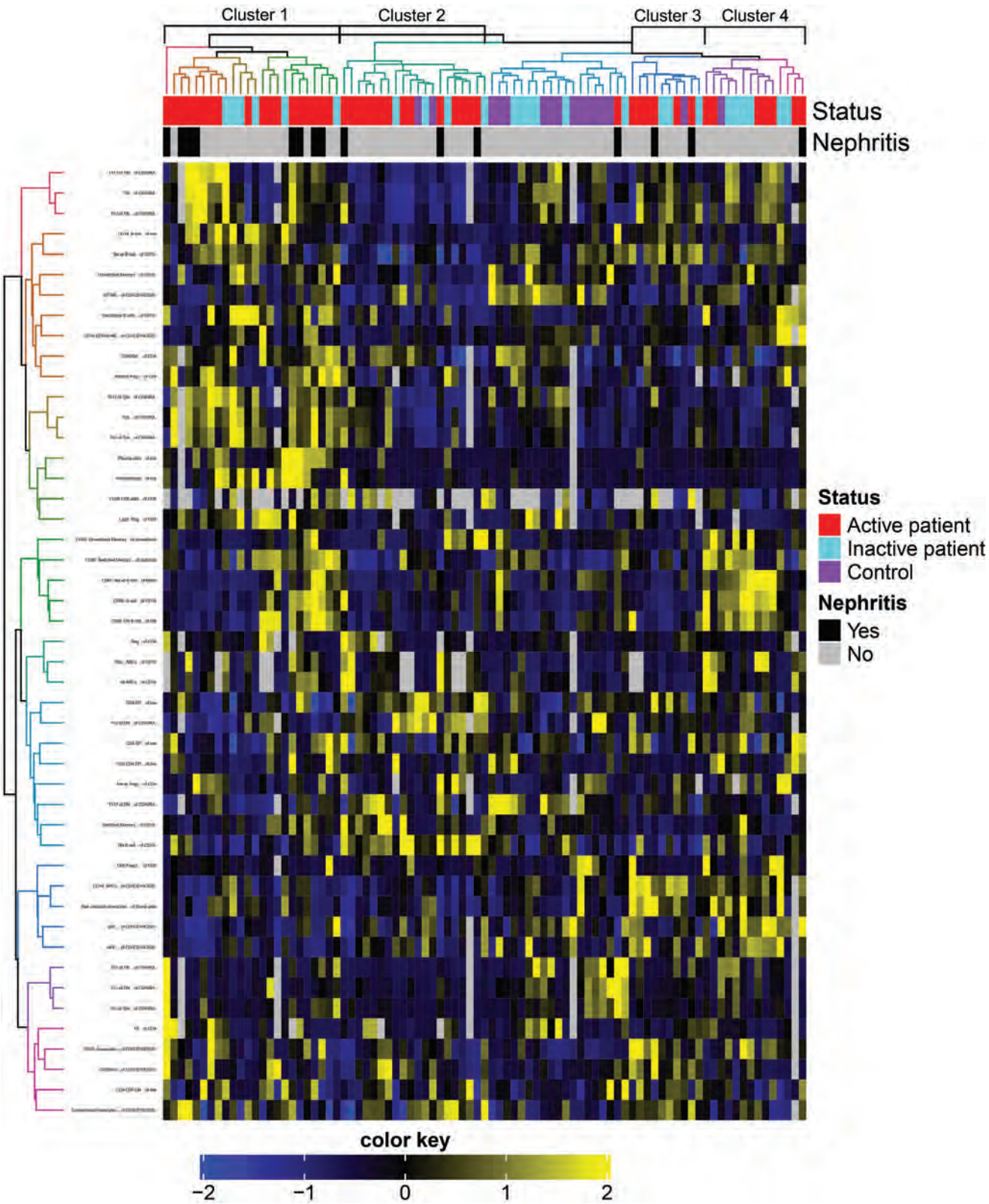

Figure 1. Heat map depicting the clustering of Z-scores for immune cell populations from healthy controls, acute flare and inactive SLE patients.

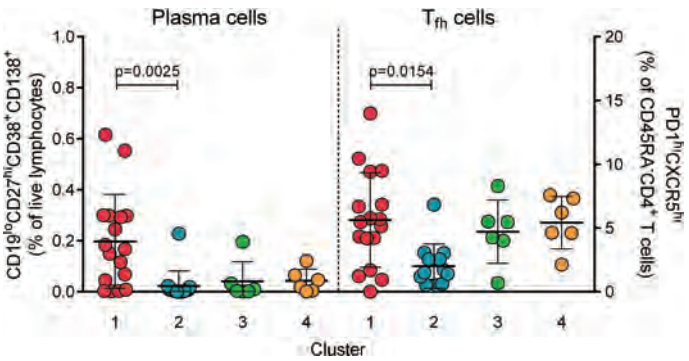

Figure 2. Plasma cells (left axis) and Tfh cells (right axis) are significantly elevated in cluster 1 of flare patients as compared with cluster 2.

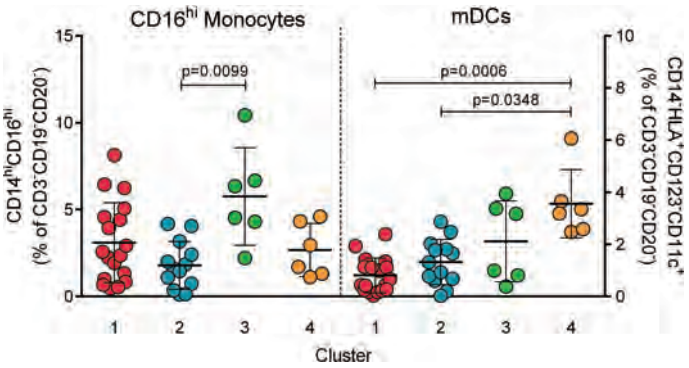

Figure 3. CD16hi monocytes (left axis) are significantly higher in cluster 3 of flare patients compared with cluster 2, while mDCs (right axis) are significantly higher in cluster 4 than in clusters 1 and 2.

examined by flow cytometry. Z-scores were calculated for the proportions of immune cell subsets from HC, flare and inactive patients. A heat map displaying immune cell subsets was generated using the ComplexHeatmap package in R (v3.6.1). For comparisons between groups, statistical significance was determined using Kruskal-Wallis non-parametric tests.

Results: While HC mostly clustered together on the heat map, flare patients stratified into four predominant clusters and inactive patients were admixed with both HC and flare groups. Looking at flare patients alone, cluster 1 had significantly elevated plasma cells ($CD19^{lo}CD27^{hi}CD38^{+}CD138^{+}$; 1 vs 2: p=0.0025), T follicular helper (T_{fh}) cells ($CD4^{+}CD45RA^{-}PD\text{-}1^{hi}CXCR5^{hi}$; 1 vs 2: p=0.0154) and $T_{fh}17$ cells ($CD4^{+}CD45RA^{-}PD\text{-}1^{hi}CXCR5^{hi}CCR6^{+}CXCR3^{-}$; 1 vs 2: p=0.0037), as well as trends to increased T peripheral helper (T_{ph}; $CD4^{+}CD45RA^{-}PD\text{-}1^{hi}CXCR5^{-}$) and regulatory T cells (T_{reg}; $CD4^{+}CD45RA^{-}CD25^{+}CD127^{-}$). Cluster 2 had similar or decreased proportions of immune subsets compared to the other groups, with the exception of expanded double negative B cells ($IgD^{-}CD27^{-}CD19^{+}$; 2 vs 1: p=0.0013, 2 vs 3: p=0.0010). In contrast, clusters 3 and 4 exhibited a more innate phenotype, with significant elevations in $CD16^{hi}$ ($CD14^{hi}CD16^{hi}CD3^{-}CD19^{-}CD20^{-}$; 3 vs 2: p=0.0099) and non-classical monocytes ($CD14^{int}CD16^{+}CD3^{-}CD19^{-}CD20^{-}$; 3 vs 2: p=0.0090), or in mDCs ($CD14^{-}HLA^{+}CD123^{-}CD11c^{+}CD3^{-}CD19^{-}CD20^{-}$; 4 vs 1: p=0.0006, 4 vs 3: p=0.0348) and NK cells ($CD16^{+}CD56^{+}CD14^{-}CD3^{-}CD20^{-}CD19^{-}$; 4 vs 3: p=0.0196), respectively. While there was no difference between the clusters with regard to age, dsDNA, complement or SLEDAI-2K score, patients in cluster 1 trended towards a longer disease duration and were more likely to have nephritis.

Conclusion: Our findings suggest that significant variations in the immune mechanisms that promote flare may exist between patients, with some patients demonstrating a more adaptive immune response in flare while others have a more innate immune response. Thus, effective treatment of SLE flare may require a more targeted approach tailored to the specific flare mechanism in each patient.

Disclosure: K. Manion, None; **C. Munoz-Grajales**, None; **M. Kim**, None; **K. Goliad**, None; **D. Bonilla**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **M. Urowitz**, None; **Z. Touma**, None; **J. Wither**, None.

Abstract Number: 0304

Type I Interferon Inhibits Glucocorticoid-Induced Leucine Zipper (GILZ) Expression and Upregulation by Glucocorticoids

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis Poster
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoids (GC) are broadly used in the treatment of inflammatory diseases, including systemic lupus erythematosus (SLE). Despite their widespread use, most SLE patients do not reach a state of low disease activity on GC treatment. Currently it is not completely understood what factors play a role in the response to this treatment. It is thought that many anti-inflammatory effects of GC are mediated through upregulation of glucocorticoid-induced leucine zipper (GILZ). GILZ expression is decreased in the blood of SLE patients compared to healthy controls. Interestingly, we have previously shown that this is inversely correlated with the interferon (IFN) signature induced by type I IFN, including IFNα and IFNβ. Given the important role of type I IFN in SLE pathogenesis, we studied whether IFNα could suppress GILZ and thereby reduce the effectiveness of GC.

Methods: Human peripheral blood mononuclear cells (PBMC) were isolated from healthy individuals and treated with 1000 IU IFNα2a, 100 nM dexamethasone (DEX) or both, with or without the Jak1/Tyk2 inhibitor tosylate salt (TS). GILZ expression in these cultures was analysed using RT-PCR. STAT1 binding sites were analyzed from public datasets and using chromatin immunoprecipitation followed by RT-PCR. Public datasets were also used to study the effect of IFNα and the interplay between GC and IFNα on GILZ expression in SLE patients.

Results: IFNα treatment reduces the expression of GILZ in human PBMC in a dose- and time-dependent manner. Interestingly, it also reduces the DEX-induced upregulation of GILZ. This corresponds to data in SLE patients, where GC treatment is less effective at inducing GILZ in patients with a high IFN score than in patients with a low IFN score. Mechanistically, we found that IFNα2a reduces GILZ expression via the Jak1/Tyk2 signalling pathway, as treatment with the specific inhibitor TS reversed the effects of IFNα2a. In public datasets, and then confirmed via ChIP, we subsequently found that the transcription factor STAT1, downstream of Jak1/Tyk2, has multiple DNA binding sites surrounding the GILZ locus. These STAT1 binding sites coincide with binding sites of the glucocorticoid receptor (GR), which may explain the mechanism by which IFNα2a reduces the DEX-induced GILZ upregulation.

Conclusion: In human PBMC, IFNα2a reduces GILZ expression and the DEX-induced upregulation of GILZ via the Jak1/Tyk2 signalling pathway and direct DNA binding of STAT1 to the GILZ locus. These data reveal a potential mechanism by which type I IFN suppress the effectivity of GC, which could be targeted to improve therapeutic efficacy in SLE.

Disclosure: W. Dankers, None; **M. Northcott**, None; **T. Bennett**, None; **B. Russ**, None; **J. Flynn**, None; **S. Jones**, None; **E. Morand**, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, 5, Merck Serono, 2, 5, Neovacs, 5, Sandoz, 5, Novartis, 8, AbbVie, 5, Amgen, 5, Biogen, 5.

Abstract Number: 0305

A Delphi Consensus Study to Standardize Terminology for the Pre-clinical Phase of Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

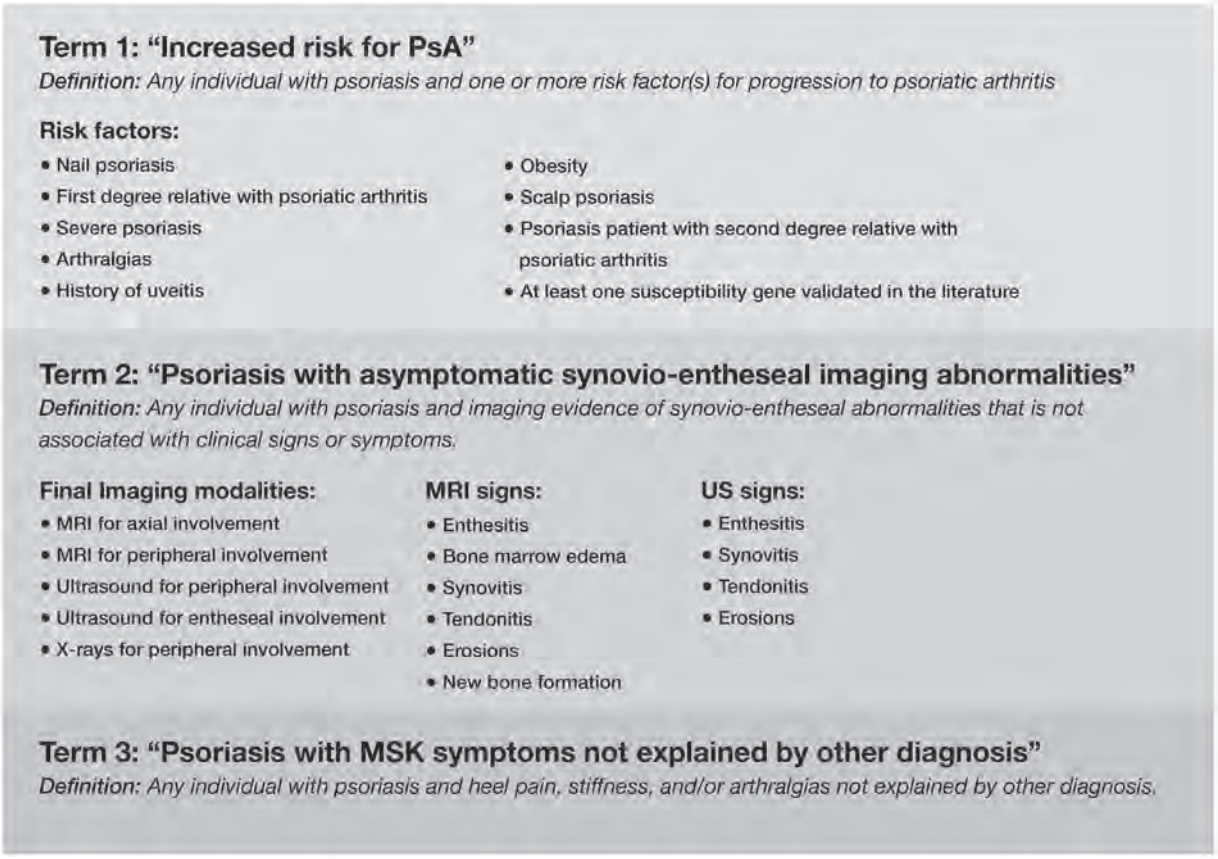
Session Time: 9:00AM–11:00AM

Background/Purpose: The concept of prevention of psoriatic arthritis (PsA) has gained increased interest given the physical limitation and poor quality-of-life experienced by PsA patients coupled with low remission rates observed with the use of currently available therapies. The transition from psoriasis to PsA offers a unique window of opportunity to identify individuals at increased risk for PsA, to study and implement preventive strategies. Herein, we propose terminology to define specific subgroups during the pre-clinical and early clinical phases of PsA to facilitate and harmonize recruitment for research studies.

Methods: We conducted a 3-round online Delphi exercise including international experts in psoriatic disease. Experts were recruited from the Group for Research and Assessment of Psoriasis and Psoriatic Arthritis (GRAPPA) and the Psoriasis and Psoriatic Arthritis Clinics Multicenter Advancement Network (PPACMAN). Participants were asked to vote on and rank their preferred (a) terms and (b) definitions to describe pre-clinical PsA populations. Consensus for multiple choice and ranking questions was defined *a priori* as ≥ 70%. For questions based on a visual analogue scale, items were retained if the median was ≥ 70. Delphi items that had < 15% of the votes or the median was < 15 were removed. If consensus was not reached, the question was carried through to the next round.

Results: A total of 29, 33, and 35 experts participated in the first, second and third Delphi round, respectively. Consensus was met for the following terms and associated definitions: "Increased risk for PsA"**,** "Psoriasis with asymptomatic synovio-entheseal imaging abnormalities", and "Psoriasis with musculoskeletal symptoms not explained by other diagnosis" (Figure). Risk factors for progression to PsA that met consensus included obesity, presence of arthralgia, severe psoriasis, history of uveitis, nail psoriasis, scalp psoriasis, and first-degree relative with PsA. Specific imaging modalities to evaluate these populations were also included in the exercises and consensus was achieved.

Conclusion: In these Delphi exercises, there was agreement on three terms and definitions that characterize the psoriasis-to-PsA transition that can to be used for research purposes. The adoption of standardized nomenclature and common definitions for research in this area should improve the communication of ideas in the field and help to enroll well-defined, homogenous cohorts of psoriasis patients, for comparison across future studies. These terms



and definitions may evolve as increasing evidence regarding the molecular, clinical, and imaging features of the psoriasis-to-PsA continuum emerges.

Disclosure: R. Haberman, Janssen, 5; **L. Perez-Chada**, None; **V. Chandran**, Abbvie, 2, 5, Amgen, 2, 5, Celgene, 2, 5, Eli Lilly, 5, Eli Lilly, 3, Janssen, 8, Novartis, 5, Pfizer, 5, UCB, 5; **C. Rosen**, Abbvie, 5, Eli Lily, 5, Novartis, 5; **C. Ritchlin**, None; **L. Eder**, AbbVie, 2, 5, 8, Eli Lilly, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5, 8, Celgene, 5, Novartis, 5; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **S. Reddy**, Amgen, 5, Novartis, 5, Janssen, 5, Pfizer, 5; **A. Ogdie**, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1; **J. Merola**, AbbVie, 1, Arena, 1, Avotres, 1, Biogen, 1, Celgene, 1, Dermavant, 1, Eli Lilly, 1, EMD Serono, 1, Janssen, 1, LEO Pharma, 5, Merck, 1, Novartis, 1, Pfizer Inc, 5, Sanofi, 1, Regeneron, 1, Sun Pharma, 1, UCB Pharma, 5; **J. Scher**, UCB, 5, Janssen, 5, Abbvie, 5, Pfizer, 5, Novartis, 5, Sanofi, 5.

Abstract Number: 0306

Characteristics of Patients with Early Oligoarticular Psoriatic Arthritis in the Corrona Psoriatic Arthritis/Spondyloarthritis Registry

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The efficacy of apremilast vs placebo for the treatment of oligoarticular PsA of ≤2 years duration is being investigated in the FOREMOST trial (NCT03747939). There is a paucity of real-world data characterizing patients (pts) with oligoarticular PsA. The Corrona PsA/SpA Registry, a prospective, observational cohort study, collects real-world data on US pts with PsA. The current analysis compared characteristics of pts with early oligoarticular PsA in the Corrona PsA/SpA Registry who would generally meet eligibility criteria for FOREMOST with the remainder of the PsA registry population.

Methods: Pts ≥18 years of age diagnosed with PsA who enrolled in the registry from March 2013 to February 2020 were included in the analysis. The FOREMOST-eligible group consisted of pts diagnosed with PsA within 2 years prior to enrollment who were naive to biologic DMARDs or targeted systemic DMARDs (apremilast or tofacitinib), had a history of ≤1 prior conventional synthetic DMARD (csDMARD [methotrexate, hydroxychloroquine, sulfasalazine, leflunomide]), and had swollen joint counts (0-66) of 2 to 4 and tender joint counts (0-68) of 2 to 4. The remainder of the PsA registry population included pts with PsA who did not meet these criteria. Data on patient demographics, clinical characteristics, treatment, disease activity, and patient-reported outcomes at enrollment are summarized descriptively.

Results: Of the 3,556 pts with PsA enrolled in the registry, 109 (3.1%) were included in the FOREMOST-eligible group and 3,447 (96.9%) comprised the remainder of the PsA registry population. Baseline characteristics among the 2

Table 1. Patient Characteristics and Treatment Experience at Time of Enrollment

Outcome	FOREMOST-Eligible (n = 109)	Remainder of PsA Registry Population (n = 3,447)
Age, mean (SD), years	50.1 (13.6)	53.7 (13.1)
Women, n (%)	65 (59.6)	1,855 (54.3)
Body mass index, mean (SD), kg/m^2	31.4 (7.4)	31.9 (7.6)
Years since PsA diagnosis, mean (SD)	0.5 (0.6)	7.6 (8.5)
Duration since onset of PsA symptoms, mean (SD), years	2.3 (3.2)	11.1 (10.3)
Prior csDMARD use, n (%)		
0	101 (92.7)	1,751 (50.8)
1	8 (7.3)	786 (22.8)
Current csDMARD therapy, n (%)	37 (37.8)	1,368 (58.7)

csDMARD = conventional synthetic DMARD; PsA = psoriatic arthritis; SD = standard deviation.

Table 2. Clinical Assessments and Disease Activity at Time of Enrollment

Outcome	FOREMOST-Eligible	Remainder of PsA Registry Population
SJC (0-66), mean (SD)	2.8 (0.9)	2.2 (4.4)
TJC (0-68), mean (SD)	2.8 (0.9)	5.2 (9.0)
Dactylitis, n (%)	28 (25.7)	359 (10.4)
Enthesitis, n (%)	13 (11.9)	796 (23.1)
Pain VAS (0-100 mm), mean (SD)	51.1 (27.1)	41.0 (30.0)
Fatigue VAS (0-100 mm), mean (SD)	47.8 (29.4)	43.3 (29.8)
PtGA of PsA VAS (0-100 mm), mean (SD)	42.5 (26.1)	40.9 (29.5)
PtGA of PsA and psoriasis VAS (0-100 mm), mean (SD)	42.4 (27.8)	40.7 (29.4)
PhGA of PsA VAS (0-100 mm), mean (SD)	35.4 (20.5)	22.3 (22.8)
Minimal disease activity, n (%)	8 (8.1)	1,186 (38.5)
cDAPSA, mean (SD)	14.9 (5.4)	15.6 (14.4)
cDAPSA category, n (%)		
Moderate disease activity, cDAPSA >13 to ≤27	66 (63.5)	944 (29.7)
High disease activity, cDAPSA >27	NA	NA
DAPSA, mean (SD)	16.3 (6.0)	16.9 (14.9)
DAPSA category, n (%)		
Moderate disease activity, DAPSA >14 to ≤28	44 (65.7)	620 (29.8)
High disease activity, DAPSA >28	NA	NA
PASDAS, mean (SD)	4.6 (1.0)	3.7 (1.6)
PASDAS category, n (%)		
Moderate disease activity, PASDAS ≥3.2 to <5.4	48 (44.0)	949 (27.5)
High disease activity, PASDAS ≥5.4	13 (11.9)	313 (9.1)
RAPID3, mean (SD)	11.0 (5.8)	9.4 (6.1)

NA refers to parameters with n <5. cDAPSA = Clinical Disease Activity Index for Psoriatic Arthritis; DAPSA = Disease Activity Index for Psoriatic Arthritis; PASDAS = Psoriatic Arthritis Disease Activity Score; PhGA = Physician's Global Assessment; PsA = psoriatic arthritis; PtGA = Patient's Global Assessment; RAPID3 = Routine Assessment of Patient Index Data 3; SD = standard deviation; SJC = swollen joint count; TJC = tender joint count; VAS = visual analog scale.

populations were generally similar, with slightly younger pts and proportionally more women in the FOREMOST-eligible group than in the remainder of the PsA registry population (Table 1). FOREMOST-eligible pts had shorter duration of PsA and shorter time to PsA diagnosis than the remainder of the PsA registry population (Table 1). Prior and current csDMARD use in the FOREMOST-eligible pts was lower than in the remainder of the PsA registry population (Table 1). FOREMOST-eligible pts had higher mean scores for patient-reported pain visual analog scale (VAS) and the Physician's Global Assessment (PhGA) of PsA VAS, in the context of comparable overall mean DAPSA, cDAPSA, PsA Disease Activity Score (PASDAS), and Routine Assessment of Patient Index Data 3 (RAPID3) scores (Table 2). Compared with the remainder of the PsA registry population, FOREMOST-eligible pts were less likely to be in minimal disease activity and more likely to have moderate disease activity based on the cDAPSA, DAPSA, and PASDAS (Table 2). Prevalence of dactylitis was higher in the FOREMOST-eligible group, whereas prevalence of enthesitis was higher in the remainder of the PsA registry population.

Conclusion: In the Corrona PsA/SpA Registry, pts with early oligoarticular PsA based on approximating FOREMOST trial criteria were the minority of the enrolled pts. Descriptive statistics of this small but understudied population indicated a higher burden of patient-reported pain and PhGA of PsA compared with the remainder of the PsA registry population, suggesting there is unmet need in this population.

Disclosure: A. Ogdie, AbbVie, 5, Amgen, 2, 5, BMS, 1, Celgene, 1, Corrona, 1, Janssen, 1, Eli Lilly, 1, Novartis, 2, 5, Pfizer, 2, 5, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 2, Rheumatology Research Foundation, 2, National Psoriasis Foundation, 2; **T. Blachley**, Corrona, LLC, 3; **K. Emeanuru**, Corrona, LLC, 3; **S. Richter**, Amgen Inc., 1; **B. Guerette**, Amgen Inc., 1; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5.

Abstract Number: 0307

Longitudinal Analysis of the Patient Pathways to Diagnosis of Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

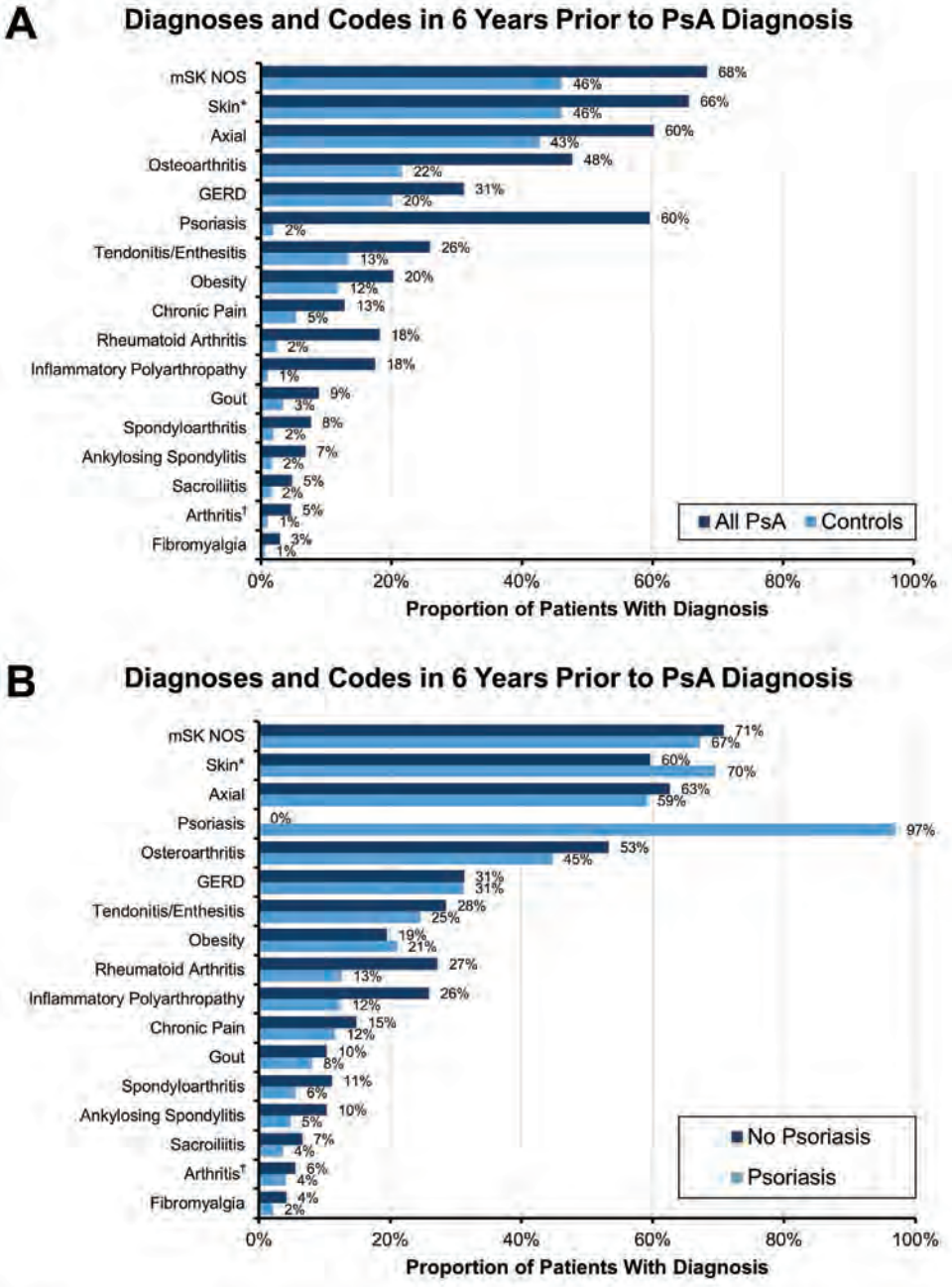
Background/Purpose: In developing algorithms within claims databases that may inform how to find patients with psoriatic arthritis (PsA) prior to diagnosis, it is important to identify meaningful potential predictors that appear prior to diagnosis. This study aims to better understand PsA patient pathways by examining the sequences of health events over the 6 years prior to PsA diagnosis, as well as differences in patients with and without PsA.

Methods: This retrospective cohort study used administrative claims data from patients in the Truven Health MarketScan® Commercial and Medicare Supplemental Databases from January 2006 to April 2019. The PsA population included all patients aged ≥ 18 years with ≥ 2 diagnoses of PsA (ICD-9-CM/ICD-10-CM) ≥ 30 days apart who had ≥ 6 years of continuous enrollment prior to first PsA diagnosis. Control (non-PsA) patients were matched 2:1 to patients with PsA by age, sex, geographic location, insurance, and enrollment duration. Sequences of health events as described by diagnosis codes, procedures performed, drugs prescribed, and physician types were examined over the 6 years prior to PsA diagnosis and for controls; results were also stratified by psoriasis vs no psoriasis prior to PsA diagnosis.

Results: Among 13,661 patients who met the inclusion criteria for diagnosis of PsA, the mean age was 55.8 years and 60.2% were women. Compared with controls, patients with PsA had an increased history of coding for arthritis and skin issues including osteoarthritis (OA; 48% vs 22%), rheumatoid arthritis (RA; 18% vs 2%), inflammatory polyarthropathy (IA; 18% vs 1%), and psoriasis (60% vs 2%) (**Figure 1A**). PsA patients without a prior diagnosis of psoriasis had higher levels of coding for other forms of arthritis compared to PsA patients with psoriasis including OA (53% vs 45%), RA (27% vs 13%), and IA (26% vs 12%) (**Figure 1B**). For many patients, diagnoses of different types of arthritis, axial symptoms, and tendonitis/enthesitis steadily increased over time prior to their PsA diagnosis (**Figure 2A**). In particular, there was a sharp rise in psoriasis diagnoses preceding the diagnosis of PsA and smaller increases in diagnoses of OA and IA prior to PsA diagnosis. Rheumatology visits were much more common just before the diagnosis of PsA (**Figure 2B**). Diagnoses made prior to diagnosis of PsA differed by the type of provider patients seen. Dermatologists were less likely than other providers to enter codes for arthritis and musculoskeletal issues, while rheumatologists were unlikely to code for psoriasis but had a fairly even distribution across different types of arthritis. General practitioners focused more on axial symptoms and general musculoskeletal codes than arthritis diagnoses (**Figure 3A**). PsA was most commonly diagnosed by rheumatologists (40%) but was diagnosed in 22% and 7% of cases by general practitioners and dermatologists, respectively (**Figure 3B**).

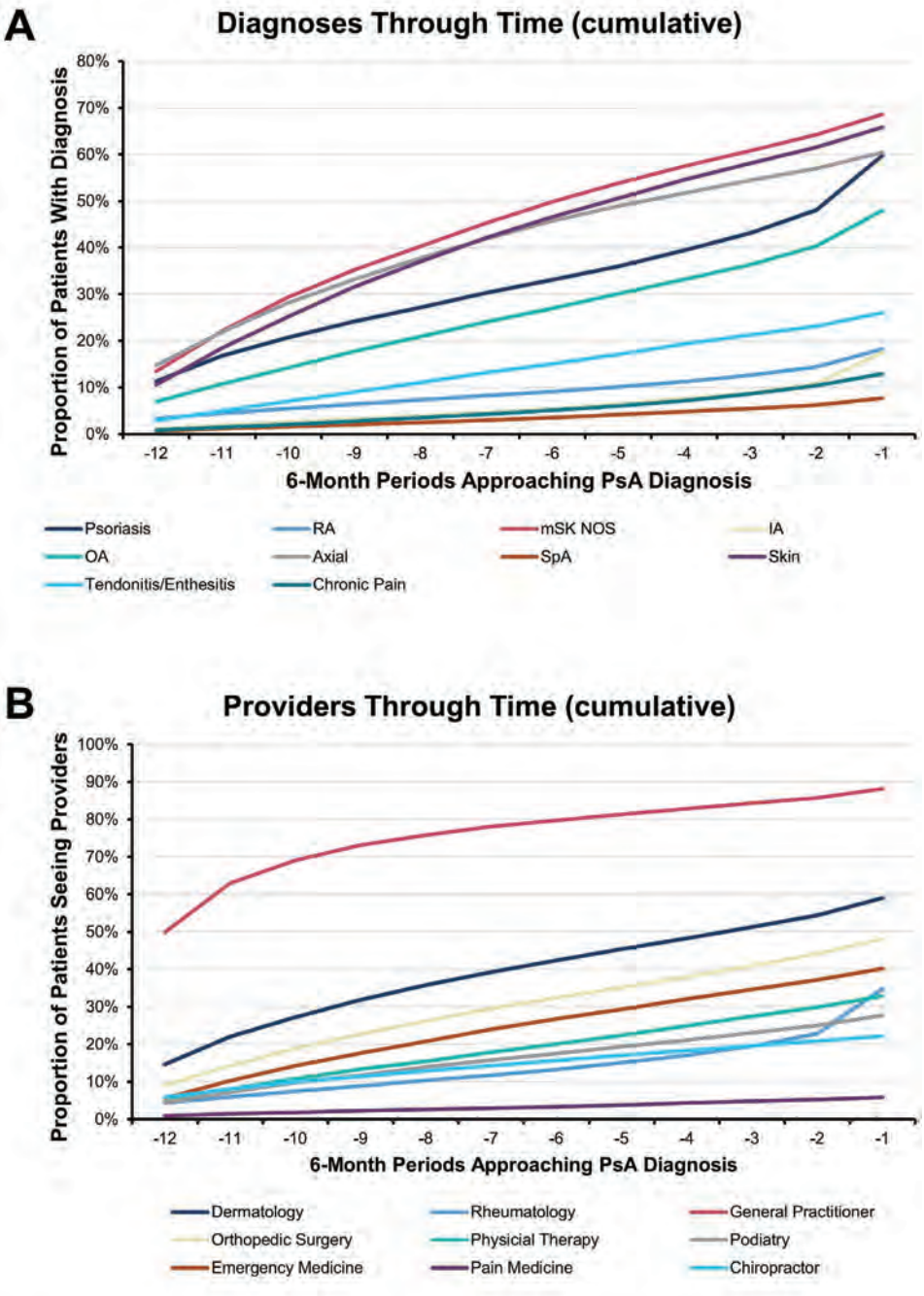
Conclusion: Rheumatologists, general practitioners, and dermatologists were responsible for diagnosing two-thirds of patients with PsA. Musculoskeletal symptoms and potential misdiagnoses are common in the years preceding diagnosis of PsA and the diagnoses and codes entered prior to PsA diagnosis varied by provider type.

Figure 1. Diagnoses and Codes in 6 Years Prior to PsA Diagnosis Among **(A)** Patients With PsA vs Controls **(B)** PsA Patients With Prior vs No Prior Psoriasis Diagnosis



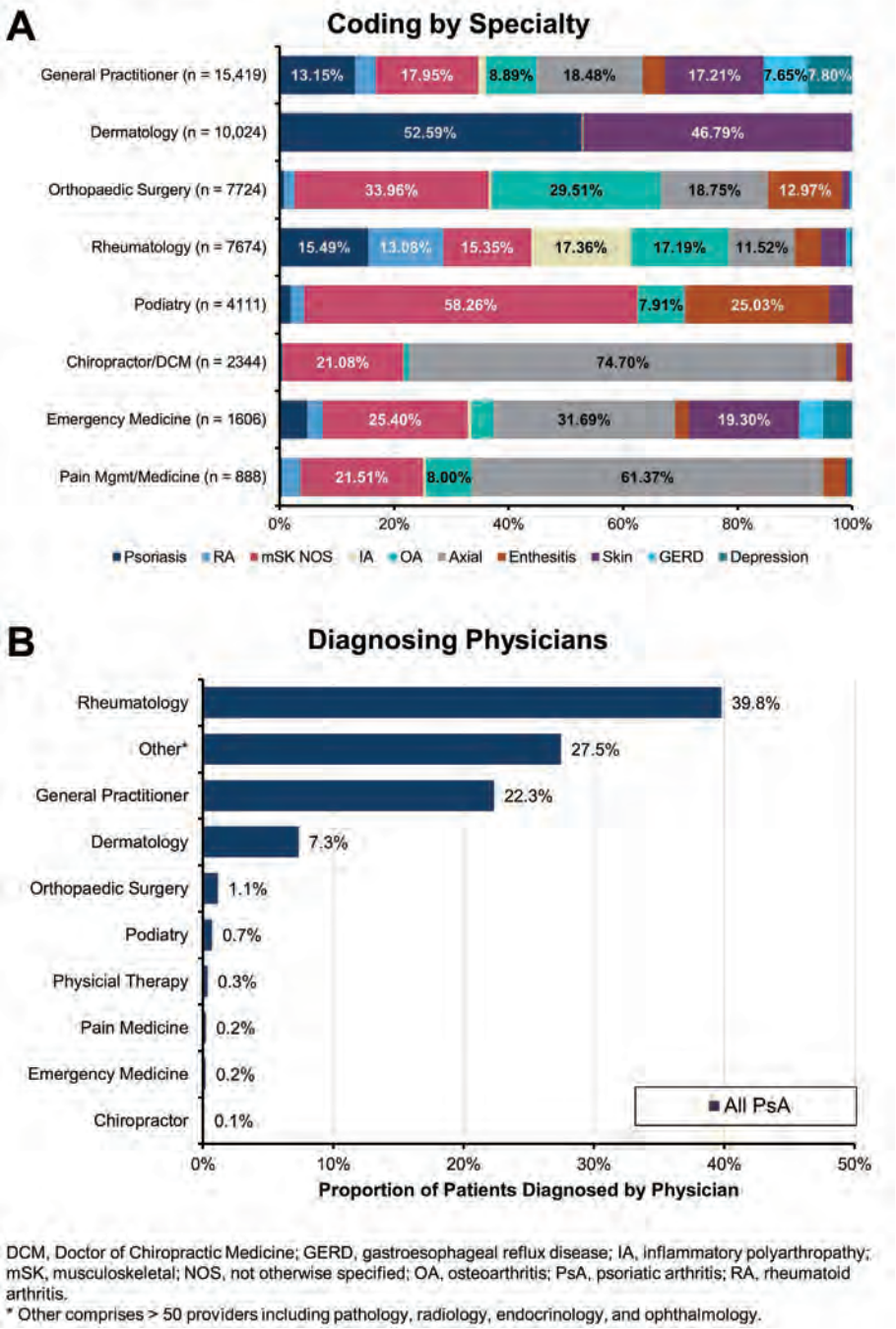
GERD, gastroesophageal reflux disease; mSK, musculoskeletal; NOS, not otherwise specified; PsA, psoriatic arthritis.
* Skin comprises 43 codes including various forms of dermatitis, rash, acne, and keratosis.
† Arthritis codes include chronic postrheumatic arthropathy (714.4); synovitis and tenosynovitis, unspecified (727.00); synovitis and tenosynovitis in diseases classified elsewhere (727.01); and secondary multiple arthritis (M153).

Figure 2. Cumulative Patient Journey Through Different **(A)** Diagnoses and **(B)** Providers in the 6 Years Prior to PsA Diagnosis



IA, inflammatory polyarthropathy; OA, osteoarthritis; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SpA, spondyloarthritis.

Figure 3. (A) Coding Patterns by Specialty—Relative Fraction of Codes Given out by Each Specialty in the 6 Years Prior to PsA Diagnosis and **(B)** the Fraction of PsA Diagnosing Physicians



DCM, Doctor of Chiropractic Medicine; GERD, gastroesophageal reflux disease; IA, inflammatory polyarthropathy; mSK, musculoskeletal; NOS, not otherwise specified; OA, osteoarthritis; PsA, psoriatic arthritis; RA, rheumatoid arthritis.
* Other comprises > 50 providers including pathology, radiology, endocrinology, and ophthalmology.

Disclosure: A. Ogdie, AbbVie, 5, Amgen, 2, 5, BMS, 1, Celgene, 1, Corrona, 1, Janssen, 1, Eli Lilly, 1, Novartis, 2, 5, Pfizer, 2, 5, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 2, Rheumatology Research Foundation, 2, National Psoriasis Foundation, 2; **M. Rozycki**, HVH Precision Analytics, 3; **T. Arndt**, HVH Precision Analytics, 3; **C. Shi**, Novartis Pharmaceuticals Corporation, 3; **N. Kim**, Novartis Pharmaceuticals Corporation, 9; **P. Hur**, Novartis Pharmaceuticals Corporation, 3.

Abstract Number: 0308

Delay in Transition from Psoriasis to Psoriatic Arthritis: A Population Based Study

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous disease which may precede, occur concurrently or after the development of psoriasis. In order to better understand the natural history of the disease we aimed to identify demographic and clinical characteristics associated with delay in transition from psoriasis to PsA.

Methods: A retrospective, population-based cohort of incident PsA patients ≥18 years of age from a geographically-defined area meeting ClASsification of Psoriatic ARthritis (CASPAR) criteria for PsA (2000-17) was identified. Onset of psoriasis was defined as confirmatory diagnosis of psoriasis by a dermatologist or rheumatologist. Date of fulfillment of CASPAR criteria was considered as the time of onset of PsA. PsA patients were divided into two groups: patients with concurrent psoriasis and PsA (within one year of each other) and patients with psoriasis onset before PsA (>1 year). Those patients with psoriasis development after PsA onset (>1 year) or only family history of psoriasis were excluded. Logistic regression models adjusted for age and sex were performed to identify factors associated with delay in transition from psoriasis to PsA.

Results: There were 157 incident cases of PsA, mean age at diagnosis was 46.3 (SD=12.0) years and 46% were females. Median lag time from psoriasis onset to PsA was 263 days (interquartile range=0, 2889). 51% (n=80) of patients had concurrent psoriasis and PsA while 49% (n=77) had onset of psoriasis before PsA (Table 1). Family history of psoriasis (OR= 2.71, 95% CI 1.24 - 5.90) and psoriasis severity (OR=1.96, 95% CI 1.26 -3.06) were more likely in those who had a delay in transition from psoriasis to PsA than those who had a concomitant diagnosis (Table 2). There were no statistically significant differences in demographic features, or any of the other psoriasis or PsA related factors between the 2 groups. Similarly, no difference in radiographic outcome was noted for the 2 groups.

Conclusion: In this population-based study, approximately half of the patients had psoriasis onset before PsA, and the other half had concurrent psoriasis and PsA. Patients with a family history of psoriasis and severe psoriasis were more likely to have a delay in transition from psoriasis to PsA. Whether this difference is secondary to earlier detection of psoriasis in patients with a family history of psoriasis and severe psoriasis or a true phenotypic difference will require further studies.

	Concurrent psoriasis and PsA (N=80)	Psoriasis before PsA (N=77)	Total (N=157)	p value
Days from PsO to PsA, median (IQR)	0 (0, 25)	2916 (1342, 6174)	263 (0, 2889)	--
Estimated years from first psoriasis eruption to psoriasis diagnosis, median (IQR)	2 (0, 4.5)	1 (0, 10)	1 (0, 8)	0.92[1]
Age at PsA incidence (yrs), mean (SD)	44.5 (11.9)	48.1 (11.9)	46.3 (12.0)	0.050[1]
Sex, female	33 (41%)	39 (51%)	72 (46%)	0.24[2]
Education Level				0.043[3]
High school or less	16 (20%)	16 (21%)	32 (21%)	
Some college or 2yr degree	23 (29%)	36 (47%)	59 (38%)	
≥4yr college degree	40 (51%)	25 (32%)	65 (42%)	
Missing	1	0	1	
Race				0.48[2]
Black	2 (3%)	1 (1%)	3 (2%)	
Asian	2 (3%)	6 (8%)	8 (5%)	
Other/Mixed	2 (3%)	2 (3%)	4 (3%)	
White	73 (92%)	68 (88%)	141 (90%)	
Unknown	1	0	1	
BMI (kg/m^2) at PsA diagnosis, mean (SD)	30.4 (6.2)	31.5 (8.0)	30.9 (7.1)	0.60[1]
Missing	1	1	2	
Smoking at psoriasis diagnosis				0.12[2]
Current smoker	13 (16%)	21 (27%)	34 (22%)	
Past smoker	23 (29%)	25 (32%)	48 (31%)	
Never smoker	44 (55%)	31 (40%)	75 (48%)	
Smoking at PsA dx				0.11[2]
Current smoker	13 (16%)	14 (18%)	27 (17%)	
Past smoker	23 (29%)	33 (43%)	56 (36%)	
Never smoker	44 (55%)	30 (39%)	74 (47%)	
Alcohol intake at psoriasis diagnosis	65 (81%)	57 (74%)	122 (78%)	0.28[2]
Alcohol intake at PsA diagnosis	63 (79%)	55 (71%)	118 (75%)	0.29[2]
Family history of psoriasis	21 (34%)	35 (54%)	56 (44%)	0.028[2]
No documentation	19	12	31	
Estimated Age at onset of first psoriasis eruption, mean (SD)	39 (13)	30 (15)	34 (15)	<0.001[1]
Psoriasis Seriousness at 1st diagnosis				0.002[2]
Mild (< 2% BSA)	44 (55%)	29 (38%)	73 (47%)	
Moderate (2-10% BSA)	29 (36%)	24 (32%)	53 (34%)	
Severe (>10% BSA)	7 (9%)	23 (30%)	30 (19%)	
No Documentation	0	1	1	
Type of psoriasis at first dx				0.10[2]
Chronic plaque psoriasis	64 (81%)	68 (88%)	132 (85%)	
Guttate psoriasis	3 (4%)	1 (1%)	4 (3%)	
Pustular psoriasis- Generalized	1 (1%)	0 (0%)	1 (1%)	
Pustular psoriasis- palms/soles	3 (4%)	3 (4%)	6 (4%)	
Sebo-psoriasis	4 (5%)	1 (1%)	5 (3%)	
Chronic plaque psoriasis & Guttate psoriasis	0 (0%)	3 (4%)	3 (2%)	
Chronic plaque & Pustular psoriasis-palms/soles	0 (0%)	1 (1%)	1 (1%)	
Chronic plaque & Sebo-psoriasis	4 (5%)	0 (0%)	4 (3%)	
No Documentation	1	0	1	
Site of psoriatic lesions at first diagnosis of psoriasis				0.15[2]
Palms and/or soles	1 (4%)	3 (18%)	4 (10%)	
Elbows and/or knees	2 (8%)	5 (29%)	7 (17%)	
Limbs arms and/or legs	8 (32%)	2 (12%)	10 (24%)	

Table 1. Baseline characteristics of patients with concurrent psoriasis and PsA, and psoriasis before PsA

	Concurrent psoriasis and PsA (N=80)	Psoriasis before PsA (N=77)	Total (N=157)	p value
Trunk	1 (4%)	0 (0%)	1 (2%)	
Face	1 (4%)	0 (0%)	1 (2%)	
Scalp	10 (40%)	6 (35%)	16 (38%)	
Intergluteal/parianal	2 (8%)	0 (0%)	2 (5%)	
Genital	0 (0%)	1 (6%)	1 (2%)	
Missing	55	60	115	
Nail involvement at first diagnosis of psoriasis	32 (47%)	15 (27%)	47 (38%)	0.021[2]
No Documentation/Missing	12	21	33	
Family history of PsA	5 (10%)	6 (12%)	11 (11%)	0.78[2]
No documentation	29	25	54	
Enthesitis/Enthespathy prior to PsA	21 (31%)	26 (40%)	47 (36%)	0.30[2]
No documentation	13	12	25	
Dactylitis prior to PsA	35 (48%)	30 (42%)	65 (45%)	0.49[2]
No documentation	7	6	13	
Inflammatory back pain prior to PsA	6 (9%)	11 (15%)	17 (12%)	0.24[2]
No documentation	11	4	15	
Uveitis	3 (5%)	4 (7%)	7 (6%)	0.99[3]
No documentation	19	16	35	
Inflammatory bowel disease	0 (0%)	1 (2%)	1 (1%)	0.47[3]
No documentation	10	15	25	
Rheumatoid factor positive	5 (7%)	1 (2%)	6 (4%)	0.21[3]
Not done	7	12	19	
ESR (mm/hr) at psoriasis diagnosis, mean (SD)	18.7 (15.5)	14.1 (14.6)	17.3 (15.2)	0.24[1]
Missing	50	64	114	
CRP (mg/L) at psoriasis diagnosis, mean (SD)	12.8 (16.3)	7.7 (8.5)	11.6 (14.9)	0.77[1]
Missing	52	68	120	
ESR (mm/hr) at PsA diagnosis, mean (SD)	19.2 (15.8)	18.6 (18.3)	18.9 (17.0)	0.44[1]
Missing	10	10	20	
CRP (mg/L) at PsA diagnosis, mean (SD)	13.8 (16.7)	17.0 (32.9)	15.5 (26.4)	0.63[1]
Missing	29	21	50	
Radiographic damage	21 (27%)	25 (32%)	46 (29%)	0.42[2]
Missing	1	0	1	

[1]Kruskal Wallis [2]Chi-Square [3]Fisher's Exact

Table 2. Logistic regression models for psoriasis before PsA adjusted for age and sex

Table 2. Logistic models for psoriasis before PsA adjusted for age and sex

Clinical features	OR (95% CI)	P-value
Family history of psoriasis	2.71 (1.24-5.90)	0.012
Severity of psoriasis	1.96 (1.26-3.06)	0.003
Type of psoriasis (Pustular psoriasis)	0.86 (0.20-3.63)	0.84
Nail involvement at psoriasis diagnosis	0.47 (0.22-1.03)	0.058
Radiographic damage	1.36 (0.66-2.79)	0.41

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Abstract Number: 0309

Diagnostic Delay in Psoriatic Arthritis: A Population Based Study

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Early diagnosis of psoriatic arthritis (PsA) is important for improving long-term outcomes. Trends in diagnostic delay of PsA in the US and factors associated with delay in diagnosis have not been well studied. The aim of our study was to 1) examine the diagnostic delay in PsA in residents of a geographically defined area from 2000-17, and 2) identify demographic and clinical characteristics associated with diagnostic delay in PsA.

Methods: A retrospective, population-based cohort of incident PsA patients ≥18 years of age from a geographically defined area meeting CIASsification of Psoriatic ARthritis (CASPAR) criteria for PsA (2000-17) was identified. Disease onset was taken as onset of any PsA related joint symptom as reported by the patient and documented by a physician in the medical records. PsA diagnosis date was the date of confirmatory diagnosis of PsA by a physician/rheumatologist. Diagnostic delay was defined as the time from disease onset to a diagnosis of PsA. Logistic regression models adjusted for age and sex were performed to identify factors associated with delay in PsA diagnosis.

Results: There were 162 incident PsA cases from 2000-17. Mean age was 41.5 (SD=12.6) and 46% were females. Median lag time from disease onset (PsA related joint symptoms) to first confirmatory diagnosis by a physician was 2.5 years (interquartile range=0.5, 7.3). At six months 23% (n=38) of the cohort received a confirmatory diagnosis of PsA, 35% (n=56) at one year and 45% (n=73) at two years of symptom onset respectively. No significant trend in diagnostic delay were observed. PsA patients with younger age at diagnosis, higher body mass index (BMI), and enthesitis before diagnosis, were associated with a diagnostic delay of greater than one and two years, while sebopsoriasis at diagnosis was associated with a lower likelihood of delay (Table 1). No significant association with sex, education level, smoking status, alcohol intake, psoriasis severity or location, nail involvement, family history of psoriasis or PsA, history of extra-articular manifestations (i.e., uveitis, inflammatory bowel disease), or high inflammatory markers at the time of diagnosis was found. Logistic regression models adjusted for age and sex showed a higher likelihood of radiographic damage at PsA diagnosis with a delay in diagnosis of six months, one year and two years, however these associations did not reach statistical significance (Table 2).

Conclusion: In this population-based study, more than half of PsA patients had a delay in diagnosis two or more years, and no significant improvement in time to diagnosis was noted from 2000-17. Patients with younger age at diagnosis, higher BMI, or enthesitis before diagnosis were more likely to have a diagnostic delay of more than two years while patients with sebopsoriasis were less likely to have a diagnostic delay. Radiographic damage may be associated with diagnostic delay, but this association did not reach statistical significance, perhaps due to the limited sample size of the cohort.

Table 1. Baseline characteristics of PsA patients with delay in diagnosis <2 years compared to ≥2 years

	<2yr (n=73)	≥2yr (n=89)	Total (n=162)	p value
Years from PsA related joint symptoms to Physician /Rheumatologist diagnosis of PsA, median (IQR)	0.5 (0.2-1.0)	6.5 (3.5-10.1)	2.5 (0.5-7.3)	--
Age (yrs) at start of inflammatory joint pain, mean (SD)	44.0 (12.4)	39.5 (12.4)	41.5 (12.6)	0.041[1]
Sex, female (%)	36 (49%)	39 (44%)	75 (46%)	0.48[2]
Education Level				0.79[2]
High school or less	16 (22%)	16 (18%)	32 (20%)	
Some college or 2yr degree	27 (38%)	36 (40%)	63 (39%)	
≥4 yr college degree	29 (40%)	37 (42%)	66 (41%)	
Missing	1	0	1	
Race				0.015[3]
Black	2 (3%)	2 (2%)	4 (2%)	
Asian	0 (0%)	8 (9%)	8 (5%)	
Other/Mixed	3 (4%)	1 (1%)	4 (2%)	
White	68 (93%)	77 (88%)	145 (90%)	
Unknown	0	1	1	
BMI (kg/m^2) at PsA diagnosis, mean (SD)	29.5 (6.1)	32.2 (7.7)	31.0 (7.1)	0.028[1]
Missing	4	5	0	
Smoking at PsA diagnosis				0.53[2]
Current smoker	12 (16%)	15 (17%)	27 (17%)	
Past smoker	23 (32%)	35 (39%)	58 (36%)	
Never smoker	38 (52%)	39 (44%)	77 (48%)	
Alcohol intake at PsA dx	56 (77%)	65 (73%)	121 (75%)	0.59[2]
Psoriasis (Current or personal history)				0.15[2]
No psoriasis	2 (3%)	5 (6%)	7 (4%)	
Current psoriasis	70 (96%)	78 (88%)	148 (91%)	
Personal history of psoriasis	1 (1%)	6 (7%)	7 (4%)	
Family history of psoriasis	24 (40%)	35 (49%)	59 (45%)	0.32[2]
No documentation	13	17	30	
Estmated age (yrs) at onset of first psoriasis eruption, mean (SD)	34 (14)	34 (15)	34 (14)	0.85[1]
Missing	2	5	7	
Psoriasis Seriousness at 1st diagnosis				0.25[2]
Mild (< 2% BSA)	38 (54%)	34 (41%)	72 (47%)	
Moderate (2-10% BSA)	20 (28%)	33 (40%)	53 (34%)	
Severe (>10% BSA)	13 (18%)	16 (19%)	29 (19%)	
No Documentation/Missing	2	6	8	
Type of psoriasis at first dx				0.033[3]
Chronic plaque psoriasis	56 (80%)	74 (88%)	130 (84%)	
Guttate psoriasis	3 (4%)	1 (1%)	4 (3%)	
Pustular psoriasis- Generalized	1 (1%)	0 (0%)	1 (1%)	
Pustular psoriasis- palms/soles	2 (3%)	4 (5%)	6 (4%)	
Sebo-psoriasis	5 (7%)	0 (0%)	5 (3%)	
Chronic plaque psoriasis & Guttate psoriasis	0 (0%)	3 (4%)	3 (2%)	
Chronic plaque & Pustular psoriasis-palms/soles	1 (1%)	0 (0%)	1 (1%)	
Chronic plaque & Sebo-psoriasis	2 (3%)	2 (2%)	4 (3%)	
No Documentation/Missing	3	5	8	
Site of psoriatic lesions at first diagnosis of psoriasis				0.49[2]
Palms and/or soles	1 (5%)	3 (14%)	4 (9%)	
Elbows and/or knees	3 (14%)	4 (19%)	7 (16%)	
Limbs arms and/or legs	5 (23%)	6 (29%)	11 (26%)	
Trunk	0 (0%)	1 (5%)	1 (2%)	
Face	1 (5%)	0 (0%)	1 (2%)	
Scalp	9 (41%)	7 (33%)	16 (37%)	
Intergluteal/Perianal	2 (9%)	0 (0%)	2 (5%)	
Genital	1 (5%)	0 (0%)	1 (2%)	
Missing	51	68	119	
Nail involvement at first diagnosis of psoriasis	24 (42%)	23 (35%)	47 (38%)	0.41[2]
No documentation	16	23	39	
Family history of PsA	6 (12%)	6 (11%)	12 (11%)	0.84[2]
No documentation	22	32	54	

	<2yr (n=73)	≥2yr (n=89)	Total (n=162)	p value
Enthesitis/Enthespathy prior to PsA diagnosis No documentation	16 (25%) 8	35 (49%) 17	51 (37%) 25	0.004[2]
Dactylitis prior to PsA diagnosis No documentation	35 (51%) 4	35 (44%) 9	70 (47%) 13	0.40[2]
Inflammatory back pain prior to PsA diagnosis No documentation	4 (6%) 7	13 (16%) 9	17 (12%) 16	0.056[2]
Uveitis No documentation	4 (7%) 14	3 (4%) 22	7 (6%) 36	0.70[3]
Inflammatory bowel disease No documentation	0 (0%) 13	0 (0%) 13	0 (0%) 26	–
ESR (mm/hr) at PsA diagnosis, mean (SD) Missing	18.9 (18.3) 4	18.2 (15.3) 17	18.5 (16.8) 21	0.95[1]
CRP (mg/L) at PsA diagnosis, mean (SD) Missing	16.5 (32.4) 22	13.6 (19.0) 29	14.9 (26.0) 51	0.87[1]
Radiographic damage Missing	17 (24%) 1	31 (35%) 0	48 (30%) 1	0.12[2]

[1]Kruskal Wallis [2]Chi-Square [3]Fisher's Exact

Table 2. Logistic models for delay in PsA diagnosis adjusted for age and sex

Table 2. Logistic models for delay in PsA diagnosis adjusted for age and sex

Variables	>6 mo, OR (95% CI), p value	>1 yr, OR (95% CI), p value	>2 yr, OR (95% CI), p value
Age at start of inflammatory joint pain per 10 year increase	0.74 (0.55-1.00), 0.047	0.79 (0.61-1.03), 0.084	0.75 (0.58-0.97), 0.026
BMI at PsA dx per 10 kg/m^2 increase	1.58 (0.89-2.81), 0.12	1.73 (1.03-2.92), 0.040	1.89 (1.15-3.10), 0.012
Enthesitis prior to PsA	3.44 (1.49-7.98), 0.004	2.07 (1.04-4.10), 0.038	2.66 (1.37-5.13), 0.004
ESR at PsA diagnosis per 10 mm/hr increase	0.82 (0.66-1.02), 0.080	0.96 (0.78-1.18), 0.69	1.00 (0.82-1.23), 0.99
Type of psoriasis at first diagnosis (sebo-psoriasis)	0.11 (0.02-0.47), 0.003	0.21 (0.05-0.92), 0.038	0.19 (0.04-0.99), 0.048
Radiographic damage	2.19 (0.87-5.52), 0.096	1.80 (0.83-3.91), 0.14	1.72 (0.83-3.53), 0.14

Disclosure: P. Karmacharya, National Center for Advancing Translational Science, 2, SPARTAN (Spondyloarthritis Research and Treatment Network), 2; **K. Wright**, None; **S. Achenbach**, None; **D. Bekele**, None; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1; **A. Ogdie**, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1; **A. Duarte-Garcia**, None; **F. Ernste**, None; **M. Tollefson**, None; **J. Davis**, Pfizer, 2, AbbVie, 5, 8, Sanofi-Genzyme, 5, 8.

Abstract Number: 0310

The Prediction of Psoriatic Arthritis Tool (PRESTO) Study – Interim Report

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: A simple, scalable tool that identifies psoriasis patients at high risk for developing PsA could improve early detection and facilitate early intervention. Our overall objective is to develop an accurate risk prediction model for the development of PsA in patients with psoriasis. This analysis focused on clinical predictors.

Methods: In this longitudinal cohort study we analyzed data from the *International Psoriasis and Arthritis Team (IP-ART) study,* a prospective cohort of psoriasis patients without PsA at the time of enrollment. The participants have been followed prospectively and their PsA status has been assessed annually by a rheumatologist. Information about their demographics, psoriasis characteristics, co-morbidities and musculoskeletal symptoms, was used to develop prediction models for PsA. Serial logistic regression models were fitted with a defined set of time-varying covariates in order to identify the optimal combination of covariates to construct risk prediction models. Prediction models were

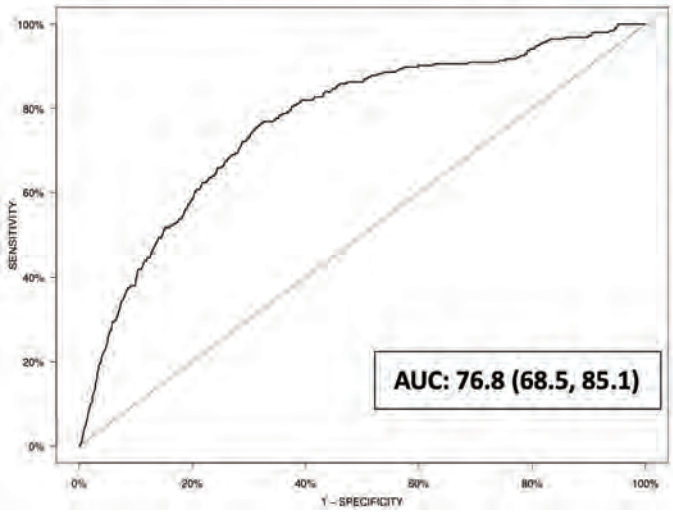
Table 1. Candidate predictors of PsA in Univariate Models at 1 year and 5 years (p<0.10)

Table 1 – Candidate Risk Factors for Psoriatic Arthritis at 1 and 5 Years (p<0.10)

	PsA within 1 year			PsA within 5 years		
	HR	95% CI	P value	HR	95% CI	P value
Back stiffness (y/n)	2.41	1.21, 4.81	0.01			
Inflammatory back pain (y/n)	3.31	1.29, 8.48	0.01			
Psoriatic nail lesion (y/n)				1.82	1.12, 2.94	0.02
Iritis (y/n)*	22.8	7.0, 74.1	<0.001	7.21	1.65, 31.61	0.009
Pustular psoriasis (y/n)*	5.6	1.7, 18.0	0.004			
Flexural psoriasis (y/n)*				2.67	0.85, 8.42	0.09
PASI				1.04	1.01, 1.07	0.009
Psoriasis BSA				1.01	0.99, 1.03	0.09
Systemic non-biologic medication/ Phototherapy (y/n)				2.11	1.27, 3.48	0.004
Stiffness level (0-10)	1.08	1.02, 1.15	0.008			
FACIT fatigue scale	0.94	0.90, 0.98	0.004	0.93	0.91, 0.96	<0.0001
FSS	1.19	1.07, 1.32	0.002	1.16	1.06, 1.27	0.0009
Global health			0.0008			0.004
• Very good	0.15	0.02, 1.42		0.25	0.08, 0.80	
• Good	0.78	0.10, 5.85		0.64	0.23, 1.82	
• Fair	1.41	0.20, 10.06		0.93	0.31, 2.82	
• Poor/Very poor (reference)	--	--				
Pain severity			0.0009			0.02
• Mild	3.17	1.43, 7.00		2.34	1.31, 4.18	
• Moderate	5.63	2.38, 13.31		2.06	0.89, 4.76	
• Severe	4.63	0.94, 22.94		4.07	1.46, 11.14	
• None (reference)	--	--				
Pain level (0-10)	1.20	1.08, 1.34	0.0006	1.13	1.03, 1.25	0.01

*Excluded from the final model due to <5 individuals in the event group; BSA; Body Surface Area CI- Confidence Interval; FACIT- Functional Assessment of Chronic Illness Therapy; FSS – Fatigue Severity Scale; HR-Hazard Ratio; PASI – Psoriasis Area and Severity Index;

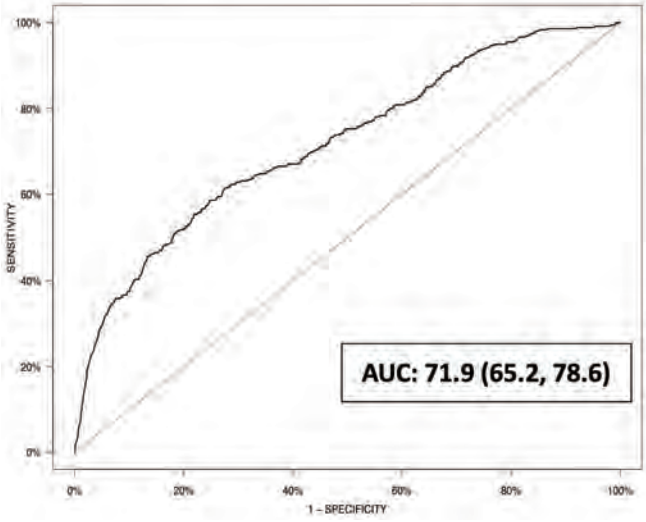
Figure 1 – The Risk of Developing PsA within 1 year – Cox Proportional Hazards Model



Variable	HR	95% CI	P value
Age	0.98	0.96, 1.00	0.08
Patient global health			0.02
Very good	0.37	0.03, 5.11	
Good	1.45	0.12, 18.13	
Fair	2.01	0.21, 20.44	
Poor/Very poor (ref)			
Pain level			0.03
Mild	2.58	1.18, 5.63	
Moderate	3.75	1.50, 9.35	
Severe/Very severe	3.43	0.48, 24.68	
None (ref)			
*Adjusted for psoriasis duration N=635, 51 events			

Figure 1 The Risk of Developing PsA within 1 year – Cox Proportional Hazards Model

Figure 2 – The Risk of Developing PsA within 5 years – Cox Proportional Hazards Model



Variable	HR	95% CI	P value
Nail lesion	1.65	1.01, 2.68	0.04
HAQ-DI	0.29	0.08, 1.09	0.07
FACIT	0.92	0.88, 0.95	<0.001
Systemic non-biologic medication/Phototherapy	1.76	1.06, 2.93	0.03
*Adjusted for psoriasis duration N=635; 71 events			

Figure 2 The Risk of Developing PsA within 5 years – Cox Proportional Hazards Model

set to estimate the risk of developing PsA over 1 and 5 years respectively. Each model was adjusted for psoriasis duration. Model selection was based on backward elimination approach ($p< 0.10$). Receiver operating characteristics curves were plotted and the predictive performance was summarized by the area under the curve (AUC).

Results: A total of 635 psoriasis patients, followed from 2016 to 2020, were analyzed (mean duration of follow up 7.7 years). 75 patients developed PsA during the study period. Univariate analysis identified various candidate predictors of PsA including the severity of musculoskeletal symptoms, psoriatic nail lesions, iritis, psoriasis type, location and severity and the use of non-biologic systemic medications or phototherapy (Table 1). The risk of developing PsA within 1 year was predicted by younger age, patient global health and pain severity (AUC 76.8, 95% confidence interval (CI) 68.5, 85.1, Figure 2). The risk of developing PsA within 5 years was predicted by psoriatic nail lesion, health as-

sessment questionnaire disability index (HAQ-DI), Functional Assessment of Chronic Illness Therapy (FACIT) fatigue scale and use of systemic non-biologic medication or phototherapy (AUC 71.9, 95% CI 65.2, 78.6, Figure 3).

Conclusion: The development of PsA within clinically meaningful time frames can be predicted with reasonable accuracy for psoriasis patients. Additional work is underway to optimize the current models and validate them in external cohorts of psoriasis patients.

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Abstract Number: 0311

The Link Between Joints and Entheses in Psoriatic Arthritis: An Ultrasound Study Supporting the Synovio-entheseal Complex Theory

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study is to explore the link between the severity of the joint and entheses involvement in psoriatic arthritis (PsA) using musculoskeletal ultrasound (US).

Methods: PsA patients from 2 centers in the Psoriatic Arthritis- International Database (PsArt-ID) (n=126) underwent an ultrasound assessment of 46 joints and 12 large entheses. The correlation between joint and enthesitis scores on the US was analyzed in addition to the clinical indices versus the US.

Results: Fifty-six of the 126 patients (44.4%) were male and the mean (SD) age was 54.8 (14.6) years. The mean PsA duration was 7.6 (8.3) years. Greyscale (GS) synovitis score for the joints was moderately correlated with the total enthesitis score ($r=0.410$, $p< 0.001$) (Table). The Global Outcome Measure in Rheumatology in Clinical Trials-European League Against Rheumatism Synovitis Score (GLOESS) score was also found in correlation with the total enthesitis score ($r=0.400$, $p< 0.001$) (Table). The link between the US and clinical examination findings only showed a poor correlation between swollen joint counts (SJC) and joint-US scores ($r=0.298$, $p=0.001$ for GLOESS). Assessment of the entheses on US showed a poor-moderate correlation between the entheseal damage scores and tender joint counts

Table. Correlation between joint and entheses ultrasound scores

		JOINTS					
	Parameters	**GS**	**p**	**PD**	**p**	**GLOESS**	**p**
ENTHESES	**Inflammation Score (A)**	0.421	**<0.001**	0.131	0.145	0.411	**<0.001**
	Damage Score (B)	0.302	**0.001**	0.045	0.616	0.295	**0.001**
	Total Enthesitis Score (A+B)	0.410	**<0.001**	0.101	0.264	0.400	**<0.001**

GS: Gray Scale, PD: Power Doppler, GLOESS: Global omeract/eular ultrasound synovitis score,

Inflammation score= Hypoechogenecity+Thickness+Power Doppler Score (0-108)

Damage Score= Calcification+Erosion+Enthesophyte (0-108)

(TJC) (r=0.217, p= 0.018) and SJC (r=0.326, p= p< 0.001). In terms of the clinical examination and activity parameters, none of the clinical parameters and acute phase reactants were correlated to Leeds Enthesitis Index.

Conclusion: Our study showed a link between the severity of the sonographic findings in the joints and the entheses. The link between these two anatomical structures supports the synovio-entheseal complex theory.

Disclosure: G. Ayan, None; **I. Tinazzi**, None; **S. Bakirci**, None; **U. Gazel**, None; **D. Solmaz**, None; **U. Kalyoncu**, Abbvie, 1, Amgen, 1, Jannsenn, 1, Lilly, 1, Novartis, 1, UCB, 1; **S. Aydin**, None.

Abstract Number: 0312

Dactylitis Is Associated with Greater Disease Severity, Ultrasound Synovitis, and Erosive Damage, in Very Early DMARD Naïve Psoriatic Arthritis

Sayam Dubash[1], Oras Alabas[2], Xabier Michelena[2], Gabriele De Marco[3], Leticia Garcia-Montoya[2], Richard Wakefield[2], Ai Lyn Tan[2], Philip Helliwell[4], Paul Emery[5], Dennis McGonagle[2] and Helena Marzo-Ortega[2], [1]The University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, UK, Leeds, England, United Kingdom, [2]The University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, UK, Leeds, United Kingdom, [3]The University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, UK, Treviglio, Italy, [4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, [5]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, UK, Leeds, United Kingdom

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Dactylitis is a hallmark feature of Psoriatic arthritis (PsA), defined as a uniform swelling of a finger or toe ("sausage digit"). It is associated with radiographic damage in chronic PsA. However, there are paucity of data on its characterisation, phenotypical significance, and disease burden in very early PsA. The objective of this study was to characterise a very early DMARD naïve PsA cohort based on the clinical presence or absence of dactylitis.

Methods: Very early PsA patients fulfilling CASPAR criteria were recruited into a prospective observational study; the Leeds Spondyloarthritis Register for Research and Observation (SpARRO). The cohort was evaluated based on presence/absence of dactylitis. Dactylitis was recorded per digit as tender ("hot") or non-tender ("cold"). Statistical differences between mean, medians, and proportions were calculated using student's t-test, quantile regression, one-sample tests, and Pearson Chi-squared test. Ultrasonography (US) of joints was conducted by trained sonog-

Table 1. Baseline characteristics of the PsA cohort by the presence or absence of dactylitis.

Variables	PsA without dactylitis (n=96)	PsA with dactylitis (n=81)	Mean/median difference
Age, mean (SD), years	44.4 (12.8)	43.7 (13.3)	0.7 (-3.2 to 4.5)
Male	38 (39.6%)	42 (51.9%)	-12.3 (-34.0 to 9.4)
Disease duration, median (IQR), months	1.1 (0-2.7)	1.2 (0.3-4.6)	0.03 (-0.9 to 1.0)
Symptoms duration, median (IQR), months	18 (10.5-36)	12 (6.0-24.0)	-6.0 (-13.1 to 1.1)
Early Morning stiffness median (IQR), minutes	50 (15.0-90.0)	60.0 (15.0-180.0)	0 (-24.1 to 24.1)
TJC (78), median (IQR)	4.0 (1.0-10)	9.0 (5-19)	5.0 (2.0 to 8.0)**
SJC (76), median (IQR)	1.0 (0.0-3.0)	7.0 (3.0-11.0)	6.0 (4.3 to 7.6)***
Current Psoriasis	96/96 (100.0%)	74/81 (91.4%)	8.6 (2.2 to 15.4)**
Family history of Psoriasis	52/94 (55.3%)	49/78 (62.8%)	-7.5 (-26.6 to 11.6)
PASI, median (IQR)	2.9 (0.8- 4.9)	1.9 (0.4-4.2)	-1.2 (-2.4 to 0.0)
Psoriatic Nail dystrophy (yes/no)	43/96 (44.8%)	36/81 (44.4%)	0.4 (-21.6 to 22.4)
mNAPSI, median (IQR)	2.0 (0.0-7.5)	0.0 (0.0-8.0)	-2.0 (-3.7 to -27.9)*
MASES, median (IQR)	0.0 (0.0-2.0)	1.0 (0.0-2.0)	1.0 (0.4 to 1.6)**
BMI, median (IQR)	28.2 (24.0-32.1)	28.6 (25.0-31.5)	0.3 (-1.7 to 2.4)
Smoking (current)	19.0 (19.8%)	9.0 (11.1%)	8.9 (-18.9 to 35.9)
Disease phenotype			
Oligoarthritis	83/96 (86.5%)	28/81 (34.6%)	51.9 (32.8 to 71.0)***
Polyarthritis	13/96 (13.5%)	53/81 (65.4%)	-50.0 (-72.6 to -27.2)**
Predominant DIP joint disease	7/93 (7.5%)	13/77 (16.9%)	-9.4 (-37.6 to 18.9)
Axial disease	17/94 (18.1%)	9/78 (11.5%)	6.6 (-21.8 to 34.3)
Arthritis Mutilans	0	0	0
Laboratory markers			
CRP (mg/L), median (IQR)	5.0 (5.0-9.3)	8.1 (5.0-18.4)	3.1 (0.9 to 5.3)**
Elevated (>10)	24 (25.0%)	36 (44.4%)	-19.4 (-43.2 to 4.3)
ESR, median (IQR)	11.0 (5.0-25.0)	16.5 (7.0-27.0)	7 (0.4 to 13.6)*
Questionnaire			
PSAQoL, median (IQR)	6.0 (0.0-13.0)	6.0 (2.0-12.0)	0 (-4.1 to 4.1)
DLQI, median (IQR)	3.0 (1.0-9.0)	2.0 (1.0-6.0)	-1.0 (-3.3 to 1.3)
HAQ, median (IQR)	0.75 (0.25-1.50)	0.75 (0.38-1.38)	0.125 (-0.23 to 0.48)
*p<0.05, **p<0.01, ***p<0.001.			

Table 2 Significantly greater synovitis and erosions in ultrasound scanned joints in PsA with dactylitis compared to PsA without dactylitis.

US	No dactylitis (n=86/155)	Dactylitis (n=69/155)	Mean difference/ Pearson Chi-squared test	P value
GS≥2	551/3422 (16.1%)	642/2721 (23.6%)	-7.5 (-12.0 to -3.0)	<0.001
PD≥1	114/3422 (3.3%)	198/2721 (7.3%)	-4.0 (-8.8 to 0.9)	<0.001
GS≥2 & PD>1	89/3422 (2.6%)	171/2721 (6.3%)	-3.7 (-4.7 to -2.6)	<0.001
Total number of US erosions	15/3206 (0.5%)	33/2557 (1.3%)	-0.8 (-1.3 to -0.3),	<0.001
Patients with US erosions	11/86 (12.8%)	22/69 (32.9%)	Pearson Chi-squared test=8.3	p=0.004

raphers blinded to clinical details. Synovitis was graded for grayscale (GS) and power Doppler (PD) using the semi-quantitative method (0-3) at 48 joints: wrists, MCP1-5, PIP1-5, DIP2-5, MTP1-5, knees, ankles, subtalar and talonavicular joints. Bone erosions were determined by US if cortical bone discontinuity was present in two perpendicular planes (longitudinal/transverse).

Results: A total of 177 patients were recruited. Dactylitis patients recorded significantly higher median difference in TJC ($p< 0.01$), SJC ($p< 0.001$), and CRP ($p< 0.01$) compared to PsA without dactylitis. Table 1 outlines the characteristics of the cohort. Dactylitis was present in 81/177 (46%) patients and 214 digits. Multiple digits (>1) were involved in 51/81 (63%) patients, asymmetrical in 52/81 (64%). Dactylitis was more prevalent in toes (146/214; 68.2%) than fingers (68/214; 31.8%). “Hot” dactylitis was more prevalent (179/214; 83.6%) than “cold” dactylitis (35/214; 16.4%). The most frequent sites for “hot” dactylitis were 2nd finger (23/179; 12.8%), 4th toe (40/179; 22.3%) and for “cold” dactylitis, 3rd finger (2/35; 8.5%), 4th toe (10/35; 28.5%). Significantly greater US synovitis was identified in PsA with dactylitis ($p< 0.001$) determined by either GS≥2, PD≥1, or GS≥2+PD≥1 as shown in table 2. Ultrasound defined erosions were also significantly greater in joints of patients with dactylitis ($p< 0.001$) overall and were identified in significantly more patients with dactylitis compared to patients without dactylitis [22/69 (31.9%) versus 11/86 (12.8%) patients; p=0.004] (table 2). Sites most prone to erosive damage were MCP2 (9/33, 27.3%), MTP5 (11/33, 33.3%).

Conclusion: This study identifies dactylitis as a clinical indicator for an aggressive phenotype with significantly greater TJC, SJC, CRP, US synovitis and US defined erosions in very early DMARD naïve PsA, compared with PsA without dactylitis. Longitudinal follow-up will determine if dactylitis represents poor prognosis at this very early disease stage. Dactylitis may be a useful discriminator for risk stratification in future PsA management strategies and clinical trials.

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Abstract Number: 0313

Swollen Joints but Not Tender Joints Are Associated with Ultrasound Power Doppler Synovitis in Very Early DMARD Naive Psoriatic Arthritis

Sayam Dubash[1], Oras Alabas[1], Xabier Michelena[1], Leticia Garcia-Montoya[1], Gabriele De Marco[2], Mira Merashli[3], Richard Wakefield[1], Philip Helliwell[4], Ai Lyn Tan[1], Dennis McGonagle[1], Paul Emery[5] and Helena Marzo-Ortega[1], [1]The University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, UK, Leeds, United Kingdom, [2]The University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, UK, Treviglio, Italy, [3]The University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, UK, Beirut, Lebanon, [4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, [5]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds and NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, UK, Leeds, United Kingdom

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

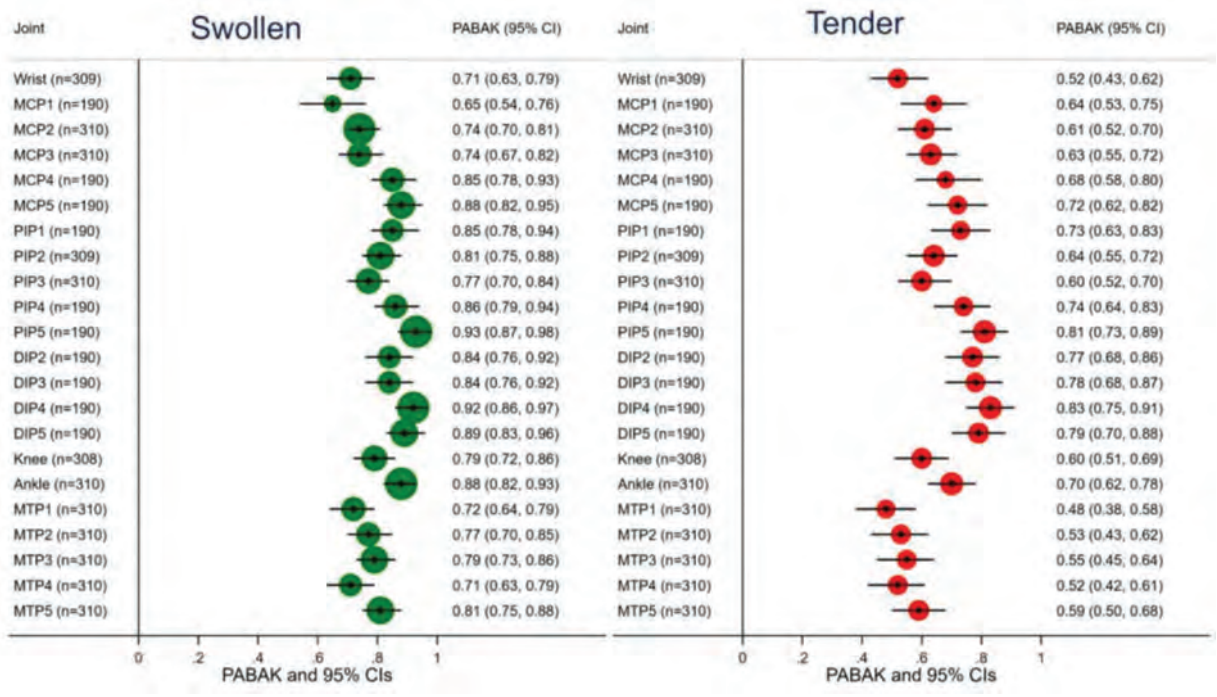

Figure 1. Percentage agreement (%) and adjusted kappa (PABAK) with 95% CIs between tender/swollen joints and ultrasound power Doppler Synovitis per joint.

Background/Purpose: Clinical tender and swollen joint counts are used for biologic drug eligibility and clinical trial inclusion criteria. Ultrasonography (US) adds to clinical examination as it is a sensitive imaging modality in the assessment of inflammatory arthritis, yet its relationship with tender and swollen joints is not fully understood. The objective of this study was to explore the relationship between clinical examination and US determined synovitis in very early, DMARD naïve psoriatic arthritis (PsA).

Table 1. Individual joint level correlation (rho) between tender non-swollen joints versus tender and swollen joints. Lack of correlation was determined by the absence of swelling.

Joint	+T -S			+T +S		
	GS≥2	PD≥1	GS≥2& PD≥1	GS≥2	PD≥1	GS≥2& PD≥1
Wrist (n=309)	-0.02	-0.03	-0.09	0.26***	0.40***	0.39***
MCP1 (n=190)	0.11	0.11	0.12	0.20**	0.36***	0.38***
MCP2 (n=310)	-0.04	-0.08	-0.07	0.24***	0.41***	0.36***
MCP3 (n=310)	0.06	0.03	0.05	0.33***	0.47***	0.46***
MCP4 (n=190)	-0.02	-0.008	0.07	0.18*	0.49***	0.34***
MCP5 (n=190)	0.003	-0.06	0.03	0.12	0.26***	0.28***
PIP1 (n=190)	0.04	-0.04	-0.04	0.30***	0.30***	0.30***
PIP2 (n=309)	-0.05	-0.01	-0.02	0.29***	0.44***	0.44***
PIP3 (n=310)	-0.02	0.003	0.02	0.25***	0.31***	0.30***
PIP4 (n=190)	-0.06	0.22**	0.22**	0.03	0.25**	0.25***
PIP5 (n=190)	0.07	-0.03	-0.03	0.11	0.39***	0.39***
DIP2 (n=190)	-0.07	-0.02	-0.04	-0.03	0.13*	0.13
DIP3 (n=190)	0.10	0.18*	0.26*	-0.09	-0.03	-0.03
DIP4 (n=190)	0.13	-0.03	-0.03	0.05	0.20**	0.20**
DIP5 (n=190)	-0.06	-0.03	-0.03	0.04	0.29***	0.16*
Knee (n=308)	-0.04	-0.07	-0.06	0.19**	0.18**	0.20**
Ankle (n=310)	-0.03	-0.04	-0.03	0.23***	0.23***	0.27***
MTP1 (n=310)	-0.15**	-0.001	0.04	0.19**	0.15**	0.17**
MTP2 (n=310)	0.14*	-0.04	-0.04	0.09	0.20**	0.18**
MTP3 (n=310)	0.06	0.04	0.04	0.32***	0.20**	0.20**
MTP4 (n=310)	-0.01	-0.01	-0.01	0.18**	0.20**	0.20**
MTP5 (n=310)	0.14*	0.13*	0.11	0.12*	0.14*	0.16**

*p<0.05, **p<0.01, ***p<0.001

Methods: Eligible PsA patients determined by CASPAR criteria underwent matched clinical and US joint assessments (44 joints). Disease activity per joint was determined by tender/swollen joints (TJ/SJ) and US synovitis defined by power Doppler (PD) ≥1. Agreement between TJ/SJ and PD≥1 was conducted at the individual joint level and patient level (TJC/SJC). Statistical agreement between clinical and US assessments was calculated using prevalence-adjusted and bias-adjusted kappa (PABAK), and the association was determined using the Spearman's rank test (rho/ρ).

Results: A total of 5,616 joints were assessed using US in 155 patients [median disease duration (interquartile range (IQR)) 1.1 months (0-3.0) from diagnosis; median symptom duration (IQR) 12 months (7-30)]. Grayscale (GS) was identified in 2273/5616 (40.4%) and PD≥1 in 292/5616 (5.2%) joints. Agreement between SJ and PD was very high at the individual joint level (82.6 - 96.3%, PABAK 0.65- 0.93) and patient level (SJ and PD≥1: 89.9%, PABAK 0.80), as per figure 1. Joints that were tender and swollen (T+ S+) demonstrated weak/moderate correlation (r=0.28, p< 0.001) with PD≥1 synovitis at the patient and individual levels. However, tender joints in the absence of swelling (T+ S-) did not correlate with PD synovitis (r=0.01) at the patient level, with negligible correlation at individual joint level (table 1).

Conclusion: In very early, DMARD naïve PsA, clinically swollen joints are associated with PD synovitis, but tender, non-swollen joints are not. Further understanding of the aetio-pathology of joint tenderness may disentangle its complex relationship in early PsA.

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Abstract Number: 0314

Accuracy of Physical Examination to Detect Synovial and Extra-synovial Pathologies in Psoriatic Arthritis in Comparison to Ultrasonography

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study to explore the comparison of physical examination (PE) and ultrasound (US) detected synovial and extra-synovial pathologies of the hands in psoriatic arthritis (PsA).

Methods: Twenty-nine PsA patients who had hand pain included the study. A detailed PE was performed to differentiate pain due to joint, tendon, and entheseal disease. At the same visit US scans of MCP (Metacarpophalangeal), PIP (Proximal Interphalangeal), DIP (Distal Interphalangeal) joints (total 696 joints), extensor and flexor tendons (464)

Table. Agreement of Physical Examination and Ultrasound in Joints, Enthesis and Tendons

			Power Doppler		Kappa/PABAK	Gray scale		Kappa/PABAK
			Absent	Present		Absent	Present	
MCP	Tender joints, n	Absent	108	2	0.084/0.043	73	37	0.089/0.077
		Present	109	13		70	52	
	Swollen joints, n	Absent	208	11	0.240/0.827	139	80	0.087/0.275
		Present	9	4		4	9	
	Tender AND Swollen joints, n	Absent	208	12	0.175/0.819	139	81	0.074/0.267
		Present	9	3		4	8	
PIP	Tender joints, n	Absent	128	4	0.099/0.206	123	9	0.208/0.284
		Present	88	12		74	26	
	Swollen joints, n	Absent	152	1	0.227/0.439	144	9	0.312/0.465
		Present	64	15		53	26	
	Tender AND Swollen joints, n	Absent	167	4	0.227/0.543	158	13	0.330/0.551
		Present	49	12		39	22	
DIP	Tender joints, n	Absent	134	1	0.003/0.163	133	2	-0.005/0.155
		Present	96	1		96	1	
	Swollen joints, n	Absent	211	2	-0.016/0.819	210	3	-0.023/0.810
		Present	19	0		19	0	
	Tender AND Swollen joints, n	Absent	217	2	-0.015/0.870	216	3	-0.021/0.862
		Present	13	0		13	0	

Tenderness on PE		Any inflammation on US within the enthesis, n		Kappa/PABAK
		Absent	Present	
EE*	Absent	149	25	-0.027/0.344
	Present	51	7	
FE	Absent	179	48	0.039/0.569
	Present	43	7	

Tenderness on PE		Any inflammation on US within the tendons, n		
		Absent	Present	
ET	Absent	158	10	0.123/0.448
	Present	54	10	
FT	Absent	151	13	0.171/0.431
	Present	53	15	

US: Ultrasound, PABAK: Prevalence Adjusted and Bias Adjusted Kappa, PE: Physical Examination
MCP: Metacarpophalangeal, PIP: Proximal Interphalangeal, DIP: Distal Interphalangeal
EE: Extensor Enthesis, FF: Flexor Enthesis, ET: Extensor Tendon, FT: Flexor Tendon
*Results are only given for the insertions of the tendons to the basis of distal phalanx.

and enthesis (696) of 2nd to 5th fingers of both hands were done by an investigator blinded to the clinical assessment. The agreement between PE and US findings was calculated with Kappa and Prevalence Adjusted and Bias Adjusted Kappa (PABAK).

Results: Fifteen of the patients were male, the mean age was 54.8 (8.4) and the mean PsA duration was 15.3 (10) years. Tender joint count was detected highest in MCP joints [n=122 (52.5%)] in 27 (93%) patients and swollen joint count was highest in PIP joints [n=79 (34%)] in 23 (79%) patients. Power Doppler (PD) positivity rate was similar in MCP (n=15, 6.5% of the joints; 7/29, 24% of the patients) and PIP joints (n=16, 7% of the joints; 8/29, 27.5 %) of the patients), but Gray Scale (GS) positivity was found highest in MCP joints [n=89, (38.4%)] and in 24 (83%) patients. Overall DIP joints had low GS and PD positivity rates (1.3% and 0.9%, respectively). Strongest agreement for joints was between "swollen joints", "tender and swollen joints" and PD in the MCP joints and GS in the PIP joints (Table). The agreement of tender entheses on PE and inflammation on US (hypoechogenicity, thickening and/or PD signals) was poor for both extensor (Kappa= -0.027 PABAK= 0.344) and flexor compartments (Kappa= 0.039 PABAK= 0.569). Similar to enthesitis, for the tendons, comparison of any PE and US findings showed a poor agreement at the extensor and flexor regions (extensor: Kappa= 0.123, PABAK= 0.448 and flexor: Kappa= 0.171, PABAK= 0.431).

Conclusion: Our study showed that there is a poor to fair agreement of PE and US findings of hands, for the joints, tendons, and entheses which may all be involved in PsA. US can add value when determining the source of pain in PsA in the small joints.

Disclosure: U. Gazel, None; **D. Solmaz**, None; **G. Ayan**, None; **C. Ivory**, None; **J. Karsh**, None; **S. Aydin**, None.

Abstract Number: 0315

The Role of Ultrasound for the Assessment of Psoriatic Arthritis Patients with Fibromyalgia

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The presence of fibromyalgia (FMS) in psoriatic arthritis (PsA) patients increases the scores of the clinical measures of disease activity.

The aim of this study is to examine whether ultrasound (US) can be used in the evaluation of disease activity in PsA patients with concomittant FMS as an objective tool that is not influenced by the presence of FMS

Methods: The study population included consecutive PsA patients that were recruited prospectively and fulfilled the CASPAR criteria. The assessment of the patients included, complete medical history and physical examination including assessment of joints (66/68 joint count), enthesitis (LEEDS and SPARCC), and fibromyalgia tender points. All the patients were assessed by the widespread pain index (WPI) and symptom severity score (SSS) for fibromyalgia criteria. Patients were classified with FMS if they fulfilled the 2016 fibromyalgia classification criteria. All the patients underwent a detailed US evaluation (gray scale and Doppler) including 52 joints, 40 tendons and 14 points of en-

Table 1. Sonographic comparison between PsA without and with fibromyalgia

Table 1: Sonographic comparison between PsA without and with fibromyalgia

	PsA without Fibromyalgia N=114	PsA with Fibromyalgia N=42	P-Value
Total US Score*, mean (± s.d)	32.3 (21.5)	33.1 (18.6)	0.83
Total US Score, mean (± s.d)	33.6 (23.1)	34.6 (20.5)	0.81
Total Gray scale score, mean (± s.d)	28.7 (18.3)	29.3 (16.0)	0.88
Total Power Doppler score, mean (± s.d)	4.9 (6.3)	5.2 (6.1)	0.79
Synovitis score, EULAR-OMERACT Score, mean (± s.d)	12.2 (10.2)	11.6 (8.9)	0.73
Synovitis score (Gray scale + Doppler), mean (± s.d)	13.3 (11.6)	13.3 (11.0)	0.99
Synovitis Gray scale score, mean (± s.d)	12.0 (10.0)	11.9 (8.8)	0.94
Synovitis Power Doppler score, mean (± s.d)	1.4 (2.2)	1.5 (2.9)	0.80
Tenosynovitis score, mean (± s.d)	3.6 (4.9)	4.0 (4.5)	0.63
Tenosynovitis Gray Scale score, mean (± s.d)	2.5 (3.8)	2.8 (3.4)	0.63
Tenosynovitis Power Doppler score, mean (± s.d)	1.1 (1.9)	1.2 (1.7)	0.77
Enthesitis score, mean (± s.d)	16.8 (12.1)	16.8 (10.7)	0.98
Enthesitis Gray Scale score, mean (± s.d)	14.3 (10.0)	14.2 (8.7)	0.97
Enthesitis Power Doppler score, mean (± s.d)	2.5 (3.7)	2.6 (3.3)	0.90

*Synovitis was based on the composite synovitis EULAR-OMERACT Score

Table 2 Correlations of US score with Clinical scores in PsA with and without Fibromyalgia

Table 2: Correlations of US score with Clinical scores in PsA with and without Fibromyalgia

	PsA without Fibromyalgia	PsA with Fibromyalgia	P-Value Differences
US SCORE & DAPSA			
Total US score & DAPSA	0.37*	0.26	0.27
GS US score& DAPSA	0.36*	0.27	0.54
PD US score & DAPSA	0.34*	0.23	0.30
US SCORE & CPDAI			
Total US score & CPDAI	0.36*	-0.04	<0.001
GS US score & CPDAI	0.34*	-0.002	0.001
PD US score & CPDAI	0.29*	-0.05	0.001
US SCORE & PASDAS			
Total US score & PASDAS	0.40*	0.15	0.01
GS US score & PASDAS	0.38*	0.20	0.09
PD US score & PASADS	0.33*	-0.1	<0.001

*<0.01, GS – Gray scale, PD – Power Doppler

theses (according to MASES index plus lateral epicondyles). The score of the US was based on the summation of a semi-quantitative score (0-3) for synovitis (based on the EULAR-OMERACT definition), tenosynovitis, and enthesitis score. All the evaluations occurred in the same day and the sonographer was blinded to the clinical data.

Results: 156 patients completed the study. Overall 7540 joints, 5800 tendons and 2030 entheses were scanned by the US. 42 patients (26.9%) classified with both PsA and FMS were compared to 114 (73.1%) PsA patients without FMS. Patients with PsA and FMS had significantly increased scores for almost all the clinical measures, including non-MDA (97.6% vs. 54.4%, p< 0.001), mean CPDAI (11.6 vs. 6.8, p< 0.001), mean DAPSA (35.1 vs. 15.9, p< 0.001) and mean PASDAS (5.8 VS. 2.7, P< 0.001). On the other hand, the total US score and its' subcategories (US synovitis, tenosynovitis and enthesitis) did not demonstrate significant differences between those with to those without FMS (Table 1). The US score significantly correlated with each clinical score (CPDAI, DAPSA and PASDAS, p< 0.01) in the PsA without FMS but not in the PsA and FMS group (Table 2). Furthermore, these correlations were significantly

Table 3. Multivariable linear regression model for association with clinical scores (DAPSA, CPDAI, PASDAS) & Total US score

Table 3: Multivariable linear regression model for association with clinical scores (DAPSA, CPDAI, PASDAS) & Total US score

Variables	DAPSA Regression coefficient	P-value	CPDAI Regression coefficient	P-value	PASDAS Regression coefficient	P-value	US Score Regression coefficient	P-value
Age	0.06	0.37	0.01	0.57	0.07	0.50	0.36	0.005
Gender	-0.52	0.78	0.68	0.20	0.05	0.86	2.4	0.44
BMI	0.39	0.03	0.08	0.11	0.04	0.09	0.24	0.41
Psoriasis duration	0.01	0.83	0.03	0.11	0.001	0.87	0.18	0.11
Fibromyalgia presence	17.6	<0.001	4.42	<0.001	2.93	<0.001	-3.5	0.31
PASI	0.09	0.7	0.11	0.11	0.05	0.16	0.04	0.9
CRP	1.77	0.02	0.13	0.55	0.19	0.09	5.14	<0.001
SJC	2.42	<0.001	0.38	<0.001	0.31	<0.001	3.4	<0.001

BMI – Body Mass Index, SJC – Swollen Joint Count

higher for the CPDAI and PASDAS in the PsA without FMS compared to PsA with FMS ($p< 0.05$). Multivariable linear regression model showed that FMS was significantly associated with higher clinical scores ($p< 0.001$) but not with the US score (Table 3).

Conclusion: Patients with PsA and FMS had increased scores of clinical measures compared to those without FMS. US scores were similar between the groups, independently of the presence of FMS**.** Hence, US has a significant additional value over composite clinical scores in the assessment of disease activity in PsA patients with fibromyalgia.

Disclosure: A. Polachek, None; **V. Furer**, None; **M. Zureik**, None; **S. Nevo**, None; **L. Mendel**, None; **D. Levartovsky**, None; **J. Wollman**, None; **V. Aloush**, None; **M. Berman**, None; **I. Kaufman**, None; **R. Tzemach**, None; **M. Anouk**, None; **O. Elalouf**, None; **H. Padova**, None; **O. Carmi**, None; **T. Eviatar**, None; **Y. Lahat goldstein**, None; **H. Sarbagil-Maman**, None; **S. Borok Lev-Ran**, None; **A. Broide**, None; **L. Eder**, None; **D. Paran**, None; **O. Elkayam**, None.

Abstract Number: 0316

High-sensitivity ^{18}F-FDG PET/CT: A Diagnostic Tool for Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To validate high-sensitivity PET/CT as a diagnostic test we have explored the association of total-body and extremity PET/CT measures with the standardized psoriatic arthritis (PsA) outcome measures (DAPSA, Leeds Enthesitis Index, etc). The *objective of our study* is to determine the association of *in vivo* PET/CT measures, and use these data to create a catalog of systemic PsA musculoskeletal pathologies and compare with that of RA and OA.

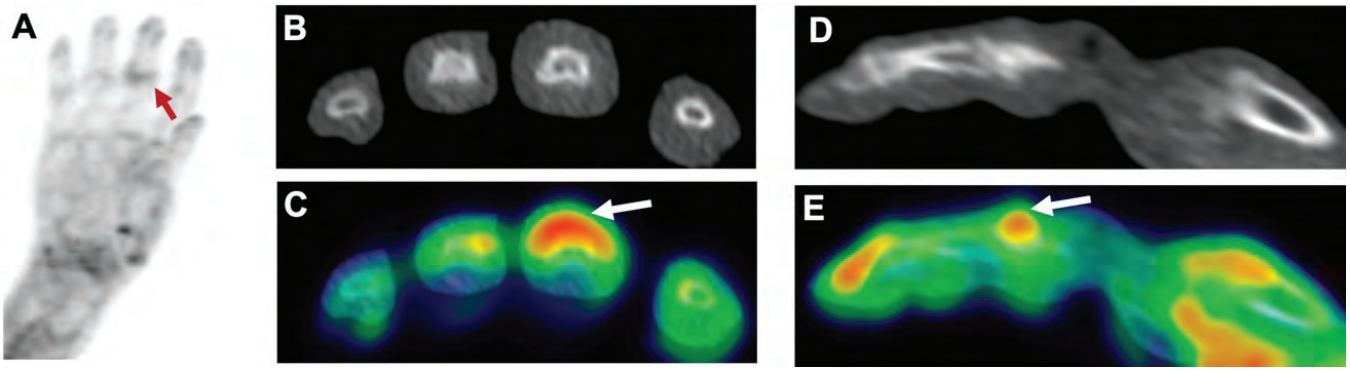

Figure 1. Enthesitis on PET/CT in PsA: Extensor digitorum tendon uptake at the central slip, showing enthesitis; (A) Maximum-intensity projection through the PET scan of the right hand of a participant with PsA showing entheseal uptake at the third PIP joint; axial (B) and sagittal (D) sections through the CT scan of the third PIP joint (grayscale); and axial (C) and sagittal (E) section from the overlay of PET (color) on CT (grayscale).

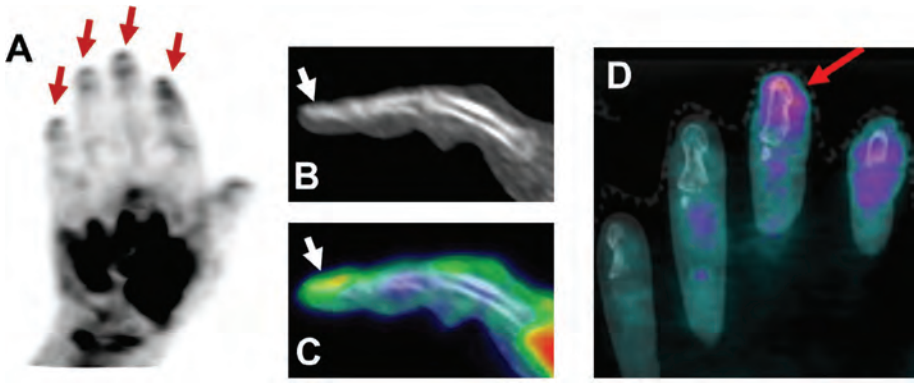

Figure 2. Nail matrix involvement in PsA: (A) Maximum-intensity projection through the PET scan of the left hand of a participant with PsA showing nail involvement; sagittal (B) CT and (C) PET/CT (PET in color, CT in grayscale) of the second digit showing nail bed inflammation. (D) shows nail bed involvement in a participant with PsA from our previous study for comparison.

Methods: Patients with RA, PsA or OA were enrolled in IRB-approved studies. All subjects underwent a single-time-point PET/CT scan on either the total body uEXPLORER scanner or the UC Davis extremity PET/CT scanner for 20 minutes starting at either 40 or 70 minutes after IV injection of ^{18}F-FDG (~1/4th of the conventional dose). Qualitative findings and different patterns for the three conditions were evaluated. We quantified the degree of inflammation in the extremities and whole-body, respectively and determine pathologic predilection for anatomical domains of bones/ligaments of hands in PsA, RA and OA.

Results: Here we will share data from recruited 20 patients, all males, with RA (n=7; median age: 67 years), PsA (n=10; median age: 68 years), OA (n=3; median age: 60 years). The RA patients had symmetric joint involvement, most commonly in the hands/knees. The following sites were involved: radio-and/or ulno-carpal compartments (n=5), MCP (n=4), PIP (n=5) joints. Joints of the feet appeared to be less frequently affected. All PsA patients demonstrated multiple sites of enthesitis (n=10/10), affected the tendons of the hands/fingers and seemed more active on the extensor side (n=5). Increased nail matrix/fingernail FDG uptake was observed to be a distinct feature (n=8/10). Several large joints showed positive findings in all patients. Less frequent features included sausage finger (n=2), plantar fasciitis (n=3); sacroiliac joint (n=2). Involvement of the interspinous ligament (n=2) and facet joints (n=2) was also noted. Patients with OA showed unilateral enhanced FDG uptake at least one big joint (shoulder, n=3; elbow, n=1; knee, n=2), and small joints of the hand/feet (1st CMC/1st MTP).

Conclusion:

1. Asymmetric synovitis of small joints of hands/feet, enthesitis, nail matrix inflammation, dactylitis and spondylitis stands out to be pathologic features for PsA.
2. There appeared to be an overall concurrence between degree of inflammation by imaging and clinical outcome measures of PsA such as DAPSA and Leeds Enthesitis Index.
3. We expect at the completion of this study these clinico-radiologic domains will provide for unique quantitative diagnostic imaging biomarkers for PsA and a single PET imaging scan will be able to differentiate from other inflammatory/non-inflammatory conditions like RA and OA.

Disclosure: S. Raychaudhuri, AbbVie, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sun Pharmaceutical Industries, Inc., 2, Amgen, 5, Eli Lilly, 5; **Y. Abdelhafez**, None; **S. Sarkar**, None; **S. Raychaudhuri**, None; **A. Chaudhari**, None.

Abstract Number: 0317

Axial Involvement in Psoriatic Arthritis in a Comprehensive Rapid Diagnosis Program (Reuma-check PsA). Analysis of Its Characteristics

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: To date, there is no consensus that allows an appropriate definition of axial involvement in PsA, that ranges between 25 to 70%. To estimate the prevalence of axial involvement in patients with newly diagnosed PsA and to describe their characteristics and differences.

Methods: An observational study included patients older than 18 who entered the fast track evaluation program (Reuma-check APS) according to the following criteria: arthritis, dactylitis or enthesitis, associated with psoriasis. Those admitted to the circuit underwent: blood test (VSG and PCR), x-ray and joint and enthesis ultrasound. Socio-demographic data, level of education and habits, DAPSA and HAQ were also recorded. If the patient reported axial symptom was re-entered into an "axial" circuit to collect: date and age of onset, characteristic of low back pain, received NSAIDs and response, VAS of pain, morning stiffness, x-ray and MRI of the sacroiliac, HLA B27, BASDAI and BASFI. The clinical assessor was blinded for the complementary studies that were collected by another observer. Statistical analysis: descriptive statistics was performed and in the low back sample, Chi2 test and Fisher's exact test and Student or Mann Whitney test was applied, logistic regression.

Results: 75 patients were diagnosed with PsA in the circuit between 2018 and 2019, 55% were women, mean age was 49 (SD 12.5), with a median duration of symptoms until the diagnosis of 3 years (RIC: 5-8).

37% (CI: 25-49) presented clinical axial involvement. The characteristics of low back pain were: inflammatory 76%, sacroiliac test 70%, HLA B27 21%, positive x-ray 40%, MRI 56%, good response to NSAIDs 55%, morning stiffness: 30 mint (15- 40), BASFI 5 (3.8-5.6), BASDAI 4.1 (3-5.8), age of onset 44 (36-50), the time between low back pain and the diagnosis of PsA 4 years (1 -9.7).

In patients with PsA and axial involvement, a higher number of enthesitis was observed median 2 (0-1) vs 0 (0-1) p 0.001, higher DAPSA: median 17 (14-19) vs 12 (5-16) p 0.02, and greater functional alteration: HAQ of 0.8 (0.5-1) vs. 0.5 (0.1-1.2). No difference was found regarding sex, smoking, peripheral ultrasound abnormalities, or acute phase reactants. In the logistic regression analysis, only the enthesitis was associated independently.

Conclusion: The prevalence of axial symptoms in our cohort was 37%, the characteristics were mostly inflammatory and with activity by BASDAI. Patients with axial symptoms had more severe PsA characteristics, with greater activity (DAPSA), functional alteration due to HAQ and enthesitis.

Disclosure: R. Garcia Salinas, None; **S. Ruta**, None; **J. Torres Chichande**, None; **E. Sanchez Prado**, None; **F. Salvatori**, None; **S. Magri**, None.

Abstract Number: 0318

Oxylipin Profile Is Associated with Skin Disease and Enthesitis in Psoriatic Disease

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA), a systemic inflammatory disease, occurs in about 25% of patients with psoriasis (PsO). At present, there are no biomarkers that reliably identify patients with PsO who will go on to develop PsA. In addition to peripheral and axial arthritis, enthesitis is common in PsA. Oxylipins are biological lipids that have been implicated in various pathological processes, including inflammation. We previously found that certain oxylipins correlated with joint disease and skin disease in a cohort with PsA patients. Here, we compare the oxylipin profile in two different cohorts of PsO patients without joint disease and PsA patients.

Methods: Patients with PsA and PsO, diagnosed based on the CASPAR criteria were recruited from the Rheumatology Outpatient Clinic at the University of Rochester, NY. A thorough clinical examination was performed, including enthesitis (using Leeds index). Patients completed a health assessment questionnaire. DAS (disease activity score) 44, Psoriasis Area and Severity Index (PASI) and body surface area (BSA) of psoriasis were also calculated. Serum oxylipins were determined by Mass Spectrometry and were classified into groups according to their precursor: arachidonic acid (AA), linoleic acid (LA), a-Linolenic acid, Docosahexaenoic acid (DHA), eicosapentaenoic acid (EPA) and Dihomo-g-linolenic acid. Data were analyzed using R version 3.6.1.

Results: Sera from 20 PsO patients were analyzed (average age 51.95 (10.83), 55% males, average body mass index BMI; 33.73 (6.84)). The average PASI was of 3.87 (4.25) and there was an average BSA of 4.5 (4.77). PsO patients were classified in 2 groups, based on the PASI. The group with higher PASI score (>2.5) had significantly lower serum concentrations of pro-inflammatory oxylipins, most of them being derived from AA. 19 PsA patients were analyzed

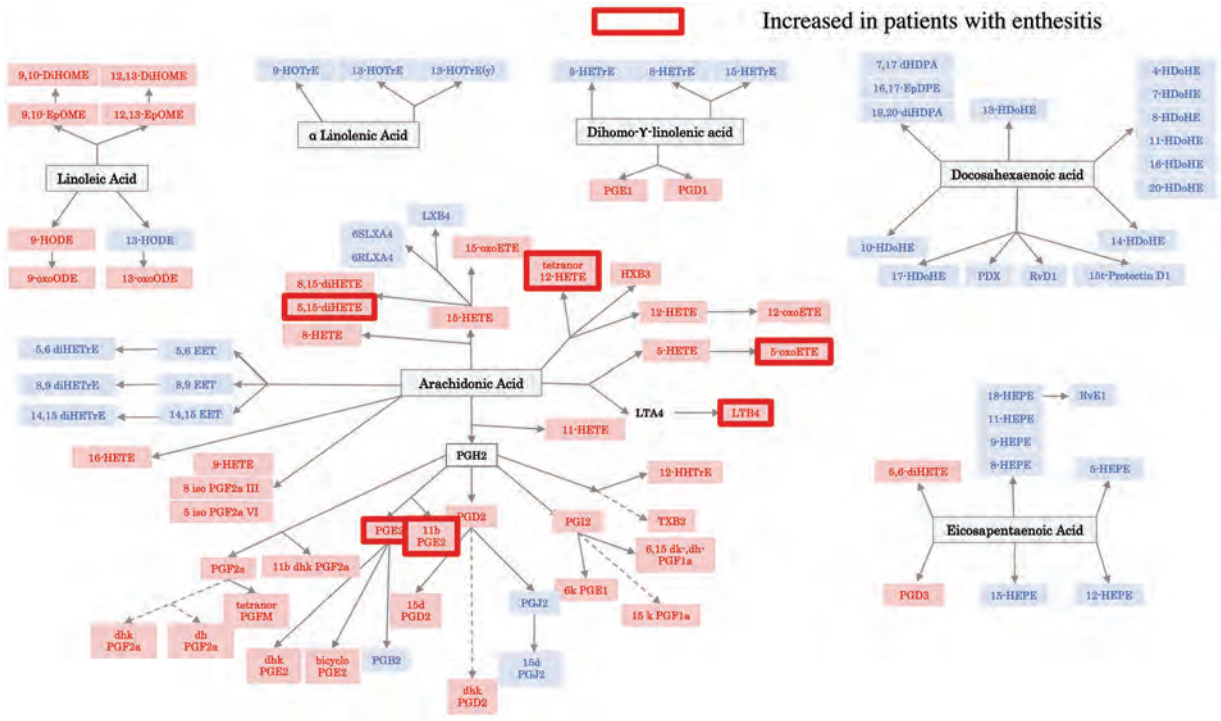

Figure 1. Oxylipins that are decreased in PsO patients with higher PASI (> 2.5) compared to lower PASI (≤ 2.5) are marked with blue squares. Red background – pro-inflammatory; blue background – anti-inflammatory.

(average age 60.5 years old (11.41), 63.15% males, with an average BMI of 31.96 (5.64)). The average number of TJC was 9.38 (10.41) and of SJC 3.77 (4.23). 63.15% patients had enthesitis (average of 2.21 (3.08)) and psoriasis (average PASI 3.02 (5.09)). Oxylipins profiling in the PsA patients with higher PASI score (>2.5) also had lower AA-derived oxylipins compared to PASI ≤ 2.5 . Oxylipin profiling did not associate with the number of SJC nor TJC. Yet, interestingly, several AA-derived oxylipins (8,15 di-HETE, 5-oxoETE, PGE2, 11bPGE2, 5-oxoETE, LTB4) were significantly associated with enthesitis. PsA patients with enthesitis had higher concentrations of oxylipins compared to PsA patients without enthesitis (Figure 1).

Conclusion: The AA-derived proinflammatory oxylipins were lower in both PsO and PsA patients with higher skin scores. Joint disease activity didn't have an effect on the concentrations of oxylipins. Yet, enthesitis was associated with an increase of AA derived pro-inflammatory oxylipins. Further studies are needed to determine whether oxylipin profiling can be a good biomarker of enthesitis in PsO patients.

Disclosure: R. Coras, None; **A. Kavanaugh**, AbbVie, 2, 9, Amgen, 2, 9, AstraZeneca, 2, 9, Bristol-Myers Squibb, 2, 9, Celgene, 2, 9, Janssen, 2, 9, Pfizer, 2, 9, Roche, 2, 9, UCB, 2, 9; **A. Kluzniak**, None; **D. Holt**, None; **A. Weilgosz**, None; **O. Quehenberger**, None; **C. Ritchlin**, None; **M. Guma**, None.

Abstract Number: 0319

Target Outcomes in Psoriatic Arthritis: Simultaneous Achievement of ACR50-Psoriasis Area and Severity Index 100 and Beyond: Insights from Open-Label, Assessor-Blinded Study at Week 24

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic Arthritis (PsA) treatment should aim to achieve robust improvement of arthritis as well as control of extra-articular manifestations like the skin. SPIRIT-H2H evaluated the efficacy of ixekizumab (IXE)

Table: Efficacy endpoints at Week 24

	ACR50 and PASI100 n=181	ACR50 only n=94	PASI100 only n=121	Neither ACR50 nor PASI100 n=170
ACR20	100.0 [b,c]	100.0	53.7	34.7
ACR70	64.6 [a,b,c]	48.9	0.0	0.0
MDA	75.7 [a,b,c]	60.6	23.1	12.4
VLDA	32.6 [a,b,c]	13.8	3.3	1.8
DAPSA LDA or Remission (≤14)	92.3 [a,b,c]	81.9	43.0	28.8
DAPSA Remission (≤4)	44.8 [b,c]	35.1	6.6	2.4
HAQ-DI score ≤0.5	75.7 [b,c]	64.9	30.6	27.4
PASI75	100.0 [a,c]	60.6	100.0	37.1
PASI90	100.0 [a,c]	36.2	100.0	14.7
SF-36 PCS change from baseline[§]	12.3±0.53 [b,c]	12.3±0.74	5.4±0.66	4.0±0.55

Data are presented as %; [§]mean±standard error.
[a] p<0.05 vs. ACR50 only; [b] p<0.05 vs. PASI100 only; [c] p<0.05 vs. Neither ACR50 nor PASI100.
ACR=American College of Rheumatology; DAPSA=Disease Activity in Psoriatic Arthritis; HAQ-DI=Health Assessment Questionnaire Disability Index; LDA=low disease activity; MDA=minimal disease activity; PASI=Psoriasis Area and Severity Index; SF-36 PCS=36-item Short Form health survey and physical component summary; VLDA=very low disease activity.
Nine patients with active psoriasis and body surface area (BSA) ≥3% were assessed as PASI=0 at baseline, a medical inconsistency that was resolved using medical judgement. These patients were considered PASI100 responders if PASI=0 and BSA=0 at post baseline visits.

and adalimumab (ADA) in patients with active PsA and psoriasis, and naïve to biologic Disease-Modifying Anti-Rheumatic Drugs (bDMARDs). At Week 24, IXE showed superiority to ADA in simultaneous achievement of ACR50 and Psoriasis Area and Severity Index (PASI) 100 as well as significant improvement of treat-to-target and other extra-articular outcomes. The objective is to examine and to compare PsA efficacy outcomes in patients beyond achievement of the primary endpoint of the SPIRIT-H2H trial at Week 24, irrespective of treatment allocation.

Methods: All patients recruited had active PsA (defined as tender joint count ≥3/68, swollen joint count ≥3/66 and body surface area [BSA] ≥3%), and inadequate response to conventional synthetic (cs)-DMARDs. Patients were randomized 1:1 to open-label, assessor-blinded IXE or ADA. We conducted post-hoc analysis of SPIRIT-H2H (NCT03151551), categorizing patients into four independent groups based on the achievement of the primary outcomes (ACR50 and PASI 100), ACR50 only, PASI 100 only or none of them, after 24 weeks of treatment. Statistical analyses consisted of mixed model for repeated measurement and logistic regression models using non-response imputation.

Results: At Week 24, patients reaching simultaneously ACR50 and PASI 100 had a statistically significant higher response in most treat-to-target endpoints than those meeting ACR50 only ($p< 0.05$). In this latter group, a high response rate was observed in ACR70, minimal disease activity (MDA), Disease Activity in Psoriatic Arthritis (DAPSA) remission and PASI 90 response (48.9%, 60.6%, 35.1%, 36.2%, respectively). In patients that did not achieve either ACR50 or PASI 100, up to 1/3 of the patients did achieve ACR20, DAPSA score ≤14, or no physical impairment.

Conclusion: Reflecting the complexity of PsA, different degrees of improvement were observed across all treat-to-target outcomes with greater improvements in patients that met ACR50 response regardless of skin resolution. These findings at Week 24 need to be confirmed with a longer duration of treatment.

Disclosure: J. Smolen, AbbVie, 2, 5, 8, AstraZeneca, 2, 5, 8, Eli Lilly, 2, 5, 8, Celgene, 5, 8, Celltrion, 5, 8, Chugai, 5, 8, Gilead, 5, 8, ILTOO, 5, 8, Janssen, 5, 8, Kabi, 5, 8, Novartis-Sandoz, 5, 8, Pfizer Inc, 5, 8, Samsung, 5, 8, Sanofi, 5, 8; **F. Behrens**, Pfizer, 2, 5, 8, Janssen, 2, 5, 8, Chugai, 2, 5, 8, Celgene, 2, 5, 8, Bionorica, 2, Roche, 2, 5, 8, Abbvie, 5, 8, Sanofi, 5, 8, Lilly, 5, 8, Novartis, 5, 8, Genzyme, 5, 8, Boehringer, 5, 8, MSD, 5, 8, Amgen, 5, 8, UCB, 5, 8, Gilead, 5, 8, Sandoz, 5, 8; **S. Liu-Leage**, Eli Lilly and Company, 3, 4; **C. Sapin**, Eli Lilly and Company, 1, 3; **I. de la Torre**, Eli Lilly and Company, 3; **G. Meszaros**, Eli Lilly and Company, 1, 3; **G. Schett**, None; **L. Gossec**, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8; **A. Östör**, AbbVie, 5, Roche, 5, Janssen, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, Gilead, 5, Paradigm, 5, UCB Pharma, 5, Bristol-Myers Squibb, 5; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **F. Van den Bosch**, AbbVie, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Gilead, 5, Merck, 5, 8.

Abstract Number: 0320

Assessment of Implementation of Treat to Target Concept Using Validated Composite Scores in Psoriatic Arthritis Patients

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To assess the implementation of the "Treat-to-Target" (T2T) concept using validated composite disease activity scores in daily management of psoriatic arthritis (PsA).

Methods: A retrospective analysis of 117 consecutive PsA patient visits during 2016-2017 was performed including patient demographics, clinical disease parameters used in the Minimal Disease Activity (MDA) and Disease Activity Index for PSoriatic Arthritis (DAPSA) composite scores, medication use, comorbidities including osteoarthritis (OA) and fibromyalgia syndrome (FMS) and treatment changes as recorded by the treating physicians. Medical records were reviewed to assess whether T2T concept was implemented. All associations were assessed using Chi square test, or Students' t-test, as appropriate. Pearson's correlation, McNemar and Cohen's kappa measures test were used to evaluate association and agreement between MDA and DAPSA parameters.

Results: Patient visits with complete data for MDA and DAPSA (116 and 114 visits, respectively) were analyzed with mean age 58.4±13 years, 65.5% women. T2T approach was implemented in 76 (65.5%) and 74 (64.9%) patient visits using MDA and DAPSA, respectively (Pearson's correlation -0.695). There was no correlation between T2T implementation and patient age, gender, alcohol and tobacco use, disease activity parameters and the various treatment regimens chosen. Physician assessment of disease activity and treatment changes did not correlate with the MDA score in 40 (34.5%) patients. In 30 of these cases (75%), the MDA status was over-estimated due to disregard of patient reported outcomes (PRO). Underestimation of the MDA status occurred in 10 cases (25%) and could be attributed to treatment changes made in patients having < 2 active joints or entheses. Underestimation of disease activity using DAPSA score occurred in 22 (19.3%) patients and could be attributed to disregarding tender joint count, patient pain visual analogue scale and C-reactive protein level. The co-existence of FMS or OA was associated with worse DAPSA scores in PsA patients (p=0.031, p=0.026, respectively), but did not affect MDA status. Achieving disease remission as a goal using the MDA score was more difficult compared to the use of the DAPSA score (Cohen's kappa=0.489).

Conclusion: In our cohort, T2T concept was implemented in about 65% of patients. The main obstacle observed in T2T implementation was the lack of use of validated, practical disease activity scores such as MDA or DAPSA and physicians' overlooking "subjective" components of these scores in daily practice. Efforts should be made in order to increase physician reliance and use of validated composite scores in PsA patient management.

Disclosure: T. Gazitt, None; **M. Abu Elhija**, None; **A. Haddad**, None; **I. Lavi**, None; **M. Elias**, None; **D. Zisman**, Pfizer, 2.

Abstract Number: 0321

Outcome Measures in Psoriatic Arthritis Registries Are Very Heterogeneous: A Systematic Literature Review of 27 Registries, or 16183 Patients

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Description of 27 ongoing PsA registries or PsA cohorts

Table 1. Description of 27 ongoing PsA registries or PsA cohorts

	Total N =16183 patients (n=27 registries)
Age of patients, weighted mean, years(SD)	49.7(9.3)
Diagnosis criteria based on Caspar, N(%)	21(78)
Gender, female, N(%)	7959(49)
Disease duration, weighted mean, years(SD)	6.8(0.2)
Study involving a single center, N(%)	12(44)
Number of patients per study, mean (SD)	599(578)
Inception cohorts for early disease (≤3years), N(%)	4/26(15)

Background/Purpose: Psoriatic arthritis (PsA) is a multidimensional inflammatory disease for which multiple outcome measures can be used, to assess disease activity e.g. through composite scores, and to assess other aspects of disease such as patient-reported outcomes (PROs)[1]. In trials, outcome measures were varied in 2012, as evi-

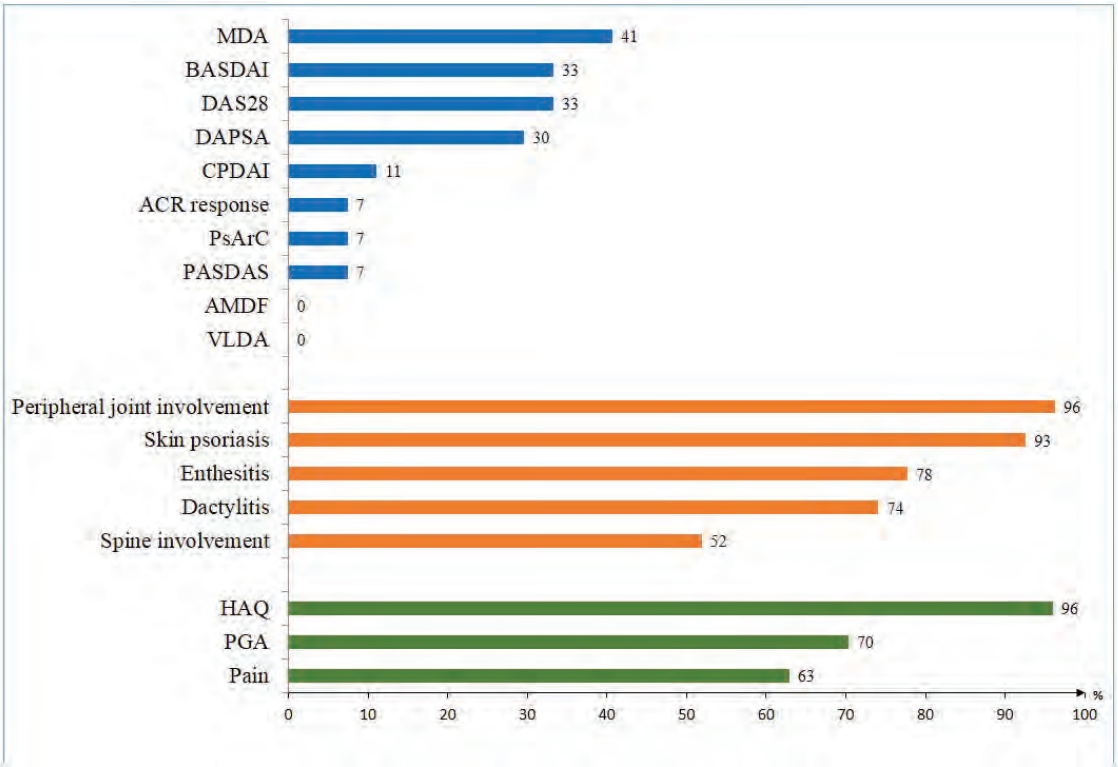

Figure 1. Outcomes reported in 27 PsA cohorts and registries. AMDF: Arithmetic Mean of the Desirability Function; ACR response: American College of Rheumatology response; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CPDAI: Composite Psoriatic Disease Activity Index; DAS28: Disease Activity Score 28; HAQ: Health assessment Questionnaire; PASDAS: Psoriatic Arthritis Disease Activity Score; PASI: Psoriasis Area Severity Index; PGA: Patient's global assessment; PsArC: Psoriatic Arthritis Response Criteria; VLDA: Very Low Disease Activity

denced in a systematic literature review [2]. Since 2012, much work has been performed on outcome measures in PsA [3]. Furthermore, registries reflect more closely real-world data than trials.

The purpose of this study was to assess outcome measures collected in ongoing PsA registries or longitudinal cohorts, through a systematic literature review.

Methods: We performed a systematic literature review in Pubmed Medline (PROSPERO CRD42020175745) to identify all studies reporting either registries or longitudinal cohorts in PsA, published between 2010 and March 2020. Registries centered on drugs or not centered on PsA (e.g., reporting outcomes for several rheumatic diseases), trials and long term extension studies were excluded. The registry principal investigators were contacted by email as needed. All publications for a single registry were analyzed together. The data collection comprised the clinical outcome measures reported, and patient characteristics, based on the largest published population for a given registry. Outcomes were classified as disease activity scores, assessments for the different domains of PsA [3], or PROs. The analysis was descriptive.

Results: Of 673 articles, 73 were relevant for analysis, corresponding to 27 registries or PsA-specific cohorts. The overall number of patients was 16,183 with a mean of 599 per study (**Table 1**). Overall, 51% were men, weighted mean age was 49.7±9.3 years and weighted mean disease duration was 6.8±0.2 years. Most of the studies (78%) were performed in Europe or the United States.

Overall, 58 different clinical outcome measures were collected. Disease activity composite scores were used in 20 registries (74%): of these, 41% reported Minimal Disease Activity, 33% DAS28 and 30% DAPSA (**Figure 1**). Regarding the different domains of PsA, joint involvement was reported in 96% (using variable joint counts, most frequently the 66/68 joint count, in 85%) and 93% of the registries reported skin psoriasis (most frequently through PASI, in 72%), whereas enthesitis, dactylitis and axial involvement were less often reported, also using variables outcome measures (**Figure 1**). Among PROs, 96% of the registries reported HAQ, and the other frequently reported PROs were patient global assessment and pain (**Figure 1**).

Conclusion: Data collection in PsA is very heterogeneous, reflecting the lack of international consensus on outcome measures. Experts need to define a core set of feasible and practical outcome measures for the clinical follow up with patients with PsA.

References

1 Orbai A-M *et al. J Rheumatol* 2017;44:1522–8.
2 Palominos PE *et al. Arthritis Care Res* 2012;64:397–406.
3 Orbai A-M *et al. Ann Rheum Dis* 2017;76:673–80.

Disclosure: K. Aouad, None; **G. Moysidou**, None; **A. Rakotozafiarison**, None; **B. Fautrel**, MSD France, 1, 2, Abbvie, 1, 2, Pfizer, 1, 2, Biogen, 1, BMS, 1, Boehringer Ingelheim, 1, Celgene, 1, Janssen, 1, Lilly, 1, Medac, 1, Nordic Pharma, 1, Novartis, 1, Roche, 1, Sanofi-Aventis, 1, SOBI, 1, UCB Pharma, 1; **L. Gossec**, None.

Abstract Number: 0322

Development and Preliminary Validation of Smartphone Sensor-based Measurement Tools for Psoriatic Arthritis

Dan Webster[1], Rebecca Haberman[2], Lourdes Perez-Chada[3], Stockard Simon[4], Woody MacDuffie[4], Michael DePhillips[5], Soumya Reddy[6], Alexis Ogdie[7], Lara Mangravite[4], Joseph Merola[8] and Jose Scher[2], [1]Sage Bionetworks, Seattle, WA, [2]NYU School of Medicine, New York City, [3]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [4]Sage Bionetworks, Seattle, [5]SDP Digital, Seattle, [6]NYU School of Medicine, New York, NY, [7]University of Pennsylvania, Philadelphia, PA, [8]Brigham and Women's Hospital, Harvard Medical School, Newton, MA

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The COVID-19 pandemic has increasingly driven clinical care into remote settings, where patients with immune-mediated and inflammatory diseases struggle to convey symptom severity to their health providers. Smartphone sensor technology has demonstrated the ability to quantitatively measure disease symptoms, however, similar tools for psoriatic arthritis (PsA) are lacking. Here, we describe preliminary data on the performance of 3 novel tools that can be self-administered by patients using the *Psorcast* iOS app to measure PsA symptoms.

Methods: Three novel smartphone sensor-based measurement tools were developed as part of *Psorcast* to assess PsA symptoms affecting joints domains (Fig 1). Patients with PsA and controls are being recruited at PPACMAN clinical sites to perform the digital measurements while being concurrently assessed by a rheumatologist.

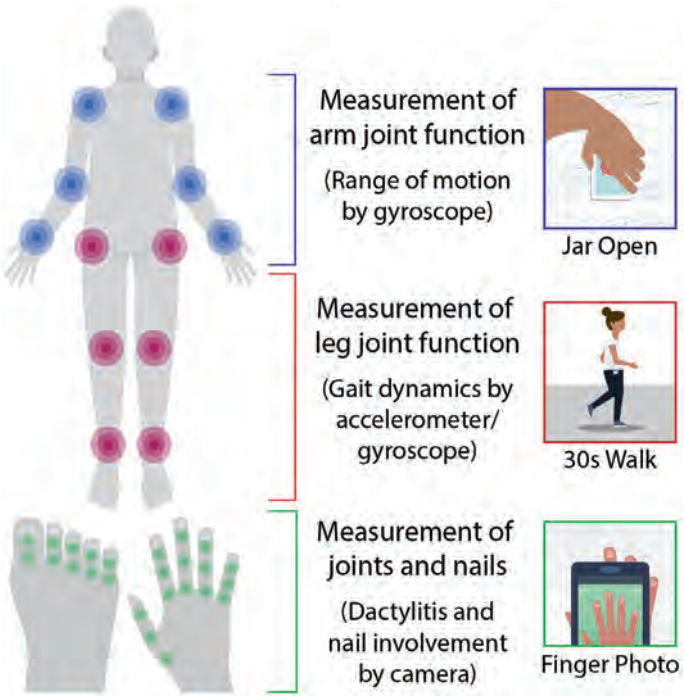

Figure 1. Interactive smartphone sensor-based measures of PsA symptoms from the Psorcast app and the joints that are assessed in each.

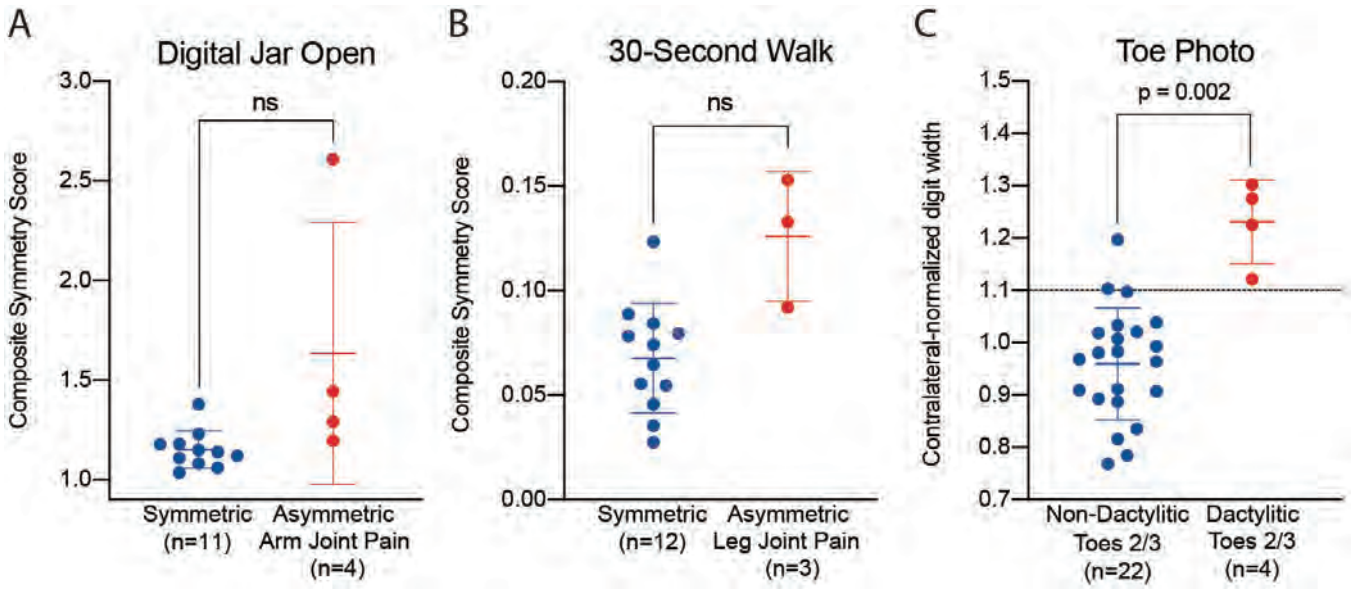

Figure 2. Preliminary results from Psorcast measures. (A) Detection of asymmetric upper extremity joint pain, (B) Detection of asymmetric lower extremity joint pain, (C) Detection of dactylitis in toes 2 and 3. All statistical comparisons use Welch's t-test.

The *Digital Jar Open* tool uses the gyroscope to measure inward and outward rotation of each arm to generate an inward symmetry score and outward symmetry score that are normalized within each participant. The *30-Second Walk* tool measures gait with the smartphone in a pocket during a walk to generate a symmetry score using PDKit. The *Finger/Toe Photo* captures finger and toe images, normalizing them with the contralateral nail bed width to measure relative digit widths.

To assess preliminary validity, *Digital Jar Open* composite symmetry scores were compared between participants with asymmetric upper extremity tenderness as determined by the examining physician and those with none. Triaxial gait asymmetry from the *30-Second Walk* was compared between participants with diagnosed asymmetric lower extremity joint tenderness and those with none. The relative widths of digits captured by the *Finger/Toe Photo* were compared to matching digits from the rest of the cohort with this data, and the resulting data was grouped by physician diagnosis of dactylitis.

Results: In all, 26 patients have been recruited to date. Of these, 15, 15, and 7 provided data to assess the *Digital Jar Open*, *30-Second Walk, and Finger/Toe Photo* tools, respectively. Results from both the *Digital Jar Open* test and *30-Second Walk* demonstrated that the asymmetric joint pain groups are markedly different from controls, but neither of these findings reach statistical significance (Fig. 2A). Finally, 3 individuals in our cohort had dactylitis, all in toes 2 and 3. The relative widths of these digits compared to the rest of the cohort showed a statistically significant separation between the two groups near the 10% difference mark (Fig. 2C). Interestingly, this is the validated cutoff for diagnosing dactylitis from the Leeds Dactylometer.

Conclusion: While validation of *Psorcast* measurements will require an expanded cohort and analysis beyond symmetry-related features, we observed that the 3 sensor-based measurements described here can distinguish some clinical features of PsA. If validated, these and other *Psorcast* tools may provide for remote self-assessment when clinical visits cannot be performed. Importantly, longitudinal and frequent symptom measurement could be of high value to study disease progression and assessing treatment response.

Disclosure: D. Webster, Otsuka Pharmaceutical, 8; **R. Haberman**, Janssen, 5; **L. Perez-Chada**, None; **S. Simon**, None; **W. MacDuffie**, None; **M. DePhillips**, Novavax, 1, Moderna, 1; **S. Reddy**, Amgen, 5, Novartis, 5, Janssen, 5, Pfizer, 5; **A. Ogdie**, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1; **L. Mangravite**, None; **J. Merola**, AbbVie, 9, Merck, 9, Dermavant, 9, Eli Lilly, 9, Novartis, 9, Janssen, 9, UCB, 9, Samumed, 9, Celgene, 9, Sanofi, 9, Regeneron, 9, GlaxoSmithKline, 9, Sun Pharmaceutical, 9, Almirall, 9, Biogen, 9, Pfizer, 9, Incyte, 9, Aclaris, 9, LEO Pharma, 9; **J. Scher**, UCB, 5, Novartis, 2, 5, Pfizer, 2, 5, Janssen, 5, Sanofi, 5, Abbvie, 5.

Abstract Number: 0323

Residual Symptoms in Patients with PsA Who Are in Very Low Disease Activity According to Physician Assessments

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Discrepancy between patient and provider assessments of disease activity is well described in psoriatic arthritis (PsA) and other inflammatory arthritides. Patients often have low tender (TJC) and swollen joint counts (SJC) but continue to have symptoms they ascribe to their PsA. Limited data exists on the specific residual symptoms that patients describe in discordance with physician assessments of very low disease activity (VLDA). Targeting these additional symptoms could improve patient outcomes without escalation of therapy. The objective of this study was to describe the residual symptoms among patients with low TJC, SJC, and enthesitis counts.

Methods: A cross-sectional observational study was conducted of consecutive PsA patients in the Psoriatic Arthritis Research Consortium (PARC) cohort between 2017-Jan 2020. Participants (pts) who started a new therapy and completed a global assessment of response to treatment, the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and Psoriatic Arthritis Impact of Disease (PsAID) questionnaire were included. We examined the prevalence of BASDAI and PSAID item scores ≥ 4 (score ≥ 4 is considered active disease) among pts with very low physician-assessed disease activity as defined by the provider portions of the VLDA criteria: SJC (0-66) of ≤ 1, TJC (0-68) of ≤ 1, and enthesitis count (Leeds + plantar fascia, 0-8) ≤ 1. Pts global assessment of response to treatment was recorded as improvement, no change, or worsening of symptoms.

Results: 244 PsA pts (mean age 51.1yrs (SD 13.9), 53% female, mean BMI 30.0 (SD 6.6) were identified with the required assessments at baseline and follow up after initiating a new therapy. Therapies initiated (pts could start more than one) included: TNFi (134), IL-17i (50), oral small molecule (88), and other (14). Mean PSAID and BASDAI scores at follow-up were significantly lower for pts in physician-assessed VLDA compared to those not in VLDA ($p< 0.001$ for almost all comparisons. Table 1); however, 47% of pts in physician-assessed VLDA had at least one residual symptom (score >=4 on BASDAI or PSAID item) compared to 85% not in physician-assessed VLDA using the PsAID. Pts global assessment of response to treatment demonstrated improvement in 42%, no change in 45%, and worsening in 12%. The most common residual symptoms were fatigue (33%), spine pain (30%), peripheral joint pain/swelling (26%), stiffness (23%), disrupted sleep (24%), and tenderness to touch (19%). Many of these symptoms

Table 1. Mean differences in patient reported outcomes by physician-assessed very low disease activity

	PhA-VLDA No. or Mean (% or SD)	Not in PhA-VLDA No. or Mean (% or SD)	p-value
Patient global assessment of response to treatment	n=91	n=153	
Improvement	39 (43%)	31 (20%)	<0.001
No change	41 (45%)	67 (44%)	
Worsening	11 (12%)	55 (36%)	
PsAID (each symptom specifically attributed to PsA)	n-=91	N=153	
Pain	2.4 (2.4)	4.9 (2.3)	<0.001
Fatigue	2.6 (2.6)	5.1 (2.6)	<0.001
Skin	1.7 (2.1)	2.5 (2.6)	0.03
Work	1.4 (2.1)	4.1 (2.8)	<0.001
Function	1.4 (1.9)	3.9 (2.7)	<0.001
Discomfort	2.3 (2.5)	4.9 (2.5)	<0.001
Sleep	2.1 (2.7)	4.3 (3)	<0.001
Coping	1.1 (2)	3.3 (2.8)	<0.001
Anxiety	1.2 (2.1)	2.9 (2.9)	<0.001
Embarrassment	0.7 (1.4)	2.1 (2.9)	<0.001
Social	0.8 (1.6)	2.7 (3)	<0.001
Depression	0.7 (1.7)	2.8 (2.9)	<0.001
BASDAI (symptoms *not* specifically attributed to PsA)	n=53*	n=90*	
Fatigue	2.9 (2.3)	5.4 (2.2)	<0.001
Spine pain	2.6 (2.3)	4.9 (2.6)	<0.001
Peripheral joints pain/swelling	2.3 (2)	4.6 (2)	<0.001
Tender to touch	1.7 (1.9)	4.8 (2.5)	<0.001
Stiffness severity	2.3 (2.2)	4.7 (2.3)	<0.001
Stiffness duration	1.8 (2.3)	3.7 (3)	<0.001

*BASDAI was added later than PsAID and thus not all patients in this cohort had an available BASDAI score
Abbreviations: BASDAI-Bath Ankylosing Spondylitis Disease Activity Index; PhA- Physician Assessed; PsAID-Psoriatic Arthritis Impact of Disease; VLDA- very low disease activity

were ascribed to PsA (PsAID items include the phrase “due to my PsA”). Furthermore, more than 10% of pts in physician-assessed VLDA still reported difficulty with function, work, and skin symptoms. Mean BMI was not significantly different between those in and not in physician-assessed VLDA.

Conclusion: Among PsA patients in VLDA according to physician measures, approximately half continue to have residual symptoms. Further studies are needed to develop comprehensive, evidence-based, patient-focused treatment plans to address these residual symptoms.

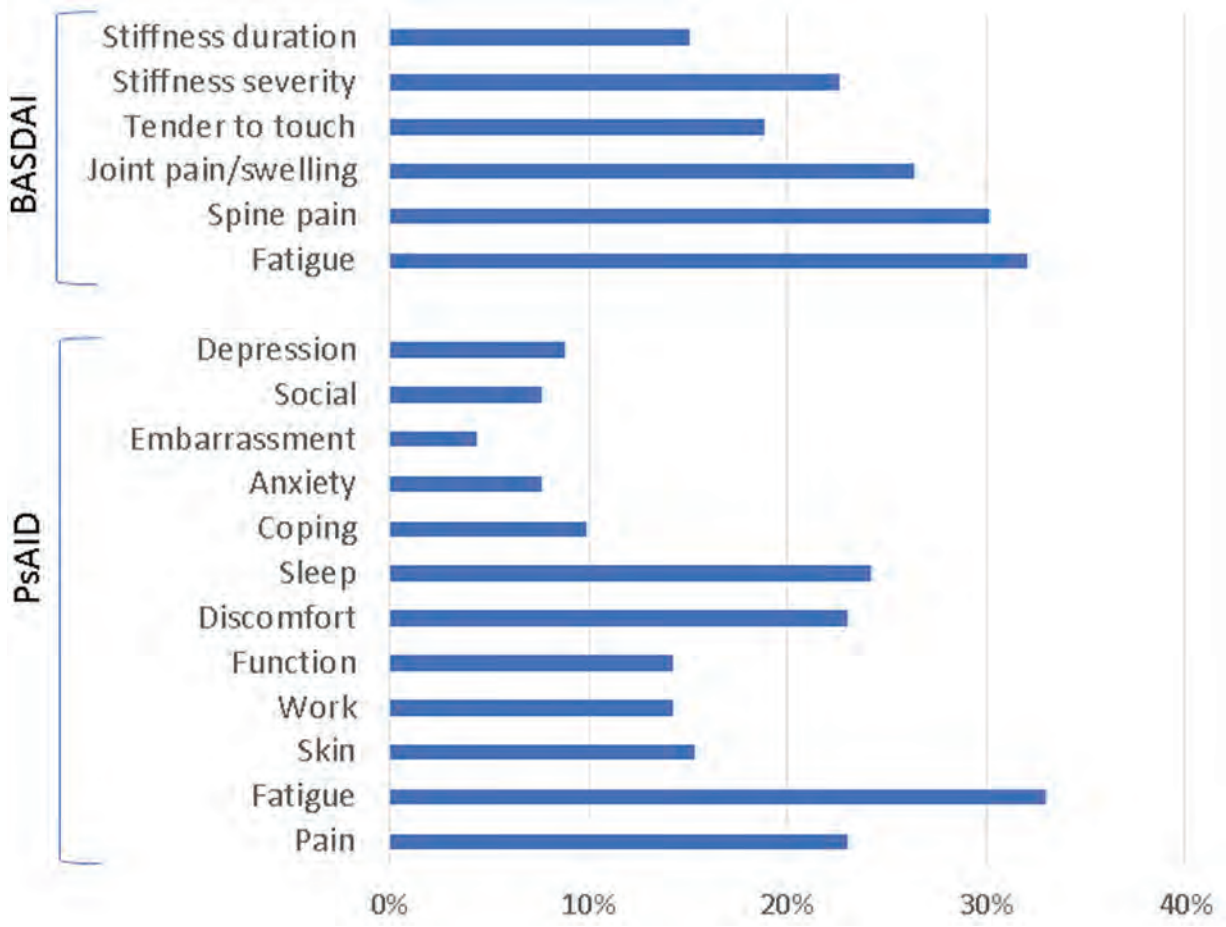

Figure 1. Residual symptoms among patients in physician-assessed very low disease activity

Disclosure: A. Ogdie, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1; **S. Reddy**, Amgen, 5, Novartis, 5, Janssen, 5, Pfizer, 5; **E. Craig**, None; **J. Scher**, UCB, 5, Janssen, 5, Abbvie, 5, Pfizer, 5, Novartis, 5, Sanofi, 5; **Y. Lee**, Highland Instruments, Inc., 1, 2, Pfizer, 1, 2, Cigna-Express Scripts, 1; **J. Walsh**, Pfizer, 2, AbbVie, 2, 5, Eli Lilly, 5, UCB, 5, Janssen, 5, Novartis, 5, Amgen, 5; **M. Husni**, Abbvie, 5, BMS, 5, Janssen, 5, Pfizer, 5, Regeneron, 5, Novartis, 5, Lilly, 5, Pfizer, 2, PASE questionnaire, 7, National Psoriasis Foundation, 6.

Abstract Number: 0324

Comparative Responsiveness of Outcome Measures in Psoriatic Arthritis: Preparation for Pragmatic Trials

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Baseline and change scores

Table 1. Outcome Measures at baseline and change at follow up					
			Baseline		Change at 16 weeks
Measure	Type	N	Mean (SD)	N	Mean (SD)
RAPID3	PRO	229	10.93 (5.88)	225	-1.11 (5.26)
HAQDI	PRO	141	0.68 (0.56)	85	-0.07 (0.42)
BASDAI	PRO	152	4.70 (2.24)	95	-0.92 (1.91)
PROMIS PH	PRO	187	42.01 (8.20)	183	1.43 (6.20)
PROMIS MH	PRO	187	46.28 (10.76)	184	0.54 (6.43)
PROMIS Depression	PRO	140	60.78 (9.59)	85	-2.68 (7.27)
PROMIS Fatigue	PRO	140	56.45 (9.93)	85	-2.86 (7.67)
PSAID	PRO	231	2.00 (1.34)	225	-0.30 (1.05)
Patient Global	PRO	234	4.11 (2.48)	234	-0.24 (2.66)
Patient Pain	PRO	234	4.81 (2.69)	234	-0.75 (2.66)
MDHAQ	PRO	229	2.05 (1.56)	225	-0.17 (1.24)
MD Global	MD	257	4.54 (2.06)	249	-0.30 (1.54)
MD Global Joint	MD	258	3.33 (2.15)	250	-0.55 (1.80)
SJC	MD	264	2.90 (4.85)	256	-0.81 (4.71)
TJC	MD	264	5.82 (7.38)	256	-0.63 (8.35)
cDAPSA	Both	234	17.29 (12.87)	225	-2.26 (12.36)

Abbreviations: RAPID3= Routine Assessment of Patient Index Data; HAQDI=Health Assessment Questionnaire Disability Index; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; PROMIS PH= PROMIS Physical Health; PROMIS MH= PROMIS Mental Health; PSAID=PsA Impact of Disease; MDHAQ=Multidimensional Health Assessment Questionnaire; MD global= physician's global assessment; SJC=swollen joint count; TJC=tender joint count; cDAPSA=clinical Disease Activity of PsA

Background/Purpose: Psoriatic arthritis (PsA) is a heterogeneous condition; this presents a challenge in how to best measure disease activity for all patients. While several outcome measures have been studied for use in traditional randomized clinical trials (RCT) of PsA, this has been done in the context of pre-defined inclusion criteria derived from a relatively homogenous population with a polyarticular phenotype and higher disease activity than is typically encountered in "real world" practice. There remains a need to determine the ideal outcomes for PsA pragmatic trials that enroll patients representative of those seen in routine care in the clinics. We aimed to investigate the responsiveness of outcome measures among patients with PsA initiating therapy in clinical practice.

Methods: Patients were enrolled in the Psoriatic Arthritis Research Consortium (PARC), a multi-center longitudinal observational cohort study, between 2017-2020. We collected data at initiation of a new treatment for PsA, including a switch in treatment, and follow-up at approximately 16 weeks. At both visits, patients completed patient-reported outcome assessments (PROs) and rheumatologists completed a comprehensive musculoskeletal exam. Change in scores were calculated for the following measures between both timepoints: Routine Assessment of Patient Index Data (RAPID3), clinical Disease Activity of Psoriatic Arthritis (cDAPSA), Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), PsA Impact of Disease (PSAID), Multi-Dimensional Health Assessment Questionnaire (MDHAQ), Health Assessment Questionnaire (HAQDI), Patient Reported Outcome Measure Information System (PROMIS) physical health (PH) subscore, PROMIS mental health (MH) subscore, PROMIS fatigue, PROMIS depression, patient pain assessment, patient global assessment, physician global assessments of joints and overall, and tender (68) and swollen (66) joint counts. Standardized response means (SRMs) were calculated as the mean change between two visits divided by the standard deviation. Responsiveness cutoffs are debatable, but SRMs may roughly be considered large at >0.8, moderate 0.5-0.8, and small < 0.5.

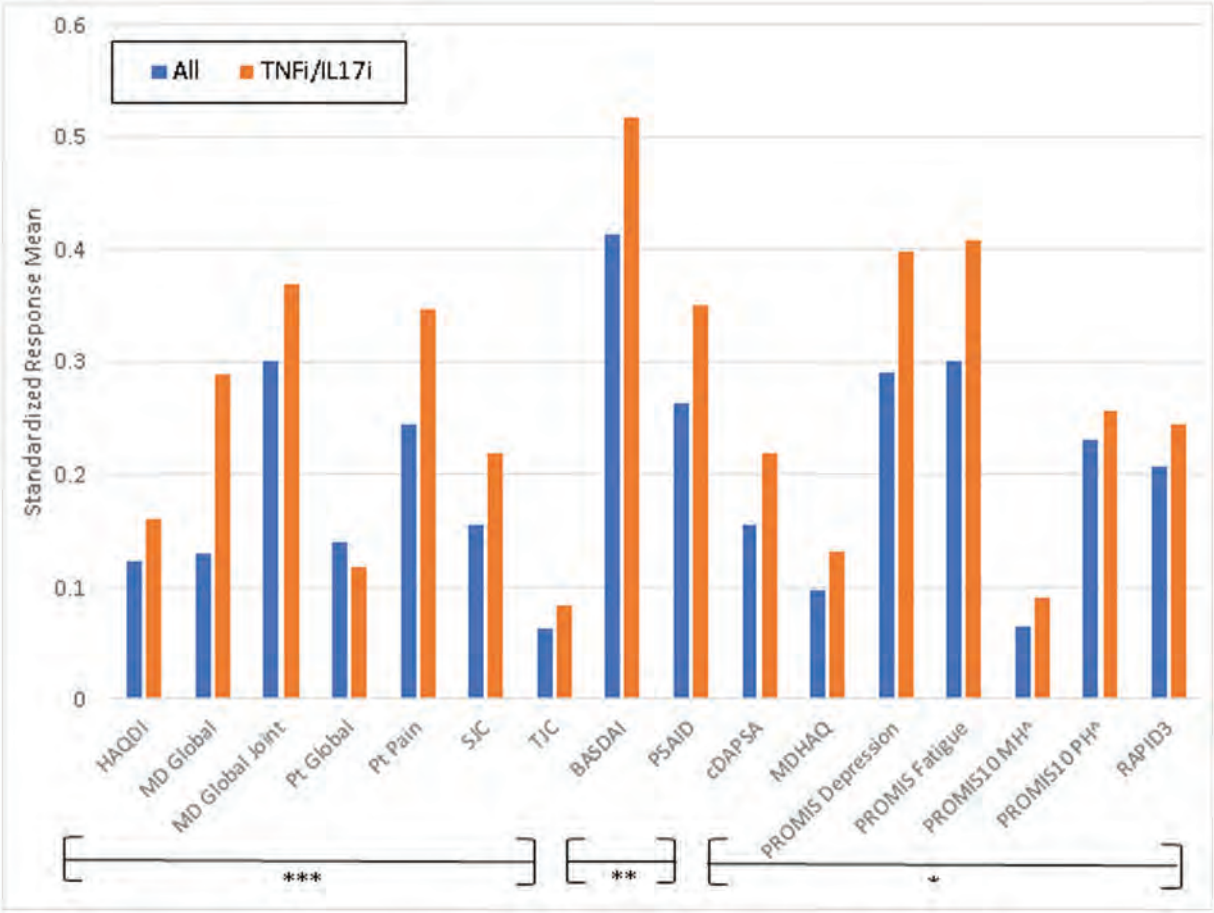

Figure 1. Standardized Response Means of Instruments Tested. ***=Outcome measures frequently used in randomized controlled trials (RCTs) for PsA **= Outcome measures sometimes used in RCTs for PsA *= Outcome measures rarely used in RCTs for PsA Abbreviations: HAQDI=Health Assessment Questionnaire Disability Index; MD global= physician's global assessment; SJC=swollen joint count; TJC=tender joint count; BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; PSAID=PsA Impact of Disease; ; cDAPSA=clinical Disease Activity of PsA; MDHAQ=Multidimensional Health Assessment Questionnaire; PROMIS MH= PROMIS Mental Health; PROMIS PH= PROMIS Physical Health; RAPID3= Routine Assessment of Patient Index Data

Results: Among 177 unique patients, 266 therapy courses met inclusion criteria. The mean age was 51 years, 53% were female, mean BMI was 29.9, and 16% had axial disease. Among the 266 visits, 145 initiated a TNFi, 55 an IL17i, 96 an OSM, and 14 started another biologic or JAKi. Mean swollen and tender joint counts (66/68) at therapy initiation were 2.9 and 5.8. Responsiveness for all measures was small to moderate (Figure 1.) BASDAI was the most responsive, and tender joint count the least responsive; SRMs were similar among those initiating a biologic therapy vs. any therapy.

Conclusion: Patients with PsA switching or starting therapy in this patient population had different clinical characteristics compared to those usually enrolling in a RCT. Similarly, responsiveness of outcome measures in clinical practice looks different than traditional PsA clinical trials, with SRMs that are generally lower. This data will be useful for selecting outcome measures and calculating sample size for pragmatic trials in PsA.

Disclosure: C. Stull, None; **S. Reddy**, Amgen, 5, Novartis, 5, Janssen, 5, Pfizer, 5; **M. Husni**, Abbvie, 5, BMS, 5, Janssen, 5, Pfizer, 5, Regeneron, 5, Novartis, 5, Lilly, 5, Pfizer, 2, PASE questionnaire, 7, National Psoriasis Foundation, 6; **J. Scher**, UCB, 5, Janssen, 5, Abbvie, 5, Pfizer, 5, Novartis, 5, Sanofi, 5; **E. Craig**, None; **J. Walsh**, Pfizer, 2, AbbVie, 2, 5, Eli Lilly, 5, UCB, 5, Janssen, 5, Novartis, 5, Amgen, 5; **A. Ogdie**, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1.

Abstract Number: 0325

The Impact of PsA Disease Control Status on Patient Treatment Satisfaction: Real-world Survey in US and Europe

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patient satisfaction associated with disease control status among PsA patients has not been extensively studied in a real-world setting. The objective of this study was to assess the impact of PsA disease control status on patient-perceived satisfaction with treatment.

Methods: A cross-sectional survey of PsA patients recruited by rheumatologists and dermatologists was conducted in France, Germany, Italy, Spain, the UK and US. Data were collected from Jun–Aug 2018 via physician- and patient-completed forms. Physicians reported if patients were currently improving, stable, unstable or deteriorating. Unstable and deteriorating patients were grouped together for this analysis. Patients reported their satisfaction with their current treatment. Patients were compared according to disease status (improving vs. unstable/deteriorating vs. stable) using parametric and non-parametric tests. Multiple ordered logistic regression analyses examined the impact

Table 1. Comparison of patient demographic and disease characteristics by physician-reported PsA disease status. *Calculated on available data: Swollen Joint Count=354, Tender Joint Count=335. Abbreviations: BMI, Body Mass Index; BSA, Body Surface Area; SD, standard deviation; tx, treatment.

	Stable (n=1,530)	Improving (n=1,018)	Unstable/Deteriorating (n=319)	p-value
Age, years, mean (SD)	49.1 (12.8)	47.1 (12.8)	48.4 (13.6)	**<0.01**
Female, n (%)	666 (43.5)	488 (47.9)	161 (50.5)	**0.02**
BMI, kg/m^2, mean (SD)	26.9 (5.1)	26.6 (6.3)	27.5 (5.3)	0.08
Caucasian, n (%)	1395 (91.2)	927 (91.1)	286 (89.7)	0.52
Full-time employment, n (%)	370 (58.5)	280 (65.1)	56 (46.3)	**<0.01**
Biologic tx, n (%)	998 (65.2)	658 (64.6)	172 (53.9)	**<0.01**
No. of lines of biologic tx, mean (SD)	0.49 (0.89)	0.48 (0.93)	0.91 (1.42)	**<0.01**
Months since diagnosis, mean (SD)	68.8 (72.6)	46.5 (57.4)	57.9 (89.3)	**0.01**
Current BSA %, mean (SD)	4.3 (7.8)	6.5 (9.2)	10.3 (11.8)	**<0.01**
*66 Swollen Joint Count, mean (SD)	3.1 (7.8)	2.7 (6.2)	6.3 (6.3)	**<0.01**
*68 Tender Joint Count, mean (SD)	3.2 (5.3)	3.5 (6.4)	8.7 (7.3)	**<0.01**
No. of joints affected, mean (SD)	2.4 (3.7)	3.3 (4.9)	6.9 (6.4)	**<0.01**
Charlson Comorbidity Index score, mean (SD)	1.1 (0.5)	1.1 (0.5)	1.2 (0.7)	0.06

Table 2. Multivariate logistic regression model for patient satisfaction with treatment as a function of PsA disease status. Abbreviations: BMI, Body Mass Index; BSA, Body Surface Area affected by psoriasis.

Covariate	Odds ratio of patient dissatisfaction	p-value
Disease status - Stable (reference) - Improving - Unstable/deteriorating	 1.00 0.95 3.67	 0.77 **<0.01**
Variables adjusted for		
Age	1.01	0.13
Sex - Female (reference) - Male	 1.00 0.74	 **0.02**
BMI	1.01	**<0.05**
BSA	0.99	0.57
No. of joints affected	1.02	0.21
Charlson Comorbidity Index score	1.36	0.07
No. of treatment lines	0.96	0.64
No. of symptoms	1.16	**<0.01**

of disease status on patient-reported satisfaction with treatment. The model controlled for gender, age, Body Mass Index (BMI), current advanced treatment line, pain, body surface area affected by psoriasis (BSA), number of joints affected, total number of symptoms experienced and Charlson Comorbidity Index score.

Results: Of 2867 patients (638 US, 2229 EU), 53% of patients were stable, 36% of patients were improving and 11% of patients were unstable/deteriorating.

Patients who were improving or stable more commonly received a biologic treatment than those who were unstable/deteriorating. Those who were unstable/deteriorating had a worse clinical profile than those who were improving (Table 1). After controlling for demographic and disease characteristics and treatment status regression analysis showed that patients who were unstable/deteriorating were at a significantly increased risk of being dissatisfied with treatment. There was no observed difference between patients who were stable and improving (Table 2).

Conclusion: After controlling for demographic and disease characteristics, and treatment status, PsA patients who were unstable/deteriorating had greater odds of being dissatisfied with treatment than stable/improving patients. Patient satisfaction was associated with therapy that provides highest degree of disease control stability. Given the importance of disease control stability for patient satisfaction, physicians should prioritise therapy that will ensure patients' disease control stability in the long term.

Disclosure: A. Orbai, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 5, UCB, 5, AbbVie, 2, Celgene, 2, Horizon, 2; **E. Holdsworth**, None; **T. Baker**, Janssen, 1, 3; **C. Middleton-Dalby**, None; **M. Shawi**, Janssen Global Services, LLC, 3; **N. Booth**, None; **J. Piercy**, Adelphi Real World, 3; **S. Peterson**, Janssen Research & Development, LLC, 3.

Abstract Number: 0326

Flares Among Patients with Psoriatic Arthritis (PsA) - Frequency and Impact on Patient Outcomes: Real-world Survey in the US and Europe

Ana-Maria Orbai[1], William Tillett[2], Suzann Grieb[3], James Piercy[4], Steven Peterson[5], Elizabeth Holdsworth[4], Sophie Meakin[4], Soumya Chakravarty[6], Nicola Booth[4] and Laure Gossec[7], [1]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, [2]Royal National Hospital for Rheumatic Diseases, Bath, UK; Department of Pharmacy and Pharmacology, University of Bath, Bath, UK, Bath, United Kingdom, [3]John Hopkins University School of Medicine, Baltimore, [4]Adelphi Real World, Bollington, United Kingdom, [5]Janssen Immunology Global Commercial Strategy Organization, Horsham, PA, [6]Janssen Scientific Affairs, LLC, Horsham, PA, USA and Drexel University College of Medicine, Horsham, PA, [7]Sorbonne University, INSERM; Pitié-Salpêtrière Hospital, Paris, Ile-de-France, France

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Flares in PsA, presenting as periods of acute disease activity, are thought to negatively impact patients' lives. This has not been extensively studied in a real-world setting. The objective of this study was to describe frequency of flares, assess flare impact on quality of life and work productivity, and explore predictors of flares.

Methods: A cross-sectional survey among patients with PsA recruited by rheumatologists and dermatologists was conducted in France, Germany, Italy, Spain, UK and US. Data were collected Jun-Aug 2018 via patient record forms and patient self-complete forms. Flares, by definition, could involve joints or skin or both simultaneously. Physicians recorded flare status (in flare currently/flared in last 12 months/longer than 12 months or never), demographics, physician perceived severity, and clinical outcomes. Patients reported quality of life [QoL] (EQ5D-5L), work productivity (WPAI), disability (HAQ-DI), pain (PsAID12 pain scale). Patients were compared by flare status using parametric or non-parametric tests. Logistic regression was used to explore predictors of flare. Multivariate regression was used to assess the impact of flare status on patient reported outcomes (PRO). The multivariate model was adjusted for gender, age, BMI, physician speciality.

Results: Data was collected for 2,238 patients (586 US, 1,652 EU). Mean age was 48.7 years (13.2 SD), 53.8% were male. Physicians reported 7.5% of patients were currently in flare and 22.0% had flared in the last 12 months. Patients had experienced 2.2 mean flares in the last 12 months (4.9 SD), lasting a mean 16.4 days (16.2 SD). Patients in

Table 1. Clinical characteristics of patients by flare status

	Currently in flare (n=168)	Flared in last 12 months (n=492)	Not flared in last 12 months/never flared (n=1578)	p-value
In remission, n (%)	4 (2.4)	157 (33.2)	799 (53.5)	<0.01
*Current BSA affected, mean (SD)	10.3 (12.0)	6.5 (7.6)	5.0 (7.7)	<0.01
*66 SJC, mean (SD)	5.4 (4.6)	4.5 (7.3)	2.4 (6.9)	<0.01
*68 TJC, mean (SD)	7.8 (5.8)	5.5 (8.3)	3.1 (5.6)	<0.01
Physician-perceived severity, n (%)				
-Mild	35 (20.8)	346 (70.3)	1297 (82.2)	<0.01
-Moderate	101 (60.1)	139 (28.3)	261 (16.5)	
-Severe	32 (19.0)	7 (1.4)	20 (1.3)	

*Calculated on available data: Total base sizes: BSA=1665; SJC=514; TJC=493; Satisfaction=931

flare were comparable demographically with those not; however, those in flare were less likely to work full time (43.6 vs. 59.3%, p< 0.01). Patients not in flare had clinically active disease (Table 1).

Results showed that flare status significantly impacted QoL, work productivity, disability, and pain (Table 2). Exploring predictors of flare in the last 12 months showed that demographic characteristics were not predictive of flare status, however patients presenting with any skin involvement or enthesitis at diagnosis were at greater risk of flare. Patients who were prescribed a bDMARD at diagnosis were at lower risk (Figure 1).

Conclusion: One third of patients surveyed were either currently in flare or had flared in the last 12 months. Being in flare adversely impacted QoL, disability and work productivity. Flare may be predicted by any degree of skin involvement or enthesitis at diagnosis.

Table 2. Impact of flare status on PROs

	Current flare status	Change in predicted PRO values	P value
EQ5D utility (n=933)	Not in flare (ref) In flare	0.83 -0.23	<0.01
EQ5D VAS (n=946)	Not in flare In flare	76.1 -21.3	<0.01
WPAI % overall work impairment (n=496)	Not in flare In flare	20.1 +28.5	<0.01
HAQ-DI (n=901)	Not in flare In flare	0.4 +0.6	<0.01
PsAID12 pain score (n=922)	Not in flare In flare	2.5 +3.0	<0.01

PRO key for worse outcome (range): EQ5D utility (0-1.0) = lower; EQ5D VAS (1-100) = lower; WPAI (0-100) = higher; HAQ-DI (0-3) = higher; PsAID12 pain (0-10) = higher

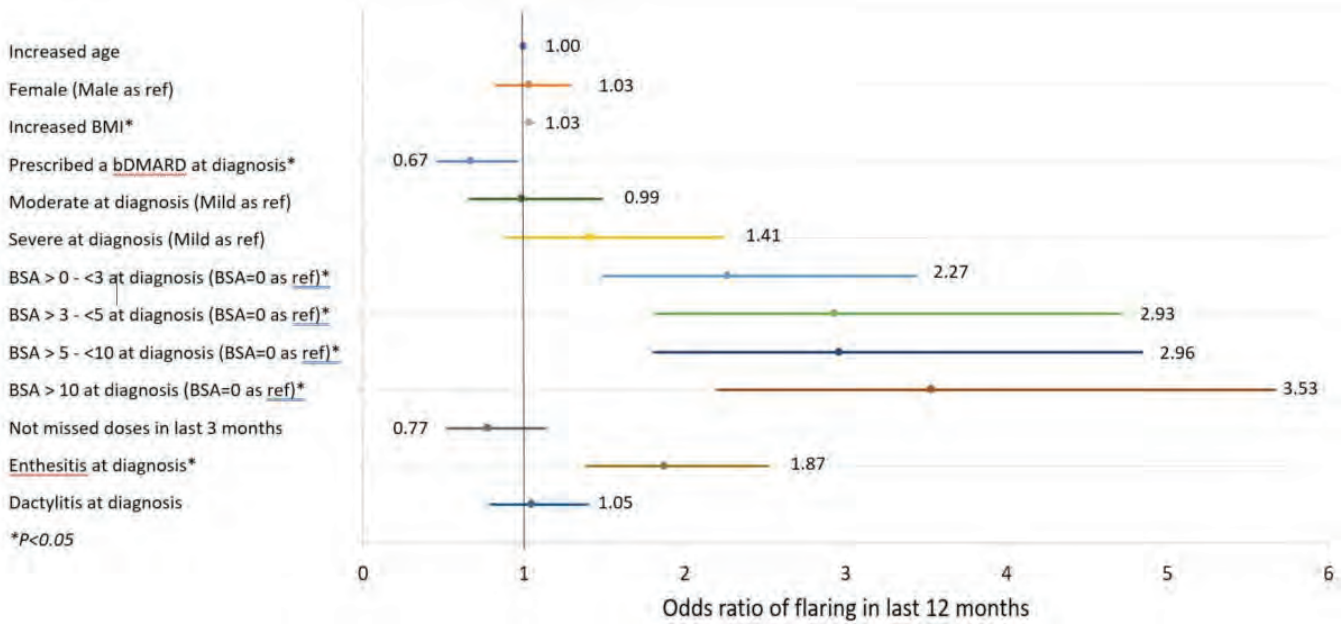


Figure 1. Predictors of flaring in last 12 months

Disclosure: A. Orbai, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 5, UCB, 5, AbbVie, 2, Celgene, 2, Horizon, 2; **W. Tillett**, AbbVie, 5, 8, Amgen, 5, 8, Eli Lilly, 5, 8, Janssen, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB Pharma, 5, 8; **S. Grieb**, None; **J. Piercy**, Adelphi Real World, 3; **S. Peterson**, Janssen Research & Development, LLC, 3; **E. Holdsworth**, None; **S. Meakin**, None; **S. Chakravarty**, Janssen Scientific Affairs, LLC, 1, 3; **N. Booth**, None; **L. Gossec**, None.

Abstract Number: 0327

Skin Involvement in Psoriatic Arthritis (PsA) - The Incremental Impact of Psoriasis on Quality of Life, Disability and Work Productivity: Real-world Survey in US and Europe

Jessica Walsh[1], Alexis Ogdie[2], Kaleb Michaud[3], Steven Peterson[4], Elizabeth Holdsworth[5], Sophie Meakin[5], Soumya Chakravarty[6], Nicola Booth[5], Agata Schubert[7], James Piercy[5] and Laure Gossec[8], [1]University of Utah School of Medicine, George E. Wahlen Veteran Affairs Medical Center, Salt Lake City, UT, [2]Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, [3]University of Nebraska Medical Center, Omaha, NE, [4]Janssen Immunology Global Commercial Strategy Organization, Horsham, PA, [5]Adelphi Real World, Bollington, United Kingdom, [6]Janssen Scientific Affairs, LLC, Horsham, PA, USA and Drexel University College of Medicine, Horsham, PA, [7]Janssen-Cilag, Janssen-Cilag, Poland, [8]Sorbonne Université and Hôpital Universitaire Pitié Salpêtrière, Paris, France

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The degree of joint and skin involvement varies across patients with PsA. Differences in patient outcomes with active joint only vs. joint plus skin involvement have not been extensively studied in a real-world setting. The objective of this study was to assess prevalence of joint-only and joint-plus-skin disease in a real-world clinical setting, and to assess the incremental impact of skin symptoms on quality of life (QoL), disability and work productivity.

Methods: A cross-sectional survey in patients with PsA recruited by rheumatologists and dermatologists was conducted in France, Germany, Italy, Spain, UK and US. Data were collected Jun-Aug 2018 via physician-completed forms and patient-completed forms. Patients were compared by joint and skin involvement (joint only, joints plus

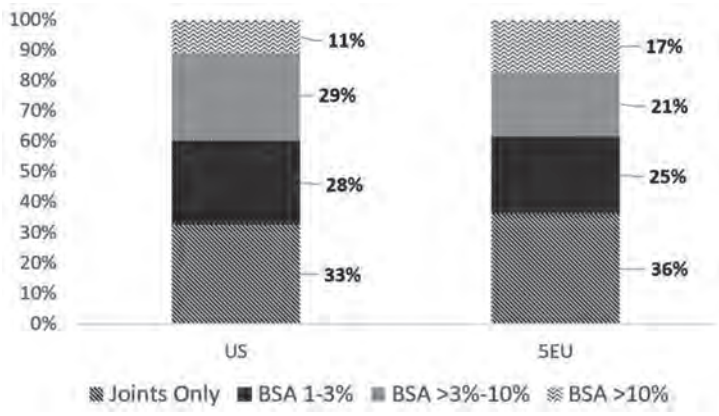


Figure 1. Prevalence of joint and skin involvement across regions.

Table 1. Comparison of patient demographic and disease characteristics by joint and skin disease involvement. *Calculated on available data, n=394.

	PsAID12 fatigue score				
	0 (n=180)	1-3 (n=445)	4-7 (n=142)	>7 (n=64)	P value
Demographic characteristics					
Age, mean (SD)	45.3 (13.0)	46.5 (13.7)	51.2 (12.6)	52.5 (12.2)	**<0.01**
Female, n (%)	62 (34.4)	213 (47.9)	78 (54.9)	37 (57.8)	**<0.01**
BMI, mean (SD)	26.8 (5.4)	26.4 (4.8)	27.1 (4.7)	26.9 (4.7)	0.53
Caucasian, n (%)	167 (92.8)	412 (92.6)	130 (91.6)	59 (92.2)	0.23
Working full time, n (%)	125 (71.0)	280 (64.2)	61 (43.6)	23 (38.3)	**<0.01**
Biologic tx, n (%)	91 (50.6)	196 (44.0)	76 (53.5)	37 (57.8)	0.06
Disease characteristics					
Years since diagnosis, mean (SD)	4.8 (2.3)	4.5 (2.2)	6.9 (4.1)	8.0 (5.6)	**<0.01**
Current severity (provider-assessed), n (%) -Mild -Moderate -Severe	 171 (95.0) 9 (5.0) 0 (0.0)	 350 (78.7) 89 (20.0) 6 (1.4)	 76 (53.5) 59 (41.5) 7 (4.9)	 26 (40.6) 32 (50.0) 6 (9.4)	**<0.01**
Current BSA %, mean (SD)	2.2 (3.7)	6.2 (7.7)	9.2 (10.2)	7.6 (10.8)	**<0.01**
*66 swollen joint count, mean (SD)	0.6 (1.8)	2.3 (3.9)	7.1 (11.3)	4.2 (4.8)	**<0.01**
*68 tender joint count, mean (SD)	1.1 (3.2)	2.8 (3.5)	7.6 (7.8)	6.2 (4.3)	**<0.01**

Table 2. Incremental impact of BSA on PROs. α PRO key for worse outcome (range): EQ5D utility (0-1.0) = lower; EQ5D VAS (1-100) = lower; WPAI (0-100) = higher; HAQ-DI (0-3) = higher; PsAID12 (0-10) = higher.

	BSA in addition to joint involvement	Change in predicted PRO values	P value
EQ5D utility (n=656)	Joint only (ref)	0.85	
	1-3%	-0.02	0.31
	>3-10%	-0.06	<0.01
	>10%	-0.06	<0.01
EQ5D VAS (n=668)	Joint only	78.14	
	1-3%	-0.58	0.74
	>3-10%	-3.78	0.03
	>10%	-3.04	0.14
WPAI % overall work impairment (n=369)	Joint only	15.88	
	1-3%	+0.32	0.91
	>3-10%	+5.11	<0.05
	>10%	+7.51	0.01
HAQ-DI (n=635)	Joint only	0.32	
	1-3%	+0.04	0.41
	>3-10%	+0.22	<0.01
	>10%	+0.27	<0.01
PsAID12 (n=642)	Joint only	1.66	
	1-3%	+0.42	0.03
	>3-10%	+1.22	<0.01
	>10%	+1.37	<0.01

1-3%, >3-10%, and >10% body surface area [BSA]) using parametric and non-parametric tests. Multiple linear regression analyses examined impact of incremental BSA on patient reported outcomes (PROs) (EQ5D, HAQ-DI, PsAID12, WPAI). Models controlled for gender, age, time since diagnosis, employment status, biologic DMARD use, BMI, number of joints affected.

Results: Of 1,909 patients (539 US, 1,370 EU), 35% of patients had joint-only disease, while 26%, 23%, and 16% experienced joint disease plus 1-3%, >3-10%, and >10% BSA respectively (Figure 1). Patients were comparable

demographically (Table 1). After controlling for demographics and number of joints involved, results showed BSA independently and significantly impacted QoL, work productivity, disability (Table 2).

Conclusion: Two thirds of this sample of actively treated PsA patients had skin involvement. Over half had moderate-severe psoriasis (BSA >3%). Joint counts increased with BSA. After controlling for joint counts, increasing skin involvement adversely impacted QoL, disability and work productivity.

Disclosure: J. Walsh, Pfizer, 2, AbbVie, 2, 5, Eli Lilly, 5, UCB, 5, Janssen, 5, Novartis, 5, Amgen, 5; **A. Ogdie**, AbbVie, 5, Amgen, 2, 5, BMS, 1, Celgene, 1, Corrona, 1, Janssen, 1, Eli Lilly, 1, Novartis, 2, 5, Pfizer, 2, 5, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 2, Rheumatology Research Foundation, 2, National Psoriasis Foundation, 2; **K. Michaud**, Rheumatology Research Foundation, 2; **S. Peterson**, Janssen Research & Development, LLC, 3; **E. Holdsworth**, None; **S. Meakin**, None; **S. Chakravarty**, Janssen Scientific Affairs, LLC, 1, 3; **N. Booth**, None; **A. Schubert**, Janssen-Cilag, 3; **J. Piercy**, Adelphi Real World, 3; **L. Gossec**, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8.

Abstract Number: 0328

Healthcare Utilization and Costs Among Patients with Psoriatic Arthritis and Psoriasis in the United States – a Retrospective Study of Claims Data from 2009 to 2020

Joseph Merola[1], Reginald Villacorta[2], Natalie Dennis[3], Soumya Chakravarty[4], Laura Mesana[5], Iris Lin[2], Maud Pacou[3], Thomas Baker[6], Yiting Wang[7] and Steven Peterson[8], [1]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [2]Janssen Immunology Global Commercial Strategy Organization, Horsham, [3]Amaris, Paris, France, [4]Janssen Scientific Affairs, LLC, Horsham, PA, USA and Drexel University College of Medicine, Horsham, PA, [5]Amaris, New York, [6]Janssen Global Services, LLC, Raritan, NJ, [7]Janssen R&D, LLC, Titusville, [8]Janssen Immunology Global Commercial Strategy Organization, Horsham, PA

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The costs of psoriasis and psoriatic arthritis (PsA) are substantial for both patients and the United States healthcare system. This study compared healthcare resource utilization and costs across three groups: patients with psoriasis, patients with PsA, and matched controls with neither psoriasis nor PsA in the United States.

Methods: The IBM MarketScan Commercial Database was used to identify three adult patient groups from 1/1/2009 through 2/29/2020: 1) Psoriasis patients: ≥ 1 inpatient or 2 outpatient psoriasis diagnoses and no PsA diagnoses; 2) PsA patients: ≥ 1 inpatient or 2 outpatient PsA diagnoses; 3) Control: absence of psoriasis and PsA diagnoses. Controls were matched 1:1 to psoriasis and PsA patients based on age, gender, and comorbidities. Healthcare resource utilization and costs (in 2019 USD) were evaluated descriptively and through mixed models for five years of follow-up.

Results: 208,434 psoriasis patients and 47,274 PsA patients were matched to the control group (N=255,708). Annual all-cause healthcare costs per patient were $7,542, $11,856, and $29,621 for the control, psoriasis, and PsA group, respectively. All-cause healthcare costs were significantly greater among patients with PsA and patients with psoriasis than controls at one year ($p< 0.0001$). These costs were also significantly greater for PsA patients than psoriasis

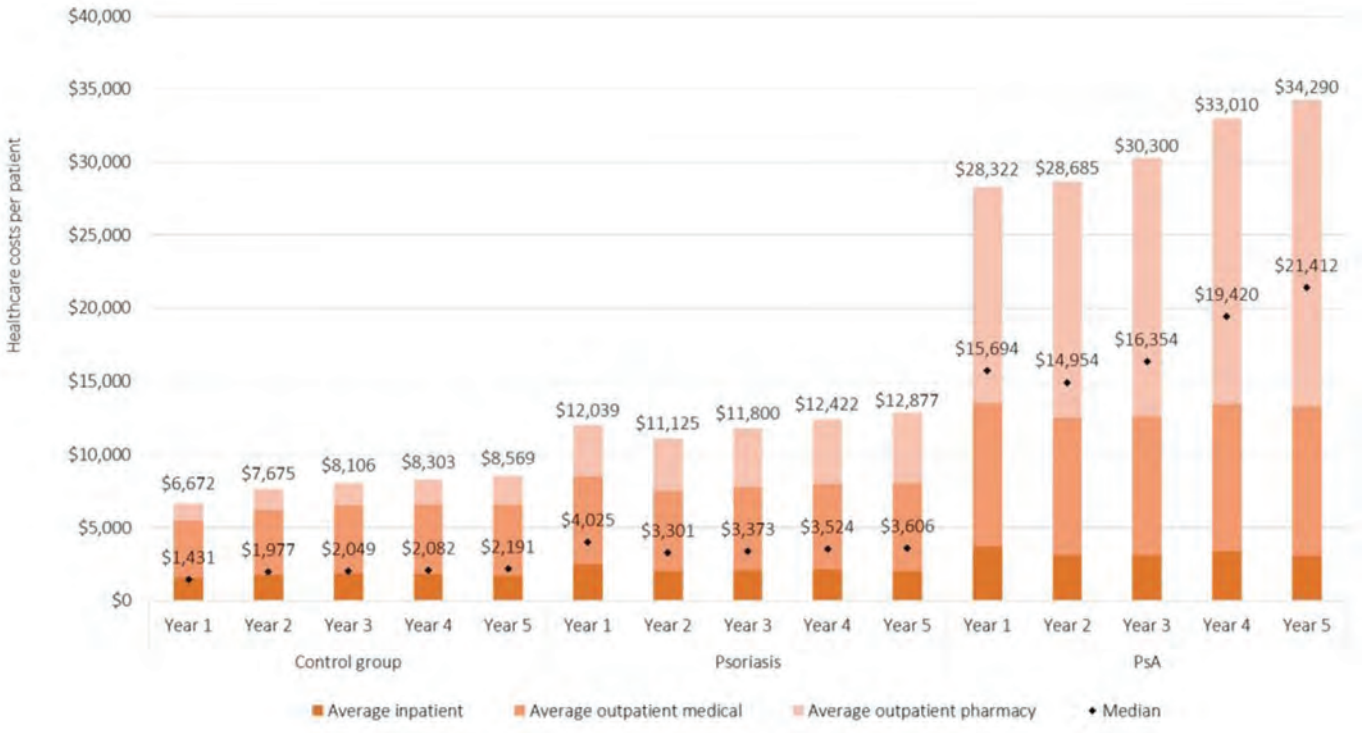


Figure 1. Mean and median all-cause healthcare costs per patient per follow-up year

patients at one year ($p < 0.0001$). This trend of increased costs for patients with PsA compared with the other groups was sustained throughout the five years of follow-up (Figure 1). Across all categories of healthcare resources, utilization was greatest among patients with PsA and lowest in the control group (Table 1). Categories included inpatient hospitalizations, physician office visits, and hospital outpatient, radiology, emergency room, laboratory, and outpatient pharmacy services.

Conclusion: Annual healthcare costs and resource utilization were significantly higher for PsA patients compared with psoriasis patients and the control group. The cost and resource utilization differences between these patient groups highlight the higher burden of illness for PsA patients as compared to patients with psoriasis, or patients without either of these diseases.

Table 1. Healthcare resource utilization during follow-up

	Control group	Psoriasis	PsA
Number of patients	**255,708**	**208,434**	**47,274**
Inpatient hospitalizations			
Patients with an admission in 1st year - N (%)	12709 (5.0%)	13978 (6.7%)	4487 (9.5%)
Number of admissions (PPPY) - Mean (SD)	0.07 (0.34)	0.08 (0.37)	0.11 (0.44)
Hospital outpatient services			
Patients with services in 1st year - N (%)	111836 (43.7%)	115962 (55.6%)	32661 (69.1%)
Number of services (PPPY) - Mean (SD)	8.29 (24.17)	9.69 (24.35)	15.50 (29.71)
Physician office visits			
Patients with visits in 1st year - N (%)	188685 (73.8%)	205532 (98.6%)	46934 (99.3%)
Number of visits (PPPY) - Mean (SD)	4.52 (5.16)	6.23 (5.92)	9.25 (7.43)
Radiology services			
Patients with services in 1st year - N (%)	113500 (44.4%)	117042 (56.2%)	36011 (76.2%)
Number of services (PPPY) - Mean (SD)	2.49 (5.57)	2.76 (5.56)	4.55 (6.41)
Emergency room visits			
Patients with visits in 1st year - N (%)	30942 (12.1%)	31745 (15.2%)	9209 (19.5%)
Number of visits (PPPY) - Mean (SD)	0.72 (3.96)	0.89 (4.63)	1.38 (7.41)
Laboratory services			
Patients with services in 1st year - N (%)	162768 (63.7%)	180941 (86.8%)	45202 (95.6%)
Number of services (PPPY) - Mean (SD)	9.01 (17.10)	11.32 (17.15)	20.67 (22.94)
Outpatient pharmacy services			
Patients with a prescription in 1st year - N (%)	155984 (61.0%)	176452 (84.7%)	40832 (86.4%)
Number of prescriptions (PPPY) - Mean (SD)	12.65 (19.27)	17.01 (20.96)	28.66 (29.08)

PPPY: per patient per year

Disclosure: J. Merola, AbbVie, 1, Arena, 1, Avotres, 1, Biogen, 1, Celgene, 1, Dermavant, 1, Eli Lilly, 1, EMD Serono, 1, Janssen, 1, LEO Pharma, 5, Merck, 1, Novartis, 1, Pfizer Inc, 5, Sanofi, 1, Regeneron, 1, Sun Pharma, 1, UCB Pharma, 5; **R. Villacorta**, Janssen Pharmaceuticals, 1, 3; **N. Dennis**, None; **S. Chakravarty**, Janssen Scientific Affairs, LLC, 1, 3; **L. Mesana**, Amaris, 3; **I. Lin**, Janssen Scientific Affairs, LLC, 1, 3; **M. Pacou**, Amaris, 3; **T. Baker**, Janssen, 1, 3; **Y. Wang**, Janssen R&D, LLC, 1, 3; **S. Peterson**, Janssen Research & Development, LLC, 3.

Abstract Number: 0329

Healthcare Utilization and Costs Associated with Functional Status in Patients with Psoriatic Arthritis

Alexis Ogdie[1], Mark Hwang[2], Phani Veeranki[3], Alexandria Portelli[3], Steven Sison[3], Jason Shafrin[3], Sofia Pedro[4], Peter Hur[5], Nina Kim[6] and Kaleb Michaud[7], [1]Perelman School of Medicine at the University of Pennsylvania, Philadelphia, PA, [2]McGovern Medical School at the University of Texas Health Science Center at Houston, Houston, TX, [3]PRECISIONheor, Los Angeles, [4]FORWARD-The National Data Bank for Rheumatic Diseases, Wichita, [5]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [6]The University of Texas at Austin; Baylor Scott and White Health, Austin, TX, [7]FORWARD-The National Data Bank for Rheumatic Diseases; University of Nebraska Medical Center, Wichita

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Demographics, Clinical Characteristics and Disease Activity Among Patients With PsA Who Completed ≥ 1 HAQ-DI Questionnaire

Characteristic	Patients With PsA (n = 828)
Age, mean (SD), years	58.5 (13.5)
Female, n (%)	599 (72.3)
White, n (%)	697 (92.3)
Education (highest year of education), n (%)	n = 753
High school graduate or less	181 (24.0)
College graduate	229 (30.4)
Master or doctorate degree	343 (45.6)
Insurance status, n (%)	n = 828
Private	263 (31.8)
Medicare	362 (43.7)
Medicaid	68 (8.2)
Other	120 (14.5)
None	15 (1.8)
Geographic location, n (%)	n = 806
Urban	638 (79.2)
Rural	168 (20.8)
Disease duration, mean (SD), years [n]	17.5 (12.4) [759]
Rheumatic disease comorbidity index (0-9), n (%)	n = 828
0	136 (16.4)
1	215 (26.0)
2	176 (21.3)
≥ 3	301 (36.4)
Smoking status, n (%)	n = 828
Never smoker	439 (53.0)
Ever smoker	318 (38.4)
Current smoker	71 (8.6)
PsA treatment history (current and past use), n (%) [n]	
DMARDs	413 (49.9) [801]
Biologics	376 (45.4) [801]
Prednisone	93 (11.2) [735]
NSAIDs	298 (36.0) [801]
Opioids	218 (26.3) [828]
PsA disease activity and quality of life, mean (SD) [n]	
HAQ-DI	0.9 (0.7) [828]
PsAID-12	3.1 (2.3) [196]
BASDAI	3.7 (2.4) [204]
EQ-5D	0.7 (0.2) [766]
Pain VAS	4.2 (2.8) [827]
Patient global assessment	4.0 (2.6) [817]

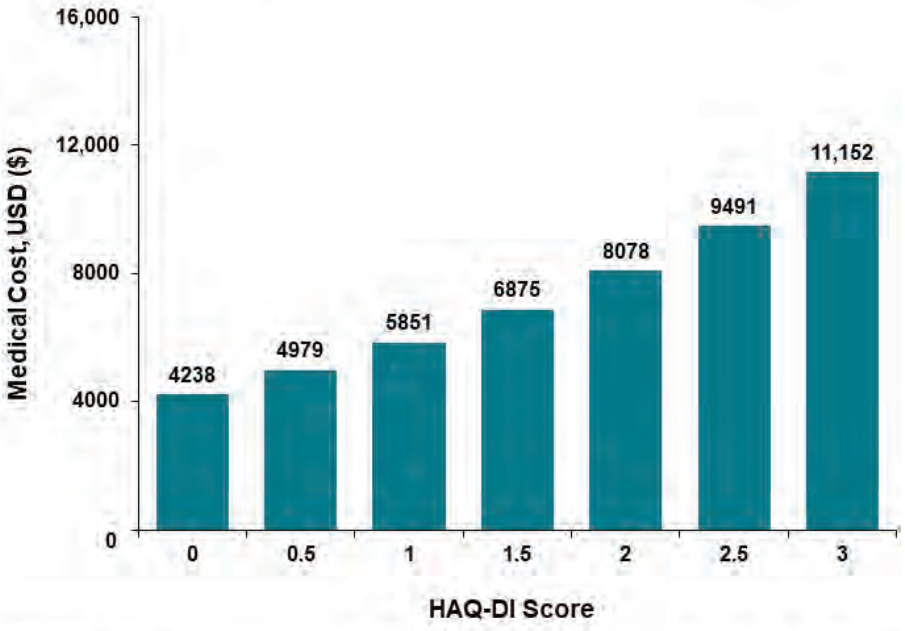
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; DMARD, disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire Disability Index; NSAID, nonsteroidal anti-inflammatory drug; PsA, psoriatic arthritis; PsAID-12, Psoriatic Arthritis Impact of Disease 12-item form; VAS, visual analog score.

Table 2. Association of HAQ-DI* With Annualized Healthcare Resource Utilization and Costs Among Patients With PsA

	Mean (SD)	RR (95% CI)*
HCRU, no. uses		
Hospitalization†	0.30 (0.94)	1.68 (1.11-2.55)**
ED visit‡	0.51 (1.27)	2.09 (1.47-2.96)††
Outpatient visit§	19.86 (14.26)	1.14 (1.05-1.24)††
Diagnostic tests¶	0.41 (1.02)	1.42 (1.16-1.74)††
Procedures‖	5.07 (6.76)	1.18 (0.88-1.58)
	Mean (SD)	**Coefficient (95% CI)**
Medical costs, USD#	6322.9 (12,698.7)	1.38 (1.13-1.69)††

DMARD, disease-modifying antirheumatic drug; ED, emergency department; HAQ-DI, Health Assessment Questionnaire Disability Index; HCRU, healthcare resource utilization; NSAID, nonsteroidal anti-inflammatory drug; PsA, psoriatic arthritis; RR, relative risk.
* HAQ-DI modeled as a continuous variable.
† Model adjusted for age, disease duration, comorbidity index, insurance type, biologic use, NSAID use.
‡ Model adjusted for education level, smoking status, comorbidity index, insurance type, and NSAID use.
§ Model adjusted for sex, geographic region, disease duration, comorbidity index, insurance type, prednisone use, and opioid use.
¶ Model adjusted for age, education level, comorbidity index, physician-reported PsA diagnosis, smoking status, insurance type, DMARD use, biologic use, prednisone use, and opioid use.
‖ Model adjusted for sex.
Includes hospital admissions, ED visits, outpatient visits, diagnostic tests, and procedures. Model adjusted for age, disease duration, comorbidity index, biologic use, NSAID use, and opioid use.
** $P < 0.05$.
†† $P < 0.01$.

Figure 1. Average Annualized Patient Medical Costs Across HAQ-DI Scores in Patients With PsA*



HAQ-DI, Health Assessment Questionnaire Disability Index; NSAID, nonsteroidal anti-inflammatory drug; PsA, psoriatic arthritis.
* Adjusted for age, disease duration, comorbidity index, biologic use, NSAID use, and opioid use.

Background/Purpose: The Health Assessment Questionnaire Disability Index (HAQ-DI) has been validated and widely used in psoriatic arthritis (PsA) clinical trials for the assessment of patient functional status. Few US studies have evaluated the economic impact of functional disability in patients with PsA. The purpose of this study was to evaluate the association of functional status with healthcare resource utilization (HCRU) and medical costs in US patients with PsA in a national data registry.

Methods: FORWARD is a longitudinal observational databank for rheumatic diseases that collects patient-reported data through questionnaires administered every 6 months. Data collected include demographics, clinical characteristics, symptoms, health and functional status, health-related quality of life, and HCRU. This cohort study included adult patients with PsA enrolled in FORWARD between July 2009 and June 2019 who completed ≥ 1 questionnaire, including the HAQ-DI, between January 2010 and December 2019. Patient demographics, clinical characteristics, and patient-reported outcomes were collected from the most recent questionnaire. HCRU and medical costs (USD 2019) for all hospitalizations, emergency department (ED) visits, outpatient visits, diagnostic tests, and procedures were assessed for the 6 months prior to survey completion. Negative binomial regression models (HCRU outcomes) and generalized linear models with gamma distribution and log-link function (cost outcomes) were used to assess the relationship between HAQ-DI and HCRU and cost outcomes adjusted for confounders.

Results: A total of 828 patients with PsA who completed HAQ-DI questionnaires were included. The mean (SD) age was 58.5 (13.5) years, 72.3% were female, and 92.3% were white. The mean (SD) disease duration was 17.5 (12.4) years, and the mean (SD) HAQ-DI score at the time of the patients' most recent questionnaire was 0.9 (0.7) (**Table 1**). Increasing HAQ-DI score was significantly associated with increased risk (relative risk [95% CI]) of hospitalizations (1.68 [1.11-2.55]), ED visits (2.09 [1.47-2.96]), outpatient visits (1.14 [1.05-1.24]), and diagnostic tests (1.42 [1.16-1.74]) (**Table 2**). There was also a significant positive association between greater HAQ-DI score and increased medical costs (coefficient [95% CI], 1.38 [1.13-1.69]) (**Table 2**). Overall, adjusted average patient medical costs increased with increasing HAQ-DI score (**Figure 1**).

Conclusion: Among patients with PsA, higher HAQ-DI scores were associated with greater HCRU and increased medical costs. These results suggest that interventions that improve functional status may reduce economic burden for patients and healthcare systems throughout the course of disease.

Disclosure: A. Ogdie, AbbVie, 5, Amgen, 2, 5, BMS, 1, Celgene, 1, Corrona, 1, Janssen, 1, Eli Lilly, 1, Novartis, 2, 5, Pfizer, 2, 5, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 2, Rheumatology Research Foundation, 2, National Psoriasis Foundation, 2; **M. Hwang**, Novartis, 5, University of Texas Health Science Center at Houston (UTHealth) Center of Clinical and Translational Sciences KL2 program, 2; **P. Veeranki**, PRECISIONheor, 3; **A. Portelli**, PRECISIONheor, 3; **S. Sison**, PRECISIONheor, 3; **J. Shafrin**, PRECISIONheor, 1, 3; **S. Pedro**, Forward, The National Databank for Rheumatic Diseases, 3; **P. Hur**, Novartis Pharmaceuticals Corporation, 3; **N. Kim**, Novartis Pharmaceuticals Corporation, 9; **K. Michaud**, Rheumatology Research Foundation, 2.

Abstract Number: 0330

Musculoskeletal Surgery in Psoriatic Arthritis: Prevalence and Risk Factors

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite optimal medical therapy, joint space disease and skeletal damage persists in a subset of patients with PsA, many of whom requiring musculoskeletal (MSK) surgery for disease related morbidity. The purpose of this study was to determine the prevalence of MSK surgery in PsA patients, describe the type/indications for surgery and associated risk factors that increase the likelihood of undergoing MSK surgery.

Table 1. Distribution and descriptions of MSK surgeries performed attributable to PsA (n=379)

Type of Surgery	N (%)	**Anatomical Location**	N (%)	**Surgical Indication**	N (%)	**Joint retaining/ sacrificing**	N (%)
Arthrodesis	102 (27%)	Knee	106 (28%)	Deformities	161 (42%)	Joint sacrificing	224 (59%)
Arthroplasty	102 (27%)	Finger	80 (21%)	Inflammation/ synovitis	156 (41%)	Joint retaining	155 (41%)
Arthroscopic synovectomy	59 (16%)	Foot	70 (18%)	Failed implant	24 (6%)		
Tendon/ ligament repair	28 (7%)	Hip	37 (10%)	Infection	9 (2%)		
Osteotomy	18 (5%)	Wrist	26 (7%)	Pain	9 (2%)		
Arthroscopic debridement/ meniscectomy	17 (4%)	Hand	17 (4%)	Avascular necrosis from corticosteroids	5 (1%)		
Revision arthroplasty	14 (4%)	Shoulder	12 (3%)	Secondary degenerative disease	5 (1%)		
Diagnostic arthroscopy	12 (3%)	Ankle	12 (3%)	Trauma/injury	4 (1%)		
Implant removal	10 (3%)	Elbow	7 (2%)	Ankylosis	3 (1%)		
Amputation	5 (1%)	Jaw	8 (2%)	Carpal tunnel syndrome	3 (1%)		
Carpal tunnel release	4 (1%)	Spine	3 (1%)				
Irrigation and debridement	3 (1%)	Pelvis	1 (1%)				
Laminectomy/ discectomy	2 (1%)						
Soft tissue excision/ debridement	2 (1%)						
Revision arthrodesis	1 (1%)						

Table 2. Multivariate cox proportional-hazards model for predictors at initial clinic visit of undergoing first MSK surgery adjusted for sex, age and duration of PsA at baseline

Variable	HR	95% CI	p-value
Male sex	0.851	(0.567, 1.279)	0.438
Age at baseline visit	1.043	(1.027, 1.059)	<0.001
PsA disease duration at baseline visit	0.989	(0.966, 1.013)	0.382
Biologic use	1.453	(0.768, 2.751)	0.251
DMARD use	1.291	(0.858, 1.941)	0.220
Elevated ESR	1.322	(0.873, 2.000)	0.187
Total active joints	1.011	(0.993, 1.030)	0.233
Total digits with dactylitis	0.973	(0.850, 1.114)	0.692
Total damaged joints	1.047	(1.024, 1.070)	<0.001
HR, hazard ratio; CI, confidence interval; MSK, musculoskeletal; PsA, psoriatic arthritis; DMARD, disease-modifying antirheumatic drug; ESR, erythrocyte sedimentation rate			

Table 3. Multivariate cox proportional-hazards model using time-dependent covariates for predictors of undergoing first MSK surgery adjusted for sex, age and duration of PsA at baseline

Variable	HR	95% CI	p-value
Male sex	0.902	(0.575, 1.413)	0.651
Age at baseline visit	1.073	(1.055, 1.090)	<0.001
PsA disease duration at baseline visit	1.020	(0.998, 1.042)	0.075
Biologic use	2.890	(1.784, 4.681)	<0.001
DMARD use	0.887	(0.569, 1.384)	0.599
Elevated ESR	1.408	(0.913, 2.171)	0.121
Presence of nail lesions	2.482	(1.530, 4.029)	<0.001
NSAID use	2.623	(1.577, 4.362)	<0.001
Total active joints	1.032	(1.011, 1.053)	0.002
Total digits with dactylitis	1.078	(0.867, 1.339)	0.499
HR, hazard ratio; CI, confidence interval; MSK, musculoskeletal; PsA, psoriatic arthritis; DMARD, disease-modifying antirheumatic drug; ESR, erythrocyte sedimentation rate; NSAID, nonsteroidal anti-inflammatory drug			

Methods: A longitudinal single center cohort was analyzed to identify PsA patients who had MSK surgery from January 1973 to December 2019 inclusive. All cohort patients fulfilled the 2006 CASPAR criteria. Data from all MSK surgeries were collected using a web-based database. Patient charts were reviewed to confirm individual surgeries were MSK related and attributable to PsA by cross-referencing to clinical records and pre and post-operative diagnoses. Descriptive statistics determined the prevalence of MSK surgeries attributable to PsA, in addition to categories, indications and anatomical locations for surgery. A cox proportional-hazards model determined predictors at initial clinic visit for undergoing first MSK surgery. Lastly, a cox proportional-hazards model using time-dependent covariates evaluated the cumulative effect of PsA disease burden on undergoing MSK surgery. All models were adjusted for sex, age and duration of PsA at baseline.

Results: Of the 1574 patients in the cohort, 185 patients had 379 MSK surgeries related to PsA (Table 1). Common surgeries were arthrodesis (27%) and arthroplasty (27%). Common anatomical locations included the knee (28%) and finger (21%) with surgical indications representing deformities (42%) and inflammation/synovitis (42%). 59% of surgeries were joint sacrificing while 41% were joint retaining. Complete covariate data for the cox proportional-hazards model at initial clinic visit and the time-dependent covariate cox proportional-hazards model was present in 97 and 90 patients respectively. At baseline visit, higher age (hazard ratio, 1.043; $p< 0.001$) and total damaged joints (hazard ratio 1.047, $p< 0.001$) were predictors for undergoing first MSK surgery (Table 2). In time-dependent covariate analysis, biologic use (hazard ratio 2.890, $p< 0.001$), nonsteroidal anti-inflammatory drug (NSAID) use (hazard ratio 2.623,

p< 0.001), the presence of nail lesions (hazard ratio 2.482, p< 0.001), higher age at baseline visit (hazard ratio 1.073, p< 0.001) and higher total actively inflamed joint count (hazard ratio 1.032, p< 0.002) were predictors for undergoing first MSK surgery (Table 3).

Conclusion: 11.8% of patients in our cohort had at least one MSK surgery attributable to PsA, with most surgeries being joint sacrificing in nature (59%). Older age at presentation and more severe disease evidenced by damaged joints at presentation, active inflammation, nail lesions and use of biologic therapy were associated with a higher risk of MSK surgery. Despite medical therapy, a significant number of patients still require surgical intervention for mainly deformities (42%) or inflammation/synovitis (42%).

Disclosure: T. Kwok, None; **M. Sutton**, None; **D. Pereira**, None; **V. Chandran**, Abbvie, 2, 5, Amgen, 2, 5, Celgene, 2, 5, Eli Lilly, 5, Eli Lilly, 3, Janssen, 8, Novartis, 5, Pfizer, 5, UCB, 5; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5.

Abstract Number: 0331

Work Absenteeism and Disability Associated with Psoriatic Arthritis and Psoriasis in the United States – A Retrospective Study of Claims Data from 2009 to 2020

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Absenteeism and work disability substantially contribute to the economic burden of psoriasis and psoriatic arthritis (PsA). This study compared work absenteeism and short-term disability among adults with psoriasis, PsA, and controls with neither psoriasis nor PsA in the United States.

Methods: Adults eligible for work absenteeism and/or short-term disability benefits between 1/1/2009 and 2/29/2020 were screened in the IBM MarketScan Commercial and Health and Productivity Management Databases. The following groups were defined: 1) Psoriasis: ≥ 1 inpatient or 2 outpatient psoriasis diagnoses and no PsA diagnoses; 2) PsA: ≥ 1 inpatient or 2 outpatient PsA diagnoses; 3) Control: absence of psoriasis and PsA diagnoses. Controls were matched 3:1 to psoriasis and PsA patients based on age, gender, and comorbidities. Absenteeism, short-term disability, and corresponding costs (in 2019 USD) were evaluated descriptively and through mixed models.

Results: 5,785 psoriasis and 1,245 PsA absentee-eligible and 35,512 psoriasis and 7,434 PsA short-term disability-eligible patients were matched to the control group. During the first year of follow-up, 9.7% of patients with PsA had short-term disability leave compared with 6.2% of patients with psoriasis and 4.8% of controls (Table 1). The

Table 1. Work absenteeism and short-term disability during follow up

	Control group	Psoriasis	PsA
Number of absentee-eligible patients	21,090	5,785	1,245
Patients with work absence during 1st follow-up year - N (%)			
Non-recreational	12559 (59.5%)	3982 (68.8%)	876 (70.4%)
Sick leaves	9422 (44.7%)	3208 (55.5%)	728 (58.5%)
Absenteeism days during follow-up - Mean (SD)			
Non-recreational (PPPY)	6.29 (13.11)	7.82 (15.53)	8.78 (17.97)
Sick leaves (PPPY)	3.37 (7.62)	4.43 (9.24)	5.10 (10.95)
Costs from hours missed from work - Mean (SD)			
Non-recreational (PPPY)	1333.04 (2778.51)	1680.40 (3350.64)	1890.88 (3878.78)
Sick leaves (PPPY)	714.90 (1614.39)	953.39 (1999.70)	1099.64 (2377.68)
Number of short-term disability-eligible patients	128,838	35,512	7,434
Patients with short-term disability during 1st follow-up year - N (%)	6217 (4.8%)	2190 (6.2%)	722 (9.7%)
Short-term disability days during follow-up - Mean (SD)	2.76 (18.21)	3.38 (21.26)	5.15 (25.71)
Costs associated with short-term disability (PPPY) - Mean (SD)	352.88 (2323.59)	436.03 (2736.99)	664.58 (3315.59)

PPPY: per patient per year

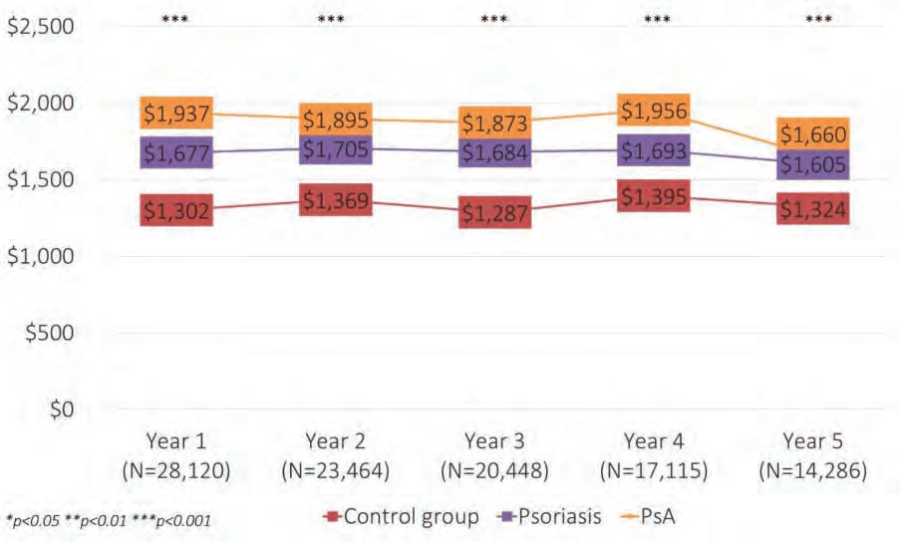


Figure 1. Average costs from non-recreational hours missed from work per patient per year

odds of short-term disability at one year were significantly greater among patients with PsA than psoriasis (OR: 1.56, 95% CI: 1.45-1.69) and controls (OR: 1.95, 95% CI: 1.82-2.10). Average costs from non-recreational work absences were $1,891, $1,680, and $1,333 per patient per year for the PsA, psoriasis, and control group, respectively. Costs associated with non-recreational work absences and short-term disability were significantly greater for patients with PsA and patients with psoriasis than controls at one year ($p< 0.0001$ for all comparisons). These costs were also significantly greater for PsA than psoriasis at one year ($p=0.001$ and $p< 0.0001$, respectively). This trend of increased costs for patients with PsA compared with the other groups was sustained throughout the five years of follow-up (Figures 1 & 2).

Conclusion: Work absenteeism and short-term disability were greater among both the psoriasis and PsA groups than the control group. Absenteeism and short-term disability were greater among patients with PsA than psoriasis. These findings demonstrate the substantial impact that psoriatic disease has on patients' work related outcomes, and highlight remaining unmet needs for patients with psoriatic disease.

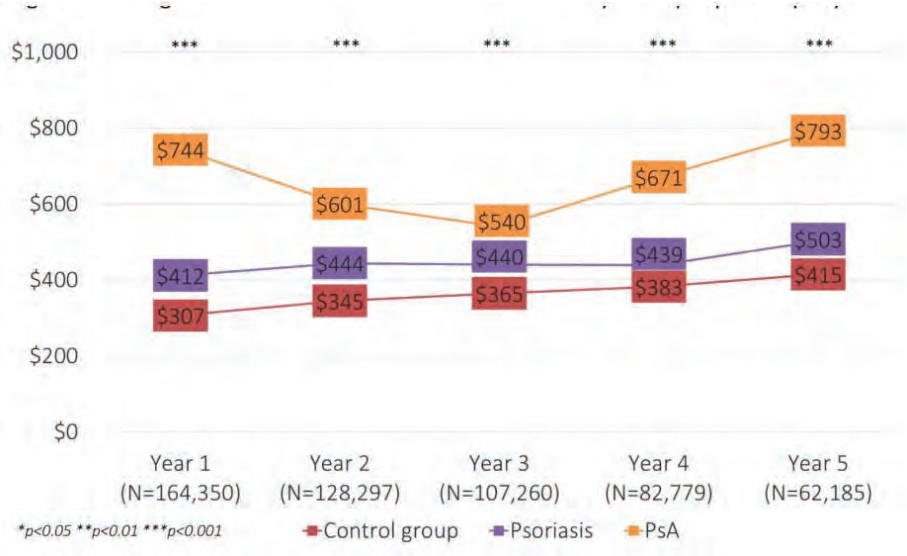


Figure 2. Average costs associated with short-term disability leave per patient per year

Disclosure: A. Orbai, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 5, UCB, 5, AbbVie, 2, Celgene, 2, Horizon, 2; **S. Reddy**, Novartis, 5, Janssen, 5, Pfizer, 5, Amgen, 5, Celgene, 2, Amgen, 2; **S. Peterson**, Janssen Research & Development, LLC, 3; **N. Dennis**, None; **R. Villacorta**, Janssen Pharmaceuticals, 1, 3; **L. Mesana**, Amaris, 3; **S. Chakravarty**, Janssen Scientific Affairs, LLC, 1, 3; **M. Pacou**, Amaris, 3; **I. Lin**, Janssen Scientific Affairs, LLC, 1, 3; **T. Baker**, Janssen, 1, 3; **Y. Wang**, Janssen R&D, LLC, 1, 3; **J. Walsh**, Pfizer, 2, AbbVie, 2, 5, Eli Lilly, 5, UCB, 5, Janssen, 5, Novartis, 5, Amgen, 5.

Abstract Number: 0332

Guselkumab Improved Work Productivity and Daily Activity in Patients with Psoriatic Arthritis: Results from a Phase 3 Trial

Jeffrey R Curtis[1], Iain McInnes[2], Proton Rahman[3], William Tillett[4], Philip Mease[5], Alexa Kollmeier[6], Elizabeth Hsia[7], Bei Zhou[8], Prasheen Agarwal[8], Steven Peterson[9] and Chenglong Han[8], [1]Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, [2]Institute of Infection, Immunity, and Inflammation, University of Glasgow, Glasgow, United Kingdom, [3]Memorial University of Newfoundland, Department of Medicine, St John's, Canada, [4]Royal National Hospital for Rheumatic Diseases, Bath, UK; Department of Pharmacy and Pharmacology, University of Bath, Bath, United Kingdom, [5]Seattle Rheumatology Associates, P.L.L.C., Seattle, WA, [6]Janssen Research & Development, LLC, La Jolla, CA, [7]Janssen Research & Development, LLC and University of Pennsylvania Medical Center, Spring House, PA, [8]Janssen Research & Development, LLC, Spring House, PA, [9]Janssen Immunology Global Commercial Strategy Organization, Horsham, PA

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: DISCOVER 2 (DISC 2) is a Phase 3 trial of anti-IL-23-specific MAb Guselkumab (GUS) in PsA patients, who experience impaired physical function, resulting in disability, work productivity loss, and economic consequences.[1] This study aimed to evaluate the effect of GUS on impaired work productivity and daily activity in DISC 2 using the Work Productivity and Activity Impairment Questionnaire: Psoriatic Arthritis (WPAI-PsA).

Table. Model-based estimates of mean change from baseline in WPAI-PsA domains. Data are % (95% CI). *p>0.05, †p<0.05, ‡p<0.001. LSmean, p values based on MMRM. LSmean diffs, p values vs PBO. GUS, Guselkumab; LSMean, least squares mean; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; WPAI-PsA, work productivity and activity impairment questionnaire: psoriatic arthritis.

	PBO		GUS 100 mg q8W		GUS 100 mg q4W	
% change from baseline	**W16**	**W24**	**W16**	**W24**	**W16**	**W24**
Work time missed (absenteeism), n	155	152	141	145	145	143
LSMean	-4.6 (-7.2, -1.9)	-3.5 (-6.4, -0.6)	-3.5 (-6.2, -0.7)	-3.1 (-6.1, -0.1)	-4.7 (-7.4, -2.0)	-3.8 (-6.8, -0.8)
LSMean diff			1.1 (-2.6, -4.8)*	0.4 (-3.7, 4.5)*	-0.2 (-3.9, 3.5)*	-0.3 (-4.4, 3.8)*
Impairment while working (presenteeism), n	131	130	125	129	133	130
LSMean	-10.3 (-13.9, -6.7)	-10.2 (-13.7, -6.7)	-16.1 (-19.7, -12.4)	-19.4 (-22.9, -15.9)	-15.1 (-18.7, -11.5)	-19.5 (-23.0, -16.0)
LSMean diff			-5.8 (-10.8, -0.8)†	-9.2 (-14.0, -4.4)‡	-4.8 (-9.7, 0.1)*	-9.3 (-14.1, -4.5)‡
Overall work productivity impairment (absenteeism + presenteeism), n	131	130	125	129	133	130
LSMean	-11.2 (-15.0, -7.5)	-10.9 (-14.6, -7.1)	-15.9 (-19.7, -12.2)	-19.7 (-23.4, -16.0)	-15.8 (-19.5, -12.1)	-20.0 (-23.7, -16.3)
LSMean diff			-4.7 (-9.9, 0.5)*	-8.8 (-14.0, -3.7)‡	-4.6 (-9.7, 0.5)*	-9.2 (-14.3, -4.0)‡
Daily activity impairment, n	244	244	247	246	243	245
LSMean	-10.6 (-13.3, -7.9)	-10.3 (-13.1, -7.6)	-17.1 (-19.8, -14.4)	-21.5 (-24.2, -18.7)	-17.0 (-19.7, -14.3)	-20.5 (-23.2, -17.7)
LSMean diff			-6.5 (-10.2, -2.8)‡	-11.1 (-15.0, -7.4)‡	-6.5 (-10.2, -2.7)‡	-10.2 (-14.0, -6.4)‡

Methods: Bio-naïve adults with active PsA despite nonbiologic DMARDs &/or NSAIDs received subcutaneous GUS 100 mg every (q) 4 weeks (W); GUS 100 mg Week 0, Week 4, q8W; or placebo (PBO). WPAI-PsA assesses, due to PsA over the previous week, work time missed (absenteeism), impairment while working (presenteeism), and impaired overall work productivity (absenteeism + presenteeism) and daily activity. Percentage change from baseline was analyzed for WPAI-PsA domains using mixed-effect model repeated measure (MMRM). Indirect savings from improved overall work productivity were estimated with 2018 US mean yearly wage estimate (all occupations).[2]

Results: At Week 24, impaired overall work productivity and daily activity were improved 20-22% in GUS-treated and 10-11% in PBO-treated patients (Table). Potential yearly indirect savings from improved overall work productivity was $10,242 with GUS q8W and $10,404 with GUS q4W vs $5,648 with PBO; $4,594 and $4,756 difference, respectively.

Conclusion: Improvement in overall work productivity and daily activity was greater with GUS versus PBO among patients with moderate-to-severe PsA, resulting in potential annual incremental economic gains.

References

1. Tillett W et al. Rheumatol (Oxford). 2012; 51:275–283.
2. US Bureau of Labor Statistics. May 2018 National Occupational Employment and Wage Estimates United States. https://www.bls.gov/oes/current/oes_nat.htm#00-000

Disclosure: J. Curtis, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **I. McInnes**, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **P. Rahman**, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5; **W. Tillett**, Abbvie, 5, 8, Amgen Inc., 5, 8, Celgene, 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB Pharma, 5, 8; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **A. Kollmeier**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **E. Hsia**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **B. Zhou**, Janssen Reserach & Development, LLC, 3, Johnson & Johnson, 1; **P. Agarwal**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **S. Peterson**, Janssen Research & Development, LLC, 3; **C. Han**, Janssen Research & Development, LLC, 3.

Abstract Number: 0333

Comparative Effectiveness of Secukinumab, Adalimumab and Other Tumor Necrosis Factor Inhibitors Used with or Without Methotrexate in the Treatment of Psoriatic Arthritis

Denis Choquette[1], Loïc Choquette Sauvageau[2], Louis Bessette[3], Isabelle Ferdinand[2], Boulos Haraoui[4], Frédéric Massicotte[2], Jean-Pierre Pelletier[1], Jean-Pierre Raynauld[1], Marie-Anaïs Rémillard[2], Diane Sauvageau[2], Édith Villeneuve[2] and Louis Coupal[2], [1]Institut de Rhumatologie de Montréal, Montreal, Canada, [2]Institut de Rhumatologie de Montréal, Montréal, QC, Canada, [3]Laval University, Quebec, Canada, [4]Rheumatology Institute of Montréal, Montreal, Canada

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

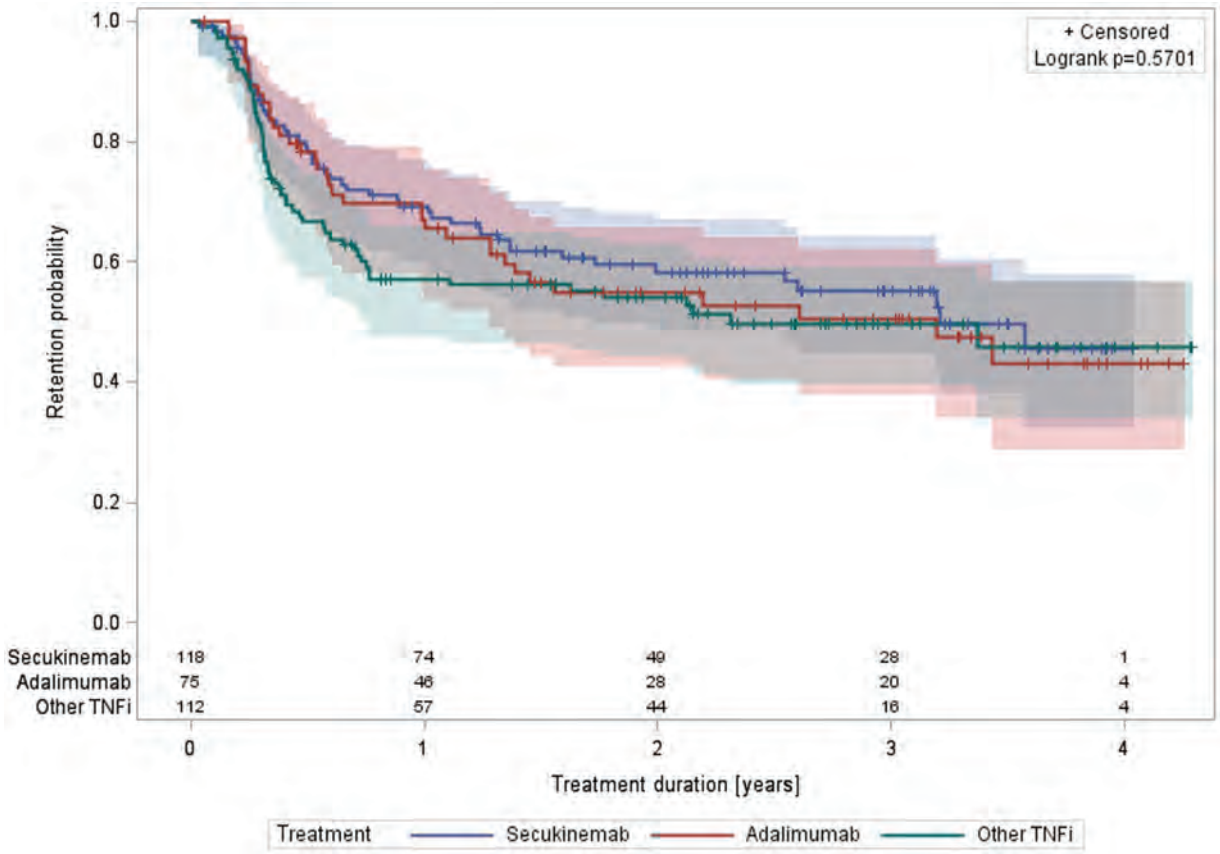
Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The treatment of psoriatic arthritis has evolved with the addition of agents targeting a different cytokine, Il-17 introduced in 2016. It has proven to be more effective than anti-TNF in controlling the cutaneous manifestation of psoriasis. Recent data have not shown clear superiority on the articular manifestations [EXCEED Study].

Methods: Patients diagnosed with PsA enrolled in RHUMADATA® were selected if they gave informed consent and were treated with secukinumab (SEC), adalimumab (ADA) or other TNF inhibitors (TNFi) on or after January 1, 2016. RHUMADATA® provides socio-demographics, comorbidities, patient-reported outcomes, disease activity indices, laboratory variables, rheumatologist exam report data, use of concomitant medications and PsA treatment. Kaplan-Meier survival curves and proportional hazard models were used to analyze time to treatment cessation.

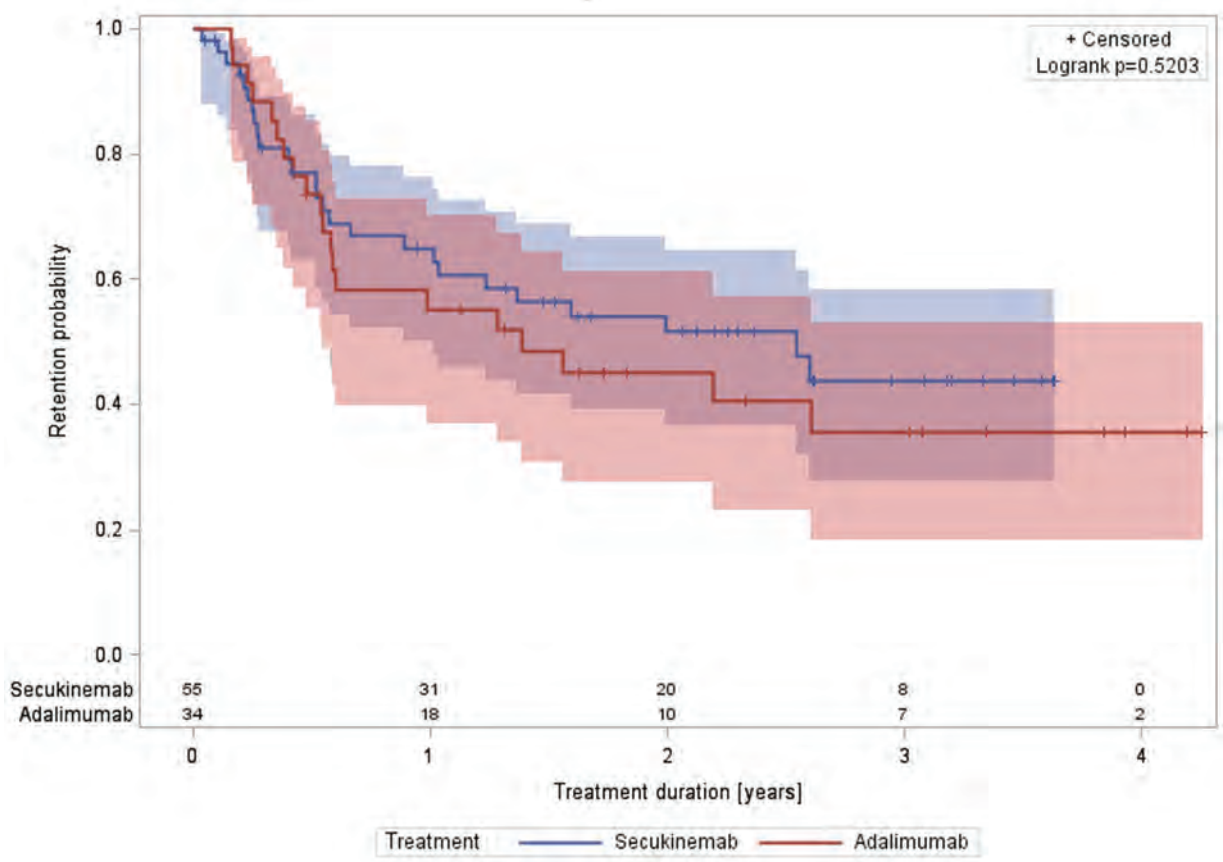
Results: A total of 305 patients with PsA were extracted from RHUMADATA®. One hundred and eighteen were treated with SEC, 75 with ADA and 112 with other TNFi (certolizumab, golimumab or infliximab. etanercept was not included



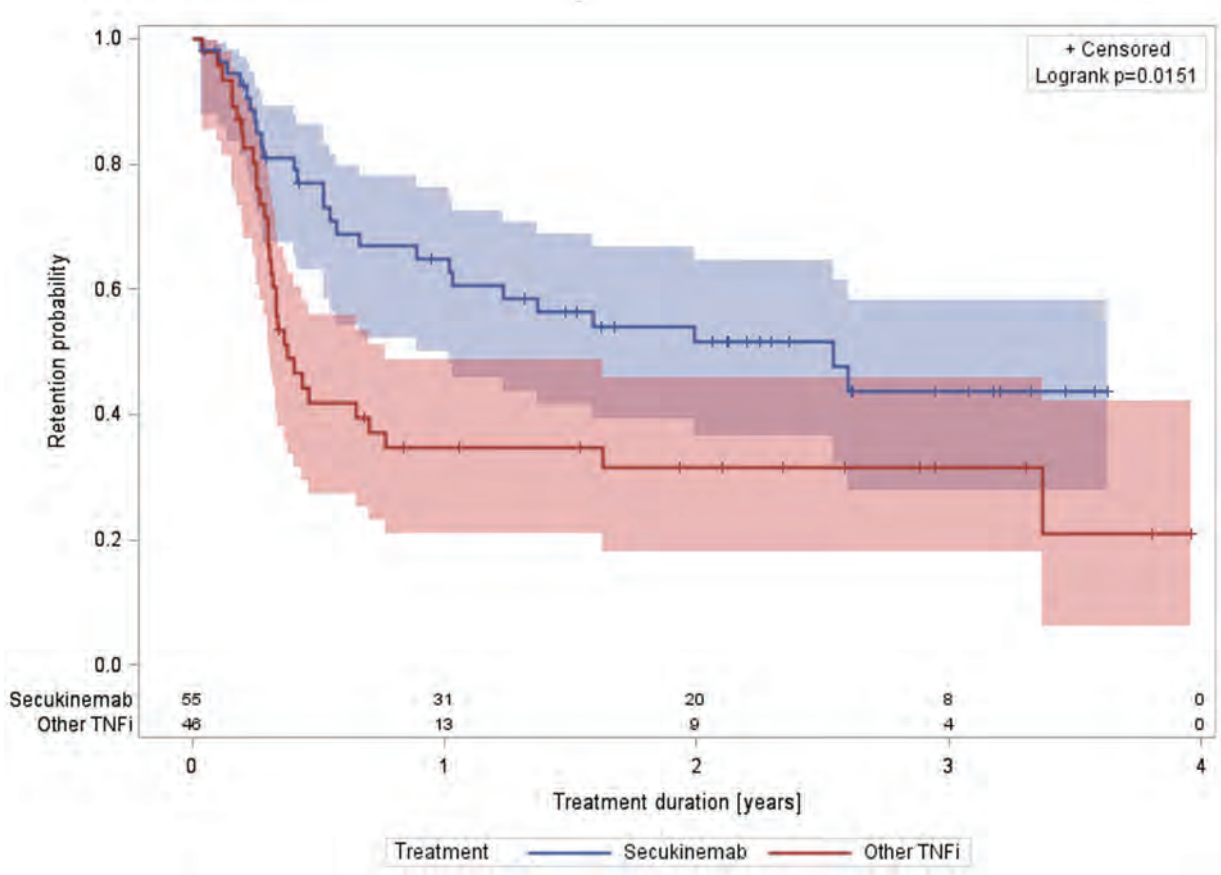
Retention of SEC, ADA and TNFi (all intentions).

as it is not an atibody targetting TNFi). Overall, 54.1% were women, average age at diagnosis and disease duration at treatment initiation were respectively 44.3 (±standard deviation (STD)=12.4) and 6.3 (7.9) years. The age-adjusted Charlson Comorbidity Index (aCCI) was 1.4 (1.8). The proportion of patients diagnosed or treated for diabetes and hypertension were 13.4% and 37.7%. The patient's assessment of disease activity, pain and fatigue were 5.5 (2.7), 6.0 (2.8) and 5.5 (3.1). Overall, BASDAI and BASFI scores were 5.6 (2.5) and 4.4 (2.8). The mean number of affected fingers and toes (dactylitis) and enthesitis were 0.9 (1.5) and 0.9 (1.7), respectively. SEC, ADA and TNFi were used in first intention in 25.4%, 61.3% and 37.5% of patients, respectively. CDAI at treatment initiation was 18.5 (11.0), 21.0 (10.2) and 16.6 (8.8) in the SEC, ADA and TNFi groups, respectively. At one-year CDAI, values were 6.1 (7.5), 5.0 (5.4) and 4.9 (3.1). Kaplan-Meier log-rank p-values comparing the three groups in all (Figure 1), first and second, and third+ intentions were 0.5701, 0.6631 and 0.3246, respectively. No pairwise comparisons of treatment (SEC vs. ADA, SEC vs. TNFi, ADA vs. TNFi) showed better retention for any agent. Pairwise comparison of these agents in monotherapy numerically favored SEC over ADA (Figure 2) but failed to reach statistical significance (log-rank p-value=0.5203), and SEC over TNFi (Figures 3) statistically favored SEC over ADA (log-rank p-value=0.0150). A Cox proportional hazard model adjusting for age at diagnosis, disease duration, aCCI, the number of prior advanced therapies, and concomitant use of MTX at treatment initiation as well as selected treatment demonstrated a statistically better retention among patients treated with MTX (Adjusted hazard ratio and 95% confidence interval: 0.487 [0.347, 0.683]. Adjusted treatment-MTX interaction terms were non-significant.

Conclusion: Secukinumab in observational data have shown similar efficacy over ADA and other TNFi. The use of these treatments in monotherapy showed similar retention for SEC over ADA , and impreoved retention for SEC over TNFi.



Retention of SEC and ADA in monotherapy (all intentions).



Retention of SEC and TNFi in monotherapy (all intentions).

Disclosure: D. Choquette, AbbVie Canada, 5, 8, Amgen Canada, 5, 8, Bristol-Myers-Squibb Canada, 5, 8, Eli Lilly Canada, 5, 8, Merk Canada, 5, 8, Novartis Canada, 5, 8, UCB Canada, 5, Janssen Canada, 5, Sandoz Canada, 5, 8, Pfizer Canada, 5, 8, Roche Canada, 5, Sanofi-Genzyme Canada, 5, 8; **L. Choquette Sauvageau**, None; **L. Bessette**, Amgen, 1, 2, 3, BMS, 1, 2, 3, Janssen, 1, 2, 3, UCB, 1, 2, 3, AbbVie, 1, 2, 3, Pfizer, 1, 2, 3, Merck, 1, 2, 3, Celgene, 1, 2, 3, Sanofi, 1, 2, 3, Lilly, 1, 2, 3, Novartis, 1, 2, 3, Gilead, 2, 6, 8; **I. Ferdinand**, Pfizer Canada, 5, 8, AbbVie Canada, 5, Amgen Canada, 5, 8, Novartis Canada, 5; **B. Haraoui**, Pfizer Canada, 5, 8, UCB Canada, 5, 8, AbbVie Canada, 5, 8, Amgen Canada, 5, Bristol-Myers-Squibb Canada, 5, Eli Lilly Canada, 5, Merck, 5, Roche Canada, 5, Sanofi-Genzyme Canada, 5, Sandoz Canada, 5, Janssen Canada, 8, Celgene Canada, 8; **F. Massicotte**, AbbVie Canada, 8, Celgene Canada, 5, Janssen Canada, 8, Pfizer Canada, 5; **J. Pelletier**, Bioiberica, 8, Bayer Canada, 5, Pierre-Fabre, 5, IBSA, 8, TEVA, 5, Sanofi-Genzyme Canada, 8, Zodiac Laboratory, 5; **J. Raynauld**, AbbVie Canada, 8, Amgen Canada, 5, 8, Bristol-Myers-Squibb Canada, 8, Celgene Canada, 8, Eli Lilly Canada, 8, Novartis Canada, 8, Pfizer Canada, 8, Roche Canada, 8, Sanofi-Genzyme Canada, 5, 8, UCB Canada, 8, Janssen Canada, 8; **M. Rémillard**, AbbVie Canada, 5, 8, Amgen Canada, 5, 8, Eli Lilly Canada, 5, 8, Novartis Canada, 5, 8, Pfizer Canada, 5, 8, Sandoz Canada, 5, 8; **D. Sauvageau**, None; **É. Villeneuve**, AbbVie Canada, 5, 8, Amgen Canada, 5, 8, Bristol-Myers-Squibb Canada, 8, Celgene Canada, 5, Merk Canada, 8, Novartis Canada, 8, Pfizer Canada, 5, 8, Roche Canada, 5, 8, UCB Canada, 5, 8; **L. Coupal**, None.

Abstract Number: 0334

Comparative Efficacy of Guselkumab in Patients with Psoriatic Arthritis: Results from Systematic Literature Review and Network Meta-Analysis

Philip Mease[1], Iain McInnes[2], Kiefer Eaton[3], Steven Peterson[4], Tim Disher[5], Soumya Chakravarty[6], Chetan Karyekar[7], Sandhya Nair[8], Wolf-Henning Boehncke[9] and Christopher Ritchlin[10], [1]Seattle Rheumatology Associates, P.L.L.C., Seattle, WA, [2]Institute of Infection, Immunity, and Inflammation, University of Glasgow, Glasgow, United Kingdom, [3]EVERSANA, Burlington, Canada, [4]Janssen Immunology Global Commercial Strategy Organization, Horsham, PA, [5]EVERSANA, Sydney, Australia, [6]Janssen Scientific Affairs, LLC, Horsham, PA, USA and Drexel University College of Medicine, Horsham, PA, [7]Janssen Global Services, LLC, Horsham, PA, [8]Janssen Pharmaceutica NV, Beerse, [9]Geneva University Hospitals, Geneva, Switzerland, [10]Department of Medicine, University of Rochester Medical Center, Rochester, NY

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

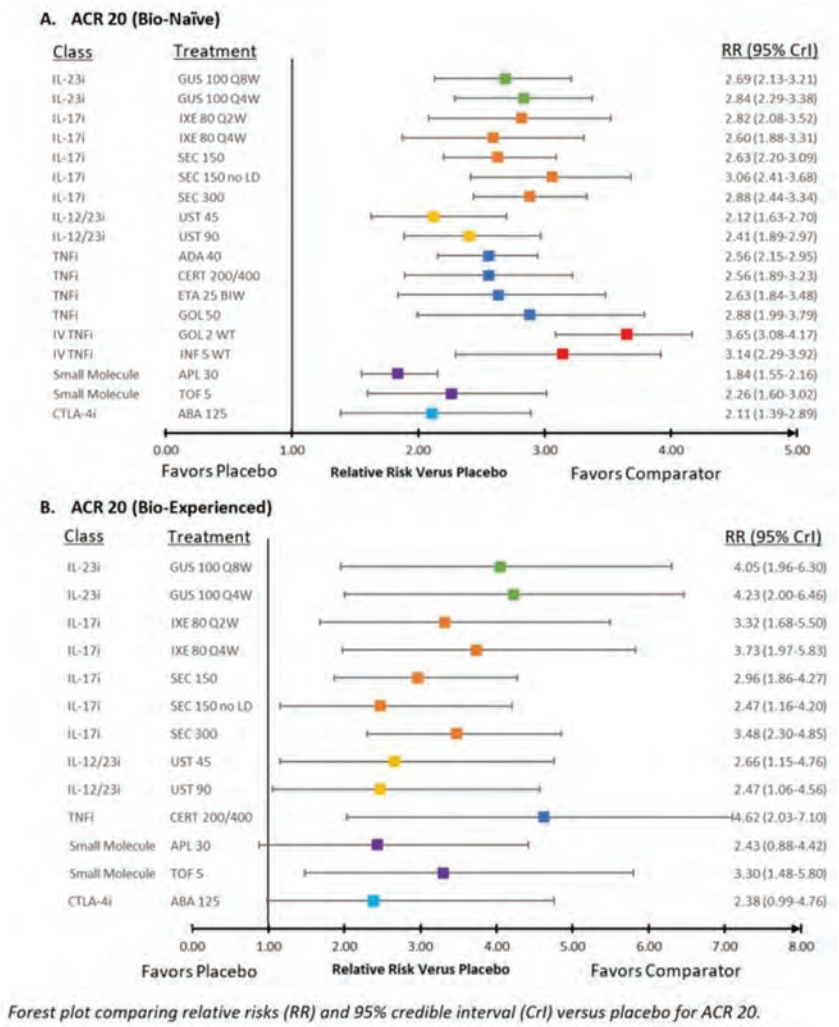


Figure 1. Forest Plot of ACR 20 Response Versus Placebo In Bio-Naïve and Bio-Experienced Populations

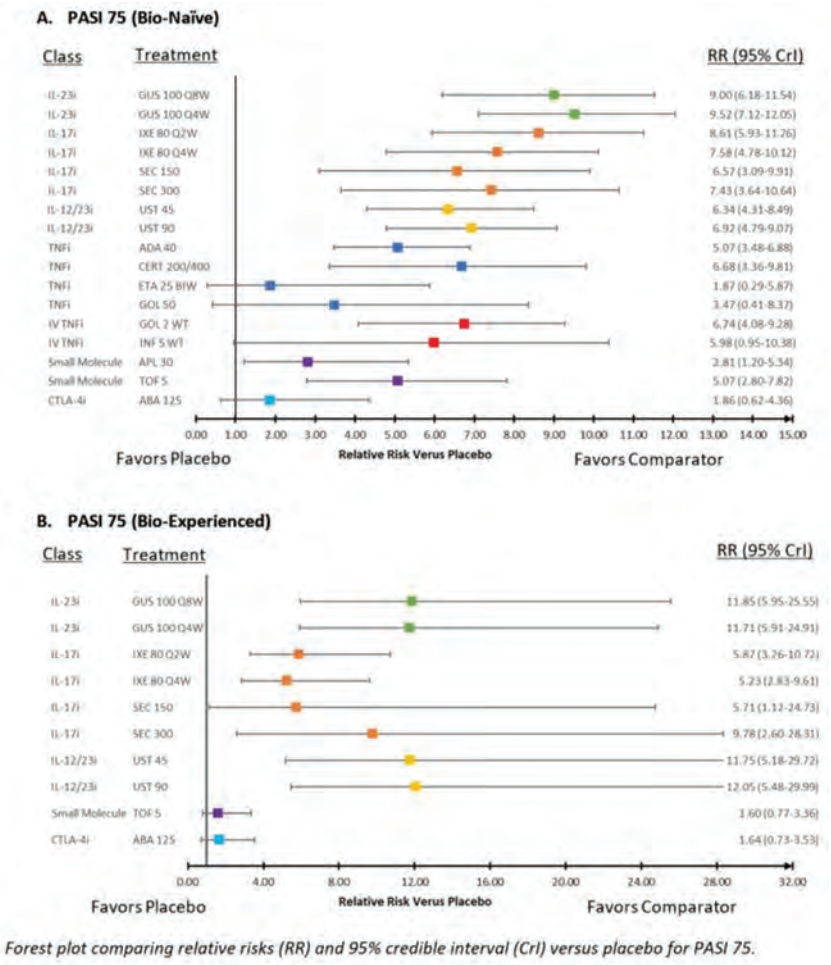
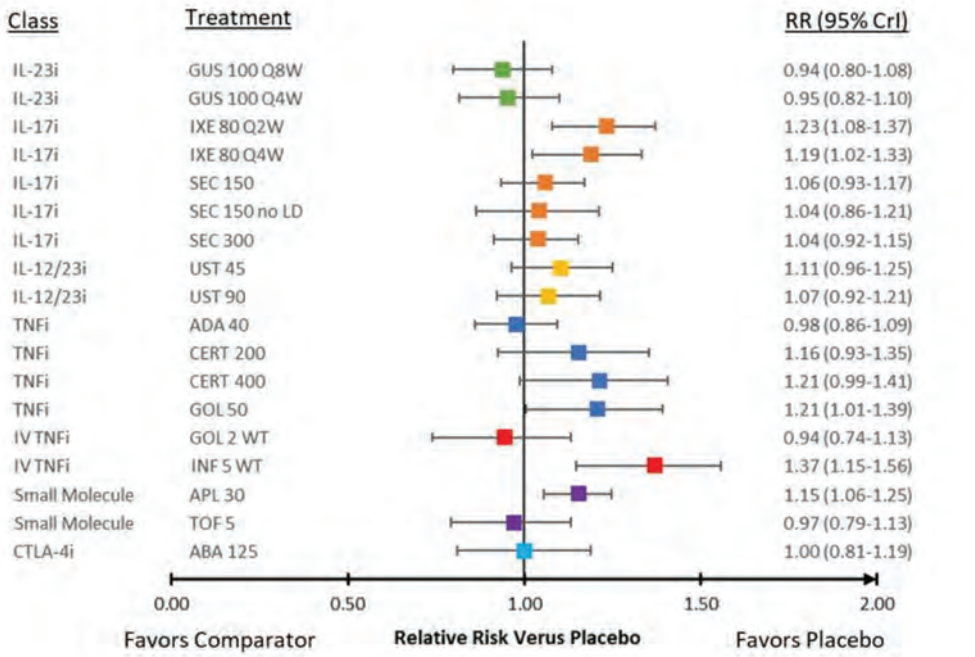


Figure 2. Forest Plot of PASI 75 Response Versus Placebo In Bio-Naïve and Bio-Experienced Populations

Background/Purpose: The efficacy of the interleukin (IL)-23 subunit p19 inhibitor guselkumab (GUS) for psoriatic arthritis (PsA) has recently been demonstrated in two Phase 3 trials (DISCOVER-1 & -2) but has not been evaluated versus existing targeted therapies for PsA. The objective of this study was to compare GUS to targeted therapies for PsA through network meta-analysis (NMA).

Methods: A systematic literature review was performed to identify PsA randomized controlled trials from 2000 to 2018. Bayesian NMAs were performed to compare treatments on American College of Rheumatology (ACR) 20/50/70 response, Psoriasis Area Severity Index (PASI) 75/90/100 response, Health Assessment Questionnaire Disability Index (HAQ-DI) score, modified van der Heijde-Sharp (vdH-S) score, adverse events (AEs) and serious adverse events (SAEs). For ACR 20 and PASI 75 response outcomes, analyses stratified according to previous exposure to biologics. Analyses adjusted for placebo response via meta-regression on baseline risk when feasible. Results are summarized by ranking treatments according responses derived from NMAs, with conclusions (ie, comparable or better/worse) derived from overlap of pairwise 95% credible intervals (CrI) between treatments.

Results: Twenty-four Phase 3 studies were included in NMAs. Studies were placebo-controlled up to 24 weeks and evaluated 13 targeted therapies for PsA. Forest plot of relative risks (RR) versus placebo for ACR 20 and PASI 75 according to previous exposure to biologics are presented in *Figure 1* and *Figure 2*, respectively. Forest plot of RRs versus placebo for AEs are presented in *Figure 3.* For ACR 20 response in the bio-naïve population, GUS 100 mg every 4 weeks (Q4W) and every 8 weeks (Q8W) ranked 5th and 8th out of 19 interventions and were comparable to



Forest plot comparing relative risks (RR) and 95% credible interval (CrI) versus placebo for patients with adverse events.

Figure 3. Forest Plot of Adverse Events Versus Placebo

IL-17 inhibitor (IL-17i) and subcutaneous tumor necrosis factor inhibitor (TNFi) agents. For ACR 20 response in the bio-experienced population, GUS Q4W and Q8W ranked 2nd and 3rd out of 14 interventions and were considered comparable to other active agents. Similar results were seen in mixed analyses of ACR 50 & 70. For PASI 75 response in the bio-naïve population, GUS Q4W and Q8W ranked 1st and 2nd out of 18 interventions and were better than most other agents. For PASI 75 in the bio-experienced population, GUS Q4W and Q8W ranked 3rd and 2nd out of 11 interventions and were better than several other agents. Similar results were seen in mixed analyses of PASI 90 & 100. For HAQ-DI score, GUS Q4W and Q8W ranked 6th and 11th out of 20 interventions and were comparable to IL-17i and subcutaneous TNFi agents. For vdH-S score, GUS Q4W and Q8W ranked 3rd and 10th out of 18 interventions, with Q8W comparable to most IL-17i and TNFi agents and Q4W likely to provide a benefit over IL-17i agents and most TNFi agents. For both AEs & SAEs, GUS Q4W and Q8W were comparable to most other agents.

Conclusion: GUS provides joint arthritis efficacy (ACR responses and modified vdH-S score), physical function (HAQ-DI score), and safety outcomes that is comparable to most targeted PsA treatments. For PASI outcomes, GUS is considered better than most other targeted PsA treatments.

Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **I. McInnes**, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **K. Eaton**, EVERSANA, 3; **S. Peterson**, Janssen Research & Development, LLC, 3; **T. Disher**, EVERSANA, 3; **S. Chakravarty**, Janssen Scientific Affairs, LLC, 1, 3; **C. Karyekar**, Janssen Global Services, LLC, 3, Johnson & Johnson, 1, Janssen, 5; **S. Nair**, Janssen Pharmaceutica NV, 1, 3; **W. Boehncke**, Janssen Research & Development, LLC, 2, 5; **C. Ritchlin**, None.

Abstract Number: 0335

Interleukin-17 Blockade Leads to Shifts from Stage-based Towards Response-based Disease Clusters- Comparative Data from Very Early and Established Psoriatic Arthritis

Eleni Kampylafka[1], Koray Tascilar[2], Veronika Lerchen[3], Chistina Linz[3], Maria Sokolova[3], Ana Zekovic[3], Arnd Kleyer[2], David Simon[2], Juergen Rech[2], Michael Sticherling[1], Georg Schett[4] and Axel Hueber[3], [1]Department of Internal Medicine 3, Friedrich-Alexander University (FAU) Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany, [2]Department of Internal Medicine 3, Friedrich-Alexander University (FAU) Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Bayern, Germany, [3]Department of Internal Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander- University Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Germany, [4]Friedrich-Alexander-Universität Erlangen- Nuremberg, Erlangen, Germany

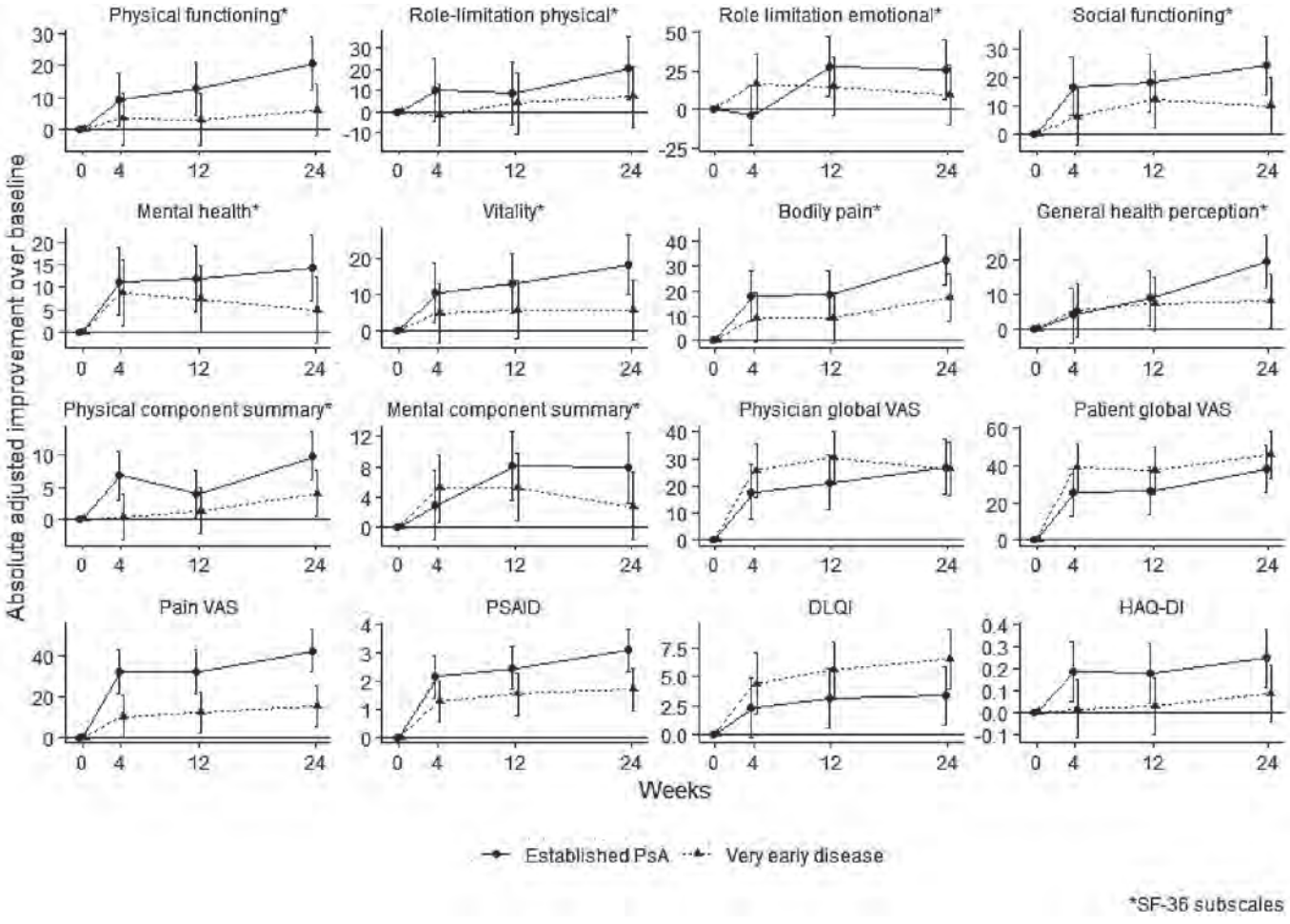
SESSION INFORMATION

Session Date: Friday, November 6, 2020

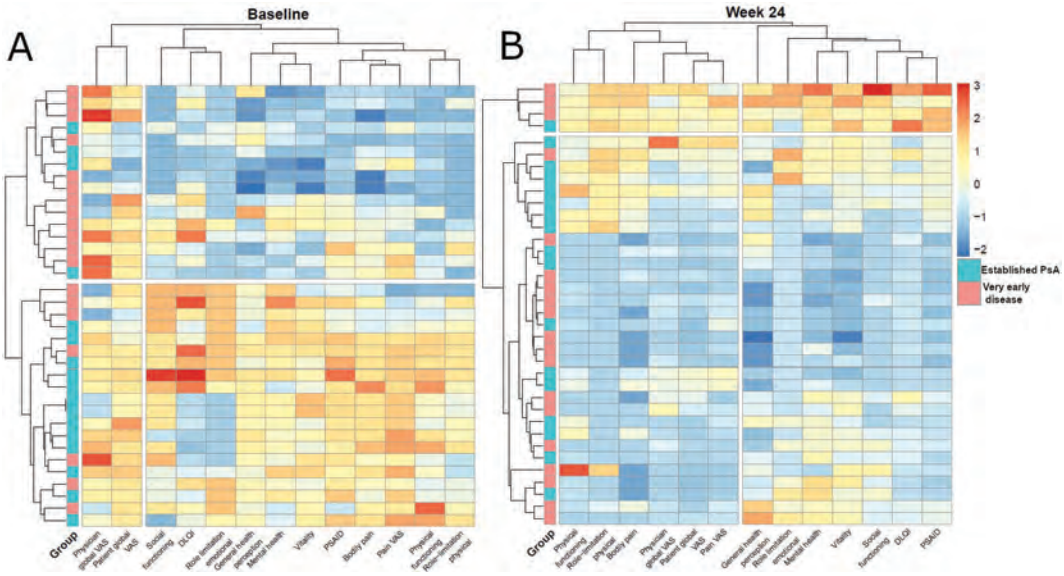
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM



Effects of secukinumab on patient-related outcomes in patients with very early disease and established psoriatic arthritis



Pre- and post-treatment patient-related outcome based cluster analysis

Background/Purpose: Limited information exists about the very early forms of psoriatic arthritis (PsA). In particular, differences and responsiveness of patient-reported outcomes (PROs) in very early disease as compared to established PsA have not been investigated to date.

Methods: Cross-sectional and prospective longitudinal evaluation of PROs related to pain (VAS pain score), physical function (HAQ-DI, SF-36 physical), mental function (SF-36 mental), impact of psoriatic skin (DLQI), joint (PsAID) and global disease (VAS global) in two small prospective observational studies on secukinumab 300 mg therapy over 6 months in 20 very early disease patients (1) and 20 established PsA patients (2). Adjusted changes from baseline were estimated using linear mixed models. We performed a cluster analysis of centered and scaled PROs at baseline and 24-weeks of follow-up using Euclidean distances.

Results: While responses in pain and physical activity-related PROs to secukinumab were more pronounced in established PsA than very early disease, effects on PROs related to general health perception, as well as those related to emotional and mental well-being, were modified in a similar way in very early disease and established PsA. The absolute adjusted improvement over baseline for the specific PROs for the 2 groups of patients is presented in figure 1. Cluster analysis based on global disease activity assessment and PROs showed that baseline clusters reflected very early disease and established PsA, while during interleukin-17 inhibition these clusters were abolished and new clusters based on differential responses to physically and mentally-oriented PROs formed (figure 2).

Conclusion: Inhibition of IL-17A leads to comprehensive improvement of PROs in patients with very early musculoskeletal involvement in PsA. Most importantly, treatment restructures original clusters based on the stage of psoriatic disease and leads to the formation of clusters that reflect their post-treatment state in physical and mental-orientated PROs.

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2. Kampylafka E *et al*: Disease interception with interleukin-17 inhibition in high-risk psoriasis patients with subclinical joint inflammation-data from the prospective IVEPSA study. *Arthritis research & therapy* 2019, 21(1):178.

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Abstract Number: 0336

Anxiety and Depression in Psoriatic Arthritis (PsA) - Prevalence and Impact on Patient Reported Outcomes: Real-World Survey in the US and Europe

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Anxiety and depression are comorbidities among PsA patients. The impact of anxiety and depression on outcomes in PsA patients has not been characterized in a real-world clinical setting. The objective of this study was to describe the prevalence of anxiety and/or depression in PsA patients, assess concordance in reported anxiety and/or depression between patients and physicians, and compare clinical and patient reported outcomes (PROs) in patients who report anxiety and/or depression and those who do not.

Methods: A cross-sectional study among patients with PsA recruited by rheumatologists and dermatologists was conducted in France, Germany, Italy, Spain, UK and US. Data were collected Jun-Aug 2018 via physician-completed patient record forms and patient self-completed forms. Physicians reported patient demographic, disease characteristics and diagnosed anxiety and/or depression. Patients reported experience of PsA-related anxiety and/or depression, quality of life [QoL] (EQ5D-5L), work productivity (WPAI), disability (HAQ-DI), and disease impact

Table 1 Demographic and clinical characteristics by patient-reported anxiety and/or depression

	No anxiety and/or depression (n=436)	Anxiety and/or depression (n=252)	P value
Demographic characteristics			
Age, mean (SD)	47.7 (12.1)	49.1 (12.6)	0.13
Female, n (%)	196 (45.0)	146 (57.9)	<0.01
BMI, mean (SD)	26.7 (5.1)	26.9 (4.4)	0.57
Caucasian, n (%)	408 (93.3)	238 (94.4)	0.46
Working full time, n (%)	293 (68.6)	107 (44.8)	<0.01
Biologic tx, n (%)	257 (58.9)	160 (63.5)	0.26
Disease characteristics			
Years since diagnosis, mean (SD)	5.7 (6.0)	6.9 (7.7)	0.04
Physician-perceived Current overall severity*, n (%) -Mild -Moderate -Severe	 277 (63.5) 145 (33.3) 14 (3.2)	 137 (54.4) 106 (42.1) 9 (3.6)	0.02
Current BSA %, mean (SD)	8.7 (12.3)	6.4 (8.2)	0.02
66 swollen joint count, mean (SD)	2.7 (3.6)	5.6 (10.4)	<0.01
68 tender joint count, mean (SD)	3.8 (4.3)	6.0 (6.2)	<0.01

Table 2. Impact of anxiety or depression on PROs*

	With or without anxiety and/or depression	Difference in predicted PRO value with anxiety and/or depression [α]	P value
EQ5D utility score, mean N=488	Without (ref) With	0.83 -0.10	<0.01
WPAI percentage overall work impairment, mean N=262	Without With	22.3 +7.4	<0.01
HAQ-DI score, mean N=480	Without With	0.53 +0.26	<0.01
PsAID12 score, mean N=482	Without With	2.32 +1.78	<0.01

* Adjusted for age, gender, employment status, BMI, no. of joints affected and BSA

[α] PRO key for worse outcome (range): EQ5D utility (0-1.0) = lower; EQ5D VAS (1-100) = lower; WPAI (0-100) = higher; HAQ-DI (0-3) = higher; PsAID12 (0-10) = higher.

(PsAID12). Patients were compared according to patient reported anxiety and/or depression using parametric tests and non-parametric tests. Multivariate regressions explored impact of anxiety and/or depression on PROs. Models adjusted for age, gender, employment status, BMI, no. of joints affected, body surface area (BSA).

Results: Data were collected from 688 physician-patient pairs (524 EU; 164 US). Physicians reported anxiety and/or depression in 14.2% of patients (EU 13.3%; US 16.2%), while 36.6% (EU 36.3%; US 37.8%) of patients self-reported anxiety and/or depression. 71.4% of physician-patient pairs agreed on anxiety and/or depression presence

or absence (Kappa = 0.31, fair agreement). Patients with anxiety and/or depression had worse QoL, higher work impairment, and greater disability (Table 2).

Conclusion: After adjusting for demographic and clinical factors, patients with anxiety and/or depression were found to have worse QoL, work productivity, and disability outcomes than those without. Differences between patient and physician reports of anxiety and/or depression suggest that physicians may not be aware of the extent to which PsA patients experience anxiety and/or depression.

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Abstract Number: 0337

Similar Impact of Psoriatic Arthritis and Rheumatoid Arthritis on Objective and Subjective Parameters of Hand Function

Anna-Maria Liphardt[1], Eva Manger[2], Sonja Liehr[2], Lisa Bieniek[2], Arnd Kleyer[3], David Simon[3], Koray Tascilar[3], Michael Sticherling[4], Juergen Rech[3], Georg Schett[5] and Axel Hueber[6], [1]Friedrich-Alexander-University Erlangen-Nuremberg, Internal Medicine 3 - Rheumatology & Immunology, University Hospital Erlangen, Erlangen, Bayern, Germany, [2]Departement of Internal Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander-University Erlangen-Nuremberg and University Hospital Erlangen, Erlangen, Bayern, Germany, [3]Department of Internal Medicine 3, Friedrich-Alexander University (FAU) Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Bayern, Germany, [4]Department of Internal Medicine 3, Friedrich-Alexander University (FAU) Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany, [5]Friedrich-Alexander-Universität Erlangen- Nuremberg, Erlangen, Germany, [6]Sozialstiftung Bamberg, Sektion Rheumatologie, Bamberg, Germany

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: To compare the impact of psoriatic arthritis (PsA) and rheumatoid arthritis (RA) on objective and subjective parameters of hand function.

Methods: Hand function was assessed by (i) vigorimetric grip strength, (ii) Moberg picking up test (MPUT) and (iii) self-reported hand function (Michigan Hand Questionnaire, MHQ). Mixed effects linear regression models were used to test the relation of hand function with age, sex and disease group.

Results: 299 subjects were tested, 101 with RA (Age: 59.1 ± 13.3 years, BMI: 27.2 ± 5 kg/m^2), 92 with PsA (Age: 58.8 ± 11.6 years, BMI: 29 ± 6.1kg/m^2) and 106 non-arthritic controls (51 with Pso (Age: 47.3 ± 14.1 years, BMI: 29.8 ± 7.3 kg/m^2) and 55 healthy controls (HC, Age: 54.6 ± 16.5 years, BMI: 25.2 ± 3.3 kg/m^2). Grip strength as a measure of muscle force (lbf) was lowest in RA patients (57.9(31)), followed by PsA (72.8(34.7)), Pso (80.4(34.1) and HC (84.1(24.9)) respectively. MPUT (seconds) of the dominant hand was best in HC (11.5(2.3)), followed by Pso patients (14.7(4.6)), PsA (16.4(8.5)) and RA (18.2(21.6)). Group means for self-reported hand function score by MHQ ranged

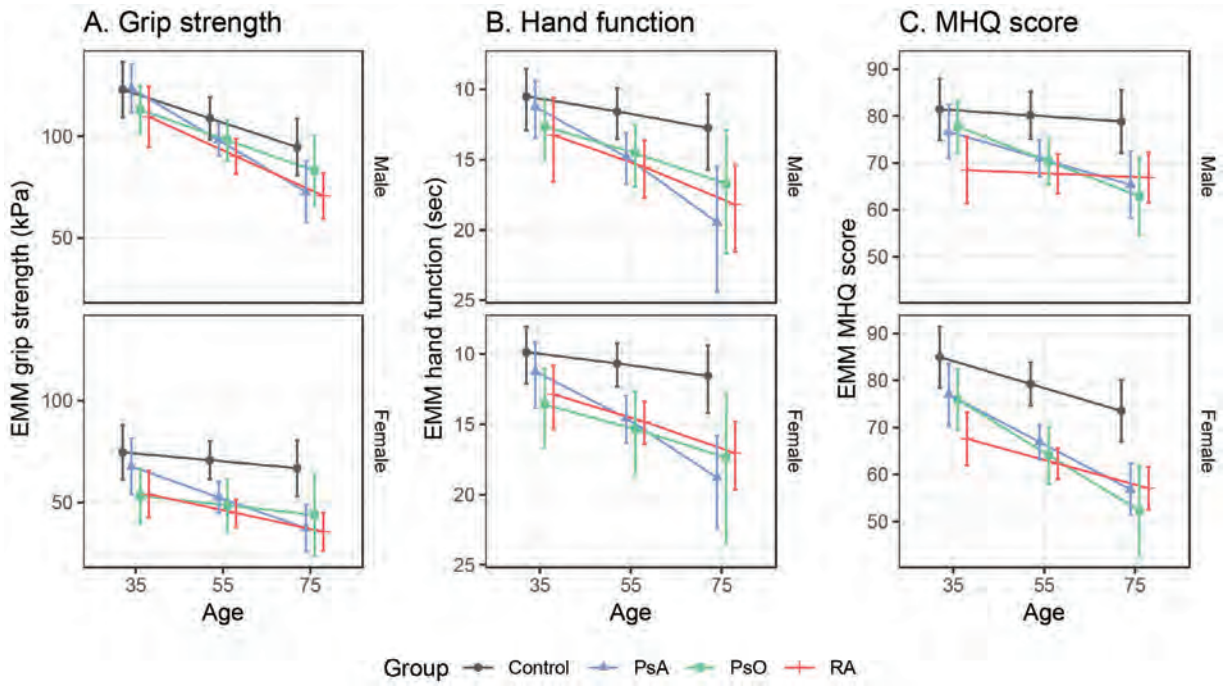

Figure 1. Estimated marginal means with multiplicity-adjusted 95% confidence intervals for psoriatic arthritis patients (PsA), rheumatoid arthritis patients (RA), psoriasis patients (PsO) and healthy controls (HC) at ages 35, 55 and 75 by gender and dominant hand.

between 77.2 (HC) and 63.8 for RA patients. Regression analysis showed that grip strength was affected by sex, age and disease group ($p < 0.001$ for all) with higher values but also greater decline with increasing age in male individuals (Figure 1A). PsA, RA and unexpectedly also psoriasis lowered grip strength in females, while in males only modest disease-related reductions of grip strength were observed. Fine motor skills as assessed by MPUT remained remarkably stable in healthy subjects during age. However, they significantly dropped with age in RA, PsA and interestingly also in psoriasis patients ($p < 0.001$ for the interaction of MPUT with age and disease Group, Figure 1B). Self-reported hand function was assessed by MHQ. Regression analysis showed that MHQ is significantly affected by age, disease status and hand dominance ($p < 0.001$ for all). The effect of disease on the MHQ increased with age and was more pronounced in females. Estimated marginal mean MHQ incrementally deviated from controls in PsA and psoriasis with increasing age, whereas in RA self-reported hand function was already low in younger subjects (Figure 1C).

Conclusion: In conclusion, the impact of PsA on hand function is similar to RA and affects muscular force, fine motor skills and self-perception of hand function. The burden of disease on hand function increased with age and affects both sexes and both hands. In addition, hand function is impaired already in psoriasis patients suggesting intrinsic functional musculoskeletal alterations in psoriatic disease, which occur independently from PsA.

Disclosure: A. Liphardt, Novartis Pharma GmbH, 2, Abbvie Deutschland GmbH & Co KG, 8, Meda Pharma GmbH & Co KG, 5; **E. Manger**, None; **S. Liehr**, None; **L. Bieniek**, None; **A. Kleyer**, Lilly, 8, Novartis, 8, BMS, 8, Sanofi, 8, Gilead, 8; **D. Simon**, Novartis, 8, Lilly, 5, 8, Janssen, 8, AbbVie, 5; **K. Tascilar**, None; **M. Sticherling**, Novartis, 2, 5, 8, Abbvie, 5, 8, Celgene, 5, 8, Janssen, 5, 8, 9, Pfizer, 8, Leo, 5, 8, Lilly, 5, 8, Sanofi, 5, 8; **J. Rech**, Abbie, Biogen, BMS, Chugai, Celgene, EliLilly, Gilead, GSK, Janssen, MSD, Novartis, Roche, Sanofi, Sobi, UCB, 5, 8; **G. Schett**, None; **A. Hueber**, Abbvie, 5, 8, BMS, 8, Gilead, 5, GSK, 5, 8, Janssen, 5, 8, Roche/Chugai, 5, Lilly, 2, 5, 8, Novartis, 2, 5, 8.

Abstract Number: 0338

Increased Risk of Lymphoproliferative Disorders in Psoriatic Arthritis

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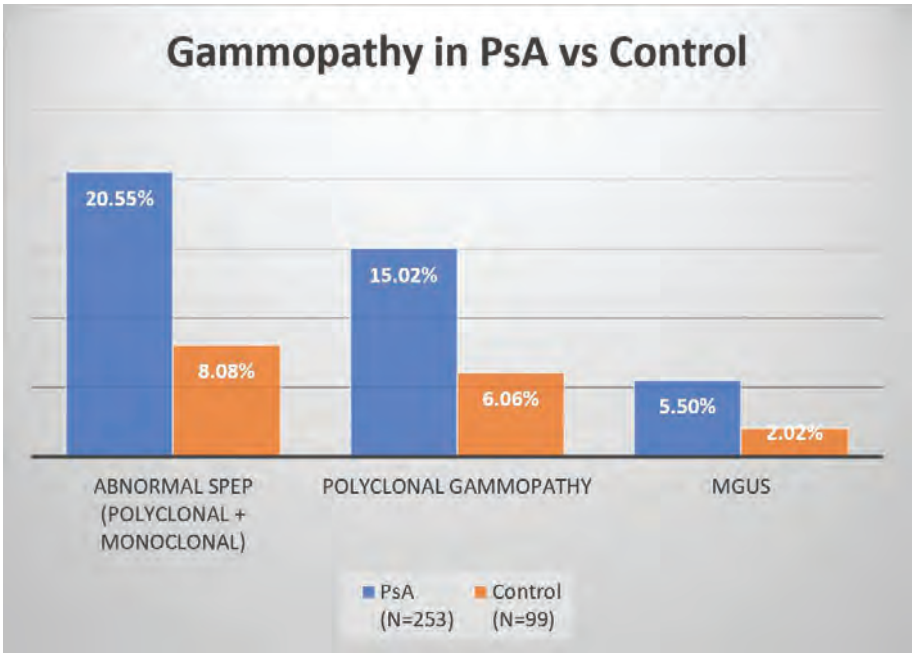
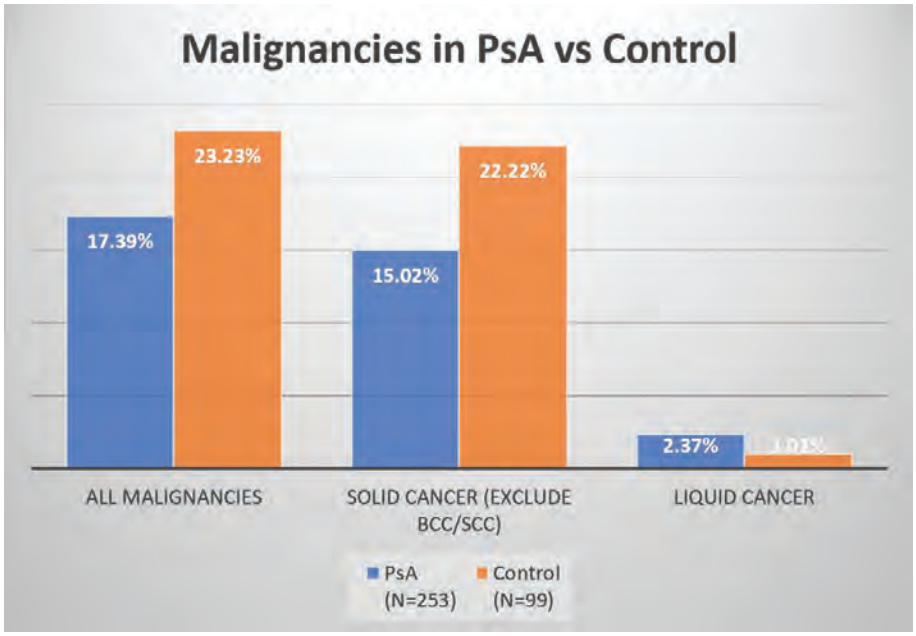
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a systemic inflammatory disease that involves musculoskeletal and skin manifestations. Such autoimmune disease has been associated with increased lymphoproliferative disease risk, which is thought to be due to abnormal immune activation and/or continual exposure of systemic immunosuppressive therapies. Such risk is well established in psoriasis but is still unclear in PsA. This study was undertaken to investigate the risk of developing lymphoproliferative disorders among patients with PsA.

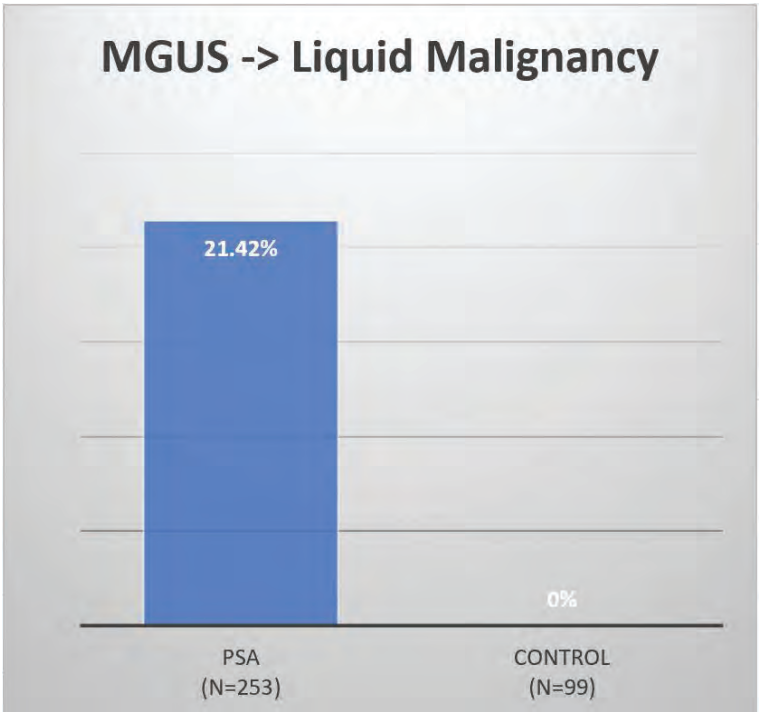
Methods: A multicenter retrospective study involving two Veterans Affairs (VA) Hospitals in Southern California, namely Long Beach and Greater Los Angeles, was performed. Patients with PsA were assembled using the ICD 9 and 10 coding from 2000 to 2019 (n=253) compared against controls (n=99) without autoimmune diseases that were matched in age, sex and race. Outcome measures were the number of patients who developed malignancies (excluding skin basal cell carcinoma and squamous cell carcinoma) and the number who had abnormal serum protein electrophoresis (SPEP). The Odds Ratio (OR) for developing abnormal SPEP, including polyclonal and monoclonal gammopathy (MGUS), as well as solid and liquid cancers (lymphoma or leukemia) were calculated. Additionally, the percentage of MGUS patients progressing to develop lymphoproliferative malignancies was compared.



The risk of developing abnormal SPEP and polyclonal gammopathy were both significantly higher in PsA patients compared to controls with $p<0.05$. The prevalence of MGUS was 5.5% among PsA patients, while 2% among controls, with p value close to but not statistically significant.



There was no significant difference in the risk of developing malignancies in PsA patients vs controls. However, we observed a trend of slightly higher liquid cancer risk in PsA patients, but not solid tumors.



Among PsA patients with MGUS, approximately 20% eventually developed lymphoproliferative cancers but none in the controls. However, the sample size was too small to reach statistical significance.

Results: PsA patients were at least twice more likely to develop abnormal SPEP (OR 2.36, CI 1.08-5.15), and in particular, polyclonal gammopathy (OR 2.74, CI 1.12-6.70), compared to controls. The prevalence of MGUS was 5.5% in PsA patients versus 2.0% in controls (OR 2.84, CI 0.63-12.74). There was no significant difference in the risk of developing any kind of malignancies, however there was a trend of a slightly higher number of PsA patients with liquid

cancers than solid tumors. Among PsA patients with MGUS, approximately 20% eventually developed lymphoproliferative cancers but none in the controls. However, the sample size was too small to reach statistical significance.

Conclusion: PsA patients have a higher risk of developing polyclonal gammopathy, likely due to abnormal immune activation of the disease and chronic inflammation. More PsA patients developed MGUS, and possibly with an increased propensity to progress to lymphoproliferative malignancy, which requires validation with a larger cohort. Additional studies on immunosuppressive therapies, disease activity and inflammatory markers are underway to elucidate their correlation with lymphoproliferative cancer risk in PsA patients. Malignancy screening by SPEP on a regular basis may be beneficial to PsA patients, especially for those who have MGUS.

Disclosure: E. Chen, None; **M. Wong**, None.

Abstract Number: 0339

Is Sex-adjusted Treatment in Early-PsA Justified?

Evangelia Passia[1], Jolanda Luime[1], Marc Kok[2], Ilja Tchetverikov[3], Marijn Vis[4], Fouchia Fodili[5], Yvonne Ruiterman[6] and Lindy-Anne Korswagen[7], [1]Erasmus MC, Rotterdam, [2]Maasstadziekenhuis, Rotterdam, [3]Albert Schweitzer Ziekenhuis, Dordrecht, [4]Erasmus UMC, Rotterdam, Netherlands, [5]RZWN, Roosendaal, [6]HAGA ziekenhuis, Den Haag, [7]Franciscus Gasthuis, Rotterdam

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: According to existing knowledge, the prevalence of psoriatic arthritis (PsA) is equal in men and women, however, women experience a higher burden of disease (pain, disability and fatigue). Recently we showed that women with newly diagnosed PsA present higher disease activity, pain and functional impairment compared to men at baseline but also at one year of follow up. Several reasons could be incriminated for the observed differences and their persistence over time. One of them could be a different therapeutic approach, maybe less aggressive, in women compared to men.

To compare applied treatment in female and male patients with early PsA.

Methods: Data were used from the Dutch south west Psoriatic Arthritis Cohort (DEPAR) which includes newly diagnosed PsA patients. Data on disease activity, medication use and patient reported outcomes is gathered at baseline and from then, during the first year, every 3 months. Exposure time (days), cumulative and mean dose per dosing interval during the first year were calculated for each conventional DMARD (csDMARD). Exposure time for biological DMARDs (bDMARDs), as a group was also calculated. T-tests and Kruskal Wallis tests were used for the comparison across sexes. Stata 16 was used for statistical analysis.

Results: In February 2019, 615 patients were available for analysis, 304 men and 311 women (51%), average age of 50 (SD 13.6) years. Oligoarthritis was the most frequent phenotype (39%), more frequently present in men (44%) than in women (33%). Polyarthritis (23%) was more prevalent in women. 523 patients had 12 months of follow-up, while the remaining 92 participated a mean 223 days in the study. Over the first year, 75% of the patients received one or more DMARDs for which the majority (82%) started within the first month after diagnosis. Not using DMARDs was equally present in both sexes. Monoarthritis was the phenotype less frequently treated by DMARDs (50%).

		Men (n=304)				Women (n=311)				
		n	p25	p50	p75	n	p25	p50	p75	p-value
Biological	days	42	106	212	319	39	83	160	260	0.10
Methotrexate	days	216	208	354	365	215	174	336	365	0.05[t]
	cumulative dose (mg)		541	809	1172		423	770	1132	0.03[t]
	dose		15	20	24		15	20	24	0.14[t]
Sulfasalazine	days	36	149	289	319	52	43	97	277	0.002
	cumulative dose (mg)		258000	549500	614000		34250	174000	433000	0.001
	dose		1741	1931	2000		1000	1925	2000	0.35
Hydroxychloroquine	days	11	24	173	289	34	116	270	344	0.13
	cumulative dose (mg)		9600	69200	115600		39600	88600	137600	0.30
	dose		400	400	400		400	400	400	0.54
Leflunomide	days	22	100	197	281	37	50	126	212	0.06
	cumulative dose (mg)		1740	2610	4940		900	2020	2775	0.07
	dose		10	20	20		10	17	20	0.59
Prednisone	days	32	34	98	171	51	38	89	183	0.66
	cumulative dose (mg)		648	1208	1820		420	814	1480	0.20
	dose		8	11	20		7	8	15	0.06

Table 1. DMARD medication frequency, median days of exposure, cumulative dose and dose per dosing interval in the first year after PsA diagnosis stratified by sex. *non-parametric comparison between men and women. t parametric t-test for comparison between men and women

Results are shown in table 1. Methotrexate was the most frequently used drug during the first year. Its frequency (70%) and dosing (median 20 mg/week) were similar for men and women.. Women received methotrexate for a shorter period (median 270 vs 290 days) and subsequently had a lower cumulative dose compared to men. Sulfasalazine, leflunomide, hydroxychloroquine and corticosteroids were more frequently prescribed in women compared to men. Retention time of sulfasalazine was substantial shorter in women. Number of days on bDMARDs was lower for women (n=39, median 160 days), but not significantly different from men(n=42, median 212 days), mainly caused by a later start of bDMARDs in women.

Conclusion: 75% of early Psoriatic Arthritis patients in DEPAR were treated by DMARDs in the first year after diagnosis. Initial treatment strategies were similar in both sexes. However, over time women received methotrexate for a shorter period, were more often switched to other csDMARDs and started later with bDMARDs. Retention time for the other csDMARDs was shorter in women. These observations raise the question whether optimal therapeutic strategies are in place for women with early PsA.

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Abstract Number: 0340

Neuropathic Pain Relationship with Comorbidity in Psoriatic Arthritis Patients and Its Influence on Disease Activity

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In psoriatic arthritis (PsA) peripheral nociceptive pain is characteristic, and is trigger by the activation of the afferent sensory fibers in the inflamed synovial membrane. The greatest ability to respond to pain in the presence of inflammation is physiological, however, pain hypersensitivity may persist after inflammation has resolved and perpetuate itself as chronic pain, a mechanism in which central hypersensitivity is involved. Inflammatory activity indices include subjective variables related to pain perception, so central hypersensitivity can overestimate disease activity. For this reason, identifying possible underlying pain mechanisms can be of great importance in clinical decision-making. Purpose: To relate the presence of neuropathic pain with disease activity and impact, and to analyze the influence of comorbidity on neuropathic pain.

Methods: Cross-sectional study of 246 PsA patients (diagnosed with CASPAR criteria). Patients with fibromyalgia, depression, anxiety or diabetes were excluded. The PAINDETECT questionnaire was used to identify neuropathic pain and to classified patients into 3 groups: a score ≥ 19 indicated a high probability of pain with a neuropathic component, between 18 and 13 was ambiguous and ≤ 12 possibly ruled out this type of pain. Disease activity was measured by DAPSA index, ESR and CRP. The therapeutic objective was the minimal disease activity (MDA) and to assess disease impact PsAID questionnaire was used. Regarding comorbidities anxious and/or depressive habit were assessed using the Hospital Anxiety and Depression Scale (HADS), fatigue (item 2 of PsAID), sleep quality by the Insomnia Severity Index (ISI) and waist-to-hip ratio, apolipoprotein A, apolipoprotein B, lipoprotein A, C-peptide, insulin, insulin resistance (HOMA) and leptin were also measured.

Results: Of the 246 patients 44.7% were female and the mean of age was 53.45 years (SD: 11.00). The average disease duration was 10.3 years (SD: 7.47). 64.6% were taking synthetic DMARDs and 14.6% were receiving biological therapy. 24.8% were in remission by DAPSA and 39.4% achieved MDA. According to the PAINDETECT questionnaire

Table 1.

	PAINDETECT≥19	PAINDETECT≤12	P
Gender (M/F)	12/30(28,6%)	104/60(63,4%)	0,001
MDA (Yes/No)	8/34(19%)	83/81(53%)	0,001
DAPSA(≤4) (Yes/No)	1/41(2,4%)	40/123(24,5)	0,001
Pain	6,26(2,28)	2,50(2,39)	0,001
HAQ	1,16(0,59)	0,47(0,53)	0,001
Tender joint count	2,73(2,42)	1,40(1,94)	0,002
MASES Index	2,52(2,71)	0,82(1,44)	0,001
Fatigue	6,26(2,26)	3,70(2,49)	0,001
ISI	14,54(6,12)	7,34(4,99)	0,001
Anxiety	9,85(3,71)	5,89(3,97)	0,001
Depression	7,61(4,10)	3,99(3,46)	0,001
PsAID	6,13(1,75)	2,66(1,95)	0,001
Leptin (ng/mL)	34,26(36,20)	14,21(13,56)	0,001

17.1% of patients had neuropathic pain and 66.7% didn't. Table 1 shows the significant variables related to neuropathic pain.

In the multivariate analysis composed of gender, ISI, HADS, fatigue, leptin and obesity, the variables that influenced the presence of neuropathic pain were fatigue $p < 0.003$ (OR: 1.34, 95% CI: 1,10-1.62), sleep quality $p < 0.001$ (OR: 1.20; 95% CI: 1.10-1.32) and leptin $p < 0.008$ (OR: 1.03; 95% CI: 1.008-1.052). Nagelkerke's $R2 = 0.51$.

Conclusion: PsA patients with neuropathic pain have higher probability of not achieving MDA or remission measured by DAPSA. More intense pain, greater number of entheses and tender joints were the main reasons. Therefore, neuropathic pain assessment in our patients may have therapeutic implications. Sleep quality and fatigue influenced the presence of neuropathic pain, and these processes (secondary to central hypersensitivity) were associated to PsA and not to other diseases such as fibromyalgia. As described in animal models, leptin levels could mediate in the presence of chronic pain.Table 1.

Disclosure: M. Acosta, None; **O. Compán**, None; **S. Pastor**, None; **G. Manzano Canabal**, None; **L. Gomez-Lechon Quiros**, None; **C. Hidalgo Calleja**, None; **O. Martinez Gonzalez**, None; **A. Turrión**, None; **J. Del Pino-Montes**, None; **C. Montilla Morales**, None.

Abstract Number: 0341

Metabolomics Profiling of Human Serum for Discovering Biomarkers to Diagnose Psoriatic Arthritis and Ankylosing Spondylitis with High Specificity

Wei Han[1], Xiaohang Wang[1], Liang Li[1], Stephanie Wichuk[2], Edna Hutchings[3], Rana Dadashova[3], Joel Paschke[3] and Walter Maksymowych[2], [1]Department of Chemistry, University of Alberta, Edmonton, AB, Canada, [2]University of Alberta, Edmonton, AB, Canada, [3]CARE Arthritis, Edmonton, AB, Canada

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In this work, we applied a high-performance chemical isotope labeling (CIL) LC-MS platform to search for biomarker candidates of PsA and AS in human serum samples. We aimed to identify metabolite biomarkers with high discriminatory power for PsA and AS versus rheumatoid arthritis and healthy controls.

Methods: Serum samples were collected from 331 subjects, including 100 healthy controls, 48 PsA patients, 52 AS patients and 131 RA patients. The average age of each group was: 52.6 (control), 50.7 (PsA), 51.8 (AS) and 53.1 (RA) years. After pre-treatment, each sample was incubated with ^{12}C-dansyl chloride, which can label the amine/phenol-containing metabolites. The reference sample for relative quantification was prepared by mixing all individual samples and then labeled by ^{13}C-dansyl chloride. With this normalization, the individual samples and the reference sample were mixed at an equal amount. Finally, we used an LC-QTOF-MS platform to analyze the mixtures and measure the ^{12}C/^{13}C peak pairs.

Results: We detected 1,149 peak pairs commonly existing in the serum samples. Using our dansyl-library of 700 dansyl-labeled standards and a prediction library, which contains the predicted retention times and mass values of

3,431 dansylated human metabolites, we identified 134 and 141 peak pairs, respectively. The relative concentrations are calculated from the intensity ratios of $^{12}C/^{13}C$ peak pairs. We first visualized the entire amine/phenol-submetabolome for all phenotypes using the partial least squares discriminant analysis (PLS-DA). We found that the most significant between-group separation was between healthy controls and all the patients. No significant sex or age effect was observed. Furthermore, among the three diseases, PsA and AS samples were closely clustering, while the RA group was well separated from them. Therefore, we chose a two-step diagnosis approach that first differentiates PsA patients from controls/RA patients and then filters out the AS patients wrongly classified as PsA in the first step. The same strategy was conducted for AS. Stipulating a fold change larger than 1.5 with the false discovery rate lower than 5%, we found 74 metabolites having significantly higher or lower concentrations in the PsA group compared to the control or the RA group. We selected two of these significant metabolites to build a classification model based on the linear support vector machine (SVM) method, and the area-under-the-curve (AUC) value of the resulting receiver operating characteristic (ROC) curve was 0.929 (95% confidence interval: 0.899-0.956). Similarly, 37 metabolites could differentiate AS samples from RAs and controls. A proposed diagnostic panel containing four metabolites demonstrated an AUC value of 0.890 (0.843-0.934). For the last step, distinguishing between PsA and AS, there were 15 significantly increased metabolites and 9 lowered ones. The biomarker panel consisting of the top three metabolites also achieved good discriminatory power with AUC = 0.827 (0.717-0.919).

Conclusion: Isotope-labeling-LC-MS-based metabolomics has revealed biomarker candidates that can specifically differentiate PsA or AS patients from control populations.

Disclosure: W. Han, None; **X. Wang**, None; **L. Li**, None; **S. Wichuk**, None; **E. Hutchings**, None; **R. Dadashova**, None; **J. Paschke**, None; **W. Maksymowych**, CARE Arthritis Limited, 9, AbbVie, 2, 5, 8, Boehringer Ingelheim, 5, Celgene, 5, Eli Lilly, 5, Galapagos, 5, Janssen, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 0342

Multimorbidity Clusters in Psoriatic Arthritis: A Population-Based Study

Paras Karmacharya[1], Dilli Poudel[2], Cynthia Crowson[3], John Davis[4], Kerry Wright[4] and Alexis Ogdie[2], [1]Mayo Clinic, Rochester MN, ROCHESTER, MN, [2]University of Pennsylvania, Philadelphia, PA, [3]Mayo Clinic, Rochester, Minnesota, USA, Rochester, MN, [4]Mayo Clinic, Rochester, MN

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) patients have a higher prevalence of cardiometabolic and other morbidities compared to the general population. Studies suggest that a single clinical variable cannot adequately predict which PsA patients will have worse outcomes; therefore studying these morbidities together will provide better insight. Multimorbidity refers to the simultaneous presence of ≥2 morbidities, and certain morbidities are more likely to cluster than others. We used The Health Improvement Network (THIN) database to identify prevalent multimorbidity clusters in PsA.

Methods: We used the THIN database (2000-14) to identify adults (aged 18–89 years) with PsA using the Read code for PsA (positive predictive value- 85%). THIN contains systematically and prospectively recorded data by general practitioners in the UK. Morbidities in PsA were selected by clinical relevance and by previous reports, and only those occurring ≥1% were included. Multimorbidity clusters were identified using K-median clustering, which is an

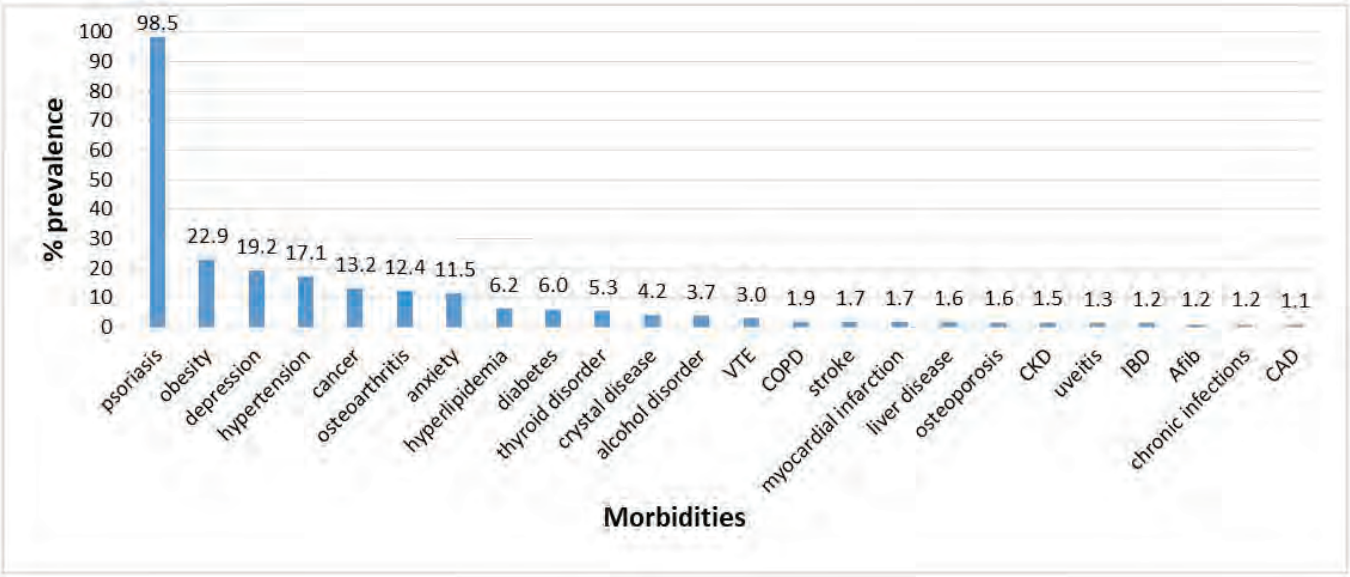

Figure 1. Prevalence of morbidities in psoriatic arthritis

unsupervised machine learning algorithm which groups data into a user-specified number (k) of clusters based on a set of variables (here morbidities). The optimal number of clusters was determined using the elbow method. K-median clustering was run on the dataset for a range of values of k (e.g., k from 1 to 10); and for each value of k, sum of squared errors (SSE) was calculated. In a scree plot of the SSE for each value of k, we identified the "elbow" on the arm (graph line), which was taken as the best value of k.

Results: There were 14,560 PsA patients identified in the THIN database from 2000-14, with a mean age of 47 ±15 years and 50% males. Psoriasis was the most prevalent morbidity (98.45%), followed by obesity (22.9%) and depres-

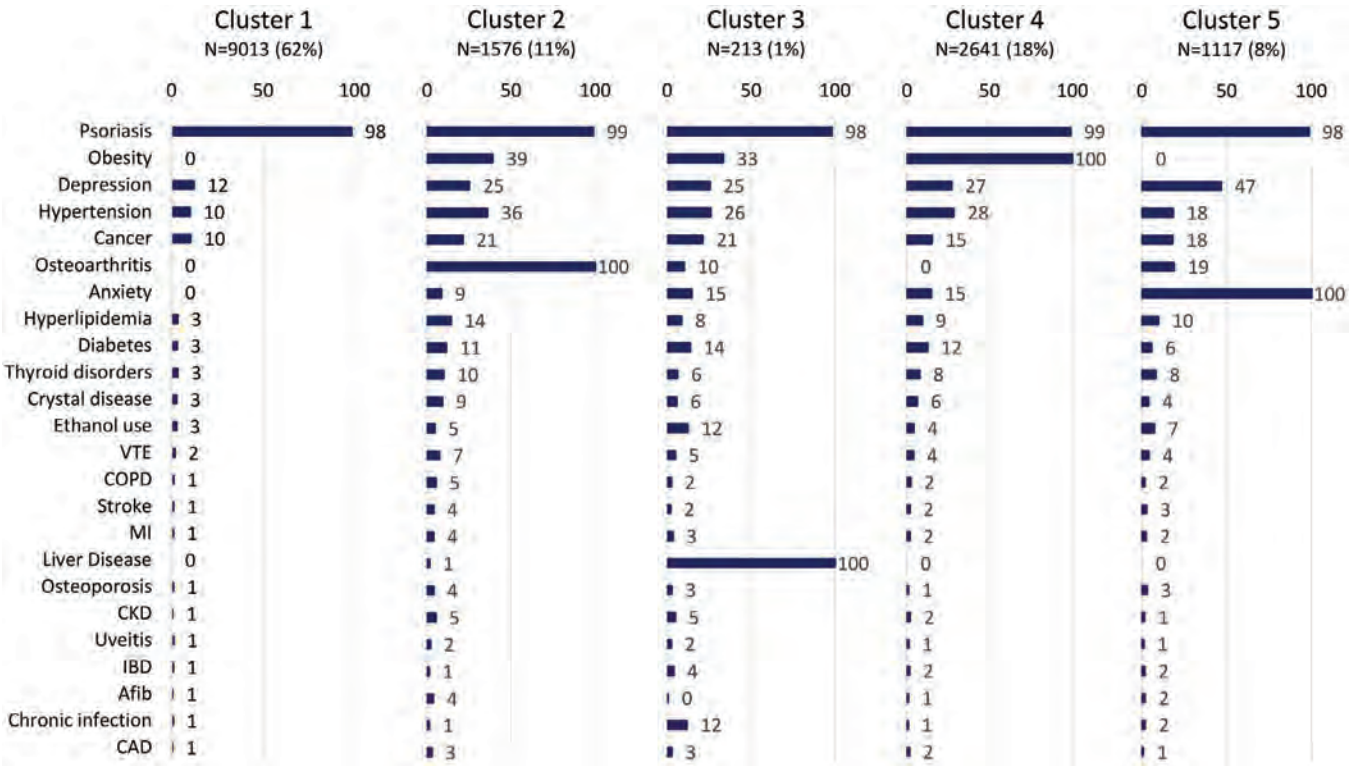

Figure 2. Multimorbidity clusters in psoriatic arthritis

sion (19.2%) (Figure 1). The optimal number of clusters determined using the elbow method was 5. The five clusters included relatively healthy (62%), osteoarthritis (11%), liver disease (1%), obesity (18%), and anxiety/depression (8%) (Figure 2). Males had higher odds of being in the anxiety/depression (OR=2.11, 95% CI 1.86 to 2.40), obesity (OR=1.54, 95% CI 1.41 to 1.68), and osteoarthritis (OR=1.47, 95% CI 1.32 to 1.64) clusters compared to the healthy cluster.

Conclusion: Distinct multimorbidity clusters were identified in PsA patients in the THIN database. Further research is needed to look for common pathophysiologic mechanisms within each clusters and comparison with the general population. The identified clusters could have different effects on important outcomes in PsA.

Disclosure: P. Karmacharya, National Center for Advancing Translational Science, 2, SPARTAN (Spondyloarthritis Research and Treatment Network), 2; **D. Poudel**, None; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1; **J. Davis**, Pfizer, 2, AbbVie, 5, 8, Sanofi-Genzyme, 5, 8; **K. Wright**, None; **A. Ogdie**, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1.

Abstract Number: 0343

Co-expression of DC-STAMP and CX3CR1: Biomarkers for Tissue Resident Osteoclasts in Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) patients often experience joint damage mediated by osteoclasts (OC). Although PsA pathogenesis is poorly understood, the production of the cytokines IL-17, IL 23, and TNF are implicated in disease initiation and progression. TNF and IL-17 induce the expression of CX3CR1 and the CX3CR1-Fractalkine (FKN) axis promotes inflammation and bone damage in rheumatoid arthritis (RA). In addition, a tissue-resident OC that expresses CX3CR1 was identified in murine arthritis and RA synovial tissue[1]. Dendritic Cell-Surface Transmembrane Protein (DC-STAMP) is expressed on OC precursors (OCP). We found that DC-STAMP$^{-/-}$ mouse fibroblasts exposed to TNF do not secrete FKN and that DC-STAMP$^{-/-}$ x TNFTg arthritic mice show impaired migration of CX3CR1^{+} monocytes to joints. The purpose of this study is to identify whether DC-STAMP and CX3CR1 are co-expressed on OCP in the blood and synovial tissue of PsA patients.

Methods: We collected blood from 23 psoriatic (Ps) and 10 PsA patients to measure serum IL-17 and TNF by multiplex assay. We assessed the frequency of CD14^{+}CX3CR1^{+}DCSTAMP^{+} monocytes in the blood of Ps and PsA patients and controls. We used immunofluorescence to enumerate TNF and IL-17-producing cells in biopsies of non-lesional (NL) and lesional (L) skin of Ps and PsA patients, and qPCR to calculate fold changes in TNF and IL-17 mRNA expression in skin biopsies (L, NL). We enumerated DC-STAMP^{+}CX3CR1^{+} monocyte subsets in 3 synovial and 5 PsA L skin biopsies.

Results: We found low serum TNF levels (Ps, 4.6 ± 1.05 vs PsA, 13.98 ± 6.8, p=0.04), high IL-17 mRNA expression (Ps, 40-fold ± 7.6 vs PsA, 4.6-fold, p = 0.04) and an increased number of IL-17$^+$ cells in L skin of Ps patients (Ps, 31.5 ± 3.3 vs PsA, 7.0 ± 2.6, p = 0.0001). In contrast, PsA patients had higher systemic levels of TNF, lower IL-17 mRNA expression, and poor infiltration of IL-17$^+$ cells in L skin. Interestingly, we visualized higher numbers of TNF-expressing cells in PsA synovial tissue than skin. Flow cytometry analysis showed an increased frequency of CD45$^+$CD14$^+$DC-STAMP$^+$CX3CR1$^+$ circulating monocytes in PsA (2.3%), compared to Ps (0.6%) and controls (0.001%). Intriguingly, DC-STAMP$^+$CX3CR1$^+$CD14$^+$ and DC-STAMP$^+$CX3CR1$^+$ CD14$^-$ monocytes were present only in synovial tissue, while a unique subset of CX3CR1$^-$DC-STAMP$^+$CD14$^+$ cells was present in PsA but not psoriasis skin biopsies.

Conclusion: These findings highlight the divergence of TNF and IL-17 expression in the serum and skin of psoriasis and PsA patients. The co-expression of CX3CR1 and DC-STAMP present only in synovial cells supports the presence of a tissue-resident OC that arises from precursors in the skin and blood.

[1]Hasegawa T. Nat Immuno. 2019;20:1631

Disclosure: M. Garcia-Hernandez, None; **J. Rangel-Moreno**, None; **A. Paine**, None; **B. Korman**, None; **M. Nuzzo**, None; **L. Eder**, AbbVie, 2, 5, 8, Eli Lilly, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5, 8, Celgene, 5, Novartis, 5; **C. Ritchlin**, None.

Abstract Number: 0344

Use of the BASDAI in Psoriatic Arthritis Patients with and Without Axial Disease

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SESSION INFORMATION

Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster I: Psoriatic Arthritis
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) is increasingly being used to assess the activity of axial disease in patients with psoriatic arthritis (PsA). However, five out of six BASDAI questions are not specific to axial disease. The objective of this study was to evaluate the specificity of BASDAI for axial disease in PsA compared to PsA without axial disease by examining differences in baseline scores, change in scores after therapy initiation, and responsiveness between the two groups.

Methods: Participants (pts) were enrolled in the Psoriatic Arthritis Research Consortium (PARC) longitudinal observational study between 2017-Jan 2020. In this study we included PsA pts initiating therapy with a BASDAI score at baseline and follow up. Pts were classified as having axial disease if they a) fulfilled the ASAS axial spondyloarthritis (axSpA) classification criteria or b) had imaging (MRI, X-ray, or CT) features of axial disease (sacroiliac joints or spine). We descriptively report scores (BASDAI, individual BASDAI items, patient global, patient pain, and the Routine Assessment of Patient Index Data (RAPID3)) at baseline and change in scores following therapy initiation by presence or absence of axial disease.

Table 1. Baseline characteristics and disease activity measures by presence or absence of axial disease in psoriatic arthritis.

Table 1. Baseline characteristics and disease activity measures by presence or absence of axial disease in psoriatic arthritis.

	All	Peripheral only	Axial* +/- Peripheral	p-value
Age (yrs)	49 (13.7)	49.5 (13.1)	48 (15)	NS
Sex (male)	55%	49%	65%	NS
Body mass index	29.7 (6.2)	29.6 (6.1)	29.8 (6.7)	NS
Body Surface Area	1.9% (3.8)	1.2% (1.7)	3.3% (6.1)	0.04
Swollen Joint Count (0-66)	4.1 (5.2)	3.6 (4.2)	4.9 (6.8)	NS
Tender Joint C (0-68)	6.5 (7.3)	6.6 (7.1)	6.4 (7.6)	NS
Enthesitis count (0-8)**	0.7 (1.1)	0.6 (1)	0.9 (1.3)	NS
Dactylitis count (0-20)	0.2 (1.1)	0.3 (1.3)	0.2 (0.6)	NS
BASDAI (0-10)	4.9 (2.1)	4.8 (2)	5.5 (2.6)	NS
Item 1 (Fatigue)	5.3 (2.5)	5.2 (2.4)	5.4 (2.6)	NS
Item 2 (Spinal Pain)	4.8 (2.7)	4.5 (2.7)	5.2 (2.8)	NS
Item 3 (Peripheral joints)	5.2 (2.5)	5.2 (2.4)	4.5 (2.9)	NS
Item 4 (Enthesitis)	4.6 (2.7)	4.7 (2.6)	5.4 (2.7)	NS
Item 5 (AM stiffness duration)	5.2 (2.5)	5.1 (2.4)	5.7 (3.2)	NS
Item 6 (AM stiffness severity)	3.6 (3.1)	3.6 (3)	5 (2.2)	NS
Patient Global (0-10)	4.5 (2.4)	4.3 (2.3)	4.9 (2.6)	NS
Patient Pain (0-10)	5.2 (2.4)	5 (2.3)	5.7 (2.6)	NS
RAPID3 (0-30)	11.7 (5.3)	11.2 (5.2)	12.8 (5.4)	NS

*Axial PsA is defined as having met ASAS classification criteria for axSpA or having an imaging finding consistent with axial PsA.

**Enthesitis count was the Leeds Enthesitis Index plus plantar fascia insertion

Abbreviations: BASDAI = Bath Ankylosing Spondylitis Index; Chg = Change; NS = not significant (p>0.05); RAPID3 = Routine Assessment of Patient Index Data; SD = standard deviation

Table 2. Responsiveness of BASDAI by presence or absence of axial disease in psoriatic arthritis.

Table 2. Responsiveness of BASDAI by presence or absence of axial disease in psoriatic arthritis.

	All (N=117)		Peripheral only (N=77)		Axial +/- Peripheral (N=40)	
	Mean Chg (SD)	SRM	Mean Chg (SD)	SRM	Mean Chg (SD)	SRM
BASDAI	-0.81 (2.0)	-0.41	-0.88 (1.9)	-0.44	-0.75 (2.1)	-0.37
Item 1	-0.77 (2.4)	-0.32	-0.75 (2.2)	-0.34	-0.80 (2.7)	-0.30
Item 2	-0.68 (2.7)	-0.25	-0.64 (2.8)	-0.23	-0.78 (2.6)	-0.29
Item 3	-1.00 (2.7)	-0.37	-1.03 (2.7)	-0.39	-0.95 (2.8)	-0.33
Item 4	-0.8 (2.4)	-0.34	-1.00 (2.4)	-0.42	-0.43 (2.3)	-0.18
Item 5	-1.07 (2.6)	-0.41	-1.05 (2.4)	-0.43	-1.10 (2.9)	-0.38
Item 6	-0.47 (3.8)	-0.12	-0.44 (3.5)	-0.13	-0.53 (4.4)	-0.12
Patient Global	-0.60 (2.7)	-0.22	-0.46 (2.4)	-0.19	-0.90 (3.3)	-0.27
Patient Pain	-1.06 (2.7)	-0.39	-0.85 (2.5)	-0.33	-1.51 (3.0)	-0.51
RAPID3	-1.78 (5.4)	-0.33	-1.38 (5.2)	-0.27	-2.7 (5.8)	-0.46

*Axial PsA is defined as having met ASAS classification criteria for axSpA or having an imaging finding consistent with axial PsA.

Abbreviations: BASDAI = Bath Ankylosing Spondylitis Index; Chg = Change; RAPID3 = Routine Assessment of Patient Index Data; SD = standard deviation; SRM = standardized response mean.

Results: Among 117 PsA pts who initiated therapy with a BASDAI at baseline and follow up, the mean age was approximately 49 years, 55% were female, and the mean BMI was 29.7 (Table 1). Among these pts, 30 (26%) had imaging evidence of axSpA, 33 (30%) met ASAS classification criteria (7 had missing data for axSpA criteria), and 40 (34%) met one or both of these criteria. The mean baseline BASDAI score at the time of therapy initiation was 5.5 among those with axial disease by either definition and 4.8 among those without axial disease. This was similar when using either ASAS criteria or imaging evidence of axSpA. Item 2 on the BASDAI, which asks about spine pain, was higher in those with axial disease (5.2) compared to those without (4.5). Item 5 (stiffness) was higher in those without axial disease compared to those with axial disease (5.1 vs 3.7). Patient pain, patient global and the RAPID3 were slightly higher in those with axial disease.

The mean change for BASDAI was -0.81 (SD 2.0) among all pts initiating therapy and similar among axial vs peripheral only (-0.75 vs -0.83). Among the subgroup of 95 pts initiating a TNFi or IL17i, mean change in BASDAI was -0.93 (SD 2.0) with similar differences in SRMs compared to the entire group (-0.47 vs -0.41 respectively) thus only the full cohort of therapy initiators is presented. The SRMs for the individual BASDAI items varied from 0.12 (item 6) to 0.41 (item 5) (Table 2). SRMs were similar across axial vs peripheral only disease for BASDAI (-0.37 vs -0.44 respectively) and individual items. The SRMs for the patient global, patient pain, and RAPID3 however were greater among pts with axial disease (Table 2).

Conclusion: While BASDAI was initially developed as an axial disease measure and works well in axSpA, it is a broad measure of disease activity and current symptoms. The BASDAI has similar scores, change in scores, and responsiveness in PsA regardless of the presence of axial disease.

Disclosure: S. Reddy, Amgen, 5, Novartis, 5, Janssen, 5, Pfizer, 5; **M. Husni**, Abbvie, 5, BMS, 5, Janssen, 5, Pfizer, 5, Regeneron, 5, Novartis, 5, Lilly, 5, Pfizer, 2, PASE questionnaire, 7, National Psoriasis Foundation, 6; **J. Scher**, UCB, 5, Janssen, 5, Abbvie, 5, Pfizer, 5, Novartis, 5, Sanofi, 5; **E. Craig**, None; **A. Ogdie**, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1; **J. Walsh**, Pfizer, 2, AbbVie, 2, 5, Eli Lilly, 5, UCB, 5, Janssen, 5, Novartis, 5, Amgen, 5.

Abstract Number: 0345

Effectiveness and Safety of Apremilast in Biologic-Naive versus Biologic-Experienced Patients with Psoriatic Arthritis in Real-World Clinical Practice Settings in Germany: Interim Analysis of an Ongoing, Multicenter, Prospective, Non-interventional Study

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

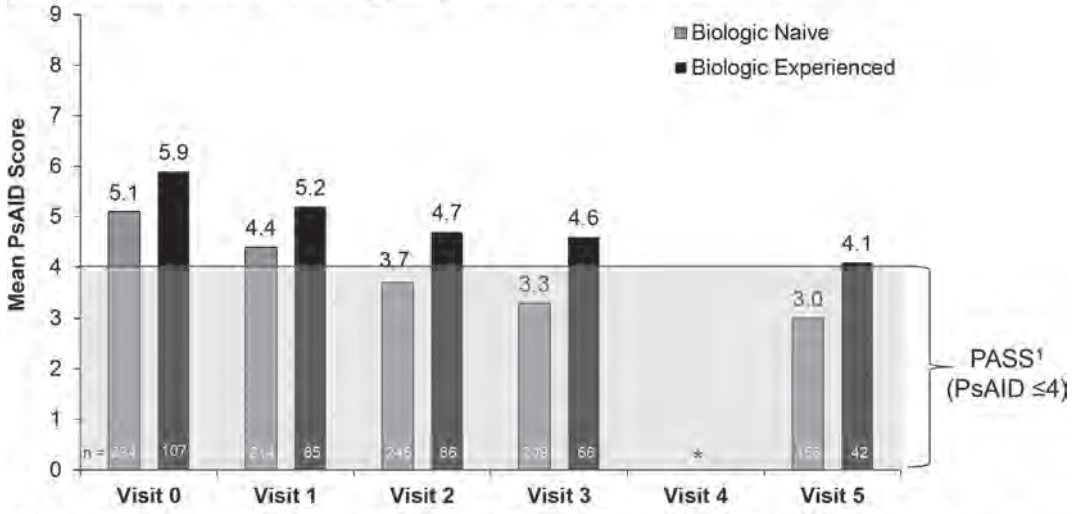
Background/Purpose: Apremilast (APR) was associated with improvements in physician-assessed and patient-reported outcomes in a large cohort of patients with PsA based on a 1-year interim analysis of LAPIS-PsA, a real-world study conducted in clinical practice settings in Germany. The current interim analysis of LAPIS-PsA evaluated the effectiveness and safety of APR in patients with and without prior biologic therapy.

Table 1. Physician- and Patient-Reported Outcomes With APR Treatment at Baseline and Follow-up

Outcome	Biologic Naive						Biologic Experienced					
	Visit 0 (n = 306)	Visit 1 (n = 232)	Visit 2 (n = 269)	Visit 3 (n = 229)	Visit 4 (n = 193)	Visit 5 (n = 170)	Visit 0 (n = 110)	Visit 1 (n = 92)	Visit 2 (n = 88)	Visit 3 (n = 69)	Visit 4 (n = 53)	Visit 5 (n = 43)
PhGA of 0 or 1, %	0	35	65	75	71	78	0	34	49	64	64	74
PtGA of 0 or 1, %	9	20	34	41	46	48	4	11	17	21	15	20
LEI score of 0*, %	0	36	51	51	61	53	0	44	51	50	45	71
Dactylitis count of 0†, %	0	49	75	77	84	87	0	42	59	70	67	90
Mean (95% CI) SJC	4.3 (3.8, 4.8)	2.3 (1.9, 2.8)	1.4 (1.1, 1.7)	0.6 (0.4, 0.8)	1.0 (0.6, 1.4)	0.7 (0.4, 1.1)	5.0 (4.0, 5.9)	3.0 (2.2, 3.9)	2.9 (1.7, 4.1)	1.4 (0.8, 2.1)	1.5 (0.7, 2.2)	1.3 (0.5, 2.2)
Mean (95% CI) TJC	11.4 (9.9, 12.9)	7.7 (5.9, 9.5)	5.0 (3.7, 6.3)	3.8 (2.3, 5.2)	3.5 (2.0, 4.9)	3.0 (1.7, 4.3)	11.3 (8.7, 14.0)	8.6 (6.0, 11.3)	8.3 (5.3, 11.3)	7.1 (3.7, 10.4)	4.6 (1.7, 7.6)	5.0 (1.3, 8.7)

*In patients with LEI >0 at baseline. †In patients with dactylitis at baseline. The n represents the total sample; the number of patients with data available may vary. CI = confidence interval; LEI = Leeds Enthesitis Index; PhGA = Physician's Global Assessment; PtGA = Patient's Global Assessment; SD = standard deviation; SJC = swollen joint count; TJC = tender joint count.

Figure 1. Lower Mean PsAID Scores Observed Over Time in Biologic-Naive Patients Compared With Biologic-Experienced Patients



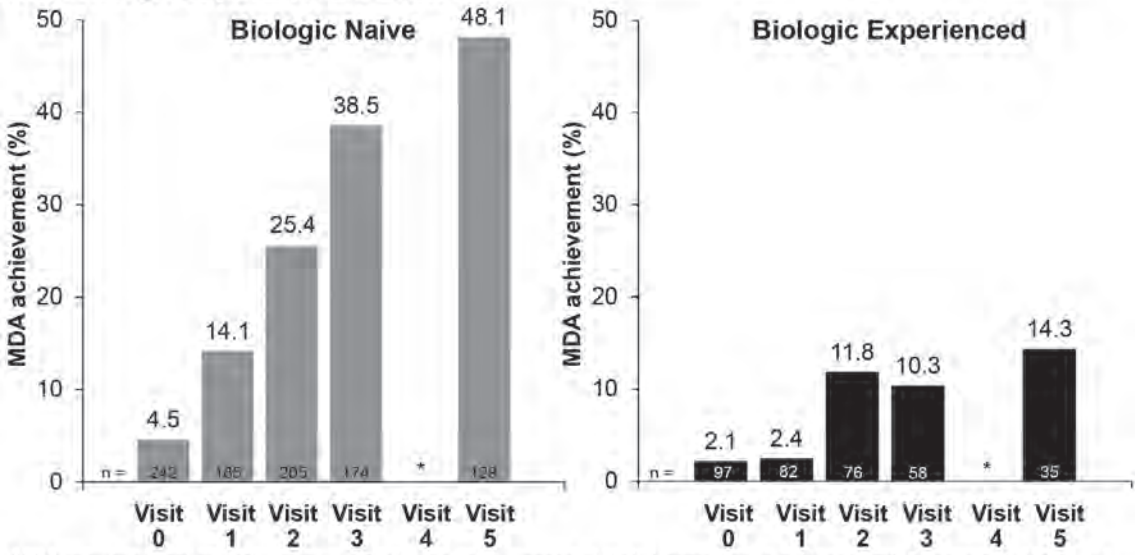
*PsAID score was not assessed at Visit 4 according to the protocol. Visit 0 (baseline); Visit 1 (~1 month after baseline); Visit 2 (~4 months after baseline); Visit 3 (~7 months after baseline); Visit 4 (~10 months after baseline); Visit 5 (~13 months after baseline). PASS = Patient-Acceptable Symptom State; PsAID = Psoriatic Arthritis Impact of Disease.

1. Gossec L, et al. *Ann Rheum Dis.* 2014;73:1012-1019.

Methods: LAPIS-PsA is a multicenter, prospective, non-interventional study enrolling patients with PsA under routine care in Germany who initiated APR according to the summary of product characteristics. Assessments included the Physician's Global Assessment of Disease Activity (PhGA), Patient's Global Assessment of Disease Activity (PtGA), Leeds Enthesitis Index (LEI), dactylitis count, swollen and tender joint counts (SJC/TJC), and Psoriatic Arthritis Impact of Disease (PsAID). Efficacy was examined descriptively at baseline and Visit 1 (~1 month), Visit 2 (~4 months), Visit 3 (~7 months), Visit 4 (~10 months) and Visit 5 (~52 weeks). Safety was evaluated based on adverse events (AEs) in the safety population (all patients who received ≥1 dose of APR).

Results: Of the 418 patients who were enrolled in the full analysis set, 306 were biologic naive and 110 were biologic experienced. For biologic-naive vs biologic-experienced patients, mean (SD) age was 54.6 (11.0) vs 55.3 (10.6) years, mean (SD) body mass index was 29.5 (5.7) kg/m^2 vs 29.6 (5.7) kg/m^2, and 56.4% vs 65.1% were women. Biologic-naive vs biologic-experienced patients had similar baseline (mean [SD]) duration of psoriasis (24.9 [17.4] vs 27.7 [17.5] years), duration of PsA (17.0 [19.6] vs 19.7 [18.2] years), enthesitis counts (LEI count: 3.0 [1.7] vs 2.9 [1.7]), and dactylitis counts (2.3 [2.2] vs 2.0 [1.4]). During follow-up, early and sustained improvements were observed in PhGA,

Figure 2. Greater MDA Achievement Over Time in Biologic-Naive Patients Compared With Biologic-Experienced Patients



*MDA calculation not possible because FFbH was not assessed at Visit 4 according to protocol. Visit 0 (baseline); Visit 1 (~1 month after baseline); Visit 2 (~4 months after baseline); Visit 3 (~7 months after baseline); Visit 4 (~10 months after baseline); Visit 5 (~13 months after baseline). FFbh = Funktionsfragebogen Hannover questionnaire; MDA = minimal disease activity.

PtGA, enthesitis, dactylitis, SJC, and TJC assessments in both groups (Table 1); achievement of PtGA score of 0 or 1 was higher in biologic-naive vs biologic-experienced patients at all study visits (Table 1). Mean PsAID scores were lower for biologic-naive vs biologic-experienced patients at all study visits; biologic-naive patients achieved mean PsAID scores exceeding the Patient-Acceptable Symptom State (PASS; PsAID ≤4) as early as Visit 2 and maintained PsAID PASS up to Visit 5 (Figure 1). A greater proportion of patients in the biologic-naive vs biologic-experienced group achieved minimal disease activity (MDA) over visits (Figure 2). Rates of AEs commonly reported (≥5%) in APR clinical trials were similar in biologic-naive (n = 358) vs biologic-experienced (n = 128) patients in the safety analysis population of LAPIS-PsA (diarrhea: 31 [8.7%] vs 17 [13.3%]; nausea: 22 [6.1%] vs 8 [6.3%]; headache: 10 [2.8%] vs 5 [3.9%]; upper respiratory tract infection: 3 [0.8%] vs 1 [0.8%]).

Conclusion: In this real-world study of patients with PsA, APR demonstrated early and sustained effectiveness in patients with and without prior biologic therapy. More biologic-naive patients achieved PtGA 0-1 and PsAID PASS at all study visits vs biologic-experienced patients and were more likely to achieve early and sustained MDA. AEs were consistent with the known safety profile of APR.

Disclosure: J. Wollenhaupt, Abbott, Bristol-Myers Squibb, Merck Sharp & Dohme, Pfizer, UCB, 2, 5; **C. Bach**, Amgen GmbH, 3; **J. Roemmler-Zehrer**, Amgen GmbH, 3.

Abstract Number: 0346

Safety Profiles of Ixekizumab versus Adalimumab: 52-Week Results from a Head-to-Head Comparison in Patients with Active Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Ixekizumab (IXE) was shown to be superior to adalimumab (ADA) in achievement of simultaneous improvement of joint and skin disease (American college of Rheumatology [ACR]50 and Psoriasis Area and Severity Index [PASI]100) in patients with active psoriatic arthritis (PsA) and inadequate response to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs).[1] The objective of this study was to compare the safety and tolerability profile of vs ADA in patients with PsA up to 52 weeks of treatment.

Methods: SPIRIT-H2H (NCT03151551) was an open-label, head-to-head, blinded assessor clinical trial which included patients with active PsA (≥3 tender joint count + ≥3 swollen joint count) and plaque psoriasis (body surface area ≥3%) who were inadequate responders to csDMARD therapy but naïve to biologic DMARDs. Patients were randomized (1:1) to approved dosing of IXE or ADA. Safety events were assessed at each patient visit up to Week 52. Frequencies of adverse events (AEs) were based on the number of patients in the safety population (patients who received ≥1 dose of study drug). Cases of inflammatory bowel disease (IBD) and cerebro-cardiovascular events were adjudicated by external committees. Kaplan-Meier analysis of time to onset of serious adverse events (SAEs) was performed.

Table: Safety results at 52 weeks

	IXE N=283 n (%)	ADA N=283 n (%)
TEAEs	209 (74)	194 (69)
Severe[a]	9 (3.2)	20 (7.1)
Related to study treatment[b]	98 (35)	87 (31)
Serious adverse events	12 (4.2)	35 (12)***
Deaths	0	0
Discontinuation due to AE	12 (4.2)	21 (7.4)
Serious infections	3 (1.1)	4 (1.4)
Injection-site reactions[c]	30 (11)	10 (3.5)**
Severe	0	1 (0.4)
Resulted in discontinuation	2 (0.7)	3 (1.1)
Anaphylaxis	0	0
Inflammatory bowel disease	2 (0.7)	0
Ulcerative colitis	1 (0.4)[d]	0
Crohn's disease	1 (0.4)	0
Cerebro-cardiovascular events	5 (1.8)	7 (2.5)
MACE	0	2 (0.7)
Malignancies	0	4 (1.4)
Depression	5 (1.8)	9 (3.2)
Interstitial lung disease	0	1 (0.4)
Cytopenias	9 (3.2)	12 (4.2)
Hepatic events	18 (6.4)	20 (7.1)

[a]Patients with multiple occurrences of the same event are counted under the highest severity. [b]The treatment-emergent adverse event 's relationship to study treatment was judged by the investigator. [c]Medical Dictionary for Regulatory Activities (MedDRA) high-level term. [d]This event was adjudicated but it was not a confirmed inflammatory bowel disease. ***p<0.001; **p<0.01 by Fisher's exact test. ADA=adalimumab, AE=adverse event; IBD=inflammatory bowel disease; IXE=ixekizumab; MACE=major adverse cardiovascular event.

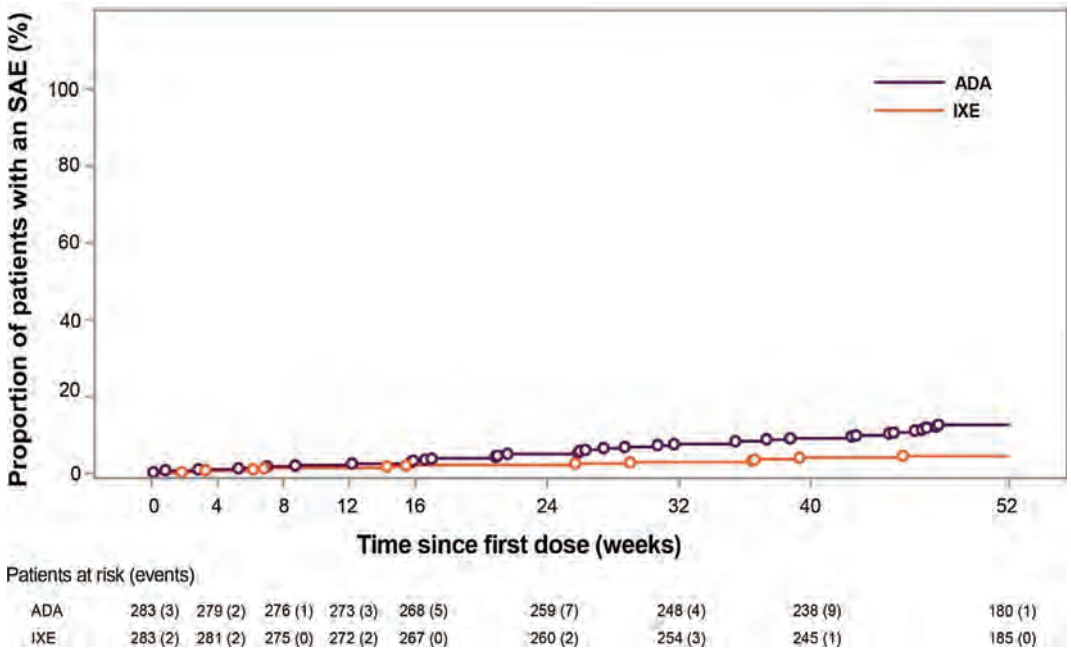

Figure 1. Time to onset of first SAE. Numbers below x-axis represent patients at risk at each time point. Open circles represent events. p<0.001 by log rank test. ADA=adalimumab; IXE=ixekizumab; SAE=serious adverse event.

Results: Of the 283 patients randomized to each treatment, 87% (246/283) of patients who received IXE and 84% (237/283) of patients who received ADA, completed 52 weeks of treatment. The frequency of treatment-emergent AEs (TEAEs) was similar between the groups (74% IXE vs 69% ADA), however fewer severe TEAEs were reported in the IXE group (3.2% IXE vs 7.1% ADA) (Table). SAEs were significantly more frequent in the ADA group compared to the IXE group (12% vs 4.2%; p< 0.001), and the time to develop a patient's first SAE was significantly shorter for ADA versus IXE (p< 0.001; Figure). Discontinuations due to AEs were numerically more frequent in the ADA group versus the IXE group (7.4% vs 4.2%; p=0.15). IXE-treated patients reported more injection-site reactions (ISR) than ADA-treated patients (11% vs. 3.5%; p=0.002). Study withdrawals due to ISR were comparable, and only one injection-site reaction was severe on ADA (Table). There were two IBD cases reported for IXE; one case was confirmed as IBD.

Conclusion: Safety results were consistent with previous trials with IXE and ADA. Compared with IXE, patients with PsA treated with ADA had significantly more serious AEs.

Reference

1. Mease PJ, et al. *Ann Rheum Dis.* 2020;79(1):123-31.

Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **J. Smolen**, AbbVie, 2, 5, 8, AstraZeneca, 2, 5, 8, Eli Lilly, 2, 5, 8, Celgene, 5, 8, Celltrion, 5, 8, Chugai, 5, 8, Gilead, 5, 8, ILTOO, 5, 8, Janssen, 5, 8, Kabi, 5, 8, Novartis-Sandoz, 5, 8, Pfizer Inc, 5, 8, Samsung, 5, 8, Sanofi, 5, 8; **A. Kavanaugh**, Eli Lilly and Company, 5; **P. Nash**, AbbVie, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8; **G. Gallo**, Eli Lilly and Company, 3, 4; **S. Liu-Leage**, Eli Lilly and Company, 3, 4; **C. Sapin**, Eli Lilly and Company, 1, 3; **M. Genovese**, Abbvie, 2, 5, Eli Lilly and Company, 2, 5, Galapagos, 2, 5, Gilead Sciences Inc., 2, 5, Pfizer, 2, 5, EMD Merck Serono, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, RPharm, 2, 5, Sanofi-Genzyme, 2, UCB, 5, Amgen, 5.

Abstract Number: 0347

In Two Phase-3 Trials, Guselkumab Reduced Fatigue over 52 Weeks in Patients with Psoriatic Arthritis and Demonstrated Independent Treatment Effects on Fatigue After Adjustment for Clinical Response (ACR20)

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

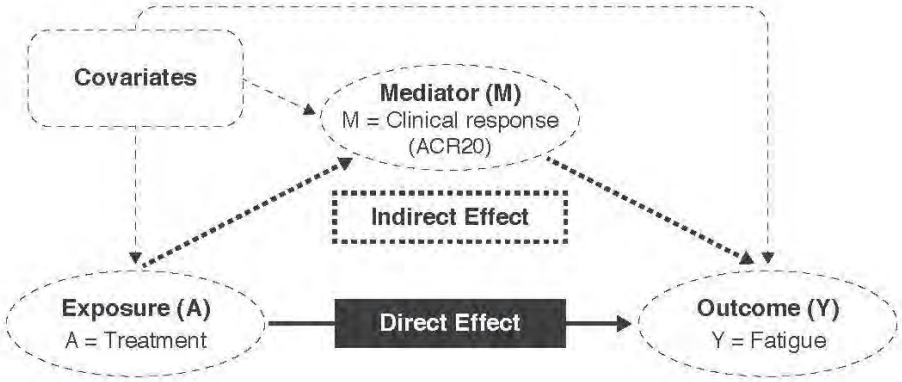
Session Time: 9:00AM–11:00AM

Background/Purpose: DISCOVER 1 & 2 are phase-3 trials of guselkumab (GUS, an IL-23 inhibitor) in patients with psoriatic arthritis (PsA). In both trials, treatment with GUS led to significantly more improvement than placebo (PBO) in the primary endpoint (ACR20) and in other measures of arthritis and psoriasis at week (w) 24,[1,2] and these improvements were maintained through 1 year of active treatment.[3,4] Here we evaluate the effect of GUS on fatigue in DISCOVER 1 & 2 using the patient reported outcome (PRO) FACIT-Fatigue, which has demonstrated content validity and strong psychometric properties in clinical trials.[5]

Methods: DISCOVER 1 & 2 enrolled patients with active PsA, despite non-biologic DMARDS or NSAIDS, who were biologic naïve except ~30% of patients in DISCOVER 1 who had received 1-2 TNFi. Patients were randomized (1:1:1) in a blinded fashion to subcutaneous GUS 100 mg at w0, w4, then every (q) 8w; GUS 100 mg q4w; or matching PBO. At w24, PBO patients were switched to GUS q4w. Concomitant treatment with select non-biologic DMARDS, oral corticosteroids, and NSAIDs was allowed. The FACIT-Fatigue is a 13-item PRO assessing fatigue and its impact on daily activities and function over the past 7 days, total score ranging from 0 to 52, higher score denoting less fatigue. A change of ≥4 points is considered clinically meaningful.[5] The change from baseline in FACIT-Fatigue presented below is based on observed data. Mediation analysis[6] was applied to the treatment effect of GUS on FACIT-Fatigue to estimate the natural direct and indirect effects, after adjusting for ACR20 response (Figure 1).

Results: At baseline in DISCOVER 1 & 2, the mean FACIT-fatigue scores (SD) were 30.4 (10.4) and 29.7 (9.7), respectively, indicating that patients with PsA experienced fatigue worse than the general population. At w24 in the DISCOVER trials, treatment with GUS led to significant improvements in FACIT-Fatigue scores compared with PBO, as early as w16 in DISCOVER 1 and w8 in DISCOVER 2. Improvements in fatigue were similar between GUS q4w and q8w doses, and the improvements at w24 were maintained through w52 (Figure 2). After a switch to GUS q4w at w24, PBO patients achieved FACIT-Fatigue scores that were comparable to those of GUS patients (Figure 2). 54%-63% of GUS patients compared with 35%-46% of PBO patients achieved clinically meaningful improvement (≥4 points) in FACIT-Fatigue at w24 ($P \leq 0.003$). At w52, 61%-70% of both GUS and PBO-to-GUS groups reached this improvement. As evaluated by mediation analysis at w24, GUS had independent positive treatment effects on fatigue (12%-36% in the q8w GUS dosing group and 69%-70% in the q4w GUS group) after adjustment for ACR20 response (Figure 1).

Figure 1. Mediation Analysis: Guselkumab has Direct Effects and Indirect Effects (mediated through ACR 20) on Fatigue in PsA.



Mediation Analysis			
	Effect	**GUS 100 mg q8W vs. PBO (95% CI)**	**GUS 100 mg q4W vs. PBO (95% CI)**
DISCOVER-1	Total Effect	3.1 (1.0, 5.2) ($p < 0.02$)	3.8 (1.9, 5.4) ($p < 0.02$)
	% Direct Effect	11.7%	68.5%
	% Indirect Effect mediated by ACR20	88.3%	31.5%
DISCOVER-2	Total Effect	4.0 (2.4, 5.5) ($p < 0.02$)	3.6 (2.1, 5.0) ($p < 0.02$)
	% Direct Effect	36.3%	69.7%
	% Indirect Effect mediated by ACR 20	63.7%	30.3%
The mediation analysis shows that for total treatment effect on fatigue, 11.7%-36.3% with GUS 100 mg q8w and 68.5%-69.7% with GUS 100 mg q4w are direct effects, indicating additional patient benefit beyond clinical response.			

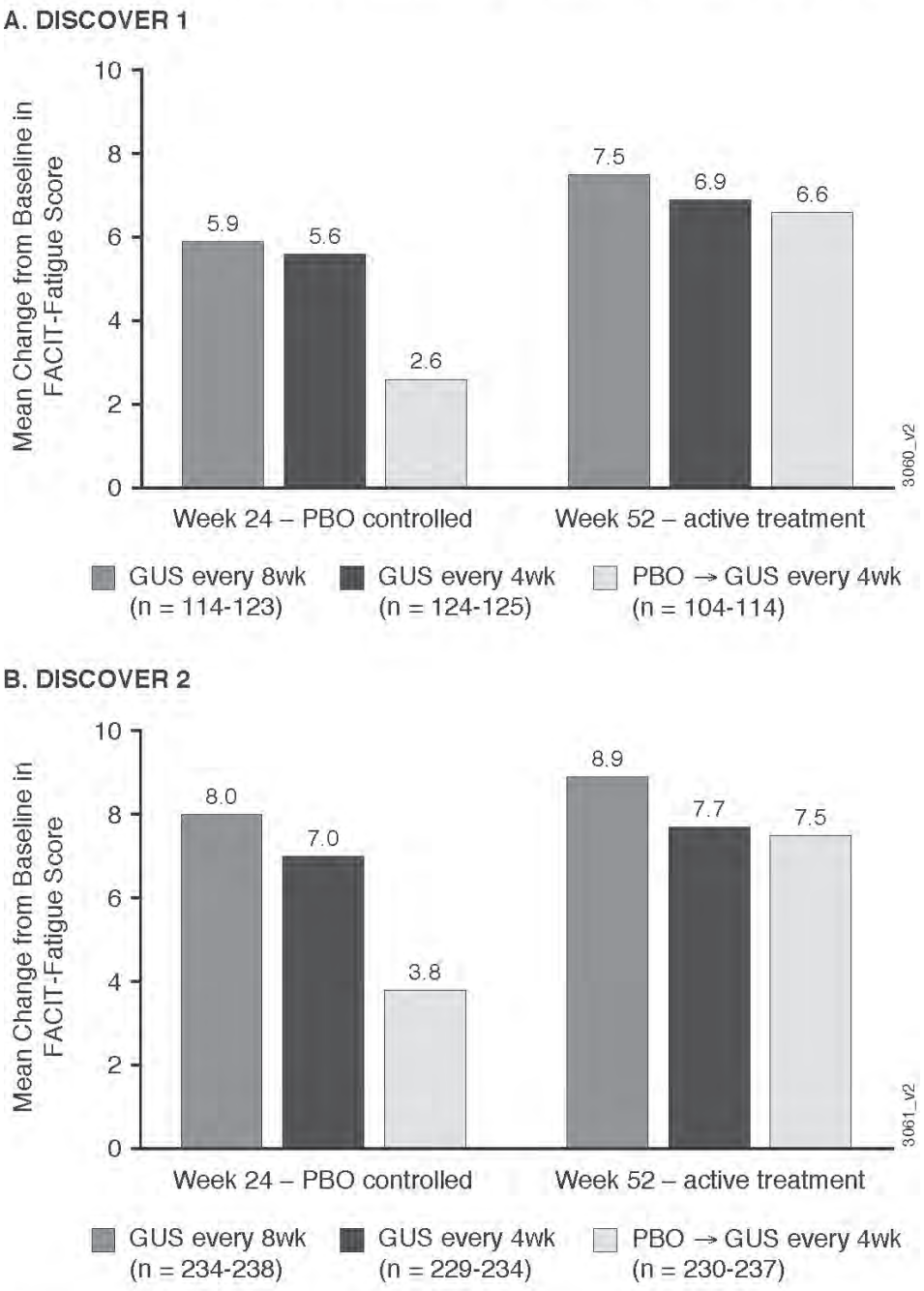
3000_v3

Conclusion: In 2 phase-3 trials, GUS treatment improved fatigue when compared to PBO during PBO-controlled periods and maintained improvements through 1 year of active treatment. Substantial proportions of those effects were independent of the effects on ACR 20, especially for the q4W dosing group.

References

1. Deodhar. *Lancet*. 2020;395:1115
2. Mease. *Lancet*. 2020;395:1126
3. Ritchlin. *EULAR20*. SAT0397
4. McInnes. *EULAR20*. SAT0402
5. Cella. *J Patient-Reported Outcomes*. 2019;3:30
6. Valeri. *Psychologic Meth*. 2013;18:137

Figure 2. Changes from Baseline in FACIT-Fatigue over 52 weeks in the DISCOVER 1 and 2 Trials of Guselkumab in Patients with Psoriatic Arthritis



FACIT = Functional Assessment of Chronic Illness Therapy, GUS = guselkumab, PBO = placebo

Disclosure: P. Rahman, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5; **P. Helliwell**, AbbVie, 2, 8, Janssen, 2, Pfizer Inc, 8, Celgene, 8, Galapagos, 8, Amgen, 8, Novartis, 2, UCB, 8; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **A. Kollmeier**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **E. Hsia**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **B. Zhou**,

Janssen Reserach & Development, LLC, 3, Johnson & Johnson, 1; **X. Lin**, Janssen Research & Development, LLC, 3; **C. Han**, Janssen Research & Development, LLC, 3; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5.

Abstract Number: 0348

Biologics History and Sex Are Linked to Golimumab Discontinuation in Axial Spondyloarthritis: A Sub-Analysis of the Post-Registration GO-Practice Study

Philippe Bertin[1], Philippe Goupille[2], Florence Tubach[3], Eric Lespessailles[4], Naoual Harid[5], Saannya Sequeira[6], Jean-Marie Fayette[6], Bruno Fautrel[7] and **Rene-Marc Flipo**[8], [1]Limoges University Hospital, Limoges, France, [2]CHU Tours, department of rheumatology, Tours, France, [3]Pierre Louis Institute of Epidemiology and Public Health, INSERM 1136, Sorbonne University and Centre of Pharmacoepidemiology, Pitié Salpêtrière Hospital, APHP.Sorbonne University, Paris, Ile-de-France, France, [4]Regional Hospital and University of Orleans, Orléans, France, [5]MSD France Puteaux, Puteaux, Ile-de-France, France, [6]ClinSearch, Malakoff, Ile-de-France, France, [7]Sorbonne University, INSERM, IPLES; Pitié-Salpêtrière Hospital, Paris, Ile-de-France, France, [8]Lille University Hospital, Lille, France

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Golimumab (**GLM**) is the latest anti-TNFα to be indicated for treating rheumatoid arthritis (**RA**), psoriatic arthritis (**PsA**) and axial spondyloarthritis (**axSpA**). The post-registration GO-PRACTICE study was performed at the request of the French Health Authorities, for the reevaluation of **GLM** in real-life.

Methods: The primary objective was to estimate **GLM** persistence at 2 years from initial prescription which was defined as the time to **GLM** discontinuation. This abstract focuses on a *post-hoc* analysis of the factors linked to **GLM** discontinuation in **axSpA** patients.

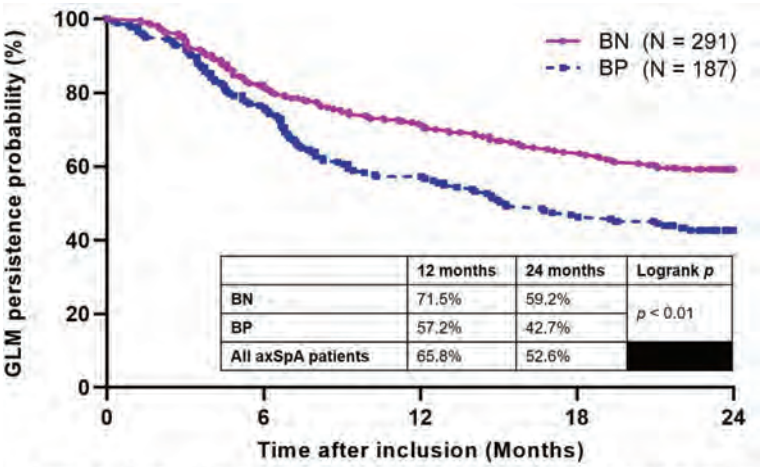


Figure 1: Kaplan-Meier curve of golimumab persistence in biologic-naïve (BN) and biologic-pretreated (BP) patients with axSpA

Figure 1. Kaplan-Meier curves of golimumab persistence in biologic-naïve and biologic-pretreated patients with axSpA

Table 1. Cox proportional hazard model results for variables of interest and their link to golimumab discontinuation in axSpA

Table 1: Cox proportional hazard model results for variables of interest and their link to GLM discontinuation in axSpA

Factor	Modalities	*p*-value	Hazard ratio (HR)	95% CI
HR for variables of interest following univariate analysis ($p > 0.20$)				
Age	Continuous variable	0.5200	1.00	0.99–1.02
Disease duration		0.5187	1.00	0.98–1.01
Inflammatory bowel disease	Yes vs. No	0.2771	0.74	0.43–1.28
Gastrointestinal disease		0.3440	1.27	0.78–2.06
Uveitis		0.2374	0.80	0.55–1.16
Psoriasis		0.2376	0.92	0.64–1.31
HR following multivariate analysis (all variables with $p < 0.20$ at univariate analysis)				
Gender	Female vs. Male	0.0065	1.59	1.14–2.23
Biologics history	Pretreated vs. naïve	0.0034	1.63	1.18–2.26
Serum CRP	Continuous variable	0.5367	1.00	0.99–1.01
DMARD history	Yes vs. No	0.2007	1.25	0.89–1.75
Ongoing corticosteroids		0.7518	1.07	0.71–1.60
Anemia		0.1002	2.06	0.87–4.88
Asthma		0.9384	0.98	0.57 – 1.68
Kidney Disease		0.6359	1.34	0.40–4.41
Other physical illness		0.5331	1.21	0.66–2.24

Observational, prospective, multicenter study, that consecutively recruited adult patients with **RA**, **PsA** and **axSpA** who were newly prescribed **GLM**. Patients were followed-up for 2 years and outcomes data were collected at baseline, 1 and 2 years. Patients' sociodemographic characteristics, disease history, comorbidities and treatment history were also collected at baseline. Persistence was estimated with the Kaplan-Meier method. Cox proportional hazard models were used to assess factors associated with persistence. Selected baseline characteristics were studied in univariate models, where those associated with *p*-value < 0.20 were included in multivariate analysis. Significance level was set at $p < 0.05$.

Results: Patients with **axSpA** (n=478) were included from Jan 2015 to Mar 2016. Mean age was 43 years and 55% were female; 61% of patients were biologic-naïve (**BN**, n=291) and 39% (n=187) were biologic-pretreated (**BP**). Median time-elapsed in years since **axSpA** diagnosis was 1.7 (range 0–45.1) and 6.9 (range 0.2–51.8) in **BN** and **BP** patients, respectively ($P < 0.001$); 97% patients were prescribed 50 mg GLM monthly and co-treatments included **DMARD** (34%), corticosteroids (17%) and **NSAIDs**/analgesics (90%).

The cumulative persistence probability of **GLM** at 2-years was 52.6% (Fig 1). Table 1 details the binary variables associated with GLM discontinuation at $p < 0.20$. Among continuous variables, baseline **CRP** level was associated with $p < 0.20$. A multivariate analysis of these factors revealed that being female (Hazard Ratio 1.59, 95%CI 1.14–2.23, $P = 0.0065$) and being **BP** (Hazard ratio 1.63, 95%CI (1.18–2.26), $P = 0.0034$) were risk factors for earlier **GLM** discontinuation (Table 1).

Conclusion: The persistence of golimumab at 2-years was 52.6% in patients with axial spondyloarthritis. Females and those who were biologics-pretreated were at greater risk for earlier golimumab discontinuation.

Disclosure: P. Bertin, MSD France, 1; **P. Goupille**, MSD France, 1, 2, Abbvie, 1, Amgen, 1, Biogaran, 1, 2, BMS, 1, Celgene, 1, Chugai, 1, Lilly, 1, Hospira, 1, Janssen, 1, Medac, 1, Nordic Pharma, 1, Novartis, 1, Sanofi-Genzyme, 1, Pfizer, 1, UCB Pharma, 1; **F. Tubach**, None; **E. Lespessailles**, MSD, 2, 5, 8, Amgen, 2, 5, 8, Lilly, 2, 5, 8, UCB, 2, Expanscience, 5, 8, Abbvie, 2; **N. Harid**, MSD France, 1; **S. Sequeira**, MSD France, 1; **J. Fayette**, MSD France, 1; **B. Fautrel**, MSD France, 1, 2, Abbvie, 1, 2, Pfizer, 1, 2, Biogen, 1, BMS, 1, Boehringer Ingelheim, 1, Celgene, 1, Janssen, 1, Lilly, 1, Medac, 1, Nordic Pharma, 1, Novartis, 1, Roche, 1, Sanofi-Aventis, 1, SOBI, 1, UCB Pharma, 1; **R. Flipo**, MSD France, 1, 2, Sanofi-Aventis, 1.

Abstract Number: 0349

Pooled Safety Results from Two Phase-3 Trials of Guselkumab in Patients with Psoriatic Arthritis Through 1 Year

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Baseline characteristics from pooled DISCOVER 1 and 2 Trials

Characteristic	PBO	GUS q8w	GUS q4w	GUS Combined*
	(n=372)	(n=375)	(n=373)	(n=748)
Age, mean years (SD)	47 (11.5)	46 (11.9)	47 (11.5)	46 (11.7)
Gender, male, n (%)	178 (48%)	197 (53%)	208 (56%)	405 (54%)
BMI, mean kg/m^2 (SD)	29.2 (6.1)	29.1 (6.3)	29.4 (5.8)	29.2 (6.0)
PsA disease duration, mean years (SD)	6.3 (6.4)	5.6 (5.7)	5.9 (6.1)	5.7 (5.9)
Number swollen joints (0-66), mean (SD)	11.5 (7.0)	11.4 (7.7)	11.4 (7.5)	11.4 (7.6)
Number tender joints (0-68), mean (SD)	21.0 (13.5)	19.9 (12.8)	20.8 (13.6)	20.4 (13.2)
CRP, median mg/dL (IQR)	0.9 (0.5; 2.4)	1.0 (0.5; 2.3)	0.9 (0.5;1.9)	0.9 (0.5; 2.2)
PsA % BSA, mean (SD)	15.4 (18.9)	15.7 (20.0)	17.1 (19.7)	16.4 (19.9)
IGA Score, VAS (0-10 cm): ≥ 2, n (%)	301 (81%)	295 (79%)	311 (83%)	606 (81%)
Previous TNFi use, n (%)	39 (10)	41 (11)	38 (10)	79 (11)
Medication Use at Baseline				
Methotrexate	227 (61.0%)	209 (55.7%)	218 (58.4%)	427 (57.1%)
Oral corticosteroids	69 (18.5%)	68 (18.1%)	62 (16.6%)	130 (17.4%)
NSAIDs	245 (65.9%)	236 (62.9%)	240 (64.3%)	476 (63.6%)

*Combined GUS q8w and q4w treatment groups.

BMI, body mass index; BSA, body surface area; CRP, C-reactive protein; IGA, investigators global assessment of psoriasis (cleared=0, minimal=1, mild=2, moderate=3, severe=4); IQR, interquartile range; PsA, psoriatic arthritis; TNFi, transforming growth factor inhibitor; VAS, visual analog scale

Table 2. Number of Patients with Adverse Events (AEs) per 100 Patient Years (PY)

Time Period	24-weeks				1 Year*			
Treatment Group	PBO	GUS SC 100 mg			Placebo→ GUS‡	GUS SC 100 mg		
Dosing Schedule	Matching	q8w	q4w	GUS Combined†	q4w	q8w	q4w	GUS Combined ‡
N	372	375	373	748	352	375	373	1100
Total PY Follow-Up	173	173	172	346	204	384	385	589
Patients with AEs per 100 PY (95% CI)								
Patients with ≥1 AEs	143 (123, 166)	148 (127, 171)	154 (132, 178)	151 (136, 167)	92 (77, 108)	114 (100, 130)	115 (101, 131)	109 (100, 117)
Patients with ≥1 serious AEs	7.1 (3.7, 12)	4.1 (1.6, 8.4)	4.7 (2.0, 9.3)	4.4 (2.5, 7.3)	7.0 (3.8, 11.8)	4.8 (2.9, 7.6)	4.0 (2.2, 6.6)	4.9 (3.6, 6.6)
Patients with ≥1 infection	50 (39, 62)	47 (37, 59)	52 (42, 65)	49 (42, 58)	39 (31, 49)	41 (34, 48)	38 (31, 45)	39 (35, 44)
Patients with ≥1 serious infections	1.7 (0.4, 5.1)	0.6 (0.0, 3.2)	1.8 (0.4, 5.1)	1.2 (0.3, 3.0)	2.5 (0.8, 5.8)	1.3 (0.4, 3.1)	0.8 (0.2, 2.3)	1.3 (0.7, 2.3)
Patients discontinued due to an AE	4.1 (1.6, 8.4)	2.9 (1.0, 6.8)	4.7 (2.0, 9.3)	3.8 (2.0, 6.5)	3.5 (1.4, 7.1)	2.1 (0.9, 4.1)	2.6 (1.3, 4.8)	2.6 (1.7, 3.8)

* Through week 60 for DISCOVER 1 and week 52 for DISCOVER 2.
†Combined GUS q8w and q4w treatment groups.
‡For subjects in PBO group who changed treatment from PBO to GUS, only data on and after first administration of guselkumab were included in this group.
AE, adverse event; CI, confidence interval; PY, patient year; q4w, every 4 weeks; q8w, every 8 weeks

Background/Purpose: DISCOVER 1 & 2, two double-blind, phase 3, psoriatic arthritis (PsA) trials of guselkumab (GUS, an IL-23 inhibitor), demonstrated significant improvement with GUS vs placebo (PBO) in signs and symptoms of PsA, with good tolerability, at week (w) 24 during the PBO-controlled period.[1,2] Beyond w24, all patients switched to GUS. Continued treatment maintained efficacy through w52.[3,4] Here, we describe pooled safety results from the DISCOVER 1 & 2 trials through 1-year of GUS treatment.

Methods: Adults with active PsA (≥3 tender/swollen joints and C-Reactive protein [CRP] ≥0.3 mg/dL in DISCOVER 1; ≥5 tender/swollen joints and CRP ≥0.6 mg/dL in DISCOVER 2) were enrolled. Patients were biologic naive except ~30% patients in DISCOVER 1 had taken 1-2 TNF inhibitors. Patients were randomized to subcutaneous GUS 100 mg at w0, w4, then every 8 w (q8w); GUS 100 mg q4w; or PBO. At w24, PBO patients were switched to GUS 100 mg q4w. Adverse events (AEs), laboratory investigations, and AEs of interest (Table 3) through w60 (end of trial) in DISCOVER 1 and through w52 in DISCOVER 2 were reported.

Results: Baseline characteristics were similar between treatment groups in the pooled studies (Table 1). Through w24 and 1 year, time adjusted results (per 100 patient years [PY]) for numbers of patients with ≥1 event were similar among treatment groups for AEs, serious AEs, infections, serious infections, and discontinuations due to an AE (Table 2). For events of interest at 1 year (Table 3), there were no cases of active tuberculosis or opportunistic infections (including *Candida*); no inflammatory bowel disease in GUS-treated patients; 2 deaths in PBO patients; and low incidences that were similar across treatment groups for malignancy, major adverse cardiac events, and injection-site reactions. Incidence of anti-GUS antibodies was 4.5%, and most were not neutralizing. Mild elevations in serum hepatic transaminases and decreases in neutrophil counts were consistent at 1 year with the results at w24 (Table 3).

Table 3. Incidence of AEs of Interest, n (%)

Time Period	6 Months				1 Year*			
	PBO	GUS SC 100 mg			PBO→ GUS‡	GUS SC 100 mg		
Dosing Schedule	Matching	q8w	q4w	GUS Combined†	q4w	q8w	q4w	GUS Combined‡
n	370	375	373	748	352	375	373	1100
Death	2 (0.5%)	0	0	0	0	0	0	0
Malignancy	1 (0.3%)	2 0.5%)	0	2 (0.3%)	1 (0.3%)	2 (0.5%)	0	3 (0.3%)
MACE	1 (0.3%)	0	1 (0.3%)	1 (0.1%)	0	0	1 (0.3%)	1 (0.1%)
Opportunistic infections	0	0	0	0	0	0	0	0
Tuberculosis	0	0	0	0	0	0	0	0
IBD	1 (0.3%)	0	0	0	0	0	0	0
Injection-site reaction	1 (0.3%)	5 (1.3%)	4 (1.1%)	9 (1.2%)	4 (1.1%)	6 (1.6%)	9 (2.4%)	19 (1.7%)
Anti-GUS antibody +	NA	6/373 (1.6%)	9/371 (2.4%)	15/744 (2.0%)	14/350 (4.0%)	18/373 (4.8%)	17/371 (4.6%)	49/1094 (4.5%)
Clinical Laboratory Investigations								
ALT Increased, n (%)**								
Grade 1	111 (30.0%)	105 (28.2%)	130 (35.0%)	235 (31.6%)	90 (25.6%)	125 (33.5%)	153 (41.2%)	368 (33.6%)
Grade 2	5 (1.4%)	4 (1.1%)	10 (2.7%)	14 (1.9%)	7 (2.0%)	6 (1.6%)	17 (4.6%)	30 (2.7%)
Grade 3	2 (0.5%)	3 (0.8%)	4 (1.1%)	7 (0.9%)	0	4 (1.1%)	4 (1.1%)	8 (0.7%)
Grade 4	1 (0.3%)	0	0	0	0	0	0	0
AST Increased, n (%)**								
Grade 1	74 (20.0%)	70 (18.8%)	80 (21.6%)	150 (20.2%)	74 (21.1%)	85 (22.8%)	103 (27.8%)	262 (23.9%)
Grade 2	2 (0.5%)	6 (1.6%)	6 (1.6%)	12 (1.6%)	6 (1.7%)	11 (2.9%)	14 (3.8%)	31 (2.8%)
Grade 3	4 (1.1%)	2 (0.5%)	6 (1.6%)	8 (1.1%)	1 (0.3%)	2 (0.5%)	6 (1.6%)	9 (0.8%)
Grade 4	0	0	0	0	0	0	0	0
Neutrophil Count Decreased, n (%)**								
Grade 1	12 (3.2%)	21 (5.6%)	22 (5.9%)	43 (5.8%)	15 (4.3%)	36 (9.7%)	29 (7.8%)	80 (7.3%)
Grade 2	3 (0.8%)	6 (1.6%)	6 (1.6%)	12 (1.6%)	3 (0.9%)	10 (2.7%)	12 (3.2%)	25 (2.3%)
Grade 3	1 (0.3%)	0	0	0	2 (0.6%)	2 (0.5%)	1 (0.3%)	5 (0.5%)
Grade 4	0	0	1 (0.3%)	1 (0.1%)	0	0	1 (0.3%)	1 (0.1%)

*Through week 60 for DISCOVER 1 and week 52 for DISCOVER 2. **National Cancer Institute toxicity grades †Combined GUS q8w and q4w treatment groups. ‡For subjects in PBO group who changed treatment from PBO to GUS, only data on and after first administration of guselkumab were included in this group.
ALT, alanine aminotransferase; AST. Aspartate aminotransferase; IBD, inflammatory bowel disease; MACE, major adverse cardiac events (cardiovascular death, non-fatal myocardial infarction, or non-fatal stroke); NA, not applicable; PBO, placebo; q4w, every 4 weeks; q8q, every 8 weeks

Conclusion: GUS regimens of q8w and q4w were well tolerated in PsA patients through 1 year of treatment in the phase 3 DISCOVER trials, consistent with the w24 results. There were no meaningful differences between incidences of AEs reported in the q8w and q4w groups. The safety profile of GUS in PsA patients is generally comparable with the previously established safety profile of GUS.

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The Impact of Age and Time Since Diagnosis on Response to Treatment with Secukinumab in Pooled Week 52 Data from 4 Phase 3 Studies in Patients with Ankylosing Spondylitis

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) is a chronic inflammatory disease involving the sacroiliac joints and spine and associated with pain, stiffness, and disability.[1] A previous analysis of 16-wk data from the phase 3 MEASURE studies showed that secukinumab (SEC), a selective inhibitor of interleukin 17A, led to significant improvements in efficacy outcomes vs placebo, regardless of age or time since diagnosis (TSD).[2] Younger patients (pts) reported better responses, possibly due to shorter TSD and higher rates of biologic inexperience. However, the relative importance of these factors was not clear.

In this hypothesis-generating analysis of pooled 52-wk data, we investigated the impact of age, TSD, TNFi exposure, and other baseline factors on responses in pts with AS treated with SEC in the MEASURE studies.

Methods: Pts with active AS from MEASURE 1 (NCT01358175), 2 (NCT01649375), 3 (NCT02008916), and 4 (NCT02159053) were included.[3-8] Pts received subcutaneous (SC) SEC every 4 wk at doses of 300 mg with an intravenous (IV) loading dose (MEASURE 3 only) or 150 mg with or without an IV or SC loading dose. Pooled efficacy outcomes (ASAS20/40; ASDAS-CRP inactive disease [ID]; change from baseline [BL] in BASDAI, BASFI, and BASMI)

at wk 52, were analyzed using logistic regression or ANCOVA with TSD and age at BL as continuous predictors along with key binary factors (eg, TNFi exposure). No adjustments were made for multiple comparisons.

Results: This analysis included 460 pts (SEC 300 mg, n = 76; SEC 150 mg, n = 384) (**Table 1**); data were available at BL and wk 52 for 393 pts (85.4%). Regression analyses (**Table 2**) revealed that ASAS20 responses were less likely with older age and prior TNFi exposure; ASAS40 responses were more likely in nonsmokers vs smokers and less likely with older age. ASDAS-CRP ID responses were more likely to occur in pts with BMI < 30 vs ≥ 30 kg/m^2. Reductions in BASDAI and BASFI were greater in nonsmokers vs smokers, and in TNFi-naive vs -treated pts (**Table 2**). Reductions in BASFI were also greater in pts with BMI < 30 vs ≥ 30 kg/m^2. TSD was not a significant covariate. Age at BL was a significant factor for reductions in BASDAI, BASFI, and BASMI scores.

Conclusion: ASAS20/40 responses at wk 52 were more likely to occur in younger pts, and age at BL was a significant covariate for predicting reductions in disease activity measures. Better outcomes in younger pts demonstrate the importance of early treatment. It is possible that the effect of age was due to longer disease duration in older pts (which would also support the importance of early treatment) and that TSD was not predictive of outcomes due to the variable time between onset of symptoms and diagnosis; age might therefore be a better surrogate for disease duration than TSD.

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Table 1. Demographics and Baseline Disease Characteristics by Time Since Diagnosis

Baseline Characteristics	Time Since Diagnosis					
	< 2 years		2 to 5 years		> 5 years	
	SEC 300 mg n = 39	SEC 150 mg n = 148	SEC 300 mg n = 14	SEC 150 mg n = 67	SEC 300 mg n = 23	SEC 150 mg n = 169
Age, mean (SD) [range], years	38.0 (10.7) [20-58]	40.4 (11.5) [19-67]	42.0 (10.6) [22-59]	37.5 (11.0) [19-65]	49.0 (11.5) [30-73]	45.7 (11.4) [24-79]
Male, n (%)	27 (69.2)	100 (67.6)	7 (50.0)	45 (67.2)	16 (69.6)	110 (65.1)
White, n (%)	28 (71.8)	119 (80.4)	14 (100.0)	54 (80.6)	17 (73.9)	140 (82.8)
BMI, mean (SD)	27.7 (5.9)	26.2 (5.1)	26.9 (4.7)	27.9 (6.0)	28.7 (5.1)	27.8 (6.5)
Current smoker, n (%)	12 (30.8)	53 (35.8)	7 (50.0)	16 (23.9)	5 (21.7)	55 (32.5)
hsCRP, mean (SD), mg/L	9.2 (13.2)	15.1 (30.7)	9.9 (10.3)	20.3 (30.4)	15.1 (14.7)	17.1 (26.5)
TNFi treated, n (%)	4 (10.3)	20 (13.5)	5 (35.7)	21 (31.3)	10 (43.5)	66 (39.1)
PGA of disease activity, VAS 0-100 mm	71.2 (15.5)	70.0 (16.1)	74.3 (19.8)	66.2 (19.0)	75.2 (16.6)	69.1 (17.9)
Total back pain, VAS 0-100 mm	72.1 (14.3)	69.7 (16.5)	78.9 (15.5)	68.1 (17.9)	74.3 (16.1)	70.2 (16.6)
Nocturnal back pain, VAS 0-100 mm	73.1 (15.4)	65.3 (20.6)	80.8 (19.3)	67.8 (19.5)	74.1 (19.1)	67.7 (18.4)
BASDAI	7.1 (1.4)	6.7 (1.4)	6.9 (1.4)	6.5 (1.7)	6.9 (1.4)	6.8 (1.4)
BASFI	6.5 (1.7)	6.0 (2.0)	6.2 (1.5)	5.7 (2.3)	6.5 (2.0)	6.4 (2.1)
BASMI (linear)	3.1 (1.3)	3.3 (1.7)	3.3 (1.4)	3.5 (1.4)	4.2 (1.7)	4.5 (1.8)
BASMI (spinal flexion)	13.1 (5.1)	12.7 (5.8)	11.9 (3.4)	11.5 (4.9)	10.4 (5.1)	9.3 (5.1)

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; BMI, body mass index; hsCRP, high-sensitivity C-reactive protein; PGA, patient global assessment; SEC, secukinumab; TNFi, tumor necrosis factor inhibitor; VAS, visual analog scale.

Table 2. Logistic Regression and ANCOVA Analyses of Key Week 52 Efficacy Outcomes

Inputs		Logistic Regression Models		
		ASAS20	ASAS40	ASDAS-CRP ID
Binary predictors				
Secukinumab dose: 300 vs 150 mg	Odds ratio (95% CI)	1.381 (0.704 to 2.707)	1.314 (0.749 to 2.304)	1.098 (0.584 to 2.065)
	P value	.3473	.3414	.7717
BMI: < 30 vs ≥ 30 kg/m²	Odds ratio (95% CI)	1.648 (0.990 to 2.746)	1.435 (0.903 to 2.282)	2.415 (1.275 to 4.576)
	P value	.0549	.1267	**.0068**
Current smoker: No vs yes	Odds ratio (95% CI)	1.368 (0.831 to 2.252)	1.641 (1.056 to 2.550)	1.536 (0.888 to 2.657)
	P value	.2183	**.0277**	.1250
hsCRP: ≥ 5 vs < 5 mg/L	Odds ratio (95% CI)	1.093 (0.668 to 1.790)	1.391 (0.907 to 2.135)	0.699 (0.380 to 1.286)
	P value	.7232	.1306	.2496
TNFi naive: No vs yes	Odds ratio (95% CI)	0.553 (0.327 to 0.933)	0.721 (0.447 to 1.165)	0.541 (0.284 to 1.028)
	P value	**.0264**	.1814	.0609
Continuous predictors				
Time since diagnosis of AS (years)	Odds ratio (95% CI)	1.010 (0.980 to 1.041)	0.991 (0.964 to 1.019)	0.967 (0.929 to 1.005)
	P value	.5290	.5284	.0907
Age (years)	Odds ratio (95% CI)	0.969 (0.947 to 0.991)	0.979 (0.960 to 0.999)	0.985 (0.962 to 1.008)
	P value	**.0063**	**.0401**	.1984
Baseline value (for ASDAS-CRP)	Odds ratio (95% CI)	-	-	0.804 (0.567 to 1.140)
	P value			.2204
Inputs		**ANCOVA**		
		Δ BASDAI	**Δ BASFI**	**Δ BASMI**
Binary factors				
Secukinumab dose: 300 vs 150 mg	Estimate (95% CI)	−0.194 (−0.756 to 0.369)	−0.230 (−0.786 to 0.326)	0.067 (−0.171 to 0.304)
	P value	.4985	.4166	.5820
BMI: < 30 vs ≥ 30 kg/m²	Estimate (95% CI)	−0.413 (−0.890 to 0.064)	−0.526 (−1.001 to −0.051)	−0.070 (−0.275 to 0.136)
	P value	.0893	**.0300**	.5049
Current smoker: No vs yes	Estimate (95% CI)	−0.776 (−1.228 to −0.325)	−0.636 (−1.082 to −0.190)	−0.010 (−0.208 to 0.187)
	P value	**.0008**	**.0053**	.9181
hsCRP: ≥ 5 vs < 5 mg/L	Estimate (95% CI)	−0.210 (−0.644 to 0.224)	−0.126 (−0.555 to 0.303)	−0.031 (−0.224 to 0.161)
	P value	.3414	.5629	.7488
TNFi naive: No vs yes	Estimate (95% CI)	0.564 (0.074 to 1.055)	0.552 (0.067 to 1.037)	0.049 (−0.163 to 0.262)
	P value	**.0243**	**.0258**	.6481
Covariates				
Time since diagnosis of AS	*P* value	0.5264	0.2766	0.1794
Age	*P* value	**.0014**	**.0002**	**.0007**
Baseline value	*P* value	**< .0001**	**< .0001**	**< .0001**

ANCOVA, analysis of covariance; ASAS, Assessment of SpondyloArthritis international Society; ASDAS-CRP-ID, Ankylosing Spondylitis Disease Activity Score (C-reactive protein) inactive disease; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; BMI, body mass index; hsCRP, high-sensitivity C-reactive protein; TNFi, tumor necrosis factor inhibitor.
Note: *P* values in bold are below the nominal significance level of .05.

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Disclosure: A. Deodhar, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **P. Machado**, Novartis, 1, 3; **E. Pournara**, Novartis, 1, 3; **X. Meng**, Novartis, 1, 3; **V. Strand**, AbbVie, 5, Amgen, 5, Celltrion, 5, Janssen, 5, Merck, 5, Novartis, 5, Regeneron, 5, Sanofi, 5, UCB, 5, Genentech/Roche, 5, GSK, 5, Pfizer, 5, Bayer, 5, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, Galapagos, 5, Lilly, 5, Gilead, 5, Samsung, 5, Servier, 5, Setpoint, 5, Arena, 5, AstraZeneca, 5, Horizon, 5, Ichnos, 5, Inmedix, 5, Sandoz, 5; **M. Magrey**, Novartis, 5, Eli Lilly, 5, AbbVie, 2, UCB, 2, Amgen, 2, Pfizer, 5, Janssen, 5.

Abstract Number: 0351

Ustekinumab-Treated Patients with Psoriatic Arthritis in a Real-world Study: Similar Clinical Responses and Treatment Persistence over One Year in Elderly and Younger Patients

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Table 1. Baseline Demographics and Clinical Characteristics of PsA Patients Treated with Ustekinumab and Stratified by Age

Mean (95% CI) unless otherwise stated	Age <60 years (N=336)*	Age ≥60 years (N=102)*
Age, years	46.1 (45.1; 47.1)	67.3 (66.1; 68.5)
Sex (male), n (%)	147 (43.8%)	45 (44.1%)
BMI, kg/m²	28.3 (27.6; 28.9)	29.5 (28.2; 30.9)
Disease duration (time since initial diagnosis), years	6.88 (6.07; 7.69)	9.54 (7.60 ;11.48)
Swollen joint count (66 joints)	5.9 (5.0; 6.9)	6.0 (4.3; 7.6)
Tender joint count (68 joints)	12.7 (11.2; 14.2)	11.7 (9.2; 14.2)
Physician Global VAS	54.0 (51.8; 56.2)	53.0 (48.5; 57.6)
Patient Global VAS	59.9 (57.2; 62.6)	63.9 (58.8; 69.0)
Patient Pain VAS	59.3 (56.5; 62.2)	64.0 (59.1; 69.0)
HAQ-DI	1.09 (1.01; 1.16)	1.25 (1.11; 1.39)
CRP (mg/dL), median (IQ range)	0.50 (0.2; 1.2)	0.70 (0.3; 1.6)
cDAPSA score, mean (95% CI) Remission, n (%) Low Moderate High	30.7 (28.2; 33.1) 9 (3.2%) 28 (10.1%) 111 (39.9%) 130 (46.8%)	30.3 (26.1; 34.5) 1 (1.3%) 8 (10.0%) 30 (37.5%) 41 (51.3%)
Co-morbidities**, n (%)		
Cardiovascular/metabolic syndrome	103 (30.7%)	81 (79.4%)
Inflammatory Bowel Disease	6 (1.8%)	2 (2.0%)
Obesity	98 (31.9%)	31 (34.1%)
Uveitis	1 (0.3%)	0 (0%)
Co-treatment, n (%) Methotrexate Corticosteroids	 101 (30.1%) 101 (30.1%)	 30 (29.4%) 42 (41.2%)

*N=numbers of enrolled patients. Values for patients with available outcome data.
**Currently present
BMI, body mass index; cDAPSA, clinical disease activity index for psoriatic arthritis; CI, confidence interval; CRP, C-reactive protein; cDMARD, conventional disease modifying anti-rheumatic drug; HAQ-DI, health assessment questionnaire disease index; VAS, Visual Analog Scale

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

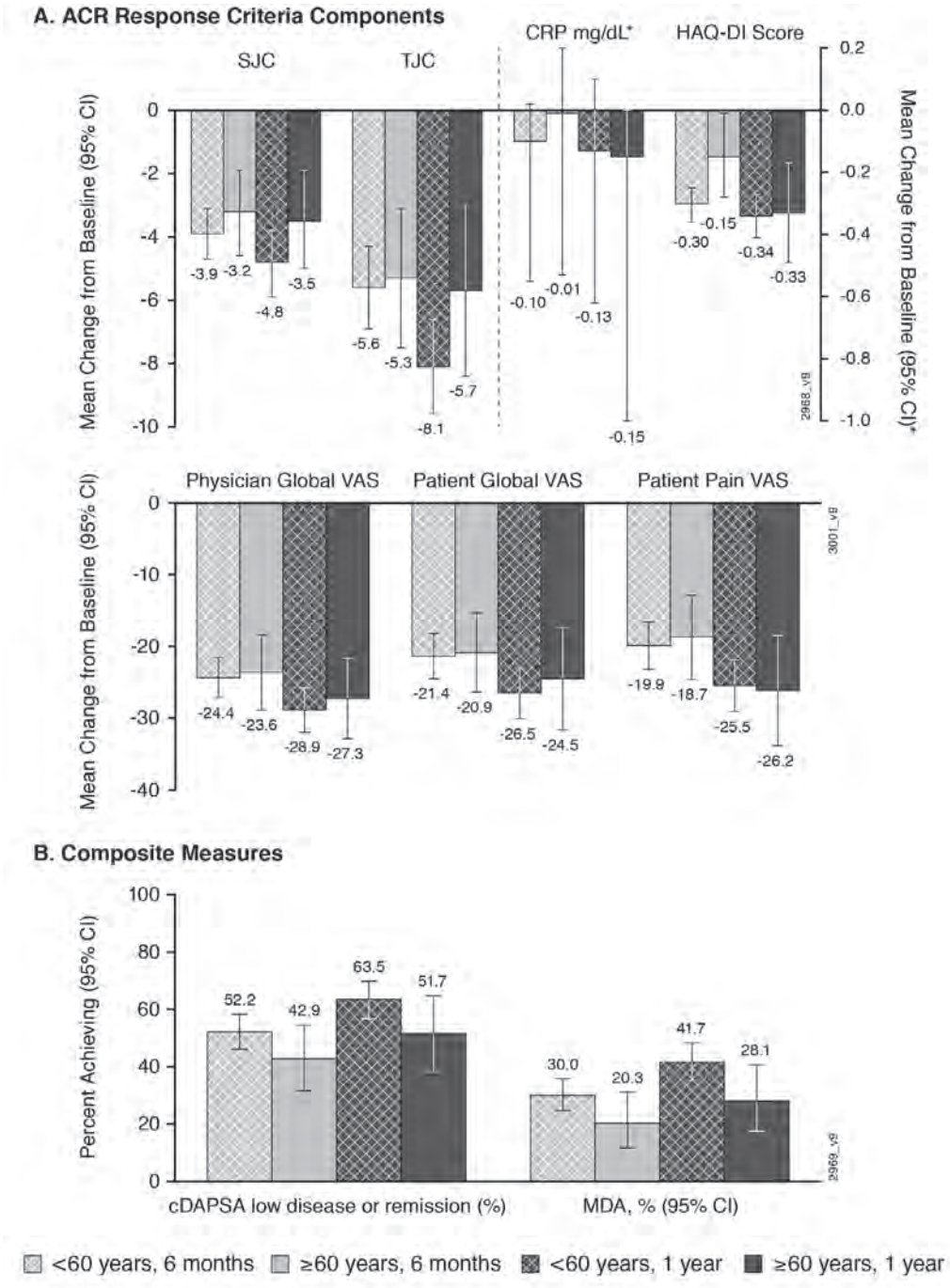

Figure 1. Psoriatic Arthritis Disease Measures by Age Subgroup after 6 and 12 Months of Treatment with Ustekinumab in the PsABio trial.

A. Change from Baseline in ACR Response Criteria Components **B.** Composite Measures

* For CRP, median change from baseline (interquartile range)

ACR, American College of Rheumatology; **cDAPSA**, clinical disease activity index for psoriatic arthritis; **CRP**, C-reactive protein; **HAQ-DI**, health assessment questionnaire disease index; **MDA**, minimal disease activity; **SJC**, swollen 66-joint count; **TJC**, tender 68-joint count; **VAS**, visual analog scale (0-100)

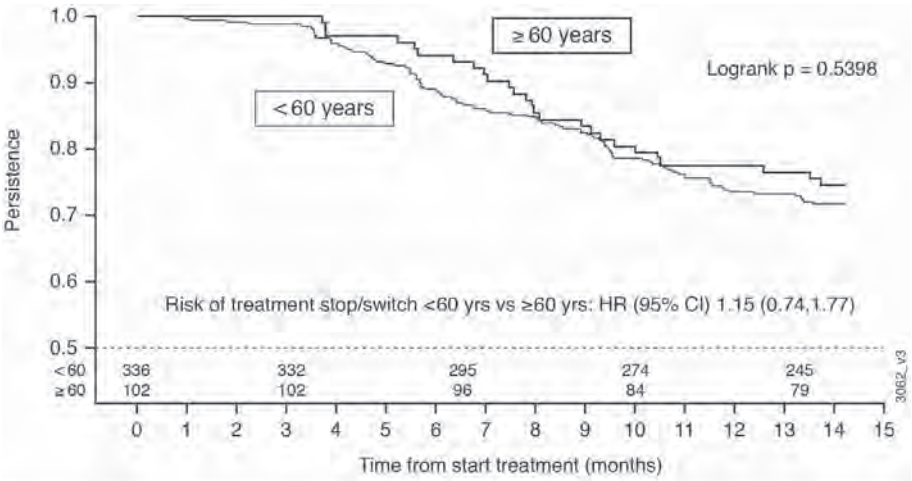

Figure 2. Kaplan-Meier Plot of Treatment Duration: ≥60 vs. <60 Years of Age in Patients Treated with UST.

Background/Purpose: In the PsABio study (NCT02627768), real-world data from patients with PsA showed comparable clinical results after treatment with ustekinumab (UST, an anti-p40 IL-12/23 inhibitor) versus TNF inhibitors (TNFi).[1,2] Patients of all ages may acquire psoriatic arthritis (PsA) and may require prolonged treatment. In general, treatment persistence is a function of effectiveness, safety, convenience, and treatment satisfaction. Elderly patients may be at increased risk of treatment interruption due to adverse events (AEs), increased comorbidities, and/or polypharmacy. Here we report PsABio results in younger versus older patients treated with UST.

Methods: PsABio is a multinational, prospective, observational study in patients with PsA prescribed either UST or TNFi (as 1st, 2nd or 3rd line treatment) at the discretion of the treating rheumatologist. This post-hoc analysis compared the effectiveness and safety in UST-treated patients by age subgroup (< 60 vs ≥60 years old). Drug persistence was compared by means of Kaplan-Meier plots and the log-rank test. Cox-regression analysis was used to compare the risk of stopping treatment before 15 months of follow-up between the age subgroups.

Results: 458 of 930 patients in PsABio received UST (77.1% were < 60 years of age; 22.9% were ≥60). Baseline characteristics (Table) were comparable across the older vs younger subgroups, except that older patients had more cardiovascular disease and trended towards greater PsA disease duration. Effectiveness after treatment with UST for 6 months and 1 year was generally comparable across age subgroups. The similarities included components of the ACR response criteria (Swollen 66-joint Count, Tender 68-joint Count, C-Reactive Protein, Health Assessment Questionnaire-Disease Index [HAQ-DI], Physician's Global Assessment, Patient's Global Assessment, and Patient's Pain Assessment) (Figure 1A) and composite measures (clinical Disease Activity Index for Psoriatic Arthritis and Minimal Disease Activity) (Figure 1B). Numerically fewer older patients reached the goals measured in the composite endpoints. Incidence of AEs, but not withdrawal due to an AE, was somewhat higher in the older patient subgroup (data not shown). Observed treatment persistence did not differ between older and younger patients (Log Rank p value=0.54), confirmed by Cox-regression analysis showing similar risk for stop/switch within the first year (Figure 2).

Conclusion: In a real-world setting, no clinically meaningful differences were observed in UST effectiveness and safety in PsA patients who were < 60 compared with ≥60 years of age. These results were generally maintained from 6 months to 1 year of treatment. Additionally, no significant differences were observed in treatment persistence over one year when comparing younger or older populations treated with UST, indicating that UST appears safe and effective in the aged PsA population.

References

1. Smolen et al. EULAR 2020. Abstract #2755; 2. Gossec et al. EULAR 2020. Abstract # 2127.

Disclosure: L. Gossec, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8; **E. Theander**, Janssen Medical Affairs, LLC, 1, 3; **S. Chakravarty**, Janssen Scientific Affairs, LLC, 1, 3; **P. Bergmans**, Janssen Medical Affairs, LLC, 1, 3; **I. Lin**, Janssen Scientific Affairs, LLC, 1, 3; **W. Noël**, Janssen Medical Affairs, LLC, 1, 3; **S. Siebert**, AbbVie, 5, 8, Celgene, 2, 8, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb, 1, Janssen, 1, 2, 3, Novartis, 2, 5, 8, UCB, 2, 5, GlaxoSmithKline, 2, Pfizer, 2, 5; **J. Smolen**, AbbVie, 2, 5, 8, AstraZeneca, 2, 5, 8, Eli Lilly, 2, 5, 8, Celgene, 5, 8, Celltrion, 5, 8, Chugai, 5, 8, Gilead, 5, 8, ILTOO, 5, 8, Janssen, 5, 8, Kabi, 5, 8, Novartis-Sandoz, 5, 8, Pfizer Inc, 5, 8, Samsung, 5, 8, Sanofi, 5, 8.

Abstract Number: 0352

Efficacy and Safety of Ixekizumab versus Adalimumab with and Without Concomitant Conventional Synthetic Disease-Modifying Antirheumatic Drugs (DMARD) in Biologic DMARD-Naïve Patients with Psoriatic Arthritis: 52-Week Results

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting IL-17A, was superior to adalimumab (ADA) at Week (Wk) 24 for simultaneous achievement of ACR50 and 100% improvement from baseline in Psoriasis Area and Severity Index (PASI 100); (primary endpoint) in patients (pts) with active PsA from SPIRIT-H2H. SPIRIT-H2H had 2 major secondary endpoints and achieved both: noninferiority of IXE to ADA for ACR50 and superiority of IXE to ADA for PASI 100, at Wk 24.The aim was to determine how concomitant conventional synthetic (cs) DMARD use affects safety and efficacy of IXE and ADA in prespecified subgroups defined by biologic monotherapy, concomitant MTX use, and concomitant csDMARD use through Wk 52 in SPIRIT-H2H.

Methods: SPIRIT-H2H was a 52-wk, multicenter, randomized, open-label, assessor-blinded, parallel-group study evaluating the efficacy and safety of IXE vs ADA in adults with PsA and naïve to biologic DMARDs. Pts were required to have active PsA fulfilling Classification for Psoriatic Arthritis (CASPAR) criteria and ≥3/68 tender and ≥3/66 swollen joints, ≥3% plaque psoriasis (PsO) body surface area (BSA) involvement, no prior treatment with biologic DMARDs, and with prior inadequate response to ≥1 csDMARD (but not necessarily current treatment with csDMARDs). Randomization (1:1) was stratified by concomitant use of csDMARD and the presence/absence of moderate-to-severe PsO (baseline: BSA≥10% + PASI≥12, + static Physician's Global Assessment≥3). Pts (N=566) received IXE/ADA through 52 wks according to the labelled dose dependent on presence/absence of moderate-to-severe PsO. In this prespecified subgroup analysis by presence/absence of csDMARDs, efficacy outcomes through Wk 52 were com-

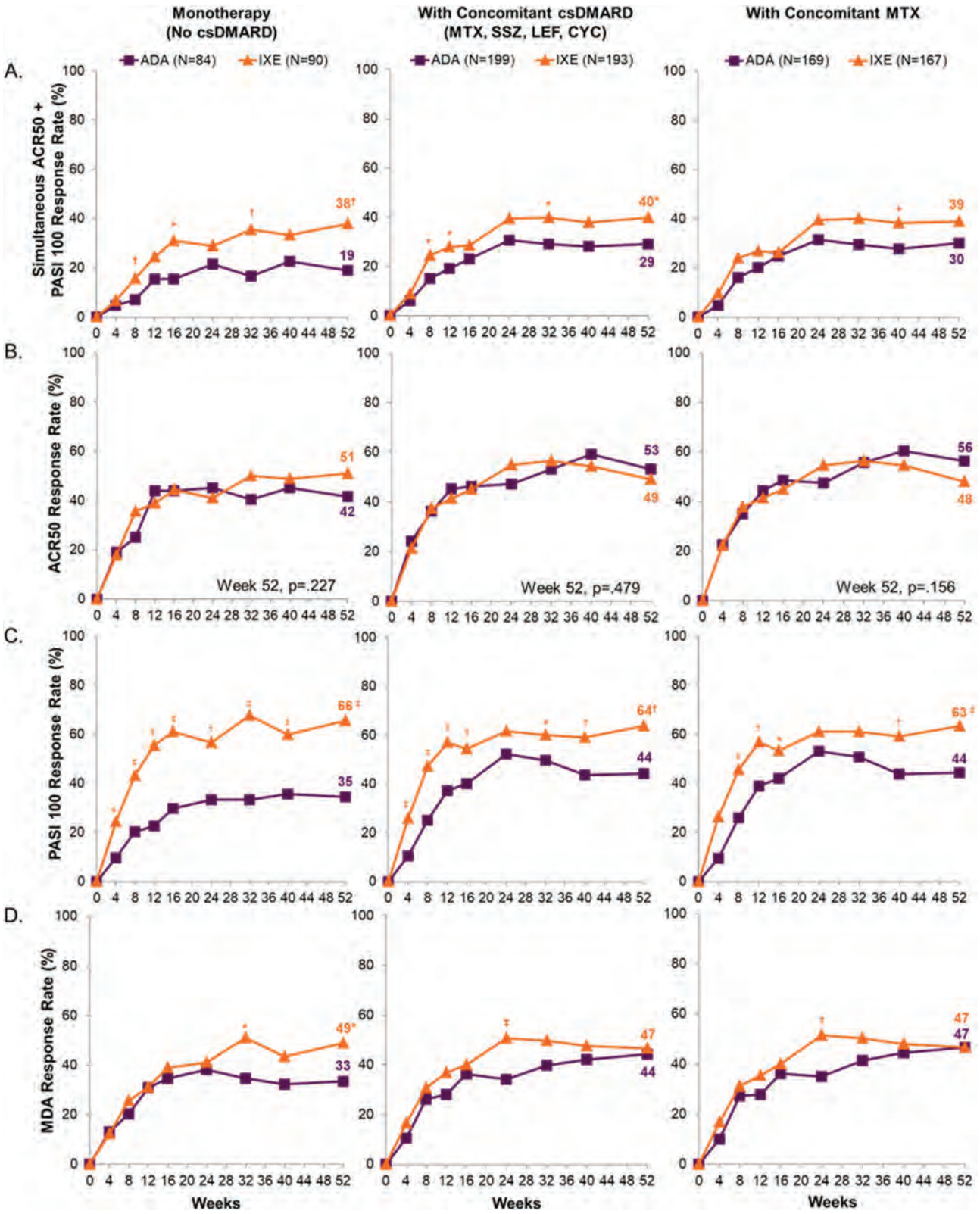

Figure 1. Proportion patients through 52 weeks with simultaneous achievement of ACR50 + PASI 100, ACR50, PASI 100, and MDA-18 Entheseal Points. Nine patients with active PsO and BSA≥3% were assessed as PASI=0 at baseline, a medical inconsistency that was resolved using medical judgement. These patients were considered PASI 100 responders if PASI=0 and BSA=0 at post baseline visit. *p≤.05 vs. ADA; †p<.01 vs. ADA; ‡p≤.001 vs. ADA. ACR=American College of Rheumatology; ADA=adalimumab; BSA=body surface area; csDMARD=conventional synthetic disease modifying anti-rheumatic drugs; CYC=cyclophoshamide; Ixe=ixekizumab; LEF=leflunomide; MDA=minimal disease activity PASI=Psoriasis Area and Severity Index; PsO=psoriasis; MTX=methotrexate; SSZ=sulfasalazine.

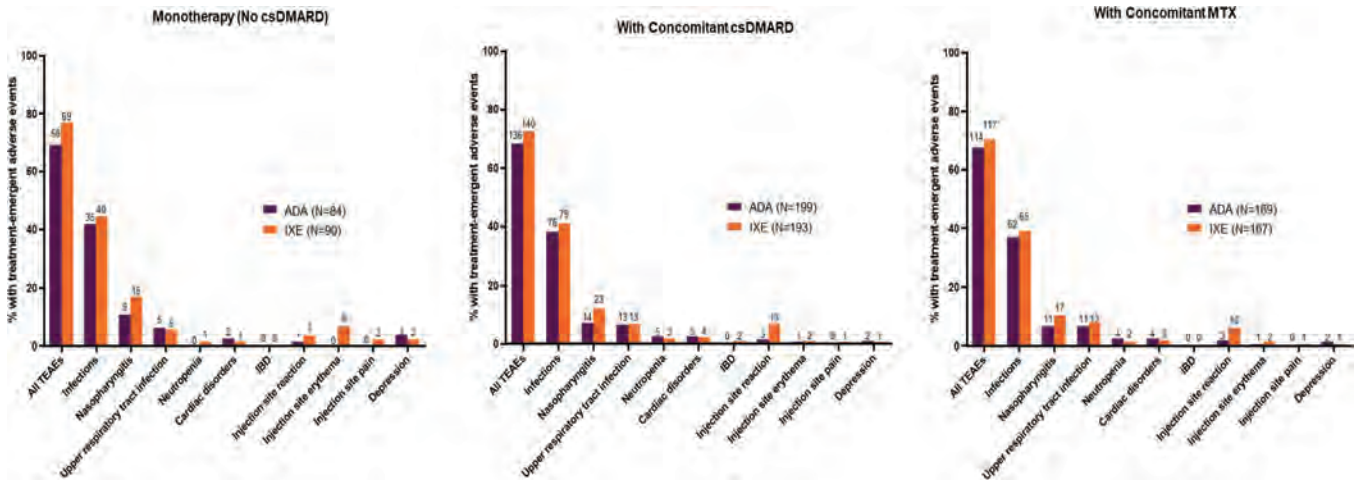

Figure 2. Safety data for patients through 52 weeks. Two events of IBD were reported in the ixekizumab treatment arm but only 1 case met the adjudication criteria of confirmed inflammatory bowel disease. ADA=adalimumab; csDMARD=conventional synthetic disease modifying anti-rheumatic drugs; IBD=inflammatory bowel disease; Ixe=Ixekizumab; MTX=methotrexate; TEAE=treatment emergent adverse event.

pared between IXE and ADA using logistic regression models and Fisher's exact tests. Missing data were imputed using non-responder imputation.

Results: At baseline, 167/283 IXE- and 169/283 ADA-treated pts had concomitant MTX use. Of these, 9.0% (15/167) and 7.1% (12/169) treated with IXE and ADA, respectively, were taking an additional csDMARD (sulfasalazine, cyclosporine, or leflunomide). A significantly greater proportion of pts on IXE vs ADA achieved the primary endpoint or PASI 100 when used as monotherapy or in combination with csDMARD (Figs. 1A and 1C). At Wk 52, the proportion of pts achieving ACR50 was not statistically different between IXE and ADA, regardless of monotherapy or concomitant csDMARD use (Fig. 1B). A significantly higher proportion of pts achieved minimal disease activity (MDA) on IXE compared to ADA in the monotherapy subgroup (49% vs 33%), while the response rates were similar in both combination subgroups (Fig. 1D). These data support consistent ACR50, PASI 100, and MDA response for IXE across all 3 subgroups. There were no significant differences in safety data across the 3 subgroups for either IXE or ADA (Fig. 2).

Conclusion: As with prior studies, consistent efficacy across multiple PsA disease-specific endpoints was observed with IXE in SPIRIT-H2H, regardless of whether IXE was taken as monotherapy or in combination with MTX or another csDMARD. Both agents were well tolerated, with no unexpected safety signals.

Disclosure: J. Smolen, AbbVie, 2, 5, 8, AstraZeneca, 2, 5, 8, Eli Lilly, 2, 5, 8, Celgene, 5, 8, Celltrion, 5, 8, Chugai, 5, 8, Gilead, 5, 8, ILTOO, 5, 8, Janssen, 5, 8, Kabi, 5, 8, Novartis-Sandoz, 5, 8, Pfizer Inc, 5, 8, Samsung, 5, 8, Sanofi, 5, 8; **A. Sebba**, Eli Lilly and Company, 5, 8; **E. Ruderman**, Eli Lilly and Company, 5, AbbVie Inc., 5, Amgen, 5, Gilead, 5, Janssen, 5, Novartis, 5, Pfizer, 2, 5; **A. Gellett**, Eli Lilly and Company, 1, 3; **C. Sapin**, Eli Lilly and Company, 1, 3; **A. Sprabery**, Eli Lilly and Company, 1, 3, Johnson and Johnson, 1; **S. Liu-Leage**, Eli Lilly and Company, 3, 4; **S. Pillai**, Eli Lilly and Company, 3; **P. Reis**, Eli Lilly and Company, 3, 4, AbbVie Inc., 4; **P. Nash**, AbbVie, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 0353

Achievement of Sustained Remission and Low Disease Activity with Secukinumab Improves Quality of Life and Physical Function in Patients with Psoriatic Arthritis: Results from a Randomized Phase 3 Study

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: A treat-to-target approach in psoriatic arthritis (PsA) was recommended by EULAR and GRAPPA to achieve remission (REM) or low disease activity (LDA), by regular disease activity assessment and therapeutic adjustment.[1,2] Disease activity index for psoriatic arthritis (DAPSA) or the minimal disease activity (MDA) are considered for defining REM/LDA in secukinumab (SEC) treated patients (pts) with PsA.[3] Very low disease activity (VLDA) is a more stringent measure compared to MDA in defining REM/LDA.[4] Currently, limited reports are available on pts with PsA achieving sustained REM in clinical trials or real-world evidence, using these stringent criteria. Here, we report an exploratory analysis on sustained REM/LDA in pts with PsA treated with SEC and its impact on health-related quality of life (QoL) and physical function, in the FUTURE 5 study (NCT02404350).

Methods: FUTURE 5 is a randomized, double-blind, placebo-controlled 2-year phase 3 trial in pts with active PsA. The study design has been previously reported.[5] Pts randomized to SEC 150 mg could be escalated to 300 mg from Week (Wk) 52 to 104, based on investigators' judgement. The pts were categorized as either achieving REM/LDA once only or sustained REM/LDA, which was defined as pts who achieved REM/LDA between Wk 24-52 and maintained the same response at least 2 of the next 6 visits (visit every 8 wks). Of pts who achieved REM/LDA (VLDA, DAPSA REM, MDA, DAPSA LDA+REM) between Wk 24 and 52, the relationship between REM/LDA, sustained REM/LDA and physical function (health assessment questionnaire disability index [HAQ-DI]), QoL (short form-36 physical component score [SF-36 PCS]) were assessed. To assure that sustainability of responses were uniformly assessed for all pts at the same time period, only pts who completed the 2-year study with no missing REM/LDA assessment at Wks 24 and 104 were evaluated.

Results: In total, 996 pts were randomized to one of 4 treatment groups: SEC 300 mg loading dose (LD; N=222), SEC 150 mg LD (N=220), SEC 150 mg no loading dose (NL; N=222), and placebo (N=332). The baseline clinical characteristics were comparable across treatment groups. A total of 48-62% and 19-36% of all SEC-treated groups, respectively achieved sustained LDA (DAPSA LDA+REM or MDA) and sustained REM (DAPSA REM or VLDA) in at least three visits (**Table 1**). Higher improvements in QoL (SF-36 PCS) (**Table 2**) and physical function (HAQ-DI) were observed from baseline to Wk 104 in pts who had achieved sustained REM or LDA when compared with pts who had not achieved this or who had achieved this only once.

Table 1. Proportion of patients achieving remission or low disease activity

REM and LDA composite indices, %	Treatment group	REM/LDA only once	Sustained REM/LDA
MDA	SEC 150 mg LD (N=184)	10.9	47.8
	SEC 150 mg NL (N=169)	11.2	49.7
	SEC 300 mg LD (N=191)	10.5	55.5
VLDA	SEC 150 mg LD (N=184)	9.8	18.5
	SEC 150 mg NL (N=169)	9.5	20.7
	SEC 300 mg LD (N=191)	9.4	23.6
DAPSA REM	SEC 150 mg LD (N=167)	8.4	29.9
	SEC 150 mg NL (N=162)	8.0	35.2
	SEC 300 mg LD (N=179)	8.4	36.3
DAPSA LDA + REM	SEC 150 mg LD (N=167)	11.4	56.9
	SEC 150 mg NL (N=162)	12.3	61.7
	SEC 300 mg LD (N=179)	14.0	60.9

Sustained REM/LDA was defined if the same response was achieved at least 2 out of the next 6 visits (every 8 weeks), respectively.
DAPSA, Disease activity in Psoriatic Arthritis; LD, loading dose; LDA, Low Disease Activity; MDA, Minimal Disease Activity; N, number of randomized patients assessed at both Week 24 and 104; NL, without loading dose; REM, remission; SEC, secukinumab; VLDA, Very Low Disease Activity.

Table 2 Summary of change from baseline in SF36-PCS at Week 104 by REM/LDA and sustained REM/LDA status

REM and LDA composite indices, Mean ± Standard Deviation (n)	Treatment group	REM/LDA only once	Sustained REM/LDA
MDA	SEC 150 mg LD	6.36 ± 9.54 (20)	9.45 ± 8.70 (87)
	SEC 150 mg NL	6.35 ± 8.78 (19)	11.38 ± 9.19 (84)
	SEC 300 mg LD	8.58 ± 6.61 (19)	10.40 ± 8.75 (104)
VLDA	SEC 150 mg LD	10.18 ± 9.12 (17)	11.14 ± 9.25 (34)
	SEC 150 mg NL	7.56 ± 9.25 (16)	13.28 ± 10.02 (35)
	SEC 300 mg LD	13.11 ± 7.08 (17)	11.67 ± 8.21 (43)
DAPSA REM	SEC 150 mg LD	3.48 ± 6.24 (14)	9.84 ± 8.57 (50)
	SEC 150 mg NL	7.71 ± 6.45 (13)	12.01 ± 9.52 (57)
	SEC 300 mg LD	9.11 ± 9.19 (15)	11.58 ± 9.05 (64)
DAPSA LDA + REM	SEC 150 mg LD	2.76 ± 6.05 (19)	7.00 ± 7.71 (94)
	SEC 150 mg NL	8.26 ± 7.92 (20)	7.82 ± 9.23 (100)
	SEC 300 mg LD	7.13 ± 8.10 (25)	8.43 ± 9.23 (107)

Sustained REM/LDA was defined if the same response was achieved at least twice out of the next 6 visits (every 8 weeks), respectively.
DAPSA, Disease Activity in Psoriatic Arthritis; LD, loading dose; LDA, Low Disease Activity; MDA, Minimal Disease Activity; n, number of evaluable patients; NL, without loading dose; REM, remission; SEC, secukinumab; SF-36 PCS, Short Form-36 Physical Component Score; VLDA, Very Low Disease Activity.

Conclusion: The majority of pts treated with SEC were able to achieve sustained REM/LDA. Sustained LDA/REM was associated with higher improvement of QoL and physical function compared to pts who achieved this response at only one visit.

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Disclosure: L. Coates, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5; **P. Mease**,

Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **S. Navarra**, Eli Lilly, 5, 8, Astra-Zeneca, 5, 8, Astellas, 8, Janssen, 5, 8, Novartis, 8, Pfizer, 8, Biogen, 2, 5; **W. Bao**, Novartis, 1, 3; **C. Gaillez**, Novartis, 1, 3.

Abstract Number: 0354

How Do TNF-alpha-Inhibitors in Medical History Affect Patient Reported Outcomes and Retention in Ankylosing Spondylitis Patients Treated with Secukinumab in Real World? – German Observational Study

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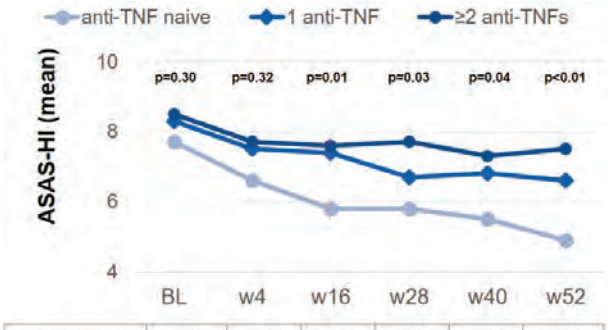
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Secukinumab (SEC), a fully human monoclonal antibody that selectively inhibits interleukin 17A, is approved for treatment of patients with ankylosing spondylitis (AS). However, there is lack of real-world evidence on SEC treatment outcomes, disease activity, physical functioning and on its retention, especially in anti-tumor necrosis factor (anti-TNF) naïve patients and patients pretreated with different anti-TNFs in medical history.[1]

The aim of this interim analysis is to evaluate SEC treatment outcomes on disease activity, physical functioning and retention rates in AS patients stratified by number of anti-TNFs (naive, 1 or ≥2) in medical history.

Methods: AQUILA is an ongoing, multi-center, non-interventional study. AS and psoriatic arthritis patients treated with SEC in daily practice are enrolled and observed from baseline (BL, d0 or d1 of study start) up to week 52 accord-



anti-TNF naive	n=79	n=69	n=75	n=60	n=59	n=56
1 anti-TNF	n=72	n=53	n=64	n=58	n=52	n=41
≥2 anti-TNFs	n=125	n=89	n=114	n=83	n=65	n=59

Figure 1. Change of health in AS patients treated with SEC stratified by anti-TNF pretreatment

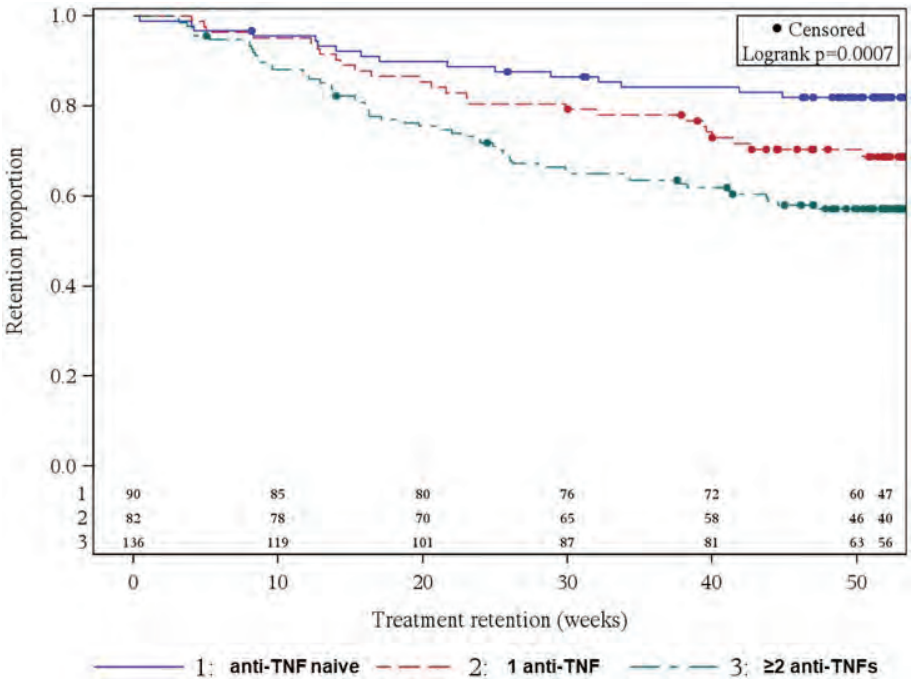


Figure 2. SEC treatment retention depending on anti-TNF pretreatment (Kaplan-Meier plot)

ing to clinical routine. Real-world effectiveness of SEC was assessed prospectively and analyzed as observed. Here, we report interim results of SEC effectiveness on different treatment outcomes in AS patients by means of validated questionnaires such as patient´s global assessment (PGA), Bath Ankylosing Disease Activity Index (BASDAI), and Assessment of Spondyloarthritis Health Index (ASAS-HI). In addition, retention rates (time from study inclusion until premature SEC treatment discontinuation) were assessed through Kaplan-Meier plots. This interim analysis focuses on *anti-TNF naïve* and AS patients treated with *1 anti-TNF* or *≥2 anti-TNFs* in medical history. Wilcoxon tests were conducted to show significant differences between the subgroups.

Results: At BL, 311 AS patients were included; 72 (23.2%) of them received SEC already for more than 1 day up to more than 6 months before BL. Most AS patients were anti-TNF-experienced (71.1%): 82 (26.4%) and 139 (44.7%) AS patients had 1 or ≥2 prior anti-TNF treatments, respectively. BL scores for PGA, BASDAI and ASAS-HI were similar between the different anti-TNF subgroups. Constant improvement was shown in all parameters from BL up to week 52, irrespective of prior anti-TNF treatment (PGA-*anti-TNF naïve*: 5.9 to 3.5, PGA-*1 anti-TNF:* 6.1 to 4.2 and PGA-*≥2 anti-TNFs:* 6.7 to 5.1; BASDAI-*anti-TNF naïve*: 5.3 to 3.4, BASDAI-*1 anti-TNF:* 5.5 to 3.7 and BASDAI-*≥2 anti-TNFs:* 5.7 to 4.7). However, overall better improvement was observed in *anti-TNF naïve* patients, as seen by the example of ASAS-HI (Fig. 1). Between 30% and 40% of patients prematurely discontinued SEC treatment in the subgroups *1 anti-TNF* and *≥2 anti-TNFs*, respectively, while only about 20% did so in the *anti-TNF naïve* AS patients (Fig. 2).

Conclusion: SEC has shown to improve disease activity, physical functioning and QoL in anti-TNF-naïve and pre-treated AS patients in a real-world setting. The benefits of SEC were numerically more distinct in anti-TNF-naïve patients. Moreover, SEC demonstrated high retention rate, particularly in anti-TNF-naïve patients, thereby confirming previously reported real-world data on SEC from EuroSpA research collaboration network.[2]

Disclosure: U. Kiltz, Abbvie, 2, 5, Biocad, 2, 5, Biogen, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Grünenthal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5; **J. Brandt-Jürgens**, Abbvie, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi-Aventis, 5, 8, Novartis, 5, 8, Lilly, 5, 8, MSD, 5, 8, UCB, 5, 8, BMS, 5, 8, Janssen, 5, 8, Medac, 5, 8; **P. Kästner**, Chugai, Novartis, 1; **E. Riechers**, AbbVie, Chugai, Lilly, Jannsen, Novartis, Pfizer, Roche, UCB, 1, AbbVie,

Chugai, Novartis, UCB, 1; **D. Peterlik**, Novartis Pharma GmbH, 1; **H. Tony**, AbbVie, 5, Astra-Zeneca, 5, BMS, 5, Chugai, 5, Janssen, 5, Lilly, 5, MSD, 5, Novartis, 5, Pfizer, 5, Roche, 5, Sanofi, 5.

Abstract Number: 0355

Collagen Turnover Markers Are Associated with Active Psoriatic Arthritis and Decrease with Guselkumab Treatment in a Phase-3 Clinical Trial

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Guselkumab (GUS), an interleukin-23p19-subunit monoclonal antibody, demonstrated efficacy compared to placebo (PBO) in reducing skin and musculoskeletal signs and symptoms in patients with active

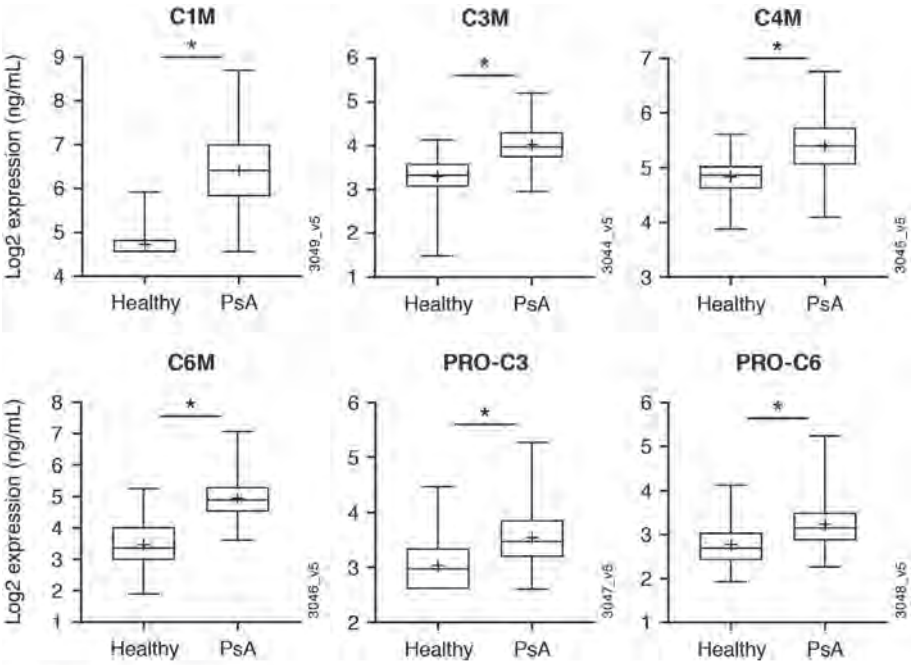

Figure 1. Upregulation of collagen degradation/formation biomarkers is detected in the serum of PsA subjects compared to healthy controls.

Healthy controls have been demographically matched (age, sex, race/ethnicity) to the PsA cohort. Median values (+ marks mean). Boxes represent the interquartile range, whiskers the minimum and maximum.

* Indicates significance defined by |fold change| ≥1.25 and FDR adjusted $p < 0.05$.

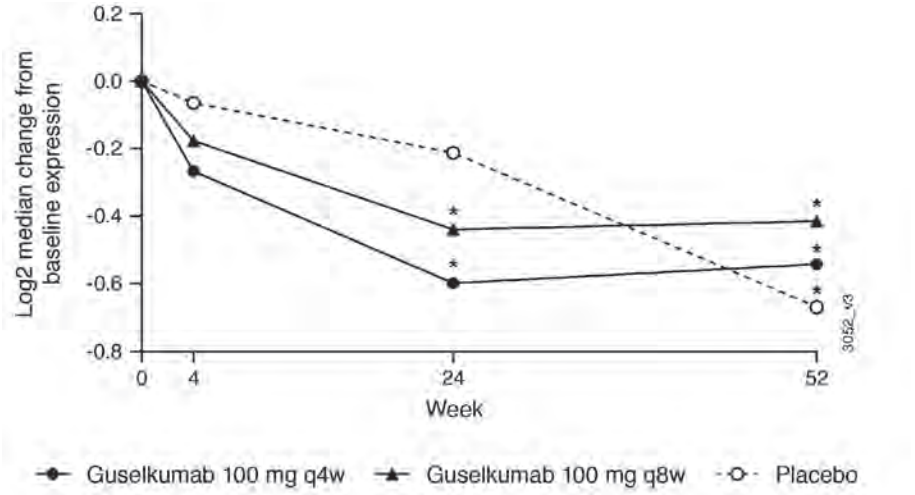

Figure 2. Collagen degradation marker C1M decreases with guselkumab treatment.
* Significant change from baseline defined by $p < 0.05$ and |fold difference| ≥1.25

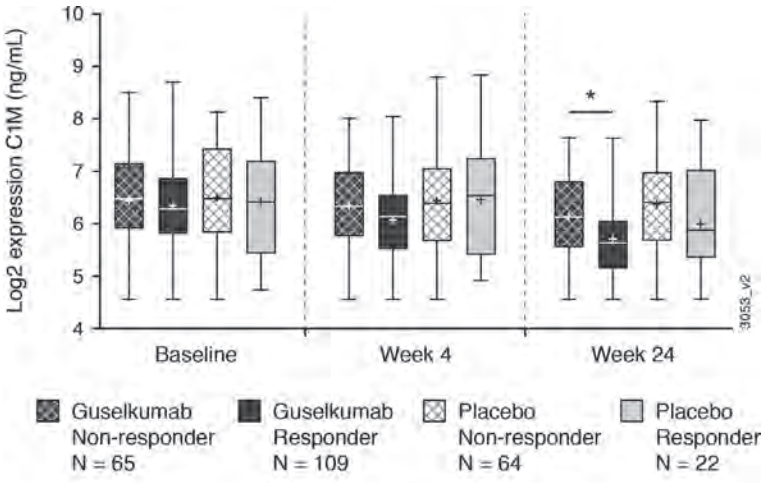

Figure 3. C1M Reductions by ACR20 Response.
Response defined by ACR20 at Week 24. Median values (+ marks mean). Boxes represent the interquartile range, whiskers the minimum and maximum.
* p=0.0065, significance between responder and non-responder defined by $p < 0.05$ and |fold difference| ≥1.25.

psoriatic arthritis (PsA) in two phase-3 studies, DISCOVER 1 & 2, and in retarding structural damage in DISCOVER 2.[1,2] Here we evaluate tissue-derived extracellular matrix (ECM) products[3,4] in serum of PsA patients in the DISCOVER 2 study and their relationship with radiographic damage, clinical response, and impact of treatment.

Methods: In DISCOVER 2, patients were treated with GUS 100 mg at Week (w) 0, 4, then every 8w (q8w); GUS 100mg every 4w (q4w); or matching PBO. At w24, PBO subjects were crossed-over to GUS q4w. 11 serum biomarkers of ECM collagen formation (PRO-C1, PRO-C2, PRO-C3, PRO-C4, PRO-C6) and degradation (C1M, C2M, C3M, C4M, C6M, and COL10) were measured (by Nordic Bioscience) in a subset of 260 patients from the DISCOVER 2 program at Weeks 0, 4, 24, & 52 and in 76 healthy controls matched for age, sex, and ethnicity. PsA patients were selected randomly, though enriching for subjects with greatest radiographic changes, at Weeks 24 and 52. Significance defined by $P < 0.05$ and $|\text{fold difference}| \geq 1.25$.

Results: At baseline, collagen degradation markers C1M, C3M, C4M, C6M and collagen formation markers PRO-C3 and PRO-C6 were significantly higher in PsA patients compared to matched healthy controls (Figure 1). Baseline C3M, C4M, and C6M were positively correlated to baseline skin and joint disease; baseline C1M, C3M, C4M, C6M, and PRO-C1 were positively correlated to baseline radiographic damage (data not shown). Levels of C1M (a maker indicating breakdown of collagen type I, the major collagen subtype in the bone) were significantly decreased after 24w treatment with GUS (Figure 2), reaching significant differences from placebo with the GUS 100 mg q4w group. For the PBO patients who crossed over to GUS at w24, there was also a reduction in this marker observed at w52 (Figure 2). In patients treated with GUS or PBO, there were not significant differences in baseline expression levels of the analytes in responders (patients achieving ACR20 at w24) compared with non-responders. However, ACR20 responders in the combined GUS group had a significantly greater reduction in C1M levels compared to non-responders (Figure 3).

Conclusion: This work provides evidence that collagen biomarkers in serum are dysregulated in patients with PsA compared to healthy controls, and that GUS impacts levels of these proteins. Importantly, C1M serves as a biomarker that tracks with joint response. We observed a greater reduction in C1M in ACR responders compared to non-responders, providing insight into how GUS may be working to protect from degradation of bone in PsA.

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Disclosure: G. Schett, None; **M. Loza**, Janssen Research & Development, LLC, 1, 3; **A. Palanichamy**, Janssen Research & Development, LLC, 1, 3; **O. FitzGerald**, AbbVie Inc., 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Janssen, 2, 5, Eli Llilly, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **C. Ritchlin**, None; **F. Baribaud**, Janssen Research & Development, LLC, 1, 3; **K. Sweet**, Janssen Research & Development, LLC, 3.

Abstract Number: 0356

Bimekizumab Improves Patient-Reported Outcomes in Psoriatic Arthritis: 48-Week Results from a Phase 2b Study and Association Between Patient-Reported Outcomes and Disease Activity

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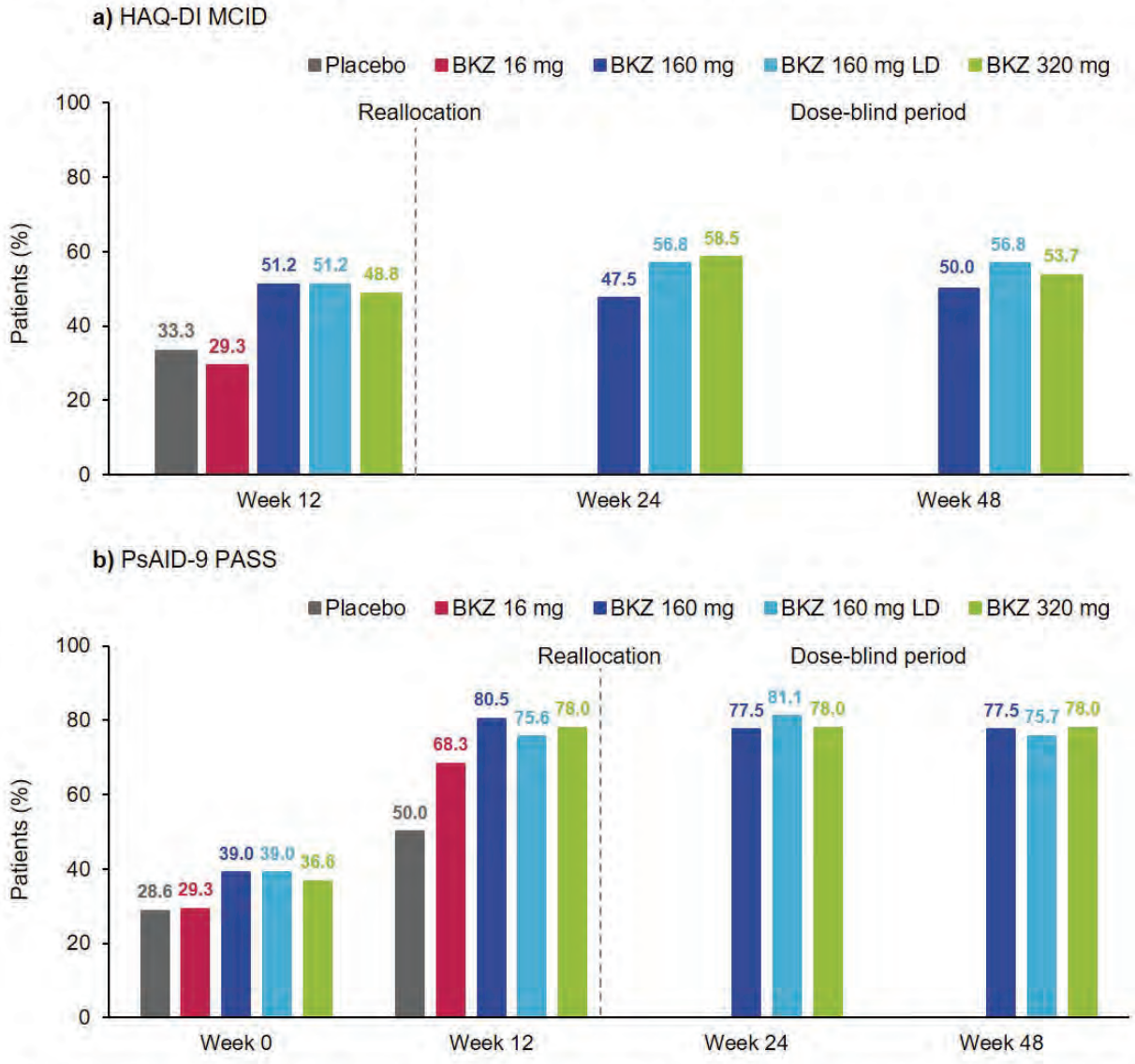
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Bimekizumab (BKZ), a humanized monoclonal IgG1 antibody that selectively neutralizes interleukin (IL)-17A and IL-17F, has shown clinical improvements in joint and skin outcomes and a favorable safety profile in patients (pts) with active psoriatic arthritis (PsA).[1] Here we report the impact of BKZ treatment over 48 weeks

Figure 1: Proportion of patients with HAQ-DI MCID and PsAID-9 PASS



The study was double-blind and placebo-controlled to Wk 12 and dose-blind to Wk 48. Patients were randomized at baseline to receive either placebo Q4W or 1 of 4 dosing regimens of BKZ Q4W (16 mg, 160 mg, 160 mg with 320 mg LD at baseline, or 320 mg). After Wk 12, patients receiving placebo or 16 mg BKZ were reallocated (1:1) to receive either 160 mg or 320 mg BKZ, while all other patients continued their original dosing regimen. Data are shown by randomized dose at baseline. FAS up to Wk 12 and DBS Wks 12–48; DBS consists of all patients who received ≥1 dose of BKZ in dose-blind period. patients with missing values were counted as non-responders. The HAQ-DI MCID is a ≥0.35 decrease from baseline. Lower PsAID-9 score corresponds to better quality of life in patients. PASS is defined as having a PsAID-9 total score ≤4. BKZ: bimekizumab; DBS: Dose-Blind Set; FAS: Full Analysis Set; HAQ-DI: Health Assessment Questionnaire Disability Index; LD: loading dose; MCID: minimal clinically important difference: PASS: patient acceptable symptom state; PsAID-9: Psoriatic Arthritis Impact of Disease-9; Q4W: every four weeks; Wk: Week.

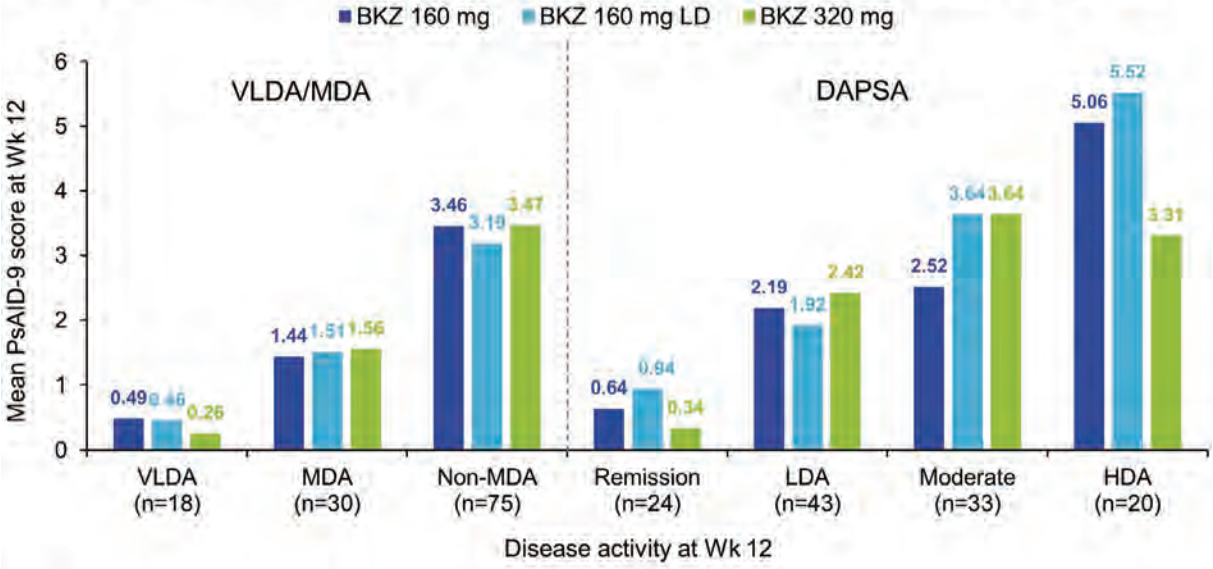
on two patient-reported outcome (PRO) measures: Health Assessment Questionnaire Disability Index (HAQ-DI) and Psoriatic Arthritis Impact of Disease-9 (PsAID-9). The PsAID-9 is a questionnaire specifically developed to assess the impact of PsA on pts' lives.[2, 3] We also examine the association between achieving high disease control states (very low disease activity [VLDA], minimal disease activity [MDA] or Disease Activity in PSoriatic Arthritis [DAPSA] remission) and PsAID-9 score.

Table: VLDA, MDA and DAPSA responder rates

Treatment arm (FAS n, DBS n)	VLDA (%) [a]			MDA (%) [a]			DAPSA remission (%) [b]		
	Wk 12	Wk 24	Wk 48	Wk 12	Wk 24	Wk 48	Wk 12	Wk 24	Wk 48
Placebo (n=42)	2.4			14.3			2.4		
BKZ 160 mg (n=41, n=40)	14.6	22.5	37.5	46.3	50.0	60.0	19.5	35.0	45.0
BKZ 160 mg LD (n=41, n=37) [c]	19.5	32.4	29.7	41.5	59.5	54.1	29.3	48.6	37.8
BKZ 320 mg (n=41, n=41)	9.8	14.5	22.0	29.3	36.6	46.3	12.2	19.5	34.1

FAS for Wk 12 and DBS for Wks 24 and 48. Data are shown by randomized dose at baseline. [a] DBS, patients with missing data were counted as non-responders; [b] DBS, missing data are imputed using last observation carried forward; [c] 160 mg with 320 mg LD at baseline. BKZ: bimekizumab; DAPSA: Disease Activity Index for Psoriatic Arthritis; DBS: Dose-Blind Set; FAS: Full Analysis Set; LD: loading dose; MDA: minimal disease activity.

Figure 2: Association between VLDA, MDA, and DAPSA disease states and PsAID-9 at Wk 12



FAS; values of n are the number of patients on the 160 mg, 160 mg LD, and 320 mg doses with the specified disease activity outcome. Missing data are imputed using multiple imputation based on the Markov-Chain Monte Carlo method for the intermittent missing data, followed by monotone regression for the monotone missing data assuming missing at random. Lower PsAID-9 score corresponds to better quality of life in patients. BKZ: bimekizumab; DAPSA: Disease Activity in Psoriatic Arthritis; FAS: Full Analysis Set; HDA: high disease activity; LD: loading dose; LDA: low disease activity; MDA: minimal disease activity; PsAID-9: Psoriatic Arthritis Impact of Disease-9; VLDA: very low disease activity; Wk: Week.

Methods: In this phase 2b dose-ranging study (BE ACTIVE; NCT02969525), PsA pts received BKZ or placebo.[1] Here we report improvements in PROs over 48 weeks using the proportion of pts who achieved a Minimal Clinically Important Difference (MCID) in the functional score HAQ-DI (≥0.35 decrease from baseline). We also show the rate of pts reporting a PsAID-9 Patient Acceptable Symptom State (PASS), which for the PsAID-9 has been proposed as a score ≤4,[2] and examine the association of VLDA/MDA (binary disease control states) or DAPSA (where remission is

0–4, low: 5–14, moderate: 15–28, and high disease activity is >28) with PsAID-9 score at Wk 12. The Full Analysis Set (FAS) is used up to and including Wk 12; the Dose-Blind Set (DBS) is used from Wk 12 to Wk 48.

Results: Across 206 randomized pts at baseline, 66.5% had psoriasis body surface area (BSA) ≥3%, 18.9% had prior tumor necrosis factor inhibitor (TNFi) exposure, and 63.6% received concomitant methotrexate. Mean baseline HAQ-DI scores were comparable across all treatment arms (including placebo), ranging from 0.9–1.0; PsAID-9 scores ranged from 4.3–4.8. The proportion of pts achieving HAQ-DI MCID for BKZ 160 mg, 160 mg plus loading dose (LD), and 320 mg treatment arms was 47.5–58.5% across Wks 12, 24 and 48 (**Figure 1a**). Additionally, more than 75% of pts receiving BKZ 160/160 LD/320 mg achieved PsAID-9 PASS across Weeks 12, 24 and 48 (**Figure 1b**). Furthermore, a substantial proportion of pts within these BKZ treatment arms also achieved VLDA, MDA and/or DAPSA remission at Wk 12; this generally increased through to Wk 24 and 48 (**Table**). PsAID-9 score at Wk 12 was consistently lower for pts with VLDA/MDA or in DAPSA remission (**Figure 2**).

Conclusion: This patient population with active PsA demonstrated rapid and sustained improvements in patient-reported physical function and psychological wellbeing over 48 weeks of BKZ treatment. Achievement of VLDA/MDA or DAPSA remission was associated with lower mean PsAID-9 scores, reinforcing evidence that achievement of higher disease control in pts with PsA is important for improved quality of life.

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Disclosure: L. Gossec, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **A. Gottlieb**, Janssen, 2, 5, Incyte, 2, 5, Novartis, 2, 5, 8, Xbiotech, 2, 9, Boehringer Ingelheim, 2, 5, UCB Pharma, 2, 5, 8, Beiersdorf, 5, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, Sun Pharma, 2, 5, Leo Pharma, 5, Avotres Therapeutics, 5; **D. Assudani**, UCB Pharma, 3; **J. Coarse**, UCB Pharma, 3; **B. Ink**, UCB Pharma, 3; **L. Coates**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5.

Abstract Number: 0357

Suppressing Inflammation Rather Than Lowering the Disease Activity Score Should Be Targeted During TNF Inhibitor Treatment to Slow Radiographic Changes in Patients with Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

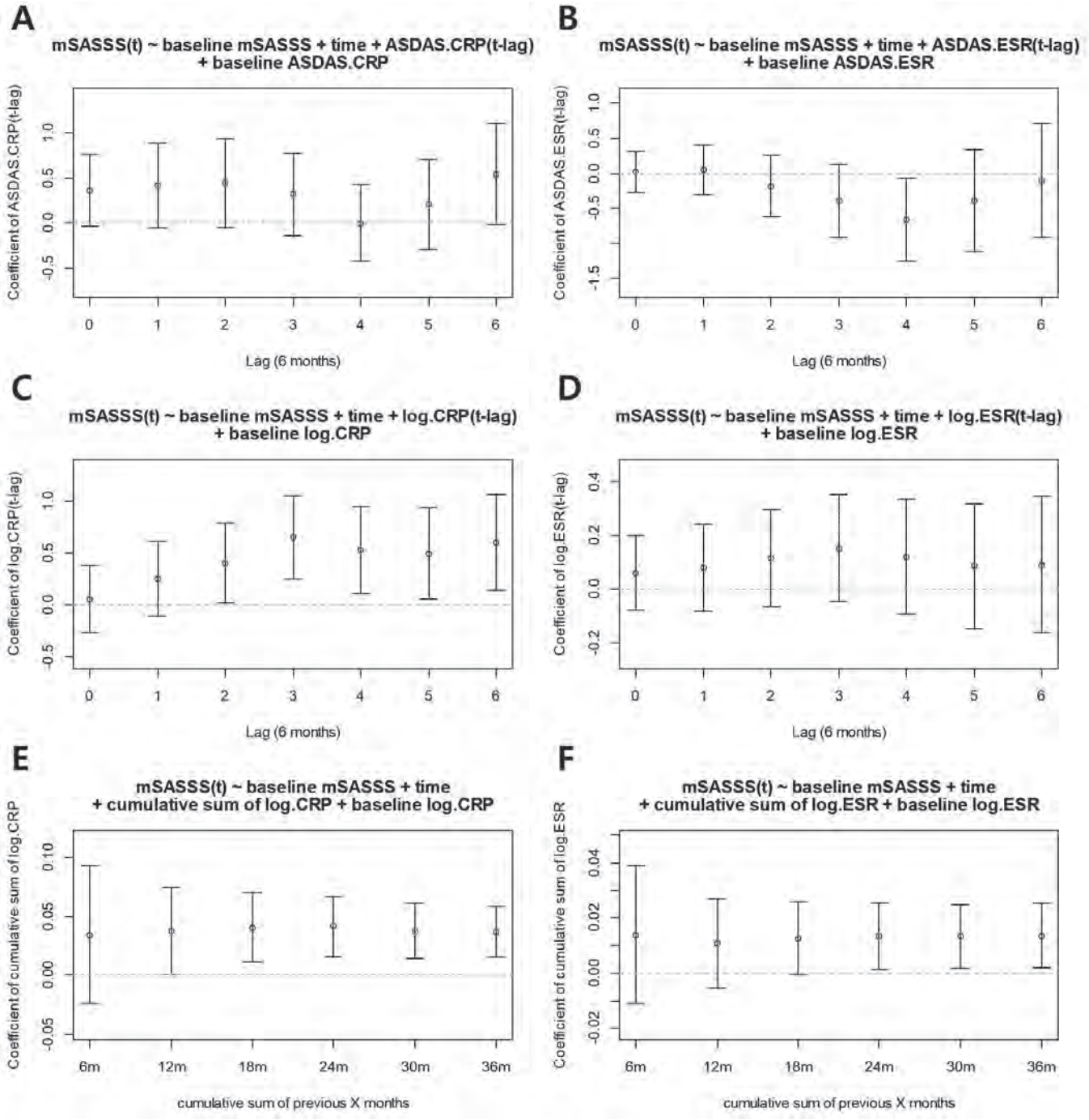

Figure 1. Relationship between mSASSS and inflammatory markers and disease activities over time using an autoregressive model

Background/Purpose: Treatment with tumor necrosis factor (TNF) inhibitors has the effect of slowing radiographic progression by improving symptoms and reducing inflammation in patients with ankylosing spondylitis (AS). However, the inflammation is still not controlled in some patients even if their symptoms improve with the TNF inhibitor treatment. The purpose of this study was to analyze the relationship between inflammation and radiographic progression in patients with AS, whose symptoms were well controlled by a TNF inhibitor treatment in a real-world observational data.

Table 1. Linear mixed model with the cumulative sum of log CRP up to 24 months as main independent variable and mSASSS at 24 months as outcome

X	Beta estimate	95% CI		p-value
		LB	UB	
Baseline mSASSS	1.047	1.013	1.080	<0.001
Time	0.466	0.433	0.500	<0.001
Cumulative sum of previous 24 months' log CRP	0.043	0.014	0.071	0.004
Female	-0.649	-2.658	1.359	0.525
Eye involvement	0.349	-0.834	1.532	0.561
Peripheral_involvement1	-1.234	-2.436	-0.032	0.044
HLA B27 positivity	-0.549	-3.639	2.540	0.726

Methods: Of the 1,280 patients who were followed-up for 18 years in a single center, the electronic medical data of 590 patients treated with TNF inhibitors were included. Among them, 333 patients with bath ankylosing spondylitis disease activity Index (BASDAI) < 4 measured at all the time points following the first TNF inhibitor dosing were included. From these patients, 898 intervals were obtained, which was the period of administration of the TNF inhibitor. To determine the relationship between the modified stoke ankylosing spondylitis spinal score (mSASSS) and inflammatory markers such as c-reactive protein (CRP), erythrocyte sedimentation rate (ESR), and disease activities such as Ankylosing Spondylitis Disease Activity Score (ASDAS)-ESR and ASDAS-CRP over time, we fitted linear mixed models with mSASSS as response variable, baseline mSASS and inflammatory marker with different lag times as fixed effects, and patients as random effects. With the inflammatory marker and the lag time with statistically significant beta coefficient, , its association with the mSASSS was further investigated with linear mixed model that includes additional clinical variables.

Results: The relationship between mSASSS and past inflammatory markers and disease activities were examined for up to 36 months using linear mixed models (Fig. 1). The cumulative sums of log CRP for the previous 18, 24, 30, and 36 months showed significantly positive correlation with mSASSS (Fig. 1E). From these results, the cumulative sum of the previous 24 months' log CRP as the main independent variable was used in the linear mixed model with mSASSS at 24 months as the outcome (Table 1). Baseline mSASSS (b=1.047, 95% CI: 1.013 to 1.080, p< 0.001), time (b=0.466, 95% CI: 0.433 to 0.500 p< 0.001), and cumulative sum of the previous 24 months' log CRP (b=0.043, 95% CI: 0.014 to 0.071, p=0.004) were significantly associated with mSASSS at 24 months.

Conclusion: The symptoms were well controlled because BASDAI was maintained below 4; however, those with a high cumulative sum of CRP showed an increased mSASSS change. In order to slow the radiographic progression in patients with AS, inflammation rather than disease activity should be targeted and actively controlled during treatment with TNF inhibitors.

Disclosure: B. Koo, None; **J. Oh**, None; **S. Park**, None; **J. Shin**, None; **B. Nam**, None; **S. Lee**, None; **K. Joo**, None; **T. Kim**, AbbVie, 1, Celltrion, 1, Kirin, 1, Lilly, 1, Novartis, 1.

Abstract Number: 0358

Does Smoking Affect Secukinumab Treatment Outcomes and Safety in Patients with Ankylosing Spondylitis? – Real World Data from German Observational Study

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: There is growing body of evidence that smoking is associated with more active and severe disease in patients (pts) with ankylosing spondylitis (AS)[1,2]. The German non-interventional study AQUILA provides real-world data on the influence of smoking on therapeutic effectiveness and safety under secukinumab (SEC), a fully human monoclonal antibody that selectively inhibits interleukin-17A.

The aim of this interim analysis is to describe selected baseline (BL) demographics, to evaluate SEC effectiveness on disease activity and global functioning and health, and to report safety profile depending on smoking status of AS pts.

Methods: AQUILA is an ongoing, multi-center, non-interventional study including up to 2700 pts with active AS or psoriatic arthritis. Pts were observed from BL up to week (w) 52. Real-world data was assessed prospectively and analyzed as observed. Assessment of CRP and validated questionnaires were used to collect data on disease activity (Bath Ankylosing Spondylitis Disease Activity Index, BASDAI), global functioning and health (Assessment of

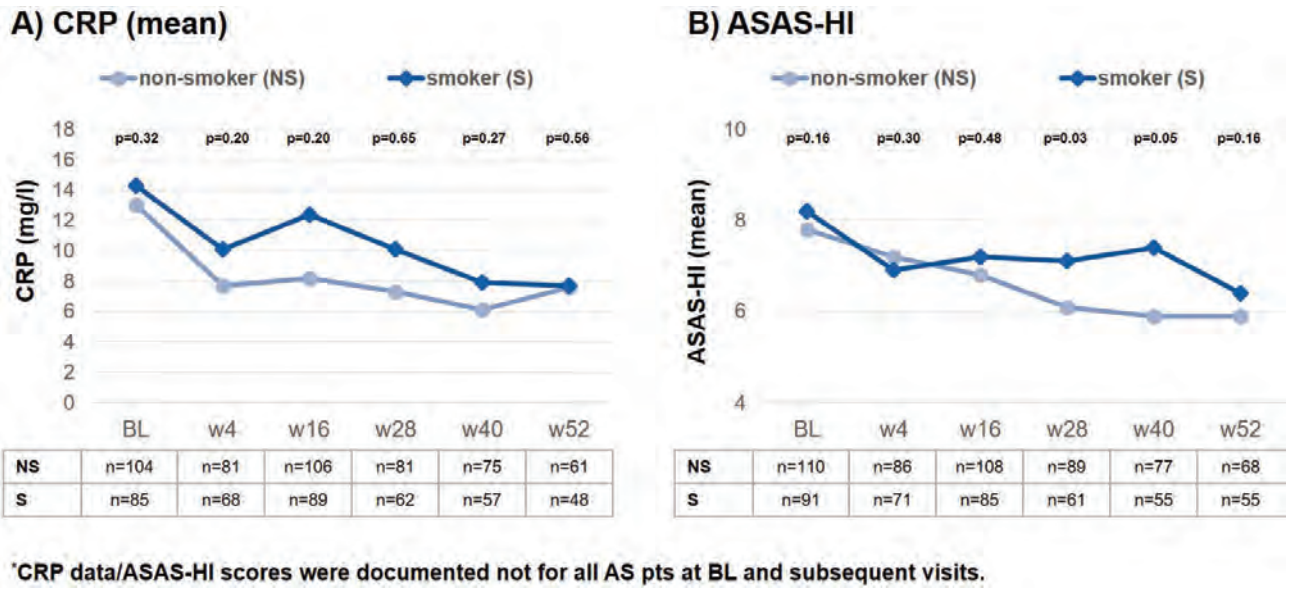

Figure 1. CRP and global functioning and health in AS pts treated with SEC depending on smoking status*

Table 1 Overview of AEs (and SAEs) under SEC treatment depending on smoking status in AS pts

Number of pts with	NS (N=140), n (%)	S (N=110), n (%)	P value
AE	95 (67.9)	78 (70.9)	0.80
AE with suspected relationship to SEC	66 (47.1)	41 (37.3)	0.29
SAE	39 (27.9)	30 (27.3)	0.95
SAE with suspected relationship to SEC	15 (10.7)	10 (9.1)	0.87

SpondyloArthritis-Health Index, ASAS-HI) and depressive mood (Beck´s Depression Inventory version II, BDI-II). For calculation of proportion of pts who experienced (serious) adverse events ((S)AEs), all AS pts were included who received at least one dose of SEC irrespective of further documentation of any study visit. This analysis focuses on the subgroups non-smoker (NS) and smoker (S).

Results: At BL, 311 AS pts were included: 42.1% (n=131) NS and 32.8% (n=102) S. Remaining subgroups were 15.1% (n=47) ex-smoker and 10.0% (n=31) of unknown smoking status. About half of AS pts in NS were male, while in S (69.6%) portion of men was more than twice as high as of women. S were slightly younger than NS (mean age: 43.9/49.0 years). During the study, CRP value decreased irrespective of smoking status with numerically higher fluctuations in S (Fig. 1A). BASDAI (NS: 5.2 at BL to 3.7 at w52, S: 5.6 at BL to 4.1 at w52) and ASAS-HI (Fig. 1B) scores numerically improved best in NS, whereas more variations were seen in S; the same was observed for BDI-II score values (NS: 11.8 at BL to 9.2 at w52, S: 13.0 at BL to 12.1 at w52). Although no major significant differences in mean values existed between NS and S, S displayed – except in w4 – overall higher mean values in the parameters mentioned above. Regarding the occurrence of AEs/SAEs with or without suspected relationship to SEC, there was no significant difference between NS and S (Table 1).

Conclusion: In a real-world setting, SEC improved disease activity and global functioning and health in AS pts with slight (mostly non-significant) differences between NS and S. Overall, this interim analysis shows that SEC is an effective treatment with a favorable safety profile up to 52 weeks, irrespective of the pts' smoking status. Further progress of the AQUILA study will reveal whether this trend will continue.

Disclosure: E. Riechers, AbbVie, Chugai, Lilly, Jannsen, Novartis, Pfizer, Roche, UCB, 1, AbbVie, Chugai, Novartis, UCB, 1; **U. Kiltz**, Abbvie, 2, 5, Biocad, 2, 5, Biogen, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Grünenthal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5; **J. Brandt-Jürgens**, Abbvie, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi-Aventis, 5, 8, Novartis, 5, 8, Lilly, 5, 8, MSD, 5, 8, UCB, 5, 8, BMS, 5, 8, Janssen, 5, 8, Medac, 5, 8; **P. Kästner**, Chugai, Novartis, 1; **D. Peterlik**, Novartis Pharma GmbH, 1; **H. Tony**, AbbVie, 5, Astra-Zeneca, 5, BMS, 5, Chugai, 5, Janssen, 5, Lilly, 5, MSD, 5, Novartis, 5, Pfizer, 5, Roche, 5, Sanofi, 5.

Abstract Number: 0359

Clinical Characteristics of Psoriatic Arthritis Patients with Physician-Identified Spondylitis, According to HLA-B27 Status: An Analysis from the Corrona Psoriatic Arthritis/Spondyloarthritis Registry

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial disease in psoriatic arthritis (PsA) has been reported to occur in anywhere from 25% to 75% of PsA patients (pts). It can be associated with more severe disease characteristics.[1] Our objective was to describe the characteristics of clinical registry PsA pts with physician-identified spondylitis, at treatment initiation and 6 months post-treatment with biologic (b) or targeted synthetic (ts) disease modifying anti-rheumatic drugs (DMARDs), and to determine whether treatment response differs by HLA-B27 status.

Methods: The Corrona Psoriatic Arthritis/Spondyloarthritis Registry is a prospective, multicenter, observational disease-based registry launched in March 2013 that currently has information on over 3000 enrolled pts. Pt assessments are completed at approximately 6-month intervals. The PsA pts included in this analysis initiated treatment with either bDMARDs or tsDMARDs at a Corrona visit (baseline) and had a 6-month follow-up, fulfilled Classification Criteria for Psoriatic Arthritis (CASPAR), had physician-reported spondylitis with Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) scores ≥4 at baseline, and had known HLA-B27 genotype. Disease characteristics at baseline and

Table 1. Baseline Characteristics of PsA Initiators in the CORRONA Registry with Physician-Reported Axial Involvement and Known HLA-B27 Genotype*

	Baseline		
	HLA-B27+	HLA-B27–	Overall
Demographics	(n=54)	(n=119)	(n=173)
Age, years	54.19 (11.47)	49.42 (12.39)	50.91 (12.28)
Sex [male], n (%)	19 (35.8)	51 (42.9)	70 (40.7)
BMI, kg/m^2	33.00 (8.410)	32.54 (7.350)	32.67 (7.670)
Time since PsA symptom onset, years	8.75 (8.910)	9.05 (8.190)	8.96 (8.390)
Time since PsA diagnosis, years	4.44 (4.450)	5.19 (5.560)	4.96 (5.250)
Current PsO	43 (79.6)	102 (85.7)	145 (83.8)
History of Comorbidities n (%)			
IBD	0	1 (0.8)	1 (0.6)
Crohn's Disease	0	1 (0.8)	1 (0.6)
Ulcerative Colitis	0	0	0
Uveitis	1 (1.9)	1 (0.8)	2 (1.2)
CVD	13 (24.1)	10 (8.4)	23 (13.3)
Osteoporosis	1 (1.9)	4 (3.4)	5 (2.9)
Therapy Initiated, n (%)**			
bDMARD	46 (85.2)	95 (79.8)	141 (81.5)
TNFi	26 (48.1)	50 (42.0)	76 (43.9)
Non TNFi	20 (37.0)	45 (37.8)	65 (37.6)
tsDMARD	8 (14.8)	24 (20.2)	32 (18.5)
Concomitant therapy, n (%)			
Monotherapy	35 (68.6)	84 (71.8)	119 (70.8)
MTX in combination	16 (31.4)	33 (28.2)	49 (29.2)

*Data are mean (SD) unless otherwise stated. **Patients may have received more than one drug over time and been included in more than one group.
BMI, body mass index; CVD, cardiovascular disease; DMARD, disease modifying anti-rheumatic drug (b, biologic; ts, targeted synthetic); IBD, inflammatory bowel disease; MTX, methotrexate; PsA, psoriatic arthritis; PsO, psoriasis; TNFi, tumor necrosis factor inhibitor

Table 2. Disease Characteristics at Baseline and 6 Months Post-Treatment of PsA Initiators in the CORRONA Registry with Physician-Reported Axial Involvement and Known HLA-B27 Genotype*

Disease Characteristics	Baseline			6 Months Post-Treatment *Change from Baseline*		
	HLA-B27+	HLA-B27–	Overall	HLA-B27+	HLA-B27–	Overall
n**	(n=54)	(n=119)	(n=173)	(n=54)	(n=119)	(n=173)
Tender joint count (TJC, 68 joints)	9.3 (9.5)	10.6(13.0)	10.2(12.0)	6.5 (9.1) *-2.4 (8.5)*	8.4 (12.6) *-2.2 (10.0)*	7.8 (11.6) *-2.3 (9.5)*
Swollen joint count (SJC, 66 joints)	4.0 (5.2)	4.7 (6.8)	4.5 (6.3)	2.5 (4.1) *-1.5 (5.2)*	3.0 (5.1) *-1.7 (6.1)*	2.8 (4.8) *-1.6 (5.8)*
Physician Global Assessment of PsA, VAS	43.5 (20.0)	40.3 (24.3)	41.3 (23.1)	30.7 (27.1) *-12.9 (28.3)*	26.9 (22.1) *-14.0 (26.7)*	28.0 (23.6) *-13.7 (27.1)*
Patient-reported Pain VAS	67.4 (20.9)	66.7 (18.6)	66.9 (19.3)	57.9 (26.1) *-9.2 (27.8)*	57.7 (25.1) *-8.8 (28.6)*	57.8 (25.3) *-8.9 (28.3)*
HAQ-DI	1.2 (0.6)	1.1 (0.7)	1.1 (0.6)	1.1 (0.7) *-0.05 (0.5)*	1.0 (0.7) *-0.07 (0.5)*	1.1 (0.7) *-0.07 (0.5)*
BSA, %	5.1 (6.8)	5.1 (8.9)	5.1 (8.3)	3.0 (4.5) *-2.2 (6.4)*	3.7 (7.8) *-1.5 (10.5)*	3.4 (6.9) *-1.7 (9.4)*
BASDAI (0-10)	6.3 (1.4)	6.5 (1.5)	6.4 (1.4)	5.5 (2.2) *-0.8 (1.8)*	5.6 (2.0) *-0.8 (2.2)*	5.6 (2.1) *-0.8 (2.1)*
BASDAI Q2, Spine Pain	6.2 (2.4)	6.2 (2.6)	6.2 (2.6)	5.5 (2.9) *-0.8 (2.3)*	5.4 (2.6) *-0.8 (2.6)*	5.4 (2.7) *-0.8 (2.5)*
mBASDAI	6.2 (1.5)	6.4 (1.5)	6.4 (1.5)	5.6 (2.3) *-0.6 (1.8)*	5.7 (2.1) *-0.8 (2.2)*	5.7 (2.2) *-0.7 (2.1)*
ASDAS-CRP	3.4 (1.0)	3.1 (0.9)	3.2 (0.9)	2.8 (1.1) *-0.4 (1.1)*	2.7 (0.9) *-0.7 (1.2)*	2.8 (1.0) *-0.6 (1.1)*
HAQ-S	1.2 (0.6)	1.1 (0.7)	1.1 (0.6)	1.1 (0.7) *-0.03 (0.5)*	1.1 (0.7) *-0.07 (0.5)*	1.1 (0.7) *-0.06 (0.5)*
Patient Reported Spine Pain, VAS	49.8 (31.7)	50.7 (29.5)	50.4 (30.1)	39.7 (29.9) *-10.2 (28.3)*	42.5 (29.6) *-8.6 (32.0)*	41.6 (29.6) *-9.1 (30.8)*
Patient-reported Nocturnal Spine Pain, VAS	39.5 (30.3)	46.6 (32.0)	44.3 (31.5)	38.2 (31.0) *-1.2 (24.9)*	40.5 (29.5) *-7.0 (31.1)*	39.8 (29.9) *-5.2 (29.3)*

*Data are mean (SD) unless otherwise stated. **Some entries have missing patient values; observations are based on unique therapy initiations, thus patients may contribute ≥1 observation
ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score-C-reactive protein (<1.3:inactive, ≥1.3-<2.1:moderate, ≥2.1-≤3.5:high, >3.5:very high); BASDAI, Bath Ankylosing Spondylitis Disease Activity Index (0-10cm, ≥4 active disease); mBASDAI, modified BASDAI (excludes Q#3); BSA, body surface area; HAQ-DI, The Stanford Health Assessment Questionnaire Disability Index (0 -1 mild to moderate difficulty, 1-2 moderate to severe disability, and 2-3 severe to very severe disability); HAQ-S, Health Assessment Questionnaire for the Spondylarthropathies; VAS, visual analog scale

6-months are described via means (SD) and counts (%) by HLA-B27 status (+/–). A multivariable-adjusted linear mixed model was used to test for association (regression coefficient) of HLA-27 status with outcomes at 6-months.

Results: Among the 173 initiations, 31% were HLA B27+ and 69% were HLA B27–. Baseline demographics, comorbidities (Table 1), and disease characteristics (Table 2) were similar between HLA-B27+ and HLA-B27– groups. Axial disease-related outcome measures, including BASDAI, BASDAI Q#2, modified BASDAI (mBASDAI, Q#3 removed), and ASDAS-CRP, all consistently indicated either active disease or high disease activity at baseline. In HLA-B27+ and HLA-B27– pts, respectively, 85% and 80% initiated a bDMARD, while 15% and 20% initiated a tsDMARD. Six-months post-treatment, axial disease-related measures reflected only mild improvement and were still indicative of active disease or high disease activity, irrespective of HLA-B27 status (Table 2). There were no statistically significant differences between HLA B27+ and HLA B27– pts in changes from baseline in the axial disease-related outcome measures assessed (Table 3). In an exploratory analysis of a subgroup of these pts with radiologic confirmation of axial involvement (n=21), similar outcomes were observed (data not shown).

Conclusion: In this registry study of PsA pts with physician-reported axial disease, after 6 months of treatment with bDMARD or tsDMARD therapy, only mild improvements in axial disease-related outcome measures were observed.

Table 3. Adjusted* Difference Between HLA-B27+ and HLA-B27– Initiators in Outcomes (Mean Change from Baseline to 6 Months)		
Disease Characteristic	**β Estimate (95% CI)**	**p-value**
Tender Joint Count (68 joints)	-0.368 (-2.926, 2.190)	0.777
Swollen Joint Count (66 joints)	-0.136 (-1.431, 1.159)	0.835
Physician Global Assessment of PsA, VAS	2.287 (-6.385, 10.959)	0.603
Patient-reported Pain VAS	1.881 (-6.562, 10.324)	0.660
HAQ-DI	-0.004 (-0.161, 0.153)	0.960
BSA, %	-1.262 (-3.231, 0.707)	0.207
BASDAI (0-10)	0.040 (-0.584, 0.665)	0.898
BASDAI Q2: Spine Pain	0.863 (-6.729, 8.455)	0.822
mBASDAI	0.077 (-0.561, 0.714)	0.812
HAQ-S	0.006 (-0.147, 0.158)	0.941
Patient-reported Spine Pain VAS	-0.269 (-8.61, 8.076)	0.949
Patient-reported Nocturnal Spine Pain VAS	3.012 (-6.376,12.399)	0.527
*Linear regression model estimates adjusted for baseline value and other potential risk factors: (age at initiation, insurance, alcohol use, history of cardiovascular disease, prior cDMARD, prior bDMARD, and prior tsDMARD). The HLA-B27– group is the reference group for this comparison. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; mBASDAI, modified BASDAI (excludes Q3); BSA, body surface area; HAQ-DI, The Stanford Health Assessment Questionnaire Disability Index; HAQ-S, Health Assessment Questionnaire for the Spondylarthropathies; VAS, visual analog scale		

Furthermore, response did not differ based on HLA-B27 status. The continued high disease activity of these pts reflects a critical unmet need for additional safe and effective therapies for PsA axial disease.

Reference

1. Mease et al. *J Rheumatol* 2018; 45:1389.

Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **S. Chakravarty**, Janssen Scientific Affairs, LLC, 1, 3; **R. McLean**, Corrona, 3; **T. Blachley**, Corrona, LLC, 3; **T. Kawashima**, None; **I. Lin**, Janssen Scientific Affairs, LLC, 1, 3; **J. Uy**, Janssen Scientific Affairs, LLC, 1, 3; **A. Kavanaugh**, Eli Lilly and Company, 5; **A. Ogdie**, AbbVie, 5, Amgen, 2, 5, BMS, 1, Celgene, 1, Corrona, 1, Janssen, 1, Eli Lilly, 1, Novartis, 2, 5, Pfizer, 2, 5, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 2, Rheumatology Research Foundation, 2, National Psoriasis Foundation, 2.

Abstract Number: 0360

Does Smoking Affect Secukinumab Treatment Outcomes and Safety in Patients with Psoriatic Arthritis? – Real World Data from German Observational Study

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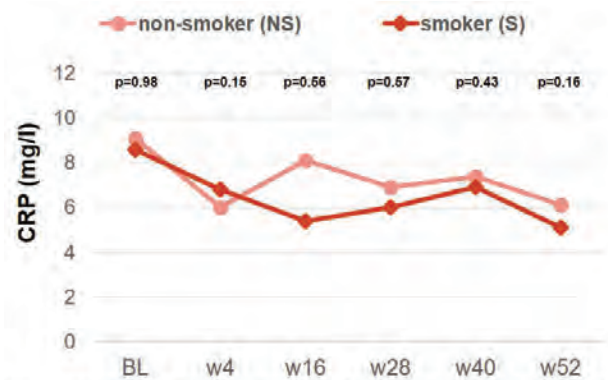
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Several studies have shown an negative association between smoking status and psoriatic arthritis (PsA) clinical outcomes[1,2]. The German non-interventional study AQUILA provides real-world data on the influence of smoking on therapeutic effectiveness and safety issues under secukinumab (SEC), a fully human monoclonal antibody that selectively inhibits interleukin-17A.

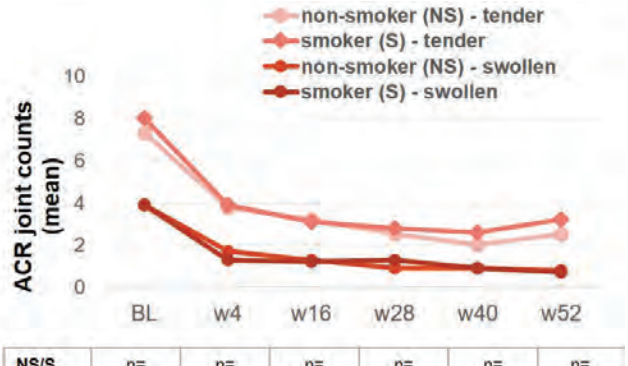
The aim of this interim analysis is to describe selected baseline (BL) demographics, to evaluate SEC effectiveness on disease activity and depressive mood and to report the safety profile depending on smoking status of PsA patients.

Methods: AQUILA is an ongoing, multi-center study including up to 2700 patients with active PsA or ankylosing spondylitis. Patients were observed from BL up to week (w) 52. Real-world data was assessed prospectively and analyzed as observed. In addition to the assessment of C-reactive protein (CRP), data was collected on patient´s disease activity (tender/swollen joint counts, TJC/SJC), skin disease activity (Psoriasis Area and Severity Index, PASI) and depressive mood (Beck´s Depression Inventory version II, BDI-II). For calculation of the proportion of patients who experienced (serious) adverse events ((S)AEs), all PsA patients were included who received at least one dose of SEC irrespective of further documentation of any study visit. This interim analysis focuses on subgroups non-smoker (NS) and smoker (S).

Results: At BL, 641 PsA patients were included: 49.8% (n=319) non-smokers (NS) and 24.3% (n=156) smokers (S). 17.5% (n=112) were ex-smoker and 8.4% (n=54) of unknown smoking status. In both, NS and S, the proportion of women was higher (58.0% in NS and 67.3% in S). NS were slightly older than S (mean age: 53.8/49.7 years). There were no significant differences between NS and S in mean CRP within the 52 weeks (Fig. 1A). Both TJC and SJC improved over time and were similar between NS and S (Fig. 1B). Although mean absolute PASI value was worse in S at BL, a similar temporal improvement was seen in both groups (NS: 7.0 at BL to 1.0 at w52; S: 9.2 at BL to 1.0 at w52). BDI-II scores decreased in both groups with overall higher values in S (NS: 10.9 at BL to 9.1 at w52; S: 12.8 at BL and 10.8 at w52). Regarding the occurrence of AEs and SAEs with or without suspected relationship to SEC,



	BL	w4	w16	w28	w40	w52
NS	n=267	n=195	n=247	n=210	n=194	n=146
S	n=134	n=103	n=120	n=102	n=79	n=63



	BL	w4	w16	w28	w40	w52
NS/S, tender	n= 215/120	n= 155/82	n= 203/105	n= 160/87	n= 138/66	n= 118/50
NS/S, swollen	n= 215/121	n= 155/83	n= 203/105	n= 162/87	n= 140/66	n= 119/50

*CRP data/ACR joint counts were documented not for all PsA patients at BL and subsequent visits.

Figure 1 Disease activity in PsA patients treated with SEC depending on the smoking status*

Table 1. Overview of AEs (and SAEs) under SEC treatment depending on smoking status in PsA patients

Number of patients with	NS (N=333), n (%)	S (N=161), n (%)	P value
AE	233 (70.0)	118 (73.3)	0.11
AE with suspected relationship to SEC	129 (38.7)	72 (44.7)	0.10
SAE	74 (22.2)	45 (28.0)	0.06
SAE with suspected relationship to SEC	29 (8.7)	18 (11.2)	0.37

NS had percentagewise less events than S (Table 1). In addition, percentage of PsA patients who discontinued SEC treatment due to an AE was lower for NS compared to S.

Conclusion: In a real-world setting, SEC improved disease activity and depressive mood of PsA patients with no obvious differences between NS and S. Overall, this interim analysis shows that SEC is an effective and reliable treatment, irrespective of the PsA patients' smoking status. Further progress of the AQUILA study as well as long-term data from other real-world observational studies with SEC, such as SERENA, will reveal whether this trend will continue.

Disclosure: E. Riechers, AbbVie, Chugai, Lilly, Jannsen, Novartis, Pfizer, Roche, UCB, 1, AbbVie, Chugai, Novartis, UCB, 1; **U. Kiltz**, Abbvie, 2, 5, Biocad, 2, 5, Biogen, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Grünenthal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5; **J. Brandt-Jürgens**, Abbvie, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi-Aventis, 5, 8, Novartis, 5, 8, Lilly, 5, 8, MSD, 5, 8, UCB, 5, 8, BMS, 5, 8, Janssen, 5, 8, Medac, 5, 8; **P. Kästner**, Chugai, Novartis, 1; **D. Peterlik**, Novartis Pharma GmbH, 1; **H. Tony**, AbbVie, 5, Astra-Zeneca, 5, BMS, 5, Chugai, 5, Janssen, 5, Lilly, 5, MSD, 5, Novartis, 5, Pfizer, 5, Roche, 5, Sanofi, 5.

Abstract Number: 0361

Response to Treatment with Ixekizumab in Patients with Active Non-Radiographic Axial Spondyloarthritis Based on HLA-B27 Status and Disease Duration

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: In this analysis, we evaluate the efficacy of ixekizumab at week 16 in patients with non-radiographic axial spondyloarthritis (nr-axSpA) with or without baseline HLA-B27 positivity and disease duration using a 5 year cutoff.

Methods: COAST-X (NCT02757352) was a phase 3, randomized, double-blind, placebo-controlled study of eligible patients with active nr-axSpA who received 80 mg ixekizumab every 4 weeks (IXE Q4W, N=96) or every 2 weeks (IXE Q2W, N=102), or placebo (PBO, N=105) up to 52 weeks. Post hoc analysis was performed on the intent-to-treat population at week 16 and included two subpopulations of patients based on baseline HLA-B27 status (positive or negative) or disease duration (< 5 or ≥5 years). Outcomes reported here are achievement of Assessment of Spondy-

loArthritis international Society 40% response (ASAS40) and Bath Ankylosing Spondylitis Disease Activity Index 50% response (BASDAI50) at week 16. Missing data were imputed using non-responder imputation. Treatment comparison was performed using Fisher's exact test.

Results: Of patients treated with IXE Q4W, IXE Q2W, and PBO through week 16, 74.0% (n=71), 71.6% (n=73), and 73.3% (n=77) respectively were HLA-B27+, and 25.0% (n=24), 27.5% (n=28), and 25.7% (n=27) respectively were HLA-B27-. Of patients treated with IXE Q4W, IXE Q2W, and PBO through week 16, 42.7% (n=41), 40.2% (n=41), 37.1% (n=39) respectively had disease duration < 5 years and 57.3% (n=55), 59.8% (n=61), 62.9% (n=66) had disease duration ≥5 years. ASAS40 and BASDAI50 response rates were higher with IXE Q4W and IXE Q2W vs. PBO at week 16 regardless of HLA-B27 status or disease duration < 5 or ≥5 years **(Figure)**. Patients who were HLA-B27+ showed a significant difference over PBO for ASAS40 response (IXE Q4W, p=.047; IXE Q2W, p=.005) and BASDAI50

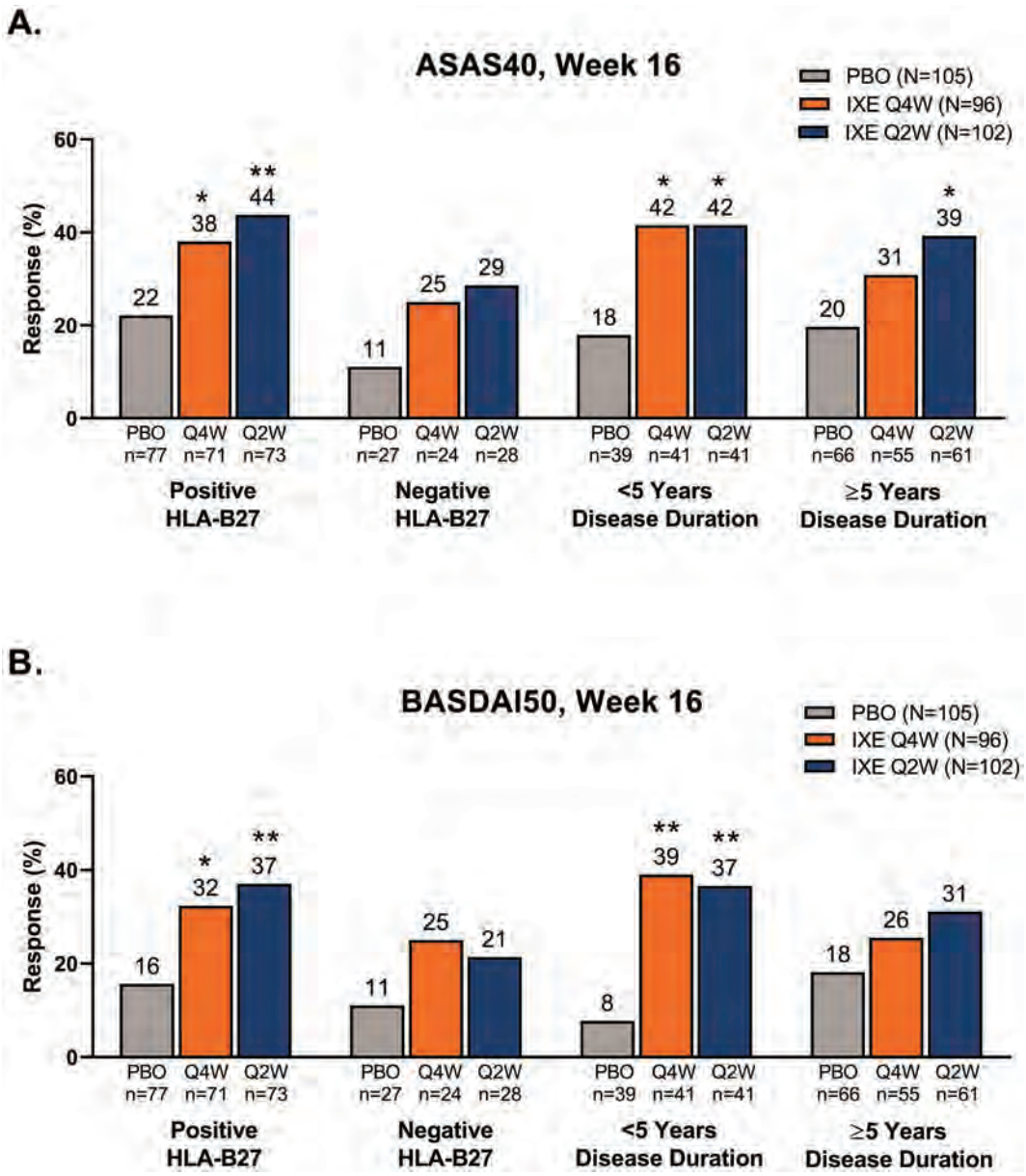

Figure. ASAS40 (A) and BASDAI50 (B) response rates at week 16 with IXE versus PBO in subpopulations of patients with non-radiographic axial spondyloarthritis. ASAS40, Assessment of SpondyloArthritis international Society 40% response, BASDAI50, Bath Ankylosing Spondylitis Disease Activity Index 50% response, IXE, ixekizumab; N, number of patients in the analysis population; n, number of patients in the specified category; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks. *p<.05, **p<.01 vs. PBO

response (IXE Q4W, p=.020; IXE Q2W, p=.003) at week 16. Patients who had disease duration < 5 years showed a significant difference over PBO for ASAS40 response (IXE Q4W, p=.029; IXE Q2W, p=.029) and BASDAI50 response (IXE Q4W, p=.001; IXE Q2W, p=.003) at week 16, and patients who had disease duration ≥5 years showed a significant difference over PBO for ASAS40 response for IXE Q2W (p=.019) at week 16.

Conclusion: Patients treated with ixekizumab saw improvement in signs and symptoms of nr-axSpA as assessed by ASAS40 and BASDAI50 responses regardless of HLA-B27 status (positive or negative) or disease duration (< 5 or ≥5 years). However, the responses with IXE Q4W and IXE Q2W were significant over placebo for the HLA-B27+ patients and those with < 5 years of disease.

Disclosure: V. Navarro-Compán, Novartis Pharma, 1, 5, 8, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, UCB, 5, 8; **J. Maldonado-Cocco**, Pfizer, 2, 5, 8, Merck Sharp Dohme, 2, 5, 8, Novartis, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Roche, 2, 5, 8, Boehringer Ingelheim, 2, 5, 8, Schering-Plough, 2, 5, 8, Abbott, 2, 5, 8, UCB, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Gilead, 2, 5, 8; **P. Rahman**, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5; **A. Kronbergs**, Eli Lilly and Company, 1, 3; **D. Sandoval**, Eli Lilly and Company, 3; **S. Park**, Eli Lilly and Company, 1, 3; **T. Hunter**, Eli Lilly and Company, 1, 3; **M. Magrey**, Novartis, 5, Eli Lilly, 5, AbbVie, 2, UCB, 2, Amgen, 2, Pfizer, 5, Janssen, 5.

Abstract Number: 0362

Patients with Psoriatic Arthritis Treated with Guselkumab Achieved Psoriasis-Related Symptom-Free State and Had No Skin Condition Impact on Their Health Related Quality of Life

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Guselkumab (GUS), a monoclonal antibody that specifically binds to the p19 subunit of IL-23, is approved for psoriasis. In the DISCOVER-2 Phase 3 trial in patients with psoriatic arthritis (PsA), the treatment effect of GUS on patient-reported symptoms and Health Related Quality of Life (HRQOL) as related to psoriatic skin was assessed.

Methods: For DISCOVER-2, adults with active PsA (≥5 swollen + ≥5 tender joints; CRP ≥0.6 mg/dL) despite standard therapies (eg, non-biologic DMARDs, apremilast, or NSAIDs) were eligible. Patients in the HRQOL analyses also had baseline ≥3% Body Surface Area (BSA) of psoriatic involvement and an Investigators Global Assessment (IGA) Score ≥2 (mild). Patients were randomized 1:1:1, stratified by Week 0 DMARD use (Yes/No) and the most recent CRP value prior to randomization (< 2.0 mg/dL vs ≥2.0 mg/dL), to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at Week 0, Week 4, then every 8 weeks (Q8W); or Placebo. Concomitant stable use of select non-biologic DMARDs, oral corti-

Table 1. Least squares mean change from baseline in DLQI subscore through Week 24 among subjects with ≥3% Body Surface Area (BSA) of psoriatic involvement and an Investigators Global Assessment (IGA) Score ≥2 (mild) at Baseline[a]

DLQI subscores	Placebo (n=183) LS mean (range)[b]	Guselkumab	
		100 mg Q8W (n=176) LS mean (range)[b]	100 mg Q4W (n=184) LS mean (range)[b]
Symptoms and feelings	-0.54 (-0.717, -0.371)	-2.31 (-2.492, -2.141)	-2.25 (-2.420, -2.074)
Daily activities	-0.45 (-0.624, -0.281)	-1.90 (-2.073, -1.725)	-1.93 (-2.101, -1.756)
Leisure	-0.55 (-0.725, -0.376)	-1.81 (-1.983, -1.628)	-1.75 (-1.923, -1.572)
Work or school performance	-0.15 (-0.266, -0.024)	-0.87 (-0.989, -0.743)	-0.82 (-0.939, -0.697)
Personal relationships	-0.255 (-0.414, -0.095)	-1.27 (-1.434, -1.110)	-1.32 (-1.477, -1.156)
Treatment	-0.17 (-0.263, -0.084)	-0.79 (-0.885, -0.703)	-0.76 (-0.849, -0.670)

DLQI=Dermatology Life Quality Index; LS=least squares; MRMM=Mixed Model Repeated Measures; Q4W=every 4 weeks; Q8W=every 8 weeks

[a] The DLQI measures the impact of psoriasis on a patient's health related quality of life. The score is calculated based on a 10-item questionnaire that assesses 6 aspects (symptoms and feelings, daily activities, leisure, work or school performance, personal relationships, and treatment). A higher score indicates more severe disease.

[b] The LS means and p-values are based on the MMRM analysis.

Table 2. Mean change (SD) from baseline in total DLQI score and domain subscores at Week 52[a]

Subjects Evaluable	Placebo → 100 mg Q4W (n=173)	Guselkumab	
		100 mg Q8W (n=170)	100 mg Q4W (n=174)
Total DLQI score	-8.82 (7.27)	-9.24 (7.38)	-9.84 (6.88)
DLQI subscores			
Symptoms and feelings	-2.25 (1.80)	-2.41 (1.71)	-2.47 (1.55)
Daily activities	-1.95 (1.74)	-1.98 (1.69)	-2.18 (1.61)
Leisure	-1.75 (1.84)	-1.72 (1.92)	-2.05 (1.85)
Work or school performance	-0.76 (1.13)	-0.92 (1.23)	-0.86 (1.15)
Personal relationships	-1.30 (1.70)	-1.35 (1.60)	-1.44 (1.51)
Treatment	-0.80 (0.90)	-0.85 (0.93)	-0.85 (0.90)

DLQI=Dermatology Life Quality Index; SD=standard deviation

[a] The DLQI measures the impact of psoriasis on a patient's health related quality of life. The score is calculated based on a 10-item questionnaire that assesses 6 aspects (symptoms and feelings, daily activities, leisure, work or school performance, personal relationships, and treatment). A higher score indicates more severe disease.

costeroids, and NSAIDs was allowed. At Week 16, patients with < 5% improvement in tender+swollen joints could initiate or increase the dose of permitted medications while continuing study treatment. Dermatology Life Quality Index (DLQI), a validated endpoint, assessed skin-related symptoms and HRQOL at Weeks 8, 16, 24, and 52. Skin-related symptom-free was defined as a DLQI item-1 score=0, and no impact of skin condition on HRQOL was defined as total DLQI score=0 or 1.

Results: Among 738 treated patients (248 GUS Q8W, 245 GUS Q4W, and 245 Placebo), baseline mean (standard deviation [SD]) DLQI score was 9.9 (7.5), indicating the great impact of skin disease on patients' HRQOL. Baseline

mean (SD) % BSA (n=736) was 17.4% (20.4%) and IGA score ≥2 (n=738) was reported for 82% of patients. A greater proportion of patients treated with GUS 100 mg Q8W (54.3%) or 100 mg Q4W (49.6%) was observed for psoriasis symptom-free at Week 24 vs Placebo (16.9%) (each nominal p< 0.001). A greater mean change from baseline was observed for DLQI total score at Week 24 in patients treated with GUS 100 mg QW8 (n=175) (-8.95 [95% CI -9.691, -8.218]) or 100 mg Q4W (n=184) (-8.85 [95% CI -9.581, -8.124]) vs placebo (n=182) (-2.13 [95% CI -2.854, -1.404]) (each nominal p< 0.001), and the least squares mean difference was observed as early as Week 8 (each nominal p< 0.001). At Week 24, a greater proportion of patients treated with GUS 100 mg Q8W (101 [63.9%]) or 100 mg Q4W (102 [59.0%]) achieved a DLQI score of 0 or 1 vs Placebo (20 [11.8%]) (each p< 0.001), indicating no impact of skin disease on their HRQOL. Similarly, greater improvements in each of the 6 DLQI domain subscores at Week 24 were observed in GUS-treated patients vs Placebo (Table 1). The greater mean changes from baseline in DLQI total and subscores observed at Week 24 were sustained through Week 52 (Table 2). Placebo-treated patients who switched to GUS 100 mg Q4W at Week 24 achieved improvement in DLQI score, which was comparable with originally randomized patients who received GUS.

Conclusion: The majority of GUS-treated patients with PsA achieved skin-related symptom-free and no impact of skin condition on their HRQOL.

Disclosure: J. Dutz, Janssen Research & Development, LLC, 2; **J. Merola**, AbbVie, 1, Arena, 1, Avotres, 1, Biogen, 1, Celgene, 1, Dermavant, 1, Eli Lilly, 1, EMD Serono, 1, Janssen, 1, LEO Pharma, 5, Merck, 1, Novartis, 1, Pfizer Inc, 5, Sanofi, 1, Regeneron, 1, Sun Pharma, 1, UCB Pharma, 5; **C. Han**, Janssen Research & Development, LLC, 3; **A. Kollmeier**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **B. Zhou**, Janssen Reserach & Development, LLC, 3, Johnson & Johnson, 1; **P. Agarwal**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **Y. Yang**, Janssen Global Services, LLC, 1, 3; **M. Shawi**, Janssen Global Services, LLC, 3, Johnson & Johnson, 1; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2.

Abstract Number: 0363

Efficacy of Ixekizumab on Disease Activity and Quality of Life in Patients with Active Nonradiographic Axial Spondyloarthritis and Objective Signs of Inflammation, Stratified by Baseline CRP/Sacroiliac Joint MRI Status

Walter Maksymowych[1], Helena Marzo-Ortega[2], Mikkel Østergaard[3], Lianne Gensler[4], Joerg Ermann[5], Atul Deodhar[6], Denis Poddubnyy[7], David Sandoval[8], Rebecca Bolce[8], Andris Kronbergs[8], Soyi Liu-Leage[9], Gabriel Doridot[8], Vladimir Geneus[8], Ann Leung[10], David Adams[9] and Martin Rudwaleit[11], [1]University of Alberta, Edmonton, AB, Canada, [2]The University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, UK, Leeds, United Kingdom, [3]University of Copenhagen, Copenhagen, Denmark, [4]University of California San Francisco, San Francisco, CA, [5]Brigham and Women's Hospital, Boston, [6]Oregon Health & Science University, Portland, OR, [7]Charité – Universitätsmedizin Berlin, Berlin, Germany, [8]Eli Lilly and Company, Indianapolis, [9]Eli Lilly and Company, Indianapolis, IN, [10]Syneos Health, Morrisville, [11]Department of Internal Medicine and Rheumatology, Klinikum Bielefeld, Germany

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

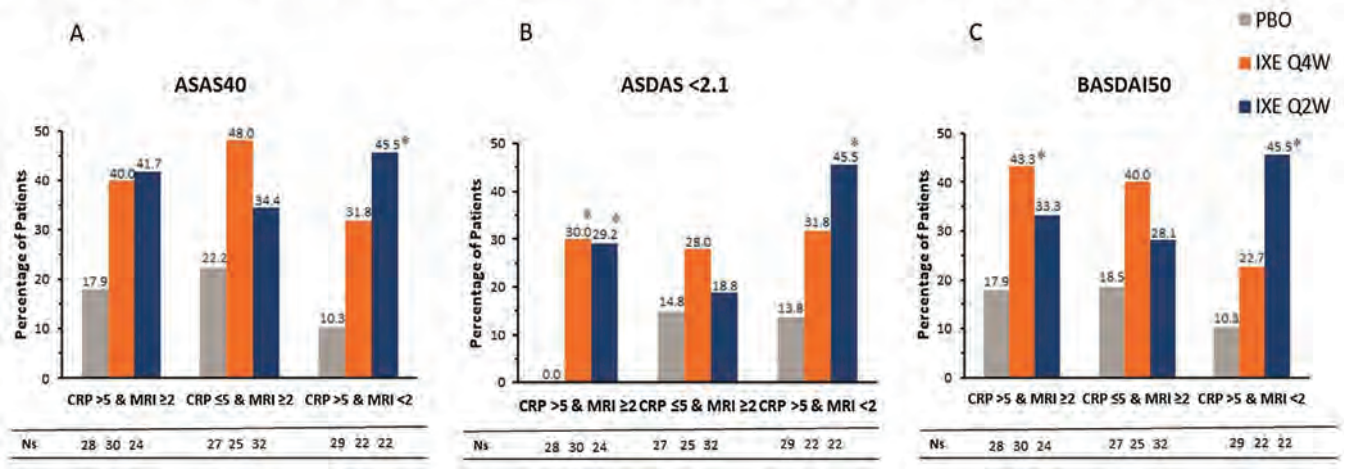
Session Time: 9:00AM–11:00AM

Background/Purpose: Ixekizumab (IXE), a high-affinity anti-interleukin-17A monoclonal antibody, is effective in patients (pts) with active non-radiographic axial spondyloarthritis (nr-axSpA), who had elevated C-reactive protein (CRP) and/or active sacroiliitis on magnetic resonance imaging (MRI).[1] The objective was to determine if disease activity and patient-reported outcomes at Week 16 were similar between groups after stratifying pts by CRP/sacroiliac joint (SIJ) MRI status at baseline.

Methods: COAST-X (NCT02757352) included pts with active nr-axSpA and objective signs of inflammation, that is, presence of sacroiliitis on MRI (Assessment of Spondyloarthritis International Society [ASAS]/Outcome Measures in Rheumatology criteria) or elevation of serum CRP (>5.0 mg/L). Pts were randomized 1:1:1 to receive subcutaneous 80 mg IXE every 4 weeks (Q4W) or every 2 weeks (Q2W), or placebo (PBO). Depending on the baseline values of CRP and MRI SIJ (Spondyloarthritis Research Consortium of Canada [SPARCC] score), pts in the intent-to-treat population (N=239) were divided into 3 subgroups (CRP >5 and MRI ≥2; CRP ≤5 and MRI ≥2; CRP >5 and MRI < 2). Logistic regression analysis with treatment, subgroup, and treatment-by-subgroup interaction was used to detect treatment group differences in ASAS40, Ankylosing Spondylitis Disease Activity Score (ASDAS) < 2.1 (low disease activity), and Bath Ankylosing Spondylitis Disease Activity Index 50 (BASDAI50) responses at Week 16. Analysis of covariance model with baseline value, treatment, subgroup, and treatment-by-subgroup interaction was used to detect the treatment group difference in change from baseline in Short Form-36 physical component score (SF-36 PCS).

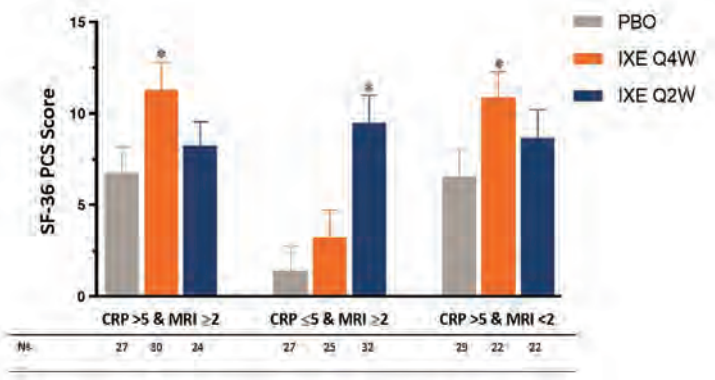
Results: The proportion of pts achieving ASAS40 (primary endpoint), ASDAS < 2.1, and BASDAI50 (secondary endpoints) was higher in IXE treatment groups compared to PBO at Week 16 (Figure 1). The response rates in IXE-treated subjects were higher in all subgroups (CRP >5 and MRI ≥2; CRP ≤5 and MRI ≥2; CRP >5 and MRI < 2) without consistent differences in efficacy between the subgroups. Similarly, pts in the IXE groups showed improvement in SF-36 PCS scores (secondary endpoint) versus pts on PBO at Week 16 (Figure 2).

Figure 1: Disease Activity and Patient Reported Outcomes (NRI) at Week 16 by baseline CRP and MRI SIJ SPARCC Score



*p<0.05 as compared to PBO. Data from ITT population in 3 subgroups, N=239. Baseline CRP is defined as the last CRP value prior to first study injection. ASAS40=Assessment of Spondyloarthritis International Society 40; ASDAS=Ankylosing Spondylitis Disease Activity Score; BASDAI50=Bath Ankylosing Spondylitis Disease Activity Index 50; CRP=C-Reactive Protein; ITT=intent-to-treat; IXE Q4W=ixekizumab every 4 weeks; IXE Q2W=ixekizumab every 2 weeks; MRI=magnetic resonance imaging; N=number of patients in the analysis population; NRI=non-responder imputation; Ns=number of patients in each subgroup; PBO=placebo; SIJ=sacroiliac joints; SPARCC=Spondyloarthritis Research Consortium of Canada Score.

Figure 2: Change from Baseline in SF-36 PCS Score at Week 16 by Baseline CRP and MRI SIJ SPARCC Score



*p<0.05 as compared to PBO. mBOCF data provided as least square mean ± standard error from ITT population in 3 subgroups, N=239. Baseline CRP is defined as the last CRP value prior to first study injection. CRP=C-Reactive Protein; ITT=intent-to-treat; IXE Q4W=ixekizumab every 4 weeks; IXE Q2W=ixekizumab every 2 weeks; mBOCF=modified baseline observation carried forward; MRI=magnetic resonance imaging; N=number of patients in the analysis population; Ns=number of patients in each subgroup; PBO=placebo; SF-36 PCS=Short Form-36 physical component score; SIJ=sacroiliac joints; SPARCC=Spondyloarthritis Research Consortium of Canada Score.

Conclusion: Pts with active nr-axSpA and objective signs of inflammation at baseline who were treated with IXE showed an overall improvement in the signs and symptoms of the disease. The efficacy was not different between pts with both elevated CRP and active sacroiliitis on MRI and pts with either elevated CRP or active sacroiliitis on MRI.

Reference

1. Deodhar A, et al. *Lancet.* 2020;395(10217):53-64.

Disclosure: W. Maksymowych, AbbVie, 2, 5, Janssen, 5, Lilly, 5, Pfizer, 2, 5, Novartis, 2, 5, Gilead, 5, UCB Pharma, 5, Boehringer Ingelheim, 5, Galapagos, 5; **H. Marzo-Ortega**, Novartis, 2, 5, 8, Janssen, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, UCB, 5, 8, AbbVie Inc., 5, 8, Celgene, 5, 8, Takeda Pharmaceutical Company, 5, 8; **M. Østergaard**, Abbvie, 2, 5, 8, BMS, 2, 5, 8, Celgene, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Boehringer-Ingelheim, 5, Eli-Lilly, 5, 8, Hospira, 5, Janssen, 5, 8, Novo, 5, Orion, 5, Pfizer, 5, 8, Regeneron, 5, Roche, 5, 8, Sandoz, 5, Sanofi, 5, 8, UCB, 5, 8; **L. Gensler**, AbbVie, 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB Pharma, 2, 5; **J. Ermann**, Boehringer-Ingelheim, 2, Pfizer, 2, 5, Abbvie, 5, Eli Lilly, 5, Janssen, 5, Novartis, 5, Takeda, 5, UCB, 5; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8; **D. Sandoval**, Eli Lilly and Company, 3; **R. Bolce**, Eli Lilly and Company, 1, 3; **A. Kronbergs**, Eli Lilly and Company, 1, 3; **S. Liu-Leage**, Eli Lilly and Company, 3, 4; **G. Doridot**, Eli Lilly and Company, 1, 3; **V. Geneus**, Eli Lilly and Company, 3, 4; **A. Leung**, Syneos Health, 3; **D. Adams**, Eli Lilly and Company, 1, 3; **M. Rudwaleit**, Bristol-Myers Squibb, 5, 8, Chugai Pharmaceutical Co., Ltd., 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Novartis, 5, 8, UCB Pharma, 5, 8, AbbVie, 5, 8, Pfizer, 5, 8, Celgene, 8, Roche, 5, 8, Merck Sharp & Dohme, 5, 8.

Abstract Number: 0364

Subcutaneous Secukinumab 150 Mg Provides Sustained Relief in Total and Nocturnal Back Pain, Morning Stiffness, Fatigue, and Low Disease Activity in Patients with Active Ankylosing Spondylitis: End-of-study (5-year) Data from the MEASURE 2 Trial

Helena Marzo-Ortega[1], Corinne Miceli-Richard[2], Sonja Gill[3], Marina Magrey[4], Paula Machado[5], Abhijit Shete[6], Jianyuan Wang[6], Susanne Rohrer[6] and Atul Deodhar[7], [1]The University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, UK, Leeds, United Kingdom, [2]Paris Descartes University, Department of Rheumatology - Hôpital Cochin, Assistance Publique - Hôpitaux de Paris, Paris, France, [3]412 – 3075 Hospital Gate, Oakville, Canada, [4]Case Western Reserve University School of Medicine, Cleveland, OH, [5]Novartis Pharmaceuticals Corporation, East Hanover, NJ, [6]Novartis Pharma AG, Basel, Switzerland, [7]Oregon Health & Science University, Portland, OR

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1. Improvement in Pain, Morning Stiffness and Fatigue Scores Through Wk 260

Endpoints	Treatment group	BL, mean ± SD	Wk 16, mean change from BL ± SD	Wk 260, mean change from BL ± SD
Pain				
Total back pain	SEC 150 mg	66.22 ± 16.67	–29.0 ± 25.08	–31.69 ± 29.93
	Placebo	69.20 ± 18.83	–12.22 ± 25.79	N/A
Nocturnal back pain	SEC 150 mg	65.88 ± 17.15	–32.57 ± 27.51	–33.41 ± 30.00
	Placebo	64.04 ± 21.76	–9.70 ± 26.85	N/A
Overall level of spinal pain	SEC 150 mg	7.24 ± 1.54	–2.54 ± 2.55	–2.64 ± 2.79
	Placebo	7.64 ± 1.25	–1.28 ± 2.36	N/A
Morning stiffness				
BASDAI average	SEC 150 mg	6.55 ± 2.09	–2.46 ± 2.91	–3.28 ± 2.47
	Placebo	6.48 ± 2.15	–0.86 ± 2.28	N/A
Physical function				
SF-36 PCS	SEC 150 mg	34.43 ± 6.54	6.93 ± 7.10	7.99 ± 8.88
	Placebo	36.21 ± 6.19	2.02 ± 6.04	N/A
BASFI	SEC 150 mg	6.22 ± 2.13	–2.32 ± 2.21	–2.53 ± 2.49
	Placebo	6.10 ± 2.01	–0.76 ± 1.89	N/A
Fatigue				
Overall level	SEC 150 mg	7.10 ± 1.42	–2.12 ± 2.38	–2.85 ± 2.62
	Placebo	7.22 ± 1.61	–1.12 ± 2.05	N/A
FACIT-Fatigue	SEC 150 mg	22.58 ± 8.77	9.35 ± 9.56	9.92 ± 11.15
	Placebo	24.28 ± 8.99	3.65 ± 8.30	N/A
ASDAS-CRP	SEC 150 mg	3.73 ± 0.89	–1.24 ± 1.11	–1.49 ± 1.28
	Placebo	3.82 ± 0.76	–0.43 ±0.93	N/A

Observed data (mean ± SD) are presented through Wk 260; SEC 150 mg, N = 72 and placebo, N = 74; n = 67 and 54 at Wk 16 and 260, respectively, in the SEC 150 mg group; n = 64 at Wk 16 in the placebo group. ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score- C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BL, baseline; FACIT, Functional Assessment of Chronic Illness Therapy; N, number of randomized pts; n, number of pts with response; N/A, not applicable; SD, standard deviation; SEC, secukinumab; SF-36 PCS, Short Form-36 Physical Component Summary; Wk, week.

Table 2. Proportion of Patients Meeting MCID Criteria Through Wk 260

Endpoints, n/M (%)	Treatment group	Wk 16	Wk 260
Pain			
Total back pain	SEC 150 mg	29/67 (43.3)	28/54 (51.9)
	Placebo	10/64 (15.6)	N/A
Nocturnal back pain	SEC 150 mg	34/67 (50.7)	30/54 (55.6)
	Placebo	11/64 (17.2)	N/A
Overall level of spinal pain	SEC 150 mg	38/67 (56.7)	33/54 (61.1)
	Placebo	24/64 (37.5)	N/A
Morning stiffness			
BASDAI average	SEC 150 mg	42/67 (62.7)	44/54 (81.5)
	Placebo	21/64 (32.8)	N/A
Physical function			
SF-36 PCS	SEC 150 mg	51/67 (76.1)	36/51 (70.6)
	Placebo	30/66 (45.5)	N/A
BASFI	SEC 150 mg	49/67 (73.1)	37/54 (68.5)
	Placebo	24/64 (37.5)	N/A
Fatigue			
Overall level	SEC 150 mg	35/67 (52.2)	35/54 (64.8)
	Placebo	21/64 (32.8)	N/A
FACIT-Fatigue	SEC 150 mg	52/67 (77.6)	37/52 (71.2)
	Placebo	33/66 (50.0)	N/A
ASDAS-CRP	SEC 150 mg	34/67 (50.7)	32/52 (61.5)
	Placebo	14/64 (21.9)	N/A

SEC 150 mg, N = 72 and placebo, N = 74
MCID definition: total and nocturnal back pain, defined as improvement of ≥50%; overall level of spinal pain, defined as improvement of ≥22.5%; BASDAI average, defined as improvement of ≥22.5%; SF-36 PCS, defined as improvement of ≥2.5 points; BASFI, defined as improvement of ≥17.5%; Overall level of fatigue/tiredness, defined as improvement of ≥22.5% (on a VAS scale of 0-10); FACIT-Fatigue: defined as improvement of ≥4 points; ASDAS-CRP, defined as improvement of ≥1.1 points
MCID, minimal clinically important difference; M, number of evaluable pts; N, number of randomized pts; n, number of pts with response.

Background/Purpose: Patients (pts) with ankylosing spondylitis (AS) report pain (70–80%), stiffness (20–40%), and fatigue (50–60%) as the most troubling symptoms. Early diagnosis and sustained improvement in these symptoms are essential for effective management of AS. Here, we report the effect of subcutaneous (s.c.) secukinumab (SEC) 150mg on these symptoms through 5 years (end-of-study) from MEASURE 2.

Methods: The MEASURE 2 study design has been reported previously. This post hoc analysis assessed the mean change from baseline to Week (Wk) 260 in total and nocturnal back pain scores (Visual analogue scale [0–100]), overall level of spinal pain (neck, back, or hip) from BASDAI score, and morning stiffness (overall level; mean of questions 5 and 6 of BASDAI score). Additionally, the SF-36 physical component summary (PCS) score, BASFI score, overall level of fatigue (BASDAI question 1), FACIT-Fatigue, ASDAS-CRP scores, and proportion of pts meeting minimal clinically important difference (MCID) criteria across multiple clinical domains were also assessed. Data are shown for pts originally randomized to SEC 150mg and placebo. Data are reported as observed for overall population and by prior tumor necrosis factor inhibitor (TNFi) therapy status (naïve vs inadequate response/intolerance [IR]).

Results: Baseline clinical characteristics were generally comparable across the treatment groups; SEC 150mg (N=72) and placebo (N=74). 73.6% (n=53) of pts originally randomized to SEC 150 mg completed 5 years of treatment. The most frequent reason of discontinuation was adverse events reported 9.7% (n=7) pts. Improvements were sustained through 5 years in pts treated with SEC 150mg in pain, morning stiffness, physical function (SF-36 PCS and BASFI), fatigue (overall level of fatigue and FACIT-Fatigue), and ASDAS-CRP (Table 1). 48.1% and 25.0% of SEC 150mg treated pts met MCID criteria for ASDAS-CRP Low Disease Activity and ASDAS-CRP Inactive Disease at 5 years, respectively (Table 2). Improvements were observed in both TNFi-naïve and -IR pts, with numerically higher improvement in TNFi-naïve pts.

Conclusion: Secukinumab 150mg provided clinically meaningful improvements in total back pain, nocturnal back pain, morning stiffness, fatigue and low disease activity through 5 years of treatment in pts with active AS.

Disclosure: H. Marzo-Ortega, Novartis, 2, 5, 8, Janssen, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, UCB, 5, 8, AbbVie Inc., 5, 8, Celgene, 5, 8, Takeda Pharmaceutical Company, 5, 8; **C. Miceli-Richard**, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 8, Novartis, 2, 5, MSD, 2, Pfizer, 2, 5, 8, UCB, 2, 5, Biogen, 2, Wyeth, 2, 8, Schering-Plough, 8, Roche, 5, 8, Merck, 2, 5, 8, Abbott, 8; **S. Gill**, AbbVie, 5, 8, Eli Lilly, 5, 8, Janssen, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Amgen, 5, 8, Sanofi-Genzyme, 5, 8; **M. Magrey**, Novartis, 5, Eli Lilly, 5, AbbVie, 2, UCB, 2, Amgen, 2, Pfizer, 5, Janssen, 5; **P. Machado**, Novartis, 1, 3; **A. Shete**, Novartis, 1, 3; **J. Wang**, Novartis, 3; **S. Rohrer**, Novartis, 1, 3; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2.

Abstract Number: 0365

Experience with Apremilast in Treatment of Psoriatic Arthritis in US Clinical Practice; Assessments from Trio Health and the American Rheumatology Network (ARN)

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Apremilast is the one targeted immune modulating (TIM) treatment for psoriatic arthritis (PsA) that may be combined with csDMARDs, biologic therapies, or used as a monotherapy. Here we describe the utilization of and experience with apremilast in a large network of community rheumatologists.

Methods: The ARN-TRIO Rheumatology registry consists of EMR (fielded and open text), lab, procedure, infusion, medical claims, and specialty pharmacy data generated in care of >75,000 patients by ARN, a network of independent practices with >200 rheumatologists across the US. For this study, registry data were limited to patients diagnosed with PsA who initiated apremilast or TNF inhibitors between Jan 2014 to Nov 2019 with ≥6 months follow-up. Disease Assessment Scores (DAS) were calculated using CDAI or RAPID3 and analyzed categorically using 4 grade scale. Comparisons between groups used Fisher's Exact Test for categorical variables. As a surrogate for clinical effectiveness, we examined time from apremilast monotherapy initiation to modification or discontinuation, defined as either drug discontinuation or addition of a csDMARD or TIM drug. Time to event analyses were conducted via KM curves and associated Log-Rank Test for difference in Hazard.

Results: Of the 581 apremilast-treated patients in the study, 325 (56%) had no prior observed PsA treatment, 129 (22%) previously were treated with csDMARDs but not TIM drugs, and 127 (22%) had previously received TIM therapies. Two or more of the apremilast treatment groups were significantly different for gender, race, age, payer, and prior

Table 1. Patient Characteristics for apremilast-treated groups

Category	Characteristic	(1)	(2)	(3)	p		
		No Prior Therapies	Prior csDMARDs	Prior TIM Therapies	1v2	1v3	2v3
Gender	F	207/325 (63.7)	93/129 (72.1)	85/127 (66.9)	0.099	0.585	0.416
Race	White	199/209 (95.2)	91/94 (96.8)	92/93 (98.9)			
	Black	10/209 (4.8)	2/94 (2.1)		0.188	0.019	0.747
	Other		1/94 (1.1)	1/93 (1.1)			
	Unknown	116/325 (35.7)	35/129 (27.1)	34/127 (26.8)			
Ethnicity	Hispanic or Latino	3/166 (1.8)	2/66 (3.0)	3/81 (3.7)	0.625	0.397	1
	Not Hispanic or Latino	163/166 (98.2)	64/66 (97.0)	78/81 (96.3)			
	Unknown	159/325 (48.9)	63/129 (48.8)	46/127 (36.2)			
Age Group	18-44	63/325 (19.4)	21/129 (16.3)	22/127 (17.3)	0.058	0.417	0.270
	45-54	75/325 (23.1)	36/129 (27.9)	41/127 (32.3)			
	55-64	113/325 (34.8)	30/129 (23.3)	38/127 (29.9)			
	65-74	32/325 (9.8)	20/129 (15.5)	11/127 (8.7)			
	75-100	42/325 (12.9)	22/129 (17.1)	15/127 (11.8)			
Payer Type	Commercial	237/325 (72.9)	82/129 (63.6)	94/127 (74.0)	0.067	0.946	0.150
	Medicare/Medicare Advantage	69/325 (21.2)	41/129 (31.8)	27/127 (21.3)			
	Other	19/325 (5.8)	6/129 (4.7)	6/127 (4.7)			
Baseline Disease Assessment	Near Remission	21/124 (16.9)	7/38 (18.4)	2/33 (6.1)	0.781	0.256	0.261
	Low	25/124 (20.2)	5/38 (13.2)	6/33 (18.2)			
	Moderate	40/124 (32.3)	12/38 (31.6)	16/33 (48.5)			
	Severe	38/124 (30.6)	14/38 (36.8)	9/33 (27.3)			
	No Baseline DAS	201/325 (61.8)	91/129 (70.5)	94/127 (74.0)			
apremilast therapy	Monotherapy	255/325 (78.5)	22/129 (17.1)	16/127 (12.6)	<0.001	<0.001	<0.001
	+csDMARD	40/325 (12.3)	101/129 (78.3)	22/127 (17.3)			
	+TIM	25/325 (7.7)	1/129 (0.8)	70/127 (55.1)			
	csDMARD + TIM	5/325 (1.5)	5/129 (3.9)	19/127 (15.0)			

therapies; groups were not different by baseline disease severity. [Table 1] Across these groups, 227 (48%) received apremilast as a monotherapy without prior TIM therapies. A comparator group of 1662 patients who received a TNF inhibitor (TNFi) as a monotherapy and without prior TIM was identified. Characteristics for the apremilast monotherapy and TNFi monotherapy groups differed significantly for gender and race but not for baseline disease severity. [Table 2] Median time from monotherapy start to modification or discontinuation was significantly different between apremilast (19.3 months) and TNFi (30.4 months, p=0.018). In subset analyses, differences in time to modification persisted between apremilast and TNFi monotherapy groups among males (p = 0.037) and patients with severe baseline DAS (p=0.009), but not among females or non-severe baseline DAS. [Figure 1]

Conclusion: The use of apremilast in US community practice is predominantly as a monotherapy. When examined as a first TIM monotherapy, time to modification or discontinuation was significantly less than comparator TNFi monotherapy-treated group. However, when stratified by gender and baseline DAS, female patients and those with low DAS had no difference in time to modification between apremilast and TNFi. These results should be viewed in light of the limitations of the study, which include potential prior treatments or other confounding variables not present in the collected data.

Table 2. Patient Characteristics for patients with qualifying first TIM monotherapy with apremilast or TNFi

Category	Characteristic	(1)	(2)	p
		TNFi	apremilast	1v2
Gender	F	909/1662 (54.7)	185/277 (66.8)	<0.001
Race	White	828/859 (96.4)	173/183 (94.5)	0.135
	Black	20/859 (2.3)	9/183 (4.9)	
	Other Race	11/859 (1.3)	1/183 (0.5)	
	Unknown	803/1662 (48.3)	94/277 (33.9)	
Ethnicity	Hispanic or Latino	32/666 (4.8)	3/143 (2.1)	0.178
	Not Hispanic or Latino	634/666 (95.2)	140/143 (97.9)	
	Unknown	996/1662 (59.9)	134/277 (48.4)	
Age Group	18-44	431/1662 (25.9)	49/277 (17.7)	0.004
	45-54	419/1662 (25.2)	62/277 (22.4)	
	55-64	409/1662 (24.6)	93/277 (33.6)	
	65-74	303/1662 (18.2)	56/277 (20.2)	
	75-100	100/1662 (6.0)	17/277 (6.1)	
Payer Type	Commercial	1200/1662 (72.2)	196/277 (70.8)	0.606
	Medicare/Medicare Advantage	356/1662 (21.4)	66/277 (23.8)	
	Other	106/1662 (6.4)	15/277 (5.4)	
Baseline Disease Assessment	Near Remission	107/544 (19.7)	18/102 (17.6)	0.975
	Low	96/544 (17.6)	18/102 (17.6)	
	Moderate	160/544 (29.4)	31/102 (30.4)	
	Severe	181/544 (33.3)	35/102 (34.3)	
	No Baseline PDA	1118/1662 (67.3)	175/277 (63.2)	
Prior Treatment	Prior csDMARD	108/1662 (6.5)	22/277 (7.9)	0.365

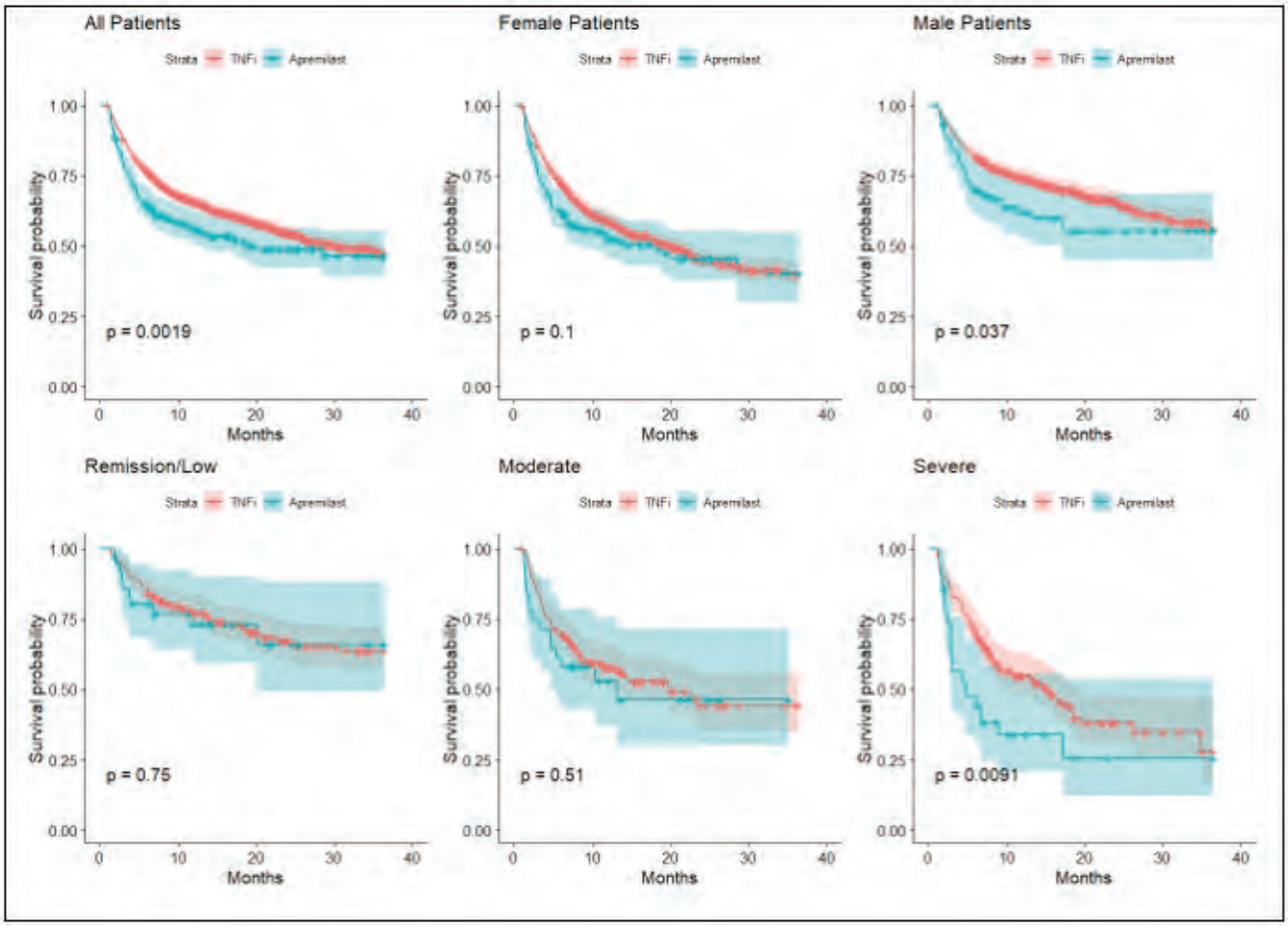

Figure 1. Time to modification or discontinuation of apremilast vs TNFi monotherapies given as first TIM

Disclosure: C. Edgerton, Sandoz, 5; **A. Frick**, None; **S. Helfgott**, Abbvie, 5; **K. Huston**, None; **J. Singh**, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **N. Soloman**, Horizon, 5, 8, Amgen, 2, 8, Abbvie, 2, 5, 8, UCB, 2, 5, 8, Novartis, 5, 8, Jannsen, 2, 8, Pfizer, 8, Lilly, 2, GSK, 2, 5, 8.

Abstract Number: 0366

Symptoms of Peripheral Arthritis Are Significantly Improved in Patients with Ankylosing Spondylitis Treated with Secukinumab

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) is a chronic inflammatory disease of the axial skeleton associated with pain, stiffness, and disability.[1] Up to 66% of patients (pts) with AS may also have peripheral involvement, including swollen and tender joints (STJs),[2,3] which are associated with worse overall disease activity.[4] A previous analysis showed that secukinumab, a selective inhibitor of interleukin 17A, led to significant improvements in efficacy outcomes vs placebo, regardless of peripheral joint involvement.[3] However, the effect of secukinumab on symptoms of peripheral arthritis in pts with AS was not assessed.

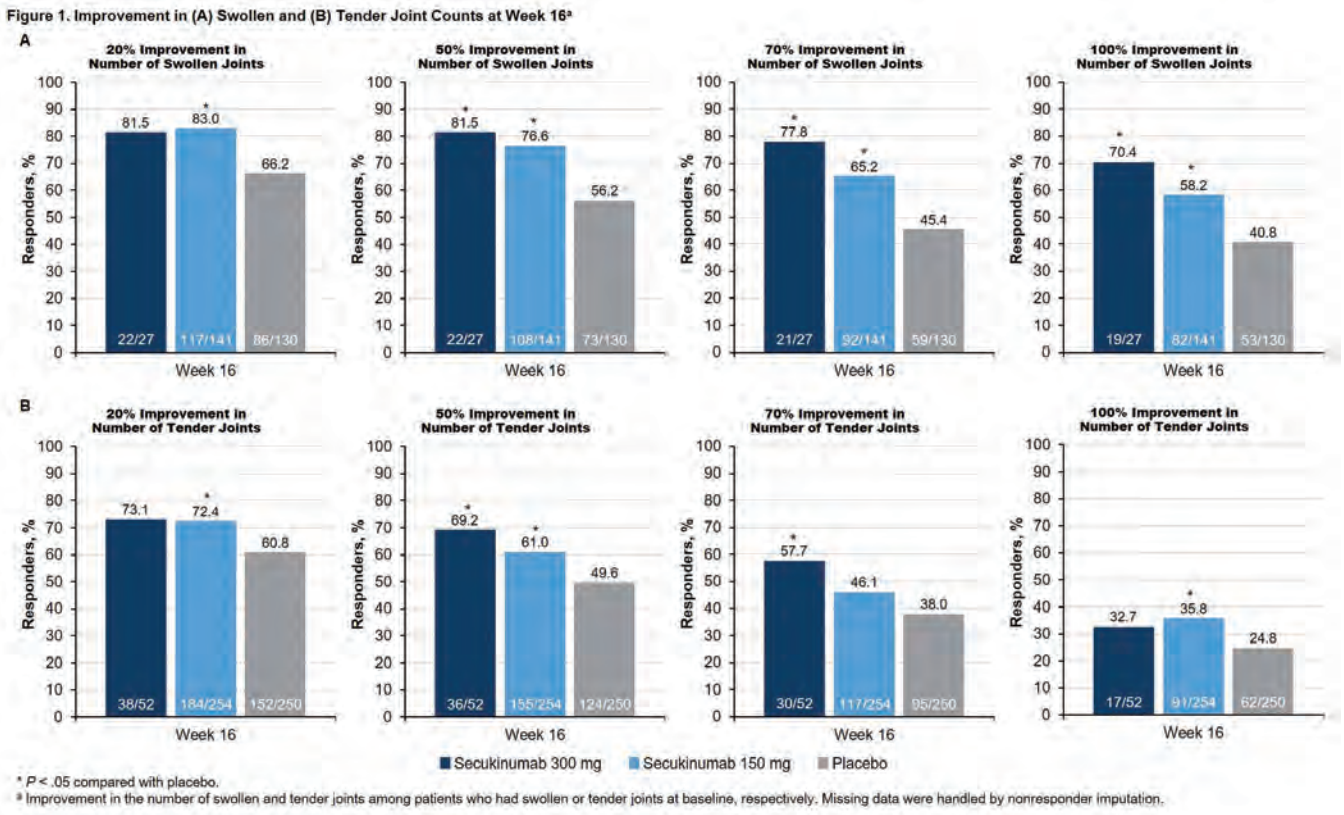
The objective of this analysis was to assess changes in peripheral symptoms in pts with AS treated with secukinumab vs placebo.

Methods: Data from pts with active AS and peripheral symptoms who were enrolled in MEASURE 1 (NCT01358175), 2 (NCT01649375), 3 (NCT02008916), and 4 (NCT02159053) were pooled in this hypothesis-generating analysis. No adjustments for multiple comparisons were made. Pts with peripheral symptoms were identified by the presence

Table 1. Pooled Baseline Patient Characteristics Across the MEASURE 1, 2, 3, and 4 Studies

Characteristic	Secukinumab 300 mg (n = 52)	Secukinumab 150 mg (n = 256)	Placebo (n = 252)
Age, mean (SD), years	43.6 (12.2)	43.7 (12.0)	44.9 (12.6)
Male, n (%)	33 (63.5)	159 (62.1)	145 (57.5)
Race, n (%)			
White	37 (71.2)	203 (79.3)	215 (85.3)
Asian	1 (1.9)	16 (6.3)	12 (4.8)
Other[a]	13 (25.0)	37 (14.5)	25 (9.9)
Unknown	1 (1.9)	0	0
BMI, mean (SD), kg/m^2	27.8 (5.9)	27.6 (6.1)	27.4 (5.4)
Current smoker at baseline, n (%)	14 (26.9)	82 (32.0)	72 (28.6)
Time since diagnosis, mean (SD), years	5.6 (7.4)	7.2 (8.9)	7.3 (9.0)
Previous TNFi use, n (%)	15 (28.8)	79 (30.9)	79 (31.3)
BASDAI, mean (SD)	7.0 (1.5)	7.0 (1.4)	6.9 (1.3)
BASDAI question 3, mean (SD)	6.3 (2.5)	6.6 (2.2)	6.4 (2.1)
hs C-reactive protein, mean (SD), mg/L	12.0 (14.7)	18.5 (32.4)	15.4 (20.5)
Patient Global Assessment (VAS 0-100), mean (SD)	73.4 (15.8)	71.7 (17.2)	70.1 (16.1)
Swollen 44-joint count, mean (SD)	1.9 (2.8)	2.6 (4.2)	2.5 (4.4)
Tender 44-joint count, mean (SD)	7.1 (7.1)	7.8 (7.5)	7.9 (8.0)

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BMI, body mass index; hs, high-sensitivity; SD, standard deviation; TNFi, tumor necrosis factor-α inhibitor; VAS, visual analog scale.
[a] Includes black or African American, American Indian or Alaskan Native, and other.



of STJs, based on 44-joint counts at baseline (BL). Pts received subcutaneous (SC) secukinumab every 4 weeks at doses of 300 mg with an intravenous (IV) loading dose (MEASURE 3 only), 150 mg with an IV or SC loading dose, or placebo. Treatment response through Week 16 was assessed based on the proportions of pts who achieved improvements of 20%, 50%, 70%, or 100% in the number of swollen and number of tender joints and improvements in the BASDAI score for question 3 and Patient Global Assessment (PGA). Changes in the number of swollen and number of tender joints were assessed in pts with swollen or tender joints at BL, respectively.

Results: This pooled analysis included 560 pts with AS and STJs at BL (**Table**). At Week 16, treatment with secukinumab led to significantly greater proportions of pts achieving reductions in the number of swollen (**Fig 1A**) or tender (**Fig 1B**) joints compared with placebo; the treatment effect was more pronounced in reduction of swollen joints. Furthermore, a greater proportion of secukinumab-treated pts achieved complete resolution of swollen or tender joints vs placebo (**Fig 1**). Secukinumab also led to significant improvements in peripheral pain/swelling (**Fig 2A**) and disease activity (**Fig 2B**) vs placebo, as assessed using BASDAI question 3 and the PGA, respectively.

Conclusion: In parallel with its previously reported efficacy in axial symptoms,[3] secukinumab led to significant improvements in symptoms of peripheral arthritis in pts with AS. Significant improvements were seen in both tender and swollen joints.

References

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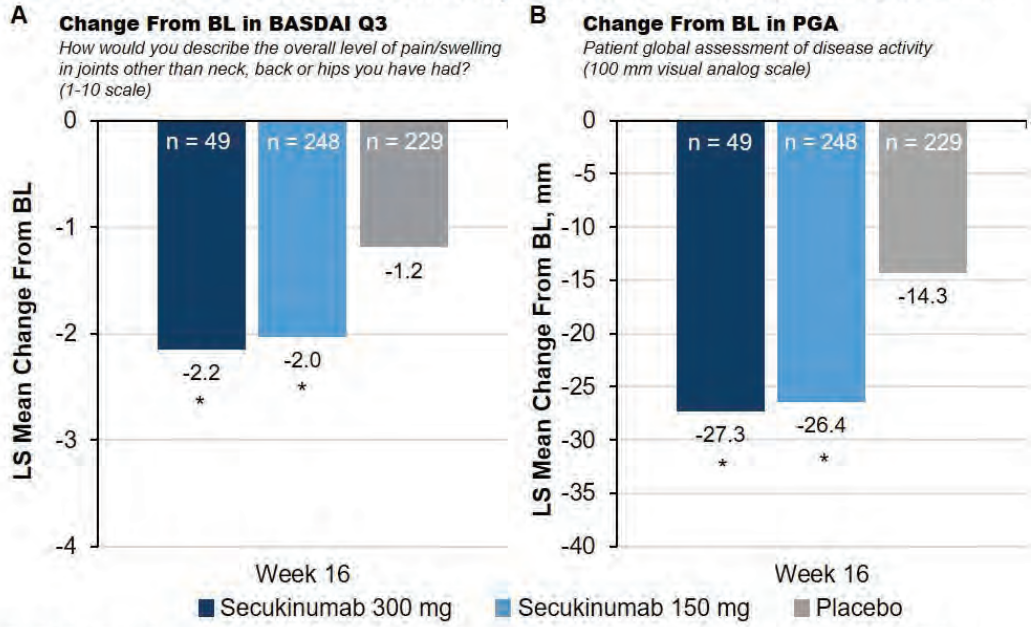
Figure 2. Change From Baseline in (A) BASDAI Question 3 and (B) Patient Global Assessment at Week 16 in Patients With Peripheral Swollen or Tender Joints at Baseline[a]



BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BL, baseline; LS, least squares; PGA, Patient Global Assessment; Q, question

* $P < .05$ compared with placebo.

[a] LS mean and P value are from mixed-effect model repeated measures analysis, with treatment, visit, and TNF-α inhibitor status as factors, baseline and weight as covariates, and treatment by visit and baseline by visit as interaction terms.

Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **R. Calheiros**, Novartis, 1, 3; **X. Meng**, Novartis, 1, 3; **T. Fox**, Novartis, 1, 3; **X. Baraliakos**, AbbVie, 2, 5, Celgene, 2, 5, Galapagos, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 2, 5, Chugai, 2, 5, MSD, 2, 5, Sandoz, 2, 5, Hexal, 2, 5.

Abstract Number: 0367

Guselkumab Induces Sustained Reduction in Acute Phase Proteins and Th17 Effector Cytokines in Active Psoriatic Arthritis in Two Phase-3 Clinical Trials (DISCOVER-1 and DISCOVER-2)

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

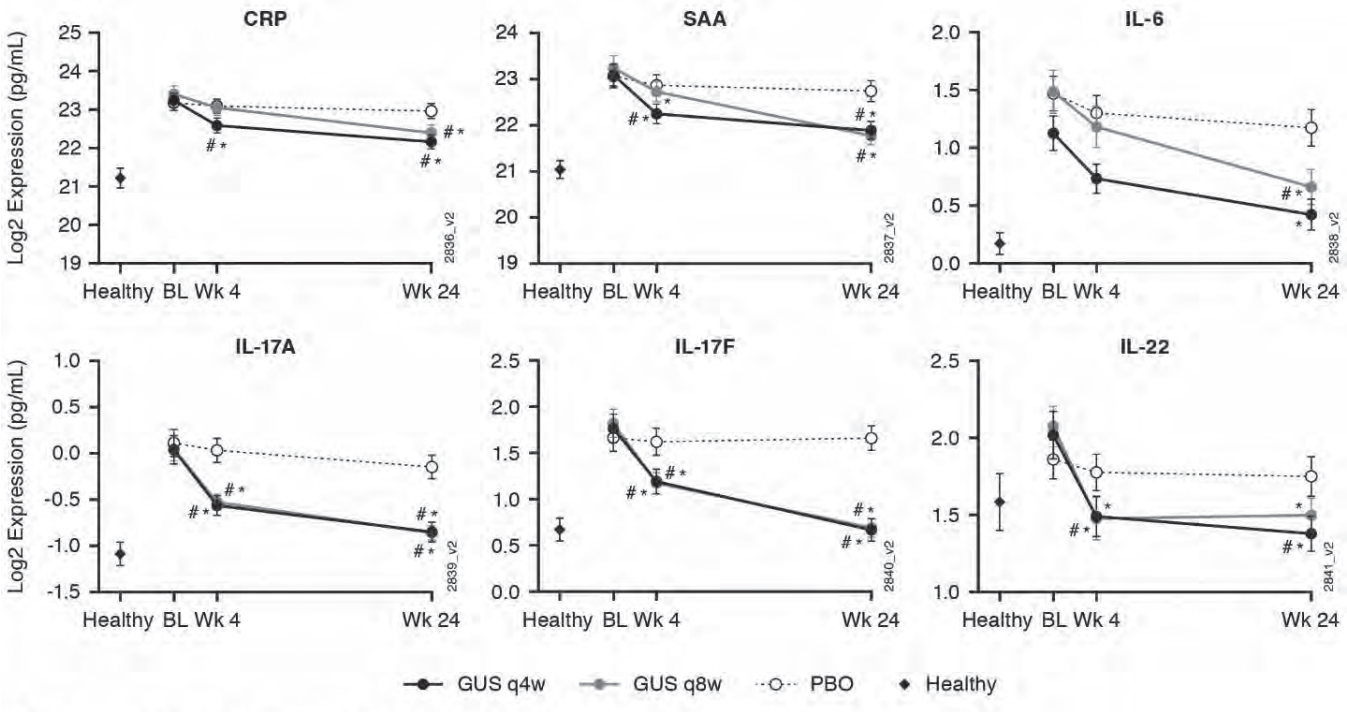
Session Time: 9:00AM–11:00AM

Background/Purpose: Guselkumab (GUS), an IL-23 inhibitor monoclonal antibody (MAb) that specifically binds the IL-23p19 subunit, demonstrated efficacy compared to placebo (PBO) in reducing skin & musculoskeletal signs & symptoms in patients (pts) with active PsA in two Ph3 studies, DISCOVER 1 & 2.[1,2] Results from a GUS PsA Ph2 trial[3] & Ustekinumab (UST, anti-IL12/23p40 MAb) PsA Ph3 trials (PSUMMIT 1 & 2)[4] showed associations of baseline IL-17A, IL-17F, & CRP with baseline disease characteristics, & associations of GUS-induced cytokine reductions with clinical responses. We investigated cytokine expression in PsA & changes post GUS therapy.

Methods: In DISCOVER 1 & 2, pts received GUS 100 mg at Week (Wk) 0, 4, then every 8Wks (q8w); GUS 100 mg q4w; or matching PBO. 21 serum biomarkers were measured in 300 PsA pts from DISCOVER at Wks 0, 4, & 24, & in 34 healthy controls matched for age, sex, & ethnicity. Serum proteins measured were acute phase reactants: CRP & SAA & inflammatory cytokines/chemokines: Th17 effector cytokines IL-17A, IL-17F, IL-22, soluble ICAM-1, soluble VCAM-1, IL-6, CXCL-8, IL-10, IL-13, IL-12p70, CCL22, IFN-γ, CCL2, CCL4, TNF-α, IL-1β, IL-2, IL-4 (MSD), & YKL-40. Serum IL-17A, IL-17B, & CRP measured in PSUMMIT[4] were compared with GUS.

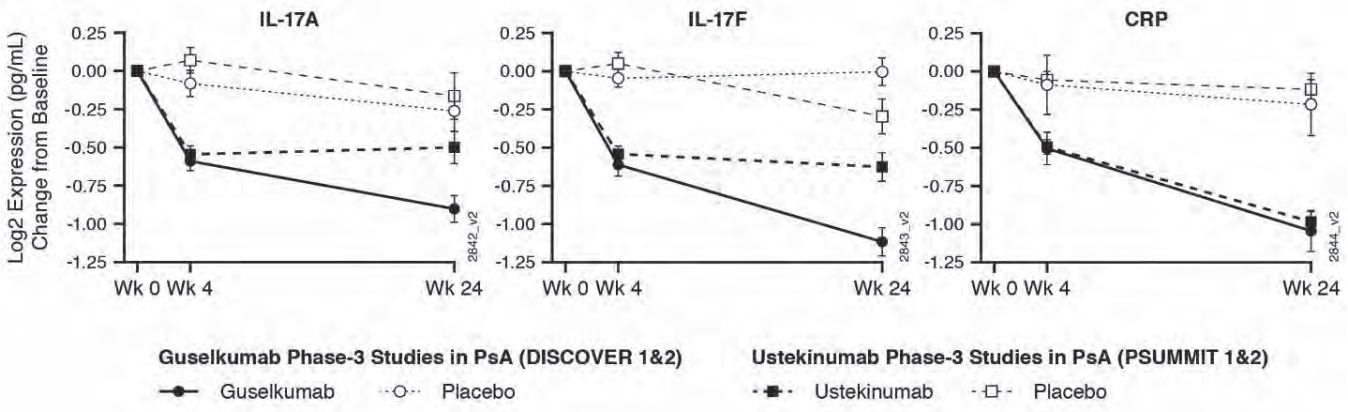
Results: Baseline serum levels of CRP, SAA, IL-6, IL-17A, & IL-17F were elevated in PsA pts vs healthy controls ($p< 0.05$, geometric mean [GM] ≥40% higher, FIG 1). No significant dysregulation in other cytokines in PsA pts vs healthy controls. Baseline IL-17A, IL-17F, IL-22, & CCL22 were significantly associated with baseline psoriasis disease activity (Body Surface Area & Psoriatic Area & Severity Index, Spearman Signed Rank $p< 0.05$, $r >0.25$). Baseline CRP, SAA, IL-6, & YKL40 were significantly associated with baseline joint disease (Disease Activity Score 28-CRP, Spearman $p< 0.05$, $r >0.25$). Baseline SAA, IL-6, IL-17A, & IL-17F were higher in pts with prior TNF inhibitor exposure than without ($p< 0.05$, GM ≥40% higher), although PsA pts with/without prior TNF inhibitor had higher levels vs healthy controls. GUS treatment resulted in decreases in serum CRP, SAA, IL-6, IL-17A, IL-17F, & IL-22 that were significantly greater than PBO as early as Wk 4 (FIG 1). These protein levels continued to decrease through Wk 24 in GUS-treated pts with both regimens ($p< 0.05$, GM decrease from baseline ≥ 33%). No significant difference in Wk 24 IL-17A & IL-

FIGURE 1.



* P vs. baseline ≤0.05, |fold difference| ≥1.4
\# P vs. placebo ≤0.05, |fold difference| ≥1.4
Error bars represent 2 standard errors of the mean (~95% confidence interval)
BL=Baseline, GUS=Guselkumab, PBO=Placebo, Wk=Week

FIGURE 2.



Error bars represent standard error of the mean
Wk=Week

17F levels for GUS vs healthy controls suggests a normalization of peripheral effector cytokines associated with the IL-23/Th17 axis post GUS treatment. Effects on IL-17A/IL-17F were greater in GUS vs UST treated pts, while CRP levels were similar in both programs (FIG 2).

Conclusion: Comprising a strong pharmacodynamic effect, GUS reduced serum protein levels of acute phase & Th17-effector cytokines (whose elevations at baseline were associated with PsA disease characteristics) & achieved comparable levels to those in healthy controls. In PsA pts, reductions of IL-17A & IL-17F by GUS were of greater magnitude than those by UST.

References

1. Deodhar et al. *Arth Rheumatol* 2019;71 S10: 1386
2. Mease et al. *Arth Rheumatol* 2019;71 S10:5247
3. Siebert et al. *Ann Rheum Dis* 2019;78 S2:293
4. Siebert et al. *Arth Rheumatol* 2019;71:1660

Disclosure: S. Siebert, AbbVie, 5, 8, Celgene, 2, 8, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb, 1, Janssen, 1, 2, 3, Novartis, 2, 5, 8, UCB, 2, 5, GlaxoSmithKline, 2, Pfizer, 2, 5; **I. McInnes**, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **M. Loza**, Janssen Research & Development, LLC, 1, 3; **K. Ma**, Janssen Research & Development, LLC, 3; **K. Leander**, Janssen Research & Development, LLC, 3; **V. Lakshminarayanan**, Janssen Research & Development, LLC, 3; **C. Franks**, Janssen Research & Development, LLC, 3; **P. Cooper**, Janssen Research & Development, LLC, 3; **K. Sweet**, Janssen Research & Development, LLC, 3.

Abstract Number: 0368

Comparable Impact and Burden of Disease of Psoriatic Arthritis Patients with Limited Joint Involvement vs. Those with More Extensive Joint Involvement: Interim Results from a Prospective, Multicenter, Real-World Study in Patients Treated with Apremilast

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is associated with a high burden of disease and an increased risk of comorbidities. Recent data suggest that patients with moderate PsA benefit most from apremilast (APR) treatment (Mease PJ, et al. *Arthritis Care Res [Hoboken].* 2020 Jan 7. [Epub ahead of print]). Results from an earlier analysis of the REWARD study suggest that patients with limited joint involvement may benefit from APR treatment, with improvements in the perceived impact of disease (Jansen TL, et al. *Ann Rheum Dis*. 2019;78:913 [abstract FRI0442]). Patients with limited joint involvement or comorbidities are underrepresented in randomised controlled trials; therefore, evidence from real-world patient cohorts is needed to assess and compare the impact and burden of disease on patients with limited vs. extensive joints who may also have comorbidities. This study compared the burden of disease and comorbidities in patients with PsA who have limited joint involvement with patients with PsA who have extensive joint involvement.

Methods: The prospective, multicenter, observational REWARD study assessed the impact of using the Psoriatic Arthritis Impact of Disease (PsAID) questionnaire (score range: 0-10), presence of domains of PsA (enthesitis, dactylitis, skin psoriasis, nail psoriasis, axial involvement), and ongoing or history of comorbidities of interest on patients with

Table 1. Patient Characteristics

Demographics	SJC ≤4 (n=53)	SJC >4 (n=24)
Age, mean	53.1	54.4
Women, %	46.2	66.7
Body mass index, mean, kg/m^2	28.6	28.7
PsA Characteristics		
SJC, mean	1.2	10.2
TJC, mean	4.3	13.7
PsAID, mean	4.4	4.8
Pain VAS, mean	45.9	53.4
Moderate to severe psoriasis (BSA >3), %	31.4	21.7
Dactylitis, %	18.9	33.3
Enthesitis, %	43.4	45.8
Nail psoriasis, %	45.3	41.7
Axial spondyloarthritis, %	3.8	8.3
Comorbidities		
Hypertension, %	30.2	37.5
Hypercholesteremia, %	13.2	16.7
Uveitis, %	1.9	8.3
Malignancy, %	0.0	8.3
Heart failure, %	5.7	8.3
Depression, %	5.7	4.2

Figure 1. Baseline SJC vs PsAID vs Pain VAS

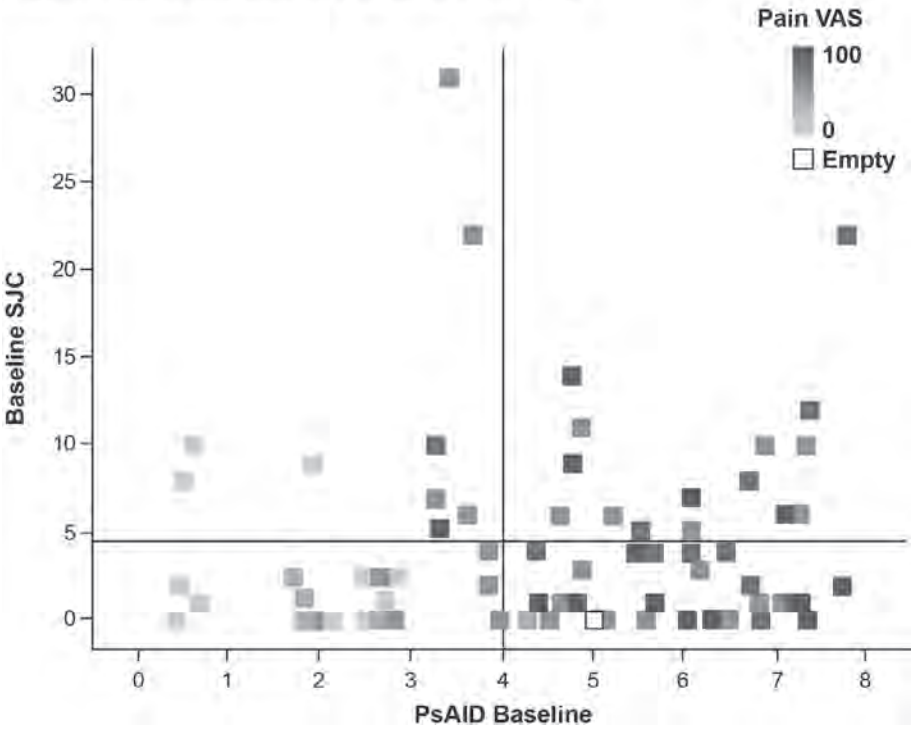
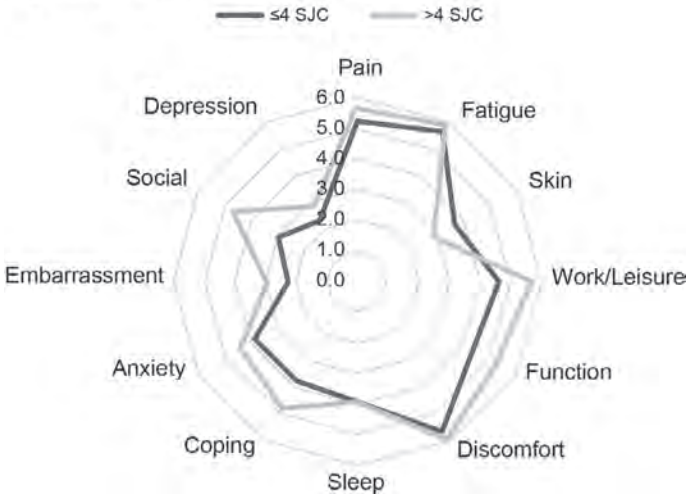


Figure 2. Baseline PsAID by Domain



PsA considered for apremilast treatment in The Netherlands. This interim analysis compared results in patients with limited joint involvement (swollen joint count [SJC] ≤4) vs. more extensive joint involvement (SJC >4).

Results: Currently, 77 patients have been included in the analysis (SJC ≤4: n=53; SJC >4: n=24) (Table 1). Mean baseline PsAID scores were 4.4 vs. 4.8 for the SJC ≤4 vs. SJC >4 groups (Figure 1). The proportions of patients who were not in the PsAID-defined Patient Acceptable Symptom State (PASS) were 58.7% for the SJC ≤4 group and 62.5% for the SJC >4 group. Mean pain visual analog scale (VAS) scores (0-100 mm) were 45.9 vs. 53.4 for the SJC ≤4 group vs. for the SJC >4 group. Mean scores for the individual PsAID domains for the SJC ≤4 vs. SJC >4 groups were generally comparable (Figure 2). Presence of specific manifestations of PsA for patients in the SJC ≤4 group vs. the SJC >4 group, respectively, were: moderate to severe psoriasis (psoriasis-involved body surface area [BSA]

>3: 31.4% vs. 21.7%), nail psoriasis (45.3% vs. 41.7%), enthesitis (Leeds Enthesitis Index >0: 43.4% vs. 45.8%), dactylitis (18.9% vs. 33.3%), and axial involvement (3.8% vs 8.3%). Comorbidities in ≥5% of either group (SJC ≤4 vs. SJC >4) included hypertension (30.2% vs. 37.5%), hypercholesterolemia (13.2% vs. 16.7%), uveitis (1.9% vs. 8.3%), malignancy (0.0% vs. 8.3%), heart failure (5.7% vs. 8.3%), and depression (5.7 vs. 4.2%).

Conclusion: In this real-world study, no strong associations between SJC and patient-reported impact of disease or pain were observed. Similar to patients with more extensive joints involvement, patients with limited joint involvement had an associated substantial burden of disease, with more than half not achieving PsAID PASS.

Disclosure: T. Jansen, Olatec, 1, Grunenthal, 1, 2, Sobi, 1, AbbVie, 1, Celgene Corporation, 1; **A. van Vliet**, Amgen B.V., 1, Celgene Corporation, 1; **M. Vis**, Novartis, 1, 2, Pfizer, 1, 2, AbbVie, 1, Celgene Corporation, 1, Eli Lilly, 1.

Abstract Number: 0369

Effect of Upadacitinib on Reducing Pain in Patients with Active Ankylosing Spondylitis and Inadequate Response to Nonsteroidal Anti-inflammatory Drugs

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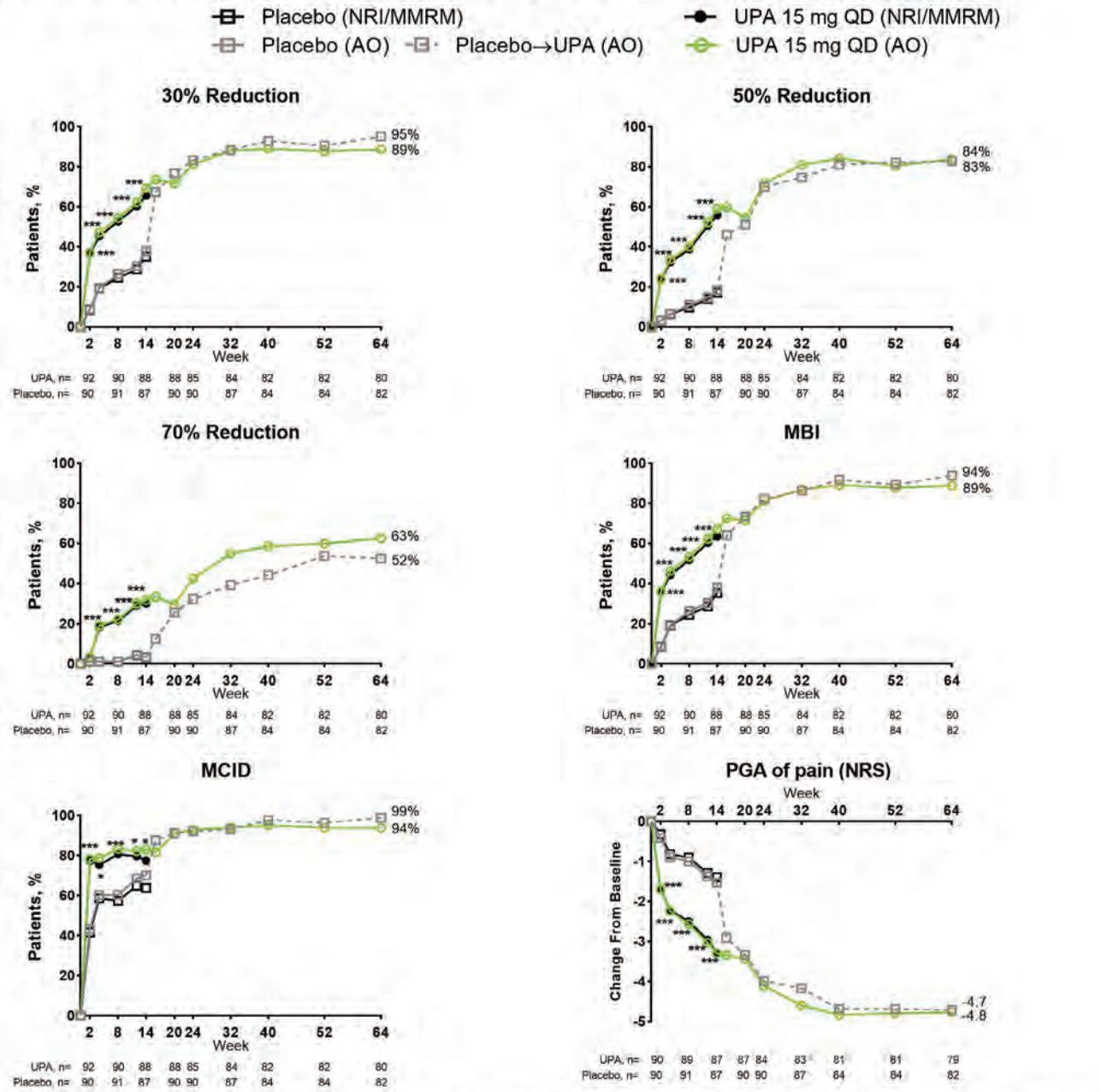
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Pain is a debilitating symptom of ankylosing spondylitis (AS) and negatively impacts patient (pt) lives. Upadacitinib (UPA), a Janus kinase (JAK) inhibitor engineered for increased selectivity for JAK1 over JAK2, JAK3, and tyrosine kinase 2, [1] showed significant efficacy vs placebo (PBO) in the randomized phase 2/3 SELECT-AXIS 1 study in active AS.[2] The objective of this analysis was to evaluate the efficacy of UPA on multiple pain assessments through 64 weeks (wks).

Methods: SELECT-AXIS 1 (NCT03178487) enrolled adults with active AS, who had an inadequate response, intolerance or contraindications to ≥2 NSAIDs, were biologic DMARD naive and met the modified New-York Criteria. Pts were randomized 1:1 to UPA 15 mg once daily (QD, n=93) or PBO (n=94) for 14 wks (Period 1), followed by open-label UPA 15 mg QD during 90-wk extension (Period 2); reported here are data through wk 64. Pain endpoints included the proportion of pts achieving ≥30%/≥50%/≥70% reduction in Pt's Global Assessment (PGA) of pain on a 0–10 numeric rating scale (NRS), minimal clinically important difference (MCID, defined as ≥1 point reduction or ≥15% reduction from baseline [BL]) in PGA of pain, and much better improvement (MBI, defined as ≥2 point reduction and ≥33% reduction from BL) in PGA of pain. In addition, mean change from baseline in PGA of pain, BASDAI questions 2 (neck/back/hip pain) and 3 (peripheral pain/swelling), and pt's assessment of total back pain and nocturnal back pain NRS scores (NRS 0–10) were assessed. Non-responder imputation (binary endpoints) and mixed-effects model for repeated measurements (continuous endpoints) were used for missing data/dropouts in Period 1; as-observed analysis was used for Period 2.

Figure 1. Proportion of Patients with ≥30%/50%/70% Reduction from Baseline, MBI, or MCID in PGA of Pain and Mean Change from Baseline in PGA of Pain NRS Score Through 64 Weeks

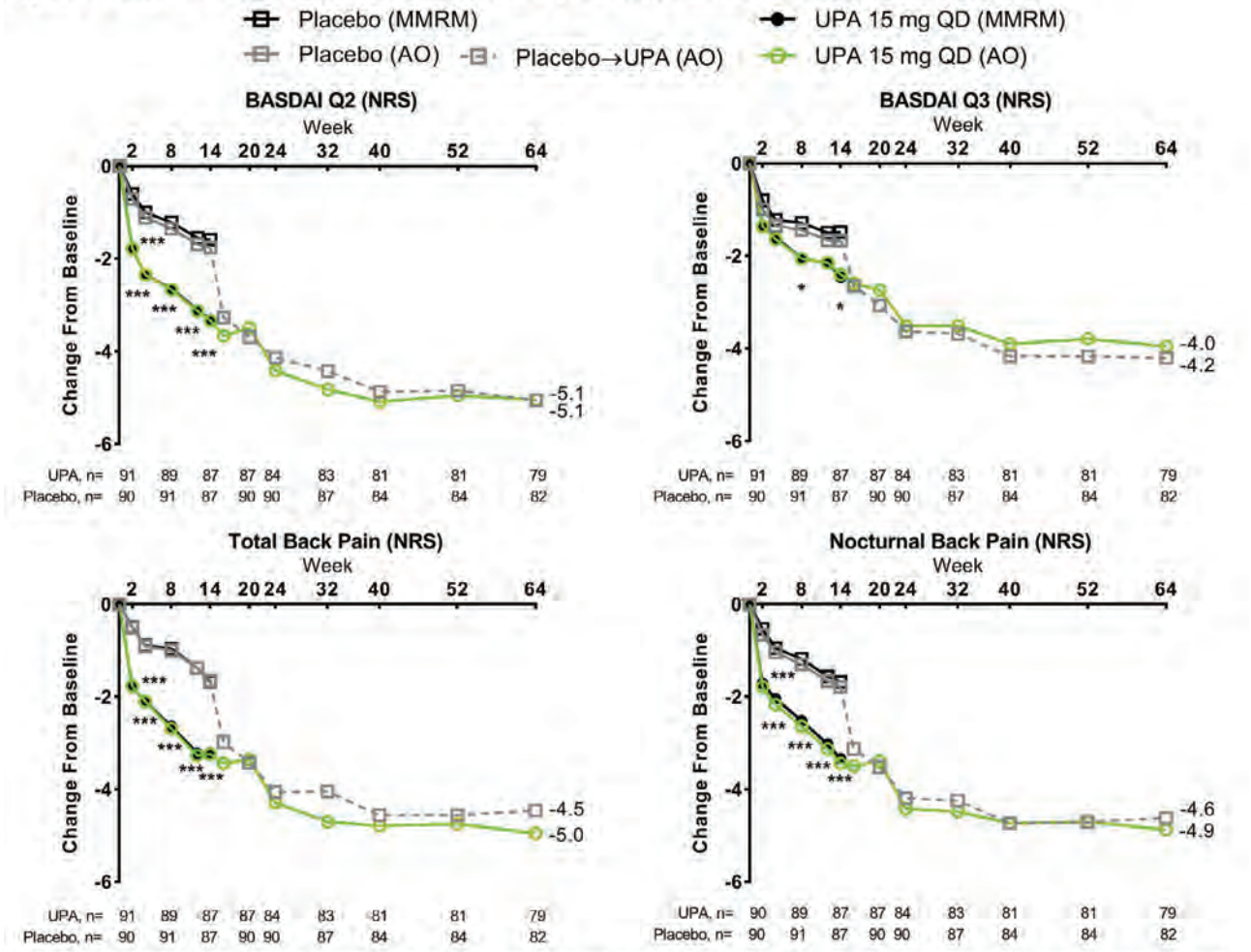


AO, as observed; MBI, much better improvement; MCID, minimal clinically important difference; MMRM, mixed-effects model for repeated measurements; NRI, non-responder imputation; NRS, numeric rating scale; PGA, patient's global assessment; UPA, upadacitinib.
Dashed line: all patients randomized to placebo received open-label UPA starting from week 14.
UPA vs PBO comparison was calculated using Cochran-Mantel-Haenszel test adjusting for stratification factor of high-sensitivity CRP level; nominal *P* values: ***$P<0.001$, *$P<0.05$.
Patient's Global Assesment of Pain based on: "How much pain have you had because of your condition during the last week?"

Figure 1

Results: A significantly higher proportion of pts receiving UPA vs PBO achieved reductions in all PGA of pain assessments as early as wk 2 that was sustained at all time points in Period 1; the only exception was ≥70% reduction in PGA of pain that was significant at wk 4 and sustained thereafter (**Fig. 1**). For ≥30%/≥50%/≥70% reduction and MBI, the response rate increased over time with UPA; the difference for UPA vs PBO also continued to increase over time for ≥50% and ≥70% reduction endpoints. For MCID, an increase from BL to wk 2 was observed and plateaued there-

Figure 2. Mean Change from Baseline in Other Pain NRS Scores Through 64 Weeks



AO, as observed; MBI, much better improvement; MCID, minimal clinically important difference; MMRM, mixed-effects model for repeated measurements; NRS, numeric rating scale; UPA, upadacitinib.
Dashed line: all patients randomized to placebo received open-label UPA starting from week 14.
UPA vs PBO comparison was calculated using Cochran-Mantel-Haenszel test adjusting for stratification factor of high-sensitivity CRP level; nominal *P* values: ***$P<0.001$, *$P<0.05$.
BASDAI Q2 based on a question: "How would you describe the overall level of AS neck, back or hip pain you have had?"
BASDAI Q3 based on a question: "How would you describe the overall level of pain/swelling in joints other than neck, back or hips you have had?"
Patient's assessment of total back pain based on question: "What is the amount of back pain that you experienced at any time during the last week?
Patient's assessment of nocturnal back pain based on a question:"What is amount of back pain at night that you experienced during the last week?"

Figure 2

after. The mean change from BL in PGA of pain, BASDAI Q2, total back pain, and nocturnal back pain NRS scores were significantly greater for UPA vs PBO at all time points in Period 1; BASDAI Q3 was significant at wk 8 and 14 (**Figs 1-2**). The effect of UPA on pain reduction was sustained through wk 64. PBO pts who switched to open-label UPA at wk 14 generally reached the same level of pain reduction as those initially randomized to UPA (**Figs 1-2**).

Conclusion: In pts with active AS and an inadequate response/contraindication to NSAIDs, a greater proportion of patients treated with UPA achieved rapid, significant, and clinically meaningful reductions in pain vs PBO through 14 wks across multiple pain assessments. The reductions in pain were sustained over time, and pts who switched from PBO to UPA reached the same level of improvement as the continuous UPA group.

1. Parmentier JM, et al. *BMC Rheumatology*. 2018;2(23).

2. van der Heijde D, et al. *Lancet*. 2019;394(10214):2108-2117.

Disclosure: A. Deodhar, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **X. Baraliakos**, AbbVie, 2, 5, Celgene, 2, 5, Galapagos, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 2, 5, Chugai, 2, 5, MSD, 2, 5, Sandoz, 2, 5, Hexal, 2, 5; **I. McInnes**, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **K. de Vlam**, Eli Lilly and Company, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5, 8, Celgene, 2, 5, 8, Pfizer, 2, 5, 8; **L. Bessette**, Amgen, 1, 2, 3, BMS, 1, 2, 3, Janssen, 1, 2, 3, UCB, 1, 2, 3, AbbVie, 1, 2, 3, Pfizer, 1, 2, 3, Merck, 1, 2, 3, Celgene, 1, 2, 3, Sanofi, 1, 2, 3, Lilly, 1, 2, 3, Novartis, 1, 2, 3, Gilead, 2, 6, 8; **A. Maniccia**, AbbVie Inc., 1, 3, 4; **R. Lippe**, AbbVie Inc., 1, 3; **C. Saffore**, AbbVie Inc., 1, 3, 4; **T. Gao**, AbbVie Inc., 1, 3, 4; **I. Song**, AbbVie, 1, 3; **A. Östör**, AbbVie, 5, Roche, 5, Janssen, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, Gilead, 5, Paradigm, 5, UCB Pharma, 5, Bristol-Myers Squibb, 5.

Abstract Number: 0370

Guselkumab-Treated Patients Achieved Clinically Meaningful Improvement in Systemic Symptoms as Measured with PROMIS Instrument: Results from Phase-3 Psoriatic Arthritis Trial DISCOVER 1

Ana-Maria Orbai[1], Laura Coates[2], Atul Deodhar[3], Philip Helliwell[4], Christopher Ritchlin[5], Alexa Kollmeier[6], Elizabeth Hsia[7], Xie Xu[8], Shihong Sheng[9], Bei Zhou[9] and Chenglong Han[9], [1]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, [2]University of Oxford, Oxford, United Kingdom, [3]Oregon Health & Science University, Portland, OR, [4]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, [5]Department of Medicine, University of Rochester Medical Center, Rochester, NY, [6]Janssen Research & Development, LLC, La Jolla, CA, [7]Janssen Research & Development, LLC and University of Pennsylvania Medical Center, Spring House, PA, [8]Janssen Research & Development, LLC, San Marcos, CA, [9]Janssen Research & Development, LLC, Spring House, PA

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with psoriatic arthritis (PsA) experience broad systemic symptoms including pain, fatigue, depression, sleep disturbance, poor physical function, and diminished social participation. DISCOVER 1 is a Phase 3 trial (NCT03162796) evaluating the efficacy and safety of guselkumab (GUS), an interleukin 23 inhibitor that binds to the p19-subunit of IL-23, in patients with active PsA. In this study, PROMIS-29 (Patient-Reported Outcomes Measurement Information System-29), a validated generic health instrument,[1] assessed the treatment effect of GUS on symptoms in patients with PsA.

Methods: Patients with active PsA despite nonbiologic DMARDs were enrolled, and ~30% of patients could have previously received ≤2 TNFi. Patients were randomized (1:1:1) to subcutaneous GUS 100 mg at Week 0 (W0), W4 then q8W (n=127), GUS 100 mg q4W (n=128), or PBO (n=126). Concomitant stable use of select csDMARDs, oral steroids, and NSAIDs was allowed. PROMIS-29 consists of 7 domains (Depression, Anxiety, Physical Function, Pain Interference, Fatigue, Sleep Disturbance, and Social Participation) and a pain intensity 0-10 numeric rating scale (NRS). The raw score of each domain is converted into a standardized T-score with a mean of 50 (general population mean) and a standard deviation (SD) of 10. Higher PROMIS scores represent more of the concept being measured. A ≥5-point improvement (1/2 SD of T-score) is defined as clinically meaningful.[1]

Table. PROMIS-29 Domain T-Scores Least Square (LS) Mean Change from Baseline

Table. PROMIS-29 Domain T-Scores Least Square (LS) Mean Change from Baseline			
	LS Mean Change from Baseline		
	PBO	GUS q8W	GUS q4W
Anxiety	-1.37	-3.23*	-2.92
Depression	-0.85	-3.4**	-2.67*
Fatigue	-1.86	-4.79**	-5.08**
Pain interference	-2.30	-5.49**	-5.69**
Physical function	1.34	3.89**	5.05**
Sleep disturbance	-1.17	-3.48**	-2.46
Social participation	1.45	4.90**	4.52**
Pain intensity	-0.56	-1.98**	-2.32**
Nominal p-values vs placebo: *<0.05, **<0.01			
GUS, guselkumab; q4W, every 4 week; q8W, every 8 week			

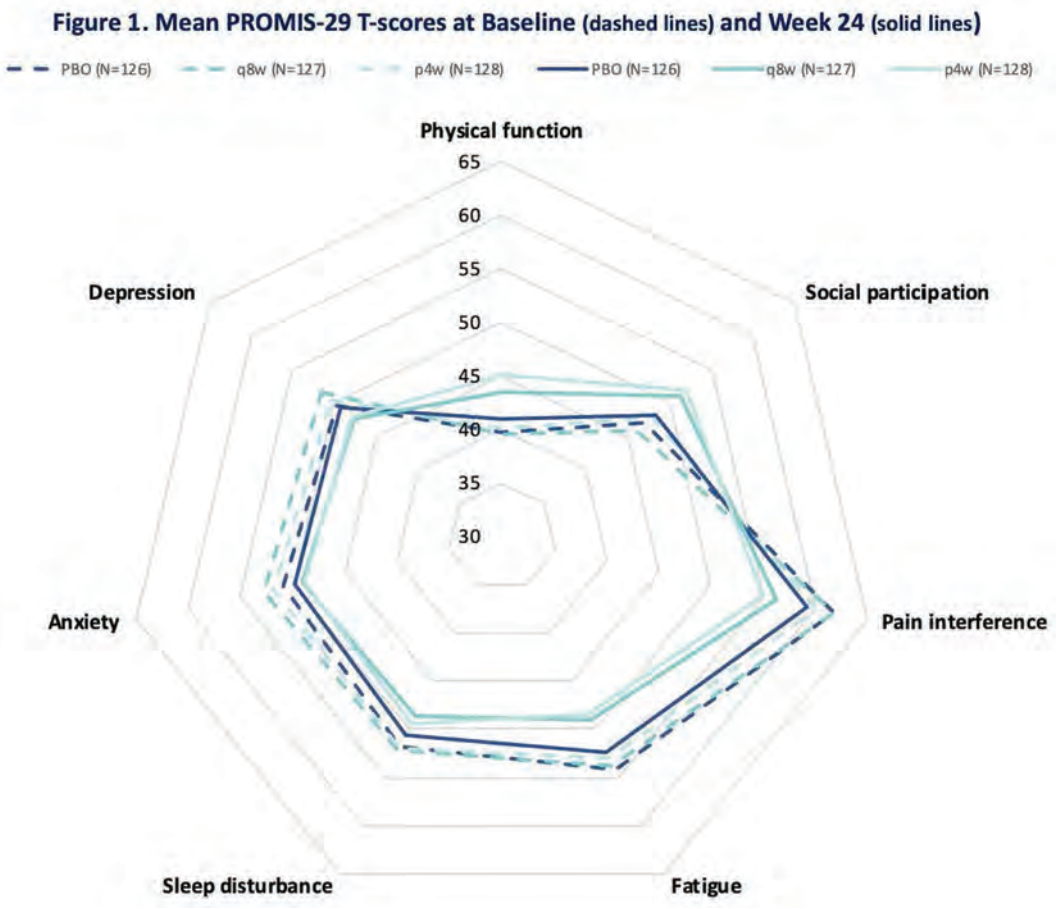


Figure 1. Mean PROMIS-29 T-Scores at Baseline (dashed lines) and Week 24 (solid lines)

Results: At baseline, mean PROMIS-29 T-scores for physical function, social participation, sleep disturbance, pain, and fatigue were worse than the general US population. At W24, GUS q8W-treated patients achieved greater improvements from baseline in all PROMIS-29 domains vs PBO ($p< 0.05$) (Table and Fig 1). Results were consistent

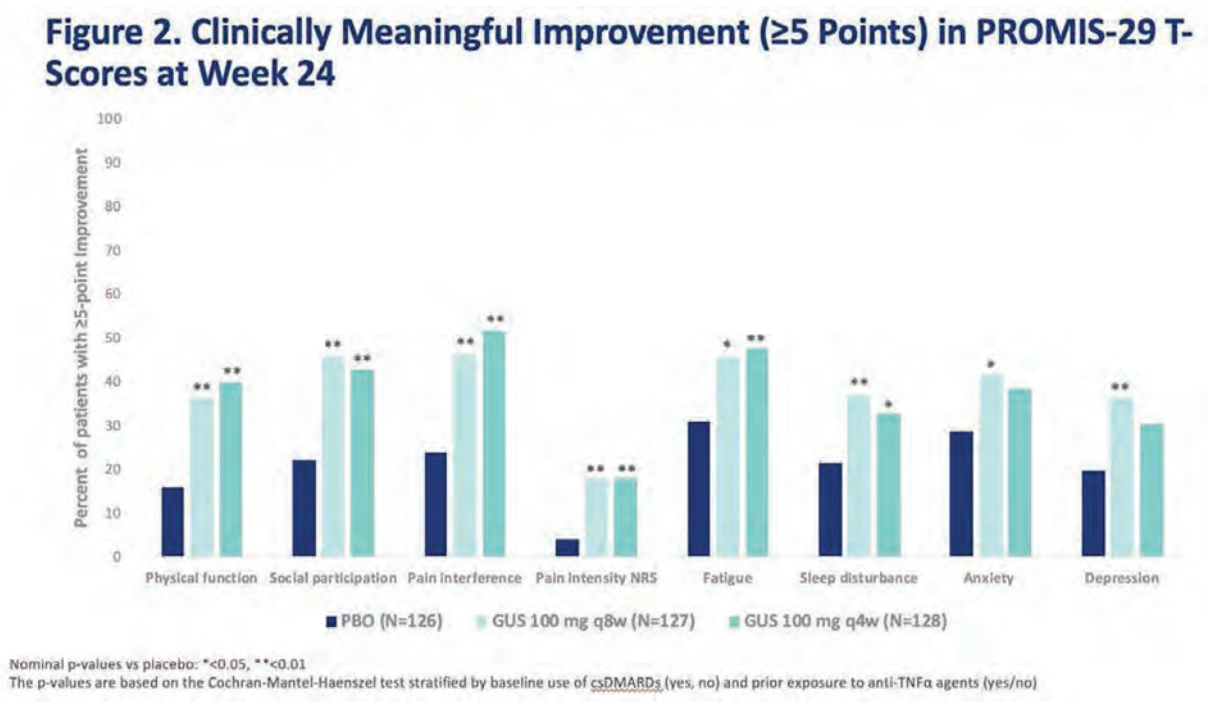


Figure 2. Clinically Meaningful Improvement (>=5-Points) in PROMIS-29 T-Scores at Week 24

in the GUS q4W group except for anxiety and sleep disturbance. More patients receiving GUS achieved clinically meaningful improvement vs PBO except for depression and anxiety in the GUS q4W group, which were numerically improved (Fig 2).

Conclusion: Active PsA patients treated with GUS achieved clinically meaningful reduction in symptoms and improvement in physical function and social participation vs PBO at W24

Reference

1. http://www.healthmeasures.net/score-and-interpret/interpret-scores/meaningful-change/165-meaningful-change

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Disclosure: A. Orbai, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 5, UCB, 5, AbbVie, 2, Celgene, 2, Horizon, 2; **L. Coates**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **P. Helliwell**, AbbVie, 2, 8, Janssen, 2, Pfizer Inc, 8, Celgene, 8, Galapagos, 8, Amgen, 8, Novartis, 2, UCB, 8; **C. Ritchlin**, None; **A. Kollmeier**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **E. Hsia**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **X. Xu**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **S. Sheng**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **B. Zhou**, Janssen Reserach & Development, LLC, 3, Johnson & Johnson, 1; **C. Han**, Janssen Research & Development, LLC, 3.

Abstract Number: 0371

Identifying Inadequate Response Among Ankylosing Spondylitis Patients Prescribed Biologics in a Real-world Commercially Insured Adult Population in the United States

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: The purpose of this analysis was to assess the frequency of inadequate response (IR) over 1 year from biologic initiation among ankylosing spondylitis (AS) patients in the United States using a claims-based algorithm that was originally developed and validated for rheumatoid arthritis[1]. Baseline factors associated with IR to biologic were also analyzed.

Methods: This was a retrospective cohort study using claims data from the HealthCore Integrated Research Database (HIRD®). Adult patients with AS who initiated a biologic (TNFi: adalimumab, certolizumab, etanercept, golimumab, infliximab; IL-17: secukinumab) from 7/1/2016 to 8/31/2018 and had continuous enrollment ≥6 months before and ≥12 months after index date (date of first biologic claim) were included. The index biologic was defined as the first biologic prescribed during the study time period. Patients were identified as having IR to their index biologic if during the 12 months after index date they had one or more of the following: low adherence (defined as proportion of days covered (PDC)< 80%), switched/added new biologic, added a new conventional disease modifying anti-rheumatic drugs (cDMARDs) (methotrexate and/or sulfasalazine), increased dose/frequency of biologic, >1 glucocorticoid injection/infusion, addition or dose increase of oral glucocorticoids, used a new pain medication, or had a spinal procedure. Baseline patient characteristics were compared between responders and IRs using Chi-square tests for categorical variables and t-tests for continuous variables. A multivariable logistic regression model was constructed to identify baseline characteristics associated with IR to index biologic.

Results: A total of 646 AS patients were included in this analysis. Mean age was 43 years, 58% were male, 93% initiated a TNFi, and 7% initiated an IL-17 as their index biologic (Table 1). Over the 1-year follow-up period, 69% of AS patients had an IR to their biologic: 56% of patients had low adherence, 14% switched/added a new biologic, 8% added a new cDMARD, 4% had a dose/frequency increase of their index biologic, 8% had >1 glucocorticoid injection/infusion, 6% had an addition/dose increase of oral glucocorticoids, 12% used a new pain medication, and 2% had a spinal procedure (Table 2). Inadequate responders were more likely to be female (odds ratio (OR)=2.05; p< 0.001), have anxiety or depression (OR=1.91; p=0.014) and other mental health issues (OR=4.57; p< 0.001), and live in the South (OR=1.61; p=0.017); while patients with baseline use of methotrexate were more likely to be responders (OR=0.48; p=0.018) (Table 3). Prior exposure to TNFi was associated with a 3.89-fold greater odds of non-response (p=0.001).

Conclusion: Over 68% of AS patients had an inadequate response to their index biologic 1 year after initiation, mostly driven by low adherence. Health plan claims data appears useful to classify inadequate responders in AS and additional research should be done to further validate this claims-based algorithm in a clinical setting.

Table 1. Demographic and Baseline Characteristics of AS Patients at Biologic Index Date

	AS Patients N=646	Responders N=203	Inadequate Responders N=443	p-value
Sex, n (%)				
Female	272 (42.1%)	62 (30.5%)	210 (47.4%)	<0.001
Age, continuous				
mean (SD)	42.88 (13.22)	43.29 (13.25)	42.69 (13.2)	0.508
Age, categorical, n (%)				
18-39	273 (42.3%)	84 (41.4%)	189 (42.7%)	0.759
40-64	344 (53.3%)	111 (54.7%)	233 (52.6%)	0.622
65-74	19 (2.9%)	<10*	13 (2.9%)	0.988
≥ 75	10 (1.6%)	<10*	<10*	0.433
Health plan type, n (%)				
HMO[1]	109 (16.9%)	34 (16.8%)	75 (16.9%)	0.955
PPO[2]	386 (59.8%)	129 (63.6%)	257 (58.0%)	0.183
CDHP[3]	150 (23.2%)	39 (19.2%)	111 (25.1%)	0.102
Other	<10*	<10*	0	0.139
Geographic region[5], n (%)				
Northeast	101 (15.6%)	39 (19.2%)	62 (14.0%)	0.090
Midwest	128 (19.8%)	44 (21.7%)	84 (19.0%)	0.422
South	213 (33.0%)	53 (26.1%)	160 (36.1%)	0.012
West	170 (26.3%)	61 (30.1%)	109 (24.6%)	0.145
Other/Unknown	34 (5.3%)	<10*	28 (6.3%)	0.075
Index year, n (%)				
2016	198 (30.7%)	59 (29.1%)	139 (31.4%)	0.554
2017	279 (43.2%)	91 (44.8%)	188 (42.4%)	0.569
2018	169 (26.2%)	53 (26.1%)	116 (26.2%)	0.984
Quan-Charlson Comorbidity Index[6]				
Mean (SD)	0.33 (0.78)	0.25 (0.71)	0.37 (0.80)	0.031
0	509 (78.8%)	170 (83.7%)	339 (76.5%)	0.037
1	88 (13.6%)	24 (11.8%)	64 (14.5%)	0.367
2	33 (5.1%)	<10*	29 (6.6%)	0.014
3+	16 (2.5%)	<10*	11 (2.5%)	0.988
Comorbid conditions[6], n (%)				
Anemia	38 (5.9%)	15 (7.4%)	23 (5.2%)	0.271
Dyslipidemia	47 (7.3%)	17 (8.4%)	30 (6.8%)	0.467
Fibromyalgia	44 (6.8%)	<10*	38 (8.6%)	0.009
Hypertension	150 (23.2%)	52 (25.6%)	98 (22.1%)	0.329
Infections	207 (32.0%)	53 (26.1%)	154 (34.8%)	0.028
Low-back pain	306 (47.4%)	90 (44.3%)	216 (48.8%)	0.296
Anxiety or depression	138 (21.4%)	24 (11.8%)	114 (25.7%)	<0.001
Other mental health issue (ex. anxiety/depression)	76 (11.8%)	7 (3.5%)	69 (15.6%)	<0.001
Osteoarthritis	155 (24.0%)	47 (23.2%)	108 (24.4%)	0.735
Osteoporosis	19 (2.9%)	<10*	15 (3.4%)	0.323
Index biologic, n (%)				
TNFi	600 (92.9%)	191 (94.1%)	409 (92.3%)	0.418
Adalimumab	349 (54.0%)	130 (64.0%)	219 (49.4%)	<0.001
Certolizumab	18 (2.8%)	<10*	12 (2.7%)	0.860
Etanercept	164 (25.4%)	35 (17.2%)	129 (29.1%)	<0.001
Golimumab	24 (3.7%)	<10*	15 (3.4%)	0.514
Infliximab	45 (7.0%)	11 (5.4%)	34 (7.7%)	0.296
IL-17				
Secukinumab	46 (7.1%)	12 (5.9%)	34 (7.7%)	0.418

[1]HMO=health management organization; [2]PPO=preferred provider organization; [3]CDHP=consumer-driven health plan; [4]Commercial plan is reference group on index date; [5]Based on US census regions; [6]6-months prior to index date; * denotes n < 10, which was blinded for privacy

Table 2. Criteria Classifying AS Patients as Inadequate Responders 1-year from initiation of a Biologic Therapy

	All AS Patients N=646	TNFi N=600	Secukinumab N=46
Inadequate Response (IR)	443 (68.6%)	409 (68.2%)	34 (73.9%)
Criteria for IR, n (%)			
Low adherence to index biologic (PDC[1]<80%)	364 (56.4%)	337 (56.2%)	27 (58.7%)
Switch/add new biologic (on-label)	88 (13.6%)	82 (13.7%)	<10*
Add new cDMARD therapy[2]	53 (8.2%)	47 (7.8%)	<10*
Dose or frequency increase of index biologic	29 (4.5%)	23(3.8%)	<10*
>1 glucocorticoid injection/IV	52 (8.1%)	46 (7.7%)	<10*
Addition or dose increase of oral glucocorticoid	42 (6.5%)	33 (5.5%)	<10*
Use of new pain medication not observed at baseline	78 (12.1%)	70 (11.7%)	<10*
Spinal procedure	11 (1.7%)	11 (1.8%)	0

[1]PDC= proportion of days covered; [2]Conventional DMARD therapy includes methotrexate or sulfasalazine; *denotes n < 10, which was blinded for privacy

Table 3. Association between Baseline Patient Characteristics and Inadequate Response to a Biologic for Ankylosing Spondylitis

Number of patients	N			
Responders, n	203			
Inadequate Responders, n	443			
	Adjusted Odds Ratio[1]	**95% CL**		**p-value[4]**
		LCL[2]	**UCL[3]**	
Covariates				
Sex (Female vs. Male)	2.05	1.40	2.99	**<0.001**
Age (40 above vs. others)	0.90	0.62	1.29	0.561
Region (South vs. others)	1.61	1.09	2.38	**0.017**
Medicare	0.28	0.08	1.00	0.051
Index Rx (Biologic/TNFi vs. Biologic/Non-TNFi)	0.88	0.42	1.85	0.743
Prior TNFi exposure[5]	3.89	1.74	8.70	**0.001**
Baseline use of methotrexate	0.48	0.26	0.88	**0.018**
Baseline mental health issues (excluding anxiety/depression)	4.57	1.99	10.46	**<0.001**
Baseline anxiety or depression	1.91	1.14	3.18	**0.014**
Baseline chronic pulmonary disease	2.11	0.97	4.57	0.059
Baseline anemia	0.52	0.24	1.11	0.090
Index provider specialty (Rheumatologist vs. Others)	0.70	0.44	1.11	0.130

[1] Odds ratio was from logistic regression model; [2] Lower Confidence Limits; [3]Upper Confidence Limits; [4]p-values obtained from logistic regression model // Model C-statistic=0.7084; Hosmer-Lemeshow test (based on 10 groups) p-value= 0.5104; [5]Prior TNFi exposure= use of TNFi at any time prior to the 6-month baseline period

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Abstract Number: 0372

Tumor Necrosis Factor-α Receptor 2 Polymorphisms and Response to TNF Inhibitor Therapy in Patients with Psoriatic Arthritis

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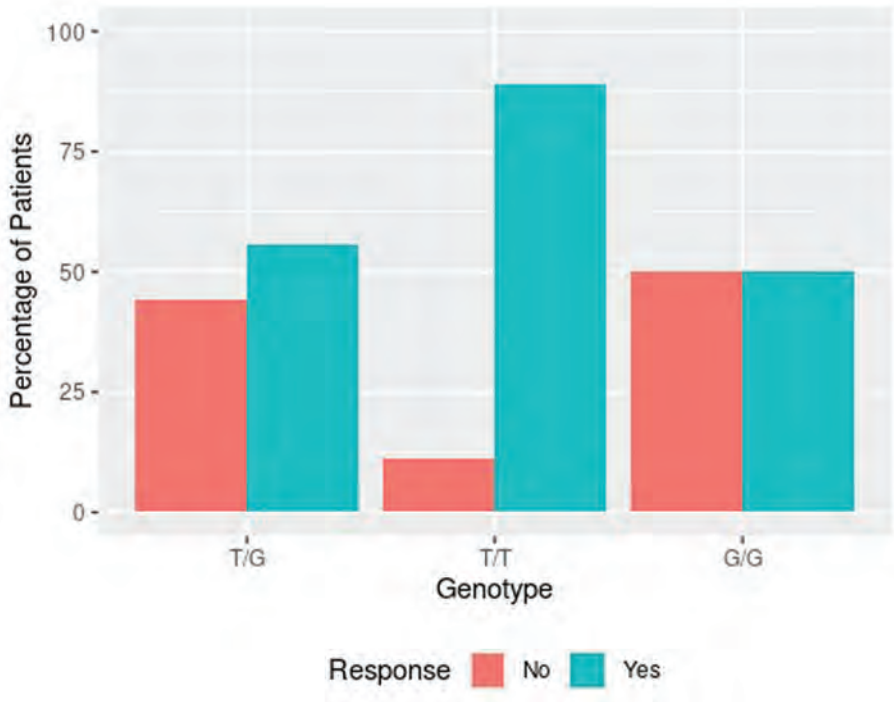
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor necrosis factor inhibitors (TNFi) have significantly improved the prognosis of patients with psoriatic arthritis (PsA); however, approximately 40% of patients do not achieve complete treatment response. There is an unmet clinical need to predict which psoriatic arthritis patients have an increased likelihood of responding to TNFi therapies. Recently published studies have demonstrated that the presence of a TNFR2 gene polymorphism (rs1061622) is linked to TNFi response in patients with immune-mediated diseases, including psoriasis. Presence of the TNFR2 gene with T/T genotype shows a significantly higher rate of response to TNFi compared to G/G genotype in these patients. However, the relationship between this specific TNFR2 gene polymorphism and TNFi response in PsA patients is not known. The aim of this study was to test the association of 3 genotypes (T/T genotype as compared to the T/G and G/G genotypes) with anti TNF response in a cohort of psoriatic arthritis patients.

Methods: Patients treated with TNFi were identified from the PsA longitudinal cohort. Genomic DNA isolated from the buffy coats of these patients were used to perform restriction fragment length polymorphism (RFLP) analysis to identify T/T, T/G or G/G genotypes. TNFi response was then evaluated through chart review by two board certified rheumatologists. Non-response was defined as change of TNFi treatment due to lack of achieving low disease activ-



	Odds Ratio (95% CI)	P-value
Genotype: T/T vs. T/G	6.4 (1.12, 36.44)	0.036
Genotype: G/G vs. T/G	0.8 (0.13, 5.09)	0.810
Genotype: T/T vs G/G	8 (0.91, 70.27)	0.061

ity in skin or joint symptoms. Response rate was studied retrospectively and groups were matched for age, gender and BMI.

Continuous variables were summarized using means and standard deviations. Categorical variables were summarized using counts and percentages. Univariable logistic regression with each genotypes as a single predictor was built to investigate the relationship between genotypes and non-response to TNFi. Results were represented using odds ratios and 95% confidence intervals. Data management and analysis were done in R software (Version 3.5; Vienna, Austria). All tests were two-sided, with an alpha level of 0.05.

Results: 42 patients were included (50.0% female, mean age 53.6 years, mean BMI 29.7) in the analyses. Our results demonstrated that 89% of patients with T/T genotype (n=18) were responders to TNFi, as compared to only 56% of patients with T/G genotype (n=18) and 50% of patients with G/G genotype (n=6) (Figure 1). The main finding in our study was that the odds of having a response in the T/T genotype is 6.4 times the odds of having a response in the T/G genotype (OR = 6.4 (1.12, 36.44), p = 0.036) (Table 1).

Conclusion: Our results suggest that PsA patients homozygous for T genotype (T/T), as compared to the T/G or G/G genotypes, show a stronger likelihood of response to TNFi. Identifying the association between these TNFR2 gene polymorphisms and TNFi response can potentially be a valuable guide in a more personalized approach to treatment options for PsA patients. Our study suggests the potential role of pharmacogenomics profiling in predicting treatment response.

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Abstract Number: 0373

Medical Cannabis in Ankylosing Spondylitis Following Recreational Legalization: A Prospective Cross-sectional Study

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Recreational legalization of cannabis has influenced the medical use by patients. When only legal medical access was available in Canada, 4.3% of all rheumatology patients reported medical use, with this number increasing to 12.6% following recreational legalization. In this study we examine the prevalence of medical cannabis use and explore factors associated with medical use in patients with ankylosing spondylitis (AS).

Methods: During a two-month period (April-May 2019), consecutive patients attending an academic, community-based rheumatology clinic staffed by 3 rheumatologists participated in an onsite survey comprising 2 questionnaires: 1) demographic and disease information completed by the rheumatologist, 2) patient anonymous questionnaire of health status, cannabis use (recreational and/or medicinal) and characteristics of use.

Table 1. Demographic and ankylosing spondylitis disease related information (part 1)

Table 1. Demographic and ankylosing spondylitis disease related information

		All patients (n=72)	Never medical cannabis users (n=55)	Ever medical cannabis users (n=17)	p-value
Demographics	Age, years, mean (SD)	50.4 (14.4)	49.3 (14.7)	53.9 (13.1)	0.252
	Female gender, n (%)	42 (58.3)	33 (60.0%)	9 (52.9%)	0.779
	Employment				
	Full-time, n (%)	36 (50.0%)	28 (50.9%)	8 (47.1%)	0.750
	Part-time, n (%)	6 (8.3%)	5 (9.1%)	1 (5.9%)	
	Disabled, n (%)	15 (20.8%)	10 (18.2%)	5 (29.4%)	
	Student, n (%)	3 (4.2%)	3 (5.5%)	0 (0.0%)	
	Retired, n (%)	12 (6.7%)	9 (16.4%)	3 (17.6%)	
	Employment: unemployed/disabled, n (%)	15 (20.8%)	10 (18.2%)	5 (29.4%)	0.325
	Fibromyalgia, n (%)	13 (18.1%)	7 (12.7%)	6 (35.3%)	0.065
Comorbid conditions	Cardiovascular, n (%)	13 (18.1%)	9 (16.4%)	4 (23.5%)	0.490
	Pulmonary, n (%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	N/A
	Gastrointestinal, n (%)	17 (23.6%)	12 (21.8%)	5 (29.4%)	0.527
	Neurological, n (%)	5 (6.9%)	2 (3.6%)	3 (17.6%)	*0.082*
	Endocrine, n (%)	9 (12.5%)	5 (9.1%)	4 (23.5%)	0.201
	Mood disorder, n (%)	15 (20.8%)	11 (20.0%)	4 (23.5%)	0.742
	Other psychiatric disorder, n (%)	1 (1.4%)	0 (0.0%)	1 (5.9%)	0.236
	Other comorbid condition, n (%)	2 (2.8%)	1 (1.8%)	1 (5.9%)	0.419
Medications for	Number of medication types for rheumatic disease, mean (SD)	1.5 (1.0)	1.2 (0.7)	2.4 (1.5)	**<0.001**
	Non-steroidal anti-inflammatory drug use, n (%)	31 (43.1%)	22 (40.0%)	9 (52.9%)	0.407

Results: In a cohort of 1000 rheumatology attendees (73% females; mean age 64 ± 14 yrs), medical cannabis (MC) had ever been used by 12.6% (95% CI: 10.7%-14.8%) with half continuing use. Inflammatory arthritis was diagnosed in 621 (62%), with 72 (7.2%) diagnosed with AS. Characteristics of AS patients are shown in Table 1. Of the 72 AS patients, 17 (24%) had used MC (95% CI: 14.4-35.1), with 9 (53%) continuing medical use. Past and current recreational cannabis use for all AS patients was 31 (43.1%) and 8 (11.1%) respectively, with no difference in ever recreational rates for medical users. AS users vs. AS non users did not differ for demographic or employment data; there was a trend for users to have more concomitant FM 35.3% vs 12.7% (p=0.065), used significantly more medication types 2.4 vs. 1.2 (p< 0.001), used more opioids 23.5% vs. 5.5% (p=0.049), had a poorer patient global assessment 5.3 vs. 3.6 (p=0.022) and had more pain 6.5 vs 4.4 (p=0.015). Inhalation was the most common method of medical cannabis use. Symptom relief was 5.1±2.1 on a 10 cm VAS.

Conclusion: AS patients had double the rate of medical cannabis use compared to other rheumatology patients. Poorly controlled pain may be the driver for an increased MC in AS, although the effect was perceived as modest.

Table 1. Demographic and ankylosing spondylitis disease related information (part 2)

rheumatic diseases	*Disease-modifying anti-rheumatic drug use, n (%)*		7 (9.7%)	5 (9.1%)	2 (11.8%)	0.665
	Biologic use, n (%)		40 (55.6%)	30 (54.5%)	10 (58.8%)	0.788
	Opioids use, n (%)		7 (9.7%)	3 (5.5%)	4 (23.5%)	**0.049**
	Tranquilizer use, n (%)		2 (2.8%)	1 (1.8%)	1 (5.9%)	0.419
	Antiepileptic use, n (%)		6 (8.3%)	3 (5.5%)	3 (17.6%)	0.139
	Antidepressant use, n (%)		1 (1.4%)	1 (1.8%)	0 (0.0%)	>0.999
	Steroid use, n (%)		3 (4.2%)	2 (3.6%)	1 (5.9%)	0.560
	Cannabis pharmaceutical		3 (4.2%)	0 (0.0%)	3 (17.6%)	N/A
	Cannabis herbal		5 (6.9%)	0 (0.0%)	5 (29.4%)	N/A
Disease assessment	Physician Global Assessment (PGA) (0-10), mean (SD)		3.0 (2.3)	2.7 (2.3)	3.9 (2.0)	*0.055*
	Patient Global Assessment (PtGA) (0-10), mean (SD)		4.0 (2.7)	3.6 (2.7)	5.3 (2.4)	**0.022**
	Pain, VAS cm, mean (SD)		4.9 (3.1)	4.4 (3.1)	6.5 (2.6)	**0.015**
Cigarette use	Non-smoker	n (%)	42 (58.3%)	32 (58.2%)	10 (58.8%)	0.419
	Past smoker	n (%)	16 (22.2%)	14 (25.5%)	2 (11.8%)	
	Current smoker	n (%)	12 (16.7%)	8 (14.5%)	4 (23.5%)	
	Missing	n (%)	2 (2.8%)	1 (1.8%)	1 (5.9%)	
Cannabis use	Recreational	Ever use, n (%)	31 (43.1%)	23 (41.8%)	8 (47.1%)	0.783
		Current use, n (%)	8 (11.1%)	5 (9.1%)	3 (17.6%)	0.382
	Medical	Ever used >10 times, n (%)	14 (19.4%)	NA	14 (82.4%)	NA
		Current medical use, n (%)	9 (12.5%)	NA	9 (52.9%)	NA
		If never used, consider medical use, n (%)	NA	40 (72.7%)	NA	NA
	Current cannabis use (any reason)[§§]	Current use, n (%)	15 (20.8%)	5 (9.1%)	10 (58.8%)	**<0.001**
		Method of herbal cannabis use[††]				
		Smoke, n (%)	12 (80.0%)[§§]	5 (100.0%)[‡]	7 (70.0%)[‡‡]	0.505
		Vaporize, n (%)	5 (33.3%)[§§]	0 (0.0%)[‡]	5 (50.0%)[‡‡]	0.101
		Oil/capsules, n (%)	5 (33.3%)[§§]	0 (0.0%)[‡]	5 (50.0%)[‡‡]	0.101
		Edible, n (%)	1 (6.7%)[§§]	0 (0.0%)[‡]	1 (10.0%)[‡‡]	>0.999
		Rub, n (%)	0 (0.0%)[§§]	0 (0.0%)[‡]	0 (0.0%)[‡‡]	N/A

Table 1. Demographic and ankylosing spondylitis disease related information (part 3)

	Current herbal cannabis use (medical reasons)	Relief of symptoms, mean (0-10) (SD)[¥]	NA	NA	5.1 (2.1)	NA

NA, not applicable.
Significant ($p<0.05$) p-values indicated in bold. Missing category is not included in the comparison.
[†] Patients may have had more than one type of inflammatory arthritis.
[§] Patients may have had more than one type of osteoarthritis.
[††] Patients may have used more than one method of herbal cannabis.
[§§] Proportions are based on the number of patients currently using herbal cannabis for any reason (All patients: n=15; Current recreational herbal cannabis users: n=5; Current medical herbal cannabis users: n=10).
[‡] Proportions are based on the number of patients in the '*Never medical cannabis users*' group currently using herbal cannabis for recreational purposes (n=5).
[‡‡] Proportions are based on the number of patients in the '*Ever medical cannabis users*' group currently using herbal cannabis for any reason (All patients n=10).
[¥] Among patients using herbal cannabis for medical reasons. Minimum (0) represents 'no relief' and maximum (10) represents 'maximum relief".

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Abstract Number: 0374

Neo-epitopes of Type I Collagen Can Be Utilized as Translational Biomarkers for Skin and Joint Turnover in Patients with Psoriasis and Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
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Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriasis (PsO) is a chronic immune-mediated skin disease. Around 30% of patients diagnosed with PsO will develop psoriatic arthritis (PsA). Patients with PsA may develop irreversible joint damage, therefore optimized screening methods identifying the patients with PsO in risk of developing PsA have become a medical priority. In the interstitial matrix of bone and soft tissue, type I collagen is the most abundant collagen and secreted by fibroblasts. During extracellular matrix (ECM) remodeling, proteases cleave type I collagen resulting in the release of metabolites into the circulation. These collagen metabolites can be quantified in serum as biomarkers of tissue remodeling and give insight to pathological process at tissue level. In this study we investigated type I collagen turnover by measuring synthesis (PRO-C1) and degradation (C1M) biomarkers in a preclinical Scar-in-a-Jar (SiaJ) model and in serum from patients with PsO or PsA.

Methods: In the SiaJ model, primary human healthy dermal fibroblasts were grown for up to 17 days in DMEM medium containing 0.4% fetal calf serum, Ficoll (to produce a crowded environment) and ascorbic acid. Cells were treated with tumor necrosis factor β1 (TGF-β1) [1 nM] and a range of Tofacitinib concentrations [0-100 nM]. Media and treatments were changed twice a week and untreated cell were used as control. PRO-C1 was quantified in the tissue culture supernatant by ELISAs (Nordic Bioscience). Furthermore, patients with PsO (n=30, mean age 41.1) and patients with PsA (n=30, mean age 50.3) were recruited through St. Vincent's University Hospital, Ireland. Study was ethically approved by their local ethics committee. Clinical disease parameters were recorded. PRO-C1 and C1M were measured in serum by ELISAs (Nordic Bioscience). Statistical analysis included one-way ANOVA on data from SiaJ model and Mann Whitney test on clinical data from patients with PsO or PsA.

Results: In the dermal fibroblasts, TGF-β1 significantly increased PRO-C1 levels compared to w/o (p<0.001). Moreover, above a concentration of 12.5nM, Tofacitinib decreased TGF-β1 induced type I collagen formation in a dose-dependent manner. The highest treatment concentration of Tofacitinib (100 nM) significantly decreased PRO-C1 to the level of controls (p< 0.001). In the clinical study, PRO-C1 levels were not different between patients with PsO and PsA (p=0.123). However, levels of C1M were elevated in patients with PsA (p=0.029) compared to PsO. The tissue turnover of type I collagen in the interstitial network-system was analyzed (PRO-C1/C1M). Patients with PsO demonstrated increased formation of type I collagen (p=0.007) compared to PsA.

Conclusion: We demonstrated that Tofacitinib decreased collagen type I production in dermal fibroblasts. Moreover, the tissue turnover profile of type I collagen in PsO patients was significantly increased compared to PsA patients, with balance toward tissue formation. The increased type I collagen formation may be due to the dermal fibroblast

activity in PsO producing extensive amounts of PRO-C1. These results suggest that serological biomarkers may be used to separate PsO and PsA patients and potentially be used to identify the 30% of PsO patients that progress to PsA.

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Abstract Number: 0375

Efficacy of Disease Modifying Anti-Rheumatic Drugs for Enthesitis in a Prospective Longitudinal Psoriatic Arthritis Cohort

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Enthesitis is a common clinical feature of psoriatic arthritis (PsA). There is limited evidence on the effect of treatment on enthesitis. Our purpose was to study the effectiveness of conventional and targeted (c and t) DMARDs in treating clinical enthesitis in an observational PsA cohort.

Methods: Patients enrolled into a large PsA cohort from 1 January 2000 to 6 May 2020, with clinical enthesitis were included in this study. Enthesitis was defined as tenderness over at least 1 of the 29 sites described by validated enthesitis scoring indices, including spondyloarthritis research consortium of Canada (SPARCC) enthesitis index, Leeds enthesitis index (LEI), and Maastricht ankylosing spondylitis enthesitis score (MASES). Baseline medications, including non-steroidal anti-inflammatory drugs (NSAIDs) and/or c/t DMARDs at the diagnosis of enthesitis, were recorded for each patient. Complete resolution of enthesitis at 12 months was the primary outcome. The pharmacological treatment prescribed was divided into the following mutually exclusive ordinal categories: I- No treatment/NSAIDs; II- cDMARDs±NSAIDs, without tDMARD; III- tDMARDs±cDMARDs/NSAIDs. Univariable and multivariable logistic regression models were created to determine the association between medication category and complete resolution of enthesitis after controlling for age, sex, body mass index (BMI), PsA duration and baseline enthesitis score. A global p-value was calculated to evaluate the overall effect of medication categories on enthesitis resolution. The results are expressed as odds ratios (OR) with a 95% confidence interval (CI).

Results: Of the 1270 patients, 628 (49.4%) had enthesitis. After excluding 102 patients for inadequate follow-up data, 526 patients (51.7% males) with a mean age of 49.02 years (sd=13.12) years were included. The mean tender entheses count was 2.13 (sd=2.16). The mean duration of PsA at baseline was 10.74 years (sd=10.73), and the mean BMI was 29.13 (sd=6.25). The proportion of patients treated with each category of medications is presented in Table 1. Complete resolution of enthesitis was noted in 453 (86%) patients, within a mean of 8.9 months. The results of the regression analysis are shown in Table 2. The global p-value for medication categories was not significant in uni-

Table 1: Number of patients on each drug category

Individual medications in each category	Number (%) (N = 526)	Numbers on the individual drug (%)
Category I	**142 (27)**	
• No medication		52 (36.7)
• NSAIDs		90 (63.3)
Category II	**196 (37.3)**	
• Methotrexate		158 (80.6)*
• Leflunomide		29 (14.8)
• Sulphasalazine		32 (16.3)
• Azathioprine		10 (5.1)
• Cyclosporine		2 (1)
Category III	**188 (35.7)**	
• Tumor necrosis factor inhibitors (TNFi)		155 (82.4)
• Interleukin-17 inhibitors (IL-17i)		14 (7.4)
• Others (IL-12/23i, IL-23i, Tofacitinib, Apremilast)		19 (10.1)

* Percentage of individual drugs do not add to 100 since some patients were treated with a combination of cDMARDs

Table 2: Association between treatment and resolution of enthesitis

	Univariable models		Multivariable Model	
Variable	**OR (95% CI)**	**P value**	**OR (95% CI)**	**P value**
Sex (Male vs. Female)	1.61 (0.97 – 2.68)	0.07	1.61 (0.96 – 2.70)	0.07
Baseline age in years	1.00 (0.98 – 1.02)	0.85	1.00 (0.98 – 1.02)	0.90
Baseline PsA duration	1.00 (0.98 – 1.03)	0.81	1.00 (0.98 – 1.03)	0.85
BMI	1.01 (0.97 – 1.05)	0.69	1.01 (0.97 – 1.05)	0.61
Number of entheses	0.96 (0.87 – 1.06)	0.45	0.96 (0.87 – 1.07)	0.47
Medication category		0.58*		0.61*
Category I	Ref	Ref	Ref	Ref
Category II	1.40 (0.74 – 2.63)	0.30	1.37 (0.72 – 2.60)	0.34
Category III	1.24 (0.67 – 2.31)	0.50	1.27 (0.67 – 2.41)	0.47

*global p value

variate and multivariable models. The models showed a trend for males to achieve complete resolution of enthesitis regardless of the medication category (OR 1.71; 95% CI 0.96-2.70; p=0.07).

Conclusion: In an observational setting resolution of clinical enthesitis occurs regardless of the treatment used. Future effectiveness studies may require evaluating patients with severe enthesitis using advanced imaging.

Disclosure: A. Mathew, None; **M. Sutton**, None; **D. Pereira**, None; **V. Chandran**, Abbvie, 2, 5, Amgen, 2, 5, Celgene, 2, 5, Eli Lilly, 5, Eli Lilly, 3, Janssen, 8, Novartis, 5, Pfizer, 5, UCB, 5; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5.

Abstract Number: 0376

Higher Intake of Carbohydrates and Free Sugar Are Associated with Higher Disease Activity in Patients with Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Diet has been described as a factor influencing the course of rheumatic diseases, such as rheumatoid arthritis and systemic lupus erythematosus (SLE). In addition, it has been previously reported that dietary sugar intake may contribute to subclinical inflammation and disease activity in SLE. However, no studies have been performed to investigate the possible association of nutritional parameters on disease activity in patients with spondyloarthritis (SpA).

Table 1. Univariable and multivariable linear regression analysis of the association between ASDAS and nutritional parameters in patients with radiographic axial SpA (n=104)

	Univariable Analysis		Multivariable Analysis*					
			Model 1		Model 2		Model 3	
	ß (95%CI)	p value	ß (95%CI)	p value	ß (95%CI)	p value	ß (95%CI)	p value
Total Energy Intake,1000 Kcal/day	**0.11 (0.04;0.18)**	**<0.01**	**0.12 (0.44;0.20)**	**<0.01**	-	-	-	-
Carbohydrates, 100g/day	**0.05 (0.01;010)**	**0.01**	-	-	**0.05 (0.02;0.08)**	**<0.01**	-	-
Sugar**, 100g/day	**0.04 (0.01;0.07)**	**0.01**	-	-	-	-	**0.05 (0.01;0.08)**	**0.01**
Total Fat, 100g/day	0.33 (-0.02;0.69)	0.07	-1.98 (-6.43;2.48)	0.38	-1.85 (-6.30;2.60)	0.41	-1.87 (-6.36;2.61)	0.41
Saturated, 100g/day	**0.80 (0.10;1.60)**	**0.02**	3.02 (-2.82;8.85)	0.31	2.99 (-2.85;8.83)	0.31	3.08 (-2.80;8.97)	0.30
Monounsaturated, g/day	0.01 (0.00;0.02)	0.06	0.01 (-0.04;0.07)	0.65	0.01 (-0.04;0.07)	0.65	0.01 (-0.04;0.06)	0.68
Polyunsaturated, 100g/day	0.30 (-1.20;1.70)	0.72	1.60 (-4.96;8.17)	0.63	1.56 (-5.01;8.13)	0.64	1.67 (-4.94;8.29)	0.62
Protein, 100g/day	0.30 (-0.10;0.70)	0.12	0.25 (-0.52;1.01)	0.52	0.30 (-0.47;1.07)	0.44	0.33 (-0.44;1.10)	0.40
Dietary fiber, 100g/day	0.30 (-1.60;0.10)	0.64	-1.28 (-2.98;.042)	0.14	-1.26 (-2.96;0.44)	0.14	-1.10 (-2.80;0.60)	0.20

Dependent Variable: ASDAS at baseline

ß, linear regression coefficient

*Adjusted for age, sex, BMI and smoker status

**includes monosaccharides and disaccharides

Table 2. Univariable and multivariable linear regression analysis of the association between BASDAI and nutritional parameters in patients with radiographic axial SpA (n=104)

	Univariable Analysis		Multivariable Analysis*					
			Model 1		Model 2		Model 3	
	ß (95%CI)	p value	ß (95%CI)	p value	ß (95%CI)	p value	ß (95%CI)	p value
Total Energy Intake,1000 Kcal/day	**0.13 (0.01;0.26)**	**0.04**	**0.16 (0.02;0.29)**	**<0.01**	-		-	
Carbohydrates, 100g/day	0.05 (-0.01;0.10)	0,06	-		**0.06 (010;1.20)**	**0.02**	-	
Sugar**, 100g/day	0.05 (-0.01;0.11)	0,06	-		-		**0.06 (0.06;0.12)**	**0.03**
Total Fat, 100g/day	0.55 (-0.06;1.16)	0,08	-0.57 (-8.21;7.06)	0.88	-0.41 (-8.04;7.21)	0.91	-0.46 (-8.12,7.19)	0.90
Saturated, 100g/day	**1.36 (0.09;2.63)**	**0,04**	1.88 (-8.06;11.82)	0.71	1.85 (-8.09;11.79)	0.71	2.00 (-7.98;11.98)	0.69
Monounsaturated, g/day	0.02 (0.00;0.04)	0,06	0.02 (-0.07;0.11)	0.66	0.02 (-0.07;0.11)	0.67	0.02 (-0.07;0.11)	0.68
Polyunsaturated, 100g/day	0.51 (-1.93;2.94)	0,68	-1.20 (-12.37;9.97)	0.83	-1.25 (-12.42;9.92)	0.82	-1.08 (-12.29;10.14)	0.85
Protein, 100g/day	0.10 (-0.57;0.77)	0,78	-0.53 (-1.84;0.79)	0.43	-0.46 (-1.78;0.85)	0.49	-0.42 (-1.74;0.90)	0.53
Dietary fiber, 100g/day	-1.41 (-3.60;0.79)	0,21	-1.62 (-4.53;1.29)	0.27	-1.60 (-4.51;1.31)	0.28	-1.39 (-4.30;1.52)	0.35

Dependent Variable: BASDAI at baseline
ß, linear regression coefficient
*Adjusted for age, sex, BMI and smoker status
**includes monosaccharides and disaccharides

Methods: Patients with radiographic axSpA (ankylosing spondylitis fulfilling the modified New York criteria) and starting a bDMARD therapy were recruited between 2015 and 2019 in an extension of the prospective German Spondyloarthritis Inception Cohort (GESPIC). Dietary habits were collected at baseline using the country-specific validated food frequency questionnaire (FFQ) developed for the use in the German Health examination Survey for Adults 2008-2011. The FFQ includes questions about the frequency and amount of 53 food items, consumed during the past 4 weeks, and enabled to compute individual mean consumptions of foods in grams per day. Total energy intake (in Kcal per day) and nutritional parameters: carbohydrates, free sugars, total fats, saturated fats, mono and poly-unsaturated fats, proteins and dietary fiber, were calculated for each patient using Prodi® software (version 6.10, Basis, Nutri-Science, Stuttgart/Germany) and the database of Federal Food Code (Bundeslebensmittelschlüssel), version 3.02. Disease activity measures (BASDAI, CRP and ASDAS), as well as height, weight and body mass index (BMI) were assessed at baseline before bDMARD treatment.

Results: A total of 129 patients with axSpA were included in this cohort. FFQ with the consequent nutritional analysis was performed in 104 patients. There were 68.3% males, and 86.5% were HLA-B27 positive. At baseline, patients presented BMI of 25.1±4.3 kg/m^2, BASDAI 5.6±1.4, CRP 14.0±18.2 mg/l, and ASDAS 3.5±1.0.

In the univariable analysis, a higher energy intake and carbohydrates at baseline were associated with higher disease activity, measured by ASDAS, BASDAI and CRP (tables 1-3). This association was attributable to the full intake of carbohydrates and specifically to the total of free sugars (monosaccharides and disaccharides) and the decrease

Table 3. Univariable and multivariable linear regression analysis of the association between CRP and nutritional parameters in patients with radiographic axial SpA (n=104)

	Univariable Analysis		Multivariable Analysis*					
			Model 1		Model 2		Model 3	
	ß (95%CI)	p value	ß (95%CI)	p value	ß (95%CI)	p value	ß (95%CI)	p value
Total Energy Intake,1000 Kcal/day	**2.94 (1.38;4.50)**	**<0.01**	**3.32 (1.59;5.04)**	**<0.01**	-		-	
Carbohydrates, 100g/day	**1.33 (0.65;2.01)**	**<0.01**	-		**1.35 (0.64;2.05)**	**<0.01**	-	
Sugar**, 100g/day	**1.31 (0.62;0.20)**	**<0.01**	-		-		**1.31 (0.60;2.01)**	**<0.01**
Total Fat, 100g/day	1.91 (-6.23;10.05)	0.64	-32.42 (-131.57;66.72)	0.52	-28.99 (-128.04;70.06)	0.56	-30.28 (-129.86;69.30)	0.55
Saturated, 100g/day	3.43 (13.62;20.48)	0.40	62.43 (-67.45;192.31)	0.34	61.65 (-68.29;191.59)	0.35	64.97 (-65.71;195.65)	0.33
Monounsaturated, g/day	0.04 (-0.24;0.32)	0.79	-0.59 (-1.77;0.60)	0.33	-0.59 (-1.77;0.60)	0.33	-0.61 (-1.80;0.58)	0.31
Polyunsaturated, 100g/day	8.19 (23.78;40.15)	0.61	69.21 (-76.88;215.30)	0.35	68.07 (-78.09;214.23)	0.36	71.79 (-75.15;218.73)	0.33
Protein, 100g/day	2.97 (-5.80;11.75)	0.50	10.28 (-6.75;27.31)	0.23	11.66 (-5.38;28.71)	0.18	12.59 (-4.55;29.73)	0.15
Dietary fiber, 100g/day	-8.41 (37.46;20.63)	0.57	-33.82 (-71.59;3.95)	0.08	-33.29 (-71.06;4.48)	0.08	-28.95 (-66.78;9.87)	0.13

Dependent Variable: CRP at baseline
ß, linear regression coefficient
*Adjusted for age, sex, BMI and smoker status
**includes monosaccharides and disaccharides

of dietary fiber as shown in the multivariable analyses (tables 1-3). This effect was independent of age, sex, smoker status and BMI.

Conclusion: A higher intake of carbohydrates and a higher consumption of free sugars are associated with higher disease activity in patients with AS.

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Abstract Number: 0377

Evaluation of Sex Differences in the Efficacy and Safety of Tofacitinib in Patients with Active Psoriatic Arthritis: A Post Hoc Analysis of Two Phase 3 Randomized Controlled Trials

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

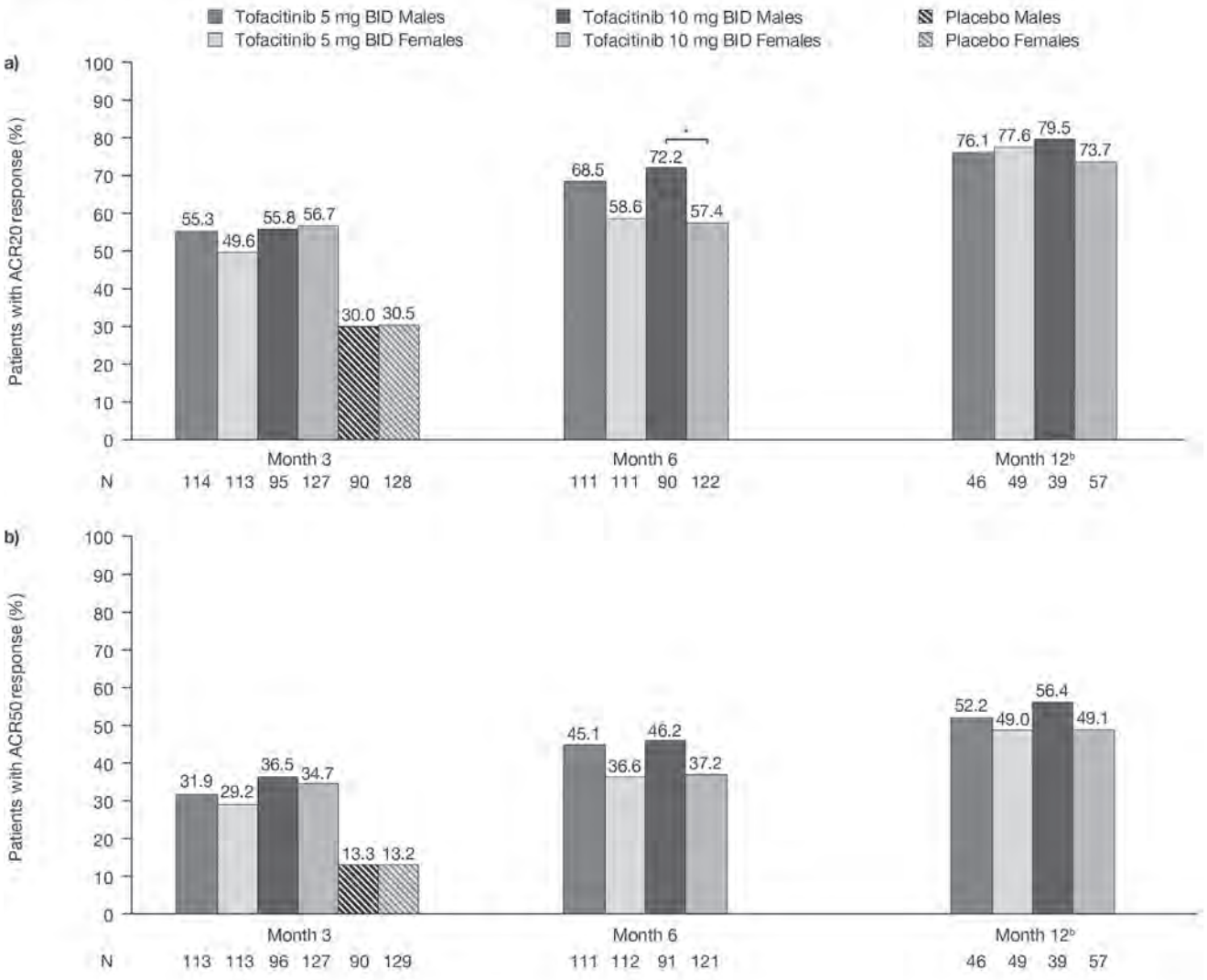
Background/Purpose: Studies indicate that sex (male vs female) is predictive of outcomes with PsA treatments, such as TNF inhibitors (TNFi).[1] Tofacitinib is an oral JAK inhibitor for the treatment of PsA. This post hoc analysis evaluated the impact of sex on tofacitinib efficacy and safety in PsA.

Methods: Data were pooled from two Phase 3, randomized, placebo-controlled studies of tofacitinib (OPAL Broaden [NCT01877668]; OPAL Beyond [NCT01882439]) in patients (pts) with active PsA and an inadequate response to ≥ 1 conventional synthetic DMARD (and were TNFi-naïve; OPAL Broaden) or ≥ 1 TNFi (OPAL Beyond). Analyses included pts randomized to tofacitinib 5 mg twice daily (BID), tofacitinib 10 mg BID, or placebo (switching to tofacitinib 5 or 10 mg BID at Month [M]3). Efficacy endpoints included ACR20/50 response rates; change from baseline (Δ) in Leeds Enthesitis Index (LEI), ΔDactylitis Severity Score (DSS), and ΔFunctional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F); and proportion of pts achieving a minimal clinically important difference (MCID) for HAQ-Disability Index (HAQ-DI) (≥ 0.35). Safety outcomes were assessed up to M6. Demographic and baseline disease characteristics were tested using one-way analysis of variance for continuous parameters and chi-squared test for categorical parameters. Analyses are based on observed cases and presented without p-value multiplicity adjustment.

Results: Overall, 710 pts (317/393, male/female) were included (tofacitinib 5 mg BID, 117/121; tofacitinib 10 mg BID, 100/136; placebo, 100/136, respectively). Baseline characteristics were broadly similar between sexes; exceptions included higher Composite Psoriatic Disease Activity Index in females (tofacitinib 5 mg), higher FACIT-F total score (less fatigue) in males, higher HAQ-DI in females (tofacitinib 5 mg BID and placebo), and higher DSS in males (placebo). ACR20/50 response rates were similar between sexes at M3. At M6, ACR20 response rates were numerically higher for males (Figure a), with a significant difference seen for tofacitinib 10 mg BID (72.2% males vs 57.4% females; p=0.0163); no significant differences in ACR50 response rates were observed (Figure b). ACR20/50 response rates were similar between sexes by M12 (OPAL Broaden). In general, no significant differences between sexes were shown in ΔLEI, ΔDSS, ΔFACIT-F, or HAQ-DI MCID at M3, 6, and 12 in all groups. Up to M6, numerically more females vs males had adverse events (AEs), serious AEs, severe AEs, discontinuations due to AEs, gastrointestinal, nervous, respiratory, thoracic and mediastinal system disorders (system organ class) with tofacitinib 5 and 10 mg BID (Table). Rates of vascular disorders were numerically higher in males.

Conclusion: In general, no clinically meaningful differences between sexes were observed in the efficacy of tofacitinib 5 and 10 mg BID up to M12. Some numerical differences in safety outcomes with tofacitinib were seen between sexes. Results further characterize the efficacy and safety of tofacitinib in pts with PsA.

Figure. a) ACR20 and b) ACR50 response rates, by sex (FAS; no imputation[a])



*p<0.05 male vs female
[a]Analyses were based on observed cases. Results of the analyses with NRI are not presented as they were similar to results without imputation; [b]OPAL Broaden only
The FAS included all patients who received ≥1 dose of study medication and had ≥1 post-baseline assessment; differences in the proportion of responders between males and females, and associated p values were estimated using the Cochran-Mantel-Haenszel approach, adjusted for study
ACR20/50, American College of Rheumatology ≥20/50% response criteria; BID, twice daily; FAS, full analysis set; N, number of patients with non-missing data; NRI, non-responder imputation

1. Eder L, Gladman DD. Expert Rev Clin Immunol 2014; 10: 763-770.

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Table. Overview of AEs (all-causality), by sex up to Month 6 (safety population)

	Tofacitinib 5 mg BID		Tofacitinib 10 mg BID	
Patients, n (%)	Male (N=117)	Female (N=121)	Male (N=100)	Female (N=136)
≥1 AE	74 (63.2)	80 (66.1)	64 (64.0)	95 (69.9)
SAE	4 (3.4)	6 (5.0)	4 (4.0)	7 (5.1)
Severe AEs	3 (2.6)	9 (7.4)	4 (4.0)	7 (5.1)
Discontinuation due to AEs	3 (2.6)	7 (5.8)	5 (5.0)	9 (6.6)
Dose reduction or temporary discontinuation due to AEs	16 (13.7)	16 (13.2)	19 (19.0)	31 (22.8)
Most frequently occurring AEs by SOC (≥5% in any treatment group)				
Eye disorders	3 (2.6)	3 (2.5)	0	9 (6.6)
GI	19 (16.2)	29 (24.0)	16 (16.0)	27 (19.9)
General and administration site	10 (8.5)	9 (7.4)	6 (6.0)	13 (9.6)
Infections and infestations	39 (33.3)	41 (33.9)	36 (36.0)	65 (47.8)
Injury, poisoning, and procedural complications	13 (11.1)	12 (9.9)	6 (6.0)	12 (8.8)
Investigations	9 (7.7)	11 (9.1)	12 (12.0)	10 (7.4)
Metabolism and nutrition	4 (3.4)	4 (3.3)	6 (6.0)	5 (3.7)
Musculoskeletal and connective tissue	11 (9.4)	17 (14.0)	6 (6.0)	19 (14.0)
Nervous system	10 (8.5)	20 (16.5)	13 (13.0)	22 (16.2)
Respiratory, thoracic, and mediastinal	3 (2.6)	12 (9.9)	2 (2.0)	7 (5.1)
Skin and subcutaneous tissue	13 (11.1)	10 (8.3)	10 (10.0)	10 (7.4)
Vascular	7 (6.0)	4 (3.3)	5 (5.0)	4 (2.9)

The safety population included all patients who received ≥1 dose of study medication; AEs were coded using MedDRA v19.0

AE, adverse event; BID, twice daily; GI, gastrointestinal; MedDRA, Medical Dictionary for Regulatory Activities; SAE, serious adverse event; SOC, system organ class

Disclosure: L. Eder, AbbVie, 2, 5, 8, Eli Lilly, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5, 8, Celgene, 5, Novartis, 5; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **S. Zehra Aydin**, AbbVie, 1, Celgene, 1, Eli Lilly, 1, Janssen, 1, Novartis, 5, Pfizer Inc, 5, UCB, 5; **A. Ogdie**, Amgen, 2, 5, 8, Novartis, 2, 5, Pfizer Inc, 2, 5, AbbVie, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Corrona, 5, Eli Lilly, 5; **H. Shi**, Pfizer Inc, 1, 2; **P. Landry**, Pfizer Inc, 1, 2; **R. Luna**, Pfizer Inc, 1, 2.

Abstract Number: 0378

Itch as the Major Mediator of the Effect of Tofacitinib on Health-Related Quality of Life in Psoriatic Arthritis: A Mediation Analysis

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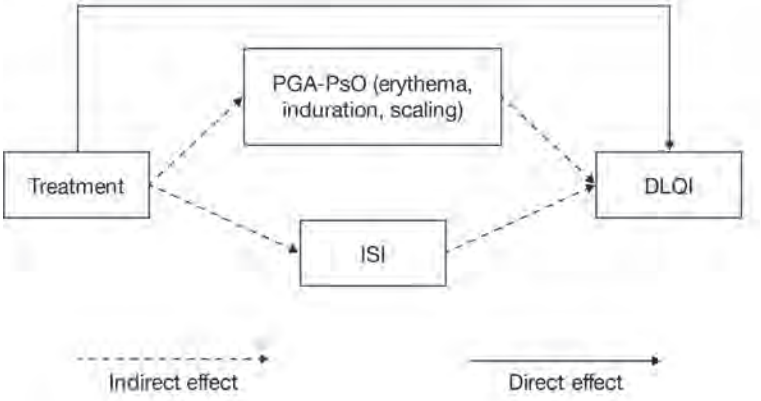
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

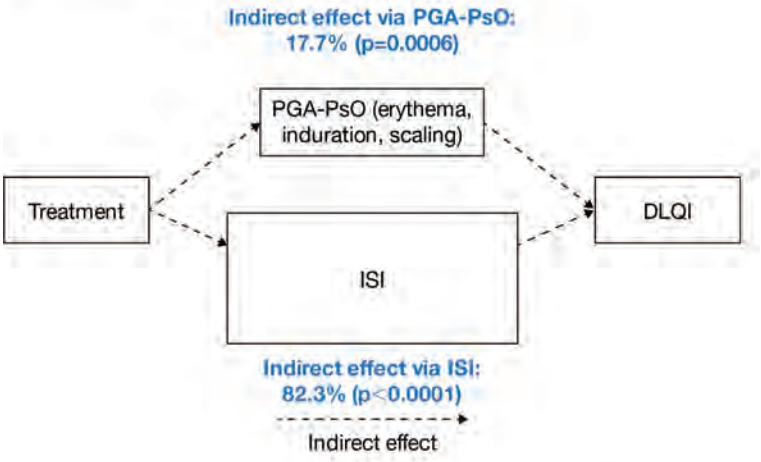
Background/Purpose: Psoriatic arthritis (PsA) is a chronic, systemic inflammatory disease with signs and symptoms across multiple domains, including cutaneous manifestations, which can impact health-related quality of life (HRQoL). Tofacitinib is an oral Janus kinase inhibitor for the treatment of PsA. In two Phase 3 randomized studies, patients (pts) with active PsA treated with tofacitinib experienced greater improvements in various dermatologic endpoints, compared with placebo. As pruritus is a bothersome symptom of skin disease in pts with PsA, we sought to determine how tofacitinib treatment affects pt-reported HRQoL via clinical improvements in dermatologic symptoms including itch.

Figure 1. Initial mediation model



Treatment is represented by a binary variable (tofacitinib 5 mg BID vs placebo).
DLQI, Dermatology Life Quality Index; ISI, Itch Severity Index;
PGA-PsO, Physician Global Assessment of Psoriasis

Figure 2. Revised mediation model



Treatment is represented by a binary variable (tofacitinib 5 mg BID vs placebo).
DLQI, Dermatology Life Quality Index; ISI, Itch Severity Index;
PGA-PsO, Physician Global Assessment of Psoriasis

Methods: Analyses used data (mean scores from Months 1 and 3) from two Phase 3 studies (OPAL Broaden [NCT01877668]; OPAL Beyond [NCT01882439]) of pts with active PsA treated with tofacitinib 5 mg twice daily or placebo; pts were tumor necrosis factor inhibitor (TNFi)-naïve or had previous inadequate response to ≥1 TNFi. All pts were treated continuously with a single conventional synthetic DMARD. Mediation modeling, a statistical method used to assess mechanisms underlying observed relationships between different variables via other explanatory variables (mediators), was applied. The mediation model included: treatment, as the independent (explanatory) binary variable (tofacitinib 5 mg BID vs placebo); HRQoL, measured by Dermatology Life Quality Index (DLQI), as the dependent (outcome) variable; and two mediators, pt-reported Itch Severity Index (ISI) and Physician's Global Assessment of Psoriasis (PGA-PsO) (a latent variable represented by erythema, induration, and scaling). The initial model designated the treatment effect on DLQI mediated via ISI and PGA-PsO as an indirect effect, and treatment effects not attributable to ISI or PGA-PsO as a direct effect (Figure 1).

Results: Data were collected from 468 pts, pooled from both studies. In the initial model (pooled data), the effect of tofacitinib treatment on DLQI was largely mediated by itch (measured by ISI) and PGA-PsO (indirect effect) ($p< 0.0001$); the effect of treatment attributable to factors other than ISI and PGA-PsO (direct effect) was not statistically significant ($p=0.66$). Results were consistent for pooled and individual study data. Because the direct effect was small and not statistically significant, the model was re-specified to exclude the direct effect of tofacitinib treatment on DLQI. In the revised model (pooled data), 17.7% of the indirect effect of treatment on DLQI was attributable to PGA-PsO ($p=0.0006$) and 82.3% was attributable to itch ($p< 0.0001$) (Figure 2). Analyses of individual studies using the revised model gave results generally consistent with pooled data.

Conclusion: Dermatology-focused mediation modeling showed that the majority of the effect (~80%) of tofacitinib treatment on DLQI is mediated by improvements in itch, with ~20% mediated via improvements in PGA-PsO.

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Abstract Number: 0379

Achievement of RAPID3 and cDAPSA Treatment Targets Is Associated with Control of Articular and Extra-Articular Manifestations of Active Psoriatic Arthritis in DMARD-Naive Patients Treated with Apremilast

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

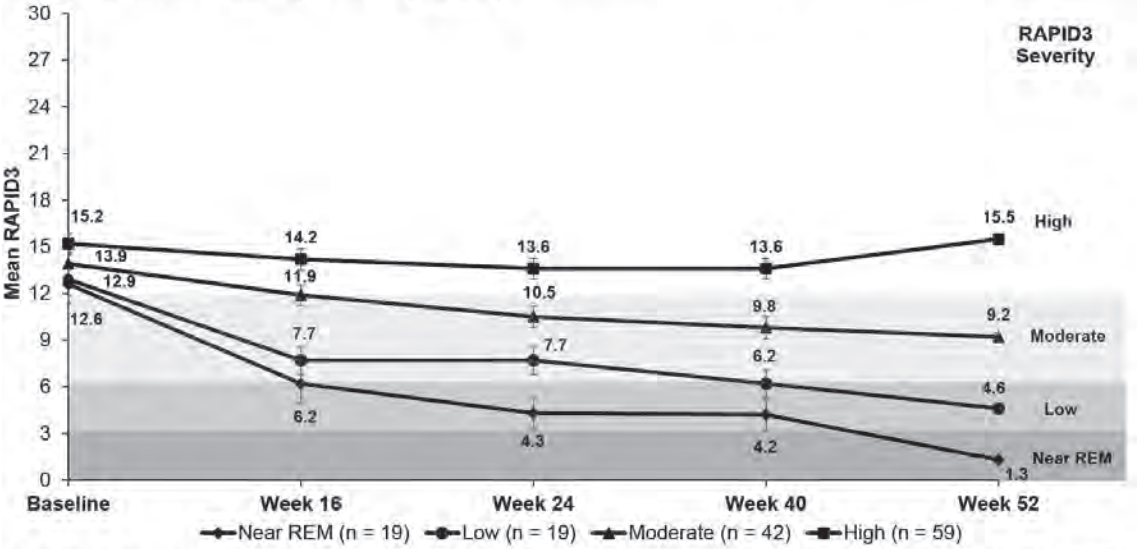
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

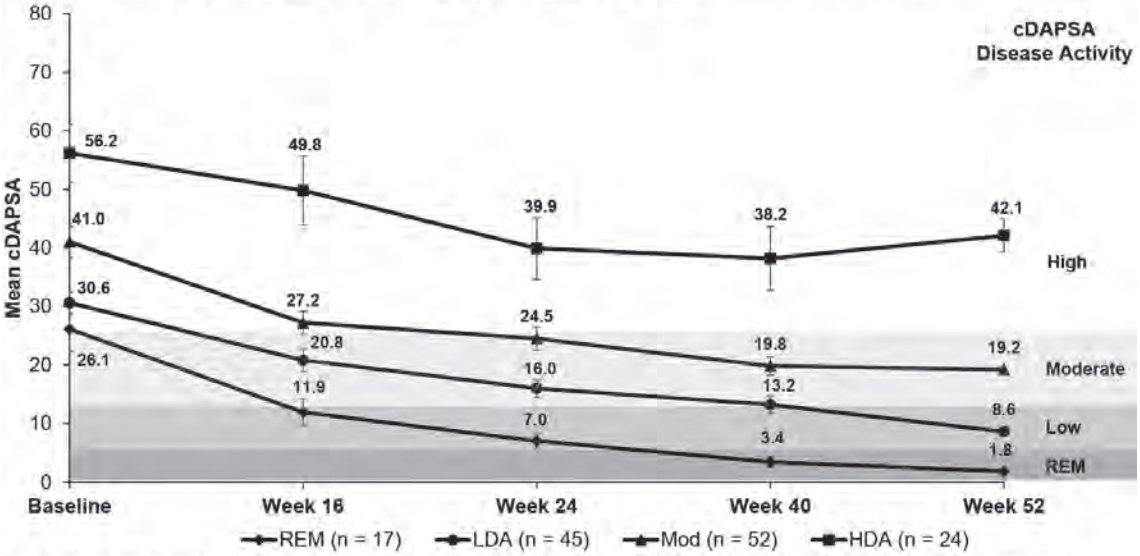
Background/Purpose: Phase III PALACE 4 (NCT01307423) assessed the efficacy of apremilast (APR) in DMARD-naive patients with PsA. The Routine Assessment of Patient Index Data 3 (RAPID3 [0-30]) evaluates disease activity derived from patients' self-reported measures, including HAQ-DI or multidimensional HAQ, Pain visual analog scale

Figure 1. RAPID3 Scores (0–30) Through Week 52 by RAPID3 Category at Week 52 in cDMARD-Naive Patients Randomized to Apremilast (N = 139)



Includes patients randomized at baseline who had RAPID3 components available at Week 52; data are as observed. RAPID3 near REM: ≤3; low severity: >3 to ≤6; moderate severity: >6 to ≤12; and high severity: >12 to ≤30. Error bars represent standard error of the mean.

Figure 2. cDAPSA Scores (0–154) Through Week 52 by cDAPSA Category at Week 52 in cDMARD-Naive Patients Randomized to Apremilast (N = 138)



Includes patients randomized at baseline who had cDAPSA components available at Week 52; data are as observed. REM: cDAPSA ≤4; low: cDAPSA >4 to ≤13; moderate: cDAPSA >13 to ≤27; high: cDAPSA >27. Error bars represent standard error of the mean.

Articular and Extra-articular Disease Activity in Patients Achieving RAPID3 and cDAPSA Treatment Targets at Week 52

Mean	RAPID3 Analysis*				cDAPSA Analysis†			
	Patients With Near REM at Week 52 n = 19		Patients With Low Severity at Week 52 n = 19		Patients With REM at Week 52 n = 17		Patients With LDA at Week 52 n = 45	
	Baseline	Week 52	Baseline	Week 52	Baseline	Week 52	Baseline	Week 52
SJC (0-66)	6.8	0.2	9.1	1.7	6.3	0.1	6.9	0.4
TJC (0-68)	12.7	1.5	18.1	6.1	10.3	0.6	13.6	2.7
PAP (VAS 0-100 mm)	42.4	4.4	52.5	15.1	42.3	3.7	51.1	26.9
PtGA (VAS 0-100 mm)	52.8	7.7	45.6	18.5	52.5	7.9	50.0	28.0
PhGA (VAS 0-100 mm)	45.2	4.6	54.3	18.0	44.4	3.6	47.6	12.2
PASI‡ (0-72)	8.3	3.7	5.2	1.9	6.6	2.4	6.4	3.2
MASES§ (0-13)	4.1	0.4	3.2	1.9	3.4	0.2	3.6	0.9
Dactylitis count¶ (0-20)	4.3	0.2	3.3	0.7	2.8	0.0	2.6	0.1
HAQ-DI (0-3)	0.9	0.0	0.9	0.4	1.0	0.1	1.0	0.6

*Includes patients randomized at baseline who had RAPID3 components available at Week 52. RAPID3 near REM: ≤3; RAPID3 low severity: >3 to ≤6. †Includes patients randomized at baseline who had cDAPSA components available at Week 52. REM: cDAPSA ≤4; low: cDAPSA >4 to ≤13. ‡Patients with baseline psoriasis body surface area involvement ≥3%. §Patients with pre-existing enthesitis at baseline. ¶Patients with pre-existing dactylitis at baseline. MASES = Maastricht Ankylosing Spondylitis Enthesitis Score; PAP = Patient's Assessment of Pain; PASI = Psoriasis Area and Severity Index; PhGA = Physician's Global Assessment of Disease Activity.

(VAS), and Patient's Assessment of Disease Activity (PtGA) VAS. The Clinical Disease Activity Index for Psoriatic Arthritis (cDAPSA [0-154]) includes objective and subjective physician assessments (ie, swollen and tender joints counts [SJC and TJC]) and the Patient's Assessment of Pain and PtGA VAS scores. Among patients receiving APR in the DMARD-naive PALACE 4 trial, we examined trajectories for improving RAPID3 scores for those achieving RAPID3 near remission (REM) or low severity, cDAPSA scores among those achieving cDAPSA REM or low disease activity (LDA), and PsA manifestations not measured by either outcome by Wk 52.

Methods: DMARD-naive patients in PALACE 4 who were randomized to receive APR 30 mg BID at baseline with available scores on RAPID3 and/or cDAPSA components at Wk 52 were included and grouped according to RAPID3 categories at Wk 52 using RA cutoffs (near REM: ≤3; low severity: >3-≤6; moderate severity: >6-≤12; and high severity: >12-30) and cDAPSA categories at Wk 52 (REM: ≤4; LDA: >4-≤13; moderate disease activity: >13-≤27; high disease activity: >27). Mean RAPID3 and cDAPSA scores were assessed from baseline through Wk 52. Other measures of PsA disease activity were reported longitudinally by RAPID3 and cDAPSA categories at Wk 52.

Results: The RAPID3 analysis included 139 APR patients; the cDAPSA analysis included 138 APR patients. Achievement of near REM or low severity (RAPID3) or REM or LDA (cDAPSA) by Wk 52 with APR were associated with improvements over time in mean RAPID3 (Figure 1) and cDAPSA (Figure 2) trajectories, with observable improvement at Wk 16. Patients achieving RAPID3 or cDAPSA treatment targets at Wk 52 had mild or resolved articular involvement at Wk 52. Achievement of treatment targets was also associated with improvements in extra-articular disease activity at Wk 52, although not all manifestations were as well controlled in patients achieving RAPID3 treatment targets (Table). In the RAPID3 and cDAPSA analyses, improvements in SJC and TJC were observed for patients with REM or low severity (RAPID3) or REM or LDA (cDAPSA) at Wk 52. In the RAPID3 analysis, mean TJC was higher than expected at Wk 52 in patients achieving low severity. The Psoriasis Area and Severity Index score was the only measure for which a pattern of greater improvement for the near RAPID3 REM/cDAPSA REM group vs the RAPID3 low severity/cDAPSA LDA group was not observed; it was numerically lower in cDAPSA REM vs LDA and numerically higher in RAPID3 REM vs low severity.

Conclusion: DMARD-naive patients achieving RAPID3 and cDAPSA targets with APR showed early and sustained improvements to Wk 52 with continued treatment. Achievement of treatment targets was associated with improvements in other domains not captured directly by RAPID3 or cDAPSA (eg, dactylitis, enthesitis). As shown in a prior analysis, RAPID3 LDA was associated with higher residual TJC than what would be expected from this categorization.

Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **A. Kavanaugh**, Eli Lilly and Company, 5; **A. Ogdie**, Lilly, 5, Amgen, 5, AbbVie, 5, BMS, 5, Celgene, 5, Janssen, 5, Norvatis, 2, 5, Pfizer, 2, 5, Takeda, 5; **A. Wells**, Abbvie, 1, 2, Eli Lilly & Co., 1, 2; **M. Bergman**, AbbVie, 5, 8, Amgen, 5, 8, Bristol-Myers Squibb, 5, 8, Genentech/Roche, 5, 8, Gilead, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Regeneron, 5, 8, Sanofi, 5, 8, Sandoz, 5, 8, JNJ (parent of Janssen), 1; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **S. Richter**, Amgen Inc., 1; **M. Brunori**, Amgen Europe GmbH, 1; **L. Teng**, Amgen Inc., 1; **B. Guerette**, Amgen Inc., 1; **J. Smolen**, AbbVie, 2, 5, 8, AstraZeneca, 2, 5, 8, Eli Lilly, 2, 5, 8, Celgene, 5, 8, Celltrion, 5, 8, Chugai, 5, 8, Gilead, 5, 8, ILTOO, 5, 8, Janssen, 5, 8, Kabi, 5, 8, Novartis-Sandoz, 5, 8, Pfizer Inc, 5, 8, Samsung, 5, 8, Sanofi, 5, 8.

Abstract Number: 0380

Efficacy and Safety of Ixekizumab in Patients with Psoriatic Arthritis and Inadequate Response to TNF Inhibitors: 3 Year Results from a Phase 3 Study

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Ixekizumab (IXE) is a high affinity monoclonal antibody that selectively targets interleukin-17A. In the SPIRIT-P2 study, IXE every 4 (Q4W) or 2 (Q2W) weeks was superior to placebo (PBO) in improving the signs and symptoms of psoriatic arthritis (PsA) at Week 24 in patients (pts) with prior inadequate response or intolerance to 1 or 2 tumor necrosis factor inhibitors (TNFi). The objective of this study was to determine efficacy and safety of IXE treatment up to 3 years in pts with PsA.

Methods: In SPIRIT-P2 (NCT02349295), 310 pts entered the extension period where pts maintained their original ixekizumab dose, and placebo pts received IXEQ4W or IXEQ2W (1:1). Pts failing to demonstrate ≥20% improvement in both tender and swollen joint counts at Week 32, or any subsequent visit, were discontinued (mandatory discontinuation criteria). Efficacy outcomes were ACR20/50/70 response, Psoriasis Area and Severity Index (PASI) 75/90/100 response, Leeds Enthesitis Index (LEI), Leeds Dactylitis Index-Basic (LDI-B), minimal disease activity (MDA), and Disease Activity in Psoriatic Arthritis (DAPSA). Ad-hoc efficacy data are presented for intent-to-treat (ITT) pts initially randomized to IXE at Week 0. Observed and modified non-responder imputation (mNRI; missing data treated as non-response for pts discontinued due to lack of efficacy or adverse events [AEs]) was applied to categorical

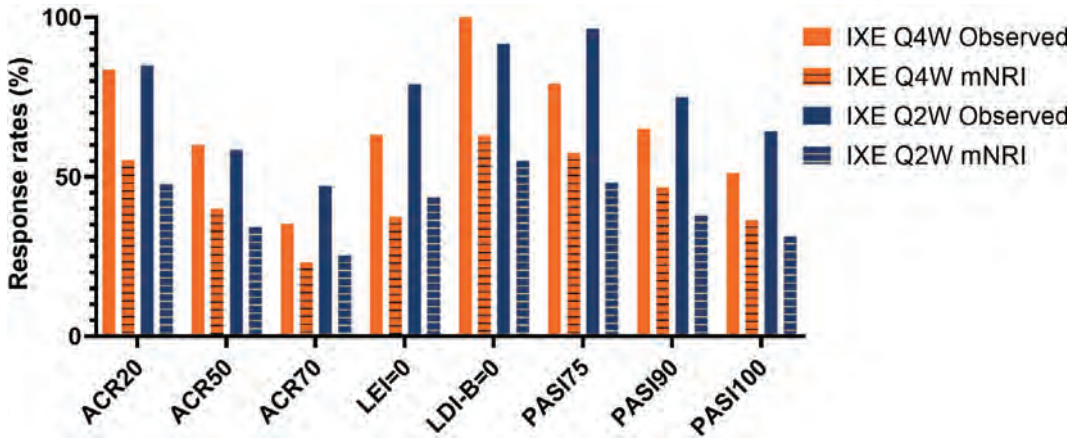

Figure 1. Efficacy Outcome Measures at Week 156 (Intent-to-treat Population). ACR=American College of Rheumatology; IXE=ixekizumab; LEI=Leeds Enthesitis Index; LDI-B=Leeds Dactylitis Index-Basic; mNRI=modified non-responder imputation; PASI=Psoriasis Area and Severity Index; Q2W=every two weeks; Q4W=every four weeks.

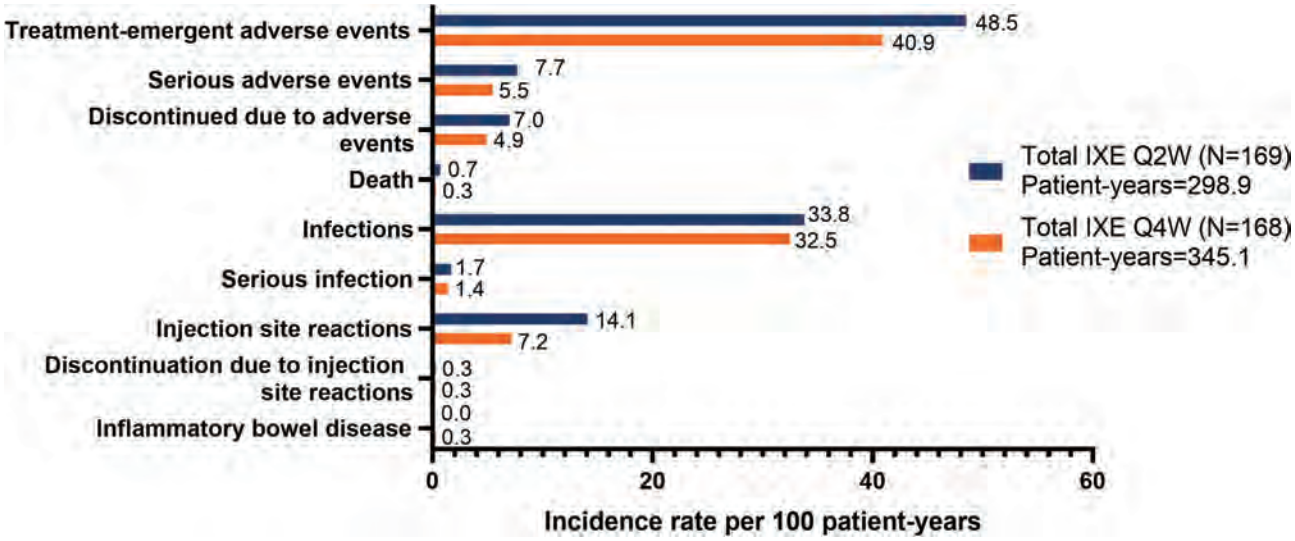

Figure 2. Safety Outcome Measures (Weeks 0-156). Safety was analyzed in patients exposed to at least one dose of ixekizumab. During the double-blind treatment period (Weeks 0-24), one patient reported serious adverse events of anal fistula and anal abscess, which were considered by the sponsor to be inflammatory bowel disease (IBD); however, an independent adjudication committee of external experts reviewed the case and determined the events to be "Not IBD." IXE=ixekizumab; Q2W=every two weeks; Q4W=every four weeks.

measures. Observed and modified baseline observation carried forward (mBOCF) was applied to continuous efficacy measures. Safety was analysed in pts exposed to at least one dose of IXE.

Results: Of the 245 pts initially randomized to IXE at Week 0 (ITT), 64 (26.1%) pts discontinued due to lack of efficacy and 22 (9.0%) pts due to mandatory discontinuation criteria. Efficacy results are summarized below (Figure 1). Pts in SPIRIT-P2 who received IXEQ4W and IXEQ2W for 156 weeks reported sustained improvement in ACR responses and manifestations of PsA, including enthesitis, dactylitis, and skin outcomes. Treat-to-target measures such as MDA and DAPSA (Low Disease Activity or Remission) were achieved by 30.8% and 47.7% of pts, respectively on IXEQ4W, and by 29.2% and 40.7% of pts, respectively on IXEQ2W. Incidence rates (IR) of treatment-emergent adverse events (TEAEs) are provided below (Figure 2). Most TEAEs were mild or moderate in severity, and 38 out of 337 (5.9%) pts (safety population) discontinued due to AEs. The most common TEAEs were infections (IR=33.1) and injection site reactions (IR=5.4). Three deaths were reported in the study.

Conclusion: In pts treated with IXE who had prior inadequate response or intolerance to 1 or 2 TNFi, improvements in the signs and symptoms of PsA persisted up to 3 years. No unexpected safety signals were observed, and the safety profile was consistent with previous studies of IXE.

Disclosure: J. Gratacós, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, 8, MSD, 5, 8, UCB, 5, 8, Novartis, 5, 8, Janssen Pharmaceutical, 5, 8, Amgen, 5, 8, BMS, 2, 5, 8, Celgene, 2, 5, 8; **A. Turkiewicz**, Novartis, 2, 8, Eli Lilly, 2, 8, Pfizer, 2, 8, UCB, 2, 8, AbbVie Inc., 2, 8, Sanofi-Genzyme, 2, 8; **E. Dokoupilova**, Eli Lilly and Company, 2, AbbVie Inc., 2, GSK, 2, Novartis, 2, Pfizer Inc., 2, UCB, 2, Sanofi-aventis, 2, Hexal AG, 2; **A. Gellett**, Eli Lilly and Company, 1, 3; **A. Sprabery**, Eli Lilly and Company, 1, 3, Johnson and Johnson, 1; **V. Geneus**, Eli Lilly and Company, 3, 4; **A. Constantin**, AbbVie Inc., 5, 8, Amgen, 5, 8, Celltrion, 5, Gilead, 5, 8, Eli Lilly and Company, 5, 8, Novartis, 5, 8, Pfizer Inc., 5, 8, UCB, 5, 8, Janssen, 8.

Abstract Number: 0381

Efficacy of Tofacitinib on Dactylitis in Individual Digits in Patients with Active Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Dactylitis, a hallmark of psoriatic arthritis (PsA), is a uniformly diffuse and sometimes painful swelling of the fingers and/or toes.[1] Up to 50% of patients (pts) with PsA may experience dactylitis;[1,2] as such, dactylitis is an accepted domain of PsA that should be considered in treatment decisions.[3] In PsA, dactylitis typically involves feet more than hands; dactylitic joints more frequently have erosive damage, compared with non-dactylitic joints.[2] There remains a need for effective therapies to treat dactylitis in pts with PsA. Improvements in dactylitis have been associated with tofacitinib, an oral Janus kinase inhibitor for the treatment of PsA.[4,5] Here, we assessed the effect of tofacitinib on dactylitis by location (hands/feet) and individual digit involvement in pts with PsA.

Methods: These post hoc analyses used data pooled from two Phase 3 studies (12-month OPAL Broaden [NCT01877668];[5] 6-month OPAL Beyond [NCT01882439][4]) in pts with active PsA treated with tofacitinib 5 mg twice daily (BID; approved dose; to Month [M]6), tofacitinib 10 mg BID (to M6), or placebo (PBO; to M3); pts were treated continuously with a single conventional synthetic DMARD. Pts were categorized by the presence of dactylitis at baseline (BL) in the hands and/or feet. Endpoints included change from BL (CFB) in Dactylitis Severity Score (DSS),[6] the number of dactylitic digits, and the proportion of pts with dactylitis in individual digits at M1, M3, and M6. Descriptive statistics were generated by visit and treatment arm.

Results: Data were pooled from 373 pts with DSS > 0 at BL. BL characteristics were similar across dactylitis groups, except pts with dactylitis in both hands and feet had higher DSS at BL, compared to those with dactylitis in hands only or feet only, likely due to having more dactylitic digits (Table). Regardless of location, pts treated with tofacitinib

had cumulative improvements from BL to M6 in DSS (Figure 1a) and in the number of dactylitic digits (Figure 1b); improvements were greater at M1 and M3, compared with PBO. Pts treated with tofacitinib 10 mg BID typically had numerically greater improvements in DSS, compared with pts treated with tofacitinib 5 mg BID (Figure 1a). Most pts treated with tofacitinib experienced improvement of dactylitis across all fingers and toes (Figure 2); mean dactylitis presence was ≤ 15% at M6 in pts treated with tofacitinib for all digits. Generally, at M1 and M3, fewer pts treated with tofacitinib had dactylitis in any digit, compared with PBO (Figure 2).

Conclusion: Among pts with pre-existing dactylitis, treatment with tofacitinib resulted in improvements in dactylitis in hands, feet, or both, and in all digits as early as M1, and up to M6.

Table. Baseline demographics and disease characteristics in patients with DSS >0, treated with tofacitinib 5 mg BID (green), tofactinib 10 mg BID (blue), and placebo (purple), stratified by BL location of dactylitis (pooled from OPAL Broaden and OPAL Beyond).

	Hands	Feet	Hands and Feet	Hands or Feet
	(N=84)	(N=97)	(N=54)	(N=127)
	(N=87)	(N=91)	(N=53)	(N=125)
	(N=80)	(N=87)	(N=46)	(N=121)
Female, n (%)	40 (47.6)	40 (41.2)	23 (42.6)	57 (44.9)
	45 (51.7)	49 (53.8)	29 (54.7)	65 (52.0)
	38 (47.5)	41 (47.1)	16 (34.8)	63 (52.1)
Age, years, mean (SD)	50.3 (12.0)	47.6 (12.5)	48.8 (12.4)	48.9 (12.3)
	48.8 (11.5)	47.9 (12.0)	48.1 (11.3)	48.5 (12.0)
	48.1 (13.8)	48.2 (12.7)	47.0 (14.5)	48.6 (12.7)
Race, n (%)				
White	80 (95.2)	90 (92.8)	51 (94.4)	119 (93.7)
	80 (92.0)	80 (87.9)	49 (92.5)	111 (88.8)
	77 (96.3)	83 (95.4)	45 (97.8)	115 (95.0)
Other	4 (4.8)	7 (7.2)	3 (5.6)	8 (6.3)
	7 (8.0)	11 (12.1)	4 (7.5)	14 (11.2)
	3 (3.8)	4 (4.6)	1 (2.2)	6 (5.0)
BMI, kg/m², mean (SD)	29.8 (6.8)	29.7 (6.2)	29.2 (6.4)	30.0 (6.5)
	29.9 (6.5)	30.1 (6.7)	29.6 (6.9)	30.2 (6.5)
	29.5 (5.9)	29.5 (5.4)	29.9 (5.4)	29.3 (5.7)
PsA duration, years, mean (SD)	9.3 (9.3)	7.7 (6.8)	8.2 (8.0)	8.5 (8.2)
	7.8 (6.2)	8.1 (7.0)	8.1 (6.7)	7.9 (6.5)
	7.8 (6.9)	8.2 (8.8)	7.3 (7.4)	8.3 (8.1)
Baseline DSS,[a] mean (SD)	10.8 (10.2)	9.4 (9.7)	14.0 (10.9)	8.4 (9.0)
	10.9 (8.8)	10.1 (8.9)	13.9 (9.3)	9.0 (8.2)
	10.6 (7.8)	9.4 (7.9)	14.3 (7.6)	8.3 (7.3)
Dactylitic digits count,[b] mean (SD)	3.2 (2.4)	3.1 (2.7)	7.4 (5.5)	4.5 (4.5)
	3.6 (2.9)	3.3 (2.6)	7.3 (5.1)	4.9 (4.4)
	3.6 (2.4)	3.0 (2.2)	7.6 (3.9)	4.5 (3.7)

[a]A blinded assessor squeezed each digit of the hands and feet with moderate pressure, and assigned a score for each digit on a scale of 0–3, where 0 = no tenderness, 1 = tender, 2 = tender and winces, and 3 = tender and withdraws. DSS is calculated as the sum of those scores, ranging from 0–60, with a score of 60 being the highest dactylitis severity[6]

[b]Dactylitis was defined as swelling of an entire digit

BID, twice daily; BL, baseline; BMI, body mass index; DSS, Dactylitis Severity Score; N, total number of patients with dactylitis in that particular location at BL; n, number of patients applicable for each category; PsA, psoriatic arthritis; SD, standard deviation

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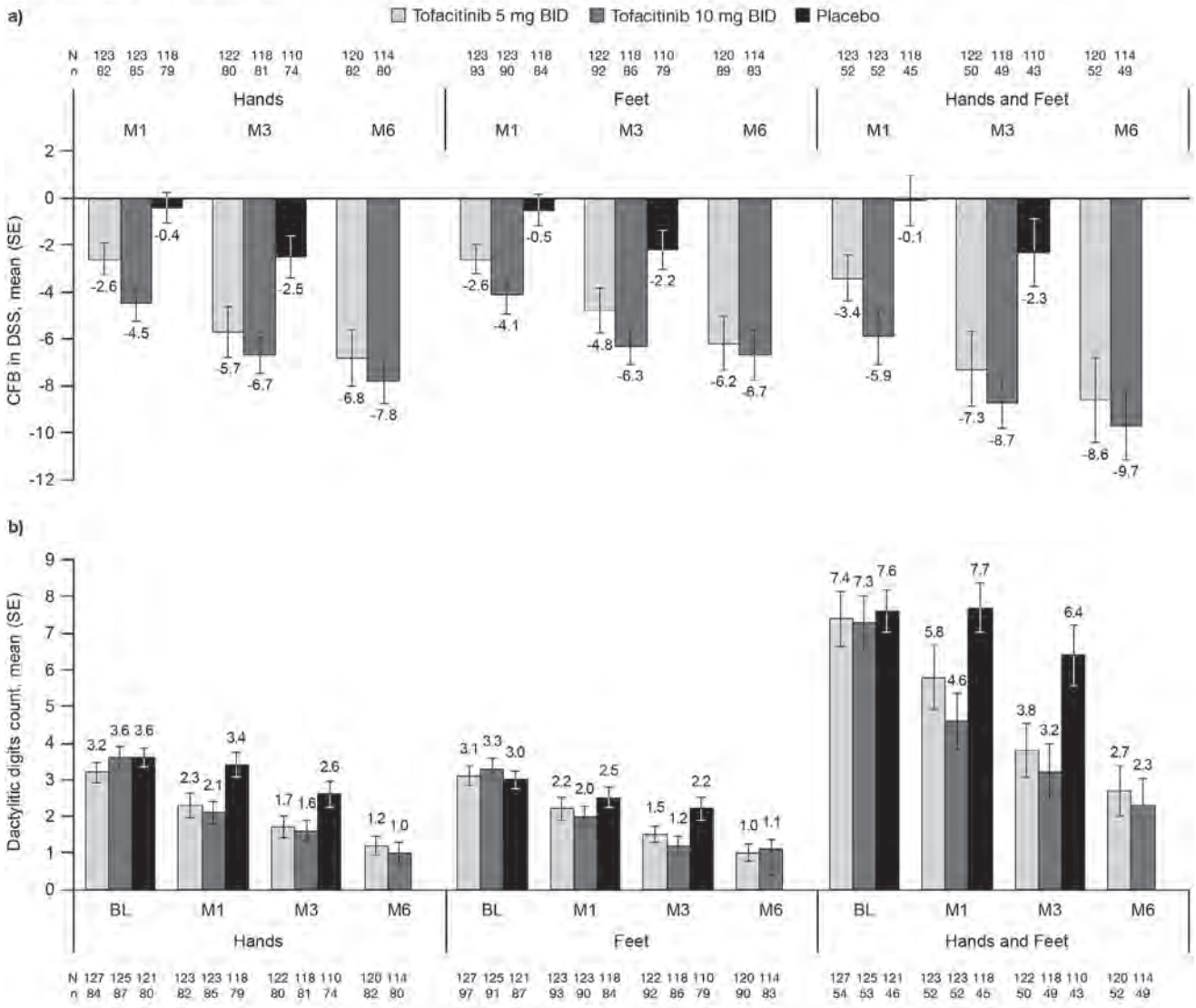
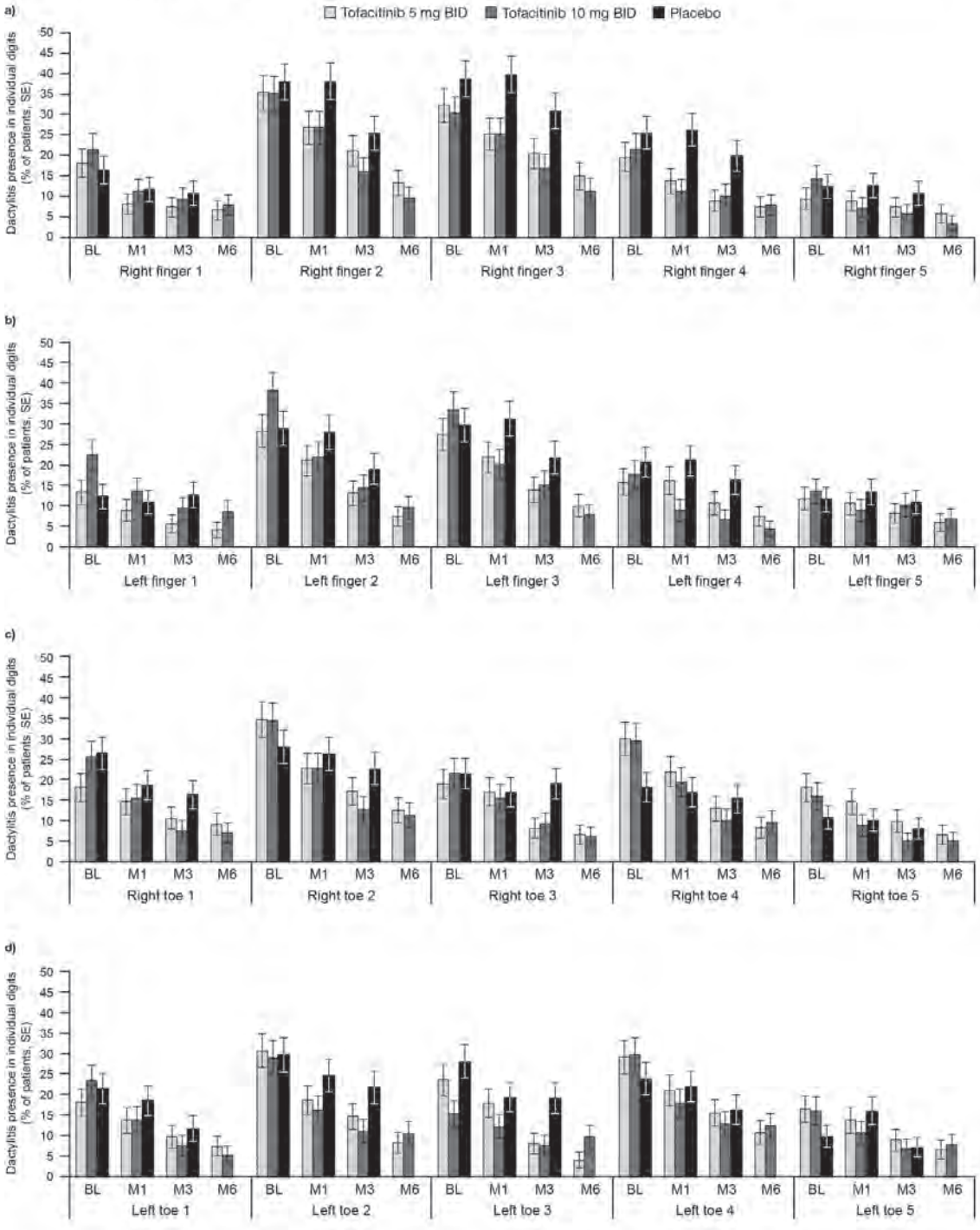
Figure 1. a) Change from baseline in DSS[a] and b) dactylitic digits count[b] in patients with DSS >0 at BL, stratified by location of dactylitis (pooled from OPAL Broaden and OPAL Beyond)



[a]A blinded assessor squeezed each digit of the hands and feet with moderate pressure, and assigned a score for each digit on a scale of 0–3, where 0 = no tenderness, 1 = tender, 2 = tender and winces, and 3 = tender and withdraws. DSS is calculated as the sum of those scores, ranging from 0–60, with a score of 60 being the highest dactylitis severity[6]
[b]Dactylitis was defined as swelling of an entire digit
BID, twice daily; BL, baseline; CFB, change from baseline; DSS, Dactylitis Severity Score; M, month; N, total number of patients with DSS >0 at BL; n, total number of patients with dactylitis in that particular location; SE, standard error

Figure 2. Proportion of patients with dactylitis[a] in patients with DSS[b] >0 at BL, stratified by a) right hand fingers, b) left hand fingers, c) right foot toes, and d) left foot toes (pooled from OPAL Broaden and OPAL Beyond)



N ranged from 121–127 at BL, 118–123 at M1, 110–122 at M3, and 113–120 at M6 for all digits
[a]Dactylitis was defined as swelling of an entire digit
[b]A blinded assessor squeezed each digit of the hands and feet with moderate pressure, and assigned a score for each digit on a scale of 0–3, where 0 = no tenderness, 1 = tender, 2 = tender and winces, and 3 = tender and withdraws. DSS is calculated as the sum of those scores, ranging from 0–60, with a score of 60 being the highest dactylitis severity[6]
BID, twice daily; BL, baseline; DSS, Dactylitis Severity Score; M, month; N, total number of patients with DSS >0 at BL; SE, standard error

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Abstract Number: 0382

Increased Rates of Obstetric Complications Prior to Systemic Sclerosis Diagnosis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Table 1 Baseline characteristics of cases and controls.

Table 1. Baseline characteristics of cases and controls.

Characteristic	Cases (N=17), %	Controls (N=170), %	P value
Maternal age at delivery			
20-29 years	5 (29.4)	45 (26.5)	0.99
30-39 years	10 (58.9)	97 (57.1)	
40-49 years	2 (11.8)	20 (11.8)	
Race			
Non-Hispanic White	3 (17.6)	86 (50.6)	0.001
Asian	4 (23.5)	48 (28.2)	
Hispanic	7 (41.1)	32 (18.8)	
Black	2 (11.8)	4 (2.4)	
Other	1 (5.9)	0	
Ever smoker	5 (29.4)	37 (21.78)	0.54
BMI at delivery (kg/m^2)	28.3±6.9	28.2±6.1	0.94
History of essential hypertension	0	10 (5.9)	0.60
Gravidity			
Primigravida	5 (29.4)	28 (16.5)	0.18
Multigravida	12 (70.6)	142 (83.5)	
Parity			
Nulliparous	7 (41.2)	49 (28.8)	0.52
Primiparous	7 (41.2)	75 (44.1)	
Multiparous	3 (17.5)	46 (27.1)	

Table 2. Conditional logistic regression analysis comparing SSc cases with controls matched on maternal age and year of delivery.

Table 2. Conditional logistic regression analysis comparing SSc cases with controls matched on maternal age and year of delivery.

Variable	Cases (N=17), %	Controls (N=170), %	OR (95% CI)
Hypertensive disorder of pregnancy	13 (17.7)	16 (9.4)	2.1 (0.5-8.4)
Premature rupture of membranes	2 (11.8)	7 (4.1)	3.6 (0.6-22.9)
Intrauterine growth restriction	1 (5.9)	3 (1.8)	3.3 (0.4-32.0)
Maternal infection	5 (29.4)	24 (14.2)	2.5 (0.8-7.6)
Neonatal intensive care unit admission	4 (23.5)	13 (7.7)	4.7 (1.2-18.8)
Preterm birth<37 weeks	2 (11.8)	17 (10.0)	1.2 (0.3-5.8)
Mode of delivery: assisted vaginal delivery or C-section*	9 (52.9)	59 (34.7)	2.3 (0.8-6.4)

*Compared to normal spontaneous vaginal deliveries.

Background/Purpose: Vasculopathy and immune dysfunction likely precede the diagnosis of systemic sclerosis (SSc) by years as evidenced by longstanding Raynaud's phenomenon prior to diagnosis. Poor obstetric outcomes may also reflect underlying vascular and immune system abnormalities in patients who later develop SSc. We investigated whether obstetric complications prior to SSc diagnosis are more common compared to the general obstetric population.

Methods: A retrospective case-control study was conducted among Kaiser Permanente Northern California (KPNC) pregnant women with subsequent SSc diagnosis (2013 ACR-EULAR classification criteria confirmed by chart review) from 2007-2016. Controls from the general obstetric population were matched 10:1 by maternal age and year of delivery. Exposures of interest included hypertensive disorders of pregnancy (including pre-eclampsia, eclampsia, and gestational hypertension), premature rupture of membranes (PROM), intrauterine growth restriction (IUGR), maternal infections, neonatal intensive care unit (NICU) admission, and preterm birth. Fischer's exact tests were used to compare categorical variables. Conditional logistic regression models estimated the odds ratio (OR) and corresponding 95% confidence intervals for the outcome SSc.

Results: Median maternal age at delivery was 34 years (range 23-46 years) for 17 SSc cases and 170 matched controls (Table 1). Median time from delivery to SSc diagnosis was 2 years (range 0.2-7.3 years), with 13/17 developing limited cutaneous disease. Compared to controls, SSc cases were more likely to be Hispanic and Black. Obstetric complications were non-significantly higher in women with an eventual SSc diagnosis compared to controls, including hypertensive disorders (17.7% vs. 9.4%), PROM (11.8% vs. 4.1%), IUGR (5.9% vs 1.8%), maternal infection (29.4% vs. 14.1%), NICU admissions (23.5% vs. 7.7%), and preterm birth (29.4% vs. 21.8%). Women with a subsequent diagnosis of SSc were found to have twice the odds of having hypertensive disorders of pregnancy compared with controls, but the results were not statistically significant). Cases had a significantly higher odds of delivering infants requiring NICU admission (Table 2).

Conclusion: Women who eventually develop SSc appeared to have more pregnancy complications, particularly NICU admissions, before overt diagnosis. Larger studies are needed to validate these findings.

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Abstract Number: 0383

Sex Differences in Severity and Progression of Interstitial Lung Disease in Systemic Sclerosis: What We Have Learned from Clinical Trials

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SESSION INFORMATION

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Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Although systemic sclerosis (SSc) disproportionately affects females compared with males [1], observational studies have demonstrated higher mortality rates in males with SSc [2]. This may be due to a higher prevalence of interstitial lung disease (ILD) in males [2], or external factors, such as delayed SSc diagnosis in males. The objective of this study was to compare short- and long-term outcomes of male and female participants of two RCTs for SSc: Scleroderma Lung Studies (SLS) I [3] and II [4].

Methods: SLS I randomized 158 SSc participants (47 Males) with ILD to 1 year of oral cyclophosphamide (CYC) versus placebo, followed by 1 year off treatment. SLS II randomized 142 SSc-ILD participants (37 Males) to 1 year of oral CYC, followed by 1 year of placebo, versus 2 years of mycophenolate (MMF). Both studies measured the FVC every 3 months during the study and performed HRCT scans at baseline and 12 (SLS I) and 24 (SLS II) months. Up to 12 (SLS I) and 8 (SLS II) years after randomization, we assessed morbidity and mortality outcomes. Joint models evaluated progression of ILD based on the course of the FVC and linear regression models evaluated radiographic changes in ILD. We compared survival using a log-rank test and used Cox proportional hazard modeling to determine the variables associated with survival.

Results: Baseline demographic and disease characteristics were similar for males and females of SLS I and II, with the exception of a higher prevalence of Caucasians in SLS I males (79% versus 58%, respectively). Additionally, males demonstrated more restrictive physiology in SLS I (lower FVC, TLC, DLCO) and II (lower DLCO) compared

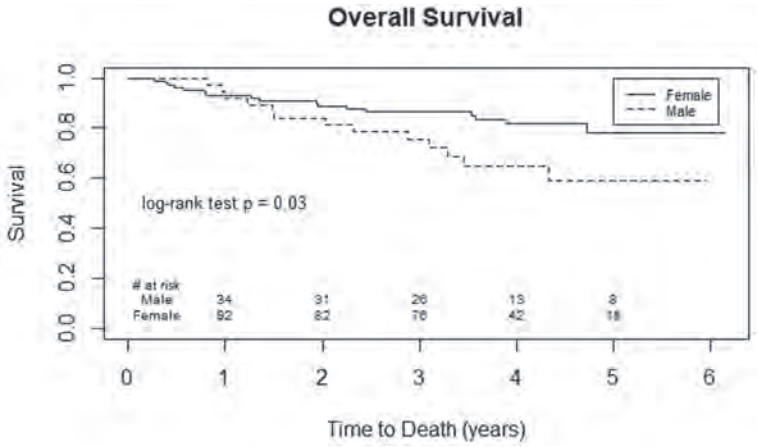

Figure 1. Time to death in males (dotted line) versus females (solid line) in SLS I.

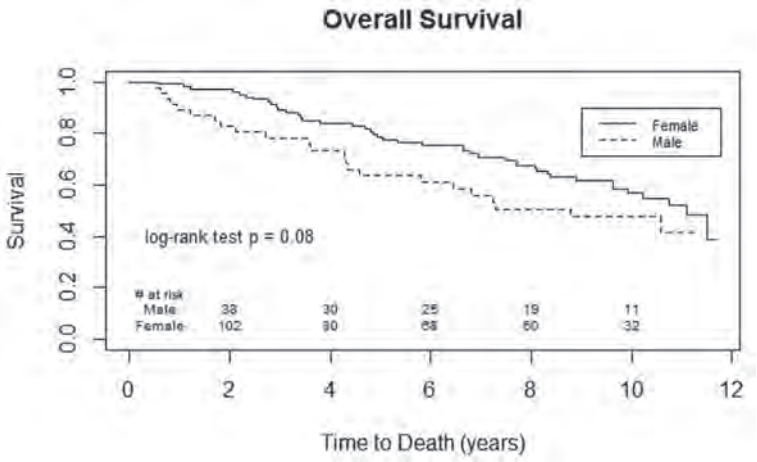

Figure 2. Time to death in males (dotted line) versus females (solid line) in SLS II.

with females. In the placebo arm of SLS I, there was a trend for increased worsening of the FVC in males compared with females from 3 to 12 months (P=0.14). In the CYC arm of SLS I, there was no difference in the course of the FVC from 3 to 12 months (P=0.84). In the CYC arm of SLS II, males experienced a decline in the FVC from 3 to 12 months, whereas females experienced an improvement (P=0.0006). In the MMF arm of SLS II, males experienced less of an improvement in the FVC from 3 to 12 months compared with females (P=0.005). In SLS II (but not SLS I), males had increased radiographic progression of ILD based on quantitative imaging analysis, even after adjusting for treatment arm. Long-term survival was worse in males compared with females in both SLS I and II (Log Rank Test: P=0.08, P=0.03, respectively). After adjustment for baseline disease severity (FVC, skin score) and age, male sex was independently associated with increased mortality compared with females in SLS II (HR 2.42; P=0.01), but not SLS I (HR 1.14; P=0.63).

Conclusion: Data from two large RCTs in SSc-ILD demonstrated that males with SSc-ILD had evidence of increased ILD severity at baseline. Males also appeared to have increased progression of ILD both with and without treatment, as well as worse long-term survival. These findings are consistent with prior observational studies, and future studies are needed to understand the genetic and hormonal underpinnings for these important sex differences.

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Abstract Number: 0384

Serum Neutrophil Count Predicts Progression of Interstitial Lung Disease and Mortality in Patients with Systemic Sclerosis Related Interstitial Lung Disease

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) patients have a prominent neutrophil gene expression signature. However, investigations into the pathophysiologic role of neutrophils in SSc are lacking. This is predominantly due to their limited survivability *in vitro* and the significantly lower proportion of neutrophils in rodent serum compared to humans. These limitations highlight the need to directly study the role of neutrophils in SSc using human specimens. In this study, we examined the prognostic significance of neutrophil count in the Scleroderma Lung Study (SLS) II.

Methods: Neutrophil counts were prospectively obtained at the baseline visit of SLS II. All subjects had clinically significant SSc related interstitial lung disease (ILD) and had a disease duration less than 7 years. Baseline neutrophil count was log-transformed with a base of 2 in all analyses. A joint model combining mixed effects and survival models was used to examine the relationship between baseline blood neutrophil count and serially obtained % predicted forced vital capacity (FVC%) as well as modified Rodnan skin scores (mRSS) from 3-12 month visits after adjustment

Table 1. Baseline neutrophil count as a predictor of worsening SSc-ILD in SLS II

	β (95% CI)	P-value
Baseline neutrophil count*	-1.11 (-1.15, -1.08)	0.030
Baseline FVC%	0.90 (0.90, 0.90)	<0.001
Time variable	0.07 (0.07, 0.08)	0.004
Treatment arm #	0.88 (0.83, 0.93)	0.185

* Neutrophil count was log-transformed using a base of 2.

Mycophenolate compared to cyclophosphamide treatment groups

Table 2. Mortality risk in SLS II patients as a function of baseline neutrophil count

	Hazard Ratio	95% CI	P-value
Baseline neutrophil count*	2.02	1.02, 4.01	0.045
Age at enrollment	1.09	1.05, 1.14	<0.001
Treatment arm #	0.73	0.34, 1.55	0.415

* Neutrophil count was log-transformed using a base of 2. This indicates that the risk of mortality increases 102% with doubling of the baseline neutrophil count.

Mycophenolate compared to cyclophosphamide treatment groups

for baseline disease severity and treatment arm. Cox proportional hazards models were created to evaluate the association between neutrophil count and long-term mortality.

Results: Of the 142 patients enrolled in SLS II, 134 (94.3%) had an available baseline neutrophil count. The majority of patients had diffuse cutaneous disease (59%) and mean disease duration was 2.6 years (±1.7). Higher neutrophil count predicted worsening of SSc-ILD based on the course of the FVC% from 3-12 months (p=0.030 – Table 1). Neutrophil count did not predict changes in mRSS. Baseline neutrophil count predicted an increased risk of mortality after adjustment for age (HR=2.02, 95% CI [1.02, 4.01], p=0.045-Table 2). The median follow-up time was 3.4 years with IQR (2.9, 4.6) for the mortality analysis. Both findings were independent of treatment arm.

Conclusion: Higher neutrophil count predicted worse ILD course and higher long-term mortality in patients with SSc-ILD. Our findings were independent of treatment with cyclophosphamide or mycophenolate. Neutrophils, largely under-investigated in SSc, might play a role in pathogenesis of SSc and warrant further mechanistic studies. Furthermore, baseline neutrophil counts may serve as a useful prognostic marker of disease progression.

Disclosure: N. Wareing, None; **N. Li**, None; **E. Volkmann**, Boehringer Ingelheim, 2, 5, Forbius, 2, 5, Corbus, 2; **M. Lyons**, None; **M. Roth**, Genentech/Roche, 1; **D. Tashkin**, None; **S. Assassi**, Momenta, 1, corbus, 1, Integrity Continuing Education, 1, Boehringer Ingelheim, 1, 2, 3.

Abstract Number: 0385

A Pilot Study to Evaluate the Safety and Efficacy of Treprostinil in the Treatment of Calcinosis in Patients with Systemic Sclerosis

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SESSION INFORMATION
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Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Calcinosis is characterized by calcium deposition in skin and subcutaneous tissues and progresses over one year in the majority of systemic sclerosis (SSc) patients. Since vascular hypoxia may contribute to calcinosis pathophysiology, we evaluated the safety and efficacy of oral treprostinil in preventing progression of SSc-associated calcinosis.

Methods: We performed a prospective, open-label, single-institution study in 12 SSc patients meeting 2013 ACR/EULAR classification criteria with confirmed radiological and physical examination evidence of ≥1 subcutaneous calcium deposit in the hands (ClinicalTrials.gov Identifier: NCT02663895). Patients received oral treprostinil for 1 year with evaluations every 3 months. Primary endpoints were safety/tolerability and percentage of patients without radiographic progression of calcinosis at 1 year assessed by the Scleroderma Clinical Trials Consortium radiographic score. Progression of calcinosis was defined as >25% increase in score, improvement as >25% decrease, and stabilization as values in-between. Radiographs were scored by a radiologist blinded to treatment history and sequence of images. Secondary endpoints included 1-year changes in the Scleroderma HAQ (SHAQ), Cochin Hand Functional Scale, SF-36, Raynaud Condition Score, and patient and physician assessment of calcinosis severity. Endpoints were assessed using Wilcoxan signed rank test.

Table 1. Baseline Patient Demographics

Table 1. Baseline Patient Characteristics	
	(n = 12)
Age, mean (range)	55 (35-68)
Female, n (%)	12 (100)
Race, n (%)	
Caucasian	9 (75)
Hispanic	2 (16.7)
Black	1 (8.3)
Diffuse disease, n (%)	6 (50)
Years from 1st symptom, median (range)	
Raynaud's phenomenon	15.1 (4.8-32.9)
Non-Raynaud's phenomenon	12.3 (5.6-20.5)
Ever smoker	4 (33.3)
Autoantibodies, n (%)	
Anticentromere	6 (50)
Anti-Scl-70	1 (8.3)
Anti-RNA-polymerase III	3 (25)
Anti-PM-Scl	1 (8.3)
Anti-Nuclear antibody	9 (75)
Antiphospholipid antibodies	2 (16.7)
Disease features, current or prior, n (%)	
Digital Ulcers	9 (75)
Gangrene	1 (8.3)
Gastrointestinal involvement	12 (100)
Gastroesophageal reflux disease	12 (100)
Esophageal/small bowel dysmotility	3 (25)
Malabsorption syndrome	1 (8.3)
Gastric antral vascular ectasia	1 (8.3)
Small intestinal bacterial overgrowth	0
Parenteral nutrition	0
Interstitial lung disease	6 (50)
Arthritis	6 (50)
Myositis	3 (25)
Scleroderma renal crisis	0
Osteopenia*	5 (42)
Osteoporosis*	4 (33)
Current therapy for Raynaud's, n (%)	
Calcium channel blocker	5 (41.7)
Aspirin	3 (25)
SSRI/SNRI	2 (16.7)
ACE inhibitor	1 (8.3)

SD = standard deviation; anti-Scl-70 = anti-topoisomerase antibody; anti-PM-Scl = anti-polymyositis-scleroderma antibody; SSRI/SNRI=selective serotonin reuptake inhibitor/selective norepinephrine reuptake inhibitor; ACE = angiotensin converting enzyme; *at time of study enrollment. Patients with pulmonary arterial hypertension excluded from trial.

Results: Twelve female patients were enrolled (half had diffuse cutaneous SSc disease), with mean age 55 years (range 35-68 years) **(Table 1)**. Five patients completed the study, tolerating up to a median dosage of 1mg TID (range 0.25-7.625 mg TID). Seven patients withdrew from the trial at a median dosage of 1.3mg TID (range 0-5mg TID) at

Table 2: Adverse events with treprostinil in SSc patients (n=12)

Table 2. Adverse events with treprostinil in SSc patients (n=12)	
Event	No. of Patients (%)
Headache	8 (67)
Abdominal pain	6 (50)
Diarrhea	5 (42)
Nausea	3 (25)
Flushing	2 (16)
Jaw pain	2 (16)
Dizziness	2 (16)
Hypotension	1 (8)
Epistaxis	1 (8)
Weight loss	1 (8)

a median follow-up of 5 months (range 0.25-10 months) due to the following: intolerable side effects (n=3, diarrhea, headaches), withdrawn by investigator for intercurrent illness unrelated to drug (n=2, cirrhosis, cancer), progressive SSc (n=1), and personal reasons (n=1). Most patients developed headaches and gastrointestinal side effects, consistent with the known side effect profile of treprostinil **(Table 2).** No serious adverse events occurred. Four of the 12 (33%) patients experienced progression of calcinosis at 1 year. Of the 5 patients who completed 12 months of treatment, 4 had stability and 1 had progression of calcinosis (1-year median % score change: 22.2%, range: 5.3-85.5%, p=0.06). Of the 6 patients who withdrew but had 1-year follow-up radiographs, 3 had stability/improvement of calcinosis while 3 progressed (1-year median % score change: 38.4%, range: -38.9%-111%, p=0.16). Including all 12 enrolled patients, worsening of the SHAQ-VAS-GI score was observed (median change/month: 0.03, range 0-0.25, p=0.016); there were no significant changes in other secondary endpoints.

Conclusion: Oral treprostinil was poorly tolerated in SSc patients with calcinosis, with most patients developing headaches and gastrointestinal side effects. Of patients who were able to complete the treatment period, most (80%) had stability of calcinosis on hand radiographs at 1 year.

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Abstract Number: 0386

Phase 1 Clinical Study of MGTA-145 in Combination with Plerixafor Shows Rapid Single-Day Mobilization and Collection of CD34+ Hematopoietic Stem Cells Without G-CSF

John DiPersio[1], **Jonathan Hoggatt**[2], Steven Devine[3], David Scadden[2], Haley Howell[4], Veit Schmelmer[4], Glen Raffel[4], Pat Falahee[4], Kevin Goncalves[4], William Savage[4] and John Davis[4], [1]Washington University, Saint Louis, [2]Massachusetts General Hospital, Boston, [3]National Marrow Donor Program, Minneapolis, [4]Magenta Therapeutics, Cambridge

SESSION INFORMATION

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Background/Purpose: Autologous hematopoietic stem cell (HSC) transplantation is a recommended therapeutic option for selected patients with scleroderma and other autoimmune diseases. HSC transplant requires collection

of HSCs via mobilization by G-CSF, which consists of 4-7 days of injections that are associated with significant side effects and potential for severe complications including disease flares (e.g., scleroderma and multiple sclerosis). MGTA-145 is a biologic that activates CXCR2 on neutrophils, and with plerixafor (a CXCR4 antagonist) rapidly mobilizes HSCs in mice and non-human primates. The combination promises to be a same-day, G-CSF-free mobilization regimen.

Methods: This healthy volunteer study consisted of four parts- Part A: single-agent MGTA-145 or placebo; Part B: MGTA-145 or placebo given immediately or 2 hours after plerixafor; Part C: MGTA-145 or placebo given 2 hours after plerixafor on 2 consecutive days; Part D: MGTA-145 given 2 hours after plerixafor, just prior to apheresis cell collection.

Results: Monotherapy of MGTA-145 mobilized CD34+ cells within minutes and peaked within 1-hour post MGTA-145 (median 11 CD34+ cells/μL, a 7-fold increase vs baseline). White blood cells and neutrophils followed a similar pattern. Importantly, markers of neutrophil activation were relatively unchanged (≤2-fold vs baseline, Fig 1).

MGTA-145 combined with plerixafor increased CD34+ cell mobilization, whether given simultaneously or 2h after plerixafor (Fig. 2). Mobilization was highly enriched for CD34+CD90+CD45RA- HSCs. At the 0.03 mg/kg dose with

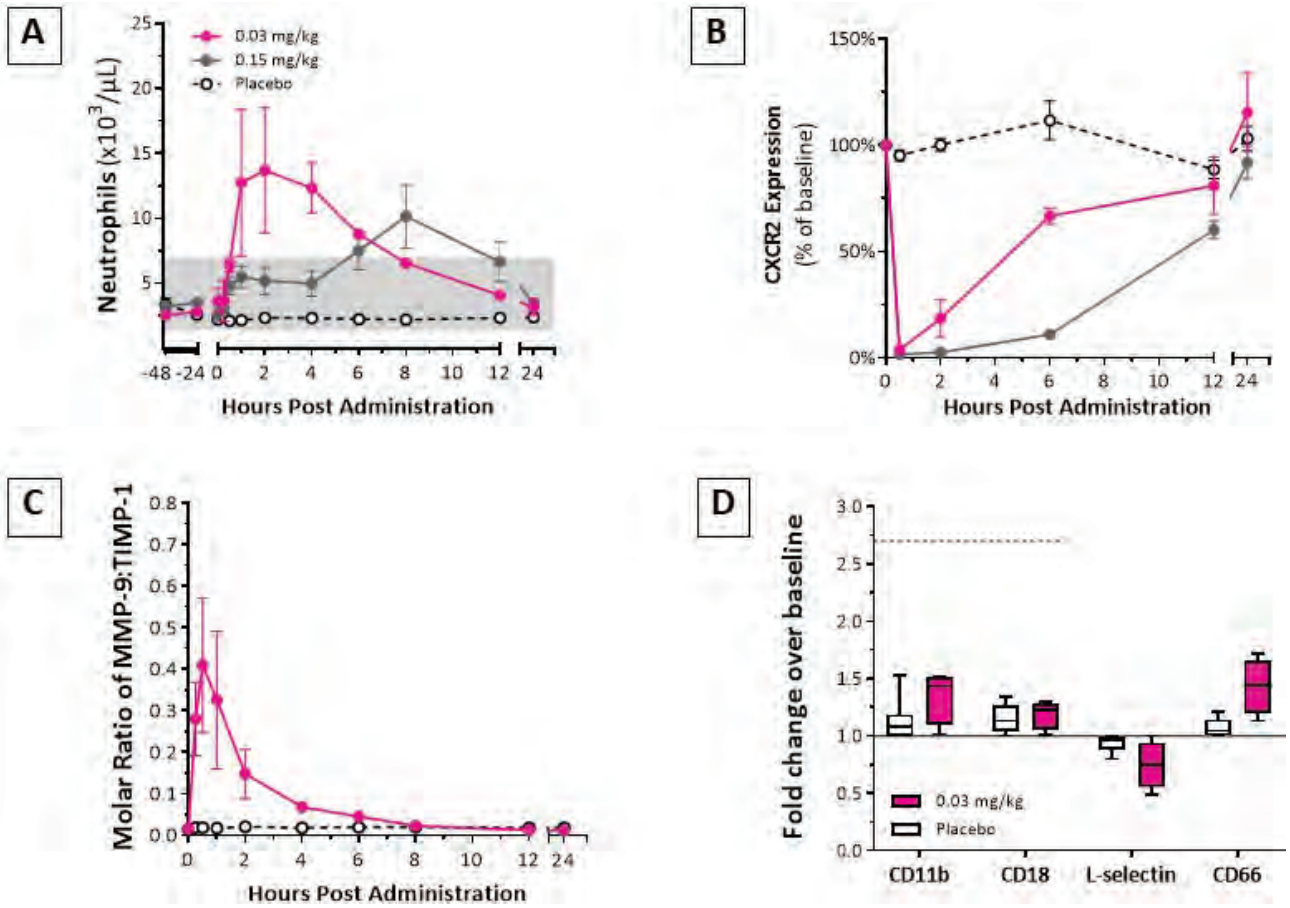

Figure 1. MGTA-145 has rapid, on-target neutrophil pharmacodynamics with minimal activation. (A) A single dose of MGTA-145 elicits dose-dependent mobilization of neutrophils into peripheral blood. (B) MGTA-145 monotherapy leads to rapid downregulation of its target receptor, CXCR2, on peripheral blood neutrophils. (C) MGTA-145 monotherapy leads to an increase in the molar ratio of the neutrophil protease, MMP-9, to its inhibitor, TIMP-1, in plasma. (D) MGTA-145 monotherapy elicits only modest changes in peripheral blood neutrophil activation markers (median ≤ 2-fold) after administration. Data represent at least 4 subjects per dose level and are expressed as mean ± SEM (A-C) or median + 10-90 percentile range (D). The shaded region in (A) represents the normal reference range for healthy subjects. The dotted line in (D) represents the anticipated effect of 5 days of G-CSF based on published data (Falanga et al, Blood. 1999).

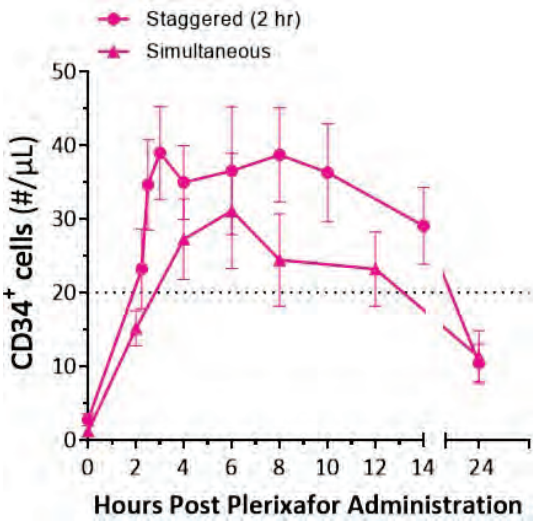

Figure 2. Peripheral blood mobilization after plerixafor + 0.03 mg/kg MGTA-145 in healthy subjects with simultaneous and 2h stagger dosing after plerixafor. Dotted line: previously reported CD34+ counts with plerixafor alone mobilization (Chen et al, Blood Advances. 2018).

Table. Single-day Mobilization and Apheresis Cell Yields in Part D

MGTA-145 dose (mg/kg)	Subjects (n)	Total CD34+ Yield (x10⁶) Median (range)	CD34+ / kg (x10⁶)			CD90+ / kg (x10⁶)a			CD90+ (% of CD34+)
			Mean	Median	Range	Mean	Median	Range	
0.015	4	310 (118-525)	4.0	3.7	1.5 - 7.0	1.4	1.2	0.5 – 2.8	37%
0.03	4	321 (239-500)	4.1	4.3	2.7 – 5.3	1.3	1.5	0.5 – 1.8	31%

2h stagger, median peak CD34+ peripheral blood mobilization was ≥40 cells/µL in Part B. On a second consecutive day of dosing, MGTA-145 + plerixafor mobilized HSCs to levels comparable to day 1. Apheresis cell collection yields in Part D showed that sufficient numbers of cells (median 4.3 x 10^6 CD34+ cells/kg) for transplant were collected in a single day. Notably, MGTA-145 + plerixafor mobilized 3-fold higher numbers of CD34+CD90+CD45RA- HSCs and demonstrated >10-fold higher engraftment in NSG mice compared to cells mobilized by G-CSF.

MGTA-145 monotherapy was well tolerated with no significant adverse events (AEs). Grade 1, transient lower back pain that dissipated within minutes was reported. The combination of MGTA-145 with plerixafor was well tolerated, with some subjects experiencing grade 1/2 gastrointestinal AEs commonly observed with plerixafor and one grade 2 back pain with MGTA-145 at 0.075 mg/kg that resolved within minutes.

Conclusion: MGTA-145 was well-tolerated and induced rapid mobilization of significant numbers of HSCs. CD34+ cell mobilization with MGTA-145 + plerixafor was immediate and superior to plerixafor alone. These data suggest that the combination enables the collection of sufficient HSCs for transplant in one day without the need for G-CSF. Further clinical development as a first line mobilization agent is warranted in scleroderma and other autoimmune diseases, as well as in gene therapy and hematologic malignancies.

Disclosure: J. DiPersio, Magenta Therapuetics, 1, 2, Wugen, 1, Incyte, 1, BioLineRx, 1; **J. Hoggatt**, Magenta Therapeutics, 1, 2; **S. Devine**, Bristol Myers, 1, Magenta Therapeutics, 1; **D. Scadden**, Magenta Therapeutics, 1; **H. Howell**, Magenta Therapeutics, 1, 2; **V. Schmelmer**, Magenta Therapeutics, 1, 2; **G. Raffel**, Magenta Therapeutics, 1, 2; **P. Falahee**, Magenta Therapeutics, 1, 2, 3; **K. Goncalves**, Magenta Therapeutics, 1, 2, 3; **W. Savage**, Magenta Therapeutics, 1, 2; **J. Davis**, Magenta Therapeutics, 1, 2, 3.

Abstract Number: 0387

Altered Iron Homeostasis and Pulmonary Haemodynamics in Systemic Sclerosis Associated Pulmonary Arterial Hypertension

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
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Session Time: 9:00AM–11:00AM

Background/Purpose: Iron deficiency (ID) is more frequent in systemic sclerosis (SSc) patients with pulmonary hypertension (PH) than those without and associated with worse prognosis. There is paucity of data on the relationship between serum iron parameters and pulmonary haemodynamics.

Methods: Right heart catheterisation (RHC) reports of SSc patients were retrospectively reviewed. Subjects were included in the study if they had serum iron studies done within 12 months of RHC and were either diagnosed as 1) pulmonary arteral hypertension (PAH, group 1 PH), defined as mean pulmonary artery pressure (mPAP) ≥25 mmHg at rest with pulmonary artery wedge pressure ≤15 mmHg; or 2) no PH. Patients with gastrointestinal disorders that may cause low iron levels and glomerular filtration rate below 60 ml/min/1.73m^2 were excluded. We recorded serum iron concentration (µmol/L), total iron-binding capacity (TIBC, µmol/L), transferrin saturation (TS, %), ferritin (µg/L), red cell distribution width (RDW, %), as well as mPAP (mmHg) and pulmonary vascular resistance (PVR, dynes/sec/cm^{-5}). Univariable associatıons were assessed using Mann-Whitney test and Spearman's correlation as appropriate. Multiple regression of log-transformed mPAP and PVR and Cox regression were used to compare iron and RDW association with haemodynamics and survival.

Results: We included 122 subjects in the analysis, 84% were female and mean age at RHC was 57 years. The majority (73%) had limited cutaneous SSc and 34% carried anti-centromere antibodies, followed by 18% with anti-Scl70 and 8% with anti-U3RNP.

At RHC, 53/122 (43%) of the patients were diagnosed with PAH. Among them we observed substantially lower levels of serum iron (8.7 vs. 12.1 µmol/L, p< 0.001), TS (15.3% vs. 22.5%, p< 0.001), ferritin (68.1 vs. 112.5 µg/L, p=0.07), significantly higher RDW (16.4% vs. 14.8%, p< 0.001) and no difference in TIBC (57.4 vs. 54.3 µmol/L, p=0.163), compared to subjects in whom PH was excluded.

mPAP showed moderately strong negative correlation with iron concentration (Spearman's rho=-0.35, p< 0.001) and TS (Spearman's rho=-0.39, p< 0.001) and positive correlation with RDW (Spearman's rho=0.46, p< 0.001).

PVR was significantly inversely correlated with iron concentration (Spearman's rho=-0.30, p=0.001), TS (Spearman's rho=-0.37, p< 0.001 and ferritin (Spearman's rho=-0.22, p=0.016), while it showed positive correlation with TIBC (Spearman's rho=0.28, p=0.003) and RDW (Spearman's rho=0.37, p< 0.001).

Compared to serum iron indices, RDW is a better predictor of mPAP and PVR. In addition, iron levels did not demonstrate any association with survival, while risk of death was significantly higher for patients with higher RDW (HR=1.18, p=0.002) and the association remained after adjusting for presence of PH (HR=1.16, p=0.013).

Conclusion: To our knowledge, this is the first study to demonstrate a significant relationship between ID state and haemodynamic measures of SSc-PAH. Our data also support RDW, as an indicator for functional iron deficiency, may serve as a biomarker for severity of pulmonary vasculopathy in SSc.

Disclosure: A. Sari, None; **C. Denton**, Janssen, 1, GlaxoSmithKline, 1, 2, Bayer, 1, Sanofi, 1, Inventiva, 1, 2, Boehringer Ingelheim, 1, Roche, 1, Bristol-Myers Squibb, 1, CSL Behring, 1, 2, UCB, 1, Leadiant Biosciences, 1, Corbus Pharmaceuticals, 1, Acceleron Pharma, 1, Horizon Therapeutics, 1, Forbius, 1, Servier, 1; **S. Nihtyanova**, GlaxoSmithKline, 3; **B. Schreiber**, None; **V. Ong**, None.

Abstract Number: 0388

Factors Prognostic of Greater Decline in Forced Vital Capacity in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD): Data from the Placebo Group of the SENSCIS Trial

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: The progression of SSc-ILD is variable and unpredictable. However, observational studies have identified patient characteristics that may be prognostic of a greater rate of decline in forced vital capacity (FVC) in patients with SSc-ILD. We used data from the placebo group of the SENSCIS trial to conduct a preliminary analysis of whether baseline variables were prognostic of a greater rate of decline in FVC over 52 weeks.

Methods: Patients with SSc-ILD with onset of first non-Raynaud symptom ≤7 years before screening, extent of fibrotic ILD ≥10% on HRCT and FVC ≥40% predicted were enrolled in the SENSCIS trial. Patients on prednisone ≤10 mg/day (or equivalent) and/or stable therapy with mycophenolate or methotrexate for ≥6 months prior to randomization were allowed to participate. Patients were randomized to receive nintedanib or placebo until the last patient had reached week 52 but for ≤100 weeks. We used data from the placebo group to investigate baseline characteristics as prognostic factors for a greater rate of decline in FVC (mL/year) over 52 weeks (Table). Our analyses were based on

Table. Baseline characteristics as prognostic factors for a greater rate of decline in FVC (mL/year) over 52 weeks in the placebo group of the SENSCIS trial

Baseline characteristic		N analyzed	Rate of decline in FVC (mL/year) over 52 weeks		
			Adjusted rate (SE)	Difference (95% CI)	p-value†
ATA status	Negative	111	-93.5 (22.9)	2.5 (-55.1, 60.2)	0.93
	Positive	177	-96.0 (18.1)		
Sex	Female	212	-88.7 (17.5)	24.2 (-52.6, 101.1)	0.54
	Male	76	-112.9 (32.1)		
Mycophenolate use	No	148	-121.5 (19.8)	-53.8 (-109.3, 1.7)	0.06
	Yes	140	-67.7 (20.1)		
FVC % predicted	≤70	129	-127.4 (23.2)	-58.5 (-123.9, 6.8)	0.08
	>70	159	-68.9 (20.4)		
Extent of fibrotic ILD on HRCT (%)*	<20	74	-84.6 (27.9)	14.0 (-49.9, 78.0)	0.67
	≥20	214	-98.7 (16.5)		
SSc subtype	Diffuse cutaneous	146	-114.2 (19.9)	-38.6 (-94.2, 17.1)	0.17
	Limited cutaneous	142	-75.7 (20.0)		
Age (years)	<65	229	-96.8 (15.9)	-8.5 (-76.3, 59.2)	0.80
	≥65	59	-88.3 (30.7)		
mRSS	<18	226	−82.4 (16.0)	−53.15 (−121.1, 14.8)	0.12
	≥18	60	−135.6 (30.5)		
C-reactive protein (mg/L)	>4.99 mg/L	74	-107.9 (28.9)	-24.3 (-91.3, 42.7)	0.48
	≤4.99 mg/L	187	-83.6 (17.9)		
Years since onset of first non-Raynaud's symptom	≤3	127	-112.5 (21.3)	-31.3 (-87.4, 24.8)	0.27
	>3	161	-81.2 (19.0)		

ATA, anti-topoisomerase I antibody. *Assessed visually in the whole lung to nearest 5%. The assessment did not include pure (non-fibrotic) ground glass opacities. †p-value for subgroup-by-time interaction.

a random coefficient regression model with effects of anti-topoisomerase I antibody status, sex, time, baseline FVC (mL), age and height, and subgroup-by-time and baseline-by-time interactions.

Results: A total of 288 patients received placebo, of whom 73.6% were female, 61.5% were ATA-positive, and 50.7% had diffuse cutaneous SSc. At baseline, mean (SD) age was 53.4 (12.6) years, FVC was 72.7 (16.6) % predicted and modified Rodnan skin score was 10.9 (8.8); median time since onset of first non-Raynaud's symptom was 3.5 years. Almost half (48.6%) of patients were taking mycophenolate at baseline. In the primary analysis, the adjusted rate (SE) of decline in FVC in the placebo group was -93.3 (13.5) mL/year. None of the baseline factors investigated in this patient population was prognostic ($p< 0.05$) of a greater rate of decline in FVC (mL/year) over 52 weeks, but baseline FVC ≤70% predicted and not taking mycophenolate at baseline showed trends toward being prognostic factors (Table).

Conclusion: Among patients with SSc-ILD who received placebo in the SENSCIS trial, no baseline characteristic was found to be prognostic of a greater rate of decline in FVC over 52 weeks, although baseline FVC ≤70% predicted

and not taking mycophenolate at baseline showed trends toward being prognostic factors. These findings support previous studies suggesting that the course of SSc-ILD is difficult to predict, that prognostic factors identified in certain populations may not apply to all populations of patients with SSc-ILD, and that new parameters or a combination of factors from different disease domains might be needed to predict the course of SSc-ILD.

Disclosure: M. Kuwana, Ono Pharmaceutical, 2, 8, Chugai, 2, 8, Astellas, 8, Mitsubishi Tanabe Pharma Corporation, 2, 8, AbbVie Inc., 8, Eisai Co., Ltd., 8; **S. Assassi**, Momenta, 1, corbus, 1, Integrity Continuing Education, 1, Boehringer Ingelheim, 1, 2, 3; **J. Avouac**, Sanofi, 5, 8, AbbVie, 5, Bristol-Myers Squibb, 8, Pfizer, 8, MSD, 8, Novartis, 8; **R. Hoyles**, Boehringer Ingelheim, 5, 8, Roche, 5, 8; **J. Pope**, AbbVie, 2, 5, Amgen, 5, 8, Lilly, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 5, 8, Sandoz, 5, 8, Roche, 2, 5, 8, Pfizer, 5, 8, Novartis, 5, 8, Merck, 2, 5, 8, Janssen, 5, 8, Gilead Sciences, Inc., 2, 5, BMS, 2, 5, 8, Abbott, 5, Actelion, 5, AstraZeneca, 5, Bayer, 5, Boehringer Ingelheim, 5, EICOS, 5, Emerald, 5, GlaxoSmithKline, 5, Medexus, 5, Seattle Genetics, 2; **V. Smith**, Boehringer Ingelheim, 2, 5, 8, Janssen, 2, 5, 8; **C. Miede**, Boehringer Ingelheim, 9; **E. Clerisme-Beaty**, Boehringer Ingelheim, 3; **M. Alves**, Boehringer Ingelheim, 3; **O. Distler**, Actelion, 2, 5, 8, Bayer, 2, 5, 8, Boehringer Ingelheim, 2, 5, 8, Medscape, 5, 8, Novartis, 8, Roche, 5, 8, Menarini, 8, Mepha, 8, MSD, 5, 8, iQone, 8, Pfizer, 5, 8, AbbVie, 5, Acceleron Pharma, 5, Amgen, 5, AnaMar, 5, Arxx Therapeutics, 5, Beacon Discovery, 5, Blade Therapeutics, 5, CSL Behring, 5, ChemomAb, 5, Corpus Pharma, 5, Curzion Pharmaceuticals, 5, Ergonex Pharma, 5, Mitsubishi Tanabe Pharma, 2, 5, Kymera Therapeutics, 2, 5, Catenion, 5, Galapagos NV, 5, GlaxoSmithKline, 5, Glenmark Pharmaceuticals, 5, Inventiva, 5, Italfarmaco, 5, Lilly, 5, Sanofi, 5, UCB, 5, IQVIA, 5, Medac, 5, Target BioScience, 5, Patent issued, 9.

Abstract Number: 0389

Organ Specific Treatment Patterns of a Real-World, Electronic Health Record Cohort of Patients with Systemic Sclerosis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Assembling large cohorts of patients with rare diseases is difficult and limits the power to assess outcomes in systemic sclerosis (SSc) studies. Treatment in SSc varies significantly and is tailored to a patient's disease manifestations. To investigate this variability, we identified a cohort of SSc patients in the EHR to examine real-world disease presentations and treatment practices.

Methods: We analyzed data from a de-identified EHR that contains over 3 million subjects with longitudinal clinical data. We identified potential SSc patients using a previously validated algorithm requiring ^{3} 4 SSc ICD-9 (710.1) or ICD-10-CM codes (M34.0, M34.1, M34.8, M34.9). We performed chart review to determine case status, disease manifestations, autoantibodies, and medication use. Patients were confirmed to have SSc if diagnosed by a rheumatologist, pulmonologist, or dermatologist. Disease manifestations were included if documented in inpatient or outpatient notes. Immunosuppressants and medications for gastroesophageal reflux disease (GERD), Raynaud's phenomenon, and pulmonary hypertension (PH) were assessed through inpatient and outpatient notes and counted if ever used.

Results: Of 223 patients identified by the algorithm, 196 were confirmed on chart review as SSc patients with an additional 4 mixed connective tissue disease patients. Of these 200, patients were predominantly female (84%) and

Table 1: Characteristics and disease manifestations of systemic sclerosis patients in an electronic health record cohort

Sex [a], *n (%)*	
Female	165 (84)
Male	31 (16)
Race [b], *n (%)*	
Caucasian	163 (87)
African American	19 (10)
Asian	3 (2)
Ethnicity, *n (%)*	
Hispanic/Latino	2 (1)
SSc subtype, *n (%)*	
Limited	166 (83)
Diffuse	28 (14)
MCTD	4 (2)
Sine	2 (1)
Organ manifestations, *n (%)*	
GERD	155 (78)
Pulmonary hypertension	71 (36)
Esophageal dysmotility/dysphagia [c]	72 (36)
Interstitial lung disease	44 (22)
Renal crisis	3 (2)
Cutaneous manifestations, *n (%)*	
Raynaud's phenomenon	164 (82)
Sclerodactyly	139 (70)
Telangiectasias	107 (54)
Digital ulceration	48 (24)
Cutaneous calcinosis	25 (13)
Autoantibodies [d], *n (%)*	
Antinuclear antibody (titer ≥ 1:160)	106 (95)
Centromere	37 (77)
Anti-Scl 70	19 (26)

[a] 4 cases with missing sex
[b] 13 cases with missing race/ethnicity
[c] Patients were counted if subjective dysphagia documented or if patient underwent EGD showing dysmotility/esophageal stricture requiring dilation
[d] Percentage is of subjects with available test results
SSc: Systemic Sclerosis
MCTD: Mixed connective tissue disease

Caucasian (87%) (Table 1). Of patients with available tests, 95% had a positive antinuclear antibody (titer ≥ 1:160). Most were of the limited cutaneous subtype (83%). Overall, 22% had interstitial lung disease (ILD), 36% PH, and 3% renal crisis. The most common disease manifestations were Raynaud's phenomenon (82%) and GERD (78%). Of the patients with Raynaud's phenomenon, 45% were ever on a calcium channel blocker and 34% were not on any medications (Table 2). Almost all patients with GERD were on acid suppression therapy (97%) with 89% on a proton pump inhibitor. Overall, immunosuppressant use varied widely, with the most commonly used medications being prednisone at any dose (40%) and methotrexate (17%). Only 16% of patients on prednisone were on doses higher than 30 mg daily, and a majority (69%) had co-existing ILD or arthritis. For the ILD patients, 91% were on immunosuppressants with the most frequently used medications being prednisone (70%) and cyclophosphamide (50%). Of the PH patients, 79% were on disease specific treatment with 21% not on therapy or on diuretics alone. A majority (60%) of the PH patients were managed with combination therapy.

Conclusion: We identified a large, real-world EHR cohort of SSc patients. The majority of SSc patients were on medications for GERD, PH, and ILD. This trend may reflect our EHR cohort being based at a tertiary care center with access to multi-disciplinary care. Despite high percentages of treatment, immunosuppressant treatments and

Table 2: Treatment patterns of systemic sclerosis patients in an electronic health record cohort

Ever immunosuppressant use, *n (%)*	
Prednisone (all doses)	79 (40)
No prior therapy	77 (38)
Prednisone (<10mg)	43 (21)
Prednisone (10-30 mg)	37 (18)
Methotrexate	34 (17)
Hydroxychloroquine	29 (14)
Cyclophosphamide	29 (14)
Mycophenolate mofetil	22 (11)
Azathioprine	20 (10)
Prednisone (>30mg)	13 (6)
Rituximab	3 (2)
Leflunomide	3 (2)
Ever Raynaud's phenomenon therapy, *n (%)*	
Calcium channel blocker	73 (45)
No prior therapy	56 (34)
Phosphodiesterase-5 (PDE5) inhibitor	28 (17)
Topical nitroglycerin	16 (10)
Endothelin receptor antagonist (ERA)	11 (7)
Ever pulmonary hypertension therapy, *n (%)*	
Diuretic only	10 (14)
PDE5 inhibitor	10 (14)
Prostacyclin + ERA + PDE5 inhibitor	9 (13)
Prostacyclin + ERA	9 (13)
Prostacyclin + PDE5 inhibitor	8 (11)
Prostacyclin	6 (8)
ERA + PDE5 inhibitor	6 (8)
ERA	5 (7)
No prior therapy	5 (7)
Calcium channel blocker + PDE5 inhibitor	2 (3)
Calcium channel blocker	1 (1)
Ever GERD therapy, *n (%)*	
Proton pump inhibitor (PPI)	138 (89)
H2 inhibitor	7 (5)
PPI + H2 inhibitor	5 (3)
No prior therapy	5 (3)
Ever immunosuppressants for ILD, *n (%)*	
Prednisone	31 (70)
Cyclophosphamide	22 (50)
Mycophenolate mofetil	13 (30)
Methotrexate	10 (22)
Azathioprine	8 (18)
Rituximab	3 (7)
Hydroxychloroquine	3 (7)

PDE5: Phosphodiesterase-5, ERA: Endothelin receptor antagonist

medications for ILD and PH varied significantly between patients. In future studies, we will evaluate how real-world management and treatment practices impact clinical outcomes in SSc.

Disclosure: K. Kidwell, None; **L. Crofford**, None; **A. Barnado**, Nashville Biosciences, 1.

Abstract Number: 0390

Baseline Characteristics of Systemic Sclerosis (SSc) Patients with Restrictive Lung Disease in a Multi-Center United States Based Longitudinal Registry

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is the leading cause of death in SSc. Several international observational studies have evaluated characteristics of ILD in their SSc patient populations, however these studies do not necessarily reflect the US SSc patient population. The purpose of this analysis was to assess the baseline characteristics of SSc patients with and without restrictive lung disease (RLD) in a US based longitudinal registry.

Methods: The Collaborative National Quality and Efficacy Registry (CONQUER) for Systemic Sclerosis is a multicenter US based registry of patients with early SSc within 5 years of first non-Raynaud's symptom enrolled at 13 expert centers. All patients are >18 years old and fulfill the 2013 ACR/EULAR Classification Criteria for SSc. All patients who had a pulmonary function test (PFT) at baseline on or before April 1, 2020 were included in this analysis. As a high-resolution computed tomography (HRCT) Chest at baseline was not available to characterize ILD for all patients, patients were characterized as RLD based on force vital capacity (FVC) % predicted < 80% or total lung capacity (TLC) % predicted < 80%. Chi-squared test and Fisher's Exact test were performed for categorical variables. T-test was performed for continuous variables. Multivariable modeling with stepwise selection was performed to predict RLD. A p-value < 0.05 was considered significant.

Results: 329 patients underwent PFTs at baseline with 147 (45%) patients characterized as RLD. There was no significant difference in age, sex or disease duration between patients with and without RLD. Patients with RLD had a mean disease duration of 2.6 years and a mean FVC of 67% at baseline. RLD patients compared to no RLD were more likely to be non-white (African American, Asian or other) and have diffuse disease, a higher modified Rodnan skin score, digital pitting scars and abnormal GI symptoms including gastric antral vascular ectasia (GAVE), esophageal dysmotility, small bowel dysfunction or malabsorption (Table 1). RLD patients who underwent HRCT also were more likely to have a patulous esophagus on HRCT compared to those patients without RLD (Table 2). In multivariable analysis, non-white race, crackles on exam, DLCO< 60%, and higher physician global health assessment scores were found to be independently associated with RLD (Table 3).

Table 1

Table 1: Patient Demographics and Key SSc Features

	Overall (N = 329)	SSc-restrictive lung disease: Yes (N = 147)	SSc-restrictive lung disease: No (N = 182)	P-value
Demographics				
Age at baseline visit: Mean (SD)	51.9 (13.67)	50.6 (14.00)	53.0 (13.33)	0.120[1]
Female Sex	273 (83.0%)	118 (80.3%)	155 (85.2%)	0.240[2]
Race				<.001[2]
White	261 (80.3%)	99 (67.8%)	162 (90.5%)	
Black or African American	36 (11.1%)	30 (20.5%)	6 (3.4%)	
Other	28 (8.6%)	17 (11.6%)	11 (6.1%)	
Smoking status				0.017[3]
Never	217 (66.0%)	104 (70.7%)	113 (62.1%)	
Former	100 (30.4%)	42 (28.6%)	58 (31.9%)	
Current	12 (3.6%)	1 (0.7%)	11 (6.0%)	
Employment status[4]				0.057[2]
Full-time	153 (48.7%)	67 (47.9%)	86 (49.4%)	
Retired	66 (21.0%)	27 (19.3%)	39 (22.4%)	
Disabled	43 (13.7%)	27 (19.3%)	16 (9.2%)	
Other	52 (16.6%)	19 (13.6%)	33 (19.0%)	
Key SSc Features				
Disease duration (years): Mean (SD)	2.6 (1.40)	2.6 (1.34)	2.7 (1.45)	0.865[1]
SSc subtype				0.002[2]
Limited	134 (40.7%)	46 (31.3%)	88 (48.4%)	
Diffuse	195 (59.3%)	101 (68.7%)	94 (51.6%)	
Antibody Testing				
ANA positive	285 (86.6%)	125 (85.0%)	160 (87.9%)	0.494[2]
Anti-centromere positive	38 (11.6%)	11 (7.5%)	27 (14.8%)	0.058[2]
Anti-Scl-70 positive	97 (29.5%)	47 (32.0%)	50 (27.5%)	0.657[2]
Anti-RNA Polymerase III positive	77 (23.4%)	32 (21.8%)	45 (24.7%)	0.187[2]
Anti-U1-RNP positive	25 (7.6%)	16 (10.9%)	9 (4.9%)	0.029[2]
Anti- SSA/Ro positive	37 (11.2%)	23 (15.6%)	14 (7.7%)	0.061[2]
Anti- SSB/La positive	6 (1.8%)	4 (2.7%)	2 (1.1%)	0.550[2]
Modified Rodnan Skin Score (mRSS): Mean (SD)	12.7 (10.71)	15.0 (11.37)	10.7 (9.76)	<.001[1]
Digital ulcers	17 (5.2%)	10 (6.8%)	7 (3.9%)	0.233[2]
Digital pitting scars	74 (22.8%)	41 (28.3%)	33 (18.4%)	0.036[2]
Gastric antral vascular ectasia (GAVE)	29 (16.6%)	18 (23.1%)	11 (11.3%)	0.038[2]
GI Tract[5]				0.028[2]
Normal	84 (25.8%)	29 (19.9%)	55 (30.6%)	
Not normal	242 (74.2%)	117 (80.1%)	125 (69.4%)	

[1] T-test with unpooled variance estimates.
[2] Chi-squared test.
[3] Fisher's exact test.
[4] Employment status of 'Other' includes part-time, homemaker, student or unemployed.
[5] GI Tract normal: normal esophagram; normal small bowel series; not GI symptoms.
GI Tract not normal: distal esophageal hypoperistalsis; small bowel abnormal (e.g. reflux, bloating, distension) or antibiotics required for bacterial overgrowth or malabsorbtion syndrome; episodes of pseudo-obstruction or hyperalimentation required.

Table 2

Table 2: Baseline Pulmonary Features and Patient/Physician Assessments

	Overall (N = 329)	SSc-restrictive lung disease: Yes (N = 147)	SSc-restrictive lung disease: No (N = 182)	P-value
Baseline supplemental oxygen use	15 (4.6%)	11 (7.6%)	4 (2.2%)	0.021[2]
Oxygen at rest (L/min): Mean (SD)	2.6 (1.16)	2.2 (0.92)	3.5 (1.29)	0.135[1]
Oxygen at exertion (L/min): Mean (SD)	3.7 (1.66)	3.2 (1.23)	4.9 (2.17)	0.224[1]
Crackles on exam	71 (21.6%)	50 (34.2%)	21 (11.5%)	<.001[2]
New York Heart Association (NYHA) functional classification[3]				<.001[2]
Class I	185 (56.6%)	68 (46.3%)	117 (65.0%)	
Class II	112 (34.3%)	57 (38.8%)	55 (30.6%)	
Class III, IV	30 (9.2%)	22 (15.0%)	8 (4.4%)	
Pulmonary Function Testing[4]				
FVC (L): Mean (SD)	3.0 (0.89)	2.4 (0.68)	3.4 (0.80)	
FVC % predicted: Mean (SD)	83.7 (20.31)	67.1 (15.65)	97.0 (12.14)	
FEV1 (L): Mean (SD)	3.0 (11.19)	2.0 (0.55)	3.8 (14.95)	0.111[1]
FEV1 % predicted: Mean (SD)	84.3 (19.46)	69.5 (15.63)	96.1 (13.14)	<.001[1]
FEV1/FVC (actual): Mean (SD)	82.6 (10.46)	85.0 (9.45)	80.8 (10.85)	<.001[1]
TLC(L): Mean (SD)	5.0 (5.33)	4.6 (7.65)	5.3 (1.20)	
TLC % predicted: Mean (SD)	89.8 (65.08)	70.7 (19.42)	107.6 (84.86)	
DLCO (mL/mmHg/min): Mean (SD)	17.5 (7.31)	13.9 (5.53)	20.4 (7.30)	<.001[1]
DLCO % predicted: Mean (SD)	70.4 (23.87)	56.6 (21.30)	81.3 (19.83)	<.001[1]
Six Minute Walk Test distance (meters): Mean (SD)	404.9 (136.22)	373.7 (141.94)	451.7 (114.88)	0.029[1]
HRCT performed at baseline	218 (66.3%)	114 (77.6%)	104 (57.1%)	<.001[2]
Ground glass opacity	98 (49.0%)	58 (53.7%)	40 (43.5%)	0.149[2]
Reticular changes	62 (34.4%)	38 (39.6%)	24 (28.6%)	0.121[2]
Honeycombing	16 (8.6%)	13 (13.4%)	3 (3.4%)	0.018[3]
Traction Bronchiectasis	53 (27.3%)	39 (37.9%)	14 (15.4%)	<.001[2]
Patulous esophagus	51 (28.7%)	40 (41.2%)	11 (13.6%)	<.001[2]
Echocardiogram	284 (86.3%)	132 (89.8%)	152 (83.5%)	0.099[2]
Estimated PASP/RSVP (mmHg): Mean (SD)	31.6 (11.05)	33.5 (10.93)	29.7 (10.96)	0.090[1]
Assessments				
Participant global health[5]: Mean (SD)	4.0 (2.58)	4.4 (2.47)	3.6 (2.63)	0.016[1]
Physician global health[6]: Mean (SD)	3.5 (2.06)	4.2 (2.13)	2.9 (1.81)	<.001[1]
Physician global damage[7]: Mean (SD)	4.0 (7.23)	4.3 (2.17)	3.7 (9.52)	0.419[1]
SHAQ breathlessness score[8]: Mean (SD)	3.4 (11.87)	5.4 (15.70)	1.9 (7.32)	0.020[1]
mMRC dyspnea scale[9]				<.001[2]
0	117 (40.6%)	34 (27.2%)	83 (50.9%)	
1	108 (37.5%)	50 (40.0%)	58 (35.6%)	
2-4	63 (21.9%)	41 (32.8%)	22 (13.5%)	
FACIT dyspnea score: Mean (SD)	6.6 (6.95)	8.5 (7.65)	5.1 (5.96)	<.001[1]

[1] T-test with unpooled variance estimates.
[2] Chi-squared test.
[3] Class I (No symptoms and no limitation to physical activity), to Class IV (severe limitations, symptoms at rest)
[4] P-values are not calculated for FVC and TLC because those variables were used to derive the outcome of RLD.
[5] How was your overall health in the last week? 0 (Excellent) to 10 (Extremely poor).
[6] How would you rate the participants overall health for the past week? 0 (Excellent) to 10 (Very poor).
[7] How much damage do you think the participant has from his/her scleroderma? 0 (No damage) to 10 (Very severe damage).
[8] In the past week how much have your breathing problems interfered with your daily activities? 0 (No interference) to 10 (Very severe interference).
[9] Describe your shortness of breath: 0 (I only get breathless with strenuous exercise) 1 (I get short of breath when hurrying on level ground or walking up a slight hill) to 4 (I am too breathless to leave the house or I am breathless when dressing).
HRCT = high resolution computed tomography of the chest; SHAQ = Scleroderma Health Assessment Questionnaire; mMRC = Modified Medical Research Council; FACIT = Functional Assessment of Chronic Illness Therapy; FVC = forced vital capacity; FEV1 = forced expiratory volume in 1 second; TLC = total lung capacity; DLCO = diffusion capacity for carbon monoxide

Conclusion: We found that SSc patients with RLD enrolled in CONQUER had more diffuse disease and significant GI manifestations compared to patients without RLD. Non-white race was independently associated with RLD. Interestingly, patients with RLD had early disease yet already significant restrictive defects on PFTs, suggesting that even

Table 3

Table 3: Multivariable model

	SSc-restrictive lung disease	
	Odds ratio (95% CI)	P-value
Race		<.001
White	Reference	
Non-white	4.67 (2.33, 9.79)	
Physician global health	1.24 (1.08, 1.42)	0.002
GI Tract		0.054
Normal	Reference	
Not normal	1.87 (0.99, 3.60)	
DLCO % predicted		<.001
≥80%	Reference	
<60%	5.47 (2.67, 11.53)	
≥60% to <80%	1.85 (0.94, 3.68)	
PFT Not performed OR Missing Predicted Value	2.83 (1.09, 7.38)	
Crackles on exam		0.004
No	Reference	
Yes	2.68 (1.37, 5.35)	

n=319
Results are based on a multivariable model, adjusting for each of the predictors in this table.

earlier detection methods are necessary. Further investigation into the factors associated with ILD and its progression is warranted as we collect long-term prospective data on this growing cohort of US SSc patients.

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Abstract Number: 0391

Defining the Optimal Disease Duration of Early Diffuse Systemic Sclerosis for Clinical Trial Design

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
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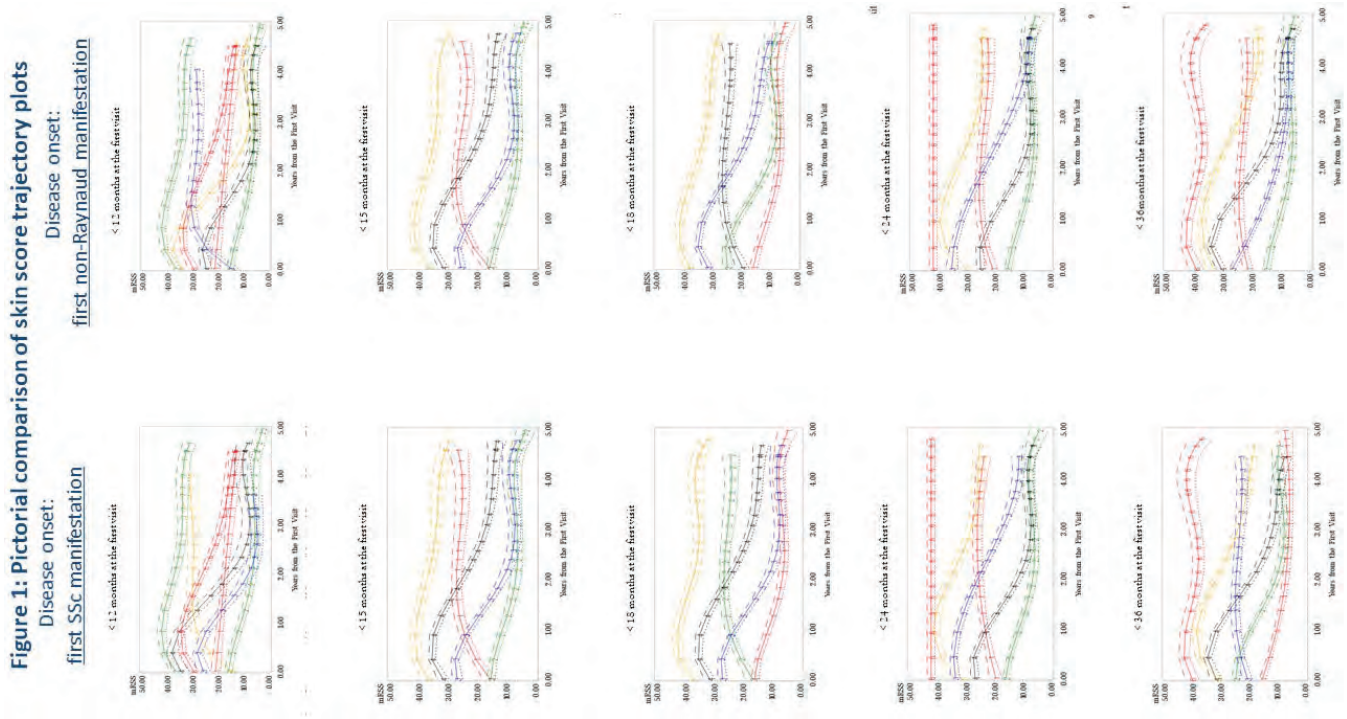
Background/Purpose: Clinical trials in early diffuse cutaneous systemic sclerosis (SSc) have historically used the modified Rodnan skin score (mRSS) as the primary outcome measure. These trials have persistently been unable to show any significant improvement in the mRSS between placebo and comparison groups. What has been demonstrated in many trials are declines in the mRSS in both groups; suggesting regression to the mean occurring in both the treatment and the comparison group. We wanted to assess how the definition of disease onset (first SSc manifestation versus first non-Raynaud manifestation), and how varying lengths of disease duration at trial entry as an inclusion criteria functioned with respect to mRSS trajectory. Our objective was to optimize trial inclusion criteria.

Methods: We used a prospective, observational cohort from a large US university, tertiary-care referral Scleroderma Center cohort. We identified early diffuse SSc patients first seen between 1980 and 2015. All had < 3 years from first SSc (n=481) or first non-Raynaud manifestation (n=514) and ≥3 mRSS scores during follow-up. We used descriptive, time to event and group-based trajectory analyses to model: 1) the two different definitions of disease onset (first SSc and first non-Raynaud manifestation), and 2) varying lengths of disease duration as inclusion criteria for clinical trials. Disease duration definitions assessed included < 12 months, < 15 months, < 18 months, < 24 months and < 36 months using both definitions of disease onset.

Results: Baseline characteristics are in Table 1. There was no appreciable difference in mRSS trajectory patterns between using first SSc manifestation compared to first non-Raynaud manifestation as the definition of disease onset

Table 1: Baseline characteristics of first SSc and first non-Raynaud manifestation onset cohorts

	First SSc manifestation <36 months (n=481)	First non-Raynaud manifestation <36 months (n=514)
Mean age at first visit (±SD)	49.8 ±13.7	49.4 ± 13.8
Female	355 (74%)	382 (74%)
Caucasian	435 (90%)	468 (91%)
Median disease duration (years) from first SSc manifestation (IQR)	0.97 (0.66, 1.53)	1.04 (0.70, 1.84)
Median follow-up time in years (IQR)	9.6 (4.3, 16.2)	10.2 (4.5, 16.3)
Median number of clinic visits (IQR)	7 (4, 14)	14 (8, 23)
SKIN CHARACTERISTICS		
Mean mRSS (±SD) at 1st visit	24.6 ± 10.7	24.5 ± 10.6
Maximum mRSS during follow-up (mean ±SD)	31.2 ± 11.2	31.1 ± 11.1
Skin Thickness Progression Rate rapid	169 (35%)	194 (38%)
intermediate	158 (33%)	163 (32%)
slow	151 (32%)	154 (30%)
NON-CUTANEOUS DISEASE CHARACTERISTICS		
Tendon friction rubs present	219 (46%)	231 (46%)
Gastrointestinal involvement	215 (45%)	235 (46%)
Fibrosis on chest imaging	95/411 (23%)	103/440 (23%)
Renal crisis	42 (9%)	50 (10%)
Joint/tendon involvement	456 (92%)	484 (92%)
Myopathy	20 (4%)	22 (4%)
Pulmonary hypertension	9 (2%)	9 (2%)
AUTOANTIBODIES		
anti-RNA polymerase III	269 (56%)	273 (53%)
anti-Scl-70	121 (25%)	137 (27%)



(Figure 1). Compared to other disease durations, < 18 months of disease had >70% of patients fitting into trajectories with worsening cutaneous disease over the first six months of follow-up. Longer disease durations demonstrated that the majority of patients had trajectories showing an improvement in mRSS (regression to the mean) over six months.

Conclusion: Regardless of whether the first SSc or first non-Raynaud manifestation is used to define disease onset, duration of < 18 months at enrollment is preferable, despite the difficulty in identifying such patients. Longer disease duration criteria more frequently results in regression to the mean of the mRSS score, and may have contributed to prior negative trials. Given the weight of the mRSS in the combined response index (CRISS), this analysis likely applies to trials using the CRISS as an outcome.

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Abstract Number: 0392

Prevalence and Survival of Systemic Sclerosis (SSc) and Associated Interstitial Lung Disease (ILD) in Ontario, Canada over 10 Years

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
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Background/Purpose: Systemic sclerosis (SSc) is an autoimmune disease characterized by skin thickening, vascular lesions and fibrotic changes in various organs, mainly the lungs, heart, intestinal tract, kidneys, muscles and joints. Pulmonary complications of SSc are one of the leading causes of morbidity and mortality. Interstitial lung disease (ILD) is among the most common forms of lung disease associated with SSc. To date, no published study has generated population-based estimates of the prevalence of SSc-ILD in Canada. The objective of this study was to develop prevalence and survival estimates of SSc and SSc-ILD in Ontario, Canada using administrative data over 10 years.

Methods: Adult patients diagnosed with SSc between April 1, 2008 and March 31, 2018 were identified from the National Ambulatory Care Reporting System (NACRS) and Discharge Abstract Database (DAD) administrative databases, using ICD 10 CA codes. Patients with SSc were identified first, using M34 ICD-10 CA codes (M34.0, M34.1, M34.2, M34.8, and M34.9). SSc-ILD patients were identified if an additional one of J84.1, J84.8, J84.9 or J99.1 codes for lung disease was used after the SSc diagnosis. Prevalence estimates were determined for both SSc and SSc-ILD, based on the population of all eligible Ontario adults (~11.0 million as of fiscal 2017). Descriptive statistics and Kaplan Meier survival curves were generated.

Results: There were 3,111 unique patients identified as having SSc over 10 years. Of those, 559 (18%) were further identified as having SSc-ILD. At the start of fiscal year 2017/18 (final year of the cohort), there were 2,114 prevalent SSc cases for a cumulative prevalence of 19.12 per 100,000 persons from 2008/9 to 2017/18. Over the same time frame, there were 257 prevalent cases of SSc-ILD, generating a prevalence of 2.32 cases per 100,000 persons. At index date, mean age was approximately 57 and 58 years of age for SSc and SSc-ILD patients with 84% and 80% females in the groups. The survival rates at one, five and ten years after diagnosis for the SSc group were 84.96%, 64.45% and 44.88%, respectively. The SSc-ILD group survival rates at one, five and ten years were lower, at 77.12%, 44.41% and 22.02%, respectively.

Conclusion: This study provides the first population based estimates of SSc-ILD in Canada. Results confirm that the prevalence of SSc-ILD may fall within a Canadian threshold for drugs for 'other' rare disease. It also demonstrates the poor survival in SSc and especially when SSc-ILD is present.

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Abstract Number: 0393

Agreement Between Physician Evaluation and the Composite Response Index in Diffuse Cutaneous Systemic Sclerosis (CRISS)

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SESSION INFORMATION

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Background/Purpose: Diffuse cutaneous Systemic Sclerosis (dcSSc) is a morbid disease involving the skin and internal organs. The American College of Rheumatology has provisionally approved a Composite Response Index in dcSSc (CRISS) (1) as a global endpoint for trials in dcSSc. Based on changes after 1 year, a CRISS score of ≥0.6 is considered improved and < 0.6 not improved. While the CRISS has been adopted in several trials, it lacks definite validation. Our goal is to assess the agreement between the CRISS score and physicians' evaluation of dcSSc patient profiles. We hypothesized that there will be agreement on whether a patient has improved after 1 year. This would further validate the CRISS.

Methods: Patient profiles were created for 100 randomly selected dcSSc patients with < 5 years disease duration from a multicenter cohort. Patients were selected such that after 1 year of observation, 50 had improved and 50 had non-improved CRISS. The profiles described features used during the development of the CRISS at baseline and 1 year: patient and physician global; HAQ; modified Rodnan skin score; forced vital capacity; body mass index; patient assessed score (0-10) of their breathing, gastrointestinal symptoms, Raynaud's, pain, digital ulcers; number of digital ulcers; presence of renal crisis and tendon friction rubs; SF-36 Vitality and Physical component scores. A total of 15 physicians with SSc expertise were involved and each patient profile was rated by 3 different physicians. The majority opinion determined consensus on whether a patient was improved (physician rated "improved") or not improved (physician rated "stable", "worsened", or "unable to tell"). Kappa agreement between the CRISS and physician ratings was calculated.

Results: The mean age of patients was 51.8 ± 12.3 years with mean disease duration of 2.2 ± 1.3 years. Physician consensus was obtained in all patient profiles. All CRISS non-improvers were also rated as non-improved by physician consensus (Table 1). 12 CRISS improvers were rated as non-improved by physician consensus because their profiles were rated as "stable" or "unable to tell". The kappa agreement was substantial, κ (95%CI) =0.76 (0.64, 0.88). The agreement between physician assessment prior to consensus and the CRISS remained substantial, κ (95%CI) = 0.70 (0.62, 0.78).

Table 1: Agreement of physician consensus rating with CRISS score

	Improved CRISS ≥ 0.6	Not improved CRISS < 0.6	Total
Improved by physician consensus (n)	38	0	38
Not improved by physician consensus (n)	12	50	62
Total (n)	50	50	100

Kappa (95%CI) = 0.76 (0.64, 0.88)

Table 1. Agreement of physician consensus rating with CRISS score; Kappa (95%CI) = 0.76 (0.64, 0.88)

Conclusion: There was substantial agreement between the dichotomous CRISS rating and physician assessment of dcSSc patients after 1 year. This supports the use of a dichotomous CRISS cut-off at 0.6 for improvement versus non-improvement. All CRISS non-improvers were also rated as not improved by physicians, although the CRISS was less conservative than physicians in assessing improvement. Physicians were more likely to report patients as stable or report that improvement was difficult to determine.

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Abstract Number: 0394

Prevalence of a Diagnosis of Osteopenia/Osteoporosis Amongst Patients with Systemic Sclerosis and Identification of Associated Clinical Factors

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

Table 1. Associations of demographic characteristics with prevalence of diagnosis of osteopenia/osteoporosis (OP) in systemic sclerosis (SSc) patients

	Sample size	Number of patients with diagnosis of OP	Prevalence of diagnosis of OP (%)	95% CI (%)	*p* value [a]
Total	348	144	41.4	(36.2,46.6)	
Age at last visit (years)					**<0.001**
>18 to 50	92	16	17.4	(9.6,25.1)	
>50 to 65	145	70	48.3	(40.1,56.4)	
>65	111	58	52.3	(43.0,61.5)	
Race					0.33
White	209	88	42.1	(35.4,48.8)	
Asian	38	20	52.6	(36.8,68.5)	
Black or Native American	15	5	33.3	(9.5,57.2)	
Other or Unknown	86	31	36.0	(25.9,46.2)	
Gender					**0.01**
Female	305	134	43.9	(38.4,49.5)	
Male	43	10	23.3	(10.6,35.9)	

Abbreviation: OP = osteopenia/osteoporosis
a. *p* values were calculated from chi-squares test

Table 2. Treatment in systemic sclerosis (SSc) patients with and without diagnosis of osteopenia/osteoporosis (OP)

	Sample size n (%) [a]	Diagnosis of OP n (%)	No diagnosis of OP n (%)	*p* value [b]
Total	348	144	204	
Corticosteroids	290(83.3)	114(87.7)	112(70.0)	**<0.001**
High dose [c]	256(73.6)	103(85.8)	96(70.6)	**<0.01**
>= 6 months	233(67.0)	63(57.3)	43(35.0)	**<0.001**
Immuno-suppressants	348(100.0)	68(47.2)	57(27.9)	**<0.001**
Mycophenolate	348(100.0)	38(26.4)	28(13.7)	**0.01**
Hydroxychloroquine	348(100.0)	15(10.4)	28(13.7)	**0.05**
Methotrexate	348(100.0)	12(8.3)	16(7.8)	0.64
Azathioprine	348(100.0)	14(9.7)	7(3.4)	**<0.01**
Cyclophosphamide	348(100.0)	6(4.2)	5(2.5)	0.67
Rituximab	348(100.0)	1(0.7)	1(0.5)	0.11
Abatacept	348(100.0)	1(0.7)	1(0.5)	0.75
Other	348(100.0)	8(5.6)	3(1.5)	**0.02**
PPI	347(99.7)	129(89.6)	167(82.3)	0.06

Abbreviation: OP = osteopenia or osteoporosis, PPI = proton-pump inhibitor
a. n is the number of patients with available test results. Percentage = n / total number of enrolled subjects (348).
b. *p* values were calculated from chi-squares test.
c. High dose of corticosteroids treatment is defined as greater than 7.5 mg of prednisone equivalent daily.

Background/Purpose: This study aims to determine the prevalence of a diagnosis of osteopenia/osteoporosis (OP) in systemic sclerosis (SSc) patients and to identify the clinical and serologic features independently associated with OP in SSc patients.

Methods: This is a cross-sectional study of 348 adult patients who visited the Stanford Rheumatologic Dermatology Clinic from January 2006 to March 2016 and were diagnosed with SSc according to the revised 2013 ACR/EULAR criteria for SSc. We compared the clinical characteristics, autoantibodies, and treatment of SSc patients with a diagnosis of OP to those without a diagnosis of OP. We used logistic regression analyses to identify clinical characteristics and autoantibodies associated with a diagnosis of OP in SSc patients.

Results: The prevalence of a diagnosis of OP in our SSc cohort was 41.4% (144/348, 95% CI: 36.2%, 46.6%) and was significantly higher in female patients and those >50 years of age (Table 1). Patients with a diagnosis of OP had longer disease duration and were more likely to have sclerodactyly, telangiectasias, interstitial lung disease (ILD), and gastroesophageal reflux. Patients with a diagnosis of OP were more commonly treated with corticosteroids and

Table 3. Odds ratios (ORs) and 95% confidence intervals (CIs) for the association between clinical characteristics and autoantibodies and the diagnosis of osteopenia/osteoporosis

	Crude model		Adjusted model [a]	
	OR	95% CI	OR	95% CI
Follow-up time (years)	**1.08**	**(1.03, 1.13)**	1.03	(0.97, 1.10)
Diffuse subtype	0.76	(0.48, 1.19)	0.87	(0.46, 1.66)
Maximum mRSS > 11	0.95	(0.60, 1.50)	0.91	(0.49, 1.71)
Disease duration from first RP symptom	**1.04**	**(1.02, 1.06)**	1.03	(1.00, 1.06)
Disease duration from first non-RP symptom	**1.06**	**(1.03, 1.09)**	**1.05**	**(1.01, 1.08)**
Calcinosis	1.61	(1.00, 2.58)	1.17	(0.63, 2.15)
Digital ulcers	1.22	(0.79, 1.88)	1.06	(0.59, 1.89)
Sclerodactyly	**1.94**	**(1.01, 3.71)**	1.63	(0.72, 3.7)
Telangiectasias	**1.89**	**(1.14, 3.13)**	1.54	(0.8, 2.96)
Chronic renal disease	0.88	(0.45, 1.73)	0.56	(0.2, 1.53)
Scleroderma renal crisis	0.86	(0.31, 2.43)	0.47	(0.12, 1.81)
ILD	**1.86**	**(1.19, 2.91)**	1.35	(0.76, 2.42)
PAH	1.43	(0.87, 2.35)	1.04	(0.55, 1.97)
GERD	**1.95**	**(1.01, 3.77)**	1.79	(0.71, 4.49)
Malabsorption	0.75	(0.18, 3.2)	0.25	(0.03, 2.49)
Esophageal dysmotility	1.39	(0.83, 2.34)	1.57	(0.78, 3.16)
Arthritis	1.38	(0.82, 2.3)	1.06	(0.55, 2.04)
ACA	1.23	(0.76, 1.98)	1.46	(0.76, 2.79)
Anti-Scl-70	1.12	(0.65, 1.94)	1.43	(0.68, 3.01)
U1-RNP	1.47	(0.7, 3.08)	1.18	(0.49, 2.86)
Anti-PM/Scl	3.89	(0.72, 21.12)	2.07	(0.28, 15.39)
Anti-beta-2-glycoprotein	1.72	(0.78, 3.81)	1.71	(0.61, 4.78)
Anti-cardiolipin	0.73	(0.34, 1.59)	0.80	(0.3, 2.17)
Immunosuppressant	**1.99**	**(1.29, 3.08)**	**2.15**	**(1.18, 3.93)**
PPI	1.85	(0.97, 3.53)	1.88	(0.7, 5.03)

Abbreviations: mRSS = modified Rodnan skin score, ILD = interstitial lung disease, PAH = pulmonary artery hypertension, GERD = gastroesophageal reflux, ACA = anti-centromere antibody, RNP = ribonucleoprotein, PPI = proton-pump inhibitor

a. Model adjusted for common risk factors including age, gender, race, smoking history, BMI, and corticosteroids treatment.

non-corticosteroids immunosuppressants (Table 2). Longer disease duration and non-corticosteroid immunosuppressant use were significantly associated with a higher odds of diagnosis of OP in logistic regression models adjusted for common risk factors for OP including age, race, gender, smoking history, body mass index, and corticosteroid treatment (Table 3).

Conclusion: More than 40% of SSc patients have a diagnosis of OP during the course of disease. Longer disease duration and non-corticosteroid immunosuppressant use increased the odds of diagnosis of OP in SSc patients.

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Abstract Number: 0395

African Ancestry-Specific Variants Regulate TGFB3 Expression in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

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Background/Purpose: African American (AA) patients have a higher prevalence of SSc than European Americans (EA). Adding to this health disparity, AA SSc patients are more likely to present with pulmonary involvement leading to significant morbidity and mortality. Samples from the Genome Research in African American Scleroderma Patients (GRASP) cohort were used for a genome-wide association analysis (GWAS) study in AA SSc patients. Intronic variants within the intraflagellar transport 43 (*IFT43)* gene were identified as the top non-*HLA* loci that were significant at the genome-wide level. These variants were in tight linkage disequilibrium with each other and were African-ancestry specific.

Methods: Expression quantitative trait loci (eQTL) analysis of fibroblast data from the Genotype-Tissue Expression (GTEx) project was performed for the *IFT43* variants. Assay for transposase-accessible chromatin with high-throughput sequencing (ATAC-seq) and DNase I hypersensitive sites sequencing (DNase-Seq) sample data from the GEO and ENCODE databases were downloaded and filtered to exclude poor-quality samples. 251 samples from primary cells and tissues, covering 76 distinct primary tissues and cell types, were analyzed further. Real-time PCR (RT-PCR) was performed on primary fibroblast cells with and without the *IFT43* risk variants. Two fibroblast cell lines, BJ and IMR-90, were obtained and processed for ATAC-Seq and RNA-Seq.

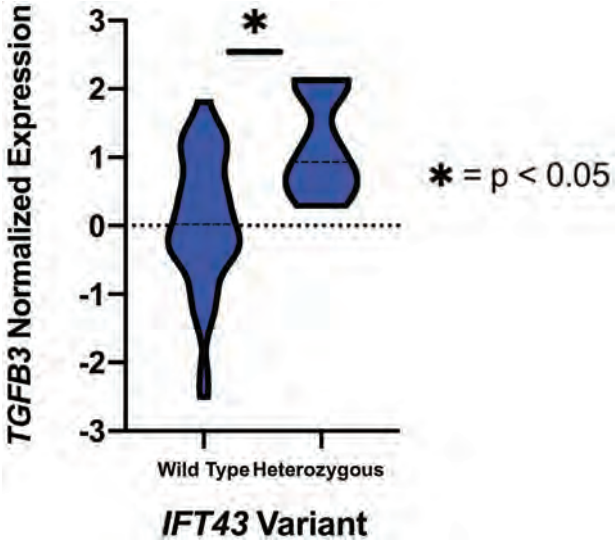

Figure 1. GTEx TGFB3 Expression.

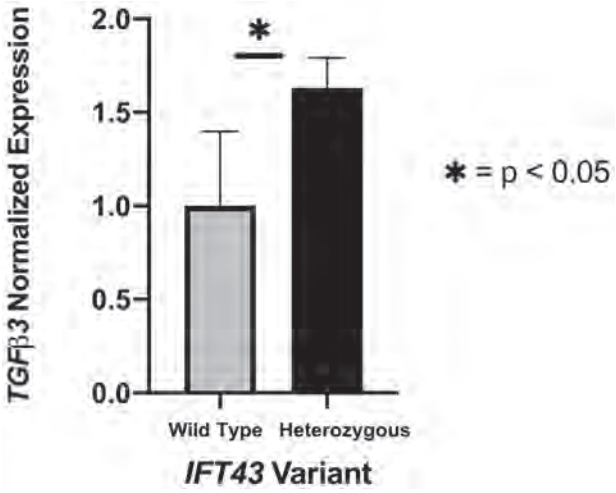

Figure 2. RT-PCR for TGFB3 expression.

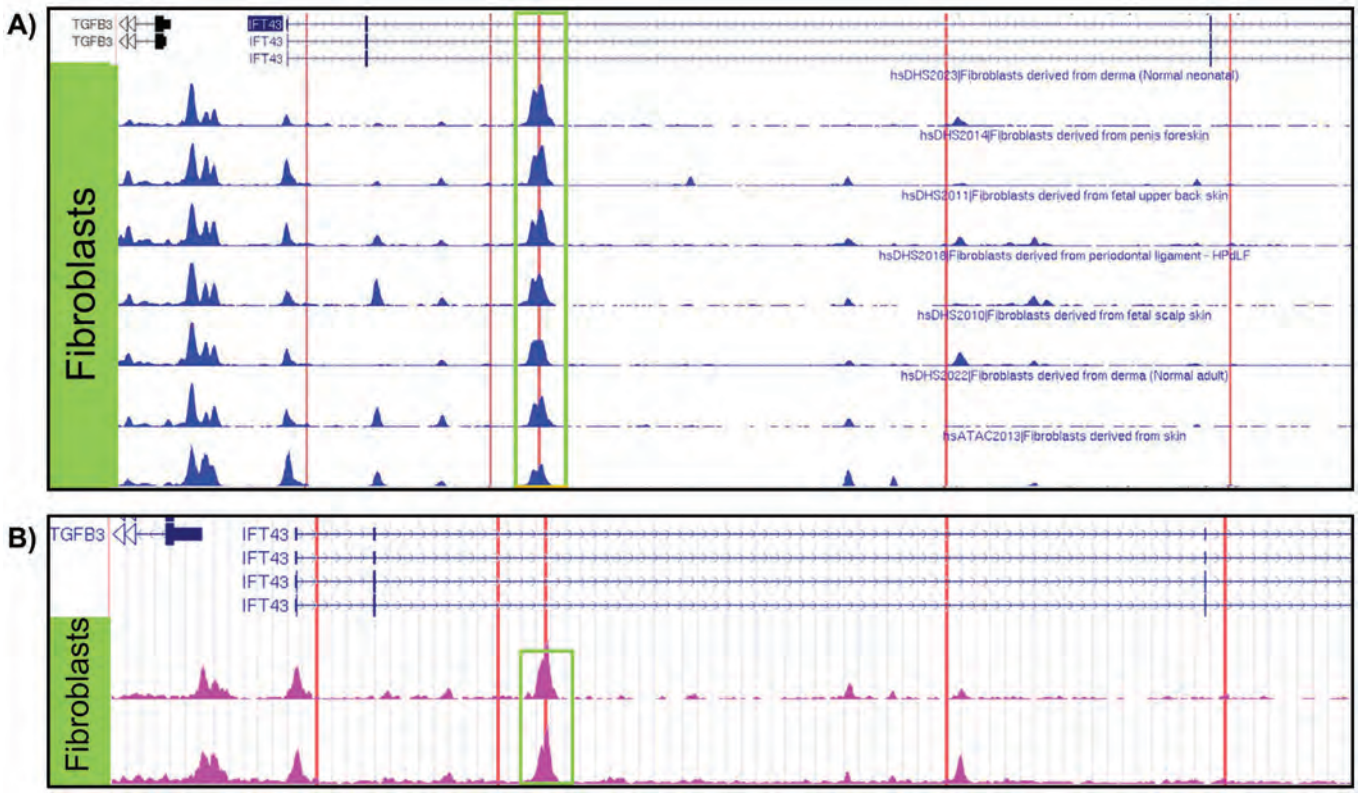

Figure 3. A) ATAC-Seq and DNAse-Seq tracks from ENCODE database showing accessible chromatin in fibroblasts. B) ATAC-Seq results from obtained BJ and IMR-90 fibroblast cell lines. Red lines represent location of IFT43 variants.

Results: eQTL analysis of fibroblast data from GTEx revealed increased expression of *TGFB3* in samples with the *IFT43* minor variants, suggesting that *TGFB3* expression was likely being regulated by these *IFT43* intronic variants (Figure 1). RT-PCR for *TGFB3* expression was performed on fibroblasts cells from healthy AA individuals. Individuals heterozygous for the *IFT43* minor variant had 1.6-fold higher *TGFB3 expression* compared to wildtype individuals (Figure 2). Bioinformatic analysis of ATAC-Seq and DNase-Seq data for fibroblasts showed that one of the SSc-associated *IFT43* variants was within an open, accessible chromatin region (Figure 3A). ATAC-Seq analysis of the BJ and IMR-90 fibroblast cell lines confirmed accessible chromatin at the site of one of the *IFT43* variants (Figure 3B).

Conclusion: Based on these results, we hypothesize that the *IFT43* variants overlap *cis*-regulatory modules (i.e. enhancer elements) and disrupt transcription factor binding, leading to altered *TGFB3* gene expression and function in SSc patients. TGFB3 could be regulating fibrosis via the canonical TGFB pathway or be inducing pathogenic Th17 cell development. Future directions include deletion of these *IFT43 cis*-regulatory modules in fibroblast cell lines utilizing CRISPR-Cas9 and assessing for changes in *TGFB3* gene expression. ChIP-Seq will be used for identifying transcription factor binding at the site of SSc-associated variants. This work implicates *TGFB3* as a novel therapeutic target in SSc, especially with regard to regulating fibrosis and autoimmunity. An isoform-selective TGFB inhibitor (blocking TGFB1 and -B3) is in early phase clinical trials in SSc. Identifying SSc patients based on variants increasing TGFB3 expression would provide an ideal target population for such a therapeutic agent.

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Safety and Efficacy of Subcutaneous Tocilizumab in Systemic Sclerosis: Results from the Open-Label Period of a Phase 3 Trial

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SESSION INFORMATION
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Background/Purpose: The anti–interleukin-6 (IL-6) receptor-α antibody tocilizumab (TCZ) demonstrated skin score improvement and forced vital capacity (FVC) preservation in patients with systemic sclerosis (SSc) in a phase 2 randomized controlled trial.[1,2] Data from the 48-week, double-blind (DB), placebo (PBO)-controlled period of the focuSSced phase 3 trial were previously presented,[3] and open-label (OL) data up to week 96 are presented to assess the long-term safety and efficacy of TCZ in SSc patients.

Methods: Adult patients with active SSc (≤60-month duration, modified Rodnan skin score [mRSS] 10-35, and elevated acute-phase reactants) treated with PBO or TCZ in the DB period received OL TCZ 162 mg SC weekly from weeks 48 to 96 in the OL period (PBO→OL TCZ and TCZ→OL TCZ, respectively). Exploratory analysis of data up to week 96 included no formal statistical analyses. Changes in mRSS and percent predicted FVC (ppFVC) were assessed. The study was conducted in accordance with the principles of the Declaration of Helsinki and received IRB approval.

Results: Overall, 92 of 105 TCZ (88%) and 89 of 107 PBO (83%) patients entered the OL TCZ treatment period at week 48, and 85 of 105 TCZ→OL TCZ (81%) and 82 of 107 PBO→OL TCZ (77%) patients completed treatment up to week 96. Continued decline in mRSS was observed in the OL period for PBO→OL TCZ and TCZ→OL TCZ patients (Table). Change in ppFVC for patients who switched from PBO to TCZ (PBO→OL TCZ) was comparable between weeks 48 and 96 (OL period) to the change in patients who received TCZ from BL to week 48 in the DB period (Table). Rates (95% CI) of serious adverse events from weeks 48 to 96 were 15.8 (8.6, 26.5) per 100 PY for TCZ→OL TCZ patients, 14.8 (7.9, 25.3) per 100 PY for PBO→OL TCZ patients, and 15.4 (11.0, 20.9) for all-TCZ exposure over 96 weeks (n = 193). Rates (95% CI) of serious infections were 2.3 (0.3, 8.1) per 100 PY for TCZ→OL TCZ patients, 3.4

Table 1. Change in Efficacy From Baseline

	Baseline to Week 48		Baseline to Week 96		Week 48 to Week 96	
	PBO	TCZ	PBO→OL TCZ	TCZ→OL TCZ	PBO→OL TCZ	TCZ→OL TCZ
mRSS, mean (95% CI)[a]	–5.3 (–6.9, –3.7) n = 92	–6.7 (–8.0, –5.4) n = 97	–8.4 (–10.0, –6.8) n = 83	–9.6 (–10.9, –8.4) n = 85	–2.5 (–3.3, –1.6) n = 82	–2.3 (–3.2, –1.5) n = 85
ppFVC, mean (95% CI) [median]	–4.1 (–5.8, –2.4) [–3.9] n = 92	–0.2 (–1.6, 1.2) [–0.7] n = 94	–3.3 (–5.1, –1.5) [–3.1] n = 79	–0.5 (–2.4, 1.3) [–1.4] n = 84	0.6 (–0.7, 1.9) [0.3] n = 78	–0.3 (–1.7, 1.1) [0.0] n = 82
Decline in ppFVC ≥10%, n/N (%)[a]	15/91 (16.5)	5/93 (5.4)	14/79 (17.7)	11/84 (13.1)	2/78 (2.6)	8/82 (9.8)
Improvement in ppFVC >0% change, n/N (%)[a]	26/91 (28.6)	43/93 (46.2)	22/79 (27.8)	35/84 (41.7)	39/78 (50.0)	40/82 (48.8)
Improvement in ppFVC ≥10% change, n/N (%)[a]	1/91 (1.1)	8/93 (8.6)	4/79 (5.1)	9/84 (10.7)	4/78 (5.1)	3/82 (3.7)

*Observed data. NA, not assessed.

(0.7, 10.0) per 100 PY for PBO→OL TCZ patients, and 3.0 (1.3, 5.9) for all TCZ exposure over 96 weeks. One death occurred during the OL period in each arm (TCZ→OL TCZ, pulmonary hypertension; PBO→OL TCZ, brain injury).

Conclusion: Although OL data have to be interpreted with caution, results from OL TCZ treatment show numeric improvements in mRSS and FVC preservation similar to those of the DB period, with a beneficial effect on trajectory of FVC decline in patients who switched from PBO to TCZ. Long-term safety results were consistent with the known safety profile of TCZ, and no new or unexpected events were observed.

References

1. Khanna D et al. *Lancet* 2016;387:2630-40; 2. Khanna D et al. *Ann Rheum Dis.* 2018;77:212-20; 3. Khanna D et al. *Arthritis Rheumatol* 2018;70(suppl 10). Abstract 898.

Disclosure: D. Khanna, Bayer, 2, BMS, 2, Horizon, 2, Pfizer, 2, NIH, 2, Immune Tolerance Network, 2, Eicos Sciences Inc, 4, Acceleron,, 5, Actelion,, 5, Abbvie,, 5, Amgen,, 5, Bayer,, 5, Boehringer Ingelheim, 5, CSL Behring, 5, Corbus,, 5, Galapagos,, 5, Genentech/Roche, 5, GSK, 5, Horizon, 5, Merck,, 5, Mitsubishi Tanabe Pharma, 5, Sanofi-Aventis, 5, United Therapeutics, 5, Impact PH, 9, Scleroderma Development, 6, CiviBioPharma/Eicos Sciences Inc, 6; **C. Lin**, Genentech/Roche, 1, 3; **H. Spotswood**, Roche Products Ltd, 1, 3; **J. Siegel**, Roche, 1, Gilead Sciences, 3; **D. Furst***, Actelion, 1, 2, Amgen, 1, 2, BMS, 1, Corbus, 1, 2, Galapagos, 1, 2, GSK, 1, NIH, 1, Norvatis, 1, 2, Pfizer, 1, 2, Sanofi, 1, Roche/Genentech, 1, Gilead, 1, Horizon, 1, 2, Kadmon, 1, Talaris, 1, 2, CMC Connect (McCann Health Company), 8, Cytori, 5, AbbVie, 5; **C. Denton**, Janssen, 1, GlaxoSmithKline, 1, 2, Bayer, 1, Sanofi, 1, Inventiva, 1, 2, Boehringer Ingelheim, 1, Roche, 1, Bristol-Myers Squibb, 1, CSL Behring, 1, 2, UCB, 1, Leadiant Biosciences, 1, Corbus Pharmaceuticals, 1, Acceleron Pharma, 1, Horizon Therapeutics, 1, Forbius, 1, Servier, 1.

Abstract Number: 0397

Assessing Adherence to Screening of Systemic Sclerosis-Related Lung Disease

Matthew Herrmann[1] and Zineb Aouhab[1], [1]Loyola University Medical Center, Maywood, IL

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Feared complications of systemic sclerosis (SSc) affect the pulmonary system, with pulmonary hypertension and interstitial lung disease being common causes of mortality. Baseline and annual transthoracic echocardiography (TTE) screening for pulmonary hypertension in asymptomatic patients is recommended by experts

Table 1: Baseline Demographics and Clinical Characteristics

Variable	*n* (%)
Sex	
Female	57 (87.69)
Male	8 (12.31)
Race	
White	40 (61.54%)
Black	14 (21.54)
Asian/Other	11 (16.92)
Antibody positivity	
Centromere	25 (38.46)
Scl-70	9 (13.85)
Nucleolar ANA	14 (21.54)
Other	17 (26.15)
Respiratory symptoms at baseline	
Yes	29 (44.62)
No	36 (55.38)

Chart 1: Primary Outcome

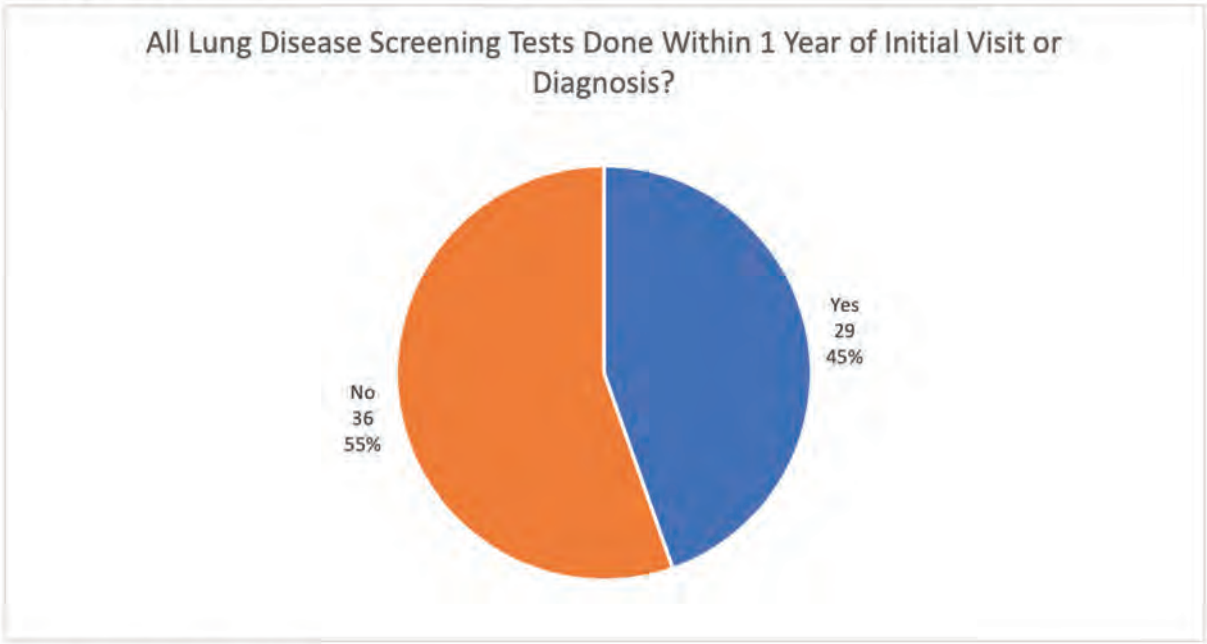
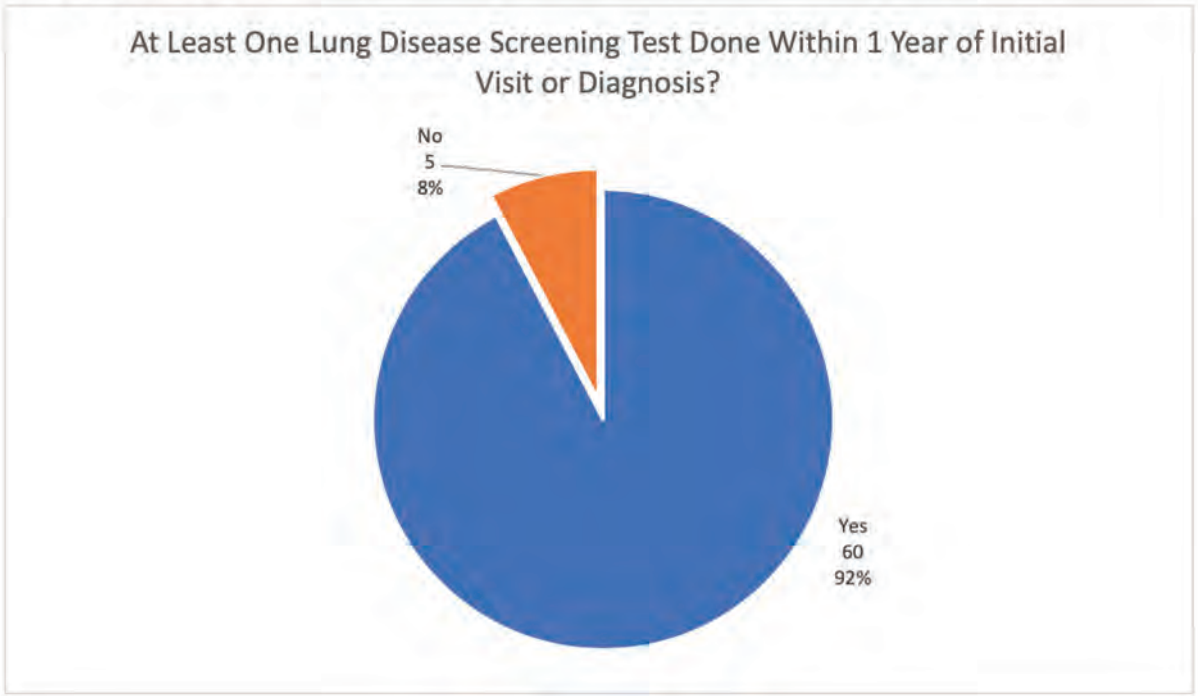


Chart 2: Secondary Outcome



from the American College of Cardiology, American Heart Association, European Society of Cardiology, and European Respiratory Society.[1] For screening of interstitial lung disease (ILD) in SSc, it is recommended that computed tomography (CT) of the chest in addition to pulmonary function tests (PFTs) be obtained at baseline. Based on expert opinion, PFTs should then be obtained every two years in asymptomatic patients with normal diffusing capacity.[2]

The aim of our quality improvement study was to assess the compliance rate of the Division of Rheumatology at Loyola University Medical Center in screening patients for SSc-related lung disease within one year of diagnosis, or at the initial encounter in those patients with a preexisting diagnosis of SSc.

Table 2: Secondary Outcomes

Variable	Median Frequency of Tests/Patient Years (IQR)
Pulmonary Function Tests	0.83 (0.19-1.0)
Transthoracic Echocardiogram	1.0 (0.41-1.75)

Methods: Patients with a diagnosis of SSc at Loyola University Medical Center between January 1, 2010 and June 1, 2019 were screened for study inclusion. Medical records were retrospectively reviewed and data collected included demographic information and dates of PFTs, TTEs, and chest CT scans. The primary endpoint was the proportion of patients who have all three lung disease screening tests done within one year of diagnosis or at the initial encounter in patients with a preexisting diagnosis of SSc. Secondary endpoints included the proportion of patients having at least one screening test done within this same time frame, as well as the frequency of follow-up PFTs and TTEs. Nonparametric univariate statistics were used to quantify the frequency in which SSc patients had PFTs and TTEs performed.

Results: A total of 122 patients were screened, and 65 fulfilled inclusion criteria. The primary outcome was reached in 29 patients (44.62%), and not reached in 36 patients (55.38%). At least one lung disease screening test was performed within one year of diagnosis or initial visit in 60 patients (92.31%), and not performed in 5 patients (7.69%). Of the three lung disease screening tests CT of the chest was obtained the most infrequently, with 35 patients (53.85%) having the test performed, and 30 patients (46.15%) not having the test performed. The median number of PFTs per patient years was 0.83 (IQR 0.19-1.0), while the median number of TTEs per patient years was 1.0 (IQR 0.41-1.75).

Conclusion: Our study showed that while the majority of SSc patients have at least one lung disease screening test within one year of diagnosis or initial visit, only about half of the patients had CT of the chest performed. Several cohorts involving SSc patients have suggested that more than half of patients may have ILD at diagnosis despite an absence of symptoms. Therefore, efforts should be made to obtain CT scans as early as possible in the course of diagnosis, and further quality improvement measures should be instituted to help achieve this goal.

1. Galie N, et al. *Eur Respir J*2015; 46: 903–975.

2. Kane GC, et al. *Respir Med* 1996; 90:223.

Disclosure: M. Herrmann, None; **Z. Aouhab**, None.

Abstract Number: 0398

Chest CT Ordering Practices at Expert Scleroderma Centers in the United States

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is the leading cause of death in patients with systemic sclerosis (SSc). Although pulmonary function tests (PFTs) are commonly used to screen for ILD in patients with SSc, studies have shown that they lack sensitivity for the detection of ILD. Moreover, although high resolution computed tomography (HRCT) scan of the chest is the gold standard test for detection of ILD, there is no consensus among rheumatologists regarding the use of HRCT to screen for ILD in their SSc patients. The aims of this study were to describe the HRCT ordering practices at expert SSc centers in the US, and to determine which patient characteristics are associated with HRCT ordering.

Methods: We performed a retrospective cohort study of patients enrolled in the Collaborative National Quality and Efficacy Registry (CONQUER) at 13 sites in the US between June 6, 2018, and February 1, 2020. CONQUER is a US-based, multicenter cohort of adults with SSc who met 2013 ACR/EULAR Classification Criteria and had a disease duration ≤5 years from the 1st non-Raynaud's symptom at enrollment. We used the Student's t test, chi square test, and Fisher's exact test, as appropriate, to compare baseline characteristics between participants who did and did not undergo HRCT. We performed univariate logistic regression (LR) followed by multivariable LR to determine which patient characteristics were associated with HRCT ordering. Each variable that attained a p-value< 0.1 in the univariate analysis was included in the final multivariable LR model, as were age and sex. Statistical significance in the univariate and multivariable models was defined as a p-value< 0.05.

Results: 356 SSc patients were enrolled in CONQUER, of whom 285 (80%) underwent HRCT at some point during their SSc disease course. Among those who underwent HRCT compared to those who did not, a smaller proportion were centromere positive (9.5% vs. 22.5%) and a greater proportion had crackles on exam (23.5% vs. 9.9%). SSc patients who underwent HRCT had lower forced vital capacity (FVC), forced expiratory volume in 1 second (FEV1), and diffusion capacity for carbon monoxide (DLCO) than those who did not (Table 1). In univariate analyses, the following variables were statistically significantly associated with HRCT ordering: crackles on pulmonary exam, FVC< 80%, FEV1< 80%, total lung capacity (TLC)< 80%, missing TLC%, and DLCO< 60% (Table 2). A positive centromere antibody was negatively associated with HRCT ordering. In the final multivariable LR model, positive centromere

Table 1. Baseline characteristics of the CONQUER cohort

Table 1. Baseline characteristics of the CONQUER cohort

	Overall (N = 356)	HRCT Ever Performed: Yes (N = 285)	HRCT Ever Performed: No (N = 71)	P-value
Age at baseline visit	53.8 (42.3, 62.7)	53.7 (42.5, 63.1)	55.0 (40.4, 61.1)	0.801[1]
Sex				0.869[2]
Female	292 (82.0%)	235 (82.5%)	57 (80.3%)	
Male	64 (18.0%)	50 (17.5%)	14 (19.7%)	
Race				0.245[3]
White	273 (76.7%)	213 (74.7%)	60 (84.5%)	
Black or African American	43 (12.1%)	38 (13.3%)	5 (7.0%)	
Other	31 (8.7%)	26 (9.1%)	5 (7.0%)	
Missing	9 (2.5%)	8 (2.8%)	1 (1.4%)	
Ethnicity				0.259[3]
Not Hispanic or Latino	306 (86.8%)	253 (88.8%)	56 (78.9%)	
Hispanic or Latino	39 (11.0%)	29 (10.2%)	10 (14.1%)	
Missing	8 (2.2%)	3 (1.1%)	5 (7.0%)	
Employment status				0.786[2]
Full-time	165 (46.3%)	131 (46.0%)	34 (47.9%)	
Not full-time	171 (48.0%)	136 (48.4%)	33 (46.5%)	
Missing	20 (5.6%)	16 (5.6%)	4 (5.6%)	
Ever smoked				0.837[2]
No	237 (66.6%)	189 (66.3%)	48 (67.6%)	
Yes	119 (33.4%)	96 (33.7%)	23 (32.4%)	
Disease duration (years)[4]	2.6 (1.3, 3.8)	2.6 (1.4, 3.8)	2.6 (1.1, 3.8)	0.710[1]
ANA				0.561[3]
Negative	23 (6.5%)	17 (6.0%)	6 (8.5%)	
Positive	305 (85.7%)	247 (86.7%)	58 (81.7%)	
Missing	28 (7.9%)	21 (7.4%)	7 (9.9%)	
Anti-Centromere				0.006[2]
Negative	228 (64.0%)	191 (67.0%)	37 (52.1%)	
Positive	43 (12.1%)	27 (9.5%)	16 (22.5%)	
Missing	85 (23.9%)	67 (23.5%)	18 (25.4%)	
Anti-Scl-70				0.661[2]
Negative	212 (59.6%)	167 (58.6%)	45 (63.4%)	
Positive	100 (28.1%)	83 (29.1%)	17 (23.9%)	
Missing	44 (12.4%)	35 (12.3%)	9 (12.7%)	
Anti-RNA Polymerase III				0.256[2]
Negative	167 (46.9%)	139 (48.8%)	28 (39.4%)	
Positive	85 (23.9%)	68 (23.9%)	17 (23.9%)	
Missing	104 (29.2%)	78 (27.4%)	26 (36.6%)	
Baseline supplemental oxygen use				0.749[2]
No	337 (94.7%)	268 (94.0%)	69 (97.2%)	
Yes	16 (4.5%)	14 (4.9%)	2 (2.8%)	
Missing	3 (0.8%)	3 (1.1%)	0 (0.0%)	
Crackles on exam				0.011[2]
No	281 (78.9%)	217 (76.1%)	64 (90.1%)	
Yes	74 (20.8%)	67 (23.5%)	7 (9.9%)	
Missing	1 (0.3%)	1 (0.4%)	0 (0.0%)	
SSc subtype				0.165[2]
Limited cutaneous	140 (39.3%)	107 (37.5%)	33 (46.5%)	
Diffuse cutaneous	216 (60.7%)	178 (62.5%)	38 (53.5%)	
Modified Rodnan Skin Score (mRSS)	9.0 (4.0, 19.5)	10.0 (5.0, 22.0)	8.0 (3.0, 15.0)	0.246[1]
Limited cutaneous subtype	4.0 (2.0, 7.0)	5.0 (2.0, 7.0)	3.0 (2.0, 5.0)	0.030[1]
Diffuse cutaneous subtype	17.0 (9.0, 26.5)	17.5 (9.0, 26.0)	14.5 (9.0, 29.0)	0.969[1]
New York Heart Association (NYHA) functional class				0.460[2]
Class I, II	321 (90.2%)	255 (89.5%)	66 (93.0%)	
Class III, IV	33 (9.3%)	28 (9.8%)	5 (7.0%)	
Unknown	2 (0.6%)	2 (0.7%)	0 (0.0%)	
Participant global health[6]	4.0 (2.0, 6.0)	4.0 (2.0, 6.0)	3.0 (2.0, 5.0)	0.098[1]
Physician global health[7]	3.0 (2.0, 5.0)	3.0 (2.0, 5.0)	2.0 (1.0, 4.0)	0.057[1]
Physician global damage[8]	3.0 (2.0, 5.0)	3.0 (2.0, 5.0)	3.0 (1.0, 4.0)	0.055[1]
SHAQ breathlessness score[9]	1.0 (0.0, 3.0)	1.0 (0.0, 3.0)	0.0 (0.0, 3.0)	0.014[1]
mMRC dyspnea scale				0.198[2]
0	119 (33.4%)	91 (31.9%)	28 (39.4%)	
1	124 (34.8%)	106 (37.2%)	18 (25.4%)	
2-4	64 (18.0%)	51 (17.9%)	13 (18.3%)	
Unknown	49 (13.8%)	37 (13.0%)	12 (16.9%)	
FACIT dyspnea score	4.0 (1.4, 10.0)	4.5 (1.4, 10.0)	3.0 (1.0, 9.0)	0.664[1]
FVC (L)	2.8 (2.4, 3.5)	2.8 (2.3, 3.4)	3.3 (2.6, 3.9)	0.005[1]
FVC % predicted	84.0 (71.0, 96.0)	81.5 (69.5, 92.5)	92.5 (81.0, 114.0)	<0.001[1]
FVC % predicted				0.006[2]
<70%	71 (19.9%)	63 (22.1%)	8 (11.3%)	
70 to <80%	57 (16.0%)	52 (18.2%)	5 (7.0%)	
≥80%	182 (51.1%)	137 (48.1%)	45 (63.4%)	
Missing	46 (12.9%)	33 (11.6%)	13 (18.3%)	
FEV1 (L)	2.3 (1.9, 2.6)	2.2 (1.8, 2.7)	2.6 (2.2, 3.2)	0.655[1]
FEV1 % predicted	85.0 (72.0, 97.0)	84.0 (69.0, 92.0)	97.0 (82.0, 110.0)	<0.001[1]
FEV1 % predicted				0.009[2]
<70%	71 (19.9%)	64 (22.5%)	7 (9.9%)	
70 to <80%	43 (12.1%)	39 (13.7%)	4 (5.6%)	
≥80%	193 (54.2%)	146 (51.2%)	47 (66.2%)	
Missing	49 (13.8%)	36 (12.6%)	13 (18.3%)	
FEV1/FVC (actual)	82.0 (78.0, 88.0)	82.0 (78.0, 88.0)	82.0 (78.0, 86.7)	0.227[1]
TLC(L)	4.5 (3.8, 5.4)	4.4 (3.8, 5.2)	4.8 (4.2, 5.6)	0.844[1]
TLC % predicted	85.0 (74.0, 97.0)	84.0 (71.0, 95.0)	93.0 (83.0, 108.0)	0.542[1]
TLC % predicted category				0.019[2]
<70%	42 (11.8%)	36 (12.6%)	6 (8.5%)	
70 to <80%	33 (9.3%)	30 (10.5%)	3 (4.2%)	
≥80%	134 (37.6%)	96 (33.7%)	38 (53.5%)	
Missing	147 (41.3%)	123 (43.2%)	24 (33.8%)	
DLCO (mL/min/mmHg)	16.7 (12.3, 21.5)	16.4 (11.9, 21.1)	18.9 (14.2, 24.7)	0.009[1]
DLCO % predicted	70.0 (52.0, 88.0)	68.0 (50.0, 85.0)	77.0 (63.0, 93.0)	0.008[1]
DLCO % predicted category				0.081[2]
<60%	97 (27.2%)	87 (30.5%)	10 (14.1%)	
60 to <70%	43 (12.1%)	34 (11.9%)	9 (12.7%)	
70 to <80%	43 (12.1%)	34 (11.9%)	9 (12.7%)	
≥80%	101 (28.4%)	76 (26.7%)	25 (35.2%)	
Missing	72 (20.2%)	54 (18.9%)	18 (25.4%)	

Continuous variables are summarized using median (IQR) and categorical variables are summarized with counts and percentages. All hypothesis tests exclude missing and unknown data, except for the autoantibody and PFT % predicted categorical variables.

[1] T-test with unpooled variance estimates.

[2] Chi-squared test.

[3] Fisher's exact test.

[4] Disease duration: From first non-raynauds symptom to baseline visit.

[5] Class I (No limitations of physical activity), to Class IV (Impossibility of performing physical activity without symptoms; symptoms at rest. Dyspnea is present at rest and is worsened by even mild effort).

[6] How was your overall health in the last week? 0 (Excellent) to 10 (Extremely poor)

[7] How would you rate the participants overall health for the past week? 0 (Excellent) to 10 (Very poor)

[8] How much damage do you think the participant has from his/her scleroderma? 0 (No damage) to 10 (Very severe damage).

[9] In the past week how much have your breathing problems interfered with your daily activities? 0 (No interference) to 10 (Very severe interference).

[10] Describe your shortness of breath: 0 (I only get breathless with strenuous exercise) 1 (I get short of breath when hurrying on level ground or walking up a slight hill) to 4 (I am too breathless to leave the house or I am breathless when dressing).

HRCT = high resolution computed tomography of the chest; SHAQ = Scleroderma Health Assessment Questionnaire; mMRC = Modified Medical Research Council; FACIT = Functional Assessment of Chronic Illness Therapy; FVC = forced vital capacity; FEV1 = forced expiratory volume in 1 second; TLC = total lung capacity; DLCO = diffusion capacity for carbon monoxide

Table 2. Univariate analyses

Table 2. Univariable analyses

	HRCT Ever Performed	
	Odds ratio (95% CI)	P-value
Age at baseline visit	1.00 (0.98, 1.02)	0.800
Sex		0.672
Male	Reference	
Female	1.15 (0.58, 2.19)	
Race		0.213
White	Reference	
Black or African American	2.14 (0.88, 6.42)	
Other	1.46 (0.58, 4.47)	
Ethnicity		0.275
Hispanic or Latino	0.64 (0.30, 1.45)	
Not Hispanic or Latino	Reference	
Employment status		0.764
Full-time	Reference	
Not full-time	1.09 (0.63, 1.86)	
Ever smoked		0.836
No	Reference	
Yes	1.06 (0.61, 1.87)	
Disease duration (years)	1.04 (0.86, 1.25)	0.702
ANA		0.578
Negative	Reference	
Positive	1.50 (0.52, 3.80)	
Missing	1.06 (0.29, 3.78)	
Anti-Centromere		0.011
Negative	Reference	
Positive	0.33 (0.16, 0.67)	
Missing	0.72 (0.39, 1.37)	
Anti-Scl-70		0.675
Negative	Reference	
Positive	1.32 (0.72, 2.49)	
Missing	1.05 (0.49, 2.46)	
Anti-RNA Polymerase III		0.263
Negative	Reference	
Positive	0.81 (0.42, 1.60)	
Missing	0.60 (0.33, 1.11)	
Baseline supplemental oxygen use		0.412
No	Reference	
Yes	1.80 (0.49, 11.65)	
Crackles on exam		0.006
No	Reference	
Yes	2.82 (1.31, 7.03)	
SSc subtype		0.171
Limited cutaneous	Reference	
Diffuse cutaneous	1.44 (0.85, 2.44)	
Modified Rodnan Skin Score (mRSS)	1.02 (0.99, 1.04)	0.211
New York Heart Association (NYHA) functional class		0.446
Class I, II	Reference	
Class III, IV	1.45 (0.58, 4.39)	
Participant global health	1.10 (0.98, 1.23)	0.106
Physician global health	1.13 (1.00, 1.29)	0.051
Physician global damage	1.12 (1.00, 1.27)	0.058
SHAQ breathlessness score	1.06 (1.00, 1.20)	0.078
mMRC dyspnea scale		0.193
0	Reference	
1	1.81 (0.95, 3.54)	
2-4	1.21 (0.58, 2.60)	
FACIT dyspnea score	1.01 (0.97, 1.05)	0.666
FVC % predicted		0.001
<80%	2.91 (1.53, 5.85)	
≥80%	Reference	
Missing	0.83 (0.41, 1.77)	
FEV1 % predicted		0.002
<80%	3.01 (1.54, 6.37)	
≥80%	Reference	
Missing	0.89 (0.44, 1.87)	
FEV1/FVC (actual)	1.02 (0.99, 1.05)	0.158
TLC % predicted		0.007
<80%	2.90 (1.37, 6.76)	
≥80%	Reference	
Missing	2.03 (1.15, 3.65)	
DLCO % predicted		0.078
<80%	1.82 (0.99, 3.34)	
≥80%	Reference	
Missing	0.99 (0.49, 2.01)	

HRCT = high resolution computed tomography of the chest; SHAQ = Scleroderma Health Assessment Questionnaire; mMRC = Modified Medical Research Council; FACIT = Functional Assessment of Chronic Illness Therapy; FVC = forced vital capacity; FEV1 = forced expiratory volume in 1 second; TLC = total lung capacity; DLCO = diffusion capacity for carbon monoxide

Table 3. Multivariable model

Table 3. Multivariable model

	HRCT Ever Performed	
	Odds ratio (95% CI)	**P-value**
Age at baseline visit	1.00 (0.98, 1.03)	0.875
Sex		0.184
Male	Reference	
Female	1.70 (0.77, 3.61)	
Anti-Centromere		0.008
Negative	Reference	
Positive	0.27 (0.11, 0.62)	
Missing	0.57 (0.28, 1.17)	
Crackles on exam		0.252
No	Reference	
Yes	1.68 (0.70, 4.52)	
Physician global health	1.03 (0.82, 1.26)	0.799
Physician global damage	1.06 (0.96, 1.34)	0.489
SHAQ breathlessness score	1.02 (0.98, 1.12)	0.359
FVC % predicted		0.625
<80%	1.50 (0.66, 3.58)	
≥80%	Reference	
Missing	1.32 (0.33, 5.23)	
TLC % predicted		0.006
<80%	2.06 (0.73, 6.30)	
≥80%	Reference	
Missing	3.54 (1.60, 8.51)	
DLCO % predicted		0.256
<80%	0.94 (0.44, 1.98)	
≥80%	Reference	
Missing	0.38 (0.12, 1.27)	

N=314
Results are based on a multivariable model, adjusting for each of the predictors in this table.
HRCT = high resolution computed tomography of the chest; SHAQ = Scleroderma Health Assessment Questionnaire; FVC = forced vital capacity; TLC = total lung capacity; DLCO = diffusion capacity for carbon monoxide

antibody remained negatively associated and missing TLC% remained positively associated with HRCT ordering (Table 3).

Conclusion: 80% of SSc patients enrolled in CONQUER at 13 expert SSc centers in the US underwent HRCT. Abnormal PFTs and crackles were associated with HRCT ordering in univariate analyses. However, in the multivariable analysis, only a positive centromere antibody remained associated with a decreased odds of HRCT ordering and a

missing TLC% remained associated with an increased odds of HRCT ordering. Given the poor sensitivity of PFTs for the detection of SSc-ILD, research is needed about how to increase rheumatologists' HRCT ordering practices in their SSc patients.

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Abstract Number: 0399

A Heavy Burden of Calcinosis Reflects Cumulative Disease Damage in Scleroderma

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SESSION INFORMATION
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Background/Purpose: Ectopic calcification, or calcinosis, is a common complication of scleroderma. However, a subset of scleroderma patients has a heavy burden of calcinosis, which may have unique risk factors compared to a light burden of calcinosis.

Methods: We determined calcinosis burden of patients in the Johns Hopkins Scleroderma Center cohort database through chart review. A heavy burden was defined as calcinosis deposits in three or more body areas excluding the hands and fingers, mass-like or bulky deposits, and/or sheet-like or plaque-like deposits on physician exam. A light burden was defined as calcinosis present but not meeting the criteria for heavy burden by chart review. No calcinosis was defined as calcinosis recorded as absent in the Scleroderma Center database. We performed exploratory analyses comparing clinical, demographic, and serologic parameters by burden status. We then performed latent class analysis to identify scleroderma phenotypic classes followed by multinomial logistic regression to determine whether latent phenotypic classes and autoantibodies are independent risk factors for a light burden or a heavy burden of calcinosis.

Results: 29.4% (997/3388) of patients with scleroderma had calcinosis. 13.5% (130/963) had a heavy burden. The phenotypic class (Class 3 in Table 1) with predominantly diffuse skin disease as well as the greatest overall disease

Table. Association between calcinosis burden, phenotypic class, and autoantibodies among 3388 scleroderma patients, adjusting for race, disease duration, and sex*

	Estimate	SE	OR	95% CI	P
Light burden					
Disease duration (per year increase)	0.04	0.00	1.04	(1.03, 1.05)	<0.001
African American race	-0.44	0.12	0.64	(0.51, 0.82)	<0.001
Male sex	-0.35	0.12	0.70	(0.56, 0.89)	0.003
Scl70	0.13	0.17	1.14	(0.82, 1.59)	0.436
CENP-A	0.91	0.37	2.48	(1.20, 5.15)	0.015
CENP-B	-0.60	0.37	0.55	(0.27, 1.13)	0.102
RP11	0.08	0.30	1.09	(0.61, 1.94)	0.783
RP155	0.18	0.31	1.19	(0.64, 2.21)	0.574
PM75	0.25	0.27	1.29	(0.76, 2.18)	0.356
PM100	0.81	0.32	2.24	(1.19, 4.22)	0.013
Class 1	-1.36	0.25	0.26	(0.16, 0.42)	<0.001
Class 2	-0.01	0.17	0.99	(0.72, 1.38)	0.967
Class 3	1.00	0.15	2.71	(2.01, 3.65)	<0.001
Heavy Burden					
Disease duration (per year increase)	0.04	0.01	1.04	(1.03, 1.06)	<0.001
African-American race	-1.82	0.44	0.16	(0.07, 0.38)	<0.001
Male sex	-0.65	0.30	0.52	(0.29, 0.93)	0.027
Scl70	-0.30	0.37	0.74	(0.36, 1.52)	0.419
CENP-A	0.61	0.76	1.84	(0.42, 8.13)	0.422
CENP-B	-0.45	0.74	0.64	(0.15, 2.71)	0.544
RP11	-0.16	0.69	0.86	(0.22, 3.33)	0.823
RP155	0.08	0.70	1.08	(0.27, 4.26)	0.911
PM75	1.12	0.47	3.07	(1.23, 7.68)	0.024
PM100	1.40	0.50	4.04	(1.53, 10.68)	0.005
Class 1	-0.35	0.43	0.70	(0.30, 1.62)	0.406
Class 2	0.00	0.40	1.00	(0.45, 2.20)	0.992
Class 3	1.84	0.31	6.29	(3.42, 11.57)	<0.001

*Light burden and heavy burden are each compared to the group without calcinosis. Phenotypic classes 1-3 are assessed relative to the reference class 4.

Table 3: Multivariable model

severity was associated with an increased risk of both a heavy burden of calcinosis (OR 6.29, 95% CI 3.42-11.57; p< 0.001) and a light burden of calcinosis (OR 2.71, 95% CI 2.01-3.65; p< 0.001) compared to the reference class with predominantly limited skin disease (Class 4). The phenotypic class with predominantly sine skin disease (Class 1) was associated with a decreased risk of a light burden of calcinosis (OR 0.26, 95% CI 0.16-0.42; p< 0.001) compared to Class 4 but was not significantly associated with a high burden. The phenotype with predominantly diffuse skin disease but less severe extra-cutaneous disease compared to Class 3 (Class 2) was not associated with either a light or heavy burden of calcinosis. Autoantibodies to PM100 (OR 4.04, 95% CI 1.53 to 10.68; p=0.005) and PM75 (OR 3.07, 95% CI 1.23 to 7.68; p=0.024) were associated with an increased risk of a heavy burden of calcinosis.

Conclusion: Calcinosis burden may reflect cumulative scleroderma-related tissue damage. Independent of disease activity, autoantibodies to the PM/Scl complex are associated with a high burden of calcinosis, indicating the possibility of excess subclinical disease activity or aberrant tissue repair in patients with this unique immunologic response.

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Abstract Number: 0400

Outcomes of Systemic Sclerosis Hospitalizations by Hospital Teaching Status: Analysis of the National Inpatient Sample

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Background/Purpose: Systemic sclerosis (SSc) is a chronic autoimmune connective tissue disease that results in hospitalizations in different hospital settings. It is unclear if outcomes of SSc hospitalizations differ between teaching and non-teaching hospitals. This study aims to compare outcomes of SSc hospitalizations between teaching and nonteaching hospitals.

Methods: Data were abstracted from the National Inpatient Sample (NIS) Database. NIS is the largest inpatient admission database in the United States. It is a nationally representative sample of 20% of hospitalizations from approximately 1000 hospitals. The numbers in the databases are weighted to optimize national estimates. The NIS was searched for SSc hospitalizations in 2016 using ICD-10 code "M34" as the principal or secondary diagnosis. Only hospitalizations for patients aged ≥ 18 years were included. The primary outcome was inpatient mortality. Multivariate logistic regression analysis was used to adjust for confounders for the primary outcome. Secondary outcomes were hospital length of stay (LOS) and total hospital charges. Multivariate linear regression analysis was used to adjust for confounders for the secondary outcomes. Confounders adjusted for include age, sex, race, median income expected for zip code, Charleston comorbidity index, insurance status, hospital location/region, and bed size. STATA software was used to analyze the data.

Results: There were over 35 million discharges included in the 2016 NIS database. 30,965 hospitalizations were for patients aged ≥18 years, who had either a principal or secondary ICD 10 code for SSc. 22,280 of these hospitalizations (72%) were in teaching hospitals, while 8,685 hospitalizations (28%) were in nonteaching hospitals. The mean age for teaching hospital hospitalizations was 61.45 vs 64.56 for nonteaching hospitals (P< 0.0001). 1,395 (4.5%) hospitalizations resulted in inpatient mortality. Inpatient mortality occurred in 4.7% of hospitalizations in teaching hospitals vs 4.1 % in nonteaching hospitals (P=0.3164). The adjusted odds ratio (AOR) of inpatient mortality in teaching hospitals compared to nonteaching hospitals was 1.05 (95% CI 0.78-1.42, P=0.75). Mean LOS for hospitalizations in teaching hospitals was 6.67 vs 5.18 days for nonteaching hospitals. Hospitalizations in teaching hospitals have a mean increase in Adjusted LOS of 1.12 days (95% CI 0.69-1.54, P< 0.0001) compared to nonteaching hospitals. Total hospital charges for hospitalizations in teaching hospital was $75,943.58 vs $51,611.54 for nonteaching hospitals. Hospitalizations in teaching hospitals have an increase in adjusted total hospital charges of $16,333 compared to nonteaching hospitals (95% CI 9,005-23,660, P< 0.0001).

Conclusion: There was no statistically significant difference in inpatient mortality for SSc hospitalizations in teaching compared to nonteaching hospitals. SSc hospitalizations in teaching hospitals had younger patients, more LOS, and total hospital charges compared to nonteaching hospitals.

Disclosure: E. Edigin, None; **P. Eseaton**, None; **P. Ojemolon**, None.

Abstract Number: 0401

Prevalence and Characteristics of Systemic Sclerosis Patients Fulfilling the 2019 EULAR/ACR Classification Criteria for Systemic Lupus Erythematosus

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Table 1 – Among SSc patients who meet 2019 EULAR/ACR Classification Criteria for SLE (n = 40), frequency of criteria fulfilled

Domain	Item	n (%)
Constitutional		
	Fever	4 (10)
Hematologic		
	Leukopenia	8 (20)
	Thrombocytopenia	4 (10)
	Autoimmune hemolysis	0 (0)
Neuropsychiatric		
	Delirium	0 (0)
	Psychosis	0 (0)
	Seizure	2 (5)
Mucocutaneous		
	Alopecia	11 (28)
	Oral ulcers	4 (10)
	Subacute cutaneous lupus erythematosus or discoid lupus erythematosus	9 (23)
	Acute cutaneous lupus erythematosus	9 (23)
Serosal		
	Effusion	11 (28)
	Acute pericarditis	5 (13)
Musculoskeletal		
	Joint involvement	32 (80)
Renal		
	Proteinuria	2 (5)
	Class II or V lupus nephritis	1 (3)
	Class III or IV lupus nephritis	0 (0)
Antiphospholipid antibodies	Antiphospholipid	10 (25)
Complements		
	C3 or C4 low	9 (23)
	C4 and C4 low	8 (20)
SLE-specific antibodies		
	Anti-Smith	15 (38)
	Anti-dsDNA	13 (33)

Background/Purpose: Literature describing the overlap syndrome of SSc and SLE is limited and has employed a range of case definitions. Our study sought to use the new EULAR/ACR SLE classification criteria to define and characterize SSc-SLE cases among our center's SSc cohort.

Table 2 – Demographic, laboratory, and clinical differences among SSc-SLE overlap and non-overlap SSc patients

	SSc-SLE overlap (n = 40)	non-overlap SSc (n = 362)	p
Age at first visit (mean ± SD)	46.3 ± 12.7	48.2 ± 13.2	0.383
Female sex	40 (100)	309 (77)	**0.009**
Black or African American ethnicity	27 (68)	175 (48)	**0.021**
Fulfilled 2013 ACR/EULAR SSc classification criteria	33 (83)	331 (91)	0.067
EULAR/ACR SLE classification score (mean ± SD)	15.6 ± 5.0	1.8 ± 3.2	**< 0.001**
Initially purported to have SLE	17 (42.5)	26 (7.2)	**< 0.001**
SSc type			
Limited	30 (75)	189 (52)	**0.006**
Diffuse	10 (25)	168 (46)	**0.010**
Unclassified	0 (0)	5 (1)	1.000 †
SSc-specific autoantibody			
Negative	0 (0)	22 (6)	0.149 †
Anti-centromere	2 (5)	56 (16)	0.095 †
Anti-Scl70	4 (10)	80 (22)	0.099 †
Anti-U1RNP	12 (30)	24 (7)	**< 0.001**
Isolated nucleolar ANA	10 (25)	71 (20)	0.420
Anti-RNA polymerase III	1 (3)	36 (10)	0.154 †
Other	11 (28)	59 (16)	0.076
No result	0 (0)	14 (4)	0.378 †
Clinical features of SSc			
Raynaud's phenomenon			
None	1 (3)	13 (4)	1.000 †
Raynaud's only	23 (58)	169 (47)	0.194
with digital pitting	0 (0)	23 (6)	0.150 †
with digital ulcers	12 (30)	135 (37)	0.363
with digital gangrene	4 (10)	22 (6)	0.312 †
Renal crisis	2 (5)	21 (6)	1.000 †
Pulmonary fibrosis by CT scan			
None	12 (30)	86 (24)	0.383
Mild/Moderate	16 (40)	128 (35)	0.561
Severe	2 (5)	26 (7)	1.000 †
Not performed	10 (25)	122 (34)	0.266
Pulmonary hypertension (any type) by right heart catheterization	8 (20)	59 (16)	0.551
Treatments used at any point			
Prednisone	23 (58)	138 (38)	**0.018**
Mycophenolate mofetil	11 (28)	114 (32)	0.605
Hydroxychloroquine	32 (80)	96 (27)	**< 0.001**

† Fisher's exact test

Methods: A single-center, retrospective study of SSc patients was performed. A previously described cohort (Moore 2019) composed of African American and non-African American SSc patients matched 1:1 by sex, age, date of first visit, disease duration at first visit, and limited vs. diffuse cutaneous disease was used. The 2013 ACR/EULAR Classification Criteria for SSc were fulfilled in 91% of these patients. Patient data were re-abstracted to evaluate specifically for fulfillment of the 2019 EULAR/ACR Classification Criteria for SLE and the 2012 SLICC Criteria for the Classification of SLE. Demographic, laboratory, and clinical features and mortality were compared among SSc-SLE overlap and non-overlap SSc patients.

Results: 402 patients with SSc were analyzed. 40 (10%) of patients fulfilled the 2019 EULAR/ACR SLE criteria, 41 (10%) fulfilled the 2012 SLICC criteria, and 33 (8.2%) fulfilled both sets of criteria. Table 1 shows the frequencies of the criteria items among patients who fulfilled the EULAR/ACR criteria. Neuropsychiatric and renal involvement were rare. Table 2 compares the features of overlap and non-overlap SSc patients. An initial diagnosis of SLE was purported in 43% of the overlap patients and 7% of non-overlap patients ($p < 0.001$). Overlap patients were more likely to be female, be African American, and have limited cutaneous SSc. Anti-U1RNP antibody positivity prevalence was only 30% among overlap patients, and lower at 6.6% among non-overlap patients ($p < 0.001$). Overlap and non-overlap patients were similar in the prevalence of other SSc-specific autoantibodies, Raynaud's phenomenon, scleroderma renal crisis, pulmonary fibrosis per CT scan, and pulmonary hypertension by right heart catheterization. Overlap patients were more likely to have received treatment with prednisone or hydroxychloroquine at any point. Death during follow-up occurred in 12 (30%) of SSc-SLE overlap patients and in 81 (22%) of non-overlap patients, but there was no difference in survival among the groups per log rank test ($p = 0.404$).

Conclusion: Approximately 10% of SSc patients fulfill the 2019 EULAR/ACR Classification Criteria for SLE. These SSc-SLE overlap patients comprise a distinct demographic, serologic, and clinical phenotype but sustain similar severe SSc-specific end-organ damage and mortality as non-overlap SSc patients. SLE patients with Raynaud's should be evaluated for SSc-specific autoantibodies and clinical features.

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Optical Coherence Tomography of the Skin Detects Scleroderma Changes in Clinically Unaffected Skin: An Opportunity for Early Detection of Systemic Sclerosis

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Background/Purpose: The Very Early Diagnosis Of Systemic Sclerosis (VEDOSS) study has shown that more than 80% of patients with Raynaud's Phenomenon, specific ANA positivity and scleroderma pattern at nailfold video-capillaroscopy will fulfill classification criteria within 5 years. This is suggesting that there is a subclinical window of opportunity to diagnose systemic sclerosis (SSc) before clinical manifestations occur. In this scenario, a non-invasive tool to diagnose SSc in clinically unaffected skin might improve the early detection of disease in at risk-patients. Optical coherence tomography (OCT) of the skin has been shown to be a sensitive and accurate biomarker of skin fibrosis in SSc. Here we aimed to assess the ability of skin OCT to "detect SSc" in clinically unaffected skin from a multicenter cohort.

Methods: Dorsal forearm skin of SSc patients and matched-healthy controls (HC) was evaluated using VivoSight scanner (Michelson Diagnostics). Mean A-scans (mean OCT signal plotted against depth-in-tissue) were derived as previously described. Minimum Optical Density (MinOD), Maximum OD (MaxOD) and OD at 300 micron-depth (OD300) were calculated. Clinical involvement was assessed by an operator blinded to OCT findings using the mRSS. Receiver-operating characteristic (ROC) curve analysis was carried out for MinOD, MaxOD, and OD300 to evaluate their ability to discriminate between SSc and HC. Statistical analysis was performed using GraphPad Prism software V.7.0.

Results: One hundred seventy four OCT images were collected from 87 subjects [43 SSc (39 Female, mean age 49.7 ± 9.1 years) and 44 gender/age-matched healthy controls (HC) (36 Female, mean age 50.2 ± 8.3 years)] in two different SSc centers. All patients fulfilled classification criteria for SSc. OCT measures demonstrated discriminative ability in SSc skin detection with any clinical skin involvement (0-3 at site of analysis) with an AUC of 0.73 (MinOD, 95%CI 0.64-0.81), 0.77 (MaxOD, 95%CI 0.7-0.85) and 0.82 (OD300, 95%CI 0.76-0.89); $p < 0.0001$ for all as previously indicated. Most importantly, all three measures showed comparable performance in detecting scleroderma also in clinically unaffected skin (mRss=0 at site of analysis), with an AUC of 0.7 (95%CI 0.6-0.81, p=0.001), 0.72 (95%CI 0.61-0.83, p=0.0003) and 0.72 (95%CI 0.61-0.83, p=0.0003) for MinOD, MaxOD and OD300 respectively.

Conclusion: Virtual biopsy by OCT recognises clinically unaffected skin of SSc patients from the HC skin. This is in line with gene array data showing that scleroderma specific signatures are consistent in affected and clinically unaffected skin. These results inform future studies on at risk patients with clinically unaffected skin which may define a role for OCT in detecting subclinical SSc.

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Abstract Number: 0403

Comparison of Immediate Post-Operative and Long-Term Outcomes in Aortitis and Non-Inflammatory Thoracic Aortic Aneurysms Undergoing Open Surgical Repair

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Background/Purpose: Around 2-12% of patients who undergo open thoracic aortic aneurysm repair are incidentally found to have aortitis on pathology. There is no standardized approach to the post-operative care of patients with incidentally-found aortitis nor extensive data on post-operative and long-term outcomes. A better understanding of the risk for recurrent vascular disease and surgical complications in this population could inform clinical surveillance and treatment. This study compared immediate post-operative and long-term outcomes between patients with pathology-diagnosed aortitis and those with non-inflammatory aortic aneurysms after undergoing open thoracic aortic aneurysm repair.

Methods: This is a single-center matched cohort study. Patients with aortitis were identified by histopathology following open thoracic aortic aneurysm repair in the University of Pennsylvania Health System between 2007 and 2017 and lacked any evidence of infection or known prior diagnosis of rheumatic disease. Two comparators who lacked significant inflammation on pathology were matched to each aortitis case by year of surgical repair. Outcomes included length of hospital stay, surgical complications, formation of new vascular abnormalities on CT/MRI imaging, and death. Differences between groups were compared using conditional logistic, Cox proportional hazards, or conditional Poisson regression models accounting for matching.

Results: For the analysis, 162 patients were included: 53 patients with aortitis and 109 matched comparators with similar follow-up time between groups (median follow-up 3.7 vs 3.3 years) (**Table 1**). Aortitis patients were more likely to be older, female and less likely to have a history of coronary artery disease. 93% of each group had an ascending thoracic aortic aneurysm that was repaired **(Table 1)**. Patients with aortitis had a significantly longer hospital length of stay even after adjusting for perioperative glucocorticoid use and referral to rheumatology (adjusted IRR 1.35 (1.19 to 1.53), $P < 0.01$). There was no difference in rates of post-operative complications or surgical revision between groups (**Table 1**). On long-term surveillance imaging, no difference was seen in new or worsening aortic aneurysms between groups, but there were significantly more vascular abnormalities in the thoracic aortic branch arteries (carotid, subclavian, brachiocephalic, and celiac arteries) in the aortitis group (39% vs. 11%, $P < 0.01$)(**Table 2, Figure**).

Conclusion: Among patients who underwent open surgical repair of a thoracic aortic aneurysm, patients with incidentally-discovered aortitis were more likely than non-inflammatory comparators to have a longer hospital length of stay and develop vascular anomalies in major aortic branch arteries. The higher rate of arterial abnormalities in patients with aortitis may reflect ongoing inflammatory changes from an underlying vasculitic process and suggest that more frequent surveillance imaging and involvement of a rheumatologist are needed in the long-term care of these patients.

Table 1. Immediate post-operative outcomes in patients with aortitis vs non-inflammatory comparators.

	All (N = 162)	Aortitis (N = 53)	Non-Inflammatory (N = 109)	P-value
Baseline Characteristics of Cohort				
Age at surgery	65 (55 to 74)	67 (59 to 76)	62 (54 to 71)	0.02
Female sex	36%	58%	25%	<0.01
Race				
White	79%	70%	83%	0.05
Black	8%	13%	6%	0.09
Asian	2%	4%	1%	0.25
Location of aneurysm repair				
Ascending aorta	93%	93%	93%	0.96
Aortic arch	3%	4%	3%	0.64
Descending aorta	3%	4%	3%	0.64
Events during hospitalization				
Total length of stay after surgery, days	7 (6 to 10)	8 (6 to 10)	7 (6 to 10)	<0.01
Post-operative systemic glucocorticoids				
Administered for any indication	–	22%	–	N/A
Administered for treatment of aortitis	–	20%	–	
Rheumatology referral				
During inpatient hospitalization	9%	30%	0%	N/A
Post-discharge within 4 weeks	5%	17%	1%	
Surgical complications				
Any	18%	15%	19%	0.53
Graft leak	1%	2%	0%	0.33
Aortic dissection	1%	2%	0%	0.33
Graft infection	0%	–	–	–
Non-graft infection	9%	8%	10%	0.78
Organ/limb ischemia	10%	9%	11%	0.76
Surgical re-exploration or revision	6%	8%	5%	0.48
Other surgery unrelated to graft	2%	2%	2%	0.99
Death	3%	4%	3%	0.66
Post-hospitalization follow-up				
Total follow-up time, years	3.3 (1.2 to 5.9)	3.7 (1.2 to 5.6)	3.3 (1.5 to 6.1)	0.64
Follow-up with rheumatologist	11%	32%	1%	N/A
Follow-up with surgeon	94%	91%	96%	0.38
Systemic glucocorticoids				
Initiated	16%	33%	7%	N/A
Time from surgery to initiation, days	8 (3 to 432)	5 (3 to 14)	1476 (360 to 2404)	
Initial dose, mg	60 (20 to 60)	60 (60 to 60)	5 (3 to 50)	
Duration of therapy, months	10 (4 to 18)	10 (6 to 16)	11 (0.4 to 27)	
Other immunosuppressive therapy				
Any	7%	13%	4%	N/A
Azathioprine	1%	4%	0%	
Methotrexate	2%	6%	1%	
TNF inhibitor	1%	2%	0%	
Other	3%	4%	3%	
Surgical revision	8%	6%	9%	0.55
Time to revision, months	35 (4 to 80)	36 (8 to 105)	44 (3 to 80)	0.49
Death	12%	11%	12%	0.97

Values expressed as median (interquartile range) or %

Table 2. Radiographic (CT or MRI) changes during follow-up in patients with aortitis vs non-inflammatory comparators.

	All (N = 131)	Aortitis (N = 44)	Non-Inflammatory (N = 87)	P-value
Total number of imaging studies performed	4 (3 to 7)	5 (3 to 8)	4 (2 to 6)	0.01
Time between first and last imaging study, months	39 (20 to 65)	39 (15 to 62)	39 (23 to 67)	0.92
New or worsening changes in aorta on imaging	67%	61%	70%	0.32
Abnormality identified in aorta				
Aneurysm	60%	50%	64%	0.13
Stenosis or occlusion	3%	5%	2%	0.60
Wall thickening	3%	9%	0%	0.01
Thrombosis	10%	16%	7%	0.11
New or worsening changes in branches of aorta on imaging	33%	45%	26%	0.03
Location of new or worsening changes in branch artery				
Thoracic branch arteries	21%	39%	11%	< 0.01
Carotid artery	5%	14%	1%	0.02
Subclavian artery	5%	9%	2%	0.11
Brachiocephalic artery	7%	16%	2%	0.02
Celiac artery	11%	20%	6%	0.02
Abdominal branch arteries	18%	23%	16%	0.37
Superior mesenteric artery	5%	9%	3%	0.20
Renal artery	6%	9%	5%	0.33
Inferior mesenteric artery	4%	9%	1%	0.06
Iliac artery	13%	16%	11%	0.50
Other	14%	20%	10%	0.09
Abnormality identified in branch artery				
Aneurysm	19%	27%	15%	0.13
Stenosis or occlusion	18%	27%	13%	0.04
Wall thickening	5%	14%	0%	< 0.01
Thrombosis	3%	9%	0%	0.01

Values expressed as median (interquartile range) or %

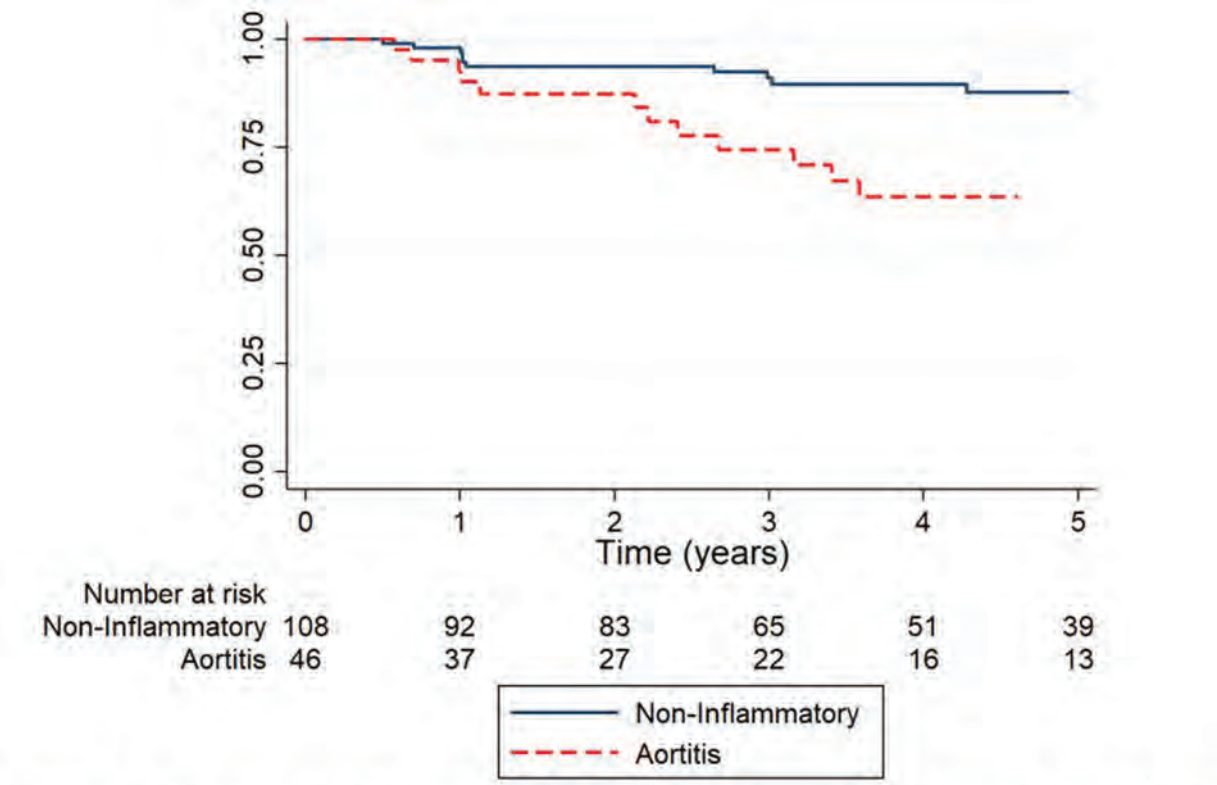

Figure. Time to development of abnormality in thoracic aortic branch arteries (carotid, subclavian, brachiocephalic, celiac). Patients with aortitis are more likely to develop arterial abnormalities on imaging over time (HR 2.70 [95% CI 1.05 to 6.93], P = 0.03).

Disclosure: A. Mayer, None; **A. Sperry**, None; **L. Quimson**, None; **R. Rhee**, None.

Abstract Number: 0404

Isolated Aortitis: Single Centre Experience of Clinical Spectrum and Management

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Aortitis was previously regarded as a rare form of large vessel vasculitis (LVV), but is now increasingly being recognised. It may occur in the context of primary systemic vasculitis, as a part of systemic autoimmune disease or in isolation. Positron emission tomography (PET) has facilitated the diagnosis of LVV which is often a challenge as the presenting clinical features are often nonspecific. The outcome and optimal management remain uncertain; EULAR 2018 recommendations on LVV have helped to address some of these issues [EULAR 2018 guidelines (Hellmich B, et al. Ann Rheum Dis 2020;79:19–30)]

We aimed to assess the presenting features, time to diagnosis, imaging methods utilized, treatment and complications in a cohort of patients with isolated aortitis.

Methods: We identified patients diagnosed with isolated aortitis presenting at our centre over the last 10-years. Patients were identified using a specifically designed database, which prospectively phenotyped all patients attending a single rheumatology department. Their medical notes were retrospectively reviewed using the electronic patient record system.

Results: We identified 63 patients who had been diagnosed with isolated aortitis (IA) over the last 10 years; 5 were excluded due to incomplete data.

Demographic data and main results are presented in Table 1. The median age at diagnosis of aortitis was 68 years (range 32 - 88); 36 (62%) were females. The median duration of symptoms was 7 months (range 2-120). The commonest presenting feature was systemic inflammatory syndrome in 28 patients (49%) followed by back/abdominal pain in 8, chest symptoms in 6 and weight loss in 4. Acute presentation with dissection/aneurysm was seen in 6 patients who also had histological confirmation of aortitis.

Patients had elevated inflammatory markers (median CRP 81 [range16-249]; median ESR 79 [range 11-139]) at presentation. 43 patients (74%) were diagnosed on PET CT with aortitis, 12 (21%) on CT angiogram aorta (CTA) and 3 (5%) on CT chest/full body performed to rule out other diagnoses. Follow up imaging included MRA in 60, CTA in 56 and PET CT in 30 patients.

Prednisolone and disease modifying anti-rheumatic drugs (DMARDs) were used in the majority of patients (90% and 93% respectively), with methotrexate being the commonest DMARD. Cyclophosphamide was used in 11 patients and 4 patients received tocilizumab.

Parameter	Overall Population (n=58)
Age at Diagnosis (yr.), mean, (S.D.)	68, (13)
Sex, Female	36 (62%)
Ethnicity	
White	49 (85%)
South Asian	7 (12%)
Others	2 (3%)
Risk Factors	
Smoker	27 (47%)
Hypertension	26 (45%)
Hyperlipidaemia	13 (22%)
Coronary artery disease	7 (12%)
Diabetes mellitus	3 (5%)
Atherosclerosis	3 (5%)
Underlying carcinoma	4 (7%)
Presentation	
Systemic inflammatory syndrome	28 (49%)
Back/Abdominal pain	8 (14%)
Chest Symptoms	6 (10%)
Dissection	5 (9%)
Weight loss	4 (7%)
Headache	2 (3%)
Neurological Symptoms	2 (3%)
Claudication	2 (3%)
Aneurysmal disease	1 (2%)
Treatment	
Corticosteroids	52 (90%)
Immunosuppressive	
First line	
Methotrexate	45 (78%)
Leflunomide	3 (5%)
Cyclophosphamide	5 (9%)
Mycophenolate	1 (2%)
Biologics	
Tocilizumab	4 (7%)

The median duration of follow up was 3 years (range 0.30 - 10). 17 patients developed vascular complications, including aneurysms (8 patients), vascular stenosis/ischaemic complications (9 patients) with 4 patients requiring subsequent vascular/surgical interventions.

Drug free remission was achieved in 13 (23%) patients and they remain in remission whilst off treatment for a median duration of 11 months (range 2-40). 4 patients died during follow up, 3 due to sepsis and 1 to unknown cause.

Conclusion: We have reviewed the clinical features, treatment and complications of a cohort of patients with isolated aortitis. Diagnostic delay remains an issue, highlighting the need for increasing awareness of this condition. Vascular complications are high in this group, despite aggressive immunosuppression and only a minority achieve sustained drug free remission.

Disclosure: N. Ahmad, None; **A. Verdiyeva**, None; **R. Luqmani**, None; **S. Dubey**, None.

Abstract Number: 0405

Disease Activity and Quality-of-Life Outcomes in Patients with Behçet's Syndrome Who Achieved and Maintained Oral Ulcer Complete Response with Apremilast Treatment

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

Background/Purpose: Recurrent, painful oral ulcers (OU) are common symptoms of Behçet's syndrome that can impact daily activities and impair quality of life (QoL) (Kokturk A. *Patholog Res Int*. 2012;2012:690390; Hatemi G, et al. *Ann Rheum Dis*. 2018;67:808-818). Apremilast (APR), an oral phosphodiesterase 4 inhibitor, demonstrated efficacy in the treatment of OU associated with Behçet's syndrome, including improvements in OU pain, disease activity, and QoL, in the phase III RELIEF study (Hatemi G, et al. *N Engl J Med*. 2019;381:1918-1928). We describe outcomes in APR-treated patients in the RELIEF study who achieved complete response of OU (ie, OU-free) by Week 6 and remained OU-free for at least an additional 6 weeks compared with those who did not.

Methods: RELIEF was a phase III, multicenter, randomized, double-blind, placebo (PBO)-controlled study (BCT-002; NCT02307513). Adult patients (≥18 years of age) with active Behçet's syndrome and ≥3 OU at randomization or ≥2 OU at screening and randomization, without active major organ involvement, were randomized (1:1) to APR 30 mg BID or PBO during the 12-week PBO-controlled phase. In patients who received APR, a post hoc analysis compared outcomes in patients who achieved an OU-free response by 6 weeks and remained OU-free for at least 6 weeks thereafter (6+6 achiever) with outcomes in those who did not achieve an OU-free response at any time point, or those who did but were not able to remain OU-free for at least 6 weeks thereafter (non-6+6 achiever). Outcomes assessed at Week 12 included OU pain visual analog scale (VAS; 0-100 mm), disease activity measures (components of the Behçet's Disease Activity Index Form: Behçet's Disease Current Activity Index [BDCAI], Patient's Perception of Dis-

Changes From Baseline at Week 12 in Efficacy Outcomes With APR 30 mg BID Treatment in 6+6 Achievers and Non-6+6 Achievers in the RELIEF Study

Outcome	APR 6+6 Achiever n = 31	APR Non-6+6 Achiever n = 73
OU pain VAS, LS mean change (SE)	−49.5 (1.8)	−35.3 (4.2)
BDCAI, LS mean change (SE)	−1.4 (0.4)	−0.7 (0.2)
Patient's Perception of Disease Activity, LS mean change (SE)	−2.4 (0.3)	−1.4 (0.2)
Clinician's Overall Perception of Disease Activity, LS mean change (SE)	−2.3 (0.2)	−1.3 (0.2)
BSAS, LS mean change (SE)	−23.9 (2.1)	−14.1 (2.2)
BDQoL, LS mean change (SE)	−5.6 (1.3)	−2.7 (0.8)

Intent-to-treat population. Last-observation-carried-forward analysis.
6+6 Achiever = patients who achieved OU-free response by 6 weeks and remained OU-free for at least 6 weeks thereafter. Non-6+6 Achiever = patients who did not achieve OU-free response by 6 weeks or did but were not able to remain OU-free for at least 6 weeks thereafter.

ease Activity, Clinician's Overall Perception of Disease Activity, and Behçet's Syndrome Activity Scale [BSAS]), and a QoL measure (Behçet's Disease Quality of Life [BDQoL]). OU pain VAS scores, disease activity measures, and BDQoL scores were analyzed using an analysis of covariance model.

Results: Of the 207 patients who were randomized and received ≥1 dose of study medication, 104 received APR; of these, 31 (29.8%) were 6+6 achievers and 73 (70.2%) were non-6+6 achievers. 6+6 achievers, as defined above, showed greater improvements from baseline in outcomes beyond OU count, such as OU pain VAS score, measures of disease activity, and QoL measures, compared with non-6+6 achievers (Table).

Conclusion: In RELIEF, patients who achieved an OU-free response by Week 6 and remained OU-free for an additional 6 weeks with APR treatment showed greater improvements in clinically relevant outcomes, including OU pain, overall disease activity, and QoL, than those who did not achieve or maintain an OU-free response.

Disclosure: G. Hatemi, BMS, 1, Celgene Corporation, 1, Silk Road Therapeutics, 1, AbbVie, 1, Mustafa Nevzat, 1, Novartis, 1, UCB, 1, Bayer, 1, Eli Lilly, 1; **A. Mahr**, Roche, 1, Chugai, 1; **M. Takeno**, Celgene Corporation, 1, Esai, 1, Tanabe-Mitsubishi, 1; **D. Kim**, None; **M. Melikoğlu**, None; **S. Cheng**, Amgen Inc., 1; **S. Richter**, Amgen Inc., 1; **M. Brunori**, Amgen Europe GmbH, 1; **M. Paris**, Amgen Inc., 1; **M. Chen**, Amgen Inc., 1; **Y. Yazici**, BMS, 1, Celgene Corporation, 1, Genentech, 1, Sanofi, 1.

Abstract Number: 0406

Infliximab in Refractory Uveitis Due to Behçet's Disease: Long Term Follow-up and Therapy Optimization. Multicenter Study of 103 Caucasian Patients

José Luis Martín-Varillas[1], Belén Atienza-Mateo[2], Vanesa Calvo-Río[3], Emma Beltran-Catalan[4], Alfredo Adan[5], Marisa Hernandez Garfella[6], Elia Valls-Pascual[7], Agustín Sellas-Fernández[8], N Ortego[9], Alejandro Fonollosa[10], Olga Maiz Alonso[11], Ignacio Torre[12], Cruz Fernández-Espartero[13], Vega Jovani[14], Diana Peiteado[15], David Díaz Valle[16], Susana Romero-Yuste[17], Elena Aurrecoechea[1], Miriam García-Arias[18], Miguel Ángel Caracuel[19], Santos Insúa[20], Senén González-Suárez[21], Amalia Sánchez Andrade[22], Luis Francisco Linares[23], Alfredo J García González[24], Raquel Almodovar[25], Carmen Carrasco Cubero[26], María Alcalde Villar[27], C Fernandez-Carballido[28], Fred A Pages[29], Eva Peña Sainz-Pardo[24], Rosalia Demetrio-Pablo[3], Santos Castañeda[30], Miguel Ángel González-Gay[31], José Luis Hernández[3] and Ricardo Blanco[3], [1]Hospital Sierrallana, Torrelavega, Spain, [2]Research group on genetic epidemiology and atherosclerosis in systemic diseases and in metabolic bone diseases of the musculoskeletal system, IDIVAL; and Department of Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [3]Hospital Universitario Marques de Valdecilla, Santander, Spain, [4]Del Mar University Hospital, Barcelona, [5]Hospital Clinic, Barcelona, Catalonia, Spain, [6]H. Valencia, Valencia, Spain, [7]H. Doctor Peset, Valencia, Spain, [8]H. Vall d'Hebron, Barcelona, Spain, [9]H. San Cecilio, Granada, Spain, [10]H. de Cruces, Bilbao, Spain, [11]Hospital Universitario Donostia, San Sebastian, Pais Vasco, Spain, [12]Hospital Basurto, Bilbao, Spain, [13]H. Mostoles, Madrid, Spain, [14]H. Alicante, Alicante, Spain, [15]Hospital La Paz - IdiPAZ, Madrid, Spain, [16]H. Clínico San Carlos, Madrid, Spain, [17]H Pontevedra, Coruna, Spain, [18]H. La Princesa, Madrid, [19]H.U. Reina Sofía, Córdoba, Spain, [20]H. Santiago de Compostela, Santiago de Compostela, Spain, [21]H. Cabueñes, Gijón, Spain, [22]H. Lucus Augusti, Lugo, Spain, [23]Hospital de la Arrixaca, Murcia, [24]H. 12 de Octubre, Madrid, Spain, [25]Fundación Alcorcón University Hospital, Madrid, [26]H. Mérida, Mérida, Spain, [27]H. Severo Ochoa, Madrid, Spain, [28]H San Juan, Alicante, Spain, [29]H. Palencia, Palencia, Spain, [30]Princesa University Hospital, Universidad Autónoma, Madrid, Madrid, Spain, [31]Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I

Session Type: Poster Session A

Session Time: 9:00AM–11:00AM

	Optimized N=18	Non Optimized N=42	P
Patients/eyes affected, n/n	18/34	42/77	
Age, mean (SD), years	39.5 (9.8)	38.8 (10.5)	0.82
Men/women, n/n (%)	10/8 (55.6/44.4)	25/17 (59.5/40.5)	0.78
Duration of uveitis before IFX, median [IQR] months	38 [18-119]	35 [10-48]	0.11
Ocular features at time of IFX onset			
- AC cells count, median [IQR]	2 [1-4]	2 [1-2]	0.29
- Vitritis, median [IQR]	2 [1.5-3]	2 [1-2]	0.02
- BCVA, mean (SD)	0.32 (0.21)	0.37 (0.26)	0.51
- OCT, mean (SD)	303.5 (23.3)	397.7 (155.7)	0.12
- Retinal vasculitis, n (%)	9 (50)	26 (66.7)	0.23
Uveitis pattern, n (%)			
- Bilateral/unilateral	16/2 (88.9/11.1)	35/7 (83.3/16.7)	0.71
- Anterior	0 (0)	6 (14.3)	0.17
- Posterior	5 (27.8)	8 (19.0)	0.50
- Panuveitis	13 (72.2)	28 (66.7)	0.67
Prednisone dose at IFX onset, mean (SD), mg/d	40.3 (20.6)	41.4 (15.5)	0.81
Regimen of IFX therapy			
Monotherapy/combined treatment, n (%)	15 (83.3)	30 (71.4)	0.33
- AZA	5 (27.8)	4 (9.5)	0.11
- CsA	9 (33.3)	8 (19.0)	0.32
- MTX	4 (22.2)	15 (35.7)	0.30
Follow-up on IFX therapy, median [IQR], months	48 [33-60]	24 [6-60]	0.007
- **Relapses, median (IQR)**	0 [0-1]	0 [0-2]	0.46
- **Remission, %**	100	75.6	0.02
- **Severe side effects, n (per 100 patients/year)**	0 (0)	3 (0.78)	0.55
- **Cost (mean), euros per year**	4826.52	9854.13	-

Background/Purpose: Biologic therapy has improved prognosis of Behçet Disease (BD) uveitis. Although infliximab (IFX) is approved in Japan, most data in Caucasian patients comes from small series and no data on IFX optimization has been published. In the present study we assessed: **a)** long-term efficacy and safety of IFX and **b)** IFX optimization when ocular remission was achieved

Methods: Multicenter study of IFX-treated patients with BD uveitis refractory to conventional immunosuppressants.103 patients were treated with IFX as 1st biologic as follows: 3-5 mg/kg i.v. at 0, 2, 6 and every 4-8 weeks. The main outcomes were anterior chamber cells, vitritis, retinal vasculitis, macular thickness, best corrected visual acuity, and the glucocorticoids sparing effect that were analysed at baseline, 1st week, 1st and 6th months and 1st and 2nd years. After remission, based on a shared decision between patient and clinician, IFX optimization was performed. Efficacy, safety, and IFX cost were evaluated

Results: In whole series (n=103), main outcomes showed a rapid and maintained improvement, reaching remission in 78 patients after a mean IFX duration of 31.5 months. Severe side-effects were observed in 9 patients.

In the optimization subanalysis, comparative study between optimized and non-optimized groups showed: **a)** no differences in clinical baseline characteristics; **b)** similar maintained improvement in most ocular outcomes; **c)** lower severe adverse events and **d)** lower IFX cost in optimized group (4826.52 vs. 9854.13 euros/patient/year) **(Table)**

Conclusion: IFX seems effective and relatively safe in Caucasian patients with refractory BD uveitis. IFX optimization is also effective, safe, and cost-effective

Main general features and follow-up of a subgroup of patients (n= 60) with Refractory Uveitis Due to BD who Achieved Remission after the standard dose of IFX therapy (5 mg/kg at 0, 2, 6 and then every 8 weeks). Differences between Optimized and Non-optimized patients

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Disclosure: J. Martín-Varillas, None; **B. Atienza-Mateo**, None; **V. Calvo-Río**, None; **E. Beltran-Catalan**, None; **A. Adan**, None; **M. Hernandez Garfella**, None; **E. Valls-Pascual**, None; **A. Sellas-Fernández**, None; **N. Ortego**, None; **A. Fonollosa**, None; **O. Maiz Alonso**, Novartis, 1; **I. Torre**, None; **C. Fernández-Espartero**, None; **V. Jovani**, None; **D. Peiteado**, None; **D. Díaz Valle**, None; **S. Romero-Yuste**, None; **E. Aurrecoechea**, None; **M. García-Arias**, None; **M. Caracuel**, None; **S. Insúa**, None; **S. González-Suárez**, None; **A. Sánchez Andrade**, None; **L. Linares**, None; **A. García González**, None; **R. Almodovar**, None; **C. Carrasco Cubero**, None; **M. Alcalde Villar**, None; **C. Fernandez-Carballido**, None; **F. Pages**, None; **E. Peña Sainz-Pardo**, None; **R. Demetrio-Pablo**, None; **S. Castañeda**, Roche, 2; **M. González-Gay**, None; **J. Hernández**, None; **R. Blanco**, None.

Abstract Number: 0407

Achievement of Early and Sustained Complete Response of Oral Ulcers with Apremilast Compared with Placebo in Patients with Active Behçet's Syndrome

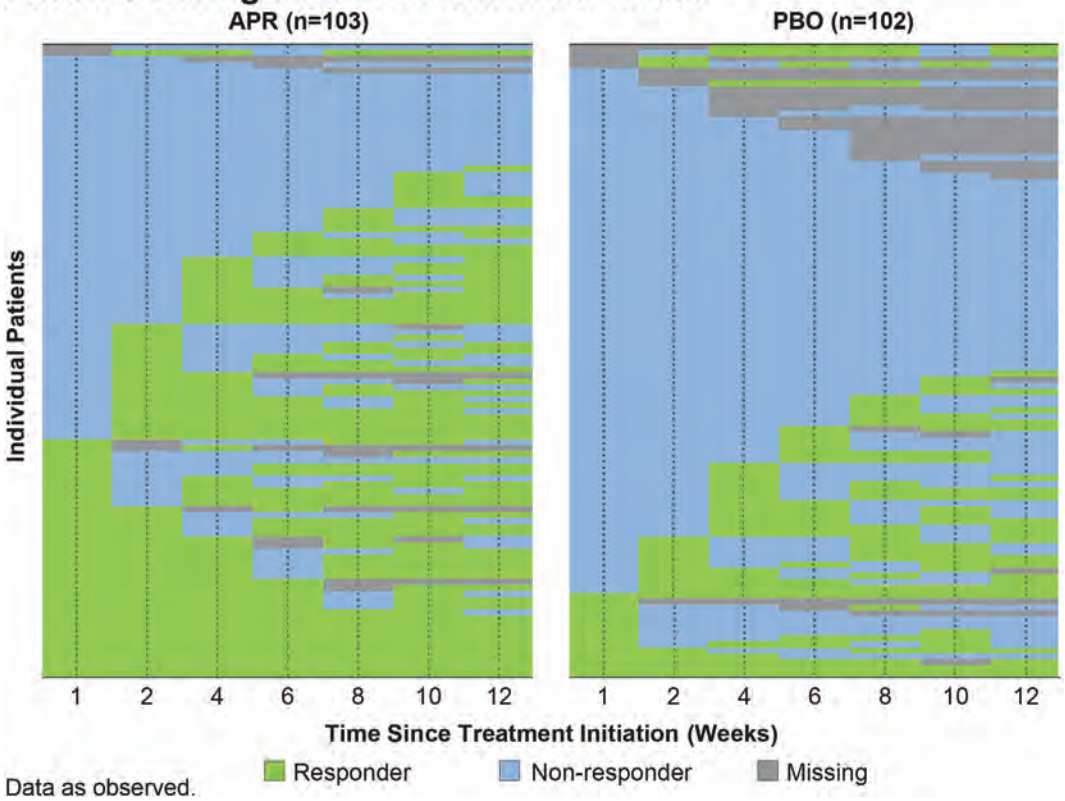
Gülen Hatemi[1], Alfred Mahr[2], Mitsuhiro Takeno[3], Doyoung Kim[4], Melike Melikoğlu[1], Sue Cheng[5], Sven Richter[5], Michele Brunori[6], Maria Paris[5], Mindy Chen[5] and Yusuf Yazici[7], [1]Istanbul University−Cerrahpaşa, Cerrahpaşa Medical School and Behçet's Disease Research Center, Istanbul, Turkey, [2]Cantonal Hospital St. Gallen, St. Gallen, Switzerland, [3]Nippon Medical School, Graduate School of Medicine, Tokyo, Japan, [4]Yonsei University College of Medicine and Severance Hospital, Seoul, Republic of Korea, [5]Amgen Inc., Thousand Oaks, [6]Amgen Europe GmbH, Rotkreuz, Switzerland, [7]New York University School of Medicine, New York

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
Session Type: Poster Session A
Session Time: 9:00AM–11:00AM

Background/Purpose: Painful and recurring oral ulcers (OU) are a common manifestation of Behçet's syndrome that can interfere with eating and have a negative impact on quality of life (Ozguler Y, et al. *Clin Exp Rheumatol*. 2019;37[6 Suppl 121]:28-34). Apremilast (APR), an oral phosphodiesterase 4 inhibitor, has demonstrated efficacy in the treatment of OU in the phase 3 RELIEF study (Hatemi G, et al. *N Engl J Med*. 2019;381:1918-1928). In RELIEF, 53% of patients treated with APR 30 mg BID and 22% who received placebo (PBO) achieved OU complete response at Week 12 (Hatemi G, et al. *N Engl J Med*. 2019;381:1918-1928). Here, we describe the achievement of OU complete response over different time points during the PBO-controlled period in RELIEF.

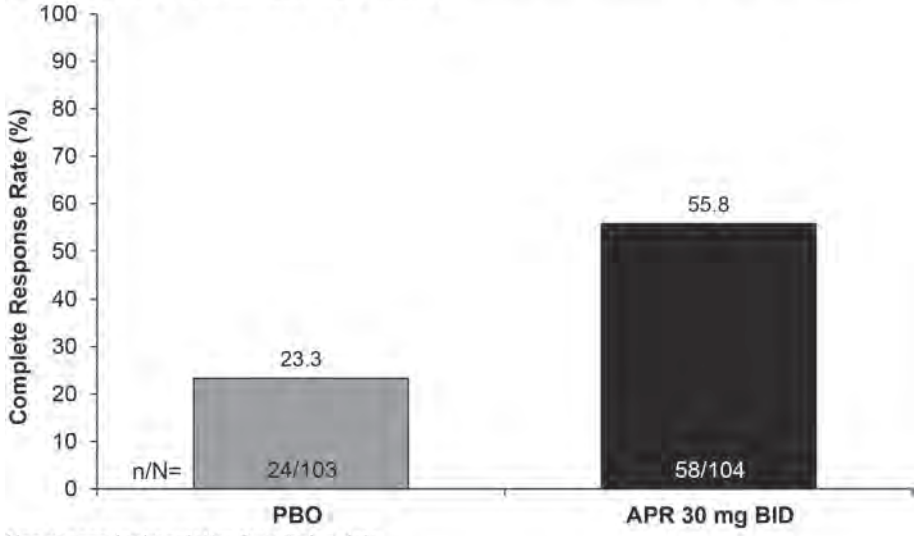
Methods: This multicenter, randomized, double-blind, PBO-controlled study (BCT-002; NCT02307513) enrolled adult patients (≥18 years of age) with active Behçet's syndrome and ≥3 OU at randomization or ≥2 OU at screening and randomization, without active major organ involvement. Patients were randomized (1:1) to receive APR or PBO during the 12-week PBO-controlled period. The current post hoc analysis assessed the proportion of individual patients who achieved OU complete response (ie, were OU-free) at any point during the PBO-controlled period and the proportion of patients who achieved complete response for OU as early as Weeks 1 or 2. The number of patients achieving OU complete response by Week 6 who remained OU-free for ≥6 additional weeks was also evaluated. Data are summarized descriptively.

Figure 1. Achievement of OU Complete Response for Individual Patients During the PBO-Controlled Period



Data as observed.

Figure 2. Achievement of Early OU Complete Response During Weeks 1 or 2 of the PBO-Controlled Period



Non-responder imputation for missing data.

Results: A total of 207 patients were randomized and received ≥1 dose of study medication, including 104 who received APR and 103 who received PBO. At baseline, the mean (SD) number of OU was 4.2 (3.7) in the APR group and 3.9 (2.7) in the PBO group. Mean (SD) duration of Behçet's syndrome at baseline was 6.7 (7.4) years in the APR group and 6.9 (8.0) years in the PBO group. The proportion of individual patients who achieved OU complete response at any time point during the 12-week PBO-controlled period was higher with APR than with PBO (Figure 1). Greater proportions of patients achieved early OU complete response during Weeks 1 or 2 with APR compared with PBO

(Figure 2). In total, 44/104 patients receiving APR and 24/103 patients receiving PBO had OU complete response by Week 6; of these, 33 patients in the APR group and 12 in the PBO group maintained OU-free response for ≥6 additional weeks.

Conclusion: In the RELIEF study, a higher proportion of patients with active Behçet's syndrome achieved OU complete response with APR treatment compared with PBO during the PBO-controlled period. Similarly, a greater proportion of patients achieved early OU complete response and maintained OU-free response with APR compared with PBO.

Disclosure: G. Hatemi, BMS, 1, Celgene Corporation, 1, Silk Road Therapeutics, 1, AbbVie, 1, Mustafa Nevzat, 1, Novartis, 1, UCB, 1, Bayer, 1, Eli Lilly, 1; **A. Mahr**, Roche, 1, Chugai, 1; **M. Takeno**, Celgene Corporation, 1, Esai, 1, Tanabe-Mitsubishi, 1; **D. Kim**, None; **M. Melikoğlu**, None; **S. Cheng**, Amgen Inc., 1; **S. Richter**, Amgen Inc., 1; **M. Brunori**, Amgen Europe GmbH, 1; **M. Paris**, Amgen Inc., 1; **M. Chen**, Amgen Inc., 1; **Y. Yazici**, BMS, 1, Celgene Corporation, 1, Genentech, 1, Sanofi, 1.

Abstract Number: 0408

Epidemiology and Treatment of Behçet's Disease Insights from the Rheumatology Informatics System for Effectiveness (RISE) Registry

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
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Background/Purpose: Behçet's disease (BD), a rare multisystem vasculitis, is prevalent among Middle Eastern populations but remains rare in North America. Data for patients with BD in the U.S. are based on cohorts from single centers and limited by small sample sizes. Therefore, we sought to characterize BD in the U.S., analyzing patient characteristics and medication use across the RISE registry. We also compared the characteristics of U.S. patients with those from the Egyptian College of Rheumatology (ECR) registry, which represents one of the largest cohorts of BD patients to date (Gheita TA, et al. *Clin Rheumatol*. 2019).

Methods: We conducted a cross-sectional study using data from the RISE Registry (2014-2018). RISE contains patient data collected during routine clinical care through EHRs of participating rheumatology practices. As of 2018, RISE held validated data from 1,113 providers in 226 practices, representing ~32% of the US clinical rheumatology workforce. Patients aged ≥ 18 years with ≥ 1 diagnosis codes (ICD-9 or ICD-10) for BD were included. Sociodemographic, laboratory, and treatment information was extracted when available. The ECR BD registry, a population-based multicenter cohort, included adults aged ≥ 18 years who fulfilled the 2014 International Study Group diagnostic criteria for BD who presented to one of the included rheumatology centers during 2017-2018. Patients' demographic, clinical, and laboratory data in the ECR were collected and entered into a standardized data abstraction form. Data were summarized with descriptive statistics and comparisons were performed using t-tests and chi-square tests, as appropriate.

Table 1. Characteristics of patients with Behçet's disease in the RISE registry

Characteristics mean±SD / N (%)			Total patients (N=1323)	
Age			48.72 (16.31)	
Sex (female)			1049 (49.0%)	
Race	White		882	66.7%
	Black or African American		65	4.9%
	Hispanic or Latino		55	4.2%
	Other*		157	11.9%
	Missing		164	12.4%
Insurance	Medicare		205	15.50%
	Medicaid		43	3.2%
	Private		557	42.1%
	Other#		75	5.7%
	Missing		443	33.5%
U.S. geographic division	East North Central		22	1.7%
	West North Central		153	11.6%
	Mid-Atlantic		159	12.0%
	Mountain		109	8.2%
	New England		396	29.9%
	Pacific		116	8.8%
	South Atlantic		153	11.6%
	East South Central		62	4.7%
	West South Central		144	10.9%
	Missing		9	0.7%
Laboratory markers	ESR	Number of patients	390	
		Mean (SD)	14.6 (13.0)	
	CRP	Number of patients	781	
		Mean (SD)	3.2 (8.1)	
	Charlson score; mean±SD		0.7 (0.6)	
Number of visits in RISE; median (IQR)			4.5 (2.5, 8)	
Duration of follow up time (years); median (IQR)			2.5 (0.9, 4.4)	
Medications; N (%)				
Colchicine			728	55.0%
Dapsone			62	4.7%
Glucocorticoids	Any prednisone or equivalent#		895	67.6%
csDMARDs	Methotrexate		288	21.8%
	Hydroxychloroquine		117	8.8%
	Azathioprine		418	31.6%
	Mycophenolate		31	2.3%
	Sulfasalazine		53	4.0%
	Cyclosporine		23	1.5%
Biologics-TNFi	Infliximab		192	14.5%
	Adalimumab		187	14.1%
	Etanercept		92	6.9%
	Certolizumab		30	2.3%
	Golimumab		20	1.5%
Biologics-non-TNFi§			65	4.9%
Targeted small molecules	Tofacitinib		11	0.8%
	Apremilast		42	3.2%

Abbreviations: RISE: Rheumatology Informatics System for Effectiveness, GC: glucocorticoid, csDMARDs: conventional disease modifying anti-rheumatic drugs, TNFi: tumor necrosis factor inhibitors. # Prednisone or equivalent included prednisone and other oral and intravenous steroids. *Other race: Asian, Not determined OMB race, and AMERICAN INDIAN OR ALASKA, NATIVE HAWAIIAN, # Other insurance: include Veteran, §include Rituximab, Abatacept, Tocilizumab, Ustekinumab, and Secukinumab. IQR: interquartile range.

Results: A total of 1323 subjects with BD from the RISE registry were included. The mean ± SD age was 48.7 ± 16.3 years, female to male ratio was 3.8:1, with 66.7% being White (Table 1). The most frequently used medications included glucocorticoids (67.6%) and colchicine (55.0%). Infliximab and adalimumab were the most commonly used biologics (14.5% and 14.1%, respectively); 3.2% of patients used apremilast.

In comparison to the ECR cohort, the RISE cohort had more women (49.0% in RISE vs. 27.8% in ECR, $p < 0.001$, Table 2) and patients were older (mean age (SD); 48.7 (16.3) in RISE vs. 35.7 (9.84) in ECR, $p < 0.001$). There were also significant differences in medication use, with methotrexate and TNFi used more commonly in RISE (21.8% and

Table 2 Comparison of BD characteristics between RISE and Egyptian college of rheumatology cohorts

Characteristics mean±SD / N (%)	RISE (N=1323)	ECR (N=1526)	P value
Demographics			
Age	48.7 (16.3)	35.7 (9.84)	<0.001
Female	1049 (79.3%)	424 (27.8%)	<0.001
Medication use			
Colchicine	728 (55.0%)	611 (82.7%)	<0.001
Prednisone or equivalent#	895(67.6%)	947 (90.2%)	0.002
Methotrexate	288 (21.8%)	67 (7.2%)	<0.001
Azathioprine	418 (31.6%)	474 (26.7%)	0.760
Cyclosporine	23 (1.7%)	282 (26.7%)	<0.001
Cyclophosphamide	8 (0.6%)	208 (20.1%)	<0.001
TNFi	491 (37.1%)	83 (8.3%)	<0.001

Abbreviations: RISE: Rheumatology Informatics System for Effectiveness, TNFi: tumor necrosis factor inhibitors.

37.1%) compared to the ECR (7.2% and 8.3%, $p < 0.001$) whereas colchicine, glucocorticoids, cyclosporine and cyclophosphamide had more widespread use in the ECR cohort.

Conclusion: We report on the largest population-based BD cohort in the U.S. using the RISE registry. Our findings suggest that U.S. patients with BD are predominantly female, which is in contrast to cohorts in the Middle East. Differences in medication use may be due to practice patterns or differences in the manifestations of BD. Further research is needed to explore the reasons for the increased prevalence of BD among women in the U.S. and its possible impact on disease severity and management.

Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

Keywords: Behçet's disease, RISE, ECR, medication

Disclosure: N. Hammam, None; **J. Yazdany**, Eli Lilly, 1, Astra Zeneca, 1; **G. Schmajuk**, None.

Abstract Number: 0409

Clinical Characteristics, Brain MRI Findings, and Diagnostic Approach of the Central Nervous System Vasculitis by Affected Vessel Size

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SESSION INFORMATION

Session Date: Friday, November 6, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster I
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Background/Purpose: Diagnosis of the central nervous system vasculitis (CNS-V) is made on the basis of image findings or brain biopsy. Recently, two different subtypes of the disease have been postulated, the small (SVV) and large-medium vessel variant (LMVV). We hypothesized that the image profiles and diagnostic approaches would vary

between the LMVV and the SVV in patients with CNS-V. The aim of this study was to clarify the clinical characteristics, brain MRI findings, and diagnostic accuracy for high-resolution vessel wall image (HR-VWI) and brain biopsy according to affected vessel size in CNS-V patients from our prospective CNS vasculopathy registry.

Methods: We extracted CNS-V patients from our prospective CNS vasculopathy registry (n=201) from 2012-2019. Arterial involvement was assessed by digital subtraction angiography (DSA) or MR angiography (MRA). LMVV was defined as patients with cerebral vasculature indicating vasculitis in proximal or middle arterial segments. SVV was diagnosed with vessel involvements in only smaller distal branch or normal angiography. We compared clinical demographics, MRI findings including high-resolution vessel wall image (HR-VWI), and diagnostic accuracy for brain biopsy between two variants.

Results: We identified 34 cases who underwent cerebral vascular studies (DSA: n=26, MRA: n=32). Among them, 11 (32.4%) were LMVV and 23 (67.6%) were SVV based on angiographical findings. LMVV had more infarcts (LMVV: 100.0 % vs. SVV: 60.9%, P=0.017) and were more likely to have concentric vessel wall enhancement on HR-VWI (LMVV: 90.0% (9/10) vs. SVV: 7.1% (1/14), P< 0.001); summary in Table1.

By contrast, meningeal/parenchymal contrast enhancement lesion was more frequently observed in the SVV group (SVV: 87.0% vs. LMVV 45.5%, P=0.006) and the majority of SVV was diagnosed by brain biopsy (SVV: 78.3% vs. LMVV: 30.8%, P=0.022). The diagnostic accuracy of the brain biopsy was 100 % (18/18) in the SVV and 57.1% (4/7) in the LMVV, respectively (P=0.015); summary inTable 2.

Table 1. Brain MRI, cerebral angiogram, and HR-VWI findings between LMVV and SVV in CNS-V patients.

	LMVV (n=11)	SVV (n=23)	P
MRI findings, n (%)			
Brain infarcts	11 (100.0)	14 (60.9)	0.017
Parenchymal hemorrhage	1 (9.1)	5 (21.7)	0.638
Subarachnoid hemorrhage	0 (0.0)	4 (17.4)	0.280
White matter lesion	2 (18.2)	12 (52.2)	0.076
Tumor-like lesion	0 (0.0)	8 (34.8)	0.034
Contrast enhancement lesion	5 (45.5)	20 (87.0)	0.033
Assessment of the cerebral vascular image, n (%)			
Both MRA and DSA	11 (100.0)	13 (56.5)	0.014
Only MRA	0 (0.0)	8 (34.8)	0.034
Only DSA	0 (0.0)	2 (8.7)	1.000
Arterial stenosis, n (%)			
Proximal segment	7 (63.6)	0 (0.0)	<0.001
Middle segment	10 (90.9)	0 (0.0)	<0.001
Smaller distal branch	10 (90.9)	8 (34.8)	0.003
None	0 (0.0)	15 (65.2)	<0.001
HR-VWI findings, n (%)			
VWE	10 (100.0)[n=10]	2 (14.3)[n=14]	<0.001
Concentric VWE	9 (90.0) [n=10]	1 (7.1) [n=14]	<0.001
Eccentric VWE	1 (10.0) [n=10]	1 (7.1) [n=14]	1.000

MRI; magnetic resonance imaging, HR-VWI; high-resolution vessel wall image, LMVV; large/medium vessel variant, SVV; small vessel variant, CNS-V; central nervous system vasculitis, MRA; magnetic resonance angiography, DSA; digital subtraction angiography, VWE; vessel wall

Brain MRI, cerebral angiogram, and HR-VWI findings between LMVV and SVV in CNS-V patients

Table 2. Brain biopsy and CSF findings between LMVV and SVV in CNS-V patients.

	LMVV (n=11)	SVV (n=23)	P
Biopsy proven CNS-V, n (%)	4 (36.4)	18 (78.3)	0.026
Biopsy positive, n (%)	4 (57.1) [n=7]	18 (100.0) [n=18]	0.015
Pathological patterns, n (%)			
Granulomatous vasculitis	1 (14.3) [n=7]	1 (11.1) [n=18]	0.490
Lymphocytic vasculitis	3 (42.9) [n=7]	12 (66.7) [n=18]	0.378
Necrotizing vasculitis	0 (0.0) [n=7]	5 (27.8) [n=18]	0.274
CSF findings, n (%)			
Abnormal *	11 (100.0) [n=11]	16 (80.0) [n=20]	0.269
Pleocytosis *	10 (90.9) [n=11]	12 (60.0) [n=20]	0.106
Elevated protein*	8 (72.7) [n=11]	13 (65.0) [n=20]	1.000

CSF; cerebral spinal fluid, LMVV; large/medium vessel variant, SVV; small vessel variant, CNS-V; central nervous system vasculitis.*Abnormal CSF is defined by either leukocyte counts >5 cells/mm^3 (pleocytosis) or protein level >45 mg/dl (elevated protein).

Brain biopsy and CSF findings between LMVV and SVV in CNS-V patients

Conclusion: Clinical and image characteristics of CNS-V seem to differ concerning the affected vessel size. LMVV is more likely to develop ischemic stroke and HR-VWI is useful for diagnosis of CNS-V with LMVV. Higher prevalence rate of mass lesion and leptomeningeal/parenchymal contrast enhancement lesion is associated with SVV; Brain biopsy is of high yield and thus should be considered in suspected CNS-V; higher yield of biopsy is associated with SVV variant but still positive in almost one third of LMVV variant

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Abstract Number: 0410

Exploring Gene Expression Profile of Primary Central Nervous System Vasculitis

Carlo Salvarani[1], Robert Brown[2], Jonas Paludo[2], Stefania Croci[3], Stephen Ansell[4], Caterina Giannini[2], Joseph Parisi[2], Kenneth Warrington[2] and Gene Hunder[2], [1]Azienda USL-IRCCS di Reggio Emilia e Università di Modena e Reggio Emilia, Reggio Emilia, Italy, [2]Mayo Clinic, Rochester, MN, [3]Azienda USL-IRCCS di Reggio Emilia, Reggio Emilia, Italy, [4]Mayo Clinic, Rochester

SESSION INFORMATION
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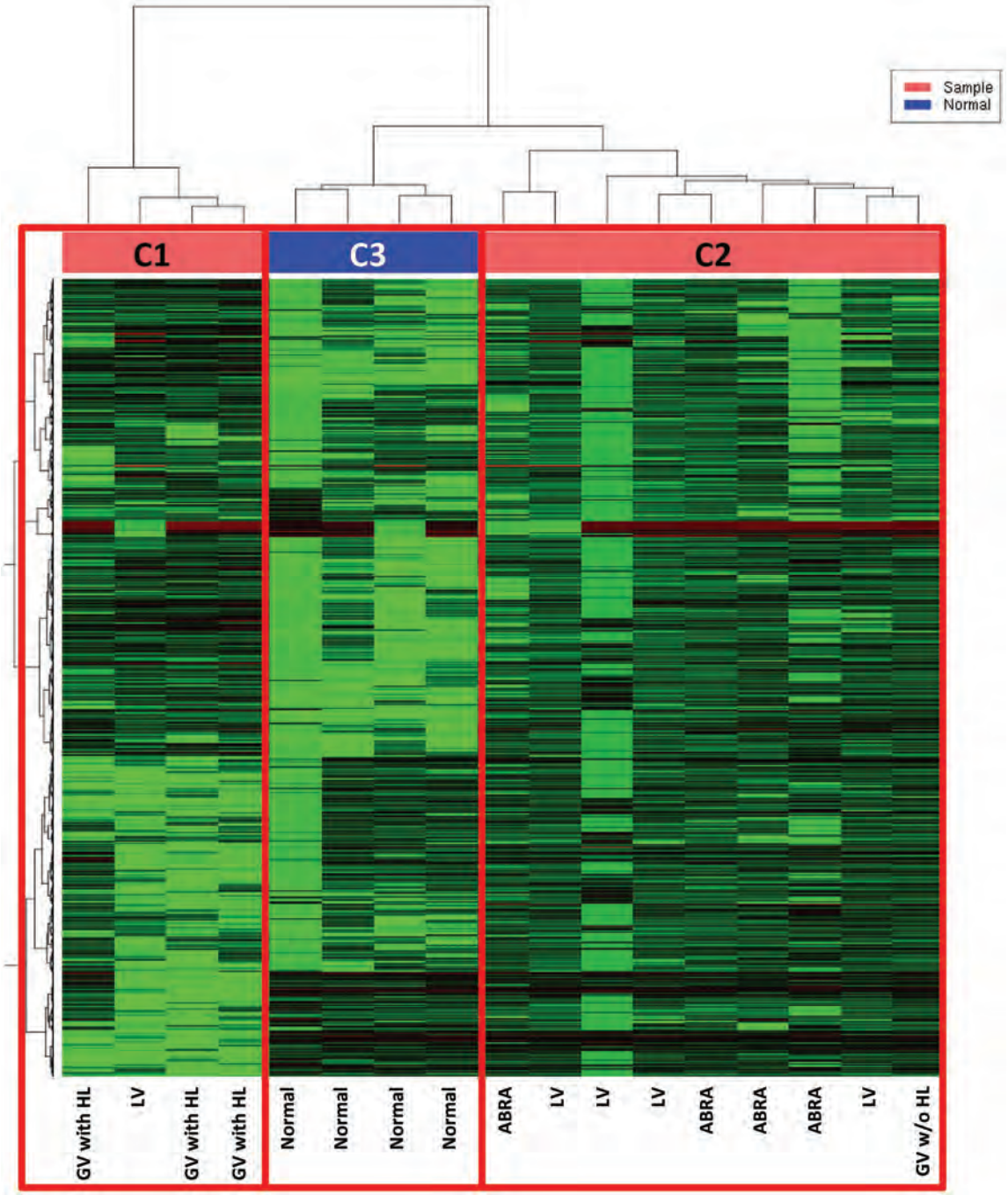
Background/Purpose: Primary CNS vasculitis (PCNSV) is an uncommon and poorly understood disease that affects the brain and spinal cord. It includes heterogeneous histopathological patterns, clinical subsets, outcomes, and re-

sponse to treatment. PCNSV has also been associated with lymphoma suggesting an immunological paraneoplastic mechanism. The molecular hallmarks of PCNSV are still unknown. We investigated the gene expression profile of granulomatous vasculitis (GV) including with Hodgkin lymphoma (HL), lymphocytic vasculitis (LV) and amyloid β-related angiitis (ABRA).

Methods: Formalin fixed paraffin embedded (FFPE) brain biopsy samples were cut for histology and RNA extraction (n=3 GV with HL, n=1 GV without HL, n=5 LV, n=4 ABRA, n=4 normal brain). RNA-sequencing was performed using Illumina® Hiseq-4000 platform and the Illumina® TruSeq® Total-RNA library. Student's t-test and false discovery



Unsupervised Clustering by RNAseq: 3 clusters are clearly defined. No cases clustered with normal samples

rate (FDR) tests were performed for each of the differentially expressed transcripts. Ingenuity Pathway Analysis® was used for the pathway expression analysis.

Results: Samples clustered in three groups by unsupervised analysis of gene expression profile. Cluster 1 (C1) included all samples of GV with HL plus one of the samples of LV. Cluster 2 (C2) included all ABRA samples plus 4/5 LV samples and the GV not associated with HL. Normal brain samples clustered together in cluster 3 (C3). Results indicated that PCNSV has specific transcriptomes compared to normal brain and GV with HL have a distinct profile from the other types of PCNSV. Pathway analysis revealed upregulation of dendritic cell maturation and antigen processing, T helper type 1 lymphocyte activation and neuroinflammation in PCNSV versus normal brain. The comparison of the different kinds of PCNSV showed that GV expressed CD28 at lower levels than LV (FDR < 0.01) suggesting a lower activation of lymphocytes. The top differentially expressed genes between GV and ABRA were TRAJ13 and CD27 suggesting an expansion of naïve and memory T cells in GV. Finally, only one gene, namely CD163, was expressed at lower levels in LV than in ABRA (FDR < 0.05) suggesting a lower presence of macrophages or the presence of anti-inflammatory mediators.

Conclusion: RNA sequencing revealed pathways deregulated in PCNSV and genes differentially expressed between the different kinds of PCNSV increasing the knowledge on PCNSV pathogenesis. It also sugested that GV with HL has an distinct gene expression profile compared to other types of PCNSV.

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Abstract Number: 0411

Serial Vessel Wall Enhancement Change on High-Resolution MRI Vessel Wall Imaging in Primary Central Nervous System Vasculitis

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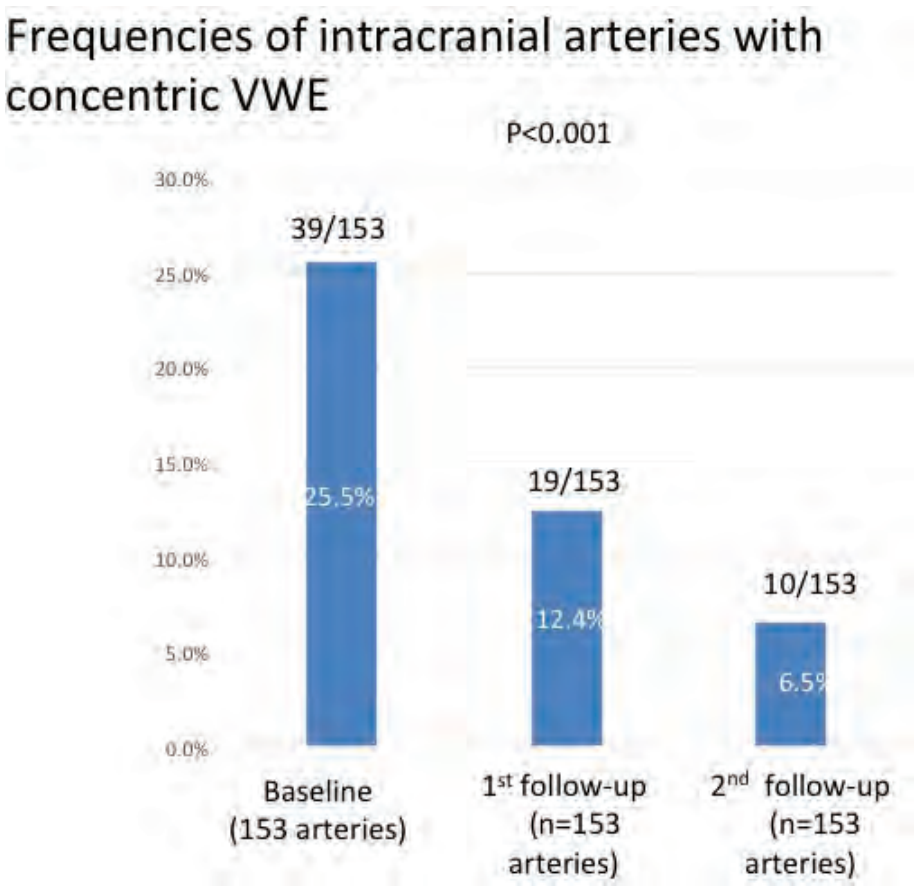
Background/Purpose: High-resolution vessel wall imaging (HR-VWI) is emerging as a tool of notable utility in the diagnosis of central nervous system vasculitis (CNS-V). However, little is known about monitoring the response to treatments in these patients. The aim of this study was to investigate the temporal vessel wall enhancement (VWE) pattern and its clinical practice through the management of patients with CNS-V

Methods: We extracted 9 patients with primary CNS-V who underwent serial high-resolution MRI vessel wall image (HR-VWI) from Cleveland Clinic prospective CNS vasculopathy registry. Visibility and VWE were analyzed in 17 intracranial artery segments (Bilateral ICA, M1, M2, A1, A2, P1, P2, VA, and BA). Intraluminal enhancement was classified into 3 categories (none, eccentric VWE, and concentric VWE).

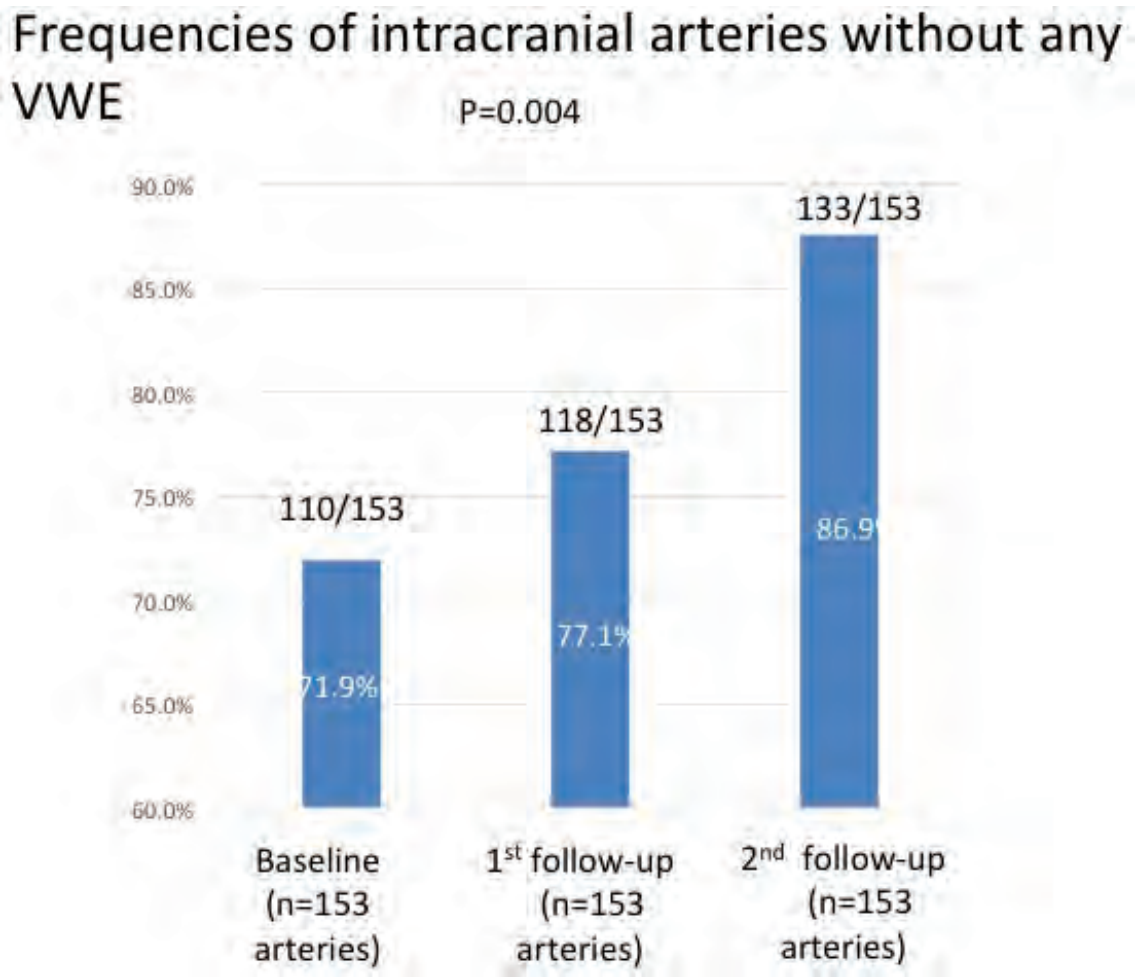
Results: In unique 153 intracranial arterial segments, 39 arteries (25.5%) had concentric VWE on baseline HR-VWI. The frequencies of intracranial arteries with concentric VWE have decreased to 12.4% (19 of 153 arteries) at 1st follow-up image and 6.5% (10 of 153 arteries) at 2nd follow-up image, respectively (P< 0.001), [figure 1]. By contrast, the



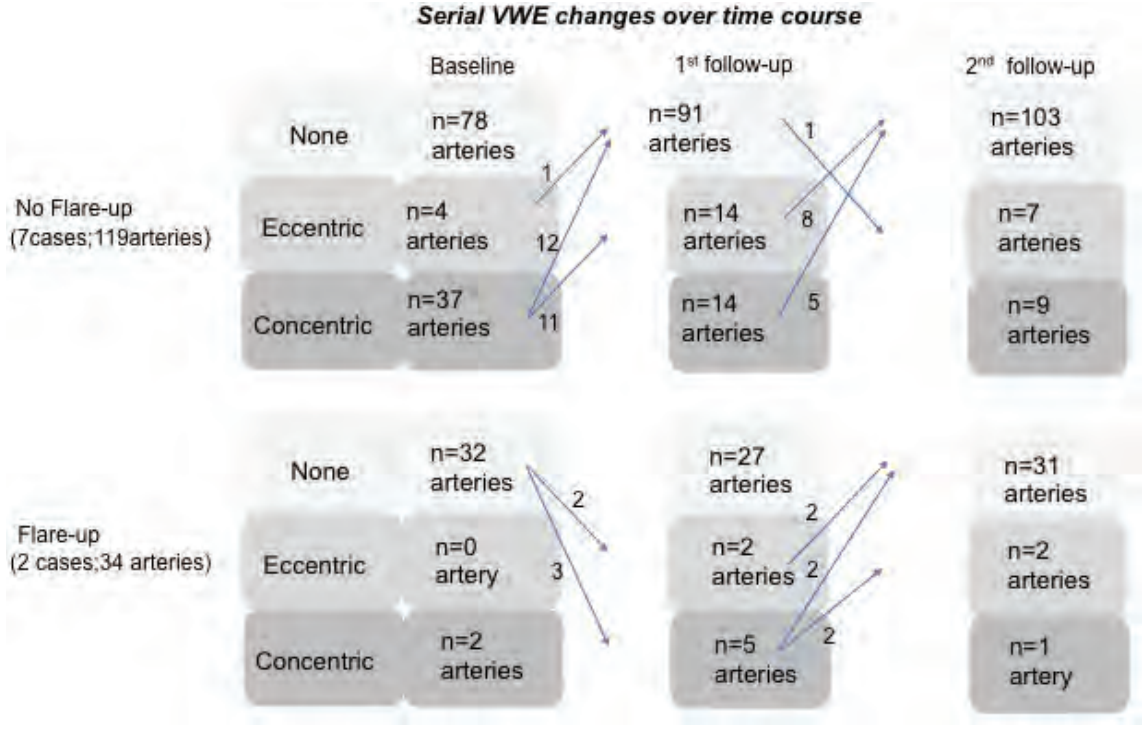
Frequencies of intracranial arteries with concentric vessel wall enhancement (VWE)

prevalence of intracranial arteries without VWE increased over time course (Baseline; 71.9% (110 of 153 arteries), 1st follow-up; 77.1% (118 of 153 arteries), and 2nd follow-up; 86.9% (133 of 153 arteries), P=0.004), [figure 2]. During the follow-up (mean follow-up 15.9 months), two patients had clinical flare-up at 1st follow-up image. New intraluminal enhancements were identified in 5 intracranial artery segments (Eccentric VWE: 0 to 2 arteries, Concentric VWE: 2 to 5 arteries). After intensive immunosuppressive treatment, VWE changes were improved at 2nd follow-up image (None: 27 to 31 arteries, Concentric VWE: 5 to 1 artery), [figure 3].

Conclusion: Decreasing contrast VWE at follow-up images were frequently observed in CNS-V patients after treatment. Patients with flare-up had temporal VWE worsening during the clinical course. Serial vessel wall enhancement pattern on HR-VWI may be useful for monitoring the response to treatment in patients with CNS-V. Larger studies are needed to validate our observation.



Frequencies of intracranial arteries without any vessel wall enhancement (VWE)



Serial vessel wall enhancement (VWE) changes over time

Disclosure: T. Shimoyama, None; **K. Uchino**, None; **L. Calabrese**, AbbVie, 1, 2, GlaxoSmithKline, 1, Bristol-Myers Squibb, 1, Genentech, 1, 2, Janssen, 1, 2, Novartis, 1, 2, Sanofi, 1, Horizon, 1, Crescendo, 1, Gilead, 1; **R. Hajj-ali**, ABBVIE, 1, Rockpoint, 1.

Abstract Number: 0412

2019 Novel Coronavirus Disease (COVID-19) in Patients with Large-Vessels Vasculitis: Single-centre Experience in Paris

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SESSION INFORMATION

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Background/Purpose: Advanced age and cardiovascular diseases are recognized as major comorbidities associated with severe forms of coronavirus disease 2019 (COVID-19) caused by the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2). Patients with large vessels vasculitis (LVV) could be considered at-risk for severe COVID-19 due to frequent age over 65 years in patients with giant cell arteritis (GCA), severe hypertension in patients with Takayasu arteritis (TAK) and current use of immunomodulating therapies in both LVV. The aim of this study was to determine the prevalence, clinical presentation and outcome of COVID-19 among LVV patients.

Methods: We retrospectively collected symptoms compatible with COVID-19 reported during SARS-CoV-2 pandemic in France, and severity, therapeutic management and outcomes of COVID-19 infection in all LVV patients followed for GCA or TAK in a single-tertiary centre.

Results: Between 04 and 20 may 2020, 148 patients with LVV were enrolled, including 84 GCA and 64 TAK. Median age at inclusion was 73 (67-82) years vs. 48 (42-62) for GCA and TAK, respectively, $p < 0.001$. Comorbidities such as hypertension, diabetes, obesity, and smoking habit were not significantly different between GCA and TAK group, except for the presence of solid cancer (19% vs 3% for GCA and TAK, respectively, $p = 0.004$). Seventy-seven percent of LVV patients were currently receiving glucocorticoids, 33% DMARDs and 20% biotherapies. Sixteen (11%) LVV patients presented a COVID-19 infection, including 9/84 (11%) GCA patients and 7/64 (11%) TAK patients. COVID-19 infections in LVV patients were confirmed by nasal PCR (n=3) and/or thoracic CT scan (n=3) and/or serological tests (n=3). Pneumonia occurred in 5 (31%) COVID-19 positive LVV patients, all requiring hospitalization and 4 oxygen therapy. LVV-COVID$^+$ patients had a more active vasculitis disease than LVV-COVID$^-$ patients ($p = 0.044$). Over a two-month period contemporary with the SARS-CoV-2 pandemic, in our LVV cohort we observed 3 COVID-19 related deaths (2 TAK and 1 GCA), leading to a mortality rate of 3/16 (18.8%).

Conclusion: Severe COVID-19 may occur in LVV requiring hospitalization in up to 30% of patients and frequent fatal issue. Active LVV or recent remission appear to increase the risk of COVID-infection.

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Abstract Number: 0413

Coronavirus Infection and Vasculitis: Identifying Associations Mining the Biomedical Literature

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SESSION INFORMATION
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Background/Purpose: Based on recent publications suggesting an association between COVID-19 and vascular inflammation, our aim was to explore new associations between coronavirus infections and vasculitis utilizing semantic mining of PubMed results.

Methods: The following literature search string: "(vasculitis OR vascular inflammation OR vascular damage) AND (coronavirus OR SARS virus OR MERS-CoV OR Covid-19)" was used to retrieve abstracts from the whole PubMed database, using Semantic MEDLINE 2 on 6/7/2020. This application represents a network of semantic predications (triples of the form subject-predicate-object, e.g. COVID-19 *causes* Disease) on a knowledge graph. The system allows for choosing the maximum number of nodes represented, the central topic, and the length of the network. For our network we chose to display all relations, COVID-19 (31 edges) as the central term, 3 lengths, and selecting the most informative nodes. Automatic summarization eliminated the less informative predications.

Results: The search string retrieved 152 citations from PubMed and identified 1,028 predications. The network (Figure 1), displayed using COVID-19 as the central term, consisted of 72 nodes and 140 edges. The 5 most connected nodes were 'Patients: 19 nodes', COVID-19: 13', 'Inflammation: 13', 'Lung: 11', and 'Disease: 11'.

Multiple links have been found between coronavirus and vasculitis. Animal coronaviruses, including the one causing feline infectious peritonitis (FIP), the murine coronavirus mouse hepatitis virus (MHV), the SARS-CoV in transgenic mice and coronavirus in ferrets, are known to cause vasculitis in animals. It is known that coronaviruses that infect animals can evolve and become new human coronaviruses. SARS produces inflammation in blood vessels. In 2005, a link between the coronavirus HCoV-NL63 or New Haven Coronavirus (HCoV-NH) and Kawasaki Disease (KD) was reported, although later studies concluded that HCoV-NH did not play a dominant role in the etiology or pathogenesis of KD. In 2014, serological testing suggested the possible involvement of HCoV-229E in the development of KD. There has also been a report of KD patients being infected by coronavirus OC43/HKU1. SARS-CoV2 may infect the vessels and trigger inflammatory reactions like those of vasculitis, including vasculitis-like cutaneous lesions. Some COVID-19 patients develop thrombosis, and increased risk of thrombosis is also present in primary vasculitic syndromes. Children, many of whom tested positive for COVID-19 antibodies, developed Multisystem Inflammatory Syndrome (MIS-C), an inflammatory condition similar to KD.

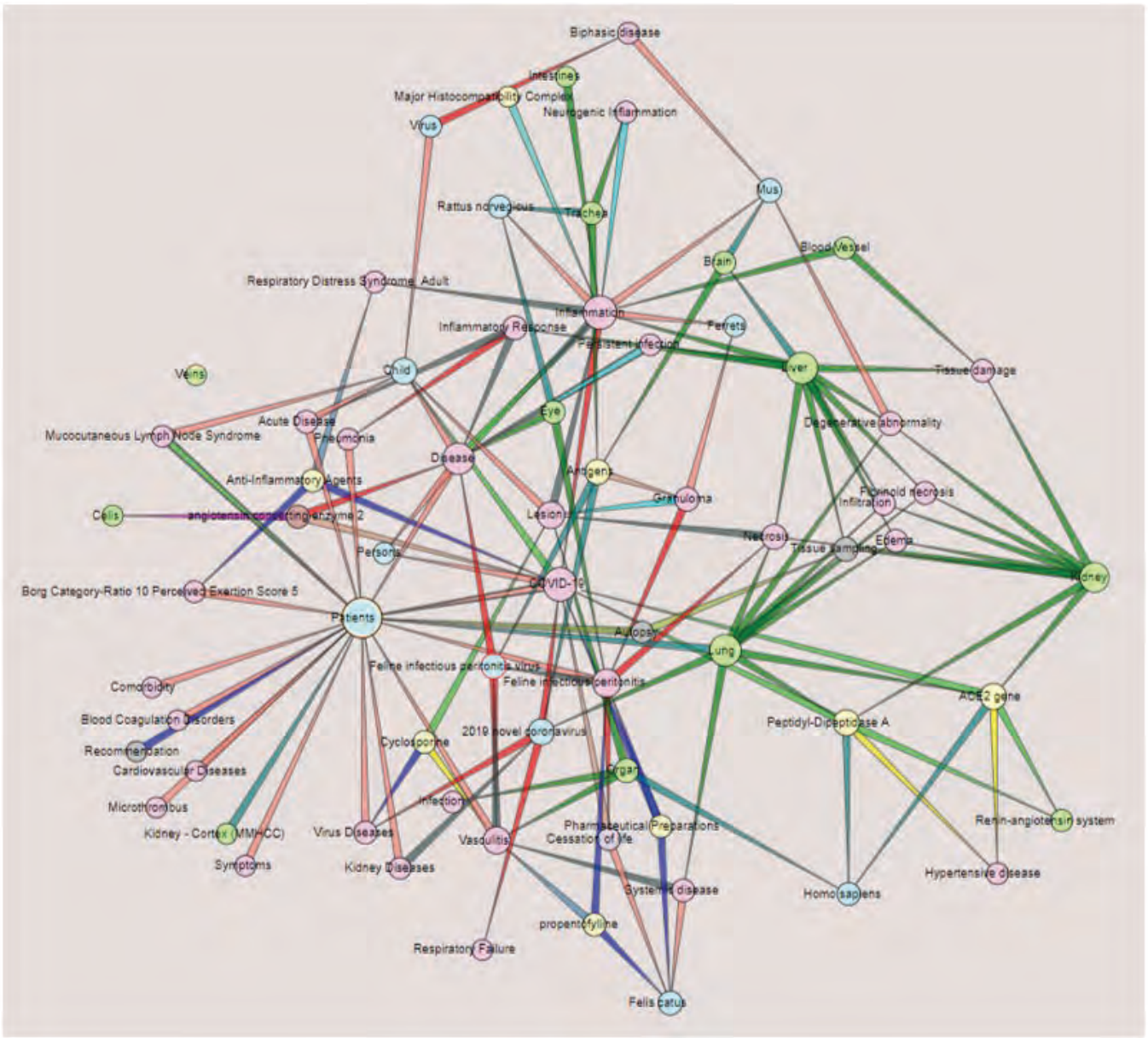

Figure 1. Semantic Network Resulting from PubMed Results

Conclusion: Knowledge integration and discovery methods are an efficient and powerful way of retrieving and analyzing relevant information from multiple papers. Their main advantages are finding relations among biomedical concepts, generating new hypotheses, and opening them to literature-based discovery.

SARS-CoV-2 may cause vasculitis or vasculitis-like syndromes. The KD-like syndrome reported mainly in children with COVID-19 revives the previous suspicion of coronavirus as a possible triggering agent of KD and the decades-old hypothesis of infection involvement in the pathogenesis of vasculitis.

Disclosure: A. Rodriguez Pla, None; **R. Cartin-Ceba**, None.

Abstract Number: 0414

Clinical Characteristics of an Internet-Based Cohort of Participants with a Self-Reported Diagnosis of Cryoglobulinemic Vasculitis or IgA Vasculitis

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SESSION INFORMATION
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Background/Purpose: Cyroglobulinemic vasculitis (CV) and IgA vasculitis are forms of small-vessel vasculitis characterized by immune complex deposition. The purpose of this study was to a) describe the characteristics of an international internet-based cohort of patients with a self-reported diagnosis of CV or IgA vasculitis and b) determine the extent to which these diagnoses agreed with established definitions of disease or classification criteria.

Methods: Participants with self-reported diagnoses of CV or IgA vasculitis were included in a prospective, internet-based, longitudinal registry from November 2014 to May 2020. All information was self-reported including diagnosis, symptoms at onset, and diagnostic testing.

Results: CV: 117 participants reported a diagnosis of CV (79% female). The racial/ethnic distribution was: 86% Caucasian/White, 3% Asian, 3% Hispanic/Latino and 2% African American/Black. Mean age at diagnosis was 48.7

Table 1: Comparison of Childhood and Adult onset IgA vasculitis

	Childhood onset*	Adult onset*	P-value
Female	17/26 (65%)	60/77 (78%)	0.203
Onset in summer	5/24 (21%)	30/74 (41%)	0.080
Manifestations			
Fevers	8/20 (40%)	19/57 (33%)	0.591
Purpura	26/26 (100%)	72/77 (94%)	0.183
Intussusception	2/25 (8%)	1/75 (1%)	0.091
GI bleed	7/23 (30%)	28/71 (39%)	0.438
Joint pains	24/25 (96%)	61/68 (89%)	0.337
Myalgia	22/23 (96%)	57/70 (81%)	0.098
Numbness	8/22 (36%)	46/65 (71%)	0.004
Hearing loss	3/23 (13%)	8/73 (11%)	0.784
Kidney involvement	17/25 (68%)	46/70 (66%)	0.836
ESRD	0/27 (0%)	1/76 (1%)	0.550
Thrombocytopenia	0/9 (0%)	10/31 (32%)	0.049

***Responses of "I don't know" were excluded from analysis.**
ESRD: end-stage renal disease

± 2.6 years. 22% had a history of hepatitis C and 13% of hematologic malignancy. 96% reported positive serum cryoglobulins. Common clinical manifestations included: purpura (94%), peripheral nerve involvement (93%), joint involvement (91%), and kidney involvement (27%). The establishment of the diagnosis was by laboratory testing (84%), symptoms (60%), and biopsy (37%). 108 participants (92%) met the Chapel Hill Consensus Conference (CHCC) definition.

IgA vasculitis: 103 participants reported a diagnosis of IgA vasculitis (75% female). The racial/ethnic distribution was: 88% Caucasian/White, 5% Asian, 5% Hispanic/Latino, 2% American Indian/Alaska Native, and 1% African American/Black. Mean age at diagnosis was 42.7 ± 3.2 years, with 77 (75%) developing symptoms in adulthood (≥18 years); there were few differences in clinical manifestations based on age of presentation (**Table 1**). 52% reported onset after an upper respiratory infection. Common clinical manifestations included: purpura (99%), joint involvement (93%), gastrointestinal pain/bleeding (70%), and kidney involvement (66%). Patients reported their diagnosis was established by biopsy results (68%), symptoms (62%), and serum laboratory testing (52%). 96 participants (93%) met the 1990 American College of Rheumatology criteria while 70 (68%) met the CHCC definition.

Conclusion: Self-reported clinical manifestations of CV and IgA vasculitis are similar to cohorts utilizing the traditional center-based approach. In addition, most patients with these diseases met established criteria or definitions for their disease. The diagnosis of CV appears to be more commonly reliant on laboratory testing as opposed to IgA vasculitis in which the diagnosis is more heavily based on biopsy results. Patients with adult-onset IgA vasculitis were more likely to develop peripheral neuropathy and thrombocytopenia. Patient-derived data from online registries is a feasible option for the conduct of future clinical trials in these rare and understudied diseases.

Disclosure: J. Springer, InflaRx, 2; **T. Kermani**, None; **D. Shaw**, None; **K. Young**, None; **C. Burroughs**, None; **P. Merkel**, AbbVie, 5, Biogen, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Insmed, 5, Jannsen, 5, Kiniksa, 5, Magenta, 5, Novartis, 5, Pfizer, 5, Sparrow, 5, Talaris, 5, AstraZeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, UpToDate, 7.

Abstract Number: 0415

Characteristics of Arthritis in Adult IgA Vasculitis

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Background/Purpose: Arthritis is one of the main clinical features in IgA vasculitis (IgAV). In children, joint involvement represents the second most common manifestation with the prevalence of ≈75%, and predilection for the knees and ankles. The aim of our study was to describe the characteristics of arthritis in adult IgAV.

Methods: We analysed medical records of histologically proven adult IgAV cases, diagnosed between January 2010 and May 2020 at our secondary/tertiary rheumatology centre. The frequency, temporal occurrence and the localization of arthritis was recorded. Additionally, we explored potential differences in other clinical features of acute IgAV between patients with and without arthritis.

Table 1. Clinical characteristics of IgA vasculitis patients with and without arthritis

Clinical characteristics	Arthritis IgAV (48)	Non-arthritis IgAV (265)	P value
Male gender (%)	56.3	61.5	0.523
Age (years)*	49.9 (36.1-66.9)	65.6 (49.0;78.2)	<0.001
Ever smoker (%)	50.0	41.9	0.343
Prior infection (%)	43.8	30.2	0.092
Generalized purpura	50.0	49.8	1.0
Skin necroses (%)	35.4	50.2	0.062
GI involvement (%)	47.9	26.4	0.005
Renal involvement (%)	47.9	46.8	1.0
Elevated serum IgA (%)	33.3 (11/33)	53.4 (111/208)	0.039

Legend: * median and IQR; GI gastrointestinal;

Results: During the 125-month observation period we identified 313 new IgAV cases (60.7 % males, median (IQR) age 64.6 (45.6; 77.1) years). Arthritis developed in 48 (15.3%) patients and was the first IgAV manifestation in 16 (5.1%) patients. Arthritis was mono-, oligo- and poly- articular (involving up to 15 joints) in 13 (4.2%), 25 (8%) and 10 (3.2%) patients, respectively. Arthritis was most common in wrists and ankles (each in 18 (37.5%) patients); metacarpophalangeal joints and knees (each in 11 (22.9%)); proximal interphalangeal joints (9 (18.8%)); elbows (8 (16.7%)) and metatarsophalangeal joints (4 (8.3%)). Table 1 shows clinical differences between IgAV patients with and without arthritis. Patients with arthritis were significantly younger, more commonly had gastrointestinal tract involvement and less frequently elevated serum IgA. Arthritis remitted in all with immunomodulatory treatment (given predominantly for necrotic skin purpura or visceral involvement). Follow up (FU) data accessible for 40/48 (83.3%) patients with arthritis showed that IgAV relapsed in 10 (25%) patients during a median (IQR) 24.6 (11.2; 41.8) month FU. Relapses were limited to skin and/or kidneys, there were no relapses of arthritis.

Conclusion: Arthritis more commonly affected younger adults with IgAV, was frequently oligoarticular, involved large and small joints of both upper and lower extremities and unlike skin lesions or renal involvement was not prone to chronic course and recurrence.

Disclosure: A. Hocevar, None; **V. Jurcic**, None; **M. Tomsic**, None; **Z. Rotar**, None.

Abstract Number: 0416

IgG4-related Retroperitoneal Fibrosis. Retrospective Cohort

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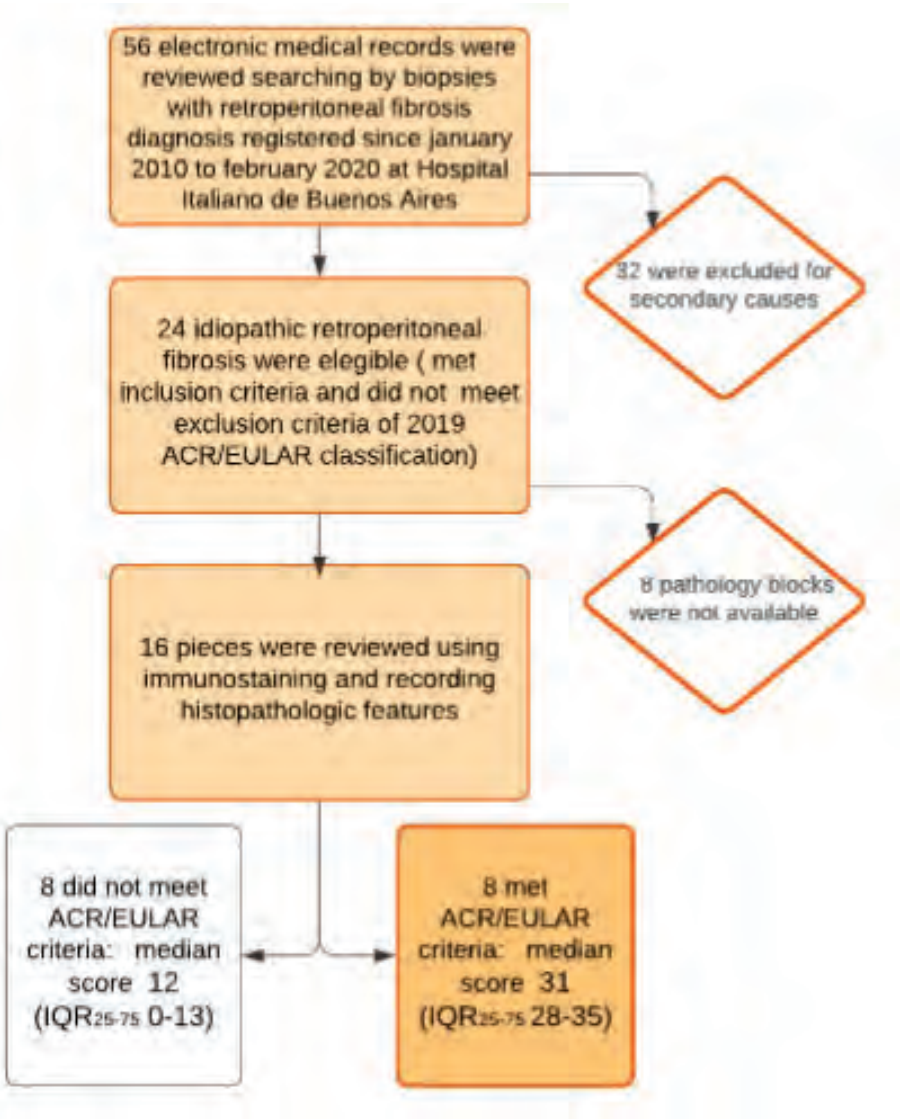

Figure 1. Overview of patient selection

Table 1. Clinical and radiologic features of IgG4- related and non - IgG4- related retroperitoneal fibrosis

	IgG4-RD (n=8)	Non IgG4-R(n=8)	*p*
Male sex*	5 (62%)	8 (100%)	0.2
Age#	61 (59 -63)	54 (47.2-60)	0.32
Allergic disease*	1 (12.5%)	2 (25%)	1
Hypertension*	3 (37.5%)	4 (50%)	1
Diabetes*	1 (12.5%)	2 (25%)	1
Collagenopathy*	0	0	-
Cardiovascular events*	1 (12.5%)	1 (12.5%)	1
Thromboembolic events*	1 (12.5%)	2 (25%)	1
Cancer*	1 (12.5%)	2 (25%)	1
Other IgG4-RD manifestation*	3 (37.5%)	0	0.06
Presenting symptoms*			
- Anorexia	2 (25%)	1 (12.5%)	1
- Low back pain	2 (25%)	2 (25%)	1
- Abdominal pain	0	2 (25%)	0.47
- Weight loss	2 (25%)	1 (12.5%)	1
- Anuria	1(12.5%)	0	1
- Acute heart failure	1 (12.5%)	0	1
- Incidental finding	0	1 (12.5%)	1
Renal failure*			
- Acute	4 (50%)	3 (37.5%)	1
- Chronic	5 (62.5%)	3 (37.5%)	0.59
Hemodialysis*	2 (25%)	1 (12.5%)	1
Location mass*			
-Infrarrenal	8 (100%)	6 (75%)	0.47
-Periaortic	8 (100%)	4 (50%)	0.19
-Periiliac	5 (62.5%)	5 (62.5%)	1
-Mesenteric	1 (12.5%)	0	1
-Presacral	1 (12.5%)	2 (25%)	1
Hydronefrosis*			
-Unilateral	2 (25%)	4 (50%)	0.6
-Bilateral	4 (50%)	2 (25%)	0.6
Drug therapy*			
- Corticosteroids	3 (37.5%)	2(25%)	1
- Azathioprine	1 (12.5%)	1 (12.5%)	1
- Mycophenolate	0	1 (12.5%)	1
- Metotrexate	0	1 (12.5%)	1
- Rituximab	0	0	
Only surgical treatment*	0	1 (12.5%)	1
Only endoscopic treatment*	1 (12.5%)	1 (12.5%)	1
Both*	6 (75%)	5 (62.5%)	1
Number of hospitalizations#	3 (2- 3,5)	2(1.5 - 2.5)	0.07

*Absolute frequency (%), #median (IQR_{25-75})

Background/Purpose: The spectrum of IgG4-related disease (IgG4-RD) includes many diseases that were thought to be confined to a single organ, as the retroperitoneal fibrosis. Many patients identified with idiopathic retroperitoneal fibrosis (IRF) could be reclassified as IgG4-RD, due to immunohistochemistry techniques. Classification criteria have

Table 2. Histopathological features of IgG4- related and non - IgG4- related retroperitoneal fibrosis

	IgG4-RD (n=8)	Non IgG4-R(n=8)	*p*
Biopsy area (mm^2)*	144 (75.5 - 258)	42 (13 - 108)	0.16
Storiform fibrosis*	8 (100%)	1 (12.5%)	0.01
Non storiform fibrosis*	0	7 (87.5%)	0.01
Dense lymphocytic infiltrate*	8 (100%)	5 (62.5%)	0.46
Obliterative phlebitis*	3 (37.5%)	1 (12.5%)	0.56
Non-obliterative phlebitis*	2 (25%)	1 (12.5%)	1
Eosinophils*	6 (75%)	1 (12.5%)	0.04
Germinal centers*	3 (37.5%)	2 (25%)	1
Fat necrosis*	0	0	-
IgG4+ cells/hpf*	17.8 (15.5 - 22.8)	1 (0.75 - 9.5)	0.01
IgG4/IgG ratio*	41 (18 - 59.5)	12.5 (10.2 - 14)	0.03
*Absolute frequency (%), *median (IQR_{25-75})			

not been uniform during last years and IgG4-related retroperitoneal fibrosis frequency is unknown in our country. We aim to describe IgG4-related retroperitoneal fibrosis (IgG4-RF) frequency using last published criteria and compare clinical, histopathologic and radiologic features with non-Ig4-RF

Methods: A dynamic retrospective cohort involving 16 adults with histopathological diagnosis of IRF at Hospital Italiano de Buenos Aires since january 2010 to february 2020 was studied. Pathology slides were reviewed, and immunohistochemistry for IgG4 and IgG was performed and assessed for each case. 2019 American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) classification criteria were used to identify IgG4-RD cases. Mann Whitney U test and the Fisher exact test were used to compare continuous and categorical variables respectively

Results: 8 (50%) patients met criteria for IgG4-RF. The median age was similar in the two subsets (61 years old in IgG4-RF versus 54, p = 0.2) and both had male predominance. 3 patients presented other manifestations of IgG4-RD in IgG4-RF group. None had either high serum IgG4 levels or eosinophilia. All of the IgG4-RF had infrarenal and circumferential retroperitoneal extension along the aorta on computed tomography but there were not significant differences with non-IgG4-RF (p= 0.4 and 0.1). Hydronephrosis, renal failure and requirement of renal replacement therapy did not differ between groups. Corticosteroids were mostly used as drug therapy, followed by azathioprine but most of the patients did not receive specific treatment. 7 (87.5%) patients needed surgical or endoscopic intervention in each group. 7 patients in each subset were admitted to hospital with a similar median number of hospitalizations (3 in IgG4-RF versus 2, p=0.07). All of Ig4-RF patients had a dense lymphocytic infiltrate and storiform fibrosis (p=0.01) and 75% presented eosinophils (p=0.04). IgG4+ cells/hpf and IgG4/IgG ratio were significantly higher than patients with non-Ig4-RF (p = 0.01 and 0.03, respectively)

Conclusion: Half of patients in our IRF retrospective cohort met criteria of IgG4-RF, first data in our region. ACR/ EULAR new criteria may be helpful in order to homogenize the identification of Ig4-RD. These findings may motivate further evaluation of this condition, increasing early recognition, accurate treatment and integral follow-up

Disclosure: E. Angarola, None; **F. Jauk**, None; **V. Peuchot**, None; **M. Orlova**, None; **M. Valeo**, None; **J. Pollan**, None; **H. Garcia Rivello**, None.

Abstract Number: 0417

Different Immunophenotypes Characterized IgG4-Related Disease Clinical Phenotypes

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Background/Purpose: Patients with IgG4-related disease (IgG4-RD) can be classified in clinical phenotypes which differ in terms of demographics, clinical and serological features. Whether there are also differences in the immunophenotype of each phenotype is unknown. Our aim was to characterize the immunophenotype of IgG4-RD patients according to their clinical phenotype.

Methods: We included consecutive patients with a diagnosis of IgG4-RD according to the Comprehensive Diagnostic Criteria for IgG4-RD who attended our Institution from Aug 2018 to Nov 2019. Healthy subjects were included as controls. We obtained peripheral blood for isolation of peripheral mononuclear cells and through negative selection, CD4+ memory T cells were obtained. We determined the percentage of the following cell subsets by flow cytometry:

- Th2 (CD4+/CD45RO+/CD14-/IL-4+; CD4+/CD45RO+/CD14-/IL-13+, CD4+/CD45RO+/CD14-/IL-5+);
- CD4+IL-21 T cells (CD4+/CD45RO+/CD14-/IL-21+);
- CD4+ cytotoxic T cells (CTLs) (CD4+/CD45RO+/SLAMF7+/IL-1β+/TGF-β1+);
- Th9 (CD3+/CD4+/ CD45RO+/IL-9);
- T follicular helper cells (Tfh) (CD4+/CD45RO+/CCR7-/ICOS+/CCCR5+/Bcl6+);
- Tfh1 (CD4+/CD45RO+/CCR7-/ICOS+/CCCR5+/Bcl6+/IFN-γ+);
- Tfh2 (CD4+/CD45RO+/CCR7-/ICOS+/CCCR5+/Bcl6+/IL-4+);
- Tfh17 (CD4+/CD45RO+/CCR7-/ICOS+/CCCR5+/Bcl6+/IL-17+);
- Tfr (CD4+/CD45RO+/CCR7-/ICOS+/CCCR5+/Bcl6+/Foxp3+);
- Tregs (CD4+/CD25hi/CD127-/Foxp3+);
- Tr1 (CD4+/CD25low/Foxp3-/IL-10+);
- Th3 (CD4+/CD25-/Foxp3-/TGF-β1+);
- Bregs (CD19+/CD24hi/CD38hi/IL-10+);
- Plasmocitoid dendritic cells (pDC) (CD86+/CD163hi/IL-10+);
- M1 macrophages (CD86+/CD127+/TNF-α+);
- M2 macrophages (CD163+/CD14+/TGF-β1+/IL-33+).

Results: We recruited 43 patients with a mean age of 52.3±16.4 years, 48.8% were male. Twelve controls were included. Eight (18.6%) patients belong to the pancreato-hepatobiliary, 7 (16.3%) to the retroperitoneal-aorta, 16 (37.2%) to the head and neck limited and 12 (27.9%) to the Mikulicz/Systemic phenotypes. Twenty two (51.2%) had active disease. The percentages of all cell subsets were statistically higher in patients vs controls, with the exception

of Tr1 cells. The percentages of the following cell subsets were different among clinical phenotypes: Th2 (CD4+/IL-4+) (p=0.029), Th2 (CD4+/IL-5+) (p=0.047), CD4+ CTLs, (p=< 0.001), Tfh17 (p=0.005), Tregs FOXP3+ (p=0.008), Th3 (p=0.02), Bregs (p=0.005) and pDC IL-10 (p=0.016). In a sensitive analysis including only the 22 patients with active disease, the same cell subsets remained significant and we also observed differences in Tfh1 (p=0.03), Tfh2 (p=0.009), Tr1 (p=0.034), and M1 macrophages (p=0.03). Patients with active IgG4-RD had higher proportions of Tfh (< 0.001), Tfh17 (p< 0.001), Tr1 (p=0.001), Th3 (p=0.01), pDC IL-10 (0.005) and M1 macrophages (p=0.017). There were no differences according to the presence of atopy or immunosuppressive treatment at recruitment.

Conclusion: Our study showed that the clinical heterogeneity of IgG4-RD might be driven by the participation of different immune cell subsets.

Disclosure: E. Martin-Nares, None; **J. Furuzawa-Carballeda**, None; **Á. Priego-Ranero**, None; **I. Chan-Campos**, None; **G. Herrera-Noguera**, None; **F. López-Verdugo**, None; **G. Hernandez-Molina**, None.

Abstract Number: 0418

Prevalence of Thyroid Disease Among Patients with Vasculitis

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Background/Purpose: Previous studies have reported higher risk of thyroid disease in patients with giant cell arteritis (GCA) and ANCA-associated vasculitis (AAV) compared to age- and sex-matched controls. The aim of this study was to compare the risk of hypothyroidism or hyperthyroidism in patients with large-vessel vasculitis (giant cell arteritis, GCA and Takayasu's arteritis, TAK), polyarteritis nodosa (PAN), and AAV.

Methods: Patients GCA, TAK, PAN, granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), and eosinophilic granulomatosis with polyangiitis (EGPA) enrolled in a prospective, multicenter, longitudinal study were included. All patients were followed with standardized data collection. Information on type of thyroid disease was systematically collected for each form of vasculitis. Odds ratios (OR) and 95% confidence intervals (CI) for risk of thyroid diseases were calculated between clinical subgroups.

Results: The study included 2,087 patients, 63% female, 90% White, mean age 54.6 (±17.2) years. Diagnoses were: GCA (427, 20%), TAK (225, 11%), PAN (108, 5%), GPA (873, 42%), MPA (170, 8%), and EGPA (285, 14%).

Thyroid disease was present in 246 patients (12% overall cohort), 83% female, mean (±SD) age 59.2 (14.8) years. The majority of the cases were hypothyroidism; 217 patients (88% with thyroid disease). The frequency of thyroid

Table 1: Thyroid Disease by Type of Vasculitis

Variable	GCA N=427	TAK N=225	PAN N=108	GPA N=873	MPA N=170	EGPA N=285
Mean age±(SD), years	72 (8.5)	38.4 (12.7)	48.6 (16.2)	50.7 (16.3)	59.7(14.5)	53.3 (13.8)
Female sex, N (%)	300 (70)	209 (93)	60 (55)	467 (54)	107 (63)	159 (56)
Ethnicity, N (%)						
White	413 (97)	182 (81)	92 (85)	800 (92)	151 (89)	248 (87)
African American	5 (1)	10 (4)	5 (5)	15 (2)	4 (2)	6 (5)
Asian	4 (1)	28 (12)	6 (6)	39 (5)	5 (3)	16 (6)
Other	5 (1)	5 (2)	5 (5)	19 (2)	10 (6)	15 (5)
Any thyroid disease, N (%)	55 (23)	20 (9)	7 (7)	107 (12)	31 (18)	26 (9)
Hypothyroidism, N (%)	51 (12)	14 (6)	6 (6)	93 (11)	30 (18)	23 (8)
Hyperthyroidism, N (%)	4 (1)	6 (3)	1 (1)	14 (2)	1 (1)	3 (1)
Any thyroid disease, OR* (95% CI)	0.58 (0.40, 0.85)	0.72 (0.43, 1.20)	0.60 (0.27, 1.32)	1.54 (1.16, 2.05)	1.70 (1.12, 2.59)	0.77 (.050, 1.20)
Hypothyroidism, OR* (95% CI)	0.61 (0.41, 0.90)	0.57 (0.31, 1.03)	0.59 (0.25, 1.38)	1.51 (1.12, 2.05)	1.81 (1.18, 2.80)	0.82 (0.52, 1.30)
Hyperthyroidism, OR* (95% CI)	0.40 (0.13, 1.30)	1.80 (0.65, 4.97)	0.69 (0.09, 5.16)	1.52 (0.72, 3.21)	0.78 (0.18, 3.33)	0.76 (0.23, 2.52)

GCA=giant cell arteritis, TAK=Takayasu arteritis, PAN=polyarteritis nodosa, GPA=granulomatosis with polyangiitis, MPA=microscopic polyangiitis, EGPA=eosinophilic granulomatosis with polyangiitis, N=number of patients, SD=standard deviation, OR=odds ratio, CI=confidence intervals

* age- and sex-adjusted

disease by type of vasculitis, and, age- and sex-adjusted OR for thyroid disease is in **Table 1.** Adjusting for age and sex, patients with LVV had lower risk of hypothyroidism (OR 0.59, 95% CI 0.42, 0.81) while risk of hypothyroidism was higher in patients with AAV (OR 1.80, 95% CI 1.31, 2.47). Patients with GCA had the lowest risk compared to the other forms of vasculitis while patients with GPA and MPA had the highest risk (**Table 1**). There were no differences in age- and sex-adjusted risk of hyperthyroidism between the different forms of vasculitis (**Table 1**).

Conclusion: There are important differences in the risk of hypothyroidism, but not hyperthyroidism, between the different forms of vasculitis. Patients with GCA have the lowest age- and sex- adjusted risk of hypothyroidism while patients with GPA and MPA had the highest risk. Possible explanations for these findings include differences in genetic susceptibilities, immune responses, or treatment exposures between the forms of vasculitis. The interplay of thyroid disease and vasculitis warrants further investigation.

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Abstract Number: 0419

Survival and Prevalent Comorbidities in Polymyalgia Rheumatica

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Background/Purpose: There is limited information on mortality in patients with polymyalgia rheumatica (PMR), and on prevalent comorbidity at the time of diagnosis of PMR. The purpose of this study was to investigate survival in a community-based sample of patients with PMR diagnosed in primary health care (PHC) compared to the general population. Furthermore, we assessed comorbidities diagnosed prior to PMR diagnosis, and their impact on mortality.

Methods: A community-based cohort of consecutive patients with a validated diagnosis of PMR at two PHC centres (1) between 2000 and 2013 was investigated. Validation was based on a review of the electronic records by an experienced rheumatologist, taking into account the disease course and differential diagnoses. Four controls, matched for age, sex and municipality were retrieved from the regional health care database. The index date was defined as the date of PMR diagnosis in cases and the corresponding date in the matched controls. Cases and controls were censored at death, emigration, 10 years of follow-up or the end date of the study (December 31, 2018). Prevalent comorbidity was defined as ≥1 ICD-code indicating a predefined condition prior to the index date. Survival in PMR cases and controls was estimated using the Kaplan-Meier method (log rank test). The impact of PMR and comorbidities was investigated in Cox regression models.

Table 1. Registered comorbidities before index date; n (%)

	PMR cases N=113	Controls N=452	p
Coronary artery disease (CAD)	8 (7.0)	55 (12.1)	0.12
Cerebrovascular disease (CeVD)	9 (7.9)	37 (8.1)	0.94
Peripheral artery disease (PAD)	4 (3.5)	21 (4.6)	0.61
Cardiovascular disease (CVD)	18 (15.9)	102 (22.5)	0.12
Hypertension	28 (24.7)	167 (36.9)	0.02
Diabetes	10 (8.8)	102 (22.5)	0.001
Malignancy	12 (10.6)	102 (22.5)	0.005
COPD	6 (5.3)	39 (8.6)	0.24

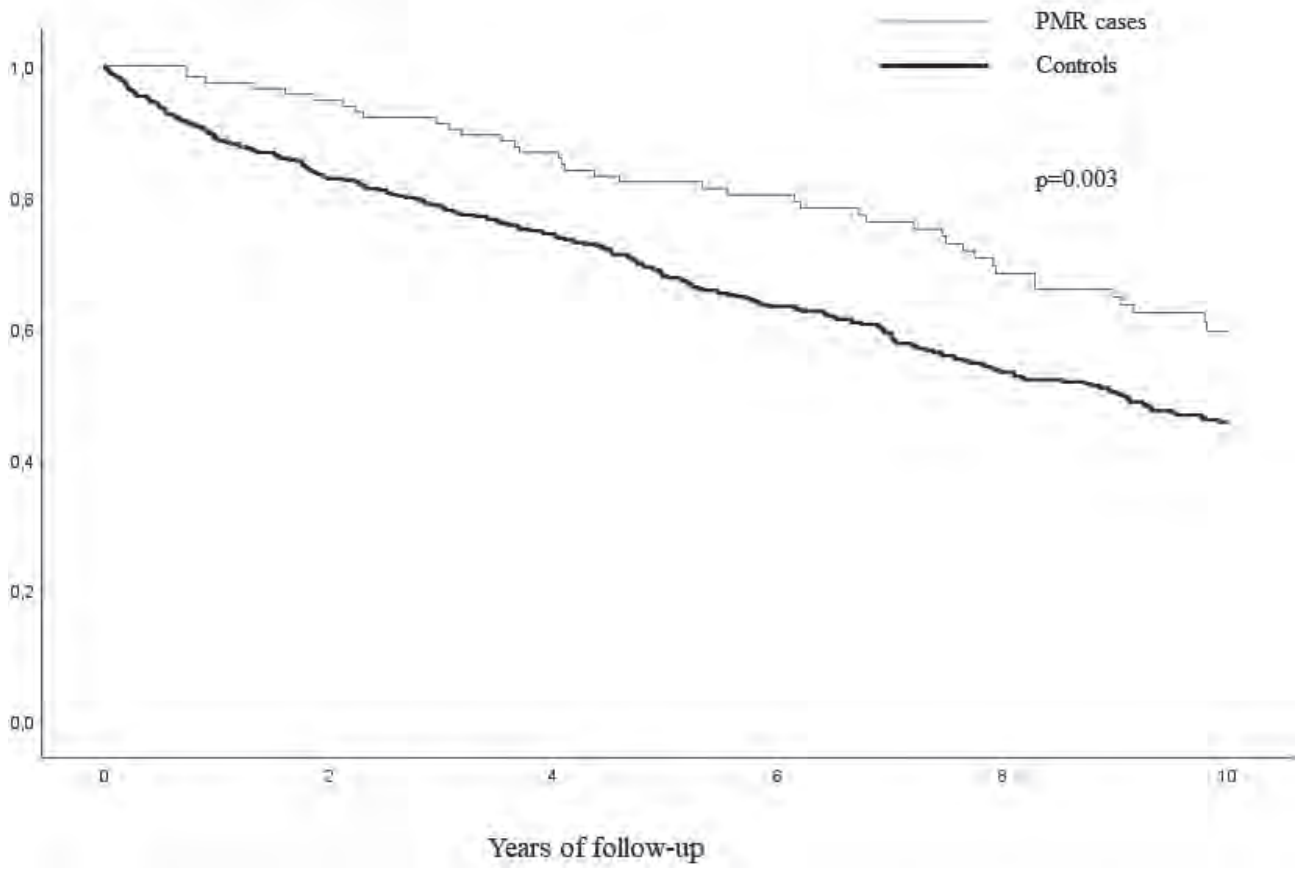
CVD: CAD and/or CeVD and/or PAD. COPD: Chronic obstructive pulmonary disease

Table 2. Predictors of mortality (Cases and controls combined)
Cox regression, univariate analyses

	Hazard ratio (95 % CI)
PMR	0.62 (0.45-0.84)
Coronary artery disease (CAD)	1.30 (0.94-1.79)
Cerebrovascular disease (CeVD)	1.49 (1.02-2.17)
Peripheral artery disease (PAD)	2.14 (1.34-3.41)
Cardiovascular disease (CVD)	1.51 (1.17-1.94)
Hypertension	1.15 (0.92-1.45)
Diabetes	1.79 (1.39–2.32)
Malignancy	1.86 (1.45-2.40)
COPD	2.36 (1.66-3.36)

CVD: CAD and/or CeVD and/or PAD.
COPD: Chronic obstructive pulmonary disease

Figure 1. Survival in cases with PMR and age-sex matched controls



Results: One hundred and thirteen patients with verified PMR (68 % women, mean age at diagnosis 75.3 years) and 452 matched controls were included. There were 40 (35.4%) deaths among the PMR cases, and 252 (55.7%) among the controls. Survival was significantly higher in PMR cases compared to controls (Figure 1). There was not a single

death during the first 0.7 years after diagnosis among the patients with PMR (Figure 1). Among the investigated comorbidities, diabetes, malignancy and hypertension were diagnosed in significantly lower proportions prior to the index date in patients with PMR compared to controls (Table 1). Prevalent malignancy, diabetes and cardiovascular disease (CVD) were all associated with increased mortality in pooled analysis of cases and controls (Table 2). In analysis adjusted for malignancy, diabetes and CVD, PMR was associated with reduced mortality (adjusted hazard ratio (HR) 0.66; 95 % CI 0.48-0.90). In a sensitivity analysis, excluding the first 0.7 years of follow-up to avoid short term survival bias after PMR diagnosis, the association between PMR and reduced mortality did not reach statistical significance (adjusted HR 0.75; 95 % CI 0.55-1.04).

Conclusion: Patients with PMR diagnosed in PHC had an improved survival compared to the background population, and were less likely to have been diagnosed with several comorbidities. The reduced mortality in PMR may be partly due to a tendency to regard PMR as a diagnosis of exclusion, and a reluctance to make a diagnosis of PMR in patients with serious comorbidities and a poor prognosis. Alternatively, factors that predispose to PMR may protect from other conditions, in particular diabetes and malignancy.

Reference

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Abstract Number: 0420

Prospective Analysis of the Prevalence of Giant Cell Arteritis in Consecutive Newly Diagnosed Patients with Polymyalgia Rheumatica

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Background/Purpose: Giant cell arteritis (GCA) is the most common form of systemic vasculitis affecting people aged 50 years and older.[1] Although it is known, that GCA often coexists with polymyalgia rheumatica (PMR)[2], to this point, the prevalence of GCA in consecutive newly diagnosed patients with PMR has not been investigated.

Methods: Consecutive patients with newly diagnosed PMR fulfilling the ACR /EULAR classification criteria[3] were included. Vascular US examination of the extracranial arteries typically involved in GCA, such as axillary arteries, vertebral arteries, common carotid arteries, superficial temporal arteries with both frontal and parietal branches, occipital arteries, facial arteries and the central retinal arteries was performed in all PMR patients. Typical symptoms of GCA and PMR were recorded. Diagnosis of GCA was made, if intima-media thickness (IMT) was above respective cut-off values.[4]

Symptoms	Group	
	PMR-group	GCA-PMR-group
Morning stiffness	22 (95%)	23 (85%)
=1 shoulder with synovits or bursitis trochanterica	12 (52%)	13 (48%)
=1 shoulder or hip with synovitis or bursitis	11 (48%)	14 (51%)
Absence of RF/ anti-CCP	5 (21%)	11 (40%)
Hip pain	23 (100%)	23 (85%)
No other joints affected	22 (95%)	26 (96%)

PMR-group: patients with diagnosis of polymyalgia rheumatica only
GCA-PMR-group: patients with diagnosis of polymyalgia rheumatica and giant cell arteritis

Table 1. Number of patients fulfilling ACR/EULAR classification criteria for polymyalgia rheumatica

Results: Fifty patients with newly diagnosed PMR were included. In 27 PMR patients, GCA was diagnosed by vascular ultrasound (GCA-PMR group), while 23 PMR patients showed no evidence of GCA (PMR-group). Mean age of the PMR-GCA group was 74 years (SD ± 9) with ten (37%) females, while mean age in the PMR-GCA group was 71 years (SD ± 10.1) with seventeen (73%) females. Mean C-reactive protein (CRP) values were 29.4 mg/l (SD±24.5) in the PMR-group and 52.2 mg/l (SD±43.2) in the GCA-PMR group. CRP values were not found to be significant between groups (p = 0.1432). Forty-five of all patients (90%) described morning stiffness. Ten patients (37%) in the GCA-PMR group did not complain of any GCA symptoms, GCA was only detected by ultrasound examination. Every patient with diagnosis of PMR had shoulder or hip inflammation on US. Characteristic symptoms of PMR and GCA and the number of patients with respective symptoms are depicted in table 1 and 2.

Conclusion: Prevalence of GCA in patients with PMR in our cohort was 54%. CRP was higher in the GCA-PMR group compared to the PMR-group. Ten (37%) patients with GCA and PMR did not have any GCA symptoms. Performing vascular US in patients with PMR can be useful to diagnose a clinical inapparent GCA. Prompt onset of the respective therapy could prevent complications of GCA, glucocorticoid therapy and probably improve disease outcome.

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Abstract Number: 0421

Polymyalgia Rheumatica Is Associated with Later Menopause: An Observational Study

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Background/Purpose: Oestrogen exposure leads to an increase in peak bone mass whereas menopause is associated with rapid bone loss. Numerous studies have linked rheumatoid arthritis (RA), systemic lupus erythematosus (SLE) and osteoarthritis to an earlier menopause; however, there are paucity of data in polymyalgia rheumatica (PMR). This study aims to establish whether PMR is associated with a later self-reported age of menopause.

Methods: Post menopausal patients who were referred for bone mineral density (BMD) estimation in a scanner in the North West of England between June 2004 and October 2015 were included in the analysis. All patients had their baseline demographics recorded at time of scan as well as risk factors for fracture including presence of PMR, RA, SLE and coeliac disease, excess alcohol intake, corticosteroid use, smoking history and parental family history of hip fracture. Bone mineral density (BMD) was measured at the left neck of femur and the lumbar spine. Patients were grouped into those with a clinician made diagnosis of PMR and those without; and initially compared using student's T-test. Univariate and multivariate linear regression models were then fitted to examine associations with age of menopause in this group. All statistical analysis was performed using STATA v13, with results expressed as coefficients with 95% confidence intervals (95%CI).

Results: We recruited 14481 post-menopausal patients with a mean (SD) age of menopause of 65.5 years (10.8). 407 patients (2.8%) had a diagnosis of PMR, 63 (0.44%) patients with SLE, 832 (5.8%) with RA and 272 (1.9%) with coeliac disease. In this cohort, 4742 (32.8%) patient had a smoking history, 810 (5.6%) drank an excess of alcohol, 3157 (21.8%) were taking corticosteroids and 2428 (16.8%) had a parental family history of hip fracture. The mean age (SD) of patients was 65.5 (10.8) years. Mean age of menopause was later in patients with PMR (49.3 vs 48.2 years, mean difference 1.1 years, p=< 0.001). Results of the univariate analysis are shown in table 1. This analysis showed that PMR, increasing age and increased BMD in the lumbar spine are associated with a later age of menopause. Smoking and SLE, however, were associated with an earlier age of menopause. In the multivariable model when adjusting for

Table 1. Linear regression analysis of patient's parameters with 95% confidence interval (CI). BMD, bone mineral density.

Predictor of menopause	Beta co-efficient	95% CI	P value
Age	0.07	0.09, 0.10	<0.001
Previous smoker	-0.95	-1.14, -0.77	<0.001
Body mass index	-0.00	-0.02, 0.01	0.756
Polymyalgia rheumatica	1.15	0.63, 1.68	<0.001
Systemic lupus erythematosus	-3.03	-4.35, -1.72	<0.001
Coeliac disease	-0.08	-0.72, 0.55	0.797
Rheumatoid arthritis	-0.19	-0.56, 0.18	0.315
History of fragility fracture	0.11	-0.07, 0.28	0.246
Parental history of hip fracture	-0.03	-0.27, 0.20	0.770
BMD left femoral neck	-0.63	-1.28, 0.02	0.06
BMD lumbar spine	0.96	0.51, 1.41	<0.001

all of the above, delayed menopause was still significantly associated with PMR (beta co-efficient 1.34 95% CI 0.72, 1.96, p< 0.001).

Conclusion: In this large observational study, women with PMR have a later onset of self reported menopause. This is the first study to establish this association between the age of menopause and PMR. Further studies will be required to confirm this association and review whether the age of menopause is a risk factor for PMR.

Disclosure: S. Dyball, None; **C. Saleh**, None; **M. Bukhari**, Bristol- Myers Squib, 1, UCB celltech, 1, 2, Roche, 1, 2, Abbvie, 1, 2, Merck, 1, 2, Mennarini, 1, 2, Sanofi-aventis, 1, 2, Elli-Lilly, 1, 2, Janseen, 1, Amgen, 1, 2, Novartis, 1, 2.

Abstract Number: 0422

Frailty and Health-Related Quality of Life in Patients with Polymyalgia Rheumatica

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Background/Purpose: Frailty is a syndrome characterized by an increased vulnerability to stressors. Frailty and pre-frailty have been reported in 10% and 44%of community dwelling elderly, respectively.[1] Chronic inflammation is a risk factor for frailty. Patients with PMR represent a population at high risk for frailty; however, there are no data on the prevalence and impact of frailty in PMR patients. The objective of this study is to describe the prevalence of frailty in a single center cohort of patients with PMR and to determine the association of frailty with health-related quality of life (HRQoL), cognition and sarcopenia.

Methods: Patients with an ICD-10 diagnosis of PMR were identified between 03/2019-03/2020. Patients fulfilling 2012 EULAR/ACR Provisional Classification Criteria, ≤ 12 months from diagnosis and on glucocorticoids (≥ 3 mg of prednisone) were included. Disease activity was measured with the PMR-activity score. Frailty and pre-frailty were

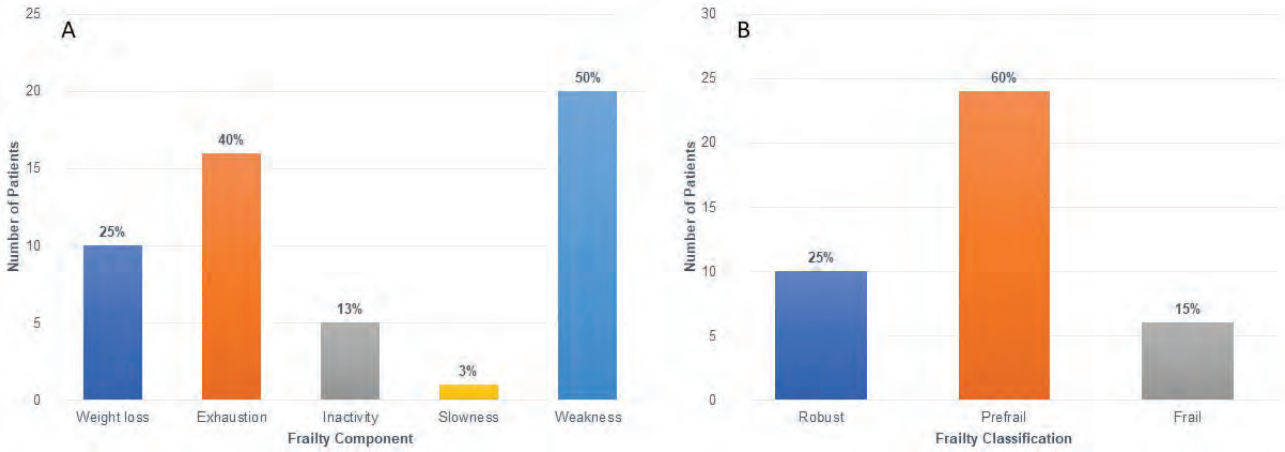

Figure 1. Fried Frailty Classification

defined according to Fried Frailty Criteria[2]. HRQoL was assessed using global Patient-Reported Outcomes Measurement Information System (PROMIS) computerized adaptive tests where 50 is the population mean. Cognition was assessed using the Mini-Mental Standard Examination (MMSE) and sarcopenia was assessed by DXA[3]. Fisher's exact test, chi-square tests and Kruskal-Wallis tests were used to describe differences among groups as appropriate. Univariate and multivariate linear regressions were used to describe the associations with frailty.

Results: 40 patients were enrolled. Overall, patients had a low burden of comorbidities and high education level (Table 1). Prevalence of frailty, pre-frailty and robustness was 15%,60% and 25%, respectively. Frail patients were older and had longer duration of disease; however, these differences were not statistically significant. Of 27 patients with

Table 1. Baseline characteristics by frailty classification

Characteristic	Robust N = 10	Pre-fail N= 24	Frail N =6	p-value
Age, years, median [IQR]	68.8 (60.8, 76.4)	73.5 (67.4, 78.0)	76.2 (72.5, 78.5)	0.25
Sex, female, n (%)	4 (40%)	10 (42%)	5 (83%)	0.19
Race, n (%)				
White/Caucasian	10 (100%)	23 (96%)	5 (83%)	0.34
Asian	0 (0%)	1 (4%)	0 (0%)	
Other	0 (0%)	0 (0%)	1 (17%)	
Ethnicity, n (%)				
Hispanic	0 (0%)	0 (0%)	1 (17%)	0.34
Non-Hispanic	10 (100%)	24 (100%)	5 (83%)	
Education, n (%)				0.43
High school/GED or less	0 (0%)	1 (4%)	1 (17%)	
Some college	0 (0%)	2 (8%)	0 (0%)	
College	2 (20%)	7 (29%)	2 (33%)	
Graduate/advanced professional degree	8 (80%)	14 (58%)	3 (40%)	
Smoking, n (%)				0.59
Never	4 (40%)	14 (58%)	2 (33%)	
Ever	6 (60%)	10 (42%)	4 (67%)	
Alcohol use, n (%)				0.49
Never	1 (10%)	5 (21%)	0 (0%)	
Ever	9 (90%)	19 (79%)	6 (100%)	
Charlson Comorbidity Index, median [IQR]	1 (1, 2)	2 (1, 3)	2 (1, 3)	0.48
Number of medications taken, median [IQR]	5 (3, 5)	5 (3, 7.5)	4 (2, 8)	0.48
Duration of disease, days, median [IQR]	173.5 (156, 314)	200 (100.5, 281.5)	228 (88, 319)	0.82
PMR-AS score, median [IQR]	3.45 (0.7, 4.7)	1.2 (0.7, 4.8)	4.2 (2.4, 5.5)	0.44
C-reactive protein, (mg/dl) median [IQR]	0.7 (0.5, 0.7)	0.7 (0.5, 0.7)	0.7 (0.7, 0.8)	0.52
Erythrocyte Sedimentation rate, (mm/hr), median [IQR]	3.5 (2, 19)	9.5 (5, 17.5)	16.5 (8, 19)	0.30
Prednisone dose (mg/day), median [IQR]	5.5 (3, 8)	6.5 (3.5, 11.5)	7.25 (5, 7.5)	0.80
Glucocorticoid exposure duration, days, median [IQR]*	173.5 (145,313)	177 (78.0,273.5)	221.5 (100.0, 319.0)	0.77
Steroid sparing agent use, n (%)*	0 (0%)	3 (12%)	0 (0%)	1.00
Body mass index (BMI), kg/m^2, median [IQR]	26.0 (24.8, 27.3)	26.5 (23.8, 29.9)	26.3 (21.3, 30.1)	0.74
Disability, n (%)				
ADL disability	3 (30%)	3 (13%)	0 (0%)	0.31
IADL dependent	0 (0%)	2 (8%)	0 (0%)	1.00

*Steroid sparing agents such as methotrexate, hydroxychloroquine, tocilizumab. PMR-AS = Polymyalgia Rheumatica Activity Score; ADL= activities of daily living assessed by Katz index; IADL = instrumental activities of daily living assed by Lawton scale.

Table 2. HRQoL, MMSE and Sarcopenia by frailty classification and Multivariate Cross-Sectional Analysis

	Robust		Pre-frail		Frail	
	Median (95% CI)	Multivariate† Coefficient (p-value)	Median (95% CI)	Multivariate† Coefficient (p-value)	Median (95% CI)	Multivariate† Coefficient (p-value)
PROMIS Physical function t-score*	53.7 (41.4, 55.2)	REF	48.5 (43.5, 53.7)	0.65 (0.98)	36.3 (34.2, 42.2)	-9.28 (<0.05)
PROMIS Fatigue t-score*	48.5 (38.2, 52.8)	REF	48.5 (45.1, 50.7)	2.55 (0.41)	59.3 (53.3, 61.4)	10.6 (<0.05)
PROMIS Pain behavior t-score*	51.3 (35.3, 57.5)	REF	35.3 (35.3, 52.6)	-2.39 (0.55)	57.5 (56.3, 59.6)	14.6 (0.04)
PROMIS Pain interference t-score*	46.6 (38.7, 54.3)	REF	46.6 (38.7, 52.6)	-0.11 (0.97)	55.9 (55.1, 60.1)	14.1 (0.01)
PROMIS Anxiety t-score*	52.0 (49, 53.5)	REF	50.8 (46.7, 52.1)	-2.43 (0.346)	55.9 (52.4, 64.8)	5.03 (0.241)
PROMIS Anger t-score*	48.2 (44.3, 52.3)	REF	47.5 (42.1, 52)	-0.36 (0.89)	51.5 (48.1, 54.9)	3.62 (0.42)
PROMIS Depression t-score*	48.2 (46.9, 50.8)	REF	46.1 (42.6, 49.9)	- 3.88 (0.137)	53.5 (41.8, 58.2)	0.48 (0.91)
PROMIS Satisfaction with social role t-score*	52.4 (47.4, 64.6)	REF	54.0 (45.8, 60.2)	-3.32 (0.40)	55.3 (49.1, 58.4)	-4.51 (0.49)
PROMIS Cognition t-score*	52.3 (49.1, 60.7)	REF	49.3 (45.8, 54.4)	-4.16 (0.26)	56.0 (42.7, 68)	-0.95 (0.88)
MMSE score	29 (29, 30)	REF	29 (28, 30)	-0.51 (0.34)	28 (28, 30)	-0.98 (0.20)
Sarcopenia**	1 (10%)#	REF	5 (21%)#	1.75 (0.65)	1 (17%)#	0.62 (0.79)

†Multivariate linear regression adjusted for age, sex, and duration of disease. #Presented as n (%). *5 points are considered a minimally clinical important difference. **Sarcopenia defined following the EWGSOP2 recommendations.
MMSE = Mini-Mental Standard Examination

body composition analysis, 26% were sarcopenic. Frail patients had worse physical function (lower scores) and more fatigue, pain behavior and interference (higher scores) compared to pre-frail and robust patients (Table 2). In the multivariate analysis, frail patients were more likely to have worse physical function, more fatigue, and more pain behavior and pain interference. No significant associations between either cognition or sarcopenia and frailty were observed.

Conclusion: In this cohort of PMR patients, we found a higher prevalence of frailty and pre-frailty than community dwelling elderly. Frailty was associated with worse physical function and increased fatigue, pain behavior and pain interference, differences that were clinically meaningful and statistically significant. Study limitations include the relatively small, homogenous sample size and missing data regarding sarcopenia. These data suggest that frailty is common in PMR and that it is associated with clinical phenotypes. Further assessment of frailty and its impact on PMR outcomes in a larger prospective cohort is warranted.

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Disclosure: S. Sattui, None; **D. Jannat-Khah**, Astrazeneca, 1, Cytodyn, 1, Walgreens Boots Alliance, 1; **L. Lally**, None; **S. Lieber**, None; **L. Mandl**, Annals of Internal Medicine, 9, UpToDate, 7, Regeneron, 2; **R. Spiera**, Roche-Genentech, 1, 2, GlaxoSmithKline, 1, 2, Bristol-Myers Squibb, 1, Boehringer Ingelheim, 1, ChemoCentryx, 1, Corbus Pharmaceuticals, 1, Sanofi, 1, InflaRx, 1, Janssen, 1, Forbius, 1, 2.

Abstract Number: 0423

Defining Ear Chondritis: Data from 685 Patients with Relapsing Polychondritis

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SESSION INFORMATION
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Background/Purpose: Ear chondritis is often considered the pathognomonic feature of relapsing polychondritis (RP). Although painful redness and swelling of the pinna and a resultant cauliflower ear are universally recognized as chondritis, the complete spectrum of symptoms associated with ear chondritis have not been well described. The study objective was to seek patient input to help characterize ear chondritis.

Methods: An online survey was administered in English or Spanish to participants with self-reported RP. Participants were asked questions about their ear pain, including quality, location, duration, aggravating/alleviating factors, timing of onset and duration. Participants were included who reported age ≥ 18 years, a diagnosis of RP confirmed by a physician, and sufficient symptoms to meet McAdams or Damiani's diagnostic criteria. Participants were categorized as having "typical ear chondritis" if they reported ear pain localized to the pinna with associated redness and swelling. Atypical presentations of ear chondritis were also considered.

Results: A total of 685 participants from five continents completed the survey. Among them, 659 met inclusion criteria for subsequent analysis. Most participants were female (n=574; 87%), white (n=548; 83%) and from the United States (n=484;74%). The median age was 50 years (interquartile range = 41-58). In total, 593 (90%) patients reported ear pain, 227 (38%) had "typical ear chondritis", and 98 (16%) had cauliflower ear.

Ear pain was most commonly described as burning (n=334, 56%) or throbbing (n=295, 50%). The most common location of pain was the pinna (n=373, 63%). Participants reported ear redness (n=454, 76%) and swelling (n=349, 53%). Some patients experienced isolated redness (n=130, 22%) or swelling (n=25, 4%). The most common aggravating factors were minor trauma (n=371, 62%) and stress (n=358, 60%). The most common alleviating factor was avoidance of touching the ear (n=374, 63%). Pain was most frequently reported during the daytime (n=355, 60%) and most likely to occur in either ear at different times (n=310, 52%). Onset could be gradual (n=198, 33%) or sudden (n=155, 26%). Pain typically lasted a few hours (n=175, 30%) or 2-3 days (n=130, 22%). The majority of patients who had pinna pain also had pain in other parts of the ear (e.g. mastoid process, inner ear, whole ear) at some point (n=394, 67%). In patients with cauliflower ear, the most common location of pain was the pinna (n=57, 58%) followed by pain inside the ear (n=53, 54%). Most participants reported at least two different types of pain (n=420, 64%).

Conclusion: Ear chondritis in patients with RP has a wide range of clinical presentations and characteristics beyond the typical triad of redness, swelling, and pain localized to the pinna. The description of pain often significantly varies within the same patient. Knowledge of the various distinct characteristics of ear involvement in RP may help physicians recognize and monitor the disease more effectively.

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Abstract Number: 0424

Anti-Collagen II Antibodies in Patients with Relapsing Polychondritis

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SESSION INFORMATION

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Background/Purpose: Relapsing polychondritis (RP) is a highly heterogenous systemic inflammatory disorder that affects many organ systems, in particular, cartilaginous structures. Clinical presentations in RP are variable, making recognition and diagnosis of the disease challenging. Testing for anti-collagen II (CII) antibodies is sometimes used to confirm the diagnosis of RP; however, the data remains inconclusive as to what percentage of RP patients have anti-CII antibodies in their serum. Our objectives were to evaluate the utility of anti-CII antibody as a diagnostic tool and as a possible objective measure of disease activity in a large cohort of patients with RP.

Methods: Patients 18 years and older were recruited into a prospective observational cohort of RP. All patients met McAdams or Damiani's diagnostic criteria for RP. Anti-CII antibodies were assayed via a clinically certified ELISA test (Mayo Clinic, Rochester, MN) in all patients evaluated from July 2019 to March 2020. Clinical features were compared between patients with RP stratified by presence of anti-CII antibody results using Fisher's exact test or Wilcoxon rank sum test as appropriate. Linear regression was used to determine if antibody titer correlated to Physician Global Assessment (PGA) score of disease activity. Clinical ELISA test results were compared to results using a different ELISA test platform (cat. no. 2065, Chondrex Inc., Redmond, WA, USA).

Results: Forty-six patients were tested, and six patients (13%) had elevated levels of anti-CII antibodies. Of four patients (8%) who had repeat testing, anti-CII antibodies were persistently negative in 3 patients and discordant positive/negative in 1 patient. Patients with elevated anti-CII antibodies compared to those without elevated antibodies were female (100 vs 63%, $p = 0.02$) with a significantly higher prevalence of oral ulcers (50 vs 15%, $p = 0.04$), genital ulcers (33 vs 5%, $p = 0.02$), costochondritis (66 vs 25%, $p = 0.048$), and Sicca symptoms (83 vs 33%, $p = 0.03$) and with a significantly lower prevalence of eye inflammation (0 vs 40%, $p = 0.018$), as well as lower absolute monocyte (median 0.33 vs 0.51 K/uL, $p = 0.02$) and white blood cell counts (median 4.54 vs 6.95 K/ul, $p = 0.049$). There was no correlation between antibody titer and PGA ($r= 0.18$; $p = 0.33$). A total of 24 patients were tested on both ELISA platforms. Twenty-three patients tested negative on both platforms, but 1 patient that tested positive by the Mayo Clinic ELISA tested negative by the Chondrex ELISA. Thus, there was little concordance between platforms.

Conclusion: Anti-CII antibodies likely have a limited role as a diagnostic test or biomarker of disease activity in RP. Few patients with RP have detectable anti-CII antibodies, and detection of these antibodies is dependent on testing platform. Presence of anti-CII antibodies may be associated with specific clinical symptoms and may be enriched in a subset of patients with RP who have mucocutaneous disease. This subset is commonly referred to as MAGIC syndrome (mouth and genital ulcers with inflamed cartilage). Whether anti-CII antibodies provide pathogenic insight for a smaller subset of patients with RP remains to be determined.

Disclosure: K. Wells, None; **M. Ferrada**, None; **E. Rose**, None; **K. Sikora**, None; **W. Goodspeed**, None; **K. Quinn**, None; **P. Grayson**, None.

Abstract Number: 0425

MAGIC Syndrome in a Cohort of Patients with Relapsing Polychondritis

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SESSION INFORMATION

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Background/Purpose: Mouth and genital ulcers with inflamed cartilage (MAGIC) syndrome is an extremely rare condition that encompasses symptoms of relapsing polychondritis (RP) and Behcet's disease (BD). Little is known about the prevalence of clinical symptoms in patients with MAGIC and to what extent patients with MAGIC are similar to other patients with RP. The study objectives were to determine the frequency of patients with MAGIC syndrome and BD in a cohort of patients with RP and compare the clinical, laboratory and radiographic characteristics as well as treatment and outcomes.

Methods: Patients who met McAdams or Damiani's diagnostic criteria for RP and were 18 years old or older were included in this analysis. The International Criteria for Bechet's Disease (ICBD) was used for the diagnosis of BD. MAGIC syndrome was defined by presence of recurrent oral and genital ulcers plus chondritis. Categorical and continuous variables were compared using the Fisher's exact test and Kruskal-Wallis test, respectively.

Results: Eighty-four patients were included in this analysis. Most of the patients were female (n=72, 86%) and white (n=73, 87%). Median age of symptom onset was 36 years (IQR 28-42). Among patients with RP, 13 (15%) met diagnostic criteria for BD, all of whom had MAGIC syndrome. Although referred for RP, MAGIC syndrome was not recognized by any of the referring care providers. When comparing patients with RP and MAGIC syndrome, there were no significant differences between race or sex (white, 85% vs 87%, p=0.68; female 83% vs 100%, p=0.20). Patients with MAGIC syndrome were more likely compared to RP to have diagnostic delay (median 10.1 years (IQR 3-18) vs 6.9 years (IQR 1-9.75), p=0.04), a higher prevalence of Raynaud's phenomena (54% vs 11%, p = 0.002), uveitis or retinal vasculitis (23% vs 4%, p =0.04), chronic GI symptoms (54% vs 13%, p = 0.002), and elevated anti-collagen II antibodies (60% vs 9 %, p=0.03). Although not statistically significant, patients with MAGIC syndrome also had a higher percentage of pulmonary embolism (15% vs 3%), unprovoked DVT (15 vs 3%), aortitis (8% vs 1%), airway chondritis (69% vs 41%), GI ulcers or inflammation (15% vs 4%) and erythema nodosum or pseudofolliculitis (8% vs 1%). There were no significant differences in the prevalence of ear or nose chondritis, costochondritis, hearing loss, joint involvement, neurologic disease, elevated inflammatory markers, or HLA-B51 status. There were no significant

Table 1. Clinical Characteristics of RP patients with and without MAGIC Syndrome

	All Patients n=84	MAGIC Syndrome n=13	Relapsing Polychondritis n=71	p value
Demographic Characteristics				
Race, White n (%)	73 (87)	11 (85)	62 (87.32)	0.68
Sex, Female n (%)	72 (86)	13 (100)	59 (83.10)	0.20
Age, Symptom onset (years, IQR)	35.5 (28-42)	31 (29-36)	36.3 (28-43)	0.08
Age, Diagnosis (years, IQR)	43 (34-52)	41.1 (35-44)	43.6 (34-52)	0.55
Diagnostic Delay (Regarding RP, years, IQR)	7.4 (2-10)	10.1(3-18)	6.9 (1-9.8)	**0.04**
Clinical Manifestations				
Chondritis n (%)	83 (99%)	13 (100%)	71 (100%)	1.00
Ear chondritis n (%)	47 (56)	7 (54)	40 (56)	1.00
Nose chondritis n (%)	70 (83)	13 (100)	57 (80)	0.11
Airway chondritis n (%)	37 (44)	9 (69)	29 (41)	0.07
Costochondritis n (%)	71 (85)	11 (85)	60 (85)	1.00
Musculoskeletal Involvement n (%)	76 (90)	12 (92)	64 (90)	1.00
Audiological Involvement n (%)	32 (38)	4 (30)	28 (39)	0.76
Eye Inflammatory Disease n (%)	26 (31)	5 (38)	21 (29)	0.52
Uveitis or retinal vasculitis n (%)	6 (7)	3 (23)	3 (4)	**0.04**
Mucusal Involvement n (%)	25 (30%)	13 (100%)	12 (17%)	**<0.01**
Genital ulcers n (%)	14 (17)	13 (100)	1 (1)	**<0.01**
Oral ulcers n (%)	24 (29)	13 (100)	11 (15)	**<0.01**
Vascular Involvement n (%)	21 (25 %)	8 (62%)	13 (19%)	**P<0.01**
Raynaud's n (%)	15 (18)	7 (54)	8 (11)	**<0.01**
Pulmonary embolism n (%)	4 (5)	2 (15)	2 (3)	0.11
Unprovoked DVT n(%)	4 (5)	2 (15)	2 (2)	0.11
Aortitis n (%)	2 (2)	1 (8)	1 (1)	0.29
Skin involvement n (%)	21 (25)	5 (38)	16 (23)	0.30
Erythema nodosum, pseudofolliculitis n (%)	2 (2)	1 (8)	1 (1)	0.29
Gastrointestinal Involvement n (%)	17 (20%)	7 (54 %)	10 (14%)	**<0.01**
Chronic GI symptoms* n (%)	16 (19)	7 (54)	9 (13)	**<0.01**
GI ulcer or inflammation n (%)	5 (6)	2 (15)	3 (4)	0.17
CNS Involvement n (%)	0 (0)	0 (0)	0 (0)	-
Laboratory abnormalities				
ANA	11 (13)	2 (15)	9 (13)	0.68
Anti-collagen II antibody	6 (15)	3 (60)	3 (9)	**0.03**
HLA-B51	64 (76)	1(8)	7 (10)	0.54
Outcomes				
Death n (%)	3 (3)	1 (8)	2 (2)	0.40
ICU admission n (%)	12 (14)	2 (15)	10 (14)	1.00
Tracheotomy n (%)	7 (8)	1 (8)	6 (8)	1.00
Medications				
Prednisone ever ≥ 60 mg n (%)	44 (52)	5 (38)	39 (55)	0.37
csDMARD ever n (%)	69 (82)	10 (77)	59 (83)	0.69
Biological or ts- DMARD ever n (%)	57 (68)	9 (69)	48 (68)	1.00
Number of csDMARDs median (IQR)	1 (1-2)	2 (1-2)	1 (1-2)	0.92

N = number; IQR = interquartile range; csDMARD = conventional synthetic DMARD; tsDMARD = targeted synthetic DMARD; *Chronic GI symptoms include chronic abdominal pain, vomiting or diarrhea, excluding a confirmed non-functional non-inflammatory cause

differences in treatment or outcome measures including mortality, ICU admissions and tracheotomy between MAGIC and RP.

Conclusion: Fifteen percent of patients with RP meet diagnostic criteria for MAGIC syndrome and BD. Patients with MAGIC syndrome have distinct clinical and laboratory characteristics including prevalent vascular symptoms such as Raynaud's, thromboembolic disease, and aortitis. Recognizing the wide pattern of organ involvement and clinical characteristics in patients with MAGIC syndrome may help identify these patients earlier. Larger studies to determine whether anti-collagen II antibodies in patients with MAGIC play a causal role in disease and/or function as a diagnostic biomarker are warranted.

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T-Cell Receptor (TCR) Sequencing Reveals Decreased Diversity and Clonotypic Expansion of T-cells in Relapsing Polychondritis (RP)

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Background/Purpose: Relapsing polychondritis (RP) is a rare, systemic inflammatory disease characterized by recurrent inflammation of cartilaginous structures, including the nose/ears, joints, and trachea. The etiology of this life-threatening and disabling disease is currently unknown and little is known about its pathogenesis. HLA association evidence supports T-cell involvement in RP; however, the extent of T-cell involvement is incompletely understood. Previous studies demonstrate that TCR repertoire diversity is decreased in individuals with autoimmune diseases, such as rheumatoid arthritis and type 1 diabetes. Here we study the TCR repertoire of individuals with RP to identify potential disease-causing clones, which may provide critical knowledge in uncovering disease etiology, serve as a biomarker, or influence treatment decisions.

Methods: Peripheral blood leukocyte DNA was collected from 13 patients with highly active RP, and TCR-β chains were sequenced by Adaptive Biotechnologies. 3 samples containing a dominant clone were re-sequenced at a time of reduced disease activity. 13 age and sex matched healthy controls were obtained from the ImmuneACCESS public database. Data was analyzed using ImmunoSEQ Analyzer to quantify Productive Entropy, Max Productive Frequencies, Differential Abundance, and TCR- β chain V family gene usage. Frequencies were compared using the Mann-Whitney U test. Physician global assessment (PGA) was used to determine disease activity in a subset of the patients.

Results: Productive Entropy values were significantly lower in patients with RP compared to healthy controls (median 15.73 vs 16.86, P=0.0015), indicating a less diverse TCR repertoire in patients with RP. 3 patients had unique dominant clones with Max Productive Frequencies over 5 % (range 5.68-10.71%). In 2 of these patients Productive Entropy values increased in parallel with improvement in PGA scores (12.316 to 12.8916 and 14.1600 to 15.5207 respectively) and Max Productive Frequencies of dominate clones decreased (5.675% to 4.961% and 10.712% to 7.476% respectively). Additionally, 3 TCR- β chain variable (V) expansions were detected for Vβ9, Vβ19, and Vβ20 families that were not expanded in controls.

Conclusion: TCR repertoire is less diverse in patients with RP compared to healthy controls. Expanded TCR- β chain V families and dominant clones not expressed in healthy controls may provide insights to antigenic drivers of RP. Further, the TCR repertoire may be less diverse during active disease compared to lower disease activity. Based upon these findings, we intend to confirm the trends in a larger cohort of patients, make comparisons to immunopheno-

types and clinical associations, and detect possible antigens by clustering TCRs with conserved CDR3 and V family motifs.

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Abstract Number: 0427

Validation of Physician Global Assessment as an Outcome Measure in Relapsing Polychondritis

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Background/Purpose: Relapsing polychondritis (RP) is a rare systemic inflammatory disorder of cartilage that lacks validated disease activity measures. Physician global assessment (PhGA) is a measure of disease activity frequently used in a variety of rheumatologic diseases to track treatment response and categorize disease states. PhGA has not been studied specifically in a cohort of patients with RP. The objective was to characterize the reliability and utility of PhGA for RP.

Methods: Adult patients in an ongoing observational cohort who meet existing diagnostic criteria for RP underwent a standardized comprehensive evaluation at approximately 6-month intervals. PhGA was scored by consensus of 3 raters on a scale of 0 (no clinical activity) to 10 (maximum disease activity) at each study visit. Ratings were considered discordant if any two ratings differed by three or more points. Change in immunosuppressive treatment between consecutive visits was recorded as increased, decreased or unchanged. Intraclass correlation coefficients (ICC) (2, 1), Spearman's correlation, Fisher's exact test and Wilcoxon signed rank were used to characterize the reliability and utility of PhGA as a measure of disease activity.

Results: 78 patients were evaluated over visits. The ICC for the ratings by the 3 raters was 0.79 (95 % confidence interval:0.73-0.84), indicating good reliability. For 6 out of 164 visits (3.7%) the ratings by the 3 raters were discordant. After adjudicating the discordant ratings, the assigned PhGA ranged from 0-7 with a median of 3 (interquartile range 2-3). PhGA was 0 at 4 visits (2%), 1 or 2 at 76 visits (46%), 3 or 4 at 63 visits (38%), and more 5 or more at 22 visits (13%). PhGA was weakly correlated with CRP ($r= 0.30$, $P< 0.001$) but not with ESR ($r=0.13$, $P=0.10$). Between the baseline and the first follow-up visit there was decrease in PhGA from median of 3 (interquartile range 2-5) to median of 2 (interquartile range of 1-3) ($P< 0.001$). There was no further change in PhGA over subsequent consecutive follow-up visits. Between consecutive visits in which there was an increase in immunosuppressive treatment, the median PhGA decreased from 3 (interquartile range 2-4) to 2 (interquartile range 2-3) ($P< 0.001$) but rarely went to 0. Between consecutive visits in which there was no change or a decrease in treatment, there were no corresponding changes in PhGA.

Conclusion: PhGA is a reliable measure to quantify disease activity and monitor treatment response in RP. Even with treatment, few patients with RP have a PhGA of 0, suggesting that a state of no clinical activity is difficult to achieve or that damage may be masquerading as low disease activity in some patients. These data provide insight into the burden of disease activity in RP and highlight a need for improved treatments.

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Abstract Number: 0428

Enrichment of Clinical Trial Recruitment Using Advanced Molecular Imaging in Takayasu's Arteritis

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Background/Purpose: Definitions of disease activity are not standardized in Takayasu's arteritis (TAK), which can lead to difficulty in determining whether a patient should be enrolled into a randomized controlled trial (RCT). FDG-PET can complement clinical assessment of disease activity. Two prior RCTs in TAK (AGATA, North American study of abatacept[1] and TAKT, Japanese study of tocilizumab[2]) used different definitions of disease activity. Neither trial considered FDG-PET findings in these definitions.

The objectives of this study were to: 1) Evaluate physician agreement about patient enrollment based on study inclusion criteria from AGATA and TAKT and 2) Determine if vascular FDG-PET impacts decision-making about trial inclusion.

Methods: Patients with TAK were recruited from an observational cohort. Each patient underwent clinical assessment and an FDG-PET-CT scan during a single study visit. A nuclear medicine physician reviewed all PET scans, blinded to clinical data, and interpreted the scans as active, indeterminate, or inactive. Two rheumatologists independently rated whether each patient met inclusion criteria for AGATA[1] and/or TAKT[2]. In Round 1, determination of disease activity was based on clinical and laboratory data only. In Round 2, determination of disease activity was based on the same data plus PET scan results. In both rounds, each reviewer recorded certainty about the decision to enroll/exclude a patient. Inter-rater reliability (IRR) was calculated using Fleiss' Kappa.

Results: 76 patients with TAK were evaluated. Using AGATA enrollment criteria, the raters agreed to enroll 31 patients (41%), exclude 33 patients (43%), and disagreed for 12 patients (16%). Using TAKT enrollment criteria, the raters agreed to enroll 34 patients (45%), exclude 29 patients (38%), and disagreed for 13 patients (17%). Disagreement was frequently driven by fatigue/malaise and/or elevated acute phase reactants, and raters were uncertain in 92%

Table: Certainty of Disease Activity Assessment for Trial Enrollment Based on Clinical and Laboratory Data (Blinded to FDG-PET Scan)

			Certain to Enroll in Round 1	Certain to Exclude in Round 1	Uncertain in Round 1
NIH Cohort N = 76	AGATA	*Rater 1* *PET Active* *PET Indeterminate* *PET Inactive*	Total n=16 n=16 (100%) n= 0 (0%) n=0 (0%)	Total n=24 n= 11 (46%) n= 5 (21%) n= 8 (33%)	Total n=36 n= 22 (61%) n= 9 (25%) n= 5 (14%)
		Rater 2 *PET Active* *PET Indeterminate* *PET Inactive*	Total n=18 n=17 (94%) n=1 (6%) n=0 (0 %)	Total n=25 n= 12 (48%) n= 6 (24%) n= 7 (28%)	Total n=33 n= 20 (61%) n= 7 (21%) n= 6 (18%)
	TAKT	*Rater 1* *PET Active* *PET Indeterminate* *PET Inactive*	Total n=20 n=19 (95%) n=1 (5%) n=0 (0 %)	Total n=25 n= 12 (48%) n= 6 (24%) n= 7 (28%)	Total n=31 n= 19 (61%) n= 7 (23%) n= 5 (16%)
		Rater 2 *PET Active* *PET Indeterminate* *PET Inactive*	Total n=21 n=19 (90%) n=2 (10%) n=0 (0%)	Total n=23 n= 11 (48%) n= 5 (22%) n= 7 (30%)	Total n=32 n= 18 (56%) n= 7 (22%) n= 7 (22%)

of these cases. Availability of PET scan results significantly improved agreement between raters (Round 1 IRR= 0.68 [95% CI (0.67-0.69)]; Round 2 IRR=0.88 [CI 0.87-0.89]; p< 0.01).

Of patients whom the rater was certain in Round 1 to enroll, no patient had an inactive PET. Conversely, of patients whom the rater was certain to exclude, approximately half of these patients had abnormal subclinical PET activity (TABLE). For patients whom the rater noted uncertainty about enrollment in Round 1, certainty improved in both raters once PET data was incorporated [Rater 1: 56% to 86% certainty, Rater 2: 57% to 87% certainty].

Conclusion: Physicians are frequently uncertain about disease activity assessment in TAK. This uncertainty leads to disagreement about which patients meet RCT requirements for enrollment. Consideration of FDG-PET findings in addition to clinical assessment improves confidence about disease activity assessment and significantly reduces disagreement about trial eligibility. Incorporation of PET findings into the definition of disease activity identifies a substantial number of patients with subclinical inflammation, which could increase the number of eligible participants for treatment trials in TAK.

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1. Langford CA, *et al* A&R 2017
2. Nakaoka Y, *et al* ARD 2018

Disclosure: K. Quinn, None; **M. Ahlman**, None; **E. Rose**, None; **P. Merkel**, AbbVie, 5, Biogen, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Insmed, 5, Jannsen, 5, Kiniksa, 5, Magenta, 5, Novartis, 5, Pfizer, 5, Sparrow, 5, Talaris, 5, Astra-Zeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, UpToDate, 7; **P. Grayson**, None.

Abstract Number: 0429

Prothrombotic Antiphospholipid Antibodies in COVID-19

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Plenary Session I
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Session Time: 11:30AM–1:00PM

Background/Purpose: Patients with coronavirus disease 19 (**COVID-19**) are at high risk for thrombosis of arteries and veins. At the same time, COVID-19 lung histopathology has revealed fibrin-based occlusion of small vessels. Antiphospholipid syndrome (**APS**) is an acquired thrombophilia in which patients develop pathogenic autoantibodies (**aPL**) targeting phospholipids and phospholipid-binding proteins. Small case series have recently detected aPL in patients with COVID-19. Here, we endeavored to comprehensively measure aPL in a large cohort of patients hospitalized with COVID-19. We also asked whether purified IgG fractions from these patients had prothrombotic properties in vitro and in vivo.

Methods: Sera from 172 patients hospitalized with COVID-19 were evaluated for eight different types of aPL: anti-cardiolipin IgG/IgM/IgA, anti-beta-2 glycoprotein I IgG/IgM/IgA, and anti- phosphatidylserine/prothrombin (**PS/PT**) IgG/IgM. IgG fractions were purified from COVID-19 patients with various aPL profiles. The prothrombotic potential of the purified IgG fractions were evaluated in neutrophil extracellular trap (**NET**) assays and in two mouse models of inferior vena cava thrombosis.

Results: We detected anticardiolipin IgM antibodies in 23% of COVID-19 patients, anti-PS/PT IgG in 24%, and anti-PS/PT IgM in 18%. Any aPL was present in 52% of patients based upon the manufacturer's threshold and in 30% using a more stringent cutoff (≥40 units) (**Table 1**). High aPL levels tended to track with more severe COVID-19. For example, anti-PS/PT IgM levels were significantly correlated with neutrophil activation (calprotectin, r=0.23, p=0.002), circulating NETs (myeloperoxidase/**MPO**-DNA complexes, r=0.23, p=0.003), and more severe respiratory disease (SpO_2/FiO_2, r=-0.16, p=0.03). Similar correlations were also seen for anticardiolipin IgM (calprotectin r=0.28, p=0.0002; MPO-DNA r=0.25, p=0.001; SpO_2/FiO_2 r=-0.19, p=0.01). Furthermore, positive testing for any aPL predicted impaired kidney function as defined by estimated glomerular filtration rate (p=0.03). Purified IgG fractions from aPL-positive COVID-19 patients (either anti-β_2GPI IgG or anti-PS/PT IgG) promoted NET release from control neutrophils, similar to IgG isolated from individuals with established APS. Furthermore, injection into mice of COVID-19 IgG fractions (isolated from four different patients with high levels of anti-PS/PT IgG) more than doubled thrombus extension and accretion in two separate models of inferior vena cava thrombosis. Administration of the COVID-19 IgG also significantly increased circulating NET remnants in mice (p=0.0004), similar to IgG from patients with catastrophic antiphospholipid syndrome (p=0.001).

Conclusion: These data demonstrate that a significant percentage of patients with COVID-19 become at least transiently positive for aPL and that these aPL are potentially pathogenic.

Table 1: Prevalence of antiphospholipid antibodies in COVID-19 patients (n=172)

aPL	Number positive (factory cut-off)	%	Number positive (titer ≥40)	%
aCL IgG	8	4.7%	2	1.2%
aCL IgM	39	23%	13	7.6%
aCL IgA	6	3.5%	1	0.58%
aβ_2GPI IgG	5	2.9%	3	1.7%
aβ_2GPI IgM	9	5.2%	7	4.1%
aβ_2GPI IgA	7	4.1%	3	1.7%
aPS/PT IgG	42	24%	21	12%
aPS/PT IgM	31	18%	21	12%
any positive aPL	89	52%	52	30%

aPL=antiphospholipid antibodies; aCL= anticardiolipin;
aβ_2GPI=anti-beta-2 glycoprotein I; aPS/PT=anti-phosphatidylserine/prothrombin
Factory cut-offs:

- aCL IgG/M/A=20 GPL/MPL/APL
- aβ2GPI IgG/M/A=20 GPL/MPL/APL
- aPS/PT IgG/M=30 units

Disclosure: Y. Zuo, None; **S. Estes**, None; **A. Ghandi**, None; **S. Yalavarthi**, None; **R. Ali**, None; **S. Hui**, None; **G. Sule**, None; **K. Gockman**, None; **J. Madison**, None; **M. Zuo**, None; **W. Woodard**, None; **S. Lezak**, None; **N. Lugogo**, None; **Y. Kanthi**, None; **J. Knight**, None.

Abstract Number: 0430

Outcomes of Coronavirus Disease 2019 Infection Among Patients Living with Rheumatic Diseases: A Matched Cohort Study from a US Multi-Center Research Network

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Plenary Session I
Session Type: Plenary Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Whether patients living with systemic autoimmune rheumatic diseases (SARDs) suffer from more severe complications of Coronavirus Disease 2019 (COVID-19) infection remains unknown.

Methods: We conducted a matched cohort study to examine COVID-19 infection outcomes of patients with SARDs using the TriNETX Research Network, which contains real-time electronic health record data from >52 million patients across 35 healthcare organizations. COVID-19 infections were identified by International Classification of Diseases

Table 1. Baseline characteristics of COVID-19 infected patients with SARD versus 1:1 age-sex-race-matched comparators without SARD.

	COVID-19 with SARD (N=716)	COVID-19 without SARD (N=716)
Age, years	57 ± 16	57 ± 16
Female	569 (79%)	569 (79%)
Race/ethnicity		
White	388 (54%)	388 (54%)
Black/African American	241 (34%)	241 (34%)
Asian	13 (2%)	13 (2%)
Latinx	47 (7%)	47 (7%)
Body mass index, kg/m^2	31 ± 8	32 ± 9
Creatinine, mg/dL	1.2 ± 1.4	1.0 ± 0.8
Hypertension	349 (49%)	228 (32%)
Diabetes mellitus	173 (24%)	120 (17%)
Asthma	129 (18%)	67 (9%)
Chronic obstructive pulmonary disease	25 (3%)	13 (2%)
Chronic kidney disease	136 (19%)	47 (7%)
Congestive heart failure	104 (15%)	38 (5%)

Continuous variables are expressed as mean ± standard deviation and categorical variables are expressed as number (percentage). COVID-19 = Coronavirus Disease 2019; SARD = systemic autoimmune rheumatic disease.

Table 2. Outcomes of COVID-19 infection in patients with SARD versus 1:1 age-sex-race-matched comparators without SARD.

COVID-19 Infection Outcome	Risk in People with SARD, N(%) (N=716)	Risk in People without SARD, N(%) (N=716)	Risk Difference, % (95% CI)	Risk Ratio (95% CI)	p-value
Hospitalization	175 (24.4%)	142 (19.8%)	4.6 (0.3, 8.9)	1.23 (1.01, 1.50)	**0.04**
Intensive care unit admission	49 (6.8%)	28 (3.9%)	2.9 (0.6, 5.3)	1.75 (1.11, 2.75)	**0.01**
Mechanical ventilation	39 (5.5%)	22 (3.1%)	2.4 (0.3, 4.5)	1.77 (1.06, 2.96)	**0.03**
Acute kidney injury*	42 (5.9%)	23 (3.2%)	2.7 (0.5, 4.8)	1.83 (1.11, 3.00)	**0.02**
Congestive heart failure	49 (6.8%)	16 (2.2%)	4.6 (2.5, 6.8)	3.06 (1.76, 5.33)	**<0.01**
Death	36 (5.0%)	31 (4.3%)	0.7 (-1.5, 2.9)	1.16 (0.73, 1.86)	0.53

COVID-19 = Coronavirus Disease 2019; SARD = systemic autoimmune rheumatic disease; CI = confidence interval.
*Includes ICD-10 codes for acute kidney injury and procedure codes for initiation of renal replacement therapy.

10th Revision (ICD-10) codes or positive COVID-19 testing by polymerase chain reaction between January 20, 2020, and June 1, 2020. Patients with SARDs (including rheumatoid arthritis [RA], systemic lupus erythematosus [SLE], Sjogren's syndrome, systemic sclerosis [SSc], idiopathic inflammatory myositis [IIM], mixed or undifferentiated connective tissue disease, systemic vasculitis, psoriatic arthritis [PsA], and ankylosing spondylitis [AS]) were identified by two ICD-10 codes for rheumatic disease greater than two months apart. For the comparison cohort, we matched one individual without SARDs based on age, sex, and race/ethnicity. Baseline characteristics were assessed in the 1 year prior to COVID-19 infection, and outcomes were assessed between 2 weeks and 3 months after COVID-19 infection. We calculated the risk difference and risk ratio (RR) for the association of SARD with each outcome.

Results: There were 716 patients with COVID-19 infection and SARD and 716 age-sex-race-matched comparators with COVID-19 infection but without SARD. After matching, the average age was 57 years, 79% were female, 54% were white, and 34% were Black or African American (**Table 1**). Patients with SARDs had higher rates of comorbidities than comparators, including hypertension, asthma, chronic kidney disease, and heart failure. Among patients with SARDs, the distribution of rheumatic disease was: 325 (45%) RA, 128 (18%) SLE, 71 (10%) Sjogren's syndrome, 25 (3%) SSc, 20 (3%) IIM, 34 (5%) mixed or undifferentiated connective tissue disease, 61 (9%) systemic vasculitis, 44 (6%) PsA, and 22 (3%) AS. Of patients with SARDs, 289 (40%) were on prednisone, 140 (20%) were on hydroxychloroquine, and 84 (12%) were on tumor necrosis factor inhibitors. Patients with SARDs had higher risk of hospitalization (RR 1.23), intensive care unit admission (RR 1.75), mechanical ventilation (RR 1.77), acute kidney injury (RR 1.83), and congestive heart failure (RR 3.06) versus comparators without SARDs (all $p < 0.05$, **Table 2**). Mortality was numerically higher in patients with SARDs than comparators, although not statistically significant.

Conclusion: Patients with SARDs who develop COVID-19 infection may have higher risks of end-organ failure (including mechanical ventilation, acute kidney injury, and heart failure) compared to matched comparators without SARDs. Further studies are needed to identify risk factors associated with severe COVID-19 infection in patients living with SARDs.

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Abstract Number: 0431

Hydroxychloroquine Use Was Not Associated with QTc Length in a Large Cohort of SLE and RA Patients

Elizabeth Park[1], Jon Giles[2], Thania Perez-Recio[1], Paloma Pina[3], Christopher Depender[1], Joan Bathon[1] and Laura Geraldino-Pardilla[4], [1]Division of Rheumatology, Columbia University Vagelos College of Physicians and Surgeons, New York, NY, [2]Columbia University, New York, NY, [3]Cardiac Electrophysiology, Northwestern Medicine, Chicago, IL, [4]Division of Rheumatology, Columbia University Vagelos College of Physicians and Surgeons, New York

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Plenary Session I
Session Type: Plenary Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Hydroxychloroquine (HCQ) is a cornerstone therapy for systemic lupus erythematosus (SLE), and is used as monotherapy and combined with other DMARDs in rheumatoid arthritis (RA). However, its use in the treatment of COVID-19 has raised concerns for the possibility of QTc prolongation and development of arrhythmia. We therefore assessed QTc length in a large SLE and RA cohort and its association with HCQ use.

Figure 1.

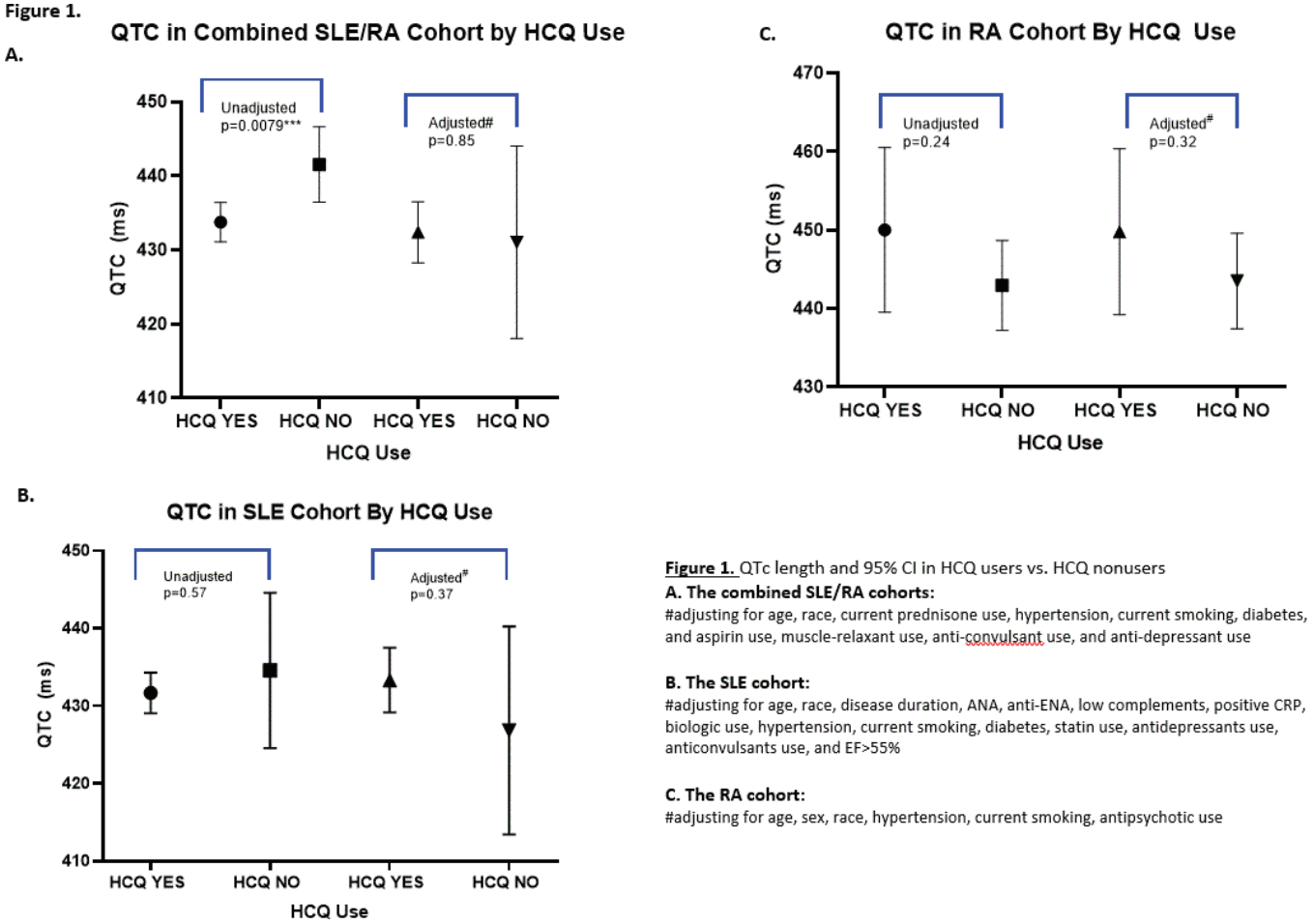

Figure 1. QTc length and 95% CI in HCQ users vs. HCQ nonusers

A. The combined SLE/RA cohorts:
#adjusting for age, race, current prednisone use, hypertension, current smoking, diabetes, and aspirin use, muscle-relaxant use, anti-convulsant use, and anti-depressant use

B. The SLE cohort:
#adjusting for age, race, disease duration, ANA, anti-ENA, low complements, positive CRP, biologic use, hypertension, current smoking, diabetes, statin use, antidepressants use, anticonvulsants use, and EF>55%

C. The RA cohort:
#adjusting for age, sex, race, hypertension, current smoking, antipsychotic use

Figure 1A-C

Methods: A total of 681 SLE and RA patients without clinical cardiovascular disease (CVD) were analyzed from two prospective RA cohorts with EKGs as part of study data collection (n=307), and one retrospective SLE cohort (n=374) with EKGs performed as part of standard of care. The participants from all three cohorts were recruited from tertiary referral centers. The association between QTc length and HCQ use was explored in regression models and adjusted for disease-specific characteristics and CVD risk factors.

Results: Of the entire (SLE+RA) cohort, 54% were HCQ users and 44% had a QTc > 440 ms. The mean QTc length was 437± 28 ms. In the entire cohort, adjusted QTc length in HCQ users was comparable to that of non-HCQ users (*Figure 1*). In multivariate logistic modeling, HCQ use was *not* a significant predictor of prolonged QTc > 440 or >500 ms for the entire cohort (OR 0.89; CI 0.25-3.2, & OR 0.11; CI 0.007-1.7, respectively), nor for the RA cohort (OR 1.1; CI 0.54-2.2, & OR 0.80; CI 0.23-2.8, respectively). HCQ use was not a significant predictor of a QTc >440 ms in the SLE subset (OR 2.0; CI 0.46-8.8). However, 9/11 SLE patients with a QTc >500 ms were on HCQ, yet these observations were too small to detect statistically significant differences between the HCQ groups. Importantly, QTc >500 ms was *not* associated with arrhythmias or deaths. No significant interactions were found between HCQ use and other QTc prolonging medications in the entire cohort. In fact, use of HCQ combined with any QTc prolonging medication was associated with a comparable QTc length (434 ms; CI 430-439) vs. use of HCQ alone (433 ms; CI 429-437). A significant interaction (p=*0.014*) was found between HCQ use and antipsychotic use in the SLE cohort, with QTc length being *longer* (441 ms; CI 428-454) for those on both vs. those only on HCQ (432 ms; CI 428-436).

Conclusion: This study demonstrates that in a large combined cohort of SLE and RA patients, QTc length does not significantly differ in HCQ users compared with non-HCQ users even while adjusting for potential clinical confound-

ers. Importantly, HCQ use was not associated with a prolonged QTc (>440 ms) in the combined and individual SLE and RA cohorts, nor was HCQ use a significant predictor of QTc length.

Disclosure: E. Park, None; **J. Giles**, AbbVie, 5, Bristol-Myers Squibb, 5, Eli Lilly, 5, Gilead, 5, Pfizer, 2; **T. Perez-Recio**, None; **P. Pina**, None; **C. Depender**, None; **J. Bathon**, None; **L. Geraldino-Pardilla**, Pfizer, 1, BMS, 1.

Abstract Number: 0432

The Effect on Renal Function of the Complement C5a Receptor Inhibitor Avacopan in ANCA-Associated Vasculitis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Plenary Session I

Session Type: Plenary Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Avacopan, a novel, orally-administered selective antagonist of C5aR, was recently evaluated in a pivotal Phase 3 randomized clinical trial where its use in patients with ANCA-associated vasculitis, also receiv-

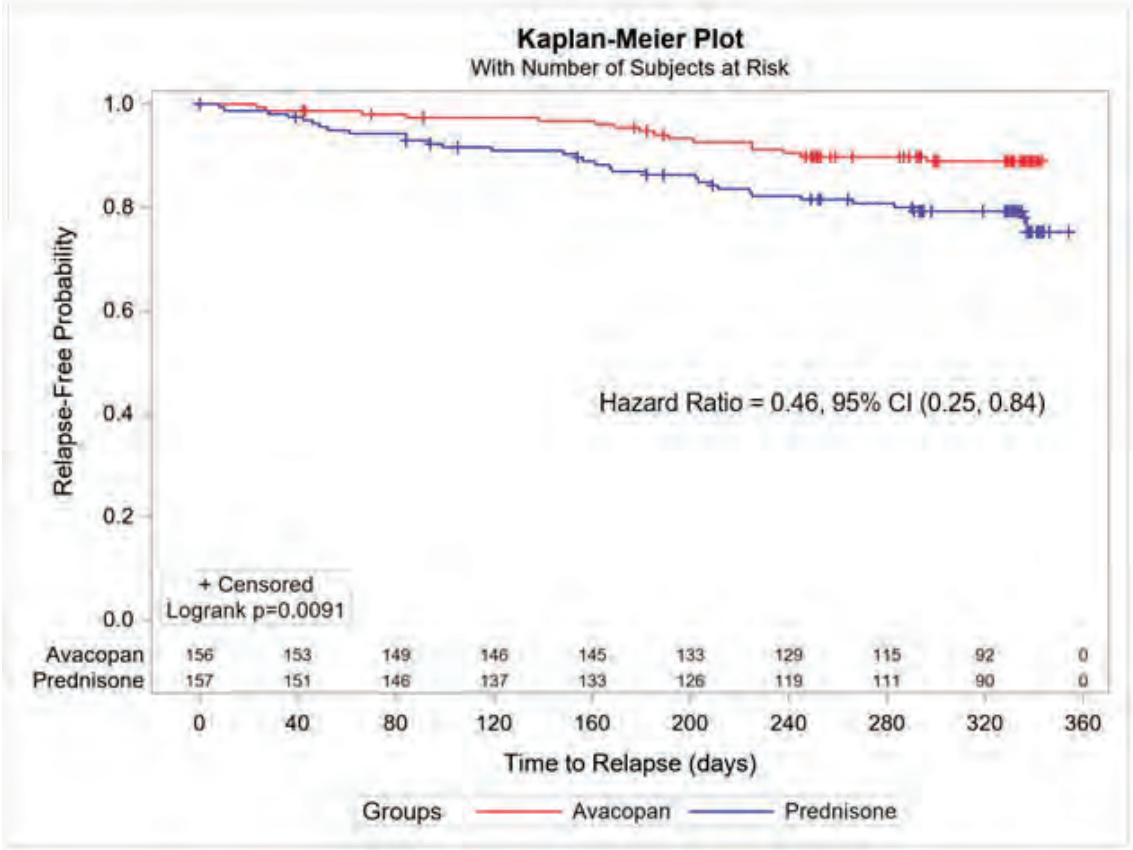
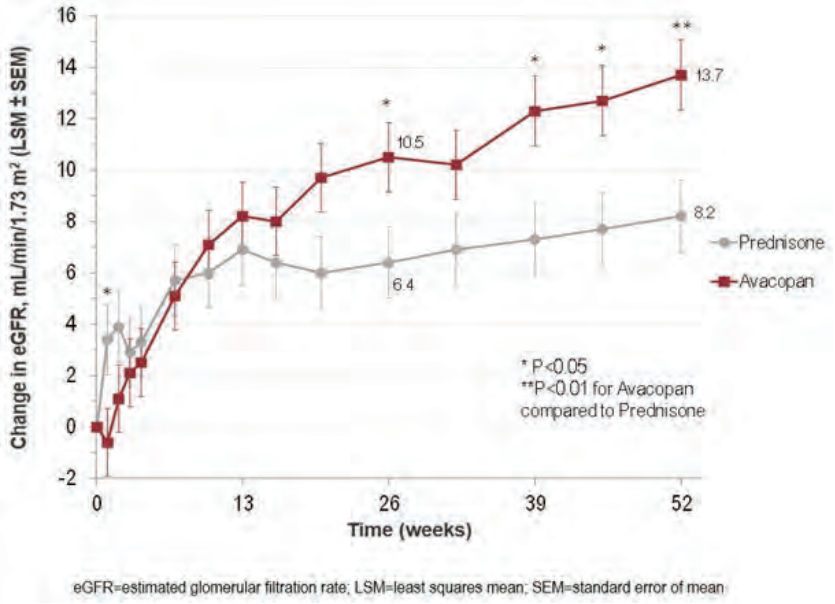


Figure 1. Time to Relapse in the ADVOCATE Study



Change in Estimated Glomerular Filtration Rate (eGFR) in Subjects with eGFR <30mL/min/1.73 m2 at Baseline

ing cyclophosphamide/azathioprine or rituximab, demonstrated superiority compared with the prednisone group. Eighty-one percent of subjects had renal vasculitis, with renal function being a major outcome predictor. This analysis focuses on changes observed in renal function during the trial.

Methods: Subjects were randomized 1:1 to receive either standard prednisone therapy or avacopan 30 mg twice daily. Both treatment groups received either cyclophosphamide followed by azathioprine, *or* rituximab. The primary efficacy endpoints were the proportion of subjects achieving disease remission at Week 26, and sustained disease remission at Week 52 as measured by the Birmingham Vasculitis Activity Score (BVAS). Renal function was assessed based on the estimated glomerular filtration rate (eGFR), and albuminuria, based on the albumin:creatinine ratio.

Results: 330 subjects were dosed: 164 in the prednisone group, 166 in the avacopan group. Primary endpoints, remission Week 26: avacopan 72.3% vs. prednisone 70.1% (P< 0.0001 non inferiority); avacopan 65.7% vs. prednisone 54.9% at Week 52 (avacopan statistically superior P=0.0066). Time to relapse from time of remission (BVAS=0) was longer for the avacopan group (P=0.0091 Log-rank test of difference). The hazard ratio of time to relapse for avacopan:prednisone was 0.46, (95% confidence interval: 0.25, 0.84), **Figure 1**. Efficacy was observed across newly-diagnosed vs. relapsed disease, PR3- vs. MPO-ANCA, granulomatosis with polyangiitis vs. microscopic polyangiitis, cyclophosphamide vs. rituximab, and men vs. women.

In subjects with renal disease at baseline, the avacopan group had a greater increase in eGFR vs. the prednisone group (7.3 mL/min/1.73 m^2 vs. 4.1 mL/min/1.73 m^2) (P=0.029). The difference was greatest in subjects with a baseline eGFR < 30 mL/min/1.73 m^2 **(Figure 2)**. There was a more rapid reduction in albuminuria in the avacopan group (-40%) compared to no change in the prednisone group at 4 weeks; the overall reduction at Week 52 was similar between groups.

The avacopan group had a favorable safety profile compared to the prednisone group. There were 166 serious adverse events in the prednisone group compared to 116 in the avacopan group, and 31 serious infections vs. 25 in the avacopan group. SAEs of WBC count decreases occurred in 4.9% of subjects in the prednisone group vs. 2.5% in the avacopan group, and liver function test increases in 3.7% vs. 5.4%, respectively.

Conclusion: Avacopan offers a new treatment option in ANCA-associated vasculitis. In addition to an improved sustained remission outcome, the avacopan group had greater improvement in renal function compared to standard prednisone therapy. These findings suggest the potential for better long-term outcomes with avacopan for patients with renal disease than current standard of care treatment and provide intriguing insights into subclinical renal disease activity in ANCA-associated vasculitis.

Disclosure: P. Merkel, AbbVie, 5, Biogen, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Insmed, 5, Jannsen, 5, Kiniksa, 5, Magenta, 5, Novartis, 5, Pfizer, 5, Sparrow, 5, Talaris, 5, AstraZeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, UpToDate, 7; **P. Bekker**, Chemocentryx, 3; **H. Yue**, Chemocentryx, 3; **C. Kelleher**, Chemocentryx, 3; **T. Schall**, Chemocentryx, 3; **D. Jayne**, Chemocentryx, 1, 2, 5, GlaxoSmithKline, 1, 2, 5, AstraZeneca, 1, 2, 5, Aurinia, 1, 2, 5, Bristol-Myers Squibb Company, 1, 2, 5, Boehringer Ingelheim, 1, 2, 5.

Abstract Number: 0433

Racial Disparities and New SLE-Specific Predictors of Stroke and Ischemic Heart Disease in Patients with Lupus

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Plenary Session I
Session Type: Plenary Session
Session Time: 11:30AM–1:00PM

Background/Purpose: In the US, cardiovascular disease (CVD) is the leading cause of disparities in life expectancy between black and white populations. We recently reported a 19-fold higher occurrence of CVD in blacks with SLE compared to non-blacks and noted disproportionately high stroke-related events around the time of SLE diagnosis. This study measured the risk and predictors of stroke and ischemic heart disease (IHD) in a predominantly black, population-based, incident cohort.

Methods: The Georgia Lupus Registry (GLR) is a population-based registry of SLE patients from Atlanta, Georgia. Incident patients in 2002-04 met ≥4 ACR SLE criteria or 3 criteria with a final diagnosis of SLE by their board-certified rheumatologist. Patients were matched to the Georgia Hospital Discharge Database and National Death Index from 2000-13. Stroke- and IHD-related hospitalizations and deaths were classified by the first three admission or cause of death codes. Stroke also included transient ischemic attack, and IHD included myocardial infarction and angina. Predictors of strokes and IHD were examined using Cox proportional hazards models.

Results: Among 336 incident SLE patients, 87% were female, 75% were black patient with a mean age at SLE diagnosis of 40 ± 17 years. There were 38 stroke-related and 25 IHD-related events or deaths, from the period 2 years before through 14 years after SLE diagnosis.

Table 1. Predictors of Incident Stroke in Systemic Lupus Patients in the Georgia Lupus Registry

Table 1. Predictors of Incident Stroke in Systemic Lupus Patients in the Georgia Lupus Registry

Variable	HR (95% CI)	p value
Age <19 years	ref	ref
Age 19-<35 years	0.4 (0.11-1.5)	0.18
Age 35-<50 years	1.6 (0.50-5.1)	0.42
Age 50-<65 years	1.1 (0.28-3.1)	0.91
Age ≥65 years	2.7 (0.43-17)	0.29
Male	ref	ref
Female	0.9 (0.39-1.9)	0.78
Non-black race	ref	ref
Black race	**3.4 (1.1-10)**	**0.028**
ACR Criteria:		
No immunologic disorder	ref	ref
Immunologic disorder	2.3 (0.82-6.1)	0.12
No serositis	ref	ref
Serositis	1.7 (0.74-3.8)	0.22
No discoid rash	ref	ref
Discoid rash	**4.6 (1.7-13)**	**0.0028**
No hematologic disorder	ref	ref
Hematologic disorder	4.3 (0.97-19)	0.054
No renal disorder*	ref	ref
Renal disorder*	**2.4 (1.1-5.4)**	**0.04**
ACR criteria total of 4 or 3 ACR criteria with a rheumatologist diagnosis of SLE	ref	ref
ACR criteria total >4	0.8 (0.58-1.2)	0.32

*p <0.1 on univariable analysis included in multivariable cox proportional hazards model; *includes ACR renal disorder at time of SLE diagnosis and/or end-stage renal disease after SLE diagnosis; All ACR criteria were within 1 year of SLE diagnosis. ESRD was through Year 2002-2015; ESRD=end stage renal disease. Ref=reference. p-values <0.05 are in bold.*

In the 11% with strokes, the mean age at first stroke was 48 years, with 78% occurring in females and 90% in blacks. The peak number of strokes occurred during the 2nd year after SLE diagnosis. We noted 8% had IHD, the mean age at first IHD was 52 years, with all occurring in females and 96% in blacks. The peak number of IHD occurred in the 14th year after SLE diagnosis.

Table 2. Predictors of Incident Ischemic Heart Disease (IHD) Occurrence

Table 2. Predictors of Incident Ischemic Heart Disease (IHD) Occurrence

Variable	HR (95% CI)	p value
Age <19 years	ref	ref
Age 19-<35 years	2.7 (0.31-24)	0.36
Age 35-<50 years	5.8 (0.63-54)	0.12
Age 50-<65 years	3.9 (0.36-41)	0.26
Age ≥65 years	**61 (5.8-647)**	**0.0007**
Non-black race	ref	ref
Black race	**24 (2.7-206)**	**0.004**
ACR Criteria:		
No oral ulcers	ref	ref
Oral ulcers	2.2 (0.81-5.8)	0.12
No neurologic disorder	ref	ref
Neurologic disorder	**4.0 (1.3-13)**	**0.018**
No immunologic disorder	ref	ref
Immunologic disorder	**4.7 (1.3-18)**	**0.02**
No discoid rash	ref	ref
Discoid rash	2.1 (0.69-6.5)	0.21
ACR criteria total of 4 or 3 ACR criteria with a rheumatologist diagnosis of SLE	ref	ref
ACR criteria total >4	0.97 (0.67-1.3)	0.83

p <0.1 on univariable analysis included in multivariable cox proportional hazards model and discoid rash; Gender not included in multivariable model as all IHD events occurred in females; All ACR criteria were within 1 year of SLE diagnosis. Ref=reference. p-values <0.05 are in bold.

Blacks had a 3-fold higher risk for stroke (HR 3.4, 95% CI 1.2-10, p 0.03) and a 24-fold higher risk for IHD (HR 24, 95% CI 3-206, p 0.004) (Table 1 & 2). Discoid rash at SLE diagnosis predicted a 5-fold (HR 4.6, 95% CI 1.7-13, p 0.003) and renal disorder predicted a 2-fold higher risk for stroke (HR 2.4, 95% CI 1.1-2.5, p 0.04) (Table 1). Neither impacted IHD (Table 2). Neurologic (HR 4.0, 95% CI 1.3-13, p 0.02) and immunologic disorder (HR 4.7, 95% CI 1.3-18, p 0.02) (Table 2) were strong predictors of IHD but not stroke.

Race stratified Cox proportional hazard models showed significantly accelerated stroke and IHD events in black compared to non-black patients ($p \leq 0.001$) (Figure 1A & B).

Conclusion: We found a 3-fold higher risk of stroke and 24-fold higher risk of IHD in blacks with SLE. We found different SLE-specific predictors of stroke and IHD: discoid rash and renal disorder predicted stroke, and neurologic and

Figure 1 Race Stratified: Panel A) Stroke-Event Free Survival, Panel B) IHD-Event Free Survival

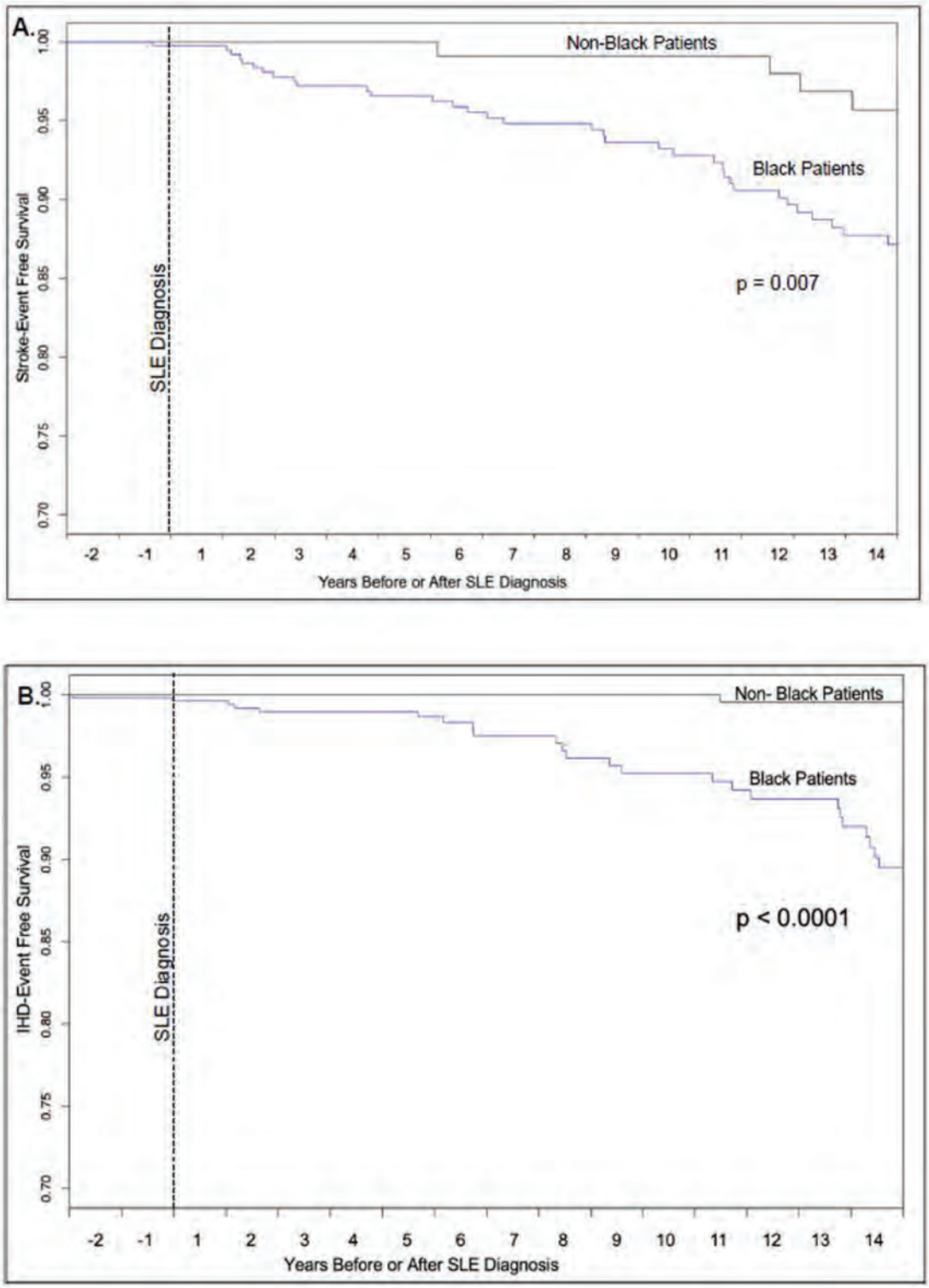

Figure 1. Race Stratified: Panel A) Stroke-Event Free Survival, Panel B) IHD-Event Free Survival

immunologic disorder strongly predicted IHD. This study provides unique insights on significantly different SLE-disease related predictors, timing and racial disparities in stroke compared to IHD in SLE. Hence, we highlight the need to consider different preventive strategies for stroke and IHD in SLE.

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Abstract Number: 0434

Changes in Mental Health During the COVID-19 Pandemic Among Individuals with Rheumatic Disease

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Clinical Practice I
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Symptoms of both depression and anxiety are often elevated among individuals with rheumatic conditions, and stress levels may play a role in each. Depression, anxiety, and stress have also been linked to worse outcomes. We examined changes in symptoms of anxiety and depression from pre-pandemic to during the pandemic, with a focus on the role of stress.

Table 1. Characteristics of Participants

	Total (n = 1504)	RA (n=1126)	OA (n=277)	SLE (n=101)
Age	66.1 ± 10.6	65.4 ± 10.7	70.4 ± 8.5	61.9 ± 11.9
Female	85.7 (1289)	84.6 (953)	(86.6) 240	95.1 (96)
Education (yrs)	15.3 ± 2.0	15.3 ± 2.0	15.4 ± 2.1	15.3 ± 2.0
Rural residence	21.6 (325)	22.2 (250)	19.1 (53)	21.8 (22)
Disease duration (yrs)	23.2 ± 12.5	22.7 ± 12.7	23.4 ± 11.0	27.7 ± 12.0
Pre-COVID Global severity rating	3.2 ± 2.4	3.1 ± 2.3	3.3 ± 2.4	3.8 ± 2.7
Stress				
COVID-19-specific	6.1 ± 1.9	6.1 ± 1.9	5.9 ± 1.8	6.4 ± 2.0
General (PSS)	2.5 ± 1.8	2.4 ± 1.8	2.4 ± 1.7	2.8 ± 1.9
PHQ4 depression				
Pre-COVID-19	0.79 ± 1.25	0.78 ± 1.25	0.66 ± 1.12	1.28 ± 1.46
During COVID-19	0.84 ± 1.24	0.84 ± 1.27	0.73 ± 1.07	1.20 ± 1.36
% with increase*	7.9 (119)	8.0 (90)	6.9 (19)	9.9 (10)
PHQ4 anxiety				
Pre-COVID-19	0.66 ± 1.18	0.67 ± 1.18	0.52 ± 1.04	0.97 ± 1.47
During COVID-19	0.99 ± 1.35	1.01 ± 1.39	0.84 ± 1.15	1.23 ± 1.47
% with increase*	10.6 (159)	10.7 (120)	8.7 (24)	14.9 (15)

PHQ4 DEP and ANX: score range = 0 – 6. Increase defined as change ≥2.
Global severity rating range 0 – 10
Both stress measures re-scaled for range 0 – 10.

Table 2. Association of stress with increases in anxiety and depression			
	Model 1	Model 2	Model 3
Increase in DEP			
COVID-19-specific	1.8 (1.6, 2.1)	---	1.6 (1.4, 1.9)
General PSS	---	1.8 (1.6, 2.1)	1.6 (1.4, 1.9)
Increase in ANX			
COVID-19-specific	2.1 (1.8, 2.3)	---	1.9 (1.7, 2.2)
General PSS	---	1.7 (1.5, 1.9)	1.5 (1.3, 1.7)
Values are odds ratio (95% confidence interval) from multiple logistic regression analyses adjusting for age, sex, education, race, rural residence, and pre-COVID global severity rating, hydroxychloroquine use, and PHQ4 depression or anxiety score. Model 1 includes PSS only, Model 2 includes COVID-19-specific stress only, Model 3 includes both			

Methods: Data are from FORWARD, The National Databank for Rheumatic Diseasesa longitudinal registry of individuals with rheumatic diseases. Data are regularly collected via semi-annual questionnaires. Participants with active emails were asked to respond to 5 COVID-19-specific questionnaires from March 25 through June 2, 2020. Both regular and COVID-19 questionnaires included the PHQ4, a validated screening measure for symptoms of anxiety (ANX) and depression (DEP). The COVID-19 questionnaire also include an item about COVID-19-specific stress ("how much stress or worry has the COVID-19 pandemic caused you? None, a little, moderate amount, great deal) and the 4-item Perceived Stress Scale (PSS), which assesses general stress. Both stress scale scores were transformed to 0 – 10 scores to facilitate comparison. Participant characteristics were taken from the most recent semi-annual (pre-COVID-19) questionnaire. Analyses examined the frequency of increases in ANX and DEP, defined as score change ≥2. Predictors of ANX and DEP increases among respondents with rheumatoid arthritis (RA), osteoarthritis (OA), and lupus (SLE) were identified using multiple logistic regression, focusing on the role of COVID-19-specific stress and PSS, and controlling for age, sex, race, education, rural residence, disease duration, and pre-COVID-19 global disease severity rating, and DEP and ANX scores.

Results: A total of 7217 participants were invited; 2000 (28%) responded at ≥1 COVID-19 questionnaire. Only those reporting diagnoses of RA, OA, or SLE (n=1504) are included in analyses. Respondent characteristics are shown in Table 1. COVID-specific stress ratings were twice as high as general stress ratings. Correlation between the two was 0.40. Increases in ANX were more common than increases in DEP (ANX: 10.6%; DEP: 7.9%), with no significant differences in frequency of increases among condition groups. Both COVID-19-specific and general stress were significantly associated with increases in DEP and ANX (Table 2).

Conclusion: Substantial increases in symptoms of both anxiety and depression were found when comparing scores from pre-pandemic to during the pandemic. Both COVID-19-specific and general stress levels were significantly associated with those changes. While the impact on disease outcomes remains to be seen, results suggest the need for assessment of stress in clinical settings and identification of effective stress management techniques.

Disclosure: P. Katz, None; **S. Pedro**, Forward, The National Databank for Rheumatic Diseases, 3; **K. Wipfler**, None; **T. Simon**, Bristol Myers Squibb, 5, Lexicon, 5; **Y. Shaw**, Amgen Inc., 9; **A. Cornish**, None; **K. Michaud**, Rheumatology Research Foundation, 2.

Abstract Number: 0435

Low Incidence of Coronavirus Disease 2019 (COVID-19) Infection in Patients on Biologic Infusion Therapies at a Community Rheumatology Practice

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SESSION INFORMATION
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Session Time: 4:00PM–4:50PM

Background/Purpose: Following the first documented Florida case of COVID-19 on March 1, 2020, our community rheumatology practice continued to administer biologic infusion therapy with concern as to the outcome of exposure to COVD-19 in this patient population.

Methods: Point-of-care COVID-19 antibody testing was initiated prior to all infusions from April 28, 2020, using the RayBiotech or Healgen COVID-19 IgM/IgG Rapid Test Kit. During this three month period a review of the medical records revealed a total of 255 unique infusion patients screened for COVID-19, 185 females and 70 males, age 16 to 92 with a mean age of 58. Underlying diagnoses included AS, GCA, hidradenitis suppurativa, IBD, MS, myasthenia gravis, PSA, RA, and SLE. Treatments included infliximab (51.8%), rituximab (12.9%), golimumab (10.2%), abatacept, belimumab, ocrelizumab, tocilizumab, ustekinumab, and vedolizumab.

IgM positive patients were not infused and were asked to get confirmatory PCR testing done, quarantine for two weeks, and needed to test negative for IgM before infusions were restarted. All staff wore appropriate PPE, had daily body temperatures checked, and were tested for COVID weekly.

Results: On April 28, 2020 there were 11,831 confirmed COVID-19 cases in Dade County (the county in which this practice resides)[1], and by June 16, 2020 Dade County reported 22,741 confirmed cases of COVID-19, with 3,497 hospitalizations (16% of all cases) and 847 reported deaths (4% of all cases)[2].

Of the 255 unique infusion patients screened in this period, six tested positive for both COVID-19 IgM and Ig G antibodies (2.67% of patients) while four patients (1.57%) tested positive for COVID-19 IgG antibodies alone. None of these patients required hospitalization and none had experienced severe COVID-19 symptoms or disease. All experienced negligible or only mild symptoms when questioned by the provider about current or historical diagnosis following their positive test results.

Conclusion: Considering the level of community spread occurring in our area, we were surprised to find how few of our patients on biologic therapy tested positive for COVID-19 antibodies, and furthermore, how few of those who tested positive experienced symptoms. This appears to support the concept that cytokine inhibition from the use of biologic infusion therapy and possibly may in fact provide some protective mechanism to this group of patients and may arguably reduce the clinical consequences following infection[3,4]. To be noted, background steroids were utilized in a high percentage of our patients. In the past, this facility, amongst others, has reported a potential benefit and lack of toxicity with the use of biologic therapies in the face of HIV and Hepatitis C infections.[5] Further investigation would

be warranted to determine if there is any anti-COVID-19 benefit prophylactically and therapeutically from the various immune modulators currently used in the clinical rheumatology space.

Disclosure: J. Keegan Strosser, None; **R. Yglesias**, None; **N. Gaylis**, None.

Abstract Number: 0436

The Addressing Lupus Pillars for Health Advancement (ALPHA) Project: Establishing Consensus and Prioritization of Global Community Recommendations to Address Major Challenges in Lupus Diagnosis, Care, Treatment and Research

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Session Time: 4:00PM–4:50PM

Background/Purpose: The Addressing Lupus Pillars for Health Advancement (ALPHA) Project is a global consensus effort to identify, prioritize and address top barriers in lupus impacting diagnosis, care, treatment and research. Prior publications outlined mixed methodology of expert interviews and surveys to identify and prioritize barriers across drug development, clinical care and access to care among global lupus stakeholders including: clinicians, researchers, biopharmaceutical and government representatives, patients and caregivers.[1,2] This abstract details methodology used to develop a roadmap of specific recommendations to address the barriers.

Methods: An in-person stakeholder meeting of ALPHA Global Advisory Committee (GAC) members and a 2-round scoring survey were used to elicit recommendations. Prior to the meeting, held in Jan. 2020 in Washington, DC, GAC members (n=15) defined 'success' across drug development, clinical care and access to care using prior identified barriers as a framework. The meeting included 14 GAC members, 2 patients, an added clinician-researcher and Lupus Foundation of America and Tufts Center for the Study of Drug Development staff. Participants were divided into 3 breakout groups, with patient and specialty representation in each group, and identified at least 1 actionable solution to achieve 'success' per pillar. After full group discussion, participants voted on 1 top solution per pillar. Post-meeting, solutions were evaluated by feasibility, impact and timeline for implementation (FIT; **Table 1**). Each meeting

Table 1. Feasibility, Impact, and Timeline (FIT) Scoring Guide

Score	Feasibility	Impact	Timeline
1	Low feasibility: Item implementation faces **many** internal and external economic, technical, legal, and operational constraints that hinder achievability	Low impact: If implemented, the item will have a **minimal to no effect** on lupus communities, practices, organizations, and systems, and the impact will be short-term.	Long timeline: Item implementation will take **more than 5 years.**
2	Moderate feasibility: Item implementation faces **some** internal and external economic, technical, legal, and operational constraints that hinder achievability	Moderate impact: If implemented, the item will have a **modest effect** on lupus communities, practices, organizations, and systems, and the impact may be short term.	Moderate timeline: Item implementation will take **between 1-5 years.**
3	High feasibility: Item implementation faces **few to no** internal and external economic, technical, legal, and operational constraints that hinder achievability	High impact: If implemented, the item will have **maximum effect** on lupus communities, practices, organizations, and systems, and the impact will last for years to come.	Short timeline: Item implementation will take **less than 1 year.**

participant completed 2 rounds of scoring in Qualtrics software. Potential FIT component values were between 1-3 and total scores between 3-9. Higher scores represent higher achievability based on the composite of the 3 criteria.

Results: Table 2 shows ranked solutions per pillar based on in-person voting, and **Table 3** shows FIT scores. Simplifying and standardizing outcomes measures, such as steroid-sparing (drug development), and defining the lupus spectrum (clinical care) ranked as the highest priority solutions during the GAC meeting and received high FIT scores.

Table 2. Ranked Solutions per Pillar Identified During GAC In-Person Meeting

Priority	Drug Development	Clinical Care	Access to Care
#1	Simplify and standardize outcomes measures, including steroid-sparing as an outcome *(10 votes)*	Define the lupus spectrum (9 votes)	Build the case for World Health Organization prioritization (9 votes)
#2	Develop data sharing approaches related to biomarkers, clinical data, and lab samples *(5 votes)*	Perform longitudinal studies of prognostic and diagnostic biomarkers (5 votes)	Develop standardized and specialized, expert-driven care pathways (5 votes)
#3	Drive quality of life driven studies (e.g. fatigue) *(3 votes)*	Drive clinical and lab-based measures for individualized treatments (3 votes)	Drive telehealth advances and reimbursement, and build upon current infrastructures (3 votes)
#4	Increase representativeness in trials (e.g. minority, pediatric) *(1 vote)*	Identify and support development of adherence strategies that work for lupus and communicate them to patients and providers (3 votes)	(0 votes) • Explore broader partnering • Leverage social media • Develop evidence base for interventions, including standardized endpoints / outcomes • Payer education and alignment

Table 3. Feasibility, Impact, and Timeline Scoring Results, Listed by Highest Average Score

Consensus Item	Feasibility 1 = low 2 = moderate 3 = high		Impact 1 = low 2 = moderate 3 = high		Timeline 1 = long 2 = moderate 3 = short		TOTAL		
	Round 1	Round 2	Round 1	Round 2	Round 1	Round 2	Round 1	Round 2	Average
Drug Development – Average Scores									
Simplify and standardize outcomes measures, including steroid-sparing as an outcome	2.44	2.61	2.72	2.94	2.11	2.11	**7.28**	**7.67**	**7.48**
Increase representativeness in trials (e.g. minority, pediatric)	2.17	2.11	2.61	2.61	1.89	1.83	**6.67**	**6.56**	**6.62**
Drive quality of life driven studies (e.g. fatigue)	2.28	2.22	2.39	2.39	1.72	1.94	**6.39**	**6.56**	**6.48**
Develop data sharing approaches related to biomarkers, clinical data, and lab samples	1.78	1.78	2.72	2.78	1.50	1.50	**6.00**	**6.06**	**6.03**
Clinical Care – Average Scores									
Identify and support development of adherence strategies that work for lupus and communicate them to patients and providers	2.44	2.39	2.72	2.67	2.00	2.17	**7.17**	**7.22**	**7.20**
Define the lupus spectrum	2.50	2.56	2.44	2.56	2.00	2.33	**6.94**	**7.44**	**7.19**
Drive clinical and lab-based measures for individualized treatments	2.00	1.78	2.61	2.78	1.44	1.33	**6.06**	**5.89**	**5.98**
Perform longitudinal studies of prognostic and diagnostic biomarkers	2.11	1.89	2.67	2.61	1.39	1.00	**6.17**	**5.50**	**5.84**
Access to Care – Average Scores									
Leverage social media	2.71	2.89	2.47	2.06	2.76	2.83	**7.94**	**7.78**	**7.86**
Explore broader partnering	2.47	2.56	2.18	2.11	2.06	2.22	**6.71**	**6.89**	**6.80**
Payer education and alignment	2.00	2.06	2.59	2.50	1.76	1.89	**6.35**	**6.44**	**6.40**
Develop standardized and specialized, expert-driven care pathways	2.12	2.17	2.53	2.44	2.00	1.83	**6.28**	**6.44**	**6.36**
Develop evidence base for interventions, including standardized endpoints / outcomes	2.12	1.83	2.71	2.72	1.53	1.44	**6.36**	**6.00**	**6.18**
Drive telehealth advances and reimbursement, and build upon current infrastructures	2.06	2.00	2.53	2.11	2.00	1.89	**6.22**	**6.00**	**6.11**
Build the case for World Health Organization prioritization	1.76	1.67	2.29	2.06	1.47	1.39	**5.52**	**5.11**	**5.32**

Leveraging social media (access to care) received the highest FIT score across all pillars. Cross-cutting themes included leveraging digital technology and applying specific considerations for pediatric populations, as drug development has been limited and outcomes may differ from adults.

Conclusion: ALPHA has developed a roster of actionable solutions to barriers collectively impacting drug development, clinical care and access to care, and assessed achievability of each to improve the quality of life of adults and children with lupus. Simplifying and standardizing outcome measures, including steroid-sparing, may be pivotal to advance lupus drug development. Further clarifying the lupus spectrum may improve time to diagnosis and aid both provider and patient understanding of lupus. These findings are also an important indicator of patient preferences, highly relevant in patient-focused drug development.

References

[1]Lupus Sci Med 2019;**6:**e000342. doi: 10.1136/lupus-2019-000342
[2]Ann Rheum Dis, volume 79, supplement 1, year 2020, page 1953

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Abstract Number: 0437

Integrating Reproductive Health in Systemic Lupus Erythematosus in a Tertiary Care Setting

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Session Title: Clinical Practice I
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Session Time: 4:00PM–4:50PM

Background/Purpose: Systemic Lupus Erythematosus (SLE) predominantly affects women of childbearing age. Women affected by SLE have higher risk for infertility, miscarriages, and other pregnancy complications due to dis-

Gender	Subjects	SLE, N(%)
Female	900 (85.1%)	777 (89.1 %)
Male	158 (14.9%)	95 (10.9 %)
female patients age between 18-50	465 (44.0%)	372 (42.7 %)
female patients seen the last two years only	325 (30.7%)	281 (32.2 %)
female patients seen last two years age between 18-50	203 (19.2%)	166 (19.0 %)
Total number of subjects	1058	872 (82.4 %)

Table 1A (Demographic History of protocol 94-AR-0066):

Female Subjects	N	Percent %
Seen in the past two years between 18-50	203.0	
Healthy Volunteers	39	19.2%
Age above 45 years old	39	19.2%
SLE patients age between 18-45 years old	122	60 %

Table 1B (Demographic History of female subjects seen in the past two years between ages 18-50):

ease activity, renal involvement, medications (like cyclophosphamide), and presence of certain autoantibodies (like anti- Ro/SSA, anti-La/SSB, antiphospholipid antibodies). Active SLE at the time of conception is a strong predictor of adverse maternal and fetal outcomes; current recommendations include attempting disease quiescence for 6 months before trying to conceive. Our goal is to improve reproductive health in patients with SLE following the ACR Guidelines. We embark on this study by assessing our current practice of addressing and documenting reproductive health issues and to develop a quality improvement process to address any deficiencies.

Methods: A retrospective chart review was conducted of the NIAMS Lupus Natural History Cohort on female patients of childbearing age with at least one clinic visit in the preceding two years were included in the study (Table 1B) to identify current practice. Data collected included documentation of obstetrics history, discussion on reproductive health, fertility preservation, and autoantibody history (anti-Ro/SSA, anti-La/SSB, and antiphospholipid antibodies).

Results: Our cohort comprises of 85% (N=900) females, with 44% (n=465) in childbearing age (Table 1A). The mean age of SLE women studied was 35 years old with a range of 21-45 years of age. Autoantibody history was documented in 98%. Contraception was documented in 92%. Out of the 112 patients, documentation of pre-pregnancy counseling occurred in only 4%. There was no documentation of discussion on fertility preservation (Table 2).

Conclusion: Reproductive health is an important topic that should be a shared decision-making process between SLE patients and providers. Studies have shown that patients desire an active role from their rheumatologist regarding initiating family planning conversations and sexual/reproductive health education. The current study reveals that, while certain aspects of reproductive health (such as autoantibodies and contraception) are documented, discussions on pre-pregnancy counseling and fertility preservation are lacking. Furthermore, although there were documentations on disease activity, there was no discussion on how disease activity may affect future pregnancy. Based on the current study, we will implement the HOP-STEP program which provides a guideline in helping providers address pre-pregnancy counseling, and acceptable options for contraception. We plan to modify our progress note template to incorporate elements from ACR reproductive health guidelines. Lastly, with our colleagues in reproductive health

Data Collection:	Percentage:
Serological History Documentation	98%
Contraception Documentation	92%
Intrauterine device (IUD)	33%
Abstinence/None	15.1%
Oral Contraception	12.5%
Tubal Ligation/Hysterectomy	10.7%
Barrier Method	10.7%
Medroxyprogesterone injection	4.4%
Etonogestrel implant	3.5%
Ovarian Failure	2.6%
Patient/Provider Pre-Pregnancy Counseling	4.4%
Patient/Provider Fertility Preservation	0

Table 2 (Retrospective Chart Review on 100% (N=112) of all females seen within the last two years between the ages of 18-45 years old):

we will develop a fertility preservation resource for our patients. With these interventions put in place, we believe will greatly impact and improve reproductive health in SLE.

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Abstract Number: 0438

Pharmacist-Led Multidisciplinary Approach to Opioid Tapering in a Large Private Rheumatology Practice

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Clinical Practice I

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: With the evolution of DMARDs, the need for opioids in the treatment of rheumatic diseases has decreased. However, rheumatology professionals are often presented with patients in whom chronic opioid ther-

apy was started prior to the availability of newer DMARDs. Current guidelines suggest opioid tapering should be considered in patients with chronic noncancer pain on ≥90 mg morphine equivalent dose (MED) daily or in combination with other high-risk medications. The aims of our project are to assess provider perspective and baseline knowledge on opioid taper regimens, provide education and support related to opioid management, and demonstrate improved patient outcomes when a pharmacist is part of the multidisciplinary team in a rheumatology practice.

Methods: The pharmacy team at a private rheumatology practice developed a three phased program including provider and staff education, updates to office workflows, and implementation of individualized patient taper plans. A baseline survey was administered to providers to characterize current practices and perspectives regarding practice-wide opioid use and confidence in managing opioids. The pharmacy team held training sessions to teach providers to appropriately identify circumstances when opioid tapering is indicated, develop individualized opioid taper regimens, recognize and manage withdrawal symptoms, and apply risk mitigation strategies during a chronic opioid therapy taper. Patients identified by providers as candidates are enrolled in the pharmacy service. The pharmacy team serves as a continuous resource to providers and works directly with patients enrolled in the service. Baseline characteristics, historical data on opioid related efficacy and side effects, and daily morphine equivalents are collected and tracked for each patient.

Results: All providers (n=10) reported having patients on chronic opioids; 70% felt they had at least one patient who would benefit from tapering. Reported barriers to tapering included time, comfort, and lack of confidence in managing withdrawal. Eighty percent of providers rated their comfort level a 5 or lower in tapering or discontinuing an opioid, on a scale of 0 to 10, with 0 being not comfortable at all and 10 being very comfortable. Nine providers stated they were hesitant or very hesitant in developing an opioid tapering plan. As of June 2020, 16 patients have been enrolled in the opioid taper service, and 2 withdrew. Five have reduced their daily MED somewhere between 25 and 100%. The remainder of patients are at stage where the focus is optimizing non-opioid analgesics, limiting high-risk concomitant medications, and minimizing use of existing opioids. A follow-up provider survey is planned. Patient survey data will also be collected.

Conclusion: Successful opioid tapering is a time intensive process and requires a multidisciplinary approach. This provides an opportunity for pharmacists to play an essential role as part of a team-based approach to ensure a successful opioid taper or discontinuation while minimizing adverse events. Our pharmacist-led opioid taper protocol can serve as an innovative model for rheumatology practices to include a clinical pharmacist as part of their healthcare team.

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Abstract Number: 0439

Hurried Communication and Low Patient Self-Efficacy Are Associated with Persistent Non-Adherence to SLE Medications

Ann Cameron Barr[1], Megan Clowse[2], Amanda Eudy[3], Jennifer Rogers[4], Rebecca Sadun[3], Lisa Criscione-Schreiber[5], Jayanth Doss[3], Lena Eder[6], Mithu Maheswaranathan[3], Amy Corneli[7], Hayden Bosworth[7] and Kai Sun[3], [1]Duke University Hospital, Durham, NC, [2]Duke University, Chapel Hill, NC, [3]Duke University, Durham, NC, [4]Duke, Durham, NC, [5]Duke University School of Medicine, Durham, NC, [6]Duke University Hospital, Chapel Hill, NC, [7]Duke University, Durham

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Healthcare Disparities in Rheumatology

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: Medication non-adherence is common among SLE patients and contributes to poor outcomes. Underrepresented racial minorities have disproportionately lower rates of medication adherence and often have more severe manifestations of SLE. In this longitudinal analysis, we aimed to identify modifiable factors associated with persistent medication non-adherence.

Table 1. Comparing those with Persistent Adherence, Inconsistent Adherence, and Persistent Non-Adherence based on the Composite Adherence measure at baseline and follow-up.

Table 1. Comparing those with Persistent Adherence, Inconsistent Adherence, and Persistent Non-Adherence based on the Composite Adherence measure at baseline and follow-up.

	Persistent Non-Adherence (n=36)	Inconsistent Adherence (n=16)	Persistent Adherence (n=25)	P-value
Age, years, median [IQR]	**39[33-49]**	**36[31-50]**	**49[43-57]**	**0.01**
Female gender, %	100%	94%	92%	0.2
African American race, %	**74%**	**50%**	**32%**	**0.005**
≥ College Education, %	53%	75%	60%	0.3
Disability, %	47%	25%	28%	0.2
Medicaid insurance, %	25%	13%	4%	0.07
Hurried communication*, median [IQR]	**1.5[1-2.3]**	**1[1-1.3]**	**1[1-1.5]**	**0.01**
Speak fast‡, median [IQR]	**2[1-3]**	**1[1-1.5]**	**1[1-1]**	**0.003**
Hard words‡, median [IQR]	**2[1-3]**	**1[1-1.5]**	**1[1-2]**	**0.005**
Self-efficacy^, general, median [IQR]	47[42-57]	52[41-65]	52[49-59]	0.2
Self-efficacy^, managing treatments & medications, median [IQR]	**43[40-57]**	**52[43-58]**	**54[48-61]**	**0.05**
# SLE medications, median [IQR]	**2.5[2-3]**	**2[2-2]**	**1[1-2]**	**0.002**
SLICC damage score, median [IQR]	**3[1-4]**	**0[0-1]**	**1[0-3]**	**0.0001**
SLEDAI, median [IQR]	2[0-5]	2[0-4]	0[0-4]	0.2
PGA, median [IQR]	**0.5[0.3-0.8]**	**0[0-0.6]**	**[0-0.5]**	**0.03**

* Interpersonal Processes of Care survey, score ranges 1-5, with higher score indicating more of the domains. 1 is best score for Hurried Communication and its sub-domains. Scores of other domains of this survey (Elicited concerns, Explained results, Patient-centered decision making, Discrimination, and Disrespectful office staff) were not significantly different between adherence groups.

‡ Subdomains of Hurried Communication, as reflected by answers to the questions "how often did doctors speak too fast?" and "how often did doctors use words that were hard to understand?"

^ Patient Reported Outcomes Measurement Information System (PROMIS®) measures, general population mean score is 50, clinically significant difference is ≥ 5

Methods: Consecutive SLE patients taking ≥1 SLE medications at a tertiary lupus clinic were enrolled. Baseline data collected 7/2018-1/2019 included demographics, patient-provider communication as measured by the Interpersonal Processes of Care survey, self-efficacy, and SLICC damage scores. Follow-up data collected 9/2019-1/2020 included SLEDAI and physician global assessment (PGA) of disease activities. Adherence data obtained at both baseline and follow-up included: 1) self-reported adherence in the preceding month from 0-100%, with ≥90% indicating High Self-Reported Adherence; and 2) pharmacy refill data in the preceding 3 months, with a medication possession ratio (MPR) of ≥80% indicating High Refills. High Composite Adherence was defined as having both High Self-reported Adherence and High Refills. Those with High Composite Adherence at both baseline and follow-up were considered to have Persistent Adherence, those with Low Composite Adherence at both time points were considered to have Persistent Non-Adherence, and the rest were considered to have Inconsistent Adherence. We compared characteristics of adherence groups.

Results: Data from 77 SLE patients were analyzed (43% white, 53% African-American, and 4% other). Median age was 44 years, 96% were female, 60% had ≥ college education, and 51% had private insurance. On average, patients were prescribed 2 SLE medications, with 84% prescribed HCQ, 57% prescribed a DMARD, and 4% prescribed Belimumab. At baseline, 73% had High Self-Reported Adherence, 51% High Refills, and 43% High Composite Adherence. Longitudinally, 32% had Persistent Adherence, 47% had Persistent Non-Adherence, and 21% had Inconsistent Adherence. Comparing adherence groups, those with Persistent Non-Adherence were younger, more likely to be African-American, took more SLE medications, and had higher PGA scores. Patients with Persistent Non-Adherence also rated more hurried communication with providers – specifically with respect to speaking fast and using hard words – and had lower self-efficacy in managing treatments and medications (Table 1).

Conclusion: Our results show that adherence rates to SLE medications are low, and persistent non-adherence is disproportionately more common among African-Americans. Potential areas for intervention in order to improve adherence include optimizing patient-provider communication, specifically avoiding difficult vocabulary and fast speech, and enhancing patient self-efficacy, particularly among young African-Americans with SLE who are at higher risk for non-adherence.

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Abstract Number: 0440

Representation of Women as Authors of Rheumatology Research Articles

Ekta Bagga[1], Sarah Stewart[2], Gregory Gamble[1], Janine Hill[1], Andrew Grey[1] and **Nicola Dalbeth**[1], [1]University of Auckland, Auckland, New Zealand, [2]The University of Auckland, Auckland, New Zealand

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Table. Proportion of articles according to author gender.

		First author gender, women		Senior author gender, women	
	Number of articles, N	n	% [95% CI]	n	% [95% CI]
All	7651	3939	51.5% [50.4%, 52.6%]	2699	35.3% [34.2%, 36.4%]
Research design					
Basic science	1801	931	51.5% [49.4%, 54.0%]	542	30.1% [28.0%, 32.2%]
Randomised controlled trial	603	201	33.3% [29.7%, 37.2%]	159	26.4% [23.0%, 30.0%]
Systematic literature review/meta-analysis	449	227	50.6% [45.9%, 55.2%]	178	39.6% [35.2%, 44.2%]
Other clinical	4798	2580	53.7% [52.4%, 55.2%]	1820	37.9% [36.6%, 39.3%]
Funding source					
Industry-funded/industry-initiated	724	284	39.2% [35.7%, 42.8%]	224	30.9% [27.7%, 34.3%]
Industry-funded/investigator-initiated	734	369	50.3% [46.7%, 53.9%]	261	35.6% [32.2%, 39.1%]
Not industry-funded	6193	3286	53.1% [51.8%, 54.3%]	2214	35.8% [34.6%, 37.0%]

Background/Purpose: In academic medicine, journal article authorship is central to career advancement and promotion. This study aimed to examine the contemporary representation of women as first and senior authors of rheumatology-related original research articles.

Methods: The gender of first and senior author, disease category, research design and funding source were extracted from rheumatology original research articles published in high impact rheumatology and general medical journals between 2015 and 2019.

Results: 7,651 original research articles were included in the analysis. In total, there were 51.5% [95% CI 50.4%, 52.6%] articles with women first authors and 35.3% [95% CI 34.2%, 36.4%] with women senior authors. Women were significantly less likely to be first and senior authors of articles reporting randomized controlled trials compared with other clinical research designs ($P < 0.001$), and of articles reporting industry-funded/industry-initiated studies compared with studies not funded by industry ($P \leq 0.01$). For articles reporting industry-funded/industry-initiated randomized controlled trials, women were first authors in 18.5% [95% CI 13.8%, 24.0%] and senior authors in 23.9% [95% CI 18.6%, 29.8%].

Conclusion: In rheumatology journal articles, there is gender parity for first authorship, but women are under-represented in senior authorship positions. Under-representation of women in authorship is particularly apparent in articles reporting randomized controlled trials, especially those that are initiated by industry.

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Abstract Number: 0441

Use of an Integrated Care Management Program to Uncover and Address Social Determinants of Health for Individuals with Lupus

Kreager Taber[1], Jessica Williams[1], Weixing Huang[2], Katherine McLaughlin[1], Christine Vogeli[3], Rebecca Cunningham[1], Lisa Wichmann[1] and Candace Feldman[4], [1]Brigham and Women's Hospital, Boston, MA, [2]Division of Rheumatology, Inflammation, and Immunity; Brigham and Women's Hospital and Harvard Medical School, Boston, [3]Massachusetts General Hospital, Boston, MA, [4]Brigham and Women's Hospital, Boston

SESSION INFORMATION
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Session Title: Healthcare Disparities in Rheumatology
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Session Time: 4:00PM–4:50PM

Background/Purpose: The burden of systemic lupus erythematosus (SLE) falls disproportionately on racial/ethnic minorities and individuals of lower socioeconomic status who often receive fragmented, inconsistent care. The Integrated Care Management Program (iCMP) enrolls patients at high risk for acute care use and adverse outcomes and connects them with a nurse and care team who help coordinate their medical care. We studied SLE patients enrolled in iCMP to understand whether social determinants of health (SDoH) needs such as food insecurity, housing instability, and financial constraints were prevalent in this population. We hypothesized iCMP teams would uncover and address SDoH issues that while likely present, would not have been documented before enrollment.

Methods: The iCMP enrolls the top 2% of medically and psychosocially complex patients within our multihospital primary care practices. Patients are identified by a system that incorporates clinical complexity, healthcare utilization

Figure. Social Determinants of Health-related Issues Documented Before and During Integrated Care Management Program (iCMP) Enrollment

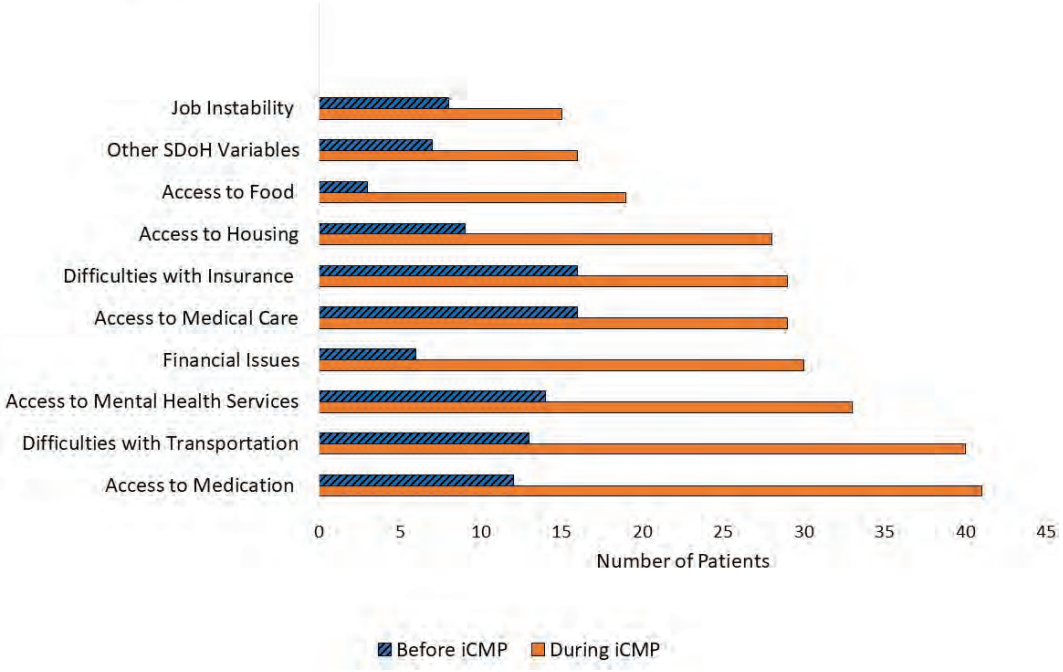

Table. Social determinants of health needs uncovered by the integrated care management program (iCMP) team and examples of strategies used to address these needs			
Social Determinants of Health (SDoH) Factors	SLE patients with issues addressed (n=56)	Example of issue	Examples of strategies used by iCMP team* to address issue
Medication Access	66%	Patient could not afford copays for medications	Connected patient with new insurance plan to make medications more affordable
Transportation Needs	61%	Patient needed transportation to medical appointments	Coordinated door-to-door transportation to appointments
Insurance Difficulties	50%	Patient's health insurance was revoked	Connected to financial services to reinstate insurance
Mental Health Service Access	48%	Patient would like to see mental health services but has significant difficulty leaving her home	Referred to at-home psychiatrist
Financial Issues	48%	Patient could not pay utility bill	Utility protection letter composed for patient
Housing Instability	46%	Patient given eviction notice from apartment after unable to pay rent	Connected with emergency housing and helped during appeal of eviction
Food Instability	32%	Patient couldn't afford to eat	Referred to Elder services and Meals-on-Wheels
Other SDoH Variables (Access to child care, personal/neighborhood safety, education access, job instability)	32%	Patient had no resources to support children while she was admitted Patient experienced domestic violence Patient not able to start school on time due to illness Patient reported difficulty finding work after catastrophic medical event	Connected with services to help with child care and home upkeep while admitted Family helped while finding a long-term care facility for patient Helped patient contact her academic advisor for assistance delaying her enrollment Helped patient search for jobs that could accommodate her functional needs
*iCMP Team includes iCMP Nurse, Social Workers, Care Coordinators, Community Resource Specialists, and Pharmacists			

indicators, and consultation with primary care providers, but does not explicitly factor in SDoH. Individuals with SLE enrolled in iCMP were identified with a validated machine learning algorithm (PPV=90%) and verified by chart review. We reviewed patients' electronic health record encounters to identify SDoH needs prior to iCMP enrollment primarily using notes from physicians and social workers, and throughout enrollment using notes from iCMP nurses and team members.

Results: There were 69 patients with SLE enrolled in iCMP. Of these, 93% were female, 55% were white, 25% black, 3% Asian/Pacific Islander, 16% other/unknown race, and 21% were Hispanic. The mean duration of iCMP enrollment was 3.8 (SD 2.4) years. Prior to iCMP enrollment, 57% of the patients had documentation of ≥1 SDoH factor, compared to 94% during enrollment **(Figure).** The iCMP nurses addressed ≥1 SDoH factor for 81% of the SLE patients and completed high risks assessments for each patient. For these patients, iCMP nurses discussed and addressed multiple SDoH issues including medication access (66%), transportation (61%), insurance (50%), financial issues (48%), housing concerns (46%) and food insecurity (32%) **(Table).** The iCMP nurses connected 75% of these patients with additional resources, including social workers/mental health resources (58%), home health (43%) and elder care (14%) services, pharmacists (14%) and substance abuse programs (6%).

Conclusion: While SDoH-related issues were not used to identify patients for iCMP, the majority of enrolled high-risk, medically complex SLE patients had these needs. The iCMP nurses and care team members uncovered and addressed numerous SDoH-related concerns that while likely present, had not been documented prior to iCMP participation. As SDoH directly impact the care that patients access and the disproportionate burden of adverse out-

comes among vulnerable populations, the healthcare system must develop and expand sustainable strategies like this integrated care management program to identify, document, and address these issues.

Disclosure: K. Taber, None; **J. Williams**, None; **W. Huang**, None; **K. McLaughlin**, None; **C. Vogeli**, None; **R. Cunningham**, None; **L. Wichmann**, None; **C. Feldman**, Merck, 5, Voyager Therapeutics, 5, Biogen, 8.

Abstract Number: 0442

Disparities in CoronaViridae Infection Are Readily Apparent in Rheumatology Patients Despite Use of Hydroxychloquine And/or Methotrexate

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology
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Session Time: 4:00PM–4:50PM

Background/Purpose: In the initial months of the SARS CoV2/COVID19 pandemic, broad use of off-label therapy with hydroxychloroquine (HCQ) was prescribed to reduce CoV2-related morbidity and mortality. Disparity in infection rates in non-Caucasians were observed even when other co-morbidities such as diabetes, obesity and smoking were accounted for. We hypothesized that if HCQ was effective against CoV2, then the rates of CoV2 infections in patients treated with HCQ for both African Americans and non-African Americans, would be lower than in those using patients methotrexate (MTX) as a control drug that was not postulated, at the time, to protect against CoV2.

Methods: A retrospective observational analysis utilizing IBM Watson Health Explorys data was performed. The Explorys database contains pooled de-identified clinical data. Explorys aggregates, standardizes and normalized clinical data from diverse electronic health records. Patient records are mapped into a systematized nomenclature of medicine- clinical terms (SNOMED-CT) hierarchy. To determine if chronic use of HCQ prevented CoV2 infection, individuals prescribed HCQ or MTX at least twice in the preceding 12 months were included. Incident disease was identified using the term SNOMED-CT diagnosis of “Disease caused by Coronoviridae” (CorV) to calculate infection rates. Cohorts were analyzed accordingly: African American (AA) or not AA, male sex, age >65, presence of obesity, cardiovascular disease (CVD), chronic kidney disease (CKD), and diabetes (DM). Rates of infection were calculated and compared to the reference populations using odds ratios (OR).

Results: At time of data collection in May 2020, Explorys included data from 68,569,460 patients. There were 14,490 total infections of CoV; Infection rates for the general population are shown in table 1, 34% were in AA patients. Table 2 shows infection rates in patients who used either HCQ or MTX . Table 3 shows a comparison of rates of infection in AA in those treated with HCQ or MTX. AA were more likely to be diagnosed with a CorV than nonAA overall in all the analyses: the odds ratio (OR) of having a corona virus ranged from 3.31-5.27 (all statistically significant). In both HCQ and MTX users, AA were more likely to be diagnosed with a CorV infection as compared with nonAA ranging from 4.43 to 7.37 in HCQ users and, 3.42-8.89 in MTX users. Comparing AA, there was a trend towards HCQ users being more likely than MTX users to be diagnosed with a CorV infection, but none of these comparisons were statistically significant. Death rates in each cohort were also calculated but too low to report (0 or < 10 each).

Conclusion: Of total CoV infections through May 2020, a higher proportion of those with a diagnosis of CorV were AA. When variables were analyzed separately, the ORs were elevated in AA with the following comorbidities: male sex, age >65, presence of obesity, CVD, CKD, DM. AA lupus and rheumatoid arthritis (RA) patients were more likely to be diagnosed with an infection compared to non-AA with lupus/RA. The data suggest that the disparities are exaggerated in rheumatology patients who contract CoV and that infection rates are not reduced in either in AA or non-AA on chronic HCQ. In contrast, rates of diagnosis of CoV were lower for patients on MTX.

Table 1. General Population	**Total COVID Infection Rate % (n)**	**African American COVID Infection Rate % (n)**	**Non-African COVID American Infection Rate % (n)**	**AA vs nonAA Odds Ratio (CI)**	***p*-value (AA v non-AA)**
General population	0.0211% (14490/68568630)	0.0696% (4950/7115350)	0.0155% (9540/61453280)	4.49 (4.33-4.64)	<.0001
Obese	0.0594% (7140/12031050)	0.1920% (3390/1763840)	0.0365% (3750/10267210)	5.27 (5.03-5.52)	<.0001
Male	0.02050% (6370/31074340)	0.0579% (1870/3228780)	0.0162% (4500/27845560)	3.58 (3.40-3.79)	<.001
>65	0.0273% (4150/15228380)	0.1093% (1220/1116240)	0.0208% (2930/14112140)	5.27 (4.93-5.63)	<.0001
CVD	0.0884% (2740/3097990)	0.2533% (790/311940)	0.0700% (1950/2786050)	3.625 (3.34-3.94)	<.0001
CKD	0.1630% (2550/1564790)	0.3852% (1040/269980)	0.1166% (1510/1294810)	3.31 (3.06-3.58)	<.0001
DM	0.0842% (4040/4795920)	0.2493% (1880/754170)	0.0534% (2160/4041750)	4.47 (4.39-4.97)	<.0001
SLE	0.0782% (150/191750)	0.2234% (80/35810)	0.0449% (70/155940)	4.99 (3.62-6.88)	<.0001
RA	0.0721% (370/513100)	0.1857% (110/59240)	0.0721% (260/453860)	3.25 (2.60-4.06)	<.0001

General population: CoV infection rate comparing African Americans and non-African Americans

	Hydroxychloroquine Users					Methotrexate Users				
Table 2. DMARD Users	Total COVID Infection Rate % (n)	African American COVID Infection Rate % (n)	Non-African American COVID Infection Rate % (n)	AA vs non-AA Odds Ratio (CI)	*p*-value (AA v non-AA)	Total COVID Infection Rate % (n)	African American COVID Infection Rate % (n)	Non-African American COVID Infection Rate % (n)	AA vs non-AA Odds Ratio (CI)	*p*-value (AA v non-AA)
General population	0.4854% (130/26780)	1.387% (90/6490)	0.1971% (40/20290)	7.12 (4.90-10.34)	<.0001	0.3085% (70/22690)	0.8427% (30/3560)	0.2091% (40/19130)	4.06 (2.52-6.52)	<.0001
Obese	0.6486% (110/16960)	1.649% (80/4850)	0.2478% (30/12110)	6.75 (4.43-10.28)	<.0001	0.3610% (50/13850)	1.160% (30/2590)	0.177% (20/11260)	6.59 (3.73-11.62)	<.0001
Male	0.5894% (30/5090)	1.8182% (20/1100)	0.2506% (10/3990)	7.37 (3.45-15.79)	<.0001	0.3053% (20/6550)	1.493% (10/670)	0.1701% (10/5880)	8.89 (3.69-21.45)	<.0001
>65	0.4883% (50/10240)	1.6216% (30/1850)	0.2384% (20/8390)	6.90 (3.91-12.17)	<.0001	0.3261% (30/9200)	0.8475% (10/1180)	0.2494% (20/8020)	3.42 (1.60-7.32)	0.0015
CVD	1.2924% (80/6190)	2.9070% (50/1720)	0.6711% (30/4470)	4.43 (2.81-6.99)	<.0001	<0.4683% * (<20/4270)	<1.5385% * (<10/650)	0.2762% (10/3620)	¥	¥
CKD	0.9975% (40/4010)	3.0303% (20/660)	0.5970% (20/3350)	5.20 (2.78-9.73)	<.0001	<0.7692%* (<20/2600)	<1.8182%* (<10/550)	<0.4878% * (<10/2050)	¥	¥
DM	1.6275% (90/5530)	3.1963% (70/2190)	0.5988% (20/3340)	5.48 (3.33-9.04)	<.0001	<0.5692% * (<30/5270)	1.6667%* (20/1200)	<0.2457%* (<10/4070)	¥	¥
SLE	<0.3480% * (30/8620)	<1.0381%* (30/2890)	<0.1160% * (<10/5730)	¥	¥	<1.3699% * (<20/1460)	<2.7778% * (<10/360)	<0.9091% * (<10/1100)	¥	¥
RA	0.3372% (40/11860)	0.9174% (20/2180)	0.2066% (20/9680)	4.47 (2.40-8.33)	<.0001	0.2867% (40/13950)	0.8733% (20/2290)	0.1715% (20/11660)	5.13 (2.76-9.55)	<.0001

*Values from Explorys database less than 10, infection rates calculated with value of 10.

¥ Data ranges too small to calculate

Comparing CoV infection rates in African Americans to non-African Americans; left panel hydroxychloroquine users; right panel methotrexate users

Table 3 Comparison African Americans	African American Hydroxychloroquine Users COVID Infection Rate % (n)	African American Methotrexate Users COVID Infection Rate % (n)	HCQ vs MTX Odds Ratio (CI)	*p*-value (AA v non-AA)
General population	1.387% (90/6490)	0.8427% (30/3560)	1.66 (1.09-2.51)	0.0163
Obese	1.649% (80/4850)	1.160% (30/2590)	1.43 (0.94-2.18)	0.94
Male	1.8182% (20/1100)	1.493% (10/670)	1.22 (0.57-2.63)	0.6033
>65	1.6216% (30/1850)	0.8475% (10/1180)	1.93 (0.939-3.96)	0.689
CVD	2.9070% (50/1720)	<1.5385% * (<10/650)	¥	¥
CKD	3.0303% (20/660)	1.8182% * (<10/550)	¥	¥
DM	3.1963% (70/2190)	1.6667% (20/1200)	1.95 (1.179-3.28)	0.0086
SLE	1.0381% (30/2890)	<2.7778% * (<10/360)	¥	¥
RA	0.9174% (20/2180)	0.8733% (20/2290)	1.05 (0.56-1.96)	0.88

*Values from Explorys database less than 10, infection rates calculated with value of 10.

¥ Data ranges too small to calculate

CoV infection rates in African American hydroxychloroquine users compared to methotrexate users

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Disclosure: M. Antonelli, None; **N. Singer**, None.

Abstract Number: 0443

Impact of the COVID-19 Pandemic on Racial and Ethnic Minority Groups Diagnosed with Rheumatic Diseases

Emily Sirotich[1], Teresa Semalulu[1], Kevin Kennedy[2], Salman Surangiwala[3], Maggie Larche[1], Jean Liew[4], Mitchell Levine[2], Graeme Reed[5], Naira Ikram[6], Carly Harrison[7], Richard Howard[8], Rashmi Sinha[9], Monique Gore-Massy[10] and Jonathan Hausmann[11], [1]McMaster University, Hamilton, ON, Canada, [2]McMaster University, Hamilton, Canada, [3]Queen's School of Medicine, Kingston, Canada, [4]University of Washington, Seattle, [5]Canadian Spondylitis Association, Vancouver, Canada, [6]Duke University, Durham, [7]Lupus Chat, NA, [8]Spondylitis Association of America, Van Nuys, CA, [9]SJIA Foundation, Cincinnati, [10]Lupus Foundation of America, Brooklyn, NY, [11]Boston Children's Hospital / Beth Israel Deaconess Medical Center, Cambridge, MA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Healthcare Disparities in Rheumatology
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: The COVID-19 pandemic has exacerbated structural and systematic barriers in access to healthcare for racial and ethnic minorities. The impact of these increased barriers on patients with rheumatic disease has not been studied. We describe the clinical characteristics and COVID-19 disease burden among racial and ethnic minority participants in an international survey of patients with rheumatic disease.

Methods: The COVID-19 Global Rheumatology Alliance (C19-GRA) Patient Experience Survey is an international, self-reported survey for adults and parents of children with rheumatic disease, with or without COVID-19 infection. The survey was distributed online by patient support organizations and social media platforms. Responses of participants living in Canada, the United States, and Europe were analyzed to compare outcomes between minority and non-minority groups. Descriptive statistics were used to describe patient characteristics and COVID-19 related outcomes.

Results: We report data on 6,581 respondents to the Patient Experience Survey. There were 5,703 (86.7%) respondents who identified as White, and 878 (13.3%) belonged to all other racial or ethnic groups (Table 1). Respondents from ethnic minority groups were mostly female (92.3%) with a mean age of 44.0 (SD 12.4). The most common rheumatic diseases include systemic lupus erythematosus (47.8%) and rheumatoid arthritis (37.2%).

A total of 455 (6.9%) participants reported a diagnosis of COVID-19; of these, 66 (14.5%) self-identified as a racial or ethnic minority including 12 (2.6%) who were Black. Among ethnic minorities, 24 patients diagnosed themselves based on symptoms and 42 were diagnosed by a physician according to symptoms or a lab result. Of patients who were hospitalized with COVID-19, 33 (73.3%) were White and 12 (26.7%) belonged to other ethnic groups.

Conclusion: This international survey reports data related to the impact of COVID-19 on racial and ethnic minorities with rheumatic disease. There were differences in high risk comorbidities, yet no difference in incidence of COVID-19 and severity of disease among various racial and ethnic groups compared to White participants. Racial and ethnic minorities were underrepresented in our survey, likely a consequence of systemic barriers that prohibit their engagement within the healthcare community.This reinforces the importance of collecting race-related data, particularly where there are concerns of inequities influencing health outcomes, and the need to implement targeted recruitment strategies to enhance representation of minority groups in research.

	Black (n=146)	Asian (n = 94)	Latin American (n=154)	Indigenous/ Native American (n=19)	Other Ethnic Groups (n=465)	White (n=5703)
Gender						
Female	141 (96.6)	78 (83)	148 (96.1)	17 (89.5)	426 (91.6)	5100 (89.4)
Male	5 (3.4)	16 (17)	6 (3.9)	2 (10.5)	32 (6.9)	592 (10.4)
Non-binary	0	0	0	0	2 (0.4)	4 (0.1)
Prefer not to answer	0	0	0	0	5 (1.1)	7 (0.1)
Age						
18-35	31 (21.2)	36 (38.3)	49 (31.8)	2 (10.5)	115 (24.7)	976 (17.1)
36-50	60 (41.1)	40 (42.6)	78 (50.6)	11 (57.9)	169 (36.3)	2019 (35.4)
50-65	47 (32.2)	16 (17)	25 (16.2)	6 (31.6)	145 (31.2)	2080 (36.5)
65+	8 (5.5)	2 (2.1)	2 (1.3)	0	36 (7.7)	628 (11)
Region						
United States	126 (86.3)	38 (40.4)	122 (79.2)	14 (73.7)	277 (59.6)	2643 (46.3)
Canada	5 (3.4)	24 (25.5)	11 (7.1)	5 (26.3)	58 (12.5)	533 (9.3)
Europe	15 (10.3)	32 (34)	21 (13.6)	0	130 (28)	2527 (44.3)
Medications						
Biologic DMARDs	35 (24)	27 (28.7)	44 (28.6)	6 (31.6)	146 (31.4)	2037 (35.7)
csDMARDs	128 (87.7)	71 (75.5)	112 (72.7)	12 (63.2)	336 (72.3)	3810 (66.8)
Steroids	71 (48.6)	27 (28.7)	60 (39)	9 (47.4)	153 (32.9)	1802 (31.6)
tsDMARDs	2 (1.4)	0	5 (3.2)	1 (5.3)	15 (3.2)	226 (4)
Other	3 (2.1)	3 (3.2)	3 (1.9)	0	13 (2.8)	109 (1.9)
Rheumatic disease diagnosis						
ANCA-associated vasculitis	1 (0.7)	1 (1.1)	0	0	9 (1.9)	255 (4.5)
Ankylosing spondylitis	1 (0.7)	5 (5.3)	6 (3.9)	3 (15.8)	37 (8)	636 (11.2)
Anti-phospholipid antibody syndrome	3 (2.1)	1 (1.1)	8 (5.2)	0	28 (6)	304 (5.3)
Autoinflammatory disease	1 (0.7)	2 (2.1)	2 (1.3)	0	11 (2.4)	120 (2.1)
Behcet's syndrome	3 (2.1)	1 (1.1)	0	0	6 (1.3)	93 (1.6)
Chronic recurrent multifocal osteomyelitis	0	0	0	0	1 (0.2)	9 (0.2)
Crystalline arthritis	4 (2.7)	1 (1.1)	1 (0.6)	0	4 (0.9)	57 (1)
Dermatomyositis	13 (8.9)	5 (5.3)	11 (7.1)	2 (10.5)	35 (7.5)	295 (5.2)
Eye inflammation	3 (2.1)	3 (3.2)	2 (1.3)	0	26 (5.6)	238 (4.2)
Giant cell arteritis	0	0	1 (0.6)	0	3 (0.6)	49 (0.9)
IgG4-related disease	0	1 (1.1)	0	0	0	14 (0.2)
Juvenile idiopathic arthritis	0	2 (2.1)	0	0	10 (2.2)	110 (1.9)
Mixed connective tissue disease	16 (11)	1 (1.1)	4 (2.6)	2 (10.5)	41 (8.8)	281 (4.9)
Other inflammatory arthritis	16 (11)	3 (3.2)	4 (2.6)	2 (10.5)	39 (8.4)	270 (4.7)
Other spondyloarthritis	0	0	0	0	7 (1.5)	113 (2)
Other Vasculitis	0	1 (1.1)	1 (0.6)	0	4 (0.9)	63 (1.1)
Polymyalgia rheumatica	0	0	1 (0.6)	0	2 (0.4)	133 (2.3)
Psoriatic arthritis	4 (2.7)	3 (3.2)	4 (2.6)	0	26 (5.6)	509 (8.9)
Rheumatoid arthritis	53 (36.3)	29 (30.9)	58 (37.7)	11 (57.9)	176 (37.8)	2182 (38.3)
Sarcoidosis	1 (0.7)	0	0	0	9 (1.9)	38 (0.7)
Sjogren's syndrome	22 (15.1)	10 (10.6)	21 (13.6)	4 (21.1)	91 (19.6)	807 (14.2)
Still's Disease	0	3 (3.2)	1 (0.6)	0	6 (1.3)	63 (1.1)
Systemic lupus erythematosus	108 (74.0)	49 (52.1)	121 (78.6)	7 (36.8)	276 (59.4)	2033 (35.6)
Systemic sclerosis	2 (1.4)	1 (1.1)	4 (2.6)	0	11 (2.4)	99 (1.7)
Undifferentiated connective tissue disease	4 (2.7)	3 (3.2)	0	1 (5.3)	13 (2.8)	173 (3)
Comorbidities						
Cancer	1 (0.7)	0	1 (0.6)	1 (5.3)	8 (1.7)	88 (1.5)
Chronic kidney disease	20 (13.7)	7 (7.4)	10 (6.5)	0	36 (7.7)	236 (4.1)
Dermatological	3 (2.1)	0	2 (1.3)	0	13 (2.8)	140 (2.5)
Diabetes	13 (8.9)	6 (6.4)	5 (3.2)	0	30 (6.5)	280 (4.9)
Gastrointestinal	5 (3.4)	7 (7.4)	10 (6.5)	2 (10.5)	39 (8.4)	452 (7.9)
Heart Disease	10 (6.8)	0	6 (3.9)	1 (5.3)	19 (4.1)	242 (4.2)
High blood pressure	62 (42.5)	12 (12.8)	29 (18.8)	4 (21.1)	130 (28)	1379 (24.2)
Immune	16 (11)	7 (7.4)	30 (19.5)	6 (31.6)	58 (12.5)	646 (11.3)
Metabolic	13 (8.9)	1 (1.1)	12 (7.8)	1 (5.3)	49 (10.5)	444 (7.8)
Neurological/ Neuromuscular	7 (4.8)	0	3 (1.9)	0	23 (4.9)	148 (2.6)
Pain Syndromes	52 (35.6)	8 (8.5)	44 (28.6)	4 (21.1)	138 (29.7)	1339 (23.5)
Psychiatric	7 (4.8)	4 (4.3)	7 (4.5)	3 (15.8)	30 (6.5)	269 (4.7)
Pulmonary	53 (36.3)	12 (12.8)	31 (20.1)	7 (36.8)	130 (28)	1381 (24.2)

Table 1. Demographic and clinical characteristics of racial and ethnic minorities from Canada, United States and Europe in the C19-GRA Patient Experience Survey (n=6581). Participants may have more than one condition and take more than one type of medication. csDMARD medications included: antimalarials (hydroxychloroquine, chloroquine), azathioprine, cyclophosphamide, cyclosporine, leflunomide, methotrexate, mycophenolate mofetil/mycophenolic acid, sulfasalazine, tacrolimus. bDMARD included: abatacept, belimumab, CD-20 inhibitors, IL-1 inhibitors, IL-6 inhibitors, IL-12/IL-23 inhibitors, IL-17 inhibitors, and anti-TNF. tsDMARD included: Janus Kinase inhibitors. Other included: IVIG, apremilast, thalidomide bDMARD, biologic DMARD; csDMARD, conventional synthetic DMARD; tsDMARD targeted synthetic DMARD, DMARD, disease-modifying antirheumatic drug.

Disclosure: E. Sirotich, Canadian Arthritis Patient Alliance, 9; **T. Semalulu**, None; **K. Kennedy**, Lyceum Health, 5; **S. Surangiwala**, None; **M. Larche**, AbbVie, 5, Amgen, 5, Boehringer-Ingelheim, 5, BMS, 5, Celgene, 5, Janssen, 5, Mallinckrodt, 5, Novartis, 5, Pfizer, 5, Roche, 5, Sandoz, 5, UCB, 5; **J. Liew**, None; **M. Levine**, None; **G. Reed**, None; **N. Ikram**, None; **C. Harrison**, None; **R. Howard**, Novartis, 1, 5, AbbVie, 1, Amgen, 1, Bristol-Myers Squibb, 1, GSK, 1, Johnson & Johnson, 1, Lilly, 1, Merck, 1, Pfizer, 1, Teva, 1; **R. Sinha**, None; **M. Gore-Massy**, Aurinia, 5; **J. Hausmann**, Novartis, 5.

Abstract Number: 0444

Chronological Order of Decrease of Synovitis, Osteitis and Tenosynovitis in Early Arthritis Patients Receiving First DMARD-treatment

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Imaging of Rheumatic Diseases
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Advanced imaging modalities have shown that not only joints but also bones and tendon sheaths can be inflamed at diagnosis of rheumatoid arthritis. We aimed to better understand the time order in which the inflamed tissues respond to DMARD-treatment and whether this differs between ACPA-subgroups.

Methods: 216 consecutive patients presenting with undifferentiated or rheumatoid arthritis, who received DMARD-treatment, were studied. 1.5T contrast-enhanced hand and foot MRIs were performed before treatment and after 4, 12 and 24-months. Cross-lagged models evaluated the influence of two time-patterns: a simultaneous pattern ("change in one inflammatory feature associated with change in another feature") and a subsequent pattern ("change in one inflammatory feature preceded change in another feature"). ACPA-stratification was performed.

Results: All pairs of inflammatory features decreased simultaneously in all time-intervals (0–4/4–12/12–24m; $p< 0.05$). Moreover, time orders were identified: synovitis decrease preceded tenosynovitis decrease (0-4m- >4-12m; $p=0.02$ & 4-12m- >12-24m; $p=0.03$). Similar results were obtained in both ACPA-subgroups. Additionally, in ACPA-positive but not ACPA-negative patients, synovitis decrease preceded osteitis decrease (4-12m- >12-24m; $p=0.002$).

Conclusion: This study increased the understanding of the response to treatment on tissue level. Additional to simultaneous decrease of inflammation, synovitis decrease preceded tenosynovitis decrease. Differences in time order of inflammation decrease between ACPA-subgroups suggest differences in underlying inflammatory pathways.

Disclosure: X. Matthijssen, None; **E. Niemantsverdriet**, None; **S. le Cessie**, None; **A. van der Helm - van Mil**, None.

Abstract Number: 0445

Dual-Energy CT in Gout Patients: Do All Color-Coded Lesions Actually Represent Monosodium Urate Crystals?

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Imaging of Rheumatic Diseases

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: Dual-Energy CT (DECT) can acknowledge differences in tissue compositions and can color-code tissues with specific features including monosodium urate (MSU) crystals. However, when evaluating gout patients DECT frequently color-codes material not truly representing MSU crystals and this might lead to misinterpretations if the reader is not aware of these potential pitfalls. The variations in properties of color-coded DECT lesions in gout patients have not yet been systematically investigated.

The objective was to evaluate the properties and locations of color-coded DECT lesions in gout patients.

Methods: DECT of the hands, knees and feet were performed in patients with suspected gout using factory default gout-settings. Location-relevant colour-coded lesions were registered. For each lesion properties [mean density (mean of Hounsfield Units (HU) at 80kV and Sn150kV), mean DECT ratio and size] and location were determined.

Subgroup analysis was performed post-hoc evaluating differences in locations of lesions when divided into definite MSU deposits and possibly other lesions. Division were made according to lesion properties: 1) *Size*—to separate small volume artefacts (*possible image noise artefacts*), 2) *DECT ratios*—to separate calcium-containing material

Figure 1: Properties of color-coded DECT lesions in gout and non-gout patients

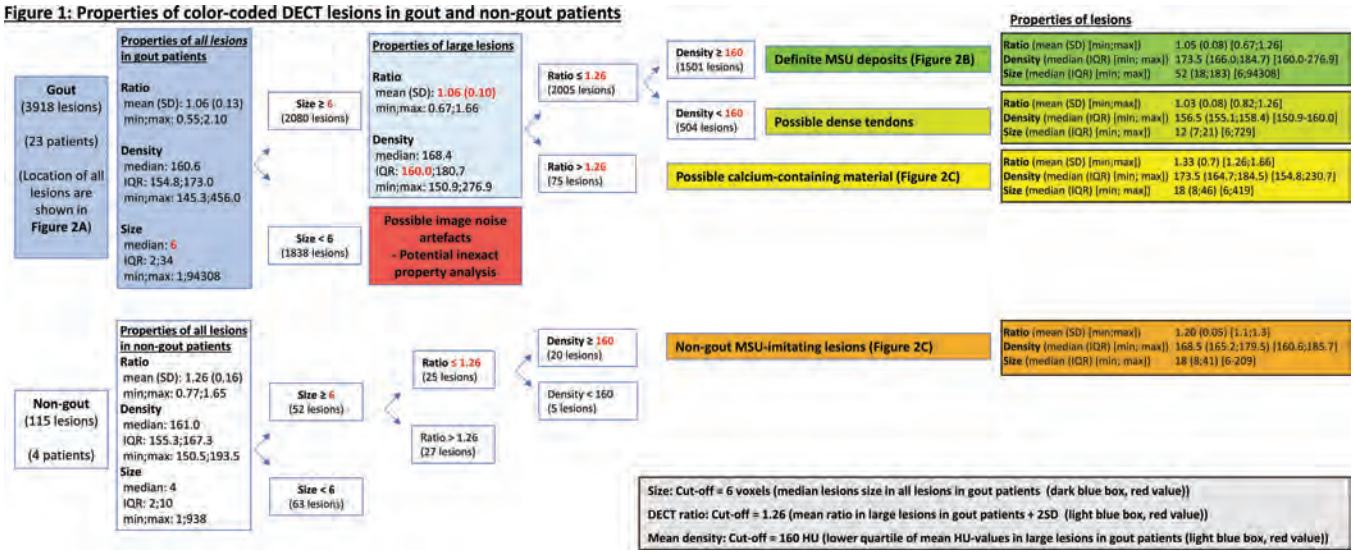
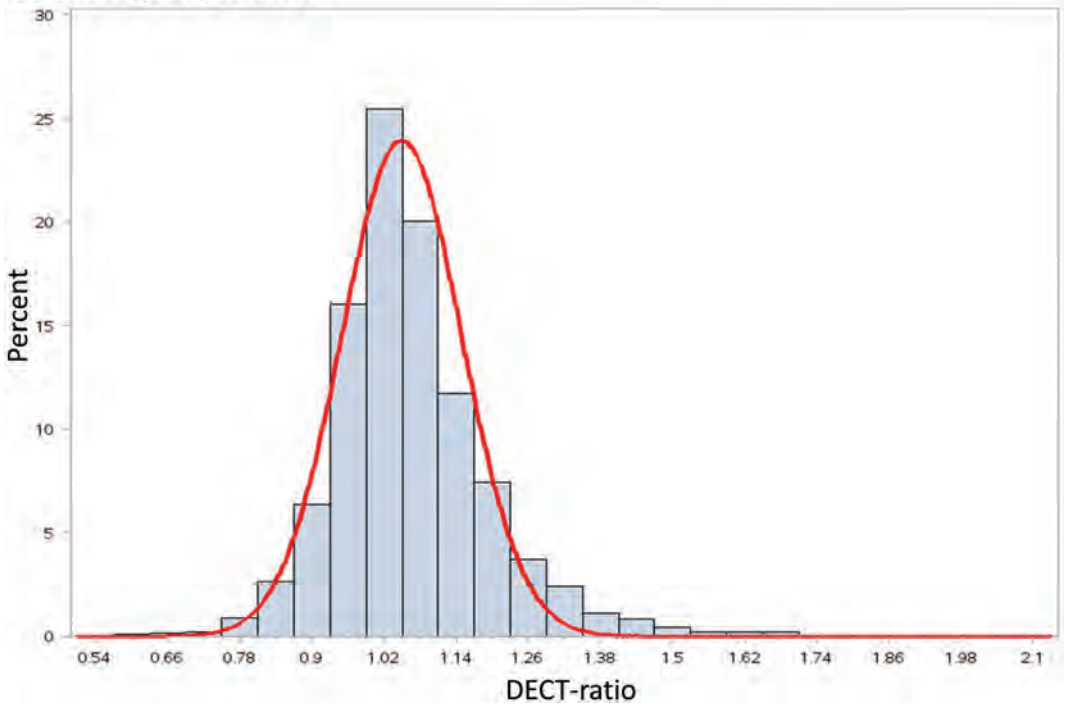


Figure 2: Distributions of DECT ratios. Evaluation of large color-coded DECT lesions in gout patients.



characterised by high DECT ratio (*possible calcium-containing material*). 3) *Density*—to separate dense tendons characterised by low DECT ratio and low HU values (*possible dense tendons*). Lesion fulfilling all MSU characteristics (large volume, low DECT ratio, high density) were labelled *definite MSU deposits*. Finally, for non-gout patients, properties of *non-gout MSU-imitating lesions* (properties as *definite MSU deposits*) were analysed.

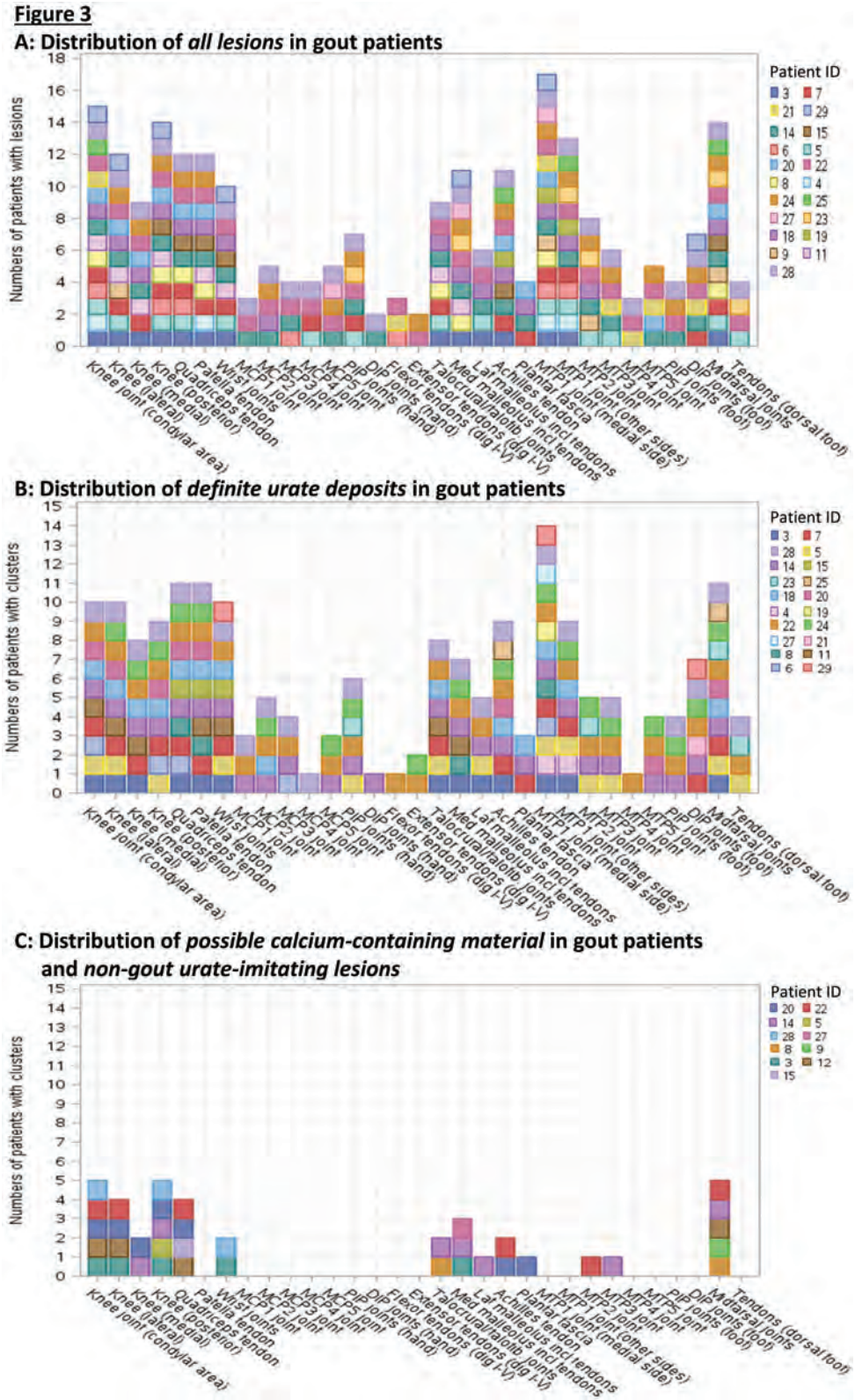
Results: In total, 3918 lesions (*all lesions*) were registered in 23 gout patients with median density of 160.6HU and median size of 6 voxels (Figure 1). DECT ratios of large lesions showed an approximated normal distribution, but with a right heavy tail consistent with presence of smaller amounts of calcium-containing lesions (Figure 2). The most common locations of *all lesions* were MTP1, knee and midtarsal joints along with quadriceps and patella tendons (Figure 3A).

Subgroup analyses showed that *definite MSU deposits* had a similar distribution pattern as *all lesion* with the same five most common locations (Figure 3B). This was also the case for *possible dense tendon* (data not shown), indicating that these lesions primarily consisted of true MSU deposits. In contrast, *possible calcium-containing material* and *non-gout MSU-imitating lesions* had distinctly different properties (DECT ratios 1.33 and 1.20, respectively) (Figure 1) and furthermore showed different distribution pattern as they were primarily found in some larger joints (knee, midtarsal and talocrural) and tendons (Achilles and quadriceps), whereas non were found in either MTP1 joints or patella tendons (figure 3C).

Conclusion: Color-coded DECT lesions in gout patients showed heterogenicity in properties and locations. MTP1 joints and patella tendons exclusively showed definite MSU deposits. Hence, a sole focus on these regions in the evaluation of gout patients may improve the specificity of DECT scans.

DECT, dual energy CT ; HU, Hounsfields Units ; ratios, DECT ratios (HU a 80kV / HU at sn150kV) ; density, (HU at 80kV+HU at sn150kV) / 2 ; size, numbers of pixels; SD, standard deviation ; IQR, interquartile range ; SD standard deviation.

Figure 3



The distributions of DECT ratios have been overlaid with a normal distribution curve with a mean at the local maxima at a DECT ratio of 1.06 and a standard deviation estimated from points below this mean to be 0.10. Notice that the right tail on the DECT ratios are heavy with more lesions having a high DECT ratio than expected by a Gaussian

distribution in agreement with a mixture of monosodium-urate deposits and calcium-containing material. DECT, Dual-Energy computed tomography; DECT ratio, HU at 80kV / HU at 150kV (with tin filter).

MCP, metacarpophalangeal joints; PIP, proximal interphalangeal joints; DIP, distal interphalangeal joints; MTP, metatarsophalangeal joints.

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Abstract Number: 0446

Novel Ultrasound Image Acquisition Protocol and Scoring System for the Pediatric Ankle

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Imaging of Rheumatic Diseases
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: The clinical decision-making process in pediatric arthritis lacks an objective, reliable bedside imaging tool. Although increasingly used for children, there is a need for reliable ultrasound (US) scanning protocols and scoring systems to provide objective assessments of various inflammatory lesions. The aim of this study was to develop a scanning protocol and assess the reliability of B-Mode and Doppler scoring systems for the pediatric ankle.

Methods: As part of the Childhood Arthritis and Rheumatology Research Alliance (CARRA) US group, 19 pediatric rheumatologists developed through a comprehensive literature review a set of standard views to assess inflammatory lesions of the synovial recesses as well as tendons of the pediatric ankle. The views included in the final acquisition protocol reached at least 80% agreement following a nominal group technique. Subsequently, a B-mode and Doppler scoring system was developed through a comprehensive literature review, then a consensus process. Three rounds of scoring of still-images were followed by one practical exercise. Agreement between raters determined using two-way single score intraclass correlation coefficients (ICC).

Results: Following published standardized guidelines, we examined the available evidence for using sonographic views to assess presence of synovitis in the tibiotalar (TTJ), subtalar (STJ) and talonavicular joints (TNJ), as well as tenosynovitis of the anterior, medial and lateral tendon compartments of the ankle. We identified 37 possible views to assess the presence of ankle synovitis and tenosynovitis in children. We further considered different positions of the ankle (extension, neutral and flexion). Following a practical exercise, a total of 9 views were chosen for each B-mode and Doppler in a nominal group technique (Table 1). The scanning protocol was feasible with a scanning time of 12-15 minutes. Scoring protocols for each structure based upon anatomic variability among the joints and tendons of interest were developed. An initial scoring exercise included 124 images. There was good to excellent agreement for B-mode on the anterior TTJ: medial and lateral views ICC 0.69 (CI 0.61-0.75) and midline view ICC 0.75 (CI 0.71-0.79). The ICC for the TNJ was fair at 0.51 (CI 0.40-0.61). Views assessing the medial and lateral aspects of the STJ had good to fair reliability 0.67 (CI 0.57-0.75) and 0.51 (CI 0.43-0.59) respectively. ICC for tendon images was 0.49 (CI 0.37-0.59). The observations from this scoring exercise are elucidating which modifications are necessary to reach good to excellent reliability of the scoring systems. Additional scoring exercises and consensus rounds will be necessary to refine the individual scores.

Conclusion: A novel pediatric ankle US scanning protocol and scoring system for the assessment of arthritis were successfully developed. Preliminary results from practical exercises indicate overall good reliability but also illustrate the challenges in certain views especially the STJ, TNJ and tendons. With further refinement and validation, this scoring system may serve as an assessment tool and outcome measure for both clinical and research applications

BM: B-mode, PD: Power Doppler, TTJ: Tibiotalar Joint, STJ: subtalar joint. Note: It is recommended to slide the probe medially to laterally and capture the area of maximal distention.

Table 1. Ankle Scanning Protocol

	View (BM/PD)		View Description
	BM	PD	
Anterior compartment: ankle in a neutral position: knee flexed at 90˚, foot flat on table.			
Midline TTJ	1a	1b	Probe is placed in line with the 3rd toe. Move the probe laterally and medially to obtain the area of maximal pathology while ensuring visualization of the joint recess, talar dome, and talar neck.
Antero-Medial TTJ	2a	2b	Probe just anterior to the medial malleolus.
Antero-Lateral TTJ	3a	3b	Probe just anterior to the lateral malleolus.
Talonavicular	4a	4b	Start midline. Obtain a longitudinal view with the proximal end of the probe on the talus and distal end of the probe over the navicular bone.
Anterior Tendon Compartment	5a	5b	Place the probe in a transverse position over the top of the talar dome visualizing the bone cortex and the cartilage covering it. Move the probe proximally and distally to find the area of maximal distension of each abnormal tendon sheath and obtain an image representing abnormality. If tendons are normal, obtain an image at the level of the talar dome.
Medial compartment: hold the leg straight with slight external rotation. For the scanning of the anterior STJ hold foot in slight eversion.			
Medial Flexor Tendons	6a	6b	Place the proximal probe tip on medial malleolus and distal end perpendicular to Achilles to visualize PTT, FDT, FHL (*heel-toe distal end of probe to observe the FHL well).* Sweep distally along the tendons to find the area of maximal distension of each abnormal tendon sheath and obtain an image. If tendons are normal, obtain an image at the level of the sustentaculum tali
Medial aspect of the Anterior STJ	7a	7b	Probe will be positioned with proximal end anterior to the medial malleolus and distal end pointing towards the heel of the foot with the sustentaculum tali in view. Move the probe just distal to the sustentaculum tali where the anterior medial STJ is visible and obtain images at the site of maximal distention.
Lateral compartment: hold the leg straight with slight internal rotation. For the scanning of the lateral STJ hold foot in slight inversion			
Lateral Tendon Compartment	8a	8b	Place the proximal end of the probe on the lateral malleolus and distal end perpendicular to the Achilles to visualize PB/PL tendons. Sweep distally along the tendons to find the area of maximal distension of each abnormal tendon sheath and obtain an image. If tendons are normal, obtain an image at the level of the lateral view of the posterior STJ.
Lateral view of the Posterior STJ	9a	9b	Place the probe perpendicular to the sole over the sinus tarsi. Slide the probe posteriorly following the lateral STJ. Obtain image at the level of maximal distention. If no pathology obtain image just anterior to the lateral malleoli.

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Abstract Number: 0447

Magnetic Resonance Imaging Characteristics in Patients with Spondyloarthritis and Clinical Diagnosis of Heel Enthesitis: Screening Data from a Phase 3 Trial

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Imaging of Rheumatic Diseases

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: Inflammation and pain at entheseal sites are the key clinical signs in patients (pts) with axial spondyloarthritis (axSpA) and psoriatic arthritis (PsA).[1] Magnetic resonance imaging (MRI) has been shown to be a sensitive tool to diagnose enthesitis in both bone and soft tissues, especially in cases of potential disconnect be-

Table 1. MRI Parameter: Qualitative

n (%)	PsA N = 128	axSpA N = 76	Total N = 204
Tendinitis	51 (39.8)	43 (56.6)	94 (46.1)
Location Achilles tendon	45 (35.2)	34 (44.7)	79 (38.7)
Location Plantar aponeurosis	14 (10.9)	19 (25.0)	33 (16.2)
Bone marrow edema	46 (35.9)	34 (44.7)	80 (39.2)
Location Achilles tendon	37 (28.9)	28 (36.8)	65 (31.9)
Location Plantar aponeurosis	14 (10.9)	13 (17.1)	27 (13.2)
Bursitis	50 (39.1)	28 (36.8)	78 (38.2)
Location Achilles tendon	49 (38.3)	28 (36.8)	77 (37.7)
Location Plantar aponeurosis	1 (0.8)	1 (1.3)	2 (1.0)
Bone erosion	39 (30.5)	22 (28.9)	61 (29.9)
Location Achilles tendon	36 (28.1)	19 (25.0)	55 (27.0)
Location Plantar aponeurosis	9 (7.0)	6 (7.9)	15 (7.4)
Location Other	0	1 (1.3)	1 (0.5)
Periarticular inflammation	23 (18.0)	18 (23.7)	41 (20.1)

N, total number of pts in a group with MRI parameter present;
Patients with tendinitis/bone marrow edema/bursitis/bone erosion at multiple locations will be counted only once in the respective overall category.

Table 2. MRI Parameter: Quantitative

n (%)		PsA N = 128	axSpA N = 76	Total N = 204
Bone marrow edema	0 = absent	82 (64.1)	42 (55.3)	124 (60.8)
	1 = 1-33%	39 (30.5)	22 (28.9)	61 (29.9)
	2 = 34-66%	5 (3.9)	8 (10.5)	13 (6.4)
	3 ≥ 67%	2 (1.6)	4 (5.3)	6 (2.9)
Bone erosion	0 = absent	89 (69.5)	54 (71.1)	143 (70.1)
	1 = 1-10%	31 (24.2)	18 (23.7)	49 (24.0)
	2 = 11-20%	7 (5.5)	3 (3.9)	10 (4.9)
	3 = 21-30%	1 (0.8)	0	1 (0.5)
	4 = 31-40%	0	1 (1.3)	1 (0.5)
N, total number of pts in a group with MRI parameter present				

Table 3. MRI Parameter: Scores

Mean score (SD)	PsA N = 128	axSpA N = 76	Total N = 204
Bone edema	0.4 (0.65)	0.7 (0.87)	0.5 (0.75)
Bone erosion	0.4 (0.63)	0.4 (0.69)	0.4 (0.65)
Composite Score (PsAMRIS)	1.0 (1.09)	1.3 (1.34)	1.1 (1.20)
Bone edema score was based on 0 = absent, 1 = 1-33%, 2 = 34-66%, 3 = >67% of bone edematous; Bone erosion score was based on 0 = absent, 1 = 1-10%, 2 = 11-20%, …, 10 = 90-100%; and composite score was a total of Periarticular inflammation 0 = absent, 1 = present + bone edema score + bone erosion score N, total number of pts in a group with MRI parameter present			

tween pain and objective signs of inflammation at entheseal sites.[2] ACHILLES (NCT02771210) is the largest prospective randomized controlled trial so far, investigating both clinical and imaging endpoints, with blinded and centrally read MRI data on heel enthesitis in pts with SpA.[3] Here, we report MRI characteristics at screening in pts clinically diagnosed with heel enthesitis (N=204) from the ACHILLES trial.

Methods: ACHILLES included pts (≥18 years) with active PsA (CASPAR criteria and ≥1 tender joint count and swollen joint count) or axSpA (ASAS axSpA criteria with objective signs of inflammation at screening and/or hsCRP >5mg/L and total BASDAI ≥4), with clinical (presence of pain and tenderness) and STIR-MRI positive heel enthesitis, refractory to standard treatment (either NSAIDs or TNF-inhibitors). MRI-positive heel enthesitis was confirmed for all pts by local investigators and was defined as tendinitis and/or bone marrow edema (BME) in the insertional area of the Achilles' tendon and/or the plantar aponeurosis. After randomization, all MRI were re-evaluated by two blinded central readers in a consensus read fashion for a priori defined qualitative and quantitative MRI parameters (based on PsAMRIS)[4].

Results: According to central reading, 114/204 (55.9%) pts presented with MRI-positive heel enthesitis. The most frequently observed MRI feature was tendinitis, affecting 46.1% (94/204) of the population (**Table 1**). A total of 61 pts (29.9%) presented with BME affecting 1-33% of the heel (PsAMRIS category 1); out of these 40/61 (65.6%) had an edema length of ≤0.5 cm and 21/61 (34.4%) had an edema length of >0.5 cm. There was no bone erosion affecting more than 40% of the calcaneus; therefore, no erosions reported in the PsAMRIS categories 5 to 10 (**Table 2**). AxSpA pts presented with more severe edema compared to PsA pts (more pts having edema in category 2 or 3), resulting in a higher bone marrow edema score based on PsAMRIS categories and a higher composite score (**Table 3**).

Conclusion: Despite clinical assessment of enthesitis, only 56% of the ACHILLES patients presented with MRI-positive heel enthesitis according to central reading. These results indicate discrepancies in MRI evaluations between

local and trained central readers. Furthermore, clinically assessed enthesitis might not necessarily correlate with imaging features of heel inflammation or chronic changes.

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Abstract Number: 0448

Disease-related factors associated to atherosclerotic disease in axial spondyloarthritis. A mutlicenter study with 806 patients.

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SESSION INFORMATION
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Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Cardiovascular (CV) mortality and morbidity is increased in ankylosing spondylitits (AS) due to a process of accelerated atherosclerosis. The disease-related factors involved in this process are not yet well known. The aim of this study is to identify factors associated with subclinical atherosclerosis in the largest series of axial spondyloarthritis (axSpA) studied so far, and to analyze possible differences in this regard between AS and non-radiographic axial spondyloarthritis (nr-axSpA).

Methods: This is a transversal observational study from the AtheSpAin cohort, a Spanish multicenter cohort to study atherosclerosis in axSpA. We included patients older than 18 years old diagnosed with axSpA according to ASAS criteria. Carotid ultrasound (US) examination was done in all patients, included the measurement of carotid intima-media wall thickness (cIMT) in the common carotid artery and the detection of plaques in the extracranial carotid tree bilaterally, according to the Mannhein consensus.

Results: 639 AS patients and 167 nr-axSpA were recruited. Baseline characteristics and clinical features are shown in **table 1**

Table 2 shows the association between three surrogate markers for subclinical atherosclerosis (unilateral and bilateral carotid plaques and cIMT) with disease features, analyzed in an unadjusted model. As expected, cardiovascular risk factors (CRF) were associated with the presence of carotid plaques and cIMT.

Concerning disease related data, a very high disease activity according to ASDAS-CPR was related with both unilateral and bilateral plaques as well as an increased cIMT. BASDAI was associated only with cIMT. The three surrogate markers for atherosclerosis were also associated with CPR and ESR at time of diagnosis. The severity of the disease measured by BASMI, BASFI or hip involvement and the radiographic damage were strongly associated with subclinical atherosclerosis. History of synovitis and extraarticular manifestations as well as the use of prednisone and DMARDs were found to be related with IMT.

After adjustment for age, sex and CRF, associations with surrogate markers for atherosclerosis remained statistically significant for BASFI (unilateral plaques: OR 1.13, p=0.01), BASMI (bilateral plaques: OR 1.22, p=0.01), use of prednisone and DMARDs (bilateral plaques: OR 2.42, p=0.03; OR 2.10, p=0.02 respectively), CRP and ESR at time of diagnosis (IMT: beta coefficient 0,31, p=0,047 and 0.77, p=0,002 respectively), and inflammatory bowel disease (bilateral plaques: OR 3.48, p=0.01).

Differences, between AS and nr-axSpA, in the effect of CV riks factors on cIMT/carotid plaque were assessed including interaction factors in the regression models. In this sense, no differences were found between both subtypes of patients in the effects of CV risks factors over CIMT/carotid plaque.

Conclusion: Apart from CRF, the atherosclerotic disease in axSpA is associated with disease-related factors such as the inflammatory response, the severity of the disease or extraarticular manifestations, without differences between AS and nr-axSpA.

TABLE 1. Association between unilateral/bilateral carotid plaques and IMT with the main clinical, analytical (unadjusted model) and radiological features in axSpA patients.

	Carotid plaque		IMT, microns
	OR (95% CI), p. Adjusted model		beta coefficient (95%CI), p. Adjusted model
	Unilateral plaque axSpA	Bilateral plaque axSpA	
Age (years)	**1.10 (1.07-1.13), 0.000**	**1.15 (1.12-1.18), 0.000**	**7 (6-8), 0.000**
Male	**1.78 (1.14-2.77), 0.011**	**1.75 (1.11-2.74), 0.015**	**53 (32-74), 0.000**
Cardiovascular data			
History of CV risk factors			
Current smoker	1.33 (0.88-2.00), 0.18	**1.60 (1.06-2.41), 0.025**	0 (-21-22), 0.97
Have ever smoked	1.40 (0.94-2.09), 0.096	**1.86 (1.23-2.81), 0.003**	**32 (12-54), 0.002**
Obesity	1.51 (0.97-2.34), 0.066	1.23 (0.77-1.94), 0.39	**52 (28-76), 0.000**
Dyslipemia	**1.90 (1.27-2.83), 0.002**	**3.37 (2.23-5.10), 0.000**	**82 (62-103), 0.000**
Hypertension	**2.11 (1.39-3.20), 0.000**	**3.15 (2.07-4.78), 0.000**	**111 (90-133), 0.000**
Diabetes Mellitus	2.11 (1.00-4.44), 0.050	**4.46 (2.35-8.49), 0.000**	**111 (72-151), 0.000**
Chronic Kidney Disease	2.28 (0.63-8.22), 0.21	**3.66 (1.16-11.55), 0.027**	**96 (27-165), 0.007**
Lipids			
Total cholesterol	1.00 (1.00-1.01), 0.39	1.00 (1.00-1.01), 0.29	2 (0-5), 0.086
HDL-cholesterol	0.99 (0.98-1.01), 0.26	0.99 (0.98-1.01), 0.26	**-9 (-2- -0), 0.002**
LDL-cholesterol	1.00 (1.00-1.01), 0.24	1.00 (1.00-1.01), 0.65	**5 (2-8), 0.002**
Atherogenic index ≥4	**1.67 (1.11-2.50), 0.013**	1.08 (0.71-1.64), 0.73	**31 (10-51), 0.004**
Triglycerides	1.00 (1.00-1.00), 0.45	**1.00 (1.00-1.01), 0.036**	**3 (1-4), 0.000**
Statins	**2.57 (1.53-4.30), 0.000**	**3.96 (2.36-6.64), 0.000**	**90 (61-119), 0.000**
Blood pressure, mm Hg			
Systolic	**1.04 (1.02-1.05), 0.000**	**1.04 (1.03-1.05), 0.000**	**3 (2-3), 0.000**
Diastolic	**1.03 (1.01-1.04), 0.009**	0.99 (0.97-1.01), 0.23	**2 (1-3), 0.000**
Carotid IMT (each 0.1 mm)	**1.84 (1.39-2.43), <0.000**	**2.19 (1.85-2.59), 0.000**	
Disease related data at time of study			
Mean disease duration, years			
Since first symptoms	**1.04 (1.03-1.06), 0.000**	**1.07 (1.05-1.09), 0.000**	**4 (3-5), 0.000**
Since diagnosis	**1.04 (1.02-1.05), 0.000**	**1.05 (1.03-1.07), 0.000**	**4 (3-5), 0.000**
ASDAS	1.21 (0.98-1.49), 0.076	**1.35 (1.09-1.68), 0.007**	
Inactive disease			
Low disease activity	1.07 (0.57-2.00), 0.84	1.35 (0.65-2.79), 0.42	**40 (9-72), 0.012**
High disease activity	1.29 (0.73-2.26), 0.38	1.77 (0.92-3.41), 0.087	**42 (13-70), 0.004**
Very high disease activity (>3.5)	**2.20 (1.00-4.43), 0.050**	**3.43 (1.54-7.65), 0.003**	**72 (33-112), 0.000**
BASDAI	1.07 (0.98-1.17), 0.16	1.09 (0.99-1.19), 0.079	**5 (0-9), 0.046**
BASDAI>4	1.20 (0.81-1.79), 0.47	1.36 (0.90-2.05), 0.14	**20 (-1-40), 0.060**
CRP at time of study, m/L	1.00 (0.98-1.02), 0.88	**1.02 (1.00-1.03), 0.044**	
ESR at time of study, mm/ 1st hour	1.00 (0.98-1.01), 0.93	1.01 (1.00-1.02), 0.086	
BASFI	**1.19 (1.10-1.29), 0.000**	**1.17 (1.08-1.27), 0.000**	**11 (7-15), 0.000**
BASMI	**1.27 (1.14-1.41), 0.000**	**1.45 (1.30-1.62), 0.000**	**18 (13-23), 0.000**
Dx MASES	1.00 (0.75-1.41), 0.97	0.88 (0.65-1.18), 0.28	24 (-34-82), 0.41
Syndesmophytes	**2.09 (1.39-3.13), 0.000**	**2.17 (1.43-3.30), 0.000**	**82 (61-103), 0.000**
Inp mSASSS	**1.30 (1.05-1.61), 0.015**	**1.77 (1.40-2.25), 0.000**	**3 (2-3), 0.000**
Grade of Sacroiliitis Rx			
Grade ≥ 3 (uni or bilateral)	**1.53 (1.01-2.30), 0.044**	**1.83 (1.19-2.82), 0.006**	**65 (44-85), 0.000**
Grade 4 (uni or bilateral)	**2.48 (1.63-3.77), 0.000**	**2.35 (1.53-3.60), 0.000**	**81 (58-104), 0.000**
Current drugs			
NSAIDs, n (%)	0.79 (0.49-1.27), 0.32	0.77 (0.48-1.26), 0.30	**-48 (-74- -21), 0.000**
Current prednisone, n (%)	1.52 (0.86-2.68), 0.15	**1.91 (1.10-3.29), 0.021**	**46 (15-76), 0.003**
DMARDs, n (%)	1.32 (0.89-1.98), 0.17	**1.63 (1.09-2.44), 0.018**	**22 (1-43), 0.041**
Methotrexate, n (%)	1.61 (0.98-2.66), 0.063	**2.21 (1.36-3.57), 0.001**	**55 (28-82), 0.000**
Sulfasalazine, n (%)	0.99 (0.61-1.59), 0.95	1.13 (0.71-1.81), 0.60	-4 (-29-21), 0.76
Anti-TNF-alpha, n (%)	1.00 (0.67-1.50), 0.99	0.95 (0.63-1.44), 0.82	**37 (16-58), 0.001**
Secukinumab, n (%)	0.47 (0.10-2.11), 0.32	0.27 (0.03-2.06), 0.20	-69 (-1434-6), 0.070
Historical disease related data			
History of synovitis	0.96 (0.59-1.56), 0.61	1.51 (1.01-2.27), 0.045	**37 (16-58), 0.001**
History of enthesitis	0.96 (0.63-1.45), 0.84	0.74 (0.48-1.14), 0.17	1 (-21-22), 0.95
History of dactilitis	1.31 (0.62-2.80), 0.48	1.09 (0.48-2.47), 0.84	14 (-29-57), 0.52
History of hip involvement	**1.63 (1.01-2.65), 0.047**	1.55 (0.95-2.55), 0.080	**35 (7-62), 0.014**
History of sacroiliitis at MRI	1.17 (0.59-2.33), 0.66	1.99 (0.91-4.37), 0.085	**28 (-58-1), 0.057**
Extraarticular manifestations			
Total	0.95 (0.64-1.44), 0.82	1.42 (0.95-2.12), 0.092	**26 (4-47), 0.018**
Psoriasis	1.11 (0.59-2.10), 0.75	1.45 (0.79-2.64), 0.23	20 (-13-53), 0.23
Uveitis	0.89 (0.55-1.45), 0.64	1.03 (0.64-1.66), 0.91	25 (-1-50), 0.055
Inflammatory Bowel Disease	1.13 (0.54-2.39), 0.74	1.18 (0.56-2.49), 0.66	-10 (-50-30), 0.63
HLA-B27 positive	0.92 (0.59-1.44), 0.71	0.97 (0.61-1.54), 0.90	1 (-23-24), 0.96
CRP at time of disease diagnosis. (m	1.01 (1.00-1.01), 0.056	1.00 (0.99-1.01), 0.96	**1 (0-1), 0.005**
CRP >3 at time of diagnosis	**1.59 (1.06-2.39), 0.025**	**1.84 (1.20-2.82), 0.005**	**35 (15-56), 0.001**
ESR at the time of disease diagnosis	**1.01 (1.00-1.03), 0.009**	**1.02 (1.00-1.03), 0.008**	**2 (1-2), 0.000**
Drugs from the disease diagnosis			
Anti-TNF-α	0.80 (0.37-1.72), 0.57	0.98 (0.44-2.21), 0.96	16 (-28-59), 0.49
IL-17 inhibitors	-	-	-49 (-158-59), 0.37
DMARDs	1.10 (0.59-2.02), 0.77	1.28 (0.66-2.48), 0.47	**53 (18-88), 0.003**

TABLE 2. Association between IMT and the main clinical, analytical and radiologycal features in axSpA patients older than 18 years old.

	IMT, microns beta coefficient (95%CI), p. Adjusted model.		
	AxSpA	AS	Nonrx AxSpA
Age (years)	**7 (6-8), 0.000**	**7 (5-8), 0.000**	**7 (6-8), 0.000**
Male	**53 (32-74), 0.000**	20 (-16-55), 0.28	**52 (26-77), 0.000**
Cardiovascular data			
History of CV risk factors			
Current smoker	0 (-21-22), 0.97	5 (-33-43), 0.79	-1 (-25-23), 0.94
Have ever smoked	**32 (12-54), 0.002**	20 (-16-56), 0.27	**31 (8-54), 0.009**
Obesitty	**52 (28-76), 0.000**	**63 (16-109), 0.009**	**44 (18-71), 0.001**
Dyslipemia	**82 (62-103), 0.000**	**70 (29-110), 0.001**	**79 (56-103), 0.000**
Hypertension	**111 (90-133), 0.000**	**77 (28-125), 0.002**	**110 (86-137), 0.000**
Diabetes Mellitus	**111 (72-151), 0.000**	**119 (25-212), 0.013**	**103 (60-146), 0.000**
Chronic Kidney Disease	**96 (27-165), 0.007**	103 (-60-266), 0.21	88 (12-164), 0.23
Lipids			
Total cholesterol x10	2 (0-5), 0.086	4 (-1-9), 0.056	2 (-1-5), 0.23
HDL-cholesterol x 10	**-9 (-2- -0), 0.002**	-1 (-2-0), 0.18	**-1 (-2- -0), 0.040**
LDL-cholesterol x 10	**5 (2-8), 0.002**	**9 (3-2), 0.04**	**4 (0-8), 0.034**
Atherogenic index ≥4	**31 (10-51), 0.004**	**42 (5-80), 0.027**	24 (-1-48), 0.051
Triglycerides x 10	**3 (1-4), 0.000**	**4 (1-6), 0.002**	**2 (1-4), 0.006**
Statins	**90 (61-119), 0.000**	57 (-20-134), 0.14	**84 (53-115), 0.000**
Blood pressure, mm Hg			
Systolic	**3 (2-3), 0.000**	**2 (1-3), 0.000**	**2 (2-3), 0.000**
Diastolic	**2 (1-3), 0.000**	**2 (0-4), 0.015**	**1 (0-3), 0.011**
Carotid IMT (each 0.1 mm)			
Disease related data at time of study			
Mean disease duration, years			
Since first symptoms	**4 (3-5), 0.000**	**6 (3-8), 0.000**	**4 (3-5), 0.000**
Since diagnosis	**4 (3-5), 0.000**	**7 (4-10), 0.000**	**4 (3-5), 0.000**
ASDAS			
Inactive disease	-	-	-
Low disease activity	**40 (9-72), 0.012**	**64 (10-117), 0.020**	**28 (-9-64), 0.14**
High disease activity	**42 (13-70), 0.004**	**52 (6-99), 0.026**	**34 (1-68), 0.044**
Very high disease activity (>3.5)	**72 (33-112), 0.000**	**86 (20-152), 0.011**	**65 (19-111), 0.006**
BASDAI	**5 (0-9), 0.046**	5 (-2-13), 0.17	**5 (0-11), 0.041**
BASDAI>4	**20 (-1-40), 0.060**	21 (-15-57), 0.26	22 (-1-46), 0.063
BASFI	**11 (7-15), 0.000**	**9 (2-16), 0.019**	**11 (6-15), 0.000**
BASMI	**18 (13-23), 0.000**	**17 (3-30), 0.014**	**17 (11-22), 0.000**
1/x MASES	24 (-34-82), 0.41	8 (-87-103), 0.87	19 (-51-88), 0.60
Syndesmophytes	**82 (61-103), 0.000**	**92 (31-153), 0.003**	**69 (45-92), 0.000**
mSASSS	**3 (2-3), 0.000**	**7 (1-13), 0.019**	**2 (1-3), 0.000**
Grade of sacroileitis Rx			
Grade ≥ 3 (uni or bilateral)	**65 (44-85), 0.000**	-	**50 (25-76), 0.000**
Grade 4 (uni or bilateral)	**81 (58-104), 0.000**	-	**68 (44-93), 0.000**
Current drugs			
NSAIDs, n (%)	**-48 (-74- -21), 0.000**	-36 (-84-12), 0.14	**-49 (-80- -18), 0.002**
Current prednisone, n (%)	**46 (15-76), 0.003**	46 (-10-102), 0.11	**44 (10-79), 0.013**
DMARDs, n (%)	**22 (1-43), 0.041**	**63 (27-99), 0.001**	11 (-13-36), 0.37
Methotrexato, n (%)	**55 (28-82), 0.000**	**81 (30-132), 0.002**	**46 (15-76), 0.003**
Sulfasalazine, n (%)	-4 (-29-21), 0.76	30 (-16-75), 0.20	-14 (-42-14), 0.32
Anti-TNF-alpha, n (%)	**37 (16-58), 0.001**	**76 (37-115), 0.000**	**22 (-2-46), 0.075**
Secukinumab, n (%)	-69 (-1434-6), 0.070	-121 (-292-50), 0.16	**-69 (-150-12), 0.096**
Historical disease related data			
History of synovitis	**37 (16-58), 0.001**	**51 (15-87), 0.005**	**37 (12-61), 0.003**
History of enthesitis	1 (-21-22), 0.95	34 (-2-71), 0.063	-3 (-29-22), 0.81
History of dactilitis	14 (-29-57), 0.52	58 (-10-126), 0.095	4 (-47-55), 0.88
History of hip involvement	**35 (7-62), 0.014**	67 (-21-155), 0.14	19 (-10-49), 0.20
History of sacroiliitis in MRi	**-28 (-58-1), 0.057**	11 (-30-52), 0.59	**-54 (-93- -15), 0.007**
Extraarticular maniphestations			
Total	**26 (4-47), 0.018**	17 (-24-58), 0.41	21 (-3-45), 0.084
Psoriasis	20 (-13-53), 0.23	12 (-48-73), 0.69	20 (-17-57), 0.29
Uveitis	25 (-1-50), 0.055	-5 (-65-56), 0.88	18 (-9-46), 0.20
Inflammatory Bowel Disease	-10 (-50-30), 0.63	18 (-51-86), 0.61	-16 (-63-30), 0.49
HLA-B27 positive	1 (-23-24), 0.96	-21 (-58-15), 0.25	-2 (-31-26), 0.88
CRP at time of disease diagnosis, (mg/dL)	**1 (0-1), 0.005**	1 (0-1), 0.13	**0 (0-1), 0.031**
CRP >3 at time of diagnosis	**35 (15-56), 0.001**	21 (-15-58), 0.25	**31 (7-55), 0.011**
ESR at the time of disease diagnosis (mm/1st h	**2 (1-2), 0.000**	**2 (1-3), 0.006**	**1 (1-2), 0.000**
Drugs from the disease diagnosis			
Anti-TNF-α	16 (-28-59), 0.49	104 (-17-225), 0.089	3 (-44-50), 0.90
IL-17 inhibitors	-49 (-158-59), 0.37	36 (-169-242), 0.72	-66 (-191-59), 0.30
DMARDs	**53 (18-88), 0.003**	**156 (81-230), 0.000**	**41 (2-79), 0.037**

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Abstract Number: 0449

Cytotoxic T Cells with a Chronic Antigen Exposure Phenotype Drive Immune Checkpoint Inhibitor Sicca

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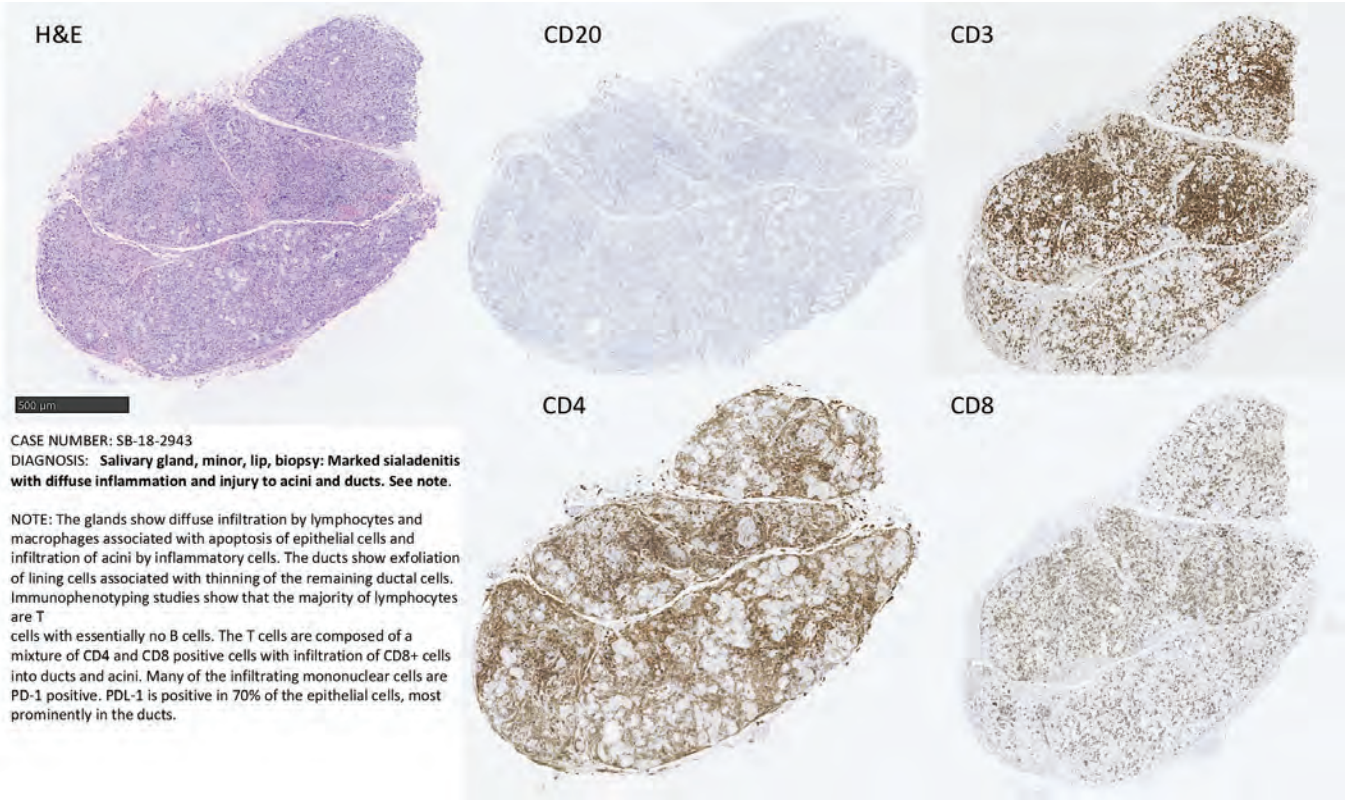
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Immunological Complications of Therapy
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Immune checkpoint inhibitors (ICI) have advanced the field of cancer therapeutics. By blocking the negative co-stimulation of T cells, ICI augment the anti-tumor immune response. However, ICI can elicit inflammatory reactions termed immune-related adverse events (irAEs). We previously reported that ICI therapy is associated an abrupt onset, oftentimes severe irAE resembling Sjögren's syndrome (Warner et al., 2019). Herein we aimed to characterize the inflammatory infiltrate of labial salivary gland biopsies (LSGB) from patients with ICI sicca.

Methods: Patients with ICI sicca (ICI, n=21) and healthy volunteers (HV, n=9) underwent saliva assessments, medical workup, and LSGBs. We measured the surface area of acini and fibrosis with histochemical stains and the density of IHC stains in LSGB using QuPath_2.0. Transcriptional profiling of immune markers was determined using RNA sequencing. Dissociated LSGB were subjected to 4h PMA/ionomycin stimulation and subsequent flow cytometry analysis. In patients with available dissociated tissues, single cell (sc)RNA sequencing was performed.

Results: LSGB form ICI sicca patients demonstrated architectural distortion including the most common findings of reduced density of acini (p=0.01), variable fibrosis (p= 0.07), and mild-to-severe sialadenitis composed chiefly of T lymphocytes. In some patients, destruction of PD-L1$^+$ epithelia with marked effacement of gland architecture was observed. IHC demonstrated the ICI inflammatory infiltrate was composed increased numbers of CD8$^+$ (p=0.039), CD4$^+$ (p=0.078), and CD3$^+$ (p=0.05) T lymphocytes. RNA sequencing exhibited significantly higher PD-1 expression in the ICI LSGB (p=0.02) with higher CD8 and CD39 expression (p=0.05). CD3, CD4, 4-1BB, TIM3, GzmB, FOXP3 and PDL1 were all upregulated in the ICI group but did not reach statistical significance. Flow cytometry confirmed increased infiltration with CD3$^+$ with significant increases in activated cytotoxic T cells (CD8$^+$CD107a$^+$). scRNAseq and confocal immunofluorescence microscopy confirmed increased density of CD8$^+$PD-1$^+$CD39$^+$ T cells in the ICI LSGB.

Conclusion: The histopathology of ICI induced sialadenitis consists primarily of a T cell infiltrate with parenchymal destruction with patchy fibrosis. IHC analysis combined with the transcriptional data show the presence of cytotoxic T-cell population (CD8, 4-1BB, TIM3, GrzB) with a chronic antigen exposure phenotype (PD-1, CD39). Further investigation is necessary to determine if this T-cell population is causing the sicca or if it constitutes a reactive population.



Example of severe sialadenitis induced by anti-PD-L1 therapy . Total effacement of the gland architecture with injury to the acini and ducts is evident. The infiltrate is composed chiefly of T cells without B cells. CD4 cells predominate, although infiltration of the acini and ducts is seen.

Disclosure: B. Warner, None; **B. Gasmi**, None; **D. Kleiner**, None; **P. Perez Riveros**, None; **D. Barber**, None; **S. Sakai**, None; **A. Baer**, Bristol Myers Squibb, 5, Sanofi, 5.

Abstract Number: 0450

In Vitro Characterization of Inflammatory Arthritis Associated with Immune Check Point Inhibition

Anne Sofie Sørensen[1], Morten Nørgaard Andersen[1], Kristian Juul-Madsen[2], Cæcilie Deisting Skejø[1], Henrik Schmidt[1], Thomas Vorup-Jensen[1] and Tue Wenzel Kragstrup[1], [1]Aarhus University, Aarhus, Denmark, [2]Aarhus University, Aarhus, Midtjylland, Denmark

SESSION INFORMATION
Session Date: Friday, November 6, 2020
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Session Time: 3:00PM–3:50PM

Background/Purpose: During treatment with immune checkpoint inhibitors (ICI) such as the anti-PD-1 antibody pembrolizumab, 2-4% of cancer patients develop inflammatory arthritis as an immune-related adverse event (IRAE). These IRAEs show striking similarities with inflammatory arthritis and are linked with immune activation. However, the underlying immunological mechanisms are not well characterized.

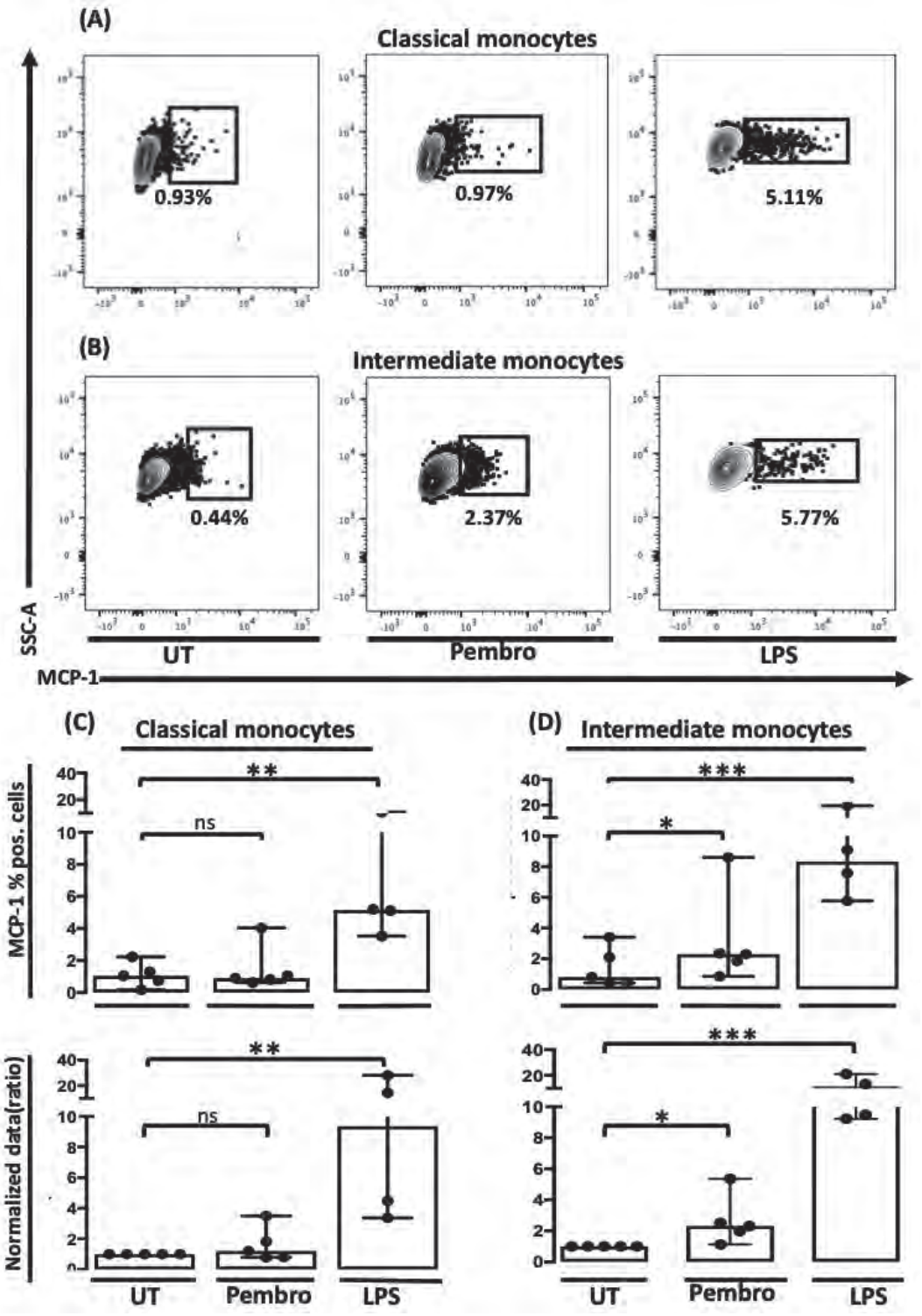

Figure 1. MCP-1 production in the monocyte subsets following treatment with pembrolizumab. (A) Representative dotplots of MCP-1 production in classical monocytes. (B) Representative dotplots of MCP-1 production in intermediate monocytes. (C) Upper panel: Frequency of MCP-1+ cells in classical monocytes in each culture. Lower panel: Data were normalized and expressed as ratios. (D) Upper panel: Frequency of MCP-1+ cells in intermediate monocytes in each culture. Lower panel: Data were normalized and expressed as ratios. All data are expressed as median + 95% Confidence interval. * p-value < 0.05, ** p-value < 0.01, *** p-value < 0.001. UT, untreated; Pembro, Pembrolizumab ; CM, Classical monocytes ; IM, intermediate monocytes.

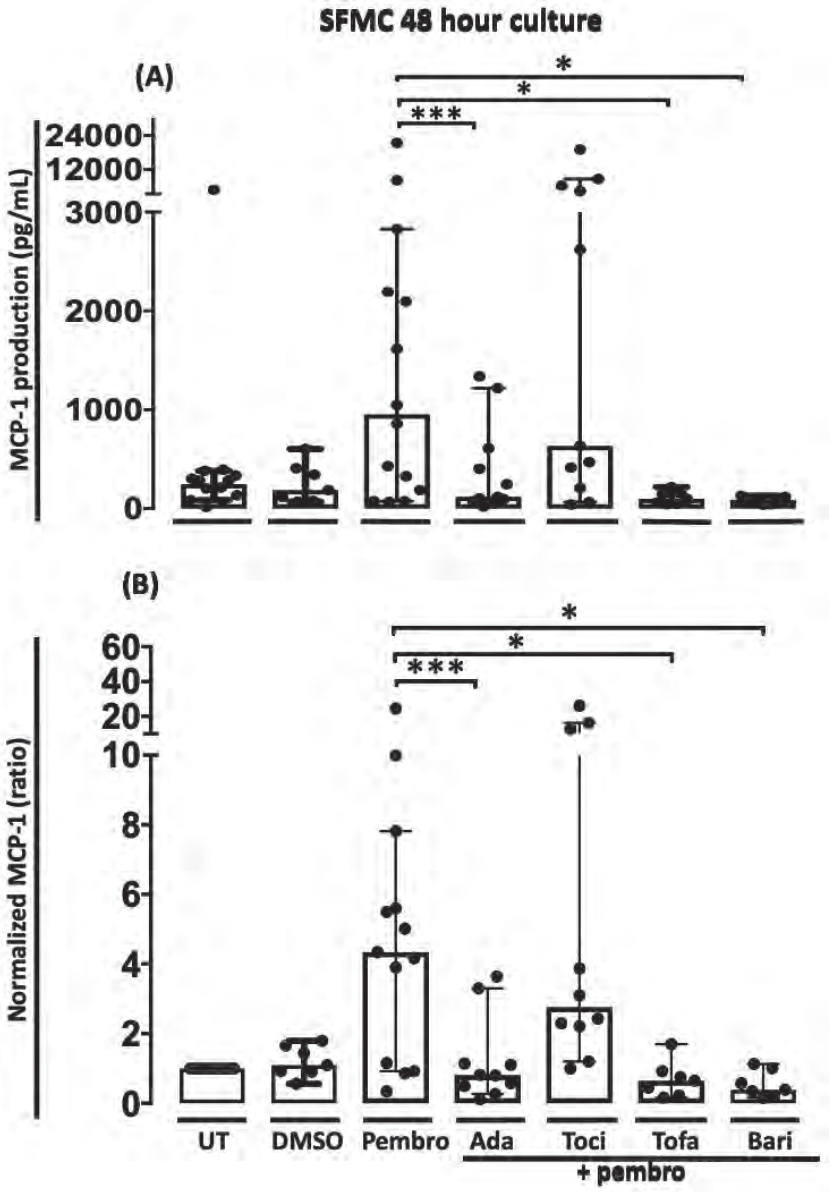

Figure 2. MCP-1 production in SFMC cultures treated with pembrolizumab combined with different DMARDs A) MCP-1 production in SFMCs cultured for 48 h untreated (UT)(n=13) or treated with DMSO (n=7), pembrolizumab (n=13), pembrolizumab + adalimumab (n=10), pembrolizumab + tocilizumab (n=10), pembrolizumab + tofacitinib (n=7) or pembrolizumab + baricitinib(n=7). B) Data were normalized to untreated cultures and expressed as ratios.

Methods: We included synovial fluid mononuclear cells (SFMCs, n=31) and peripheral blood mononuclear cells (PBMCs, n=6) from patients with rheumatoid arthritis and peripheral spondyloarthritis and PBMCs from healthy controls (n=6).Pembrolizumab-treated cells were analyzed using flowcytometry and pro-inflammatory multiplex assays. The mitigation of the effects of pembrolizumab treatment was compared for the disease modifying anti-rheumatic drugs (DMARDs) adalimumab, tocilizumab, tofacitinib, and baricitinib.

Results: Pembrolizumab significantly increased MCP-1 production by arthritis SFMCs (P=0.0031) but not by PBMCs from patients or healthy controls (P=0.77 and P=0.43). In SFMCs, pembrolizumab increased the production of TNFα(P=0.049), IFNγ (P=0.047), and IL-12p70 (P=0.031), but did not change the production of IL-6 (P=0.98). The SFMCs treated with pembrolizumab showed an increased frequency of intermediate monocytes (P=0.044) and increased the

MCP-1 production only within the intermediate monocyte subset (P=0.028) (Figure 1). Lastly, adalimumab, baricitinib, and tofacitinib treatment were able to attenuate the pembrolizumab-induced MCP-1 production (P=0.0004, P=0.033, and P=0.025, respectively) while this was not seen with tocilizumab treatment (P=0.75) (Figure 2).

Conclusion: We have established an in vitro model to study the immunological reactions caused by pembrolizumab. In this model, pembrolizumab specifically activated intermediate monocytes and induced TNFα, IFNγ, and IL-12p70 production, whereas IL-6 was unchanged.

Data is expressed as median + 95% Confidence interval. * p-value < 0.05, ** p-value < 0.01, *** p-value < 0.001. DMSO, Dimethyl sulfoxide; Pembro, Pembrolizumab; Ada, Adalimumab; Toci, Tocilizumab ; Tofa, Tofacitinib ; Bari, Baricitinib.

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Abstract Number: 0451

Prevalence, Therapy and Tumor Response in Patients with Rheumatic Immune-related Adverse Events Following Immune Checkpoint Inhibitor Therapy: A Single-Centre Analysis

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SESSION INFORMATION
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Session Title: Immunological Complications of Therapy
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Session Time: 3:00PM–3:50PM

Background/Purpose: Immune checkpoint inhibitors (ICIs) have improved cancer therapy [1] by inducing a higher immune system activity and subsequent attack of tumor cells. However, this effect can cause rheumatic immune-related adverse events (rh-irAE), which have not yet been extensively studied.

Methods: We analysed 437 patients between January 2014 and October 2019, treated with ipilimumab (anti-CTLA-4) and / or nivolumab (anti-PD-1) or pembrolizumab (anti-PD-1) at the Department of Oncology, Hematology and Rheumatology at the University Hospital in Bonn, Germany.

Results: Of the 437 patients, 260 (60%) were males, 177 (40%) were females with a mean age of 64 years (SD ± 14) at the beginning of the ICI-therapy. 163 patients (37.3%) displayed at least one irAE, including rh-irAE. Most common other non-rheumatic irAE (non-rh-irAE) were rash, colitis and hepatitis.

We identified 19 patients (4.3%) with a minimum of one rh-irAE due to ICI-therapy, three of those had a pre-existing rheumatological disease. Clinical characteristics of patients with rh-irAE, including types of rh-irAE and therapy, are displayed in table 1. Rh-irAE occurred in one patient (2.6%) with ipilimumab, in ten patients (5.3%) with nivolumab

	Number of patients (%)
Patients with rh-irAE	19 (100)
Median onset time of rh-irAE	109.0 days (IQR 40 – 420 days)
Types of rh-irAE	
Arthralgia only[1]	8 (42.1)
Arthritis	7 (36.8)
Rheumatoid arthritis	3
Psoriatic arthritis	2
Juvenile idiopathic arthritis	1
Undifferentiated arthritis	1
Myalgia	2 (10.5)
Myositis	3 (15.8)
Immunosuppressive treatment	
Glucocorticosteroids (GC) only	11 (57.9)
GC plus MTX	3 (15.8)
GC plus tocilizumab	1 (5.3)
Other treatments	
NSAIDs	6 (31.6)
Opioids	1 (5.3)

Table 1. Clinical characteristics of rheumatic immune-related adverse events (rh-irAE). 1= Excluding patients with arthritis. IQR: interquartile range, MTX: methotrexate, NSAIDs: non-steroidal anti-inflammatory drugs

	Patients without irAE n=200 (%)	Patients with non-rh-irAE n=135 (%)	Patients with rh-irAE n=18 (%)
Responders*	65 (32.5)	82 (60.7)	17 (94.4)
Non-responders*	135 (67.5)	53 (39.3)	1 (5.6)

Table 2. Comparison of best tumor response to immune checkpoint inhibitors (ICIs) in patients without immune-related adverse events (irAE), patients with non-rheumatic irAE (non-rh-irAE) and in patients with rheumatic irAE (rh-irAE). *Response to ICI-therapy includes complete response, partial response and stable disease. Non-responders were affected by progressive disease. Patients who suffered from rh-irAE and non-rh-irAE were classified as rh-irAE cohort.

and in eight patients (5.0%) with pembrolizumab. Thirteen patients with rh-irAE received ICI-therapy (percentage within each malignancy given in brackets) for melanoma (6.2%), three patients for lung cancer (3.8%), two patients for head and neck tumor (5.9%) and one patient for gastrointestinal carcinoma (8.3%). Most rh-irAE were classified as moderate severe (CTCAE [Common Terminology Criteria of Adverse Events] grade 2: 68.4%). Even though patients benefited from ICI treatment, therapy had to be discontinued in six of them as a consequence of rh-irAE.

Interestingly, patients with rh-irAE had a significantly higher tumor response rate compared to patients without irAE (94.4% vs. 32.5%; $p< 0.0001$). The comparison of best tumor response in different cohorts (patients without irAE, with non-rh-irAE and with rh-irAE) is listed in table 2. In order to calculate progression-free survival (PFS), we performed a Kaplan-Meier analysis (Fig. 1) and compared thereby the PFS in the three cohorts mentioned above. Using the log-rank test, a significant difference in PFS was found in these three cohorts ($p=0.003$).

Conclusion: Rh-irAE occur under ICI-therapy and in patients with higher tumor response. However, they are not the most frequent irAE after ICI exposure: 9.3% of all irAE were rheumatic (20 rh-irAE cases in 19 patients of a total of

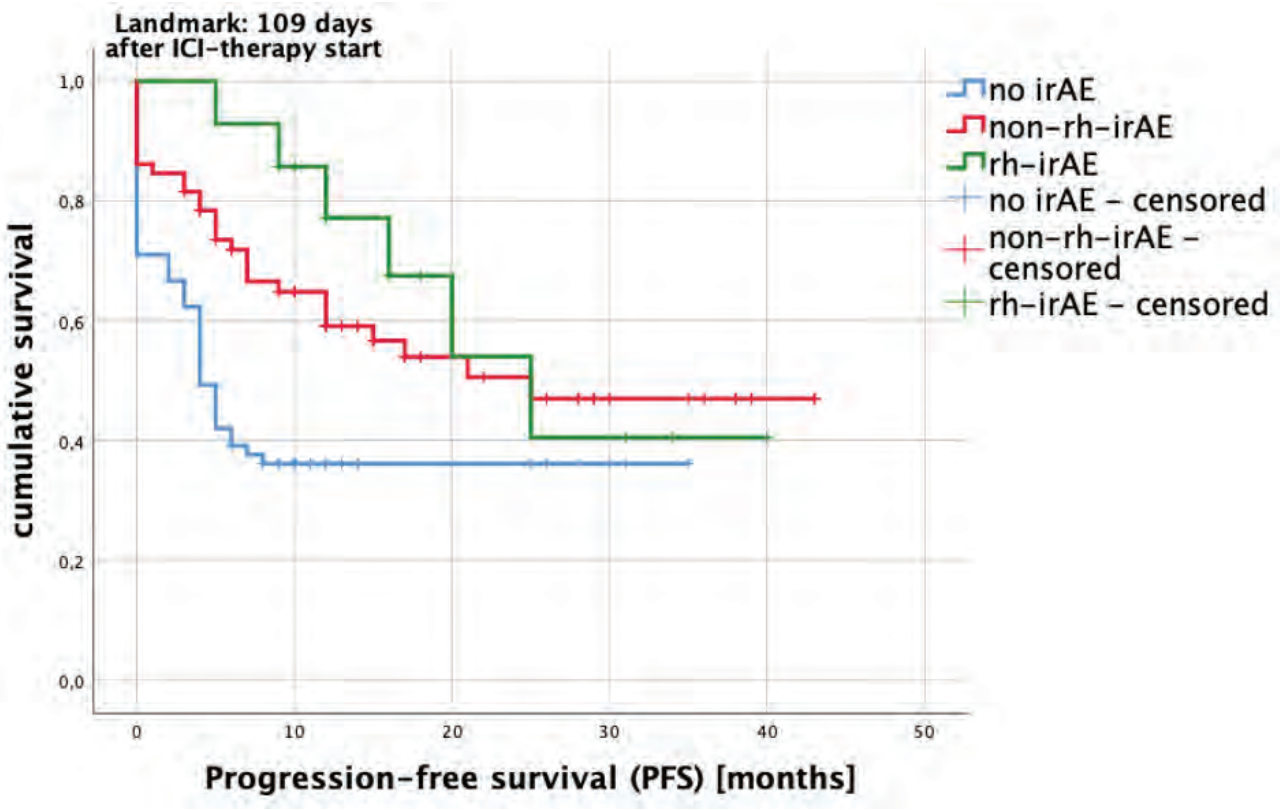

Figure 1. Kaplan-Meier analysis estimated PFS (progression-free survival) after immune checkpoint inhibitor (ICI) therapy. Compared were patients with no side effects (no irAE=blue line), patients with other non-rheumatic immune-related adverse events (non-rh-irAE=red line) and patients with rheumatic immune-related adverse events (rh-irAE=green line). Patients who suffered from rh-irAE and non-rh-irAE were classified as rh-irAE cohort. Patients with a therapy duration of 109 days or more were included in the analysis (landmark 109 days after ICI-therapy start). Log rank test: p=0.003.

215 irAE cases in 163 patients). As the use of ICIs is increasing for different malignancies the incidence of rh-irAE can be expected to increase.

References

1. Ribas A et al. Cancer immunotherapy using checkpoint blockade. *Science*. 2018

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Abstract Number: 0452

Recombinant Zoster Vaccine in Patients with Rheumatic Diseases: A Retrospective Study of 622 Patients

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Immunological Complications of Therapy

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: The recombinant herpes zoster vaccine (RZV) was FDA-approved in 2017 but patients with rheumatic diseases were excluded from initial pivotal trials because of theoretical risk of flares given the vaccine's potent immunogenicity. Its use in patients with RA, SLE and vasculitis raises particular concern.

Methods: Patients followed in the Cleveland Clinic Rheumatology Department who received RZV between February 2018 and March 2020 were identified and retrospectively included in this study. Inclusion criteria were: age > 18 years, at least one RZV dose during the study period, available data on the clinical status before and after the vaccine. Data were collected from the electronic medical record. An immune mediated inflammatory disease (IMID) flare was defined as a) a documentation of flare in the rheumatology office notes, telephone encounter or patient portal communication or b) new prednisone prescription, occurring in the 12 week period following each dose. Adverse events (AE) attributed to RZV and occurrence of herpes zoster (HZ) were also assessed. The statistical analysis was performed with R studio v.1.2.5042. Categorical variables were compared using chi-square tests and multivariable analysis were performed using logistic regression and Cox model (tests were two-sided, significance level was 0.05).

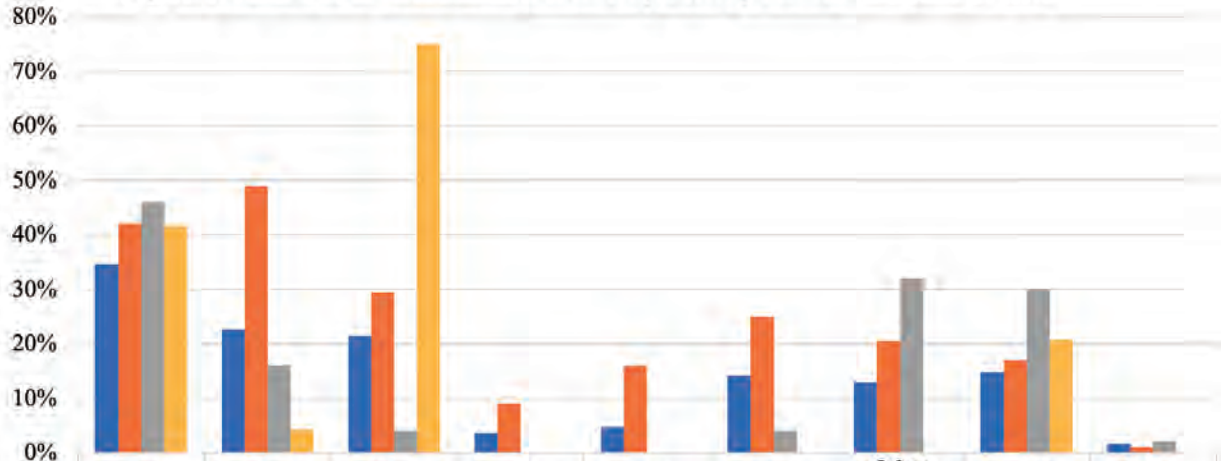
Results: In the study period, 622 patients met the inclusion criteria; the majority were female (67%), and median age was 67 years. Of the group, 15% reported a history of HZ and 43% had previously received live attenuated zoster vaccine. 147 patients (24%) received 1 dose of RZV, while 475 (76%) received both dsoses with a median interval of

Table 1. Statistical analysis of risk factors for IMID flare after RZV

	No flare (n=301)	Flare (n=57)	Univariate analysis	Multivariate analysis adjusted on significant factors	
			p value	Adjusted OR [IC95%]	p value
Median age (years)	66	67	0.973		
Gender (female)	66%	65%	0.861		
Ethnicity (Caucasian)	84%	86%	0.461		
Rheumatoid arthritis (vs others)	22%	37%	**0.019**	1.66 [0.85-3.17]	0.129
Treatment at RZV					
Glucocorticoids	31%	53%	**0.002**	**2.31 [1.29-4.15]**	**0.005**
Jak-inhibitors	4%	11%	**0.025**	2.11 [0.64-6.41]	0.199
Hydroxychloroquine	21%	26%	0.335		
Methotrexate	22%	26%	0.468		
TNF inhibitors	14%	18%	0.437		
Other biologic	13%	14%	0.77		
Other immunosuppressant	14%	19%	0.297		
Baseline laboratory findings					
Positive CRP	14%	9%	0.43		
Median CRP (mg/L)	0.3	0.3	0.862		
Positive ESR	31%	26%	0.539		
Median ESR (mm)	9	10	0.982		
Positive RF	19%	25%	0.329		
Positive CCP	14%	21%	0.17		
Positive ANA	27%	26%	0.926		
Positive ANCA	6%	0%	0.051		

Legend: IMID: Immune Mediated Inflammatory Disease; RZV: Recombinant Zoster Vaccine; OR: Odd-ratio; IC: Confident Interval

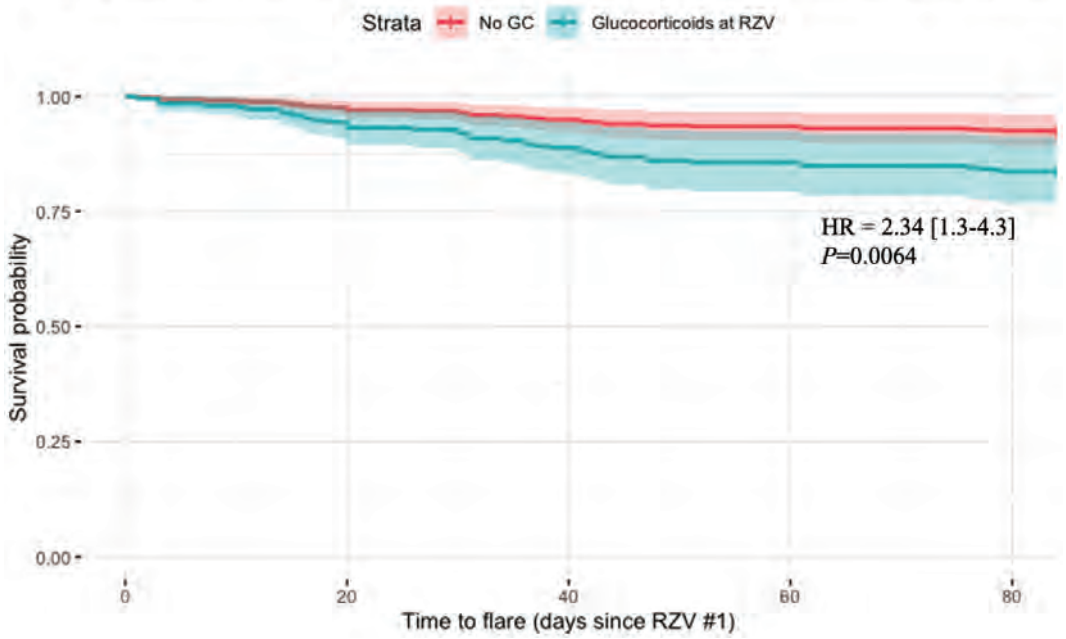
Figure 1. Pannel of the treatments received by IMID patients at the time of RZV



	GC	MTX	HCQ	SSA	Jak-i	TNF-i	Other biologic	Other IS	IVIG
IMID (n=358)	35%	23%	22%	4%	5%	14%	13%	15%	2%
RA (n=88)	42%	49%	30%	9%	16%	25%	20%	17%	1%
Vasculitis (n=50)	46%	16%	4%	0%	0%	4%	32%	30%	2%
SLE (n=24)	42%	4%	75%	0%	0%	0%	0%	21%	0%

Legend. IMID: Immune Mediated Inflammatory Disease; RZV: Recombinant Zoster Vaccine; RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus; GC: Glucocorticoids; MTX: Methotrexate; HCQ: Hydroxychloroquine; SSA: Sulfasalazine; Jak-i: Jak-inhibitors; TNF-i: TNF inhibitors; Other biologic: abatacept, apremilast, belimumab, mepolizumab, rituximab, secukinumab, tocilizumab, ustekinumab; Other IS: Other Immunosuppressant, azathioprine, leflunomide, ciclosporine, mycophenolate mofetil, tacrolimus; IVIG: Intravenous Immunoglobulin.

Figure 2. Glucocorticoid use at time of vaccine was associated with a higher risk of IMID flare after the first RZV dose



Legend: This figure shows a survival analysis of the time-to-flare with estimated risk of being on glucocorticoids at the time of first RZV dose (multivariate Cox-model). IMID: Immune Mediated Inflammatory Disease; RZV: Recombinant Zoster Vaccine; GC: Glucocorticoids; HR: Hazard Ratio

2.9 months. The AE rate was 8.5% with mostly mild events (71%). After a median 35.8 weeks of follow-up, the HZ incidence was 0.6%.

Of 358 IMID patients the most common were RA (n=88, 25%), vasculitis (n=50, 14%), and PMR (n=29, 8%). Baseline treatment in this group included glucocorticoids (GC) (35%, median dose 5 mg/day), conventional and biologic DMARDs (Fig 1). Fifty-seven (16%) experienced a flare: 34 (60%) after the first dose, 16 (28%) after the second, and 7 (12%) flared after both. RA patients had the highest flare rate (n=21, 24%). Flares occurred in temporal relation to a treatment change in 18 cases (31%). Flares were most often treated with GC (44%, median dose 20 mg/day) and 14 (25%) required a change in immunosuppressive therapy. Among IMID patients, univariate analysis revealed more flares in patients on GC and Jak-inhibitors (p=0.002 and 0.025 respectively), and in RA patients (p=0.019) (Table 1). A multivariate analysis showed that only GC use at time of vaccine remained significantly associated with flares (OR = 2.31 [1.29-4.15], p=0.005). A time-to-flare survival analysis was conducted with a multivariate Cox-model: glucocorticoids remained the only significant predictor of the first IMID flare (HR = 2.34 [1.3-4.3], p=0.006) (Fig 2).

Conclusion: In this retrospective cohort of rheumatic disease patients, we found the incidence of AEs and HZ after RZV to be consistent with the existing literature. GC at time of RZV was associated with a significantly higher rate of flares, suggesting that delaying RZV administration in patients with active disease may be prudent

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Abstract Number: 0453

Monitoring of BK Reactivation and Long-term Safety on JAK1/2 Inhibition with Baricitinib

Kader Cetin Gedik[1], Gema Souto Adeva[2], Jenna Wade[1], Gina Montealegre Sanchez[3], Adriana de Jesus[4] and Raphaela Goldbach-Mansky[5], [1]Translational Autoinflammatory Disease Section (TADS)/NIAID/NIH, Bethesda, MD, [2]Translational Autoinflammatory Disease Section (TADS)/NIAID/ NIH, Bethesda, [3]Translational Autoinflammatory Disease Section (TADS)/NIAID/NIH, Rockville, MD, [4]Translational Autoinflammatory Disease Section (TADS)/NIAID/NIH, Silver Spring, MD, [5]Translational Autoinflammatory Disease Section (TADS)/NIAID/NIH, Potomac, MD

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Immunological Complications of Therapy
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Baricitinib has been used to treat pediatric patients (pts) with Type 1 Interferonopathies[1]. Safety profile including BK viral reactivation in urothelium and pharmacokinetic model have been reported[1,2]. Given the association of BK nephropathy with BK viremia[3], we assessed long term safety and consequences of chronic BK viruria on renal function.

Methods: Between October 2011 and August 2018, 25 pts [10 CANDLE (Chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperatures), 7 SAVI (Stimulator of IFN genes–associated [STING-associated] vasculopathy with onset in infancy) and 8 other interferonopathies] were enrolled in an institutional review board

Table 1: Severe Adverse Events[A]

Severe Adverse Events	CANDLE (n=10), number of SAEs	Other (n=8),[B] number of SAEs	SAVI (n=7), number of SAEs	Total (n=25), number of SAEs
Total	60	19	35	114
Viral infection	22	3	8	33
-Reactivation	9	1	3	13
BK viremia	7	1	3	11
Herpes zoster	2	0	0	2
-Primary[C]				
Upper respiratory tract[D]	3	0	1	4
Gastrointestinal	1	0	1	2
Other[E]	0	1	0	1
Bacterial Infection[F]	6	3	8	17
Pneumonia[G]	3	1	1	5
Blood and lymphatic system disorders	5	1	1	7
Gastrointestinal disorders	1	3	0	4
Musculoskeletal and connective tissue disorders	1	1	0	2
Respiratory disorders	2	0	3	4
Renal disorders	4	2	1	7
Metabolic/endocrine/ nutrition	5	0	0	5
Nervous system disorders	1	3	0	4
Dermatologic disorders	1	0	7	8
Elective surgery/ hospitalization	3	2	6	11
Other[H]	6	0	0	6

SAE: severe adverse event

[A]Patients with multiple occurrences of a specific event are counted once for the event. Multiple patients with same SAE counted as separate SAEs.

[B]NEMO-NDAS=2, SAMD9L_SAAD=1, Aicardi-Goutières syndrome=1, undifferentiated=4

[C]Admitted to hospital (n=6), prolongation of hospitalization (n=1)

[D]Influenza B (n=2), upper respiratory infection-metapneumovirus (n=1), presumed viral syndrome (n=1).

[E]Respiratory syncytial virus infection

[F]Wound infection (n=3), clostridium difficile infection (n=2), urinary tract infection (n=2), foot infection (n=2), portacath infection (n=2), cellulitis (n=2), H. influenza bacteremia (n=1), pyelonephritis/urosepsis (n=1), osteomyelitis (n=1), methicillin-resistant staphylococcus aureus infection (n=1).

[G]Pneumonia/lower respiratory tract infection (n=4), PCP pneumonia (n=1)

[H]CANDLE flare (n=2), pyrexia (n=2), congenital anomaly [cleft lip/cleft palate s/p surgical repair] (n=1), deviated nasal septum (n=1).

approved protocol (NCT01724580). Safety was longitudinally assessed during study period (cut off May 2020). After detection in an index pt in June 2015, BK viral load and renal function were monitored longitudinally, with baseline assessments in 7 additionally enrolled pts. Dichotomous adverse events (AEs and SAEs) were descriptively analyzed, for continuous outcomes (BK viral load) paired t-tests were used.

Results: The mean age at enrollment was 11.5 years [range 1.2-24.2]. The mean baricitinib exposure was 4.2 years [104.6 pt.-years]. Of 25 pts, 1 CANDLE (azotemia in the context of BK viremia) and 4 pts with undifferentiated disease discontinued (4/4 inadequate response; 1/4 osteonecrosis). Nine pts are receiving commercial baricitinib and discontinued from study. During the study period, 114 SAEs were reported [66 were treatment related] (Table 1). Of 23 pts monitored, 20 developed BK viruria (1/20 pre-baricitinib). All except the index pt. had stable renal function over a mean of 4.9±2.4 years on baricitinib. Out of 8 pts with no BK viruria at baseline, 5 (63%) developed viruria after a mean of 8.3±10.3 months on baricitinib at a mean age of 5.8±2.3 years. Two pts had BK viremia prior to baricitinib (1 on tacrolimus and 1 azathioprine) and 10 additional pts developed viremia [mean 3.08±1.1 log copy/ml] after a mean of 1.7±1.4 years on baricitinib. The mean urine BK load was 7.7±2 log copy/ml at the time of first viremia (Table 2). Herpes zoster developed in 2 pts and resolved without holding baricitinib. The most frequent treat-

Table 2: BK viral reactivation in interferonopathy patients with baricitinib treatment

BK viral load [A] n=23	Pre-baricitinib Baseline Screening n (%) (Mean±SD)	On-baricitinib June 2015 n (%) (Mean±SD)	On-baricitinib May 2020 n (%) (Mean±SD)	p-value
BK viremia [log copy/ml] (n=12/23)	2/23 (8%) 0.21±0.72		9/23 (39%) 1.55±2.08	0.012[B]
BK viruria[C] [log copy/ml] (n=15/16)	Not tested in 16/23 pts prior to baricitinib	14/16 (88%) 5.56±3.17	15/16 (94%) 6.11±2.66	ns[D]
BK viruria[E] [log copy/ml] (n=5/7)	1/7 (14%) 2.88±1.02		4/7 (57%) 4.57±3.65	ns[F]

[A]Results reported in [log_{10}] copies/mL; n (%) represents the number and (percentage) of patients who tested positive for BK virus.
[B]The BK viral load in blood at baseline (prior to baricitinib) was compared to the last visit (n=23)
[C]Baseline urine samples had not been collected and therefore baseline BK urine viral load could not be obtained. Of 23 patients enrolled, 16/23 had their first evaluation of BK viral load in urine in/around June 2015, while already on baricitinib.
[D]The first BK titer assessment in urine at the time of the identification of the first case (post-baricitinib - June 2015) was compared to the last visit (n=16)
[E]Of 23 patients, 7 patients who enrolled after June 2015 had BK assessment in blood and urine prior to baricitinib.
[F]The BK titer assessment in urine at baseline (prior to baricitinib) was compared to the last visit (n=7).

ment-emergent infectious AEs were upper respiratory tract infections, gastroenteritis, sinusitis and pneumonia (in 76%, 36%, 36%, 28% of the pts respectively).

Conclusion: Overall, baricitinib was well tolerated. BK reactivation in urine occurred or was present in 20/23 (87%) pts. In 19/23 who were prospectively monitored, baricitinib dose adjustments to keep BK viremia negative or low were made and renal function remained unchanged during the study period. Our data suggest that BK viral load should be monitored on baricitinib. The presence of BK viremia/ viruria prior to baricitinib treatment suggests evaluation of BK viral load in pts on other chronic immunosuppressive regimens.

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Abstract Number: 0454

Anticytokine Therapies for Inflammatory Rheumatic Disease (IRD) Are Associated with Reduced Hospitalisation Following Community COVID-19 Infection; Results of the Trinity Rheumatology and Covid-19 Registry - TRACR

Rachael Flood[1], Richard Conway[2], David Kane[1] and Ronan Mullan[1], [1]Tallaght University Hospital, Dublin, Ireland, [2]St James's Hospital, Dublin, Ireland

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Infection-related Rheumatic Disease
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Anticytokine biological disease modifying anti-rheumatic drugs (bDMARD), which are widely prescribed for Inflammatory Rheumatological Diseases (IRD) are currently undergoing clinical trials for the treatment of Covid-19. Despite indicators that bDMARDs ought to reduce adverse outcomes through inhibition of hyperinflammatory cytokine storm events, only one global registry of 600 Covid-19 IRD patients has indicated that pre-treatment with the tumour necrosis factor inhibitor class of bDMARD protects against hospitalisation. Furthermore global registry reports of admission rates of 46% in IRD are at variance with lower rates recently published in the NEJM,

	IRD Only (n=40)		All Patients (n=68)	
Parameter	Non-Hospitalisation	Hospitalisation	Non-Hospitalisation	Hospitalisation
COVID-19 Positive (n, %)	34 (85)	6(15)	53 (77.9)	15 (22.1)
Age in Years (Mean, SD)	48.7 (15)	68.9* (15.1)	59.6 (13.8)	68.1*(12.2)
Female (n, %)	26 (76.5)	5 (83.3)	41 (77.4)	10 (66.7)
CVS Disease (n, %)	2 (5.9%)	2 (33.3)	6 (11.3%)	8*(53.3)
BMI >30 (n, %)	7 (20.6)	2 (33.3)	10 (18.9)	3 (20)
T2DM (n, %)	1 (2.9)	2 (33.3)	1(1.9)	3* (20)
csDMARD (n, %)	14 (41.2)	4 (66.7)	N/A	
HCQ (n,%)	7 (20.6)	2 (33.3)	N/A	
bDMARD (n,%)	16 (47.1)	0 (0)	N/A	
tsDMARD (n,%)	0 (0)	0 (0)	N/A	
GC (n, %)	0 (0)	2* (33.3)	0(0)	3* (20)

Table 1: Baseline Data in Community Acquired COVID-19 Infection.
CVS – Cardiovascular Disease. BMI – Body Mass Index. T2DM – Type 2 Diabetes Mellitus. csDMARD- conventional synthetic disease modifying antirheumatic drug. HCQ – hydroxychloroquine. bDMARD- biologic disease modifying antirheumatic drug. tsDMARD- targeted synthetic disease modifying antirheumatic drug. GC – Glucocorticosteriods.
* P=<0.01 † P=<0.05

Parameter	IRD	nIRD
COVID-19 Positive (n, %)	40 (58.9)	28 (41.2)
Age in Years (Mean, SD)	51.8 (16.5)	56.46 (13.6)
Female (n, %)	31 (77.5)	20 (71.4)
CVS Disease (n,%)	4 (10)	10* (35.7)
BMI >30 (n, %)	9 (22.5)	4 (14.3)
T2DM (n, %)	3 (7.5)	1 (3.6)
GC (n, %)	2 (5)	1 (3.6)
Incidence (per 100,000)	884	940
Diagnosis	RA 14 PsA 7 SLE 4 Sjogren's 2 JIA 2 HUVS. 1 uCTD 5 PMR 1 AS 4	Costochondritis 1 Fracture 9 Fibromyalgia 6 Gout 1 EDS 1 OA 8 Functional 1 Mechanical 1

Table S1: Baseline Data between IRDs and nIRDs

CVS – Cardiovascular Disease. BMI – Body Mass Index. T2DM – Type 2 Diabetes Mellitus. GC – Glucocorticosteriods. RA – Rheumatoid Arthritis. PsA – Psoriatic Arthritis. SLE – Systemic Lupus Erythematosus. JIA – Juvenile Idiopathic Arthritis. uCTD – Undifferentiated Connective Tissue Disease. PMR – Polymyalgia Rheumatica. AS- Ankylosing Spondylitis, EDS -Ehlers Danlos Syndrome. OA – Osteoarthritis. HUVS – Hypocomplementemic Urticarial Vasculitis Syndrome.

suggesting a potential reporting bias in registry data towards hospitalised patients, including those who may only become infected during hospitalisation for an unrelated condition.

Methods: To eliminate reporting bias we contacted 7,500 patients comprising 4,524 with IRDs and 2,976 with non-inflammatory disease (nIRDs) attending Trinity College Dublin aligned academic Rheumatology centres, collecting data up to the end of the 1st pandemic wave in Ireland on 03rd June 2020. Cross-referencing with test-centre positive polymerase chain reaction (PCR) results and mortality data was performed to ensure complete collation of cases.

Results: We identified 77 cases of PCR or physician diagnosed COVID-19, of whom 68 were community acquired (supplementary table 1) and 9 were hospital acquired. No differences were seen in cumulative incidence/100,000 of COVID-19 between IRD (884), non-inflammatory rheumatic disorders (nIRD, 940), or incidence rates for metropolitan Dublin (887). In subgroup analysis of community acquired infection, hospitalisation was statistically less likely in patients receiving long-term anticytokine biological therapies ($P< 0.05$). This significance was lost when hospital acquired cases were included. In further analysis of the 40 IRD and 28 nIRD community acquired cases, hospitalisation was more likely to occur in those receiving glucocorticosteroids ($p< 0.01$) or those diagnosed with type 2 diabetes ($p< 0.05$). Lower hospitalisation rates for community acquired Covid-19 in IRD (15%), equivalent to national figures (13%) were observed.

Conclusion: Unintentional bias in reporting hospitalised COVID-19 cases to IRD registries and the inclusion of hospital acquired cases during data analysis, may lead to spurious overestimates of overall morbidity while masking critically important information on the role of anticytokine therapies in preventing hospitalisation. Although our dataset is

small, these results suggest a much more powerful role for anticytokine therapies in treating COVID-19 than existing published registry data indicate. Further analysis using existing datasets on community acquired cases, are likely to more rapidly identify existing drugs to treat COVID-19, which are urgently required to improve health outcomes.

Disclosure: R. Flood, None; **R. Conway**, None; **D. Kane**, None; **R. Mullan**, None.

Abstract Number: 0455

HLA-B27 and Host Immune Response: Lessons from Reactive Arthritis

Sophie Wojcik[1], Davina Morris[2], Gillian Fitzgerald[3], Steve Ramkissoon[4], Nigil Haroon[2] and Robert Inman[5], [1]UHN, Montreal, QC, Canada, [2]University of Toronto, Toronto, ON, Canada, [3]Toronto Western Hospital, Toronto, ON, Canada, [4]UHN, Toronto, ON, Canada, [5]University Health Network, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Infection-related Rheumatic Disease
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: The natural history of reactive arthritis (ReA) remains poorly understood. Certain patients with ReA will go on to develop a chronic course while others will have a self-limited course. The goal of this study is to identify prognostic factors for chronicity of disease.

Methods: ReA patients were identified via two methods; from a Spondyloarthritis clinic database and from an urgent Rheumatology clinic, both located within the University Health Network in Toronto, Canada. Baseline data at presentation, including history, physical exam, X-rays and clinical laboratory results were collected. Patients whose arthritis resolved and were discharged from clinic were defined as self-limited ReA, whereas patients with persisting arthritis with long term follow-up in the clinic were defined as chronic ReA.

Results: A total of 57 patients with ReA were identified. Of these patients, 23 were classified as self-limited ReA (mean disease duration 2.5 years +/- 4.0) and 34 were classified as chronic ReA (disease duration 14.2 years +/- 10.7), $p < 0.01$. The most striking difference was the presence of HLA-B27: 82.4% in the chronic group *vs*45.0% in the self-limited ($p= 0.004$). The nature of the antecedent infection was not a prognostic marker. There was a difference in the presence of inflammatory back pain at disease onset (59.4% *vs* 30.0% $p= 0.04$) and in CRP (15.0 mg/L *vs* 1.5, $p = 0.04$) in the chronic *vs* self-limited group, respectively. In multivariate analysis, the presence uveitis *trended* towards an increased risk of chronic ReA (OR 6.71 (95% CI 0.44-102.12) as did male gender (OR 3.22 (95% CI 0.59- 16.67), but neither reached statistical significance. A subgroup analysis of chronic ReA patients revealed an increased incidence of both uveitis and SI joint involvement over time; 25.8% patients presented with uveitis; however over time, 53.9% developed uveitis. Similarly, 38.9% of chronic ReA patients initially presented with sacroiliitis vs. 56.3% over time.

Conclusion: HLA-B27 is the predominant risk factor for chronicity in ReA, as it is for ankylosing spondylitis (AS). In contrast, the type of antecedent infection is not a prognostic factor for the course of ReA. This suggests that host immune response orchestrated by HLA-B27, rather than a particular antigenic specificity, determines outcome in ReA by setting stage for chronic inflammation. This may have direct relevance to deciphering the inciting events in AS.

Table 1: Clinical features of combined groups, self-limited ReA and chronic ReA group at presentation of disease

	Combined N= 57	Self-limited N= 23	Chronic N= 34	P value
Duration of disease Mean (SD)	9.7 (10.4)	2.5 (4.0)	14.2 (10.7)	<0.01
Age at diagnosis Mean (SD)	29.8 (10.8)	31.8 (11.7)	28.4 (10.1)	0.24
CRP Mean (SD)	22.2 (33.1)	1.5 (0.0, 16.8)	15.0 (5.0, 26.0)	0.04
ESR Mean (SD)	26.7 (29.0)	5.5 (4.0, 18.8)	19.8 (7.0, 32.0)	0.75
Male N (%)	36 (63.2)	12 (52.2)	24 (70.6)	0.16
Antecedent infection N (%)	51 (89.5)	21 (91.3)	30 (88.2)	0.71
Infection type N (%) GI GU Other	 33 (64.7) 11 (21.6) 7 (13.7)	 15 (71.4) 2 (19.5) 4 (19)	 18 (60.0) 9 (30.0) 3 (10.0)	
Family history N (%)	6 (10.5)	1 (4.5)	5 (15.2)	0.22
Conjunctivitis N (%)	10 (20)	3 (14.3)	7 (24.1)	0.39
Uveitis N (%)	10 (17.5)	2 (9.5)	8 (25.8)	0.14
Inflammatory back pain N (%)	25 (48.1)	6 (30.0)	19 (59.4)	0.04
HLA-B27 positivity N (%)	37 (68.5)	9 (45.0)	28 (82.4)	0.004
Dactylitis N (%)	17 (40.5)	6 (33.3)	11 (45.8)	0.41
Pattern of arthritis N (%) 1-4 joints More than 5 joints	 34 (59.6) 22 (38.6)	 14 (60.9) 9 (39.1)	 14 (58.8) 13 (38.2)	 0.88 0.95
Sacroiliac joint involvement N (%)	12 (36.4)	5 (33.3)	7 (38.9)	0.74

Table 2: Multivariate analysis for all variables with p values inferior or equal to 0.2 in univariate analysis

	Univariate OR (95% CI)	P value	Multivariate OR (95% CI)	P value
Gender	2.17 (0.73- 6.67)	0.16	3.22 (0.59- 16.67)	2.17 (0.73-6.67)
HLA-B27 positive	5.7 (1.6 – 19.8)	0.01	5.56 (1.13-27.29)	0.03
Uveitis	3.30 (0.63-17.46)	0.16	6.71 (0.44-102.13)	0.17
Inflammatory back pain	3.41 (1.04-11.19)	0.04	5.98 (1.03-34.73)	0.046

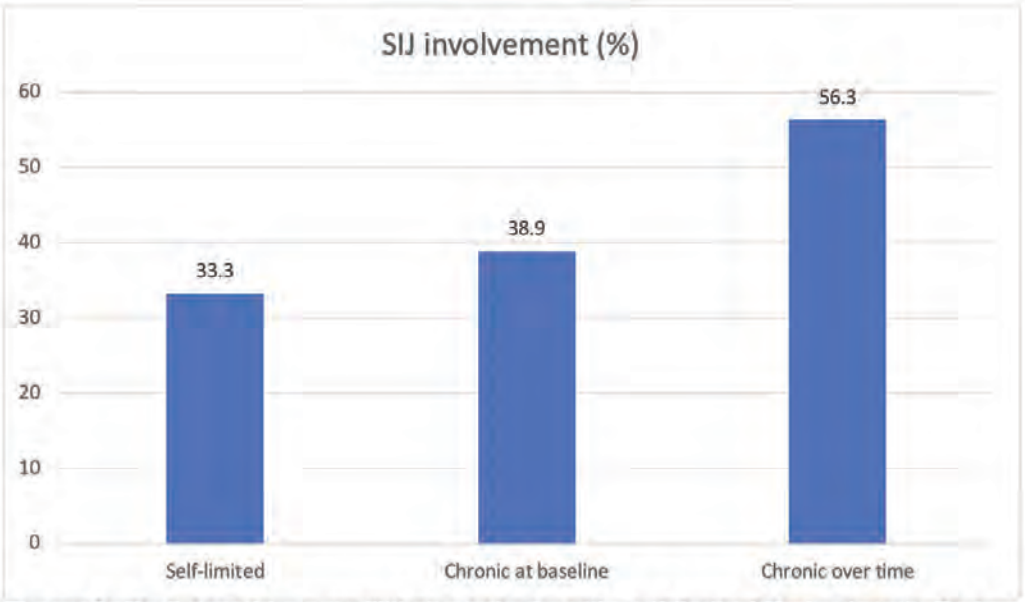

Figure 2: Radiographic sacroiliitis in patients with self-limited ReA, chronic ReA at baseline and chronic ReA over time.

Disclosure: S. Wojcik, None; **D. Morris**, None; **G. Fitzgerald**, None; **S. Ramkissoon**, None; **N. Haroon**, Amgen, 1, Eli Lilly, 1, Novartis, 1, Janssen, 1, UCB, 1; **R. Inman**, Abbvie, 5, Amgen, 5, Janssen, 5, Lilly, 5, Novartis, 5.

Abstract Number: 0456

Reduced Risk of Serious Pneumococcal Infection up to 10 Years After Immunization with 7-valent Conjugated Pneumococcal Vaccine in Patients with Inflammatory Arthritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Infection-related Rheumatic Disease
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: The aim was to examine the rates of putative pneumococcal infections up to 10 years before and after administration of heptavalent conjugated pneumococcal vaccine (PCV7) in patients with inflammatory arthritis compared to non-vaccinated arthritis patients.

Methods: Adult patients with rheumatoid arthritis (RA) and spondylarthropathy (SpA) including psoriatic arthritis (PsA) patients, at the Department of Rheumatology at Skåne University Hospital, Sweden were offered one single

Table. Relative risk (RR) and ratio of relative risk (RRR) of pneumonia and all serious pneumococcal infections among vaccinated and non-vaccinated individuals before and after date of vaccination.

	Vaccinated patients (n=595)	Non-vaccinated references (n=2379)
Events of pneumonia, *before* vaccination, n	42	77
Events of pneumonia *after* vaccination, n	76	263
Risk ratio (after/before) (95% CI)	1.74 (1.14-2.64)	3.65 (2.70-4.93)
RRR of pneumonia (vaccinated /non-vaccinated) (95% CI): 0.47 (0.28-0.77)		
Events of serious infection, *before* vaccination, n	48	103
Events of serious infection *after* vaccination, n	85	307
Risk ratio (after/before) (95% CI)	1.72 (1.12-1.63)	3.09 (2.33-4.10)
RRR of serious pneumococcal infection, vaccinated /non-vaccinated (95% CI): 0.54 (0.33-0.89)		

RRR, ratio of relative risk

intramuscular dose of PCV7 between May 2008 and February 2012. 595 patients participated (RA=342; 80% women, and SpA=253; 45% women). Mean age was 62 and 51 years, mean disease duration was 16 and 14 years respectively. For each patient, 4 reference subjects were identified, matched for arthritis diagnosis, age, sex, and geographical area, and date of vaccination of the patient was also used as index date for its references. References were presumed to be non-vaccinated for pneumococci, following the current national guidelines.

At the time of vaccination, 420 patients were treated with bDMARDs including anti-TNF agents (n=330), tocilizumab (n=15), abatacept (n=18), anakinra (n=1) and rituximab (n=56). Methotrexate (MTX) was given as monotherapy (n=86), or in combination with bDMARD (n=220). Eighty-nine of the SpA patients were treated with NSAIDs without DMARD. Thirty percent (n=176) of the patients were treated with prednisolone, mean weekly dose 41 (1-140) mg.

The Skåne Healthcare Register was searched for ICD-10 diagnostic codes for serious putative pneumococcal infections between January 2000 and December 2018 for both patients and reference subjects. The outcome events included community acquired pneumonia, lower respiratory tract infection, septicemia, meningitis, and septic arthritis. We compared the frequency of outcome events after vs before date of vaccination by calculating relative risks (RRs). The ratio of relative risk (RRR) was calculated comparing the RR of vaccinated patients vs non-vaccinated references. A generalized estimated equation (GEE) was used to handle correlated data for several events in the same individual and included time of follow up as a covariate. We also did a survival analysis (Kaplan-Meier) and Cox regression to investigate time to first event after vaccination.

Results: The point estimate of RRR for pneumonia only was 0.47, 95% CI 0.28-0.77 and for all serious putative pneumococcal infections the RRR was 0.54, 95% CI 0.33-0.89 (Table). Time to first pneumonia or other serious infection after vaccination was significantly shorter among vaccinated patients compared to references (Figure), but after adjusting for number of the same type of infection before vaccination, there was no longer a statistically significant difference after vaccination (p=0.12) and (p=0.09), respectively.

Conclusion: A single dose of heptavalent pneumococcal conjugate vaccine may decrease the risk of putative serious pneumococcal infection up to 10 years after vaccination in adult patients with inflammatory arthritis receiving immunomodulating treatment. However, the vaccine does not seem to prolong the time to first serious infection.

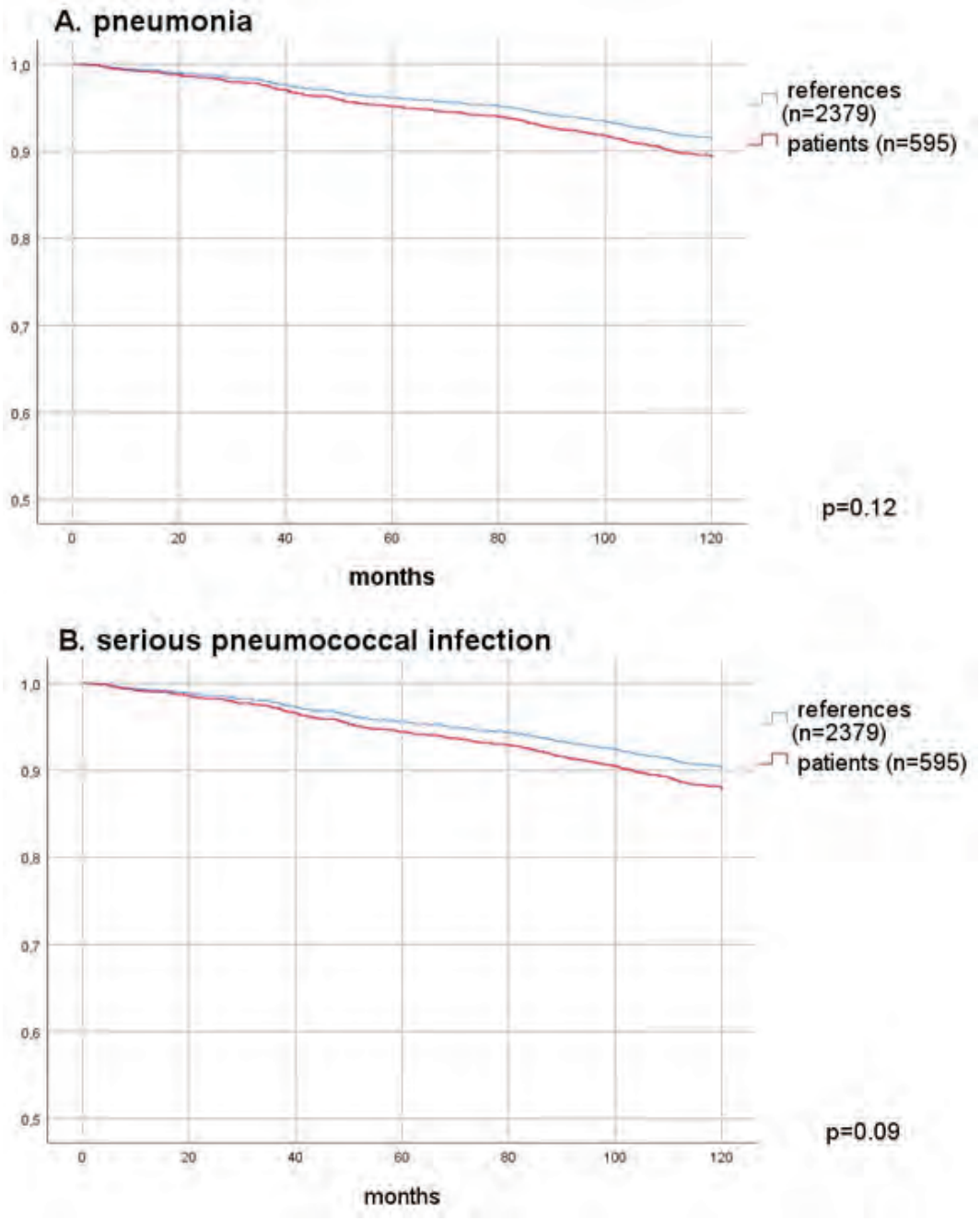

Figure. Cox regression; Time to first event, death or loss of follow-up after date of vaccination for pneumonia only (A), all serious pneumococcal infections (B), adjusted for number of events before date of vaccination.

Disclosure: J. Nagel, None; **G. Jönsson**, None; **J. Nilsson**, None; **C. Manuswin**, None; **M. Englund**, Pfizer, 5; **T. Saxne**, None; **P. Geborek**, None; **M. Kapetanovic**, None.

Abstract Number: 0457

Improving Pneumococcal Vaccination Rates in Immunosuppressed Rheumatology Patients

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Infection-related Rheumatic Disease

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: The Centers for Disease Control and Prevention recommends pneumococcal vaccination of high-risk patients, including patients on iatrogenic immunosuppression. Many patients seen in the rheumatology clinic are at increased risk of invasive pneumococcal infection secondary to primary or acquired immunodeficiencies. A quality improvement project to increase pneumococcal vaccination rates in patients with systemic lupus erythematosus (SLE) and mixed connective tissue disease (MCTD) was started in September 2016. After increasing the

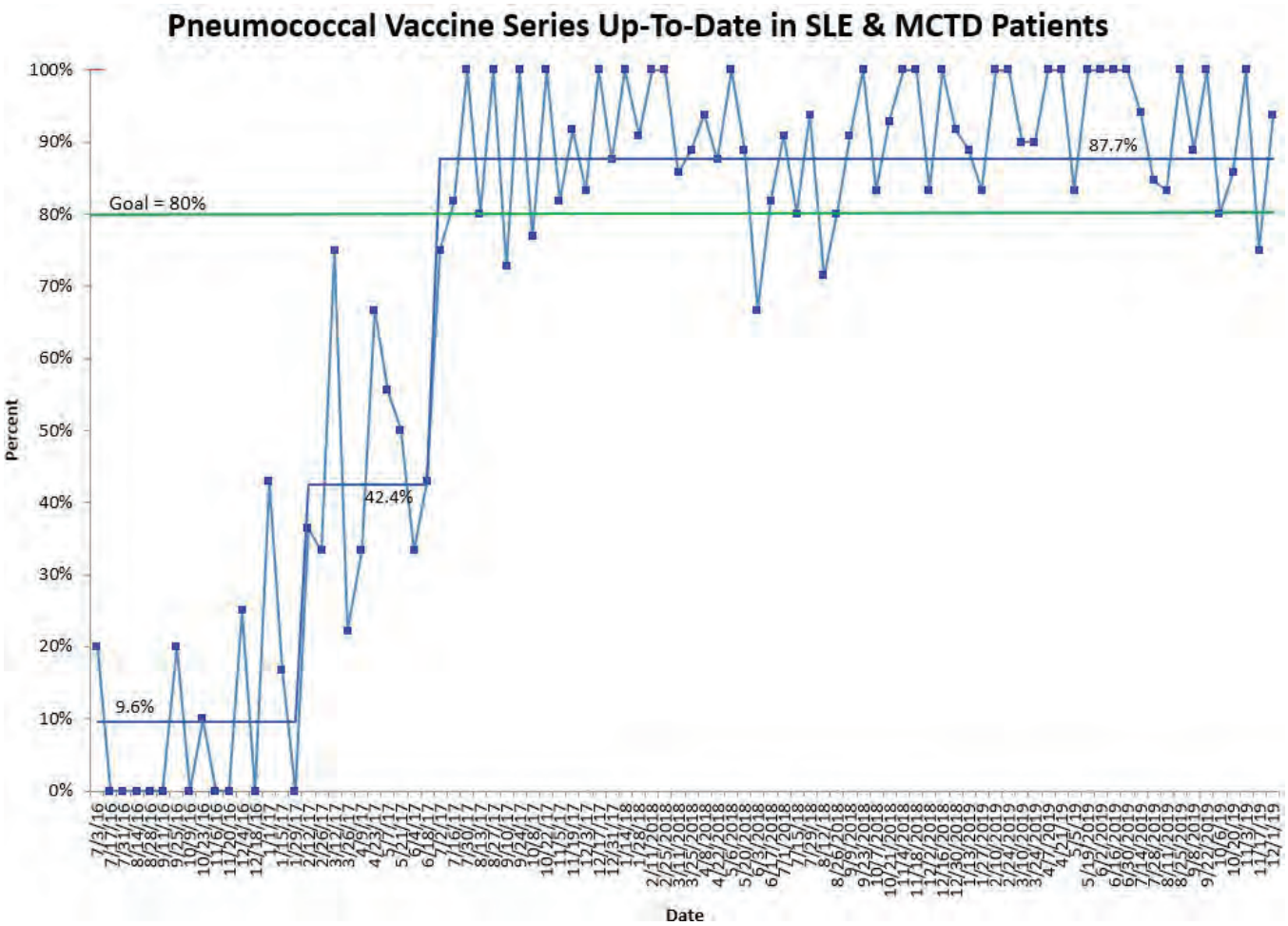

Figure 1. Pneumococcal vaccine series up-to-date in SLE and MCTD patients.

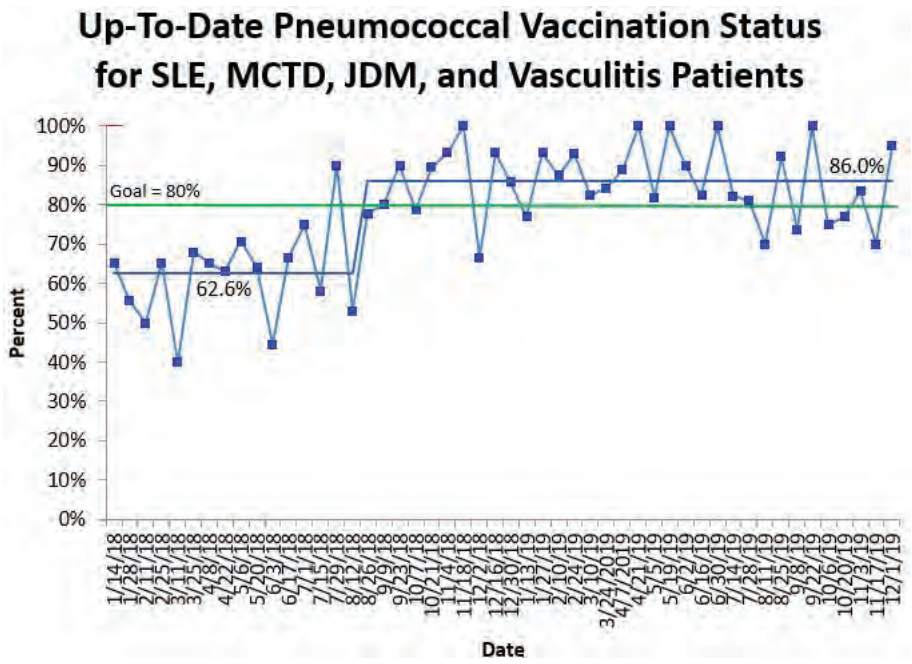

Figure 2. Pneumococcal vaccinations up-to-date in SLE, MCTD, JDM and vasculitis patients on immunosuppression.

combined pneumococcal vaccination rate to 87.7% for those with SLE and MCTD, our new aim in July 2018 was to have 80% of patients on immunosuppression with SLE, MCTD, juvenile dermatomyositis (JDM) and systemic vasculitis up-to-date on pneumococcal vaccinations by July 2019.

Methods: Our division established a project team and utilized quality improvement methodology including a driver diagram, process map, fishbone diagram, and plan-do-study-act cycles. Two process measures were created: 1) being up-to-date on the 13-valent pneumococcal conjugated vaccine (PCV13) and 2) being up-to-date on the 23-valent pneumococcal polysaccharide vaccine (PPSV23). Our outcome measure was being completely up-to-date on pneumococcal vaccinations. Eligible patients from September 2016 to June 2018 were all SLE and MCTD patients. From July 2018 onward, JDM and vasculitis patients on immunosuppression were eligible along with all SLE and MCTD patients. Interventions included: generating an immunization algorithm, creating a report of eligible patients, providing physician and nurse education, sending email reminders, and performing pre-visit planning. Control charts were made to evaluate for change over time.

Results: Data collection of pneumococcal immunization rates began in July 2016 and is ongoing. There were shifts in the center line for all three quality measures in both phases of our project indicating a significant increase in vaccination rates. Average PCV13 rate for SLE and MCTD patients increased from 32.1% to 91.5%, and PPSV23 rate went from 17.1% to 89.9%. Combined pneumococcal vaccination rate for SLE and MCTD patients increased from 9.6% to 87.7%, and this mean has been sustained for over two years (**Figure 1**). Pneumococcal vaccination rates also significantly increased for phase 2 with SLE, MCTD, JDM, and vasculitis patients: 70.5% to 92.2% for PCV13, 63.8% to 86% for PPSV23, and 62.6% to 86% for the combined pneumococcal vaccination rate (PCV13 and PPSV23) (**Figure 2**). There have been no significant known adverse events related to the vaccinations.

Conclusion: Using quality improvement methodology, pneumococcal vaccination rates significantly increased and have been sustained in our immunosuppressed pediatric rheumatology patients. We continue to prioritize this important initiative through a multi-specialty project and through pre-visit planning by identifying additional rheumatology patients on immunosuppression that are eligible for pneumococcal vaccination.

Disclosure: J. Harris, None; **M. Holland**, None; **E. Fox**, None; **A. Ivy**, None; **M. Ibarra**, None; **C. Hoffart**, None; **J. Jones**, None; **L. Favier**, None; **A. Cooper**, None.

Abstract Number: 0458

Rapid Implementation of a Multidisciplinary COVID-19 Cytokine Storm Syndrome Task Force

Bibi Ayesha[1], Anand Kumthekar[1], Ruchi Jain[2], Sneha Patel[3], Manish Ramesh[1], Denisa Ferastraoaru[4], Golda Hudes[4], Merhunisa Karagic[4], Sheema Zafar[1], Rachel Bartash[4], Natalia Vasquez-Canizares[5], Elizabeth Kitsis[6], Clement Tagoe[7], Dawn Wahezi[5], Tamar Rubinstein[8] and Anna Broder[3], [1]Montefiore Medical Center, Bronx, NY, [2]Montefiore Medical Center, Irvington, NY, [3]Albert Einstein College of Medicine/Montefiore Medical Center, Bronx, NY, [4]Montefiore Medical Center, Bronx, [5]Albert Einstein College of Medicine, Bronx, NY, [6]Albert Einstein College of Medicine, New York, NY, [7]Albert Einstein College of Medicine, Fresh Meadows, NY, [8]Albert Einstein College of Medicine / Montefiore Medical Center, White Plains, NY

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Infection-related Rheumatic Disease

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: Coronavirus disease (COVID-19) infected patients present with a state of ongoing inflammation and an exaggerated inflammatory state due to unregulated cytokine release called the cytokine storm syndrome (CSS).Early identification and timely, management of CSS is needed for avoiding an untoward outcome. Multi-disciplinary involvement is needed because of the complexity of the syndrome and the multi-systemic presentation. We summarize a novel approach and our experience in the formation and functioning of multidisciplinary COVID-19 CSS task force at Montefiore Medical Center in the Bronx, New York City (NYC).

Methods: As adult and pediatric rheumatologists, allergy and immunologists (AI) are well versed with managing inflammatory disorders, after input of infectious disease (ID) and critical care team (CCM) specialists, with consensus developed a set of 4 clinical and 6 laboratory parameters to potentially help in early identification of COVID 19 patients progressing towards CSS

Every consulted patient was reviewed by a sub-specialist and discussed in daily multidisciplinary virtual conference. A consensus recommendation was made regarding steroid therapy or biologic therapy if deemed appropriate. All

Clinical Parameters	Laboratory Parameters
Persistent Fever ≥ 101°F for 48 hours	Ferritin ≥1000 ug/L
Systolic BP ≤ 90 (not responding to IV fluids)	CRP ≥ 30 mg/dl or change in CRP ≥ 15 mg/dl
PaO2/FiO2 ≤ 200 in intubated patients or Increasing oxygen requirement in non-intubated patients.	AST ≥ 150 IU/L
	Hemoglobin ≤ 9 g/L
	Platelets ≤ 100 K/ul
	Absolute neutrophil count ≤ 7.7 K/ul

Abbreviations: BP: Blood pressure, CRP: C-reactive protein, AST: Aspartate Amino transferase

Table 1. Clinical and Laboratory Parameters based on consensus recommendations of the COVID-19 CSS Task Force.

Variable	Total (N=288)	Biologic Therapy (N=31)	No Biologic Therapy (N=257)	P value
Age, years- Median (IQR)	62 (51-70)	53 (32-63)	62.5 (52-70)	0.01
Male - no (%)	197 (68)	22 (71)	175 (68)	0.75
Ethnicity - no (%)				0.63
Non-Hispanic	149 (52)	15 (48)	134 (52)	
Hispanic	122 (42)	13 (42)	109 (42)	
Race - no (%)				0.56
Black or African American	88 (31)	9 (29)	79 (31)	
White	25 (9)	1 (3)	24 (9)	
Asian	24 (8)	2 (6)	22 (9)	
Presenting Symptoms - No/Total no (%)				
Subjective Fever	197 (68)	26 (84)	171 (67)	0.05
Cough	188 (65)	20 (65)	168 (65)	0.86
Dyspnea	245 (85)	27 (87)	218 (85)	0.74
Hyperglycemia	109 (38)	16 (52)	94 (37)	0.21
Acute Kidney Injury	116 (40)	13 (42)	103 (40)	0.86
Diarrhea	230 (80)	5 (16)	51 (20)	0.81
DVT	20 (7)	1 (3)	19 (7)	0.39
PE	9 (3)	2 (7)	7 (3)	0.26
CVA	15 (5)	1 (3)	14 (5)	0.60
Required ICU Admission	177 (61)	26 (84)	151 (59)	0.01
New Onset Dialysis	60 (21)	6 (19)	54 (21)	0.83
Anoxic Brain Injury	8 (3)	0	8 (3)	0.32

Table 2. Characteristics of COVID-19 patients evaluated by the CSS Task Force

biological therapy recommended by the CSS task force required a final approval from designated physician from ID or CCM.

Results: Between April 4,2020 and May 7,2020, the CSS consult service evaluated a total of 288 patients. Patients who received biologic therapy were younger with a median age of 53 years (IQR= 32-63 years) versus 62.5 years (52-70 years) in the no-biologic group (p=0.008). A higher proportion of patients receiving biologics were in the critical care setting {26 (84%) vs 151 (59%), p= 0.006}, were on mechanical ventilation {26 (84%) vs 146 (57%), p=0.003} and on vasopressors {22 (71%) vs 111 (43%), p=0.003}. Patients who received biologics were more likely to have a longer median duration of steroid therapy 12.5 days (IQR= 6-15 days) vs 8 days (IQR= 5-12 days) (p=0.01).

Conclusion: To our knowledge, this is the first multi-disciplinary team model collaborative effort to provide consensus recommendations for COVID-19 patients at risk of developing CSS, which is a unique experience at our institution where multiple sub-specialities came together to create a consult service to help early identify and treat patients with COVID-19 CSS, at a time of unparalleled COVID-19 surge with limited resources in NYC.

Variable	Total (N=288)	Biologic Therapy- Yes (N=31)	BiologicTherapy- No (N=257)	P value
CSS consult Steroid Recommendations no (%)				0.361
No steroids	61 (21)	5 (16)	56 (22)	
Continue same steroid regimen	133 (46)	17 (55)	116 (45)	
New Steroid initiation	49 (17)	8 (26)	41 (16)	
Increase steroids	16 (6)	0	16 (6)	
Decrease steroids	29 (10)	1 (3)	28 (11)	
Pulse Steroids	1 (<1)	0	1 (<1)	
Total days of steroid therapy - Median (IQR)	8 (5-13)	12.5 (6-15)	8 (5-12)	0.01
Anticoagulation	264 (91)	30 (97)	234 (91)	0.36
Enrolled in Clinical Trial	38 (13)	3 (10)	35 (14)	0.54

Table 3. Treatment Profile of Patients Evaluat-ed by the COVID-19 CSS Task Force

Disclosure: B. Ayesha, None; **A. Kumthekar**, None; **R. Jain**, None; **S. Patel**, None; **M. Ramesh**, None; **D. Ferastraoaru**, None; **G. Hudes**, None; **M. Karagic**, None; **S. Zafar**, None; **R. Bartash**, None; **N. Vasquez-Canizares**, None; **E. Kitsis**, None; **C. Tagoe**, None; **D. Wahezi**, None; **T. Rubinstein**, None; **A. Broder**, None.

Abstract Number: 0459

Autologous Hematopoietic Stem Cell Transplantation for Behçet's Disease: A Retrospective Survey of Patients Treated in Europe, on the Behalf of the Autoimmune Diseases Working Party of the European Society for Blood and Bone Marrow Transplantation

Mathieu Puyade[1], Patel Amit[2], Yeong Jer Lim[3], Norbert Blank[4], Manuela Badoglio[5], Francesca Gualandi[6], David D Ma[7], Raffaella Greco[8], Natalia Maximova[9], Tobias Alexander[10] and John A Snowden[11], [1]Service de Médecine Interne et Maladies Infectieuses ,CIC-1402 Centre Hospitalier Universitaire de Poitiers, Poitiers, France, [2]The Christie NHS Foundation Trust, Manchester, United Kingdom, [3]University of Liverpool, Liverpool, United Kingdom, [4]Department of Hematology, Oncology and Rheumatology, Internal Medicine V, University Hospital of Heidelberg, Eppelheim, Germany, [5]EBMT ADWP Office, Paris, France, [6]U.O. EMATOLOGIA Centro Trapianti Midollo - OSPEDALE POLICLINICO SAN MARTINO, GENOVA, Italy, [7]Department of Haematology and BM Transplantation, St Vincent's Hospital Sydney and St Vincent's Clinical School, Faculty of Medicine, Sidney, New South Wales, Australia, [8]Ematologia Trapianto Midollo San Raffaele, Milano, Italy, [9]Institute for Maternal and Child Health – IRCCS Burlo Garofolo, Trieste, Italy, [10]Charité - Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Rheumatology and Clinical Immunology, Berlin, Deutsches Rheuma-Forschungszentrum, Berlin, Germany, [11]Sheffield Teaching Hospitals NHS Foundation Trust, Sheffield, United Kingdom

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases I: Mechanisms of Disease

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Table 1 Characteristics of the patients and outcomes.

	Median (range) or % (N=10)	Missing data
Sex (Female)	40 %	0
Age at onset (years)	24 (9-50)	0
Age at transplantation (years)	32 (26-51)	0
Number of previous lines	4 (2-11)	0
Active disease before mobilization	100 %	1
Mobilization		1
Cyclophosphamide + G-CSF	8	
G-CSF alone	1	
Dose of cyclophosphamide during mobilization	2 (1.5-4)	0
Conditioning regimen		0
Melphalan 200mg/m²	5	
Cyclosphosphamide 200 mg/kg –ATG 4.5 mg/kg	2	
BEAM	3	
Number of days before engraftment:		
Neutrophils > 0.5 x10⁹/L	11.5 (6-13)	0
Platelets > 50 x10⁹/L	14 (13-20)	1
Complications before Day +100		
Fever of Unknown Origin	2 patients/2 episodes	
Infectious	2 patients/2 episodes	
Other:	1 patient /3 episodes	
Atrial Fibrillation, Line associated DVT, Depression		
Complications after Day 100	0	0
Overall Response		0
CR	8	
DDPR	1	
No response	1	
Major Relapse (n=1)		0
Uveitis	1	
Minor Relapse (n=2)		0
Aphtosis	2	
Arthralgia	1	
Median Follow-up (months)	48 (6-252)	0

ATG : Anti Thymocyte Globulin, BEAM : BCNU – Etoposide- Cytarabine- Melphalan, CR = Complete Remission : no evidence for disease activity in patients with daily prednisolone equivalent dosage ≤ 7.5mg and absence of disease-modifying drugs, DVT : Deep Venous Thrombosis, DDPR : Drug-Dependent Partial Response *ig* any documented clinical and/or laboratory response in patients receiving glucocorticoids ≥7.5mg daily prednisolone dosage and/or disease-modifying drugs.

Background/Purpose: Behçet's Disease (BD) is a rare autoimmune disease mostly presenting with recurrent oral and genital aphtosis, ulcers, and uveitis. Rare patients are refractory to conventional treatments. Autologous hematological stem cell transplantation (AHSCT) is a standard of care in other autoimmune diseases. Some patients with BD have been treated with AHSCT based on compassionate use.

Methods: Evaluate the outcome of AHSCT in adult patients with BD treated in member centers of the European Society for Blood and Marrow Transplantation (EBMT). Adults who received AHSCT primarily for BD were identified retrospectively in the EBMT registry and/or in published literature. Data were extracted from either medical records of the patient or from publications.

Results: Eight out of 9 cases reported to the registry and extracted data of 2 further patients from literature were analyzed. Four were female, median age at onset of BD was 24y (range 9-50). Median age at AHSCT was 32y (27-51). Patients had received median 4 (2-11) prior lines of therapy (89% corticosteroids, 50% methotrexate, anti-TNFa or cyclophosphamide). All patients had active disease before mobilization. Conditioning regimen was heterogeneous. Median follow-up was 48 months (range 6-240 months). No treatment-related mortality was reported. At last

Table 2 Individual characteristics and outcome for patients with Behçet's disease treated with autologous stem cell transplantation in European Society of Blood and bone Marrow Transplantation centers (N=10)

a) Before transplantation

Patient	Center	Sex	Age at onset	Organ involvement	Previous treatments	Status of the disease before transplantation	Indication of transplantation
1	Trieste	F	29	G,O, Oc, V, GI	TS, SC, CSA, AZA	Active	G, O, Oc, V, GI
2	Heidelberg	M	48	G,O, Oc, V, N, K, L	SC, iCYC, oCYC	Active	G, O, Oc, K, L
3	Heidelberg	M	25	G,O, S, V, CI	SC, MTX	Active	G, O, Oc, CI
4	Foggia	M	22	N*	SC, CLB	Active	N
5	Foggia	M	23	N*	SC, CLB	Active	N
6	Genova	F	20	G,O, Oc, S, A, N, GI	TS, SC, iCYC,	Active	N, GI
7	Sydney	F	16	G,O, Oc, S	SC, MTX, IFN, IFX, RTX, PYX, oCYC, CSA, TCZ	Active	Oc
8	Liverpool	M	24	G,O, Oc, S, V	SC, MTX, IFX, iCYC, TCL, MMF, ETN	Unknown	Unknown
9	Liverpool	F	9	G,O, S, P , A, GI	TS, SC, COL, DAP, MTX, IFX, ADA, ATZ, AZA, LF, ETN	Active	O, GI
10	Liverpool	M	50	G,O, S, V, A, N, GI, CI	IFN, ATZ, AZA, MMF, ETN, CTZ	Active	V, GI, CI

* patients extracted from the literature, fulfilling International Study Group criteria of Behcet's Disease, A = Arthritis, ADA = Adalimumab, ATZ=Alemtuzumab, AZA = Aziathoprine, CI = Cardiac Involvement, CLB = Chlorambucil COL= Colchicine, SC = Systemic Corticoids, CSA= Cyclosporine, CTZ = Certolizumab, DAP = Dapsone, ETN = Etanercept, FU = Follow-up, iCYC = intravenous Cyclophosphamide, IFX = Infliximab, IFN = Interferon alpha, G = Genital aphtosis, GI = Gastro-Intestinal Involvement, K= Kidney, L = Lung, LF = Leflunomide, MMF = Mycophenolate Mofetil, MTX = Methotrexate, N= Neurological involvement, O = Oral aphtosis, Oc = Ocular involvement, oCYC = Oral Cyclophosphamide, P = Pathergy test positive, PYX = Pentoxifylline, RTX = Rituximab, S = Skin involvement (skin ulcer or erythema nodosum), TCL = Tacrolimus, TCZ = Tocilizumab, TS = Topical Steroids.

Table 2
b) Characteristics of the transplantation and outcome

Patient	Year of transplant	Age at transplant	Mobilization	Conditioning regimen	Complications before D100	OR	FU in this study (months)	Case previously published (FU reported in months)
1	1999	33	G-CSF	iCYC+ATG		CR	48	No
2	1999	49	iCYC + G-CSF	Melphalan	Fever of unknown origin	CR	252	Yes (96)
3	1999	31	iCYC + G-CSF	Melphalan	Fever of unknown origin	CR	252	Yes (72)
4	Before 2002	26	iCYC + G-CSF	BEAM		CR	48	Yes (48)
5	Before 2002	26	iCYC + G-CSF	BEAM		CR	48	Yes (48)
6	2002	30	iCYC + G-CSF	BEAM		NR	6	No
7	2011	49	iCYC + G-CSF	iCYC+ATG		DDPR*	48	No
8	2009	29	iCYC + G-CSF	Melphalan		CR*	24	No
9	2016	42	iCYC + G-CSF	Melphalan	Pneumonia (Rhinovirus + Klebsiella Pneumoniae), AF, Line-DVT, Depression	CR*	37	No
10	2016	51	iCYC + G-CSF	Melphalan	Pneumonia	CR	96	No

* : Relapse, AF : Atrial Fibrillation, ATG = Anti Thymocyte Globulin, BEAM = Bicnu, Etoposide, Aracytine, Melphalan,, CR = Complete Remission : no evidence for disease activity in patients with daily prednisolone equivalent dosage ≤ 7.5mg and absence of disease-modifying drugs, DDPR : Drug- Dependent Partial Response = any documented clinical and/or laboratory response in patients receiving glucocorticoids ≥7.5mg daily prednisolone dosage and/or disease modifying drugs, DVT : Deep Venous Thrombosis, iCYC = intravenous Cyclophosphamide, G-CSF : Granular Colony Stimulating Factor, NR : No Response, OR : Overall Response,

follow-up, one patient did not respond, 3 patients relapsed with pan-uveitis (n=1), aphtosis (n=2) and arthralgia (n=1). Six patients were in CR without any further treatment. No late complications were reported.

Conclusion: AHSCT is feasible and safe in multi-refractory patients with BD and has the potential to stabilize BD in patients with life-threatening involvements.

Disclosure: M. Puyade, None; **P. Amit**, None; **Y. Lim**, None; **N. Blank**, None; **M. Badoglio**, None; **F. Gualandi**, None; **D. Ma**, None; **R. Greco**, None; **N. Maximova**, None; **T. Alexander**, None; **J. Snowden**, Sanofi, 8, Jazz Pharmaceuticals, 8, Janssenn and Jansenn, 8, Actelion Pharma, 8, Mallinckrodt, 8, Gilead, 8, Kiadis, 6.

Abstract Number: 0460

Lymphocyte Clonal Expansion Distinguishes Different Forms of Uveitis

Michael Paley[1], Lynn Hassman[1], Philip Ruzycki[1], Ekaterina Esaulova[1], Grace Paley[1], Jennifer Laurent[1], Luke Springer[1], Lacey Feigl[1], Maxim Artyomov[1] and Wayne Yokoyama[2], [1]Washington University, Saint Louis, [2]Washington University, St Louis, MO

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases I: Mechanisms of Disease
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Anterior uveitis is a form of ocular inflammation associated with rheumatologic disease and can be categorized as granulomatous or non-granulomatous. Whether different ocular manifestations are associated with distinct immune responses, however, remains unclear. Here, we evaluated lymphocyte clonal expansion in granulomatous and non-granulomatous uveitis to determine whether putative antigen-driven T or B cell responses distinguish clinical presentations of ocular inflammation.

Methods: We performed single cell RNA-sequencing (scRNAseq) to obtain an unbiased gene expression survey of aqueous and blood immune cells in subjects with different forms of uveitis. This analysis allowed quantification, cell type identification, and transcriptional profiling of individual lymphocytes within the inflamed eye as compared to cells in circulation, along with T cell receptor and B cell receptor sequencing to determine clonotype distribution.

Results: The majority of aqueous immune cells were CD4 T cells, with smaller contributions of CD8 T cells, B cells, NK cells, and myeloid cells. Analysis of clonal expansion in granulomatous uveitis revealed highly expanded lymphocyte clonotypes, but only in one T or B cell lineage. Coincident with the clonal expansion were transcriptional signatures of T cell receptor signaling and effector differentiation. In contrast, non-granulomatous uveitis was not associated with robust clonal expansion in any T or B cell lineage analyzed.

Conclusion: Here, these data suggest that the clinical presentation of uveitis may be the result of distinct pathogenic mechanisms, with granulomatous inflammation arising from a select few antigen-specific T or B cells. Furthermore, this extensive clonal expansion was seen in a different lymphocyte lineage for each individual, suggesting a distinct antigen-specific response in each patient and highlighting the potential to identify personalized therapeutic targets.

Disclosure: M. Paley, None; **L. Hassman**, None; **P. Ruzycki**, None; **E. Esaulova**, None; **G. Paley**, None; **J. Laurent**, None; **L. Springer**, None; **L. Feigl**, None; **M. Artyomov**, None; **W. Yokoyama**, None.

Abstract Number: 0461

High-Throughput Single-Cell Analysis Reveals Unique Lung Cellular Subsets in a Murine Model of Rheumatoid Arthritis-Inflammatory Lung Disease

Rohit Gaurav[1], Ted Mikuls[1], Geoffrey Thiele[1], Amy Nelson[1], Meng Niu[1], Chittibabu Guda[1], James Eudy[1], Austin Barry[1], Debra Romberger[1], Michael Duryee[1], Bryant England[1] and Jill Poole[1], [1]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases I: Mechanisms of Disease

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: Rheumatoid arthritis (RA)-associated inflammatory lung disease is an extra-articular manifestation of RA associated with increased morbidity and mortality, whose precise molecular mechanisms remain undetermined. We established a novel mouse model of combining the collagen-induced arthritis (CIA) model with the organic dust extract (ODE)-induced airway inflammatory disease model to demonstrate that combined exposures (CIA+ODE) increased arthritis, autoantibody levels, and polarized the lung towards pre-fibrotic inflammatory processes. Utilizing this animal model, we aimed to identify relevant cellular and protein mediators through high-throughput single-cell analysis.

Methods: Arthritis-prone DBA/1J mice were assigned to 1 of 4 treatment groups: Sham, CIA, ODE, and CIA+ODE for 5 weeks. Whole lung cells were processed for single cell RNA-sequencing (scRNA-seq). In separate studies, 4 defined myeloid-derived immune cell populations consisting of macrophages, monocytes/macrophages, monocytes, and neutrophils were isolated from whole lung of exposed mice by fluorescence activated cell sorting (FACS) with gene expression determined by NanoString (771 genes). Data are represented as fold-change compared to Sham from 3 experiments (2-3 mice/group/experiment) using two-way ANOVA.

Results: By scRNA-seq, 14 discrete lung immune cell populations were identified through unsupervised clustering and respective gene expression. Cell populations included 3 neutrophils (inflammatory, resident/transitional, autoreactive/myeloid derived suppressor), 5 macrophages (airspace, differentiating/recruited, recruited, resident/interstitial, and proliferative airspace), 2 T-cells (differentiating and effector), and a population of inflammatory monocytes, dendritic cells, B-cells and natural killer cells (**Figure 1)**. Inflammatory monocytes, autoreactive/suppressor neutrophils, and recruited/differentiating macrophage subpopulations were predominantly ascribed to arthritis induction (CIA and

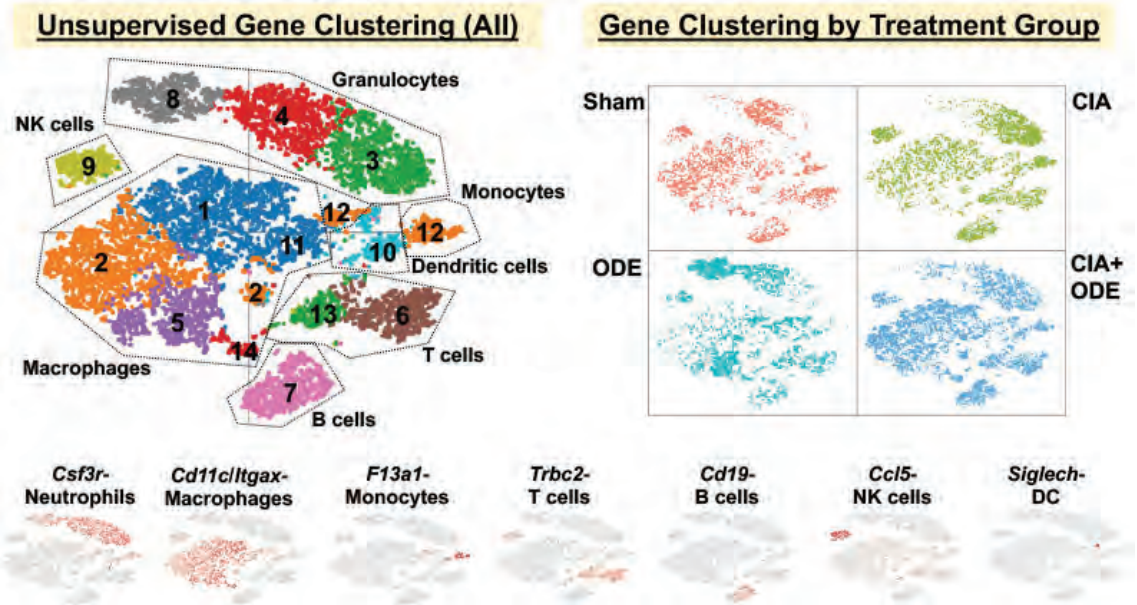

Figure 1. Single-cell RNA-sequencing analysis. Top left panel shows unsupervised gene clustering of all CD45+ gene expressing lung cells when all treatment groups are aggregated. Cell names are ascribed based upon gene expression (bottom panel). Top right panel depicts clustering of the defined aggregated clustering across treatment groups with dotted circles highlighting macrophages, monocytes, and granulocytes. Arbitrary numbers (1, 2, etc.) designate unique gene clusters determined by unsupervised clustering.

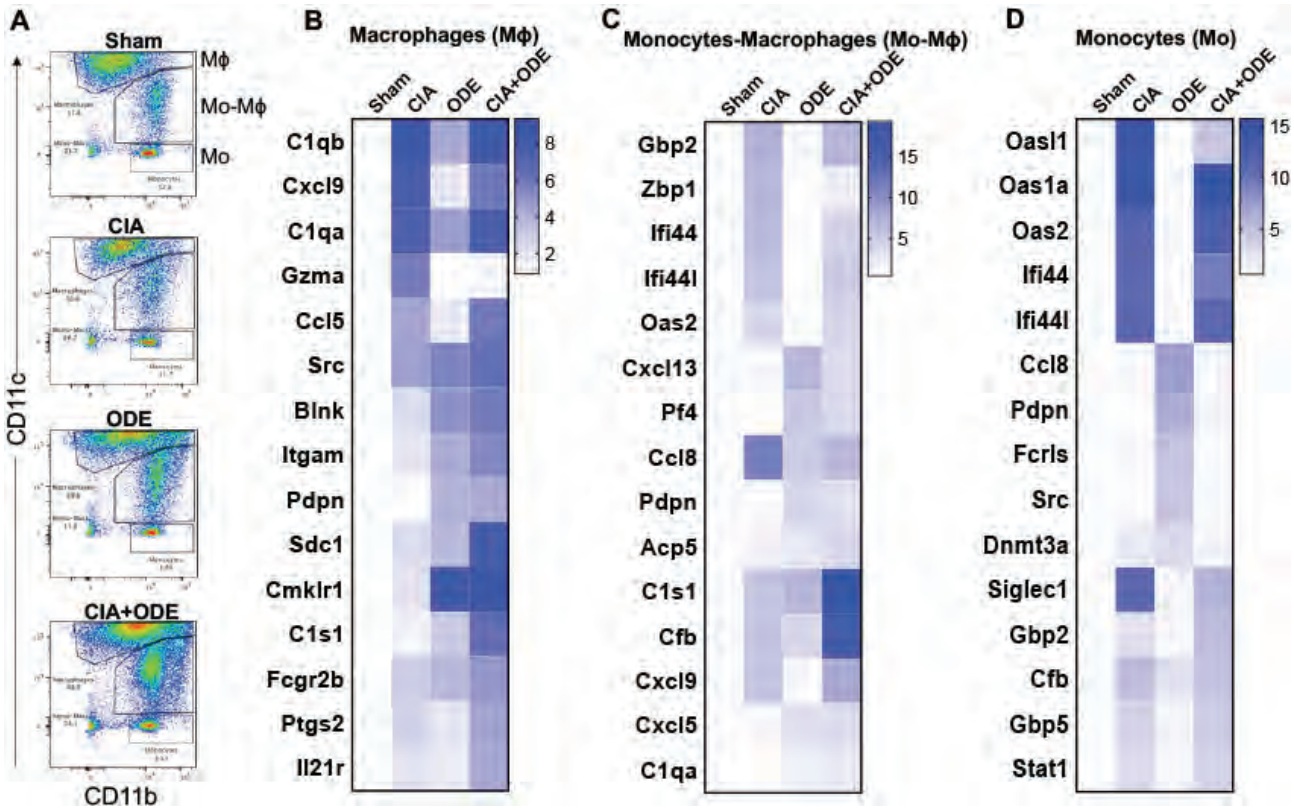

Figure 2. Lung cell populations of macrophages (MΦ) and monocytes (Mo) isolated by FACS and gene expression analysis among treatment groups. A, Representative dot plots of macrophages (CD11chigh CD11bvariable), monocytes-macrophages (CD11cintermediate CD11bhigh), and monocytes (CD11c– CD11bhigh) from each treatment of Sham, CIA, ODE, and CIA+ODE shown. B, C, and D Heatmaps of each cell population depicting the fold-change of top 5 genes/treatment group (CIA, ODE and CIA+ODE), normalized to 20 housekeeping genes and compared to Sham.

CIA+ODE). Genes highly expressed with arthritis induction across lung cell populations of myeloid origin included interferon-related, autoimmunity, and suppressive genes (e.g. *Ifit3b*, *Ifit3*, *S100a8*, and *S100a9*). NanoString analysis of the 4 isolated lung myeloid-derived populations were consistent with scRNA-seq findings (**Figure 2,3**). Several immunosuppressive and autoimmune genes (e.g. *Oasl1*, *Oas2*, *Ifit3*, *Gbp2*, *Ifi44*, *Ifi44l*, *Zbp1*, and *Ifit1*) were disproportionately expressed in lung cell populations of neutrophils and macrophages/monocytes among CIA and CIA+ODE groups. Complement cascade genes (e.g. *C1s1*, *Cfb*, *C1qa*, and *C1ra*) were uniquely increased in the co-exposure (CIA+ODE) across all 4 cell populations.

Conclusion: Recruited and inflammatory macrophages/monocytes and neutrophils expressing suppressive and autoimmune genes in systemic autoimmunity might contribute towards pro-fibrotic inflammatory responses in the lung following airborne biohazard exposures. Targeting these cellular features and/or signature genes could lead to novel approaches in RA-associated inflammatory lung disease.

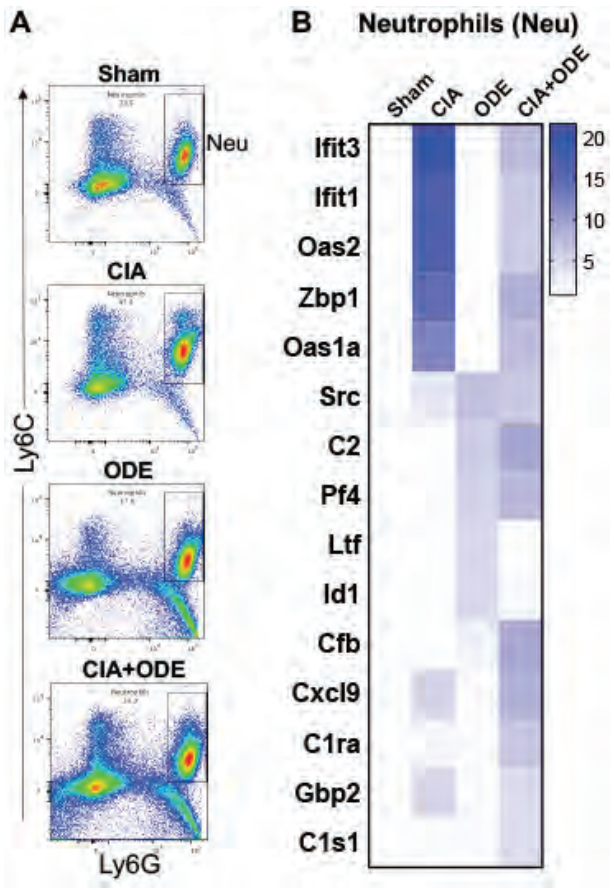

Figure 3. Lung cell populations of neutrophils (Neu) isolated by FACS and gene expression analysis among treatment groups. A, Representative dot plots of neutrophils (Ly6C+ Ly6G+) from each treatment of Sham, CIA, ODE, and CIA+ODE shown. B, Heatmap depicting the fold-change of top 5 genes/treatment group (CIA, ODE and CIA+ODE), normalized to 20 housekeeping genes and compared to Sham.

Disclosure: R. Gaurav, None; **T. Mikuls**, Horizon Therapeutics, 2; **G. Thiele**, None; **A. Nelson**, None; **M. Niu**, None; **C. Guda**, None; **J. Eudy**, None; **A. Barry**, None; **D. Romberger**, None; **M. Duryee**, None; **B. England**, None; **J. Poole**, None.

Abstract Number: 0462

Lupus-like Autoimmunity and Increased Interferon Response in Patients with STAT3-deficient Hyper-IgE Syndrome

Brian Dizon[1], Rishi Goel[2], Shuichiro Nakabo[2], Amanda Urban[2], Meryl Waldman[2], Lilian Howard[2], Dirk Darnell[2], Munir Buhaya[2], Sarfaraz Hasni[3], Mariana Kaplan[4], Alexandra Freeman[2] and Sarthak Gupta[1], [1]National Institutes of Health, BETHESDA, MD, [2]National Institutes of Health, Bethesda, [3]Lupus Clinical Trials Unit, NIAMS/NIH, Bethesda, MD, [4]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases I: Mechanisms of Disease

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: Autosomal dominant hyper-IgE syndrome (AD-HIES), also known as Job's syndrome, is a rare primary immunodeficiency caused by dominant-negative loss-of-function (LOF) mutations in signal transducer and activator of transcription 3 (STAT3). STAT3 LOF patients develop dermatitis, recurrent infections, and elevated serum IgE. Autoimmunity and auto-inflammation are common complication of primary immune deficiencies; however, systemic autoimmune features and the role of innate immune system are not well-characterized in AD-HIES.

Methods: A retrospective chart review of patients with STAT3 LOF seen at the National Institutes of Health was performed to identify patients who also had clinical and serologic features of systemic lupus erythematosus (SLE), as defined by American College of Rheumatology (ACR) 1997 classification criteria. To characterize lupus-associated innate immune dysregulation, type I interferon (IFN) stimulated genes (ISGs) were quantified by RT-PCR in neutrophils, *in vitro* neutrophil extracellular trap (NET) formation was measured by immunofluorescence, and serum anti-NET IgG autoantibodies were quantified by ELISA.

Results: We identified 10 out of 158 individuals (prevalence ~6.3%) with genetically confirmed STAT3 LOF mutations who developed systemic lupus erythematosus (SLE) or SLE-like manifestations, including immune complex glomerulonephritis (40%), cytopenias (50%), cutaneous disease (40%), and arthritis (40%). STAT3 LOF patients with SLE features were predominantly female (70%), and the onset of lupus and lupus-like disease features occurred between 12-24 years of age. All patients had positive ANA (100%), with a majority having anti-double-stranded DNA antibodies (90%), and hypocomplementemia (70%). Other lupus-associated-autoantibodies were also detected (**Table 1**). Immunosuppressive medications were required in 8 patients with systemic autoimmune features, which were well-tolerated and led to improvement in clinical symptoms. STAT3 LOF subjects with and without clinical features of SLE had increased expression of ISGs in neutrophils when compared to healthy controls. Increased spontaneous NET formation and anti-NET autoantibodies were observed in LOF STAT3 subjects, independent of the presence or absence of lupus-like symptoms and at higher levels than healthy controls (**Figure 1**).

Conclusion: Although autoimmunity is not a common finding in STAT3 LOF patients, we have identified SLE or SLE-like disease in about 6% of our cohort, with a high incidence of kidney involvement. These findings are associated

PATIENT	SEX	RACE	AGE[1]	STAT3 MUTATION	CLINICAL	RENAL	HEME	ANA	Anti-dsDNA	C3/C4	SEROLOGIES	ACR 1997	SLICC 2012	ACR 2017	DIAGNOSIS	MEDICATIONS	DISEASE STATUS
1	F	W	8	K658E	Alopecia, arthritis	Class III and V	ITP	+	+	Low	-	+	+	+	Lupus	IVIG, prednisone, hydroxychloroquine, methotrexate	Inactive
2	F	W	Teens	R382W	Discoid lupus, alopecia	No	Leukopenia	+	+	Low	+RF, anti-Sm, anti-RNP	+	+	+	Lupus	Methotrexate, hydroxychloroquine	Inactive
3	F	AA	21	I653del	Arthritis	Class IV and V progressing to ESRD and renal transplant	No	+	+	Low	+anti-ENA, SSA, and anti-SmRNP	+	+	+	Lupus	Mycophenolate, prednisone, tacrolimus, hydroxychloroquine	Inactive
4	F	AA	22	I653del	Arthritis, discoid lupus	Class III	No	+	+	Low	-	+	+	+	Lupus	Mycophenolate, prednisone, hydroxychloroquine	Inactive
5	M	AA, W	12	R382W	Jaccoud's arthropathy	Microscopic hematuria	AIHA	+	+	Low	-	+	+	+	Lupus	IVIG, prednisone, hydroxychloroquine	Active
6	M	PI, L	12	R417G	No	No	AIHA	+	-	Low	-	-	+	-	Lupus-like	IVIG, prednisone, rituximab	Active
7	F	W	24	R382W	No	C3 glomerulopathy	No	+	+	Normal	-	-	-	+	Lupus-like	Mycophenolate, hydroxychloroquine	Unclear[2]
8	M	W	22	R382W	Alopecia	No	No	+	+	Normal	-	-	-	-	Lupus-like	None	Inactive
9	F	W	18	V463E	No	IgA nephropathy	No	+	+	Normal	-	-	-	+	Lupus-like	None	Unclear[2]
10	F	W	11	V637M	No	No	Leukopenia, ITP	+	+	Low	+anti-Sm	-	+	+	Lupus-like	Hydroxychloroquine	Inactive

Table 1. Clinical characteristics of STAT3 LOF patients with lupus and lupus-like autoimmunity. Patients (n=10) with STAT3 LOF mutations were identified to have clinical and serologic features of lupus. Demographic information, disease manifestations, clinical laboratory data, and historic treatment protocols are shown. Diagnosis of lupus and lupus-like disease was made on the basis of fulfilling ACR 1997 classification criteria. Updated classification criteria for systemic lupus, SLICC 2012 and ACR 2017, are shown for comparison. Abbreviations are the following: W= white, AA= African-American, L= Latino, PI= Pacific Islander, ESRD= end-stage renal disease, ITP= idiopathic thrombocytopenic purpura, AIHA= autoimmune hemolytic anemia, IVIG= intravenous immunoglobulin, IVIG= intravenous immunoglobulin. 1Age at onset of lupus symptoms. 2Delineation of lupus and non-lupus symptoms is unclear at this time.

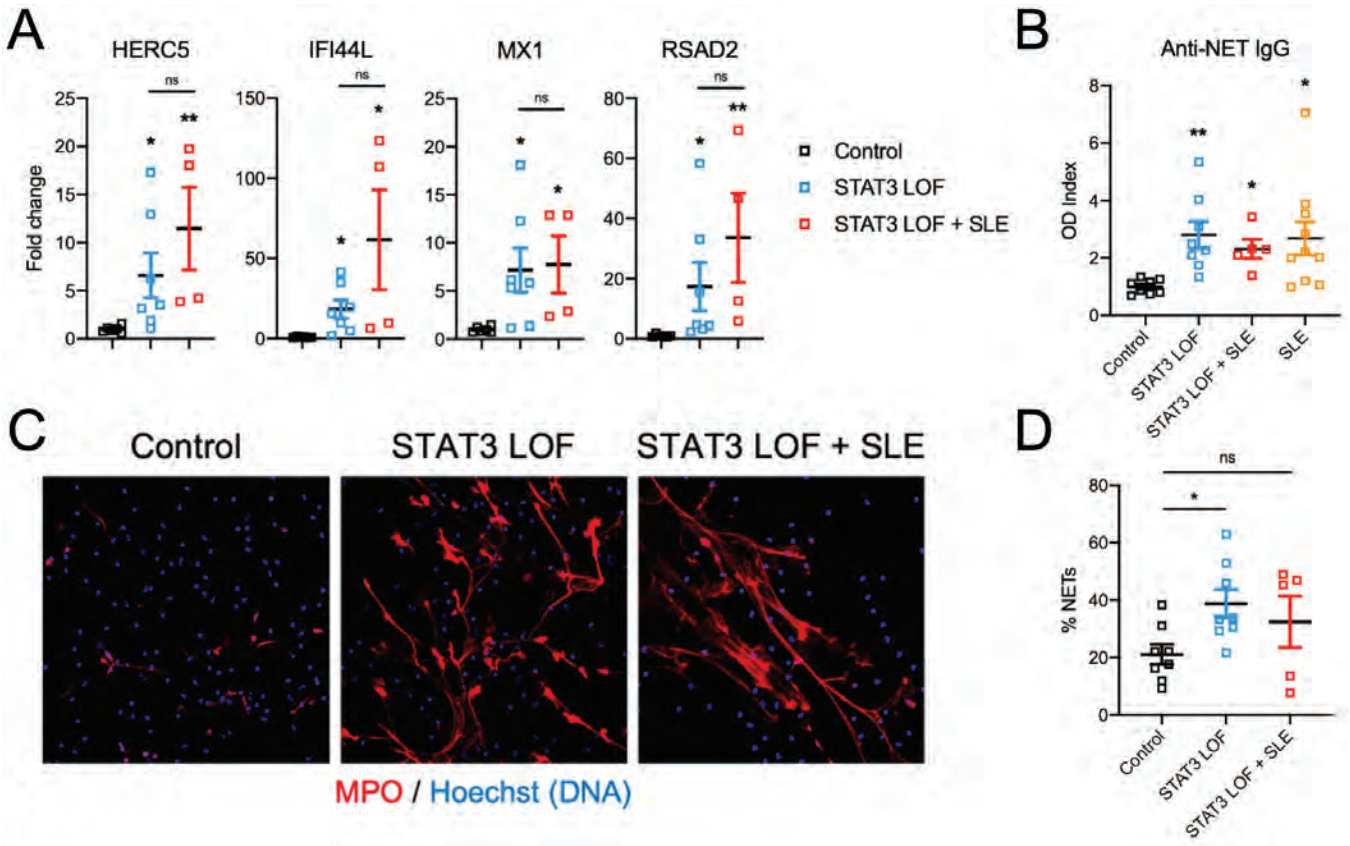

Figure 1. Increased interferon response, neutrophil extracellular trap (NET) formation, and anti-NET antibodies in patients with AD-HIES. (A) RT-PCR for interferon-stimulated gene expression in neutrophils from healthy controls (n=6), STAT3 LOF (n=7), and STAT3 LOF + SLE (n=4) patients. (B) Anti-NET IgG antibodies were measured in serum by ELISA in healthy controls (n=8), STAT3 LOF (n=8), STAT3 LOF + SLE (n=5), and SLE (n=10) patients. (C) Immunofluorescence for spontaneous NET formation in healthy controls (n=8), STAT3 LOF (n=7), and STAT3 LOF + SLE (n=5) patients; MPO (red), DNA (Hoechst, blue). (D) NETs were further quantified as percentage of neutrophils forming extracellular traps. Statistics were calculated by non-parametric Kruskal-Wallis test with Dunn's correction (A,B,C) or non-parametric Mann-Whitney test (D). *p>0.05, **p>0.01, ns=not significant.

with immune dysregulation characteristic of SLE including an increased IFN signature, NET formation, and various autoantibodies, including anti-NET antibodies. Significant immune dysregulation associated with dominant-negative STAT3 LOF mutations may explain the increased prevalence of systemic autoimmunity in these patients. Given this association, we recommend that patients with STAT3 LOF mutations be considered for rheumatology consultation for early recognition and treatment of SLE. The increased IFN signature also raises the potential for JAK-STAT modulation for therapy in these patients.

Disclosure: B. Dizon, None; **R. Goel**, None; **S. Nakabo**, None; **A. Urban**, None; **M. Waldman**, None; **L. Howard**, None; **D. Darnell**, None; **M. Buhaya**, None; **S. Hasni**, None; **M. Kaplan**, None; **A. Freeman**, None; **S. Gupta**, None.

Abstract Number: 0463

Molecular Diagnosis of Childhood Immunodysregulation, Endocrinopathy and Enteropathy X-linked (IPEX)-Like Syndrome and Implications for Clinical Management

Sarah Baxter[1], Tom Walsh[1], Silvia Casadei[1], Suleyman Gulsuner[1], Eric Allenspach[2], David Hagin[3], Gesmar Segundo[4], Troy Torgerson[5] and Mary-Claire King[1], [1]University of Washington, Seattle, [2]Seattle Children's Research Institute, Seattle, [3]Tel Aviv Medical Center, Tel Aviv, Israel, [4]Universidade Federal de Uberlandia, Uberlandia, Brazil, [5]Allen Institute, Seattle

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases I: Mechanisms of Disease
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Patients with early-onset immunodysregulation, endocrinopathy and enteropathy but without identified mutations in *FOXP3* are termed "IPEX-like," and undergo trial-and-error immunosuppressive treatment with highly variable outcomes. The scope of genetic variation in these patients has not been well studied, even though genetic diagnosis can be critical to determining appropriate medical treatment.

We sought to investigate the prevalence and breadth of genetic diagnoses in patients with early-onset immune dysregulation, polyendocrinopathy, and/or enteropathy who had previously normal *FOXP3* sequencing, in order to determine the clinical utility of broad panel sequencing in these patients.

Methods: Patients with IPEX-like disease who were referred from around the world for analysis of *FOXP3* but who had apparently normal sequencing were re-evaluated using an extensive targeted sequencing panel encompassing 464 genes associated with innate disorders of immunity. Prediction pipelines were used to identify potentially damaging mutations, including copy number variants (CNVs) and splice site alterations, which were validated by whole genome sequencing (WGS) and RT-PCR, respectively.

Results: A likely genetic diagnosis was identified in 59 of 131 (44%) patients. Seven patients were found to have *FOXP3* mutations not previously detected. Likely damaging variants in alternative genes were identified in 52 of the 124 (42%) remaining patients with intact *FOXP3.* Twenty-one patients had variants in genes known to cause IPEX-like Syndrome. The remaining genes belong to a wide array of phenotypic categories and biologic pathways. Within the patients carrying a known or candidate gene, over 75% had diagnoses which would have significantly altered therapeutic recommendations.

Conclusion: Patients with severe and early-onset immune dysregulation, polyendocrinopathy and/or enteropathy but without *FOXP3* mutations (IPEX-like syndrome) have a high mutational burden with a very high rate of clinically actionable findings. These patients should undergo broad genetic screening for innate diseases of immunity, with technologies capable of detecting coding variants, splice-site variants, and CNVs.

Disclosure: S. Baxter, None; **T. Walsh**, None; **S. Casadei**, None; **S. Gulsuner**, None; **E. Allenspach**, None; **D. Hagin**, None; **G. Segundo**, None; **T. Torgerson**, None; **M. King**, None.

Abstract Number: 0464

Assessment of the COVID-19 Pandemic from the Perspective of People with Rheumatic Musculoskeletal Diseases in Europe. Preliminary Results from the REUMAVID Study

Marco Garrido-Cumbrera[1], Helena Marzo-Ortega[2], José Correa-Fernández[3], Sergio Sanz-Gomez[4], Laura Christen[5] and Victoria Navarro-Compán[6], [1]Health & Territory Research (HTR), Universidad de Sevilla / Spanish Federation of Spondyloarthritis Associations, Sevilla, Spain, [2]The University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, UK, Leeds, United Kingdom, [3]Health & Territory Research (HTR), Universidad de Sevilla, Sevilla, Spain, [4]Health & Territory Research, Seville, Spain, [5]Novartis Pharma AG, Basel, Switzerland, [6]Hospital Universitario La Paz IdiPaz, Madrid, Pais Vasco, Spain

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes I: COVID-19
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: The COVID-19 pandemic is an unprecedented public health crisis affecting people worldwide, including those with rheumatic and musculoskeletal diseases (RMDS). REUMAVID aims to assess the impact of the COVID-19 pandemic and lockdown on the wellbeing, mental health, disease activity and function, access to healthcare and treatment, support services, and hopes and fears of people RMDs.

Methods: REUMAVID is an international collaboration led by the Health & Territory Research group at University of Seville, Spain, together with a multidisciplinary team including patient organizations and rheumatologists. The study consists of an online survey gathering data from patients with a diagnosis of 15 RMDs in Cyprus, France, Greece, Italy, Portugal, Spain, and the United Kingdom. Participants are recruited by patient organizations. Data is collected in two phases: 1) during the first peak of the COVID-19 pandemic (Spring 2020), and 2) either during the predicted second peak, or as a follow-up if a second peak does not occur (Fall 2020). This analysis presents preliminary descriptive results of the aggregated data, summarizing continuous and categorical variables.

Results: A total of 1,707 RMD patients have participated in Phase 1 so far (from early April to mid-June 2020). The most frequent reported diagnosis were axial spondyloarthritis (47.5%), 618 (36.2%), rheumatoid arthritis (36.2%) and osteoarthritis (22.0%). Mean age was 50.9±17.1 years, 78.2% were female, 68.8% were in a relationship or married and 28.4% had university studies. In total, 1.4% had tested positive for COVID-19, 11.5% reported symptoms but were not tested, while 87.0% did not experience symptoms. 45.0% reported worsening health during the pandemic. 59.7% perceived their health status to be “fair to very bad” and 52.4% reported poor wellbeing according to the WHO-5 scale. Psychological health during the pandemic was also poor, with 55.3% marking as anxiety and 44.3% as depression in the HADS scale. Access to care was limited with 60.6% being unable to keep the rheumatologist appointment, of which 92.5% were cancelled by the provider. 15.3% changed their medication, for which 60.4% were changed by the provider and 28.1% own decision. Reported wellbeing and psychological health during the pandemic was poor, with 52.4% reporting poor wellbeing according to the WHO-5 scale, 55.3% marking as anxiety and 44.3% as depression in the HADS scale. During the pandemic, 25.0% smoked and 17.2% drank more than before and 42.9% were unable to exercise at home.

Conclusion: Preliminary results show disturbance of the healthcare quality, substantial changes to harmful health behaviors and an unprecedented impairment of mental health in REUMAVID participants. REUMAVID will continue

to collect information in order to assess the impact of the COVID-19 pandemic in people affected by RMDs across Europe.

Disclosure: M. Garrido-Cumbrera, None; **H. Marzo-Ortega**, Novartis, 2, 5, 8, Janssen, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, UCB, 5, 8, AbbVie Inc., 5, 8, Celgene, 5, 8, Takeda Pharmaceutical Company, 5, 8; **J. Correa-Fernández**, None; **S. Sanz-Gomez**, None; **L. Christen**, Novartis Pharma AG, 3; **V. Navarro-Compán**, Novartis Pharma, 1, 5, 8, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, UCB, 5, 8.

Abstract Number: 0465

The COVID-19 Pandemic and Its Effect on Patients with Chronic Rheumatologic Disease Regarding the Value of Vaccination Recommendations

Rebecca Overbury[1], Gregory Stoddard[2] and Tracy Frech[3], [1]University of Utah and Primary Children's Hospital, Salt Lake City, UT, [2]University of Utah, Salt Lake City, UT, [3]University of Utah and Salt Lake Veterans Affair Medical Center, Salt Lake City, UT

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes I: COVID-19
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Vaccinations are an important component of care in rheumatology as many patients are immunocompromised by treatment therapies. Patients are sometimes reticent to receive recommended vaccinations for various reasons. A contributing reason could be an under-appreciation of the positive protective benefit of vaccinations. We hypothesize that patients' experience with the COVID-19 pandemic may shift this understanding.

Methods: On April 15, 2020, a link to an anonymous online survey was sent to patients cared for in an academic outpatient rheumatology clinic (RO) via the protected electronic medical record email communication system. Formal institutional review board (IRB) approval was obtained for completion of anonymous surveys. As this research was low risk, this study qualified for IRB exemption. Statistical analysis included two-tailed Fisher exact test and binary Poisson regression.

Results: A total of 83 patients responded to the survey. Most were female. The majority had "rheumatoid arthritis or other autoimmune arthritis" (Table 1). 34.9% (n = 29) had been, or knew someone who had been, affected by COVID-19. 14.5% (n = 12) reported that COVID-19 had changed their opinion on the importance of vaccinations. There was no association between age group, gender, or diagnosis and having a changed opinion on the importance of vaccinations. Those who were affected or knew someone affected by COVID-19 were less likely to change their opinion on the importance of vaccinations due to COVID-19 (p=0.049). However, those who had ever declined a vaccination recommend by their doctor were almost three times more likely to change their opinion on the importance of vaccinations due to the COVID-19 pandemic (RR = 2.96, 95% CI [1.05 - 8.36]). 85.5% (n = 71) reported full compliance with previous vaccination recommendations by their doctor and 97.8% (n = 76) reported that they were now "likely" or "very likely" to have a vaccine recommended by their doctor; there was not a statistically significant difference when comparing these responses (p = 0.059). When asked if participants would want a COVID-19 vaccine were it available today, 8.4% (n = 7) would decline. When asked if participants would want a COVID-19 vaccine for their child, were it available today, 3.6% (n = 3) would decline (Figure 1).

Table 1. Demographics *(n = 83)*

Variables	%
Ages	
18-24 (n=8)	9.6
25-34 (n=12)	14.5
35-44 (n=14)	16.9
45-54 (n=14)	16.9
55-64 (n=14)	16.9
65-74 (n=17)	20.5
75-84 (n=4)	4.8
85+ (n=0)	0
Gender	
Male (n=20)	24.1
Female (n=63)	75.9
Diagnosis	
Rheumatoid arthritis or other autoimmune arthritis (n=47)	56.6
Lupus or other autoimmune connective tissue disease (n=16)	19.3
Gout, pseudo-gout, osteoarthritis (n=3)	3.6
Vasculitis (n=2)	2.4
Periodic fever syndromes (n=3)	3.6
Fibromyalgia (n=1)	1.2
Other or I don't know (n=11)	13.3

Table 1. Demographics

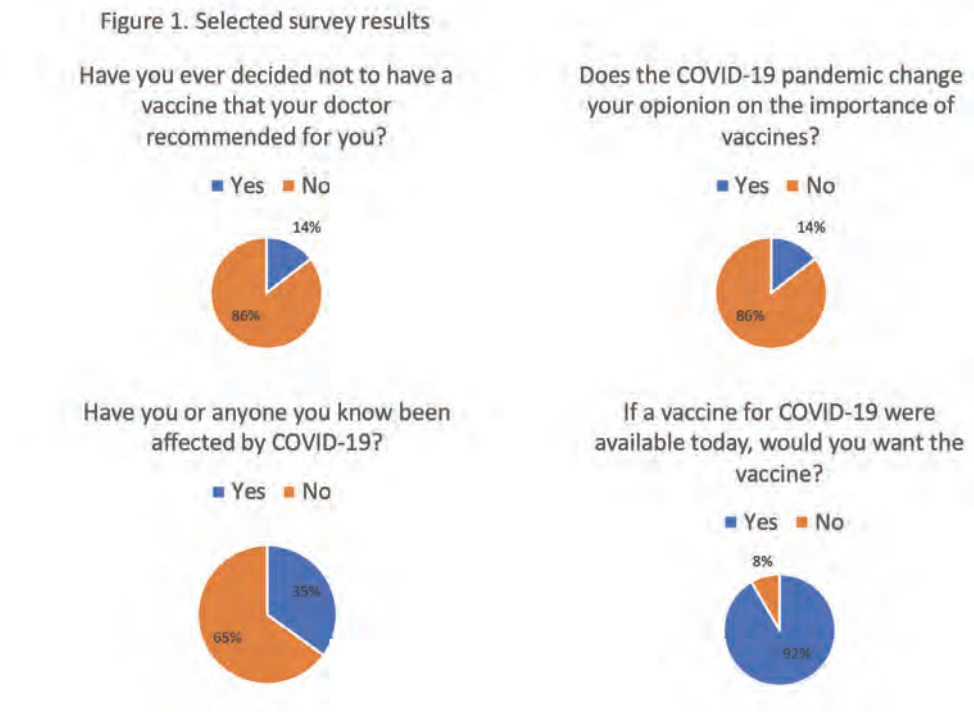

Figure 1. Selected survey results

Conclusion: Based on this research, most patients in an academic rheumatology clinic would desire a COVID-19 vaccination were it available today, both for themselves and for their children. Personal experiences or exposure to COVID-19 did not change opinions on the importance of vaccinations. However, patients who had previously opted to forgo vaccinations, were more likely to change their opinion on the importance of vaccinations due to the COVID-19 pandemic. Although it did not reach statistical significance, there is a trend towards patient expressed intention of compliance with vaccination recommendations after the COVID-19 pandemic. This research suggests that the COVID-19 pandemic may positively affect the likelihood of patients with chronic rheumatologic disease to value and comply with vaccination recommendations offered by their doctor.

Disclosure: R. Overbury, None; **G. Stoddard**, None; **T. Frech**, None.

Abstract Number: 0466

Dosage Modification of Immunomodulatory Medications by Rheumatology Patients in New York City During the Peak of the COVID-19 Pandemic

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes I: COVID-19
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Due to concerns about underlying immune dysregulation and immunosuppression, patients with systemic rheumatic diseases living in COVID-19 "hot spots" may have modified their immunomodulatory medications during the peak of the pandemic in an effort to minimize risk and severity of infection. We aimed to assess the degree of immunomodulatory medication modification at a large specialty hospital.

Methods: We emailed a secure web-based survey to 26,045 patients aged ≥18 years evaluated at least once by a rheumatologist between April 1, 2018-April 21, 2020 at a tertiary care academic center in New York City. Patients were invited to complete the survey by email or phone between April 24, 2020 and May 26, 2020. Detailed information was collected, including potential COVID-19 exposure, symptoms, and outcomes, as well as rheumatic disease history and medications. Patients were asked to report any immunomodulatory medication use in the previous six months and to indicate whether they increased, decreased or discontinued the medication during the COVID-19 pandemic, as well as reasons for reduction or discontinuation.

Results: 6,908/26,045 patients (26.5%) responded to the survey. Mean age was 59.6±15.6 years, 76.3% were female, 86.7% were white, and 7.4% were Hispanic/Latinx. 3,230 patients (46.8% of respondents) reported any use of antimalarial drugs, biologic therapies, conventional DMARDs), and/or corticosteroids in the previous six months. 1275/6,908 (18.5%) patients used antimalarials, 1033 (15.0%) used biologic therapies, 1208 (17.5%) used conventional DMARDs, and 1100 (15.9%) used corticosteroids. Among 3,230 patients, there were 4,701 individual reports of immunomodulatory drug use (2,109 used 1 medication, 843 used 2 medications, 278 used ≥2 medications). Medication dosages were increased 156 times (3.3% of reports), decreased 523 times (11.1%), unchanged 3,382 times

Table 1. Immunomodulatory Medication Dosage Modification Among 3,230 Rheumatology Patients Who Reported Use in the Last 6 months During the April to May 2020 COVID-19 Pandemic "Surge" in New York City

Immunomodulatory Medication History	Overall Use	Increased Dosage	Decreased Dosage	Medication Discontinued*	No Change
Medication usage (N reports)	***4701†***	***156***	***523***	***560***	***3382***
Antimalarials (Chloroquine or Hydroxychloroquine)	1275 (27.1%)**	30 (19.2%)	76 (14.5%)	41 (7.3%)	1049 (31.0%)
Biologics	1059 (22.5%)	18 (11.5%)	158 (30.2%)	98 (17.5%)	785 (23.2%)
• **Abatacept**	• 73 (6.9%)	• 0	• 6 (3.8%)	• 13 (13.3%)	• 49 (6.2%)
• **Belimumab**	• 53 (5.0%)	• 1 (5.6%)	• 8 (5.1%)	• 3 (3.1%)	• 38 (4.8%)
• **TNF inhibitors**	• 662 (62.5%)	• 9 (50.0%)	• 98 (62.0%)	• 49 (50.0%)	• 465 (59.2%)
• **IL-6 inhibitors**	• 87 (8.2%)	• 2 (11.1%)	• 12 (7.6%)	• 7 (7.1%)	• 60 (7.6%)
• **IL-1 inhibitors**	• 10 (0.9%)	• 0	• 3 (1.9%)	• 1 (1.0%)	• 6 (0.8%)
• **IL-12/23 inhibitors**	• 21 (2.0%)	• 0	• 1 (0.6%)	• 5 (5.1%)	• 14 (1.8%)
• **IL-17 inhibitors**	• 103 (9.7%)	• 4 (22.2%)	• 14 (8.9%)	• 9 (9.2%)	• 67 (8.5%)
• **Cyclophosphamide**	• 8 (0.8%)	• 0	• 0	• 3 (3.1%)	• 3 (0.4%)
• **Rituximab**	• 126 (11.9%)	• 2 (11.1%)	• 16 (10.1%)	• 8 (8.2%)	• 83 (10.6%)
Conventional DMARDs	1267 (27.0%)	38 (24.4%)	103 (19.7%)	104 (18.6%)	1022 (30.2%)
• **Leflunomide**	• 125 (9.9%)	• 3 (7.9%)	• 4 (3.9%)	• 14 (13.5%)	• 90 (8.8%)
• **Methotrexate**	• 783 (61.8%)	• 26 (68.4%)	• 63 (61.2%)	• 60 (57.7%)	• 572 (56.0%)
• **Mycophenolate**	• 196 (15.5%)	• 3 (7.9%)	• 23 (22.3%)	• 9 (8.7%)	• 155 (15.2%)
• **Azathioprine**	• 82 (6.5%)	• 2 (5.3%)	• 5 (4.9%)	• 6 (5.8%)	• 64 (6.3%)
• **Sulfasalazine**	• 187 (14.8%)	• 4 (10.5%)	• 8 (7.8%)	• 15 (14.4%)	• 141 (13.8%)
Corticosteroids (Methylprednisolone, Prednisone)	1100 (18.2%)^	70 (44.9%)	186 (35.6%)	317 (56.6%)	526 (15.6%)

Column percentages are shown for all numbers
†Among 3,230 respondents: 2,109 individuals reported taking 1 medication of interest in the last six months, 843 reported 2 medications, 222 reported 3, 44 reported 4, 10 reported 5, 1 reported 6, and 1 reported 8
*Since January 1, 2020
**79 did not answer follow-up questions about dosage modifications or discontinuation
^1 did not answer follow-up questions about dosage modifications or discontinuation

Table 2. Reasons for Immunomodulatory Medication Dosage Reductions and Discontinuation Among 3,230 Rheumatology Patients Who Reported Usage in the Last 6 months in New York City During the Peak of the COVID-19 Pandemic

Immunomodulatory Medication History	Decreased Dosage in setting of pandemic	Medication Discontinued after 1/1/20
Medication usage (Number of reports, %)	**523**	**560**
Antimalarials**	76 (14.5%)	41 (7.3%)
• **By rheumatologist**	47 (61.8%)	19 (46.3%)
• **By another physician**	5 (6.6%)	11 (26.8%)
• **By patient**	22 (28.9%)	10 (24.4%)
• **Most common reason selected for patient modification (N, %)**	Lack of supply in my area (14, 63.6%)	Other* (5, 50%)
Biologics	158 (30.2%)	98 (17.5%)
• **By rheumatologist**	85 (53.8%)	55 (56.1%)
• **By another physician**	15 (9.5%)	11 (11.2%)
• **By patient**	58 (36.7%)	30 (30.6%)
• **Most common reason selected for patient modification (N, %)**	Concerns about immunosuppression (45, 77.6%)	Concerns about immunosuppression (23, 76.7%)
Conventional DMARDs	103 (19.7%)	104 (18.6%)
• **By rheumatologist**	65 (63.1%)	62 (59.6%)
• **By another physician**	9 (8.7%)	11 (10.6%)
• **By patient**	29 (28.2%)	31 (29.8%)
• **Most common reason selected for patient modification (N, %)**	Concerns about immunosuppression (22, 75.9%)	Concerns about immunosuppression (20, 64.5%)
Corticosteroids	186 (35.6%)	317 (56.6%)
• **By rheumatologist**	115 (61.8%)	93 (29.3%)
• **By another physician**	31 (16.7%)	155 (48.9%)
• **By patient**	39 (21.0%)	64 (20.2%)
• **Most common reason selected for patient modification (N, %)**	Other (22, 56.4%)**	I no longer needed this medication (26, 40.6%)

* Taken for COVID-19 prevention or treatment, or due to side effects
** Side effects, short-term or tapered prescription

(71.9%), and discontinued 560 times (11.9%) **(Table 1).** We collected only one modification per medication during the study time period. Among dosage reduction reports, 35.6% were corticosteroids, 30.2%r biologics, 19.7% conventional DMARDs, and 14.5% antimalarials. Medication discontinuation was highest for corticosteroids (56.6%), less for conventional DMARDs (18.6%) and biologics (17.5%), and lowest for antimalarials (7.3%). 19.2% of reported increases in medication doses were for antimalarials. Medication reductions were advised >50% of the time by a physician, whereas up to a third of discontinuations were self-directed **(Table 2)**.

Conclusion: During the peak of the COVID-19 pandemic, nearly a quarter of immunomodulatory drugs used by surveyed rheumatology patients at a large, tertiary care, specialty center in NYC were reduced or discontinued. These findings provide insight into real-world medication management of patients with rheumatic disease during an infectious disease pandemic. Understanding patient and physician behavior during this public health crisis will help guide planning for a second Sars-CoV-2 spike or future pandemic. Longitudinal studies will evaluate the impact of changes to routine medications on disease activity among these patients.

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Abstract Number: 0467

Incidence of COVID-19 in Patients Treated with Infliximab Compared to Patients Treated with Rituximab

Cathy Melong Pianta[1], Kim Lauper[1], Delphine Courvoisier[1], Tim Cunningham[2], Daniéle Allali[3] and Axel Finckh[4], [1]Division of rheumatology, Geneva University Hospitals, Geneva, Switzerland, [2]Private practice, Geneva, Geneva, Switzerland, [3]Division of immunology, Geneva University Hospitals, Geneva, [4]Division of Rheumatology, University Hospitals of Geneva, Geneva, Switzerland

SESSION INFORMATION
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Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: The prevalence of anti-SARS-CoV-2 IgG infection was estimated at 9.7% in the Geneva population end of April 2020. (1) Immunosuppressed patients may be at increased risk of developing severe forms of COVID-19. It is unknown whether the increasing risk is due to immune-mediated diseases by themselves or to specific immunosuppressive therapies. We postulated that long-lasting cell-depleting therapies may increase the risk of severe COVID-19 more than targeted anti-cytokine therapies.

Methods: We included all patients who received infliximab or rituximab at the Rheumatology Division of the Geneva University Hospitals between September 1st 2019 and February 29, 2020 (last 6 months). We called each patient and administrated a questionnaire with predefined questions on incident COVID-19 symptoms and COVID-19 diagnosis between March 1st, 2020 and end of May 2020, which represents the first wave of the COVID 19 pandemic in Switzerland.

Table 1: Patient characteristics by treatment group

Characteristics	Infliximab (n=64)	Rituximab (n =78)	p value
Age (yr, median [IQR]))	49.17 [39.67, 56.85	56.92 [47.2, 67.4]	0.005
Sex (male)	31(48.4)	15 (19.2)	<0.001
Tobacco consumption (ever, n(%))	7 (13.7)	5 (19.2)	0.526
Comorbidities, n(%)	23 (45.1)	14 (53.8)	0.428
Type of immune-mediated disease			
RA (n=33)	14 (21.6)	54 (96.2)	<0.001
SpA (n=44)	45(70.3)	0 (0.0)	
Other (n=10)	5(7.8)	22(28.2)	

We compared patient characteristics using Wilcoxon test for continuous variables and Fisher test for categorical variables. We calculated prevalence, incidence and their crude and adjusted prevalence and incidence ratio with generalised estimating equations using a Poisson distribution. We adjusted the prevalence and incidence ratio by quartiles of a propensity score based on age, gender, disease (rheumatoid arthritis (RA) vs other), smoking and presence of a comorbidity.

Results: During the study period, 151 patients received either rituximab (RTX, n=86) or infliximab (IFX, n=65). We were able to retrieve complete COVID-19 information from 142 (94.0%) patients. RTX patients were older than IFX patients with an average of 56.6 (47.2, 67.4), and significant different in the underlying diagnoses (more RA on RTX and more spondyloarthritis (SpA) on IFX) (Table 1).

Overall, 15 (10.5%) patients have reported symptoms of plausible COVID-19; 9 (13.8%) on IFX and 6 (7.0%) on RTX (p= 0.18). All 15 patients (RTX=7, IFX=8) were tested for Sars-Cov2 using nasopharyngeal swab PCR. Three patient developed severe pulmonary manifestations requiring hospitalisation (two hospitalized in intensive care units, one died). These patient's were 74, 62, 45 years of age respectively, without any of the established at risk comorbidities, but tobacco smoking.

During this first wave of COVID-19 epidemic, the prevalence of plausible COVID-19 in these immunosuppressed patients was 13.8% (95%CI: 7.5-25.4) on IFX, compared to 7.0% (95%CI: 3.2-15.1) on RTX (crude p=0.17, adjusted p=0.03). The incidence rate of COVID-19 was 2.10 (95% CI: 0.94-3.92) cases/1000 patients-days on IFX, compared to 0.97 (0.35-2.10) cases/1000 patients-days on RTX, a significantly increased rate with IFX compared to RTX (crude p< 0.001, adjusted p=0.03).

The incidence rate of severe COVID-19 was null on IFX (95%CI: 0.0-0.76) compared to 0.47 (0.10-1.38) cases/1000 patients-days on RTX. On RTX, tree out of six patients had a severe evolution compared to zero out of 9 patients on IFX (p=0.04).

Conclusion: The incidence of severe COVID-19 tended to be higher in patients on RTX compared to IFX. The study is ongoing, with an analysis of a broader patient sample.

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Abstract Number: 0468

Concerns and Health-Related Behaviors During the COVID-19 Pandemic in Patients with or Without Autoimmune Rheumatic Disease in a Large Physician Network

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SESSION INFORMATION
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Background/Purpose: Patients with autoimmune rheumatic diseases (ARD) may be particularly concerned about COVID-19. We aimed to compare concerns and health-related behaviors of patients with common autoimmune rheumatic conditions versus patients with non-autoimmune rheumatic conditions during the COVID-19 pandemic.

Methods: Adults cared for by members of a multi-state rheumatology provider network (AARA) were invited to complete an online survey (completed April 22 to May 27, 2020). Demographics and rheumatic diagnoses were obtained from the electronic health record data warehouse (Columbus) and linked to the survey. Analyses were restricted to patients with primary diagnoses of common ARD (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, or systemic lupus erythematosus) or patients with non-autoimmune rheumatic disease (osteoarthritis or osteoporosis) who had no ARD diagnoses or DMARD use. Concerns about COVID-19 and health-related behaviors were compared in patients with autoimmune versus non-autoimmune disease using logistic regression, adjusting for demographics, rural residence, and zip-code based measures of COVID-19 activity, income, and education.

Results: Among 18219 respondents with completed surveys, 9004 met criteria for a primary diagnosis of interest, 7176 with and 1828 without autoimmune disease. Patients with ARD were younger (mean age 58 vs. 69) and less commonly female (78% vs. 85%) (Table 1). Respiratory illnesses were reported by 353 (3.9%) and COVID-19 diagnoses by 66 (0.7%). After multivariable adjustment, patients with and without autoimmune disease expressed similar concerns about COVID-19 and similar social distancing behaviors (Figure 1). Older age, female sex, Black race, urban residence, and higher county COVID-19 cases per capita were associated with higher levels of concern (all $p< 0.001$). Patients with ARD had greater concerns related to their rheumatic condition (Figure 1, $p < 0.001$). Among patients with ARD, those with lupus and those treated with biologics/janus kinase inhibitors (JAKi) or glucocorticoids had greater COVID-19-related concerns (all $p < 0.01$). Among the 5543 patients receiving a DMARD, 571 (10.3%) stopped a medication because of concerns about COVID-19. Patients with ARD were less likely to avoid a doctor's visit or laboratory tests and were more likely to have had a telehealth visit (38% versus 33%, Figure 2, all $p < 0.01$) compared to those with non-autoimmune disease.

Conclusion: Concerns about COVID-19 and degree of social distancing were similar in patients with ARD vs. those with non-autoimmune rheumatic disease. Those with ARD had more concerns specific to their rheumatic condition, especially patients with lupus and those treated with biologics/JAKi or glucocorticoids. Patients with ARD were less likely to

Table 1: Cohort characteristics

	Autoimmune Disease	No Autoimmune Disease
Sample size, N	7176	1828
Age (years)	58.5 +/- 14.1	68.7 +/- 10.2
Female	5594 (78.0%)	1561 (85.4%)
Race		
White	5873 (81.8%)	1543 (84.4%)
Black	557 (7.8%)	59 (3.2%)
Other	222 (3.1%)	38 (2.1%)
Missing	524 (7.3%)	188 (10.3%)
Hispanic	704 (9.8%)	162 (8.9%)
Rural	386/7070 (5.5%)	59/1806 (3.3%)
County cases of COVID-19 per capita*		
Lowest tertile	1786/7070 (25.3%)	396/1806 (21.9%)
Middle tertile	3048/7070 (43.1%)	618/1806 (34.2%)
Highest tertile	2236/7070 (31.6%)	792/1806 (43.8%)
Autoimmune/rheumatic condition		
Rheumatoid arthritis	4581 (63.8%)	-
Psoriatic arthritis	1276 (17.8%)	-
Systemic lupus erythematosus	980 (13.7%)	-
Ankylosing spondylitis	339 (4.7%)	-
Osteoarthritis	-	1046 (57.2%)
Osteoporosis	-	782 (42.8%)
Medications		
Biologic DMARD	2700 (37.6%)	-
JAKi	459 (6.4%)	-
Methotrexate	2152 (30.0%)	-
Hydroxychloroquine	1740 (24.2%)	-
Glucocorticoids	1494 (20.8%)	99 (5.4%)
NSAIDs	2054 (28.6%)	630 (34.5%)
Illness/COVID-19		
No reported respiratory illness	6824 (95.1%)	1761 (96.3%)
Reported a respiratory illness but not COVID-19	296 (4.1%)	57 (3.1%)
Reported a physician diagnosis of COVID-19	56 (0.8%)	10 (0.5%)

Number (%) and mean +/- standard deviation shown

*Tertiles in cumulative COVID-19 cases per capita in the United States on the day in which the patient completed the survey, with counties weighted by population

DMARD: disease modifying anti-rheumatic drug; JAKi: Janus kinase inhibitor; NSAIDs: non-steroidal anti-inflammatory drugs

avoid office visits and testing and more likely to have telehealth visits, perhaps reflecting the need for closer monitoring of these conditions. These results emphasize the impact of the pandemic across patients with rheumatic disease and the need to ensure adequate follow-up and address concerns specific to patients with autoimmune disease as the pandemic continues.

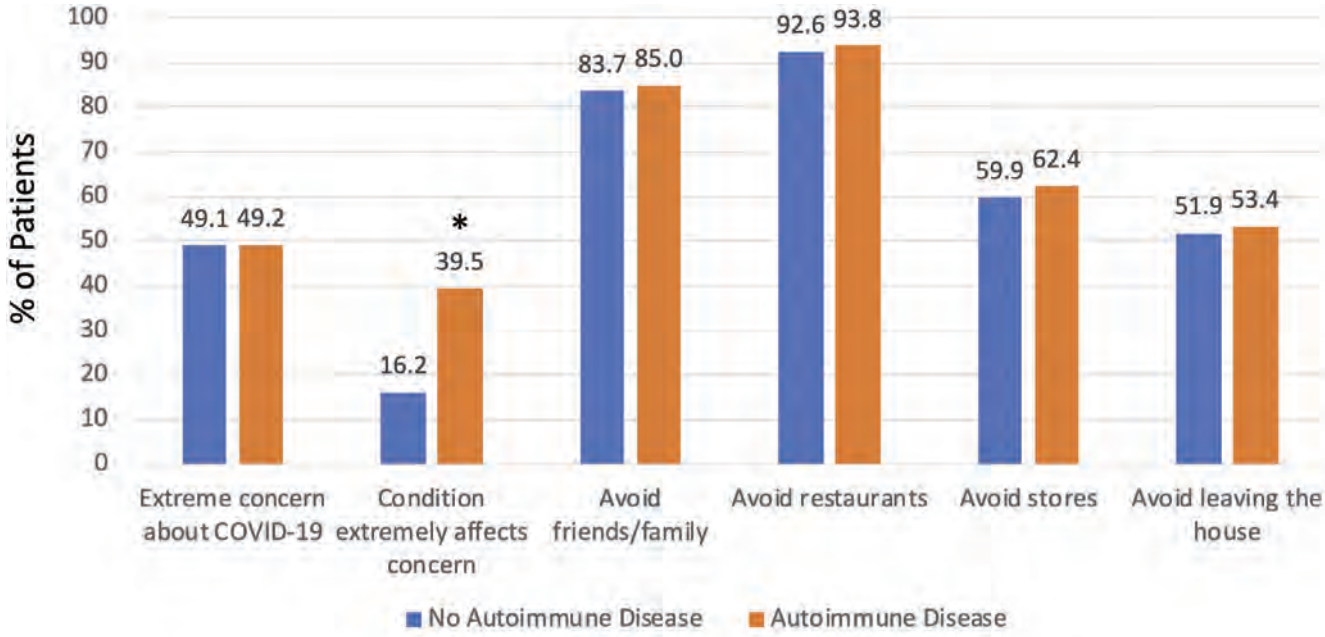

Figure 1: Comparison of concerns about COVID-19 and social distancing behaviors in patients with autoimmune disease (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, or systemic lupus erythematosus) compared to those without autoimmune disease (osteoarthritis or osteoporosis). Proportions shown are based on predicted probabilities from multivariable logistic regression to adjust for age, sex, race, rural residence, tertiles of county-based COVID-19 activity, and tertiles of zip-code based median household income and education. Concerns about COVID-19 and degree to which the patient's autoimmune/rheumatic condition affects these concerns were based on a 5-point Likert scale ranging from 1 (not at all) to 5 (extremely). Patients who indicated "not applicable" for questions about each social distancing measure were excluded

* $p < 0.05$

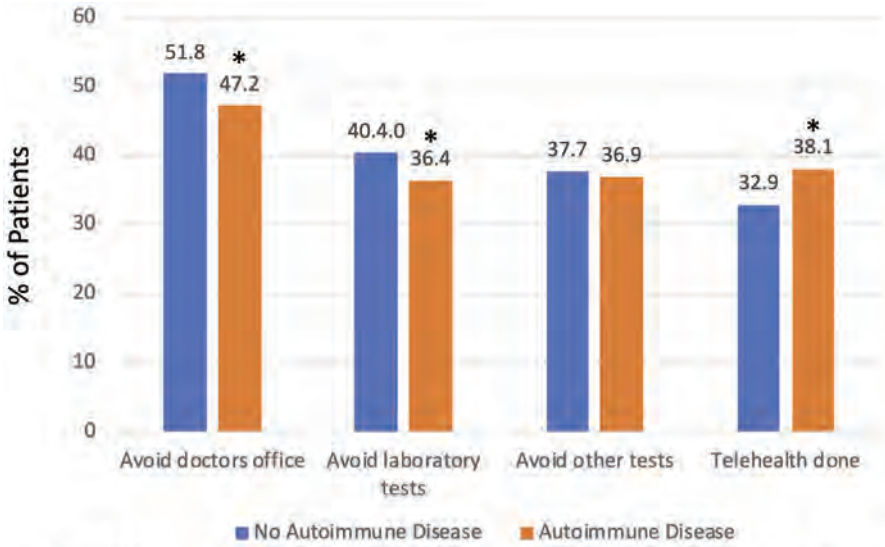

Figure 2: Comparison of health-related behaviors in patients with autoimmune disease (rheumatoid arthritis, psoriatic arthritis, ankylosing spondylitis, or systemic lupus erythematosus) compared to those without autoimmune disease (osteoarthritis or osteoporosis). Proportions shown are based on predicted probabilities from multivariable logistic regression to adjust for age, sex, race, rural residence, tertiles of county-based COVID-19 activity, and tertiles of zip-code based median household income and education. Patients who indicated "not applicable" for each question were excluded.

* $p < 0.05$

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Abstract Number: 0469

IFNγ Is Essential for Alveolar Macrophage Driven Lung Inflammation in Macrophage Activation Syndrome

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SESSION INFORMATION
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Background/Purpose: Macrophage activation syndrome (MAS) is a life-threatening cytokine storm syndrome frequently complicating systemic juvenile idiopathic arthritis (SJIA) and driven by IFNγ. MAS is also associated with an emerging and severe inflammatory lung disease (SJIA-LD). The causes and pathogenesis of SJIA-LD are unknown, but have been proposed to include introduction of anti-cytokine therapies, allergic reactions, or other environmental factors, along with recurrent MAS. Our recent work supports activation of IFNγ pathways in the lungs of children with SJIA-LD, supporting a pathologic link between pulmonary inflammation and MAS. The objective of this study was to mechanistically define the novel observation of pulmonary inflammation in the TLR9 mouse model of MAS.

Methods: Pulmonary inflammation was examined by histopathology, cytokine/chemokine levels and alveolar macrophage gene expression profiling. IFNγ signaling was inhibited through neutralizing antibodies as well as using mice with macrophages insensitive to IFNγ.

Results: In acute MAS, lungs exhibit mild but diffuse lymphocyte-predominant, primarily perivascular interstitial inflammation with elevated IFNγ, elevated levels of the IFN-induced chemokines CXCL9 and CXCL10, and alveolar macrophage expression of IFNγ-induced genes. We have further developed the TLR9 model system by for the first time characterizing the resolution phase of MAS. MAS resolution was associated with alveolar macrophage expansion and increased interstitial mononuclear cell infiltration. Alveolar macrophage microarrays confirmed IFNγ-induced proinflammatory polarization during acute MAS. However, this switches towards an anti-inflammatory phenotype during MAS resolution with activation of STAT6-induced genes and repression of STAT1-induced genes. As many patients with SJIA-LD have repeated episodes of MAS, we retreated mice with CpG to model recurrent MAS. Interestingly, recurrent MAS led to increased alveolar inflammation, and reset alveolar macrophage polarization towards a persistent proinflammatory state. Furthermore, using both direct IFNg blockade and macrophages insensitive to IFNγ (MIIG) mice, both systemic feature of MAS and pulmonary inflammation were markedly attenuated.

Conclusion: These findings demonstrate that experimental MAS induces IFNγ-driven pulmonary inflammation that replicates key features of children with SJIA-LD. These findings support a model whereby MAS induces IFNγ-driven pulmonary inflammation and dynamic changes in alveolar macrophage polarization, contributing to development of SJIA-LD.

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Abstract Number: 0470

Th1 Polarization Defines the T Cell Compartment in the Joints of Oligoarticular Juvenile Idiopathic Arthritis Patients

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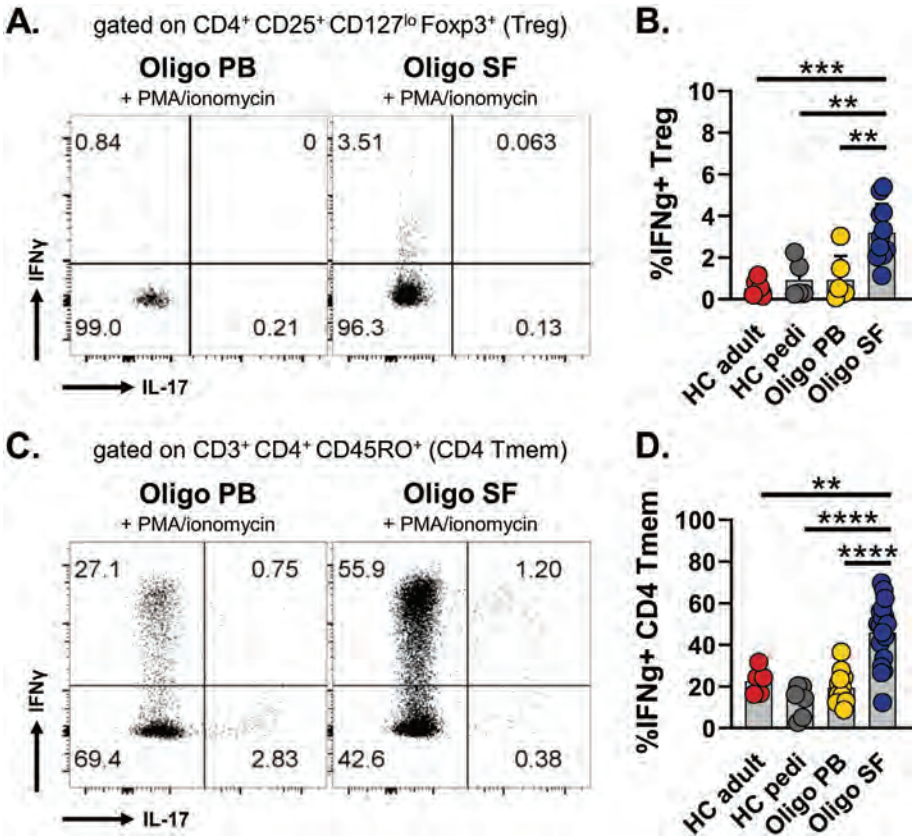
Background/Purpose: Oligoarticular juvenile idiopathic arthritis (oligo JIA) is defined by limited joint involvement at disease onset. Some children achieve long-term remission while others continue to have chronic arthritis in a few joints or extend to a polyarticular course. The mechanisms driving persistent or extended disease in a subgroup of patients are unknown. To better understand how $CD4^+$ T cell responses evolve in oligo JIA, we characterized regulatory (Treg) and effector (Teff) T cells found in the joints of patients at disease onset and during recurrent arthritic flares.

Methods: Synovial fluid (SF) and paired peripheral blood (PB) samples were collected from oligo JIA patients, defined by ILAR criteria. PB was also obtained from healthy controls (HC). Tregs ($CD3^+CD4^+CD25^+CD127^{lo}$) and Teffs ($CD3^+CD4^+CD25^-$) were sorted from SF and PB, and processed for bulk RNA sequencing, single-cell RNA sequencing coupled with T cell receptor (TCR) repertoire analysis (10x genomics), DNA methylation studies (EpigenDx), or *in vitro* Treg suppression assays. PB and SF mononuclear cells were evaluated with flow cytometry.

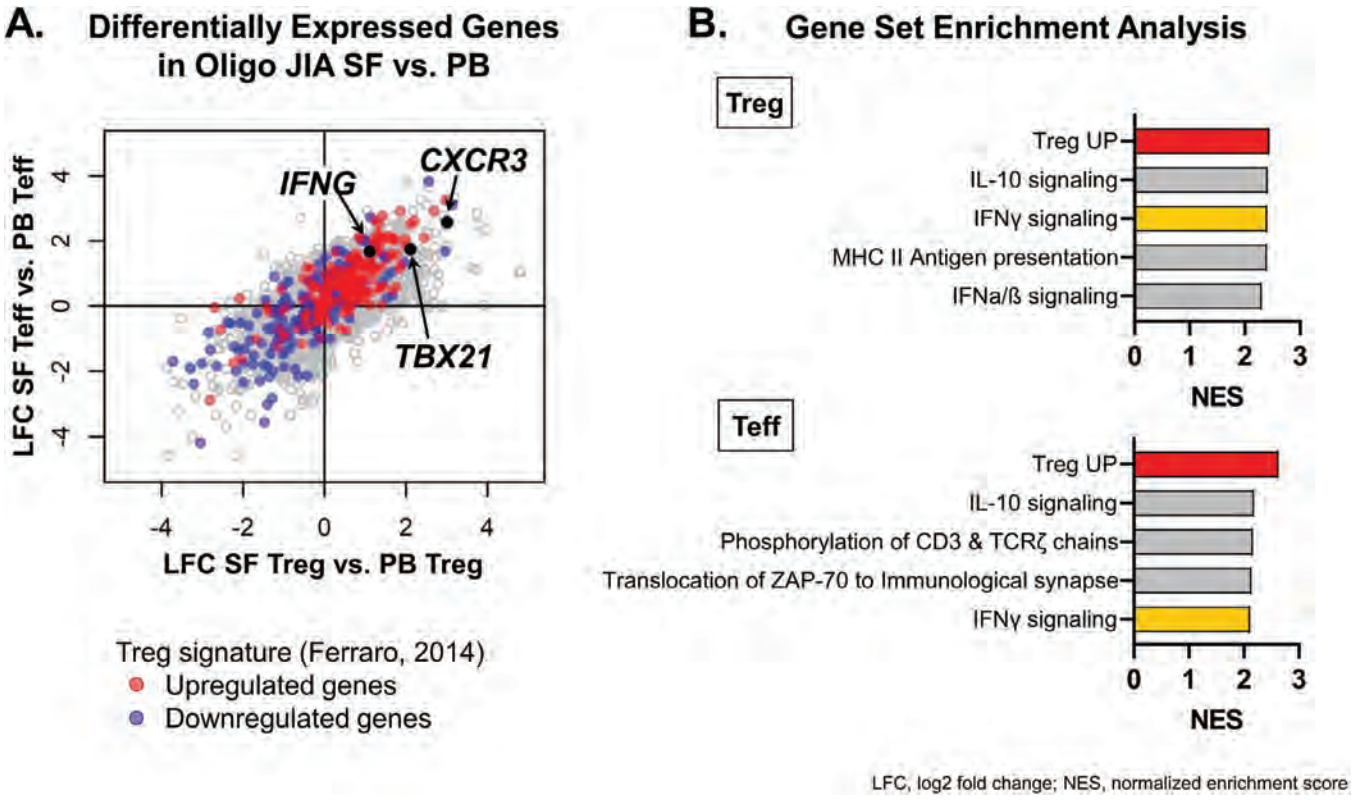
Results: 34 oligo JIA patients and 15 controls were studied. In SF, flow cytometry demonstrated significantly increased frequencies of memory $CD4^+$ T cells ($CD3^+CD4^+CD45RO^+$) expressing Th1 related cytokines (IFNγ) and chemokine receptors (CXCR3). Th17 cells were not enriched in the joint. SF Tregs ($CD4^+CD25^+CD127^{lo}Foxp3^+$) were markedly skewed to a Th1 phenotype: 76.3% ± 6.0% (SEM) expressed CXCR3, and 3.2% ± 0.4% secreted IFNγ after stimulation *in vitro* (Fig1). Bulk RNA sequencing confirmed a Th1 signature in SF Tregs and SF Teffs at disease onset and relapse, with elevated levels of *TBX21* (T-bet, master regulator of the Th1 fate), *CXCR3* and *IFNG* transcripts in oligo JIA SF compared to oligo JIA PB and HC PB. Gene set enrichment analysis uncovered IFNγ signaling as one of the most enriched pathways in SF Tregs and SF Teffs (Fig2). The Treg transcriptional signature was preserved in

SF Tregs. In addition, *FOXP3* locus demethylation and Treg suppressive capacity was maintained in Th1-like Tregs (CXCR3^{+} Tregs), confirming the regulatory identity of this population. Single-cell RNA sequencing uncovered heterogeneity in oligo JIA SF Tregs, with 5 distinct subsets: (1) 'classical' Tregs, (2) IL2RA^{low} Tregs, (3) activated, HLA-DR^{hi} Tregs, (4) Th1-like Tregs expressing *FOXP3* and *IL2RA* jointly with *TBX21* and *IL12RB2*, and (5) Tregs expressing other IFNγ induced genes. Except for IL2RA^{lo} Tregs, all other Treg clusters were enriched in expanded TCR clones, with 22.0 to 37.0% of cells per cluster having at least 3 clonal copies across the single-cell dataset.

Conclusion: Our results identify a strong Th1 polarization in the joints of oligo JIA patients that encompasses both regulatory and effector CD4^{+} T cells and persists longitudinally. While the majority of SF Tregs display Th1 features, this population is heterogeneous with at least 5 subpopulations. Th1-like Tregs retain their regulatory gene expression signature, methylation patterns and functional capacity. These results suggest that augmenting the function of Th1-like Tregs may be key in controlling Th1 mediated inflammation in the joint and restoring tolerance in oligo JIA.



CD4+ T cells from oligo JIA SF express IFNγ upon stimulation in vitro. A) and C) Representative flow cytometry dot plots for Tregs (A) and memory CD4+ T cells (C). B) and D) Mean frequencies +SD of IFNγ+ Tregs (B) and memory CD4+ T cells (D), as measured by flow cytometry (ANOVA with correction for multiple comparisons, **p<0.01, ***p<0.001, ****p<0.0001). PB, peripheral blood; SF, synovial fluid; HC, healthy control; pedi, pediatric.



Oligo JIA SF Treg and SF Teff show markers of a Th1 transcriptomic profile. A) Log2 fold change vs. Log2 fold change plot of the outcomes from the differential expression analysis of oligo JIA SF (n=14, including 7 new-onset and 7 persistent oligo JIA) versus PB (n = 22, including 8 oligo JIA and 14 HC) in Tregs and Teffs. Genes upregulated (red) and downregulated (blue) in the Treg signature described in Ferraro (2014) are highlighted. Th1-related genes (CXCR3, TBX21, IFNG) are labeled. B) Top enriched gene sets in oligo JIA SF Tregs vs. PB Tregs and oligo JIA SF Teffs vs. PB Teffs based on the normalized enrichment score (NES) from the gene set enrichment analysis against the Reactome Database (Immune system and Metabolism subsets) and the Treg signature (Ferraro, 2014).

Disclosure: A. Jule, None; **K. Hoyt**, None; **K. Wei**, Gilead, 5; **S. Case**, None; **M. Chang**, None; **E. Cohen**, None; **F. Dedeoglu**, Novartis, 1; **M. Hazen**, None; **J. Hausmann**, Novartis, 5; **O. Halyabar**, None; **E. Janssen**, None; **P. Lee**, None; **J. Lo**, None; **M. Lo**, None; **E. Meidan**, None; **J. Roberts**, None; **M. Son**, None; **R. Sundel**, None; **T. Chatila**, None; **P. Nigrovic**, Novartis, 2, 5, BMS, 2, 5, Pfizer, 2, 5, Sobi, 5, Miach Orthopedics, 5, Simcere, 5, XBiotech, 5, Quench Bio, 5, Siglion, 5, Cerecor, 5, UpToDate, 7, American Academy of Pediatrics, 7, CARRA, 9; **L. Henderson**, Adaptive Biotechnologies, 5, Sobi, 5, CARRA, 9.

Abstract Number: 0471

Splice Site Variants in *IKBKG,* Encoding NEMO, Detected by a Customized Analysis of Next-Generation Sequencing Data Cause an Early-onset Autoinflammatory Syndrome of Panniculitis and Cytopenias in Male and Female Patients

Adriana de Jesus[1], Sofia Torreggiani[2], Bin Lin[2], Jacob Mitchell[2], Eric Karlins[3], Andrew Oler[3], Sara Alehashemi[4], Dana Kahle[5], Katelin R. Honer[2], Gema Souto Adeva[2], Eric Hanson[6], Gina Montealegre Sanchez[7], Amer Khojah[8], Timothy Moran[9], Eveline Wu[9], Chris Scott[10], Timothy Ronan Leahy[11], Emma Jane MacDermott[11], Orla Killeen[12], Thaschawee Arkachaisri[13], Zoran Gucev[14], Kathryn Phillippi[15], Vafa Mammadova[16], Gulnara Nasrullayeva[16] and Raphaela Goldbach-Mansky[17], [1]Translational Autoinflammatory Disease Section (TADS)/NIAID/NIH, Silver Spring, MD, [2]Translational Autoinflammatory Disease Section (TADS)/NIAID/NIH, Bethesda, MD, [3]Bioinformatics and Computational Biosciences Branch/NIAID/NIH, Bethesda, MD, [4]Translational Autoinflammatory Disease Section (TADS)/NIAID/NIH, Clarksville, MD, [5]Translational Autoinflammatory Disease Section (TADS)/NIAID/NIH, Bethesda, [6]Indiana University School of Medicine, Indianapolis, IN, [7]NIAID/NIH, Rockville, MD, [8]Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, [9]UNC Chapel Hill, Chapel Hill, NC, [10]University of Cape Town, Cape Town, South Africa, [11]Our Lady's Children's Hospital, Dublin, Ireland, [12]National Centre for Paediatric Rheumatology, CHI at Crumlin, Dublin, Ireland, [13]Duke-NUS Medical School, Singapore, Singapore, [14]University Children's Hospital, Medical Faculty Skopje, Skopje, Macedonia, [15]Akron Children's Hospital, Akron, OH, [16]Azerbaijan Medical University, Baku, Azerbaijan, [17]Translational Autoinflammatory Disease Section (TADS)/NIAID/NIH, Potomac, MD

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Pediatric Rheumatology – Basic Science

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: The Inhibitor of Kappa-B Kinase Regulatory Subunit Gamma (*IKBKG*) is located on the X chromosome and encodes the NF-κB essential modulator (NEMO). Loss-of-function mutations in *IKBKG* cause immunodeficiency with ectodermal dysplasia in males and incontinentia pigmenti in females. We have recently reported 4 patients (pts) with gain-of-function (GOF) splice site variants in *IKBKG* causing an autoinflammatory disease (AID) that mimics chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE)[1]. This AID has been called NEMO-deleted exon 5 autoinflammatory syndrome (NDAS). The presence of an *IKBKG* pseudogene (*IKBKGP1*) makes the genetic diagnosis of NEMO-associated diseases challenging. We sought to develop a customized bioinformatics approach as screening tool to facilitate the discovery of disease-causing splice site variants.

Methods: Pts enrolled in an IRB-approved protocol underwent whole exome/genome sequencing (WES/WGS) and trio analysis. A bioinformatics pipeline was developed to computationally mask the *IKBKGP1* pseudogene and improve sensitivity of the discovery of splice site mutations. An interferon (IFN) response gene (IRG) score was assessed by Nanostring.

Results: Eight female pts with 5 different de novo splice-site variants in *IKBKG* were identified. The clinical phenotype of the 8 female pts was similar and, in some cases, more severe than the clinical phenotype of male pts with GOF *IKBKG* mutations previously reported. All female pts had early disease onset (2 days to 6 months-old) with nodular skin rashes, fever and increased inflammatory markers (ESR and CRP). Other frequent clinical manifestations included failure to thrive (8/8), lipodystrophy (4/8), hepatosplenomegaly (5/7), anemia (8/8), thrombocytopenia (6/8) and B-cell lymphopenia (5/7). All pts were cortico-dependent and partially responded to anti-TNF (n=5) or JAK inhibitor (n=5) therapies, and one pt deceased due to opportunistic infections (3 years-old). Analysis of pts' WES/WGS data using

a custom approach to mask *IKBKG* pseudogene revealed that two pts had variants in intron 5 (*IKBKG* NM_003639.4 c.671+5G >A in Pt1 and c.671+1G >A in Pt2); and 6 pts had variants in intron 4 (c.519-2A >G in Pt3-Pt6, c.519-22_519-14delGTCTGCTCT in Pt7 and c.519-7_519-6insGGCCCTGG in Pt8). None of the *IKBKG* variants had previously been detected by pts' WES/WGS using standard analysis methods. Reverse transcription followed by cDNA sequencing showed exon 5 skipping in the 7 pts tested and Western blot confirmed the splice product in 2/2 pts. All 8 pts had high 28-gene IFN scores with a relatively higher expression of IRG's that have transcription factor binding sites for NF-κB (*CXCL10*, *GBP1* and *SOCS1*) and a high 3 NF-κB/25 IFN-gene ratio[1].

Conclusion: We describe de novo splice-site variants in the X chromosome gene, *IKBKG* (encoding NEMO), in 8 female pts with a CANDLE-like phenotype. Analysis of WES/WGS masking the *IKBKG* pseudogene provided a remarkably better diagnostic yield than standard methods, and could be used for the diagnosis of pts with NEMO-NDAS.

[1]de Jesus AA et al. J Clin Invest. 2020;130:1669-1682

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Disclosure: A. de Jesus, None; **S. Torreggiani**, None; **B. Lin**, None; **J. Mitchell**, None; **E. Karlins**, None; **A. Oler**, None; **S. Alehashemi**, None; **D. Kahle**, None; **K. Honer**, None; **G. Souto Adeva**, None; **E. Hanson**, None; **G. Montealegre Sanchez**, None; **A. Khojah**, None; **T. Moran**, None; **E. Wu**, None; **C. Scott**, None; **T. Leahy**, None; **E. MacDermott**, None; **O. Killeen**, None; **T. Arkachaisri**, None; **Z. Gucev**, None; **K. Phillippi**, None; **V. Mammadova**, None; **G. Nasrullayeva**, None; **R. Goldbach-Mansky**, None.

Abstract Number: 0472

ApoB:ApoA1 Ratio Could Predict Atherosclerotic Risk in Juvenile-SLE Patients Associated with Altered Interferon Signalling in CD8+ T-cells

George Robinson[1], Kirsty Waddington[2], Leda Coelewij[2], Junjie Peng[2], Meena Naja[2], Chris Wincup[2], Anna Radziszewska[2], Hannah Peckham[2], David Isenberg[2], Yiannis Ioannou[2], Ines Pineda Torra[2], Coziana Ciurtin[2] and Elizabeth Jury[2], [1]University College London, Hertford, United Kingdom, [2]University College London, London, United Kingdom

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Pediatric Rheumatology – Basic Science
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune rheumatic disease characterised by immune-dysregulation, chronic inflammation, type-I interferon (IFN) signatures and increased cardiovascular disease (CVD) risk (CVR); CVD is a major cause of morbidity and mortality in SLE. Juvenile-SLE (JSLE) has a more severe disease phenotype and CVR than adult SLE. All patients with SLE should receive careful monitoring and treatment of modifiable CVR factors. However, no guidelines exist for CVR management in SLE and it is not possible to predict the CVR of patients using traditional factors. This study used a multi-omic approach to investigate CVR in JSLE patients.

Methods: NMR-based serum metabolomic biomarker analysis (including 113 lipoprotein measures assessing size/lipid content) was performed on a discovery cohort of JSLE patients (n=31, median age 19). Data were analysed using cluster, receiver operating characteristic (ROC) and logistic regression analysis. Results were validated in a second

JSLE cohort (n=31, median age 19). All patients were assessed clinically over 3-6 years of follow up. Flow cytometry evaluated 28 immune cell subsets and RNAseq assessed gene expression in matched patient samples.

Results: Unbiased hierarchical clustering of metabolomic data identified 2 JSLE patient groups, each with a complex and unique lipoprotein profile. Group-1 had decreased high density lipoproteins (HDL) and increased very low and low density lipoproteins (VLDL/LDL) and Group-2 had elevated HDL but reduced VLDL/LDL, indicating an association with high and low CVR respectively. This pattern was verifed by the measurement of lipid biomarkers associated with pre-clinical atherosclerotic plaque in adult SLE patients. The groups were validated the second JSLE cohort and the Apolipoprotein(Apo)B:A1 ratio was identified as a predictive and longitudinally stable biomarker of CVR (ROC area under the curve >0.99).

Patients with a high ApoB:A1 ratio had significantly increased circulating CD8+ T-cells. Transcriptomic and pathway enrichment analysis of differentially expressed genes (DEGs) from isolated JSLE CD8+ T-cells identified significantly increased interferon (IFN) signaling pathways in high ApoB:A1 ratio patients which overlapped with CD8+ T-cells from human and mouse atherosclerotic plaque. When DEGs associated with disease activity were removed from the analysis, we observed a unique dysregulation of the IFN-stimulated gene factor 3 transcription complex (ISGF3), including significantly increased expression of JAK2, STAT1/2 and IRF9.

Finally, a higher baseline ApoB:A1 ratio predicted an increased average Systemic Lupus Erythematosus Disease Activity Index (SLEDAI) over an average of 5 years (p=0.0009), suggesting worsened clinical outcome.

Conclusion: Multi-omic analysis identified a putative predictive biomarker (ApoB:A1 ratio) and novel immunopathogenic pathways, involving CD8+ T-cells and ISGF3 signalling, associated with increased CVR in JSLE. Patient stratification using the measurement of ApoB:A1 may therefore provide an opportunity for tailored disease treatments using lipid modification therapy and/or diet modification to control disease severity and CVR outcome.

Disclosure: G. Robinson, None; **K. Waddington**, None; **L. Coelewij**, None; **J. Peng**, None; **M. Naja**, None; **C. Wincup**, None; **A. Radziszewska**, None; **H. Peckham**, None; **D. Isenberg**, None; **Y. Ioannou**, UCB Pharma, 3; **I. Pineda Torra**, None; **C. Ciurtin**, None; **E. Jury**, None.

Abstract Number: 0473

Characterization of *DOCK8* as a Novel Gene Associated with Cytokine Storm Syndrome

Mingce Zhang[1], Remy Cron[2], Devin Absher[3], Prescott Atkinson[1], Winn Chatham[1] and **Randy Cron**[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]University of Alabama at Birmingham, Birmingham, [3]HudsonAlpha Institute for Biotechnology, Huntsville, AL

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Pediatric Rheumatology – Basic Science
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Cytokine storm syndrome (CSS), also known as macrophage activation syndrome (MAS) or secondary hemophagocytic lymphohistiocytosis (HLH), is a life threatening condition that commonly presents with unremitting fever and shock like multi-organ dysfunction (MOD). Laboratory studies show pancytopenia, elevated liver enzymes, elevated ferritin, and hemophagocytosis. Familial forms of HLH result from homozygous defects in

Table. DOCK8 rare mutations and polymorphisms identified in CSS patients.

Table. *DOCK8* rare mutations and polymorphisms identified in CSS patients.

#	Age (yrs)	Sex	Disease	Trigger	Mutation	Frequency
1	16	M	?	*Bartonella*	c.782C>T, p.Ala261Val	novel
2	19	M	T cell leukemia	?	c.54-1G>T (splice acceptor)	0.03%
3	24	M	Still disease	?	c.187G>A, p.Asp63Asn	12%
4	36	F	Polyarteritis nod.	*Streptococcus*	c.187G>A, p.Asp63Asn	12%

genes involved in perforin mediated cytolysis by NK cells and CD8 T cells. As many as 30-40% of CSS patient cohorts studied have heterozygous defects in the same HLH genes resulting in decreased cytolytic function, prolonged interaction with antigen presenting cells, and subsequent increased pro-inflammatory cytokines resulting in MOD. Since NK cell dysfunction is common in CSS, there are likely other genes that contribute to CSS via decreased cytolysis. Using gene sequencing, mutations in potentially novel HLH genes present in 2 or more CSS patients were explored.

Methods: Pediatric and adult patients with CSS at UAB were screened for genetic mutations, potentially contributing to CSS, via whole genome sequencing or a commercial immunodeficiency exomic genetic panel of 207 genes. Four patients were noted to have mutations in the guanine nucleotide exchange factor *DOCK8* critical to NK cell function. *DOCK8* mutations from this CSS cohort, or wild-type (WT) sequence controls, were introduced exogenously into human NK-92 NK cell lines by foamy virus (FV) transduction. Alternatively, the endogenous NK-92 *DOCK8* genes were cut and repaired to express WT sequence or patient derived *DOCK8* mutations by CRISPR/Cas9 technology. WT and mutant *DOCK8* expressing NK-92 cells were incubated with K562 target cells and compared for cytolytic activity, degranulation (CD107a), and cytokine [interferon-g (IFNg), tumor necrosis factor (TNF)] production by flow cytometry.

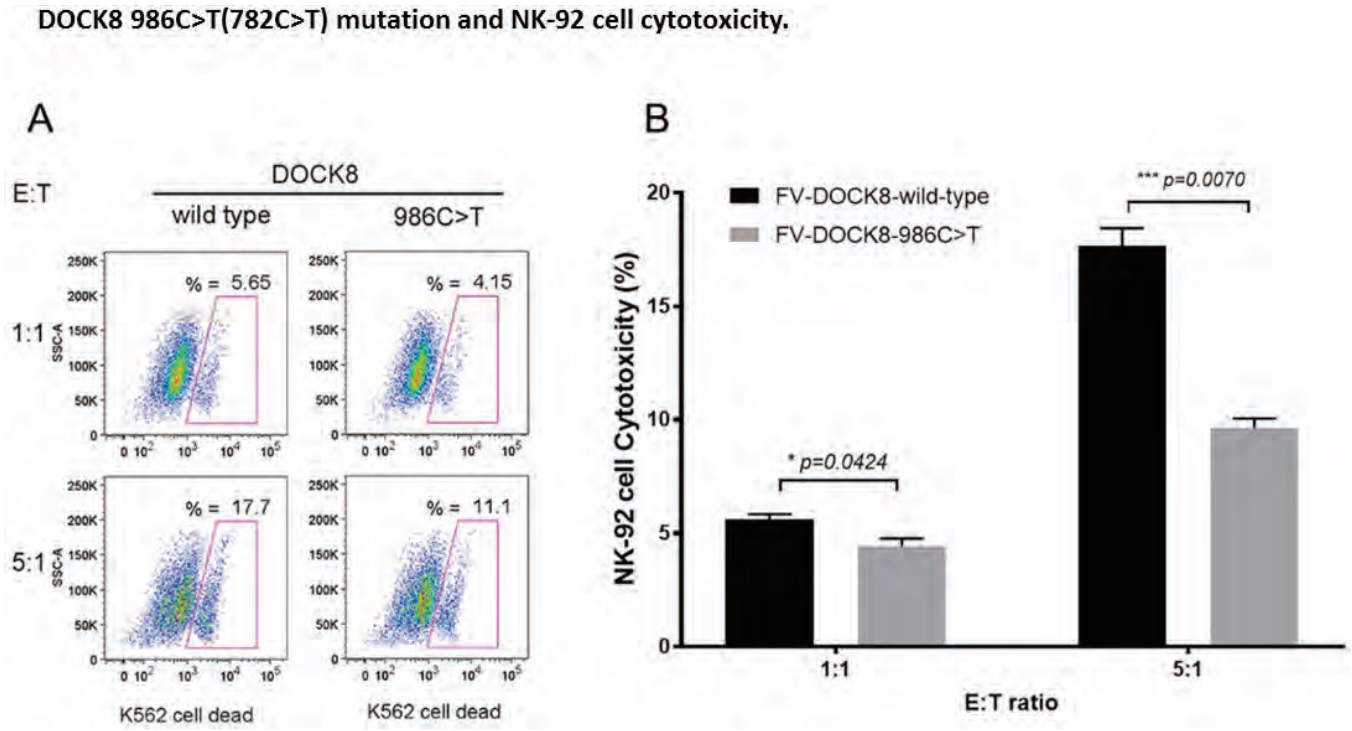


Figure 1. Cytolytic activity of patient #1 DOCK8 missense mutation in NK-92 cells. NK-92 cells were transduced with WT or patient mutation DOCK8-expressing FV and incubated with K562 target cells. A. K562 lysis detected by near-IR fluorescence at 2 E:T ratios. B. N=3, means +/- SEMs.

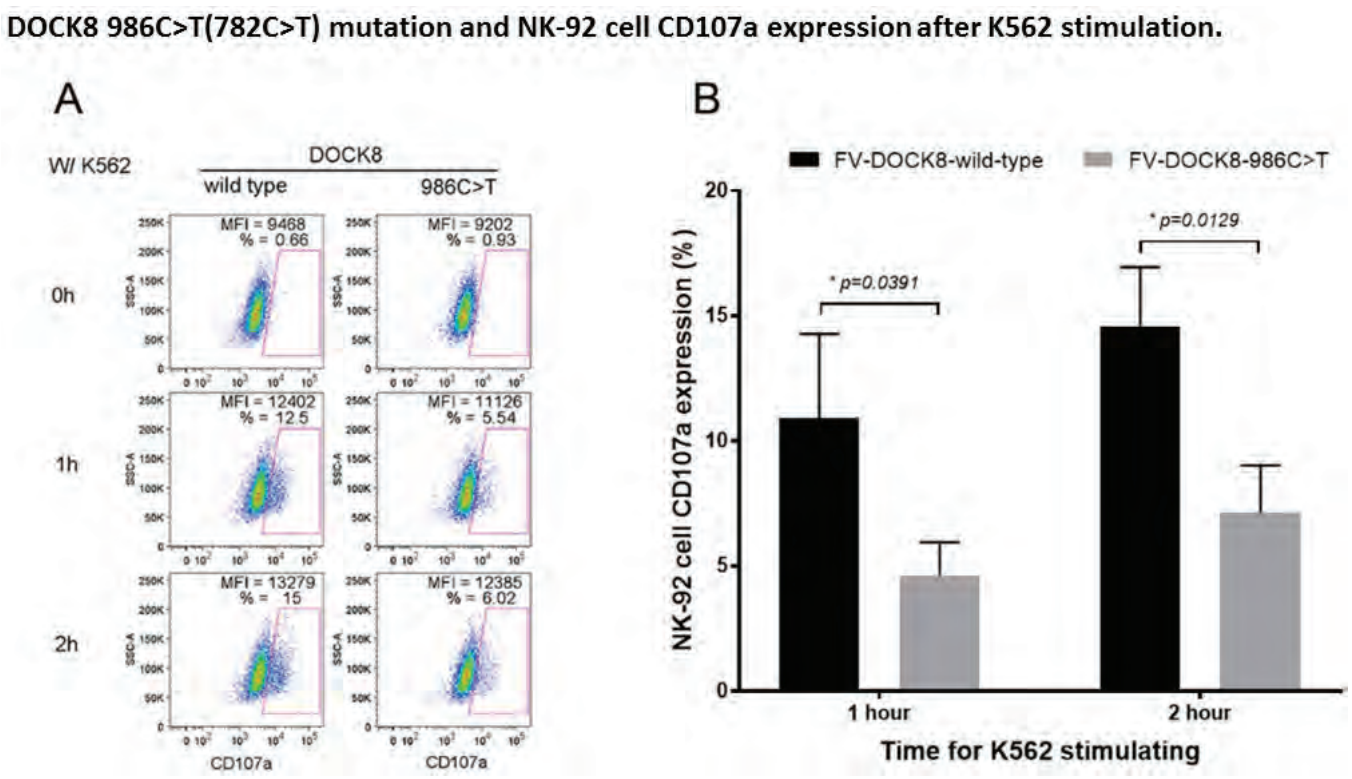


Figure 2. Degranulation of patient #1 DOCK8 missense mutation in NK-92 cells. NK-92 cells were transduced with WT or patient mutation DOCK8-expressing FV and incubated with K562 target cells. A. NK-92 cell degranulation detected by CD107a surface expression at 3 time points. B. N=3, means +/- SEMs.

Results: Two CSS patients were identified with rare heterozygous *DOCK8* mutations, and 2 others with CSS were noted to have the same *DOCK8* polymorphism (c.187G >A, p.Asp63Asn) present in 12% of the population (Table). One of the rare mutations was missense (c.782C >T, p.Ala261Val – novel), and one was a splice acceptor variant (c.54-1G >T, 0.03%). The novel *DOCK8* mutant consistently decreased NK cell lytic activity when introduced by either CRISPR/Cas9 (n=2) or FV (n=3, decreased by ~50% compared to WT, p=0.007) (Fig. 1). Similarly, the novel mutant decreased degranulation by >50% (n=3, p=0.013) (Fig. 2). During the incubation of the NK-92 cells with K562 targets, NK cells expressing the novel *DOCK8* mutant increased expression of IFNg and TNF by >200% (p=0.019 & p=0.003, respectively). The *DOCK8* polymorphism decreased lysis and degranulation to a lesser degree. The *DOCK8* splicing mutation disrupted RNA splicing by an exon trapping assay and a novel assay developed in the lab.

Conclusion: Heterozygous mutations in *DOCK8*, a novel CSS associated gene, likely contribute to CSS pathology through a partial dominant-negative or hypomorphic effect resulting in decreased cytolysis and increased pro-inflammatory cytokine production.

Disclosure: M. Zhang, None; **R. Cron**, None; **D. Absher**, None; **P. Atkinson**, None; **W. Chatham**, Sobi, 2, 5; **R. Cron**, Sobi, 2, 5, 8, Pfizer, 5, Novartis, 5.

Abstract Number: 0474

Assessment of Teaching Behavior and Knowledge Among Faculty to Inform an Active Teaching Intervention Within a Rheumatology Fellowship Curriculum

Stefanie Wade[1], Vasileios Kyttaris[1], Jason Freed[2] and Jonathan Hausmann[3], [1]Beth Israel Deaconess Medical Center, Harvard Medical School, Boston, MA, [2]Beth Israel Deaconess Medical Center / Harvard Medical School, Boston, MA, [3]Boston Children's Hospital / Beth Israel Deaconess Medical Center, Cambridge, MA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Professional Education
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: The science of learning has provided us with evidence-based tools to enhance learning. Studies show that greater learning occurs in interactive workshops that tackle real-life problems, as compared to traditional lectures. We sought to determine the use of active learning techniques during fellowship didactics and to assess faculty knowledge regarding active teaching strategies.

Methods: We assessed faculty use of active learning strategies during the "Introduction to Rheumatology" curriculum by using a cognitive learning assessment tool that was created by Saunders S and Freed JA (manuscript in progress). An "Active Learning Score" was calculated based on questions that measured active learning (Table 1). A pair of observers (JSH, VCK, or SDW) scored each of the lectures, which took place from July to September 2019. We surveyed faculty knowledge and behavior regarding current teaching practices. Unprecedented teaching challenges brought on by the COVID-19 pandemic prompted us to survey faculty comfort teaching within a virtual learning environment. This project was determined to be exempt by the Beth Israel Deaconess Medical Center IRB.

Results: We surveyed 14 faculty members within the Division of Rheumatology. Faculty demographics are shown in Table 2. Faculty placed the highest value on "understanding concepts" and "applying information to new cases" as

Active Learning Score Items	Score
1. Uses questions in the beginning to determine prior knowledge related to the topic	0 or 3
2. Uses questions periodically during lecture to revisit key concepts	0 to 3
3. Encourages audience participation (i.e., through non-rhetorical questions to group or audience response systems)	0 to 3
4. Asks learners to explain their reasoning with follow-up questions	0 to 3
5. Creates hypothetical situations or asks "what if" questions	0 or 3
6. Utilizes techniques such as "think-pair-share" to facilitate discussion	0 to 3
7. Asks audience to share experiences of taking care of patients with 'x' (i.e., "how many of you have ever taken care of a patient with RA")	0 or 3
8. Asks learners to identify or share with a neighbor key take-home points or concepts	0 or 3
	/24

Table 1. Active Learning Score items from a cognitive learning lecture assessment tool designed by Saunders S, Freed JA (manuscript in progress).

Faculty Surveyed, n	14
Response Rate, n (%)	14 (100)
Years since fellowship, n (%)	
0 to 5	3 (21.4)
6 to 9	2 (14.3)
10 to 19	3 (21.4)
20 or more	6 (42.9)
Advanced Training in Medical Education, n	
Education Track During Training	1
Medical Education Fellowship	0
Graduate Degree in Education	0
Other:	
Firm Chief (Teaching Medical Residents)	1
CME Courses in Education	1
Masters in Public Health	1
Academic Rank, n	
Instructor	7
Assistant Professor	5
Associate Professor	1
Professor	1

Table 2. Faculty Demographics.

opposed to "remembering facts." A minority of faculty (42.9%) were familiar with the concept of a flipped classroom. Only 50% of faculty felt that virtual teaching could be as effective as in-classroom teaching.

A total of 12 faculty members delivered 16 lectures on core rheumatology topics. 93.8% of lectures incorporated case-based examples that fellows could relate to. Mean baseline Active Learning Scores were 7.8 +/- 5.3 out of 24. We had strong agreement between raters as measured by intraclass correlation (0.86, 95% CI: 0.64-0.95). Faculty asked learners to explain their reasoning with follow up questions an average of 1.25 +/- 1.14 times per lecture. Techniques to facilitate small-group discussion, such as "think-pair-share," were used in 1 out of the 16 lectures (6.25%). Learners were asked to identify or share key take-home points or concepts in 1 out of 16 (6.25%) lectures.

Conclusion: Faculty use of active teaching techniques in fellowship didactics was low. A minority of faculty were familiar with the flipped classroom, and the majority of faculty expressed hesitancy regarding teaching in a virtual environment. Based on these results, we plan to use a multifaceted approach to improve the use of active teaching strategies in the "Introduction to Rheumatology" curriculum (Figure 1). We designed a faculty development workshop to provide strategies for increasing active learning in a virtual environment and will seek input from the department regarding how best to implement these educational changes. We will compare Active Learning Scores pre- versus post-intervention.

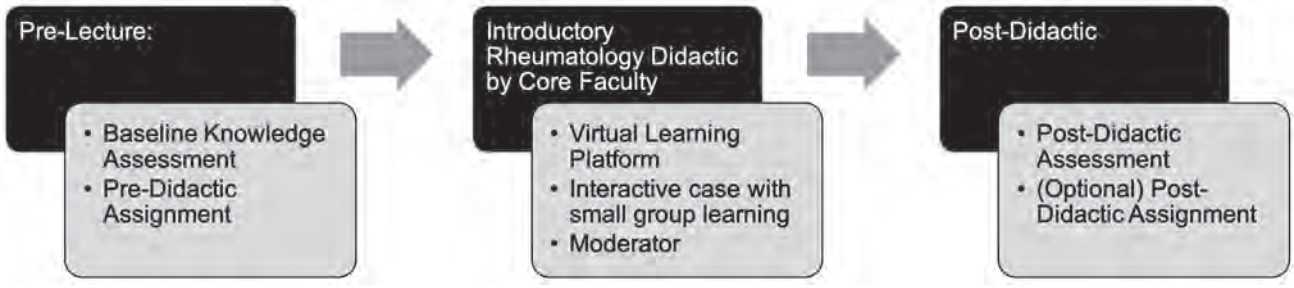


Figure 1. Proposed framework for increasing active teaching within the "Introduction to Rheumatology Curriculum" via virtual learning environment.

Disclosure: S. Wade, None; **V. Kyttaris**, GlaxoSmithKline, 5, Exagen Diagnostics, 2, 5; **J. Freed**, None; **J. Hausmann**, Novartis, 5.

Abstract Number: 0475

To Attend or Note to Attend; The Medical Student's Dilemma

Benjamin Widener[1], Amy Cannella[1] and Sarah McBrien[1], [1]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Professional Education
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: We present a comparison of student's outcomes with remote video-based learning versus lecture attendance in pre-clinical medical students during a musculoskeletal curriculum, thus allowing insight to optimizing educational formats for pre-clinical medical students. Our purpose was to assess academic outcomes (Rheumatology exam, overall course exam, and overall second year rank) among second year medical students in a musculoskeletal course at the University of Nebraska Medical Center College of Medicine (UNMC COM) varying by percentage of remote learning versus attended lecture for this musculoskeletal block. As remote learning becomes increasingly common during the ongoing COVID-19 pandemic, it is prudent to understand how this may impact medical student's acquisition of pre-clinical knowledge of Rheumatology.

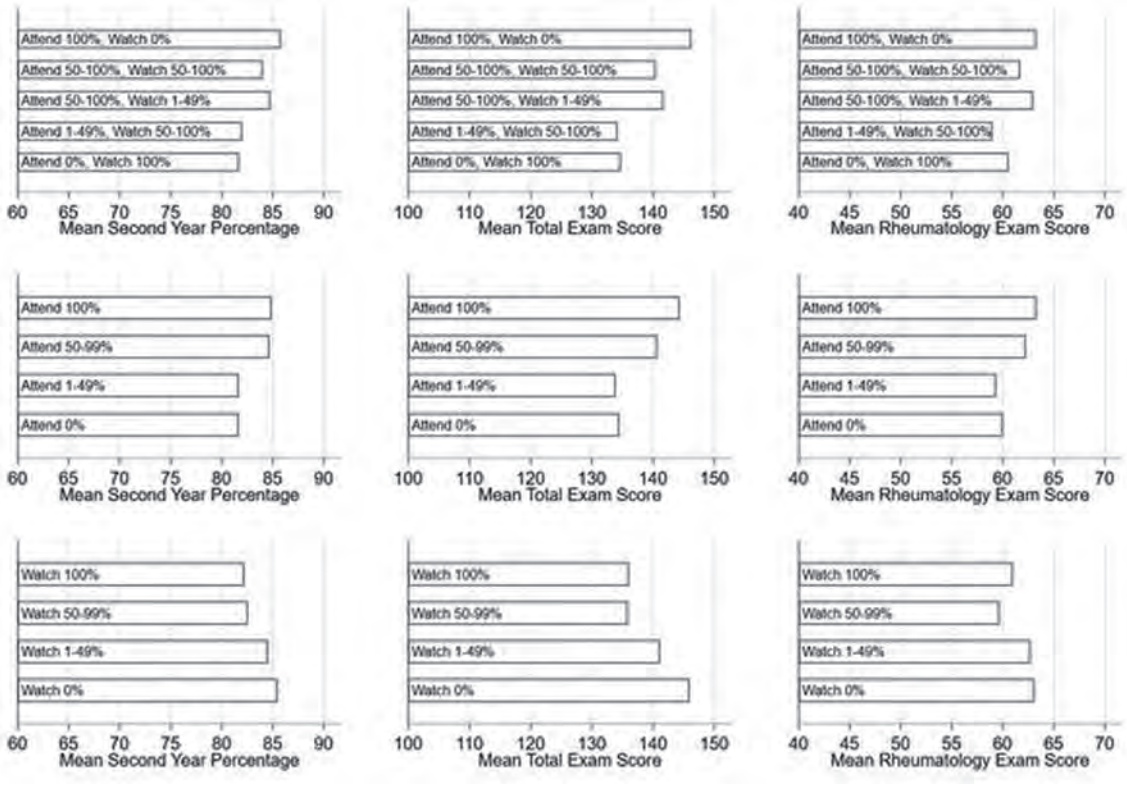


Figure 1 Outcomes 2nd year percentage, Mean total exam (overall course) and mean rheumatology Exam Score.

Methods: Our study is a prospective cohort study conducted at UNMC COM during the M-ID-640 Musculoskeletal, Dermatology & BLS Core from March 23, 2015 to April 10, 2015. We compared the outcomes of 126 second year medical students during this time period. Outcomes were compared based upon confirmed variations in percentage of class attendance and remote lecture viewing. We directly took lecture attendance and had automated record of remote viewing of the material using Echo 360. Our outcomes of interest were the Rheumatology subject exam score, M-ID-640 (course) overall exam score, and the second year cumulative GPA. Investigators reviewed the attendance and echo 360 viewing data and assigned each student to one of the following groups 1) Attend 100%, Watch 0%; 2) Attend 50-100%, Watch 50-100%; 3) Attend 50-100%, Watch 1-49%; 4) Attend 1-49%, Watch 50-100%; 5) Attend 0%, Watch 100%. The outcomes or these groups were compared by regression analysis.

Results: Increased lecture attendance when compared to remote viewing of the lectures, correlated with improved scores in all three of the measured academic outcomes (overall second year percentage, mean overall course grade and mean rheumatology exam score.) There was no statistical difference in undergraduate GPA's among the cohorts that would help explain the outcome differences we observed.

Conclusion: Increased lecture attendance had a positive correlation with multiple scholastic measures in a pre-clinical musculoskeletal course at the UNMC COM when compared to remote video learning. As remote learning is becoming increasingly commonplace, particularly in the setting of the current COVID-19 pandemic, careful consideration of medical school curricula delivery should be undertaken to best achieve academic success and knowledge acquisition in pre-clinical medical students.

Disclosure: B. Widener, None; **A. Cannella**, USSONAR, 6; **S. McBrien**, None.

Abstract Number: 0476

Using Consensus Building to Guide Rheumatology Curriculum Development for Internal Medicine Residents

Sarah Goglin[1] and Jennifer Babik[2], [1]University of California San Francisco, Burlingame, CA, [2]University of California San Francisco, San Francisco, CA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Professional Education
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: In spite of the increasing burden of rheumatic diseases in the United States, many patients have limited access to rheumatologists. As a result, internists provide much of the care for these patients. However, the current state of rheumatology education for internal medicine (IM) residents is inadequate. No national rheumatology curriculum exists for IM residents. At the University of California San Francisco (UCSF), 20% of IM residents report dissatisfaction with their clinical and didactic experience in rheumatology and in-training exam scores in rheumatology are consistently in the bottom 3 specialties. The purpose of this study was to determine expert consensus on the most important topics to include in a curriculum for UCSF IM residents.

Methods: We conducted a modified, 2-round Delphi process to develop consensus on rheumatology topics that all graduating IM residents should know. Through review of the literature for common diagnoses and the ABIM Blueprint

Topics Meeting Consensus		
	Clinical Features/Diagnostics	Treatment
Gout	x	x
CPPD	x	x
Osteoarthritis	x	x
Psoriatic arthritis	x	
Rheumatoid arthritis	x	x
Infectious arthritis	x	x
Systemic lupus	x	
Drug induced lupus	x	
Antiphospholipid antibody syndrome	x	
Sjogren's syndrome	x	
Raynaud's phenomenon	x	
Inflammatory myopathies	x	
Giant cell arteritis	x	x
Polyarteritis nodosa	x	
ANCA-associated vasculitis	x	
Leukocytoclastic vasculitis	x	
Polymyalgia rheumatica	x	x
Osteoporosis	x	x
Avascular necrosis	x	
Occupational/sports-related overuse syndromes	x	x
Adverse effects of non-biologic antirheumatic drugs	x	
Adverse effects of biologic drugs used by rheumatologists	x	
New topics suggested for Round 2 only		
Indications for a rheumatology consult/referral	x	
How to initiate a rheumatologic work up in cost effective way	x	
Rheumatologic emergencies	x	
Approach to patient with inflammatory arthritis	x	

Table 1. Topics meeting consensus after Round 2 of Delphi process categorized as either clinical features/diagnostics or treatment of specific rheumatologic condition

in rheumatology, we generated an initial list of 78 topics. We surveyed 50 expert faculty educators from general internal medicine, hospital medicine, and rheumatology, and asked them to rate each topic's importance using a 4-point Likert scale (0 = absolutely do not include, 1 = not very important, 2 = kind of important, 3 = important, 4 = very important). We considered a content validity index (the percentage of respondents who rated the topic as ≥3 in Round 2) of at least 80% as our definition for having reached consensus.

Results: 35 of 50 (70%) completed Round 1 of the survey, and 27 of 35 (77%) completed Round 2 (total response rate 54%). In Round 1, 63.6% of topics were scored as ≥3, with a significant difference in scoring between rheumatologists and general medicine faculty (56.2% vs. 69%, p=0.009). 30 of 78 topics met our consensus definition (scored as ≥3 by at least 80% of respondents), with 21 of 78 meeting consensus by rheumatologists compared with 31 of 78 by general internists (p=0.09). 8 additional topics proposed by participants in Round 1 were included in Round 2. Af-

ter Round 2, 35 of 86 topics met the consensus definition, with rheumatologists reaching consensus on fewer topics than general internists (33.7% versus 44.2% of topics, p=0.16). 74.2% of the topics meeting consensus addressed clinical features and/or diagnostics of rheumatologic conditions, while the remainder focused on treatment.

Conclusion: The Delphi consensus method was used to determine which topics should be included in a rheumatology curriculum for IM residents. This process can be used as a blueprint for development of curricula in other medicine specialties in our and other residency programs. Interestingly, rheumatologists considered more topics to be of lower importance to include in a curriculum for IM residents compared with ratings by general internists. The potential differences in opinion between rheumatologists and general internists highlights the need to include both specialists and general medicine physicians in developing subspecialty curricula.

Disclosure: S. Goglin, None; **J. Babik**, None.

Abstract Number: 0477

Rheumatology Fellowship Program Directors in the United States: Analysis of Demographics, Educational and Scholarly Achievements

Aakanksha Khanna[1], Dawid Czarny[2], Vibhor Wadhwa[3] and Alysia Kwiatkowski[4], [1]Department of Medicine, University at Buffalo, Jacobs School of Medicine and Biomedical Sciences, Buffalo, NY, [2]University at Buffalo, Amherst, NY, [3]Department of Radiology, University of Arkansas for Medical Sciences, Little Rock, AR, [4]State University of New York at Buffalo, Clarence, NY

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Professional Education
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Rheumatology program directors (PDs) play a vital role in developing, improving and overseeing the fellowship programs. Although PDs have an important role to play in the education and training of future rheumatologists, there is paucity of literature about the educational and demographic background of the current PD workforce in the United States (US). The main aim of the study was to analyze the demographic variables, educational background, and scholarly achievements of rheumatology fellowship PDs in the US.

Methods: The Accreditation Council for Graduate Medical Education (ACGME) website was accessed to obtain a list of all accredited rheumatology fellowships, and PDs of all programs were included. Publicly available sources including individual program/institutional websites, HealthGrades© and Doximity© websites, and the Scopus© database were accessed. Each PD's age, gender, educational background, appointment age, interval between fellowship completion and appointment as PD, additional degrees, and scholarly metrics (publications, citations, h-index) were recorded. Nonparametric statistics including Mann-Whitney U and Kruskal-Wallis tests were used to compare differences between groups and P-value of < 0.05 was considered significant.

Results: A total of 121 PDs were included in the study, of which 61 (50.4%) were females. The average age was 52.69±9.17 years (median 52, range 33-). There was no statistical difference in of male versus female PDs (p=0.112). The average age at appointment was 46.06±7.9 years (range 32-71) and mean tenure duration was 6.53±5.71 years (median 4.8, range 0.17-27.42). International medical graduates comprised 42 (34.7%) of the PDs, with the most common country of international medical school being India (13, 10.7%). Six (5%) received a Doctor of Osteopathic Medicine (DO) degree. The mean (and median) number of publications, citations and h-index for PDs were

31.98±45.47 (median 14), 1344.21±3035.96 (median 384) and 11.94±13.05 (median 8). There was no statistical difference between male and female PDs with regards to distribution of publications (p=0.108), citations (p=0.204) and h-index (p=0.12). There was no statistical difference between PDs from American and international medical schools with regards to distribution of publications (p=0.261), citations (p=0.367) and h-index (p=0.337).

Conclusion: Rheumatology fellowship PD positions demonstrate gender equality with 50% being female, and with no significant difference in scholarly metrics between male and female PDs. International medical graduates comprise thirty five percent, a sizeable minority. This study provides a single snapshot of the current rheumatology PD workforce in the US in 2020, and will be helpful for those interested in an academic career, with a focus on medical education. Furthermore, this study will serve as a baseline for future comparative studies.

Disclosure: A. Khanna, None; **D. Czarny**, None; **V. Wadhwa**, None; **A. Kwiatkowski**, None.

Abstract Number: 0478

Increasing Awareness of Advocacy During Early Career – a Web-Based Educational Program

Sirisha Gokaraju[1], Angus Worthing[2], Katherine Maher[3], Grace Wright[4] and Gail Kerr[5], [1]Georgetown University hospital, Bethesda, MD, [2]Arthritis & Rheumatism Associates, PC, Washington, DC, [3]Arthritis & Rheumatism Associates, PC, Alexandria, VA, [4]Association of Women in Rheumatology, New York, NY, [5]Washington DC VA Medical Center, Washington, DC

SESSION INFORMATION

Session Date: Friday, November 6, 2020
Session Title: Professional Education
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: In 2015, the American College of Rheumatology (ACR) began Advocacy 101 in person-education for Fellows in Training (FIT) and physicians to encourage participation in federal regulatory and legislative issues that relate to access to care, research funding, and contemporaneous matters. However, FIT participation has

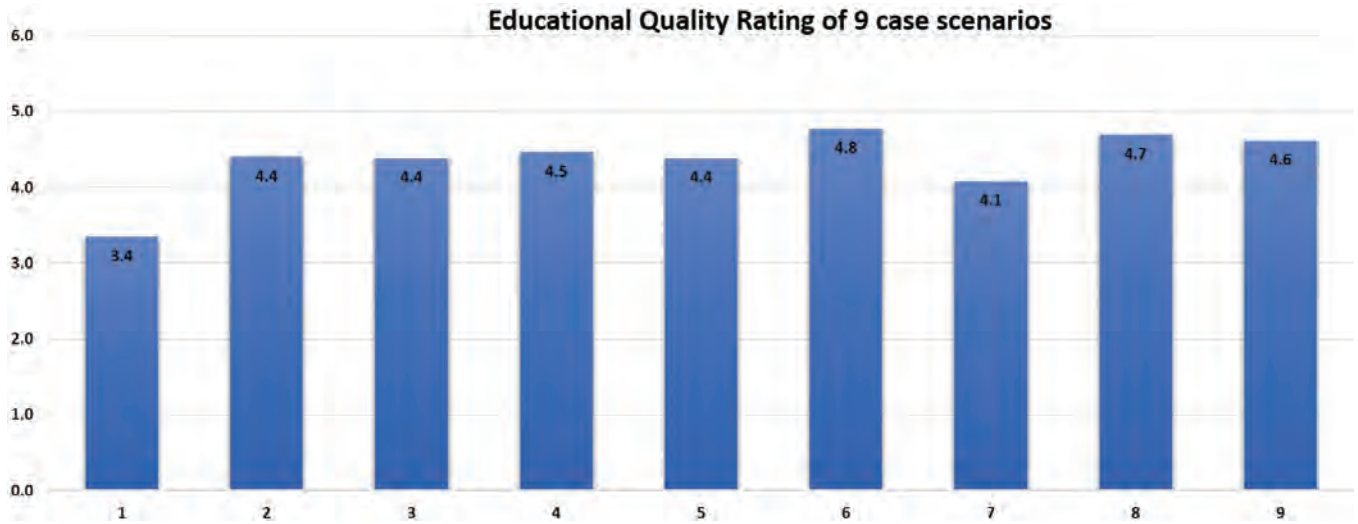


Table 1. Rating of Educational Quality of 9 case scenarios

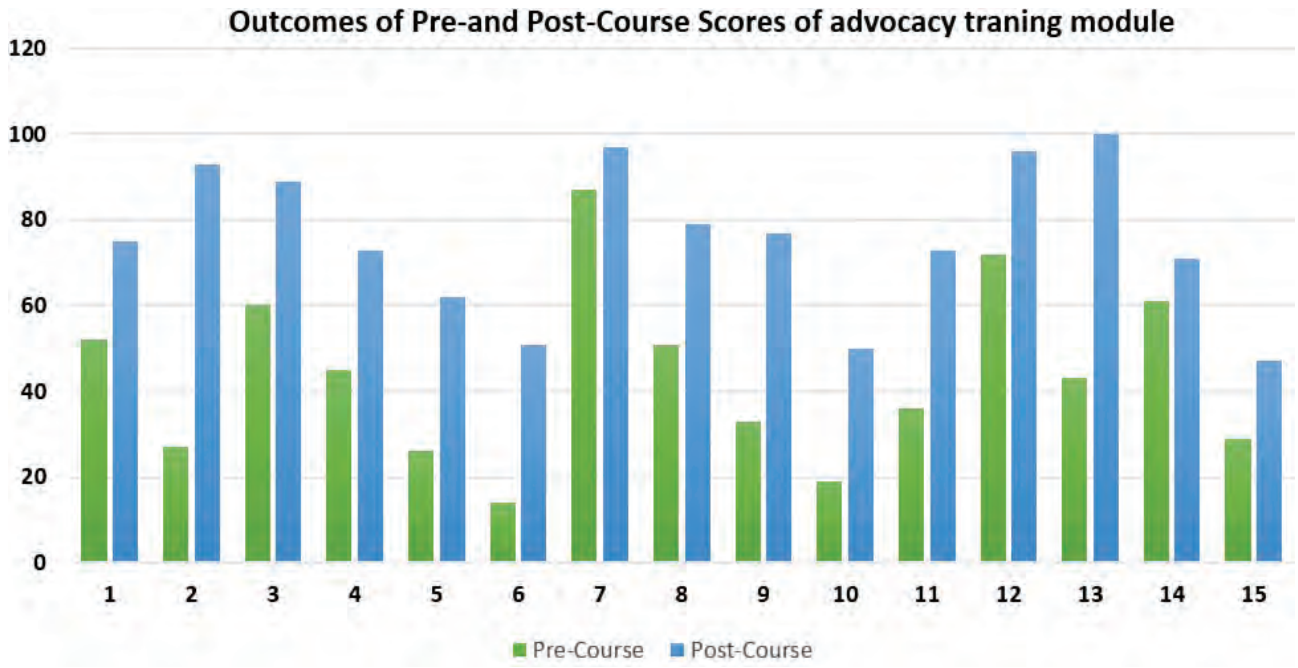


Table 2. Pre- and Post-course Questionnaire scores for Advocacy Training

been undersubscribed, with 50% - 80% of adult and pediatric trainees unexposed, particularly in single-Fellow programs. Though knowledge of the Advocacy process improved by 30%, there was minimal increase in ACR Advocacy awareness (5%), or increased investment in the Rheum PAC® (3%). FIT reported that while in-person training was acceptable, 48% were receptive to on-line training. To date, no web-based Advocacy Training tool exists.

Objective: To evaluate the impact of a web-based Rheumatology Advocacy Training tool on Increasing Awareness in Early Career.

Methods: Early career rheumatologists who attended the 2019 ACR-Advocacy 101 were invited to participate. Email notification for the 9-step, case-based, web-hosted Advocacy training program was sent every 28 days. Content included ACR and other sources of legislative and regulatory material. Tasks related to improving access to care, writing letters of appeals were included. Single multiple-choice questions were assigned to each case scenario, with continuing medical education credit. Participants were invited to 2 web-based teleconferences; 1) at mid-point - to clarify technical questions, 2) at completion - to review and discuss cases, responses, and obtain feedback from participants. Outcomes of pre- and post-questionnaires, completed, correct answers, narrative summations of responses, and suggestions for improvement were collected.

Results: Early Career Rheumatology physicians (≤ 2years) from 9 academic institutions accepted the invitation to participate. Of 20 trainees who started the program, 75% completed all 9 cases. Correct CME answers were scored on 85% of cases. Overall educational quality of content received a mean rating of 4.3 (Likert scare: 1-5). Seven of the 9 cases achieved positive ratings related to relevance of case content, achievement of training goal, objectivity and helping improve competence. Cases relevant to Medicare drug coverage structures, Tele-Health, Biosimilars, Medicare Sequestration, Prior Authorization, and how to translate Advocacy training into action, were rated as having the greatest impact. All cases were assessed free of bias. Feedback indicated ~ 30 minutes was dedicated for completion of each case, and that a combination of skill set and content learning to be most effective. Pre- and post-questionnaire scores indicated significant improvement in knowledge of advocacy matters ($p < 0.0001$,Table).

Conclusion: A web-based, case-scenario Advocacy tool permitted access to training, increased participation and awareness of pertinent federal regulatory and legislative issues related to the care of rheumatic patients. A follow-up evaluation 2 years post-training to assess enduring Advocacy engagement is planned.

Disclosure: S. Gokaraju, None; **A. Worthing**, None; **K. Maher**, None; **G. Wright**, Amgen, 1, 2, Abbvie, 1, 2, Bristol Myers Squibb, 1, 2, Janssen, 1, Myriad, 1, 2, Pfizer, 1, Eli Lilly, 1, 2, UCB, 1, 2, Gilead, 1, Association of Women In Rheumatology, 1, Novartis, 1, 2; **G. Kerr**, Novartis, 1, BMS, 1, 2, Gilead, 1, Regeneron, 1, Janssen, 1.

Abstract Number: 0479

Early DAS Response After DMARD-start Increases Probability of Achieving Sustained DMARD-free Remission in Rheumatoid Arthritis

Marloes Verstappen[1], Ellis Niemantsverdriet[2], Xanthe Matthijssen[2], Saskia le Cessie[2] and Annette van der Helm - van Mil[3], [1]Leiden University Medical Center, Leiden, Zuid-Holland, Netherlands, [2]Leiden University Medical Center, Leiden, Netherlands, [3]Leiden University Medical Center, Erasmus Medical Center, Leiden, Netherlands

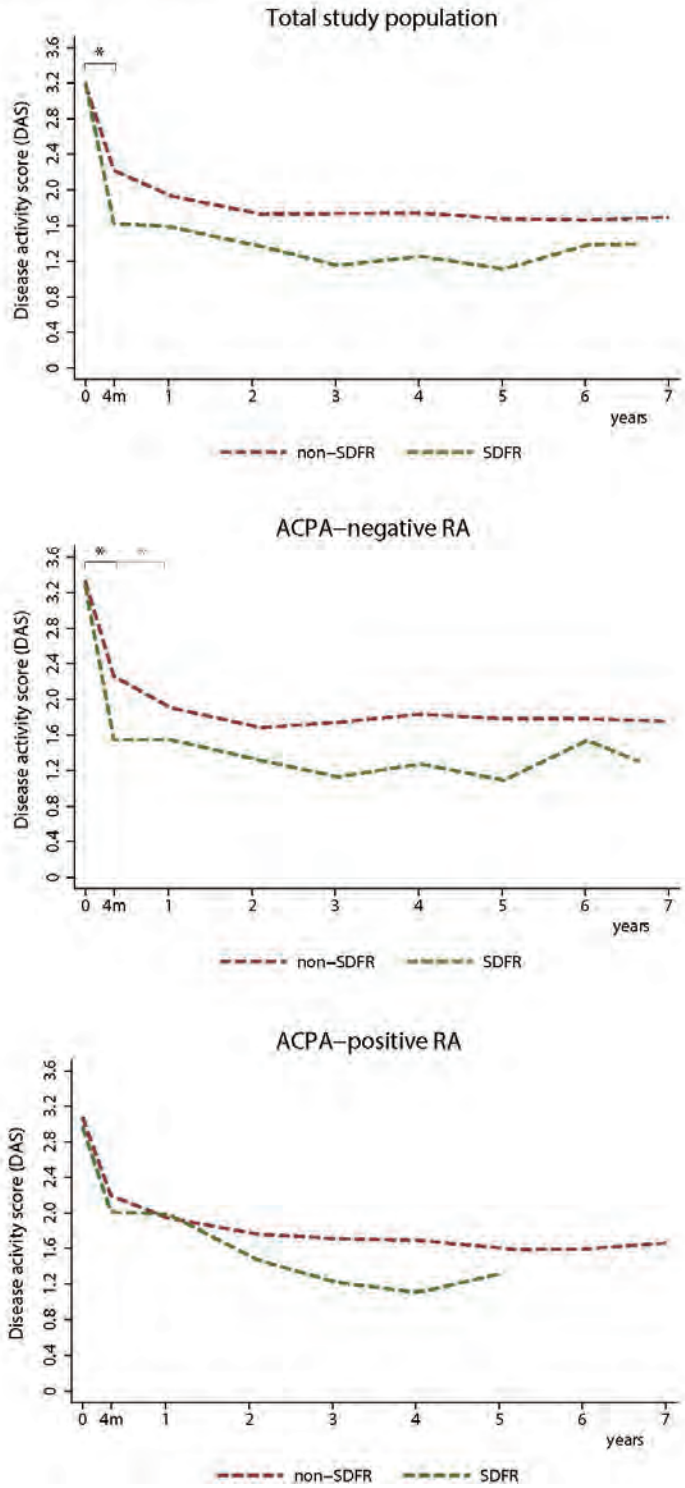
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes I: Pre-Onset & Early RA
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Sustained DMARD-free remission (SDFR) is increasingly achievable. The pathogenesis underlying SDFR-development is unknown and patient-characteristics at diagnosis poorly explain whether SDFR will be achieved. To increase the understanding, we studied the course of disease activity scores (DAS) over time in relation to SDFR-development. Subsequently, we explored whether DAS-course could be helpful identifying patients likely to achieve SDFR.

Methods: 772 consecutive RA-patients, promptly treated with csDMARDs (mostly methotrexate and treat-to-target treatment adjustments), were studied for SDFR-development (absence of synovitis, persisting minimally 12-months after DMARD-stop). The course of disease activity scores (DAS) were compared between patients with and without SDFR-development within 7-years, using linear mixed models, stratified for ACPA. The relation between 4-months DAS and the probability of SDFR-development was studied with logistic regression. Cumulative incidence of SDFR within DAS-categories (< 1.6, 1.6-2.4, 2.4-3.6, ≥3.6) at 4-months was visualized using Kaplan-Meier-curves.

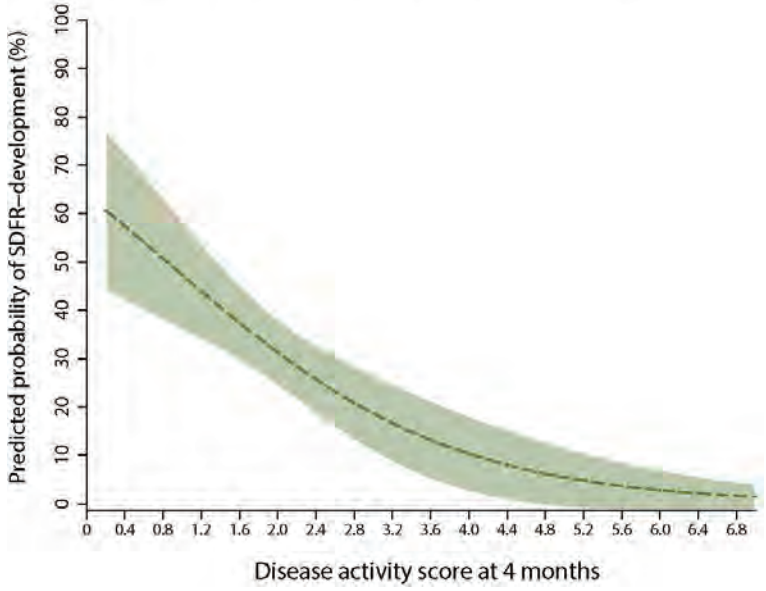
Results: In ACPA-negative patients, those achieving SDFR showed a remarkably stronger DAS-decline within the first 4-months, compared to patients without SDFR; -1.73 units (95%CI,1.28-2.18) versus -1.07 units (95%CI,0.90-1.23) (p< 0.001). In APCA-positive patients such a difference was not observed. In ACPA-negative RA, DAS-decline in the first 4-months and absolute DAS-levels at 4-months (DAS4months) were equally predictive for SDFR-development. Incidence of SDFR in ACPA-negative patients was high (70.2%) when DAS4months was < 1.6, whilst SDFR was rare (7.1%) when DAS4months was ≥3.6. In ACPA-negative patients, those achieving SDFR showed a remarkably stronger DAS-decline within the first 4-months, compared to patients without SDFR; -1.73 units (95%CI,1.28-2.18) versus -1.07 units (95%CI,0.90-1.23)(p< 0.001). In APCA-positive patients such a difference was not observed. In ACPA-negative RA, DAS-decline in the first 4-months and absolute DAS-levels at 4-months ($DAS_{4months}$) were equally predictive for SDFR-development. Incidence of SDFR in ACPA-negative patients was high (70.2%) when $DAS_{4months}$ was < 1.6, whilst SDFR was rare (7.1%) when $DAS_{4months}$ was ≥3.6.

Figure 1. Course of DAS over time for the SDFR and non-SDFR group in the total RA population studied, and for ACPA-negative RA and ACPA-positive RA separately.



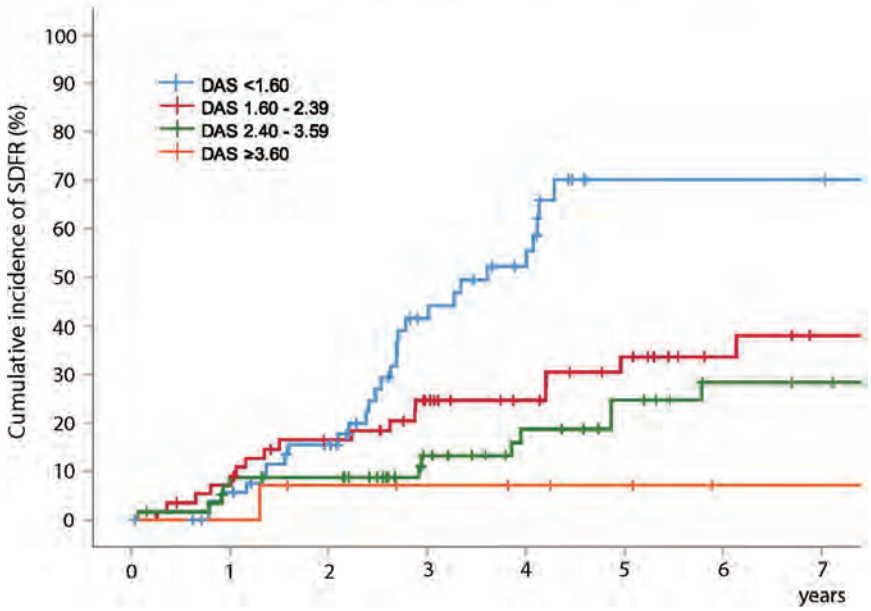
Legend: Course of DAS over time of patients achieving sustained DMARD-free remission (SDFR) within 7 years of follow-up (n=149), and those not (n=623). In ACPA-positive patients, the line of the SDFR-group was restricted to 5 years follow-up because of insufficient data thereafter. Statistically significant differences in course of DAS over time, between the SDFR-group and non-SDFR-group, were indicated by with: * ACPA: anti-citrullinated protein antibody, DAS: Disease activity scores, RA: Rheumatoid arthritis, SDFR: Sustained DMARD-free remission.

Figure 2. Predicted probability of SDFR-development in ACPA negative RA in relation to DAS at 4 months.



Legend: Predicted probability of achieving SDFR during follow-up in ACPA-negative RA, based on multivariate logistic model including DAS at 4 months, age, gender and symptom duration (table 2). For this graph, age, gender and symptom duration were set at the mean value of each covariable. An inverse relation is seen between DAS at 4-months and the predicted probability of achieving SDFR (within 7 years). ACPA: anti-citrullinated protein antibody, DAS: Disease Activity Score, SDFR: Sustained DMARD-free remission.

Figure 3. Kaplan-Meier curves for SDFR-development within 7-years follow-up based on disease activity scores at 4 months in ACPA-negative RA



Legend: Time-to-event was defined as time from 4-months visit until SDFR-development (yes/no), i.e. the absence of clinical arthritis for minimally 12-months after DMARD-stop. ACPA: anti-citrullinated protein antibody, DAS: Disease activity score, SDFR: sustained DMARD-free remission.

Conclusion: In ACPA-negative RA, early response to treatment, i.e. a strong DAS-decline within the first 4-months, is associated with a higher probability of SDFR-development. DAS-values at 4-months could be useful for later decisions to stop DMARDs.

Disclosure: M. Verstappen, None; **E. Niemantsverdriet**, None; **X. Matthijssen**, None; **S. le Cessie**, None; **A. van der Helm - van Mil**, None.

Abstract Number: 0480

Impact of Targeting Remission or Low Disease Activity on 10-year Severity in Rheumatoid Arthritis: Data from ESPOIR Cohort

Julia Dupont[1], Gregory Guernec[2], Yannick Degboé[3], Frédéric Lioté[4], Olivier Vittecoq[5], Arnaud Constantin[6] and Adeline Ruyssen Witrand[7], [1]University Hospital of Thoulouse, Toulouse, [2]Inserm UMR 1027, TOULOUSE CEDEX 9, France, [3]University Hospital of Toulouse, Toulouse, [4]AP-HP, Paris, France, [5]University Hospital of Rouen, Rouen, France, [6]Rheumatology Department, Toulouse University Hospital, Toulouse, France, [7]Rheumatology center, University Hospital of Toulouse, Inserm 1027, University Paul Sabatier, Toulouse, France, Toulouse, France

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes I: Pre-Onset & Early RA
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

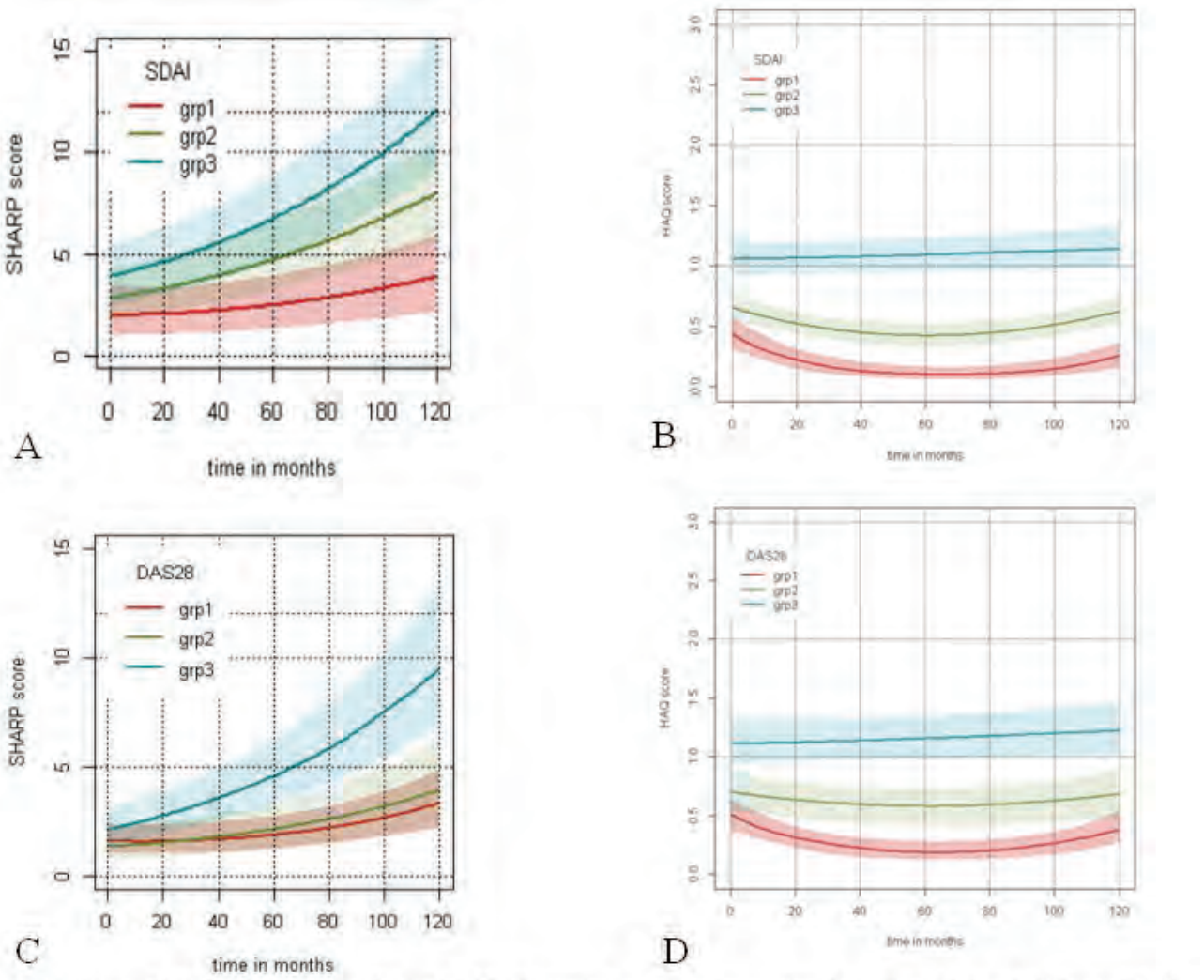
Background/Purpose: The aim of rheumatoid arthritis (RA) treatment is to target remission or at least low disease activity (LDA). We previously showed that SDAI remission at one year decreased the risk of 3-year structural progression in RA compared to patients in LDA.

The aim of the study was to compare 10-year severity outcomes including structural progression, function and orthopaedic surgery in RA patients with sustained remission versus patients with sustained LDA.

Methods: *Patients:* 813 patients with DMARDs-naïve early arthritis were included in the ESPOIR cohort and followed for 10 years. We analyzed data from with disease activity scores available at least at 6 visits out of 11 (n=523 with SDAI scores and n=527 with DAS28 scores).

Data analyzed: Remission was defined by SDAI ≤ 3.3 or DAS28< 2.6; LDA by 3.3 < SDAI score ≤ 11 or 2.6 ≤ DAS28 ≤ 3.2. Radiographs were centrally scored using the Total Sharp Score modified by Van der Heijde (mTSS) at baseline and at 10-year visits. Health Assessment Questionnaires (HAQ) and RA orthopaedic procedures were collected at each visit.

Analysis: patients were classified in 3 groups according to the SDAI at each visit between 1-year and 10-year visits. Group 1: patients with sustained SDAI remission. Group 2: patients with sustained SDAI LDA. Group 3: patients with moderate or high sustained disease activity. Patient with instable disease activity over time were excluded. A process latent mixed model were used to assess the impact of SDAI status over time on mTSS progression and mHAQ-DI evolution until 10-year visit was performed. A Cox proportional model was used to assess the impact of SDAI status over time on the risk of surgery. The following cofounding factors were included in the model: age, gender, disease duration, clinical center, erosions at baseline, ACPA positivity and titer , smoking habits, DMARDs use, time to start



A: predicted means of mTSS over time according to the SDAI groups (1=sustained remission, 2= sustained LDA, 3=MDA or HDA)
B : predicted means of HAQ over time according to SDAI groups (1=sustained remission, 2=sustained LDA, 3=MDA or HDA)
C: predicted means of mTSS over time according to the DAS28 groups (1=sustained remission, 2= sustained LDA, 3=MDA or HDA)
D: predicted means of HAQ over time according to DAS28 groups (1=sustained remission, 2=sustained LDA, 3=MDA or HDA)

DMARD, biologic agents use and glucocorticoid use. Comparisons between remission and LDA fort the 3 outcomes over 10 years were obtained from the multivariate model with contrasts method. Analyses were repeated using DAS28.

Results: After classification of patients according to SDAI over time, group 1 included 48 patients in remission (9.2%), and group 2 included 135 patients in LDA (25.8%), while 79 patients (14.9%) could be classified in remission group 1 and 53 patients (10.1%) could be classified in LDA group 2 using the DAS28.

Patients with sustained SDAI remission had lower 10-year structural progression compared to patients in LDA ($p=0.0014$) and lower 10-year HAQ means ($p< 0.0001$). After 10 year follow-up only 53 patients have undergone orthopaedic procedures (10%) of whom 3 were in the group 1 according to SDAI and 14 in group 2 ($p=0.14$). When

using DAS28 as disease activity score to classify patients, we identified a lower structural progression in the sustained DAS28 remission group compared to the LDA group (p=0.02) and patients in remission had lower 10-year HAQ means (p=0.0008) (figure), while no difference was observed for the risk of orthopaedic procedures between groups.

Conclusion: Aiming for SDAI or DAS28 remission rather than LDA during monitoring leads to better radiographic and functional outcomes at 10 years in early RA patients.

Disclosure: J. Dupont, None; **G. Guernec**, None; **Y. Degboé**, None; **F. Lioté**, LILLY FRANCE, 5, 8, SANOFI GENZYME, 8, SANDOZ, 5, NORDIC PHARMA, 8, LILLY FRANCE, 3; **O. Vittecoq**, BMS, 5, Novartis, 8, Pfizer, 8, ABBVIE, 5, 8; **A. Constantin**, None; **A. Ruyssen Witrand**, None.

Abstract Number: 0481

Subclinical Synovitis in Arthralgia: How Often Does It Result in Clinical Arthritis? A Longitudinal Study to Reflect on Starting Points for DMARD Treatment

Cleo Rogier[1], Fenne Wouters[2], Laurette van Boheemen[3], Dirkjan van Schaardenburg[4], Pascal de Jong[1] and Annette van der Helm - van Mil[5], [1]Erasmus MC, Rotterdam, Netherlands, [2]Leiden University Medical Center, Leiden, Netherlands, [3]Amsterdam Rheumatology and immunology Center | Reade, Amste, Netherlands, [4]Amsterdam Rheumatology and immunology Center | Reade and Amsterdam UMC, Amsterdam, Netherlands, [5]Leiden University Medical Center, Erasmus Medical Center, Leiden, Netherlands

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes I: Pre-Onset & Early RA
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: According to guidelines, clinical arthritis is mandatory for diagnosing rheumatoid arthritis (RA). However, in the absence of clinical synovitis, imaging-detected subclinical synovitis is increasingly used instead, and considered as starting point for DMARD-therapy. We searched for evidence of the natural course and determined in arthralgia-patients with subclinical synovitis from three longitudinal cohorts the frequencies of non-progression to clinically apparent inflammatory arthritis (IA) (i.e 'false-positives').

Methods: Subclinical synovitis in hands or feet of arthralgia-patients was visualized with ultrasound (two cohorts, subclinical synovitis definition: greyscale≥2 and/or power doppler≥1) or MRI (one cohort, subclinical synovitis: synovitis score ≥1 by two readers). Patients were followed for 1-year on IA-development; two cohorts also had 3-year data. Analyses were stratified for anti-citrullinated protein antibody (ACPA).

Results: Subclinical synovitis at presentation was present in 36%, 41% and 31% in the three cohorts. Of the ACPA-positive arthralgia-patients with subclinical synovitis 54%, 44% and 68%, respectively, did not develop IA (Figure 1A). These percentages were even higher in the ACPA-negative arthralgia-patients: 66%, 85% and 89% (Figure 1A). Similar results were seen after 3-years follow-up (Figure 1B).

Conclusion: Replacing clinical arthritis by subclinical synovitis to identify RA introduces a high false positive rate (44-89%). DMARD-initiation in absence of clinical arthritis may lead to considerable overtreatment.

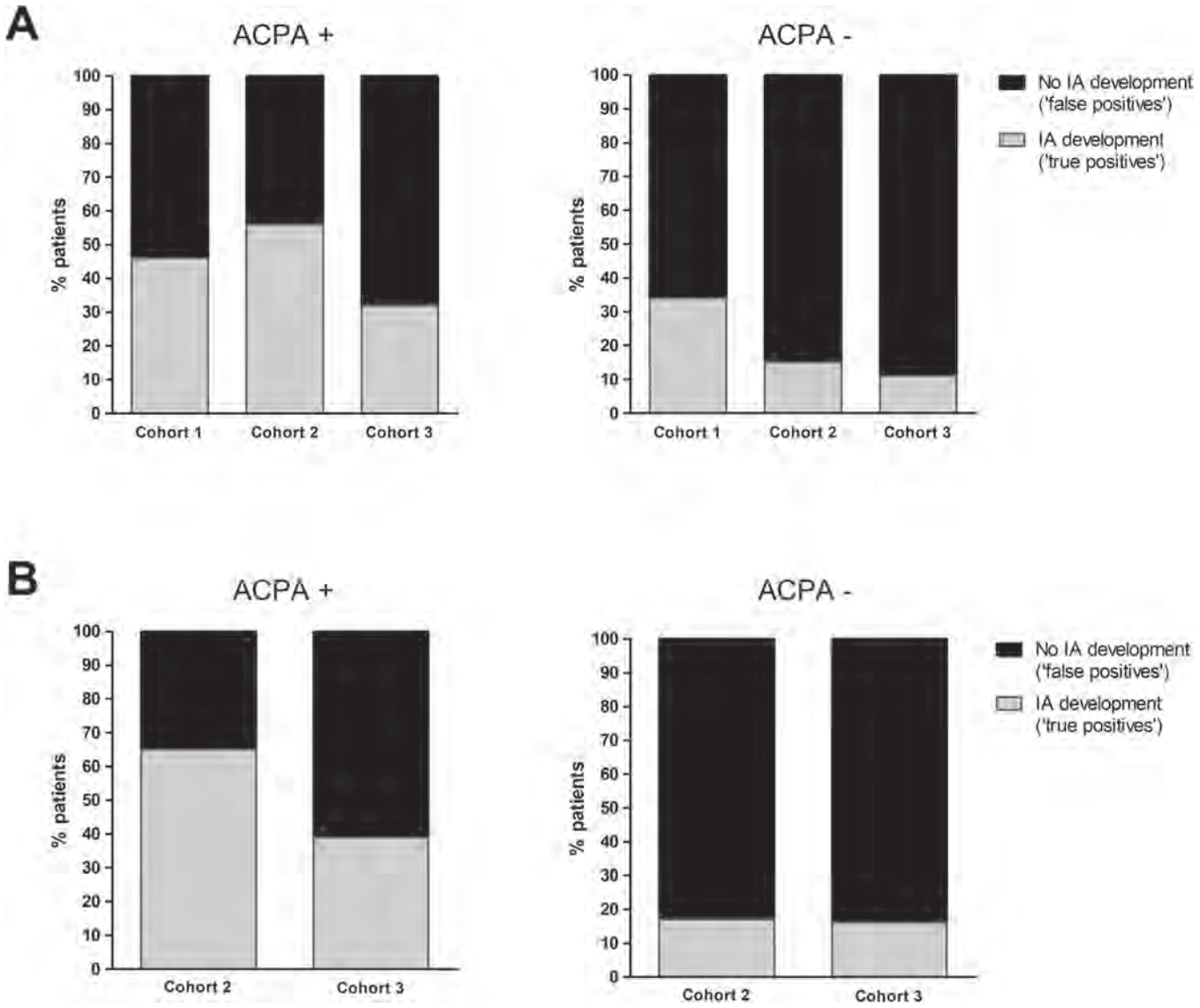


Figure 1 Percentage of arthralgia-patients with subclinical synovitis at baseline that did and did not develop inflammatory arthritis after 1-year (A) and 3-years follow-up (B), stratified for ACPA-status. Legend: (A) Percentage of patients with subclinical synovitis at baseline that did and did not progress to inflammatory arthritis after one year follow-up in three independent cohorts (ACPA-positive patients n=13, n=36, n=31, respectively; ACPA-negative patients n=47, n=157, n=19, respectively). (B) Percentage of patients with subclinical synovitis at baseline that did and did not progress to inflammatory arthritis after three year follow-up, in two independent cohorts (ACPA-positive patients n= 26, n=31, respectively; ACPA-negative patients n=121, n=19, respectively).

Disclosure: C. Rogier, None; **F. Wouters**, None; **L. van Boheemen**, None; **D. van Schaardenburg**, None; **P. de Jong**, None; **A. van der Helm - van Mil**, None.

Abstract Number: 0482

Differential Influence of CDAI Components Based on Disease State in Rheumatoid Arthritis Patients: Real World Results from a Rheumatoid Arthritis Cohort

Edward C Keystone[1], Mohammad Movahedi[2], Angela Cesta[3], Claire Bombardier[4], John Sampalis[5] and **Emmanouil Rampakakis**[5], [1]Mount Sinai Hospital, Toronto, ON, Canada, [2]Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada, [3]Toronto General Hospital Research Institute, Toronto, ON, Canada, [4]Institute for Work and Health, Toronto, ON, Canada, [5]JSS Medical Research, St-Laurent, QC, Canada

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes I: Pre-Onset & Early RA
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Treat-to-target recommendations for rheumatoid arthritis (RA) dictate that remission or low disease activity should be aimed. Although numerous composite indices are available, the clinical disease activity index (CDAI) is commonly used in routine clinical care due to its simplicity and non-reliance on acute phase reactants. The purpose of this analysis was to evaluate the CDAI properties both cross-sectionally and longitudinally in a cohort of RA patients followed in Canadian routine care.

Methods: RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI), with available follow-up for ≥6 months and data on CDAI, disease activity score based on 28 joints (DAS28), health assessment questionnaire (HAQ), and ACR/EULAR Boolean remission were included. For both the CDAI score and its change from baseline to 6 months, construct validity was assessed with principal component analysis, internal consistency with the Cronbach's alpha coefficient (α), correlational validity with the Spearman's rho coefficient, agreement in disease state classification with percent concordant pairs and the kappa statistic. Stratified analysis by presence of CDAI low disease activity (LDA) or remission was performed.

Results: 1,582 patients met the inclusion criteria. Principal component analysis showed that CDAI could be reduced to a single component when CDAI is >10 with SJC28 accounting for most variance in score and patient global assessment (PtGA) the least; whereas, when CDAI is ≤10, two distinct components were identified, the first comprising PtGA and physician global assessment (PhGA) and the second SJC28 and TJC28. In terms of internal consistency, high levels were observed for both CDAI at baseline (α=0.83) and its change from baseline to 6 months (α=0.81); however, the consistency between CDAI components was very low when CDAI is ≤10 (α=0.23).

Overall, a strong positive correlation was observed between CDAI and DAS28 (rho=0.86) and their changes (rho=0.87) while its correlation with HAQ was weak. When stratifying by CDAI levels, the correlation of CDAI with DAS28 was moderate when CDAI is ≤10 and very weak when CDAI is ≤2.8. Similarly, agreement in the classification of LDA between CDAI and DAS28 or HAQ was fair to moderate, and agreement in classification of remission was poor to fair.

Conclusion: CDAI and DAS28 correlate well when disease activity is moderate or high and poorly in LDA or remission. PtGA had a stronger influence on CDAI at LDA or remission state compared to moderate or high disease state. Thus, careful interpretation of PtGA is necessary particularly in patients who are identified as CDAI non-remitters.

Disclosure: E. Keystone, AbbVie, 2, 5, 8, Celltrion, 2, 5, 8, Eli Lilly, 2, 5, 8, Pfizer Inc, 2, 5, 8, Merck, 2, 5, 8, Sandoz, 2, 5, 8, Samsung Bioepsis, 2, 5, 8, Myriad Autoimmune, 2, 5, 8, Purapharm, 2, 5, 8, Janssen, 2, 5, 8, Sanofi-Gen-

zyme, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, F. Hoffman-La Roche Ltd., 2, 5, 8, Genentech, 2, 5, 8, Gilead, 2, 5, 8, UCB, 2, 5, 8; **M. Movahedi**, None; **A. Cesta**, None; **C. Bombardier**, CIHR, 2, MOHLTC, 2, Abbvie, 2, Amgen, 2, Janssen, 2, Medexus, 2, Merck, 2, 5, Novartis, 2, Pfizer, 2; **J. Sampalis**, None; **E. Rampakakis**, None.

Abstract Number: 0483

Can a Clinical Disease Activity Index Based on Patient-Reported Joint Counts (PT-CDAI) Be Used to Inform Target-Based Care in Telemedicine? An Analysis of 2 Early RA Cohort Studies

Caroline Benson[1], Marie-France Valois[2], Orit Schieir[3], Gregory Vitone[1], Aidan Tirpack[1], Michelle Jones[4], Louis Bessette[5], Gilles Boire[6], Glen Hazlewood[7], Carol Hitchon[8], Edward C Keystone[9], Janet Pope[10], Carter Thorne[11], Susan Bartlett[2], Clifton Bingham III[12], **Vivian Bykerk**[1] and Canadian Early Arthritis Cohort (CATCH) Investigators[13], [1]Hospital for Special Surgery, New York, NY, [2]McGill University, Montreal, Canada, [3]Canadian Early Arthritis Cohort Study, Montreal, Canada, [4]Johns Hopkins Arthritis Center, Baltimore, MD, [5]Laval University, Quebec, Canada, [6]Universite de Sherbrooke, Sherbrooke, Canada, [7]University of Calgary, Calgary, AB, Canada, [8]University of Manitoba, Winnipeg, MB, Canada, [9]Mount Sinai Hospital, Toronto, ON, Canada, [10]Department of Medicine, University of Western Ontario, St. Joseph's Health Centre, London, ON, Canada, [11]Southlake Regional Health Centre, Newmarket, ON, Canada, [12]Johns Hopkins University, Baltimore, MD, [13]Canadian Early Arthritis Cohort (CATCH) Study, Toronto, Canada

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes I: Pre-Onset & Early RA
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: COVID-19 mitigation strategies have forced rheumatologists to shift from in-person clinical visits to telemedicine, limiting their ability to carry out complete joint exams needed to score disease activity and provide target based-care for RA patients. The purpose of this study was to estimate agreement between the validated Clinical Disease Activity Index (CDAI), and an alternative patient-based CDAI (PT-CDAI) scored using patient-reported joint counts.

Methods: Data were from early RA patients (sx < 1 year) enrolled in 2 North American prospective cohort studies, CATCH (Canadian early ArThritis CoHort) and CATCH-US (Consortium of early ArThritis Cohorts-USA), from Mar 2017-Jan 2020 and Jan 2015-Feb 2020 with complete data needed to calculate the MD-CDAI and PT-CDAI including concurrently measured patient (PT) and physician (MD) assessed 28-tender and 28-swollen joints counts (28-TJC/28-SJC) using a homunculus, MD and PT global assessments (NRS 0-10) and other PROs (pain, stiffness, fatigue, function and mental health) at baseline, 6- and 12-months follow up. MD-CDAI and PT-CDAI were scored by summing (28-TJC and 28-SJC, MD and PT global assessments) though the former was scored using MD assessed joint counts and the latter with PT assessed joint counts. The established CDAI cut-off of 10 was applied to both scores to classify patients in REM/LDA vs. MDA/HDA disease states. Descriptive statistics were used to summarize and compare baseline cohort characteristics. Bland-Altman plots were used to estimate agreement between the MD-CDAI and the PT-CDAI. Cohen's Kappa was used to estimate agreement between scores at classifying patients into controlled (REM/LDA) vs. active (MDA/ HDA) disease states. Mixed-effects linear regression was used to identify potential predictors of greater discrepancies between MD-CDAI and PT-CDAI.

Results: Baseline characteristics of 358 ERA patients enrolled in CATCH and 102 ERA patients enrolled in CATCH-US are summarized in Table 1. Mean differences in PT vs. MD assessments were lower for swollen than tender joints (Figure). Both studies showed higher agreement at lower ranges of the CDAI and more spread in scores at higher

Patient Characteristics at Baseline	COHORT 1 Canadian Early Arthritis Cohort (N=358)	COHORT 2 Consortium of Early Arthritis Cohorts USA (N=102)
Socio-Demographic		
Age (years)	57 (14)	47 (15)
Female, n (%)	230 (64%)	90 (85%)
Caucasian (White /European), n (%)	297 (83%)	72 (68%)
Education > high school, n (%)	217 (61%)	95 (90%)
Current Smoker, n (%)	53 (15%)	11 (10%)
Obese BMI (≥ 30), n (%)	92 (30%)[§]	26 (25%)[§]
RDCI^ (0-9)	1.3 (1.4)	1.0 (1.3)
RA Characteristics		
Symptom duration (months)	5.4 (2.9)	6.3 (3.1)
Meet RA criteria (1987 or 2010), n (%)	248 (69%)	99 (93%)
RF+/CCP+, n (%)	194 (56%)[§]/206 (63%)[§]	69 (68%)[§]/64 (66%)[§]
MD-CDAI	25.8 (14.0)	15.3 (12.3)
MD TJC (28) / SJC(28)	8 (6) / 7 (6)	4 (5) / 4 (5)
MD Global (0-10)	5.1 (2.5)	3.7 (2.2)
RA Medications		
Any csDMARDs, n (%)	324 (91%)	55 (52%)
MTX monotherapy, n (%)	122 (34%)	22 (21%)
MTX combination therapy, n (%)	139 (39%)	10 (9%)
Biologics or JAKi, n (%)	2 (1%)	12 (11%)
Oral steroids use, n (%)	106 (30%)	44 (41%)
PROs		
Patient Global (0-10)	4.7 (2.7)	3.3 (2.6)
Function - MD-HAQ (0-10)	2.7 (2.0)	1.4 (1.5)
RAFQ Domain Ratings (NRS 0-10)		
Pain Severity	5.5 (2.8)	3.6 (2.6)
Difficulty physical activities	5.5 (2.9)	3.2 (2.7)
Fatigue	5.2 (2.9)	3.5 (2.9)
Stiffness	5.8 (2.8)	3.7 (3.0)
Participation	5.1 (3.0)	2.7 (2.8)
RAFQ Sum of 5 Domains (0-50)	27.1 (13.3)	16.9 (12.4)
PHQ8 (0-24)	6.8 (5.9)	4.9 (4.8)
PT TJC (28) / SJC (28)	10.3 (7.8)/7.3 (7.8)	4.9 (5.8)/ 3.1 (4.8)
PT-CDAI	27.5 (16.7)	15.1 (12.0)
Regional non-articular pain (NAP), n (%)	122 (34%)	27 (25%)
Widespread non-articular pain (NAP), n (%)	76 (21%)	4 (4%)
RDCI Rheumatic Disease Comorbidity Index (0-9)		
Data are mean (SD) unless noted. N (%) refers to the frequency of observed values		

Table 1. Baseline Characteristics show more are older, have higher BMI and non-articular pain and are current smokers in Canadian Cohort; more are female, younger and recruited with lower disease activity in CATCH-US.

ranges of the CDAI (Figure). Agreement between MD-CDAI and PT-CDAI scores were moderate to substantial at classifying patients with controlled vs. active disease (Table 2). Predictors of greater differences in MD-CDAI vs. PT-CDAI

CATCH Joint Count Values (N=664)			CATCH-US Joint Count Values (N=211)		
Joint Count, mean (SD)	**MD**	**PT**	**Joint Count, mean (SD)**	**MD**	**PT**
SJC28 (0-28)	4.7 (5.5)	4.7 (6.7)	SJC28 (0-28)	3.4 (4.6)	2.9 (5.3)
TJC28 (0-28)	5.3 (6.1)	7.5 (7.5)	TJC28 (0-28)	3.1 (4.6)	4.5 (6.2)
CDAI, mean (SD)	**MD-CDAI**	**PT-CDAI**	**Measure, mean (SD)**	**MD-CDAI**	**PT-CDAI**
CDAI (0-76)	17.0 (14.9)	19.2 (16.4)	CDAI	12.6 (11.8)	13.5 (13.4)

Agreement between PT and MD-CDAI Scores in Those with Active or Controlled RA As Defined by MD-CDAI Grouped DA States		
CATCH (N = 664)	**MD-CDAI**	**PT-CDAI**
Active RA (N=280)	384 (58%)	418 (63%)
Controlled RA (N=384)	280 (42%)	246 (37%)
Simple Kappa (95% CI)	**0.67 (0.62, 0.73)**	

CATCH-US (N=211)	**MD-CDAI**	**PT-CDAI**
Active RA (N=111)	100 (47%)	100 (47%)
Controlled RA (N=100)	111 (53%)	111 (53%)
Simple Kappa (95% CI)	**0.72 (0.62, 0.81)**	

Data comparing MD / PT joint Counts and MD and PT-CDAI are from all visits (baseline, 6 months, 12 months combined, mean (SD))
Active RA is defined using MD-CDAI DA states combining those who are in moderate and high disease activity (MDA/HDA) and controlled RA as those in low disease activity and remission (LDA/REM)

Table 2. Comparisons of MD vs. PT Joint Counts and CDAI Scores

in mixed-effects linear regression were greater tender joints and worse stiffness in CATCH and tender joints, obesity and male sex in CATCH-US.

Conclusion: The newly calculated PT-CDAI had good agreement with the MD-CDAI at identifying active vs. controlled RA disease activity. Results suggested that PT-based swollen joints were more consistent with MD assessments than PT tender joint counts. Moreover, predictors of higher discrepancies between PT-CDAI and MD-CDAI may help identify patient subsets that could benefit most from more MD guided training at joint self-assessments and/or more probing questioning during a telehealth visit to confirm active synovitis. Although there are other validated PROs to assess disease activity, none directly assess joint involvement which is critical to informing treatment decisions.

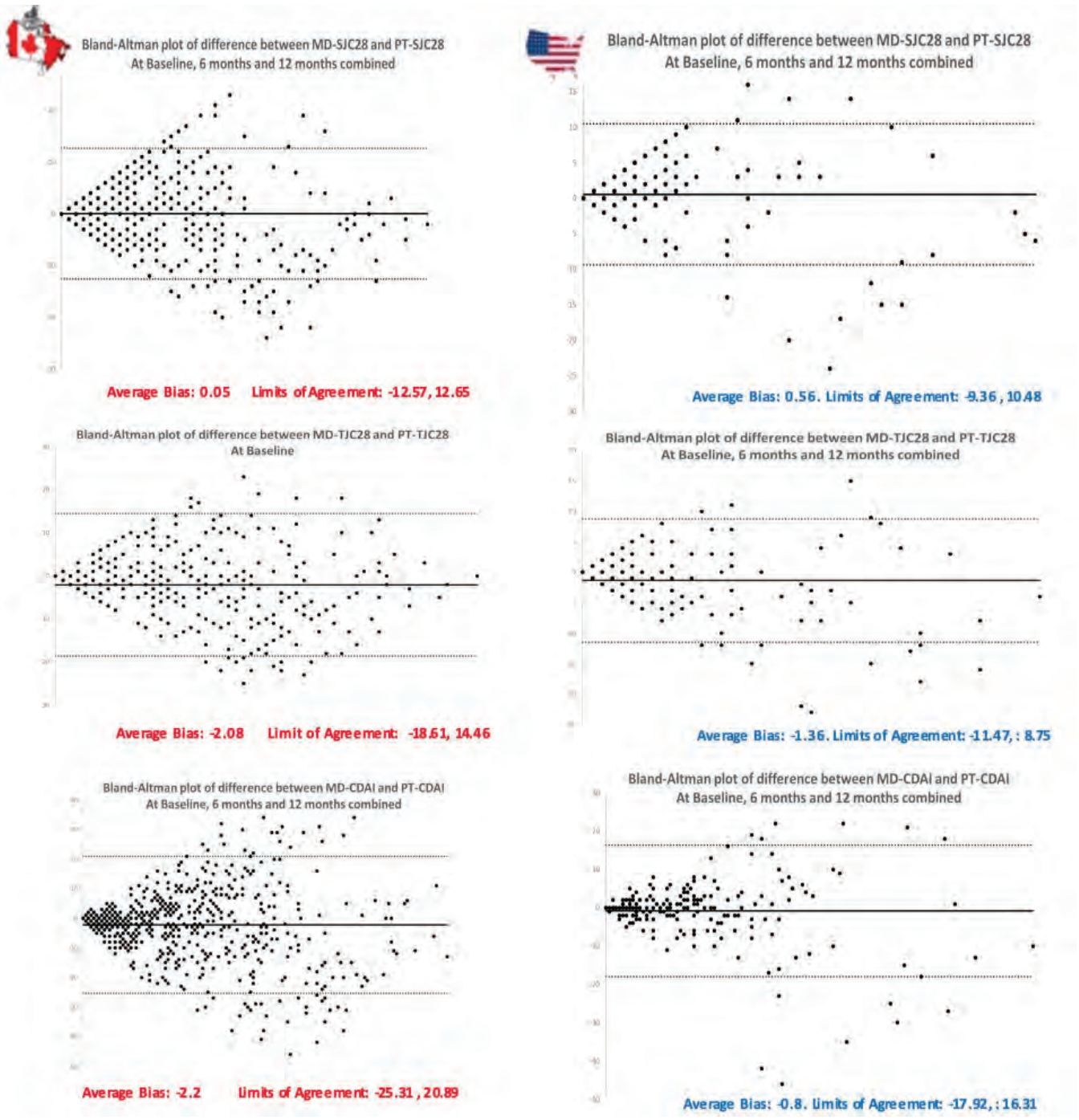


Figure. Agreement between Physician and Patient Assessed 28 Swollen and Tender Joint Counts and PT-CDAI vs. MD-CDAI in 2 Early RA Cohorts

Disclosure: C. Benson, None; **M. Valois**, None; **O. Schieir**, None; **G. Vitone**, None; **A. Tirpack**, None; **M. Jones**, None; **L. Bessette**, Amgen, 1, 2, 3, BMS, 1, 2, 3, Janssen, 1, 2, 3, UCB, 1, 2, 3, AbbVie, 1, 2, 3, Pfizer, 1, 2, 3, Merck, 1, 2, 3, Celgene, 1, 2, 3, Sanofi, 1, 2, 3, Lilly, 1, 2, 3, Novartis, 1, 2, 3, Gilead, 2, 6, 8; **G. Boire**, Amgen, 1, 2, BMS, 1, 2, 3, Celgene, 1, Merck, 1, 2, Pfizer, 1, 2, 3, Eli Lilly, 1, 2, Janssen, 1, Abbvie, 1, Novartis, 1, Sandoz, 1; **G. Hazlewood**, None; **C. Hitchon**, Pfizer, 1, UCB Canada, 1; **E. Keystone**, AbbVie, 2, 5, 8, Celltrion, 2, 5, 8, Eli Lilly, 2, 5, 8, Pfizer Inc, 2, 5, 8, Merck, 2, 5, 8, Sandoz, 2, 5, 8, Samsung Bioepsis, 2, 5, 8, Myriad Autoimmune, 2, 5, 8, Purapharm, 2, 5, 8, Janssen, 2, 5, 8, Sanofi-Genzyme, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, F.

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Abstract Number: 0484

Relationship Between Paraoxonase-1 Genotype, Activity, and Major Adverse Cardiovascular Events in Patients with Rheumatoid Arthritis Receiving Tofacitinib

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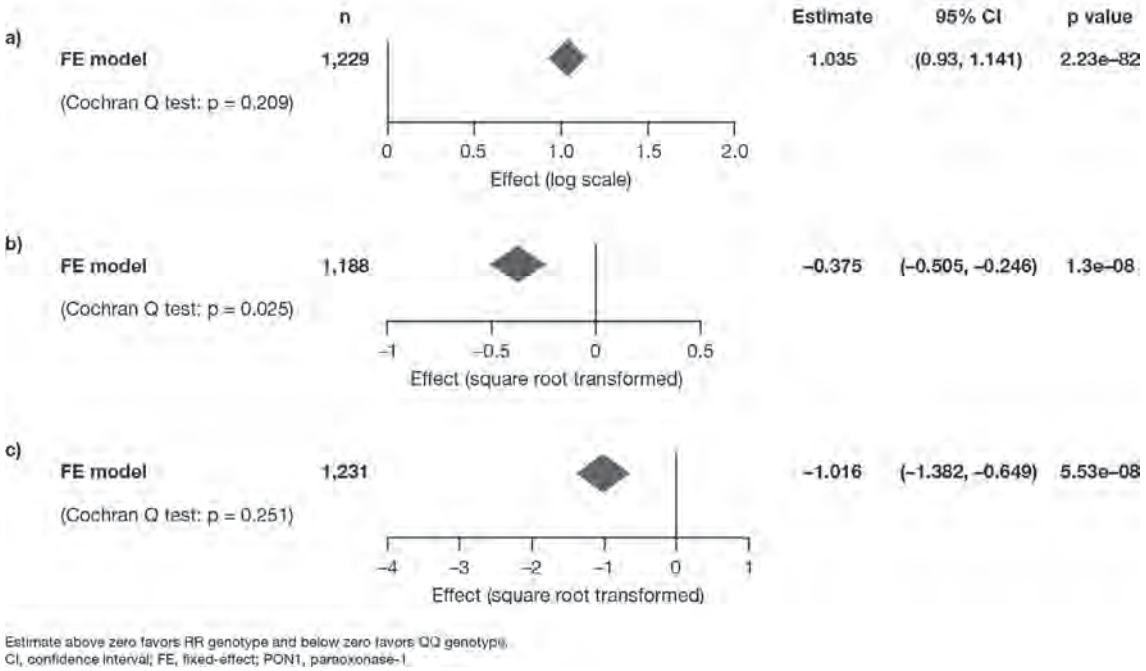
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes II: The Heart of the Matter
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Paraoxonase 1 (PON1) is a high-density lipoprotein (HDL)-associated enzyme with paraoxonase, lactonase, and arylesterase activities. PON1 contributes to the antioxidant properties of HDL, and is being investigated for its atheroprotective properties.[1] Patients (pts) with RA that are homozygous for the RR genotype of the Q192R gene polymorphism on PON1 (rs662) have increased paraoxonase activity, and a lower risk of carotid plaques, vs those with QQ or QR genotypes.[2] Tofacitinib is an oral Janus kinase inhibitor for the treatment of RA. This post hoc analysis investigated the relationship between PON1 genotype/activity and risk of major adverse cardiovascular events (MACE) in the tofacitinib RA clinical program.

Methods: Data were pooled from pts enrolled in nine Phase 2/3 studies of tofacitinib in RA. Enzyme activities in pt plasma samples were measured at individual study baseline (BL) and at follow-up visits using three substrates: paraoxon (paraoxonase activity), dihydrocoumarin (lactonase activity), and phenylacetate (arylesterase activity). The effect of the PON1 Q192R genotype (QQ, QR, or RR) on BL paraoxonase/lactonase/arylesterase activity was determined using linear regression for each study with age and sex as covariates, and then fixed-effect meta-analysis assessed effects across studies. The risk of MACE by enzyme activity was determined using Cox proportional hazards regression stratified by clinical studies. Univariate regression against BL enzyme activity and other risk factors, as well as both minimally and fully adjusted multivariable regressions against time-varying enzyme activity, are presented.

Results: The analysis included 1,969 pts with RA who received ≥ 1 dose of tofacitinib and had PON1 activity measures available at BL; 39 pts had ≥ 1 MACE event. Compared with the QQ genotype, the RR genotype had a highly significant positive association with BL paraoxonase activity, and a highly significant negative association with BL

Figure 1. Effect of PON1 Q192R genotype (RR vs QQ) on a) paraoxonase, b) lactonase, and c) arylesterase enzyme activities



Estimate above zero favors RR genotype and below zero favors QQ genotype.
CI, confidence interval; FE, fixed-effect; PON1, paraoxonase-1

Figure 1

lactonase and arylesterase activity (Figure 1). A univariate analysis identified several BL covariates significantly associated with risk of MACE (Figure 2a). Time-varying models found a highly significant association of increased paraoxonase activity over time with lower risk of future MACE, even after controlling for low-density lipoprotein or HDL cholesterol levels, and other traditional cardiovascular (CV) risk factors identified in univariate analysis (Figure 2b), with similar findings for lactonase and arylesterase (data not shown).

Conclusion: Higher activity of the HDL-associated protein, PON1, over time was associated with a significantly reduced risk of future MACE in pts with RA receiving tofacitinib, after controlling for traditional CV risk factors and cholesterol levels. Further investigation of PON1 as a novel functional lipid biomarker to assess CV risk in RA pts is warranted.

1. Mackness M, Mackness B. Gene 2015; 567: 12-21.

2. Charles-Schoeman C et al. Arthritis Rheum 2013; 65: 2765-2772.

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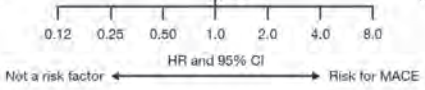
Figure 2. Associations between a) baseline covariates and occurrence of MACE (univariate analysis) and b) baseline and time-varying covariates and occurrence of MACE (univariate and multivariable adjusted analyses)

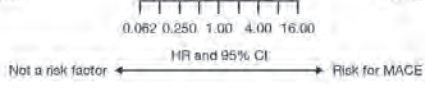
a)

Covariate	Events / Patients	HR	95% CI	p value (nominal)	p value (FDR)
Log (Paraoxonase)[a]	39 / 1,429	0.714	(0.51, 1)	0.0502	0.143
sqrt (Lactonase)[a]	38 / 1,375	0.759	(0.544, 1.06)	0.105	0.19
sqrt (Arylesterase)[a]	39 / 1,432	0.838	(0.607, 1.16)	0.283	0.404
Age (10 years)	39 / 1,434	2.16	(1.56, 3)	3.98e-06***	7.96e-06***
Sex (male/female)	39 / 1,434	1.32	(0.603, 2.89)	0.487	0.573
Average tofacitinib dose (10 mg/5 mg)	39 / 1,434	0.529	(0.227, 1.23)	0.14	0.233
BMI (kg/m^2)	39 / 1,434	1.05	(1.01, 1.09)	0.00653**	0.0435*
RA duration (years)	39 / 1,434	0.979	(0.936, 1.02)	0.347	0.433
Glucocorticoid use (Y/N)	39 / 1,434	0.722	(0.382, 1.36)	0.316	0.421
Methotrexate use (Y/N)	39 / 1,434	0.614	(0.13, 2.91)	0.539	0.599
Statin use (Y/N)	39 / 1,434	1.3	(0.499, 3.41)	0.588	0.619
Smoking status (ex-smoker/never smoked)	39 / 1,434	2.35	(1.09, 5.1)	0.0302*	0.101
Smoking status (smoker/never smoked)	39 / 1,434	2.58	(1.2, 5.53)	0.0151*	0.0748
Hypertension (Y/N)	39 / 1,434	2.14	(1.13, 4.03)	0.0187*	0.0748
Diabetes (Y/N)	39 / 1,434	3.76	(1.63, 8.63)	0.00182**	0.0182*
Total cholesterol[b]	28 / 1,154	1.33	(0.88, 2.01)	0.176	0.27
LDL cholesterol[b]	27 / 1,143	1.5	(0.973, 2.32)	0.0662	0.147
HDL cholesterol[b]	28 / 1,153	0.713	(0.487, 1.04)	0.0824	0.165
Triglycerides[b]	28 / 1,154	1.4	(0.985, 1.99)	0.0608	0.147



b)

Covariate	Model	#Events / #Observation	HR	95% CI	p value
Time varying log (Paraoxonase)[a]	Univariate	39 / 3,971	0.553	(0.408, 0.748)	0.000125***
Time varying log (Paraoxonase)[a]	Minimally adjusted	39 / 3,971	0.514	(0.371, 0.711)	5.75e-05***
Time varying log (Paraoxonase)[a]	Fully adjusted	39 / 3,971	0.494	(0.346, 0.705)	1e-04***
Time varying log (Paraoxonase)[a]	Fully adjusted + HDL cholesterol[c]	29 / 3,281	0.517	(0.349, 0.766)	0.001**
Time varying log (Paraoxonase)[a]	Fully adjusted + LDL cholesterol[c]	28 / 3,264	0.507	(0.34, 0.755)	0.000848***
Time varying log (Paraoxonase)[a]	Fully adjusted + Total cholesterol[c]	29 / 3,282	0.497	(0.333, 0.74)	0.000568***
Time varying log (Paraoxonase)[a]	Fully adjusted + Triglycerides[c]	29 / 3,282	0.505	(0.338, 0.756)	0.00089***
Time varying log (Paraoxonase)[a]	Fully adjusted + rs662 in EUR patients	31 / 2,704	0.674	(0.379, 1.201)	0.181
Baseline log (Paraoxonase)[a]	Fully adjusted baseline model	39 / 1,429	0.792	(0.555, 1.131)	0.199
Baseline log (Paraoxonase)[a]	Fully adjusted baseline model + rs662	31 / 953	0.902	(0.557, 1.46)	0.675
rs662 QR vs QQ	rs662 multivariate baseline model	31 / 956	1.473	(0.702, 3.093)	0.306
rs662 RR vs QQ	rs662 multivariate baseline model	31 / 956	0.35	(0.045, 2.746)	0.318
rs662 QR vs QQ	Fully adjusted + rs662 in EUR patients	31 / 2,704	2.149	(0.861, 5.365)	0.101
rs662 RR vs QQ	Fully adjusted + rs662 in EUR patients	31 / 2,704	0.566	(0.064, 4.98)	0.608
HDL cholesterol[c]	Fully adjusted + HDL cholesterol[c]	29 / 3,281	0.573	(0.396, 0.828)	0.00301**
LDL cholesterol[c]	Fully adjusted + LDL cholesterol[c]	28 / 3,264	1.289	(0.855, 1.941)	0.225
Total cholesterol[c]	Fully adjusted + Total cholesterol[c]	29 / 3,282	1.225	(0.821, 1.829)	0.321
Triglycerides[c]	Fully adjusted + Triglycerides[c]	29 / 3,282	1.476	(1.06, 2.055)	0.0212*
Age (10 years)	Fully adjusted	39 / 3,971	2.31	(1.592, 3.351)	1.03e-05***
Average tofacitinib dose (10 mg/5 mg)	Fully adjusted	39 / 3,971	0.708	(0.31, 1.616)	0.412
BMI (kg/m^2)	Fully adjusted	39 / 3,971	1.035	(0.991, 1.081)	0.122
Diabetes (Y/N)	Fully adjusted	39 / 3,971	2.357	(0.944, 5.88)	0.0662
Smoking status (ex-smoker/never smoked)	Fully adjusted	39 / 3,971	1.741	(0.778, 3.894)	0.177
Smoking status (smoker/never smoked)	Fully adjusted	39 / 3,971	3.253	(1.489, 7.107)	0.00309**



*p≤0.05, **p<0.01, ***p<0.001
[a]All paraoxonase activities were standardized (mean = 0, SD = 1); [b]All lipids were log transformed and standardized (mean = 0, SD = 1); [c]All lipids analyzed were time-varying, log transformed and then standardized (mean = 0, SD = 1).
Risk of MACE by BL enzyme activity was determined using Cox proportional hazards regression stratified by clinical studies. BL univariate regression models included BL paraoxonase/lactonase/arylesterase activities and pt demographic/disease characteristics. Time-varying univariate regression models included time-varying PON1 activity. Minimally and fully adjusted multivariable regression models included time-varying PON1 activity and additional covariates of significance/interest in univariate models.
After FDR multiplicity adjustment, age, BMI, diabetes mellitus, and smoking status were significant or nominally significant and included in the fully adjusted model; tofacitinib dose was also included. Heterogeneity was measured using the Cochran Q test. In the event of significant heterogeneity, random-effect (DerSimonian and Laird) meta-analysis was also conducted.
BMI, body mass index; BL, baseline; CI, confidence interval; EUR, European; FDR, false discovery rate; HDL, high-density lipoprotein; HR, hazard ratio; LDL, low-density lipoprotein; MACE, major adverse cardiovascular events; N, no, PON1, paraoxonase-1; RA, rheumatoid arthritis; rs662, Q192R gene polymorphism on PON1; SD, standard deviation; sqrt, square root, Y, yes

Figure 2

Disclosure: C. Charles-Schoeman, AbbVie, 2, 5, Regeneron-Sanofi, 5, Gilead, 5, Bristol-Myers Squibb, 2, Pfizer Inc, 2, 5; **C. Hyde**, Pfizer Inc, 1, 3; **S. Guan**, Pfizer Inc, 1, 3; **N. Parikh**, None; **J. Wang**, None; **A. Shahbazian**, None; **L. Stockert**, Pfizer Inc, 1, 3; **J. Andrews**, Pfizer Inc, 1, 3.

Abstract Number: 0485

Non-obese Rheumatoid Arthritis Patients with Low Low-density Lipoprotein Have Higher Coronary Atherosclerosis Burden, Greater Plaque Progression and Cardiovascular Event Risk

George Karpouzas[1], Sarah Ormseth[1], Elizabeth Hernandez[1] and Matthew Budoff[1], [1]Harbor-UCLA Medical Center and the Lundquist Institute, Torrance, CA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes II: The Heart of the Matter
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: RA patients with low body weight incur higher mortality than obese patients. Paradoxically, RA patients in the lowest low-density lipoprotein group (LDL < 70 mg/dl) also experience unexpectedly high cardiovascular disease (CVD) risk. We here explored whether abdominal obesity (waist-to-height ratio >0.58 in females and >0.63 in males) might moderate the effect of low LDL (< 70mg/dl) on coronary atherosclerosis burden, progression and long-term CVD event risk in RA.

Methods: One hundred fifty patients without symptoms or diagnosis of CVD underwent coronary computed tomography angiography. Plaque progression was evaluated 6.9±0.3 years later in 101 patients. Coronary artery calcium, number of segments with plaque (segment involvement score), and extensive (>4 segments with plaque) or obstructive disease (>50% stenosis) were assessed. CVD events were prospectively recorded, including cardiac death, myocardial infarction, unstable angina, revascularization, stroke, claudication, and heart failure hospitalization over 6.0±2.4 years of follow-up. Lipoprotein classes were directly measured. Oxidized LDL (oxLDL) was assessed with monoclonal antibody E06. Adjusted robust linear regression evaluated interactions between abdominal obesity and LDL groups on plaque outcomes. Per segment, adjusted robust logistic regression models explored obesity x LDL group interactions on new plaque formation and stenotic progression of prevalent plaques. Robust Cox regression models stratified by abdominal obesity evaluated the effect of LDL group (< 70 vs. >70mg/dl) on CVD events.

Results: Non-obese patients with low LDL had the highest plaque burden (Figure 1A, all $p < 0.02$). Obesity further moderated the effect of LDL on likelihood of extensive/obstructive disease (*P* for interaction = 0.061); specifically, LDL< 70 associated with an increased likelihood of extensive/obstructive plaque in non-obese (adjusted OR 4.75 [95% CI 1.18-19.07], *P* = 0.028) but not obese patients (adjusted OR 1.55 [95% CI 0.39-6.08], *P* = 0.532). No differences in disease activity or inflammatory markers were seen across groups. Compared to LDL >70 mg/dl, low LDL predicted an increased likelihood of high oxLDL (>median) in non-obese patients (adjusted OR 5.10 [95% CI 1.46-17.75], *P* = 0.011) but not obese patients (adjusted OR 0.50 [95% CI 0.11-2.21], *P* = 0.36). In non-obese patients, low LDL further associated with a greater likelihood of plaque forming in coronary segments without baseline plaque (adjusted OR 4.68 [95% CI 2.26-9.66], *P* < 0.001) and worsening stenotic severity in segments with prevalent plaque (OR 5.35 [95% CI 1.62-17.67], *P* = 0.006). This was not observed in obese patients (Figure 1B). Notably, in non-obese patients, low LDL associated with higher CVD event risk compared to those with LDL >70 mg/dl (HR 7.94 [95% CI 1.52-41.36], *P* = 0.015). This was not the case in obese patients (HR 0.32 [95% CI 0.04-2.40], *P*= 0.27, Figure 1C).

Conclusion: In non-obese RA patients, LDL< 70 mg/dl may reflect higher LDL oxidation and was associated with higher baseline coronary atherosclerosis burden, new plaque formation, stenotic plaque progression and greater CVD risk than LDL >70 mg/dl.

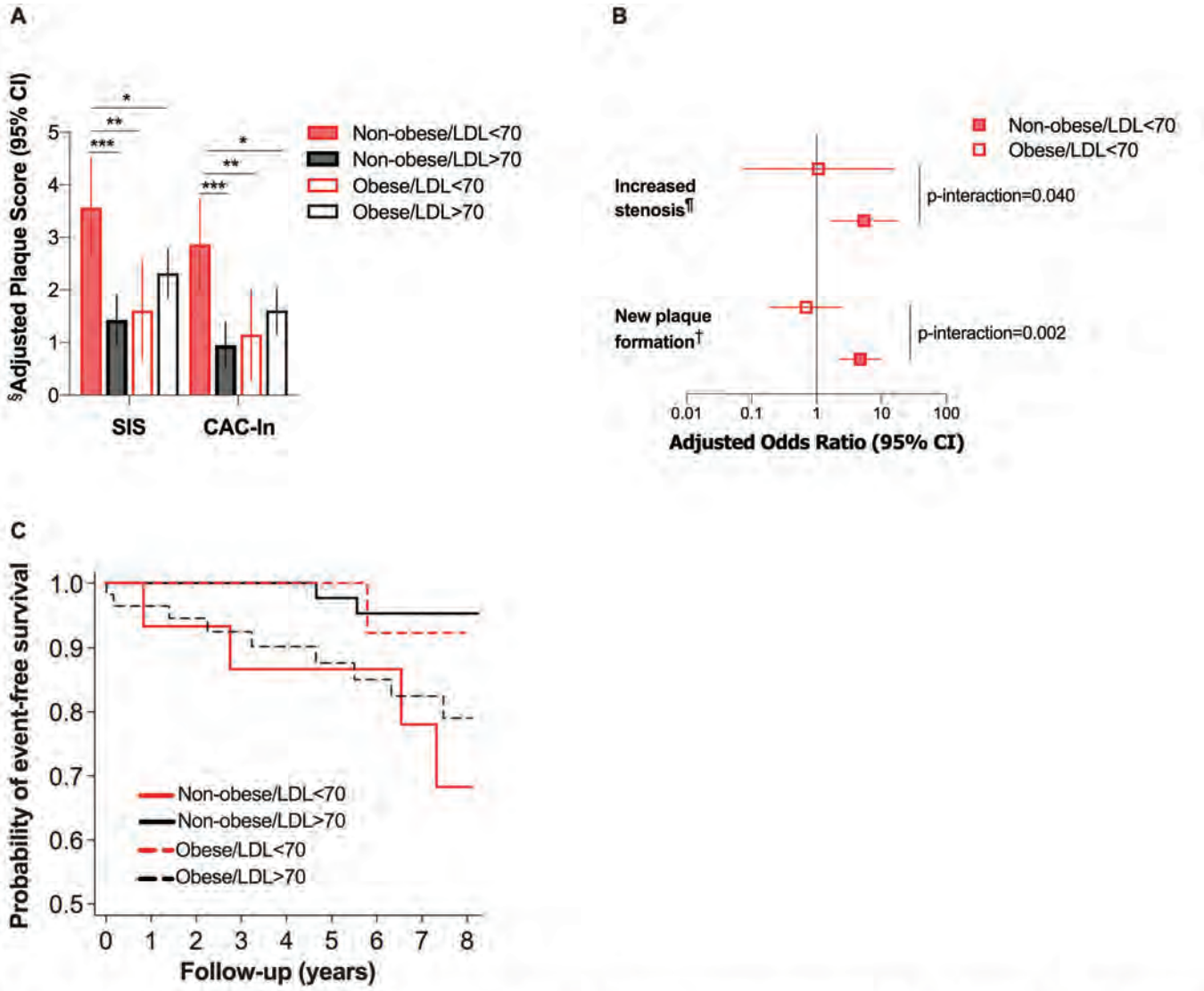


Figure 1. Abdominal obesity moderates the effect of low LDL (<70mg/dl) on **(A)** coronary atherosclerosis burden at baseline. §Model adjusted for age, gender, diabetes and statin use. **(B)** Effect on coronary plaque progression over time. ¶Stenotic severity model adjusted for age, time between scans, segment location, time-averaged CRP, prednisone dose and statin duration. †New plaque formation model adjusted for age, time between scans, segment location, prednisone dose, statin duration and bDMARD duration. **(C)**. Effect on long-term cardiovascular event risk in RA. SIS= segment involvement score, CAC-ln= natural log-transformed coronary artery calcium score.
*p<0.05, **p<0.01, ***p<0.001.

Disclosure: G. Karpouzas, Pfizer, 2; **S. Ormseth**, None; **E. Hernandez**, None; **M. Budoff**, None.

Abstract Number: 0486

Differences in Low-density Lipoprotein (LDL) Particle Composition and Oxidation May Underlie the Paradoxical Association of Low LDL with Higher Coronary Atherosclerosis Burden in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes II: The Heart of the Matter
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Rheumatoid arthritis (RA) patients in the lowest LDL group (< 70mg/dl) experience unexpectedly high cardiovascular risk. We first explored whether this group (Group 1) had higher coronary atherosclerosis burden compared to other LDL groups (Group 2: 70≤ LDL ≤130 and Group 3: LDL >130). We then evaluated whether differences in LDL particle composition, oxidation, or inflammation associated with low LDL in Group 1.

Methods: One hundred fifty RA patients without cardiovascular disease underwent coronary atherosclerosis evaluation with computed tomography angiography. Coronary artery calcium, number of segments with plaque (segment involvement score), stenotic severity (segment stenosis score), and extensive (>4 segments with plaque) or obstructive disease (>50% stenosis) were assessed. Lipoprotein classes and subclasses were directly measured. Oxidized LDL (oxLDL) was measured with monoclonal antibody E06. Chemiluminescence Elisa quantified IgG and IgM antibodies to oxLDL (anti-oxLDL) and apoB100 immune complexes. Proinflammatory cytokines were measured with Erenna Immunoassay. Robust linear and logistic regression models- adjusted for Framingham D'Agostino score and statin treatment- evaluated associations between LDL groups and plaque outcomes. Similar models evaluated adjusted differences in LDL subclasses, oxLDL, anti-oxLDL, ApoB100 immune complexes, and cytokines across LDL groups.

Results: Patients in Group 1 had higher coronary plaque burden (Figure 1A) and 2.8 times greater likelihood of extensive or obstructive disease (adjusted OR 2.82 [95% CI 1.12-7.17], *P* = 0.031) compared to LDL >70 groups. Group 1 had higher anti-oxLDL IgG and ApoB100 IgG immune complexes compared to other groups (Figure 2A). Among statin naïve patients, those with LDL< 70 also had higher oxLDL (Log transformed EMM 2.55 [95%CI 2.34-2.77] vs.

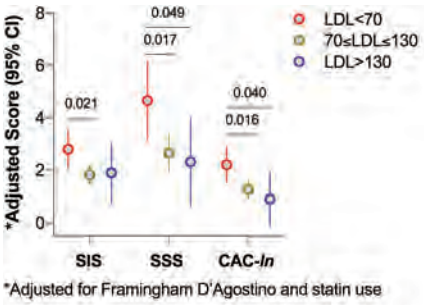

Figure 1. Coronary atherosclerosis burden across different LDLgroups. SIS=segment involvement score, SSS= segment stenosis score, CAC-ln=log-transformed coronary artery calcium score.

Figure 1. Coronary attherosclerosis burden across different LDLgroups. SIS=segment involvement score, SSS= segment stenosis score, CAC-ln=log-transformed coronary artery calcium score.

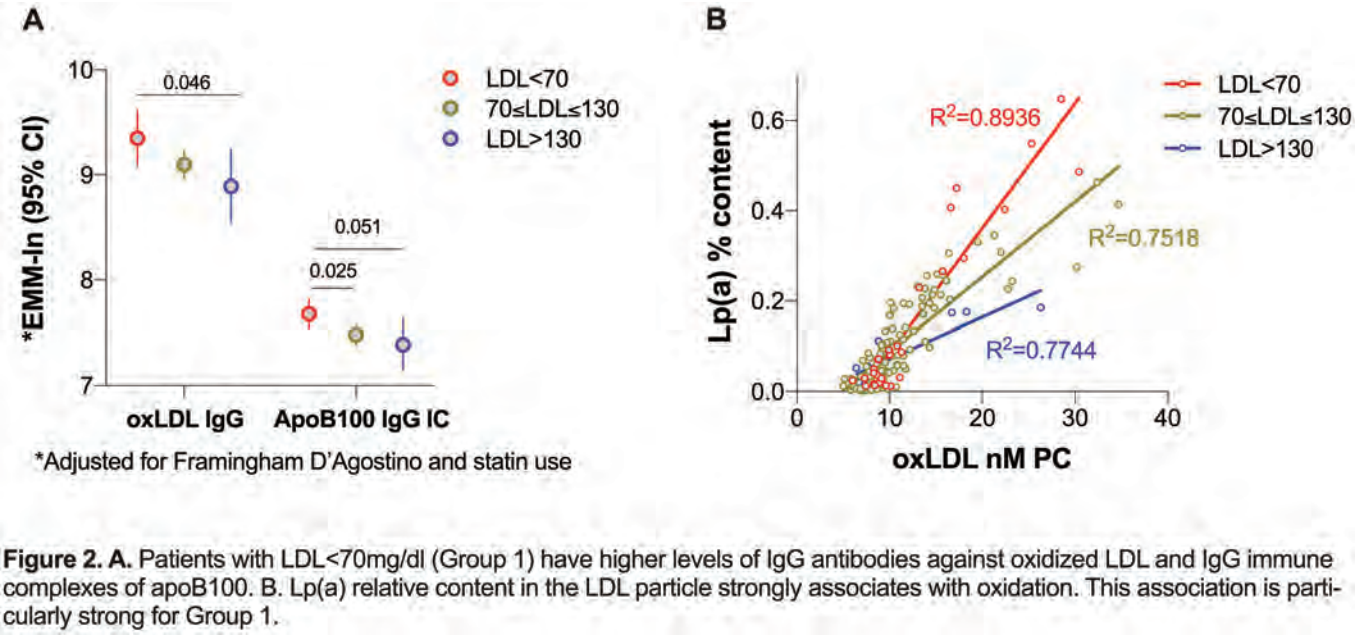

Figure 2. A. Patients with LDL<70mg/dl (Group 1) have higher levels of IgG antibodies against oxidized LDL and IgG immune complexes of apoB100. B. Lp(a) relative content in the LDL particle strongly associates with oxidation. This association is particularly strong for Group 1.

Figure 2. A. Patients with LDL<70mg/dl (Group 1) have higher levels of IgG antibodies against oxidized LDL and IgG immune complexes of apoB100. B. Lp(a) relative content in the LDL particle strongly associates with oxidation. This association is parti- cularly strong for Group 1.

2.27 [95%CI 2.19-2.36], P = 0.018 for LDL >70). LDL subclass relative content in the LDL particle differed across groups. Lp(a) was higher in LDL particles in Group 1 (EMM 16.04% [95% CI 11.75-20.33], vs. 10.48% [95% CI 8.20-12.75] in Group 2, p = 0.026 and 7.41% [95% CI 0.77-14.04] in Group 3, p = 0.033). Notably, Lp(a) content strongly associated with oxLDL overall (r = 0.83, p< 0.0001). This association was stronger for Group 1 compared to others (p< 0.005, Figure 2B). No differences in RA activity, CRP, TNF-α, IL-17A, or IL-17F were seen across groups. However, Group 1 had higher IL-6 (log-transformed EMM= 1.98 [95% CI 1.64- 2.32] vs. 1.57 [1.45-1.70],*P* = 0.028 in Group 2 and 1.32 [95% CI 0.84-1.80],

P = 0.031 in Group 3). IL-6 associated with both IgG anti-oxLDL (p=0.015) and apoB100 immune complexes (p=0.016). IL-6 further associated with higher CAC (adjusted B 0.41 [95% CI 0.01-0.81], *P*= 0.049).

Conclusion: RA patients with LDL< 70 had higher coronary atherosclerosis burden. Low circulating LDL in that group may reflect higher oxidation; this was mostly linked to the larger Lp(a) relative content of LDL and its significantly higher oxidation potential in that group. Greater oxLDL further associated with higher IL-6 elaboration which may in turn augment atherosclerosis burden in Group1.

Disclosure: G. Karpouzas, None; **S. Ormseth**, None; **E. Hernandez**, None; **M. Budoff**, None.

Abstract Number: 0487

Association Between an Extended Lifestyle Score and Adverse Health-related Outcomes in People with Rheumatoid Arthritis: A Study of 5295 UK Biobank Participants

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes II: The Heart of the Matter
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic autoimmune disorder characterised by inflammation of the synovial joints. Traditional lifestyle factors, such as smoking and poor diet, have been associated with adverse outcomes in people with RA. However, the effect of emerging lifestyle factors, such as sleep duration and sedentary behaviour, remain unclear as does their combined effect. We examined the association between an extended lifestyle score (based on traditional and emerging lifestyle factors) and all-cause mortality and major adverse cardiac events (MACE) in an RA population.

Methods: Data were sourced from the population-based cohort, UK Biobank (N = 502,503). Data were collected from 2006 to 2010 and linked to mortality and hospital admissions records. Participants with RA were assigned one point for each unhealthy lifestyle behaviour: frequent alcohol intake, four poor dietary habits (low fruit and vegetable or oily fish intake, and high processed or red meat intake), physical inactivity, short/long sleep duration, current smoker and prolonged television viewing time, giving a lifestyle score of 0-9. Participants were categorised as most healthy (score 0-2), moderately healthy (score 3-5) and least healthy lifestyle (score 6-9). Cox proportional hazards models were used to examine the association between lifestyle score categories and all-cause mortality and MACE (including myocardial infarction and stroke). All analyses were adjusted for age, sex, socioeconomic status, body mass index and other long-term conditions count.

Results: 5295 participants with RA and a lifestyle score (aged between 40 and 70; mean age (SD) 59.19 (7.10); 69.97% Female) were included in this study. There were 390 deaths and 290 MACE recorded. The adjusted hazard ratio (HR) for all-cause mortality in the least healthy category, compared with the most healthy (reference) category, was 2.42 (95% confidence interval (CI) 1.42-4.12) and 2.04 (95% CI 1.03-4.06) for MACE. The adjusted HR in the moderately healthy category, compared with the most healthy (reference) category, was 1.23 (95% CI 0.99-1.51) for all-cause mortality and 1.39 (95% CI 1.09-1.77) for MACE.

Conclusion: Combinations of unhealthy lifestyle factors are associated with higher risk of adverse health-related outcomes in people with RA. People in the least healthy category experience over twice the risk of all-cause mortality or MACE compared to those in the most healthy category. Examining the impact of combined traditional and emerging lifestyle factors may inform health policy reducing avoidable adverse health-related outcomes.

Disclosure: J. Canning, None; **S. Siebert**, AbbVie, 5, 8, Celgene, 2, 8, Boehringer-Ingelheim, 2, 5, Bristol-Myers Squibb, 1, Janssen, 1, 2, 3, Novartis, 2, 5, 8, UCB, 2, 5, GlaxoSmithKline, 2, Pfizer, 2, 5; **B. Jani**, None; **F. Mair**, None; **B. Nicholl**, None.

Abstract Number: 0488

Incidence of Dementia in Patients with Rheumatoid Arthritis and Association with DMARDs – Analysis of a National Claims Database

Sebastian Sattui[1], Iris Navarro-Millan[2], Fenglong Xie[3], Mangala Rajan[2], Huifeng Yun[4] and Jeffrey R Curtis[4], [1]Hospital for Special Surgery, New York, NY, [2]Weill Cornell Medicine, New York, [3]University of Alabama at Birmingham, Birmingham, AL, [4]Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes II: The Heart of the Matter

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: There is growing interest regarding the role of neuroinflammation in the development of dementia and the potential role for anti-inflammatory therapy, including TNF-inhibitors (TNFi), in its prevention. Previous studies suggest that inflammatory diseases like rheumatoid arthritis (RA) can increase risk for dementia, yet the effect of DMARDs on reducing this risk is unclear. The objective of this study was to evaluate the risk of incidence dementia associated with the use of biologics or targeted synthetic DMARDs (b/tsDMARD) compared to csDMARDS only in RA patients.

Methods: This longitudinal analysis used 2006-2017 Medicare claims data. Patients must have had continuous enrollment >12 months in Medicare Part A, B, and D, be ≥40 years old and have no prior diagnosis of dementia. RA

Characteristics	Incident Dementia During Follow-up Period	
	No N = 229,477	Yes N = 3794
Age, years, n (%)		
40-54	30,774 (13.4)	56 (1.5)
55-64	40,280 (17.6)	212 (5.6)
64-74	107,873 (47.0)	1,346 (35.5)
74-84	44,259 (19.3)	1,698 (44.8)
85 and over	6,291 (2.7)	482 (12.7)
Male, n (%)	43,576 (19.0)	682 (18.0)
Race, n (%)		
White	172,002 (75.0)	2,994 (78.9)
Black	25,057 (10.9)	301 (7.9)
Asian	4,615 (2.0)	90 (2.4)
Other	3,913 (1.7)	43 (1.2)
Hispanic, n (%)	22,879 (10.0)	358 (9.4)
Charlson-Deyo score, mean (SD)	2.81 (1.83)	3.38 (2.12)
1-2	124,533 (54.3)	1,617 (42.6)
3-4	66,988 (29.2)	1,177 (31.0)
≥5	37,956 (16.5)	1,000 (26.4)
Cardiovascular disease, n(%)*	49,614 (21.6)	1,298 (34.2)
Hypertension, n (%)	177,460 (77.3)	3,262 (86.0)
Hyperlipidemia, n (%)	152,509 (66.5)	2,719 (71.7)
Diabetes mellitus, n (%)	69,413 (30.2)	1,308 (34.5)
Cardiovascular medications		
Statins	109,395 (47.7)	1,994 (52.6)
ACEI/ARBs	100,789 (43.9)	1,864 (49.1)
Beta-blockers	80,991 (35.3)	1,646 (43.4)
Diuretics	146,467 (63.8)	2,735 (72.1)

*Define as history myocardial infarction, heart failure, stroke, peripheral vascular disease, history of coronary artery bypass graft, history of percutaneous coronary intervention and history of carotid endarterectomy. ** Defined as hypertension, diabetes mellitus, hyperlipidemia, obesity.
ACEI = angiotensin converting enzyme inhibitor; ARB = angiotensin receptor blocker.

Table 1. Characteristics of Patients with RA and Incident Dementia

RA Medication	N	No. of events	Person years	Crude IR per 100 person-years (95% CI)	Crude HR (95% CI)	Adjusted HR (95% CI)*
csDMARDs	121,010	1711	85,268.0	2.0 (1.9-2.1)	REF	REF
b/tsDMARDS	112,261	2083	159,809.3	1.3 (1.2-1.4)	0.63 (0.59-0.67)	0.83 (0.78-0.89)
TNFi-bDMARDs	62,717	1210	91,115.1	1.3 (1.3-1.4)	0.64 (0.59-0.69)	0.88 (0.81-0.94)
Non-TNFi-bDMARDs	42,667	816	62,167.9	1.3 (1.2-1.4)	0.63 (0.58-0.69)	0.78 (0.72-0.85)
tsDMARDs	6877	57	6256.4	0.9 (0.7-1.1)	0.46 (0.35-0.59)	0.68 (0.52-0.89)

* Adjusted for age, sex, race, cardiovascular disease, cardiovascular risk factors, cardiovascular medications, any hospitalizations, number of physician visits, dual eligibility and original reason for Medicare enrollment.

Table 2. Events, person-years, crude, and age-adjusted incidence rates (IRs), and crude and adjusted hazard ratios (HRs) for incident dementia

defined as: two RA diagnoses (ICD-9-CM 714.xx/ICD-10 M0.5.x or M06.x) by a rheumatologist > 7 and < 365 days apart. Patients had to meet RA definition on or before DMARD initiation. Person-time was classified as either: 1) b/tsDMARD exposed, which included TNFi-bDMARDs, non-TNFi-bDMARDs or tsDMARDs with or without csDMARDs; 2) csDMARD-exposed: any csDMARD without b/tsDMARD. Patients could contribute time to different exposure groups if they changed medications. Incident dementia was defined as: 1 inpatient claim for dementia (ICD-9-CM codes for 290.xx, 294.1x, or 331.xx and ICD-10 codes for F00.x, F01.x, F03.x,G30.x, G31.x) OR 2 outpatient claims for dementia OR prescription of a dementia specific medication (rivastigmine, galantamine, memantine, donepezil, tacrine). Incidence rates (IR) were estimated using Poisson models. Cox proportional hazard models (HR) were used to examine the risk for incident dementia among patients receiving b/tsDMARDs compared to those receiving csDMARD, adjusting for the competing risk of death. A sensitivity analysis was done that re-grouped the b/tsDMARD category as TNFi-bDMARDs, non-TNFi-bDMARDs and tsDMARDs.

Results: We identified 141,326 eligible RA patients; 80% female and 75.3% white, median age 67 years and a mean (SD) exposure time of 1.1 (1.5) years. Censoring events included incident dementia, death, change in bDMARD and discontinuation of fee for service. There were 233,271 initiations of c/b/tsDMARDS and 3,794 events of incident dementia (Table 1). The crude IR of dementia was 2.0 (95% CI 1.9-2.1) per 100 person-years for patients on csDMARDs and 1.3 (95% CI 1.2-1.4) for patients on any bDMARD (Table2). Patients on b/tsDMARDs had an adjusted 17% lower risk for dementia than patients on csDMARDs [HR 0.83 (95% CI 0.78-0.89)]. Sensitivity analysis found comparable risks between TNFi, non-TNFi, and tsDMARDs on the risk of dementia (Table 2).

Conclusion: The incidence of dementia in patients with RA was lower in patients receiving b/tsDMARDs when compared to patients on csDMARD only. No differences were observed between different classes of b/tsDMARDs, suggesting that decreased risk is possibly explained by the overall decrease in inflammation rather than a specific mechanism of action.

Disclosure: S. Sattui, None; **I. Navarro-Millan**, None; **F. Xie**, None; **M. Rajan**, Veterans Health Administration, 3; **H. Yun**, Pfizer, 2; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5.

Abstract Number: 0489

Prevalence, Incidence, and Cause-Specific Mortality of Rheumatoid Arthritis-Associated Interstitial Lung Disease Among Older Patients with Rheumatoid Arthritis: A Nationwide Cohort Study

Jeffrey Sparks[1], Yinzhu Jin[1], Soo-Kyung Cho[2], Seanna Vine[1], Rishi Desai[1], Tracy J. Doyle[3] and Seoyoung Kim[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [3]Brigham and Women's Hospital, West Roxbury, MA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes III: Major Comorbidities in RA
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Rheumatoid arthritis-associated interstitial lung disease (RA-ILD) is one of the most serious extra-articular RA manifestations and is more common in older patients. Registry-based RA-ILD studies have been limited to investigate incident RA-ILD and cause-specific mortality due to small sample size. Previous nationwide studies were limited due to the previous lack of a validated RA-ILD algorithm in administrative data. Therefore, we aimed to investigate prevalence, incidence, and cause-specific mortality of RA-ILD using a recently validated claims-based algorithm.

Methods: We performed a retrospective cohort study using US nationwide claims data from Medicare (2008-2017). RA was identified using a previously validated algorithm (2+ ICD-9/10 codes for RA separated by 7+ days and DMARD prescription [PPV 86%]; RA date [index date] was the date these criteria were met). RA-ILD was identified using a recently validated algorithm (2+ ICD-9/10 codes for ILD by a rheumatologist or pulmonologist separated by 7+ days [PPV 72%]; ILD date was the 2nd ILD code). We identified prevalent RA-ILD and covariates as of 365 days prior to index date. Among RA without ILD at baseline, Cox regression estimated HRs for incident RA-ILD by baseline covariates. We compared the risk for total mortality between patients with RA-ILD to RA without ILD using multivariable Cox regression adjusting for baseline covariates. For cause-specific mortality, Fine and Gray subdistribution hazard ratios (sdHR) were estimated to handle competing risks of alternative causes of mortality.

Results: Among a total of 509,787 patients with RA in Medicare (mean age 72.6 years; 76.2% female), 10,306 (2.0%) had prevalent RA-ILD at initial RA observation. Among RA without ILD at baseline, 13,372 (2.6%) developed RA-ILD during 1,873,127 person-years of follow-up (median 3.0 years/person). The incidence rate of RA-ILD was 7.14 per 1,000 person-years. Several baseline factors were associated with incident RA-ILD: male sex (HR 1.31, 95%CI 1.26-1.36), smoking (HR 1.35, 95%CI 1.29-1.41), biologic/targeted DMARD use (HR 1.34, 95%CI 1.29-1.40), and glucocorticoid use (HR 1.45, 95%CI 1.39-1.50, Table 1). During follow-up, 38.7% of RA-ILD died compared to 20.7% of RA without ILD (unadjusted HR 2.36, 95%CI 2.28-2.45). After multivariable adjustment that included confounders and possible mediators (such as comorbidities after RA-ILD onset), the association of RA-ILD with total mortality remained significant (HR 1.66, 95%CI 1.60-1.72, Table 2). Accounting for competing risk of other causes of death, RA-ILD had a sdHR of 4.39 (95%CI 4.13-4.67) for respiratory mortality and a sdHR of 1.56 (95%CI 1.43-1.71) for cancer mortality compared to RA without ILD.

Baseline characteristic	Incident RA-ILD cases	Person-years	RA-ILD incidence rate*	Incidence rate* 95% CI	Multivariable** HR (95%CI)
Female	9,732	1,457,405	6.68	6.55-6.81	1.00 (Ref)
Male	3,640	415,722	8.76	8.47-9.04	1.31 (1.26-1.36)
No asthma	11,356	1,679,179	6.76	6.64-6.89	1.00 (Ref)
Asthma	2,016	193,948	10.39	9.95-10.86	1.57 (1.49-1.64)
No COPD	9,974	1,602,565	6.22	6.10-6.35	1.00 (Ref)
COPD	3,398	270,561	12.56	12.14-12.99	2.00 (1.93-2.09)
No smoking	11,190	1,641,339	6.82	6.69-6.94	1.00 (Ref)
Smoking	2,182	231,788	9.41	9.03-9.82	1.35 (1.29-1.41)
No glucocorticoid use	4,274	759,305	5.63	5.46-5.80	1.00 (Ref)
Glucocorticoid use	9,098	1,113,821	8.17	8.00-8.34	1.45 (1.39-1.50)
No biologic or targeted DMARD use	9,704	1,462,943	6.63	6.50-6.77	1.00 (Ref)
Biologic or targeted DMARD use	3,668	410,184	8.94	8.66-9.24	1.34 (1.29-1.40)
No non-biologic DMARD use	1,061	127,826	8.30	7.81-8.81	1.00 (Ref)
Non-biologic DMARD use	12,311	1,745,301	7.05	6.93-7.18	0.86 (0.81-0.92)

*per 1,000 person-years
**Adjusted for age, sex, and US region.

Table 1. Incidence rates and hazard ratios (HRs) for incident RA-ILD by selected characteristics among patients with RA and no prevalent ILD at initial observation in Medicare (n=499,481).

	Unadjusted HR (95%CI) for total mortality	Unadjusted sdHR (95%CI) for cardiovascular mortality	Unadjusted sdHR (95%CI) for cancer mortality	Unadjusted sdHR (95%CI) for respiratory mortality	Unadjusted sdHR (95%CI) for infection mortality	Unadjusted sdHR (95%CI) for other mortality
RA without ILD	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
RA-ILD	2.36 (2.28-2.45)	1.42 (1.32-1.54)	2.08 (1.90-2.27)	7.08 (6.67-7.51)	1.89 (1.55-2.30)	1.78 (1.66-1.90)
	Multivariable* HR (95%CI) for total mortality	Multivariable* sdHR (95%CI) for cardiovascular mortality	Multivariable* sdHR (95%CI) for cancer mortality	Multivariable* sdHR (95%CI) for respiratory mortality	Multivariable* sdHR (95%CI) for infection mortality	Multivariable* sdHR (95%CI) for other mortality
RA without ILD	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
RA-ILD	1.66 (1.60-1.72)	1.01 (0.93-1.09)	1.56 (1.43-1.71)	4.39 (4.13-4.67)	1.19 (0.97-1.45)	1.30 (1.21-1.40)

*Adjusted for age, sex, US region, smoking, methotrexate use, hydroxychloroquine use, tumor necrosis factor inhibitor use, other biologic or targeted DMARD use, glucocorticoid use, combined comorbidity score, and number of physician visits.

Table 2. Hazard ratios (HRs) for total mortality and subdistribution hazard ratios (sdHRs) for cause-specific mortality comparing RA-ILD to RA without ILD in Medicare (n=509,787).

Conclusion: RA-ILD was present or developed in nearly 5% in this nationwide study of older patients with RA. RA-ILD was associated with excess total mortality that was not explained by measured factors. Male sex, smoking, biologic/targeted DMARD use, and glucocorticoid use were associated with incident RA-ILD. RA-ILD was strongly associated with increased respiratory mortality compared to RA without ILD. The novel association of RA-ILD with increased cancer mortality requires further investigation.

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Abstract Number: 0490

Fine Specificity Anti-Citrullinated Protein Antibodies as Biomarkers for Prediction of Incident Rheumatoid Arthritis-Associated Interstitial Lung Disease

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes III: Major Comorbidities in RA

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: Seropositivity for anti-citrullinated protein antibodies (ACPA) has been shown to increase risk for RA-associated interstitial lung disease (RA-ILD). However, RA-related autoantibodies used in clinical care are unable to accurately predict future RA-ILD. Previous investigations of specific ACPA and RA-ILD were cross-sectional and had inconsistent results. Therefore, we aimed to investigate fine specificity ACPA and subsequent risk of RA-ILD.

Methods: We performed a nested case-control study among patients with RA in a single center prospective registry. Three radiologists/pulmonologists confirmed RA-ILD through research review of the images of chest computed tomography imaging (index date). We matched each incident RA-ILD case to three RA controls (without patient/physician report or billing codes for ILD) on age, sex, RA duration, rheumatoid factor (RF) status, and time from blood draw to index date. Reactivities to three isotypes of 26 different fine specificity ACPA were measured from serum using a previously developed multiplex bead-based platform. The primary analysis investigated log-transformed levels of IgG ACPA. Secondary analyses considered IgA1 and IgA2 isotypes. Covariates at time of blood draw included smoking pack-years, BMI, and RA clinical factors. Conditional logistic regression estimated ORs for RA-ILD, adjusting for matching factors and covariates. We accounted for multiple comparisons using a 10% false discovery rate.

Results: We identified 84 incident RA-ILD cases and 243 RA controls without ILD. Mean age was 65.8 years, 79.2% were female, 89.0% were seropositive for ACPA/RF, and median RA duration was 19 years. Blood was drawn a medi-

	IgG ACPA biomarker by targeted protein and epitope position	OR (95%CI) per log-transformed unit conditioned on matching factors[1]	Multivariable[2] OR (95%CI) per log-transformed unit
1	B_actin_191_216_cit3	1.04 (0.82,1.30)	1.00 (0.78, 1.28)
2	Biglycan_247_266_cit_cyclic	1.05 (0.81,1.37)	1.02 (0.77,1.34)
3	Clusterin_221_240_cit_cyclic	1.11 (0.88,1.4)	1.04 (0.80,1.34)
4	Clusterin_231_250_cit_cyclic	**1.35 (1.15,1.59)*** **	**1.24 (1.04,1.48)***
5	Collagen_Type_II_281_298_cit	0.80 (0.61,1.06)	0.80 (0.60,1.08)
6	Enolase_1A_5_21_cit	1.18 (0.97,1.42)	1.08 (0.88,1.34)
7	FibrinogenA_211_230_cit_cyclic	0.77 (0.56,1.07)	0.79 (0.57,1.11)
8	FibrinogenA_27_43_cit	1.09 (0.88,1.35)	1.00 (0.79,1.27)
9	FibrinogenA_41_60_cit3_cyclic	0.94 (0.68,1.29)	0.96 (0.69,1.34)
10	FibrinogenA_563_583_cit_57	1.01 (0.80,1.26)	0.98 (0.77,1.25)
11	FibrinogenA_616_635_cit3_cyclic	1.00 (0.77,1.28)	0.92 (0.70,1.22)
12	FibrinogenB_246_267_cit	1.02 (0.79,1.31)	0.98 (0.74,1.29)
13	FibrinogenB_285_305_cit	1.17 (0.92,1.50)	1.11 (0.85,1.45)
14	FibrinogenB_36_52_cit	0.80 (0.59,1.09)	0.78 (0.57,1.08)
15	FibrinogenB_54_74_cit_72	1.03 (0.78,1.37)	1.00 (0.73,1.36)
16	FibrinogenB_62_81_cit_72	0.88 (0.68,1.15)	0.83 (0.63,1.09)
17	FibrinogenB_62_81_cit_74	0.94 (0.74,1.19)	0.87 (0.68,1.13)
18	Fibronectin_cit_1035_1036	**1.21 (1.04,1.41)***	**1.20 (1.02,1.42)***
19	Filaggrin_48_65_cit2_cyclic	**3.38 (1.78,6.42)*****	**3.08 (1.63,5.84)*****
20	H2A_a_1_20_cit_cyclic	1.05 (0.84,1.32)	0.97 (0.76,1.24)
21	H2A_a_2_1_20_cit	1.05 (0.81,1.37)	0.96 (0.72,1.28)
22	H2B_a_62_81_cit_cyclic	0.87 (0.66,1.13)	0.80 (0.61,1.05)
23	H4_33_48_cit39	1.24 (1.00,1.54)	1.22 (0.96,1.54)
24	H4_33_48_cit39_40	**1.26 (1.08,1.47)****	**1.23 (1.04,1.46)***
25	Vimentin_1_16_cit	0.84 (0.62,1.13)	0.87 (0.63,1.20)
26	Vimentin_58_77_cit3_cyclic	1.07 (0.85,1.35)	0.99 (0.78,1.27)

*p<0.05 at false discovery rate of 10%
**p<0.01 at false discovery rate of 10%
***p<0.0001 at false discovery rate of 10%

[1]All models were conditioned on matching factors (age, sex, RA duration, RF status, and time from blood draw to index date).
[2]Additionally adjusted for smoking pack-years (continuous) and body mass index (continuous).

Table 1. Associations of log-transformed IgG fine specificity ACPA with incident RA-ILD in 84 RA-ILD cases and 243 RA controls without ILD.

an of 1.7 years prior to the index date of RA-ILD. After accounting for multiple comparisons, four IgG ACPA biomarkers were significantly associated with subsequent risk of RA-ILD (Table 1). Filaggrin_48_65_cit2_cyclic was strongly associated with increased risk for incident RA-ILD (multivariable OR 3.08 per each log-transformed unit, 95%CI 1.63-5.84) adjusted for matching factors, smoking pack-years, and BMI. Clusterin_231_250_cit_cyclic (OR 1.24, 95%CI 1.04-1.48), fibronectin_cit_1035_1036 (OR 1.20, 95%CI 1.02-1.42), and H4_33_48_cit39_40 (OR 1.23, 95%CI 1.04-1.46) were also associated with incident RA-ILD. The association of filaggrin_48_65_cit2_cyclic with RA-ILD was also observed in the IgA1 (OR 1.83, 95%CI 1.03-3.26) and IgA2 (OR 4.36, 95%CI 1.13-16.90) isotype analyses.

Conclusion: We identified several fine specificity ACPA associated with subsequent risk of RA-ILD that may inform pathogenesis. In particular, autoimmunity to a specific citrullinated epitope of filaggrin was associated with RA-ILD across all isotypes investigated and is potentially a novel predictive biomarker for RA-ILD. External replication is in process, but these results suggest that fine specificity ACPA biomarkers may have utility in RA-ILD prediction.

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Amgen, 1, AbbVie, 5, Amgen, 2, 5, Arena, 5, Bristol Myers Squibb, 2, 5, Canfite, 1, 5, Corrona, 5, Crescendo, 2, 5, GlaxoSmithKline, 5, Gilead, 9, Horizon, 9, Johnson and Johnson, 9, Lilly, 2, 9, Pfizer, 9, Scipher, 1, 9, Set Point, 9, Roche, 9, Canfite, 1, Inmedix, 1, Lycera, 1, Vorso, 1, Scipher, 1; **N. Shadick**, Sanofi, 2, Crescendo Biosciences, 2, Lilly, 2, Bristol-Myers Squibb Company, 2, 5, Amgen, 2, Mallinckrodt, 2; **T. Doyle**, None; **J. Sparks**, Optum, 1, Janssen, 1, Inova, 1, Gilead, 1, Amgen, 1, Bristol-Myers Squibb, 1, 2.

Abstract Number: 0491

Relationship Between Rheumatoid Arthritis and Pulmonary Function in the UK Biobank

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes III: Major Comorbidities in RA

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: Established pulmonary manifestations of RA include restrictive processes such as interstitial lung disease and obstructive processes such as bronchiectasis, but clinically detected forms of these diseases are relatively uncommon. Emerging research suggests that airways disease may be common in RA and not explained by smoking. However, prior studies investigating the relationship of RA with restriction or obstruction were limited by small sample size, insufficient smoking data, or lack of a control group without RA. Therefore, we aimed to investigate the relationship of RA with type and severity of pulmonary function test (PFT) abnormalities compared to the general population, accounting for smoking.

Methods: We performed a cross-sectional study investigating the association of RA and PFT abnormalities among subjects who had PFTs performed for research purposes in the UK Biobank. RA cases were identified by self-report and current DMARD use (as previously published in this dataset). We compared RA cases to general population controls in the UK Biobank that denied RA and other systemic rheumatic disease. Outcomes were: continuous PFT results, type of PFT abnormality (restrictive pattern, obstructive pattern, and either abnormality), and level of severity (mild, moderate, and severe) according to standard clinical PFT cutpoints from population prediction equations. Covariates included age, sex, smoking status, and pack-years. We used linear regression to compare RA cases to

	FEV_1 % predicted β (95%CI)	FVC % predicted β (95%CI)	FEV_1/FVC β (95%CI)
Unadjusted			
Controls	Ref	Ref	Ref
RA cases	-4.25 (-4.98, -3.52)	-3.12 (-3.77, -2.44)	-0.013 (-0.016, -0.010)
*Multivariable**			
Controls	Ref	Ref	Ref
RA cases	-3.11 (-3.82, -2.39)	-2.28 (-2.94, -1.63)	-0.008 (-0.010, -0.004)

*Adjusted for age, sex, smoking status (never/past/current), and smoking pack-years (continuous).

CI, confidence interval; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; RA, rheumatoid arthritis.

Table 1. Linear regression analyses of continuous pulmonary function test results, comparing rheumatoid arthritis to general population controls (n=319,288).

Table 2. Odds ratios for pulmonary function test abnormalities, comparing rheumatoid arthritis to general population controls (n=319,288).

	Either Abnormality (FVC % predicted <80 and/or FEV_1/FVC <0.7) **OR (95%CI)**	**Restrictive Pattern** (FVC % predicted <80) **OR 95%CI**	**Obstructive Pattern** (FEV_1/FVC <0.7) **OR 95%CI**
Unadjusted			
Controls	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
RA cases	**1.59 (1.44, 1.75)**	**1.62 (1.46, 1.81)**	**1.45 (1.29, 1.63)**
*Multivariable**			
Controls	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
RA cases	**1.41 (1.28, 1.56)**	**1.42 (1.27, 1.59)**	**1.28 (1.14, 1.45)**
Among only never smokers (n=172,860)			
Unadjusted			
Controls	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
RA cases	**1.52 (1.31, 1.77)**	**1.64 (1.39, 1.94)**	**1.26 (1.02, 1.54)**
*Multivariable***			
Control	1.00 (Ref)	1.00 (Ref)	1.00 (Ref)
RA	**1.47 (1.26, 1.70)**	**1.53 (1.30, 1.81)**	**1.26 (1.02, 1.55)**

*Adjusted for age, sex, smoking status (never/past/current), and smoking pack-years (continuous).
**Adjusted for age and sex.

CI, confidence interval; FEV_1, forced expiratory volume in 1 second; FVC, forced vital capacity; OR, odds ratio; RA, rheumatoid arthritis.

Table 2. Odds ratios for pulmonary function test abnormalities, comparing rheumatoid arthritis to general population controls (n=319,288).

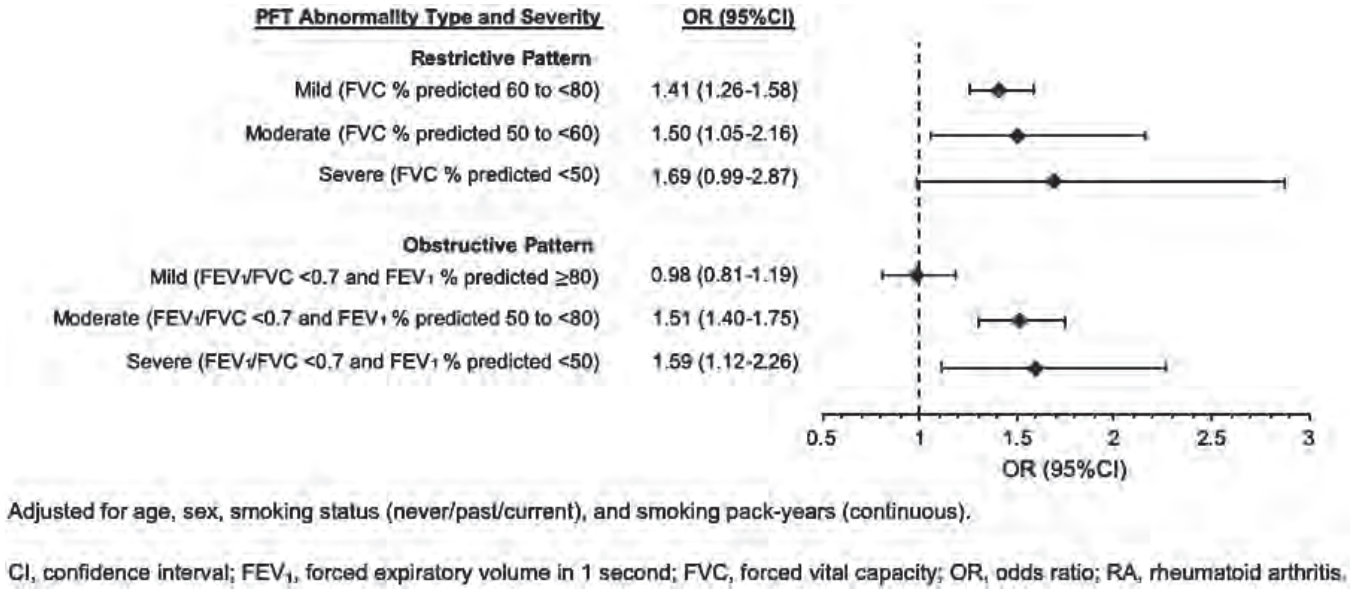

Figure 1. Multivariable odds ratios for level of severity of pulmonary function test abnormalities, comparing rheumatoid arthritis to general population controls (n=319,288).

controls for continuous PFT results. We used logistic regression to estimate adjusted ORs for type and severity of PFT abnormality, comparing RA cases to controls.

Results: Among 319,288 analyzed subjects with PFTs performed (mean age 56.4 years, 56% female, and 46% ever smokers), we identified 1,853 (0.6%) cases of treated RA. Among RA cases, 72% were female and 84% were RF+. Among the entire sample, 16% had restrictive pattern and 14% had obstructive pattern on PFTs. RA was strongly associated with lower % predicted forced expiratory volume 1 second (FEV_1), % predicted forced vital capacity (FVC), and FEV_1/FVC results than general population controls, independent of smoking and other confounders (**Table 1**). RA

was also associated with increased odds of restrictive (multivariable OR 1.42, 95%CI 1.27-1.59) and obstructive (OR 1.28, 95%CI 1.14-1.45) patterns (**Table 2**). RA was associated with increased odds of either PFT abnormality (OR 1.41, 95%CI 1.28-1.56) compared to controls. RA was associated with higher odds of restrictive pattern across all severity levels and higher odds of moderate and severe, but not mild, obstructive pattern (**Figure 1**). Findings were similar among never smokers.

Conclusion: RA cases were more likely than general population controls to have restrictive or obstructive pattern abnormalities on PFTs obtained for research purposes, and this relationship was not explained by smoking and other measured confounders. The independent association of RA with obstructive pattern adds to the growing literature implicating RA and airways disease. In addition to restrictive lung disease, clinicians should also be aware that obstructive lung diseases may be a pulmonary manifestation of RA independent of smoking history.

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Abstract Number: 0492

Microbiota-induced Intestinal Barrier Dysfunction Initiates the Shuttling of Immune Cells from the Gut to the Joints

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes III: Major Comorbidities in RA
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: While it is known that microbial dysbiosis is associated with the onset of rheumatoid arthritis, mechanistic insights how it facilitates the development of arthritis remained largely elusive to date. It is especially interesting how microbial dysbiosis affects the transition from asymptomatic autoimmunity to arthritis. We speculated that a breakdown of intestinal barrier function caused by microbial dysbiosis allows immune cells to shuttle from the gut to the joints. The purpose of this study was to test whether intestinal barrier function is impaired before the onset of human RA and experimental arthritis and to seek for evidence that immune cells from the gut migrate to the joints.

Methods: In a longitudinal cohort of RA-at risk individuals markers of disturbed intestinal barrier function, such as zonulin, were analyzed and linked to RA onset. Furthermore, new-onset RA patients were assessed for gut leakiness and their intestinal biopsies for the expression of tight junction proteins and immune cell infiltration. In the murine model of collagen-induced arthritis, sequential analysis of intestinal dysbiosis, intestinal barrier function and arthritis onset was carried out. Additionally, barrier function was assessed on intestinal organoids exposed to faecal super-

natants from eu- and dysbiotic mice with and without inhibition of zonulin. Furthermore, three types of interventions restoring intestinal barrier function were carried out for testing their effects on the inhibition of arthritis onset. Finally, photo- converted cells from the gut were traced in the joints and further identified in more detail to test for cellular trafficking from one to the other compartment.

Results: Zonulin, a potent regulator for intestinal tight junctions, was elevated in autoimmune mice and men before the onset of arthritis and predicted the onset of human RA. Intestinal barrier functions as well as epithelial tight junctions were decreased before the onset of experimental arthritis and at onset of human RA. In mice, induction of autoimmunity was followed by rapid intestinal dysbiosis followed by gut leakiness before arthritis started. Faecal supernatants of arthritic mice induce epithelial barrier dysfunction in intestinal organoids in zonulin dependent manner. Restoration of the intestinal barrier in the pre-phase of arthritis using butyrate, CB1R agonist or zonulin antagonist larazotide inhibited the development of arthritis. Finally, using photoconvertible mice, gut-borne immune cells were identified that homed to the joints when barrier function was impaired.

Conclusion: In summary, these data show the intestinal barrier dysfunction precedes the onset of RA and allows the trafficking of immune cells from the gut to the joints. Targeting of intestinal tight junction function may therefore allow preventing the onset of RA.

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Abstract Number: 0493

Automatic Joint Space Assessment in Hand Radiographs with Deep Learning Among Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Session Title: RA – Diagnosis, Manifestations, & Outcomes III: Major Comorbidities in RA
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Assessment of joint space is the fundamental radiographic task to diagnose rheumatoid arthritis (RA) and to assess the severity and progression of the disease. The clinical assessment of joint space is a visual task, and the current scoring systems, such as the modified Sharp's score, generally follow the semiquantitative grading.(1) The inter- and intra-observer variation impede the development of computer-aided detection and diagnosis software to help physicians.(2) This exploratory study aims to assess the performance of a deep-learning model for detecting and scoring joint space automatically and compare it with the physician's performance.

Methods: We collected 1,397 conventional hand radiographs from 450 RA patients (training: 309; validation, 141) whose diagnoses were based on the 2010 ACR/EULAR criteria for RA. Three rheumatologists assessed the joint space independently according to the van der Heijde-modified Sharp scoring method. The consensus was the ground truth for training data. We trained a model to detect joints automatically using the Deep Adaptive Graph (a landmark detection technique based on graph convolutional network; figure 1). The extracted region of interest was fed into the joint space assessment algorithm to predict the joint space score and compare it with rheumatologists'

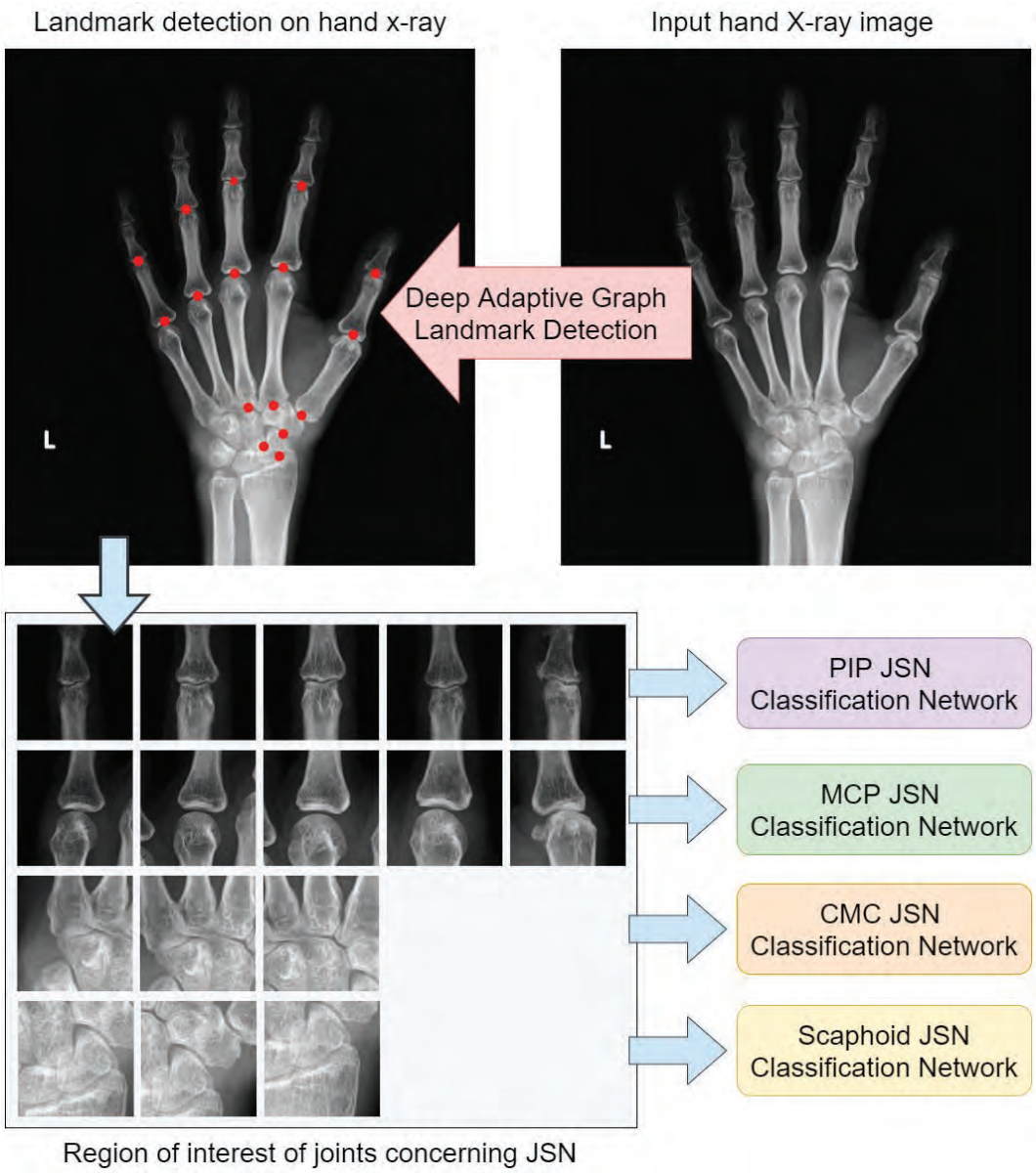

Figure 1. Flow chart for the development of joint detection and joint space scoring algorithms.

scoring. The model-rheumatologist agreement was compared to the inter-rater agreement between rheumatologists as an assessment for model performance. The accuracy of the model to predict an exact joint space score of rheumatologist consensus, a joint space score of rheumatologist consensus by one score, and score a joint space score ≥ 2 were also performed.

Results: Among 141 RA patients in the validation set, the mean age was 57.9 years, and 82.3% were female. The overall model-rater agreement was similar to the inter-rater agreement with Kappa statistics of 0.568 and 0.565, respectively. The accuracy to predict exact the joint space score of rheumatologist consensus and to predict the joint space score of rheumatologist consensus by one score were 0.674 and 0.973. The model sensitivity, specificity, and positive predictive value to detect a joint space score ≥ 2 were 0.808, 0.919, and 0.884, respectively. The performance was consistent across different joint areas as shown in Table 1.

Joint areas	Model performance			Comparison of model-rater and inter-rater reliability	
	Exact accuracy*	One-score accuracy**	PPV for a score≥2	Inter-rater Kappa statistic	Model-rater Kappa statistic
PIP	0.698	0.986	0.855	0.578	0.589
MCP	0.764	0.987	0.900	0.629	0.674
CMC	0.570	0.946	0.877	0.434	0.426
Wrist	0.594	0.952	0.906	0.537	0.477
All	0.675	0.972	0.884	0.565	0.568

* Predicted score matched rheumatologist consensus exactly.

** Predicted score matched rheumatologist consensus by one score.

Table 1. Performance of joint space scoring algorithm.

Conclusion: This study indicates that deep learning models are useful to detect specific joint area and score the joint space with performance comparable with rheumatologists.

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Abstract Number: 0494

Genetic-epigenetic Interaction and the Relationship Between DNA Methylation Patterns and Disease Activity in a Longitudinal Cohort of Lupus Patients

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Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Genetic factors and epigenetic dysregulation are implicated in the pathogenesis of lupus. We performed a longitudinal analysis of DNA methylation in lupus patients for the first time. We assessed epigenetic changes over time and across disease activity status. Combining genomic and epigenomic analyses, we also examined ancestry-specific DNA methylation and DNA methylation changes influenced by genetic variants across the genome.

Methods: A total of 54 female lupus patients, including 32 European-American and 22 African-American, were followed over a period of up to 43 months. Blood samples were obtained at routine follow up visits and during disease flares, with a total of 229 samples collected. Disease activity at each blood draw was determined by SLEDAI. Granulocytes were isolated and DNA extracted. Genotyping was performed using the Infinium Global Screening Array v2.0, and genome-wide DNA methylation was assessed at each time-point using the Infinium MethylationEPIC array. Ancestry-specific DNA methylation changes were determined, and methylation quantitative trait loci (meQTL) analysis was performed. A linear mixed effects model was implemented to identify DNA methylation alterations that vary with disease activity.

Results: We identified 487 hypomethylated and 420 hypermethylated CpG sites in African-American compared to European-American lupus patients, annotated to 391 and 316 unique genes, respectively. Differentially methylated genes include type I interferon-response genes such as *IRF7* and *IFI44,* and genes related to the NFkB pathway. After adjusting for age, medications, and genetic background, DNA methylation levels in 142 (15.7%) differentially methylated sites were found to be allele-specific and influenced by at least one genetic variant located within 1kb. *TREML4*, which plays a vital role in toll-like receptor signaling, was hypomethylated in African-American patients and demonstrated a strong *cis*-meQTL association (R^2=0.91). The associated genetic variant (rs9369265) significantly differs in allele frequencies between African-American and European-American patients, and is located within an active enhancer region in neutrophils and modifies *TREML4* expression. Interestingly, the DNA methylome was highly stable across different disease activity levels and over time. Methylation levels in *SNX18* and *FGD1* showed correlation with disease activity in African-American patients (P= 4.6 x 10^{-8} and P= 3.7 x 10^{-7}, respectively). FGD1 is a guanine nucleotide exchange factor that activates the GTPase Cdc42 which has been shown to regulate neutrophil morphology during migration and apoptotic response to immune complex signaling.

Conclusion: Lupus granulocytes demonstrate significant differences in DNA methylation patterns between African-American and European-American patients. DNA methylation profiles in lupus patients are influenced by ancestry-specific genetic variants and are highly stable over time independent of disease activity levels. Progressive demethylation in *SNX18* and *FGD1* was observed with increasing disease activity in granulocytes from African-American lupus patients.

Disclosure: P. Coit, None; **L. Ortiz-Fernandez**, None; **E. Lewis**, None; **W. McCune**, None; **K. Maksimowicz-McKinnon**, ChemoCentryx, 5, AstraZeneca, 9, Gilead, 9, GSK, 9, Merck, 9; **A. Sawalha**, None.

Abstract Number: 0495

Epstein Barr Virus (EBV), an Etiologic Factor for Systemic Lupus Erythematosus (SLE), Interacts with SLE Risk Loci Through EBV-encoded Transcription Co-factors (co-TFs)

Viktoryia Laurynenka[1], Xiaoting Chen[1], Sreeja Parameswaran[1], Shruti Eswar[2], Kenneth Kaufman[3], Bahram Namjou[4], Matthew Weirauch[5], Leah Kottyan[4] and John Harley[6], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, [3]Cincinnati Children's Hospital Medical Center;US Department of Veterans Affairs Medical Center, Cincinnati, OH, [4]Cincinnati Children's Hospital Medical Center/Univ of Cincinnati, Cincinnati, OH, [5]Cincinnati Children's Hospital Medical Center/Univ of Cincinnati, 535 Terrace Ave, [6]Cincinnati Children's Hospital Medical Center/Univ of Cincinnati College of Medicine, Cincinnati, OH

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: SLE affects millions worldwide. The etiology of this complex autoimmune disease is the consequence of both strong genetic and environmental components. Genome-wide association studies (GWAS) have identified many variants associated with SLE that mostly localize to incompletely understand regulatory regions. EBV has been nominated as potential triggering environmental factors in SLE from immunochemical, virologic, epidemiologic and genomic studies. Recent work reveals a possible mechanism via the concentration of the EBV-encoded transcription cofactor (co-TF), Epstein-Barr virus nuclear antigen 2 (EBNA2) at SLE risk loci (Nat Genet 50:699 2018).

Methods: In 124 GWAS and candidate-gene studies ~500 variants have been associated with SLE at p< 5E-08. By literature curation and linkage disequilibrium pruning, we identify 187 independent SLE loci when requiring r^2< 0.2 or regression modeling to separate loci. Most loci (132, 71%) are ancestry specific. The most studied ancestries, European (100 loci) and East Asian (94 loci), share only 31 loci.

The simulation algorithm, RELI, first presented in (Nat Genet 50:699, 2018), has been improved and applied to 53 viral and 11,781 human ChIP-seq (chromatin immunoprecipitation with DNA sequencing) datasets, a collection 8-times larger than previously available, to assess DNA binding of 1,467 regulatory proteins (TFs & co-TFs).

Results: We confirm association with EBNA2 DNA binding complexes (OR=2.4, Pc= $3.1x10^{-12}$) and discover association with EBV Latency III genes EBNA3C (OR=2.7, Pc= $1.44x10^{-23}$) and EBNA-LP (OR=2.0, Pc= $3.18x10^{-15}$) that bind 33% to 51% of the 187 SLE loci. Among human TFs & co-TFs 193 significantly associated (Pc< 10^{-6}) with SLE risk loci. In GO Enrichment Analysis these 193 human TFs & co-TFs show involvement in JAK/STAT, Toll receptor, interleukin, apoptosis signaling pathways, oxidative stress response and transcription regulation pathways and enriched in such biological processes as T and B cell regulation and differentiation, dendritic cell, megakaryocyte and erythrocyte differentiation, cellular response to interleukin-6, -7, -9, 15, type I interferon, positive regulation of interleukin-10 and -12 biosynthetic processes, chromatin modification, mitosis, and viral transcription.

The EBV co-TFs EBNA2, EBNA3C, and EBNA-LP and human regulatory proteins, tend to cluster together at the same subset of the SLE risk loci (p< 10^{-300}). The associated human TFs have a powerful tendency to be from EBV transformed B cells (OR≈56, P< E-100) and to be known components of the super-enhancer complexes that form upon EBV infection and transformation of B cells (OR >30, p< 10^{-25}). Meanwhile, genetic associations for many other diseases, such as depression, anxiety, and schizophrenia and other complex genetic phenotypes (n >400) show no such relationships.

Conclusion: These new results confirm previous results and extend evidence supporting an etiologic role for EBV in SLE. At this moment, the most attractive hypothesis of mechanism is that the EBV alters a substantial proportion of SLE genetic risk through gene expression changes that occur in EBV transformed B cells as a consequence of the action of the Latency III EBV gene expression program.

Disclosure: V. Laurynenka, None; **X. Chen**, None; **S. Parameswaran**, None; **S. Eswar**, None; **K. Kaufman**, None; **B. Namjou**, None; **M. Weirauch**, None; **L. Kottyan**, None; **J. Harley**, Now Diagnostics, Inc, 1, 6, GSK, 5.

Abstract Number: 0496

A Role of Lipid-Peroxidation in Systemic Lupus Erythematosus-Associated Cardiovascular Disease

David Patrick[1], Justin van Beusecum[1], Michelle Ormseth[2], Leslie J. Crofford[2], Sean Davies[3], Sergey Dikalov[1] and David Harrison[1], [1]Vanderbilt University Medical Center, Nashville, [2]Vanderbilt University Medical Center, Nashville, TN, [3]Vanderbilt University, Nashville

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: In SLE, cardiovascular complications are a significant contributor to morbidity and death. Importantly, there is an increased prevalence of hypertension in SLE patients compared to healthy controls. We have identified a critical role of isolevuglandins (isoLGs) as activators of the immune system in essential hypertension. IsoLGs are peroxidized products of fatty acids that form as a result of reactive oxygen species. These isoLG adducts participate in the activation of T-cells and contributed. We hypothesize that isoLGs are important for the development of hypertension and systemic immune activation in SLE.

Methods: To determine the presence of isoLG's in monocytes of human subjects we recruited 11 subjects with SLE and 10 controls subjects. IsoLG adduct accumulation within antigen presenting cells was performed by flow cytometry and mass spectrometry. Superoxide was measured by incubation with dihydroethidium and subsequent high performance liquid chromatography. Flow cytometry was performed with a single chain antibody that recognizes isoLG adducted lysine residues independent of the peptide backbone. $CD11c^+$ and $CD14^+$ monocytes were analyzed for the presence of isoLG adducts. To determine a causative role of isoLG adducts in immune activation and hypertension in SLE, we employed the *B6.SLE123* and *NZBWF1* mouse models of SLE. Animals were treated with the specific isoLG scavenger 2-hydroxybenzylamine (2-HOBA) or vehicle beginning at 7 weeks. Animals were sacrificed at 32 weeks of age and *C57BL/6* and *NZW* were used as controls. Blood pressure was analyzed by radiotelemetry. Immune cell accumulation was determined by flow cytometry and the presence of anti-isoLG adduct antibodies was determined by a capture enzyme linked immunosobent assay (ELISA).

Results: By flow cytometry and mass spectrometry we found marked accumulation of isoLG adducts within $CD11c^+$ and $CD14^+$ antigen presenting cells in SLE subjects compared to control. This was accompanied by an increase in superoxide production in $CD14^+$ monocytes. In animals, treatment with 2-HOBA attenuated blood pressure in both mouse models. Immune cell accumulation in primary and secondary lymphoid organs is significantly attenuated by 2-HOBA. Moreover, treatment with 2-HOBA reduced albuminuria and renal injury in the *B6.SLE123* model of SLE as measured by urinary albumin/creatinine ratio and histologic scoring. Similarly, there is a significant reduction in bone marrow plasma cell accumulation and anti-double stranded DNA (anti-dsDNA) titers in treated animals. Finally we have detected anti-isoLG-adduct IgG in serum collected from both mouse models.

Conclusion: These studies define a critical role of isoLG adduct accumulation in both systemic immune activation and hypertension in SLE. Moreover, they suggest a potential therapeutic strategy for the treatment of SLE and associated cardiovascular disease.

Disclosure: D. Patrick, None; **J. van Beusecum**, None; **M. Ormseth**, None; **L. Crofford**, None; **S. Davies**, Metabolic Technologies Inc, 9; **S. Dikalov**, None; **D. Harrison**, None.

Abstract Number: 0497

Interleukin-23 Acts Directly on Podocytes and Contributes to the Development of Glomerulonephritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: SLE – Etiology & Pathogenesis

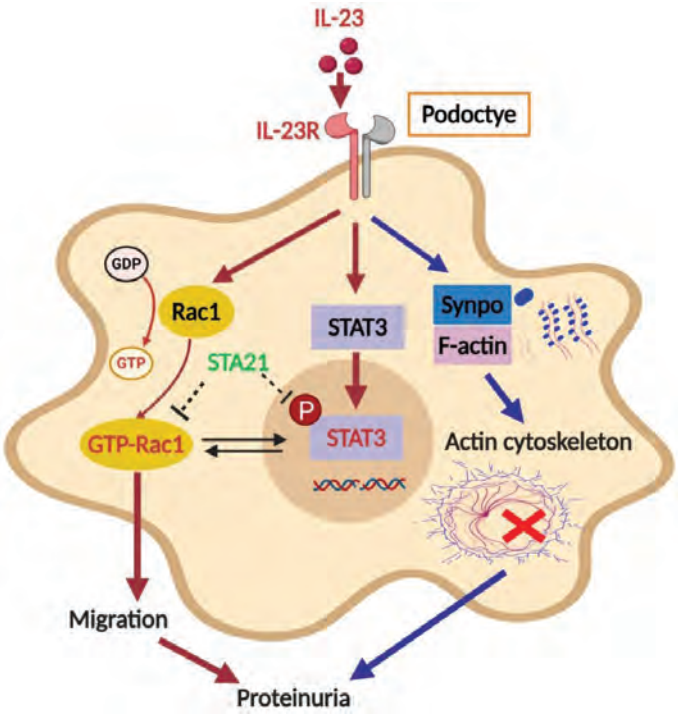
Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: Interleukin (IL)-23 is central in the advancement of an inflammatory response and has been shown to be involved in the pathogenesis of autoimmune diseases. Therapeutic targeting of IL-23-mediated signaling is being exploited for therapeutic purposes. It is still unknown whether IL-23 can affect the function of tissue resident cells and promote organ damage. Disruption of podocyte structure and function represents a common feature of several inflammatory kidney diseases.

Methods: Podocytes were cultured on an advanced decellularized matrix (doi.org/10.1002/adfm.201908752).

Results: Using podocytes cultured on an advanced decellularized matrix, we demonstrated that in the presence of IL-23 the expression of IL-23 receptor on the surface membrane of podocytes increases significantly followed by increased levels of phosphorylated STAT3. We found that phosphorylated STAT3 associated with Rac1 and this re-



sulted in decreased actin and synaptopodin, two proteins which are important in the structure of podocytes. Using a wound healing assay we showed that the presence of IL-23 increases the motility of podocytes. The presence of a small drug inhibitor of STAT3 prevented all aspects of IL-23-induced podocyte injury.

To determine the role of IL-23-instigated signaling in podocytes in the development of glomerulonephritis we constructed a mouse which lacked IL-23 receptor in podocytes (*Il-23*$^{f/f}$*.Nphs2*^{cre}*)* and exposed it to a nephrotoxic serum. *Il-23*$^{f/f}$*.Nphs2*^{cre}mice, unlike control mice, developed minimal proteinuria, histologically defined glomerulonephritis and maintained normal levels of synaptopodin in their podocytes.

Conclusion: Our results present first evidence that IL-23 acts directly on tissue resident cells and contributes directly to the development of kidney disease. We propose that approaches to block IL-23 signaling should benefit people with glomerulonephritis.

Disclosure: S. Yu, None; **H. Li**, None; **A. Satyam**, None; **S. Rose**, Janssen, 1, 3; **J. Jordan**, Janssen Research & Development, LLC, 1, 3; **G. Tsokos**, None.

Abstract Number: 0498

Exploring the Role of Lipocalin-2 in Neuropsychiatric SLE Pathogenesis

Chaim Putterman[1], Elise Mike[1] and **Sayra Garcia**[1], [1]Albert Einstein College of Medicine, Bronx, NY

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: SLE – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: While the etiology of neuropsychiatric lupus (NPSLE) is not fully understood, blood brain barrier (BBB) disruption and localized neuroinflammation are potential mechanisms that contribute to disease progression. Lipocalin-2 (LCN2) is a multi-functional acute phase protein known to affect immune cell function, BBB integrity, and glial cell activation. Previous studies in our laboratory demonstrated the amelioration of behavioral deficits in a LCN2 deficient, lupus-prone mouse model, B6.Sle1.Sle3 (Sle1,3), indicating a potential role of LCN2 in NPSLE. At the transcriptional level, we found that LCN2 deficiency restored genes involved in cognitive function that were down-regulated in Sle-1,3 mice. Moreover, LCN2 regulated *MMP-9* and *Plp1,* genes involved in blood brain barrier function

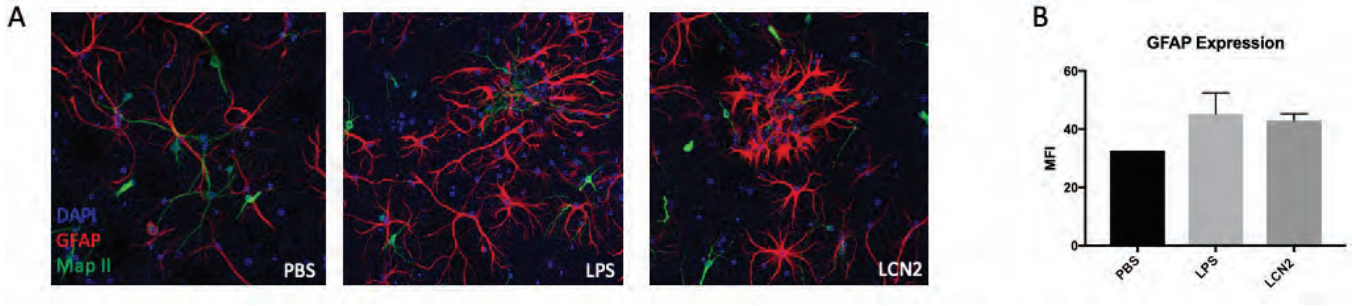


Figure 1. Immunofluorescent staining of neuron-astrocyte co-cultures stimulated with LCN2, LPS, and PBS revealed that LCN2 stimulation leads to activated astrocyte morphology. We observed increased cell volume and cell process extension, indicating higher levels of astrocyte activation in the LPS treated positive control and in the LCN2 experimental group (1A). GFAP mean fluorescence intensity (MFI) was measured using ImageJ software (1B). Green = MAP-II (neurons), Red = GFAP(astrocytes), Blue = DAPI.

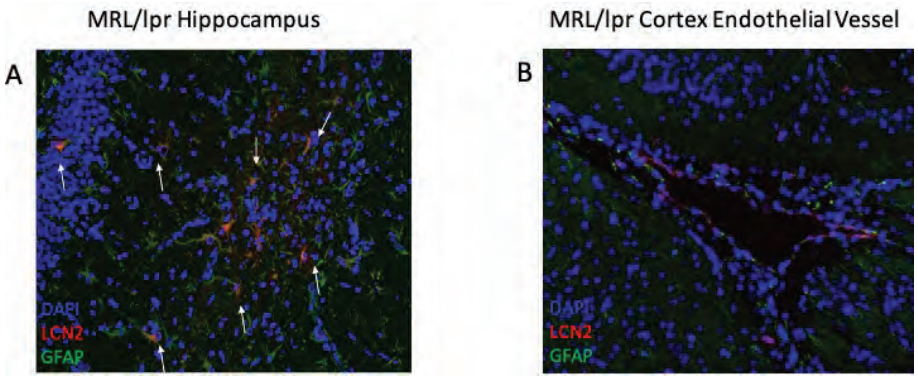


Figure 2. Immunofluorescent staining of MRL/lpr cortex and hippocampus reveals astrocyte-LCN2 co-staining (indicated by white arrows) in MRL/lpr mice injected with LPS, suggesting that under inflammatory stimulus, astrocytes are the main source of LCN2 in MRL/lpr brains. We observed co-staining of astrocytes with LCN2 in the hippocampus (2A) and localization of LCN2 and astrocytes around cortical endothelial vessels (2B). Green = GFAP (astrocytes), Red = LCN2, Blue = DAPI.

and glial cell activation in the brain. In the following studies we examined the role of LCN2 in the neuroinflammation present in the well established MRL/lpr lupus prone strain, as well as the potential role of astrocytes in NPSLE

Methods: Astrocytes and neurons from P1 C57BL/6 pups were isolated and co-cultured for 13 days. On day 14, the co-cultures were treated with either LPS at 100 ng/mL, LCN2 at 5 mcg/ml, or PBS. After 8 hours the cells were fixed and stained for neuron and astrocyte markers by immunofluorescence. Astrocyte activation was analyzed by measuring glial fibrillary acid protein (GFAP) expression through mean fluorescence intensity. For the *ex vivo* experiments, female 10 week old MRL/lpr mice received an intraperitoneal LPS injection to accelerate systemic inflammation. Eight hours post injection, mice were sacrificed, and their brains paraffin embedded for immunofluorescent staining.

Results: To examine astrocyte activation by LCN2 in the *in vitro* studies, we analyzed astrocyte morphology and GFAP expression in stimulated cells. Measurement of mean fluorescence intensity showed an increase in GFAP expression with LCN2 stimulation that was similar to the increase seen in the positively treated LPS stimulated cells when compared to the control (Fig. 1B). Additionally, astrocyte morphology in LPS and LCN2 treated cultures showed a similar increase in cellular processes as well as total cell volume size, both indicators of an activated astrocyte morphology (Fig. 1A). Next, we examined the brains of MRL/lpr mice. We found co-staining of LCN2 with GFAP, an astrocyte marker, in the hippocampus and cortex in injected MRL/lpr mice. Additionally, LCN2 was localized around brain endothelial vessels (Fig. 2).

Conclusion: These preliminary results begin to shed light on the significant behavioral improvement we saw in previous experiments in LCN2 deficient mice. Our *in vitro* results suggest that LCN2 can promote astrocyte activation. Moreover, astrocytes may be the primary source of LCN2 in the brain of MRL/lpr mice. Increased astrocyte LCN2 expression *in vivo* was mainly localized to the cortex and hippocampus, brain regions that are involved in cognitive function and emotional behaviors, respectively. Our findings of astrocyte activation by LCN2 and the colocalization of LCN2 and astrocytes suggest astrocyte derived LCN2 acting in an autocrine manner to promote pathological neuroinflammation in this NPSLE model.

Disclosure: C. Putterman, Equillium, 1, 2; **E. Mike**, None; **S. Garcia**, None.

Abstract Number: 0499

WITHDRAWN

Abstract Number: 0500

Genomic, Phenomic, Proteomic Predictors of Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: Psoriatic Arthritis

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: Delays in diagnosis of psoriatic arthritis (PsA) are common and impair quality of life and function. The study objective was to identify phenotypes, genetic variants, and plasma biomarkers that may predict PsA in patients with psoriasis.

Table 1. Demographics and baseline characteristics

	Phenotype analysis¥		Gene analysis (WES)		Protein analysis (PEA)	
	Psoriasis only (n= 506)	Psoriasis + PsA ¶ (n= 132)	Healthy Controls (n= 1176)	Early onset PsA £ (n= 247)	Psoriasis only (n= 162)	Psoriasis + PsA (n= 65)
Demographics						
Age	45.9 (17.0)	46.9 (12.7)	45.7 (17.4)	47.4 (14.3)	46.2 (16.7)	48.5 (13.3)
Male gender	275 (54.3%)	58 (43.9%)	463 (39.5%)	117 (47.4%)	71 (43.8%)	31 (47.7%)
Age at psoriasis onset	28.3 (17.5)	29.0 (14.9)	NA	32.8 (15.4)	28.5 (17.4)	31.2 (16.7)
Age at PsA diagnosis*	NA	52.9 (13.2)	NA	45.4 (15.9)	NA	49.3 (14.3)
PsA prior to psoriasis onset	NA	11 (8.3%)	NA	73 (29.6%)	NA	12 (19.4%)
BMI at age 18	22.3 (4.1)	22.2 (4.6)	NA	22.9 (4.5)	22.7 (4.7)	22.4 (5.0)
Psoriatic fingernails	208 (41.4%)	85 (65.4%)	NA	134 (57.5%)	63 (39.4%)	33 (53.2%)
Worst-ever induration	2.0 (1.2)	2.5 (1.2)	NA	2.2 (1.3)	2.6 (1.2)	2.9 (1.1)
Worst-ever erythema	3.1 (1.0)	3.4 (1.1)	NA	3.4 (1.2)	3.3 (1.1)	3.4 (1.1)
Worst-ever desquamation	3.0 (1.2)	3.3 (1.2)	NA	3.2 (1.2)	3.2 (1.2)	3.3 (1.1)
Worst-ever BSA	17.9 (24.2)	22.6 (27.3)	NA	19.1 (25.1)	20.2 (25.9)	18.8 (26.1)
Koebner phenomenon	178 (37.8%)	70 (57.4%)	NA	100 (45.2%)	59 (40.4%)	29 (49.2%)
Pustular psoriasis	15 (3.1%)	15 (11.7%)	NA	21 (8.6%)	9 (5.9%)	8 (12.7%)

Numbers in this table are mean (standard deviation) for continuous variables or number of observations (percentage) for binary variables. ¥ Phenotype analysis included psoriasis patients who reported no diagnosis of PsA at the time of phenotyping. ¶ Psoriasis+PsA patients in the phenotype analyses were diagnosed with PsA after the date of phenotyping. £ Early onset PsA was defined as the PsA patients with the shortest time tertile between patient-reported psoriasis onset and PsA onset. *PsA or ankylosing spondylitis diagnosed by a rheumatologist per patient report. WES = whole exome sequencing. PEA = Proximity Extension Assay. Worst ever induration, erythema, and desquamation were estimated by patients on a scale of 0-5.

Table 2. Phenotypes in psoriasis patients associated with subsequent PsA diagnosis

	Univariate		Multivariate	
Phenotype	Hazard Ratio [95% CI]	p-value	Hazard Ratio [95% CI]	p-value
Worst-ever induration	1.46 [1.27-1.68]	**<0.001** *	1.37 [1.19-1.58]	**<0.001** *
Psoriatic fingernails	2.54 [1.75-3.68]	**<0.001** *	2.20 [1.50-3.23]	**<0.001** *
Pustular psoriasis	3.32 [1.92-5.77]	**<0.001** *		
Palmoplantar pustulosis	3.30 [1.57-6.93]	0.002		
Generalized pustular Ps	3.14 [1.43-6.90]	0.004		
Koebner phenomenon	2.15 [1.49-3.11]	**<0.001** *		
Depression	1.72 [1.18-2.51]	0.005		
Inflammatory bowel disease	3.59 [1.43-9.01]	0.006		
Worst-ever desquamation	1.23 [1.06-1.42]	0.006		

Table 3. Gene and protein associations with PsA.

Phenotype	Populations	# Genes/ proteins	Pathway or name	p-value
Genes (Whole exome sequencing)				
Early onset PsA[£]	Early onset PsA vs. Healthy controls	12 genes	Glycosphingolipid metabolic process	**$2x10^{-6}$** *
Early onset PsA	Early onset PsA vs. Healthy controls	34 genes	Upregulation of genes in CD4 T helper cells Th0	$7x10^{-6}$
Early onset PsA	Early onset PsA vs. Healthy controls	2 genes	Hepatocyte growth factor (HGF) and HGF activator	**$2x10^{-6}$** *
PsA before Ps	PsA before psoriasis vs. Healthy controls	2 genes	Hepatocyte growth factor (HGF) + HGF activator	**$3x10^{-7}$** *
Proteins (Plasma Extension Assay)[£]				
PsA	PsA vs. PsC	1 protein	Hepatocyte growth factor (HGF)	0.03
PsA duration	PsA	1 protein	Tumor necrosis factor	**$6x10^{-5}$** **
PsA duration	PsA	1 protein	PI3 (Elafin)	0.02
PsA duration	PsA	1 protein	MCP-3	0.03

Whole exome sequencing results were selected by p<0.00001, without filtering based on biology of the genes or pathways. [£]Early onset PsA was defined as the PsA patients with the shortest time tertile between patient-reported psoriasis onset and PsA onset. *Significant after Bonferroni correction for the number of genes or pathways. **Significant after Bonferroni correction for the number of proteins. PsC = psoriasis without PsA. [£]PEA analyses were adjusted for age, sex and body mass index.

Methods: Clinical data and specimens were collected from 1360 psoriasis patients participating in the Utah Psoriasis Initiative (UPI) between 2002 and 2014. Three concurrent analyses were performed for identifying 1) phenotypes,

2) genes, and 3) plasma protein biomarkers associated with PsA. For the phenotype analysis, proportional hazard Cox regression was used to identify variables associated with an increased risk of developing PsA in the subset of patients with psoriasis phenotyping prior to PsA diagnosis. For the genotype analysis, whole exome sequencing (WES) and primary data analysis were performed by the Regeneron Genetics Center. Variant filtering was completed with the deleterious score BayesDel. Participants with early-onset PsA were compared to healthy controls using an in-house software suite PERCH. Cox regression was also used to assess genotype associations in PsA patients vs. psoriasis patients. For the biomarker analysis, 273 proteins were quantified with Proximity Extension Assay (PEA) and compared in psoriasis subsets with and without PsA.

Results: The mean ages of the phenotype, genotype, and biomarker populations ranged from 45.9 to 48.5 and 39.5% to 54.3% were male (Table 1). Phenotypes associated with a subsequent diagnosis of PsA in the multivariate analysis included worst-ever induration and fingernail involvement (Table 2). With WES analysis, early-onset PsA had a significantly higher burden of deleterious or loss-of-function variants in the glycosphingolipid metabolic process pathway and the gene set hepatocyte grow factor (*HGF*) and HGF activator (*HCFAC*) than healthy controls (Table 3). The association of *HGF*+*HGFAC* was genome-wide significant among the subset of patients who developed PsA before psoriasis. Cox regression in PsA (n=402) vs. psoriasis patients (n=1019) also demonstrated that *HGF* and *HGFAC* associated with an increased risk of PsA (p=0.01). With PEA, associations were newly discovered between 1) PsA and HGF and 2) PsA duration and TNF, P13, MCP-3 proteins.

Conclusion: Multiple phenotypes, genes, and proteins associate with PsA. Patient-reported psoriatic nails and worst-ever induration associate with the subsequent development of PsA in psoriasis patients. Genetic analyses demonstrate the newly discovered associations with *HGF* and *HGFAC* genes that differentiated between PsA and cutaneous psoriasis. The association between PsA and plasma HGF concentration also suggests that HGF may be a useful protein biomarker for PsA. Additional plasma protein biomarkers for PsA may include TNF, PI3, and MCP-3. After validation and additional discovery of phenotypes, genotypes, and biomarkers, we anticipate using these variables to develop a predictive model for identifying psoriasis patients at high risk for PsA.

Disclosure: J. Walsh, Pfizer, 2, AbbVie, 2, 5, Eli Lilly, 5, UCB, 5, Janssen, 5, Novartis, 5, Amgen, 5; **S. Belman**, None; **C. Carroll**, None; **M. Milliken**, None; **B. Haaland**, Astra Zeneca, 5, Flatiron Health, 9, Prometic Life Sciences, 5, Value Analytics Labs, 5; **K. Callis Duffin**, Amgen, 2, Abbvie, 2, 5, Novartis, 2, 5, 8, Lilly, 2, 5, Boehringer-Ingelheim, 2, 5, Pfizer, 2, UCB, 2, Janssen, 2, Anaptys-Bio, 5, Celgene, 2; **G. Krueger**, None; **B. Feng**, Ambry Genetics, 7, Regeneron, 2, Pfizer, 2, Astra Zeneca, 2.

Abstract Number: 0501

Structural Entheseal Lesions in Psoriasis Patients Are Associated with an Increased Risk Ofprogression to Psoriatic Arthritis - A Prospective Cohort Study

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SESSION INFORMATION

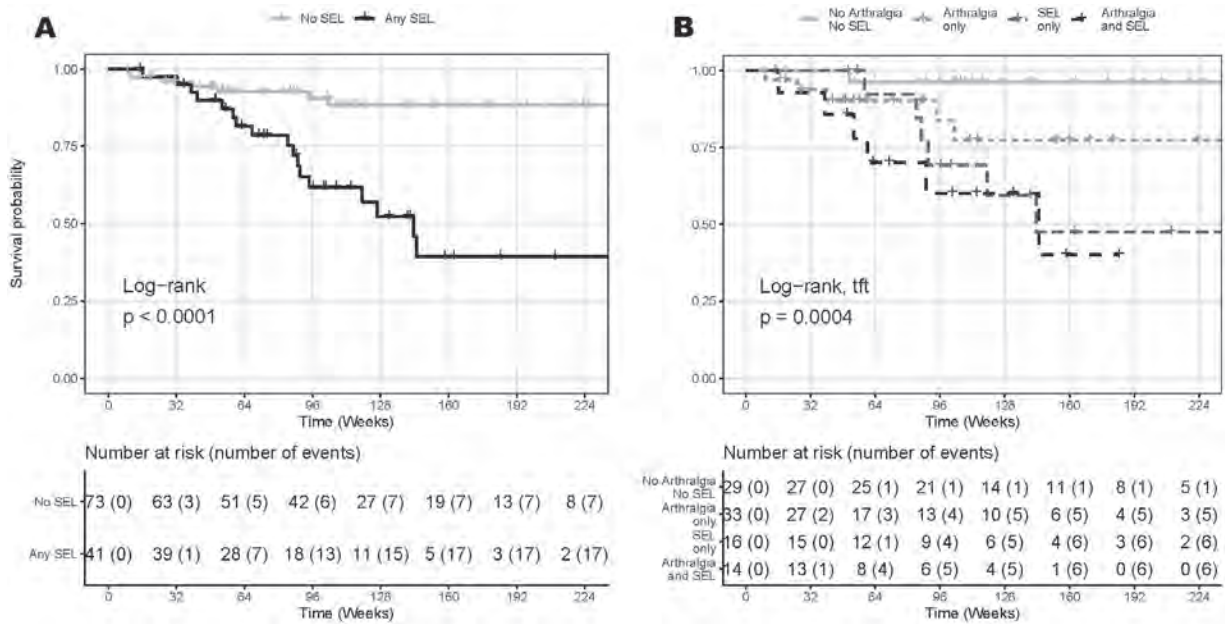
Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: Psoriatic Arthritis

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: We have previously reported that the presence of musculoskeletal pain in psoriasis patients is associated with a higher risk of developing psoriatic arthritis (PsA) (1). Furthermore, a subset of psoriasis patients shows evidence for structural entheseal lesions (SEL) in their hand joints (2), sometimes also referred as “Deep Koebner Phenomenon”, which are highly specific for psoriatic disease and virtually absent in healthy controls, rheumatoid arthritis and hand osteoarthritis patients (2-4). However, it remains unclear whether SEL alone or in combination with



(A) Kaplan-Meier plots of psoriatic arthritis-free survival by presence/absence of structural entheseal lesions (SEL) at baseline. P value by log-rank test;, (B) Kaplan-Meier plots of psoriatic arthritis-free survival by four groups; 1, no arthralgia and no SEL at baseline; 2, arthralgia but no SEL (Arthralgia only) ; 3, no arthralgia but SEL(SEL only) ; 4, arthralgia and SEL

musculoskeletal pain are associated with the development of PsA. Therefore, we aimed to test whether the presence of SEL in psoriasis patients increases the risk for progression to PsA and how this is related to the presence of musculoskeletal pain.

Methods: Psoriasis patients without evidence of PsA were enrolled in a prospective cohort study between 2011 and 2018. All patients underwent baseline assessment of SEL in their 2nd and 3rd MCP joints by high-resolution peripheral quantitative computed tomography (HR-pQCT). The risk of PsA development associated with SEL and arthralgia was explored using survival analyses and multivariable Cox regression models.

Results: 114 psoriasis patients (72 men/42 women) with a mean (SD) follow-up duration of 28.2 (17.7) months were included, 24 of whom developed PsA (9.7 /100 patient-years, 95%CI 6.2 to 14.5) during the observation period. Patients with SEL (N=41) were at higher risk of developing PsA compared to patients without such lesions (21.4/100 patient-years, 95%CI 12.5 to 34.3, HR 5.10, 95%CI 1.53 to 16.99, p=0.008) (Kaplan Meier plot A). Furthermore, while patients without arthralgia and without SEL had a very low progression rate to PsA (1/29; 3.4%), patients with arthralgia but no SEL showed higher progression (5/33; 15.2%), which was in line with previous observations (1) (Kaplan Meier plot B). Presence of SEL further enhanced the risk for progression to PsA both in the absence (6/16; 37.5%) and presence (6/14; 42.8%) of arthralgia with the highest progression rate in those subjects with both arthralgia and SEL ($p< 0.001$ by log rank test for trend) (Kaplan Meier plot B).

Conclusion: Presence of SEL is associated with an increased risk of developing PsA in patients with psoriasis. If used together with pain, SEL allow defining subsets of psoriasis patients with very low and very high risk to develop PsA.

References

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(2) Simon D et al. Ann Rheum Dis. 2016;75:660-6
(3) Finzel S et al. Ann Rheum Dis. 2011;70:122-7
(4) Finzel S et al. Arthritis Rheum. 2011;63:1231-6

Disclosure: D. Simon, Novartis, 8, Lilly, 5, 8, Janssen, 8, AbbVie, 5; **K. Tascilar**, None; **A. Kleyer**, Lilly, 8, Novartis, 8, BMS, 8, Sanofi, 8, Gilead, 8; **S. Bayat**, Novartis, 8; **E. Kampylafka**, Novartis, 8, Bristol-Myers-Squibb, 8, Janssen, 8; **A. Hueber**, Abbvie, 5, 8, BMS, 8, Gilead, 5, GSK, 5, 8, Janssen, 5, 8, Roche/Chugai, 5, Lilly, 2, 5, 8, Novartis, 2, 5, 8; **J. Rech**, Abbie, Biogen, BMS, Chugai, Celgene, EliLilly, Gilead, GSK, Janssen, MSD, Novartis, Roche, Sanofi, Sobi, UCB, 5, 8; **L. Schuster**, None; **K. Engel**, None; **M. Sticherling**, Novartis, 2, 5, 8, Abbvie, 5, 8, Celgene, 5, 8, Janssen, 5, 8, 9, Pfizer, 8, Leo, 5, 8, Lilly, 5, 8, Sanofi, 5, 8; **G. Schett**, None.

Abstract Number: 0502

Integration of Clinical and Protein Markers Through Machine Learning to Distinguish Patients with Psoriasis Arthritis from Those with Psoriasis Without Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: Psoriatic Arthritis

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: Psoriatic Arthritis (PsA) is a progressive inflammatory arthritis that occurs in about 24% of psoriasis patients. Early diagnosis of PsA is associated with better outcomes. Since almost 90% of patients develop PsA either simultaneously or after the onset of cutaneous psoriasis, careful evaluation of psoriasis patients may increase early identification of PsA. Although several candidate protein markers have been demonstrated to be associated with PsA, individually the power to discriminate between PsA and psoriasis without PsA (PsC) is poor. Here, we have developed a computational approach to identify 9 alternative signatures by combining clinical and protein markers to improve discrimination between PsA and PsC.

Methods: Serum samples were obtained from 192 PsA and 191 PsC patients (Table 1). Sixteen protein markers identified in previous studies were assayed in serum samples using ELISA and combined with four clinical features associated with PsA and easily identified by non-rheumatologists (Table 1). To classify patients, we used Support Vector Machines (SVM). To identify the best performing signatures (markers and classifier parameters) we used a three-layer approach. In the first two layers, for training and testing classifiers, we used data only from patients with polyarticular PsA (tender or swollen joint count > 4), while in the third layer, we used all PsA samples. Evaluation of signatures was done using 10-fold cross-validation. First, using a greedy algorithm we identified 41 signatures with accuracy above 75%. Next, we identified 9 signatures using four different measures based on frequency of features and AUCs of these 41 signatures. In the third layer, we used three sample sets for training and testing 2700 classifiers: all samples, only oligoarticular (tender or swollen joint count ≤ 4) PsA, and only polyarticular PsA. All 9 classifiers were trained and tested on similar training and testing sets. Finally, we prioritized the 9 signatures based on their AUC ranks (Table 2).

Results: Demographics and clinical features of patients are provided in Table 1. We propose 9 signatures as alternative signatures to use for distinguishing PsA from PsC, depending on available data, all of which share four features:

List of sixteen measured protein markers		
LEP, SPP1, SOST, POSTN, TNFSF11, TFCP2_CPII, TFCP2_C2C, COMP, TNFSF14, DEFA1, S100A8, ITGB5, LGALS3BP, TNFRSF11B, CXCL10, CRP		
Clinical features	**PsC**	**PsA**
Number of patients	191	192
***Sex (% female)**	28%	56%
Age at psoriasis diagnosis in years - Mean (S.D)	27.53 (14.41)	31.32 (16.77)
***Psoriasis duration in years - Mean (S.D)**	15.69 (14.35)	20.74 (13.61)
***PASI - Mean (S.D)**	4.76 (8.35)	4.75 (6.76)
***Presence of nail psoriasis**	59%	56%
Tender or swollen joint count - Mean (S.D)	-	7.16 (7.63)

* Clinical features used for classifying patients

Table 1. Clinical and demographic information about samples

	Score based on rank of AUC using each feature set in 100 runs of the classifier			
Signature	**All samples**	**oligoarticular**	**polyarticular**	**Total**
Nail psoriasis, CRP, DEFA1, LEP, SOST, SPP1, TFCP2_CPII, TNFRSF11B	669	607	636	1912
Nail psoriasis, CRP, LEP, PASI, SOST, SPP1, TFCP2_CPII, TNFRSF11B, TNFSF11	548	604	551	1703
Nail psoriasis, CRP, ITGB5, LEP, SOST, SPP1, TFCP2_CPII	538	591	510	1639
Nail psoriasis, CRP, ITGB5, LEP, SOST, SPP1, TFCP2_CPII, TNFRSF11B, TNFSF11	531	546	510	1587
Nail psoriasis, CRP, CXCL10, DEFA1, LEP, S100A8, SOST, SPP1, TNFRSF11B	553	454	543	1550
Nail psoriasis, PASI, COMP, CRP, DEFA1, LEP, SOST, SPP1, TNFRSF11B	572	414	563	1549
Nail psoriasis, CRP, ITGB5, LEP, SOST, SPP1, TFCP2_CPII, TNFSF11	459	561	481	1501
Nail psoriasis, CRP, CXCL10, DEFA1, ITGB5, LEP, SOST, TFCP2_CPII, TNFSF11	325	435	350	1110
Nail psoriasis, PASI, COMP, CRP, DEFA1, ITGB5, LEP, SOST, TFCP2_CPII	305	288	356	949

Table 2. 9 identified feature sets sorted based on their score (the higher the score, the better) We used same combinations of samples to train and test all 9 classifiers. To obtain the scores, for each training and testing set, we ranked all of the 9 classifiers from 1 to 9 (1 for the lowest and 9 for the highest AUC). Next, for each signature, we multiplied its frequency at each rank by the rank. The scores in this table are the sum up of these 9 values for each of the three categories of samples.

nail psoriasis, LEP, CRP, and SOST (Table 2). Importantly, the lowest ranked signatures were those without SPP1, suggesting its importance in classifying patients. Our top feature set (Table 2) obtained AUC of up-to 90% on polyarticular samples (median 75%). Performance slightly dropped when we considered all samples, or only oligoarticular samples (Figure 1). Median AUC of 68% (max AUC = 86%) for distinguishing oligoarticular PsA cases from PsC is significant considering high similarity between patients of these two groups.

Conclusion: Integration of clinical and biomarker data through machine learning improves discrimination of PsA from PsC patients. Nail psoriasis and CRP followed by SPP1 are the most important features influencing performance of classifiers. *Nail psoriasis, CRP, DEFA1, LEP, SOST, SPP1, TFCP2_CPII, TNFRSF11B* provided best discrimination between PsA and PsC and needs further validation.

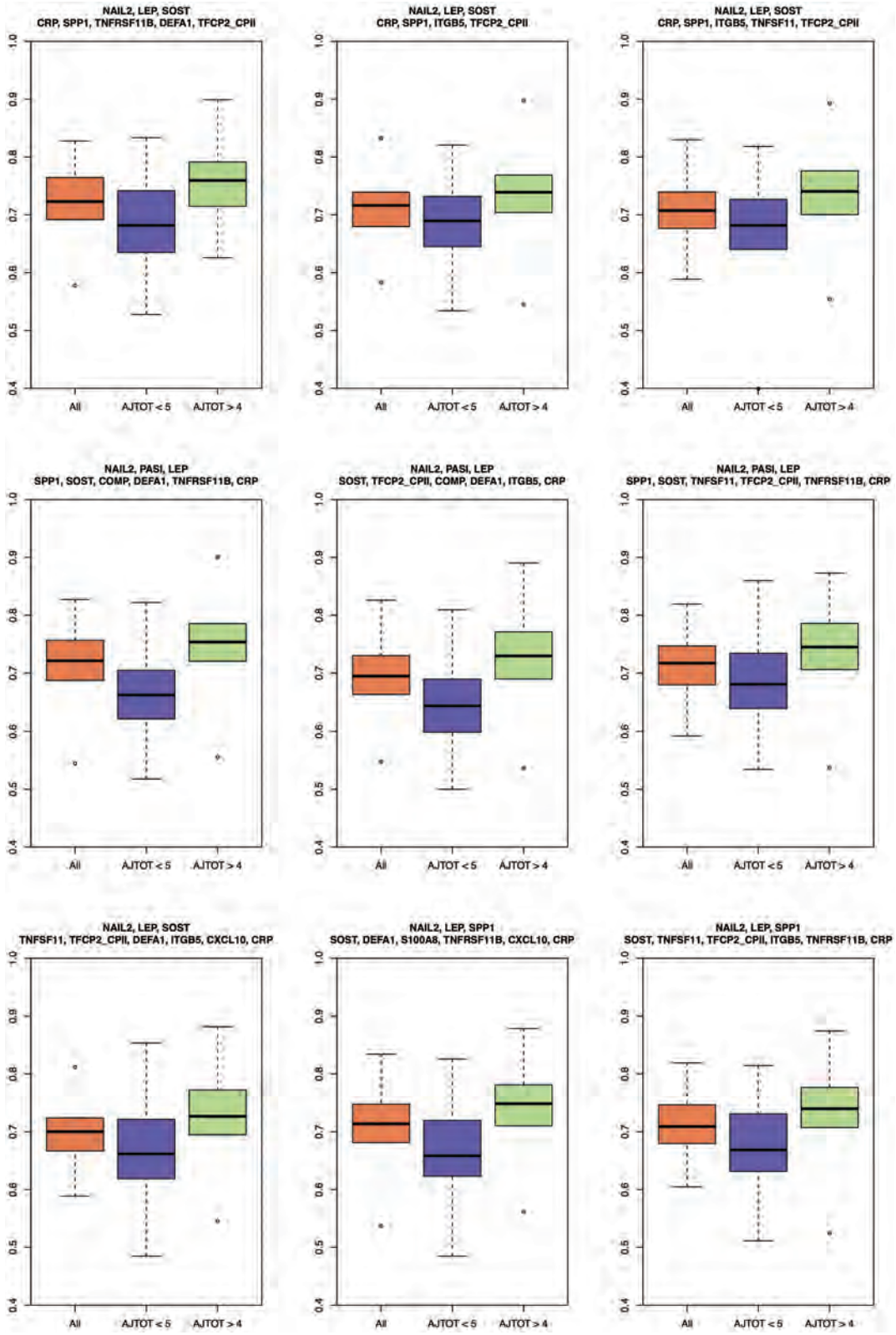

Figure 1. Distribution of AUC of SVMs (y-axis) using each of the 9 identified signatures (listed above each panel) as their feature sets. Each classifier was trained and tested 100 times using three different samples sets: all PsC samples and 1) only polyarticular samples; 2) only oligoarticular samples; 3) all samples. Three boxplots in each panel shows AUC distribution relevant to these three sample sets. For all 9 classifiers, similar training and testing sets were used, making their performance comparable. While all 9 signatures are among high performing signatures, the top left panel was the highest rank in our list.

Disclosure: S. Rahmati, None; **F. Abji**, None; **P. Rahman**, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5; **V. Chandran**, Abbvie, 2, 5, Amgen, 2, 5, Celgene, 2, 5, Eli Lilly, 5, Eli Lilly, 3, Janssen, 8, Novartis, 5, Pfizer, 5, UCB, 5.

Abstract Number: 0503

Targeted Metabolomic Profiling and Prediction of Cardiovascular Events: A Prospective Study of Patients with Psoriatic Arthritis and Psoriasis

Keith Colaco[1], Ker-Ai Lee[2], Shadi Akhtari[3], Raz Winer[4], Paul Welsh[5], Naveed Sattar[5], Iain McInnes[6], Vinod Chandran[7], Paula Harvey[8], Richard Cook[2], Dafna Gladman[7], Vincent Piguet[8] and Lihi Eder[9], [1]Institute of Medical Science, University of Toronto; Women's College Research Institute, Women's College Hospital; and Toronto Western Hospital, University Health Network, Toronto, ON, Canada, [2]University of Waterloo, Waterloo, ON, Canada, [3]Women's College Hospital, University of Toronto, North York, ON, Canada, [4]Rambam Health Care Campus, Haifa, Israel, [5]University of Glasgow, Glasgow, Scotland, United Kingdom, [6]Institute of Infection, Immunity, and Inflammation, University of Glasgow, Glasgow, United Kingdom, [7]Krembil Research Institute, Toronto Western Hospital, Toronto, ON, Canada, [8]Women's College Hospital, University of Toronto, Toronto, ON, Canada, [9]Women's College Research Institute, University of Toronto, Toronto, ON, Canada

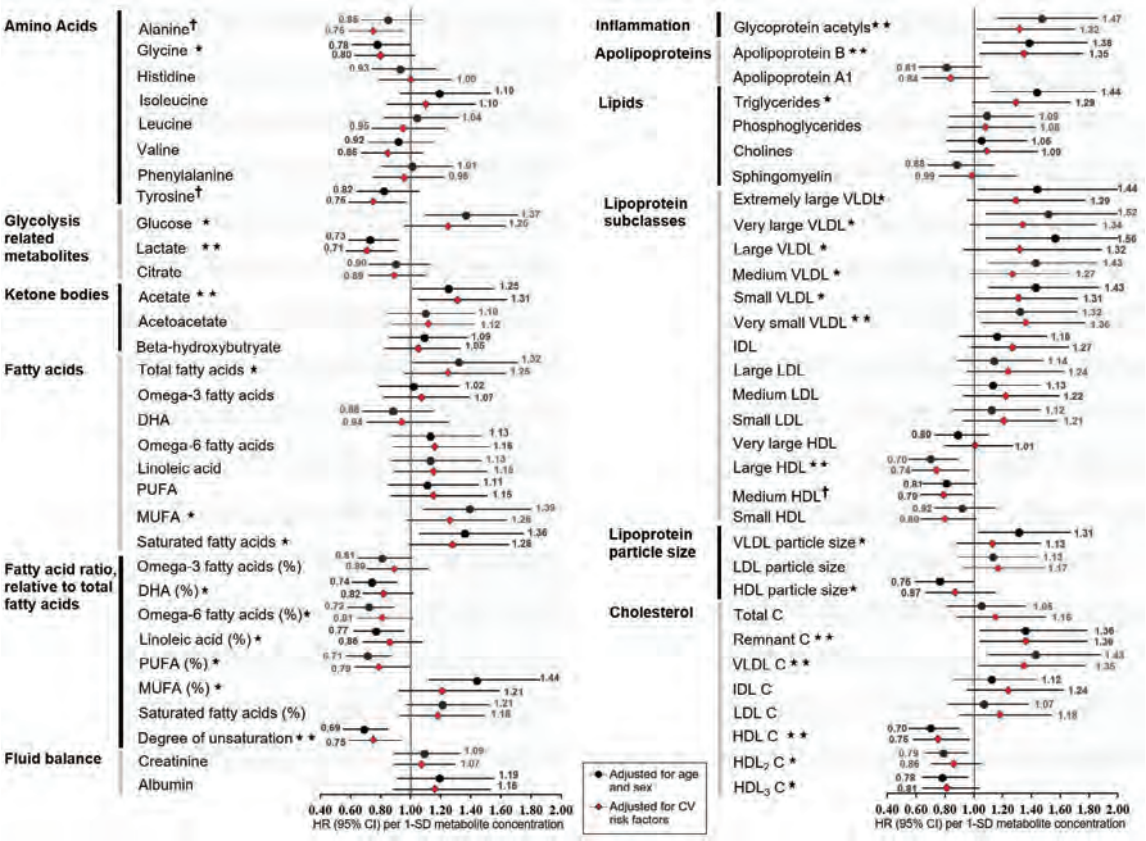

Figure 1. Metabolite associations with future cardiovascular events in patients with psoriatic disease. Hazard ratios of 64 metabolite measures with incident CV events during follow-up (n=977, 70 events). Hazard ratios are per 1-SD log-transformed metabolite concentration, adjusted first for age and sex, and subsequently in another model for CV risk factors that included age, sex, smoking, diabetes, hypertension and body mass index. Error bars denote 95% confidence intervals. *P<0.05 (in age and sex-adjusted model only). **P<0.05 (in both models adjusted for age and sex, and CV risk factors. †P<0.05 (in model adjusted for CV risk factors only). C indicates cholesterol; CI, confidence interval; CV, cardiovascular; DHA, docosahexaenoic acid; HR, hazard ratio; HDL, high-density lipoprotein; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein; MUFA, monounsaturated fatty acids; PUFA, polyunsaturated fatty acids; SD, standard deviation; and VLDL, very low-density lipoprotein.

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes I: Psoriatic Arthritis

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: Psoriatic arthritis and psoriasis, collectively termed psoriatic disease (PsD), are associated with increased cardiovascular (CV) risk. Metabolites comprise biomarkers that may add predictive value over traditional CV risk factors. We aimed to identify metabolites associated with CV events (CVEs) and to determine whether they could improve CV risk prediction beyond traditional CV risk factors.

Methods: Patients from a longitudinal PsD cohort without a prior history of CVEs were included. In the first available serum sample, a targeted nuclear magnetic resonance (NMR) metabolomics platform was used to quantify 64 metabolite measures comprised of lipoprotein subclasses, fatty acids, glycolysis precursors, ketone bodies and amino acids. The study outcome included any of the following CVEs occurring within the first 10 years of biomarker assessment: angina, myocardial infarction, congestive heart failure, transient ischemic attack, cerebrovascular accident, revascularization procedures and CV death. The association of each metabolite with incident CVEs were analyzed separately using Cox proportional hazards regression models first adjusted for age and sex, and subsequently for traditional CV risk factors. Variable selection was performed using penalization with boosting after adjusting for age and sex. The added predictive value of the selected metabolites to improve risk prediction beyond traditional CV risk factors was assessed using the area under the receiver operator characteristic curve (AUC).

Selected Serum Metabolite	Cross-validation coefficient
Acetate	0.0853
Acetoacetate	0.0984
Albumin	0.0781
Average diameter for LDL particles	0.0077
Beta-hydroxybutyrate	0.0091
Glucose	0.0678
Glycoprotein acetyls	0.1692
Phenylalanine	0.0311
Triglycerides in IDL	0.1878
Concentration of large HDL particles	-0.0290
Concentration of medium HDL particles	-0.0238
Degree of unsaturation	-0.1233
Glycine	-0.0071
HDL_3 cholesterol	-0.0384
Lactate	-0.2487
Ratio of DHA to total fatty acids	-0.0845
Tyrosine	-0.1303

DHA, docosahexaenoic acid; HDL, high-density lipoprotein; IDL, intermediate-density lipoprotein; LDL, low-density lipoprotein.

Table 1. Selected serum metabolites associated with incident cardiovascular events, based on 5-fold cross-validation and a proportional subdistribution hazard model adjusted for age and sex.

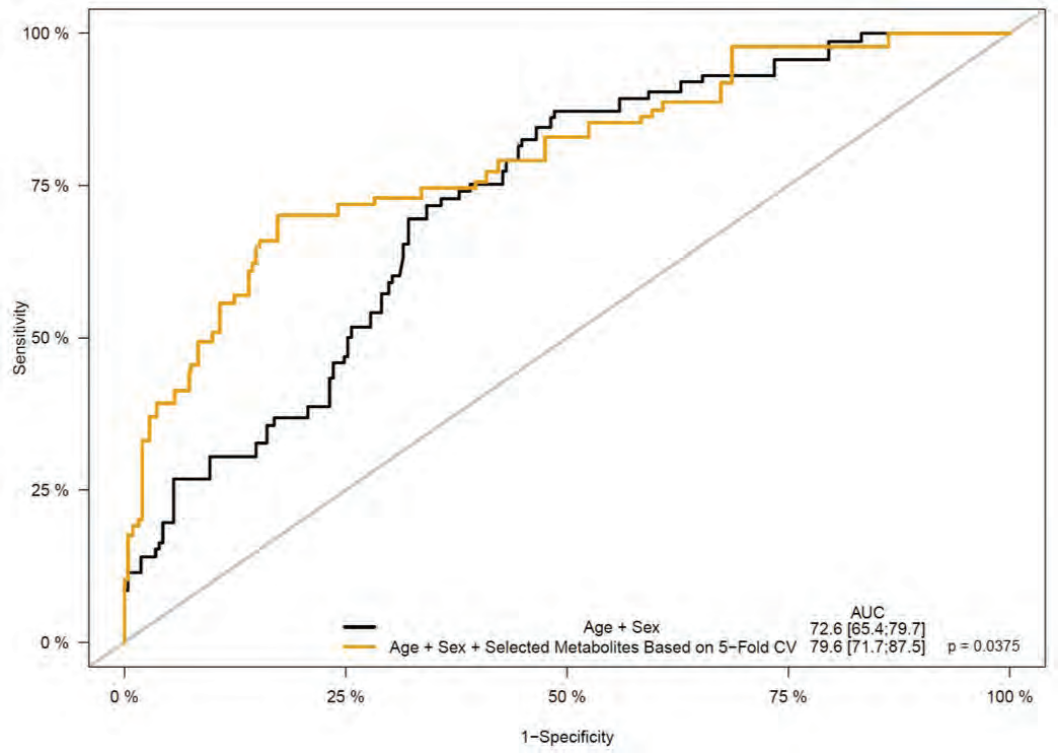

Figure 2. Comparison of the predictive performance of the base model (age and sex alone) and expanded model (age and sex plus selected metabolites) for prediction of cardiovascular events in patients with psoriatic disease. AUC indicates area under the receiver operator characteristic curve; CV, cross-validation.

Results: A total of 977 patients with PsD, followed between 2005 and 2019, were analyzed (mean age 49.1 ± 12.6 years, 45.1% female). During a mean follow-up of 7.1 years, 70 (7.2%) patients developed incident CVEs. In Cox regression models adjusted for CV risk factors, alanine, tyrosine, lactate, degree of unsaturation, high-density lipoprotein (HDL) cholesterol, and medium and large HDL particles were significantly associated with decreased CV risk. Acetate, glycoprotein acetyls, apolipoprotein B, remnant cholesterol, very low-density lipoprotein (VLDL) cholesterol, and very small VLDL particles were associated with an increased CV risk (**Figure 1**). In proportional sub-distribution hazards regression models adjusted for age and sex, 17 metabolites were selected (**Table 1**). The age- and sex-adjusted expanded model (base model + 17 metabolites) significantly improved prediction of CVEs beyond the base model (only age and sex) with an AUC of 79.6 vs. 72.6, respectively (p=0.038) (**Figure 2**).

Conclusion: Using NMR metabolomics profiling, we identified a variety of metabolites associated with a lower and higher risk of developing CVEs in patients with PsD. Further study of their underlying association with CVEs is needed to clarify the clinical utility of these biomarkers to guide CV risk assessment in this population.

Disclosure: K. Colaco, None; **K. Lee**, None; **S. Akhtari**, None; **R. Winer**, None; **P. Welsh**, None; **N. Sattar**, None; **I. McInnes**, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **V. Chandran**, Abbvie, 2, 5, Amgen, 2, 5, Celgene, 2, 5, Eli Lilly, 5, Eli Lilly, 3, Janssen, 8, Novartis, 5, Pfizer, 5, UCB, 5; **P. Harvey**, None; **R. Cook**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **V. Piguet**, None; **L. Eder**, AbbVie, 2, 5, 8, Eli Lilly, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5, 8, Celgene, 5, Novartis, 5.

Abstract Number: 0504

Efficacy and Safety of Upadacitinib in Patients with Active Psoriatic Arthritis and Inadequate Response to Biologic Disease-Modifying Anti-Rheumatic Drugs: A Double-Blind, Randomized Controlled Phase 3 Trial

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: Psoriatic Arthritis
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

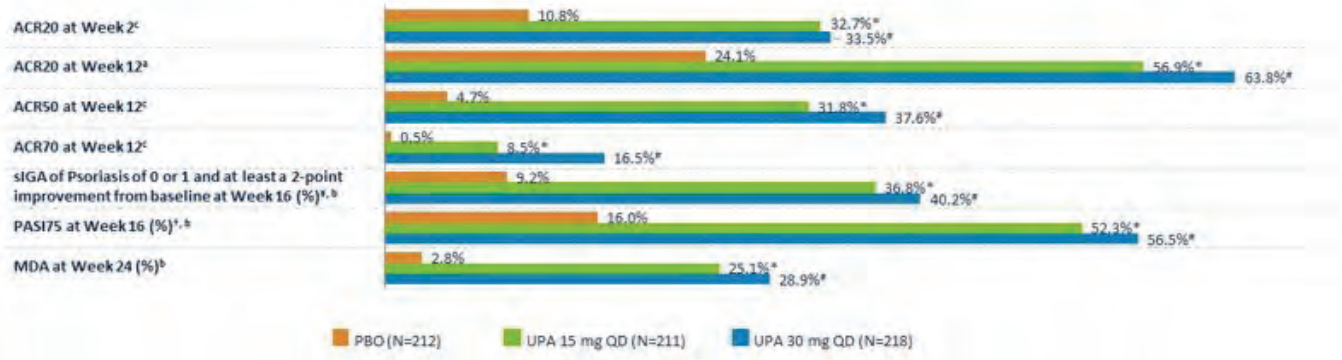
Background/Purpose: Upadacitinib (UPA) is an oral, reversible, JAK inhibitor approved for treatment of moderate to severe rheumatoid arthritis (RA) and currently under evaluation for treatment of psoriatic arthritis (PsA). We assess the efficacy and safety of UPA versus placebo (PBO) in patients (pts) with PsA and prior inadequate response or intolerance to ≥1 biologic disease-modifying anti-rheumatic drug (bDMARD).

Methods: In SELECT-PsA-2, pts were randomized 1:1:1 to once daily UPA 15 mg (UPA15), UPA 30 mg (UPA30), or PBO. Pts were stratified by baseline DMARD use, number of prior failed bDMARDs, and extent of psoriasis. The primary endpoint was the proportion of pts achieving ACR20 response at Wk 12. Multiplicity controlled secondary endpoints included change in HAQ-DI, FACIT-Fatigue (FACIT-F), and SF-36 Physical Component Summary (PCS) at Wk 12; static Investigator Global Assessment (sIGA) of Psoriasis of 0 or 1 and at least a 2-point improvement from baseline, PASI75, and change in Self-Assessment of Psoriasis Symptoms (SAPS) at Wk 16; and proportion of pts achieving MDA at Wk 24. Additional key secondary endpoints were ACR50 and ACR70 at Wk 12, and ACR20 at Wk 2. Treatment-emergent adverse events (TEAEs) are reported for pts who received ≥1 dose of study drug.

Results: 641 pts were randomized and received study drug; 54.3% were female with mean age of 53.4 years, and mean duration since PsA diagnosis of 10.1 years. 61% of pts failed 1 bDMARD, 18% failed 2 bDMARDs, and 13% failed ≥3 bDMARDs. 543 (84.6%) pts completed Wk 24 study drug.

At Wk 12, a significantly greater proportion of pts receiving UPA15 and UPA30 vs PBO achieved ACR20 (56.9% and 63.8% vs 24.1%; $p < .0001$ for both comparisons). Statistically significant improvements were observed in the UPA15 and UPA30 arms vs PBO in all multiplicity controlled secondary endpoints, including ΔHAQ-DI (PBO, -0.10; UPA15, -0.30; UPA30, -0.41), ΔSF-36 PCS (PBO, 1.6; UPA15, 5.2; UPA30, 7.1), ΔFACIT-F (PBO, 1.3; UPA15, 5.0; UPA30, 6.1), and ΔSAPS (PBO, -1.5; UPA15, -24.4; UPA30, -29.7; $p < .0001$ for all endpoints; **Figure 1**). In addition, a greater proportion of pts achieved ACR50 and ACR70 at Wk 12 with UPA vs PBO.

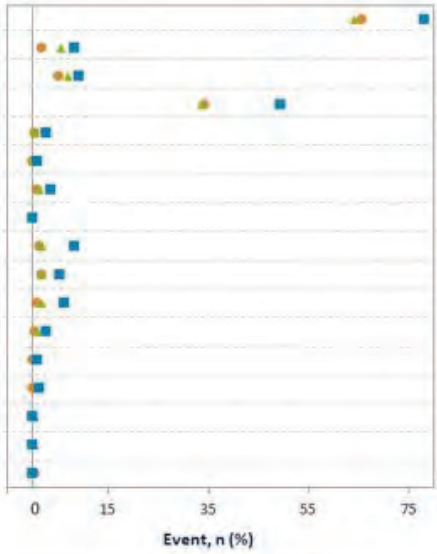
Figure 1. Efficacy Endpoints



[a] Primary endpoint; [b] Multiplicity controlled ranked secondary endpoints; [c] Additional key secondary endpoints.
[d] for patients with baseline sIGA ≥2; [e] for patients with ≥ 3% body surface area psoriasis at baseline
PBO, placebo; UPA, upadacitinib; QD, once daily; ACR, American College of Rheumatology; sIGA, static Investigator Global Assessment; PASI, Psoriasis Area Severity Index; MDA, Minimal Disease Activity; *, p < 0001 for UPA15 vs. PBO; #, p < .0001 for UPA30 vs. PBO. Nominal p-value is provided for ACR50/70 at Week 12 and ACR20 at Week 2. Multiplicity adjustments were applied to the primary and ranked key secondary endpoints.

Results for binary endpoints are based on non-responder imputation (NRI) analysis; each of the two UPA arms was compared to PBO using the Cochran-Mantel-Haenszel (CMH) test, adjusting for the main stratification factor of current use of at least 1 DMARD.
Results for MDA at week 24 are based on NRI with additional rescue handling, where patients rescued at Week 16 are imputed as non-responders.
A graphical multiple testing procedure is used to control the overall type I error rate at the 0.05 level for all primary and ranked key secondary endpoints.

Figure 2. Safety Summary Through Week 24



	PBO; N=212; n (%)	UPA 15mg QD; N=211; n (%)	UPA 30mg QD; N=218; n (%)
Any Adverse Event	139 (65.6)	135 (64.0)	170 (78.0)
Serious AE	4 (1.9)	12 (5.7)	18 (8.3)
AE Leading to Discontinuation of Study Drug	11 (5.2)	15 (7.1)	20 (9.2)
Infection	73 (34.4)	71 (33.6)	108 (49.5)
• Serious Infection	1 (0.5)	1 (0.5)	6 (2.8)
• Opportunistic Infection excl. tuberculosis and herpes zoster[a]	0	0	2 (0.9)
• Herpes Zoster[b]	2 (0.9)	3 (1.4)	8 (3.7)
• Active Tuberculosis	0	0	0
Hepatic Disorder	3 (1.4)	4 (1.9)	18 (8.3)
Creatine Phosphokinase elevation	4 (1.9)	4 (1.9)	12 (5.5)
Anemia	2 (0.9)	4 (1.9)	14 (6.4)
Neutropenia	1 (0.5)	2 (0.9)	6 (2.8)
Lymphopenia	0	2 (0.9)	2 (0.9)
Malignancy (including NMSC)[c]	0	3 (1.4)	3 (1.4)
MACE (adjudicated)[d]	0	1 (0.5)	0
VTE (adjudicated)[e]	0	1 (0.5)	0
Deaths[f]	1 (0.5)	0	0

NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular event; VTE, venous thromboembolic events

[a]Opportunistic infections: UPA30: 1 candidiasis of the trachea, 1 oropharyngeal candidiasis; [b]Herpes zoster: All events of herpes zoster were mild or moderate in severity with the exception of 1 severe event of herpes zoster involving 2 dermatomes in 1 pt on UPA30. Three pts had involvement of 3 dermatomes (1 on UPA15 and 2 on UPA30); [c]Malignancies: UPA15: 1 pt basal cell carcinoma, 1 pt prostate cancer, 1 pt rectal cancer; UPA30: 1 pt rectal adenocarcinoma, 1 pt ovarian cancer and endometrial cancer, 1 pt basal cell carcinoma; [d]MACE (includes CV death, non-fatal myocardial infarction [MI], non-fatal stroke): UPA15: 1 non-fatal myocardial infarction; [e]VTE: UPA15: 1 pulmonary embolism; [f]Deaths: PBO: 1 motor vehicle accident

Generally, TEAEs were reported at similar frequencies in the PBO and UPA15 arms and at a higher frequency in the UPA30 arm (**Figure 2**). Numerically higher rates of serious AEs were reported in the UPA arms. Herpes zoster was more frequent with UPA30. Three malignancies occurred in each of the UPA arms. One adjudicated non-fatal myocardial infarction and one adjudicated pulmonary embolism were reported with UPA15.

Conclusion: In this bDMARD-IR PsA population, UPA15 and UPA30 demonstrated significant improvements across PsA domains including improvements in joint and skin signs and symptoms vs PBO through Wk 24 with improvement

observed by Wk 2. A greater percentage of pts treated with UPA achieved MDA and ACR50/70, stringent composite measures of disease control. No new safety signals were identified compared to what has been observed with UPA in RA.

Disclosure: M. Genovese, Abbvie, 2, 5, Eli Lilly and Company, 2, 5, Galapagos, 2, 5, Gilead Sciences Inc., 2, 5, Pfizer, 2, 5, EMD Merck Serono, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, RPharm, 2, 5, Sanofi-Genzyme, 2, UCB, 5, Amgen, 5; **A. Lertratanakul**, AbbVie Inc., 1, 3; **J. Anderson**, AbbVie Inc., 1, 3, 4; **K. Papp**, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Astellas, 2, 5, 8, Baxalta, 2, 5, 8, Baxter, 5, 8, Boehringer Ingelheim, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Centocor, 2, 5, 8, Dermira, 2, 5, 8, Eli Lilly, 2, 5, 8, Forward Pharma, 5, 8, Galderma, 2, 5, 8, Genentech, 2, 5, 8, GlaxoSmithKline, 2, 5, 9, Janssen, 2, 5, 8, Kyowa-Hakko Kirin, 2, 5, 8, Leo Pharma, 2, 5, 8, Medimmune, 2, 5, 8, Merck-Serono, 2, 5, 8, Merck Sharp & Dohme Corp, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Regeneron, 2, 5, 8, Roche, 2, 5, 8, Sanofi-Genzyme, 2, 5, 8, Stiefel, 2, 5, 8, Sun Pharma, 5, 8, Takeda, 2, 5, 8, UCB, 2, 5, 8, Valeant, 2, 5, 8; **W. Tillett**, AbbVie, 5, 8, Amgen, 5, 8, Eli Lilly, 5, 8, Janssen, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB Pharma, 5, 8; **F. Van den Bosch**, AbbVie, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Gilead, 5, Merck, 5, 8; **S. Tsuji**, AbbVie Inc., 1, Asahi Kasei, 1, Chugai, 1, Daiichi Sankyo, 1, Eli Lilly, 1, Eisai, 1, Mitsubishi Tanabe, 1, Celgene, 1, Novartis Pharma K.K., 1; **E. Dokoupilova**, None; **M. Keiserman**, Pfizer, 5, 9, Abbott, 5, Actelion, 5, Astra Zeneca, 5, 9, Amgen, 5, 9, Roche, 5, 9, Bristol-Myers Squibb, 5, 9, Janssen, 5, Anthera Pharmaceuticals, 9, Biogen Idec Inc, 9, Celltrion, 9, Eli Lilly, 9, Human Genome Sciences, 9, Novartis, 9, Sanofi, 9, UCB, 9; **X. Wang**, AbbVie Inc., 1; **S. Zhong**, AbbVie, 1, 3; **P. Zueger**, AbbVie Inc., 1, 3; **A. Pangan**, AbbVie, 1, 3; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5.

Abstract Number: 0505

Secukinumab Provides Sustained Improvements in Clinical and Imaging Outcomes in Patients with Psoriatic Arthritis and Axial Manifestations: Results from the MAXIMISE Trial

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: Psoriatic Arthritis

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Axial disease may affect up to 25–70% of psoriatic arthritis (PsA) patients, depending on the definition used. Current evidence on efficacy of biologics in the treatment of axial manifestations is limited,[1] particularly as validated classification criteria for this subtype of PsA are not yet available. MAXIMISE (NCT02721966); the first randomized controlled trial evaluating the efficacy of a biologic drug in the management of the axial manifestations of PsA, showed that secukinumab (SEC) 300 and 150 mg provided rapid and significant improvement in ASAS20 responses through Week (Wk) 12.[2] Here, we report the effect of SEC on clinical and imaging outcomes through 52 wks from the MAXIMISE trial.

Criteria	SEC 300 mg s.c. (N = 164)	SEC 150 mg s.c. (N = 157)	Placebo to SEC 300 mg s.c. (N = 81)	Placebo to SEC 150 mg s.c. (N = 80)
Clinical endpoints				
ASAS20, % Responders (n/M)*	75.5 (123/163)	77.3 (119/154)	74.1 (60/81)	74.7 (59/79)
ASAS40, % Responders (n/M)*	62.6 (102/163)	60.4 (93/154)	63.0 (51/81)	50.6 (40/79)
BASDAI50, % Responders (n/M)#	68.3 (95/139)	58.5 (83/142)	55.6 (40/72)	54.1 (40/74)
Spinal pain VAS, mean change from BL (SD), n#	-42.4 (27.0), 140	-43.8 (26.2), 142	-43.1 (25.0), 72	-36.4 (25.2), 74
Imaging endpoint				
Berlin MRI score for Entire Spine, mean change from BL (SD), n#	-0.6 (2.3), 121	-0.3 (1.3), 124	-0.8 (2.7), 63	-0.4 (1.3), 60
Berlin MRI score for SIJ, mean change from BL (SD), n#	-0.7 (2.2), 122	-0.5 (1.7), 122	-0.9 (2.4), 63	-1.0 (2.7), 59

N, total number of patients in the group; n, number of patients with response; M, number of evaluable patients
*Intermediate missing data as well as any data missing in the case of study discontinuation is imputed using LOCF; #observed data
Patients with initial placebo treatment were re-randomized to SEC 300 mg or 150 mg at Wk 12
ASAS, Assessment of Spondyloarthritis International Society criteria ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BL, baseline; LOCF, Last observation carried forward; MRI, magnetic resonance imaging; s.c., subcutaneous; SEC, secukinumab; SIJ, sacroiliac joints; VAS, visual analogue scale, Wk, week.

Table. Endpoints at Wk 52

Methods: This phase-3, double-blind, placebo-controlled, multicentre trial included 498 patients (≥18 years) diagnosed with PsA and fulfilling CASPAR criteria presenting with spinal-pain VAS-score ≥40/100 and BASDAI-score ≥4 and inadequate response to ≥2 NSAIDs. Patients were randomized to SEC 300 mg (N=167); 150 mg (N=165) or placebo (N=166) wkly for 4 wks and every 4 wks thereafter. At Wk 12, placebo patients were re-randomized to SEC 300/150 mg. The primary endpoint was ASAS20 response with SEC 300 mg at Wk 12. Assessments at Wk 52 were exploratory and included ASAS20/40, BASDAI50, spinal pain (VAS), and improvement in Berlin MRI score for the spine and the sacroiliac joints. Multiple imputation and last observation carried forward (LOCF) were used to account for missing data for analysis of ASAS20/40 at Wk 12 and Wk 52, respectively. All other data were reported as observed.

Results: The primary endpoint was met.[2] ASAS20/40 responses at Wk 12 were 62.9%/43.6% (SEC 300 mg) and 66.3%/39.5% (SEC 150 mg) versus 31.2%/12.2% (placebo), respectively (P< 0.0001). ASAS20/40 responses improved further with SEC 300/150 mg treatment from baseline through 52 wks. 74.1%/75.0% and 63.0%/50.0% of placebo patients re-randomized at Wk 12 to SEC 300/150 mg, achieved ASAS20/40 response at Wk 52. At baseline, 59.5% (SEC 300 mg), 53.5% (SEC 150 mg) and 64.2% (placebo) of the pts had positive MRI scores for the sacroiliac joints and/or the spine. The reductions of Berlin MRI score for entire spine and sacroiliac joints were sustained with SEC 300/150 mg from baseline through 52 wks (**Table**). 64.6%, 69.1% and 33.6% of patients with inflammatory back pain at baseline as confirmed by the ASAS, Calin et al. and Berlin criteria in the secukinumab 300 mg, 150 mg and placebo groups, respectively, achieved an ASAS20 response at Wk 12.

Conclusion: Secukinumab provided further improvement in signs and symptoms of axial disease as assessed by ASAS20/40 through 52 wks and showed reduced inflammatory MRI lesions in the spine and sacroiliac joints in patients with PsA with axial manifestations. Efficacy responses at Wk 52 were comparable in patients who switched at Wk 12 from placebo to SEC 300/150 mg.

References

1. McInnes IB, et al. *Lancet.* 2015;386(9999):1137–46.
2. Baraliakos X, et al. *Arthritis Rheumatol*. 2019;71(suppl 10).

Disclosure: X. Baraliakos, AbbVie, 2, 5, 8, Novartis, 2, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Pfizer, 5, 8, UCB, 5, 8, BMS, 5, 8, Merck, 5, 8, Galapagos, 5; **L. Gossec**, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8; **E. Pournara**, Novartis, 1, 3; **S. Jeka**, Pfizer, 2, 8, Novartis, 2, 8, Abbvie, 2, 8, UCB, 2, 8, MSD, 2, 8, Roche, 2, 8, Sandoz, 2, 8, Egis, 2, 8, Lilly, 2, 8, Celgene, 2, 8; **R. Blanco**, AbbVie, 2, 5, 8, MSD, 2, 5, 8, Roche, 2, 5, 8, Pfizer, 5, 8, Bristol-Myers Squibb, 5, 8, Janssen, 5, 8, Eli Lilly, 5, 8, UCB Pharma, 5, 8; **S. D'Angelo**, AbbVie, 5, 8, Biogen, 5, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, MSD, 5, Novartis, 5, 8, Pfizer, 8, Sanofi, 8, UCB, 5; **G. Schett**, None; **B. Schulz**, Novartis, 3; **M. Rissler**, Novartis, 1, 3; **D. Whyms**, Novartis, 3; **C. Perella**, Novartis, 1, 3; **L. Coates**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5.

Abstract Number: 0506

Efficacy and Safety of Guselkumab, a Monoclonal Antibody Specific to the p19-Subunit of Interleukin-23, Through Week 52 of a Phase 3, Randomized, Double-blind, Placebo-controlled Study Conducted in Biologic-naïve Patients with Active Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: Psoriatic Arthritis

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Guselkumab (GUS), a monoclonal antibody that specifically binds to the p19-subunit of IL-23, is approved to treat psoriasis. Through Week24 (W24) of the Ph3, double-blind, placebo (PBO)-controlled trial in biologic-naïve pts with active PsA (DISCOVER-2), GUS every 4 or 8 weeks (Q4W or Q8W) demonstrated efficacy for joint & skin symptoms and inhibition of structural damage progression (Q4W), and was well tolerated. This study assessed GUS efficacy and safety through W52.

Methods: Biologic-naïve adults with active PsA (≥5 swollen+≥5 tender joints; CRP ≥0.6mg/dL) were randomized (1:1:1) to GUS 100 mg Q4W; GUS 100 mg at W0, W4, Q8W; or PBO. At W24, PBO pts switched to GUS 100 mg Q4W (PBO X Q4W). ACR response rates at W52, based on nonresponder imputation (NRI) for missing data and as observed in pts who continued study agent at W24, are shown. Observed data for additional endpoints, including PsA-modified van der Heijde Sharp (vdH-S) scores derived from blinded radiographic images collected at W0, W24, W52 (or at d/c) and scored in a new Read Campaign, are shown.

Results: 712/739 (96.3%) randomized & treated pts continued study agent at W24; 689/739 (93.2%) completed Wk52. NRI ACR20 response rates continued to increase after W24, and at W52 were 70.6% for GUS Q4W and 74.6% for GUS Q8W (Fig1A). Similar response patterns were observed for the more stringent ACR50/70 criteria

Table 1. Observed Efficacy[1]	GUS Q4W		GUS Q8W		PBO (W0-24) X	GUS Q4W (W24-52)
Data are % unless otherwise stated	W24	W52	W24	W52	W24	W52
Dactylitis at W0, n	116	111	107	105	95	93
Resolution	68.1	81.1	60.7	81.9	41.1	78.5
Enthesitis at W0, n	165	160	151	148	172	168
Resolution	45.5	60.0	57.6	65.5	32.6	67.3
≥3% BSA psoriasis, IGA ≥2 at W0, n	176	173	172	170	176	172
IGA 0/1 + ≥2-grade decrease	71.0	84.4	72.1	77.1	19.9	84.3
PASI75	81.8	91.9	80.8	88.8	23.3	88.4
PASI90	63.6	81.5	70.3	77.1	10.2	76.7
PASI100	46.6	61.3	46.5	54.7	2.8	55.2
HAQ-DI, n	234	229	238	234	237	230
Mean change	-0.4	-0.5	-0.4	-0.5	-0.2	-0.4
SF-36 scores, n (mean change)	234	229	238	234	237	230
Physical Component - PCS	7.2	9.0	7.8	9.5	3.8	8.1
Mental Component - MCS	4.1	4.1	4.5	4.5	2.2	4.3
MDA/VLDA, n	234	228	238	234	238	231
MDA	19.7	36.8	26.5	32.9	6.3	31.6
VLDA	5.1	12.2[2]	4.6[3]	17.1	1.3	6.9

[1]Randomized pts still on study agent at W24; [2]N=229; [3]N=237

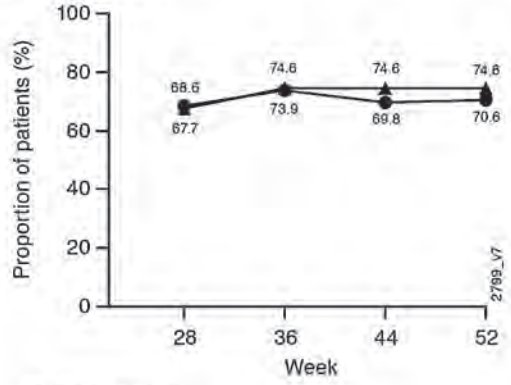
Table 1. Observed Efficacy

(Fig1C,E). Observed ACR (Fig, 1B,D,F), IGA, PASI & MDA/VLDA responses; dactylitis & enthesitis resolution; and mean improvements in HAQ-DI and SF-36 PCS/MCS scores were also sustained through W52 in pts receiving Q4W & Q8W; W52 data for PBO X Q4W pts were generally consistent with other GUS-treated pts (Fig1, Table1). Changes in vdH-S scores were similar for W24-52 (0.62) and W0-24 (0.46) for Q4W; less radiographic progression occurred from W24-52 v W0-24 for Q8W (0.23 v 0.73) & PBO X Q4W (0.25 v 1.00). In 731 GUS-treated pts, 4.2% had SAEs; 1.2% had serious infections; no pt died; and no pt had IBD, opportunistic infections or active TB, or anaphylactic or serum sickness-like reactions.

Conclusion: In biologic-naïve pts with active PsA, GUS elicited sustained improvements in joint & skin symptoms; inhibition of radiographic progression & improvements in physical function, quality of life & composite indices through W52. GUS safety in PsA was similar at W24[1] & W52 and consistent with GUS safety in psoriasis.

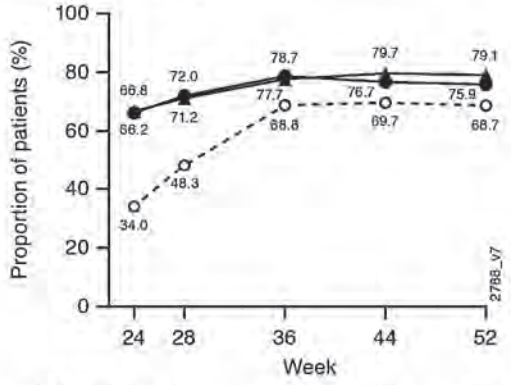
Fig 1. NRI and Observed ACR20 (**A & B**), ACR50 (**C & D**), and ACR70 (**E & F**) responses through W52 (Note: patients randomized to PBO crossed over to GUS Q4W at W24)

A. ACR 20 (NRI)*



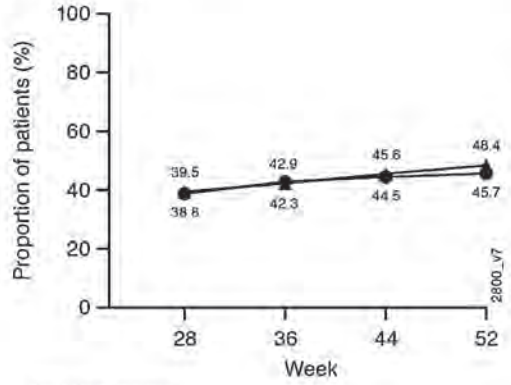
GUS Q4W, n = 245
GUS Q8W, n = 248

B. ACR 20 (Observed)



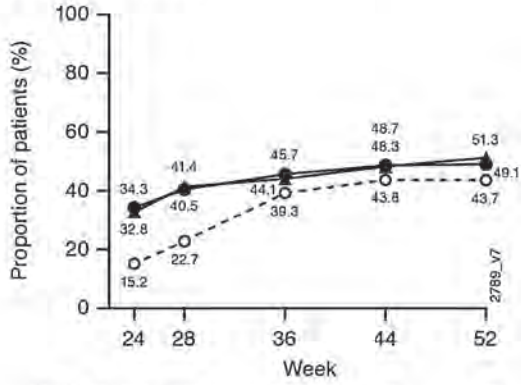
GUS Q4W	234	232	230	223	228
GUS Q8W	238	236	238	232	234
PBO→GUS Q4W	238	238	231	234	230

C. ACR 50 (NRI)*



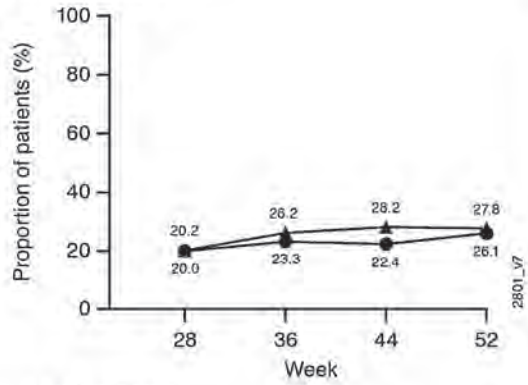
GUS Q4W, n = 245
GUS Q8W, n = 248

D. ACR 50 (Observed)



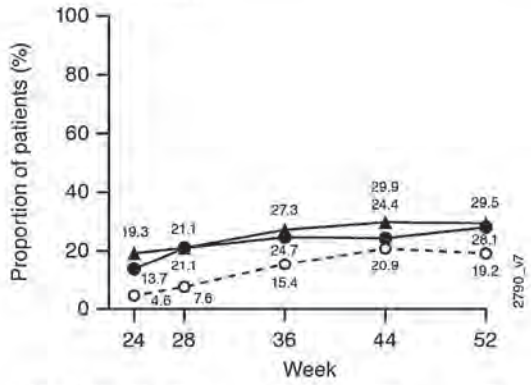
GUS Q4W	233	232	230	224	228
GUS Q8W	238	237	238	234	234
PBO→GUS Q4W	237	238	234	235	231

E. ACR 70 (NRI)*



GUS Q4W, n = 245
GUS Q8W, n = 248

F. ACR 70 (Observed)



GUS Q4W	233	232	231	225	228
GUS Q8W	238	237	238	234	234
PBO→GUS Q4W	238	237	234	235	229

* NRI analysis includes pts randomized to Q4W and Q8W at W0 who received ≥1 dose of study treatment.

GUS 100 mg Q4W — GUS 100 mg Q8W - - PBO→GUS 100 mg Q4W

Reference

1. Mease et al. *ACR 2019, abs #L13*. *Arth Rheumatol*. 2019;71 S10:5247
NRI and Observed ACR20 (A & B), ACR50 (C & D) and ACR70 (E & F) responses through W52 (Note: patients randomized to PBO crossed over to GUS Q4W at W24)

Disclosure: I. McInnes, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **P. Rahman**, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5; **A. Gottlieb**, Janssen, 2, 5, Incyte, 2, 5, Novartis, 2, 5, 8, Xbiotech, 2, 9, Boehringer Ingelheim, 2, 5, UCB Pharma, 2, 5, 8, Beiersdorf, 5, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, Sun Pharma, 2, 5, Leo Pharma, 5, Avotres Therapeutics, 5; **E. Hsia**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **A. Kollmeier**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **X. Xu**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **R. Subramanian**, Janssen Research & Development, LLC., 3; **P. Agarwal**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **S. Sheng**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **Y. Jiang**, None; **B. Zhou**, Janssen Reserach & Development, LLC, 3, Johnson & Johnson, 1; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5.

Abstract Number: 0507

Comparison of Secukinumab versus Adalimumab Efficacy by Sex in Psoriatic Arthritis from a Phase 3b, Double-blinded, Randomized, Active-controlled Study

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: Psoriatic Arthritis
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Lower efficacy to anti-tumor necrosis factor treatment has been reported in female patients with psoriatic arthritis (PsA) as compared to males in clinical registries.[1] The EXCEED study (NCT02745080) evaluated efficacy and safety of secukinumab (SEC) *versus* adalimumab (ADA) as first-line monotherapy in biologic-naïve patients with PsA. Here, we report the impact of sex on efficacy outcomes with SEC *versus* ADA at Week 52 from the EXCEED study.

Methods: Eligible patients were randomized 1:1 to receive SEC 300 mg subcutaneous at baseline, Week 1-4, followed by dosing every 4 weeks until Week 48 or ADA 40 mg subcutaneous at baseline followed by same dosing

every 2 weeks until Week 50. The detailed study design and objectives have been previously described.[2] The primary analysis was to demonstrate superiority of SEC *versus* ADA on ACR20 response at Week 52 using logistic regression model with treatment as a factor and baseline weight as a covariate. A *post-hoc* analysis for ACR20 response was performed using the same model with treatment, sex and smoking status as factors to adjust for imbalances observed in the baseline characteristics. Comparative *post-hoc* analysis was performed with SEC *versus* ADA by sex for other efficacy outcomes through Week 52.

Results: A total of 853 patients were randomized to receive SEC (N=426) or ADA (N=427) with similar baseline demographics except for higher proportion of females (51% in SEC; 46% in ADA) and smokers (21·8% in SEC; 17·8% in ADA) in the SEC group.[2] The primary endpoint for ACR20 response at Week 52 was not met. ACR20 response at Week 52 was, SEC (67·4%) *versus* ADA (61·4%); p=0·0227, after adjusting for sex and smoking status. The female patients had higher tender joint count, patient global assessment, HAQ-DI, PsA pain and enthesitis compared to males (**Table 1**). A greater proportion of patients with SEC (83·0% females; 91·3% males) completed Week 52 *versus* ADA (74·2% females; 83·4% males). SEC was associated with numerically higher efficacy on joints in females at Week 52 without any notable differences in the ACR core components *versus* ADA. Overall, higher efficacy was demonstrated in males versus females at Week 52 (**Table 2**).

Conclusion: Females had greater baseline disease severity than males. Secukinumab was associated with higher retention rate in both males and females at Week 52. Secukinumab provided numerically higher clinical responses in females *versus* adalimumab in musculoskeletal and skin endpoints and physical function at Week 52. In males, similar efficacy on musculoskeletal endpoints for both treatments and greater efficacy on skin with secukinumab were observed. These interesting findings warrant further investigation for reproducibility or uniqueness.

References

1. Højgaard P, et al. *Rheumatology.* 2018;57(9):1651-60.
2. McInnes IB, et al. *Lancet.* 2020;395:1496–505.

Characteristic	Female			Male		
	SEC 300 mg, N = 218	ADA 40 mg, N = 198	Total N=416	SEC 300 mg, N = 208	ADA 40 mg, N = 229	Total N=437
TJC, mean (SD)	21·4 (15·7)	22·1 (14·9)	21·7 (15·3)	17·2 (11·3)	19·3 (14·7)	18·3 (13·2)
SJC, mean (SD)	9·6 (7·1)	10·4 (8·3)	10·0 (7·7)	9·9 (7·6)	10·0 (7·5)	9·9 (7·5)
Patient global assessment, mean (SD)	65·1 (19·9)	63·9 (20·4)	64·5 (20·1)	62·8 (19·5)	60·1 (21·0)	61·4 (20·3)
HAQ-DI, mean (SD)	1·4 (0·6)	1·4 (0·6)	1·4 (0·6)	1·1 (0·6)	1·1 (0·6)	1·1 (0·6)
PsA pain (0-100), mean (SD)	60·3 (23·3)	60·0 (22·6)	60·2 (23·0)	56·7 (23·6)	56·2 (22·1)	56·4 (22·8)
Presence of enthesitis, n (%)	139 (63·8%)	133 (67·2%)	272 (65·4%)	95 (45·7%)	131 (57·2%)	226 (51·7%)
CRP >= 10 mg/L, n (%)	70 (32·1%)	52 (26·3%)	122 (29·3%)	61 (29·3%)	76 (33·2%)	137 (31·4%)

ADA, adalimumab; CRP,C-reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; n, number of available patients; N, total number of randomized patients; PsA, Psoriatic Arthritis; SD, standard deviation; SEC, secukinumab; SJC, Adjusted swollen joint total score for PsA 76 joints; TJC, adjusted tender joint total score for PsA 78 joints

Table 1. Baseline clinical characteristics

Endpoints, % response rate	Female			Male		
	SEC 300 mg, N = 218	ADA 40 mg, N = 198	*p-value	SEC 300 mg, N = 208	ADA 40 mg, N = 229	*p-value
ACR20	61·0	51·5	0·0496	74·0	70·2	0·3719
ACR50	43·0	32·6	0·0284	55·3	55·3	0·9521
[1]PASI90	64·0	37·6	0·0003	66·9	48·2	0·0050
HAQ-DI, >= 0·35	53·7	43·9	0·0487	56·1	57·9	0·6209
[2]Resolution of enthesitis (LEI)	52·1	46·5	0·3338	72·6	62·0	0·0637
MDA	36·2	24·2	0·0063	51·0	49·8	0·8886
DAPSA LDA+Remission	52·2	41·7	0·0382	71·6	63·1	0·1023
DAPSA Remission	20·7	12·0	0·0224	30·3	35·0	0·2282

*p-value are from a logistic regression model with treatment as a factor and baseline weight as a covariate; N, total number of randomized patients
[1]PASI reported only in patients with at least 3% body surface area affected with PsO at baseline. (N=102 and 94 females in SEC and ADA group, respectively; N = 113 and 108 males in SEC and ADA group, respectively)
[2]number of patients with enthesitis (LEI index) at baseline, (N=139 and 133 females in SEC and ADA group, respectively; N = 95 and 131 males in SEC and ADA group, respectively)
Patients who discontinued study treatment prematurely or took csDMARDs after week-36 were considered non-responders. Multiple imputation was used for all other missing data.

ACR, American College of Rheumatology; ADA, adalimumab; csDMARD, conventional synthetic disease modifying antirheumatic drugs; DAPSA, Disease Activity in Psoriatic Arthritis; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDA, Low Disease Activity; LEI, Leeds enthesitis index; MDA, Minimal Disease Activity; PASI, Psoriasis Area Severity Index; PsO, Psoriasis; SEC, secukinumab

Table 2. Efficacy outcomes by sex at Week 52

Disclosure: G. Wright, Exagen, 5, 8, AbbVie, 5, 8, Amgen, 5, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly and Company, 5, 8, Myriad Autoimmune, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Regeneron Pharmaceuticals, Inc., 5, 8, Sanofi Genzyme, 5, 8, UCB, 5, 8; **P. Nash**, AbbVie, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8; **L. Coates**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5; **J. Gratacós**, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, 8, MSD, 5, 8, UCB, 5, 8, Novartis, 5, 8, Janssen Pharmaceutical, 5, 8, Amgen, 5, 8, BMS, 2, 5, 8, Celgene, 2, 5, 8; **F. Behrens**, Pfizer, 2, 5, 8, Janssen, 2, 5, 8, Chugai, 2, 5, 8, Celgene, 2, 5, 8, Bionorica, 2, Roche, 2, 5, 8, Abbvie, 5, 8, Sanofi, 5, 8, Lilly, 5, 8, Novartis, 5, 8, Genzyme, 5, 8, Boehringer, 5, 8, MSD, 5, 8, Amgen, 5, 8, UCB, 5, 8, Gilead, 5, 8, Sandoz, 5, 8; **K. Ding**, Novartis, 3; **W. Bao**, Novartis, 1, 3; **L. Pricop**, Novartis, 1, 3; **C. Gaillez**, Novartis and BMS, 1, Novartis, 3; **I. McInnes**, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9.

Abstract Number: 0508

Maintenance or Achievement of Minimal Disease Activity Following Therapy Optimization with Adalimumab or Methotrexate in Patients with Psoriatic Arthritis: Results from Part 2 of a Randomized, Open-Label Phase 4 Study

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment I: Psoriatic Arthritis

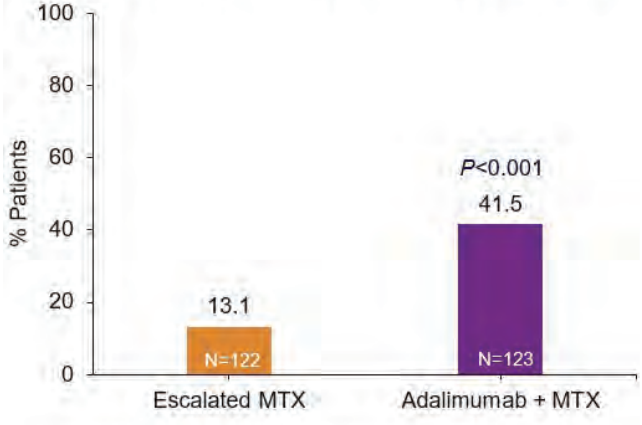
Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Minimal Disease Activity (MDA) is suggested as an appropriate treat-to-target outcome for patients (pts) with PsA. Results from Part 1 of the CONTROL study demonstrated that the introduction of adalimumab (ADA) after an initial course of MTX 15 mg resulted in significantly higher MDA rates at week (wk) 16 compared with escalating MTX dose (**Fig 1**).[1] Here we present results from Part 2 of the CONTROL study, in which therapy was either maintained or modified based upon MDA response at wk 16.

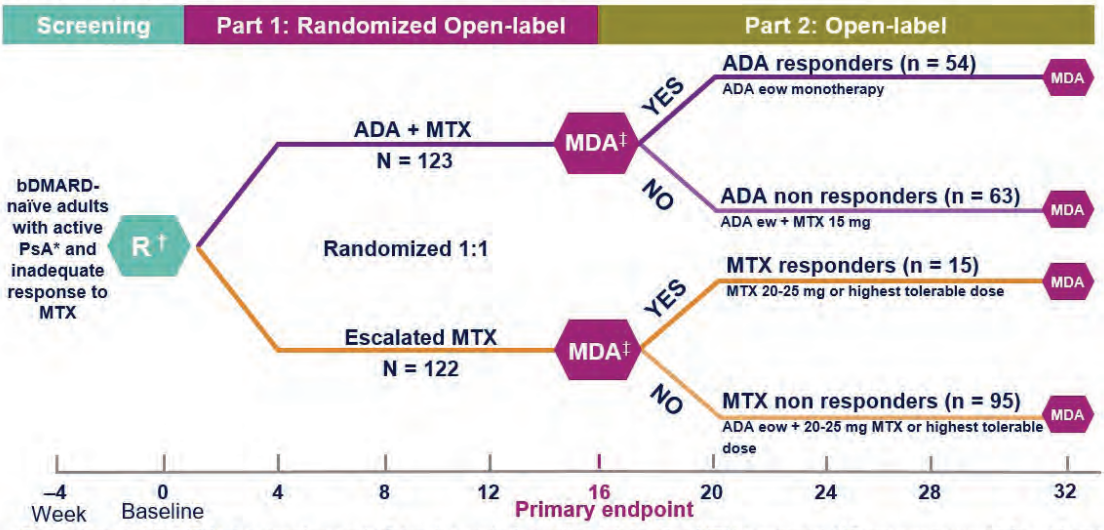
Methods: The open-label, 2-part CONTROL study enrolled bDMARD-naive adult pts with active PsA (not in MDA at screening and ≥3 tender and ≥3 swollen joints) despite MTX 15 mg every wk (ew) for ≥4 wks.[1] During Part 1, pts were randomized to ADA 40 mg every other wk (eow) + MTX 15 mg (ADA + MTX) or escalated MTX to 20–25 mg ew or highest tolerable dose for 16 wks (**Fig 2**). In Part 2 (wk 16 through 32), pts initially randomized to ADA + MTX who

Figure 1. MDA at Week 16 (Primary Endpoint)



MDA, minimal disease activity; MTX, methotrexate.

Figure 2. Study Design

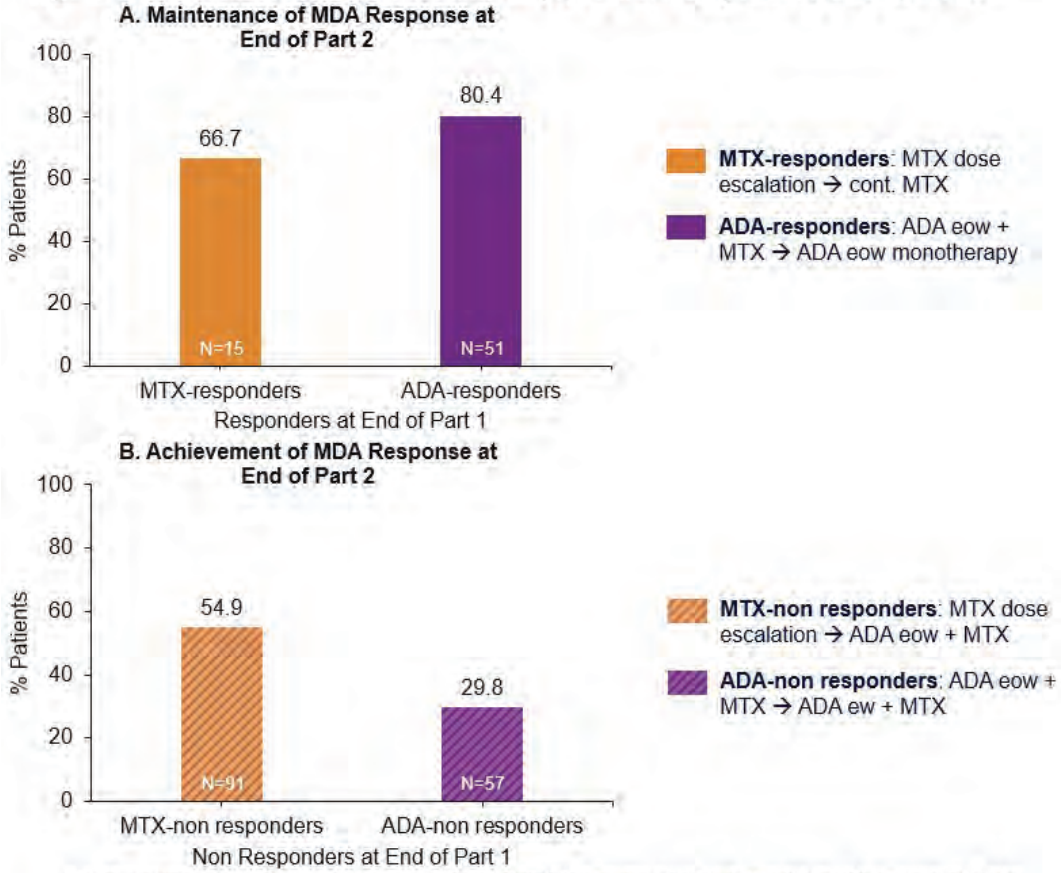


*Defined as not in MDA at screening and ≥3 tender and ≥3 swollen joints after MTX treatment (15 mg every week) for at least 4 weeks.
†Patients stratified by duration of prior MTX (MTX 15 mg/week for ≤3 months or >3 months).
‡Patients were assigned to treatment arms based on their MDA status.

ADA-responders: ADA eow + MTX → ADA eow monotherapy
ADA-non responders: ADA eow + MTX → ADA ew + MTX
MTX-responders: MTX dose escalation → cont. MTX
MTX-non responders: MTX dose escalation → ADA eow + MTX

ADA, adalimumab; bDMARD, biologic disease-modifying antirheumatic drug; eow, every other week; ew, every week; MDA, minimal disease activity; MTX, methotrexate; PsA, psoriatic arthritis.

Figure 3. Maintenance (A) or Achievement (B) of MDA Response at End of Part 2[a]



[a]MDA status was inaccurately identified by the investigator at wk 16 for 6 patients (MTX-responders, n=1; MTX-non responders, n=2; ADA-responders; n=3). Rescue therapy was available starting at wk 24; patients who were rescued were considered non responders for MDA analysis.
ADA, adalimumab; eow, every other week; ew, every week; MDA, minimal disease activity; MTX, methotrexate.

achieved MDA at wk 16 (ADA responders) discontinued MTX and continued ADA 40 mg eow as monotherapy; those initially randomized to ADA + MTX who did not achieve MDA (ADA-non responders) escalated therapy to ADA 40 mg ew + MTX 15 mg ew. For pts initially randomized to escalated MTX, if MDA was achieved at wk 16 (MTX responders), weekly MTX (20-25 mg or highest tolerable dose ew) was continued; if MDA was not achieved (MTX non-responders), pts were switched to ADA 40 mg eow + MTX 20-25 mg or highest tolerable dose ew. Data are reported as observed.

Results: At wk 16, 54 and 15 pts achieved MDA on ADA + MTX or escalated MTX (ADA responders and MTX responders, respectively) (**Fig 2**). There were 63 ADA-non responders and 95 MTX-non responders who did not achieve MDA at wk 16. In the responder groups, 80% of ADA responders were in MDA state at the end of Part 2 after switching from ADA + MTX to ADA monotherapy; whereas 67% of MTX responders were in MDA after maintaining their escalated MTX therapy during Part 2 (**Fig 3A**). Among MTX-non responders who switched from escalated MTX to ADA eow + MTX in Part 2, 55% achieved MDA at the end of Part 2 (**Fig 3B**). Thirty percent of ADA-non responders who did not respond to ADA eow + MTX in Part 1 were able to achieve MDA following escalation of therapy to ADA ew + MTX (**Fig 3B**). In Part 2, the proportion of pts with treatment-emergent adverse events (AE) was as follows: ADA responders: 44.4% (24/54); ADA-non responders: 66.7% (42/63); MTX responders: 33.3% (5/15); MTX-non responders: 56.8% (54/95). Serious AEs were reported infrequently (< 5%) across all groups. Two malignancies were reported: one each in the ADA responder and ADA-non responder groups. There were no opportunistic infections, tuberculosis, or deaths or new safety signals identified in Part 2.

Conclusion: Patients who achieved MDA response in Part 1 generally maintained efficacy through Part 2 despite a reduction in or maintenance of current therapy, with numerically higher proportions of patients achieving MDA response in ADA responders vs MTX responders at wk 32. For patients who did not achieve MDA after 16 wks in Part 1, modification of therapy by addition or escalation of ADA resulted in increased proportions of patients achieving MDA at the end of Part 2. The safety profile of ADA was consistent with the known safety profile.

Reference

1. Coates et al. *Ann Rheum Dis* 2020;79(s1):33

Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **P. Conaghan**, AbbVie, 1, 2, EMD Serono, 1, Flexion Therapeutics, 1, 2, Galapagos, 1, Gilead, 1, Novartis, 1, 2, Regeneron, 1, Samumed, 1, 2, GlaxoSmithKline, 5, Janssen, 5, Pfizer Inc, 5, Bristol-Myers Squibb, 2, Eli Lilly, 5; **W. Tillett**, AbbVie, 5, 8, Amgen, 5, 8, Eli Lilly, 5, 8, Janssen, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB Pharma, 5, 8; **M. D'Agostino**, AbbVie, 5, 8, Bristol Myers Squibb, 5, 8, Novartis, 5, 8, Roche, 5, 8; **P. Rahman**, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5; **F. Behrens**, Pfizer, 2, 5, 8, Janssen, 2, 5, 8, Chugai, 2, 5, 8, Celgene, 2, 5, 8, Bionorica, 2, Roche, 2, 5, 8, Abbvie, 5, 8, Sanofi, 5, 8, Lilly, 5, 8, Novartis, 5, 8, Genzyme, 5, 8, Boehringer, 5, 8, MSD, 5, 8, Amgen, 5, 8, UCB, 5, 8, Gilead, 5, 8, Sandoz, 5, 8; **E. Blondell**, AbbVie, 1, 3; **X. Bu**, AbbVie, 1, 3; **L. Chen**, AbbVie, 1, 3; **M. Kapoor**, AbbVie, 1, 3; **L. Coates**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5.

Abstract Number: 0509

Classification of Patients with Relapsing Polychondritis Based on Somatic Mutations in *UBA1*

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders I: GCA, Behçet's, & Relapsing Polychondritis

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Relapsing polychondritis (RP) is a rare, heterogenous, systemic inflammatory disease with a predilection for cartilaginous structures. Recently we discovered myeloid-restricted somatic mutations in *UBA1* in patients with a spectrum of adult-onset inflammatory diseases, and 60% of these patients were diagnosed with RP. Hematologic mosaicism for variants within a single residue of *UBA1* now defines a novel syndrome called VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory,somatic). The study objectives were to determine the prevalence of VEXAS in a cohort of patients with RP, to compare their clinical, laboratory, and immunologic features and to develop a clinical algorithm to inform genetic screening for VEXAS among patients with RP.

Methods: Patients that met diagnostic criteria for RP and were ≥18 years old were included. All patients were screened by whole-exome sequencing and *UBA1* variants of interest were confirmed by Sanger sequencing. To determine prevalence of VEXAS within RP, *UBA1* variants were tested in all patients enrolled in a large, prospective, observational cohort of RP. Additional patients with VEXAS were recruited from other cohorts and included in subsequent analyses. Immune populations were quantified by multipanel flow cytometry. Categorical and continuous variables were compared using the chi square or Kruskal-Wallis test. Random forest was used to create an algorithm to identify patients with VEXAS based on key clinical features. $P < 0.05$ defined statistical significance.

Results: Within a prospective cohort of 92 patients with RP, 7 patients were confirmed to have *UBA1* variants consistent with VEXAS (prevalence=8%). Six additional patients with VEXAS from other cohorts were included for subsequent analyses. Compared to RP, patients with VEXAS were all male, older at disease onset, and more likely to have fever, ear chondritis, periorbital edema, skin involvement, deep vein thrombosis, and pulmonary infiltrates. Patients with RP as compared with VEXAS had a significantly higher prevalence of airway chondritis, costochondritis, tenosynovitis/arthralgias, and vestibular symptoms (**Table**). Mortality was significantly greater in VEXAS than RP (27% vs 2% p=0.01). Maximum ESR, CRP, and mean corpuscular volume (MCV) values were significantly greater in VEXAS. Absolute monocyte, lymphocyte, and platelet counts were significantly lower in VEXAS. Reduction of B lymphocytes

Table 1. Clinical Characteristics of Patients with RP vs VEXAS

	All Patients n=98	RP n=85	VEXAS n=13	p value
Demographic Characteristics				
Race, White n (%)	90 (92)	77 (91)	13 (100)	0.59
Sex, Male n (%)	26 (27)	13 (15)	13 (100)	<0.0001
Age, Current visit, years, Median (IQR)	47 (38-57)	45 (36-55)	62 (56-70)	<0.0001
Disease Duration, years, Median (IQR)	8 (3.25-13)	8 (4-15)	4 (2-5)	0.0068
Age, Symptom onset, years, Median (IQR)	38 (30-47)	37 (28-43)	56 (54-64)	<0.0001
Clinical Symptoms				
Fever n (%)	33 (34)	20 (24)	13 (100)	<0.0001
Ear chondritis n (%)	61 (62)	48 (56)	13 (100)	0.0015
Nose chondritis n (%)	83 (85)	71 (84)	12 (92)	0.68
Airway chondritis n (%)	37 (38)	37 (44)	0 (0)	0.0015
Costochondritis n (%)	72 (73)	72 (85)	0 (0)	<0.0001
Tenosynovitis/arthalgias n (%)	83 (85)	77 (91)	6 (46)	0.0005
Vestibular symptoms n (%)	65 (68)	62 (73)	3 (27)	0.0044
Skin involvement n (%)	33 (34)	22 (26	11 (85)	<0.0001
Periorbital edema n (%)	6 (6)	2 (2)	4 (32)	0.0025
Laboratory Values				
ESR, mm/hr, median (IQR)	12 (6-22)	11 (5-19)	66.5 (42-110)	<0.0001
CRP, mg/L, median (IQR)	2.9 (0.8-9.6)	1.9 (0.6-6.3)	17.7 (9.6-99.5)	<0.0001
Platelet count (k/uL)	246(201-299)	258 (227-312)	145 (100-169)	<0.0001
Hemoglobin (g/dL)	13.2 (12-14)	13.4 (12-14)	10 (8-12)	<0.0001
MCV (fL)	93.05 (90-98)	92.2 (89-95)	105 (102-115)	<0.0001
Absolute lymphocyte count	1.6 (1.1-2.3)	1.78(1.4-2.4)	0.92 (0.5-1.2)	<0.0001
Absolute monocyte count	0.49 (0.3-0.6)	0.5(0.4-0.6)	0.26(0.1-0.3)	<0.0001
CT Scan Abnormalities				
Pulmonary infiltrates n (%)	16 (16.33)	6 (7.06)	10 (77)	<0.0001
Complications				
Death n (%)	6 (6)	3 (4)	3 (23)	0.029
ICU admission n (%)	20 (21)	16 (19)	4 (33)	0.24
Need for transfusion n (%)	6 (6)	0 (0)	6 (46)	<0.0001
Unprovoked DVT n (%)	12 (12)	4 (5)	8 (62)	<0.0001
Medications				
Prednisone dose, (mg), mean (IQR)	7.25 (0-20)	5 (0-20)	17.5 (5-30)	0.065
Prednisone n (%)	61 (63)	51 (60)	10 (91)	0.045
Number of steroid sparing agents ever, mean (IQR)	3 (2-4)	2 (2-4)	4 (3-7)	0.0043

N = number; IQR = interquartile range

and nonclassical monocytes (CD14-/CD16+) relative to healthy controls was observed in both RP and VEXAS, but was more marked in VEXAS. Increased Th17 cells was observed only in RP. A decision tree based on 1) Male sex or age at onset >50, 2) MCV >100 and 3) platelet count< 200 classified between VEXAS and RP with 100% sensitivity and 96% specificity.

Conclusion: Mutations in *UBA1* are causal for disease in 8% of patients with RP. These patients have unique clinical characteristics that readily distinguish them from other patients with RP. A screening algorithm based on four, easily measurable clinical variables differentiates between VEXAS and RP with near-perfect accuracy. Early disease detection and improved clinical management is important in VEXAS given the high rate of mortality in this genetic subset of RP.

Disclosure: M. Ferrada, None; **K. Sikora**, None; **S. Savic**, Novartis, 5, 8, SOBI, 2, 5, 8; **Y. Luo**, None; **K. Wells**, None; **E. Rose**, None; **K. Quinn**, None; **W. Goodspeed**, None; **A. Jones**, None; **M. Le**, None; **A. Ombrello**, None; **Z. Deng**, None; **M. Gadina**, None; **W. Tsai**, None; **I. Aksentijevich**, None; **D. Kastner**, None; **D. Beck**, None; **P. Grayson**, None.

Abstract Number: 0510

Expression and Functional Activity of the Angiotensin II System in Temporal Artery Lesions from Patients with Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders I: GCA, Behçet's, & Relapsing Polychondritis

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Giant cell arteritis (GCA) is a large and medium size-vessel granulomatous vasculitis that predominantly affects the aorta and its major branches. The renin-angiotensin-aldosterone system (RAAS) is a multiple-step cascade of vasoactive peptides that plays a major role in the regulation of blood pressure and electrolyte balance. Angiotensin II (ATII), the major effector molecule of the RAAS, has emerged as a powerful pro-inflammatory peptide and pharmacological blockade of this system results in anti-inflammatory effects. In this line, a previous observational study suggested that treatment with angiotensin II blockers (ARB) was associated with lower relapse rate and glucocorticoid (GC)-sparing effect in patients with GCA (Alba MA, Semin Arthritis Rheum. 2014). Our objective was to investigate the expression and functional activity of the ATII system in GCA temporal arteries (TA).

Methods: 40 involved TA from patients with GCA and 18 normal arteries from controls were included. Angiotensinogen (AGT), angiotensin-converting enzyme (ACE), ATII receptor 1 (ATR1), and counter-regulatory ACE2 expression was investigated by quantitative real-time PCR in TA. Distribution of ATII system components was assessed by confocal microscopy. The effect of ATII and ATR1-blockade on pro-inflammatory cytokine production was investigated in a co-culture system of peripheral blood mononuclear cells (PBMC) and TA-derived vascular smooth muscle cells (VSMC). In addition, modulation of the ATII system by GC was addressed using an *ex vivo* model of cultured TA.

Results: A local ATII system, mainly characterized by constitutive expression of ATG, overexpression ACE mRNA transcripts and a down-regulation of ACE2 was identified in GCA inflamed arteries (figure 1). By confocal microscopy, ATII, ACE, and ATR1 expression was identified to be qualitatively higher in GCA sections in comparison with a control TA. The local ATII system appears to require multi-cellular cooperation as VSMC were the main cells expressing ATII and ATR1 while ACE was predominantly expressed by inflammatory infiltrating cells. *In vitro*, ATII was able to induce a pro-inflammatory phenotype in PBMC and co-cultured VSMC: IL-1β, IL-6, TNF-α, CCL-2, ICAM-1, and VCAM-1 mRNA expression measured by real-time quantitative PCR was increased in PBMC whereas IL-1β, IL-6, CCL-2, ICAM-1, and VCAM transcripts increased in VSMC co-cultured with PBMC. Losartan, an ARB, was able to reverse

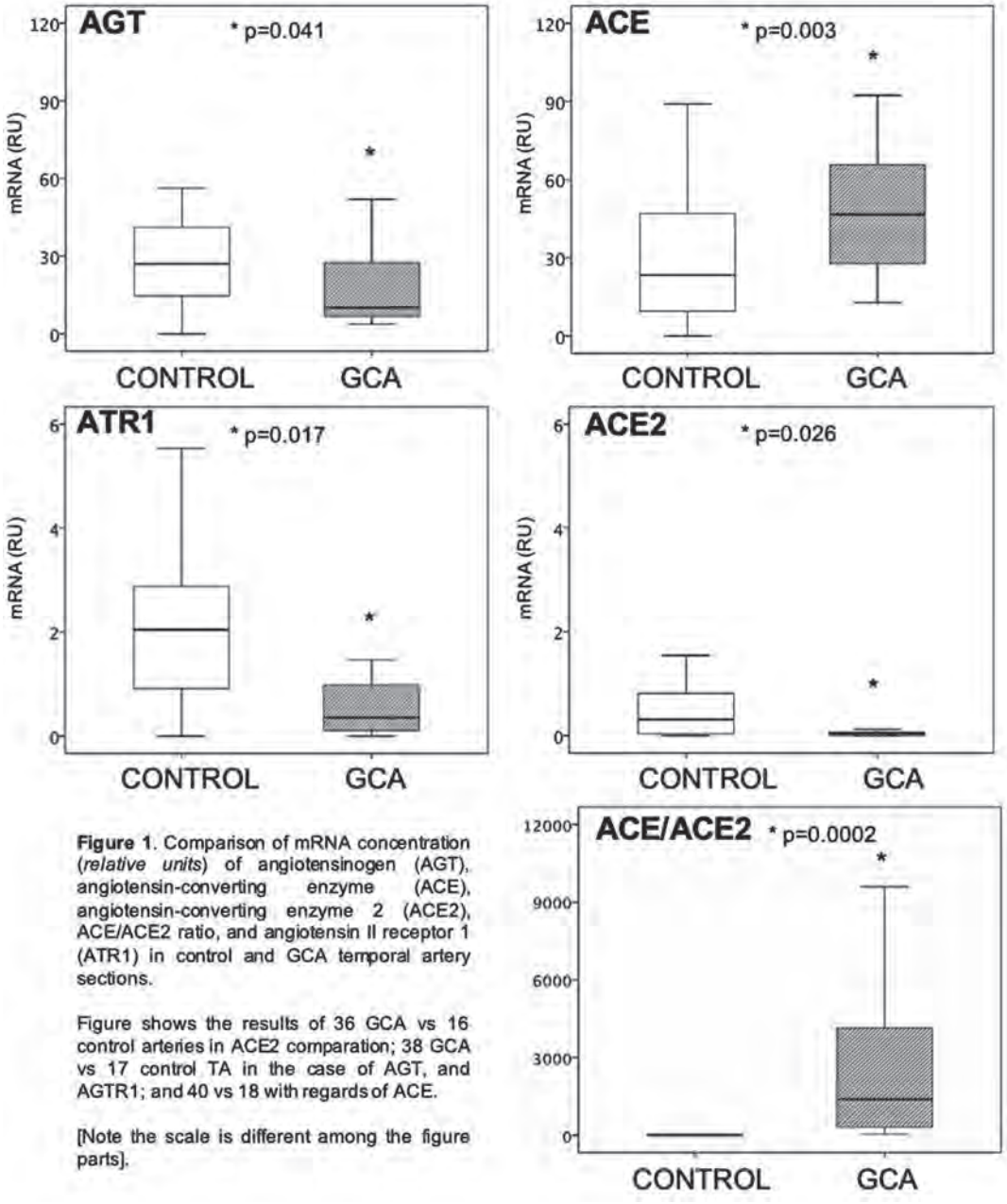

Figure 1. Comparison of mRNA concentration (*relative units*) of angiotensinogen (AGT), angiotensin-converting enzyme (ACE), angiotensin-converting enzyme 2 (ACE2), ACE/ACE2 ratio, and angiotensin II receptor 1 (ATR1) in control and GCA temporal artery sections.

Figure shows the results of 36 GCA vs 16 control arteries in ACE2 comparation; 38 GCA vs 17 control TA in the case of AGT, and AGTR1; and 40 vs 18 with regards of ACE.

[Note the scale is different among the figure parts].

these changes and interestingly, it reduced basal expression of IFN-γ, CCL-2, ICAM-1, and VCAM-1 in PBMC. Finally, we observed that dexamethasone was able to modulate the expression of the ATII system by reducing ACE gene expression and increasing ATR1 and ACE2 in an *ex-vivo* model of cultured temporal arteries.

Conclusion: Our findings suggest that the ATII system may play a role in vascular inflammatory lesions of GCA. Thus, interference of the RAAS system may be a potential adjunctive therapeutic option for patients with GCA.

MA Alba and E Planas-Rigol contributed equally to this study. Supported by Ministerio de Economía y Competitividad (SAF 2017/88275-R). MA Alba was supported by BITRECS.

Disclosure: M. Alba, None; **E. Planas-Rigol**, None; **M. Corbera-Bellalta**, None; **N. Terrades-García**, None; **A. García-Martínez**, None; **S. Prieto-González**, None; **R. Alba-Rovira**, None; **G. Espígol-Frigolé**, None; **J. Marco-Hernández**, None; **J. Hernández-Rodríguez**, None; **J. Grau**, None; **M. Cid**, Kiniksa, 2.

Abstract Number: 0511

ERAP1-mediated Immunogenicity and Immune-phenotypes in HLA-B51+ Behçet's Disease Point to Pathogenic CD8 T Cell Effector Responses

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders I: GCA, Behçet's, & Relapsing Polychondritis

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: HLA-B51 is a definite risk factor for Behçet's disease (BD). A coding variant of ERAP1, Hap10 – with low peptide-trimming activity – vastly potentiates this risk, but is mechanistically unclear. Here, we aimed to test the hypothesis that low or absent ERAP1 activity alters CD8 T cell immunogenicity through changes in the HLA-B51 peptidome and shapes the CD8 T cell immune response in affected subjects.

Methods: We generated HLA-B51^{+}ERAP1 KO LCL clones using CRISPR-Cas9, performed mass spectrometry of the immunoprecipitated MHC-class I peptidome with subsequent computational deconvolution for HLA-B51-binding peptides. We then assessed single cell (ICS), bulk (ELISA) and proliferative (CFSE) CD8 effector (IFNG, granzyme-B, perforin) T cell responses through stimulation of allogeneic donor cells with WT vs KO LCL and determined ERAP1 haplotypes in 49 untreated Turkish BD subjects with ocular and/ or vascular involvement as well as healthy donors (HD) whose PBMC were profiled using 6 multicolor flow cytometry panels.

Results: WT and KO peptidomes differed significantly ($p< 0.0005$ Fisher's exact test) with a distinct shift of peptide length frequencies exceeding 9-mer (binding optimum) in the KO vs WT. This held true for computationally deconvoluted HLA-B51 binders. IFNG secretion from CD8 T cells stimulated with KO LCL was significantly different from WT (ICS, $p=0.0006$; ELISA, $p=0.0059$) as were CD8 T cell proliferation and ICS of perforin/ granzyme-B^{+} CD8 T cells. Analysis of 133 T, B, NK, and monocyte cell populations revealed a predominance of CD8 T and NKT cell subset in HLA-B51+/Hap10+ BD vs HLA-B51+/Hap10- BD and HD, accounting for 80% of all populations reaching significance ($p< 0.05$, Mann-Whitney). Naive and effector memory CD8 T cell subsets were inversely correlated. Cohen's effect sizes were large (>0.8) or very large (>1.2).

Conclusion: We show that the absence of functional ERAP1 alters human CD8 T cell immunogenicity. This is mediated by an HLA-class I peptidome with a propensity for longer peptides above 9mer and suggests a loss or de-novo presentation of peptide-HLA-B51 complexes to cognate CD8 TCR. The reciprocal changes in antigen-experienced vs naive CD8 T cell subsets in affected subjects point to the biologic significance of HLA-B51/Hap10 in BD. Collectively, our findings suggest that an altered HLA-B51 peptidome modulates the immunogenicity of CD8 effector T cells in ERAP1-Hap10 carriers with BD and identifies targets for future drug development.

Disclosure: A. Cavers, None; **Y. Ozguler**, None; **O. Manches**, None; **A. Al-Obeidi**, None; **H. Zhong**, None; **B. Ueberheide**, None; **G. Hatemi**, BMS, 1, Celgene Corporation, 1, Silk Road Therapeutics, 1, AbbVie, 1, Mustafa Nevzat, 1, Novartis, 1, UCB, 1, Bayer, 1, Eli Lilly, 1; **M. Kugler**, None; **J. Nowatzky**, None.

Abstract Number: 0512

Efficacy of Apremilast for the Treatment of Manifestations of Behçet's Syndrome Other Than Oral Ulcers, Including Skin Lesions and Arthritis

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SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders I: GCA, Behçet's, & Relapsing Polychondritis

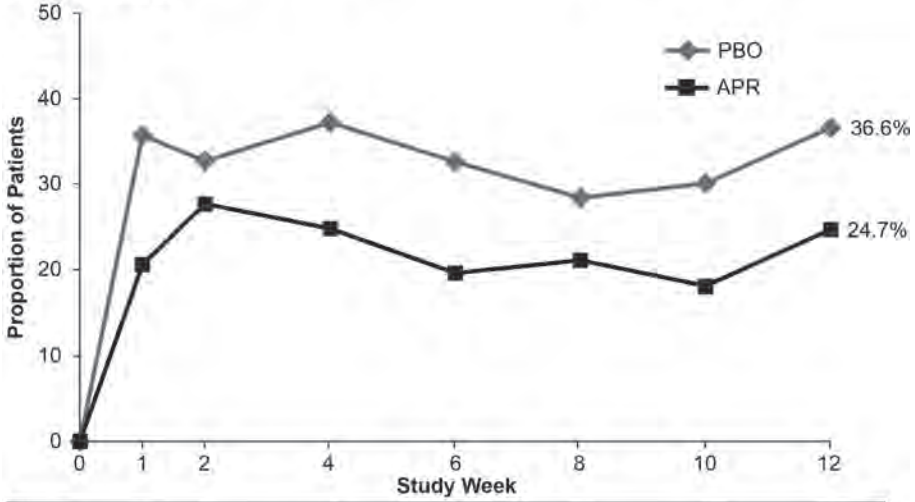
Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Behçet's syndrome is a chronic, multi-system inflammatory disorder characterized by painful and recurrent oral ulcers (OU) and other manifestations, such as skin lesions and arthritis, that have a significant impact on quality of life (Hatemi G. *Ann Rheum Dis*. 2018;77:808-818). Apremilast, an oral phosphodiesterase 4 inhibitor, demonstrated efficacy in the treatment of OU in the phase 3 RELIEF study (Hatemi G, et al. *N Engl J Med*. 2019;381:1918-1928). We describe outcomes for non-OU manifestations of Behçet's syndrome in patients (pts) treated with apremilast (APR) 30 mg BID vs placebo (PBO) in RELIEF.

Methods: RELIEF was a multicenter, randomized, double-blind, PBO-controlled study (BCT-002; NCT02307513). Eligible pts were adults with active Behçet's syndrome and ≥3 OU at randomization or ≥2 OU at screening and randomization, without active major organ involvement. Pts were randomized (1:1) to receive APR or PBO up to Week 12 and stratified by region (Japan/other). The proportions of pts with ≥1 new, recurrent, or worsening non-OU manifestations

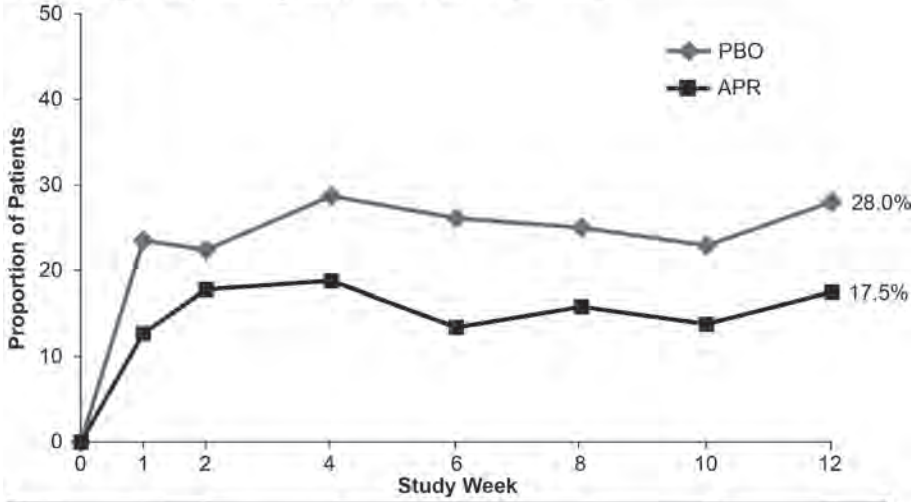
Figure 1. Proportion of Patients in the Overall Population With ≥1 New, Recurrent, or Worsening Behçet's Syndrome Non-OU Manifestations* From Baseline



Weeks	1	2	4	6	8	10	12
PBO, n	98	98	94	92	88	83	82
APR, n	102	101	101	97	95	94	97

Intent-to-treat population. Data as observed. *Skin lesions, arthritis, uveitis, and gastrointestinal, central nervous system, or vascular manifestations. n = number of patients.

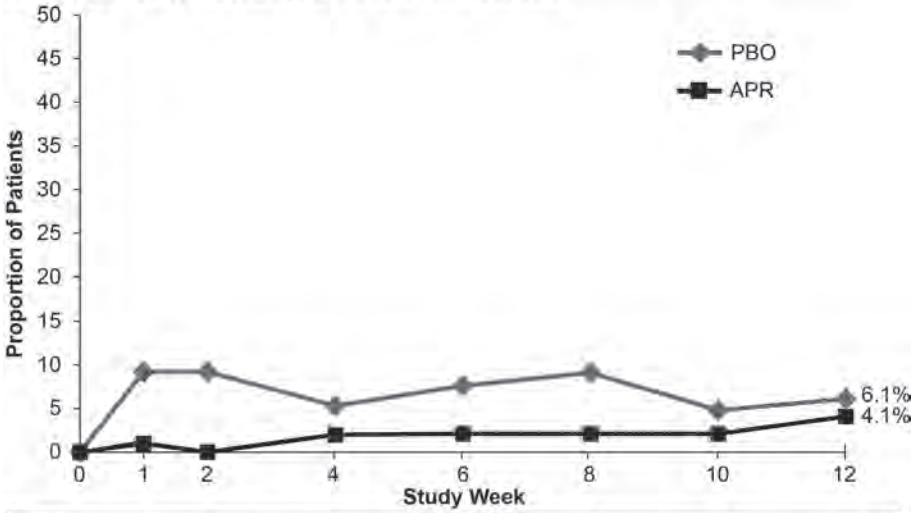
Figure 2. Proportion of Patients in the Overall Population With ≥1 New, Recurrent, or Worsening Skin Lesion From Baseline



Weeks	1	2	4	6	8	10	12
PBO, n	98	98	94	92	88	83	82
APR, n	102	101	101	97	95	94	97

Intent-to-treat population. Data as observed. n = number of patients.

Figure 3. Proportion of Patients in the Overall Population With ≥1 New, Recurrent, or Worsening Arthritis From Baseline



Weeks	1	2	4	6	8	10	12
PBO, n	98	98	94	92	88	83	82
APR, n	102	101	101	97	95	94	97

Intent-to-treat population. Data as observed. n = number of patients.

(ie, skin lesions, arthritis, uveitis, and gastrointestinal, CNS, or vascular manifestations) were assessed up to Week 12 in the overall population and in a Japanese subgroup. Change from baseline (BL) at Week 12 in scores on the Physician's Global Assessment (PGA) of skin lesions, swollen joint count (SJC), and tender joint count (TJC) in pts with skin lesions, SJC >0, and TJC >0 at BL, respectively, were assessed in the overall and Japanese subgroup populations.

Results: A total of 207 pts were randomized and received ≥1 dose of study medication in the overall population (APR: n=104; PBO: n=103), including 39 pts in the Japanese subgroup (APR: n=19; PBO: n=20). During the 12-week PBO-controlled period, the proportions of pts with ≥1 new, recurrent, or worsening non-OU manifestations (Figure 1), skin lesions (Figure 2), or arthritis (Figure 3) were lower in pts treated with APR vs PBO in the overall population. In

the Japanese subgroup, lower proportions of pts in the APR vs PBO group had new, recurrent, or worsening non-OU manifestations (5.9% [1/17] vs 31.3% [5/16]), skin lesions (5.9% [1/17]) vs 18.8% [3/16]), and arthritis (0.0% [0/17] vs 6.3% [1/16]) at Week 12. In the overall population treated with APR vs PBO, mean (SD) BL values were 3.4 (3.1) vs 5.7 (7.1) for SJC and 6.5 (8.5) vs 6.0 (8.0) for TJC; LS mean (95% CI) changes from BL at Week 12 were –0.9 (–1.1, –0.6) vs –0.8 (–1.0, –0.5) for PGA of skin lesions, –3.1 (–5.2, –1.0) vs –2.9 (–5.0, –0.8) for SJC, and –4.4 (–6.3, –2.4) vs –2.7 (–4.5, –0.9) for TJC. In the Japanese subgroup treated with APR vs PBO, mean (SD) BL values were 1.5 (0.7) vs 3.7 (3.8) for SJC and 6.4 (10.5) vs 4.3 (4.8) for TJC; LS mean (95% CI) changes from BL at Week 12 were –0.7 (–1.4, –0.1) vs –0.5 (–1.1, 0.2) for PGA of skin lesions, –3.0 (–9.6, 3.6) vs –2.3 (–8.6, 4.0) for SJC, and –3.7 (–6.1, –1.2) vs –2.4 (–4.4, –0.5) for TJC.

Conclusion: Pts with active Behçet's syndrome in the overall population and the Japanese subgroup of RELIEF achieved lower rates of new, recurrent, or worsening non-OU manifestations, including skin lesions and arthritis, and numerically greater improvements in PGA of skin lesions, SJC, and TJC with APR vs PBO over 12 weeks.

Disclosure: G. Hatemi, BMS, 1, Celgene Corporation, 1, Silk Road Therapeutics, 1, AbbVie, 1, Mustafa Nevzat, 1, Novartis, 1, UCB, 1, Bayer, 1, Eli Lilly, 1; **A. Mahr**, Roche, 1, Chugai, 1; **M. Takeno**, Celgene Corporation, 1, Esai, 1, Tanabe-Mitsubishi, 1; **D. Kim**, None; **M. Melikoğlu**, None; **S. Cheng**, Amgen Inc., 1; **S. Richter**, Amgen Inc., 1; **M. Brunori**, Amgen Europe GmbH, 1; **M. Paris**, Amgen Inc., 1; **M. Chen**, Amgen Inc., 1; **Y. Yazici**, BMS, 1, Celgene Corporation, 1, Genentech, 1, Sanofi, 1.

Abstract Number: 0513

Mass Spectrometry Identifies Novel Biomarkers in Giant Cell Arteritis, Useful in Patients on Interleukin-6 Receptor Blockade

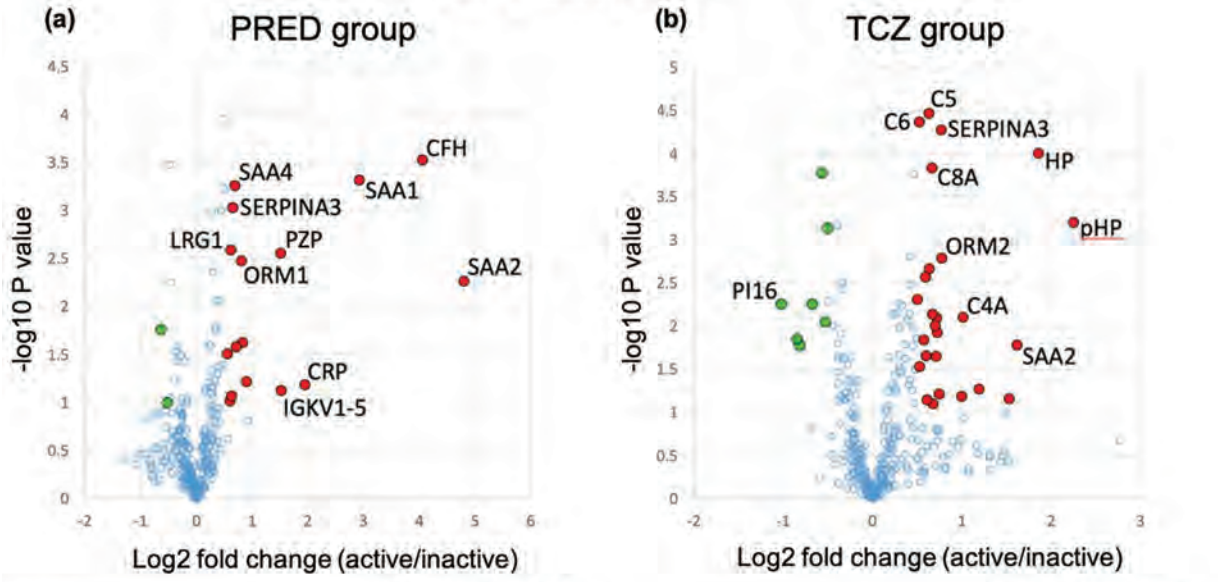
Sebastian Unizony[1], Robert Morris[2], Johannes Kreuzer[2], Wilhelm Haas[2] and John H. Stone[1], [1]Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA, [2]Massachusetts General Hospital, Boston, MA

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders I: GCA, Behçet's, & Relapsing Polychondritis
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: We aimed to identify biomarkers of disease activity in giant cell arteritis (GCA) patients treated with prednisone monotherapy and with prednisone in combination with tocilizumab (TCZ)

Methods: We mapped the serum proteome of GCA patients with active and inactive disease in an unbiased manner using high-throughput multiplexed mass spectrometry. Proteomic analyses were performed in 5 µl serum samples with 11-plexed tandem mass tag (TMT) technology using an Orbitrap Lumos mass spectrometer. A SEQUEST-based database search engine was employed for peptide identification. Quantification was based on TMT reporter ion intensities. All patients were sampled during their participation in the GiACTA trial,[1] in which they received TCZ plus 26 weeks of prednisone (TCZ group) or placebo plus 26 or 52 weeks of prednisone (PRED group). Active disease was defined as the presence of cranial or PMR symptoms requiring treatment intensification regardless of ESR and CRP levels. Samples were selected if patients were in clear states of active or inactive disease at GiACTA systematic sample collection timepoints (baseline and weeks 4, 12, 24, 48). An exhaustive leave-2-out strategy was used to identify classification markers. Proteins with an absolute log2 fold concentration difference ≥0.5 between active and inactive samples and a P-value < 0.1 were retained and sorted based on the metric -log10(P-value)*absolute(log2

Figure 1. Differentially expressed serum proteins in giant cell arteritis patients with active and inactive disease

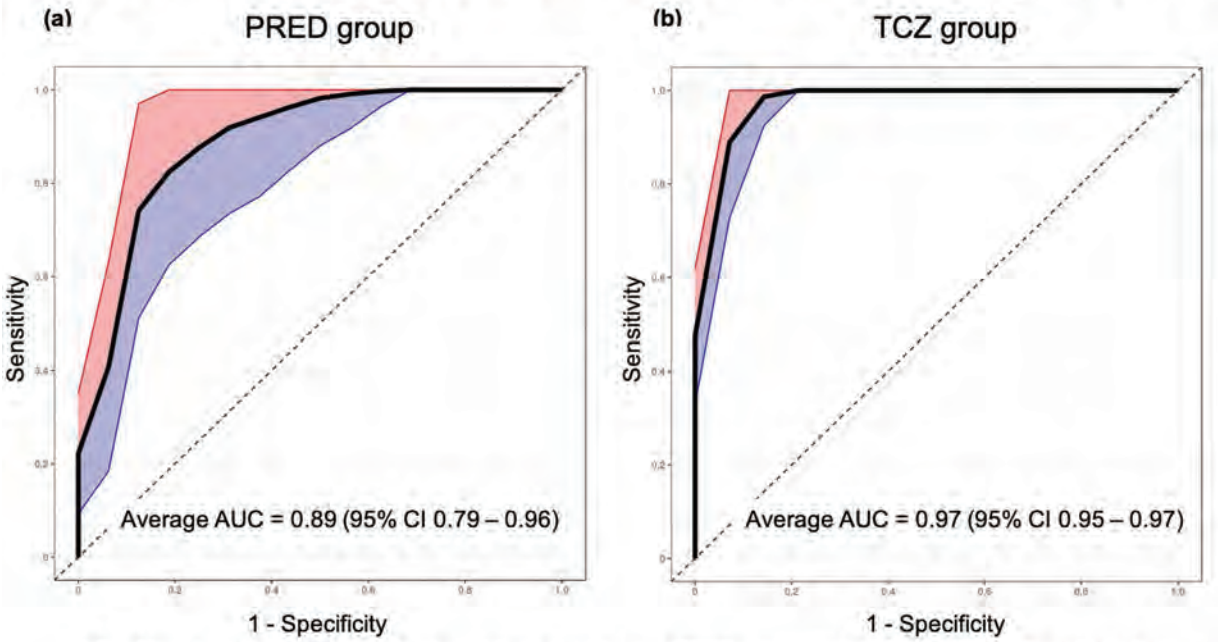


	log2 fold change	P-value
Serum amyloid A2 (SAA2)	4.8	0.0054
Complement factor H (CFH)	4.1	0.0003
Serum amyloid A1 (SAA1)	2.9	0.0005
C-reactive protein (CRP)	2	0.0650
Pregnancy zone protein (PZP)	1.5	0.0028
Immunoglobulin Kappa Variable 1-5 (IGKV1-5)	1.5	0.0746
Alpha-1-acid glycoprotein 1 (ORM1)	0.8	0.0033
Serum amyloid A4 (SAA4)	0.7	0.0005
Alpha 1-antichymotrypsin (SERPINA3)	0.7	0.0009
Leucine-rich alpha-2-glycoprotein 1 (LRG1)	0.6	0.0026

	log2 fold change	P-value
Haptoglobin precursor (pHP)	2.3	0.0006
Haptoglobin (HP)	1.9	0.0001
Serum amyloid A2 (SAA2)	1.6	0.0165
Complement factor 4A (C4A)	1	0.0079
Alpha-1-acid glycoprotein 2 (ORM2)	0.8	0.0016
Alpha 1-antichymotrypsin (SERPINA3)	0.8	0.0001
Complement factor 8A (C8A)	0.7	0.0001
Complement factor 5 (C5)	0.6	<0.0001
Complement factor 6 (C6)	0.5	<0.0001
Peptidase Inhibitor 16 (PI16)	-1	0.0055

(a) Top 10 markers in patients treated with prednisone monotherapy (PRED group); (b) top 10 markers in patients treated with tocilizumab and prednisone (TCZ group)

Figure 2. Accuracy of top biomarkers for discrimination between active and inactive giant cell arteritis



(a) Top 10 markers in patients treated with prednisone monotherapy (PRED group); (b) top 10 markers in patients treated with tocilizumab and prednisone (TCZ group)

fold change). The accuracy of the top 10 biomarkers for classification of active versus inactive disease in each group was evaluated by determining areas under the curves (AUC) of receiver operator characteristic (ROC) curves.

Results: The PRED group included 21 patients (active, n = 16; inactive, n = 5) and the TCZ group included 21 patients (active, n = 14; inactive, n = 7). Compared to inactive PRED-treated patients, active PRED-treated patients showed significant overexpression of several acute phase reactants including serum amyloid A1 and 2 (SAA1, SAA2) and complement factor H (CFH) (**Fig. 1a**). The magnitude of concentration change and the level of statistical significance observed for SSA1, SSA2 and CFH in PRED-treated patients were higher than those of CRP (**Fig. 1a**). Compared to inactive TCZ-treated patients, active TCZ-treated patients demonstrated significant overexpression of multiple biomarkers including haptoglobin, haptoglobin precursor, SSA2 and complement factor 4A, and underexpression of peptidase inhibitor 16 (**Fig. 1b**), a protein involved in vascular and regulatory T cell biology. Sets of 10 biomarkers resulted in a classification of active versus inactive disease with ROC AUCs of 0.89 (95% CI 0.79-0.96) in the PRED group (**Fig. 2a**) and 0.97 (95% CI 0.95-0.97) in the TCZ group (**Fig. 2b**).

Conclusion: We identified several differentially expressed serum proteins in GCA patients with active and inactive disease receiving prednisone monotherapy or TCZ-based treatment regimens. In both treatment groups, a signature of biomarkers classified disease activity status with high accuracy. Haptoglobin, a readily available laboratory test, may be useful in monitoring disease activity in GCA patients receiving IL-6 blockade therapy.

Disclosure: S. Unizony, Genentech, Inc., 2; **R. Morris**, None; **J. Kreuzer**, None; **W. Haas**, None; **J. Stone**, Roche, 2, 5, Genentech, 2, 5.

Abstract Number: 0514

Feasibility of 18F-fluorodeoxyglucose Positron Emission Tomography to Monitor the Effect of Tocilizumab on Vascular Inflammation in Giant Cell Arteritis: A Prospective Observational Cohort Study

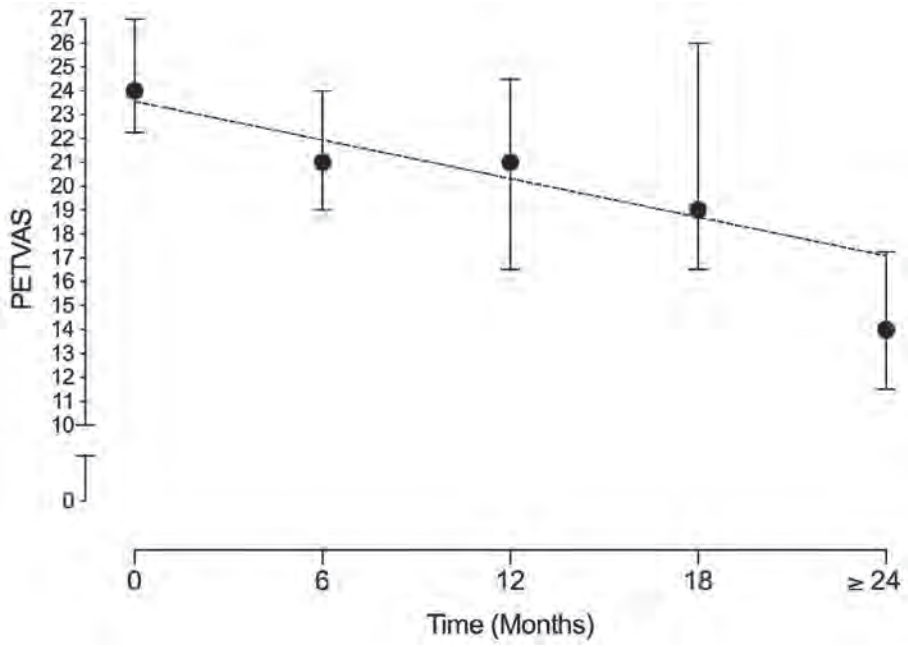
Kaitlin Quinn[1], Himanshu Dashora[2], Mark Ahlman[3], Elaine Novakovich[2] and Peter C. Grayson[2], [1]Systemic Autoimmunity Branch, National Institutes of Health, NIAMS, Bethesda, [2]Systemic Autoimmunity Branch, National Institutes of Health, NIAMS, Bethesda, MD, [3]National Institutes of Health, Clinical Center, Radiology and Imaging Sciences, Bethesda, MD

SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders II: GCA Clinical & Epidemiology
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Two randomized controlled trials have demonstrated the clinical efficacy of tocilizumab for treatment of giant cell arteritis (GCA) (1,2). In these trials, response to treatment was defined by improvement in clinical and laboratory-based assessment of disease activity, but direct assessment of the large arteries by vascular imaging was not systematically evaluated.

The objective of this study was to evaluate the longitudinal effects of tocilizumab on vascular inflammation as measured by ^{18}F-fluorodeoxyglucose positron emission tomography (FDG-PET) in giant cell arteritis (GCA).

Methods: Patients with GCA treated with tocilizumab were selected from an ongoing prospective, observational cohort. All patients fulfilled modified 1990 American College of Rheumatology (ACR) Classification Criteria for GCA.



Patients underwent FDG-PET computed tomography (CT) at the baseline visit prior to the initiation of tocilizumab and at subsequent follow-up visits. In a subset of patients in whom tocilizumab was discontinued due to established remission, a repeat FDG-PET scan was obtained after therapy discontinuation.

A single reader reviewed all PET scans, blinded to clinical data. Qualitative assessment of FDG uptake relative to liver uptake by visual assessment (scale 0-3) was assessed in 9 arterial territories. A summary score, PET Vascular Activity Score (PETVAS), was calculated (scale 0-27).

Wilcoxon signed rank test was used to compare change in PETVAS between study visits. Linear regression was used to determine change in PETVAS over multiple timepoints.

Results: Twenty-five patients with GCA were included. All patients had clinically active disease with associated active vasculitis by FDG-PET imaging at the baseline visit. PETVAS was significantly reduced in association with tocilizumab treatment from the baseline to the most recent follow-up visit [24.0 (IQR 22.3-27.0) vs. 18.5 (IQR 15.3-23.8); $p< 0.01$]. A significant reduction in PETVAS was observed over a two-year treatment period ($p< 0.01$ for linear trend), with a similar degree of improvement in both the first and the second years of treatment (Figure).

In a subset of six patients who discontinued tocilizumab due to established remission [median PETVAS 18.5 (16.5-21.0) at time of remission], a repeat FDG-PET scan at least 6 months after treatment discontinuation showed worsening PET activity in 5 out of 6 patients [median PETVAS 21.5 (17.3-23.0)]. Two of these patients subsequently experienced a clinical relapse.

Conclusion: Treatment of patients with GCA with tocilizumab was associated with both clinical improvement and reduction of vascular inflammation as measured by serial FDG-PET. There was continued improvement of vascular inflammation at both year 1 and year 2 of treatment, and this preliminary evidence suggests a rebound of vascular inflammation when tocilizumab was discontinued. These data support the use of FDG-PET as a novel outcome measure in clinical trials in GCA.

References

1. Stone JH, et al. N Engl J Med 2017;377:317-28.
2. Villiger PM, et al. Lancet 2016;387:1921-7.

Disclosure: K. Quinn, None; **H. Dashora**, None; **M. Ahlman**, None; **E. Novakovich**, None; **P. Grayson**, None.

Abstract Number: 0515

A Proof of Concept Study to Assess the Efficacy of Tocilizumab in Combination with Ultra-Short Glucocorticoid Administration to Treat Newly Diagnosed Giant Cell Arteritis – a 24 Week Analysis

Lisa Christ[1], Luca Seitz[1], Lukas Buetikofer[2], Godehard Scholz[1], Adela-Cristina Sarbu[1], Jennifer Amsler[1], Florian Kollert[1], Stephan Reichenbach[1] and Peter Villiger[1], [1]Department of Rheumatology, Immunology and Allergology, University of Bern, Inselspital, Switzerland, Bern, Switzerland, [2]Clinical Trials Unit, University of Bern, Bern, Switzerland, Bern, Switzerland

SESSION INFORMATION

Session Date: Friday, November 6, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders II: GCA Clinical & Epidemiology

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: Two randomized controlled trials [Villiger et al. Lancet 2016; Stone et al. NEJM 2017] demonstrated a glucocorticoid (GC)-sparing effect of tocilizumab (TCZ) of at least 50%. The GUSTO (GCA treatment with Ultra-Short GC and TCZ) trial was set up to unravel the efficacy and safety of TCZ-monotherapy after ultra-short GC treatment in new-onset GCA. Data up to week 24 are presented.

Methods: In this investigator-initiated, single-arm, single-center, open-label clinical trial with Simon's two stage design, 18 patients with newly diagnosed GCA were enrolled (NCT03745586). Patients received 500mg methylprednisolone intravenously for three consecutive days. Thereafter, GC treatment was discontinued and TCZ (8mg/kg body-weight) was administered intravenously, followed by weekly subcutaneous TCZ injections (162mg) from day 10 until week 52. The primary endpoints included the proportion of patients (i) achieving remission within 31 days and (ii) without relapse at week 24. Remission was defined as disappearance of GCA symptoms; partial remission included the presence of mild symptoms (defined as non-ischemic with NRS < 5/10, reported as mild, not occurring on most days of the week). An interim analysis of the primary endpoint was performed after the first 12 patients reached the primary endpoint, analysis of the 24-week outcome after all patients reached 24 weeks.

Results: Baseline characteristics include 12/18 female patients with a median age of 72 (range 64-78) years, 11/18 with median 1 (range 1-7) day of prior GC-treatment, 15/18 with cranial symptoms (10/18 with jaw claudication, 6/18 with visual involvement), 10/18 with PMR-symptoms, 16/18 with positive cranial ultrasound, 14/18 with aortitis on MRI, 14/18 with vasculitis on cranial MRI and 13/18 with GCA-findings in temporal biopsy.

At the interim analysis, 3/12 patients achieved remission at 31 days and stayed relapse-free until week 24 (25%, 95% confidence interval (CI) 5-57%), i.e. less than necessary to continue to the second stage. We could therefore not reject the null hypothesis that the proportion of responders is smaller than 40% (p=0.92). 11/12 patients achieved remission within 24 weeks after a mean of 74 days (95% CI 50-98) and 10 stayed relapse-free up to 24 weeks (83%, 95% CI 52-98%).

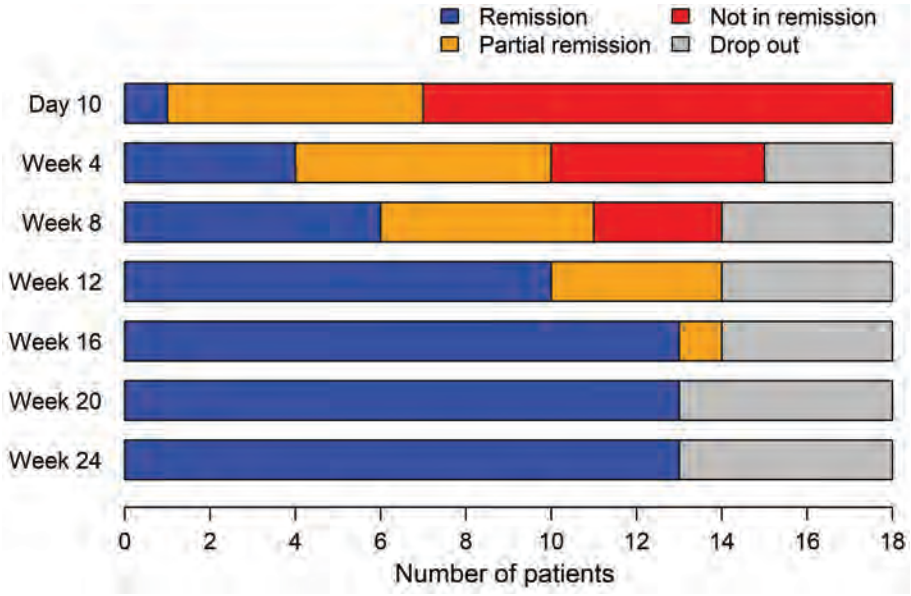


Figure 1. Disease status of patients at each visit (Day 0 - week 24, n=18).

Of the 18 patients recruited up to the time point of the interim analysis, 14 achieved remission within 24 weeks after a mean of 78 days (95% CI 58-97) and 13 stayed relapse-free up to 24 weeks (72%, 95% CI 47-90%).

3/18 patients (17%) were non-responders and started on rescue GC-treatment (2/3 with persistent cranial symptoms including one new-onset anterior ischemic optic neuropathy (AION); 1/3 with persistent PMR symptoms), 2/18 (11%) discontinued the study due to an adverse event (hepatopathy and diverticulitis, respectively; 1/2 after induction of remission). Figure 1 demonstrates remission status over time.

Conclusion: After a 3-days pulse of methylprednisolone, ensuing TCZ monotherapy induced and maintained remission until week 24 in 13/18 patients. Although the primary end-point was not met, the data add an important piece of evidence regarding the potency of blocking the IL-6 pathway in GCA.

Disclosure: L. Christ, None; **L. Seitz**, None; **L. Buetikofer**, None; **G. Scholz**, None; **A. Sarbu**, None; **J. Amsler**, None; **F. Kollert**, None; **S. Reichenbach**, None; **P. Villiger**, None.

Abstract Number: 0516

Characteristics of Giant Cell Arteritis Flares After Successful Treatment with Tocilizumab: Results from the Long-Term Extension of a Randomized Controlled Phase 3 Trial

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders II: GCA Clinical & Epidemiology
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: To investigate the characteristics of disease flare after successful treatment with tocilizumab (TCZ) in patients with giant cell arteritis (GCA).

Methods: We performed a post hoc analysis of data from part 2 of the GiACTA trial. GiACTA consisted of a 52-week, double-blind, randomized controlled treatment period (part 1) and a 2-year long-term follow-up (part 2). In part 1, patients received TCZ 162 mg subcutaneously every week or every other week with a 26-week prednisone taper (TCZ+Pred) or placebo plus a 26-week or a 52-week prednisone taper. Patients who achieved the primary outcome of sustained remission through week 52 while adhering to the protocol prednisone taper entered part 2 on no treatment. Any treatment during part 2 was administered open-label at the investigator's discretion. We analyzed the characteristics of first disease flare in patients originally assigned to the TCZ+Pred arms who were in sustained remission at the end of part 1 (week 52) and experienced flare in part 2. Flare was defined as the reappearance of cranial symptoms (headaches, jaw claudication, visual manifestations, scalp tenderness) or polymyalgia rheumatica (PMR) symptoms or as the elevation of erythrocyte sedimentation rate (ESR) ≥30 mm/h that was attributable to GCA and necessitated treatment. ACR GCA classification criteria were fulfilled by 78% of patients

Results: Among 149 patients treated with TCZ+Pred in part 1, 81 (54%) were in sustained remission at week 52 upon entering part 2 (Table 1). Of these 81 patients, 37 (46%) experienced at least one flare during part 2, including 17 patients with new-onset GCA and 20 patients with relapsing GCA at the start of the trial. Flares among patients with new-onset GCA presented with cranial symptoms (53%) more often than PMR symptoms (18%). In contrast, the incidence of cranial (60%) and PMR (60%) symptoms was balanced in patients with relapsing GCA. Visual manifestations occurred in two patients (5%) who experienced flare (Table 2). ESR and CRP were elevated in 68% and 36% of patients, respectively, at the time of flare. Median ESR and CRP values around the time of flare were 37.0 mm/h and 5.44 mg/L, respectively, in patients with new-onset GCA and 35.0 mm/h and 8.6 mg/L, respectively, in patients with relapsing GCA. Only three (8%) of the flares were identified as ESR elevation without cranial or PMR symptoms.

Conclusion: Overall, 46% of GCA patients successfully treated with TCZ for 12 months experienced disease flare within the following 2 years. Flares in patients with new-onset disease at the time of TCZ initiation occurred more often with cranial symptoms than PMR symptoms. Visual manifestations were rare at the time of flare, and no cases of blindness occurred. ESR was within the normal range in one-third of the patients who experienced flare.

Table 1. Baseline Demographics and Disease Characteristics

Characteristic	Part 1 Treatment[a]	
	TCZ QW+Pred n = 56	TCZ Q2W+Pred n = 25
Age, mean (SD)	68.4 (8.3)	70.0 (8.6)
Female, n (%)	44 (78.6)	14 (56.0)
Race white, n (%)	56 (100)	24 (96.0)
Positive TAB, n (%)	29 (82.9)	18 (85.7)
Positive vascular imaging, n (%)	30 (53.6)	12 (48.0)
New onset GCA, n (%)	28 (50.0)	14 (56.0)
Prednisone dose, mg/day, mean (SD)	34.8 (12.1)	37.4 (12.8)

TAB, temporal artery biopsy.
[a]Patients from part 1 TCZ+Pred groups who were in sustained remission at week 52; these patients entered part 2 on no treatment.

Table 1

Table 2. Signs and Symptoms of First Flare in Part 2 for Patients Who Received TCZ in Part 1, Were in Sustained Remission at Week 52, and Experienced Flare in Part 2

Clinical manifestations during flare in part 2	Part 1 Treatment[a]		
	TCZ QW+Pred	TCZ Q2W+Pred	All TCZ
New-onset disease at the beginning of part 1			
Number of patients	28	14	42
Patients with ≥1 flare, n (%)[b]	9 (32.1)	8 (57.1)	17 (40.5)
Patients with ESR ≥30 mm/h during flare, n (%)[b]	6 (66.7)	6 (75.0)	12 (70.6)
Patients with GCA signs or symptoms during flare, n (%)[c]	7 (77.8)	7 (87.5)	14 (82.4)
PMR symptoms	1 (11.1)	2 (25.0)	3 (17.6)
Cranial symptoms[d]	4 (44.4)	5 (62.5)	9 (52.9)
Amaurosis fugax	0	0	0
Blurred vision	1 (11.1)	0	1 (5.9)
Diplopia	0	0	0
Blindness	0	0	0
Ischemic optic neuropathy	0	0	0
Fever	1 (11.1)	0	1 (5.9)
Other[e]	3 (33.3)	2 (25.0)	5 (29.4)
Relapsing disease at the beginning of part 1			
Number of patients	8	11	39
Patients with ≥1 flare, n (%)[b]	14 (50.0)	6 (54.5)	20 (51.3)
Patients with ESR ≥30 mm/h during flare, n (%)[b]	8 (57.1)	4 (66.7)	12 (60.0)
Patients with GCA signs or symptoms during flare, n (%)[c]	14 (100)	6 (100)	20 (100)
PMR symptoms	8 (57.1)	4 (66.7)	12 (60.0)
Cranial symptoms[d]	8 (57.1)	4 (66.7)	12 (60.0)
Amaurosis fugax	1 (7.1)	0	1 (5.0)
Blurred vision	0	0	0
Diplopia	0	0	0
Blindness	0	0	0
Ischemic optic neuropathy	1 (7.1)	0	1 (5.0)
Fever	0	0	0
Other[e]	6 (4.3)	1 (16.7)	7 (35.0)

[a]Patients from part 1 TCZ+Pred groups who were in sustained remission at week 52; these patients entered part 2 on no treatment.
[b]Percentage based on N in disease-onset group.
[c]Percentage based on number of flare patients in disease-onset group. Individual signs or symptoms are shown as number of patients with each symptom; patients could have ≥1 sign or symptom at the time of flare.
[d]New-onset localized headache, scalp tenderness, temporal artery tenderness or decreased pulsation, ischemia-related vision loss, or jaw pain claudication.
[e]Other signs and symptoms included fatigue, malaise, subjective weakness, and night sweats.

Table 2

Disclosure: S. Unizony, Genentech, Inc., 2; **S. Mohan**, Genentech, Inc., 1, 2; **J. Han**, Genentech, Inc., 1, 2; **J. Stone**, Roche, 2, 5, Genentech, 2, 5.

Abstract Number: 0517

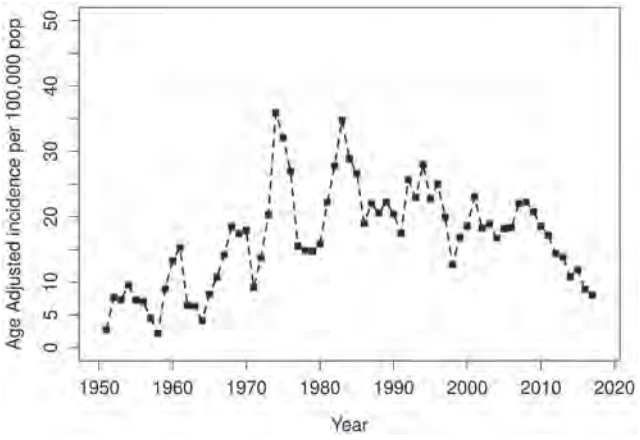
Trends in the Incidence and Use of Diagnostic Modalities for Giant Cell Arteritis over Seven Decades: A Population-based Study

Thomas Garvey[1], Cynthia Crowson[2], Matthew J. Koster[3] and Kenneth Warrington[3], [1]Mayo Clinic Rochester, Apple Valley, MN, [2]Mayo Clinic, Rochester, Minnesota, USA, Rochester, MN, [3]Mayo Clinic, Rochester, MN

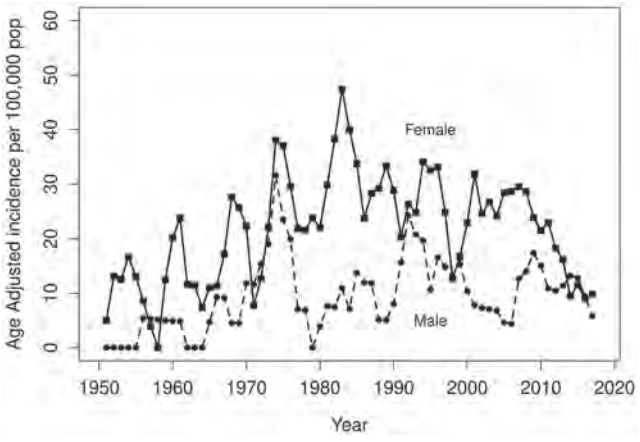
SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders II: GCA Clinical & Epidemiology
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Diagnostic methods for giant cell arteritis (GCA) have evolved over recent decades, and large vessel imaging plays an increasing role in disease detection. The purpose of this study is to examine the incidence of GCA in recent decades, and to analyze trends in the frequency of GCA subsets according to diagnostic modalities.

Methods: A pre-existing population-based cohort of patients diagnosed with GCA between 1950 and 2009 was extended with incident cases from 2010 to 2018. The diagnosis of GCA was confirmed by review of medical records



Trends in the incidence of GCA in Olmsted County (1950-2018)



Trends in the incidence of GCA in Olmsted County by sex (1950-2018)

of patients with ICD9/10 codes for GCA between 1/1/2010 and 12/31/2018. Incident cases that met either one of the following sets of inclusion criteria were added to the cohort: one, American College of Rheumatology 1990 GCA classification criteria; or two, patients aged ≥50 years with elevation of erythrocyte sedimentation rate or C-reactive protein and radiographic evidence of large vessel vasculitis attributed to GCA. Incident cases were classified into one of three groups: group 1, temporal artery biopsy (TAB) positive; group 2, TAB negative or not done with positive large-vessel imaging; or group 3, clinical diagnosis of GCA.

Results: The study cohort included 302 patients diagnosed with GCA from 1950 until 2018. Fifty-two incident cases were diagnosed between 2010 and 2018; 34 females (65%) and 18 males (35%). The age and sex adjusted incidence rates (95% CI) per 100,000 between 2010 and 2018 for females, males, and the total population were 13.6 (9.0, 18.1), 9.8 (5.2, 14.3), and 11.6 (8.4, 14.7), respectively. The corresponding incidence rates from 2000-2009 were 28.1 (21.0, 35.2), 10.2 (5.0, 15.5), and 20.5 (15.9, 25.1), respectively. This represents a significant decline in the incidence rates in females ($p< 0.001$) and the total group ($p< 0.001$) between the 2000-2009 and 2010-2018 cohorts but no change in males ($p=0.92$). Of the 52 patients diagnosed between 2010 and 2018, there were 35 (67%) in group 1, 10 (19%) in group 2, and 7 (13%) in group 3. In contrast, of the 250 patients diagnosed between 1950 and 2009 there were 209 (84%) in group 1, 4 (2%) in group 2, and 37 (15%) in group 3. There was a significant difference between the 1950-2009 and 2010-2018 cohorts in the composition of these groups ($p< 0.001$).

Conclusion: In this population-based cohort of patients with GCA diagnosed over a 69-year period, the incidence of GCA has declined in recent years. The total decline is driven by a decline in females but not in males. The reasons for this are unclear but should be followed over time and investigated in other population-based cohorts. There has also been a shift in the diagnostic modalities for GCA. In recent years, there are fewer TAB positive patients, and more patients diagnosed with large vessel imaging. This is the first population-based incidence cohort demonstrating a trend towards increased use of large vessel imaging for the diagnosis of GCA.

Disclosure: T. Garvey, None; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1; **M. Koster**, None; **K. Warrington**, Lilly, 2, Kiniksa, 2.

Abstract Number: 0518

The Impact of Large Vessel Vasculitis of the Axillary Artery on Cumulative Glucocorticoid Dose and Relapse Rate in Giant Cell Arteritis

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SESSION INFORMATION
Session Date: Friday, November 6, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders II: GCA Clinical & Epidemiology
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Prognostic markers for clinical outcomes in giant cell arteritis (GCA) are urgently needed. While large vessel GCA (LV-GCA) has been associated with higher glucocorticoid (GC) dose and increased relapses, data are still controversial (Muratore et al. 2015). The axillary artery is almost always affected in LV-GCA patients (axG-

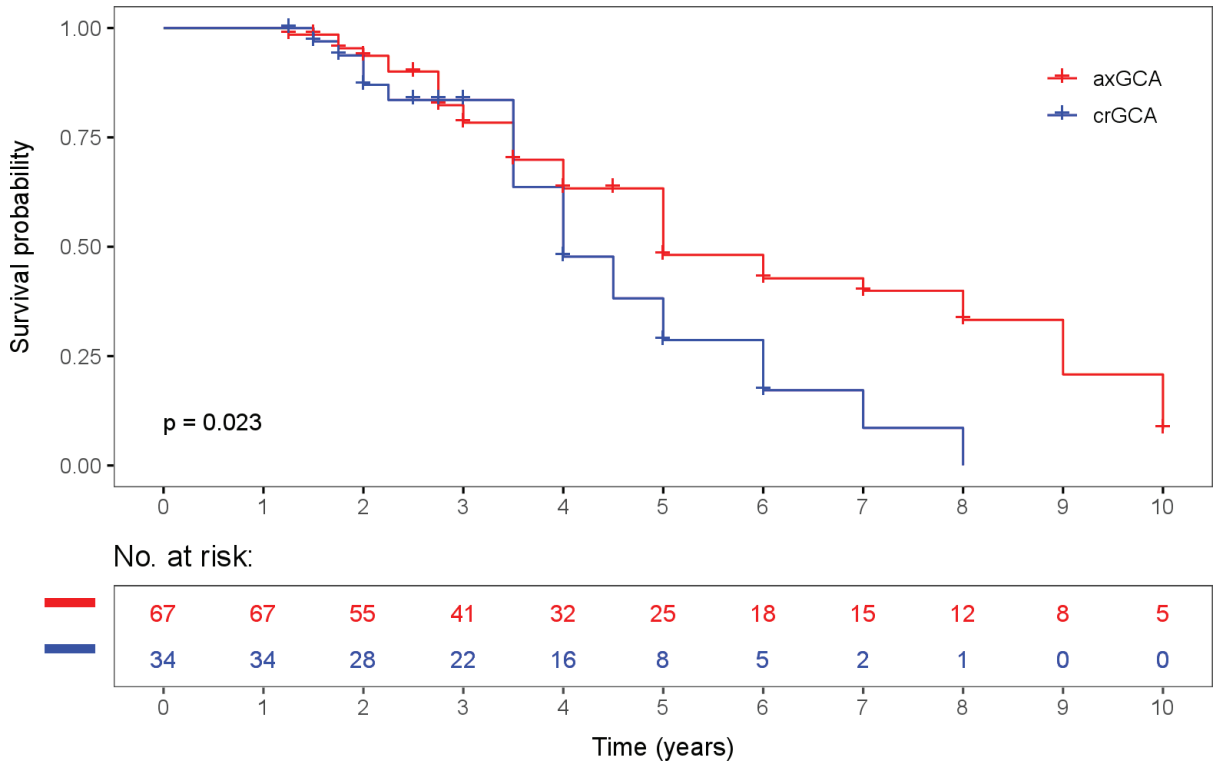

Figure 1. Kaplan-Meier curves assessing time until cessation of glucocorticoid treatment in patients with giant cell arteritis with (axGCA) and without (crGCA) vasculitis of the axillary artery.

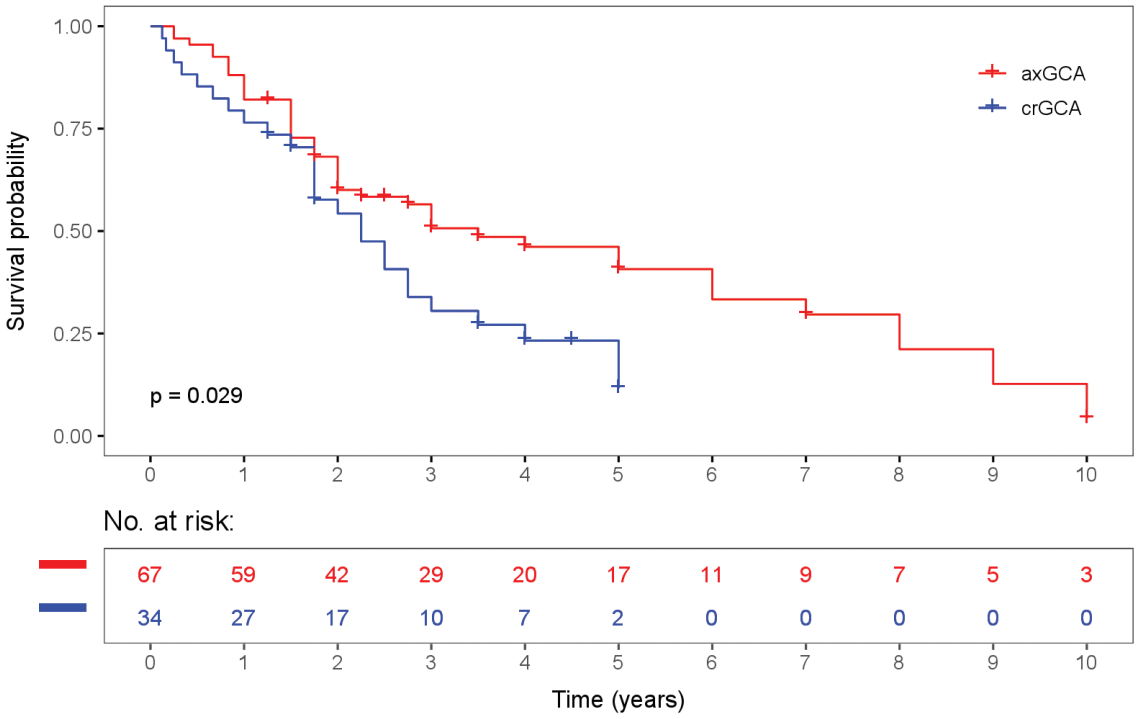

Figure 2. Kaplan-Meier curves assessing the time until the first clinical relapse in patients with giant cell arteritis with (axGCA) and without (crGCA) axillary artery involvement.

CA) (Schmidt et al. 2008; Czihal et al. 2012), however, it is not yet clear whether axGCA patients have more relapses and a higher GC need, compared to GCA with exclusive cranial vessel involvement (crGCA).

The aim of this study was to determine the prognostic value of axillary artery involvement in GCA in respect to cumulative GC doses and relapse rates.

Methods: Ultrasound (US) of the axillary arteries was performed in GCA patients at the time of diagnosis and at multiple follow-up visits. Patients with US signs of axillary artery vasculitis at the time of diagnosis were compared with patients in whom US was exclusively positive in cranial arteries. Cumulative GC doses and relapse rates were calculated for the most recent study visit and survival analysis was performed to determine differences between the groups concerning the time until the first relapse and the cessation of GC treatment. Linear mixed models were used to assess the effect of GC and relapses on the axillary artery wall in axGCA patients.

Results: Sixty-seven patients had US signs of vasculitis of the axillary arteries at baseline (=axGCA group), while 34 patients had exclusively signs of vasculitis in the cranial arteries (=crGCA group). Mean (SD) age at diagnosis was 68.0 (7.3) years in the axGCA group and 72.4 (6.5) years in the crGCA group; 72% and 56% were female, respectively. Time from diagnosis was 48 months in both groups (range: axGCA: 16-137, crGCA: 16-102). Median time until GC cessation was 60 months (95% CI: 60-108) in the axGCA group compared to 48 months (95% CI: 42-72) in the crGCA group (p=0.0239), while median time until the first relapse was 42 months (95% CI: 24-84) vs 27 months (95% CI: 21-42; p=0.029), as depicted in figure 1 and 2. Median cumulative GC doses were higher in the axGCA group with 6801mg (range: 1748-34169), compared to the crGCA group with 5633mg (range: 2553-19967; p=0.052), while median cumulative number of relapses were similar with 2 (range: 0-16) and 1 (range: 0-13) in the axGCA and crGCA group, respectively (p=0.67). While we observed a continuous decline of the intima media thickness (IMT) over the entire study period, the cumulative GC dose had no significant effect on IMT decrement. In contrast, a clinical relapse resulted in an increase of the IMT by 0.18mm (95% CI: 0.07-0.30; p=0.003).

Conclusion: GCA patients with vasculitis of the axillary artery have longer GC treatment and higher cumulative GC doses compared to GCA patients without vasculitis of axillary arteries. Relapse rates are similar between the groups but occur later in patients with axillary artery involvement. Also, relapses lead to an IMT increase of axillary arteries.

Disclosure: P. Bosch, None; **C. Dejaco**, Abbvie, 5, 8, BMS, 8, Janssen, 5, 8, Celgene, 2, Lilly, 8, Novartis, 8, Pfizer, 8, Roche, 8, Sanofi, 5, 8; **W. Schmidt**, None; **A. Krause**, None; **K. Schlüter**, None; **G. Pregartner**, None; **V. Schaefer**, None.

Abstract Number: 0519

Thrombotic and Obstetric Associations of Non-Criteria Antiphospholipid Immunoassays That Detect Antibodies to Neutral and Negatively-Charged Phospholipid

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Criteria antiphospholipid (aPL) antibodies that identify antiphospholipid syndrome (APS) patients, anticardiolipin (aCL) and anti-β2glycoprotein-I (anti-β2GPI), have demonstrated inconsistent specificity and sensitivity in this regard respectively. The purpose of this study was to evaluate the performance characteristics of non-criteria anti-phosphatidic acid (anti-PA), anti-phosphatidylglycerol (anti-PG) and anti-phosphatidylethanolamine (anti-PE) assays (IgG/IgM) in identifying APS related clinical manifestations in a large group of patients with aPL-related diseases.

Methods: Serum samples from 520 patients from the Hopkins (n=344) and Jamaican SLE cohorts (n=42), the PROMISSE cohort (n=77), as well as APS patients (n=29) and healthy controls (n=28) from the Antiphospholipid Standardization Laboratory were examined for IgG/IgM positivity in aCL (in-house), anti-β2GPI (INOVA Diagnostics), anti-PA, anti-PG and anti-PE (Louisville APL) ELISA assays. Assay cut-offs were aCL IgG/IgM (10GPL/10MPL), anti-β2GPI (20SGU/20SMU), anti-PA, anti-PG, anti-PE (15GPL/15MPL). Correlation of assay positivity with clinical manifestations expressed as odds ratio (OR) with 95%CI, the effect of increasing antibody titers, logistic regression multivariate analysis, quantitative and qualitative inter-assay agreement, and various analytical measures of assay performance including sensitivity, specificity, positive (PPV) and negative (NPV) predictive values were evaluated.

Results: The prevalence of IgG/IgM anti-PA positivity was 30.4%, anti-PG was 27.7%, anti-PE was 30.8%, aCL was 24.2% and anti-β2GPI was 18.3%. The IgG isotypes of all assays were associated with at least one or more thrombotic and/or obstetric manifestation, while IgM isotypes of non-criteria assays were associated with obstetric manifestations. All criteria and non-criteria assays (IgG/IgM) were associated with APS diagnosis (Table 1). There was a 3 to 10-fold increased risk for thrombotic manifestations, particularly venous thrombosis, associated with high

Assay	Venous Thrombosis	Arterial Thrombosis	Any Thrombosis	Pre-eclampsia Eclampsia	Miscarriage	Any Preg Morbidity	APS
aCL G	4.2(2.6-6.8)**	2.3(1.4-3.9)**	3.6(2.3-5.6)**	1.8(0.9-3.6)	1.7(1.0-2.7)*	1.7(1.1-2.8)	6.7(4.2-11.0)**
aCL M	1.4(0.8-2.7)	1.8(0.9-3.4)	1.5(0.9-2.7)	1.1(0.4-2.7)	1.1(0.6-2.1)	1.2(0.7-2.3)	3.0(1.7-5.4)**
aCL GM	3.1(2.0-4.9)**	2.1(1.3-3.4)**	2.7(1.8-4.1)**	1.5(0.8-2.9)	1.6(0.9-2.3)	1.6(1.0-2.4)*	5.8(3.8-9.0)**
aB2 G	2.8(1.7-5.0)**	1.5(0.8-2.7)	2.1(1.3-3.6)**	1.6(0.7-3.5)	2.8(1.6-4.9)**	2.7(1.5-4.7)**	5.3(3.0-9.3)**
aB2 M	1.2(0.6-2.4)	1.2(0.6-2.5)	1.2(0.6-2.2)	1.7(0.7-4.1)	1.5(0.8-2.8)	2.2(1.2-4.1)**	2.6(1.5-4.8)**
aB2 GM	2.1(1.3-3.5)**	1.4(0.8-2.4)	1.8(1.1-2.8)*	1.4(0.7-2.8)	2.4(1.5-3.9)**	2.6(1.6-4.2)**	4.8(3.0-7.7)**
aPA G	2.6(1.7-4.1)**	2.1(1.3-3.3)**	2.6(1.7-3.9)**	2.5(1.3-4.7)**	2.0(1.2-3.0)**	2.3(1.5-3.6)**	3.7(2.4-5.7)**
aPA M	0.8(0.4-1.5)	1.3(0.7-2.5)	1.2(0.7-2.0)	1.7(0.8-3.6)	1.6(0.9-2.8)	2.2(1.3-3.8)**	2.4(1.5-4.2)**
aPA GM	2.1(1.4-3.3)**	2.0(1.3-3.1)**	2.3(1.5-3.3)**	2.0(1.1-3.7)*	2.2(1.4-3.3)**	2.7(1.8-4.0)**	4.0(2.7-5.9)**
aPG G	2.1(1.3-3.3)**	1.1(0.7-1.9)	1.6(1.0-2.5)*	1.5(0.8-3.0)	2.4(1.5-3.8)**	2.3(1.4-3.6)**	3.7(2.3-5.9)**
aPG M	1.0(0.5-1.8)	1.1(0.6-2.0)	1.1(0.7-1.9)	1.0(0.4-2.3)	1.7(1.0-2.8)*	2.1(1.2-3.4)**	1.9(1.2-3.2)**
aPG GM	1.7(1.1-2.6)*	1.3(0.8-2.0)	1.5(1.0-2.3)*	1.2(0.6-2.3)	2.7(1.8-4.1)**	2.7(1.8-4.1)**	3.8(2.5-5.7)**
aPE G	1.5(0.9-2.4)	2.0(1.3-2.2)**	2.0(1.3-3.0)**	1.3(0.7-2.5)	1.6(1.0-2.4)*	1.6(1.0-2.3)*	1.5(1.0-2.3)*
aPE M	0.8(0.3-2.0)	1.9(0.8-4.1)	1.7(0.9-3.5)	0.9(0.3-3.0)	0.8(0.4-1.7)	0.8(0.4-1.6)	2.3(1.2-4.8)*
aPE GM	1.3(0.9-2.1)	2.2(1.4-3.5)**	2.1(1.4-3.1)**	1.2(0.7-2.3)	1.4(0.9-2.1)	1.3(0.9-2.0)	1.7(1.1-2.5)*

*p-value <0.05. ** p-value <0.01.

Table 1. Association of antiphospholipid assay positivity with APS-related clinical manifestations – Odds Ratios with 95% Confidence Intervals

vs low positive titers in IgG assays. There was moderate to excellent quantitative and qualitative agreement among most assays of corresponding isotypes. Overall, sensitivity (26.3-39.5%), specificity (85.3-94.1%), PPV (39.3-68.0%) and NPV (70.4-76.1%) for APS diagnosis were relatively similar among IgG assays, which performed better than their IgM counterparts. IgG aCL was the only independent predictor for venous thrombosis OR 3.6(2.1-6.1) and arterial thrombosis OR 1.9(1.1-3.4) while IgG anti-PA was the only independent predictor for placental insufficiency due to pre-eclampsia/eclampsia OR 2.4(1.3-4.6) and recurrent miscarriage OR 1.9(1.2-3.0).

Conclusion: IgG anti-PA, anti-PG and anti-PE antibodies were associated with thrombotic and obstetric APS-related manifestations, while their IgM counterparts were associated with mainly obstetric manifestations. Increasing titers of IgG assays imparted an increased risk, particularly for venous thrombosis. These non-criteria PL assays are promising biomarkers for particular APS manifestations and their independent value in APS classification requires further investigation.

Disclosure: R. Willis, Louisville APL Diagnostics Inc, 5, Pfizer, 2; **E. Harris**, Louisville APL Diagnostics Inc, 4; **V. Murthy**, None; **Z. Romay-Penabad**, None; **A. Schleh**, Louisville APL Diagnostics Inc, 4; **M. Smikle**, None; **K. De Ceulaer**, None; **A. Tebo**, None; **T. Jaskowski**, None; **M. Guerra**, None; **D. Branch**, None; **J. Salmon**, UCB, 1, 2, BMS, 1, 2, Abbott, 1, Pfizer, 1, Johnson & Johnson, 1, Lilly, 1, Merck, 1, Regeneron, 1; **M. Petri**, AbbVie, 5, Amgen, 5, AstraZeneca, 2, 5, BMS, 5, Decision Resources, 5, GSK, 2, 5, INOVA, 5, IQVIA, 5, Janssen, 5, Eli Lilly, 2, 5, Merck EMD Serono, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5, Exagen, 2; **E. Gonzalez**, None.

Abstract Number: 0520

Antiphospholipid Antibodies and Thrombotic Events in COVID-19 Patients Hospitalized in Medicine Ward

Alexandre Le Joncour[1], Corinne Frere[1], Isabelle Martin-Toutain[1], Paul Gougis[1], Pascale Ghillani-Dalbin[1], Georgina Maalouf[1], Matheus Vieira[1], Anne-Genevieve Marcelin[1], Joe-Elie Salem[1], Yves Allenbach[2], David Saadoun[3], Olivier Benveniste[4] and Patrice Cacoub[1], [1]APHP, paris, France, [2]Sorbonne Université, Paris, Ile-de-France, France, [3]AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Department of Internal Medicine and Clinical Immunology, F-75013, Paris, France, Centre national de références Maladies Autoimmunes et systémiques rares et Maladies Autoinflammatoires rares, PAris, France, [4]Sorbonne Université, paris, France

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: A high prevalence of thrombotic events has been reported in critically ill COVID-19 patients but data on the prevalence of thrombosis in ward patients are scarce. The presence of antiphospholipid antibodies (aPL) and whether aPL are involved in the risk of thrombosis in this setting has not been addressed.

Our objective was to study the prevalence of aPL in non-ICU COVID-19-patients and their relationship with thrombotic events.

Methods: This is a prospective single-center observational cohort study of COVID-19 patients admitted in the Internal Medicine and Clinical Immunology Department of a tertiary care university hospital (Paris, France). Included patients were older than 18 years with an initial requirement for hospitalization in a medical ward and a positive SARS-CoV-2 RT-PCR assay from nasal swabs. Patients were tested for the presence of aPL antibodies. Limit of

Table 1: Patients characteristics and antiphospholipid markers in a prospective cohort of COVID-19 patients :

	All patients	Patients without thrombotic event	Patients with thrombotic event	P value
Number of patients	**N=104**	**N=93**	**N=11**	
Demographics				
Age, mean [IQR] years	71 [59-81]	71 [59-80.5]	80 [60-84]	0.328
Male, no. (%)	60 (57.7)	53 (57)	7 (63.6)	0.756
Smoking, n (%)	10 (9.8)	10 (10.9)	0 (0)	0.592
BMI (kg/m^2)	24.4 [22.5-28.6]	25.7 [23.1-29.6]	24.2 [21.26.3]	0.359
Past medical history, n (%)				
Venous thrombosis	16 (15.4)	12 (13.9)	4(36.4)	0.064
Cancer	27 (26.2)	25 (27.2)	2 (18.2)	0.753
Active cancer	18 (17.3)	16 (17.2)	2 (18.2)	1
Coronary ischemic disease	18 (17.3)	16 (17.2)	2 (18.2)	1
Stroke	11 (10.6)	10 (10.8)	1 (9.1)	1
Peripheral arterial disease	9 (8.7)	8 (8.6)	1 (9.1)	1
Hypertension	61 (58.7)	55 (59.1)	6 (54.5)	0.759
Dyslipidemia	39 (37.5)	32 (34.4)	7 (63.6)	0.096
Diabetes	25 (24)	21 (22.6)	4 (36.4)	0.454
Platelet inhibitor	24 (23.1)	20 (21.5)	4 (36.4)	0.273
Oral anticoagulant	15 (14.4)	14 (15.1)	1 (9.1)	0.506
Covid-19 symptoms, n (%)				
Fatigue	65 (62.5)	60 (64.5)	5 (45.5)	0.393
Dyspnea	59 (56.7)	51 (54.8)	8 (72.7)	0.342
Cough	45 (43.3)	39 (41.9)	6 (54.5)	0.577
Diarrhea	21 (20.2)	20 (21.5)	1 (9.1)	0.301
Dysgueusia	20 (19.2)	18 (19.4)	2 (18.2)	1.0
Thoracic pain	19 (18.3)	15 (16.1)	4 (36.4)	0.313
Anosmia	12 (11.5)	11 (11.8)	1 (9.1)	1.0
Hemoptysis	2 (1.9)	0 (0)	2 (18.2)	**0.016**
Covid-19 course				
Nasal oxygen (L /min)	2 [2-4]	2 [2-3]	4 [3-11.5]	**0.01**
ICU transfer D14, n (%)	17 (16.3)	14 (15)	3 (27)	0.437
Mortality Day 14, n (%)	14 (13.5)	11 (11.8)	3 (27.3)	0.16
Baseline laboratory findings				
Neutrophils, /mm^3	4535 [3185-6047]	4420 [2930-5615]	6460 [4537-8755]	**0.019**
Lymphocytes, /mm^3	955 [710-1237]	950 [710-1210]	1020 [717-1480]	0.600
Haemoglobin, g/dl	12.1 [11.1-13.9]	12.3 [11.1-13.9]	12 [11.2-13.0]	0.534
Platelet count, G/mm^3	220 [159-288]	220 [159-282]	231 [153-368]	0.355
CRP, mg/L	69 [30-107]	64.2 [28.3-104.1]	124 [64.7-253]	**0.021**
Fibrinogen, g/L	6.0 [4.83-6.98]	5.95 [4.88-6.93]	6.5 [4.5-8.15]	0.861
D-Dimer, µg/L	950 [480-1920]	890 [450-1615]	5860 [2555-17750]	**<0.001**
Ferritin, µg/L	876 [364-1463]	867 [356-1526]	979 [368-1413]	1.0
IL-6, pg/mL	60 [34-83]	61.5 [34.8-91.8]	54 [31.8-123]	0.980

positivity was fixed at 15 and 10 units/mL (99th percentile of a control population) for aCL and aβ2GPI antibodies respectively. Continuous variables are presented as median (interquartile range, IQR) and were compared using Wilcoxon's- test. Categorical variables are presented as count (percent) and were compared using Fisher's-test.

Table 1 (...)				
Anti-phospholipid Ab markers				
IgG anticardiolipin Ab	8 (7.7)	5 (5.4)	3 (27.3)	**0.037**
IgG titer (fold UNL)	1.5 [1.3-2]	1.6 [1.2-2]	1.3 /1.5 / 2.3*	0.786
IgM anticardiolipin Ab	8 (7.7)	3 (3.2)	5 (45.5)	**< 0.001**
IgM titer(fold UNL)	1.6 [1.4-2.2]	1.2 / 1.5 / 1.6 *	1.7 [1.5-2.5]	0.143
IgA anticardiolipin Ab	31 (28)	26 (28)	5 (45.5)	0.297
IgA titer (fold UNL)	1.5 [1.4-1.7]	1.4 [1.3-1.7]	1.7 [1.6-2.6]	0.081
IgG anti-β2-GPI Ab	5 (4.8)	4 (4.3)	1 (9.1)	0.435
IgG titer (fold UNL)	4.5 [1.8-14]	6.9 [1.6-15.1]	4.5*	-
IgM anti-β2-GPI Ab	3 (2.9)	2 (2.2)	1 (9.1)	0.287
IgM titer(fold UNL)	1 / 4 / 26 *	4 / 26*	1*	-
IgA anti-β2-GPI Ab	6 (5.8)	3 (3.2)	3 (27.3)	**0.015**
IgA titer (fold UNL)	10 [3.1-13]	2.6 / 3.3 / 15.2	10/10/12	0.7
Lupus anticoagulant, yes/nb tested	21/53 (39.6)	18/48 (37.5)	3/5 (60)	0.374
Anti-phospholipid markers positivity#				
Single positivity	35 (33.7)	31 (33.3)	4 (36.4)	0.740
Double positivity	12 (11.5)	11 (11.8)	1 (9.1)	1
Triple positivity	2 (1.9)	0 (0)	2 (18.2)	**0.01**

*IQR : InterQuartil Range ; BMI : Body Mass Index ; CRP : C reactive protein ; Ab : antibody. # Positivity of anti-phospholipid marker among anticardiolipin Ab, anti-β2-GPI Ab and lupus anticoagulant. * when n≤3, singles values are given*

Results: A total of 104 patients (57.7% males, 71 years) were included. Eleven (10.6%) patients had a thrombotic event (9 acute pulmonary embolisms, 1 deep vein thrombosis and 1 aortic thrombus). They had more frequently a history of venous thrombosis, and increased C- reactive protein and D-Dimer levels versus patients without thrombotic events. Overall, 49/104 (47.1%) patients had a least one positive aPL marker while double or triple antiphospholipid seropositivity was found in 11.1% and 1.9%, respectively. Anticardiolipin (aCL) and anti-beta2 glycoprotein I (aβ2GPI) were noted in 35/104 (33.7%) and 9/104 (8.7%) patients. A lupus anticoagulant was found in 21 out of 53 (39.6%) patients. IgG aCL, IgM aCL, IgA β2-GPI and triple positivity were significantly associated with the occurrence of thrombotic events (details are shown in table 1).

If we consider only highly positive aPL (cut off > 30 U/mL), 27/103 (26.2%) non-ICU patients had at least one positive aPL [5/11 (45%) vs 22/91 (24%) patients with or without thrombosis, p=0.051]. The presence of at least two positive aPL (>30 U/ml) was associated with thrombosis [3/11 (27.3%) vs 1/93 (1.1%), p =0.003].

Conclusion: Although aPL are frequently found in Covid-19 non-ICU patients, their role in thrombotic events needs dedicated studies.

Disclosure: A. Le Joncour, None; **C. Frere**, None; **I. Martin-Toutain**, None; **P. Gougis**, None; **P. Ghillani-Dalbin**, None; **G. Maalouf**, None; **M. Vieira**, None; **A. Marcelin**, None; **J. Salem**, None; **Y. Allenbach**, None; **D. Saadoun**, None; **O. Benveniste**, None; **P. Cacoub**, None.

Abstract Number: 0521

Avoiding Misclassification of Primary Antiphospholipid Syndrome as Systemic Lupus Erythematosus: What Are the Best-performing SLE Classification Criteria?

Flavio Signorelli[1], Gustavo Balbi[2], Eloisa Bonfa[3], Eduardo Borba[4] and Danieli Andrade[5], [1]Universidade de São Paulo, Rio de janeiro, Rio de Janeiro, Brazil, [2]Universidade de São Paulo, Juiz de Fora, Minas Gerais, Brazil, [3]Hospital das Clínicas, Faculdade de Medicina da Universidade de Sao Paulo (HCFMUSP), Sao Paulo, Sao Paulo, Brazil, [4]Rheumatology Division, Hospital das Clinicas HCFMUSP, Faculdade de Medicina, Universidade de São Paulo, São Paulo, Brazil, [5]University of Sao Paulo, Sao Paulo, Brazil

SESSION INFORMATION

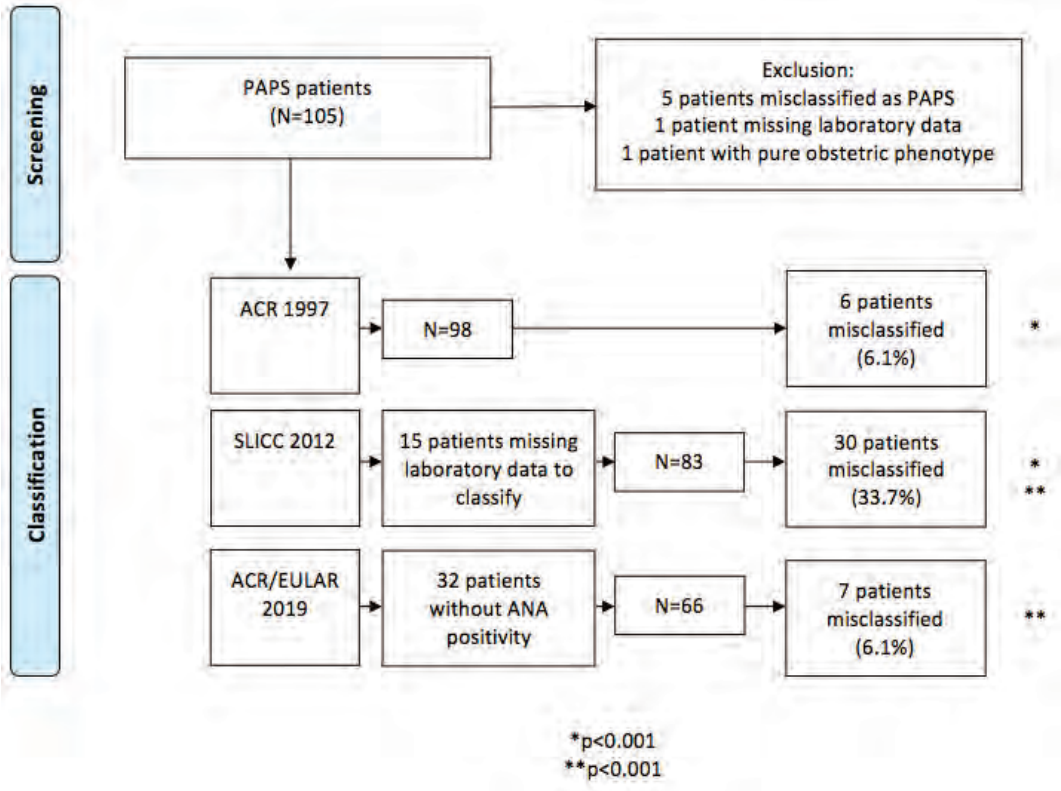
Session Date: Saturday, November 7, 2020

Session Title: Antiphospholipid Syndrome Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Antiphospholipid Syndrome (PAPS) patients, when submitted to Systemic Lupus Erythematosus (SLE) classification criteria, can be misclassified. The new 2019 ACR/EULAR classification criteria have never been applied for PAPS patients. The main objective of this study is to evaluate the risk of misclassifying thrombotic PAPS (Sidney) as SLE in a cohort of a tertiary Hospital.



Data	
Female sex, n (%)	86 (87.8)
Age at diagnosis (years), n (median, IQ)	29 (23-26)
Age at study (years), n (median, IQ)	46 (37.8-56)
Time since APS diagnosis (years), n (median, IQ)	14 (10-21)
Arterial thrombosis, n (%)	39 (39.8)
Venous thrombosis, n (%)	68 (68.4)
Obstetric criteria, n=72, n (%)	40 (55.6)
Valvulopathy, n (%) (MD)	16 (16.3) (59)
Nephropathy, n (%)	10 (10.2)
Livedo, n (%) (MD)	44 (52.4) (14)
Thrombocytopenia, n (%)	7 (7.1)
LA positivity, n (%) (MD)	91 (93.8) (1)
aCL positivity, n (%)	63 (63.4)
aB2GP1 positivity, n (%)	50 (51.0)
Triple positivity, n (%)	41 (41.8)
Anticoagulation therapy (warfarin/LWH)*, n (%)	96 (98)
Antiaggregating therapy**, n (%)	12 (12.4)
Hydroxychloroquine, n (%)	43 (43.9)

Legend: n (%)= number (%), IQ- interquartile range, (MD)= missing data, LA=lupus anticoagulant, aCL= anticardiolipin, aB2GPI= antibeta2 glycoprotein 1,LWH= low weight heparin. *warfarin, n=93 and LWH=3, **acid acetylsalicylic, n=9 and clopidogrel, n=3.

Methods: A retrospective analysis of our PAPS cohort was performed using electronic chart database. The three current classification criteria for SLE (ACR 1997, SLICC 2012 and 2019 ACR/EULAR) were applied in parallel focusing on the latter. Flowchart of the study is shown in Figure 1. Categorical variables were analyzed by x^2 or two-tailed Fisher's exact test, and continuous variables were analyzed by Student's T test or Mann–Whitney-U test, as applicable. The misclassification rates of the three different criteria were compared using McNemar's test. A p-value of < 0.05 was considered statistically significant.

Results: All patients had thrombotic PAPS and 55.6% presented obstetric criteria manifestations. Venous and arterial thrombosis were detected in 69.4% and 39.8%, respectively. Ninety-eight PAPS patients were submitted to ACR 1997 and 2019 ACR/EULAR. SLICC 2012 was applied in only 83 patients due to missing data (lack of direct Coombs test). Our patients were mostly female (87.8%), with a median age at study inclusion of 46 years (38-56) and median disease duration of 14 years (10-21). LA was the most frequent antiphospholipid antibody, identified in 91 patients (93.8%). Main characteristics of the studied patients are shown in Table 1. The comparison of different criteria two-by-two according to their rates of misclassification found that 2019 ACR/EULAR and ACR 1997 performed similarly (N=98; 6.1 vs. 6.1%, p=1.00). On the other hand, SLICC 2012 demonstrated a poor performance compared to both 2019 ACR/EULAR (N=83, 36.1 vs. 6.1%, p< 0.001) and ACR 1997 criteria (N=83, 36.1 vs. 6.1%, p< 0.001). When the 3 classification criteria were used simultaneously, only 1 patient was misclassified as SLE. Hematological manifestations were the most frequent criteria related to misclassification in PAPS patients, encompassing 100% of misclassified patients (vs. 52.2%, p=0.025) in ACR 1997, 90% (vs. 11.3%, p< 0.001) in SLICC 2012 and 71.4% (vs. 18.6%, p=0.01) in 2019 ACR/EULAR.

Conclusion: 2019 ACR/EULAR is very accurate in differentiating PAPS from SLE, with only 6.1% of misclassification rates (similar to those observed in ACR 1997 and lower than those found in SLICC 2012).

Disclosure: F. Signorelli, None; **G. Balbi**, None; **E. Bonfa**, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4), 2, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #305068/2014-8), 2; **E. Borba**, None; **D. Andrade**, None.

Abstract Number: 0522

Development of New International Classification Criteria for Antiphospholipid Syndrome: Phase III Case Collection Results

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: An international multi-disciplinary effort is underway to develop rigorous, new, consensus- and evidence-based classification criteria for Antiphospholipid Syndrome (APS). The methodological approach includes four phases; we have previously presented Phase I (item generation) and II (item reduction), resulting in 27 candidate criteria organized into laboratory and clinical domains. Phase III (item weighting/threshold identification) is currently underway; here we report initial Phase III case collection results.

Methods: We used REDCap, a secure web-based data system, for Phase III international case collection. The 27 candidate criteria items from Phase II were represented in a standardized case collection form. We asked 17 physicians specializing in APS from Europe, North and South America to provide cases and to rate them using a Likert scale from +3 to -3 (highly likely to highly unlikely to be APS). Cases with higher scores (+2 or +3) were categorized as "highly likely" APS based on treating physician assessment, whereas lower scores (+1 to -3) were categorized as "equivocal or unlikely" APS. We calculated risk ratios to represent the probability that a laboratory or clinical candidate criterion would be associated with a "highly likely" compared to "equivocal or unlikely" APS case.

Results: We collected 314 potential APS cases (mean age 43.8 +/- 14.4 years; 79% female; and 77% white) between 6/2019-8/2019 from 17 sites in Europe (n=8, 47%), North America (n=7, 41%), and South America (n=2, 11%). Majority of cases were potential primary APS (n=201, 64%). Out of 314 cases, 137 (44%) were rated as "highly likely" and 177(56%) as "equivocal or unlikely" APS. The table demonstrates frequency of laboratory and clinical manifestations of potential APS cases (overall and categorized by physician assessment) as well as the risk ratios; the three criteria with the lowest risk ratios (< 1.5) were superficial vein thrombosis, transient ischemic attack, and embryonic loss < 10 weeks 0 days.

Conclusion: In Phase III of the development of new APS classification criteria, a large international collection of cases spanning the spectrum of "highly likely" to "equivocal or unlikely" APS was used to identify the observation frequency of each of the candidate criterion from Phase II in real world clinical settings. In next steps, these proposed candidate criteria will be further refined and weighted using multi-criteria decision analysis methodology, and a preliminary threshold for APS classification will be determined.

Table. Laboratory and Clinical Manifestations of 314 International Potential APS Cases, Overall and Categorized by Physician Assessment				
Candidate Relative Criteria (*Number of individuals, %*)	**Total (n=314)**	**Highly Likely APS (n=137)**	**Equivocal or Unlikely APS (n=177)**	**Risk Ratios**
LABORATORY				
Lupus Anticoagulant Test Positive (persistent)	136 (43%)	92 (67%)	44 (25%)	2.70
Anticardiolipin Antibody Positive (persistent[¥])				
• IgG	113 (36%)	78 (57%)	35 (20%)	2.88
• IgM	78 (25%)	43 (31%)	39 (22%)	1.59
Anti-β_2-glycoprotein-I Antibody Positive (persistent)				
• IgG	72 (23%)	55 (40%)	17 (10%)	4.18
• IgM	52 (17%)	33 (24%)	19 (11%)	2.24
CLINICAL				
Macrovascular				
• Superficial Vein Thrombosis	15 (5%)	4 (3%)	11 (6%)	0.47
• Venous Thromboembolism	95 (30%)	63 (46%)	32 (18%)	2.54
• Transient Ischemic Attack	27 (9%)	13 (10%)	14 (8%)	1.20
• Arterial Thrombosis	82 (26%)	58 (42%)	24 (14%)	3.12
Microvascular*	70 (22%)	41 (30%)	29 (16%)	1.83
Obstetric (otherwise unexplained) **				
• Embryonic loss (<10 weeks 0 days)	85 (45%)	34 (42%)	51 (48%)	0.86
• Fetal loss (10 weeks 0 days – 15 weeks 6 days)	20 (11%)	9 (11%)	11 (10%)	1.86
• Fetal loss (16 weeks 0 days – 34 weeks 0 days)	42 (22%)	32 (40%)	19 (18%)	4.13
• Severe preeclampsia (< 34 weeks)	27 (14%)	18 (22%)	9 (8%)	2.58
• Severe placental insufficiency (<34 weeks)	22 (12%)	13 (16%)	9 (8%)	1.87
Cardiac Valve Disease***	27(9%)	18 (13.1%)	9 (5.1%)	2.58
Hematologic (platelet count <150 10^9/L)	93 (30%)	57 (42%)	36 (20%)	2.05

*Livedo racemosa, livedoid vasculopathy, adrenal hemorrhage, acute ischemic enceophalopathy, cardiac microvascular disease, pulmonary hemorrhage, acute antiphospholipid-related nephropathy, and/or chronic antiphospholipid-related nephropathy; **Total number of patients ever pregnant: 188 (highly likely APS: 81; unlikely APS: 107) ***Cardiac valve thickening and/or vegetation. ¥Persistent defined as positive on at least two occasions, at least 12 weeks apart.

Acknowledgement: The project is supported by ACR/EULAR.

Disclosure: M. Barbhaiya, None; **S. Zuily**, None; **Y. Ahmadzadeh**, None; **K. Costenbader**, Glaxo Smith Kline, 5, UpToDate, 7, Lupus Foundation of America, 6, Neutrolis Inc, 5; **R. Naden**, ACR/EULAR, 1, 2; **D. Erkan**, None.

Abstract Number: 0523

Characterization of Antiphospholipid Antibody-Associated Nephropathy: An International Survey of Renal Pathology Society Members

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Antiphospholipid Syndrome Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid antibody (aPL)-associated nephropathy (aPL-N) is recognized as a distinct complication of APS. However, it remains unclear whether pathologists worldwide use uniform diagnostic criteria to distinguish aPL-N from other forms of thrombotic microangiopathy. In parallel with international efforts to develop new classification criteria for antiphospholipid syndrome (APS), we conducted a pilot study to assess the renal pathologic features used by academic pathologists to diagnose aPL-N.

Methods: We conducted a web-based survey of 780 members of an international Renal Pathology Society in 50 countries. We asked respondents to determine whether two acute and eight chronic aPL-N features were consistent with acute or chronic aPL-N without providing aPL serology. and rate each item using a Likert scale (from +5 to -5): "Please consider two renal biopsies which are exactly the same except that one has the pathologic feature presented below and the other does not. Please rate how specific each feature is in differentiating "acute" or "chronic" aPL nephropathy from other diagnoses. They were also asked to rate their confidence in diagnosing aPL nephropathy on renal biopsy in two scenarios: 1) without aPL laboratory test results, or 2) with known lupus.

Results: Survey response rate was 14% (111/780) and 91% of participants self-identified as renal pathologists from 33 countries and in clinical practice for a mean (SD) of 19.1 (15.1) years. Over 92% of respondents agreed that thrombotic microangiopathy lesions in the glomeruli, arterioles, or arteries were consistent acute aPL-N, and >75% gave a positive Likert scale score (>0), with >50% indicating Likert score +3 to +5. For chronic aPL-N, >83% agreed with the pathologic features of organized arterial or arteriolar microthrombi with or without recanalization, organized

Table. Laboratory and Clinical Manifestations of 314 International Potential APS Cases, Overall and Categorized by Physician Assessment

Candidate Relative Criteria (*Number of individuals, %*)	Total (n=314)	Highly Likely APS (n=137)	Equivocal or Unlikely APS (n=177)	Risk Ratios
LABORATORY				
Lupus Anticoagulant Test Positive (persistent)	136 (43%)	92 (67%)	44 (25%)	2.70
Anticardiolipin Antibody Positive (persistent[¥])				
• IgG	113 (36%)	78 (57%)	35 (20%)	2.88
• IgM	78 (25%)	43 (31%)	39 (22%)	1.59
Anti-β_2-glycoprotein-I Antibody Positive (persistent)				
• IgG	72 (23%)	55 (40%)	17 (10%)	4.18
• IgM	52 (17%)	33 (24%)	19 (11%)	2.24
CLINICAL				
Macrovascular				
• Superficial Vein Thrombosis	15 (5%)	4 (3%)	11 (6%)	0.47
• Venous Thromboembolism	95 (30%)	63 (46%)	32 (18%)	2.54
• Transient Ischemic Attack	27 (9%)	13 (10%)	14 (8%)	1.20
• Arterial Thrombosis	82 (26%)	58 (42%)	24 (14%)	3.12
Microvascular*	70 (22%)	41 (30%)	29 (16%)	1.83
Obstetric (otherwise unexplained) **				
• Embryonic loss (<10 weeks 0 days)	85 (45%)	34 (42%)	51 (48%)	0.86
• Fetal loss (10 weeks 0 days – 15 weeks 6 days)	20 (11%)	9 (11%)	11 (10%)	1.86
• Fetal loss (16 weeks 0 days – 34 weeks 0 days)	42 (22%)	32 (40%)	19 (18%)	4.13
• Severe preeclampsia (< 34 weeks)	27 (14%)	18 (22%)	9 (8%)	2.58
• Severe placental insufficiency (<34 weeks)	22 (12%)	13 (16%)	9 (8%)	1.87
Cardiac Valve Disease***	27(9%)	18 (13.1%)	9 (5.1%)	2.58
Hematologic (platelet count <150 10^9/L)	93 (30%)	57 (42%)	36 (20%)	2.05

*Livedo racemosa, livedoid vasculopathy, adrenal hemorrhage, acute ischemic enceophalopathy, cardiac microvascular disease, pulmonary hemorrhage, acute antiphospholipid-related nephropathy, and/or chronic antiphospholipid-related nephropathy; **Total number of patients ever pregnant: 188 (highly likely APS: 81; unlikely APS: 107) ***Cardiac valve thickening and/or vegetation. ¥Persistent defined as positive on at least two occasions, at least 12 weeks apart.

Acknowledgement: The project is supported by ACR/EULAR.

glomerular thrombi, and fibrous and fibrocellular (arterial or arteriolar) occlusions, and >50% indicated a positive Likert score (>0), while there was less consensus for other chronic features (Table). The majority of respondents (76%) reported either an equivocal (Likert score of 0, 18%) or lack of confidence (score from -1 to -5, 58%) in diagnosing aPL-N on renal biopsy without of aPL laboratory test results. However, 80% indicated confidence (Likert score >0) in diagnosing aPL-N with concomitant lupus (69%) indicated Likert score +3 to +5.

Conclusion: Consensus exists among over 90% of pathologists worldwide that the following renal pathologic features are most specific for aPL-N: 1) non-inflammatory glomerular or small arterial microthrombi and 2) organized microvascular thrombi with recanalization. However, in the absence of serologic aPL status, over 75% of pathologists indicated lack of specificity of chronic glomerular or small arterial changes for aPL-N. Over 80% of pathologists indicated high confidence in diagnosing aPL nephropathy in patient with concomitant lupus. These findings indicate the importance of aPL serologic test results in biopsy interpretation and suggest higher specificity for certain acute or chronic features.

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Abstract Number: 0524

Determination of Homogenous Subgroups of Antiphospholipid Syndrome: A Cluster Analysis Based on 509 Cases

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SESSION INFORMATION
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Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid syndrome (APS) is a heterogeneous disease, with different phenotypes which may widely vary from classical thrombotic or obstetrical manifestations to catastrophic antiphospholipid syndrome (CAPS). APS can be associated with other auto-immune diseases, such as systemic lupus erythematosus (SLE). We aimed to determine distinct homogenous phenotypes among APS patients, using a non-supervised hierarchical cluster analysis.

Methods: We performed an observational, retrospective study on APS patients satisfying Sydney classification criteria and enrolled in the French multicentre “APS and SLE” registry. The clustering process involved an unsupervised multiple correspondence analysis followed by hierarchical ascendant clustering analysis, using 27 selected variables

Table 1. Main characteristics according to devised cluster (N=509).

	N available data	Cluster 1	Cluster 2	Cluster 3	Cluster 4	*P*
N	509	181	130	102	96	
Demographic						
Age, *mean (SD)*	509	34.4 (13.3)	**45.8 (15.0)**	30.7 (12.6)	33.1 (13.1)	<0.001
Gender, female	509	149 (82.3)	**84 (64.6)**	94 (92.2)	69 (71.9)	<0.001
Classification criteria						
Arterial thrombosis	509	10 (5.5)	**115 (88.5)**	21 (20.6)	66 (68.8)	<0.001
Venous thrombosis	**509**	**141 (77.9)**	25 (19.2)	**75 (73.5)**	41 (42.7)	<0.001
Small vessel thrombosis (biopsy proven)	509	3 (1.7)	1 (0.8)	2 (2.0)	**30 (31.2)**	<0.001
Pregnancy morbidity¶	396	55 (29.1)	10 (11.9)	**34 (36.2)**	**25 (36.2)**	<0.001
≥1 foetal death >10 wg¶	396	24 (16.1)	5 (6.0)	**27 (28.7)**	15 (21.7)	<0.001
≥1 premature birth <34 wg due to eclampsia, PE or placental insufficiency¶	396	**21 (14.1)**	4 (4.8)	6 (6.4)	9 (13.0)	0.037
≥3 consecutive foetal losses <10 wg¶	396	13 (8.7)	2 (2.4)	2 (2.1)	4 (5.8)	0.053
Associated manifestations						
CAPS	509	10 (5.5)	3 (2.3)	3 (2.9)	**74 (77.1)**	<0.001
APS-associated nephropathy	494	2 (1.1)	4 (3.2)	7 (7.0)	**88 (92.6)**	<0.001
Renal hypertension	480	0 (0.0)	2 (1.6)	3 (3.0)	**51 (61.4)**	<0.001
Livedo reticularis	488	10 (5.7)	**44 (35.2)**	18 (18.8)	**33 (35.9)**	<0.001
Seizures	486	2 (1.1)	10 (8.0)	8 (8.4)	**13 (14.3)**	0.001
Migraine	486	10 (5.7)	**26 (20.8)**	9 (9.5)	10 (11.0)	0.001
Chorea	486	0 (0.0)	1 (0.8)	1 (1.1)	**4 (4.4)**	0.020
Valvular involvement	490	0 (0.0)	**26 (21.1)**	7 (7.2)	**41 (43.6)**	<0.001
Associated diseases						
SLE	509	1 (0.6)	7 (5.4)	**78 (76.5)**	37 (38.5)	<0.001
Other autoimmune disease*	509	4 (2.2)	12 (9.2)	**31 (30.4)**	8 (8.3)	<0.001
Arterial hypertension	487	14 (8.0)	**60 (48.8)**	11 (11.2)	**45 (49.5)**	<0.001
Diabetes mellitus	486	4 (2.3)	**22 (17.7)**	1 (1.0)	5 (5.5)	<0.001
Dyslipidaemia	485	12 (6.9)	**65 (52.4)**	12 (12.2)	11 (12.4)	<0.001
Biology						
Haemolytic anaemia	486	1 (0.6)	2 (1.7)	**13 (13.5)**	7 (7.8)	<0.001
Lymphopenia	480	5 (2.9)	7 (5.8)	**22 (22.9)**	2 (2.2)	<0.001
Thrombocytopenia	490	17 (9.7)	25 (20.5)	**47 (48.0)**	**43 (45.7)**	<0.001
Lupus anticoagulant	509	128 (70.7)	85 (65.4)	**86 (84.3)**	**84 (87.5)**	<0.001
Anticardiolipin antibodies	509	134 (74.0)	100 (76.9)	82 (80.4)	**92 (95.8)**	<0.001
Anti-β2-GPI antibodies	509	114 (63.0)	86 (66.2)	53 (52.0)	**70 (72.9)**	0.019
Triple positivity	509	77 (42.5)	53 (40.8)	46 (45.1)	**63 (65.6)**	0.001
ANA	432	71 (51.1)	63 (59.4)	**98 (98.0)**	71 (81.6)	<0.001
Low C3	286	8 (9.3)	15 (21.1)	**51 (65.4)**	28 (54.9)	<0.001

Data are expressed as number (% of available data) unless stated otherwise.
Comparisons between different subgroups were performed with Chi-2 tests and ANOVAs.
¶Percentage of obstetrical manifestations were calculated among women only.
*Other autoimmune diseases included Sjögren syndrome, systemic sclerosis, rheumatoid arthritis, or chronic lymphocytic thyroiditis.
Abbreviations: N=number; wg= weeks of gestation; PE= preeclampsia; SLE=systemic lupus erythematosus; ANA=anti-nuclear antibody.

Table 1. Main characteristics according to devised cluster (N=509).

to widely cover APS clinical and biological manifestations. Comparisons between different subgroups were performed with Chi-2 tests and ANOVAs.

Results: We included 509 patients in the analyses, mainly women (78%). Mean (± SD) age at APS diagnosis was 36.3 ± 14.7 years, and mean follow-up duration after APS diagnosis was 10.3 ± 8.5 years. Cluster hierarchical classification yield in four homogenous groups of patients. Their main characteristics are described in *Table 1*.

1. Cluster 1 (n=181) included mostly patients with venous thrombosis (78%) and premature births due to placenta insufficiency (14%) history, without associated auto-immune disease (only 2.2%).
2. Cluster 2 (n=130) included older patients (mean 45.8 years), less frequently women (65% of women), with arterial events history (89%). Valvular involvement (21%), migraine (21%), livedo (35%), arterial hypertension (49%), and cardiovascular risk factors were relatively frequent.
3. Cluster 3 (n=102) included younger patients, frequently women (mean 30.7 years; 92% women), with associated SLE (76%) or other autoimmune diseases (30%). They frequently had history of venous thrombosis (74%) and of pregnancy morbidity (36%). Thrombocytopenia (48%), haemolytic anaemia (14%), and lupus anticoagulant (84%) were frequent.
4. Cluster 4 (n=96) included mainly patients with a history of CAPS (77%) and/or APS-associated nephropathy (93%), and pregnancy morbidity (36%). Renal hypertension (61%), livedo (36%), seizures (14%), valvular involvement (44%) and triple positivity (66%) were relatively frequent.

Conclusion: Using an unsupervised clustering method, our study highlighted four distinct homogenous subgroups of APS patients that were predominantly venous; arterial; associated with SLE or other autoimmune disease; and microthrombotic. It confirms the underlying idea of heterogeneous pathophysiological mechanisms.

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Abstract Number: 0525

Epidemiology of Thromboembolic Complications Among Hospitalized Patients with Antiphospholipid Syndrome in the United States

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SESSION INFORMATION
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Background/Purpose: Antiphospholipid syndrome (APLS) is characterized by arterial and venous thrombosis, often in the setting of an underlying systemic disease. Few studies have described the varied clinical presentations of this disease. This study aims to characterize healthcare expenditure and inpatient clinical outcomes of APLS using a nationally representative sample.

Methods: Patients with a diagnosis of APLS admitted to U.S. hospitals were identified using the ICD 10 CM classification system. The NIS is an all-payer inpatient database that estimates over 37 million annual U.S. hospitalizations

Table 1. In hospital thrombotic complications among hospitalized APLS patients in the United States, NIS 2016-2017		
Complication	**N (weighted)**	**%**
Venous Thromboembolism	6100	7.6
Stroke, ischemic	4445	5.6
Pulmonary Embolism	4015	5
Myocardial Infarction	2320	2.9
Stroke, hemorrhagic	1035	1.3
Portal and hepatic thrombosis	814	1
Mesenteric Ischemia	640	<1
Thrombophlebitis	619	<1
Renal Infarction	590	<1
Splenic Infarction	510	<1
Retinal Occlusion	116	<1
Intrauterine Demise	100	<1

and is maintained by the Healthcare Cost and Utilization Project. The primary outcomes were prevalence of APLS among hospitalized patients. Secondary outcomes included mortality, rate of acute thrombotic complications, and cost of care. Multivariate hierarchical regression analysis was used adjusting for demographics, hospital factors, and comorbid conditions.

Results: Of 79,835 patients identified in this retrospective cohort, 915 were primarily admitted for APLS. Patients were most commonly admitted for cardiovascular (22%), pregnancy-related (10.5%), gastrointestinal (9.3%) and infectious (6.5%) etiologies. Most patients were female (71.1%), white (66.5%) and had a mean age of 51.9 (51.5-52.2, 95% CI) years. Most patients were admitted to urban academic centers (77.7%) and had an average length of stay of 6.5 (6.3-6.6, 95% CI) days. The average hospitalization cost was $18,776 ($18,093-$19,458, 95% CI). 1,720 (2.2%) deaths occurred. The rates of acute arterial and venous thrombotic complications are summarized in Table 1. 21.7% of patients were diagnosed with systemic lupus erythematosus (SLE).

Conclusion: Acute thrombotic events remain a significant cause of morbidity and mortality among patients admitted for APLS. The prevalence of life-threatening thrombotic complications including pulmonary embolism, stroke, myocardial infarction and fetal demise were lower than previously reported [1,2]. These results may reflect overall improvements in disease detection and anticoagulation practices in the community setting and merit further investigation.

1. Cervera R. et al “Antiphospholipid Syndrome: Clinical and Immunologic Manifestations and Patterns of Disease Expression in a Cohort of 1,000 Patients” Arthritis Rheum. 2002 Apr;46(4);1019-27

2. Andreoli L. et al. “Estimated Frequency of Antiphospholipid Antibodies in Patients With Pregnancy Morbidity, Stroke, Myocardial Infarction, and Deep Vein Thrombosis: A Critical Review of the Literature.” Arthritis Care Res. 2013 Nov; 65(11):1869-73

Disclosure: L. Mathias, None; **A. Mantha**, None; **K. Mathias**, None; **G. Ehresmann**, None.

Abstract Number: 0526

Patient-Reported Outcomes in Antiphospholipid Syndrome

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SESSION INFORMATION
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Session Type: Poster Session B
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Background/Purpose: PROMIS® (Patient-Reported Outcome Measurement Information System) is a set of person-centered measures that evaluates and monitors the physical, emotional, and social aspects of health. PROMIS® measures have been used to assess health-related quality of life (HRQoL) in patients with rheumatic diseases1 and cut-points of severity in impairments have been identified for specific domains (like physical function). These measures have not been carefully evaluated in patients with persistent antiphospholipid antibodies (**aPL**) or with antiphospholipid syndrome (**APS**).

Methods: At an academic medical center, patients (n = 78) with persistent aPL seen in the rheumatology clinic prospectively completed PROMIS® Physical Function (**PF**) Short Form 10A v2.0, Cognitive Function (**CF**) Short Form 8A, and self-perceived pain intensity (**PI**, the scale of 1-10, with 10 being the most pain). Of the 78 patients, 51 had primary APS, 17 had secondary APS, and 10 had persistent aPL without a history of thrombotic event or pregnancy loss. Data regarding serologies and clinical manifestations associated with APS were captured; also, medications taken for mental health, pain, or seizures were recorded. Groups were compared by unpaired t-tests or one-way ANOVA; correlations were tested by Pearson's method.

Results: For the general United States population, the T-score average is standardized at 50 ± 10 for PF and CF. For the 78 patients studied here, the average T-scores for PF and CF were 45.0 ± 9.8 and 47.5 ± 10.9, respectively; the average score for PI was 3.2 ± 2.6. Patients who endorsed more impairment on one measure endorsed more impairment on another measure (PF vs. CF, r=0.51, p< 0.0001; PF vs. PI, r=-0.55, p< 0.0001; and CF vs. PI, r=-0.33, p=0.004). About a third of the patients endorsed moderate to severe impairment in PF (**Table 1**). A quarter of the patients had a T-score of < 40 for CF. While clinical markers of disease (specific aPL, previous thrombotic events, etc.) did not predict PROMIS® scores, several general health and lifestyle factors (especially sedentary lifestyle) were predictive of impairments in PF and CF (**Table 2**). The use of medications for mental health or pain was associated with more endorsed impairments in PF and CF (**Table 3**).

Conclusion: In this single-center cohort of patients with positive aPL (most of whom have APS), a large minority of patients endorsed impairments in PF and CF. Health and lifestyle factors such as sedentary lifestyle and smoking and

Table 1: Physical and cognitive PROs for 78 persistently aPL-positive individuals

	T-score ranges, N (%)			
	>45	40-45	30-40	<30
Physical function	43 (55%)	13 (17%)	16 (21%)*	6 (8%)**
Cognitive function	47 (60%)	13 (17%)	13 (17%)	5 (6%)

*Moderate impairment in physical function
**Severe impairment in physical function

Table 1

Table 2: Effects of health and lifestyle on PROs for 78 persistently aPL-positive individuals									
	History of smoking			Sedentary lifestyle			Obesity		
	Yes (n=34)	No (n=44)	p	Yes (n=57)	No (n=21)	p	Yes (n=47)	No (n=31)	p
Physical function	42 ± 10	47 ± 9	**0.03**	43 ± 10	51 ± 8	**0.0003**	43 ± 9	48 ± 10	**0.03**
Cognitive function	45 ± 13	49 ± 9	0.07	46 ± 11	52 ± 9.1	**0.03**	46 ± 11	50 ± 11	0.19
Pain intensity*	3.9 ± 2.7	2.6 ± 2.5	**0.04**	3.6 ± 2.6	2.1 ± 2.4	**0.02**	3.6 ± 2.8	2.5 ± 2.2	0.067
*Pain intensity is on a scale of 1-10 (with 10 being the most pain) and is not a PROMIS® measure.									

Table 2

Table 3: Medications and PROs for 78 persistently aPL-positive individuals						
	Mental health medications			Pain medications		
	Yes (n=31)	No (n=47)	p	Yes (n=66)	No (n=12)	p
Physical function	42 ± 9	46 ± 10	0.07	35 ± 9	47 ± 10	**<0.0001**
Cognitive function	43 ± 11	50 ± 10	**0.01**	44 ± 10	50 ± 11	**0.006**
Pain intensity*	3.8 ± 2.7	2.8 ± 2.6	0.17	3.6 ± 2.6	2.8 ± 2.5	**0.0005**
*Pain intensity is on a scale of 1-10 (with 10 being the most pain) and is not a PROMIS® measure.						

Table 3

the use of certain medications (for mental health or pain) were associated with higher self-reported impairments in PF and CF. Future directions for this study include: (a) increasing the size of the cohort, (b) tracking these PROMIS® measures over time, (c) identifying cut-points of self-reported impairment in CF in comparison with legacy measures, and (d) identifying any correlation with biomarker data.

1. Nagaraja, V., Mara, C., Khanna, P.P. *et al.* Establishing clinical severity for PROMIS® measures in adult patients with rheumatic diseases. *Qual Life Res* **27,** 755–764 (2018).

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Abstract Number: 0527

Rituximab for Refractory Manifestations of the Antiphospholipid Syndrome: A Multicenter Israeli Experience

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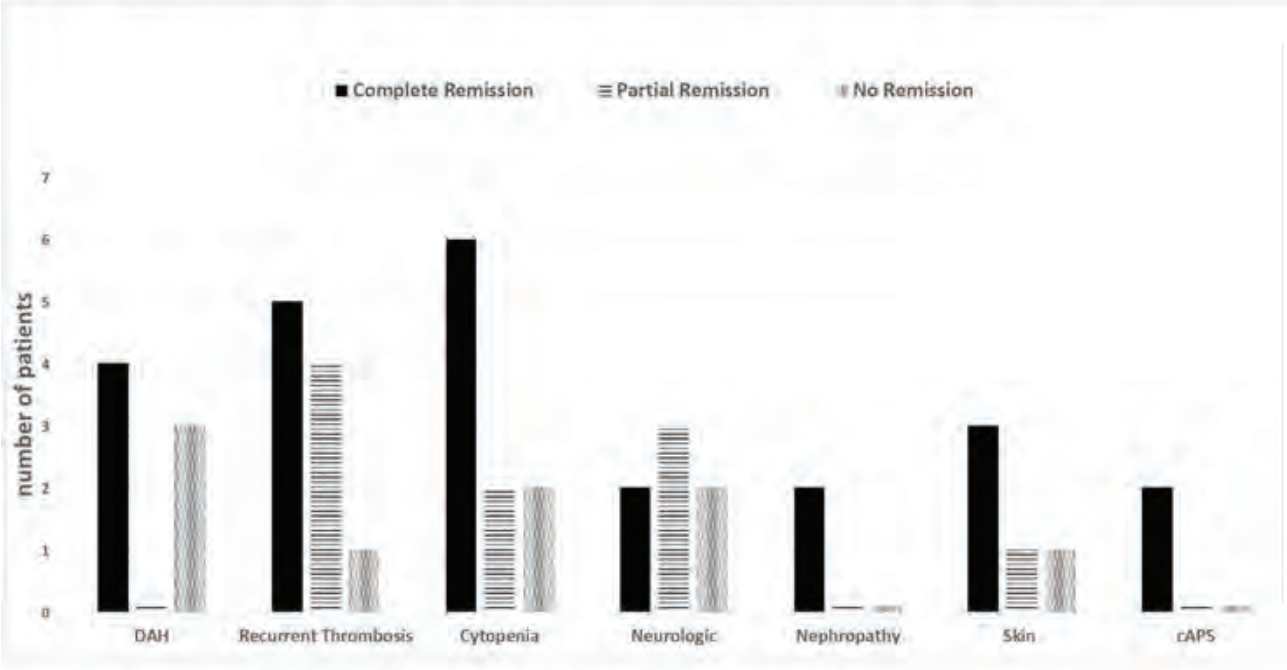
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The clinical manifestations of the antiphospholipid syndrome (APS) are heterogeneous and related to anti-phospholipid antibodies (aPL). There is some evidence that B cells are involved in the pathogenesis of this condition. Thus the ability of rituximab (RTX) to deplete B cells makes it an appealing potential therapy for refractory antiphospholipid syndrome (APS). Real world data on RTX treatment of APS is still lacking. This study was conducted to report outcomes of RTX administration in the treatment of different aspects of APS.

Methods: This is a retrospective case series study on APS patients from 3 medical centers in Israel who were treated with RTX during 2010-2019 for refractory manifestations of APS including diffuse alveolar hemorrhage, recurrent thrombosis, thrombocytopenia, neurological and skin manifestations. Medical records were reviewed regarding the clinical indication for RTX treatment, concomitant medications, RTX protocol, aPL status and response to treatment. Outcomes were defined as complete response if full resolution of the "indicated manifestation" was achieved and maintained for at least 12 months, partial response or no response

Results: We identified 40 patients who were treated with RTX for refractory APS, 31 patients had primary APS (78%), 24 (60%) were female, mean age was 40 years. A favorable response to RTX was documented in 32 patients (80%) including complete response in 22 (55%). A RTX regimen of 375mg/m2 X 4 was more effective than a regimen of 1000 mgx2 (100% vs. 65%; p=0.01).

Fig. 1 Response to treatment with Rituximab according to APS manifestations



DAH – diffuse alveolar hemorrhage; cAPS- catastrophic APS.

Complete response was associated with a decrease in aPL titers 4-6 months post treatment. No significant change in aPL titers was observed in patients with partial or no response.

Conclusion: Consistent with previous small case series, we report a good therapeutic response to RTX in patients with difficult to treat manifestations of APS. In this cohort, treatment protocols were associated with outcomes. Although further studies are required to verify our observations, our data support a plausible role for B cell depletion in refractory APS.

Disclosure: N. Agmon-Levin, None; **M. Berman**, None; **L. Harel**, None; **M. Lidar**, None; **S. Hajyahia**, None; **D. Paran**, None.

Abstract Number: 0528

The Complex Relationship Between C4b Binding Protein, Warfarin and Antiphospholipid Antibodies

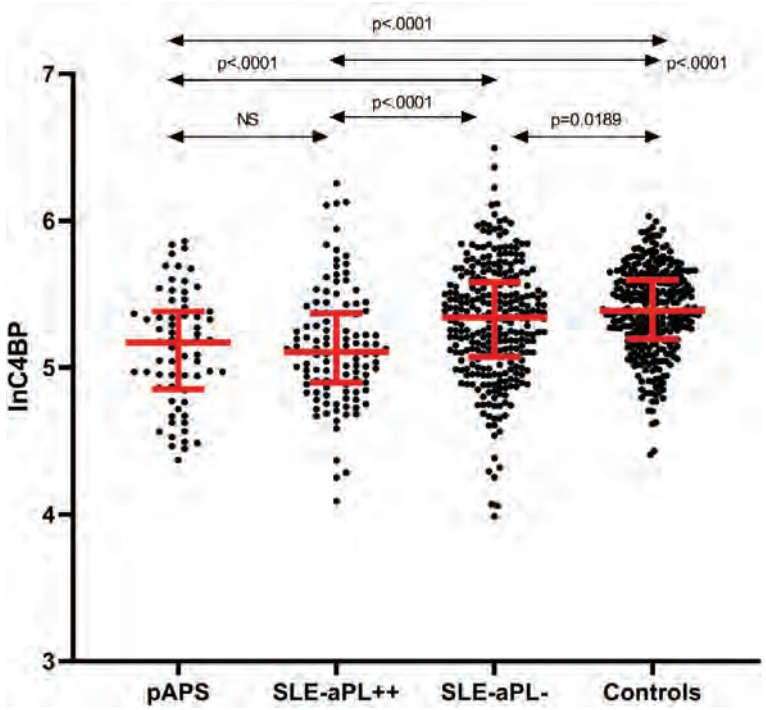
Giorgia Grosso[1], Kerstin Sandholm[2], Aleksandra Antovic[1], Iva Gunnarsson[1], Agneta Zickert[1], Anna Vikerfors[3], Lennart Truedsson[4], Maria Bruzelius[1], Bo Nilsson[5], Kristina Nilsson Ekdahl[5] and Elisabet Svenungsson[1], [1]Karolinska University Hospital, Stockholm, Sweden, [2]Linnaeus Center for Biomaterials Chemistry, Linnaeus University, Kalmar, Sweden, [3]Swedish Medical Products Agency, Uppsala, Sweden, [4]Lunds University, Lund, Sweden, [5]Uppsala University, Uppsala, Sweden

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

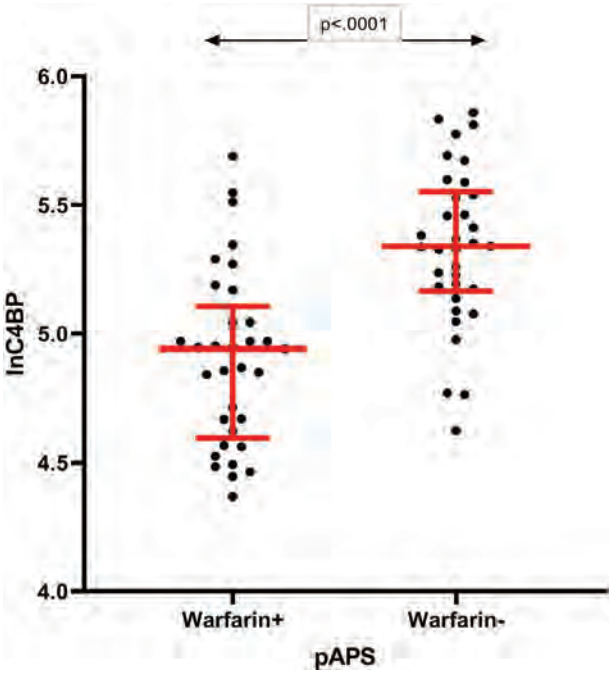
Background/Purpose: C4b Binding Protein (C4BP) is the main inhibitor of the classical complement pathway. Both β2glycoprotein-I (β2GPI), the main antigen in the antiphospholipid syndrome (APS), and C4BP, belong to the Complement Control protein (CCP) family. C4BP binds to protein S (PS) in circulation. Low C4BP levels are reported in the presence of antiphospholipid antibodies (aPL) and during treatment with vitamin K antagonists (VKA). / To investigate if levels of C4BP vary with aPL profile, clinical manifestations and anticoagulant treatment in primary (p) and secondary (s) APS.

Methods: C4BP, complement proteins and PS were investigated in 67 patients with pAPS, 67 age and sex matched controls and 15 individuals with repeated positivity (++) for aPL (nonSLE-aPL++) without clinical manifestations. Moreover, 118 SLE-aPL++, of which 56 with sAPS, 291 aPL negative SLE patients (SLE-aPL-) and 322 controls were included. Clinical characteristics, including treatment, were tabulated. C4BP was determined with a magnetic bead-beased sandwich immunoassay. Additional proteins in the complement cascade (C1q, C2, C3, C4, C3a, C3dg, sC5b-9, Factor I) were measured.

Results: C4BP is 20% decreased in aPL++ patients, independently of SLE or clinical manifestations (fig. 1). We report positive associations between C4BP and complement proteins C1q, C2, C3, C4, whereas C4BP associates negatively with complement activation products (C3a, C3dg) ($p < 0.05$ for all). Treatment with warfarin contributes to C4BP reduction by 9% (fig.2) according to mediation analysis performed in the SLE group: since warfarin is mostly prescribed to aPL+ patients, it is considered a mediator in the reducing effect of aPL on C4BP.



Levels of C4BP in different subgroups of patients: pAPS (n=67), SLEaPL++ (n=118), SLEaPL- (n=291) and controls (n=322)



C4BP in 67 pAPS patients, 33/67 on warfarin

Conclusion: Both the presence of aPL and warfarin treatment are associated with decreased levels of C4BP. Furthermore, higher complement degradation products are observed in patients with low C4BP levels, indicating that depressed levels of C4BP may, through reduced inhibition, contribute to complement activation in APS.

Disclosure: G. Grosso, None; **K. Sandholm**, None; **A. Antovic**, None; **I. Gunnarsson**, None; **A. Zickert**, None; **A. Vikerfors**, None; **L. Truedsson**, None; **M. Bruzelius**, None; **B. Nilsson**, None; **K. Nilsson Ekdahl**, None; **E. Svenungsson**, None.

Abstract Number: 0529

A Prospective Study on the Incidence of a First Thrombo-embolic Event in Patients with Systemic Lupus Erythematosus and Anti-phosphatidylserine/prothrombin Antibodies

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

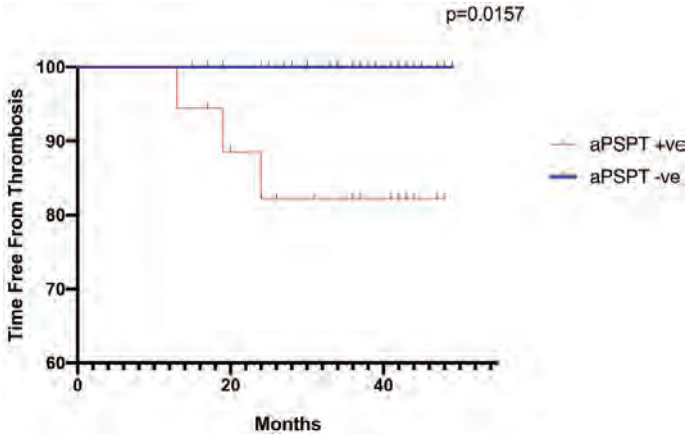
Background/Purpose: Prospective data confirming the role of anti-phosphatidylserine/prothrombin antibodies **(**aPS/PT) in the absence of other aPL tested by β2–glycoprotein I-depend assays are missing.

Methods: Since 2015 aPSPT was implemented as part of the routine testing in our SLE patients as part of the autoantibody screening. Patients with the revised criteria for SLE and fulfilling the following criteria were included in this study and prospectively followed-up.

- No previous TEs
- No concomitant anticoagulant therapy
- Negative tests aCL, anti-β2GPI (confirmed at least twice, at least 12 weeks apart)

All included patients were tested for aPS/PT at study inclusion. Positivity aPS/PT was defined as having at least two positive test results (IgG and/or IgM), at least 12 weeks apart.

Reports for objectively diagnosed TEs during follow-up had to include type, site, and the status of antithrombotic treatment at the time of event.



Results: This study included a total of 52 patients with SLE (42, 80.8% women). Of those 18 patients (34.6%) were found to be positive for aPS/PT (IgG and/or IgM). During a total follow-up of 238 years, there were 3 TEs (1.26% per year). The overall cumulative incidence of TEs was 5.8% after 2 years, being up to 16.7% when focusing on aPS/PT+ve patients (Figure 1). All the TEs events (2 cerebrovascular events and 1 thrombotic kidney microangiopathy) occurred in the aPS/PT+ve group. TEs not included among end-points were superficial thrombophlebitis in 2 subjects. No patient died and no pregnancy was recorded during the follow-up. The 3 patients with TEs were compared with the controls who did not have this complication. All patients tested negative for aB2GPI Domain 1 IgG.

aPS/PT was found to be associated with a trend in conferring an increased risk for TE (HR 12.9, 95% CI 0.70 to 236.74 p= 0.0851). When focusing on IgG aPS/PT we found that patients tested positive were at a significant higher risk for TEs (HR 19.6, 95% CI 1.0741 to 357.6416 p= 0.0446) when compared to controls.

Patients with TEs had a higher GAPSS when compared to those without, even if it failed to reach a statistically significance [6±2.64 Vs. 2±5.37, p=0.0971], probably due to sample size.

On multivariate analysis of considered variables (demographic factors, SLE features, arterial and venous risk factors), no factors was found to be statistically associated with the TEs.

Conclusion: Our prospective data validated previous retrospective studies demonstrating that aPS/PT, especially IgG, confers an increased risk for TEs in SLE patients.

Disclosure: S. Sciascia, None; **M. Radin**, None; **I. Cecchi**, None; **D. Rossi**, None; **D. Roccatello**, None.

Abstract Number: 0530

Pediatric APS: Clinical Features, Therapeutic Interventions, and Damage in a Series of 22 Cases

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Antiphospholipid Syndrome Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Pediatric antiphospholipid syndrome (APS) is a thromboinflammatory disease classically defined by the presence of circulating antiphospholipid antibodies and either thrombotic events or pregnancy morbidity. Despite its potential to cause significant morbidity in children, pediatric APS is an understudied condition that lacks classification criteria specific to the pediatric age group. The objective of this study was to review a large institution's experience with pediatric APS in pursuit of a better understanding of the characteristics of children with APS.

Methods: We conducted a retrospective review of pediatric APS at a tertiary referral center. The electronic medical record system was queried for patients aged 21 and younger with a diagnosis of APS from 2000 through 2019. Fifty cases were evaluated further, and 22 were ultimately included in this study based on meeting the revised Sapporo Classification criteria by age 18 or younger.

Table 1: Demographics and clinical manifestations of pediatric APS patients

Characteristics	APS patients (n=22)
Median age at diagnosis	16 years (range 8-18)
Median duration of follow-up	5.8 years (range 0.8-15.3)
Sex, N (%)	
Male	6 (27.3%)
Female	16 (72.7%)
Primary APS	10 (45.5%)
Secondary APS	12 (54.5%)
SLE	10 (45.5%)
Ulcerative colitis	1 (4.5%)
Microscopic polyangiitis	1 (4.5%)
Type of APS	
Obstetric	1 (4.5%)
Thrombotic	21 (95.5%)

Table 2: Clinical and laboratory features of pediatric APS patients

Disease Features	Primary APS (n=10)		Secondary APS (n=12)		p value
Clinical Manifestations	Number	(%)	Number	(%)	
Obstetric	0	(0%)	1	(8.3%	0.55
Thrombotic	10	(100%)	11	(91.7%)	0.55
Venous	8	(80%)	6	(50%)	0.16
Arterial	1	(10%)	6	(50%)	0.05
Small Vessel	3	(30%)	3	(25%)	0.80
Catastrophic APS	0	(0%)	1	(8.3%)	0.54
Non-criteria Manifestations					
Thrombocytopenia	6	(60%)	6	(50%)	0.65
Autoimmune hemolytic anemia	4	(40%)	6	(50%)	0.65
Livedo reticularis/racemosa	3	(30%)	2	(16.7%)	0.47
APS nephropathy	1	(10%)	1	(8.3%)	0.71
Seizure	1	(10%)	2	(16.7%)	0.66
White matter lesions	1	(10%)	2	(16.7%)	0.66
Skin ulcer	0	(0%)	2	(16.7%)	0.48
Valve abnormality	1	(10%)	0	(0%)	0.45
Cognitive changes	0	(0%)	1	(8.3%)	0.55
Multiple sclerosis-like features	0	(0%)	1	(8.3%)	0.55
Laboratory Manifestations					
Anti-beta-2-glycoprotein I	8	(80%)	8	(66.7%)	0.49
Anti-cardiolipin	9	(90%)	8	(66.7%)	0.20
Lupus anticoagulant	6	(60%)	6	(50%)	0.65
Triple Positive	8	(80%)	7	(58.3%)	0.29
ANA	0	(0%)	10	(83.3%)	**0.0001**
Anti-double-stranded DNA	1	(10%)	10	(83.3%)	**0.0008**
Anti-chromatin	1	(10%)	7	(58.3%)	**0.02**
Anti-Smith	0	(0%)	3	(25%)	0.10
Recurrence of Thrombosis	5	(50%)	3	(25%)	0.24
Mean DIAPS[1] Score (95% CI)	1.50 (+/- 1.14)		1.25 (+/- 0.43)		0.69

[1] Damage Index in Patients with Thrombotic APS

Results: Twenty-two patients were included with a median age at diagnosis of 16 years and median follow-up of 5.8 years (**Table 1**). Of the cases, 72.7% were in female patients (**Table 1**). Secondary APS was slightly more common than primary APS (12 versus 10 cases) and was primarily diagnosed in the context of SLE (10/12 cases). With regards to clinical features, 1 patient had obstetric APS and 21 patients had thrombotic APS (**Table 1**). Many patients (both primary and secondary APS) had so-called "non-criteria" manifestations of APS includingthrombocytopenia, autoimmune hemolytic anemia, and livedo reticularis/racemosa (**Table 2**). Patients had durably positive anti-beta-2-glycoprotein I antibodies in 73% of cases, anticardiolipin antibodies in 77%, and lupus anticoagulant in 55%. Secondary

APS patients were more likely to be positive for ANA, anti-double-stranded DNA, and anti-chromatin antibodies (**Table 2**). Two patients were tested for anti-phosphatidylserine/prothrombin antibodies, and both were positive. Both primary and secondary groups had recurrent thromboses without any significant difference in rates between the groups (**Table 2**), often when patients were subtherapeutic foranticoagulation. Although two patients were treated with aspirin alone, the majority (86%) received anticoagulation with warfarin or heparinoids; 41% (9/22) were treated with both aspirin and anticoagulation. Direct oral anticoagulants and fondaparinux were used in four patients each. The Damage Index in Patients with Thrombotic APS (DIAPS) scores indicate a significant burden of disease (**Table 2**).

Conclusion: This is the largest case series to date of pediatric APS in a United States population, and thereby provides important context regarding potential phenotypes displayed by children with APS. There was a high prevalence of non-criteria clinical manifestations, highlighting the need to consider these additional characteristics when developing pediatric-specific classification criteria and, most importantly, when considering this rare diagnosis in pediatric practice.

Disclosure: J. Madison, None; **K. Gockman**, None; **J. Knight**, None.

Abstract Number: 0531

The Prevalence of Systemic Sclerosis, Dermatomyositis/Polymyositis, and Giant Cell Arteritis in the United States by Race and Ethnicity: An Analysis Using Electronic Health Records

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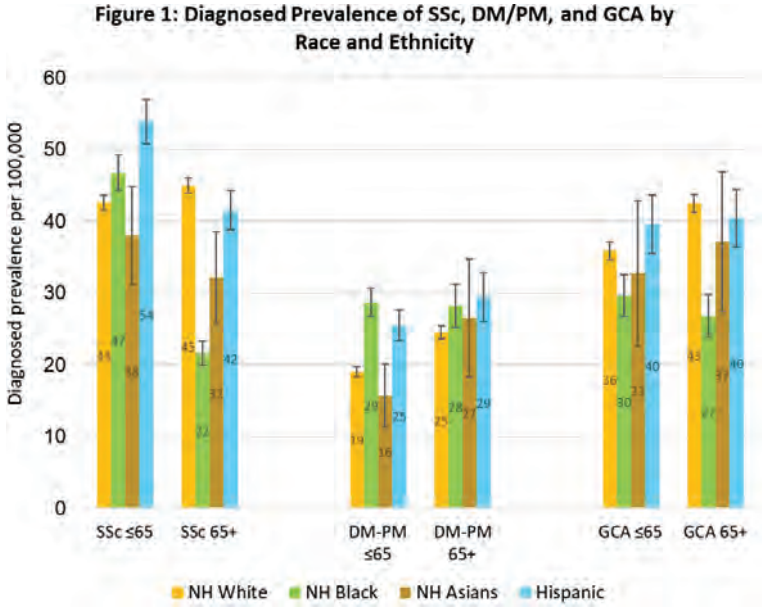
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Epidemiological studies suggest differences in the prevalence and disease severity of certain autoimmune diseases by race and ethnicity. In this study, we evaluate the distribution of three rare connective-tissue diseases i.e., systemic sclerosis (SSc), dermatomyositis/polymyositis (DM/PM), and giant cell arteritis (GCA), in different racial/ethnic groups in the United States using data from electronic health records (EHR).

Methods: We restricted the study population to patients aged 20 or older, who had submitted at least two insurance claims in 2018 (Real World Data. Decision Resources Group, 2020), and had no missing information in their EHR regarding age, gender, and race/ethnicity. We categorized the patients with respect to age (≤65 versus 65+ for SSC and DM/PM; 50-65 versus 65+ for GCA) and race/ethnicity (non-Hispanic White (NHW), non-Hispanic Black (NHB), Hispanic, and non-Hispanic Asian (NHA)). To be considered a case, a patient was required to have at least two diagnoses recorded for each autoimmune disease in 2018. For each racial/ethnic category, we estimated the age-group-specific diagnosed prevalence of SSc, DM/PM, and GCA, and calculated the diagnosed prevalence ratios for NHBs, Hispanics, and NHAs using NHWs as the referent population.

Results: In persons aged ≤65, we observed a significantly increased risk of SSc in NHBs (RR=1.10; 95% CI = 1.04-1.16) and Hispanics (RR = 1.26, 95% CI = 1.19-1.35) as compared to the NHW population, but not in NHAs (RR =



Diagnosed prevalence of SSc, DM/PM, and GCA by race and ethnicity

Table 1: Risk Ratios (95% Confidence Intervals) for SSc, DM/PM, and GCA _ minority ethnicities versus non-Hispanic Whites

	SSc ≤65	SSc 65+	DM/PM ≤65	DM/PM 65+	GCA ≤65	GCA 65+
Non-Hispanic White (Referent)	1.0	1.0	1.0	1.0	1.0	1.0
Non-Hispanic Black	1.1 (1.0-1.2)*	0.5 (0.4-0.5)***	1.5 (1.4-1.6)***	1.2 (1.0-1.3)*	0.8 (0.7-0.9)**	0.6 (0.6-0.7)***
Non-Hispanic Asian	0.9 (0.7-1.1)	0.7 (0.6-0.9)**	0.8 (0.6-1.1)	1.1 (0.8-1.5)	0.9 (0.7-1.2)	0.9 (0.7-1.1)
Hispanic	1.3 (1.2-1.4)***	0.9 (0.9-1.0)*	1.3 (1.2-1.5)***	1.2 (1.1-1.4)*	1.1 (1.0-1.2)	1.0 (0.9-1.1)

*$p < 0.05$; **$p < 0.001$; ***$p < 0.0001$

Risk ratios (95% confidence intervals) for SSc, DM/PM, and GCA _ minority ethnicities versus non-HIspanic Whites

0.89, 95% CI = 0.74-1.07). Interestingly, the pattern was reversed in NHBs aged 65+, with a significantly lower diagnosed prevalence of SSc (RR = 0.48; 95% CI = 0.44-0.52) as compared to NHWs. We also observed a reduced risk of SSc in Hispanics (RR=0.92, 95% CI = 0.86-0.99) and in NHAs (RR = 0.71; 95% CI = 0.58-0.87) in the older age-group. The risk of DM/PM in both age-groups was elevated in NHBs (ages ≤65: RR = 1.51, 95% CI = 1.40-1.63; ages 65+: RR = 1.15, 95% CI = 1.03-1.29) and Hispanics (ages ≤65: RR = 1.34, 95% CI = 1.22-1.47; ages 65+ RR = 1.20, 95% CI = 1.06-1.35) as compared to NHWs, but not in NHAs (ages ≤65: RR = 0.83, 95% CI = 0.62-1.10; ages 65+: RR = 1.08, 95% CI = 0.79-1.48). We observed a significantly reduced risk of GCA in NHBs in both age groups (ages ≤65: RR = 0.83, 95% CI = 0.75-0.92; ages 65+: RR = 0.63, 95% CI = 0.56-0.71) as compared to NHWs, while no significant difference was observed in Hispanics (ages ≤65: RR = 1.10, 95% CI = 0.99-1.23; ages 65+: RR = 0.95, 95% CI = 0.86-1.05) and in NHAs (ages ≤65: RR = 0.91, 95% CI = 0.67-1.25; ages 65+: RR = 0.87, 95% CI = 0.67-1.14).

Conclusion: Our results concur with findings of other epidemiological studies that have observed a higher prevalence of SSc and DM/PM and a lower prevalence of GCA in certain ethnic groups as compared to NHWs. However,

the lower prevalence of SSC observed in NHBs and Hispanics aged 65+ warrants further investigation, as it may indicate early mortality in these patients known to experience more severe disease.

Disclosure: S. Goonesekera, None; **A. Bansal**, None; **S. Tadwalkar**, None; **A. Isherwood**, None.

Abstract Number: 0532

State-Specific Percentage of Adults with Arthritis Who Report Both Severe Joint Pain and Physical Inactivity and Their Characteristics, United States, Behavioral Risk Factor Surveillance System, 2017

Dana Guglielmo[1], Louise Murphy[1], Jennifer Hootman[1], Michael Boring[1], Kristina Theis[1], Charles Helmick[1], Susan Carlson[1], Yong Liu[1], Hua Lu[1] and Janet Croft[1], [1]Centers for Disease Control and Prevention, Atlanta, GA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: About one in four (27%) US adults with arthritis have severe joint pain, and only 36% meet the Physical Activity Guidelines for Americans. While low-impact physical activity can relieve arthritis pain, improve physical functioning, and prevent or delay arthritis-related disability, pain itself is the most frequently reported barrier to physical activity among adults with arthritis. The study purpose was to estimate, among adults with arthritis, percentages of reporting both severe joint pain and physical inactivity: 1) for each of the 50 states and District of Columbia, and 2) overall by selected sociodemographic and health-related characteristics.

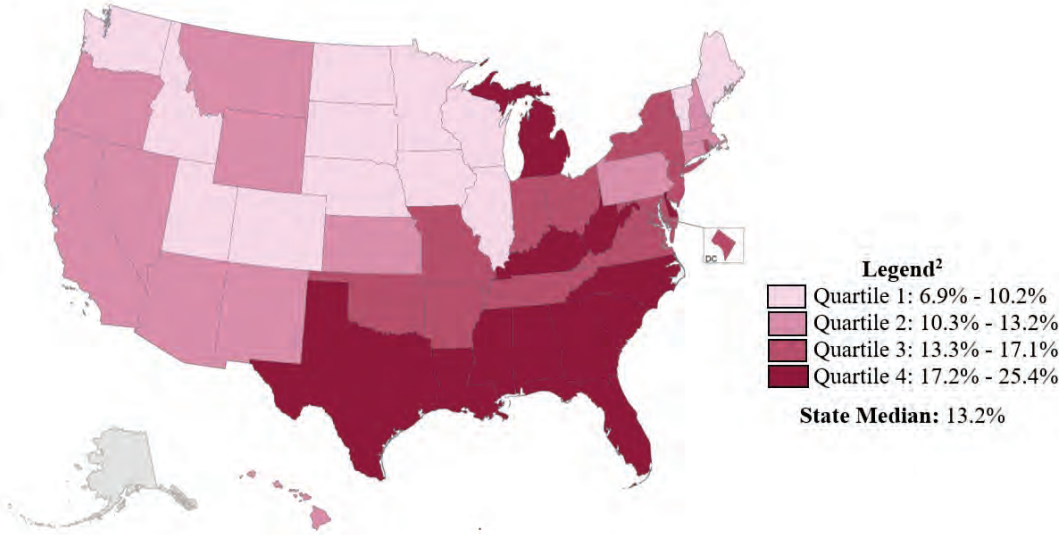
Methods: We analyzed 2017 Behavioral Risk Factor Surveillance System data (unweighted n=134,405 adults with arthritis). We used standard definitions of arthritis, severe joint pain, and physical inactivity (Table). We generated age-specific or age-adjusted percentages with 95% confidence intervals (CIs) for all outcomes. Differences between subgroups were assessed using t-tests and linear patterns in ordinal variables using tests for trends (i.e., orthogonal linear contrasts) (α=0.05). We accounted for the complex survey design by applying sampling weights and adjusting variance.

Results: In 2017, the median state age-adjusted percentage of reporting both severe joint pain and physical inactivity among adults with arthritis was 13.2% (range: 6.9% [Wisconsin]-25.4% [Mississippi]), with higher percentag-

Table. Variable Definitions

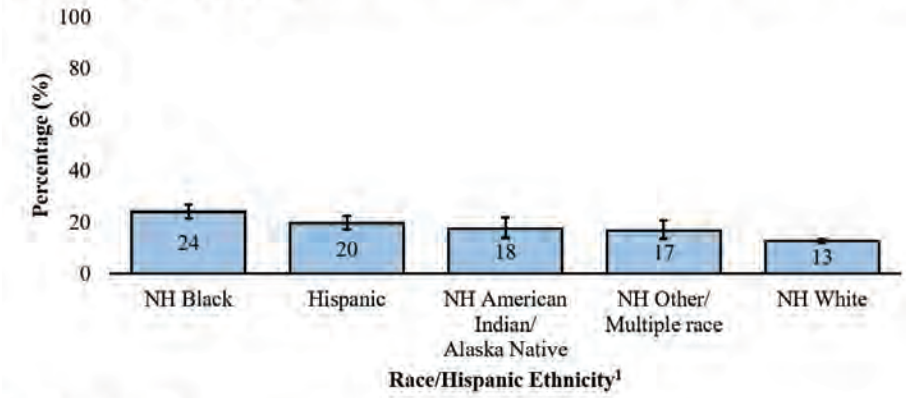
Variable	Definition
Arthritis	Response of "yes" to "Have you ever been told by a doctor or other health care professional that you have arthritis, rheumatoid arthritis, gout, lupus, or fibromyalgia?"
Severe Joint Pain	Response of "7," "8," "9," or "10" to "Please think about the past 30 days, keeping in mind all of your joint pain or aching and whether or not you have taken medication. On a scale of 0 to 10 where 0 is no pain or aching and 10 is pain or aching as bad as it can be, during the past 30 days, how bad was your joint pain on average?"
Physical Inactivity	Response of "no" to "During the past month, other than your regular job, did you participate in any physical activities or exercises such as running, calisthenics, golf, gardening, or walking for exercise?"

Figure 1. Age-Adjusted[1] State-Specific Percentage of Adults Aged ≥18 Years with Arthritis who Report Both Severe Joint Pain and Physical Inactivity — Behavioral Risk Factor Surveillance System, 50 states and District of Columbia, 2017



[1]Estimates were age-standardized to the 2000 projected U.S. population aged ≥18 years using three groups (18–44 years, 45–64 years, and ≥65 years).
[2]Estimates for Nevada and Hawaii were unreliable (relative standard error 20-30%); estimate for Alaska was suppressed (relative standard error >30%).

Figure 2. Age-Adjusted Percentage of Adults with Arthritis who Report Both Severe Joint Pain and Physical Inactivity, by Race/Hispanic Ethnicity, Behavioral Risk Factor Surveillance System, 50 States and District of Columbia



NH: Non-Hispanic
[1]Estimate for non-Hispanic Asians was suppressed (relative standard error >30%).

es in South and Southeast states (Figure 1). Age-specific percentage was higher among those aged 45-64 years (17.3% [95% CI: 16.6-18.1]) compared with those aged 18-44 years (14.2% [95% CI: 12.9-15.6]) and those aged >65 years (13.2% [95% CI: 12.6-13.9]). Age-adjusted percentages were highest in their respective subgroups for females (17.2% [95% CI: 16.1-18.3]), those with < high school graduation (27.9% [95% CI: 25.0-31.0]), non-Hispanic blacks (24.2% [95% CI: 21.5-27.0]) (Figure 2), Hispanics (19.7% [95% CI: 17.3-22.4]) (Figure 2), and those with obesity (18.5% [95% CI: 17.2-19.9]). Age-adjusted percentage for those unable to work/disabled (36.7% [95% CI: 34.4-39.0]) was more than four times higher than for those employed/self-employed (8.8% [95% CI: 8.0-9.6]). Age-adjusted percentage was similar across urban/rural geographic areas, ranging from 14.9%–17.1% in all areas, except for a slightly lower prevalence (13.1%) in large fringe metro areas.

Conclusion: Across states, about 1-in-8 adults with arthritis reported both severe joint pain and physical inactivity. The percentage was even higher among specific subgroups (e.g., 1-in-3 adults unable to work/disabled, 1-in-4 non-Hispanic blacks), making them an important target for evidence-based physical activity programs. These programs, available in most states, can safely reduce the compound effects of severe joint pain and physical inactivity by helping adults with arthritis reduce pain and increase physical functioning and quality-of-life.

Disclosure: D. Guglielmo, None; **L. Murphy**, None; **J. Hootman**, None; **M. Boring**, None; **K. Theis**, None; **C. Helmick**, None; **S. Carlson**, None; **Y. Liu**, None; **H. Lu**, None; **J. Croft**, None.

Abstract Number: 0533

Characterization of Older Male Patients with a Fragility Fracture

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoporosis is associated with significant burden in terms of adverse patient outcomes, mortality, and cost; and is particularly common in the older Medicare population. Approximately a quarter of patients with fractures are male. Emerging evidence suggests worse outcomes related to osteoporotic fractures in male compared to female patients.The objective of this study was to examine baseline characteristics of male Medicare patients who experienced a fragility fracture.

Methods: We studied Medicare fee-for-service (FFS) beneficiaries with a closed fragility (or osteoporosis-related) fracture between 01 January 2010 and 30 September 2014 (identification period). Additional inclusion criteria included age ≥65 years as of the index date, continuous enrollment in Medicare FFS with medical and pharmacy benefits (parts A+B+D-C) for a minimum of one year prior to the index date, through at least 1 month after (i.e. beneficiaries were excluded if they died within 30 days of the index date). Patients with Paget's disease or malignancy (except for non-melanoma skin cancer) at baseline were excluded. Patients were classified into four cohorts based on the observed diagnoses and/or treatment of osteoporosis at baseline. Diagnoses of osteoporosis could be in any position on any medical claim.

Results: A total of 9,876 beneficiaries met eligibility criteria. Sixty-one percent were ≥75 years of age and 90.3% were white. Fewer than 6% had undergone bone mineral density testing with DXA in the 2 years prior to their fracture. 62.8% had a history of musculoskeletal pain and 48.5% had a history of opioid use 1 year prior to index fracture. The most commonly observed fracture sites were spine (n=3,060; 31.0%), hip (n=2,759; 27.9%), and ankle (n=965; 9.8%). Of all patients with a qualifying fracture, approximately 92.8% (n=9,163) did not have a claim for diagnosis or treatment of osteoporosis at baseline. 2.8% (n=279) were diagnosed but not treated, 2.3% (n=227) were treated but not diagnosed, and only 2.1% (n=207) were diagnosed and treated. There was a trend in declining DXA scans from 2012 to 2014 (65-69 years; 6.3 to 5.5% AND 70-74 years; 4.7 to 4.0%) especially pronounced in the ≥75 age group (6.0 to 4.3%).

Conclusion: Our findings suggest a high level of underdiagnosis and undertreatment of osteoporosis in the older male population who experience fracture. Further documentation of cost of illness following an osteoporosis-related fracture, including identification of drivers of high costs and earlier identification high risk patients who may benefit from more targeted screening and osteoporosis therapies, will be of value.

Disclosure: S. Williams, Radius Health, Inc., 1, 2; **S. Daigle**, Radius Health, Inc., 1; **R. Weiss**, Radius Health,Inc., 1, 2; **Y. Wang**, Radius Health, Inc., 1, 2; **T. Arora**, Radius Health, Inc., 1; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5.

Abstract Number: 0534

National Variation and Factors Associated with Long-term Opioid Use for Non-cancer Pain in the First Year of Use

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Physician prescribing behaviour has been described as a key driver of rising opioid prescriptions and long-term opioid use. However, the effect of prescribers requires interpretation within context. No studies have investigated the extent to which regions, practices, prescribers, vary in opioid prescribing by considering this hierarchy together, whilst accounting for case-mix. Objectives: (i) quantify and identify risk factors for the transition from new-users to long-term opioid users (ii) quantify variation of long-term use attributed to region, practice, prescriber, accounting for patient mix and chance variation.

Methods: We conducted a retrospective observational study between 2006-2017 using Clinical Practice Research Datalink. New users of opioids, ≥18 years, without cancer were identified. Long-term opioid use was defined as ≥3 opioid prescriptions within a 90-day period from index date, or ≥1 opioid prescription lasting at least 90-days in the first year. A multi-level random-effects logistic regression model was used to examine the association of patient characteristics with the odds of becoming a long-term opioid-user. To examine variation in opioid use amongst prescribers, GP-practices and region after adjusting for case-mix, we used a nested random-effect structure. A 'high-risk' region, prescriber or practice was defined as those where the entire adjusted 95% CI lay above population average.

Results: 1,968,742 new opioid users were included; 14.6% transitioned to long-term use. In the fully-adjusted model, factors associated with higher-odds of long-term use included older-age, deprivation, fibromyalgia, rheumatological conditions, higher morphine milligram equivalents (MME)/day at initiation and prior surgery (Table). After adjustment for case-mix, the North-West, Yorkshire and South-West were found to be high-risk regions for long-term use. 103 practices (25.6%) and 540 prescribers (3.5%) were associated with a significantly higher-risk of long-term use. The odds of becoming a long-term user for patients belonging to these prescribers reached up to >3.5 times than the population average.

Individual factors	Adjusted Odds Ratio (95% CI) *
Prescribing factors	
Index daily MME >200	7.59 (6.29, 9.16)
Index daily MME 100-200	1.12 (1.03, 1.21)
Index daily MME 50-100	1.58 (1.49, 1.68)
Index daily MME <50	Ref
Gabapentinoid use	2.51 (2.43, 2.60)
Psychotropic use	1.28 (1.17, 1.40)
Age	
>75	4.35 (4.26, 4.45)
65-75	3.57 (3.50, 3.65)
55-65	3.03 (2.96, 3.09)
35-55	1.91 (1.88, 1.95)
Age <35	Ref
Deprivation (Townsend score)	
Quintile 5 (Most deprived)	1.54 (1.51, 1.57)
Quintile 4	1.34 (1.31, 1.36)
Quintile 3	1.20 (1.18, 1.22)
Quintile 2	1.09 (1.07, 1.11)
Quintile 1 (Least deprived)	Ref
Pre-existing conditions/ prior procedures	
Fibromyalgia	1.81 (1.49, 2.20)
Substance use disorder	1.76 (1.70, 1.83)
Suicide and self-harm	1.56 (1.51, 1.61)
Rheumatological conditions Ψ	1.54 (1.49, 1.59)
Alcohol abuse	1.50 (1.45, 1.55)
Depression	1.28 (1.26, 1.30)
Major Surgery	1.09 (1.06, 1.13)
Abbreviations: MME, Morphine Milligram Equivalent; *p<0.05. Index daily MME/day is the MME/day at first prescription (MME= daily dose in milligrams X opioid conversion ratio). Ψ Defined by Charlson score including rheumatoid arthritis, SLE, myositis.	

Factors associated with long term opioid use using a multi-level model accounting for clustering of individuals within prescriber, practice and region

Conclusion: Prescribing factors, age, deprivation and conditions including fibromyalgia and rheumatological conditions were associated with higher odds of long-term opioid use. In the first UK study evaluating long-term opioid prescribing with patient-level characteristics adjustment, variation in regions, especially practices and prescribers were observed. Our findings support greater calls for action to reduce practice/prescriber variation by promoting safe practice in opioid-prescribing.

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Abstract Number: 0535

Provider Opinion and Support for Shared Decision-making in Gout Treatment: A Quality Improvement National Survey of Veterans Affairs Rheumatologists

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: To assess rheumatologists' views and practices related to shared decision making (SDM) in gout treatment.

Methods: We performed a cross-sectional electronic survey of rheumatologists at U.S. Veterans Affairs (VA) medical centers, assessing views and practices related to SDM in gout.

Table 1. Characteristics of survey respondents (n=90 providers)

	N (%) unless specified otherwise*
Female Sex	45 (58%)
Age in years, mean (standard deviation)	51 (9.6)
Age group	
≤ 50 years	34 (47%)
>50 to 65 years	34 (47%)
>65 years	4 (6%)
U.S. region	
Northeast	18 (27%)
West	15 (22%)
Midwest	12 (18%)
South	68 (34%)
Years in Practice	
0-5 years	6 (11%)
6-10 years	12 (16%)
11-20 years	23 (31%)
21-30 years	23 (31%)
>30 years	9 (12%)
*Missing: Sex, n=13; age, n=18; Region, n=22; years in practice, n=15	

Table 1. Characteristics of survey respondents (n=90 providers)

Appendix 1. Provider practices for choice for the patient regarding gout treatment decisions

	Yes	No
Do you routinely offer your gout patients a choice regarding the following?		
1. Starting urate-lowering therapy (ULT) vs. doing nothing?	70%	30%
2. Choosing among non-steroidal anti-inflammatory drugs (NSAIDs), steroids, or colchicine for the treatment of acute flares?	67%	33%
3. Choosing among NSAIDs, steroids, or colchicine for prophylaxis when starting ULTs	51%	49%
4. Choosing allopurinol vs. febuxostat as a first ULT?	16%	84%
5. Choosing whether to take daily ULT and continue taking it long-term vs. intermittently (e.g., during a flare)?	15%	85%

Appendix 1. Provider practices for choice for the patient regarding gout treatment decisions

Table 2. Provider view of patient difficulties and their role in shared decision-making (SDM) process in gout

	Often	Sometimes	Rarely	Never	Don't know
Q1. How common is it for your patients to have difficulty starting urate-lowering therapy vs. doing nothing…					
a. Unsure about the best choice for them?	11 (14%)	41 (51%)	25 (31%)	2 (2%)	1 (1%)
b. Uninformed about both benefits and risks?	28 (36%)	23 (29%)	22 (28%)	5 (6%)	0 (0%)
c. Unclear about the personal importance of the benefits and risks?	32 (58%)	26 (33%)	16 (20%)	4 (5%)	1 (1%)
d. Unsupported in decision-making?	8 (10%)	29 (37%)	25 (32%)	11 (14%)	5 (6%)
Q2. How common is it for your patients to have difficulty choosing between non-steroidal anti-inflammatory drugs (NSAIDs), steroids or colchicine for the treatment of acute flares…					
a. Unsure about the best choice for them?	20 (26%)	35 (45%)	23 (18%)	9 (6%)	4 (5%)
b. Uninformed about both benefits and risks?	22 (28%)	28 (36%)	18 (23%)	7 (9%)	3 (4%)
c. Unclear about the personal importance of the benefits and risks?	22 (28%)	33 (42%)	12 (15%)	7 (9%)	4 (5%)
d. Unsupported in decision-making?	10 (13%)	27 (35%)	19 (25%)	12 (16%)	8 (10%)
Q3. How common is it for your patients to have difficulty choosing between NSAIDs, steroids, or colchicine for prophylaxis when starting ULTs…					
a. Unsure about the best choice for them?	22 (28%)	32 (42%)	13 (17%)	5 (7%)	4 (5%)
b. Uninformed about both benefits and risks?	25 (33%)	22 (29%)	16 (21%)	9 (12%)	4 (5%)
c. Unclear about the personal importance of the benefits and risks?	26 (35%)	23 (32%)	14 (19%)	7 (9%)	4 (5%)
d. Unsupported in decision-making?	11 (14%)	29 (38%)	17 (22%)	12 (16%)	8 (10%)
Q4. How common is it for your patients to have difficulty choosing between allopurinol vs. febuxostat as a first urate-lowering therapy (ULT)…					
a. Unsure about the best choice for them?	15 (20%)	12 (16%)	24 (32%)	12 (16%)	13 (16%)
b. Uninformed about both benefits and risks?	17 (23%)	16 (21%)	17 (23%)	12 (16%)	13 (17%)
c. Unclear about the personal importance of the benefits and risks?	19 (25%)	21 (28%)	11 (15%)	14 (13%)	14 (19%)
d. Unsupported in decision-making?	9 (12%)	18 (24%)	17 (23%)	17 (23%)	14 (19%)
Q5. How common is it for your patients to have difficulty choosing whether to take daily ULT and continue taking it long-term vs. intermittently…					
a. Unsure about the best choice for them?	18 (24%)	16 (21%)	22 (29%)	13 (17%)	8 (10%)
b. Uninformed about both benefits and risks?	19 (25%)	19 (25%)	19 (25%)	11 (15%)	8 (10%)
c. Unclear about the personal importance of the benefits and risks?	20 (26%)	20 (26%)	10 (24%)	11 (14%)	8 (10%)
d. Unsupported in decision-making?	12 (16%)	18 (24%)	20 (26%)	15 (20%)	11 (14%)
Missing data: Q1, n=10; Q4, n=15; Q5, n=13; Q2, n=12; Q3, n=13					

Table 2. Provider view of patient difficulties and their role in shared decision-making (SDM) process in gout

Results: Of the 154 VA rheumatology providers eligible, 90 responded (response rate, 58%). Fifty-eight percent were female, the mean age was 51 years (standard deviation, 9.6), 42% had >20 years of experience in medical practice (**Table 1**).

Rheumatologists reported routinely offering a choice to their patients for: (1) starting urate-lowering therapy (ULT) for gout vs. doing nothing (70%); (2) choosing NSAIDs, corticosteroids, or colchicine for the treatment of acute flares (67%); and (3) choosing NSAIDs, corticosteroids, or colchicine for anti-inflammatory prophylaxis when starting ULT (51%; **Appendix 1**). Very few rheumatologists offered choice regarding: (4) choosing allopurinol vs. febuxostat as the first ULT (16%); and (5) taking daily ULT long-term vs. intermittently (15%).

Rheumatologists perceived that large proportion of patient were often or sometimes unsure of the best choice for these five decisions, respective proportions were 34%, 76%, 76%, 52%, and 54%. Similar proportions were often or sometimes uninformed about both medication benefits and risks, unclear about the personal importance of the benefits and risks, and unsupported in decision-making (**Table 2**). The rheumatologists reported that 44-64% of the patients were uninformed about both benefits and risks, 52-73% were unclear about the personal importance of the benefits and risks, and 36-52% were unsupported in decision-making (**Table 2**).

Conclusion: The majority of VA rheumatologists incorporated SDM in several gout treatment decisions. Rheumatologists also recognized that patients need better support to participate in SDM in gout.

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Abstract Number: 0536

Systematic Geriatric Assessment in Older Patients with Rheumatic Diseases - The RheuMAGIC Pilot Study

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Current demographic data predict that the number of older adults with rheumatic diseases will considerably increase in the coming years. Geriatric patients differ from younger adults in many ways including their clinical presentation, co-morbidities and response to medication. The management of such patients is often

Geriatric Problem	% present
Problems with Daily Activities	67
Problems with Vision	28
Problems with Hearing	38
Problems with Falls	11
Problems with Urinary Incontinence	38
Problems with Depression	57
Lack of Social Support	10
Incomplete Vaccinations	53
Problems with Cognition	31
Problems with Chronic Pain	90
Problems with Dizziness	44
Problems with Mobility	41
Problems with Unintentional Weight Loss	30
Inappropriate Medications present	17
Polypharmacy present	81
Frailty present	46
Short Physical Performance Battery low	57

Table 1. Frequency of Geriatric Problems

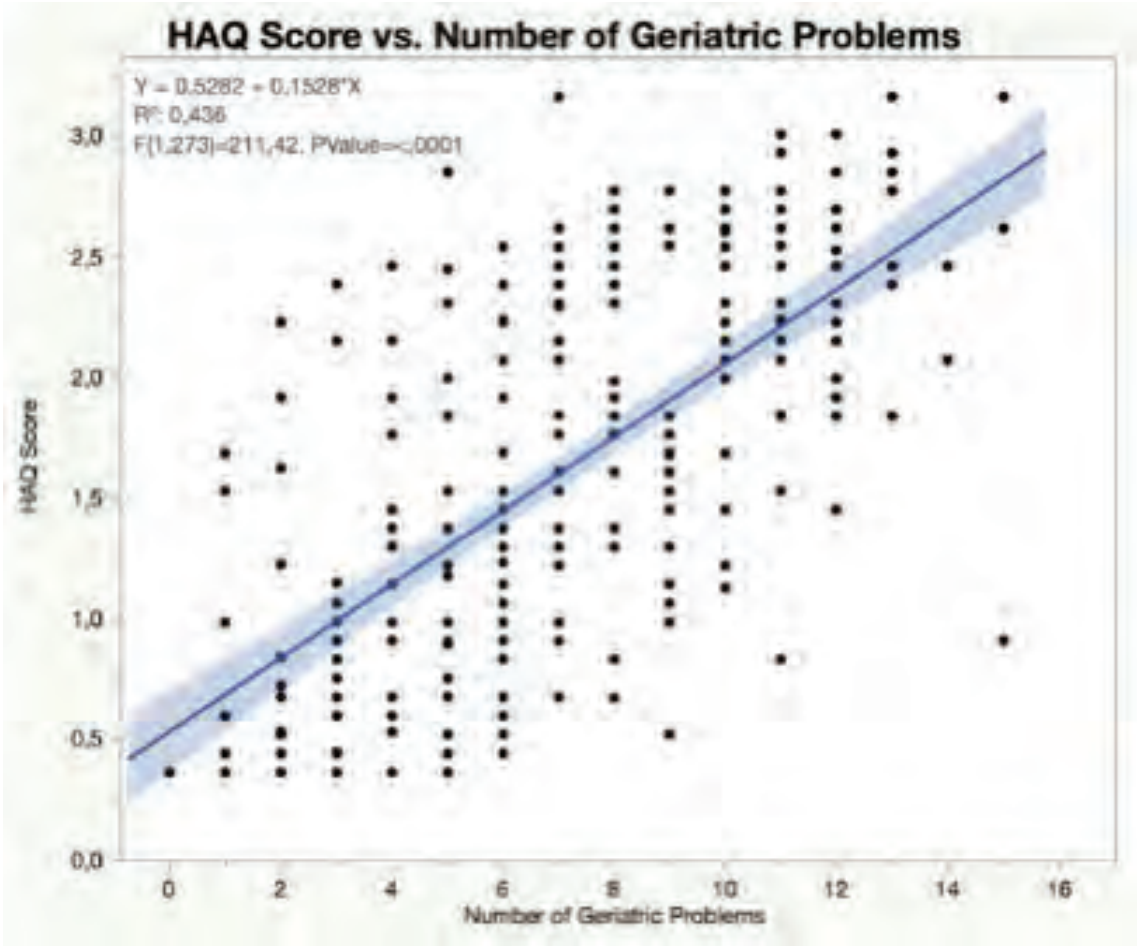

Figure 1. Relationship of Number of Geriatric Problems and Health Assessment Questionnaire (HAQ) Score. A significant linear relationship was found between the number of geriatric problems and HAQ score indicating that a higher number of geriatric problems is associated with greater difficulty in daily function

challenging due to the presence of multimorbidity, polypharmacy and geriatric syndromes (i.e. conditions in which symptoms result from impairments in multiple systems rather than a discrete disease). To systematically assess geriatric patients, specific tools have been developed; however, they are not routinely utilized by rheumatologists. Using these tools could improve patient management and satisfaction in rheumatologic care. The aim of this study was to examine the prevalence of 17 common geriatric health problems using validated geriatric assessment tools in older patients with rheumatic and musculoskeletal diseases.

Methods: Adults 65 years and older who presented to a tertiary rheumatologic hospital were included after informed consent. All patients recruited were assessed using the MAngable GeriatrIC Assessment (MAGIC) which addresses 14 common geriatric health problems. In addition, polypharmacy (≥ 5 medication), muscle function using the Short Physical Performance Battery and frailty applying the Fried definition were assessed. Disability was quantified with the "Funktionsfragebogen Hannover" (FFbH), a validated tool for patients with rheumatologic diseases that can be easily converted to Health Assessment Questionnaire (HAQ) scores. Primary outcome was the frequency of the selected 17 geriatric health problems; the correlation of the total number of problems with HAQ scores was a secondary outcome.

Results: Of the 300 individuals included 67% were female with a mean age of 73±6.6 years; 85% (> 50% with rheumatoid arthritis) had a rheumatologic diagnosis. The remaining participants had either a chronic pain syndrome or degenerative joint/spine disease. On average participants had 7 out of 17 assessed geriatric problems. Females had

more such problems than males (8 vs. 6, p< 0.0001). Chronic pain and polypharmacy were most common but several others were also seen in more than 50% of patients (see Table). The mean HAQ Score was 1.67±0.79. There was a positive correlation (see Graph) between the number of problems and the HAQ Score (R2 0.44, p< 0.0001).

Conclusion: A systematic geriatric assessment can be successfully used to discover and quantify geriatric health problems in older patients with rheumatic and musculoskeletal diseases. These problems appear to be very common and importantly, patients with more problems had poorer functional status. Frailty, depression, incomplete vaccination status, cognitive impairment or polypharmacy are all known to negatively impact patient care. Recognizing and addressing geriatric problems has the potential to lead to health care improvements including adherence and medication side effects and might increase patient satisfaction and functional status independent of disease activity.

Disclosure: B. Buehring, GE/Lunar, 1, 2, Kinemed, 1, Gilead, 1, AbbVie, 1, 2, Lilly, 1, Janssen, 1, Amgen, 1, 2, UCB, 1, 2, 3, MSD, 1; **A. Berrisch**, None; **I. Andreica**, None; **S. Tsiami**, None; **D. Kiefer**, None; **U. Kiltz**, Abbvie, 2, 5, Biocad, 2, 5, Biogen, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Grünenthal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5; **X. Baraliakos**, None; **J. Braun**, None.

Abstract Number: 0537

Hip Abductor Strength and Its Association with New or Worsening Knee Pain: The MOST Study

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Background/Purpose: Hip abductors are important for controlling pelvic orientation and rotation of the femur during gait, both of which affect knee mechanics. Thus hip abductor weakness may influence the development or worsening of knee pain. The purpose of this study was to evaluate the relation of hip abductor strength to worsening or new onset of frequent knee pain, with and without adjusting for quadriceps strength.

Methods: We used data from the Multicenter Osteoarthritis Study (MOST). For the existing cohort, the 144-month study visit was considered baseline for the current analysis. At this visit, a new cohort was recruited, with their initial visit considered as the baseline. Participants had hip abductor and quadriceps muscle strength measured in each limb. Strength was measured as maximal isometric torque with hip abduction and isotonic torque with knee extension, respectively. Sex-specific quartiles were created for both hip and knee strength. Participants also filled out the WOMAC questionnaire and answered questions about frequent knee pain at baseline, 8, 16 and 24 months later.

We characterized two knee pain outcomes. First, using the WOMAC questionnaire, we defined worsening as an increase in pain score by at least 2 on the 0-20 scale. We characterized each knee as having worsening pain if worse pain was reported at 2 or more of the 3 follow-ups. For those who did not report frequent knee pain (FKP) at baseline, we characterized the knee as having new FKP if they responded ‘yes’ to the frequent knee pain question at greater

Table 1: Cohort characteristics: mean (standard deviation) or percent of participants.

Variables		n = 2259 participants
Age (years)		63.4 (10.3)
Body mass index (BMI) (kg/m^2)		29.4 (5.6)
Women (%)		56.5
Clinic Site = Iowa (%)		52.9
Depressive Symptoms (%)		11.1
Race (%)	Black or African-American	16.5
	White or Caucasian	80.7
	Other	2.7
WOMAC Pain Worsening (%)		13.7
New Frequent Knee Pain (%)		9.8
Hip Abductor Torque (Nm/kg)		1.10 (0.40)

Table 2: Odds ratios and 95% confidence intervals (CI) for each quartile of hip abductor strength. Analyses adjusted for age, sex, race, BMI, depressive symptoms, and baseline WOMAC pain score.

	WOMAC Pain Worsening		New Frequent Knee Pain	
Hip Abductor Strength Quartiles	Odds Ratio (95% CI)	Odds Ratio adjusted for Quadriceps Strength (95% CI)	Odds Ratio (95% CI)	Odds Ratio adjusted for Quadriceps Strength (95% CI)
Q1 (Weakest)	1.47 (1.03, 2.09) P = 0.03	1.27 (0.87, 1.85) P = 0.22	1.84 (1.11, 3.06) P = 0.02	1.52 (0.87, 2.66) P = 0.14
Q2	1.24 (0.90, 1.69) P = 0.19	1.14 (0.81, 1.59) P = 0.45	1.48 (0.94, 2.34) P = 0.09	1.30 (0.79, 2.14) P = 0.31
Q3	1.14 (0.84, 1.54) P = 0.40	1.10 (0.80, 1.50) P = 0.55	1.37 (0.86, 2.19) P = 0.18	1.27 (0.77, 2.09) P = 0.35
Q4 (Strongest)	1 (referent)	1 (referent)	1 (referent)	1 (referent)
P for Trend	0.031	0.228	0.018	0.161

than 50% of 2 or more follow-ups. Non-cases were those with no reports of worsening or new FKP on follow-up. We carried out hip and knee specific analyses testing hip abductor strength as a risk factor for ipsilateral worsening and new knee pain, accounting for the correlation between limbs with GEE and adjusting for age, sex, race, body mass index (BMI), depressive symptoms, and baseline WOMAC pain score in that knee. After initial analyses, we added quadriceps strength as a covariate.

Results: Of 2391 participants with hip abductor strength measurements, sufficient follow-up data were available from 2259 participants for WOMAC pain worsening and 1891 participants for incident frequent knee pain. Characteristics of the participants are in Table 1. In analyses unadjusted for quadriceps strength, hip abductor strength demonstrated a significant association with worsening WOMAC knee pain and new onset FKP (Table 2). However, when we adjusted additionally for quadriceps strength, the associations between hip abductor strength and knee pain became much weaker and nonsignificant. Quadriceps strength was associated with pain outcomes; trend tests were significant for WOMAC pain worsening (p=0.023) and for new onset frequent knee pain (p=0.038).

Conclusion: Hip abductor strength is not independently associated with worsening or incident knee pain in this cohort. Instead, the relation of abductor strength with knee pain appears to be substantially due to its association with quadriceps strength.

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Abstract Number: 0538

Autoimmune Disease Outcomes of Women with Breast Implants: A Population-Based Study

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Background/Purpose: The long-term safety of breast implants has been a debated topic; two recent studies have raised new concerns about their potential negative health effects (Watad A et al., *Int J Epidemiol.* 2018; Coroneos C et al., *Annals of Surgery.* 2018). While these reports suffer from methodological weaknesses, previous studies indicating no association between silicone breast implants and systemic disease may have been under-powered for rare outcomes. Since disease diagnostic criteria have been expanded in modern times, we felt these recent reports required a re-examination of whether autoimmune conditions occurred more frequently in women after silicone and saline breast implantation compared to those with no history of implants.

Methods: In this retrospective cohort study, all women who received a breast implant in a geographically defined region between January 1, 1998 and December 31, 2017 were identified. Implant cases were individually reviewed to confirm implant status and determine implant date, type, and reason. Each subject was matched to 3 women of the same age and region with no history of implants. Index date was defined as date of implantation or matched date. Both cohorts were screened for 26 autoimmune conditions using diagnostic codes (Table 1). Using a previously validated method, confirmed autoimmune conditions were defined by the presence of ≥1 inpatient encounter as the primary diagnosis, or ≥2 codes ≥30 days and ≤2 years apart (Ong MS et al., *JAMA Neurol.* 2014). Comparisons of autoimmune disease occurrence in women with and without implants were performed using Cox models adjusted for age and calendar year.

Results: We identified 835 women who received breast implants during the study period and 2505 comparators with no history of implants. Women with implants were 89.2% white with a mean age of 41.4 years at implantation. Roughly half the implants were for cosmetic reasons (n = 422; 50.5%), with 310 (37.1%) for breast cancer, and 103 (12.3%) for prophylaxis or reasons related to another condition. The median length of prior medical history for implant patients was 24.9 years (IQR: 11.3, 36.1). After implant placement, these women had a median follow-up of 9.3 years (IQR: 4.8, 14.2). Prior to receiving implants, 129 (15.4%) women had an autoimmune condition compared to 381 (15.2%) comparators (p = 0.87). Excluding women with prior autoimmune disease, 74 women with implants (cumulative incidence at 10 years: 11.0%; 95% CI: 8.5-14.1%) and 222 comparators (cumulative incidence at 10 years: 11.3%; 95% CI: 9.8-13.0%) developed an autoimmune condition during follow-up. We found no evidence of an increase in the risk of autoimmune disease for women with implants compared to those without (HR: 0.98; 95% CI: 0.75-1.27). When assessing the risk of autoimmune disease for implant reason subtypes, we did not observe any differences (Table 2).

Table 1. Diagnostic codes for autoimmune conditions

Autoimmune Disease	ICD-9	ICD-10
Addison's disease	255.4	E27.1, E27.2
Ankylosing spondylitis	720	M45.x, M08.1
Antiphospholipid syndrome	-	D68.61
Celiac disease	579	K90.0
Crohn's disease	555.x	K50.x
Dermatomyositis/Polymyositis	710.3, 710.4	M33.x
Guillain-Barre syndrome	357	G61.0
Hepatitis, autoimmune	571.42	K75.4
Grave's disease	242.x	E05.x
Hashimoto's thyroiditis	245.2, 244.9	E06.3, E03.5, E03.9
Multiple sclerosis	340	G35
Myasthenia gravis	358	G70.0
Pernicious anemia	281	D51.0
Polymyalgia rheumatica	725	M31.5, M35.3
Primary biliary cirrhosis	571.6	K74.3
Psoriasis or psoriatic arthritis	696.x	L40.x
Rheumatoid arthritis	714.x	M05.x, M06.x, M08.0, M08.2
Systemic sclerosis, limited or diffuse	701.0, 710.1	L94.0, M34.x
Sjögren's syndrome	710.2	M35.0
Systemic lupus erythematosus	710	M32.x
Takayasu arteritis	446.7	M31.4
Type 1 diabetes	250.[0-9]1, 250.[0-9]3	E10.x, O24.0
Ulcerative colitis	556.x	K51.x
Uveitis	360.12, 364.01, 364.02, 364.1	H20.01, H20.02, H20.1, H44.1
Vasculitis, either granulomatosis with polyangiitis (GPA), eosinophilic GPA, or polyarteritis nodosa	GPA: 446.4, EGPA: -, PAN: 446.0	GPA: M31.3, EGPA: M30.1, PAN: M30.0
Vitiligo	709.01	H02.7, L80

Table 2. Risk of autoimmune disease in implant patients by reason for breast implant

Reason for breast implant	Number of events*		Cumulative incidence at 10 years (95% CI)**		Hazard ratio (95% CI)***	p-value
	Implant cases	*Comparators*	*Implant cases*	*Comparators*		
Any reason	74	222	11.0 (8.5, 14.1)	11.3 (9.8, 13.0)	0.98 (0.75, 1.27)	0.86
Cosmetic	41	121	10.2 (7.2, 14.3)	9.8 (8.0, 11.9)	0.96 (0.68, 1.37)	0.84
Cancer	25	76	12.5 (7.9, 20.0)	13.9 (11.0, 17.6)	1.04 (0.66, 1.63)	0.88
Prophylactic	7	23	13.6 (6.7, 27.5)	15.0 (9.8, 23.0)	0.85 (0.36, 2.00)	0.72

*The number of events is the number of patients who develop any autoimmune disease

**Adjusted for the competing risk of death

***Adjusted for age and calendar year of index date

Conclusion: This study observed no increase in the modern era for the risk of autoimmune diseases in women with breast implants compared to those without. Additional analyses are currently underway for saline vs. silicone subsets as well as analyses focusing on length of implant exposure.

Disclosure: M. Peterson, None; **T. O'Byrne**, None; **J. Davis**, Pfizer, 2, AbbVie, 5, 8, Sanofi-Genzyme, 5, 8; **V. Kronzer**, None; **L. Peterson**, None; **M. Weisman**, None; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1.

Abstract Number: 0539

Sports with a Bat or Racket Are Not Associated with Thumb-base Osteoarthritis: Data from the Osteoarthritis Initiative

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Sports that require the use of a racket or bat to propel a ball (e.g., baseball, softball, tennis) expose the thumb-base to repetitive high-velocity loading. However, it remains unclear if these sports increase the risk of thumb-base osteoarthritis (OA). We aimed to determine if a history of participation in racket or bat sports is associated with prevalent thumb-base OA.

Methods: We studied men and women from the Osteoarthritis Initiative (OAI) – a multicenter cohort study recruited from the community. Eligible participants had dominant hand radiographic readings, hand symptom assessments, and historical physical activity survey data. A history of participation in racket or bat sports (i.e., baseball/softball, racquetball/squash, badminton, table tennis, tennis [doubles/singles]) was based on self-reported recall data covering 3 age ranges (teens: 12-18 years, young adult: 19-34 years, adult: 35-49 years). As a sensitivity analysis, we examined people who indicated that participation in these sports was among their top 3 commonly performed physical activities during each age range. Prevalent radiographic thumb-base OA was defined as Kellgren-Lawrence grade≥2 in the first carpometacarpal joint or scaphotrapezoidal joint at the OAI baseline visit. Symptomatic thumb-base OA was defined as the presence of radiographic OA and hand symptoms. We used a series of logistic regression models to assess the association between a history of racket or bat sports within each age range with prevalent radiographic thumb-base OA (primary outcome) or symptomatic thumb-base OA (secondary outcome). These models were performed stratified by sex and completed with and without adjusting for confounders (see Tables).

Results: The 2309 participants tended to be 60 (9) years of age, female (55%), white (80%), and educated with at least some college experience (87%). Among 1049 men, 355 (34%) and 56 (5%) had radiographic or symptomatic

Table 1. Association Between History of Racket/Bat Sport Participation and Radiographic Thumb-base Osteoarthritis (rTBOA)

	Men			Women		
Variable	No rTBOA n = 694 n (%)	Prevalent rTBOA n = 355 n (%)	Adjusted OR* (95% CI)	No rTBOA n = 735 n (%)	Prevalent rTBOA n = 525 n (%)	Adjusted OR* (95% CI)
Teens (12-18 years): Any Racket/Bat Sports	580 (83.6)	280 (78.9)	0.98 (0.69, 1.39)	504 (68.6)	312 (59.5)	0.84 (0.64, 1.11)
Racket/Bat Sports among Top 3 Sports	346 (49.9)	169 (47.6)	0.95 (0.72, 1.25)	230 (31.3)	129 (24.6)	0.82 (0.62, 1.09)
Young Adult (19-34 years): Any Racket/Bat Sports	516 (74.4)	259 (73.0)	1.34 (0.97, 1.84)	371 (50.5)	247 (47.0)	0.98 (0.75, 1.27)
Racket/Bat Sports among Top 3 Sports	295 (42.5)	131 (36.9)	0.87 (0.66, 1.15)	168 (22.9)	111 (21.1)	1.08 (0.79, 1.48)
Adult (35-49 years): Any Racket/Bat Sports	352 (50.7)	183 (51.5)	1.16 (0.88, 1.54)	177 (24.1)	143 (27.2)	1.05 (0.78, 1.41)
Racket/Bat Sports among Top 3 Sports	162 (23.3)	87 (24.5)	1.06 (0.77, 1.45)	79 (10.7)	48 (9.1)	0.70 (0.46, 1.08)

Note. * adjusted for age, race, and education.
Further adjusting for other physical activities related to racket or bat sports and rTBOA led to similar results (data not shown).
OR = odds ratio, 95% CI = 95% confidence interval.

Table 1.

Table 2. Association Between History of Racket/Bat Sport Participation and Symptomatic Thumb-base Osteoarthritis (sxTBOA)

	Men			Women		
Variable	No sxTBOA n = 993 n (%)	Prevalent sxTBOA n = 56 n (%)	Adjusted OR* (95% CI)	No sxTBOA n = 1090 n (%)	Prevalent sxTBOA n = 170 n (%)	Adjusted OR* (95% CI)
Teens (12-18 years): Any Racket/Bat Sports	817 (82.3)	43 (76.8)	0.98 (0.50, 1.91)	709 (65.1)	107 (62.9)	1.01 (0.71, 1.44)
Racket/Bat Sports among Top 3 Sports	487 (49.0)	28 (50.0)	1.13 (0.65, 1.96)	314 (28.8)	45 (26.5)	0.97 (0.67, 1.41)
Young Adult (19-34 years): Any Racket/Bat Sports	739 (74.4)	36 (64.3)	0.88 (0.49, 1.60)	532 (48.8)	86 (50.6)	1.08 (0.77, 1.51)
Racket/Bat Sports among Top 3 Sports	405 (40.8)	21 (37.5)	1.03 (0.58, 1.82)	243 (22.3)	36 (21.2)	0.99 (0.66, 1.49)
Adult (35-49 years): Any Racket/Bat Sports	508 (51.2)	27 (48.2)	1.08 (0.61, 1.90)	271 (24.9)	49 (28.8)	1.07 (0.73, 1.55)
Racket/Bat Sports among Top 3 Sports	233 (23.5)	16 (28.6)	1.43 (0.77, 2.65)	107 (9.8)	20 (11.8)	1.13 (0.67, 1.91)

Note. * adjusted for age, race, and education.
Further adjusting for other physical activities related to racket or bat sports and rTBOA led to similar results (data not shown).
OR = odds ratio, 95% CI = 95% confidence interval.

Table 2

thumb-base OA, respectively. Among 1260 women, 525 (42%) and 170 (13%) had radiographic or symptomatic thumb-base OA, respectively. After adjusting for age, race, and education level, we found no significant associations between a history of any racket or bat sport participation and thumb-base OA (radiographic or symptomatic; odds ratios range from 0.84 to 1.34; Tables 1 and 2). Sensitivity analyses among people who listed racket/bat sports among their top 3 sports in each age range supported the primary analyses (Tables 1 and 2).

Conclusion: Within a community-based cohort, a self-reported history of participation in racket or bat sports was not associated with having radiographic or symptomatic thumb-base OA in the dominant hand.

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Abstract Number: 0540

Risk of Hydroxychloroquine Retinopathy in the Community

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is used in the treatment of a wide variety of autoimmune diseases. HCQ retinopathy is a feared complication of long-term use. The reported prevalence of this complication increased with the advent of optical coherence tomography (OCT) or visual field assessment (VFA), and is estimated

Table 1. Selected Study Population and Case Characteristics

Characteristic	Study Population N=372	Cases N= 8
Age at First HCQ Prescription in years (Mean (SD); Range)	54.3 (15.6); 16.9-84.4	55.7 (11.5); 38.8-70.9
Sex N, (%)	294 (79) Female 78 (21) Male	8 (100) Female
Race/Ethnicity N, (%)	339 (91) White 13 (3) Asian 10 (3) other/mixed 6 (2) Black 3 (1) American Indian 14 (4) Hispanic Ethnicity	7 (88) White 1 (13) other/mixed 0 (0) Hispanic Ethnicity
Indication for HCQ N, (%)	211 (57) RA 91 (24) SLE 17 (5) Sjogren's 3 (1) DM 14 (4) Dermatological 36 (10) other autoimmune conditions	6 (75) RA 1 (13) Sjogren's 1 (13) Other autoimmune conditions
Presence of CKD N, (%)	45 (12)	1 (13)
Dose of HCQ in mg/day* (Mean (SD); Range)	358.9 (83.6); 100-800	400 (0); 400-400
Dose of HCQ in mg/kg/day* (Mean (SD); Range)	4.6 (1.4); 1.5-8.0	5.9 (1.0); 4.4-6.7
Length of Follow up in years (Mean (SD); Range)	9.6 (3.0); 4.2-17.1	7.7 (2.5); 4.7-12.7
*Actual body weight; kg, kilogram; HCQ, hydroxychloroquine; CKD, chronic kidney disease.		

Table 1. Selected Study Population and Case Characteristics

Table 2. HCQ Retinopathy Rates

Time to Retinopathy in Years (N=372, Events=8)	Cumulative incidence (risk), % (95% CI)
5	0
6	0.3 (0.0-2.3)
7	0.6 (0.2-2.6)
8	1.3 (0.5-3.5)
9	2.0 (0.9-4.5)
10	2.5 (1.2-5.2)

Table 2. HCQ Retinopathy Rates

Table 3. Risk factors for HCQ Retinopathy

Risk factor	HR (95% CI)	p-value
Age at HCQ start, years	1.01 (0.97, 1.06)	0.58
Male sex	—	0.99
BMI at 4 years HCQ, kg/m^2	0.96 (0.86, 1.07)	0.43
Daily HCQ dose per 100mg	1.19 (0.69, 2.06)	0.54
Cumulative HCQ dose per 100,000 mg	1.65 (0.98, 2.80)	0.061
Daily dose mg/kg*	1.28 (0.88, 1.87)	0.20
Daily dose =5mg/kg* (vs. < 5)	2.59 (0.64, 10.43)	0.18
CKD	0.86 (0.11, 7.02)	0.89
*Actual body weight; Kg, kilogram; HCQ, hydroxychloroquine; CKD, chronic kidney disease; BMI, Body Mass Index.		

Table 3. Risk factors for HCQ Retinopathy

to be approximately 7.5% after five years of use. This led to guideline recommendation of using lower doses of HCQ. However, the reliance on prevalence rather than on incidence to predict the risk of developing a non-fatal and irreversible condition such as retinopathy leads to risk overestimation. To better estimate the risk of this complication, we estimated the incidence (risk) of retinopathy among new HCQ users.

Methods: A cohort of new HCQ users in a geographically defined 27-county region was identified using population-based research infrastructure. Prescription data was available starting in 2003 for one county and since 2010 for the rest of the counties. The patients were followed until HCQ toxicity incidence, migration out of the region, death or December 31, 2018. Medical records of these patients were reviewed for the development of HCQ retinopathy. HCQ

retinopathy was defined based on characteristic paracentral visual field defects and parafoveal retinal photoreceptor layer changes on OCT. Indication for HCQ, demographics and risk factors for retinopathy were abstracted. Incidence rates were age- and/or sex-adjusted to the estimated 2010 white population of the US. To compute 95% confidence intervals for incidence rates, it was assumed that the number of incident cases followed a Poisson distribution. The cumulative incidence rates after 4 years of HCQ use were estimated adjusting for the competing risk of death. Risk factors for HCQ retinopathy were estimated using Cox models.

Results: The study cohort identified 372 new HCQ users who had taken HCQ for four or more years. The average age was 54 years and 79% were female. The most common indications for HCQ were RA and SLE. The average follow up was 9.6 years after the first HCQ prescription (range 4.2 to 17.1). The mean dose in mg was 358.9, while the mean daily dose per weight was 4.6 mg/kg. Eight patients developed HCQ retinopathy, all were females and 88% were white. The majority used HCQ for RA treatment. The mean daily dose per weight was 5.9 mg/kg (Table 1). Table 2 references the risk of HCQ retinopathy. After five years of use, the risk was 0% and progressively increased up to 2.5% at ten years. Age at onset of therapy, daily dose per 100 mg, male sex, and presence of CKD did not increase the risk of retinopathy (Table 3). Those taking ≥5mg/kg of HCQ had a hazard ratio of 2.6 (0.64, 10.43) compared to those who took less than 5mg/kg, however this did not reach statistical significance.

Conclusion: The risk of HCQ retinopathy at ten years of use is lower compared to previous prevalence-based estimations. The number of cases was low for risk factor assessment; however, a dose higher than 5mg/kg may be associated with higher HCQ retinopathy risk.

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Abstract Number: 0541

Suboptimal Vaccination Coverage with Influenza, Pneumococcal and Herpes Zoster Vaccines Among Adult Patients with Autoimmune Inflammatory Rheumatic Diseases in a Nationwide Health Care Plan

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune inflammatory rheumatic diseases (AIIRD) increase the susceptibility to infections. Immunisation against vaccine-preventable diseases is recommended for patients with AIIRD by most international medical societies. Yet, evidence points to a suboptimal adherence to vaccination recommendations among the AIIRD population.[1-3]

The purpose of this study is to assess the vaccination coverage with influenza, pneumococcal and herpes zoster (HZ) vaccines among adult patients with AIIRD in a real-world setting.

Table 1. Vaccination coverage with influenza, pneumococcal and herpes zoster vaccines among adults diagnosed with autoimmune inflammatory rheumatic diseases (30/4/2019).

Vaccine	Coverage (look-back)	RA	PsA	SLE	Mixed AIIRD	Total AIIRD
Age ≥18y: Total N		6,932	4,395	1,951	1,250	14,528
Influenza	Past year*	45.1%	36.2%	33.7%	46.0%	41.0%
	Ever	74.2%	65.8%	65.8%	74.7%	70.6%
PCV13	Past 5y*	5.1%	4.1%	4.0%	6.6%	4.8%
	Ever	5.2%	4.1%	4.2%	6.6%	4.8%
PPSV23	Past 5y*	19.6%	16.2%	12.6%	17.7%	17.5%
	Ever	49.4%	31.1%	29.3%	42.6%	40.6%
PCV13+	Past year	0.8%	0.8%	0.5%	0.6%	0.7%
PPSV23**	Past 5y*	2.9%	2.3%	2.1%	2.8%	2.6%
	Ever	4.4%	3.0%	3.3%	5.0%	3.9%
Age ≥50y: Total N		5,514	2,954	962	912	10,342
HZ	Past 5y*	4.0%	3.6%	2.0%	3.1%	3.6%

AIIRD, autoimmune inflammatory rheumatic diseases; HZ, herpes zoster; Mixed AIIRD, >1 diagnosed AIIRD (defined here as RA, PsA, SLE); PCV13, pneumococcal conjugate vaccine; PPSV23, pneumococcal polysaccharide vaccine; PsA, psoriatic arthritis; RA, rheumatoid arthritis; SLE, systemic lupus erythematosus. *Defined as optimal vaccination coverage. **Prime boost vaccination strategy – consecutive vaccination with PCV13 followed by PPSV23

Table 1. Vaccination coverage with influenza, pneumococcal and herpes zoster vaccines among adults diagnosed with autoimmune inflammatory rheumatic diseases (30/4/2019).

Methods: A retrospective cross-sectional study was performed using the databases of Maccabi Healthcare Services (MHS), a large healthcare provider in Israel. The AIIRD population was defined as adults (≥ 18 years old) alive on 30/04/2019, with ≥12 months of continuous enrolment, diagnosed with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and systemic lupus erythematosus (SLE). Point prevalence rates among MHS members were age-adjusted. Optimal coverage was defined as vaccination documented in the past year for influenza and 5 years for pneumococcal (PPSV23 and/or PCV13) and HZ vaccines.

Results: A total of 14,528 AIIRD patients were included. Overall, 41.0%, 17.5%, 4.8%, and 3.6% of AIIRD patients had optimal influenza, PPSV23, PCV13 and HZ vaccination coverage, respectively (Table 1). The highest age-specific

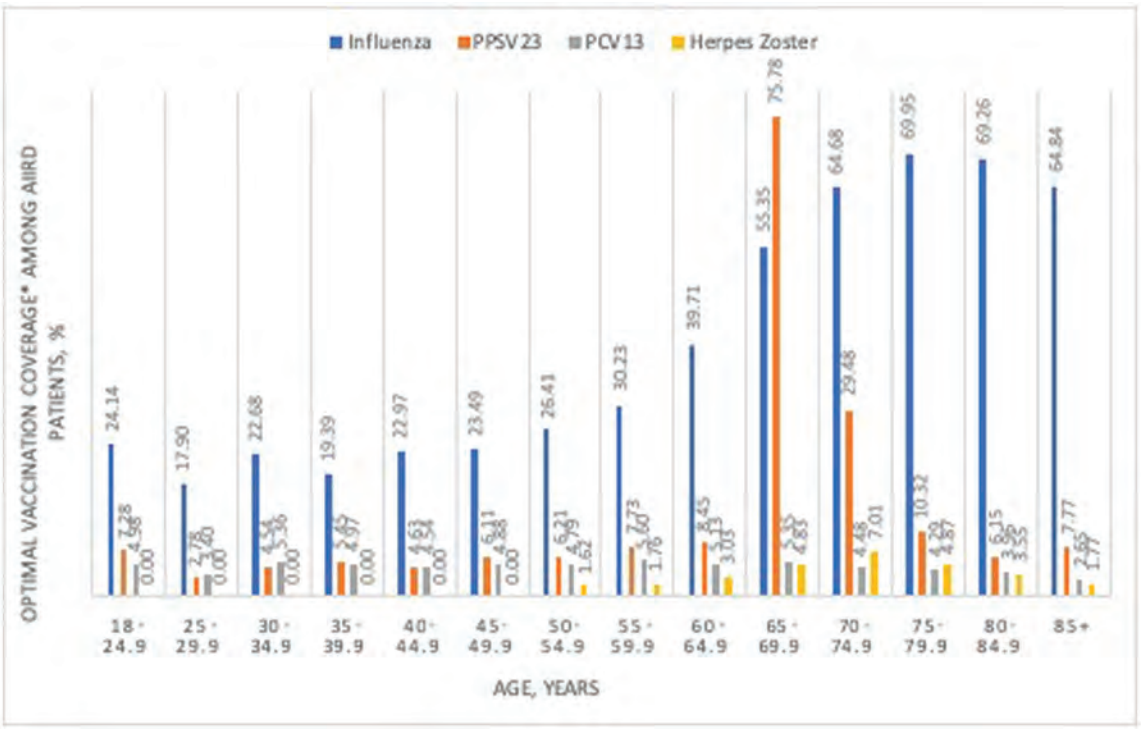

Figure 1. Age-specific optimal vaccination coverage with influenza, pneumococcal and herpes zoster vaccines among adults diagnosed with autoimmune inflammatory rheumatic diseases (30/4/2019). AIIRD, autoimmune inflammatory rheumatic diseases (defined here as rheumatoid arthritis, psoriatic arthritis, and/or systemic lupus erythematosus); PCV13, pneumococcal conjugate vaccine; PPSV23, pneumococcal polysaccharide vaccine. *Optimal coverage defined as vaccination in the past year for influenza, and vaccination in the past 5 years for pneumococcal and herpes zoster vaccines.

vaccination rates were observed in age group 75-79y for influenza, 65-69y for PPSV23, 55-59y for PCV13, and 70-74y for HZ respectively (Figure 2). Influenza vaccination was significantly ($p< 0.05$) associated with older age (≥60y) after adjusting for patient characteristics and potential confounders. Among the elderly (≥65y), AIIRD patients had comparable vaccine coverage rates to those reported in the general population in Israel[4] for influenza (past year: 63.2% vs. 61.0%) and PPSV23 (past 5y or at least once since age 65y: 83.4% vs. 77.7%). The uptake of PCV13 and HZ vaccines was remarkably low in all age groups.

Conclusion: This study provides real-world evidence of suboptimal influenza, pneumococcal, and HZ vaccination coverage of patients with AIIRD, in particular among younger adults. There remains significant scope to improve uptake of vaccinations in patients with AIIRD.

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Abstract Number: 0542

Examining the Long-Term and Short-Term Day-To-Day Pain Variability in Inflammatory and Non-Inflammatory Rheumatic and Musculoskeletal Diseases Using Multilevel and Markov Transition Models: Cloudy with a Chance of Pain, a National U.K. Smartphone Study

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

	RA	axSpA	OA	CWPFM
N	921	216	758	630
Female gender, N(%)	756 (82.1)	143 (66.2)	623 (82.2)	568 (90.2)
Age, mean(SD)	47.40 (12.51)	43.55 (11.02)	55.74 (11.04)	41.25 (10.75)
Pain site - head, N(%)	48 (5.2)	14 (6.5)	24 (3.2)	190 (30.2)
Pain site - face, N(%)	17 (1.8)	2 (0.9)	5 (0.7)	102 (16.2)
Pain site - mouth/jaw, N(%)	140 (15.2)	26 (12.0)	26 (3.4)	170 (27.0)
Pain site - neck/shoulder, N(%)	505 (54.8)	138 (63.9)	284 (37.5)	397 (63.0)
Pain site - back, N(%)	298 (32.4)	191 (88.4)	339 (44.7)	412 (65.4)
Pain site - abdomen, N(%)	46 (5.0)	27 (12.5)	31 (4.1)	195 (31.0)
Pain site - hip, N(%)	384 (41.7)	123 (56.9)	376 (49.6)	363 (57.6)
Pain site - knee, N(%)	568 (61.7)	95 (44.0)	516 (68.1)	376 (59.7)
Pain site - hands, N(%)	716 (77.7)	86 (39.8)	373 (49.2)	346 (54.9)
Pain site - feet, N(%)	574 (62.3)	71 (32.9)	256 (33.8)	301 (47.8)
Pain site - multi-site, N(%)	426 (46.3)	86 (39.8)	128 (16.9)	396 (62.9)
Pain site - all over body, N(%)	107 (11.6)	8 (3.7)	22 (2.9)	331 (52.5)
Analgesia use - none, N(%)	85 (9.2)	11 (5.1)	65 (8.6)	32 (5.1)
Analgesia use - paracetamol, N(%)	410 (44.5)	89 (41.2)	393 (51.8)	302 (47.9)
Analgesia use - NSAIDs, N(%)	580 (63.0)	156 (72.2)	478 (63.1)	336 (53.3)
Analgesia use - simple analgesia, N(%)	277 (30.1)	55 (25.5)	224 (29.6)	221 (35.1)
Analgesia use - weak opioids, N(%)	221 (24.0)	60 (27.8)	186 (24.5)	262 (41.6)
Analgesia use - strong opioids, N(%)	63 (6.8)	21 (9.7)	44 (5.8)	76 (12.1)
Analgesia use - neuropathic pain agent, N(%)	51 (5.5)	26 (12.0)	55 (7.3)	267 (42.4)
Analgesia use - other, N(%)	20 (2.2)	7 (3.2)	49 (6.5)	100 (15.9)

Table 1. Baseline characteristics for 2,525 study participants stratified by rheumatic and musculoskeletal diseases

Background/Purpose: Chronic pain is common in rheumatic and musculoskeletal diseases (RMDs), yet the patterns and the extent of variability over time are poorly understood. Real-time longitudinal capture of pain symptoms using smartphones enables the assessment of temporal patterns of pain, which are important indicators of disease activity. We examined the day-to-day pain variability in inflammatory and non-inflammatory RMDs using *Cloudy With a Chance of Pain*, a national U.K. smartphone study.

Methods: 10,584 study participants (aged ≥18 years; chronic pain for ≥3 months) entered their daily pain using a downloaded smartphone app (on a five-point ordinal scale of 1 - no pain/ 2 - mild pain/ 3 - moderate pain/ 4 - severe pain/ 5 - very severe pain). 2,525 participants diagnosed with single RMD (rheumatoid arthritis - RA, axial spondyloarthropathy - axSpA, osteoarthritis - OA, chronic widespread pain/fibromyalgia - CWP/FM) were included (median symptom entry days: 165 [IQR 82-284]). Long-term and short-term day-to-day pain variability for the first one-month period were analyzed using multilevel and Markov transition models respectively.

Results: From 29,705 daily pain scores (83% female; mean age 48 years; median symptom entry days: 24 [IQR 15-29]), the average pain scores for the first one-month period were higher in participants with axSpA and OA compared with participants with RA (2.74±0.98, 2.61±0.96, and 2.53±0.98 respectively), although participants with CWP/FM had the highest average pain score of 3.06±1.04. In addition, participants with CWP/FM had the highest overall pain

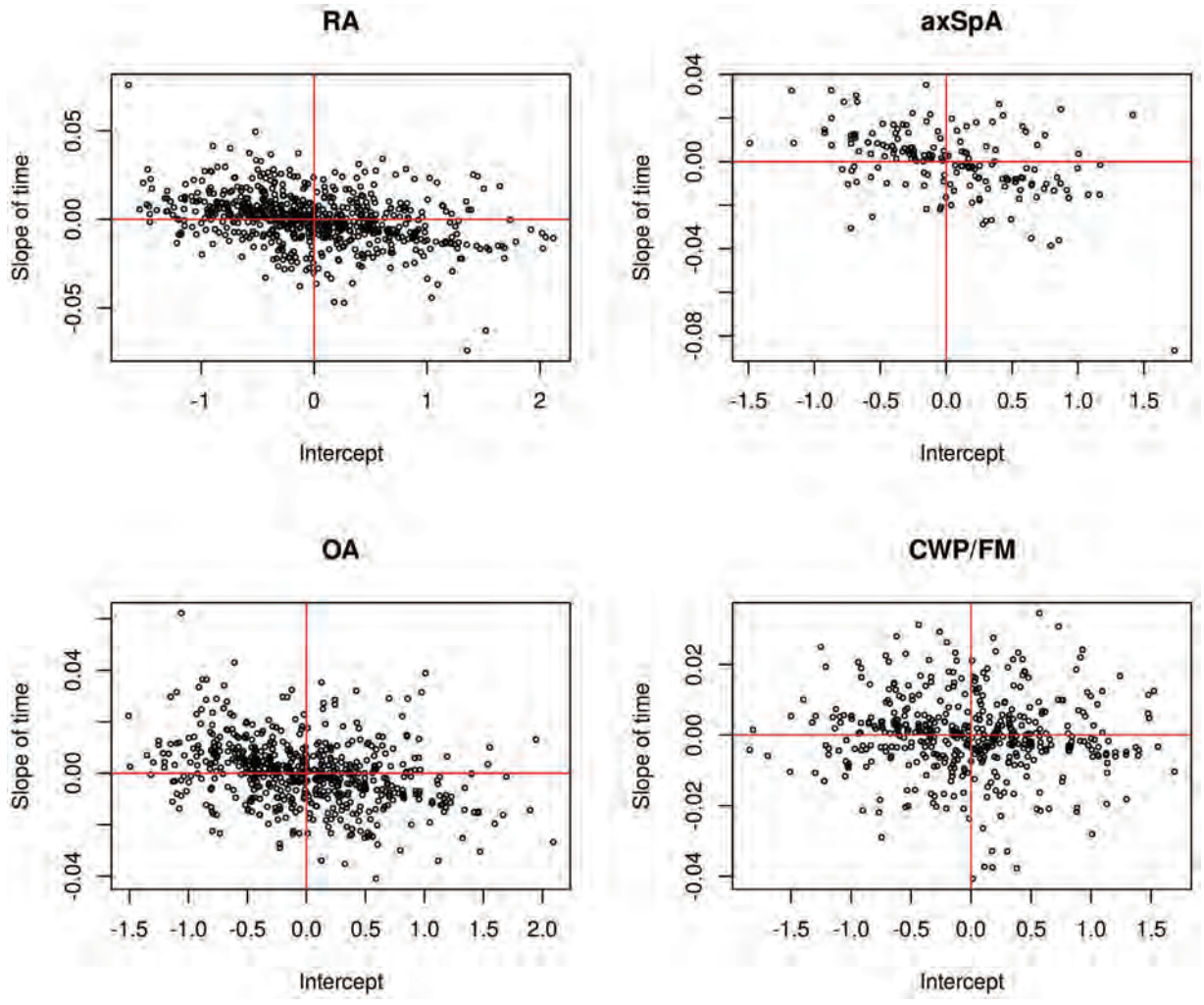

Figure 1. Slope-intercept plots for the multilevel model stratified by rheumatic and musculoskeletal diseases

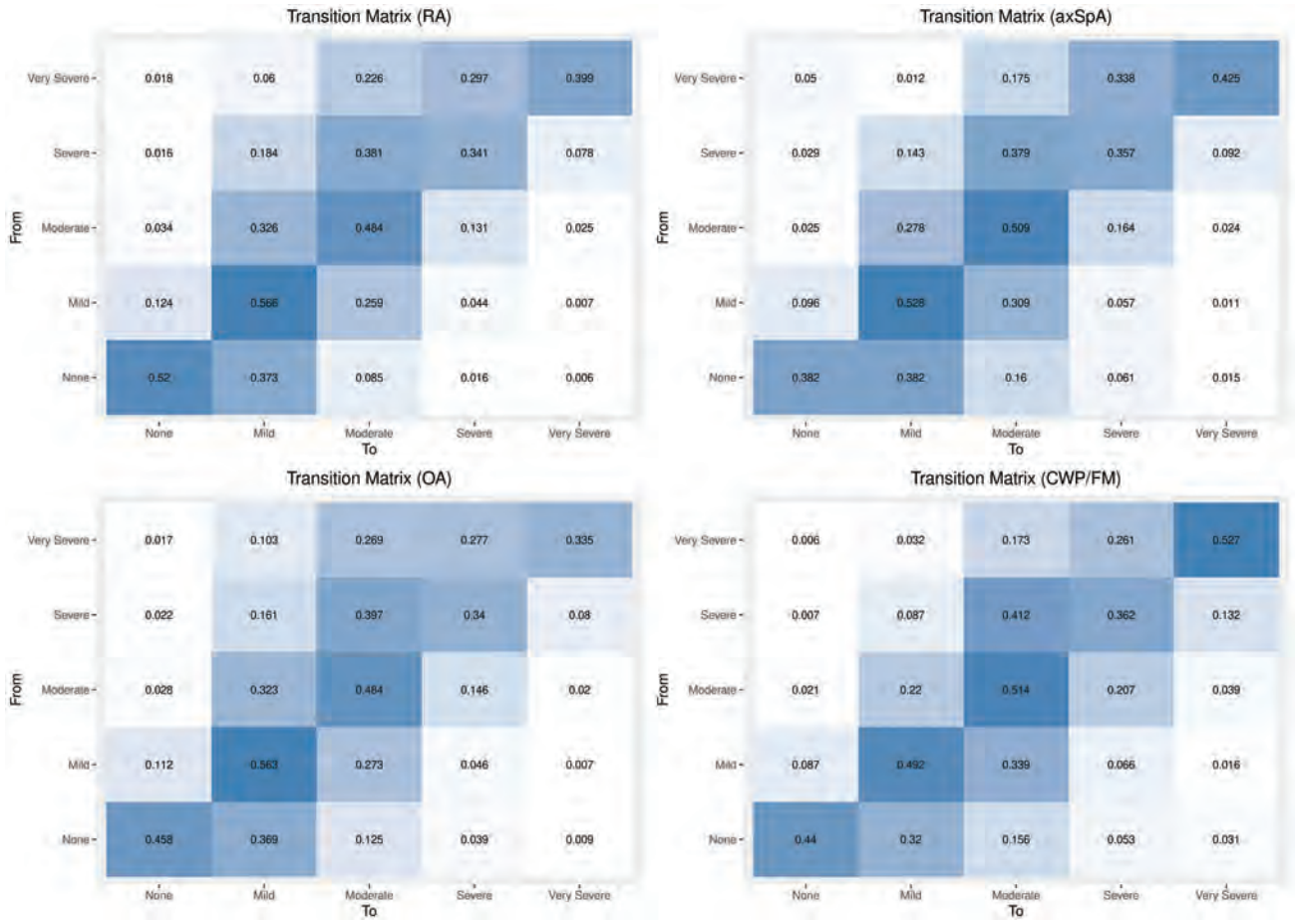

Figure 2. Heat map plots for the Markov transition model stratified by rheumatic and musculoskeletal diseases

level (71.1% reported moderate-very severe pain), followed by participants with axSpA, OA, and RA (57.8%, 52.0%, and 47.9% reported moderate-very severe pain respectively). The long-term change in pain was significantly different between participants, with steeper time-based improvements in pain for participants with higher initial pain scores across all diseases. The day-to-day pain state transitions were unchanged in 50% of days across diseases, although the event of any increase in pain state was noted in 25% of days (e.g., ≥2-point increase was noted in 4% of days). 53% of those with CWP/FM remained in the 'very severe' pain state with minimal variation.

Conclusion: Participants with CWP/FM had the highest overall pain level followed by participants with axSpA, OA, and RA. These daily pain scores allow the assessment of gradual day-to-day changes through time. Patterns of improvement in those with higher initial pain scores were seen across diseases, perhaps representing regression to the mean. The volatility of changing pain states was comparable across diseases, suggesting no difference in flares. Our future work in identifying patterns of day-to-day pain will focus on analyzing the magnitude of day-to-day change in pain and the constructs of pain volatility.

Disclosure: H. Pisaniello, None; **M. Lunt**, None; **J. McBeth**, None; **W. Dixon**, Google, 1, Bayer, 1.

Abstract Number: 0543

Exercise Among Older Adults Living with Rheumatic Disease: Physical Activity Habits and Patient Reported Outcomes

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Among patients with rheumatic disease, physical activity is important for maintaining health and improving outcomes. EULAR recommendations suggest at least 30 min of vigorous exercise three times weekly. This may be particularly important for older adults in whom it is important to maintain strength and physical function. The objective of this study was to describe patient-reported level of physical activity across different diagnoses as well as the association between activity level and patient reported outcomes (PROs) among adults age 65 and older with rheumatic disease.

Methods: We performed a cross-sectional analysis among adults age 65 and older using data from Forward, The National Databank for Rheumatic Diseases, a patient registry based in the U.S. As a part of the registry, participants (pts) complete a survey every 6 months. Three questions about physical activity were added to the survey in 2019: level of physical activity, number of days per week during the month the participant exercised for 30 min or more, and perceived activity level compared to others their age. Pts also complete several other PROs including the PROMIS29 assessment, medication use, side effects, and interactions with the health care system. Proportion of pts with each disease reporting levels of disease activity and mean PRO scores by level of disease activity were descriptively reported.

Results: Among 5,335 pts completing the first questionnaire, 3,343 were age 65 or older and among these, 2,278 pts had rheumatoid arthritis (RA), 681 osteoarthritis (OA), 111 spondyloarthritis (SpA, including both axial SpA and psoriatic arthritis), 161 systemic lupus erythematosus (SLE) and 137 fibromyalgia syndrome (FMS, diagnosed by physician) (diagnoses were not mutually exclusive). The mean age overall was 74.4 (SD 6.6). Most pts were female

	RA	OA	SpA	SLE	FMS
Age (mean, SD)	74.4 (6.6)	75.4 (6.9)	72.6 (6.1)	72.8 (5.4)	72.2 (5.9)
Sex	82%	83%	75%	96%	91%
Disease duration (mean, SD)	25.2 (13)	25.1 (12.2)	27.1 (14.7)	30.8 (14)	29.5 (13.4)
Comorbidity index (mean, SD)	2.3 (1.7)	2.6 (1.8)	2.6 (1.9)	2.8 (1.9)	2.6 (1.6)
Obese	32%	40%	39%	32%	45%
College education	43%	51%	54%	44%	48%
Depression	12%	14%	14%	16%	26%

Abbreviations: RA = rheumatoid arthritis, OA = osteoarthritis, SpA = spondyloarthritis, SLE = systemic lupus erythematosus, FMS = fibromyalgia syndrome, SD = standard deviation

Table 1. Patient Demographics

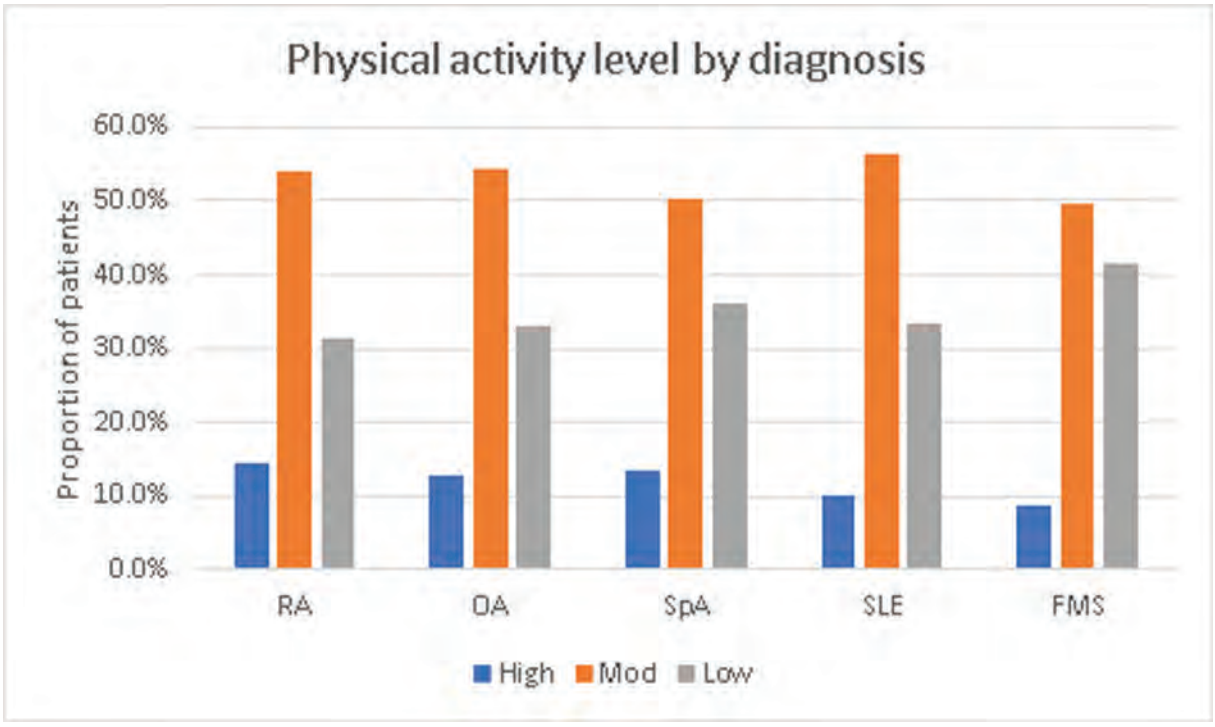

Figure 1. Physical activity level by diagnosis. Physical activity level was categorized as high (vigorously active for at least 30 min, 3 times per week), moderate (moderately active for at least three times per week) or low (seldom active).

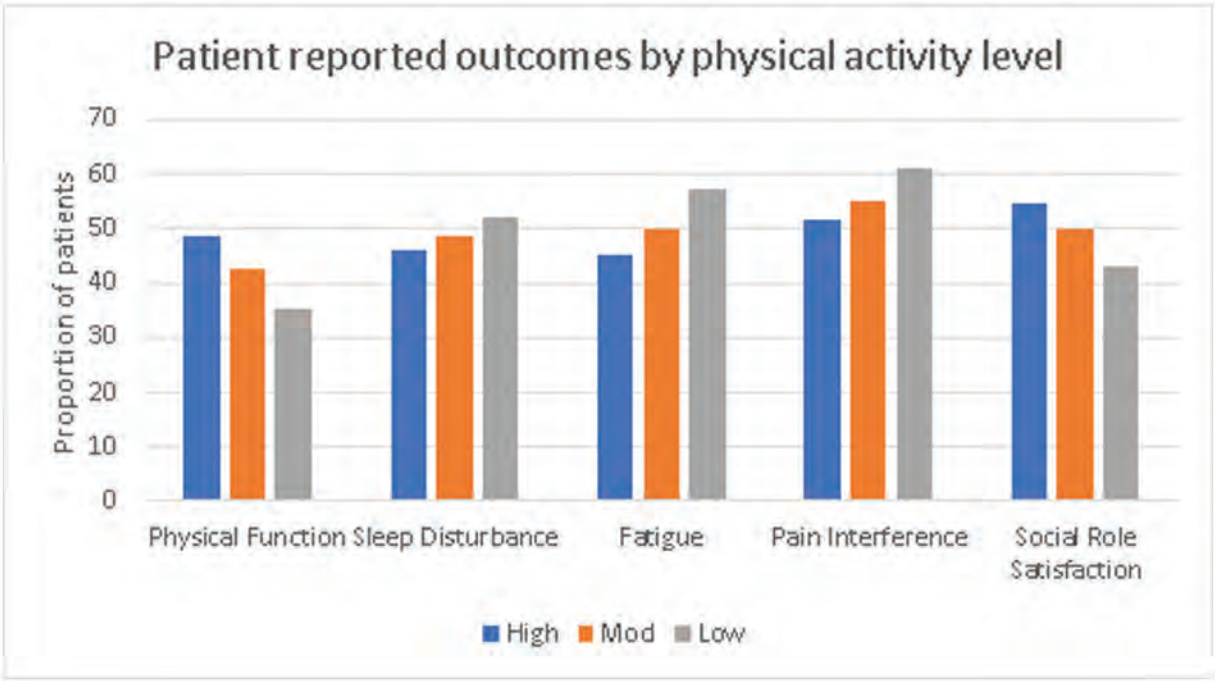

Figure 2. Patient reported outcomes by level of physical activity. Physical activity level was categorized as high (vigorously active for at least 30 min, 3 times per week), moderate (moderately active for at least three times per week) or low (seldom active). PROMIS scores increase for a patient having 'more' of the construct (i.e., higher physical function scores are good, higher pain scores are bad).

(83%). Overall, 468 (14%) pts reported vigorous physical activity for at least 30 minutes 3 or more days were week, 1,799 (54%) reported moderate activity 3 or more days per week, and 1,076 (32%) reported seldom being active. This was similar across diseases. (**Figure 1**) Overall, participants reported a median of 7 days of physical activity

per month (IQR 0-15). Obese participants were significantly more likely to report low levels of activity (44% of obese compared to 25% of non-obese individuals). Similarly, among patients with depression, 48% reported a low level of activity compared to 30% of those without depression. Finally, diminishing levels of physical activity were associated with poorer sleep, fatigue, physical function, pain, and pt global assessment of disease (**Figure 2**).

Conclusion: Levels of physical activity were relatively low among older pts with RA, OA, SpA, SLE and fibromyalgia. Because people tend to over-report their amount of exercise, the actual proportion exercising is likely even lower. Participants with the lowest level of physical activity were more likely to have depression, poor sleep, and fatigue and more likely to be obese. As these factors can improve with activity, these patients may be ideal targets for physical activity engagement strategies.

Disclosure: A. Ogdie, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1; **S. Pedro**, Forward, The National Databank for Rheumatic Diseases, 3; **J. Baker**, Gilead, 5, Bristol-Meier Squibb, 5; **K. Michaud**, Rheumatology Research Foundation, 2; **P. Katz**, None.

Abstract Number: 0544

Risk Factors for Lumbar Vertebral Osteoporosis Do Not Reflect Factors Traditionally Associated with Osteoporosis at the Hip

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The most common site of osteoporotic fragility fractures is the thoracic spine. However, bone mineral density (BMD) measurements at the hip are used to predict fracture risk using tools like FRX™, while spinal measurements only assess response to treatment. Dual energy X-ray absorptiometry (DEXA) measures BMD at lumbar vertebrae L1-3 and L1-4, user-dependant. It is not known if predictors of hip osteoporosis and fracture mimic those for vertebral osteoporosis.

Aim:

1. Evaluate factors associated with osteoporosis in the lumbar spine in female patients presenting for BMD estimation.

Methods: Female patients presenting for BMD estimation at a district general hospital in North West England, 2004-2016, were studied. In addition to BMD in L1-4, demographics, fracture history, and risk factors were recorded. Logistic regression models at each lumbar vertebral level were used to identify predictors of osteoporosis (T-score≤-2.5).

Results: 26119 unique patients underwent BMD estimation during our study period, mean age of 65.0 years (SD 12.4). Other characteristics are shown in Table 1. Fragility fractures were significantly associated with increased osteoporosis risk at all lumbar levels. Current aromatase inhibitor-use and hormone replacement therapy (HRT) were associated with significantly decreased likelihood of osteoporosis at all lumbar levels. All other demographics, co-morbidities, and medications investigated were associated with osteoporosis at varying lumbar levels.

Vertebral level	Outcome														
	L1			L2			L3			L4			L1-4		
Sample size (n)	3580			3483			3362			3440			3466		
% osteoporosis	34.3%			33.4%			35.0%			35.1%			35.5%		
%fragility fracture	40.1%			40.2%			41.9%			40.4%			41.6%		
Predictor/ Odds ratio (95%CI)	OR	2.5%	97.5%	OR	2.5%	97.5%	OR	2.5%	97.5%	OR	2.5%	97.5%	OR	2.5%	97.5%
Prev aromatase inh	1.46	0.82	2.57	0.96	0.47	1.85	0.92	0.47	1.75	1.01	0.53	1.86	0.94	0.48	1.80
Current aromatase inh	0.59	0.48	0.73	0.56	0.45	0.70	0.52	0.41	0.65	0.52	0.41	0.64	0.58	0.47	0.72
Cancer	1.57	0.88	2.76	1.47	0.83	2.55	1.16	0.60	2.20	0.85	0.47	1.47	1.37	0.76	2.41
Coeliac	1.37	0.93	2.00	0.99	0.64	1.52	0.82	0.52	1.24	0.66	0.41	1.01	1.02	0.65	1.57
Depo-provera	0.53	0.30	0.86	0.84	0.47	1.41	0.37	0.17	0.67	0.70	0.43	1.06	0.65	0.34	1.12
Prev etoh	0.74	0.40	1.29	1.12	0.60	2.01	1.03	0.55	1.85	0.56	0.29	1.02	0.63	0.30	1.21
Current etoh	0.84	0.59	1.17	0.77	0.54	1.09	0.57	0.39	0.80	0.83	0.59	1.15	0.61	0.42	0.86
Fam hist of fracture	1.36	0.91	2.02	1.10	0.76	1.58	1.49	0.99	2.21	1.60	1.09	2.33	1.12	0.74	1.67
Fragility fracture	1.89	1.64	2.18	2.11	1.83	2.44	1.91	1.65	2.20	1.84	1.60	2.12	1.91	1.66	2.20
HRT	0.42	0.28	0.61	0.45	0.30	0.66	0.45	0.31	0.64	0.52	0.35	0.75	0.49	0.34	0.70
Prev hyperparathyroid	1.04	0.39	2.54	2.19	0.92	5.27	1.87	0.64	5.47	1.04	0.32	3.01	0.91	0.24	2.89
Current hyperparathyroid	1.54	0.89	2.64	0.64	0.31	1.23	1.13	0.61	2.06	1.67	0.98	2.86	1.19	0.66	2.12
Prev hyperthyroidism	1.67	0.98	2.84	0.78	0.43	1.35	1.52	0.93	2.47	1.68	1.00	2.82	1.06	0.64	1.71
Current hyperthyroid	1.29	0.43	3.58	0.44	0.07	1.71	0.68	0.19	2.00	0.56	0.13	1.83	3.29	1.13	10.72
IBD	0.92	0.66	1.26	1.18	0.83	1.66	1.12	0.79	1.58	0.89	0.62	1.26	1.13	0.83	1.55
SLE	0.38	0.12	0.92	0.92	0.45	1.79	0.65	0.24	1.58	0.23	0.05	0.66	0.43	0.16	0.99
PMR	1.11	0.74	1.63	0.72	0.47	1.07	1.41	0.98	2.02	0.67	0.43	1.01	0.76	0.52	1.11
RA	1.00	0.76	1.31	1.11	0.85	1.44	0.75	0.56	1.00	0.78	0.59	1.03	0.93	0.70	1.22
Prev smoker	0.93	0.79	1.10	1.06	0.89	1.26	0.95	0.80	1.13	0.95	0.80	1.12	0.90	0.76	1.07
Current smoker	0.87	0.70	1.09	0.91	0.72	1.14	0.79	0.62	0.99	0.99	0.80	1.22	0.87	0.70	1.08
axSpa	1.92	0.53	6.90	0.66	0.10	2.88	0.62	0.03	4.84	2.23	0.67	7.74	2.55	0.81	8.63
Prev steroids	0.94	0.77	1.14	0.93	0.76	1.14	0.90	0.74	1.10	0.84	0.69	1.03	0.89	0.73	1.08
Current steroids	0.81	0.64	1.12	1.04	0.83	1.30	0.73	0.57	0.93	0.63	0.49	0.80	0.61	0.48	0.78
Vit D deficiency	0.89	0.44	1.68	0.96	0.49	1.79	0.59	0.25	1.26	1.09	0.58	1.96	0.79	0.41	1.46

Table 1. Odds ratios for risk of osteoporosis, associated with co-morbidities and medication-use, in the lumbar vertebral spine

Conclusion: Our results show a clear difference in co-morbidities and medication-use associated with osteoporosis at different lumbar levels. Traditional risk factors for osteoporosis are not associated with decreased BMD in the lumbar spine. Patients with vertebral osteoporosis were more likely to sustain fragility fractures as expected. HRT is bone-protective and was therefore associated with decreased likelihood of osteoporosis. Current aromatase inhibitor use was associated with decreased likelihood of osteoporosis at all lumbar levels, while current corticosteroid use was associated with decreased likelihood of osteoporosis in the lower lumbar region. Both medications are known to reduce BMD- these results are confounded by concurrent use of calcium, vitamin D, and bisphosphonate treatment.

SLE was associated with reduced likelihood of osteoporosis at the superior and inferior lumbar spine, also likely confounded by treatment. Current hyperthyroidism was associated with significantly increased risk of osteoporosis averaged throughout the lumbar spine, consistent with previous studies. Current alcohol intake was associated with decreased risk of osteoporosis at L3, consistent with previous work demonstrating a protective effect of low-moderate alcohol intake on bone health.

In conclusion, we demonstrate risk factors for low BMD are not equal throughout the lumbar spine, and differ from traditional osteoporotic risk factors, including those commonly used in predictive scores for fracture. Our results suggest a need to consider risk factors specific to lumbar spine osteoporosis when planning prevention and management of vertebral fragility fractures.

Disclosure: M. Bukhari, Bristol- Myers Squib, 1, UCB celltech, 1, 2, Roche, 1, 2, Abbvie, 1, 2, Merck, 1, 2, Mennarini, 1, 2, Sanofi-aventis, 1, 2, Elli-Lilly, 1, 2, Janseen, 1, Amgen, 1, 2, Novartis, 1, 2; **M. Dey**, None.

Abstract Number: 0545

The Use of Tocilizumab and Tofacitinib in Patients with Resolved Hepatitis B Infection: A Case Series

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The use of immunosuppressive medications in patients with a history of hepatitis B virus (HBV) infection is associated with an increased risk of HBV reactivation which can lead to liver failure and death. Rates of HBV reactivation have been reported in up to 24% of people with resolved HBV (positive core antibody [HBcAb], negative surface antigen [HBsAg], and positive or negative surface antibody [HBsAb]) and 34% of people with chronic HBV (positive HBsAg) in patients who are treated with tumor necrosis factor inhibitors, rituximab, and other biologics. Outside of Asia, there are limited data regarding the risk of reactivation in patients taking tocilizumab or tofacitinib, both of which have emerged as potential treatments for the systemic inflammatory manifestations of coronavirus disease 2019.

Methods: In this retrospective study, we identified patients in the Mass General Brigham (MGB) healthcare system who had ≥ 1 prescription for either tocilizumab or tofacitinib and resolved or chronic HBV between 1995 and 2018. Details regarding demographics, medical history, and laboratory results were extracted from the electronic health record. HBV reactivation was defined as a greater than 10-fold increase in HBV deoxyribonucleic acid (DNA) levels from baseline, an absolute increase > 10^5 copies/mL, or a positive HBsAg when previously negative.

Results: Twenty patients, all with resolved HBV, were included (**Table 1**). Four patients received tofacitinib and tocilizumab sequentially such that there were 24 medication exposures. The median age at treatment initiation was 59 years (tofacitinib) and 66 years (tocilizumab) and the majority were female. The majority of patients treated with tocilizumab (16, 100%) and tofacitinib (7, 88%) were HBsAb positive at baseline. Concurrent immunosuppression was used in 12 (75%) tocilizumab-treated patients and 6 (75%) tofacitinib-treated patients. Anti-viral treatment was prescribed in 25% of cases in both groups. Median follow-up time after treatment initiation was 4.0 years in the tocilizumab group and 3.1 years in the tofacitinib group. During follow-up, all patients had aminotransferases measured at least once, and no patients had transaminitis attributed to HBV reactivation. Among the patients who had ≥ 1 HBV polymerase chain reaction or HBsAg assessed after treatment initiation (13 [81%] in the tocilizumab group and 4 [50%] in the tofacitinib group), none were positive.

Conclusion: We found no instances of HBV reactivation in patients with resolved HBV exposed to tocilizumab or tofacitinib. A quarter of people in our study were prescribed antivirals and many had no follow up serologic studies to evaluate for reactivation, reflecting the uncertainty regarding best practices for patients with resolved HBV. Our findings suggest that tocilizumab or tofacitinib may be safely used in patients with resolved HBV infection.Table 1. Demographics, clinical characteristics, and follow up of study population

Table 1. Demographics, clinical characteristics, and follow up of study population

Characteristic	Tocilizumab-treated patients (N=16)	Tofacitinib-treated patients (N=8)
Age (years); median (IQR)	66.1 (45.4, 71.3)	59.4 (42.4, 70.9)
Female, n (%)	9 (56)	7 (88)
Race, n (%)		
White	7 (44)	3 (38)
Black or African-American	4 (25)	4 (50)
Asian	4 (25)	0 (0)
Unknown/ Other	1 (6)	1 (12)
Ethnicity, n (%)		
Non-Hispanic	15 (94)	8 (100)
Unknown	1 (6)	0 (0)
Positive HBV serologies, n (%)		
HBcAb	16 (100)	8 (100)
HBsAg	0 (0)	0 (0)
HBsAb	16 (100)	7 (88)
Cirrhosis, n (%)*	1 (6)	1 (13)
Follow-up time (years), median (IQR)	4.0 (1.6, 5.9)	3.1 (0.9, 5.7)
Concurrent immunomodulatory therapy, n (%)†	12 (75)	6 (75)
Oral glucocorticoids	7/12 (58)	4/6 (67)
csDMARD‡	7/12 (58)	4/6 (67)
Rituximab	1/12 (8)	0/6 (0)
Antiviral treatment, n (%)§	4 (25)	2 (25)
Reactivation of HBV virus during or within 2 years following treatment, n (%)¶		
Yes	0 (0)	0 (0)
No	13 (81)	5 (63)
Unknown (no follow-up HBV DNA or HBsAg)	3 (19)	3 (38)

HBV: hepatitis B virus; HBcAb: hepatitis B core antibody; HBsAg: hepatitis B surface antigen; HBsAb: hepatitis B surface antibody; IQR: interquartile range; csDMARD: conventional synthetic disease-modifying antirheumatic drug; DNA: deoxyribonucleic acid

*Cirrhosis was defined by presence of this diagnosis in the electronic health record.
†Percentages do not add up to 100% as some patients received multiple types of immunomodulatory medications within the two-year study period.
‡csDMARDs included methotrexate, leflunomide, and sulfasalazine in the tocilizumab group, and methotrexate and sulfasalazine in the tofacitinib group.
§Refers to patients who received antiviral treatment at any point within the two-year follow-up period. In the tocilizumab group, three patients received entecavir and one received tenofovir, one of which was after the study medication. In the tofacitinib group, one patient received tenofovir and one patient received entecavir, though both after study medication.
¶Percentages in tofacitinib group do not add up to 100% due to rounding.

Table 1. Demographics, clinical characteristics, and follow up of study population

Disclosure: N. Serling-Boyd, None; **A. Mohareb**, None; **A. Kim**, Biomarin, Inc, 7; **E. Hyle**, None; **Z. Wallace**, Bristol-Myers Squibb, 2.

Abstract Number: 0546

Stepping up for Inflammatory Arthritis (SUFIA): A Pilot Trial to Test Behavioral Economics Strategy to Increase Physical Activity in Inflammatory Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease

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Session Time: 9:00AM–11:00AM

Background/Purpose: Regular physical activity may have benefits for patients with rheumatoid arthritis (RA) and psoriatic arthritis (PsA), but patients with active disease are often reluctant to increase activity. Principles from behavioral economics (BE), a field combining psychology and economics, have been applied to motivate increased physical activity in non-arthritis patients. The objective of this study was to assess the feasibility and efficacy of a loss aversion financial incentive for increasing step counts and improving disease symptoms in RA and PsA patients with active disease.

Methods: A double-blind randomized controlled pilot trial was performed among patients with RA and PsA. Participants were required to have active disease defined by having at least one swollen joint and a Routine Assessment of Patient Index Data-3 (RAPID3) score >3 (range 0-30 with < 3 indicating remission). The primary goal of this study was to establish feasibility of the platform and study conduct. The primary outcome was change in RAPID3 between the two arms. The trial included two visits (Figure 1) and weekly check-ins via virtual trial platforms, Way to Health and the ArthritisPower app. Patients were given a Fitbit Alta at baseline and completed a two-week run-in period to assess average step count. Patients were then prompted to select a step count goal (30, 40, or 50% above baseline daily step count) and complete a commitment contract. After selection of a goal, participants randomized to the

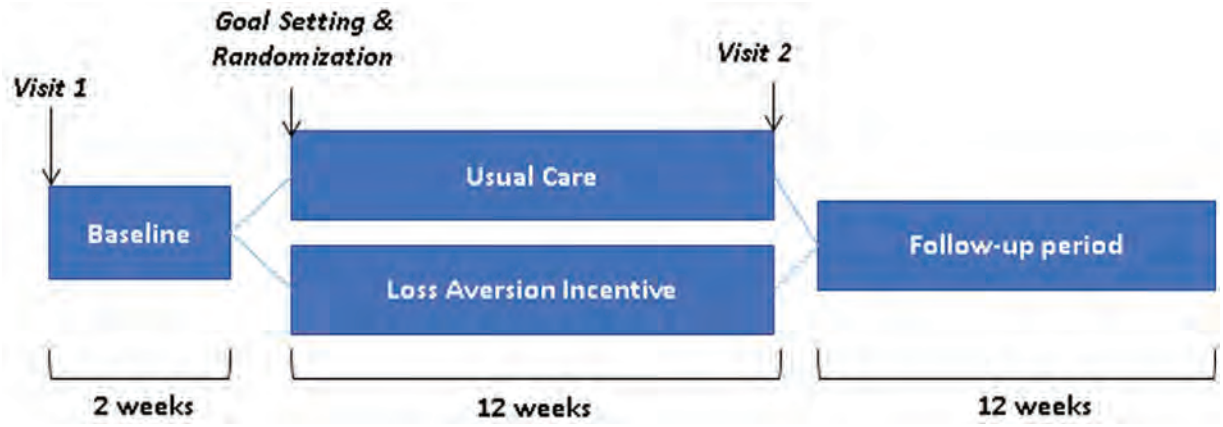

Figure 1. Study diagram. There were two study visits (weeks 0 and 14). The first two weeks served as a baseline period to establish a baseline step count. Patients then selected a step count goal which was either 30%, 40%, or 50% above the baseline step count and signed a commitment contract. Patients were then randomized to a financial incentive or no incentive. The primary outcome (change in RAPID3) occurred at week 14.

Table 1. Baseline Characteristics of Patients Enrolled in Pilot SUFIA Study

N	27
Age	50 (13)
Women	85%
Body Mass Index	30.6 (7.7)
Rheumatoid Arthritis	10 (37%)
Psoriatic Arthritis	17 (63%)
Disease duration (yrs)	9 (10)
Swollen Joint Count (0-66)*	6.2 (5.6)
Tender Joint Count (0-68)*	8.1 (9.1)
Lower extremity involvement**	
Knee	
Ankle	56%
Midfoot	37%
Toes	19%
	37%
RAPID3	10.4 (4.6)
PROMIS Fatigue	53.4 (7.8)
PROMIS Sleep Disturbance	49.7 (3.3)

All patients are on therapy for IA. *We used the 66/68 joint count for assessment of all patients to capture lower extremity involvement. **Lower extremity involvement could be swelling or tenderness.

Table 1. Baseline Characteristics of Patients Enrolled in Pilot SUFIA Study

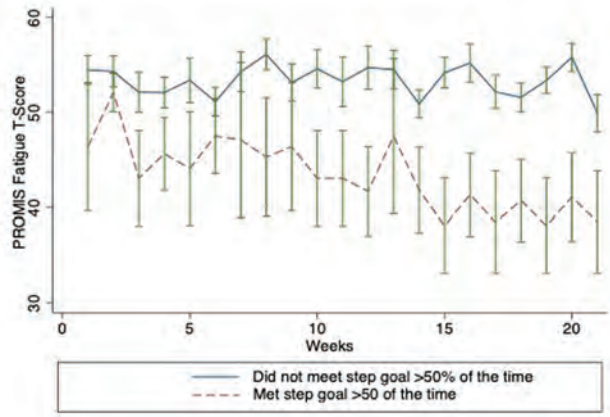

Figure 2. Change in fatigue severity among those with greater adherence to step count goals. The PROMIS fatigue score increases with worse fatigue and decreases with improving fatigue.

intervention arm received a financial loss aversion incentive (each month, patients started with $75 in their account and lost $2.50 for each day they did not reach their goal). All patients received weekly text message prompts providing feedback about their performance over the past week and completed weekly PROs. After 12 weeks of the intervention (at week 14), the incentive was removed and patients were followed to 26 weeks to determine how long the effect persisted.

Results: In the pilot trial, 71 patients were verbally consented for screening, 34 underwent screening (of these, two were ineligible), 27 were randomized, and 22 patients completed the 14-week study visit. The mean step count at baseline was 5,962. By 28 days, 65% of patients increased their step count. Participants receiving the incentive had an average of 714 more steps per day over the first 14 weeks and a greater probability of reaching 10,000 steps per day during follow-up (30% v. 21%, p=0.41). Among patients who achieved their step count goals more than 50% of days, we observed more improvement in sleep quality, fatigue, and overall well-being ($p< 0.05$) (Figure 2). After adjusting for baseline RAPID3, the 14-week RAPID3 scores were lower in the group that achieved their step goals 50% of the time [B: -3.91 (-11.8, 3.99); a difference that approximates the minimal clinically important difference (MCID) for the RAPID3 (3.6).

Conclusion: While financial incentives have worked well in patients without arthritis, the estimated effect of the financial incentive in this small study was more modest in patients with RA and PsA. Those that were able to increase their physical activity and meet their step goals had greater improvements in symptoms over the course of the study.

Disclosure: A. Ogdie, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1; **K. Bush**, None; **M. George**, Bristol-Myers Squibb, 2; **M. Patel**, None; **W. Nowell**, None; **K. Gavigan**, None; **J. Curtis**, AbbVie, 1, 2, Amgen, 1, 2, Bristol-Myers Squibb, 1, 2, Corrona, 1, 2, Crescendo, 1, 2, Janssen, 1, 2, Pfizer, 1, 2, Sanofi, 1, 2, UCB, 1, 2; **J. Baker**, Gilead, 5, Bristol-Meier Squibb, 5.

Abstract Number: 0547

Transgender Patients in the Rheumatology Setting

Chantelle Carneiro[1], Jessica Chee[2], Karen Beattie[2] and Kimberly Legault[2], [1]McMaster University, Toronto, ON, Canada, [2]McMaster University, Hamilton, ON, Canada

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Minimal medical research exists regarding transgender patients, particularly within the field of rheumatology. A few case reports note that male to female transitions may precede presentation of autoimmune disease, with a possible link to exogenous estrogen, while exogenous testosterone was noted to improve a case of subacute cutaneous lupus. There is currently no research assessing transgender demographics and disease presentation in the rheumatologic setting.

Methods: We conducted a retrospective chart review of transgender patients who presented to our academic and community clinics or inpatient rheumatology service. We collected information on patients' medical history and rheumatologic diagnoses, transition (legal, social and medical), presenting symptoms and treatment.

Results: From 25 rheumatologists contacted, 12 transgender patients were identified. Patients' ages ranged from 22-66 years old and had the following diagnoses: PsA, seronegative SpA, PM with SSc overlap, SSc, PMR, FM, leucocytoclastic vasculitis, periodic fever syndrome and osteopenia. Five (42%) patients had uncontrolled disease or relapse of their disease requiring adjustment of their treatment regimens. The most common co-morbidity was depression and anxiety (n=7, 58% patients). A family history of autoimmune disease was documented in 5 (42%) patients. Nine (75%) of patients were transgender males, 8 of whom were using intramuscular testosterone and 2 of whom had hysterectomies with bilateral salpingoopherectomies. Only 3/9 transgender male patients had a docu-

mented start time of testosterone therapy. However, 7 patients had either been on testosterone at diagnosis or were on it for at least 1 year before being diagnosed with their rheumatologic conditions. Of 3 transgender females, 2 were exposed to estrogen therapy prior to presentation. One patient had only a one-time use of exogenous estrogen and significant silica exposure for >20 years that was her major risk factor for developing systemic sclerosis.

Conclusion: The majority of patients presenting in our rheumatology clinics and inpatient service were transgender males undergoing transition. These data correlate with prior research that most rheumatologic diseases have a higher prevalence for biologic females. However, of the diseases with female prevalence in our study (PM, PMR, SSc, osteopenia and FM), almost half the patients diagnosed were biologically male (3/7). We believe larger studies need to be done to assess whether hormone transitions, either via gonadectomy and/or with exogenous hormones, can affect the prevalence of these diseases in transgender patients. In addition, we recommend rheumatologists carefully document when medical transitions occur relative to their rheumatologic condition in order to track timing of new diagnoses or changes in their disease. Additionally, given the high prevalence of depression seen in our study, we recommend that physicians pay particular attention to the mental health of their transgender patients at each follow-up and direct them to supports as needed.

Disclosure: C. Carneiro, None; **J. Chee**, None; **K. Beattie**, None; **K. Legault**, None.

Abstract Number: 0548

Incidence of First Cardiovascular Event in Spanish Patients with Chronic Inflammatory Rheumatic Diseases. Prospective Data After Five Years of Follow Up

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Sevilla, Spain, [44]Hospital El Escorial, Madrid, Spain, [45]Hospital Infanta Leonor, Madrid, Spain, [46]Hospital Universitario 12 de Octubre, Madrid, Spain, [47]Hospital dos de Maig, Barcelona, Spain, [48]Hospital Universitario Son Dureta, Palma de Mallorca, Spain, [49]School of Medicine, University of Cantabria, and CIBER Epidemiología y Salud Pública (CIBERESP), Santander, Spain, [50]Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: To determine the incidence and risk factors implicated in the development of first cardiovascular (CV) event (CVE) in patients with chronic inflammatory rheumatic diseases (CIRD) attending Spanish rheumatology clinics after 5 years of follow-up.

Methods: Analysis of data of patients included in an observational prospective study [CARdiovascular in rheuMAtology (CARMA) project] after 5 years of follow-up. The study includes a cohort of patients with CIRD [rheumatoid arthritis (RA, n=775, ankylosing spondylitis (AS, n=738), and psoriatic arthritis (PsA, n=721)], and another cohort of matched individuals (n=677) without CIRD attending outpatient rheumatology clinics from 67 public hospitals in Spain. Cumulative incidence per 1000 patients of CVE was estimated in both cohorts at 5 years from the start of the project. Weibull proportional hazard model was used to calculate the Hazard Ratio (HR) and 95% confidence intervals (95% CI) of the risk factors involved in the development of CV events. Losses to follow-up and their causes were also analyzed.

Results: The total number patient who completed the follow-up visit at 5 years was 2.382 (81.9% of those who started the study). Fifteen patients died due to CVE and sixty due to non-CVE. Cardiovascular cumulative incidence of CVE in patients with CIRD was higher in PsA patients (48.9; 95% CI: 40.7-57.1). The higher risk of developing a first CVE during the 5 years of follow-up was seen in patients with AS (HR: 4.60 ; 95% CI: 1.32-15.99; p=0.02), those with older age (HR:1.09; 95% CI: 1.05-1.13; p< 0.001), higher systolic blood pressure (HR: 2.64; 95% CI: 1.32-5.25; p=0.006), and those with longer duration of the rheumatic disease (HR: 1.07; 95% CI: 1.03-1.12; p=0.002). In contrast, woman gender was a protective factor (HR: 0.45; 95% CI: 0.21-0.99; p=0.047).

Conclusion: Patients with AS prospectively followed-up at rheumatology outpatient clinics showed higher risk of developing a CVE than those with RA or PsA. Besides traditional CV disease risk factors, a longer time course of the disease is a risk factor for the development of CV disease in patients with CIRD.

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Abstract Number: 0549

Developing an Algorithm for Identifying Mortality in MarketScan Claims Data Using Machine Learning

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: In 2016, MarketScan data no longer included information about inpatient mortality, compromising the ability to study fatal hospitalization events. Using data through 2015 when mortality remained available, we developed an algorithm to accurately identify in-hospital mortality using coverage patterns, proximate healthcare claims diagnoses, and corresponding information for family members.

Methods: We selected the latest hospital claim in 2011-2015 MarketScan data for each individual. Hospitalizations with discharge status of (20, 40, 41) were defined as death, and (21, 87, missing) as alive. Predictors included age, sex, coverage disenrollment post hospitalization, diagnosis codes and timing of last submitted claim, and corresponding information from family members linked by family ID (to confirm family members remained enrolled). Individual predictors were optimized using the c (concordance) index. Datasets were split into Training (80% random sample of hospitalizations, 2011-2013); Test1 (80% in 2014-2015) and Test2 (remaining 20%, 2011-2015). Machine learning (ML) methods included decision tree (DT), random forest (RF), elastic-net regularization (ER) and XGBoost methods. Hyper-parameters were tuned using a random search method with 10-fold cross validation across a preset range. was used to assess model performance. Each model was validated in Test1 and Test2 datasets separately. Sensitivity, specificity, positive predicted value (PPV) and accuracy were calculated in all datasets.

Results: 1,307,532 hospitalizations were selected among patients; mean age was 47.4 (standard deviation 25.9) years and 43.6% were male. Training data included 727,887 hospitalizations, 23.1% ending in death. Disenrollment

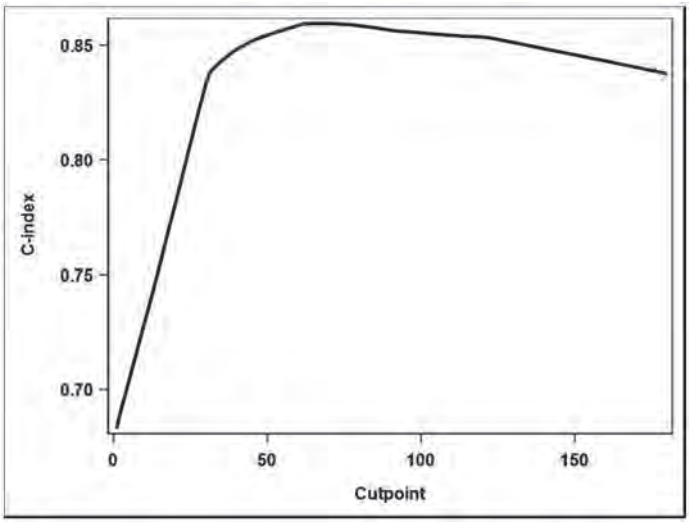

Figure 1. Optimization of cut-point for disenrollment

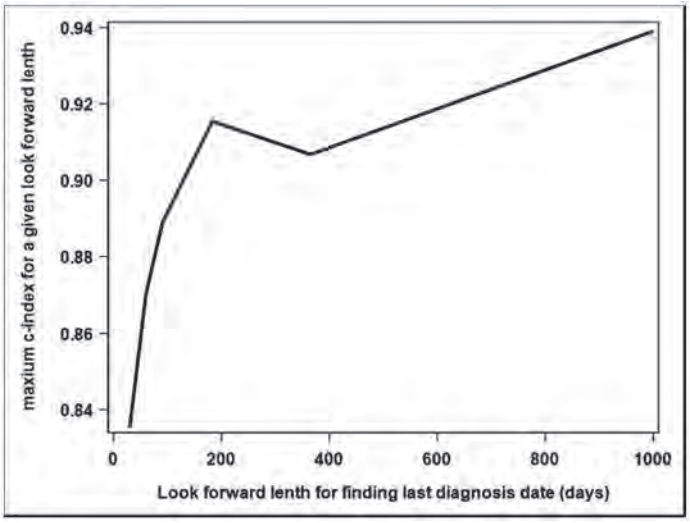

Figure 2. Optimization of interval from hospital discharge date to last claim

Dataset	Train				Test1				Test2			
ML Method	SN	SP	PPV	ACC	SN	SP	PPV	ACC	SN	SP	PPV	ACC
Decision Tree	0.83	0.95	0.82	0.92	0.88	0.96	0.87	0.94	0.84	0.95	0.84	0.93
Random Forest	0.93	0.96	0.88	0.96	0.93	0.96	0.88	0.95	0.93	0.96	0.88	0.95
Elastic Net	0.86	0.97	0.89	0.94	0.89	0.97	0.91	0.95	0.87	0.97	0.89	0.94
XG Boost	0.94	0.96	0.87	0.95	0.94	0.96	0.88	0.95	0.94	0.96	0.87	0.95

ACC: Accuracy; DT: Decision tree; ER: elastic-net regularization; ML: Machine Learning;
PPV: Positive predicted value; RF: random forest; SN: sensitivity; SP: Specificity; XGB: XGBoost.

Table Model performance to classify in hospital mortality in Training and Test datasets

ending within 30 days (Figure 1), and last claim within 90 days were optimized as single predictors (Figure 2). Models using different ML methods performed well in all datasets, albeit with a trend for less optimal parameters with decision tree methods. In test datasets, PPV and accuracy was as high as 0.91 and 0.95 respectively.

Conclusion: We derived and validated an algorithm for identifying in-hospital mortality in Marketscan claims data which performed well with >90% accuracy. This represents filling of a key gap for health outcomes research with Marketscan data.

Disclosure: F. Xie, None; **H. Zhao**, None; **H. Yun**, Pfizer, 2; **S. Bernatsky**, None; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5.

Abstract Number: 0550

Mapping Multimorbidity Using Drug Concept Unique Identifiers (RxCUIs) via the Rx-Risk Comorbidity Index

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease

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Background/Purpose: Identifying and accurately classifying comorbid conditions in large, real-world data sources is crucial for cohort establishment and confounder adjustment. However, the ability to conduct proper confounding control may be challenging when data for diagnosis codes and lab tests are incomplete, such as in a single-specialty EHR system where comorbidities are incompletely recorded by specialists. Thus, we updated a method to allow researchers to identify comorbid conditions using only medication information in circumstances where diagnosis codes are under-captured.

Using the RxNorm application program interface (API) and its web-based clients, RxMix and RxClass, we mapped Drug Concept Unique Identifiers (RxCUIs) to the Rx-Risk. In an established RA cohort in the ACR RISE registry, we compared Rxrisk with other comorbidity indices. These included the Charlson comorbidity index, Rheumatic Disease Comorbidity Index (RDCI) and Elixhauser.

Methods: For each of the 46 Rx-Risk categories, we identified corresponding RxNorm ingredients via RxClass and expanded them to all RxCUI term types (TTYs) using RxMix (RxNorm May 2020 release) based on FDA indications. Glucocorticoid products were confined to the comorbidity categories: Allergies, Chronic airway disease, and steroid-responsive disease by administration route. After finalizing the Rxrisk categories, we conducted descriptive analyses and compared the distribution of Rxrisk with more traditional diagnosis-based comorbidity scores among RA patients who were 18 years of age with $^{3}2$ consecutive visits with ICD-10 codes for RA using ACR RISE data, a rheumatologist-based RA registry. Medications and comorbidity diagnoses were assessed using all available data prior to the 2nd RA diagnosis code.

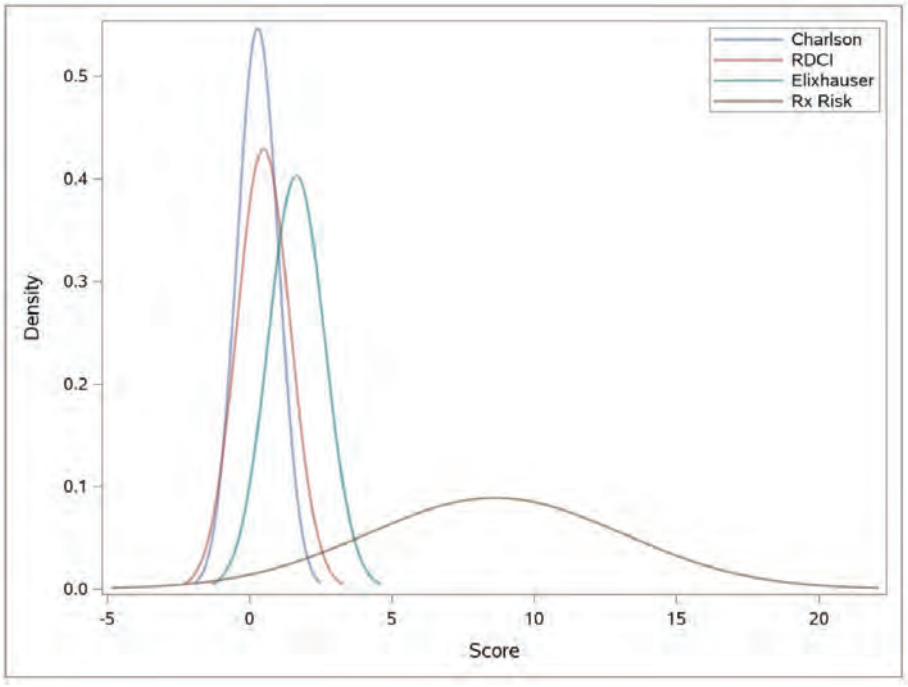

Figure Distribution of Rx Risk, Charlson, RDCI and Elixhauser among RA patients identified from ACR RISE registry.

Results: We identified 913 ingredient RxCUIs representing the 46 Rx-Risk comorbidity categories. 65,895 RxCUIs for all TTYs were returned from our initial query. After excluding Dosage Form related RxCUIs, a total of 56,217 RxCUIs were included in our analysis. The most common TTYs were Semantic Clinical Drug (19.8%), Demantic Brand Drug (13.0%), and Semantic Branded Drug Component (11.9%), while pain (17.7%), allergy (11.7%), and malignancy (6.2%) products were most frequent among the 46 comorbidity categories. The median score (25^{th}/75^{th} percentile) for Rxrisk was much greater: 8 (5,12) than for charlson index: 0 (0,0); Elixhauser: 1 (1,2); RDCI: 0 (0,1). For patients with Charlson score of 0 (85% of total), both the RDCI and Elixhauser were close to 1, but the Rxrisk score ranges from 0 to 20 (Figure).

Conclusion: The misclassification and under ascertainment of comorbidities in a single specialty EHR can largely be overcome by using a medication-focused comorbidity index that we have recently updated.

Disclosure: J. Vanderbleek, None; **J. Owensby**, None; **A. Mccannaly**, None; **L. Chen**, None; **B. England**, None; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **H. Yun**, Pfizer, 2.

Abstract Number: 0551

Physical Performance as a Mediator of the Association Between Depression and Pain in Knee Osteoarthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Background/Purpose: Depression is common in knee osteoarthritis (OA), and leads to reduced physical function, which may mediate the effect of depression on pain. However, research has used self-reported functional measures and assumed that depression is additively related to pain both directly (unmediated) and indirectly (mediated) by physical function. The aim was to assess the direct effect of depression on pain and indirect effect mediated, possibly synergistically, through physical function using an objective physical performance measure among individuals with radiographic knee OA.

Methods: Participants were from the Osteoarthritis Initiative (n=2,484) who had radiographic disease (Kellgren-Lawrence [K-L] grade ≥ 2) and complete data on variables measured at baseline (time *t)*. Depression was measured on a severity continuum using the Center for Epidemiologic Studies Depression (CES-D) Scale as a continuous score (range=0-60) from baseline to third annual follow-up visit (time *t*+3). Physical performance was assessed via 20-meter gait speed (meters per second [m/s]) from the first (time *t*+1) through fourth (time *t*+4) annual follow-up visit. Pain was measured with the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) pain subscale (rescaled range=0-100) from the second (time *t*+2) to fifth (time *t*+5) annual follow-up visit. Time-invariant confounders were age, sex, race, marital status, education, smoking, alcohol consumption, employment status, health insurance, Charlson comorbidity index, and presence of frequent knee symptoms. Time-varying confounders measured concurrent to depression were knee injections, analgesic medication use, body mass index, K-L grade, gait speed,

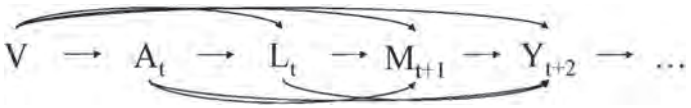

Figure 1. Directed acyclic graph illustrating the repeated measures study design with time-invariant confounders (V), and time-varying depression exposure (A), confounders (L), and physical performance mediator (M), as well as pain outcome (Y), where the subscript t corresponds to time point.

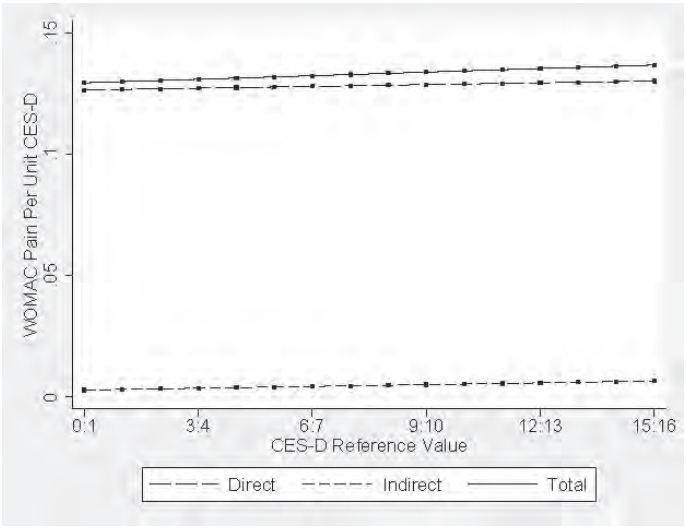

Figure 2. Incremental direct, indirect, and total effects.

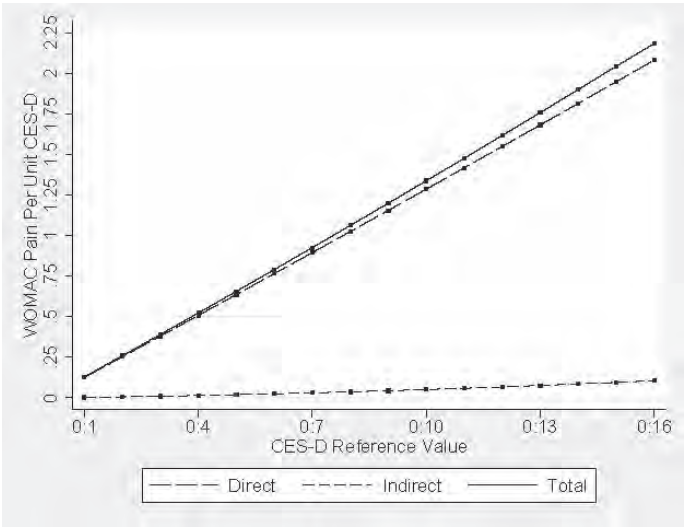

Figure 3. Cumulative direct, indirect, and total effects.

and WOMAC pain. A two-stage marginal structural model approach for effect decomposition in scenarios with exposure-mediator interaction estimated direct, indirect, and total effects between depression, physical performance, and pain (Figure 1).

Results: Incremental effects for one-unit differences in CES-D score indicated that associations (Figure 2) increased with higher depression severity. Direct effects of depression on pain were 0.126 (95% CI: 0.124, 0.128) and 0.130 (95%: 0.128, 0.132) WOMAC units for a CES-D score difference of 1 vs. 0 compared to 16 vs. 15, respectively. Indi-

rect effects of depression on pain mediated by physical performance were smaller in magnitude but showed larger proportional increases: CES-D score 1 vs. 0 = 0.003 (95% CI: 0.002, 0.004) WOMAC units; and CES-D score 16 vs. 15 = 0.066 (95% CI: 0.003, 0.009) WOMAC units. Cumulative effects (Figure 3) implied a 16-unit CES-D score difference (16 vs. 0) yielded a direct effect of 2.082 (95% CI: 2.052, 2.112) WOMAC units and indirect effect mediated by physical performance of 0.105 (95% CI: 0.054, 0.157) WOMAC units.

Conclusion: Effects of depression on pain increase with higher depressive symptom severity, but the proportion of the association mediated by physical performance is small. Findings suggest that exercise interventions for depression may reduce pain by acting directly on depressive symptoms or by increasing physical activity rather than function.

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Abstract Number: 0552

Fast Food Habits and Serum Urate Change in Young Adults: 15-Year Prospective Cohort Analysis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Fast food consumption has strong positive associations with weight gain and insulin resistance. Obesity and insulin resistance are, in turn, strongly associated with elevated serum urate (SU) levels. This is largely mediated by the anti-uricosuric ability of insulin. The objective of this study was to investigate the relationship between fast food consumption and changes in SU over a 15-year period among young black and white adults in the United States.

Methods: Coronary Artery Risk Development in Young Adults (CARDIA) is a longitudinal study of cardiovascular disease risk factors and development among black and white adults in the United States who were 18-30 years of age in 1985-86 who underwent repeated dietary questionnaires and clinical and laboratory examinations. Our analysis included data from participants who had SU data available both at baseline and Year 15. Frequency of fast food consumption (fast food frequency, FFF) was quantified on a semicontinuous scale and classified as < 1, 1-2, or >2 times per week. Multivariable linear regression models were used to investigate the association of FFF at baseline as well as change in FFF with 15-year changes in SU. Difference in baseline FFF was defined as a difference in FFF

Table 1. Participant Characteristics

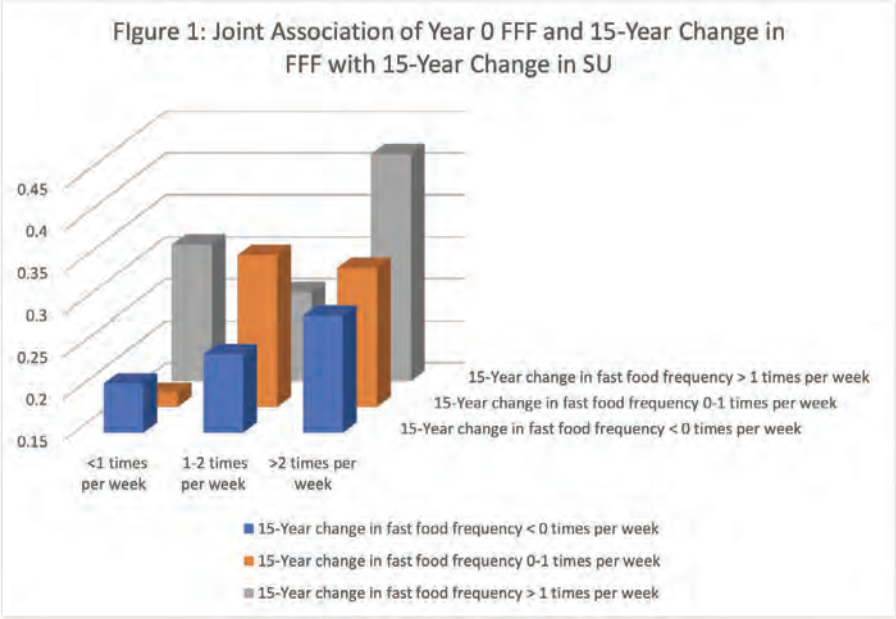
Characteristic	Blacks (n=1468)	Whites (n=1654)
Age, years (Year 0)	24.4 (3.8)	25.6 (3.3)
Male (%)	44	48
Weight, kg (Year 0)	72.8 (16.7)	70.0 (14.0)
Weight, kg (Year 15)	87.9 (20.9)	80.7 (18.6)
Serum urate, mg/dL (Year 0)	5.1 (1.4)	5.4 (1.4)
Serum urate, mg/dL (Year 15)	5.6 (1.4)	5.5 (1.4)

All values reported as mean (SD) unless otherwise noted.

Table 2. Mean Adjusted Change in Serum Urate by Baseline and Change in Fast Food Frequency

	Fast Food Variable	Blacks		Whites	
		Beta (SE)	p	Beta (SE)	p
Model 1	Baseline	0.11 (0.04)	0.01	0.11 (0.04)	0.01
	Change	0.003 (0.033)	0.93	0.09 (0.04)	0.01
Model 2	Baseline	0.12 (0.04)	0.01	0.09 (0.04)	0.02
	Change	0.004 (0.03)	0.88	0.08 (0.04)	0.03

Model 1: age, sex, education, baseline height and weight, baseline SU
Model 2: model 1 + alcohol, physical activity, and smoking (both baseline and year 15 change



consumption of 3 times a week (approximately the mean difference between individuals with low vs. high FFF) between participants. Change in FFF was defined as 3 times a week (approximately the mean range in change over time between individuals with low vs. high FFF) 15-year change within participants.

Results: Our analysis included data from 3,122 participants (**Table 1**). After adjustment for age, sex, education, baseline height and weight, and baseline SU, Year 15 SU increased by 0.11 mg/dL per 3 times a week difference in Year 0 FFF among both black and white participants (p=0.01 for both) (**Table 2**). SU increased by 0.09 mg/dL per 3 times a week increase in FFF from Year 0 to Year 15 among white participants (p=0.01) but not black participants (beta =0.003, p=0.93) (**Table 2**). There was a significant correlation between weight change and SU change (correlation coefficient 0.34, p< 0.001). **Figure 1** depicts the joint associations of Year 0 FFF and 15-year changes in FFF with change in weight. Compared to the average 15-year SU change among participants with baseline FFF < 1 time per week and 15-year FFF change < 0 time per week, those with high FFF at both baseline and follow-up had an extra

0.21 mg/dL increase (i.e., 75% of overall population SU increase over 15 years [0.28 mg/dL]) in SU during that time. After adjusting for covariates in model 2, change in weight (beta=0.03, p< 0.001) and homeostasis model for insulin resistance (HOMA) (beta=0.05, p< 0.001) remained significantly associated with SU change.

Conclusion: Fast food consumption has strong positive associations with SU, suggesting that fast food increases the risk of hyperuricemia and gout. The observed association is likely mediated by weight gain and resultant changes in insulin resistance.

Disclosure: C. Yokose, None; **N. Lu**, None; **N. McCormick**, None; **J. Choi**, None; **Y. Zhang**, None; **H. Choi**, Astra-Zeneca, 2, Takeda, 5, Selecta, 5, GlaxoSmithKline, 5, Horizon, 5.

Abstract Number: 0553

The US Prevalence of Ulcerative Colitis Associated Peripheral Arthralgias and Arthritis: Data from the National Health & Nutrition Examination Survey (NHANES)

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

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Session Time: 9:00AM–11:00AM

Background/Purpose: An association between ulcerative colitis (UC) and peripheral arthritis has been known since the 1930's and more recently has been described as a part of the spectrum of peripheral Spondyloarthritis (p-SpA).

Table 1. UC Questionnaire Peripheral Joint Arthralgia Distributions in US Adults: NHANES II.

	All UC (n=131)		No UC (n=10,273)		
Peripheral Arthralgias:	n	% (95%CI)	n	% (95%CI)	*p-value*
Arthralgias Any Joint	55	34.4 (23.8-45.0)	2163	20.7 (19.1-22.3)	0.01
Pauciarticular (1-5 joints)	32	18.2 (9.7-28.1)	1678	16.2 (14.9-17.5)	0.60
Polyarticular (≥ 5 joints)	22	15.1 (7.0-23.3)	468	4.3 (3.5-5.1)	0.01
Symmetric	43	27.5 (18.0-37.0)	1104	10.0 (9.0-10.9)	0.01
Asymmetric	11	6.5 (1.5-11.6)	1042	10.5 (9.6-11.5)	0.12
Upper Extremities	39	23.5 (14.0-33.0)	1371	13.5 (12.1-15.0)	0.04
Hand-Wrist	32	17.1 (10.9-23.2)	819	8.0 (6.9-9.1)	0.01
Elbow	18	12.3 (5.5-19.2)	469	4.9 (4.1-5.7)	0.03
Shoulder	23	16.0 (7.4-24.5)	759	7.1 (6.3-7.9)	0.04
Lower Extremities	44	28.5 (18.9-38.1)	1462	13.4 (12.2-14.6)	0.01
Hips	24	16.8 (8.6-25.0)	532	4.9 (4.3-5.5)	0.01
Knee	29	20.6 (11.9-29.3)	1057	9.6 (8.6-10.7)	0.01
Foot-Ankle	21	15.4 (7.1-23.8)	586	5.3 (4.6-6.1)	0.01

Symmetric joint involvement is 1 or more pair of symmetrically involved joints.

Pauci- and polyarticular definitions are from Orchard et al. Gut. 1998. 42:387–91

Table 2. UC Questionnaire Peripheral Joint Arthritis Distributions in US Adults: NHANES II.

	All UC (n=131)		No UC (n=10,273)		
Peripheral Joint Arthritis:†	n	% (95%CI)	n	% (95%CI)	*p-value*
Arthritis Any Joint	31	19.8 (12.3-27.3)	1148	10.8 (9.6-12.0)	0.02
Pauciarticular (1-5 joints)	24	14.3 (8.1-20.5)	932	8.9 (7.8-10.0)	0.09
Polyarticular (≥ 5 joints)	7	5.5*	179	1.5 (1.1-1.8)	*
Symmetric	23	14.5 (8.7-20.2)	591	5.2 (4.5-5.8)	0.01
Asymmetric	8	5..3*	520	5.2 (4.4-6.0)	*
Upper Extremities	22	13.3 (8.0-18.5)	627	6.0 (5.1-6.9)	0.01
Hand-Wrist	18	11.3 (6.5-16.1)	513	4.9 (4.1-5.7)	0.01
Elbow	9	6.5*	157	1.5 (1.2-1.8)	*
Shoulder	7	5.5*	177	1.4 (1.0-1.8)	*
Lower Extremities	21	14.2 (7.1-21.3)	741	6.6 (5.8-7.3)	0.04
Hips	5	4.4*	102	0.8 (0.6-1.0)	*
Knee	13	9.2 (5.3-13.2)	478	4.3 (4.0-5.0)	0.01
Foot-Ankle	11	8.4*	417	3.5 (3.1-4.0)	*

†Reported peripheral joint arthralgia plus joint swelling and palpable tenderness ≥1 month.

*Insufficient sample size for reliable statistical estimation

Table 3. Current Peripheral Symptoms and Examination Findings: US Adults NHANES II.

	All UC (n=131)		No UC (n=10,273)		
	n	% (95%CI)	n	% (95%CI)	*p-value*
Interview Data:					
Current SR Arthralgias	38	28.4 (18.8-37.9)	1110	12.1 (10.9-13.3)	0.01
Current SR Arthritis	21	12.4 (7.0-17.7)	569	6.1 (5.2-6.9)	0.03
Examination Data:					
Current Positive Exam Findings:	24	14.8 (8.0-21.6)	943	8.3 (5.6-11.1)	0.03
Upper Extremity Joints	12	5.9*	483	4.4 (2.6-6.2)	*
Lower Extremity Joints	16	10.9 (4.8-17)	633	5.5 (3.6-7.4)	0.04
Palpable Joint Tenderness	13	7.6*	544	4.8 (2.3-7.3)	*
Joint Pain on Passive Motion	18	11.9 (6.3-17.5)	744	6.6 (4.1-9.1)	0.03
Palpable Joint Swelling	6	2.9*	326	2.9 (2.0-3.8)	*
Exam Joint Pain and Swelling	4	2.0*	242	2.0 (1.2-3.0)	*
Heberden's Nodes- DIP Joints	35	13.3 (6.6-20)	1405	10.2 (6.6-13.8)	0.32
Symptomatic Heberden's Nodes	2	0.4*	54	0.4*	*

*Insufficient sample size for reliable statistical estimation

Prevalence rates of p-SpA in UC have been reported with varying estimates from clinical and cohort studies. To our knowledge there are no US population-based studies to estimate the prevalence of UC-associated peripheral arthritis or arthralgia. We describe herein population-based rates of peripheral arthritis and arthralgia among those with and without UC using previously unreported data from NHANES II (1976-80), a nationally-representative survey of the US population.

Methods: NHANES II participants ages 20-69 were interviewed and examined by physicians at mobile examination centers and defined as having UC if they reported having been diagnosed with UC by a physician. Previous analysis of NHANES II and NHANES 2009-10 data showed these self-reports to be consistent with true UC given corresponding high rates of colonoscopy, surgery, UC-related comorbidities, and UC-related symptoms.

Interview data was collected for a present or past history of peripheral arthralgias for ≥6 weeks (Table 1) and of arthritis signs and symptoms (arthralgias plus joint swelling and tenderness for ≥1 month) (Table 2). A physician joint exam was also performed (Table 3). Statistical analysis used SASTM 9.4 using survey design variables and sample weights to produce nationally representative estimates.

Results: 10,404 participants were interviewed and examined, 131 with a history of UC. 34% of those with UC reported present or past peripheral arthralgias (an estimated 400,000 persons nationwide) compared to 21% of those without ($p=0.01$). Rates of overall present or past polyarticular arthralgias, and of arthralgias at the hand and wrist, elbow, shoulder, hip, knee, and foot and ankle were all elevated among those with UC (all $p< 0.05$) (Table 1). 20% of participants with UC reported present or past peripheral arthritis compared to 11% without ($p=0.02$; Table 2). Rates of arthritis at the hand and wrist and knee were significantly elevated in UC ($p< 0.05$ for both). Rates of arthritis at the elbow, shoulder, hip, and foot and ankle were all elevated, but sample size precluded statistical evaluation (Table 2).

Overall, those with UC had significantly increased exam findings (28% vs. 12% without; $p=0.03$), notably increased pain on passive joint motion (12% with UC vs. 7% without; $p=0.03$). The rates of joint swelling on exam were similarly low in both groups (Table 3). On exam, Heberden's Node prevalences were similar between both groups.

Conclusion: Rates of self-reported peripheral arthralgia and arthritis were elevated in NHANES II participants who reported a history of UC compared to the general population. However, while rates of joint pain with motion on exam were elevated in UC, rates of examination-based swelling were not. This may suggest that much of much of UC patients' joint pain is due to peri-articular structure involvement, including possible tenosynovitis and enthesitis, and that point-prevalence of true arthritis is low consistent with p-SpA patients.

Disclosure: O. Stens, None; **H. Kim**, None; **J. Hou**, Redhill Biopharma, 2, Janssen, 2, 5, Abbvie, 2, 5, Celgene, 2, Genentech, 2, Eli Lilly, 2, Lycera, 2, Pfizer, 2, 5; **M. Weisman**, Novartis, 5, GSK, 5, UCB, 5, Lilly, 5.

Abstract Number: 0554

Increased Burden of Painful Arthritis and Rheumatism Following the Chikungunya Epidemic 2006: India Rural Population Survey 2018

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: A spectrum of post Chikungunya (Chik) arthritis , often RA like, were referred to an urban rheumatology centre (Pune India)during the 2006 epidemic (Arthritis & Rheumatism 2008). We examined 449 (51.3%) adult cases of acute Chik in a nearby rural survey (Bavi, Solapur) in 2006 ; 35% cases persisted with arthritis which reduced substantially by 6 months. Only 5% cases suffered non-specific arthralgias (mostly knees, elevated IL-6) by 24 months (Epidemiol Infect 2012. In a prior rural survey (Ralegaon Sidhi) in 2003, we reported 27% painful MSK (0.8% undifferentiated IA, 0.3% clinical RA, 0.3% SpA (Ind J Rheumatol 2015). Sporadic cases of Chik related arthritis continue. In the current study, we demonstrate the impact of the earlier Chik epidemic 2006 on the current MSK arthritis landscape.

Methods: The WHO Community oriented program for control of rheumatic diseases Bhigwan model (J Rheumatol 2009) was used to identify MSK disorders arthritis (> 16 years age) using standard questionnaire in a house to house survey in Bavi; May-Aug 2018. We verified residency from village records (including electoral) and interviews. 2131 population (70% response, 49% women, 15% aged 65 years +) was screened and classified: 784 residents also surveyed in 2006 (BRS), 1120 residents not included in the 2006 survey (BRNS), 227 post 2006 migrants (BM); 127 had died. Most of the BRNS lived in the outskirts of Bavi. Clinical diagnosis was based on standard rheumatology approach. Blood samples (26% population) were assayed in the urban centre. Standard statistics included crude point prevalence; significant $p< 0.05$.

Results: 549 (25.7%) subjects suffered from painful MSK disorders, predominantly (¬80%) mild moderate and with mild HAQ disability. 206 cases (39.9%) recalled past acute Chik illness. 422 (61.7%) healthy subjects and 362 (80.6%) cases from the 2006 survey cohort were available; correspondingly 17.5% healthy and 44.8% cases reported painful MSK (2018 survey).10 patients were diagnosed clinical RA (50% seropositive RF). 13 (2.5%) cases (1 RA) in 2006 survey were seropositive (cut off 40 IU/ml) for RF; correspondingly 22 (4%) cases (5 RA, 440-1170 IU/ml) in 2018 survey. 6/22 seropositive RF cases (5 RA) tested seropositive for anti CCP. Table 1 & Table 2 show the classification break up (proportion) in the 2018 survey, and compares MSK per se with and without onset following CHIK; Abbreviations in text

2018 Survey subjects	BRS	BRNS	Total
Number Screened	784	1120	2131
MSK	30.1	25.0	25.8
WOMEN Cases	59.3	54.6	58.8
Post Chik MSK	20.7	4.3	10.2
RA	0.6	0.2	0.5
IA-Undifferentiated	2.8	1.3	1.9
SpA	0.0	0.4	0.2
OA	11.7	11.8	10.9

2018 Survey subjects	BRS	BRNS	Total
Non Specific Arthralgia	14.8	10.3	11.5
Soft Tissue Rheumatism	0.1	1.1	0.8

	POST CHIK MSK	NON CHIK MSK	'p'
Number of Cases	217	332	
RA	1.8	1.8	0.77
IA-Undifferentiated	10.6	5.1	0.02
SPA	0.0	1.5	0.17
OA	42.4	42.2	0.96
Non Specific Arthralgia	44.2	45.2	0.83
Soft Tisuue Rheumatism	0.9	4.2	0.02

Conclusion: A substantial burden and spectrum of painful MSK disorders, in particular related to Chik was demonstrated in this rural survey. There seemed to be an increase in inflammatory arthritis (not necessarily RA) following the Chik 2006 epidemic in this otherwise robust population.

Disclosure: A. Chopra, None; **R. Ghorpade**, None; **A. Venugopalan**, None; **M. Saluja**, None; **K. Adam**, None.

Abstract Number: 0555

Utilization and Adherence Among Infliximab Biosimilar Initiators in a U.S. National Commercial Insurance Database

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
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Background/Purpose: Infliximab Biosimilar, the first biosimilar to infliximab, was approved for multiple indications in the U.S. in 2016. Since the utilization of biosimilar in the U.S. has not been studied, it is unclear if patients on Infliximab Biosimilar are adherent to their treatment. Therefore, we evaluated the characteristics of Infliximab Biosimilar initiators and their adherence using national commercial administrative data.

Methods: We identified Infliximab Biosimilar initiators based on procedure and pharmacy codes in 2016-2017 IBM Marketscan data. Using all available data, we classified Infliximab Biosimilar initiators as naïve Infliximab Biosimilar users (never used infliximab), infliximab early switchers with < 2yr of infliximab use, and late switchers with long-term (>2yr) use of infliximab. Eligible patients were ≥18 years of age and continuously enrolled with medical and pharmacy coverage in 2014-2017. The date of the first prescription for infliximab biosimilar was considered as "Index date". Baseline was defined as 365 days prior to the index date. Follow up period started from the index date and ended at the earliest date of death, loss of coverage, and 12/31/2018.We evaluated baseline characteristics in all patients and calculated the proportion of days covered (PDC) at the 12 months of follow up among patients who had >=12m of coverage during follow-up. The PDC adherence level was further categorized as < 50%, 50 to 80%, and > 80%.

Adherence among individuals with at least 12 Months of follow up period.

Cohort	N	Follow up adherence N (%)		
		<50%	50%-80%	80%
Naïve Inflectra cohort.	69	21(30.4%)	11(15.9%)	37(53.6%)
Inflectra (with one to 2 years of infliximab exposure).	88	41(46.6%)	8(9.1%)	39(44.32%)
Inflectra (with prevalent use of infliximab).	66	18(27.3%)	11(16.7%)	37 (56.1%)

Results: We identified 98 Naïve Infliximab Biosimilar users, 114 early switchers, and 113 late switchers. Compared to (early or late) switchers, naive users were younger and more likely to be female. The highest proportion of auto-immune disease was inflammatory bowel disease (40.9-45.4%), followed by rheumatoid arthritis (15.4-29.6%) and psoriasis (9.7-13.9%). Among patients who had >=12m of follow-up, 53.6% naive users, 44.3% early switchers, and 56.1% late switchers continued to be adherent (>80%) at 12 months (Table).

Conclusion: Approximately half of the Infliximab Biosimilar initiators were highly adherent at 12 months. Further studies are needed to evaluate the long-term adherence among Infliximab Biosimilar users.

Disclosure: S. Sarvesh, None; **J. Alanaeme**, None; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **H. Yun**, Pfizer, 2.

Abstract Number: 0556

Recent Use, Missed Doses and Discontinuation of Infliximab in New-users: Comparisons of Biosimilar and Originator Exposures

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Background/Purpose: Biosimilar infliximab offers a potentially lower-cost treatment option compared to its bio-originator. However, uptake of biosimilars in general in North America has been slow. To describe new users of infliximab in the US, comparing biosimilar and bio-originator, in terms of missed doses and discontinuation.

Methods: We used from data Marketscan® Commercial Claims and Encounters and the Medicare Supplemental and Coordination of Benefits databases (January 1st, 2017 to December 31st, 2018). We studied adult individuals (age≥18 years), who were infliximab-naïve (new users). The date of first infliximab claim was defined as the index date. We assessed i) first missed dose and, ii) occurrence of complete discontinuation. Missed dose was defined as any gap between infusions beyond recommended intervals (0, 2, and 6 weeks during the induction phase and 8 weeks in the

Table 1 – Baseline characteristics of new users of infliximab biosimilar and infliximab originator, Marketscan, 2017-2018.

	New users (a)	
Characteristic	**INF-B (n=301)**	**INF-O (n=5295)**
Female sex, N (%)	186 (61.8)	3149 (59.5)
Mean age in years, (SD)	47.1 (16.3)	43.5 (14.8)
Year/Quarter, N (%)		
2017Q1	2 (0.66)	748 (14.1)
2017Q2	29 (9.6)	732 (13.8)
2017Q3	41 (13.6)	756 (14.2)
2017Q4	36 (12.0)	704 (13.3)
2018Q1	46 (15.3)	721 (13.6)
2018Q2	57 (18.9)	660 (12.5)
2018Q3	59 (19.6)	731 (13.8)
2018Q4	31 (10.3)	243 (4.6)
Rheumatic disease[1,2], N (%)	145 (48.2)	1919 (36.2)
IBD[1], N (%)	150 (49.8)	3321 (62.7)
Past ever use of medications, N (%)		
Corticoids	246 (81.7)	4050 (76.5)
sDMARDs	109 (36.2)	1476 (27.9)
Biologic DMARDs[4]	107 (35.6)	1684 (31.8)
Tofacitinib	5 (1.7)	88 (1.7)

[1]Based on the date of diagnosis closest to the start of treatment with infliximab.

[2]Includes rheumatoid arthritis, ankylosing spondylitis, and psoriatic arthritis

[3]Includes Crohn's disease and ulcerative colitis.

[4]Including abatacept, golimumab, certolizumab, tocilizumab, and rituximab.

Table 1. Baseline characteristics of new users of infliximab biosimilar and infliximab originator, Marketscan, 2017-2018.

maintenance phase). If there was no record of an infliximab infusion at the expected date of the next injection (plus a grace period of 7 days), a discontinuation event was assigned.

Results: In the new-user cohort there were 5,596 new users of infliximab, including 301 biosimilar users. Baseline characteristics of individuals included in the analysis are shown in Table 1. Among patients initiating treatment with infliximab biosimilar, 30.9% missed at least one scheduled infusion during the induction phase, similar to the percent (28.6%) among the originator infliximab users. After multivariable adjustment for age, sex, date of treatment initiation, medication use (other biologic medications, synthetic DMARDs, and corticosteroids), and underlying diseases, we were unable to detect if first missing dose in the induction phase differed between the two groups (adjusted hazard ratio, aHR = 1.14; 95% CI = 0.92-1.41). For patients completing the induction phase (n=3,282), 33.1% of biosimilar users missed at least one infusion within one year during the maintenance phase, which was not statistically different from the originator users (40.1%). The adjusted analysis showed no clear difference for first missed dose between groups (aHR = 0.94, 95% CI =0.71;1.24). Complete discontinuation in the maintenance phase (a gap more than 90 days beyond the expected infusion date without restarting therapy), was similar in the biosimilar group (13.1%) and originator group (15.5%). In adjusted analysis, we were unable to show significant difference among groups for complete discontinuation (aHR = 1.00, 95% CI =0.63;1.59)

Conclusion: Biosimilar infliximab use in the United Sates continues to be low over 2017-2018. In new users, we were unable to detect differences between biosimilar and bio-originator, in terms of missed doses and discontinuation.

Disclosure: C. Moura, None; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **D. Choquette**, AbbVie Canada, 5, 8, Amgen Canada, 5, 8, Bristol-Myers-Squibb Canada, 5, 8, Eli Lilly Canada, 5, 8, Merk Canada, 5, 8, Novartis Canada, 5, 8, UCB Canada, 5, Janssen Canada, 5, Sandoz Canada, 5, 8, Pfizer Canada, 5, 8, Roche Canada, 5, Sanofi-Genzyme Canada, 5, 8; **G. Boire**, Amgen, 1, 2, BMS, 1, 2, 3, Celgene, 1, Merck, 1, 2, Pfizer, 1, 2, 3, Eli Lilly, 1, 2, Janssen, 1, Abbvie, 1, Novartis, 1, Sandoz, 1; **V. Bykerk**, None; **C. Thorne**, None; **W. Maksymowych**, AbbVie, 2, 5, Janssen, 5, Lilly, 5, Pfizer, 2, 5, Novartis, 2, 5, Gilead, 5, UCB Pharma, 5, Boehringer Ingelheim, 5, Galapagos, 5; **P. Lakatos**, None; **L. Svenson**, None; **L. Targownik**, None; **W. Afif**, None; **S. Bernatsky**, None.

Abstract Number: 0557

The Joint Association of Steps/day and Typical Sedentary Bout Length with Worsening Knee Cartilage Damage over Two Years: The MOST Study

Dana Voinier[1], Tuhina Neogi[2], Joshua Stefanik[3], Ali Guermazi[2], Frank Roemer[4], Hiral Master[5], Louise Thoma[6], Meredith Christiansen[7], Jason Jakiela[1], Michael Nevitt[8], Cora Lewis[9], James Torner[10] and Daniel White[1], [1]University of Delaware, Newark, DE, [2]Boston University School of Medicine, Boston, MA, [3]Northeastern University, Boston, MA, [4]Boston University School of Medicine, Boston, MA, and Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany, Erlangen, Germany, [5]Vanderbilt University Medical Center, Nashville, TN, [6]University of North Carolina at Chapel Hill, Chapel Hill, NC, [7]University of Delaware, New York, NY, [8]University of California San Fransisco, Orinda, CA, [9]University of Alabama Birmingham, Birmingham, AL, [10]University of Iowa, Iowa City, IA

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Knee cartilage requires loading, e.g., walking, to remain healthy. When cartilage is deprived of loading, i.e., during bouts of sedentary time, it becomes vulnerable to damage. Thus, achieving more steps/day, and distributing steps throughout the day, may be important for cartilage health. However, the joint effects of walking and sedentary bouts on cartilage health are not known.

We conducted an exploratory analysis to examine the joint association of walking and sedentary bouts with worsening cartilage damage in the medial tibiofemoral joint (TFJ), a common site for knee osteoarthritis (OA), in adults with or at risk for knee OA. We also stratified our analysis by obesity status, as it may modify the above relationship.

Methods: We used data from the Multicenter Osteoarthritis (MOST) Study, a NIH-funded cohort study of adults with or at risk of knee OA. Participants had minute-by-minute accelerometry data collected via the StepWatch Activity Monitor (Orthocare Innovations) at baseline. We included participants with ≥4 days of ≥10 hours/day of wear. For each participant, we estimated **average steps/day** and **typical sedentary bout length (SED, minutes)**; the latter was estimated using an established weighted median approach (Chastin, 2010). We dichotomized steps/day by the sample median: **Active** (≥9,300 steps/day) and **Not Active** (< 9,300 steps/day). We dichotomized typical sedentary bout length by the median: **Short SED** (< 30 min) or **Long SED** (≥30 min). This yielded four groups: 1) Active/Short SED (REF); 2) Not Active/Short SED; 3) Active/Long SED; 4) Not Active/Long SED.

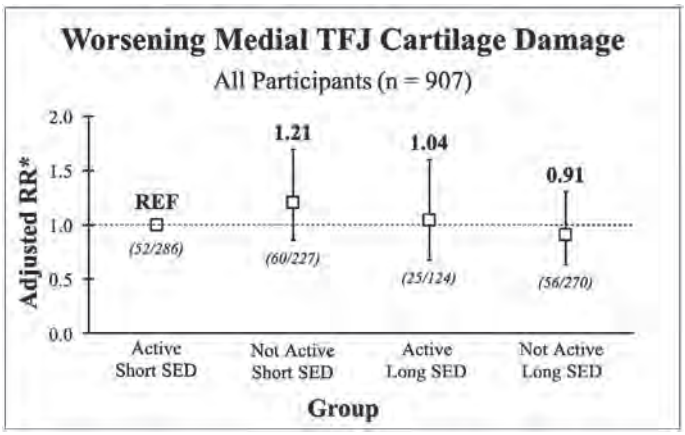

Figure 1. RR and 95%CI (represented by error bars) for worsening medial TFJ cartilage damage in all participants. *Analyses were adjusted for age, sex, and BMI.

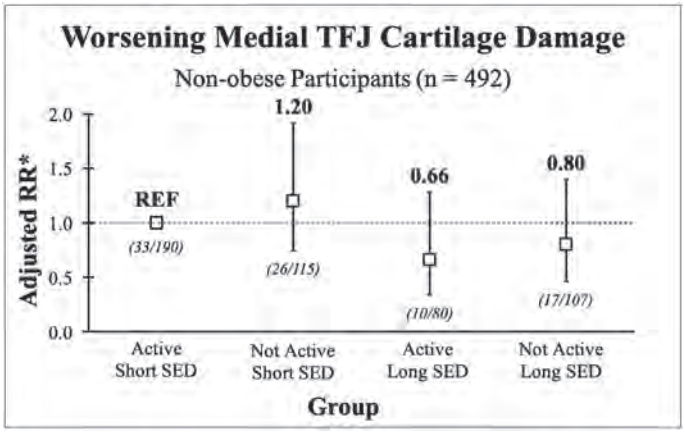

Figure 2. RR and 95%CI (represented by error bars) for worsening medial TFJ cartilage damage in participants who are non-obese. *Analyses were adjusted for age, sex, and BMI.

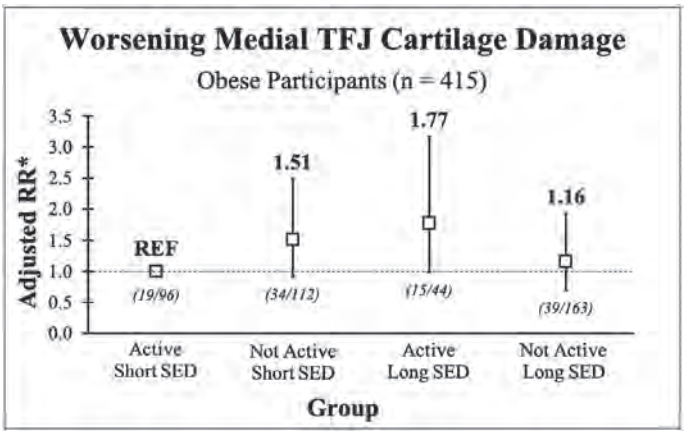

Figure 3. RR and 95%CI (represented by error bars) for worsening medial TFJ cartilage damage in participants who are obese. *Analyses were adjusted for age, sex, and BMI.

Participants had knee MRIs (1.0T, OrthOne) at baseline and two years. Cartilage morphology was scored from 0-6 in 5 subregions of the medial TFJ using the Whole Organ Magnetic Resonance Imaging Score by two musculoskeletal radiologists. Our outcome, worsening medial TFJ cartilage damage over 2 years, was defined as an increased score

in any medial TFJ subregion, including within-grade changes. We used binomial regression with robust variance estimation to calculate risk ratios (RR) and 95% confidence intervals (95% CI) for worsening damage in each group. Analyses were adjusted for age, sex, and body mass index (BMI). We also separately analyzed those who were non-obese (BMI < 30 kg/m^2) vs. obese (BMI ≥ 30 kg/m^2).

Results: We included 907 participants (66.7 years, 62% female, BMI: 29.7 kg/m^2). Risk for worsening medial TFJ cartilage damage was not different between groups in the full sample or in non-obese participants (n=492). However, among obese participants (n=415), those in the Not Active/Short SED and Active/Long SED groups had 1.51 [0.92-2.48] and 1.77 [0.99-3.17] times the risk for worsening damage, respectively, compared with those in the Active/Short SED (REF) group, though neither reached statistical significance. Participants in the Not Active/Long SED group did not have greater risk (1.16 [0.70-1.93]) for worsening damage compared with the REF group.

Conclusion: For adults with or at risk for knee OA who are obese, either lower steps/day or longer typical sedentary bout length may be related to worsening medial TFJ cartilage damage; however, the combination of fewer steps/day and longer sedentary time was not related to worsening damage.

Disclosure: D. Voinier, None; **T. Neogi**, Lilly, 1, EMD Merck Serono, 1, Novartis, 1, Regeneron, 1, Pfizer/Lilly, 1; **J. Stefanik**, None; **A. Guermazi**, AstraZeneca, 1, Pfizer, 1, MerckSerono, 1, Galapagos, 1, Roche, 1, TissueGene, 1, Boston Imaging Core Lab, 1; **F. Roemer**, Boston Imaging Core Lab (BICL), LLC, 1, Calibr - California Institute for Biomedical Research, 1; **H. Master**, None; **L. Thoma**, None; **M. Christiansen**, None; **J. Jakiela**, None; **M. Nevitt**, None; **C. Lewis**, None; **J. Torner**, None; **D. White**, None.

Abstract Number: 0558

Statin Use Pattern in Patients with Inflammatory Joint Disease in a Single Site VA Medical Center

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with inflammatory joint disease, including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and ankylosing spondylitis (AS) carry increased risk of cardiovascular disease (CVD). Mechanisms underlying this increased risk are thought to be attributable to a combination of traditional and novel CVD risk factors (engaged pathogenic inflammatory pathways). Lipid lowering statin therapy is one of the most commonly used CVD preventive

	RA	AS	PsA	Control	P value[1]
Number	200	41	94	19	
ASCVD-10 year score median (IQR)	21.8 (13.8; 32.7)*	13 (4.2; 17.4)	14.15(7.1; 31.6)	8.5 (3.4; 11.7)	<0.001
Subset with ASCVD ≥ 7.5[2] Number (% of parent population)	176 (88%)	27 (65.8%)	69 (73.4%)	11(57.8%)	
ASCVD-10 year score median (IQR)	23.8 (16.9; 34.8)	15 (13.0; 25.2)	26 (11.2;35.0)	9.6 (9.0;16.5)	0.005
Age,median(IQR)(years)	70(65;73)	63 (56; 70)	65 (56;70)	61 (54; 72)	<0.001
Gender (male)(%)	174 (98.8%)	27 (100%)	66 (96.6%)	11 (100%)	0.4
Diabetes Mellitus (%)	60 (34.4%)	8 (29.6%)	40 (57.9%)*	3 (27.3%)	0.003
Hypertension (%)	126 (71.5%)*	12(44.5%)	47 (68.1%)	6(54.5%)	0.03
On Statin (%)	92 (51.8%)	10 (37%)	47 (68.1%)	9 (81.8%)	0.06

medications. We explored statin use patterns in patients with inflammatory joint disease (RA, PsA and AS) accounting for traditional CVD risk factors.

Methods: This was a retrospective chart review study conducted at the Cleveland VA Medical Center. ICD 10 diagnoses for RA, AS and PsA identified local populations of these patients. Medical charts of 200 RA (all seropositive for either RF or CCP in this sample set), 41 AS, 94 PsA and 19 patients with no inflammatory joint disease (general medical clinic patients) were reviewed. Diagnoses were verified using rheumatology clinic visit information and ACR, ASAS, or CASPAR criteria. Records were reviewed for ASCVD risk score components (age, gender, race, presence of hypertension or diabetes, lipid profile, and smoking status). We examined patient race, body mass index (BMI), and treatment history. When calculating ASCVD Risk Score, if age or lipid levels were above or below the limitations of the calculator, either the upper or lower limit values were used, respectively.

Results: Clinical characteristics are shown in **Table 1**. Most of the patients were male, consistent with the VA patient population. Patients with RA had higher ASCVD scores compared to patients with AS and PsA. In the subgroups with ASCVD score above or equal to 7.5, RA and PsA patients more commonly had diabetes mellitus, while RA patients were older and more commonly had hypertension. Only 51.8% of RA, 37% of AS and 68% or PsA patients with ASCVD score at or above 7.5 were prescribed statin compared to 81.8% of patients with no inflammatory joint disease (p=0.06). Chart review for reasons patients were not on statin included: 1) undergoing a trial of dietary change and weight loss; 2) patient declining recommended medication; and 3) other.

Conclusion: Patients with inflammatory joint disease and traditional CVD risk factor with indication for statin may benefit of provider education and improvement of CVD risk assessment and initiation of proper preventive measures in these high risk inflammatory joint disease patient populations.

Disclosure: L. Kostadinova, None; **S. Damjanovska**, None; **A. Gupta**, None; **I. Gad**, None; **S. Syed**, None; **A. Lange**, None; **C. Kowal**, None; **C. Shive**, None; **C. Burant**, None; **B. Wilson**, None; **D. Canaday**, None; **D. Zidar**, None; **D. Anthony**, None; **M. Mattar**, None.

Abstract Number: 0559

Low Frequency of ANA/DFS70 Pattern Positive Result in a Large Cohort of Autoimmune/autoinflammatory Diseases Compared with First Degree Relatives and Healthy Controls Evaluated in a Single Hospital from Colombia

Consuelo Romero-Sanchez[1], **Omar-Javier Calixto**[2], Veronica Romero[2], Diana Rincon Riano[3], Julio Amador[2], Luis Castro[2], Pedro Lopez-Mojica[4], Daniela Marin[2], Diana Àcero[5], Monica Acevedo[5], Wilson Bautista-Molano[6] and Juan Manuel Bello-Gualtero[7], [1]Hospital Militar Central, Rheumatology and Immunology Department, Universidad Militar Nueva Granada / Clinical Immunology Group, Hospital Militar Central, School of Medicine, Universidad Militar Nueva Granada /Universidad El Bosque, Cellular and Molecular Immunology Group -InmuBo-, School of Dentistry, Bogotá D.C., Colombia, [2]Hospital Militar Central, Universidad Militar Nueva Granada, Bogota, Colombia, [3]Universidad Militar Nueva Granada, Bogota, Colombia, [4]Hospital Militar Central, Universidad Militar Nueva Granada, BOGOTA, Distrito Capital de Bogota, Colombia, [5]Hospital Militar Central, Bogota, Colombia, [6]University Hospital Fundación Santa Fé de Bogotá and Universidad El Bosque, Bogotá, Colombia, [7]Hospital Militar Central, Rheumatology and Immunology Department, Universidad Militar Nueva Granada/ Clinical Immunology Group, Hospital Militar Central, School of Medicine, Universidad Militar Nueva Granada, Bogotá D.C., Colombia

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Autoimmune systemic rheumatic disease (SARD) diagnostic approach is complex and recently there are some diagnostic tools to rule-out autoimmune disease diagnoses. ANAS/DFS70 antibodies have attracted interest as a positive result in patients without clinical evidence of SARD, but we are scarce on data validation

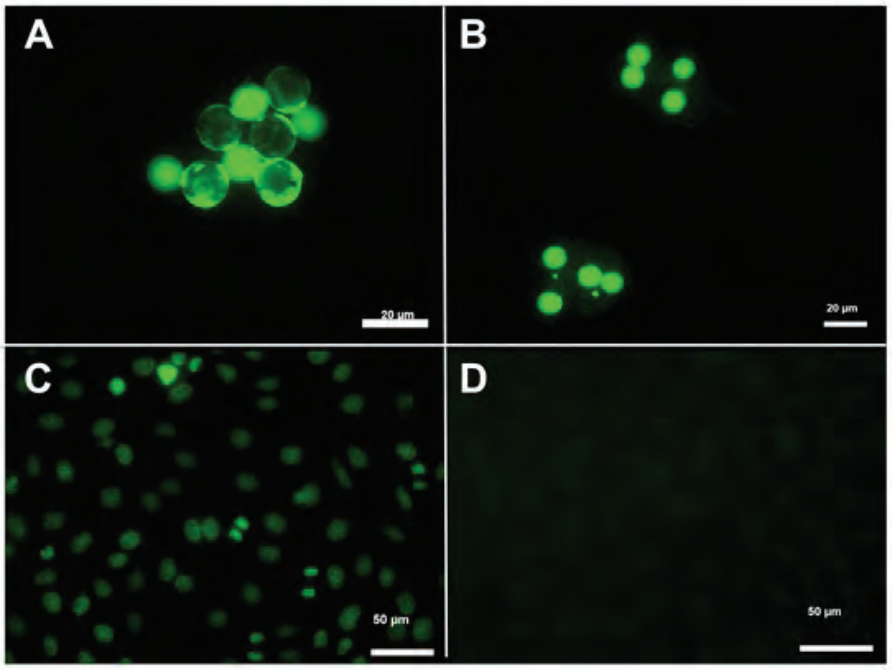

Figure 1. Indirect immunofluorescence for ANA: A: Postive Cytobeads ANA for DFS70, B: positives control beads for cytobeads, C: ANA: AC-2 - Nuclear dense fine speckled (Speckled pattern distributed throughout the interphase nucleus with characteristic heterogeneity in the size and D: ANA: AC-0 – Negative.

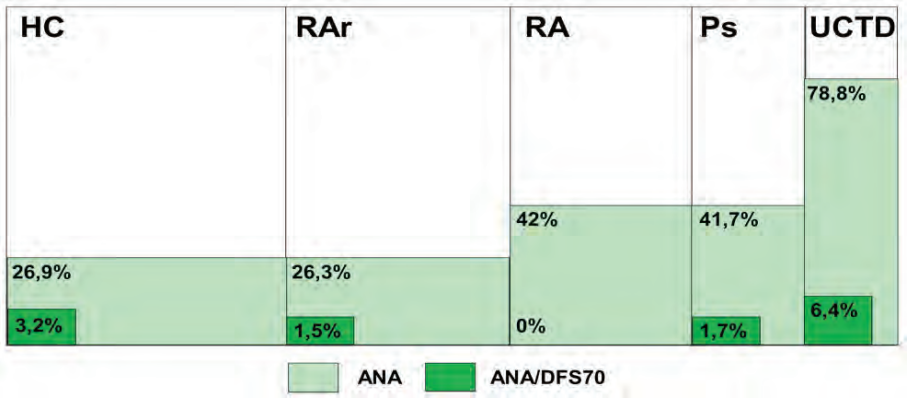

Figure 2. Participants were RA 19%, 25,8% RA first degree relatives, Ps 11,3%, UCTD 8,9%, and 35% healthy controls. ANA/DFS70 was positive in a 6,4% in UCTD, 3,2% in healthy controls, 1,7% in Ps, 1,5% in relatives of RA, no RA had positive results.

in Latin American countries population. The objective of this study was to assess ANA/DFS70 performance in a large population with SARD compared with first degree relatives and healthy controls.

Methods: A cross-sectional study was conducted. We analyzed 531 individuals between 18-65 years old, 101 early rheumatoid arthritis (eRA) patients (ACR/EULAR 2010 classification criteria), 137 first degree relatives (FDR) from RA, 60 psoriasis (Ps) patients (Colombian classification consensus), 47 Undifferentiated connective tissue diseases (UCTD) patients and 186 healthy controls matched by age and sex. The healthy control group were individuals who lived and work similarly like those patients those criteria of exclusion criteria were to present autoimmune or auto-inflammatory disease, infectious, neoplasms, diabetes, antibiotic treatment, pregnancy or lactation, consanguinity with autoimmune entities.

The determination of ANA-HEp2 antibodies (ANA-Hep-2 AESKU.Dignostic®, Autoantiboy test SYSTEM IMCO DIAGNOSTICS REF 1103® and ANA-Hep-2 AESKU.Dignostic®) was carried out. The positive results (standard AC-2) are used as a confirmatory test the determination of ANAS / DFS70: AUTOANTIBOY TEST SYSTEM IMMCO DIAGNOSTICS (Knocked out, for the psip gene) REF 1108® and CytoBead ANA Generic Assays ref 8065 ® by indirect immunofluorescence-IFI technique (Figure 1). In addition, serum levels of C-reactive protein (CRP), erythrocyte sedimentation rate (ESR), IgG/IgA antibodies against citrullinated peptide (ACPA), and rheumatoid factor (RF). Absolute and relative frequencies were established.

Results: 531 participants were included: eRA 19%, 25,8% RA FDR, Ps 11,3%, UCTD 8,9%, and 35% healthy controls. eRA mean age was 41,8±12,2 years, female 82,2%, with ANA test(+) result 42%. In Ps mean age 49,1±15,7 years, female 53,3%, ANA test(+) 41,7%. UCTD mean age 41,3±15,2 years, female 85,1%, and ANA test(+) 78,7%. RA FDR mean age 38,7±12,2 years, female 73%, ANA test(+) 26,3%. And healthy controls mean age 41,3±12,2 years, female 74,7%, and ANA test(+) 26,9%. ANA/DFS70 was positive in a 6,4% in UCTD, 3,2% in healthy controls, 1,7% in Ps, 1,5% in RA FDR, no eRA had positive results (Figure 2). These 12 participants were negative for acute phase reactants (ESR[-] 83,3% and CRP[-] 66,6%), as well as they were all negative for RF and two were positive for APCA from UCTD.

Conclusion: ANAS/DFS70 autoantibodies were present in very low frequency in patients with SARD, specially no eRA patient had a positive test result. Thus, patients with a positive result tend to have a mild or non-progressing phenotype of SARD, as UTCD. This is the first time ANA/DFS70 are tested in a large population cohort in Latin American countries which coincide with previous results in RA and RA relatives.

Disclosure: C. Romero-Sanchez, None; **O. Calixto**, None; **V. Romero**, None; **D. Rincon Riano**, None; **J. Amador**, None; **L. Castro**, None; **P. Lopez-Mojica**, None; **D. Marin**, None; **D. Àcero**, None; **M. Acevedo**, None; **W. Bautista-Molano**, None; **J. Bello-Gualtero**, None.

Abstract Number: 0560

Mortality Burden of Immune-Mediated Inflammatory Diseases (IMID): Race/Ethnicity, Sex, and Geographic Variation in the United States

Ram Singh[1], Eric Yen[2] and Meifang Wu[2], [1]UCLA David Geffen School of Medicine, Los Angeles, CA, [2]UCLA, Los Angeles, CA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Almost every organ system can be affected by immune-mediated inflammatory diseases (IMID) characterized by inflammation and therapeutic response to immune-suppressive or anti-inflammatory drugs. Since IMID are purported to have shared pathogenic mechanisms, it would be important to understand their burden of disease together. Our goal is to determine 1) the burden of IMID deaths relative to the leading causes of death published by the Centers for Disease Control and Prevention (CDC) and 2) the mortality associations of IMID with major demographic/geographic variables.

Methods: This is a nationwide population-based study using a U.S. national mortality database and census data from 2013 to 2017. A list of forty-four IMID was compiled based on their relative high prevalence. Crude death rates for each IMID were calculated by dividing death counts of each IMID by the U.S. population between 2013 and 2017 and ranked. Pooled death counts of the fifteen IMID with highest crude death rates were further ranked among CDC's official leading-causes-of-death ranklist for eleven age groups and charted. Mortality associations with four demographic/geographic variables were analyzed with multinomial logistic regression.

Results: 362,150 deaths were attributed to the top fifteen IMID from 2013 to 2017. Of these deaths, IMID were recorded as the underlying cause in 202,430 deaths and as the contributing cause in 159,720 deaths. These IMID deaths (underlying + contributing) ranked 6th to 9th for all age groups in relation to the CDC's official leading causes of death. The ranking was even higher in Black persons, particularly in young females. IMID deaths ranked number 4 in Black females at 35-54 age groups. Multinomial logistic regression analysis revealed that young (< 45 years) and middle (45-64 years) ages, female sex, race/ethnicity of non-Hispanic Black or American Indian/Alaska Native, and census region of West or Midwest were independently associated with higher IMID mortality. IMID caused premature mortality in several race/ethnic groups, especially in Blacks and American Indians/Alaska Natives. American Indians/Alaska Natives living in the Midwest or West had the highest risk for IMID mortality.

Conclusion: IMID is an unrecognized leading cause of death. IMID caused premature mortality, especially in Black females, and in American Indians/Alaska Natives living in the Midwest and West. These data highlight that IMID is a major public health problem. Similar to various forms of cancer, various IMIDs should be considered as a collective disease entity. The recognition of IMID as a leading cause of death may influence healthcare prioritization and research funding, which may help to reduce their disease burden. Our data have implications for developing precision public health strategies to target IMID high-risk vulnerable populations including Black females and American Indians/Alaska Natives living in the Midwest and West.

Disclosure: R. Singh, None; **E. Yen**, None; **M. Wu**, None.

Abstract Number: 0561

Risk Factors for Falls Among Individuals with Knee OA: A Longitudinal Community-based Study

Jessica Wilfong[1], Anthony Perruccio[2] and Elizabeth Badley[2], [1]Krembil Research Institute, University Helath Network, Toronto, ON, Canada, [2]Krembil Research Institute, UHN; University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Knee osteoarthritis (OA) is a known risk factor for falling, but little is known about what factors contribute to the risk of falling among people with knee OA. Our purpose was to identify factors that contributed to an individual with knee OA experiencing one or multiple (≥2) falls within an 18-month follow-up period.

Methods: Data from the baseline and 18-month follow-up of the Canadian Longitudinal Study on Aging (CLSA) of individuals aged 45-85 who reported doctor diagnosed knee OA at baseline were analyzed. At the follow-up, individuals reported if they experienced 0, 1, ≥2 falls in the past year where they were hurt enough to limit some of their normal activities. A multinomial logistic regression model was used to assess predictors of reporting falls at follow-up (≥2, 1, 0 (referent group)). Self-reported and performance-based predictors were considered: age, sex, body mass index, alcohol use, sleeping problems, vision problems, previous fall, neurological condition, respiratory condition, incontinence, depression, other types of arthritis, other chronic conditions, and the timed up and go, chair rise, 4-metre walk, and standing balance tests.

Results: 4,495 individuals reporting knee OA at baseline were included (15% of the CLSA sample). Fourteen percent reported a fall(s) at follow-up: 10% reported 1 fall, 4% reported ≥2 falls. Reporting a past fall, taking depression medication, and having a worse standing balance time was associated with an increased risk of any number of future falls. Being female and having troubles sleeping were associated with an increased risk of having 1 fall, while specific comorbidities (e.g. diabetes, depression) were associated with an increased risk of ≥2 falls. Older individuals were not more likely than younger individuals to experience multiple falls.

Conclusion: There are differences between the predictors of one versus multiple falls among individuals with knee OA. Some of these are potentially modifiable with opportunities for clinical intervention and fall prevention strategies. Relationships between risk factors and falling among individuals with knee OA can be complex. There is a need for better understanding these relationships in OA.

Disclosure: J. Wilfong, None; **A. Perruccio**, None; **E. Badley**, None.

Abstract Number: 0562

The Relationship Between Heart Disease Risk Profile and Osteoarthritis, Overall and by Multi-/Single-Joint Involvement

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) and heart disease (HD) are among the most common chronic conditions. Several studies have shown that OA increases the risk of HD later in life, even after adjusting for socioeconomic factors, functional limitations and obesity. Much of the literature considers OA of a specific joint, but there is increasing realization that OA is a multi-joint disease for many, with a greater potential for systemic inflammatory load, a risk factor for HD. Our objective was to compare the burden of HD risk factors between those with and without OA, and consider differences between those with single- and multi-joint OA.

Methods: Data are from cycle 1 of the Canadian Longitudinal Study on Aging, a national study of a representative sample of individuals aged 45-85. Respondents indicated a doctor diagnosis of OA in the knees, hips or hands. Those reporting arthritis other than OA, any form of HD, or use of HD medications were excluded. A 1:1 age and sex

Table 1: Distribution of heart disease (HD) risk score by OA status.

		No OA (%)	OA (%)	Single-joint OA (%)	Multi-joint OA (%)
HD Risk Score	0 – 6	30.1	22.1	23.8	16.7
	7 – 9	28.6	26.7	27.6	23.9
	10 – 11	17.1	19.4	19.0	20.6
	12+	24.2	31.9	29.6	38.8

Table 2: Multinomial logistic regressions* investigating relationship between HD risk score (0-6 (ref), 7-9, 10-11, 12+) and a) OA overall and b) single- and multi-joint OA.

Predictor	Outcome: HD risk score (ref: 0-6)		
	Risk score 7-9	Risk score 10-11	Risk score 12+
	Odds Ratio (95% Confidence Interval)		
OA overall vs. no OA	**1.21 (1.05 - 1.39)**	**1.43 (1.22 - 1.68)**	**1.59 (1.38 - 1.83)**
Single-joint OA vs. no OA	**1.18 (1.02 - 1.37)**	**1.35 (1.14 - 1.59)**	**1.45 (1.24 - 1.68)**
Multi-joint OA vs. no OA	**1.33 (1.04 - 1.71)**	**1.82 (1.39 - 2.37)**	**2.21 (1.75 - 2.80)**

*Models are age-sex matched and adjusted for education, income, physical activity score, timed up and go test, and chronic conditions.

non-OA match was randomly selected for every individual with OA. OA was characterized as single or multi-joint OA. HD risk factors: high sensitivity C-reactive protein (hsCRP), high density lipoprotein (HDL), triglycerides, cholesterol, body fat %, body mass index, blood pressure, waist size, Hemoglobin A1c, and smoking history. Each risk factor was scored 0, 1, or 2 using established cut-offs for low/medium/high HD risk, then summed to give an HD risk score and categorized as 0-6, 7-9, 10-11 and 12+ based on quartiles. Covariates: age, sex, education, income, physical activity score, timed up and go functional test and comorbidity count. The association between HD risk score category and a) OA overall and b) single- and multi-joint OA was quantified using multinomial logistic regressions, adjusting for covariates.

Results: The matched sample consisted of 6098 respondents (3049 with OA). The median age was 63 years, 55.8% were female. Several HD risk factors were elevated among those with OA vs. without, including hsCRP, a systemic inflammation marker. Individuals with OA were in the 'high' risk category more frequently than non-OA individuals for all but 3 (HDL, cholesterol, and smoking) risk factors. This was reflected in the overall HD risk score: the proportion of OA respondents in the higher score categories was also more frequent for multi- vs. single-joint OA (Table 1). The age-sex matched and covariate adjusted regressions showed that those with OA had significantly greater odds of higher HD risk score than those without OA, with a significant trend of increasing odds for increasing quartile of HD risk score (Table 2). The trend of increasing odds was greater for those with multi-joint than single-joint OA.

Conclusion: Individuals with OA and without HD, and more so those with multi-joint OA, had a worse HD risk profile than individuals without OA. Greater joint involvement and systemic features may be an additional link between OA and HD. Improving overall HD risk-stratification for people with OA is important for enhanced approaches to prevention/intervention. Furthermore, the findings suggest that an exclusive focus on individual joints in OA care and research may limit our ability to effectively manage, treat and understand OA.

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Abstract Number: 0563

Relation of Pain Sensitization to Isokinetic Knee Extension Torque: The MOST Study

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Background/Purpose: Central and local alterations in nociception are related to heightened pain severity and can be present in people who have knee osteoarthritis (OA). Yet, it is unknown if pain sensitization independently contributes to alterations in muscle function beyond the effect of pain severity. Thus, we aimed to examine the relation of pain sensitization to knee extension torque in adults with or at risk for knee OA.

Methods: Data from the 60-month visit of the MOST Study were used for this cross-sectional analysis. MOST is a cohort study of persons with or at risk for knee OA. Pain pressure threshold (PPT) and temporal summation (TS) were assessed at the right wrist and patella. PPT was measured with mechanical algometry (tip size=1 cm^2; rate=0.5 kg/s), and defined as the minimum pressure that caused slight pain. Three trials were performed at each site and averaged. For analysis, PPTs were divided into sex-specific tertiles. TS was assessed by repeatedly touching the skin (rate=1 Hz) with a 60 g monofilament for 30 s, and the presence of TS was defined as new or increased pain. Isokinetic knee extension torque was measured for the right leg at 60°/s with a computerized dynamometer. Maximum concentric knee extension torque was extracted from 4 maximal-effort trials, and normalized to body mass. Separate general linear regression models determined the relation of PPT and TS at the right wrist and patella to maximal knee extension torque of the right leg. Models were adjusted for age, sex, body mass index (BMI), clinic site, depressive symptoms, pain catastrophizing, average knee pain severity in the past month (Visual Analog Scale; VAS), and the presence of radiographic OA (ROA). Additionally, analyses were repeated after stratifying by sex and the presence of pain (VAS > 0) separately.

Results: 1702 participants (60% female) were included, with a mean (SD) age of 67.3 (7.7) years, BMI of 30.3 (5.6) kg/m^2, VAS of 15.3 (19.6) mm, and maximum knee extension torque of 1.03 (0.41) Nm/kg. Mean PPTs at the right wrist and patella were 3.4 (1.5) and 5.2 (2.2) kg/cm^2, respectively. Knee extension torque was significantly less in those with lower PPTs (i.e., higher pain sensitivity) compared to those with high PPTs (Table 1). Notably, those with the lowest PPTs at the patella were 14.3% weaker than those with the highest PPTs. For TS, the prevalence was 40.8% at the right wrist and 39.7% at the patella. Knee extension torque was significantly less in those with TS compared to those without TS, but the difference was small (i.e., < 5% weaker) (Table 1). In sex-specific analyses, lower PPTs were significantly associated with lower knee extension torques for both sexes, but the presence of TS was only associated with lower knee extension torques for females (Table 2). Lastly, low PPTs were associated with lower knee extension torques regardless of the presence of pain, but the presence of TS was only associated with lower knee extension torques for those with pain (Table 3).

Table 1. Relation of pain sensitization to maximum normalized knee extension torque (Nm/kg).

	Adjusted Mean Torque (95% CI)*	Adjusted Mean Torque (95% CI) **
Wrist PPT:		
Lowest Tertile	0.98 (0.95-1.01) †	1.01 (0.98-1.03) †
Middle Tertile	1.04 (1.01-1.06) †	1.06 (1.03-1.08)
Highest Tertile	1.09 (1.06-1.12)	1.10 (1.07-1.12)
Right Patella PPT:		
Lowest Tertile	0.96 (0.93-0.99) †	0.99 (0.97-1.02) †
Middle Tertile	1.03 (1.01-1.06) †	1.05 (1.02-1.07) †
Highest Tertile	1.12 (1.09-1.14)	1.13 (1.10-1.15)
Wrist TS:		
Present	1.01 (0.98-1.03) ‡	1.03 (1.00-1.05) ‡
Absent	1.05 (1.03-1.07)	1.07 (1.05-1.09)
Right Patella TS:		
Present	1.01 (0.98-1.03) ‡	1.03 (1.01-1.05) ‡
Absent	1.06 (1.04-1.08)	1.07 (1.05-1.09)

PPT – Pain Pressure Threshold (kg/cm^2). TS – Temporal Summation. *Adjusted for age, sex, BMI, clinic site, depressive symptoms, and pain catastrophizing. ** further adjusted for VAS pain and ROA. † Significantly different from highest PPT tertile. ‡ Significantly different from those without TS.

Table 2. Relation of pain sensitization to maximum normalized knee extension torque (Nm/kg) stratified by sex.		
	Adjusted Mean Torque (95% CI) *	Adjusted Mean Torque (95% CI) **
Wrist PPT:		
Males		
Lowest Tertile	1.20 (1.15-1.25) †	1.23 (1.18-1.28) †
Middle Tertile	1.26 (1.21-1.31)	1.29 (1.24-1.34)
Highest Tertile	1.32 (1.27-1.37)	1.34 (1.29-1.39)
Females		
Lowest Tertile	0.83 (0.80-0.86) †	0.86 (0.83-0.89) †
Middle Tertile	0.89 (0.86-0.91)	0.90 (0.87-0.93)
Highest Tertile	0.93 (0.90-0.96)	0.94 (0.91-0.97)
Right Patella PPT:		
Males		
Lowest Tertile	1.21 (1.16-1.26) †	1.24 (1.19-1.28) †
Middle Tertile	1.22 (1.17-1.26) †	1.24 (1.20-1.29) †
Highest Tertile	1.37 (1.32-1.41)	1.39 (1.34-1.44)
Females		
Lowest Tertile	0.82 (0.79-0.85) †	0.83 (0.80-0.86) †
Middle Tertile	0.92 (0.89-0.95)	0.92 (0.89-0.95)
Highest Tertile	0.97 (0.94-0.99)	0.96 (0.93-0.98)
Wrist TS:		
Males		
Present	1.25 (1.20-1.30)	1.26 (1.22-1.31)
Absent	1.27 (1.23-1.30)	1.30 (1.26-1.34)
Females		
Present	0.84 (0.82-0.87) ‡	0.87 (0.85-0.90) ‡
Absent	0.91 (0.89-0.93)	0.92 (0.90-0.94)
Right Patella TS:		
Males		
Present	1.26 (1.22-1.31)	1.29 (1.24-1.33)
Absent	1.27 (1.23-1.30)	1.29 (1.25-1.33)
Females		
Present	0.84 (0.81-0.87) ‡	0.86 (0.84-0.89) ‡
Absent	0.92 (0.89-0.94)	0.92 (0.90-0.95)

PPT – Pain Pressure Threshold (kg/cm²). TS – Temporal Summation. *Adjusted for age, sex, BMI, clinic site, depressive symptoms, and pain catastrophizing. ** further adjusted for VAS pain and ROA. † Significantly different from highest PPT tertile. ‡ Significantly different from those without TS.

Conclusion: Increased pain sensitivity, centrally and locally, is related to lower knee extension torque in adults with or at risk for knee OA. This relation is independent of knee pain severity and provides support that nervous system alterations may not only affect pain severity, but also muscle function.

Table 3. Relation of pain sensitization to maximum normalized knee extension torque (Nm/kg) stratified by presence of pain (VAS>0).		
	Adjusted Mean Torque (95% CI) *	Adjusted Mean Torque (95% CI) **
Wrist PPT:		
Painful		
Lowest Tertile	0.90 (0.87-0.93) †	0.92 (0.89-0.96) †
Middle Tertile	0.98 (0.95-1.01)	1.01 (0.97-1.04)
Highest Tertile	1.01 (0.97-1.04)	1.03 (0.99-1.06)
Nonpainful		
Lowest Tertile	1.15 (1.11-1.20)	1.16 (1.11-1.21) †
Middle Tertile	1.17 (1.12-1.21)	1.17 (1.12-1.21)
Highest Tertile	1.23 (1.19-1.27)	1.24 (1.19-1.28)
Right Patella PPT:		
Painful		
Lowest Tertile	0.89 (0.86-0.92) †	0.92 (0.89-0.95) †
Middle Tertile	0.97 (0.94-1.00) †	0.98 (0.95-1.01) †
Highest Tertile	1.05 (1.02-1.08)	1.07 (1.04-1.10)
Nonpainful		
Lowest Tertile	1.12 (1.07-1.17) †	1.13 (1.08-1.17) †
Middle Tertile	1.17 (1.12-1.22)	1.18 (1.13-1.22)
Highest Tertile	1.24 (1.20-1.28)	1.24 (1.20-1.28)
Wrist TS:		
Painful		
Present	0.94 (0.91-0.97) ‡	0.96 (0.93-0.98) ‡
Absent	0.98 (0.95-1.00)	1.00 (0.98-1.03)
Nonpainful		
Present	1.17 (1.12-1.21)	1.16 (1.12-1.21)
Absent	1.20 (1.17-1.23)	1.21 (1.17-1.24)
Right Patella TS:		
Painful		
Present	0.94 (0.91-0.96) ‡	0.95 (0.92-0.98) ‡
Absent	0.99 (0.96-1.01)	1.01 (0.98-1.03)
Nonpainful		
Present	1.18 (1.13-1.23)	1.18 (1.13-1.23)
Absent	1.19 (1.16-1.22)	1.20 (1.16-1.23)

PPT – Pain Pressure Threshold (kg/cm^2). TS – Temporal Summation. *Adjusted for age, sex, BMI, clinic site, depressive symptoms, and pain catastrophizing. ** further adjusted for ROA. † Significantly different from highest PPT tertile. ‡ Significantly different from those without TS.

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Incidence and Progression of Foot Osteoarthritis

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SESSION INFORMATION

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Background/Purpose: Foot osteoarthritis (OA) is a common cause of disability in older adults yet remains an understudied area. The purpose of this study was to examine the incidence and progression of foot osteoarthritis (OA), as well as potential risk factors, in a large population-based cohort.

Methods: Data were from the Johnston County Osteoarthritis Project (JoCoOA), a prospective population-based cohort of African American and White adults. Participants completed foot radiographs at baseline (2013-2015) and follow-up (2016-2018), which were scored using the La Trobe Foot Atlas to examine osteophytes (OP, score 0-3) and joint space narrowing (JSN, score 0-3) in the first metatarsophalangeal (1st MTP), first cuneometatarsal (1st CMT), second cuneometatarsal (2nd CMT), naviculocuneiform (NC), and talonavicular (TN) joints. Incident foot radiographic OA (rOA) was defined as baseline score < 2 OP and JSN in all 5 joints with ≥2 OP or JSN at follow-up in any of the 5 joints. Progression was defined as worsening score of OP or JSN in a joint with baseline foot rOA. At baseline and follow-up,

Table 1. Characteristics of the study sample by foot radiographic osteoarthritis (rOA) status at baseline and frequency of outcomes.

Characteristics	All participants (n=541)	No Foot rOA at baseline	Foot rOA at baseline
Age, mean (years)	69.4	69.2	70.2
Men	29.4%	31.1%	23.3%
African-American	35.1%	33%	42.5%
BMI, mean (kg/m^2)	31.2	30.6	33.2
Current smoker	7.9%	8.8%	5.0%
NSAID use in past two weeks	60.1%	58.9%	64.2%
Work disability	22.0%	21.1%	25.0%
Gout	6.2%	6.4%	5.2%
Foot injury	2.4%	2.2%	3.9%
Joints involved:			
1st MTP	5.9%	n/a	41.6%
1st CMT	1.2%	n/a	8.4%
2nd CMT	3.1%	n/a	22.1%
NC	3.5%	n/a	24.7%
TN	4.4%	n/a	31.2%

BMI=body mass index. Current smoker=smoking any amount of cigarettes during time of questionnaire. NSAID=non-steroidal anti-inflammatory and does exclude use of low-dose aspirin (81 mg daily).

Table 2. Association (adjusted odds ratio [95% confidence interval]) between covariates, foot radiographic osteoarthritis (rOA) incidence and progression, and worsening pain, aching or stiffness (PAS) in sample size of n=1082

Risk Factors	Incidence or progression	Incidence or progression and PAS present	PAS worsening
Women vs men	n/a	2.35 (0.77, 7.22)	1.58 (0.93, 2.71)
• No rOA at baseline	**4.10 (1.22, 13.8)**	n/a	n/a
• rOA at baseline	0.46 (0.19, 1.08)	n/a	n/a
BMI: 5 kg/m^2 increase	n/a	n/a	1.16 (0.97, 1.38)
• No rOA at baseline	**1.60 (1.31, 1.97)**	**1.81 (1.39, 2.36)**	n/a
• rOA at baseline	1.11 (0.90, 1.36)	1.07 (0.78, 1.47)	n/a
Age: 5 years older	1.14 (0.97, 1.34)	1.101 (0.76, 1.35)	n/a
• No rOA at baseline	n/a	n/a	1.02 (0.85, 1.23)
• rOA at baseline	n/a	n/a	**0.70 (0.50, 0.99)**
Work disability	0.74 (0.39, 1.42)	1.24 (0.43, 3.63)	**1.81 (1.07, 3.04)**
Gout	**2.75 (1.25, 6.07)**	2.01 (0.68, 5.92)	1.42 (0.81, 2.49)
Foot injury	2.75 (0.73, 10.4)	**4.99 (1.57, 15.9)**	1.59 (0.61, 4.13)

Bolded text indicates statistical significance.

BMI=body mass index, NSAID=nonsteroidal anti-inflammatory drug. Work disability was patient reported and included individuals that received work disability payments from either government or disability insurance. Gout was defined as self-report of being told by a physician of having gout at the feet. Foot injury was defined as injury that limited an individual's ability to walk for at least two days. Models adjusted for race, work disability, NSAID use, any foot PAS at baseline

For PAS worsening, a sample size of n=1080 was used.

Table 3. Association (adjusted odds ratio [95% confidence interval]) between covariates and worsening by Foot and Ankle Outcome Score (FAOS) subscale scores.

Risk Factors	Worsening FAOS Symptoms (n=1080)	Worsening FAOS Pain (n=1080)	Worsening FAOS-Activities of Daily Living (n=1080)	Worsening FAOS Sports & Recreation (n=1080)	Worsening FAOS Quality of Life (n=1080)
Women vs men	n/a	1.41 (0.93, 2.13)	**1.58 (1.04, 2.42)**	**1.57 (1.01, 2.43)**	1.31 (0.89, 1.94)
No rOA at baseline	**1.47 (0.95, 2.27)**	n/a	n/a	n/a	n/a
rOA at baseline	0.60 (0.26, 1.37)	n/a	n/a	n/a	n/a
BMI: 5 kg/m^2 increase	**1.40 (1.19, 1.66)**	**1.22 (1.05, 1.41)**	**1.21 (1.04, 1.41)**	**1.31 (1.11, 1.54)**	**1.24 (1.06, 1.44)**
Age: 5 years older	1.13 (0.99, 1.31)	n/a	n/a	n/a	1.01 (0.89, 1.15)
No rOA at baseline	n/a	1.01 (0.88, 1.16)	1.09 (0.94, 1.26)	1.12 (0.97, 1.29)	n/a
rOA at baseline	n/a	**0.74 (0.58, 0.96)**	**0.77 (0.60, 0.98)**	0.89 (0.71, 1.13)	n/a
Work disability	1.39 (0.85, 2.27)	**2.08 (1.26, 3.43)**	**2.09 (1.33, 3.27)**	**2.19 (1.35, 3.55)**	**1.60 (1.02, 2.50)**
Gout	0.98 (0.65, 1.47)	0.87 (0.54, 1.40)	**1.59 (1.09, 2.31)**	**1.47 (1.10, 1.96)**	1.56 (0.93, 2.62)
Foot injury	n/a	1.52 (0.56, 4.13)	**2.57 (1.18, 5.61)**	1.17 (0.43, 3.19)	1.21 (0.55, 2.68)

Bolded text indicates statistical significance.

BMI=body mass index. Work disability was self-reported and included participants that received work disability payments from either government or disability insurance. Gout was defined as self-report of being told by a physician of having gout and included his/her feet. Foot injury was defined as injury that limited the participant's ability to walk for at least two days. Models adjusted for race, work disability, NSAID use, any foot PAS at baseline.

participants were asked to rate their pain, aching, or stiffness [PAS] in each foot as 0-10 (none to extreme) on most days of any month in the past 12 months. PAS worsening was defined as an increase in the PAS from baseline to follow-up. The Foot and Ankle Outcome Score (FAOS) (pain, other symptoms, activities of daily living [ADL], sport and recreation function [Sports & Rec], foot and ankle-related quality of life [QOL]) was also obtained at both time points. Joint-based logistic regression models with generalized estimating equations were used to examine associations of foot rOA incidence and progression and covariates of interest (Table 1). Two-way interactions between risk factors and foot rOA status at baseline were assessed at a 0.10 alpha level and adjusted odds ratios and 95% confidence intervals (aOR [95% CI]) were shown by baseline status if significant; otherwise overall associations were reported.

Results: A total of 541 participants (1082 feet) were included (71% women, mean age 69 years; 35% African American, 53% obese; Table 1). Among 928 feet without baseline rOA, 4% developed incident foot rOA and roughly 2% of those had PAS of the same foot at follow-up (Table 1). Among 154 feet with baseline foot rOA, 55% had radiographic progression and 16% of those had PAS of the same foot at follow-up. Female sex and higher BMI were associated with incident foot rOA, while history of gout was associated with both incidence and progression of foot rOA (Table 2). History of foot injury was associated with foot OA with PAS present. Work disability was associated with PAS and FAOS worsening particularly for pain, ADL, and Sports & Rec subscales (Table 3). BMI was associated with worsening of all FAOS subscales, and history of gout was associated with worsening for FAOS ADL and Sports & Rec subscales.

Conclusion: Progression of foot rOA is relatively common, although it is not necessarily related to worsening symptoms. Given the increased risk of foot OA outcomes with higher BMI, foot injury, and history of gout, further studies could examine interventions (e.g., weight loss, injury prevention, intensive gout control) to reduce or manage foot OA.

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In Those with Unilateral Frequent Knee Pain, Between-Limb Differences in Stance Time During Walking Increase the Risk of Frequent Pain in the Other Knee: The MOST Study

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SESSION INFORMATION

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Background/Purpose: Knee osteoarthritis (OA) commonly begins as a unilateral disease, with pain in only one knee. Yet 88% of persons with unilateral knee OA develop bilateral disease within 10 years. Between-limb differences in stance time while walking may be a modifiable risk factor that plays a role in the progression from unilateral to bilateral disease. Therefore, the purpose of this study was to determine if stance time asymmetry while walking is a risk factor for incident frequent pain in the contralateral knee for older adults with unilateral frequent knee pain (FKP).

Methods: Participants with unilateral FKP (i.e., pain on most days of the past month) at the 60-month visit of the MOST study were included in this analysis. MOST is a NIH-funded cohort study of persons with or at risk for knee OA. Participants performed 4 walking trials at their usual walking speed over a 4.9 m instrumented walkway. Average stance time was calculated for each leg with all steps taken during the walking trials. A stance time limb symmetry index (LSI) was calculated as (Stance Time without FKP / Stance Time with FKP) x100, with values >100% indicating longer stance time on the leg without FKP, values < 100% indicating longer stance time on the leg with FKP, and 100% indicating equal stance times. Incident FKP was defined by the presence of FKP at the 84-month visit for the knee without FKP at the 60-month visit. Logistic regression models determined the relation of stance time LSI to incident FKP. Covariates included age, sex, BMI, race, gait speed, previous surgery or injury to the knee without FKP, and knee pain severity of the knee without FKP. Analyses were repeated for females and males independently.

Results: 300 participants in the MOST cohort had unilateral FKP at the 60-month visit. 63% were female, 86% were white, mean (SD; min-max) age was 66.9 (8.1; 55.5-84.9) years, and BMI was 31.2 (6.8; 20.4-62.4) kg/m^2. For the gait evaluation, mean stance time was 708 (69; 529-986) ms on the leg with FKP and 712 (72; 514-970) ms on the leg without FKP, with a mean LSI of 100.6 (2.8; 83.9-111.3) %. Of the 300 participants, 97 (32%) developed FKP by the 84-month visit in the knee without FKP originally. Stance time LSI was significantly associated with incident FKP, with a five-unit increase in LSI (i.e., 5% longer time spent on the leg without FKP) associated with a 67% increased odds of incident FKP (OR 1.67, 95%CI 1.03-2.69, p=0.04). For females, a five-unit increase in stance time LSI was associated with a 86% increased odds in incident FKP (OR 1.86, 95%CI 1.01-3.43, p=0.048), while for males a five-unit increase was associated with a 65% increased odds in incident FKP (OR 1.65, 95%CI 0.71-3.83, p=0.24).

Conclusion: A high proportion (32%) of individuals with unilateral FKP have frequent pain in their contralateral knee at 2-year follow-up. A longer stance time on the leg without FKP compared to the leg with FKP appears to be a risk factor for developing frequent pain in the knee without FKP originally. The effect was similar for females and males independently. Future research is needed to determine how to best intervene.

Disclosure: P. Corrigan, None; **D. Felson**, None; **C. Lewis**, None; **K. Gross**, None; **M. Nevitt**, None; **B. Lewis**, None; **J. Torner**, None; **J. Stefanik**, None.

Abstract Number: 0566

Healthcare Utilization and Costs Prior to Diagnosis of ANCA Vasculitis in Medicare Beneficiaries

Shirley Huang[1], Xintong Li[2], Joehl Nguyen[2], Jacob Robinson[2], Susan Hogan[3], Vimal Derebail[3] and Carolyn Thorpe[2], [1]University of North Carolina at Chapel Hill, Chapel Hill, [2]University of North Carolina Eshelman School of Pharmacy, Chapel Hill, [3]University of North Carolina Kidney Center, Chapel Hill

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Epidemiology & Public Health Poster II: OA, Osteoporosis, & Other Rheumatic Disease
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Antineutrophil cytoplasmic antibody (ANCA) vasculitis (AV) is a complex group of autoimmune disorders affecting blood vessels in multiple organ systems. Delays in diagnosis are common because AV symptoms can be non-specific and present heterogeneously. This may result in increased healthcare utilization in the months preceding diagnosis. We examined whether Medicare beneficiaries with AV experience increased healthcare utilization and costs in the year before the first diagnosis was recorded in claims, relative to Medicare beneficiaries without AV.

Methods: This retrospective cohort study used 2015-16 Medicare Part A/B medical claims and Part D prescription drug data. Beneficiaries with newly diagnosed AV were identified by having ≥1 inpatient claim or ≥2 non-inpatient claims at least 7 days apart in 2016 with an ICD-10 code for granulomatosis with polyangiitis, microscopic polyangiitis, or eosinophilic granulomatosis with polyangiitis, with no AV claims in the year prior. Beneficiaries with AV were matched 1:1 on age and sex to beneficiaries without any diagnosis codes for any type of systemic vasculitis in 2016. The study index date for AV beneficiaries was the first AV claim in 2016, which also served as the index date for the matched control. Beneficiaries were required to have continuous enrollment in Parts A, B, and D in the year prior to index. Outcomes included annual Medicare and beneficiary expenditures for Part A/B medical services, Part B and D medications, and annual counts of events in 12 categories of medical services (e.g., inpatient stays, outpatient visits, tests), for the year prior to the index date. Linear regression was used to test for differences, controlling for race/ethnicity, dual Medicaid enrollment or the Part D low-income subsidy, entitlement due to disability, and US region. Bias-corrected bootstrapped standard errors were used to calculate 95% confidence intervals (CI), accounting for non-normal distributions of dependent variables.

Results: A total of 1,626 AV beneficiaries and 1,626 matched controls met study criteria (mean age = 70.4 years, 62% female). The mean (SD) unadjusted Medicare and beneficiary Part A/B payments in the year prior to diagnosis were $23,445.23 (33,646.70) and $4,380.64 (5,064.45) for AV beneficiaries, respectively, and $10,136.05 (19,944.70) and $1,907.44 (3,292.49) for matched controls (Table 1). Adjusted regression analyses revealed that AV beneficiaries had significantly higher Medicare and beneficiary payments for all cost categories, and higher number of all types of utilization events, compared to matched controls ($p< 0.001$). Of note, AV beneficiaries on average incurred an additional $13,726 (95% CI: $11,946-$15,845) in Medicare Part A/B expenditures and had 21.2 (95% CI: 18.3-24.5) more hospital outpatient visits vs. matched controls.

	Descriptive Statistics				Adjusted Regression Model*	
	Beneficiaries without AV N=1,626		Beneficiaries with AV N=1,626			
Medical Service Payments (USD)	Mean (SD)	Median (Q1,Q3)	Mean (SD)	Median (Q1,Q3)	Coefficient	95% CI
Total Medicare Parts A and B Payments	10,136.05 (19,944.70)	2,990.91 (1131.26, 8896.26)	23,445.23 (33,646.70)	11,094.14 (4052.26, 31413.09)	13,726.08	[11,945.85 – 15,845.02]
Total Beneficiary Parts A and B Payments	1,907.44 (3292.49)	800.22 (366.02, 2079.78)	4,380.64 (5064.45)	2,582.16 (1105.51, 5359.57)	2,531.78	[2,268.24 – 2,841.29]
Healthcare Utilization	Mean (SD)	Median (Q1,Q3)	Mean (SD)	Median (Q1,Q3)	Coefficient	95% CI
Acute Inpatient Stays	0.28 (0.75)	0 (0,0)	0.66 (1.20)	0 (0,1)	0.40	[0.33 - 0.47]
Hospital Outpatient Visits	8.39 (17.05)	3 (1,9)	29.35 (56.29)	8 (3,21)	21.19	[18.29 - 24.54]
Emergency Room Visits	0.80 (2.12)	0 (0,1)	1.35 (2.98)	0 (0,2)	0.64	[0.45 - 0.82]
Part B Drug Events	4.09 (8.67)	2 (0,4)	6.96 (13.31)	3 (1,6)	2.83	[2.06 - 3.56]
Part B Physician Office Services	9.12 (8.21)	7 (3,13)	14.05 (11.90)	11 (6,19)	5.02	[4.27 - 5.75]
Dialysis	0.14 (1.54)	0 (0,0)	1.88 (7.20)	0 (0,0)	1.78	[1.45 - 2.21]
Imaging	7.76 (16.32)	2 (0,7)	11.85 (20.49)	6 (2,13)	6.26	[5.70 - 6.92]
Tests	4.89 (6.26)	3 (1,7)	11.01 (10.82)	8 (4,15)	14.49	[12.49 - 16.57]
Other Procedures	18.02 (24.99)	11 (3,23)	32.34 (34.15)	21 (9,43)	3.98	[2.74 - 5.20]
Durable Medical Equipment	3.55 (8.48)	0 (0,2)	4.93 (9.17)	0 (0,6)	1.53	[0.93 - 2.12]
Other Part B Carrier Events	5.71 (11.98)	2 (0,6)	11.09 (29.09)	4 (1,11)	5.35	[3.95 - 7.00]
Drug Payments (USD)	Mean (SD)	Median (Q1,Q3)	Mean (SD)	Median (Q1,Q3)	Coefficient	95% CI
Total Medicare Part B Drug Payments	492.96 (3081.29)	47.04 (0, 205.93)	1,215.66 (5669.67)	63.70 (8.02, 282.79)	710.01	[398.52 - 1,040.15]
Total Beneficiary Part B Drug Payments	113.88 (790.38)	0.00 (0, 7.55)	301.53 (1451.22)	2.78 (0, 48.93)	184.87	[105.66 - 270.49]
Total Medicare Part D Drug Payments	3,429.82 (12567.90)	811.08 (108.09, 2371.81)	5,089.79 (16042.1)	1,476.03 (333.44, 3122.53)	1,732.44	[797.29 - 2,692.57]
Total Beneficiary Part D Drug Payments	581.47 (1098.25)	203.52 (56.24, 643.19)	1,046.73 (3429.69)	353.88 (89.29, 1026.17)	461.42	[314.39 - 644.60]

*p<0.001 for all comparisons of AV vs. non-AV beneficiaries
AV: ANCA vasculitis, SD: standard deviation, Q1: quartile 1, Q3: quartile 3, CI: confidence interval

Table 1. Total one-year utilization and costs prior to diagnosis for AV beneficiaries and matched controls

Conclusion: In the year prior to AV diagnosis, Medicare beneficiaries have significantly higher healthcare utilization and costs when compared to age- and sex-matched beneficiaries without AV. This study highlights that pre-diagnosis manifestations in AV can be costly and further improvement may be needed to allow for timely diagnosis.

Disclosure: S. Huang, GlaxoSmithKline, 1; **X. Li**, None; **J. Nguyen**, Bristol Myers Squibb, 1; **J. Robinson**, None; **S. Hogan**, None; **V. Derebail**, Novartis, 1, Retrophin, 1; **C. Thorpe**, None.

Abstract Number: 0567

Rheumatologist's Perception of the Efficacy, Safety and Willingness to Prescribe Infliximab and Use Alternate Drug Supply Programs to Lower Cost of Rheumatoid Arthritis Care

Cesar Galan[1], Alan Puric[2], Guy Cozzi[2], **Michele Hamburger**[3], Elisea Avalos-Reyes[4] and Kjel Johnson[1], [1]CVS Health, Lincoln, RI, [2]CVS Health, Northbrook, IL, [3]Frances Hamburger Institute, Hauppauge, NY, [4]CVS Health, Irving, TX

SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: There is interest in employing biosimilar therapies for patients with rheumatoid arthritis (RA), which have been shown comparable to originator biologics in safety and efficacy but lower in cost; another strategy is “white bagging” where rheumatologist administered drugs are sent by a specialty pharmacy to the rheumatologist’s office.To date, four infliximab biosimilars are available and various payors have implemented white bagging programs. We assessed what drives rheumatologists to prescribe an infliximab biosimilar and participate in white bagging drug programs.

Methods: We conducted an online cross-sectional survey of hospital and community-based rheumatologists in July 2019 and June 2020. Questions assessed willingness to prescribe biosimilars, the quality, safety and effectiveness of biosimilars compared to originator biologics, what influences a rheumatologist’s decision to prescribe a biosimilar and reasons rheumatologists would not switch from buy-and-bill to white-bagging. We used a Likert scale rating of “Never,” “Seldom,” “Sometimes,” “Often” and “Always.” Descriptive statistics and percentages are reported (n=43).

Results: Rheumatologists reported prescribing an originator biologic drug often or always 58% of the time. When asked to what degree a biosimilar matches the originator biologic in terms of safety, effectiveness and quality, rheumatologists reported the biosimilar as being the same 77%, 74% and 72% of the time, respectively. In spite of this, when asked to report their expected likelihood of prescribing a biosimilar in the future, only 35% of rheumatologists believed they would often or always prescribe a biosimilar. Provided financial equivalence, rheumatologists reported being more likely to prescribe a biosimilar 65% of the time to new patients and 47% of the time to existing patients. The top 3 reasons for prescribing a biosimilar are the patient’s out of pocket cost, cost to the practice and the value of reimbursement, 72%, 67% and 56%, respectively in fee-for-service reimbursement arrangements and 72%, 63% and 51%, respectively, in value-based reimbursement arrangements. When asked why rheumatologists would not switch from buy-and-bill to white-bagging, financial benefit to the rheumatologists’ practice (63%) and control of the drug (58%) were the top 2 reasons.

Conclusion: The majority of rheumatologists in this study reported currently prescribing originator biologics most of the time at their practice. The rheumatologists also perceived biosimilars to be as safe and effective as the originator biologic. Additionally, the surveyed rheumatologists expressed a willingness to prescribe biosimilars in the future, provided income would not be reduced. RA is associated with considerable economic burden; lower-cost biosimilars may provide an opportunity to reduce overall patient and health system costs; white bagging programs are not supported by rheumatologists due to revenue loss and chain of control concerns. Supporting provider income in any cost reduction program is key to program success.

Disclosure: C. Galan, CVS Health, 1, 3; **A. Puric**, CVS Health, 1, 3; **G. Cozzi**, CVS Health, 1, 3; **M. Hamburger**, None; **E. Avalos-Reyes**, CVS Health, 3; **K. Johnson**, CVS Health, 1, 3.

Abstract Number: 0568

Clinical Timelines and Management Delays in Suspected Giant Cell Arteritis

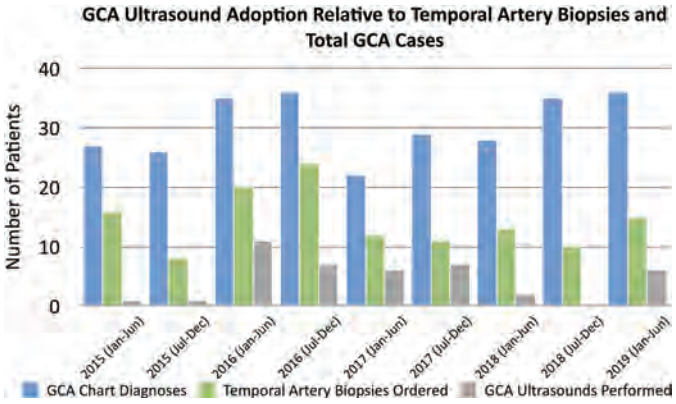
Stephen Slade[1], Cindy Chiu[1], Erin Bauer[1] and Amish Dave[1], [1]Virginia Mason Medical Center, Seattle, WA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

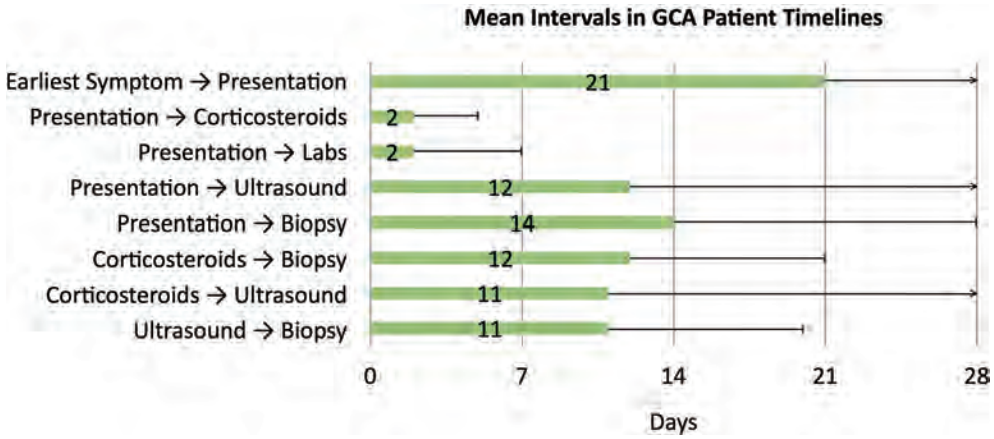
Background/Purpose: Giant cell arteritis (GCA), the most common systemic vasculitis, may have diagnostic and treatment delays that can increase risk of vascular complications. Diagnostic color doppler ultrasound (US) has potential to decrease time to diagnosis, limit corticosteroid exposure, and avoid need for a surgical procedure, all at lower cost than temporal artery biopsy (TAB).

Identification of bottlenecks in patient workup and delays in treatment can guide targeted quality improvement interventions. Our goal was twofold: to determine institutional use of US and TAB and to construct a timeline of key clinical events for patients with suspected GCA.

Methods: All data was obtained from the integrated electronic health record at our community-based multi-site health system from a 4.5-year timeframe starting in 2015 with GCA by International Classification of Diseases-9 or 10 diagnostic codes, and TAB order dates were determined by current procedural terminology codes. Because our outcomes were agnostic to final diagnosis, we did not designate GCA classification criteria for all patients. Using retrospective chart review, we identified dates of milestone events for patients who underwent GCA US: earliest of common GCA symptoms from a predefined list, medical presentation, corticosteroid initiation, inflammatory marker evaluation, US, and TAB.



Comparing US and TAB among 274 patients with new GCA diagnoses, 100 (36%) had TAB only ordered, 29 (11%) had both TAB ordered and had US, and 12 (4%) had US only.



Timeline mean intervals with standard deviation. Symptom onset to presentation 21 ± 43, presentation to corticosteroids 2 ± 3, presentation to labs 2 ± 5, presentation to US 12 ± 23, presentation to TAB 14 ± 14, corticosteroids to TAB 12 ± 9, corticosteroids to US 11 ± 27, and US to TAB 11 ± 9. Time from presentation to US versus TAB was not significantly different (p=0.77).

Where available, we calculated intervals by subtraction of event dates, and where unavailable, approximated based on clinical documentation. Mean durations were rounded to the nearest whole day and excluded negative integers (e.g. patient excluded if prescribed corticosteroids for different indication days prior to presentation with suspected GCA and new, high-dose corticosteroid indication).

Results: Comparing US and TAB among 274 patients with new GCA diagnoses, 100 (36%) had TAB only ordered, 29 (11%) had both TAB ordered and had US, and 12 (4%) had US only. Timeline values were as follows (mean ± standard deviation, in days): symptom onset to presentation 21 ± 43, presentation to corticosteroids 2 ± 3, presentation to labs 2 ± 5, presentation to US 12 ± 23, presentation to TAB 14 ± 14, corticosteroids to TAB 12 ± 9, corticosteroids to US 11 ± 27, and US to TAB 11 ± 9. Time from presentation to US versus TAB was not significantly different (p=0.77). Ten of 37 patients (27%) with calculable corticosteroid dates were not prescribed high-dose empiric corticosteroids within two days of presentation.

Conclusion: Patients with suspected GCA had widely variable times to key events in their clinical courses, including initial presentation. US was used in only a minority of suspected GCA cases. Future work could target interventions to reduce variability in diagnostic access and empiric therapy initiation, such as through a fast-track clinic model.

Disclosure: S. Slade, None; **C. Chiu**, None; **E. Bauer**, None; **A. Dave**, None.

Abstract Number: 0569

Ability and Willingness to Utilize Telemedicine Among Rheumatology Patients – a Cross Sectional Survey

Steve Kong[1], **Lilian Otalora Rojas**[2], Amnie Ashour[3], Mathew Robinson[1] and Neha Bhanusali[1], [1]University of Central Florida College of Medicine, Orlando, [2]University of Central Florida HCA Healthcare GME, Orlando, [3]Stony Brook University School of Medicine, New York

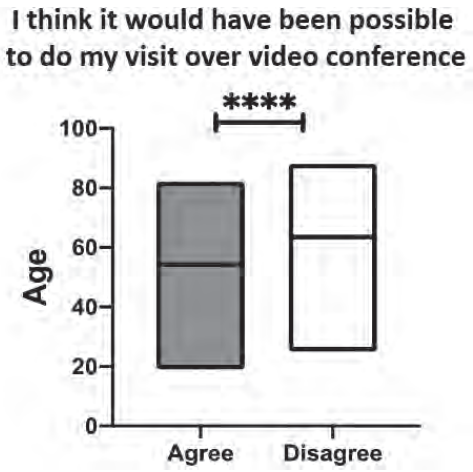
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Telemedicine (TM) is the delivery of health care services using information and communication technologies. TM presents unique opportunities and benefits specifically in rheumatology as most rheumatic illnesses are chronic requiring frequent disease monitoring, outpatient therapies, and a strong patient-physician relationship. This study aims to assess the patients' ability and willingness to utilize telemedicine along with some of the barriers to a more widespread adoption of TM in rheumatology.

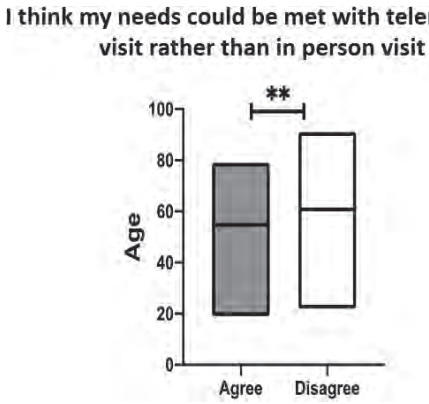
Methods: A cross sectional survey of patients visiting a rheumatology clinic in Florida from March-August 2018 was conducted. We used a Tele-Rheumatology Questionnaire to assess patients' attitude on the effectiveness of TM versus in-person visits, patients' access to technology (telephone, front facing camera, and high-speed internet), distance traveled by the patient to attend the clinic visit, and demographic parameters (age, sex, race, new patient vs follow-up, and diagnosis). Data was analyzed using Statistical Package for Social Sciences and descriptive statistics were calculated.

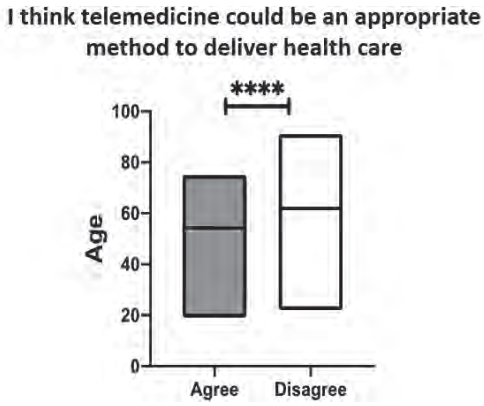
Results: 214 rheumatology patients participated in this study. 82.7% were women and 17.3% were men with an average age of 58.3 ±13.5. We found statistically significant associations between age and the following responses: access to—front facing camera (mean difference -12.8), —telephone (mean difference -14.4), and —stable internet connection (mean difference -15.1); conflict in appointments and work hours (mean difference -11.73); willingness to—utilize telephone consultation (mean difference -3.97) or —live video consultation (mean difference -8.09); —try TM with a new rheumatologists (mean difference -7.82); —try TM with an established rheumatologist (mean difference -11.19); —try TM for other specialties (mean difference -8.16); —try TM to reduce time between appointments (mean difference -10.79).

Follow-up patients were more likely to feel that their visit could have been possible over the phone (mean difference -1.13) or video conferencing (mean difference -1.13) compared to new patients.

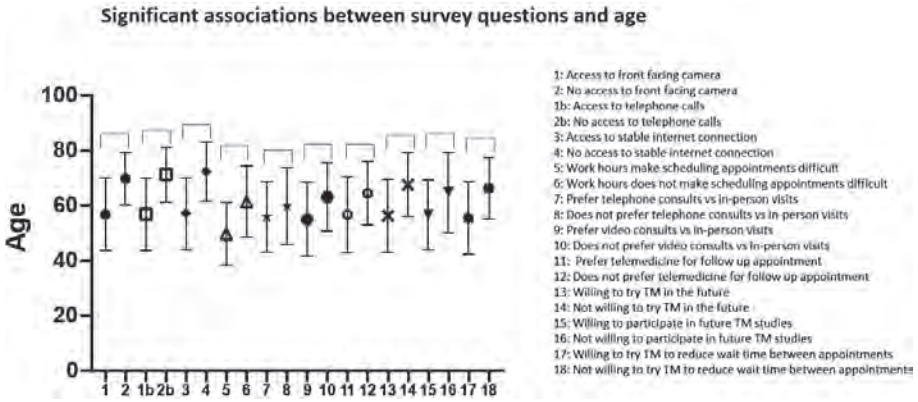


Left: Statistically significant correlation between age and patients who responded that the purpose of the clinic visit could have been possible over telephone, in which a negative correlation of -0.207 ($p=0.003$) was seen. Right: statistically significant correlation between age and patients who responded that the purpose of the clinic visit could have been possible over video conference, in which a negative correlation of -0.333 ($p<0.001$) was seen.





Left: Statistically significant correlation between age and patients who responded that their needs could have been met with telemedicine, in which a negative correlation of -0.224 ($p<0.001$) was seen. Right: Statistically significant correlation between age and patients who responded that telemedicine could be an appropriate method of healthcare, in which a negative correlation of -0.298 ($p<0.001$) was seen.



Statistically Significant correlation between age and "yes and no" questions on the TRQ. The mean difference in age between 1 and 2 = -12.837 ($p<0.001$), between 1b and 2b = -14.417 ($p<0.001$), between 3 and 4 = -15.107 ($p<0.001$), between 5 and 6 = -11.733 ($p<0.001$), between 7 and 8 = -3.973 ($p<0.040$), between 9 and 10 = -8.099 ($p<0.001$), between 11 and 12 = -7.826 ($p<0.001$), between 13 and 14 = -11.193 ($p<0.001$), between 15 and 16 = -8.167 ($p<0.001$), between 17 and 18 = -10.797 ($p<0.001$).

Older patients were less likely to think that the purpose of their rheumatology visits could be achieved over the phone (r-.207, p=0.003) or video conferencing (r -.331, p=0.001). Negative correlations were found between increase in age and believing that their needs could be met through TM (r -.224, p< 0.001) and thinking that TM could be an appropriate alternative method of healthcare (r -.298, P< 0.001).

The further the distance traveled, the more the patients were willing to utilize telephone consultation compared to in-person visits (r 0.167,p=0.019).

Conclusion: With the COVID-19 pandemic, rheumatology clinics are increasingly turning to TM as the main, and sometimes only, method of seeing patients. The results of this study suggest that technology may still be limited in certain demographics, particularly the elderly. This study helps to understand some of the limitations of TM that can be crucial in the development of solutions to make it a better option for all rheumatological patients. Futures studies are needed to evaluate if this sample population felt the same once telehealth was actually utilized.

Disclosure: S. Kong, None; **L. Otalora Rojas**, None; **A. Ashour**, None; **M. Robinson**, None; **N. Bhanusali**, None.

Abstract Number: 0570

The Patient Perspective on Using Digital Resources to Address Unmet Needs in Systemic Lupus Erythematosus

Jennifer Ra[1], Jerik Leung[2], Elizabeth Baker[2] and Alfred Kim[1], [1]Washington University School of Medicine, St. Louis, MO, [2]Saint Louis University, College for Public Health and Social Justice, St. Louis

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The clinical variability of systemic lupus erythematosus (SLE) caused by the unpredictability of flares contributes to patients experiencing a diminished sense of social support. Digital health interventions (DHI) – interventions accessible through digital technologies (i.e. apps, internet) on devices such as mobile phones, tablets, and computers – have the potential to improve this eroded social support. Digital resources have shown to improve disease self-management and health-related quality of life in other chronic diseases like rheumatoid arthritis and chronic pain. However, DHIs for SLE have yet to be studied extensively. Our objective was to assess: 1) general and SLE-specific internet usage and 2) specific suggestions for SLE-related digital resources and tools among SLE patients at the Washington University Lupus Clinic.

Methods: Fifty-six patients with American College of Rheumatology or Systemic Lupus International Collaborating Clinics classified SLE were recruited from the Washington University Lupus Clinic. Because SLE affects mostly women, only female patients were considered. No other specific characteristics were sought.

Ten-minute structured interviews were conducted. Multiple choice questions assessed internet access, types of devices used to access the internet, how patients currently use the internet for their SLE, what topics they would be interested to see in the future, and demographics. Open-ended questions assessed what other SLE-related information or support they would like to use the internet for and what would make them more likely to use it for their SLE needs. Descriptive statistical analysis was conducted with the quantitative data, while the qualitative data was analyzed using an open coding approach, where similar or recurring responses were categorized into themes and subthemes.

Results: Nearly all respondents indicated having access to the internet (98.2%, n=55). Currently, 80.0% (n=44) use the internet to locate SLE-related information, all of whom were interested in continuing or increasing this use. Participants indicated that they were interested in most topics presented (i.e. connecting with other SLE patients, nutrition and SLE, new/alternative treatments). The qualitative data indicated that SLE patients: 1) used the internet for understanding flares, changes in their symptoms, and/or lab results; 2) wanted a greater variety of SLE information; 3) wanted to exchange personal experiences and knowledge of SLE with others; and 4) desired increased diversity in the methods of delivering digital SLE information.

Conclusion: Our findings indicate that patients were not only already using the internet for their SLE, but also eager to provide suggestions to improve current digital resources. A primary suggestion from patients was a desire for dynamic, interactive resources that would enable patients to access content according to the symptomatology they are experiencing. Other considerations include developing interventions that are customizable to the patient and provide SLE information that is consistent with that received from their healthcare providers. We believe that our findings will aid future development of DHIs for SLE patients.

Disclosure: J. Ra, None; **J. Leung**, None; **E. Baker**, None; **A. Kim**, Exagen Diagnostics, Inc., 5, 8, GlaxoSmithKline, 2, 5, 8, Alexion Pharmaceuticals, 5, Annexon Biosciences, 5, JPMorgan Chase & Co., 5.

Abstract Number: 0571

Improving Care for Patients with Inflammatory Arthritis by Enabling Physical Therapists to Directly Refer to Rheumatologists: A Qualitative Study

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Health Services Research Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Early referral to rheumatology of persons with suspected inflammatory arthritis is associated with better outcomes. Typically, patients are first seen by a family physician who assesses the need for referral to a rheumatologist. However, many people who do not have a regular family physician may consult a physical therapist where no physician referral is required. Enabling direct referral from a physical therapist to a rheumatologist could enhance early access to a rheumatologist; recent evidence indicates that physical therapists can appropriately identify patients with inflammatory arthritis. Our objective was to explore perceptions of professionals and patients regarding enabling physical therapists to refer patients with inflammatory arthritis directly to rheumatologists.

Methods: We conducted 5 focus groups with a total of 29 participants. There were 4 homogeneous groups with: 1) 5 rheumatologists, 2) 7 family physicians, 3) 6 physical therapists and 4) 6 patients. The fifth group was mixed and included 3 physical therapists and 2 patients. We used purposive and snowball sampling to recruit participants. All 8 patients with inflammatory arthritis were recruited via the Canadian Arthritis Society. Meetings were audio-taped and transcripts were analyzed using thematic analysis.

Results: Two common core themes were identified from all focus groups: 1) difficulties accessing care, and 2) interprofessional relationships. The first theme included aspects such as waiting times to consult rheumatologists and physical therapists in the public sector, as well as financial barriers related to consulting physical therapists in the private sector. The second theme included perceptions of physical therapists' roles and abilities, appropriateness of referrals, multidisciplinary vs. solo practitioners, communication pathways and traditionalist vs. contemporary style of practice by family physicians. Besides these two main themes, several groups discussed other issues. The health care groups (rheumatologists, family physicians and physical therapists) talked about lack of awareness of the new agreement that physical therapists can directly refer to rheumatologists. In the physician groups, 2 other issues were discussed: professional responsibilities (e.g. scope of practice, gatekeeping and coordination of care) and the consult fee for rheumatologists. In the physical therapist focus group, self-confidence in identifying inflammatory vs. non-inflammatory conditions was also raised.

Conclusion: Regarding difficulties accessing care, waiting time to see a rheumatologist remains the biggest barrier for patients with new-onset inflammatory arthritis followed by the lack of access to physical therapists and family physicians. Further developing the relationship among the health professionals involved with these patients could optimize patient care. This could be done through education about everyone's role, building efficient communication pathways and creating opportunities for interprofessional connections. In addition, professional regulatory bodies

should increase awareness about the new agreement regarding direct referral by physical therapists to rheumatologists.

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Abstract Number: 0572

Two-year Cost-effectiveness Between Two Gradual Tapering Strategies in Rheumatoid Arthritis: Cost-utility Analysis of the TARA Trial

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Session Time: 9:00AM–11:00AM

Background/Purpose: The benefits of tapering are a decreased risk of long-term adverse events and a reduction of health care costs, especially when bDMARDs are tapered. However, tapering treatment may lead to more transient or persistent disease flares, which have a direct impact on patients' lives and societal costs. We aimed to evaluate the two year cost-utility ratio between tapering the csDMARD first followed by the TNF-inhibitor, and tapering the TNF-inhibitor first followed by the csDMARD.

Methods: The TARA trial is a multicenter single-blinded randomized controlled trial. RA patients that used a csDMARD(s) plus a TNF-inhibitor and who had a well-controlled disease for at least 3 months, defined as a DAS≤2.4 and a swollen joint count (SJC) ≤1, were included. Patients were randomized into gradual tapering their csDMARD in the first year followed by the TNF-inhibitor in the second year, or vice versa. Medication was tapered in three steps over the course of 6 months. Gradual tapering was done by cutting the dosage into half, a quarter and thereafter it was stopped. Data on quality adjusted life years (QALYs, measured with the Dutch EuroQol [EQ5D]), health care costs and productivity costs were used to calculate the Incremental Cost Effectiveness Ratio (ICER). The ICER, the cost-effectiveness acceptability curve (CEAC), and the incremental net monetary benefit (iNMB) were used to assess cost-effectiveness between both tapering strategies.

Results: Of the 189 included patients, 94 started tapering their TNF-inhibitor first, while the other 95 tapered their csDMARD first. QALYs (sd) were, respectively, 1.64 (0.22) and 1.65 (0.22). Medication costs were significantly lower in the patients who tapered the TNF-inhibitor first, while indirect cost were higher due to more productivity loss (p=0.10). Therefore, total costs (sd) were €38,833 (€39,616) for tapering csDMARDs first, and €39,442 (€47,271) for tapering the TNF-inhibitor first (p=0.88). The ICER (95% CI) between tapering csDMARDs first minus the TNF-inhibitor first was €60,919 per QALY (95% CI, -€90,638 per QALY to €212,475 per QALY)(figure 1). The iNMB was €1134 (95% CI €761 to €1507) in favor of tapering TNF-inhibitor first for a willingness-to-pay (WTP) level of €50,000, which is the current level of WTP in the Netherlands for treatment of RA (figure 1). According to the CEAC, for WTP levels < €53,800 tapering the csDMARD first has the highest probability of being cost-effective, while for WTP levels >€83,800 tapering the TNF-inhibitor first has the highest probability (figure 2).

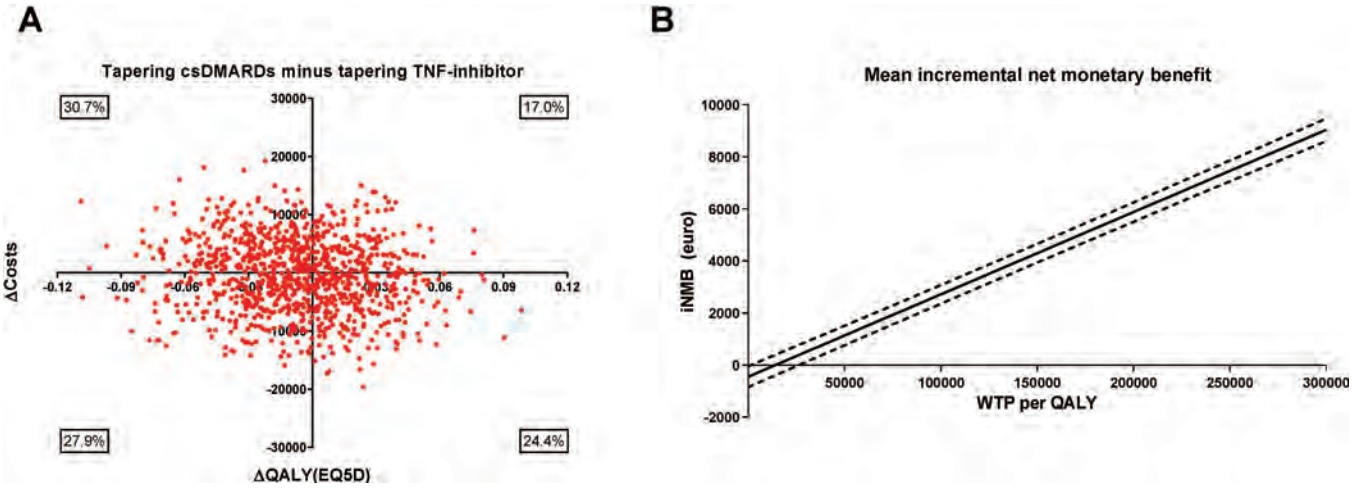

Figure 1. Summary of economic evaluation of tapering csDMARDs first minus tapering TNF-inhibitor first. (A) Results of 1000 bootstrapped replications, presented in a cost-effectiveness plane which represents uncertainty of the cost-effectiveness ratio. (B) Mean incremental net monetary benefit (iNMB) for tapering csDMARDs minus tapering TNF-inhibitors with 95% confidence intervals plotted against different levels of willingness to pay (WTP) per quality adjusted life year (QALY). The iNMB was calculated as the incremental benefit times different levels of WTP, minus the incremental costs. csDMARDs: conventional synthetic DMARDs; iNMB: incremental net monetary benefit; QALY: quality adjusted life year; WTP: willingness to pay.

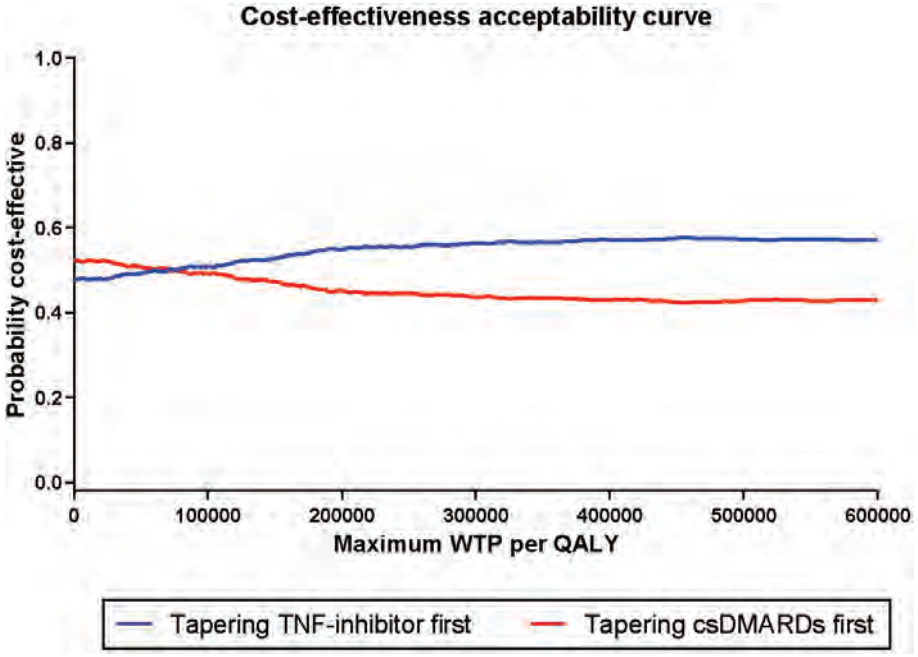

Figure 2. Cost effectiveness acceptability curve for tapering csDMARDs first versus tapering TNF-inhibitor first. Results of 1000 bootstrapped replication, presented for several levels of willingness to pay, indicated per quality adjusted life year (QALY). csDMARDs: conventional synthetic DMARDs; QALY: quality adjusted life year; WTP: willingness to pay.

Conclusion: Our economic evaluation shows that costs are similar for both tapering strategies. Depending on the WTP threshold, either tapering the TNF-inhibitor first or csDMARD first has the highest probability of being cost-effective.

Disclosure: E. van Mulligen, None; **A. Weel**, None; **M. Hazes**, None; **A. van der Helm - van Mil**, None; **P. de Jong**, None.

Abstract Number: 0573

Effects of Successive Switches of Two Different Biosimilars of Etanercept on Outcomes in Inflammatory Rheumatic Diseases in Daily Practice

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SESSION INFORMATION
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Background/Purpose: A single *switch* from an originator to a *biosimilar* product has been shown to be safe and effective in the treatment of rheumatic musculoskeletal diseases (RMDs). The availability of biosimilars has created a financial incentive to encourage switching to cheaper products ("non-medical switch"). This is naturally associated with multiple switches. However, the effect of multiple switching between biosimilars of the same reference product has not been thoroughly investigated to date. To assess the effectiveness and safety of systematic non-medical switching from innovator etanercept (ETN) to biosimilar ETN (SB4) and successive to another biosimilar ETN (GP2015) in adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) or axial spondyloarthritis (axSpA) in a real-life setting.

Methods: This retrospective study was performed in a tertiary center in adult patients with RA, PsA or axSpA who had been treated with the innovator ETN and who had been switched to two ETN biosimilars for economic reasons thereafter. The first switch from innovator ETN to the first biosimilar ETN occurred between February-May 2017 and the second switch from the first to the second biosimilar ETN occurred between September-December 2017. The end of the observation period was October 2019. Disease activity, function and adverse events (AE) were regularly assessed, and any changes in outcome were recorded during the follow-up period. The scores documented at week 12 week after the second switch were taken as primary outcome.

Results: A total of 100 patients (54 RA, 27 axSpA, 19 PsA, mean age 54.3±15.1, 46% male) who switched twice to those ETN biosimilars over a follow-up period of 21.1±7.4 months were included. The retention rate after the second ETN biosimilar switch was 89% about 6 months after the second switch. While 2 patients were lost to follow-up and 1 patient died (cardiac arrest), 7 patients discontinued due to inefficacy or AE, including one pancreatic cancer.

	Assessment	Baseline (n=100)	SB4 Follow-up 12 weeks (n=100)	SB 4 Follow-up 24 weeks (n=100)	Second switch to GP2015 (n=100)	GP2015 Follow-up 12 weeks (n=97)	GP2015 Follow-up 24 weeks (n=89)
RA	DAS28	3,0 (1,2)	2,9 (1,4)	3,1 (1,2)	2,8 (1,4)	3,4 (2,5)	3,0 (1,4)
	HAQ	1,4 (0,8)	1,6 (0,9)	1,0 (0,9)	1,5 (0,8)	1,5 (0,8)	1,6 (0,9)
PsA	DAS28	3,8 (1,4)	1,9 (1,4)	2,8 (1,5)	3,1 (1,1)	4,5 (2,6)	3,6 (2,6)
	HAQ	1,2 (0,9)	1,0 (0,9)	0,9 (0,9)	1,0 (0,8)	1,0 (0,9)	1,2 (0,8)
axSpA	BASDAI	5,1 (2,7)	4,5 (2,6)	5,1 (3,8)	4,1 (2,2)	4,6 (2,5)	4,3 (2,4)
	ASDAS	3,4 (0,8)	2,5 (0,8)	2,7 (0,8)	3,2 (1,8)	2,7 (1,2)	2,5 (0,9)
	BASFI	4,4 (2,7)	4,3 (2,7)	4,3 (3,2)	4,6 (2,6)	4,5 (2,7)	4,8 (3,0)

*Values are mean ± standard deviation

One patient was withdrawn due to pregnancy. Overall, 14 AEs were reported in 8 patients. Among them, 4 patients switched back to originator etanercept in month 6, 1 patient re-administered GP2015 successfully in month 3 after suffering from mucosal erosions and in 3 patients another mode of action was prescribed. The scores at week 12 of both, disease activity and function, remained unchanged (Table 1).

Conclusion: The retention rate after multiple switches from innovator ETN to two ETN biosimilars was close to 90%. No major changes in disease activity and function were observed in all three indications.Table 1: Patient characteristics

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Disclosure: U. Kiltz, Abbvie, 2, 5, Biocad, 2, 5, Biogen, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Grünenthal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5; **S. Tsiami**, None; **X. Baraliakos**, None; **J. Braun**, None.

Abstract Number: 0574

Is Hydroxychloroquine Use a Proxy for Health Care Access? Predictors of First Dispensing Among Medicaid Beneficiaries with Incident Lupus

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SESSION INFORMATION
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Background/Purpose: Hydroxychloroquine/chloroquine (HCQ/CQ) is considered to be the backbone of systemic lupus erythematosus (SLE) care. Differences in receipt of HCQ/CQ may exacerbate disparities in adverse events, as well as bias observational studies examining the association between HCQ/CQ use and outcomes. We investigated factors associated with first dispensing of HCQ/CQ among individuals with incident SLE. We hypothesized that individuals receiving HCQ/CQ may have better health care access, as measured by outpatient visits and preventive care (e.g., cancer screening and vaccinations), and fewer comorbidities.

Methods: Using Medicaid claims from 2000-2006 (47 states) and 2007-2010 (29 states), we identified individuals age 18-65 years with incident SLE (≥3 SLE ICD-9 codes separated by ≥30 days within 24 months. We required 24 months of continuous enrollment without SLE codes and without HCQ/CQ use prior to the first SLE code (index date). The primary outcome was the first dispensing of HCQ/CQ on or within 24 months of the index date. We used Cox proportional hazards regression models to examine the association (HR, 95% CI) between baseline sociodemographic factors, comorbidities, health care utilization, preventive care and medication use and time to first HCQ/CQ dispensing in the first 24 months following SLE diagnosis.

Results: We identified 9560 Medicaid beneficiaries with incident SLE; 41% received HCQ (N=3949) or CQ (N=14) within 24 months of diagnosis. The mean age was 35.7 (SD 11.7) years for HCQ/CQ users and 39.9 (SD 12.2) years for non-users. Seventy-two percent received any glucocorticoids within 24 months of diagnosis; of these, 51% also received HCQ/CQ. Cox models demonstrated that younger patients (age 18-25) were 2.3 times more likely to receive HCQ/CQ compared with 51-65 year-olds (**Table 1**). All racial/ethnic groups were more likely to receive HCQ/CQ than whites. Alcohol use disorder, opioid use, diabetes, end-stage renal disease and smoking were associated with a lower rate of dispensing. Receiving 1-2 preventive care services was associated with 29% higher rate of receipt; ≥2

Table 1. Baseline factors associated with first hydroxychloroquine or chloroquine* dispensing among Medicaid beneficiaries with incident SLE (n=9560)	
	Hazard ratio† (95% CI)
Male sex (ref=female)	0.88 (0.75-1.02)
Age (ref=age 51-65 years)	
• 18-24 years	**2.33 (2.05-2.64)**
• 25-31 years	**1.99 (1.76-2.24)**
• 32-38 years	**1.74 (1.54-1.95)**
• 39-45 years	**1.31 (1.17-1.48)**
• 46-50 years	**1.15 (1.01-1.32)**
Race/ethnicity (ref=white)	
• Asian	**1.61 (1.34-1.94)**
• American Indian/Alaska Native	**1.49 (1.10-2.02)**
• Hispanic	**1.36 (1.24-1.50)**
• Black	**1.29 (1.20-1.40)**
• Other	1.05 (0.85-1.29)
Region (ref=Northeast)	
• Midwest	0.94 (0.85-1.04)
• West	**0.90 (0.82-0.99)**
• South	**0.76 (0.70-0.83)**
Medication use (ref= no use)	
• Prescription NSAID use	**1.53 (1.43-1.64)**
• Glucocorticoid use	**1.27 (1.18-1.36)**
• Opioid use	**0.75 (0.59-0.96)**
• Immunosuppressive use	**0.48 (0.40-0.57)**
Comorbidities	
• Renal disease (excluding ESRD)	1.07 (0.96-1.17)
• Cardiovascular disease	1.06 (0.98-1.15)
• Smoking	**0.90 (0.83-0.98)**
• Diabetes mellitus	**0.84 (0.77-0.90)**
• Chronic pain	**0.83 (0.76-0.91)**
• Pregnancy	**0.80 (0.74-0.87)**
• Alcohol Use Disorder	**0.74 (0.65-0.85)**
• ESRD	**0.72 (0.61-0.84)**
*Preventive care** (ref=0)*	
• 1-2	**1.29 (1.16-1.43)**
• >2	**1.46 (1.30-1.64)**
Heath Care Utilization (ref=none)	
• 1-5 Outpatient visits	1.08 (0.99-1.18)
• >5 Outpatient visits	**1.10 (1.00-1.21)**

with a 46% higher rate. Individuals with more outpatient visits were more likely to receive HCQ/CQ while those with more hospitalizations were less likely.

Conclusion: HCQ/CQ use is central to SLE treatment however only 41% of Medicaid beneficiaries with SLE received HCQ/CQ within 2 years of diagnosis. Preventive care and outpatient visits, markers of access to health care, were associated with higher rates of initial HCQ/CQ dispensing, whereas frequent hospitalizations, high-risk lifestyles and complex comorbidities were associated with lower rates. All non-white races had higher rates of first dispensing

compared to whites suggesting that in this Medicaid population, initial HCQ/CQ dispensing differences likely do not explain racial/ethnic disparities in adverse outcomes. Overall these findings suggest that we must cautiously interpret potential physiologic effects of HCQ/CQ on outcomes in observational studies comparing users to non-users as they may be biased by differences in access to care and measured and unmeasured confounders.

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Abstract Number: 0575

The Impact of an Integrated Care Management Program on Acute Care Utilization and Outpatient Appointment Attendance Among High-Risk Patients with Lupus

Jessica Williams[1], Weixing Huang[2], Jamie Collins[3], Kreager Taber1, Katherine McLaughlin[1], Rebecca Cunningham[1], Christine Vogeli[4], Lisa Wichmann[1] and Candace Feldman[3], [1]Brigham and Women's Hospital, Boston, MA, [2]Division of Rheumatology, Inflammation, and Immunity; Brigham and Women's Hospital and Harvard Medical School, Boston, [3]Brigham and Women's Hospital, Boston, [4]Massachusetts General Hospital, Boston, MA

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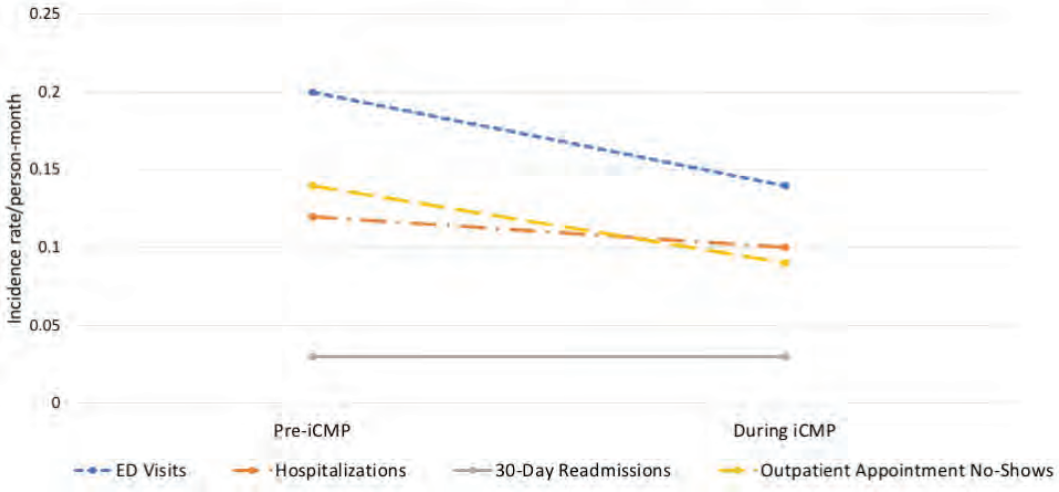
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) are often members of disadvantaged groups and some struggle with high acute care utilization and missed outpatient appointments. An integrated care management program (iCMP) was established at our multihospital system whereby nurses lead care coordination efforts for patients considered high risk for frequent emergency department (ED) visits and hospitalizations. We aimed to determine whether this program was effective at decreasing acute medical care use and outpatient no-show rates among patients with SLE.

Figure. Rates of Medical Care Utilization and Outpatient Appointment No-Shows Among High-Risk Patients with SLE Before and During iCMP



Methods: The top two percent of medically and psychosocially complex patients within our multihospital system are enrolled in iCMP – a longitudinal primary care-embedded care management program. We used a validated electronic health record (EHR) machine learning algorithm (PPV 90%) to identify adults ≥18 with SLE enrolled in iCMP from January 2012-February 2019 and verified the diagnosis with EHR review. We used EHR data linked to insurance claims to compare the incidence rates of ED visits, hospitalizations, 30-day readmissions, and outpatient appointment no-shows during iCMP enrollment to the 12-months prior. We used Poisson regression to examine the incidence rate ratios (IRR) during versus pre-iCMP enrollment for each of these utilization measures, adjusting for age, sex, race/ethnicity, number of comorbidities and calendar year of entry, accounting for within-patient clustering.

Results: We identified 67 iCMP enrollees with SLE and linked EHR-claims data. Fifty-five met 1997 ACR criteria for SLE, 9 met 2012 SLICC criteria, and 3 did not meet criteria but were diagnosed and treated by a rheumatologist. The mean duration of iCMP enrollment was 46 (SD 29) months. The mean age was 60 (SD 17) years and 93% were female. Enrollees were 55% white, 25% black, 16% other race and 3% Asian, and 21% were Hispanic. Twenty patients had commercial insurance, 59 had Medicare, 4 had Medicaid and 16 had ≥1 one insurance. The rate of ED visits averaged 0.14/person-month during iCMP enrollment compared to 0.20/person-month pre-iCMP (IRR 0.66, 95% CI 0.48-0.92, p=0.01), the rate of hospitalizations averaged 0.10/person-month during iCMP compared to 0.12/person-month pre (IRR 0.89, 95% CI 0.64-1.24, p=0.5), and the rate of outpatient appointment no-shows was 0.09/person-month during iCMP compared to 0.14/person-month pre (IRR 0.74, 95% CI 0.57-0.97, p=0.03); see **Figure**. After adjusting for demographics, enrollment year, comorbidities, and repeated measures, there was a 37% reduction in the rate of ED visits during iCMP compared to the year prior (p=0.003) and trends towards reduced hospitalizations (IRR 0.88, 95% CI 0.65-1.19, p=0.39) and fewer missed appointments (IRR 0.80, 95% CI 0.62-1.04, p=0.097).

Conclusion: In a single arm, pre-post observational study, we found that a nurse-led, primary care-based integrated care management program appeared effective at decreasing the rate of ED visits for high-risk SLE patients and likely also reduced rates of missed appointments. Further studies are needed to determine the root causes of high utilization patterns for vulnerable patients and to develop strategies to comprehensively address these issues.

Disclosure: J. Williams, None; **W. Huang**, None; **J. Collins**, None; **K. Taber**, None; **K. McLaughlin**, None; **R. Cunningham**, None; **C. Vogeli**, None; **L. Wichmann**, None; **C. Feldman**, Merck, 5, Voyager Therapeutics, 5, Biogen, 8.

Abstract Number: 0576

Medical Savings of Timely Rheumatoid Arthritis Diagnoses

Kathryn Johnson[1], Christine Sawicki[1], Cristina Sotelo[2], Tanvi Kalevar[3], Sylvie Lardeux[4], Fabio Casadio[3], David Baghdadi[5], **Michele Hamburger**[6], Elisea Avalos-Reyes[7] and Kjel Johnson[1], [1]CVS Health, Lincoln, RI, [2]CVS Health, Austin, TX, [3]CVS Health, New York, NY, [4]CVS Health, Wellesley, MA, [5]CVS Health, Woonsocket, RI, [6]Frances Hamburger Institute, Hauppauge, NY, [7]CVS Health, Irving, TX

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Background/Purpose: Previous studies suggest that early rheumatoid arthritis (RA) recognition and treatment provides greater clinical benefits than treatment started later in the disease course. However, the impact of early treatment initiation on the total cost of care in RA patients has not been well studied. Additional data on the clinical and economic impact of RA in the US are required to provide better information for healthcare and health policy deci-

	Diagnosed in an ED/IP setting (N = 4,249)	Diagnosed in other setting (N = 38,101)
Age, years (mean, SD)	65.9 (16.9) ***	58.5 (16.6) ***
Gender, n(%)		
Female	2,928 (68.9%)	26,442 (69.4%)
Male	1,321 (31.1%)	11,659 (30.6%)
Newly diagnosed RA patients, n(%)		
Commercial	1,298 (30.6%) ***	22,971 (60.3%) ***
Medicare	2,951 (69.5%) ***	15,130 (39.7%) ***

**p< 0.01, *** p< 0.001
A t-test was used for continuous variables and χ^2 test was used for dichotomous variables.

Table 1. Demographic Characteristics of Newly Diagnosed RA Patients in 2019.

sion-making. The purpose of this study was to determine the medical cost savings of a timely RA diagnosis 6 months pre-and post-diagnosis.

Methods: This retrospective cohort study evaluates newly diagnosed RA patients insured by a large commercial and Medicare health plan in the United States between January 1, 2019 and December 31, 2019. We defined a "late" RA diagnosis as a patient diagnosed for the first time as part of an emergency department (ED)/inpatient (IP) setting as these patients likely had symptoms of RA prior to this visit but were not properly diagnosed. We defined a "timely" RA diagnosis as a patient diagnosed for the first time in an in-office setting. We defined newly diagnosed as a patient who had medical insurance but no paid claim for RA for at least six months before the initial claim with an RA diagnosis. We defined diagnosis in the ED/IP setting as patients with their first RA claim in an ED/IP setting. A Targeted Likelihood Estimation Model (TMLE) was used to assess relationships between patient characteristics and the total cost of care per member (PM) 6 months before and 6 months after diagnosis.

Results: The study included 42,350 patients with a new RA diagnosis in 2019, the majority were female (69.3%) and the mean age was 59.4 years (SD = 16.8). Ten percent of the new RA cases were diagnosed in an ED/IP setting (late diagnosis). The total cost of care 6 months pre-diagnosis was driven by an increase in ED costs (a $418 PM over 6 months increase for commercial patients (p< 0.001) and a $547 PM over 6 months increase for Medicare patients (p<

	Commercial	Medicare
Total Spend (6 months pre-diagnosis)	**$2,676**	**$2,512**
Inpatient	$2,712	$1,341
Emergency Room	$418	$547
Pharmacy	$271	-$34
Office visits	$34	$151
Lab	-$24	$47
Other	-$734	$460
Total Spend (12 months 6 pre and 6 post-diagnosis)	**$4,055**	**$1,670**
Inpatient	$2,220	$1,074
Emergency Room	$1,261	$353
Pharmacy	$13	-$52
Office visits	$102	$33
Lab	-$41	-$43
Other	$443	$306

Total spend calculated as total cost of newly diagnosed in an ED/IP setting – newly diagnosed in other settings.
Targeted Likelihood Estimation Model (TMLE) was used to assess total spend and adjusted for risk score and demographic characteristics.

Table 2. Total Spend Differences Between Patients Diagnosed in an ED/IP Setting and Patients Diagnosed in Other Settings by Type of Insurance

0.001)) and IP costs (a $2,712 PM over 6 months increase for commercial patients (p< 0.001) and a $1,341 PM over 6 months increase for Medicare patients (p< 0.001)). After adjusting for risk score and demographic characteristics, the adjusted total cost of care PMPY for new RA patients diagnosed in an ED/IP setting was higher than new RA patients diagnosed in other settings by a $4,055 PM over 12 months increase (p< 0.01) in commercial patients and a $1,670 PM over 12 months increase (p< 0.01) in Medicare patients. Most of the increase in cost occurred during the 6 month period pre-diagnosis, there was no significant difference in total cost of care in the 6 month post-diagnosis period.

Conclusion: In this study, a late RA diagnosis was associated with a significantly higher total cost of care, compared to a timely RA diagnosis; a trend that was observed for both commercial and Medicare patients. Newly diagnosed RA patients in an ED/IP setting spent significantly more on IP and ED costs prior to their RA diagnosis. Future studies are needed to identify and predict patients at risk of developing RA to reduce unnecessary healthcare costs of a delayed diagnosis.

Disclosure: K. Johnson, CVS Health, 1, 3; **C. Sawicki**, CVS Health, 1, 3; **C. Sotelo**, CVS Health, 1, 3; **T. Kalevar**, CVS Health, 3; **S. Lardeux**, CVS Health, 3; **F. Casadio**, CVS Health, 1, 3; **D. Baghdadi**, CVS Health, 3; **M. Hamburger**, None; **E. Avalos-Reyes**, CVS Health, 3; **K. Johnson**, CVS Health, 1, 3.

Abstract Number: 0577

Qualitative Review of Unsuccessful Pilot Study of Super-Utilizer Systemic Lupus Erythematosus (SLE) Patients Enrollment into Team Based Program to Improve Patient Outcomes

Sarah Min[1], Devy Setyono[2], Sunghye Kim[3], Feben Girma[1], Melanie Martin[1] and Rachel Wolfe[1], [1]Wake Forest Baptist Medical Center, Winston-Salem, NC, [2]Emkey Arthritis and Osteoporosis Clinic, Wyomissing, PA, [3]W.G. Hefner VA Medical Center, Salisbury, NC

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is a chronic multi-system autoimmune disease, affecting mostly women of child-bearing age and more racial minorities, with a wide spectrum of outcomes: from long-standing remission to frequent flares and mortality. Although survival rate of SLE has improved, healthcare utilization among SLE patients is still high, including hospitalizations. Our internal data indicate that 30-day readmission rate among SLE patients is 28%. CarePlus is a team-based primary care for healthcare super-utilizers at Wake Forest Baptist Medical Center (WFBMC). The objective of the initial pilot study was to test if team-based care through CarePlus with comprehensive services (i.e. mental health care, medication education, social assistance and patient hotline) would help reduce healthcare utilization of those SLE patients with the highest utilization (>3 admissions/ED visits in 18 months). Their primary rheumatologists contacted each patient to determine interest in enrollment in the CarePlus program. Only those interested at that time were included in the pilot study. The initial study was prematurely discontinued due to difficulty of contacting patients, scheduling, and no showing to appointments. The aim of this study was to characterize patient factors in declining CarePlus and barriers to attending the initial CarePlus appointment.

Methods: In the initial pilot study, a cohort of patients with SLE were identified as healthcare super-utilizers and 12 agreed to be scheduled with CarePlus. For those 12 patients, demographics were obtained via chart review.

Study-eligible SLE patients were interviewed over the phone about reasons for declining CarePlus and barriers to attending the initial appointment.

Results: Median age was 44 years (range 27-64) with 92% female. Thirty-three percent were Caucasian, 50% African-American, and 17% Hispanic. Two-thirds had previously no-showed to rheumatology appointments. Three patients were successfully enrolled in CarePlus (only 1 during the 5 month study enrollment period). All 3 enrolled patients live in the county in which the clinic is located or adjacent county; the 8 patients who did not enroll lived further out of these counties. Of the 9 patients who did not enroll, eight patients could be contacted and interviewed. Factors in declining CarePlus and barriers to attending appointments included: personal health issues (3), did not want to switch primary care physician (2), transportation (2), and forgetfulness (2). Subsequent to the interview, two patients still wanted to enroll in CarePlus.

Conclusion: The qualitative review of the factors that led patients to fail to establish in the CarePlus program provides new insights into how to better structure a patient-centered home for our SLE healthcare super-utilizers. Specific factors such as the established relationship with their current primary care doctors and proximity to the clinic were limitations to our study's enrollment. The recent increased implementation of telemedicine may be a unique and helpful tool in developing a more effective team-based approach for the care of SLE super-utilizers in the future especially to address the barriers noted in this particular study.

Disclosure: S. Min, None; **D. Setyono**, None; **S. Kim**, None; **F. Girma**, None; **M. Martin**, None; **R. Wolfe**, None.

Abstract Number: 0578

Going Digital Due to COVID 19 Crisis: A Rapid Reorganisation of Medication Clinics

Rian Penford[1], Angela Reith[1], Elaine Wren[1] and **Kirsten Mackay**[1], [1]Torbay and South Devon NHS Foundation Trust, Torquay, United Kingdom

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Until the COVID 19 crisis we initiated DMARD(s) and Biologic therapies using shared medical clinics. More than 30 patients could seen per week, with a maximum of 6 per group, for each different medication to be started, (see fig 1). This allowed us to manage the increase in workload, and start patients efficiently on their medications, both safely, and within 10 working days. This took 3-4 hours per week of Rheumatology nurse time.

However, with the onset of the pandemic, we had to stop these clinics immediately, but, we did not have capacity to start everyone on their medications in a timely manner by telephone. Telephoning each individual took > 9 hours per week.

Methods: We scripted and organised the filming of 10 short healthcare videos very rapidly (www.torbayandsouthdevon.nhs.uk), to give patients all the information they required to start a range of DMARDs and biologics.

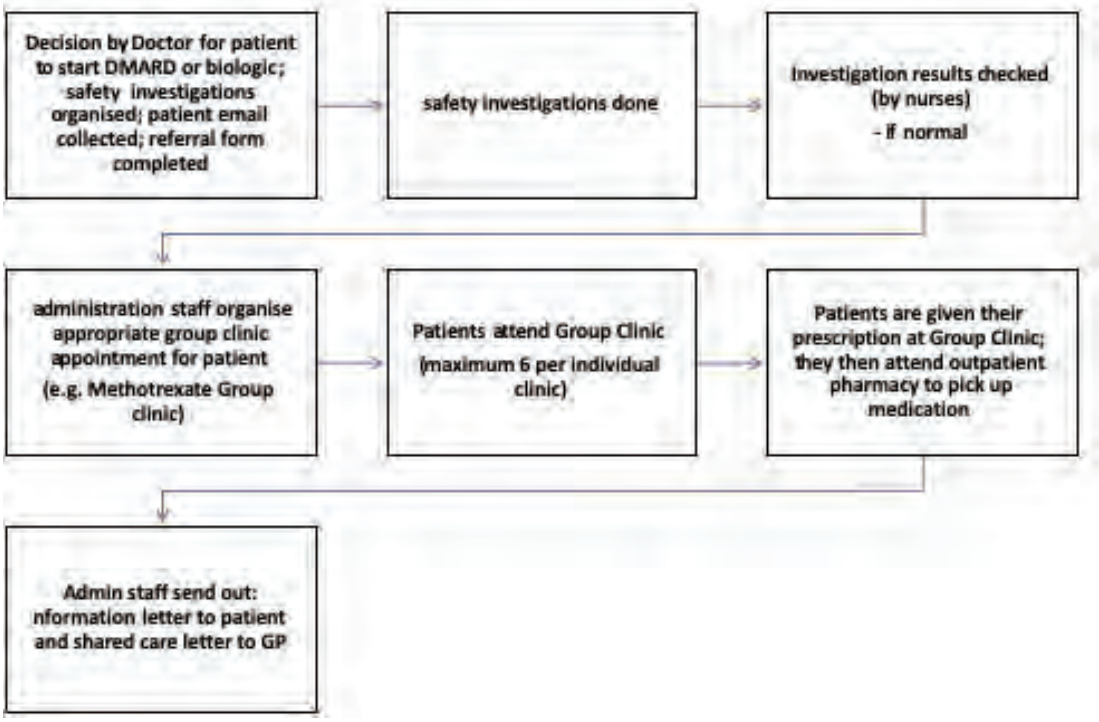

Figure 1. Our original Shared Medical Appointment Approach to start DMARDs and Biologics

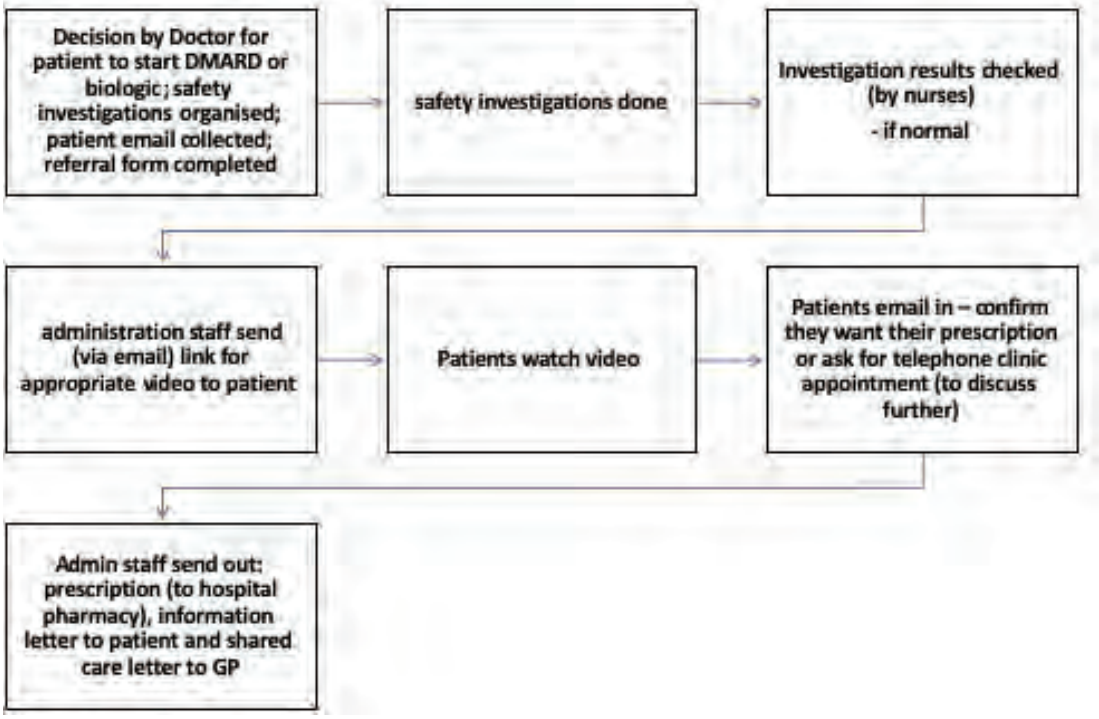

Figure 2. Our digital solution for medication clinics

We developed a new algorithm (Fig 2) and now patients are asked to view the relevant video, contact our department to confirm they understand the safety monitoring, risks, potential side effects, dose increases etc. As soon as they confirm by email they are happy to start treatment, a prescription is generated and emailed to the hospital outpatient pharmacy, where it is dispensed and delivered to the patient's home (usually within 3 working days). We also send

them a follow up reminder letter about blood test monitoring etc (with copy to their GP) and a 'shared care agreement' to their GP. Alternatively, if they are uncertain about anything, we organise for them to have a telephone clinic appointment with a specialist nurse.

Results: Of those requiring DMARDs, 55% reviewed the video, completed the checklist and confirmed by email they were happy to start treatment, within 24-hours. A further 26% completed the process within 3 days.

Almost half the patients (48%) were starting DMARDs for the first time, of those 8% requested a telephone consultation to discuss treatment further with the Rheumatology nurses. None of the patients already taking a DMARD and due to start a second medication required a telephone clinic appointment.

As this is a new service, we asked for feedback, receiving replies from 26%, all scoring between 9/10 and 10/10.

Conclusion: This has altered the way we work and we will continue with this approach over the long term. It has reduced the necessity for face-to-face appointments, enabled us to start patients on their rheumatology medications more quickly and efficiently than previously, allowed the nursing staff time to spend more time working in our telephone clinic and we have had excellent feedback. Although, we are aware, this is at a cost of no peer-to-peer interaction, which has been of value in the past.

Disclosure: R. Penford, None; **A. Reith**, None; **E. Wren**, None; **K. Mackay**, None.

Abstract Number: 0579

Risk Factors of Nonadherence in New Rheumatoid Arthritis Patients

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SESSION INFORMATION
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Background/Purpose: Biologic disease-modifying antirheumatic drug (bDMARD) therapies are commonly prescribed for rheumatoid arthritis (RA) treatment. However, their high out-of-pocket (OOP) cost may limit patient access to therapy. While insurance typically covers bDMARDS, they often require cost-sharing. Prior studies have shown that cost-sharing can have negative consequences, such as nonadherence and increased use of medical services. However, no study has examined adherence changes by drug class across OOP cost ranges in the commercial population. The purpose of this study is to assess the impact of patient OOP cost range, drug class and referral source on adherence in patients with RA.

Methods: This is a retrospective cohort study of RA patients insured by a large commercial health plan in the United States who reported a first RA drug fill for (medical or pharmacy benefit) from March 1, 2018, to February 28, 2019 (index fill), from a single specialty pharmacy. Demographic characteristics, OOP cost, drug class and referral source were obtained from the specialty pharmacy's dispense data. We defined a direct referral as any incoming referral from a prescriber, another specialty pharmacy, a payor or a patient. We defined a hub referral as a referral from the manufacturer. All other referrals were included in the "other" category. Medication adherence was calculated using the medication possession ratio (MPR). MPR was defined as the sum of the days' supply for all fills of RA drugs

Variables	
Age, years (mean, SD)	50.8 (12.0)
Race, n(%)	
White	13,842 (85.4%)
Black	1,662 (10.3%)
Asian	696 (4.3%)
Gender, n(%)	
Female	12,096(74.7%)
Male	4,104 (25.3%)
Annual Income, (mean, SD)	$61,705 ($23,949)
Co-pay per day, (mean, SD)	$0.89 ($5.79)
Used a drug coupon, n(%)	
Yes	13,193 (81.4%)
No	3,007 (18.6%)
Used a 90-day supply, n(%)	
Yes	1,724 (10.6%)
No	14,476 (89.4%)
Drug Class	
TNF-alpha inhibitors	12,375 (76.4%)
Janus kinase inhibitors	1,844 (11.4%)
T-cell blockers	1,118 (6.9%)
IL-6 inhibitors	863 (5.3%)
Referral Source, n(%)	
Direct	12,761 (78.8%)
Other	3,266 (20.2%)
Hub	173 (1.1%)

§Due to rounding percent's may not add up to 100%
TNF-alpha inhibitors include: etanercept, certolizumab, adalimumab, infliximab-dyyb, infliximab, infliximab-abda, and golimumab
IL-6 inhibitors include: tocilizumab and sarilumab
T-cell blockers include abatacept
Janus kinase inhibitors include: tofacitinib, baricitinib and upadacitinib

Table 1. Demographic Characteristics (N=16,200)

during a year after the index fill, divided by 365. A generalized linear model (GLM) was used to estimate predictors of adherence.

Results: The study included 16,200 patients, the majority were female (74.7%) and the mean age was 50.8 years (SD = 12.0). The average copay per day supply was $0.89 (SD = $5.79). Most (81.4%) patients used a coupon at least once to pay for their medication. Patients in the lowest copay category, compared to the other copay categories, were more likely to use a coupon (83.2%) to pay for their medication ($p < 0.001$). After adjusting for the variables in the model, MPR decreased as OOP cost increased. Above an OOP cost of $181 per month, MPR decreased significantly ($p = 0.0004$). MPR was significantly different by drug class ($p < 0.01$), IL6 = 59.9%, TCB = 64.2%, TNF = 66.8% and JAK = 66.8%. Patients who received a direct referral had a significantly higher MPR (66.5%) compared to patients who received a referral from an "other" source (61.1%) ($p < 0.0001$).

Conclusion: This study suggests that as member OOP costs increase adherence decreases and adherence differs by drug class and referral source. Source of referral and an appropriate formulary and patient copayment structure must be considered when assessing adherence.

Characteristics	MPR	p-value
Therapy		
IL-6 inhibitors	59.9%	Reference
T-cell blockers	64.2%	**0.0029**
TNF-alpha inhibitors	66.8%	**<0.0001**
Janus kinase inhibitors	66.8%	**<0.0001**
Co-pay category (OOP cost per month)		
$0-$60	67.3%	Reference
$61 -$180	64.5%	0.0593
> $181	61.4%	**0.0004**
Referral Source, n(%)		
Other	61.1%	Reference
Hub	65.7%	0.0632
Direct	66.5%	**<0.0001**

Adjusted for therapy, age, gender, patient zip code characteristics (race, annual income), utilization of 90-day supply, copay, coupon use, index date, insurance and referral source
TNF-alpha inhibitors include: etanercept, certolizumab, adalimumab, infliximab-dyyb, infliximab, infliximab-abda, and golimumab
IL-6 inhibitors include: tocilizumab and sarilumab
T-cell blockers include abatacept
Janus kinase inhibitors include: tofacitinib, baricitinib and upadacitinib

Table 2. Adjusted Generalized Linear Model

Disclosure: G. Cozzi, CVS Health, 1, 3; **P. Kyrychenko**, CVS Health, 1, 3; **M. Hamburger**, None; **E. Avalos-Reyes**, CVS Health, 3.

Abstract Number: 0580

Risk of Severe Acute Localized Reactions for Different Intra-Articular Hyaluronic Acid Knee Injections in a Real World Setting

Kevin Ong[1], Jack Farr[2], Louis McIntyre[3], Andrew Gudeman[2], Iain Murray[4], Charles Hummer[5], Wilson Ngai[6], Heather Good[7], Edmund Lau[8] and **Roy Altman**[9], [1]Exponent, Philadelphia, [2]Indiana University Department of Orthopaedic Surgery, Indianapolis, [3]US Orthopedics, Tarrytown, [4]Department of Orthopaedics, The University of Edinburgh, Edinburgh, United Kingdom, [5]Premier Orthopaedics and Sports Medicine, Glen Mills, [6]Sanofi US, Bridgewater, [7]Sanofi US, Bridgewater, FL, [8]Exponent, Menlo Park, [9]David Geffen School of Medicine, University of California, Agua Dulce, CA

SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Case reports of severe acute localized reactions (SALR) following intra-articular (IA) hyaluronic acid (HA) injections for knee osteoarthritis (OA) have been described. These have been speculated to be related to the crosslink of hylan or an allergic reaction to avian-derived hyaluronan, but reactions have also been reported for non-crosslinked, non-animal, and/or naturally derived HA. We compared surrogate SALR measures between patients using hylan G-F 20 and specific non-hylan G-F 20 HA products.

Methods: Knee OA patients were identified from the Optum Clinformatics dataset (Jan 2006-June 2016), stratified into hylan G-F 20 and non-hylan G-F 20 HA users, matched by single or multiple injection products. Occurrences of surrogate SALR measures including inflammation/infection, intra-articular corticosteroid (CS) injections, arthrocentesis/aspiration, arthrotomy/incision and drainage, arthroscopy, and office visits were evaluated (with ICD/CPT codes)

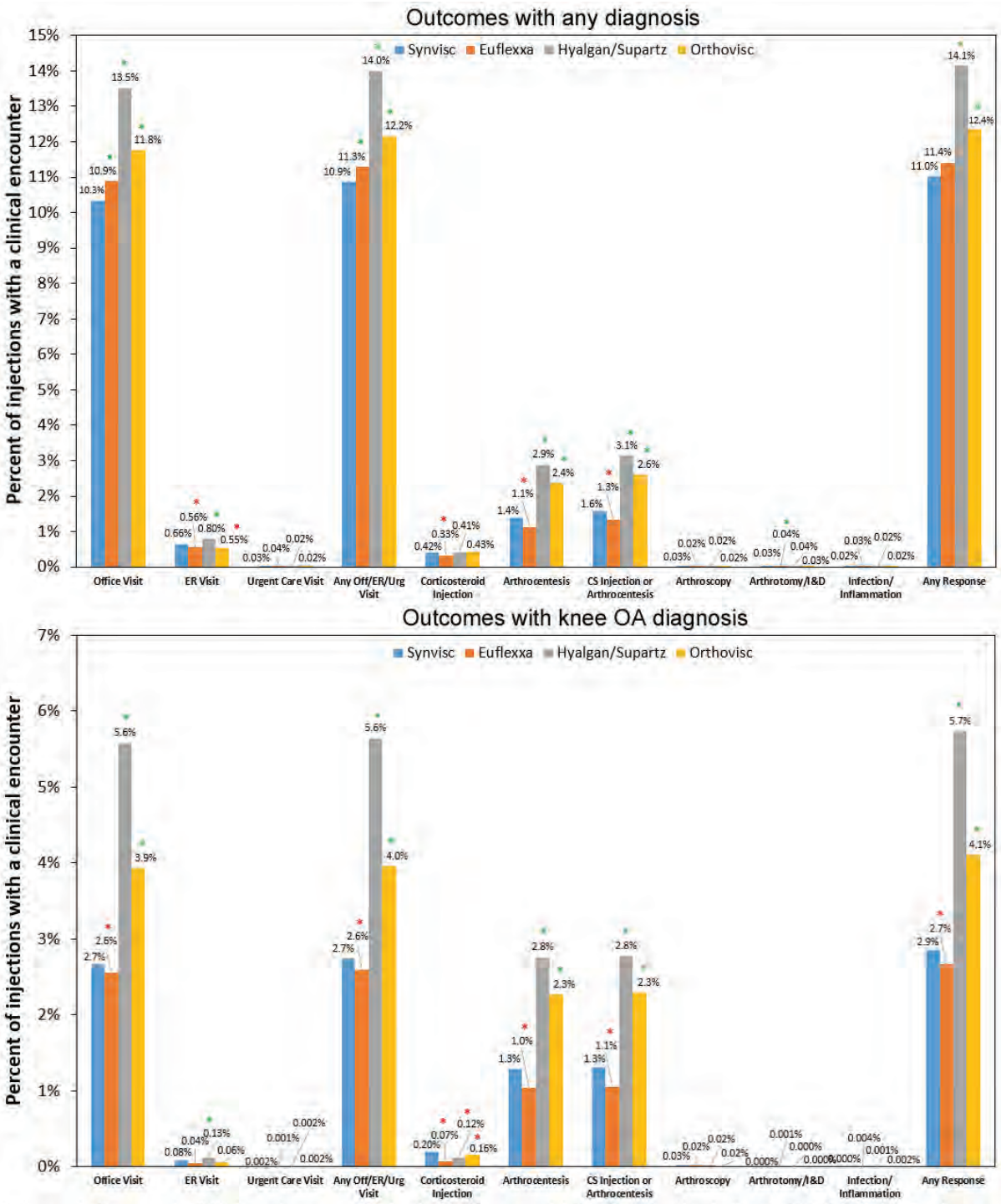

Figure 1. Surrogate SALR outcomes within three days post-injection for the hylan G-F 20 (3-injection), Euflexxa, Hyalgan/Supartz, and Orthovisc patient groups (top: outcomes with any diagnosis on the claims; bottom: outcomes with knee OA diagnosis on the claims). Statistically significant differences are indicated with an asterisk (* p<0.05; green and red for lower and greater adjusted risks in the hylan G-F 20 (3-injection) group, respectively).

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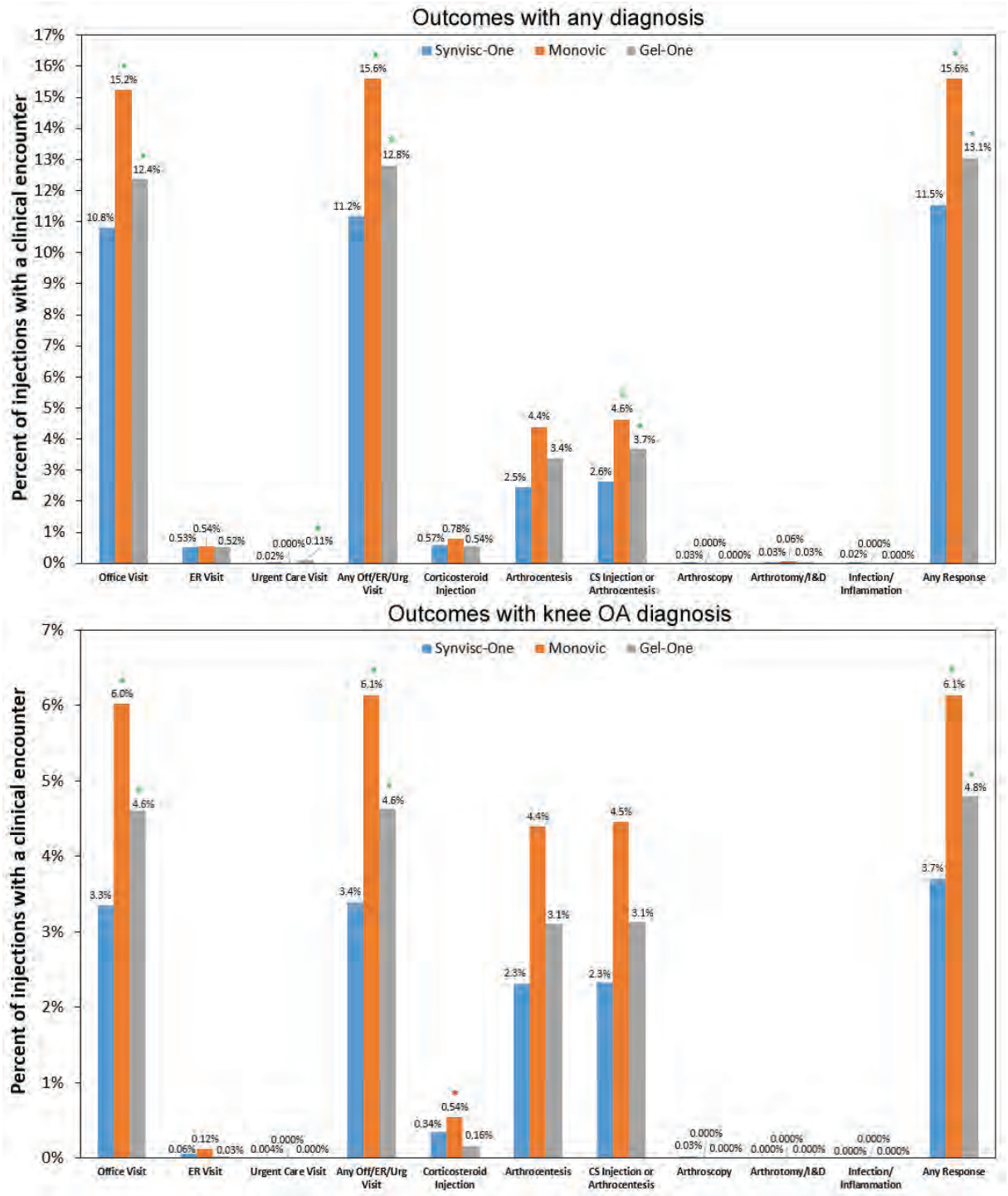

Figure 2. Surrogate SALR outcomes within three days post-injection for the hylan G-F 20 (1-injection), Monovisc, and Gel-One patient groups (top: outcomes with any diagnosis on the claims; bottom: outcomes with knee OA diagnosis on the claims). Statistically significant differences are indicated with an asterisk (* p<0.05; green and red for lower and greater adjusted risks in the hylan G-F 20 (1-injection) group, respectively).

Figure 2. Surrogate SALR outcomes within three days post-injection for hylan G-F 20 (1-injection), Monovisc, and Gel-One patient groups (top: outcomes with any diagnosis on the claims; bottom: outcomes with knee OA diagnosis on the claims). Statistically significant differences are indicated with an asterisk (* p<0.05; green and red for lower and greater adjusted risks in the hylan G-F 20 (1-injection) group, respectively).

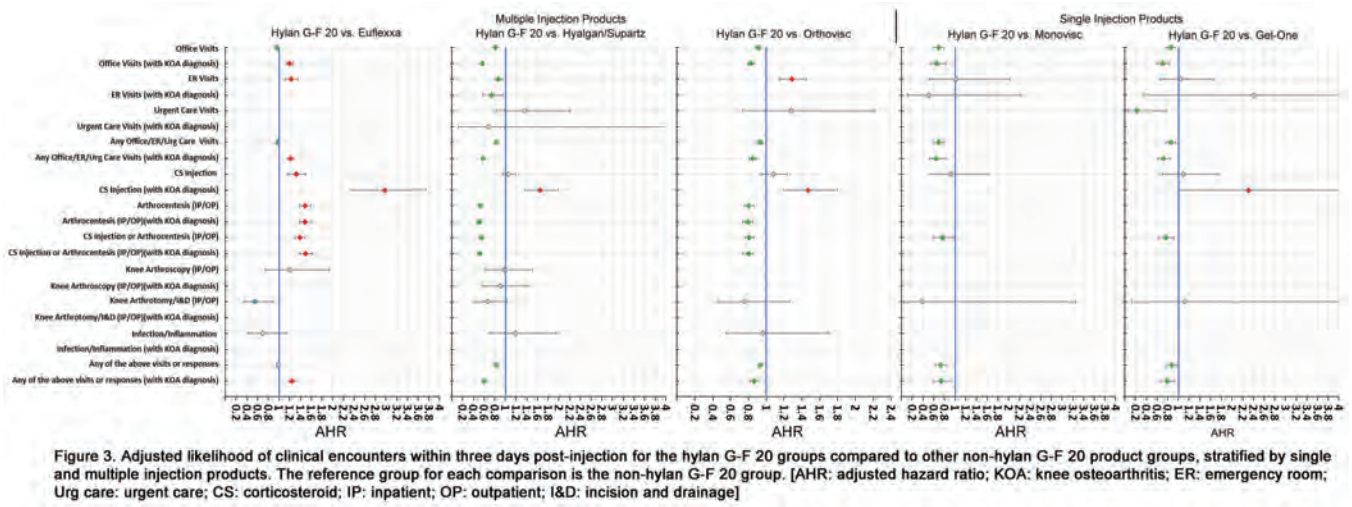

Figure 3. Adjusted likelihood of clinical encounters within three days post-injection for the hylan G-F 20 groups compared to other non-hylan G-F 20 product groups, stratified by single and multiple injection products. The reference group for each comparison is the non-hylan G-F 20 group. [AHR: adjusted hazard ratio; KOA: knee osteoarthritis; ER: emergency room; Urg care: urgent care; CS: corticosteroid; IP: inpatient; OP: outpatient; I&D: incision and drainage]

within three days of HA use, adjusting for demographics and clinical factors. These were stratified by single/multiple injection products and evaluated for claims that had a corresponding knee OA diagnosis (knee OA related), as well as those that did not (any diagnosis).

Results: A total of 694,404 HA injections were included in the study. Inflammation/infection rate (with any diagnosis) was rare within three days of HA use (hylan G-F 20 (3-injection): 0.02%; Euflexxa: 0.03%; Hyalgan/Supartz: 0.02%; Orthovisc: 0.02%; hylan G-F 20 (1-injection): 0.02%; Monovisc: none; Gel-One: none) (Figs. 1 and 2); no statistical differences between hylan G-F 20 and non-hylan G-F 20 groups were observed (Table 1). The risk of arthrocentesis was greater for hylan G-F 20 (3-injection; 1.4%) than Euflexxa patients (1.1%) (adjusted hazard ratio (AHR) 1.48; $p< 0.001$), but lower than Hyalgan/Supartz (2.9%) (AHR 0.53; $p< 0.001$) and Orthovisc (2.4%) (AHR 0.80; $p< 0.001$) patients. When considering the collective occurrence of any of the surrogate SALR outcomes, the risk was found to be similar between hylan G-F 20 (3-injection) and Euflexxa cohorts ($p=0.062$), except when limited to those with corresponding knee OA diagnoses (AHR 1.24 for hylan G-F 20; $p< 0.001$). The overall risks were lower for hylan G-F 20 (3-injection) than Hyalgan/Supartz ($p< 0.001$) or Orthovisc ($p< 0.001$) patients and lower for hylan G-F 20 (1-injection) than Monovisc ($p< =0.007$) or Gel-One patients ($p< =0.012$).

Conclusion: The present study examined potential SALR risk in a real-world setting of almost 700,000 HA injections. Diagnoses of inflammation or infection diagnoses were extremely rare (0 to 0.03%) within three days of HA injections. While our arthrocentesis results are consistent with a randomized controlled trial (Kirchner 2006), which reported a greater rate of local reactions in terms of effusions, in hylan G-F 20 (3-injection) than Euflexxa patients, the collective risk of any of the surrogate SALR outcomes was not found to be significantly different between hylan G-F 20 and non-hylan G-F 20 products (single or multiple injection products).

Disclosure: K. Ong, Medtronic, 9, Sanofi, 9, Ferring Pharmaceuticals, 9, Pacira Pharmaceuticals, 9, Relievant Medsystems, 9, International Society for the Advancement of Spine Surgery, 9, SI-Technology, LLC, 9, Zimmer Biomet, 9, Ethicon, 9, Karl Storz Endoscopy-America, 9, Rex Medical, 9; **J. Farr**, Organogenesis, 2, 5, 7, 8, Zimmer Biomet, 2, Samumed, 2, Novartis, 2, Fidia Pharma, 2; **L. McIntyre**, AAOS, 6, Active Implants, 5, Advocacy for Improvement in Mobility, 6, Arthroscopy Association of North America, 6, Delegate Medical Society of the State of New York, 6, Embody, 5, 7, Flexion, 5, Mininvasive, 5, Orthopedic Practice Management, Inc, 6, Orthopedics Today, 6, Sanofi-Aventis, 8, Smith & Nephew, 5, 8, Westchester County Medical Society, 6; **A. Gudeman**, None; **I. Murray**,

Bone and Joint Research, 6, British Orthopaedic Research Society, 6, Journal of Bone and Joint Surgery - British, 6; **C. Hummer**, Sanofi, Flexion Therapeutics, 5, AAOS Board of Councilors, 6; **W. Ngai**, sanofi, 1, 3; **H. Good**, Sanofi, 1, 3; **E. Lau**, Medtronic, 9, Stryker Orthopaedics, 9, Sanofi, 9, Ferring Pharmaceuticals, 9, Paradigm Spine, 9, Boston Scientific, 9, Pacira Pharmaceuticals, 9, Alcon, 9, Relievant Medsystems, 9, American Association of Orthopaedic Surgeons, 9; **R. Altman**, GlaxoSmithKline, 5, Norvartis, 5, Pfizer, 5, Sanofi-Aventis, 9.

Abstract Number: 0581

A Proposed Economic Framework to Model the Consequences of Psoriatic Arthritis Disease Domains

Jacquelyn Chou[1], Ervant Maksabedian[2], David Collier[3] and **Howard Thom**[4], [1]PRECISION heor, Los Angeles, CA, [2]Amgen Inc., LOS ANGELES, CA, [3]Amgen, Thousand Oaks, CA, [4]University of Bristol, Bristol, England, United Kingdom

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Treatment	Target	Peripheral Arthritis	Skin disease	Nail disease	Psoriatic Spondylitis	Dactylitis	Enthesitis
secukinumab	Cytokines: IL-17A		✓	✓	✓	✓	✓
adalimumab	TNF	✓	✓	✓	✓	✓	✓
etanercept	TNF	✓	✓	✓	✓	✓	✓
apremilast	small-molecule inhibitor that modulates inflammatory cytokine production via inhibition of phosphodiesterase-4 (PDE-4 inhibitor)	✓	✓	✓		✓	✓
certolizumab	TNF	✓	✓	✓	✓	✓	✓
golimumab	TNF	✓	✓	✓	✓	✓	✓
infliximab	TNF	✓	✓	✓	✓	✓	✓
ustekinumab	Cytokines: IL-12 and IL-23	✓	✓	✓	✓	✓	✓

Table 1. Identified outcomes in PsA disease and the GRAPPA treatment guidelines specifying which disease domains are treated using specific treatments.

Background/Purpose: Psoriatic arthritis (PsA) manifests heterogeneous signs and symptoms (e.g., dactylitis, enthesitis, axial involvement, skin- and nail disease), which may respond to treatments differently. While a wide variety of treatments are available for psoriatic arthritis (PsA), variability in treatment response across different patient types is not well-documented. Understanding patient heterogeneity and its consequences on outcomes is critical to making appropriate treatment decisions. Our objective is to characterize the heterogeneity of PsA and develop a conceptual framework to explore the therapeutic and financial impacts of specific treatments on these five PsA manifestations.

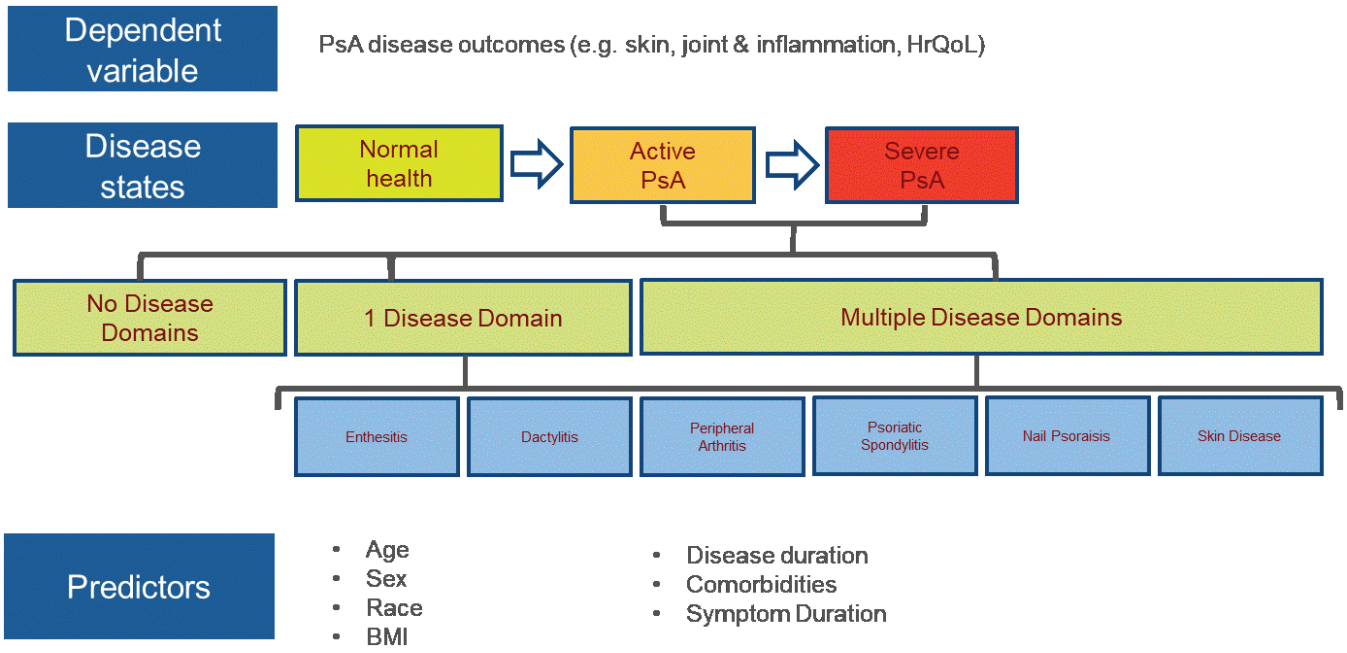

Figure 1. PsA Outcome Risk Model Components

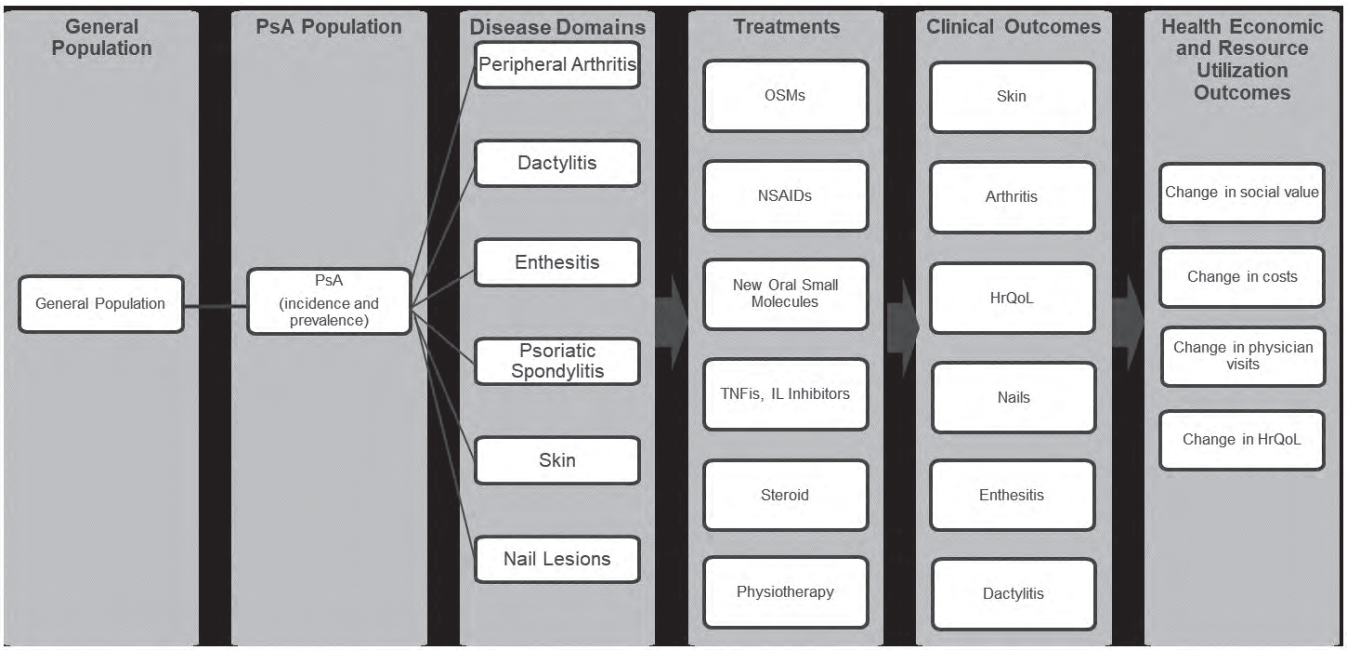

Figure 2. Treatments and clinical outcomes can be grouped by type to simplify the conceptualization of PsA disease manifestation and treatment.

Methods: We conducted a narrative literature review to determine the key prevalent PsA disease domains. We present the existing evidence base to measure the treatment effects of existing PsA treatments on the various disease domains. Finally, we propose an economic modeling framework that could estimate the economic value of treatments for addressing specific PsA disease domains.

Results: The key prevalent disease domains in PsA include peripheral arthritis, dactylitis, enthesitis, psoriatic spondylitis, skin, and nail lesions. However, the evidence base for the effect of a specific treatment on a given domain was less robust, as was the comparative evidence base of how existing market PsA treatments perform on one or more disease domains relative to each other (Table 1). Our review of clinical trials and the literature of the relevant outcomes also found no comparative effectiveness analysis of PsA domains. Our economic modeling framework to estimate the economic value of treatments for addressing specific PsA disease domains requires further clinical and real-world evidence to be generated on the relative efficacy or effectiveness on each disease domain. Given the evidence challenges, we would suggest a cohort-level model, with potential parallel modeling for the different disease domains, to estimate total social value calculated as quality-adjusted life-years as well as the cost per grouped outcome and changes in cost per symptom avoided. An individual/patient-level simulation would be the ideal design to represent patient heterogeneity but may not be feasible due to limited available data. As PsA is a chronic lifelong disease, we propose that this model use a lifetime horizon. We believe that a model as outlined in Figure 1-2 would provide valuable economic input to help inform treatment decision making.

Conclusion: Psoriatic arthritis is a heterogeneous disease, with patients presenting a variety of disease manifestations. A more granular understanding of the interaction between disease domains and treatments, such as the one proposed in Figure 3, would benefit both providers and patients in making value-based, personalized treatment decisions.

Disclosure: J. Chou, PRECISIONheor, 1, 3; **E. Maksabedian**, Amgen Inc., 1, 2; **D. Collier**, Amgen Inc., 1, 2; **H. Thom**, Amgen Inc., 9.

Abstract Number: 0582

Mortality and Cost of Hospitalization: Do Hospitals Caring for More SLE Patients Perform Better?

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Background/Purpose: Individuals with systemic lupus erythematosus (SLE) have an increased risk of hospitalization throughout their lifetime, potentially leading to higher patient mortality and healthcare costs. Establishing minimum volume thresholds for other medical and surgical conditions has been proposed as a way to improve outcomes. We evaluated the relationship between a hospital's yearly SLE volume and two outcomes: mortality and cost of hospitalization.

Methods: We used the National Inpatient Sample (NIS), which after weighting provides annual estimates for more than 35 million community hospitalizations in the US. Analysis was limited to adults without missing relevant variables hospitalized in 2017. Admissions with SLE were captured in ICD-10-CM codes (M32.1x, M32.8, M32.9). Hospital specific costs were obtained using NIS cost-to-charge ratio files. We used linear regression to model average cost for admissions with a diagnosis of SLE based on the number of yearly SLE discharges at the treating hospital (analysis conducted with continuous variable of SLE volume per year, and repeated with a categorical variable establishing 50 or more SLE discharges yearly), controlling for the Ward systemic lupus-specific risk adjustment index[1] modified for ICD-10, demographics (age, sex, race/ethnicity), health insurance, income quartile in the ZIP Code of residence, and hospital characteristics (bed size, rural/urban/teaching status). In addition, we used Poisson regression to model mortality risk based on hospital SLE volume and the covariates listed above. All analyses accounted for the complex sampling design of the NIS.

Results: Adults with SLE included in the analysis accounted for a nationally estimated 172,135 discharges in 2017 (0.48% of all hospital discharges). Mean cost per SLE discharge was $14,420 (SE $207); 2% of hospitalizations resulted in death. In adjusted analysis, cost per SLE discharge was higher for hospitals caring for more SLE patients per year. Approximately 18.6% of included hospitals had a yearly SLE volume greater than 50. Hospitals with a yearly SLE volume greater than 50 had a higher average cost per SLE discharge compared to those with an SLE volume less than 50 (cost difference $3,399; 95% CI $1,803 to $4,996). Risk of inpatient mortality did not significantly vary based on SLE hospital volume.

Conclusion: Higher yearly SLE hospital volume was associated with greater cost per discharge, without significant differences in mortality rates compared to hospitals with lower SLE volumes. If the lupus-specific risk adjustment index we used does not fully capture patient disease severity or if there were coding differences between hospitals, this could have potentially affected the results. Our findings do not suggest a minimum volume threshold for SLE care that can be used to improve inpatient outcomes.

Reference

1. Ward, MM. Development and testing of a systemic lupus-specific risk adjustment index for in-hospital mortality. *J Rheumatol* 2000; 27(6):1408-1413.

Disclosure: C. Anastasiou, None; **L. Trupin**, None; **P. Katz**, None; **Z. Izadi**, None; **M. Gianfrancesco**, None; **G. Schmajuk**, None; **J. Yazdany**, Eli Lilly, 5, Astra Zeneca, 5.

Abstract Number: 0583

Cost of Illness in Patients with Psoriasis and Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriasis (Ps) and psoriatic arthritis (PsA) have a major impact on patients' health-related quality of life. Cost of illness of patients with Ps, PsA and both diseases (PsA+Ps) is an important subject as they are associated with a substantial economic impact, with implications from a health management perspective.

The objective of our work was to describe the economic burden of direct non-healthcare and indirect resources of patients with Ps, PsA and PsA+Ps in Spain.

Methods: COEPSO ("Evaluation of Costs in patients with Psoriatic Disease") was an observational, retrospective, cross-sectional study performed in 22 Spanish centers (17 Dermatology and 14 Rheumatology Services), from February 2017 to February 2018, including moderate to severe Ps and PsA patients (with or without Ps), naive to biologics. Direct non-healthcare (social services, home care, physical adaptations, private health and non-health professionals, non-reimbursed and non-pharmaceutical therapies), indirect (loss of productivity) and total costs (direct non-healthcare and indirect costs) related to the disease during the previous year to the study were obtained. Unitary costs (€, 2018) were calculated: out-of-pocket costs were specified directly by patients and loss of productivity costs by means of average salaries based on occupation specified by patients. The information was collected through a case report form filled out by the investigators and a telephone survey administered to the patients.

Results: A total of 318 patients were included (196 Ps; 43 PsA and 79 PsA+Ps), mean age 48.7 years and 51.3% males. Metabolic syndrome was the most frequent comorbidity in all groups. The average annual total cost per patient was 1,042.71€ (SD 3,817.55), 1,137.84€ (SD 3,070.39) and 1,830.26€ (SD 5,835.81) for Ps, PsA and PsA+Ps, respectively. The average annual direct non-healthcare cost per patient was 749.57€ (SD 2,393.77), 750.50€ (SD 1,641.82) and 1,247.56€ (SD 4,467.19) for Ps, PsA and PsA+Ps, respectively. The average annual indirect cost per patient was 293.14€ (SD 2,855.27), 387.35€ (SD 2,409.63) and 582.71€ (SD 3,842.12) for Ps, PsA and PsA+Ps, respectively. Patients with combined PsA+Ps had higher annual total cost (direct non-healthcare and indirect costs) than patients with only one of these manifestations separately (75.5% and 60.9% above patients with Ps and PsA, respectively). Total costs in patients with Ps and PsA were similar. Direct non-healthcare costs represent between 66.0% (patients with PsA) to 71.9% (patients with Ps) of total cost. Indirect costs represent between 28.1% (patients with Ps) to 34.0% (patients with PsA) of total cost.

Conclusion: PsA and Ps have proved to be diseases with a high economic burden, and the total costs were mainly driven by direct non-healthcare costs. Moreover, although annual total costs in patients with PsA were similar to those of Ps patients, the combination of both manifestations yielded the highest costs suggesting the importance of the increased disease load.

Disclosure: S. Castañeda, Roche, 2; **E. Vicente-Rabaneda**, Roche, 8, BMS, 2, 8; **M. Llamas-Velasco**, Abbvie, 2, 5, 8, Almirall, 2, 5, 8, Amgen, 2, 5, 8, Boehringer, 5, 8, Celgene, 5, 8, Janssen, 2, 5, 8, Leo, 2, 5, 8, Lilly, 2, 5, 8, Novartis, 2, 5, 8, 9, UCB, 5, 8; **J. Sánchez-Pérez**, None; **J. Pardo**, None; **R. Cabeza-Martínez**, None; **M. Miranda-Fontes**, None; **J. Márquez**, None; **J. Calvo-Alén**, None; **S. Armesto**, None; **I. Belinchón**, None; **A. Gómez**, None; **M. Miranda**, None; **S. Martínez-Pardo**, None; **L. Merino Melendez**, None; **M. Casado**, None; **M. Yébenes**, None; **A. Casado**, None.

Abstract Number: 0584

Total Cost of Care for Patients with Rheumatoid Arthritis

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: The range of medical costs associated with rheumatoid arthritis (RA) is, in part, related to the various treatment options. Treatment for RA focuses on the control and management of inflammation. Patients with new RA diagnoses or less severe disease are usually prescribed less expensive non-biologic disease-modifying anti-rheumatic drugs (DMARDs). In contrast, patients who do not respond to DMARD treatment or exhibit more advanced disease are treated with biologics. It is estimated that treating RA with biologic therapies is three times more expensive than nonbiologic DMARDs. However, the initial cost of biologic therapy may be offset through reduced disease progression, health care utilization, and health care expenditures throughout the disease. The purpose of this study was to estimate the total cost of care among RA patients with commercial health insurance.

Methods: We identified patients with RA using medical claims data from January 1, 2019, to December 31, 2019. We defined total cost of care as the sum of allowed costs paid for medical and pharmacy claims per year. We compared the allowed costs of fully-insured and self-insured commercial patients with health insurance through a large national insurer.

Results: From January 2019 to December 2019, we identified 7,489 fully-insured RA patients and 11,824 self-insured RA patients. The average annual total cost of care for fully-insured and self-insured patients was $31,561 and $33,753, respectively. Pharmacy costs (both medical and pharmacy benefits) accounted for 70% of total costs for fully-insured and self-insured patients. Inpatient facility, specialist physician and ambulatory facility costs accounted for 9%, 7% and 5%, respectively, of total costs for fully-insured and self-insured patients. In 2019, 622 patients were

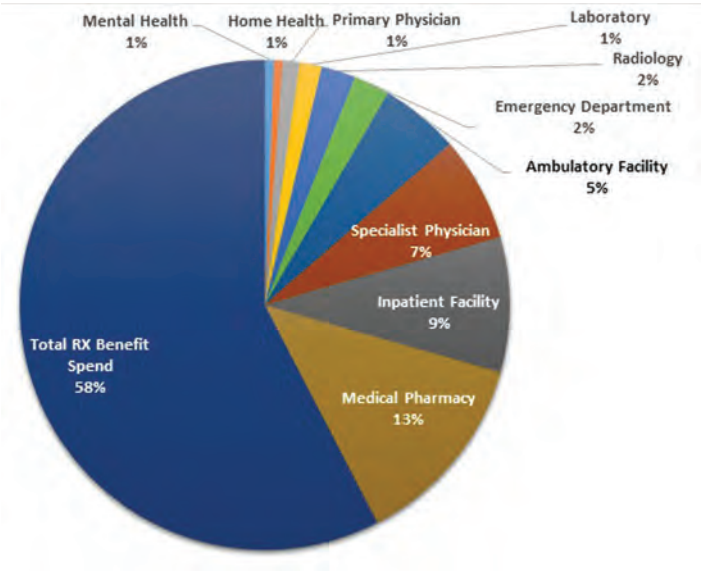

Figure 1. Total Cost of Care Distribution for Members with Rheumatoid Arthritis, 2019

prescribed infliximab for the treatment of RA, the majority of these patients (72%) received infusions in their doctor's office. The annual total cost of care for patients on infliximab ranged from $57,612 for those receiving infusions in their doctor's office to $131,616 for those receiving infusions in a hospital.

Conclusion: Direct medical costs for patients with RA are significant. In this study, pharmacy costs comprised a substantial portion of RA total cost of care. While pharmacy costs comprise a significant portion, the actual amount spent varies significantly by type of therapy and site of care, which presents an opportunity of future study and potential optimization of cost outcomes.

Disclosure: K. Johnson, CVS Health, 1, 3; **R. Karos**, CVS Health, 3; **E. Avalos-Reyes**, CVS Health, 3; **F. Casadio**, CVS Health, 1, 3; **M. Hamburger**, None; **C. Leprai**, CVS Health, 1, 3.

Abstract Number: 0585

Cost-effectiveness of Motivational Counselling and SMS-reminders on Daily Sitting Time in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The "Joint Resources – Sedentary Behaviour" randomised controlled trial (RCT) (1,2,3) aimed to reduce sedentary behaviour in patients with rheumatoid arthritis (RA) by means of a 16-week intervention consisting of motivational counselling and text message reminders. The results showed significant between-group differences on behavioral, patient-reported and cardio-metabolic outcomes, both after 4 and 22 months. This secondary, protocolised cost-effectiveness analysis compared the intervention costs and improvement in HAQ and EQ-5D health utility between the intervention and control group.

Methods: Eligible RA patients (meeting the ACR classification criteria for RA) were randomised to the intervention (IG) or control group (CG). The healthcare perspective was applied for the cost analysis and outcomes were reported in terms of objectively measured daily sitting time, HAQ and EQ-5D scores during the 22-month observation period. Cost-effectiveness was reported as incremental cost-effectiveness ratios (ICER) and cost-effectiveness acceptability curve.

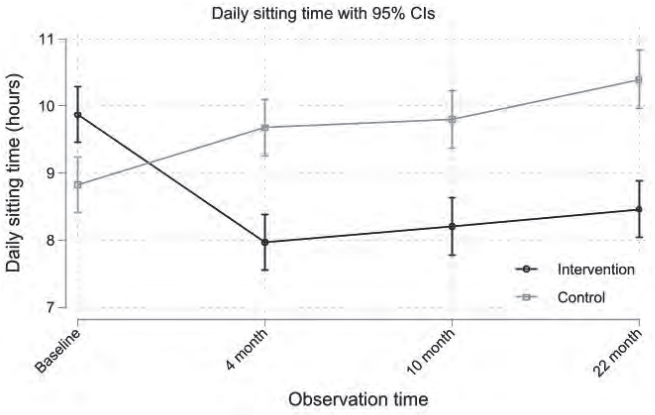
Outcomes were assed at baseline, at 4 months (after completed intervention), 10 and 22 months after baseline. Intervention mean cost included fixed planning costs and variable running cost. The incremental time weighted outcomes were related to the intervention cost. The ratio of intervention cost and gain in QALYs were illustrated in a scatterplot and cost-effectiveness acceptability curve.

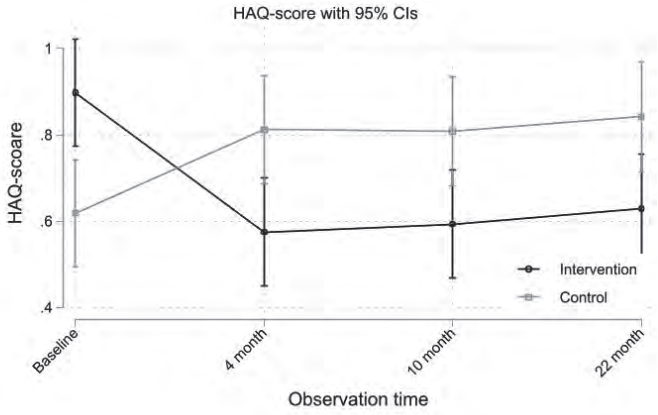
Results: The intervention cost was estimated at €145 per participant. The difference in mean outcomes are shown in Figure 1. At follow-up the intervention group had shorter daily sitting time, better HAQ and EQ-5D scores. The time weighted outcomes and ICERs are shown in Table 1. Figure 2 shows A) the relation between bootstrapped intervention cost and incremental quality-adjusted life years (QALY) based on EQ-5D outcomes and B) the cost-effectiveness acceptability curve. These figures suggest that the intervention is cost-effective at a threshold value of €3800 per QALY.

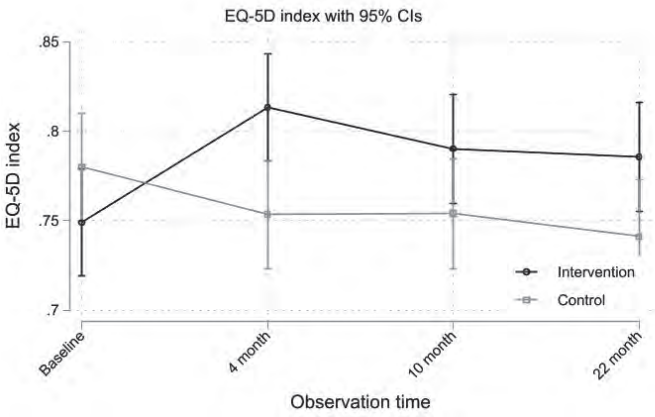
Table 1. Time-weighted outcomes (mean and 95% confidence interval)

	Intervention group (n=75)	Control group (n=75)	Incremental difference
Outcomes			
Daily sitting time (hours)	8.4 (8.1-8.8)	9.8 (9.5-10.2)	-1.4 (-1.9 - -0.9) p<0.001
HAQ score (low value better)	0.62 (0.52-0.73)	0.80 (0.67-0.92)	-0.17 (-0.33 - -0.01) p=0.035
EQ-5D utility (high value better)	0.79 (0.77-0.81)	0.75 (0.73-0.78)	0.04 (0.02 - 0.074) p=0.037
Incremental Cost-Effectiveness ratio			ICER (2019-€)
Cost per reduced daily sitting hour			101
Cost per reduced HAQ score			844
Cost per gain in QALY			3800

Missing observations replaced with last observation carried forward. Mean intervention cost per participant: €1





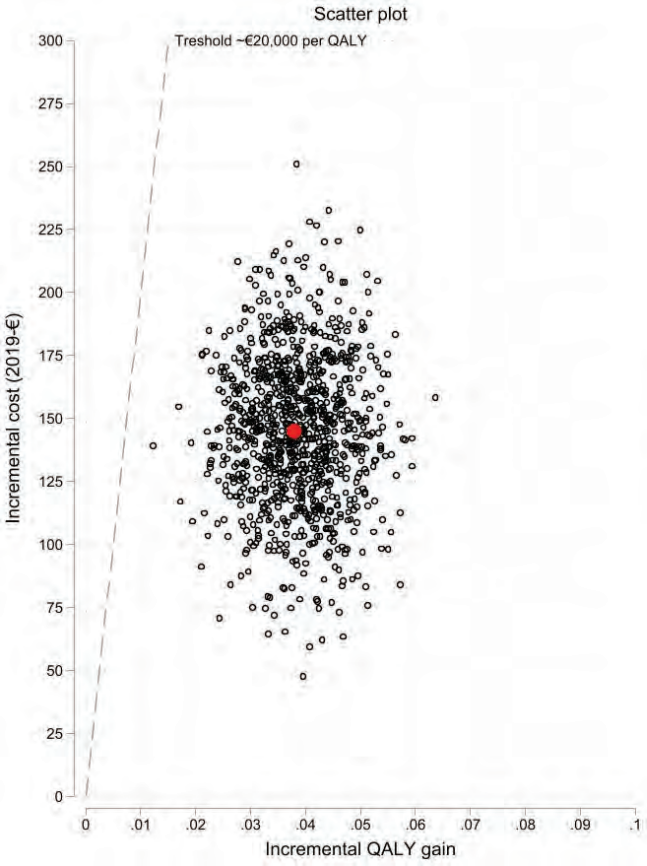


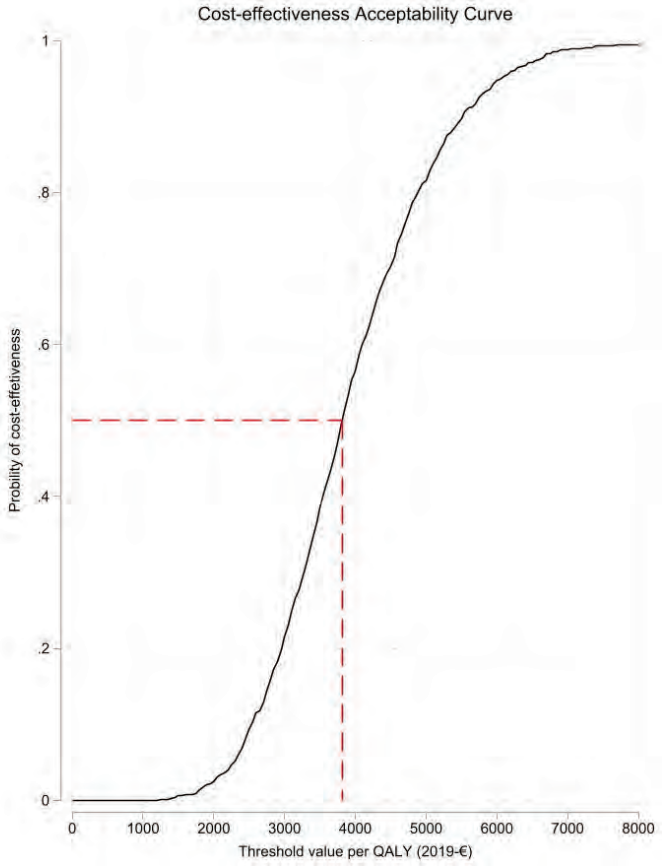
Conclusion: This secondary, protocolised cost-effectiveness analysis was based on data from an RCT with high participation rates and good completion of return outcome measurements. The results suggest that the ICER of the individually tailored, behavioural intervention is €3800 per QALY which is well below traditional threshold values. These results suggest that the intervention is cost effective to implement in routine care.

(1) Esbensen BA et al. Trials 2015; 16:23

(2) Thomsen T et al. Ann Rheum Dis 2017; 76(9):1603-6

(3) Thomsen T et al. Arthritis Care Res 2019; sept 10





Disclosure: J. Sorensen, None; **M. Aadahl**, None; **M. Hetland**, Novartis, 2, Bristol-Myers Squibb, 2, MSD Denmark, 5, AbbVie, 2, Roche A/S, 2, Orion Pharma, 2, Eli Lilly Denmark, 2, CellTrion Healthcare Co Ltd, 5, Merck A/S, 2, Samsung Bioepis, 2, Janssen Biologics B.V, 5, Biogen, 2, Pfizer, 2, Diankonhjemmet Sykehus, 5; **B. Appel Esbensen**, None; **T. Thomsen**, None.

Abstract Number: 0586

Performance Characteristics of ANA by Elisa and Immunofluorescence

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The ANA is a critical test in the evaluation of patients with suspected lupus and other connective tissue diseases. Clinical laboratories have relied increasingly on automated solid phase methods for its detection and, more recently, on automated pattern recognition systems for the indirect immunofluorescence (IFA) technique.

Table 1. ANA by Elisa and IFA

	N	+ ANA by Elisa (%)	+ ANA by IFA (%)	Concordant Results (%)	Discordant Results (%)
Total pts	312				
Positive N (%)		165 (52.9)	204 (65.4)		
				207 (66.3)	105 (33.7)
Final Dx					
RA	20	8 (40.0)	13 (65.0)	13 (65.0)	7 (35.0)
SLE	37	27 (73.0)	24 (64.9)	22 (59.5)	15 (40.5)
IPA[1]	28	12 (42.9)	18 (64.3)	22 (85.7)	6 (21.4)
UCTD	52	40 (76.9)	38 (73.1)	38 (73.1)	14(26.9)
SSC	8	7 (87.5)	8 (100)	7 (87.5)	1 (12.5)
SS	13	9 (69.2)	10 (76.9)	10 (76.9)	3 (23.1)
DM	3	-	-	-	-
PM	1	-	-	-	-
CTD	62	46 (74.2)	45 (72.6)	41 (66.1)	21 (33.9)
EUCTD[2]	142	98 (69.0)	101 (71.3)	101 (71.1)	41 (28.9)
IRD[3]	162	106 (65.4)	114 (70.4)	114 (70.4)	48 (29.6)

1: inflammatory polyarthritis; 2: early undifferentiated connective tissue disease; 3: inflammatory rheumatic disease

The performance characteristics of both methods have not been rigorously evaluated and have not been studied prospectively.

Methods: Patients who were seen by an academic rheumatologist, who had ANA's obtained within 30 days by both Elisa (Zeus Elisa™) and IFA (Euroimmune ANA Diagnostics ™), and whose diagnosis had yet to be established, were evaluated. Patients were followed to establish a diagnosis. Patients were classified at their last office visit by clinical diagnosis, confirmed by independent review, and were further grouped into those with: 1) Connective tissue disease (CTD) including pts with definite and probable CTD who were also receiving DMARD/ immunomodulating therapy; 2) Early undifferentiated connective tissue disease (EUCTD) which included CTD, possible CTD, as well as undiagnosed inflammatory polyarthritis (IPA); and, 3) inflammatory rheumatic diseases (IRD) which included all with EUCTD as well as patients with RA.

Sensitivity, specificity, predictive values, likelihood and diagnostic odds ratios and their confidence intervals were calculated and compared.

Results: 312 patients were identified and followed for a median of 9.96 months (IQR: 1.9, 18.5). At their last visit the following diagnoses were established: CTD- 62 (SLE-37, SS-13, SSC-8, DM-3, PM-1), EUCTD-142, IRD-162. Percent positive ANAs by Elisa and IFA were 52.9% and 65.4% respectively. Concordance of results was found in 66.3% The performance characteristics of the two ANA techniques are shown in Table 1 and Table 2.

Table 2. Performance Characteristics of ANAs by Elisa and by IFA

	RD (95% CI)	EUCTD (95% CI)	CTD (95% CI)
Elisa Sensitivity	0.654 (0.581, 0.728)	0.690 (0.614, 0.766)	0.742 (0.633, 0.851)
IFA Sensitivity	**0.704 (0.633,0.774)**	**0.711 (0.637, 0.786)**	**0.726 (0.615, 0.837)**
Elisa Specificity	0.607 (0.529, 0.685)	0.601 (0.532, 0.679)	0.524 (0.462, 0.586)
IFA Specificity	**0.400 (0.322, 0.478)**	**0.394 (0.321, 0.468)**	**0.364 (0.304,0.424)**
Elisa PPV[1]	0.642 (0.569, 0.716)	0.594 (0.519, 0.669)	0.278 (0.210, 0.347)
IFA PPV	**0.559 (0.491, 0.627)**	**0.495 (0.4265, 0.564)**	**0.221 (0.164, 0.278)**
Elisa NPV[2]	0.619 (0.541, 0.698)	0.701 (0.627, 0.775)	0.891 (0.841, 0.942)
IFA NPV	**0.556 (0.462, 0.649)**	**0.620 (0.529, 0.712)**	**0.842 (0.774, 0.911)**
Elisa Accuracy	0.631 (0.575, 0.685)	0.644 (0.588, 0.697)	0.567 (0.510, 0.623)
IFA Accuracy	**0.558 (0.501, 0.614)**	**0.541 (0.485, 0.598)**	**0.496 (0.380, 0.458)**
Elisa LR+[3]	1.66 (1.32, 2.09)	1.75 (1.41, 2.17)	1.56 (1.28, 1.90)
IFA LR+	**1.17 (0.99, 1.38)**	**1.19 (1.01, 1.40)**	**1.14 (0.95, 1.37)**
Elisa LR-[4]	0.57 (0.44, 0.73)	0.51 (0.39, 0.67)	0.49 (0.32, 0.76)
IFA LR-	**0.74 (0.54, 1.01)**	**0.72 (0.52, 0.99)**	**0.75 (0.49,1.17)**
DOR[5] Elisa	2.91 (1.84, 4.63)	3.42 (2.14, 5.48)	3.16 (1.70, 5.89)
DOR IFA	**1.52 (0.99, 2.53)**	**1.60 (1.00, 2.58)**	**1.52 (0.82, 2.80)**

1: Positive Predictive Value; 2: Negative Predictive Value; 3: Positive Likelihood Ratio; 4: Negative Likelihood Ratio; 5: Diagnostic Odds Ratio

In general, the test methodologies provided comparable results. IFA was somewhat more sensitive (NS) while Elisa was more specific ($p < 0.05$). Diagnostic accuracy was higher with Elisa than with IFA for definite CTD (0.567 vs 0.436, $p < 0.05$). Diagnostic odds ratios where higher with Elisa (2.91-3.42) than with IFA (1.52-1.60) although the differences did not achieve statistical significance.

Conclusion: ANA by Elisa and ANA by IFA performed similarly in this short-term, prospective study. Elisa appears to be more specific and possibly more accurate in patients who had developed a definite CTD. Further observation will be necessary to definitively determine any meaningful differences in testing approaches.

Disclosure: G. Lobo, None; **M. Luggen**, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Genentech, 2, 5, 8, Eli Lilly, 2, 5, 8, Nichi-Iko, 2, 5, 8, Novartis, 1, 5, 8, Pfizer, 2, 5, 8, Sun Pharmaceutical Industries, Inc., 2, 5, 8, R-Pharm, 2, 5, 8; **C. Crutchfield**, None.

Abstract Number: 0587

Barriers to Rheumatologic Care and Antimalarial Refills Among a Cohort of Patients with Systemic Lupus Erythematosus During the COVID-19 Pandemic

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The pandemic of coronavirus disease 19 (COVID-19) has led to widespread disruptions across the spectrum of healthcare. We sought to investigate barriers to medical care, including access to ambulatory rheumatology appointments and routine medications such as antimalarials among patients with systemic lupus erythematosus (SLE) in the San Francisco Bay Area using a diverse, population-based cohort.

Methods: Subjects with SLE in the longitudinal California Lupus Epidemiology Study (CLUES) were administered a structured telephone interview during the COVID-19 pandemic. Participants were asked about SLE disease activity, COVID-19 exposures and infection, demographic factors and patient-reported outcomes. We collected data on access to ambulatory rheumatology appointments. Participants were also asked about difficulties in obtaining timely antimalarial refills since March 2020, encompassing partially filled, delayed or denied refills. Using a multivariable logistic regression model, we investigated demographic (age, female sex, nonwhite race) and disease-related factors (Systemic Lupus Activity Questionnaire, or SLAQ) associated with barriers to timely antimalarial refills.

Results: 202 CLUES cohort members participated in this interview. The mean age was 50 (±13 SD), 91% were female, and 64% reported a nonwhite race/ethnicity. 89 of 99 (90%) participants who tried to access ambulatory rheumatologic care were able to obtain an appointment; 79% of this care was delivered via telephone or video visits. Of the 111 participants who attempted to refill their antimalarial since March 2020, 39 (35%) reported partially filled, delayed or denied refills. Barriers to timely antimalarial refills were not associated with age, female sex, nonwhite race or SLAQ score.

Conclusion: These data suggest that in the San Francisco Bay Area, there were minimal disruptions in access to rheumatologic care for people with SLE, which parallels the high rate of virtual care provided during the first months of the pandemic. However, participants with SLE did report considerable difficulties in obtaining antimalarial refills. This highlights the importance of ensuring an adequate supply and appropriate stewardship of a critical medication for patients with chronic diseases during the COVID-19 pandemic.

Disclosure: A. Aguirre, None; **L. Trupin**, None; **S. Patterson**, None; **K. DeQuattro**, None; **P. Katz**, None; **C. Lanata**, None; **S. Rush**, None; **L. Criswell**, None; **M. Dall'Era**, Janssen, 5, AstraZeneca, 5; **J. Yazdany**, Eli Lilly, 1, Astra Zeneca, 1.

Abstract Number: 0588

Feast or Famine? An Institutional Assessment of Hydroxychloroquine Screening Practices

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SESSION INFORMATION
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Background/Purpose: Hydroxychloroquine (HCQ) is a generally safe and widely used rheumatologic drug. Maculopathy is an adverse effect in < 1% in the first 5 years of use; risk rises with exposure and presence of comorbidities. The American Academy of Ophthalmology (AAO) screening guidelines for HCQ maculopathy recommend a baseline within the 1st year and, if normal, annual screening after 5 years. Patients are screened at baseline with a fundus examination at minimum and per the provider's discretion may also undergo additional testing.

We evaluated our institutional screening practices and determined the cost of excess services provided and whether this practice led to an increase in detection of toxic maculopathy. We hypothesize that patients in our system are over screened, leading to waste.

Table 1
Demographics of Participants

Gender	
Female	132
Male	25
Weight Based Dosing (mg/kg/day)	
Average	4.5
Range	1.5-8.8
Patients on <5 mg/kg/day	97
Patients on >5 mg/kg/day	46
Unknown dose	13
Age	
Average	52.8
Range	4-99
Time on Hydroxychloroquine	
Less than 1 yr	41
1-5 yrs	59
> 5 yrs	57
CKD Status	
Present	28
Absent	129
Tamoxifen use	
Yes	2
No	155

Table 1. Demographics of included patients on hydroxychloroquine. CKD = Chronic Kidney Disease

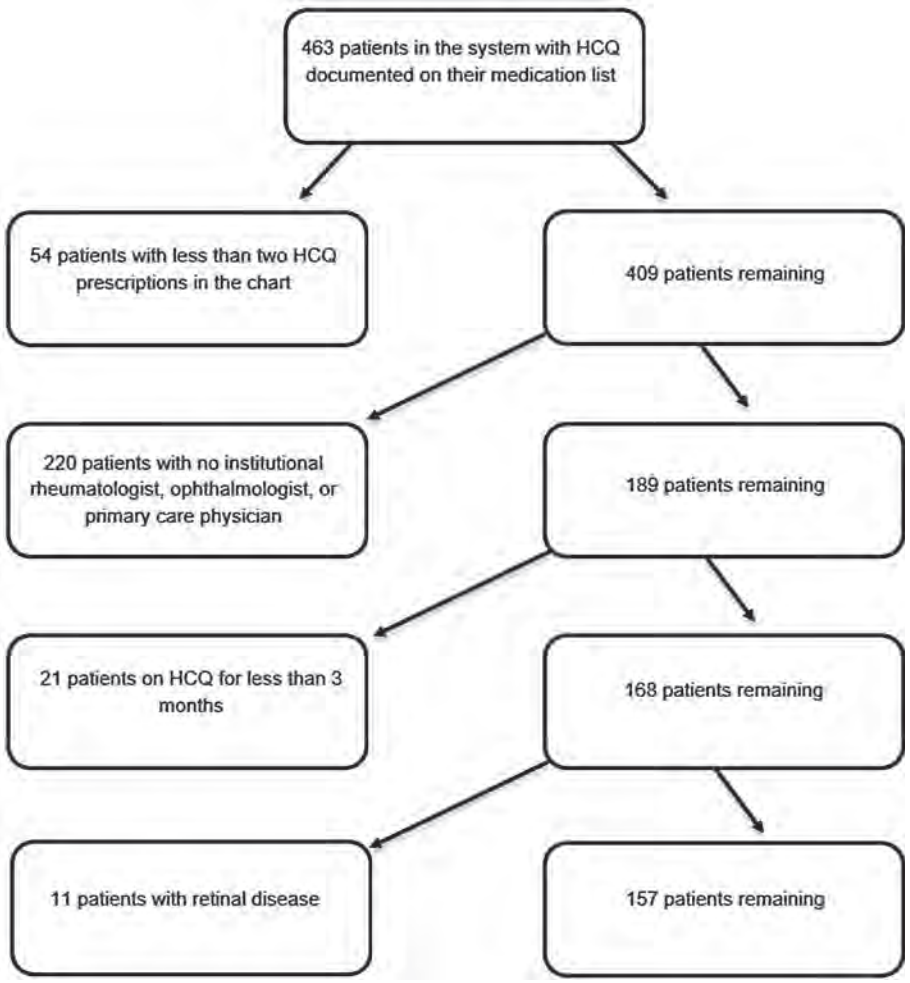

Figure 1. Diagram of method of patient exclusion from study

Methods: All patients with an HCQ prescription in their medication list were included. Exclusions were: macular disease, single prior prescription, never-users or those with adverse effect with < 3 months of use, and those without appointments with rheumatology, ophthalmology or primary care within the institution. Electronic chart-based data collection included: weight-based dose of HCQ, duration of treatment (< 1, 1-5, or >5 years), tamoxifen use, history of kidney disease, and presence of toxic maculopathy. Screening recommendations were evaluated in compliance with the AAO recommendations for baseline and follow-up screening.

Results: 463 patients were prescribed HCQ between January 2010 and April 2020; 157 were included. HCQ use duration was distributed into 3 groups: < 1 year (n= 41), 1-5 years (n= 59), and >5 years (n= 57).

Of the 157 included patients, 38.7% underwent baseline ophthalmologic exam within one year of starting HCQ, 27.7% did not, and 33.6% had no documentation of a retinal exam. 33.6% of patients were inappropriately recommended to be screened again after baseline exam within 1 year. Only 2% of patients were advised to rescreen following baseline exam after 5 years exposure per AAO guidelines. 9% of patients on HCQ for more than 5 years were appropriately receiving annual screening; 12.2% were not. All 3 cases of HCQ maculopathy in our system were diagnosed in appropriately screened patients. Over screening resulted in an additional $1853 per patient.

Length of Time on HCQ	<1 year		1-5 years		>5 years		Cumulative Data	
	n	%	*n*	%	*n*	%	*n*	%
Baseline Screen								
Appropriate	17	42.5	28	48.3	15	26.3	60	38.7
Not Done	0	0	25	43.1	14	24.6	39	25.1
Not Applicable	19	10	0	0	0	0	19	12.2
Unknown	4	47.5	5	8.6	28	49.1	37	23.9
Recommended Follow-Up from Baseline Screen								
Within 1 year	11	30.6	23	41.8	15	27.3	49	33.6
At 5 years of treatment	0	0	1	1.8	2	3.6	3	2.0
Not Applicable	21	58.3	16	29.1	16	29.1	53	36.3
Unknown	4	11.1	15	27.3	22	40	41	28.1
5 Year Screen								
Appropriate	0	0	4	6.9	24	42.1	28	18
Not Done	0	0	0	0	10	17.5	10	6.4
Not Applicable	41	100	50	86.2	7	12.2	98	62.8
Unknown	0	0	4	6.9	16	28	20	12.8
Annual Screening after 5 years								
Yes	0	0	0	0	14	24.6	14	9
No	0	0	0	0	19	33.3	19	12.2
Not Applicable	41	100	58	100	19	33.3	118	75.6
Unknown	0	0	0	0	5	8.8	5	3.2

Table 2. Screening practices and follow up recommendations for patients divided into length of time on hydroxychloroquine (HCQ)

Conclusion: Our analysis of institutional screening practices for HCQ reveal that only 41% of patients are being appropriately screened. Contrary to our hypothesis, of the inappropriately screened patients, 29% were over screened and 71% were under screened. Of patients who had recorded follow-up recommendations after baseline exam, 94% were inappropriately recommended to follow up in 1 year, while only 6% were recommended to follow up after 5 years of HCQ use per AAO guidelines. Insurance demands regarding specialty care may be a cause of over screening as follow up visits greater than one year out require more administrative burden. Limitations to this study include inadequate available data and reliance on clinical documentation to establish screening methods. In those over screened, utilization costs were high, an additional $1853/patient. For those under screened, the health and financial consequences remain unknown.

Disclosure: A. James, None; **K. Kam**, None; **V. Sandhu**, GSK, 8; **C. Downey**, None.

Abstract Number: 0589

The Ideal Mhealth Application for Rheumatoid Arthritis: Qualitative Findings from Stakeholder Focus Groups

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Background/Purpose: Early access to specialized rheumatological care is under increasing pressure. Many countries are currently confronted with a relative shortage of practicing rheumatologists, while recent shifts in the management strategies of rheumatoid arthritis (RA) have made ambulatory care more labor intensive. These developments have prompted the exploration of innovative care models for RA, including the use of mobile health (mhealth) applications, such as mobile apps and wearables. Mhealth applications could facilitate the monitoring of disease activity in between clinic visits and thus offer opportunities to provide personalized care for RA patients at the right time. This could potentially result in a significant reduction in the number of unnecessary clinic visits and reduce waiting times for an appointment. In Belgium, mhealth applications have only sparsely been integrated in routine care for RA patients. Little is known about their applicability in Belgian rheumatology care. The aim of this study was to gain more insight in possible barriers and facilitators of mhealth applications for the ambulatory care for RA patients, according to different stakeholders.

Methods: We performed a qualitative study with focus group interviews. Focus groups were organized with the following stakeholders: nurses specialized in the care of patients with RA, patients with RA and rheumatologists. The qualitative analysis guide of Leuven (QUAGOL) was used to analyze the data obtained during the focus groups by 3 researchers (MVDP, RVM, DDC).

Results: In total, 2 focus groups with nurses (n=16), 2 with patients (n=17) and 2 with rheumatologists (n=19) took place. Due to the Covid-19 pandemic, 1 focus group with patients was cancelled, and 1 with rheumatologists was performed online.

Most stakeholders expressed some form of familiarity with mhealth applications. However, reluctance of seeing these applications as a care innovation was observed. Especially rheumatologists underlined such applications were suitable for only a subgroup of patients. Some stakeholders feared the complexity of mhealth applications and doubted the added benefit versus a face-to-face visit. However, the evolution towards mhealth applications was expressed as inevitable in modern society. Mhealth tools were viewed as complementary to routine care. Especially rheumatologists underlined their role as experts of RA care, fearing to be replaced by mhealth techniques. Expectations of such an application were high. An ideal tool was said to aggregate as much practical, clinical and educational aspects for a patient as possible and to incorporate easy access for all stakeholders to stimulate application use while ensuring privacy.

Conclusion: Although stakeholders expressed doubts towards mhealth applications in daily practice, many saw this evolution as inevitable. Therefore, it would be wise to develop an app integrating the viewpoints of all parties involved in the care of patients with RA to ensure implementation in practice.

Disclosure: D. De Cock, None; **M. Vandeputte**, None; **R. Van Melder**, None; **M. Doumen**, None; **D. Bertrand**, None; **V. Stouten**, None; **S. Pazmino**, None; **R. Westhovens**, Celltrion, Inc., 2, 5, Galapagos NV, 2, 5, Gilead Sciences, Inc., 2, 5; **P. Verschueren**, Pfizer, 9.

Abstract Number: 0590

A Web-Based Data Capture System Can Successfully Collect Detailed and Quantifiable Physical Therapy Intervention Data Post Total Knee Replacement

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SESSION INFORMATION
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Background/Purpose: Variation in clinical care of patients post total knee replacement (TKR) is well-known. Experts suggest that electronic health records (EHR) can be used to decrease unwarranted practice variation and to provide real world evidence for comparative effectiveness research (CER). However close examination of EHRs shows that they rarely include adequate intervention detail to replicate or replace randomized controlled trials. Using content recommendations from PT experts we designed a web-based data capture system to collect detailed, quantifiable intervention data from physical therapists (PTs) treating patients following TKR. PTs were instructed to enter every intervention provided at every visit using drop-down menus. If unable to describe their intervention using the menus, PTs provided explanations of the interventions in a Clinical Notes text box. We deployed the system to 8 outpatient physical therapy practices and 33 sites in 3 different US states. The purpose of this study was to evaluate the system's ability to capture detailed quantifiable intervention data from multiple clinical sites and practitioners by describing the use of the Clinical Notes text box to identify interventions.

Methods: 81 PTs entered intervention data for 153 patients over a total of 2442 visits. All clinical notes were reviewed by at least two trained physical therapy reviewers to determine if the interventions in the clinical notes were: 1) additional information about interventions already identified by the PT in the menus; 2) additional interventions that were available but not identified in the menu by the PT; or 3) additional interventions not represented in the menus. We identified the frequency of visits when interventions were entered into the clinical texts but not entered using the menus. We determined the number of PTs who included interventions in the clinical notes but not in the menus. We also determined what interventions listed in the text box were unavailable in the menus.

Results: 46 PTs (57 %) used the Clinical Notes text box to include interventions they had not chosen from the menus. Clinical Notes from 424 visits (17%) included interventions which had not been identified in the menus. The most common reason (148 visits) for including interventions in the text box but not in the menu was because the therapist exceeded the maximum allowable number (10) of strengthening exercises. In 257 visits (11%) the PT listed interventions in the text box that had been available in the menus. 19 visits (0.008%) included interventions in the text box that could not have been identified in the menus. PTs reported documentation was quick and easy.

Conclusion: It is possible to use a structured, menu-driven data capture system to collect detailed and quantifiable intervention data across multiple practice sites and among multiple PTs in patients post TKR. While many PTs used text to describe their interventions, better training of the PTs and minor changes to the capture system will minimize the need for text in data capture, making detailed and quantifiable descriptions of interventions and dosages straight forward across treatment sites and practitioners. This will allow large pragmatic CER and may lead to decreased practice variation.

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Abstract Number: 0591

Intervention to Improve SLE Medication Adherence Using Surescripts Pharmacy Refill Data

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Background/Purpose: Medication nonadherence is as high as 80% among SLE patients and leads to higher morbidity, mortality, and healthcare costs. Few studies have tested interventions to improve adherence in SLE patients, and none was effective among adults with SLE in the US. We developed an intervention based on prior study results and data from Surescripts, the largest health information network in the US, in collaboration with lupus clinic stakeholders, including patients, providers, and staff. The intervention uses Surescripts pharmacy refill data which draws from nearly all pharmacies and electronic health record systems, to monitor nonadherence and prompt tailored discussions surrounding medication use during the clinic encounter. We pilot-tested this intervention to assess feasibility, acceptability, appropriateness, and to explore its effect on adherence.

Methods: We conducted a 12-week pilot intervention at an university lupus clinic among consecutive follow-up patients on SLE medications, including HCQ, MTX, AZA, MMF, LEF, and belimumab. Adherence was assessed by medication possession ratio (MPR) based on Surescripts refill data, using MPR ≥80% as a cutoff for being adherent. During an encounter, the clinic note template prompted the provider to share the screen with the patient and review pharmacy refill data together (Figure 1). Patients with MPR ≥80% received encouraging statements. For those with MPR < 80%, providers asked open-ended questions to elicit and address adherence barriers. Discussions were documented in the note. We measured feasibility, acceptability, and appropriateness using patient and provider surveys. Feasibility was also assessed by medical record documentation. We explored change in adherence by comparing MPR in the 3-month periods before and after the intervention visit.

Results: All 6 lupus clinic rheumatologists participated, and 134 follow-up SLE patients were seen during the pilot period (mean age 43, 96% female, and 53% black). Provider surveys showed high scores for acceptability (4.4/5), appropriateness (4.6/5), and feasibility (4.7/5) of the intervention. Among 48 patients who completed surveys, the most common reactions to the intervention visit were feeling determined (24%), empowered (21%), and proud (12%). No patient reported being angry, upset, or embarrassed. Ninety percent of clinic notes contained documentation of reviewing Surescripts data with the patient. Adherence rates comparing 3 months before and after the intervention visit increased for HCQ (n=121) from 60% to 71% (p=0.02), for DMARDs (n=85) from 49% to 61% (p=0.06), and for MMF (n=37) from 50% to 59% (p=0.1).

Conclusion: We developed an intervention based on formative results in collaboration with lupus clinic stakeholders that showed excellent acceptability, appropriateness, and feasibility among patients and providers. The intervention led to a statistically significant improvement in HCQ adherence and a trend for improvement in DMARD and MMF

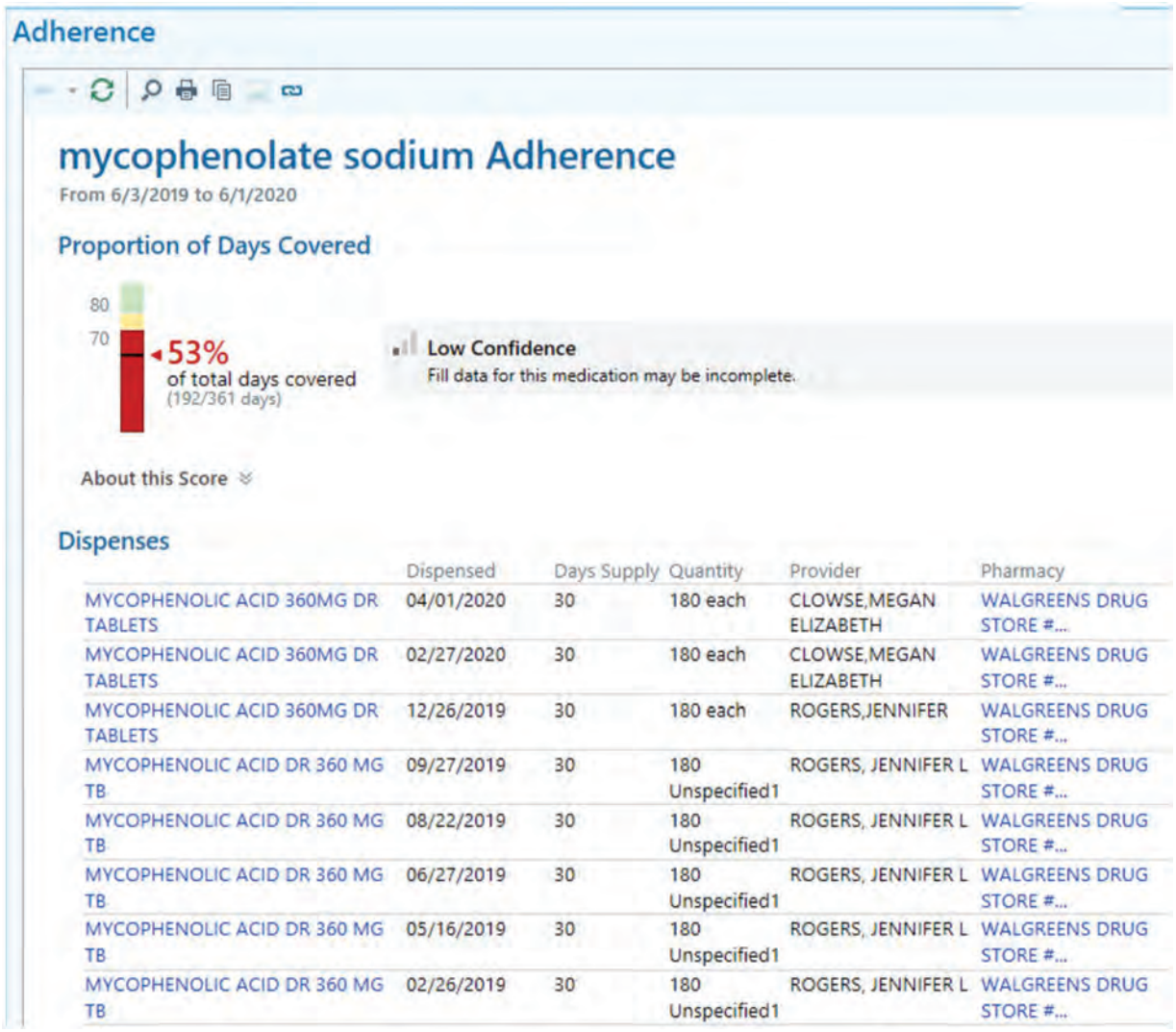

Figure 1. Screen shot of Surescripts pharmacy refill information providers review with patients during the clinical encounter.

adherence. Future work should elucidate the mechanisms by which this intervention works, assess its efficacy in a controlled setting, and adapt its use among other chronic rheumatic conditions.

Disclosure: K. Sun, None; **J. Rogers**, None; **R. Sadun**, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 2, Pfizer, 2; **J. Doss**, None; **L. Criscione-Schreiber**, None; **A. Barr**, None; **L. Eder**, None; **M. Maheswaranathan**, None; **A. Corneli**, None; **H. Bosworth**, None; **M. Clowse**, UCB, 5, GSK, 2, 5, Astra Zeneca, 5, Pfizer, 2.

Abstract Number: 0592

A Rheumatology-Driven Protocol and Treatment Algorithm of SARS-CoV-2 Cytokine Release Syndrome and Its Associated Outcomes

Sandy Lee[1], Neha Chiruvolu[2], Muntarin Karim[3], Patil Injean[4], Loomee Doo[5], Donna Jose[6], Deepa Panikkath[1], Micah Yu[5], Anna Lafian[5], Wendy De La Pena[7], Albert Chow[8], Karina Torralba[9], Vaneet Sandhu[10], Mehrnaz Hojjati[5], Marven Cabling[5] and Christina Downey[1], [1]Loma Linda University Medical Center, Redlands, CA, [2]UC Riverside School of Medicine, Riverside, CA, [3]Loma Linda University Health System, Loma Linda, CA, [4]LOMA LINDA UNIVERSITY MEDICAL CENTER - RHEUMATOLOGY, Redlands, CA, [5]Loma Linda University Medical Center, LOMA LINDA, CA, [6]Loma Linda University Medical Center, Ontario, CA, [7]PRCSG, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [8]Loma Linda University, San Bernardino, CA, [9]Loma Linda University School of Medicine, Redlands, CA, [10]Loma Linda University, Loma Linda, CA

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Background/Purpose: The newly identified SARS-CoV-2 has brought Cytokine Release Syndrome (CRS) to a level of prominence not often seen in adult medicine. Mortality rates of CRS in JIA, Kawasaki disease and SLE are between 30-60%. There is no published mortality rate due to SARS-CoV-2-CRS. A rheumatology division handling inpatient consultation services at an academic medical center and a county hospital developed institutionally mandated treatment algorithms with the goal to identify and treat patients with CRS. We are unaware of any other rheumatology division in the USA that has taken an institution-level role in managing SARS-CoV-2-CRS. The objective of this study is to determine if this algorithm was effective in preventing mortality rates of more than 30%.

Methods: Representatives from the Divisions of Rheumatology, Infectious Disease, Pulmonary and Critical Care Medicine, and the head of Pharmacy and the Pharmacy and Therapeutics (P&T) Committee were involved in institutional protocol development at each hospital. With the acknowledgement that CRS is a rheumatologic condition, four rheumatologists and five fellows reviewed rheumatologic and hematologic medical literature on CRS in JIA, SLE, Kawasaki Disease and hemophagocytic lymphohistiocytosis to define clinical features that would guide diagnosis and treatment of CRS. Consensus was reached for laboratory tests and result thresholds for early CRS monitoring and diagnosis, and for first and second-line agents including contraindications and precautions for each (Figure 1, Table 1). Final approval was done by the protocol development committee. During implementation, further revisions

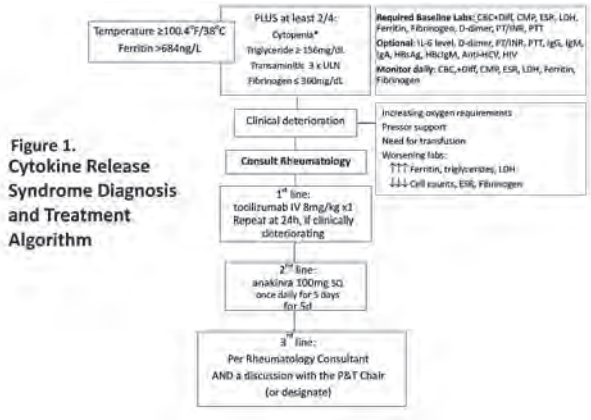

Figure 1. Cytokine Release Syndrome Diagnosis and Treatment Algorithm

Figure 1. Cytokine Release Syndrome Diagnosis and Treatment Algorithm

Table 1. Treatment Considerations for Cytokine Release Syndrome due to SARS-CoV-2 for patients referred to a Rheumatology Consultation Service

	Therapy	Dose	Comments
1st Line	tocilizumab (anti-IL6)	8mg/kg IV x 1 (800mg maximum dose); repeat if no clinical improvement within 24-48 hours For dosing, consider rounding to the nearest available vial size: 80mg, 200mg, 400mg	• Pertinent Drug Interaction: CYP3A4 Substrates (High risk with Inducers) • No renal adjustment; • Contraindications: Known hypersensitivity to Tocilizumab or any component • Caution: Monitor liver enzymes, platelet counts, neutrophils • Risks: GI perforation risk; thrombocytopenia, neutropenia; liver enzyme elevation; Herpes zoster reactivation
2nd Line	anakinra (anti-IL1)	100 mg SQ once daily x 5 days	• Not to be combined with other biologic DMARDs; clozapine; live vaccines • Contraindications: Hypersensitivity to E.coli derived proteins, anakinra or any component of the formulation; use with caution: CrCl<30mL/minute or ESRD
3rd Line	Per Rheumatology Consultant AND after discussion with the P&T Committee Chair (or designate)		
	Any use of the above immunomodulatory drugs intended as treatment of COVID-19 complications which deviates from this table, including administration route &/or dosing, requires a discussion with the P&T Committee Chair (or designate) before the drug is verified by the Pharmacist, or administered by Nursing.		

Table 1. Treatment Considerations for Cytokine Release Syndrome due to SARS-CoV-2 for patients referred to a Rheumatology Consultation Service

Table 2. Outcomes of SARS-CoV-2-CRS patients managed using a Rheumatology-Driven Treatment Algorithm at a University Medical Center and County Hospital

Patients diagnosed with SARS-CoV-2 referred to rheumatology for CRS evaluation	Total N = 150	University Hospital, N= 64	County Hospital N=86
Patients diagnosed with CRS and received a biologic agent	71 (47.3%)	21 (32.8%)	50 (58.1%)
Deaths	31 (20.7%)	16 (25%)	15 (17.4%)
Deaths attributed to MAS/CRS or its complication	20 (28.2%)	9 (42.9%)	11 (22%)
Patients requiring ICU admission	65 (43.3%)	31 (48.4%)	34 (39.5%)
Patients with CRS requiring ICU admission	43 (60.6%)	16 (76.2%)	27 (54%)
Patients with CRS not needing ICU level of care	29 (40.8%)	5 (23.8%)	24 (48%)
Patients with CRS discharged from the ICU	19 (26.8%)	7 (33.3%)	12 (24%)
Patients with CRS still hospitalized in the ICU	5 (7%)	1 (4.8%)	4 (8%)
Patients with worsening labs but did not meet criteria to make the diagnosis of CRS, treated with corticosteroids	27 (18%)	14 (21.9%)	13 (15.1%)

Table 2. Outcomes of SARS-CoV-2-CRS patients managed using a Rheumatology-Driven Treatment Algorithm at a University Medical Center and County Hospital

to biologic contraindications and third-line agent options were made. Regular updates to biologic supplies were coordinated between rheumatology and pharmacy. Outcome assessments included tracking 1) mortality rates among the general SARS-CoV-2 population vs those with CRS, 2) number of CRS patients requiring admission to the intensive care unit (ICU), 3) number of CRS patients who received biologics vs those who received corticosteroids.

Results: Rheumatology was consulted on 150 patients diagnosed with SARS-CoV-2 infection for evaluation for possible CRS between March 15, 2020 through May 30, 2020. Protocol criteria for CRS was met by 71 patients (Table 2) with 43 of those patients requiring ICU admission. There were 19 patients stable for transfer back to non-COVID medicine service. There were 27 patients who did not formally meet CRS criteria who were given corticosteroids for a suspicion for impending CRS. With overall hospital mortality rate of 20.7%, 31 deaths from the referral cohort were noted, with 20 attributed to CRS, rendering a mortality rate 28.2%.

Conclusion: Using our protocols, we met our goal to minimize mortality rates below 30%. Advantages to having a rheumatology protocol include regulation of hospital pharmacy supplies of biologics, gaining experience in handling medication side effects in consideration of past and current medical issues, and improving interdisciplinary care across pharmacy and various medical services.

Disclosure: S. Lee, None; **N. Chiruvolu**, None; **M. Karim**, None; **P. Injean**, None; **L. Doo**, None; **D. Jose**, None; **D. Panikkath**, None; **M. Yu**, None; **A. Lafian**, None; **W. De La Pena**, None; **A. Chow**, None; **K. Torralba**, None; **V. Sandhu**, GSK, 8; **M. Hojjati**, None; **M. Cabling**, None; **C. Downey**, None.

Abstract Number: 0593

Patient Characteristics and Factors Affecting Decision-Making Regarding Total Knee Replacement by Different Types of Physicians Treating Patients with Knee OA

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Background/Purpose: Total knee replacement (TKR) is considered an effective knee OA treatment and is a commonly performed orthopedic procedure that relieves pain and improves function and quality of life.[1] However, up to 20% of patients may not achieve good clinical outcomes.[2] Also, comorbidities and patient factors may limit the ability to safely perform the TKR. The objective of this was to identify the percentage and distribution of TKR surgical candidates across specialties (rheumatologists [RH], orthopedic surgeons [OS], sports medicine [SM] physicians, and pain specialists [PS]) to gain insight into patient characteristics influencing TKR candidacy.

Methods: Board-certified physicians with >2 years in practice and >10 knee OA patients per week participated in an interview about their two most recent knee OA patients. Interviews were conducted from March to April 2019 and assessed demographics, referral patterns, comorbidities, time to treatment, imaging use, candidacy for TKR, and reasons for noncandidacy. Multiple reasons for TKR noncandidacy per patients were allowed. Since no patient-iden-

	Total N=854	Orthopedist (OS) n=352	Rheumatologist (RH) n=250	Sports Medicine (SM) n=152	Pain Specialist (PS) n=100
Mean age		C	C		C
65 years of age or older (total)		C	C		C
Mean age when symptoms started		BCD			
Male		B			
Female			A		
Mean BMI				AB	AB
BMI ≥35				AB	AB
Not currently employed (total) due to inability to perform function					ABC
Bilateral OA (total)			ACD		ABC

Figure 1: Patients' path to TKR

% of Patients Who Had a TKR
Among total patients (n=854)

Yes 14% | No 86%

Years from diagnosis to first TKR	TKR patients with diagnosis dates n=59
Within a year of diagnosis	20%
2–3 years after diagnosis	31%
4–10 years after diagnosis	27%
More than 10 years after diagnosis	22%
Mean # of years	5.34

16% of Ortho TKR patients (n=43) had the TKR within a year of diagnosis, 33% 2–3 years post diagnosis, 28% 4–10 years post diagnosis, and 23% more than 10 years post diagnosis

% of Patients Who Are Candidates for TKR
Among patients who have not had two TKRs (n=779)

Yes 49% | No 37% | 15%

Time frame for TKR	TKR candidates n=380
Within next 12 months	38%
Ortho	53%
Rheum	21%
SM	33%
Pain	16%
Next 1–2 years	29%
In more than 3 years	11%
No time frame	23%

Reasons why not a candidate	TKR non candidates n=286	
Mild disease	65%	Ortho: 70% Rheum: 66% SM: 74% Pain: 31%
Patient preference	29%	Ortho: 23% Rheum: 30% SM: 30% Pain: 44%
Age	16%	
Overall health	12%	
Weight	10%	Ortho: 14% Rheum: 5% SM: 13% Pain: 13%
Smoking status	5%	

tifying information was included, this project was exempt from IRB review and HIPAA consent. As this study was designed to assess multiple characteristics and associated effect modifications, a confidence level of 90% was used.[3]

Results: Overall, the mean age of knee OA patients was 65 years (range: 63 years for SM patients to 66 years for PS patients) (Table 1). Primary care physicians were the most common referrers to RH (83%) and the reported mean time from symptom onset to diagnosis was 3.4 years (longest in RH patients; 4.5 years). Overall, the mean number of comorbidities was 2.6, with the most common being hypertension and obesity (Table 2). The mean pain score was 5.5 (0–10 NRS) and 58% of RH patients had moderate pain. RH saw predominantly KL grade 3 (55.6%) patients whereas OS saw more KL grade 4 (45.3%) patients. TKR candidacy was assessed for 779 patients; approximately half of these were identified as future surgical candidates, with 38% projected to undergo TKR within the next 12 months. Overall, of 286 (37%) identified as TKR noncandidates, 65% had mild disease or well-controlled symptoms. Among RH noncandidates (42%, n=105), additional reasons for TKR exclusion included patient preference (30%), age (11%), overall health (10%), weight (5%), and smoking habits (5%) (Table 2). Limitations to this study included potential

Table 2: Comorbidities and reasons for TKR noncandidacy

Comorbidities	Total N=854	Orthopedist (OS) n=352	Rheumatologist (RH) n=250	Sports Medicine (SM) n=152	Pain Specialist (PS) n=100
Average # of comorbidities	2.6	2.3	2.6[A]	2.8[A]	3.2[AB]
Hypertension	57% (n=485)	59% (n=206)	57% (n=142)	57% (n=87)	50% (n=50)
Obesity	38% (n=326)	33% (n=117)	40% (n=99)[A]	46% (n=70)	40% (n=40)
Hyperlipidemia	33% (n=279)	28% (n=98)	36% (n=89)[A]	41% (n=63)[AD]	29% (n=29)
Type 2 diabetes	25% (n=210)	22% (n=76)	22% (n=54)	33% (n=50)[AB]	30% (n=30)[A]
Chronic back pain	21% (n=182)	17% (n=-60)	19% (n=48)	24% (n=36)[A]	38% (n=38)[ABC]
Anxiety/depression	19% (n=160)	17% (n=59)	16% (n=41)	21% (n=32)	28% (n=28)[AB]
CVD	18% (n=155)	18% (n=64)	15% (n=38)	17% (n=26)	27% (n=27)[ABC]
Reason for noncandidacy	**Total N=286**	**Orthopedist (OS) n=80**	**Rheumatologist (RH) n=105**	**Sports Medicine (SM) n=69**	**Pain Specialist (PS) n=32**
Mild disease/ symptoms controlled	65% (n=186)	70% (n=56)[D]	66% (n=69)[D]	74% (n=51)[D]	31% (n=10)
Patient preference	29% (n=84)	23% (n=18)	30% (n=31)	30% (n=21)	44% (n=14)[A]
Age	16% (n=45)	18% (n=14)	11% (n=12)	17% (n=12)	22% (n=7)
Overall health	12% (n=35)	14% (n=11)	10% (n=11)	9% (n=6)	22% (n=7)
Weight	10% (n=29)	14% (n=11)[B]	5% (n=5)	13% (n=9)[B]	13% (n=4)
Smoking status	5% (n=14)	6% (n=5)	5% (n=5)	---	13% (n=4)

Key: Statistical significance, $P<0.1$; A: versus orthopedist, B: versus rheumatologist, C: versus sports medicine physician, D: versus pain specialist

selection bias, confounding by risk factors, inability to show causation, small n's, missing data, and pre-COVID-19 proposed timeline for TKR.

Conclusion: In this observational chart review, of the 42% of TKR noncandidates who were RH patients, several patient factors were identified as reasons for exclusion (patient preference, age, overall health, and lifestyle choices [such as smoking]). Patient preference contributed the largest impact (30%) and other influences were well characterized, suggesting further investigation of patient-focused factors that impact decision-making regarding TKR is warranted.

References

1. NEJM 2015; 373:1597-1606
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Disclosure: A. Bedenbaugh, Samumed, 3; **V. Lee**, Samumed, 5; **G. Oderda**, Samumed, LLC, 5; **S. Kennedy**, Samumed, LLC, 1, 3; **J. Tambiah**, Samumed LLC, 1, 3, Samumed LLC, 1, 3; **D. Brixner**, Samumed, 5; **T. McAlindon**, Pfizer, 1, Sanofi Aventis US, 1, Kolon Tissuegene, 1, Samumed, 1, Seikagaku, 1, Kiniksa Pharmaceuticals, 1, Anika Therapeutics, 1.

Abstract Number: 0594

Mechanical and Temperature Stress During Biologic Shipments to Rheumatology Patients

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SESSION INFORMATION
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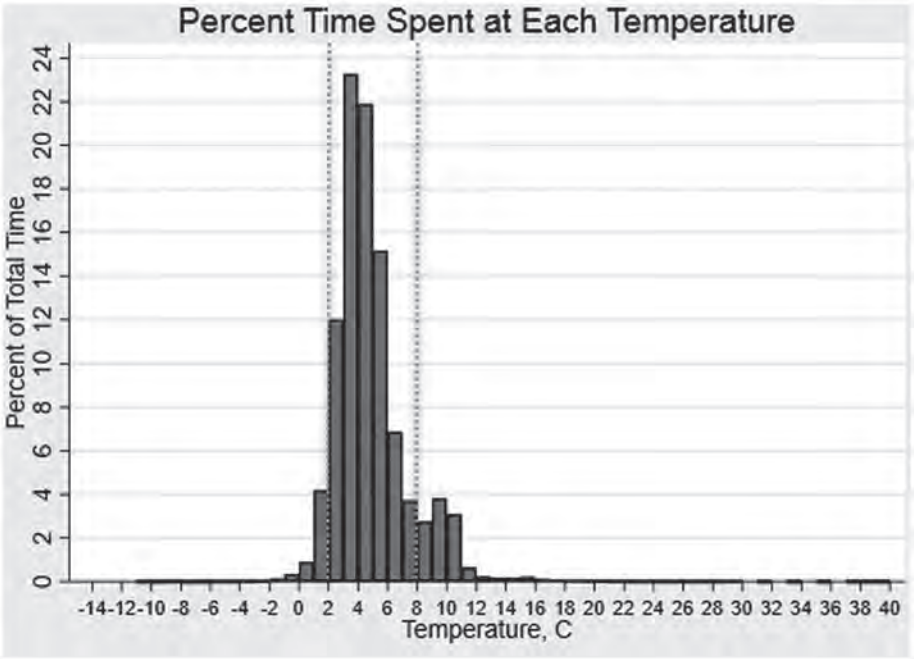
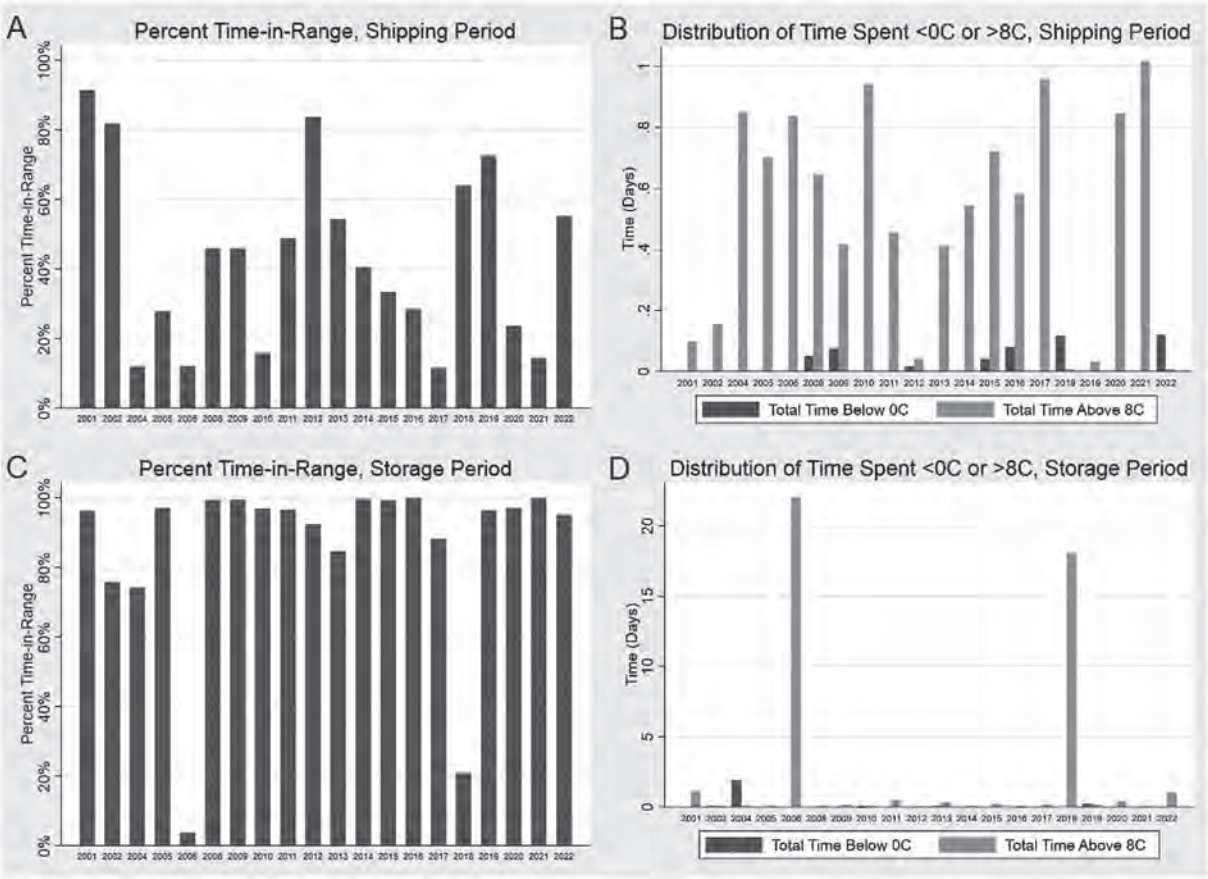
Background/Purpose: Biologic medications are expensive, and unfortunately their immunogenicity contributes to loss of efficacy over time. Protein particles may form as a result of medication mishandling and are known to enhance the immunologic response to biologics. In order to identify factors contributing to mishandling, we evaluated the temperature excursions and mechanical shock exposures during shipment of biologic medications to patients and described the storage practices of these medications by patients.

Methods: Colorimetric shock indicators registered the highest forces sustained during shipments. During both shipment and patient storage, thermocouple data loggers recorded temperatures every 2 minutes. After medication administration, patients completed and returned a questionnaire along with the data logger. The questionnaire evaluated factors like patient storage habits, refrigerator age, and frequency of adverse medication events. Temperature differences were compared between transit and storage intervals using the Wilcoxon rank-sum test. We also determined if refrigerator location was associated with temperature percent time-in-range and number of excursions out of range under controlled conditions.

Results: Twenty shipments were analyzed. Shock sensor results showed that 95%, 25%, and 5% of sensors experienced an impact of 25*g*, 50*g* and 75*g*, respectively. Medications were in-range (2-8^{0}C) temperatures only 84% of the total time (Fig. 1). The shipping period had an overall percent time-in-range of 43%, compared to 86% during the storage period (Fig 2A,C). In both shipping and storage periods, time spent over 8^{0}C was more common than time spent below 0^{0}C (Fig. 2B,D). Under controlled experimental conditions for biologic packaging, we identified a relationship between refrigerator location and both percent time in range (p=0.05) and number of excursions (p=0.004) (Fig. 3A,C). The interior rear of the refrigerator near the cold output accounted for this difference with only 68%



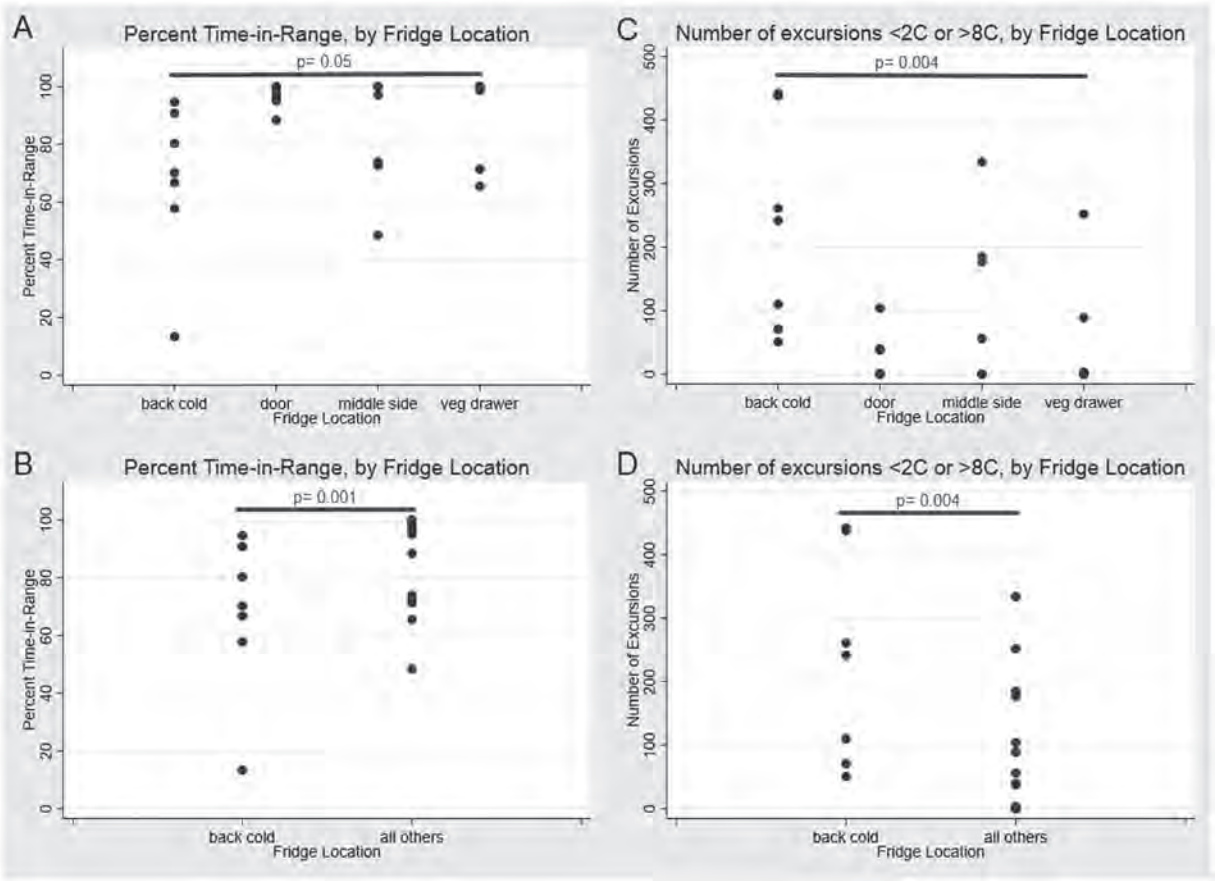
Percent time at each temperature for all trips in aggregate. Dashed lines indicate recommended temperature range.



Depicts the percent time in range and the distribution of time spent "hot" (>8^{0}C) or "cold" (<0^{0}C), for shipping (3A, 3B) and storage (3C, 3D) periods.

percent time-in-range and 231 average excursions, (p=0.01 and p=0.004 vs. other locations, Wilcoxon rank sum) (Fig. 3B,D). Dermatologic reactions were the most common adverse event, but there was no association between frequency of adverse events and mishandling (temperature excursions and mechanical shock).

Conclusion: Our current packaging strategy is insufficient both to maintain recommended temperatures during shipping and to mitigate mechanical shocks. Patients maintained biologics at more appropriate storage temperatures compared to temperature control during shipping, but additional patient education may lead to further improvements.



Scatter plots comparing each location overall for percent time-in-range (4A) and number of excursions (4B). Also comparing the back cold (near cold output) to all other areas, percent time-in-range (4C) and number of excursions (4D).

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Abstract Number: 0595

High Satisfaction with Tele-medicine in a New York City Clinic

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
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Background/Purpose: The face of medicine is changing with the time. A twenty-first century technological revolution in medicine happened in March 2020 as the COVID-19 pandemic reached the US. As it quickly became clear that face-to-face clinical medicine could not continue, at least not for some time, medical practices across the country were forced to offer virtual medicine encounters to the vast majority of patients. This change, while protecting patients, also had a cost that we are still trying to ameliorate. In Rheumatology, and other cognitive specialties, the physical exam is a critical component of the evaluation of patients with rheumatic diseases and the ability of current

technology to allow for accurate evaluations are limited. As we are struggling to understand the correct balance between face-to-face and telemedicine over the next several months, we sought to evaluate patients' satisfaction with telemedicine in a New York City rheumatology practice.

Methods: Questionnaires asking about the level of satisfaction with their telemedicine experience were offered to patients that had had a recent telemedicine encounter. The questionnaires asked about their experience and satisfaction with telemedicine and communication with the provider. The abstract reports these responses.

Results: Of the 100 patients, 91% were women, mean age 44.3, 25% black, 26% Hispanic, all insured, and over 90% had a diagnosis of SLE or other types of inflammatory arthritis (RA, UCTD, SS, PsA, SpA). Patients were asked how satisfied they were with telemedicine, and the results were unexpected: 84% reported high levels of satisfaction

Table 1. Telemedicine Evaluation Survey

Respondents ($n = 100$)	*n= 100*
How satisfied were you with your previous telemedicine visit?	
Highly satisfied	50 (50%)
Satisfied	34 (34%)
Neither satisfied not unsatisfied	11(11%)
Not Satisfied	5 (5%)
Highly Unsatisfied	0 (0%)
Reasons for satisfaction	73 (73%)
Avoid coming into the office	77 (77%)
Call went smoothly	75 (75%)
Decrease their concerns over condition, medications and risks of COVID	
Reasons for dissatisfaction	4 (4%)
Technical difficulties.	2 (2%)
Visit was too short.	4 (2%)
Visit was too basic for their needs.	
How comfortable were you with your previous telemedicine visits?	
Very comfortable	62 (62%)
Comfortable	24 (24%)
Neither comfortable nor uncomfortable	11 (11%)
Uncomfortable	3 (3%)
Highly uncomfortable	0 (0%)
The physician was able to address what was bothering me through the telemedicine visit	
Strongly agree	54 (54%)
Agree	37 (37%)
Don't Know	5 (5%)
Disagree	4 (4%)
Strongly disagree	0 (0%)
Overall, compared to an in-person visit, the telemedicine visit was?	
Much better	10 (10%)
Better	6 (6%)
Same	57 (57%)
Worse	25 (25%)
Much worse	2 (2%)
I would have a telemedicine appointment in the future, if given the option.	
Yes	77 (77%)
Unsure	14 (14%)
No	9 (9%)

Table 2. Demographic of patients	
Characteristics	Subjects (N=100)
Gender, n (%)	
Male	9 (9%)
Female	91 (91%)
Age, mean ± SD (range), years	44.3 ± 14.6 (20-75)
20-30	18 (18%)
30-40	22 (22%)
40-50	22 (22%)
50-60	21 (21%)
60-70	13 (13%)
70-80	4 (4%)
Race, n (%)	
White	41 (41%)
Black or African American	25 (25%)
Asian	7 (7%)
Ethnicity, n (%)	
Hispanic	26 (26%)
Health Insurance	
Insured	100 (100%)
Diagnoses	
SLE	60 (60%)
Rheumatoid Arthritis	7 (7%)
UCTD	7 (7%)
Psoriatic Arthritis	5 (5%)
Sjogren's Syndrome	4 (4%)
Spondylitis	3 (3%)
Other (Sarcoidosis, Myositis, OA, FM, MCTD, Uveitis, Vasculitis)	14 (14%)

(highly satisfied or satisfied) with only 5% reporting that they were not satisfied. 86% of patients reported that they were comfortable with the new format. In 92% of patient reports, physicians were able to satisfactorily address the issues and concerns that prompted the visit. 57% of patients reported that the experiences were very similar to the in person experiences. Finally, when asked whether they would use telemedicine in the future, 77% of patients responded "yes". See further details in the table below. None of the demographic variables correlated with satisfaction or comfort with telemedicine visits.

Conclusion: These data support a high level of patient satisfaction and comfort with telemedicine, suggesting that the transition from in person medicine to telemedicine has been successful. The balance for each subspecialty between face-to-face, when signs and symptoms need to be elicited, and telemedicine remains to be determined. Further data that comprise wider demographics, socio-economics, disease manifestations, and insurance are needed to fully understand the impact of telemedicine on patient care in Rheumatology practices.

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Abstract Number: 0596

Clinical Academic Rheumatology: A Boon for Health Systems

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Background/Purpose: Finding a balance between clinical and scholarly productivity is a challenge for many academic clinician-educator (CE) rheumatologists. An examination of workload and practice-generated downstream revenue serves to determine if the financial value generated by services rendered by rheumatologists are proportionate to the financial value created for a health system. A 2005 study found that academic rheumatologists generate $10.02 for every $1.00 they receive for an office visit.[1] 15 years later, this study aims to determine the financial gains an academic health system can expect from CE rheumatologists.

Methods: A retrospective analysis of ordering practices from August 2017 - February 2019 was done.

Individual workload as averaged full-time equivalents (FTEs) based on time spent on inpatient consultation, outpatient faculty practice income-generating activities, academic and administrative duties. Revenue-generating activities were classified as those that benefited the hospital directly (downstream revenue) and the rheumatology division directly through the faculty practice (Table 1). CPT codes for all charges were assigned based on Medicare Allowable Charges for 2019.

Table 1. Academic productivity by 5 academic rheumatologists over an 18-month period

Academic marker	Outcome
Promotion/Rank	1 full professor (achieved within 5 years of start of employment), 1 associate professor (within 4 years), 3 assistant professors
Teaching time	2 half-days of trainee supervision on average per week, 1 monthly lecture for trainees
Peer Reviewed publications	In total, 12 publications in high quality rheumatology journals
ACR abstracts	12 accepted and presented
Book Chapters	1 book chapter each by 2 faculty
Ongoing research projects including clinical trial	1 NIH funded research, 1 investigator initiated pharmaceutical company sponsored research, 4 industry sponsored trials, 7 non-funded investigator initiated research
Centers development	7 virtual centers approved and under development (Lupus, Inflammatory arthritis, Bone Health and Osteoporosis, Vasculitis, Scleroderma, Myositis, Sjogren's Disease)

Table 2. Revenues generated per clinical activity by rheumatologists August 2017 - February 2019

Activity	Average Revenue
Direct Rheumatology In-Office Clinical Revenue (Non-Hospital Based Clinic)	
Procedures (I,e, Arthrocentesis)	$5,903
Point-of-care ultrasounds	$5242
Infusions*	$48,372
Downstream Revenue to Hospital from Rheumatology Clinics	
Referred procedures to other specialties	$60,310
Inpatient consultations	$300,189
Laboratory tests	$347,542
Radiology (i.e. MRI, CT, xrays, DXA)	$123,900
Hospital Infusion Center** Single Drug revenue based on	$35,748,000 Reference drug: Rituximab 100mg vial cost: $9818.09 Estimated 340b pricing: 60% below WAC 100 infusions, $10,000 base charge
Contracted Services***	

Legend: MRI, magnetic resonance imaging; CT, computed tomography, DXA, dual energy absorptiometry; US, ultrasound, WAC, wholesale acquisition price *In-office infusion revenues were based solely on procedure codes for infusions. We currently do not engage in drug buy & bill or other reimbursement programs. **Estimates of revenue as numbers of patients on various medications referred, 340b pricing and hospital charges for each drug, and each infusion procedure (J) code, for were not made available by administrators. Notes. Faculty also provide services at a county hospital, and 2 FQHCs. Average faculty salary $225,000 based on 80% private practice area salary and 20% academic salary

One limitation encountered was the unavailability of hospital-based infusion center revenue. We extrapolated data based on infusion drug costs and reimbursement values of the most commonly prescribed drug prescribed (Rituximab 1000mg). We also reviewed academic productivity of faculty in the said period (Table 1).

Average FTE allocation is 0.2 FTE academic time, and 0.8 clinical duties with 0.4 FTE allocated for clinic care with trainees, and 0.4 FTE faculty practice clinic care. Faculty practice care was reduced for on-call hospital consultations (0.5 FTE). Additional FTEs allowances were given for clinical directorships (0.1 FTE), division chief (0.1 FTE) and fellowship program directorship (0.3 FTE). Academic productivity was notable (Table 1).

Results: An average of $229,041 between the five physicians for office visits was generated in evaluation and management services. The total downstream revenue generated from these visits averaged $36,579,941 per physician (Table 2). To calculate hospital infusion revenues, Rituximab 1000mg x 2 doses was used as a reference point dosed

every six months (3 doses during the study time frame). 100 vials totaling 1,000mg at $9,818.09 per vial with 340b pricing considered gross revenue was $35,748,000 per physician.

Conclusion: For every $1 generated though office visits by the five practicing Academic Rheumatologists at our institution $159.70 dollars were generated through downstream revenue, nearly 16 times the 2005 study. Most likely this is an underestimation as this study is unable to account for eleven other infusion products. Consideration must be made to consider hospital-based support for by academic rheumatologists, and for additional compensation mechanisms that consider academic productivity.

[1] Wickersham, Pendleton, Diane Golz, and Sterling G. West. "Clinical academic rheumatology: getting more than you pay for." *Arthritis Care & Research: Official Journal of the American College of Rheumatology* 53.2 (2005): 149-154.

Disclosure: K. D'Anna, None; **K. Torralba**, None; **C. Downey**, None; **C. Silva Lynch**, None.

Abstract Number: 0597

Telemedicine in Pediatric Rheumatology During COVID-19: The PR-COIN Experience

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Background/Purpose: Healthcare teams were forced to rethink the way they practiced medicine during the COVID-19 pandemic. Many teams transitioned from conducting in-person visits to virtual telemedicine visits with limited knowledge, experience with, or infrastructure for telemedicine. PR-COIN, a quality improvement collaborative of 20 North American pediatric rheumatology centers, set out to capture the experience of the rapid adoption of telemedicine, understand its usage and acceptability, and gather opinions on its continued use.

Methods: A REDCap® survey was sent to a representative from each PR-COIN site to collect data about their experience with telemedicine and its use during COVID-19. Quantitative data were analyzed using descriptive statistics and qualitative data were thematically analyzed.

Results: 19/20 of the PR-COIN sites responded to the survey. All sites transitioned from in-person to virtual telemedicine visits during the COVID-19 state of emergency (Figure 1). Most centers reported using both videoconferencing system and telephone to conduct their telemedicine visits (Table 1). All centers reported seeing both new consultations and follow up patients over telemedicine.

13/19 (68%) reported at least 50% of their providers consistently used pediatric Gait Arms Legs and Spine (PGALS) to document musculoskeletal exams in patients with juvenile idiopathic arthritis (JIA). Items that were not well-doc-

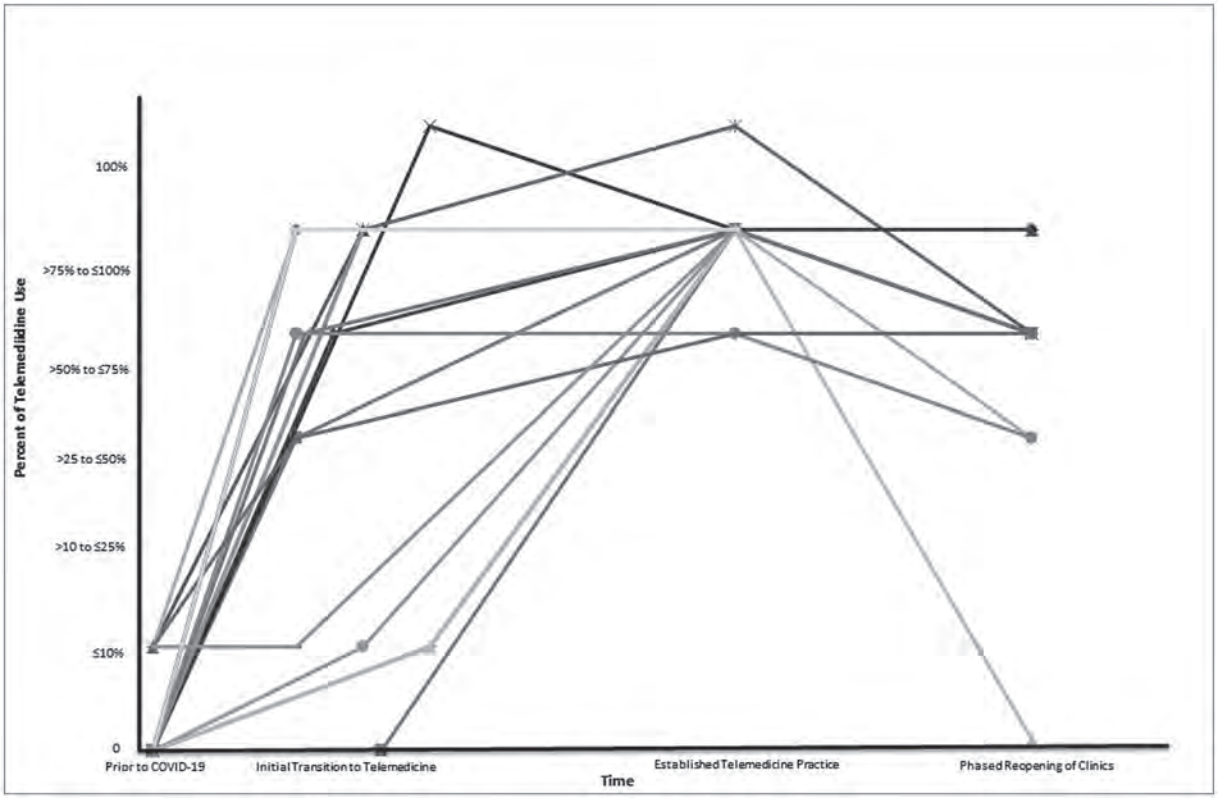

Figure 1. Use of Telemedicine Over Time

Medium Used to Conduct Virtual Telemedicine Visits	Number of Centers
Videoconferencing system, telephone	7
Videoconferencing system	3
Videoconferencing system, electronic health record patient portal	2
Videoconferencing system, telephone, telemedicine center	2
Videoconferencing system, telephone, electronic health record	2
Electronic health record patient portal	1
Electronic health record, telephone	1
Videoconferencing system, telephone, electronic health record patient portal, telemedicine center	1

Table 1. Mediums Used to Conduct Virtual Telemedicine Visits

umented during telemedicine visits included: weight, height, disease activity, and treatment targets. 11/19 (58%) centers reported collecting patient global assessment, pain intensity and morning stiffness during the telemedicine visits. Two sites indicated they did not collect any patient reported outcome measures (PROMs), while three indicated they collected more complex PROMs.

7/19 (37%) centers reported performing research-related activity during telemedicine visits. 2/7 (29%) reported the ability to consent patients over telemedicine and 6/7 (86%) reported performing follow-up visits for observational studies.

All responding PR-COIN centers agreed that telemedicine visits were able to meet provider needs and the providers from all but one center believed that telemedicine visits were able to meet patient needs. Reasons to justify an in-person visit included presence of active disease, worsening of condition, and parent request/desire.

Identified benefits of telemedicine visits included convenience, no travel, and continuity of care for families who were hesitant to have an in-person visit. Identified challenges with telemedicine visits included limited ability to perform physical exams, difficulty assessing disease activity, and access to technology.

All centers supported the continued use of telemedicine after the pandemic. Centers indicated that they would be willing to see both new [15/19 (79%)] and follow up [14/19 (74%)] patients over telemedicine.

Conclusion: Healthcare providers have recognized the potential of incorporating telemedicine into their routine practice to serve a portion of their patients. PR-COIN plans on identifying best practices and creating tools to address existing barriers.

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Abstract Number: 0598

Impact of a Dedicated Lupus Nephritis Clinic to Improve Time to Biopsy and Care Quality

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Background/Purpose: Lupus nephritis (LN) contributes to a 10-fold higher risk to develop kidney failure and 26-fold higher mortality compared to peers. Kidney biopsy remains a gold-standard to diagnose LN and start therapy. Yet, our prior study highlighted that the average wait time to see a specialist and undergo a kidney biopsy was >50 days, with no change over 20 years (1997-2017). Further, studies report that high-impact quality process measures, such as ACE inhibitors use and addressing social needs, are often missed during routine SLE visits, contributing to poor LN outcomes. Therefore, we implemented a multidisciplinary LN clinic to provide targeted strategies to overcome such barriers to improve care and LN outcomes. We aimed to examine time to biopsy and quality measures provided to LN patients before and after the implementation of LN clinic.

Methods: All validated adult LN patients with diagnostic kidney biopsy preformed between 2011-2020 were identified from our comprehensive native kidney biopsy database at an academic center. Data on sociodemographic, disease characteristics and biopsy date were abstracted from this database. We manually abstracted data on medications, date of abnormal labs or LN specialist referral, vaccinations and social needs to examine quality process measures. Time to biopsy was defined as time from abnormal labs or LN specialist referral until biopsy. Pre- and post-LN clinic period included patients who underwent biopsies between 2011-2017 and 2018-2020, respectively. We used KM analysis to compare time to biopsy during the two periods, and Cox Proportional hazards models to examine predictors of time to biopsy. We used Fisher and two-sample t-tests to compare socio-demographics and quality measures during these two periods.

Table 1. Demographics of Adult LN Patients During Pre- and Post-LN Clinic Periods

	Pre-LN Clinic n = 53	Post-LN Clinic n = 21	OR (95% CI)*	p value**
Socio-Demographics				
Age, Mean ± SD years	36±14	35.6±13		0.9
Female, n(%)	40 (75%)	13 (62%)	0.5 (0.2-1.8)	0.3
Non-White Race, n(%)	14 (26%)	10 (48%)	2.5 (0.8-8.2)	0.1
Smoking Ever, n(%)	20 (38%)	6 (29%)	0.6 (0.2-2)	0.4
CKD Stage ≥ 3, n(%)	17 (32%)	10 (48%)	1.7 (0.5-5.5)	0.4
Time to LN Biopsy				
Mean ± SD days	**202±489**	**22±26**		**0.01**
Median (IQR) days	**26 (7-120)**	**16 (8-21)**		**0.014**
Time to LN Therapy				
Median (IQR) days	7 (1-16)	7 (3-12)		0.2
LN Therapy Started/Used				
MMF, n(%)	35 (66%)	18 (86%)	3 (0.7-18)	0.15
CYC n(%)	9 (17%)	0	0 (0-1.2)	0.053
Others (RTX, AZA, Tacrolimus) n(%)	**2 (4%)**	**5 (24%)**	**7.7 (1.1-88)**	**0.017**
HCQ Use, n(%)	41 (77%)	20 (95%)	5.8 (0.8-262)	0.09
Quality Measures, n(%)				
ACE-I/ARB Present, n(%)	**32 (60%)**	**20 (95%)**	**13 (1.8-567)**	**0.008**
Flu Vaccination (Year of Dx), n(%)	43 (81%)	18 (85%)	1.3 (-.03-8)	0.99
Pneumococcal Vaccination, n(%)	**19 (36%)**	**18 (86%)**	**10 (2.6-62)**	**0.0002**
Pharmacist Consultation, n(%)	0	7 (33%)	-	<0.0001
Social Needs & Referral, n(%)	**4 (8%)**	**11 (52%)**	**15 (4-81)**	**<0.0001**

**OR and **p calculated using Fisher test for qualitative data & t-test for quantitative data; AZA Azathioprine; CKD Chronic Kidney Disease; CYC Cyclophosphamide; DM Diabetes Mellitus; Dx Diagnosis; IQR Inter-Quartile Range; HCQ Hydroxychloroquine; RTX Rituximab*

Table 1. Demographics of Adult LN Patients During Pre- and Post-LN Clinic Periods

Results: The pre-LN clinic period included 53 LN patients, the mean age was 36 years, 75% were female and 74% were white (Table 1). During the post-LN clinic period, 21 LN patients underwent diagnostic biopsy. The mean age was 35.6 years, 62% were female and 51% were white.

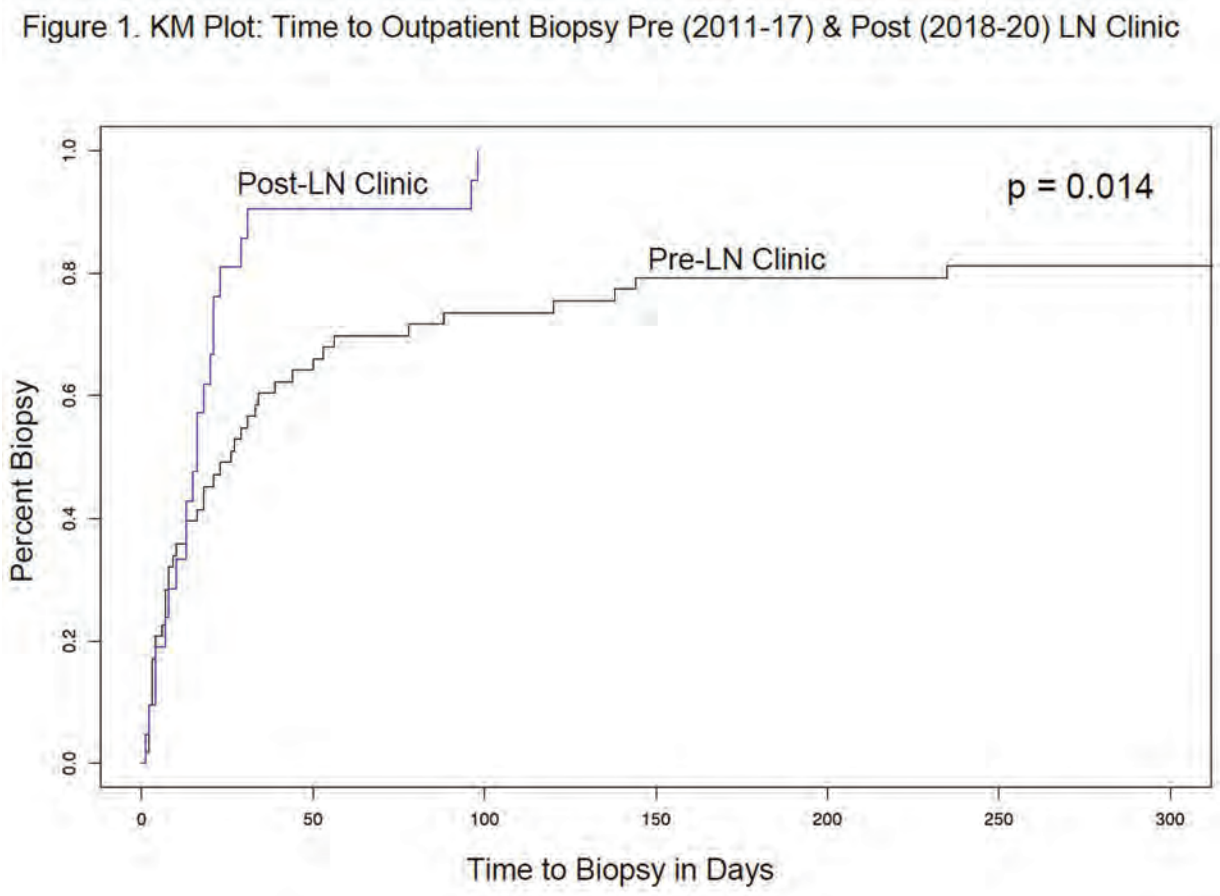

Figure 1. KM Plot: Time to Outpatient Biopsy Pre (2011-17) & Post (2018-20) LN Clinic

Table 2. Cox Proportional Hazards Model to Examine Predictors of Time to Biopsy

Variable	HR (95% CI)	p value
Age at LN Biopsy	0.98 (0.9-1.0)	0.6
Non-White Race	1.3 (0.5-3.2)	0.6
Female	1.3 (0.5-4.0)	0.5
Social Needs Identified	**4.1 (1.2-12)**	**0.007**
Urine Protein Creatinine Ratio, Time of Biopsy	1.1 (0.95-1.3)	0.2
CKD Stage 3 or above	2.2 (0.7-6.0)	0.2

Model includes all variables with p < 0.1 on univariate analysis; CKD Chronic Kidney Disease; LN Lupus Nephritis

Table 2. Cox Proportional Hazards Model to Examine Predictors of Time to Biopsy

The mean and median time to biopsy in the pre-LN clinic period were 202 and 26 (IQR 7-120) days, and during the post-LN clinic period were 22 and 16 (IQR 8-21) days. The median time to biopsy decreased by 10 days after starting the LN clinic (*p 0.014*; Figure 1). We found social barriers as the strongest predictor of longer wait times (*HR 4.1, 95% CI 1.2-12, p 0.007;* Table 2).

We found 13-fold higher odds of ACE inhibitors use in LN, 10-fold higher odds to complete pneumococcal vaccination, and 15-fold higher odds to address social needs during the post-LN clinic period compared to the previous period (Table 1). We noted a trend of increased hydroxychloroquine use in the post-LN clinic period.

Conclusion: This is one of the first studies to report significant improvement in wait times to diagnose LN after establishing a multidisciplinary LN clinic. Our study highlights that system and social barriers predict a delay in diagnosis, which can be addressed by including a social worker in specialized clinics. Finally, our study supports previous reports on higher quality measure performance in SLE subspecialty clinics.

Disclosure: S. Garg, None; **C. Plafkin**, None; **T. Singh**, None; **S. Panzer**, None; **C. Bartels**, Independent Grants for Learning and Change (Pfizer), 2.

Abstract Number: 0599

Evaluation of Telephone Consultations in Germany as an Additional Tool in Outpatient Rheumatology Clinics During the COVID-19 Pandemic

Ulrich Drott[1], Axel Braner[1], Thomas Kollewe[2], Harald Burkhardt[3] and **Florian Meier**[1], [1]Department of Rheumatology, University Hospital Frankfurt, Goethe University, Frankfurt, Germany, Frankfurt, Germany, [2]J. W. Goethe-Universität Frankfurt, FB Medizin, Frankfurter Arbeitsstelle für Medizindidaktik, Frankfurt, Germany, Frankfurt, Germany, [3]Department of Rheumatology, University Hospital Frankfurt, Goethe University, Frankfurt, Germany, Frankfurt am Main, Germany

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The Covid-19 pandemic holds multiple challenges for the healthcare system. Quick adoptions and adjustments are the mainstays during these times. Hygiene management and plans in a primary care center for Covid-19, especially for prone patients such as patients with inflammatory rheumatic diseases receiving immunosuppressive or immunomodulatory therapies, are difficult. Nonetheless, monitoring of these treatments must be ensured. As a result, implementation of telephone visits was sought and rapidly achieved for most of the outpatient consultations.

The aim of this retrospective analysis was to evaluate the opinion of the patients regarding telephone consultations as a substitute for regular outpatient visits during the COVID-19 pandemic.

Methods: Patients were pre-screened for applicability and availability of a telephone consultation. After four weeks of mixed outpatient clinics (physical visits and majorly telephone visits), we performed a survey to inform our current concept during the outbreak. Patients (n=104) were randomly selected assuring to pick visits throughout the consulting hours. A 14-item questionnaire was developed and applied (graduation from 1 [do not agree at all]) to 5 [fully agree]). Additionally, we noted changes in therapy.

Results: On average, patients were 54 years old and for the most part female (69.2%). In general, patients reported an high agreement for the telephone visit (median 5 for the first six items: questions were equally answered as in regular visits; symptoms were reported sufficiently, and readily; telephone visit adequate if no acute problems were

present; time saving; nonetheless well looked after). The quality of the connection did not influence the consultation and many (median 4) would participate in future telephone visits. Patients highly agreed to implement telephone visits as an additional tool for outpatient clinics despite the pandemic (median 5), however patients were divided as to favour physical visits or telephone or video consultations. Dosage adjustments were made in 14.4%, change of therapy at least in 5.7% of cases.

Conclusion: The participation in a pre-screened telephone consultation as an additive tool in the outpatient care of patients with rheumatic disease showed a high level of acceptance. It remains a matter of ongoing health services research as to which extent telephone and/or video consultations should steadily be implemented in outpatient rheumatology clinics, even after the Covid-19 outbreak, with regard to the current deficits in rheumatologic care, especially in Germany.

Disclosure: U. Drott, None; **A. Braner**, None; **T. Kollewe**, None; **H. Burkhardt**, AbbVie, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Boehringer Ingelheim, 5, 8, Bristol Myer Scripps, 5, 8, Chugai, 5, 8, Eli Lilly, 5, 8, Janssen, 5, 8, Novartis, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **F. Meier**, None.

Abstract Number: 0600

Gout Increases Length of Stay in Patients Hospitalized for Heart Failure Exacerbation

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: There is growing evidence that both the prevalence of gout and its burden on healthcare costs has increased over recent decades. It has been shown that hospitalization increases the risk of acute gout flare, which may prolong hospital stay compared to those without gout flare. It is unclear whether patients with history of gout would have longer hospital stays in general, or only when they have a flare. The objective of this study is to examine the effect of gout diagnosis and flare on the length of stay in patients admitted for heart failure exacerbation in a health care system.

Methods: We conducted a case control study using electronic medical record data from Columbia University Irving Medical Center. We searched for patients ≥18 years, with an inpatient hospitalization for a primary discharge diagnosis of heart failure exacerbation from 7/1/2012 to 6/30/2017 using ICD-9 and ICD-10. Cases were defined as those with two or more gout diagnoses prior to their heart failure admission. Controls were defined as patients without any diagnosis of gout prior to their admission. Cases were matched 1:2 to controls on the basis of age, sex, and total number of heart failure admissions during the study period. Gout flare was defined as any clinician documentation of gout flare during a hospitalization, and was ascertained by manual review. Primary outcome was length of stay (LoS). We used two-sample t-test to compare the log LoS between cases and controls. We used linear mixed effect model

Table 1.

	Controls (n= 492)	Cases (n = 246)
Age, *years*	71.67 (±13.95)	71.67 (± 13.95)
Sex, *no. (%)*		
Male	304(61.7%)	152(61.7%)
Female	188 (38.2%)	94(38.2%)
Insurance, *no.(%)*		
Commercial	243 (49.4%)	111 (45.1%)
Medicare	217 (44.1%)	126 (51.2%)
Self-Pay	7 (1.4%)	2 (0.8%)
Medicaid	25 (5.1%)	7 (2.9%)
Number of Admissions , *days*	1.325 (± 0.61)	1.325 (± 0.61)
Ejection Fraction, %	36.97 (± 18.97)	38.96 (± 18.55)
BMI	28.28 (± 11.55)	29.04(±8.00)
Elevated Troponin, *no.(%)*	111(22.6%)	39 (15.9%)
Baseline Na, *mEq/L*	137.78 (± 4.78)	138.51 (± 4.43)
Baseline BNP, *mEq/L*	5539.3 (± 11574.2)	5145.41 (± 8596.18)
Baseline Cr, *mEq/L*	1.76 (±1.48)	2.22 (± 1.60)

Baseline characteristics of patients with prior gout diagnosis (cases) and patients without prior gout diagnosis (controls). Except where indicated otherwise, values are mean ± SD. BMI: body mass index; Na: sodium; BNP: brain natriuretic peptide; Cr: creatinine, SD: standard deviation.

with random intercept to adjust for potential confounders and compared the adjusted LoS of gout patients with flare, gout patients without flare, and controls.

Results: We identified 545 admissions for heart failure exacerbation in 293 patients with a history of gout, and 5461 admissions for heart failure exacerbation in 3798 patients without a history of gout. A total of 978 admissions, consisting of 246 cases and 492 matched controls, were included in our analysis. Baseline data for cases and controls are summarized in *Table 1*. The log LoS was significantly longer in cases (1.86 ± 0.95) compared with controls (1.72 ± 0.94; $p = 0.0278$). Out of 326 case admissions, a gout flare was confirmed to have occurred in 42 (13%) admissions. The median LoS for those gout patients who flared was 10 days (interquartile range (IQR) = 10), compared to 6 days in those without flare (IQR = 8), and 6 days in patients without a history of gout (IQR = 9). The log LoS was significantly longer in those with gout who flared (2.41 ± 0.96) compared to those without gout (1.77 ± 0.90, $p < 0.0001$). The log LoS in those with gout who did not flare was not different from controls (1.82 ± 0.83; $p = 0.2465$). After adjusting for age, baseline electrolytes, body mass index, cardiac function, and socioeconomic status, the log LoS of patients that flared ($p < 0.0001$) remained significantly longer than controls, but not those who did not flare ($p = 0.042$).

Conclusion: Heart failure patients with gout had significantly longer hospitalizations than those without gout, an effect driven primarily by those gout patients who flare during hospitalization. Future work will focus on identifying risk factors for gout flares and its prevention in hospitalized patients.

Disclosure: D. DeMizio, None; **G. Wu**, None; **Y. Wei**, None; **J. Bathon**, None; **R. Wang**, Eli Lilly, 1, Novartis, 1.

Abstract Number: 0601

The "Why" of Drug Discontinuation; Clinical Review of EMR Notes for 2,545 Patients with Rheumatic Diseases

Kent Kwas Huston[1], Simon Helfgott[2], Scott Milligan[3], Jasvinder Singh[4], Nehad Soloman[5], Brandon Weil[3] and Colin Edgerton[6], [1]Kansas City Physician Partners, Kansas City, MO, [2]BWH- HMS, Boston, MA, [3]Trio Health, Louisville, CO, [4]University of Alabama at Birmingham, Birmingham, AL, [5]Arizona Arthritis & Rheumatology Associates, P.C., Peoria, AZ, [6]Articularis Healthcare, Summerville, SC

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Persistence on therapy is an important consideration in rheumatic diseases. There are multiple treatment options that influence long term disease management and a better understanding of the causes for medication discontinuation are needed. Possible reasons for discontinuation may be inferred from fielded data, when present, in EMR, claims, or specialty pharmacy records; however, actual reasons may be different. We reviewed open text notes within the EMR to understand why drugs were discontinued for patients with rheumatic diseases.

Methods: The ARN-TRIO Rheumatology registry contains EMR (fielded and open text), lab, procedure, infusion, medical claims, and specialty pharmacy data generated in care of >75,000 patients by ARN, a network of independent practices with >200 rheumatologists across the US. Data present in open text notes are extracted by clinically trained scribes who review the full patient histories for each patient and collect supplemental information into customized data forms. The collected data undergo a two-level audit process. Open text notes assessed were those specific to patients who discontinued csDMARD and/or targeted immune modulating drugs (TIM) between 2015 to 2019. Only the last discontinuation event per patient drug was considered for this study. Comparisons were made using chi-square with column proportions compared by z-test.

Results: Open text notes were reviewed for 2545 patients receiving 3616 regimens for which 4027 drugs were discontinued. Study population characteristics: 75% (1918) female, 77% (1325/1712) white, mean (range) age 57 (18-89), 67% (1706) with rheumatoid arthritis (RA). Reasons for discontinuation differed by drug type. [FIGURE 1] Perceived association or complication with one or more medical conditions was most commonly indicated for csDMARDs (44% [725/1644]) with 49% (350/715) indicated as gastrointestinal. [FIGURE 2] Lack or loss of efficacy was listed as the predominant reason for TIM discontinuation (53% [1260/2382]). To assess alignment of fielded data with recorded discontinuation reasons within the notes, we examined disease activity scores (RAPID3 or CDAI [DAS]) closest but preceding drug discontinuation for the subset of patients with RA. Of 2780 drug discontinuations, DAS were recorded for 73% (2042); 68% (1891) within 6 months prior to discontinuation. For TIM (but not for csDMARD discontinuations), DAS scores were significantly different for those indicated as "lack or loss of efficacy" v. not. [FIGURE 3] Approximately 15% (TIM) and 16% (csDMARD) of discontinuations indicated as "lack or loss of efficacy" had near remission or low DAS.

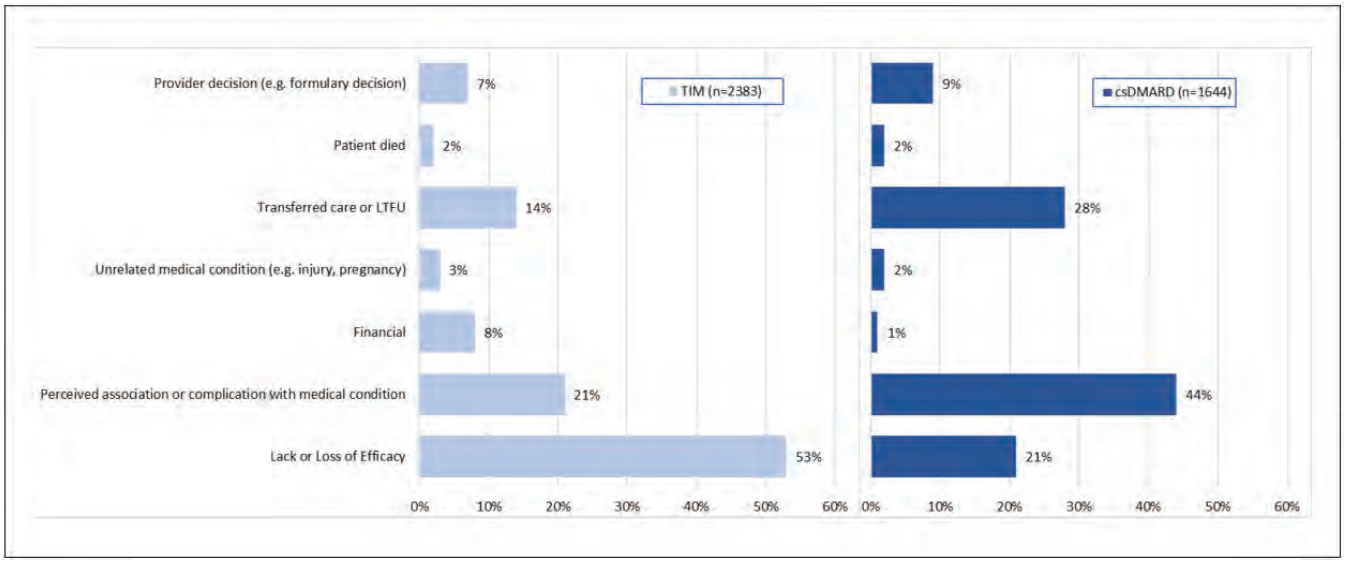

Figure 1. Reasons for discontinuation by type of discontinued drug. An individual patient may have >1 discontinuation reason

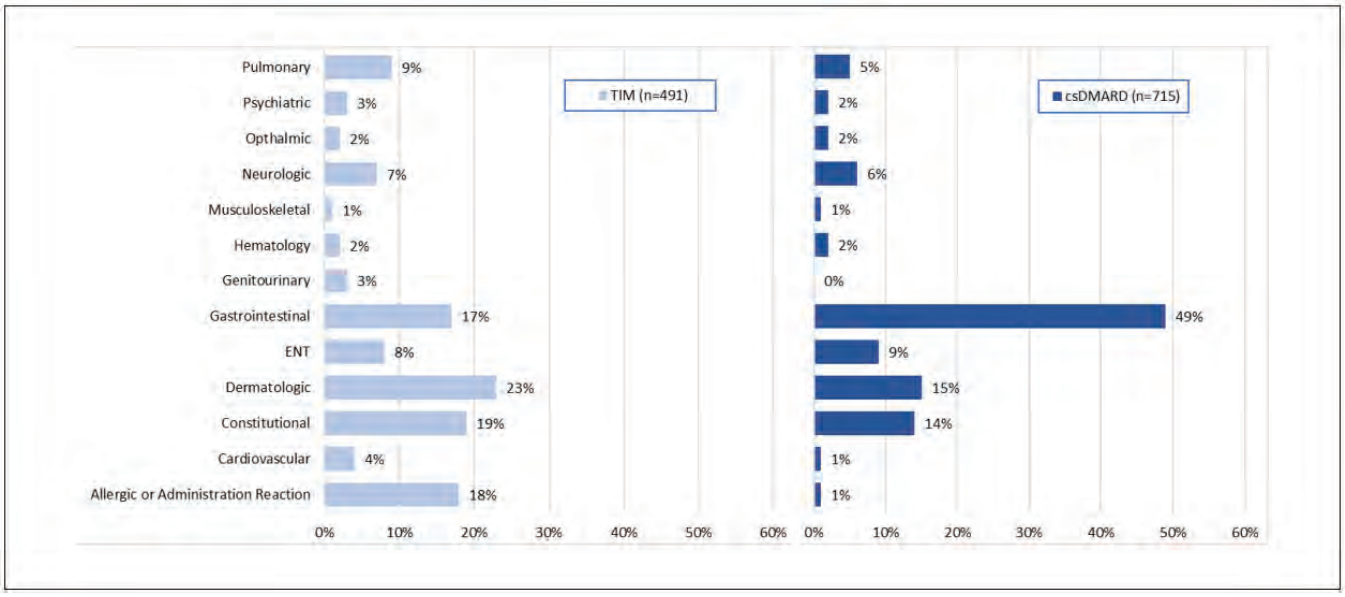

Figure 2. Systems indicated when discontinuation associated with 1 or more medical condition

Conclusion: Actual reasons for discontinuation may be directionally aligned with recorded data in the EMR, though the lack of fielded data for ~30% of evaluated discontinued drugs limits full understanding of what drives drug discontinuation. In addition, reported data that would appear to be at odds with the discontinuation reason suggest that other measures or inputs may contribute to how physicians or patients define successful treatment. To fully understand care, ongoing chart review along with full data extraction are necessary.

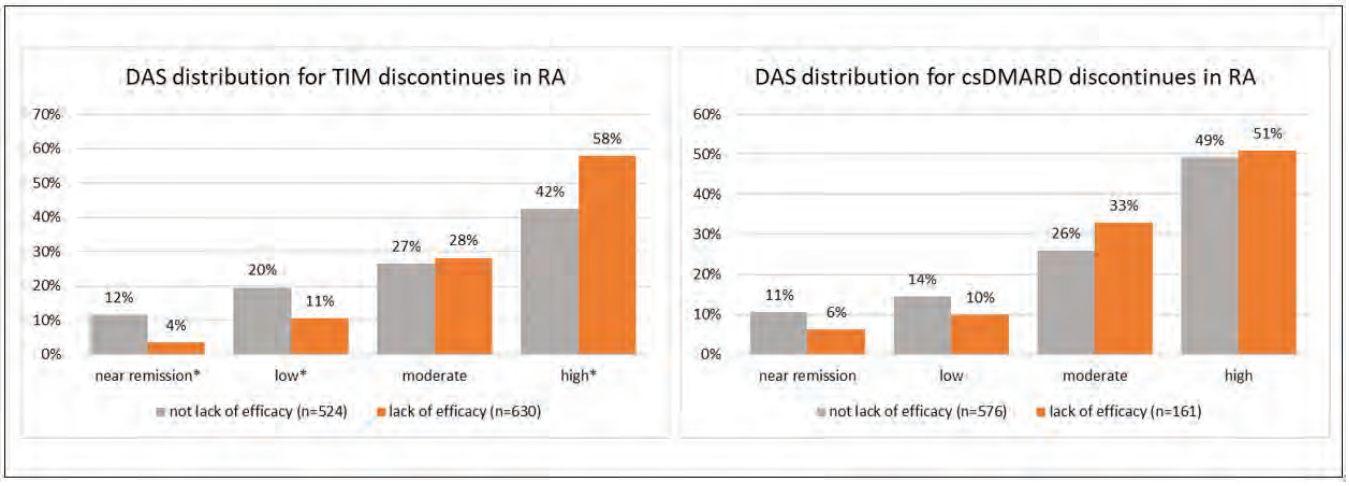

Figure 3. Distribution of DAS scores by discontinued drug type and reason of loss/lack of efficacy v. not in patients with RA. * indicates proportions that are significantly different ($p<0.05$)

Disclosure: K. Huston, None; **S. Helfgott**, Abbvie, 5; **S. Milligan**, Gilead, 2; **J. Singh**, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **N. Soloman**, Horizon, 5, 8, Amgen, 2, 8, Abbvie, 2, 5, 8, UCB, 2, 5, 8, Novartis, 5, 8, Jannsen, 2, 8, Pfizer, 8, Lilly, 2, GSK, 2, 5, 8; **B. Weil**, None; **C. Edgerton**, Sandoz, 5.

Abstract Number: 0602

Labor Impact of SARS-COV-2 Pandemic in Argentine Rheumatologists

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
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Session Time: 9:00AM–11:00AM

Background/Purpose: The novel coronavirus SARS2-COV-2 has precipitated the present outbreak of COVID-19, the worldwide spread has strong impact on general population and on healthcare workers. The objective of the present study was to describe the impact of the COVID-19 outbreak on Argentinian rheumatologists. Also to describe the current employment situation of the specialty.

Methods: A voluntary survey was carried out by e-mail to Argentine Society of Rheumatology (SAR) associates, during the mandatory preventive isolation (quarantine) ordered in Argentina by the national state (March 18th, 2020). After a brief explanation, the physicians were invited to join a fully anonymous online closed survey and the access link was sent. A 27-items survey was designed and developed by the authors. Transferred to STATA 14 for analysis:

descriptive statistics, Mann-Whitney or T-test for continuous variables and Fisher's exact test or Chi2 for categorical ones, p 0.05 was considered significant.

Results: More than one thousand physicians registered in SAR were invited. Responses were collected from April 22nd to May 22nd, 2020, (days: 34-64 the of quarantine). For the final analysis, 272 were included.

Women 65.59%, median age 44 years (ICR 38-52). Most (85.03%) lives in big cities (more than 100,000 h). 9.68% were in trainee. Only 17 rheumatologist (6.09%) works exclusively at public sector.

In total, 96.06% of the physicians has been in virtual contact with patients, the most frequent via was WhatsApp (78.8%). The most frequent reason was: request medical prescription (81.8%), 90% (RIC 70-100) were able to obtain medications in digital format, although 52.7% contacted again for same reason. Of the large number of non-face-to-face consultations, only in 5% (RIC 0-40) have received payment. On average, reported a 65% drop (RIC 50-80) in their monthly income.

The 34% reported having had some change in their job functions, 30% were assigned to COVID-19 patient care. A similar proportion has had, unilaterally by their employer, decrease in their workload, and even nine have lost a job in this period. Only 57.66% reported having the proper personal protective equipment (PPE).

About 40% of the population of the country lives in the metropolitan area of Buenos Aires (AMBA), being this one´s that concentrates the largest number of cases of patients with SARS2-COV-2 infection (at the time of conducting the survey and of making this report). Sub-analysis: 43.7% of the physicians were from AMBA and 56.3% from others regions. Before the quarantine, outside AMBA have a greater number of weekly outpatient clinic (average) [60 (RIC 40-80) vs 50 (RIC 30-70), p: 0.009] and currently the residents in AMBA have consultations [5 (RIC 2-10) vs 10 (RIC 3-15) p: 0.03]. Outside AMBA report a greater drop in their monthly income [70% (RIC 50-90) vs. 50% (RIC 30-80) p: 0.004].

Conclusion: The lack of safe and effective systems to virtual consultations make rheumatology patients unable to continue with the adequate follow-up. The deteriorated quality of work and poor payment of doctors in Argentina is deepened at the moment, sharing with much of the rest of the world's doctors the lack of PPE to perform tasks related to the pandemic.

Disclosure: S. Santiago, None; **E. Buschiazzo**, None; **M. Martire**, None; **C. Graf**, None; **R. Garcia Salinas**, None.

Abstract Number: 0603

Multisite Study of the Impact of COVID-19 Era Telemedicine Expansion on Reduction in No-Show Rates

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
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Session Time: 9:00AM–11:00AM

Background/Purpose: The COVID-19 pandemic led to rapid expansion of telemedicine in all fields, including rheumatology. We hypothesized that increased use of telemedicine would reduce no-show visits, given greater convenience and reduced barriers such as travel or transportation, which could also potentially reduce disparities in visit attendance.

Table 1. Comparison of Gundersen, MCW, and UW Health system population characteristics

Group	Primary County	Academic/ Community	Rural %	Population Density/ sq. mi	White non-Hispanic	Black	Hispanic/ Latino	Asian	Other Race
Gundersen	La Crosse	Community	17%	254	90%	2%	2%	5%	2%
MCW	Milwaukee	Academic	<1%	3,926	53%	27%	14%	4%	4%
UW Health	Dane	Academic	30%	408	81%	5%	6%	6%	3%

Table 2. Monthly clinic visits, telemedicine, and no-show rates pre-post telemedicine expansion

	Baseline									Safer at Home Order		
	Jun-19	Jul-19	Aug-19	Sep-19	Oct-19	Nov-19	Dec-19	Jan-20	Feb-20	Mar-20	Apr-20	May-20
UW Clinic Visits	1447	1403	1326	1229	1148	1086	1226	1425	1257	762	111	276
UW Telemed	6	3	3	5	8	3	7	3	5	409	1172	1115
UW No-shows	74	79	86	91	97	72	66	93	73	51	8	13
UW Scheduled	1527	1485	1415	1325	1253	1161	1299	1521	1335	1237	1331	1434
UW % No-shows	5.1%	5.6%	6.5%	7.4%	8.4%	6.6%	5.4%	6.5%	5.8%	5.4%	3.7%	3.1%
GHS Clinic Visits	464	504	490	462	495	407	434	460	330	349	13	202
GHS Telemed	0	0	0	0	0	0	0	0	0	234	662	311
GHS No-shows	26	42	28	23	23	24	17	20	10	12	14	13
GHS Scheduled	490	546	518	485	518	431	451	480	340	595	689	526
GHS % No-shows	5.3%	7.7%	5.4%	4.5%	4.4%	5.6%	3.8%	4.2%	2.9%	2.0%	2.0%	2.5%
MCW Clinic Visits	1009	1184	1176	1083	1278	1013	1152	1185	1120	705	67	244
MCW Telemed	0	0	0	0	0	0	0	0	0	104	758	740
MCW No-shows	71	102	106	109	112	103	123	98	98	82	65	81
MCW Scheduled	108	1286	1282	1192	1390	1116	1275	1283	1218	891	890	1065
MCW % No-shows	6.6%	7.9%	8.3%	9.1%	8.1%	9.2%	9.7%	7.6%	8.1%	9.2%	7.3%	7.6%
Combined Visits	2920	3091	2992	2774	2921	2506	2812	3070	2707	1816	191	722
All Telemed	6	3	3	5	8	3	7	3	5	747	2592	2166
All No-shows	171	223	220	223	232	199	206	211	181	160	127	137
All Scheduled	3097	3317	3215	3002	3161	2708	3025	3284	2893	2723	2910	3025
All % No-shows	5.5%	6.7%	6.8%	7.4%	7.3%	7.4%	6.8%	6.4%	6.3%	5.9%	4.4%	4.5%

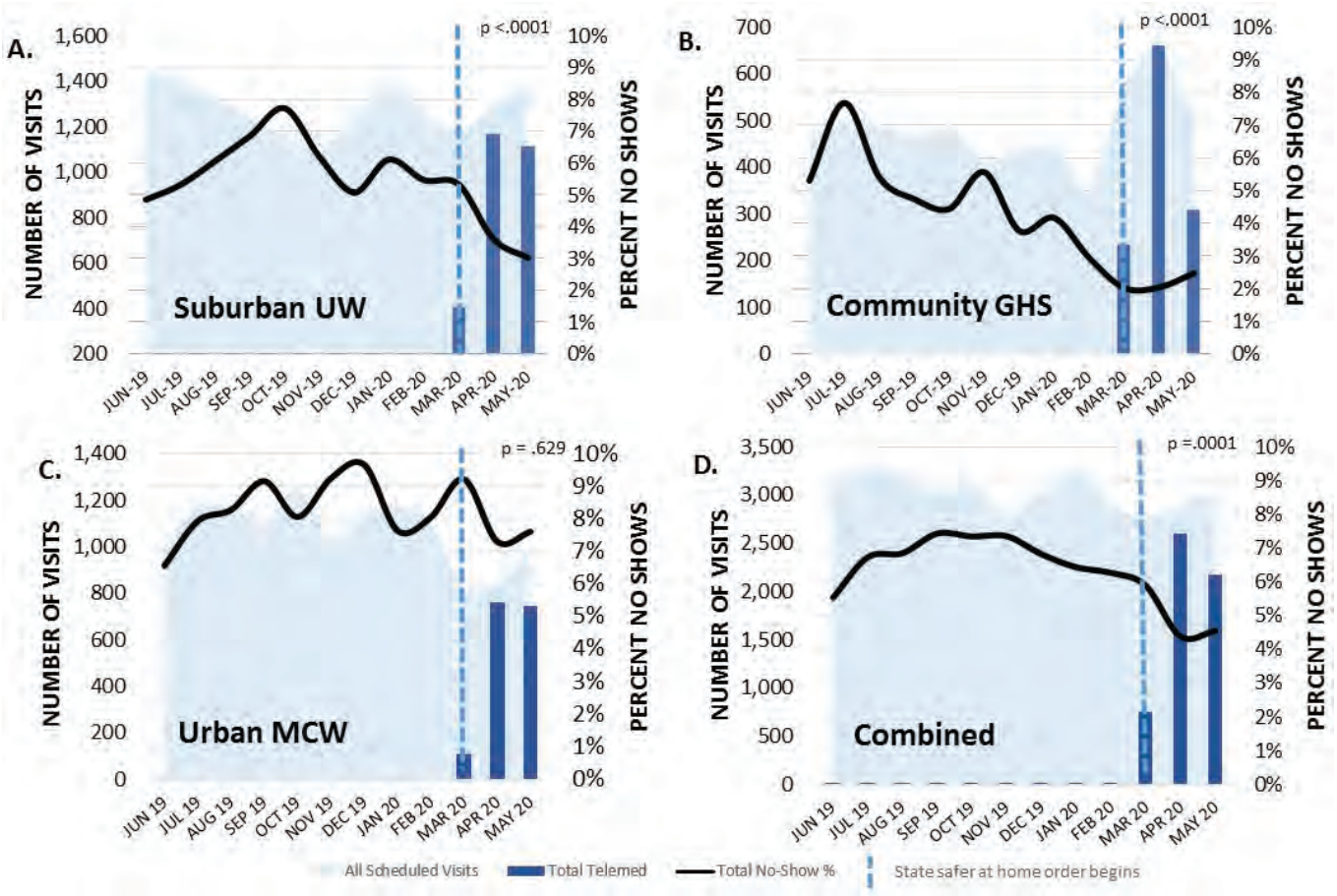

Figure 1. Total visits, telemedicine visits & no-show encounters by month at three centers and overall combined

Methods: We conducted an observational study with three rheumatology groups in one state (Table 1) serving diverse academic urban (Medical College of Wisconsin-MCW in Milwaukee), suburban (University of Wisconsin-UW in Madison), and community populations (Gundersen Health System-GHS in Lacrosse). To compare rates of no-shows before and after a statewide safer at home order 3/26-5/26/2020, electronic health record (EHR) data were queried for monthly rates of in-clinic visits, telemedicine visits, and no-show counts across one year, 6/1/2019-5/31/2020. Telemedicine included scheduled telephone or video encounters versus in-person clinic visits; most were via telephone. No-show rates were defined as the proportion of visits that did not successfully reach a patient divided by the total number of scheduled clinic or telemedicine visits. Chi square calculations compared no-shows and completed visits before and after March 2020 at each site and combined. The project was exempted by local IRBs.

Results: At baseline, only one center used telemedicine with a mean of five visits per month. In March 2020, telemedicine visits increased at all centers. By April, telemedicine outnumbered clinic visits 13-fold, while total volumes remained high (Table 2). Two sites saw no-show rates decline from 4.2-8.4% before to 2.0-5.8% after March 2020. As hypothesized, rates declined in months with higher telemedicine volumes at two centers (Fig 1A & B black lines $p< 0.0001$). However, declines were not statistically significant at the urban center (Fig 1C). Combined data (Fig 1D) showed declines in no-show rates at the time of telemedicine expansion (p.0001).

Limitations include limited information regarding telemedicine implementation across sites (e.g., live pre-visit reminder calls with telemedicine vs. automated reminders), possible missed no-show visits, and the lack of adjustment in our observational study. Personal interaction via reminder calls from office staff, or the novelty of telemedicine might have also reduced no-show rates and merits further study.

Conclusion: Our findings suggest that in the period of increased telemedicine visits after March 2020, no-show rates decreased while overall total visit volumes remained high. Two centers serving more rural populations showed particular gains in reducing no shows. The urban center did not see reduced no-show rates, potentially predicting ongoing healthcare delivery disparities with telemedicine or a need for more implementation support in urban populations. Future studies should follow longitudinal trends and compare multivariable predictors (e.g., race, age group, travel distance) of no-shows for in-clinic versus telemedicine. Likewise, further work should examine how to optimize telemedicine implementation overall and with vulnerable populations, and how policy can support optimal telemedicine use.

Disclosure: C. Bartels, Independent Grants for Learning and Change (Pfizer), 2; **D. Gazeley**, None; **A. Rosenthal**, None; **S. Ferguson**, None; **E. Ramly**, None; **M. Messina**, None; **D. White**, None.

Abstract Number: 0604

Increasing the Rate of Pneumococcal Vaccination in an Academic Rheumatology Outpatient Clinic

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
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Background/Purpose: Many patients with rheumatic diseases are at increased risk of infection, including invasive pneumococcal infection, due to both disease-related abnormalities of the immune system as well as the use of immunomodulatory medications. The Centers for Disease Control and Prevention recommends that people with immunocompromising conditions receive vaccination with both a pneumococcal conjugate vaccine (PCV-13), and pneumococcal polysaccharide vaccine (PPSV-23). However, significant confusion persists in rheumatology clinics regarding

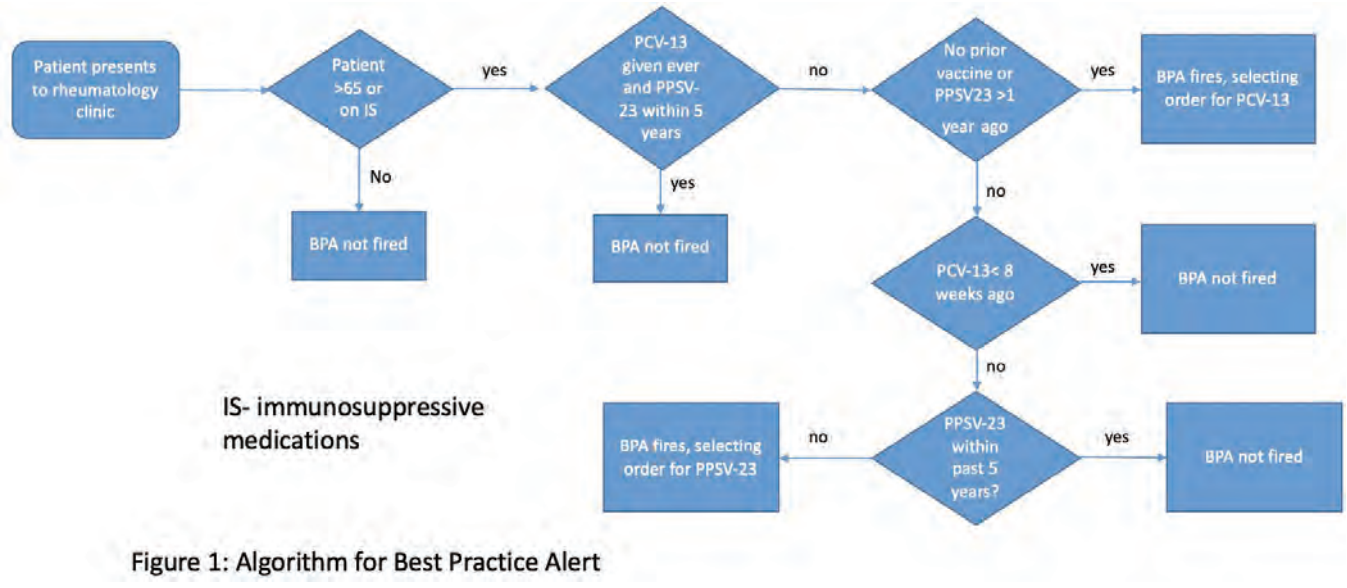

Figure 10. Vaccine Algorithm

Table 1: Data from Intervention

Pre-intervention Data

	Up to date	Not up to date	Not due yet	percent up to date
Pneumovax	23	26	1	49.0%
PCV13	10	34	6	31.4%

Post-intervention Data

	Up to date	Not up to date	Not due yet	percent up to date
Pneumovax	32	11	7	78.0%
PCV13	28	20	2	60.0%

Table 1. Intervention Data

Table 2: Patient Characteristics

Patients	Pre-intervention N=50	Post-intervention N=50
Age, ≥65	22%	24%
Gender, male	24%	18%
Rheumatologic Medications		
Abatacept	0.8%	0.0%
Adalimumab	0.8%	6.0%
Apremilast	0.8%	0.0%
Azathioprine	0.8%	8.0%
Belimumab	0.8%	2.0%
Cyclophosphamide	1.7%	0.0%
Etanercept	2.5%	10.0%
Infliximab	4.2%	4.0%
IVIG	4.2%	0.0%
Leflunomide	4.2%	4.0%
Methotrexate	5.9%	40.0%
Mycophenolate mofetil	5.9%	6.0%
Prednisone alone	8.4%	0.0%
Rituximab	9.2%	12.0%
Sulfasalazine	15.1%	16.0%
Tofacitinib	34.5%	2.0%

Table 2. Patient characteristics

pneumococcal vaccine indications and algorithms for administering the vaccine. Furthermore, multiple competing demands in clinic often leave inadequate time to discuss indicated vaccinations with patients. The aim of our quality improvement initiative was to improve the percentage of patients who are up to date on pneumococcal vaccines in an academic county hospital rheumatology clinic from 33% to 53% for PCV-13 and from 49% to 70% for PPSV-23 from January 2019 to January 2020.

Methods: We created a Best Practice Alert (BPA) in our electronic medical record that would alert the provider when a patient is due for either a PCV-13 or PPSV-23 vaccine (Figure 1). The BPA opens an order set with the appropriate vaccine preselected. The provider then has to sign the vaccine order and a nurse will administer it as part of the checkout process. A comprehensive list of immunosuppressive medications was given to the hospital information technology department to incorporate into the BPA algorithm. The BPA went live in December 2019. In order to have consistent results, we reviewed 50 patient charts from the first week of January 2019 and 50 patient charts from the first week of January 2020. Patients seen by the authors, who refused vaccination, or who did not have an indication for pneumococcal vaccination were excluded. Patients who had received one vaccination but were not yet due for the other were counted as up to date on vaccination status.

Results: Of 50 patient charts reviewed pre-intervention from January 2019, 31% were up to date on PCV-13 and 49% were up to date on PPSV-23 vaccination. In January 2020, post-intervention, 60% were up to date on PCV-13 and 78% of patients were up to date on PPSV-23, exceeding our goal. The vast majority of patients were on at least one immunosuppressive medication (Tables 1 and 2).

Conclusion: Patients with rheumatic conditions have an indication for pneumococcal vaccination, but are not always vaccinated. This quality improvement project utilizes the medical record to remind providers to discuss appropriate pneumococcal vaccination based on an algorithm and rapidly order the vaccine if the patient agrees. We have shown in our clinic that BPAs are effective at increasing pneumococcal vaccination rates in our outpatient rheumatology clinic. Further data will be needed to assess sustainability of the intervention.

Disclosure: M. Bacalao, None; **S. Reddy**, None; **N. Syed**, None.

Abstract Number: 0605

How Did SARS-CoV2/COVID-19 Pandemic Affected Rheumatology Practice in Latin America? A Regional Survey from PANLAR

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SESSION INFORMATION
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Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Since December 2019, a novel coronavirus (SARS-CoV-2) pandemic was declared. Social isolation became a mainstay for the prevention of disease expansion. Outpatient follow-up of patients with rheumatic diseases was restricted. Thus, a revolution in rheumatology practice has been observed. Attitudes, behaviors, and practice studies are used to investigate patterns of community reactions to a disease. The aim of this study was to explore the influence of COVID-19 pandemic in the practice of rheumatologists in Latin America.

Methods: We performed a cross-sectional observational study by means of a digital anonymous survey (RedCap®). We included rheumatologists from PANLAR non-English-speaking countries. We retrieved demographics, COVID-19 diagnosis and perceived risk of being infected, information on practice prior and during the pandemic, the quantitative impact on wage and employment, practices concerning communication with patients and adjustment of immunomodulators, attitudes and behaviors regarding telehealth, the rheumatologist's role on the pandemic, and the perceived discrimination as a health worker. We calculated median and interquartile range (IQR) for quantitative variables and frequencies and percentages for qualitative variables.

Results: Our interim results include 476 rheumatologists from 18 countries. The median age is 48 (39-58) years, most of them are women (55%). The most frequent practice scenarios are private practice (73.9%) and institutional

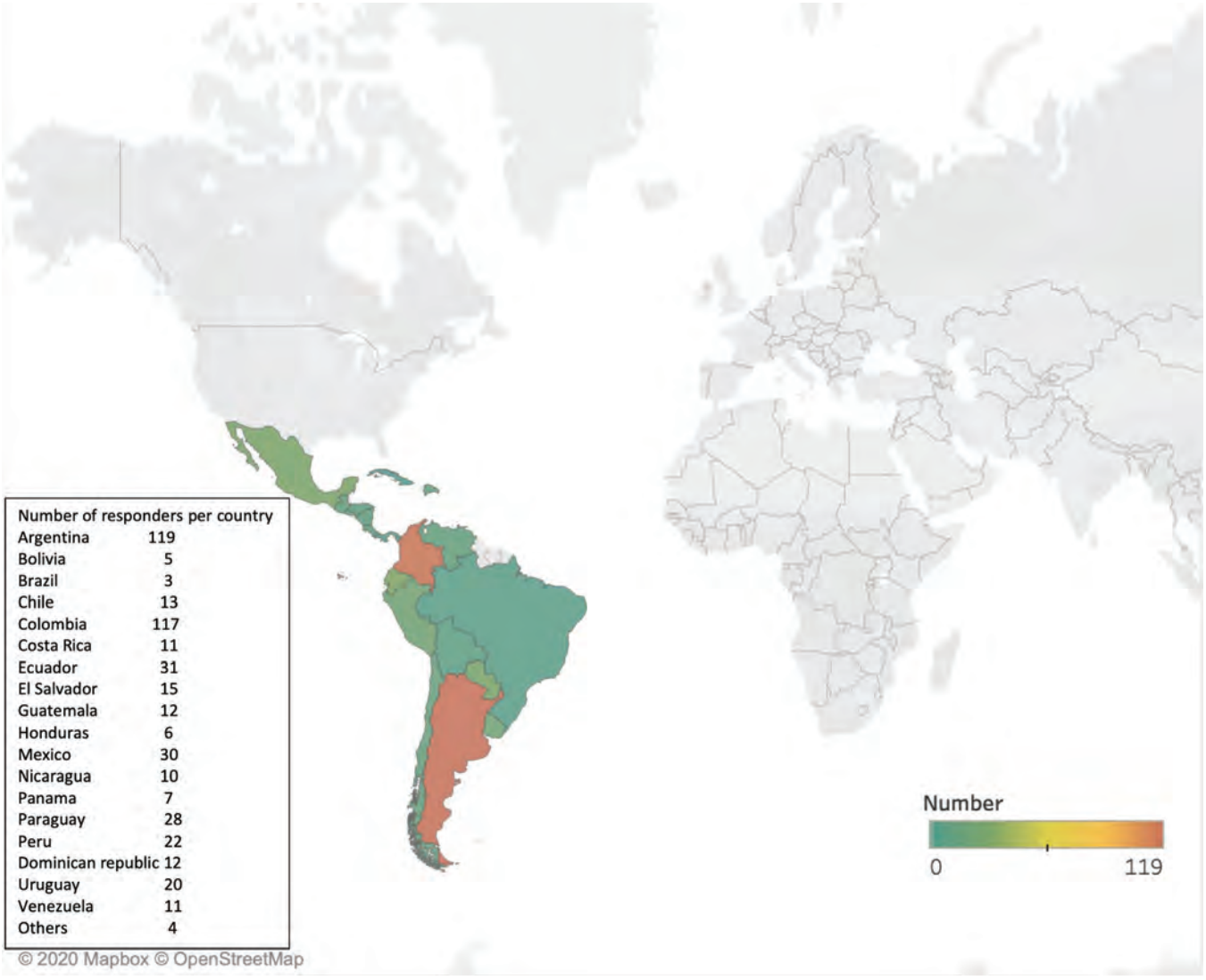

Figure 1. Number of rheumatologists filling the survey per country

Variable n (%)	n = 476
Demographics	
Age in years (IQR)	48 (39-58)
Women	263 (55.2)
Adult/Pediatrics	454 (95.4) / 22 (4.6)
Years of experience (IQR)	14 (6-25)
Practice scenarios	
Private practice	352 (73.9)
Institutional outpatient clinic	280 (58.8)
In-patient care	251 (52.7)
Teaching	187 (39.3)
Research	139 (29.2)
Pharmaceutical industry	75 (15.8)
Other	12 (2.5)
In-person practice (hours)	
Prior to the pandemic (IQR)	28 (15-40)
During the pandemic (IQR)	10 (4-15)
Median proportion of cancelled appointments (IQR)	80 (50-100)
Telehealth	
Did perform during pandemic	415 (87.2)
Telephone call	272 (57.1)
Whatsapp call	198 (41.6)
Whatsapp video call	189 (39.7)
Other	98 (20.6)
Microsoft Teams video call	35 (7.3)
Skype video call	28 (5.9)
Skype call	11 (2.3)
Hours per week (IQR)	8 (3-16)
Did reduce consult fee	195 (47)
Median % of reduction from baseline fee (IQR)	50 (25-60)
Agree is valid during the pandemic	427 (89.7)
Agree is valid after the pandemic	265 (55.7)
Individual economic impact	
Perceived a reduction in monthly wage	422 (88)
Median % of reduction in monthly wage (IQR)	50 (40-70)
Lost their job	43 (9)
Required to care for internal medicine patients	69 (14.5)
Practices regarding medication	
Perceived a reduction in patient adherence to medication (Synthetic / Biologics)	214 (45) / 219 (46)
Did no adjustment to DMARDs due to the pandemic (Synthetic / Biologics / Glucocorticoids)	467 (98.1) / 298 (93.1) / 443 (62.6)
Rheumatologist participation in COVID-19 local guidelines development	
Consider they should participate	365 (76.7)
Did actually participate	155 (32.6)
At least one episode of discrimination as a health worker during the pandemic	49 (10.3)
Median percentage of perceived risk of being infected with SARS-CoV-2/COVID19 during the pandemic (IQR)	50 (30-60)

Table 1. Demographics, attitudes and practices prior and during COVID-19 pandemic of rheumatologists in non-English-speaking PANLAR countries.

outpatient clinics (58.8%). Fifteen (3.2%) responders were diagnosed with COVID-19. A reduction of in-person practice hours was observed prior and during the pandemic; the median proportion of cancelled appointments was 80% (50-100). Forty-five percent perceived a reduction in patient's adherence during the pandemic. Most rheumatologists continued DMARDs at the same doses. Most of the responders have performed telehealth, with a median of 8 (3-16) hours/week. Forty-seven percent of responders have reduced their consult fee, with a median reduction of 50% (30-60) from baseline. Most of the responders (88%) reported a reduction of monthly wage, with a median reduction of 50% (40-70). Although 89.7% consider telehealth as a valid strategy during the pandemic, this reduces to 55.7% as a hypothetical alternative after the pandemic. More than two-thirds of responders believe that rheumatologists should take part of the development of local COVID-19 guidelines, however, only a third actually got involved in in-

stitutional panels. Ten percent reported an episode of perceived discrimination during the pandemic. Nine percent of rheumatologists have lost their jobs and 14.5% have being required to care for internal medicine patients, including COVID-19 cases.

Conclusion: SARS-CoV2/COVID-19 pandemic has reshaped rheumatology practice in Latin America and has had a profound impact on rheumatologists' behaviors. Telehealth is perceived as a valid alternative to in-person consults during the pandemic. A larger effort to participate in the elaboration of disease management strategies should be pursued. Our study is still ongoing and we present interim results; it is planned to collect data until July 31th, 2020.

Disclosure: D. Fernández-Ávila, None; **J. Barahona-Correa**, None; **D. Romero-Alvernia**, None; **S. Kowalski**, None; **A. Sapag Durán**, None; **A. Cachafeiro Vilar**, None; **B. Meléndez Muñoz**, None; **C. Pastelín**, None; **D. Palleiro Rivero**, None; **D. Arrieta**, None; **G. Pons-Estel**, None; **J. Then Báez**, None; **M. Ugarte-Gil**, Janssen, 2, Pfizer, 2; **M. Cardiel**, None; **N. Colman**, None; **N. Chávez Pérez**, None; **P. Burgos**, None; **R. Montufar**, None; **S. Sandino**, None; **Y. Fuentes-Silva**, None; **E. Soriano**, AbbVie Inc., 2, 5, 8, Amgen, 2, 5, 8, Bristol Myers, 2, 5, 8, Celgene, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8.

Abstract Number: 0606

A Systematic Review Exploring Pre-COVID-19 Telehealthcare Models Used in the Management of Patients with Rheumatological Disease

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Session Date: Saturday, November 7, 2020
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Background/Purpose: Recent advancements in the delivery and utilization of information and communication technologies (ICTs) have led to an increased application of telehealthcare services. Global coronavirus disease (COVID-19) has further accelerated pressure on healthcare systems. Patients with rheumatological disease, particularly those on immunosuppressant therapy, are potentially at increased risk of COVID-19 and developing the severe consequences of the disease. Furthermore, this group have been advised to shield during the COVID-19 pandemic. This review aims to assess the baseline use of telehealthcare in rheumatology before COVID-19, to which future comparisons of newer interventions adapted during the crisis can be made.

Methods: A registered systematic literature search (CRD42020180695) was performed using MEDLINE, EMBASE, CENTRAL and PubMed databases. All full-length articles comparing telehealthcare delivery models to standard care in the management of patients with rheumatic conditions were assessed for inclusion. This systematic review was conducted in accordance with The Cochrane Collaboration principles of Systematic Reviews and reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guidelines.

Results: 4809 studies were identified. 108 studies were suitable for review by full text of which 13 studies met full criteria for this review. Five studies (38%) included patients with rheumatoid arthritis, four studies (31%) included patients with mixed disease cohorts, two studies (15%) included patients with osteoarthritis, one study (8%) included patients with juvenile idiopathic arthritis and one study (8%) included patients with fibromyalgia. The majority of

patients were female representing 38-100% of patients and the average age of patients ranged from 13.1-64.4 years. Six studies (46%) used telephone, three studies (23%) used mixed method communication, three studies (23%) used videoconferencing and one study (8%) used website delivered telecommunication as their method of telehealthcare delivery. Modality of telehealthcare intervention ranged throughout studies with six studies (46%) delivering virtual consultation, three studies (23%) delivering a self-management program, two studies (15%) delivering a health education program, one study (8%) delivering cognitive behaviour therapy and one study (8%) delivering a self-efficacy program. Seven studies (54%) identified the telehealthcare intervention to be effective and superior to standard care and six studies (46%) identified the telehealthcare intervention as non-inferior to standard care.

Conclusion: Current evidence for telehealthcare in rheumatology is lacking and the evidence for superiority or non-inferiority is limited by methodological bias and clinical heterogeneity of telehealthcare interventions. With a paradigm shift in the nature of patient consultation, fit for purposeful assessment is essential in rheumatology following the COVID-19 crisis. Scrutinous assessment of the current telehealthcare interventions used during COVID-19 is required to accommodate recommendations directed from international working groups.

Disclosure: A. Nelson, None; **M. Anderson**, Boehringer-Ingelheim, 5, Lilly, 9.

Abstract Number: 0607

The Evolution of Rheumatologist's Practice in Response to the COVID19 Pandemic

Maria Bacalao[1], Kathryn Dao[2] and John Cush[2], [1]UT Southwestern, Dallas, TX, [2]University of Texas Southwestern Medical School, Dallas, TX

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Background/Purpose: The COVID19 pandemic was a turning point for Rheumatology. This survey of rheumatologists (rheums) assessed its impact on care delivery, patient counseling and drug use in the first 3 months of the pandemic.

Methods: 2406 rheums were surveyed by email in June 2020. The 26 questions assessed respondent demographics, geography, practice type, care delivery, counseling, risks and prevalence of COVID in rheumatic disease (RMD) patients (pts).

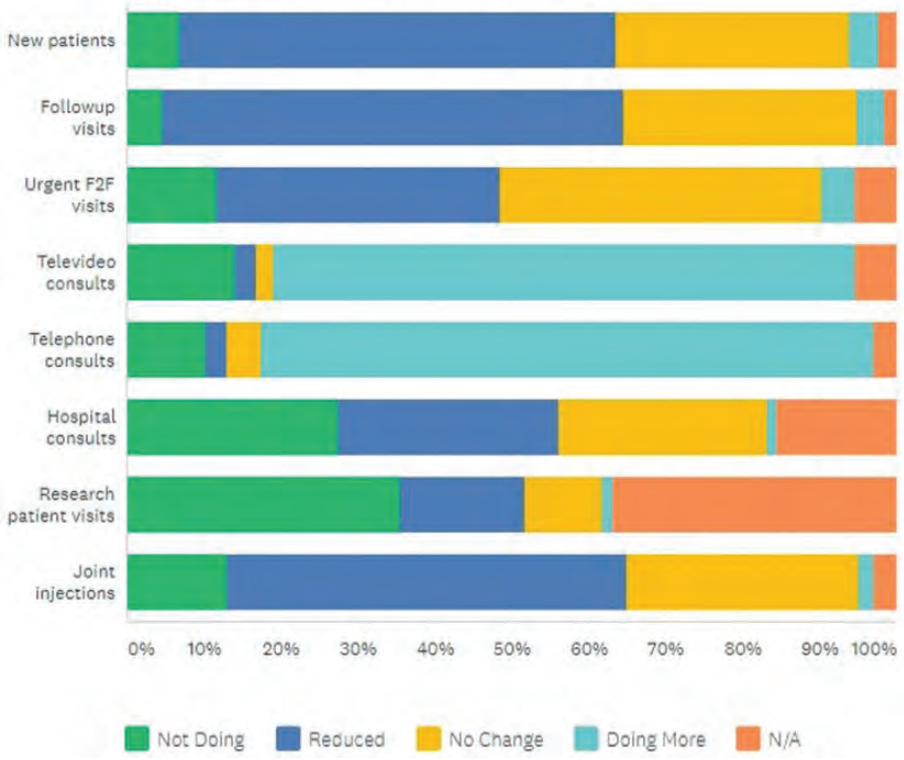
Results: 400 responses (16.7%) were received. Average respondent age was 54 yrs, 61% male, in practice for 21 years, avg 67 pts seen per week; most were in private practice (group 27%, solo 27%, multispecialty 22%) or academics (24%). 5% of respondents practiced outside the US.

Care Delivery: Figure 1 shows substantial reductions in number of new pt visits (64%), hospital consults (56%), follow-ups visits (55%), joint injections (55%), urgent (49%) and research visits (42%). Major service increases were seen in telehealth (>75%) visits. Many noted < 20% patients had no telemedicine access. Rheums temporarily closed their clinics, for either 4 weeks (32%), 6-8wks (28%) or 12 wks (14%); 19% have still not reopened. A major

Table. 1 COVID Infection Rates by US Region

	COVID infections	COVID deaths	#infections per Rheum	#Deaths per Rheum
Northeast	235	16	5.3	0.36
Atlantic	23	6	2.3	0.6
Southeast	182	8	2.6	0.11
Midwest	82	1	1.9	0.02
Southwest	34	2	1.2	0.07
Northwest	16	0	1.6	0
Western	40	3	1.7	0.13
Rest of world	54	2	4.5	0.15
Overall	875	52	2.5	0.15

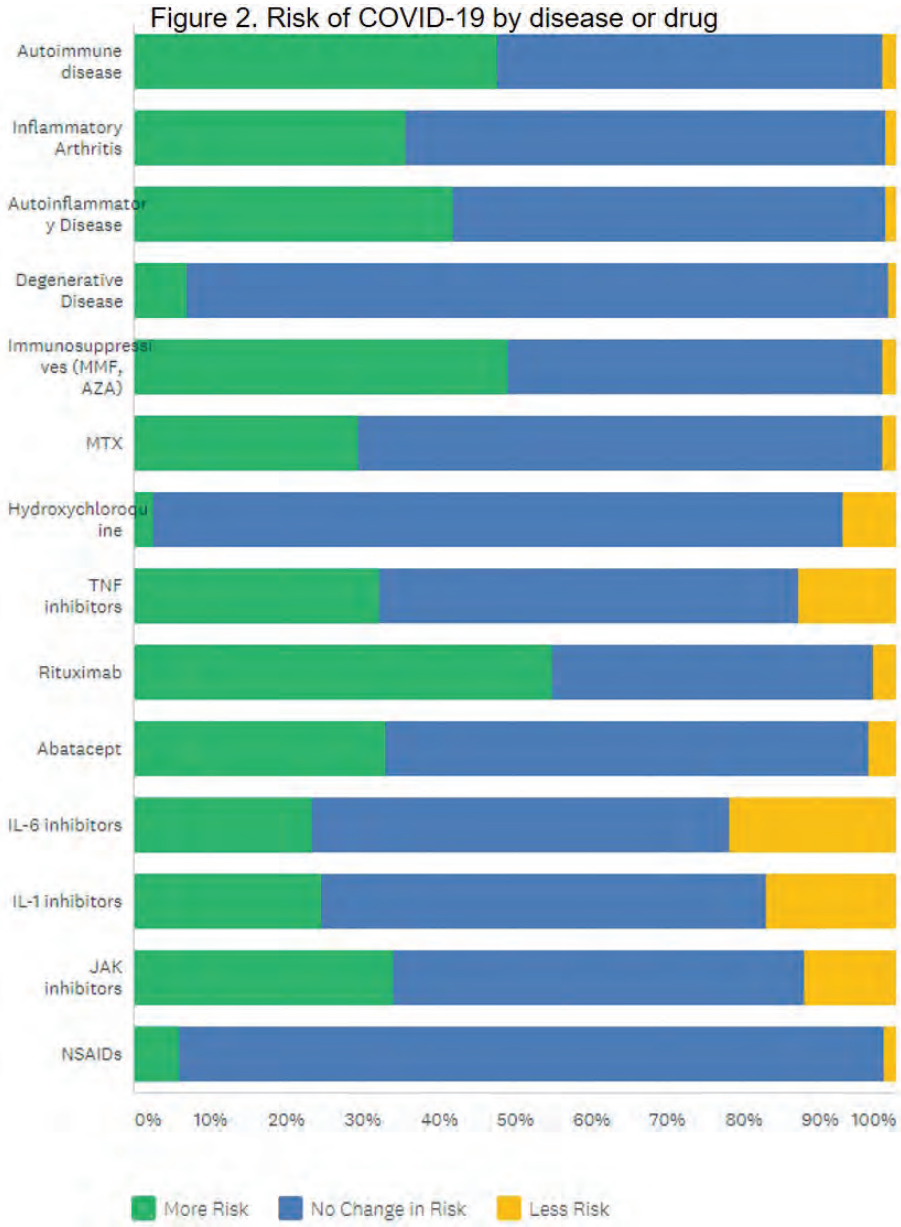
Fig 1. Practice Changes Since COVID-19



disruption to practice was noted by 46% rheums; 4% had no change. A major income loss was claimed by 31%, and 17% had no income loss.

Patient Counseling: 40% rheums noted ongoing patient confusion about COVID. Two-thirds informed pts their disease does NOT increase COVID risk. RA & SLE pts were told risk is not higher if they are well controlled on stable meds (27%) or that risk was due to comorbidities & age (21%); rather than meds (9%). Majority noted no COVID risk imposed by NSAIDs (93%), OA (92%), HCQ (91%), MTX (69%), abatacept (64%) or inflammatory arthritis (63%). Rheums suggested an increased risk with rituximab (55%), immunosuppressives (49%) or active autoimmune disease (47%). Rheums perceptions of COVID risk are shown in Figure 2.

Prescribing Habits: Overall, rheums did not change their use of NSAIDs, MTX, HCQ, TNF inhibitors abatacept, IL-6 inhibitors, or MMF. Prednisone use decreased 41%, as did rituximab 26%, cyclophosphamide 19% and denosumab 18%; antidepressants (9%) and hydroxychloroquine (7%) increased. Nearly all rheums (94%) said ≤25% of patients



reduced or discontinued meds without seeking advice. 10% prescribed antimalarials as COVID prophylaxis, and 82% of rheums reported patients had difficulty getting antimalarials (shortages/cost issues).

Rheums Role: Most (61%) have not been involved in COVID-19 care, while 30% were consulted about DMARD/biologics; only 6% have managed cytokine storm (CSS). The preferred agent for CSS was IL-6 inhibitor (66%), and 14% did not know what to use. A total of 348 rheums reported 875 cases of COVID, (2.51 patients/Rheum). With an average Rheum patient panel of 1350 patients, the COVID infection rate was 0.18% in RMD pts. Total of 52 deaths were reported, with a COVID death rate of 0.01% in RMD patients.

Conclusion: Rheums substantially changed their practices, counseling and health care delivery during the pandemic. COVID infection and death rates among RMD patients appears to be lower than the general US population. Maintenance of drug therapy and patient compliance appears potentially protective to SARS-CoV-2.

Disclosure: M. Bacalao, None; **K. Dao**, None; **J. Cush**, AbbVie, 2, 5, AstraZeneca, 2, Aurinia, 2, Bristol-Myers Squibb, 2, 5, Genentech, 2, 5, Novartis, 2, 5, Pfizer, 2, Amgen, 5, Boehringer Ingelheim, 5, Gilead, 5, Eli Lilly, 5, UCB, 5.

Abstract Number: 0608

Patient and Parent Perspectives in a Academic Pediatric Rheumatology Transition Clinic

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Background/Purpose: In November 2018 we initiated a transition clinic called ACCORD (Adult Center for Childhood Onset Rheumatic Disease). Our unique structure integrates an adult rheumatologist in a pediatric rheumatology clinic setting to initiate clinical transition of our patients. Patients are seen when they are ≥ 16 years old. All patients and parents receive education on transition planning and provide feedback on their experience.

Methods: Metrics collected in the ACCORD clinic include the 'Transition Readiness Assessment' (Got Transition$_{TM}$) and the 'Mind the Gap' scale, a validated metric using 7-point Likert scales to assess satisfaction with transitional health care among adolescents and young adults (AYA) with chronic illness and their parents. The preliminary data from these metrics were analyzed to evaluate the perspectives and satisfaction of our AYA as well as their parents.

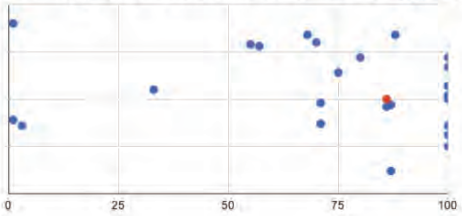
Table 1. Demographics of Transition Clinic *

	Sex		Mean Age (years)		Race					
	Male n (%)	*Female n (%)*	*Male/ Female*	*White n (%)*	*Black n (%)*	*Asian n (%)*	*American Indian or Alaskan Native n (%)*	*Native Hawaiian or Pacific Islander n (%)*	*Unknown/Not Reported/Other n (%)*	*Total*
Juvenile Idiopathic Arthritis or Rheumatoid Arthritis	4 (11.4)	19 (54.3)	22.1	19.7	17 (48.6)	1 (2.9)	1 (2.9)	0	1 (2.9)	3 (8.6)	23
SLE (or other CTD)	1 (2.9)	8 (22.9)	18.5	19.9	5 (14.3)	0	2 (5.7)	1 (2.9)	0	1 (2.9)	9
Other	0	3 (8.6)	N/A	18.4	3 (8.6)	0	0	0	0	0	3
Total											35

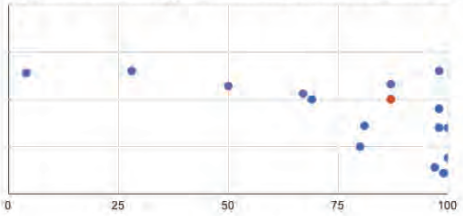
*All percentages are of entire cohort (n = 35)

Figure 1. Transition Readiness Assessment

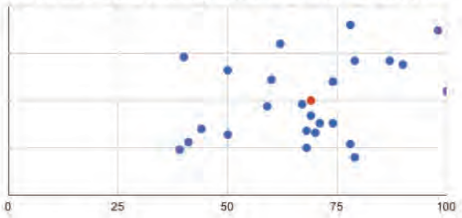
AYA: "How Important is it to you to prepare for/change to an adult doctor before age 22?"



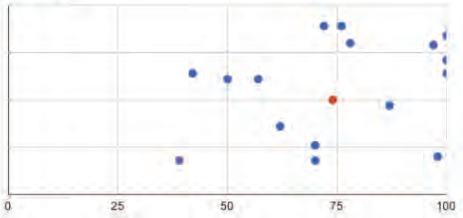
Parents: "How important is it for your child to prepare for/change to an adult doctor before age 22?"



AYA: "How confident do you feel about your ability to prepare for/change to an adult doctor?"



Parents: "How confident do you feel about your child's ability to prepare for/change to an adult doctor?"



Discrete variables are reported as percentages. Linear variables are reported as means and compared using independent one-tailed t-test ($p < .05$).

Results: 35 families have participated in our transition clinic (Table 1). 25 AYA and 16 parents completed a 'Transition Readiness Assessment'. On an importance scale from 0 (not) – 100 (very), AYA rated "the importance of preparing for/changing to an adult doctor before the age of 22" as 73.3 (M = 73.3, SD = 32.2). For parents, "how important is it for your child to prepare for/change to an adult doctor before age 22" was rated 77.1 (M = 77.1, SD = 29.3). When asked "how confident do you feel about your ability to prepare for/change to an adult doctor" 0 (not) – 100 (very), AYA responded 67.8 (M = 67.8, SD = 17.2). When asked "how confident do you feel about your child's ability to prepare for/change to an adult doctor" parents responded 74.9 (M = 74.9, SD = 21.0) (Figure 1). Parents were more confident than AYA, but this change did not reach statistical significance ($t(39) = -1.1808$, $p = .12$). AYA and 6 parents completed a 'Mind the Gap' scale. For AYA, those variables felt "extremely important" by the majority of respondents included: "does not waste my time at clinic," and "has staff who are very knowledgeable about my disease and latest treatments" (n = 8, 61.5% for each). For parents, those variables felt "extremely important" by the majority of respondents included: "provides me with honest explanations of my child's condition and treatment options (including side-effects)," "provides my child with honest explanations of their condition and treatment options (including side-effects)," and "helps me and my child prepare for their move to adult services," (n = 6, 100.0% for each).

Conclusion: This research shows that AYA and their parents believe transition planning and successful clinical transition to an adult sub-specialist is important. Although the difference is not statically significant in this small sample, parents are more confident than AYA in their child's/own ability to successfully make this transition. Of most value to both AYA and their parents are efficient clinic processes, which include deliberate transition preparation, and are led by knowledgeable staff. Parents especially value honest explanations of their child's condition and treatment that target both the parent and the AYA.

Disclosure: R. Overbury, None; **T. Frech**, None; **J. Bohnsack**, AbbVie, 2, Bristol-Myers Squibb, 2, Janssen, 2, Pfizer Inc, 2, Roche, 2; **C. Inman**, None; **S. Stern**, None; **K. James**, None; **E. Treemarcki**, None; **A. Hersh**, None.

Abstract Number: 0609

Impact of Depressive Symptoms, Anti-depression Treatment on Direct Medical Costs Among Medicare Beneficiaries with Knee Osteoarthritis (KOA)

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Depressive symptoms are prevalent among knee OA (KOA) patients and likely lead to additional medical costs. We sought to quantify the prevalence of depressive symptoms among Medicare Beneficiaries with KOA and patterns of depression treatment in this population. We compared annual direct medical costs in KOA Medicare beneficiaries with and without depressive symptoms.

Methods: We identified a Knee Osteoarthritis (KOA) cohort using Medicare Current Beneficiary Survey (MCBS) Cost and Use files (2009-2015) among community-dwelling Medicare survey responders who had at least one outpatient visit resulting in Medicare Part A or Part B claims. We used ICD-9/10 diagnostic codes in both Part A and Part B claims to identify KOA cohort. We determined the prevalence of depressive symptoms using self-reported data on sadness or anhedonia during the past year, consistent with DSM-IV criteria. We divided KOA patients into three groups: 1. No reported depressive symptoms; 2. Reported depressive symptoms, no depression-related treatments costs; 3. Reported depressive symptoms and depression-related treatment costs. We ascertained claim payments to physician/suppliers, hospitals, outpatients, skilled nursing facilities, hospice, durable medical equipment, and home health agency. We used these payment data to estimate direct medical costs for each of three groups. We used a generalized linear model to compare mean annual total direct medical cost across three groups, adjusting for general health, comorbid conditions, year of MCBS, and interaction of MCBS year with depressive symptoms/treatment.

Table. Annual direct medical costs stratified by depressive symptoms and depression treatment status

	Mean Annual Medical Cost (SD)	Adjusted Mean Annual Medical Cost (SD)	Adjusted Mean Annual Medical Cost Difference (95%CL)	
			Comparing to no depressive symptoms	Comparing treated and non-treated groups among those with depressive symptoms
Treated Depression Symptoms	$21,627 (2,008)	$17,504 (2,003)	$6,390 ($1,387, $11,393)	$5,290 ($16, $10564)
Untreated Depression Symptoms	$13,563 (1,022)	$12,214 (1,048)	$1,100 (-$1,748, $3,948)	(REF)
No depressive Symptoms	$9,499 (573)	$11,114 (711)	(REF)	

Results: We identified 1,918 individuals with KOA. 28% self-reported depressive symptoms and 5% received depression-related billable medical services. The mean adjusted annual direct medical cost ranged from $11,114 for Medicare beneficiaries with KOA without depressive symptoms, to $12,214 among those with KOA and depressive symptoms who did not accrue depression treatment related costs to $17,504 among those with KOA and depressive symptoms who received depression-related treatment (Table). Subjects with depressive symptoms who were treated had $5,290 (43%) higher direct medical cost compared to those with depressive symptoms who were not treated and $6,390 (57%) higher direct medical costs compared to those without depressive symptoms.

Conclusion: Over one quarter of Medicare beneficiaries with KOA self-reported depressive symptoms but just 5% of the population received treatment for depression. The presence of depressive symptoms leads to higher direct medical costs that are somewhat attenuated after accounting for other medical comorbidities.

Disclosure: S. Song, None; **J. Katz**, Samumed, 2, Flexion, 2; **E. Losina**, Pfizer, 9, Samumed, 2, JBJS, 9.

Abstract Number: 0610

Change in Utilization of Outpatient Services at US Community Rheumatology Practices During COVID-19 Outbreak

Kent Kwas Huston[1], Nehad Soloman[2], Janna Radtchenko[3], Simon Helfgott[4], Jasvinder Singh[5] and Colin Edgerton[6], [1]Kansas City Physician Partners, Kansas City, MO, [2]Arizona Arthritis & Rheumatology Associates, P.C., Peoria, AZ, [3]Trio Health, Louisville, CO, [4]BWH- HMS, Boston, MA, [5]University of Alabama at Birmingham, Birmingham, AL, [6]Articularis Healthcare, Summerville, SC

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients (pts) with autoimmune diseases managed by rheumatologists represent vulnerable population with risk of serious complications if exposed to novel coronavirus SARS-CoV2. The first case of COVID-19, disease caused by SARS-CoV2, was diagnosed in the US on January 20, 2020. By the beginning of April, 42 states implemented stay-at-home advisories limiting non-essential activity including non-emergency healthcare services leading to the majority of routine healthcare visits being conducted via telehealth method using audio and/or video technology. In May states began lifting stay-at-home orders and gradually renewing economic activity. We evaluated impact of these policies on volume and type of care provided by US community rheumatology practices.

Methods: EMR records from the American Rheumatology Network (ARN) - Trio Health Rheumatology registry were used for the study. The ARN is a physician led and owned organization that supports some of the largest independent practices with over 200 practicing rheumatologists across the US. Pts with rheumatic diseases in care in Jan'19-May'20 were selected for analysis. Trends were evaluated for in-office drug administrations, new starts on targeted immune modulating therapy (TIM) both in-office and self-administered, drug administration, new and existing patient visits, telehealth visits, telephonic services, labs, x-rays, minor surgical procedures, and other diagnostic and treatment procedures.

Results: Of 120,780 pts treated in the study period, 19,449 (16%) were treated in central region, 44,055 (36%) in western, and 57,276 (48%) in southern; there were no practices representing northeast hardest hit by COVID-19.

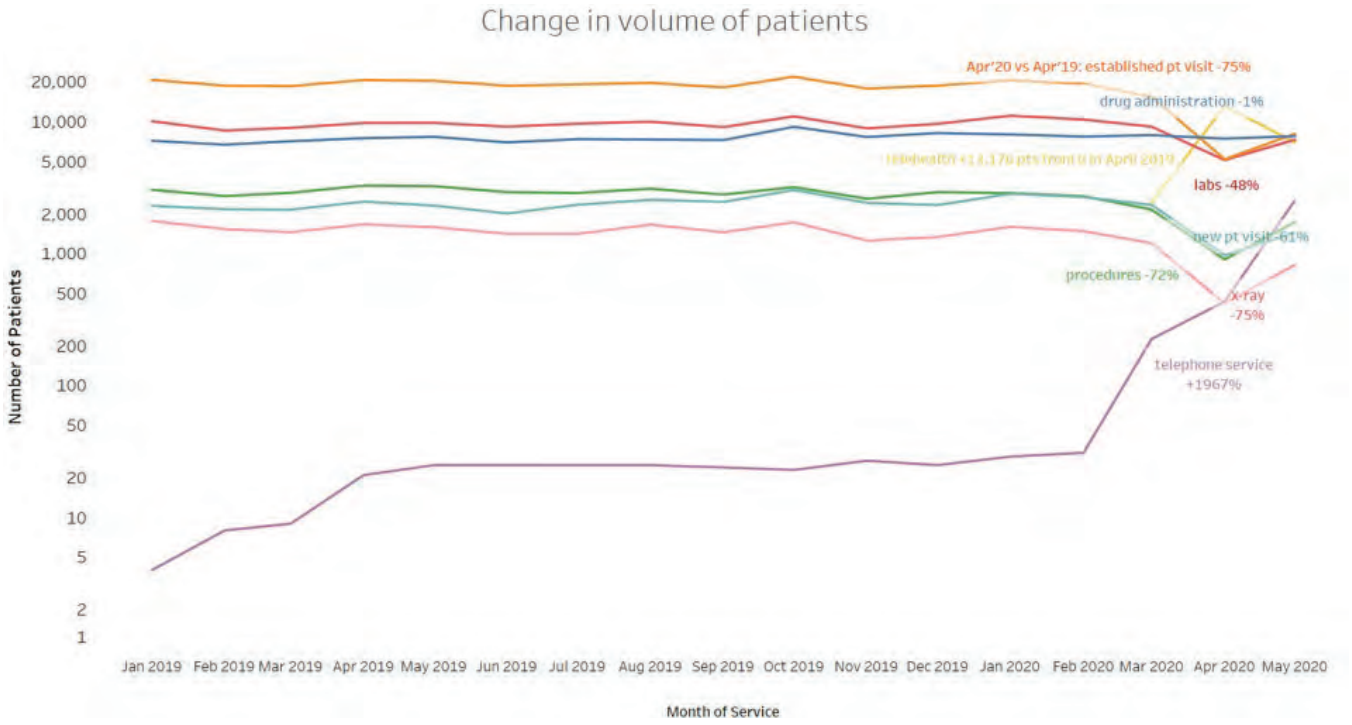

Figure 1. Change in patient volume

In Mar'20, treated pt number declined 6% vs Feb'20 and 0.4% vs Mar'19; in Apr'20 pt number declined 4% vs Mar'20 and 13% vs Apr'19, while in May'20 pt number was flat vs Apr'20 and down 12% vs May'19. Considering all services delivered by the practices, there was 12% decline in service volume in Mar'20 vs Feb, 28% decline in Apr'20 vs Mar, and 22% increase in May'20 vs Apr; there was 2% decline in Mar, 36% in Apr, and 23% in May'20 vs corresponding months of 2019.

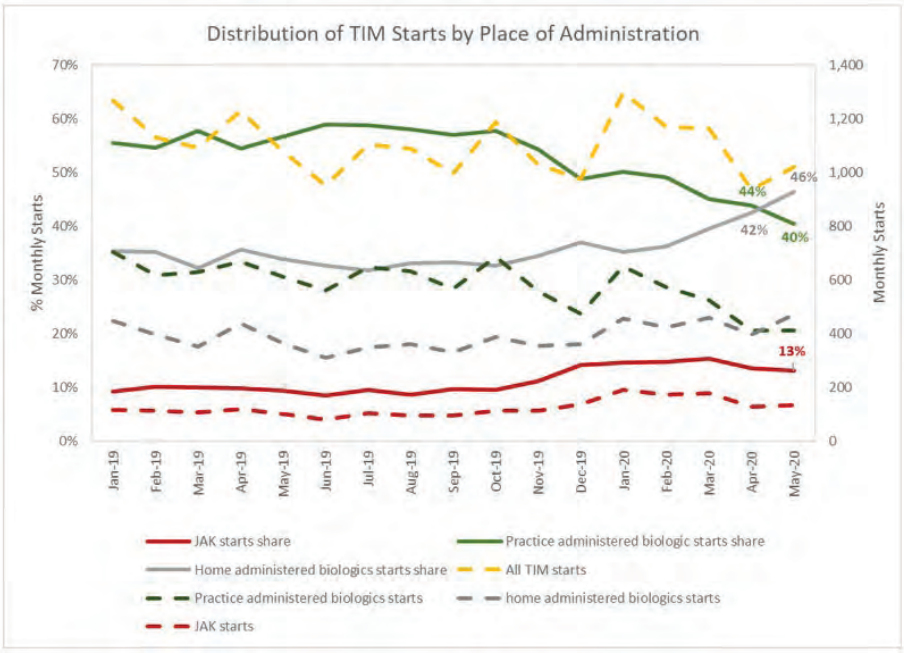

Figure 2. Distribution of starts on targeted immune modulating therapy (TIM)

Most affected services in Mar-Apr were procedures, new and established pt visits, x-rays, and labs [Figure 1]. Telehealth was implemented in Mar'20 with 2,449 pts seen via telehealth visits. Telehealth grew 438% in Apr from Mar reaching 13,176 pts and declined 47% in May over Apr. Telephone services were provided to 226 pts in Mar'20 vs 9 pts in Mar'19, telephone services were up 92% in Apr'20 vs Mar and 487% in May vs Apr. Drug administrations were + 3% in Mar'20 vs Feb, -6% in Apr vs Mar, and +7% in May vs Apr.

Growing pre-COVID trend towards home administration of biologics continued during stay-at-home advisory: in May pt starts on home administered biologics overtook starts on practice administered biologics [Figure 2].

Conclusion: During COVID-19 outbreak in the US stay-at-home advisory period significantly influenced care patterns of pts with rheumatic diseases with sharp growth of telehealth and decline in in-person visits, drug administrations, and diagnostic testing. Further research is needed to evaluate these trends as the pandemic continues.

Disclosure: K. Huston, None; **N. Soloman**, Horizon, 5, 8, Amgen, 2, 8, Abbvie, 2, 5, 8, UCB, 2, 5, 8, Novartis, 5, 8, Jannsen, 2, 8, Pfizer, 8, Lilly, 2, GSK, 2, 5, 8; **J. Radtchenko**, Gilead, 2, ViiV, 2; **S. Helfgott**, Abbvie, 5; **J. Singh**, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **C. Edgerton**, Sandoz, 5.

Abstract Number: 0611

Disease Activity and Disability Are Not Associated with Rehabilitation Utilization in African Americans with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Health Services Research Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Considerable advances in pharmacological care for adults with rheumatoid arthritis (RA) over the last 25 years have reduced disease activity in individual patients, but disability has not improved to the same extent. Rehabilitation, including physical therapy (PT) and occupational therapy (OT), is recommended to address disability and functional limitations, yet utilization of rehabilitation for adults with RA in the United States is low. Reductions in RA disease activity and disability are associated with utilization of rehabilitation services in Caucasian adults with RA, but it is unclear if associations are similar in African Americans. Thus, we examined the association of disease activity and disability with rehabilitation utilization in African Americans with RA.

Methods: We analyzed baseline data from the Consortium for the Longitudinal Evaluation of African Americans with RA (CLEAR) I Registry (disease duration < 24 months) and the CLEAR II Registry (any disease duration). Data were collected in a single visit for each participant at one of four southeastern US institutions. The clinical variables of

	Full Sample	Early RA	Established RA	p-value^
	Mean ± SD or Median [IQR] or % (n)			
n	1067	445	622	
Age, years	54.2 ± 12.2	51.3 ± 13.0	56.3 ± 11.1	<0.001
Sex, women	86% (916)	84% (373)	87% (543)	0.11
BMI, kg/m^2	31.6 ± 7.7	31.6 ± 7.7	31.6 ± 7.5	0.97
Education, more than HS	43% (459)	43% (187)	44% (272)	0.75
Household income, >$30k	25% (263)	30% (130)	22% (133)	0.003
Comorbidities, number	3 [2, 5]	3 [1.5 , 4]	3 [2, 5]	<0.001
Disease duration, months	37 [13, 137]	11 [6, 17]	117 [60, 213]	*n/a*
DMARD use, yes	84% (903)	82% (364)	87% (539)	0.04
Disease Activity (DAS28-CRP), score*	3.9 ± 1.4	4.0 ± 1.5	3.8 ± 1.3	0.05
Disability (HAQ), score	1.3 ± 0.73	1.3 ± 0.76	1.3 ± 0.72	0.52
Rehabilitation utilization in the last 6 months, yes	14% (150)	13% (59)	15% (91)	0.60
Rehabilitation utilization ever, yes	41% (432)	31% (137)	48% (295)	<0.001

^comparing Early RA & Established RA using independent t-test, Mann-Whitney U test or Chi-squared as indicated; *missing n=157

Table 1. Participant Characteristics

	Full Sample	Early RA	Established RA
Disease Activity (DAS28-CRP)			
Utilization in the last 6 months			
Unadjusted OR (95% CI)	1.02 (0.89, 1.17)	1.07 (0.89, 1.30)	0.98 (0.81, 1.18)
Adjusted OR (95% CI)*	1.00 (0.85, 1.18)	1.13 (0.87, 1.47)	0.93 (0.75, 1.15)
Utilization ever			
Unadjusted OR (95% CI)	1.01 (0.92, 1.11)	1.13 (0.98, 1.30)	0.95 (0.83, 1.08)
Adjusted OR (95% CI)*	1.04 (0.92, 1.17)	1.21 (0.99, 1.47)	0.96 (0.82, 1.13)
Disability (HAQ)			
Utilization in the last 6 months			
Unadjusted OR (95% CI)	1.18 (0.93, 1.50)	0.98 (0.68, 1.40)	1.36 (0.99, 1.86)
Adjusted OR (95% CI)*	1.17 (0.84, 1.62)	0.98 (0.57, 1.70)	1.29 (0.84, 1.98)
Utilization ever			
Unadjusted OR (95% CI)	1.10 (0.94, 1.31)	1.11 (0.85, 1.46)	1.09 (0.88, 1.36)
Adjusted OR (95% CI)*	1.00 (0.79, 1.27)	0.86 (0.58, 1.29)	1.02 (0.75, 1.38)

*adjusted for age, BMI, gender, disease duration, comorbidities, DMARD, household income, education, DAS28/HAQ; no models were significant

Table 2. Association of disease activity and disability with rehabilitation utilization

interest were disease activity, defined by the Disease Activity Score 28 with C-Reactive Protein (DAS28-CRP), and disability, measured with the Health Assessment Questionnaire (HAQ). Rehabilitation utilization variables were self-reported recall of PT or OT in the prior 6 months (yes/no) and any prior PT or OT utilization (yes/no). We examined the association of disease activity and disability with rehabilitation utilization using separate binary logistic regression models to estimate odds ratios and 95% confidence intervals. We adjusted for age (years), sex, body mass index (BMI, kg/m^2), disease duration (months), use of disease modifying anti-rheumatic drugs (DMARD; yes/no), comorbidities (number), household income (>$30k vs. ≤$30k), and education (more than high school vs. high school grad or less). We repeated the analyses with the sample stratified by disease duration: early RA and established RA.

Results: Of 1067 participants, 14% reported utilizing rehabilitation in the prior 6 months, and 41% reported ever utilizing rehabilitation (Table 1). Rehabilitation utilization in the prior 6 months was similar among those with early and established RA (13% vs. 15%), but a greater proportion of those with established RA reported any past rehabilitation utilization (31% vs. 48%). Disease activity and disability at the time of baseline visit were not associated with rehabilitation utilization in the past 6 months or ever, in unadjusted and adjusted models (Table 2).

Conclusion: Among African Americans with RA, rehabilitation utilization was low (14%) in the 6 months prior to enrollment into CLEAR, and was not associated with disease activity or disability level. Factors driving rehabilitation

utilization in African Americans with RA, as well as success in reducing disease activity and disability, are unclear, and should be a focus of future research to facilitate delivery of appropriate and effective rehabilitation services.

Disclosure: L. Thoma, None; **R. Cleveland**, None; **S. Bridges**, None; **B. Jonas**, None; **L. Callahan**, Gilead, 5.

Abstract Number: 0612

Differences in 30-Day Rehospitalization Risk and Predictors by Age Group Among Patients with Lupus in Medicare

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SESSION INFORMATION
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Background/Purpose: Although our recent research demonstrates that young adult Medicare beneficiaries (age 18-35) with lupus (SLE) have higher risk of 30-day rehospitalization, predictors specific to young SLE patients have not been evaluated. The objectives of this study are to assess the risk of and predictors for 30-day rehospitalization in young adults with SLE on Medicare compared to non-SLE and older SLE Medicare beneficiaries to inform targeted efforts for readmission reduction.

Table 1. Patient Characteristics of Hospitalizations of Medicare Beneficiaries

Patient Characteristic n (%)		Non-SLE n= 1,378,654	SLE Age 18-35 n= 1,133	SLE Age 36-64 n= 4,855	SLE Age 65+ n= 4,880
Female Sex		776,803 (56)	1,037 (92)	4,331 (89)	4,355 (89)
Age (median, IQR)		75.0, 67.2-83.2	29.8, 26.8-32.5	52.5, 45.4-59.0	73.4, 69.3-79.7
Race/Ethnicity	Asian	14,920 (1)	24 (2)	52 (1)	37 (1)
	Black	168,877 (12)	586 (52)	1,880 (39)	987 (14)
	Hispanic	27,180 (2)	170 (15)	297 (6)	71 (1)
	Native American	10,068 (1)	26 (2)	64 (1)	39 (1)
	White	1,378,654 (83)	253 (22)	2,493 (51)	3,992 (82)
	Other/Unknown	19,022 (1)	74 (7)	69 (1)	54 (1)
Neighborhood Deprivation Rank (mean ± sd)		51.0 ± 27.0	61.2 ± 26.9	59.7 ± 26.6	49.5 ± 27.1
Ever Received Medicaid		411,694 (30)	1,036 (91)	2,912 (60)	1,059 (22)
Disability on Enrollment		440,957 (32)	898 (79)	4,590 (95)	1559 (32)
Length of Stay (median, IQR)		4, 2-6	4, 2-6	4, 2-6	4, 2-6
HCC Score (median, IQR)		2.27, 1.26-3.89	3.92, 2.24-6.07	3.25, 1.90-5.32	2.8, 1.70-4.42
Renal Failure		308,476 (22)	745 (66)	1839 (38)	1244 (25)
Coagulopathy		94,073 (7)	363 (32)	830 (17)	488 (10)
Congestive Heart Failure		291,295 (21)	345 (30)	1139 (23)	1134 (23)
Deficiency Anemia		429,475 (31)	900 (79)	2547 (52)	1917 (39)
Drug Use Disorder		55,168 (4)	308 (27)	630 (13)	78 (2)
Fluid or Electrolyte Disorder		406,930 (30)	794 (70)	2234 (46)	1674 (34)
Hypertension w/ Complications		983,804 (71)	895 (79)	3566 (73)	3601 (74)

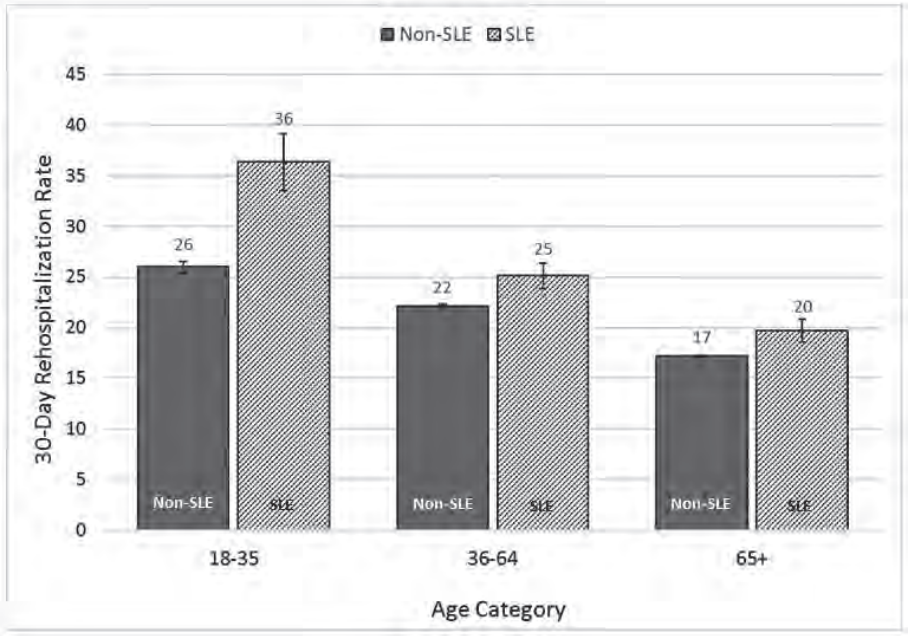

Figure 1. 30-Day Rehospitalization Rates by Age Group for Medicare Beneficiaries with and without SLE. Percentage of hospitalizations resulting in re-hospitalization within 30 days from discharge by age group among Medicare beneficiaries with (hatched bar) and without (solid bar) SLE. Error bars represent 95% confidence intervals.

Methods: This retrospective cohort study utilized a 20% random sample of all adult hospitalizations in Medicare from 2013-2014. Inclusion required at least 1 year of continuous Medicare AB coverage before hospitalization; hospitalizations with a SLE diagnosis code were included in the SLE sub-cohort. Observations from HMO or Railroad beneficiaries or specialty care hospitals were excluded.

Table 2. Multivariable Models for Rehospitalization within 30-Days in Patients with SLE by Age Group

		SLE Age 18-35 N= 1,133	p	SLE Age 36-64 N= 4,855	p	SLE Age 65+ N= 4,880	p
Age at Index Admission		**0.94 (0.90, 0.98)**	**0.002**	**0.98 (0.97, 0.99)**	**<0.001**	1.00 (0.98, 1.01)	0.58
Sex	Female	1.32 (0.79, 2.20)	0.29	0.89 (0.69, 1.16)	0.40	0.88 (0.67, 1.15)	0.33
Race/Ethnicity	White	ref		ref		ref	
	Asian	0.40 (0.15, 1.07)	0.07	0.75 (0.35, 1.59)	0.45	0.80 (0.36, 1.79)	0.58
	Black	0.74 (0.49, 1.11)	0.15	1.13 (0.94, 1.36)	0.21	1.06 (0.94, 1.34)	0.62
	Hispanic	**0.59 (0.35, 0.98)**	**0.04**	0.98 (0.71, 1.36)	0.93	0.84 (0.41, 1.73)	0.64
	Native American	1.01 (0.46, 2.19)	0.98	1.26 (0.74, 2.13)	0.40	1.04 (0.56, 1.96)	0.90
	Other/Unknown	0.78 (0.42, 1.44)	0.42	0.66 (0.35, 1.25)	0.21	1.19 (0.56, 2.50)	0.65
Ever Received Medicaid		1.06 (0.61, 1.86)	0.84	0.93 (0.78, 1.11)	0.43	0.97 (0.78, 1.21)	0.79
Disability on Enrollment		0.91 (0.60, 1.37)	0.65	0.94 (0.67, 1.31)	0.71	0.99 (0.82, 1.2)	0.95
Length of Stay (days)		**1.03 (1.01, 1.06)**	**0.001**	**1.04 (1.02, 1.05)**	**<0.001**	**1.03 (1.01, 1.04)**	**<0.001**
Neighborhood Deprivation Rank		1.00 (0.99, 1.01)	0.97	1.00 (1.00, 1.00)	0.24	1.00 (1.00, 1.00)	0.32
HCC Community Score		**1.08 (1.01, 1.15)**	**0.03**	**1.18 (1.14, 1.23)**	**<0.001**	**1.20 (1.16, 1.25)**	**<0.001**
Deficiency Anemia		1.26 (0.74, 2.14)	0.40	1.00 (0.82, 1.23)	0.98	1.02 (0.84, 1.23)	0.86
Congestive Heart Failure		**2.03 (1.43, 2.88)**	**<0.001**	1.16 (0.94, 1.43)	0.18	**1.31 (1.07, 1.61)**	**0.008**
Coagulopathy		**1.51 (1.07, 2.12)**	**0.02**	1.08 (0.86, 1.36)	0.49	1.15 (0.90, 1.46)	0.26
Drug Use Disorder		**1.60 (1.11, 2.31)**	**0.01**	**1.73 (1.31, 2.28)**	**<0.001**	1.22 (0.75, 2.00)	0.42
Hypertension with Complications		1.15 (0.71, 1.86)	0.58	0.93 (0.75, 1.15)	0.50	1.04 (0.85, 1.27)	0.72
Electrolyte Disorder		**2.29 (1.48, 3.53)**	**<0.001**	**1.27 (1.05, 1.53)**	**0.01**	1.15 (0.96, 1.39)	0.13
Renal Failure		1.03 (0.70, 1.53)	0.87	1.12 (0.90, 1.39)	0.98	1.01 (0.82, 1.24)	0.95

Thirty-day rehospitalization rates were calculated by age group among SLE and non-SLE patients. Initial generalized logistic regression clustered by individual estimated the odds of rehospitalization by age group, presence of SLE, and interactions between age group and SLE. Multivariable regressions were then performed within each SLE age group strata based on *a priori* and LASSO selected predictors of rehospitalization in young adults including socioeconomic, hospitalization, and comorbidity factors.

Results: Among 1,378,654 non-SLE and 10,868 SLE Medicare hospitalizations (Table 1), the observed 30-day rehospitalization rate in young adults without SLE was 26% (Figure 1). For young adults with SLE, the rehospitalization rate was 36%, decreasing to 20% in those over 65. Both young adult age (aOR 1.69, CI 1.60-1.78) and having SLE (aOR 1.18, CI 1.08-1.28) significantly increased odds of rehospitalization compared to patients of older age or without SLE; young adults with SLE had further increased odds (interaction term aOR 1.38, CI 1.11-1.71).

In multivariable models within age strata of SLE patients, each added day of index hospitalization length was associated with increased odds of rehospitalization in all age groups (Table 2). Among 18-64 year olds, increasing age was protective against rehospitalization. Medicare's hierarchical condition category (HCC) score (designed to predict expenditures and mortality) was significantly associated with greater odds of rehospitalization in each age group, although the magnitude of effect was lower in young adults who had additional predictive factors such as heart failure, drug use, and coagulopathy.

Conclusion: Hospitalized young adults with SLE in the Medicare population are more racial diverse, from more disadvantaged areas, and have more comorbid conditions, and more than 1 in 3 are rehospitalized within 30 days of discharge. Comorbidities such as coagulopathy, drug use disorder, and heart failure conferred a greater increase in odds of 30-day rehospitalization in young adults with SLE than in older adults with SLE. Together these findings suggest a critical need to develop targeted interventions with young adults to support these high-risk patients and reduce rehospitalizations.

Disclosure: M. Schletzbaum, None; **Y. Chen**, None; **A. Sheehy**, None; **F. Kaiksow**, None; **R. Powell**, None; **A. Gilmore-Bykovskyi**, None; **A. Kind**, None; **C. Bartels**, Independent Grants for Learning and Change (Pfizer), 2.

Abstract Number: 0613

Modeling the Effects of Covid-19 Protective Behaviors and Healthcare Delivery on the Health of Patients with Rheumatic Disease

Kevin Kennedy[1], Emily Sirotich[2], Salman Surangiwala[3], Maggie Larche[2], Mitchell Levine[1] and Jonathan Hausmann[4], [1]McMaster University, Hamilton, Canada, [2]McMaster University, Hamilton, ON, Canada, [3]Queen's School of Medicine, Kingston, Canada, [4]Boston Children's Hospital / Beth Israel Deaconess Medical Center, Cambridge, MA

SESSION INFORMATION
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Session Title: Health Services Research Poster
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Background/Purpose: COVID-19 has caused global disruptions in the management of chronic illnesses. The extent to which patients with rheumatic disease have been affected by COVID-19 and the related changes to methods of health service delivery is unknown. We present a model capturing the effects of the pandemic on the physical and mental health of a sample of adult patients with rheumatic disease.

Disclaimer: The views expressed here are those of the authors and participating members of the COVID-19 Global Rheumatology Alliance and do not necessarily represent the views of the American College of Rheumatology, the European League Against Rheumatism (EULAR), or any other organization.

Methods: The COVID-19 Global Rheumatology Alliance Patient Experience Survey was disseminated online to patients with rheumatic disease. Patients reported age, gender, WHO region, employment status, ethnicity, change in employment status, smoking status, current rheumatic disease control, methods of communicating with rheumatologist, medications, possible exposure to COVID-19, COVID-19 diagnosis, hospitalization due to COVID-19, mental/physical health, and methods taken to protect from COVID-19, were entered in two multivariable regression models. The two models assessed the associations with the entered variables with PROMIS Global Health Mental and Global Health Physical scales.

Results: Out of 9,393 patients, 1,544 were removed due to missingness. PROMIS Global Health Physical was associated with the additive independent predictors entered into the model with a large effect size ($R2adj = 0.41$, $F = 123.744, 7804$, $p < 0.001$). After adjusting for employment status, region, ethnicity, age, disease activity, smoking status, medications, and gender, patients unable to communicate with their rheumatologist reported a decreased physical health (-0.25, $p < 0.001$). Patients who quarantined, or those with COVID-19 diagnosis, experienced worse physical health (-0.18, $p < 0.001$; -0.21, $p < 0.001$). PROMIS Global Health Mental was associated with the independent predictors with a moderate effect size ($R2adj = 0.27$, $F = 67.9444, 7804$, $p < 0.001$). Patients who have not needed to communicate with their rheumatologist, were hospitalized with COVID-19, and had COVID-19 expressed better mental health (0.14, $p = 0.022$; 0.67, $p < 0.01$; 0.31, $p < 0.01$). Patients who identified possible contact with COVID-19 expressed a lower mental health state (0.15, $p < 0.001$).

Conclusion: By modeling the effects of COVID-19 behaviors and health care service delivery, we demonstrated that patients unable to communicate with their rheumatologist, quarantined, and/or with COVID-19, experienced decreased physical health. In contrast, patients experienced better mental health if they reported no need to communicate with their rheumatologist, had COVID-19, and/or were hospitalized due to COVID-19.

It is evident that COVID-19 caused worse physical health, however, having or surviving COVID-19 paradoxically led to improved mental health. It is possible that these patients perceived a reduced mortality risk, despite the consequences to their physical health.

In contrast, patients who reported potential COVID-19 exposures endorsed poorer mental health, perhaps due to a greater perceived risk of mortality. Further exploration of patient characteristics and behaviors in a principal component analysis may provide additional insight into the experience of patients with rheumatic disease amidst a global pandemic.

Disclosure: K. Kennedy, Lyceum Health, 5; **E. Sirotich**, Canadian Arthritis Patient Alliance, 9; **S. Surangiwala**, None; **M. Larche**, AbbVie, 5, Amgen, 5, Boehringer-Ingelheim, 5, BMS, 5, Celgene, 5, Janssen, 5, Mallinckrodt, 5, Novartis, 5, Pfizer, 5, Roche, 5, Sandoz, 5, UCB, 5; **M. Levine**, None; **J. Hausmann**, Novartis, 5.

Abstract Number: 0614

Impact of COVID-19 Pandemic on the Rheumatology Practice in Mexico: Mexican College of Rheumatology Survey

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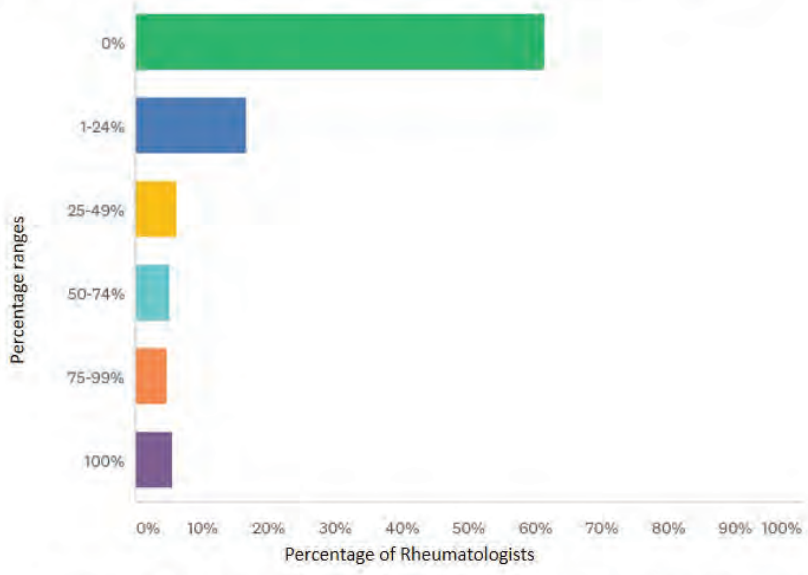
Background/Purpose: COVID-19 pandemic is an evident challenge for healthcare systems and daily clinical practice in developing countries. Particularly, chronic diseases attention has faced difficulties. The Mexican College of Rheumatology (MCR) is a professional membership organization committed to helping the development, communication of knowledge, and the improvement for the care of patients with rheumatic diseases, with 619 active members from the 32 regions in Mexico. We aimed to explore the impact of COVID-19 pandemic on the rheumatology practice among MCR members.

Methods: An anonymous web-based survey was developed and distributed via social media groups and e-mail to all members of the MCR from May 14th to June 12th, 2020. The survey included 27 questions exploring sociodemo-

Fig 1. Percentage of Mexican rheumatologists attending COVID-19 patients.



*Responses to the question ¿Which percentage of your activities are aimed to give attention to COVID-19 patients? Answer options: 0%, 1-24%, 25-49%, 50-74%, 75-99% and 100%.

graphic aspects, the impact of the pandemic in rheumatology practice and, the economic impact for the Mexican rheumatologists. Descriptive statistics were used.

Results: A total of 239 respondents from 24 regions of Mexico completed the survey. By gender, 130 (54.4%) were women and 109 (45.6%) men. The median (IQR) age was 46 years (36-56). Rheumatologist practice was private only in 82 (34.3%) of cases, public only in 8 (4.4%), and both in 144 (60.3%); 5 rheumatologists (2.1%) did not have clinical practice. Among those with private practice, 147 (84.0%) reported a reduction of more than 50% in the number of patient visits and 27 (12.4%) closed their practice. The main protective measures used in private practice were increasing hygienic measures (83.2%) and reducing the number of patients by hour/day (63.1%). Rheumatologist reported expenses in more than 25% of their total income to implement protective measures in their practices in 34.4% of the cases. Different online platforms were used by 76.3% rheumatology specialists, 80% reported they have reduced their fees and 14.1% did not charge when giving online consultation. Those having public practice, 118 (82.9%) reported a reduction of more than 50% in the number of patient visits and 43 (29.9%) did not give rheumatology consultations anymore. The reduction of more than 50% of consultations number was not associated with age neither in private, nor in public practice (p=0.25 and p=0.53, respectively) and no association with gender was found (p=0.52 and p=0.30, respectively). Most of the rheumatologists working in public practice (83.3%) have bought themselves the protective equipment needed. Of all rheumatologists who answered the survey, 15.7% reported more than 50% of their activities were aimed to see patients with COVID-19, and 11 (5.1%) had been diagnosed with the disease.

Conclusion: The survey shows the negative impact in the Mexican rheumatology clinical practice of COVID-19 outbreak with the reduction of overall public and private consultations and supports the need to establish appropriate measures to keep the attention of patients with rheumatic diseases during COVID-19 pandemic.

Disclosure: N. Ruiz, None; **J. Ruiz Guizar**, None; **E. Zamora Tehozol**, None; **I. Colunga Pedraza**, None; **C. Hernández-Díaz**, None; **V. Rivera-Terán**, None; **C. Pacheco Tena**, None; **D. Alpizar-Rodriguez**, None.

Abstract Number: 0615

Rheumatology Going Digital: Developing a Rheumatology App for Use by All Patients Attending Our Department to Aid Remote Working and Self-management

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Background/Purpose: Patients with a rheumatological condition require information regarding the disease itself and treatments regimes. This is particularly important for new patients.

Our local patient focus group asked for reliable information, produced by their rheumatology team with the aim to help self-management. They wanted readily accessible information in one place, that they could review, replay and access, as required.

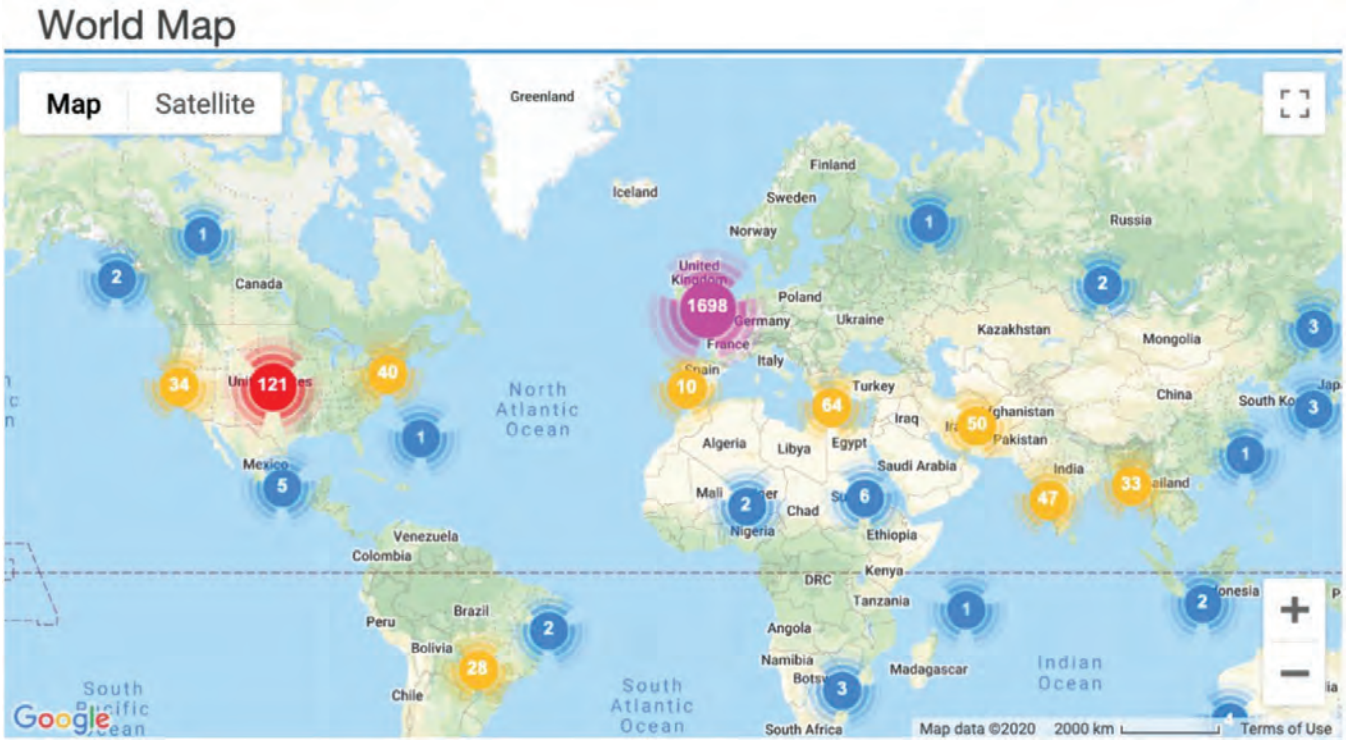

Figure 1. Downloads and where the App is being used

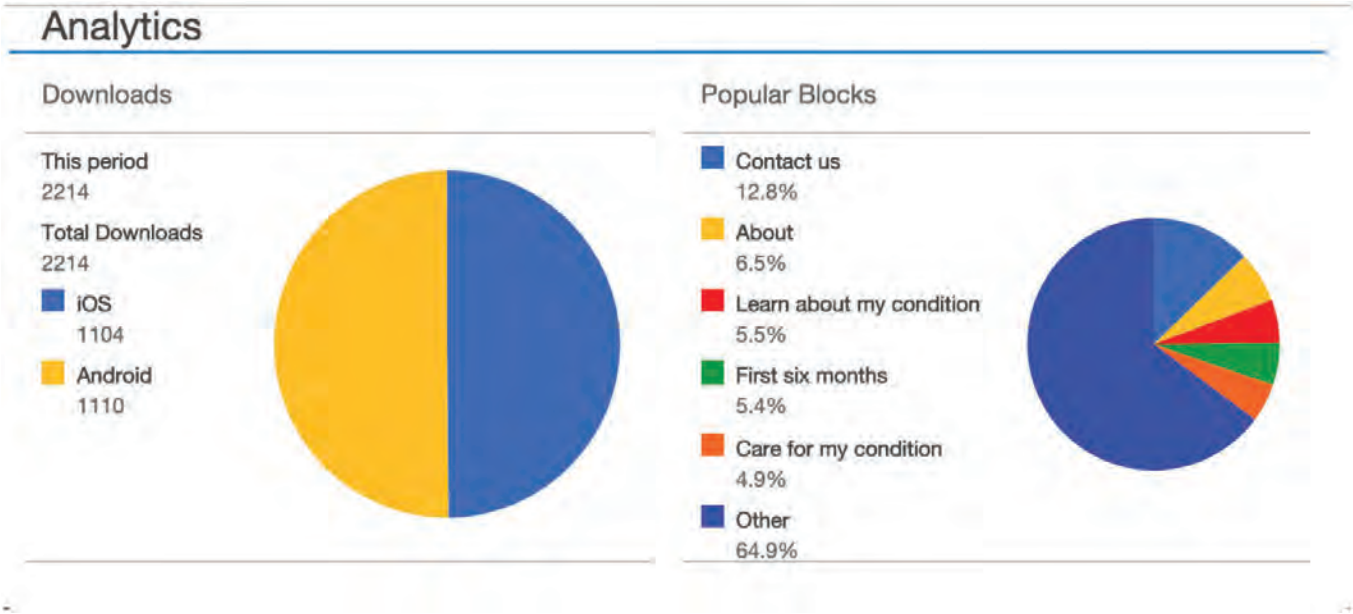

Figure 2. Most frequently viewed sections of the App

Methods: We decided the way forward was to produce a Rheumatology App, thus we gathered together a number of patients with a rheumatological condition, of various ages, the Rheumatology multi-disciplinary team (MDT) and identified an industry partner, hci.digital, who was able to advise on the development of an appropriate Application. We called this App 'Rheumatology Connect'.

A picture is worth a thousand words, hence we developed over 40 short videos. Then, we provided links to other relevant patient websites e.g. NASS, Versus Arthritis, NRAS etc. We produced written information about various dis-

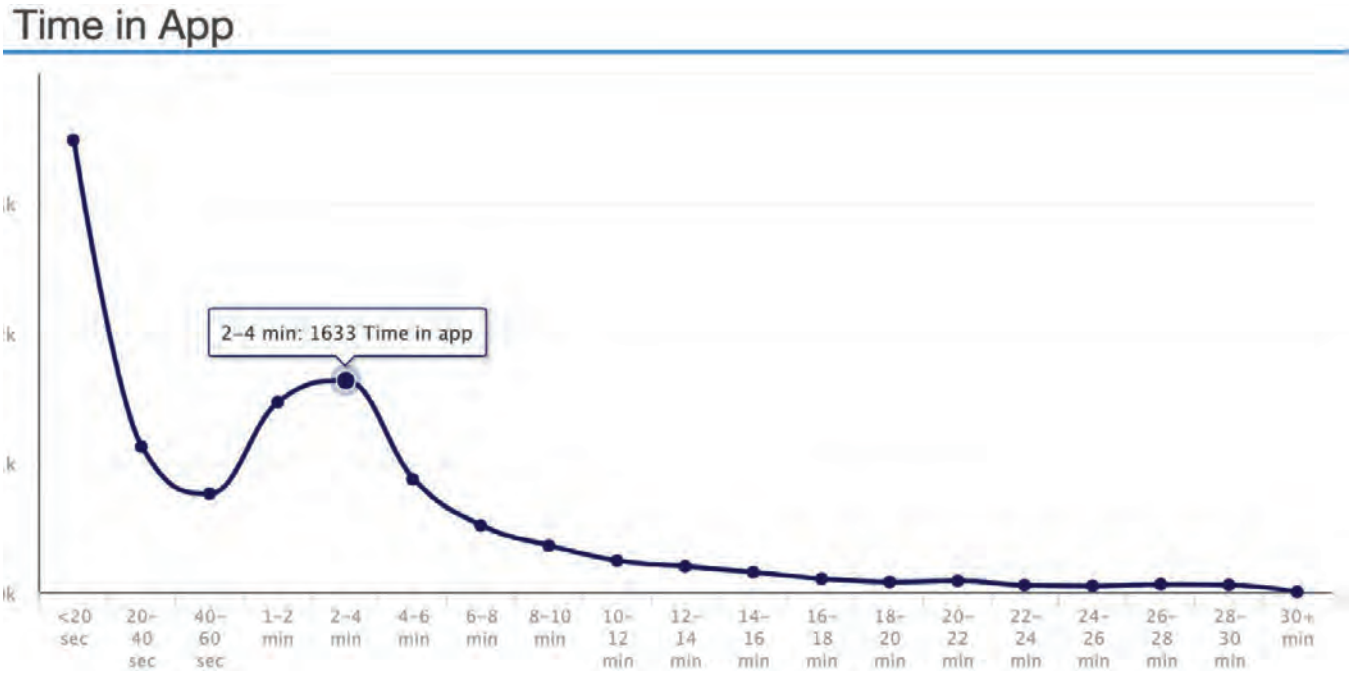

Figure 3. Time spent in App

eases and treatments e.g. Methotrexate. We also provided direct contact details, information about the local hospital and where to park. The written content, including video scripts, was provided by the authors and filmed by hci.digital.

Naturally, our patients were involved at all times and helped considerably in ensuring the App is easily navigable by all.

The results were presented to our patients in June 2018, who gave us their candid opinion of our efforts and how they would like us to develop the App further.

Results: Our App has been downloaded 2214 times, with over 10,000 visits and 35,000 page views, with peaks around the time of our monthly education sessions when we advertise the App to new patients.

Over 73% spent between 2-4 minutes in the App on each occasion with most of the videos being between 2-3 minutes long. Common hits include: videos on medications, contact details, different conditions, services available and clinic locations.

Patients have made spontaneous contact saying how valuable they find the information we have given them.

Emails and telephone calls can be made directly from the App, helping patients and aiding an efficient service by allowing direct phone calls or emails to the correct member of the MDT e.g. rheumatology physio, rather than going through the secretaries. Emailing rather than telephoning helps the department by making our services more efficient, as it frees up secreatarial time for other work.

Conclusion: Our patients have continued to download and use the App and it has become an important part of our patient education efforts, in particular, for those with a new diagnosis.

We can respond to patient queries more quickly now patients are contacting us by email rather than telephone and avoiding difficult to hear ansa-phone messages.

Our patient steering committee has asked us to develop interactive PROMS, a calendar reminder function and medicines management function and this is in process, having raised funds to develop this. The update of the App should be available by the end of the Summer 2020.

Download free from App store (search '*Rheumatology Connect'*) or go to www.rheumatologyconnect.info.

Disclosure: K. Mackay, None; **M. Clemence**, None; **R. Penford**, None.

Abstract Number: 0616

Correlation Between Disease Activity and Perceived Economic Barriers to Care in a Population of African American Women with Systemic Lupus Erythematosus

Ashley White[1], Trevor Faith[1], Aissatou Ba[1], Viswanathan Ramakrishnan[2], Hetlena Johnson[3], Jillian Rose[4], Clara Dismuke-Greer[5], Jim Oates[6], Leonard Egede[7] and Edith Williams[1], [1]Medical University of South Carolina, Charleston, SC, [2]medical university of south carolina, south carolina, [3]LupusCSC, Columbia, SC, [4]Hospital for Special Surgery, New York, [5]Palo Alto VA, Palo Alto, CA, [6]Medical University of South Carolina, Charleston, SC, Charleston, SC, [7]Medical College of Wisconsin, Milwaukee, WI

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is a complex, multifactorial disease with heterogeneous presentation. Disease activity – the number and severity of symptoms – can be influenced by a multitude of patient level and environmental factors. This examination seeks to explore the relationship between economic barriers to care and self-reported disease activity among a cohort of patients diagnosed with the disease.

Methods: Data for this study were aggregated from the baseline (pre-intervention) visits of the Peer Approaches to Lupus Self-Management (PALS) and Care Coordination Approaches to Learning Lupus Self-Management (CALLS) studies. Disease activity was assessed using the Systemic Lupus Activity Questionnaire. We used a Pearson Correlation to evaluate the correlation between disease activity and economic hardship in this using the "Systemic Lupus Activity Questionnaire" as an indicator of disease activity and questions from financial/travel surveys as indicators of economic hardship. The PALS study enrolled African American women with SLE at the Medical University of South Carolina while the CALLS study enrolled recently hospitalized SLE patients at the same institution. The CALLS study was not limited to African American women; however, the cohort was disproportionately made up of this population.

Results: There was no correlation between the indicator of disease activity during the past four weeks from and the indicators of economic barriers and financial barriers to care outside the MUSC hospital setting. As well as no correlation between disease activity and healthcare utilization outside of MUSC. There was no correlation between our indicator of disease activity during the past three months from the Systemic Lupus Activity Questionnaire and our indicators of economic barriers and financial barriers to care outside the MUSC hospital setting. As well as no

correlation between our indicator of disease activity during activity during the past three months and health utilization outside of MUSC.

Conclusion: These results indicate that economic and financial barriers to care and healthcare utilization outside the MUSC hospital setting are not statistically significant to estimate short term disease activity among this cohort of lupus patients. However, the majority of Lupus Quality of Life scores were high, indicating less interference of health and emotional issues on work and daily routine. These findings suggest that long-term studies are needed to further elucidate the impact of economic barriers on disease activity among lupus patients. Impaired access to care has profound implications for chronic and progressive disease care. With limited access to appropriate primary and specialty care, SLE patients are likely to seek care in emergency departments which increases the cost of care and diverts resources from acute care needs. Moreover, patients who forgo standard care are more likely to experience disease flares and develop organ damage which can be life threatening.

Disclosure: A. White, None; **T. Faith**, None; **A. Ba**, None; **V. Ramakrishnan**, None; **H. Johnson**, None; **J. Rose**, None; **C. Dismuke-Greer**, None; **J. Oates**, None; **L. Egede**, None; **E. Williams**, None.

Abstract Number: 0617

Support Methodologies for African American Women with Lupus – Comparing Two Study's Effects on Patient Activation

Ashley White[1], Trevor Faith[1], Aissatou Ba[1], Viswanathan Ramakrishnan[2], Hetlena Johnson[3], Jillian Rose[4], Clara Dismuke-Greer[5], Jim Oates[6], Leonard Egede[7] and Edith Williams[1], [1]Medical University of South Carolina, Charleston, SC, [2]medical university of south carolina, south carolina, [3]LupusCSC, Columbia, SC, [4]Hospital for Special Surgery, New York, [5]Palo Alto VA, Palo Alto, CA, [6]Medical University of South Carolina, Charleston, SC, Charleston, SC, [7]Medical College of Wisconsin, Milwaukee, WI

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Background/Purpose: Systemic Lupus Erythematosus (SLE) is a chronic inflammatory disease in which the immune system of affected individuals attacks their own healthy tissues. While pharmaceutical therapies are an important part of disease management, many behavioral interventions have been implemented to increase patients' disease self-management skills, provide social support, and encourage patients to take a more active role in their care. This study seeks to compare two studies providing support to SLE patients and their subsequent effect on patient activation.

Methods: Within these two studies three interventions are considered. A peer-to-peer methodology and patient support group were evaluated in the Peer Approaches to Lupus Self Management (PALS) and a patient navigator mediated program was evaluated in the Care-Coordination Approach to Lupus Self-Management (CALLS). Both studies were implemented for patients with SLE at the Medical University of South Carolina (MUSC). The outcomes of interest for this examination are the Patient Activation Measure and Lupus Self Efficacy Score. We used a Least Squares Means model to analyze change in the total Patient Activity Measure and Lupus Self Efficacy scores independently in each cohort. We adjusted for demographics such as age, education, income, employment, and insurance. Participants in this study were largely African American women with SLE. Participants in the peer-to-peer arm and support group arms (PALS) were entirely African American women and recruited at the MUSC. The patient navigator arm

(CALLS) was not exclusively made up of African American women, but was disproportionately so. These subjects were identified due to recent hospitalizations at MUSC.

Results: Within the PALS study, the model that adjusted for demographic covariates described the data better but there was not a statistically significant difference between patient activation measures and lupus self-efficacy measures from baseline to post intervention measures. Within the CALLS study, the model that adjusted for demographic covariates described the data better but there was not a statistically significant difference between patient activation measures and lupus self-efficacy measures from baseline to post intervention measures. Comparing PALS to CALLS, the difference between baseline and postintervention measures seems to greater for the PALS study, thus warranting further investigation of the differing methodologies of the two studies.

Conclusion: These findings suggest that there is a difference between the two studies and their effects on patient activation and lupus self-efficacy.

Tailored interventions are a critical pathway towards improving disease self-management among SLE patients. Ideal interventions may look to include the peer mentoring approach.

Disclosure: A. White, None; **T. Faith**, None; **A. Ba**, None; **V. Ramakrishnan**, None; **H. Johnson**, None; **J. Rose**, None; **C. Dismuke-Greer**, None; **J. Oates**, None; **L. Egede**, None; **E. Williams**, None.

Abstract Number: 0618

The Effect of Travel Burden on Depression and Anxiety in African American Women Living with Systemic Lupus

Trevor Faith[1], Ashley White[1], Aissatou Ba[1], Viswanathan Ramakrishnan[2], Hetlena Johnson[3], Jillian Rose[4], Clara Dismuke-Greer[5], Jim Oates[6], Leonard Egede[7] and Edith Williams[1], [1]Medical University of South Carolina, Charleston, SC, [2]medical university of south carolina, south carolina, [3]LupusCSC, Columbia, SC, [4]Hospital for Special Surgery, New York, [5]Palo Alto VA, Palo Alto, CA, [6]Medical University of South Carolina, Charleston, SC, Charleston, SC, [7]Medical College of Wisconsin, Milwaukee, WI

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Background/Purpose: The United States has a deficit of rheumatology specialists. This leads to an increased burden accessing care for patients with autoimmune and connective tissue disorders requiring specialized care. Given that most rheumatologists are located in urban centers at large hospitals, many Systemic Lupus Erythematosus (SLE) patients must travel long distances for routine appointments. The present work aims to determine whether travel burden is associated with increased levels of depression and anxiety among these patients.

Methods: Data for this study were collected from the baseline visits of patients participating in two SLE studies at MUSC. At the baseline time point a travel/economic burden survey was assessed as well as the Patient Health Questionnaire 8 and the Generalized Anxiety Disorder 8 survey as measures of depression and anxiety respectively. A linear regression model was used to determine if travel burden contributes to depression/anxiety. Travel burden was determined using the “Travel Burden” questionnaire while depression/anxiety were measured using the total “Personal Health Depression Questionnaire (PHQ) 8” or total Generalized Anxiety Disorder Screener (GAD) 8” scores.

Both models adjusted for the systemic lupus activity questionnaire. Participants in these studies were largely African American women, all of whom were diagnosed with SLE.

Results: Indicators of travel burden did not have a statistically significant association with indicators of depression and anxiety during the time frame of two weeks measured by the total Personal Health Questionnaire assessment scores. However, specifically, 'transportation issues for medical care increasing stress' was a statistically significantly associated with Personal Health. After adjusting for disease activity during the past three months, travel burden did have a statistically significant association with indicators of depression and anxiety. Additionally, indicators of travel burden did have a statistically significant association with indicators of depression and anxiety during the time frame of two weeks measured by the total Generalized Anxiety Disorder assessment score. However, after adjusting for disease activity during the past three months the association was no longer statistically significant.

Conclusion: Previous studies have identified patient travel costs as being problematic. Our findings support the impact of travel burden on depression and anxiety among lupus patients. The difference in the impact of disease activity with associations of travel burden indicators, the Personal Health Questionnaire and the Generalized Anxiety Disorder assessment suggest a potentially larger role with disease activity during the past three months. Our findings suggest investigating long term disease activity to further examine the influence of travel burden. Travel burden remains a significant barrier to care for many SLE patients. Not only does inadequate access to care lead to greater direct healthcare costs but it can also result in the development or worsening of comorbid conditions. Compounding chronic conditions further complicates the treatment process for these patients and impedes appropriate resource delivery.

Disclosure: T. Faith, None; **A. White**, None; **A. Ba**, None; **V. Ramakrishnan**, None; **H. Johnson**, None; **J. Rose**, None; **C. Dismuke-Greer**, None; **J. Oates**, None; **L. Egede**, None; **E. Williams**, None.

Abstract Number: 0619

Pharmacist Intervention: Reducing Insurance Denials of Specialty Medications

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Background/Purpose: Insurance companies have inconsistent formularies that do not align with Rheumatology clinical treatment guidelines. We are faced with the ongoing challenge of insurance companies denying access to specialty medications for patients with very individualized needs. This abstract will examine the common reasons for insurance denials of specialty medications and how pharmacist intervention can impact these denials.

Methods: A retrospective analysis of pharmacist interventions pertaining to insurance denials of prescribed specialty medications was conducted. The interventions consisted of pharmacist written appeal letters for 41 denials (98%) and providing supporting literature for 1 denial (2%). Another data point considered was the number of medication claims for off-label use versus FDA-approved use. The data was compiled from pharmacy intervention records which occurred from July 2019 through May 2020.

The denials involved the following specialty medications for reference: abatacept, adalimumab, anakinra, apremilast, canakinumab, certolizumab, etanercept, infliximab, ixekizumab, pirfenidone, rituximab, secukinumab, sildenafil, tadalafil, tocilizumab, and tofacitinib.

The denials involved the following diagnoses for reference: Adult-Onset Still's Disease, AS, Autoimmune Inner Ear Disease, Behcet's Disease, Checkpoint Inhibitor-induced Arthritis, Chronic Recurrent Multifocal Osteomyelitis, Familial Mediterranean Fever, IgG4-Related Disease, Myhre Syndrome, Psoriatic Arthritis, Raynaud Phenomenon, Recurrent Pericarditis, Relapsing Polychondritis, Rheumatoid Arthritis, SAPHO Syndrome, Schnitzler's Syndrome, and SLE.

Results: Of the 42 insurance denials that required pharmacist intervention, 32 (76%) were medication claims for off-label use and 10 (24%) were for FDA-approved use.

Of the 42 challenged insurance denials, 30 denials were overturned (71%) and 12 denials were upheld (29%). Of the 30 overturned denials, 24 (80%) of the approvals were for medication claims for off-label use and 6 (20%) were for FDA-approved use.

Of all appeal approvals, the average time from date of denial to date of approval was 9 days.

The reasons for initial insurance denials were as follows: non-FDA approved use (27; 64%), step therapy requirements (12; 29%), and quantity limits (3; 7%).

Conclusion: Rheumatologic conditions are progressive and debilitating. In consequence, it is necessary to tailor treatments to the individual patient and not allow medication access to be at the discretion of the insurance company. Based on the data presented, a significant percentage of insurance denials were due to non-FDA approved use or step therapy requirements. Greater than two-thirds of the analyzed insurance denials were overturned, with a remarkable average turnaround time of 9 days. Pharmacists have advanced clinical training and skills to conduct literature review, making them very effective in overturning insurance medication denials, and increasing patient access to medications as a result. It is indicated that pharmacists are a valuable asset to increase the focus on unchallenged insurance denials and reduce existing burden on providers to improve patient care in a timely manner.

Disclosure: N. Sharma, None; **N. Girardi**, None; **K. Wong**, None.

Abstract Number: 0620

Do Physical Therapists Follow Evidence-Based Practice Recommendations for Treatment of Inflammatory Arthritides?

Debbie Ehrmann Feldman[1], Tatiana Orozco[1], Sasha Bernatsky[2], François Desmeules[1], Maude Laliberté[3], Kadija Perreault[4], Jonathan El-Khoury[5], Jean Légaré[4] and Linda Woodhouse[6], [1]Université de Montréal, Montreal, QC, Canada, [2]The Research Institute of the McGill University Health Centre, Montreal, ON, Canada, [3]Integrated Health and Social Services University Network for West-Central Montreal, Montreal, Canada, [4]Université Laval, Québec, QC, Canada, [5]Université de Sherbrooke, Montreal, QC, Canada, [6]Curtin University, Perth, Australia

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Session Time: 9:00AM–11:00AM

Background/Purpose: Physical therapy plays an important role in the global management of rheumatoid arthritis (RA) and ankylosing spondylitis (AS). Therapeutic exercises (mobility, strength and aerobic) and patient education are recommended whereas passive modalities, such as electrotherapy, are more controversial. Our purpose was to document the type of interventions used by physical therapists for patients with RA and AS, to assess whether intervention choices follow current evidence-based practice recommendations, and to explore factors associated with such choices.

Methods: We sent an online survey to physical therapists in the province of Quebec, Canada. Participants were asked about what kind of treatment they would provide for 2 patients showing typical signs and symptoms of RA and AS. Descriptive statistics were used to illustrate the proportions for each treatment chosen by physical therapists. We explored associations between choice of treatments with physical therapists' demographic and practice related factors, using inferential statistics and regression analyses.

Results: A total of 298 physical therapists responded to the online survey. For both RA and AS respectively, the most common interventions were mobility exercises (91.0%; 98.3%) and patient education (90.1%; 92.8%). For both cases, just over 60% selected strength exercises. Passive manual forms of therapy were chosen by 36% of PTs for RA and 58% for AS, and electrotherapy was chosen by 30% for RA and 40.9% for AS. Aerobic exercise was rarely selected as a mode of treatment (less than 3% of the PTs for both RA and AS). For RA, choosing electrotherapy ($p= 0.006$) and passive manual forms of therapy ($p< 0.001$) were highly associated with working in the private sector. For AS, selecting passive manual forms of therapy were highly associated with working in the private sector ($p< 0.001$) and having taken post-graduate related courses ($p< 0.001$).

Conclusion: Most physical therapists chose mobility exercises and patient education, which both represent evidence-based treatment approaches for RA and AS. Despite evidence recommending strength and aerobic exercise for these clienteles, physical therapists underutilize these interventions, especially aerobic exercise. There is a need for better knowledge translation to physical therapists regarding the importance of strength and aerobic exercise for patients with RA and AS.

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Abstract Number: 0621

Effectiveness of Screening in Patients with Rheumatic Disease Before Commencing Biologic Therapy and Risk of Active Tuberculosis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment with biologic therapy has been associated with a high risk of reactivation of latent tuberculosis (TB). Preventive strategies for tuberculosis remain a crucial step before initiating biologics in rheumatic disease.

The study aimed to access the effectiveness of TB screening recommendations before the initiation of biological therapy and identify the incidence of active TB among these patients.

Methods: We performed a hospital-based retrospective cohort study among rheumatic disease patients on biological therapy in two centers in Jeddah between January 2005 to December 2019. Medical files were retrospectively reviewed for demographics data, baseline screening for TB, use of prophylaxis, information on DMARDs and biological therapies, and outcomes results were collected.

Results: A total of 365 patients were included over a period of 14 years. Two hundred ninety-two (80%) had Rheumatoid arthritis (RA),13% psoriatic arthritis (PSA), 9% spondyloarthritis (SPA), 2% SLE, and 4% others. The mean age was 47.54 (±14.2), 311 (85%) were females with a mean duration of disease 8.45 years (± 6.58). Hundred forty-nine (42.3%) were on steroids. Anti TNFs were prescribed in 213 (58.4%) patients, Non Anti-TNFs 124 (36.6%) patients, and Jak inhibitors 18 (5%) patients.TB screening was done to all patients except 3 patients (data missing) before commencing biologics. Forty-four (12.1%) patients had latent TB at baseline and all received chemoprophylaxis with isoniazid before starting biologics. There was no significant difference in patients with latent TB and those without regarding the demographics, comorbid illnesses, old TB, inflammatory markers, BMI, or steroid use.

Four patients with active TB were identified (one with Behcet's disease and three with RA). One patient had a reactivation of latent TB and 3 patients developed de novo TB. Three out of four had an infection in the first 6 months of treatment (one on infliximab and two on rituximab) and one case after 1 year of stopping adalimumab. Two cases had pulmonary TB and two others with extrapulmonary TB (pericarditis and brain abscess each). All four patients with active TB were treated with standard anti TB medications. Three had complete resolution of their TB and one died.

Conclusion: Baseline screening has been effectively carried out in our cohort as per recommendations. Physicians should be vigilant for symptoms and signs of active TB as not only reactivation of latent TB can occur with patients on biologics but also de novo TB can occur.

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Abstract Number: 0622

Infection-induced MPO-ANCA Associated Vasculitis: A Systematic Review of Published Case Reports

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Infection-related Rheumatic Disease Poster
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Background/Purpose: Anti-myeloperoxidase (MPO) antineutrophil cytoplasmic antibody (ANCA) has been implicated in the pathogenesis of microscopic polyangiitis (MPA) and an MPO-ANCA associated glomerulonephritis; both conditions are considered part of the MPO-ANCA associated vasculitis (AAV) spectrum. Recent reports have highlighted that MPO-ANCA AAV can develop during or after an infectious process. We performed a systematic review

Author, year	Clinical characteristics	GN	Duration of infection prior to vasculitis	Causative pathogen	Diagnosis	Anti-infective treatment	Immunosuppressive regimen	Outcome
Meyer et al. (2000)	69 F, weakness and paresthesias of right upper limb, bilateral hearing impairment, peripheral neuropathy, and lung crepitations.	Possible*	Does not clarify	CMV	MPA	Ganciclovir	Prednisolone 80mg/d.	Remission of vasculitis
Nakayama et al. (2000)	53 F, Productive cough, fever and exertional dyspnea for 27 months. Imaging: cavitary lesion of right upper lobe and pulmonary artery stenosis.	No	27 months	MAC	AAV	Anti-mycobacterial regimen	None	Relapse of vasculitis
Hellmich, et al. (2001)	53 M, 3-month history of fever, weight loss, myalgias, leg weakness, dyspnea. PMH of recurrent bacterial endocarditis for 10 years, AV and MV replacement	Possible*	3 months	*S. aureus*	MPA	Not at this presentation - 10-day course of vancomycin 3 months ago	Prednisolone (starting dose 1 mg/kg) and oral cyclophosphamide (2 mg/kg).	Partial remission
Chaiamnuay et al. (2005)	75 F, chronic nonproductive cough, migratory polyarthralgias, microscopic hematuria, cavitary lesion of right upper lobe	Possible*	Does not clarify	MAI	AAV	Anti-mycobacterial regimen	IV methylprednisone (1 g/day for 3 days), followed by oral prednisone 60 mg/day and oral cyclophosphamide 2 mg/kg/day	Remission of vasculitis
Chan et al. (2006)	74 M, Knee monoarthritis, fever, acute renal failure, 3 months after a surgical would infection and abdominal abscess formation, following resection of colorectal cancer	Yes	3 months	*E. coli*	MPA	Ampicillin, gentamicin, metronidazole, cefotaxime and ciprofloxacin	High dose prednisolone and cyclophosphamide	Died, likely from vasculitis complication
Miranda Filloy et al. (2006)	71 F, fever, abdominal pain, palpable purpura and mononeuritis multiplex. Diagnosed with *S. aureus* endocarditis. Three weeks before admission, gangrenous cholecystitis and *S. aureus* bacteremia.	No	3 weeks	*S. aureus*	MPA	IV Cloxacillin, oral rifampicin	Methylprednisolone 60 mg/d	Remission of vasculitis
Nickerson et al (2012)	47 M, fever, decreased urine output, abdominal pain, hypotension and petechial rash. PMH of 2-month history of lymphadenopathy.	No	2 months	*R. rickettsii*	AAV	Broad spectrum antibiotics including doxycycline	Hydrocortisone 1200 mg/dayfor 7 days and then tapered to prednisone 40 mg daily.	Remission of vasculitis
Oumerzouk et al. (2013)	40 M, muscle weakness evolving to flaccid tetraparesis, diffuse myalgia, arthralgia, 10 kg weight loss for 2 months before admission.	No	Does not clarify	CMV	AAV	No	IVIG (0.4 g/kg/day) 5 days followed by methylprednisolone 500 mg/d. Switched to oral prednisolone 1 mg/kg/d, without improvement. Administration of Cyclophosphamide led to partial recovery.	Remission of vasculitis

Mirsaeidi et al. (2013)	25 M, 2-day history of cough, hemoptysis, fevers and 1day hematuria. Nausea, vomiting, abdominal pain and reduced urine output over the last 2 weeks.	Yes	Does not clarify	EBV in the setting of HIV/AIDS	AAV	No	Prednisone and cyclophosphamide	Remission of vasculitis
Xu et al. (2014)	16 F, fever for 3 weeks. Microscopic hematuria and nephrotic range proteinuria. Diagnosed with acute EBV and given ganciclovir plus NSAIDS. Within a week severe anemia and acute kidney injury ensued.	Yes	4 weeks	EBV	AAV	Gancyclovir	IV methylprednisolone 1 mg/kg/d	Remission of vasculitis
Yamaguchi et al. (2014)	80 F, PMH of MAC infection 2 years prior, p/w 2-month history of hearing loss and 1-month history of fever. Workup demonstrated necrotizing GN.	Yes	2 months	EBV	MPA	No	Methylprednisolone pulse therapy, followed by mizoribine and low-dose prednisolone	Remission of vasculitis
Lizarraga et al. (2015)	66 F, fever, fatigue, puffy eyes, frothy urine, hypertention and rapidly progressive GN	Yes	4 weeks	Dengue virus	AAG	No	Methylprednisolone pulses, prednisone, plasma exchange, IV cyclophosphamide	Remission of vasculitis
Asano et al. (2016)	73 F, untreated pulmonary MAC infection for 1 year, fever, polyarthritis, livedo reticularis, purpura, crescentic GN	Yes	11 months	MAC	AAV	Anti-mycobacterial regimen	Prednisolone 1 mg/kg/d	Remission of vasculitis
Addy et al. (2018)	70 F, recurrent chest infections, middle lobe bronchiectasis, purpuric rash, small joint arthralgia, peripheral neuropathy.	No	10 years and 3 months	*M. abscessus*	MPA	Anti-mycobacterial regimen	High dose prednisolone and cyclophosphamide	Relapse of infection and vasculitis
Alnaser et al. (2018)	27 M, lung cavitation, miliary nodules, and necrotizing glomerulonephritis	Yes	2 months	*M. kansasii*	MPA	Anti-mycobacterial regimen	Prednisone 60mg/d.	Died from infection and vasculitis, following treatment discontinuation
Azar et al. (2020)	64 M, fevers, malaise, mild cough, and pain in the left flank. Diagnosed with persistent focal pneumonia and GN	Yes	4,5 months	*Coccidioides* spp.	AAG	Amphoteracin B, after the dissemination of infection from immunosuppressive Tx	IV methylprednisolone, followed by oral cyclophosphamide, therapeutic plasma exchange and rituximab	Died from infection
Hashimoto et al. (2020)	11 F, PMH: chronic back pain for 1 year and proteinuria/hematuria for 3 months history with positive MPO-ANCA. Workup revealed MSSE osteomyelitis of T11.	Yes	9 months	*S.epidermidis*	AAG	2 weeks of IV cefazolin followed by a 3-month course of oral cefaclor	Prednisolone 1 mg/kg per alternate day	Remission of GN

*Possible glomerulonephritis due to the presence of acute kidney injury or proteinuria or hematuria. Patient did not consent to biopsy. CMV, Cytomegalovirus; EBV, Epstein-Barr Virus; MPO-ANCA, Myeloperoxidase specific antineutrophil cytoplasmic antibody; AAV, ANCA associated vasculitis; AAG, ANCA associated glomerulonephritis; GN, glomerulonephritis; M, male; F, female; AV, atrial valve; MV, mitral valve; MPA, Microscopic polyangiitis; MAC, *Mycobacterium avium complex*; MAI, *Mycobacterium avium intracellulare*; MSSE, Methicillin sensitive *Staphylococcus epidermidis*; IV, intravenous; PMH, Past medical history; IVIG, intravenous immunoglobulin.

to identify and describe all infections that induce MPO-ANCA AAV and describe the patients' clinical characteristics and outcomes.

Methods: PubMed/Medline and Scopus databases were searched without any restrictions, from inception to March 2020, in accordance with PRISMA guidelines. Published articles were included, describing the development of

MPO-ANCA AAV during or after infection. The data retrieved were including the causative pathogen, patients' clinical features, the reported diagnosis, the therapeutic regimen used, and the patient outcomes. Two authors independently selected the studies, extracted data and assessed risk of bias.

Results: Among the 595 abstracts identified, 17 case reports articles were included, each describing a single patient (Table 1 and 2). The mean age was 53.8 (range 11-80 years), and the majority were female (58.8%). Seven patients (41.2%) were diagnosed with MPA, 7 (41.2%) with MPO-ANCA AAV, and 3 (17.6%) with MPO-ANCA associated glomerulonephritis. The median time between infection and development of vasculitis was 3 months (range: 3 weeks - 10 years).

The most common pathogens associated with the preceding infections were viruses (35.2%), followed by mycobacterial (29.4%) and bacterial infections (29.4%). The viral infections were caused by EBV, CMV, and 1 case by Dengue virus infection. Mycobacterium avium complex was the most frequent mycobacterial species pathogen, and infective endocarditis due to staphylococcus aureus was the common bacterial infection.

Renal involvement was the most frequent clinical manifestation (70.5%) with renal biopsy-proven glomerulonephritis in 53% of cases, followed by respiratory, musculoskeletal, cutaneous, and nerve involvement. Glucocorticoids and anti-infective agents were administered in the vast majority of patients, and cyclophosphamide in 47%. Three (17.6%) patients expired during follow-up. Vasculitis regressed after the resolution of infection in 10/17 (58.8%). MPO-ANCA titers decreased significantly on follow-up in all 10 cases where they were estimated.

Conclusion: Several infectious agents can lead to the development of MPO-ANCA and the clinical manifestations of MPO-ANCA AAV, which appear to regress with the resolution of infection. Clinicians should be alert for the presence of an underlying infection in patients presenting with MPO-ANCA associated vasculitis, as early detection will enable prompt treatment with the combination of anti-infective and immunosuppressive regimens.

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Abstract Number: 0623

Cytokine Storm: Outcomes in SARS-CoV-2 Patients Treated with Biologics in a Rheumatology Cohort

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SESSION INFORMATION
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Session Title: Infection-related Rheumatic Disease Poster
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Background/Purpose: Cytokine Release Syndrome (CRS) or Macrophage Activation Syndrome (MAS) is a life threating hyperinflammatory condition that can complicate rheumatic disease as well as infections like SARS-CoV-2 (SARS-CoV-2-CRS). Immunomodulators are traditionally used to treat MAS in SLE, Kawasaki disease, and systemic

JIA, but have the potential to treat SARS-CoV-2-CRS. An institution-mandated rheumatology SARS-CoV-2-CRS management algorithm was developed for 2 health systems with use of tocilizumab (TOC) and anakinra (ANA) as first and second-line agents. The objective of this study is to determine characteristics of patients from a SARS-CoV-2-CRS cohort with the overall goal to understand the clinical disease course of these patients and the impact of biologic management.

Methods: A retrospective chart review was completed on SARS-CoV-2 patients at an academic medical center and a county hospital for whom rheumatology consultations were completed for CRS evaluation from March 15-May 30, 2020. Both institutions shared the same electronic medical record system. Patients meeting CRS diagnostic criteria who were treated with biologic therapy were compared to those without CRS not given biologic therapy for the following outcomes: survival, deaths, infections, intensive care unit (ICU) admissions and duration, length of hospitalization, thrombosis and trends in laboratory markers including blood cell counts, liver enzymes, and acute phase reactants.

Results: Out of 150 patients with SARS-CoV-2 referred for rheumatology consultation, 71 (47%) were diagnosed with CRS and were treated with the following biologics: TOC only in 63 (89%), ANA only in 1 (1%), abatacept only in 1 (1%), and 6 (8%) patients who received both TOC and ANA separately. Steroids were given in 64 (90%) CRS patients. Comparing baseline characteristics of all 150 patients (Table 1), CRS patients required more ICU admissions (61%), but had similar need for ventilator support (23%). Biologic treatment resulted in improved ferritin, platelets, and ESR; yet, other laboratory tests remained similar or worse 3-5 days after the first dose (Table 2). Death occurred in 20 (28%) while 36 (51%) were discharged from the hospital (Table 3). Bacterial co-infection at time of diagnosis was noted in 10 (14%); 10 (14%) patients developed a second co-infection after biologic treatment.

Table 1. Characteristics of SARS-CoV-2 patients evaluated for Cytokine Release Syndrome

Characteristic	**SARS-CoV-2-CRS (n= 71)**	**SARS-CoV-2 without CRS (n= 79)**
Age (average years (range))	60 (20-88)	63 (33-102)
Steroid treatment[a]		
Average initial steroid dose	226 mg[b]	129 mg
Average daily steroid dose	162 mg[b]	67 mg
ICU admissions, n (%)	43 (61)	30 (38)
Ventilator support, n (%)	16 (23)	18 (23)
Hypoxia at admission, n (%)	56 (79)	51 (66)
Requiring oxygen during hospitalization, n (%)[d]	69 (97)	70 (89)
Underlying Comorbidities		
Type 2 Diabetes Mellitus, n (%)	36 (51)	36 (46)
Hypertension, n (%)	46 (65)	43 (54)
Hyperlipidemia, n (%)	35 (49)	27 (34)
Coronary artery disease, n (%)	14 (20)	11 (14)
History of CVA, n (%)	10 (14)	13 (16)
Pulmonary disease, n (%)	14 (20)	14 (18)
History of Smoking, n (%)	26 (37)	26 (33)[c]
Co-infection at time of diagnosis n, (%)	10 (14)	25 (32)

[a]Prednisone equivalents
[b]Post-biologic dosing
[c]7 with unknown smoking history
[d]Including those requiring ventilator support

Characteristics of SARS-CoV-2 patients evaluated for Cytokine Release Syndrome

Table 2. Laboratory results in SARS-CoV-2-CRS patients pre- and post-biologic therapy		
Routine labs for CRS monitoring and D-dimer (n=71)	**1-3 days pre-biologic median, (range)**	**3-5 days post-biologic median, (range)**
WBC *(normal range 4.3-11.3 x 10^9/L)*	8.6 (1.1-30.1)	10.5 (1.4-40)
Platelets *(normal range 147-409 x 10^9/L)*	189 (27-694)	296 (33-960)
AST *(normal range 15-37 U/L)*	51 (13-3297)	53 (11-452)
ALT *(normal range 12-78 U/L)*	42 (5-919)	69 (6-932)
LDH *(normal range 87-241 U/L)*	456 (156-5680)	478 (188-1025)
Triglycerides *(normal range 30-150 mg/dL)*	139 (58-365)	169 (84-525)
Ferritin *(normal range 26-388 ng/mL)*	1025 (492-42128)	983 (407-16082)
ESR *(normal range 0-10 mm/hr)*	93 (12-140)	69 (5-140)
Fibrinogen *(normal range 249-494 mg/dL)*	715 (111-1200)	465 (35-1200)
D-dimer *(normal range <0.55 ug/mL)*	2.1 (0.2-28)	3.1 (0.2-21)
Cytokine levels, n = 42		
IL-6 level *(normal range <5 pg/mL)*	35 (1-113607)	34 (1-1698)

Laboratory results in patients with Cytokine Release Syndrome pre- and post-biologic therapy

Table 3. Outcomes in SARS-CoV-2-CRS treated with biologic and Non-SARS-CoV-2-CRS not treated with biologic		
Events	SARS-CoV-2-CRS treated with biologic[a] (n = 71)	Non-SARS-CoV-2-CRS not treated with biologic (n = 79)
Thrombosis/Thromboembolic disease, n (%)	8 (11)[b]	2(3)
Transfer to ICU,[c] n (%)	2(3)	-
Duration of ICU stay (mean number of days)	11	9
Duration from first dose of therapy to downgrade from ICU[d] (mean number of days)	11	-
Hospitalization length (mean number of days)[e]	17	11
Infections, n (%)[f]	10 (14)	-
Clinical Status as of May 30, 2020		
Discharged, n (%)	36 (51)	57 (72)
Days post-treatment	13	-
Death, n (%)	20 (28)	11 (14)
Days post-treatment	14	-
Still Hospitalized, n (%)	15 (21)	11 (14)
ICU	4 (6)	3 (4)
Non-ICU	10 (14)	8 (10)

ICU- Intensive Care Unit
[a]Tocilizumab, Anakinra, and/or Abatacept
[b]5 developed thrombosis prior to biologic
[c]3 days or more after first dose of biologic administered
[d]Calculated for patients that were in the ICU during first dose of biologic
[e]Calculated for patients discharged
[f]5 urinary tract infection, 3 bacteremia, 1 pneumonia, 1 both pneumonia and bacteremia

Outcomes in SARS-CoV-2-CRS treated with biologic and Non-SARS-CoV-2-CRS not treated with biologic

Conclusion: SARS-CoV-2-CRS patients had similar baseline comorbidities to patients without CRS except for co-infections at time of diagnosis that were more common in the latter group. Within the time frame laboratory tests were reviewed, only the ferritin, platelets, and ESR improved after biologic treatment, but overall, patients with CRS had more critical laboratory test results compared to those without CRS. Death was noted to be two-fold higher in CRS patients. All deceased were in the ICU at the time, suggesting a sicker population at greater risk for death. Additional studies are needed including a longitudinal evaluation of trends in laboratory tests post-biologic use in consideration of drug pharmacokinetics and more robust cytokine profiling. Furthermore, outcomes in CRS patients that received biologics should be compared to a control arm that did not receive biologics.

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Abstract Number: 0624

Association of Regional Body Composition and Physical Function Using the Short Physical Performance Battery Among Peruvian Women with HIV

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SESSION INFORMATION

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Background/Purpose: The musculoskeletal (MSK) system is significantly affected by HIV and its treatment. Changes in body composition can reflect important changes in bone and MSK health, particularly among populations at risk for developing fat redistribution syndromes, like HIV-positive women (HpW). Although more than half of HIV-infected population worldwide are women, there are limited data about characteristics of women aging with HIV in Latin American and the Caribbean (LAC). No studies from LAC have focused on the relationship between body composition changes and physical function among these individuals. We aimed to explore the scope of this problem among Peruvian women aging with HIV.

Methods: We enrolled HpW and HIV-negative women (HnW) ≥40 years of age receiving care at a large HIV clinic in Lima, Peru. Dual X-ray absorptiometry (DXA) was used to measure trunk and limb lean mass (LM) and fat mass (FM). Physical performance was assessed with the well-established Short Physical Performance Battery (SPPB) and physical strength with the grip strength test (GST) using a hand hydraulic dynamometer. We used linear regression to model associations between HIV status, body composition and physical test scores.

Results: 104 HpW and 212 HnW were enrolled with a mean age of 52.4±8.2 and 56.4±8.8 years (p< 0.001) and BMI of 26.4±5.1 and 27.6±4.1 kg/m^2 (p=0.03), respectively. Among HpW, the mean years since HIV diagnosis was 11.8±6

Characteristics	HIV-positive women N= 104	HIV-negative women N = 212	P-value
SPPB			
Overall score, mean (SD)	9.99 (1.4)	10.81 (1.12)	**<0.001**
score ≤8 N(%)	17 (16.35)	10 (4.72)	0.099
score >8 N(%)	87 (83.65)	202 (95.28)	**<0.001**
Balance test, mean (SD)	3.68 (0.51)	3.86 (0.36)	**<0.001**
Gait test, mean (SD)	3.56 (0.55)	3.71 (0.48)	**0.01**
Chair stand test, mean (SD)	2.75 (0.71)	3.14 (0.77)	**<0.001**
Grip Strength			
Score (kg), mean (SD)	19.93 (5.91)	19.78 (5.44)	0.8251

SPPB, short physical performance battery; SD, standard deviation

Overall SPPB score, balance test, gait test, chair stand test and grip strength score were tested using two independent samples T-test; proportion SPPB ≤8 and >8 were tested using Fisher's exact test

Table 1. Overall SPPB Scores and Sub-scores and Grip Strength according to HIV status

Independent variables	SPPB				Grip strength test			
	Unadjusted		Adjusted		Unadjusted		Adjusted	
	B	95% C.I.	B	95% C.I.	B	95% C.I.	B	95% C.I.
Body composition measurements								
Trunk FM	**-0.050**	**-0.094 to -0.006***	**-0.079**	**-0.117 to -0.040¥**	0.115	-0.067 to 0.298	-	-
Trunk BMC	0.832	-0.808 to 2.473	-	-	**17.025**	**10.516 to 23.534¥**	-	-
Trunk LM	-0.021	-0.074 to 0.031	-	-	0.418	0.207 to 0.628	-	-
Trunk %fat	-0.029	-0.059 to 0.001	-	-	-0.091	-0.215 to 0.033	-	-
Lower extremity FM	-0.018	-0.081 to 0.045	-	-	0.147	-0.113 to 0.408	-	-
Lower extremity BMC	**1.998**	**0.677 to 3.318‡**	-	-	**16.500**	**11.288 to 21.713¥**	-	-
Lower extremity LM	0.001	-0.079 to 0.081	-	-	0.865	0.549 to 1.181	-	-
Lower extremity %fat	0.003	-0.021 to 0.027	-	-	-0.085	-0.183 to 0.013	-	-
Upper extremity FM	**-0.115**	**-0.204 to -0.027‡**	-	-	0.128	-0.242 to 0.498	-	-
Upper extremity BMC	**3.734**	**0.304 to 7.164***	-	-	**43.553**	**30.350 to 56.756¥**	-	-
Upper extremity LM	**-0.060**	**-0.268 to 0.148***	-	-	**2.035**	**1.207 to 2.863¥**	**2.220**	**1.398 to 3.042¥**
Upper extremity %fat	-0.015	-0.034 to 0.005	-	-	**-0.086**	**-0.165 to -0.006***	**-0.149**	**-0.227 to -0.072¥**
Total body FM	**-0.021**	**-0.043 to 0.000***	-	-	0.057	-0.032 to 0.147	-	-
Total body BMC	**0.697**	**0.196 to 1.197‡**	-	-	**6.361**	**4.395 to 8.327¥**	-	-
Total body LM	-0.005	-0.033 to 0.023	-	-	**0.284**	**0.174 to 0.395¥**	-	-
Total body %fat	-0.025	-0.056 to 0.007	-	-	-0.118	-0.247 to 0.011	-	-
Sociodemograpgic and clinical characteristics								
Age	**-0.051**	**-0.067 to -0.035¥**	**-0.058**	**-0.073 to -0.043¥**	**-0.178**	**-0.246 to -0.111¥**	**-0.165**	**-0.232 to -0.098¥**
BMI	**-0.041**	**-0.074 to -0.008***	-	-	0.091	-0.047 to 0.228	-	-
Smoking ever	0.322	-0.044 to 0.688	**0.438**	**0.122 to 0.754‡**	0.477	-1.039 to 1.993	-	-
Current alcohol use	**0.569**	**0.236 to 0.902¥**	**0.298**	**0.005 to 0.592***	0.925	-0.469 to 2.319	-	-
Rheumatoid arthritis diagnosis	**-1.506**	**-2.595 to -0.418‡**	**-1.163**	**-2.110 to -0.216***	-3.907	-8.43 to 0.614	-	-
HIV status	**-0.727**	**-1.036 to -0.417¥**	**-1.107**	**-1.392 to -0.823¥**	0.148	-1.171 to 1.467	-0.944	-2.205 to 0.317
Years since HIV diagnosis	0.022	-0.022 to 0.067	-	-	0.046	-0.142 to 0.234	-	-
Years since antiretroviral treatment start	0.035	-0.017 to 0.087	-	-	0.091	-0.128 to 0.311	-	-
Nadir CD4+ count	0.000	-0.002 to 0.001	-	-	0.005	-0.001 to 0.012	-	-
Current CD4+ count	0.000	-0.001 to 0.001	-	-	**0.004**	**0.000 to 0.008***	-	-
Menopause status	**-0.663**	**-1.041 to -0.284¥**	-	-	**-2.310**	**-3.880 to -0.740‡**	-	-
Bone nutritional supplements, ever	-0.108	-0.794 to 0.577	-	-	-1.207	-4.031 to 1.617	-	-

*SPPB, short physical performance battery; FM, fat mass; LM, lean mass; BMC, bone mineral content; BMI, body mass index; %fat, percentage of FM; *p ≤ 0.05; ‡p ≤ 0.01; ¥p ≤ 0.001*

Table 2. Unadjusted and Adjusted Linear Regression for SPPB and Grip Strength

and everyone was on antiretroviral treatment (9.9±5.3 years). Fat mass index (FMI) was 9.6±3 vs 10.9±2.7 kg/m^2 (p< 0.001) between HpW and HnW, respectively. Overall mean SPPB score was 9.9 vs 10.8 between HpW and HnW, respectively (p< 0.001). Mean grip strength was 19.9±5.9 vs 19.8±5.4 kg (p=0.83) between HpW and HnW, respectively. In multivariate models adjusted by age and HIV status, increased trunk FM was independently associated with decreased SPPB score (p< 0.001), increased arm LM was independently associated with increased GST(p< 0.001) and increased arm %fat was independently associated with decreased GST (p< 0.001).

Conclusion: In this study, trunk FM and arm LM were independent predictors for the physical performance and function tests described, and HIV status was independently associated with SPPB score. Larger prospective studies are needed among PWH in LAC to help identify individuals at high risk for declines in physical function, and to inform prevention guidelines.

Disclosure: D. Cabrera, None; **M. Cornejo Ortega**, None; **Y. Pinedo**, None; **P. Garcia**, None; **E. Hsieh**, None.

Abstract Number: 0625

Machine Learning Model to Predict Culture Positivity in Suspected Septic Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Infection-related Rheumatic Disease Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Arthrocentesis is typically performed on patients with an acutely inflamed joint of unclear etiology. This is most often done to rule out septic arthritis, especially in patients with a red, swollen, and painful joint.

In the absence of a positive gram stain, an elevated synovial fluid (SF) white count of >25,000 is usually suggestive of an infected joint. However, there does not appear to be a reliable cut off to make a diagnosis of septic arthritis. Missing a diagnosis or a delay in the treatment can lead to extensive damage to the articular cartilage. Hence making an early diagnosis is especially important.

Baseline characteristics (Mean ± SD)	
Demographics and population characteristics	
Age	60 ± 18.5
Sex	Males: 71, Females: 27
Type 2 DM	29 of 98
CKD	25 of 98
Prosthetic joint	16 of 98
Laboratory characteristics	
CRP	137 ± 104
ESR	62 ± 35
SF WBC	31.6k ± 18k

Figure 1

	Predicted False	Predicted True
Actual False	12	0
Actual True	1	7

Figure 2

Artificial intelligence (AI) applications in healthcare have seen a steady rise over the past decade. Machine learning and deep learning models have been extensively used to discover patterns and predict patient outcomes. AI applications have shown promise in a number of fields, from radio diagnostics to infectious diseases. Our study was aimed at developing and accessing a machine learning model to predict the likelihood of septic arthritis before synovial fluid culture results are available.

Methods:

- We retrospectively collected data on 98 patients that had synovial fluid aspirations done at our community hospital over a 4-year period. A diagnosis of septic arthritis was confirmed based on the results of the synovial cultures on day 5.
- Medical history, presenting clinical features, and corresponding laboratory values were recorded (Fig 1).
- Prior to building the model, the data was preprocessed and normalized. Boolean values were converted to binary representations and categorical features were converted to numerical values.
- The dataset was then split into a training and test set, with an 80:20 randomly sampled split.
- A Random Forest Classifier algorithm was used to build the model, which was then evaluated using the test set.
- Feature importance was plotted, and a confusion matrix generated to view the false positives/negative count (Fig 2).
- Finally, column correlations were generated using a heatmap (Fig. 3) to explore the data and validate the features that the model had selected.

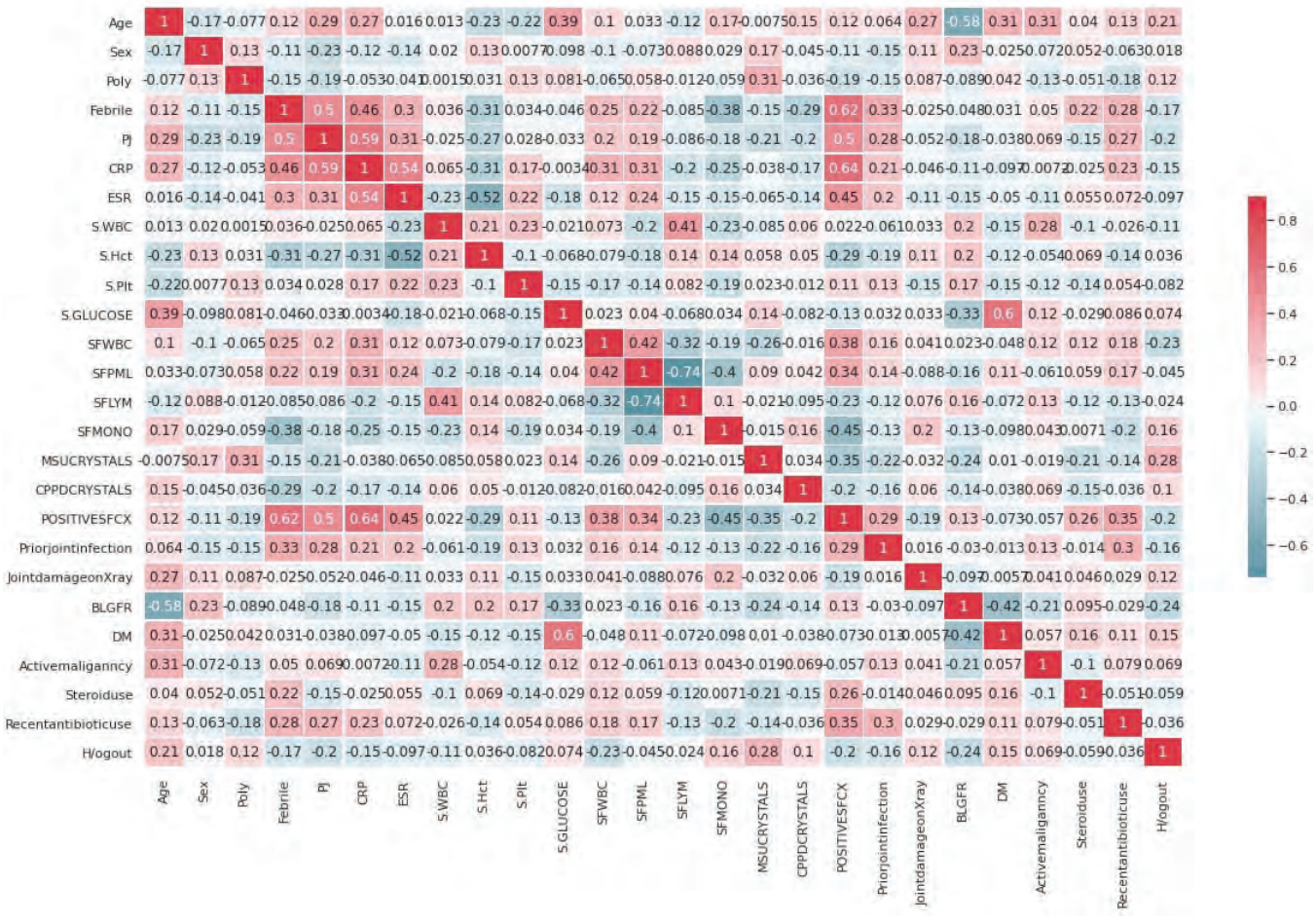

Figure 3

Results:

- In total, 33 of the 98 (33.6%) SF cultures came back positive.
- The most common organism identified was methicillin-sensitive staphylococcus aureus (42% of positive cultures).
- 22 of the 65 patients (33.8%) with ultimately negative cultures were empirically started on antibiotics at presentation, while, 3 of the 33 patients (9%) with positive cultures had not been initiated on antibiotics.
- Our feature importance plot indicated that CRP and SF monocytes were the strongest positive and negative predictors of SA, respectively.
- When evaluated with the test set, our prediction model proved to be quite accurate with a sensitivity of 87% and a specificity of 100% (accuracy of 95%).

Conclusion: Our proof of concept indicated that it is possible to build a well-performing model to predict septic arthritis cases using machine learning. With a larger sample size, more robust methods can be leveraged for predictive modeling and higher performance and accuracy. Ultimately, the output can be used to generate a risk score to determine a patient's likelihood of septic arthritis.

Disclosure: V. Gilvaz, None; **E. Mody**, None; **A. Rapose**, None; **S. Radhakrishnan**, None; **S. Abaalkhail**, None; **S. Vibhavari Guntupalli**, None.

Abstract Number: 0626

Early Rise in CRP Is Associated with Progression to Respiratory Failure and Intubation in COVID-19 Patients

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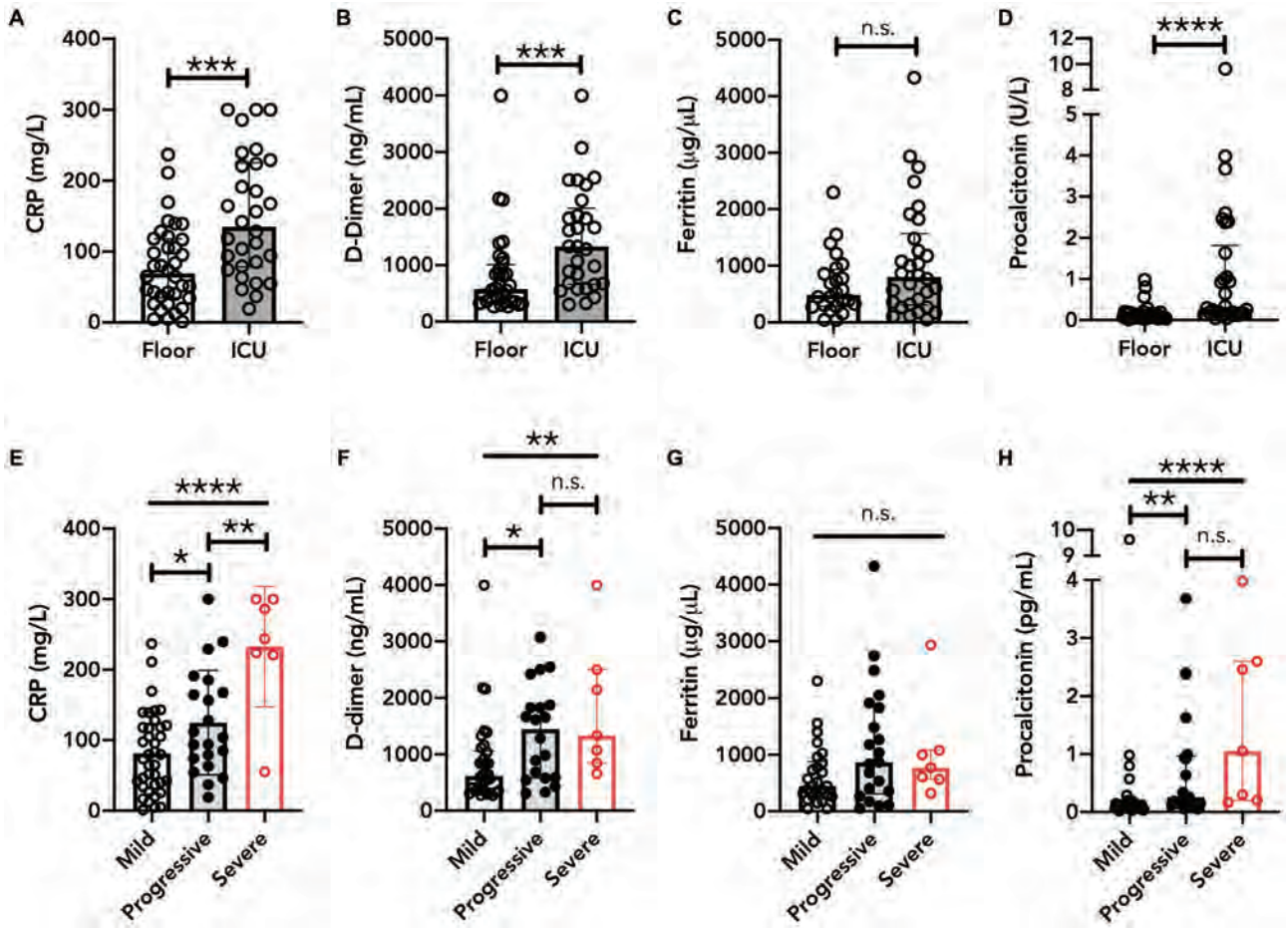
Background/Purpose: During the course of hospitalization, it is often unclear which COVID-19 patients will progress from non-critical to critical illness. Timely identification of these patients is crucial to guiding triage and early immunomodulatory intervention. Biomarkers linked with inflammation, such as CRP, D-dimer, ferritin, and procalcitonin are associated with critical illness or mortality in COVID-19 infection. These laboratory values are of particular interest due to their correlation with pathologic mechanisms related to IL-1 and IL-6 signaling as well as coagulopathy. We sought to determine whether these markers could be predictive in assessing whether a patient with non-critical illness would progress to critical disease.

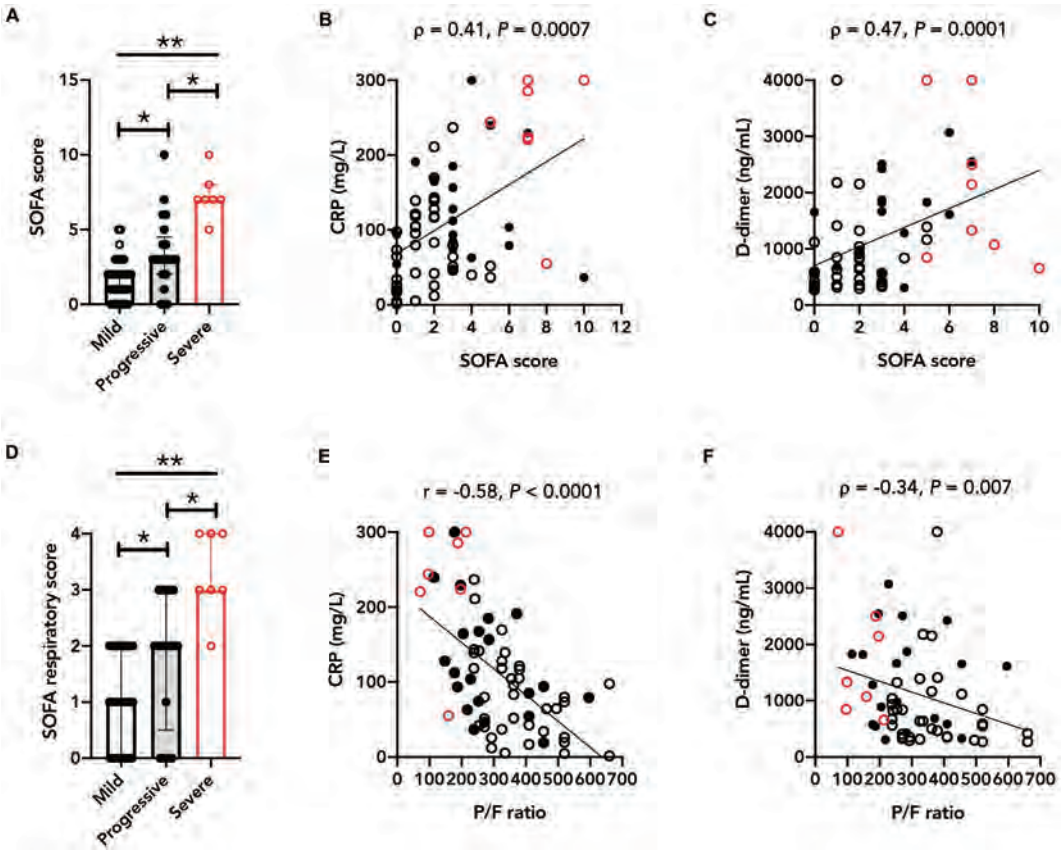
Methods: In our single-center retrospective cohort analysis of the first 66 patients admitted for COVID-19 infection, we examined inflammation biomarkers to distinguish non-critically ill inpatients who remained stable from those that had progressive respiratory failure requiring intubation and ICU transfer. Unlike the typical approach where patients are grouped into the two categories of non-critical and critical illness, COVID-19 patients in our study were classified



into three cohorts by severity and stability of respiratory failure: stable non-critical illness ("mild", 38 [58%]); non-critical illness at admission that progressed to critical illness ("progressive", 21 [32%]); and critical illness at admission ("severe", 7 [11%]). This approach allowed us independently profile patients with progressive disease from those who were already critically ill on admission.

Results: We found that while admission CRP level was weakly associated with future progressive respiratory failure, it had limited clinical utility as the progressive cohort showed modestly increased levels of CRP compared to the mild cohort, with significant overlap (125.0 ± 74 vs. 81.3 ± 57 mg/L, $P = 0.05$) (Figure 1). Despite the limited predictive value of admission CRP levels, these measurements were indeed clinically relevant as they correlated with SOFA score ($\rho = 0.41$, $P < 0.001$) and hypoxemic respiratory failure (P_aO_2/F_iO_2, $r = -0.58$, $P < 0.001$) (Figure 2). A closer examination of CRP trend showed that dynamic trend of CRP levels within the first 72 hours of admission rather than the static CRP level at admission showed a much stronger association with respiratory deterioration. Specifically, rise in CRP levels most clearly distinguished mild and progressive cohorts (24-48h post-admission: 170.6 ± 95 vs. 91.0 ± 67 mg/L, $P = 0.03$; 48-72h post-admission: 185.0 ± 92 vs. 81.6 ± 63 mg/L, $P = 0.002$) (Figure 3).

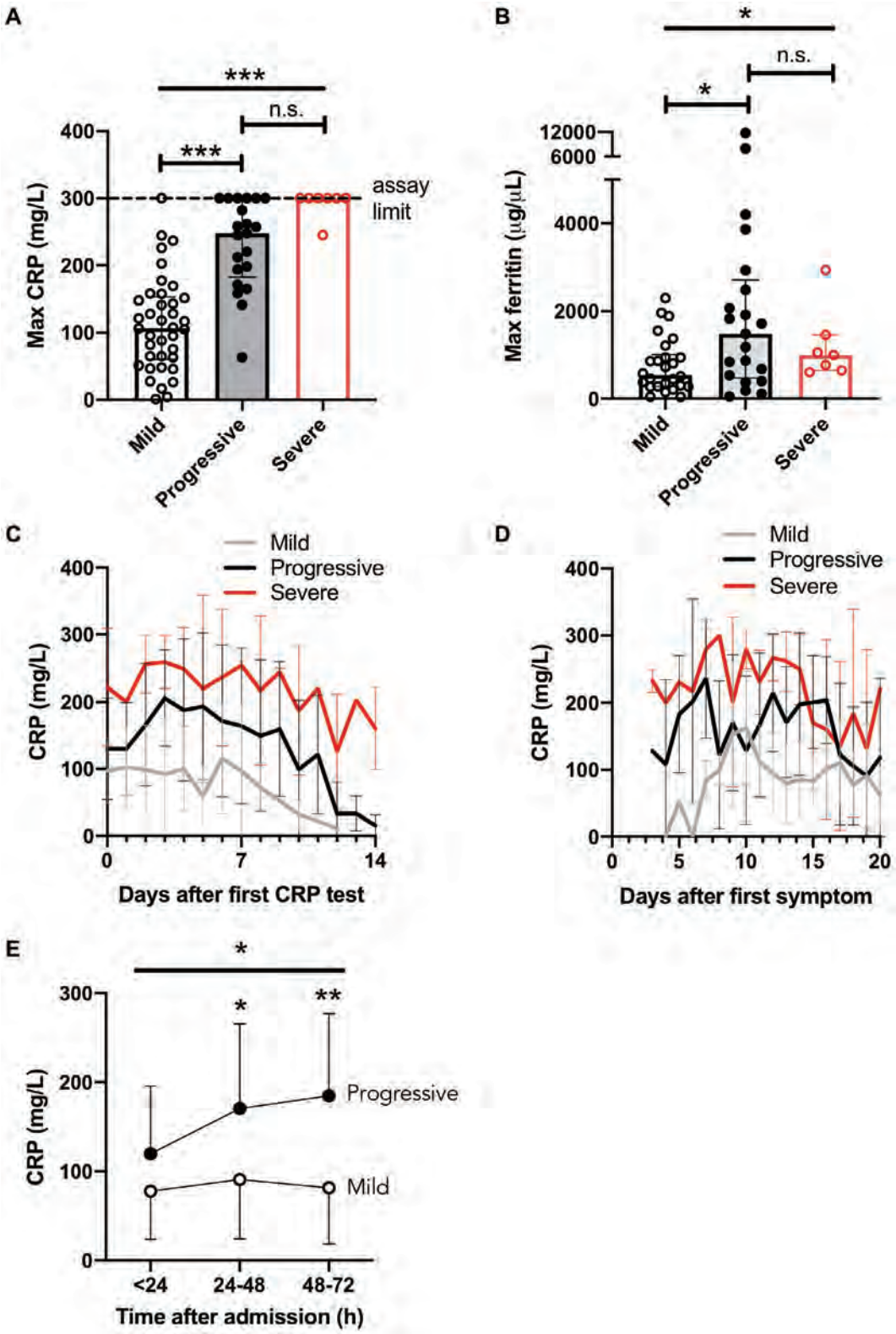
Conclusion: Closely tracking the CRP levels in the hyper-acute phase of admission for COVID-19 patients was predictive of progression to critical illness, suggesting that trends of inflammatory biomarkers, rather than absolute admission values, may have most utility for clinical triage and targeting therapeutic immunomodulation. Moreover, separating out patients with progressive disease identified a unique biomarker phenotype, indicating that clinical trials of anti-IL6 receptor monoclonal antibodies should pay parti



Admission CRP and D-dimer values associate with mild, progressive and severe respiratory failure. A-D: Initial levels of A) CRP; B) D-dimer; C) Ferritin; D) Procalcitonin are shown for patients with non-critical illness ("Floor"; n = 36) or with critical illness ("ICU"; n = 30). E-H: Patients grouped into "mild" (stable, non-critical respiratory failure; n = 38), "progressive" (initial non-critical respiratory failure that progressed to intubation during admission; n = 21), and "severe" (intubation on day of admission; n = 7) cohorts. Initial levels of E) CRP, F) D-dimer, G) Ferritin, and H) Procalcitonin are shown. Mann-Whitney U test performed for A-G. ANOVA and Tukey's multiple comparison performed for H. *P < 0.05, **P < 0.01, ***P < 0.001, ****P < 0.0001. Kruskal-Wallis test with Dunn's multiple comparison used for E-H. CRP, C-reactive protein; n.s., non-significant.

Admission CRP values associate with SOFA score and PaO2/FiO2 (P/F) ratio. COVID-19 inpatients are grouped into mild, progressive or severe cohorts defined by respiratory failure. A) SOFA scores on admission. B-C: Correlation of SOFA scores to initial B) CRP; C) D-dimer. D) SOFA respiratory scores on admission. E-F: Correlation of P/F ratios to initial E) CRP; F) D-dimer. Open black circles, mild; filled black circles, progressive; open red circles, severe. Kruskal-Wallis test and Dunn's multiple test were performed for A and D; Spearman rank correlation for B, C, and F; Pearson correlation for E. *P < 0.05, **P < 0.01. CRP, C-reactive protein; P/F, PaO2/FiO2; SOFA, Sequential Organ Failure Assessment.

Hyper-acute CRP trend distinguishes stable and progressive respiratory failure. COVID-19 inpatients are grouped into mild, progressive or severe cohorts defined by respiratory failure. A-B: Maximum values during hospital course are shown for A) CRP; B) ferritin. C-D: Mean CRP values are shown as a function of C) days after first recorded CRP level; D) days after onset of first symptom. E) CRP values for patients with mild or progressive disease taken 0-24, 24-48, and 48-72 hours after admission. A-B, median and interquartile range are plotted; C-E, mean and standard deviation are plotted. Open black circles, mild; filled black circles, progressive; open red circles, severe. Kruskal-Wal-



lis test and Dunn's multiple test were performed for A and B; a mixed effect model was used for E. *P < 0.05, **P < 0.01, ***P < 0.001. CRP, C-reactive protein; Max, maximum; n.s., non-significant.

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Abstract Number: 0627

Complications of COVID-19 Infection in Patients with Rheumatic Disease: A Case Series

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SESSION INFORMATION
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Background/Purpose: People with rheumatic diseases may be at high risk for poor outcomes related to COVID-19; on the other hand, immunomodulatory medications are used as therapy for severe COVID-19. Here, we report a case series of 26 patients with known rheumatic disease who were confirmed as having COVID-19 and compared medication use and other characteristics of hospitalized patients with those who were not hospitalized.

Methods: Established patients being followed at Temple Rheumatology Associates as well as patients admitted to Temple University Hospital in Philadelphia who tested positive for SARS-CoV2 were identified. We analyzed the demographic and clinical characteristics of patients with rheumatic disease and COVID-19 as well as associated outcomes.

Results: Of the patients in our case series, most common rheumatic conditions seen in both hospitalized and non-hospitalized groups were RA and SLE (35%, 23%) (Table 1). The majority of patients in both the hospitalized and non-hospitalized groups were in remission or low disease states (58%).

23% were receiving biologic medications and 20% were on no therapy. The most common therapy among both hospitalized and non-hospitalized patients was HCQ (40%, 50%), with 25% and 33% on HCQ monotherapy, respectively.

The most prevalent comorbidities were obesity (35%), hypertension (46%), COPD/asthma (27%), and diabetes (27%).

Conclusion: We report a case series of 26 patients with rheumatic disease and COVID-19 followed at an academic medical center in a geographic "hot spot." High numbers of patients who are Black or of Latinx ethnicity in this case series are in line with prior published reports. Our rate of hospitalization (77%) is also relatively high; however, this calculation as well as assessment of frequency of complications is likely confounded by low testing rates in our area for asymptomatic or minimally symptomatic patients, and our baseline number of COVID-19 patients may be much larger.

The most frequent complication in hospitalized patients was hyperinflammatory syndrome (65%), a complication of severe COVID-19 (Table 2); in our center, this was treated aggressively with further immunosuppression such as IL-1 and IL-6 inhibitors and systemic steroids. There was only one death among all included patients. The cause of this discrepancy between severity of illness and death is not clear and may be related to the local rate of infection as well as treatment practices at our center.

In terms of treatment, the most common therapy among our patients was HCQ (42%). Interestingly, no patients were on IL-1, IL-6, IL-17, IL-12/23, CTLA4-Ig, or tsDMARDs. However, absence of evidence is not evidence of absence, and this finding may reflect the social distancing measures being practiced by our patients.

Table 1. Baseline characteristics of patients with rheumatic disease and COVID-19

Characteristic	All patients (N=26)	Hospitalized patients (N=20)	Non-hospitalized (N=6)
Mean age – years (range)	56 (25-84)	59 (25-84)	45 (32-54)
Female sex – no. (%)	21 (81%)	16 (80%)	5 (83%)
Primary rheum dx- no. (%)			
Rheumatoid arthritis	9 (35%)	7 (35%)	2 (33%)
Systemic lupus erythematosus	6 (23%)	3 (15%)	3 (50%)
Systemic sclerosis	2 (8%)	2 (10%)	0
Sjogren's syndrome	1 (4%)	1 (5%)	0
Inflammatory myopathy	2 (8%)	2 (10%)	0
Sarcoidosis	3 (12%)	3 (15%)	0
Small vessel vasculitis	2 (8%)	2 (10%)	0
Antiphospholipid syndrome	1 (4%)	1 (5%)	0
Discoid lupus erythematosus	2 (8%)	2 (10%)	0
Inflammatory osteoarthritis	1 (4%)	0	1 (17%)
Rheum disease status - no. (%)			
Remission	2 (8%)	2 (10%)	0
Low disease	13 (50%)	7 (35%)	6 (100%)
Moderate	3 (12%)	3 (15%)	0
Severe	1 (4%)	1 (5%)	0
Unknown or not applicable	7 (27%)	7 (35%)	0
Comorbidities - no. (%)			
Obesity	9 (35%)	8 (40%)	1 (17%)
Hypertension	12 (46%)	11 (55%)	1 (17%)
Diabetes	7 (27%)	6 (30%)	1 (17%)
Coronary artery disease	3 (12%)	3 (15%)	0
Heart failure	3 (12%)	3 (15%)	0
Pulmonary hypertension	1 (4%)	1 (5%)	0
COPD or asthma	7 (27%)	6 (30%)	1 (17%)
Interstitial lung disease	2 (8%)	2 (10%)	0
Obstructive sleep apnea	3 (12%)	2 (10%)	1 (17%)
Cancer	1 (4%)	1 (5%)	0
Glomerulonephritis	1 (4%)	1 (5%)	0
Organ transplant	1 (4%)	1 (5%)	0
Smoking status			
Never	14 (54%)	9 (45%)	5 (83%)
Former	10 (38%)	10 (50%)	0
Current	2 (8%)	1 (5%)	1 (17%)
Race – no. (%)			
White	3 (12%)	2 (10%)	1 (17%)
Black or African-American	13 (50%)	10 (50%)	3 (50%)
Asian	0	0	0
Other or not recorded	10 (38%)	8 (40%)	2 (33%)
Hispanic or Latinx ethnicity no. (%)	8 (31%)	6 (30%)	2 (33%)
Long-term medications - no. (%)*			
No therapy	5 (19%)	5 (25%)	0
Oral glucocorticoid	8 (31%)	7 (35%)	1 (17%)
Prednisone >5 mg/day	5 (19%)	4 (20%)	1 (17%)
Hydroxychloroquine (HCQ)	11 (42%)	8 (40%)	3 (50%)
HCQ monotherapy	7 (27%)	5 (25%)	2 (33%)
bDMARDs			
TNF inhibitors	2 (8%)	1 (5%)	1 (17%)
Belimumab	1 (4%)	0	1 (17%)
Rituximab	3 (12%)	3 (15%)	0
csDMARDs			
Methotrexate	4 (15%)	3 (15%)	1 (17%)
Leflunomide	3 (12%)	2 (10%)	1 (17%)
Mycophenolate	1 (4%)	1 (5%)	0
Sulfasalazine	1 (4%)	1 (5%)	0
Azathioprine	1 (4%)	1 (5%)	0
Tacrolimus	1 (4%)	1 (5%)	0

* No patients were on IL-1, IL-6, IL-17, IL-12/23, CTLA4-Ig, or tsDMARDs.

Table 2. COVID-19-associated outcomes in hospitalized patients with rheumatic disease

Characteristic	Hospitalized patients (N=20)
Respiratory support	
Oxygen supplementation	4 (20%)
Non-invasive ventilation	9 (45%)
ICU or mechanical ventilation	3 (15%)
Myocarditis	1 (5%)
ARDS	6 (30%)
Hyperinflammatory syndrome	13 (65%)
Death	1 (5%)

Many hospitalized patients were affected with severe COVID requiring ventilatory support or associated with a hyperinflammatory state.

Disclosure: T. Buckey, None; **M. Jurkowski**, None; **K. Lu**, None; **R. Caricchio**, None; **A. Jayatilleke**, None.

Abstract Number: 0628

Factors Associated with Knee Osteoarthritis in an Outpatient HIV-1 Clinic over a 26 Year Interval

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Background/Purpose: With the advent of combined antiretroviral therapy (cART), patients with HIV-1 began living longer and started to develop diseases associated with aging such as osteoarthritis (OA). This study examined the epidemiologic, clinical, and immunological data in patients with concomitant HIV-1 and knee OA.

Methods: We examined with knee OA treated at a HIV-1 outpatient clinic seen between 1994 and 2020. At baseline visit, demographic parameters, lymphocyte subsets, HIV-1 viral load, knee OA date of diagnosis, pertinent lab findings, knee radiographs, and relevant clinical information were collected. All patients met the American College of Rheumatology Classification Criteria for knee OA. Antiretroviral medications were categorized into protease inhibitors, nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and integrase inhibitors. Univariate and multivariate analyses were conducted that looked at age, BMI, ethnicity, gender, CD4 count, HIV viral load, antiretroviral medication use, and time of knee OA diagnosis on the risks of developing knee OA.

Results: Comparing the pre-HAART (1994-1997) to the era after the introduction of HAART (1998-2020), the frequency of DILS and reactive arthritis fell whereas the osteoarthritis, particularly of the knee, and carpal tunnel syndrome

Table 1. Harris County HIV Rheumatology Clinic Distribution of Diagnoses in the Pre-and Post-HAART Eras

Diagnosis	Before 1998 N=319 (%)	After 1998 N=1352 (%)	p-value
Carpal Tunnel Syndrome	0.0	5.0	<0.001
Creatine Phosphokinase Elevation	2.4	1.3	<0.001
Diffuse Infiltrative Lymphocytosis Syndrome	9.2	5.0	<0.001
Fibromyalgia	1.1	2.8	0.67
Gout	1.9	2.9	0.42
Hepatitis C Arthralgia	2.2	2.9	0.63
HIV Arthralgia	6.3	4.7	0.29
HIV Arthritis	3.4	5.4	0.19
Low Back Pain	9.1	10.8	0.43
Osteoarthritis (all)	4.1	20.9	<0.001
Osteoarthritis Knee	2.2	15.5	<0.001
Reactive Arthritis	3.4	0.9	<0.001
Rheumatoid Arthritis	0.0	0.9	0.19
Systemic Lupus Erythematosus	0.9	1.4	0.7
Soft Tissue rheumatism	21.0	24.0	0.28
Spondyloarthritis	0.9	1.4	0.7
Vasculitis	0.9	0.5	0.63

Table 1. Harris County HIV Rheumatology Clinic Distribution of Diagnoses in the Pre-and Post-HAART Eras

Table 2. Demographic and Clinical Parameters in HIV Rheumatology Patients with and without Knee Osteoarthritis+

Parameter	Knee OA Group (n=217)	Non-Knee OA (n=1454)	p-value	OR	C.I.
Age at Presentation (yrs)	51.1 (±9.05)	46.7 (±9.75)	<0.001	1.05	1.04, 1.08
CD4 count	548.4 (±292.1)	502.9 (±321.5)	0.001	n.a.	n.a.
CD4 count > 200 cells/μL (%)	94.5	85.3	0.001	3.00	1.60, 6.15
Undetectable Viral Load (%)	87.4	74.6	<0.001	2.37	1.50-3.91
Body Mass Index	32.8 (±7.95)	28.5 (±6.62)	<0.001	1.08	1.06, 1.11
Female (%)	61.0	44.5	<0.001	1.95	1.06, 2.17
White (%)	8.2	18.8	Comparison group		
Black (%)	69.2	60.8	0.04*	2.60 *	1.52, 4.75
Hispanic (%)	22.5	20.3	0.004*	2.53*	1.37, 4.90
Protease Inhibitor (%)	44.5	41.5	0.41	1.14	0.86, 1.52
Nucleoside Reverse Transcriptase Inhibitors (%)	89.0	82.5	0.02	1.70	1.09,2.66
Non-Nucleoside Reverse Transcriptase Inhibitors (%)	25.8	23.6	0.53	1.13	0.81, 1.56
Integrase Inhibitor (%)	24.7	18.1	0.02	1.50	1.07, 2.10
Number of Antiretroviral Meds	1.84 (±0.67)	1.66 (±0.77)	0.001	n.a.	n.a.
No therapy (%)	9.3	14.8	Comparison group		
Mono-therapy (%)	3.3	8.1	0.38**	0.65	0.22-1.64
Multi-therapy (%)	87.4	77.1	0.03**	1.80	1.08-3.18

+ univariate analysis *compared to whites ** compared to no therapy

Table 2. Demographic and Clinical Parameters in HIV Rheumatology Patients with and without Knee OA

rose dramatically (Table 1). A total of 217 patients with HIV-1 infection and knee OA were identified out of the 1671 patients referred to the HIV Rheumatology Clinic. Patients with knee OA were more likely to be female and to be black or Latino than white (Table 2). The knee OA patients were older (average age of 51.1 [±9.1] years compared to 46.7 [±9.8] years in the non-knee OA group). In addition, knee OA patients had a greater body mass index (BMI-average of

32.8 [±7.9] compared to 28.5 [±6.6] in the non-knee OA group). Patients with knee OA were more likely to have CD4 >200 cells/μL at baseline than those with other diagnoses. Medication use with NRTI and integrase inhibitors respectively, were significantly associated with knee OA. However, on multivariable analysis, independent associations of CD4 count, HIV viral load, NRTI and integrase inhibitor usage were not observed. When stratifying antiretroviral usage into the categories of no therapy, mono-drug therapy, and multi-drug therapy, those on multidrug-therapy had higher odds of having knee OA that those on no therapy. However, in the multivariable analysis, this association was not independently observed. Moreover, between the period of 1994 and 2020, we noted an increase in the frequency of knee OA over time on both the univariable ($p< 0.001$) and multivariable analyses ($p< 0.001$).

Conclusion: To date, this is the largest cohort of concomitant HIV-1 and knee OA patients followed longitudinally to date. Our cohort confirmed the risk factors of BMI, age, ethnicity, and female gender as well as demonstrating that there is a relationship with CD4 >200 cells/μL and an increase in the frequency of knee OA diagnoses over the period 1994-2006, probably reflecting the longer survival of patients with HIV with effective treatment and factors associated with HIV treatment itself.

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Abstract Number: 0629

COVID-19 Among Patients with Immune-mediated Inflammatory Diseases: A Descriptive Study

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with immune-mediated inflammatory diseases (IMID) have a higher risk of infections related to their disease, comorbidities or immunosuppressive treatments, but recent studies addressing severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) infection (COVID-19) didn´t support more frequent or severe disease in these patients. Our objective is to describe our cohort of patients with IMID who had a probable or confirmed SARS-CoV-2 infection.

Methods: Patients with IMID currently followed in the Rheumatology Department of Ramón y Cajal University Hospital with probable or confirmed SARS-CoV-2 infection diagnosed between 01-02-2020 and 22-05-2020 were selected. Confirmed infection was defined if the patient had a positive nasopharyngeal swab for SARS-CoV-2 or characteristic bilateral infiltrates on chest radiograph/computerized tomography (CT); probable infection was defined by 2 or more symptoms related to COVID-19 (fever, dry cough, dyspnoea, myalgia, anosmia or ageusia) if other causes were excluded. We analysed the demographic and clinical data on patients who had IMID with symptomatic COVID-19.

	Total (n=80)	Outpatient (survived) (n=31)	Inpatient (survived) (n=38)	Inpatients (deceased) (n=11)	p-value
Basal characteristics					
Age≥65 years	32 (40%)	3 (9.7%)	20 (52.6%)[a]	9 (81.8%)[a]	**0.000***
Female	50 (62.5%)	23 (74.3%)	22 (57.9%)	5 (45.5%)	0.176
Smoking	12 (15%)	7 (22.6%)	5 (13.2%)	0	0.234
Hypertension	36 (45%)	6 (19.4%)	22 (57.9%)[a]	8 (72.7%)[a]	**0.001***
Diabetes	15 (18.8%)	2 (6.5%)	10 (26.3%)	3 (27.3%)	0.061
BMC>30	10 (12.5%)	3 (9.7%)	7 (18.4%)	0	0.299
COPD/asthma	13 (16.3%)	1 (3.2%)[a]	8 (21.1%)[a,b]	4 (36.4%)[b]	**0.011***
CKD	8 (10%)	2 (6.5%)	3 (7.9%)	3 (37.3%)	0.147
CVD	8 (10%)	1 (3.2%)[a]	3 (7.9%)[a,b]	4 (36.4%)[b]	**0.015***
IMID					
RA	24 (30%)	7 (22.6%)	13 (34.3%)	4 (36.4%)	0.558
Sjögren	6 (7.6%)	1 (3.2%)	5 (13.2%)	0	0.283
RA+Sjögren	3 (3.8%)	2 (6.5%)	1 (2.6%)	0	0.735
SpA	18 (22.5%)	9 (29%)	9 (23.7%)	0	0.120
Polymyalgia Rheumatica	8 (10%)	0[a]	6 (15.8%)[a,b]	2 (18.2%)[b]	**0.032***
JIA	5 (6.3%)	4 (12.9%)	1 (2.6%)	0	0.213
SLE/APS	6 (7.6%)	2 (6.5%)	2 (5.3%)	2 (18.2%)	0.343
IIM/Scleroderma	3 (3.8%)	2 (6.5%)	1 (2.6%)	0	0.735
Systemic vasculitis	6 (7.5%)	2 (6.5%)[a,b]	1 (2.6%)[b]	3 (27.3%)[a]	**0.043***
Other diseases	2 (2.5%)	1 (3.2%)	1 (2.6%)	0	1.000
Comorbidities associated with IMID					
Associated ILD	8 (10%)	0[a]	5 (12.2%)[a,b]	3 (27.3%)[b]	**0.012**
Lymphopenia	7 (8.7%)	3 (9.7%)	2 (5.2%)	2 (18.2%)	0.344
Treatment					
GC <10 mg/day	33 (41.3%)	10 (33.2%)	17 (44.7%)	6 (54.5%)	0.380
GC≥10 mg/day	5 (6.3%)	0[a]	2 (5.3%)[a,b]	3 (27.3%)[b]	**0.006***
Hydroxychloroquine	4 (5%)	4 (12.9%)	3 (7.9%)	1 (9.1%)	0.874
Methotrexate	32 (40%)	17 (54.8%)	13 (34.3%)	2 (18.2%)	0.076
Leflunomide	4 (5%)	2 (6.5%)	1 (2.6%)	1 (9.1%)	0.476
Sulfasalazine	5 (6.3%)	0	4 (10.5%)	1 (9.1%)	0.123
Azathioprine	4 (5%)	2 (6.5%)	2 (5.3%)	0	1.000
Mycophenolate	2 (2.5%)	1 (3.2%)	0	1 (9.1%)	0.125
Anti TNF	16 (20%)a	10 (32.3%)[a]	6 (15.8%)[a]	0[a]	**0.049***
Rituximab	12 (15%)	4 (12.9%)	5 (13.2%)	3 (27.3%)	0.513
Tocilizumab	4 (5%)	4 (12.9%)[a]	0[a]	0[a]	**0.043***
Abatacept	1 (1.3%	0	1 (2.6%)	0	1.000
JAK inhibitors	1 (1.3%)	1 (3,2%)	0	0	0.525
Anti-IL-1	1 (1.3%)	0	1 (2.6%)	0	1.000

Table 1. Demographic and clinical characteristics.
*BMC=body mass index, COPD= chronic obstructive pulmonary disease, CKD=chronic kidney disease, CVD=cardiovascular disease, RA=rheumatoid arthritis, SpA=Spondyloarthritis, PMR=polymyalgia rheumatica, JIA=juvenile idiopathic arthritis
SLE=systemic lupus erythematosus, APS=antiphospholipid syndrome, IIM=idiopathic inflammatory myopathy, ILD=interstitial lung disease, GC=glucocorticoids.
**Superscripts are used to indicate differences between subgroups.

Results: Eighty patients were selected (58 patients with confirmed COVID-19, and 22 patients with probable COVID-19). Median age at diagnosis was 61.50 years (Interquartile range [IQR], 37.5-85.5). Fifty patients (62.5%) were

	Total (n=49)	Inpatients survived (n=38)	Inpatients deceased (n=11)	p-value
Outcomes				
Unilateral infiltrates*	13 (26.5%)	10 (26.3%)	3 (27.3%)	1.000
Bilateral infiltrates*	34 (69.3%)	26 (68.4%)	8 (72.7%)	1.000
Worsening on 2nd X-ray/CT	14/33 (42.4%)	9 /25 (36%)	5/11 (62.5%)	0.238
ARDS	16 (32.6%)	7 (18.4%)	9 (82.8%)	**0.000***
Lymphopenia	35 (71.4%)	25 (65.8%)	10 (90.9%)	0.103
AKD	8 (16.3%)	5 (12.2%)	3 (27.3%)	0.355
Heart failure	3 (6.1%)	0	3 (27.3%)	**0.009***
PE	2 (4%)	1 (2.6%)	1 (9.1%)	0.402
Supplementary O2	25 (51%)	22 (57.9%)	3 (27.3%)	0.095
NIMV	6 (12.2%)	1 (2.6%)	5 (45.5%)	**0.001***
Treatments received				
Hydroxychloroquine	43 (87.8%)	34 (89.5%)	9 (81.8%)	0.605
Azithromycin	24 (49%)	16 (42.1%)	8 (72.7%)	**0.074***
Lopinavir/Ritonavir	30 (61.2%)	25 (65.8%)	5 (45.5%)	0.298
Remdesivir	3 (6.1%)	0	3 (7.9%)	1.000
Glucocorticoids	23 (46.9%)	15 (39.5%)	8 (81.8%)	**0.013***
Tocilizumab	7 (14.2%)	1 (9.1%)	6 (12.2%)	1.000

Table 2. Outcomes and treatment received.
*On x-ray or computerized tomography (CT).
ARDS=acute respiratory distress syndrome, AKD=acute kidney disease, PE= pulmonary embolism, NIMV= non-invasive mechanical ventilation.

female. Thirty-one patients were treated as outpatients, 49 were admitted in our hospital, out of them 11 died. Their characteristics are described and compared in table 1.

All patients that were hospitalised (n=49) suspended their conventional and biologic DMARDs at the time of admission. Their outcome and treatment prescribed during hospitalization is represented in table 2.

Conclusion:

- We found that patients with IMID share risk factors for hospitalization/death described for the general population.
- Patients with systemic vasculitis, polymyalgia rheumatica (PMR) and IMID-associated interstitial lung disease had a worse prognosis (more frequent hospitalization and/or higher mortality). Patients treated with moderate/high GC doses for their IMID had a worse outcome, while patients treated with anti-TNF or tocilizumab had a better prognosis.
- Among the patients that were hospitalised, those who developed ARDS or heart failure and those who required non-invasive mechanical ventilation (NIMV) had higher mortality.
- Nevertheless, these results must be interpreted with caution, given the relatively low number of patients, interaction between variables associated with mortality couldn´t be analysed.

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Abstract Number: 0630

"No Benefit from a Strict Immobilization in Vertebral Osteomyelitis" Vertebral Immobilization and Neurological Complication in Acute Pyogenic Vertebral Osteomyelitis: SPONDIMMO, a Prospective Cohort of 250 Patients

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SESSION INFORMATION

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Background/Purpose: Vertebral osteomyelitis (VO) can be associated with neurological complications. We showed in a previous study that they occurred in 40% of patients with VO. Spine immobilization is recommended to prevent those complications but with poor evidence from the literature.

The aim of our study was to describe the practice of spine immobilization in a large multicentered cohort of patients with VO, and to evaluate the association between immobilization and neurological complications.

Methods: We prospectively recruited patients with VO from 2016 and 2019 in 11 centers. We included adults patients with VO confirmed by imaging and identification of causative agent or a good response to antibiotic therapy if all samples were sterile. We collected clinical, microbiologic, imaging and therapeutic characteristics at admission and during follow up, at 3 and 6 months. Characteristics of the type and duration of immobilization were especially recorded.

Results: 250 patients were included. Mean age was 66.7 +/- 15 years old, mostly men (67.2%, n=168). Median duration of pain before diagnosis was 25 (0-427) days. Lumbo-sacral level was the most frequently involved (54.4%), cervical level was involved in 12.8% of cases. Staphylococcus aureus was the most frequent pathogen (33.6%).

At diagnosis, 25.6% patients (n=64) had minor neurological symptoms (radicular pain, reflex abolition, sensitive loss) and 9.2% (n=23) major neurological complications (motor weakness or sphincter dysfunction). During follow up, new minor neurological complications occurred in 9.2% (n=23) of patients, and major ones in 6.8% of patients (n=17) medianly 11 (1 to 45) days.

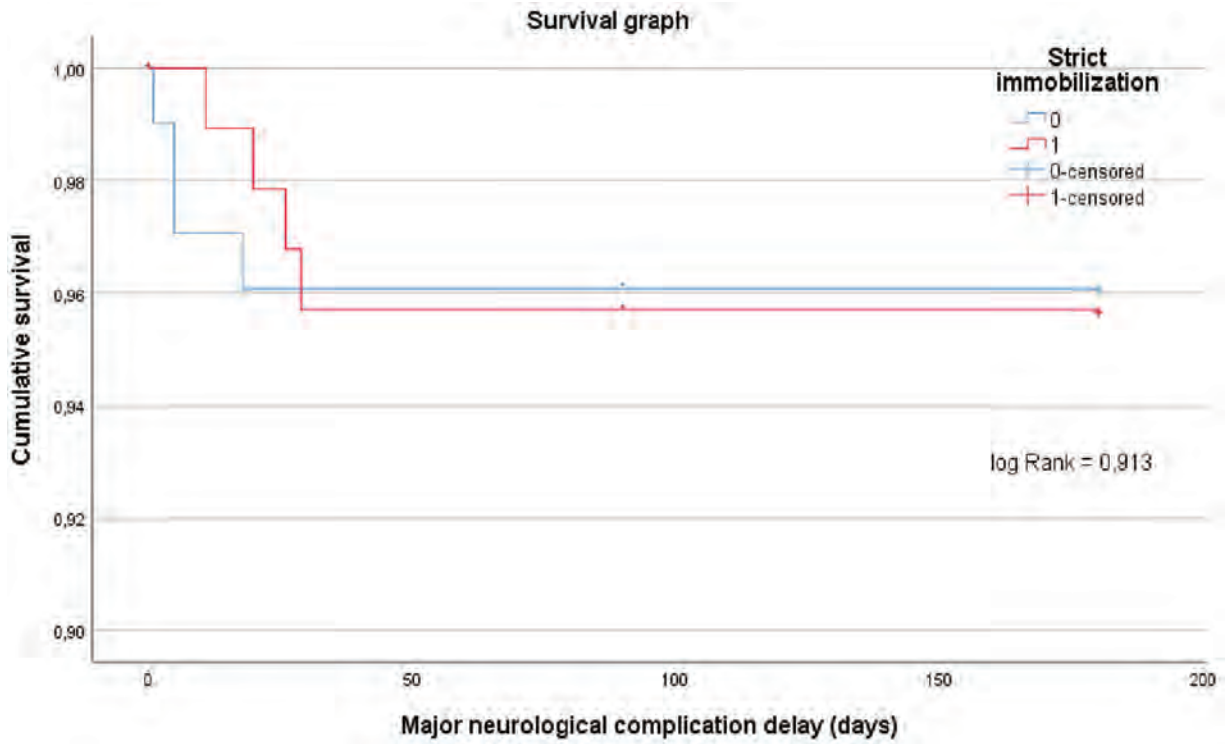
Table 1 : Population characteristics	Total 250 (100%)	Strict Immobilization 110 (44%)	No strict immobilization 119 (47.9%)	p
Male	67.2% (168/250)	71.8% (79/110)	61.3% (73/119)	0.094
Age : mean (standard deviation)	66.7 (15.0)	63.45 (15.2)	69.37 (13.9)	**0.002**
Diagnosis delay : median (min-max)	25 (0-427)	24 (0-207)	26.5 (0-427)	0.861
Anterior back surgery	5.6% (14/250)	7.3% (8/110)	4.2% (5/119)	0.316
Frailty (0 "very fit" to 5 "severely frail") : mean (standard deviation)	1.3 (1.031)	0.9 (0.901)	1.41 (1.039)	**0.005**
Level involved:				
Cervical	12.8% (32/241)	18.7% (20/107)	7.7% (9/117)	**0.014**
Cervico-thoracic	1.6% (4/241)	0.9% (1/107)	1.7% (2/117)	0.61
Thoracic	22.4% (56/241)	25.2% (27/107)	23.9% (28/117)	0.82
Thoraco-lumbar	5.2% (13/241)	3.7% (4/107)	6.8% (8/117)	0.30
Lumbar	54.4% (136/241)	51.4% (55/107)	59.8% (70/117)	0.20
Endocarditis	22.4% (56/249)	17.3% (19/110)	28.8% (34/118)	**0.039**
MRI	87.2% (218)			
Multifocal	24.4% (61/239)	25% (27/108)	23.7% (27/114)	0.819
Vertebral destruction > 50%	9.2% (23/234)	10.3% (11/107)	9.1% (10/110)	0.767
Destruction of posterior arc	7.6% (19/226)	10.8% (11/102)	5.6% (6/107)	0.171
Sagittal angulation	18.8% (47/224)	25.5% (26/102)	17.1% (18/105)	0.142
Epidural inflammation	54% (135/221)	70.6% (72/102)	51.5% (53/103)	**0.005**
Epidural abscess	17.6% (44/224)	24.5% (25/102)	15.1% (16/106)	0.088
Spinal cord hypersignal	7.6% (19/218)	14.1% (14/99)	2.9% (3/103)	**0.004**
Subarachnoid space effacement	17.6% (44/221)	28.7% (29/101)	12.5% (13/104)	**0.004**
Dural sac compression	20% (50/222)	32.7% (33/101)	13.3% (14/105)	**0.001**
Duration of antibiotherapy : median (min-max)	45 (5-417)	46 (5-417)	45 (9-377)	0.153
Surgery	11.2% (28/250)	17.3% (19/110)	5.1% (6/118)	**0.03**
Initial pain evaluation: mean (standard deviation)	53.6 (28,65)	54.7 (27,17)	51.8 (30,42)	0.595
Minor neurological symptom	25.6% (64/250)	28.2% (31/110)	22.7% (27/119)	0.34
Major neurological symptom	9.2% (23/250)	14.5% (16/110)	5% (6/119)	**0.015**

Median duration of antibiotherapy was 45 (5-417) days, 11.2% of patients (n=28) underwent surgery.

Immobilization was prescribed in 69.2% (n=173) of cases, 94.2% (n=162) were rigid bracing. However a strict immobilization (defined by a rigid brace for at least 6 weeks) was prescribed for only 44% of the patients (n=110). In multivariate analysis, factors significantly associated with strict immobilization were: Centre (p=0.035), younger age (p=0.005), dural sac compression (p=0.005) and major neurological signs at diagnosis (p=0.036). Vertebral destruction or epidural abscesses were not associated with strict immobilization. Lumbar localization was not less strictly immobilized.

There was no significant difference in the apparition of new minor neurological complications between strictly immobilized patients and others (10.9% (n=12) and 5.9% (n=7) respectively; log Rank = 0.315). Same results were found for new major complications (4.5% (n=5) and 6.7% (n=8) respectively; log Rank = 0.913).

Duration of immobilization prescription was not associated with apparition of severe complications.



In patients without prescription of any rigid bracing, subarachnoid space effacement was significantly associated with apparition of major neurological complications in multivariate analysis (p=0.016).

Conclusion: Only 44% of the patients were strictly immobilized in our cohort. We did not observe significant differences in terms of neurological complications between strictly immobilized patients and others.

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Abstract Number: 0631

Clinical Manifestations and Outcomes in DMARD-Naïve Patients with Chronic Chikungunya Arthritis

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SESSION INFORMATION
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Background/Purpose: Chikungunya virus (CHIKV) is characterized by fever, maculopapular rash, and severe polyarthralgia and polyarthritis. Up to 80% of affected individuals may develop chronic CHIKV arthralgias and arthritis. Most studies on chronic CHIKV arthritis include patients treated with disease-modifying anti-rheumatic drugs (DMARDs),

Table 1. Demographic features, lifestyle behaviors, comorbidities, and clinical manifestations in patients with and without chronic CHIKV arthritis.

Features	Chronic CHIKV Arthritis (n=33)	Resolved CHIKV arthritis (n=28)	p value
Gender, %women	69.7	64.3	0.786
Age, mean years (SD)	52.5 (10.5)	48.3 (13.7)	0.205
Time period, mean months (SD)	25.3 (10.8)	21.1 (7.0)	0.651
Educational level, mean years (SD)	16.3 (3.9)	17.0 (3.9)	0.631
Lifestyle behaviors, %			
Smoking	12.1	14.3	>0.999
Exercise	21.2	57.1	0.004
Comorbidities, %			
Overweight/obese (BMI ≥ 25)	87.9	78.6	0.490
Arterial hypertension	24.2	28.6	0.775
Diabetes mellitus (type 1 or type 2)	18.2	0.0	0.027
Dyslipidemia	18.2	25.0	0.517
Chronic back pain	24.2	0.0	0.006
Osteoarthritis	15.2	14.3	>0.999
Clinical manifestations on acute infection, %			
Arthralgia	100	96.4	0.459
Arthritis	87.9	71.4	0.107
Fever	97.0	78.6	0.041
Tiredness	100	82.1	0.017
Morning stiffness	97.0	82.1	0.085
Myalgia	97.0	75.0	0.019
Maculopapular rash	93.9	75.0	0.067
Treatment on acute infection, %			
Acetaminophen	90.9	85.7	0.693
NSAIDs	75.8	50.0	0.037
Prednisone	33.3	14.3	0.085

most likely altering the expression of clinical manifestations during the chronic phase. Therefore, we sought to evaluate the clinical features and correlates in patients with chronic CHIKV arthritis who did not receive therapy with DMARDs.

Methods: We conducted a cross-sectional study in adult (≥21 years) patients with serologically-confirmed CHIKV infection in Puerto Rico. All patients had inflammatory polyarthritis in the acute phase of infection. None received treatment with corticosteroids one year before study visit and, none receive DMARDs at any time. Demographic features, lifestyle behaviors, clinical manifestations, comorbidities, disease activity (per Clinical Disease Activity Index [CDAI]), functional status (per Health Assessment Questionnaire [HAQ]), and pharmacologic treatment were ascertained. Patients with and without chronic CHIKV arthritis were compared. Furthermore, a sub-analysis was performed among patients with chronic CHIKV who presented with low disease activity (CDAI < 10) versus moderate-high disease activity (CDAI ≥ 10) at study visit. Statistical analyses were performed using Fisher's exact test, Pearson Chi-squared test, and Wilcoxon rank-sum test, as appropriate.

Table 2. Demographic features, lifestyle behaviors, comorbidities, and clinical manifestations on acute infection and at study visit in patients with chronic CHIKV presenting with mild and moderate/high activity.

Features	All chronic CHIKV arthritis (n=33)	Low disease activity (n=14)	Moderate-High disease activity (n=19)	p value
Gender, % women	69.7	85.7	57.9	0.131
Age, mean years (SD)	52.5 (10.5)	51.7 (11.5)	53.1 (10.0)	0.771
Time period, mean months (SD)	25.3 (10.8)	23.0 (10.7)	27.1 (10.8)	0.084
Educational level, mean years (SD)	16.3 (3.9)	17.4 (2.7)	15.6 (4.5)	0.049
Lifestyle behaviors, %				
Smoking	12.1	0.0	21.1	0.119
Exercise	21.2	21.4	21.1	>0.999
Comorbidities, %				
Overweight/obese (BMI ≥ 25)	87.9	85.7	89.5	>0.999
Arterial hypertension	24.2	37.50	62.50	>0.999
Diabetes mellitus	18.2	14.3	21.1	>0.999
Dyslipidemia	18.2	28.6	10.5	0.363
Chronic low back pain	24.2	28.6	21.1	0.695
Osteoarthritis	15.2	14.3	15.8	>0.999
Clinical manifestations on acute infection, %				
Arthralgia	100	100	100	---
Arthritis	87.9	78.6	94.7	0.288
Fever	97.0	92.9	100	0.424
Tiredness	100	100	100	---
Morning stiffness	97.0	92.9	100	0.424
Myalgia	97.0	92.9	100	0.424
Maculopapular rash	93.9	100	89.5	0.496
Treatment on acute infection, %				
Acetaminophen	90.9	92.9	89.5	>0.999
NSAIDs	75.8	85.7	68.4	0.416
Prednisone	33.3	35.7	31.6	>0.999
Clinical manifestations at study visit, %				
Tiredness	66.7	50.0	79.0	0.136
Joint swelling	54.6	42.9	63.2	0.247
Morning stiffness	90.9	78.6	100	0.067
HAQ mean score (SD)	0.95 (0.56)	0.63 (0.50)	1.19 (0.47)	0.006
HAQ categories, mean score (SD)				
Dressing & grooming	0.8 (0.7)	0.4 (0.5)	1.2 (0.6)	<0.001
Arising	1.2 (0.7)	0.8 (0.7)	1.4 (0.5)	0.009
Eating	0.6 (0.7)	0.4 (0.6)	0.8 (0.8)	0.070
Walking	1.1 (0.7)	0.9 (0.7)	1.3 (0.7)	0.083
Hygiene	0.7 (0.6)	0.5 (0.7)	0.9 (0.5)	0.034
Reaching	1.2 (0.9)	0.9 (0.9)	1.5 (0.8)	0.025
Grip	0.8 (0.8)	0.6 (0.6)	1.0 (0.8)	0.121
Activities	1.1 (0.8)	0.7 (0.8)	1.4 (0.7)	0.006

Results: In total, 61 patients were studied; 41 (67.2%) were women and the mean (standard deviation [SD]) period between onset of CHIKV infection and study visit was 23.4 (9.4) months. Thirty-three patients had chronic arthritis and 28 had resolved arthritis. Patients with chronic arthritis were more likely to have diabetes mellitus, chronic back pain, other symptoms on the acute phase (fever, tiredness, and myalgia), and to receive treatment with NSAIDs on the acute phase (Table 1). Among patients with chronic CHIKV arthritis, joint tenderness was most common in MCP joints (54.6%), shoulders (51.5%), PIP joints (45.5%), and knees (39.4%) at study visit. Swelling was observed in PIP joints (15.2%), MCP joints (12.1%), shoulders (9.1%), wrists (6.1%), ankles (6.1%), and MTP joints (3.0%). The mean (SD) HAQ score was 0.95 (0.56) and 57.6% had moderate-high disease activity per CDAI. Patients with moderate-high disease activity were more likely to have higher scores in overall HAQ and HAQ categories (dressing & grooming, arising, hygiene, reaching, and activities) when compared to those with mild activity (Table2).

Conclusion: In this group of DMARD-naïve patients with chronic CHIKV arthritis, nearly 58% had moderate to severe disease activity. Those patients had major functional disability, including significant dysfunction in several HAQ categories. Diabetes mellitus, chronic low back pain, and some manifestations on acute infection (fever, tiredness, and myalgias) were associated with chronic CHIKV arthritis.

Disclosure: N. Medina-Cintrón, None; **I. Martínez**, None; **N. Pérez-Ríos**, None; **Y. Berríos-López**, None; **L. Vilá**, None.

Abstract Number: 0632

Systems Approach to Understanding Reasons for Influenza Vaccine Hesitancy in Rheumatic Diseases

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: A vaccination coverage goal of 80% with the seasonal influenza vaccine was established to protect people at high-risk for influenza-related complications or hospitalizations (e.g. rheumatic diseases - RD). Inactivated influenza vaccine (IIV) coverage in RD patients remains below target. Vaccine hesitancy (i.e. delay in acceptance or refusal of vaccination despite availability of vaccination services) is a complex issue that threatens vaccine uptake. Understanding the reasons for influenza vaccine hesitancy among RD patients is fundamental to enhance vaccination coverage.

Methods: Between November and March 2020, we conducted a cross-sectional study of consecutive RD patients presenting to a rheumatology clinic at a Canadian university hospital. Patients indicated in a 10-point scale how likely they were to get the IIV. Three groups were defined: (a) refuse IIV (values 0-1-2), (b) accept IIV (values 8-9-10), and (c) uncertain (values 3-7). Demographic data, education, employment, RD diagnosis, treatment, and smoking status were compared between groups. Patients completed the WHO-Strategic Advisory Group of Experts (SAGE) questions on vaccine hesitancy (i.e. vaccine hesitancy determinants matrix). Multivariate logistical regression analyses were performed to evaluate predictors of vaccine hesitancy.

Table 1 (*Accept IIV as reference group*)	Refuse vs Accept		Uncertain vs Accept	
	OR (95% CI)	P values	OR (95% CI)	P values
Sex				
Female	0.23 (0.04, 1.23)	0.086	0.26 (0.07, 1.01)	0.052
Male	Ref		Ref	
Age	1.02 (0.96, 1.08)	0.586	0.96 (0.92, 1.01)	0.105
School Degree				
Other degrees	0.60 (0.13, 2.68)	0.500	1.77 (0.52, 6.07)	0.359
Bachelor/University level or above	Ref		Ref	
Employment				
Not employed	Ref		Ref	
Employed	3.63 (0.37, 35.48)	0.268	2.51 (0.46, 13.81)	0.291
Retired	2.58 (0.13, 52.13)	0.538	3.15 (0.30, 33.76)	0.342
Ever received IIV				
No	**144.01 (7.70, >999.99)**	<0.001	**46.78 (3.31, 661.79)**	0.004
Yes	Ref		Ref	
Trusts pharma provides safe/effective IIV				
No	**261.95 (9.63, >999.99)**	0.001	4.11 (0.22, 77.95)	0.346
Yes	Ref		Ref	
Not sure	3.69 (0.62, 21.78)	0.150	0.92 (0.27, 3.08)	0.892
Concerns about adverse effects				
No	Ref		Ref	
Yes	**10.47 (1.67, 65.44)**	0.012	1.52 (0.33, 6.90)	0.591
Enough info about IIV and its safety				
No	1.06 (0.22, 5.11)	0.942	1.27 (0.34, 4.66)	0.723
Yes	Ref		Ref	
Feels social pressure to get IIV				
No	Ref		Ref	
Yes	**0.03 (0.01, 0.75)**	0.033	0.21 (0.03, 1.92)	0.119
Believes Influenza disease is serious				
No	Ref		Ref	
Yes	43.47 (0.11, >999.99)	0.214	35.61 (0.53, >999.99)	0.097
Not sure	157.67 (0.30, >999.99)	0.114	84.73 (0.84, >999.99)	0.060
Thinks IIV is safe				
No	39.27 (0.84, >999.99)	0.061	**34.26 (1.02, >999.99)**	0.049
Yes	Ref		Ref	
Not sure	2.42 (0.18, 32.50)	0.506	1.92 (0.34, 10.98)	0.464
Would take time off work to get IIV				
No	**42.79 (3.87, 473.25)**	0.022	3.13 (0.79, 12.35)	0.104
Yes	Ref		Ref	
Would pay to get IIV				
No	**5.22 (1.03, 26.60)**	0.047	**5.49 (1.50, 20.09)**	0.010
Yes	Ref		Ref	

Results: 294 patients (101 rheumatoid arthritis-RA, 107 SLE/vasculitis-SARD, 55 spondyloarthropathies-SpA, 31 osteoarthritis-OA) were included in the analysis. Over a third them did not receive IIV in the previous year (RA 38.4%, SARD 39.1%, SpA 48.2%, OA 38.7%). According to how likely they were to get the IIV, three groups were defined: refused (n=67), accepted (n=165) and uncertain (n=40). Demographics, education, and smoking status did not differ between the three groups. Retired patients were more frequent among those who refused IIV (35% vs 12% in the uncertain group). The use of biologics was higher in the group that 'accepted IIV' (27% vs 13.4% in those who refused IIV). Reported reasons for hesitancy according to the WHO-SAGE matrix was similar across diseases. Table 1 summarizes the predictors of vaccine hesitancy.

Conclusion: Forty percent of RD patients, irrespective of their education, either refuse or express uncertainty about getting IIV. Concerns about adverse events and doubts that pharmaceutical companies are providers of safe and effective vaccines are key determinants of IIV hesitancy.

Disclosure: V. Valerio, None; **M. Useche**, None; **E. Field**, None; **M. Wang**, None; **E. Hazel**, None; **B. Ward**, None; **I. Colmegna**, None.

Abstract Number: 0633

Vitamin D Serum Status in a Cohort of COVID-19 Patients

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Vitamin D serum levels have been inversely associated with risk of pulmonary infections and autoimmune inflammatory disease activity and severity [1,2]. A possible role of vitamin D in patients with SARS-Cov-2 infection was also recently reported [3].

The aim of the study was to evaluate 25OH-vitamin D serum levels in a cohort of patients hospitalized for SARS-Cov-2 infection, looking in particular for correlations with parameters of lung involvement.

Methods: Sixty consecutive COVID-19 patients (mean age 76±8 years, mean disease duration 13±13 days, 26 males and 34 females) and sixty sex- and age-matched healthy subjects (CNT) were evaluated. Pulmonary involvement (radiological findings), respiratory parameters (PaO_2/F_IO_2, pO_2, sO_2), clinical parameters, duration of hospitalization and global disease duration were recorded.

Results: Vitamin D serum levels were found significantly lower in COVID-19 patients than in CNT (median 7.8 vs 16.0 ng/ml, p=0.0003). Among COVID-19, vitamin D sufficiency (>30 ng/ml), insufficiency (between 20 and 30 ng/ml) deficiency (between 10 and 20 ng/ml) and severe deficiency (< 10 ng/ml) were observed respectively in 11, 12, 20 and 57 % of patients. In CNT, the same vitamin D distribution occurred in 21, 22, 34 and 23 % of subjects respectively.

A statistically significant positive correlation was observed between vitamin D serum levels and PaO_2/F_IO_2 (p=0.02), pO_2 (p=0.04), sO_2 (p=0.05), while a statistically significant negative correlation was found between vitamin D serum levels and percentage of O_2 in Venturi Mask (p=0.04). Vitamin D serum levels negatively correlated also with C-reactive protein (p=0.04), D-dimer (p=0.04), and parathyroid hormone (p=0.05).

A negative correlation was also found between vitamin D levels and severity of radiographic pulmonary involvement, but this did not reach the statistical significance (median vitamin D levels in patients with Mild, Moderate and Severe lung involvement were respectively 10.9, 7.7 and 5.5 ng/dl; p=0.11). However, vitamin D serum levels were found significantly lower in COVID-19 patients with either multiple lung consolidations or severe interstitial lung involvement than in those with either normal or mild interstitial lung involvement (p=0.02).

Finally, lower vitamin D serum levels were found associated with longer global disease duration (p=0.05).

Conclusion: Deficiency of 25OH-vitamin D serum levels seem associated with more severe lung involvement and longer disease duration in COVID-19 patients.

References

1. Zittermann A et al. *Eur J Med Res (2016)* 21:14. **2.** Cutolo M et al. *Ann N Y Acad Sci (2014)* 1317:39-46. **3.** Weir EK et al. *Clin Med (Lond) (2020)* 20:4.

Disclosure: A. Sulli, None; **E. Gotelli**, None; **S. Paolino**, None; **A. Casabella**, None; **C. Pizzorni**, None; **E. Alessandri**, None; **V. Smith**, Boehringer Ingelheim, 2, 5, 8, Janssen, 2, 5, 8; **M. Cutolo**, None.

Abstract Number: 0634

Influenza Knowledge and Barriers to Vaccination in Immunosuppressed Patients in the Pediatric Rheumatology Clinic

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Many pediatric rheumatology patients are at increased risk of influenza due to immunosuppressive medication use. Annual influenza vaccination is recommended for all children by the Centers for Disease Control and Prevention. Our division has tracked influenza vaccination rates since 2015 and have done quality improvement efforts to increase our vaccination rate. The vaccination rate plateaued at 71%, which prompted a survey to assess patient-reported vaccination rate, knowledge of influenza, and barriers to influenza vaccination.

	Parent (n=21)	Patient (n=14)	Total (n=35)
1. I think the flu shot can cause the flu	19%	35.7%	25.7%
2. The flu shot makes you sick	19%	14.3%	17.1%
3. The injection is painful	4.8%	7.1%	5.7%
4. I worry the vaccine will flare/worsen my child's/my rheumatic disease	42.9%	7.1%	28.6%
5. I do not think the vaccine will work	23.8%	14.3%	20%
6. My child does/I do not get the flu, so it is not worth getting the vaccine	9.5%	7.1%	8.6%
7. The flu is not that serious	4.8%	0%	2.9%
8. I would have given my child/gotten the vaccine but forgot to get it	9.5%	28.6%	17.1%
9. I would have given/gotten the flu vaccine, but the doctor's office did not have it available	0%	0%	0%
10. I do not give any vaccinations to my child	14.3%	N/A	N/A
11. My parent does not believe in any vaccinations	N/A	0%	N/A
12. I choose not to receive any vaccinations	N/A	0%	N/A
13. I would have gotten the flu shot but my parent refused	N/A	0%	N/A

*Respondents were able to select more than one answer

Table 1. Reasons why influenza vaccine not received*

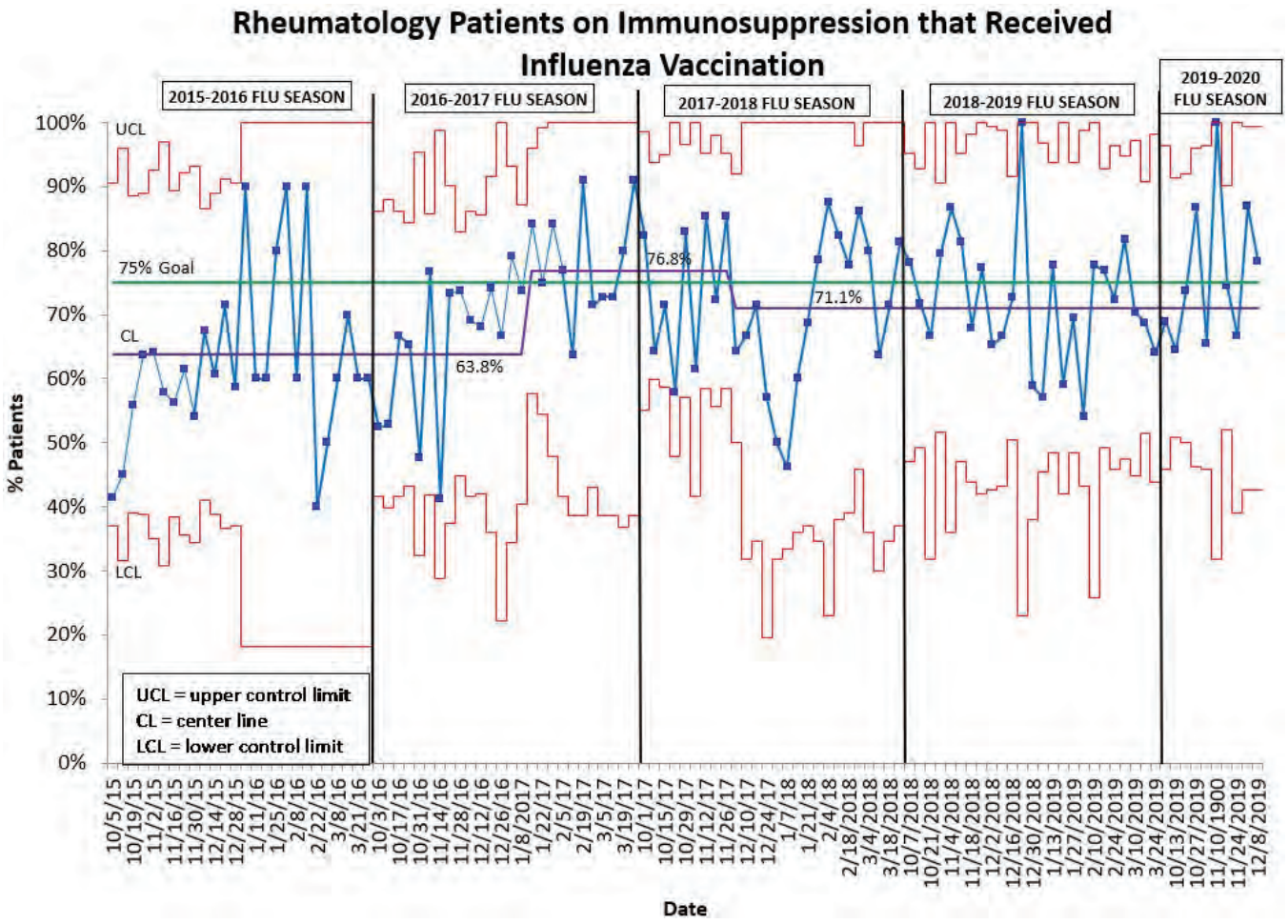

Figure 1. Control chart demonstrating influenza vaccination rates in immunosuppressed rheumatology patients

Methods: In the Rheumatology Clinic, a parent or patient (15 years and older) on immunosuppressive medication was eligible to complete a REDCap survey. Survey questions assessed demographics, rheumatology diagnosis, immunosuppressive medication type, medical providers recommendation of the influenza vaccination, influenza knowledge, and barriers to influenza vaccination. Self-reported vaccination rate referred to the 2018-2019 influenza season; if no vaccine received, a follow-up question asked for reasons why. The survey began in July 2019, and this project is ongoing. Influenza vaccination rates of immunosuppressed patients are acquired each flu season via chart review and tracked on a control chart that our division has maintained since 2016.

Results: Of 212 surveys, 139 (65.6%) were completed by parents and 73 (34.4%) by patients. The patients had an average age of 11.4 years for those under 17 years of age, and 13.2% of respondents were 18 years or older. The majority (61.3%) were diagnosed with juvenile idiopathic arthritis, while 8.5% had juvenile dermatomyositis and 8% had systemic lupus erythematosus. Methotrexate was the most common (52.4%) immunosuppressive medication followed by a tumor necrosis factor inhibitor (41%). The majority (84.9%) of parents reported their child received an influenza vaccine while patient report was 80.8%. The most common reasons for not receiving the influenza vaccine included: worry about disease flare (28.6%), concern the vaccine will cause influenza (25.7%), and presumed lack of vaccine effectiveness (20%) (**Table 1**). When asked for the two most common symptoms of influenza, 82.5% correctly answered fever and 73.5% correctly answered cough and/or congestion; however, 23.1% answered gastrointestinal symptoms and 9.6% joint swelling. Almost all the respondents (95.3%) were aware that influenza could cause death and that the prescribed medication increased risk of infection. The average weekly influenza vaccination rate

from October to December 2019 was 76.6%, which was higher than the 72.1% vaccination rate from the 2018-2019 season (**Figure 1**).

Conclusion: The influenza survey of immunosuppressed patients indicates that patients and parents understand the potential severity of influenza and the increased risk of infection due to medication use, however, many respondents inaccurately identified the most common symptoms of influenza. Additionally, self-reported vaccination rate was higher than expected. The barriers identified in this survey will help drive further improvement efforts to increase influenza vaccination rates in this high-risk population.

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Abstract Number: 0635

Hydroxychloroquine Is Not Associated with Reduced Influenza Admissions in Rheumatoid Arthritis Patients

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is commonly used as a disease-modifying anti-rheumatic drug (DMARD) for patients with rheumatoid arthritis (RA). HCQ has previously been the subject of interest for its in-vitro antiviral activity against influenza A strains, although in-vivo studies have yielded conflicting results. There has recently been renewed interest in the use of HCQ as prophylaxis and treatment for respiratory viral infections. Patients with RA are known to have increased risk of influenza infections and influenza-associated hospitalizations. They thus potentially provide the opportunity to explore the antiviral effects of HCQ. Our study aims to examine the association of HCQ use among RA patients with hospital inpatient admissions for influenza.

Methods: We examined general medical inpatient admissions for patients with a diagnosis of RA in a large tertiary hospital between January 2014 and December 2018. Natural language processing, ICD-10 codes, and medical record review were utilized to determine patient demographic data (age, gender, and smoking history), medical diagnosis, and medication use. Major confounders (smoking status, chronic obstructive pulmonary disease (COPD), age, gender, and other DMARD use) were selected. DMARD use was defined as medical record documentation of use at time of admission. Multivariate logistic regression models were used to assess the association of HCQ use and inpatient admission for influenza. The strength of association was assessed using adjusted odds ratios (OR) and associated 95% confidence intervals (CI).

Results: From 909 inpatient admissions during the study period, 23 admissions were primarily for influenza. There were no statistical differences in patient demographics or DMARD medication between the two groups (Table 1). A

Variable	No Influenza Diagnosis	Influenza Diagnosis	p-value
Admissions	886	23	
Age (years)	77.0	77.2	0.9037
Length of stay (hours)	382	218	0.0723
Smoking	47 (9%)	3 (13%)	0.8122
COPD	97 (19%)	4 (17%)	1.000
Proportion of admissions on DMARDs			
Hydroxychloroquine	265 (30%)	9 (39%)	0.4707
Methotrexate	301 (34%)	8 (35%)	1.000
Corticosteroid	483 (55%)	14 (61%)	0.6948

Table 1. Characteristics of rheumatoid arthritis patients admitted for influenza compared to those admitted for other indications.

total of 265 (30%) non-influenza admissions and 9 (39%) influenza admissions used HCQ at time of admission. In our multivariate regression model, HCQ use among patients with RA was not associated with a statistically significant difference in inpatient admission for influenza when adjusted for confounders (OR 1.45, CI 0.58 – 3.59). Likewise, the lack of association was persistent when adjusted for methotrexate (OR 1.42, CI 0.58 – 3.50) and corticosteroid use (OR 1.40, CI 0.56 – 3.54).

Conclusion: There was no association in our cohort to support the contention that HCQ use prevents inpatient admission for influenza among RA patients, and in fact may even favour the possibility of increased risk. This study contributes to the growing evidence that HCQ does not confer a protective effect for respiratory viral infections.

Disclosure: B. Liu, None; **V. Yang**, None; **C. McMaster**, None; **R. Buchanan**, None; **A. Frauman**, None; **D. Liew**, None.

Abstract Number: 0636

Rheumatology Patient Experience and Trends During the SARS-COV-2 Pandemic

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatic disease patients are counseled on the immunosuppressive aspect of their rheumatic disease treatment and their increased risk of infection. Little is known about the experience of rheumatic disease patients during a pandemic, their medication trends, or resource utilization.

Methods: Rheumatologist-created 32 question electronic questionnaire was shared through social media platforms including Facebook, Reddit, and Twitter on disease-specific pages from April-June 2020 with goal of being by patients with any rheumatic disease.

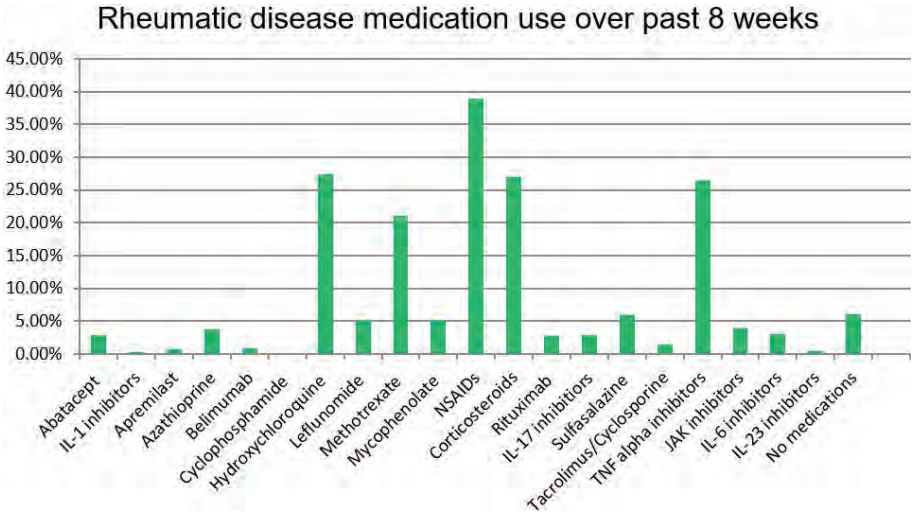

Figure 1.

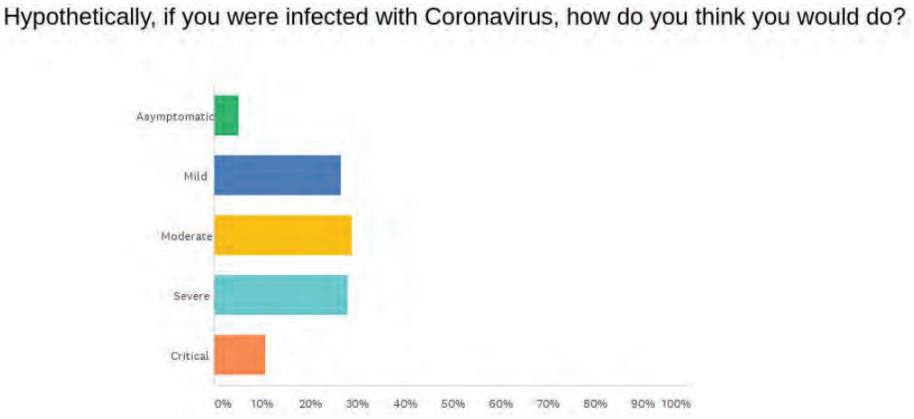

Figure 2.

Results: 2244 questionnaires were completed, the majority by Caucasian women (88%) ages 35-64 from across the United States (85%) who had obtained higher education. Multiple self-declared diagnoses could be chosen, the majority had any form of inflammatory arthritis (59%) with systemic lupus, mixed connective tissue disease, and Sjogren's syndrome noted by 23%. All categories of rheumatic diseases were represented. Most commonly used medications were: Corticosteroids, TNF inhibitors, NSAIDs, and Methotrexate, 5% were on no medications (Figure 1). One quarter of subjects had a pulmonary, renal, and/or cardiac condition. Eighty percent of those surveyed considered themselves immunocompromised, with 4% of these on no immunosuppressive medications. When typically ill almost half of patients reported they continue all of their medications.

Across all diseases, almost 50% had contacted their rheumatologist or another medical provider with questions regarding the novel coronavirus in the past 8 weeks prior to the survey completion, with those on no medications more likely to reach out. In this time period, 20% held at least one of their medications. Of those, 15% held their rheumatic medication as directed by their rheumatologist due to the SARS-Cov-2 pandemic (not infected) and 30% held medication without medical consultation. Specifically 10% stopped taking NSAIDs due to concern of SARS-CoV-2. Patients felt they would do poorly if infected with SARS-CoV-2 (Figure 2) this correlated with underlying pulmonary, renal, or cardiac conditions but also correlated with the patient reported taking no medications. Medications popularized at time of survey with potential to treat SARS-CoV-2 were not correlated with presumption of less severe outcomes.

Very few had been diagnosed with SARS-CoV-2 (0.7% tested, 3% presumed), nor had their household contacts. Only about 40% were working from home, 12% of those surveyed were unemployed or furloughed. Traditional news sources was the most often consulted resource as knowledge in regard to how coronavirus affects those with rheumatic diseases, followed by disease-specific foundations and the CDC.

Conclusion: In the initial months of the SARS- CoV-2 pandemic, patients were either told to stop or self-stopped their rheumatic disease medications. Patients overall felt they would do worse than those without a rheumatic disease, however did not correlate to specific medication or disease but with organ involvement. Disease specific foundations were seen as a resource for reliable information pertaining to their disease.

Disclosure: C. Edens, None; **K. Ko**, None; **K. Trotter**, None.

Abstract Number: 0637

Clinical and Treatment Features of Rheumatoid Arthritis in HIV-Infected Individuals Followed Longitudinally over Time

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: With the successful treatment of HIV-1 infection with combination anti-retroviral treatment, immune-mediated diseases that were rarely encountered in HIV positive individuals in the pre-treatment era have emerged, including rheumatoid arthritis. The management of RA poses a particular challenge since the use of immunomodulatory medications could increase immunosuppression. The purpose of this study was to examine the clinical features and treatment outcomes of HIV-infected individuals with rheumatoid arthritis (RA) in a large outpatient HIV rheumatology clinic.

Methods: A retrospective chart review of patients with concomitant RA and HIV-1 were evaluated at the Harris County HIV Rheumatology Clinic from 1994-2020. All patients met the American College of Rheumatology criteria for RA and were seen by the same investigators (FMW, JDR). At baseline visit the following were collected: demographic data, disease features, laboratory data, medications, and follow up visit data. Antiretroviral medications were stratified into protease inhibitors, nucleoside reverse transcriptase inhibitors (NRTIs), non-nucleoside reverse transcriptase inhibitors (NNRTIs), and integrase inhibitors.

Results: From 1994-2020, we saw 27 patients with concomitant RA and HIV-1 infection from a total cohort of 1671 HIV-1 rheumatology patients (Table 1). The first case of RA noted in our clinic was 2003 with an average of 7.3 (±4.9) years of follow up. Mean age at presentation was 51.9 (±9.6) years, 14 were female and 13 patients male. Ethnically, the RA patients included three white, 14 black, and 10 Latino patients. Average BMI on presentation was 29.13 (±6.57) compared to 27.98(±8.25) on follow up. Average CD4 count at presentation was 629.3 (±432.2) cells/μL with five patients having a CD4< 200 cells/μL compared to 634.7 (±422.2) cells/μL at their most recent visit. Only one patient had a CD4< 200 at follow up. Four patients had a detectable viral load at presentation; however, at subsequent follow up only one of these still had a detectable viral load. Twelve patients were seropositive by either positive

Age at Diagnosis	Gender	Ethnicity	Date of Diagnosis	Base-line CD4	DMARD	Prednisone	TNF	NSAID	Protease Inhibitors	NRTI	NNTRI	Integrase Inhibitors	Last Seen
45	M	W	6/1/2003	528	Yes	Yes	Yes	Yes	No	Yes	Yes	No	2/13/2020
62	F	W	6/9/2003	627	No	No	No	Yes	No	Yes	Yes	No	Lost to follow up
30	F	B	7/28/2003	168	No	No	No	Yes	No	Yes	Yes	No	Lost to follow up
48	M	B	9/29/2003	826	Yes	No	No	No	No	Yes	No	No	2/18/2020
44	F	B	4/12/2004	1300	Yes	No	Yes	Yes	N/A	N/A	N/A	N/A	2/25/2020
36	M	H	8/9/2004	127	No	No	No	Yes	No	Yes	Yes	No	1/9/2014
46	F	W	11/12/2007	195	N/A	No	N/A	No	Yes	Yes	No	No	Lost to follow up
55	F	B	11/26/2007	171	No	No	No	No	Yes	Yes	No	No	3/25/2014
69	M	H	1/14/2008	311	Yes	Yes	Yes	No	Yes	Yes	No	No	10/20/2015
60	M	H	9/14/2009	476	Yes	Yes	Yes	Yes	No	No	No	No	5/1/2020
47	F	B	2/3/2010	75	No	No	No	Yes	Yes	Yes	Yes	No	6/3/2020
71	F	B	9/27/2010	388	Yes	Yes	No	Yes	No	Yes	Yes	No	2/18/2020
61	M	H	9/12/2011	289	No	Yes	No	Yes	Yes	Yes	No	No	5/7/2020
48	M	H	6/27/2011	620	Yes	No	No	No	Yes	Yes	No	No	3/2/2015
49	M	B	7/11/2011	548	No	No	No	No	No	Yes	Yes	No	5/17/2018
60	F	B	9/10/2012	305	No	Yes	No	Yes	Yes	Yes	No	No	8/13/2018
48	M	B	1/14/2013	1608	Yes	Yes	Yes	No	No	No	No	No	5/13/2020
54	M	H	8/12/2013	254	No	No	No	Yes	No	Yes	Yes	No	10/28/2019
37	M	H	7/27/2015	470	Yes	No	No	Yes	No	Yes	No	Yes	6/26/2019
58	M	B	6/27/2016	1050	No	No	No	Yes	Yes	Yes	No	No	3/18/2019
54	F	B	8/22/2016	518	No	No	No	No	No	Yes	No	Yes	2/20/2020
63	F	B	8/22/2018	1167	Yes	No	No	No	No	Yes	No	Yes	6/13/2019
46	F	H	10/31/2018	1400	No	Yes	No	Yes	No	Yes	No	Yes	4/27/2020
56	F	B	7/2/2019	638	Yes	Yes	No	No	No	Yes	No	Yes	5/6/2020
51	F	B	10/23/2019	868	Yes	No	No	Yes	No	Yes	No	Yes	2/4/2020
50	M	H	6/10/2020	717	Yes	No	No	No	No	Yes	No	Yes	6/10/2020
52	F	H	6/10/2020	1347	Yes	Yes	No	No	No	Yes	No	Yes	6/10/2020

rheumatoid factor (RF) or anti-cyclic citrullinated peptides (anti-CCP). In regards to RA medications we have used methotrexate since 1994 (on non RA patients). Fourteen patients were on DMARDs, 10 on prednisone (at doses of < 10 mg/day) , 15 were taking NSAIDs and four were treated with TNF blockers (with no adverse effects). As far as antiretroviral medications are concerned, seven took protease inhibitors, 22 on NRTI, eight on NNRTI, and six integrase inhibitors. Two patients were on no HIV therapy and only one patient was on mono-drug therapy with the rest of the patients being on two or more anti-retroviral medications. With follow up, 18 patients had clinical remission on treatment, seven patients were treatment noncompliant, and two patients had no improvement on methotrexate.

Conclusion: Patients treated for rheumatoid arthritis in the setting of HIV-1 with anti-rheumatic and antiretroviral medications had improvement in laboratory values in regard to CD4 and viral loads. Additionally, our cohort demonstrated a high prevalence of seronegative rheumatoid arthritis cases compared to what has been reported in the literature.

Features of Concomitant Rheumatoid Arthritis and HIV-1

Disclosure: B. Naovarat, None; **F. Williams**, None; **J. Reveille**, Eli Lilly, 2, UCB, 5, Janssen, 2.

Abstract Number: 0638

Serological Evidence of SARS-CoV-2 in Symptomatic Patients Under Biological Treatment in a Rheumatology Service

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: In mid-March 2020, state of alarm was declared in Spain due to the novel coronavirus disease 2019 (COVID-19) pandemic. Patients with rheumatic diseases (RD) under immunosuppressive drugs are considered at high risk of severe outcome. Some commonly used treatments in RD such as corticosteroids, hydroxychloroquine or anti-IL6 drugs are also hypothesized to help treat COVID-19. We set out to determine the prevalence of SARS-CoV-2 infection among patients who reported respiratory symptoms during COVID-19 pandemic from March up to June 2020 in a group of patients treated with biological agents such as anti-TNF, anti-IL6, abatacept and JAK inhibitors like baricitinib or tofacitinib.

Methods: A registry of all patients under treatment with adalimumab, anti-IL6, abatacept, baricitinib and tofacitinib in our Rheumatology Service was obtained. All the patients were called and asked to participate in a telephone survey screening for infectious respiratory symptoms in the past 4 months (phone calls were made from mid-April to early-June)**.** Other epidemiological data (previous contact with a suspected case, number of household members and confinement measures) were collected. Reported symptoms were evaluated by a clinician to assess whether or not these were suggestive of acute respiratory disease. Those who presented new onset acute respiratory symptoms were tested for SARS-Cov-2 serology (IgM/IgG).

Results: A total of 355 patients participated in the survey, 66.5% were females. Mean age (S.D.) was 54.7 years (16.5). Rheumatoid arthritis was the most common diagnosis (56%), followed by spondyloarthritis (16.3%), psoriasic arthritis (11.3%), idiopathic juvenile arthritis (6.8%) and others (9.6%). Adalimumab (46%) and tocilizumab (20.9%) were the most common treatment groups, followed by abatacept (12.4%), tofacitinib (12.1%), baricitinib (6.5%) and sarilumab (2.3%). Mean time under current treatment was 59.8 months.

Patients were asked for the presence of respiratory symptoms out of a list with 20 items. Follow-up questions were asked when necessary to determine the acute or chronic nature of the symptoms. The most common reported symptoms were cough (8.2%), odynophagia (6.8%), fatigue (5.4%), shortness of breath (4.8%), joint or muscular pain (3.7%) and diarrhea (3.4%). 87.24% complied with the confinement measures. 4.94% reported contact with people with symptoms suspicious of COVID-19. No patient required hospital care.

A total of 25 were selected for serological testing based on reported symptoms compatible with COVID-19 disease. The remaining 330 patients reported no symptoms or had symptoms not attributable to infection. Peak incidence of reported symptoms occurred in March (n = 10). All patients tested negative for IgM and only one patient was positive for IgG.

Conclusion: Patients with RD showed a high level of compliance to confinement measures. COVID-19 was extremely low among patients with RD treated with biological agents or JAK inhibitors. Confinement measures are key to prevent SARS-Cov-2 transmission.

Disclosure: C. Pavez Perales, None; **S. Leal Rodriguez**, None; **M. De la Rubia Navarro**, None; **R. Gonzalez Mazario**, None; **E. Grau Garcia**, None; **C. Alcañiz Escandell**, None; **I. Chalmeta Verdejo**, None; **J. Fragio Gil**, None; **L. Gonzalez Puig**, None; **J. Ivorra Cortes**, None; **I. Martinez Cordellat**, None; **R. Negueroles Albuixech**, None; **J. Oller Rodriguez**, None; **F. Ortiz Sanjuan**, None; **E. Vicens Bernabeu**, None; **J. Roman Ivorra**, None.

Abstract Number: 0639

Immunological Abnormalities in a SARS-CoV-2-Cytokine Release Syndrome Rheumatology Cohort

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Infection-related Rheumatic Disease Poster

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Background/Purpose: Cytokine release syndrome (CRS) is a condition characterized by a sepsis-like condition and laboratory abnormalities such as high ferritin, low ESR, and low fibrinogen which has a mortality rate of up to 60%. Patients with SARS-CoV-2 can develop CRS (SARS-CoV-2-CRS). There have been reports of features of antiphos-

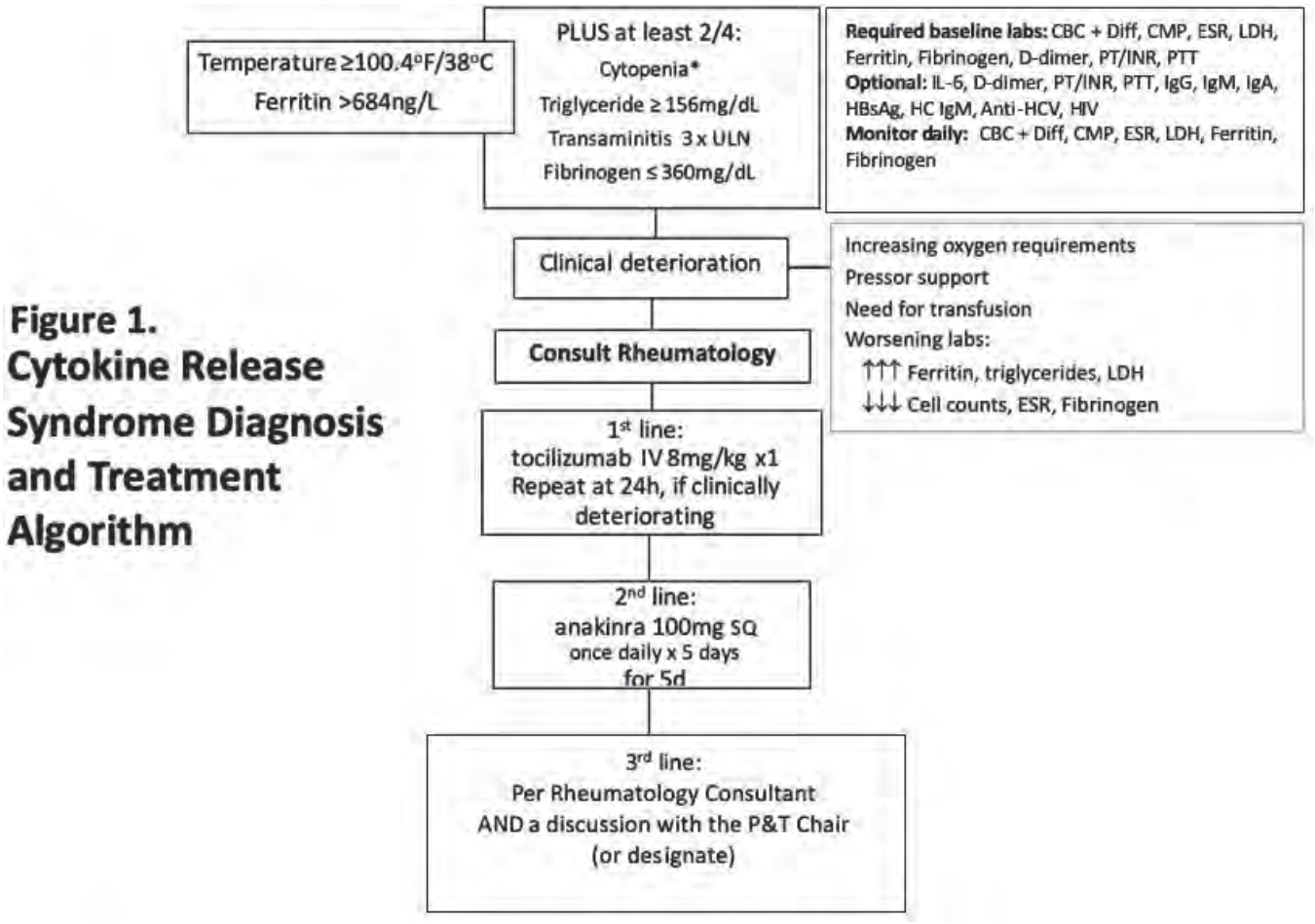

Figure 1. Cytokine Release Syndrome Diagnosis and Treatment Algorithm

Table 1. Treatment Considerations for Cytokine Release Syndrome due to SARS-CoV-2 for patients referred to a Rheumatology Consultation Service

	Therapy	Dose	Comments
1st Line	tocilizumab (anti-IL6)	8mg/kg IV x 1 (800mg maximum dose); repeat if no clinical improvement within 24-48 hours For dosing, consider rounding to the nearest available vial size: 80mg, 200mg, 400mg	• Pertinent Drug Interaction: CYP3A4 Substrates (High risk with Inducers) • No renal adjustment; • Contraindications: Known hypersensitivity to Tocilizumab or any component • Caution: Monitor liver enzymes, platelet counts, neutrophils • Risks: GI perforation risk; thrombocytopenia, neutropenia; liver enzyme elevation; Herpes zoster reactivation
2nd Line	anakinra (anti-IL1)	100 mg SQ once daily x 5 days	• Not to be combined with other biologic DMARDs; clozapine; live vaccines • Contraindications: Hypersensitivity to E.coli derived proteins, anakinra or any component of the formulation; use with caution: CrCl<30mL/minute or ESRD
3rd Line	Per Rheumatology Consultant AND after discussion with the P&T Committee Chair (or designate)		
	Any use of the above immunomodulatory drugs intended as treatment of COVID-19 complications which deviates from this table, including administration route &/or dosing, requires a discussion with the P&T Committee Chair (or designate) before the drug is verified by the Pharmacist, or administered by Nursing.		

Table 1. Treatment Considerations for Cytokine Release Syndrome due to SARS-CoV-2 for patients referred to a Rheumatology Consultation Service

pholipid antibody syndrome, lupus and Kawasaki disease occurring in SARS-CoV-2 patients, but no other study has looked at these features in patients with CRS. Studies are needed to determine if immunological laboratory abnormalities occur in SARS-CoV-2-CRS patients, and can help predict poor outcomes. Institution-mandated rheumatology treatment protocols for SARS-CoV-2-CRS were developed at a university medical center and county Hospital (Figure 1, Table 1). This study aims to establish if immunological abnormalities and poorer outcomes are present in SARS-CoV-2-CRS patients when compared to those without CRS.

Methods: SARS-CoV-2 patients referred to Rheumatology SARS-CoV-2-CRS for CRS evaluation (March 15-May 30, 2020) were included in this retrospective chart review. Demographics (age, sex, and ethnicity) and histories of diabetes, autoimmune disease, and medications were noted. Laboratory data reviewed included white blood cell count, hemoglobin, platelets, ferritin, fibrinogen, liver enzymes, complement, immunoglobulin levels, antinuclear antibody and antiphospholipid antibody panels and interleukin 6. Clinical outcomes tracked included oxygen and ventilation requirements, development of infections, and mortality. Descriptive statistics were used.

Results: 150 patients were included in this chart review. Majority were 109 (73%) males, with a mean age of 61.6. 28 (19%) were health facility residents, 11 (7%) health care workers, and 34 (23%) inmates. Ethnicities included 44 (30%) white non-Hispanic, 64 (43%) Hispanic, 24 (16%) Asian, 14 (9%) Black, and 2 (1%) other. 71 (47%) of patients were diagnosed with SARS-CoV-2-CRS. Compared to patients without CRS, greater proportions of patients with CRS were noted to have lower Ig, complement and platelet levels, higher liver enzyme, triglyceride, ferritin, IL6 and IL2 receptor levels, positive antiphospholipid antibody tests, (Table 2). Bacterial co-infections were actually higher among non-CRS patients. CRS patients had a higher rate of death and thrombosis compared to those without CRS.

Conclusion: A larger proportion of SARS-CoV-2-patients who developed CRS had certain immunological laboratory abnormalities when compared to those without CRS. This data serves as preliminary analysis of an ongoing study. More detailed analysis of categorized deviations of laboratory abnormalities relative to the timed occurrence of adverse outcomes (i.e. death) and to the use of therapies, and how these correlate with other features such as physical

Table 2. Laboratory features and clinical outcomes in a patient population referred to Rheumatology for SARS-CoV-2-CRS diagnosis and management

	Met diagnostic criteria for SARS-CoV-2-CRS, N = 71	Did not meet Diagnostic criteria for SARS-CoV-2-CRS, N = 79
Specific Immunology Laboratory tests (Cut offs for abnormal and units where applicable)	N (%)	N (%)
Positive ANA	7 (10)	5 (6)
low C3 (<70 mg/dL)	7 (8)	1 (1)
low C4 (<11 mg/dL)	5 (7)	1 (1)
High Immunoglobulin M (>230mg/dL)	1 (1)	1(1)
High Immunoglobulin G (680-1490mg/dL)	7 (10)	4(5)
Low Immunoglobulin G (<680 mg/dL)	3 (4)	1 (1)
Low Immunoglobulin M (<54 mg/dL)	7 (10)	0 (0)
High Interleukin 6 (>1.8 pg/mL)	29 (41)	24 (30)
High Interleukin 2 Receptor (>1,033 pg/mL)	12 (17)	2 (3)
Positive Anticardiolipin IgG or IgM or IgA (U/mL)	8 (11)	2 (3)
Positive Beta2 Glycoprotein IgG or IgM or IgA(U/mL)	4 (6)	0 (0)
Positive Lupus Anticoagulant	10 (14)	5 (6)
High D-Dimer (>0.4 ug/mL)	65 (92)	70 (89)
Laboratory tests for diagnosis of CRS (cut offs for abnormal)		
Hyperferritinemia(>350 ng/mL)	64 (90)	65 (82)
Leukopenia (<4.0 bil/L)	13 (15)	15 (19)
Thrombocytopenia (<150 bil/L)	17 (24)	12 (15)
Transaminitis (AST > 35 U/L, ALT >45 U/L)	62 (87)	60 (76)
Elevated ESR (>30mm/hr)	65 (92)	71 (90)
Inappropriately low ESR*	4 (6)	2 (3)
Hypertriglyceridemia (>150mg/dL)	47 (66)	44 (56)
Clinical Outcomes		
Need for increased Oxygen requirement Mechanical ventilation	69 (97) 16 (23)	70 (89) 18 (23)
New thrombosis	8 (11)	2 (3)
Bacterial co-infection	10 (14)	25 (32)
Deceased	20 (28)	11 (14)

*An inappropriately low ESR was defined as a an ESR that was normal or low or only mildly elevated despite a critical clinical course defined by increasing oxygenation requirements, need for mechanical ventilation or having a sepsis-like picture

Table 2. Laboratory features and clinical outcomes in a patient population referred to Rheumatology for SARS-CoV-2-CRS diagnosis and management

exam findings and imaging results are needed. Autopsy data also need to be included. Follow up of survivors are being done to determine if these abnormalities persist, and if other clinical features suggestive of autoimmune diseases and immunodeficiency disorders develop.

Disclosure: P. Injean, None; **S. Lee**, None; **N. Chiruvolu**, None; **M. Karim**, None; **L. Doo**, None; **D. Ragesh Panikkath**, None; **D. Jose**, None; **M. Yu**, None; **A. Lafian**, None; **V. Sandhu**, GSK, 8; **K. Torralba**, None; **C. Downey**, None; **M. Cabling**, None; **M. Hojjati**, GlaxoSmithKline, 8.

Abstract Number: 0640

Covid-19 and Rheumatic and Musculoskeletal Disease Patients: Infection Rates, Attitudes and Medication Adherence

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SESSION INFORMATION

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Background/Purpose: Covid-19 has caused >400,000 deaths. The relationship between RMDs, immunosuppressive medications and Covid-19 is unclear. This study explores Covid-19 prevalence, DMARD adherence, information sources and attitudes to virtual clinics amongst RMD patients during the current pandemic.

Methods: An anonymous online survey to assess Covid-19 status, RMD diagnoses, adherence and information sources was performed. The respondents' primary information source was assessed for quality and readability using validated scoring systems. Binary logistic regression was used to calculate odds ratios for symptoms of Covid-19.

Gender	
Female	1207 (87.8%)
Male	168 (12.2%)
Age	
<40	331 (24.1%)
41-60	814 (59.2%)
>60	230 (16.7%)
RMD*	
Rheumatoid Arthritis	726 (52.9%)
Spondyloarthropathy	451 (32.9%)
CTD/Vasculitis	77 (5.6%)
Other RMD	193(14.1%)
None	118(8.6%)
Covid-19 status	
Asymptomatic, without infected contact risk	1176 (91.8%)
Asymptomatic, with infected contact risk	58 (4.5%)
Symptomatic, without infected contact risk	39 (3.0%)
Symptomatic, with infected contact risk	8 (0.6%)
Covid-19 test status	
Not tested	1203 (92.7%)
Negative	89 (6.9%)
Positive	6 (0.5%)
RMD medications	
Biologic/JAKi	664 (51.8%)
csDMARD (excluding HCQ/chloroquine)	526 (40.8%)
Glucocorticoid	116 (12.9%)
HCQ/chloroquine	118 (9.2%)
None of the above	290 (22.5%)

*Some respondents had more than one RMD

Table 1. Respondent characteristics

	Covid-19 symptoms (%)	Odds ratio (95% CI)	p
Gender			
Female	38 (3.4%)	0.67 (0.31-1.45)	NS
Male	8 (5.0%)	1.50 (0.69-3.28)	
Age, years			
<41	16 (5.0%)	1.63 (0.88-3.04)	
41-60	24 (3.2%)	0.73 (0.41-1.32)	NS
>60	6 (3.1%)	0.82 (0.34-1.96)	
RMD			
Rheumatoid Arthritis	21 (3.1%)	0.72 (0.40-1.29)	NS
Spondyloarthropathy	24 (5.5%)	2.06 (1.14-3.70)	0.015
Connective Tissue Disease/Vasculitis	4 (5.7%)	1.16 (0.57-4.71)	NS
Other RMD	12 (6.7%)	2.16 (1.10-4.26)	0.025
No RMD	2 (2.0%)	0.50 (0.12-2.10)	NS

Table 2 Odds ratios of Covid-19 symptoms by demographics and disease

Results: Table 1 shows respondent characteristics (n=1,381). RA was the most common diagnosis. 47 (3.7%) respondents had symptoms of Covid-19 and 6 (0.5%) tested positive, consistent with the general Irish population.

	Covid-19 symptoms (%)	Odds ratio (95% CI)	p
Medications			
Biologic/JAKi	19 (2.9%)	0.66 (0.36-1.21)	NS
csDMARD (excluding HCQ/chloroquine)	9 (1.7%)	0.35 (0.17-0.72)	0.005
Glucocorticoid	7 (4.4%)	1.28 (0.56-2.92)	NS
HCQ/chloroquine	1 (4.5%)	1.4 (0.43-4.60)	NS
Any immunosuppressive agent*	27 (2.9%)	0.48 (0.27-0.88)	0.018
No immunosuppressive agent	18 (5.8%)	2.08 (1.13-3.84)	0.018
Number of immunosuppressive drug classes*			
None	18 (5.8%)	2.60 (1.42-4.78)	0.002
1	21 (3.5%)	0.965 (0.54-1.75)	NS
2 or more	6 (1.7%)	0.39 (0.16-0.93)	0.034
Information source			
Health authority guidance	16 (2.4%)	0.47 (0.25-0.89)	0.020
Other	18 (2.9%)	0.68 (0.37-1.28)	NS
None	17 (5.8%)	2.17 (1.15-4.10)	0.017

*excludes HCQ/chloroquine

Table 3. Odds ratio of COVID-19 symptoms by medications and information source

Odds ratios for Covid-19 symptoms were higher amongst those with a SpA and other RMDs and lower in those on immunosuppression, csDMARDs, multiple immunosuppressives and those compliant with health authority guidance (Tables 2 and 3). Adherence to RMD medications was high at 84.1%. The most common reason for non-adherence was concern of an increased risk of infection (58.8%). 57.1% report using health authority guidelines for information on medication use. Importantly, adherence rates were higher amongst those who cited guidelines ($p< 0.001$), and conversely lower in those with Covid-19 symptoms ($p=0.004$). Moreover, we found the health authority guidance good quality and highly readable.

68.9% were unsure about potential Covid-19 therapies. Hydroxychloroquine was the most commonly selected potential agent (10.6%). Those with Covid-19 symptoms were more likely to think NSAIDs had a role in treating Covid-19 (20.9% versus 8.4%, $p=0.010$) amongst those with Covid-19 symptoms.

Finally, the use of virtual clinics was supported by 70.4% of respondents.

Conclusion: The rate of Covid-19 positivity in RMD patients was similar to the general population. Covid-19 symptoms were lower amongst respondents on immunosuppressive medication and those adherent to medication guidelines. Adherence rates were higher than previous studies. Interestingly, a higher proportion of respondents adherent with medications cited health authority guidelines. This study suggests provision of high quality, readable information may significantly influence behaviour with better awareness of social distancing and cocooning guidance and increase adherence and decrease the spread of Covid-19. Respondents were supportive of health authority advice and virtual clinics.

Disclosure: K. Murray, None; **S. Quinn**, None; **M. Turk**, None; **A. O'Rourke**, None; **E. Molloy**, None; **L. O'Neill**, None; **A. Mongey**, None; **U. Fearon**, None; **D. Veale**, AbbVie, 2, Health Beacon, 1, Janssen, 2, 8, Pfizer, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5.

Abstract Number: 0641

Cohort of Rheumatic Patients Treated with Rituximab and COVID-19: Does Rituximab Treatment Increases the Severity of SARS-COV2 Infection?

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SESSION INFORMATION
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Background/Purpose: There are very few studies reporting COVID-19 in patients with rheumatic diseases, without clear evidence supporting more frequent or severe disease in these patients. Nevertheless, to our knowledge, there are no studies analysing Rituximab effect within autoimmune diseases. The aim is t o describe the impact and outcome of SARS-CoV-2 infection in our cohort of patients with rheumatic diseases treated with Rituximab.

Methods: A retrospective, descriptive study was conducted on patients treated with Rituximab followed in the rheumatology unit of a referral hospital. Patients were screened by telephone interview and a comprehensive review of health records from 01/02/2020 to 22/05/2020. Patients were classified in 4 groups: Non suspected infection (asymptomatic), suspected infection (compatible symptoms not confirmed), inpatients with confirmed infection, deceased patients with confirmed infection. The clinical characteristics and outcome of these 4 groups were described.

Results: Seventy-six patients treated with Rituximab were reviewed. Among the 76 patients, 63 (82,8%) were classified as non suspected SARS-COV 2 infection, 5 (6,6%) had a suspected non confirmed infection, 5 (6,6%) were admitted to hospital with confirmed infection and 3 (4%) were admitted to hospital and died during hospitalization. Their baseline characteristics according to infection severity are described in table 1. At the beginning of COVID19 outbreak, 76,9% of patients were on remission of their rheumatic disease, 15,4% had low disease activity and 7,7% had active disease despite treatment.

	Non suspected infection patients (n= 63)	Suspected infection patients, not confirmed (n=5)	Hospitalized with confirmed infection patients (n=5)	Deceased with Confirmed infection patients (n=3)	TOTAL (n=76)
Age years median, (range)	61 (18-89)	54 (28-69)	68 (55-72)	69 (68-76)	62,5 (18-89)
Sex, n %					
Female	54 (85,7)	4 (80)	3 (60)	1 (33,3)	62 (81,6)
Male	9 (14,3)	1 (20)	2 (40)	2 (66,7)	14 (18,4)
Diagnosis, n %					
- RA	29 (46)	1 (20)	1 (20)	1 (33,3)	32 (42,2)
- RA+ 2º SS	6 (9,5)	2 (20)	1 (20)	0 (0)	9 (11,8)
- 1º SS	4 (6,3)	0 (0)	2 (40)	0 (0)	6 (7,9)
- SLE	5 (7,9)	1 (20)	0 (0)	1 (33,3)	7 (9,2)
- Vasculitis	3 (9,5)	1 (20)	1 (20)	1 (33,3)	6 (7,9)
- Systemic Sclerosis	8 (12,7)	0 (0)	0 (0)	0 (0)	8 (10,5)
- Myositis	6 (9,5)	0 (0)	0 (0)	0 (0)	6 (7,9)
- Polyarticular JIA	1 (1,6)	0 (0)	0 (0)	0 (0)	1 (1,3)
- Sarcoidosis	1 (1,6)	0 (0)	0 (0)	0 (0)	1(1,3)
Comorbidities, n %					
HTA	23 (36,5)	1 (20)	4 (80)	3 (100)	31 (40,8)
DM	8 (12,7)	0 (0)	0 (0)	1 (33,3)	9 (11,8)
DL	23 (36,5)	4 (80)	1 (20)	1 (33,3)	29 (38,2)
CV disease	7 (9,7)	0 (0)	1 (20)	3 (100)	11 (14,5)
COPD	8 (12,7)	0 (0)	1 (20)	3 (100)	12 (15,8)
Comorbidities, n %					
=2	11 (17,5)	1(20)	0(0)	0 (0)	12 (15,8)
≥3	10 (15,9)	0(0)	1(20)	3 (100)	14 (18,4)
Pulmonary involvement 2º to rheumatic disease, n %	17 (27)	1 (20)	4 (80)	2 (66,7)	24 (31,6)
Corticosteroids use, n %	35 (55,6)	2 (40)	2 (40)	3 (100)	42 (55,3)
cDMARDs, n %					
Methotrexate	16 (25,4)	4(80)	1 (20)	1 (33,3)	22 (28,9)
Hydroxychloroquine	2 (31,7)	1 (20)	0 (0)	0 (0)	3 (3,9)
Leflunomide	8 (12,7)	0 (0)	0 (0)	0 (0)	8 (10,5)
MMF	5 (7,9)	0 (0)	0 (0)	0 (0)	5 (6,6)
Azathioprine	4 (6,3)	0 (0)	0 (0)	0 (0)	4 (5,3)
Time from rituximab to COVID19, months median(range)	4 (0-13)	6 (4-9)	5 (2-12)	8 (0-9)	4 (0-13)

Table 1: Baseline Characteristics. RA= Rheumatoid arthritis, SLE= Systemic lupus erythematosus, SS= Sjögren's Syndrome, JIA= Juvenile idiopathic arthritis, HTA= Arterial hypertension, DM=Diabetes mellitus, DL= dislipemia, CV= cardiovascular, COPD= Chronic obstructive pulmonary disease, MMF= Mycophenolate mofetil.

First symptom reported was fever (30,8%) followed by cough (23,1%) and myalgia (15,4%). SARS-COV2 treatment and chest-x-ray findings are reported in table 2.

	Suspected infection patients, not confirmed (n=5)	Hospitalized with confirmed infection patients (n=5)	Deceased with Confirmed infection patients (n=3
SARS-COV-2 infection treatment, n %			
None	4 (80)	0 (0)	0 (0)
AZT	1 (20)	0 (0)	0 (0)
HCQ+AZT	0 (0)	1 (20)	1 (33,3)
HCQ+ L/R	0 (0)	2 (40)	2 (66,7)
HCQ+AZT+L/R	0 (0)	2 (40)	0 (0)
Corticosteroids, n %			
None	5 (100)	1 (20)	0 (0)
<1mg/kg/day	0 (0)	2 (40)	0 (0)
>1mg/kg/day	0 (0)	2(40)	1 (33,3)
Bolus	0 (0)	0 (0)	2 (66,7)
Tocilizumab, n %	0 (0)	0 (0)	1 (33,3)
Use of supplementary oxygen, n %	0 (0)	7 (87,5)	0 (0)
NIMV, n %	0 (0)	0 (0)	3 (100)
Chest x-ray, n %			
Normal	NA	0 (0)	0 (0)
Unilateral/unilobar pneumonia	NA	1 (20)	0 (0)
Bilateral Pneumonia	NA	4 (80)	3 (100)
PAFI <300, n %	NA	2 (40)	3 (100)

Table 2: SARS-COV-2 Treatment. AZT= Azithromycin, HCQ= Hydroxychloroquine, L/R= Lopinavir/Ritonavir, NIMV= non-invasive mechanical ventilation.

Severe SARS-COV2 infection was developed in 61,5% of patients (8/13), requiring hospitalization. Patients were hospitalized a median of 10 days [range (4-29)] and 62,5% (5/8) of patients experienced a clinical worsening after >10 days from symptoms onset. Inpatients had a higher rate of comorbidities: mainly HTA, COPD and CV disease. Up to 75% of inpatients had pulmonary involvement, being ILD the most frequent (4/6 66,7%). Respiratory insufficiency was present in 87,5% of hospitalized patients, 3/7 (42,9%) required non-invasive mechanical ventilation and 5/8 (62.5%) fulfilled ARDS criteria (PAFI< 300 and bilateral pneumonia).

Three out of eight (37,5%) patients died during hospitalization, all having 3 or more comorbidities. One longstanding RA patient with ILD complicated with a pulmonary embolism despite prophylactic heparin, a SLE patient with Evans Syndrome and COPD with chronic supplementary oxygen and an ANCA-vasculitis with renal and pulmonary involvement.

Conclusion: In our cohort of patients treated with Rituximab we found a high rate of hospitalization and death. Rituximab treatment might be taken into consideration as a risk factor for severe SARS-COV-2 infection in rheumatic pati ents.

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Abstract Number: 0642

COVID-19 Infection in Rheumatologic Patients on Treatment with Targeted Therapies

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: SARS COV 2 pandemic has been an issue which has challenged the health care systems around the world. Rheumatology has been involved in two ways: in the one hand, due to the use, in its treatment, of specific agents usually indicated in rheumatologic conditions and, on the other hand, the fear that our patients could be at higher risk due to the use of immunosuppressive agents.

The main objective of our study was to analyze the incidence of COVID infection in rheumatologic patients on treatment with targeted therapies (TT) (b and stDMARD) and to compare the incidence of such infection in the general population.

Methods: All patients with rheumatologic inflammatory conditions and COVID infection (confirmed by PCR of nasopharyngeal swab or serology) followed at three university referral centers from Basque Country (Spain) were identified. Patients on treatment with TT were selected. Characteristics of rheumatologic condition, type of TT and outcome of the infection were registered. Infection rates with the different TT were calculated and compared with the general population.

Results: Among 97 rheumatologic patients with COVID-19 infection 19 (12 with TNFi, 2 with anti-IL6 and 1 with abatacept, rituximab, ustekinumab, anakinra and baricitinib) were on treatment with TT at the COVID-19 infection diagnosis. Although, no significant differences were observed with those not taking TT with regards to severe disease outcome (hospital admission or death), the admission rate was 31.8% (greater than that commonly reported in general population ≈ 20%) and the mortality rate 13.8%, higher than that observed in our region (7.8%). In comparison with the general population of our region, the total infection rate for patients on TT was 4% vs 0.9%.

Specifically, in those taking TNFi the infection rate was of 3.5% and in those taking anti-IL6 of 3.1%.

Conclusion: Rheumatologic patients taking TT present higher rates of COVID infection than those seem in the general population (under the same criteria for infection definition). The admission rates observed in these patients suggest also a more severe course of the infection.

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Abstract Number: 0643

Use of Biologic Treatment and Risk to Be Admitted for COVID-19 Infection

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: To analyze the risk of admission for COVID19 infection and outcome of patients treated with b/tsDMARD from our center, to compare with all patients admitted for COVID-19 infection.

Methods: Records of the b/tsDMARD patients admitted for COVID-19 infection between March 8 and June 8, 2020 were analyzed retrospectively. Age, gender, and outcome of all patients admitted to our hospital for COVID19 infection on the same dates were collected. Chi-square, Student's t and Man-Whitney U tests were used when appropriate.

Results: 1,668 patients with IMID treated with b/tsDMARD were included. Median age 53.0 years (range 17-91), 52.4% women. Diagnoses and DMARD distribution are shown in tables 1 and 2. 21/1668 (1.3%; 4.2/100 patient-years) were admitted for severe COVID19 infection. Mortality ratio: 4/21 (19.0%). Median age of the admitted patients was higher: 61.0y (SD 14.7) vs 53.0y (SD 15.0); $p < 0.006$. Median age of deceased patients was also higher 69.5y (SD 20.3) vs 53.0y (SD 15.0); p: NS. Female gender had a worse prognosis trend: 52.4% of all group, 61.9% of those hospitalized, 75.0% of those who died. Females had a higher median age than men: 55.0y (SD 14.9) vs. 50.0y (SD 14.9); $p < 0.001$.

When comparing patients treated with DMARD admitted for COVID19 infection with all patients hospitalized for the same reason (2,684 patients), no differences were found neither in age (61.0y [SD 14.7] vs 60.0y [SD 19.0]; NS) nor gender (female: 61.9% vs 50.2%; NS). Mortality rate was not different: 4/21 (21.0%) vs 551/2684 (20.5%); p: NS, but patients treated with b/tsDMARD died at a younger age: 69.5y (SD 20.3) vs 81.5 (SD 11.3); p: NS.

Rheumatoid arthritis patients were admitted more frequently: (9/392 (2.3%) vs 12/1276 (0.9%); $p < 0.035$. And were older: median 62y (SD 13.5) vs 50.0y (SD 14.4); $p < 0.001$.

Patients treated with anti-TNF suffered less admissions: 6/1055 (0.6%) vs 15/613 (2.4%); p< 0.001 and were younger: median 51.0y (SD 15.0) vs 55.0y (SD 14.7); p < 0.001. Anti-TNF were less used in patients with rheumatoid arthritis 188/392 (48.0%) vs 867/1276 (67.9%); p< 0.001.

Table 1:

Disease	N (%)	Admitted	deaths
Rheumatoid arthritis	392 (23.5%)	9/392 (2.3%)	1
Spondylarthritis	277 (16.6%)	3/277 (1.1%)	1
Psoriatic arthritis	124 (7.4%)	1/124 (0.8%)	0
JIA	30 (1.8%)	0/30 (0.0%)	0
CTD	31 (1.9%)	1/31 (3.2%)	1
Vasculitis	20 (1.2%)	0/20 (0.0%)	0
IBD	582 (34.9%)	4/578 (0.7%)	1
Psoriasis	202 (12.1%)	3/202 (1.5%)	0
others	10 (0.6%)	0/10 (0.0%)	0
TOTAL	1,668 (100%)	21/1668 (1.3%)	4/21 (19.0%)

Table 2:

Treatment	N (%)	Admitted	deaths
Anti-TNF	1055 (63.2%)	6/1055 (0.6%)	2
Anti-CD20	79 (4.7%)	3/79 (3.8%)	1
Anti-IL6	96 (5.8%)	3/96 (3.1%)	0
CTLA4-Ig	44 (2.6%)	3/44 (6.8%)	1
Anti-IL17	92 (5.5%)	3/92 (3.3%)	0
Anti-IL12/23	143 (8.6%)	1/143 (0.7%)	0
Anti-integrin	79 (4.7%)	0/79 (0.0%)	0
JAK inhibitor	34 (2.0%)	1/34 (2.9%)	0
PDE4 inhibitor	32 (1.9%)	1/32 (3.1%)	0
Anti-IL23	14 (0.8%)	0/14 (0.0%)	0
TOTAL	1,668 (100%)	21/1668 (1.3%)	4/21 (19.0%)

Conclusion: It is reasonable that patients with inflammatory diseases treated with b/tsDMARD continue their treatment during the COVID19 epidemic. The different rates of hospitalization based on the diagnosis or DMARD may be due to comorbidity, confounding by indication and other bias. The study is not powerful enough to study these confounders.

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Abstract Number: 0644

Characterizations of Cytokine Storm Associated with COVID19

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SESSION INFORMATION
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Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: COVID-19, the name given to the clinical syndrome associated with the newly recognized virus SARS-CoV-2 has become pandemic with mortality estimated based on reports from China between 1-3% and complications among hospitalized patients leading to up to 15-25% admissions to the ICU. The clinical presentation includes both upper and lower respiratory tract infection, but patients may also be asymptomatic. The term "cytokine storm" calls up vivid images of an immune system gone awry and an inflammatory response flaring out of control. The term has captured the attention of the public and the scientific community alike and is increasingly being used in both the popular media and the scientific literature. Indeed, a few publications have indicated an important part of the complications in COVID19 are related to a cytokine storm.

Methods: Over 100 patients were hospitalized at Hadassah-Hebrew University Hospital, Jerusalem, in the recent 3 months with the diagnosis of COVID19. We summarized the clinical outcomes and their correlation (using NEWS2) to a cytokine storm at Hadassah. 30 different cytokines/chemokines/ hematopoietic growth factors were analyzed and compared to clinical manifestations. Serum cytokine/chemokine measurement was performed using the Luminex MAGPIX system (Luminex Corp, Texas, USA) and analyzed with Milliplex analysis software (Millipore MA, USA). The following cytokine/ chemokines were measured by sandwich ELISA kits: IL-18 (R&D), MCP-3 (R&D), TNFR1 (R&D), TREM-1 (R&D), procalcitonin (PCT) (IBL-America, MN, USA).

Results: We were able identify a correlation between disease severity (NEWS2), and 16 immunological biomarkers including IL6, TNF-alpha, IL18, IFN-a, IFN-b, IFN-g, IL-2R, IL-8, IL-10, TNF-R1, IL-1Ra, MCP-1, MIP-1 alpha, IP-10, IL8 and GM-CSF that have been associated with disease severity. IL-1 was not markedly elevated. The NEWS2 severity was strongly supported by a correlation to CRP, ferritin, d-dimer, and lymphopenia.

Conclusion: In this cohort of patients with COVID19, cytokine storm surprisingly did not include IL-1b and is typically characterized by both pro-inflammatory and anti-inflammatory cytokines/ chemokines / hematopoeitic growth factors. Typ1 1 IFN were not decreased upon development of the storm.

Disclosure: O. Perzon, None; **A. Abutbul**, None; **S. Sviri**, None; **D. Mevorach**, None.

Abstract Number: 0645

Prevalence and Clinical Features of COVID-19 in a Large Cohort of 199 Patients with Sarcoidosis

Anne-Claire Desbois[1], **Cindy Marques**[1], Leila Lefèvre[1], Serge Barmo[1], Camille Lorenzo[1], Mathilde Leclercq[1], Gaëlle Leroux[1], Chloé Comarmond[1], Catherine Chapelon-Abric[1], Fanny Domont[1], David Saadoun[1] and Patrice Cacoub[1], [1]AP-HP, Groupe Hospitalier Pitié-Salpêtrière, Department of Internal Medicine and Clinical Immunology, F-75013, Paris, France, Centre national de références Maladies Autoimmunes et systémiques rares et Maladies Autoinflammatoires rares, Paris, France

SESSION INFORMATION
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Session Title: Infection-related Rheumatic Disease Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate the prevalence, clinical features and outcomes of coronavirus disease 2019 (COVID-19) among sarcoidosis patients.

Methods: We retrospectively collected clinical features, treatments and outcomes of COVID-19 in a cohort of patients with sarcoidosis followed in a single tertiary university hospital.

Results: Among 199 sarcoidosis patients [mean age 58.8 (±14) years, 86 (43.2%) men], 26 (13%) were diagnosed with COVID-19 [definite (n=7), probable (n=12) and possible (n=7)]. Twenty-four out of 26 patients (92%) had at least one comorbidity, and 11/26 (42%) had two or more comorbidities. Demographic and clinical features of patients COVID-19 positive were similar to those of sarcoidosis patients COVID-19 negative. The administration of hydroxychloroquine or immunosuppressant was not associated with the occurrence or the severity of COVID-19. Four out of 26 (15.4%) COVID-19 positive patients required admission to hospital and two of them died. Hospitalized patients [mean age of 61 (±11.5) years] were receiving higher doses of long-term treatment with corticosteroids than non-hospitalized patients; 4/4 had pulmonary and 2/4 cardiac involvement of sarcoidosis, and all one or more comorbidity.

Conclusion: The prevalence of COVID-19 in sarcoidosis is slightly higher to that of the general population. Almost half of the COVID-19 positive patients have two or more comorbidities and about 15% present a severe course.

Disclosure: A. Desbois, None; **C. Marques**, None; **L. Lefèvre**, None; **S. Barmo**, None; **C. Lorenzo**, None; **M. Leclercq**, None; **G. Leroux**, None; **C. Comarmond**, None; **C. Chapelon-Abric**, None; **F. Domont**, None; **D. Saadoun**, None; **P. Cacoub**, None.

Abstract Number: 0646

"An Apple Pie a Day Does Not Keep the Doctor Away". Fictional Depictions of Gout in Contemporary Film and Television

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Views about gout as a self-inflicted condition of dietary excess can contribute to stigma and lead to ineffective management strategies. Fictional portrayals of illness and medical management in film and television may perpetuate cultural stereotypes about illness. The aim of this study is to analyse fictional depictions of gout in contemporary film and television.

Methods: We conducted a search for English language depictions of gout in film and television since 1990 using the Internet Movie Database (IMDb), other internet media databases, a google search and member contributions from the Gout, Hyperuricemia and Crystal-Associated Disease Network (G-CAN). Film and television shows depicting gout were analysed (n=44).

Results: Gout was used as a plot device to represent nobility or to explain the absence of characters from important events. Characters with gout were most often male and frequently portrayed as overweight and ageing. The most

Table 1. Fictional depictions of dietary associations with gout

Food/drink portrayed as triggers or causes of gout	Food/drink portrayed as protective or recommended for gout
Alcohol	Drink plenty of water
Apple pie	Fish
Bacon	Fruit and vegetables
Blood gravy	Omelette
Champagne	Salad
Chopped chicken liver	
Deli foods	
Drinkable cheese	
Garlic	
Lard cakes	
Liver balls	
Lung loaf	
Mackerel	
New York style food	
Organ meats: kidney, hearts, liver	
Pancakes	
Preserved fish like anchovies or herrings	
Red wine	
Rich food	
Skillet dripping	
Smothered chicken fried bacon	
Smothered chicken fried bananas	
Smothered pork chops	
Wine	

commonly depicted causes of gout were overindulgence of food and alcohol (61%), and numerous dietary causes of gout were portrayed (Table). Depictions of biological causes were infrequent (12%). Common management strategies described were change in diet (36%) and pain relief (32%), with only one mention of urate-lowering therapy (5%). The majority of films and television episodes depicted gout as humorous (59%) and embarrassing (50%).

Conclusion: In contemporary film and television, gout is portrayed as a humorous and embarrassing condition, caused by dietary indulgence. These negative depictions may reinforce inaccurate beliefs about the causes of gout and its management.

Disclosure: R. Murdoch, None; **C. Derksen**, None; **K. Petrie**, None; **N. Dalbeth**, AstraZeneca, 1, 2, Abbvie, 1, Arthrosi, 1, Dyve BioSciences, 1, Selecta, 1, Janssen, 1.

Abstract Number: 0647

Dual-energy CT versus Ultrasound, Alone or in Combination, for the Diagnosis of Gout: A Diagnostic Performance Study

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: To examine the diagnostic accuracy of dual-energy computed tomography (DECT) vs. ultrasound or their combination for the diagnosis of gout.

Methods: Using data from an outpatient rheumatology clinic, we examined the sensitivity, specificity, positive and negative predictive value (PPV, NPV) and area under the receiver operating characteristic (ROC) curve (AUC) of either modality or their combination for gout diagnosis. We used two standards: (1) demonstration of monosodium urate (MSU) crystals in synovial fluid (gold); and (2) 2015 American College of Rheumatology and European League Against Rheumatism (ACR-EULAR) classification criteria for gout, modified to exclude points based on DECT and ultrasound findings (silver), since these were test standards.

Results: Of the 147 patients who provided data, 48 had synovial fluid analysis performed (38 had MSU crystals and 10 were MSU-crystal negative). The mean age of 64.7 years (standard deviation, 14.3) and a mean symptom duration of 9.2 years. 113 (77%) met the silver standard, i.e. modified ACR-EULAR classification criteria for gout, and 34 (23%) did not.

Compared to the gold standard of synovial fluid MSU crystal positivity, the accuracy statistics for feet DECT, knee DECT, feet ultrasound double contour (DC) sign, combined feet DECT and feet ultrasound diagnosis (DC sign or tophus), and combined knee and feet DECT and ultrasound were: (1) sensitivity, 87%, 91%, 76%, 95%, 97%; (2) specificity, 100%, 87%, 60%, 60%, 50%; (3) PPV, 100%, 97%, 88%, 90%, 88%; (4) NPV, 67%, 75%, 40%, 70%, 83%; (5) AUC, 0.93, 0.89, 0.68, 0.77, and 0.74 (**Table 1**). These findings were replicated compared to the modified ACR-EULAR gout classification criteria, but with lower numbers (**Table 2**). Feet DECT, followed by knee DECT had the highest accuracy for the diagnosis of gout (**Figure 2**); ultrasound DC sign or the combination of DECT and ultrasound or across joints had lower accuracy.

Conclusion: In a single-center rheumatology clinic study, feet or knee DECT had the best overall accuracy statistics for the diagnosis of gout. DECT/ultrasound combination or multiple joint imaging may offer no additional increase in overall diagnostic accuracy.

Table 1. Diagnostic accuracy of DECT and ultrasound modalities for gout with MSU positivity as the gold standard (n=48)

Anatomical region	Imaging technique	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	AUC (95% CI)
Feet and ankles	US	84% (79-89%)	60% (53-67%)	89% (84-94%)	50% (43-57%)	0.72 (0.52-0.92)
	US – DC sign	76% (70-82%)	60% (53-67%)	88% (83-93%)	40% (33-47%)	0.68 (0.48-0.89)
	US – tophus	60% (53-67%)	90% (86-94%)	96% (93-99%)	37% (30-44%)	0.75 (0.60-0.91)
	DECT	87% (82-92%)	100% (100-100%)	100% (100-100%)	67% (60-74%)	0.93 (0.86-1.00)
	US and DECT combined (either diagnostic)	95% (92-98%)	60% (53-67%)	90% (86-94%)	75% (69-81%)	0.77 (0.58-0.97)
	US and DECT combined (both diagnostic)	76% (70-82%)	100% (100-100%)	100% (100-100%)	53% (46-60%)	0.88 (0.79-0.98)
Knees	US	58% (51-65%)	80% (86-94%)	92% (93-99%)	33% (29-43%)	0.66 (0.46-0.87)
	US – DC sign	46% (39-63%)	80% (86-94%)	89% (91-97%)	29% (29-43%)	0.62 (0.41-0.83)
	US – tophus	47% (40-54%)	100% (100-100%)	100% (100-100%)	33% (24-38%)	0.73 (0.57-0.89)
	DECT	91% (87-95%)	87% (81-91%)	97% (94-100%)	70% (60-74%)	0.89 (0.75-1.00)
	US and DECT combined (either diagnostic)	92% (88-96%)	60% (63-77%)	90% (88-96%)	67% (63-77%)	0.80 (0.75-1.00)
	US and DECT combined (both diagnostic)	53% (45-61%)	100% (100-100%)	100% (100-100%)	33% (23-37%)	0.76 (0.61-0.91)
Feet/ankles and knees combined	US	84% (79-89%)	60% (53-67%)	89% (84-94%)	50% (43-57%)	0.72 (0.52-0.92)
	US – DC sign	82% (76-88%)	60% (53-67%)	89% (84-94%)	46% (39-53%)	0.71 (0.51-0.90)
	US – tophus	60% (53-67%)	80% (74-86%)	92% (88-96%)	35% (28-42%)	0.70 (0.53-0.88)
	DECT	92% (88-96%)	90% (86-94%)	97% (95-99%)	75% (69-81%)	0.91 (0.79-1.00)
	US and DECT combined (either diagnostic)	97% (95-99%)	50% (43-57%)	88% (83-93%)	83% (78-88%)	0.74 (0.53-0.94)
	US and DECT combined (both diagnostic)	79% (73-85%)	100% (100-100%)	100% (100-100%)	56% (49-62%)	0.89 (0.81-0.98)

AUC = area under the receiver operating characteristic curve, CI = confidence interval, DC = double contour, DECT = dual-energy computed tomography, NPV = negative predictive value, PPV = positive predictive value, US = ultrasound

Table 1. Diagnostic accuracy of DECT and ultrasound modalities for gout with MSU positivity as the gold standard (n=48)

Table 2. Diagnostic accuracy of DECT and ultrasound modalities for gout with **modified ACR/EULAR gout classification criteria** as the silver standard (N=147)

Anatomical region	Imaging technique	Sensitivity (95% CI)	Specificity (95% CI)	PPV (95% CI)	NPV (95% CI)	AUC (95% CI)
Feet and ankles	US	85% (82-88%)	29% (25-33%)	80% (77-83%	37% (33-41%)	0.57 (0.46-0.69)
	US – DC sign	73% (69-77%)	35% (31-39%)	79% (76-82%)	28% (24-32%)	0.54 (0.43-0.65)
	US – tophus	62% (58-66%)	71% (67-75%)	87% (84-90%)	36% (32-40%)	0.66 (0.56-0.76)
	DECT	82% (79-85%)	76% (72-80%)	92% (90-94%)	56% (52-60%)	0.79 (0.70-0.89)
	US and DECT combined (either diagnostic)	98% (97-99%)	27% (23-31%)	82% (79-85%)	82% (79-85%)	0.62 (0.50-0.74)
	US and DECT combined (both diagnostic)	69% (65-73%)	79% (76-82%)	92% (90-94%)	43% (39-47%)	0.74 (0.65-0.83)
Knees	US	37% (33-41%)	85% (82-88%)	89% (86-92%)	29% (25-33%)	0.60 (0.49-0.70)
	US – DC sign	28% (24-32%0	88% (85-91%)	89% (86-92%)	27% (23-31%)	0.57 (0.46-0.68)
	US – tophus	26% (22-30%)	97% (96-98%)	97% (96-98%)	28% (24-32%)	0.60 (0.50-0.86)
	DECT	72% (68-76%)	80% (76-84%)	93% (91-95%)	44% (39-49%)	0.76 (0.66-0.86)
	US and DECT combined (either diagnostic)	73% (69-77%)	68% (64-72%)	88% (85-91%)	43% (39-47%)	0.71 (0.60-0.81)
	US and DECT combined (both diagnostic)	34% (30-38%)	97% (96-98%)	97% (96-98%)	29% (25-33%)	0.65 (0.55-0.75)
Feet/ankles and knees combined	US	89% (86-92%)	29% (25-33%)	81% (78-84%)	44% (40-48%)	0.59 (0.47-0.70)
	US – DC sign	78% (75-81%0	32% (28-36%)	79% (76-82%)	31% (27-35%)	0.55 (0.44-0.66)
	US – tophus	64% (60-68%)	68% (64-72%)	87% (84-90%)	36% (32-40%)	0.66 (0.55-0.76)
	DECT	85% (82-88%)	71% (67-75%)	91% (89-93%)	58% (54-62%)	0.78 (0.68-0.88))
	US and DECT combined (either diagnostic)	98% (97-99%)	23% (20-26%)	81% (78-84%)	80% (77-83%)	0.61 (0.49-0.73)
	US and DECT combined (both diagnostic)	75% (71-79%)	76% (72-80%)	91% (89-93%)	48% (44-52%)	0.76 (0.66-0.85)

AUC = area under the receiver operating characteristic curve, CI = confidence interval, DC = double contour, DECT = dual-energy computed tomography, NPV = negative predictive value, PPV = positive predictive value, US = ultrasound

Table 2. Diagnostic accuracy of DECT and ultrasound modalities for gout with modified ACR/EULAR gout classification criteria as the silver standard (N=147)

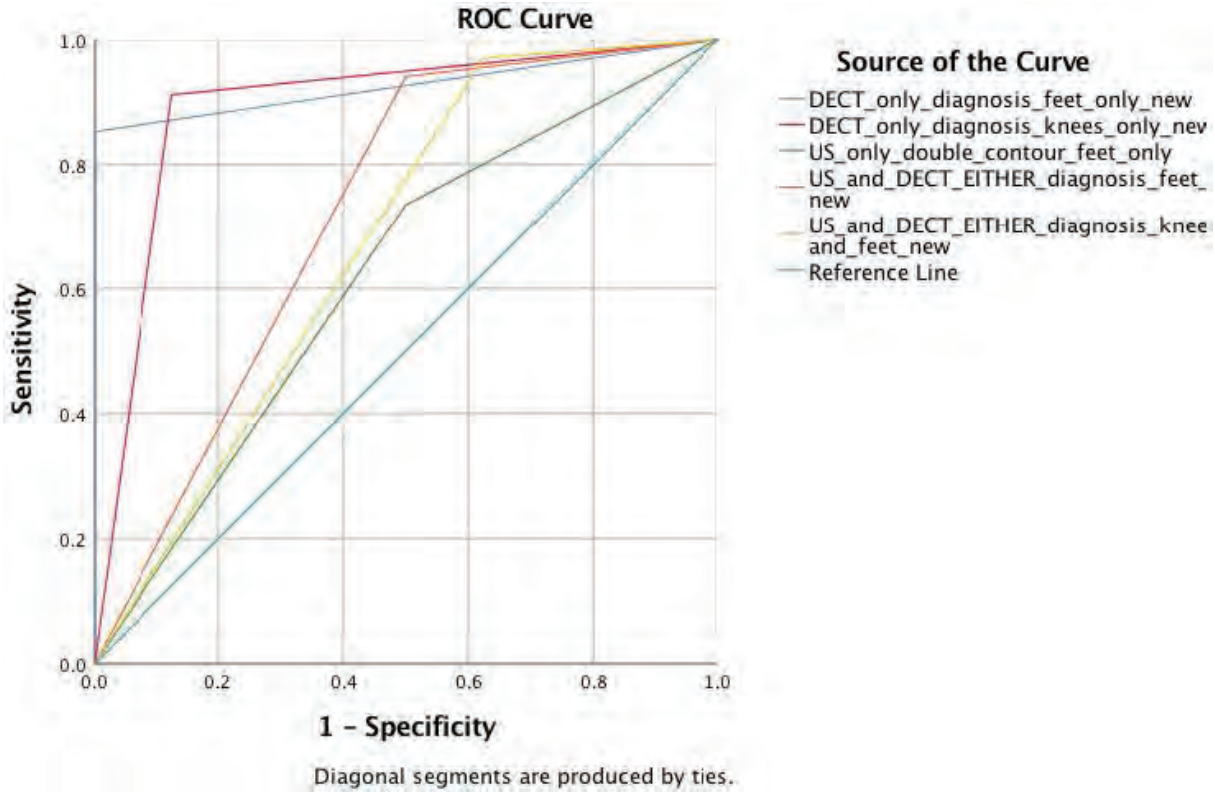

Figure 1. Area under the curve for the DECT and ultrasound modalities, alone or combined for feet/ankles, knees and both areas combined against the gold standard of synovial fluid monosodium urate (MSU) crystals Figure legend: The X-axis represents 1-specificity and Y-axis represents sensitivity. The null hypothesis is the diagonal line with an area of 0.50; the greater the area, the higher the overall accuracy of each modality. The area was highest for feet DECT (0.93) and lowest for feet ultrasound double contour (DC) sign (0.68).

Disclosure: J. Singh, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **F. Becce**, Horizon Therapeutics, 5; **J. Budzik**, None; **T. Pascart**, novartis, 8, Horizon, 2.

Abstract Number: 0648

Dual Energy CT Has Additional Prognostic Value over Clinical Measures in Gout Including Tophi: Best Evidence Synthesis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Dual Energy CT Scan (DECT) can detect monosodium urate crystals in joints and periarticular tissues. EULAR gout guidelines (Richette, 2020) recognized DECT's value in making a clinical diagnosis, when joint aspiration is difficult. DECT demonstrates crystal depositions in 50% of gout patients without tophi (Dalbeth 2017).

Since clinical tophi predict excess all-cause and cardiovascular mortality (Vincent 2017 & Perez-Ruiz 2013) it's possible that subclinical urate depositions on DECT could provide more prognostic information. To have prognostic value, DECT should be reliable and valid. Validity should be evident on measures of death, disability and distress (pain, gout flares). We used a best evidence synthesis framework to and summarize the evidence for DECT as a prognostic gout tool.

Methods: PUBMED and EMBASE were searched from initiation to December 2019, keywords (DECT, gout, tophaceous gout, chronic gout, monosodium urate crystals OR monosodium urate burden OR tophi OR monosodium urate volume OR flares OR pain OR distress OR death OR disability OR function). Titles, abstracts and full articles were identified and supplemented with a manual search of secondary sources. Data extraction was conducted by both authors; final data inclusion represents consensus.

Results: Of 344 eligible articles, 76 titles/abstracts met screening inclusion criteria (22%); a full manuscript was pulled. Thirty-nine articles informed this analysis (11.3%). Four systematic reviews showed high DECT reliability; intra-class correlations, 0.78-0.99. DECT has content validity. Dalbeth (2015) showed DECT and X-Rays correlate

Table 1. Construct Validity for DECT in Gout Patients

Stage of Gout / Consequence	Hyperuricemia	Clinical Gout: DECT positive, No tophi	Clinical Gout: DECT positive and Palpable tophi	Clinical Gout: DECT not measured, Palpable Tophi
Distress (Pain)	No Data	No Data	No Data	No Data
Distress (Flares)	Dalbeth N, et al. *A&R* 71(11), 2019	No Data	Dalbeth N, et al. *A&R* 71(10), 2019 Dalbeth N, et al. *ARD* 77(3), 2017 Pascart T, et al. *ART* 20(1), 2018	No Data
Disability	No Data	No Data	No Data	Dalbeth N, et al. *Rheumatology*. 46, 2007
Death	Perez-Ruiz F, et al. *ARD* 73(1), 2013	No Data	Gamala M, et al. *Clin Rheumatol* 37(7), 2017 Vincent Z, et al. *J Rheum* 44, 2017	Perez-Ruiz F, et al. *ARD* 73(1), 2013 Vincent Z, et al. *J Rheum* 44 (3), 2017

Table 2. Validity Articles: Authors, Journal and Year

Authors	Journal, Volume, Issue	Year
Araujo, E. G., Bayat, S., Petsch, C., et al.	*RMD Open*	2015
Dalbeth, N., Billington, K., Doyle, A., et al.	*Arthritis Rheumatol*, 71(10)	2019
Dalbeth, N., Nicolaou, S., Baumgartner S., et al.	*Ann Rheum Dis*, 77(3)	2017
Dalbeth, N., Aati, O., Kalluru, R., et al.	*Ann Rheum Dis*, 74(6)	2015
Dalbeth, N., Collis, J., Gregory, K., et al.	*Rheumatology*, 46(12)	2007
Gamala, M., Linn-Rasker, S. P., Nix, M., et al.	*Clinical Rheumatol*, 37(7)	2017
Pascart, T., Capon, B., Grandjean, A., et al.	*Arthritis Res and Therapy*, 20(1)	2018
Perez-Ruiz, F., Martínez-Indart, L., et al.	*Ann Rheum Dis,* 73(1)	2013
Richette, P., Doherty, M., Pascual, E., et al.	*Ann Rheum Dis*, 79(1)	2020
Vincent, Z., Gamble, G., House, M., et al.	*J Rheumatol,* 44(3)	2017

with feet erosion scores in tophaceous gout patients, r=0.70, p< 0.001. Vincent (2017) and Perez-Ruiz (2013) showed clinical tophi associated with increased mortality; no study has examined mortality against DECT volume. Dalbeth (2007) showed hand function, (Sollerman Hand Disability Score), correlated with tophi burden (r^2=0.59, p=0.024); no study has examined DECT volume with foot or knee function. Higher DECT volumes associate with gout flares. Dalbeth (2017) showed DECT associated with greater flare recall over 3 and 12 months (p< 0.01) in 152 patients. Pascart (2018) showed an odds ratio of 2.03 (95% CI: 1.15-4.38) for flares in 36 patients over 1 year; flared subjects had near doubled DECT knee volumes vs. non-flaring subjects (0.6 cm^3 vs 1.1 cm^3). Dalbeth (2019) correlated DECT volume and flares at 2 years, r=0.36, p< 0.001. Dalbeth (2017) showed DECT is abnormal in controlled and uncontrolled gout. DECT scans of hands/wrists, feet/ankles/Achilles, knees were abnormal in 47% of those with uric acid < 6.0 mg/dL and no palpable tophi; DECT was abnormal in 90% with uric acid >6.0 mg/dL and palpable tophi. DECT is sensitive to change with therapy. Araujo (2015) showed a 95% change in DECT volume in 152 patients receiving pegloticase. DECT volume decreased from 9.15 to 1.89 cm^3 over 12 months.

Conclusion: DECT imaging is highly reliable and has content validity in gout. There is evidence of added prognostic value with DECT, especially for future gout flares. DECT is sensitive to change with urate lowering therapy. Future studies should evaluate DECT's ability to predict mortality and disability in gout.

Disclosure: S. Stauder, None; **P. Peloso**, Horizon Therapeutics plc, 1, 2.

Abstract Number: 0649

A Multicenter, Open-Label, Efficacy and Safety Study of Pegloticase in Patients with Uncontrolled Gout Who Have Undergone Kidney Transplantation: Early Data Report

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout's high prevalence in kidney transplant (KT) recipients has been associated with heavy residual urate burden, decreased urate excretion related to reduced renal function, and high calcineurin inhibitor use in this population. The management of gout can be particularly challenging in KT patients due to decreased urate lowering therapy (ULT) renal clearance and drug-drug interactions. Pegloticase (pegylated recombinant uricase) is a treatment indicated for uncontrolled gout and tophi burden that rapidly metabolizes uric acid to allantoin which is readily cleared from the circulation. The use of pegloticase with immunomodulation therapy has been rising in order to reduce anti-drug antibody generation that decreases treatment efficacy and can increase risk of infusion reactions (IRs). Immunomodulator/pegloticase co-therapy markedly improves treatment responder rates[1-3]. However, only a few case reports[4,5] of pegloticase use in solid organ transplant patients have been published and phase 3 pegloticase

Table. Serum uric acid and kidney function parameters in kidney transplant recipients undergoing pegloticase treatment for uncontrolled gout

Patient	sUA (mg/dL)			eGFR (mL/min/1.73m^2)			UACR	
	Last Visit Prior to Data Cut	Baseline	Last Value	Last Visit with eGFR and UACR values	Baseline	Last Value	Baseline	Last Value
1	Week 24	9.1	<1	Week 24	61.2	51.0	376	56
2†*	Week 20	7.9	<1	Week 14	41.6	45.5	56	40
3*	Week 21	9.3	<1	Week 14	41.8	49.7	2196	1406
4†	Week 2	10.9	<1	Week 2	41.1	34.9	305	572
5*	Week 6	9.7	<1	Week 6	40.1	40.1	22	20
6*	Week 6	10.9	<1	Week 6	40.8	32.7	317	407
7*	Week 4	12.2	<1	Week 2	20.4	23.2	407	342

*ongoing pegloticase therapy. †experienced an SAE (Patient 1, SAE of stomach ulcer deemed unrelated to pegloticase; Patient 4, SAE of cellulitis deemed unrelated to pegloticase).

trials excluded organ transplant recipients. We conducted the PROTECT trial (NCT04087720) to examine pegloticase use in KT recipients with uncontrolled gout.

Methods: We are examining pegloticase treatment (12 biweekly 8 mg infusions over 24 weeks) in adult KT recipients (KT >1 year ago, eGFR ≥15 mL/min/1.73m^2) with uncontrolled gout (serum uric acid [sUA] ≥7 mg/dL, ULT contraindication/inefficacy, and either tophi, chronic gouty arthritis, or ≥2 flares in past year). The primary endpoint is the proportion of pegloticase responders (sUA < 6 mg/dL for ≥80% of time during Month 6). We are also examining sUA levels, eGFR, urine albumin-to-creatinine ratio (UACR), and health assessment questionnaire (HAQ) pain scores.

Results: At the time of this analysis (April 30, 2020), 7 patients who had undergone KT 15.3 ± 5.0 years earlier had enrolled (age: 52.0 ± 11.2 years, sUA: 10.0 ± 1.4 mg/dL, gout duration: 5.9 ± 4.3 years; COVID-19 reduced enrollment). All patients were on stable doses of ≥2 immunosuppressants. 1 patient had completed the 24-week treatment, 5 were in treatment, and 1 had discontinued early due to COVID-19 (non-infection) reasons (Table); the number of infusions received ranged from 2 to 12. In the 5 ongoing patients, all post Day 1 central lab sUA levels were < 1 mg/dL, indicative of treatment response. No notable changes in eGFR were observed; 2 patients with baseline albuminuria >300 mg/g showed >35% reduction in UACR by week 14. HAQ pain (0 to 100 VAS) decreased by 33.8 ± 2.7 (n=3) from baseline at week 20. 2 patients experienced flares; no IRs occurred. 2 SAEs (stomach ulcer, cellulitis), deemed unrelated to pegloticase, were reported.

Conclusion: Early findings of the ongoing PROTECT clinical trial suggest that pegloticase can safely and effectively be used in KT recipients to treat uncontrolled/refractory gout. Further efficacy and safety data in the KT population are pending.

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Disclosure: A. Abdellatif, Horizon Therapeutics plc, 5, 8; **L. Zhao**, Horizon Therapeutics plc, 1, 2; **P. Peloso**, Horizon Therapeutics plc, 1, 2; **K. Cherny**, Horizon Therapeutics plc, 1, 2; **B. Marder**, Horizon Therapeutics plc, 1, 2; **J. Scandling**, Horizon Therapeutics, 5; **K. Saag**, Arthrosi, 5, Horizon Therapeutics plc, 2, 5, Atom Bioscience, 5, LG Pharma, 5, Takeda, 5, Mallinkrodt, 5, SOBI, 2, 5, Shanton, 2.

Abstract Number: 0650

Risk of Vertebral Fractures at Lateral Chest Radiographies in Patients with Gout

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
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Background/Purpose: Osteoporosis causes significant morbidity and mortality through the development of fragility fractures, including vertebral fractures (VF). Patients with gout may show an increased risk of osteoporotic fractures, as the urate crystals-led inflammatory state has been associated with an accelerated bone resorption, though data to date is conflicting. This field study aims to evaluate the risk of osteoporotic VF associated with gout.

Methods: Patients admitted for cardiovascular events were screened for gout by face-to-face interview following 2015 ACR/EULAR criteria; 40 gout patients, out of the 266 assessed (15%), were identified. Participants with available lateral view of chest radiography (at admission or in the previous six months) were selected for the present analysis (n=126). Two observers, blinded to clinical data and trained by web-based program on VF assessment by the International Osteoporosis Foundation, simultaneously reviewed the radiographies. Presence of VF (defined as height loss ≥20%), number and severity (by Genant semi-quantitative scale), were registered. Chi-squared and Mann-Whitney's U tests were used for group comparisons. To analyze the relation between gout and presence of VF, odds ratios (OR) with 95% confidence interval (95%CI) were calculated, adjusting for age, female gender and chronic kidney disease by multiple logistic regression.

Results: Chest radiographies from 126 participants were analyzed, 21 of them (16.67%) identified as gout patients. Prevalence of VF in the whole sample was 14.3% (n=18). Results are shown in Table 1. Presence of VF was more frequent in gout patients, while there were no differences in number and severity. Across subgroups, VF numerically predominated in gout at lower age tertile (≤64.0 years: 50.0% vs 5.5%; p=0.184) and in males (23.5% vs 4.1%; p=0.022), compared to controls.

The OR for the presence of VF in gout was 3.10 (95%CI 1.01-9.52), persisting the association after multivariate adjustment (adjusted OR 5.21, 95%CI 1.32-20.61).

Table 1. Vertebral fractures and comparison across subgroups (#).

Conclusion: An independent association between gout and vertebral fractures at lateral chest radiographies was confirmed in patients with a cardiovascular event. Further studies should confirm this finding in other settings.

Disclosure: M. Ferrández-Jiménez, None; **I. Calabuig**, None; **M. Peral**, None; **M. Gómez-Garberí**, None; **M. Andrés**, Grünenthal, 2, 8, Horizon, 8, Menarini, 8.

Abstract Number: 0651

Readmission Risk and Quality of Care in Patients Presenting to the Emergency Department with Gout Flares

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is the most common inflammatory arthritis and its economic burden is substantial, with estimates for the overall cost exceeding $20 billion (US) annually. Contributing to the economic burden are hospital admissions and iatrogenic events associated with pharmacotherapy. Identification of modifiable risk factors would be an important contribution to clinical practice.

The purpose of this study was to identify opportunities for enhancing gout care in patients presenting to the Emergency Department (ED) with gout flares.

Methods: This retrospective cohort study used data from electronic medical records (EMR) at a large community hospital. All consecutive patients visiting the medical center ED with a primary diagnosis of gout from 1/1/2016 to 7/1/2019 were included. Patients were then followed for 90 days to determine whether they were readmitted to the ED for any reason. A chart review identified whether they were on appropriate medications in terms of gout flare management. All data were summarized using descriptive statistics. A multiple logistic regression was constructed to identify risk factors for ED utilization within 90 days of the index visit.

Results: A total of 214 patients were included in the analysis. Most patients were male (79%), mean age was 59.4 ± 15.6 years, and mean Charlson comorbidity index was 0.5 ± 1.14. The most common medications prescribed during the ED visit included NSAIDs (41.6%), opioids (28%), corticosteroids (26.6%), and colchicine (21%). Allopurinol and febuxostat were initiated in the ED in 4.7% and 0.9%, respectively. Discharge medications for the management of gout included NSAIDs (37%), corticosteroids (34.6%), opioids (23.8%), colchicine (14%), febuxostat (7%), and allopurinol (6.5%). Of the patients sent home with an opioid, 40% were newly prescribed. An anti-inflammatory medication was not prescribed in 29.6% of patients discharged from the ED. Readmission within 90 days was recorded in 16.8% of patients. Of these readmissions, 33.3% were gout-related and 11.1% were cardiac related.

After adjusting for age and comorbidity index, patients receiving colchicine were 2.8 times more likely (OR, 2.81; 95% CI, 1.12 to 7.02; p=0.027) to return to the ED within 90 days. The most common cause of readmission in this subset was gout-related (54.5%).

Conclusion: Approximately 30% of patients were discharged from the ED without an anti-inflammatory medication, whereas initiation of urate lowering therapy was rare. Opiates were used frequently, but the indication was uncertain. Only 5.6% of subjects revisited the ED for gout-related diagnoses in the subsequent 3 months. Colchicine prescription was associated with an increased risk of gout-related ED utilization within 90 days. Treatment of gout in the ED is sub-optimal and often does not follow established guidelines.

Disclosure: L. Brunetti, CSL Behring, 2, Astellas Pharma, 2, Horizon Blue Cross Blue Shield of New Jersey, 5; **J. Vekaria**, None; **P. Lipsky**, Horizon Therapeutics, 3; **N. Schlesinger**, Johnson and Johnson, 5, Horizon, 5, IFM, 5, Pfizer, 2, AMGEN, 2.

Abstract Number: 0652

Changes in Serum Urate, in the First 6-months of Initiation or Change of Urate-Lowering Therapy, Associate with Immediate Health-Related Quality of Life Outcomes in People with Gout

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SESSION INFORMATION
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Background/Purpose: Few studies, if any, have found association of the biochemical cause of gout (high serum urate) with functional limitation and health-related quality of life (HRQoL) and productivity decrements in gout. We examined the associations of changes in serum urate in the immediate term with HRQoL using data from five intervention clinical trials of urate-lowering therapies (ULT).

Methods: Data were obtained from the following trials: Combining Lesinurad With Allopurinol in Inadequate Responders (CLEAR1 and CLEAR2; 1217 participants, 12 months); Long-term Allopurinol Safety Study Evaluating Outcomes in Gout (LASSO;1735 participants, 6 months); Lesinurad Monotherapy in Gout Subjects Intolerant to Xanthine Oxidase Inhibitors (LIGHT; 214 participants, 6 months; Combination Treatment Study in Subjects With Tophaceous Gout With Lesinurad and Febuxostat (CRYSTAL; 330 participants, 12 months). We excluded participants in LASSO who had also taken part in CLEAR or LIGHT (n=154). HRQoL measures were assessed at baseline and at 3 monthly intervals (LASSO only at baseline and 6 months), serum urate was measured monthly in each trial.

Primary outcome measures were physical (PCS) and mental (MCS) health functioning taken using the respective component summary scores from Short-form 36 (SF-36) data, Health Assessment Questionnaire Disability Index

Table1: Associations of absolute change in urate in preceding month with patient reported outcomes in first six months with initiation or change of urate-lowering therapy

	Urate (mg/dL)		Absolute urate change (mg/dL)		
HRQoL	Beta	95% CI	Beta	95% CI	N subjects (N observations)
PCS	-0.334	-0.45 - -0.22	-0.120	-0.26 - -0.08	3295 (7231)
MCS	-0.240	-0.35 - -0.13	-0.345	-0.49 - -0.20	3295 (7231)
HAQ-DI Score	-0.003	-0.008 - 0.002	0.013	0.007 - 0.019	3295 (7251)
SDS Score	0.335	0.23 - 0.44	0.175	0.04 - 0.31	3199 (6484)
PGA	0.792	0.49 - 1.10	0.500	0.10 - 0.90	3302 (8488)
Pain	0.828	0.38 - 1.28	0.666	0.17 - 1.17	1731 (4604)

PHYS and MENT negative scores indicate increased disability. HAQ-DI, SDS, PGA and pain positive scores indicate increased disability. HRQoL, health-related quality of life measure; CI, confidence interval.

Table 2: Associations of absolute change in urate in preceding month with patient reported outcomes, stratified into increasing and decreasing observations, in first six months with initiation or change of urate-lowering therapy

	Decreasing urate (mg/dL)			Increasing urate (mg/dL)		
HRQoL	Beta	95% CI	N observations	Beta	95% CI	N observations
PCS	-0.266	-0.47 - -0.07	4013	0.291	-0.09 - 0.68	2902
MCS	-0.375	-0.57 - -0.18	4013	-0.186	-0.56 - 0.19	2902
HAQ-DI Score	0.019	0.01 - 0.029	4023	0.000	-0.08 - 0.02	2910
SDS Score	0.323	0.14 - 0.51	3589	-0.113	-0.46 - 0.23	2623
PGA	0.954	0.41 - 1.50	4679	-0.714	-1.67 - 0.24	3433
Pain	1.226	0.56 - 1.89	2681	-0.419	-1.72 - 0.88	1722

PHYS and MENT negative scores indicate increased disability. HAQ-DI, SDS, PGA and pain positive scores indicate increased disability. HRQoL, health-related quality of life measure; CI, confidence interval.

Score (HAQ-DI), Sheehan Disability Scale (SDS) score, Patient Global Assessment (PGA), and pain in the last week. For each outcome, we investigated the underlying distribution and then a series of corresponding random intercept and slope (month) generalized linear mixed models were used to test the adjusted effect of the fixed predictors on the outcome across all timepoints over the first six month. Serum urate, change in urate in the last month, number of flare-affected days in the last month, baseline BMI, age, number of comorbidities, sex, ethnicity, trial and treatment, and tophi status were modelled as fixed effects. Subject, and the month of trial were modelled as random effects.

Results: Higher current serum urate correlated with reduced physical and mental health functioning, and increased disability and pain but not with HAQ-DI Score (Table 1). However absolute change in serum urate levels associated with poorer outcomes on the HAQ-DI scale (β (95% CI) = 0.013 (0.007 - 0.019)) and the five other measures. Observations were stratified into those which followed a month of serum urate reduction (n = 4023) or increase (n = 2910) (Table 2). Reduction of serum urate levels was associated with poorer outcomes in all six measures. Timepoints with increasing serum urate levels showed no significant associations with the outcomes.

Conclusion: High serum urate levels associate with poorer HRQoL outcomes. Importantly, very recent fluctuations in serum urate levels associate with reduced HRQoL, primarily driven by effects of reduction in serum urate. Clinical emphasis on maintaining stable and reduced concentrations of serum urate may improve patient reported functional outcomes. This study provides further support for serum urate as central to disease pathophysiology and its impact on an individual's health.

Disclosure: R. Topless, None; **T. Merriman**, None; **S. Noorbaloochi**, None; **J. Singh**, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1.

Abstract Number: 0653

Nutrient Content of Gout Flare Trigger Foods

Tanya Major[1], Ruth Topless[1], Elsa Sanchez-Lopez[2], Jennie Harré Hindmarsh[3], Lisa Stamp[4], Nicola Dalbeth[5], Monica Guma[6], Robert Terkeltaub[7] and **Tony Merriman**[1], [1]University of Otago, Dunedin, New Zealand, [2]University of California San Diego, San Diego, CA, [3]Ngāti Porou Hauora, Te Puia Springs, New Zealand, [4]University of Otago Christchurch, Christchurch, New Zealand, [5]University of Auckland, Auckland, New Zealand, [6]University of California San Diego, La Jolla, CA, [7]VA/UCSD, San Diego, CA

SESSION INFORMATION
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Session Title: Metabolic & Crystal Arthropathies Poster
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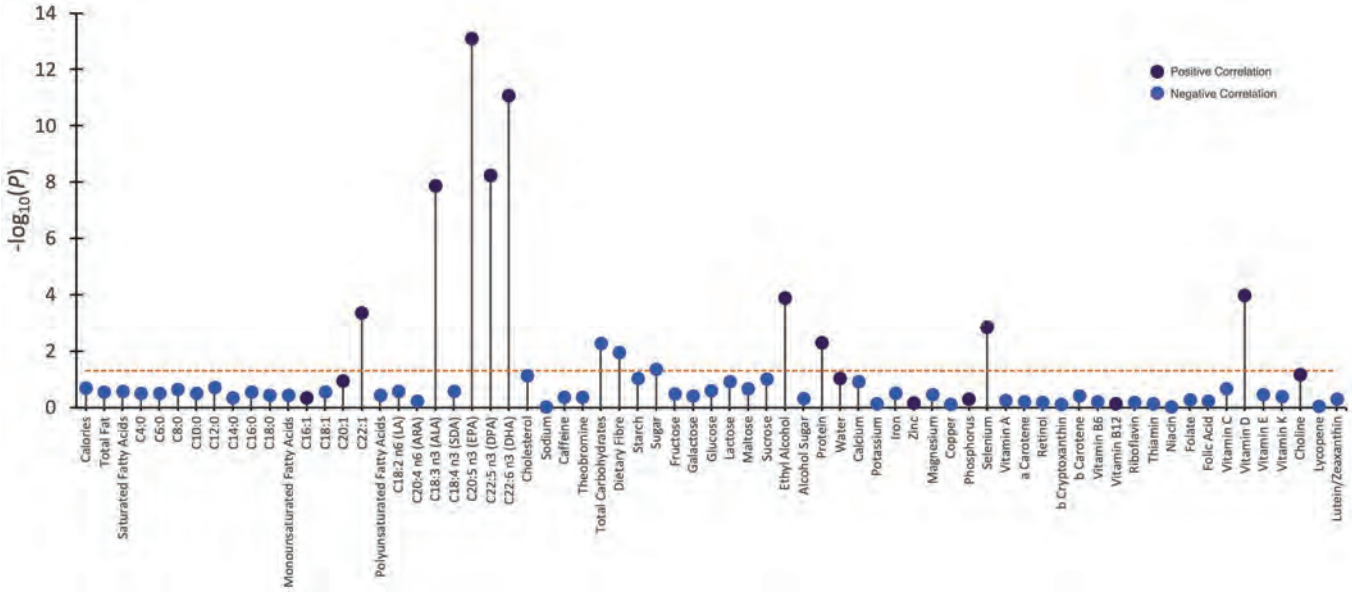
Background/Purpose: A wide variety of foods are reported by patients to be triggers of gout flares. Some of these foods have been associated with serum urate levels and onset of gout, and their possible mechanism for involvement in gout explained through their high purine content and subsequent influence on the purine metabolism pathway (e.g. red meat and seafood). However, not all reported gout flare trigger foods have a high purine content and acute increases in serum urate are not thought to be the primary mechanism leading to inflammation. This study aimed to assess which nutrients are commonly found within gout flare trigger foods.

Methods: Participants with gout recruited across Aotearoa/New Zealand (n = 2,106) were asked to list their dietary gout flare triggers in an open-text format. Their answers were aligned with a list of 115 foods commonly included in food frequency questionnaire forms. The nutrient content (per 100 g) of these 115 foods was estimated using the USDA Food Central database and the Cronometer website (https://cronometer.com; 70 different nutrients, vitamins, and minerals). The proportion of participants who included each food as a gout flare trigger was calculated and this proportion was associated with the estimated nutrient content of these foods using a linear regression.

Results: Nine of the food nutrients analysed were more likely to be present within foods listed as gout flare triggers; protein (β = 4.28 g, P = 0.005), vitamin D (β = 45.70 ug, P = 1.1x10-4), ethyl alcohol (β = 12.60 g, P = 1.34x10-4), selenium (β = 2.43 ug, P = 0.001), the monounsaturated fatty acid C22:1 (β = 1.40 mg, P = 4.5x10-4), and four omega 3 polyunsaturated fatty acids C18:4 (β = 7.97 mg, P = 1.4x10-8), C20:5 (β = 2.50 mg, P = 8.0x10-14), C22:5 (β = 8.84 mg, P = 5.7x10-9), and C22:6 (β = 1.30 mg, P = 8.4x10-12). Three of the food nutrients analysed were less likely to be



present within foods listed as gout flare triggers by participants with gout. These three nutrients were; carbohydrates (β = -1.39 g, *P* = 0.005), dietary fibre (β = -10.08 g, *P* = 0.011), and sugars (all types combined; β = -1.48 g, *P* = 0.044).

Conclusion: This study identified nine nutrients commonly found in foods reported by people with gout to trigger their flares. Another three nutrients were less likely to be found in gout flare trigger foods. The link between increased vitamin D and selenium content of foods listed as gout flare triggers is a novel finding; as is the reduced carbohydrate, dietary fibre, and sugar content of these foods. The association of ethyl alcohol, several fatty acids, and protein (a proxy for purine-content) aligns with current knowledge of pathways involved in gout flare onset and reinforce the robustness of our analysis methodology. This work provides greater insight into the mechanisms involved in the triggering of a gout flare.

Correlations between 70 different nutrients, vitamins and minerals and frequency of food items being listed as gout flare triggers by participants. Purple points indicate positive correlations, blue points indicate negative correlations. Points above the orange dashed line are significant at P<0.05.

Disclosure: T. Major, None; **R. Topless**, None; **E. Sanchez-Lopez**, None; **J. Harré Hindmarsh**, None; **L. Stamp**, None; **N. Dalbeth**, AstraZeneca, 1, 2, Abbvie, 1, Arthrosi, 1, Dyve BioSciences, 1, Selecta, 1, Janssen, 1; **M. Guma**, None; **R. Terkeltaub**, SOBI, 5, Selecta, 5, Horizon, 5, Astra Zeneca, 2, Genentech, 5; **T. Merriman**, None.

Abstract Number: 0654

The Effects of Dietary Macronutrients on Serum Urate: A Secondary Analysis of the OmniHeart Trial

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SESSION INFORMATION

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Session Title: Metabolic & Crystal Arthropathies Poster

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Background/Purpose: Diet is a significant determinant of hyperuricemia and risk for gout. Dietary recommendations to prevent gout emphasize reducing purine intake; however, low-purine diets are often ineffective in preventing gout and have unknown effects on cardiovascular disease risk factors, such as hypertension and hyperlipidemia, which often accompany gout. Meanwhile, studies suggest that the DASH diet reduces serum urate while also lowering blood

Table 1. Baseline Change in Serum Urate, mg/dL (N=163)

	Mean, 95% CI	Mean Change from Baseline, 95% CI	*P*
Baseline	5.1 (4.9, 5.3)	-	-
Carbohydrate Diet			
4-week	5.1 (4.9, 5.3)	0.02 (-0.09, 0.12)	0.72
6-week	5.0 (4.9, 5.2)	-0.03 (-0.15, 0.09)	0.63
Combined 4-week and 6-week measures	5.1 (4.9, 5.2)	-0.00 (-0.11, 0.10)	0.93
Protein Diet			
4-week	5.0 (4.8, 5.2)	-0.08 (-0.19, 0.03)	0.16
6-week	4.9 (4.7, 5.1)	**-0.16 (-0.28, -0.05)**	**0.006**
Combined 4-week and 6-week measures	4.9 (4.8, 5.1)	**-0.12 (-0.23, -0.02)**	**0.02**
Unsaturated Fat Diet			
4-week	5.1 (4.9, 5.3)	0.01 (-0.10, 0.12)	0.85
6-week	5.1 (4.9, 5.2)	-0.01 (-0.11, 0.09)	0.81
Combined 4-week and 6-week measures	5.1 (4.9, 5.2)	-0.00 (-0.10, 0.10)	0.98

Table 2. Mean difference between diets (combined 4-week and 6-week measures), overall and stratified by baseline serum urate

	Mean Difference (95% CI)	*P*		Mean Difference (95% CI)	*P*		Mean Difference (95% CI)	*P*	*P*-interaction
Overall			**Baseline SUA < 6 mg/dL, N=134**			**Baseline SUA ≥ 6 mg/dL, N=29**			
CARB vs baseline	0.00 (-0.11, 0.10)	0.93	**CARB vs baseline**	0.08 (-0.02, 0.18)	0.126	**CARB vs baseline**	**-0.39 (-0.68, -0.10)**	**0.01**	**0.003**
PROT vs baseline	**-0.12 (-0.23, -0.02)**	**0.02**	**PROT vs baseline**	-0.04 (-0.15, 0.07)	0.508	**PROT vs baseline**	**-0.52 (-0.79, -0.24)**	**< 0.001**	**0.001**
UNSAT vs baseline	0.00 (-0.10, 0.10)	0.98	**UNSAT vs baseline**	0.08 (-0.02, 0.18)	0.106	**UNSAT vs baseline**	**-0.39 (-0.62, -0.16)**	**0.001**	**< 0.001**
PROT vs CARB	**-0.12 (-0.20, -0.04)**	**0.005**	**PROT vs CARB**	**-0.12 (-0.20, -0.03)**	**0.007**	**PROT vs CARB**	-0.13 (-0.38, 0.13)	0.33	0.931
PROT vs UNSAT	**-0.12 (-0.20, -0.05)**	**0.001**	**PROT vs UNSAT**	**-0.12 (-0.20, -0.05)**	**0.00**	**PROT vs UNSAT**	-0.13 (-0.36, 0.11)	0.29	0.962
CARB vs UNSAT	0.00 (-0.07, 0.07)	0.92	**CARB vs UNSAT**	0.00 (-0.07, 0.06)	0.89	**CARB vs UNSAT**	0.00 (-0.23, 0.23)	1.00	0.962

Abbreviations: CARB represents carbohydrate diet; PROT represents protein diet; UNSAT represents unsaturated fat diet; SUA represents serum urate

pressure and lipids. Whether DASH-pattern diets that emphasize different macronutrient proportions might enhance serum urate reduction is not known.

Methods: We conducted a secondary analysis of the Optimal Macronutrient Intake Trial to Prevent Heart Disease (OmniHeart) feeding study, a 3-arm, crossover design, randomized trial of 191 adults with prehypertension or stage I hypertension (defined at the time of the trial as systolic blood pressure 120-159 mm Hg or diastolic blood pressure 80-99 mm Hg) who were not on antihypertensive medications. Participants were randomized to one of three DASH-pattern diets that emphasized either carbohydrates (CARB), protein (PROT), or unsaturated fat (UNSAT). Calories were adjusted as needed to maintain body weight throughout the study. We compared the effects of these diets on serum urate at weeks 4 and 6 of each feeding period.

Results: A total of 163 participants were included in the final analysis (mean age 53.5 yrs, 45% women, 55% black). The mean BMI was 30.2 kg/m^2 and 56.7% had hypertension. The PROT diet reduced serum urate from baseline at the end of the 6-week feeding period (-0.16 mg/dL; 95% CI: -0.28, -0.05; P = 0.006) (**Table 1**). In contrast, neither the CARB diet (-0.03 mg/dL; 95% CI: -0.15, 0.09; P = 0.63) or the UNSAT diet (-0.01 mg/dL; 95% CI: -0.11, 0.09; P = 0.81) reduced serum urate. Compared with the CARB and UNSAT diets, the PROT diet lowered serum urate by 0.12 mg/dL (95% CI: -0.20, -0.04; P = 0.005) and 0.12 mg/dL (95% CI: -0.20, -0.05; P = 0.001), respectively (**Table 2**). When stratified by baseline serum urate ≥ 6 mg/dL (n = 29), all diets significantly reduced serum urate from baseline (-0.39 to -0.52 mg/dL) and there was no significant difference between diets.

Conclusion: A DASH-pattern diet emphasizing plant-based protein lowered serum urate compared with those emphasizing carbohydrates or unsaturated fat. These findings suggest that a DASH-pattern diet emphasizing plant-based protein may enhance serum urate reduction. Overall, a DASH-pattern diet emphasizing plant-based protein has the potential to lower serum urate while also improving hypertension and hyperlipidemia. A definitive trial to test the ability of a DASH-pattern diet emphasizing plant-based protein to lower the incidence of gout is warranted.

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Abstract Number: 0655

Weight Loss as Treatment for Gout in Patients with Concomitant Obesity: A Proof-of-Concept Randomized Controlled Trial

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SESSION INFORMATION
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Background/Purpose: Despite scarce evidence regarding the effects of weight loss in gout[1], international guidelines recommend dietary advice and weight loss as a core management strategy in people with gout and concomitant obesity. We explored whether there are potential clinical benefits associated with intensive weight loss in obese individuals with gout.

Objectives: To compare in a proof-of-concept randomized trial the effect of an intensive, 16-weeks weight loss program (full meal replacement with hypocaloric products and weekly visits to a dietician), relative to a dietary advised control group (ordinary food and visits to a dietician only at baseline and at week 8), on primarily changes in body weight and secondarily serum urate, fatigue and pain in people with gout and concomitant obesity.

Methods: Participants were randomized using permuted blocks and stratification (i.e. sex (male vs. female), obesity (BMI< 40kg/m^2 vs BMI≥40kg/m^2), serum urate (< 6mg/dL vs ≥6mg/dL)). he primary outcome was change in body weight at 16 weeks, analyzed using repeated measures mixed models. According to the Statistical Analysis Plan, the key secondary outcomes were changes in serum urate, VAS gout pain, and VAS fatigue after 16 weeks. ClinicalTrials.gov (NCT03664167).

Results: Overall, 61 participants were enrolled and randomized, of whom 29 were assigned to intensive weight loss and 32 to dietary control. The participants had an average age of 60.3 (SD, 9.9) years, average BMI of 35.6 (SD, 5.0) kg/m^2 and 59 (97%) were men. There was a statistically and clinically significant difference in the change in body weight from baseline to 16 weeks between the dietary and control groups (least squares means: -15.4 kg and -7.7 kg, respectively; difference: -7.7 kg (95%CI -10.9 to -4.7, p< 0.001). Mean changes in serum urate levels at the 16 weeks visit were -0.6 mg/dL and -0.3 mg/dL, respectively, with a difference between groups of -0.3 mg/dL (95%CI -0.9 to 0.3, p=0.744). The corresponding mean change in VAS fatigue was -17.4 mm compared to -8.6 mm, with a group difference of -8.8 mm (95%CI -25.5 to 7.9). Mean change in VAS pain corresponded to -2.5 mm compared to -12.5 mm, with a group difference of 9.9 mm (95% CI -11.1 to 31.0).

Conclusion: An intensive dietary intervention can effectively lower body weight in people with gout and concomitant obesity. Although absolute differences were present, we were not able to reject the null hypotheses for serum urate, fatigue, and pain in this proof-of-concept study with a small sample size

[1]Nielsen SM, Bartels EM, Henriksen M, et al. Weight loss for overweight and obese individuals with gout: a systematic review of longitudinal studies. *Ann Rheum Dis*. 2017. https://doi.org/10.1136/annrheumdis-2017-211472

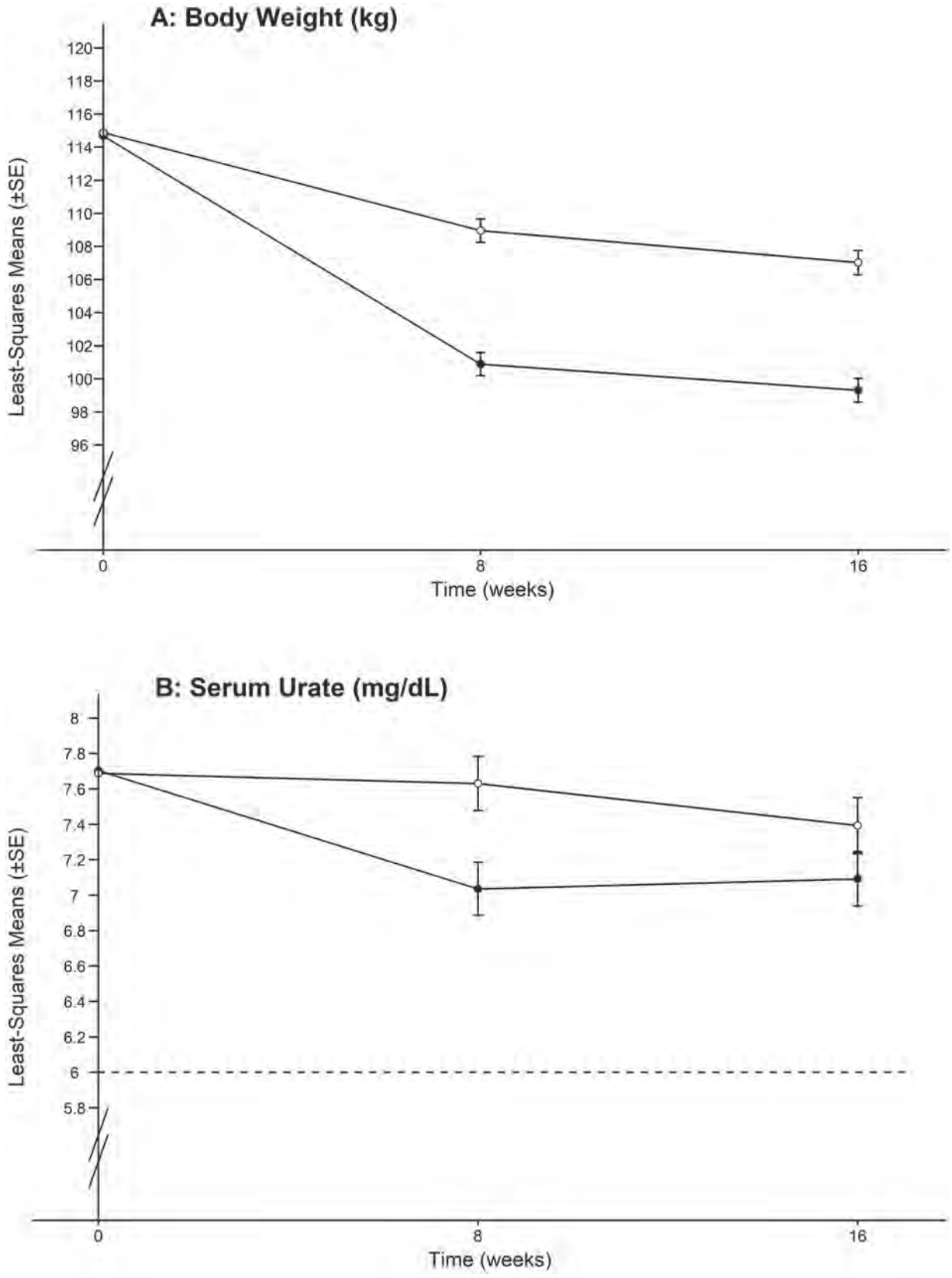

Figure A. Effect of diet on weight B: Effect of diet on serum urate. Open dots = control group, Closed dots = intensive diet.

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Abstract Number: 0656

A Sugar Tax Results in Reduced Incident Gout, Quality Adjusted Life Years Lost and Economic Cost from Gout: A Health Economic Analysis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Background/Purpose: Intake of sugar is associated with increased incident gout. Sugar taxes have been effective at reducing the intake of sugar in several jurisdictions. We aimed to model the impact of a sugar tax on incident gout (assuming causality through increased serum urate levels and a consequent increase in incident gout), quality adjusted life years (QALY) lost and the excess economic cost of new incident gout.

Methods: We modelled the effect of a sugar tax on incident gout in the US population (n=330M) on the study by Choi and colleagues (Arthritis Care & Research 2008;59:109-116). Our model assumptions were a 20% *ad velorum* (value of the item) taxation level, a price elasticity of -0.95 (defined as the percentage change in the quantity demanded over the percentage chance in price). A passthrough rate of 100% (the amount of tax passed through from the manufacturer to the consumer), a 2.5% per annum discount rate, healthcare inflation rate of 6.5% per annum, and a marginal disutility rate of 0.05 (this is the impact on QALY of a diagnosis of gout). We modelled incident gout rates using the Atherosclerosis Risk in Communities Study (ARIC), Coronary Artery Risk Development in Young Adults Study (CARDIA), and both the Original and Offspring cohorts of the Framingham Heart Studies (FHS). We modelled 3, 5, 10 and 15 year incident gout from < 3.0mg/dL up to 6mg/dL in 0.1mg/dl increments. Our outcomes were incident gout, increases in QALY and economic savings from the reduced gout. In modelling all time points we simulated death using US life tables. We assumed a societal perspective for costs (i.e. costs of treatment were considered regardless to whom they accrue), and a marginal cost of gout over non-gout of US$6,560 per annum. We undertook sensitivity analyses of key input parameters. We did not model the revenue to the government of the sugar tax.

Results: We fitted linear models to the raw incident gout rates from < 3mg/dL to 6mg/dL from the combined cohorts. This enabled fine scale prediction of the effect of sugar tax on reducing SU and consequent incident gout.

	3 years	5 years	10 years	15 years
Reduction in incident gout (n)	1,485	7,915	49,233	84,830
QALY saved	1,602	3,876	13,108	26,398
Economic savings (US$)	203.2M	482.5M	1.56B	3.00B

Table 1: Main model Results

We found a reduction in incident gout was achievable (n=84,830) with a 20% *ad velorum* sugar tax over 15 years (Table 1). Based on this reduction in incident gout we were also able to model a saving of 26,398 QALY over 15 years. This led to a saving of 3.15B in net present value.

Sensitivity analyses demonstrated the model was robust to changes in key inut variables.

Conclusion: Assuming a causal relationship, based purely on the reduction in incident gout, QALY savings and economic savings, we provide evidence supporting a sugar tax to be an effective public health measure to address the growing incidence of gout. The reduction in gout and the consequent savings of QALY and costs should be included when considering the implementation of a sugar tax.Table 1: Main model Results

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Disclosure: P. Robinson, Novartis, 2, 5, 8, UCB, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 5, Pfizer, 5, Abbvie, 5, 8, BMS, 9; **N. Dalbeth**, AstraZeneca, 1, 2, Abbvie, 1, Arthrosi, 1, Dyve BioSciences, 1, Selecta, 1, Janssen, 1; **C. Frampton**, None; **T. Merriman**, None; **A. Phipps-Green**, None; **P. Donovan**, None.

Abstract Number: 0657

Gout and Heart Failure in the US

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Background/Purpose: Heart failure (HF) is the eighth leading cause of death in the US, with a 38% increase in the number of deaths due to HF from 2011 to 2017 (1). Gout and hyperuricemia have previously been recognized as significant risk factors for heart failure (2), but there is little nationwide data on the clinical and economic consequences of these comorbidities. The objective was to study heart failure hospitalizations in patients with gout in the United States (US) and estimate their clinical and economic impact.

Methods: The Nationwide Inpatient Sample (NIS) is a stratified random sample of all US community hospitals. It is the only US national hospital database with information on all patients, regardless of payer, including persons covered by Medicare, Medicaid, private insurance, and the uninsured. We examined all inpatient hospitalizations in the NIS in 2017, the most recent year of available data, with a primary or secondary diagnosis of gout and heart failure. Over 69,800 ICD 10 diagnoses were collapsed into a smaller number of clinically meaningful categories, consistent with the CDC Clinical Classification Software.

Results: There were 35.8 million all-cause hospitalizations in patients in the US in 2017. Of these, 351,735 hospitalizations occurred for acute and/or chronic heart failure in patients with gout. These patients had a mean age of 73.3

years (95% confidence intervals 73.1 – 73.5 years) and were more likely to be male (63.4%). The average length of hospitalization was 6.1 days (95% confidence intervals 6.0 to 6.2 days) with a case fatality rate of 3.5% (95% confidence intervals 3.4% – 3.7%). The average cost of each hospitalization was $63,992 (95% confidence intervals $61,908 - $66,075), with a total annual national cost estimate of $22.8 billion (95% confidence intervals $21.7 billion - $24.0 billion).

Conclusion: While gout and hyperuricemia have long been recognized as potential risk factors for heart failure, the aging of the US population is projected to significantly increase the burden of illness and costs of care of these co-morbidities (1). This calls for an increased awareness and management of serious co-morbid conditions in patients with gout.

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Disclosure: G. Singh, Horizon Therapeutics, 2; **M. Sehgal**, None; **A. Mithal**, None.

Abstract Number: 0658

Identification of Two Novel Dysfunctional Variants in a Physiologically Important Urate Transporter *ABCG2* in Paediatric-onset Familial Hyperuricemia and Gout Patients in Three Generations

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

Background/Purpose: *ABCG2* is a high-capacity urate transporter gene. Common dysfunctional variants of *ABCG2* that result in decreased urate excretion in humans are major causes of hyperuricemia and gout, especially in pediatric-onset patients [1]. In the present study, we identified and functionally characterized a novel *ABCG2* variants in a family with three generations of early-onset hyperuricemia and gout.

Methods: A 12-year-old girl was examined for chronic asymptomatic hyperuricemia (397–405 µmol/L) with decreased fractional excretion of uric acid (2.2–3.5%). From positive family history of early hyperuricemia and gout < 35 year (her mother, maternal uncle and maternal grandfather), we performed a metabolic investigation. The results suggested that their hyperuricemia were mainly due to a defect in the urate excretion system and did not result from an excess production of urate. Since this type of hyperuricemia is reportedly related to ABCG2 dysfunction, we analyzed *ABCG2* coding regions of our patients using their genomic DNA. We carried out a series of biochemical analyses for

the functional validation of the identified ABCG2 variants using ABCG2-expressing plasma membrane vesicles as we report previously [2]. This study was approved by the Ethics Committee of the Institute of Rheumatology in Prague (no. 6181/2015).

Results: We identified two novel heterozygous variants: c.393G >T (p.M131I) and c.706C >T (p.R236X) in *ABCG2* gene in the proband. The segregation analysis showed existence of those variants in her mother, maternal brother and maternal grandfather. Immunoblotting for *N*-glycosidase treated whole cell lysates of 293A cells transiently-expressing each ABCG2 variant demonstrated that p.M131I had minimal effect on the protein level and *N*-linked glycosylation status, while the p.R236X variant was detected as truncated forms with weaker band intensity compared with that of ABCG2 wild-type. Confocal microscopy showed that similar to ABCG2 wild-type, p.M131I variant localized on the plasma membrane; the p.R236X variant exhibited little plasma membrane localization. Functional assay revealed that contrary to the wild-type, p.M131 had limited ATP-dependent urate transport activity; ABCG2-mediated urate transport activity of this variant was calculated as 14 ± 2% of wild-type control. Moreover, p.R236X variant was functionally null.

Conclusion: We found a representative case of paediatric hyperuricemia with familial gout that harboured two dysfunctional variants of a physiologically important urate transporter *ABCG2*. Biochemical analyses revealed that ABCG2 p.M131I and p.R236X were functionally deficient and null, respectively. Our identification of novel dysfunctional ABCG2 variants confirmed a key role of ABCG2 transporter and its link with early-onset hyperuricemia and gout.

References

1. Stiburkova B, et al. Arthritis Res Ther. 2019 Mar 20;21(1):77.
2. Toyoda Y, et al. Cells. 2019 Apr 18;8(4). pii: E363.
Supported by the grants from the Czech Republic Ministry of Health RVO 00023728 (Institute of Rheumatology) and by the JSPS KAKENHI Grant Numbers 18KK0247 (to T.T.).

Disclosure: B. Stiburkova, None; **Y. Toyoda**, None; **K. Pavelcova**, None; **J. Bohata**, None; **P. Ješina**, None; **Y. Kubota**, None; **T. Takada**, None; **H. Suzuki**, None.

Abstract Number: 0659

Polynesian-Specific Gout-Associated Frameshift Variant in *PRPSAP1*

Megan Leask[1], Nicola Dalbeth[2], Lisa Stamp[3], Tony Merriman[4], Amanda Phipps-Green[4], Ruth Topless[4], James Boocock[5], Hyon Choi[6], Keresoma Leaupepe[1] and Eli Stahl[7], [1]University of Otago, Dunedin, Otago, New Zealand, [2]University of Auckland, Auckland, New Zealand, [3]University of Otago Christchurch, Christchurch, New Zealand, [4]University of Otago, Dunedin, New Zealand, [5]David Geffen School of Medicine at UCLA, Los Angeles, CA, [6]Massachusetts General Hospital, Department of Medicine, Division of Rheumatology, Lexington, MA, [7]Mt Sinai School of Medicine, New York, NY

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Polynesian (NZ Māori and Pacific) populations have increased prevalence of gout. Hyperuricaemia is contributed to by increased urate production in the liver via the purine pathway. PRPSAP1 (phosphoribosyl

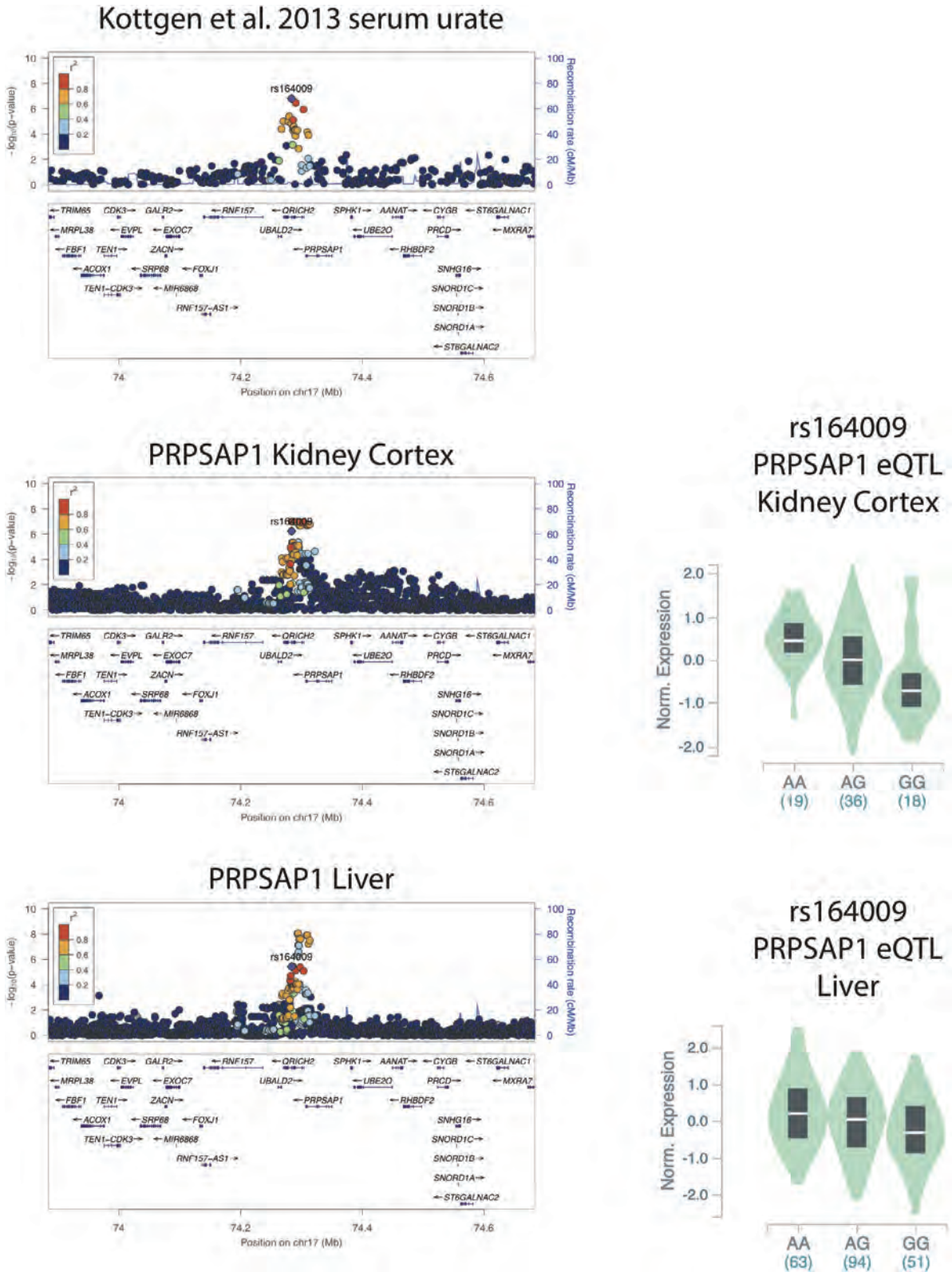

Figure 1. Regional association plots for serum urate (Köttgen et al. 2013) and gene expression of PRPSAP1 in Kidney Cortex and Liver tissue. eQTL violin plots for directionality of expression for the lead Köttgen SNP at PRPSAP1.

pyrophosphate (PRPP) synthetase-associated protein 1) binds PRPP synthetase and negatively regulates the production of PRPP and urate. Genetic variants in close proximity to *PRPSAP1* have been associated with serum urate and colocalize with an expression quantitative trait locus (eQTL) for *PRPSAP1* (Boocock et al. 2020 PMID 31985003), implicating *PRPSAP1* as a causal gene for hyperuricemia. We hypothesize that functional variants within genes that function in the purine pathway (*PRPS1* and *PRPSAP1*) could contribute to the risk of gout.

Methods: *PRPS1* and *PRPSAP1* were sequenced from 811 individuals of Polynesian or European ancestry in order to identify protein-altering variants. A second cohort of 3203 individuals of Polynesian ancestry of gout cases and controls was used to test association with gout using TaqMan®. eQTL data from the latest Genotype Tissue Expression Project release (GTEx v8), that now includes kidney, was used to test for a kidney eQTL.

Results: Two variants within *PRPSAP1* predicted to be protein altering and splice site acceptor variants (rs749392722 and rs201995246, respectively) were identified. No protein-altering variants were identified in *PRPS1*. rs749392722 is a frameshift variant, found only in 19 Polynesian participants, predicted to abolish almost the entirety of exon 3 of *PRPSAP1*. rs201995246 was identified in one hyperuricaemic male (8.1 mg/dL) of European ancestry. In the larger cohort of Māori and Pacific cases and controls (n = 3203) rs74939722 had a minor allele frequency of 0.025. rs749392722 significantly associates with increased risk of gout in Eastern Polynesian people (OR = 2.074, $p = 9.0 \times 10^{-3}$) and this association was confirmed in a meta-analysis (OR = 2.19, $P_{overall} = 4.0 \times 10^{-3}$) carried out on all Polynesian groups.

The maximal urate-associated SNP at the *PRPSAP1* locus, identified previously by genome-wide association study (rs164009; Boocock et al.), is tightly correlated with the maximally associated SNPs for the *PRPSAP1* eQTL in Kidney Cortex (Figure 1). rs164009_A raises serum urate and increases *PRPSAP1* expression in the Kidney Cortex. In contrast rs164009 is not amongst the maximally associated SNPs at the *PRPSAP1* eQTL in Liver, where there is an eQTL with a different genetic pattern of genetic control.

Conclusion: A *PRPSAP1* frameshift Polynesian genetic variant increases risk to gout perhaps by increased production of urate in the liver. The GTEx expression data indicate that the common serum urate association at *PRPSAP1* overlaps a kidney eQTL for *PRPSAP1*, where the urate-raising allele increases *PRPSAP1* expression, which would be expected to decrease production of urate via the purine pathway. *PRPSAP1* expression in the kidney may be important in serum urate control and this could be independent of any role of PRPSAP1 in regulating PRPP synthetase activity in the liver.

Disclosure: M. Leask, None; **N. Dalbeth**, AstraZeneca, 1, 2, Abbvie, 1, Arthrosi, 1, Dyve BioSciences, 1, Selecta, 1, Janssen, 1; **L. Stamp**, None; **T. Merriman**, None; **A. Phipps-Green**, None; **R. Topless**, None; **J. Boocock**, None; **H. Choi**, AstraZeneca, 2, Takeda, 5, Selecta, 5, GlaxoSmithKline, 5, Horizon, 5; **K. Leaupepe**, None; **E. Stahl**, None.

Abstract Number: 0660

Sodium-Glucose Co-Transporter-2 Inhibitors and the Risk for Gout – a Comparison Among Canagliflozin, Dapagliflozin and Empagliflozin

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Sodium-glucose co-transporter-2 inhibitors (SGLT2-i) are anti-diabetic drugs that have a urate-lowering effect. SGLT2-i had a more favorable impact on gout risk than glucagon-like peptide-1 (GLP-1) recep-

Table 1. Baseline characteristics

	Canagliflozin (n=3,287)	Dapagliflozin (n=12,504)	Empagliflozin (n=6,258)
Female, n (%)	1,334 (40.6)	5,347 (42.8)	2,646 (42.3)
Age, years, mean ± SD	59.1 ± 10.9	58.0 ± 10.5	59.2 ± 10.7
BMI, kg/m^2, mean ± SD	34.1 ± 6.6	34.7 ± 6.8	34.5 ± 6.7
Duration of type 2 diabetes mellitus, years, mean ± SD	8.6 ± 5.4	8.4 ± 5.3	9.0 ± 5.8
HbA1c, %, mean ± SD	8.3 ± 1.6	8.4 ± 1.6	8.2 ± 1.5
Diabetic nephropathy, n (%)	65 (2.0)	333 (2.7)	123 (2.0)
Diabetic neuropathy, n (%)	84 (2.6)	281 (2.2)	148 (2.4)
Diabetic retinopathy, n (%)	663 (20.2)	2,507 (20.0)	1,228 (19.6)
GFR, mL/min/1.73m^2, mean ± SD	89.1 ± 22.8	90.6 ± 22.5	90.2 ± 22.6
Chronic kidney disease*, n (%)	3 (0.1)	9 (0.1)	9 (0.1)
Coronary artery disease, n (%)	441 (13.4)	1,519 (12.1)	959 (15.3)
Heart failure, n (%)	88 (2.7)	274 (2.2)	225 (3.6)
Hypertension, n (%)	1,948 (59.3)	7,420 (59.3)	3,780 (60.4)
Peripheral vascular disease, n (%)	92 (2.8)	272 (2.2)	179 (2.9)
Insulin, n (%)	559 (17.0)	2,417 (19.3)	1,148 (18.3)
Diuretic, n (%)	1,221 (37.1)	4,757 (38.0)	2,447 (39.1)
Losartan, n (%)	337 (10.3)	1,294 (10.3)	611 (9.8)
NSAID, n (%)	2,521 (76.7)	9,674 (77.4)	4,721 (75.4)

*Chronic kidney disease (CKD) defined as CKD stage 4, CKD stage 5, or renal replacement therapy (dialysis or transplant). BMI: body mass index; GFR: glomerular filtration rate; HbA1c: glycated hemoglobin; NSAID: non-steroidal anti-inflammatory drug; SD: standard deviation.

Table 2. Hazard of developing gout among SGLT2-i users

	Canagliflozin (n=3,287)	Dapagliflozin (n=12,504)	Empagliflozin (n=6,258)
New cases of gout (n)	63	195	51
Total follow-up time (person-years)	5,497	28,247	8,057
Mean follow-up time (years)	1.7	2.3	1.3
Incidence Rate (per 1,000 person-years)	11.5	6.9	6.3
Unadjusted Hazard Ratio (95% CI)	1.59 (1.19 – 2.11)	1.0	0.84 (0.61 – 1.15)
Adjusted* Hazard Ratio (95% CI)	1.57 (1.18 – 2.09)	1.0	0.81 (0.59 – 1.11)

* Potential confounders (assessed at baseline) included in the adjusted hazards ratio model: 1) general (age, gender, body mass index); 2) duration of type 2 diabetes mellitus; 3) complications of type 2 diabetes mellitus (diabetic nephropathy, diabetic neuropathy, diabetic retinopathy); 4) comorbidities (chronic kidney disease, coronary artery disease, heart failure, hypertension, peripheral vascular disease) 5) medication use (diuretics, insulin, losartan, non-steroidal anti-inflammatory drug). CI: confidence interval; SGLT2-i: sodium-glucose co-transporter 2 inhibitors.

tor agonists. In a post-hoc analysis of a randomized controlled trial (RCT), canagliflozin, a SGLT2-i, decreased risk of gout that seemed to be more than may be expected by serum urate reduction, suggesting potential anti-inflammatory effects beyond urate reduction. *In-vitro*, canagliflozin, but not dapagliflozin or empagliflozin, activated AMPK and suppressed IL-1β stimulated secretion of IL-6 and monocyte chemoattractant protein-1 (MCP-1). However, dapagliflozin and empagliflozin activated AMPK in other studies. Whether there may be differences in gout risk between SGLT2-i's is not known.

Methods: We performed a cohort study using data from The Health Improvement Network (THIN), a UK general practitioner (GP) electronic health records (EHR) database. We included subjects aged 18–89 with type 2 diabetes mellitus and incident use of a SGLT2-i (canagliflozin, dapagliflozin, empagliflozin) between 01/01/2013 and 12/ 31/2018 who had been enrolled in the GP practice for 6 months prior to study entry. We excluded individuals with gout diagnosis (Read code), use of gout medications (allopurinol, febuxostat, probenecid, sulfinpyrazone, or colchicine) or without body mass index assessment prior to SGLT2-i initiation. Follow-up started from the index date (date of first SGLT2-i prescription) and continued until incident gout diagnosis (diagnostic Read code or prescription of gout medications), switch to another SGLT2-i, death, or end of study. We compared the risk of developing gout across the 3 SGLT2-i's using multivariable Cox proportional hazards regression, adjusting for potential confounders.

Results: Of 22,049 subjects with type 2 diabetes mellitus, there were 3,287 incident users of canagliflozin, 12,504 incident users of dapagliflozin and 6,258 incident users of empagliflozin. Baseline characteristics are shown in Table 1. After adjusting for potential confounders, canagliflozin had 1.57 (95% confidence interval (CI) of 1.18 to 2.09) times the risk of developing gout, while empagliflozin had 0.81 (95% CI 0.59–1.11) times the risk compared with dapagliflozin, although the latter the effect estimate was not statistically significant (Table 2).

Conclusion: While SGLT2-i agents as a class and canagliflozin in particular have been shown to reduce the risk of gout in prior studies, in this cohort study from a UK EHR database, the beneficial effects appeared to be strongest for dapagliflozin and empagliflozin, with no significant differences noted between the two of them. Although canagliflozin reduced risk of gout compared with placebo in a RCT, in these data, it had a less favorable effect than dapagliflozin. The clinical relevance of the *in vitro* data on the potential anti-inflammatory effects of the various agents in this drug class is not clear.

Disclosure: A. Vargas-Santos, Abbvie, 8; **C. Peloquin**, None; **S. Kim**, Pfizer, 1, Roche, 1, AbbVie, 1, Bristol-Myers Squibb, 1; **T. Neogi**, Lilly, 1, EMD Merck Serono, 1, Novartis, 1, Regeneron, 1, Pfizer/Lilly, 1.

Abstract Number: 0661

Genomic Regions Jointly Associated with eGFR and Serum Urate: Implications for Shared Genetic Etiology of Hyperuricemia and Chronic Kidney Disease

Nick Sumpter[1], Alexa Lupi[2], Megan Leask[3], Tony Merriman[4], Ana Vazquez[2] and Richard Reynolds[1], [1]University of Alabama at Birmingham, Birmingham, AL, [2]Michigan State University, East Lansing, MI, [3]University of Otago, Dunedin, Otago, New Zealand, [4]University of Otago, Dunedin, New Zealand

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout and hyperuricemia (HU), serum urate (SU) > 6.8 mg/dL, often present in the context of chronic kidney disease. It has long been known that estimated glomerular filtration rate (eGFR) and SU levels are correlated. Recent GWAS studies of SU and eGFR indicate nine overlapping large effect variants including *GCKR, A1CF,* and *VEGFA*, which suggests that the traits are also correlated genetically. Here we estimate the local genetic covariance of eGFR/SU across the genome and test whether expression quantitative trait loci (eQTL) are a potential source of the shared genetic effects on eGFR/SU.

Methods: We computed eGFR/SU genetic covariance estimates from the UK Biobank, consisting of SNP genotypes and clinical data measured on a total of 333,542 unrelated individuals, all of European ancestry. Estimates were generated from sets of SNPs comprising 511,828 genomic windows distributed across the genome. SNPs were included in the same window if they had pairwise linkage disequilibrium (LD) greater than 0.1. Genetic covariance was computed using estimates of variance explained by sets of SNPs on the outcomes from three separate models: 1) eGFR alone 2) SU alone 3) eGFR + SU. Variances were estimated using Bayesian inference, and bootstrap 95% confidence intervals of selected covariance estimates were generated. The Gene and Tissue Expression (GTEx) database (version 8) was used to test *cis*-eQTLs for variants comprising windows with significant covariance estimates on eGFR/SU. Colocalization of eQTL and GWAS signals was assessed using COLOC.

Results: The cohort was 53.7% female with an average age of 56.9 ± 8.0 years old. The average (SD) for eGFR was 112.8 ± 39.4 ml/min/1.73 m2, and the average (SD) for SU was 4.1 ± 1.1 mg/dL. Out of 511,828 genomic windows, 268 produced genetic covariance estimates between eGFR/ SU with 95% confidence intervals which did not overlap zero (Figure 1). Seven of the 15 largest magnitude covariance estimates validate shared loci from the marginal GWAS of eGFR/SU with the remainder representing novel shared eGFR/SU loci (Table 1). Sixteen shared eGFR/SU loci also colocalized with gene expression (posterior probability of colocalization (PPC) > 0.8). At the *A1CF* locus the eGFR/SU associations colocalize (PPC = 0.99) with an eQTL for *A1CF* (Figure 2). Furthermore, eQTL for *FGF5* in kidney cortex, *CD86* in whole blood and two transporter genes *SLC15A2* and *SLC7A9* were also identified.

Conclusion: Using our novel approach allowing direct estimates of the genetic covariance of eGFR/SU in specific windows of the genome, we demonstrate a set of loci contributing to the association between SU and eGFR. Many shared genomic regions also associate with gene expression thereby highlighting their potential functional signifi-

Chr	Locus	Window size	Genetic covariance [95% CI]	Novel
11	*DCDC1*	10 [30,749,090 - 30,768,678]	-0.786 [-0.918, -0.669]	Yes
2	*GCKR*	16 [27,656,822 - 27,748,624]	0.586 [0.301, 0.890]	No
7	*UNCX*	13 [1,270,699 - 1,307,501]	-0.536 [-0.676, -0.402]	Yes
7	*PRKAG2*	10 [151,415,041 - 151,442,897]	-0.440 [-0.607, -0.264]	No
2	*CPS1*	1 [211,540,507]	0.391 [0.217, 0.585]	Yes
2	*LRP2*	6 [169,985,418 - 170,010,985]	0.391 [0.093, 0.636]	No
6	*VEGFA*	1 [43,806,609]	-0.368 [-0.488, -0.215]	No
8	*STC1*	6 [23,731,875 - 23,757,657]	-0.366 [-0.494, -0.233]	No
19	*SLC7A9*	16 [33,347,439 - 33,408,977]	0.321 [0.012, 0.608]	Yes
11	*OVOL1*	7 [65,506,822 - 65,553,306]	-0.316 [-0.460, -0.167]	Yes
12	*R3HDM2*	7 [57,778,221 - 57,849,768]	-0.296 [-0.429, -0.126]	No
1	*MTX1*	5 [155,172,725 - 155,194,980]	-0.276 [-0.491, -0.072]	Yes
10	*A1CF*	7 [52,581,892 - 52,637,925]	0.267 [0.101, 0.466]	No
2	*HOXD10*	5 [176,962,989 - 176,978,833]	-0.234 [-0.329, -0.145]	Yes
2	*GLI2*	7 [121,305,604 - 121,310,704]	-0.211 [-0.299, -0.117]	Yes

Table 1. List of 15 genomic windows with largest magnitude significant genetic covariance estimates. Chr column defines chromosome. Window size column contains # SNP markers/ window followed by its width [starting base pair position - ending base pair position]. Novel is defined as a locus that has not previously been implicated as a shared locus for eGFR/SU.

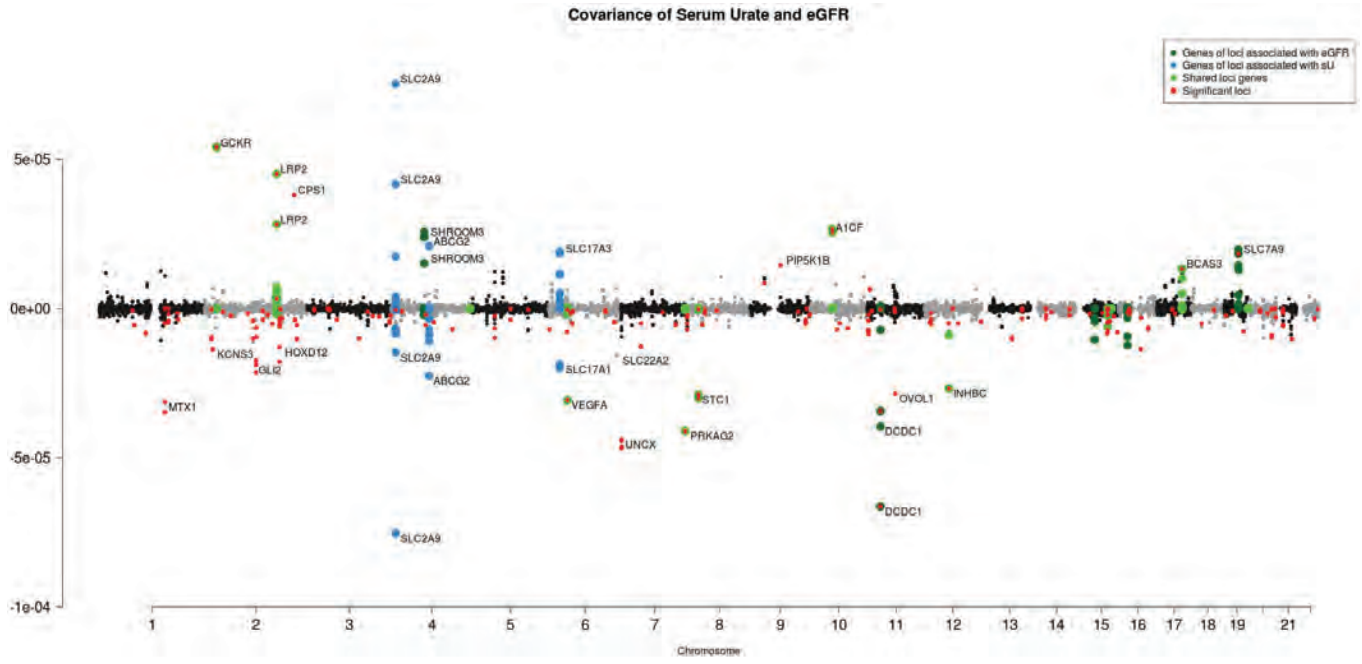


Figure 1. Covariance estimates of LD windows in the UK Biobank. Windows that contained SNPs in genes associated with known eGFR genes are highlighted in dark green, windows that contained SNPs in genes associated with serum urate are highlighted in blue, and windows that contained SNPs in genes associated with both serum urate and eGFR (from comparing separate GWAS, Johnson et al.5) are highlighted in lime green. Windows with confidence limits not overlapping zero are highlighted in red.

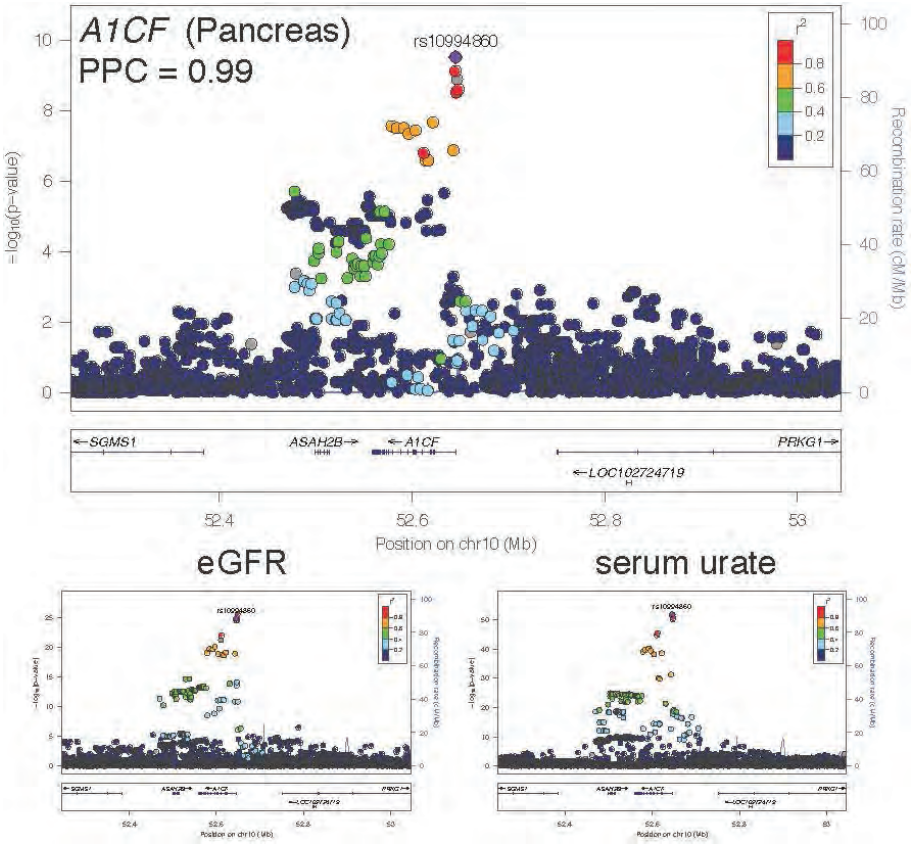


Figure 2. Regional association plots at the A1CF locus for an A1CF eQTL in pancreas (above) and corresponding urate and eGFR associations (below). The color of the surrounding SNPs indicates the strength of LD with the lead A1CF eQTL SNP (in purple) according to the key in the left top hand corner, measured as r2 found in the European HapMap data (hg19/1000 genomes Nov 2014). The plots were generated using LocusZoom.

cance. The extensive genetic signal shared between eGFR/SU suggests that pleiotropy, acting through gene expression differences, contributes to the genetic basis of the association between gout/HU and CKD.

Disclosure: N. Sumpter, None; **A. Lupi**, None; **M. Leask**, None; **T. Merriman**, None; **A. Vazquez**, None; **R. Reynolds**, None.

Abstract Number: 0662

Cause-Specific Mortality in Patients with Gout in the Veteran's Health Administration: A Matched Cohort Study

Lindsay Helget[1], Bryant England[1], Punyasha Roul[1], Harlan Sayles[1], Alison Petro[1] and Ted Mikuls[1], [1]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Table 1. Baseline characteristics*

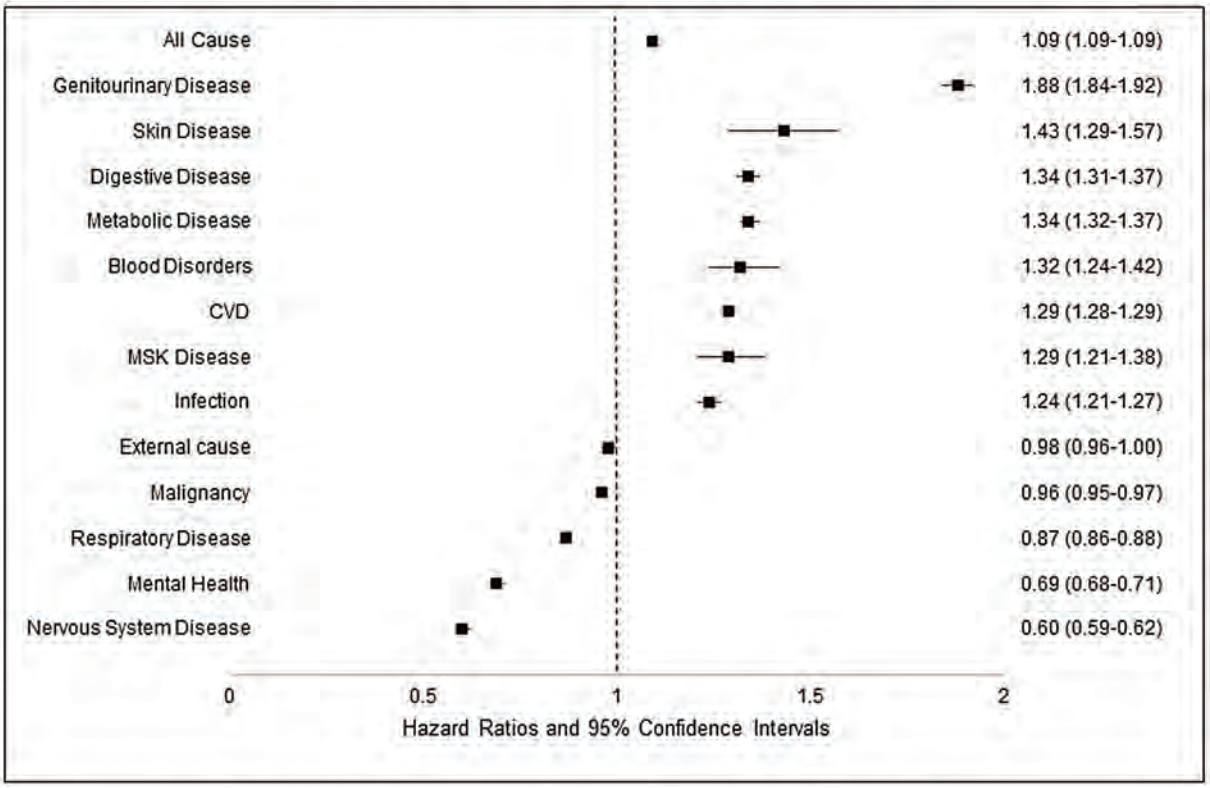
Characteristic	Gout	Non-gout
Demographics		
Age, years	67 (12)	67 (12)
Male sex, %	99	99
Race/ethnicity, %		
White Hispanic	2	3
White non-Hispanic	62	59
Black Hispanic	0	0
Black non-Hispanic	16	10
Asian	1	1
Other	3	3
Missing	15	24
Health factors		
Body mass index, %		
<20 kg/m^2	1	1
20 to <25 kg/m^2	6	14
25 to <30 kg/m^2	21	29
≥30 kg/m^2	72	56
Alcohol use disorder, % (ICD 9cm codes)	8	6
RDCI score (range 0-9)	2.0 (1.5)	1.3 (1.5)
MI or atherosclerosis, %	4	2
Other CVD, %	36	22
Stroke, %	3	2
HTN, %	73	43
Lung disease, %	12	9
Depression, %	15	12
Diabetes mellitus, %	30	19
Ulcer or stomach problem, %	5	3
Cancer, %	12	9

*Gout and non-gout cases matched on age and sex; all other factors shown differed ($p < 0.05$) between groups

Background/Purpose: Gout is the most common type of inflammatory arthritis, with a prevalence in the Veteran's Health Administration (VHA) of nearly 6%. While gout flares prompt patients to seek medical attention, the longer-term consequences of gout are important considerations for patients, clinicians, and health systems. Associated with increased all-cause mortality, an understanding of the cause-specific mortality risk in gout remains incomplete. The purpose of this study was to compare all-cause and cause-specific mortality risk between gout and non-gout patients in the VHA.

Methods: We performed a retrospective, matched cohort study, identifying patients with gout using the VHA administrative data from 1/1999-9/2015 based on the presence of ≥2 ICD-9 codes for gout (274.X). The index date was defined as the date of the 2nd diagnostic code. Gout patients were matched up to 1:10 on birth year, sex, and year of VHA enrollment with non-gout patients (no prior diagnostic codes or urate lowering therapy). Patients were followed from the index date until death, censoring due to end of study period or subsequently fulfilling the gout algorithm (non-gout patients could cross-over and contribute to gout "at risk" observation). Vital status and cause of death (20

Figure 1. Associations of Gout with All-Cause and Cause-Specific Mortality in the Veteran's Health Administration



*Top causes by category: Malignancy (lung, prostate, and colon); Respiratory (COPD and pneumonia); Metabolic disease (diabetes mellitus and hyperlipidemia); Genitourinary disease (CKD, acute renal failure, and urinary tract infections); Digestive disease (cirrhosis and GI bleed); Nervous system disease (Alzheimer's disease and Parkinson's disease); Mental Health (dementia and vascular dementia); MSK disease (osteomyelitis and rheumatoid arthritis); Skin disease (cellulitis and decubitus ulcer); Blood disease (anemia and coagulation defect).

unique ICD-10 chapters) were obtained from the National Death Index (through 12/2017). Associations of gout with all-cause and cause-specific mortality were examined using Cox regression.

Results: Gout patients (n = 559,253) were matched to 5,431,582 non-gout controls. Gout patients had a higher BMI and greater comorbidity (**Table 1**). There were 246,291 deaths over 4,250,477 patient-years in gout patients and 1,995,863 deaths over 40,469,354 patient-years of follow-up in controls. Associations of gout with all-cause and cause-specific mortality are shown in **Figure 1**. The strongest associations of gout with cause-specific mortality were observed with genitourinary conditions. Kidney failure was the most common specific cause of death in this category. Of the 20 unique ICD-10 chapters examined, mortality was increased among gout patients for 8 specific causes. In contrast, gout patients were at lower risk from death related to neurologic (e.g., Alzheimer's, Parkinson's, and other neurodegenerative disorders), mental health, respiratory, and malignancy related conditions.

Conclusion: Using data from the largest integrated health system in the U.S, we found that gout patients in the VHA have an ~10% higher rate of all-cause mortality. Although patients with gout are well recognized to have higher all-cause and cardiovascular mortality, these results suggest that survival is negatively impacted by a number of other health conditions with genitourinary causes acting as the most over-represented cause of death in gout. Likewise, these data suggest that gout patients exhibit a survival advantage for both neurologic and mental health causes. Additional research examining factors associated with cause-specific survival in this Veteran population are needed as this could inform future strategies aimed at improving long-term outcomes in gout.

Disclosure: L. Helget, None; **B. England**, None; **P. Roul**, None; **H. Sayles**, None; **A. Petro**, None; **T. Mikuls**, Horizon Therapeutics, 2.

Abstract Number: 0663

Analysis of Common Gout Comorbidities in the UK Biobank Cohort Reveals Sex-Specific Effects and Genetic Differentiation

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: This study aimed to estimate the extent to which gout associated genetic variants are associated with the presence/absence of common comorbidities in gout patients of the UK Biobank cohort. Previous studies have shown that the odds-ratios of comorbidities tend to be higher among women in comparison to men (Dirken-Heukensfeldt et al., 2010; Zhu et al., 2012).

Methods: The total cohort size for this study was 332,360 (mean [SD] age was 57.1 [7.9] years old; 48% male). Common gout comorbidities (hypertension, type 2 diabetes, obesity, dyslipidemia, chronic kidney disease (CKD), liver disease, coronary heart disease, heart failure, cerebrovascular disease and sleep apnea) were defined using self-report data, ICD-10 codes, medications and measured biomarkers/metrics.

Trait	Number (whole cohort)	Percentage (whole cohort)	Number (gout only)	Percentage (gout only)
Gout	7,131	2.15	7,131	100.00
Hypertension	117,129	35.24	4,949	69.40
Dyslipidemia	77,061	23.19	3,581	50.22
Type 2 diabetes	20,352	6.12	1,278	17.92
Renal failure	163	0.05	28	0.39
CKD stage 3	13,255	3.99	894	12.54
CKD stage 4	664	0.20	148	2.08
CKD stage 5	431	0.13	100	1.40
Obesity	76,625	23.05	3,428	48.07
Coronary heart disease	31,685	9.53	1,549	21.72
Heart failure	5,938	1.79	465	6.52
Cerebrovascular disease	11,078	3.33	490	6.87
Sleep apnea	4,503	1.35	312	4.38

Table 1. Prevalence of comorbidities.

Trait	OR (whole cohort) [95% CI]	OR (male) [95% CI]	OR (female) [95% CI]
Hypertension	3.19 [3.02; 3.36] ****	2.98 [2.83; 3.15] ****	7.18 [5.82; 8.93] ***
Dyslipidemia	2.27 [2.16; 2.39] ****	2.16 [2.05; 2.28] ****	3.95 [3.31; 4.71] ***
Type 2 diabetes	2.42 [2.27; 2.58] ****	2.27 [2.12; 2.42] ****	5.25 [4.25; 6.45] ***
Renal failure	8.23 [5.25; 12.51] ***	6.61 [4.00; 10.50] **	28.43 [10.85; 61.76] **
CKD stage 3	3.57 [3.31; 3.85] ****	3.32 [3.05; 3.60] ****	5.62 [4.59; 6.85] ***
CKD stage 4	10.50 [8.59; 12.76] ****	8.31 [6.66; 10.30] ***	34.06 [22.64; 49.58] ***
CKD stage 5	11.03 [8.64; 13.98] ***	8.62 [6.60; 11.16] ***	45.47 [27.15; 72.41] ***
Obesity	3.00 [2.86; 3.15] ****	2.90 [2.76; 3.05] ****	4.99 [4.21; 5.93] ***
Coronary heart disease	1.62 [1.53; 1.72] ***	1.54 [1.44; 1.64] ***	3.43 [2.78; 4.20] ***
Heart failure	2.44 [2.20; 2.69] ***	2.22 [1.99; 2.46] ***	7.58 [5.63; 10.01] ***
Cerebrovascular disease	1.52 [1.38; 1.67] **	1.40 [1.27; 1.55] **	3.40 [2.55; 4.44] **
Sleep apnea	2.35 [2.09; 2.65] ***	2.19 [1.93; 2.48] ***	7.20 [4.67; 10.58] ***

Table 2. Results of generalized linear models for each comorbidity in gout cases vs controls. P-values represented as: * = P < 0.05, ** = P < 0.001, *** = P < 10-20, **** = P < 10-100.

Model	OR [95% CI]	P-value
Full GRS	0.90 [0.84; 0.96]	0.0025
rs1967017 (*PDZK1*)	1.07 [0.97; 1.18]	0.21
rs780093 (*GCKR*)	0.96 [0.87; 1.06]	0.44
rs13129697 (*SLC2A9*)	0.90 [0.79; 1.03]	0.12
rs2231142 (*ABCG2*)	0.88 [0.78; 0.99]	0.033
rs1229984 (*ADH1B*)	0.69 [0.54; 0.89]	0.0029
rs1165196 (*SLC17A1*)	0.92 [0.83; 1.02]	0.12
rs3812316 (*MLXIPL*)	1.04 [0.88; 1.22]	0.64
rs1171619 (*SLC16A9*)	0.90 [0.79; 1.03]	0.13
rs505802 (*SLC22A11*)	0.95 [0.85; 1.05]	0.29
rs2229357 (*R3HDM2*)	0.98 [0.87; 1.11]	0.79
rs28508560 (*IDH2*)	0.90 [0.80; 1.00]	0.056
rs738409 (*PNPLA3*)	1.11 [0.98; 1.26]	0.085

Table 3. Genetic analysis of the presence of any comorbidity among gout patients.

Each comorbidity was tested for association with gout using generalized linear models, adjusted for age and sex, and in sex-specific models, adjusted for age.

Variant genotypes from 12 genome-wide significant gout loci (from the UK Biobank) were used to calculate an effect size weighted gout genetic risk score (GRS). The GRS was tested for association, using a generalized linear model, with the presence of any comorbidity within the gout cohort (N = 7,131), adjusting for age and sex. Each variant was also tested separately.

Results: The prevalence of comorbidities in the whole cohort ranged from 1.8% (heart failure) to 35.2% (hypertension) (Table 1). All comorbidities were roughly 2-3x as common in gout patients alone relative to the entire cohort,

ranging from 6.5% (heart failure) to 69.4% (hypertension) (Table 2). Additionally, we showed that these comorbidities are more prevalent in female gout cases, with all odds ratios showing higher, non-overlapping confidence intervals in females compared to males.

The GRS was confirmed to associate with gout in the entire cohort (OR = 1.73 [95%-CI: 1.69; 1.77], $P < 10^{-300}$). The GRS associated with a reduced likelihood of having any comorbidity among gout patients (Table 3). This was largely driven by variants at the *ABCG2* locus and the *ADH1B* locus, which associated significantly on their own.

Conclusion: This study showed evidence for a stronger likelihood of comorbidities among female gout cases in comparison to males. We also established that there is a significant contribution of gout genetic risk variants to the presence or absence of any comorbidity in gout patients. Variants at the *ABCG2* and *ADH1B* loci contributed the most to this association, showing significance when modeled alone with presence of any comorbidity. This likely represents the concept of primary versus secondary gout, with a higher genetic risk amongst individuals without comorbidities (primary gout) and a second group of individuals with lower genetic risk but prevalent comorbidities (secondary gout).

Disclosure: N. Sumpter, None; **M. Cadzow**, None; **A. So**, None; **R. Reynolds**, None; **T. Merriman**, None.

Abstract Number: 0664

Uric Acid Level Is Associated with Severity of Heart Failure with Preserved Ejection Fraction

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Hyperuricemia (HUC) has been shown to have an impact in the left atrium and left ventricle remodeling leading to the development of heart failure (HF).

Experimental studies have shown that the increase of HUC results in cardiomyocyte hypertrophy, myocardial oxidative stress, interstitial fibrosis, and impaired diastolic relaxation. Ultimately, patients with HUC may also develop heart failure with preserved ejection fraction (HFpEF).

Methods: We conducted a cross-sectional study to determine the correlation between serum uric acid levels and the severity of HFpEF, after receiving the Institutional Review Board (IRB) approval (IF2467628). HUC was defined as a mean serum uric acid level equal to or more than 7.0 mg/dL. 161 patients with a diagnosis of HUC were screened by chart review between January 2016 to December 2018 following these inclusion criteria: 1) reported HUC at least one year before the echocardiogram (TTE) was performed, 2) echocardiographic parameters to classify the severity of diastolic dysfunction.

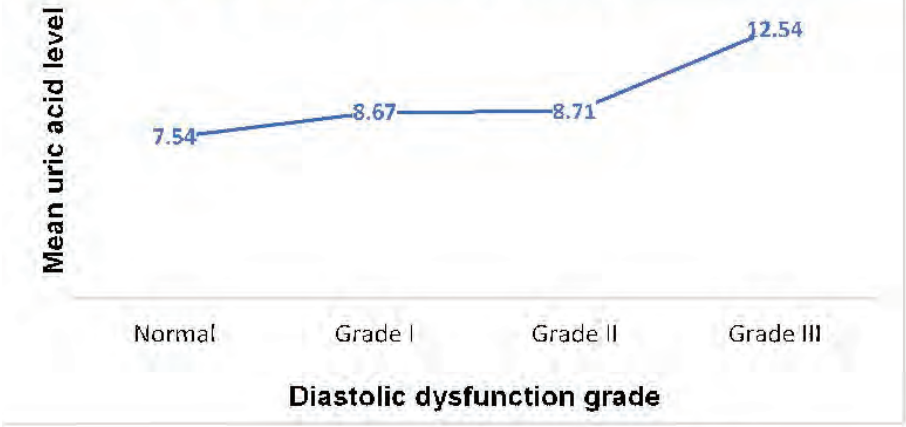
Fisher's exact test was used for qualitative variables and Pearson chi-square test for quantitative variables. Multiple regression analysis, including potential confounders factors (age, gender, race, use of uric acid lowering agents, use of Losartan, low-dose Aspirin, diuretic agent, use of more than 3 blood pressure-lowering agents, history of comorbid

Variable	Normal and impaired relaxation (Normal and Grade I) N= 40 (%)	High-grade diastolic dysfunction (Grade II and III) N= 16 (%)	*P* value
Age (years)	65.8 ±13.6	60.1 ±20.8	0.161
Females	10 (25%)	5 (31%)	0.741
Race/ethnicity • White • Black • Hispanic • Other	 4 (10%) 20 (50%) 10 (25%) 6 (15%)	 3 (19%) 9 (56%) 3 (19%) 1 (6%)	0.567
Mean uric acid level (mg/dL)	8.06 ±0.29	9.36 ±1.09	0.898
Hypertension	35 (88%)	15 (94%)	0.308
Mean systolic blood pressure (mmHg)	128.8 ±18.9	129.4 ±44.7	0.525
Mean diastolic blood pressure (mmHg)	74.9 ±11.9	73.1 ±20.5	0.369
On three blood pressure lowering agents or more	15 (38%)	11 (69%)	**0.043**
Resistant hypertension	2 (5%)	6 (38%)	**0.003**
On a Beta blocker	21 (53%)	13 (81%)	**0.029**
On a RAAS inhibitor	18 (45%)	10 (63%)	0.390
On Losartan	7 (18%)	1 (6%)	0.423
On a diuretic agent	17 (43%)	11 (69%)	**0.046**
On low-dose Aspirin	29 (73%)	11 (69%)	0.990
On uric acid lowering agent	19 (48%)	10 (63%)	0.149
Chronic kidney disease	24 (60%)	12 (75%)	0.365
Overweight and obesity	36 (90%)	9 (56%)	**0.008**
Diabetes mellitus	15 (38%)	8 (50%)	0.414
Atrial fibrillation	3 (8%)	15 (94%)	**< 0.001**
Atherosclerotic vascular disease	16 (40%)	10 (63%)	0.193
Gout	34 (85%)	15 (94%)	0.173
Mean ejection fraction (%)	59.9 ±9.7	37.9 ±22.7	**< 0.001**

Table 1. Baseline Characteristics

conditions related to diastolic dysfunction (HTN, resistant HTN, Afib, DM, obesity, CKD), presence of Gout and mean ejection fraction) was performed. Calculation of coefficient ratios and their 95% confidence interval for the association between mean uric acid level and grade of severity of diastolic dysfunction was performed. P-value < 0.05 was considered statistically significant. STATA (IC-15.1; Stata Corp) was used for the statistical analysis.

Diastolic dysfunction grade	Mean uric acid level (+/- SD)	P value
Normal Grade I Grade II Grade III	7.54 +/- 1.64 8.67 +/- 1.91 8.71 +/- 3.44 12.54 +/- 3.10	< 0.001



	Normal	Grade I	Grade II
Grade I	1.12 P=0.752		
Grade II	1.16 P=0.999	0.04 P=0.999	
Grade III	4.99 P < 0.001	3.86 P=0.009	3.83 P=0.020

Table 2. Mean uric acid level across diastolic dysfunction grades

	Mean uric acid level in normal and impaired relaxation vs higher grade diastolic dysfunction	Coef. (95% CI)	P value
Unadjusted risk of higher-grade diastolic dysfunction with mean uric acid level	8.06 ±0.29 vs 9.36 ±1.09	0.034 (-0.009 to 0.077)	0.119
Adjusted* risk of higher-grade diastolic dysfunction with mean uric acid level		**0.053 (0.001 to 0.106)**	**0.047**
***Adjusted** to age, gender, race, use of uric acid lowering agents, use of Losartan, use of low-dose Aspirin, use of a diuretic agent, use of more than 3 BP lowering agent, history of comorbid conditions related to diastolic dysfunction (HTN, resistant HTN, Afib, DM, obesity, CKD), presence of gout and mean ejection fraction.			

Table 3. Correlation between mean uric acid level and the severity of HFpEF

Results: Out of the 161 patients, 56 patients met our inclusion criteria of which 78.6 % had a mean uric acid level above 7 mg/dL. For normal left ventricle function and Grade I diastolic dysfunction group, the mean age was 65.8 (±13.6) years and mean uric acid level was 8.06 (±0.29) mg/dL, as compared to 60.1 (±20.8) years and mean uric acid of 9.36 (±1.09) mg/dL for Grade II and III diastolic dysfunction group. 47.5% of patients with normal and impaired relaxation were on a uric acid lowering agent versus 62.5% of patients in the group with higher grade diastolic dysfunction. 85% of the low-grade diastolic dysfunction group had a co-existing diagnosis of Gout versus 93.7% of the group with grade II and III diastolic dysfunction. The difference of mean uric acid level between Grade III diastolic dysfunction and normal diastolic function was of 4.99 mg/dL ($p< 0.001$), 3.86 mg/dL ($p= 0.009$) for Grade I and 3.83 mg/dL ($p= 0.020$) for Grade II diastolic dysfunction. Our results (Table 4) showed that the risk of severe diastolic dysfunction increases by 0.053 (95%-CI 0.001-0.106; $p= 0.047$) for every unit of increase in mean of uric acid level.

Conclusion: There is a directly proportional correlation between the level of uric acid and the severity of diastolic dysfunction. The group with higher diastolic dysfunction had a higher prevalence of Gout independent of confounding variables.

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Abstract Number: 0665

Trends in Immunomodulation/pegloticase Co-therapy from 2015-2019: A Claims Database Study

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
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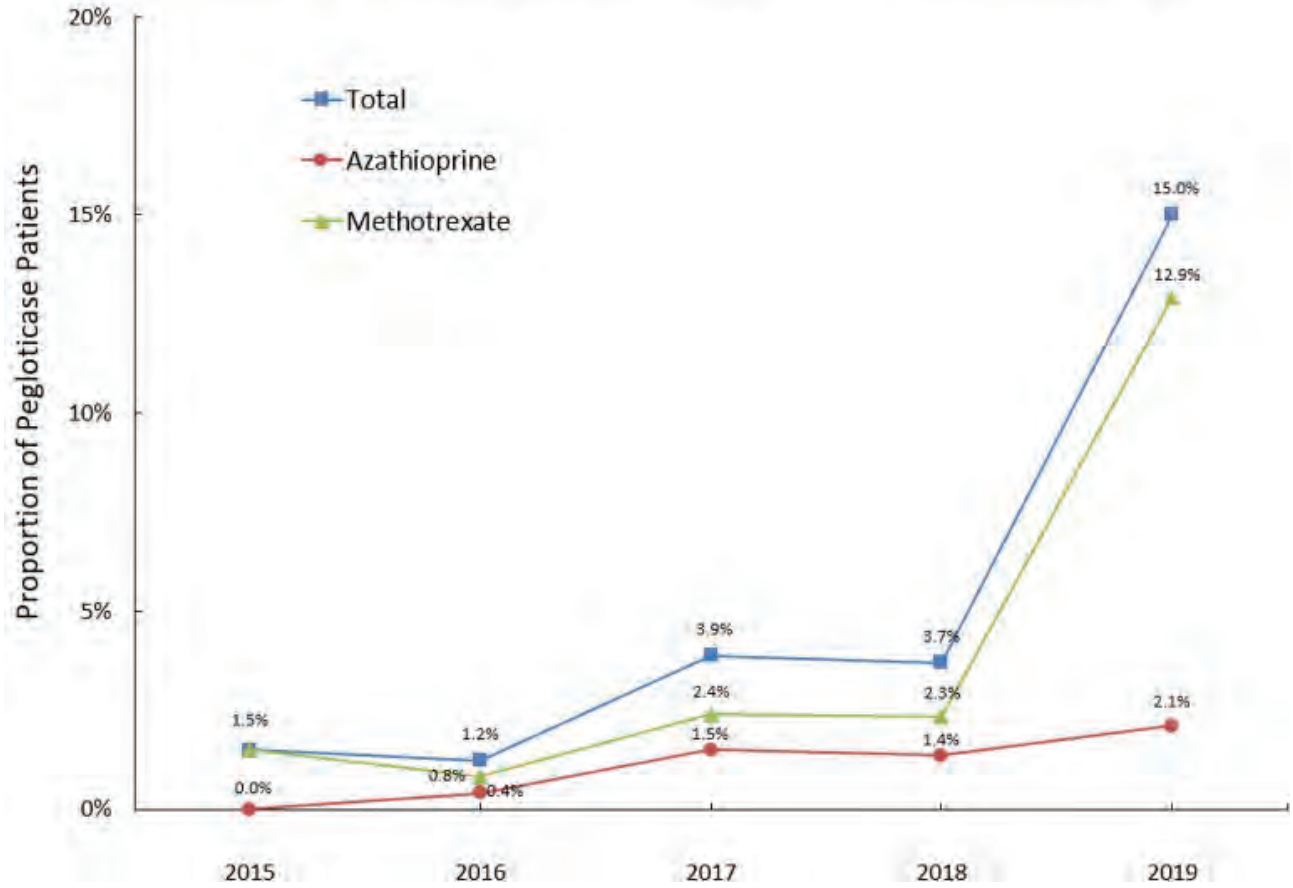
Background/Purpose: Pegloticase, a recombinant, PEGylated uricase enzyme, is used to treat uncontrolled gout in patients who do not improve on or are intolerant of oral urate-lowering therapies. As with other biologics, anti-drug antibodies (ADAs) against pegloticase can develop and cause infusion reactions and loss of treatment efficacy.[1] As a result of ADA formation, the pegloticase response rate in clinical trials was 42%.[2] DMARDs (e.g., azathioprine, methotrexate) are frequently used when treating autoimmune diseases with biologics to attenuate ADA development, often resulting in a more successful response to biologic therapy, and lower adverse event rates.[3] Starting with a case-series presentation in late 2018, growing evidence in the literature supports using pegloticase with immunomodulation co-therapy, consistently showing a marked increase in treatment responder rates.[4-8] However, little is known about whether this practice is being implemented in clinical practice and, if so, how treatment patterns have changed over time. This study examined a large medical claims database to better understand immunomodulator use with pegloticase in the United States.

Methods: The IQVIA database contains 1.3 billion claims (made from November 2014 thru December 2019) of 30 million patients diagnosed with gout or chronic kidney disease. Patients who had received pegloticase were identified and classified based on immunomodulator use. Patients who were prescribed methotrexate or azathioprine within 60 days (before or after) of receiving the first pegloticase infusion were considered to have received co-administration of pegloticase/immunomodulator.

Figure 1: Proportion of pegloticase patients receiving immunomodulation therapy by year



Note – Immunomodulation/pegloticase co-therapy usage defined as any patient starting either methotrexate or azathioprine within 60 days before or after their first pegloticase infusion, excluding immunotherapy usage one year before starting pegloticase.

Results: Pegloticase/immunomodulation co-therapy rates were consistently low (1.2%-3.9%) from 2015 through 2018 (Figure 1). However, this rate markedly increased to 15.0% in 2019. The majority of patients (86%) who started an immunomodulator did so within 30 days of their first pegloticase infusion. Methotrexate was more commonly used as the immunomodulator compared to azathioprine.

Conclusion: A dramatic increase in the use of immunomodulators with pegloticase was observed in 2019, most likely sparked by a case series presented in November 2018 that showed a marked improvement in treatment response rate with methotrexate/pegloticase co-therapy[4,5] compared to pegloticase alone.[2] Therefore, physicians appear to be using DMARDs with increasing frequency in patients with uncontrolled gout who are treated with pegloticase to potentially maximize treatment response rates. Controlled trials are currently ongoing to further validate this therapeutic approach.

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Abstract Number: 0666

Identification of Intracellular Vacuoles in Synovial Fluid with Calcium Pyrophosphate and Monosodium Urate Crystals

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Synovial fluid analysis using polarized microscopy is the gold standard for the diagnosis of crystal-related arthritis. In our experience, we have noted that, when calcium pyrophosphate(CPP) crystals are observed, they sometimes appear within intracellular vacuoles. However, this phenomenon is not seen in those samples containing monosodium urate (MSU) crystals.This finding has been scantly reported in the literature, but may be useful in clinical practice to ensure accurate crystal identification.

Objectives: our study aims to assess hether the presence of vacuoles contributes to identifying the type of crystal, and also to gauge the frequency of their presentation.

Methods: We conducted an observational study in a rheumatology unit between February and June of 2019. Synovial fluids containing CPP or MSU crystals, obtained in daily clinical practice, were consecutively included for analysis. Two observers simultaneously analyzed the presence of vacuoles by ordinary light and phase contrast microscopy in less than 24 hours after their extraction, using a microscope equipped with two viewing stations. The primary study variable was to determine whether CPP and MSU crystals are seen inside intracellular vacuoles, and to calculate the frequency of this finding for each type of crystal, stimating their 95% confidence interval (95% CI) and comparing rates using Fisher's exact test.

Results: Twenty-one samples were obtained. Data is given in the Table. MSU crystals were present in 7 (33.3%) and CPP crystals in 14 (66.6%). Interestingly, none of the MSU samples showed crystal-containing vacuoles (95% CI 0-35.4%). On the contrary, cytoplasmic vacuoles containing crystals were present in all of the CPP samples (95% CI 78.5-100%). The findings were confirmed by phase-contrast microscopy. Differences were statistically significant ($p< 0.001$).

SAMPLES ACCORDING TO TYPE OF MICROCRYSTAL (n=21)	SAMPLES WITH VACUOLES (UNDER ORDINARY LIGHT)	SAMPLES WITH VACUOLES (UNDER PHASE CONTRAST)
CPP (14; 66.6%)	14 (100%) *(95%CI 78.5-100%)*	14 (100%) *(95%CI 78.5-100%)*
MSU (7; 33.3%)	0 (0%) *(95%CI 0-35.4%)*	0 (0%) *(95%CI 0-35.4%)*

Table 1. Results

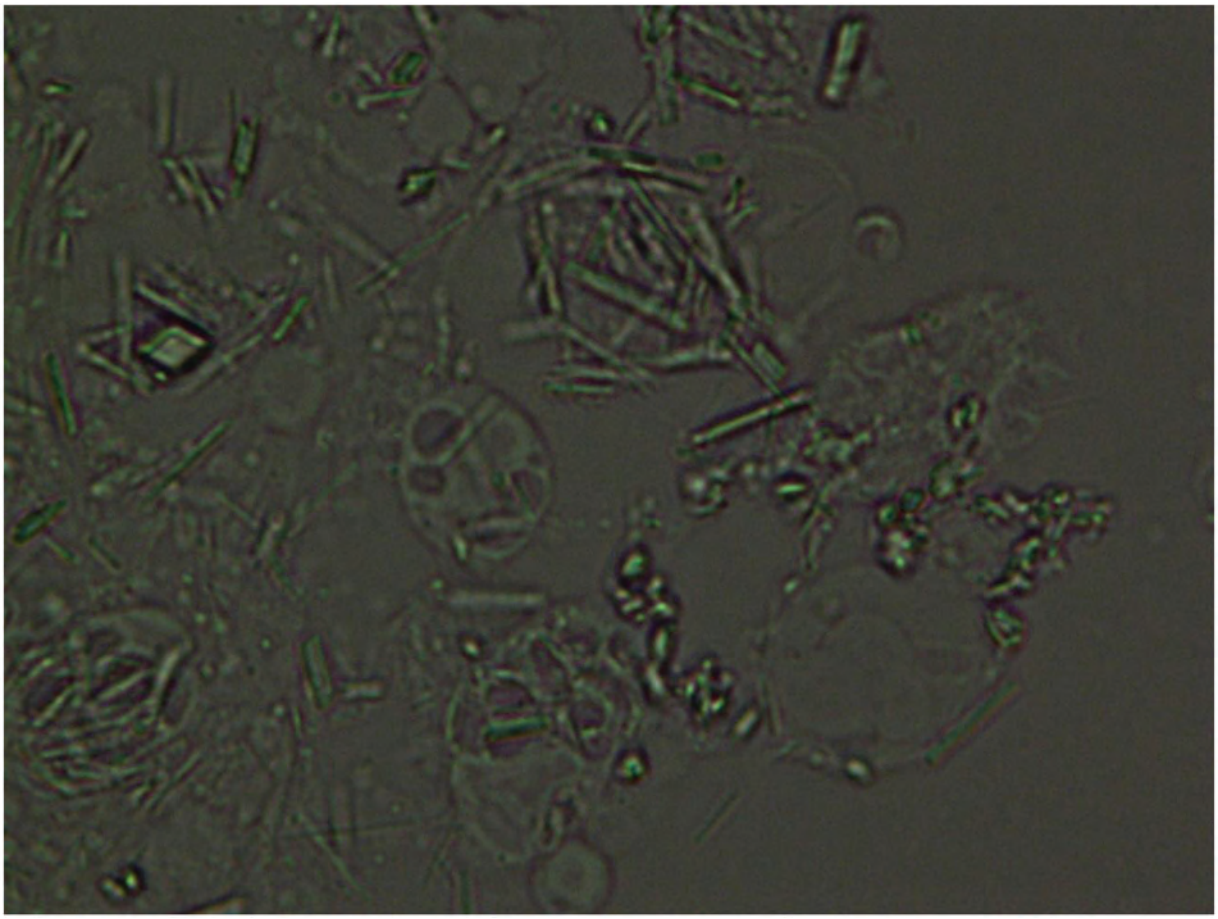

Image 1. Microscopy with ordinary light. Cells with cytoplasmic vacuoles are observed, as well as abundant intra and extracellular CPP crystals.

Conclusion: The presence of vacuoles may be a useful and easy way to differentiate MSU and CPP crystals when performing synovial fluid microscopy in clinical practice, since it appears to be a distinctive feature in CPP crystal fluids.

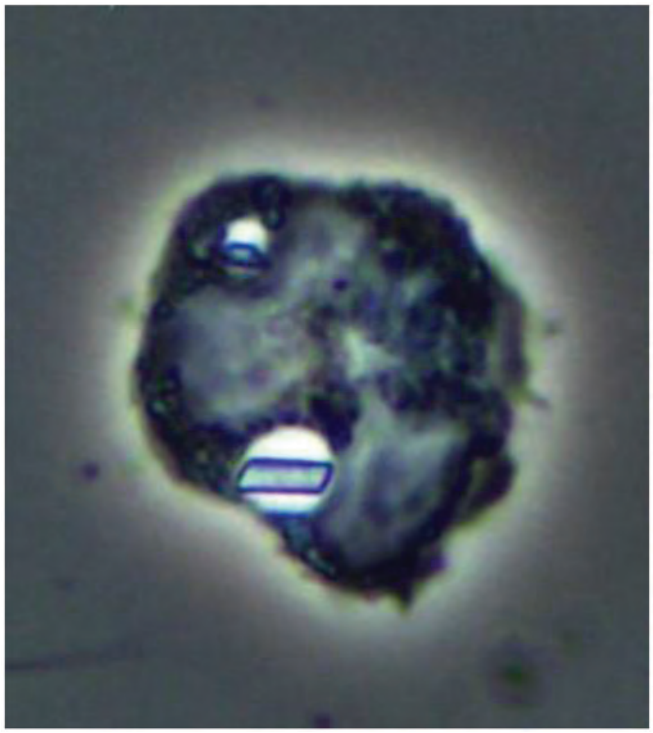

Image 2. Microscopy with phase contrast technique. Cells with intracellular vacuoles are observed inside which have microcrystals with parallelepiped morphology, compatible with CPP.

Disclosure: M. Peral, None; **I. Calabuig**, None; **A. Martín-Carratalá**, None; **M. Andrés**, Grünenthal, 2, 8, Horizon, 8, Menarini, 8; **E. Pascual**, None.

Abstract Number: 0667

Gout Management Beyond Prescription Writing: The Role of the Pharmacist

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SESSION INFORMATION
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Session Title: Metabolic & Crystal Arthropathies Poster
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Background/Purpose: Urate lowering therapy (ULT) is recommended for long-term gout management. However, gout flares are common at the time of starting ULT, and these flares can impact on adherence to ULT. Co-prescription of low dose colchicine as anti-inflammatory prophylaxis is recommended for the first 6 months of ULT. Pharmacists play a key role in community gout education. We investigated pharmacist knowledge of gout treatment. In response to the findings, an educational intervention was developed and assessed in a cohort of Irish pharmacists.

Methods: A ten-question questionnaire about gout management was developed as per Kelley (2003 (1)). Non-random sampling was used. The survey was disseminated through the Pharmaceutical Society of Ireland, PharmaBuddy

Knowledge of Gout Management Survey	Answer Options	Frequency
Where is your primary area of practice?	Community	155 (89.6%)
	Hospital	14 (8.1%)
	Academia	1 (0.6%)
	Industry	1 (0.6%)
	Other	2 (1.2%)
Urate-lowering therapy (ULT) is targeted to serum urate level	True	126 (72.8%)
	False	17 (9.8%)
	Don't Know	28 (16.2%)
First-line therapy for gout involves a combination of a xanthine oxidase inhibitor (e.g. allopurinol) combined with a prophylactic agent (e.g. colchicine)	True	61 (35.3%)
	False	109 (63.0%)
	Don't Know	3 (1.7%)
Colchicine at a dose of 0.5mg twice daily should be given in combination with urate lowering therapy (ULT) for at least 6 months after initiation of ULT, as a prophylaxis for gout flares	True	50 (28.9%)
	False	109 (63.0%)
	Don't Know	14 (8.1%)
It is common for gout to flare when. . .	Starting ULT	66 (38.2%)
	Stopping ULT	28 (16.2%)
	Increasing ULT	3 (1.7%)
	All of the Above	64 (37.0%)
	None of the above	12 (6.9%)
Patients should stop ULT during a gout attack	True	42 (24.3%)
	False	116 (67.1%)
	Don't Know	15 (8.7%)
Patients are advised to take colchicine continuously for six months or longer after initiation of ULT	True	39 (22.5%)
	False	117 (67.6%)
	Don't Know	17 (9.8%)
Patients should dose-reduce rather than stop colchicine if they experience side-effects (e.g. diarrhoea)	True	77 (44.5%)
	False	72 (41.6%)
	Don't Know	24 (13.9%)
Which information sources for colchicine do you find helpful?	BNF	148 (85.5%)
	SPC	100 (57.8%)
	Guidelines (e.g. EULAR or ACR)	15 (8.7%)
Cost of gout medication is a factor in patient non-adherence	Agree	40 (23.1%)
	Disagree	87 (50.3%)
	Neither Agree nor Disagree	46 (26.6%)

Knowledge Of Gout Management Survey

(a pharmacist-only closed forum) and word-of-mouth. Survey analysis employed factor analysis with varimax principal component analysis (PCA) and frequency analysis. An educational intervention was co-developed between a consultant rheumatologist and a general practitioner who also works as a community pharmacist in the form of a 13-minute video tutorial on pharmaceutical gout management. The effectiveness of this intervention was assessed via the same questionnaire in a cohort of n=53 (n=25 intervention group; n=28 control group of pharmacists who had not watched the video). Data was analysed via frequency analysis using Pearson's Chi-Square test for association between groups.

Results: There was n=173 pharmacist respondents to the initial survey. 63% did not know that first-line therapy for gout involves a combination of a xanthine oxidase inhibitor combined with a prophylactic agent. 22.5% of respondents knew patients were advised to take colchicine continuously for six months or longer after initiation of ULT. 28.9% selected 'true' to the statement that colchicine twice daily in combination with ULT acted as a prophylaxis for gout flares. Regarding side-effects, 45% believed patients should dose-reduce rather than stop colchicine if they experience side-effects such as diarrhoea, with 42% selecting false and 14% unsure. (Table 1).

Following educational intervention, pharmacists where more likely to know patients are advised to take colchicine continuously for six months after initiation of ULT (84% intervention group compared to 36% control, p=*0.002*). Furthermore, they understood colchicine was given up to twice daily in combination with ULT as a prophylaxis for gout flares (84% intervention, 32% control, *p=0.001*) and that the goal of ULT is to reduce serum urate level (96% intervention, 68% control, *p= 0.029*). There was no difference in community: hospital practice between intervention and control groups (*p=0.74*).

Conclusion: Gout management recommendations can be impeded if translation into pharmacy practice is neglected. Pharmacists are a valuable information resource for patients. Low-cost educational interventions can greatly improve their knowledge of gout management and in turn empower patients to assume self-management of gout.

Disclosure: E. Dorris, None; **P. Ryan**, None; **M. Kieran**, None; **N. Dalbeth**, AstraZeneca, 1, 2, Abbvie, 1, Arthrosi, 1, Dyve BioSciences, 1, Selecta, 1, Janssen, 1; **G. McCarthy**, None.

Abstract Number: 0668

Outcomes and Resource Utilization After Total Knee Arthroplasty in Calcium Pyrophosphate Crystal Deposition Disease Patients: Insights from the National Inpatient Sample Database

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Total knee arthroplasty (TKA) is one of the most frequently performed orthopedic procedures in patients with joint cartilage destruction. Calcium pyrophosphate crystal deposition (CPPD) disease is a crystal-induced arthropathy characterized by the deposition of calcium pyrophosphate crystals in the articular and periarticular tissues that might lead to inflammatory arthritis, joint damage and the need for TKA. No prior studies exist evaluating the outcomes of CPPD patients after TKA. We aim to determine the in-hospital complications, mortality, and resource utilization following TKA in patients with and without CPPD.

Methods: We queried the US National Inpatient Sample (NIS) Database from 2009-2014 in order to identify patients who had TKA. The ICD-9 code was used to identify the patients who underwent primary TKA (81.54, V43.65), and of those, we classified the patients into two groups: (i) with ICD-9 codes defining CPPD (275.49 and 712.1–712.39) and (ii) those without any CPPD code. Data collection included patient demographics and co-morbidities. Outcomes after-TKA were in-hospital mortality, length of hospitalization, hospital charges, in-hospital complications such as surgical site infections, blood loss and need for transfusion, re-operation, thromboembolism, popliteal artery injury, peroneal nerve palsy. Associations between CPPD and specific morbidity were evaluated with chi-square tests. Wilcoxon rank-sum tests were used for continuous variables.

Results: Among the 4,180,274 (adjusted for sampling weight) patients who have undergone TKA during the 7-year period (2009-2014), 7660 (0.18%) had CPPD, with a median age of 73 years and 57.9% were females (Table). Compared with patients without CPPD, patients with CPPD patients were more likely to be older (median age78 vs 73 years; $p< 0.0001$). Co-morbidities that were more frequent among CPPD patients included chronic kidney disease, gout and knee fracture. Regarding postoperative complications, the need for re-operation was significantly more common in CPPD patients ($p < 0.0001$). Further, TKA in CPPD patients was associated with prolonged median length of stay than those without CPPD (4 vs 3 days; $p < 0.0001$), although the median total charges were higher in the CPPD

Table. Demographics, clinical characteristics, outcomes and resource utilization of patients with and without CPPD who undergone total knee arthroplasty.

	No CPDD, n (%)	CPPD, n (%)	P-value*
Age in years at admission, median (mean ± SD)	71 (72.0 ± 26.2)	78 (75.7 ± 24.2)	<0.001†
Female	2623105 (62.8)	4439 (57.9)	<0.001
Comorbidities			
Diabetes Mellitus	1222731 (29.3)	1859 (24.2)	<0.0001
Congestive heart failure	640450 (15.3)	1090(14.2)	0.071
CKD	600360 (14.3)	1499 (19.5)	<0.001
Obesity	922730 (22.1)	1253(16.3)	<0.001
Gout	215410 (5.1)	682 (8.9)	<0.001
Avascular necrosis	99 (<0.2)	0(0.0)	0.27
Knee fracture	5864(0.14)	25(0.32)	<0.001
Complications during hospitalization			
Surgical site infection	55497 (1.3)	69(0.9)	<0.001
Sepsis	204 (0.01)	<0.1	0.54
Blood loss	232 (<0.01)	0(0.0)	0.51
Reoperation	150 (<0.01)	5(<0.06)	<0.001
Thromboembolism	(1.49)	99 (1.29)	0.15
Myocardial infarction	348355 (8.3)	634 (8.2)	0.83
Intraoperative fracture	6883 (0.16)	0 (0.0)	<0.001
Popliteal artery injury	216 (<0.01)	0 (0.0)	0.52
Peroneal nerve palsy	291 (<0.01)	0 (0.0)	0.46
Resource utilization			
Length of stay, median (mean ± SD)	3 (4.67 ± 10.23)	4 (5.54 ± 12.21)	<0.001†
Total hospital charges, median (mean ± SD)	$30,272 (43753 ± 111227)	$30, 718 (45092 ± 123920)	0.440†
Death during hospitalization	51354 (1.2)	50 (0.65)	<0.001

*Chi-square P except †Wilcoxon rank-sum

group, this finding was not statistically significant ($30,718 vs $30,272; p=0.44). The in-hospital mortality was lower in the CPPD patients (0.65 vs 1.2; p< 0.001).

Conclusion: To our knowledge, this the first study demonstrating that patients with CPPD patients who had undergone TKA were more likely to be older than those without CPPD, had increased length of stay; however, the in-hospital mortality was lower. These findings merit further study.

Disclosure: K. Parperis, None; **M. Hadi**, None; **B. Bhattarai**, None.

Abstract Number: 0669

Calcium Pyrophosphate Crystal Deposition in Gouty Tophi

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SESSION INFORMATION
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Background/Purpose: The coexistence of calcium pyrophosphate (CPP) and monosodium urate crystals is rarely reported in gouty tophi. We investigated CPP crystal deposits in a series of gouty tophi removed by surgery and associated factors.

Methods: 25 tophi from 22 patients were analyzed by light microscopy, field-emission-scanning electron microscopy (FE-SEM) and μ Fourier transform infrared (FTIR) spectroscopy

Results: Tophi consisted of multiple lobules separated by fibrous septa and surrounded by a foreign-body giant cell reaction. CPP crystal aggregates were identified in 8 of 25 tophi from 5 patients. CPP crystals were dispersed or highly compacted, localized at the edge or inside the tophus lobules or filled some of them. Both monoclinic and triclinic CPP crystal phases were identified by FE-SEM and μ FTIR. As compared with patients without CPP, those with CPP-containing tophi were older (mean 61.2 vs 47.8 years, p=0.009), and had long-term gout (mean 19.0 vs 9.0 years, p=0.007) and tophus (mean 11.4 vs 4.7 years, p< 0.0001). None had radiological chondrocalcinosis of the knee or wrist

Conclusion: CPP crystal formation seems to be a late and frequent event of tophus maturation and could contribute to the apparent persistence of tophus sometimes observed even after long-lasting and efficient urate-lowering therapy.

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Abstract Number: 0670

Risk Factors for Pseudogout: An Electronic Medical Record Case-Control Study

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Metabolic & Crystal Arthropathies Poster

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Background/Purpose: Prior studies of calcium pyrophosphate crystal deposition disease (CPPD) epidemiology either focused on the entire spectrum of CPPD or identified patients with its acute manifestation, pseudogout, using single non-validated diagnosis codes. We investigated previously identified risk factors for CPPD or pseudogout—including bisphosphonates, diuretics, osteoarthritis, and hyperparathyroidism—among well-defined pseudogout patients.

Methods: We performed a case-control study by applying a validated algorithm to identify pseudogout cases using electronic medical record (EMR) data (PPV 81%) at an academic medical center. Case index date was the earlier of 1st positive synovial fluid calcium pyrophosphate crystal analysis or 1st natural language processing concept "pseudogout" in narrative notes. Cases were matched to up to 4 general EMR controls not classified as pseudogout by the algorithm. Matching occurred on year of 1st EMR encounter and index date (encounter ±30d of case index date). We required age ≥50 at index date and ≥2 encounters in the 365 days before index date for cases and controls. We pre-specified covariates of interest: (1) comorbidities previously associated with CPPD in the literature, identified by ≥1 billing code from 1st EMR encounter through index date and (2) prescriptions for medications previously associated with CPPD in the literature, recorded in the 90 days prior to and including index date. A multimorbidity score was calculated for each patient using a validated method based on billing codes for 40 conditions. A multivariable logistic regression model estimated the odds ratio (OR) and 95% CI for each pre-specified covariate adjusted for age, total number of encounters from 1st EMR encounter through index date, multimorbidity score, and all pre-specified covariates.

Table. Characteristics and odds ratios (95% CI) for pseudogout

	Acute CPP crystal arthritis cases n=1856	General patient controls n=7180	Multivariable-adjusted odds ratio (95% CI)*
Male	47.7	43.0	1.42 (1.25, 1.61)
Race			
White	82.3	80.2	1.00 (Ref)
Black	7.4	10.9	0.53 (0.42, 0.67)
Other or unknown	10.2	9.0	1.03 (0.84, 1.26)
Comorbidities*			
Osteoarthritis	66.4	30.2	3.92 (3.43, 4.48)
Hyperparathyroidism	4.4	1.2	2.36 (1.54, 3.64)
Hypomagnesemia	2.9	0.6	2.07 (1.18, 3.62)
Hypophosphatasia	0.8	0.2	1.20 (0.50, 2.85)
Hemochromatosis	0.7	0.1	6.43 (2.02, 20.43)
Medications**			
Proton pump inhibitor	26.3	9.6	2.00 (1.69, 2.37)
Loop diuretic	15.7	5.8	1.75 (1.42, 2.15)
Thiazide diuretic	10.7	6.4	1.38 (1.11, 1.72)
Bisphosphonate	3.9	2.4	1.06 (0.75, 1.49)

Values are percentages or odds ratio (95% CI)

*Multivariable model includes all covariates listed in the table, age at index date, total number of encounters from 1st EMR encounter through index date, and multimorbidity score based on ICD-9 billing codes for 40 chronic conditions (Radner H, et al. Seminars Arthritis Rheum 2015;45:167-73)

*Defined by ≥ 1 ICD-9 or ICD-10 from 1st EMR encounter through index date

**Prescribed at any time from 90 days before index date through index date (oral or intravenous)

Results: We identified 1856 cases matched to 7180 controls. Mean age was 73 years, 56.0% were female, 80.6% white, 10.2% black, and 9.2% other/unknown race. Among pseudogout patients, 12.8% were age 50-59, 25.9% age 60-69, 31.7% age 70-79, and 29.6% age ≥80. Each of the pre-specified covariates were more common in pseudogout cases than controls (Table). Risk for pseudogout was significantly higher for patients with osteoarthritis (OR 3.92), male sex (OR 1.42), proton pump inhibitors (OR 2.00), loop diuretics (OR 1.75), thiazides (OR 1.38), and rare metabolic disorders including hyperparathyroidism, hypomagnesemia, and hemochromatosis. Bisphosphonates were not significantly associated with pseudogout. Black race was associated with significantly lower risk for pseudogout compared to white race (OR 0.53).

Conclusion: Using a validated algorithm to identify >1800 pseudogout cases, we identified important metabolic correlates of this acute manifestation of CPPD. This is the first study to report higher risk for pseudogout among men and lower risk among black compared to white patients. We confirmed several previously published risk factors, but in contrast to prior studies we did not identify an association between bisphosphonates and pseudogout.

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Abstract Number: 0671

Structured Cardiovascular Assessment in Gout Incorporating Carotid Ultrasound: Analysis of Subsequent Events in the Follow-Up

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SESSION INFORMATION
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Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is an independent cardiovascular (CV) risk factor. This excess of morbidity and mortality requires optimal management, especially in high-risk individuals. Therefore, the inclusion of subclinical atherosclerosis screening by carotid ultrasound in the initial evaluation may help to accurately stratify the CV risk. However, longitudinal outcomes using this approach are not available in gout. This study aimed to analyze the new CV events occurred in patients with gout after structured CV assessment incorporating carotid ultrasound.

Methods: Retrospective analysis of an inception cohort of patients with crystal-proven gout. At baseline, a structured CV assessment was performed considering age, gender, traditional risk factors, CV and renal disease, laboratory data, SCORE and Framingham risk tools, and carotid ultrasound; according to 2013 ESC guidelines, CV risk was stratified as low, moderate, high or very high. The cohort includes 356 patients, mean (SD) aged 64 years (14.0), mostly males (86.0%), 21.8% with tophaceous gout and mean serum urate at diagnosis of 8.2mg/dL (1.8). The CV risk stratification at baseline was low in 20 patients (5.6%), moderate in 47 (13.2%), high in 34 (9.6%), and very high in 242 (68.0%). Major CV events (coronary heart disease (CHD), heart failure (HF), stroke, peripheral artery disease (PAD) and CV death) were recorded during the follow-up by electronic case reports review. A binary composite endpoint of *new major CV events* was used. The incidence after inclusion in the cohort was estimated. To evaluate potential baseline predictors (clinical and gout-related) of CV events, a Cox regression model was built.

	Simple Cox regression		Multiple Cox regression	
	Hazard ratio (95%CI)	*P*	Hazard ratio (95%CI)	*P*
Very high CV risk at baseline	9.54 (2.30-39.64)	**0.002**	4.11 (0.89-19.02)	0.070
Age	1.07 (1.04-1.11)	**<0.001**	1.04 (1.00-1.08)	**0.031**
Female gender	3.27 (1.68-6.33)	**<0.001**	1.24 (0.55-2.81)	0.605
Body mass index	1.00 (0.94-1.06)	0.863	-	-
Glomerular filtration rate	0.98 (0.97-0.99)	**<0.001**	1.00 (0.99-1.01)	0.766
Serum urate at diagnosis	1.19 (1.00-1.42)	0.052	1.12 (0.94-1.33)	0.227
ULT at diagnosis	0.81 (0.29-2.27)	0.688	-	-
Tophi	1.33 (0.66-2.66)	0.422	-	-
Years since first flare	1.00 (0.97-1.03)	0.772	-	-
Number of flares suffered	0.99 (0.97-1.00)	0.255	-	-
Number of involved joints	1.00 (0.89-1.12)	0.976	-	-
Joint pattern at presentation				
- *Monoarticular*	1.00 (ref)	-	1.00 (ref)	-
- *Oligoarticular*	1.86 (0.91-3.80)	0.089	1.35 (0.65-2.82)	0.421
- *Polyarticular*	2.75 (1.05-7.22)	**0.039**	1.34 (0.48-3.76)	0.579

Table. Analysis of baseline predictors of new cardiovascular events in the follow-up.

Results: Mean (SD) follow-up in the cohort was 41.5 months (16.8). Forty new major CV events have been identified (incidence 3.25 /100patient-year), distributed as follows: HF 1.46 (n=18), CV death 0.65 (n=8), CHD 0.49 (n=6), stroke 0.33 (n=4), and PAD 0.33 /100patient-year (n=4). Per risk stratification, the incidence of a new event was 0.16/100patient-year in the high-risk group and 3.01 /100patient-year in the very high-risk, while no events occurred in low and moderate groups. Noteworthy, five events occurring in the moderate (three) and high-risk (two) groups formed without considering carotid findings, were captured in the very-high risk group after the complete assessment.

The table shows the univariate and multivariate analysis of baseline predictors. An independent association and a trend towards significance were noted for age and to be classified at a very-high CV risk at baseline, respectively.

Conclusion: First longitudinal study assessing the use of subclinical atherosclerosis screening as part of CV risk assessment in new patients with gout. Those classified at the very high-risk group presented the majority of events, being HF the most frequent. Age, and likely being classified as very-high risk, independently predicted a new CV event during follow-up, data that may be of interest for the management of patients with gout at the time of diagnosis.

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Abstract Number: 0672

Prospective Study of the Patterns of Joint Involvement for Sequential Gout Flares

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SESSION INFORMATION
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Background/Purpose: Cross-sectional radiologic evidence suggests monosodium urate crystal deposition among gout patients is a symmetrical phenomenon,[1] but no study has examined the longitudinal patterns in the locations of clinically symptomatic gout flares. We used data from a longitudinal follow-up study of individuals with gout to evaluate patterns in joint involvement for sequential gout flares.

Methods: We used data from the Boston Online Gout Study, a longitudinal internet-based case-crossover study conducted between 2003 and 2012. Gout patients who had at least one gout flare in the past year and lived in US were recruited online. Diagnosis was confirmed by medical record review. Participants were followed prospectively online. When a participant experienced a gout flare, s/he logged into the study website and answered a series of questions, indicating (on a homunculus) the joint(s) where the gout flare occurred. Possible joints included were the big toe, other toes, instep (mid-foot), heel, ankles, knees, elbows, wrists, and fingers.

Among subjects who reported at least two gout attacks during the follow-up period, we calculated the risk of the second gout flare occurring at the ipsilateral same location, according to the first gout flare in a given joint during the study, using Generalized Estimating Equations with log-binomial distribution model. We repeated the same analyses for the risk of having gout flare at the contralateral same location.

Results: We included 374 participants (mean age 55±12 years, 78% male, 37% overweight, 55% obese, mean gout duration 8.6±9.3 years) who experienced at least two gout attacks. Overall, the risk of flare was highest at the big toe, followed by the instep and ankle (**Table 1**).

For all nine sites evaluated, the magnitude of association between the first gout flare at a specific joint, and the risk of subsequent flare at the ipsilateral same location (e.g., left 1st MTP à left 1st MTP), was much stronger than the risk for the contralateral same joint (e.g., left 1st MTP à right 1st MTP) (**Table 2**). For example, participants affected in the left big toe during the first flare were 2.52-times more likely to experience their second flare in the left big toe (95%

Site	First Flare	Subsequent Flare	
	N Affected (% of all Joints)	Risk of Occurrence at Ipsilateral Same Location (vs. other sites)	Risk of Occurrence at Contralateral Same Location (vs. other sites)
Big Toe	233	0.39	0.16
Instep	159	0.36	0.13
Ankle	138	0.36	0.11
Knee	78	0.29	0.06
Heel	58	0.24	0.06
Other Toe	57	0.19	0.07
Finger	54	0.39	0.05
Wrist	40	0.43	0.04
Elbow	28	0.43	0.03

Table 1. Prevalence of Sites Affected During the First Flare, and Risk of Occurrence in Same Site During the Second Flare

Site	RR (95% CI) for Ipsilateral Same Location*	RR (95% CI) for Contralateral Same Location **	Ratio of RR: Ipsilateral/Contralateral
Big Toe	2.52 (1.93 to 3.29)	1.21 (0.90 to 1.62)	2.08
Instep	2.79 (2.07 to 3.77)	1.41 (1.03 to 1.94)	1.98
Ankle	3.07 (2.18 to 4.33)	1.64 (1.14 to 2.34)	1.87
Knees	4.17 (2.62 to 6.63)	1.82 (1.07 to 3.10)	2.29
Heel	4.06 (2.15 to 7.65)	1.35 (0.57 to 3.21)	3.01
Other Toe	3.09 (1.65 to 5.75)	0.60 (0.21 to 1.73)	5.15
Fingers	5.30 (2.70 to 10.40)	2.11 (1.02 to 4.35)	2.51
Wrist	9.25 (5.01 to 17.06)	1.59 (0.81 to 3.10)	5.82
Elbow	9.53 (4.84 to 18.79)	1.67 (0.78 to 3.55)	5.71

*mutually adjusted for the same joint on the contralateral side
**mutually adjusted for the same joint on the ipsilateral side

Table 2. Relative Risk (RR) of a Second Flare Occurring in the Same Site as the First Flare, on the Ipsilateral and Contralateral Sides

CI 1.93 to 3.29), versus a different site, and 1.21-times more likely to experience their next flare in the right big toe (95% CI 0.90 to 1.62), versus a different site. Ratio of relative risk ranged from 1.87 at the ankle to 5.82 at the wrist.

Conclusion: Among this community-based cohort of gout patients, the risk of recurrent gout flare was highest at big toe joint, and at all sites, subsequent flares were more likely to occur at the ipsilateral same joint than the contralateral same joint. These flare patterns facilitate diagnosis of gout flares during subsequent episodes and may also have pathogenetic implications such as sufficient composition of causal factors repeated in the same location.

[1]Yokose C *et al*. Radiologic evidence of symmetric and polyarticular monosodium urate crystal deposition in gout – A cluster pattern analysis of dual-energy CT. *Sem Art Rheum*. 2020; 50(1):54-8.

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Abstract Number: 0673

Gout Is an Independent Risk Factor for Undergoing an Amputation Procedure

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Background/Purpose: Gout can cause uric acid deposition in joints, soft tissues, and organs (1) and is associated with heart disease, kidney disease, hypertension, hyperlipidemia, diabetes, and metabolic syndrome (2). Infected tophi, osteomyelitis, and diabetic ulcers can appear clinically similar which can cause clinical challenges in diagnosis and treatment (3). Uncontrolled gout can lead to amputation, but amputations in patients with gout are rarely described in the literature. It is well known that patients with diabetes are at increased risk for requiring amputation procedures, along with subsequent adverse health sequelae and mortality (4,5). The current population-based study assessed and compared amputation risk in populations with gout, diabetes, and concomitant gout and diabetes to investigate a potential association between gout and increased risk of amputation. Patients without gout or diabetes were examined as a control group.

Methods: The TriNetX "Diamond" network is a large U.S. claims database that contains data from 190 million patients. Data were used to examine the occurrence of amputation procedural codes (foot, toes, hand, fingers) in adult patients with gout and in those with diabetes. Groups were further stratified into patients with diabetes only, gout only, both diabetes and gout, and neither diabetes nor gout (control).

Results: A total of 4,467,721 patients with gout and 25,972,726 patients with diabetes were identified. Amputation rate in patients with diabetes (regardless of gout comorbidity) and gout (regardless of diabetes comorbidity) was comparable at 0.484% and 0.434%, respectively. However, non-overlapping gout and diabetes cohorts had different amputation rates (gout only: 0.162%, n=2,471,430; diabetes only: 0.461%, n=23,976,435), but both were higher than in the control population (no gout or diabetes: 0.035%, n=144,705,645; 4.6- and 13.2-fold higher, respectively). Patients with both gout and diabetes (n=1,996,291) had the highest amputation rate of 0.770%, which was 1.7-fold higher than the diabetes only population and 22.0-fold higher than the control population. The amputation rate in all groups differed significantly from the control ($p< 10^{-16}$).

Conclusion: This large population-based study demonstrated that patients with gout only, diabetes only, and comorbid gout and diabetes had amputation rates 4.6, 13.2, and 22.0 times higher than patients without gout or diabetes, respectively. These findings indicate that increased risks of amputation incurred by patients with diabetes and gout are independent and synergistic. Given that both conditions are associated with cardiovascular, renal, and metabolic complications, independent risk was expected, but additive risk was not. More research is needed to understand prognostic patient features underlying this amputation rate increase.

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Disclosure: B. LaMoreaux, Horizon Therapeutics plc, 1, 2; **M. Francis-Sedlak**, Horizon Therapeutics plc, 1, 2; **S. Neville**, Horizon Therapeutics plc, 1, Integra Life Sciences, 1, Flower Orthopedics, 1; **R. Holt**, Horizon Therapeutics plc, 1, 2.

Abstract Number: 0674

Disease Control of Hyperuricemia Newly Detected by Medical Check-up: A Retrospective Cohort Study of Health Insurance Claims Data in Japan

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Japanese guidelines for managing gout and hyperuricemia recommend the initiation of urate-lowering therapy (ULT) to prevent gouty arthritis in subjects having asymptomatic hyperuricemia with serum uric acid (sUA) ≥8.0 mg/dL under certain conditions [Yamanaka H. Japan Med Assoc J. 2012;55:324-9.]. This is a distinctive difference from policies in Europe and the US. However, we lack clear documentation of the extent of clinical treatment for asymptomatic hyperuricemic subjects and of correlations between such treatment and the prevention of gouty arthritis. This study evaluated the association between disease control, defined as the relationship among prescription of ULT, occurrence of gouty arthritis, and level of sUA after 1 year, and gouty arthritis in subjects with asymptomatic hyperuricemia newly detected at medical check-up.

Methods: This research is based on Japanese health insurance claims and medical check-up data from April 2012 through June 2019. We identified subjects who had sUA ≥8.0 mg/dL in one or more medical check-ups from April 1, 2013 to March 31, 2016. The earliest available measurement date during that period was considered the index date. Subjects of analysis were health insurance subscribers whose records did not show the disease name of “gout” or “asymptomatic hyperuricemia” and for whom ULT had not been prescribed during the 1-year period prior to the index date. From the index date to the medical check-up 1 year later (follow-up date) was considered Period 1, and from the day after the follow-up date was considered Period 2. Disease control was investigated during Period 1, and disease burden (incidence rate of gouty arthritis) was assessed in relation to disease control during Period 2 (Figure 1).

Results: The analysis population consisted of 19,261 health insurance subscribers who met the eligibility criteria. During Period 1, ULT was initiated in 8.4% of that group (1,625 /19,261). Gouty arthritis was experienced by 3.1% (597/19,261), of whom 32.3% (193/597) were not under treatment with ULT. For 90.6% (17,443/19,261), no ULT was prescribed and no gouty arthritis was experienced during Period 1. Within that group, 40.4% (7,049/17,443) showed sUA ≥8.0 mg/dL on the follow-up date. Only 2.3% (438/19,261) had been prescribed ULT and had achieved sUA ≤6.0 mg/dL by the follow-up date (Figure 2). During Period 2, the incidence rate of gouty arthritis was calculated for each

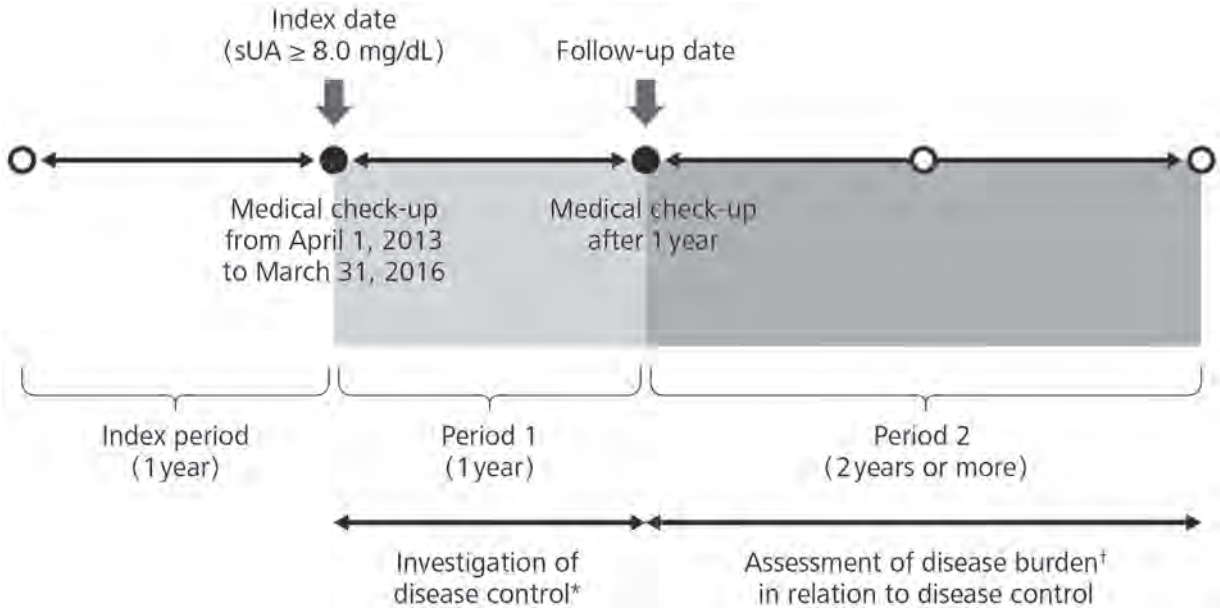

Figure 1 Study design * Disease control: Relationships among prescription of ULT, occurrence of gouty arthritis, and level of sUA after 1 year † Incidence rate of gouty arthritis sUA, serum uric acid; ULT, urate-lowering therapy

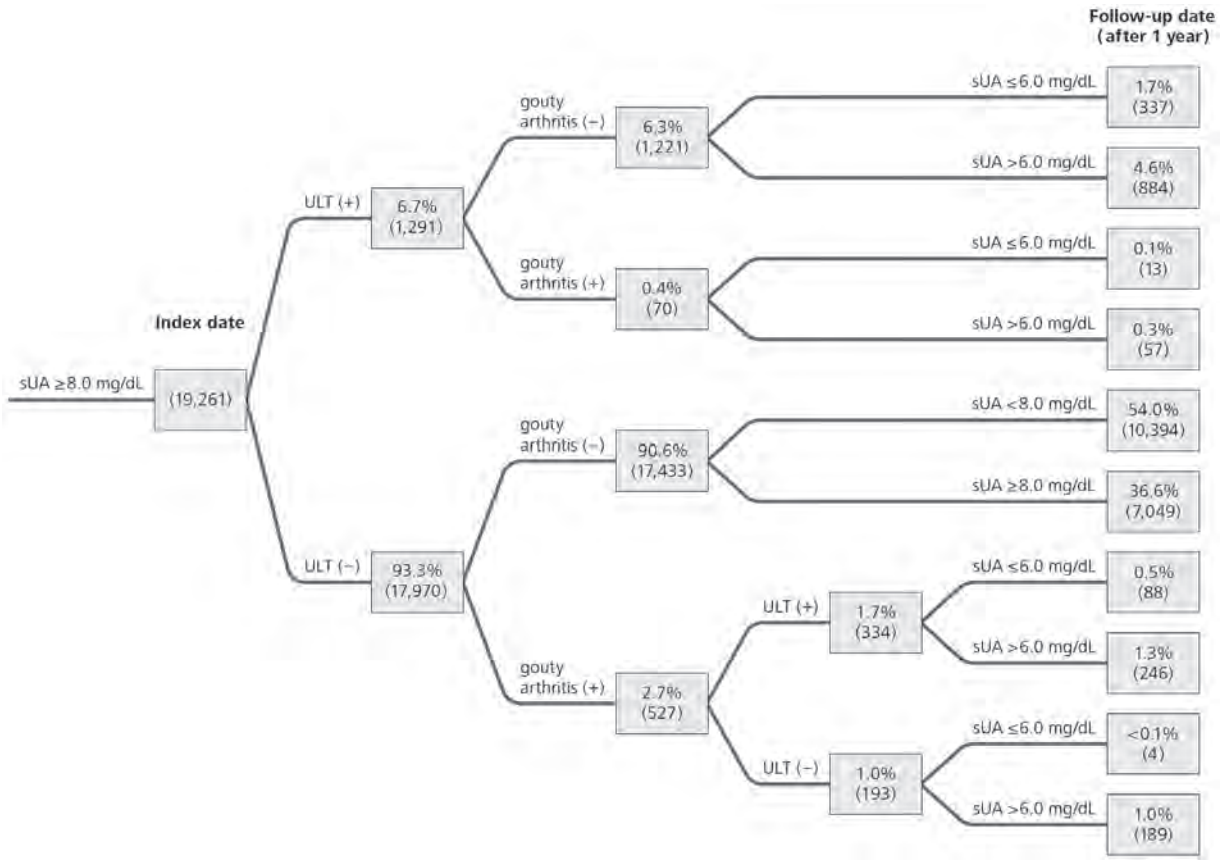

Figure 2 Event tree analysis of disease control from index date to follow-up date (Period 1) Parentheses indicate the number of subjects. For percentages, the denominator was 19,261 subscribers. sUA, serum uric acid; ULT, urate-lowering therapy

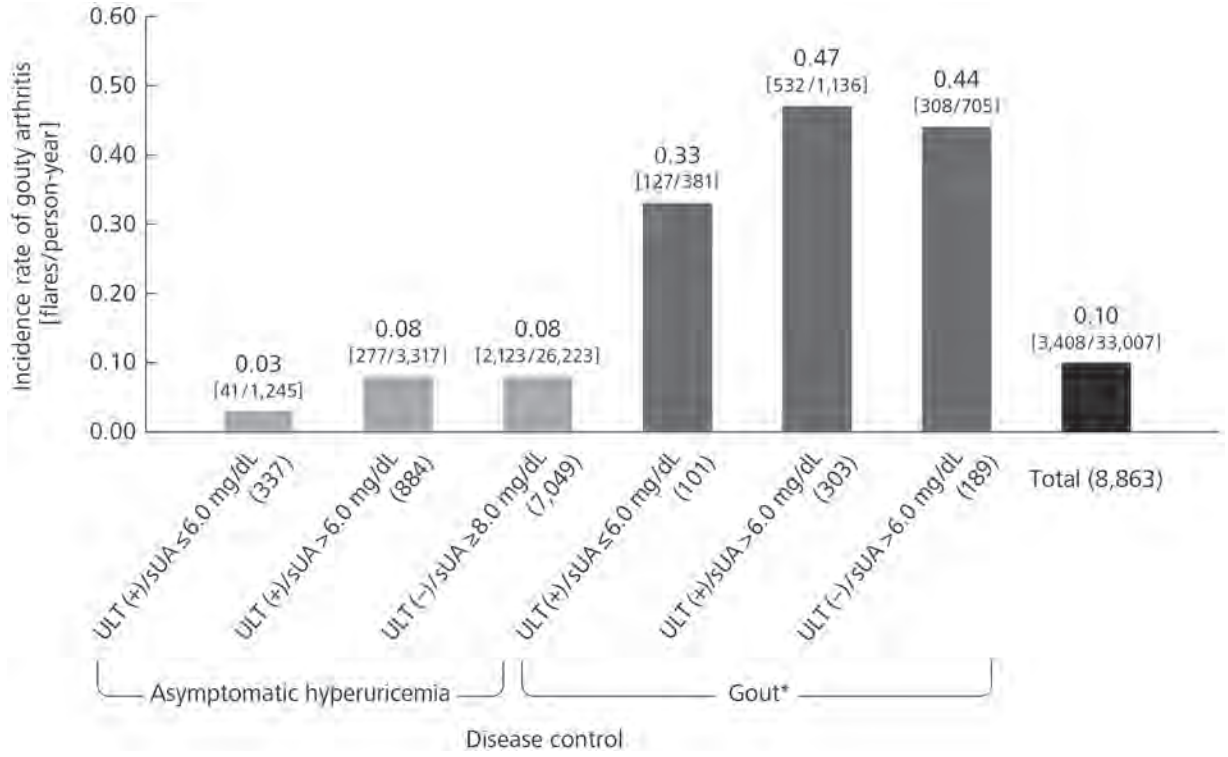

Figure 3 Incidence rate of gouty arthritis during Period 2 Parentheses indicate the number of subjects. Brackets indicate the number of flares/person-years. * Subjects who had experienced at least one incident of gouty arthritis during Period 1. sUA, serum uric acid; ULT, urate-lowering therapy

type of disease control assessed during Period 1. Both for asymptomatic hyperuricemia and for gout in subjects who had experienced at least one incident of gouty arthritis during Period 1, the incidence rate of gouty arthritis during Period 2 was lower in subjects who had sUA ≤6.0 mg/dL than in those whose sUA was >6.0 mg/dL, with or without ULT (Figure 3).

Conclusion: Of those subscribers with newly detected hyperuricemia according to medical check-up records, only 2.3% had been prescribed ULT and had achieved sUA ≤6.0 mg/dL for the 1-year period. Both for asymptomatic hyperuricemia and for gout, the incidence rate of gouty arthritis was lower in subjects whose sUA was ≤6.0 mg/dL than those whose sUA was >6.0 mg/dL, with or without ULT. Further analysis by adjusting for confounding will be required to discuss causality.

Disclosure: R. Koto, Teijin Pharama Limited, 3; **A. Nakajima**, Teijin Pharma Limited, 3; **H. Horiuchi**, Teijin Pharma Limited, 3; **H. Yamanaka**, Teijin Pharma Limited, 8.

Abstract Number: 0675

AR882, a Potent and Selective Uricosuric Agent, Significantly Reduced Serum Urate Levels Following Multiple Ascending Once-Daily Doses in Healthy Subject Volunteers

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: AR882 is a potent and selective uric acid transporter 1 (URAT1) inhibitor under development for the treatment of hyperuricemia or gout. AR882 exhibited linear pharmacokinetic (PK) properties, dose-dependent serum urate (sUA) lowering effect and was well tolerated in a single ascending dose (SAD) study in humans. A multiple ascending dose (MAD) study was therefore conducted in healthy subjects to evaluate the PK, pharmacodynamic (PD) and safety profiles of AR882 following once-daily (QD) doses for 10 days.

Methods: In this randomized, double-blind, placebo-controlled MAD study, 30 healthy male volunteers received AR882 oral capsules under fasted conditions at 25, 50, or 75 mg (ten subjects per group [8 active and 2 placebo]). On Day -1, Day 1 and Day 10, serial blood samples were collected for measurement of AR882 plasma concentrations and sUA levels for PK/PD assessments. Urine samples were collected at 6- to 12-hour intervals for assessment of uric acid excretion. Adverse events, laboratory safety tests, vital signs, and electrocardiograms were collected throughout the study.

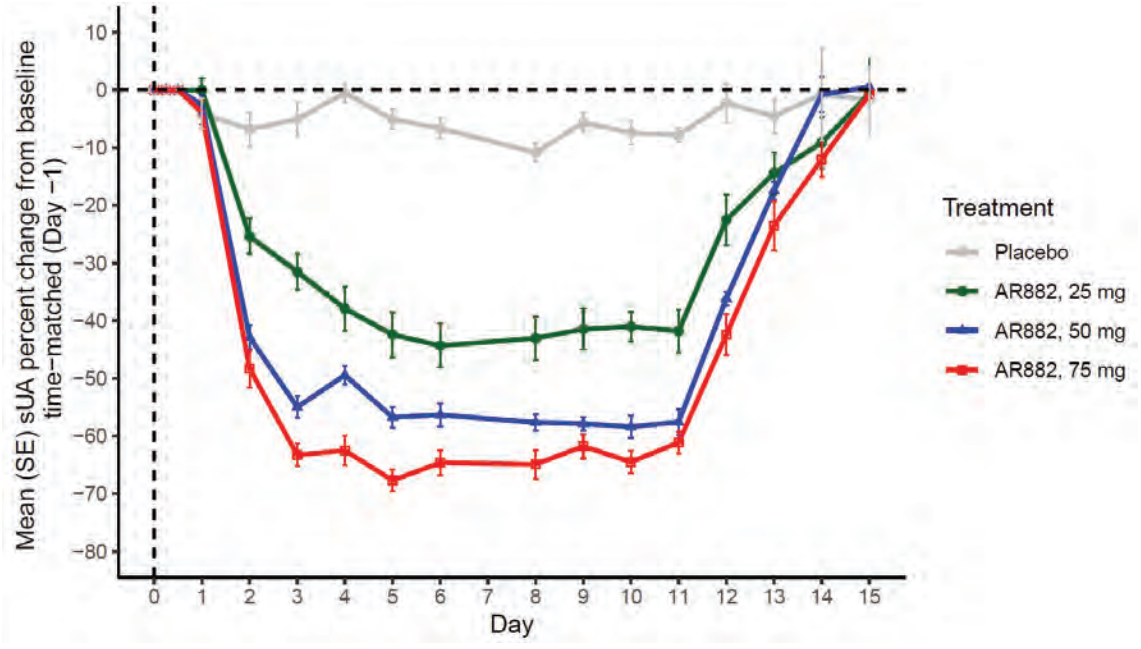

Figure Mean Serum Urate Concentrations: Percent Change from Baseline Following Once-Daily Oral Doses of AR882

Results: Following QD administration, AR882 plasma levels exhibited dose proportional increases between 25 and 75 mg. AR882 exposures were well below those observed at the no-observed-adverse-effect level (NOAEL) in preclinical studies. The median T_{max} ranged between 1.5 and 3.5 hours postdose, and accumulation in C_{max} and AUC was between 30-50%. On Day 10 predose, AR882 showed significant PD effects by reducing sUA concentrations by 41%, 58%, and 65%, respectively, following 25, 50, and 75 mg doses. Steady-state sUA lowering effect was achieved after approximately 5 days. Higher amounts of uric acid were eliminated through urine on Day 1 at all collection intervals. On subsequent days, daily urine uric acid gradually decreased. Fractional excretion of uric acid (FEUA) showed dose-dependent increases on Day 1 and Day 10, consistent with reduction in serum urate levels. AR882 was well tolerated at all doses tested. All AEs were mild, there were no discontinuations due to AEs, and no serious adverse events (SAEs) were reported. There were no clinically significant laboratory or ECG abnormalities noted.

Conclusion: Following once-daily doses over a 10-day treatment period, AR882 exhibited significant sUA lowering effects at all doses tested (58% at Day 10 predose and up to 67% maximum intraday reduction at 50 mg). These results support the potential utility of AR882 when given once-daily to treat hyperuricemia or gout. Studies in patients are underway.

Disclosure: Z. Shen, None; **E. Polvent**, arthrosi therapeutics, 3; **V. Hingorani**, None; **A. Clouser-Roche**, MedImpact PBM, 3, MedImpact PBM, 3; **C. Mikelatis**, None; **R. Yan**, None; **S. Yan**, None; **L. Yeh**, None.

Abstract Number: 0676

Surveying Practicing Rheumatologists Regarding Gout Management and Barriers in Gout Care

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The management of gout is heterogeneous across specialties and clinical settings. Gout has been demonstrated to be one of the most poorly managed conditions in healthcare. Identifying the gaps in gout management can help in focusing research to identify novel interventions or models of care that may enhance gout management and improve clinical outcomes. The purpose of this study was to assess current practices and perspectives in gout management regarding the etiology of substandard gout management amongst rheumatologists internationally.

Methods: A cross-section non-compensated survey of rheumatologists across the world was distributed to practicing rheumatologist members of the ACR and Gout, Hyperuricemia and Crystal-Associated Disease Network (G-CAN) using a 28-item questionnaire designed to evaluate current clinical practice of gout management and to assess barriers to optimal gout management. This was an anonymous internet survey open from 05/1/2020 to 05/14/2020.

Results: The survey had a response rate of 8.5% (161/1900) with 60.2% being male. The age groups of respondents was evenly distributed from under 35 to great than 66 years. Majority of respondents had greater than 10 years of

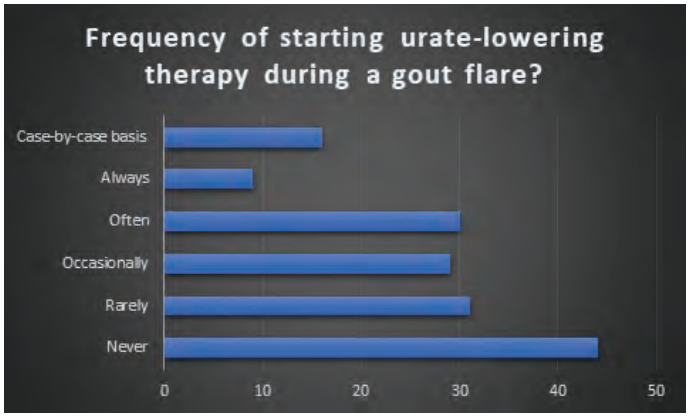


Figure 1

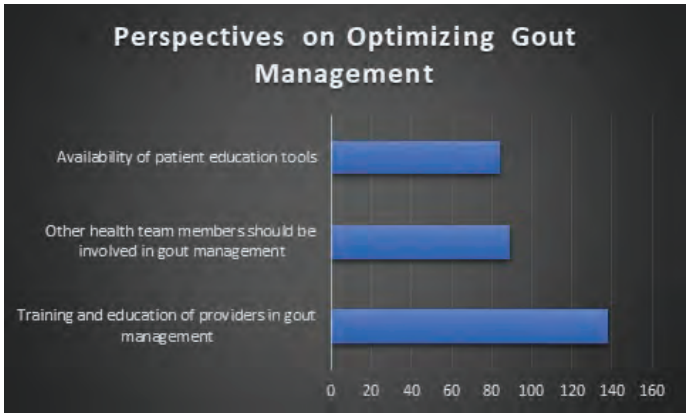


Figure 2

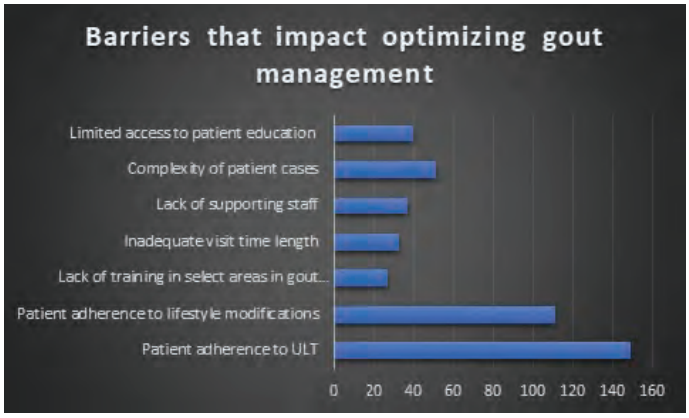


Figure 3

clinical practice (65.6%). 70.2% were academic rheumatologists. 71.4% practiced in the United States. 31.3% of respondents were G-CAN members. The mean number of gout cases seen per month by respondents was 21.3 with a median of 10. The overall survey results were concordant with the 2020 ACR guidelines. Two areas of discordance with these guidelines were identified. 1) 64.6% of respondents preferred not to start ULT during an acute flare. (Figure 1) 2) 59.6% of respondents reported “never” or “rarely considered” HLA-B*58:01 genetic testing.

Regarding improving gout management, respondents identified patient compliance with ULT (94.3%) and lifestyle changes (70.3%) as the predominant factors(Figure 2). From the perspective of healthcare improvement of gout care,

physician education, involvement of other members of the healthcare team, and better access to patient education tools, were all identified as areas of potential improvement(Figure 3).

Conclusion: Despite the modest response rate, our study highlights a variety of targets to improve care of patients with gout. Education for physicians regarding the potential benefits of initiation of ULT during an acute flare appears to be a straightforward concept to address. The polled rheumatologist's current gout management practices per our survey results are consistent with the 2020 ACR gout management guidelines. This consistency in guideline directed care of gout patients provides evidence for a rheumatologist directed gout care team.

We identified two main areas of focus for future studies based on our results: 1) Methods of assisting patients with adherence to ULT and lifestyle changes 2) Enhanced inclusivity of the entire healthcare team in treatment of gout patients. Programs targeting these gaps may lead to better management of gout by the healthcare system and aid in reducing the prevalence of this burdensome disease.

Disclosure: J. Gavin, None; **Y. KC**, None; **E. Dombrosky**, None; **N. Shah**, None; **Y. Roman**, None.

Abstract Number: 0677

A Multicenter, Efficacy and Safety Study of Methotrexate to Increase Response Rates in Patients with Uncontrolled GOut Receiving Pegloticase (MIRROR): 12-Month Results of an Open-Label Study

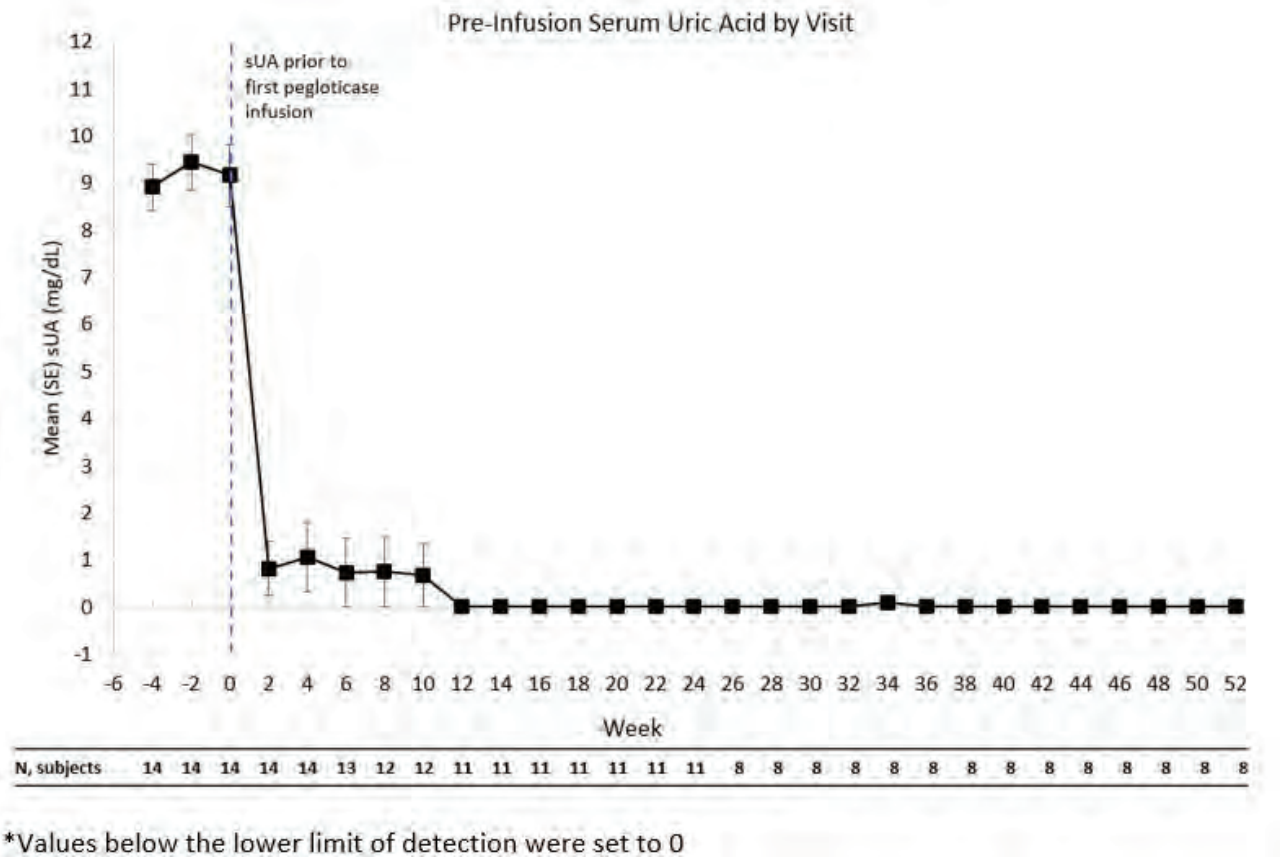
John Botson[1], Paul Peloso[2], Katie Obermeyer[3], Brian LaMoreaux[3], Lin Zhao[3], Michael Weinblatt[4] and Jeff Peterson[5], [1]Orthopedic Physicians Alaska, Anchorage, AK, [2]Horizon Therapeutics plc, Gurnee, IL, [3]Horizon Therapeutics plc, Lake Forest, IL, [4]Brigham and Women's Hospital, Boston, MA, [5]Western Washington Medical Group Arthritis Clinic, Bothell, WA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Consistent, though limited, published data suggests that methotrexate (MTX) improves treatment response in patients treated with pegloticase for uncontrolled (refractory) gout. Recent case series[1-3] (25 patients total) showed an 80%-100% response rate in patients co-treated with MTX and pegloticase, versus the 42% response rate reported in clinical trials with pegloticase monotherapy. The current clinical trial prospectively examined efficacy and safety of pegloticase in patients with uncontrolled gout who were co-treated with oral MTX.

Methods: This study included adult patients from 6 sites. Uncontrolled gout was defined as serum uric acid (sUA) ≥6 mg/dL with ≥1 of the following: sUA ≥6 mg/dL despite oral urate lowering therapy (ULT), intolerance to ULT, or functionally limiting tophaceous deposits. Key exclusion criteria included immunocompromised status, G6PD deficiency, severe renal impairment, and MTX contraindication. Oral MTX (15 mg/wk) and folic acid (1 mg/day) were initiated 4 wks prior to the first pegloticase infusion and were continued during pegloticase therapy (8 mg every 2 wks). The protocol originally consisted of 24 wks of co-therapy, but was amended to extend to 52 wks. Primary outcome was the proportion of responders during Month 6 (sUA < 6 mg/dL for ≥80% of time). Analyses were performed on the modified intent-to-treat (mITT) population (patients who received ≥1 pegloticase infusion).

Figure. Pre-infusion serum uric acid levels (sUA) during the MTX Run-in and Pegloticase + MTX treatment period.



*Values below the lower limit of detection were set to 0

Results: 14 patients made up the mITT population. All patients were male with a mean age 49.3 ± 8.7 yrs. The time since diagnosis of gout was 13.8 ± 7.4 yrs. Mean sUA was 9.2 ± 2.5 mg/dL before the first pegloticase infusion. 12 patients had visible tophi. Eleven patients (78.6%, 95%CI: 49.2-95.3%) were considered 6-month pegloticase responders and 3 non-responders discontinued pegloticase after 2 consecutive sUA levels >6 mg/dL. Of the 11 patients who were responders in month 6, 1 did not extend (pre-protocol amendment), 2 discontinued pegloticase due to meeting their treatment goals (continued on allopurinol; 1 met responder definition during month 12), and 8 continued pegloticase/MTX co-therapy and remained responders at Month 12. Mean sUA over time is displayed in Figure. Gout flares occurred in 13/14 patients (92.9%) in the first 12 weeks and in 2/8 (25%) patients in weeks 36-52. A serious adverse event (AE) of sepsis occurred in 1 patient in the first 6 months; AEs that occurred in >1 patient during co-treatment were diarrhea, nasopharyngitis, sinusitis, upper respiratory tract infection, muscle strain, arthralgia, and hypertension. No new safety issues were observed.

Conclusion: The 6-month response rate of MTX/pegloticase co-therapy was 78.6%. Responders at month 6 who remained on treatment continued to be responders at month 12 with sUA remaining below 1 mg/dL. The MTX/pegloticase co-therapy was well tolerated over this 12 month period with a reduced incidence of gout flares over time.

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[3] Albert J, et al. Arthritis Rheumatol 2019, 71(suppl 10).

Disclosure: J. Botson, Horizon Therapeutics plc, 1, 2, 3, Radius Health, 1, Celgene, 1, 2, Novartis, 1, 2, Abbvie, 1, 2; **P. Peloso**, Horizon Therapeutics plc, 1, 2; **K. Obermeyer**, Horizon Therapeutics plc, 1, 3; **B. LaMoreaux**, Horizon Therapeutics plc, 1, 2; **L. Zhao**, Horizon Therapeutics plc, 1, 3; **M. Weinblatt**, Crescendo Bioscience, 1, Bristol Myers Squibb, 1, Sanofi, 2, Lilly, 1, Amgen, 1, AbbVie, 5, Amgen, 2, 5, Arena, 5, Bristol Myers Squibb, 2, 5, Canfite, 1, 5, Corrona, 5, Crescendo, 2, 5, GlaxoSmithKline, 5, Gilead, 9, Horizon, 9, Johnson and Johnson, 9, Lilly, 2, 9, Pfizer, 9, Scipher, 1, 9, Set Point, 9, Roche, 9, Canfite, 1, Inmedix, 1, Lycera, 1, Vorso, 1, Scipher, 1; **J. Peterson**, AbbVie, 5, 8.

Abstract Number: 0678

Patient Characteristics and Patterns of Urate-lowering Treatments in Older Patients with Incident Gout

Kazuki Yoshida[1], Jun Liu[2], Daniel H Solomon[3] and Seoyoung Kim[3], [1]Brigham & Women's Hospital and Harvard Medical School, Boston, MA, [2]Brigham and Women's Hospital, Boston, [3]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is a common inflammatory arthritis caused by monosodium urate crystal deposition in the joints. Despite this well-understood pathophysiologic mechanism of disease and ACR and EULAR recommendations for a treat-to-target strategy with urate-lowering therapy (ULT), management of gout is generally suboptimal. ULT initiation in older patients with gout can be challenging as many of them have substantial comorbidities. We aimed to examine characteristics of older patients newly diagnosed with gout and their patterns of ULT initiation.

Methods: Using Medicare claims data (2007–2016 Parts A/B/D) linked to EHR from 2 health care provider networks, we identified patients newly diagnosed with gout based on the first gout diagnostic code (ICD9 274.00–03, 81, 82, 39, 9; ICD10 M10) after the baseline period of at least 365 days. All patients were required to be continuously enrolled during the baseline period. Patients with age < 65 or use of any gout-related medications (allopurinol, febuxostat, probenecid, colchicine, lesinurad, and pegloticase) in this period were excluded. We described these incident gout patients for their baseline characteristics, subsequent ULT initiation, and treatment patterns at the initiation.

Results: We identified a total of 20,193 patients who we regarded as incident gout patients by our definition. The mean (SD) age was 77.3 (7.7) years and 48.4% were male. Many patients had comorbidities prior to the gout diagnosis (**Table 1**). Hypertension was the most common comorbidity (86%) followed by hyperlipidemia (75%), diabetes (36.7%), malignancy (30%), and heart failure (25%). Use of cardiovascular medication was also common (e.g., ACE/ARB 53%, diuretics 55%, and statin 60%). 34% experienced hospitalization during the baseline 365-day period. On average, they visited physician offices 14 times (median 12), emergency department 1.6 times, and took 10.8 discrete medications during the baseline period. During the entire follow-up (median 656 days [25th 168, 75th 1454]), only 24.3% had a ULT initiation. Cumulative incidence of ULT initiation was 17.8% at 1 year 21.2% and at 2 years after the diagnosis, handling disenrollment (55%) as censoring and death (21%) as a competing event. Most ULT initiators (95%) started allopurinol. Febuxostat was used in 3% and probenecid in 2%. The median starting doses were low consistent with ACR guidelines (**Table 2**). However, concomitant use of colchicine for flare prophylaxis was low (allopurinol 26%; febuxostat 31%), except probenecid (80%), which included a combination formulation.

Conclusion: Older patients with incident gout had a substantial comorbidity and medication burden. The overall rate of ULT initiation was low (< 25%) and suboptimal, particularly in the first year after the diagnosis (18%). While the initial ULT doses were appropriately low as recommended; less than a third used gout flare prophylactic treatments at the time of ULT initiation. As the treat-to-target strategy for gout is contingent upon ULT initiation, better understanding of patient and physician barriers to ULT is essential to improving the quality of care in older patients with gout.

Disclosure: K. Yoshida, OM1, 1, Corrona, 1; **J. Liu**, None; **D. Solomon**, AbbVie, 2, Amgen, 1, Genentech, 1, Janssen, 1, Corrona, 1; **S. Kim**, Pfizer, 1, Roche, 1, AbbVie, 1, Bristol-Myers Squibb, 1.

Abstract Number: 0679

Epidemiology of Intra-Articular Mineralization on Knee Dual-Energy Computed Tomography: The Multicenter Osteoarthritis Study

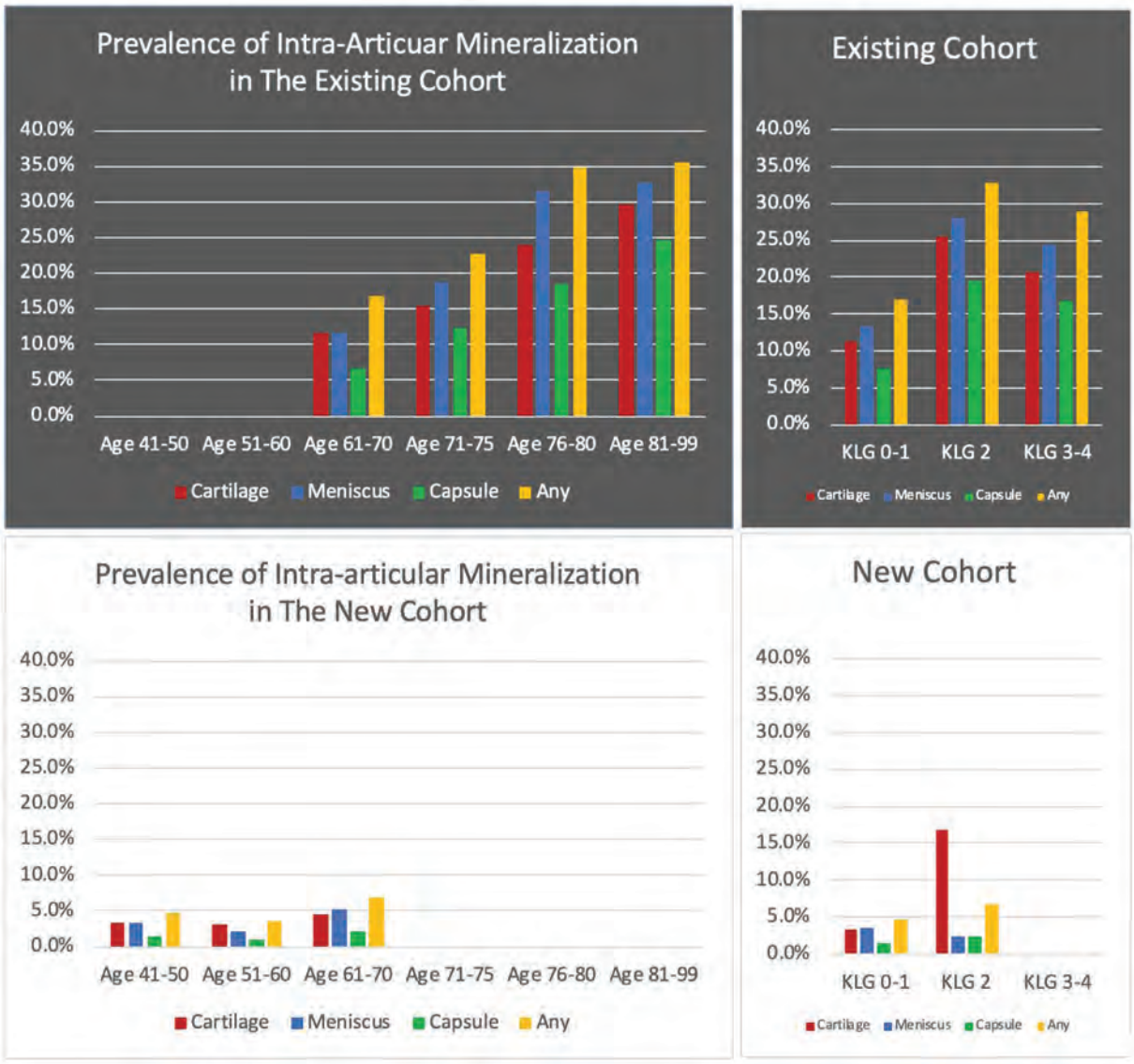
Mohamed Jarraya[1], **Tuhina Neogi**[2], John Lynch[3], David Felson[2], Piran Aliabadi[4], Michael Nevitt[3], Cora Lewis[5], James Torner[6] and Ali Guermazi[2], [1]Boston University School of Medicine, Boston, [2]Boston University School of Medicine, Boston, MA, [3]University of California at San Francisco, San Francisco, [4]Brigham and Womens Hospital, Boston, [5]University of Alabama Birmingham, Birmingham, AL, [6]University of Iowa, Iowa City, IA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Computed tomography (CT) has a higher sensitivity for the detection of intraarticular mineralization in comparison with commonly used imaging techniques in knee osteoarthritis (OA) including radiographs and MRI. The role of intra-articular mineralization in knee OA has been unclear, contributed to by inadequate imaging assessment of this phenomenon. The aim of this study is to report the prevalence of CT-detected intra-articular mineralization in older adults with or at risk of knee OA.

Methods: We used data from the Multicenter Osteoarthritis (MOST) Study, a NIH-funded cohort of people with or at risk of knee OA. The existing cohort was recruited in 2003-2005 (age 50-79), with the current analysis focusing on the 12th-year visit as the baseline for this analysis as this was the first study visit at which bilateral dual energy knee CTs were obtained. In addition coinciding with the 12th year study visit in 2016-2017, a new cohort was recruited (age 45-69) who had Kellgren Lawrence (KL) grade < =2 in both knees, and either no knee pain or if they had knee pain, it could not be severe or constant. Participants also had bilateral PA knee radiographs obtained, scored for KL grade by a musculoskeletal radiologist blinded to the CTs. A separate musculoskeletal radiologist scored multiplanar CT images using an ordinal score (0-3) for degree of mineralization in each of the MOAKS subregions of cartilage and menisci, as well as ligaments, capsule, and vasculature. Prevalence of intra-articular mineralization was computed for the total sample, and stratified by age and KL grade.

Results: The existing cohort included 635 subjects (1270 knees) (57.3 % female, mean age 71.8, mean BMI 29.9). The new cohort included 1473 subjects (2946 knees) (56 % female, mean age 56.6, mean BMI 28.4). CT-detected intra-articular mineralization (of either cartilage, meniscus, and/or capsule) was 23.3% in the existing cohort and 4.9% in the new cohort. For the existing cohort, the prevalence in specific locations was: 16.7% articular cartilage (vs. 3.6% in the new cohort), 19.5% meniscus (vs. 3.5% in the new cohort), and 12% capsule (vs. 1.5% in the new cohort). Articular and meniscal mineralization increased with age and was most prevalent in KL grade 2, both for the existing and new cohorts (**Figure**). The prevalence of intra-articular mineralization among KL grade 3 and 4 was lower



Prevalence of Intra-Articular Mineralization in the Existing and New Cohorts of the MOST Study

in comparison with KL grade 2 in the existing cohort, though this was unadjusted for age and could reflect less cartilage present at higher KL grades to allow for mineralization to be detected. Overall, the prevalence of vascular calcifications was 52.9% in the existing cohort (vs. 19.9% for the new cohort), which increased with age in both cohorts.

Conclusion: CT provides good visualization of intra-articular mineralization within the hyaline articular cartilage, meniscus, and soft tissue, which will provide novel opportunities to evaluate the longitudinal relation of intra-articular mineralization to adjacent articular tissue pathology and overall OA progression.

Disclosure: M. Jarraya, None; **T. Neogi**, Lilly, 1, EMD Merck Serono, 1, Novartis, 1, Regeneron, 1, Pfizer/Lilly, 1; **J. Lynch**, None; **D. Felson**, None; **P. Aliabadi**, None; **M. Nevitt**, None; **C. Lewis**, None; **J. Torner**, None; **A. Guermazi**, AstraZeneca, 1, Pfizer, 1, MerckSerono, 1, Galapagos, 1, Roche, 1, TissueGene, 1, Boston Imaging Core Lab, 1.

Abstract Number: 0680

Sustained Treat to Target Uric Acid Lowering Therapy Markedly Lowers Fatty Acids Levels in Gout Patients

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Though hyperuricemia is implicated in cardiovascular disease, the metabolic syndrome, and type 2 diabetes in both gout and in asymptomatic patients, the core metabolism pathways involved in these associations are unknown. Metabolomics provides valuable information about disease status. We conducted a prospective study, in which we characterized gout patient metabolic profiles at baseline and 12 and 24 weeks of treat to target uric acid (UA)-lowering therapy (ULT), to gain new mechanistic insight into association of metabolic and cardiovascular comorbidities with gout and hyperuricemia.

Methods: Recruited patients meeting the 2015 ACR/EULAR gout classification criteria (n=20) had hyperuricemia (serum UA 7-11.3 mg/dL at baseline, and 45% patients (9 out of 20) had flare rate ≥5/year at baseline. Six patients were already on ULT but hyperuricemic (at serum UA 6.8 mg/dL or higher), and 14 patients started xanthine oxidase inhibitor with allopurinol or febuxosat at recruitment. Blood was collected at time zero (baseline), and 12 and 24 weeks as all patients underwent ULT titration to attempt to achieve serum UA target < 6 mg/dL. Serum MS spectra were aquired with Ultrahigh Performance Liquid Chromatography-Tandem Mass Spectroscopy (UPLC-MS/MS). Raw data was extracted, peak-identified and processed using Metabolon hardware and software. Principal component analysis (PCA) with hierarchical clustering analysis (HCA) as well as random forest (RF) analysis was performed. Metabolites altered by ULT were identified using 2-way repeated measures ANOVA.

Results: Serum UA levels at week 12 (mean 5.9651.734SD) and week 24 (mean 5.6551.763SD) were significantly lower compared to baseline (mean 8.211.139SD), and 80% and 90% patients achieved reduced serum UA to < 7 mg/dL at week 12 and week 24, respectively. PCA along with HCA with all the samples demonstrated overlap between samples collected at time zero, as well as 12 and 24 weeks following treatment clustered based on the subject but not treatment itself. Yet, RF analysis resulted in predictive accuracy of 52%. RF analysis also identified several metabolites contributing most to the separation between baseline and 24 weeks. Top metabolites generated by RF analysis pointed heavily towards changes in selected metabolic pathways (Figure 1), including nucleotide *(urate, xanthine, adenosine and cytosine)* and lipid metabolism. Two-way repeated measures ANOVA identified 115 metabolites (89 downregulated and 26 upregulated) significantly differing between baseline and 24 weeks. Other than purine metabolites, short, medium and long chain fatty acids, and biliary acids were significantly decreased at 24 weeks, suggesting an association between urate levels and fatty acid synthesis in both the liver and adipose tissue (Figure 2).

Conclusion: The metabolomic blood profiles linked with patient response to xanthine oxidase inhibitor ULT, indicated a reduction of fatty acid synthesis. Although further studies are required to investigate how urate modulates lipid metabolism in liver and adipose, our findings point fatty acid synthesis reduction in response to ULT therapy in gout as being highly pertinent to comorbid metabolic and cardiovascular disease in gout.

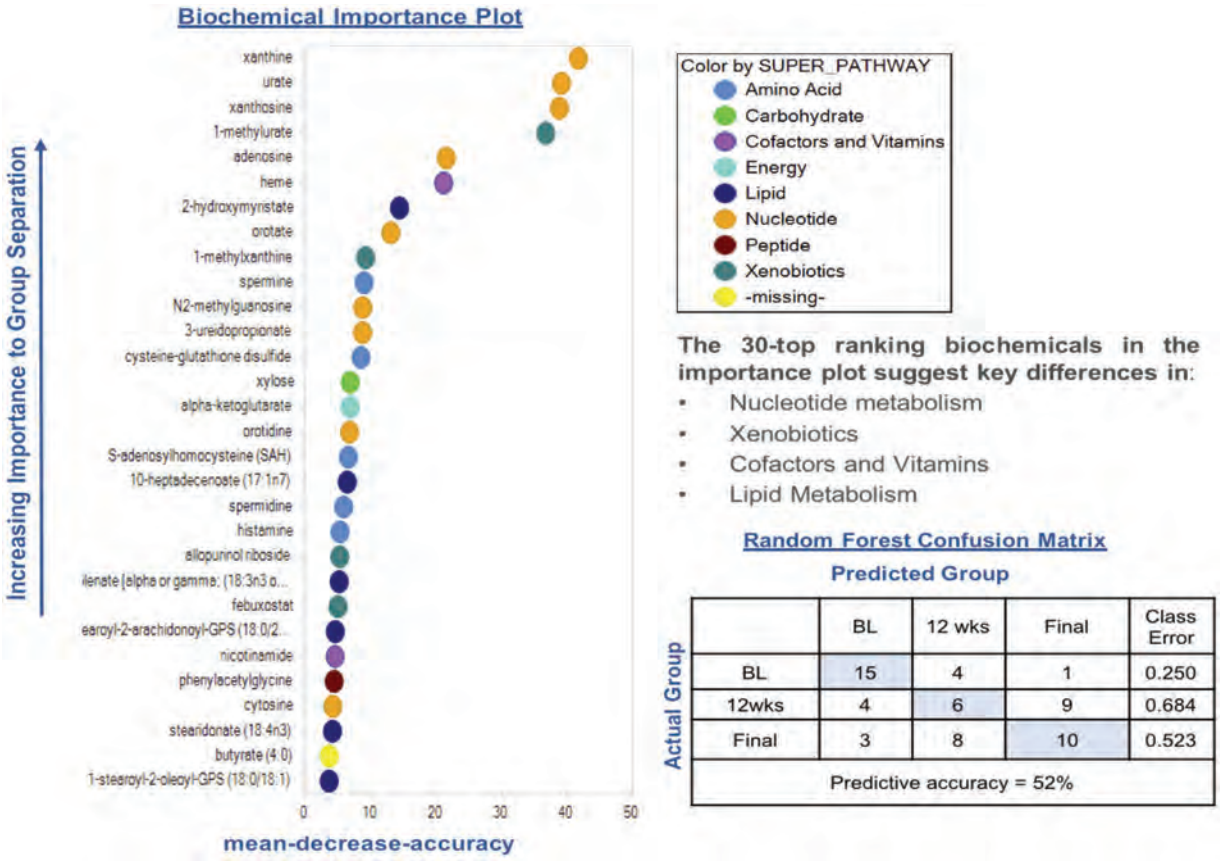

Figure 1. Random Forest classification using named metabolites detected in human serum collected from gout patients undergoing a treatment identified several metabolites contributing most to the separation of the groups. BL: baseline (time zero); wks: weeks. Final (24 weeks of ULT titrated to target).

A

Sub Pathway	Biochemical Name	Fold of Change: ANOVA Contrasts 12wk BL	Final BL	Final 12wk	Two-Way ANOVA: Group Main Effect
Purine Metabolism, (Hypo)Xanthine/Inosine containing	hypoxanthine	0.93	0.81	0.87	
	xanthine	3.00	3.00	1.00	
	xanthosine	3.89	3.44	0.88	
	urate	0.76	0.74	0.97	
	allantoin	0.79	0.76	0.95	
Purine Metabolism, Adenine	adenosine 5'-monophosphate (AMP)	0.61	0.09	0.14	
	adenosine	1.16	0.56	0.49	
Purine Metabolism, Guanine	guanosine	0.64	1.15	1.78	
	N2-methylguanosine	1.97	1.91	0.97	

B

Sub Pathway	Biochemical Name	Fold of Change: ANOVA Contrasts 12wk BL	Final BL	Two-Way ANOVA: Group Main Effect
Long Chain Polyunsaturated Fatty Acid (n3 and n6)	tetradecadienoate (14:2)*	0.83	0.73	
	stearidonate (18:4n3)	0.59	0.38	
	eicosapentaenoate (EPA; 20:5n3)	1.01	0.59	
	heneicosapentaenoate (21:5n3)	0.89	0.57	
	docosapentaenoate (n3 DPA; 22:5n3)	0.88	0.59	
	docosahexaenoate (DHA; 22:6n3)	0.88	0.60	
	docosatrienoate (22:3n3)	0.94	0.69	
	nisinate (24:6n3)	1.03	0.61	
	hexadecadienoate (16:2n6)	0.82	0.60	
	linoleate (18:2n6)	0.73	0.65	
	linolenate [alpha or gamma; (18:3n3 or 6)]	0.72	0.59	
	dihomo-linoleate (20:2n6)	0.77	0.60	
	dihomo-linolenate (20:3n3 or n6)	0.81	0.79	
	arachidonate (20:4n6)	0.82	0.75	
	docosatrienoate (22:3n6)*	0.73	0.54	
	adrenate (22:4n6)	0.80	0.60	
	docosapentaenoate (n6 DPA; 22:5n6)	0.83	0.66	
	docosadienoate (22:2n6)	0.80	0.82	
	mead acid (20:3n9)	0.89	0.74	

Figure 2. Two-way repeated measures ANOVA identified metabolites from purine metabolism and lipid metabolism significantly differing between baseline and 24 weeks ULT titration to target. BL: baseline (time zero); wks: weeks. Final (24 weeks of ULT titrated to target). Red: indicates significanlty upregulated vs baseline. Green: indicated significantly downregulated vs baseline. Blue: indicates significant two-way ANOVA test.

Disclosure: M. Guma, None; **R. Coras**, None; **R. Liu-Bryan**, CymaBay, 2; **R. Terkeltaub**, Astra-Zeneca, 2, Selecta, 5, Horizon, 5, Genentech, 5, SOBI, 5.

Abstract Number: 0681

Gout and Serum Urate Levels Are Associated with Lumbar Spine Monosodium Urate Deposition and Chronic Low Back Pain: A Dual-Energy CT Study

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Spinal gout is reported as a rare event, presenting as acute back pain, neuropathy, and spinal compression. Diagnosis is commonly based on identification of a mass, followed by tissue confirmation of monosodium urate (MSU) deposition. It is likely that many more cases of gout involve the spine asymptomatically or with non-specific or under-recognized symptoms.

Methods: Using dual-energy CT (DECT), we are determining the prevalence/extent of MSU deposition in the lumbosacral spines of patients with gout vs without gout, and with tophaceous vs non-tophaceous gout. We are recruiting 25 controls, 25 non-tophaceous and 25 tophaceous gout patients, 50-80 years old. Exclusion criteria include known CPPD disease, RA, spondyloarthropathy or active spinal malignancy. All gout subjects meet ACR classification criteria and have entry serum urate (sU) of >6.8 mg/dL, or sU >6.0 mg/dL on ULT for < 6 months. Demographics, gout history, Aberdeen back pain scale, sU, ESR, and CRP are collected. Subjects undergo DECT of the lumbosacral spine to assess for MSU deposition and osteoarthritic changes.

Results: 61 subjects are enrolled to date (25 control, 24 non-tophaceous and 12 tophaceous gout). Control and gout (all pooled) subjects have similar mean age in years (controls, 61.8±3.8 vs gout, 64.1±7.32, p=0.15), but differ in BMI (controls, 28.3±6.5 kg/m^2 vs gout, 32.35±6.9 kg/m^2, p=0.02) and creatinine (controls, 1.0±0.2 mg/dL vs gout, 1.5±0.7 mg/dL, p< 0.05). Mean sU and ESR are higher in gout subjects (sU-controls, 5.3±1 mg/dL vs gout, 8.7±1.7 mg/dL, p< 0.05; ESR-controls, 13.7±13.8 mm/h vs gout, 25.3±18.3 mm/h, p< 0.05). Using default threshold settings for MSU visualization, greater MSU deposition is observed in the spine of gout patients (controls, 2.2±1.2 cm^3 vs gout, 10.8±32.2 cm^3, p=0.18; Fig 1). When a single gout outlier with excessively high sU and spinal MSU is excluded, spinal MSU deposition between controls and gout patients becomes significant (controls, 2.2±1.2 cm^3 vs gout, 5.6±7.8 cm^3, p=0.04). Reanalysis of several scans using narrower threshold settings to limit possible artifact confirms increased MSU signal among gout patients. Although many subjects in each group do not have excessive MSU deposition, deposition is more common in both gout groups (Fig 2). Thus far, MSU deposition is not different between non-tophaceous and tophaceous gout patients (non-tophaceous, 12.3±2.92 cm^3 vs tophaceous, 7.9±3.2 cm^3, p = 0.7). No subject demonstrated a frank spinal tophus. Gout patients report higher back pain scores (controls, 5.7±8.3, vs gout, 11.8±14.3, p=0.06). Across all groups deposition is greater in patients with higher sU.

Conclusion: Based on preliminary results, gout patients have higher inflammatory markers, more spinal MSU deposition, and increased back pain versus controls. Preliminary results with more stringent DECT threshold settings suggests these differences are not artifact, but analysis is ongoing. These data suggest that non-tophaceous MSU

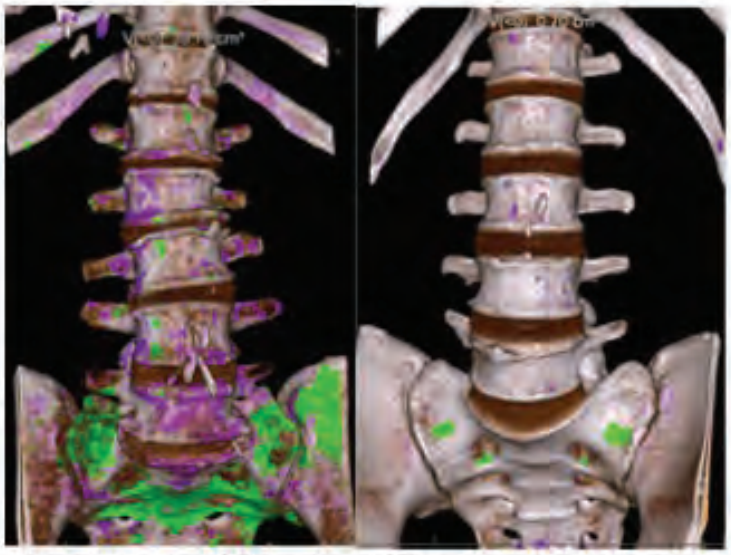

Figure 1: DECT of the spine. (A) Patient with tophaceous gout (SU 8.9mg/dL, DECT volume 39.76cm³). (B) Control patient (SU 4.5mg/dL, DECT volume 0.70cm³).

Figure 1. DECT of the spine. (A) Patient with tophaceous gout (SU 8.9mg/dL, DECT volume 39.76cm3). (B) Control patient (SU 4.5mg/dL, DECT volume 0.70cm3).

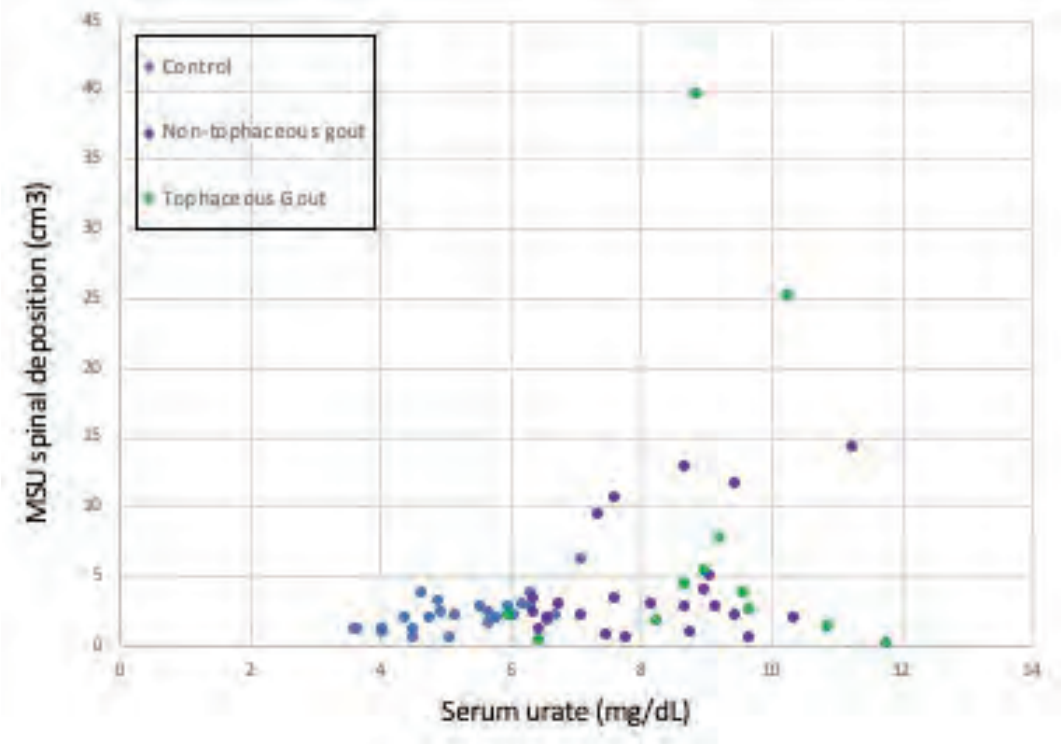

Figure 2. SU versus MSU spine deposition in control and gout patients

deposition in the spine occurs in a subset of gout patients, is associated with sU level, and may be associated with low back pain.

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Disclosure: M. Toprover, None; **M. Mechlin**, None; **A. Slobodnick**, None; **V. Pike**, None; **C. Oh**, None; **C. Davis**, None; **T. Fields**, Horizon Pharmaceuticals, 5; **F. Becce**, Horizon Therapeutics, 5; **M. Pillinger**, Horizon Pharma, 2.

Abstract Number: 0682

Role of Inflammatory and Oxidative Stress Pathway Biomarkers in Renal Disease in Gout

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: To understand the role of inflammatory cytokines and oxidative stress biomarkers in the renal disease in people with gout. We hypothesized that higher gout severity, the lack of urate-lowering treatment (ULT) use and elevated inflammatory cytokines and oxidative stress markers will be associated with the presence of advanced renal disease in people with gout.

Methods: We prospectively enrolled patients with clinically diagnosed gout in the UAB Rheumatology Arthritis Database and Repository (RADAR) from January 2018 to December 2019. All except one patient (score of 7; the threshold of >=8) met ACR-EULAR gout classification criteria. Demographic and clinical data including gout severity and allopurinol use were collected. Serum and plasma were assayed for key inflammatory markers and oxidative stress pathway metabolites, and renal function tests and other clinical end points were assessed. Gout severity was assessed on the basis of: (1) High disease activity defined as treating physician's impression or ≥ one gout flare in the last 3-6 month, or serum urate level above target (6 mg/dl) necessitating escalation of ULT; (2) presence of tophi (yes/no); and (3) the current serum urate. We used analysis of variance (continuous) and chi-square (categorical) to examine association of gout severity, ULT use and cytokines and oxidative stress markers with advanced renal disease, defined as glomerular filtration rate (GFR) ≤ 60 ml/min.

Results: Our study included a total of 90 patients with gout, 73% males, 48% African American, 48% Caucasian and 11% active smokers. Of these, 54% (N=49) hadat least one gout attack in this period, 89% had non-tophaceous gout and 74% had hypertension (**Table 1**). The mean serum urate level, serum creatinine and glomerular filtration rate (GFR) were 6.48 mg/dl (2.21), 1.83 mg/dl (3.34), 38.6 ml/min (16.4) respectively. Four inflammatory markers were increased in patients with advanced renal disease (GFR ≤60 ml/min) versus non-renal disease (GFR >60 ml/min); IL-1beta, PDGF-AA, A PDGF-BB and TNF- alpha, which statistically significant (P=0.03, 0,02, 0,03, 0.02; **Table 2**). 8-Isoprostane levels were low in people with advanced renal disease with no significant differences in other oxidative stress pathway markers including nitrotyrosine, carbonyl content, oxyHb, MetHb, nitrite or nitrates. Severity of gout disease, the presence of tophi, current allopurinol use and serum urate < 6 mg/dl were not associated with the presence of advanced renal disease (**Table 3**).

Conclusion: High level of oxidative stress and inflammatory cytokine markers were associated with the presence of advanced renal disease in patients with gout. These associations need further study in larger samples.

Table 1. Clinical and demographic characteristics

Characteristics	N (%)
Age	
≤65 years	51 (56.7)
>65 years	39 (43.3)
Race	
African American	43 (47.8)
White	43 (47.8)
Asian	3 (3.3)
Hispanic or Latino	1 (1.1)
Sex	
Female	24 (26.7)
Male	66 (73.3)
Current Alcohol use	
No	46 (51.1)
Yes	44 (48.9)
Current Smoking	
No	50 (55.5)
Former	29 (32.2)
Yes	11 (12.2)
BMI (kg/m^2)	
<30	26 (28.9)
≥30	64 (71.1)
Tophaceous Gout	
No	80 (87)
Yes	10 (10.9)
Gout	
Well controlled	58 (64.4)
Poor controlled	10 (11.1)
Unknown	22 (24.4)
Gout attacks in the last 6 month	
< 1	19 (21.1)
≥ 1	49 (54.4)
Unknown	22 (24.4)
Comorbidities	
Renal disease	21 (23.3)
Hyperlipidemia	40 (44.4)
Hypertension	67 (74.4)
Diabetes	29 (32.2)
Heart Disease	14 (15.6)
Serum urate	
≤ 6mg/dl	42 (46.7)
>6 mg/dl	48 (53.3)

Table 2. Association of oxidative/inflammatory cytokines and renal disease

	Renal function		p-value
	GFR ≤60 ml/min Mean (SD)	GFR >60 ml/min Mean (SD)	
Aldosterone (pg/mL), n=36	**210.37 (159.97)**	**483.81 (415.52)**	**0.01**
Renin (pg/mL), n=37	1937.65 (3502.54)	1773.31 (1784.43)	0.87
IL-1 Beta (pg/mL), n=27	**10.21 (9.95)**	**1.57 (1.63)**	**0.03**
PDGF-AA (pg/ml), n=26	**984.67 (555.96)**	**450.60 (225.58)**	**0.02**
CCL2/MCP (pg/mL) n=27	239.57 (75.00)	328.45 (153.62)	0.05
PDGF-BB (pg/mL), n=27	**7223.80 (4805.17)**	**2995.34 (1805.13)**	**0.03**
TNF-Alpha (pg/mL), n=27	**7.42 (3.55)**	**4.04 (2.26)**	**0.03**
Total protein (mg/ml) , n=78	53.09 (8.86)	49.36 (11.11)	0.13
Nitrotyrosine (nmol/g), n=77	4.60 (2.10)	5.00 (2.19)	0.46
Carbonyl content (nmol/mg), n=41	4.83 (4.76)	6.75 (9.58)	0.39
OxyHb (μM), n=39	2.88 (2.32)	3.41 (3.23)	0.56
MetHb (μM), n=39	0.01 (0.03)	0.03 (0.08)	0.47
8-Isoprostane (pg/ml), n=88	**10.52 (4.86)**	**15.11 (12.56)**	**0.01**
Heme (μM), n=39	19.42 (12.98)	20.23 (9.30)	0.83
Total heme (μM), n=39	22.31 (13.33)	23.67 (10.57)	0.74
Nitrite (nmol/g), n=39	8.87 (4.48)	9.08 (4.45)	0.89
Nitrate (nmol/g), n=39	5.60 (4.27)	7.38 (6.40)	0.31
CRP (μg/mL) , n=27	73.48 (42.14)	69.98 (39.13)	0.84
IL-6 (pg/mL), n=27	10.34 (7.12)	5.60 (2.05)	0.98
Bold font indicates significant differences with a p-value of <0.05			

Table 3. Association of renal disease and gout disease severity, current allopurinol use, presence of tophi and Serum urate

	Renal function		p-value
	GFR ≤60 ml/min N (%)	GFR >60 ml/min N (%)	
Gout disease severity			0.65
No	41 (91)	17 (74)	
Yes	4 (9)	6 (26)	
Current Allopurinol use			0.37
No	23 (36)	11 (42)	
Yes	41 (64)	15 (56)	
presence of tophi			0.31
No	58 (91)	22 (87)	
Yes	6 (9)	4 (15)	
Serum urate			0.35
≤6 mg/dl	27 (49.1)	10 (42)	
>6 mg/dl	28 (51)	14 (58)	

Disclosure: F. Alduraibi, None; **K. Ricart**, None; **R. Patel**, None; **A. Szalai**, None; **J. Melnick**, None; **J. Singh**, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1.

Abstract Number: 0683

Pharmacokinetics of Pegloticase and Methotrexate Polyglutamate(s) in Patients with Uncontrolled Gout Receiving Pegloticase and Co-treatment of Methotrexate

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
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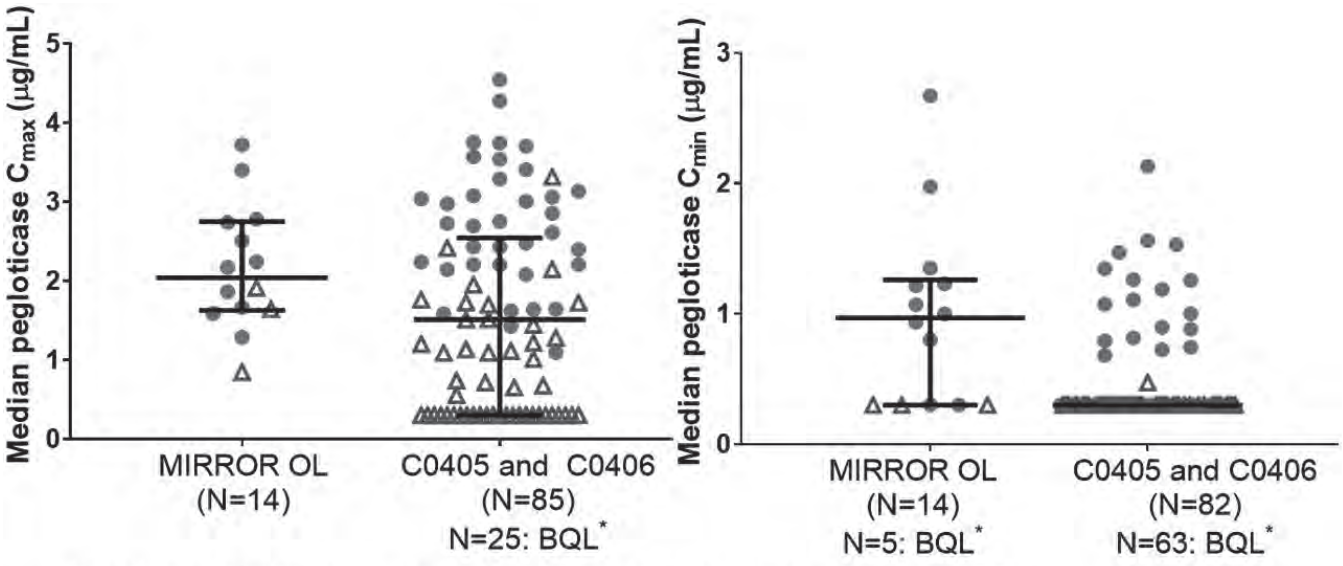
Background/Purpose: In an open-label trial in adult patients with uncontrolled gout (MIRROR open-label [OL] trial) evaluating pegloticase co-treatment with methotrexate (MTX), 78.6% patients maintained serum uric acid < 6 mg/dL for at least 80% of the time during month 6 [weeks 20, 22, and 24] versus 42% in pegloticase historical monotherapy trials (C0405 and C0406)[1]. MTX co-treatment can affect the pharmacokinetics (PK) of biologics by attenuating the formation of anti-drug antibodies[2]. The aim of this analysis was to determine the systemic exposures of pegloticase and methotrexate polyglutamate(s) (MTX-PGs) in uncontrolled gout patients receiving pegloticase and MTX and to evaluate the effect of MTX on the PK and immunogenicity of pegloticase in comparison to historical pegloticase monotherapy trials (C0405 and C0406)[3,4].

Methods: In the MIRROR OL trial, MTX (15 mg/week) was given orally 4 weeks prior to the 1st pegloticase dose and continued weekly, in combination with pegloticase 8 mg given intravenously every 2 weeks, for a treatment duration of 52 weeks. Pre-infusion samples were collected to measure MTX-PGs in red blood cells. Pre- and post-infusion blood samples were obtained to measure the peak (C_{max}) and trough (C_{min}) concentrations of pegloticase at multiple visits. Anti-drug antibody blood samples were collected at multiple visits. The impact of MTX on pegloticase PK was evaluated by comparing pegloticase exposures with MTX from this trial to historical monotherapy data (C0405 and C0406)[3,4]. The observed pegloticase concentrations with MTX were also overlaid with the 90% prediction interval based on the population PK model from C0405 and C0406[5].

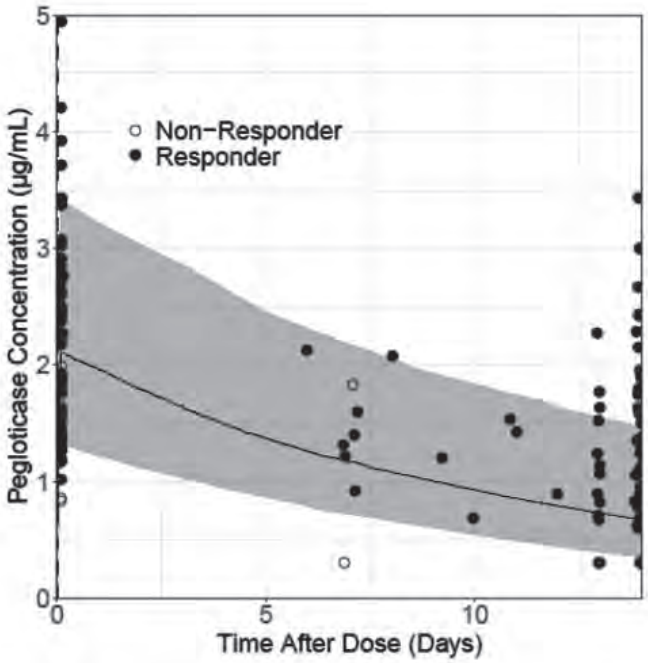
Results: Pegloticase and MTX-PG levels were determined in fourteen patients. Responders (11/14) were generally associated with higher pegloticase exposures, especially C_{min} (**Figure 1**). Concomitant treatment of MTX resulted in fewer patients with C_{min} below quantitation limit (BQL) (5/14 [36%] with MTX vs 63/82 [77%] without MTX), and higher overall C_{min} (median: 0.97 µg/ml with MTX vs BQL without MTX); C_{max} was slightly higher (median [Q1, Q3]: 2.04 [1.65, 2.68] µg/mL with MTX vs 1.51 [BQL, 2.48] µg/mL without MTX). Pegloticase co-treatment with MTX resulted in more concentrations above the predicted median value of pegloticase, compared to monotherapy (**Figure 1,2**). This may be due to the effect of MTX in reducing the immunogenicity of pegloticase. Concentrations of MTX-PGs were maintained during the treatment course, suggesting compliance of MTX administration. There was no apparent relationship between response and MTX-PGs exposures.

Conclusion: Pegloticase 8 mg IV every 2 weeks co-treatment with MTX 15 mg weekly resulted in fewer patients with pegloticase C_{min} BQL, and higher overall C_{min} compared to pegloticase monotherapy and was associated with an improved response rate for pegloticase in patients with uncontrolled gout.



*Data that are BQL (Below quantitation limit of 0.6 µg/mL) were imputed as 0.3 µg/mL (LLOQ/2).
Closed circles: Responders (11/14 in MIRROR OL; 36/85 in C0405 and C0406);
Open triangles: Non-responders (3/14 in MIRROR OL; 49/85 in C0405 and C0406).
Lower, middle and upper lines represent Q1, median and Q3 of data range.
Median pegloticase Cmin and Cmax were calculated based on observed values across visits.

Figure 1. Comparison of pegloticase exposures (Cmax and Cmin) in methotrexate co-treatment (MIRROR OL) and monotherapy trials (C0405 and C0406)



Circle: Observed data (MIRROR OL)
Shaded area: Post-hoc simulated 90% confidence interval (C0405 and C0406)
Black line: Post-hoc simulated median concentration (C0405 and C0406)

Figure 2. Comparison of observed pegloticase concentrations in MIRROR OL and stimulated PK profile of pegloticase as monotherapy

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Abstract Number: 0684

The Shrinking Toe: A Sign of Crystal Dissolution During Urate Lowering Treatment of Severe Gouty Arthropathy

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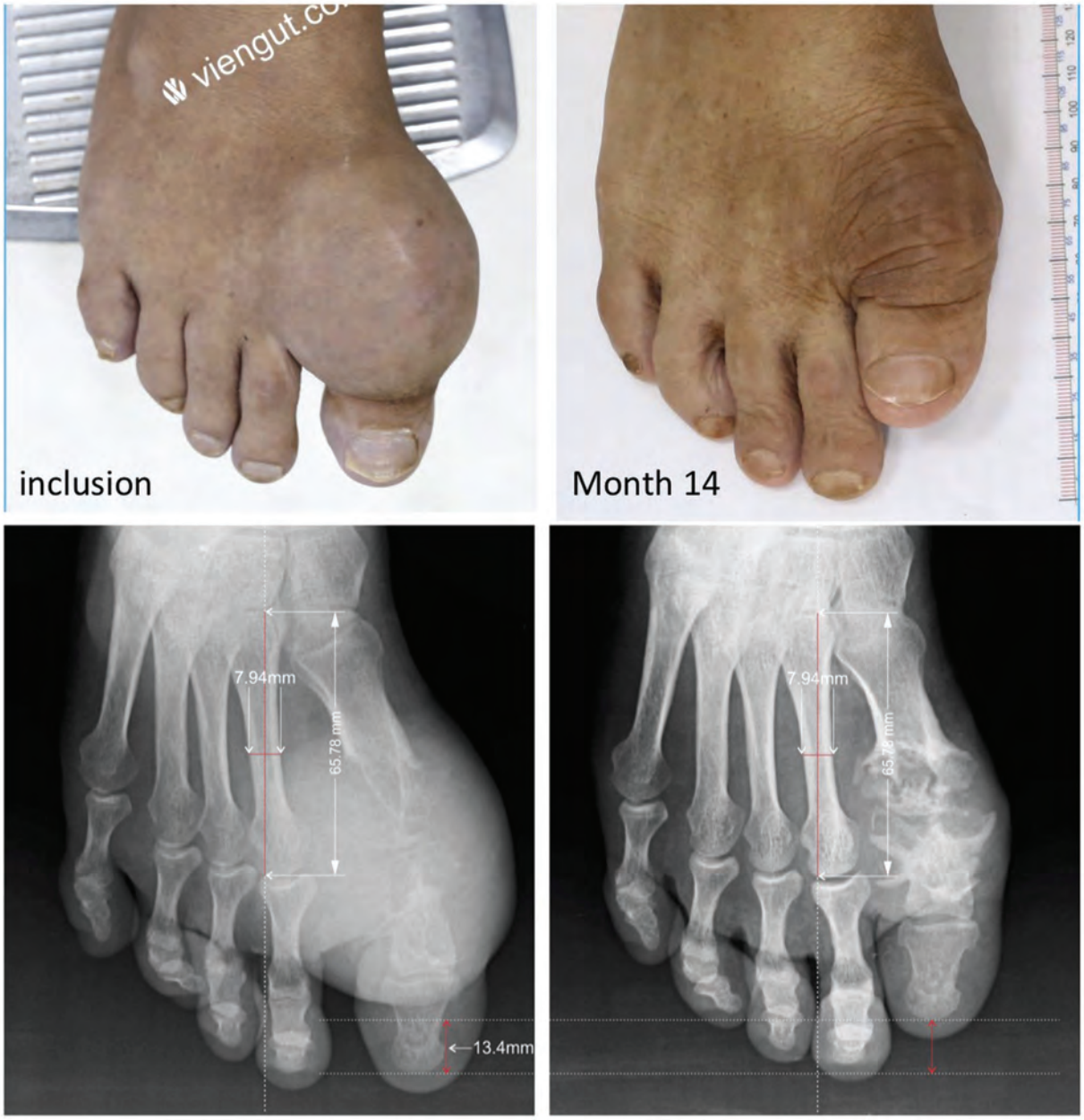
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Serum urate (SU) lowering has been reported to improve gout erosions. We observed that it may also lead to compaction of toe MTP or IP joints involved by severe gouty arthropathy.

Methods: We performed a retrospective analysis of 10 patients with severe tophaceous gout and destructive arthropathy, who did not receive urate-lowering drugs (ULDs) before inclusion and developed toe shortening (a sign we called the shrinking toe sign) during urate lowering treatment (ULT) at the Vien Gut Medical Center (Ho Chi Minh City, Vietnam). Data were retrieved from anonymized electronic files, including sequential foot radiographs and photographs. Antero-posterior non-weight bearing digital radiographs of the feet taken before ULT start, and during follow-up, were analyzed by using the COREL DRAW software (Corel Corporation, CANADA), which allowed standardization of the size and orientation of patients' radiographs, and measurement of toe shortenings.

Results: The 10 patients were men with a mean age of 39 +/- 6.6 years at gout onset. At inclusion, their mean age was 51.4 (SD 9.6) years, mean gout duration 12.4 (3.8) years, mean uricemia 528.2 (51.9) micromoles/l, mean BMI 22.5 (3.8) kg/m^2. Patients were treated by progressively increased doses of allopurinol (n=6; mean maintenance dose: 650 mg/d; range 450-900), or febuxostat (n=4; mean maintenance dose 130 mg/d; range 80-160). All patients achieved the < 300 micromoles/l serum urate (SU) target after a mean of 7.4 months (range 1-15).



Example of the shrinking toe sign

During a mean total radiological follow-up of 27 (15) months (range 6-48), the 10 patients had a mean of 1.8 radiographs each (range 1-4). The shrinking toe sign involved 12 toes: 7 first MTPs (Fig.) (mean shortening 8.7 mm; range: 3-13.8), 3 second MTPs (mean 12.4 mm; range: 9.5-17.9), and 2 second toe DIPs (9.5 and 4.4 mm). Toe shortening was also observed clinically, as confirmed by sequential photographs (Fig.).

In one patient, subchondral lytic bone collapse of P1 basis was observed 9 months before the SU target was reached, leading to shortening of a big toe, with no sign of tophus decrease, suggesting that the shrinking toe sign can occur in poorly treated gout. In the other 9 patients, shrinking toes were observed after the target had been reached at a mean follow-up of 22.9 months (range 2-47). Dissolution of MSU deposits within the joint space and/or subchondral bone lytic areas, leading to their collapse, despite the frequent observation of bone reconstruction, appeared to be the main explanation for toe shortening, associated with subluxation of the involved joint in 3 patients. 5 patients

underwent multiple follow-up radiographs; in 4, toes shortened progressively with time in parallel with decrease of tophus opacities, whereas the 5th, who had 3 follow-up radiographs up to 27 months, exhibited maximum shortening at the first follow-up radiograph (month 11), when tophus opacities had already vanished.

Conclusion: The shrinking toe sign that we described in this study involved the 1st and 2d toes, where constraints are maximized. It may be a feature of severe gouty arthropathy, but was mainly observed during MSU dissolution under ULT, which appeared to fragilize the involved joints.

Disclosure: T. Bardin, None; **N. Quang**, None; **H. Nghia**, None; **T. Khoi**, None; **H. EA**, None; **V. Bousson**, None; **P. Richette**, AbbVie Inc., 1, Biogen, 1, Janssen, 1, BMS, 1, Roche, 1, Pfizer, 1, Amgen, 1, Sanofi-Aventis, 1, UCB, 1, Lilly, 1, Novartis, 1, Celgene, 1.

Abstract Number: 0685

The Impact of Azathioprine on the Frequency of Persistent Responsiveness to Pegloticase in Patients with Chronic Refractory Gout

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SESSION INFORMATION
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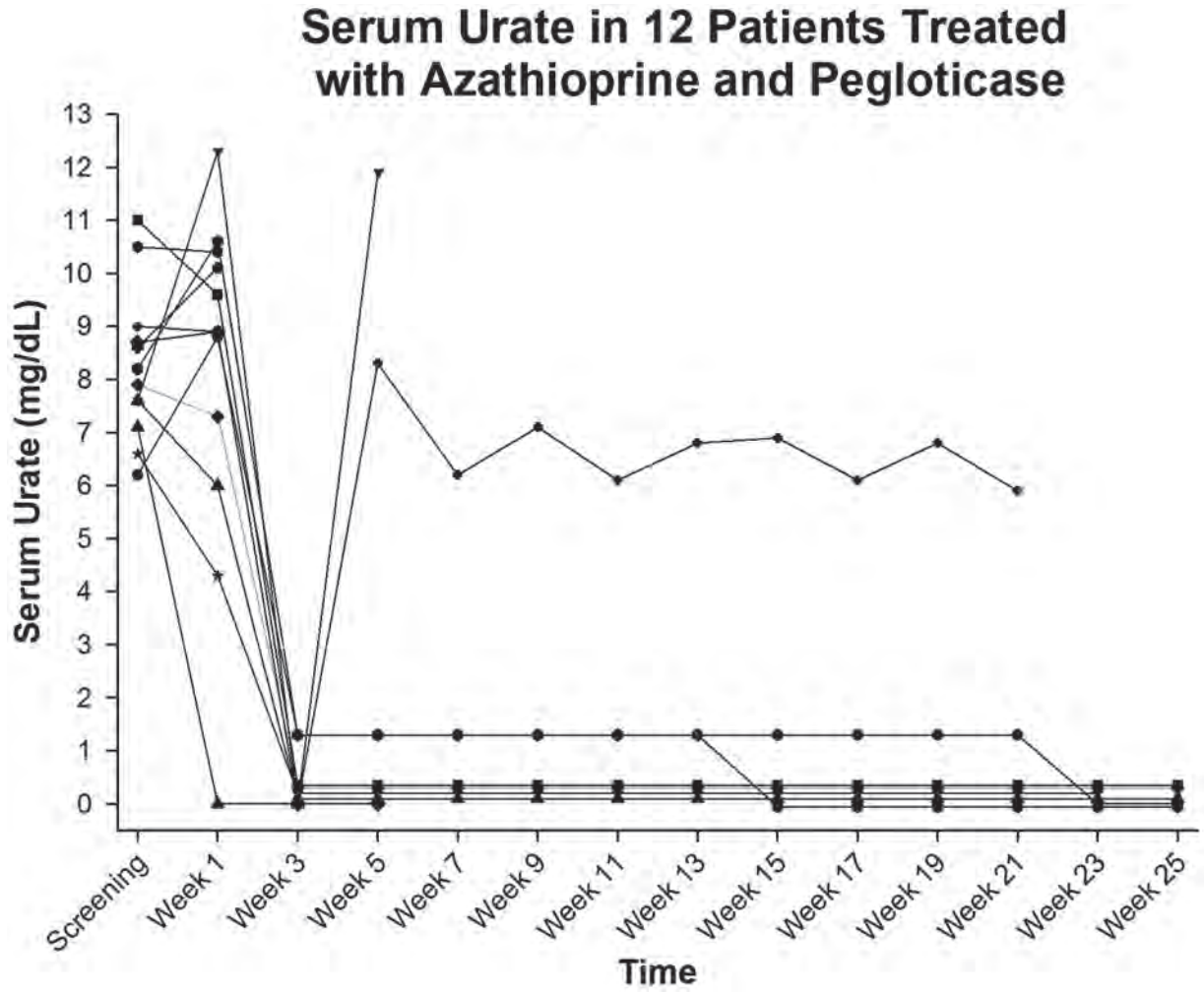
Background/Purpose: Pegloticase is a mammalian recombinant uricase coupled to monomethoxy polyethylene glycol that is approved in the US for treatment of patients with chronic refractory gout and causes profound reductions in serum urate. However, treatment with pegloticase is limited by the induction of anti-drug antibodies and loss of responsiveness in nearly half of treated patients.

The goal of this study was to determine whether co-therapy with azathioprine (AZA) would increase the frequency of chronic refractory gout patients who had persistent urate lowering from pegloticase therapy.

Methods: This open label multicenter study enrolled subjects with chronic gout who failed to lower serum urate to < 6 mg/dL despite medically indicated doses of urate lowering therapy (NCT02598596). Patients were screened for adequate levels of the AZA metabolizing enzyme thiopurine methyl transferase and then started on daily oral AZA 1.25 mg/kg for 1 week and then 2.5 mg/kg for the remainder of the trial. Blood levels of AZA metabolites 6-thioguanine and 6-methylmercaptopurine were measured biweekly. After receiving 2 weeks of AZA, patients were started on pegloticase (8 mg IV) and were treated biweekly for 24 weeks. The primary endpoint was the persistent lowering of serum urate to < 6 mg/dL at the last three consecutive study visits. Patients who had an increase in serum urate to >6 mg/dL while on therapy did not receive additional pegloticase. All patients received infusion prophylaxis with hydrocortisone as well as gout flare prophylaxis.

Results: To date, 12 patients have been enrolled. All patients were male, 75% white and 25% African American. Mean age was 62.4 ± 14.7 years, the mean BMI was 31.1 ± 4.5 and the mean duration of gout was 13.8 ± 9.2 years. At baseline, all patients had visible tophi; 58.3% suffered from gout flares; 81.8% had hypertension; 45.5% had dyslipidemia and 9.0% had coronary artery disease. Of the 12 patients, 6 have completed the full course of treatment



with persistent urate lowering and 2 remain on treatment also with persistent urate lowering (figure). 2 patients lost the urate lowering effect, both after 2 doses of pegloticase, and did not receive additional therapy. 1 patient experienced an infusion reaction during the first dose (1 infusion reaction in 90 infusions [1.1%] in the entire trial to date) and 1 subject had subjective symptoms of AZA intolerance with no laboratory abnormalities; these subjects discontinued the study and were not evaluable for the endpoint. No adverse events related to AZA were reported and gout flares were noted in 6 subjects (mean 1.5 flares/patient with flares).

Conclusion: AZA can be used safely in subjects with chronic refractory gout and appears to increase the frequency of subjects experiencing long term lowering of serum urate.

Disclosure: H. Baraf, AbbVie, 2, 8, Horizon, 2, 8, Gilead Sciences, Inc., 2, 8, Pfizer, 2, 8, Janssen, 2, 8, Merck, 2, 8; **H. Rainey**, None; **P. Lipsky**, Horizon Therapeutics, 3; **P. Lipsky**, Janssen Research & Development, LLC, 1.

Abstract Number: 0686

Renal Evolution During the First Year of Urate-lowering Therapy According to Sonographic Joint Deposition: Data from the Lille-Alicante Inception Cohort

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SESSION INFORMATION
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Session Title: Metabolic & Crystal Arthropathies Poster
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Background/Purpose: Gout is associated with chronic kidney disease, but how the kidney function evolves when gout is treated with urate lowering therapy (ULT) is still a matter of debate. Gouty nephropathy is led by crystal deposition in renal medulla, so we hypothesized that patients with a high monosodium urate (MSU) crystal burden could have the highest potential of benefiting from effective crystal depletion in the kidneys. Joint ultrasound provides an assessment of the extent of MSU crystal deposition within joints (the double contour (DC) sign) and within tissues (tophi). The objective of this study was to determine if the burden of MSU crystals as assessed by ultrasound could predict kidney response to ULT in gout patients.

Methods: Gout patients from two referral centers in Spain (Alicante) and France (Lille) requiring ULT initiation were recruited to undergo baseline ultrasound scans and a 1-year follow-up. Ultrasound scans assessed 6 joints for the presence of the DC sign and tophi. Demographic data, comorbidities, treatments, gout history, biological data including the estimated glomerular filtration rate (eGFR) and serum urate levels, were collected at the baseline visit and at the month 12 visit. A 5-point change in the eGFR at month 12 was considered significant. The number of joints affected with the DC sign and presence of tophi were compared between patients improving, preserving and degrading their eGFR using the Khi-2 and Mann-Whitney-Wilcoxon tests respectively.

Results: A total of 165 patients were recruited (n=81 from Alicante and n=84 from Lille) aged 63 years old (±14.5), predominantly male (86.1%) and with 7.5 years (±9.8) of gout duration. Baseline eGFR was 75.2 ml/min/1.73m^2 (±23.9) and serum urate levels were 8.4 mg/dL (±1.8). Overall, 81.0% of patients had ultrasound tophi and the number of joints with the DC sign was 1.4 (±1.3).

At month 12, 37 patients were lost to follow-up. A target serum urate level below 6.0mg/dL was reached for 88 patients (70.4%) and eGFR was 72.6 ml/min/1.73m^2 (±23.4). Overall, 16.4% of patients had significantly improved their eGFR, while 31.2% degraded. Patients improving their eGFR numerically achieved more frequently the serum urate target below 6.0mg/dL (83.3%) than those degrading their eGFR (64.9%) (p=0.27). Neither the presence of ultrasound tophus (p=0.53 and 0.75) nor the number of joints with the DC sign (p=0.23 and 0.18) were associated to the improvement or degradation of the renal function. In the subgroup of patients achieving serum urate levels below 6.0mg/dL at month 12, all (100%) patients improving their eGFR had an ultrasound tophus versus 87% in those not improving (p=0.35), and the number of joints with the DC sign was 1 [1 ; 2] versus 1 [0 ; 2] (p=0.83).

Conclusion: The MSU crystal burden assessed by ultrasound does not help predict the evolution of renal function during the first year of ULT, likely because ultrasound signs of depositions (especially tophi) are quite constant in pa-

tients with gout. The study was not sufficiently powered to establish a clear link between reaching the target serum urate level and preserving/improving the renal function.

Disclosure: I. Calabuig, None; **A. Marty-Ané**, None; **L. Norberciak**, None; **J. Budzik**, None; **A. Martínez-Sanchis**, None; **M. Andrés**, Grünenthal, 2, 8, Horizon, 8, Menarini, 8; **T. Pascart**, Horizon Therapeutics, 2, Novartis, 8.

Abstract Number: 0687

Musculoskeletal Manifestations in Patients with CD73 Deficiency

Cornelia Cudrici[1], Kam Newman[2], Deepak Lakshmipathy[1], Elisa Ferrante[1], Rebecca Huffstutler[1], Katherine Carney[1], Blas Betancourt[2], Markku Miettinen[3], James Katz[4], Leon Nesti[5], Han Wen[1], Manfred Boehm[6] and Alessandra Brofferio[1], [1]National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD, [2]National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [3]National Cancer Institute, National Institutes of Health, Bethesda, MD, [4]NIH NIAMS, Bethesda, MD, [5]Clinical and Experimental Orthopaedics, Walter Reed National Military Medical Center, Bethesda, MD, [6]Center for Molecular Medicine, National Heart, Lung, and Blood Institute, National Institutes of Health, Bethesda, MD

SESSION INFORMATION
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Background/Purpose: Arterial calcification due to deficiency of CD73 (ACDC) is a hereditary autosomal recessive ectopic mineralization syndrome caused by loss-of-function mutations in the 5'-nucleotidase Ecto (*NT5E*) gene that encodes for CD73also known as ecto-5′-nucleotidase. In ACDC patients, arterial calcification predominantly involves the lower extremities causing early onset of intermittent claudication. Periarticular calcification has been reported in the first reports of ACDC, but the clinical characterization of arthritis has not been systematically investigated. Here, we describe the musculoskeletal manifestations in eight ACDC patients and characterize the microstructure and chemical composition of periarticular calcifications and synovial fluid crystals.

Methods: Eight ACDC patients with either homozygous or compound heterozygous mutations in the *NT5E* gene were included in this study and underwent extensive rheumatological and radiological evaluation over a period of 11 years. Periarticular and synovial biopsies were obtained from four ACDC patients with pathological evaluation of synovial tissue and synovial fluid, as well as characterization of crystal composition by compensated polarized light microscopy and Alizarin red staining for synovial fluid along with x-ray diffraction and x-ray micro tomosynthesis for periarticular calcification.

Results: Arthritis in ACDC patients has a distinctive presentation with episodic inflammatory manifestations of small joints along with mixed erosive-degenerative joint changes, as shown by x-ray, CT and MRI with a median age of onset of arthritis symptoms at 17. Over several decades, arthritis in these patients frequently leads to the development of fixed deformities and functional limitations. Large joints also become involved later in life with bulky periarticular calcifications and presence of enthesophytes. X-rays of cervical and thoracic spine vertebrae show osteoarthritis, osteophytes, intervertebral disk calcification, and arthritis of the facet joints. Further, we have identified calcium pyrophosphate and hydroxyapatite crystals in synovial fluid collected in four ACDC patients. With these samples, we identified by x-ray diffraction that periarticular calcifications are mostly composed of *hydroxyapatite* crystals. Some patients have multiple spherical calcifications with fibrosis showing histology similar to calcific tendinitis or tumoral calcinosis-like lesions.

Conclusion: This is the largest study to describe the musculoskeletal manifestations of ACDC patients over a period of 11 years and is the first study to report the crystal composition of periarticular calcifications and the presence of synovial fluid crystals in these patients. Based on the findings in this study, the joint involvement is best defined as an erosive arthropathy that includes peripheral and axial enthesopathic calcifications along with periarticular calcifications. Joint biopsy samples analysis reveals that calcium hydroxyapatite crystals are the main component of periarticular calcifications and synovial fluid, although pyrophosphate crystals were also found in the synovial fluid.

Disclosure: C. Cudrici, None; **K. Newman**, None; **D. Lakshmipathy**, None; **E. Ferrante**, None; **R. Huffstutler**, None; **K. Carney**, None; **B. Betancourt**, None; **M. Miettinen**, None; **J. Katz**, None; **L. Nesti**, None; **H. Wen**, None; **M. Boehm**, None; **A. Brofferio**, None.

Abstract Number: 0688

The Discontinuation of Allopurinol in the Inpatient Setting and the Risk of Gout Flare: A Community-Hospital Experience

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

Background/Purpose: The discontinuation of urate-lowering therapy (ULT) in the outpatient setting increases the risk of gout flare. It was reported that in hospitalized patients with gout flare in almost a quarter of admissions allopurinol was discontinued or decreased on day of admission. We have reviewed the hospitalizations of patients with a history of gout presenting to our hospital for conditions other than gout. The aim of the study was to determine if there was an association between the discontinuation of allopurinol upon admission to the hospital and the risk of developing a gout flare during hospitalization.

Methods: This was a retrospective chart review of patients with a history of gout, on chronic ULT with allopurinol, who were admitted to our hospital for conditions other than gout from 03/01/2017 - 03/31/2019. We only included patients hospitalized for at least 2 days. Charts were reviewed for patient demographics, length of stay, allopurinol discontinuation, gout flare, and corresponding risk factors. Data were summarized using descriptive statistics for baseline characteristics and outcomes. Inferential statistics were performed where appropriate to compare patients with and without continued allopurinol treatment during hospitalization. All p-values were two-tailed and a level of < 0.05 was considered significant.

Results: A total of 401 patients with a history of gout and allopurinol listed as an outpatient medication on the day of admission were included in the study. The mean age of the included population was 75+/- 13 years old (ranging between 40 and 99 years old). The majority of included patients were males (296 subjects comprising 74% of the population). The mean length of stay (LOS) was 6.29 days (ranging between 2 and 57 days). Most of the patients were obese with the mean body mass index (BMI) of 30 kg/m2 (17-61 kg/m2). The baseline characteristics (age, gender, BMI, use of loop and thiazide diuretics, history of renal failure, smoking status) of no-allopurinol (allopurinol discontinued on admission) and yes-allopurinol (allopurinol continued on admission) groups were not significantly different be-

tween the two groups. 23.3% (7/30) of patients who had allopurinol discontinued on admission (no-allopurinol group) developed gout flare during hospitalization. In contrast, only 2.2% (8/371) of patients in the yes-allopurinol group developed gout flare during hospitalization. The odds of having gout flare in the no-allopurinol group were significantly higher than in the yes-allopurinol group (Fisher exact probability test OR 13.8, CI 4.6 - 41.4, p=< 0.0001). In our study, the LOS was not affected by the development of gout flare during hospitalization (6.2 vs 6.3 days, respectively).

Conclusion: Hospitalized patients who have allopurinol discontinued upon admission are almost 14 times more likely to develop gout flare than those patients in whom allopurinol is continued during their hospital stay. Medication reconciliation remains an important step in providing care to hospitalized patients. Understanding the role of continuation of ULT in the inpatient setting is of paramount importance in decreasing the risk of gout flare in hospitalized patients.

Disclosure: A. Minalyan, None; **W. Ullah**, None; **S. Khanal**, None; **B. Basyal**, None; **Q. Zhang**, None.

Abstract Number: 0689

The Changing Epidemiology of Inpatient Gout and Associated Mortality: A 17-year National Study

Jasvinder Singh[1] and John Cleveland[1], [1]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Knowledge gaps exist regarding time-trends for the main causes (Cardiac/renal disease vs. infections) hospitalizations in gout. Therefore, we examined whether specific causes (cardiovascular, renal, musculoskeletal, pulmonary, infection) of non-gout hospitalizations and mortality, have changed over time in people with gout.

Methods: We used the U.S. National Inpatient Sample (NIS) data from 1998 to 2014, the last calendar year with International Classification of Diseases, ninth revision, clinical modification (ICD-9-CM) in the U.S. NIS represents a 20% stratified sample of discharges for the U.S., a part of the Agency for Healthcare Research and Quality's (AHRQ) healthcare cost and utilization project (HCUP).

Our study cohort included people hospitalized with a secondary diagnosis of gout based on an ICD-9-CM code, 274.xx, a valid approach with high sensitivity (90%), specificity (100%) and positive predictive value (80%). We assessed whether the rank (and % hospitalizations) of specific diseases in the top 25 Clinical Classifications Software (CCS; and top 5) categories associated with hospitalizations in gout changed between the first (1998-99) and the last study periods (2013-14). CCS is a tool for clustering patient diagnoses and procedures (primary or secondary) into manageable clinically meaningful categories [5]. We chose 2014 as the last study year, due to switching from ICD-9-CM to ICD-10-CM in 2015.

Results: Non-gout Hospitalizations in people with gout: There were 501,847 non-gout hospitalizations in 1998-99 and 1,665,355 in 2013-14. The top four CCS categories did not change rank from 1998-99 to 2013-14, but both top 2-ranked categories, circulatory system and heart diseases, decreased by 9-10%. Infection categories increased from three in the top 25 CCS categories in 1998-99 (rank # 11, 15 and 20) to five in 2013-14 (rank #10, 11, 12, 18 and

21; **Figure 1A**), and included pneumonia, respiratory infections, infections/parasitic diseases and sepsis. Musculoskeletal diseases were rank #5 for hospitalization in 2013-14 and osteoarthritis was also newly added to the top 25 ranks for non-gout hospitalizations.

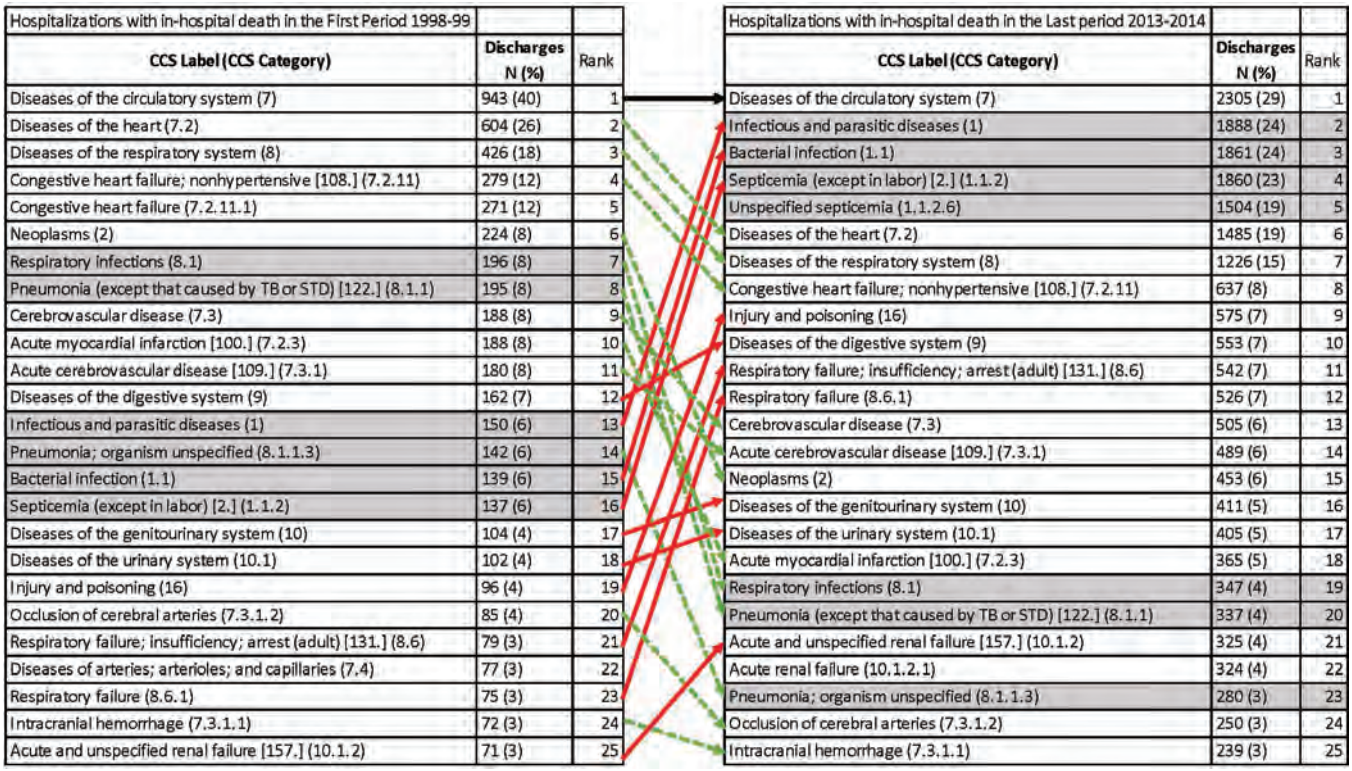
In-hospital mortality: Circulatory system disease was rank #1 in both in 1998-99 and 2013-14, but the attributed proportion decreased from 40% to 29%. Two infection categories were in the top ten in 1998-99 (respiratory infection, rank #7; pneumonia, rank #8) versus four infection categories in the top five CCS categories in 2013-14 (rank #2, #3, #4 and #5; **Figure 1B**). Most cardiac diseases and neoplasms were less frequent, while infection, respiratory failure, renal disease were more frequent in 2013-14 (**Figure 1B**).

Conclusion: Non-gout hospitalizations in people with gout increased over 2-decades. In-hospital mortality in patients with gout showed a replacement of cardiac/respiratory causes in ranks #2-5 in 1998-99 by infectious disease/sepsis in 2013-14. Cardiovascular diseases were the main reasons for non-gout hospitalizations in people with gout in both periods; but more importantly, their relative contribution decreased over 2-decades, while relative contributions of infectious and musculoskeletal diseases (including osteoarthritis) increased.

1998-1999 (501,847 non-primary gout claims)		
CCS Label (CCS Category)	Discharges N(%)	Rank
Diseases of the circulatory system (7)	191,503 (38.2)	1
Diseases of the heart (7.2)	135,647 (27.0)	2
Diseases of the digestive system (9)	52,364 (10.4)	3
Diseases of the respiratory system (8)	48,212 (9.6)	4
Congestive heart failure; nonhypertensive [108.] (7.2.11)	46,894 (9.3)	5
Congestive heart failure (7.2.11.1)	45,471 (9.1)	6
Coronary atherosclerosis and other heart disease [101.] (7.2.4)	33,361 (6.6)	7
Injury and poisoning (16)	32,631 (6.5)	8
Diseases of the musculoskeletal system and connective tissue (13)	32,348 (6.4)	9
Coronary atherosclerosis (7.2.4.4)	28,404 (5.7)	10
Respiratory infections (8.1)	26,472 (5.3)	11
Cerebrovascular disease (7.3)	25,399 (5.1)	12
Diseases of the genitourinary system (10)	25,164 (5.0)	13
Neoplasms (2)	24,963 (5.0)	14
Pneumonia (except that caused by TB or STD) [122.] (8.1.1)	23,878 (4.8)	15
Symptoms; signs; and ill-defined conditions and factors infl (17)	23,635 (4.7)	16
Diseases of the urinary system (10.1)	20,703 (4.1)	17
Endocrine; nutritional; and metabolic diseases and immunity (3)	20,413 (4.1)	18
Acute myocardial infarction [100.] (7.2.3)	18,874 (3.8)	19
Pneumonia; organism unspecified (8.1.1.3)	18,456 (3.7)	20
Complications (16.10)	17,610 (3.5)	21
Cardiac dysrhythmias [106.] (7.2.9)	16,419 (3.3)	22
Non-traumatic joint disorders (13.2)	16,086 (3.2)	23
Acute cerebrovascular disease [109.] (7.3.1)	15,104 (3.0)	24
Lower gastrointestinal disorders (9.6)	14,810 (3.0)	25

2013-2014 (1,665,355 non-primary gout claims)		
CCS Label (CCS Category)	Discharges N(%)	Rank
Diseases of the circulatory system (7)	461,745 (27.7)	1
Diseases of the heart (7.2)	321,175 (19.3)	2
Diseases of the digestive system (9)	177,205 (10.6)	3
Diseases of the respiratory system (8)	155,240 (9.3)	4
Diseases of the musculoskeletal system and connective tissue (13)	143,095 (8.6)	5
Injury and poisoning (16)	141,265 (8.5)	6
Congestive heart failure; nonhypertensive [108.] (7.2.11)	128,570 (7.7)	7
Diseases of the genitourinary system (10)	127,820 (7.7)	8
Diseases of the urinary system (10.1)	120,750 (7.3)	9
Infectious and parasitic diseases (1)	104,720 (6.3)	10
Bacterial infection (1.1)	98,145 (5.9)	11
Septicemia (except in labor) [2.] (1.1.2)	97,475 (5.9)	12
Non-traumatic joint disorders (13.2)	84,505 (5.1)	13
Osteoarthritis [203.] (13.2.2)	79,125 (4.8)	14
Complications (16.10)	76,340 (4.6)	15
Acute and unspecified renal failure [157.] (10.1.2)	74,635 (4.5)	16
Acute renal failure (10.1.2.1)	74,605 (4.5)	17
Unspecified septicemia (1.1.2.6)	71,700 (4.3)	18
Endocrine; nutritional; and metabolic diseases and immunity (3)	70,735 (4.2)	19
Osteoarthritis; localized (13.2.2.1)	68,040 (4.1)	20
Respiratory infections (8.1)	65,595 (3.9)	21
Neoplasms (2)	65,065 (3.9)	22
Symptoms; signs; and ill-defined conditions and factors infl (17)	62,060 (3.7)	23
Cerebrovascular disease (7.3)	58,850 (3.5)	24
Cardiac dysrhythmias [106.] (7.2.9)	58,500 (3.5)	25

Figure 1. Top 25 healthcare cost and utilization project (HCUP) Clinical Classifications Software (CCS) category ranks based on diagnosis or procedures for hospitalizations (1A) and in-hospital death (1B) in people with gout comparing the first study (1998-1999) to the last study period (2013-2014) Figure 1 legend. Solid red arrows show the categories whose rank increased from 1998-1999 to 2013-2014, dashed green arrows whose rank decreased and solid black arrows with the same rank. Each CCS category label and category are shown in the first column. Square brackets refer to single-level CCS categories and regular brackets refer to multi-level CCS categories.



Hospitalizations with in-hospital death in the First Period 1998-99		
CCS Label (CCS Category)	Discharges N (%)	Rank
Diseases of the circulatory system (7)	943 (40)	1
Diseases of the heart (7.2)	604 (26)	2
Diseases of the respiratory system (8)	426 (18)	3
Congestive heart failure; nonhypertensive [108.] (7.2.11)	279 (12)	4
Congestive heart failure (7.2.11.1)	271 (12)	5
Neoplasms (2)	224 (8)	6
Respiratory infections (8.1)	196 (8)	7
Pneumonia (except that caused by TB or STD) [122.] (8.1.1)	195 (8)	8
Cerebrovascular disease (7.3)	188 (8)	9
Acute myocardial infarction [100.] (7.2.3)	188 (8)	10
Acute cerebrovascular disease [109.] (7.3.1)	180 (8)	11
Diseases of the digestive system (9)	162 (7)	12
Infectious and parasitic diseases (1)	150 (6)	13
Pneumonia; organism unspecified (8.1.1.3)	142 (6)	14
Bacterial infection (1.1)	139 (6)	15
Septicemia (except in labor) [2.] (1.1.2)	137 (6)	16
Diseases of the genitourinary system (10)	104 (4)	17
Diseases of the urinary system (10.1)	102 (4)	18
Injury and poisoning (16)	96 (4)	19
Occlusion of cerebral arteries (7.3.1.2)	85 (4)	20
Respiratory failure; insufficiency; arrest (adult) [131.] (8.6)	79 (3)	21
Diseases of arteries; arterioles; and capillaries (7.4)	77 (3)	22
Respiratory failure (8.6.1)	75 (3)	23
Intracranial hemorrhage (7.3.1.1)	72 (3)	24
Acute and unspecified renal failure [157.] (10.1.2)	71 (3)	25

Hospitalizations with in-hospital death in the Last period 2013-2014		
CCS Label (CCS Category)	Discharges N (%)	Rank
Diseases of the circulatory system (7)	2305 (29)	1
Infectious and parasitic diseases (1)	1888 (24)	2
Bacterial infection (1.1)	1861 (24)	3
Septicemia (except in labor) [2.] (1.1.2)	1860 (23)	4
Unspecified septicemia (1.1.2.6)	1504 (19)	5
Diseases of the heart (7.2)	1485 (19)	6
Diseases of the respiratory system (8)	1226 (15)	7
Congestive heart failure; nonhypertensive [108.] (7.2.11)	637 (8)	8
Injury and poisoning (16)	575 (7)	9
Diseases of the digestive system (9)	553 (7)	10
Respiratory failure; insufficiency; arrest (adult) [131.] (8.6)	542 (7)	11
Respiratory failure (8.6.1)	526 (7)	12
Cerebrovascular disease (7.3)	505 (6)	13
Acute cerebrovascular disease [109.] (7.3.1)	489 (6)	14
Neoplasms (2)	453 (6)	15
Diseases of the genitourinary system (10)	411 (5)	16
Diseases of the urinary system (10.1)	405 (5)	17
Acute myocardial infarction [100.] (7.2.3)	365 (5)	18
Respiratory infections (8.1)	347 (4)	19
Pneumonia (except that caused by TB or STD) [122.] (8.1.1)	337 (4)	20
Acute and unspecified renal failure [157.] (10.1.2)	325 (4)	21
Acute renal failure (10.1.2.1)	324 (4)	22
Pneumonia; organism unspecified (8.1.1.3)	280 (3)	23
Occlusion of cerebral arteries (7.3.1.2)	250 (3)	24
Intracranial hemorrhage (7.3.1.1)	239 (3)	25

Figure 1B. See title and legend with the panel above

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Abstract Number: 0690

AR882, a Potent and Selective Uricosuric Agent, Significantly Reduced Serum Urate in Patients with Gout in a Phase 2a Study

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: AR882 is a potent and selective uric acid transporter 1 (URAT1) inhibitor under development for the treatment of hyperuricemia or gout. Phase 1 single ascending dose and multiple ascending dose clinical studies in healthy adult male subjects demonstrated linear pharmacokinetics and dose-dependent serum uric acid (sUA) lowering effect. A phase 2a study in patients with gout is ongoing to evaluate efficacy following a three-week treatment regimen comparing AR882 with 40 mg febuxostat.

Methods: In a phase 2a, single-center, two-sequence, cross-over study, adults with gout (sUA > 7 mg/dL) were randomized to receive a once-daily, three-week treatment with AR882 50 mg alone or in combination with febuxostat 40 mg. Eleven patients have been enrolled in this ongoing study. Serial blood samples were collected for measurement of sUA, AR882 or febuxostat pharmacokinetics and pharmacodynamics at the end of each treatment week (Day 7, Day 14 and Day 21). Urine samples were collected for assessment of uric acid excretion. Laboratory safety tests, vital signs, and electrocardiograms were collected throughout the study.

Results: Following treatment of AR882, 100% of patients had sUA levels below 6 mg/dL, with 63% of patients below 5 mg/dL. AR882 reduced sUA from baseline (9.0 ± 1.3 mg/dL) to 4.7 ± 0.7 mg/dL at 24 hours postdose following multiple doses, corresponding to 47.1 ± 9.4% reduction. In comparison, febuxostat 40 mg reduced sUA levels to 6.1 ± 1.3 mg/dL (33.7 ± 6.7% reduction), with 50% and 13% patients below 6 and 5 mg/dL, respectively. The combination of AR882 and febuxostat further reduced sUA levels to 3.5 ± 1.1 mg/dL (61.0 ± 10.0% reduction) at 24 hours postdose with percentage of patients < 6, 5, 4 mg/dL at 100%, 78%, 67%, respectively. Fractional excretion of uric acid following AR882 treatment was higher than baseline. Exposure of AR882 in gout patients was slightly lower than in healthy subjects presumably due to higher BMI and body weight. AR882 showed similar exposure between patients with normal renal function and mild renal impairment. In mildly renal impaired patients, AR882 reduced sUA from 8.6 ± 1.1 mg/dL mg/dL to 4.5 ± 0.8 mg/dL. AR882 was well tolerated. There were no clinically significant laboratory or ECG abnormalities noted. All adverse events were mild or moderate in severity. One subject with viral bronchitis was discontinued due to concern of COVID-19.

Conclusion: AR882 produced marked reductions in sUA, with all patients achieving and maintaining levels below 6 mg/dL following multiple dosing of AR882. These data provide clear guidance for dose selection in future large phase 2 studies and support continued development of AR882 alone or in combination with XO inhibitors for treatment of gout.

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Abstract Number: 0691

Denosumab Did Not Improve Computerized Tomography Erosion Scores When Added to Intensive Urate-Lowering Therapy in Gout: Results from a Pilot Study

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SESSION INFORMATION
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Background/Purpose: Bone erosion is a common complication of tophaceous gout. Disordered osteoclast activity has been implicated in the pathogenesis of gouty bone erosion. We sought to determine if the addition of denosumab

to intensive urate-lowering therapy (ULT) improves gouty bone erosion through targeting receptor activator of nuclear factor kappa-B ligand (RANKL).

Methods: Open-label, parallel-group pilot randomized controlled trial in which 20 participants with gout with at least one confirmed conventional radiographic foot bone erosion were assigned in a 1:1 allocation to receive denosumab (60 mg subcutaneous every 6 months) added to intensive ULT (serum urate ≤5 mg/dL or 300 μmol/L at the time of randomization and continued for the duration of the study) or intensive ULT alone. The primary outcome was the change in the foot computed tomography (CT) bone erosion score from baseline to 12 months. Erosion score was assessed by an experienced musculoskeletal radiologist blinded to study assignment. Secondary outcomes included change in serum c-terminal telopeptide (CTX), functional status by Health Assessment Questionnaire-II, physical and mental health by Short Form Health Survey 12 and pain scores by visual analogue scale (VAS).

Results: The mean age of all study participants was 65.0 (SD 12.4) years and 19/20 were men. Mean disease duration was 15 (SD 9.3) years, serum urate at randomization was 4.3 (0.6) mg/dL and the mean CT erosion score was 6.8

	Denosumab + Urate-lowering therapy N=10	**Urate-lowering therapy alone N=10**
Age, years	67.0 ± 15.0	63.0 ± 9.4
Men (%)	90%	EN
Enrollment site		
Birmingham	5 (50%)	4 (40%)
Auckland	5 (50%)	6 (60%)
Ethnicity		
European descent	6 (60%)	5 (50%)
Asian	1 (10%)	1 (10%)
Māori	0 (0%)	2 (20%)
Other	3 (30%)	2 (20%)
Disease age of onset, years	52.5 ± 19.0	47.2 ± 12.9
Disease duration, years	14.10± 11.1	15.9 ± 7.7
Tophi (%) at screening	6 (60%)	5 (50%)
Serum urate at randomization (mg/dL)	4.3± 0.5	4.2 ± 0.7
Estimated glomerular filtration rate (mL/min/1.73 m2)	76.5 ± 32.0	72.0 ± 15.3
Serum CTX	316.6 ± 152.6	286.9 ± 111.5
Health Assessment Questionnaire-II	0.20 ± 0.2	0.17 ± 0.2
Short Form Health Survey (SF-12) scores	PCS 44.7 ± 11.9 MCS 46.0 ± 7.4	PCS 46.0 ± 7.4 MCS 54.0 ± 10.2
Pain score (VAS)	2.2 ± 3.8	1.3 ± 1.5
CT erosion score	6.6± 5.4	7.0 ± 5.1

CTX = C-terminal telopeptide, PCS = Physical Component Score of SF 12, MCS = Mental Component Score of SF-12, VAS = Visual Analog Scale, CT = Computerized Tomography

Table 1. Baseline characteristics of participants. Unless stated, data are shown as mean ± SD.

	Denosumab + Urate-lowering therapy	Urate-lowering therapy alone
Change in CT erosion score after one year	0.0 ± 0.0	0.0 ± 0.0
Change in CTX after one year	-152.6 ± 144.1	25.9 ± 111.7
Change in Health Assessment Questionnaire-II (HAQ-II) after one year	0.08 ± 0.2	-0.1 ± 0.12
Change in Short Form Health Survey (SF-12) scores after one year	PCS 13.9 ± 16.1 MCS -1.2 ± 8.1	PCS 7.9 ± 10.0 MCS -2.0 ± 9.31
Change in Pain Score (VAS) after one year	-0.9 ± 3.4	-0.1 ± 1.7

CTX = C-terminal telopeptide, PCS = Physical Component Score of SF 12, MCS = Mental Component Score of SF-12, VAS = Visual Analog Scale, CT = Computerized Tomography

Table 2. Primary and Secondary Study Endpoints. Unless stated, data are shown as mean ± SD.

(SD 5.1). Baseline characteristics were balanced between the denosumab and active comparator groups (Table 1). There was no interval change in CT erosion score in either the denosumab or active comparator group after one year of follow-up (Table 2). Serum CTX declined markedly in the denosumab group compared with the active comparator group. Other secondary outcomes did not change between groups (Table 2). One patient developed atrial fibrillation (on denosumab) and another atrial flutter (on active comparator). There were no serious adverse events and no events led to study discontinuation.

Conclusion: In this one-year pilot study, denosumab did not offer additional benefit to intensive urate lowering therapy for gouty bone erosion.

Disclosure: A. Gaffo, Amgen, 1; **K. Saag**, Arthrosi, 5, Horizon Therapeutics plc, 2, 5, Atom Bioscience, 5, LG Pharma, 5, Takeda, 5, Mallinkrodt, 5, SOBI, 2, 5, Shanton, 2; **A. Doyle**, None; **J. Melnick**, None; **A. Horne**, None; **J. Foster**, None; **A. Mudano**, None; **S. Biggers**, None; **D. Redden**, None; **N. Dalbeth**, AstraZeneca, 1, 2, Abbvie, 1, Arthrosi, 1, Dyve BioSciences, 1, Selecta, 1, Janssen, 1.

Abstract Number: 0692

Pre-Operative Opioid Usage Increases Length of Stay for Rheumatoid Arthritis Patients Undergoing Total Hip Arthroplasty and Total Knee Arthroplasty

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
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Background/Purpose: Total Hip (THA) and total knee arthroplasty (TKA) are cost-effective procedures that improve the health-related quality of life for patients with advanced symptomatic joint damage, including patients with rheumatoid arthritis (RA). However, increasing utilization has led to marked increase in cost with inpatient costs representing the largest proportion of expenditures for TKA. For this reason, it is important for cost containment efforts to address length of stay (LOS). Preoperative opioid usage has been associated with increased LOS and postoperative complications in osteoarthritis (OA) patients. Patients with RA have a longer LOS after THA/TKA than OA patients, yet the factors contributing to LOS, including preoperative opioid use, have not been investigated.

Methods: We retrospectively reviewed data from a prospectively collected cohort of 252 RA patients undergoing either THA or TKA. Demographics, RA characteristics, medications, and disease activity were systematically collected pre-operatively. Disease activity was measured utilizing the DAS28 and CDAI, PROMs included HOOS/KOOS and MDHAQ, and ESR, CRP, and serologies were drawn pre-operatively. Baseline characteristics were summarized using descriptive statistics and compared using Chi-squared, Fisher's exact test, or two-sample t-test or Wilcoxon rank-sum test as appropriate. Linear Regression analysis was performed to explore the relationship between LOS

Table 1: Multivariate Analysis for Predictors of Length of Stay following Total Hip and Total Knee Arthroplasty in Patients with Rheumatoid Arthritis.

Multivariate variable	Level	Estimated model coefficient (standard error)	Percentage change in the original scale of length of stay with 1 unit increase of a continuous predictor, or a comparison of one category to the reference category for a categorical predictor * (95% CI)	p-value
Sex	Female vs. Male	0.18 (0.08)	19.72% (2.35%, 40.05%)	0.04
TKA	No vs. Yes	0.04 (0.07)	4.08% (-9.26%, 19.38%)	0.61
Type of Surgery	Hip vs. Knee	-0.22 (0.06)	-19.75% (-28.65%, -9.73%)	0.0002
Opioid	No vs. Yes	-0.20 (0.06)	-18.13% (-27.21%, -7.91%)	0.0007
Post-op Transfusion	No vs. Yes	-0.25 (0.09)	-22.11% (-34.71%, -7.10%)	0.006
Hemoglobin at baseline		0.03 (0.02)	-2.96% (-6.69%, 0.92%)	0.18
Das28_esr at baseline		0.07 (0.04)	7.25% (-0.84%, 16.00%)	0.053
CDAI at baseline		-0.003 (0.004)	-0.30% (-1.08%, 0.49%)	0.51

*Percentage change in the original scale of length of stay with 1 unit increase of a continuous predictor, or a comparison of one category to the reference category for a categorical predictor: (exponential (estimated model coefficient)-1)*100

(log-transformed) and predictors. The final multivariate model was constructed through backward selection among predictors that were found statistically significant ($p< 0.05$) in the univariate analysis.

Results: RA cases were predominantly women (83%), with median disease duration (14.1 +/-12 years), and moderate disease activity (mean DAS28= 3.7±1.3, CDAI=18.4±10.9). 240(95%) cases had LOS data available. 88 (37%) patients were taking opioids pre-operatively. The mean LOS was 3.4±1.5 days with those undergoing THA having a LOS of 3.1±1.6 and TKA with a LOS of 3.7±1.4. In the univariate analysis, post-operative transfusion (p=0.01), baseline DAS 28 (p=0.02), sex (p=0.001), BMI (p=0.03), Employment status (p=0.04), type of surgery ($p< 0.001$), opioid usage (p=0.001), duration of surgery (p=0.01), HOOS/KOOS baseline pain score (p=0.01), HOOS/KOOS baseline function score (p=0.003), duration of disease (0.03), baseline MD-HAQ (p=0.01), baseline ESR (p=0.03) were significantly associated with extended LOS. The multivariate analysis revealed several factors that impact LOS. LOS was decreased for patients who underwent THA (p=0.002), male gender (p=0.04), did not have a post-op transfusion (p=0.006) and did not take opioids pre-operatively (p=0.0007) (**Table 1**).

Conclusion: Patients who receive a post-operative transfusion, undergo knee surgery, women, and increased opioid usage were associated with increased length of stay. While gender and surgical type are non-modifiable risk factors, pre-operative optimization should focus on transfusion risk factors and pre-operative opioid reduction. We recommend that patients undergo pre-operative opioid cessation counseling, and multimodal pain management should be used peri-operatively to reduce opioid usage.

Disclosure: K. Morse, None; **N. Heinz**, None; **J. Abolade**, None; **J. Wright-Chisem**, None; **L. Russell**, None; **M. Zhang**, None; **S. Mirza**, None; **D. Orange**, None; **M. Figgie**, wishbone, 1, 2, 3, 4, 5, insight, 1, hs2, 1, mekanika, 1, lima, 1, 2; **P. Sculco**, EOS imaging, 1, Intellijoint Surgical, 1, Depuy Synthes, 1, Lima Corporate, 1; **S. Goodman**, Pfizer, 1, Novartis, 1, UCB, 1, regenosine, 1, 2, Horizon, 1.

Abstract Number: 0693

Effect of Physical Activity on Cartilage Degradation and Inflammation in Individuals with Lumbar Spinal Stenosis

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Background/Purpose: Guidelines recommend 150 minutes a week in moderate-intensity physical activity (MPA) to improve health in individuals with chronic disease such as those with lumbar spinal stenosis (LSS). LSS affects older adults' physical function and limits their mobility, which leads to reduced activity participation that might result in further disability. Because of the anatomical changes found in LSS and symptoms presented by patients, health professionals are hesitant in promoting MPA as they are fearful of worsening the condition. Therefore, it is imperative to understand whether MPA affects the concentration of plasma biomarkers in individuals with LSS. Our study aimed to determine the associations between MPA and concentration of plasma biomarkers (i.e., cartilage degeneration

Biomarkers	Concentration in pg/ml median (Q25, Q75)	Moderate Physical Activity (min/day)	
		Spearman's rho	p-value
IL-2 §	-3.00 (-15.00, 10.15)	-.18	.066
IL-1β §	-.35 (-14.65, 12.28)	-.15	.130
IL-5 §	-.50 (-14.60, 11.83)	**-.19**	**.049**
IL-6 §	-2.00 (-14.95, 14.05)	**-.24**	**.011**
IL-10 §	.50 (-16.50, 11.38)	**-.20**	**.037**
IL-12p70 §	.10 (-12.00, 8.45)	**-.20**	**.042**
IL-13 §	-.60 (-5.93, 8.00)	-.07	.464
IFN-γ §	-.60 (-12.78, 8.15)	**-.23**	**.016**
COMP ¶	-20.83 (-122.65, 86.35)	.03	.791
CTX-II ¶	6.55 (-201.31, 209.31)	-.16	.091
CS846 ¶	-73.21 (-303.97, 165.61)	**.26**	**.007**
TIMP-1 ¶	8441.13 (-42366.19, 44697.94)	**.22**	**.029**

Pg/ml: picogram per milliliter; Q25: quartile 25; Q75: quartile 75; min/day: minutes per day; IL: interleukin; IFN: interferon; COMP: Cartilage Oligomeric Matrix Protein; CTX-II: Carboxy-Terminal Telepeptides of Type II Collagen; CS846: aggrecan Chondroitin Sulfate 846 epitope; TIMP-1: Tissue Inhibitor of Metalloproteinase-1.

and inflammation) in individuals with LSS, and to also explore associations between changes in MPA and changes in concentration of biomarkers.

Methods: We performed a secondary analysis from a randomized trial that compared three non-surgical approaches to manage LSS. Participants with available blood samples and MPA measured at baseline and 2-month follow-up were included (N=109). Cartilage degradation was assessed by analyzing the concentration (volume expressed in pg/ml) of different biomarkers (COMP, CTX-II, CS864 and TIMP-1) using enzyme-linked immunosorbent assay kits specific to each biomarker. A panel of 8 inflammatory biomarkers (interleukin [IL]-1β, IL-2, IL-5, IL-6, IL-10, IL-12p70, IL-13 and IFN-γ) were assessed using a MILLIPLEX® MAP Human High Sensitivity T Cell Magnetic Bead Panel. Daily time (min/day) in MPA was assessed using the Sensewear Armband activity monitor for 7 days. Changes (i.e. follow-up minus baseline) in concentration of each biomarker and MPA were calculated. Associations between changes in concentration of biomarkers and in MPA were computed as Spearman's rho with an alpha of .05. Statistical analyses were performed using IBM SPSS Statistics 26 (IBM Corp, Armonk, NY, USA).

Results: Participants were 52% female, 72.9±7.5 years old, with a BMI of 29.7±5.8. They barely changed their time in MPA from baseline to 2-month follow-up (-4.4±30.8 min/day; median [Q25, Q75] = 0.0 [-8.5, 5.5] min/day). This change in MPA was inversely associated with changes in concentration of inflammatory biomarkers: IL-5 (rho=-.19; p=.049), IL-6 (rho=-.24; p=.011), IL-10 (rho=-20; p=.037), IL-12p70 (rho=-.20; p=.042), IFN-γ (rho=-.23; p=.016); and directly associated with changes in concentration of cartilage degradation biomarkers (pg/ml): CS864 (rho=.26; p=.007) and TIMP-1 (rho=.22; p=.029).

Conclusion: This exploratory analysis in individuals with LSS showed a trend indicating that increases in time spent in MPA may reduce inflammation, however, it may increase cartilage degradation. Promoting MPA in those with LSS may be challenging as few individuals engage in it and the benefit/risk ratio in terms of disease modulation needs further investigation.

Disclosure: G. Almeida, None; **S. Khoja**, None; **L. Terhorst**, None; **G. Sowa**, None; **S. Piva**, None; **M. Schneider**, None.

Abstract Number: 0694

Relationships Among Adherence and Patient Outcomes in a Cognitive Behavioral Plus Physical Activity Intervention for Older Adults with Osteoarthritis and Hypertension

Xiaojun Shi[1], Elizabeth Schlenk[2] and Susan Sereika[1], [1]University of Pittsburgh School of Nursing, Pittsburgh, [2]University of Pittsburgh School of Nursing, Pittsburgh, PA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster
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Background/Purpose: Osteoarthritis of the knee (OAK) affects nearly 14 million older adults and more than half are diagnosed with hypertension (HTN). Cognitive behavior therapy (CBT) has demonstrated inconsistent effectiveness on OAK symptoms. The purpose of this secondary analysis was to examine if patient adherence to CBT influences its effectiveness for OAK outcomes (pain, function, stiffness, health-related quality of life [HRQoL], and fatigue) among people with comorbid HTN.

Methods: This longitudinal comparative study analyzed data from a randomized controlled trial of a CBT plus physical activity (Staying Active with Arthritis or STAR) intervention vs. a control intervention in older adults with OAK and HTN. Participants who completed at least one session of the STAR or control interventions were included (n=172). STAR intervention consisted of 15 sessions including six weekly face-to-face physical therapy (lower extremity exercise and walking) sessions and nine biweekly telephone sessions for support (mean adherence was 10.8±0.6). Patient adherence was derived by dichotomizing participants into adherers who completed 15 STAR sessions (n=37) and non-adherers who completed < 15 STAR sessions (n=51). Control intervention consisted of 15 telephone sessions on senior health topics (n=84). Pain, function, and stiffness were measured by WOMAC Osteoarthritis Index subscales, HRQoL was measured by Short Form-36v2 Physical Component Summary and Mental Component Summary, and fatigue was measured by Brief Fatigue Inventory at baseline, immediate post-intervention, and 6 months post-intervention. Linear mixed modeling controlling for baseline outcome value, time, significant demographics and medical factors (age, sex, race, marital status, education, employment status, duration of OAK and HTN, and number of comorbidities) were used to compare within-group and between-group differences in the outcomes.

Results: The sample was primarily female (n=126, 73.3%), non-Hispanic white (n=130, 75.6%), married/partnered (n=86, 50.0%), and not working/retired (n=86, 50.0%) with mean (±SD) age of 65.0±8.0 years. On average, the duration of OAK and HTN was 11.3±9.3 and 13.6±9.2 years, respectively, and the number of comorbidities was 8.4±3.6. Regardless of adherence group, STAR participants had significant improvement in pain, function, and stiffness from baseline to immediate post-intervention and 6 months post-intervention. Compared with adherers, controls reported significantly greater knee pain (b=0.69, p=0.035) and a trend for worse function (b=2.24, p=0.051), but the difference between non-adherers and controls was not significant. There was no significant difference between adherers and non-adherers in pain, function, stiffness, HRQoL, and fatigue.

Conclusion: Both adherers and non-adherers showed improved OAK-specific outcomes of pain, function, and stiffness, but not HRQoL and fatigue. There was no difference in OAK outcomes between adherers and non-adherers or between non-adherers and controls. Adherers had less knee pain and a trend for better function compared to

controls. Patient adherence to intervention sessions was a significant factor influencing the effectiveness of the intervention.

Disclosure: X. Shi, None; **E. Schlenk**, None; **S. Sereika**, None.

Abstract Number: 0695

Chronic Inflammatory Back Pain Occurring Later in Life: A Neglected Concept

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SESSION INFORMATION

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Background/Purpose: Chronic back pain (CBP) is a common musculoskeletal complaint and a significant cause of disability (Weisman et al., 2013). A subset of CBP, chronic inflammatory back pain (CIBP) occurs in about one third of CBP patients in the NHANES 2009-2019 survey, especially in younger individuals (Weisman et al., 2013). For older individuals, there is little known about CIBP. Although older age is not an exclusion factor in many criteria for inflammatory back pain (IBP) (Weisman, 2012), it is generally thought IBP begins in patients less than 45 years old. Thus, we endeavored to review CIBP in individuals 50 years and older by i) a systematic literature review, ii) evaluating prevalence using National Health and Nutrition Examination (NHANES) data from the 2009-2010 survey, and iii) reporting clinical features of late onset ankylosing spondylitis (AS) from a longitudinal AS cohort.

Methods: The design of the present analysis was based on a systematic literature review using "chronic inflammatory back pain" and "chronic low back pain" as search terms to identify articles of interest between January 1, 2013,

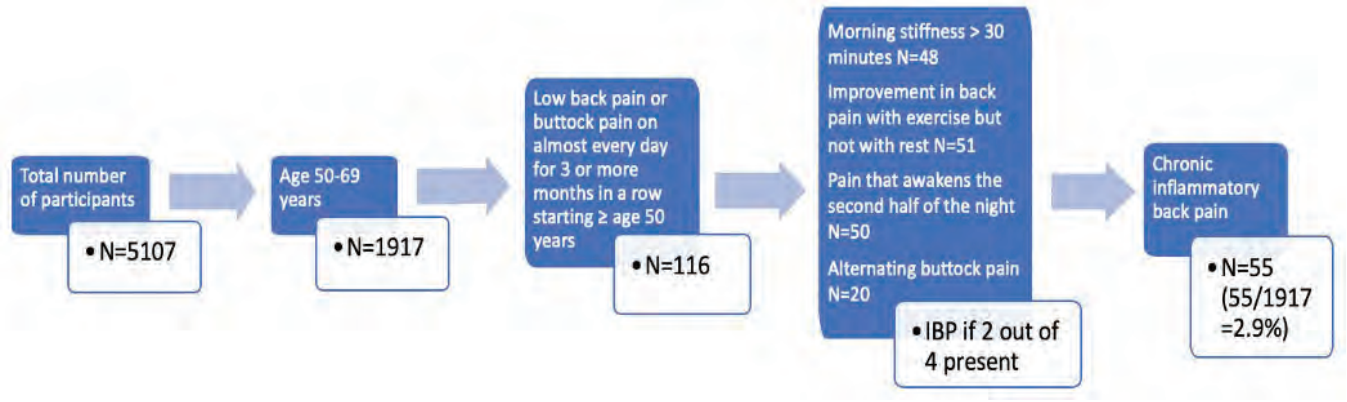

Figure 1. Late Onset "Chronic Inflammatory Back Pain" in NHANES 2009-2010

Authors	Year	Journal	Title
March et al	1998	Med J Aust	Musculoskeletal disability among elderly people in the community
Palm et al	2002	J Rheumatol	Prevalence of ankylosing spondylitis and other spondyloarthropathies among patients with inflammatory bowel disease: a population study (the IBSEN study)
Bennett et al	2010	Ann Rheum Dis	The fatty Romanus lesion (FRL): a non-inflammatory spinal MRI lesion specific for axial spondyloarthropathy
Nguyen et al	2010	J Rheumatol	Assessment of ankylosing spondylitis criteria in patients with chronic low back pain and vertebral endplate Modic I signal changes
Weisman et al	2013	Ann Rheum Dis	The prevalence of inflammatory back pain: population-based estimates from the US National Health and Nutrition Examination Survey, 2009-10
Bandinelli et al	2014	Clin Exp Rheumatol	Occult radiological sacroiliac abnormalities in patients with inflammatory bowel disease who do not present signs or symptoms of axial spondylitis
Hamilton et al	2015	BMC Musculoskelet Disord	The prevalence of axial spondyloarthritis in the UK: a cross-sectional cohort study
Kreis et al	2015	Health Qual Life Outcomes	Relationship between optimism and quality of life in patients with two chronic rheumatic diseases: axial spondyloarthritis and chronic low back pain: a cross sectional study of 288 patients
Thom et al	2015	Arthritis Care Res (Hoboken)	Prevalence of chronic axial pain, inflammatory back pain, and spondyloarthritis in diagnosed psoriasis
Burgos-Varga et al	2016	Arthritis Res Ther	The prevalence and clinical characteristics of nonradiographic axial spondyloarthritis among patients with inflammatory back pain in rheumatology practices: a multinational, multicenter study
Shmagel et al	2016	Arthritis Care Res (Hoboken)	Epidemiology of Chronic Low Back Pain in US Adults: Data From the 2009-2010 National Health and Nutrition Examination Survey
Hashem et al	2018	Spine (Phila Pa 1976)	Exploration of the Inter-Relationships Between Obesity, Physical Inactivity, Inflammation, and Low Back Pain
Tomczyszyn et al	2018	Med Pr	Assessment of the type of farmers' low back pain
Yesmin et al	2018	Int J Rheum Dis	Inflammatory back pain and associated disease conditions among patients with chronic low back pain in Bangladesh
Sigaux et al	2019	Semin Arthritis Rheum	High prevalence of spondyloarthritis in sarcoidosis patients with chronic back pain
Zwolak et al	2019	Wiad Lek	Reasons for diagnostic delays of axial spondyloarthritis
Angioni et al	2019	Rheumatismo	Spa therapy induces clinical improvement and protein changes in patients with chronic back pain
Ye et al	2019	Clin Rheumatol	MRI compared with low-dose CT scanning in the diagnosis of axial spondyloarthritis

Table 1. Results of Systematic Review

Variable	Age onset of AS <20 n=411	Age onset of AS ≥50 n=33	p value
Male%	73.5	78.8	0.50
White%	82.7	87.9	0.45
Arthritis%	65.7	72.7	0.41
Uveitis%	39.7	21.2	0.036
Ulcerative colitis%	6.33	0	0.14
Crohn's disease%	6.33	3.03	0.45
HLA-B27positive%	86.7	53.1	<0.0001

Table 2. Characteristics of Late Onset AS from 1253 Patients in the PSOAS Cohort

and March 1, 2020. The search was restricted to articles about human subjects, in English, and including subjects >65 years of age. The data from the arthritis questionnaire in the 50-59 age group of the 2009-2010 NHANES were analyzed using the Berlin 7b criteria looking at prevalence of CIBP. Lastly, the clinical features of AS patients in the Prospective Study of Outcomes in AS (PSOAS)/Australo-Anglo-American Spondyloarthritis Cohorts (TASC) were examined comparing patients with age of onset less than 20 years old to those 50 years and older, using Chi-square test to look at significance.

Results: Using the search term "chronic inflammatory back pain," the literature search identified 1,203 articles. The second search using "chronic low back pain" identified 2,245 articles. Eighteen articles were included in the review that met search criteria for CIBP in the elderly. Fifteen articles were cross-sectional studies, one was case-control, one longitudinal, and one was a randomized trial (*Table 1*). In NHANES 2009-2010, 55 (2.9%) subjects otherwise met Berlin criteria for CIBP but that started over the age of 50 years (*Figure 1*). Of the 1,253 patients in the PSOAS cohort, 33 (2.6%) had disease onset ≥ 50 years old. There was markedly lower frequency of HLA-B27 and lower frequency of uveitis with late onset disease (*Table 2).*

Conclusion: In a systematic review of articles about CIBP, we found a wide range of studies on chronic back pain from different specialties: rheumatology, pain management, orthopedic surgery, neurosurgery, chiropractic, imaging, and general medicine. However, there was not one article addressing CIBP in the older population. Based on the NHANES data, if the age restriction is omitted, nearly 3% of the population has chronic inflammatory back pain commencing on or after the age of 50 years. Moreover, from the PSOAS/TASC data, one in 40 AS patients may have disease onset after age 50. These are unmet needs for this population group, for non-rheumatologists to identify at-risk patients and refer appropriately, and for rheumatologists to consider as an important clinical entity.

Disclosure: L. Ridley, None; **N. Rianon**, None; **M. Hwang**, Novartis, 5, University of Texas Health Science Center at Houston (UTHealth) Center of Clinical and Translational Sciences KL2 program, 2; **M. Lee**, None; **L. Gensler**, AbbVie, 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB Pharma, 2, 5; **M. Ward**, None; **M. Brown**, None; **A. Tahanan**, None; **M. Rahbar**, None; **M. Ishimori**, None; **M. Weisman**, None; **J. Reveille**, Eli Lilly, 2, UCB, 5, Janssen, 2.

Abstract Number: 0696

Femoral Cartilage Ultrasound Echo-Intensity Associates with Arthroscopic Cartilage Damage in People Following Anterior Cruciate Ligament Reconstruction

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SESSION INFORMATION
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Background/Purpose: Over one-third of people will develop knee osteoarthritis within 10 years of an anterior cruciate ligament (ACL) injury. Ultrasound may be used to monitor early pathological cartilage changes that occur after an ACL injury. However, it is unclear if a non-invasive quantitative ultrasound assessment correlates with arthroscopic

cartilage damage. The purpose of our study was to compare quantitative cartilage ultrasound metrics between people with and without arthroscopic cartilage damage following an ACL injury.

Methods: We recruited individuals between 18 and 35 years of age with a primary unilateral ACL injury at a pre-operative visit with an orthopaedic surgeon. Participants were excluded if they had a history of lower extremity surgery, injured either knee within the last 6 months (other than ACL injury), or previously been diagnosed with any form of arthritis. A knee ultrasound assessment occurred pre-operatively prior to an arthroscopy. With the knee in maximal knee flexion, a transverse suprapatellar ultrasound assessment was used to image the femoral cartilage in the individual's injured knee. One reader manually segmented the cartilage. Next, a custom program automatically divided the cartilage into standardized medial and lateral femoral condyle regions and calculated 3 measures (Figure): 1) mean cartilage thickness (cartilage cross-sectional area divided by the cartilage length), 2) echo-intensity mean (average grey-scale pixel value ranging from 0–255), and 3) echo-intensity heterogeneity (standard deviation of the pixel intensity within the region). During a clinical arthroscopy, an orthopaedic surgeon with a sub-specialty in sports medicine graded the medial and femoral condyle using the Outerbridge grading system and operationally defined cartilage status as: *normal cartilage*: Outerbridge = 0 or *cartilage damage*: Outerbridge ≥1 (i.e., Outerbridge 1 = cartilage

Demographics		Overall	Medial Cartilage		Lateral Cartilage	
			Damage*	Normal	Damage*	Normal
n		24	12	12	12	12
Sex (% female)		33%	33%	33%	33%	33%
Height (cm)		173.8 ± 9.8	175.3 ± 10.5	172.3 ± 9.3	172.9 ± 7.7	174.6 ± 11.9
Mass (kg)		76.5 ± 15.3	79.0 ± 15.8	73.8 ± 15.1	**70.1 ± 11.9**	**83.5 ± 16.1**
Age (years)		24.0 ± 4.6	22.8 ± 4.6	25.3 ± 4.4	25.0 ± 5.2	23.0 ± 3.8
IKDC (0 - 100)		57.4 ± 14.6	54.3 ± 17.2	61.0 ± 10.4	59.1 ± 15.1	55.7 ± 14.7
Injury to surgery (days)		49.8 ± 51.9	50.6 ± 68.9	49.0 ± 29.7	53.9 ± 66.9	45.7 ± 33.5
Knee angle during US (°)		127.6 ± 12.0	125.0 ± 13.5	130.3 ± 10.2	131.3 ± 10.8	124.0 ± 12.4
Outerbridge Score (n)	0	-	0	12	0	12
	I	-	5	0	11	0
	II	-	5	0	1	0
	III	-	2	0	0	0
	IV	-	0	0	0	0

Table 1. Participant Demographics. mean ± standard deviation unless otherwise noted. Bold text indicates statistically significant differences between participants with and without cartilage damage ($p<0.05$). *Dichotomous cartilage damage variable based on the Outerbridge grade: 1) normal cartilage: Outerbridge = 0; 2) cartilage damage: Outerbridge >1. cm = centimeters, kg = kilograms; US = ultrasound

Medial Femoral Condyle				
Cartilage Outcomes	Normal	Damage	t (p-value)	*d* (95% CI)
Mean Thickness (mm)	2.02 ± 0.34	2.22 ± 0.38	-1.37 (0.19)	0.56 (-0.28, 1.35)
Echo-intensity mean (0-255)	**79.37 ± 6.85**	**71.64 ± 4.64***	3.24 (0.004)	-1.32 (-2.15, -0.40)
Echo-intensity SD (0-255)	**10.47 ± 2.08**	**8.08 ± 0.97***	3.60 (0.002)	-1.47 (-2.32, -0.52)
Lateral Femoral Condyle				
Cartilage Outcomes	Normal	Damage	t (p-value)	*d* (95% CI)
Mean Thickness (mm)	1.94 ± 0.31	1.84 ± 0.28	0.78 (0.44)	-0.32 (-1.11, 0.50)
Echo-intensity mean (0-255)	72.85 ± 7.81	76.62 ± 5.00	-1.25 (0.17)	0.57 (-0.26, 1.37)
Echo-intensity SD (0-255)	8.48 ± 0.98	8.83 ± 1.49	-0.63 (0.50)	0.28 (-0.53, 1.07)

Table 2. Comparison of Femoral Cartilage Ultrasound Outcomes Between People With and Without Arthroscopic Cartilage Damage. SD = standard deviation; d = Cohen's d effect size; 95% CI = 95% confidence intervals. *statistically significant compared to people with arthroscopically normal cartilage; Bold text indicates statistically significant and large magnitude effect sizes between people with and without cartilage damage

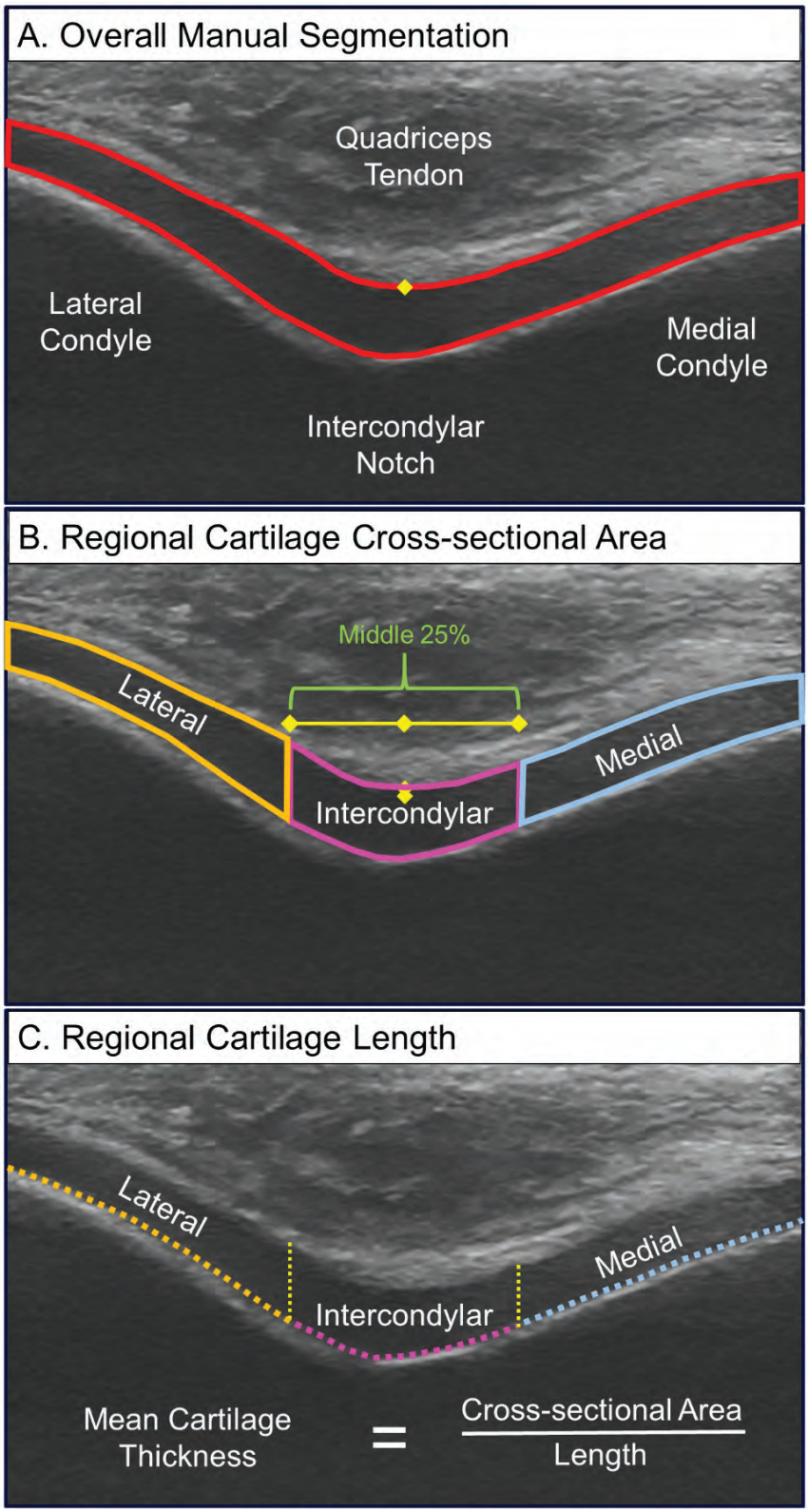

Figure Standardized Femoral Cartilage Segmentation. We used a custom program to take an overall cartilage manual segmentation (A), and use a standardized method to automatically separate the cartilage (B). This abstract focused on cartilage in the medial and lateral regions. The custom program calculated the mean cartilage thickness by dividing the regional cartilage cross-sectional area (B) by the regional cartilage length (C).

softening and swelling). We performed independent samples t-tests and used Cohen's *d* effect sizes to compare the quantitative ultrasound metrics between individuals with (n=12) and without (n=12) arthroscopic cartilage damage.

Results: The 24 participants were primarily male (n=16) and on average 24 ± 5 years old and 50 ± 52 days since ACL injury (Table 1). In the medial femoral condyle, echo-intensity mean and heterogeneity are greater in individuals with normal cartilage compared to those with cartilage damage (Table 2). In the lateral femoral condyle, there are no differences between cartilage ultrasound outcomes between individuals with and without arthroscopic cartilage damage.

Conclusion: Following ACL injury, an ultrasound assessment detects hypo-intense and less heterogeneous medial femoral cartilage in people with arthroscopically identified medial femoral cartilage damage. Future studies are needed to identify the prognostic importance of cartilage ultrasound echo-intensity characteristics, and validate these clinically-accessible metrics against more sophisticated markers of cartilage health.

Disclosure: M. Harkey, Pfizer, Inc., 1; **E. Little**, None; **M. Thompson**, None; **M. Zhang**, None; **J. Driban**, Pfizer, Inc., 1, 2, Eli Lilly and Company, 1; **M. Salzler**, None.

Abstract Number: 0697

Inferior Tendon Structure and Function Seen in Patients with Achilles Tendinopathy and Neovascularization of the Achilles Tendon

Brian Honick[1], Haraldur Sigurdsson[1] and Karin Silbernagel[1], [1]University of Delaware, Newark, DE

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Orthopedics, Low Back Pain, & Rehabilitation Poster
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Background/Purpose: In prior research, the incidence rate of neovascularization with Achilles tendinopathy ranged between 47-88% of cases. The purpose of this study was to identify the incidence rate of neovascularization in individuals with midportion Achilles tendinopathy, and to examine if there were differences in tendon structure, hopping performance, and symptom severity based on the presence or absence of neovessels.

Methods: Eighty-three participants (41 females) with a mean ± SD age of 48 ± 12 years, and BMI of 28 ± 5 with midportion Achilles tendinopathy were recruited. A standardized clinical examination confirmed the diagnosis of midportion Achilles tendinopathy. Tendon morphology was examined with diagnostic ultrasound to measure thickness and cross-sectional area (CSA) at the thickest free portion of the tendon. Power Doppler assessed whether neovessels were present within the tendon. Functional performance was measured with a single-leg hopping task and the plyometric quotient was used for analysis. The Victorian Institute of Sport Assessment-Achilles questionnaire (VISA-A) and Numeric Pain Rating Scale (NPRS) quantified the symptom severity. Participants with and without neovascularization were separated into groups. The differences between groups were assessed with independent t-tests.

Results: On the side with Achilles tendinopathy, neovascularization occurred in 28/83 (34%) of participants. The group with neovascularization, had a significantly greater degree of tendon thickness with a median (interquartile range [IQR]) of 0.3 (0.2-0.4) cm compared to 0.1 (0.1-0.2) cm in the group without neovascularization. The neovascularization group also had a greater CSA (mean ± SD 1.2 ± 0.4 cm^2) compared to those without neovascularization (mean ± SD 0.7 ± 0.3 cm^2). Those with neovascularization had worse jumping performance (plyometric quotient mean

± SD 0.3 ± 0.2) than those without neovascularization (mean ± SD 0.3=5 ± 0.1). There were no differences were observed in pain with hopping [present, mean ± SD3.7 ± 2.7; absent 2.7 ± 2.3)] or on the VISA-A [present, mean ± SD 48.1 (3.2); absent, 53.0 (2.5)].

Conclusion: Patients with Achilles tendinopathy and neovascularization had reduced jumping performance and worse tendon structure but similar symptom severity as those without neovascularization. Additional research is needed to understand the impact of neovascularization in response to treatment. Neovessels identified through power Doppler ultrasound may assist clinicians in diagnosing the stage of tendinopathy.

Disclosure: B. Honick, None; **H. Sigurdsson**, None; **K. Silbernagel**, None.

Abstract Number: 0698

Baseline Factors Are Not Associated with Rehabilitation Dose over Six Months Among Adults with RA

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SESSION INFORMATION
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Background/Purpose: Functional limitation is common in adults with rheumatoid arthritis (RA). Rehabilitation services, like physical therapy (PT) and occupational therapy (OT), are effective in improving function; however little is known regarding rehabilitation utilization patterns in adults with RA. The purpose of this study was to evaluate the association of baseline factors (demographic and clinical characteristics) with rehabilitation dose (number of subsequent PT/OT visits) among adults with RA who received PT/OT services. We hypothesize that worse disease activity and functional status will associate with more PT/OT visits.

Methods: We used data from the FORWARD registry. Participants in the FORWARD registry completed questionnaires every six months regarding health care utilization and patient reported outcomes. The analytic sample includes adults with doctor-diagnosed RA who reported new PT/OT utilization after at least 1 year with no PT/OT utilization. We excluded those with total joint replacement or skilled nursing/inpatient rehab within one year prior to first report of PT/OT or during the first episode of care. The baseline factors of interest were extracted from the preceding study visit 6 months before the study visit with reported PT/OT utilization. These baseline factors included demographic and clinical characteristics: age, sex, body mass index, race, disease duration, disease activity (Patient Activity Scale), functional status (Health Assessment Questionnaire Disability Index), pain severity (Visual Analog Scale), and fatigue severity (Visual Analog Scale). The study outcome was rehabilitation dose (number of PT/OT visits) in the past 6 months. The number of PT/OT visits was self-reported as one of five categories: 1-2, 3-4, 5-6, 7-8, or >8 visits. We examined the association of the baseline factors with rehabilitation dose (more PT/OT visits) using logistic regression (proportional odds model), and mutually adjusted for the other baseline factors.

Results: In the FORWARD registry, 979 adults received rehabilitation after a minimum one-year period with no reported rehabilitation (Table 1). Worse functional status, greater disease severity, and higher pain severity were associated with a higher dose of rehabilitation in unadjusted models, however the associations were attenuated in adjusted mod-

	Mean ± SD or % (n)
Sex, % women	82% (800)
Age, years	60.2 ± 11.3
Body mass index, kg/m²	28.6 ± 7.1
Disease Duration, years	17.2 ± 11.7
Race, % white	95% (900)
Disease activity, PAS Score	3.2 ± 2.1
Functional Status, HAQ-DI Score	0.82 ± 0.68
Pain severity	3.5 ± 2.7
Fatigue severity	3.7 ± 2.9
PT/OT visits during study period	
1-2	26% (259)
3-4	17% (165)
5-6	15% (142)
7-8	11% (109)
>8	31% (304)

*PAS – Patient Activity Scale; HAQ-DI – Health Assessment Questionnaire Disability Index

Table 1. Sample demographics and characteristics

	Unadjusted OR (95% CI)	Adjusted* OR (95% CI)
Sex (REF = Men)	**1.73 (1.29, 2.32)**	**1.65 (1.20, 2.26)**
Age (per 1 year older)	0.998 (0.988, 1.01)	1.001 (0.989, 1.01)
BMI (per 1 kg/m² more)	0.996 (0.980, 1.01)	0.991 (0.974, 1.01)
Disease Duration (per 1 year longer)	0.998 (0.989, 1.01)	0.996 (0.986, 1.01)
Disease activity (per 1 point higher on PAS)	**1.06 (1.00, 1.11)**	0.916 (0.738, 1.14)
Functional Status (per 1 point HAQ-DI Score)	**1.22 (1.03, 1.43)**	1.24 (0.862, 1.78)
Pain severity (per 1 point higher on VAS)	**1.05 (1.01, 1.09)**	1.08 (0.97, 1.21)
Fatigue severity (per 1 point higher on VAS)	1.03 (0.990, 1.07)	0.996 (0.939, 1.06)

*Mutually adjusted for other factors

Table 2. Association of demographic and baseline clinical characteristics with rehabilitation dose

els (Table 2). Women had higher odds of more rehabilitation in unadjusted and adjusted models. Other demographics and clinical characteristics were not associated with rehabilitation dose.

Conclusion: Rehabilitation dose was higher among women compared to men. Other demographic and clinical characteristics were not associated with rehabilitation dose. Further research is needed to understand factors associated with rehabilitation dose in adults with RA.

Disclosure: L. Thoma, None; **E. Wellsandt**, None; **K. Wipfler**, None; **K. Michaud**, Rheumatology Research Foundation, 2.

Abstract Number: 0699

Lumbar Spine Stenosis Treatment : Is Surgery Better Than Medical Treatment in Afro-Descendant Populations ?

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

Background/Purpose: Lumbar spinal stenosis (LSS) is a disabling condition, mostly prevalent in the aging population and associated with significant healthcare cost. Clinical presentation involving neurogenic claudication and low back pain results from congenital or degenerative narrowing of the spinal canal. Greater narrowing of the lumbar spinal canal has been described in African which contrasts with a lower incidence of the condition in this population. In clinical trials and meta-analysis of LSS treatment, the majority of the study populations are of Caucasian origin, accounting for 70% to 95% of the patients[1,2,3]. No difference between surgery, physiotherapy or epidural corticosteroid injection in LSS has been reported in those studies. To our knowledge, none has been performed in Afro-descendant populations (AD). We aim to assess efficacy of 3 different treatment approaches for lumbar spine stenosis in Martinique, a French Caribbean island with a high level of care in the region and an aging population mostly composed of AD.

Methods: Prospective cohort of 138 Afro-Caribbean patients with LSS, evaluated at 3 months from a first course of epidural corticosteroid injections in combination with standardized physiotherapy then assigned to 3 arms of treatment according to clinical evolution and wishes: rehabilitation (R: physiotherapy and oral medication), second course of epidural corticosteroid injections (ECI) or decompression surgery (DS). The primary endpoint was change in Oswestry Disability index (ODI) at 3 months (M3), M12, M18, M24. Secondary endpoints were change in leg pain and back pain measured by Visual Analog Scale (respectively L-VAS and B-VAS).

Results: Seventy-one patients were assigned to the R arm, 37 to the second ECI arm, 30 patients to the DS arm. All arms were comparable in age (62.3 +/- 13.1 years), sex (male/female ratio 0.75) and BMI with an average of 27.0 +/- 5.97 kg/m^2. ODI and L-VAS were significantly higher in the DS arm at baseline ($p< 0.01$). No difference in B-VAS was observed at baseline (Table1). A significantly higher decrease in ODI was observed in the DS arm at M3 and M12 (respectively $P< 0.001$ and $P< 0.01$). Results were not replicated at M18 and M24. A significantly higher decrease in L-VAS was observed in the DS arm at M3, M12, M18 (respectively $P< 0.01$, $P=0.011$, $P< 0.01$), not replicated at M24. No difference was observed between the 3 arms for B-VAS at no time (Table 2).

Conclusion: This is the first comparative treatment study in LSS performed in an AD population. We report a significant superiority of DS in evolution of ODI, a composite functional score, and L-VAS at M3 and M12. These results are very similar to those of major studies comparing surgical to non-surgical therapies for LSS in Caucasian cohorts[2,3]. If long terms (M24) favorable outcomes of L-VAS and ODI is not replicated in our study contrary to others, there is clearly a tendency in favor of surgery. Absence of statistical significance could be explained by important loss to follow up.

References

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2. Delitto A et al. , Ann Intern Med. 2015;162(7):465-73.
3. Malmivaara A et al. , Spine (Phila Pa 1976). 2007;32(1):1-8.

	Rehabilitation (N = 71)	2nd Epidural injection (N = 37)	Decompression Surgery (N= 30)	N=138	P
Age (years) – Mean (SD)	62.3 (±12.9)	62.4 (±14.5)	62.3 (±11.9)	138	0.87
Male – N (%)	28 (39%)	18 (49%)	13 (43%)	59	0.65
BMI (kg/m^2) – Mean (SD)	27.2 (±5.61)	26.3 (±7.56)	27.1 (±4.63)	134	0.91
ODI at baseline (percentage) – Mean (SD)	35.2 (±19.0)	41.6 (±15.0)	48.8 (±20.0)	137	**<0.01**
Back pain VAS at baseline – Mean (SD)	38.0 (±22.8)	41.1 (±24.5)	51.9 (±28.3)	130	0.065
Leg pain VAS at baseline – Mean (SD)	46.3 (±25.5)	42.5 (±27.3)	65.4 (±24.7)	129	**<0.01**

	Rehabilitation (N = 71)	2nd Epidural injection (N = 37)	Decompression surgery (N = 30)	N=138	P
Change in Back pain VAS at 3 months (mm) – Mean (SD)	-4.41 (±24.5)	0.529 (±20.0)	-15.2 (±26.4)	120	0.066
Change in Back pain VAS at 12 months (mm) – Mean (SD)	2.30 (±23.8)	0.294 (±23.1)	-15.5 (±33.2)	65	0.16
Change in Back pain VAS at 18 months (mm) – Mean (SD)	-14.3 (±25.0)	-10.1 (±24.1)	-7.11 (±27.7)	38	0.98
Change in Back pain VAS at 24 months (mm) – Mean (SD)	0.111 (±28.5)	-10.6 (±11.4)	-3.70 (±43.9)	27	0.67
Change in Leg pain VAS at 3 months (mm) – Mean (SD)	0.810 (±22.4)	1.41 (±28.3)	-24.1 (±32.4)	120	**<0.01**
Change in Leg pain VAS at 12 months (mm)– Mean (SD)	-7.70 (±25.0)	-2.44 (±20.7)	-31.2 (±28.7)	64	**0.011**
Change in Leg pain VAS at 18 months (mm) – Mean (SD)	-12.9 (±17.5)	0.769 (±19.4)	-34.4 (±20.2)	37	**<0.01**
Change in Leg pain VAS at 24 months (mm) – Mean (SD)	-18.1 (±25.5)	-6.71 (±14.1)	-25.5 (±27.1)	26	0.31
ODI change at 3 months (absolute value) – Mean (SD)	-1.15 (±14.5)	-2.89 (±11.7)	-20.7 (±23.4)	136	**<0.001**
ODI change at 12 months (absolute value) – Mean (SD)	1.44 (±14.5)	0.368 (±11.3)	-17.5 (±23.0)	72	**<0.01**
ODI change at 18 months (absolute value) – Mean (SD)	-5.94 (±14.2)	-2.57 (±11.5)	-21.7 (±24.3)	40	0.053
ODI change at 24 months (absolute value) – Mean (SD)	-6.89 (±16.5)	-2.50 (±11.6)	-16.1 (±24.3)	28	0.24

Disclosure: F. Louis-sidney, None; **S. Arfi**, None; **M. Drame**, None; **C. Deligny**, None; **P. Cabre**, None; **M. de Bandt**, None.

Abstract Number: 0700

Lipoxin A4 Induces Lipid Class Switching and Inflammation Resolution at the Genomic Level in Human Osteoarthritis

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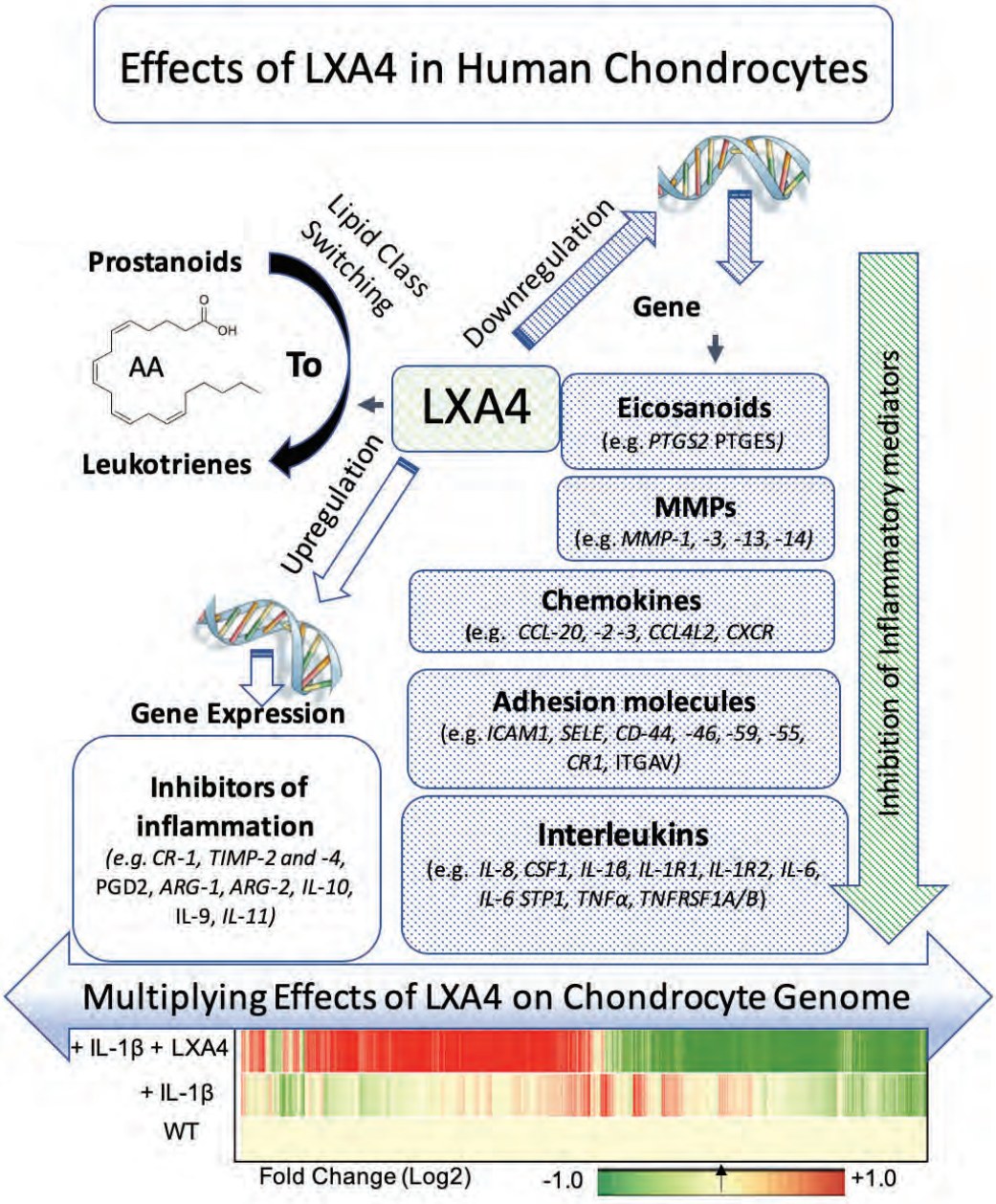
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Human OA-affected cartilage does not show the cardinal signs of inflammation (redness and swelling with heat and pain—*rubor et tumor cum calore et dolor*) because of its unique architecture (avascular, aneural and alymphatic) of the cartilage. However, there is an upregulation of inflammatory mediators at the molecular and biochemical levels [1]. We examined if the human OA-affected cartilage [a] induced innate anti-inflammatory mediators like Lipoxin A4 [LXA4] to counter and promote inflammation resolution in OA, [b] if so, what was the range and mechanism of action of LXA4 at the genomics level in human OA-affected chondrocytes.

Methods: Primary human OA-affected cartilage or chondrocytes were examined for spontaneous release of LXA4 [in *ex-vivo*] condition using liquid chromatography-tandem mass spectrometry and LXA4-specific ELISA. Furthermore, the effects of recombinant LXA4 [rLXA4] were validated in TNFα induced primary human neutrophils *in vitro*. The rLXA4 and then tested in spontaneous or IL-1β induced primary human OA-affected cartilage or human or bovine chondrocytes. Gene expression arrays and bioinformatic analysis examined the total genome. Inflammatory mediators were ELISA or RIA.

Results: LXA4 and 15-epi-LXA4 was spontaneously released [or augmented by IL-1β] in *ex-vivo* conditions in human OA-affected cartilage and chondrocytes. Exogenously added LXA4 (1nM) significantly [$p \leq 0.01$] inhibited 77% TNFα-induced PGE_2 production in human neutrophils. 1-100 nM of LXA4 significantly [$p \leq 0.01$] inhibited IL-1β induced nitric oxide (NO), and PGE_2, in human OA-affected cartilage, -chondrocytes or bovine chondrocytes. IL-1β and LXA4 exhibited an antagonistic pattern of gene expression in human chondrocytes. Specifically, LXA4 inhibited (basal and/or IL-1β-induced) gene expression of inflammatory mediators, their receptors and signaling apparatus [e.g., *IL-8, CSF1, IL-1β, IL-1R1, IL-1R2, IL-6, IL-6STP1, TNFα, TNFRSF1A/B, ICAM1, SELE, CD44, ITGAV, CCL-20, -2 -3, CCL4L2, CXCR- 5, -7, MMP-1, -3, -13, -14, CD-46, -55, -59, LTC4, LTB4, LTA4, PTGS2* and *PTGES*]. Furthermore, LXA4 upregulated the expression of inhibitors of inflammation such as *CR-1, TIMP-2 and -4, ARG-1, -2, IL-10,* and *IL-11*. Unlike IL-1β, LXA4 induced lipoxygenases [*ALOX5, ALOX5AP, ALOX15B*], phospholipases [*PLA2G1B, PLA2G7*], and PGD synthase of the eicosanoid pathway. LXA4 significantly dampened the cycloxygenase pathway and related prostaglandins.

Conclusion: Human OA-affected cartilage spontaneously releases LXA4 and 15-epi-LXA4. rLXA4 inhibits gene expression of [basal and IL-1β-induced] inflammatory mediators. Furthermore, LXA4 induced lipid class switching by shifting the regulation of cyclooxygenases towards the leukotriene pathway discretely from IL-1β. LXA4 exhibits multiple targets and mechanisms during anti-inflammatory, pro-resolving, and tissue repairing activity in human cartilage and chondrocytes.



The effects Lipoxin A4 in human chondrocytes in inducing lipid class switching from prostanoids to leukotrienes, downregulation of multiple inflammatory mediators, and upregulation of several inhibitors of inflammation. The effect of Lipoxin A4 on genomic expression in IL-1B-stimulated chondrocytes is depicted on a log2 fold change heat map exhibiting their antagonistic pattern of gene expression.

References

1. Attur *et al.* Osteoarthritis or osteoarthrosis: The definition of inflammation becomes a semantic issue in the genomic era of molecular medicine. Osteoarthritis and Cartilage, (2002) 10, 1–4.

Disclosure: M. Dave, None; **A. Islam**, None; **A. Parekh**, None; **J. Patel**, None; **A. Chawla**, None; **A. Amin**, None.

Abstract Number: 0701

miRNome Sequencing Identifies a Unique Profile of Circulating MicroRNAs in Early Knee Osteoarthritis

S. Amanda Ali[1], Rajiv Gandhi[2], Pratibha Potla[2], Sareh Keshavarzi[2], Osvaldo Espin-Garcia[2], Konstantin Shestopaloff[2], Chiara Pastrello[3], Dylan Bethune-Waddell[2], Starlee Lively[2], Anthony Perruccio[4], Raj Rampersaud[2], Christian Veillette[2], Jason Rockel[2], Igor Jurisica[2], Tom Appleton[5] and Mohit Kapoor[6], [1]Henry Ford Health System, Detroit, MI, [2]Krembil RI, Toronto, Canada, [3]University Health Network, Toronto, ON, Canada, [4]Krembil Research Institute, UHN; University of Toronto, Toronto, ON, Canada, [5]The University of Western Ontario, LONDON, ON, Canada, [6]Krembil RI, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: MicroRNAs have been shown to contribute to osteoarthritis (OA) pathophysiology, yet little is known about the circulating miRNome in OA. The circulating miRNome (e.g. all microRNAs in blood plasma) may include promising biomarkers of disease given that microRNAs are relatively stable, easy to detect, and easy to quantify. Since there are currently no validated biomarkers for detecting early stages of OA, profiling the circulating miRNome in different stages of OA holds potential for biomarker discovery. Next generation sequencing is an advantageous approach for profiling microRNAs because it offers the sensitivity and specificity to detect novel and low abundance microRNAs that are potentially unique to disease stages. Therefore, we hypothesize that sequencing will identify unique signatures of circulating microRNAs in symptomatic patients with early radiographic knee OA as compared to late radiographic knee OA.

Methods: Early knee OA patients were defined based on radiographic Kellgren-Lawrence grades 0 and 1 (N=41), and late knee OA patients defined based on Kellgren-Lawrence grades 3 and 4 (N=50). All patients were symptomatic and showed clinical features of knee OA. Of note, patients with Kellgren-Lawrence grade 2 were excluded in an effort to clearly demarcate early from late stage OA. Plasma from each patient (N=91) was subjected to microRNA library preparation and sequencing on the Illumina NextSeq550 platform. Sequencing reads were aligned and counts were generated for both known microRNAs (documented in miRBase v22.1) and novel microRNAs (predicted using bioinformatic tools). Demographic, anthropometric, and clinical data collected for all patients were considered as covariates in statistical analyses. Further statistical, bioinformatics, and computational biology approaches were taken to refine and interpret the final list of microRNAs and their predicted gene targets.

Results: Sequencing data were first explored in an unbiased manner using principal component (PC) analysis. This revealed clear separation of samples according to OA stage, with late OA samples forming a distinct cluster from early OA samples (PC1 = 58.2%). Differential expression analysis identified 215 microRNAs at FDR < 0.01 in early OA versus late OA. Refining this list for microRNAs that were consistently increased or decreased across ≥ 85% of samples in the early OA group as compared to their median expression in the late OA group, we found 97 microRNAs. At a threshold of ≥ 95%, 7 microRNAs were identified, one of which was consistently found to be increased in 100% of early OA samples. Exploring novel microRNAs, 4 were found in ≥ 50% of early OA samples. Interestingly, gene target predictions showed several common targets between the 97 shortlisted microRNAs and the 4 novel microRNAs, including SMAD2 and associated TGF-beta signaling pathway.

Conclusion: Sequencing the circulating miRNome identified a unique signature of 11 microRNAs, which included 4 novel microRNAs, in patients with early knee OA. Future studies should be directed towards understanding the role, mechanisms, and utility of these microRNAs as OA biomarkers.

Disclosure: S. Ali, None; **R. Gandhi**, None; **P. Potla**, None; **S. Keshavarzi**, None; **O. Espin-Garcia**, None; **K. Shestopaloff**, None; **C. Pastrello**, None; **D. Bethune-Waddell**, None; **S. Lively**, None; **A. Perruccio**, None; **R. Rampersaud**, None; **C. Veillette**, None; **J. Rockel**, None; **I. Jurisica**, None; **T. Appleton**, Abbvie, 2, 5, 8, CaRE Arthritis, 2, Gilead, 2, 5, 8, Pfizer, 2, 5, 8, Servier/Galapagos, 2, Amgen, 5, 8, BMS, 5, 8, Celgene, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Hoffman LaRO=oche, 5, 8, Sandoz, 5, 8, Sanofi-Genzyme, 5, 8, UCB, 5, 8, Ontario Rheumatology Association, 6, Canadian Rheumatology Association, 6, American College of Rheumatology, 6; **M. Kapoor**, None.

Abstract Number: 0702

Distinct Murine Cartilage Microbial DNA Signatures Are Seen in High Fat Diet-Induced Obesity and Aging

Christopher Dunn[1], Cassandra Garman[2], Jake Martin[2], Vladislav Izda[2], Cassandra Velasco[2] and **Matlock Jeffries**[2], [1]University of Oklahoma Health Sciences Center, Oklahoma Cityq, [2]University of Oklahoma Health Sciences Center, Oklahoma City, OK

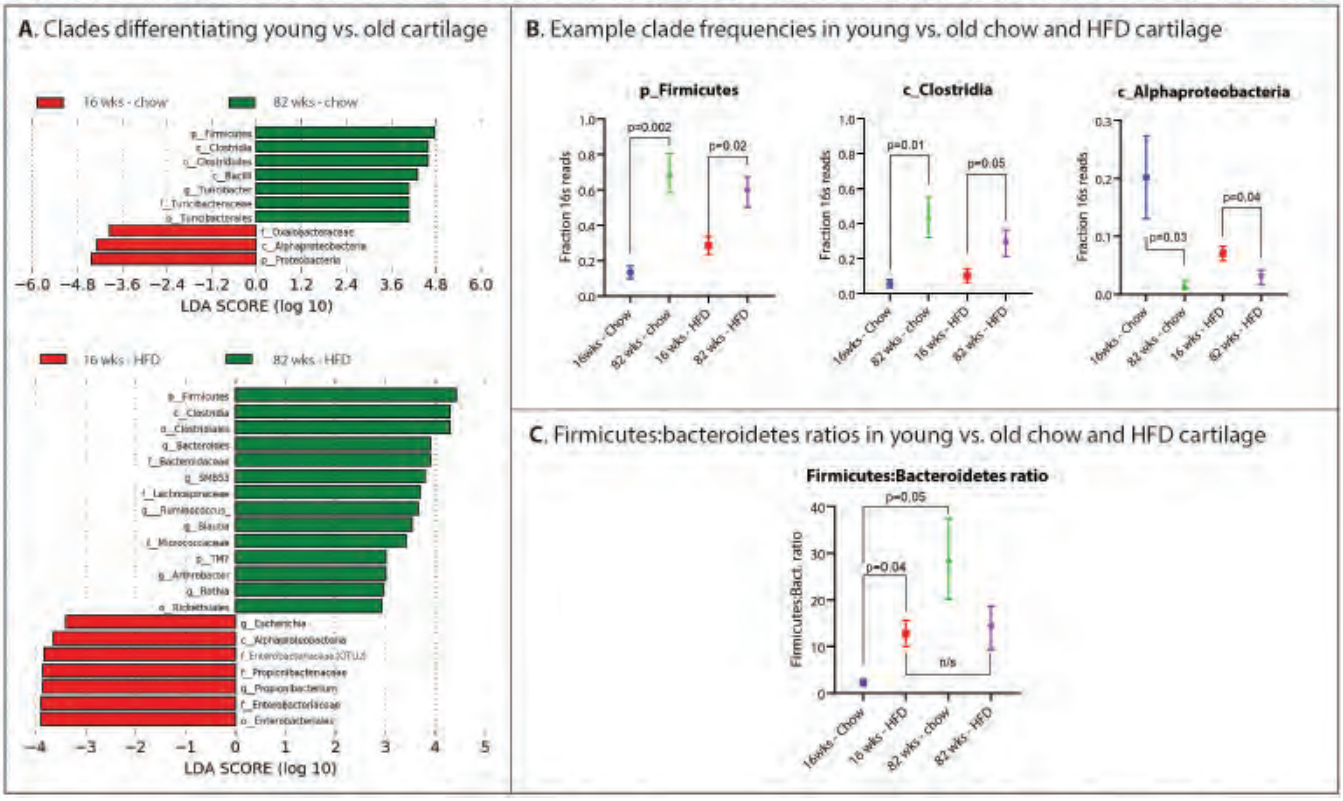
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The strongest nongenetic risk factors for primary knee OA are advanced age and obesity. We have previously shown a human cartilage microbial DNA signature associated with OA. In this study, we hypothesized that aging and obesity, known to cause gut microbiome shifts, would also produce shifts in cartilage microbial DNA patterns.

Methods: Young (8 week old, n=10) and old (74 week old, n=10) male C57BL/6J mice were divided into equal groups and randomly assigned to chow (NIH-31) or high fat (RD D12492, 60% kcal fat) diet for 8 weeks. Mice were sacrificed at 16 weeks and 82 weeks of age and knee cartilage collected using sterile technique, and DNA extracxted. The V3 and V4 regions of the bacterial rRNA gene were amplified and deep sequenced on an Illumina HiSeq. Operational taxonomic units (OTUs) were assigned in QIIME 1.9.1 using the Greengenes 13_8 97% representative reference set. Group composition differences were compared by Linear Discriminant Analysis Effect Size (LEfSe, LDA-effect sizes ≥ 2 or ≤ -2 were considered significant) following rarefaction.

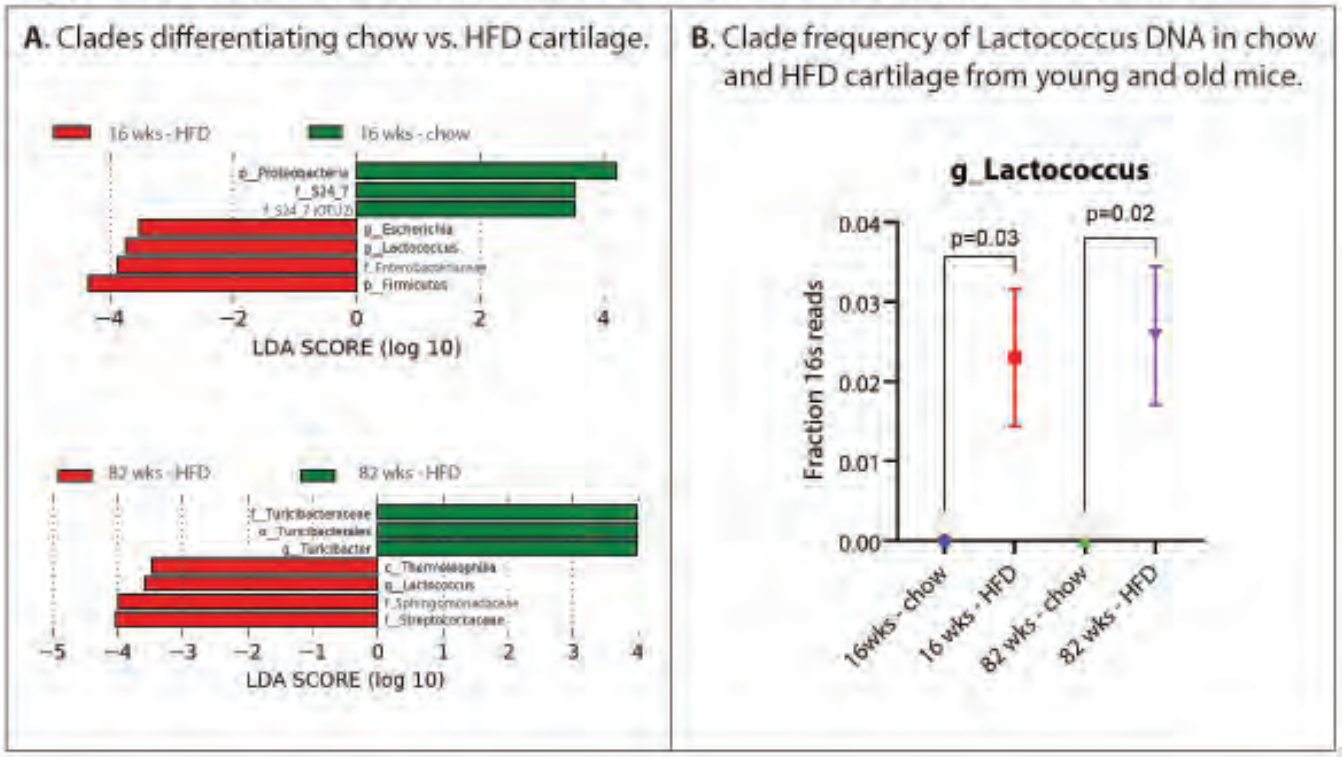
Results: In both HFD and chow animals, aging was associated with expansion of DNA from members of the phylum *Firmicutes* (LDA ES 4.8, p=0.009 for chow young vs. old, LDA ES 4.4, p=0.04 for HFD young vs. old, Figure 1A,B), specifically class *Clostridia* (LDA ES 4.6, p=0.009 for chow, LDA ES 4.3, p=0.03 for HFD, Figure 1A,B) , along with reductions in DNA from members of class *Alphaproteobacteria* with age (LDA ES 4.3, p=0.02 for chow, LDA ES 3.6, p=0.04 for HFD, Figure 1A,B). Comparing chow to HFD young mice, phylum *Proteobacteria* was expanded in chow (LDA ES 4.2, p=0.03) whereas members of phylum *Firmicutes* were expanded in HFD mice (LDA ES 4.3, p=0.02, Figure 2A), specifically including genus *Lactococcus* (LDA ES 3.7, p=0.005 Figure 2 A,B). Comparing chow to HFD old mice, chow were enriched in order *Turicibacterales* (LDA ES 4.0, p=0.02, Figure 2A), whereas HFD were enriched in class *Thermoleophilia* (LDA ES 3.5, p=0.02, Figure 2A) and genus *Lactococcus* (LDA ES 3.6, p=0.02, Figure 2A,B).

Figure 1: Comparison of microbial DNA clades in young vs. old cartilage from chow and HFD mice.



Microbial clades identified in cartilage of young and old mice fed chow or high-fat diet.

Figure 2: Comparison of microbial DNA clades in chow and HFD mice.



Comparison of microbial clades identified in cartilage of chow-fed and high-fat-diet-fed mice.

We also noted significant increases in the Firmicutes:Bacteroidetes ratio in both HFD and aging (chow young vs. old 2.3±0.7 vs. 29±9, p=0.05, young chow vs HFD 2.3±0.7 vs. 13±3, p=0.04) Figure 1C.

Conclusion: Cartilage microbial DNA patterns vary with nongenetic OA risk factors, including obesity and aging. Previous studies have shown increases in the Firmicutes:Bacteroidetes ratio in the gut microbiome associated with both obesity and aging, we identified a similar pattern within articular cartilage. Future studies should investigate the relationship between cartilage microbial DNA patterns and the gut microbiome, as well as localized innate immune activation driven by intraarticular microbial DNA.

Disclosure: C. Dunn, None; **C. Garman**, None; **J. Martin**, None; **V. Izda**, None; **C. Velasco**, None; **M. Jeffries**, None.

Abstract Number: 0703

Liraglutide as a Potential Intra-Articular Treatment for Cartilage Regeneration in Osteoarthritis: *In Vitro* and *In Vivo* Studies Supporting a Pro-Chondrogenic Effect

Francis Berenbaum[1], Coralie Meurot[2], Laure Sudre[3], Keren Bismuth[2], Revital Rattenbach[2], Patrice Denefle[2], Celine Martin[2] and Claire Jacques[3], [1]AP-HP, Hôpital Saint-Antoine, Service de Rhumatologie, Centre de Recherche Saint-Antoine, INSERM UMR_S 938,Sorbonne Université, Paris, 75012, France, Paris, France, [2]Campus Institut Pasteur Lille, 4P Pharma, Lille, France, [3]Inserm, UMR_S938, Hospital Saint-Antoine, Paris, France

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is an age-related joint disease affecting millions of individuals worldwide and associated with an extremely high burden largely attributable to disability. To date, there are only symptomatic treatments and no disease-modifying OA drugs (DMOADs) acting on both symptoms and structure are yet approved. Although OA is a disorder of the whole joint, progressive cartilage degeneration is considered as its hallmark. Indeed, differentiation and function of chondrocytes are impaired in OA, resulting in the breakdown of the cartilage matrix. Liraglutide is a Glucagon-Like-Peptide 1 Receptor (GLP-1R) agonist widely prescribed for the treatment of type 2 diabetes. We have previously shown that intra-articular (IA) liraglutide exerts anti-inflammatory and anti-degradative effects1. In this study, liraglutide was assessed for its pro-chondrogenic properties.

Methods: IA injection of liraglutide or vehicle was performed 2 days after injection of monoiodoacetate (MIA) or saline in mice. RTqPCR analyses of knee joint was performed 10 days following saline or MIA injection. The capacity of liraglutide (10-500nM) to induce chondrogenesis was evaluated using human mesenchymal stem cells (hMSCs) and mouse embryonic fibroblasts (MEFs) high-density micromass in-well culture systems. Safranin O and/or alcian blue staining was used to assess differentiation into chondrocytes. Exendin 9-39, a GLP-1R antagonist, was used to confirm target specificity. A commercial differentiation medium and bone morphogenetic protein 2 (BMP-2) were used as positive controls for hMSC and MEFs models, respectively.

Results: Col2a1 gene expression was significantly increased in total knee joints from MIA-induced mice treated with 30µg of liraglutide compared to vehicle (At Day 11, Liraglutide= 1.96±1.34, vs vehicle= 0.64±0.46, $p< 0.05$, fold change related to saline treatment). Moreover, there was a significant induction of Sox9 gene expression in MIA mice treated with 30µg and 20µg of liraglutide (Fold 2.46±1.84; 2.08±1.36, respectively, $p\leq0.05$) compared to vehi-

cle (0.92±0.67). Using hMSC, after 21 days of treatment, liraglutide but not vehicle induced their differentiation into chondrogenic 3D spheroids (Liraglutide 10nM= 5 alcian-blue positive spheroids out of 6 counted wells, $p< 0.05$; Liraglutide 100nM= 4/6, p=0.06, vs vehicle= 0/6). 5/6 alcian-blue positive spheroids were also observed for the positive control. Both Liraglutide or BMP-2 induced MEFs to differentiate into chondrocytes as revealed by cytologic analysis using alcian blue and safranin O staining. Spectroscopic quantification (in arbitrary unit, AU) of the Safranin O stain in MEFs after 21 days of chondrogenic differentiation indicated a significant increase of absorbance for liraglutide 500nM (2.90±0.03 AU, $p< 0.001$) and BMP-2 (3.17±0.06, $p< 0.001$) vs vehicle (1.99±0.34). The use of exendin 9-39 confirmed that the effect of liraglutide on chondrogenesis was GLP-1R dependent in both in vitro models.

Conclusion: Liraglutide promotes chondrocyte differentiation, which could facilitate cartilage regeneration in OA, and thus represents a potential DMOAD treatment for knee OA.

1. Berenbaum et al, Arthritis Rheumatol. 2019; 71 (s10).

Disclosure: F. Berenbaum, Pfizer, 1, Eli Lilly, 1; **C. Meurot**, None; **L. Sudre**, None; **K. Bismuth**, None; **R. Rattenbach**, None; **P. Denefle**, None; **C. Martin**, None; **C. Jacques**, None.

Abstract Number: 0704

The Murine Ear Wound Cartilage Superhealer Trait, Mediated by the Gut Microbiome, Is Transgenerationally Heritable Following Cecal Transplantation

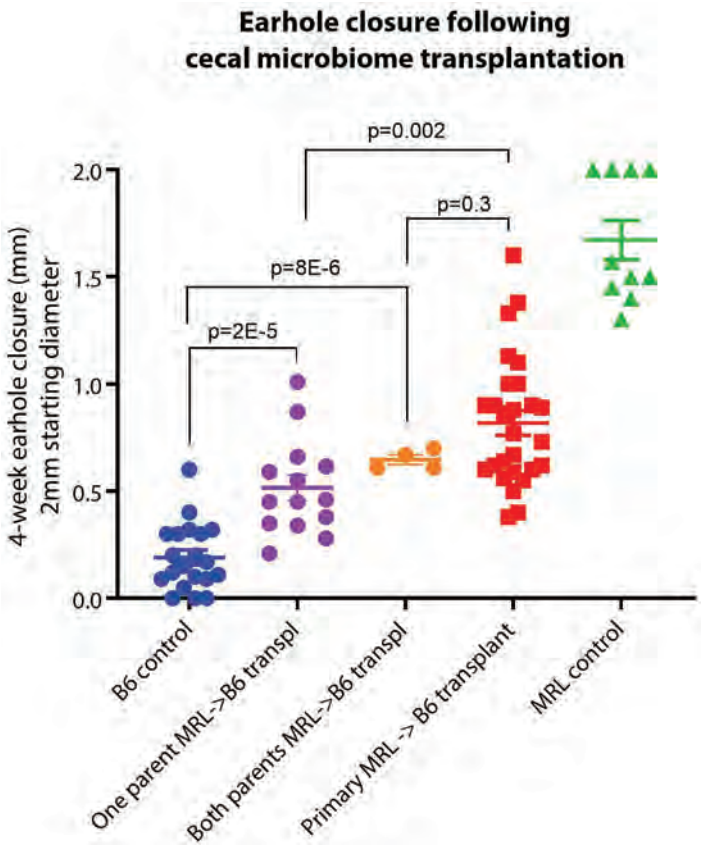
Christopher Dunn[1], Cassandra Garman[2], Cassandra Velasco[2], Vladislav Izda[2], Jake Martin[2] and **Matlock Jeffries**[2], [1]University of Oklahoma Health Sciences Center, Oklahoma City, [2]University of Oklahoma Health Sciences Center, Oklahoma City, OK

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: MRL/MpJ mice are substantially protected from developing post-traumatic osteoarthritis (OA), a trait with strong correlation to the ability to heal ear wounds. We have previously shown that this ear wound healing trait is partially determined by the gut microbiome, and that gut microbial transplantation into non-healer mice can confer the healing phenotype. In this study, we sought to examine whether the earhole healing phenotype associated with microbiome transplantation can be transgenerationally inherited.

Methods: Three-week-old C57BL6/J mice were inoculated by oral gavage with diluted cecal contents from adult male MRL/MpJ mice, or with vehicle control. Mice were then segregated into breeding cages, including cages where both parents were transplanted and cages where only one parent was transplanted. Offspring of these breeding pairs (n=4 for 'both parents transplanted', n=14 for 'one parent transplanted') received a 2mm earhole punch at 6 weeks of age, and final hole size was measured 4 weeks later. Group differences were compared to previous data on earhole closure from B6 vehicle, MRL vehicle, and primary B6- >MRL transplant mice.

Results: First-generation offspring wherein both parents received microbiome transplantation healed well (mean earhole closure at 4 weeks, mm, 0.65±0.02, p=8E-6 vs. B6 vehicle control) and were statistically indistinguishable



Earhole closure in animals following microbiome transplant, and their progeny.

from primary transplant mice (p=0.3). First-generation offspring wherein one parent was transplanted and the other also healing compared to vehicle B6 mice (earhole closure 0.52±0.08, p=2E-5 vs. B6 vehicle control), but worse than primary transplanted mice (p=0.002), Figure 1. 16S profiling of cecal microbiomes in each of these groups is ongoing.

Conclusion: The ear wound healing phenotype seen following cecal microbiome transplantation from healer MRL mice into nonhealer B6 mice is present in first generation offspring of transplanted mice. Further work will focus on identifying the key microbial clades being inherited which correlate with this phenotype, and examining any differences in healing based on mouse sex. Future studies should examine whether first generation offspring of transplanted mice are also protected against post-traumatic osteoarthritis.

Disclosure: C. Dunn, None; **C. Garman**, None; **C. Velasco**, None; **V. Izda**, None; **J. Martin**, None; **M. Jeffries**, None.

Abstract Number: 0705

lncRNA H19 and Micro RNA 675-3p Are Altered by Visfatin During Osteogenesis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Osteoarthritis & Joint Biology – Basic Science Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Long non-coding (lnc-)RNAs are transcribed from DNA similar to mRNA. lncRNA are able to interact directly with DNA, RNA and proteins. Some lncRNAs contain micro (mi-)RNAs in their sequence. The miRNAs can be released by splicing leading to active miRNA molecules. lncRNA H19 includes two miRNAs 675-3p and -5p in its sequence. Adipose tissue derived adipokines are involved in inflammation processes as well as osteoarthritis (OA) development. The proinflammatory adipokine visfatin is able to alter osteogenic differentiation (OD) of pluripotent mesenchymal stem cells (MSCs). Visfatin reduces elastic fiber expression, increases matrix mineralization and proinflammatory factor production.

Methods: MSCs isolated from OA hip or knee bone (phMSCs) and commercially obtained healthy human hMSCs were differentiated towards osteoblasts stimulated with or without visfatin, resistin, leptin as well as TNF and Wnt/TGFβ1 pathway inhibitors. Supernatants were collected at days 2, 7, 9, 14 and 21 of OD, cell lysates at day 2, 7, 9, 14. Matrix mineralization assays were performed at day 21. lncRNA H19 and miRNA expression was evaluated by real-time PCR after miRNA and total RNA isolation. IL-6 was measured by ELISA.

Results: Visfatin increased matrix mineralization and IL-6 release (hMSC: p=0.03, phMSC: p=0.01) (1). lncRNA H19 was continuously upregulated in unstimulated controls during OD as well as with leptin or resistin. Stimulation with visfatin significantly decreased lncRNA H19 (d2 to d14 of OD, phMSC: p=0.01, h-MSC: p=0.04). TNF stimulation during OD did not lead to downregulation of H19 nor increased matrix mineralization. lncRNA H19 endogenous miRNA 675-5p was reduced in parallel with H19: increased during OD and downregulated by visfatin significantly (e.g. d14 p=0.02). However, H19 endogenous miRNA 675-3p was inversely regulated: downregulated during OD while visfatin attenuated this effect (e.g. d14 p=0.03). Altered Wnt-signaling or TGFβ1 pathway were not observed.

Conclusion: lncRNA H19 is upregulated during OD playing a regulatory role during osteogenesis. During OD, visfatin showed proinflammatory effects and increased matrix mineralization while reducing elastic fiber production. These effects were associated with a reduction of lncRNA H19, an effect not triggered by other adipokines or TNF. We demonstrated that the lncRNA H19 endogenous miRNA 675-5p was regulated in parallel to H19, whereas miRNA 675-3p was inversely regulated and increased continuously upon visfatin stimulation. These results indicate that miRNA 675-3p is released out of the lncRNA H19 sequence leading to H19 reduction representing an effector mechanism

of visfatin. We hypothesize that this is a restrictive process in which either microRNA 675-5p or -3p is liberated from H19 and, in this setting, of miRNA 675-3p.

Disclosure: D. Küppers, None; **L. Tsiklauri**, None; **M. Hülser**, None; **K. Frommer**, None; **S. Rehart**, None; **C. Ospelt**, None; **U. Müller-Ladner**, Biogen, 8; **E. Neumann**, None.

Abstract Number: 0706

Adenosine A2A Receptor Activation Reduces Markers of Chondrocyte Senescence and Cartilage Inflammation Associated with Osteoarthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis is an aging-associated disorder linked to dysfunctional metabolism, chronic inflammation, oxidative stress, and cellular senescence. Cellular senescence is associated with stable cell cycle arrest, resistance to apoptosis, and the senescence-associated secretory phenotype with NFkB activation and inflammation with upregulation of senescence markers p16, p21, and p53. Importantly, senescence causes chondrocyte dysfunction by disrupting local cartilage homeostasis and promoting ECM degradation.

Methods: TC28α2 human chondrocytes were treated with or without the A2AR agonist CGS21680 (CGS, 1μM). WB, IF, and RT-qPCR were employed to evaluate *in vitro* markers of senescence and inflammation. IHC staining was used to evaluate *in vivo* markers in mice with obesity-induced OA. A resazurin assay was used to measure cell viability.

Results: We demonstrated that the deacetylase Sirt1, which is known to enhance metabolism and reduce senescence, accumulates in the nucleus by WB within 30 minutes following A2AR stimulation *in vitro* (1.7±0.2 vs 1.0±0.2, p=0.021, n=3). This is supported by a decrease in the nuclear-to-cytoplasmic ratio of acetylated nuclear NFkB by IF (0.67±0.14 vs 1.0±0.2 , p=0.038, n=3, 20-30 cells per representative 40x HPF per experiment). We have previously shown that A2AR binding likely increases Sirt1 deacetylase activity on known target p53 because total cellular p53 and nuclear acetylated p53 were reduced. Interestingly, while full length p53 levels decrease with A2AR ligation, there was a concomitant increase in an anti-senescent, pro-longevity, stem-cell associated 35 kDa transcriptional splice variant d133p53 as assessed by western blot ratio of the isoform to full length p53 (3.0±0.8 vs 1.0±0.06, p=0.005, n=3-4). This increase was also clearly apparent by IF. Accordingly, TC28α2 chondrocyte viability was increased *in vitro* with A2AR activation by resazurin assay over 3 hours (1.15±0.08 vs. 1.0±0.08, p< 0.001, n=10). We evaluated p53-induced senescence *in vivo* by staining for target p21 in an obese mouse OA model. We observed a cytoplasmic shift in signal throughout the cartilage layers in mice treated with liposomal-CGS joint injections. Untreated mice had increased nuclear p21 most notable in the superficial cartilage layers. In concordance, preliminary *in vitro* experiments cells displayed a moderate A2AR-mediated reduction and cytoplasmic shift of p21 and p16 in TC28α2 chondrocytes.

Conclusion: These results indicate that A2AR binding decreases markers associated with chondrocyte senescence both *in vitro* and *in vivo* likely via activation of metabolic proteins Sirt1 and AMPK. Activation of A2AR demonstrates the integral link between healthy metabolism and organismal and cellular longevity and suggests that targeting me-

tabolism can also reduce aging/senescence. This highlights the importance of studying the obesity-induced OA model in addition to other key OA models. Lastly, to our knowledge, the d133p53 p53 variant has not been identified in cartilage or chondrocytes and hence could provide further explanation for the specific mechanism of A2AR-mediated cartilage homeostasis and also further the general understanding the effect of senescence in OA.

Disclosure: B. Friedman, None; **B. Cronstein**, Regenosine, Inc., 4, 5, AstraZeneca, 1, 5, CanFite Biopharmaceuticals, 9, Horizon Pharmaceuticals, 9.

Abstract Number: 0707

Contribution of NOTUM and Glypicans to the Development of Osteoarthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a degenerative disease characterized by altered homeostasis of joint cartilage and bone, the functionality of which relies on chondrocytes and osteoblasts, that leads to the formation of a defective extracellular matrix (ECM). The ECM plays an essential role in bone biology as it provides the structure of cartilage which serves as a template for bone formation. Collagen X, main component of the ECM, has been described by our group as down-regulated in OA. Our data also points to an important role of the Wnt pathway in OA. Furthermore, Wnt proteins have been reported to inhibit chondrogenesis, and the Wnt pathway and its modulators have gained attention. Glypicans (GPC1 to GPC6) and NOTUM have been identified as modulators of this pathway. Notably, due to its highly specific inhibition of the Wnt pathway, NOTUM has been proposed as a therapeutic target in conditions with a high activity of the Wnt pathway is involved, such as OA.

We hypothesize that modulators of the Wnt pathway are involved in the development of OA. The aim of this study is to evaluate the presence of Glypicans and NOTUM in the serum, and their gene expression on BM-MSCs of OA patients and healthy individuals in order to determine whether significant differences exist and could clarify their likely involvement in OA.

Methods: Peripheral blood samples were obtained from OA patients, according to the ACR criteria, during routine rheumatologist visits. Samples from healthy individuals were obtained from the local Blood Bank. In both cases, serum was obtained. BM-MSCs form OA patients and healthy donors were isolated and expanded.

Quantitative ELISA assays for GPC1-6 and NOTUM were carried out using commercial kits (GPC1, #E-EL-H1710, Elabscience; GPC2, #E-EL-H1711, Elabscience;GPC3, #E-EL-H1712, Elabscience;GPC4, #E-EL-H1713, Elabscience;GPC5, #ELH-GPC5, RayBiotech;GPC6, #CSB-EL009708HU, Cusabio;NOTUM, #EK3787, Sab Biotech).

Expression of *GPC1-6* was evaluated by RT-qPCR using gene-specific probes (Applied Biosystems; Assay ID: GPC1 Hs00892476_m1; GPC2 Hs00242584_m1; GPC3 Hs01018936_m1; GPC4 Hs00155059_m1; GPC5 Hs00270114_m1; GPC6 Hs00170677_m1).

Table 1		
Cohort description		
	Control Group (n=40)	OA group (n=40)
Age	66,82±5,75	69,59±11,24
Woman (%)	32 (80%)	30 (75%)

Table 1. Cohort description.

Table 2			
ELISA Results			
Protein	Median OA (ng/ml)	Median Control (ng/ml)	*p*-value
GPC1	0.1346	0.1190	0.2379
GPC2	2.593	2.955	0.7489
GPC3	2.024	1.422	0.3574
GPC4	0.1254	0.1596	0.0767
GPC5	3.663	5.529	0.8829
GPC6	0.3922	0.3558	0.3212
NOTUM	**0.4451**	**0.8263**	**0.0013**

Table 2. ELISA test results.

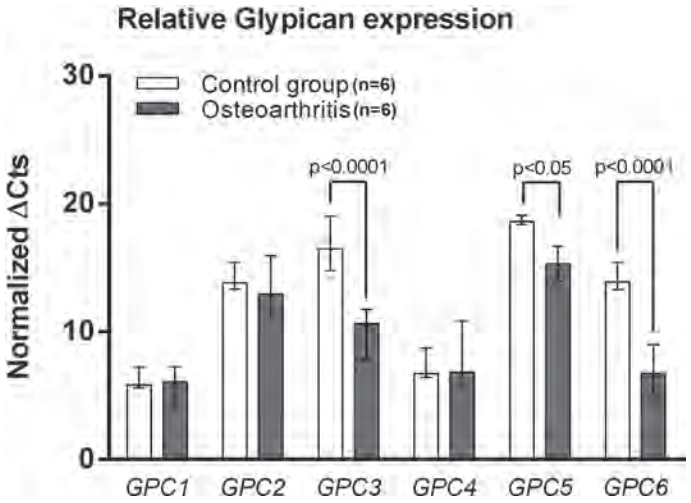

Figure 1. Glypican 1-6 gene expression on BM-MSCs form OA patients and healthy donors (ΔCts normalized to house-keeping genes β-actin and RNA18S5).

Protein concentration in serum and ΔCt for each gene was calculated using GraphPad Prism 7 software. Differences between samples were analysed with Mann-Withney U and multiple t-test. Significance level set was $p< 0.05$.

Results: A total of 40 OA patients and 40 healthy donors were included (Table 1).

Out of 7 proteins analyzed, only NOTUM showed a significant difference groups (Table 2): $Median_{OA}$=0.4451ng/mL, $Median_{CONTROL}$=0.8263ng/mL, p=0.0013.

Gene expression analysis showed a significant down-expression of 3 genes (Figure 1): GPC1, $Mean_{OA}$=5.74, $Mean_{CONTROL}$=6.48 , p=0.53; GPC2, $Mean_{OA}$=13.32, $Mean_{CONTROL}$=14.53 , p=0.34; **GPC3, $Mean_{OA}$=10.07, $Mean_{CONTROL}$=16.73 , p< 0.0001**; GPC4, $Mean_{OA}$=7.94, $Mean_{CONTROL}$=7.63 , p=0.79; **GPC5, $Mean_{OA}$=15.31, $Mean_{CONTROL}$=18.71 , p=0.042**; **GPC6, $Mean_{OA}$=6.94, $Mean_{CONTROL}$=14.17 , p< 0.0001**.

Conclusion: Our results suggest that low levels of *GPC3*, *GPC5*, *GPC6* and NOTUM may contribute to the development of OA. The lack of these inhibitors promotes the activation of the Wnt pathway, high activity of which has been related with OA.

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Abstract Number: 0708

Differences in Treating Knee Osteoarthritis by Clinician Specialty

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Current treatment of knee osteoarthritis (OA) is focused primarily around pain relief offering sustained mobility and prioritizing symptom relief over disease progression potentially impacts treatment outcome in the longer term for patients. With candidate therapies being investigated to address disease progression, it is important to examine if and where differences exist, with the prescribing behavior of current treaters of knee OA.

Methods: A cross-sectional chart review survey was conducted in Q2 2019 among US rheumatologists (rheums), orthopedic surgeons (orthos), primary care physicians with a focus in sports medicine (SM PCPs), and pain specialists practicing across hospital and private practices. Recruited from a large access panel, physicians were screened for duration of practice in their specialty (3-50 years) and caseload (35 or more knee OA patients, at least 10 of which must be classified as moderate-severe). Participants were asked to complete a 3-part survey: (1) a doctor demographic questionnaire, (2) a perceptual questionnaire, assessing perception of available and upcoming OA therapies, and (3) patient charts for the next 5 knee OA patients seen following receipt of the survey, capturing demographics and treatment history. Data were analyzed using descriptive statistics.

Results: A total of 275 physicians were recruited, reporting on 1375 patients in total (Table 1). When focusing primarily on patients with moderate-severe knee OA, this represented 65% of patients for SM PCPs and orthos. Pain specialists and rheums by comparison, had a significantly larger caseload of moderate-severe patients, at 79% and 77% respectively.

When looking at the proportion of patients treated with prescription medication for their knee OA, pain specialists and rheums stated an average of 69% and 68% of their managed patients, while SM PCPs stated 66%. Orthos stated a significantly lower proportion of patients treated with prescription therapy, at 55%.

Looking at therapies across specialties, orthos state greater use of traditional NSAIDs to treat their knee OA patients compared to pain specialists and SM PCPs (53% vs 36% vs 44%), with a significant difference to the stated use of

	Rheumatologists	Orthopedic Surgeons	SM PCPs	Pain Specialists
Physicians	55	111	56	55
Patient charts	275	555	280	265

Table 1. Physician and patient sample size

Table 1. Physician and patient sample size

rheums (35%). Rheums on the other hand, state significantly greater use of opioids compared to orthos, 18% vs 12% for mild opioids and 8% vs 1% for strong opioids.

From commonly used imaging techniques, X-ray and Magnetic resonance imaging (MRI) were used in greater proportion over ultrasound or computed tomography (CT) scan and when considering evidence of radiographic progression from imaging, rheums reported a significantly lower proportion of patients demonstrating radiographic evidence of bone erosion, compared to all specialties researched- 36% compared to 65% reported by orthos, 65% by SM PCPs and 75% by pain specialists.

Conclusion: From the sample surveyed, knee OA patients may exhibit differing outcomes based on the management adopted by their presiding clinician. With candidate therapies offering alternatives to how we currently treat knee OA, understanding nuances between treaters may prove an important consideration, when examining treatment outcomes in the longer term.Table 1. Physician and patient sample size

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Disclosure: D. Baldock, None; **C. Zhang**, None.

Abstract Number: 0709

Anatomical Distribution of Mrgprd-expressing Nonpeptidergic C-fibers in the Mouse Knee

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Osteoarthritis & Joint Biology – Basic Science Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The voltage-gated sodium channel, $Na_V1.8$, marks the majority of C-fiber nociceptors. We have used $Na_V1.8$ tdTomato reporter mice to describe the nociceptive innervation of the mouse knee (PMID: 31351964). We reported that 16 weeks after destabilization of medial meniscus (DMM), osteoarthritic (OA) joint damage is accompanied by extensive remodeling of nociceptors in the medial compartment of the knee, including increased $Na_V1.8$+ innervation in the medial synovium and within subchondral bone channels. Distinct functional classes of C-fibers have been identified, where it has been proposed that TRPV1+ C-fibers mediate heat sensitivity and C-fibers that express the G protein-coupled receptor (GPCR), Mrgprd, mediate behavioral sensitivity to mechanical stimuli. Their potential role in mechanosensation makes Mrgprd neurons an interesting subject in the context of OA pain, which is why we developed Mrgprd-EGFP reporter mice and investigated if they are present in the murine joint.

Methods: DMM surgery was performed in the right knee of 10-week old male C75BL/6 Mrgprd-EGFPf mice. Knees were harvested from 10-week old naïve mice (n=5), 26-week old naïve mice (n=3), and 16 weeks after DMM (n=3). Mice were perfused transcardially with paraformaldehyde. Knees were harvested, decalcified and cryo-sectioned. Twenty-µm thick coronal sections were collected throughout the joint. Sections were imaged using laser-scanning

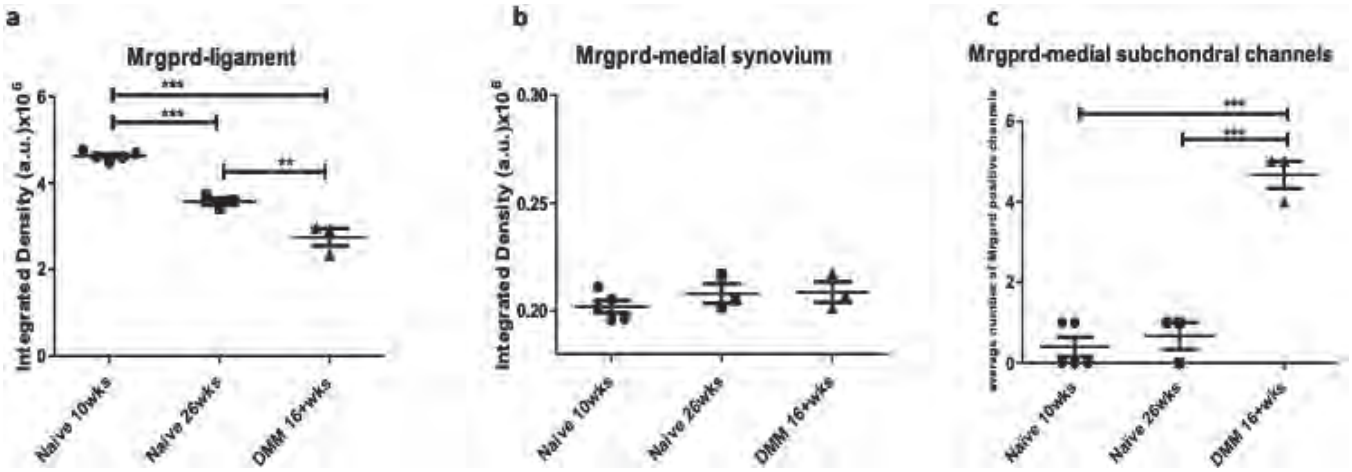

Figure 1. Quantification of MRGPRD+ signal in knees of 10- and 26-week old naïve mice and 16 weeks after DMM surgery, in (a) cruciate ligament insertions; (b) medial synovium; (c) within subchondral channels.** p<0.01 , *** p < 0.001; mean±SEM

confocal microscope (Olympus IX70) and the fluorescence signal was quantified using image J by an observer blinded to the groups.

Results: Mrgprd signal was present in the knee joint of 10-week old naïve mice, specifically at the insertions of the cruciate ligaments and in bone marrow cavities. By the age of 26 weeks, Mrgprd+ innervation decreased significantly in the cruciate ligament insertions (Fig 1a), which is similar to the age-related decline seen in the cruciate ligaments of $Na_V1.8$-tdTomato mice. No signal was observed in the medial synovium of young or old naïve mice (Fig 1b). Sixteen weeks after DMM, OA knees showed further decrease in the Mrgprd+ innervation of the cruciate ligament insertions, compared to 26-week old naïve knees (Fig 1a). In contrast to the increase in the medial synovial $Na_V1.8$+ innervation we previously observed in $Na_V1.8$-tdTomato mice, no change was observed in the Mrgprd+ innervation of the medial synovium after DMM (Fig 1b). Interestingly, Mrgprd signal was present in channel like structures in the subchondral bone of the medial femoral condyle and tibial plateau of the OA knee (Fig 1c), similar to findings in $Na_V1.8$-tdTomato mice.

Conclusion: The intra-articular Mrgprd innervation changed markedly with age and after DMM. The innervation pattern of this mechanosensitive subset was different than the pattern we observed for $Na_V1.8$, which marks all nociceptors. Sixteen weeks after DMM, at which point there is extensive joint damage, mechanosensitive Mrgprd nerve fibers were recruited in subchondral bone channels, but not in the synovium. In contrast, Mrgprd fibers declined significantly in cruciate ligament insertions with age and after DMM. The biological significance of these findings needs to be further explored

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Disclosure: A. Obeidat, None; **R. Miller**, None; **A. Malfait**, Pfizer, 5, Eli Lilly, 5.

Abstract Number: 0710

Early Start of Biological Treatment in Juvenile Idiopathic Arthritis: Does a Therapeutic Window Exist in Real Life?

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: JIA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Data about when is the best moment to start BT in Juvenile Idiopathic Arthritis (JIA) patients and the impact of this prompt initiation are scarce.Our aim is to analyze the response to BT of JIA patients according to the time when the BT was started.

Methods: A retrospective, descriptive study of JIA patients followed up in a referral hospital that started BT up to 24 months after diagnosis from 2000 to 2018. Disease activity was measured, at 2 years after diagnosis, according to Wallace criteria for remission for at least 6 months.

Results: 55 JIA patients that started BT up to 24 months from diagnosis were analyzed. 69,1% were girls. The median age at diagnosis was 8 years IQR(3-13) and the median age at the start of BT was 9 years IQR(3-13). Regarding JIA categories: 25,5% were Oligoarticular Persistent (OligP), 18,2% Systemic JIA (sJIA), 16,4% Entesitis related Arthritis (ERA), 12,7% Psoriatic Arthritis (APso) and Polyarticular RF- (PolyRF-), 5,5% Oligoarticular Extended (OligE) and Polyarticular RF+ (PolyRF+), 3,6% Undifferentiated (Und). 20% of patients had uveitis during followup.

Conventional DMARD (cDMARD) was indicated in 83,6% of patients (95,7% Methotrexate) at diagnosis [median 0 months IQR(0-2,3)]. At the end of followup only 30,9% of patients continued with cDMARDs. The main causes of discontinuation were: adverse events (46,7%), remission (36,7%). TNF inhibitors were prescribed in 81,8% of patients and 18,2% of patients received two BT during the study period. 54,5% of BT were indicated during the first 6 months from diagnosis, 27,3% from 7 to 12 months, 12,7% from 13 to 18 months, 5,5% from 19 to 24 months.

After 2 years from diagnosis, 78,2% of patients were on remission and 21,8% active. Among patients with active disease: 75% had arthritis, 16,7% had uveitis and 8,3% had both. There were no differences regarding disease activity among patients with uveitis and neither taking cDMARDs. Regarding JIA categories: 66,7% of OligE, 57,1% of PolyRF- and 57,1% of APso patients were active at 2 years from diagnosis when compared to the other categories (p=0.004).

Patients on remission at 24 months from diagnosis started sooner the BT than active patients [CI 95% (0,46-8,29) p=0,029]. The time when the BT was started was correlated to the activity at 2 years (K= 0,294 p=0,029). When the BT was prescribed after 7,5months from diagnosis it was correlated, in a COR curve, with a higher probability of active disease at 2 years (S=0,67 E=0,63). There was a correlation, among patients on remission at 2 years, between prompt start of BT and less time to reach remission (K= -0,345 p=0,024). Patients with active disease at 2 years, regardless of moment of BT initiation, required more BT during follow-up (p=0,002).

Conclusion: Prompt initiation of BT was correlated with a better outcome. JIA patients that started BT early after diagnosis had a higher probability of remission after 2 years. Starting BT after 7,5 months was correlated with a higher probability of active disease at 2 years. Active disease at 24 months was correlated with presistent active disease during follow-up

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Disclosure: A. Boteanu, AbbVie, 8, Novartis, 8, Roche, 8; **A. Briones-Figueroa**, None; **L. Calvo-Sanz**, None; **. Andreu Suárez**, None; **A. García-Fernández**, None.

Abstract Number: 0711

Alternative Dosing of Biologic Therapies Is Frequent Among Children with Juvenile Idiopathic Arthritis in the Childhood Arthritis and Rheumatology Research Alliance Registry

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: JIA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Biologic agents are integral to the treatment of juvenile idiopathic arthritis (JIA) and associated uveitis. Pediatric rheumatologists may increase the dosage of biologics beyond the labeled ranges in order to achieve better disease control or decrease the dosage when the disease is well-controlled. Though alternative dosing of biologics in the treatment of JIA and uveitis is often discussed anecdotally, there have been few published studies. We used the Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry to describe alternative dosing of biologics.

Methods: Patients with JIA enrolled in the CARRA Registry and ever treated with a biologic after enrollment were eligible for the study. We defined high-dose and low-dose as 40% higher or lower than the upper or lower limits of the labeled dose (standard dose), respectively, to exclude instances of minor dose variations due to changes in patients' body weight or rounding of doses for convenience. When a labeled dose was not available, we determined a standard dose using phase 3 clinical trials and published studies. We assessed the number of patients with use of low- and high-dose biologics (patients could be counted in more than one dose category). We also reported the subset patients who initiated treatment with a biologic for the first time following Registry enrollment and who initiated low-, standard- and high-dose.

Results: We assessed 5,352 patients treated with 6,740 different biologics following enrollment. At the patient-level, 1,080 (20%) patients ever received high-dose, and 434 (8%) patients ever received low-dose (Table 1). Commonly used biologics that had the highest proportion of patients ever receiving high-dose included infliximab (47%), adalimumab (21%), and anakinra (18%). Commonly prescribed biologics that had the highest proportion of patients ever receiving low-dose included tocilizumab (15%) and anakinra (13%). There were 951 new biologic users after Registry enrollment; 3% were prescribed low-dose, 87% standard-dose, and 11% high-dose.

Conclusion: More than 25% of patients with JIA treated with biologics received doses well outside the standard dose range, despite the fact that there are very little data on the safety and efficacy of such dosing. The vast majority of patients (87%) received standard-dose when initiating their first biologic; therefore, low-dose and high-dose use are generally the result of subsequent dose adjustments rather than disregard for standard dosing. TNF-inhibitors were commonly used at higher doses, especially the monoclonal antibodies that may be used to treat uveitis. Anakinra was commonly used at both high-dose and low-dose, and this may possibly result from variability in individual patient's responses to anakinra and the relative lack of published data and consensus on recommended dosing. Given the frequent use of low-dose and high-dose biologics in clinical practice, there is an urgent need to assess the relative safety and effectiveness of alternative biologic dosing strategies.

Table 1: Frequency of non-standard biologic dosing ever used in patients with JIA after enrollment in the CARRA

Biologic	N	Low dose	High dose
Any	5,352	434 (8.11%)	1,080 (20.18%)
Abatacept	351	12 (3.42%)	49 (13.96%)
Adalimumab	2,502	61 (2.44%)	521 (20.82%)
Anakinra	245	31 (12.65%)	45 (18.37%)
Canakinumab	230	9 (3.91%)	6 (2.61%)
Certolizumab	24	6 (25.00%)	7 (29.17%)
Etanercept	2,165	215 (9.93%)	215 (9.93%)
Golimumab	68	2 (2.94%)	8 (11.76%)
Infliximab	506	4 (0.79%)	236 (46.64%)
Rilonacept	6	0 (0.00%)	0 (0.00%)
Tocilizumab	643	96 (14.93%)	100 (15.55%)

CARRA = Childhood Arthritis and Rheumatology Research Alliance, JIA = juvenile idiopathic arthritis

* Please note that the two columns are not necessarily mutually exclusive. A patient with high-dose biologic therapy can later have a low-dose therapy and would be included in both categories.

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Abstract Number: 0712

Switching from Reference to Biosimilars Does Not Reduce Efficacy and Safety in Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: JIA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

		0 Time of switch	3 months	6 months	12 months
Amgevita (N=5)	n	5	5	3	2
	Number of active joints	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
	JADAS10	0 (0-0.1)	0 (0-1)	0 (0-0)	0.1 (0-0.2)
Benepali (N=13)	n	13	11	9	10
	Number of active joints	0 (0-0)	0 (0-0)	0 (0-0)	0 (0-0)
	JADAS10	0 (0-6)	0 (0-0.8)	0 (0-0.4)	0 (0-0.8)
Imraldi (N=24)	n	24	20	19	12
	Number of active joints	0 (0-0.5)	0 (0-0)	0 (0-0)	0 (0-0)
	JADAS10	0 (0-3.4)	0 (0-2.8)	0 (0-0)	0 (0-0)

Background/Purpose: Limited data about the use of biosimilar are available in children with Juvenile Idiopathic Arthritis (JIA). To evaluate the long-term efficacy and safety of switching from the etanercept (ETA) and adalimumab (ADA) originators to their biosimilars, in children with JIA.

Methods: Medical charts of JIA children who switched from ETA or ADA originators to the biosimilars were retrospectively evaluated. Efficacy of anti-TNF therapy was evaluated at last follow-up during the originator therapy and at 3, 6 and 12 months following the switch to biosimilar, assessing number of inflamed joints, CRP, ESR, Juvenile Arthritis Disease Activity Score (JADAS 10), Visual Analog Scale (VAS) and Childhood Health Assessment Questionnaire (CHAQ). Occurrence of adverse event (AE) during treatment was evaluated. Continuous variables were reported as median value and interquartile range (IQR) and compared using the Wilcoxon test for paired data, and csquare analysis.

Results: 43 children (31 Female, median age at onset 65 months (IQR 31-125) received originator ETA (n=14) or ADA (n=29), as first-line anti-TNF treatment for refractory JIA. Due to healthcare politics, patients have been switched to the biosimilar: Benepali®(n=13), Erelzi® (n=1) for ETA; Imraldi® (n=24), Amgevita® (n=5) for ADA, after 40.5 months (IQR 19.1-73.8) duration of originator treatment. At time of switch, 10/14 patients on ETA and 19/29 on ADA were on complete disease remission. No significance difference of entered parameters has been found at 3, 6 and 12 months thereafter the switch. Nine patients discontinued biosimilars, due to disease remission (5), to family willing (2), to occurrence of burning at injection site (2, on Benepali). The number of patients who experienced an AE was not different in different frame follow-up when comparing exposure to the originator and that to biosimilar, respectively: during 0-3 months, 15/42 (35.7%) *vs* 7/37 (18.9%), c^2: 2.76; during 3-6 months, 16/40 (40.0%) *vs* 17/31 (54.8%), c^2: 1.54; during 6-12 months, 15/39 (38.5%) *vs* 11/24 (45.8%), c^2: 0.33 . Most frequent AEs were upper respiratory tract infections (31) and injection site reactions (7).

Conclusion: Data from this small, retrospective inception cohort, showed similar efficacy and safety of the originator and a type of ETA and ADA biosimilars in JIA.

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Longitudinal Effectiveness of Abatacept in JIA: Results from an Ongoing JIA Registry

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SESSION INFORMATION

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Session Title: Pediatric Rheumatology – Clinical Poster II: JIA

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Background/Purpose: Abatacept is a selective T-cell co-stimulation modulator approved for use in JIA. Efficacy and safety of abatacept in patients with JIA has been demonstrated previously in two Phase III studies.[1,2] The objective of this analysis was to provide data from a real-world setting for longitudinal effectiveness of IV and SC abatacept in patients with JIA.

Methods: By protocol, clinical sites in the Pediatric Rheumatology Collaborative Study Group and Paediatric Rheumatology International Trial Organization enrolled patients meeting the ILAR criteria for one of the categories of JIA[3] currently taking or starting IV or SC abatacept. Planned duration of follow-up (FU) is 10 years; data were collected up to March 31, 2018. Effectiveness was assessed at day of entry into registry (baseline [BL]), 3 and 6 months and 1, 2, 3, 4 and 5 years. Safety data were collected at each visit.

Results: Of the 438 patients enrolled, 435 were included in the analysis; 346/435 (80%) were female. At BL, 17 (4%) patients were aged 2–5 years, median age was 13.6 years, JIA disease duration was 4.4 years, abatacept treatment duration was 6.5 months and number of active joints was 1 (mean 2.7). JIA categories were systemic (2%), oligo (23%), polyarticular RF– (55%), polyarticular RF+ (10%), psoriatic (3%), enthesitis-related (3%) and undifferentiated (4%). Total abatacept exposure was 474.0 patient-years. At 1-year FU, patients had low Physician Global Disease Activity, low Juvenile Arthritis Multidimensional Assessment Report scores and improved joint assessments (**Table 1**). A higher percentage of patients achieved clinically inactive disease after 1 year of FU vs BL (32 vs 45; **Table 1**). This trend continued despite low numbers of patients with 4 and 5 years of FU. There were 5 serious infections reported (incidence rate [IR] 0.66 /100 patient-years of FU, 95% CI: 0.22, 1.55; IR 0.79/100 patient-years on treatment, 95% CI: 0.26, 1.84). There were 15 autoimmune events (9 new onset) in 14 patients (IR 1.98/100 patient-years of FU, 95% CI: 0.66, 4.65; IR 2.37/100 patient-years on treatment, 95% CI: 0.78, 5.52). No malignancies or tuberculosis were reported. There was 1 death (unrelated pre-existing cardiac problems).

Table 1. Assessment of disease activity and impact

Endpoint	BL (n=435)	3 months (n=348)	6 months (n=319)	1 year (n=296)	2 years (n=189)	3 years (n=75)	4 years (n=21)	5 years (n=3)
Physician Global Disease Activity[a]	2.0 (0.1)	1.6 (0.1)	1.6 (0.1)	1.2 (0.1)	1.1 (0.1)	1.0 (0.2)	1.0 (0.3)	1.0 (0.6)
Clinical inactive disease (Wallace criteria), %	32	31	37	45	49	47	48	33
No. joints with active arthritis	2.7 (0.3)	2.1 (0.2)	2.2 (0.2)	1.8 (0.2)	1.7 (0.3)	1.8 (0.5)	1.1 (0.4)	0.3 (0.3)
JAMAR functional scale[b]								
Child	5.4 (0.3)	4.7 (0.3)	4.3 (0.3)	4.1 (0.4)	3.6 (0.4)	3.8 (0.6)	4.5 (1.2)	0.7 (0.3)
Parent	6.1 (0.4)	5.7 (0.4)	4.5 (0.4)	3.8 (0.4)	3.2 (0.4)	3.8 (0.8)	4.3 (2.1)	1.0 (–)
JAMAR HRQoL[c]								
Child	7.2 (0.3)	6.0 (0.3)	5.7 (0.3)	5.2 (0.3)	4.5 (0.4)	6.2 (0.7)	7.0 (1.4)	1.0 (0.6)
Parent	7.2 (0.3)	6.4 (0.3)	6.1 (0.3)	5.3 (0.4)	4.4 (0.5)	4.7 (0.8)	6.4 (2.2)	1.0 (–)

Mean (SE), unless otherwise indicated.
[a]Visual analog scale 0–10; 0=inactive; [b]Range 0–15, 0=no functional limitation; [c]Range 0–15, 0=best possible HRQoL.
BL=baseline; HRQoL=health-related quality of life; JAMAR=Juvenile Arthritis Multidimensional Assessment Report.

Conclusion: In this real-world JIA cohort, abatacept was safe and well-tolerated with no new safety risks identified. This longitudinal analysis further supports the persistent effectiveness of abatacept in patients with JIA.

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Response to Abatacept in JIA Categories: Results from the PRCSG/PRINTO JIA Abatacept Phase IV Registry

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SESSION INFORMATION

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Background/Purpose: Abatacept, a selective T-cell co-stimulation modulator, has been demonstrated to be well tolerated and effective in JIA in 2 Phase III studies.[1,2] The ongoing Phase IV Pediatric Rheumatology Collaborative Study Group and Paediatric Rheumatology International Trial Organization (PRCSG/PRINTO) registry aims to provide monitoring data from a real-world setting regarding longitudinal effectiveness and safety of abatacept in JIA. Here we assess the effectiveness of abatacept in JIA categories in patients who enrolled ≤1 month after starting abatacept treatment.

Methods: Using a standardized protocol and data collection process, clinical sites enroll patients with JIA currently receiving/starting IV/SC abatacept and follow them for up to 10 years. Patients are assessed at baseline and at 3, 6, 9, 12, and 24 months. Disease-related quality of life and physical function were quantified using the Juvenile Arthritis Multidimensional Assessment Report scale.[3] Proportions of patients with JIA-ACR 30, 50, 70, and 90 level of responses were determined using validated definitions based on 5/6 JIA core set measures (CRP/ESR not included).[4] The clinical 10-joint Juvenile Arthritis Disease Activity Score (cJADAS10) used validated cut-offs for low disease (LD) and inactive disease (ID) activity.[5] Disease remission was defined as cJADAS10-validated ID for ≥6 months. As-observed analysis is presented.

Results: As of March 31, 2018, 115 patients were included. Of these, 93 (80.9%) were female, the baseline mean (median) age at enrollment was 12.8 (13.1) years, and disease duration was 60.0 (42.1) months. The JIA categories identified were: polyarticular RF–, 52 (45.2%); oligoarticular, 36 (31.3%); polyarticular RF+, 11 (9.6%); enthesitis-related arthritis (ERA), 9 (7.8%); psoriatic and undifferentiated, 3 (2.6%) each; systemic, 1 (< 1%) (**Table 1**; patient with systemic JIA excluded). The proportions of patients achieving JIA-ACR responses, cJADAS10 LD, cJADAS10 ID and cJADAS10 remission are shown in **Figure 1** (patient with systemic JIA excluded).

Conclusion: Abatacept treatment resulted in rapid, clinically important and sustained JIA-ACR responses in all JIA categories with polyarticular or oligoarticular disease course and few achieved cJADAS10 ID and cJADAS10 remis-

Table 1. Disease activity measures by JIA category (baseline to 24 months)

Parameter	Baseline	3 months	6 months	9 months	12 months	24 months
Overall patients at each visit, n	115	85	84	61	60	34
Physician global assessment 0–10 VAS)	3.7 (3.5)	2.4 (2.0)	2.4 (2.0)	1.7 (1.0)	1.8 (1.0)	1.3 (0.3)
No. of active joints (0–71)	5.8 (3.0)	3.1 (1.0)	3.0 (1.0)	2.1 (0.0)	1.5 (0.0)	1.9 (0.0)
Overall well-being – parent (0–10 VAS)	4.5 (5.0)	3.2 (3.0)	3.2 (2.5)	3.0 (2.5)	2.6 (2.0)	2.1 (1.5)
JAMAR QoL score – parent (0–30)[a]	9.2 (8.0)	7.2 (6.0)	5.2 (6.7)	7.3 (6.0)	5.4 (4.0)	4.4 (3.5)
JAMAR Functional score – parent (0–30)[a]	8.3 (6.0)	7.2 (5.0)	5.2 (2.0)	6.3 (3.0)	4.3 (2.0)	3.0 (0.5)
Patients with polyarticular RF– JIA at each visit, n	52	40	36	26	28	14
Physician global assessment (0–10 VAS)	4.5 (4.5)	3.2 (3.0)	3.2 (3.0)	2.2 (1.5)	2.5 (2.0)	1.4 (1.5)
No. of active joints (0–71)	8.8 (6.0)	5.1 (3.0)	4.7 (2.5)	3.2 (0)	2.0 (0.5)	3.0 (0)
Overall well-being – parent (0–10 VAS)	4.7 (5.0)	3.5 (4.0)	2.3 (3.0)	3.0 (3.1)	2.7 (2.0)	2.4 (2.0)
JAMAR QoL score – parent (0–30)[a]	10.1 (10.0)	8.6 (7.0)	6.9 (7.0)	8.4 (8.0)	6.6 (5.0)	5.3 (4.5)
JAMAR Functional score – parent (0–30)[a]	9.9 (8.5)	9.5 (8.0)	5.8 (3.0)	8.1 (7.0)	5.7 (4.0)	4.0 (2.0)
Patients with oligoarticular JIA at each visit, n	36	29	30	21	19	13
Physician global assessment (0–10 VAS)	3.1 (3.0)	1.8 (1.5)	1.7 (1.5)	1.1 (0.5)	1.7 (0.5)	1.2 (0)
No. of active joints (0–71)	2.5 (1.0)	1.1 (0)	1.5 (0)	0.8 (0)	1.4 (0)	1.5 (0)
Overall well-being – parent (0–10 VAS)	3.9 (4.0)	3.0 (2.5)	3.3 (3.0)	3.2 (3.0)	3.3 (3.0)	2.3 (1.8)
JAMAR QoL score – parent (0–30)[a]	7.0 (4.5)	5.1 (4.0)	6.2 (6.0)	7.1 (6.0)	5.3 (4.0)	4.2 (0)
JAMAR Functional score – parent (0–30)[a]	4.8 (2.0)	4.4 (3.0)	4.5 (2.0)	4.8 (1.0)	4.6 (2.0)	3.3 (0.0)
Patients with polyarticular RF+ JIA at each visit, n	11	6	7	6	5	2
Physician global assessment (0–10 VAS)	2.6 (2.0)	0.9 (1.0)	1.4 (1.0)	0.9 (0.5)	0.3 (0)	1.3 (1.3)
No. of active joints (0–71)	2.0 (0.0)	0.7 (0.5)	0.7 (1.0)	1.2 (1.0)	0.4 (0)	0.5 (0.5)
Overall well-being – parent (0–10 VAS)	4.0 (3.3)	1.3 (1.0)	2.4 (2.0)	1.0 (1.5)	0.8 (0.8)	2.0 (2.0)
JAMAR QoL score – parent (0–30)[a]	6.8 (6.0)	2.7 (3.0)	4.0 (4.0)	3.0 (3.0)	2.3 (2.0)	8.0 (8.0)
JAMAR Functional score – parent (0–30)[a]	4.0 (4.0)	0 (0)	0.4 (0)	0 (0)	0.3 (0)	0 (0)
Patients with ERA at each visit, n	9	5	7	4	4	1
Physician global assessment (0–10 VAS)	3.6 (4.5)	2.0 (1.0)	1.4 (1.5)	3.1 (2.8)	0.3 (0.0)	0 (0.0)
No. of active joints (0–71)	4.3 (4.0)	2.4 (0.0)	0.9 (0.0)	3.5 (3.5)	0.3 (0.0)	0 (0.0)
Overall well-being – parent (0–10 VAS)	6.0 (7.5)	2.2 (2.0)	4.8 (5.8)	5.0 (5.0)	1.0 (1.0)	0 (0.0)
JAMAR QoL score – parent (0–30)[a]	13.7 (16.0)	6.6 (9.0)	10.5 (11.5)	8.3 (8.5)	3.0 (3.0)	0 (0.0)
JAMAR Functional score – parent (0–30)[a]	10.4 (9.0)	4.2 (3.0)	9.8 (7.5)	9.8 (6.5)	1.0 (0.0)	0 (0.0)
Patients with psoriatic JIA at each visit, n	3	2	2	2	2	2
Physician global assessment (0–10 VAS)	1.5 (2.0)	1 (1.0)	0.8 (0.8)	0.3 (0.3)	1.0 (1.0)	0 (0)
No. of active joints (0–71)	1.0 (1.0)	1.5 (1.5)	0.5 (0.5)	0 (0)	0 (0)	0 (0)
Overall well-being – parent (0–10 VAS)	2.0 (2.0)	0 (0)	0 (0)	0.5 (0.5)	1.3 (1.3)	0.5 (0.5)
JAMAR QoL score – parent (0–30)[a]	3.5 (3.5)	3.0 (3.0)	0 (0)	2.0 (2.0)	4.0 (4.0)	0.5 (0.5)
JAMAR Functional score – parent (0–30)[a]	3.0 (3.0)	0 (0)	0 (0)	1.5 (1.5)	1.0 (1.0)	0 (0)

Data are mean (median) unless otherwise stated; overall number of patients included.

[a]0=normal, 30=worst.

ERA=enthesitis-related arthritis; JAMAR=Juvenile Arthritis Multidimensional Assessment Report; QoL=quality of life; VAS=visual analog scale.

sion status. Quality of life was also improved across JIA categories over time, as per JAMAR QoL scores. Limitations of the study include a low number of patients with ERA, psoriatic, undifferentiated, and systemic JIA.

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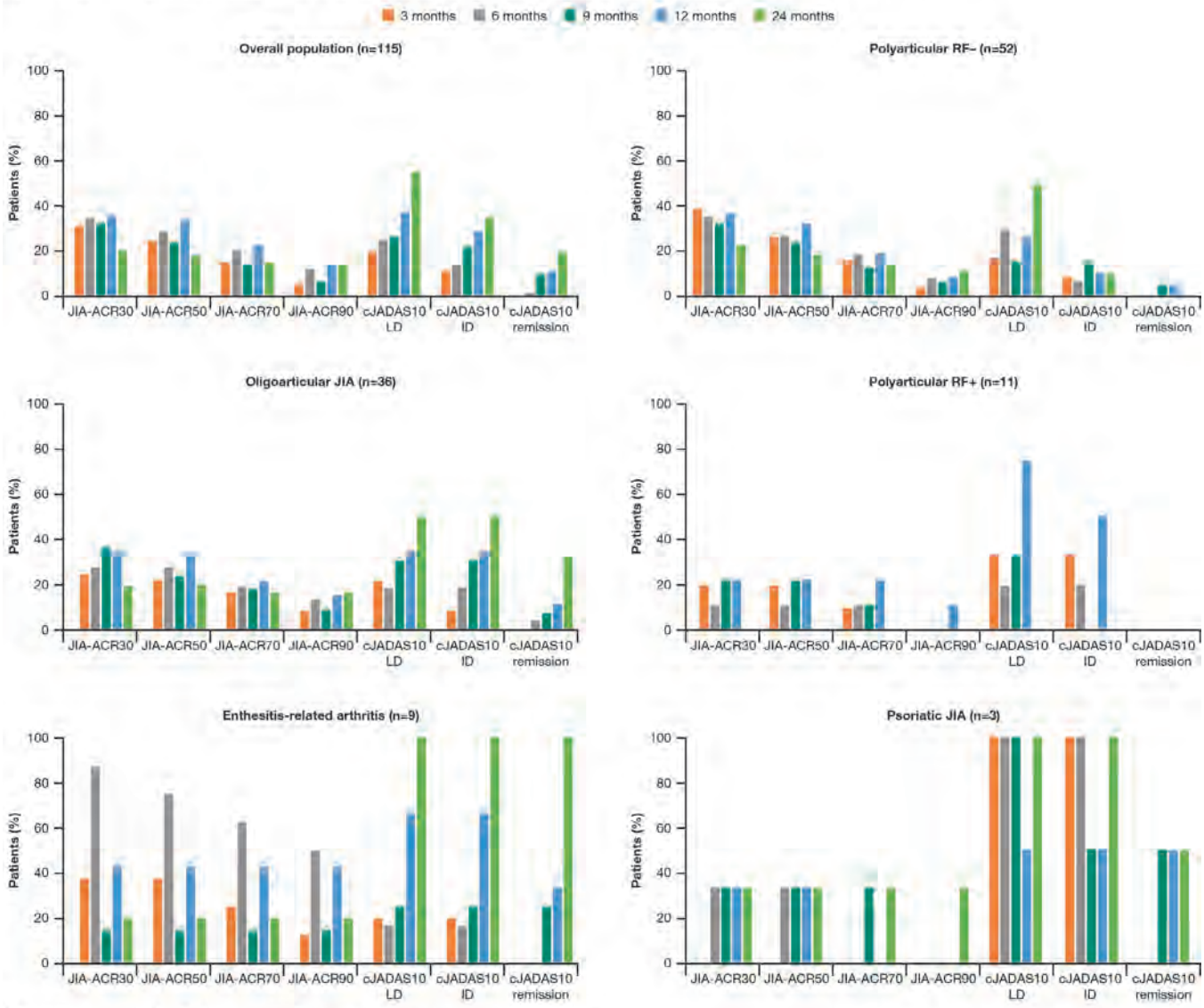
Medical writing: Katerina Kumpan, PhD (Caudex).

Figure 1. Proportion of patients achieving JIA-ACR responses, cJADAS10 LD, cJADAS10 ID and cJADAS10 remission



Data are expressed as n (%); as-observed analysis.
Overall population: 3 months n=85; 6 months n=84; 9 months n=61; 12 months n=60; 24 months n=34.
Polyarticular RF–: 3 months n=40; 6 months n=38; 9 months n=26; 12 months n=28; 24 months n=14.
Oligoarticular JIA: 3 months n=29; 6 months n=30; 9 months n=21; 12 months n=19; 24 months n=13.
Polyarticular RF+: 3 months n=6; 6 months n=7; 9 months n=6; 12 months n=5; 24 months n=2.
Enthesitis-related arthritis: 3 months n=5; 6 months n=7; 9 months n=4; 12 months n=4; 24 months n=1.
Psoriatic JIA: 3 months n=2; 6 months n=2; 9 months n=2; 12 months n=2; 24 months n=2.
cJADAS10=clinical 10-joint Juvenile Arthritis Disease Activity Score; ID=inactive disease; JIA-ACR30/50/70/90=30/50/70/90% improvement in JIA-ACR criteria; LD=low disease.

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Company, 1, 3, 4; **A. Martini**, AbbVie, 8, Eli Lilly, 8, EMD Serono, 8, Janssen, 5, 8, Pfizer Inc, 5, 8, Novartis, 5, 8; **H. Brunner**, Abbott, 5, Amgen, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, GlaxoSmithKline, 5, 8, F Hoffman-La Roche, 5, 8, Novartis, 5, 8, Pfizer, 5, Takeda, 5, UBC, 5, Wyeth, 5; **N. Ruperto**, Ablynx, 5, 8, Astrazeneca-Medimmune, 5, 8, Biogen, 5, 8, Boehringer, 5, 8, Bristol Myers Squibb, 2, 5, 8, 9, Eli Lilly, 2, 5, 8, 9, EMD Serono, 5, 8, GlaxoSmithKline, 2, 5, 8, 9, F Hoffmann-La Roche, 2, 5, 8, 9, Janssen, 2, 5, 8, 9, Merck, 5, 8, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, R-Pharma, 5, 8, Sanofi, 5, 8, Servier, 5, 8, Sinergie, 5, 8, Sobi, 2, 5, 8, 9, AbbVie, 5, 8, Takeda, 5, 8.

Abstract Number: 0715

JIA-ACR50 Response as a Predictor of Minimal Disease Activity in Patients Aged 2–17 Years with Polyarticular-Course JIA Treated with SC Abatacept

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: JIA

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Effectiveness of SC abatacept in patients with polyarticular-course JIA (pJIA) was shown in a 2-year, open-label Phase III international study (NCT01844518). Here we assess potential predictors of Juvenile Arthritis Disease Activity Score 27-CRP (JADAS27-CRP) minimal disease activity (MDA), inactive disease (ID) and remission.

Methods: Patients with pJIA aged 2–17 years received weight-tiered SC abatacept (10–< 25 kg: 50 mg; 25–< 50 kg: 87.5 mg; ≥50 kg: 125 mg) weekly for 4 months.[1] JIA-ACR30 responders at Month 4 could receive SC abatacept for another 20 months.[1] Potential predictors of response over 11 time points to Month 21 were determined with a multivariate logistic regression (MVR) analysis; Month 4, 13 and 21 data are presented. MVR variables assessed were baseline age, sex, race, weight, geographic region, CRP, MTX use, prior biologic use, number of active joints, number of joints with limitation of motion, physician's global assessment of disease activity, Childhood HAQ-DI (CHAQ-DI), parental assessment of well-being (PaGA) and JIA-ACR50 or JIA-ACR70 responses at Month 3. Variables were deemed significant if corresponding p values were < 0.05 at ≥6 of the 11 time points. Missing values were imputed as non-responders. Baseline continuous variable cut-offs (high/low) were determined by receiver-operator curve analysis. Outcomes analyzed included JADAS27-CRP MDA (≤3.8), ID (≤1) and remission (JADAS27-CRP ID for ≥6 months) rates. Odds ratios and 95% CIs were computed.

Table 1. ORs (95% CI) for variables potentially predictive of JADAS27-CRP MDA, ID or remission at Month 13[a]

	MDA		ID		Remission	
	Cut-off	OR (95% CI)	Cut-off	OR (95% CI)	Cut-off	OR (95% CI)
CRP	>1 vs ≤1	0.58 (0.23, 1.42)	>0.6 vs ≤0.6	0.33 (0.13, 0.83)*	>0.7 vs ≤0.7	0.08 (0.01, 0.78)*
CHAQ-DI	>0.75 vs ≤0.75	0.38 (0.15, 0.94)*	>0.75 vs ≤0.75	0.53 (0.23, 1.18)	>0.5 vs ≤0.5	0.39 (0.13, 1.24)
PaGA	>43.16 vs ≤43.16	0.48 (0.21, 1.10)[b]	>39 vs ≤39	0.41 (0.18, 0.91)*	>27.37 vs ≤27	0.24 (0.08, 0.75)*
JIA-ACR50	Yes vs No	6.93 (2.20, 21.89)*	Yes vs No	1.65 (0.47, 5.73)	Yes vs No	1.15 (0.12, 11.08)
JIA-ACR70	Yes vs No	1.53 (0.58, 4.00)	Yes vs No	3.01 (1.09, 8.29)*	Yes vs No	4.14 (0.72, 23.82)

*Statistically significant (p<0.05).

[a]n=217; [b]Showing trend (p=0.05–0.1).

CHAQ-DI=Childhood HAQ-DI; ID=inactive disease; JADAS27-CRP=Juvenile Arthritis Disease Activity Score 27-CRP; MDA=minimal disease activity; OR=odds ratio; PaGA=parental global assessment.

Table 2. ORs (95% CI) for variables potentially predictive of JADAS27-CRP MDA, ID or remission at Month 21[a]

	MDA		ID		Remission	
	Cut-off	OR (95% CI)	Cut-off	OR (95% CI)	Cut-off	OR (95% CI)
CRP	>1 vs ≤1	0.46 (0.19, 1.10)[b]	>0.9 vs ≤0.9	0.26 (0.09, 0.78)*	>0.7 vs ≤0.7	0.28 (0.08, 1.02)[b]
CHAQ-DI	>1.5 vs ≤1.5	0.24 (0.10, 0.62)*	>1.13 vs ≤1.13	0.31 (0.13, 0.71)*	>1.13 vs ≤1.13	0.34 (0.13, 0.90)*
PaGA	>45.65 vs ≤45.65	0.85 (0.40, 1.81)	>48.91 vs ≤48.91	0.60 (0.27, 1.32)	>39.0 vs ≤39.0	0.38 (0.16, 0.92)*
JIA-ACR50	Yes vs No	4.04 (1.40, 11.65)*	Yes vs No	2.93 (0.82, 10.45)[b]	Yes vs No	3.76 (0.72, 19.78)
JIA-ACR70	Yes vs No	2.10 (0.84, 5.24)	Yes vs No	1.96 (0.74, 5.20)	Yes vs No	2.13 (0.70, 6.49)

*Statistically significant (p<0.05).

[a]n=217; [b]Showing trend (p=0.05–0.1).

CHAQ-DI=Childhood HAQ-DI; ID=inactive disease; JADAS27-CRP=Juvenile Arthritis Disease Activity Score 27-CRP; MDA=minimal disease activity; OR=odds ratio; PaGA=parental global assessment.

Results: In all treated patients (N=219), median (range) baseline characteristics were: age 11.0 (2.0–17.0) years, CRP 0.2 (0.1–21.1) mg/dL, CHAQ-DI 1.0 (0.0–2.9) and PaGA 47.2 (0.0–95.8). Variables with the highest number of significant p values (≤0.05) were baseline CRP, CHAQ-DI, PaGA, and Month 3 JIA-ACR50 and JIA-ACR70. Baseline CRP, PaGA and CHAQ-DI were predictive of JADAS27-CRP MDA, ID and/or remission at multiple time points (Month 13: **Table 1**; Month 21: **Table 2**). JIA-ACR50 response at Month 3 was statistically significant at predicting achievement of JADAS27-CRP MDA at Month 13 (**Table 1**) and Month 21 (**Table 2**), and showed a statistical trend at Month 4 (data not shown). JIA-ACR50 response was statistically significant (p< 0.05) at five consecutive time points between Months 10 and 21.

Conclusion: Clinically important JIA-ACR50 response at Month 3 was predictive of the attainment of JADAS27-CRP MDA status at Month 13 and Month 21 in patients aged 2–17 years with pJIA treated with SC abatacept.

Reference

1. Brunner HI, et al. *Arthritis Rheumatol* 2018;70:1144–1154.
Medical writing: Rachel Rankin (Caudex)

Disclosure: N. Ruperto, Ablynx, 5, 8, Astrazeneca-Medimmune, 5, 8, Biogen, 5, 8, Boehringer, 5, 8, Bristol Myers Squibb, 2, 5, 8, 9, Eli Lilly, 2, 5, 8, 9, EMD Serono, 5, 8, GlaxoSmithKline, 2, 5, 8, 9, F Hoffmann-La Roche, 2, 5, 8, 9, Janssen, 2, 5, 8, 9, Merck, 5, 8, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, R-Pharma, 5, 8, Sanofi, 5, 8, Servier, 5, 8, Sinergie, 5, 8, Sobi, 2, 5, 8, 9, AbbVie, 5, 8, Takeda, 5, 8; **H. Brunner**, Bristol-Myers Squibb, 2, 5, MedImmune, 2, Novartis, 2,

8, Pfizer Inc, 2, 5, AbbVie, 5, AstraZeneca-MedImmune, 5, Bayer, 5, Biocon, 5, Boehringer Ingelheim, 5, Janssen, 5, Eli Lilly, 5, R-Pharm, 5, Roche, 5, 8, Cincinnati Children's Hospital Medical Center, 3, GlaxoSmithKline, 8; **A. Berman**, None; **F. Ávila-Zapata**, None; **G. Horneff**, Pfizer, 5, 8, AbbVie, 5, 8, Novartis, 5, 8, Sanofi, 5, 8; **M. Alessio**, None; **M. Becker**, CARRA, 9; **A. Belot**, None; **R. Burgos-Vargas**, None; **A. Boteanu**, None; **C. Goldenstein-Schainberg**, None; **I. Scheibel**, None; **M. Terreri**, None; **L. Zemel**, None; **R. Wong**, Bristol-Myers Squibb Company, 1, 3, 4; **M. Askelson**, Bristol-Myers Squibb Company, 5; **M. Nys**, Bristol Myers Squibb, 1, 3; **A. Martini**, AbbVie, 8, Eli Lilly, 8, EMD Serono, 8, Janssen, 5, 8, Pfizer Inc, 5, 8, Novartis, 5, 8; **D. Lovell**, AstraZeneca, 5, Boehringer Ingelheim, 5, Bristol-Myers Squibb, 2, Forest Research, 5, GlaxoSmithKline, 5, Janssen, 2, Novartis, 2, 5, Roche, 2, 5, UBC, 2, 5, AbbVie, 2, Pfizer Inc, 2, 5, Abbott, 5, Amgen, 5, Celgene, 5, Takeda, 5, Wyeth, 5.

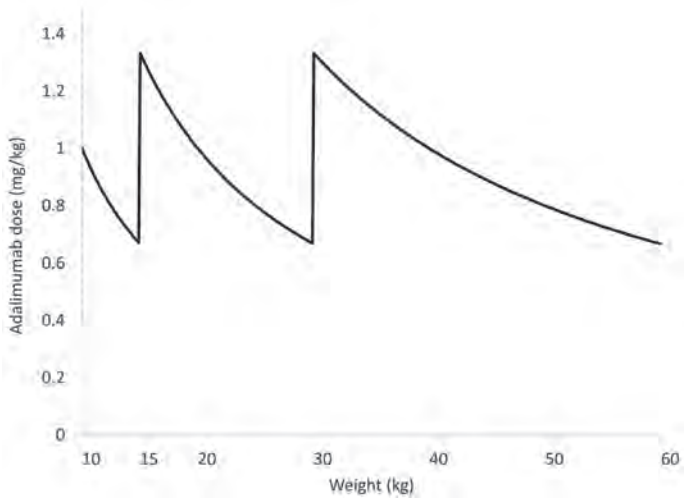
Abstract Number: 0716

Variations in Adalimumab and Etanercept Dosing in Juvenile Idiopathic Arthritis and Their Effect on Treatment Outcome: A Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry Study

Ruud Verstegen[1], Peter Shrader[2], Stephen Balevic[3], Timothy Beukelman[4], Colleen Correll[5], Anne Dennos[6], Thomas Phillips[2] and Brian Feldman[1], [1]The Hospital for Sick Children, Toronto, ON, Canada, [2]Duke University, Durham, [3]Duke University Medical Center, Durham, [4]University of Alabama at Birmingham, Birmingham, AL, [5]University of Minnesota, Minneapolis, MN, [6]Duke University, Durham, NC

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: JIA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Different dosing strategies of adalimumab and etanercept have been used over the past decade in the treatment of juvenile idiopathic arthritis (JIA). With regards to adalimumab, dosing was initially 24 mg/m^2 body surface area (BSA) every other week (eow) but changed to fixed dosing by weight categories (10-15 kg: 10 mg eow; 15-30 kg: 20 mg eow; ≥30 kg: 40 mg eow), resulting in large variation in body weight-adjusted exposure (See



Recommended Adalimumab dose according to product monograph in mg/kg/every other week. Dosing categories: 10 mg (body weight 10-15 kg), 20 mg (body weight 15-30 kg) and 40 mg (body weight >30 kg) biweekly.

	Adalimumab (dose per 2 weeks)			Etanercept (dose per week)		
Outcome variable	**No**	**Yes**	***P*-value**	**No**	**Yes**	***P*-value**
PediACR30	**63**	**62**		**31**	**81**	
Weight-adjusted dose (mg/kg)	1.07 (1.10)	0.98 (0.36)	0.55	0.80 (0.23)	0.86 (0.20)	0.14
BSA-adjusted dose (mg/m²)	34.09 (31.32)	29.45 (10.10)	0.27	25.66 (6.95)	26.14 (5.98)	0.72
PediACR50	**68**	**57**		**41**	**71**	
Weight-adjusted dose (mg/kg)	1.06 (1.06)	0.99 (0.37)	0.65	0.84 (0.25)	0.85 (0.19)	0.98
BSA-adjusted dose (mg/m²)	33.47 (30.19)	29.77 (10.47)	0.35	26.58 (7.35)	25.66 (5.53)	0.49
PediACR70	**86**	**39**		**56**	**56**	
Weight-adjusted dose (mg/kg)	1.05 (0.97)	0.98 (0.32)	0.57	0.84 (0.22)	0.85 (0.21)	0.94
BSA-adjusted dose (mg/m²)	33.11 (27.89)	28.93 (6.53)	0.20	25.89 (6.70)	26.12 (5.80)	0.85
PediACR90	**100**	**25**		**74**	**38**	
Weight-adjusted dose (mg/kg)	1.02 (0.90)	1.07 (0.34)	0.65	0.86 (0.24)	0.81 (0.15)	0.14
BSA-adjusted dose (mg/m²)	32.14 (25.96)	30.43 (7.10)	0.57	26.35 (6.78)	25.31 (5.04)	0.42
PediACR100	**101**	**24**		**78**	**34**	
Weight-adjusted dose (mg/kg)	1.02 (0.90)	1.07 (0.34)	0.63	0.86 (0.23)	0.80 (0.15)	0.11
BSA-adjusted dose (mg/m²)	32.22 (25.84)	30.00 (6.92)	0.45	26.32 (6.67)	25.25 (5.13)	0.42
cJADAS10 ≤1 *(all patients)*	**172**	**47**		**106**	**59**	
Weight-adjusted dose (mg/kg)	1.02 (0.87)	0.95 (0.36)	0.41	0.89 (0.22)	0.83 (0.26)	0.10
BSA-adjusted dose (mg/m²)	31.97 (24.83)	28.84 (8.96)	0.18	27.53 (6.33)	24.79 (7.27)	0.01
cJADAS10 ≤2 *(oligoarticular course only)*	**16**	**16**		**10**	**24**	
Weight-adjusted dose (mg/kg)	1.04 (0.50)	0.89 (0.23)	0.28	0.84 (0.16)	0.86 (0.29)	0.78
BSA-adjusted dose (mg/m²)	31.54 (15.17)	25.85 (4.35)	0.17	25.90 (6.85)	24.53 (6.60)	0.59
cJADAS10 ≤3.8 *(polyarticular course only)*	**70**	**53**		**47**	**51**	
Weight-adjusted dose (mg/kg)	0.97 (0.57)	0.98 (0.46)	0.90	0.87 (0.18)	0.86 (0.26)	0.83
BSA-adjusted dose (mg/m²)	30.76 (16.95)	28.35 (9.86)	0.33	27.39 (6.01)	26.28 (8.06)	0.45
Change in biologic treatment within 6 months after start	**232**	**62**		**200**	**28**	
Weight-adjusted dose (mg/kg)	0.98 (0.75)	0.98 (0.64)	0.97	0.89 (0.25)	0.81 (0.21)	0.12
BSA-adjusted dose (mg/m²)	30.45 (20.56)	31.80 (20.08)	0.65	27.07 (7.14)	25.61 (5.06)	0.19

Dose comparison between patients (all ages) who achieved the outcome of interest, and those who did not. BSA, body surface area. Numbers in bold represent the number of patients. Underlined results reached statistical significance ($p<0.05$).

Figure). For etanercept, the dosing recommendations remained 0.8 mg/kg per week, but the presence of single-dose prefilled syringes (25 or 50 mg) unintentionally promotes rounding of doses. These practices contribute to variable drug exposure in patients with JIA. In addition, metabolism of therapeutic proteins is increased in younger children especially in those aged < 6 years, which reduces drug exposure (i.e., serum drug concentrations). We hypothesize that a higher relative dose (mg/kg or mg/m^2) improves the treatment response of children with JIA who start adalimumab or etanercept.

Methods: This is a retrospective cohort study of CARRA Registry data, which contains prospectively collected data from children with rheumatic diseases. Patients aged < 18 years old were included in the analysis if they had a diagnosis of JIA (systemic JIA excluded), started adalimumab or etanercept after Registry enrollment as their first biologic DMARD, and had follow-up data available. The following outcomes were determined between 4-7 months after start of treatment: pediACR100, 90, 70, 50, 30, clinical juvenile arthritis disease activity score (cJADAS; clinically inactive disease: ≤ 1; low disease activity ≤ 2 for oligoarticular course, ≤ 3.8 for polyarticular course), as well as treatment continuation for > 6 months, as a surrogate marker for treatment efficacy. The weight- and BSA-adjusted dose (mg/

kg and mg/m^2, respectively) were compared using Student's t-tests (significance $p < 0.05$; no adjustment for multiple comparisons) between patients with and without the outcome and stratified by age group (< 6 years, 6-12 years, 12-18 years).

Results: This analysis included 406 and 296 patients treated with adalimumab and etanercept, respectively. Children < 6 years old attaining pediACR90/100 received higher adalimumab dosing (1.32 vs 1.06 mg/kg [p = 0.03] and 31.78 vs 25.42 mg/m^2 [p = 0.02]). For etanercept, children (all ages) who achieved cJADAS ≤ 1 received lower doses by BSA (24.79 vs 27.53 mg/m2, p=0.01; See Table). In the subgroup analysis, this was only true for 6-12 years (cJADAS ≤ 1: 22.98 vs 27.60 mg/m^2 [p = 0.007]; cJADAS ≤ 2: 21.80 vs 29.52 mg/m^2 [p = 0.003]). All other analyses did not show associations between dose and outcome variable.

Conclusion: This study provides some evidence that children younger than 6 years old have improved treatment response (pediACR90/100) when treated with a relatively higher dose of adalimumab, while lower etanercept dosing was associated with improved cJADAS outcome. As these analyses are unadjusted, further studies using a Bayesian approach with propensity score matching will follow to adjust for patient characteristics that may contribute to receiving a higher treatment dose (e.g., age, disease activity, uveitis, etc).

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Abstract Number: 0717

Predictors of Clinical Remission in Children with Extended Oligoarticular Arthritis, Enthesitis-related Arthritis, or Psoriatic Arthritis Treated with Etanercept in the CLIPPER Studies

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: JIA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: CLIPPER is an ongoing, 8-year, phase 3b, multicenter, open-label study of the safety and efficacy of etanercept in the treatment of juvenile idiopathic arthritis (JIA) categorized as extended oligoarticular arthritis (eoJIA), enthesitis-related arthritis (ERA), or psoriatic arthritis (PsA). The aim of this study was to identify predictors of sustained 6-month clinical remission on medication using long-term data from CLIPPER.

Methods: Previously reported baseline characteristics of the 127 children enrolled in CLIPPER (60 eoJIA [2–17 years], 38 ERA [12–17 years], and 29 PsA [12–17 years])[1] were analyzed post hoc as possible predictors of the attainment of clinical remission on medication (per the JIA ACR criteria or Juvenile Arthritis Disease Activity Score 71-joint [JADAS] criteria) sustained for 6 consecutive months using univariate logistic regression models and stepwise multivariate

Table. Predictors of sustained 6-month clinical remission on medication during the CLIPPER studies

Univariate analyses		
	Definition of remission	
	JIA ACR (N=127)	JADAS (N=127)
Patient characteristic	OR (95% CI)	OR (95% CI)
Age at onset (≤7.61 years vs older)	5.17 (2.31, 11.57)	1.93 (0.90, 4.14)
Patient/Parent Global Assessment score (≤2.5 vs >2.5)	2.67 (1.13, 6.28)	2.75 (1.13, 6.67)
JIA ACR IA at Week 12 (Yes vs No)	5.06 (1.51, 16.99)	4.64 (1.24, 17.38)
JADAS LDA at Week 12 (Yes vs No)	5.83 (2.60, 13.06)	7.06 (3.02, 16.51)
JADAS IA at Week 12 (Yes vs No)	7.00 (2.14, 22.89)	4.10 (1.26, 13.29)

Multivariate analyses	
Definition of remission and patient characteristic	OR (95% CI)
JIA ACR	
Age at onset (≤7.61 years vs older)	7.19 (2.71, 19.09)
JADAS LDA at Week 12 (Yes vs No)	6.29 (2.46, 16.06)
JADAS	
JADAS LDA at Week 12 (Yes vs No)	7.68 (3.08, 19.14)

CI: confidence interval; IA: inactive disease; LDA: low disease activity; OR: odds ratio.

models. Clinical response and disease activity status after 4, 8, and 12 weeks of treatment were also evaluated as predictors. Analyses were based on observed cases in CLIPPER and 6-year follow-up data from the CLIPPER2 extension.

Results: Univariate analyses showed that baseline Patient/Parent Global Assessment score, JIA ACR inactive disease (IA) at Week 12, JADAS low disease activity (LDA) at Week 12, and JADAS IA at Week 12 were associated with the attainment of 6-month remission according to both JIA ACR criteria and JADAS criteria (**Table**). Multivariate analyses showed that age at onset and JADAS LDA at Week 12 were predictors of 6-month remission according to JIA ACR criteria, whereas JADAS LDA at Week 12 was a predictor according to JADAS criteria.

Conclusion: JADAS LDA at Week 12 of etanercept treatment was a predictor of attaining sustained 6-month clinical remission on medication according to JIA ACR criteria and JADAS criteria during the CLIPPER studies. Younger age at onset was also a predictor according to JIA ACR criteria.

References

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Borlenghi, Pfizer, 1, 2; **B. Vlahos**, Pfizer, 1, 2; **C. Zang**, Pfizer, 1, 2; **N. Ruperto**, AstraZeneca-MedImmune, 5, 8, Biogen, 5, 8, Eli Lilly, 2, 5, 8, EMD Serono, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, Sobi, 2, 5, Bristol-Myers Squibb, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Roche, 2, 5, 8, AbbVie, 5, 8, Ablynx, 5, 8, Merck, 5, 8, R-Pharm, 5, Sanofi, 5, Servier, 5, Sinergie, 5, Takeda, 5, Boehringer Ingelheim, 5, 8.

Abstract Number: 0718

Obesity Impairs Achievement of Clinical Inactive Disease (CID) in Patients with Juvenile Idiopathic Arthritis (JIA) Treated with TNF Inhibitors

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SESSION INFORMATION
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Session Title: Pediatric Rheumatology – Clinical Poster II: JIA
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: to assess prevalence and disease features associated with obesity in juvenile idiopathic arthritis (JIA) and to evaluate the impact of obesity on the achievement of clinical inactive disease (CID) at six months from the start of treatment with tumor necrosis factor inhibitors (TNFi).

Methods: retrospective analysis of demographic, clinical and laboratory features and body mass index (BMI) collected at the start of TNFi treatment in patients with oligoarticular and rheumatoid factor (RF)-negative polyarticular JIA. Patients were divided into obese and non-obese; demographic, clinical and disease features were compared in the two groups. The distribution of obese, overweight, healthy-weight and underweight patients according to the achievement of CID at 6 months was investigated.

Results: 234 patients with JIA (39% RF-negative polyarthritis, 25% extended oligoarthritis, 36% persistent oligoarthritis) were enrolled in the study. Obesity (BMI $\geq 95^{th}$ percentile for age and gender) was present in 31 patients (13.2%). Obese patients compared to non-obese patients, had an older age at disease onset (p=0.020), lower frequency of antinuclear-antibody positivity (p=0.043), a higher number of active joints at baseline (p=0.0048) and higher C-reactive protein at baseline (p=0.043). Obese JIA patients achieved clinical inactive disease (CID) at 6 months with a lower frequency compared to non-obese patients (p=0.005). In multivariate regression analysis obesity at baseline was confirmed as an independent risk factor for non-achievement of CID at 6 months from starting TNFi (OR 2.42 [95% CI 1.04-5.61]; p=0.040).

Conclusion: obesity negatively affects response to TNFi in oligo- and RF-negative polyarticular JIA, independently from other disease-associated variables.

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Abstract Number: 0719

Anti-adalimumab Antibodies Detection Using a Novel Peptide-based Assay in a Cohort of Pediatric Patients with Chronic Rheumatic Disorders: A Pilot Study

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SESSION INFORMATION

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Background/Purpose: Immunogenicity and development of anti-drug antibodies have been associated with treatment failure and adverse events during biologic treatment. Anti-drug antibodies (ADAs) have been reported in 21% of Juvenile Idiopathic Arthritis patients treated with Adalimumab. However, their role in reducing adalimumab efficacy is still debated due to conflicting results. No study has been directed toward identification of neutralizing ADAs in paediatric rheumatic disorders.

Aim of our study was to detect ADAs, along with their clinical relevance, using a new theranostic peptide-base assay in a cohort of children with inflammatory chronic diseases on Adalimumab treatment.

Methods: ix candidate Adalimumab derived peptide antigens (HC-CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR 2, LC CDR3) have been developed and optimized to be tested. Their performance has been compared with commercial ELISA kit and a SPR-based optical assay (Biacore®). Assays have been performed in sera of a cohort of children receiving Adalimumab due to an inflammatory chronic disease. Mean age, disease duration, concomitant treatment with methotrexate (MTX), ANA positivity, disease activity parameters and scores at the time of ADA determination have been recorded. Chi-square, and Fisher exact test were used to compare data. Pearson's and Spearman's correlation tests were used to determine correlation coefficients for entered variables.

Results: Eighteen (14 F, median age 12.6, range 3.8-16, yrs) patients were enrolled: 16 affected by Juvenile Idiopathic Arthritis, 7 of whom complicated by JIA -associated chronic uveitis, and 2 patients affected by chronic idiopathic uveitis. Peptide assay revealed ADAs in 8 children, Biacore in 6, commercial Elisa in 5. Of note, we found total concordance among the 3 tests just in 2 patients. No significant correlation has been proven among the 3 ADA determinations. Biacore and ELISA determination showed significant concordance (r_s: 0.72, $p< 0.006$). The presence of HC CDR3 and LC CDR 3 resulted significantly correlated with disease activity (r_s: 0.57, $p< 0.05$), and, inversely, with disease remission on treatment (r_s= -0.523, $p< 0.05$). No patient experienced severe adverse events and no correlation with ADAs has been revealed.

Conclusion: In chronic rheumatic disorders, novel reliable methods are urgently required to guide clinical decision and support decisions about switching within or between drugs in refractory children. The 3 different methods, since based on different antigenic probes, detect different antibody populations. The present peptide-based assays might contribute to identify neutralizing ADAs in patients treated with Adalimumab. Further validation in larger cohort is required.

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Abstract Number: 0720

Long Term Efficacy and Safety of Triamcinolone Hexacetonide versus Triamcinolone Acetonide Intraarticular Injection for Juvenile Idiopathic Arthritis

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Background/Purpose: Juvenile idiopathic arthritis (JIA) is the most common rheumatic disease of childhood. Intra-articular corticosteroids joint injection (IAJI) with Triamcinolone hexacetonide (TH) or triamcinolone acetonide (TA) is considered as the first-line therapy for oligoarticular JIA. Previous studies showed benefit of TH vs. TA; however TA is still used in most of Israeli pediatric rheumatology centers. Our unit has experience with both regimens and therefore we aimed to compare the efficacy and safety of TA versus TH for JIA patient.

Methods: Chart review of JIA patients who were randomly (based on drug availability) treated with TA or TH IAJI between 2010-2019 was conducted. Primary outcome for efficacy was defined as full recovery of arthritis one month after IAJI and recurrence of arthritis 3 months month after IAJI. Primary outcome for safety was defined as the occurrence of adverse events (AEs) one month after IAJI.

Results: Overall 292 joints of 102 JIA patients were treated (138 TA/154 TH joints). Complete recovery after one month was documented in 107 (69.6%) TA treated joints and 96 (69.5%) TH treated joints (P=0.232). However, rate of relapse after 3 months was significantly higher in TA treated joints [27 (20.1%) vs. 13 (8.8%); (P< 0.01)]. No AEs were documented except of minor scar at 2 joints injection sites.

Conclusion: Although arthritis recovery was similar (~70%) with both regimens, relapse rate was more than doubled in TA injected joints vs. TH. These findings are specifically important due to contemporary shortage of TH in the US market.

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Validation of New Antirheumatic Drug Use as a Proxy for Increased JIA Disease Activity

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SESSION INFORMATION

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Background/Purpose: Administrative claims databases are valuable tools for studying treatment effects in large JIA populations but do not contain direct measures of disease activity, limiting conclusions about treatment effectiveness. We sought to validate a claim-based algorithm based on new medication use as a proxy for worsening JIA disease activity.

Methods: We queried clinical and prescription data in electronic medical records from 3 participating centers (2004-2019) for patients with JIA age < 21. We randomly selected a group of subjects who met a prespecified definition for new antirheumatic drug: 1) newly prescribed conventional or biologic DMARD ≥90 days after diagnosis and ≥90 days after starting the most recent DMARD; 2) DMARD re-initiation ≥180 days since the end of the most recent prescription; 3) systemic steroid prescribed ≥180 days since the most recent prescribed systemic steroid; or 4) intra-articular glucocorticoid injection (IAGC) ≥180 days after the most recent injection and after starting the most recently prescribed JIA drug. One eligible new antirheumatic drug event was randomly selected per subject. We excluded subjects for prior diagnoses of inflammatory bowel disease, immunodeficiency, and non-JIA systemic rheumatic disease (e.g., lupus). We estimated the positive predictive value (PPV) based on the proportion of subjects for whom new antirheumatic drug use was accompanied by documentation of increased disease activity within the prior 90 days. Increased disease activity was defined as: worsening joint symptoms (degree or extent of pain, stiffness, or swelling), new or recurrent joints with active arthritis on exam, new or worsening uveitis, new or recurrent symptoms or signs of systemic inflammation (e.g., fever, rash; systemic JIA only), or worsening disease activity per treating rheumatologist. We also examined the PPV of alternate definitions of new antirheumatic drug use.

Results: 87 subjects were included (Table 1). Of 66 subjects with use of a new conventional or biologic DMARD, 35 (53%) had taken a prior DMARD, and 9 (13.6%) were restarting the same DMARD that was previously stopped. Overall, among subjects who used a new antirheumatic drug, 75% (95% CI 65%, 83%) had evidence of worsening disease activity within the prior 3 months (Table 2). The PPV was lower for those starting a new DMARD (65%) than for those restarting a prior DMARD (89%), starting systemic steroids (91%), or receiving IAGC (93%). The PPV increased with longer durations of time since the last new medicine was prescribed and with longer times after diagnosis (Table 2). Reasons for new prescriptions in subjects without worsening disease activity were: inadequate response to prior treatment (86%), intolerance or side effects (23%), and patient/family preference (5%) (not mutually exclusive).

Table 1. Select characteristics of subjects sampled

	Total (n=87)
Age at diagnosis, median years (IQR)	7.2 (4.3, 12.9)
Female, n (%)	58 (67%)
Type of JIA, n (%)	
Oligoarticular	27 (31%)
Polyarticular, RF negative	28 (33%)
Polyarticular, RF positive	7 (8%)
Psoriatic	6 (7%)
Enthesitis related	7 (8%)
Systemic	7 (7%)
Undifferentiated	5 (6%)
Disease duration at index date, median years (IQR)	2.1 (0.9, 4.6)
Drug at index date[1], n (%)	
DMARD	66 (76%)
Conventional DMARD	35 (40%)
Biologic DMARD	33 (38%)
Systemic glucocorticoid	11 (13%)
Intra-articular glucocorticoid	14 (16%)

DMARD disease modifying antirheumatic drug, IQR interquartile range, RF rheumatoid factor 1 Some subjects were started on more than 1 drug at the index date

Table 2. Positive predictive value of definitions of new antirheumatic drug use as proxies for worsening JIA disease activity

	n with worse JIA / n total (%)
New antirheumatic drug use	65/87 (75%)
New DMARD (not restart)	37/57 (65%)
Restarted DMARD	8/9 (89%)
New systemic steroid	10/11 (91%)
New IAGC	13/14 (93%)
Type of new DMARD	
New conventional DMARD	17/27 (63%)
New biologic DMARD	21/31 (68%)
History of prior DMARD use	
New DMARD (not restart), no prior DMARD	19/27 (70%)
New DMARD (not restart), prior other DMARD	18/30 (60%)
Time since last new drug was first prescribed	
≥6 months since last new drug was first prescribed	39/49 (80%)
≥12 months since last new drug was first prescribed	32/35 (91%)
Time since JIA diagnosis	
≥6 months since JIA diagnosis	57/74 (77%)
≥12 months since JIA diagnosis	53/64 (83%)
≥24 months since JIA diagnosis	44/52 (85%)
JIA category	
Oligoarticular or RF negative polyarticular	43/55 (78%)
RF positive polyarticular	6/7 (86%)
Enthesitis related or psoriatic arthritis	9/13 (69%)
Systemic JIA	4/6 (67%)

DMARD disease modifying antirheumatic drug, IAGC intra-articular glucocorticoid injection, JIA juvenile idiopathic arthritis, RF rheumatoid factor

Conclusion: New prescriptions of antirheumatic drugs may serve as a reasonable proxy for worsening JIA disease activity in claims data. Restricting new use events to at least 6 months after the last newly prescribed drug or after JIA diagnosis may improve the likelihood that these events correspond to worsening disease activity.

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Abstract Number: 0722

Evaluation of Flare Rate and Tapering Strategies in Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Background/Purpose: Biological treatment (BT) has changed the perspectives of Juvenile Idiopathic Arthritis (JIA) patients, but it remains unclear when and how to taper or to withdraw treatment, neither the effect of treatment withdrawal after remission is achieved.

Our aim is to assess the course of the disease after tapering or stopping BT in a cohort of JIA patients. Tapering strategies and median time to flare were analyzed.

Methods: A retrospective, descriptive study was conducted in a cohort of JIA patients followed up in a Pediatric and Transition Unit of a referral hospital and who had received BT between 2000 and 2019. All JIA patients with at least one attempt of tapering were included. Remission was defined according to Wallace criteria.

Results: 131 JIA patients and 219 BT were reviewed. 198 deescalations in 108 (49,3%) BT in 95 (72,5%) JIA patients were included. 67,7% were female. The median age at diagnosis was 5 years [IQR (2-12)] and the median age at the beginning of tapering was 17 years [IQR (11,8-26)]. Patients were in remission a median of 9 months [IQR (6-17)]. Main BT tapered were: TNF inhibitors (76,3%), IL6 inhibitors (15,2%) and IL1 inhibitors (6,5%).Conventional DMARDs were administrated in combination with BT in 40,4% of the deescalations. Regarding JIA categories: 44 (22,2%) were Oligoarticular Persistent, 36 (18,2%) were Oligoarticular Extended, 32 (16,2%) were Systemic, 31 (15,7%) were Enthesitis related Arthritis, 19 (16,2%) were Psoriatic Arthritis, 16 (8,1%) were Polyarticular RF+, 16 (8,1%) were Polyarticular RF- and 5 (2,5%) were Undifferentiated. 8 (6,3%) patients were lost in follow-up.

171/198 (86,3%) cases started a deescalation. The most frequent tapering strategy was prolonged interval between applications (90,6%), combined strategy (5,8%) and lower dosage (3,5%). The median remaining dose administrated was 50% [IQR (50, 75)].

Twenty-seven (13,6%) cases withdrawn BT abruptly. The main causes of abrupt BT withdrawal were: remission (33,3%), pregnancy (29,6%).

Forty-five (26,3%) cases stopped BT after tapering. Median time to withdrawal was 11 months [IQR (6-22)]. The main causes of withdrawal after tapering were remission (66,7%), pregnancy (11,1%). There was no difference in remission rates after withdrawal among cases with previous tapering (PT) or abrupt discontinuation(AD) [Median PT 5 +-(1,1), median AD 7 +- (2,6), Log rank=0,946]. After 6 months of withdrawal 48,1% of AD cases and 56,1% of PT

Time, months	Cases on remission, n.%
6	101 (79,8)
12	86 (68,1)
24	60 (47,4)
Currently on remission	40 (31,8)

Table 1: Remission rates among cases tapered without withdrawal during follow-up. n=126.

cases had presented a flare. 10/72 (13,8%) cases are currently on remission without BT during follow-up, 9,7% without any treatment and 4,1% with cDMARDs.

BT was tapered without withdrawal in 126 (63,6%) cases. Remission rates during tapering are specified in table 1. 40 (20%) cases continue tapered without a flare after a median of 77 months [IQR (36,3-111,3)] of follow-up.

Conclusion: - There was no difference in remission rates among patients that discontinuated BT after tapering or after abrupt discontinuation. After 6 months of withdrawal 48,1% of cases that stopped abruptly and 56,1% of cases that stopped after tapering had presented a flare.

- Tapering without withdrawal is safe: 79,8% of cases at 6 months and 47,4% of cases at 24 months that tapered without withdrawal remained on sustained remission.

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Abstract Number: 0723

Social Determinants of Health and Time to First Pediatric Rheumatology Appointment in Polyarticular Juvenile Idiopathic Arthritis

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Background/Purpose: Patients with polyarticular JIA (pJIA) have a refractory disease course with increased risk for joint damage resulting in poor functional outcome and decreased quality of life. The highest risk is in patients who are younger at diagnosis. Therefore, it is important for patients to receive timely access to pediatric rheumatology for management. The objective of this study is to examine the association of social determinants of health (SDoH) on

	Overall (n=1684)
Gender	
Female	1322 (78.5%)
Male	362 (21.5%)
Age at Diagnosis	
Mean (SD)	7.47 (4.57)
Median (min, max)	7.0 (0,15)
Household Income	
<$25,000	150 (8.9%)
$25,000- 49,999	188 (11.2%)
$50,000-99,999	414 (24.6%)
>$100,000	483 (28.7%)
Missing	449 (26.7%)
Highest Level of Completed Parent/Guardian Education	
High School or Less	260 (15.4%)
College (1-4 year college, trade school)	656 (39.0%)
Graduate School	289 (17.2%)
Missing	479 (28.5%)
Time from onset of symptoms to seeing a rheumatologist (months)	
Median (IQR)	3 (1, 6)
Missing	331 (19.7%)

Table 1. Patient Characteristics and demographics

time from reported symptom onset (pain, joint stiffness, swelling) to first appointment with pediatric rheumatology in pJIA patients.

Methods: We retrospectively analyzed Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry from July 2015 through February 2020. Inclusion criteria were USA residency and pJIA diagnosis with recorded >4 joints involved in first 6 months of disease, exclusion criteria were invalid zip code and additional diagnosis of systemic inflammatory or autoimmune disease. The SDoH we studied were family income, guardian's highest level of ed-

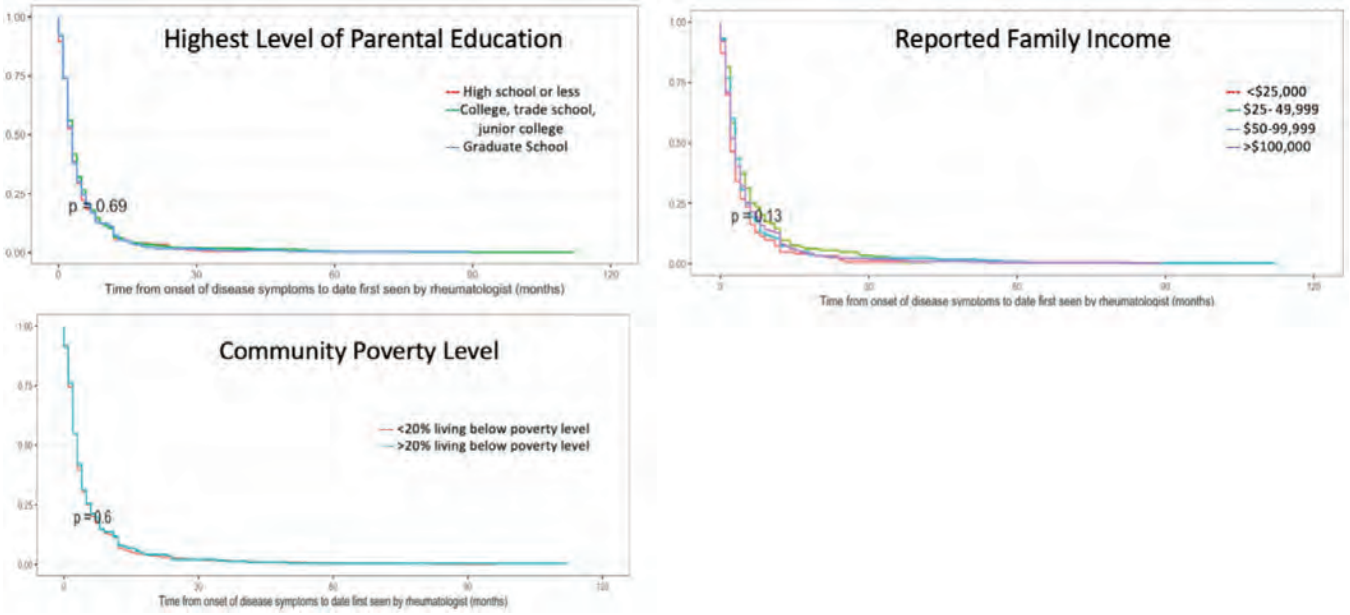

Figure 1. Kaplan- Meier curves for time from symptom onset to date first presentation to pediatric rheumatologist

[/]Hazard Ratio, Confidence Interval, *HS or less is referent, **<25,000 is referent ***<20% population/ZCTA is referent, **** Negative is referent

	Unadjusted			Adjusted for Age at Diagnosis		
Characteristic	HR[/]	95% CI[/]	p-value	HR[/]	95% CI[/]	p-value
Highest Level of Parent/ Guardian Education *						
College	0.93	0.79- 1.1	0.4	0.9	0.77-1.06	0.2
Graduate School	0.98	0.81- 1.18	0.8	0.95	0.79-1.15	0.6
Family Income **						
$25-49,999	0.76	0.6-0.97	**0.025**	0.78	0.61-1.0	**0.046**
$50-99,999	0.83	0.67- 1.02	0.075	0.83	0.68- 1.02	0.08
>$100,000	0.86	0.7- 1.05	0.15	0.88	0.72- 1.07	0.2
Community Poverty Level ***						
> 20% population/ ZCTA	0.96	0.84-1.11	0.6	0.96	0.84-1.1	0.6

Table 2. Association of social determinants of health with time to first presentation to pediatric rheumatologist

ucation, and community poverty level. Demographics, approximate date of symptom onset, were queried. Five-digit zip-codes were used to extrapolate community poverty levels using 2014-2018 American Community Survey data. The Kaplan-Meier method was used to estimate rheumatology visit-free survival. The log-rank test was used to compare rheumatology visit-free survival between the SDoH. Cox proportional-hazards models were utilized to estimate hazard ratios for the outcome mentioned above, adjusted for age of diagnosis.

Results: 1684 patients fit criteria for this study. Demographics are listed in Table 1. Twenty percent of patients had missing time to first appointment. The median time from symptom onset to first pediatric rheumatology visit was 3 months (IQR: 1,6). Kaplan-Meier curves showing the probability of first rheumatology visit for time from symptom onset are shown in figure 1. Children with family reported income in the range of $25,000-49,999 were likely to have longer time to first appointment (unadjusted HR 0.76, CI 0.6-0.97, p = 0.025). These relationships remain consistent when additionally adjusted for age at diagnosis (table 2). Guardian's highest level of education, and community poverty level did not affect the time to first appointment.

Conclusion: Family reported income, guardian education, and community poverty did not impact time to first appointment. Children within the income bracket of $25,000-49,999 may have less access to subspecialists, transportation, or advocacy compared to other children. Ascertainment bias into the registry may skew the cohort to a wealthy and educated population. Recall bias on symptom onset is possible. Future directions for research include stratification of community poverty levels and evaluation of public vs private insurance on time to first appointment.

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Abstract Number: 0724

Anxiety and Depressive Symptoms in Juvenile Idiopathic Arthritis (JIA) Correlate with Pain and Stress Using Patient-Reported Outcomes Measurement Information System (PROMIS®)

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SESSION INFORMATION
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Background/Purpose: Children with chronic diseases have higher rates of mental health issues and less favorable outcomes than the general pediatric population. Children with JIA experience pain and limited mobility which may affect their mental health. Prior studies of mental health and the relationship to disease manifestations in JIA have had variable results, partly due to a lack of a standard assessment tool. PROMIS has recently been developed to help standardize and validate assessments on patient-reported outcomes. The aims of this study were to describe anxiety and depressive symptoms in children with JIA using PROMIS measures and to evaluate potential correlations with disease manifestations.

Methods: We conducted a two-center, cross-sectional study of JIA patients and their parents. JIA ILAR subtypes included: 36% oligoarticular (52% extended; 48% persistent), 32% polyarticular (81% RF –; 19% RF +), 7% systemic, 3.5% psoriatic, 3.5% enthesitis-related, and 18% undifferentiated (Table 1). Participants completed PROMIS measures on depression, anxiety, psychological stress experiences, and pain interference to assess psychosocial functioning, and the Childhood Health Assessment Questionnaire (CHAQ) to assess physical functioning. Disease activity was measured using the clinical juvenile arthritis disease activity score (cJADAS10). A general pediatric reference population served as the control group. The Pearson correlation and Kruskal-Wallis tests were used to determine the relationship between mental health PROMIS T-scores and disease manifestations.

Results: Eighty-five JIA patients completed the study; 75% female, 86% Caucasian, median age of 14 years, and median disease duration of 4.77 years (range 0.28-16.86 years). Patients had a median active joint count of 0 joints (range 0-11) and a median cJADAS10 score of 2 (range 0-23). The median CHAQ score was 0 (range 0-1.75) (Table 1). Using the cJADAS10, 58 patients (68%) had inactive or low disease activity. Mean PROMIS T-scores for depressive and anxiety symptoms were significantly lower in JIA patients compared to the general pediatric reference population ($p < 0.0001$). Nineteen patients (23%) had moderate to severe symptoms of anxiety and/or depression (Table 2). Age correlated with depressive symptoms ($r=0.38$; $p=0.0004$) but not anxiety ($r=0.21$; $p=0.056$). Depressive and anxiety symptoms correlated with pain ($r=0.64$ and $r=0.46$, respectively; $p < 0.0001$) and stress ($r=0.78$ and $r=0.74$, respectively; $p < 0.0001$), but not with JIA subtype, disease duration, physical function, or disease activity (Table 3).

Conclusion: Using PROMIS, approximately one-quarter of JIA patients reported moderate to severe symptoms of anxiety and depression. JIA patients in our study experienced less anxiety and depressive symptoms compared to the general pediatric reference population. Anxiety and depressive symptoms in JIA patients are associated with pain and stress, but they are not associated with other disease manifestations.

Variables	Number (%) or Median (Range)
Gender	
Female	64 (75%)
Race	
Caucasian or White	73 (86%)
Black or African American	5 (6%)
Asian	5 (6%)
Native Hawaiian/Pacific Islander	1 (1%)
Multiple	1 (1%)
Current age (years)	14 (8.04-17.87)
Length of Disease (years)	4.77 (0.28-16.86)
JIA Subtype	
Oligoarticular	31 (36%)
Extended Oligoarticular	16 (19%)
Persistent Oligoarticular	15 (18%)
Polyarticular	27 (32%)
RF - Polyarticular	22 (26%)
RF + Polyarticular	5 (6%)
CCP +	4 (5%)
CCP -	1 (1%)
Systemic	6 (7%)
Psoriatic	3 (3.5%)
Enthesitis-Related	3 (3.5%)
Undifferentiated	15 (18%)
Medications	
NSAIDs	48 (56%)
Biologics	45 (53%)
DMARDs	34 (40%)
Oral Steroids	3 (4%)
Intra-articular steroids	10 (12%)
Active Joint Count	0 (0-11)
cJADAS10 score (range 0-30)	2 (0-23)
CHAQ score (range 0-3)	0 (0-1.75)
Other Chronic Diseases	
Yes	35 (41%)
Types	
Celiac	1 (1%)
Asthma	5 (6%)
Diabetes	3 (4%)
Chronic Pain	6 (7%)
Hypermobility	2 (2%)
MAS	2 (2%)
Uveitis	9 (11%)
Thyroid Disease	2 (2%)
Cardiovascular Disease	1 (1%)
Other*	13 (15%)

* Other includes: attention deficit hyperactivity disorder, autoimmune hepatitis, chronic headaches, allergies, aspergers, avascular necrosis, scoliosis, linear scleroderma, spherocytosis, pharyngo-esophageal dysphagia, and pituitary hypoplasia with secondary adrenal insufficiency

JIA: Juvenile Idiopathic Arthritis; RF: Rheumatoid Factor; CCP: Cyclic Citrullinated Peptide; NSAIDS: Non-Steroidal Anti-Inflammatory Drugs; DMARDS: Disease Modifying Anti-Rheumatic Drugs; cJADAS10: Clinical Juvenile Arthritis Disease Activity Score; CHAQ: Childhood Health Assessment Questionnaire; MAS: Macrophage Activity Syndrome

Table 1. Patient Demographics

PROMIS Survey/Score*	Mean T-score (SD)	Number (%)
Depression	45.15 (± 9.28)	
T-score < 50 = normal		56 (67%)
T-score 50 -- ≤ 54 = mild symptoms		13 (15%)
T-score 55 -- ≤ 64 = moderate symptoms		14 (17%)
T-score ≥ 65 = severe symptoms		1 (1%)
Anxiety	44.41 (± 9.13)	
T-score < 50 = normal		59 (70%)
T-score 50 -- ≤ 54 = mild symptoms		11 (13%)
T-score 55 -- ≤ 64 = moderate symptoms		13 (16%)
T-score ≥ 65 = severe symptoms		1 (1%)

*1 patient did not complete the PROMIS surveys

JIA: Juvenile Idiopathic Arthritis; PROMIS: Patient-Reported Outcome Measurement Information System; SD: Standard Deviation

Table 2. PROMIS Mental Health Scores

Disease Manifestation	PROMIS Depression r values	PROMIS Depression P values	PROMIS Anxiety r values	PROMIS Anxiety P values
JIA Sub-type	--	p = 0.88	--	p = 0.26
Age	r = 0.38	p = 0.0004	r = 0.21	p = 0.056
Total active joint count	r = -0.01	p = 0.94	r = -0.05	p = 0.64
cJADAS10 score				
Oligoarticular*	--	p = 0.20	--	p = 0.52
Polyarticular[X]	--	p = 0.30	--	p = 0.60
CHAQ	r = 0.19	p = 0.08	r = -0.02	p = 0.87
Disease Duration	r = 0.06	p = 0.57	r = -0.04	p = 0.71
PROMIS Pain Interference	r = 0.64	p <0.0001	r = 0.46	p <0.0001
PROMIS Stress Experiences	r = 0.78	p <0.0001	r = 0.74	p <0.0001

* Included persistent oligoarticular JIA and patients with ≤ 4 joints during their disease duration

[X] Included polyarticular JIA, extended oligoarticular JIA, and patients with > 4 joints during their disease duration

JIA: Juvenile Idiopathic Arthritis; PROMIS: Patient-Reported Outcome Measurement Information System; cJADAS10: Clinical Juvenile Arthritis Disease Activity Score; CHAQ: Childhood Health Assessment Questionnaire

Table 3. Correlation between PROMIS Mental Health Scores and JIA Disease Manifestations

Disclosure: D. Fair, None; **J. Olson**, Abbvie, 1, BMS, 1; **J. Lemke**, None; **S. Protopapas**, None; **K. Yan**, None; **J. Zhang**, None.

Abstract Number: 0725

A Data Science Evaluation of the Juvenile Arthritis Multidimensional Assessment Report (JAMAR) Questionnaire for Improving Management of JIA Patients

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Background/Purpose: The Juvenile Arthritis Multidimensional Assessment Report (JAMAR) is a questionnaire developed to comprehensively assess Juvenile Idiopathic Arthritis (JIA) patients. Despite being translated into 54 languages, there is still limited literature about it. The length of the questionnaire could have been influencing its clinical practicality. The purpose of this study is to answer the following questions:

1. "Which are the most informative questions?";
2. "How well do the collected data correlate with other clinical variables?";
3. "Are there discrepancies between the perceptions of patients and parents?";

Methods: We included 71 children with JIA according to ILAR criteria, all of them receiving treatment and we followed them up for a year. JAMAR questionnaires were answered by both children and parents at baseline, 6 and 12 months. Also, a thorough clinical examination was performed in every visit: all the joints were clinically assessed for swelling, tenderness, and limited range of motion, and Juvenile Arthritis Disease Activity Score (JADAS), disease activity state, parents and patients assessment through Visual Analogue Scale (VAS), physician's VAS, Erythrocyte Sedimentation Rate (ESR) and C-reactive protein (CRP) were recorded. We applied state of the art machine learning methods in order to find the most relevant questions in JAMAR. Additionally, we utilized tensor decomposition to identify relevant patient clusters. Furthermore, we correlated these critical questions with clinical and biological parameters recorded. We have compared the discordance rate between patients vs parents responses in 5 of JAMAR parameters as previously reported (Vanoni F, et al. *Pediatr Rheumatol Online J*. 2016;14(1):2). We explored the relation between discordance and demographic and clinical variables.

Results: A total of 374 JAMAR questionnaires are analyzed with our Machine Learning algorithms. First, we identify a small group of questions as the most relevant for patients and parents. The identified questions exhibit better correlations with the JADAS scores than the non-relevant ones. Second, 96% of the pairs (child-parent) are discordant for at least one item, but the differences are small and VAS well being is the only score with a statistically significant difference ($P < 0.0001$). We observe a higher rate of activity in the patients exhibiting discordant evaluations with their parents. In addition, the observation patient-parent agreement in Juvenile Arthritis Functionality Scale (JAFS) is better than Pediatric Rheumatology Quality of Life Scale (PRQL).

Conclusion: In this study, we revisit the JAMAR questionnaire by applying modern data mining techniques in a longitudinal dataset. Our results suggest that a small number of questions in the JAMAR questionnaire provide significant information and correlate well with the JADAS scores. We argue that this reduced set of questions could make the data collection easier by trading off the number of questions for frequency and ease of self-reported data collection.

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Who Ordered the Stiff One? Characteristics of Polyarticular Juvenile Idiopathic Arthritis Patients Associated with the Presence and Increased Duration of Joint Stiffness

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SESSION INFORMATION

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	Overall (n=1684)
Gender	
Female	1322 (78.5%)
Male	362 (21.5%)
Age at Diagnosis	
Mean (SD)	7.47 (4.57)
Median (min, max)	7.0 (0,15)
Household Income	
<$25,000	150 (8.9%)
$25,000- 49,999	188 (11.2%)
$50,000-99,999	414 (24.6%)
>$100,000	483 (28.7%)
Missing	449 (26.7%)
Highest Level of Completed Parent/Guardian Education	
High School or Less	260 (15.4%)
College (1-4 year college, trade school)	656 (39.0%)
Graduate School	289 (17.2%)
Missing	479 (28.5%)
Time from onset of symptoms to seeing a rheumatologist (months)	
Mean (SD)	5.18 (8.66)
Median (min, max)	3.0 (0,112)
Missing	331 (19.7%)
CHAQ	
Mean (SD)	0.505 (0.680)
Physician Global	
Mean (SD)	2.4 (2.6)
Rheumatoid Factor status	
Negative	1204 (71.5%)
Not done	171 (10.2%)
Positive	309 (18.3%)
Anti- CCP	
Negative	786 (46.7%)
Not Done	646 (38.3%)
Positive	252 (15.0%)

Table 1. Patient characteristics and demographics at first pediatric rheumatology visit

[1]Odds Ratio, Confidence Interval, *HS or less is referent, **<25,000 is referent *** <20% population/ZCTA is referent, **** Negative test result is referent

	Family Education*		Family Income **			Community Poverty Level***	RF****		Anti-CCP****	
	College	Grad School	$25-49K	$50 - 99K	>$100K	>20% population/ ZCTA	Not done	Positive	Not done	Positive
Unadjusted OR[1] (95% CI[1])	1.28 (0.82-2.05) P=0.3	0.83 (0.47-1.45) P=0.5	1.41 (0.79-2.58) P=0.3	0.83 (0.49-1.46) P=0.5	0.54 (0.31-0.96) **P=0.031**	1.15 (0.78-1.65) P=0.5	1.36 (0.72-2.4) P=0.3	2.3 (1.62-3.23) **P=<0.001**	1.05 (0.72-1.51) P=0.8	2.44 (1.65-3.58) **p<0.001**
Adjusted OR [1] (95% CI[1])	1.38 (0.88-2.21) P=0.2	0.9 (0.51-1.59) P=0.7	1.39 (0.77-2.56) P=0.3	0.85 (0.49-1.5) P=0.6	0.54 (0.31-0.97) **P= 0.035**	1.11 (0.75-1.6) P=0.6	1.45 (0.77-2.57) P=0.2	1.79 (1.24-2.58) **P=0.002**	1.16 (0.8-1.68) P=0.4	1.97 (1.31-2.95) **P<0.001**

Table 2. Unadjusted and Age at Diagnosis Adjusted Odds Ratios for >60 minutes of morning stiffness at baseline

Background/Purpose: Joint stiffness as a sign of intra-articular inflammation may be an early presenting symptom of JIA. Studies following pain in chronic disease have shown that pediatric patients from lower socioeconomic brackets report less pain compared to severity matched disease in affluent patients, it is unknown if joint stiffness in JIA follows a similar trend. The objective of this study is to assess the relationship between social determinants of health (SDoH) and presence and duration of morning joint stiffness. Polyarticular JIA (pJIA) patients were studied as they are older cohort of patient more likely to accurately describe presence of stiffness.

Methods: We retrospectively analyzed Childhood Arthritis and Rheumatology Research Alliance (CARRA) registry from July 2015 through February 2020. Inclusion criteria were USA residency and pJIA diagnosis with recorded >4 joints involved in first 6 months of disease; exclusion criteria were invalid zip code and additional diagnosis of systemic inflammatory or autoimmune disease. The primary outcomes of interest are presence and duration of morning stiffness. SDoH we studied were reported family income, highest level of completed guardian education, and community poverty level. Demographics, RF and anti-CCP status were included as covariates. Five-digit zip-codes were used to extrapolate community poverty levels using 2014-2018 American Community Survey data. Chi-square tests were utilized to assess the bivariate relationships between SDoH and study outcomes. We used logistic regression models to determine association of SDoH with duration of morning stiffness (>60min vs < 60min) and adjusted for age at diagnosis.

Results: 1684 patients were included in the study. Demographics and baseline disease severity are listed in table 1. On unadjusted analysis, guardian education (p=0.018), reported family income (p< 0.001), RF IgM status (p< 0.001), and anti-CCP IgG status (p< 0.001) were significantly associated with increased risk for presence and longer duration of morning stiffness, while community poverty level was not (p=0.6). Children who came from families with >$100,000 income were half as likely to report greater than 60 minutes of morning stiffness at baseline (OR 0.54, CI 0.31-0.97, p= 0.035). This was consistent after adjusting for age at diagnosis, CCP and RF status (table 2).

Conclusion: We found a significant inverse association between family income level and duration of morning stiffness. It is possible that this may be a reflection of increased reporting of stiffness in low income families. Further

studies to see association of SDoH on morning stiffness are warranted not only in pJIA but also in other forms of JIA to further understand these associations.

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Abstract Number: 0727

Hip Involvement Leads to Poor Outcome in Adulthood in Children with Enthesitis Related Arthritis (ERA) Category of Juvenile Idiopathic Arthritis (JIA)

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Background/Purpose: Enthesitis related arthritis (ERA) is the commonest category of JIA seen in India and constitutes 30-40% of all JIA patients. There are many studies on long term outcomes in adult Spondyloarthritis but the data in children with ERA is scant. The available data is also mostly from developed countries. Thus, we studied outcome of ERA in adulthood in resource constrained setting where there is limited availability of anti-TNF agents.

Methods: Patients with ERA (ILAR classification) having >5 years of disease and above the age of 18 years were included in the study. Data on clinical features, Bath indices (BASMI, BASDAI, BASFI), health assessment questionnaire disability index (HAQ DI) was collected. CRP was measured by Nephelometry. X-ray pelvis including hips was obtained and compared with baseline X-ray available at first visit to our hospital for progression of radiological sacroiliitis and hip arthritis. The X-rays were assessed by two radiologists. In addition, fulfilment of adult criteria of Spondyloarthropathy (SpA), assessment of Spondylarthritis International Society (ASAS) and modified New York (NY)] were assessed.

Results: 73 patients (72 male) of median age 20 (18-23) years and median disease duration of 8 (5.5-11) years were recruited. There was delay in diagnosis of 4 (1.75-6) years. Nearly all (96%) had active disease (BASDAI >0) and median CRP was 2.1 (0.6-4.8) mg/dl. Three-fourth (75.3%) had functional disability (HAQ DI >0) and median BASFI was 1.95 (0.6-3.5). 67 patients fulfilled axial ASAS criteria, while 71 fulfilled peripheral SpA criteria.

Overall, 81% had radiological sacroiliitis and 37% had hip involvement. Nearly half (46.6%) of the patients had radiological progression in sacroiliitis and one-fourth (25%) had progression of hip arthritis over 3.5 (2.5-5.5) years. Patients with radiological sacroiliitis had higher CRP (2.5 vs 1 mg/dl) and more hip arthritis (37 vs 7%) than those without it.

Those with radiological hip arthritis had longer delay in diagnosis (6 vs 3 years) than those without it. They also had higher BASDAI, BASMI, BASFI and HAQ DI. Hip arthritis correlated with radiological sacroiliitis (r= 0.301). Fulfillment of modified NY criteria was seen more often in patients with hip arthritis (95% vs 63%; p< 0.002) (Table 1).

Table 1. Differences in baseline characteristics and outcomes between groups			
	Radiological hip arthritis (n=27)	**No radiological hip arthritis (n=46)**	**P**
Duration of disease in years median (IQR)	9 (7-11)	6.5 (5-10)	0.063
Age in years	21 (19-23)	19.5 (18-22.5)	0.137
Age of onset of disease (years)	13 (10-15)	14 (12-15)	0.198
Delay in diagnosis (years)	**6 (2-9)**	**3 (1-5)**	**0.011**
Duration between initial and latest X- ray pelvis (years)	3.5 (2-5.5)	3.5 (2.5-5.5)	0.377
School years lost (in years)	1 (0.26-2)	0.5 (0-2)	0.648
Clinical features n (%)			
Arthritis	27 (100)	42 (91.3)	0.115
Enthesitis	24 (88)	42 (91)	0.735
IBP	24 (88)	43 (93.9)	0.491
Sacroiliitis	18 (66)	25 (54)	0.302
Hip involvement	**17 (63)**	**6 (13)**	**0.000**
Tarsitis	18 (66)	25 (54)	0.335
Uveitis	4 (14)	9 (16)	0.609
Lab parameters			
Hemoglobin (g/dl)	12.1 (10.9-13)	12.4 (11.5-13.3)	0.391
ESR (mm/hr)	26 (17-50)	20 (14-39)	0.200
CRP (mg/dl)	**3 (2.1-6.1)**	**1.1 (0.2-4.23)**	**0.014**
Platelets ($x10^5$/dl)	2.3 (1.8-2.9)	2.2 (1.8-2.7)	0.391
HLA B27+ (%)	11/11 (100)	21/23 (91)	0.313
Outcome measures			
BASDAI	**5 (3.2-6.5)**	**2.6 (1.2-4.8)**	**0.002**
BASMI	**2 (1.6-4.6)**	**1.2 (0.7-1.8)**	**0.000**
BASFI	**3.4 (2.1-4.8)**	**1.3 (0.35-2.3)**	**0.000**
HAQ DI	**0.45 (0.2-0.75)**	**0.15 (0-0.35)**	**0.000**
BASDAI>0 (%)	27 (100)	43 (93)	0.175
HAQ DI >0 (%)	**25 (92)**	**30 (65.2)**	**0.009**
Radiological sacroiliitis (%)	**26 (96.3)**	**33 (71.7)**	**0.010**
Progression of Radiological Sacroiliitis (%)	13 (48)	21 (48)	0.995
Fulfilment of adult criteria			
ASAS criteria	26 (96)	45 (97)	0.699
Modified NY criteria	**25 (96)**	**29 (63)**	**0.002**
Treatment received			
NSAIDS alone	7 (25)	13 (28)	0.829
DMARDS+ NSAIDS	20 (74)	32 (69)	0.681

Conclusion: Most adults with ERA have active disease even after 8 years of disease Hip involvement is associated with poorer outcome.

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Abstract Number: 0728

Clinical Outcomes of Juvenile Arthritis in Adulthood: A Systematic Review

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Background/Purpose: Juvenile arthritis (JA) is the most common pediatric rheumatic disease, with potentially permanent functional impacts on patients long after initial diagnosis. Little is known about adulthood outcomes. This systematic review aims to summarize clinical outcomes in adults with JA (age >16), identify gaps of knowledge and recommend future research directions.

Methods: MEDLINE and EMBASE searches were developed and conducted with an academic librarian. We focused on studies 2000-2017 for contemporary management outcomes. We excluded: non-English publications, studies evaluating the transition process, qualitative studies, obstetric outcomes, short reports/letters, case series. Mixed population studies were included if the mean/median age at assessment was >16 years. The Quality in Prognosis Studies (QUIPS) tool was used to assess risk-of-bias in 6 study domains: population, attrition, outcomes, prognostic factors, confounding, statistics. Each publication was assessed by 2 reviewers. Study data were extracted using a standard form.

Results: 56 of 12 243 papers were included in this study for analysis. The majority (52%) of studies were retrospective cohorts, and the most common study queries were disease (34.9%), functional status/psychosocial (22.2%), temporomandibular joint (11.1%), and uveitis (9.5%) outcomes. 13 publications (21%) were repeat publications of non- unique cohorts, with the majority of these using the same cohort from Norway. Moderate-high risks of bias were present especially in study confounding (95%), participation (81%) and attrition (82.1%) domains.

In disease outcomes, the most common reported were remission (36%), and use of DMARDs (71%). HAQ functional status was reported with a median score of 0.49, signifying mild disability. VAS pain scale had a median score of 6.51 cm. DMARDs and NSAIDs usage ever were reported with 42.8% and 63.3% respectively. Uveitis was reported in 22.9% patients. Out of 56 papers, 35 performed statistical multivariable modelling. Within each study topic there were no multivariable models of similar outcomes to allow for identification of consistent prognostic factors.

Conclusion: Only 2 (3.1%) truly longitudinal studies focused on the adult outcomes of JA patients. Although there have been many studies published on outcomes in JA adults, they have moderate-high risks of bias in crucial study domains that limited interpretation of results. Prognostic factors were non-reproducible and could not be summarized. Attention to selection of study population and accounting for attrition and confounding will improve quality of future studies. There should be a discussion among investigators to establish reporting of core outcomes in future adult JA studies to allow comparisons and facilitate future meta-analysis. In future studies we aim to categorize outcomes by duration of disease and start formulating a potential standard reporting format for future JIA research.

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Abstract Number: 0729

Morbidity of JIA-associated Uveitis: Half of Patients Despite Systemic Treatment Still Show Ocular Damage During a Long-term Follow-up

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: JIA

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Background/Purpose: Uveitis is the most common extra-articular complication of juvenile Idiopathic arthritis (JIA). Due to its typical indolent and chronic course, children with this condition are at risk for ocular morbidity with a significant impact on their quality of life. The aim of this study is to describe demographic and clinical features, treatment approaches and outcome of a population of patients with JIA-associated uveitis.

Methods: Charts of patients with JIA-associated uveitis, followed in two tertiary Pediatric Rheumatology Centres were retrospectively reviewed with regard to clinical features, therapeutic choices and outcome

Results: Data from 162 JIA patients with uveitis were analysed (81.5% female), with a mean follow up of 8.9 years (SD ± 2.56). Mean age at JIA onset was 3.6 years (SD± 3.1) and the mean JIA duration at uveitis onset was 2.5 years (SD ± 4.3). Uveitis was diagnosed at JIA onset in 9.9% of patients. The most frequent JIA category was oligoarthritis (88.9%), which was persistent in 72.8% of cases, followed by RF- polyarthritis (9.3%). No systemic JIA was reported. Uveitis was predominantly anterior (96.9%), and reported bilateral in 65.4% of cases. In almost all patients (87.6%) antinuclear antibodies (ANA) were positive. Systemic medications were required in 134 (82.7 %) patients. Methotrexate and cyclosporine were used in 66.0% and 7.4% of cases, respectively, while 86 patients (53.1%) required biologic therapy, mainly adalimumab (34.6%), followed by infliximab (10.5%) and tocilizumab (3.7%). In 28.4% of cases more than 1 biologic was needed. Mean recurrence rate in our cohort was 1.3 per year (SD ±1.1). In 79 patients (49.8%) uveitis was complicated by ocular damage, which is summarized in Table 1. A best-corrected visual acuity (BCVA) ≤ 0.4 and ≤ 0.1 were observed in 14.2% and 10.5% of patients, respectively.

Table 1. Ocular damage in the cohort (total JIA patients with uveitis, n = 162)

	Number of patients with complication (%)
Synechiae	56 (34.6%)
Band keratopathy	32 (19.8%)
Cataract	29 (17.9%)
Glaucoma	9 (5.6%)
Cystoid macular edema	7 (4.3%)
Any surgery	28 (17.3%)
Cataract	24 (14.8%)
Synechiotomy	2 (1.2%)
Other (band keratopathy, glaucoma)	2 (1.2%)

Conclusion: Despite continue improvement in JIA therapeutic options, uveitis remains a complication with high morbidity. Clinical predictors and biomarkers are needed to identify patients at higher risk of unfavourable outcome. Careful monitoring and follow-up are crucial for timely detection of ocular inflammation and prevention of damage.

Disclosure: F. Minoia, None; **L. Marelli**, None; **G. Beretta**, None; **M. Romano**, None; **E. Miserocchi**, None; **C. Mapelli**, None; **A. Petaccia**, None; **S. Lanni**, None; **I. Pontikaki**, None; **G. Filocamo**, None; **R. Cimaz**, None.

Abstract Number: 0730

To Taper or Not to Taper in Juvenile Idiopathic Arthritis: Is There a Risk of Development of Uveitis Flares?

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

Background/Purpose: To determine the association between the occurrence of uveitis flares in patients with Juvenile Idiopathic Arthritis (JIA) and the de-intensification of immunosuppressive treatment.

Methods: We conducted a retrospective longitudinal cohort study, including a single-centre consecutive cohort of patients diagnosed with oligoarticular JIA antinuclear antibody (ANA) positive, who had had at least one uveitis flare during their follow-up up to 19.5 years. Patiens with the same JIA category, ANA positive, with no history of uveitis flare were considered controls. Epidemiological data, age of first uveitis flare, number of previous episodes, treatments prescribed at the time of the flare and time since the last treatment modification were recorded. Treatment tapering was defined as a reduction in dose or increase in the inter-doses period, according to datasheet of the corresponding treatment. The relative risk (RR) for the development of uveitis flare and treatment tapering were determined by contingency tables.

Results: We included 68 patients of which 22 had had uveitis flares during their follow-up, and 46 controls. The mean age of patients at JIA diagnosis was3.56 ± 2.17 years. A total of 107 uveitis flares were recorded with an average of 4.54 ± 4.70 episodes per patient. The first uveitis flare was registered at an average age of 6.57 ± 5.79 years. Four patients (18.1%) had had only one episode. Among patients with more than one flare, the inter-flare period was 17.84 ± 21.8 months. Thirty flares (27%) were registered in patients without immunosuppressive treatment. Twenty patients (90%) required the initiation of biological therapy specific for uveitis. Adalimumab (ADA) was chosen in 19 (86.3%) patienst and avoided further uveitis flares in 15 (68%) cases. Treatment with Tocilizumab (TCZ) was used in 6 (27.7%) cases and avoided further uveitis flares in 5 (27.3%). Thirty-three episodes (33.1%) were registered in patients with Methotrexate (MTX) of which, 8 (7.5%) were receiving doses below datasheet (< 10mg/m2). Forty-four uveitis flares (41%) took place in patients on biological treatment, of which 27 were receiving ADA (25.3%), 2 (1.9%) TCZ and 15 (14%) other therapies. Thirty-seven flares (32.1%) took place in patients on tapered treatments and 11 (10.3%) after non scheduled withdrawal. In terms of risk of developing a new uveitis flare, tapering had a RR of 2.79 (CI 2.01-3.7; $P< 0.05$) while therapy withdrawal had a RR of 5.91 (CI 3.23-10.8; $P< 0.05$). MTX tapering had a RR of 12.5 (CI 6.4-24.5 $P< 0.05$). Patients with ADA had a RR of 0.88 (CI 0.4-1.6; $P=0.84$) of developing uveitis flares, with TCZ a RR

of 4,65 (CI 1.2-17.8; *P*< 0.05) and with other biological therapy (Etanercept, Infliximab, Abatacept) a RR of 3.56 (CI 2.05-6.2; *P*< 0.05).

Conclusion: Tapering immunosuppressive treatment in oligoarticular JIA ANA positive patients, increases the risk of developing uveitis flares.

Disclosure: M. Teran, None; **A. Boteanu**, AbbVie, 8, Novartis, 8, Roche, 8; **C. Guillen**, None; **C. Pijoan**, None; **J. Quinones**, None; **V. Garcia**, None; **I. Del Bosque-Granero**, None; **L. Calvo-Sanz**, None; **M. Vázquez**, None.

Abstract Number: 0731

Comparing S100 Proteins and Cytokine Levels in Tears Based on Uveitis Activity Laterality in Children with JIA-associated Uveitis and Non-JIA-U

Jackeline Rodriguez-Smith[1], Virginia Miraldi Utz[2], Amy Cassedy[1], Sherry Thornton[1], Grant Schulert[3], Alyssa Sproles[4], Najima Mwase[1], Theresa Hennard[1], Mekibib Altaye[2], Alexei Grom[1] and Sheila Angeles-Han[1], [1]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, [3]PRCSG, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [4]Cincinnati Children's Hospital, Cincinnati

SESSION INFORMATION
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Session Title: Pediatric Rheumatology – Clinical Poster II: JIA
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Session Time: 9:00AM–11:00AM

Background/Purpose: The pathogenesis of pediatric uveitis remains unclear. Studies of biomarkers using aqueous humor (AqH) identified S100 proteins, cytokines, and chemokines as potential biomarkers of uveitis activity. AqH collection is invasive and less feasible. Tears may serve as a surrogate as the same biomarkers present in AqH were detected in tears of uveitis patients. We showed that S100A12, IL-8, and sICAM-1 levels differ based on uveitis activity in JIA-associated uveitis (JIA-U). We aim to determine if tear-based biomarkers differ in a patient's eyes based on uveitis activity by laterality and diagnoses.

Methods: Tears were collected by Schirmer strips from children ≥5 years old with diagnosis of bilateral uveitis. Uveitis activity was graded by SUN criteria. Anterior chamber (AC) cell grade < 0.5 was inactive. AC grades ≥0.5+ were active. S100A8, A9 and A12 were measured by ELISA, and IL-18, IL-8, IP-10, MCP-1, RANTES and sICAM-1 by Luminex assays. Biomarkers levels were assessed between paired eyes of a person by 1) unilateral activity (active eye and inactive contralateral eye), 2) bilateral activity (both active eyes), and 3) diagnosis (JIA-U vs non-JIA-U).

Results: Fifteen children contributed 34 tear samples (JIA-U n=8; idiopathic chronic anterior uveitis n=5; and idiopathic uveitis n=2). At time of tear collection, 53% had bilateral active uveitis (53% AC cell grade 0.5+). Treatment included topical (82%) and systemic therapy (76%) (Table 1). Stratifying by laterality, all biomarker levels were similar between the active uveitic eye and the inactive contralateral uveitic eye in those with unilateral active uveitis. In bilateral active uveitis, levels were also similar in both eyes except for S100A12 that was lower in the higher-grade uveitic eye (7979 pg/ML-/+SD 7835) compared to the lower-grade (25,727+/- 39,154; P=0.032). Stratifying by diagnosis, children with JIA-U relative to non-JIA-U group, primarily had unilateral active uveitis (78 vs 25%) with AC cell grade 0.5+ (100 vs 53%), greater use of systemic therapy (89 vs 63%) with similar use of topical steroids (83 vs 81%). Regardless of uveitis activity, biomarkers levels between both eyes of children with JIA-U were similar. In non-JIA-U, only S100A12 was higher in the lower-grade or inactive eye. All other biomarkers levels were similar. Comparing eyes

Table 1. Characteristics of children with a history of bilateral JIA-U and non-JIA-U

Characteristics N (%) unless otherwise indicated	All Cohort 34 sample (n=15 people)	JIA-U+ 18 samples (n=8 people)	Non-JIA-U& 16 samples (n=7 people)
% sample of people	100	53	47
Female (%)	20 (60)	18 (100)	2 (13)
Age at time of tear collection, mean	13.2	13.5	14.1
Caucasian/Hispanic/ AA/Asian	28 (82)/2 (6)/ 2 (6)/ 2(6)	16(88)/ 2(11)/ 0 (0)/ 2(11)	14(88)/ 0(0)/ 2 (13)/ 0(0)
Active arthritis at time of tear collection	4 (12)	4 (22)	0 (0)
Uveitis Characteristics			
Unilateral activity at tear collection	16 (47)	14 (78)	4 (25)
Bilateral activity at tear collection	18 (53)	4 (22)	12 (75)
AC grade			
<0.5	10 (29)	7 (39)	3 (19)
0.5	18 (53)	11 (61)	7 (44)
1	3 (9)	0	3 (19)
2	1 (3)	0	1 (6)
3	2 (6)	0	2 (13)
4	0 (0)	0	0 (0)
Medications			
Topical steroids	28 (82)	15 (83)$	13 (81)^
Not on systemic treatment	8 (24)	2 (11)	6 (37)
Systemic medications	26 (76)	16 (89)	10 (63)
Methotrexate	16 (47)	8 (44)	8 (50)^
Anti TNF-α	19 (56)	13 (72)	6 (38)^
Tocilizumab	4 (12)	4 (22)	0

+JIA were poly or oligo JIA
& The 16 samples (n=7 people) of the Non-JIA group; 12 samples (n=5 people) were collected from patients with idiopathic chronic anterior uveitis (iCAU) and 4 samples (n=2 people) had idiopathic uveitis (IU).
$ one of the JIA-U patients contributed 2 sets of paired samples that were on two different medication regiments: on paired tear sample was topical steroids and the other paired tear sample was on no topical steroids
^One of the iCAU patients contributed two sets of paired samples and also had two different medication regimens. In one pair tear sample both eyes were on topical glucocorticoids and methotrexate. The other pair tear sample, only 1 eye was treated with topical steroids and patient was on methotrexate and infliximab.

Table 1. Clinical characteristics

Table 2. Biomarker comparisons by Diagnosis Group (JIA-U vs non-JIA-U)

	Eye with Highest AC Grade Value		
	JIA-U	Non-JIA-U	p-value
S100 proteins			
S100A8 (mean -/+SD)	1119.24 (1347.45)	409.76 (318.27)	0.1615
S100A9	5296.68 (4501.37)	2065.14 (1351.08)	0.0653
S100A12	35356.34 (38834.89)	5028 (4855.33)	0.0033
Cytokines and chemokines			
IL-8	93.75 (90.21)	42.92 (32.26)	0.0384
IL-18	59.18 (76.84)	12.28 (18.05)	0.1034
IP-10	1263.93 (660.34)	1126.16 (714.43)	0.5742
MCP-1	33.37 (60.48)	47.07 (59.63)	0.3232
RANTES	12.68 (7.72)	2.51 (2.08)	0.004
sICAM-1	20307.89 (12134.98)	5317.13 (4505.96)	0.0006

*<p=0.05; IL: interleukin; IP-10/CXCL10: interferon gamma-induced protein/chemokine (C-X-C motif) ligand; RANTES/CCL5: Regulated on activation, normal T expressed, and secreted/chemokine (C-C motif) ligand; sICAM-1: soluble intracellular adhesion molecule 1; MCP-1:monocyte chemoattractant protein.

Table 2. Tear biomarker levels between JIA-U and non-JIA-U

of children with JIA-U and non-JIA-U, the JIA-U group had significantly higher S100A12, IL-8, RANTES, and sICAM than non-JIA-U (Table 2).

Conclusion: Our results suggest that S100A12 levels may differ in the eyes of children with a history of bilateral uveitis who have bilateral active disease especially non-JIA-U. Although we expected a difference in biomarker levels of paired eyes of children with unilateral active uveitis, earlier damage to the blood-ocular barrier may allow crossing of biomarkers to the inactive uveitic eye. Use of topical steroids may also dampen the inflammatory response. Elevated S100A12, sICAM, and IL-8 in children with JIA-U compared to non-JIA-U supports the potential role of neutrophils in JIA-U. A limitation of our study is sample size. Further work is needed to clarify the impact of topical steroids on biomarkers levels and the role of S100A12, sICAM1, and IL-8 in uveitis activity.

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Abstract Number: 0732

Changing Evidence over Time: Updated Meta-analysis Regarding Anti-TNF Efficacy in Childhood Chronic Uveitis

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SESSION INFORMATION
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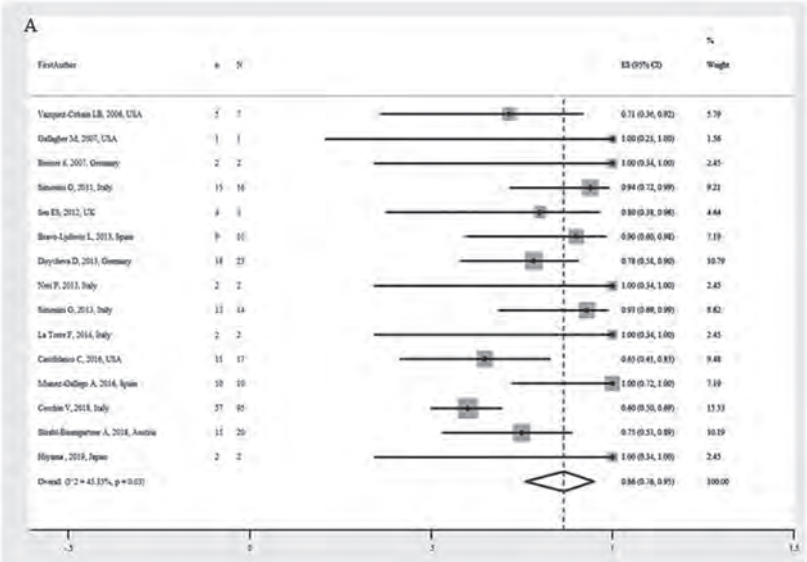
Session Time: 9:00AM–11:00AM

Background/Purpose: To summarize evidence regarding efficacy of anti-tumour necrosis factor-α (anti-TNFα) in childhood autoimmune chronic uveitis (cACU), refractory to common disease modifying antirheumatic drugs (DMARDs).

Methods: An updated systematic search was conducted between November 2012 and January 2020. Studies investigating the efficacy of anti-TNFα therapy, in children ages < 16 years, as the first biologic treatment for cACU, refractory to topical and/or systemic steroid and at least one DMARD, were eligible for inclusion. The primary outcome measure was the improvement of intraocular inflammation according to Standardization of Uveitis Nomenclature Working Group criteria. A combined estimate of the proportion of children responding to etanercept (ETA), infliximab (INF), and adalimumab (ADA) was determined.

Results: We identified 1677 articles and 37 articles were eligible. Three were randomized clinical trials (RCTs), one on ETA and 2 on ADA, and were excluded from pooled analysis. From the observational studies, a total of 487 children were identified: 226 received ADA, 213 INF and 48 ETA. The proportion of responding children was 86% (95% CI 76–95%) for ADA, 68% (95% CI 50–85%) for INF, and 36% (95% CI 9–67%) for ETA. Pooled analysis showed clear


A
FirstAuthor
ES (95% CI)
%
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Seo ES, 2012, UK
Bravo-Ljubetic L, 2013, Spain
Dzychova D, 2013, Germany
Neri P, 2013, Italy
Simonini G, 2013, Italy
La Torre F, 2014, Italy
Castiblanco C, 2016, USA
Munoz-Gallego A, 2016, Spain
Cecchin V, 2018, Italy
Binder-Baumgartner A, 2018, Austria
Hiyama , 2018, Japan
Overall (I^2 = 45.35%, p = 0.03)
0.71 (0.36, 0.92)
1.00 (0.21, 1.00)
1.00 (0.34, 1.00)
0.94 (0.72, 0.99)
0.80 (0.38, 0.98)
0.90 (0.60, 0.98)
0.78 (0.54, 0.90)
1.00 (0.34, 1.00)
0.93 (0.69, 0.99)
1.00 (0.34, 1.00)
0.65 (0.45, 0.83)
1.00 (0.72, 1.00)
0.60 (0.50, 0.69)
0.75 (0.53, 0.89)
1.00 (0.34, 1.00)
0.86 (0.76, 0.95)
5.79
1.58
2.45
9.21
4.64
7.19
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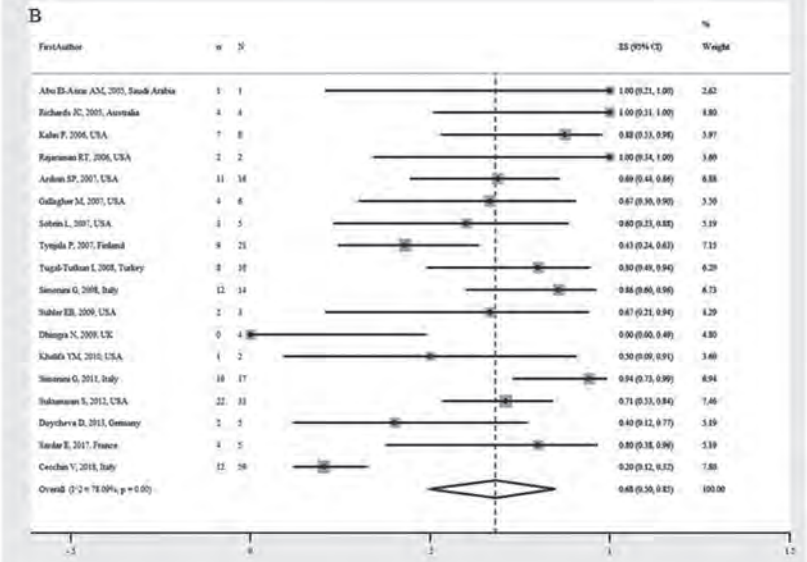
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Arshon SP, 2007, USA
Gallagher M, 2007, USA
Sobrin L, 2007, USA
Tynjala P, 2007, Finland
Tugal-Tutkun I, 2008, Turkey
Simonini G, 2008, Italy
Stubler EB, 2009, USA
Dhingra N, 2009, UK
Khalifa YM, 2010, USA
Simonini G, 2011, Italy
Sukumaran S, 2012, USA
Dzychova D, 2013, Germany
Yardar E, 2017, France
Cecchin V, 2018, Italy
Overall (I^2 = 78.09%, p = 0.00)
1.00 (0.21, 1.00)
1.00 (0.31, 1.00)
0.88 (0.53, 0.98)
1.00 (0.34, 1.00)
0.69 (0.44, 0.86)
0.67 (0.30, 0.90)
0.60 (0.23, 0.88)
0.43 (0.24, 0.63)
0.80 (0.49, 0.94)
0.86 (0.60, 0.96)
0.67 (0.21, 0.94)
0.00 (0.00, 0.49)
0.50 (0.09, 0.91)
0.94 (0.73, 0.99)
0.71 (0.33, 0.94)
0.40 (0.12, 0.77)
0.80 (0.38, 0.96)
0.20 (0.12, 0.52)
0.68 (0.50, 0.82)
2.62
4.80
5.97
3.89
8.88
5.50
5.19
7.35
6.29
6.73
6.29
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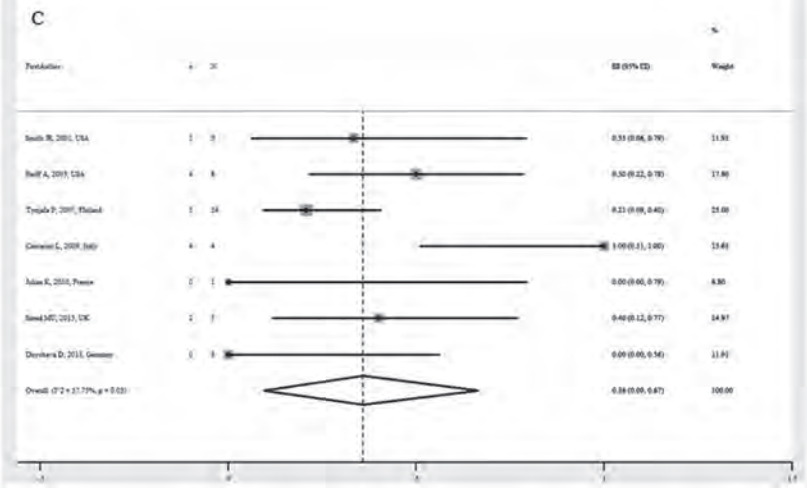
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%
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Reiff A, 2010, USA
Tynjala P, 2007, Finland
Cimino L, 2009, Italy
Islam K, 2010, France
Sood MF, 2013, UK
Dzychova D, 2013, Germany
Overall (I^2 = 57.77%, p = 0.03)
0.33 (0.06, 0.79)
0.50 (0.22, 0.78)
0.21 (0.08, 0.40)
1.00 (0.31, 1.00)
0.00 (0.00, 0.79)
0.40 (0.12, 0.77)
0.00 (0.00, 0.54)
0.26 (0.09, 0.47)
11.91
17.80
25.00
13.41
8.86
14.87
11.91
100.00

differences ($\chi2$= 32.2, p< 0.0001): ADA and INF were both significantly superior to ETA ($\chi2$ =26.8, p< 0.0001, and $\chi2$= 7.41, p< 0.006 respectively), ADA significantly superior to INF ($\chi2$= 13.4, p< 0.0002).

Conclusion: This metanalysis, consistent with recent RCT data, suggests the efficacy of ADA and INF in cACU treatment. However, ADA results superior to INF in this clinical setting.

Disclosure: I. Maccora, None; **E. Fusco**, None; **E. Marrani**, None; **A. Ramanan**, Abbvie, 5, 8, UCB, 8, Roche, 8, EliLilly, 8; **G. Simonini**, None.

Abstract Number: 0733

Practice Patterns for Tapering Medications in the Treatment of JIA-associated Uveitis

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Background/Purpose: Juvenile idiopathic arthritis associated uveitis (JIAU) is the most common extra-articular manifestation of JIA, and occurs in approximately 10% of affected children. Although there are effective medications to treat JIAU, guidelines and large studies that inform of tapering treatment after disease remission are lacking.

Methods: We surveyed vie email international pediatric rheumatologists: 1. Multinational Interdisciplinary Working Group for Uveitis in Childhood (MIWGUC), 2. Pediatric Rheumatologic Email-Listserve, 3. CARRA uveitis workgroup, and international ophthalmologic specialized in children with JIAU. Survey questions focused on the definition of remission, duration of remission prior to initiation of medication tapering, and method of tapering. Specific medications included methotrexate (MTX), adalimumab (ADA), infliximab (IFX), abatacept (ABA), and tocilizumab (TOC).

Results: Of 45 responses, 88% were from pediatric rheumatologists with a mean work experience of 18 years. The regional distribution was 31 form Europa, 9 from North-America, 3 from South-America and 2 from Asia. The responding colleagues managed a mean number of 43 JIAU patients. Remission on medication was defined as no cells in the anterior chamber (78%), followed by no need for eye drops (36%), and no uveitis flares (32%). Tapering practices were described for MTX monotherapy (100%) ADA (100%), IFX (80%), TOC (56% [25% s.c.]) and ABA (46% [30% s.c.]).

Standardized protocol for tapering exists in 32% of centers for MTX, in 26% for ADA, and 20% for IFX. The timepoint for tapering was after 6 months of remission on medication by 14% of respondents, 12 months for 38%, 24 months for 56% and 36 months for 12%.

MTX was tapered by dose in 42%, dose and interval in 40%, and interval in 15%. The lowest dose of MTX was 6mg/m2/week at the time of tapering and the longest mean interval 2.5 weeks (1 to 4 weeks). ADA was first tapered to

every 3 weeks by 76% of the responders and then to every 4 weeks by 49% before discontinuing. Fewer respondents used or tapered IFX, TOC or ABA. Around 65% tapered the interval and 20% tapered the dose and interval for ABA, 26% for TOC and 37% IFX

There were differences in the duration of tapering prior to discontinuation of specific medications. For ADA it was 6 months in 62%, 12 months in 36% ,and 24 months in 10%. For IFX it was 6 months in 27%, 12 months in 45%, and 24 months in 33%. For TOC it was 40% after 4 weeks, 87% after 6 weeks and 53% after 24 weeks. For ABA i.v. it was 30% after 8 weeks, and 90% after 12 weeks.

If combination therapy was used, 36% tapered the bDMARD first, 62% csDMARD first, and 12% both simultaneously.

Conclusion: This is the first survey to describe "real world" medication tapering and discontinuation practices of pediatric rheumatologists and ophthalmologists globally. Most physicians start to taper medication after 24 months of remission on medication and discontinue after the 6 to 12 months of tapering.

Disclosure: I. Foeldvari, Sanofi, 5, Chugai, 5, Amgen, 5, GSK, 5, Lilly, 5, BMS, 5, Abbvie, 5, Novartis, 5, gilead, 5; **J. Klotsche**, None; **S. Angeles-Han**, Nation Institutes of Health, 2, Emory University, 7, Knights Templar Eye Foundation, 2, Emory University, 2; **J. Anton**, Sobi, 1, 2, 3, Novartis, 1, 2, 3, GSK, 1, 2, 3, Pfizer, 1, 2, BMS, 1, Chemocentryx,, 1, Lilly, 1, Novimmune, 1, Sanofi, 1, Roche, 1; **G. Simonini**, Novartis, 5, 8, AbbVie, 5, 8; **N. Groesch**, None; **J. Baer**, None.

Abstract Number: 0734

Differences and Similarities Between down Syndrome-associated Arthritis and Juvenile Idiopathic Arthritis in the New Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: JIA
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Session Time: 9:00AM–11:00AM

Background/Purpose: Down syndrome-associated arthritis (DA) is under-recognized with delay in diagnosis (1). The majority of those with DA present with polyarticular, rheumatoid factor (RF) and anti-nuclear antibody (ANA) negative disease, which is different compared to those with juvenile idiopathic arthritis (JIA). Therapy for JIA has been used to treat DA, but appear to be poorly tolerated, more toxic and less effective in patients with DA (1). The objective of this study was to characterize differences between those with DA and JIA, using the new Childhood Arthritis and Rheumatology Research Alliance Registry (nCARRA).

Methods: The nCARRA began prospectively collecting data on children with JIA in the United States and Canada in July 2015. Down syndrome (DS) is documented in the CARRA Registry as a coexisting condition. Between the dates of July 2015 and March 2019, patients with a diagnosis of JIA *and* DS were identified and matched (in a 1:5 ratio) on

Table 1. Demographics of patient with and without Down syndrome at baseline visit

Demographics and clinical variables	Down Syndrome (n = 36)	Without Down syndrome (n = 165)
Female, n (%)	24 (67)	116 (70)
Age at arthritis diagnosis, years (range)	6.9 (2 - 15)	7.7 (1 - 17)
Time to diagnosis*, months (range)	8.3 (0 - 49)	9.8 (0 – 112)
Arthritis subtype, n (%)		
Oligoarticular	3 (8)	14 (9)
Polyarticular RF-	24 (67)	115 (67)
Polyarticular RF+	0 (0)	0 (0)
Systemic	1 (3)	5 (3)
Psoriatic	3 (8)	14 (9)
Enthesitis-related	3 (8)	12 (8)
Undifferentiated	2 (6)	5 (4)
Laboratory test, n (%)		
Normal testing†	16 (44)	1 (5) – 19 with all testing
Elevated antinuclear antibody	12 (33)	86 (57) – 152 tested
Elevated rheumatoid factor	0 (0)	0 (0)
Elevated erythrocyte sedimentation rate	6 (17)	17 (77) – 22 tested
Elevated c-reactive protein	6 (17)	12 (63) – 19 tested
Positive HLA-B27	2 (11) – 18 tested	21 (24) – 86 tested
Imaging, n (%)**	**n = 24**	**n = 105**
Damage present	9 (38)	23 (22)
Damage absent	15 (62)	82 (78)
Morning stiffness, n (%)	**n = 31**	**n = 165**
Yes	14 (45)	84 (51)
No	17 (55)	81 (49)

*Time to diagnosis is the time between first documented musculoskeletal complaint consistent with inflammatory joint disease and diagnosis of arthritis.

† Normal is defined as erythrocyte sedimentation rate and c-reactive protein in normal range and negative antinuclear antibody, rheumatoid factor and HLA-B27

**Imaging evidence of damage at diagnosis. Specific imaging modality data not collected.

Table 2. Outcome measures at diagnosis and last recorded visit for patients with and without Down syndrome (DS)

Arthritis and Outcome measures	At baseline visit Mean (SD)		p-value	At last visit Mean (SD)		p-value
	With DS	Without DS		With DS	Without DS	
Physician assessment of disease activity (MD-Global) *	2.7 (2.6)	2.5 (2.4)	0.74	1.2 (1.4)	1.0 (1.8)	0.06
Patient/Parent assessment of overall well-being (Pt-Global) **	4.0 (3.2)	2.0 (2.4)	**< 0.01**	2.3 (2.5)	1.3 (1.7)	**0.03**
Joints with active arthritis	4.4 (7.0)	4.0 (6.5)	0.99	2.9 (5.6)	0.8 (2.0)	**< 0.01**
Joints with limited range of motion	4.3 (6.3)	2.5 (4.2)	0.32	3.3 (5.5)	0.8 (2.0)	**< 0.01**
Childhood Health Assessment Questionnaire (CHAQ)†	1.2 (0.8)	0.4 (0.5)	**< 0.01**	1.1 (0.7)	0.2 (0.5)	**< 0.01**
Clinical Juvenile Arthritis Disease Activity Score 10 (cJADAS10) ‡	6.1 (5.6)	7.2 (7.2)	0.91	4.4 (4.5)	2.6 (4.5)	**< 0.01**

* MD-global; 10-point Likert visual analog scale, 0 = clinically inactive disease

** Pt-global; 10-point Likert visual analog scale, 0 = very good

† CHAQ; eight domains, questionnaire scores averaged to obtain disability Index score (0 - 3), 0 = no disability

‡ cJADAS10; composite disease activity (0 - 30), sum of the MD-global (0-10 VAS), Pt-Global (0-10 VAS) and number of joints with active arthritis capped at a maximum of 10, ≤ 1.0 = inactive disease

age, sex, and JIA subtype to patients with a diagnosis of JIA and without DS. Collected data included demographics, disease characteristics, laboratory results, treatment exposure, and outcomes measures.

Results: Thirty-six patients were identified with DS and 165 patients without DS. Those with DS had a mean follow-up period of 4.5 years (SD 3.2), while those without had 4.7 years (SD 3.9). Most patients were female and had polyarticular, RF negative disease (Table 1.). The treatment approach at diagnosis for both groups were similar with no significant difference (p-value < 0.05) in initiation of disease modifying antirheumatic drug (DMARD)(44% for those with DS, and 32% for those without DS) or biologic therapy (17% those with DS, and 7% for those without DS). DMARD therapy was used in 78% of those with DS and 87% of those without DS. Methotrexate was the most used DMARD for both groups, but those with DA had more DMARD adverse events (93% versus 25%). Biologic therapy was used

in 75% of those with DS and 70% of those without DS, and biologic therapy ineffectiveness was much higher in those with DS (60% versus 17%). At entry into the nCARRA, there was no significant difference between joints with active arthritis, limited range-of-motion (ROM) or clinical juvenile arthritis disease activity score (cJADAS10), however, at last reported visit there was significant (p-value < 0.05) difference in almost all outcomes measures (Table 2.).

Conclusion: This study from a large multicenter registry reveals that children with DA have a similar presentation to children with JIA without DS, however, their disease course and disease burden is significantly worse. There is also more drug adverse events and higher rates of therapeutic ineffectiveness. This raises concern for possible physiologic reasons that place them at higher risk for resistant disease and treatment ineffectiveness. Collective work is needed to characterize DA, understand the pathophysiology, and understand clinical pharmacologic factors that will help identify the most effective and tolerated therapies to treat arthritis in children with Down syndrome.

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Abstract Number: 0735

Paediatric Sarcoidosis: Phenotype of a Retrospective Cohort of Biopsy-proven Patients

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: JIA
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Session Time: 9:00AM–11:00AM

Background/Purpose: Paediatric sarcoidosis is a multisystemic inflammatory condition characterised by the formation of non-caseating granulomata that may lead to end-organ damage. Diagnosis is challenging as a compatible clinical-radiographic presentation with histopathologic confirmation is needed. Caution must be exercised to exclude granulomata of infectious aetiology as well as those seen in immunodeficiencies associated with immune dysregulation. Little is known about this rare disease's presentation and outcome in children. We report a retrospective cohort of children with biopsy-confirmed sarcoidosis, their treatment and the course of the disease.

Methods: Patients' notes were reviewed retrospectively, and multisystem involvement identified. We included patients with biopsies, performed or reviewed at our centre between 2010 and 2020, which were consistent with sarcoidosis and a compatible clinical phenotype.

Results: We identified 42 children with biopsy-proven sarcoidosis. Mean age at diagnosis was 9.4 years; male to female ratio 0.68. Twenty-seven of 42 patients were of Afro-Caribbean descent. Tissues biopsied included lymph node, skin, kidney, liver, lung, submandibular, lacrimal and salivary gland, eye, spleen, bone, brain and synovium.

28 patients had lymphadenopathy, 16 glandular involvement, 17 liver, 17 pancreas, 13 renal, 11 spleen, 27 skin, 14 lung involvement, 11 arthritis, 4 tenosynovitis, 3 hearing loss, 2 bone, 1 cerebral, and 25 eye involvement.

Remarkable laboratory findings included raised levels of serum calcium in 9, amylase in 16, lipase in 4 and ACE in 30 patients; 12 patients had abnormal renal function, 13 abnormal liver function; 13 patients were tested for NOD2 mutations, which were present in 5.

38 patients received treatment for sarcoidosis. Of those, 37 received steroids, 16 intravenous followed by oral steroids, 18 oral steroids only and 18 received steroid eye drops; 36 patients received disease-modifying antirheumatic drugs (DMARDs) including 26 methotrexate, 11 mycophenolate mofetil and 10 azathioprine; 4 patients received hydroxychloroquine, 5 cyclophosphamide; 10 received biologic therapy including anti-TNF, interleukin-1 and IL-6 blockade, JAK inhibitor and rituximab.

All patients had a good response to steroids, and most responded to methotrexate. The treatment of a subset of patients was escalated to include a biologic agent, owing to grumbling disease activity. Although most of the patients were able to wean off regular steroids, the majority remained on long-term DMARDs to maintain disease control.

Conclusion: Our study suggests that non-caseating granulomatous inflammation on biopsy, multiorgan involvement, response to steroids and chronic course are hallmarks of paediatric sarcoidosis. DMARDs, in particular methotrexate, were used with efficacy. When response was partial, addition of a biologic agent was beneficial, particularly in ocular disease. Additional organ involvement occurs over time when the disease is not fully controlled. However, no biomarkers are available to assess disease activity apart from ACE, which demonstrated low sensitivity. Prospective cohort studies are needed to define this rare paediatric disease.

Disclosure: K. Nott, None; **V. Nott**, None; **S. Compeyrot-Lacassagne**, None.

Abstract Number: 0736

Identification of Salient Resilience Domains Among Adolescents with Chronic Musculoskeletal Pain and Their Parents

Lauren Pianucci[1], Maitry Sonagra[2], Daneka Stryker[3] and **Sabrina Gmuca**[4], [1]Arcadia University, Philadelphia, [2]Children's Hospital of Philadelphia, Cherry Hill, NJ, [3]Drexel University College of Medicine, Philadelphia, PA, [4]Children's Hospital of Philadelphia, Philadelphia, PA

SESSION INFORMATION
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Session Title: Pediatric Rheumatology – Clinical Poster II: JIA
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Background/Purpose: Adolescents with chronic musculoskeletal pain (CMP) and their parents have been found to have low to moderate levels of resilience and resilience levels are associated with symptom severity. However, the causal role of resilience in CMP has not yet been established. We aimed to identify resilience domains that differ among youth with high versus low levels of resilience, as well as their parents, in order to elucidate salient resilience domains relevant to symptom severity in adolescent CMP.

Methods: This was a cross-sectional study of patients aged 13-17 years diagnosed with CMP, and one of their parents, seen in a pediatric Rheumatology subspecialty pain clinic for an initial consultation between March and May 2018. A series of online questionnaires, including the Resilience Scale 14-item (RS-14), were administered to the patient-parent pairs within 12 weeks of the initial clinic visit. Questionnaires were complemented by data abstraction from the electronic medical record. The RS-14 was re-categorized into three resilience levels: low (14-73), average

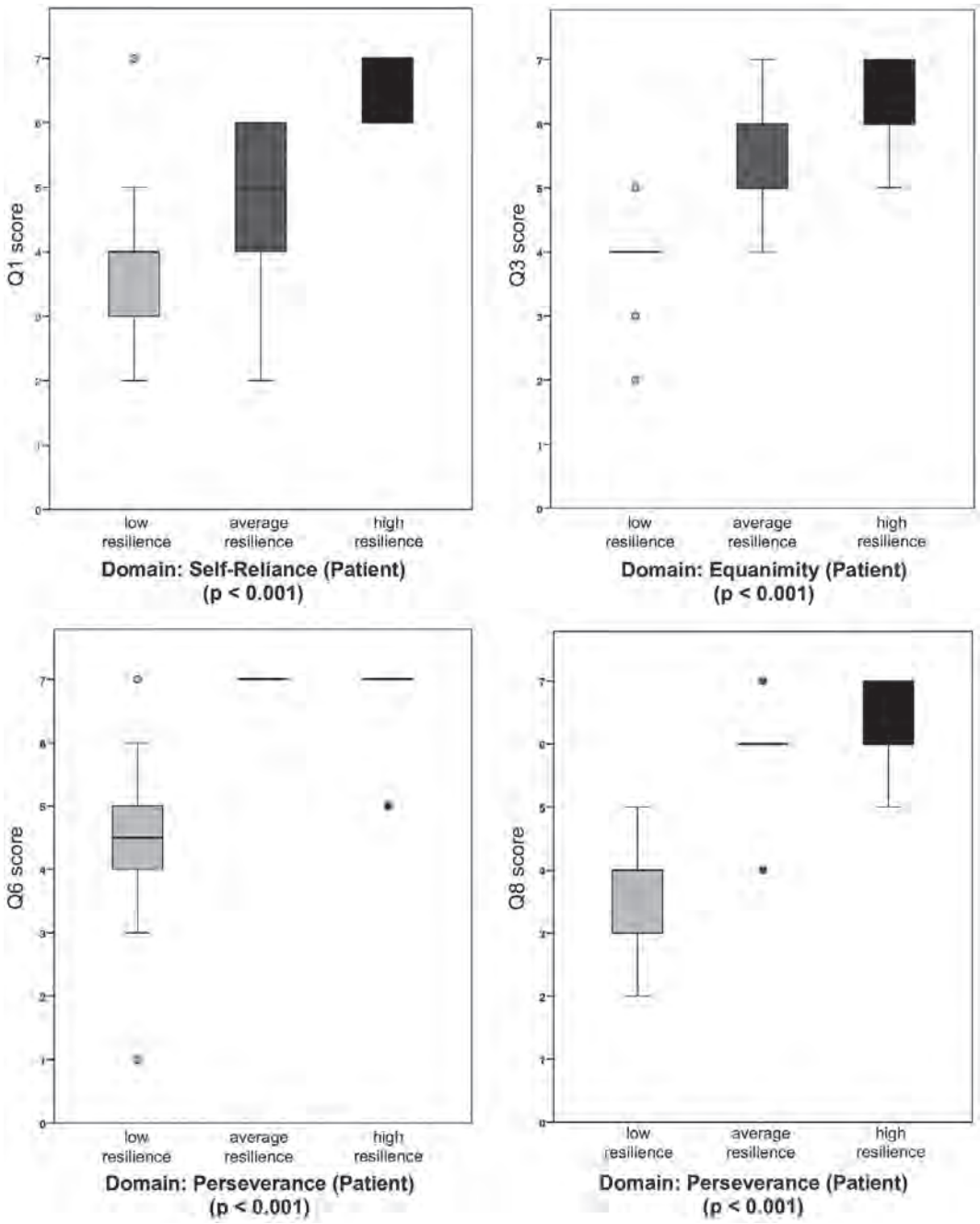

Figure 1. Box-plots of Scores in Salient Domains Identified on the RS-14 Stratified Across Levels of Resilience Among Patients. Legend. Patients with high resilience scored highest on RS-14 questions representing the salient domains of self-reliance, equanimity, and perseverance when compared to patients with low and average resilience.

(74-81), and high (82-98). Scores on each question of the RS-14 were summarized for each resilience level (low, average, and high). Differences in question scores and variables of interest between resilience groups were assessed with Kruskal-Wallis tests and Freeman Halton Fischer's exact tests, as appropriate.

Results: A total of 28 patient-parent pairs were included. The majority of patients (71.4%) and parents (92.9%) were female. Patient-parent pairs were predominantly non-Hispanic whites (75.0%) with most residing in a suburban area (60.7%). The median age of parents was 48 years (IQR 45-51) and the median age of patients was 15 years (IQR 14-16). Half of the patients had low resilience (n=14) and a little more than half (53%) of parents had high resilience (n=15). The questions with the most significant differences ($p < 0.001$) between resilience groups for patients were

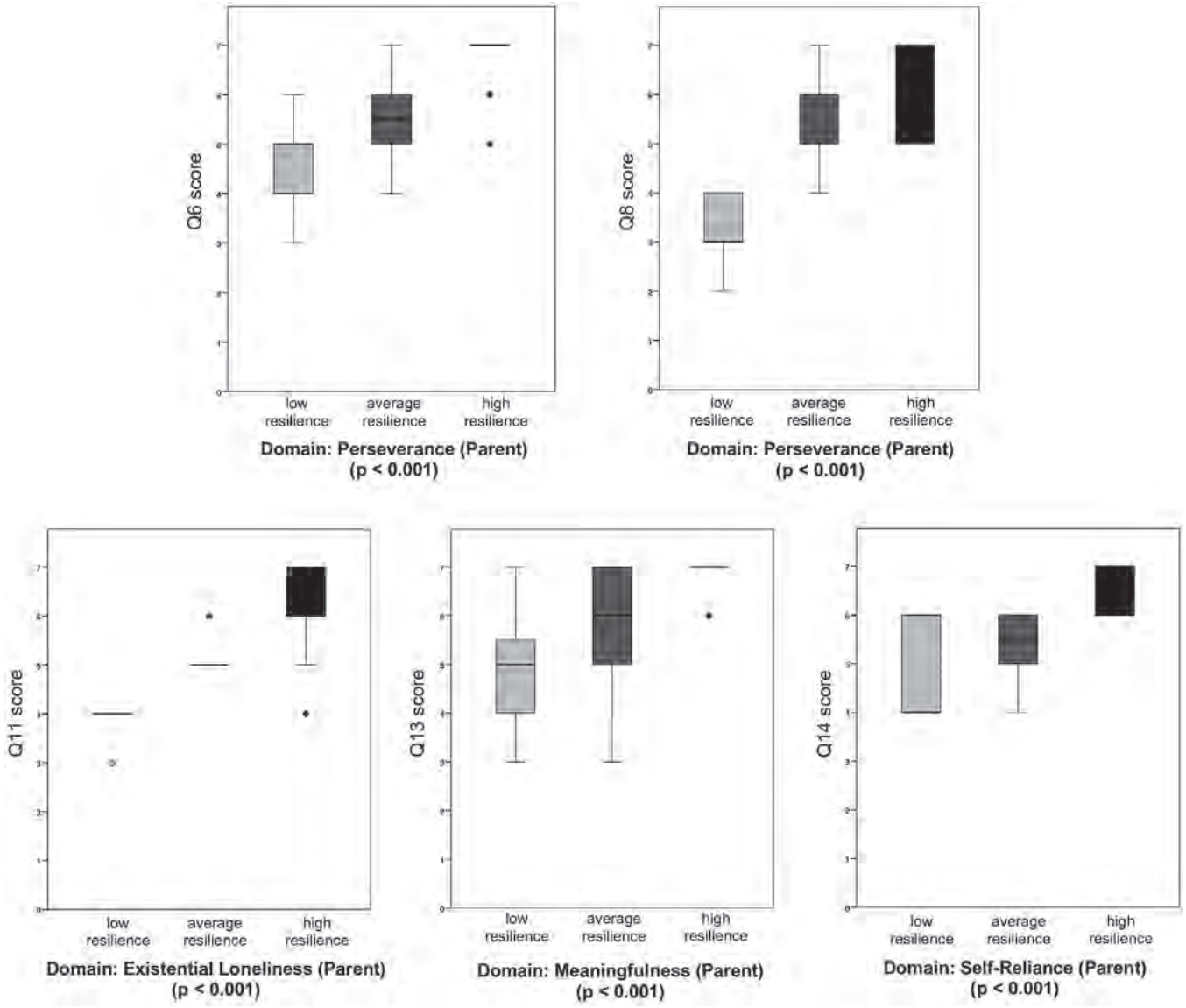

Figure 2. Box-plots of Scores in Salient Domains Identified on the RS-14 Stratified Across Levels of Resilience Among Parents. Legend. Parents with high resilience scored highest on RS-14 questions representing the salient domains of perseverance, existential loneliness, meaningfulness, and self-reliance when compared to parents with low and average resilience.

within the domains of equanimity, perseverance, and self-reliance (Figure 1). The questions with the most significant differences ($p < 0.001$) between resilience groups for parents were within the domains of existential aloneness, meaningfulness, perseverance, and self-reliance (Figure 2). Overall health-related quality of life (HRQoL) as defined by the PROMIS Pediatric Global Health 7 (PGH-7) score varied significantly across resilience levels for patients ($p < 0.01$) as did a history of suicidality ($p = 0.03$) (Table).

Conclusion: Domains of resilience most prominent among both youth with CMP and their parents included self-reliance and perseverance. Differences in patient-level resilience were associated with overall HRQoL and a history of suicidality. These findings lay the groundwork for future mixed methods research to better characterize and target these salient domains of resilience as they relate to adolescent CMP and guide novel treatment interventions.

Table. Differences in Clinical Characteristics by Patient Resilience Level

	all patients (n=28)	low resilience (n=14)	average resilience (n=5)	high resilience (n=9)	p-value
Clinical Characteristics, median (IQR) or n (%)					
Pain intensity (VAS [0-100])	61.5 (30.0-82.3)	64.0 (54.0-83.8)	80.0 (13.5-88.0)	31.0 (28.5-64.0)	0.44
Energy level (0-100)	55.0 (40.0-78.8)	50.0 (28.8-65.5)	43.6 (40.0-75.0)	75.0 (55.0-92.5)	0.06
Widespreadness of pain (WPI [0-19])	5.0 (2.3-11.0)	3.5 (1.8-10.3)	6.0 (1.5-16.5)	7.0 (3.5-12.5)	0.38
Symptom severity (SS score [0-12])	6.0 (4.3-7.8)	7.0 (4.8-9.3)	6.0 (4.0-8.5)	6.0 (3.5-7.5)	0.70
Functional disability (FDI [0-60])	23.5 (14.0-37.0)	28.5 (20.5-40.3)	36.0 (10.5-43.0)	22.0 (8.0-25.5)	0.22
Health-related quality of life (PGH-7 [0-35])	23.5 (20.3-26.8)	23.0 (19.3-40.3)	19.0 (18.5-24.5)	28.0 (25.5-31.0)	<0.01*
Self-reported Anxiety	18 (64.3)	9 (64.3)	3 (60.0)	6 (66.7)	1.00
Self-reported Depression	11 (39.3)	5 (35.7)	4 (80.0)	2 (22.2)	0.12
History of Suicidality	7 (25.0)	4 (28.6)	3 (60.0)	0 (0.0)	0.03*
Family Characteristics, n (%)					
Parent has college degree or higher	18 (64.3)	9 (64.3)	3 (60.0)	6 (66.7)	1.00
Parents divorced or separated	6 (21.4)	2 (14.3)	2 (40.0)	2 (22.2)	0.51
Household income					
<$100,000	14 (50.0)	9 (64.3)	2 (40.0)	3 (33.3)	0.18
$100,000-$149,000	4 (14.3)	0 (0.0)	1 (20.0)	3 (33.3)	
>$150,000	7 (25.0)	4 (28.6)	1 (20.0)	2 (22.2)	
Family history of anxiety	9 (32.1)	3 (21.4)	3 (60.0)	3 (33.3)	0.36
Family history of depression	9 (32.1)	4 (28.6)	2 (40.0)	3 (33.3)	1.00
Pain Diagnosis, n (%)					
CRPS	2 (7.1)	0 (0.0)	1 (20.0)	1 (11.1)	0.59
JFMS	10 (35.7)	5 (35.7)	2 (40.0)	3 (33.3)	
Other idiopathic chronic musculoskeletal pain	16 (57.1)	9 (64.3)	2 (40.0)	5 (55.6)	

*Statistically significant difference between groups, $p < 0.05$; VAS = visual analog scale, rating of level of pain (0-100); WPI = widespread pain index (0-19), measure of widespreadness of pain; SS score = Symptom severity score (0-12), measure of condition severity; WPI and SS score defined according to the 2010 College of Rheumatology Criteria for Fibromyalgia Syndrome; FDI = functional disability inventory, measure of disability (0-60) with higher scores indicating greater pain-related functional disability; PGH-7 = Patient Reported Outcomes Measurement Information System (PROMIS) Pediatric Global Health Measure, measure of health related quality of life (HRQoL) (0-35), with higher scores indicating better HRQoL; CRPS = complex regional pain syndrome; JFMS = juvenile fibromyalgia syndrome

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Abstract Number: 0737

"It'll Go Away. There's Nothing Wrong with you:" the Experience of Pain-Related Stigma Among Adolescents with Pain Amplification Syndrome

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: JIA

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Background/Purpose: Chronic pain in adolescence is a complex and significant medical condition, with a reported prevalence of 11-38%.[1] Pain amplification syndrome (PAS), which includes fibromyalgia, is a common chronic pain syndrome in adolescents characterized by allodynia without specific somatic injury or illness.[2] Physicians are often puzzled by pain reports that seem disproportionate to medical findings. As a result, the complaints of adolescents with chronic pain are often viewed with skepticism by others. This disbelief is a phenomenon referred to as pain-related stigma.[3] Pain-related stigma has not been studied in adolescents with chronic pain. Pain-related stigma may account for poor health outcomes in this population, such as depression,[4] anxiety,[5] problems in school[6] and social impairment.[7] In the current study, we sought to evaluate pain-related stigma in adolescents with PAS using focus group methodology.

Methods: Five focus groups of 3-5 adolescents with PAS (*N*=18), ages 12-17, were conducted to evaluate the impact of, and reaction to, pain-related stigma. Patients were recruited from an outpatient pediatric pain management clinic. Patients with a comorbid chronic medical condition, such as juvenile idiopathic arthritis, were excluded to reduce the bias of other disease-related stigma. Using a semi-structured interview, we asked questions targeting stigma in an open-ended manner. Focus group length ranged from 36-106 minutes with a total of 363 responses. Transcripts were validated for accuracy and coded independently by two raters (90.34% agreement) who identified pain-related themes using grounded theory.

Results: Findings suggest evidence of pain-related stigma among medical providers, school staff, peers and family members. Adolescents described sources of the pain-related stigma as the invisibility of pain and diagnostic uncertainty. Additionally, several incidents of peer bullying were also described secondary to respondent references to having chronic pain. There is evidence that adolescents with chronic pain attempt to conceal their symptoms from others to avoid negative social interactions, and that they internalize their pain-related stigma experiences.

Conclusion: Our findings indicate that adolescents with PAS experience pain-related stigma among medical providers, peers, school personnel and family members. Disbelief of pain symptoms may be critical in understanding disease-related burden and social disruptions in this population. There are several potential clinical implications of pain-related stigma among adolescents with chronic pain, including healthcare utilization, poor health outcomes and quality of healthcare.

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Disclosure: E. Wakefield, None; **W. Zempsky**, None; **R. Puhl**, None; **M. Litt**, None.

Abstract Number: 0738

Systemic Administration of Novel Hydroxyl Dendrimers to Target Inflammation in Arthritic Tissues

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SESSION INFORMATION
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Background/Purpose: Chronic inflammation observed in arthritis and other autoimmune disorders is mediated primarily by pro-inflammatory reactive macrophages. Systemic administration of anti-inflammatory agents does not selectively target the affected tissue, or the reactive macrophages and often has significant side effects. Hydroxyl dendrimers have been observed to selectively target reactive macrophages and have been well tolerated in humans. Hydroxyl dendrimer-drug conjugates may provide a superior method for treating localized inflammation, from systemic administration.

Methods: The binding affinity of the dendrimer-alendronate conjugate (D-ALN) was evaluated against hydroxyapatite (HAP) using UV/Vis spectrophotometry. Lewis rats were immunized with an emulsion of type II bovine collagen in incomplete Freund's adjuvant intradermally on Day 1 and Day 7 to establish collagen-induced arthritis (CIA). Groups of CIA rats and naïve rats (N=5/group) were administered by IV on Day 19 either hydroxyl dendrimer labelled with Cy5 (D-Cy5), D-Cy5 conjugated with alendronate (ALN-D-Cy5), or vehicle control. On Day 21, animals were sacrificed for imaging of hind limbs, kidney and liver. Immunohistochemistry was also performed on hind limbs using CD68 (macrophages), CathK (osteoclasts) and DAPI.

Results: *In vitro*, D-ALN demonstrated strong binding affinity toward HAP with >85% of D-ALN bound to HAP in less than 10 minutes. Upon intravenous administration, more than 100-fold greater radiant intensity from Cy5 was noted in the paw and knee joint of the CIA rats compared to the naïve rats, indicating significant selective uptake of the D-Cy5 into the regions of inflammation. While a comparable radiant intensity was noted in the joints of CIA rats treated with D-Cy5 or ALN-D-Cy5, a two-fold greater radiant intensity was noted in the paws for CIA rats treated with D-Cy5. A single dose of ALN-D-Cy5 reduced paw volumes by in CIA rats ~10% after 2 days and clinical scores were comparable in all CIA groups.

Conclusion: Systemically administered hydroxyl dendrimer-drug conjugates localize to sites of inflammation in arthritic tissues. Alendronate, which binds bone, conjugated to the hydroxyl dendrimer appears to concentrate only in regions of the bone with potentially less uptake in reactive macrophages away from the bone. These results indicate the types of dendrimer constructs to utilize for drug conjugates to treat inflammation or bone metabolism. Efficacy studies are planned with dendrimer drug conjugates to evaluate modulators of bone resorption and inflammation.

Disclosure: J. Cleland, Ashvattha Therapeutics, 1, 3, 6; **R. Sharma**, Ashvattha Therapeutics, 1, 3; **M. Sun**, Ashvattha Therapeutics, 1, 3; **S. Appiani La Rosa**, Ashvattha Therapeutics, 1, 3; **R. Kannan**, Ashvattha Therapeutics, 1, Ashvattha Therapeutics, 1, 6.

Abstract Number: 0739

Toll-like Receptor Inhibitor Peptide Improves the Clinical, Immunologic, and Pathologic Manifestations of Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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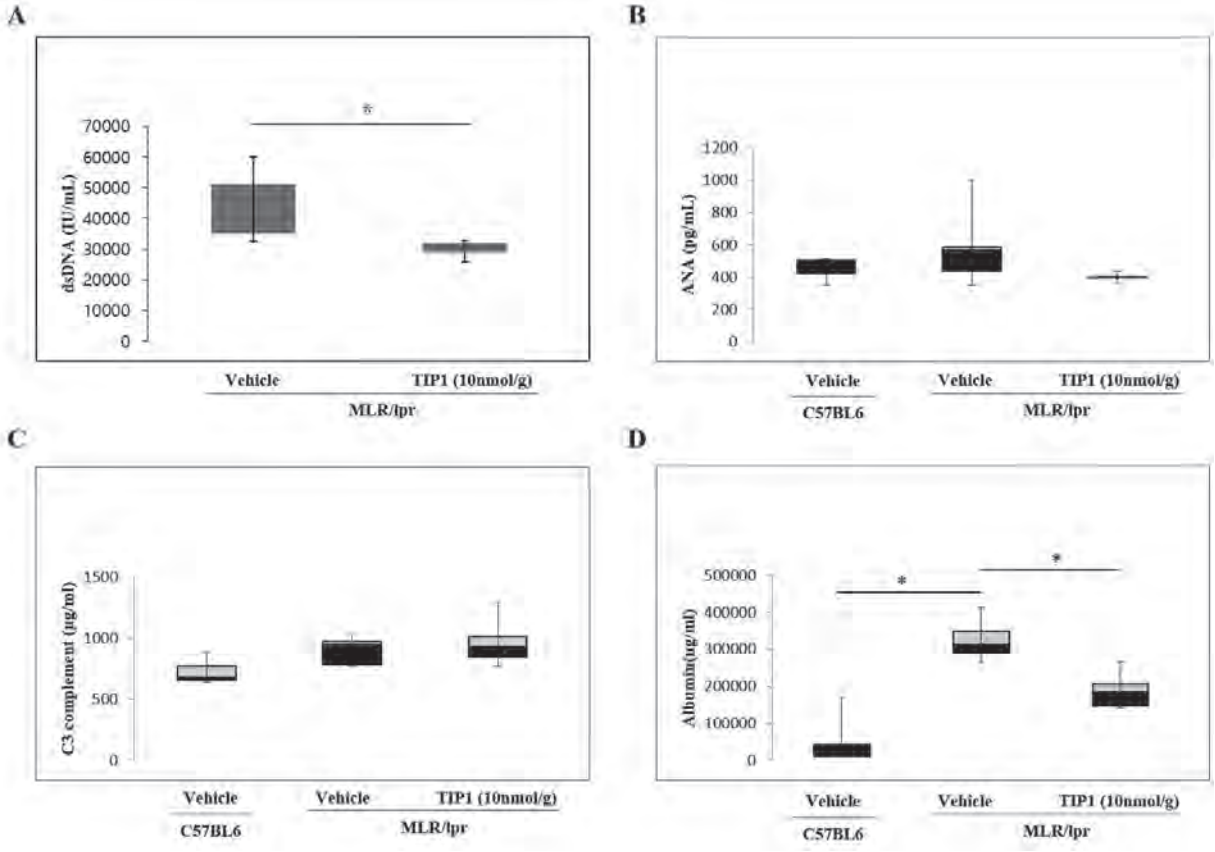
Fig. 1.



Background/Purpose: Toll-like receptors (TLRs) are a type of protein that plays a major role in the innate immune system. In recent years, several studies have shown that TLR-mediated pathways regulate in immune and inflammatory diseases. Also, dysregulated TLRs within the endosomal compartments such as TLR 7/9 trafficking can cause systemic lupus erythematosus (SLE). The TLR signaling pathways are fine-tuned by Toll/interleukin-1 receptor (TIR) domain-containing adapters, which leading to interferon (IFN)-α production. This study reports a Toll-like receptor inhibitor (TIP)1, that primarily suppresses TIR domain-containing adapters mediated downstream signaling in the animal model of lupus and patients with lupus.

Methods: MMRL/lpr mice were received an intraperitoneal injection of as a single daily dose, at a dose of 10 nmol/g/day for 4 weeks beginning at 14 weeks to 18 weeks of age. The concentration of cytokines in mice serum was measured by enzyme-linked immunosorbent assay (ELISA), and pathological analysis of kidney and spleen was analyzed by immunohistochemistry. In addition, protein expression levels of mouse major tissues and peripheral blood mononuclear cells (PBMC) of patients with SLE were analyzed by western blot.

Results: We examined the major organ size of the MRL/lpr mouse treated with TIP1. Kidney, spleen and lymph node of MRL/lpr mice were significantly increased in size but, after the administration of TIP1, the size of kidneys, spleen and lymph node were greatly reduced compared to vehicle treatment group. We next evaluated whether TIP1 can be useful for treatment of SLE in a murine model by assessing the ability of TIP1 to reduce circulating autoantibody levels, hallmarks of SLE. We performed ELISA for antinuclear antibody and anti-dsDNA antibody in serum collected from the treated lupus-prone mice. As a results, TIP1 significantly reduced the production of anti-dsDNA antibody and urine albumin (Fig 1). When assessed the expression of proteins involved in TLR 7/9 signaling in major tissues such as kidney, spleen and lymph nodes, most downstream proteins of the TLR 7/9/MyD88/IRF7 signaling pathway were reduced in the mice with TIP1 treatment compared to vehicle treatment. Furthermore, pathological analysis of mouse kidney tissue confirmed that TIP1 could improve the inflammation in MRL/lpr mice. In addition, the TIP1 treat-

ment reduced many downstream proteins in the TLR signaling such as Myeloid differentiation primary response 88 (MYD88), Interleukin-1 receptor-associated kinase (IRAK), Tumor necrosis factor receptor–associated factor (TRAF) and Interferon-alpha (IFN-α) in the PBMC of patients with SLE.

Conclusion: Our data suggest that TIP1 can be developed as a potential candidate for the treatment of SLE.

Disclosure: C. Suh, Celltrion, 5; **W. Baek**, None; **J. Kim**, None; **Y. Choi**, None; **S. Lee**, None; **I. Son**, None; **K. Jeon**, None; **S. Choi**, None.

Abstract Number: 0740

Card9 Promotes Th17-mediated Arthritis and Spondylitis via Control of Acute Pathogenic Neutrophil Responses in SKG Mice

Holly Rosenzweig[1], Emily Vance[1], Ellen Lee[1] and **Ruth Napier**[1], [1]Oregon Health & Science University and VA Portland Health Care System, Portland, OR

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Caspase recruitment domain-containing protein 9 (CARD9) is an intracellular signal transduction molecule that mediates antimicrobial responses following activation of C-type lectin receptors (ie. Dectin-1) by fungal ligands including β -glucans (zymosan). CARD9-deficient patients have defects in Th17 immunity and succumb to systemic candidiasis, and single nucleotide polymorphisms in *CARD9* have been associated with susceptibility to Th17-mediated autoimmune diseases including ankylosing spondylitis. However, how dysregulation of CARD9 may regulate autoimmunity remains unknown. Here we sought to investigate the role of CARD9 in arthritis and spondylitis (spinal inflammation) as modeled in SKG mice.

Methods: Arthritis was induced in SKG vs. Card9$^{-/-}$ SKG mice by intraperitoneal injection of 1.5mg β-glucan (zymosan) and evaluated clinically for 8 weeks, by near-infrared imaging, and histologically. CD4^{+} T cells from draining lymph nodes were stimulated *in vitro* with PMA/ionomycin and Th effector subsets were quantified by intracellular cytokine staining and flow cytometry. For lavage studies, peritoneal fluid collected 4h post-zymosan was analyzed for immune cellular composition by flow cytometry and ELISA. Neutrophils were depleted in SKG mice with anti-Ly6G (1A8) or isotype control (2A3) beginning 24h prior to zymosan and every 2 d for 5 d. For all studies, three independent experiments were performed (n=5-6 mice/genotype), and data analyzed using non-parametric statistics.

Results: In stark contrast to SKG mice that developed chronic arthritis and features of spondylitis by 8 weeks post zymosan, Card9$^{-/-}$SKG mice were completely protected from both diseases. Cell composition analysis of the ankle-draining lymph nodes at both 5 d and 8 wk post-zymosan revealed reduced numbers of neutrophils and effector Th17 responses in Card9$^{-/-}$SKG mice. CARD9 promoted acute (pre-arthritic) neutrophil responses in SKG mice as Card9$^{-/-}$SKG mice had reduced numbers of neutrophils, but not dendritic cells or macrophages, in lavage fluid as early as 4 h post-zymosan. Furthermore, neutrophils from Card9$^{-/-}$SKG lavage fluid had similar surface expression of Dectin-1 to neutrophils from SKG mice, yet had decreased activation status (retention of CD62L) and reduced degranulation of primary (CD63) and secondary (CD66b) granules. These data suggest that Card9 may function downstream of Dectin-1 ligation to promote activation and degranulation of neutrophils. Akin to Card9$^{-/-}$SKG mice,

neutrophil-deplete SKG mice had delayed onset of arthritis and decreased Th17 responses 5 d post-zymosan, supporting a pathogenic function for early neutrophil responses in induction of arthritis. Cumulatively, these data support an integral role for Card9 in regulation of early neutrophil responses that promote Th17 cells and induction of arthritis.

Conclusion: These data show a direct link between Card9 signaling and neutrophil-intrinsic induction of autoreactive Th17 responses in arthritis. Further investigation of how Card9 functions within neutrophils to drive autoimmunity may serve to unveil novel therapeutic avenues for human Th17-mediated diseases including ankylosing spondylitis.

Disclosure: H. Rosenzweig, None; **E. Vance**, None; **E. Lee**, None; **R. Napier**, None.

Abstract Number: 0741

Constitutive Inhibitor Kappa B (IκB) Kinase 2 (IKK2) Activation Induces an Inflammatory State in Fibroblast-Like Synoviocytes

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Fibroblast-like synoviocytes (FLS) are key players involved in the production of inflammatory mediators that trigger joint tissue damage in inflammatory arthritis (IA). The most important mechanism proposed for FLS activation is the NF-κB-dependent signalling pathway. Inhibitor kappa B (IκB) kinase 2 (IKK2) plays a critical role in the activation of NF-κB, resulting in transcription of several inflammation-associated genes. The aim of this research was the characterization of a constitutive IKK2 activation (IKK2ca) in FLS as a strategy to study tissue-specific inflammation in the joint.

Methods: In order to acquire new information regarding pathological pathways underlying IA, we develop an *R26Stop*^{FL}*ikk2ca-Prg4*^{CreERT2} mouse model, which expresses a constitutive active form of IKK2 restricted to Prg4-expressing cells in the joints. Cre-recombinase activation was induced by tamoxifen (TMX) intraperitoneal injection to 2-month old mice. Samples were collected after 4 weeks of TMX injection. Isolation of FLS was performed and NF-κB signalling pathway activation was analyzed by RT-qPCR and western blot. Additionally, flow cytometry was carried out to identify IKK2ca FLS population (Prg4 red cells). FLS at passages 2 to 4 were used for all experiments. R26-tdTomato-*Prg4*^{CreERT2} and TNF$^{tg/0}$rtTA$^{tg/0}$ FLS were taken as Wild type (WT) for RT-qPCR, western blot, and FACS analysis.

Results: Preliminary results showed high expression of IKK2 in IKK2ca FLS compared with WT FLS, as well as decreased expression of IκBα in the cytoplasm because of IKK2 constitutive activation. However, we did not observe differences in RelA nuclear expression between IKK2ca and WT FLS. In addition, we identify higher expression of *Il1b*, *Il6*, *Nanog*, and *Sox2* genes in IKK2ca than in WT FLS, which is consistent with the inflammatory state of IKK2ca FLS established in IA. Regarding FACS results, we identified a specific synovial sub-lining inflammatory population of IKK2ca-Prg4 CD14^{-} Thy1^{+} tdTomato^{+} FLS, which has reported as key player in IA.

Conclusion: Constitutive IKK2 activation in FLS induces an inflammatory phenotype characterized by increased expression of proinflammatory mediators, and represents an interesting strategy to study tissue-specific inflammation in the joint.

Disclosure: S. Ramirez-Perez, None; **U. Gangishetti**, None; **K. Jones**, None; **P. Bhattaram**, None.

Abstract Number: 0742

Effect of IA OnabotulinumtoxinA and Vanilloids on Substance P and Neurokinin 1 Receptor Expression in the Dorsal Root Ganglia of Mice with Monoarthritis

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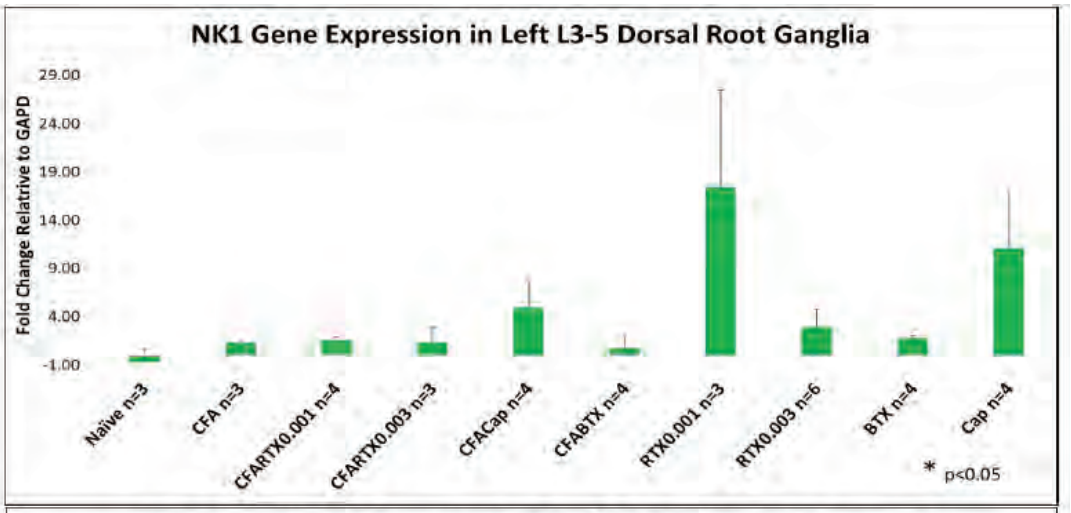
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

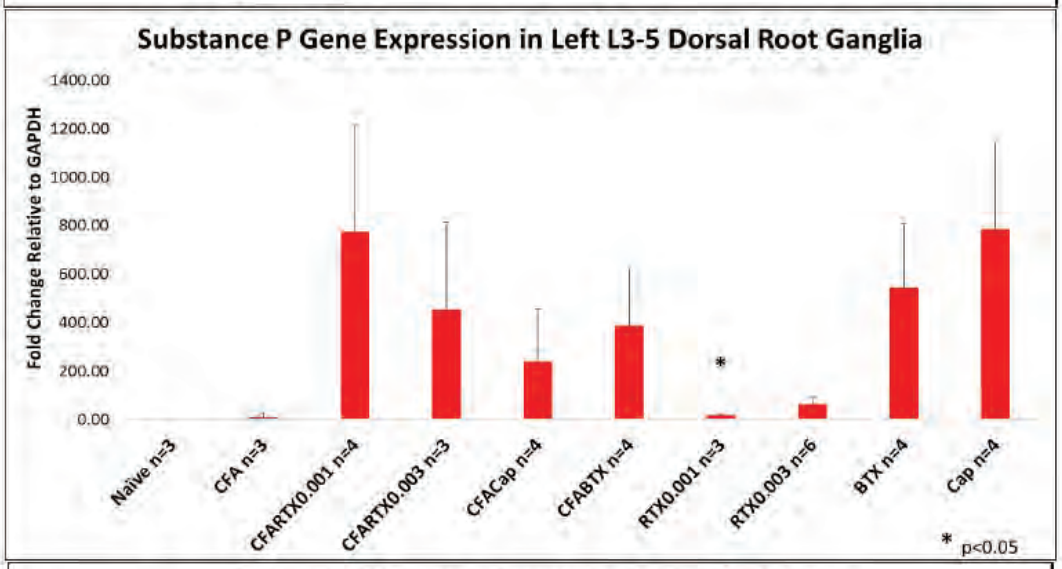
Background/Purpose: Neurotoxins are increasingly being proposed as analgesics for arthritis pain. Phase II and III clinical trials have shown efficacy but with potential toxicities such as rapidly progressive osteoarthritis that may be neurally mediated. We have shown efficacy of intra-articular (IA) onabotulinumtoxinA (BTX) and the vanilloids capsaicin (CAP) and resiniferatoxin (RTX) in monoarthritis in mice. To better understand the effect of these toxins on the sensory nervous system we examined their effect on the expression of substance P (SP) and neurokinin 1 receptor (NK1) in the dorsal root ganglion (DRG).

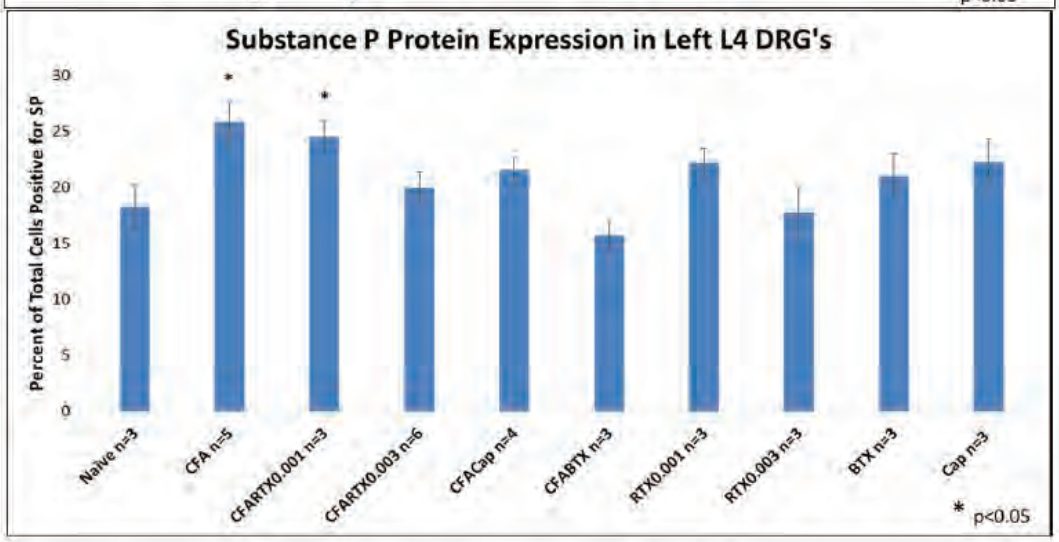
Methods: C57/Bl6 male mice received intra-articular (IA) Complete Freund's Adjuvant (CFA) to produce chronic inflammatory monoarthritis. IA therapies were given at appropriate intervals before examination and DRG harvest. Tissue samples were obtained after arthritis induction at 12 weeks of age from mouse dorsal root ganglia (DRG) and were subjected to immunohistochemistry and real-time reverse transcription polymerase chain reaction (RT-PCR). Neurotransmitter substance P (SP) protein expression was measured as percent of DRG neurons expressing SP. Both SP and receptor neurokinin-1 (NK1) gene expression were quantified using RT-PCR and expressed as a fold change relative to GAPDH values.

Results: CFA induction resulted in a significant increase in % SP protein expressing cells in DRG's but gene expression of SP and NK1 were not significantly changed from naïve. Neither vanilloids nor BTX had any effect on SP protein expression in nonarthritic animals. Only low dose RTX significantly increased SP gene expression in nonarthritic animals but had no effect onNK1 gene expression . High dose RTX, CAP and BTX all normalized % SP protein expressing cells in the DRG of arthritic animals but NK1 and SP gene expression was not significantly different from naïve. Interestingly, SP gene expression was more variable in all treated arthritic animals and in nonarthritic animals treated with BTX and CAP. NK1 gene expression in low dose RTX and CAP treated non arthritic animals was also more variable than in other groups. In general, BTX and CAP produced an increase in SP gene expression in nonarthritic animals but this was not significant.

Conclusion: Alterations in SP protein expression in the DRG of mice with chronic monoarthritis does not appear to be related to increased gene expression of either SP or NK1. Although the mechanism of action of BTX and vanilloids is hypothesized to be quite different, there does not appear to be a consistent effect of impaired neurotransmitter







release (BTX) or enhanced release (vanilloids) on SP or NK1 gene expression. Although numbers were small in this experiment, variability may be due to inherent differences in the animals' pain perception, pain behavior and response to therapy. Further studies to correlate pain behavior to SP and NK1 expression and to TRPV1 expression would be informative.

Substance P and NK 1 Receptor Gene and Protein Expression in the DRG of Mice with Inflammatory Monoarthritis: Effect of Neurotoxin Treatment.

Disclosure: H. Krug, None; **N. Blanshan**, None; **C. Dorman**, None; **S. Frizelle**, None.

Abstract Number: 0743

Higher Baseline Fine-Specificity ACPAs Predict Greater Treatment Response with Abatacept + MTX versus MTX Monotherapy in Seropositive RA: A Post Hoc Analysis

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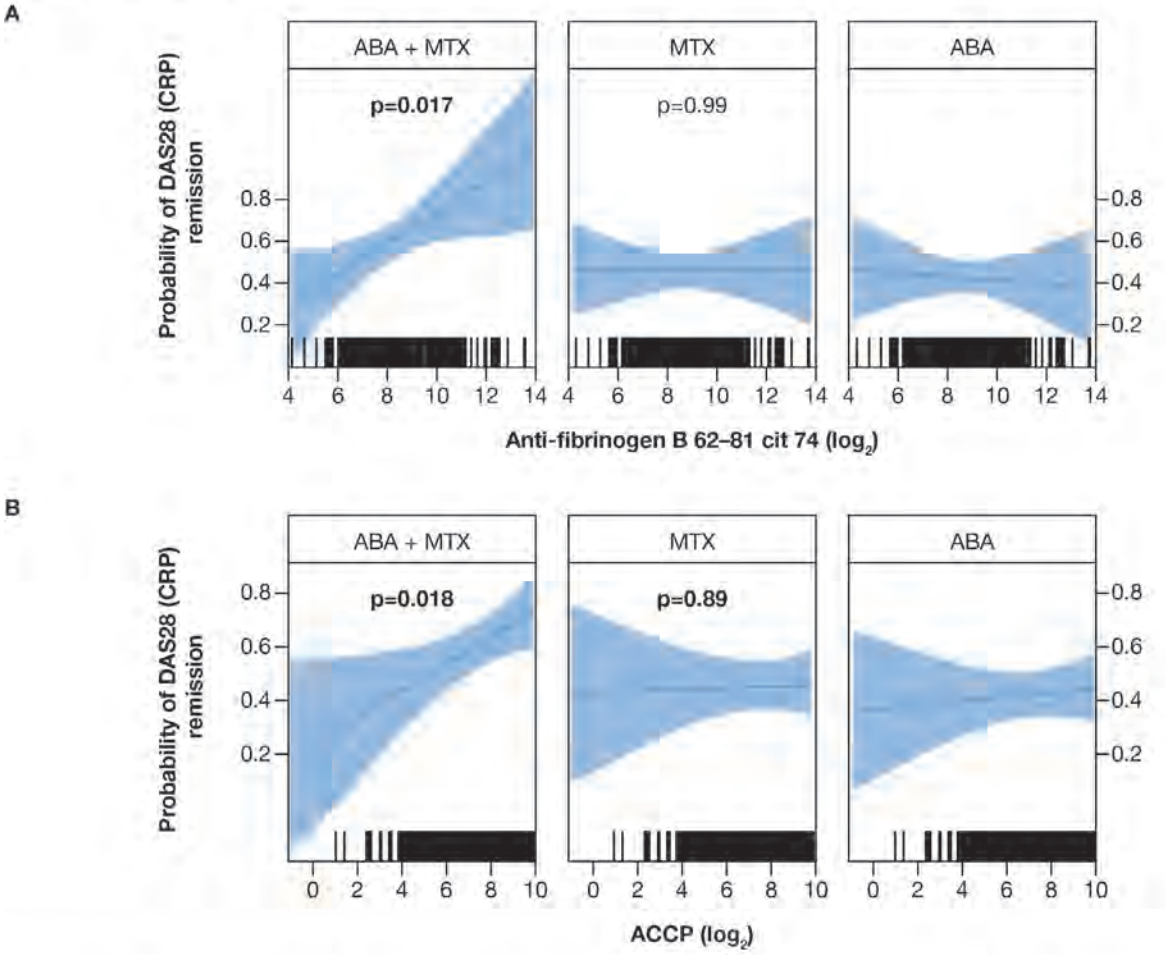
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: ACPAs are sensitive, highly specific markers of RA. Current tests cannot differentiate ACPA+ RA subtypes. Fine-specificity ACPAs (FS) can distinguish between ACPA+ RA subtypes to explore predictors of treatment (tmt) response. Higher vs lower baseline (BL) ACPA levels have been associated with improved response to abatacept (ABA).[1] In the Phase IIIb AVERT study, ABA + MTX was more effective than MTX in early RA: 61% vs 45% of patients (pts) achieved DAS28 (CRP) remission (< 2.6) at 12 mths.[2] We investigated FS as biomarkers to predict tmt response in pts with seropositive RA in AVERT.

Methods: Pts in AVERT (NCT01142726) were randomized to double-blind weekly SC ABA 125 mg + MTX, SC ABA 125 mg or MTX for 12 mths. In this *post hoc* analysis, predictive value of 29 BL FS and 10 non-citrullinated control antibodies (Ab) for efficacy measures (DAS28 [CRP], SDAI) was explored using logistic or linear regression models for remission rates (RR; SDAI remission ≤3.3) and change from BL (CfB) outcomes, respectively, with tmt arm, BL disease activity, age, sex, prior CS use, BL FS (continuous or categorized into tertiles [T; specific for each FS and control Ab]) and FS-by-tmt arm interaction as covariates. Linear mixed-effects model with repeated measures was used for time series analysis. Pairwise comparisons (unadjusted p values) between tmt arms were performed for DAS28 (CRP) and SDAI RR or adjusted mean CfB in each T. FS were analyzed with custom Bio-Plex™ bead-based autoantibody assay.[3]

Results: BL characteristics were comparable in overall (N=351) and target biomarker (n=340) populations and across tmt arms (not shown). Of 29 BL FS, 15 significantly correlated with anti-CCP Ab (ACCP; surrogate of ACPA). Of 29 FS or ACCP, higher BL anti-fibrinogen B 62–81 cit 74 (ABA + MTX p=0.017; MTX p=0.99) and ACCP (ABA + MTX p=0.018; MTX p=0.89) levels were significantly associated with higher probability of DAS28 (CRP) remission in pts who received ABA + MTX but not MTX (**Figure 1**); levels of non-citrullinated control anti-fibrinogen B 62–81 did not correlate with tmt response (p=0.324). For DAS28 (CRP) RR, tmt differences (ABA + MTX vs MTX) were greater in medium (T2) and high (T3) subgroups vs overall population: ACCP (T2; p≤0.01), 28%; anti-fibrinogen B 62-81 cit 74 (T3; p≤0.01), 32%; overall population, 16% (**Figure 2**). Tmt differences in adjusted mean DAS28 (CRP) CfB for ABA + MTX vs MTX and ABA vs MTX were greater in medium (T2; Mth 6) and high (T3; Mths 6, 12) vs low (T1) anti-fibrinogen B 62–81 cit 74 subgroups (**Figure 3**); similar findings were seen for SDAI. Anti-fibrinogen B 62–81 cit 74 (vs ACCP) better predicted DAS28 (CRP) CfB improvement with ABA + MTX vs MTX (not shown).

Figure 1. Probability of DAS28 (CRP) remission (<2.6) with ABA + MTX, MTX or ABA as predicted with A) anti-fibrinogen B 62–81 cit 74 and B) ACCP



The following FS and control antibodies were tested: B-actin 191–216 cit 196, biglycan 247–266 cit cyclic, clusterin 221–240 cit cyclic, clusterin 231–250 cit cyclic, collagen Type II 281–298 cit 290, collagen Type II 281–298, enolase 1A 5–21 cit, fibrinogen A 211–230 cit cyclic, fibrinogen A 27–43 cit, fibrinogen A 41–60 cit3 cyclic, fibrinogen A 563–583 cit 573, fibrinogen A 616–635 cit3 cyclic, fibrinogen B 246–267 cit, fibrinogen B 285–305 cit, fibrinogen B 285–305, fibrinogen B 36–52 cit, fibrinogen B 54–74 cit 60, fibrinogen B 54–74, fibrinogen B 62–81 cit 72, fibrinogen B 62–81, fibrinogen B 62–81 cit 74, fibrionectin cit 1035, filaggrin 48–65 cit2 cyclic, filaggrin 48–65 cyclic, H2A/a 1–20 cit cyclic, H2A/a 1–20 cyclic, H2A/a-2 1–20 cit, H2A/a-2 1–20, H2B/a 62–81 cit cyclic, H2B/a 62–81 cyclic, H4 33–48 cit39, tenascin C1, tenascin C5, vimentin 1–16 cit, vimentin 1–16, vimentin 265–278, vimentin 58–77 cit3 cyclic, vimentin 58–77 cyclic and ACCP BL levels.
ABA=abatacept; ACCP=anti-CCP antibody; FS=fine-specificity anti-citrullinated protein antibody.

Conclusion: BL FS predicted improved DAS28 (CRP), SDAI RR and CfB with abatacept + MTX vs MTX; higher BL T showed greater differentiation in tmt response with abatacept + MTX vs MTX. Anti-fibrinogen B 62–81 cit 74 (vs ACCP) better predicted DAS28 (CRP) improvement with abatacept + MTX vs MTX. These data support anti-fibrinogen B 62–81 cit 74 as a predictor of tmt response to abatacept.

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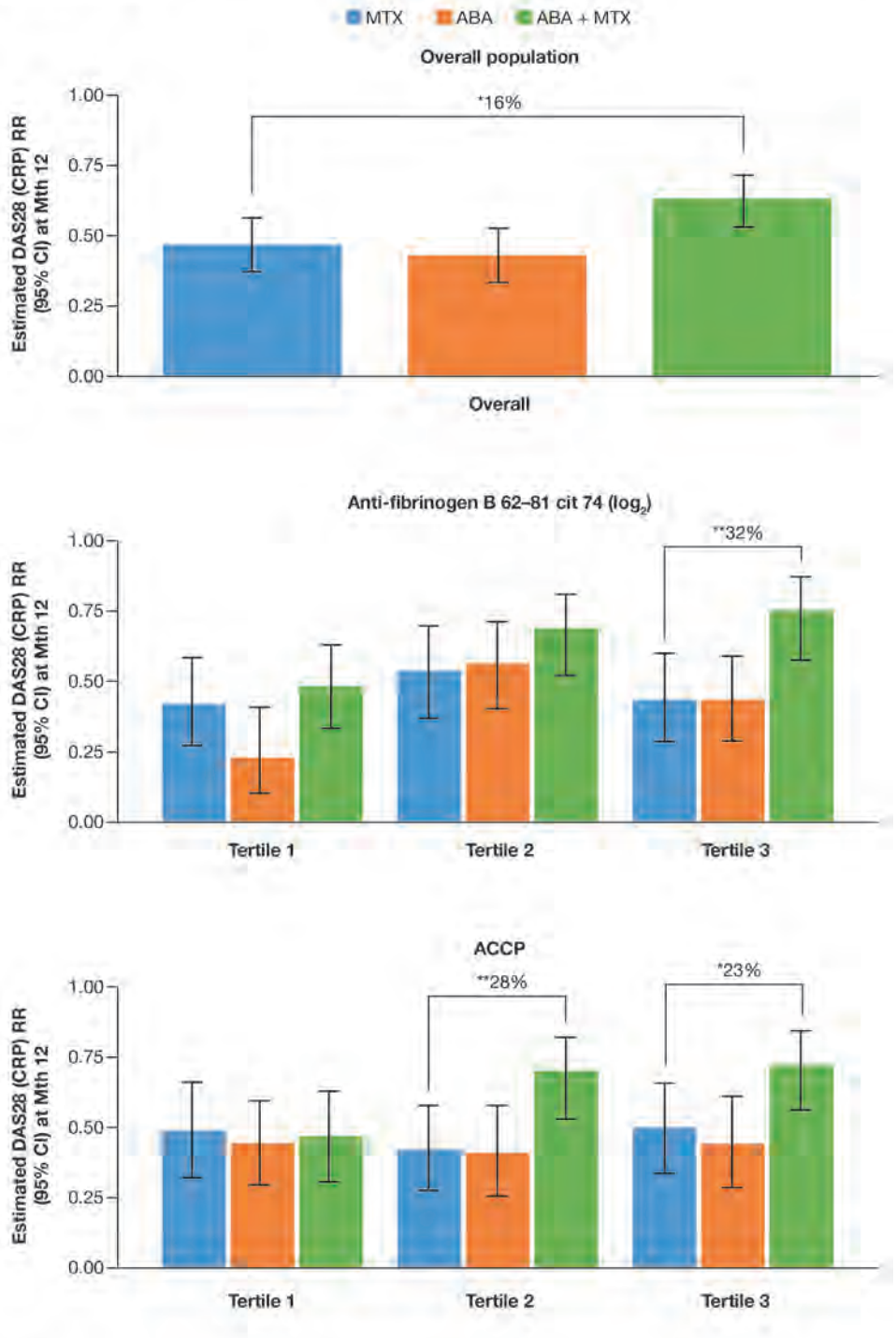
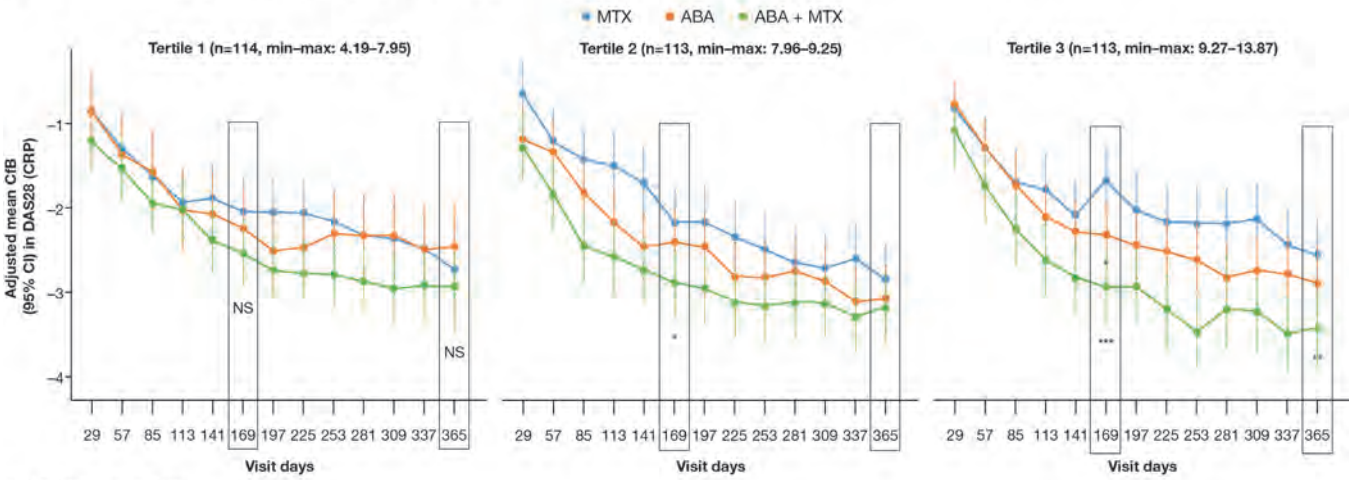
Medical writing: Katerina Kumpan (Caudex).

Figure 2. DAS28 (CRP) RR in the overall population and in the biomarker population by anti-fibrinogen B 62–81 cit 74 and ACCP tertiles



*p≤0.05; **p≤0.01.
ACCP=anti-CCP antibody; RR=remission rate.

Figure 3. Adjusted mean CfB in DAS28 (CRP) by anti-fibrinogen B 62–81 cit 74 tertiles



Day 169=Mth 6, Day 365=Mth 12.
*p≤0.05; **p≤0.01; ***p≤0.001.
CfB=change from baseline; NS=not significant.

Disclosure: W. Robinson, None; **C. Wu**, Bristol-Myers Squibb Company, 3; **S. Hu**, Bristol-Myers Squibb Company, 1, 3, 4; **S. Connolly**, Bristol-Myers Squibb Company, 1, 3, 4; **S. Mukherjee**, Bristol-Myers Squibb Company, 1, 3, 4.

Abstract Number: 0744

Circulating Fibroblast Growth Factor-21 Levels in Rheumatoid Arthritis: Associations with Disease Characteristics, Body Composition, and Physical Functioning

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) can lead to changes in body composition, including muscle loss and excess adiposity, which are in turn associated with physical disability. It is of interest to identify biomarkers that could help identify patients most at-risk for these changes. Fibroblast Growth Factor (FGF)-21, an adipokine associated with obesity, insulin resistance, and metabolic stress, is known to be elevated in patients with muscle stress conditions but has not been well-described in RA patients. In this study, we evaluated associations between FGF-21 and adverse changes in body composition and physical functioning in patients with RA, hypothesizing that levels of FGF-21 at baseline would be associated with worsening muscle deficits and physical functioning over time.

Methods: At baseline and follow-up, RA patients meeting 2010 ACR criteria, aged 18-70, completed whole-body Dual Energy Absorptiometry (DXA) and peripheral quantitative computed tomography (pQCT) to quantify lean mass, fat mass, visceral fat area, and muscle density. Dynamometry was used to measure strength at the hand and knee, and physical functioning was measured with the Health Assessment Questionnaire (HAQ) and the Short Physical Performance Battery (SPPB). Cytokines and inflammatory markers were measured at baseline, and serum FGF-21

was assessed using ELISA. Linear and logistic regression analyses assessed associations between FGF-21 levels, and body composition and physical functioning over 2-5 years of follow-up.

Results: 113 patients with RA were enrolled, and 84 (74%) returned for follow-up at a median (IQR) time of 2.7 years (2.30, 3.56). At baseline, higher FGF-21 levels were independently associated with older age, smoking, lack of methotrexate use, and greater adiposity (both total and visceral) (**Table 1**). The highest quartile of FGF-21 was associated with worse HAQ and SPPB scores, independent of other baseline characteristics (p=0.03 and p=0.01, respectively; data not shown). FGF-21 was not associated with common measures of RA activity or severity, including DAS28(CRP) and radiographic damage scores, but was associated with higher levels of specific inflammatory cytokines including TNF-RI, YKL-40, VEGF, and Resistin, before and after adjusting for visceral fat area (all p< 0.05, data not shown). Over time, higher baseline FGF-21 levels were numerically, but not statistically significantly, associated with greater worsening per year in muscle density and area z-scores [β=-0.056 (-0.12, 0.008), p=0.08; β=-0.049 (-0.10, 0.006), p=0.08], and the fourth FGF-21 quartile was associated with greater worsening in SPPB score [β=-0.57

Table 1. Associations Between FGF-21 Levels and Participant Demographics and RA Disease Characteristics at Baseline

	Univariate Model		**Multivariable Model**	
	β (95% CI)	p	β (95% CI)	p
Age (per 1 yr)	0.019 (0.004, 0.034)	0.01	0.014 (0.0005, 0.028)	0.04
Female	0.002 (-0.37, 0.38)	0.99	0.13 (-0.21, 0.46)	0.46
Black	-0.053 (-0.45, 0.34)	0.79	--	--
BMI (per 1 kg/m^2)	0.043 (0.019, 0.066)	0.001	--	--
ALMI Z-Score (per 1 unit)	0.15 (-0.026, 0.33)	0.09	--	--
FMI Z-Score (per 1 unit)	0.25 (0.10, 0.40)	0.001	--	--
Visceral Fat Area (per 1 cm)	0.006 (0.004, 0.009)	<0.001	0.006 (0.004, 0.008)	<0.001
Diabetes	-0.029 (-0.62, 0.56)	0.92	--	--
Cardiac Disease	0.59 (0.23, 0.95)	0.001	--	--
EGFR (per 1 unit)	-0.008 (-0.015, -0.0006)	0.03	--	--
Current Smoker	0.45 (0.011, 0.88)	0.05	0.37 (-0.021, 0.75)	0.06
MDAS (CRP)	0.087 (-0.068, 0.24)	0.27	--	--
DAS-28 (CRP)	0.083 (-0.073, 0.24)	0.29	--	--
vdHS Score	-0.0007 (-0.005, 0.003)	0.72	--	--
RA Duration (per 1 yr)	0.013 (-0.004, 0.029)	0.14	--	--
Current Methotrexate	-0.35 (-0.74, 0.037)	0.08	-0.45 (-0.80, -0.10)	0.01
Current Biologic	0.016 (-0.36, 0.39)	0.93	--	--
Current Prednisone	0.052 (-0.32, 0.43)	0.79	--	--

β coefficients represent differences in FGF-21 level associated with changes in each respective measure. FMI Z-score, waist circumference, and visceral fat area are all highly collinear, and therefore only visceral fat area was included in multivariable model because it was the most correlated with FGF-21. All other variables that were moderately associated (p<0.2) with FGF-21 in a univariate model were initially tested in the multivariable model. Variables remaining moderately significant (p<0.10) in the multivariate model were included in the final model, along with basic demographic characteristics (age, gender).

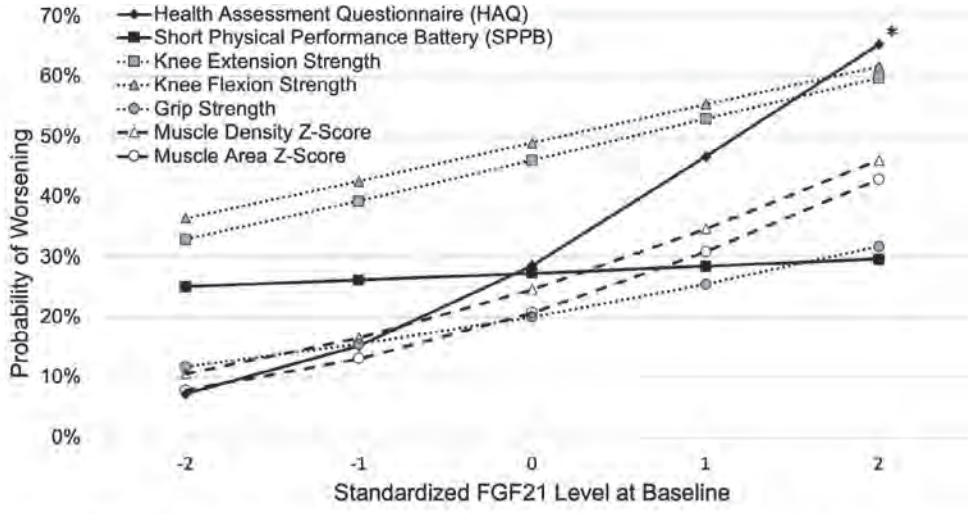
Table 1. Associations Between FGF-21 Levels and Participant Demographics and RA Disease Characteristics at Baseline

Table 2. Associations Between FGF-21 Values and RA Outcomes Over Time		
	Association with Rate of Change of Outcome	
	β (95% CI)	p
Muscle Density Z-Score		
FGF-21 (Continuous)	-0.056 (-0.12, 0.008)	0.08
FGF-21 in Top Quartile	-0.074 (-0.20, 0.056)	0.26
Muscle Area Z-Score		
FGF-21 (Continuous)	-0.049 (-0.10, 0.006)	0.08
FGF-21 in Top Quartile	-0.034 (-0.15, 0.081)	0.55
Grip Strength (kg)		
FGF-21 (Continuous)	0.10 (-0.62, 0.83)	0.77
FGF-21 in Top Quartile	-1.39 (-2.79, 0.014)	0.05
Health Assessment Questionnaire (HAQ)		
FGF-21 (Continuous)	0.025 (-0.015, 0.064)	0.22
FGF-21 in Top Quartile	0.034 (-0.045, 0.11)	0.29
Short Physical Performance Battery (SPPB)		
FGF-21 (Continuous)	-0.14 (-0.37, 0.088)	0.22
FGF-21 in Top Quartile	-0.57 (-1.04, -0.091)	0.02
All models include adjustments for age, gender, visceral fat area, current smoking, and methotrexate use (all at baseline). Models involving grip strength include an adjustment for height at baseline. β coefficients represent differences in the rate of change of each outcome associated with either a 1 SD higher FGF-21 level at baseline, or a FGF-21 value in the fourth quartile (as compared to the bottom three together).		

Table 2. Associations Between FGF-21 Values and RA Outcomes Over Time

(-1.04, -0.091), p=0.02] (**Table 2**). Higher FGF-21 (per SD) was also associated with a greater probability of clinically meaningful worsening of HAQ score [OR=2.37 (1.21, 4.64), p=0.01] (**Figure 1**).

Conclusion: FGF-21 levels were associated with obesity, physical functioning, and inflammatory mediators at baseline, and with worsening in muscle quality and physical functioning over time. These associations support the hypothesis that FGF-21 serves as a biomarker of metabolic stress that could predict greater functional declines in RA patients.



*p value <0.05. Models include adjustments for age, gender, visceral fat area, current smoking, and methotrexate use (all at baseline). Clinically meaningful worsening was defined as follows (or as patient death before visit):

- HAQ: increased by 0.2
- SPPB: decreased by 1
- Extension and flexion strength: decreased by 10%
- Grip strength: decreased by 6.5 kg
- Muscle density and muscle area z-score: decreased by 0.5

Figure 1. Probability of a Clinically Meaningful Negative Change in Selected RA Outcomes at Second Visit, by Baseline FGF-21 Z-Score

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Disclosure: P. Gould, None; **B. Zemel**, None; **E. Taratuta**, None; **J. Baker**, None.

Abstract Number: 0745

Development of Functional Assays to Pre-qualify Human Mesenchymal Stem Cells for Rheumatoid Arthritis Treatment

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Sero-positive rheumatoid arthritis (RA) is a chronic autoimmune disease that without effective treatment, leads to joint damage and disability. Not all patients respond to currently available medications. Human mesenchymal stem cells (hMSCs) have the potential to be used therapeutically to attenuate immune-mediated diseases. To understand how to select hMSCs for RA therapy 1) hMSC culture medium was tested for the ability to suppress RA and healthy control allogeneic T-cells; 2) the degree of T-cell suppression was compared using hMSCs

from distinct donors; 3) preconditioning of hMSCs with cytokines was tuned for maximal suppressive effect and likely mediators of suppression measured.

Methods: CD4+ T-cells obtained from healthy controls (HC) and RA patients were stimulated for 4 days to proliferate. Medium used in suppression assays were:1) culture conditioned medium (CCM) in which hMSCs were preconditioned by a single cytokine; TNFα, IFNγ, IL-1β or a combination of the three cytokines (all-3) or 2) unconditioned control medium (UC) that was cultured like CCM but was not preconditioned with cytokines. T-cell proliferation was measured using eFluor670 vital dye and proliferation was measured using flow cytometry. IDO mRNA and protein were quantified by qRT-PCR and western blot, respectively. Statistical analyses were performed using two-tailed Student's t-test and one-way ANOVA was used for multiple comparison tests in GraphPad Prism 8.1.2.

Results: RA and HC CD4+ T-cell proliferation was suppressed by all-3-CCM compared to UC (76%±2 of UC $p< 0.0001$). IFNγ-CCM was also suppressive (43%±6 of UC $p< 0.001$). CCM containing all-3 cytokines suppressed HC CD4+ T-cell proliferation best (68%±9 $p< 0.05$) when hMSCs were preconditioned with cytokines for 48 hours compare to 24 hours (42%±8). CCM from different donors varied in potency of suppression in both RA and HC. Differences between individual hMSC donors were best detected using all-3-CCM and IFNγ-CCM. CD4+ T-cell suppression was positively correlated with increases in IDO mRNA and IDO protein in both RA and HC.

Conclusion: The data demonstrate that hMSC can be tuned using cytokines to maximally suppress HC and RA T-cells. IDO mediates hMSC effects on T-cells, but hMSC also secrete other molecules that contribute toT-cell suppression. Standardizing cell-based therapy using functional assays *ex vivo* should facilitate comparing potency of distinct cellular products across disease indications. The suppression assays described directly test an admixture of soluble mediators that arise from hMSC rather than just describing mRNA or protein levels. Whether hMSCs should be cytokine primed prior to therapeutic infusion, is of great interest and has implications for hMSC-therapy in RA.

*This project was supported by the Clinical and Translational Science Collaborative (CTSC) of Cleveland which is funded by the National Institutes of Health (NIH), National Center for Advancing Translational Science (NCATS), Clinical and Translational Science Award (CTSA) grant, UL1TR002548. The content is solely the responsibility of the authors and do not necessarily represent the official views of the NIH. And David and Virginia Baldwin Foundation.

Disclosure: M. Breitman, None; **T. Bonfield**, None; **A. Caplan**, None; **H. Lazarus**, None; **M. Haghiac**, None; **J. Reese**, None; **N. Singer**, None.

Abstract Number: 0746

HDL-bound yRNA-derived Small RNAs Are Altered in Patients with Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

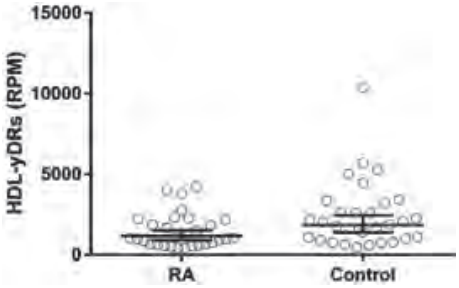

Figure 1. HDL-bound yRNA-derived sRNAs as a class are significantly reduced 36% among patients with RA compared to control subjects(P=0.03). Each dot represents an individual subject's total HDL-yDR reads per million. Bars indicate geometric mean and 95% confidence intervals.

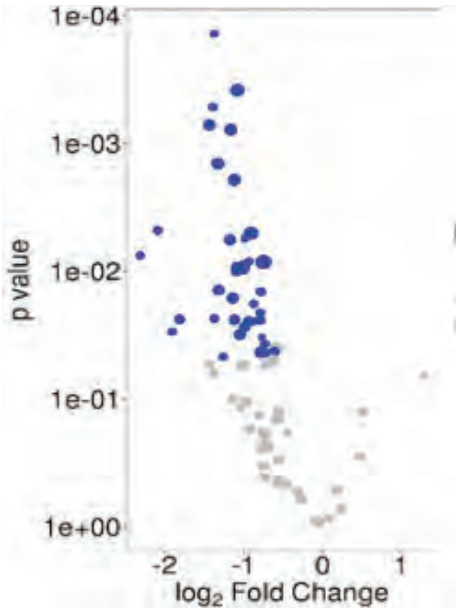

Figure 2. Volcano plot displaying difference in HDL-bound yDR sequences in RA versus control subjects. Blue dots indicate sequences which are reduced among RA patients.

Background/Purpose: Small RNAs (sRNAs), including microRNAs (miRNAs) and yRNA-derived sRNAs (yDRs), are important gene regulators and markers of disease. HDL, while known for its anti-atherogenic function, can traffic sRNAs between cells to alter gene expression and thus cellular function. Additionally, HDL interacts with cells of the immune system and synovial fibroblasts, making it an important sRNA carrier to examine in rheumatoid arthritis (RA). HDL carries yDRs, some of which are known to promote apoptosis. Apoptosis is impaired in RA, particularly in the synovial fibroblasts of RA patients. The purpose of this study was to determine if HDL-bound yDRs are altered in RA and if they are associated with disease measures.

Methods: HDL was purified from 30 patients with RA and 30 control subjects matched for age, race and sex subject plasma by density gradient centrifugation and fast protein liquid chromatography. Total RNA was extracted from the purified HDL. Next generation sequencing (NGS) was performed on sRNA libraries by Illumina NextSeq500. The TIGER pipeline was used to quantify yDRs. The yDRs were compared between RA and control subjects by DESeq2 with 5% false discovery rate multiple comparison adjustment by Benjamini-Hochberg method. Spearman correlation was used to determine relationship between sRNAs and disease measures.

Results: HDL-bound yDRs as a class were significantly reduced 36% among patients with RA compared to control subjects (p=0.03) (Figure 1). Eighteen yDR sequences were significantly reduced up to 5-fold among RA versus con-

trol subjects (Padj < 0.05) (Figure 2). Among these altered yDRs, 17 map to the 5' and 3' ends of RNY4 (Ro60-associated yRNA 4), with only minor sequence variation. Based on NGS the two most abundant sequences aligning to each end of RNY4 were significantly associated with swollen joint count (ydr-ccccccactgctaaatttgactggctt, Rho=0.39, p=0.04; and ydr-ggctggtccgatggtagtgggttatcagaact, Rho=0.40, p=0.03), but were not altered based on disease modifying antirheumatic drug use, seropositivity or erosive disease (all P >0.05).

Conclusion: HDL-bound yDRs are reduced in patients with RA and several yDRs are associated with swollen joint count. Further work will be necessary to validate these findings and to determine the functional role of these HDL-bound yDRs in RA.

Disclosure: Q. Wu, None; **Q. Sheng**, None; **J. Solus**, None; **D. Michell**, None; **K. Vickers**, None; **R. Allen**, None; **C. Stein**, None; **M. Ormseth**, None.

Abstract Number: 0747

Isotope-Labeling-LC-MS-based Metabolic Profiling of Multiple Serum Sample Sets for the Discovery of High-confidence Rheumatoid Arthritis Biomarkers

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Early diagnosis of rheumatoid arthritis (RA) is hampered by suboptimal accuracy of currently available serological biomarkers. In this work, we applied a high-performance chemical isotope labeling (CIL) LC-MS technique for in-depth profiling of the amine/phenol-submetabolome in serum samples. To avoid false positives and obtain high-confidence biomarker candidates, we analyzed three independent sets of serum samples collected from RA patients and healthy controls to examine the common effects.

Methods: Serum samples were taken from 3 RA cohorts, which comprised 50, 49, and 131 RA patients, respectively. Within each cohort, there were sex/age-matched healthy controls: 50 in Cohort 1, 50 in Cohort 2, and 100 in Cohort 3. Amine/phenol-containing metabolites were labeled by ^{12}C-dansyl chloride to improve the LC-MS detection. For each cohort, a pooled sample was prepared and labeled by ^{13}C-dansyl group to serve as the reference sample for relative quantification. Individual samples and the pooled sample were mixed 1:1 and an LC-QTOF-MS platform analyzed the mixtures and output the intensity ratios of ^{12}C/^{13}C peak pairs.

Results: 1,149 amine/phenol-containing metabolites were commonly detected across the three sample sets. Among them, 134 were positively identified by our dansyl-labeling standard library, and 141 were matched to predicted retention times and mass values of dansyl-labeled human metabolites. Visualized by the partial least squares discriminant analysis (PLS-DA), the overall amine/phenol-submetabolome demonstrated clear and consistent differences between healthy controls and the RA groups, with cross-validation Q2 = 0.765, 0.745, 0.793, respectively. The selection of significant metabolites was conducted according to the fold change and false-discovery-rate-adjusted Welch's

t-test. Cohort 1 demonstrated 85 metabolites having higher and 89 with lower concentrations in the RA samples than the controls. The numbers of increased/decreased metabolites in Cohort 2 and 3 were 87/26 and 90/53, respectively. Importantly, there were 59 significantly discriminatory metabolites commonly found in the three data sets (49 increased and 9 decreased). We picked the top three with the highest univariate classification performance to form a biomarker panel. We implemented the linear support vector machine (SVM) to build the classifier and the receiver operating characteristic (ROC) analysis to measure the performance. The area-under-the-curve (AUC) values (95% confidence interval) were 1.000 (1.000-1.000), 0.992 (0.967-1.000) and 0.902 (0.858-0.945) for the three cohorts, respectively. The results revealed the importance of examining multiple sample sets and even in the worst case (Cohort 3), our biomarker candidates could differentiate RA at 82.5% sensitivity and 82.5% specificity. Particularly, in Cohort 3, there were 30 RA patients negative for anti-cyclic citrullinated peptide and rheumatoid factor, and our metabolite panel demonstrated consistently high performance for differentiating these specific subjects from healthy controls.

Conclusion: Metabolites showing significant and consistent changes associated with RA have been identified with high discriminative power.

Disclosure: X. Wang, None; **W. Han**, None; **L. Li**, None; **S. Wichuk**, None; **E. Hutchings**, None; **R. Dadashova**, None; **J. Paschke**, None; **W. Maksymowych**, CARE Arthritis Limited, 9, AbbVie, 2, 5, 8, Boehringer Ingelheim, 5, Celgene, 5, Eli Lilly, 5, Galapagos, 5, Janssen, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 0748

Joint Space Narrowing Precedes Erosive Radiographic Damage in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory disease characterized through symmetric polyarthritis leading to joint destruction over time in many patients. Radiographic damage is an important outcome in RA clinical trials, most commonly assessed by conventional radiographs and quantified/reported by the modified total Sharp van der Heijde Score (mTSS). The mTSS is assessing erosive (ERO) changes as well as joint space narrowing (JSN; reflecting cartilage wasting) in the small joints of the hands and feet. While erosions are the hallmarks of RA, loss of cartilage has been reported to be highly relevant for functional limitations in RA. The sequence of occurrence of these events is not completely understood.

Methods: Radiographs of RA patients from a large prospective clinical routine cohort were scored using the mTSS by one experienced reader (G.S.) unaware of the aim of this project. Time-to-JSN and time-to-ERO was estimated using survival analyses utilizing the Kaplan-Meier estimator. In additional analyses, patients were stratified based on JSN and/or ERO damage at baseline. Further, potential predictors (demographics, csDMARD/bDMARD treatment/combination therapy) of time-to-ERO and time-to-JSN were evaluated using Cox-regression techniques. All statistical analyses were conducted using SAS v9.4 (Cary, New York, USA).

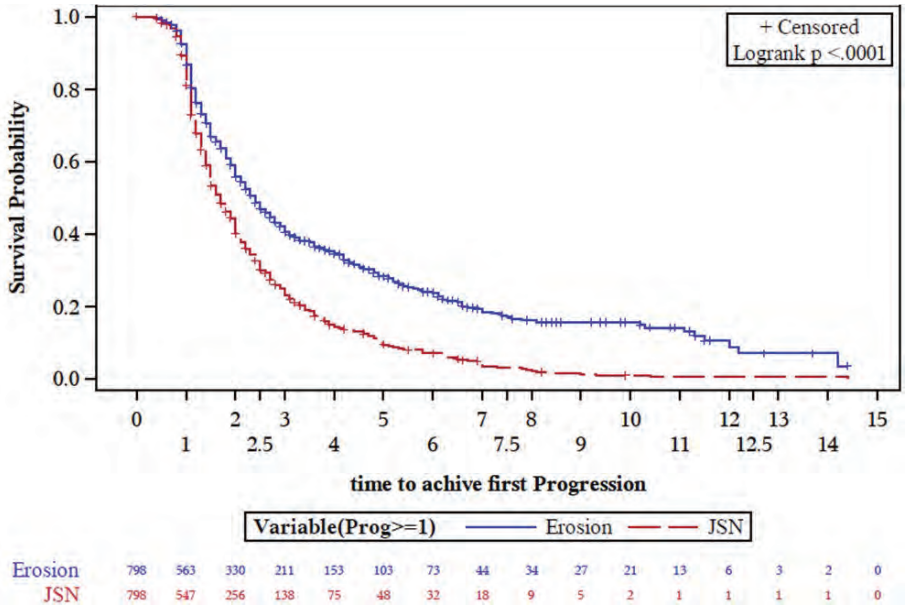


Figure 1. Kaplan-Meier analysis showing time to progression of radiographic progression. Curves represent time to first occurance of joint space narrowing (red) and erosive (blue) progression.

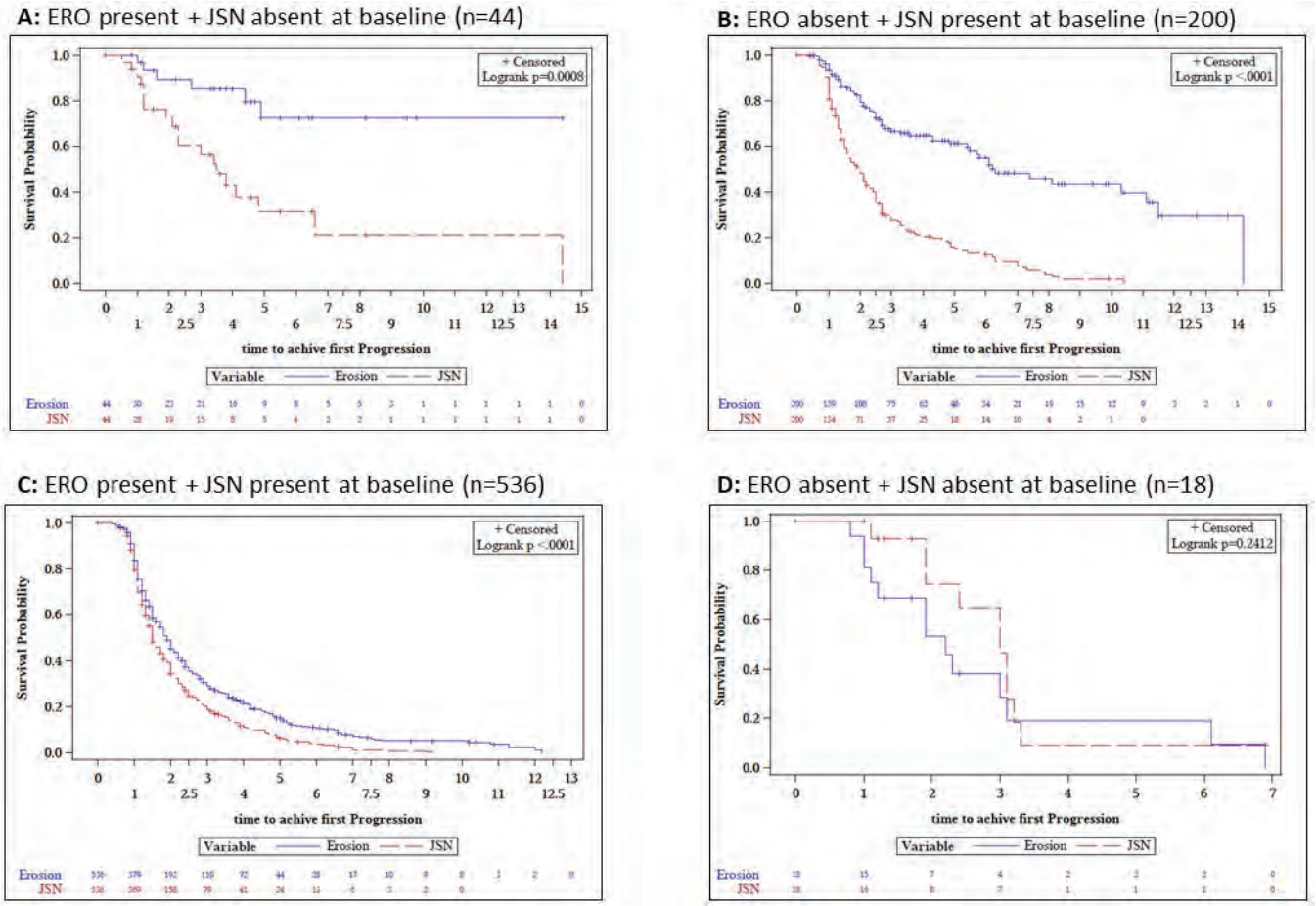


Figure 2. Time to progression of structural damage after stratification for baseline damage. A: Patients with erosions and absence of joint space narrowing; B: Patients with absence of erosions and presence of joint space narrowing; C: patients with presence of erosions and joint space narrowing; D: patients with erosions and absence of joint space narrowing.

Results: We assessed 798 patients longitudinally for radiographic progression. JSN occurred significantly earlier than erosions ($p < 0.001$, Figure 1). After stratification for baseline damage (Figure 2), these differences remained significant with a shorter time-to-JSN in patients without any baseline ERO or JSN (n=44, p=0.008), patients with JSN but no ERO at baseline (n=200, $p < 0.001$), and patients with baseline ERO and JSN (n=536, $p < 0.001$). Only in the small group of patients with isolated erosions (without JSN) at baseline there was no difference in time-to-progression of ERO vs. JSN (n=18, p=0.241). Overall, shorter time to progression of ERO was significantly predicted by positivity for rheumatoid factor or anti-citrullinated peptide antibodies (CCP; $p < 0.003$), as well as by erosions at baseline ($p < 0.001$) in Cox regression. In contrast, seropositivity for neither RF nor CCP was associated with shorter time to JSN progression (p=0.226); however, baseline concomitant JSN and ERO damage did show to be a significant predictor ($p < 0.001$).

Conclusion: We identified a significantly shorter time to progression of JSN compared to ERO in this longitudinal cohort of RA patients. JSN remains an important radiographic outcome, as it is strongly associated with impairment of physical function. This calls for a stronger focus on cartilage damage in RA, and a stronger consideration of JSN in routine evaluation of RA radiographs in clinical practice.

Disclosure: A. Kerschbaumer, Bristol-Myers Squibb, Celgene, Eli-Lilly, Merck Sharp and Dohme, Novartis, Pfizer, 8, Gilead, 9; **G. Supp**, None; **F. Alasti**, None; **J. Smolen**, AbbVie, 2, 5, 8, AstraZeneca, 2, 5, 8, Eli Lilly, 2, 5, 8, Celgene, 5, 8, Celltrion, 5, 8, Chugai, 5, 8, Gilead, 5, 8, ILTOO, 5, 8, Janssen, 5, 8, Kabi, 5, 8, Novartis-Sandoz, 5, 8, Pfizer Inc, 5, 8, Samsung, 5, 8, Sanofi, 5, 8; **D. Aletaha**, UCB, 5, 8, Eli Lilly, 5, 8, Gilead Sciences, Inc., 2, 5, Janssen, 5, Sanofi/Genzyme, 5, 8, AbbVie, 2, 5, 8, Amgen, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, Roche, 2, 5, 8, Merck Sharp & Dohme, 2, 5, 8, Bristol-Myers Squibb, 8, Celgene, 5, 8, Medac, 5, 8, Sandoz, 5, 8.

Abstract Number: 0749

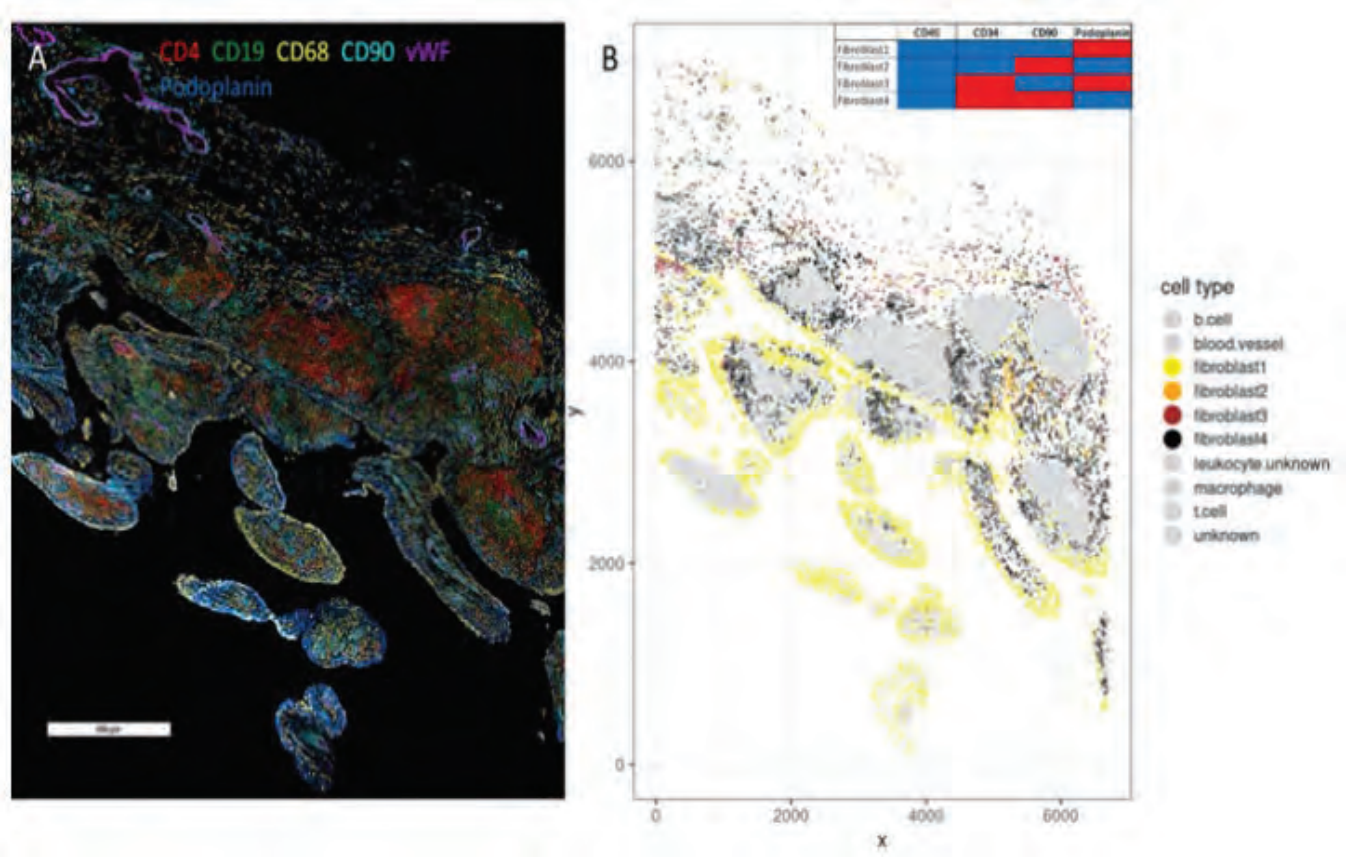
Locating Cellular Subsets in Rheumatoid Arthritis Synovium Using CO-Detection by IndEXing (CODEX)

Isabella Wulur[1], David Boyle[2], Lin Zhang[1], Andrea Martin[1], Robert Benschop[3] and **Gary Firestein**[4], [1]Eli Lilly, Indianapolis, IN, [2]UC San Diego, San Diego, CA, [3]Eli Lilly and Company, Indianapolis, IN, [4]University of California, San Diego, La Jolla, CA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: To better understand site-of-disease mechanisms in arthritis, the phenotypes and organization of synovial cells and infiltrates are critical. Conventional histology-based approaches are limited in the number of proteins that can be detected and quantification can be difficult due to non-linear detection systems. Tissue disaggregation techniques have advantages for some techniques, but disrupt tissue organization, might not liberate all cell types with equal efficiency and can result in loss of cell surface markers. To address this, we applied a novel multiplex immunofluorescence imaging platform (CODEX) to synovial tissue obtained from patients with rheumatoid arthritis (RA) or osteoarthritis (OA).

Methods: CODEX was performed by simultaneously applying 20 different antibodies, each labeled with a unique tag, to a 6 μm frozen tissue section. This technique was followed by iterative marker imaging, data processing and single



Representative CODEX image of RA synovium with CD4 staining in red, CD19 in green, CD68 in yellow, CD90 in cyan, von Willebrand factor (vWF) in magenta and podoplanin in blue. B) Location of 4 distinct phenotypes of putative fibroblasts defined by combinations of podoplanin, CD90, and CD34 expression. Fibroblast type 1 (Fb1) cells are almost exclusively found in the intimal lining, whereas Fb2, Fb3 and Fb4 are all located in the sublining.

cell segmentation to generate high resolution images along with marker intensities of each cell. These were used to create a model of cell phenotype, quantification and spatial organization of all identified cell types.

Results: In our initial analysis of 20 markers, we identified the location of multiple subsets, including macrophages, B cells, T cells and mesenchymal cells (Fig 1A). Signals for individual subsets correlated with standard histology in leukocyte-rich and leukocyte-poor tissue sections. One example of how CODEX can identify phenotypically defined cells was fibroblasts, where 4 distinct phenotypes of putative fibroblasts (CD45-) were defined by combinations of podoplanin, CD90, and CD34 (Fig 1B). Type 1 cells (Fb1; podoplanin+ CD34-, CD90-) are almost exclusively found in the intimal lining, whereas Fb2 (CD90+, CD34-, podoplanin-), Fb3 (CD34+, podoplanin+, CD90-), and Fb4 (CD34+, CD90+, podoplanin-) are all located in the sublining. In our small test cohort (4 RA, 3 OA) we noted a nonsigificant numerical increase in total cells in leukocyte-rich RA vs. OA (4994 vs. 2469 average cells/mm2, respectively). The percentage of Fb4 cells was numerically higher in leukocyte-rich RA compared with OA (13.6% vs. 7.5%, respectively).

Conclusion: CODEX technology allows the accurate simultaneous spatial mapping of a multiple cellular phenotypes in situ as suggested here by the location of fibroblast subtypes. Future direction includes combining CODEX with transcriptomics to provide additional characterization of potential pathogenic cells in RA.

Disclosure: I. Wulur, Eli Lilly & Co., 1, 3, 4; **D. Boyle**, None; **L. Zhang**, Eli Lilly and Company, 1, 3; **A. Martin**, Eli Lilly, 3; **R. Benschop**, Eli Lilly and Company, 1, 3, 4; **G. Firestein**, Eli Lilly, 2.

Abstract Number: 0750

Nuclei Detection in Rheumatoid Arthritis Synovial Tissue Using Artificial Intelligence

Steven Guan[1], David Slater[1], James Thompson[1], Edward DiCarlo[2], Diyu Pearce-Fisher[2], Susan Goodman[3], Bella Mehta[4] and Dana Orange[5], [1]MITRE, McLean, VA, [2]Hospital for Special Surgery, New York, [3]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [4]Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, [5]Rockefeller University, New York

SESSION INFORMATION

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Background/Purpose: Hematoxylin and eosin (H&E) stained rheumatoid arthritis synovium are routinely used to assess inflammation [1]. In this work, we propose an automated approach using artificial intelligence (AI) to quantify all cell nuclei in whole slide H&E stained images. This approach provides quantitative information on the number and

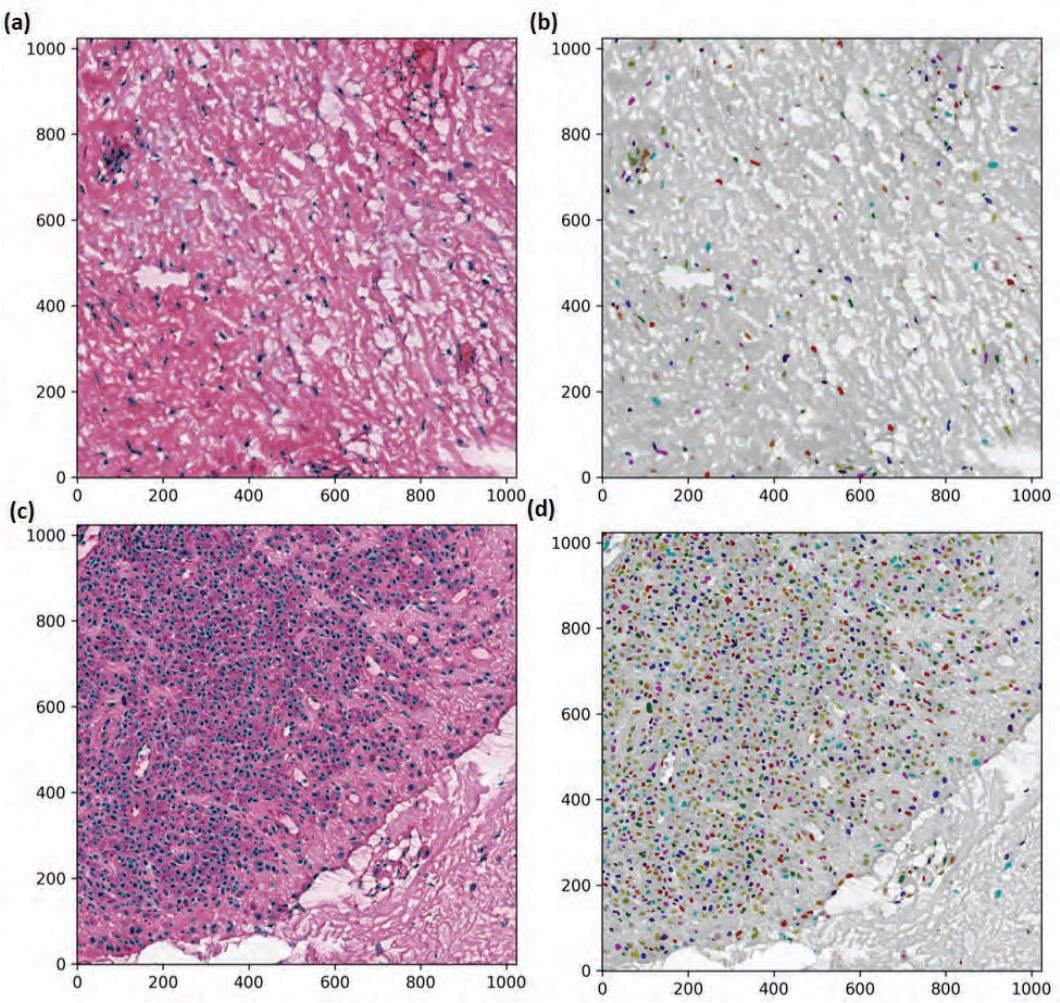

Figure 1. Nuclei identified using the proposed AI algorithm and visualized with boundaries and masks for tiles with mild (a-b) and band-like (c-d) lymphocytic inflammation.

	Class	n	Nuclei Count	Nuclei Density
RNA Subtype	Low	11	89,990 ± 56,555	303 ±114
	Mixed	13	69,360 ± 57,985	284 ± 116
	High	11	147,288 ± 56,820	417 ± 138
Lymphocytic Inflammation	0 (None)	39	65,106 ± 47,923	271 ± 111
	1 (Mild)	46	77,244 ± 52,852	285 ± 96
	2 (Moderate)	39	90,224 ± 64,876	310 ± 97
	3 (Marked)	33	140,118 ± 96,961	398 ± 142
	4 (Band-like)	9	202,084 ± 92,717	459 ± 185

Table 1. RA cohort description of nuclei count and density by RNA subtypes and pathologist lymphocytic inflammation scores.

density of nuclei in synovial images. Given nuclei density is generally increased in sites of inflammation, this approach can identify areas of interest for further evaluation [2].

Methods: The proposed AI algorithm was used to segment cell nuclei in H&E-stained images. First, we split the whole slide image into 1024x1024 tiles with a resolution of 50 µm. Each tile was then processed as follows: 1) separate stained components using color deconvolution, 2) binarize image using local adaptive thresholding, 3) split clustered nuclei using the watershed algorithm, and 4) remove false-positive detected nuclei using shape analysis. Finally, the total nuclei count normalized for area of tissue and the nuclei density were calculated. In total, 166 H&E stained images were analyzed, and corresponding synovial tissue samples were classified by pathologist score of lymphocytic inflammation (0-4). Of which, 35 samples were also classified by RNA sequencing gene expression

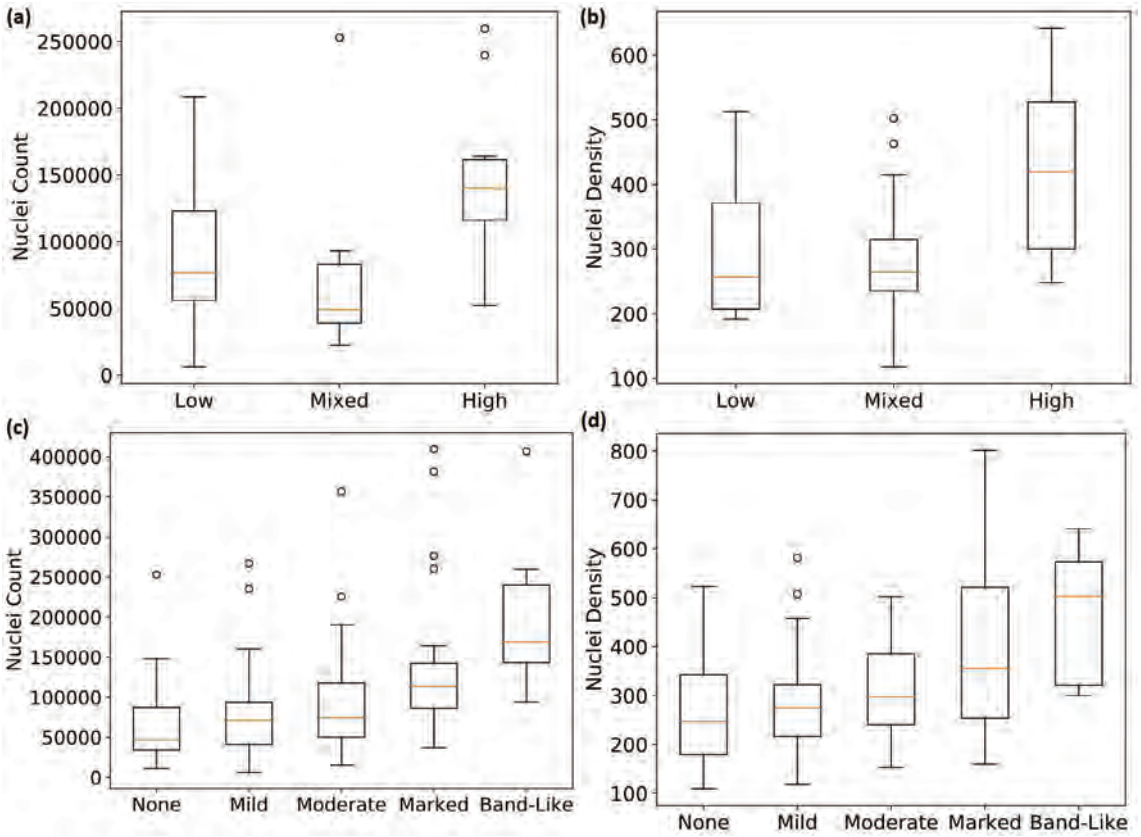

Figure 2. Boxplots to visualize distribution of nuclei count and density by RNA subtypes (low, mixed, and high inflammatory) (a-b) and lymphocytic inflammation scored by pathologist (c-d).

cluster (low, mixed, and high inflammatory gene expression) as previously described [1]. A one-way ANOVA test and post-hoc analysis using the Tukey's test corrected for multiple comparisons were conducted.

Results: Upon visual inspection, the algorithm identified majority of the nuclei in a tile, as seen in Figure 1. There was a statistically significant difference in the mean nuclei count and nuclei density between the gene expression subtypes ($p=0.01$, $p=0.03$) as well as pathologist scores of lymphocytic infiltration ($p< 0.01$, $p< 0.01$), as seen in Table 1 and Figure 2. The post-hoc analysis revealed that the mean normalized nuclei count and nuclei density was significantly different between the mixed and high-inflammatory subtypes ($p=0.01$, $p=0.03$) and between the lowest and highest lymphocyte pathologist scores ($p< 0.01$, $p< 0.01$).

Conclusion: Automated image quantification of H&E stained nuclei suggests that nuclei count and density are increased in synovial samples with high inflammatory gene expression and high pathology scores of synovial lymphocytic inflammation. Additional algorithm validation is needed to better understand its limitations. This approach provides a quantitative framework to score stained images and identify abnormal or inflamed areas. Future efforts will attempt to identify other histological features which might be clinically useful for assessing RA synovium.

Disclosure: S. Guan, None; **D. Slater**, None; **J. Thompson**, None; **E. DiCarlo**, None; **D. Pearce-Fisher**, None; **S. Goodman**, Pfizer, 1, Novartis, 1, UCB, 1, regenosine, 1, 2, Horizon, 1; **B. Mehta**, None; **D. Orange**, None.

Abstract Number: 0751

Serum Interferon-Alpha Levels Could Help Identify a Subgroup of Rheumatoid Arthritis with Poorer Physical Function and Higher Physician Global Assessment

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
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Background/Purpose: Our objective was to identify the clinical significance of serum interferon-alpha levels in patients with established rheumatoid arthritis (RA).

Methods: Serum samples and clinical data including demographic information, body mass index measured in kg/m^2, seropositivity, medications were obtained for 173 RA patients who were enrolled in the University of Pittsburgh Rheumatoid Arthritis Comparative Effectiveness Registry (RACER). Patients who underwent clinical evaluations and completed three self-report questionnaires (PainDETECT, Patient-Reported Outcomes Measurement Information System (PROMIS) 29, Widespread Pain Index/Symptom Severity Scale) were included. Serum cytokines including interleukin (IL)-1 beta, IL-6, and interferon (IFN)-alpha were measured on serum samples using enzyme-linked immunosorbent assay.

Results: Among those patients (N=18) who had detectable IFN-alpha, there were significant differences observed for physician global assessment, physical function, depression, and abilities to participate in social roles, compared with patients who did not have IFN-alpha detected. (Table 1) Those who had detectable IFN-alpha had a poorer physical function and impaired abilities to participate in social roles. (Figure 1) Although there was no statistically significant difference, those who have detectable IFN-α tend to have a higher number of swollen joints, higher seropositivity, and higher pain interference. Interestingly, inflammatory cytokines such as IL-1 beta, IL-6, and C-reactive protein (CRP), pain levels, and RA disease activity scores such as disease activity score 28-CRP and clinical disease activity index were not different between the patients with detectable IFN-alpha and without. (Table 1)

Conclusion: This study highlights the potential roles of serum IFN alpha as a biomarker in identifying a distinct subgroup of patients among those who have similar RA disease activity scores.

Table 1. Comparison of clinical characteristics and serum cytokine levels by Interferon alpha status

Characteristics	Undetected (N=142)	Detected (N=18)	P value
Age (median [IQR])	60 [51-68]	59 [55-72]	0.185
Gender (N(%))			
Female	119 (84.4)	15 (88.2)	0.953
Race (N (%))			
White	122 (87.8)	16 (94.1)	0.711
Body mass index	29.39 (7.08)	29.87 (7.05)	0.792
Seropositivity			
Rheumatoid factor	88 (72.7)	10 (100.0)	0.126
Anti-cyclic citrullinated peptide	81 (74.3)	9 (100.0)	0.182
Disease activity (mean (SD))			
Total swollen joint	1.55 (2.72)	3.00 (4.34)	0.056
Total tender joint	1.80 (2.65)	2.59 (4.37)	0.288
Physician global assessment	2.02 (1.72)	3.35 (3.04)	0.007
Patient global assessment	3.84 (2.64)	3.86 (2.83)	0.974
Clinical disease activity index	9.16 (7.46)	12.68 (12.74)	0.096
DAS28-CRP*	2.41 (0.98)	2.52 (1.47)	0.698
PROMIS score (mean t score (SD)) *			
Physical function	42.33 (8.64)	37.26 (8.08)	0.023
Anxiety	49.57 (9.63)	52.53 (12.13)	0.246
Depression	48.14 (8.54)	53.68 (10.33)	0.015
Fatigue	51.88 (10.28)	53.88 (10.55)	0.452
Sleep disturbance	51.81 (8.41)	53.65 (9.07)	0.398
Abilities to participate in social role	50.97 (9.22)	45.65 (9.21)	0.026
Pain interference	55.52 (8.89)	59.54 (9.37)	0.082
1-wk average pain level (mean (SD))	4.16 (2.52)	4.12 (2.83)	0.945
Fibromyalgia (N (%))	13 (9.6)	2 (11.8)	1
Neuropathic pain by PainDETECT (N (%))	15 (10.9)	3 (16.7)	0.579
CRP (mean (SD))	1.01 (1.82)	0.74 (0.85)	0.541
IL1 beta (mean (SD))	0.18 (0.73)	0.17 (0.60)	0.969
IL6 (mean (SD))	4.01 (3.28)	3.28 (3.17)	0.383

*IQR: interquartile range, PROMIS: Patient-Reported Outcomes Measurement Information System, IL: interleukin, CRP:C reactive protein

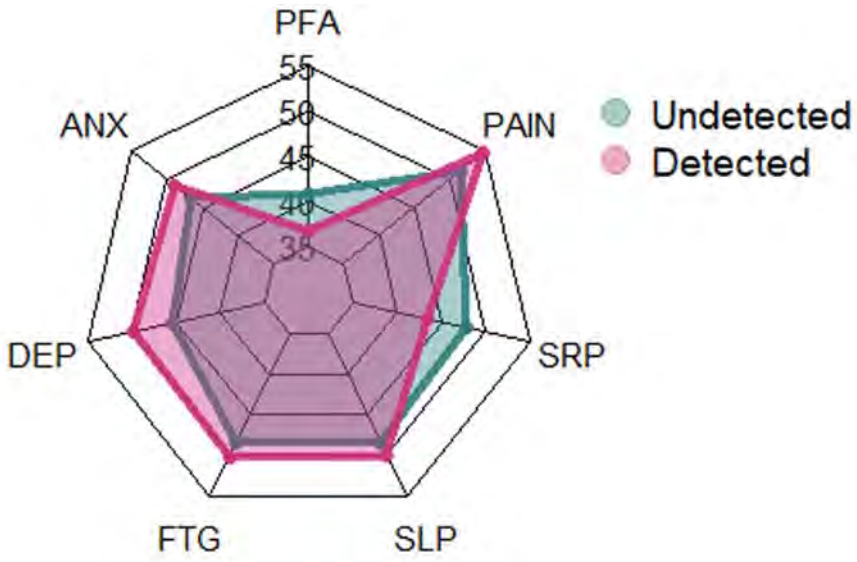

Figure 1. Comparison of 7 patient-reported outcomes measurement information system (PROMIS) domains by serum interferon alpha status (PFA: physical function, ANX: anxiety, DEP: depression, FTG: fatigue, SLP: sleep disturbance, SRP: Abilities to participate in social role, PAIN: pain interference)

Disclosure: Y. Hwang, None; **L. Zhu**, None; **D. Wu**, None; **L. Moreland**, None.

Abstract Number: 0752

Serum Proteomics Implicates Neutrophil Degranulation in Rheumatoid Arthritis Disease Activity

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Though targeted therapeutics have improved outcomes in Rheumatoid Arthritis (RA) treatment, the understanding of the underlying biological mechanisms that mediate inflammatory arthritis in RA is incomplete. We aimed to use unsupervised proteomics to identify serum proteins and active mechanistic networks that are associated with disease activity in RA.

Methods: Using the SOMAscan (slow off-rate modified aptamer) array, we generated quantitative levels of 1307 proteins in serum samples from 68 RA patients. Differentially expressed proteins between patients with high disease activity (HDA, DAS28 > 3.2) relative to low disease activity (LDA) were determined using linear modeling and visualized with hierarchical clustering. Spearman correlation was used to determine the relationship between individual proteins and DAS28, a disease activity score widely use in RA. Correlation adjusted mean rank (CAMERA) competitive gene

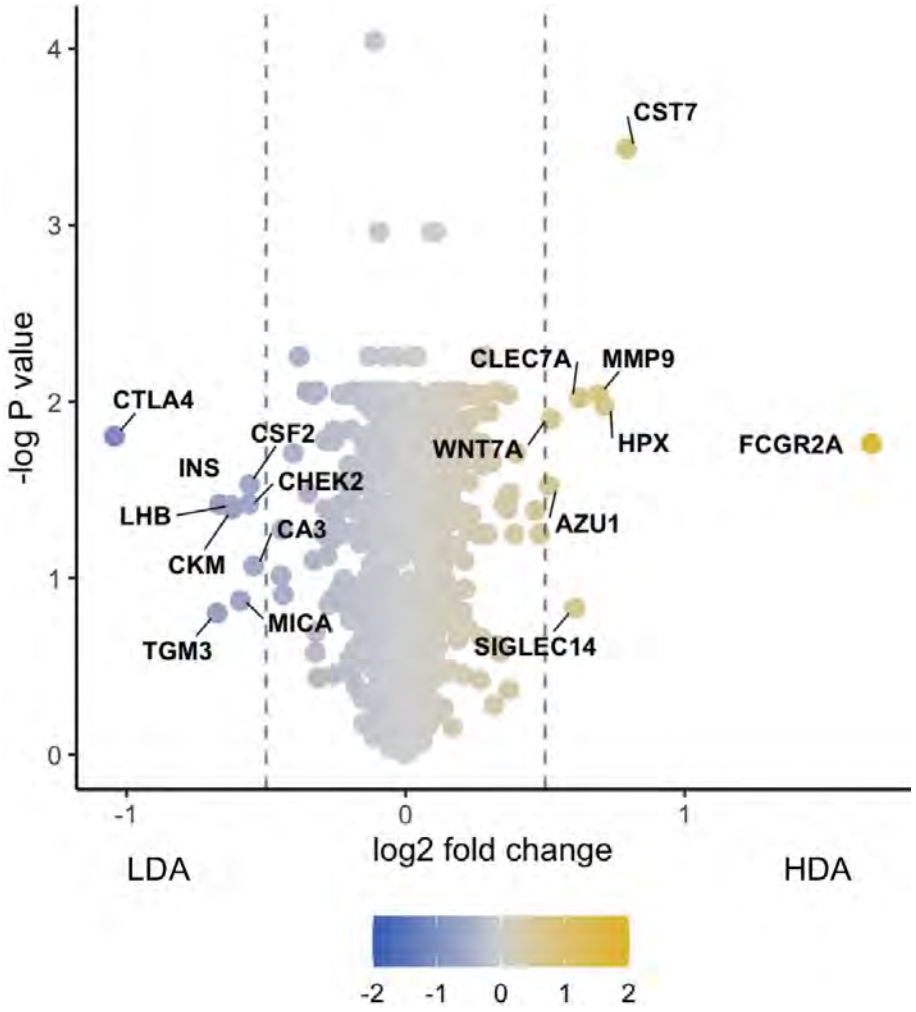

Figure 1. Volcano plot depicting fold differences between low disease activity RA patients (LDA) and high disease activity RA patients (HDA), coloured by magnitude of fold change.

set testing was performed to identify pathway enrichment while accounting for inter-gene correlation. Network analysis was then performed using Clusterprofiler and gene-concept network.

Results: 50% (n = 34) of the cohort were classified as HDA DAS28 (median 4.49 +/- 0.89) while 50% (n = 34) were LDA DAS28 (median 2.68, +/- 0.82). Principle components analysis based on expression of all proteins did not clearly separate HDA from LDA patients. *CST7 (*Fold Change (FC) = 6.2)) , *ELANE* (FC = 1.1), *S100A12* (FC = 1.9, $p < 0.001$) were all highly upregulated in HDA, while *CTLA4* (FC = 11.1) was the highest upregulated protein in LDA. Correlation between DAS28 and SERPINA3 ($R = 0.53$, $p = 2.4 \times 10^{-6}$) and S100A12 ($R = 0.46$, $p = 8.6 \times 10^{-5}$) were numerically higher than CRP (0.42, $p = 0.0003$). Gene-concept plotting linked *extracellular matrix disassembly*, *endopeptidase activity*, *platelet degranulation*, *and leukocyte migration/antimicrobial humoral response* with 19 upregulated proteins. Gene set enrichment identified *Immature Neutrophil* upregulation as one of the highest enriched gene networks in HDA ($p = 1.49 \times 10^{-4}$).

Conclusion: Our rich proteomic dataset provides a foundation for understanding of the underlying biological processes that underpin active RA. In particular, we identified proteins that implicate systemic neutrophil degranulation as a highly active process in RA, which may link systemic inflammation and tissue destruction in these individuals.

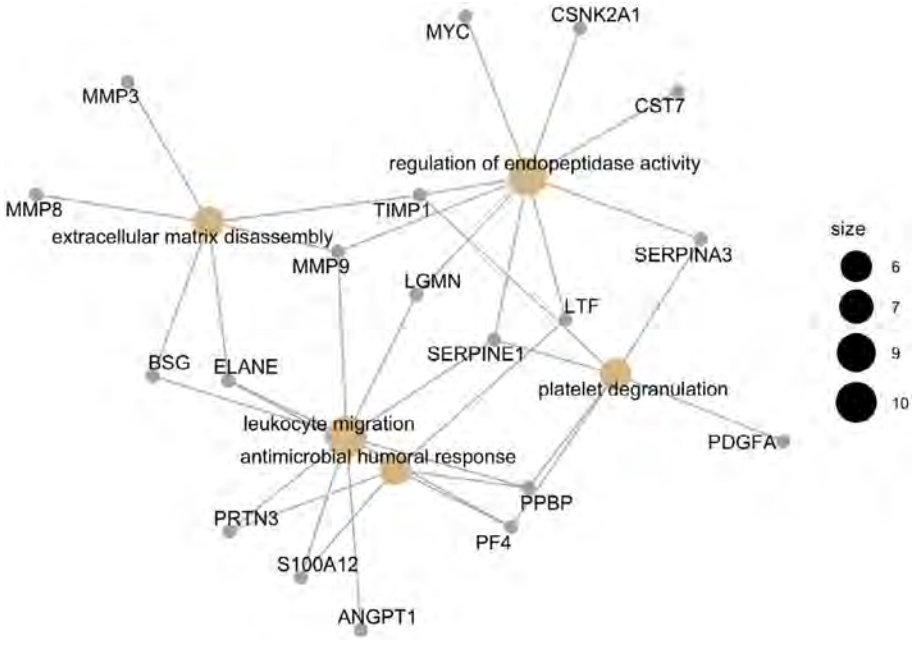

Figure 2. Gene network of protein interactions linked with GO biological processes using gene-concept plotting. Size of nodes are reflective of member inclusion. All protein members are upregulated in high disease activity relative to low disease activity.

Disclosure: L. O'Neil, None; **V. Anaparti**, None; **D. Wiens**, None; **I. Smolik**, None; **X. Meng**, None; **H. El-Gabalawy**, None.

Abstract Number: 0753

Synovial Tissue Histopathology Findings in Early RA. Is It Useful? Analysis of the Belgian CAP48 Cohort

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers

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Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis is a heterogeneous disease with different clinical presentation and prognostic factors including the immune process in the synovium. The development of ultrasound-guided synovial biopsy will enable synovial tissue collection from small joints and will facilitate histopathological studies, thus improving the understanding of the immunopathology in early rheumatoid arthritis (ERA).

	Total N=152	Pauci-immun N=33	Inflammatory N=119	Hyperplasia No Score 0-1 N=76	Hyperplasia Yes Score >1 N=76
Sex F/H, % F	96/56, 63.2%	21/12, 63.6%	75/44, 63.0%	50/26, 65.8%	46/30, 60.5%
ACPA No/Yes, % ACPA+	57/94, 62.3%	8/25, 75.8%	49/69, 58.5%	21/55, **72.4%** *	36/39, **52%** *
FR No/Yes, % FR+	53/97, 64.7%	7/25, 78.1%	46/72, 61.0%	21/54, 72.0%	32/43, 57.3%
Baseline erosions No/Yes, % Yes	93/58, 38,4%	24/9, 27.3%	69/49, 41.5%	48/28, 36.8%	45/30, 40.0%
Age at diagnosis, years mean±SD	48.3±15.2	44.5±14.4	49.4±15.2	47.5±13.7	49.2±16.5
CRP, mean±SD	2.72±3.75	**1.22±1.05***	**3.14±4.11***	**1.67±1.90***	**3.97±4.76***
DAS28-CRP, mean±SD	4.8±1.2	4.7±1.2	4.8±1.2	4.7±1.3	4.9±1.1

Table 1. Baseline characteristics of the cohort ; (*) P<0,05

The objectives of this ERA cohort are to compare the baseline clinical, biological and radiological characteristics and the clinical response on methotrexate (MTX) according to the histological "inflammatory pattern" of the synovial tissue.

Methods: 152 ERA patients fulfilling the ACR/EULAR 2010 criteria and naïve to DMARDs therapy were recruited from our Brussels Louvain ERA cohort. Synovial biopsies before treatment were obtained using an ultrasound guided needle biopsy (US-NB) of the small joints or miniarthroscopy of the knee. RA disease activity measures including DAS28-CRP were evaluated every 3 months on MTX treatment. Tissues were assessed for quality. Retrieved tissue was fixed, stained and paraffin embedded for blinded tissue pathotype description.

The pathotypes were divided in 2 groups according the absence or presence of *inflammatory infiltrates* (pauci-immune, score 0-1 *vs* inflammatory, score 1-6) and absence or presence of *synovial hyperplasia* (score >1).

Results: The average age of population is 48.3 years. 63.2% of the patients are women. 24.6% are smokers and 62.3% are positive for anti-citrullinated protein antibody (ACPA). Baseline characteristics of the cohort are summarized in Table 1. There was a significant predominant presence of ACPA+ (%) in the group without synovial hyperplasia. CRP levels were significantly higher in patients with the inflammatory pattern than those with the pauci-immune pattern. Synovial hyperplasia was also associated with these parameters.

A significantly higher rate of SJC was observed in the group with synovial hyperplasia compared to the group without hyperplasia.

Clinical response (DAS-44, SJC and CRP) was statistically better after 3 months of MTX treatment in patients with baseline inflammatory and hyperplasia pathotypes and CRP remained lower at 6 and 12 months compared to the pauci-immune group.

Conclusion: Synovial tissue analysis allows us to better define the spectrum of ERA. We have demonstrated a predominance of ACPA positive patients in pauci-immune synovial pathotypes. A better clinical response to MTX was observed in patients presenting inflammatory infiltrates or synovial hyperplasia. Further studies should validate a step change towards personalized medicine in daily clinical practice for disease stratification and treatment selection of ERA.

Disclosure: S. de Montjoye, None; **T. Sokolova**, None; **E. Sapart**, None; **B. Lauwerys**, None; **S. Dierckx**, None; **C. Galant**, None; **L. Meric de Bellefon**, None; **A. Nzeusseu Toukap**, AbbVie, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, UCB, 1, 2, Novartis, 1, Celgene Corporation, 1, Pfizer, 1; **C. Triaille**, None; **P. Durez**, None.

Abstract Number: 0754

The Association Between Continuous Decreases in Serum RF Titers and Radiographic Remission of Joint Damage in RA Patients Treated with Biological or Targeted Synthetic DMARDs

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid factors (RFs) are RA-related autoantibodies like anti-cyclic citrullinated peptide antibodies, and are used for classifying and diagnosing RA. In addition, positivity and high titers in serum RFs are risk or prognostic factors of joint damage for both early and established RA patients. However, it remains unclear whether the changes in serum RF titers are correlated with progressions of joint damage in RA. The purpose of this study is to clarify whether continuous decreases in RF titers during treatment with biological or targeted synthetic DMARD (b/tsDMARD) were associated with radiographic remission in progression of RA joint damage.

Methods: 130 RA patients were enrolled, who filled RA criteria 2010, were treated with b/tsDMARD for more than 4 months, had serum RF titers above 45 IU/ml at starting therapy (month 0), and were followed up until month 12. Serum RF titers were measured at month 0, 4 and 12 after starting b/tsDMARD therapy, and continuous RF decreases were defined as not less than 10% decreases in RF titers during both month 0-4 and 4-12. RA disease activity was assessed by DAS28-ESR at month 0, 4 and 12, and time-integrated DAS28-ESR was calculated. Joint damage was assessed by modified total Sharp score (mTSS) at month 0 and 12, and radiographic remission was defined as yearly mTSS progression below 0.5. Their medical records were reviewed retrospectively. In case of withdrawal from b/tsDMARD therapy during month 4-12 due to some causes, data upon the discontinuation of b/tsDMARD was used as that at month 12 using the last observation carried forward method. Baseline demographic, disease- and RF-related variables were included in univariate and multivariate logistic regression analysis for identifying the factors related to radiographic remission.

Results: Subjects were 102 female, were median age 61.7 years with 4.8 years of disease duration, and were treated with abatacept (n=27), JAK inhibitors (n=9), tocilizumab (n=39) and TNF inhibitors (n=55) in addition to MTX (median dose; 8 mg/week). Serum RF titers decreased from 127 IU/ml (month 0, median) to 89.5 (month 4, $p=0.0022$) and 84.5 (month 12, $p=0.0115$). DAS28-ESR improved from 3.92 (month 0, median) to 2.65 (month 4, $p< 0.0001$) and 2.58 (month 12, $p< 0.0001$). 65 of 130 subjects achieved radiographic remission in mTSS at month 12. During b/tsDMARD therapy, 46 of 130 patients showed continuous decreases in serum RF titers (CD group), and 84 cases did not (non-CD group). Compared with non-CD patients, CD had younger age of RA onset ($p=0.0456$), higher ratio of anti-TNF therapy ($p=0.0170$), lower DAS28-ESR at month 12 ($p=0.0404$) and higher ratio of radiographic remission in mTSS

(p=0.0056). In multivariate analysis, continuous decreases in serum RF titers were associated with radiographic remission in mTTS (OR=3.7316; 95% CI:1.5427–9.5980) in addition to time-integrated DAS28-ESR.

Conclusion: Continuous decreases in serum RF titers were associated with radiographic remission of mTSS in RA patients treated with b/tsDMARD. The changes in serum RF titers may become a prognostic factor for joint damage in RA.

Disclosure: T. Owada, None; **A. Tanaka**, None; **H. Hirata**, None; **M. Arima**, None; **Y. Fukushima**, None; **K. Kurasawa**, None.

Abstract Number: 0755

Exploring the Significance of Anti-Nuclear Antibody Positivity in the Medical Management of Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: ANA testing has been a well-established screening tool for autoimmune conditions such as SLE. Current practice for classification of RA does not include ANA positivity; however, ANA testing is performed in many patients who are ultimately diagnosed with RA. In the general population, ANA positivity is thought to be increasing in prevalence and has been associated with elevated rates of all-cause mortality and cardiovascular events (1-2). ANA positivity has also been studied in patients with RA who are taking TNF-α inhibitors who develop "lupus-like syndrome" (3). There is a gap in the understanding of the role a positive ANA has in the management of

Table 1:Patient Characteristics by ANA Testing

	ANA tested * (N=161)	ANA not tested (N=91)	Total (N=252)	p value
Age at fulfilment of 1987 or 2010 criteria, years, mean (SD)	54.0 (14.1)	58.5 (15.1)	55.6 (14.6)	0.031
Sex, female	109 (68%)	61 (67%)	170 (67%)	0.91
Smoker				
Never	95 (59%)	44 (48%)	139 (55%)	0.19
Current	22 (14%)	19 (21%)	41 (16%)	
Former	44 (27%)	28 (31%)	72 (29%)	
Obesity (BMI ≥30 kg/m^2)	61 (38%)	39 (43%)	100 (40%)	0.44
RF and/or CCP positive	105 (65%)	45 (49%)	150 (60%)	0.014

*ANA tested within +/- 90 days of RA diagnosis

Table 2: Patient Characteristics by ANA Positivity				
	Positive* (N=41)	Negative (N=120)	Total (N=161)	p value
Age at fulfilment of 1987 or 2010 criteria, years , mean (SD)	51.0 (12.5)	55.0 (14.6)	54.0 (14.1)	0.080
Sex, female	33 (80%)	76 (63%)	109 (68%)	0.043
Smoker				0.10
Never	29 (71%)	66 (55%)	95 (59%)	
Current	2 (5%)	20 (17%)	22 (14%)	
Former	10 (24%)	34 (28%)	44 (27%)	
Obesity (BMI ≥30 kg/m^2)	17 (41%)	44 (37%)	61 (38%)	0.58
RF and/or CCP positive	27 (66%)	78 (65%)	105 (65%)	0.92

*ANA positivity defined ANA level ≥1U by ELISA or IF titer of ≥1:80

Table 3 : Patient characteristics of RF/CCP positive and negative patients by ANA positivity						
	ANA+, RF/CCP+ (N=27)	ANA-, RF/CCP+ (N=78)	p value	ANA+, RF/CCP- (N=14)	ANA-, RF/CCP- (N=42)	p value
Age at earlier of fulfilment of 1987 or 2010years, mean (SD)	48.9 (12.3)	55.1 (14.5)	0.05	54.9 (12.5)	54.9 (14.8)	0.895
First DMARD used			0.19			0.48
MTX	13 (48%)	55 (71%)		8 (57%)	15 (36%)	
HCQ	12 (44%)	18 (23%)		5 (36%)	22 (52%)	
Leflunomide	0 (0%)	2 (3%)		0 (0%)	0 (0%)	
Sulfasalazine	1 (4%)	1 (1%)		1 (7%)	3 (7%)	
Other	1 (4%)	2 (3%)		0 (0%)	2 (5%)	
MTX used first	13 (48%)	55 (71%)	0.036	5 (36%)	22 (52%)	0.28
HCQ used first	12 (44%)	18 (23%)	0.034	8 (57%)	15 (36%)	0.16
Days from first joint swelling to fulfillment of 1987 criteria, median (IQR)	16 (0, 120)	0 (0, 12)	0.022	2 (0, 354)	21 (0, 121)	0.26
Days from first joint swelling to fulfillment of 2010 criteria, median (IQR)	3 (0, 59)	0 (0, 10)	0.067	4 (0, 196)	0 (0, 91)	0.56
Days from first joint swelling to first DMARD, median (IQR)	41 (5, 160)	13 (0, 73)	0.084	98 (14, 283)	16 (3, 125)	0.20
Days from first joint swelling to first steroid, median (IQR)	50 (4, 567)	7 (0, 53)	0.036	1 (0, 47)	0 (0, 12)	0.43

RA. The aim of this study is to describe differences in the clinical course, treatment, and outcomes of patients with RA who are ANA positive as compared to those who are ANA negative.

Methods: The study design is a retrospective, population-based cohort study of 252 residents of a geographically-defined area who first fulfilled 1987 ACR criteria for RA in 1999-2014 assembled using the resources of the Rochester Epidemiology Project (REP). Data was collected on first documentation of joint swelling, RF or CCP antibody

testing, ANA level ≥1U by ELISA or IF titer of ≥1:80, and pharmacotherapies. Comparisons between groups were performed using chi-square and rank sum tests.

Results: Sixty-four percent of RA patients in the cohort were tested for ANA within ±90 days of RA criteria fulfillment. Patients tested for ANA were more likely to be younger and to be RF or CCP seropositive. In the 161 patients with ANA testing, 25% were ANA positive (Table 1). ANA positive patients were slightly younger, were less likely to be male and somewhat less likely to be current smokers (Table 2). In terms of diagnostics, there were no differences in RF/CCP or RA criteria met, though in patients with seropositivity, the time from joint swelling to fulfillment of RA criteria was increased for ANA positive patients. The length of time to first DMARD initiation in the ANA positive patients was also increased. ANA positive patients were more likely to receive HCQ over MTX as a first treatment (Table 3). ANA positive patients were less likely to receive biologic therapy, but this association did not reach statistical significance.

Conclusion: ANA positivity does not differ between seropositive and seronegative RA patients. However, there is a difference in the time to fulfillment of RA criteria, time to treatment with DMARD, as well as in choice of initial pharmacotherapy with more ANA positive patients receiving HCQ over MTX. These findings may indicate a difference in patient presentation or clinical perception of RA patients with ANA positivity. Further research is needed to better understand what drives the treatment rationale for ANA positive, RA patients and what implications that may have for their health outcomes.

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Abstract Number: 0756

Increased Risk of Hospitalization in Patients with RA Who Are ACPA Positive and Shared Epitope Positive

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: A strong genetic association between *HLA-DRB1* alleles containing the shared epitope (SE) and RA has been described.[1] The SE has been associated with ACPA positivity,[2] earlier onset of RA,[3] harder-to-treat

Table 1. Baseline demographics and disease characteristics

Parameter	ACPA+ (n=641)			ACPA– (n=320)		
	SE+ (n=466)	SE– (n=175)	p value (std. difference) for SE+ vs SE–[a]	SE+ (n=154)	SE– (n=166)	p value (std. difference) for SE+ vs SE–[a]
Age, years	57.3 (13.7)	59.1 (14.0)	0.1913 **(0.13)**	56.6 (14.7)	54.6 (14.2)	0.200 **(0.13)**
Female, n (%)	379 (81.3)	152 (86.9)	0.0983 **(0.15)**	128 (83.1)	134 (80.8)	0.5786 (0.06)
Education level, n (%)[b]						
0	14 (3.0)	10 (5.7)	0.1074 **(0.13)**	4 (26.0)	4 (2.4)	1.0000 (0.01)
1	81 (17.4)	36 (20.6)	0.3517 (0.08)	21 (13.6)	26 (15.7)	0.6088 (0.06)
2	246 (52.8)	84 (48.0)	0.2797 (0.10)	80 (51.9)	83 (50.0)	0.7276 (0.04)
3	120 (25.8)	45 (25.7)	0.9924 (0.00)	46 (29.9)	52 (31.3)	0.7778 (0.03)
Missing	5 (1.1)	0 (0.0)		3 (1.9)	1 (0.6)	
RA duration, years	16.2 (12.3)	15.1 (12.2)	0.2258 (0.10)	12.1 (12.0)	8.9 (10.1)	**0.0087 (0.29)**
Erosive disease, n (%)	302 (64.8)	109 (62.3)	0.4437 (0.08)	62 (40.3)	57 (34.3)	0.4553 (0.09)
Missing	83 (17.8)	42 (24.0)		28 (18.2)	38 (22.9)	
Extra-articular manifestation, n (%)	193 (41.4)	67 (38.3)	0.4720 (0.06)	32 (20.8)	37 (22.3)	0.7426 (0.04)
DAS28 (CRP)	4.2 (1.6)	4.0 (1.5)	0.4169 (0.08)	3.6 (1.5)	3.6 (1.6)	0.4845 (0.05)
RF+, n (%)	404 (86.7)	151 (86.3)	0.801 (0.02)	37 (24.0)	23 (13.8)	**0.02 (0.26)**
Missing	7 (1.5)	2 (1.1)		1 (0.6)	2 (1.2)	
BMI, kg/m^2	26.6 (5.8)	27.1 (5.8)	0.1626 (0.10)	26.6 (5.6)	26.7 (5.1)	0.4124 (0.04)
Missing	12 (2.6)	12 (6.9)		12 (7.8)	8 (4.8)	
Smoking, n (%)	218 (46.8)	77 (44.0)	0.7745 (0.03)	55 (35.7)	68 (41.0)	0.4306 (0.09)
Missing	36 (7.7)	19 (10.9)		17 (11.0)	14 (8.4)	
Cardiovascular flag, n (%)	71 (15.2)	23 (13.1)	0.5045 (0.06)	17 (11.0)	24 (14.5)	0.3606 (0.10)
Number of co-morbidities	2.0 (2.0)	2.0 (1.9)	0.5694 (0.02)	1.8 (1.8)	1.6 (1.6)	0.7317 (0.08)
Baseline DMARD use						
No cs/bDMARD	50 (10.7)	22 (12.6)	0.5108 (0.06)	23 (14.9)	32 (19.3)	0.3038 **(0.12)**
csDMARD	188 (40.3)	92 (52.6)	**0.0054 (0.25)**	84 (54.5)	90 (54.2)	0.9530 (0.01)
bDMARD	106 (22.7)	26 (14.9)	**0.0278 (0.20)**	18 (11.7)	21 (12.7)	0.7926 (0.03)
csDMARD & bDMARD	122 (26.2)	35 (20.0)	0.1050 **(0.15)**	29 (18.8)	23 (13.9)	0.2280 **(0.14)**

Data are mean (SD) unless otherwise stated. Patient characteristics, namely BMI, smoking status, cardiovascular flag and number of co-morbidities, are captured on index visit; closest non-null value to the index date has been used. Significant p values (<0.05) and standardized differences (>0.10) for the SE+ vs SE– patients are shown in bold.

[a]Calculated using Chi squared (categorical variables) and Kruskal–Wallis (continuous variables) tests

[b]Education level: 0 – did not graduate high school, 1 – high school graduate, 2 – any college education, 3 – graduate education

bDMARD=biologic DMARD, csDMARD=conventional synthetic DMARD, SE=shared epitope

disease[2] and poor prognosis.[4] The purpose of this analysis was to assess whether ACPA and SE status are associated with risk of hospitalization in RA.

Table 2. Hospitalizations and causes of hospitalizations in ACPA+ and ACPA– patients stratified by SE status

Parameter	ACPA+ (n=641)			ACPA– (n=320)		
	SE+ (n=466)	SE– (n=175)	p value (std. difference) for SE+ vs SE–[a]	SE+ (n=154)	SE– (n=166)	p value (std. difference) for SE+ vs SE–[a]
Outcomes at 6 months after index date						
Hospitalization	422 (90.6)	151 (86.3)		135 (87.7)	143 (86.1)	
Yes	52 (12.3)	8 (5.3)	**0.0156 (0.24)**	11 (8.1)	17 (11.9)	0.3004 **(0.12)**
No	370 (87.7)	143 (94.7)		124 (91.9)	126 (88.1)	
Missing	44 (9.4)	24 (13.7)		19 (12.3)	23 (13.9)	
Cause of hospitalization						
Infection	3 (5.8)	1 (12.5)	0.4448 **(0.24)**	1 (9.1)	0 (0.0)	0.4231 **(0.45)**
Joint replacement	16 (30.8)	2 (25.0)	1.000 **(0.13)**	0 (0.0)	2 (11.8)	0.4923 **(0.56)**
CV condition	10 (19.2)	0 (0.0)	0.3301 **(0.69)**	3 (27.3)	2 (11.8)	0.6196 **(0.35)**
Other[b]	23 (44.2)	5 (62.5)	0.4544 **(0.37)**	7 (63.6)	11 (64.7)	0.0709 **(0.21)**
Missing	0 (0.0)	0 (0.0)		0 (0.0)	2 (11.8)	
Outcomes at 24 months after index date						
Hospitalization	455 (97.6)	166 (94.9)		146 (94.8)	153 (92.2)	
Yes	132 (29.0)	35 (21.1)	**0.0487 (0.13)**	31 (21.2)	37 (24.2)	0.5430 (0.07)
No	323 (71.0)	131 (78.9)		115 (78.8)	116 (75.8)	
Missing	11 (2.4)	9 (5.1)		8 (5.2)	13 (7.8)	
Cause of hospitalization						
Infection	13 (9.9)	7 (20.0)	0.1417 **(0.28)**	4 (12.9)	0 (0.0)	**0.0374 (0.57)**
Joint replacement	30 (22.7)	5 (14.3)	0.2588 **(0.23)**	3 (9.7)	6 (16.2)	0.4943 **(0.20)**
CV condition	26 (19.7)	4 (11.4)	0.2432 **(0.24)**	6 (19.4)	6 (16.2)	0.7174 (0.09)
Other[a]	61 (46.2)	19 (54.3)	0.4392 **(0.15)**	16 (51.6)	23 (62.2)	0.1064 **(0.22)**
Missing	2 (1.5)	0 (0.0)		2 (6.5)	2 (5.4)	

Hospitalizations recorded within 6 months of the index date and within 24 months of the index date. Significant p values (<0.05) and standardized differences (>0.10) for the SE+ vs SE– patients are shown in bold.

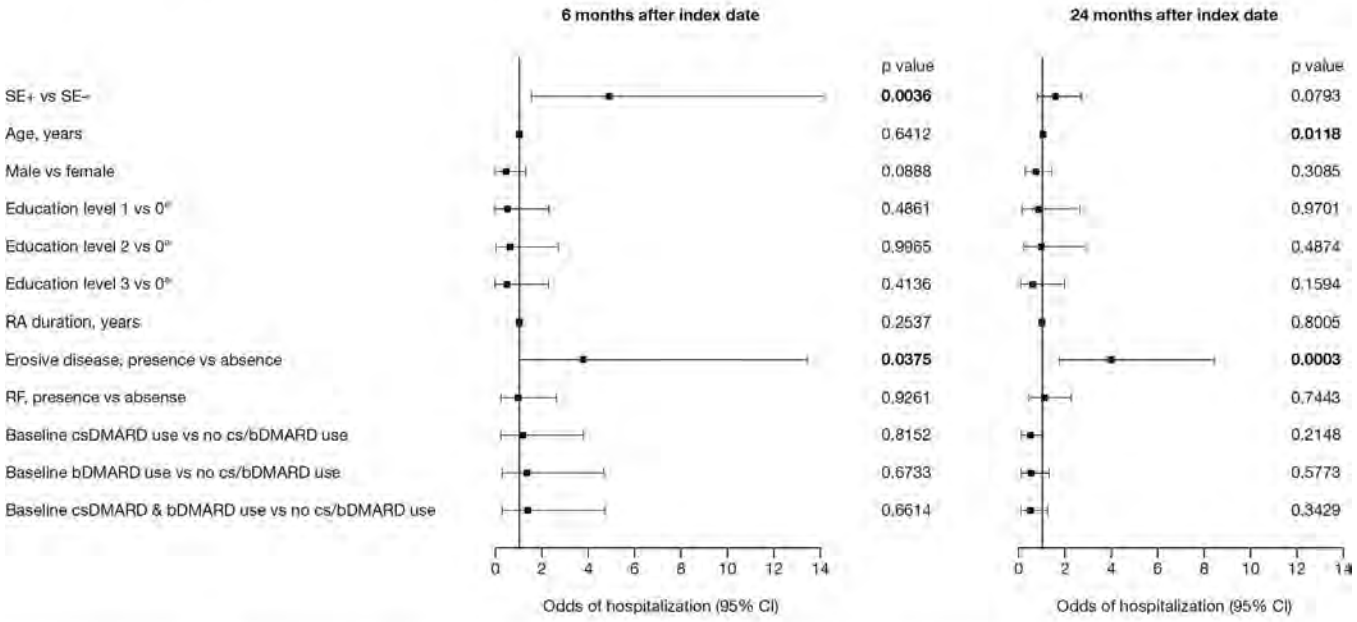
[a]Calculated using Chi squared tests.

[b]Common reasons include: gynecological surgery, colonoscopy, eye surgery, oral surgery, partial hysterectomy and gastric bypass.

CV=cardiovascular; SE=shared epitope

Methods: This was a retrospective analysis of patients (pts) enrolled in the Brigham and Women's Rheumatoid Arthritis Sequential Study (NCT01793103; BRASS) registry between March 2003 and June 2019. Pts with known ACPA and SE status were included. *HLA-DRB1* SE status (1 or 2 alleles [+], 0 alleles [–]) was determined by allele-specific polymerase chain reaction and DNA sequencing for most pts and by genome-wide association study-based imputation for the others. Pts were stratified by ACPA and SE status. Index date was the date of the baseline visit. Baseline demographics and disease characteristics, hospitalization rates (yes/no) and causes of hospitalization over 6 and 24

Figure 1. Odds of hospitalization at 6 and 24 months among ACPA+ patients



Total number of observations: 641 (6 and 24 months); number of observations used: 454 (6 months) and 491 (24 months). Significant p values are shown in bold.
[a]Education level: 0 (reference) – did not graduate high school, 1 – high school graduate, 2 – any college education, 3 – graduate education.
bDMARD=biologic DMARD; csDMARD=conventional synthetic DMARD; SE=shared epitope.

months were reported descriptively. Associations between SE status and hospitalization were examined using multivariable adjusted logistic regression models.

Results: Of 961 pts with known ACPA and SE status included in the analysis, 641 were ACPA+ and 620 were SE+ (466 [48%] were both ACPA+ and SE+). In ACPA+ pts, most baseline characteristics were similar between those who were SE+ and SE– (**Table 1**); SE+ vs SE– pts were more likely to receive conventional synthetic or biologic DMARDs. Among ACPA– pts, SE+ vs SE– pts had longer RA duration and were more likely to be RF+. Among ACPA+ pts 6 months after index date, the rate of hospitalization in SE+ pts was twice that for SE– pts (12.3% vs 5.3%; p=0.0156); joint replacement and cardiovascular (CV) conditions combined were more common causes of hospitalization in SE+ pts (50%) than SE– pts (25%; **Table 2**). Similarly, among ACPA+ pts 24 months after index date, the rate of hospitalization remained significantly higher for SE+ vs SE– pts (29% vs 21%; p=0.0487), with joint replacement and CV conditions combined being more common causes of hospitalization (SE+, 42% vs SE–, 26%; **Table 2**). No noTable differences were seen in ACPA– pts. Among ACPA+ pts, the adjusted risk of hospitalization was 4.84-fold higher in SE+ vs SE– pts at 6 months (p=0.0036) and 1.56-fold higher at 24 months (p=0.0793; **Figure 1**). Overall, joint replacement and CV conditions combined accounted for 46.0% and 24.0% of hospitalizations at 6 months in SE+ vs SE– pts and 39.9% and 29.2% of hospitalizations at 24 months, respectively.

Conclusion: In ACPA+ pts with established RA, being SE+ increased the risk of hospitalization over 6 months approximately 5-fold. The majority of the increased risk in hospitalization was accounted for by joint replacement and CV conditions, indicating the more rapidly progressive disease and greater co-morbidity burden associated with SE+ in this pt population.

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Abstract Number: 0757

Sunlight Exposure, Sun-protective Behaviour, and Anti-citrullinated Protein Antibody Positivity: A General Population-based Study in Quebec, Canada

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Sunlight exposure has been associated with lower rheumatoid arthritis (RA) risk, but to our knowledge, no one has ever studied sunlight exposure and anti-citrullinated protein antibodies (ACPA). Our objective was to examine associations between sunlight exposure and ACPA using general population data from Quebec, Canada.

Methods: A random sample of 7600 individuals (including 786 positive ACPA subjects and 201 self-reported rheumatoid arthritis, RA cases) from the CARTaGENE cohort was studied cross-sectionally. All subjects were nested in four census metropolitan areas, and mixed effects logistic regression models were used to calculate odds ratios (OR) and 95% confidence intervals (CIs) for ACPA positivity related to sunlight exposure, adjusting for sun-block use, industrial fine particulate matter ($PM_{2.5}$) exposures, smoking, age, sex, French Canadian ancestry, and family income. We also performed sensitivity analyses excluding subjects with RA, defining ACPA positivity by higher titers, and stratifying by age.

Results: The adjusted ORs and 95% CIs did not suggest conclusive associations between ACPA and sunlight exposure or sun-block use, but robust positive relationships were observed between industrial $PM_{2.5}$ emissions and ACPA (OR 1.19 per $\mu g/m^3$**,** 95% CI 1.03 – 1.36 in primary analyses).

Table 1. Adjusted odds ratios, OR (95% confidence intervals, CIs) for associations between sunlight exposures and ACPA positivity (>20 U/ml)

Variables		Overall	Excluding RA
Sunlight exposure for weekdays	<30 minutes	Reference	
	30 to 60 minutes	0.89 (0.70 – 1.12)	0.85 (0.67 – 1.07)
	1 to 2 hours	1.08 (0.83 – 1.41)	1.04 (0.79 – 1.36)
	2 to 3 hours	0.87 (0.62 – 1.21)	0.79 (0.56 – 1.12)
	3 to 4 hours	0.83 (0.53 – 1.31)	0.83 (0.53 – 1.31)
	>4 hours	0.80 (0.48 – 1.35)	0.76 (0.45 – 1.29)
Sunlight exposure for weekends	<30 minutes	Reference	
	30 to 60 minutes	1.03 (0.78 – 1.36)	1.04 (0.78 – 1.39)
	1 to 2 hours	0.85 (0.63 – 1.14)	0.85 (0.63 – 1.15)
	2 to 3 hours	1.01 (0.74 – 1.38)	1.04 (0.76 – 1.44)
	3 to 4 hours	0.99 (0.68 – 1.43)	1.03 (0.71 – 1.49)
	>4 hours	1.22 (0.82 – 1.82)	1.29 (0.86 – 1.93)
Sun-block use	Rarely	Reference	
	Sometimes	0.88 (0.70 – 1.12)	0.89 (0.70 – 1.12)
	Often	1.00 (0.83 – 1.21)	0.98 (0.81 – 1.19)
Industrial $PM_{2.5}$ exposure*		**1.19 (1.03 – 1.36)**	**1.19 (1.03 – 1.36)**
Age		1.01 (1.00 – 1.02)	1.01 (1.00 – 1.03)
Sex	Male	Reference	
	Female	1.01 (0.85 – 1.20)	0.98 (0.82 – 1.16)
Ancestry	French Canadian	Reference	
	Other	0.98 (0.83 – 1.17)	1.05 (0.88 – 1.25)
Smoking	Never	Reference	
	Occasional	0.96 (0.74 – 1.23)	0.93 (0.72 – 1.21)
	Daily	1.09 (0.85 – 1.42)	1.08 (0.83 – 1.41)
Annual income level (Canadian $)	<25,000	Reference	
	25,000 to 49,999	0.98 (0.72 – 1.33)	1.00 (0.72 – 1.37)
	50,000 to 74,999	0.99 (0.73 – 1.34)	1.03 (0.75 – 1.41)
	75,000 to 149,999	0.93 (0.69 – 1.25)	0.95 (0.70 – 1.30)
	≥150,000	1.02 (0.72 – 1.44)	1.07 (0.74 – 1.53)

*OR reported per increase in 1 µg/m3 – a value well above median levels.

Table 1. Adjusted odds ratios, OR (95% confidence intervals, CIs) for associations between sunlight exposures and ACPA positivity (>20 U/ml)

Conclusion: We did not see clear links between ACPA and sunlight exposure or sun-block use, but we did note positive associations with industrial $PM_{2.5}$. Future studies of sunlight and RA (or ACPA) should consider taking air pollution exposures into account.

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Abstract Number: 0758

Anti-citrullinated Protein Antibodies Are Associated with Functional Disability in Unaffected First-degree Relatives of Rheumatoid Arthritis Patients

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The preclinical stage of Rheumatoid Arthritis (RA) is characterized by seropositivity for anti-citrullinated protein antibodies (ACPA). We (PubMed ID 30861615), and others, have shown that ACPA seropositivity is prevalent in the first-degree relatives (FDR) of RA patients. While ACPA is highly predictive of RA development in individuals who were selected by healthcare providers based on having joint symptoms such as arthralgia, the association between ACPA and self-reported symptoms in an unselected population of at-risk FDR has not been well studied. Because it has been proposed that the ACPA themselves may induce joint symptoms in the absence of joint inflammation, we sought to determine whether ACPA seropositivity is associated with self-reported symptoms and functional impairment in a large, unselected, cohort of at-risk Indigenous North American (INA) FDR of RA patients.

Methods: Baseline demographics, Health Assessment Questionnaire (HAQ), and arthritis symptom survey data were obtained from a cohort of 607 unaffected FDR of RA patients. ACPA were detected using commercial kits (CCP2 or CCP3.1) and the manufacturer's cut-off was used to define seropositivity. Associations between ACPA status and the self-report variables were analyzed by unsupervised univariate correlation, followed by logistic regression to identify variables that were independently associated with ACPA seropositivity.

Results: 51 (8.4%) individuals were ACPA positive at baseline. Because smoking was prevalent in the cohort (85.4%), we were not able to demonstrate a clear relationship with ACPA seropositivity. Although joint symptoms were common amongst FDR (53.6%), they were not associated with ACPA seropositivity. Mean HAQ scores were higher in ACPA positive individuals compared to ACPA negative (0.313 vs 0.197, $p = 0.14$), but this did not reach statistical significance. Unexpectedly, we found that compared to FDR from urban settings, FDR from rural communities were twice as likely to be ACPA seropositive (11.5% vs. 5.2%, $p < 0.001$). Logistic regression modelling showed that *Rural status* (odds ratio (OR) 3.2, 1.5 to 7.6), *Difficulty lifting a glass* (OR 4.3, 1.1 to 17.2), and *Difficulty walking on a flat surfaces* (OR 2.9, 1.1 to 7.6) were independently associated with ACPA seropositivity, after adjusting for age and sex.

Conclusion: Although we were unable to demonstrate a relationship between joint symptoms and ACPA seropositivity, functional disability is associated with ACPA, even in the absence of detectable joint inflammation. The discordance in ACPA seropositivity between rural and urban locations is intriguing and warrants further investigation.

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Abstract Number: 0759

Presence of Ultrasound Imaging Biomarkers Are Good Predictors of Arthritis Development in a Population at Risk for Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Ultrasound (US) imaging biomarkers in the context of Anti-Citrullinated Protein Antibody (ACPA) autoimmunity might play an important role in the very early detection of Rheumatoid Arthritis (RA).

Methods: Individuals with musculoskeletal complaints suspicious for rheumatic disease, and having a positive anti-CCP2 test were referred to the Rheumatology Unit. Sixty eight joint counts as well as hands, feet and any symptomatic joints by US examination were performed. US were scored for synovial hypertrophy (SH) and Doppler activity according to EULAR-OMERACT definitions. Individuals not having arthritis defined by clinical examination and ultrasound were included in the RISK RA prospective cohort. Finger and wrist tendons were examined for any signs of tenosynovitis, including evaluations between joints for bursitis. The associations of US biomarkers with arthritis development was tested (comparing proportions) using Chi-Squared or Fisher's exact tests.

Results: 288 individuals were included in the RISK RA study from year 2014 to October 2019 (79% female, 35% RF positive, median age 48 yrs: IQR: 36-58). Within a median of 38 months (IQR: 1-72) since recruitment, 28% (84/288) progressed to arthritis.

At any scan done prior to diagnosis (either inclusion or follow-up visits), two thirds (193/288) of all individuals lacked any signs of US changes with only 16% (31/193) of them developing arthritis. One third (95/288) of all individuals had at least one type of US change (tenosynovitis, synovial hypertrophy without Doppler and/or bursitis) and 56% (53/95) of them developed arthritis. A majority, 64% (61/95), of individuals with any US changes had only one type of US change.

Tenosynovitis was detected in 22% (64/288) of all individuals, more frequently in those developing arthritis (44%, 37/84) as compared to those not developing arthritis (13%, 27/204), $p< 0.0001$. The extensor-carpi-ulnaris wrist tendons were mostly affected. Synovial hypertrophy (grade 1 or 2) was detected in 11% (32/288) of all individuals, more frequently noted among those developing (21%,18/84) as compared to those not developing arthritis (7%,14/204), $p< 0.0001$. The MCP joints were mostly affected. Bursitis between MTP joints were detected in 9% (25/288) of all individuals, more frequently among those developing (13%, 11/84) as compared to those not developing arthritis (7%, 14/204), $p=0.09$.

Conclusion: Tenosynovitis, synovial hypertrophy and bursitis are useful ultrasound biomarkers for predicting arthritis development in a population at-risk for RA.

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Abstract Number: 0760

X-rays Bone Erosions Are Uncommon in Anti-CCP Positive Individuals At-risk of Rheumatoid Arthritis with Musculoskeletal Symptoms Without Clinical Synovitis, and Do Not Predict the Development of Inflammatory Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: In individuals at-risk of RA, the identification of reliable biomarkers for the future development of clinical arthritis is of critical importance for risk-stratification and management of these individuals. Imaging, in particular US and MRI, has demonstrated the potential to predict the development and timing of RA in individuals at-risk, raising important implications on disease prevention studies.

To date, there is no consensus or guideline for the most appropriate investigations to perform in this population and clinicians would often request x-rays for the assessment of joint damage in at-risk individuals who present with hand and foot symptoms. To our knowledge, no previous study has evaluated the role of x-rays in this context.

The aims of this study were to investigate the prevalence and distribution of bone erosions (BE) in the x-rays of the hands and feet in CCP positive (CCP+) at-risk individuals, and their association with the development of inflammatory arthritis (IA).

Methods: Baseline x-rays of the hands and feet and a full US protocol were performed as part of the current study. X-rays BE were reported as standard by MSK radiologists and confirmed by subsequent reading by a second independent MSK radiologist, blinded to the clinical and US findings. The Simple Erosions Narrowing Score (SENS) was calculated for BE. The presence of US synovitis and BE was explored in the areas in which x-rays BE were reported. A subset of CCP+ individuals (n=73) had repeated x-rays at the time of progression. Subjects with ≥1 follow-up visit were included in the progression analysis (n=394).

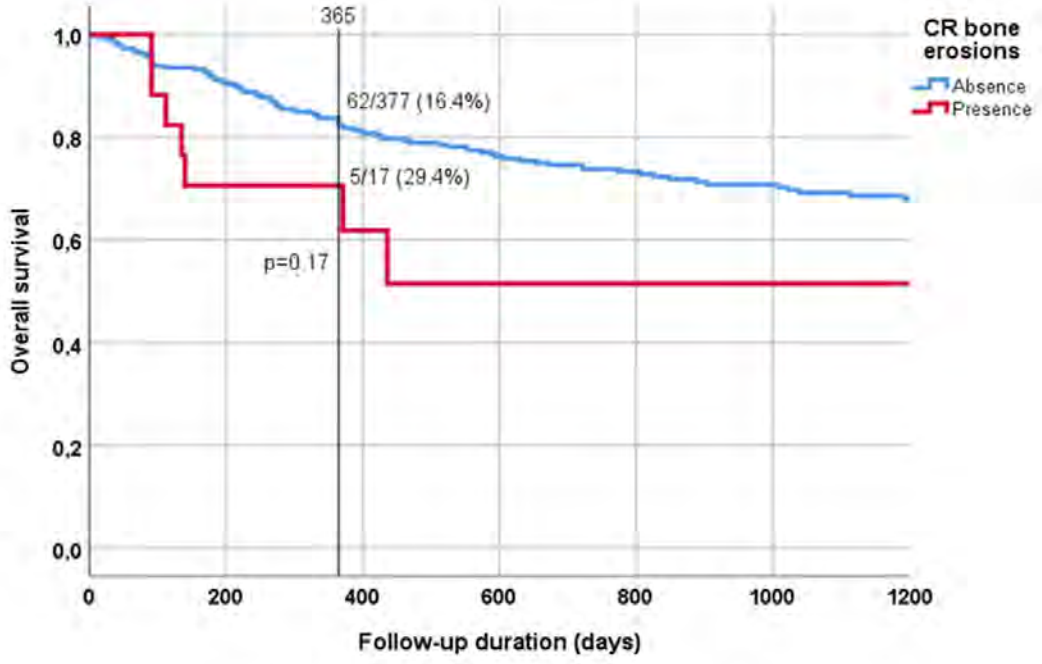
Results: The hands and feet x-rays of 418 CCP+ individuals were analysed. X-rays BE were found in 17 (4.1%), most frequently in the feet (64.7% individuals). The median SENS score was 2.0 (IQR: 1.0-2.0). Of the 17 CCP+ individuals with x-rays detected BE, 7 (41.2%) developed IA and 10 (58.8%) did not progress to IA. The clinical and imaging characteristics of the CCP+ individuals with x-rays BE detected are shown in Table 1.

Table 1. Clinical and imaging characteristics of the CCP+ at-risk individuals with x-rays bone erosions (n=17)

	Hands/wrists BE (x-rays)	Feet BE (x-rays)	SENS score	US synovitis	US BE	X-rays pattern (IA)	Hands/feet tenderness	Anti-CCP (high titre)	RF	Smoking exposure
Progressors (n=7)	42.9%	71.4%	2 (IQR 1-2)	42.9%	57.1%	71.4%	57.1%	100%	100%	71.4%
P value	*NS*	*NS*	*NS*	*NS*	*NS*	*NS*	*NS*	*NS*	***P<0.01***	*NS*
Non progressors (n=10)	60%	60%	2 (IQR 1-2.8)	40%	10%	50%	70%	90%	30%	50%

Legend. Ab: antibodies, BE: bone erosions, CCP: cyclic citrullinated peptide; EMS: early morning stiffness, IA: inflammatory arthritis, IQR: interquartile range; min: minutes, NS: not significant; RF: rheumatoid factor, SENS: Simple Erosions Narrowing Score, US: ultrasound.

Figure 1. Kaplan-Meier curves showing IA free survival time according to the presence/absence of x-rays bone erosions.



Legend. Percentages refer to the individuals progressing at 12 months follow-up (black line).

A total of 123/394 (31.2%) CCP+ at-risk individuals developed IA (median follow-up: 336 days; IQR: 167-748). Seven out of 17 (41.2%) individuals with x-rays detected BE, and 116/377 (30.8%) individuals without x-rays detected BE, developed IA (p=0.37) (Figure 1). New BE were found in only 4/73 (5.4%) CCP+ individuals on repeated x-rays at the time of progression.

Both in the univariable and multivariable analysis, CR detected BE were not predictive for the development of IA [OR: 1.60 (95%CI: 0.60-4.20) p=0.37 and OR: 1.00 (95%CI: 0.30-2.90) p=1.0, respectively], also when these analyses were carried out in individuals with BE in ≥ 3 joints and individuals with radiographic pattern indicating IA (according to the MSK radiologist's diagnosis). In individuals in which BE were detected by both x-rays and US, borderline results were observed in the univariable analysis [OR=9.08 (95%CI: 1.00-82.06) p=0.05].

Conclusion: In CCP+ individuals at-risk of RA, x-rays BE are uncommon and do not predict the development of clinical arthritis. Prevention studies should be able at least to prevent radiographic damage in CCP+ at-risk individuals.

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Abstract Number: 0761

Anti-Peptidylarginine Deaminase Antibodies in the Individuals with Arthralgia at Risk of Progression to Rheumatoid Arthritis

Nora Petrovská[1], Klára Prajzlerová[1], Ivana Půtová[2], Monika Gregová[1], Petra Hánová[2], Heřman Mann[3], Karel Pavelka[1], Jiří Vencovský[1], Ladislav Šenolt[1] and Mária Filková[1], [1]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [2]Institute of Rheumatology, Prague, Czech Republic, [3]Institute of Rheumatology, Prague, Czech Republic. Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic

SESSION INFORMATION
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Background/Purpose: In order to identify the individuals at risk of imminent progression to rheumatoid arthritis (RA), EULAR has established a definition of clinically suspect arthralgia (CSA). Individuals carrying autoantibodies e.g. anti-citrullinated protein antibodies (ACPA) and rheumatoid factors (RF) are at high risk of developing RA. Peptidyl arginine deaminases (PAD) are enzymes responsible for producing autoantigens by citrullination of proteins and, importantly, may themselves represent as an autoantigen. Similar to ACPA and RF, anti-PAD antibodies are detectable years before the disease onset. We aimed to determine the prevalence of anti-PAD autoantibodies and their coincidence with RF and ACPA in sera of the individuals at risk-of developing RA.

Methods: Our prospective study included 86 individuals at-risk of progression to RA defined as having arthralgia without arthritis and being either ACPA+ or meeting the clinical CSA definition. Antibodies against PAD3 and PAD4 were analyzed in serum using commercially available ELISA kit (MyBioSource).

Results: Of the 86 at-risk individuals, 65 were seropositive (RF+ and/or ACPA+) and 54 met the CSA definition (33 were seropositive) with median duration of arthralgia 12 months. Of all individuals, 30 (34.8%) were anti-PAD+ (spe-

cifically, 14% were anti-PAD3+ and 21% were anti-PAD4+). Of 21 individuals who were both RF+ and ACPA+, 57% were anti-PAD+. Thirty % of RF- and 26% of ACPA- individuals were anti-PAD+. Of 21 seronegative (RF- and ACPA-) individuals, 33% were anti-PAD+. A third of individuals who met the CSA definition were anti-PAD+, irrespective of RF and ACPA positivity, 33% of seropositive CSA individuals were also anti-PAD+.

Sixteen patients progressed to RA within a median of 7.5 months of follow up with median DAS28(CRP) 2.28. Of these, 14 were RF+ and/or ACPA+ and 9 were anti-PAD+. All RF, ACPA and anti-PAD autoantibodies were positive in 5 individuals, both seronegative individuals were also anti-PAD-.

Conclusion: A third of the at-risk individuals with arthralgia, originally assessed as seronegative, were carriers of anti-PAD autoantibodies, however, none of them was both anti-PAD3 and anti-PAD4 positive. Similarly, a third of seropositive at-risk individuals were anti-PAD positive. The predictive value of anti-PAD antibodies for future development of RA in the at-risk individuals with arthralgia needs to be investigated.

Disclosure: N. Petrovská, None; **K. Prajzlerová**, None; **I. Půtová**, None; **M. Gregová**, None; **P. Hánová**, None; **H. Mann**, None; **K. Pavelka**, AbbVie, 8, Merck Sharp & Dohme, 8, Bristol-Myers Squibb Company, 8, Roche, 8, Amgen, 8, Pfizer, 8, Novartis, 8, Egis, 8, Biogen, 8, UCB, 8; **J. Vencovský**, Eli Lilly, 5, 8, Abbvie, 5, 8, Boehringer, 5, Octapharma, 5, Sanofi, 8, Merck, 8, Biogen, 8, UCB Biopharma, 8, Roche, 8, Pfizer, 8; **L. Šenolt**, AbbVie, 2, 5, 8, Amgen, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 8, Merck Sharp and Dohme, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8, Takeda, 8; **M. Filková**, None.

Abstract Number: 0762

Anti-Protein-Arginine Deiminase (PAD) 1 IgG Is a Promising Novel Autoantigen in Rheumatoid Arthritis (RA) and Increases Diagnostic Performance in Combination with Anti-PAD4 IgG Using a Composite Biomarker Score

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SESSION INFORMATION
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Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
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Session Time: 9:00AM–11:00AM

Background/Purpose: Over the past years, novel biomarkers have been identified in the sera of rheumatoid arthritis (RA) patients, including autoantibodies to the protein-arginine deiminase (PAD) enzymes. These proteins are involved in the disease pathogenesis, and a total of five PAD family members (PAD1, 2, 3, 4 and 6) have been described in humans, of which PAD2, PAD3 and PAD4, and more recently PAD1, have been identified as autoantigenic targets. Nevertheless, fewer studies have explored the clinical value of anti-PAD1 antibodies. Especially anti-PAD4 antibodies have been shown to help in the diagnosis of RA. The objective of this study was to evaluate the presence of anti-PAD1 and anti-PAD4 IgG in the sera of RA patients and to investigate the utility of an anti-PAD1/PAD4 composite score.

Methods: Serum samples from RA patients (n=262) and controls (n=270) were used to evaluate the discriminatory power of antibodies targeting the individual PAD enzymes. All samples included in this study were tested for an-

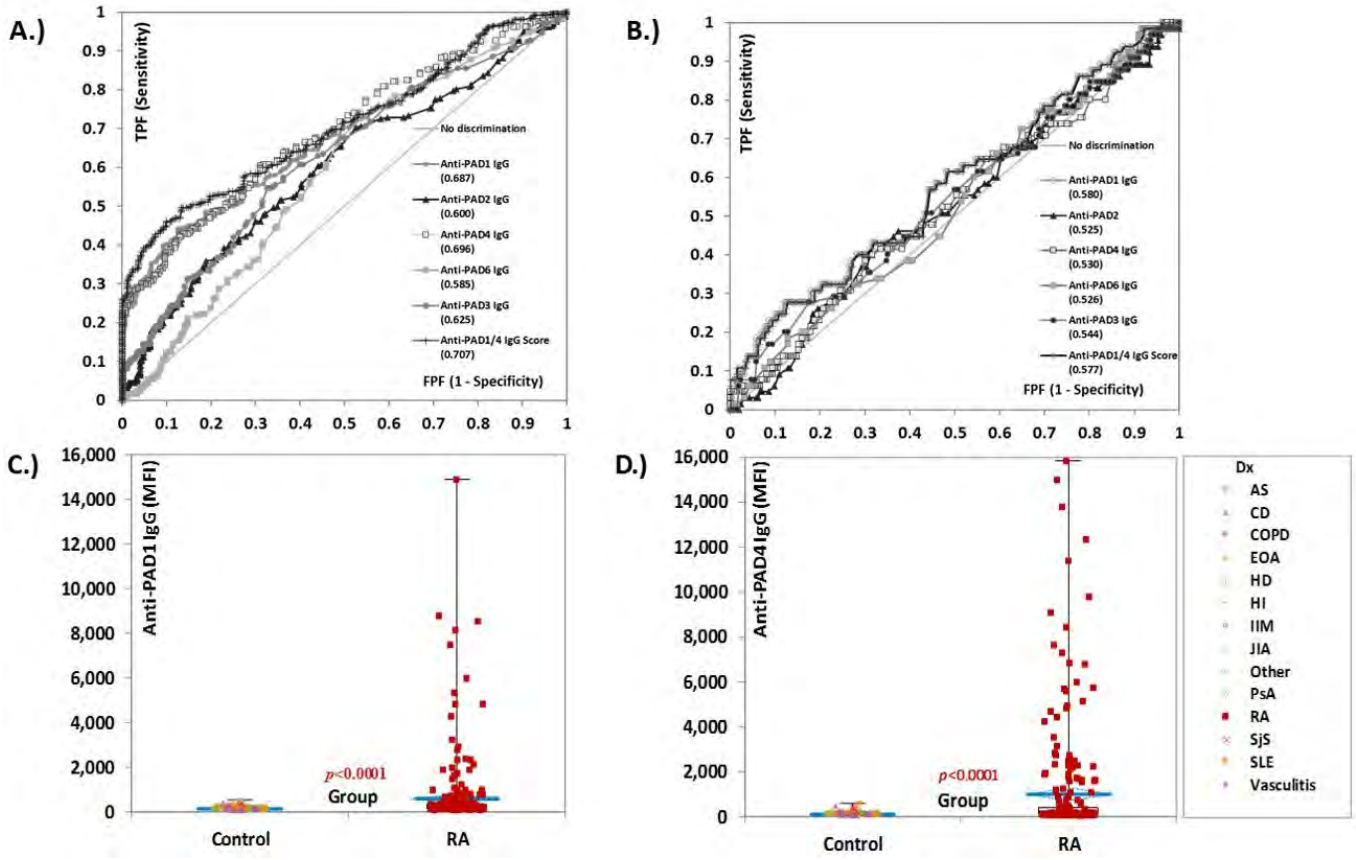

Figure 1. Diagnostic performance of individual antibodies to the protein-arginine deiminase (PAD) enzymes and of the anti-PAD1/4 IgG composite score. Receiver operating characteristic (ROC) analysis comparing the five individual anti-PAD antibodies and the anti-PAD1/4 composite score in their ability to discriminate between RA and controls in the total population (n=532) in panel A.), and in the ACPA negative individuals (n=321) in panel B.). Varying discrimination ability was observed, with anti-PAD1 and 4 showing the best diagnostic performance. The compositive PAD1/4 score shows improved discrimination between rheumatoid arthritis (RA) and controls. Area under the curve (AUC) values are shown for each of the anti-PAD antibodies. The pairwise comparison of the levels of anti-PAD1 and anti-PAD4 in patients with RA (n=262) vs controls (n= 270) are shown in C.). Panel D.) shows the same data for for anti-PAD4 IgG. Results are expressed in median fluorescence intensity (MFI). Abbreviations: AS: ankylosing spondylitis; CD: Chron's disease; CI: confidence interval; COPD: chronic obstructive pulmonary disease; EOA: erosive osteoarthritis; FPF: false positive fraction; HD: Hashimoto's disease; HI: healthy individuals; IIM: idiopathic inflammatory myopathies; JIA: juvenile idiopathic arthritis; MFI: median fluorescent intensity; PAD: protein-arginine deiminase; PsA: psoriatic arthritis; RA: Rheumatoid arthritis; SjS: Sjogren's syndrome; SLE: systemic lupus erythematosus; TPF: true positive fraction.

ti-PAD1, PAD2, PAD3, PAD4, and PAD6 IgG using the novel particle-based multi-analyte technology (PMAT, research use only, Inova Diagnostics, San Diego, USA). Anti-citrullinated protein antibodies (ACPA) IgG was also measured in these patients by QUANTA Lite CCP3 enzyme-linked immunoassay (ELISA, Inova Diagnostics, San Diego, US).

Results: Autoantibodies against all five PAD proteins were detected. Interestingly, anti-PAD1 were preferentially observed in patients with RA resulting in good discrimination between RA and controls from receiver operating characteristic (ROC) analysis (Figure 1). The area under the curve (AUC) for anti-PAD1 was comparable to the AUC obtained for anti-PAD4 antibodies, in both the total (AUC= 0.687, 95% CI 0.642-0.732 and AUC=0.696, 95% CI 0.652-0.740, respectively), and the ACPA negative population (AUC= 0.580, 95% CI .500-0.660 and AUC=0.530, 95% CI 0.450-0.610, respectively). Combining anti-PAD1 and anti-PAD4 in a composite score improved the discrimination between RA and controls substantially (Table 1). In addition, anti-PAD1 and anti-PAD4 were found in the ACPA negative RA group where anti-PAD1 had slightly higher positivity than anti-PAD4.

Entire cohort (n=532)	Anti-PAD1	Anti-PAD4	PAD1/4 Score
Sensitivity, % [95% CI]	27.1 [22.1-32.8]	28.2 [23.1-34.0]	36.3 [30.7-42.2]
Specificity, % [95% CI]	97.0 [94.3-98.5]	98.1 [95.7-99.2]	96.3 [93.3-98.0]
LR+, % [95% CI]	9.1 [4.6-18.4]	15.3 [6.5-36.3]	9.8 [5.3-18.3]
LR-, % [95% CI]	0.75 [0.69-0.91]	0.73 [0.67-0.79]	0.66 [0.60-0.72]
OR [95% CI]	12.2 [5.8-25.5]	20.9 [8.5-51.2]	14.8 [7.6-28.9]
Youden's index	0.241	0.264	0.326
Cut-off for 95% specificity	257	189	260
Sensitivity at 95% Specificity, % [95% CI]	30.9 [25.6-36.8]	29.8 [24.6-35.6]	39.3 [33.6-45.3]
OR at 95% Specificity, [95% CI]	8.8 [4.8-16.3]	8.4 [4.6-15.4]	12.8 [7.0-23.4]
ACPA negative cohort (n=321)	**Anti-PAD1**	**Anti-PAD4**	**PAD1/4 Score**
Sensitivity, % [95% CI]	9.2 [4.3-18.7]	6.2 [2.4-14.8]	10.8 [5.3-20.6]
Specificity, % [95% CI]	98.4 [96.1-99.4]	97.3 [94.5-98.7]	98.4 [96.1-99.4]
LR+, % [95% CI]	5.9 [1.8-18.9]	2.3 [0.72-6.9]	6.9 [2.2-21.4]
LR-, % [95% CI]	0.92 [0.83-0.98]	0.97 [0.88-1.0]	0.91 [0.81-0.97]
OR [95% CI]	6.4 [1.9-21.9]	2.3 [0.71-7.8]	7.6 [2.3-25.2]
Youden's index	0.077	0.034	0.092
Cut-off for 95% specificity	249	182	257
Sensitivity at 95% Specificity, % [95% CI]	13.8 [7.5-24.3]	6.2 [2.4-14.8]	13.8 [7.5-24.3]
OR at 95% Specificity, [95% CI]	3.3 [1.3-7.8]	1.3 [0.44-4.1]	3.3 [1.3-7.8]

Table 1 Diagnostic performance characteristics of anti-PAD1 and anti-PAD4 antibodies individually and in a composite score. Abbreviations: ACPA= anti-citrullinated protein antibodies; LR= likelihood ratio; OR= odds ratio; PAD= protein-arginine deiminase.

Conclusion: Our study is one of the first to confirm PAD1 and PAD6 as autoantigenic targets in RA. Interestingly, anti-PAD1 antibodies were mostly found in patients with RA with high disease specificity and although a high degree of overlap with anti-PAD4 was observed, they were also observed in the absence of these anti-PAD antibodies. Anti-PAD1 antibodies hold promise to help to close the serological gap in RA and might be superior to anti-PAD4 in the ACPA negative population, but future studies are warranted to validate in larger populations. Moreover, the observation that anti-PAD1 and anti-PAD4 antibodies combined in a composite score increases the discrimination between RA and control has the potential to further improve the diagnosis of RA.

Disclosure: M. Lopez-Hoyos, None; **C. Bentow**, Inova Diagnostics, 3; **A. Ishii**, Inova Diagnostics, 3; **L. Martinez-Prat**, Inova Diagnostics, 3; **M. Mahler**, Inova Diagnostics, 3.

Abstract Number: 0763

Plasmatic Proteome in Individuals with Arthralgia at Risk of Developing Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
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Session Time: 9:00AM–11:00AM

Background/Purpose: The presence of antibodies against citrullinated proteins (ACPA) significantly increases the risk of developing rheumatoid arthritis (RA). EULAR characterised individuals with arthralgia suspicious for progression to RA based on their clinical features (clinically suspect arthralgia, CSA). We aimed to analyse proteins at different stages of RA development with special interest in the at-risk individuals with arthralgia.

Methods: Plasma samples were obtained from 28 at-risk individuals with arthralgia and no previous history of arthritis, who were either ACPA+ or met the CSA definition. Samples collected at baseline or at the time of manifestation of arthritis were analysed by tandem mass spectrometry (nLC-MS2) using Q-OT-qIT mass spectrometer (Thermo Scientific™) followed by MaxQuant software quantification and normalization. Data were analysed using Mann Whitney or Wilcoxon pairs tests and presented as median and interquartile range [IQR]. Protein interaction networks were analysed using STRING v11.0.

Majority protein IDs	Protein names	Gene names	Baseline* vs. RA manifestation‡ p-value	Baseline ongoing arthralgia* vs. future RA‡ p-value	ACPA+* vs. ACPA-‡ p-value
P00751	Complement factor B	CFB	0.0435 ‡	NS	NS
P02745	Complement C1q subcomponent subunit A	C1QA	0.0480 ‡	NS	0.0028 ‡
P13671	Complement component C6	C6	0.0420 ‡	NS	0.0162 ‡
P02671	Fibrinogen alpha chain	FGA	NS	0.0197 ‡	NS
P02790	Hemopexin	HPX	NS	0.0468 *	NS
P05546	Heparin cofactor 2	SERPIND1	NS	0.0033 *	0.0356 ‡
P19827	Inter-alpha-trypsin inhibitor heavy chain H1	ITIH1	NS	0.0007 *	0.0315 ‡
P00734	Prothrombin	F2	NS	0.0117 *	NS
P04114	Apolipoprotein B-100	APOB	NS	0.0426 *	0.0001 ‡
P02749	Beta-2-glycoprotein 1	APOH	NS	0.0367 *	NS
P35858	Insulin-like growth factor-binding protein complex acid labile subunit	IGFALS	NS	0.0275 *	0.0276 ‡
P68871	Hemoglobin subunit beta	HBB	0.0465 *	NS	0.0391 ‡
Q14520	Hyaluronan-binding protein 2	HABP2	0.0500 ‡	0.0033 *	0.0027 ‡
P35542	Serum amyloid A-4 protein	SAA4	0.0482 ‡	NS	0.0001 ‡
*; ‡ symbols indicate the upregulated group					

Table 1. List of differentially expressed proteins Table 1: List of differentially expressed proteins

Results: Out of 28 individuals with arthralgia (96% females), 13 were ACPA+ and 23 met the CSA definition (8 were ACPA+). Median age was 47 [15] years, median symptom duration 12 [17] months and CRP 3.18 [3.56] mg/L. Thirteen individuals developed RA (10 were ACPA+) within a median of 7 months of follow up with CRP 3.25 [13.10] mg/l and DAS28(CRP) score 4.39 [2.18].

Out of 393 identified proteins, 90 proteins were detected in all tested samples. In individuals who progressed to RA, 6 proteins were differentially expressed at baseline and the manifestation of arthritis (Table 1): complement factor B (CFB), complement C1q subcomponent subunit A (C1QA) and complement component C6 were significantly higher at the time of RA onset. Protein interaction network linked C1QA to C6 by CFB. Moreover, these proteins are involved in innate immune response and regulation of acute inflammatory response. Hemoglobin subunit beta (HBB) was significantly lower at the time of RA onset.

Nine proteins showed differential baseline expression between individuals with ongoing arthralgia (median follow up 12 months) and individuals who have developed RA (Table 1): fibrinogen alpha chain (FGA) was significantly higher in future RA patients while heparin cofactor 2 (SERPIND1), prothrombin (F2), apolipoprotein B-100 (APOB) and beta-2 glycoprotein 1 (APOH) were significantly lower compared to individuals with ongoing arthralgia. Protein interaction networks linked all these four proteins involved in metabolic processes.

Nine proteins were differentially expressed at baseline between ACPA+ and ACPA- individuals (Table 1).

Conclusion: Using proteome analysis we identified several differentially expressed proteins in the at-risk individuals with arthralgia during the progression to RA that were mostly involved in innate immune and acute inflammatory response. Their predictive value as prognostic biomarkers for future development of RA in the at-risk individuals with arthralgia needs to be confirmed in larger patient cohorts.

Disclosure: K. Prajzlerová, None; **N. Petrovská**, None; **M. Gregová**, None; **J. Baloun**, None; **P. Hánová**, None; **K. Pavelka**, AbbVie, 8, Merck Sharp & Dohme, 8, Bristol-Myers Squibb Company, 8, Roche, 8, Amgen, 8, Pfizer, 8, Novartis, 8, Egis, 8, Biogen, 8, UCB, 8; **J. Vencovský**, Eli Lilly, 5, 8, Abbvie, 5, 8, Boehringer, 5, Octapharma, 5, Sanofi, 8, Merck, 8, Biogen, 8, UCB Biopharma, 8, Roche, 8, Pfizer, 8; **L. Šenolt**, AbbVie, 2, 5, 8, Amgen, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 8, Merck Sharp and Dohme, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8, Takeda, 8; **M. Filková**, None.

Abstract Number: 0764

Uncovering Novel Biomarkers for Rheumatoid Arthritis from Feature Selection and Machine Learning Approaches on Synovium and Blood Gene Expression Data

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: There is an urgent need to develop objective biomarkers for early diagnosis and monitoring of disease activity in Rheumatoid arthritis (RA). Here we define a RA meta-profile using publicly available cross-tis-

sue gene expression data and apply machine learning to identify putative biomarkers, which we further validate on independent datasets.

Methods: We carried out a comprehensive search for publicly available microarray gene expression data at NCBI Gene Expression Omnibus database for whole blood and synovial tissues in RA and healthy controls. The raw data from 13 synovium datasets with 284 samples and 14 blood datasets with 1,885 samples were downloaded and processed. The datasets were merged and batch corrected separately for each tissue. We further developed a robust feature selection pipeline to identify genes dysregulated in both tissues and highly associated with RA. Within training sets for each tissue, two sets of selected differentially expressed genes were identified and overlapped followed by the condition of co-directionality. Each gene in the resulting set was evaluated on the testing sets using AUROC. The process was repeated 100 times. 2 synovium and 3 blood independent datasets were used to validate the feature selected (FS) genes. We used the averaged AUC 0.8 threshold for the final filtering to define the RAScore, composed of a geometric mean of the selected genes.

Results: The result of the feature selection pipeline was a set of 25 upregulated and 28 downregulated genes. To confirm the robustness of the feature selected genes, we trained a Random Forest machine learning model with this set of 53 genes and the set of 32 common differentially expressed genes and tested on the validation cohorts. The model with FS genes outperformed the model with common DE genes with AUC 0.89 ± 0.04 vs 0.86 ± 0.05. The FS genes were further validated and thresholded on the 5 independent datasets resulting in 10 upregulated genes, TNFAIP6, S100A8, TNFSF10, DRAM1, LY96, QPCT, KYNU, ENTPD1, CLIC1, ATP6V0E1, that are involved in innate immune system pathways, including neutrophil degranulation and apoptosis and expressed in granulocytes, dendritic cells, and macrophages; and 3 downregulated genes, HSP90AB1, NCL, CIRBP, involved in metabolic processes and T-cell receptor regulation of apoptosis and expressed in lymphoblasts.

To investigate the clinical utility of the FS genes, RAScore was composed and found to be highly correlated with DAS28 ($r = 0.33 \pm 0.03$, $p = 7e\text{-}9$) and able to distinguish RA and OA samples (t-test, $p = 2.3e\text{-}6$). However, it did not show any difference between RF-positive and RF-negative RA sub-phenotypes (t-test, $p = 0.9$) suggesting the generalizability of this score in clinical applications. The RAScore was also able to monitor the treatment effect among RA patients (t-test of treated vs untreated, $p = 2e\text{-}4$) and separate polyJIA from healthy individuals in 7 independent pediatric cohorts (t-test, $p = 2e\text{-}4$).

Conclusion: This novel list of biomarkers, identified through a robust feature selection procedure on public data and validated using multiple independent data sets, coupled with the RAScore may be useful in the early diagnosis and disease and treatment monitoring of RA.

Disclosure: D. Rychkov, None; **J. Neely**, None; **M. Sirota**, None.

Abstract Number: 0765

High Disease Activity at Baseline and Seropositivity Are Associated with Treatment Response at One Year Post Synovial Biopsy in RA Patients

Kieran Murray[1], Candice Low[2], Francis Young[3], Monika Biniecka[4], Eimear Mylod[4], Ursula Fearon[5] and Douglas Veale[6], [1]Saint Vincent's University Hospital, Dublin 4, Dublin, Ireland, [2]EULAR Centre for Arthritis and Rheumatic diseases, St Vincents University Hospital, UCD, Dublin, Ireland, [3]Saint Vincent's University Hospital, Dublin 4, [4]Saint Vincent's University Hospital, Dublin 4, Ireland, [5]Molecular Rheumatology, Trinity College Dublin, Dublin, Dublin, Ireland, [6]EULAR Centre for Arthritis and Rheumatic Diseases, St Vincents University Hospital, UCD, Dublin, Dublin, Ireland

SESSION INFORMATION

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Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite recent therapeutic advances, our ability to predict prognosis and therapeutic response in RA remains imprecise. This study examines for biomarkers predictive of outcome at one year following arthroscopy.

Methods: RA patients were prospectively recruited and underwent knee arthroscopy performed under local anaesthetic. Each patient underwent a careful systematic assessment of demographic, clinical, and serologic factors on the day of arthroscopy and were reviewed at 2 weeks, 3, 6 and 12 months post arthroscopy. Erosive disease was defined based on plain-film radiographs of hands and feet. Disease activity at one year was used to define treatment response into responders (moderate/good EULAR Response) and non-responders.

Clinical characteristics, synovial tissue cell profiles and immunohistochemistry were analysed for T Cells (CD3), B Cells (CD20, CD138), macrophages (CD68) and vascularity (Factor VIII) to establish predictors of treatment response. All areas of each biopsy section were examined and the sub-lining layer independently scored by 2 observers using a well-validated semiquantitative scoring method, ranging from 0 to 4 (0=no staining, 1=< 25%, 2=25–49%, 3=50–74%, and 4=75–100% staining). Factor 8 was scored by calculating the mean count of stained blood vessels per high-power field (at 20X magnification).

Results: Baseline features of the study participants are presented in Table 1. There were no significant differences in gender, age, disease duration, medications, erosive status, ESR, CRP or synovitis or vascularity at arthroscopy. Interestingly, rates of RF and ACPA positivity, tender and swollen joint counts, DAS28 and DAS28CRP were all higher amongst treatment responders. One year outcomes are shown in Table 2. Immunohistochemistry was a very poor

	Responder (n=30)	Non-responder (n=18)	p value
Female	20 (66.7%)	14 (77.8%)	NS
Age	51.5 (11.2)	54.2 (10.9)	NS
Disease duration, years	0.5 (0-16)	0.5 (0-10)	NS
RF positive	22 (73.3%)	5 (27.8%)	0.003
ACPA positive	22 (73.3%)	8 (44.4%)	0.045
Erosions	8 (26.7%)	5 (27.8%)	NS
Medications			
No DMARD	23 (76.7%)	10 (55.6%)	NS
csDMARD only	4 (13.3%)	3 (16.7%)	NS
TNFi	2 (6.7%)	3 (16.7%)	NS
Other bDMARD	1 (3.3%)	2 (11.1%)	NS
Patient global health, VAS (mm)	54.2 (10-100)	51.5 (0-90)	NS
SJC (28 Joints)	4.5 (0-16)	1 (0-18)	0.001
TJC (28 Joints)	7 (1-25)	1 (0-15)	0.001
ESR, mm/hr	23 (2-120)	24 (2-81)	NS
CRP, mg/L	5 (1-95)	6.5 (1-64)	NS
DAS28	5.01 (1.95-7.36)	3.93 (1.40-6.62)	0.003
DAS28CRP	4.78 (2.82-7.13)	3.39 (1.21-6.26)	0.002
Synovitis, VAS	65 (10-100)	70 (30-100)	NS
Vascularity, VAS	60 (10-90)	70 (30-100)	NS

Data presented as n (%) or median (range)

Table 1. Baseline characteristics

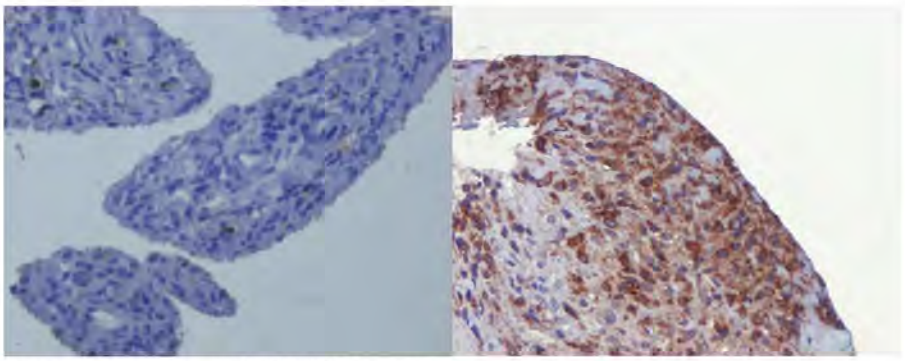
	Responder (n=30)	Non-responder (n=18)	p value
Medications			
No DMARD	3 (10%)	1 (5.6%)	NS
csDMARD only	14 (47.6%)	8 (44.4%)	NS
TNFi	12 (40%)	5 (27.8%)	NS
Other bDMARD	1 (3.3%)	4 (22.2%)	NS
Patient global health, VAS, mm	30 (0-100)	60 (0-100)	0.015
SJC (28 Joints)	0.6 (0-4)	1 (0-4)	NS
TJC (28 Joints)	0 (0-14)	2 (0-28)	0.048
ESR, mm/hr	11.5 (2-95)	19 (7-61)	NS
CRP, mg/L	3 (1-66)	7.5 (1-110)	NS
DAS28	2.87 (0.49-5.81)	4.13 (1.78-6.54)	0.002
DAS28CRP	2.47 (1.35-4.92)	3.92 (1.36-5.34)	0.006
ΔDAS28	-1.84 (-4.4 to -0.72)	0.24 (-0.55 to 1.93)	<0.001
ΔDAS28CRP	-1.78 (-3.7 to -0.64)	0.21 (-0.93 to 3.02)	<0.001

Data presented as n (%) or median (range)

Table 2. One year outcomes

	Responder (n=30)	Non-responder (n=18)	p value
CD3 SL Score	1 (1-2.5)	1 (0.5-3)	NS
CD20 SL Score	1 (1-2)	1 (1-2)	NS
CD68 SL Score	1 (1-2.5)	1 (1-3)	NS
CD138 SL Score	1 (0.5-2)	1 (0.5-3)	NS
F8 Score*	25.5 (6-71)	29 (9-58)	NS

Data presented as median (range)
*Vessels per high powered field



Representative images (CD68 Sub-lining)

Table 3. Immunohistochemistry scores

predictor of treatment response. There were no significant differences between the two groups in CD3, CD20, CD138, CD68 or Factor 8 score (Table 3).

Conclusion: In this small study, seropositivity and disease activity were higher in responders. Baseline immunohistochemical staining was not a good discriminator of treatment response.

Disclosure: K. Murray, None; **C. Low**, None; **F. Young**, None; **M. Biniecka**, None; **E. Mylod**, None; **U. Fearon**, None; **D. Veale**, AbbVie, 2, Health Beacon, 1, Janssen, 2, 8, Pfizer, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5.

Abstract Number: 0766

ACPA and Cholesterol Titers as Predictors of Good Clinical Response at One Year in an Argentine Cohort

Rodrigo Garcia Salinas[1], Alvaro Ruta[1], Santiago Ruta[1], Einer Sanchez Prado[1], Jessica Torres Chichande[1] and Sebastian Magri[1], [1]Hospital Italiano La Plata, La Plata, Argentina

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster II: Biomarkers
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoantibody positivity, erosions, activity level, and functional capacity were classically defined as poor prognosis. Paradoxically, many of them also predict a good response to treatment. Objective: To estimate the proportion of patients achieving remission and low activity by CDAI and SDAI per year in a cohort of patients with RA. To assess the impact of basal ACPA titers and total cholesterol level on response to treatment.

Methods: An observational study, where patients older than 18 who entered the Reumacheck program were included, in the first visit it was carried out: laboratory (including ACPA and total cholesterol: CT), Rx, ultrasound, and interview where were collected sociodemographic data (age, sex, schooling, occupation, toxic habits), clinical data (time of evolution, comorbidities, family history) and CDAI, SDAI, HAQ; each evaluator did not know the data from the other studies and evaluations, ACPA levels were measured in titles and divided into quartiles (Q1: 0-5, Q2: 5-50, Q3:50 -200, Q4: > 200). Those who were diagnosed with RA one year underwent a new control (FR and ACPA) where the same laboratory, clinical and treatment data were collected, and CDAI and SDAI remission and low activity (LDA) were calculated. Statistical analysis: descriptive statistics, Chi2 test and Fisher's exact test were performed. T-test of student and Mann Whitney. Multiple logistic regression. ROC curve analysis to estimate cutoff values for cholesterol.

Results: Of the 183 patients diagnosed with RA between 2018-19, 83 performed a new check-up per year. The baseline characteristics are in Table 1. They achieved CDAI - SDAI remission at one year, CDAI-SDAI LDA (%): 21, 22.4, 55.3, 55 respectively. Reaching CDAI LDA (≤ 10) was associated at baseline to: ACPA (yes-no) 64.4% p 0.05 RR 2.5 (1.02-6.4), ACPA quartile 3-4 76.5% p 0.016 RR 3.3 (1.2-11.5), ACPA title 79.5 vs. 3.95 p 0.04, initiation of anti TNF

Table 1: Baseline RA patient characteristics (N: 83)

Symptom onset less 6 months (%)	22,7	Age (IQR)	57 (43-64)
Female (%)	83	Education time (years)(IQR)	12 (8,5-15)
RF + (%)	68,4	Disease duration (months) (IQR)	48 (12-84)
ACPA + (%)	59,2	Weight (DS)	76,4 (18,3)
Double-sero + (%)	54	FR title (IQR)	34,5 (11,8-132)
Seronegative (%)	26,3	ACPA title (IQR)	28 (0,5-184)
CRP + (%)	27,6	Cholesterol (IQR)	185 (163-223)
Comorbidities (%)	59,2	ESR (IQR)	25 (10,5-40,7)
Lung disease (%)	10,5	CRP (IQR)	3 (1-7)
DMARc started (%)	89,5	CDAI (DS)	14,4 (8,9)
Prednisone ≤ 10mg (%)	22,4	SDAI (DS)	15, (9,3)
Prednisone> 10mg (%)	4	DAS28 (DS)	3,88 (1,2)
Biological - DMARtd (%)	45	TBQ (%)	32

66% p 0.04 RR 2.6 (1.3-6), CT levels 185 vs 207 p 0.04, HAQ 0.5 vs 0.8 p 0.047 and swollen joints 1 (0-3) vs 2 (0-6) p 0.05. CDAI remission (≤ 2.8) was associated only with lower baseline total cholesterol levels: 170 (38) vs. 202 (47) p 0.025.

Reaching SDAI LDA (≤ 11) was associated at baseline to: ACPA (yes-no) 69% p 0.05 RR 2.5 (1.01-6.4), ACPA quartile 3-4 76% p 0.016 RR 3 , 3 (1,2-11), ACPA titer 80 vs 3.45 p 0.047, initiation of anti TNF 66.7% p 0.04 RR 2.6 (1.2-6), levels CT 184 vs 206 p 0.04, HAQ 0.5 vs 0.78 p 0.047 and swollen joints 1 (0-3) vs 2 (0-6) p 0.05. SDAI remission (≤ 3.3) was associated only with lower baseline total cholesterol levels: 168 (36) vs. 203 (47) p 0.025. Two logistic regression models were made, where the predictor variables, sex, age, dyslipidemia, use of statins and treatment were included: both for CDAI and SDAI LDA was independently associated with ACPA quartile 3-4 p 0.02 expB 3 and high cholesterol p 0.016 expB 0.21. In the ROC curve analysis, the best cut-off value was estimated for the baseline CT level predicted by CDAI LDA: AUC 0.67 (0.54-0.8): value 180 (S: 70% E: 50%) for both.

Conclusion: Patients with RA at one-year follow-up reached CDAI - SDAI remission, CDAI-SDAI LDA (%): 21, 22.4, 55.3, 55 respectively. High ACPA titers and low cholesterol levels were associated with achieving remission and LDA by these methods.

Disclosure: R. Garcia Salinas, None; **A. Ruta**, None; **S. Ruta**, None; **E. Sanchez Prado**, None; **J. Torres Chichande**, None; **S. Magri**, None.

Abstract Number: 0767

Anti-acetylated Protein Antibodies in Rheumatoid Arthritis (RA): Clues for the Starting Point of Autoantibody Responses in RA

Tineke van Wesemael[1], Nazike Salioska[2], Annemarie Dorjée[1], Thomas Huizinga[1], Annette van der Helm - van Mil[3], René Toes[1] and Diane van der Woude[1], [1]Leiden university medical center, Leiden, Netherlands, [2]leiden university medical center, Rotterdam, Netherlands, [3]Leiden University Medical Center, Erasmus Medical Center, Leiden, Netherlands

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is characterized by autoantibodies such as rheumatoid factor (RF) and anti-modified protein autoantibodies (AMPAs) like anti-citrullinated protein antibodies (ACPA) and anti-carbamylated protein antibodies (anti-CarP). Recently, another AMPA: anti-acetylated protein antibodies (AAPA) have been found in RA patients [1]. The prevalence of AAPA antibodies and their isotypes have yet to be determined. Since isotype profiles reflect the breadth of an immune response, the prevalence of AAPA isotypes in arthritis patients with and without RA can help to understand the relevance of this autoantibody response in RA.

Objective: To describe the prevalence of AAPA isotypes in arthritis patients with and without RA.

Methods: In 650 RA patients fulfilling the 1987 RA criteria and 555 non-RA arthritis patients from the Leiden Early Arthritis Cohort, baseline serum samples were screened by ELISA for IgG, IgM and IgA to an acetylated- and control peptide that was based upon the CCP-2 backbone . The cutoff for positivity was based on 80 controls (mean + 2SD).

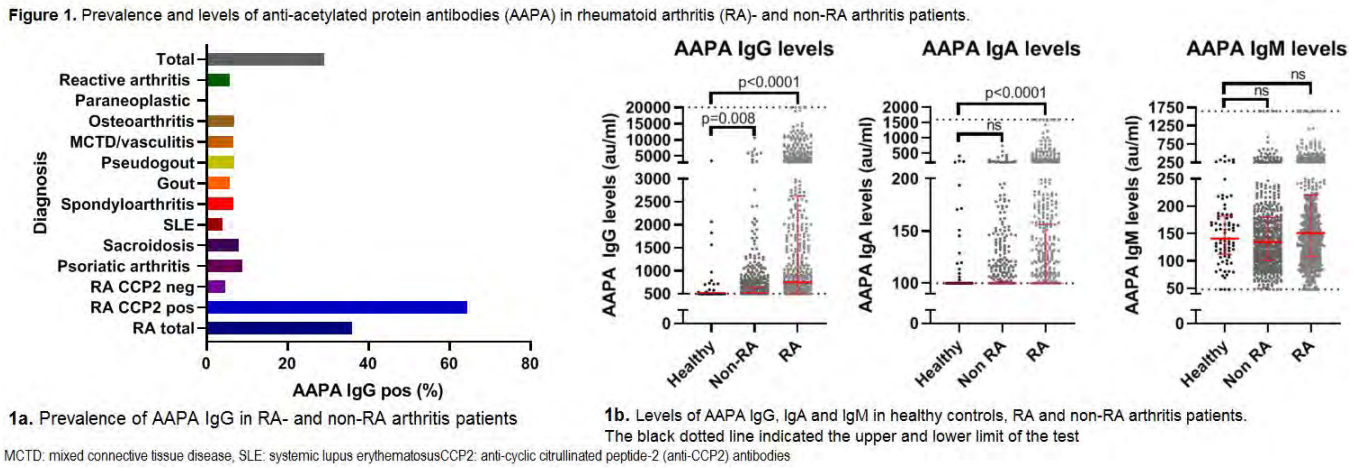


Figure 1. Prevalence and levels of anti-acetylated protein antibodies (AAPA) in rheumatoid arthritis (RA)- and non-RA arthritis patients. 1a. Prevalence of AAPA IgG in RA- and non-RA arthritis patients, 1b. Levels of AAPA IgG, IgA and IgM in healthy controls, RA and non-RA arthritis patients

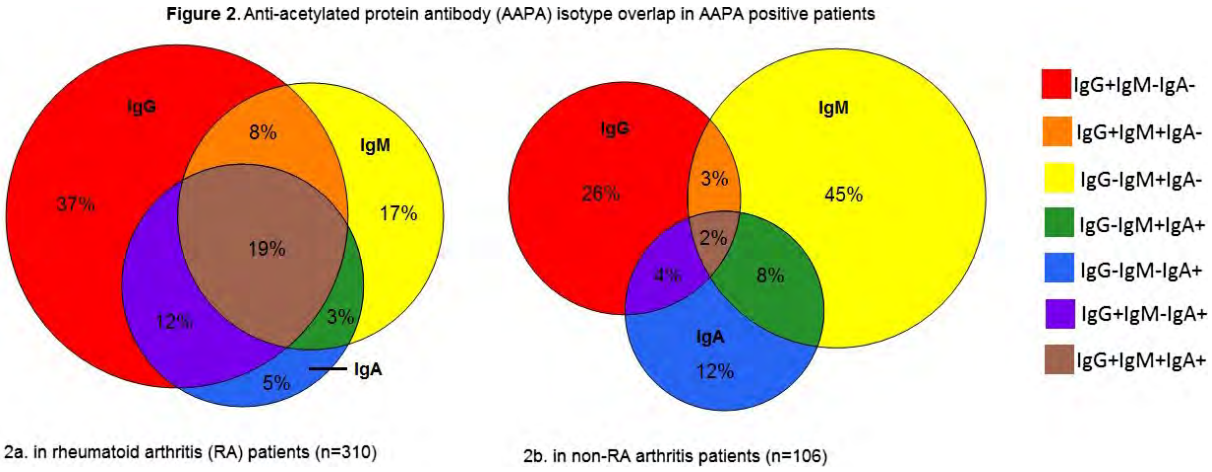


Figure 2. Anti-acetylated protein antibody (AAPA) isotype overlap in AAPA positive patients. 2a. in rheumatoid arthritis (RA) patients (n=310), b. in non-RA arthritis patients (n=106)

A sample was considered positive if it was above the cutoff and was 0.1 optical density higher on the acetylated peptide than on the control peptide.

Results: AAPA IgG was found in 36% of RA patients versus 6.7% of non-RA arthritis patients (Figure 1a). Within RA patients, AAPA IgG antibodies were mostly present in the ACPA-(CCP-2) positive group (64% in ACPA-positive, compared to 5% in ACPA-negative). Levels of AAPA IgG and IgA were higher in RA patients than in healthy controls and non-RA arthritis patients (Figure 1b), however, surprisingly, no difference in levels was found for IgM.

If isotypes profiles in AAPA- positive arthritis patients were compared, patients with RA were more often positive for two or more isotypes then patients without RA, and thus displayed considerably more overlap in AAPA isotypes compared to non-RA patients (Figure 2). Intriguingly, IgM AAPA was the most prevalent isotype in non-RA patients, versus IgG in RA patients.

Conclusion: AAPA are detected in a minority of RA patients, and mainly in the ACPA-positive subgroup. The predominance of IgM AAPA in non-RA arthritis patients and healthy controls suggests that healthy persons can develop AAPA IgM without the development of RA. These results also suggest that in healthy individuals, AAPA responses can occur, but do not mature past the IgM-stage, while in RA patients, the AAPA-response does mature and might form a "starting point" for development of other AMPA leading to the concurrent present of several AMPA in disease.

Disclosure: T. van Wesemael, None; **N. Salioska**, None; **A. Dorjée**, None; **T. Huizinga**, Bristol-Myers Squibb Company, 2, 8, Pfizer, 2, 8, Eli Lilly, 2, 8, LUMC, 9; **A. van der Helm - van Mil**, None; **R. Toes**, LUMC, 9; **D. van der Woude**, None.

Abstract Number: 0768

Dynamics of Follicular Helper T Cells Subsets in Rheumatoid Arthritis Patients Before and After Treatment

Paola Virginia Ferrero[1], Luisina Onofrio[1], Cristina del Valle Acosta[1], Estefania Raquel Zacca[1], Nicolas Eric Ponce[2], Eduardo Mussano[1], Ignacio Isaac Cadile[1], Laura Onetti[1], Marina Werner[1], Alicia Beatriz Costantino[1], Eva Virginia Acosta Rodriguez[3] and Adriana Gruppi[2], [1]HOSPITAL NACIONAL DE CLINICAS, FACULTAD DE MEDICINA, UNIVERSIDAD NACIONAL DE CORDOBA, CORDOBA, Cordoba, Argentina, [2]FACULTAD DE CIENCIAS QUIMICAS, UNIVERSIDAD NACIONAL DE CORDOBA. CENTRO DE INVESTIGACIONES EN BIOQUIMICA CLINICA E INMUNOLOGIA, CORDOBA, Cordoba, Argentina, [3]FACULTAD DE CIENCIAS QUIMICAS, UNIVERSIDAD NACIONAL DE CORDOBA. CENTRO DE INVESTIGACIONES EN BIOQUIMICA CLINICA E INMUNOLOGIA, CORDOBA, Argentina

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) is a chronic inflammatory disease characterized by the production of autoantibodies like rheumatoid factor and anti- citrullinated protein. $CD4^+$ follicular helper T cells (Tfh) play a critical role in immunity by supporting several events involved in antibody (Ab) production by B cells, including class-switch recombination, germinal center B cell differentiation, and affinity maturation. Remarkably, high levels of Tfh are associated with humoral autoimmunity. We aimed to evaluate the frequency of Tfh in RA patients under different treatment conditions and to characterize the Tfh according their ability to produce Interleukin (IL)-17 and Interferon (IFN)-γ, cytokines with opposite roles in Ab production.

Methods: One hundred subjects over 18 years diagnosed with RA according to ACR/EULAR 2010 criteria untreated and under different treatments were recruited. Twenty-seven of these patients were re-evaluated after 3 months of treatment and treatment response was determined according to EULAR response criteria. Forty-six healthy donors (HD) sex- and age-matched were recruited as controls (Table 1). Ex-vivo Tfh frequency was analyzed by flow cytometry (Figure 1a). Cryopreserved peripheral blood mononuclear cells were used to determine the frequency of IL-17- and IFN-γ-producing Tfh. GraphPad Prism version 7.00 software was used for statistical analysis and p values < 0.05 were considered significant.

Results: The frequency of total Tfh (tTfh: $CD3^+CD4^+CD45RA^-CXCR5^+CD25^{lo}CD127^{hi}$) and of $CCR7^{lo}PD1^{hi}$ Tfh, a subset with demonstrated increased ability to promote Ab response, were significantly increased in RA patients in comparison to HD (p=0.004, p=0.01, respectively) (Figure 1b). When the RA patients were segregated according to the presence of autoAbs, the increase in Tfh was limited to seropositive patients (p=0.04; p=0.03; respectively) (Figure 1c). The activated Tfh subset $CCR7^{lo}PD1^{hi}ICOS^+$ was also increased in RA patients (p=0.01) (Figure 1b) but not in

Table 1. Demographic and clinical characteristics of RA patients and healthy donors

		RA					
				Treatment			
	HD (n=46)	All pts (n=100)	*P value*	Untreated (n= 53)	DMARDs (n=24)	TNF Inh (n=14)	Tofa (n=9)
Age,* years	50±13	54±14	0.14[&]	52±15	54±13	53±14	62±10
Sex, n° F/M	39/7	87/16	0.84[#]	46/7	17/7	12/2	9/0
WBC,* n° .10^9/L	6.2±1.5	7.6±2.8	0.0002[^]	7.9±2.4	8.3±3.6	6.6±2.2	6.2±2.2
Hb,* g/L	13.6±1.3	13.0±1.9	0.019[^]	12.8±1.5	13.2±2.8	12.9±1.8	13.6±1.2
Plat,* n° .10^9/L	226±56	274±90	0.0001[^]	278±91	286±96	264±88	258±95
ERS,** mm/h	7(4-11)	17(5-32)	0.0001[&]	20(8-36)	9(4-24)	16(3-30)	13(7-25)
CRP,** mg/L	3(1-5)	6(3-20)	<0.0001[^]	7.0(3.0-23.1)	7.0(3.0-35.5)	4.1(2.0-9.4)	6.0(1.0-11.3)
DAS28-ERS*	--	4.12±1.32	--	4.57±1.15	3.87±1.46	3.16±0.91	3.39±1.27
RF , n° (+/-)	1/45	69/34	<0.0001[#]	39/14	13/11	8/6	7/2
Anti-CCPhs,** U/mL	2.6(1.5-5.0)	71(4.6-1237.5)	<0.0001[^]	105.0(7.3-1300.0)	34.0(3.7-1519.0)	45.0(5.2-320.0)	55.0(3.1-207.5)

*valor expressed by mean±SD; **valor expressed by median and interquartile range ($P_{25\ 75}$); [&]Student´s *t*-test; [^]Welch´s test; [#]Chi-square test.
RA= Rheumatoid Arthritis; HD= Healthy Donors; pts=patients; DMARDs= Disease Modifying Anti-Rheumatic Drugs; TNF inh= Tumour Necrosis Factor inhibitors drugs; Tofa= tofacitinib; F/M= Female/Male; WBC= White Blood Cells; Hb=Hemoglobin; Plat= Platelets; ERS= Erythrocyte Sedimentation Rate; CRP= C-Reactive Protein; DAS28=Disease Activity Score in 28 joints; RF=Rheumatoid Factor (RV<1/20); anti-CCPhs= anti-cyclic citrullinated peptide high sensitive (RV<20U/mL).

Table 1

seropositive group of patients (p=0.13) (Figure 1c). Interestingly, RA patients showed a tendency to increase the percentage of Tfh IL-17^+IFN-γ^- (p=0.057) but no changes were observed in the frequency of IFN-γ^+IL-17^- producing Tfh (p=0.82) respect to HD. When analyzing the effect of treatment, we determined that only untreated patients showed increased frequency of tTfh compared to HD (p=0.03) (Figure 2a). *There were* no statistically *significant differences* in the percentage of tTfh in RA patients after 3 months of treatment (p=0.36), even in the group with good/moderate response (p=0.16) (Figure 2b). Noteworthy, a decrease in the percentage of TfhCCR7^{lo}PD1^{hi} subset (p=0.004) (Figure 2c) was observed after treatment.

Conclusion: The RA patients had increased frequencies of tTfh and the subsets TfhCCR7^{lo}PD1^{hi} and TfhCCR7^{lo}PD1^{hi}ICOS$^+$, with the better capacity to induce Ab responses. tTfh and the subset CCR7^{lo}PD1^{hi}, were increased only in patients with ongoing autoreactive humoral response, and treatments only decrease the subset CCR7^{lo}PD1^{hi}. Studies aimed to understand the dynamics of Tfh subsets may be of relevance to understand and treat pathologies with uncontrolled Ab-responses.

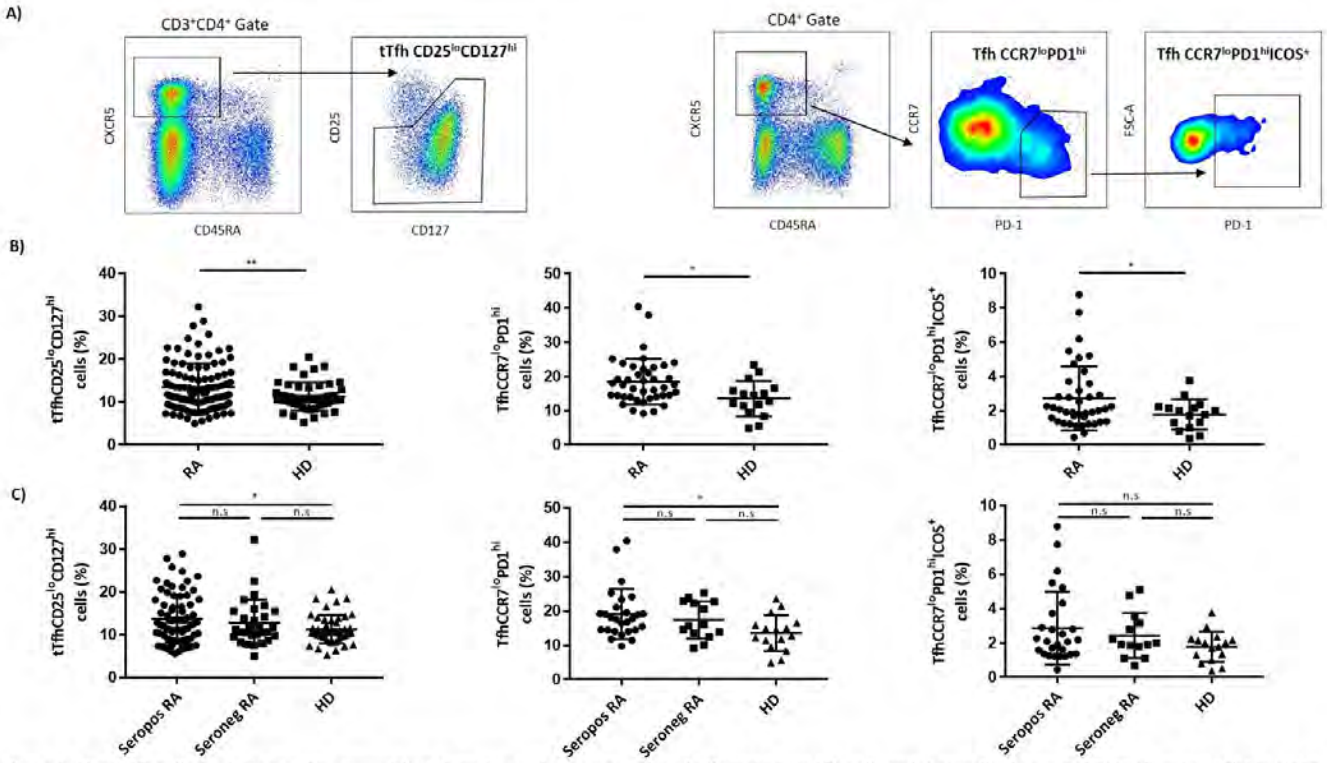


Figure 1. Blood Tfh cells are increased in seropositive RA patients. a) Gate strategies of tTfh CD25^{lo}CD127^{hi} cells and their cell subsets: CCR7^{lo}PD1^{hi} and CCR7^{lo}PD1^{hi}ICOS^{+} cells. **b)** Percentage of tTfh CD25^{lo}CD127^{hi} cells (n=103); Tfh CCR7^{lo}PD1^{hi} subset (n=41) and Tfh CCR7^{lo}PD1^{hi}ICOS^{+} activated cell subset (n=41) in RA patients and HD (n=46 and 16, respectively). Welch-test; t-test *P<0.05 **p<0.01. **c)** Percentage of tTfh CD25^{lo}CD127^{hi} cells (n=103), Tfh CCR7^{lo}PD1^{hi} cell subset (n=41) and Tfh CCR7^{lo}PD1^{hi}ICOS^{+} activated cell subset (n=41) in seropositive, seronegative patients and HD. One-way ANOVA test; Tukey-Kramer Multiple Comparisons Test *p<0.05; n.s.= not significant. RA= Rheumatoid Arthritis; HD= Healthy Donors; Seropos= seropositive; Seroneg= seronegative.

Figure 1

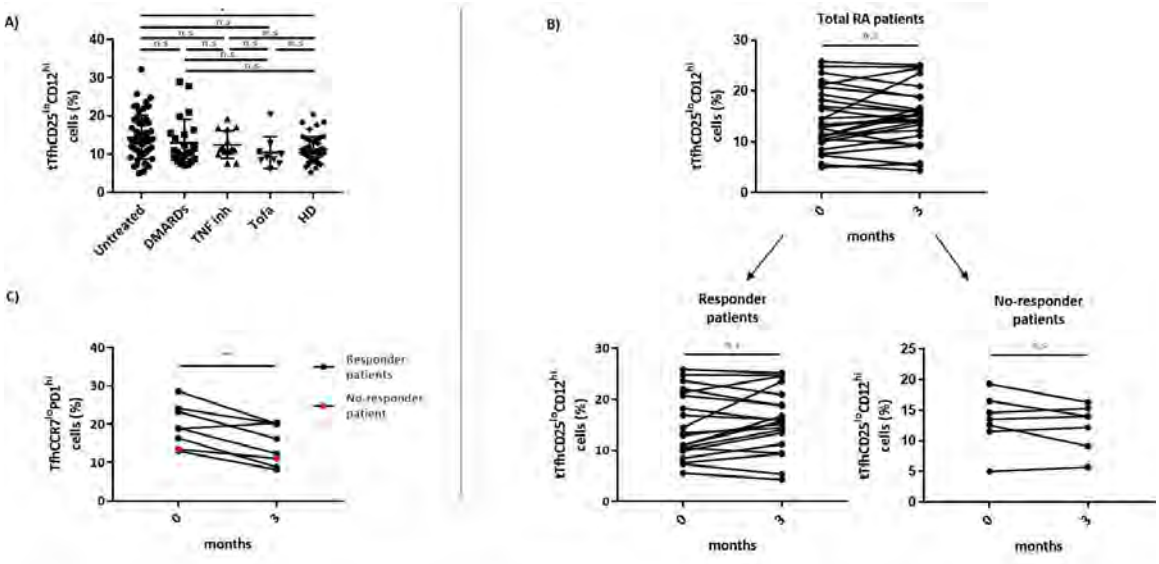


Figure 2. Blood tTfhCD25^{lo}CD127^{hi} cells are increased in untreated RA patients and TfhCCR7^{lo}PD1^{hi} subset decrease after treatment initiation. a) Percentage of tTfh CD25^{lo}CD127^{hi} cells in patients untreated (n=53) or treated with different drugs: DMARDs (n=24), TNF inh (n=14), Tofa (n=9) and HD (n=46). One-way ANOVA test; Tukey-Kramer Multiple Comparisons Test *p<0.05. **b)** Percentage of tTfh CD25^{lo}CD127^{hi} cells at the begining and after 3 months of treatment in all patients (n=27) and in responder (n= 20) and no-responder (n=7) patients to treatment. Paired samples t-test n.s.= not significant. **c)** Percentage of TfhCCR7^{lo}PD1^{hi} cell subset at the begining and after 3 months of treatment in RA patients (n=8). Paired samples t-test ** p<0.01. RA= Rheumatoid Arthritis; HD= Healthy Donors; DMARDs= Disease Modifying Anti-Rheumatic Drugs; TNF inh= Tumour Necrosis Factor inhibitors drugs; Tofa= tofacitinib.

Figure 2

Disclosure: P. Ferrero, None; **L. Onofrio**, None; **C. Acosta**, None; **E. Zacca**, None; **N. Ponce**, None; **E. Mussano**, None; **I. Cadile**, None; **L. Onetti**, None; **M. Werner**, None; **A. Costantino**, None; **E. Acosta Rodriguez**, None; **A. Gruppi**, None.

Abstract Number: 0769

Does the Autoantibody-Response Mature Between Presentation with Arthralgia and Development of Rheumatoid Arthritis? – a Longitudinal Serological Study

Fenne Wouters[1], Ellis Niemantsverdriet[1], Nazike Salioska[1], Annemarie Dorjée[1], René Toes[1] and Annette van der Helm - van Mil[2], [1]Leiden University Medical Center, Leiden, Netherlands, [2]Leiden University Medical Center, Erasmus Medical Center, Leiden, Netherlands

SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Auto-antibodies in rheumatoid arthritis (RA) are often present years before disease onset but their mere presence does not seem enough to induce RA. Several nested-case control studies have shown that autoantibody-response maturation precedes disease onset, suggesting its role in disease triggering. At present, it is

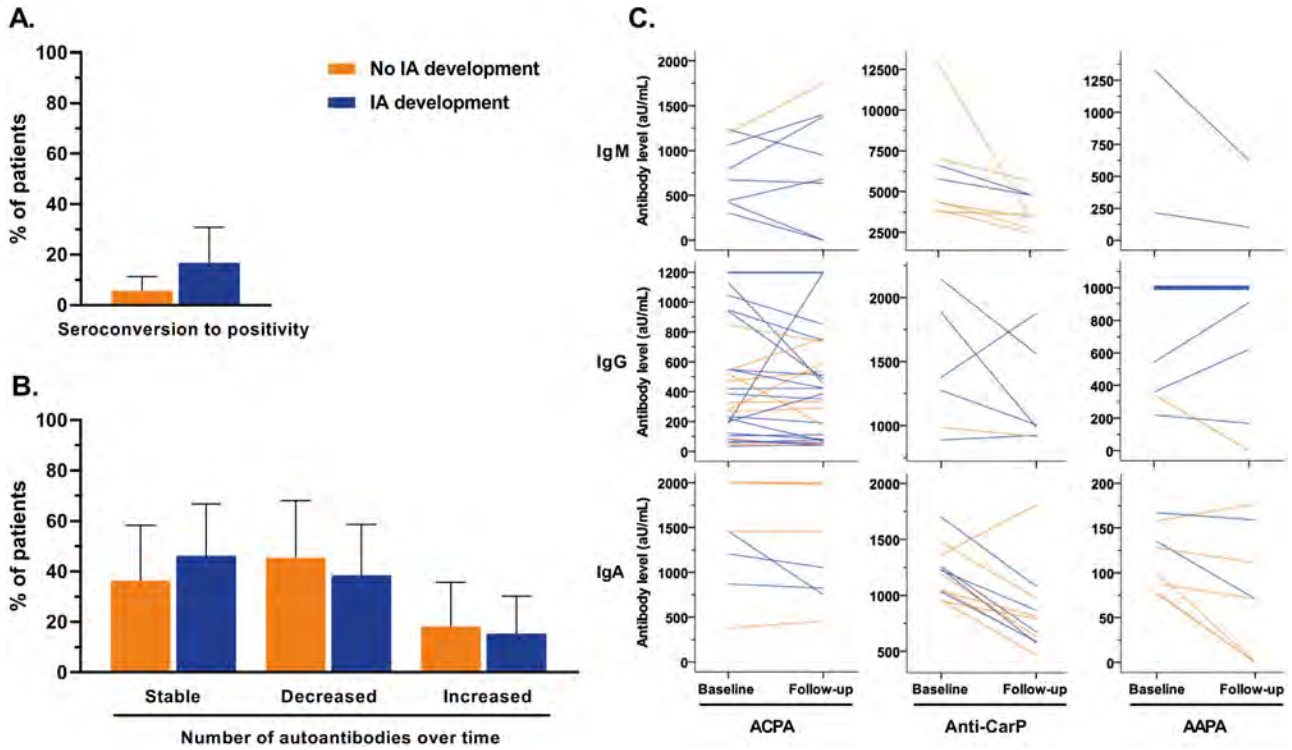


Figure 1 Changes in autoantibodies over time: A) percentage of patients with seroconversion to positive in patients negative for all autoantibodies at baseline (n=100), B) percentage of patients that has an increasing, decreasing or stable number of positive measurements over time in patients positive for ≥1 autoantibodies at baseline (n=48), C) autoantibody levels over time in patients positive for the respective autoantibody at baseline. IA: clinical inflammatory arthritis, ACPA: anti-citrullinated protein antibodies, anti-CarP: anti-carbamylated protein antibodies, AAPA: anti-acetylated protein antibodies

undetermined whether autoantibody-response maturation occurs in the symptomatic phase preceding clinical arthritis (i.e. clinically suspect arthralgia, CSA), or whether it only occurs earlier, in the asymptomatic phase. Likewise, if autoantibody-response maturation relates to disease-development, maturation is expected to be more pronounced in CSA-patients that progress to clinical arthritis compared to CSA-patients that do not. To better understand the relation between autoantibody-response maturation in time and RA-development, we performed a longitudinal study on autoantibody-response maturation in CSA-patients that did and did not progress to clinical inflammatory arthritis (IA).

Methods: In serum from 148 CSA-patients, we determined the presence and levels of anti-citrullinated, anti-carbamylated and anti-acetylated antibodies (ACPA, anti-CarP and AAPA), with three isotypes each (IgM, IgG and IgA), resulting in 9 autoantibody measurements per patient per time-point. In-house ELISA was used for all measurements. CSA-patients with paired samples at first presentation at the outpatient clinic and at IA-development (n=56) or else after 2-years (n=92) were selected. First, in patients negative for all measurements at baseline, we determined the frequency of conversion to seropositivity. Second, in patients with ≥1 positive autoantibody at baseline, we studied the frequency of autoantibody positivity over time. Finally, we determined changes in autoantibody levels in patients positive for the respective autoantibodies at baseline.

Results: In patients negative for all autoantibodies at baseline, 17% of patients that progressed to IA became positive, compared to 6% of ”non-progressors” (Figure 1A, p=0.12). In patients with ≥1 autoantibody at baseline progressing to IA, the median number of autoantibodies was 1.5 (IQR 1-3, max. 6) at baseline and 1.0 (IQR 1-4, max. 6) at IA-development (p=0.18). In CSA-patients with ≥1 autoantibody at baseline not progressing to IA, this was 1.0 (IQR 1-2, max. 4) at baseline and 1.0 (IQR 0-2, max. 5) after 2-years (p=0.07). As shown in Figure 1B; an increase in the

number of autoantibodies was infrequent (15% in progressors, 18% in non-progressors (p=1.00)). Levels of autoantibodies did not significantly change over time (p-values ranging 0.25-1.00) both in progressors and non-progressors (Figure 1C).

Conclusion: The presence and levels of IgM, IgG and IgA ACPA, anti-CarP and AAPA autoantibodies did not significantly increase over time in patients with CSA; this was similar for patients that did and did not develop clinical arthritis. These findings indicate that autoantibody-response maturation, as measured in this study, occurs in the vast majority of CSA-patients before presenting with symptoms and broadening of the autoantibody-response is not specific for progression from arthralgia to RA.

Disclosure: F. Wouters, None; **E. Niemantsverdriet**, None; **N. Salioska**, None; **A. Dorjée**, None; **R. Toes**, LUMC, 9; **A. van der Helm - van Mil**, None.

Abstract Number: 0770

Effect of Citrullination on the Processing and Presentation of Rheumatoid Arthritis Autoantigens

Ashley Curran[1], Jonathan Crawford[1] and Erika Darrah[1], [1]Division of Rheumatology, Johns Hopkins University, Baltimore, MD

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Citrullinated proteins are hallmark targets of the autoimmune response in rheumatoid arthritis (RA), but the mechanism by which immune tolerance is broken to these self-proteins is poorly understood. $CD4^+$ T cells are implicated as important drivers of the autoimmune response due to the high-affinity, class-switched nature of anti-citrullinated protein antibodies (ACPAs) present in the majority of RA patients and the prominent genetic contribution of certain HLA-DR alleles to RA susceptibility. However, the precise effect of citrullination on MHC class II antigen processing and presentation of autoantigens to $CD4^+$ T cells remains unknown. Here we aimed to examine the hypothesis that citrullination impacts the processing and presentation of RA autoantigens via destabilization of protein folding and modification of protease cleavage sites, altering the peptide repertoire presented by antigen-presenting cells (APCs).

Methods: Using fibrinogen as a model RA autoantigen, the native and citrullinated forms were digested *in vitro* by a cocktail of lysosomal cathepsins (cathepsins B, S, and H) for proteolytic mapping, or incubated with monocyte-derived dendritic cells (mo-DCs) in a natural antigen processing assay (NAPA). Peptides generated by digestion with the cathepsin cocktail or presented by HLA-DR molecules on mo-DCs were then isolated and identified by mass spectrometry.

Results: We found that the repertoire of peptides generated by each method was altered by citrullination. By proteolytic mapping, we detected both changes in the pattern of cathepsin cleavage and an increased number of peptides in the citrullinated samples. Utilizing NAPA, we observed the creation of newly presented peptides in the citrullinated samples in some cases, and loss of presented peptides in others (Fig. 1). Strikingly, all peptides whose presentation

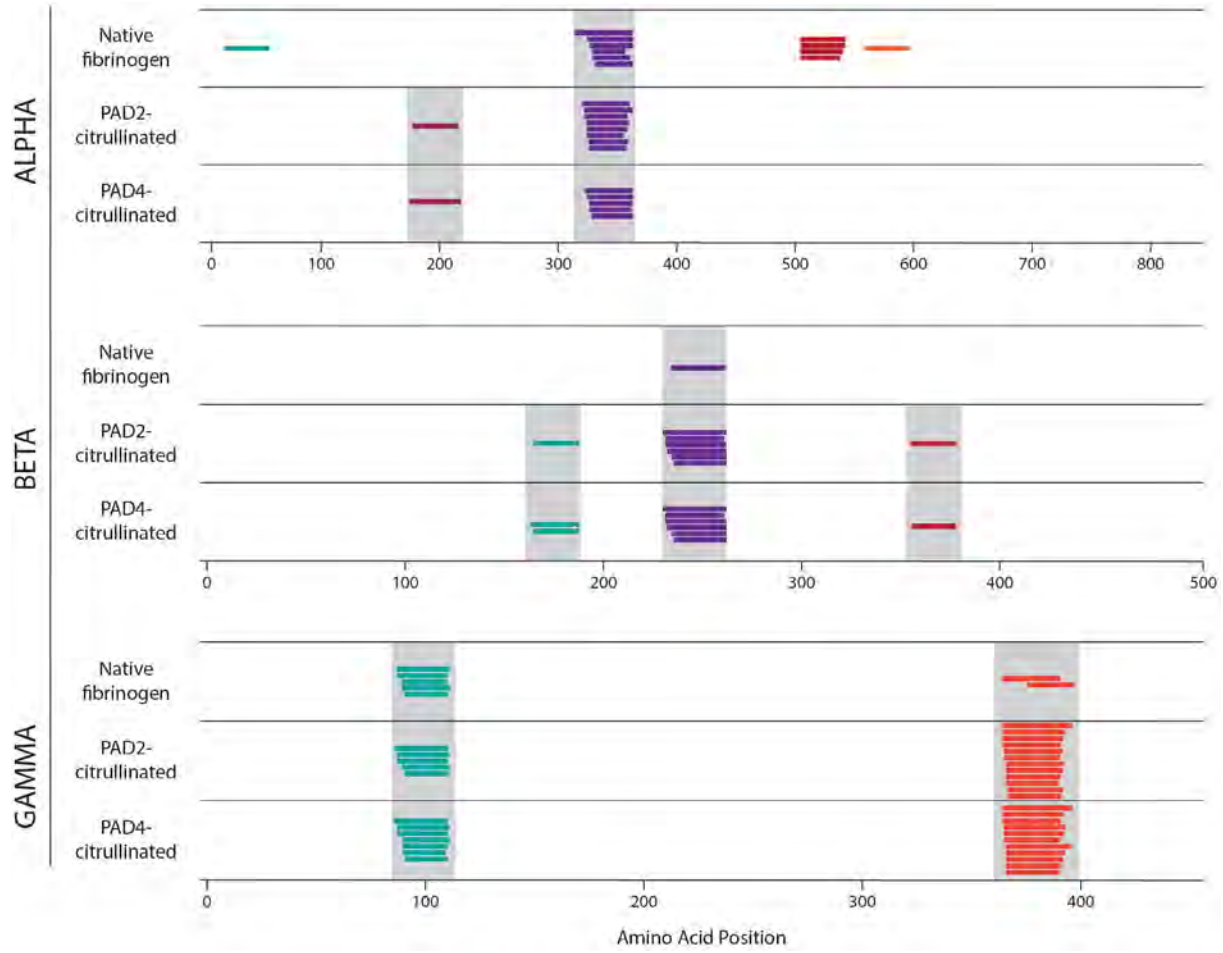


Figure 1. NAPA performed on healthy donor mo-DCs incubated with native, PAD2-citrullinated, and PAD4-citrullinated fibrinogen. Alpha, beta, and gamma chains of fibrinogen are shown separately. Each colored line represents a unique peptide. Nested peptides with a common core motif are shown in the same color within each chain. Grey bar denotes peptides with identical core motif between samples.

was destroyed by citrullination contained a citrullination site. Together these results suggest that both protease cleavage and selection of peptides by HLA-DR are impacted by citrullination.

Conclusion: Citrullination alters the peptide repertoire presented by APCs. Interestingly, no citrullinated peptides were identified by NAPA, suggesting that presentation of citrulline-containing peptides to T cells may not be the primary mechanism by which tolerance is broken to citrullinated antigens. Rather, citrullination-induced destabilization of protein folding and modification of protease cleavage sites, leading to the generation of a new peptide repertoire, could play a role in activating autoreactive T cells. This mechanism could thus drive the loss of immune tolerance to the citrullinated forms of RA autoantigens.

Disclosure: A. Curran, None; **J. Crawford**, None; **E. Darrah**, Bristol Myers Squibb, 2, Pfizer, 2, Celgene, 2, Gilead, 5.

Abstract Number: 0771

Factors Associated to Clinical and Radiographic Disease Progression in Patients with Early RA and First-degree Relatives: A 1-year Follow-up

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: In rheumatoid arthritis (RA), autoimmunity towards citrullinated peptides driven the hypothesis, in which periodontal disease (PD) is strongly related to the pathogenesis. Given the genetic association, first degree relatives (FDR) of RA-patients are considered a high-risk population to develop RA. The objective is to assess the evolution of clinical disease activity and radiographic progression associated with PD in early RA (eRA) and FDR at one-year follow-up

Methods: Patients fulfilling 2010 ACR/EULAR classification criteria and disease duration less than 2 years, additionally, relatives of patients with RA having a first degree of consanguinity were included. The following parameters were assessed: disease activity (DAS-28, SDAI), radiographic assessment of hands/feet (SENS score) for eRA, joint count assessment, serological bio-markers and a clinical periodontal evaluation was performed. Data was collected at baseline and one-year follow-up. The statistical analyses were done using the chi-square test. Ethical committee approval was obtained

Results: In total 46 eRA-patients and 83 FDR-individuals were included. In eRA the mean age was (47.8 ± 11.7 years). The increasing disease activity by DAS-28 was associated with the presence of RF ($p = 0.020$), ACPA($p = 0.008$), tender joints ($p = 0.001$), swollen joints ($p = 0.016$) and SDAI ($p = 0.005$). In all patients increasing their disease activity, the presence of *P. gingivalis* bacteria in sub-gingival plaque was observed ($p = 0.016$). With regard to periodontal condition, the incremental disease activity was associated with the presence of periodontal pockets (4-5 mm) ($p = 0.018$) and the bleeding at probing ($p = 0.046$). The change in total SENS score was observed in 55 % of progressors, associated with the presence of ACPA ($p = 0.009$). Additionally, in 100% of eRA patients who had radiological progression, a diagnosis of PD was established ($p = 0.003$). Moreover, in those who had radiological progression, the average loss of tooth insertion increased more than three times, ($p = 0.001$) and more than 50% of the sites evaluated had insertion loss ≥3 mm ($p = 0.014$)

In the FDR group (76% women), the increasing number of swollen joints at one-year follow-up was associated with active smoking (p=0.050), overweight (p=0.026), obesity (p=0.003) and fewer teeth (p=0.041). The periodontal pockets were associated with an increase of 30% in CRP levels (p=0.05), and the number of erosions (hands/feet) were associated with higher ESR levels (p=0.004). The increase in foot radiographic score was associated with higher levels of CRP (p=0.039). Finally, 2 out of 83 FDR were diagnosed with RA at one year of follow-up, for an accumulated incidence of 2.4 in individuals having genetic-risk. These 2 individuals (women) has PD and were ACPA positive.

Conclusion: In patients with eRA, disease activity and radiographic progression were directly related to periodontal involvement and ACPA levels at one-year follow-up. In FDR individuals the swollen joints and positivity of acute-phase reactants were associated to overweight/obesity and periodontal parameters. The incidence of RA in FDR is significant in this population

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Disclosure: C. Romero-Sanchez, None; **J. Bello-Gualtero**, None; **J. De Avila**, None; **G. Lafaurie**, None; **P. Chalem Choueka**, None; **C. Pacheco Tena**, None; **S. Giraldo-Q**, None; **J. Chaparro-Sanabria**, None; **A. Ramos-Casallas**, None; **L. Chila-M**, None; **W. Bautista-Molano**, None.

Abstract Number: 0772

Modification of THP-1 Cells with Malondialdehyde-Acetaldehyde Increases Cellular Calcium Load Rendering Cells Susceptible to Citrullination of Self-Proteins

Nozima Aripova[1], Michael Duryee[1], Xiarepati Tieliwaerdi[1], Xiaoting Jiang[1], Lynell Klassen[2], James O'Dell[1], Bryant England[1], Ted Mikuls[1] and Geoffrey Thiele[1], [1]University of Nebraska Medical Center, Omaha, NE, [2]Univerisity of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The post translational modification of self-proteins with malondialdehyde-acetaldehyde (MAA) has been shown to alter protein function and antibodies to MAA are increased in both ACPA positive and negative RA patients. Recently, we have shown that immunization of mice with MAA-modified proteins increases both ACPA and T-cell responses to MAA modified and citrullinated proteins. However, few if any, MAA modified and/or citrullinated proteins have been identified *in vivo*. One protein that is of interest and has been recently identified by our group is matrix Gla protein (MGP), one of the most powerful naturally occurring inhibitors of calcification. While much is known about this protein, there has been limited investigation examining whether this protein could be MAA-modified and/or citrullinated. Therefore, it was the purpose of this study was to evaluate whether MGP could be "naturally" modified with MAA and/or citrulline.

Methods: Human THP-1 monocytes were activated into macrophages with Phorbol 12-myristate 13-acetate (PMA). To evaluate whether MGP could be modified *in vitro*, THP-1 activated cells were incubated with 0.5mM MDA and 0.25mM AA (to form MAA modified proteins) ionomycin (a calcium ionophore) or media alone for 24 hours. Cell lysates were then assayed using a unique capture assay to confirm MGP could be MAA adducted and/or citrullinated. In separate experiments, activated THP-1 cells were incubated as above and then loaded with a Fluo-4 calcium indicator and observed for fluorescence at 488nm to evaluate intracellular calcium level efflux and retention.

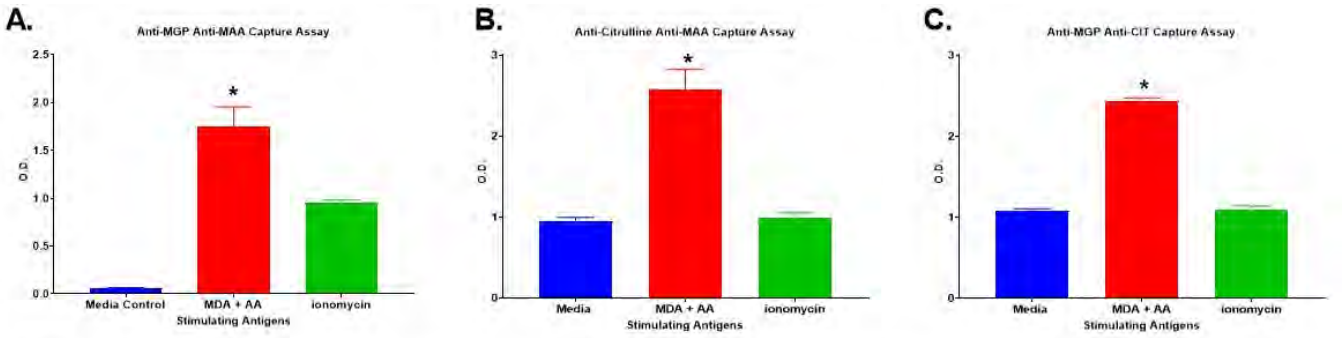

Figure 1. Identification of MAA/Citrulline and MGP on the Same Protein. Activated THP-1 cells were incubated in the presence of 0.5mM MDA and 0.25mM AA, media only, and ionomycin for 24 hours to induce MAA protein antigens. Cell lysates were assayed by ELISA capture assay for: (A) proteins both MAA adducted and Citrullinated *P<0.0001 significantly increased compared to ionomycin and media control (B) MGP MAA adducted *P<0.001 significantly increased compared to ionomycin and media control (C) MGP citrullined *P<0.0001 significantly increased compared to ionomycin and media control. N=5

Figure 1

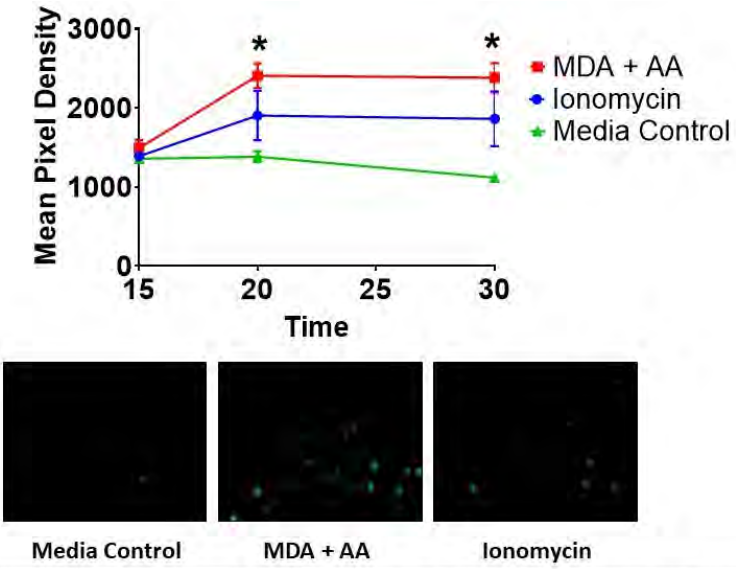

Figure 2. Increase Calcium Levels following MAA Stimulation. Activated THP-1 cells were incubated with media only, MDA + AA to create the MAA Antigen or ionomycin for 30 minutes. Cells were then loaded with a Fluo-4 and observed at 488nm for increased calcium levels. *P<0.01 significantly increased compared to the media control. N=5

Figure 2

Results: THP-1 cell lysates assayed, using the antigen capture ELISA, confirmed that MGP was both MAA-adducted and citrullinated when incubated with MDA and AA ($p < 0.0001$) as compared to ionomycin incubated and media controls (Figure 1). This was interesting as the cells were not exposed to peptidyl arginine deiminase (PAD) suggesting that citrullination was a secondary effect during the modification of cellular proteins MAA. In previous experiments, it has been shown that exogenously added MAA modified proteins decrease calcium efflux which may contribute to the activation of endogenous PAD and the citrullination of proteins. In this study, MDA and AA incubated THP-1 cells

showed significantly increased ($p< 0.01$) levels of intracellular calcium as compared to both the ionomycin and media controls (Figure 2), suggesting that calcium was indeed retained inside the cell.

Conclusion: Incubating THP-1 cells with the precursors (AA and MDA) of MAA modifies cellular proteins including MGP, which was also citrullinated in the absence of adding exogenous PAD. PAD activity is calcium dependent and we were able to show that these THP-1 macrophages incubated with AA and MDA, retained more calcium than those incubated with with appropriate controls. Mechanisms linking MAA formation to citrullination need to be identified, but it is possible that MGP function (binds calcium) is altered to help retain calcium and initiate this response. It is interesting to speculate that MGP is playing a role in the retention of calcium and the increased citrullination observed in these studies.

Disclosure: N. Aripova, None; **M. Duryee**, None; **X. Tieliwaerdi**, None; **X. Jiang**, None; **L. Klassen**, None; **J. O'Dell**, None; **B. England**, None; **T. Mikuls**, Horizon Therapeutics, 2; **G. Thiele**, None.

Abstract Number: 0773

The Anti-carbamylated Fibrinogen Response in Rheumatoid Arthritis Targets a Specific Epitope on the γ-chain and Is Associated with a More Active Disease

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SESSION INFORMATION
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Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-carbamylated protein autoantibodies (anti-CarP Abs) of IgG and/or IgA isotype have potential diagnostic and prognostic value Carbamylated Fetal Calf Serum (FCS) is the substrate for the ELISA tests being currently developed (gold standard) for their detection. However, the precise target(s) of these Abs remained undetermined *in vivo*, even though some works suggest that carbamylated fibrinogen would be the most recognized protein by them, particularly the β chain. The objectives were (i) to identify the targets recognized by anti-CarP *in situ*, (ii) to determine whether these anti-CarP Abs recognizing one or several in situ targets have a cross-reactivity with ACPA and (iii) to evaluate their diagnostic and prognostic value in a well-documented cohort.

Methods: All the sera used are from the VeRA cohort of 310 early inflammatory rheumatic diseases (median inclusion at 4 months) including 185 RA (meeting ACR 2010 criteria). To identify new carbamylated targets *in situ*, we performed mass spectrometry on sera from RA patients. An epitopic mapping was performed on the γ-chain of the carbamylated fibrinogen (target identified in the previous step) using 15 27-mer peptides overlapping on 3 amino acids, carbamylated *in vitro* (i). Two immuno-dominant epitopes were identified. The specificity of these targets was asked by performing inhibition assays with the major antigens of the citrulline response (ii). An anti-CarP FCS IgG

ELISA test on the one hand and anti-CarP Fib IgG ELISA test on the other hand were developed. An analysis with clinical, biological (CRP) and radiological data (*van der Heijde* score) at inclusion, 6 months 2 years was performed to determine the diagnostic and prognostic value of these antibodies (iii).

Results: Using a label free proteomic approach, we have identified in RA sera the γ chain of fibrinogen as a potential new target epitope mapping of this chain led to the identification of 2 immuno-dominant epitopes (peptides 5 and 13). Inhibition tests by immunodominant epitopes targeted by ACPA revealed that only peptide 13 has a specific reactivity distinct from that of anti-citrullinated fibrinogen.

The prevalence of Anti-CarP-Fib in VeRA cohort, regardless the patient status (RA or not) is 37% at baseline, which is similar to that of anti-CarP-FCS. Anti-CarP-Fib IgG has diagnostic value since 10.9% of ACPA negative RA are immuno-positive for anti-CarP-Fib IgG at early stage of the disease.

In ACPA-negative patients, anti-CarP-Fib positivity is associated with more inflammatory (higher CRP levels) and erosive disease at baseline ($p< 0.05$). However, this autoantibody population is not associated with radiological progression, which remains strongly related to the presence of ACPA.

Conclusion: One of the primary antigen targeted by the anti-CarP response in RA is carbamylated fibrinogen, particularly 2 epitopes of the γ chain whose one of them does not overlap with the ACPA response. This specificity seems to be associated to a distinct clinical phenotype since anti-CarP-Fib IgG are linked to systemic inflammation, notably in the early stage of RA.

Disclosure: P. Brevet, None; **M. Freret**, None; **P. Rottenberg**, None; **C. Guillou**, None; **T. Lequerre**, None; **P. Cosette**, None; **O. Boyer**, None; **O. Vittecoq**, BMS, 5, Novartis, 8, Pfizer, 8, ABBVIE, 5, 8.

Abstract Number: 0774

Nr4a1-high Arthritogenic T Cells from SKG Mice Are Associated with Markers of Recent and Chronic Antigen-stimulation and an Altered T Cell Receptor Repertoire

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: T cells can either be activated through their T cell receptor (TCR) in an antigen-specific manner, or in response to cytokines. Identification of antigen-reactive T cells in rheumatoid arthritis (RA) would allow us to investigate arthritogenic clones and elucidate early events in disease pathogenesis. We developed a model to identify and study such T cell responses in RA using a specific marker of TCR signaling—Nur77 (*Nr4a1*)—and identified antigen-reactive T cells in the SKG arthritis model and in RA synovial tissue. The immediate early gene *Nr4a1* (encoding the orphan nuclear hormone receptor Nur77) is upregulated in response to antigen, but notably is not induced by cytokine stimulation. Using a fluorescent reporter of Nur77 expression in SKG mice, we found that higher levels of Nur77-eGFP (GFP^{hi}) in SKG CD4 T cells were more arthritogenic and autoreactive and found an analogous

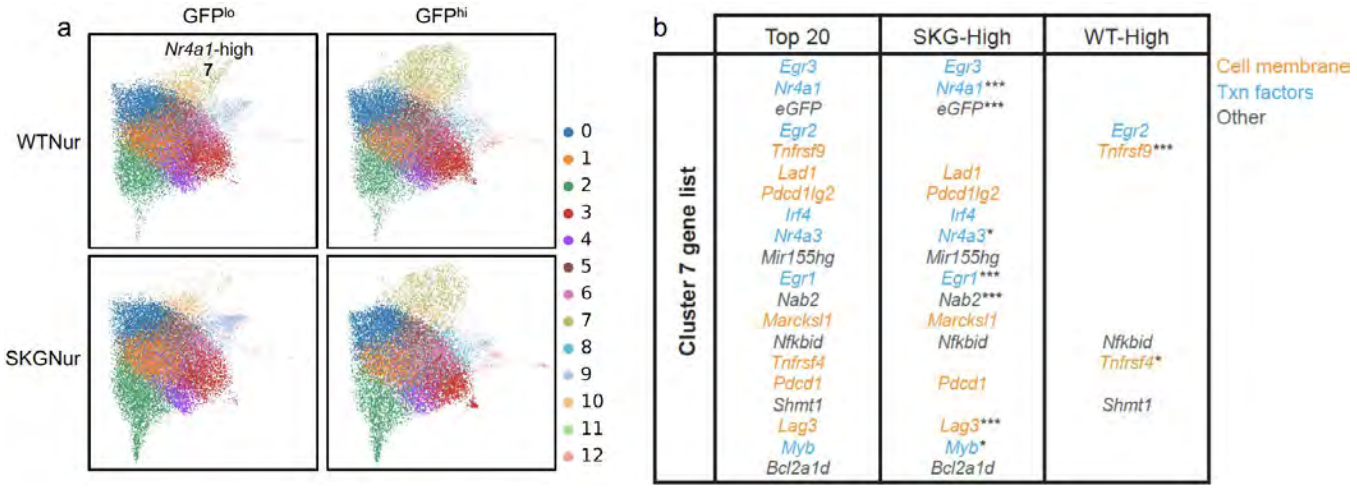

Figure 1. Nr4a1-high cluster 7 memory-like cells associated with markers of TCR signaling and enriched in SKG GFPhi CD4 T cells Transcriptional analysis of SKG and WT GFPhi and GFPlo CD4 naïve (CD4+CD25-CD62LhiCD44lo) T cells sorted based on Nur77-eGFP expression. Unbiased leiden clustering demonstrates high Nr4a1 expression in cluster 7, which is enriched with GFPhi T cells (a) and is associated with expression of immediate early genes and markers of anergy and exhaustion (b). DEG analysis by Wilcoxon rank-sum test P *< 0.05, **< 0.01, ***<0.001

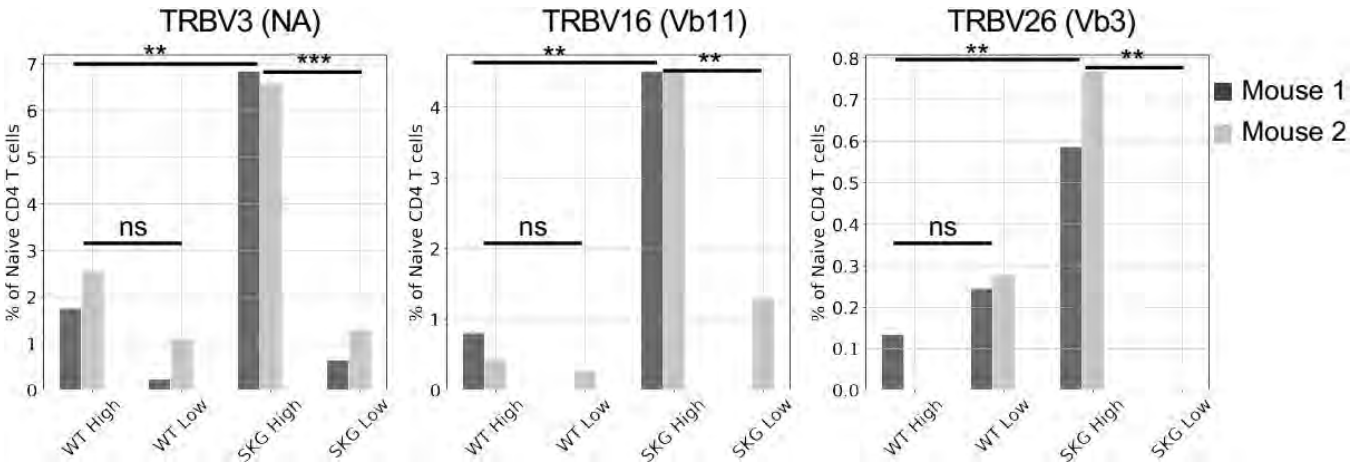

Figure 2. Altered SKG GFPhi TCR Vb repertoire. Bar graphs of TCR beta variable gene usage that are significantly enriched in SKG GFPhi T cells in cluster 7. Graph labels: TRBV gene name (TCR Vb protein name). Significance determined by one-way ANOVA followed by Tukey's HSD. NA – no named TCR Vb protein, ns: P > 0.05, **P < 0.01, ***P < 0.001

population in RA synovial tissue. Here, we set-out to examine the transcriptional program and TCR repertoire of the more antigen-experienced SKG GFP^{hi} T cells that may contribute to disease.

Methods: Paired single cell transcriptional and TCR repertoire analysis was performed on sorted naïve SKG and Balb/c (WT) CD4 T cells from 2 mice based on their Nur77-eGFP levels (GFP^{hi} and GFP^{lo}) using the 5' 10X single-cell platform. We examined our dataset for differentially expressed genes (DEG) and TCR variable genes enriched in the arthritogenic SKG GFP^{hi} T cells.

Results: After filtering, there were 99,074 cells with a mean of 12,384 cells per condition (min 9,979, max 14,899). Using leiden clustering of nearest neighbors, 12 heterogeneous cell clusters were identified from SKG and WT GF-

P^{hi} and GFP^{lo} naïve CD4 T cells. DEG analysis by Wilcoxon rank-sum test identifies a cluster marked by high *Nr4a1* expression (cluster 7). Cells in cluster 7 are associated with a memory-like phenotype, which is enriched in the SKG GFP^{hi} T cells (Fig 1). Within cluster 7 there are two highly variable gene (hvg) modules that correlate with either *Egr2* and *Egr3* (both immediate early gene transcription factors), or *Tnfrsf9* (4-1BB – the TCR inducible co-stimulatory receptor) expression using Spearman's correlation for all cells within cluster 7. The *Egr* module correlates with additional immediate early genes or markers of early T cell activation, whereas the *Tnfrsf9* module is associated with markers of chronic or prolonged TCR input. Furthermore, the SKG GFP^{hi} T cells in *Nr4a1*-high cluster 7 are associated with a biased TCR variable beta (Vb) repertoire. We find significantly higher expression of TCR Vb genes *TRBV3* ($P < 0.001$) , *TRBV16* ($P < 0.0049$), and *TRBV26* ($P < 0.001$) in SKG GFP^{hi} T cells compared to SKG GFP^{lo} and WT GFP^{hi} groups (Fig 2).

Conclusion: This scRNA and TCR sequencing dataset highlights the surprising heterogeneity found within naïve CD4 T cells and identifies a memory-like cluster marked by high *Nr4a1* expression with 2 hvg modules that likely segregate acute from chronic antigen-activated T cells. Moreover, the altered SKG GFP^{hi} TCR Vb repertoire may be an important contributor to their autoreactivity and arthritogenicity and suggests further peripheral repertoire pruning.

Disclosure: J. Ashouri-Sinha, None; **E. McCarthy**, None; **S. Yu**, None; **C. Ye**, None; **A. Weiss**, None.

Abstract Number: 0775

T and B Cell Responses to Common Tenascin-C Peptides in RA

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Session Time: 9:00AM–11:00AM

Background/Purpose: Although autoreactive CD4+ T cell and antibody responses against citrullinated antigens are known to contribute to loss of immune tolerance in rheumatoid arthritis (RA), identifying the immunodominant antigens remains an important priority. In this study, we focused on tenascin-C, an extracellular matrix protein with proinflammatory properties, based on our previous studies reporting the presence of autoantibodies targeting a citrullinated epitope in the fibrinogen-like globe of tenascin-C in patients with established RA and patients with early synovitis. Here, we extend these findings utilizing a systematic discovery approach to identify novel citrullinated tenascin C epitopes that elicit T and B cell responses in patients with RA.

Methods: An algorithm was used to predict HLA-DRB1*0401 restricted epitopes along the entire length of the tenascin-C monomer. Predicted epitopes were then tested for their ability to bind HLA-DRB1*0401 and to elicit a T cell response *in vitro*. Multiplex HLA class II tetramer staining combined with cell surface marker antibodies was used

to assess the frequency and phenotype of T cells specific for the immunogenic citrullinated-tenascin-C peptides in peripheral blood. Fluorospot assays were used to measure cytokines produced by synovial fluid mononuclear cells in response to citrullinated-tenascin-C peptides. Antibodies to citrullinated-tenascin-C peptides were detected in sera and synovial fluid using ELISAs and an extracellular matrix peptide microarray. The relationship between antibody seropositivity and clinical variables was modeled using logistic regression models with age and sex as co-variates. All RA subjects met the 2010 American College of Rheumatology criteria, and ACPA positivity was determined based on clinical testing for CCP.

Results: We identified five novel citrullinated-tenascin-C epitopes that were restricted by HLA-DRB1*0401. Notably, CD4 T cells specific for these epitopes were increased in the peripheral blood of patients with RA compared to healthy control subjects, and were present in synovial fluid. Furthermore, two of these citrullinated tenascin-C epitopes were also B cell epitopes that were recognized by antibodies in sera and synovial fluid from RA subjects. Strikingly, antibodies were present in 75% of the patients for one of these epitopes. Serum levels of these citrullinated-tenascin-C reactive antibodies were associated with rheumatoid factor, CCP seropositivity, the shared epitope, and smoking.

Conclusion: Taken together this work demonstrates the importance of citrullinated-tenascin C as an autoantigen in RA. Furthermore, our findings suggest that a unique set of epitopes recognized by both CD4 T cells and B cells have the potential to amplify autoimmunity and promote the development and progression of RA.

Disclosure: J. Song, None; **A. Schwenzer**, None; **S. Turcinov**, None; **A. Wong**, None; **C. Rims**, None; **L. Rodriguez Martinez**, None; **D. Arribas-Layton**, None; **C. Gerstner**, None; **V. Muir**, Janssen, 3; **J. Carlin**, None; **K. Midwood**, None; **V. Malmström**, Pfizer, 2; **E. James**, Pfizer, 2, Janssen, 2, Sanofi, 2, Novartis, 2; **J. Buckner**, Bristol-Myers Squibb, 2, 5, Janssen, 2.

Abstract Number: 0776

The Influence of Adipokine Profile and Periodontal Infection in Early Stages of Rheumatoid Arthritis and First-degree Relatives

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SESSION INFORMATION
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Background/Purpose: Early RA (eRA) patients have a significant incidence of periodontal inflammation and overweight/obesity. A similar degree of disease activity, functional disability and health-related quality of life has been observed in comparison to established disease. Based on the evidence with regard to the relationship between obesity and periodontitis, these two conditions could be linked because of the production of adipokines. Therefore, the aim

of this study is to evaluate the association of adipokines with of rheumatologic parameters, body mass index (BMI) and periodontitis in eRA and first-degree relatives of RA (FDR).

Methods: A cross-sectional study was conducted including 62 eRA patients (fulfilling the 2020 ACR/EULAR criteria), 124 FDR (genetic risk for developing RA according to EULAR recommendations) and 186 healthy controls matched by age and gender for each group. A complete medical history and joint count was performed. Adiponectin, adipsin, resistin and vaspin levels measured using Luminex technology, IL6 and leptin were measured by ELISA and *Porphyromonas gingivalis* by qPCR. Serum markers such as RF, ACPA, ESR and CRP were evaluated. Disease activity and radiographic assessment were evaluated using DAS-28 CRP, DAS-28 ESR, SDAI, RAPID3 and SENS score (hands/feet). An association analysis was made to evaluate the relationship between adipokines levels, rheumatologic parameters and *P.gingivalis* using X2, Fisher's Exact or U Mann Whitney test. A logistic regression model was performed to confirm associations.

Results: In patients with eRA, 35.8% were ACPA plus *P. gingivalis positive*, whereas 57.9% had high levels of adipsin. In total, 53.8% had both *P. gingivalis* plus high leptin levels, and 37.7% had both *P. gingivalis plus* high adipsin levels. High disease activity (DAS28ESR >3.2) was observed in 63.6%. Patients ACPA plus *P. gingivalis positives*, had high leptin levels (68.4%), and high disease activity (DAS28ESR >3.2) (62.53%). The following associations were found: high leptin levels (OR, 8.22; 95% CI, 2.7–24.5; p = 0.001), high adipsin levels (OR, 3.06; 95% CI, 1.0–8.9; p = 0.041) and DAS-28 ESR >3.2 (OR, 2.59; 95% CI, 1.4–4.5; p = 0.001).

In the FDR group, the *P. gingivalis* presence was associated to lower levels of adipsin (p = 0.002), resistin (p = 0.001), adiponectin (p = 0.003) and a statistical tendency to high levels of leptin (p = 0.060). Tender joints were related to low levels of adipsin (p = 0.019), and high levels of resistin (p = 0.040) and leptin (p=0.040). High levels of leptin were associated with radiographic damage SENS in hands (p = 0.037), total SENS (p=0.026), narrowing joint space in feet (p=0.020) and ACPA positivity (p=0.038).

Conclusion: High levels of leptin and adipsin were associated with clinical disease activity in patients with early RA and periodontal infection, presented simultaneously. In the genetic risk group (FDR) the adipokine profile was associated with the presence of *P. gingivalis* and joint parameters. This factor may modulate the inflammatory environment and increase the risk of developing RA.

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Abstract Number: 0777

CLEC12A Expression as a Potential Predictor of Disease Activity in Early Rheumatoid Arthritis

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Background/Purpose: Rheumatoid arthritis (RA) develops as a result of the dysregulation of immune activating and inhibitory pathways. Several lines of evidence indicate that inhibitory receptors on circulating leukocytes are potential predictors of disease activity, seropositivity and/or inflammation markers. Although myeloid cells play an important role in the pathogenesis of RA, less is known about the correlation between the expression of their inhibitory receptors and clinical outcomes in RA compared to inhibitory receptors on lymphocytes. CLEC12A is a myeloid inhibitory receptor that negatively regulates neutrophil activation *in vitro* and whose polymorphisms have been associated with RA. Moreover, CLEC12A knock-out mice with collagen-induced arthritis exhibit enhanced joint inflammation and impaired resolution of joint injury indicative of a potential role for this inhibitory receptor in RA. The goal of this study was to determine whether CLEC12A is differentially expressed in circulating neutrophils and monocytes of human early RA (eRA) patients and if its expression correlates with clinical parameters and cytokine production.

Methods: Seventeen patients with early RA (eRA), symptom duration of >6 weeks but less than 15 months of symptoms, were recruited as part of the Systemic Autoimmune Rheumatic Disease biobank and database repository of the CHU de Québec-Université Laval. Clinical data and serum samples were obtained at the first visit (baseline), 3, 6, 12 and 18 months and a one-time control sample was obtained from healthy donors. Simple disease activity index (SDAI) was determined at each visit, and autoantibody levels at baseline and 12 months. CLEC12A receptor expression was determined on circulating neutrophils and monocytes by flow cytometry at baseline and 3, 6, 12 and 18 months follow-up. Serum cytokines were quantified at baseline. Group generalized estimating equations model, Student's *t* test and Spearman's correlations were performed to identify correlations between CLEC12A expression and clinical parameters.

Results: Cell-surface expression of CLEC12A is significantly higher on neutrophils of early rheumatoid arthritis patients at baseline compared to healthy donors ($p = 0.014$). Cross-sectional analyses indicate a negative correlation of CLEC12A expression at baseline with the SDAI at baseline ($r_s = -0.55$; $p = 0.032$). The same observation was observed at 3 months ($r_s = -0.65$; $p = 0.01$). CLEC12A expression at baseline was predictive of the SDAI score at 6 months ($r_s = -0.52$; $p = 0.046$) and correlated positively with eotaxin levels at baseline ($r_s = 0.71$; $p = 0.003$). Similar observations were made for monocytes. No correlations were identified between CLEC12A expression and autoantibodies.

Conclusion: Our observations provide further support to the recurring theme that the expression of inhibitory receptors on circulating leukocytes changes during disease and predictive of disease parameters. The correlations we observed in this discovery cohort between CLEC12A expression and disease activity as well as cytokines strongly suggests that CLEC12A modulates the immune response that drives the early stages of this autoimmune disease.

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Abstract Number: 0778

Bacterial Families *Lachnospiraceae/Ruminococcaceae* Are Immunologically Targeted in Individuals At-risk for RA and a Specific Strain Is Arthritogenic in Monocultured Gnotobiotic Mice

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Background/Purpose: Circulating autoantibodies, including anti-CCP and RF, develop years before physical manifestations of rheumatoid arthritis (RA), with several lines of evidence suggesting that these autoantibodies may be driven in part by microbial-mucosal interactions. We hypothesized that discrete bacterial strains in the gut may drive autoantibody generation, inducing a systemic breach of tolerance in the autoantibody positive preclinical RA period that leads to the future development of joint inflammation.

Methods: Human fecal samples were obtained from 16 healthy controls (HC), 12 at-risk individuals (AR) (serum anti-CCP+ in the absence of current or prior arthritis), and 13 individuals with early RA (< 1 year duration). Antibody-seq was performed by flow sorting bacteria endogenously coated with human IgA, followed by 16S rRNA sequencing. Plasmablasts (PB) were isolated from 4 additional AR individuals, defined by serum CCP+ (83%) and/or RF+ (83%), and from 2 individuals with early RA (CCP+). Subdomains of the antigen binding region from PB-produced antibodies were selected by sequence analysis for their origin in a dual IgA/IgG isotype family, cloned onto a mouse IgG2a framework and expressed as monoclonal antibodies (mAbs). 94 mAbs were chosen for further study based on recombinant antibody reactivity with synovial antigens. *Lachno(spiraceae)/Rumino(coccaceae)* strains were isolated from the feces of an AR subject. After culture in anaerobic media, 7 strains of interest were identified by 16S sequencing.

Results: The closely related families *Lachno*/*Rumino* were expanded in AR and RA compared to HC. This expansion was accompanied by increased IgA coating of *Lachno*/*Rumino* in AR when compared to family abundance. 62% of 94 PB-derived mAbs that bound synovial antigens also targeted intestinal bacteria, specifically *Lachno*/*Rumino*. Together these suggest altered mucosal responses to these families and cross-reactivity between *Lachno*/*Rumino* bacterial and host self-antigens in RA joints. To analyze phenotypic effects of these families, primary human bacterial strain isolates within *Lachno*/*Rumino* were verified as targeted by representative PB-derived mAbs. Germ-free DBA/1j mice were mono-colonized with *Lachno*/*Rumino* strain isolates, *Prevotella copri*, or culture media. Within 14 days arthritis, characterized by joint swelling and bone loss, was observed in mono-colonized mice receiving one *Lachno*/*Rumino* strain.

Conclusion: In a cohort of AR and RA individuals, we identified altered mucosal and systemic immunity to *Lachno*/*Rumino*. Germ-free mice mono-colonized with a strain derived from an AR individual developed arthritis. Although

the full mechanism has not been fully elucidated, the observed cross-recognition of *Lachno*/*Rumino* and joint derived antigens by AR and early RA PB-derived mAbs, and induction of joint inflammation by such bacteria in mono-colonized mice, suggests that bacterial antigens and/or arthritogenic factors derived from these families drive a breach in tolerance during human preclinical RA and contribute centrally to the development of arthritis and classified RA.

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Abstract Number: 0779

Antibody Responses to Epstein-Barr Virus Are Altered in the Pre-Clinical Period of Rheumatoid Arthritis

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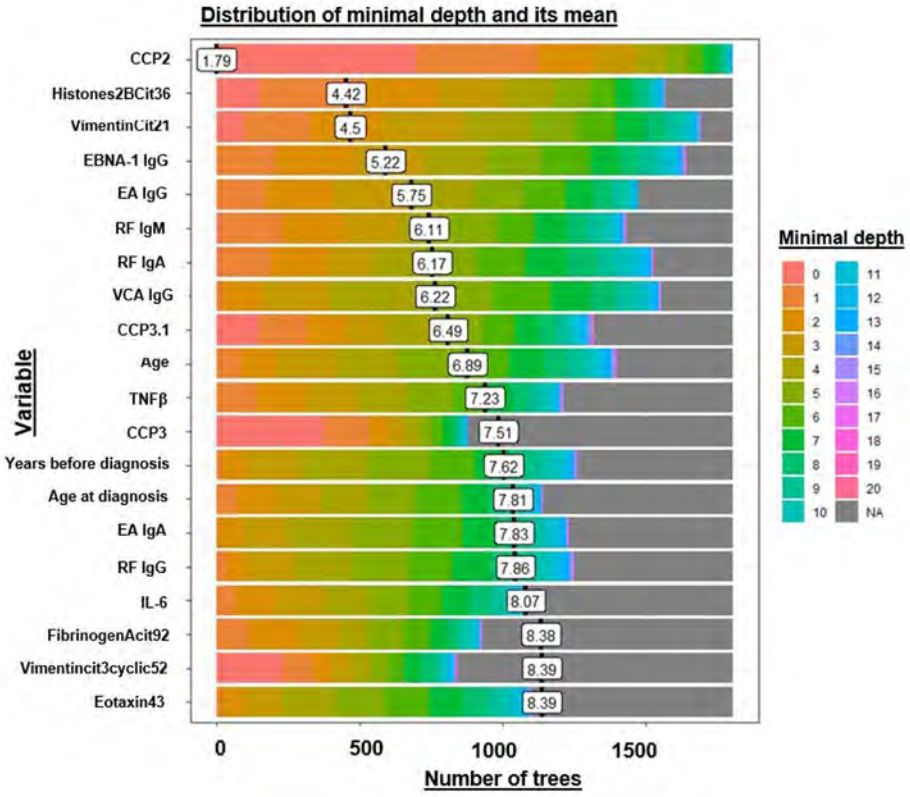
Background/Purpose: Viral infections, including infection with Epstein-Barr virus (EBV), have been suggested as environmental risk factors for rheumatoid arthritis (RA). EBV infections are known to be nearly ubiquitous in adults, life long, and asymptomatic. EBV infection status has been determined using circulating levels of IgG antibodies to Epstein Barr viral capsid antigen (VCA), nuclear antigen 1 (EBNA-1), and early antigen (EA). Prior studies have shown that patients with established RA have altered immune responses to EBV; however, the presence and role(s) for this altered immune response has not been fully understood in the autoantibody positive early period before clinically apparent RA develops. We hypothesize that EBV infection, as evidenced by an altered anti-EBV antibody response in preclinical RA, can play an important role in driving the expansion of RA-related autoimmunity.

Methods: 83 subjects had a date of RA diagnosis established by chart review and stored serum samples available through the Department of Defense Serum Repository (DoDSR) that include the pre and post RA diagnosis period based on 1987 ACR criteria. Controls (n=83) were matched to RA cases based on age, race, sex, region, and timing of blood draw. Subjects' sera were tested for 5 anti-EBV antibodies (EBNA-1-IgG, VCA-IgG, EA-IgG, VCA-IgA, and EA-IgA), 7 RA-related autoantibodies (RF-neph, -IgA, -IgM, -IgG, CCP2, CCP.3, CCP3.1), 22 cytokine/chemokine markers, and 36 APCAs. Random forest classification modelling included pre-selected biomarkers based on bivariate association with RA case versus control outcome using Mann-Whitney test ($p< 0.20$). Mixed models were used to estimate the earliest time point when the case's least-squares mean estimate was significantly higher than the control estimate for each marker. The time when an RA subject's marker level was outside the upper 95% CI for their matched control was also identified. These times were compared across each maker using an analysis of variance



The distribution of minimal depth for the top 20 significant variables among the trees of the forest is shown in different colors for each value of minimal depth. The mean minimal depth for each variable is marked by a vertical black bar and labeled with the mean depth inside the box. The lower the mean minimal depth of a variable the more important the variable is in classification of RA cases and controls.

to identify the mean time that each case differed from their control and how the mean time of each antibody relates to the others in time.

Results: Random forest analysis identified anti-EBNA1 IgG, EA-IgA, EA-IgG, and VCA-IgG among the top 20 important RA-related preclinical markers based upon mean minimal depth in trees and gini decrease importance measures that classify RA cases from controls *(Figure 1)*. Results of serologic analyses showed that EBNA-1 IgG levels are significantly higher in RA cases, whereas EA-IgA and VCA-IgG levels are significantly higher overall and in the pre-diagnosis period *(Table 1)*. Mixed modeling analysis of anti-EBV antibody levels identified the earliest divergence of EA IgG, EBNA-1 IgG, and VCA IgG levels between cases and controls are at 8.3, 3.5, and 1.9 years prior to RA diagnosis respectively. The difference in the timing of these case/control mean biomarker level differences is significant between each antibody and each group.

Conclusion: Our study suggests that several anti-EBV antibody levels are significantly elevated in the preclinical time of RA. In addition, altered EBV antibody titers suggests that this virus may contribute to a specific endotype of preclinical RA.

	RA Case	Control	p value
EBNA-1 IgG (OD) positive ever: N (%yes)	82 (98.8%)	82 (98.8%)	1.00
EBNA-1 IgG (OD) level: *mean ± SD	**0.84 ± 0.27**	**0.77 ± 0.21**	**0.05**
pre-RA visits: *mean ± SD	0.86 ± 0.29	0.79 ± 0.23	0.06
post-RA visits: †mean ± SD	0.73 ± 0.25	0.68 ± 0.20	0.27
VCA IgG (ISR**) positive ever: N (%yes)	79 (95.2%)	81 (97.6%)	0.68
VCA IgG (ISR) level: *mean ± SD	**4.44 ± 1.68**	**3.88 ± 1.27**	**0.02**
pre-RA visits: *mean ± SD	**4.39 ± 1.68**	**3.82 ± 1.24**	**0.01**
post-RA visits: †mean ± SD	4.86 ± 1.91	4.32 ± 1.71	0.15
EA IgG (ISR) positive ever: N (% yes)	**28 (33.7%)**	**9 (10.8%)**	**0.0004**
EA IgG (ISR) level: *mean ± SD	**0.82 ± 0.72**	**0.49 ± 0.28**	**0.0002**
pre-RA visits: *mean ± SD	**0.82 ± 0.72**	**0.49 ± 0.29**	**0.0002**
post-RA visits: †mean ± SD	**0.86 ± 0.61**	**0.56 ± 0.31**	**0.01**
VCA IgA (ISR**) positive ever: N (% yes)	6 (7.2%)	2 (2.4%)	0.28
VCA IgA (ISR**) level: *mean ± SD	0.34 ± 0.22	0.29 ± 0.19	0.14
pre-RA visits: *mean ± SD	0.34 ± 0.23	0.29 ± 0.19	0.17
post-RA visits: †mean ± SD	0.32 ± 0.24	0.25 ± 0.17	0.09
EA IgA (ISR) positive ever: N (% yes)	51 (61.5%)	43 (51.8%)	0.21
EA IgA (ISR) level: *mean ± SD	**0.97 ± 0.49**	**0.79 ± 0.46**	**0.02**
pre-RA visits: *mean ± SD	**1.02 ± 0.50**	**0.82 ± 0.48**	**0.01**
post-RA visits: †mean ± SD	0.78 ± 0.77	0.68 ± 0.63	0.48

**ISR- Immune Status Ratio
*mean level calculated for each subject using all visits then compared across case/control status
†only 1 sample max per subject post-RA. 94 subjects have post-RA sample.

Table 1. Anti-EBV Antibody Levels in Cohort

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Subsets of Synovial Fluid Derived Fibroblast-like Synoviocytes in Rheumatoid Arthritis

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Background/Purpose: In rheumatoid arthritis (RA), fibroblast-like synoviocytes (FLS) secrete inflammatory cytokines and chemokines, invade and degrade cartilage, and stimulate osteoclast that cause bone erosion. Recently, it is reported that the subsets of RA FLS in fresh human synovial tissues were characterized by the expression of podoplanin (PDPN), CD34, and THY1 (also known as CD90). Especially $PDPN^+CD34^-THY1^+$ FLS may be pathogenic since these cells secrete proinflammatory cytokines and are proliferative and invasive. Adherent cells with FLS appearance are observed when the cells in synovial fluid (SF) are cultured. The aim of this study is to investigate the subsets of SF-derived FLS in RA.

Methods: We collected the SFs aspirated from the knee joint of RA patients, who were not treated with DMARDs at the onset or at the flare. The SFs were centrifuged and the cell pellets were resuspended in RPMI-1640 medium supplemented with 10% FBS and 1% Pen-Strep. The attached cells were cultured until 80% confluent growth was observed, and these cells were harvested and passaged. The profile of cell surface markers expressed by SF-derived adherent cells were analyzed using flow cytometry. Flow cytometry was performed by triple staining with PDPN, CD34 and THY1. The data are reported as the mean ± SE.

Results: We got the synovial fluid from 17 patients with RA. The characteristics of the 8 patients, whose SF-derived adherent cells were able to be passaged, were long duration of arthralgia (102.1 ± 35.1 vs 11.0 ± 6.9 months, $p< 0.05$), lower levels of serum rheumatoid factor (30.9 ± 15.5 vs 152.0 ± 48.9 IU/mL, $p< 0.05$) and lower proportion of lymphocytes of white blood cells in SF (11.4 ± 3.2 vs 39.0 ± 10.6 %, $p< 0.05$). At the passage 0 (n=8), $PDPN^+$ cells were lower than $PDPN^-$ cells (35.6 ± 4.1 % and 64.4 ± 4.1 %, respectively, $p< 0.05$). The proportion of $CD34^-THY1^+$, $CD34^-THY1^-$, $CD34^+THY1^+$, and $CD34^+THY1^-$ in the $PDPN^+$ cells were 54.2 ± 10.8 %, 25.7 ± 12.2 %, 23.1 ± 9.2 %, and 2.2 ± 0.3 % respectively. Among the 3 patients whose cells were passaged up to P2, the rate of $PDPN^+$ cells were increased with every repeated the passage (P0: 28.8 ± 4.4 %, P1: 60.3 ± 7.7 %, P2: 71.4 ± 3.2 %). In addition, the rate of $CD34^+THY1^+$ cells in the $PDPN^+$ cells were increased (P0: 4.4 ± 1.7 %, P1: 16.9 ± 6.8 %, P2: 25.4 ± 6.0 %).

Conclusion: These data show that $PDPN^+$ SF-derived FLS have the subsets, and $CD34^-THY1^+$ cells would be major subsets. $PDPN^+$ SF-derived FLS, particularly $CD34^+THY1^+$ cells, are proliferative. Considering SF-derived FLS have the merit of easy accessibility, these cells could substitute for ST-derived FLS in studying the pathogenesis of RA.

Disclosure: K. Wakabayashi, None; **T. Isozaki**, None; **S. Ohta**, None; **T. Kasama**, None.

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Phenotypic and Functional Characterisation of Synovial Fluid-derived Fibroblast-like Synoviocytes in Rheumatoid Arthritis

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Background/Purpose: Fibroblast-like synoviocytes (FLS) are central cellular components in persistent inflammatory joint diseases such as rheumatoid arthritis (RA). Pathological subsets of FLS have been identified from synovial tissue. However, the synovial tissue obtained from arthroplasty procedures is aquired at late disease stages and the cellular yield obtained from synovial tissue biopsies can be low. Challenging the establishment of human RA *in vivo* and *in vitro* models. FLS obtained from the synovial fluid (SF-FLS) are proposed as an alternative source of FLS, but a detailed phenotypical and functional characterization of FLS subsets from the synovial fluid has not been performed.

Methods: In the present study, paired peripheral blood mononuclear cells (PBMC) and SF-FLS from patients with RA were obtained (n=7). FLS were isolated from the synovial fluid by a strict trypsinization protocol and their cellular characteristics and functionality were evaluated at passage 4. Monocultures (SF-FLS) and autologous co-cultures (SF-FLS+PBMC) were established from five patients with RA and subsequently evaluated by flow cytometry, Western blotting and multiplex immunoassays. Human cartilage-sponges (n=3) with SF-FLS and without SF-FLS (n=3) were co-implanted subcutaneously in 15 SCID mice, mice with only cell-free human cartilage-sponges were used as controls (n=12). After 45 days, the implants were evaluated using stained sections to determine the SF-FLS invasion score based on perichondrocytic cartilage degradation. Data are expressed as median (25-75 percentile). P-values < 0.05 were considered statistically significant.

Results: The homogeneous subpopulations of FLS, isolated from the synovial fluid, were negative for CD34 and CD45 [98.9%, (97.5-99.7]) and positive for Thy-1 and PDPN [94.6%, (79.9-97.4]). Without stimulation, RA SF-FLS showed high and comparable levels of NFκB related pathway proteins and secreted multiple pro-inflammatory cytokines and chemokines dominated by IL-6 [2648 pg/mL, (1327-6116)] and MCP-1 [2458 pg/mL, (692-8719)]. SF-FLS increased their ICAM-1 and HLA-DR expression after encountering autologous PBMCs ($p< 0.01$), ($p< 0.05$). Further, SF-FLS and PBMC interacted synergistically in a co-culture model of RA and significantly increasing the secretion of several cytokines (IL-1β, IL-2, IL-6, ($p< 0.01$)) and a chemokine (MCP-1, ($p< 0.01$)). The invasion score of the human SF-FLS *in vivo* was at primary site, [1.6, (1.3-1.7)] and contralateral implantation site [1.5, (1.1-2.2)]. The invasion score of the human SF-FLS-containing implants both at primary and contralateral site were significantly higher compared with cartilage-sponges evaluated from SF-FLS-free control mice ($p< 0001$).

Conclusion: This phenotypical and functional characterization of SF-FLS, do not deviate from synovial tissue FLS and lay a foundation for establishing *in vivo* and *in vitro* FLS models. These FLS models will be beneficial in our understanding of the role of this cellular subset in arthritis and for characterization of drugs specifically targeting this pathological RA FLS subset.

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Abstract Number: 0782

Epigenetic Regulation of Metabolic Transporters in Rheumatoid Arthritis Fibroblast-Like Synoviocytes

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
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Background/Purpose: Epigenetic changes contribute to the pathogenesis of rheumatoid arthritis (RA) and a comprehensive epigenomic characterization of RA fibroblast-like synoviocytes (FLS) has recently been described. Nutrient transporters, with the SLC transporter families that contain 400 genes and 52 subfamilies among others, serve as 'metabolic gate' of cells by mediating the transport of a wide range of essential nutrients and metabolites such as glucose, amino acids, vitamins, neurotransmitters, and inorganic/metal ions. As previous studies indicate that metabolism is altered in RA FLS, we hypothesize that ChIP mark changes in nutrient transporters genes would correlate with differences in expression of these genes and would help to identify activated metabolic pathways.

Methods: ChIP-sequencing data, for six different ChIP marks (H3K4me1, H3K4me3, H3K9me3, H3K27ac, H3K27me3, H3K36me3), and DNA methylation from a publicly available data set from FLS derived from 11 RA patients and 11 OA patients were compared to identify regions with a difference in these histone modifications. Single nearest genes to regions of interest were then utilized for pathway analyses (REACTOME classification) to determine if particular cellular processes and pathways are associated with these chromatin changes. Pathways associated with nutrient transporters were enriched near ChIP mark changes commonly associated with active transcription (H3K4me1,

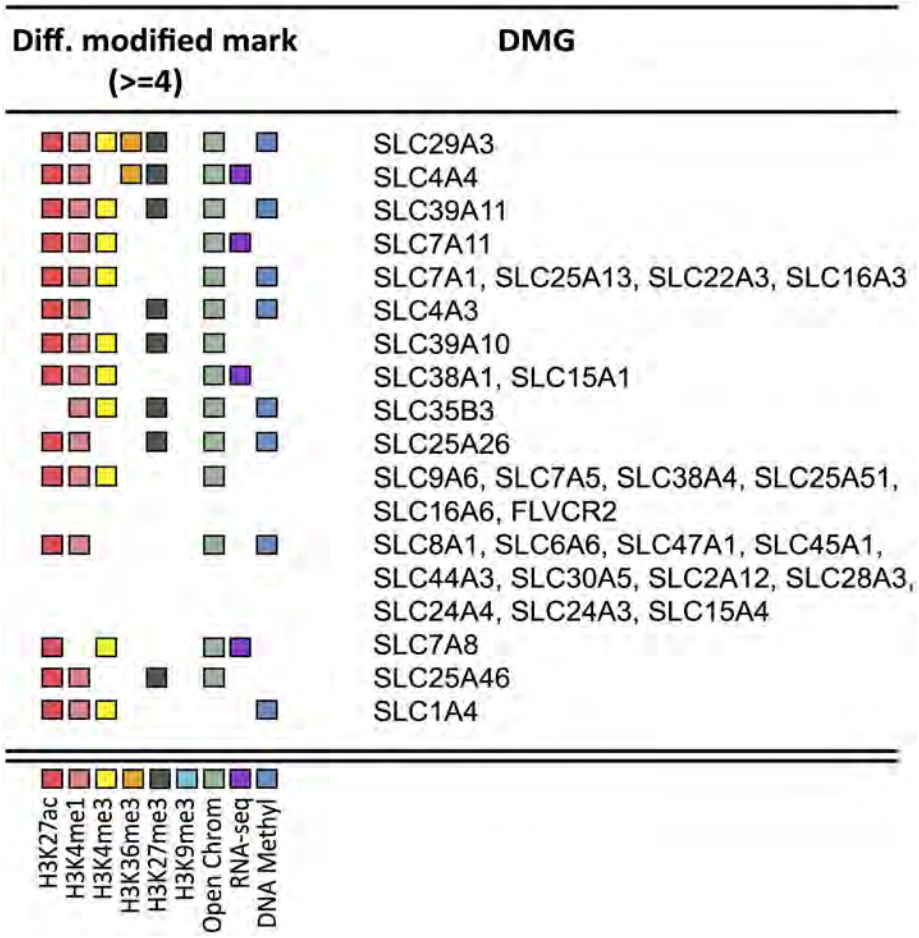

Figure 1. Shown the 34 differentially modified nutrient transport genes with differentiated modified marks.

H3K4me3, H3K27ac) with the use of the whole genome as a reference. To further elucidate these findings, single nearest genes associated with any ChIP mark change and transporters were utilized for a secondary pathway analysis. Changes in transcription of genes associated with the ChIP mark changes were assessed using RNA-sequencing data from the same cells. ATAC-Seq to study the open chromatin regions in FLS was also assessed.

Results: As per the unbiased pathway analysis, 21 pathways significantly associated with at least 3 either epigenetic marks, RNA-Seq or ATAC-Seq changes were associated with energy metabolism. "SLC-mediated transmembrane transport" was one of these pathways and associated with 4 changes. 34 different genes involved in nutrient transportation were associated with a change in at least 4 epigenetic marks (Figure 1). These genes were then used in a Reactome pathway analysis. Amino acids and oligopeptide SLC transporters (including SLC38A4, SLC38A1, SLC6A6, SLC7A8, SLC7A5, SLC7A11, SLC7A1, SLC1A4, SLC15A1, SLC15A4) was one of the top ranked pathways (adjusted p= 5.13e-13). Of note, most of these transporters are known to be glutamine transporters. Transporters for organic and metal ions were also heavily epigenetic regulated. Interestingly, ATAC-Seq analysis showed a significant enrichment of open chromatin regions near those genes.

Conclusion: This study of RA FLS demonstrates changes in epigenetic marks of genes related to nutrient transporters and suggests that metabolism is critical in RA pathogenesis and may be involved in the imprinted aggressive phenotype displayed by RA compared to OA FLS. Additionally, this dataset has the potential to identify RA-specific targets that can be used to develop novel therapeutic agents.

Disclosure: B. Pedersen, None; **R. Ai**, None; **A. Torres**, None; **W. Wang**, None; **G. Firestein**, Eli Lilly, 2; **M. Guma**, None.

Abstract Number: 0783

Role of Glutamine Metabolism in Rheumatoid Arthritis Fibroblast-Like Synoviocyte Aggressive Phenotype

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Fibroblast-like synoviocyte (FLS) activation is a key component of rheumatoid arthritis (RA) inflamed synovium. Their aggressive phenotype in RA contributes to initiation and perpetuation of destructive joint inflammation. Understanding changes in RA FLS metabolism is becoming a new focus of research in RA. We previously showed that the glutaminase gene, which encodes for the enzyme that generates glutamate from glutamine, is highly epigenetically regulated in RA FLS compared to osteoarthritis (OA) FLS. Here, we determined the importance of glutamine (gln) as an alternate carbon source to glucose for FLS and whether or not interference of this pathway can decrease the aggressive phenotype of FLS in RA.

Methods: Uptake of glutamine was determined by Glutamine/Glutamate-Glo kit by Promega. Dependence of glutamine by RA FLS was determined by functional assays, including invasion (matrigel assay), proliferation assays (EdU assay), and a migration assay (scratch assay), that were conducted using DMEM without glucose supplemented with

dialyzed fetal bovine serum. We then used increasing amounts of glutamine before and after PDGF stimulation in the presence or absence of glucose. RA FLS were also incubated with CB-839 (300nM), a glutaminase inhibitor.

Results: Glutamine/glutamate luminescence test displayed significant glutamine uptake in FLS starved of glucose after PDGF stimulation (3938±10425 vs 1165±371.8, p< 0.0001). Functional assays revealed that 6mM glutamine (FLS cultured in a media without glucose) is sufficient as an alternate source of energy to 6mM glucose (FLS cultured in media without gln) in proliferation (6mM gln 0.3±0.07 vs 6mM glucose 0.37±0.21; ns) and invasion (6mM gln 21.47±1.34 vs 6mM glucose 20.91±1.3; ns). In addition, the use of glutamine allows for an increase of invasion (0mM gln 12.87±3.316 vs 6mM 18.83±3.236; p< 0.002), proliferation (0mM gln 8.752±4.7 vs. 6mM gln 40.55±14.07; p< 0.02), and migration (0mM gln 219.8±49.88 vs 6mM gln 186.4±45.90; p=0.0002) in the absence of glucose. Of interest, OA FLS do not migrate more on 6mM glutamine compared to 0mM glutamine (0mM gln 216.1±46.35 vs 6mM gln 219.4±58.64; ns). Experiments with CB-839 showed significant decrease in invasion (vehicle 23.11±3.161 vs CB-839 14.46±2.036 p< 0.0001) and proliferation (vehicle 0.2548±0.03589 vs CB-839 0.1278±0.02861 p< 0.0001) of RA FLS under glucose depletion with varying amounts of glutamine compared with vehicle control.

Conclusion: RA FLS are able to utilize glutamine as an alternative carbon source in the absence of glucose, which mimics the starvation conditions within the joint. Glutaminase could potentially be a good target to reduce the aggressive phenotype of FLS in RA.

Disclosure: A. Torres, None; **B. Pedersen**, None; **G. Firestein**, Eli Lilly, 2; **E. Sanchez-Lopez**, None; **M. Guma**, None.

Abstract Number: 0784

Upregulation of Tyro3TK on $CD14^+CD16^-$ Monocytes Promotes Osteoclast Formation in Rheumatoid Arthritis

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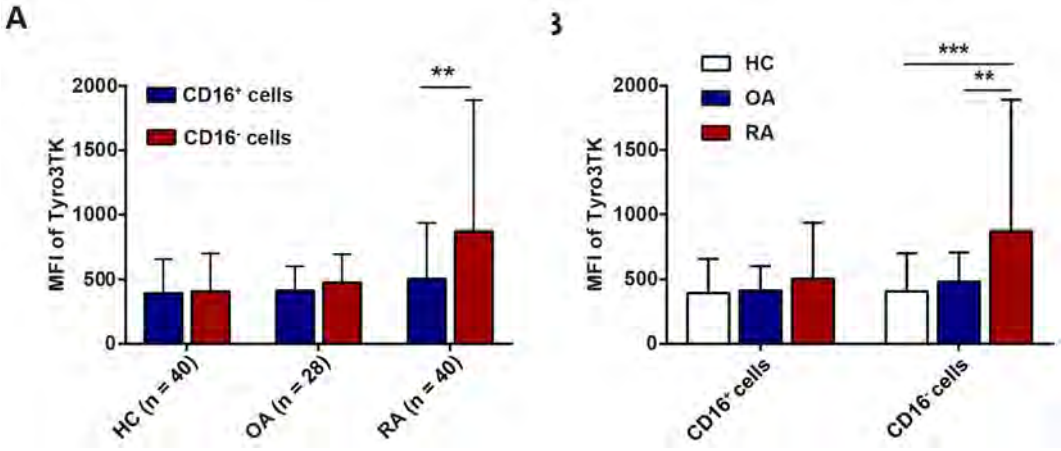
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The study aimed to investigate the expression and clinical significance of Tyro3TK on $CD14^+CD16^+$ and $CD14^+CD16^-$ monocyte subsets and explore the effect of Tyro3TK on osteoclast formation in rheumatoid arthritis (RA).

Methods: Osteoclasts were induced by $CD14^+CD16^+$ and $CD14^+CD16^-$ monocyte subsets isolated from healthy control (HC) and RA in vitro, and evaluated by tartrate-resistant acid phosphatase (TRAP) staining. Then, the expression of Tyro3TK on $CD14^+CD16^+$ and $CD14^+CD16^-$ monocyte subsets were evaluated in peripheral blood of RA by flow cytometry, and the correlation between the expression of Tyro3TK on $CD14^+CD16^+$ and $CD14^+CD16^-$ monocyte subsets with RA patient clinical data were analyzed. At last, the role of Tyro3TK on $CD14^+CD16^-$ monocyte in RA patient osteoclastogenesis was further performed by osteoclast differentiation assay.



The expression of Tyro3TK on CD14+CD16- monocytes is increased in RA. (A) The expression of Tyro3TK on CD14+CD16+ and CD14+CD16- monocytes in HC (n = 40), OA (n = 28), and RA patients (n = 40, **P = 0.008) were analyzed, and presented as mean fluorescence intensity (MFI). (B) The expression of Tyro3TK on CD14+CD16+ monocytes and CD14+CD16- monocytes were compared between HC, OA, and RA patients (**P = 0.008, ***P < 0.001).

Results: The results revealed that $CD14^+CD16^-$ monocytes were the main source of osteoclasts. The expression of Tyro3TK on $CD14^+CD16^-$ monocytes was significantly upregulated in RA patients as compared with HC and osteoarthritis (OA) patients, which was positively correlated with the disease manifestations. Moreover, anti-Tyro3TK antibody could dose-dependently inhibited Gas6-mediated osteoclast differentiation in $CD14^+CD16^-$ monocytes.

Conclusion: These findings indicate that elevated Tyro3TK on $CD14^+CD16^-$ monocytes serves as a critical signal for osteoclast differentiation in RA, but its mechanism needs to be further studied.

Disclosure: J. Xue, None; **L. Xu**, None; **F. Hu**, None; **Y. Su**, None.

Abstract Number: 0785

Identification of Recruited CCR2+ Inflammatory Monocytes in a Mouse Model of RA-associated Lung Disease with Potential Role for resolvin-D1 in Reducing Monocyte Inflammatory Responses

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) are at an increased risk for comorbid chronic lung disease, with premature mortality. Therapies for RA-associated lung disease are limited. Organic dust extract (ODE)-induced airway inflammation model was previously combined with the collagen-induced arthritis (CIA) model to model RA-related lung disease. The combination of CIA+ODE resulted in increased arthritis severity and higher levels of an-

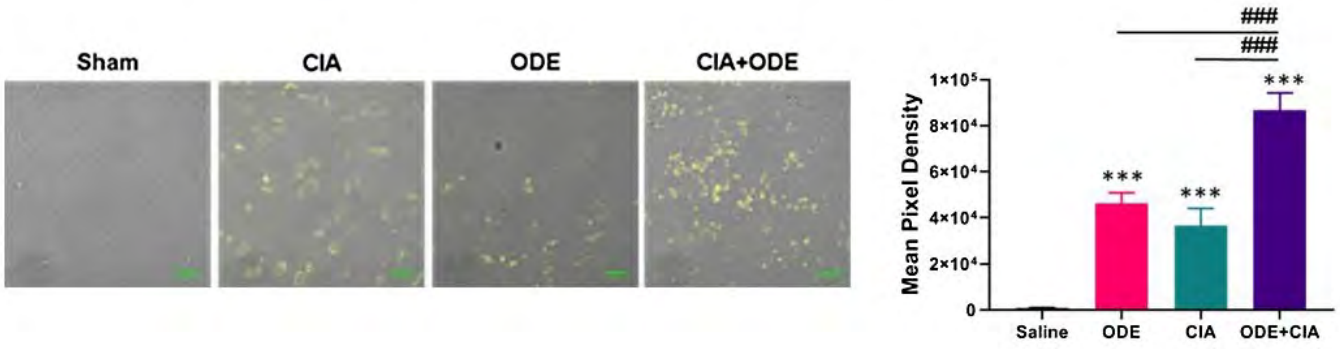

Figure 1. CCR2+ monocytes are increased with ODE and CIA treatment conditions in murine lungs. Representative image (1 of 5) of CCR2 expression (yellow) of lung tissue from each treatment group. Bar graph depicts mean with standard error bars of CCR2 staining (N=5). Statistical difference ***p<0.001 vs. saline/sham control and ###p<0.001 denoted by line between groups

ti-malondialdehyde-acetaldehyde (MAA) and anti-cyclic citrullinated (CIT) protein antibodies (vs. CIA or ODE alone). Co-exposure also promoted pro-fibrotic lung inflammatory features. $CCR2^+$ monocytes migrate to lung tissues under inflammatory conditions to influence inflammatory fibrotic consequences and may be a target for therapies. We aimed to determine whether $CCR2^+$ monocytes were recruited to the lungs in this mouse RA-lung disease model, and whether anti-inflammatory omega-3 fatty acid derivatives (DHA, resolvin-D1, and maresin-1) would reduce inflammatory responses *in vitro* from monocyte stimulation with ODE and/or autoreactive antigens.

Methods: Arthritis prone DBA/1J mice were assigned to 1 of 4 groups: Sham (saline injection/saline inhalation), CIA (CIA injection/saline inhalation), ODE (ODE inhalation/saline injection), or CIA+ODE treatment for 5 weeks as previously established. CCR2 expression was quantified using confocal microscopy in murine lung sections. In cell culture studies, human THP-1 monocytes were exposed to varying doses of: ODE, CIT peptides, and MAA-adducted protein, and the combination of ODE + autoantigens. In parallel experiments, cells were pre-treated for one hour with docosahexaenoic acid (DHA) or its metabolites (maresin-1 and resolvin-D1) before stimulation. TNF-α was quantitated in cell-free culture supernatant by ELISA.

Results: In animal studies, CCR2 expression was significantly increased in lung tissues of treated animals CIA+ODE >CIA >ODE vs. sham (Figure 1; N=5 mice/group). In monocyte studies, TNF-α levels were significantly increased following stimulation with ODE (mean ± SEM pg/ml; 1104.2 ± 91.7), MAA (167.8 ± 19.3), and CIT (75.7 ± 22.4) as compared to control (7.4 ± 4.0) (N=9; $p< 0.05$). No additive effects were demonstrated when agents were combined. Pretreatment with resolvin-D1 significantly reduced ODE-induced TNF-α at 4 hours (75% reduction) and reduced MAA (58%) and CIT (55%) stimulated TNF-α release at only 48 hours. Pretreatment with DHA or maresin-1 did not reduce ODE or autoantigen stimulated TNF-α release. No cytotoxicity was detected with respective treatments.

Conclusion: Arthritis induction promotes the recruitment of $CCR2^+$ monocytes to the lung and this response is augmented by airborne biohazard exposures to suggest that targeting recruited inflammatory monocytes may be a potential strategy. Reduction in TNF-α levels with resolvin-D1 pretreatment in monocytes strengthens the need of future *in vivo* studies to define whether specific dietary interventions focused on the omega-3 fatty acid resolvin-D1 might help in the prevention and/or treatment of RA-related lung disease..

Disclosure: A. Barry, None; **G. Thiele**, None; **T. Mikuls**, Horizon Therapeutics, 2; **M. Duryee**, None; **A. Nelson**, None; **R. Gaurav**, None; **B. England**, None; **J. Poole**, None.

Abstract Number: 0786

A Combination of Dimensionality Reduction Techniques Reveals Novel HLA-DR+ 'Candidate' Antigen-Presenting Cell Subsets (cAPC) in Patients with Rheumatoid Arthritis (RA)

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Etiology & Pathogenesis Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

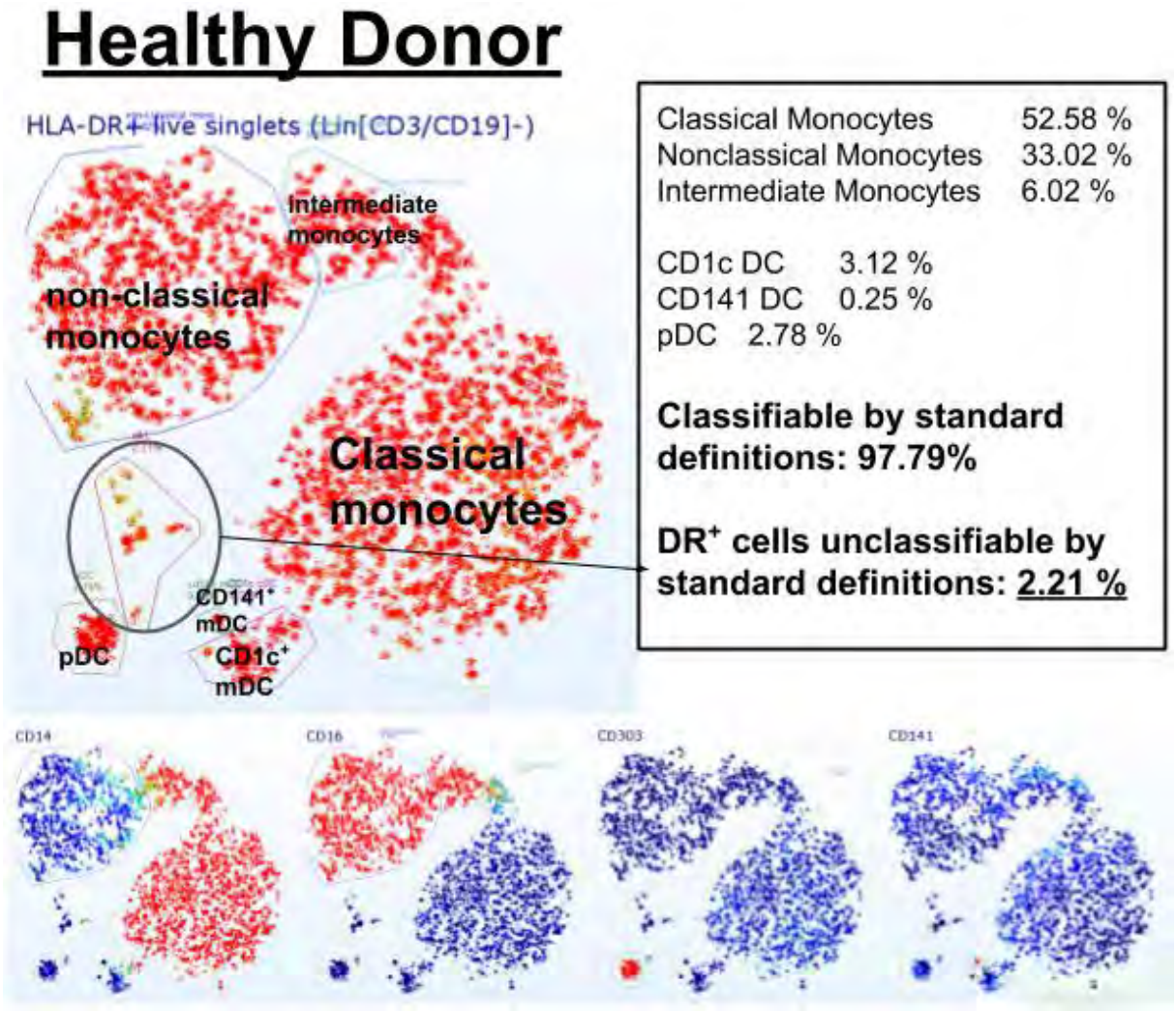

Figure 1. Example of t-distributed Stochastic Neighbor Embedding (t-SNE) guided manual annotation of high-dimensional flow cytometry data of a healthy blood donor. Non-lymphoid cells with antigen-presenting potential (DR positive, Lin negative) can be classified into established lineages in 97.79%. Bottom row shows color coded overlays of expression intensity (red positive, blue negative) of select monocyte and DC markers (CD14, CD16, CD303, CD141). Dimensions not shown: CCR2, XCR1, CD1c, CD11c, CD45RA, CD56, CD163, CD123, CD172a (SRPα)

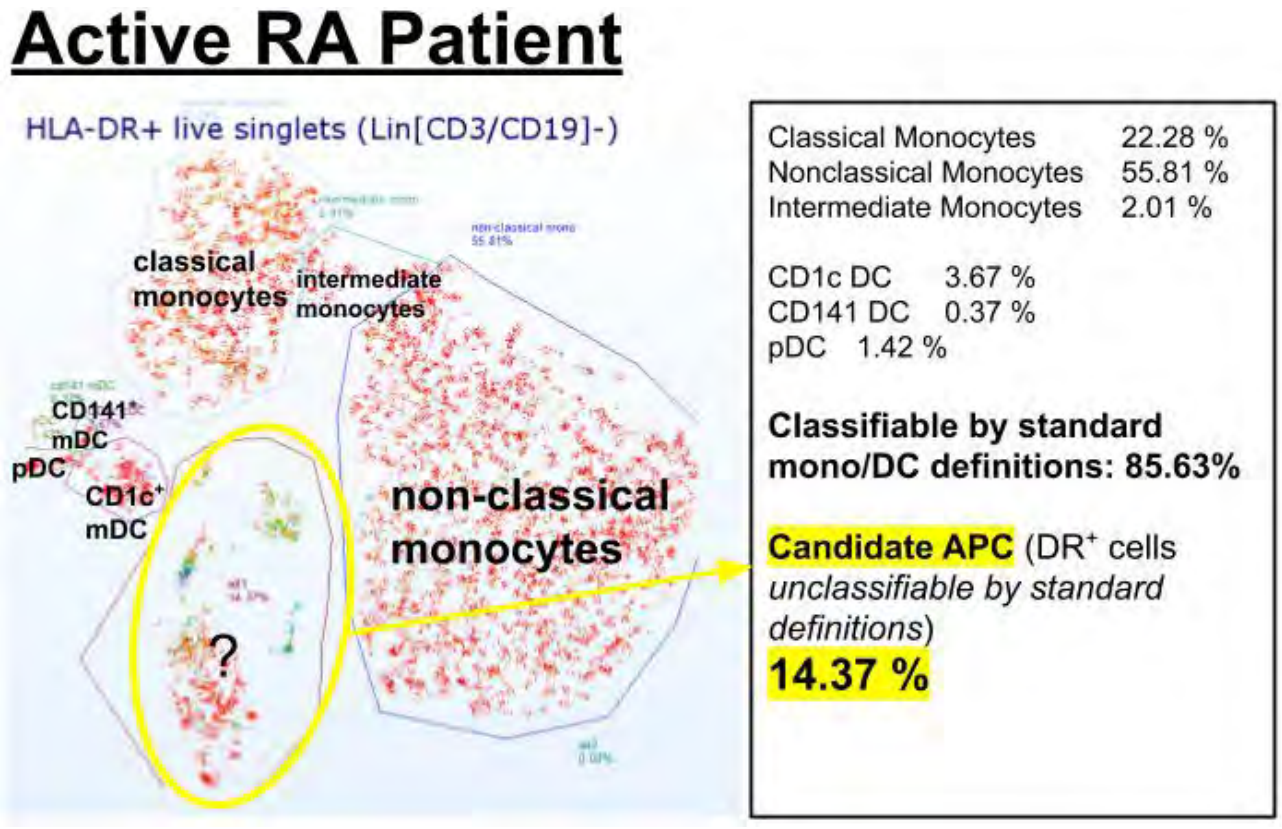

Figure 2. Example of t-SNE guided manual annotation of flow cytometry data of an active RA patient (CDAI 29), showing the emergence of 14.37% of phenotypes with antigen-presenting potential (HLA-DR positive) which are unclassifiable using standard definitions (candidate APC).

Background/Purpose: The presentation of MHC-peptide complexes to T lymphocytes via antigen-presenting cells (APC) is a crucial step in the initiation of immune responses. Dendritic cells (DC) are potent APC with remarkable plasticity that are classically divided into DC1 (141^+), DC2 ($1c^+$) and plasmacytoid (pDC) subsets. Decreases in these classic blood DC occur in patients suffering from autoimmune conditions including RA. We have previously reported that in RA, peripheral decreases of DC2 are strongly associated with clinical RA features including measures of cardiovascular disease (CVD), the main driver of RA related mortality. We reasoned that — given the importance of DC in immune activation — their apparent decrease might be more adequately explained by phenotypic alteration rather than 'true' disappearance. We hypothesized that this highly plastic compartment under inflammatory conditions might harbor alternative phenotypes that lack classic combinations of DC markers while retaining potential APC function (HLA-DR).

Methods: Patients with RA and SLE — two prototypical autoimmune rheumatic diseases (ARD) — and healthy donors (HD) underwent immunophenotyping; to capture the presumed candidate APC we first gated all viable HLA-DR^+ cells. By eliminating the lymphoid lineage ($CD3^-$,$CD19^-$) we created an HLA-DR^+Lin^- superset containing classic DCs, monocytes and candidate APC. We next classified HLA-DR^+Lin^- cells into established non-lymphoid APC [classic DC and Monocyte] by using a combination of t-distributed stochastic neighbor embedding (t-SNE) and manual annotation. HLA-DR^+Lin^- cells that did not meet established APC criteria we designate candidate APC. To screen for common characteristics across patients within this subset we performed Uniform Manifold Approximation and Projection (UMAP).

Results: Strikingly, candidate APC were higher in ARD (n=21) (7.3% vs. 3.9%; [median %DR+, Kruskall-Wallis tests), particularly SLE (11.8% vs 3.9%; p=0.01). UMAP of RA cAPC identified a dominant cluster of $CD45RA^+CD14^{lo}$ as a feature present across RA samples. $CD14^{int}CCR2^+$ cAPC represented a second major cluster. Confirming traditional

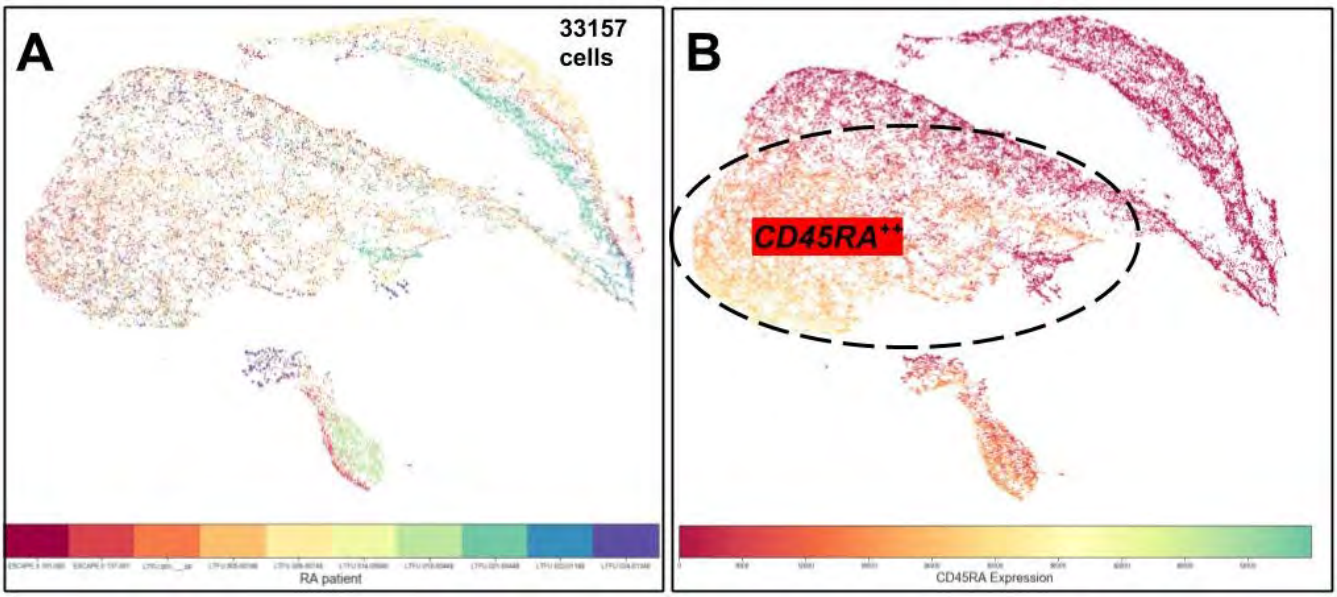

Figure 3. Uniform Manifold Approximation and Projection (UMAP) using 33157 candidate APC which were concatenated from 10 RA patients. A. Color coded by donor, showing three main clusters with cells derived from multiple donors. B. Same UMAP Heat-coded overlay showing expression of CD45RA in majority of the dominant cluster. Dimensions not shown: CD14, CD16, CD141, 303, CCR2, XCR1, CD1c, CD11c, CD45RA, CD56, CD163, CD123, CD172a (SRPα).

gating approaches, DC classical subsets were decreased in ARD when compared with HD (n=10): DC1 0.1% vs 0.4% (p=0.01), DC2 2.6% vs 5.3% (p=0.03) and pDC 1.5% vs 2.9% (p=0.03). Classical ($CD14^+CD16^-$) monocytes were not different (p=0.19) whereas intermediate monocytes ($CD14^+CD16^+$) were higher in RA than SLE and HD (13.2% vs. 8.9% vs. 6.2; p=0.01).

Conclusion: Using a combination of dimensionality reduction techniques on an unbiased $HLA\text{-}DR^+Lin^-$ APC superset we observed the appearance of $HLA\text{-}DR^+$ candidate APC. These cells do not conform to traditional APC gating definitions and were increased in ARDs relative to healthy controls. Their dominant cluster showed widespread expression of CD45RA suggesting, despite lack of CD1c expression, a developmental relationship with DC2. CD14/CCR2 co-expression was seen in three patients, supporting a relationship to monocyte-derived DC in these individuals. The novel subsets may be implicated in the pathophysiology of ARDs including RA associated cardiovascular disease, potentially via anomalous presentation of self-antigen to T lymphocytes..

Disclosure: C. Geier, None; **J. Giles**, Gilead, 5, Eli Lilly, 5, Bristol Myers Squibb, 5, Pfizer, 2; **S. Gaines**, None; **C. Depender**, None; **J. Bathon**, None; **R. Winchester**, None.

Abstract Number: 0787

MerTK Synovial Expression Correlates with Disease Activity and Treatment Response in Rheumatoid Arthritis Patients

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Despite valuable improvements in long-term clinical outcomes, a significant portion of rheumatoid arthritis (RA) patients still do not adequately respond to available treatments, and early prognostic biomarkers of response are missing. Single-cell transcriptomic studies on RA synovial tissue (ST) revealed that MerTK is highly expressed in "anti-inflammatory" macrophages [1]. Moreover, synovial macrophages isolated from RA patients in remission show a typical CD206+/MerTK+ signature [2]. Finally, monocyte-derived macrophages from RA patients treated with TNF-inhibitors (TNF-i) up-regulate MerTK on their surface.

In this study, we aim at i) assessing the modulation of synovial tissue MerTK+ macrophages upon treatment with conventional synthetic (cs) disease-modifying anti-rheumatic drugs (DMARDs) and ii) evaluating the relationship between baseline MerTK synovial gene expression and future response to TNFi.

Methods: Patients with early (< 12 months) treatment-naïve RA (as per ACR/EULAR 2010 criteria) underwent a US-guided synovial biopsy of an inflamed peripheral joint at baseline and a second biopsy of the same joint six months after starting treatment with single or multiple csDMARDs. ST was collected and used for histology and RNA extraction. ST (n=15) was stained for CD68, MerTK and CD206 by immunofluorescence using a tyramide amplification signal system. The percentage of single- (MerTK+ or CD206+) and double-positive (CD206+MerTK+) CD68+ macrophages was quantified by digital image analysis (Image J). Gene expression analysis was performed on RNA sequences of 22 baseline ST-samples (treatment-naïve).

Results: Before treatment, the percentage of MerTK+CD206+ macrophages was significantly higher in RA patients with low (DAS28< 3.2) versus high (DAS28 >5.1) disease activity (24.5±20.1 versus 4.8±4.8, p< 0.05). No differences were detected in the relative number of MerTK+ or CD206+ or MerTK+CD206+ macrophages at baseline in relationship with the clinical response to csDMARDs at 6-months. Patients (n=5) achieving remission (DAS< 2.6) at 6-months significantly increased the number of MerTK+ macrophages from baseline in comparison with patients (n=5) who were still active post-treatment (23.6±23.8 to 55.5±15.4, p< 0.05 versus 18±15.6 to 30.4±11.17, p=ns). MerTK synovial gene expression at baseline (i.e., in newly diagnosed treatment-naïve RA patients) was significantly higher in patients who subsequently responded to TNFi (n=14, good/moderate EULAR) in comparison with those who did not respond (n=8) (p = 0.003).

Conclusion: Our whole-tissue expression data further corroborate the hypothesis that a selective expansion of the MerTK+ macrophage subset defines patients achieving remission. Moreover, the up-regulation of the MerTK gene at baseline in patients future responders to TNFi suggest that MerTK is involved in modulating synovial inflammatory responses and might be exploited as a therapeutic target in RA.

Disclosure: A. Nerviani, None; **M. Boutet**, None; **G. Ghirardi**, None; **G. Lliso-Ribera**, None; **F. Rivellese**, None; **M. Lewis**, None; **M. Bombardieri**, None; **F. Humby**, None; **C. Pitzalis**, None.

Abstract Number: 0788

Rigorous Plasma Microbiome Analysis Method Enables Disease Association Discovery

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: The mucosal microbiome contributes to disease pathogenesis via local and systemic interaction with the host. The hallmark of this interaction in the physiological condition is the varying ability of bacterial products to translocate into the circulation via mucosa. Thus, the blood microbiome is important to investigate microbial-host interactions and the effects on systemic immune perturbations. However, this effort has met with major challenges due to low microbial biomass and background artifacts.

Methods: In the current study, microbial 16S DNA sequencing was applied to analyze the plasma microbiome. We have developed a quality-filtering strategy to evaluate and exclude low levels of microbial sequences, potential contaminations, and artifacts from plasma microbial 16S DNA sequencing analyses. Furthermore, we have applied our technique in individuals with systemic lupus erythematosus (SLE) and corresponding healthy controls.

Results: We first analyzed the potential contamination sources from the collection of blood samples, microbial DNA extraction, to microbial DNA sequencing. Notably, the β-diversity of plasma microbial 16S rDNA was significantly

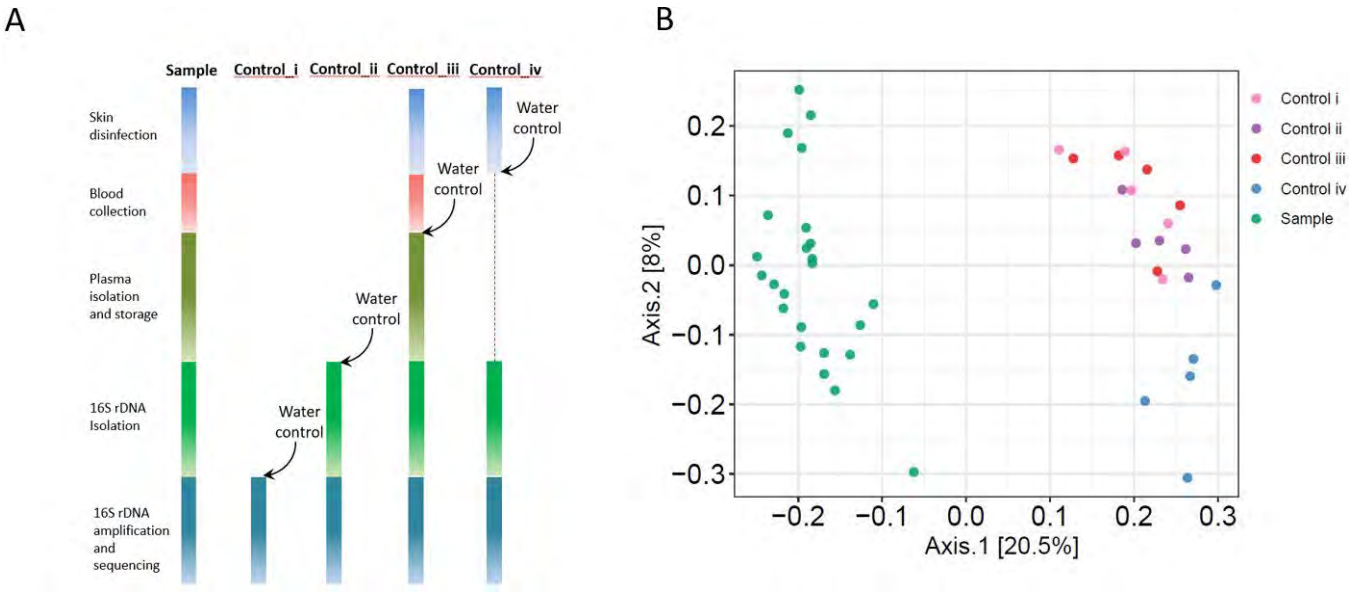

Figure 1. Overall 16S rDNA plasma microbiome analysis. (A) A workflow diagram is shown to collect blood samples and each control. (B) Principal coordinate analysis (PCoA) was conducted based on the unweighted UniFrac distance to determine the beta diversity of plasma microbial community among each controls and plasma samples.

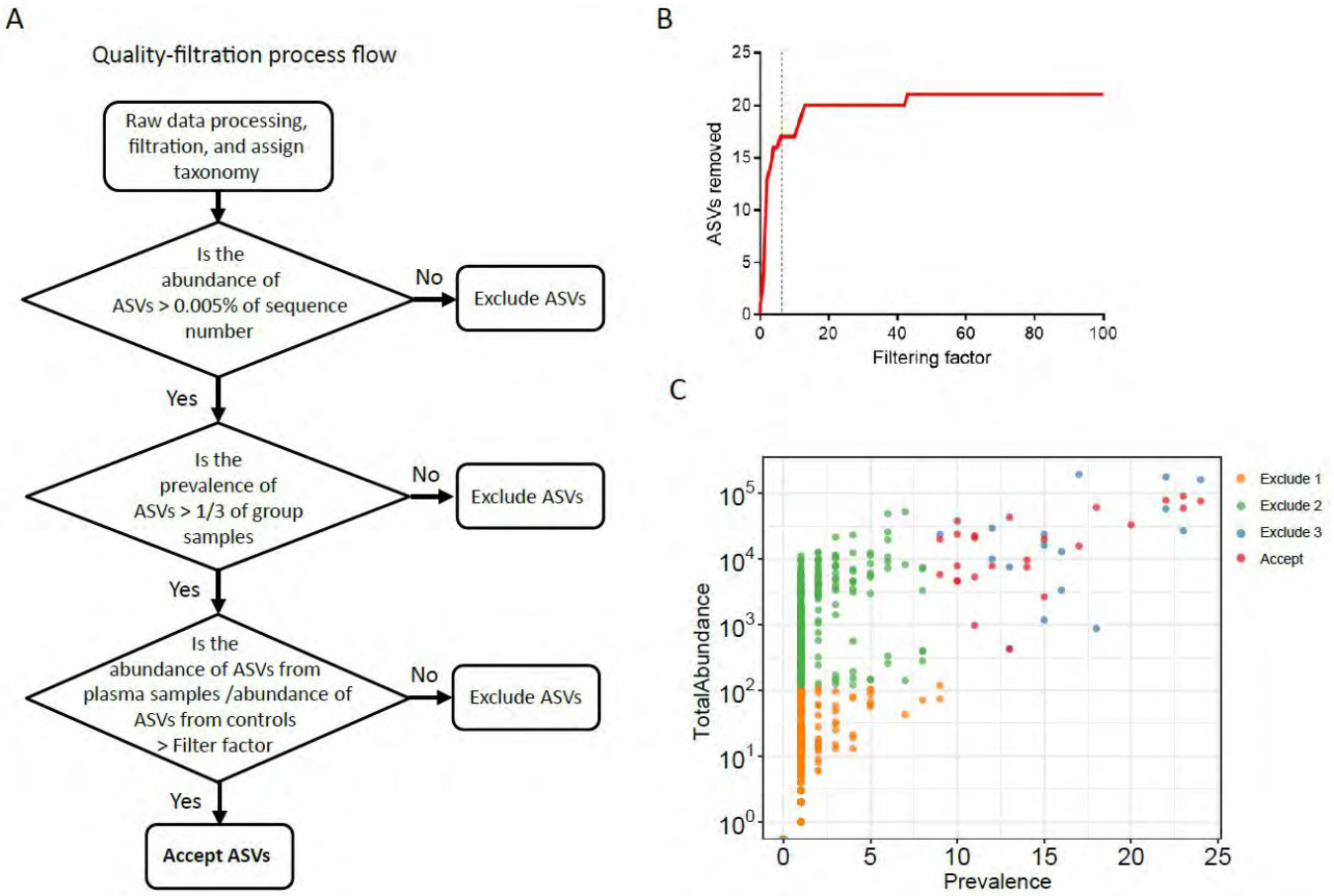

Figure 2. Strategies for removing background and potential artifacts from plasma microbiome. (A) A workflow diagram of user-defined quality-filtering strategy to exclude the background and artifacts. (B) The number of removed amplicon sequence variants ASVs with different filtering factors, we chose the filtering factor of 6 which showed the lowest number of removed ASVs during the plateau effect. (C) The abundance and prevalence of ASVs in each step of filtration. The "exclude 1" step is removing low abundance of ASVs across samples, in which a 0.005% minimum abundance threshold was applied. The "exclude 2" step is removing low prevalence of ASVs in each sample; we retained ASVs only if its prevalence was more than 1/3 across study groups. If the prevalence of ASVs was lower than 1/3 in both control and case groups, it would be removed, because it was not considered the representative disease associated ASVs. The "exclude 3" step is removing potential contaminants and artifacts using filtering factors.

different from those of the controls ($P < 0.001$, Multivariate Welch *t*-test, Figure 1). To identify the microbial amplicon sequence variants (ASVs) that are associated with disease pathogenesis, 97%-99% of total sequence data was removed using stringent quality-filtering strategy analyses; those removed ASVs were low levels of microbial sequences, contaminations, and artifacts (Figure 2). The specifically enriched pathobiont bacterial ASVs have been identified in plasmas from individuals with SLE but not from the control subjects (Nonparametric Mann-Whitney's *U* tests, Figure 3). The associations between these ASVs and plasma levels of SLE-related autoantibodies were demonstrated (Spearman correlation tests, $P < 0.05$, Figure 3).

Conclusion: The whole-genome sequencing technique has been applied to analyze the blood microbiome (Poore GD, et al, Nature, 2020); in this study, more than 90% of total sequence data was removed after decontamination analysis. In the current study, we present a quality-filtering strategy to identify abundant plasma microbial ASVs. This strategy can be used to discover translocated microbial DNAs that correlate with biological conditions. Our approach provides a cost-saving method for the diagnosis of subclinical microbial infection as well as for understanding the roles of microbiome-host interaction in disease pathogenesis.

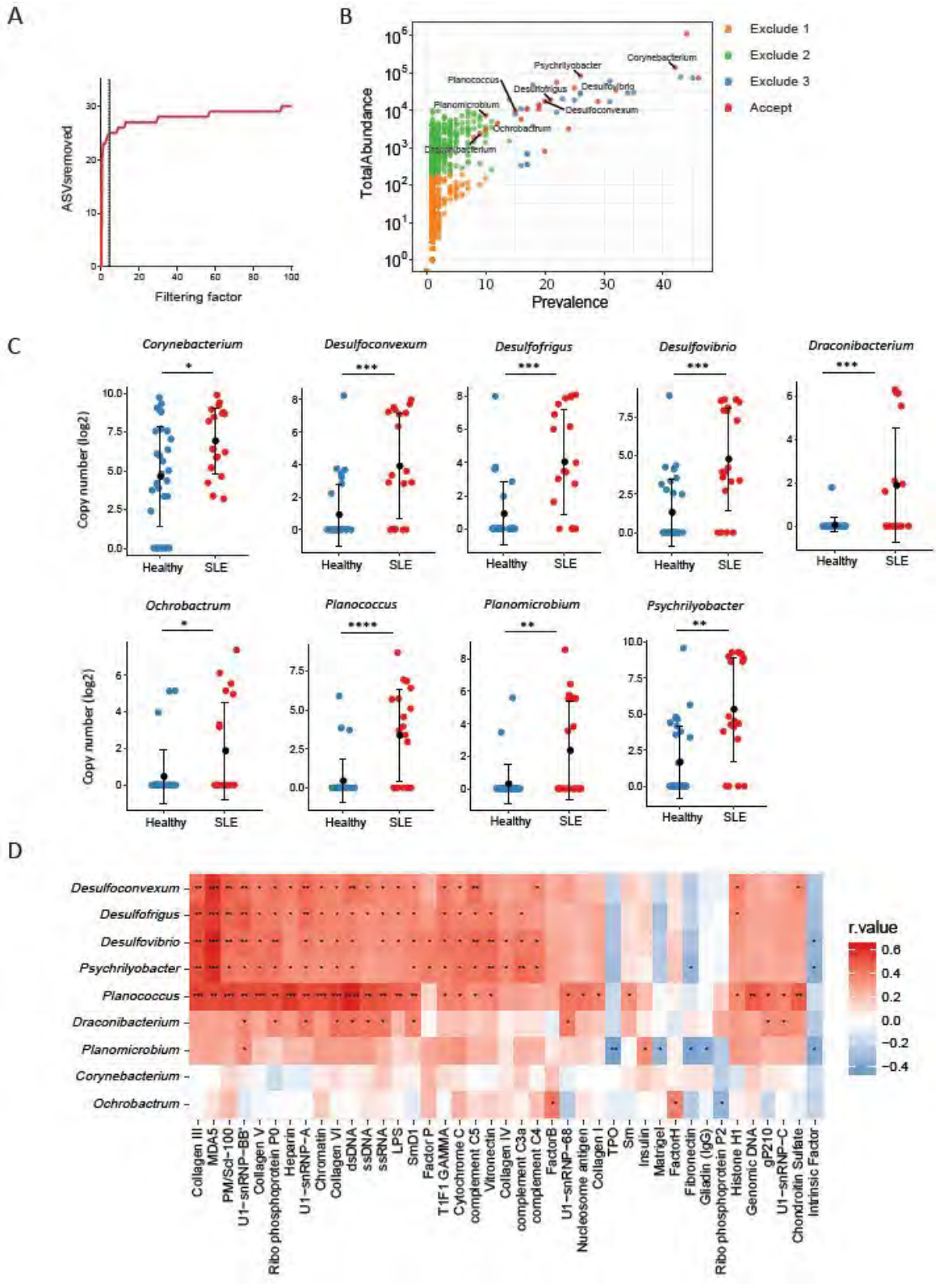

Figure 3. Plasma microbiome in female SLE patients and healthy female controls. (A) The number of removed ASVs with different filtering factor, we chose the filtering factor of 3 which showed the lowest number of removed ASVs during the plateau effect. (B) The abundance and prevalence of ASVs in each step of plasma microbiome filtration are shown, and the significantly different taxa in SLE patients compared with healthy controls are labeled in black (enriched in SLE patients). (C) The significantly different taxa in SLE patients compared with healthy controls. (D) Correlations between plasma levels of autoantibodies and differential plasma taxa levels in the two study groups. Correlation coefficient r values are indicated by color from red (directly correlations) to blue (inversely correlations); p-value significance is shown in the heatmap. Nonparametric Mann-Whitney's U and Spearman's rank tests. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$, **** $p < 0.0001$.

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Abstract Number: 0789

Matrix Gla Protein (MGP) Modified with Malondialdehyde/Acetaldehyde Is Increased in Rheumatoid Arthritis and Cardiovascular Patients

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with an increased cardiovascular disease (CVD) burden, dramatically increasing the risk of mortality. Circulating antibodies to Malondialdehyde-Acetaldehyde (MAA) modified proteins have been found in patients with RA and CVD. MAA-modified protein adducts have also been identified in RA joint tissues, atherosclerotic lesions, and plaques. However, the proteins found in these tissues have been difficult to identify. Matrix gla protein (MGP) is a robust inhibitor of calcification, binds calcium, is a constituent of atherosclerotic lesions and is thought to play a pathogenic role in CVD. The purpose of this study to determine if MAA-modified MGP is present in both RA and CVD tissues.

Methods: Joint tissues from 3 RA and 3 OA controls, along with 3 aortic lesions and 3 plaques obtained from patients with cardiovascular disease (CVD), were stained by immunohistochemistry (IHC) for the presence of MAA and MGP using zenon labeled 405 and 568 antibodies, respectively. Human vascular smooth muscle cells (VSMC) were

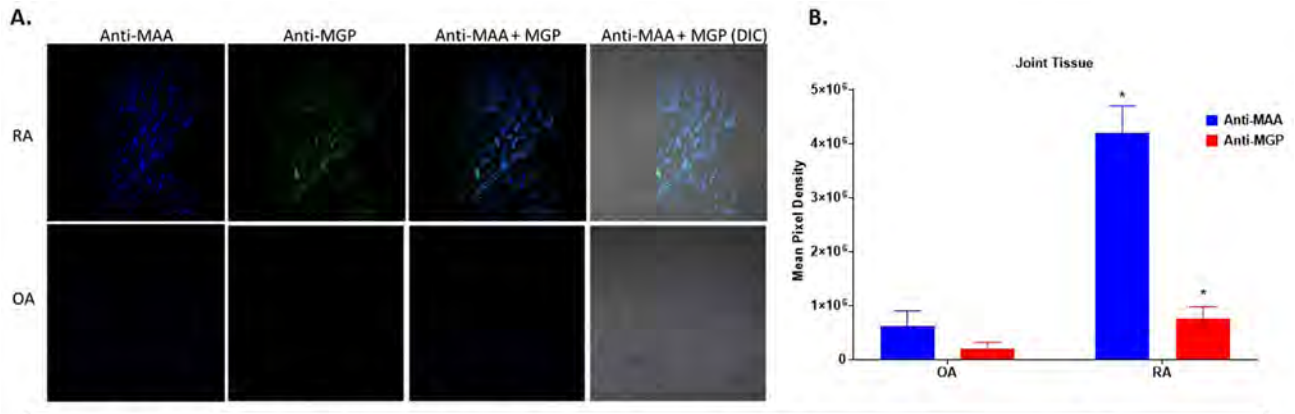

Figure 1. Anti-MAA and Anti-MGP Staining in Joint Tissue from OA and RA Patients. Joint tissue from OA and RA patients was IHC stained for the presence of MAA and MGP antigens. Detection of antibodies was done using a Ziess 710 confocal microscope and images analyzed using Image J. MAA antigens were significantly present in the RA joint tissue ($p<0.0001$) compared to the OA controls. MGP antigen were significantly present in the RA joint tissue ($p<0.05$) compared to the OA controls. Image J Coloc2 software revealed R^2 value of 0.71 when comparing MAA to MGP for colocalization. (A) Raw confocal images from OA and RA joint tissues. (B) Mean pixel density of calculated images. N=6

Figure 1

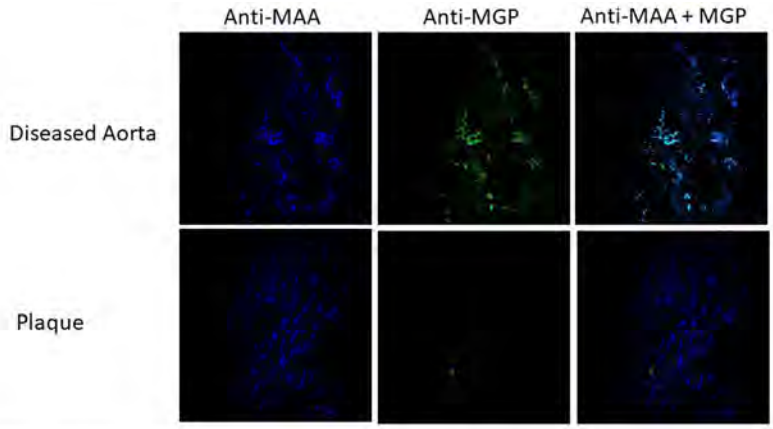

Figure 2. Anti-MAA and Anti-MGP Staining in Diseased Aorta and Plaque from Cardiovascular Patients. Aortic and plaque tissue from CVD patients was IHC stained for the presence of MAA and MGP antigens. Detection of antibodies was done using a Ziess 710 confocal microscope and images analyzed using Image J. MAA and MGP antigens were increased in all tissues. Image J Coloc2 software revealed R^2 value of 0.53 for diseased aorta and 0.45 for plaque when comparing MAA to MGP for colocalization. Representative images of 3 separate tissues.

Figure 2

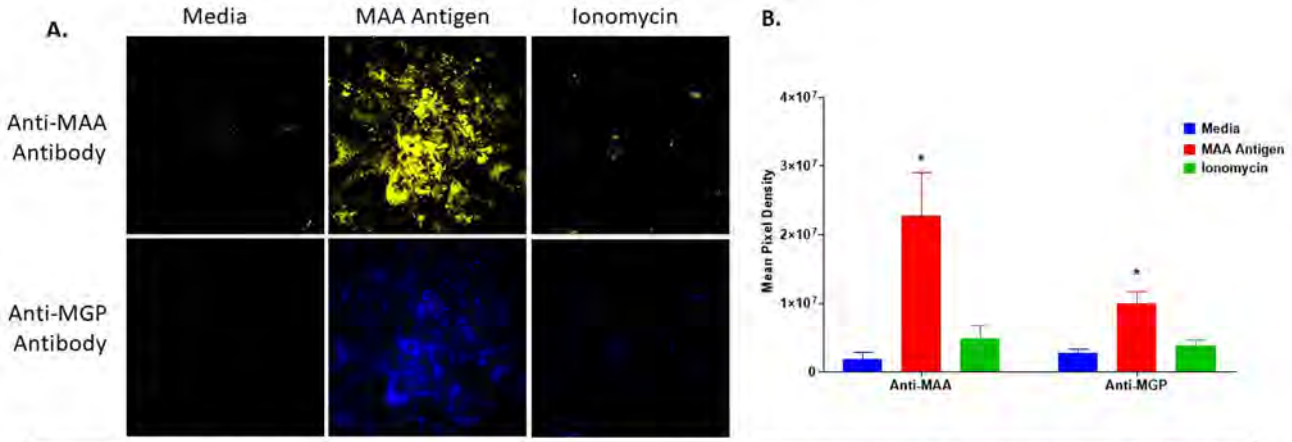

Figure 3. Anti-MAA and Anti-MGP Staining in Vascular Smooth Muscle Cells Stimulated with Acetaldehyde (AA) and Malondialdehyde (MDA). Vascular smooth muscle cells (VSMC) were incubated in the presence of 0.5mM MDA and 0.25mM AA, media only, and ionomycin for 24 hours to induce MAA protein antigens. Cells were washed and IHC stained for the presence of MAA and MGP antigens. Detection of antibodies was done using a Ziess 710 confocal microscope and images analyzed using Image J. MAA antigens were significantly present in the VSMC incubated with AA and MDA ($p<0.0001$) compared to controls. MGP antigen was significantly present in the VSMC incubated with AA and MDA ($p<0.01$) compared to controls. Image J Coloc2 software revealed R^2 value of 0.93 when comparing MAA to MGP for colocalization. (A) Raw confocal images from VSMC. (B) Mean pixel density of calculated images. N=8.

Figure 3

incubated in the presence media, ionomycin, or MAA precursors, malondialdehyde (MDA; 0.5mM) and 0.25mM acetaldehyde (AA; 0.25mM), for 24 hours, fixed and stained for MGP and MAA using specific antibodies. A Ziess 710 confocal microscope was used to determine antibody reactivity and images analyzed using Image J for mean pixel density to quantitate the amount antibody present in tissue sections. For colocalization, Image J Coloc2 plug in was used to generate a correlation coefficient as means of quantifying the magnitude of overlapping colors.

Results: MAA expression was significantly increased in RA joint tissues ($p < 0.0001$) compared to joint tissues of OA controls. Likewise, MGP was expressed significantly more ($p < 0.05$) in RA joint tissues vs. OA controls (Figure 1). Co-localization of ($r = 0.71$) was present between MGP and MAA in the RA tissues. Although less than that seen in RA joint tissues, MGP was also co-localized with MAA in aortic lesions and plaques ($r = 0.53$; $r = 0.45$ Figure 2). Human VSMC incubated with MAA precursors demonstrated increased ($p < 0.0001$) expression of both MAA antigen and MGP ($p < 0.01$) compared to media or ionomycin controls (Figure 3) with evidence of strong MAA/MGP co-localization ($r = 0.93$).

Conclusion: Previous studies have shown that MAA-modified antigen characterizes diseased tissues in both RA and CVD. To date, however, identification of the precise proteins are MAA-modified in these lesions is unknown. Findings from this study suggest that MGP, a calcium binding protein, is present in diseased tissues in both RA and CVD and appears to be MAA adducted. Indeed, findings using human tissues were confirmed with *in vitro* experiments identifying MGP as a target for MAA modification. As MAA modification has been shown to alter the biologic function of other proteins, it is possible that MAA adduction could similarly alter MGP function, increasing calcium binding, causing tissue calcification, or impacting other calcium-dependent pathways. The presence of this unique protein modified with MAA in both RA and CVD tissue could be a potential link between the two diseases providing a mechanism as to why patients with RA experience a higher comorbidity with CVD.

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Abstract Number: 0790

Vitamin D Polygenetic Risk Score and the Association with RA Autoantibodies Among First-Degree Relatives of RA Subjects

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SESSION INFORMATION
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Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a complex autoimmune disease whose etiology remains largely unknown. Vitamin D has been widely studied due to its association with numerous autoimmune diseases such as systemic lupus erythematous, multiple sclerosis, and type 1 diabetes. Genome-wide association studies (GWAS) have identified single nucleotide polymorphisms (SNPs) that are associated with levels of 25-hydoxyvitamin D3 ($25(OH)D_3$) (Jiang et al). We hypothesize that a polygenetic risk score (PRS) comprised of alleles from SNPs associated with in-

Table 1 Cohort characteristics of RA FDRs

Characteristic	aAb+ RA FDR	aAb- RA FDR	p-value
N	189	181	
Sex: % female	75.7	86.2	**0.01**
Age: mean ± SD	51.7 ± 16.2	47.4 ± 15.5	**0.01**
*Vitamin D Supplement% yes	68.5	73.3	0.30
BMI: mean ± SD	26.8 ± 5.5	26.9 ± 6.1	0.88
*Ever Smoker: % yes	40.2	41.7	0.78
Shared Epitope: % positive	53.4	52.5	0.85
Anti-CCP and RF neph/iso +: % yes	9.5	NA	NA
Anti-CCP+ only: % yes	22.2	NA	NA
RF neph/iso+ only: % yes	68.3	NA	NA
25(OH)D_3 PRS: mean ± SD	4.6 ± 1.4	4.9 ± 1.4	**0.03**
25(OH)D_3 PRS High: % yes	49.2	60.2	**0.03**
*Missing data 3 subjects missing vitamin D supplement data 1 subject missing smoking data			

Table 2 Association between vitamin D SNPs/PRS and RA aAbs among RA FDRs

	Any aAb+ (yes/no) N=370	
SNP/PRS	*OR (95% CI) p-value	P-value
GC: rs4588	0.96 (0.70-1.32)	0.81
NADSYN1: rs12785878	0.84 (0.60-1.17)	0.30
CYP2R1: rs10741657	0.85 (0.63-1.15)	0.29
AMDHD1: rs6538691	0.90 90.68-1.20)	0.46
SEC23A: rs8018720	**0.65 (0.43-0.99)**	**0.04**
† 25(OH)D PRS	**0.85 (0.74-0.99)**	**0.03**
‡ High PRS	**0.66 (0.43-0.99)**	**0.046**
*Models adjusted for sex and age †Sum of allele copies associated with increasing 25(OH)D_3 levels (range: 0-10 continuous) ‡High PRS: ≥5 copies of alleles associated with increasing 25(OH)D_3 levels		

creasing levels of serum 25(OH)D_3 will be inversely associated with the presence of RA autoantibodies (aAbs) among at-risk first-degree relatives (FDRs) of RA subjects.

Methods: The FDR study population was derived from the prospective Study of the Etiologies of Rheumatoid Arthritis (SERA). We tested the following RA-related aAbs; anti-CCP2, anti-CCP3.1, RF-neph, RF IgA, RF IgM, and RF IgG. We selected 189 non-Hispanic white (NHW) FDRs that tested positive for any aAb (aAb+) and compared them to 181 NHW FDRs that tested negative for all autoantibodies (aAb-). FDRs were genotyped using the Illumina MEGA^{EX} BeadChip per Illumina protocols. Five SNPs associated with serum 25(OH)D_3 levels were analyzed individually as well as in a PRS: rs4588 (GC), rs12785878 (NADSYN1), rs10741657 (CYP2R1), rs6538691 (AMDHD1), and rs8018720 (SEC23A). A proxy SNP (R^2=1.0) was chosen if the GWAS identified SNP was not typed on the MEGAchip. The PRS was calculated by summing the number of copies of the allele associated with increasing serum 25(OH)D_3 and ranged from 0 to 10. The PRS was also analyzed as a dichotomous variable (high PRS ≥5 v. low PRS < 5). In a subset of the cohort on whom we had previously measured 25(OH)D_3 (N=28), we tested whether the PRS was associated with

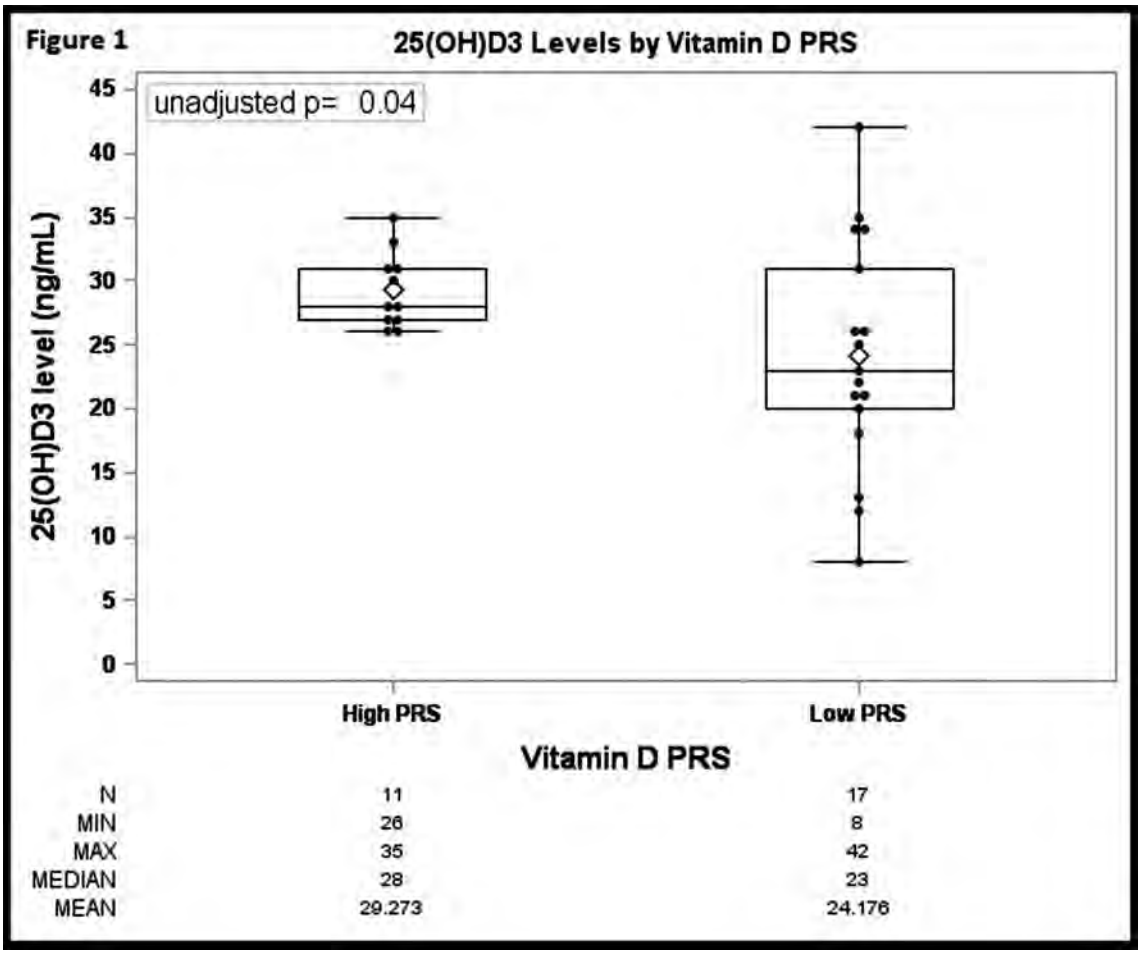

Figure 1. Comparison of mean 25(OH)D3 serum levels by high and low PRS. Subjects with a high vitamin D PRS (≥5 alleles associated with increasing 25(OH)D3 levels) had significantly higher levels of serum 25(OH)D3 (p=0.04).

25(OH)D_3 levels. Logistic regression models were used to test the association between each individual SNP and the PRS variables with the aAb+ outcome. We tested the additive interaction between the SNPs or PRS and vitamin D supplement use.

Results: The aAb+ subjects were significantly older and more likely to be male compared to the aAb- subjects (Table 1). High PRS was associated with higher levels of 25(OH)D_3 compared to low PRS (unadjusted p=0.04 and adjusted for season of blood draw p=0.08, Figure 1). We observed a significant inverse association between the SEC23A SNP rs8018720 and RA aAb+. In addition, both PRS variables were inversely associated with RA aAb+ (Table 2). There was no evidence of an additive interaction between SNPs and vitamin D supplement use.

Conclusion: A higher vitamin D PRS (reflecting higher 25(OH)D_3 levels) was inversely associated with RA aAb+. This finding indicates that genes associated with vitamin D regulation may play a protective role in the development of RA aAbs. In particular, the SEC23A SNP may be of interest for future investigation since it was the only vitamin D related SNP individually associated with the aAb+ outcome.

Reference: Jiang X, O'Reilly PF, Aschard H, et al. Genome-wide association study in 79,366 European-ancestry individuals informs the genetic architecture of 25-hydroxyvitamin D levels. *Nat Commun*. 2018;9(1):260. Published 2018 Jan 17. https://doi.org/10.1038/s41467-017-02662-2

Disclosure: E. Bemis, None; **K. Young**, None; **J. Seifert**, None; **M. Feser**, None; **K. D. Deane**, None; **M. Demoruelle**, Pfizer Inc., 2; **J. O'Dell**, None; **M. Weisman**, Novartis, 5, GSK, 5, UCB, 5, Lilly, 5; **P. Gregersen**, None; **R. Keating**, None; **W. Robinson**, None; **J. Buckner**, Bristol-Myers Squibb, 2, 5, Janssen, 2; **C. Langefeld**, Lupus Research Alliance, 2; **J. Guthridge**, None; **J. James**, None; **V. Holers**, None; **J. Norris**, None.

Abstract Number: 0791

Peficitinib Inhibits Angiogenesis via Suppression of VEGF Production in Rheumatoid Arthritis Fibroblast-like Synoviocytes

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Peficitinib is a novel Janus kinase (JAK) inhibitor developed for the treatment of rheumatoid arthritis (RA). Peficitinib has approved in 2019 in Japan, but elucidation of its mechanism of action in RA involving the inflammatory process is still inadequate. So far, we clarified JAK1, JAK2 and JAK3 were expressed in RA synovial tissue and fibroblast-like synoviocytes (FLS), and peficitiib suppress the activation of JAK-STAT pathway on RA FLS. In this study, we examined the role of peficitinib in RA angiogenesis.

Methods: To examine the functional analysis of peficitinib, we performed a proliferation and chemotaxis assays with FLS using THP-1 (human acute monocyte leukemia cell line) and peripheral blood mononuclear cells (PBMC). RA FLS supernatant was obtained from RA FLS-conditioned medium stimulated with IL-6 (100 ng/ml) and IL-6R (100 ng/ml) with or without adding peficitinib (5 μM). RA FLS were stimulated with IL-6 and IL-6R after treated peficitinib for 24 h. Next, to evaluate the effects of peficitinib on RA angiogenesis, we performed in vitro Matrigel tube formation assays using human umbilical vein endothelial cells (HUVECs). Finally, we investigated whether peficitinib suppresses the secretion of FLS inflammatory mediator using ELISA kit. The amounts of VEGF, RANTES/CCL5, MCP-1/CCL2, MMP-3, fractalkine/CX3CL1, ENA78/CXCL5 and IL-8 in IL-6 and IL-6R stimulated peficitinib treated RA FLS conditioned medium were determined.

Results: We found peficitinib treated RA FLS conditioned medium reduced THP-1 migration compared to nontreated RA FLS conditioned medium (number of THP-1 cells migrated ± SEM; 42 ± 3 and 66 ± 6 cells migrated, respectively, $p< 0.05$). Peficitinib treated RA FLS conditioned medium also reduced PBMC migration compared to nontreated RA FLS conditioned medium (number of PBMC migrated ± SEM; 36 ± 5 and 63 ± 9 cells migrated, respectively, $p< 0.05$). In addition, peficitinib treated RA FLS showed a 14 ± 2 % decrease in proliferation of RA FLS compared with nontreated RA FLS. In addition, peficitinib treated RA FLS condition medium decreased HUVEC tube formation compared to nontreated RA FLS condition medium (number of endothelial cell tubes formed ± SEM; 9 ± 1 and 13 ± 1, respectively, $p< 0.05$). Finally, we found peficitinib suppress the secretion of inflammatory mediators in RA FLS. VEGF and MCP-1/CCL2 in RA FLS supernatant was suppressed in peficitinib compared to nontreated (mean ± SEM; VEGF: 77.1 ± 69.5 and 110.4 ± 81.0 pg/ml, MCP-1/CCL2 160.1 ± 65.6 and 846.0 ± 107.1 pg/ml, respectively, $p< 0.05$).

Conclusion: We demonstrated that peficitinib is involved in the suppression of FLS proliferation, and inhibits the chemotaxis of THP1 and PBMC through inhibition of MCP-1/CCL2. Furthermore, peficitinib suppressed RA angiogenesis through inhibition of VEGF.

Disclosure: Y. Ikari, None; **T. Isozaki**, None; **K. Wakabayashi**, None; **T. Kasama**, None.

Abstract Number: 0792

LY294002 Improves the Collagen-induced Arthritis by Inducing Neutrophil Apoptosis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Neutrophils play a central role in host defense, but they also play important effectors on acute and chronic inflammation. Neutrophil apoptosis is essential for the resolution of inflammation. Previous studies have shown that delayed apoptosis of neutrophils correlate with the pathogenesis of rheumatoid arthritis (RA). This study aimed to investigate the effects of LY294002, the PI3K inhibitor, on neutrophil apoptosis in RA patients and collagen-induced arthritis (CIA) in mice.

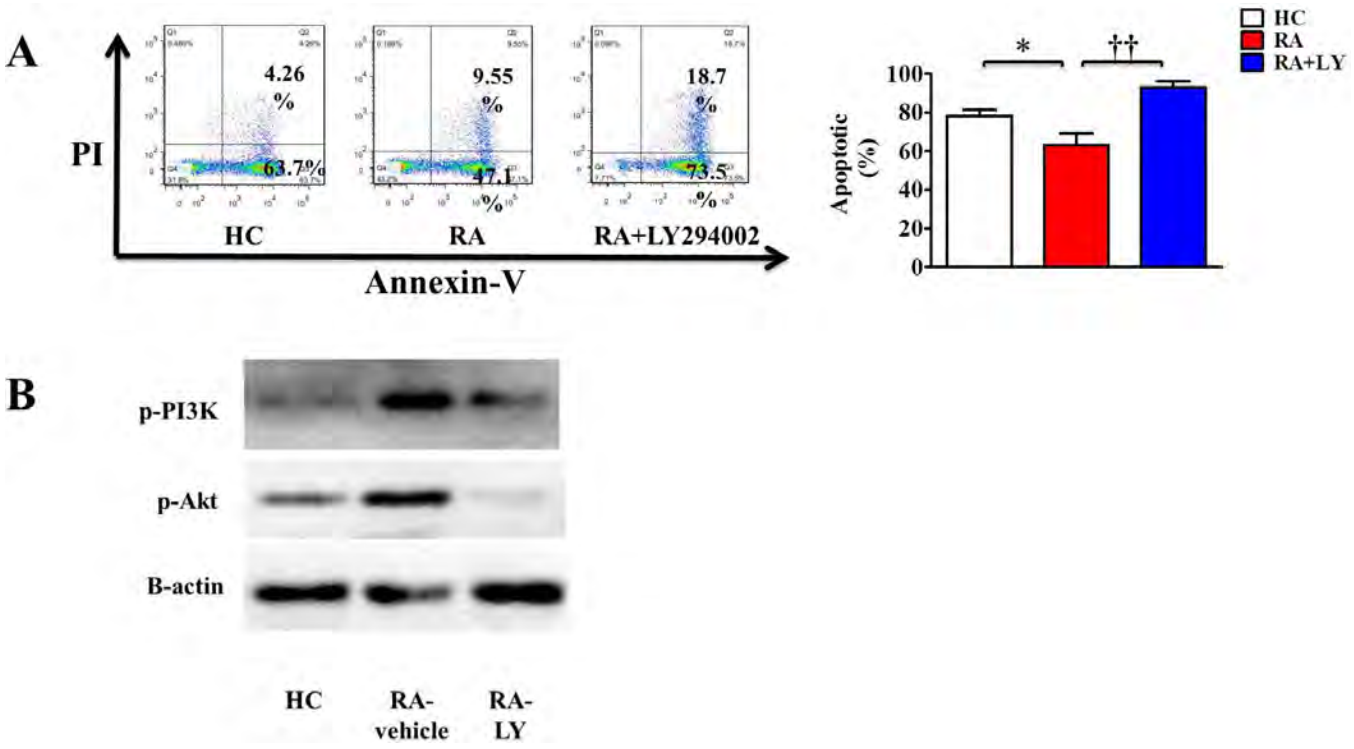

Figure1 (A) Apoptosis rate of neutrophils in peripheral blood of healthy controls (HC) or rheumatoid arthritis (RA) patients.(B) The expression of p-PI3K and p-Akt in HC and RA. *HC compare with RA **p < 0.01 † LY294002(LY) treatment group compare with untreated group † † p < 0.01

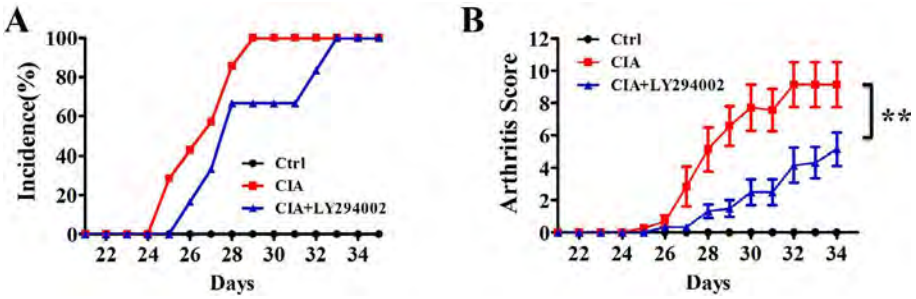

Figure 2. LY294002 treatment delayed the onset(A), reduced the severity (B)of arthritis in CIA mice.*CIA+LY294002 compare with CIA **p < 0.01

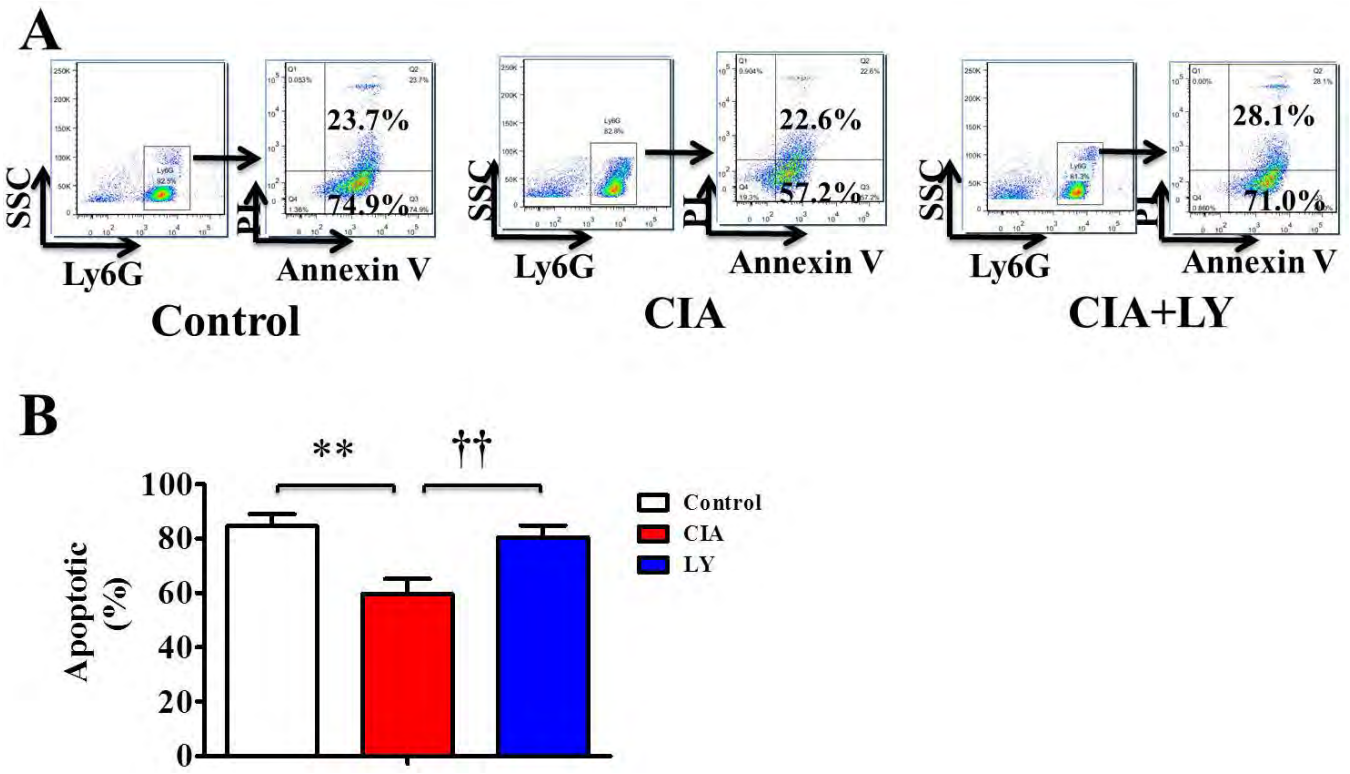

Figure 3 Apoptosis rate of neutrophils in peripheral blood of Collagen-Induced Arthritis(CIA) mice. *Control compare with CIA **p < 0.01 † LY294002(LY) treatment group compare with untreated group † † p < 0.01

Methods: The peripheral blood from untreated RA patients (n=25) and healthy volunteers (HC) (n=15) were isolated the neutrophils by density gradient centrifugation and cultured with or without LY294002(LY) in vitro for 18 h. The rate of neutrophils apoptosis were analyzed by flow cytometry and the intracellular protein of PI3K-Akt pathway in neutrophils were measured by Western blot. CIA mice were treated with vehicle or LY294002, and then analyzed the effect of LY294002 on arthritis as well as the apoptosis rate of neutrophils from peripheral blood of CIA mice.

Results: The peripheral blood neutrophils apoptosis delayed in RA patients as compared with neutrophils from HC**.** LY294002 could significantly promote neutrophils apoptosis in peripheral blood from RA patients **(Figure1 A)**. The expression of phosphorylation PI3K(p-PI3K), p-Akt were increased in RA patients and LY294002 inhibited the expression of p-Akt **(Figure1 B)**. Moreover, LY294002 treatment delayed the onset, reduced the severity of arthritis in CIA

mice **(Figure2)**.The peripheral blood neutrophils apoptosis delayed in CIA mice as compared with the control group, and LY294002 treatment facilitated the neutrophil apoptosis **(Figure3)**.

Conclusion: This data suggested that delayed apoptosis of neutrophils played an important role in the development of RA, therefore, inhibition of PI3K pathway to facilitate neutrophil apoptosis are possible approaches to reduce inflammatory arthritis which might open new doors to future clinical treatment of RA.

Disclosure: X. Huang, None; **T. Li**, None; **S. Chen**, None; **Z. Huang**, None; **J. Chen**, None.

Abstract Number: 0793

Topological Laser Capture Microscopy (LCM)-RNAseq to Map the Rheumatoid Arthritis (RA) Synovial Transcriptome

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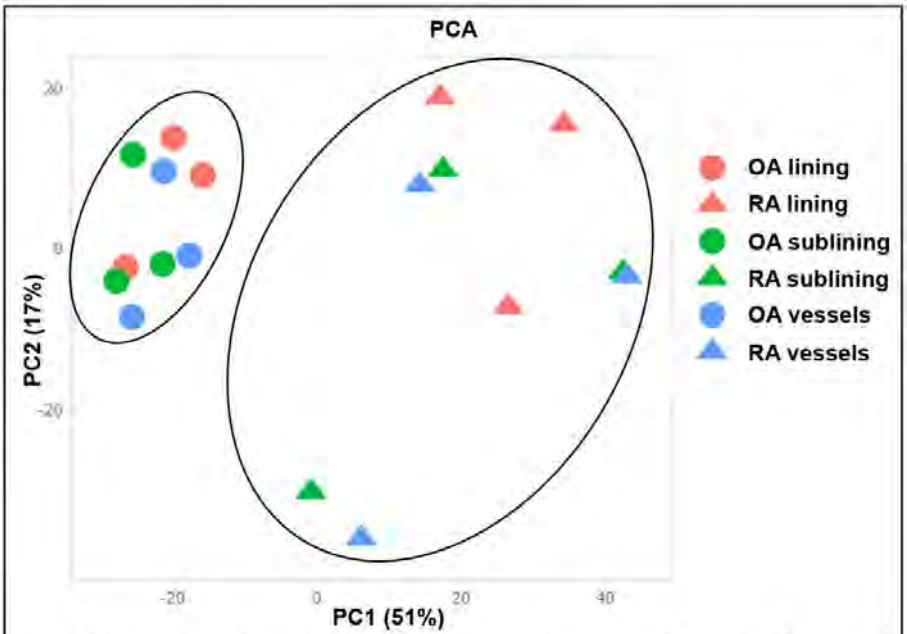
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Understanding pathogenic processes in the diseased tissue in rheumatoid arthritis (RA) is a critical step to defining disease pathogenesis and identifying novel therapeutic targets. However, the use of enzymatically dispersed cells can lead to changes in the gene transcription and bias due to cell death. Therefore, we established laser capture microscopy followed by RNAseq (LCM-RNAseq) to study the regional transcriptome.

Methods: Synovial tissue was captured by LCM after H&E staining from lining, sublining, and blood vessels from 3 RA and 3 osteoarthritis (OA) patients. RNA was extracted and subjected to RNAseq. Principal component analysis (PCA) by disease state was performed on the top 500 most variable genes among the sample set. Analysis of differentially expressed genes (DEGs) between disease state was performed using the Bioconductor DESeq2 package. DEGs had adjusted p-values of < 0.05 and log2 fold change >1 or < -1. Pathway analysis on the unique DEGs for each substructure was performed using the Canonical Pathways function in Ingenuity Pathway Analysis (IPA) platform. The significance of the pathways was calculated using a right-tailed Fisher's exact test and adjusted using the Benjamini-Hochberg method.

Results: PCA revealed striking separation between RA and OA transcriptomes (see Figure), indicating that the transcriptomes could be readily distinguished. Pairwise comparisons of synovial lining, sublining and blood vessels between RA and OA revealed substantial differences in transcriptional patterns between each region. Pathway analysis of DEGs unique to each substructure revealed that each region displayed distinct phenotypic abnormalities in RA. For example, RA synovial lining was marked by anomalies of innate immunity, including Role of Pattern Recognition Receptors in Recognition of Bacteria and Virus ($p< 0.001$) and LPS/IL-1 Mediated Inhibition of RXR Function ($p< 0.01$) pathways. Intriguingly, RA sublining abnormalities were primarily in metabolic pathways involving fatty acid regulation, such as Fatty Acid Activation ($p< 0.01$) and Mitochondrial L-carnitine Shuttle Pathway ($p< 0.01$). RA synovial vessels displayed evidence of alterations in pathways indicative of dysregulated angiogenesis, including Melatonin Signaling ($p< 0.0001$) and Apelin Cardiomyocyte Signaling ($p< 0.001$).



Principal component analysis (PCA) of transcriptomes of RA and OA synovial substructures. PCA was performed using the prcomp function in R statistical software on the top 500 most variable genes among the entire sample set. Proportion of variability explained for PC1 and PC2 is shown in parentheses.

Conclusion: Through use of LCM, we established a method for RNAseq-quality extraction of RNA and showed large differences between RA and OA synovial substructures that are difficult to detect using single cell analysis. This technology can supplement disaggregation techniques to provide key information on in situ gene expression profiles and identify disease and substructure-specific targets for RA.

Disclosure: B. Van Espen, Eli Lilly, 2; **A. Wilson**, Eli Lilly, 2; **G. Seumois**, None; **N. Perumal**, Eli Lilly and Company, 1, 3; **R. Benschop**, Eli Lilly and Company, 1, 3, 4; **G. Firestein**, Eli Lilly, 2; **N. Bottini**, Gilead Sciences, 2, Kyowa Kirin Pharmaceutical Research, 2, Eli Lilly, 2; **S. Stanford**, Eli Lilly, 2.

Abstract Number: 0794

Peripheral Blood T and B Lymphocyte Subsets in Arthritis in the Elderly

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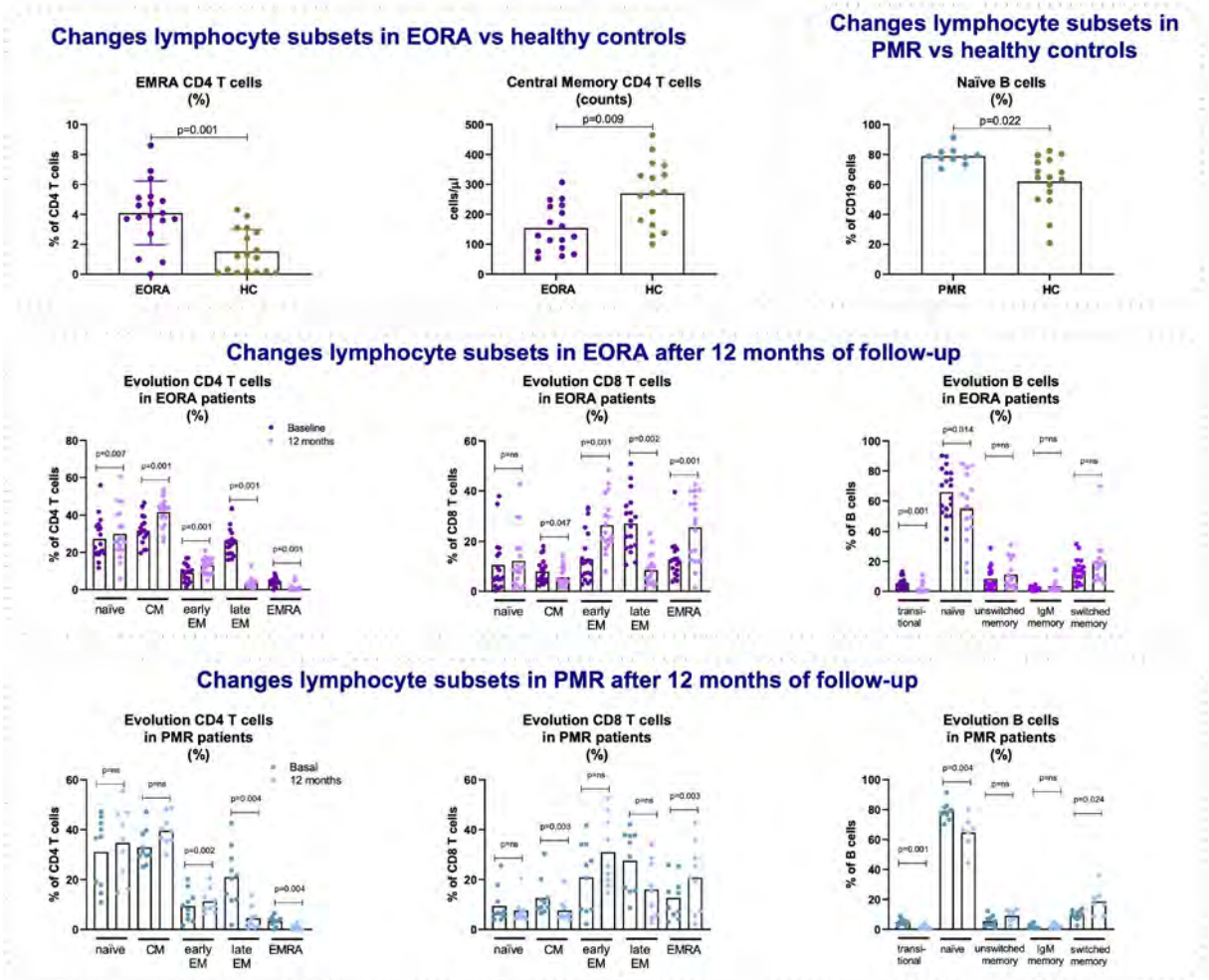
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Multiple lymphocyte subsets like T and B cells have been connected to joint infiltration and inflammation in rheumatoid arthritis (RA). Identification of leucocyte subsets that are dysregulated in arthritis development could provide insight into the aetiology of RA. Elderly-onset RA, EORA, which is defined as rheumatoid arthritis (RA) starting at > 60 years of age, has received less attention than young-onset RA. Polymyalgia rheumatica (PMR) is another common rheumatic disease in the elderly. This study aimed to investigate the composition of the peripheral blood component. We hypothesize that by defining lymphocyte subsets we might be able to define elements of inflammation pathobiology in this population.

Methods: ARTIEL (Arthritis in the Elderly) is a collection cohort with newly diagnosed arthritis in patients older than 60 years, with blood samples collected at baseline (pre-treatment) and 12 months after treatment, along with physician and patient outcome measures through 12 months. They are compared with randomly control individuals of the same age and gender. A thorough clinical examination was conducted. Patients completed a health assessment questionnaire (HAQ). Disease activity score (DAS)28CRP was calculated. Absolute numbers of lymphocyte subsets in whole EDTA blood were determined with complete blood counts and flow cytometry fluorescent labelled antibodies for T and B cell subsets. Data processing and statistical analysis were performed in SPSS.

Results: 29 patients (average: 75.15, standard deviation (SD) 6.80) and 18 controls (C; average: 75.39, SD, 6.04) were analyzed. Of these, 19 were diagnosed with RA and 10 with PMR. At the start of the study, patients had a mean DAS28CRP of 5.72 (SD, 1.05), mean HAQ was 1.64 (SD, 0.73). In addition, 84% of the patients reported scapular



pain, and 56% of the patients reported pelvic pain at baseline. Several lymphocyte subsets were different between populations. In patients with EORA, significant increase in percentage and numbers of CD4+ effector subset (EMRA; defined as $CD3^+CD4^+CD45RA^+CCR7^-CD27^-$) and significantly decrease in numbers of CD4+ central memory (CM; defined as $CD3^+CD4^+CD45RA^-CCR7^+CD27^+$). In patients with PMR, a trend towards different B cell subsets were observed with an increase in percentage of naïve B cells ($CD19^+CD27^-IgM^+IgD^+$) was observed compared to HC and a significant increase in percentage and numbers of CD8 + CM ($CD3^+CD8^+CD45RA^+CCR7^-CD27^-$). Longitudinal analysis showed that several B and T cell subsets were significantly different at 12 months in both EORA and PMR patients (see Figure) suggesting an effect of therapy in the lymphocyte subsets.

Conclusion: This study revealed that patients with EORA and PMR demonstrate a change in cellular immune parameters apparent in the periphery. More studies are needed to show whether these subsets before and after treatment might be related to clinical and therapeutic outcomes in these populations.

Disclosure: A. Teniente-Serra, None; **L. Mateo**, None; **A. Prior**, None; **M. Guma**, None; **E. Martinez-Caceres**, None; **M. Martinez-Morillo**, None.

Abstract Number: 0795

Minimum Clinically Important Improvement in Patients with Rheumatoid Arthritis Associates with Gut Microbiome

Vinod Gupta[1], Kevin Cunningham[2], Benjamin Hur[1], John Davis[1] and Jaeyun Sung[1], [1]Mayo Clinic, Rochester, MN, [2]University of Minnesota, Minneapolis, MN

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Within the past decade, there have been several major discoveries in cross-sectional gut microbiome studies suggesting that dysbiosis of the gut microbiota is a key hallmark in Rheumatoid arthritis (RA). However, the association of gut microbiome with improvement in disease activity in RA patients remains unknown. In this study, we aimed to investigate the association of minimum clinically important improvement (MCII) in RA disease activity with gut microbiome of RA patients. In addition, we generated a machine-learning model, incorporating gut microbiome and clinical data, that could predict the course of RA irrespective of the treatment strategy.

Methods: Illumina based DNA shotgun sequencing was performed on 72 stool samples, which were collected at two time-points, from 36 RA patients. Disease activity and gut microbiomes were assessed in order to investigate the association of gut microbiome with MCII (i.e., CDAI change of at least 1 for low (CDAI less than 10); of 6 for moderate (CDAI 10–22); and of at least 12 for high (CDAI greater than 22) disease activity) in RA disease activity. Machine-learning models based on XGBoost were also generated based on gut microbiome composition and clinical data at baseline to predict the future disease activity in RA patients.

Results: We found that distributions of gut microbiome profiles were significantly different in patients of $MCII^+$ (i.e., patients who show improvement in disease activity) and $MCII^-$ groups (i.e., patients who did not show improvement). At baseline, Fisher's alpha diversity and species richness were significantly higher (**Fig.1b**), and five microbial taxa, including Negativicutes, Selenomonadales, Prevotellaceae, Coprococcus, and *Ruminococcus sp.*, were significantly

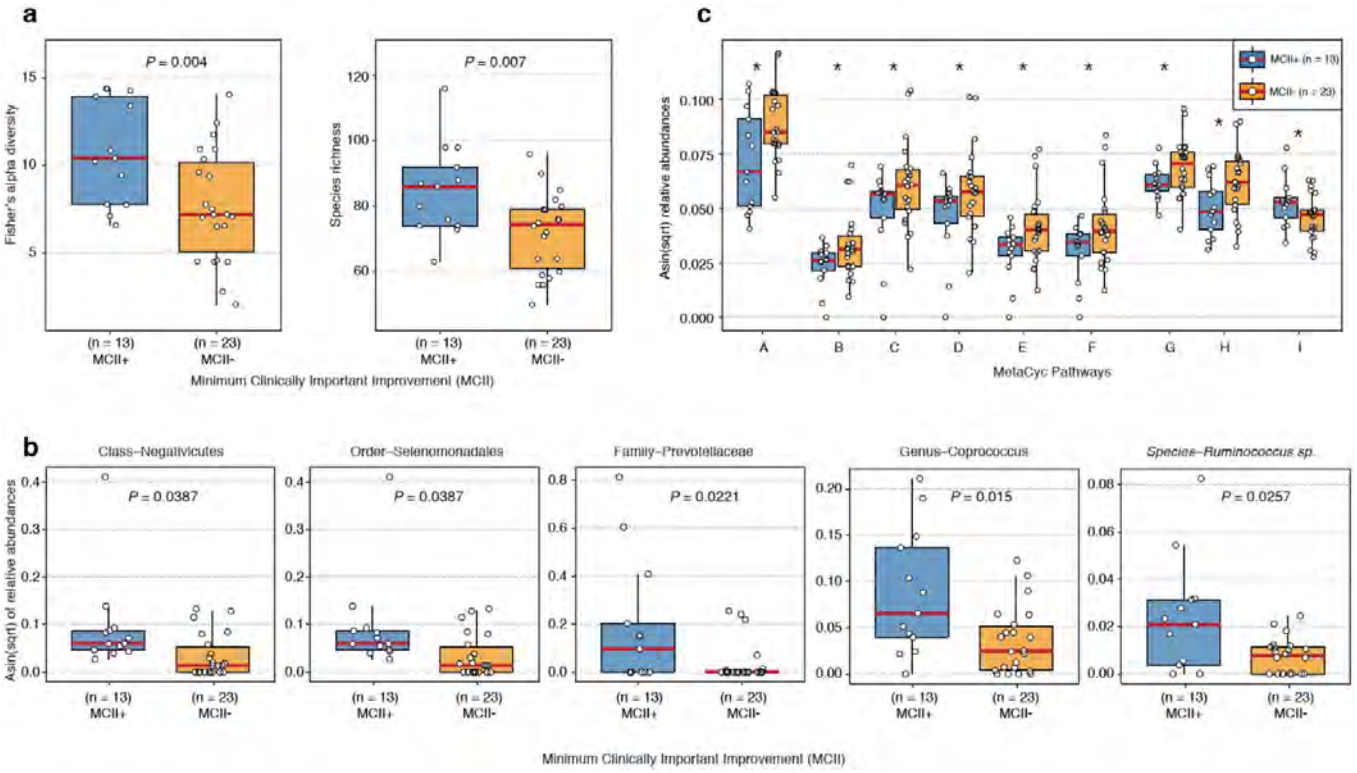


Figure 1. Significant differences in gut microbiomes of baseline stool samples between MCII+ and MCII- groups. (a) Higher distributions of Fisher's alpha diversity and species richness were observed in baseline stool samples of patients of MCII+ group than in those of MCII- group. (b) Five taxa, Ruminococcus sp, Coprococcus, Prevotellaceae, Prevotellaceae, and Negativicutes, were significantly more abundant in baseline stool samples of patients of MCII+ group than those of MCII- group. (c) MetaCyc pathways that were significantly differentiated between MCII+ and MCII- groups in baseline stool samples. P-values shown above the box plots were found using multiple linear regression models on arcsine square-root transformed relative abundances of microbial taxa and MetaCyc pathways, while adjusting for age group (middle age: age < 64 years; and old age: age >= 64 years), sex, smoking status and use of csDMARDs (conventional synthetic Disease-Modifying Antirheumatic Drugs). *, P < 0.05; ns, not significant. Pathway codes: A, L-ornithine de novo biosynthesis; B, L-ornithine biosynthesis; C, L-arginine biosynthesis IV; D, L-arginine biosynthesis I; E, L-arginine biosynthesis III; F, L-arginine biosynthesis II; G, L-rhamnose degradation I; H, CMP-3-deoxy-D-manno-octulosonate biosynthesis I; I, tetrapyrrole biosynthesis I.

more abundant among patients of $MCII^{+}$ group than those of $MCII^{-}$ group (**Fig.1b**). Biochemical pathway-level analysis of baseline stool metagenomes suggested that eight MetaCyc pathways, including ornithine biosynthesis, arginine biosynthesis, and rhamnose degradation were significantly decreased in RA patients of $MCII^{-}$ group (**Fig.1c**). For the machine-learning model, the Pearson correlation coefficient between predicted and actual disease activity score (CDAI) at follow-up visits was 0.77 ($P = 2.9 \times 10^{-12}$), which shows that our machine-learning model, incorporating gut microbiome and clinical data, is very effective in forecasting the disease activity in RA patients.

Conclusion: Our findings confirm the association of gut microbiome with MCII in disease activity in RA patients, and highlights the importance of gut microbiome in predicting the course of RA irrespective of the treatment strategy.

Disclosure: V. Gupta, None; **K. Cunningham**, None; **B. Hur**, None; **J. Davis**, Pfizer, 2, AbbVie, 5, 8, Sanofi-Genzyme, 5, 8; **J. Sung**, None.

Abstract Number: 0796

Development of a Tool to Assess Synovial Tissue Infiltrates and Derive Histological Pathotype in Inflammatory Arthritis: Relationship to Clinical and Ultrasound Variables

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Etiology & Pathogenesis Poster

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Evidence suggests that histological pathotypes are linked to pathogenic mechanisms in inflammatory arthritis and may be useful as biomarkers of outcome. The frequently used Krenn score was developed and validated to distinguish inflammatory from non-inflammatory synovitis using longstanding disease and does not distinguish the degree of histological organisation from the degree of infiltrate. We therefore developed discrete semi-quantitative indices of infiltrate density and aggregate size from which a simple pathotype grade could be derived in H&E stained tissue and examined their relationship with clinical and ultrasound variables in baseline synovial tissue biopsies from the BEACON early arthritis inception cohort.

Methods: Synovial tissue biopsies were obtained at baseline from unselected treatment naïve patients presenting to the Birmingham BEACON cohort with at least one clinically swollen joint. Final diagnosis was assigned after 18 months. 71 samples were analysed: RA (46), PsA (7), unclassified arthritis (8), and other inflammatory arthritis (10). Ultrasound (US) greyscale (GS) hypertrophy and Power Doppler (PD) were graded in joints prior to biopsy. 4 point semi-quantitative scales (0-3) were developed for discrete variables of cellular infiltrate density and aggregate size and number, with written definitions and an extensive image atlas. The BEACON density and aggregate scores were then used to create a summary pathotype: lymphoid (≥ grade 1 aggregates); diffuse (immune infiltrate in absence of aggregates); pauci-immune (absence of immune infiltrate). Following iterative assessments for face and construct

	US GS	US PD	CRP	DAS28-CRP	MD global
Krenn lining layer module	0.27 (0.026)	-0.061 (0.62)	0.087 (0.47)	0.18 (0.14)	0.051 (0.67)
Krenn infiltrate module	**0.34* (0.0052)**	0.15 (0.23)	**0.37* (0.0023)**	**0.33* (0.0056)**	**0.40* (0.0009)**
BEACON density	**0.39* (0.0008)**	0.22 (0.068)	**0.45* (0.0001)**	0.22 (0.066)	**0.35* (0.0025)**
BEACON aggregates	**0.31* (0.01)**	**0.28* (0.02)**	0.22 (0.07)	0.12 (0.32)	0.19 (0.10)

Table 1. Spearman rank correlations of Krenn lining layer and infiltrate modules, BEACON density and aggregate scores with ultrasound and clinical variables. Spearman r (p value) *Significant after Benjamini Hochberg correction

validity, 3 independent scorers blindly graded 10 representative H&E sections using the atlas and the Krenn lining layer and infiltrate modules.

Results: Reliability of the BEACON scoring system was good (mean BEACON density ICC=0.69, BEACON aggregate Kappa=0.69, pathotype Kappa=0.72).

The BEACON density and aggregate scores correlated moderately with the Krenn lining layer module (r=0.48, p< 0.001 and r=0.43, p=< 0.001 respectively) and highly with the Krenn infiltrate module (r=0.92, p< 0.001; r=0.76, p< 0.001).

Table 1 shows correlation analysis for Krenn lining layer and infiltrate modules, BEACON density and aggregate scores vs US and clinical variables (CRP, DAS28-CRP, MD global score). The Krenn infiltrate module and BEACON density correlated with US GS, CRP, and MD global assessment; BEACON aggregate score correlated with US PD and GS. The Krenn infiltrate module alone correlated with DAS28-CRP. There were no correlations with the Krenn lining layer module.

There was a greater proportion of higher US GS grades in lymphoid than diffuse and pauci-immune pathotypes (X^2(4, N=70)=11.18, p=0.025).

Conclusion: The BEACON scores and derived pathotype showed good inter-observer reliability and correlated significantly with US and clinical variables. Derived histological pathotype was also associated with US GS hypertrophy. This suggests that these variables have utility in describing infiltrate extent and complexity in early arthritis samples.

Disclosure: H. Carr, None; **I. Sahbudin**, None; **M. Maybury**, None; **B. Dyke**, None; **J. Turner**, None; **N. Gullick**, Abbvie, 5, 8, Celgene, 2, 5, Eli Lilly, 5, 8, Izana, 5, 8, Janssen, 5, 8, Novartis, 5, 8, UCB, 5, 8; **K. Raza**, Pfizer, 2; **D. Scheel-Toellner**, None; **A. Filer**, roche, 2, abbvie, 8.

Abstract Number: 0797

Comparison of the Efficacy and Safety of Janus Kinase Inhibitors and DMARDs in Patients with Active Rheumatoid Arthritis: A Bayesian Network Meta-Analysis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Janus Kinase (JAK) inhibitors have shown long term benefit in patients with active RA with inadequate response to conventional or biologic DMARDs (1). Due to a lack of head-to-head comparison trials, the relative efficacy and safety of JAK inhibitors remains unclear. Consequently, previous network meta-analysis had assessed the relative efficacy and safety of JAK inhibitors but were restricted to studies with adalimumab (2).

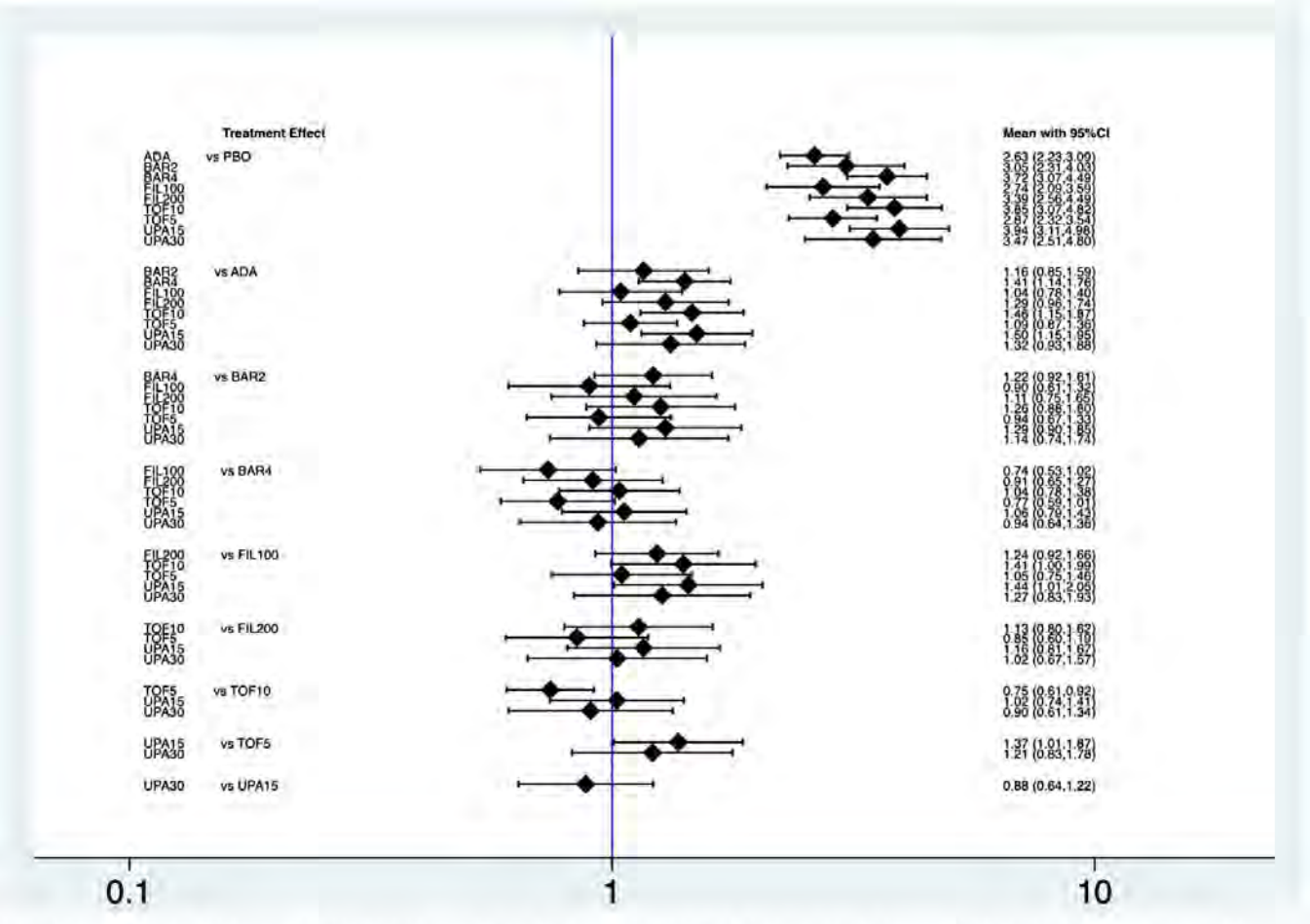

Figure 1. Predictive interval plot for active RA network for the ten-intervention analysis for ACR20.

The purpose of this study was to investigate the relative efficacy and safety of tofacitinib, baricitinib, filgotinib and upadacitinib in patients with active RA with inadequate response to conventional or biologic DMARDs.

Methods: Bayesian random-effects network meta-analysis was performed to combine the direct and indirect evidence from randomized controlled trials (RCTs) reporting efficacy and safety outcomes of tofacitinib + MTX, baricitinib + MTX, filgotinib + MTX and upadacitinib + MTX in patients with active RA despite treatment with conventional or biologic DMARDs.

Results: Twenty RCTs including 13.178 patients met the inclusion criteria. There were 45 pairwise comparisons including 18 direct comparisons of 10 interventions. The American College of Rheumatology 20% (ACR20) response rate was significantly higher for all the intervention groups other than placebo (Figure 1). The ranking probability based on the surface under the cumulative ranking curve (SUCRA) indicated that upadacitinib 15mg + MTX (SUCRA = 0.9), tofacitinib 10mg + MTX (SUCRA = 0.8). and baricitinib 4mg + MTX (SUCRA = 0.8) had the highest probability of being the best treatment in terms of the ACR20 response rate. This was followed by upadacitinib 30mg + MTX (SUCRA = 0.6), filgotinib 200mg + MTX (SUCRA = 0.6), baricitinib 2 mg + MTX (SUCRA 0.4), tofacitinib 5mg + MTX (SUCRA = 0.3), filgotinib 100mg + MTX (SUCRA = 0.3), adalimumab + MTX (SUCRA = 0.2) and placebo + MTX (SU-

UPA15	5.38 (0.81,35.88)	1.54 (0.46,5.10)	1.92 (0.57,6.45)	0.98 (0.19,5.03)	1.03 (0.20,5.42)	1.77 (0.43,7.36)	1.33 (0.25,7.00)	1.12 (0.36,3.52)	1.54 (0.58,4.09)
1.02 (0.74,1.41)	**TOF10**	3.50 (0.62,19.73)	2.81 (0.36,21.68)	5.52 (0.69,43.85)	5.23 (0.64,42.59)	3.04 (0.59,15.63)	7.16 (0.89,57.75)	4.80 (0.95,24.21)	**8.27 (1.56,43.76)**
1.06 (0.79,1.43)	1.04 (0.78,1.38)	**BAR4**	1.25 (0.30,5.13)	1.58 (0.36,6.87)	1.49 (0.41,5.43)	1.15 (0.36,3.65)	2.05 (0.46,9.11)	1.37 (0.65,2.91)	**2.36 (1.10,5.10)**
1.13 (0.82,1.56)	1.11 (0.75,1.64)	1.07 (0.74,1.55)	**UPA30**	1.97 (0.32,11.91)	1.86 (0.30,11.49)	1.08 (0.21,5.48)	2.55 (0.41,15.75)	1.71 (0.43,6.84)	2.95 (0.88,9.91)
1.16 (0.81,1.67)	1.13 (0.80,1.62)	1.10 (0.79,1.53)	1.02 (0.67,1.57)	**FIL200**	1.06 (0.16,6.91)	1.82 (0.36,9.29)	1.30 (0.34,4.90)	1.15 (0.29,4.59)	1.50 (0.39,5.78)
1.29 (0.90,1.85)	1.26 (0.88,1.80)	1.22 (0.92,1.61)	1.14 (0.74,1.74)	1.11 (0.75,1.65)	**BAR2**	1.72 (0.32,9.13)	1.37 (0.21,9.12)	1.09 (0.26,4.55)	1.58 (0.40,6.22)
1.37 (1.01,1.87)	**1.34 (1.09,1.65)**	1.30 (0.99,1.70)	1.21 (0.83,1.78)	1.18 (0.84,1.66)	1.06 (0.75,1.50)	**TOF5**	2.36 (0.45,12.27)	1.58 (0.64,3.92)	2.72 (0.89,8.36)
1.44 (1.01,2.05)	1.41 (1.00,1.99)	1.36 (0.98,1.88)	1.27 (0.83,1.93)	1.24 (0.92,1.66)	1.12 (0.76,1.64)	1.05 (0.75,1.46)	**FIL100**	1.49 (0.37,6.07)	1.16 (0.29,4.57)
1.50 (1.15,1.95)	**1.46 (1.15,1.87)**	**1.41 (1.14,1.76)**	1.32 (0.93,1.88)	1.29 (0.96,1.74)	1.16 (0.85,1.59)	1.09 (0.87,1.36)	1.04 (0.78,1.40)	**ADA**	1.72 (0.82,3.65)
3.94 (3.11,4.98)	**3.85 (3.07,4.82)**	**3.72 (3.07,4.49)**	**3.47 (2.51,4.80)**	**3.39 (2.56,4.49)**	**3.05 (2.31,4.03)**	**2.87 (2.32,3.54)**	**2.74 (2.09,3.59)**	**2.63 (2.23,3.09)**	**PBO**

ACR20	Intervention	HZ

Drugs are reported in order of ACR20 ranking according to SUCRAs. Comparisons should be read from left to right. The efficacy (ACR20) and safety (herpes zoster infection) estimate is located at the intersection of the column-defining treatment and the row-defining treatment. Significant results are in bold and underlined.

Table 1. Network league of estimated effects of ACR20 and herpes zoster infection.

CRA = 0). The SUCRAs for the ACR50 indicated that upadacitinib 30mg + MTX (SUCRA = 0.9) and upadacitinib 15mg (SUCRA =0.8) had the highest probability of being the best treatment. Safety based on number of severe adverse events did not differ significantly among the ten interventions within 12 weeks suggesting comparable safety among the different regimens and the placebo. However, it was observed an increased risk of herpes zoster infection in the group of tofacitinib 10mg + MTX (odds ratio (OR) 8.27, 95% credible interval (CrI) 1.56 – 43.7) and baricitinib 4mg + MTX (OR 2.36, 95% CrI 1.1 – 5.1) in comparison with placebo group (Table 1).

Conclusion: In patients with active RA with inadequate response to conventional or biologic DMARDs the JAK inhibitors are an effective and safe alternate therapy. The two with the best relative efficacy were upadacitinib 15mg/30mg and baricitinib 4 mg. In terms of serious infectious events, there was an increase of herpes zoster infections with tofacitinib 10mg and baricitinib 4mg.

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Disclosure: A. Castro, Novartis, 1; **J. Diaz**, Novartis, 1; **G. Quiceno**, None.

Abstract Number: 0798

A Randomized, Double-blind Phase 3 Study Comparing the Efficacy, Safety and Immunogenicity of PF-06410293 (Abrilada™), an Adalimumab (ADL) Biosimilar, and Reference ADL (Humira®) in Patients with Moderate to Severe Active RA: Results from Weeks 52-92

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the long-term safety, immunogenicity (IG), and efficacy of the adalimumab (ADL) biosimilar, PF-06410293 (ADL-PF), in patients (pts) with moderate to severe active RA who continued ADL-PF treatment throughout 78 weeks (wks) or who switched from reference ADL sourced from the European Union (ADL-EU) to ADL-PF at wk 26 or wk 52 in a randomized, double-blind, comparative clinical trial (NCT02480153). This report includes results from wks 52-92 (including 16-wk follow-up [FU]).

Methods: Eligible pts met 2010 ACR/EULAR RA diagnosis criteria for ≥4 months, had an inadequate response to MTX, and had received ≤2 doses of 1 lymphocyte-depleting or non-ADL biologic. Pts stratified by geographic regions were initially randomized (1:1) in treatment period 1 (TP1) to ADL-PF or ADL-EU (40 mg subcutaneously every other wk), both with MTX (10–25 mg/wk). The primary endpoint was ≥20% clinical improvement of ACR criteria (ACR20) at wk 12. Secondary efficacy endpoints included ACR20 other than at wk 12, DAS28; 4 components based on high-sensitivity CRP (DAS28-4[CRP]), and other measures of clinical response or remission. At wk 26 (start of TP2), pts receiving ADL-EU were blindly re-randomized (1:1) to remain on ADL-EU or transition to ADL-PF for 26 wks. At wk 52 (start of TP3), all pts received open-label treatment with ADL-PF for 26 wks; 3 groups (gps) were evaluated corresponding to the treatment sequence during the study: biosimilar; wk 26 switch; wk 52 switch.

Results: Of the randomized TP1 pts (N=597), 552 pts entered TP2. At wk 52, all pts remaining on ADL-EU were switched to ADL-PF; 507 pts continued to participate in TP3. The majority of TP3 pts were female (78.1%) and White (86.6%). ACR20 response rates and DAS28-4(CRP) scores were sustained and comparable across gps (**Table**). ADL-PF was generally well tolerated, with a comparable safety profile across gps. Incidence of treatment-emergent adverse events (AEs) during TP3 and FU was 42.6% (biosimilar), 37.0% (wk 26 switch), and 50.8% (wk 52 switch); 3 (0.6%) pts overall (all in the wk 52 switch gp) reported treatment-related serious AEs. There was 1 death (wk 52 switch gp). Pre-dose (TP3) anti-drug antibody (ADA) prevalence at wk 52 was 41.5%, 42.5%, and 48.3% for the biosimilar, wk 26, and wk 52 switch gps, respectively. The incidences of pts with a first positive ADA result during TP3 or FU, among pts who were ADA negative on entry to TP3, were 8.9%, 6.3%, and 8.3% for the biosimilar, wk 26, and wk 52 switch gps, respectively; overall, incidences of pts with ADAs in TP3 and FU were comparable among gps (46.1%, 46.5%, and 54.2%, respectively).

Efficacy Endpoints by Visit (TP3 ITT Population)			
Group[a]	Biosimilar[b] (N = 259)	Week 26 switch[c] (N = 127)	Week 52 switch[d] (N = 121)
ACR20 Response, n (%)			
Week 52	229 (88.4)	112 (88.2)	106 (87.6)
Week 78	216 (83.4)	109 (85.8)	102 (84.3)
DAS28-4(CRP) Score, Mean (SD)			
Week 52	3.0 (1.15)	2.8 (1.14)	3.2 (1.26)
Week 78	2.7 (1.12)	2.6 (1.16)	3.0 (1.33)

[a]Treatment sequence TP1/TP2/TP3; [b]ADL-PF/ADL-PF/ADL-PF; [c]ADL-EU/ADL-PF/ADL-PF; [d]ADL-EU/ADL-EU/ADL-PF.

Abbreviations: ADL-EU, reference adalimumab sourced from the European Union; ADL-PF, PF-06410293; DAS28-4(CRP), Disease Activity Score-28; 4 components based on high-sensitivity C-reactive protein; ITT, intent-to-treat; N, number of patients in the TP3 ITT population; SD, standard deviation; TP, treatment period.

Conclusion: Results from TP3 and FU (wks 52–92) are consistent with earlier findings from this study, demonstrating no clinically meaningful differences in safety, IG, and efficacy between treatment gps, independent of a single treatment switch from ADL-EU to ADL-PF at wk 26 or wk 52.

Disclosure: R. Fleischmann, Pfizer, 2, 5; **D. Alvarez**, Pfizer, 1, 2; **A. Bock**, Pfizer, 1, 2; **C. Cronenberger**, Pfizer, 1; **I. Vranic**, Pfizer, 1, 2; **W. Zhang**, Pfizer, 1, 2, AbbVie, 1, Abbott, 1; **R. Alten**, Pfizer, 2, 8, Gilead Sciences, Inc., 2, Novartis, 2, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 5, Lilly, 2, 5, UCB, 2, 5.

Abstract Number: 0799

Effectiveness of Electronic Drug Monitoring Feedback in Order to Increase Adherence in RA Patients Starting with a Biological DMARD

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Medication non-adherence in rheumatoid arthritis (RA) is associated with disease flares, increased disability and increased costs. Electronic Monitoring Feedback (EMF) to improve adherence has shown promising effects in various chronic diseases, however, it has never been studied in RA nor with biological DMARDs. This study aims to assess the effectiveness of EMF on medication adherence in RA patients starting with or switching to a new bDMARD.

	12 months		
	Feedback	Control	p
DAS28-ESR (SD)	2.71 (1.3)	2.63 (1.5)	0.801
ΔDAS28-ESR (baseline to 12 months)	-1.63 (1.2)	-1.14 (1.3)	0.105
ΔDAS28-ESR (baseline to average of month 3, 6, 9, 12)	-1.16 (1.2)	-0.990 (1.1)	0.325
Proportion with LDA (DAS28<3.2) at 3 months, %	60	68	0.307
Proportion with LDA (DAS28<3.2) at 6 months, %	42	51	0.260
CQR Z-score adherent, %	75.6	81.7	0.446
MPR (SD)	0.95 (0.11)	0.92 (0.13)	0.048
BMQ			
-Necessities	20.3	20.8	0.390
-Concerns	14.3	14.3	0.952
HAQ (SD)	0.82 (0.7)	0.83 (0.7)	0.932
bDMARD stop	46	43	0.810
Number, reason	14, AE's	11, AE's	
	22, ineffective	26, ineffective	
	10, other	6, other	

Table 1. results for both groups. Means and number of patients are presented, unless otherwise stated. CQR Zk- score combined with DAS score was available for 64 patients.

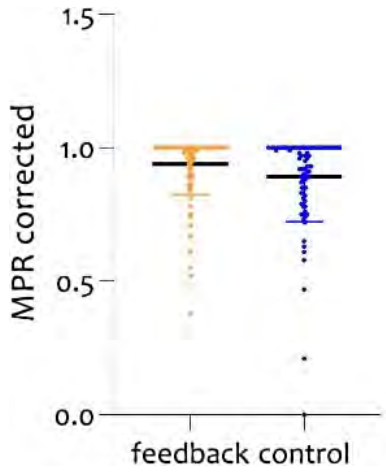

Figure 1. MPR for both groups. Scores >1 were truncated to 1.0.

Methods: In this RCT, RA patients starting a (new) bDMARD were 1:1 assigned to the intervention or control group and followed for 1 year. The intervention group received a special needle container which was equipped with a Medication Event Monitoring System (MEMS) cap registering patient's adherence to subcutaneous medication injections. During the intervention, adherence score was read out every 3 months with MEMS, on which motivational interviewing feedback based on patient's medication adherence was given. Furthermore, reasons for non-adherence were explored and counselled. The control group received usual care. At the start and after 12 months, Compliance Questionnaire in Rheumatology (CQR), Beliefs about Medicines Questionnaire (BMQ) and Health Assessment Questionnaire (HAQ) were obtained. The feedback group also received BMQ and HAQ at months 3, 6 and 9. Effectiveness of EMF on adherence was assessed with the validated discriminant CQR-Z score for taking compliance ≤80% and medication possession ratio (MPR, total day's supply in period divided by total period, truncated to 1.0). Patients taking >80% of their medication were considered adherent. Effectiveness of EMF on DAS28-ESR and side effects was also assessed.

Results: 207 consecutive patients were included,105 in feedback group and 102 control (mean age 52 years, 74% female, 88% Caucasian ethnicity, 5.3 years since diagnosis of RA, 51 used a bDMARD before). At baselins there were no differences with respect to the DAS28 and HAQ (intervention 3.95 vs control 3.74 and 1.15 vs 0.98 respectively) in both groups. Most patients started with etanercept (95) or adalimumab (91).

The percentage of CQR adherent patients increased for both groups from 68.5 and 63.1 (baseline) to 75.6 and 81.7 (12 months) for intervention and controls respectively (no difference between groups at baseline and 12 months, p=0.534 and p=0.446.

MPR was 0.95 in the feedback group and 0.92 in the control group (p=0.048, Figure 1), corrected for returned defect syringes and medical indicated postponing

Correct dosing measured by MEMS decreased slightly from 92.6% (after 3 months) to 90.5% (after 12 months).

Methotrexate, prednisolone and other csDMARD use throughout the study was similar for both groups and BMQ and HAQ scores remained nearly equal.

Side effects such as infections did not differ between groups (47% and 57% of the patients reported any side effect, p=0.142).

Conclusion: Taking compliance and correct dosing were relatively high in RA patients starting with or switching to a biological DMARD, as measured with MPR, CQR and MEMS. Since high rates were found in the control group too, probably because of a ceiling and a placebo effect, EMF did not increase adherence. Presumably the effect of EMF should be targeted to non-adherent patients.

Disclosure: R. Hebing, None; **W. Bos**, None; **M. Nurmohamed**, None; **B. van den Bemt**, None.

Abstract Number: 0800

A Randomized, Double-Blind, Phase 3 Study to Compare the Efficacy and Safety of a Proposed High Concentration (100 mg/mL) Adalimumab Biosimilar (CT-P17) with Reference Adalimumab in Patients with Moderate-to-Severe Active Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: CT-P17 (100 mg/mL) is the first proposed biosimilar of the high concentration and citrate-free formulation of reference adalimumab. The purpose of this study was to compare the efficacy and safety of CT-P17 with reference adalimumab in patients with active moderate-to-severe RA up to Week 52.

Methods: Patients with active moderate-to-severe RA despite methotrexate treatment were randomly assigned to receive 40 mg of CT-P17 or reference adalimumab every 2 weeks up to Week 24. Prior to dosing at Week 26, patients in the reference adalimumab group were re-randomized either to continue receiving reference adalimumab or to switch to CT-P17 until end of study. All patients initially randomized to CT-P17 continued CT-P17. The primary endpoint was ACR20 response rate at Week 24. Secondary measures of efficacy, pharmacokinetics (PK) and safety, including immunogenicity, were also evaluated.

Table 1. Efficacy Results at Week 24 (ITT population)

	CT-P17 N=324	Reference Adalimumab N=324
ACR20, n (%)	268 (82.7)	268 (82.7)
ACR50, n (%)	195 (60.2)	206 (63.6)
ACR70, n (%)	132 (40.7)	144 (44.4)
DAS28-CRP, change from baseline, mean (SD)	-2.7 (1.19)	-2.7 (1.21)
CDAI remission, %	82 (25.3)	86 (26.5)
SDAI remission, %	86 (26.5)	93 (28.7)
EULAR (good) response, %	208 (64.2)	208 (64.2)

Abbreviations: CDAI, clinical disease activity index; ITT, intent-to-treat; SD, standard deviation; SDAI, simplified disease activity index.

Figure 1. ACR20 Response Rates (ITT population)

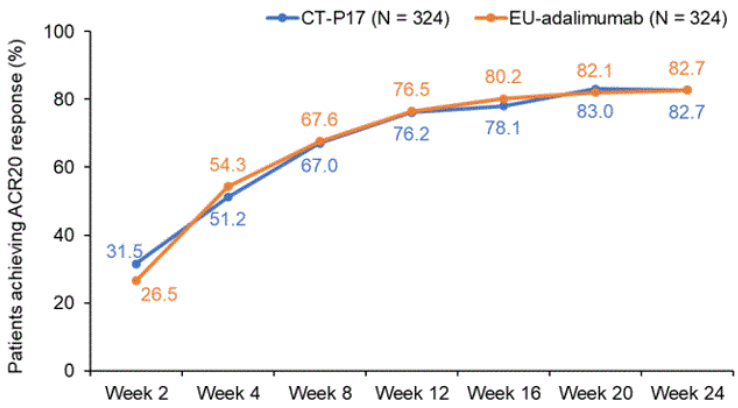

Table 2. Overview of TEAEs up to Week 24 (Safety population)

Patients, n (%)	CT-P17 N=324	Reference Adalimumab N=324
≥1 TEAE	169 (52.2)	184 (56.8)
≥1 TESAE	10 (3.1)	16 (4.9)
≥1 TEAE leading to study drug discontinuation	5 (1.5)	8 (2.5)
≥1 TEAE classified as hypersensitivity/allergic reactions	2 (0.6)	4 (1.2)
≥1 TEAE classified as injection site reactions	16 (4.9)	22 (6.8)
≥1 TEAE classified as infection	97 (29.9)	103 (31.8)
≥1 TEAE classified as malignancy	1 (0.3)	0

Abbreviation: TEAE, treatment-emergent adverse event; TESAE, treatment-emergent serious adverse event.

Results: 648 patients initiated treatment (324 patients in each arm). Baseline characteristics were similar between groups.

The ACR20 response rate at Week 24 was 82.7% (268/324) and 82.7% (268/324) for CT-P17 and reference adalimumab and the confidence intervals of the treatment difference (95% CI: -5.94 to 5.94, 90% CI: -4.98 to 4.98) were entirely within the equivalence margins agreed upon with EMA (±15%) and FDA (-12% to +15%). Secondary efficacy endpoints were also similar between groups (Table 1).

In terms of PK, geometric mean trough serum concentration was slightly higher in CT-P17; 5.3 μg/mL in CT-P17 vs. 4.3 μg/mL in reference adalimumab at Week 24 (p=0.0501).

Overall, 353 (CT-P17: 169 [52.2%] vs. reference adalimumab: 184 [56.8%]) patients experienced at least 1 treatment-emergent adverse event (TEAE). The most common TEAEs were injection site reactions (16 [4.9%] vs. 22 [6.8%]). 26 patients experienced at least 1 treatment-emergent serious adverse event (TESAE). Similar proportions of patients in both groups experienced at least 1 TEAE that was classified as hypersensitivity/allergic reactions and infections (Table 2). One malignancy (breast cancer; unrelated) was reported in a patient receiving CT-P17.

The proportion of patients who had anti-drug antibodies (ADAs) at Week 24 (209 [32.3%]), was slightly lower for CT-P17 (93 [28.7%]) than for reference adalimumab (116 [35.8%]) (p=0.0643). Of these, 83 (25.6%) receiving CT-P17 and 103 (31.8%) receiving reference adalimumab also had neutralizing ADAs.

Conclusion: Over 24 weeks, CT-P17 has equivalent efficacy to reference adalimumab, with ACR20 response rates of 82.7% for each, and similar additional secondary efficacy endpoints. Considering the ACR20 response rate of 64.0% - 82.5% [1-4] reported in previous studies of low concentration (50 mg/mL) adalimumab biosimilar, further investigation is needed to ascertain the factors associated with the slightly higher response rate in this study.

CT-P17 was well tolerated with a safety profile comparable to that of reference adalimumab.

References:

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2. Cohen SB et al. Ann Rheum Dis.2018 Jun; 77(6):914-921
3. Weinblatt ME, Arthritis Rheumatol. 2018 Jan; 70(1):40-48
4. US FDA, Multi-disciplinary Evaluation and Review for PF-06410293, 2019

Disclosure: J. Kay, Pfizer Inc., 9, Alvotech Suisse AG, 1, Arena Pharmaceuticals, Inc., 1, Boehringer Ingelheim GmbH, 1, Celltrion Healthcare Co. Ltd., 1, Mylan Inc., 5, Novartis AG, 5, Samsung Bioepis, 5, Sandoz Inc., 5, Gilead Sciences, Inc., 9; **J. Jaworski**, None; **R. Wojciechowski**, None; **P. Wiland**, Celltrion, Inc., 1, Novartis, Pfizer, Abbvie, Gedeon-Richter, Lilly, Roche, Sandoz, 1; **A. Dudek**, None; **M. Krogulec**, Celltrion, 1; **S. Jeka**, Pfizer, 2, 8, Novartis, 2, 8, Abbvie, 2, 8, UCB, 2, 8, MSD, 2, 8, Roche, 2, 8, Sandoz, 2, 8, Egis, 2, 8, Lilly, 2, 8, Celgene, 2, 8; **A. Zielinska**, None; **J. Trefler**, None; **K. Bartnicka-Maslowska**, None; **M. Krajewska-Wlodarczyk**, None; **P. Klimiuk**, None; **D. Furst***, Actelion, 1, 2, Amgen, 1, 2, BMS, 1, Corbus, 1, 2, Galapagos, 1, 2, GSK, 1, NIH, 1, Norvatis, 1, 2, Pfizer, 1, 2, Sanofi, 1, Roche/Genentech, 1, Gilead, 1, Horizon, 1, 2, Kadmon, 1, Talaris, 1, 2, CMC Connect (McCann Health Company), 8, Cytori, 5, AbbVie, 5; **S. Lee**, Celltrion, Inc., 1; **Y. Bae**, CELLTRION, Inc., 1; **G. Yang**, Celltrion, Inc., 1; **J. Yoo**, Celltrion, INC., 1; **H. Lee**, Celltrion, Inc., 1; **E. Keystone**, AbbVie, 2, 5, 8, Celltrion, 2, 5, 8, Eli Lilly, 2, 5, 8, Pfizer Inc, 2, 5, 8, Merck, 2, 5, 8, Sandoz, 2, 5, 8, Samsung Bioepsis, 2, 5, 8, Myriad Autoimmune, 2, 5, 8, Purapharm, 2, 5, 8, Janssen, 2, 5, 8, Sanofi-Genzyme, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, F. Hoffman-La Roche Ltd., 2, 5, 8, Genentech, 2, 5, 8, Gilead, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 0801

The Comparative Effectiveness of Abatacept versus TNF Inhibitors in Patients Who Are ACPA Positive and Have the Shared Epitope: Results from a US National Observational Study

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Table 1. Baseline characteristics in the overall population and patients who were biologic experienced

Characteristic	Overall population				Biologic-experienced patients			
	After PS trimming		After PS matching		After PS trimming		After PS matching	
	ABA (n=170)	TNFi (n=157)	ABA (n=111)	TNFi (n=111)	ABA (n=145)	TNFi (n=129)	ABA (n=92)	TNFi (n=92)
Age, years	56.6 (12.9)	56.9 (12.4)	56.2 (12.5)	57.6 (12.3)[a]	56.0 (12.6)	56.5 (12.4)	56.2 (12.4)	56.8 (12.2)
Female, n (%)	126 (74.1)	108 (68.8)[a]	82 (73.9)	81 (73.0)	107 (73.8)	87 (67.4)[a]	65 (70.7)	67 (72.8)
RA duration, years	11.4 (10.2)	10.4 (10.8)	10.5 (10.6)	11.4 (10.8)	11.9 (9.8)	10.9 (10.6)[a]	11.1 (10.3)	11.5 (10.4)
RF+, n (%)	155 (91.2)	138 (87.9)[a]	99 (89.2)	99 (89.2)	135 (93.1)	113 (87.6)[a]	85 (92.4)	81 (88.0)[a]
CDAI score	27.8 (11.8)	27.5 (11.9)	27.5 (12.4)	27.2 (11.6)	28.2 (12.3)	27.7 (12.4)	27.6 (13.0)	27.3 (12.1)
SJC	7.7 (5.4)	7.7 (4.9)	7.6 (5.4)	7.4 (4.5)	7.8 (5.6)	8.0 (5.2)	7.7 (5.6)	7.7 (4.6)
TJC	9.9 (6.3)	9.8 (7.0)	9.6 (6.4)	9.4 (6.9)	10.2 (6.5)	9.7 (7.2)	9.8 (6.6)	9.4 (7.1)
DAS28 (CRP)	4.7 (1.1)	4.7 (1.0)	4.7 (1.1)	4.7 (1.0)	4.7 (1.1)	4.6 (1.0)	4.7 (1.1)	4.6 (1.1)
Physician global assessment, VAS 0–100 mm	48.3 (19.5)	50.8 (18.9)[a]	49.8 (21.0)	51.3 (17.4)	48.6 (19.8)	50.5 (19.2)	49.9 (21.7)	51.2 (17.5)
Patient global assessment, VAS 0–100 mm	54.0 (23.5)	49.9 (24.8)[a]	53.0 (23.4)	52.0 (23.8)	53.4 (24.4)	49.4 (24.5)[a]	51.4 (24.1)	50.8 (23.6)
Patient-reported pain, VAS 0–100 mm	54.8 (24.4)	51.2 (28.3)[a]	53.1 (23.9)	53.0 (27.2)	56.0 (25.1)	51.2 (28.3)[a]	53.2 (25.0)	52.5 (27.1)
Patient-reported fatigue, VAS 0–100 mm	56.1 (27.7)	51.9 (29.4)[a]	55.5 (28.3)	54.1 (29.5)	57.6 (27.6)	52.2 (28.9)[a]	56.0 (28.7)	53.5 (29.0)
mHAQ	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.5 (0.5)	0.6 (0.5)	0.5 (0.5)[a]	0.5 (0.5)	0.5 (0.5)
Prior biologic use, n (%)								
0	25 (14.7)	28 (17.8)	19 (17.1)	19 (17.1)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
1	54 (31.8)	83 (52.9)[a]	49 (44.1)	49 (44.1)	54 (37.2)	83 (64.3)[a]	49 (53.3)	49 (53.3)
2	57 (33.5)	38 (24.2)[a]	28 (25.2)	37 (33.3)[a]	57 (39.3)	38 (29.5)[a]	28 (30.4)	37 (40.2)[a]
3+	34 (20.0)	8 (5.1)[a]	15 (13.5)	6 (5.4)[a]	34 (23.5)	8 (6.2)[a]	15 (16.3)	6 (6.5)[a]

Data are mean (SD), unless otherwise stated.

[a]Standardized difference >0.1.

ABA=abatacept; mHAQ=modified HAQ; PS=propensity score; TNFi=TNF inhibitor; VAS=visual analog scale.

Background/Purpose: The *HLA-DRB1* shared epitope (SE) is associated with joint destruction in ACPA+ patients (pts) with RA.[1] In the Early AMPLE trial, among ACPA+ pts with early RA, efficacy responses with abatacept (ABA) but not adalimumab were numerically higher in pts who were SE+ vs SE–.[2] This real-world analysis compared the mean change (Δ) from baseline to the 6-mth follow-up visit in CDAI score among ACPA+/SE+ pts treated with ABA or TNF inhibitors (TNFi).

Methods: Using data from CERTAIN (Comparative Effectiveness Registry to study Therapies for Arthritis and Inflammatory CoNditions; NCT01625650)[3], this study included pts with RA who initiated ABA or a TNFi, were CCP3+ (>20 U/mL), SE+ (presence of SE on *HLA-DRB1* allele) and had moderate or high CDAI score (>10) at initiation and 6-mth follow-up (+/– 3 mths). The primary outcome was mean Δ in CDAI score over 6 mths; secondary outcomes included achievement of remission (CDAI ≤2.8) and low disease activity (CDAI ≤10) and mean Δ in pain, fatigue and pt global assessment. Analyses were conducted using both propensity score (PS)-trimmed and -matched populations. PS was calculated within each line of therapy. The PS-trimmed cohort included pts with scores overlapping both

Table 2. Clinical outcomes in the overall PS-trimmed and -matched populations

Outcomes	PS-trimmed analysis[a]			PS-matched analysis		
	ABA (n=170)	TNF (n=157)	p value[b]	ABA (n=111)	TNF (n=111)	p value[b]
Primary outcome						
CDAI[b]	−11.6 (1.0)	−10.0 (1.0)	0.212	−12.1 (1.2)	−10.1 (1.2)	0.226
Secondary outcomes						
Patient-reported pain, VAS 0–100 mm[c]	−14.4 (1.8)	−10.9 (1.9)	0.174	−15.3 (2.4)	−13.1 (2.4)	0.524
Patient-reported fatigue, VAS 0–100 mm[c]	−9.8 (2.0)	−11.5 (2.1)	0.521	−10.6 (2.6)	−12.9 (2.7)	0.561
Patient global assessment, VAS 0–100 mm[c]	−14.5 (2.1)	−10.9 (2.2)	0.220	−16.4 (2.3)	−12.7 (2.3)	0.265
Achievement of LDA[d]	1.8 (0.5, 5.9)	Ref	0.358	1.6 (0.4, 6.6)	Ref	0.553
Achievement of remission[d]	1.4 (0.6, 3.5)	Ref	0.471	1.6 (0.6, 4.3)	Ref	0.371
Drug retention						
Patients who remained on drug at 6-mth visit, n (%)	117 (68.8)	101 (64.3)	0.389	79 (71.2)	73 (65.8)	0.386

[a]The PS-trimmed cohort included pts with scores overlapping both populations.

[b]p values for primary and secondary outcomes were from the adjusted mixed-effects models. Drug retention was assessed using the chi-square test.

[c]Mean (standard error) change from baseline to 6 mths.

[d]OR (95% CI) for difference between treatments at 6-mth visit.

ABA=abatacept; LDA=low disease activity; OR=odds ratio; PS=propensity score; ref=reference; VAS=visual analog scale.

populations. After PS trimming, TNFi initiators were PS matched 1:1 to ABA initiators within each line of therapy. A sensitivity analysis was conducted in biologic-experienced pts only. Mixed-effects models were used for primary and secondary outcomes and included baseline characteristics that remained unbalanced (standardized difference [sDiff] >0.1) between treatment groups.

Results: In the overall PS-trimmed cohort (ABA, n=170; TNFi, n=157), baseline characteristics that were imbalanced (sDiff >0.1) between treatments included sex, RF+, physician and pt global assessments, pain, fatigue and prior biologic use (**Table 1**). Baseline characteristics in the overall PS-matched cohort (ABA, n=111; TNFi, n=111) were generally well balanced. Similar trends for imbalances in baseline characteristics were seen in biologic-experienced cohorts. In the overall population for both the PS-trimmed and -matched cohorts, there were numerically greater improvements in mean Δ in CDAI and nearly all secondary efficacy outcomes between ABA and TNFi (**Table 2**). There was no significant difference in the percentage of pts who remained on study medication at 6 mths. Similar trends for efficacy outcomes were seen for biologic-experienced pts; statistical significance was reached for mean Δ in CDAI in the PS-trimmed cohort (**Table 3**).

Conclusion: There was a consistent numerical improvement in efficacy outcomes with abatacept over TNFi in pts with long-standing RA who were SE+ and ACPA+ over 6 mths in all four study cohorts. After adjusting for covariates that remained imbalanced between groups in the biologic-experienced PS-trimmed cohort, the improvement in CDAI with abatacept vs TNFi was significant. Additional studies to explore these findings in a larger population would be of interest.

Table 3. Clinical outcomes in the biologic-experienced PS-trimmed and -matched populations

Outcomes	PS-trimmed analysis[a]			PS-matched analysis		
	ABA (n=145)	TNF (n=129)	p value[b]	ABA (n=92)	TNF (n=92)	p value[b]
Primary outcome						
CDAI[c]	–12.2 (1.1)	–9.3 (1.1)	0.045	–12.8 (1.4)	–9.7 (1.4)	0.091
Secondary outcomes						
Patient pain, VAS 0–100 mm[c]	–15.2 (1.9)	–11.2 (2.0)	0.165	–15.8 (2.7)	–12.9 (2.7)	0.447
Patient fatigue, VAS 0–100 mm[c]	–9.1 (1.9)	–10.8 (2.1)	0.553	–9.4 (2.9)	–12.0 (2.9)	0.540
Patient global assessment, VAS 0–100 mm[c]	–13.6 (2.2)	–10.9 (2.3)	0.390	–14.8 (2.6)	–12.4 (2.5)	0.524
Achievement of LDA[d]	2.1 (0.5, 8.9)	Ref	0.298	1.9 (0.3, 10.3)	Ref	0.471
Achievement of remission[d]	1.7 (0.5, 5.5)	Ref	0.377	2.1 (0.6, 7.9)	Ref	0.283
Drug retention						
Patients who remained on drug at 6-mth visit, n (%)	99 (68.3)	82 (63.6)	0.411	65 (70.7)	60 (65.2)	0.430

[a]The PS-trimmed cohort included pts with scores overlapping both populations.

[b]p values for primary and secondary outcomes were from the adjusted mixed-effects models. Drug retention was assessed using the chi-square test.

[c]Mean (standard error) change from baseline to 6 mths.

[d]OR (95% CI) for difference between treatments at 6-mth visit.

ABA=abatacept; LDA=low disease activity; OR=odds ratio; ref=reference; VAS=visual analog scale.

References:

1. Huizinga TWJ, et al. *Arthritis Rheum* 2005;52:3433–3438.
2. Rigby W, et al. Presented at EULAR 2019. Poster LB008.
3. Pappas DA, et al. *BMC Musculoskelet Disord* 2014;15:113.

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Abstract Number: 0802

Real-World DMARD Experience and Outcomes for Rheumatoid Arthritis Patients in Japan: Effectiveness

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: There are several conventional synthetic, targeted synthetic and biological disease-modifying anti-rheumatic medications (DMARDs) approved for the treatment of rheumatoid arthritis (RA) in Japan. Little is known regarding the characteristics of patients treated by these DMARD classes and their respective effectiveness in a real-world cohort of patients in Japan.

Methods: We identified RA patients in the Corrona RA Japan Registry who initiated a DMARD (methotrexate [MTX], TNFi, nonTNFi, tofacitinib) between March 1, 2016 to December 31, 2019 with enrollment capping for some drug classes. We characterized the four drug groups in terms of sociodemographics, comorbidities, disease characteristics, medications (current and prior), disease activity, and patient-reported outcomes (PROs). Drug effectiveness in each of the drug groups was assessed for all initiators with baseline and 6-month follow-up (FU) visits available by change in Clinical Disease Activity Index (CDAI) and PROs (pain, fatigue, patient global assessment, and J-HAQ), as well as the achievement of minimal clinically important difference (MCID) in CDAI and modified ACR20/50/70s in the six months following medication initiation.

N	MTX# 275	n*	TNFi 331	n*	nonTNFi 525	n*	tofacitinib 162	n*
Demographics								
Age (years), Mean (SD)	59.7 (14.2)	275	60.6 (14.1)	331	65.9 (12.6)	525	61.5 (13.9)	162
Female gender, n (%)	205 (74.5%)	275	262 (79.2%)	331	402 (76.6%)	525	133 (82.1%)	162
Comorbidities								
Prior CVD, n (%)	24 (8.7%)	275	36 (10.9%)	331	70 (13.3%)	525	15 (9.3%)	162
Prior serious infection, n (%)	22 (8.0%)	275	34 (10.3%)	331	76 (14.5%)	525	22 (13.6%)	162
Prior herpes zoster, n (%)	32 (11.6%)	275	33 (10.0%)	331	73 (13.9%)	525	16 (9.9%)	162
Prior malignancy, n (%) (excluding non-melanoma skin cancer)	19 (6.9%)	275	20 (6.0%)	331	81 (15.4%)	525	8 (4.9%)	162
Disease Characteristics								
Disease duration (years), Mean (SD)	2.4 (5.9)	275	7.2 (9.3)	331	9.8 (11.2)	525	11.8 (11.3)	162
Seropositive (RF or CCP) ever, n (%)	171 (63.6%)	269	234 (72.0%)	325	405 (79.4%)	510	116 (76.8%)	151
Concomitant Medications								
Prednisone (yes/no), n (%)	47 (17.1%)	275	106 (32.0%)	331	180 (34.3%)	525	43 (26.5%)	162
Receiving medication in combination with csDMARDs, n (%)*	33 (12.0%)	275	302 (91.2%)	331	400 (76.2%)	525	130 (80.2%)	162
Prior Biological DMARD/JAKi Medications								
0	273 (99.3%)	275	254 (76.7%)	331	329 (62.7%)	525	43 (26.5%)	162
1	2 (0.7%)	275	56 (16.9%)	331	112 (21.3%)	525	57 (35.2%)	162
2	0 (0.0%)	275	12 (3.6%)	331	49 (9.3%)	525	34 (21.0%)	162
3+	0 (0.0%)	275	9 (2.7%)	331	35 (6.7%)	525	28 (17.3%)	162
Disease Activity								
CDAI, Mean (SD)	19.0 (11.5)	268	22.6 (12.8)	324	21.9 (11.6)	508	23.1 (13.6)	155
DAS 28 (ESR), Mean (SD)	4.6 (1.2)	225	4.9 (1.3)	297	5.1 (1.3)	434	4.9 (1.3)	143
Patient Reported Outcomes								
Pain, Mean (SD)	46.1 (27.6)	272	49.4 (27.0)	327	52.1 (26.6)	520	52.6 (27.6)	162
Fatigue, Mean (SD)	39.3 (26.8)	272	42.2 (27.4)	326	45.9 (27.3)	518	50.8 (28.0)	162
Patient global assessment, Mean (SD)	42.8 (27.1)	272	48.0 (25.7)	329	51.2 (25.6)	522	53.0 (26.5)	162
J-HAQ	0.7 (0.7)	273	1.0 (0.8)	329	1.2 (0.8)	523	1.2 (0.8)	162

CVD includes cardiac arrest, myocardial infarction, acute coronary syndrome, unstable angina, coronary artery disease, ventricular arrhythmia, congestive heart failure, cardiac revascularization procedure, other cardiovascular event, stroke, transient ischemic attack, deep vein thrombosis, peripheral arterial disease, pulmonary embolism, carotid artery disease; CDAI, Clinical Disease Activity Index; DAS28, Disease Activity Score-28 joints; J-HAQ, Japanese version of the Stanford Health Assessment Questionnaire; ‡Outcomes were calculated for all starters with baseline and 6-month FU visits available, regardless of whether they were on same drug at their 6-month FU visit; #Excluding those who initiated MTX with other biologicals (TNFi or nonTNFi) or Janus Kinase inhibitor (JAKi); *Number of non-missing observations; *For the MTX group, combo therapy = receiving any conventional synthetic disease-modifying anti rheumatic drugs (csDMARDs) other than MTX. For the TNFi, nonTNFi, and JAKi group: combo therapy = receiving any csDMARDs. The use of the following csDMARDs is collected in the RA Japan registry: methotrexate, bucillamine, iguratimod, leflunomide, sulfasalazine, and tacrolimus.

Table 1. Baseline Characteristics of the Effectiveness Cohort by Drug Group‡

N	MTX# 275	n*	TNFi 331	n*	nonTNFi 525	n*	tofacitinib 162	n*
Disease Characteristics								
CDAI, Mean (SD)	-9.9 (10.9)	267	-11.6	316	-11.8	492	-12.4 (13.0)	150
Achieving CDAI MCID, n (%)[£]	164 (61.0%)	269	199	318	332	495	100	150
Achieving mACR20, n (%)	129 (46.9%)	275	141	331	253	525	73 (45.1%)	162
Achieving mACR50, n (%)	98 (35.6%)	275	109	331	181	525	51 (31.5%)	162
Achieving mACR70, n (%)	58	275	69 (20.8%)	331	108	525	33 (20.4%)	162
Patient Reported Outcomes								
Pain, Mean (SD)	-21.5 (27.4)	272	-20.2	323	-19.1	514	-21.2 (27.0)	161
Fatigue, Mean (SD)	-13.0 (26.3)	270	-10.9	321	-11.2	501	-15.9 (25.6)	159
Patient global assessment, Mean	-18.4 (27.1)	272	-19.0	326	-17.5	514	-20.3 (27.6)	161
J-HAQ, Mean (SD)	-0.3 (0.5)	273	-0.3 (0.5)	327	-0.3 (0.6)	522	-0.3 (0.6)	162
Change in Use Over Time								
Remain on drug (n,%)[¥]	219 (79.6%)	275	274	331	447	525	138	162

CDAI: Clinical Disease Activity Index; MCID, minimal clinically important difference; J-HAQ, Japanese version of the Stanford Health Assessment Questionnaire; #Excluding those who initiated methotrexate (MTX) with other biologicals (TNFi or nonTNFi) or Janus Kinase inhibitor (JAKi); *Number of non-missing observations; £Reference: Curtis et al. Determining the Minimally Important Difference in the Clinical Disease Activity Index for Improvement and Worsening in Early Rheumatoid Arthritis Patients. *Arthritis Care & Research*. 2015;67(10):1345; ¥Patients who did not remain on drug had either switched to another medication or were not being treated.

Table 2. Unadjusted Effectiveness Outcomes (Baseline to 6-month follow-up) by Drug Group

Results: There were 1293 patients in the registry with 275 MTX, 331 TNFi, 525 nonTNFi, and 162 tofacitinib initiators that had both baseline and 6-month FU visits available. Mean disease duration was 2.4, 7.2, 9.8, and 11.8 years, respectively, in the MTX, TNFi, nonTNFi, and tofacitinib groups. Almost all MTX initiators (99.3%) were biological naïve. Among TNFi initiators, 76.7%, 16.9%, 3.6%, and 2.7% received their drug as their 1st, 2nd, 3rd, and 4th biological/Janus Kinase inhibitor (JAKi), respectively. For patients in the nonTNFi group, it was 62.7% 21.3%, 9.3%, and 6.7%, respectively. Among tofacitinib initiators, 26.5% of patients received the drug as their 1st, 35.2% as their 2nd, 21.0% as their 3rd, and 17.3% as their 4th biological/JAKi. At initiation, mean disease activity, as measured by CDAI, was 19.0, 22.6, 21.9, and 23.1 for the MTX, TNFi, nonTNFi, and tofacitinib patients, respectively (Table 1).

At the 6-month FU visit following initiation, mean change in CDAI was -9.9, -11.6, -11.8 and -12.4 in the MTX, TNFi, nonTNFi, and tofacitinib initiators, respectively. Additionally, the majority of the patients (61.0%, 62.6%, 67.1%, and 66.7% for the MTX, TNFi, nonTNFi, and tofacitinib initiators, respectively) reached MCID in CDAI. Almost half of all initiators achieved ACR20 responses (46.9%, 42.6%, 48.2%, and 45.1% of the MTX, TNFi, nonTNFi, and tofacitinib initiators, respectively). Approximately 80% or more initiators remained on the drug until their 6-month FU visit (79.6%, 82.8%, 85.1%, and 85.2% for MTX, TNFi, nonTNFi, and tofacitinib, respectively) (Table 2).

Conclusion: There were distinct patient profiles for those initiating each of the four drug classes in Japan. Overall, the majority of patients receiving MTX, TNFi, nonTNFi, and tofacitinib all had good responses. This positive patient response to DMARDS in a Japanese population adds to the growing scientific literature for those seeking to understand real-world outcomes.

Disclosure: Y. Tanaka, AbbVie, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 2, 5, 8, Asahi-kasei, 2, 5, 8, Novartis, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Astellas, 2, 5, 8, Chugai, 2, 5, 8, Daiichi-Sankyo, 2, 5, 8, Eisai, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Janssen, 2, 5, 8, Mitsubishi-Tanabe, 2, 5, 8, Pfizer, 2, 5, 8, Takeda, 2, 5, 8, YL Biologics, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8; **H. Yamanaka**, Chugai Pharmaceutical Co. Ltd., 1, 2, Astellas Pharma Inc., 1, 2, Bristol-Meyers Squibb, 1, 2, Daiichi-Sankyo Co. Ltd, 1, 2, Mitsubishi-Tanabe Pharma Corp., 1, 2, Takeda Pharmaceutical Co. Ltd., 1, 2, Teijin Pharma Ltd., 1, 2, Pfizer Japan Inc, 1, 2, YLbio, 1, 2, Ayumi Pharmaceutical Co. Ltd., 1,

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Abstract Number: 0803

Real-World DMARD Experience and Outcomes for Rheumatoid Arthritis Patients in Japan: Safety

Mitsumasa Kishimoto[1], Yoshiya Tanaka[2], Leslie Harrold[3], Alina Onofrei[3], Christine Barr[4], Ekta Agarwal[5], Jose L Rivas[6], Naonobu Sugiyama[7], Jeffrey Greenberg[8] and Hisashi Yamanaka[9], [1]Department of Nephrology and Rheumatology, Kyorin University School of Medicine, Yokohama, Japan, [2]The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, [3]Corrona, LLC, Waltham, MA, [4]Corrona, LLC, Albany, NY, [5]Pfizer, Inc., Princeton Jct, NJ, [6]Pfizer SLU, Madrid, Spain, [7]Pfizer Japan Inc, Tokyo, Japan, [8]Corrona, LLC and NYU School of Medicine, Waltham, MA, [9]Sanno Medical Center, Tokyo, Japan, Tokyo, Japan

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: There is limited information on the real-world safety of disease-modifying anti-rheumatic drugs (DMARDs) approved for treating rheumatoid arthritis (RA) in Japan. Using a Japanese RA registry, rates of serious adverse events among initiators of methotrexate (MTX), TNFi, nonTNFi, and tofacitinib were calculated.

Methods: We identified RA patients (pts) in the Corrona RA Japan Registry who initiated a DMARD between 03/01/2016 to 12/31/2019 and had at least one follow-up (FU) visit or had an adverse event before the first FU visit. If pts switched to another drug in the same drug class, they remained in the original drug group. Each initiation was considered so pts could be in ≥ 1 drug group. Adverse events of interest were cardiovascular disease (CVD), serious infections, Herpes Zoster [(HZ) serious and non-serious], and malignancy, excluding non-melanoma skin cancer (NMSC). The incidence of adverse events was calculated. For all events except malignancy, person-time at risk was estimated from time of drug initiation until the occurrence of the first event or 90 days after discontinuation. For risk of malignancies, the risk window for any therapy included all person-time in the designated period (time since starting therapy) and extended until the end of data collection. Incidence rates (IR), expressed as number of first events per 100 person-years (PY), were calculated with 95% confidence intervals (CI) assuming a Poisson distribution.

Results: There were 1,546 pts with first-time use of MTX, TNFi, nonTNFi, or tofacitinib who had at least one FU visit or had an adverse event before the first FU visit. Drug groups included 296 MTX, 491 TNFi, 560 nonTNFi, and 199 tofacitinib initiators. History of prior CVD, serious infection, HZ, and malignancy ranged from 8-14%, 9-15%, 10-14%, and 6-16%, respectively (Table 1).

The average PY of FU time was 2.0, 1.6, 1.5, and 1.4 PY for MTX, TNFi, nonTNFi, and tofacitinib initiators, respectively (Table 2). The IR for serious infections was (IR=6.47, 95% CI, 4.70-8.68) for nonTNFi, (3.86, 1.77-7.33) for tofacitin-

N	MTX[a] 296	n[b]	TNFi 491	n[b]	nonTNFi 560	n[b]	tofacitinib 199	n[b]
Demographics								
Age, Mean (SD)	59.8 (14.0)	296	60.2 (15.4)	491	65.8 (12.8)	560	61.7 (13.5)	199
Female gender, n (%)	222 (75.0%)	296	393 (80.0%)	491	429 (76.6%)	560	164 (82.4%)	199
Lifestyle Characteristics								
Currently smoking, n (%)	60 (21.9%)	274	51 (11.3%)	453	55 (10.5%)	524	21 (11.4%)	184
Alcohol use in the past year, n (%)	160 (54.1%)	296	217 (44.2%)	491	213 (38.0%)	560	85 (42.7%)	199
Comorbidities								
Prior CVD[c], n (%)	25 (8.4%)	296	50 (10.2%)	491	77 (13.8%)	560	23 (11.6%)	199
Prior serious infection, n (%)	26 (8.8%)	296	51 (10.4%)	491	81 (14.5%)	560	30 (15.1%)	199
Prior herpes zoster, n (%)	35 (11.8%)	296	50 (10.2%)	491	77 (13.8%)	560	26 (13.1%)	199
Prior malignancy (excluding non-melanoma skin cancer), n (%)	22 (7.4%)	296	27 (5.5%)	491	88 (15.7%)	560	11 (5.5%)	199
Disease Characteristics								
Disease duration, Mean (SD)	2.3 (5.7)	296	7.4 (9.7)	491	9.7 (10.9)	559	11.8 (11.2)	199
Seropositive (RF or CCP) ever, n (%)	185 (63.8%)	290	341(71.5%)	477	431(79.4%)	543	142(77.6%)	183
Concomitant Medications								
MTX (yes/no), n (%)	296 (100.0%)	296	379 (77.2%)	491	284 (50.7%)	560	137 (68.8%)	199
Dose of MTX if on MTX, mg/week (median, IQR)	8.0 (2.0)	293	10.0 (4.0)	365	10.0 (4.0)	273	10.0 (4.0)	122
Prednisone (yes/no), n (%)	51 (17.2%)	296	154 (31.4%)	491	196 (35.0%)	560	53 (26.6%)	199
Dose of prednisone if on prednisone, mg/day (median, IQR)	5.0 (4.0)	49	5.0 (5.0)	142	5.0 (4.0)	177	5.0 (5.2)	43
Prior Biologic/JAKi Medications[d]								
0	292 (98.6%)	296	360 (73.3%)	491	345 (61.6%)	560	50 (25.1%)	199
1	4 (1.4%)	296	80 (16.3%)	491	125 (22.3%)	560	69 (34.7%)	199
2	0 (0.0%)	296	27 (5.5%)	491	51 (9.1%)	560	39 (19.6%)	199
3+	0 (0.0%)	296	24 (4.9%)	491	39 (7.0%)	560	41 (20.6%)	199
Disease Activity								
CDAI, Mean (SD)	19.0 (11.5)	288	23.7 (13.2)	466	22.1 (11.8)	531	23.6 (13.8)	183
DAS 28-ESR, Mean (SD)	4.6 (1.2)	242	5.0 (1.3)	432	5.0 (1.3)	454	5.0 (1.3)	171

[a]Excluding those who initiated methotrexate (MTX) with other biologicals (TNFi or nonTNFi) or Janus Kinase inhibitor (JAKi); [b]Number of non-missing observations; [c]Prior CVD includes hypertension requiring hospitalization, cardiac revascularization procedure (CABG, stent, angioplasty), ventricular arrhythmia, cardiac arrest, myocardial infarction, acute coronary syndrome, unstable angina, CHF requiring hospitalization, stroke, transient ischemic attack, other cardiovascular event, deep vein thrombosis, peripheral arterial thromboembolic event, urgent peripheral arterial revascularization, peripheral ischemia or gangrene (necrosis) and pulmonary embolism; [d]For example, if a patient was in the tofacitinib group and had used MTX, etanercept, and abatacept prior to tofacitinib, the patient would be listed as having MTX, TNFi, and nonTNFi.

Table 1. Baseline Characteristics of the Safety Cohort

	Years of follow-up in Corrona		
Drug group	**Total**	**Mean**	**Median**
MTX*	598.5	2.0	2.1
TNFi	796.0	1.6	1.6
nonTNFi	838.5	1.5	1.5
Tofacitinib	285.3	1.4	1.4

* Excluding those who initiated MTX with other biologics (TNFi or nonTNFi) or JAKi.

Table 2. Follow-up Time for Each Drug Group

ib, (3.46, 2.17-5.24) for TNFi, and (2.16, 1.04-3.97) for the MTX groups. The tofacitinib group had the highest IR for HZ (9.31, 5.76-14.23) and nonTNFi (2.02, 1.11-3.40), TNFi (0.93, 0.34-2.03), and the MTX (0.86, 0.23-2.20) groups were lower. All the HZ events were non-serious (e.g., did not require hospitalization or intravenous antivirals). Total CVD was (0.43, 0.05-1.54), (0.77, 0.25-1.80), (1.57, 0.79-2.82), and (1.27, 0.26-3.72 in the MTX, TNFi, nonTNFi, and the tofacitinib groups, respectively. For malignancy excluding NMSC, the IRs were (1.65, 0.88-2.82) in TNFi, (1.52,0.70-2.89) in MTX, (1.20, 0.58-2.21) in nonTNFi, and (0.35, 0.01-1.96) in the tofacitinib groups (Table 3).

Conclusion: There were similar rates of serious infection, CVD, and malignancy adverse events among pts initiating MTX, TNFi, nonTNFi, and tofacitinib. Yet, the rate of HZ, due to non-serious events, was greater in those initiating tofacitinib, which is consistent with what is known from Japanese tofacitinib clinical trial data.

Total Counts of Events of Interest	MTX		TNFi Initiators		nonTNFi Initiators		Tofacitinib Initiators	
	N/PYR	Rate (95% CI)	N/PYR	Rate (95% CI)	N/PYR	Rate (95% CI)	N/PYR	Rate (95% CI)
CVD[a]	2/469.46	0.43 (0.05-1.54)	5/647.66	0.77 (0.25-1.8)	11/698.79	1.57 (0.79-2.82)	3/235.42	1.27 (0.26-3.72)
Serious Infections[b]	10/462.98	2.16 (1.04-3.97)	22/635.82	3.46 (2.17-5.24)	44/680.14	6.47 (4.70-8.68)	9/232.96	3.86 (1.77-7.33)
Herpes Zoster[c]	4/465.45	0.86 (0.23-2.2)	6/644.5	0.93 (0.34-2.03)	14/691.8	2.02 (1.11-3.4)	21/225.58	9.31 (5.76-14.23)
Cancer excluding NMSC[d]	9/591.36	1.52 (0.7-2.89)	13/787.32	1.65 (0.88-2.82)	10/830.37	1.20 (0.58-2.21)	1/284.78	0.35 (0.01-1.96)

[a]CVD includes hypertension requiring hospitalization, cardiac revascularization procedure (CABG, stent, angioplasty), ventricular arrhythmia, cardiac arrest, myocardial infarction, acute coronary syndrome, unstable angina, CHF requiring hospitalization, stroke, transient ischemic attack, other cardiovascular event, deep vein thrombosis, peripheral arterial thromboembolic event, urgent peripheral arterial revascularization, peripheral ischemia or gangrene (necrosis) and pulmonary embolism; [b]Serious infections includes pneumonia, sepsis, joint/bursa, cellulitis/skin, sinusitis, diverticulitis, bronchitis, gastroenteritis, meningitis/encephalitis, urinary tract infection, upper respiratory infection, tuberculosis and other infections meeting serious adverse event criteria (resulting in hospitalization (new or prolonged) death, disability, congenital anomaly, was immediately life-threatening or otherwise deemed serious in the opinion of the investigator), and/or requiring treatment with an IV antibiotic; [c]Herpes zoster includes both serious and non-serious herpes zoster; [d]Cancer excluding non-melanoma skin cancer

Table 3. Crude Incidence Rates (number of first events/100 PY) for MTX group, TNFi Initiators, nonTNFi Initiators, and Tofacitinib Initiators

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Disclosure: M. Kishimoto, AbbVie, 5, 8, Amgen-Astellas Pharm, 5, 8, Asahi-Kasei Pharm, 5, 8, Ayumi Pharm, 5, 8, BMS, 5, 8, Chugai, 5, 8, Daiichi Sankyo, 5, 8, Eisai, 5, 8, Eli Lilly, 5, 8, Gilead, 5, 8, Janssen, 5, 8, Kyowa Kirin, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Tanabe Mitsubishi, 5, 8, Teijin, 5, 8, UCB, 5, 8; **Y. Tanaka**, AbbVie, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 2, 5, 8, Asahi-kasei, 2, 5, 8, Novartis, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Astellas, 2, 5, 8, Chugai, 2, 5, 8, Daiichi-Sankyo, 2, 5, 8, Eisai, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Janssen, 2, 5, 8, Mitsubishi-Tanabe, 2, 5, 8, Pfizer, 2, 5, 8, Takeda, 2, 5, 8, YL Biologics, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8; **L. Harrold**, Bristol-Myers Squibb Company, 5; **A. Onofrei**, Corrona, LLC, 3; **C. Barr**, Corrona, LLC, 3; **E. Agarwal**, Pfizer Inc, USA, 1, 3; **J. Rivas**, Pfizer Inc, 1, 3; **N. Sugiyama**, Pfizer Japan Inc, 1, 3; **J. Greenberg**, Corrona, LLC, 1, 3; **H. Yamanaka**, Chugai Pharmaceutical Co. Ltd., 1, 2, Astellas Pharma Inc., 1, 2, Bristol-Meyers Squibb, 1, 2, Daiichi-Sankyo Co. Ltd, 1, 2, Mitsubishi-Tanabe Pharma Corp., 1, 2, Takeda Pharmaceutical Co. Ltd., 1, 2, Teijin Pharma Ltd., 1, 2, Pfizer Japan Inc, 1, 2, YLbio, 1, 2, Ayumi Pharmaceutical Co. Ltd., 1, Boehringer Ingelheim, 1, AbbVie Japan Co. Ltd, 1, Eisai Co., Ltd, 1, Kaken Pharmaceutical Co., Ltd., 1, Nippon-Shinyaku, 1, Novartis Pharma K. K., 1, Ono Pharmaceutical Co., Ltd, 1, Taisho Toyama Pharmaceutical Co., Ltd., 1, Torii Pharmaceutical Co., Ltd, 1, UCB Japan Co. Ltd, 1.

Abstract Number: 0804

Factors That Influence Biological Survival in Rheumatoid Arthritis: Results of a Real-world Cohort from the Netherlands

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Data on biological survival, stratified for discontinuation reasons, and predictors that influence survival time have not been explored extensively. Therefore, we aim to explore real-world first and second-line biological survival and determine its influenceability in rheumatoid arthritis (RA) patients.

Methods: Data from the local pharmacy database and patient records of a university hospital in the Netherlands were used. RA patients who started a biological between 2000-2020 were included. Data on age, anti-citrullinated protein

	RA patients, n=318
Demographic	
• Age at diagnosis, mean (sd)	40.9 (16)
• Gender, female, n (%)	264 (83)
• BMI, mean (sd)	26.9 (6.3)
Disease characteristics	
• ACPA positive, n (%)	224 (70)
• RF positive, n (%)	226 (71)
• Erosive disease, n (%)	141 (44)
Medication	
• Time to first biological, years, median (IQR)	3.6 (1-7)
• First-line biologicals	
o Etanercept, n (%)	142 (45)
o Adalimumab, n (%)	90 (28)
o Certolizumab Pegol, n (%)	59 (19)
o Infliximab, n (%)	15 (5)
o Golimumab, n (%)	5 (2)
o Anakinra, n (%)	3 (1)
• csDMARDs used with first-line biological	
o MTX, n (%)	66 (21)
o MTX + SASP and/or HCQ , n (%)	147 (46)
o Other csDMARDs (SASP, HCQ, LEF), n (%)	53 (17)
o No combination therapy, n (%)	52 (16)

ACPA: anti-citrillunated protein antibody, BMI: body mass index, csDMARD: conventional synthetic disease modifying anti-rheumatic drug, HCQ: hydroxychloroquine, IQR: inter quartile range, LEF: leflunomide, MTX: methotrexate, RF: rheumatoid factor, SASP: sulfasalazine, sd: standard deviation

Table 1 Characteristics of patient population

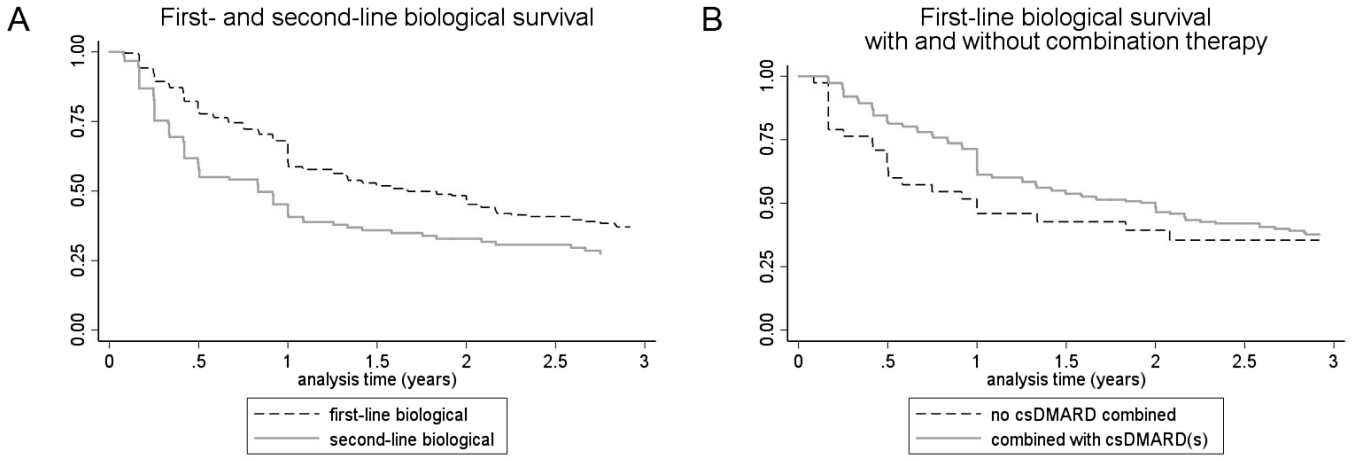

Figure 1 Kaplan Meier curves for biological survival. (A) Biological survival of first- and second-line biological in rheumatoid arthritis patients. (B) Biological survival with and without combination therapy with a csDMARD.

antibody (ACPA) and rheumatoid factor (RF)-status, presence of erosions, gender, body mass index, time to first biological, biological survival time, use of csDMARDs and discontinuation reasons were collected.

Results: Of the included 318 patients, 39 (12%) started their first biological within 6 months after diagnosis. Median time between diagnosis and first biological prescription was 3.6 years (95% confidence interval (CI) 1.0-7.2). 50%

of patients started their first biological after 2013. Median survival time of the first- and second-line biological was respectively 1.7 years (95%CI 1.3-2.2) and 0.8 years (95%CI 0.5-1.0)(p=0.0001)(Figure 1A). Discontinuation reasons for the first-line biological were ineffectiveness (47%), adverse events (17%), remission (16%), pregnancy (30%), or patient preference (10%)(Table 1). Multivariable Cox regression analyses, performed on the population that discontinued due to inefficacy or adverse events, showed that use of csDMARDs (HR=1.32, p< 0.001) positively influenced biological survival (Figure 1B) RF positivity on the other hand (HR=0.82, p=0.03) negatively influenced biological survival. Biological survival in ACPA positive patients was longer compared to ACPA negative patients taking in to account discontinuation due to remission (HR=1.43, p=0.023). This indicates that ACPA positive patients were less likely to discontinue their biological due to remission. Second-line TNF-inhibitor survival did not differ between patients with a primary, < 6 months, and secondary, ≥6 months, non-response on the first-line TNF-inhibitor (HR=1.28, p=0.34).

Conclusion: Biological survival diminishes with the number of biologicals used. Biological survival is prolonged if patients use concomitant csDMARDs, and is shortened when patients are RF positive. ACPA positivity lowers the chance to discontinue biologicals due to remission.

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Abstract Number: 0805

The PROPER Study: Results of the First Interim Analysis of a Pan-EU Real-World Study of SB5 Biosimilar Following Transition from Reference Adalimumab in Patients with Rheumatoid Arthritis, Axial Spondyloarthritis or Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: SB5, an adalimumab biosimilar received EU marketing authorisation in August 2017, based on the totality of evidence from pre-clinical and clinical Phase I and III studies that demonstrated bioequivalence, similar efficacy, and comparable safety and immunogenicity to reference adalimumab (ADL). There are few published data on the transition from reference ADL to SB5 outside the controlled, randomised, clinical trial setting. This study aims to evaluate candidate predictors of persistence on SB5 in EU patients across multiple indications.

Methods: This ongoing observational study will enrol approximately 1200 subjects with rheumatoid arthritis (RA), axial spondyloarthritis (axSpA) or psoriatic arthritis (PsA), ulcerative colitis or Crohn's disease who initiated SB5 as part of routine clinical practice following a minimum of 16 weeks' treatment with reference ADL, at clinics in Belgium, Germany, Ireland, Italy, Spain and the UK. Data are captured from clinic records retrospectively for the 24 weeks prior to transition, and prospectively and/or retrospectively for 48 weeks following transition. The primary objective is to

Table 1: Patient baseline characteristics

	RA (N=85)		axSpA (N=86)		PsA (N=85)	
	Mean (SD)	Q1, Q3	Mean (SD)	Q1, Q3	Mean (SD)	Q1, Q3
Age (years)	59.9 (12.8)	53, 68	52.7 (13.5)	40, 63	54.5 (12.6)	46, 63
Duration of disease (years)	12.6 (17.0)	1, 20	21.9 (14.2)	12, 30	12.2 (10.3)	3, 20
			n (%)			
Women	59	(69.4)	27	(31.4)	37	(43.5)
Received biologic therapy prior to reference ADL	18	(22.2)	11	(13.3)	17	(20.5)
Dosing regimen ADA to SB5						
40mg Q2W: 40mg Q2W	63	(75.9)	74	(87.1)	74	(87.1)
Other*	20	(24.1)	11	(12.9)	11	(12.9)
Clinical Status (physician opinion)						
Remission	13	(16.3)	15	(19.5)	15	(19.5)
Stable	67	(83.8)	55	(71.4)	62	(80.5)
Active	0	(0.0)	7	(9.1)	0	(0.0)

SD standard deviation; Q1 1st quartile, Q3 3rd quartile; CI Confidence interval

*Other includes all other reported doses and/or dosing intervals: 40mg QW, 80mg Q2W, and unspecified frequency

Table 2: SB5 Dose Regimen and Disease Score

		RA (N=85)		axSpA (N=86)		PsA (N=85)	
Dose Regimen		**n**	**(%)**	**n**	**(%)**	**n**	**(%)**
Baseline	40mg Q2W	70	(82.4)	76	(88.4)	76	(89.4)
	*Other	15	(17.6)	10	(11.6)	9	(10.6)
Week 12	40mg Q2W	46	(79.3)	57	(87.7)	46	(93.9)
	*Other	12	(20.7)	8	(12.3)	3	(6.1)
Week 24	40mg Q2W	34	(77.3)	44	(89.8)	37	(94.9)
	*Other	10	(22.7)	5	(10.2)	2	(5.1)
Disease Score		**n**	**mean (95% CI)**	**n**	**mean (95% CI)**	**n**	**mean (95% CI)**
			DAS28		**BASDAI**		**PsARC (tender joint)**
Baseline		76	2.59 (2.39, 2.79)	71	2.9 (2.44, 3.36)	63	2.3 (1.0, 3.6)
Week 12		47	2.68 (2.42, 2.94)	27	3.97 (3.18, 4.55)	18	3.3 (0.9, 5.7)
Week 24		38	2.55 (2.25, 2.85)	35	2.79 (2.16, 3.43)	25	3.5 (0.5, 6.5)
			FFbH				**PsARC (swollen joint)**
Baseline		32	76.8 (70.2, 83.3)	-	-	63	0.3 (0.0, 0.7)
Week 12		25	77.9 (70.1, 85.7)	-	-	18	1.8 (0.5, 3.0)
Week 24		17	71.4 (60.7, 82.0)	-	-	25	0.9 (-0.5, 2.3)

*Other includes all other reported doses and/or dosing intervals: 40mg QW, 80mg Q2W, and unspecified frequency

DAS-28 Disease Activity Score 28; FFbH Hannover Functional Ability Questionnaire; BASDAI Bath Ankylosing Spondylitis Disease Activity Index; PsARC Psoriatic Arthritis Activity Score

evaluate candidate predictors of persistence; primary outcome measures include baseline clinical characteristics, disease activity scores and clinical management over time. This interim analysis provides an overview of baseline characteristics, and disease scores and dose regimen up to 24 weeks post-initiation of SB5 in subjects with RA, axSpA or PsA enrolled at 16 specialist sites (11 in Germany, 5 in UK), followed up to the data extract date of 1st May 2020.

Results: Of the 256 patients included in this interim analysis 85 with RA and 23 with PsA were enrolled in Germany, and 86 with axSpA and 62 with PsA in U.K.

Conclusion: This interim analysis provides an early insight into a contemporary cohort of EU patients with established RA, axSpA and PsA, switched from reference to biosimilar ADL in clinical practice. The majority of patients had sTable disease at transition, with no meaningful difference seen in disease score by Week 24 post-transition, while 75% or more of each cohort transitioned to the same dose regimen of SB5 as received for reference ADL prior to transition, and the majority of patients continued the same SB5 regimen to Week 24. With ongoing enrolment and longer follow-up, the study will provide pertinent information about clinical outcomes of transition from reference to biosimilar ADL in real-world practice and in indications not investigated in controlled studies.

Disclosure: U. Müller-Ladner, Biogen, 8; **K. Gaffney**, Abbvie, 2, 5, 8, Celgene, 2, 5, 8, Lilly, 2, 5, 8, Pfizer, 2, 5, 8, Gilead, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5, 8; **D. Jadon**, Biogen, 2, 5, 8, Eli Lilly, 2, 5, 8, MSD, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 5, 8, Janssen, 5, 8, AbbVie, 5, 8, Sandoz, 5, 8, Gilead, 5, 8, Roche, 8, Oxfrod University Press, 7; **U. Freudensprung**, Biogen International GmbH, 1, 3; **J. Addison**, Biogen Idec, 1, 3.

Abstract Number: 0806

Identification and Adjustment for Factors Associated with Clinical Response in Rheumatoid Arthritis Clinical Trials to Improve Comparisons of Treatment Efficacy

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Numerous clinical trials have been published in rheumatoid arthritis (RA), but comparing efficacies of disease-modifying anti-rheumatic drugs (DMARDs) is complicated by a lack of head-to-head studies and because study populations are heterogeneous. We aimed to identify and adjust for patient/trial characteristics associated with clinical response to enable fairer comparisons between different drugs/drug classes, e.g. abatacept (co-stimulation modulator) vs. adalimumab (TNFi).

Methods: We reviewed 565 DMARD clinical trial papers using the following criteria: studies had to be randomized, controlled, Phase III trials published after 1995 reporting ACR20/50/70 with follow-up ≥ 6 months. 73 met criteria. We explored associations between 33 patient/trial characteristics and ACR response. We constructed models incorporating these factors to compute predicted ACR response rates for each trial arm and their residual differences from actual response rates. Some factors associated with response weren't reported in every study, so ACR20, 50, and 70 each required constructing multiple models to allow for different numbers of independent variables. The model used for a given trial arm was selected based on the information available (algorithm for ACR50 shown in Fig. 1).

Results: Based on linear regressions, multiple patient/trial characteristics were associated with ACR response, including age, calendar year of publication, DAS28-CRP, disease duration, and prior MTX/biologic use (Table 1). Trials with patients having greater disease duration at enrollment had lower response rates. Similarly, previous therapy

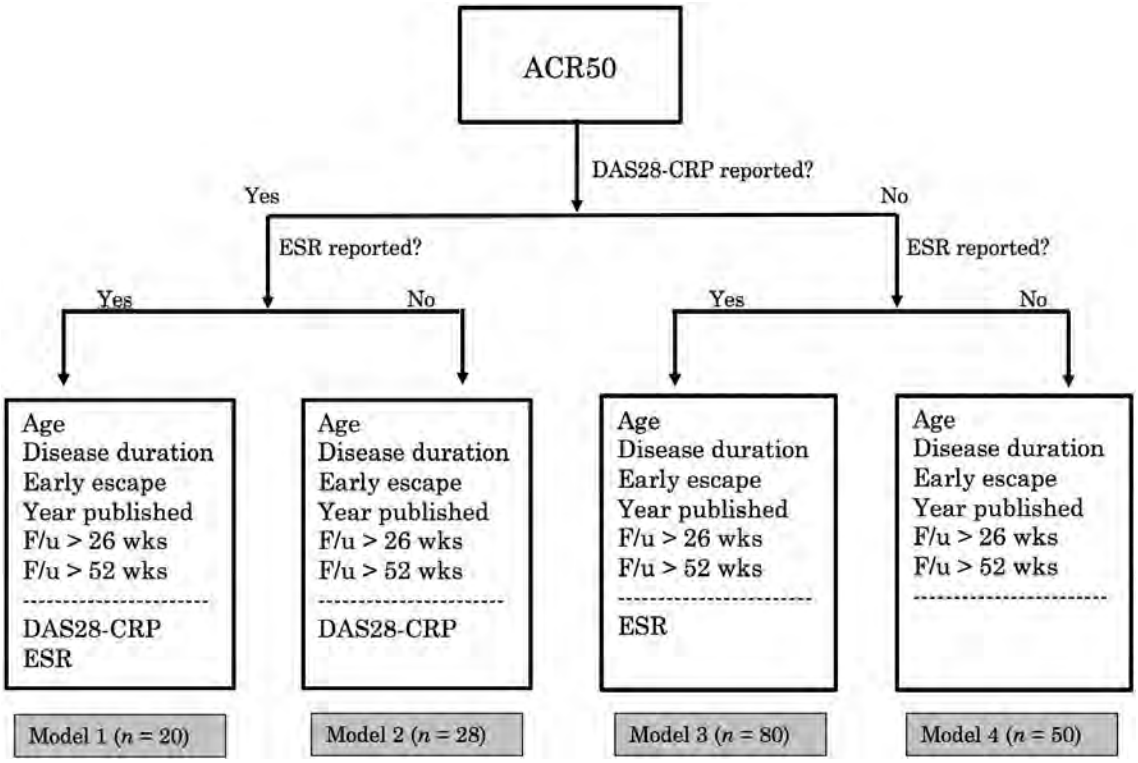

Figure 1: Choosing among four models for predicting an ACR50 score. Here n denotes the number of treatment arms for which a given model applied. Variables above the dashed line were reported in every treatment arm and are included in every model. Those below the line were not reported in some treatment arms. Calculating ACR50 scores for such arms required models not taking those variables as inputs.

failure (MTX or biologics) was associated with poorer response in trials. Conversely, trials with patients having higher baseline disease activity as characterized by DAS28-CRP (but not by DAS28-ESR) had higher response rates. Sex, white race, swollen/tender joint counts, and RF serostatus weren't associated with response. Several variables were associated with ACR70 response only, including steroid usage, anti-CCP serostatus, and ESR.

Before adjusting for the model predictions, ACR response rates were higher for abatacept compared to TNFi (both with MTX). The differences in average ACR20, 50, and 70 response rates, respectively, were 10.6 (p = 0.063), 13.3 (p = 0.018), and 15.3 (p = 0.005) percentage points, in favor of abatacept (Fig. 2). After adjustment, the differences were smaller and non-significant: 6.7 (p = 0.214), 3.9 (p = 0.421), and 6.6 (p = 0.087) points. These findings are more comparable to those reported in a direct head-to-head study by Schiff et. al. in 2014—between-group differences of -0.4, -1.9, and 1.8 points, respectively.

Conclusion: We identified factors associated with ACR response in RA clinical trials, awareness of which may inform interpretation of therapy response rates. Adjusting for them could enable more appropriate efficacy comparisons across therapies studied in different settings. In the case of abatacept vs. TNFi, adjustment via the predictive models we developed yielded results more similar to results of an existing head-to-head trial. These models may be useful for comparing other drugs/drug classes, particularly when no head-to-head trial exists.

Patient/trial characteristic	β_ACR20 (95% CI)	β_ACR50 (95% CI)	β_ACR70 (95% CI)
Calendar year published (N = 176)	**0.52*** (0.08 – 0.97)	**0.61**** (0.23 – 1.00)	**0.54***** (0.25 – 0.83)
DAS28-ESR (N = 116)	0.20 (-7.78 – 8.17)	1.65 (-5.26 – 8.58)	2.09 (-3.18 – 7.37)
DAS28-CRP (N = 48)	**12.0**** (4.07 – 20.0)	**12.5**** (5.52 – 19.6)	**7.22*** (1.00 – 13.4)
Age, yr (N = 178)	**-1.59**** (-2.59 – -0.59)	**-1.84***** (-2.70 – -0.98)	**-1.60***** (-2.23 – -0.97)
% Female (N = 176)	0.012 (-0.40 – 0.43)	-0.07 (-0.43 – 0.29)	-0.10 (-0.37 – 0.17)
% White (N = 95)	0.04 (-0.06 – 0.15)	0.06 (-0.03 – 0.15)	0.05 (-0.02 – 0.12)
% Smokers (N = 5)	-1.43 (-3.10 – 0.25)	-1.03 (-2.37 – 0.31)	-0.66 (-1.55 – 0.23)
BMI, kg/m^2 (N = 19)	-1.06 (-5.87 – 3.75)	-0.62 (-4.37 – 3.13)	-0.53 (-2.94 – 1.88)
HAQ (N = 161)	-3.61 (-15.1 – 7.92)	1.72 (-8.56 – 12.0)	2.84 (-5.08 – 10.8)
SJC (28) (N = 26)	-1.52 (-3.81 – 0.78)	-1.39 (-3.49 – 0.71)	-1.22 (-2.92 – 0.49)
TJC (28) (N = 26)	-1.06 (-2.22 – 0.092)	-0.95 (-2.01 – 0.11)	-0.87 (-1.73 – -0.02)
SJC (66/68) (N = 150)	-0.43 (-1.20 – 0.33)	-0.28 (-0.95 – 0.39)	-0.20 (-0.69 – 0.29)
TJC (66/68) (N = 150)	-0.39 (-0.90 – 0.13)	-0.23 (-0.68 – 0.22)	-0.09 (-0.43 – 0.24)
Patient Pain (VAS) (N = 101)	0.26 (-0.33 – 0.86)	0.22 (-0.30 – 0.75)	0.16 (-0.23 – 0.55)
Patient Global (N = 105)	-0.11 (-0.57 – 0.35)	-0.12 (-0.54 – 0.28)	-0.03 (-0.33 – 0.27)
Evaluator Global (N = 105)	-0.05 (-0.65 – 0.55)	-0.17 (-0.71 – 0.36)	-0.14 (-0.53 – 0.25)
Sharp score (N = 80)	-0.17 (-0.35 – 0.01)	**-0.22**** (-0.37 – -0.07)	**-0.21***** (-0.33 – -0.10)
% using steroids (N = 127)	-0.01 (-0.20 – 0.18)	-0.10 (-0.26 – 0.08)	**-0.14*** (-0.26 – -0.015)
Disease duration, yr (N = 178)	**-1.09**** (-1.77 – -0.41)	**-1.40***** (-1.98 – -0.83)	**-1.41***** (-1.82 – -1.00)
% RF + (N = 134)	0.13 (-0.15 – 0.41)	0.17 (-0.07 – 0.41)	0.16 (-0.02 – 0.34)
% anti-CCP + (N = 55)	-0.26 (-0.70 – 0.18)	0.17 (-0.24 – 0.59)	**0.37*** (0.03 – 0.71)
ESR (N = 100)	0.30 (-0.11 – 0.70)	0.33 (-0.00 – 0.68)	**0.28*** (0.05 – 0.52)
CRP (N = 158)	-0.01 (-0.28 – 0.26)	-0.04 (-0.27 – 0.20)	-0.03 (-0.21 – 0.15)
% MTX naïve (N = 164)	**0.07*** (0.01 – 0.13)	**0.10***** (0.05 – 0.15)	**0.10***** (0.07 – 0.14)
% Biologic naïve (N= 164)	**0.14*** (0.03 – 0.26)	**0.12*** (0.03 – 0.22)	**0.08*** (0.01 – 0.15)
Pharma sponsor (y/n) (N = 178)	-0.55 (-7.59 – 6.49)	0.94 (-5.08 – 6.96)	1.86 (-2.63 – 6.35)
Follow up > 26 wks (y/n) (N = 178)	3.45 (-1.69 – 8.58)	**7.74**** (3.38 – 12.10)	**8.51***** (5.38 – 11.63)
Follow up > 52 wks (y/n) (N = 178)	1.02 (-8.06 – 10.1)	3.07 (-4.92 – 11.1)	3.07 (-2.90 – 9.04)
Early escape (y/n) (N = 178)	**-8.89**** (-13.92 – -3.85)	**-7.09**** (-11.54 – -2.63)	**-5.49**** (-8.81 – -2.16)

Table 1. Simple linear regression coefficients from modeling ACR response rates as functions of patient/trial characteristics. N represents the number of observations for a given association, i.e. how many treatment arms contained both the independent and dependent variables of interest. Statistically significant associations are bolded with * = $p < 0.05$, ** = $p < 0.01$, and *** = $p < 0.001$.

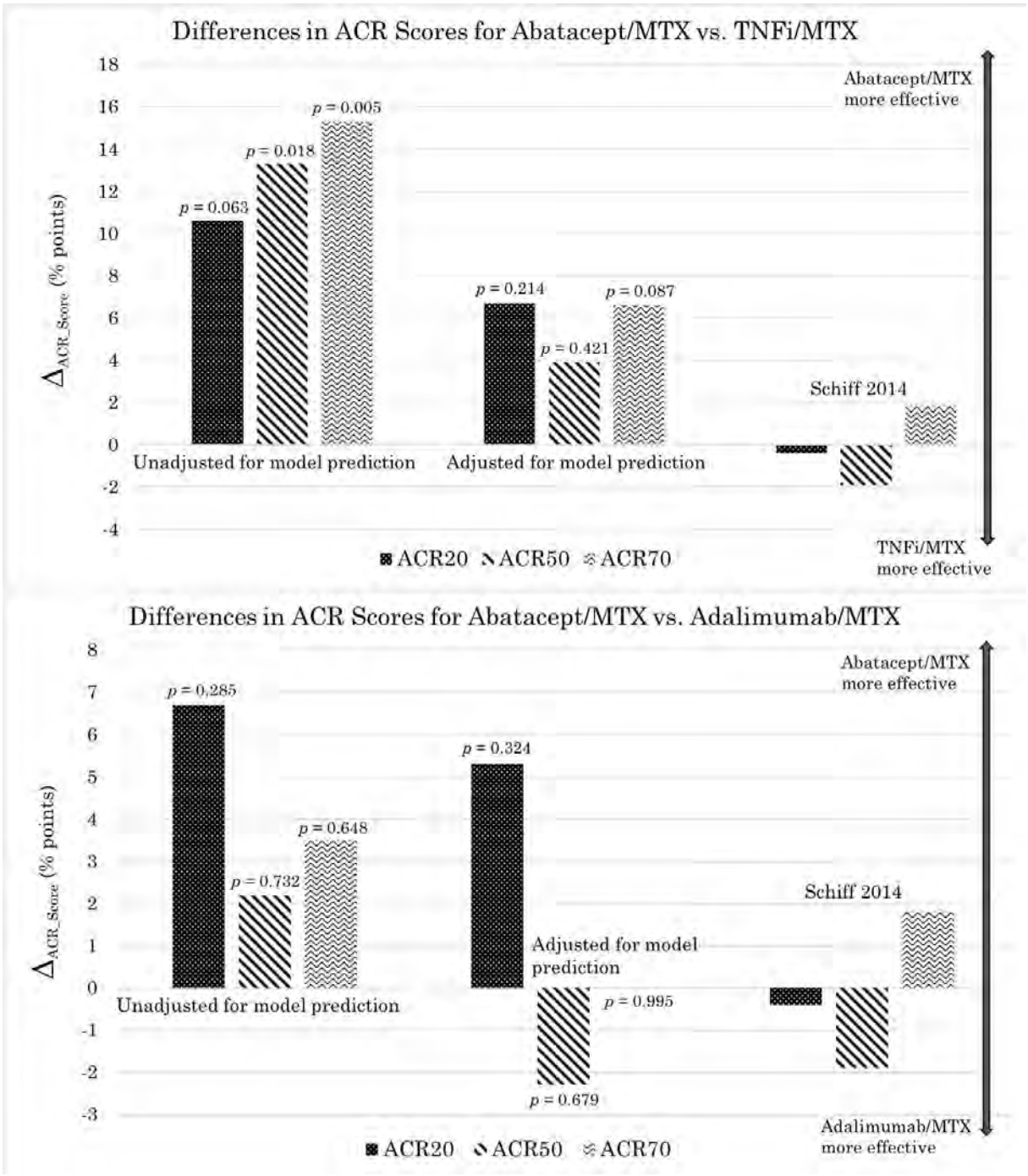

Figure 2. Differences in ACR response rates for abatacept vs. TNFi (comparison based on drug class) and abatacept vs. adalimumab (comparison based on drug)—all combined with MTX—unadjusted and adjusted for predictive models. Here ACR response rates for TNFi or adalimumab have been subtracted from those for abatacept, thus the positive vertical axis corresponds to superior efficacy for abatacept.

Disclosure: A. Cordisco, None; **J. Baker**, Gilead, 5, Bristol-Meier Squibb, 5.

Abstract Number: 0807

Safety of Biologic & Targeted Therapies Among Elderly Patients with Rheumatoid Arthritis: A Systematic Review and Meta-analysis

Akhil Sood[1], Soham Al Snih[1], Vijaya Murthy[2], Emilio Gonzalez[1] and Mukaila Raji[1], [1]University of Texas Medical Branch, Galveston, TX, [2]University of Texas Medical Branch, League City, TX

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Recent developments in biologic and targeted therapy have led to better control of disease activity and improved quality of life in patients with rheumatoid arthritis (RA). Many patients with RA are living longer, adding to the growing elderly population. A critical appraisal of extant data from studies on safety of these immunomodulatory therapies in the elderly can inform decision-making by patients and their physicians. We thus conducted a systematic review and meta-analysis of research studies on safety of biologics and targeted therapy in patients aged >60 years with RA.

Methods: We systematically searched Pubmed/Medline and Scopus from January 1, 1999 to June 1, 2020 to identify eligible studies that examined the safety of biologic & targeted therapies in older patients with rheumatoid arthritis. Included studies provided information on patients who received biologic (anti-TNF, IL-1, IL-6, B cell, or T cell) or targeted therapy (Janus kinase inhibitor), patients older than 60 years and a control population (younger users on biologics). Information on overall pooled rates of infections and malignancy was extracted from the studies. Meta-analysis was performed using RevMan software.

Results: We identified 823 studies; of these, 16 were included in the final analysis (12 observational studies and 4 randomized clinical trials) that comprised 8992 older users on biologics and 25,564 younger users of biologics. The pooled prevalence of infections in older and younger users of biologics was 11% and 7%, respectively, yielding a

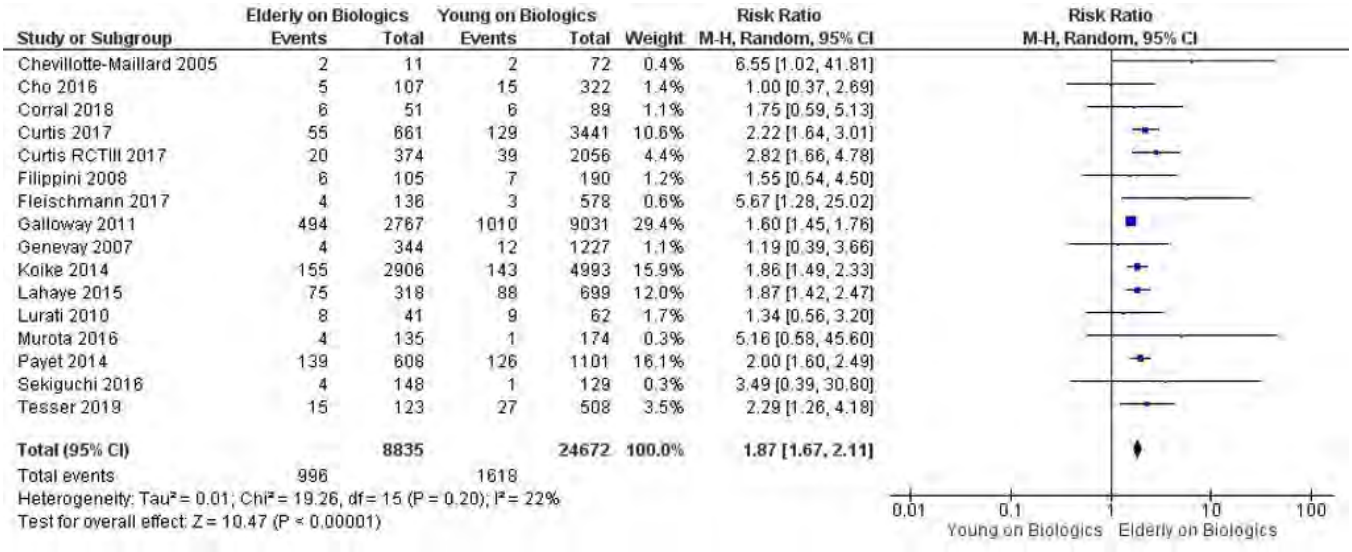

Figure 1. Forest plot on risk of infection among older patients (>60 years) on biologics compared to younger patients on biologics

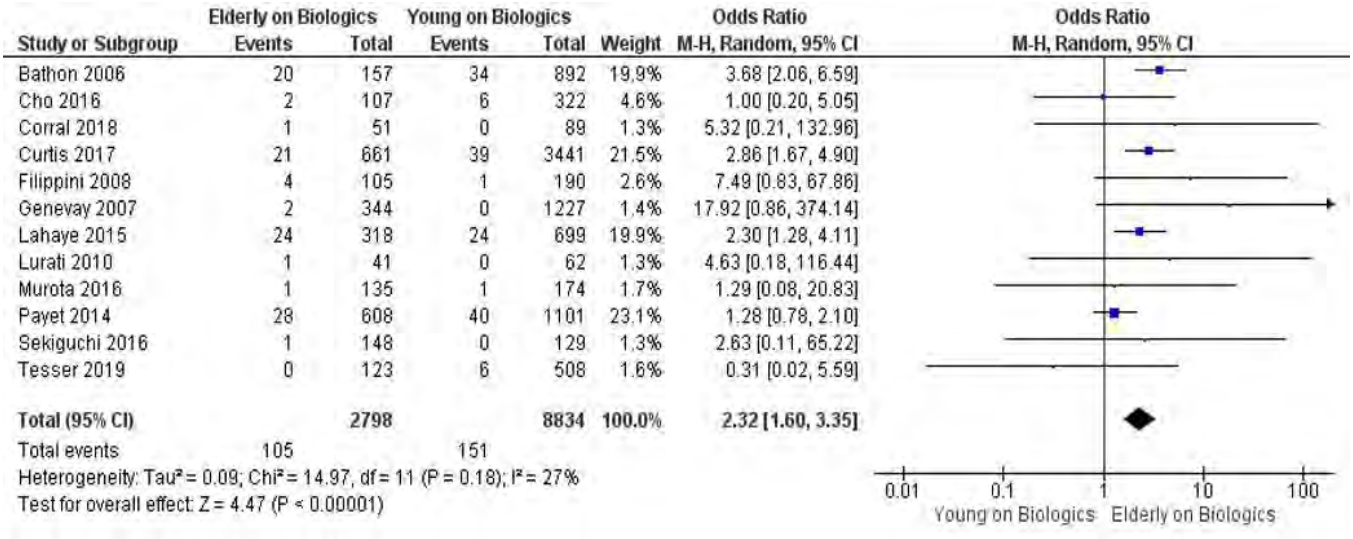

Figure 2. Forest plot on risk of malignancy among older patients (> 60 years) on biologics compared to younger patients on biologics

pooled random effects odds ratio of 1.87 (95% CI, 1.67–2.11). Older age was associated with a significant increase in risk of malignancy (OR, 2.32; 95% CI, 1.60–3.35) compared to younger users on biologics. The majority of the eligible studies were conducted in White population.

Conclusion: In a systematic review and meta-analysis, older patients with RA on immunomodulatory therapies were at significantly increased risk of infection and malignancy compared to younger patients on these treatments. Additional studies involving more racially and ethnically diverse cohorts are necessary to broaden our understanding of safety profile of biologics in different populations of older patients with RA. Furthermore, studies which include elderly patients on non-biologics as comparison would be necessary to better assess safety of biologics within elderly population.

Disclosure: A. Sood, None; **S. Al Snih**, None; **V. Murthy**, None; **E. Gonzalez**, None; **M. Raji**, None.

Abstract Number: 0808

Time to Discontinuation of Tofacitinib and TNF Inhibitors in Rheumatoid Arthritis Patients with and Without Methotrexate: Real World Results from a Rheumatoid Arthritis Cohort

Mohammad Movahedi[1], Angela Cesta[2], Xiuying Li[3], Edward C Keystone[4] and Claire Bombardier[5], [1]Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada, [2]Toronto General Hospital Research Institute, Toronto, ON, Canada, [3]Toronto General Hospital Research Institute, Toronto, Canada, [4]Mount Sinai Hospital, Toronto, ON, Canada, [5]Institute for Work and Health, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX). TOFA can be used as an alternative to biologic disease mod-

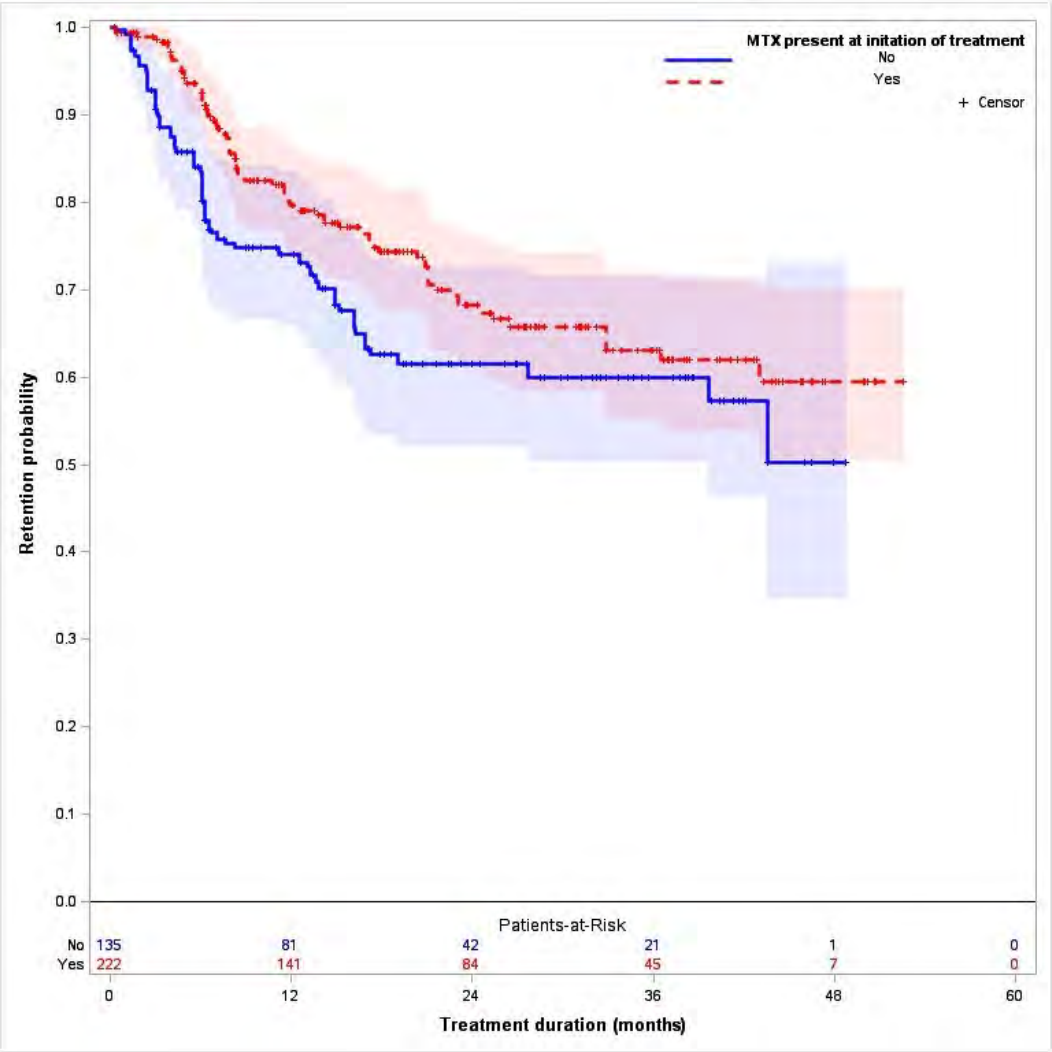

Figure 1. Drug discontinuation TNFi and TOFA; with and without MTX A. TNFi

ifying antirheumatic drugs (bDMARDs) including tumor necrosis factor inhibitors (TNFi). We aimed to evaluate the discontinuation rate of this drug, with and without concurrent MTX in comparison with TNFi, in patients with RA in the Ontario Best Practices Research Initiative (OBRI).

Methods: RA patients enrolled in the OBRI initiating their TOFA or TNFi (adalimumab, certolizumab, etancercept, golimumab, and infliximab) between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2018 were included. Time to discontinuation (due to any reason) were assessed using Kaplan-Meier survival (adjusted for propensity score using inverse probability of treatment weight) to compare patients with and without MTX use at initiation of TOFA or TNFi. We used multiple imputation (N=20) to deal with missing data for covaraites at treatment initiation.

Results: A total of 565 patients initiated TOFA (n=208) or TNFi (n=357). Of those, 106 (51%) and 222 (62%) were treated with MTX in the TOFA and TNFi group, respectively. There was no significant difference for sociodemographic , comorbidity, and disease profile between MTX groups in TOFA users. In TNFi users, compared with no MTX group, patients with MTX were significantly less likely to be women (77.9% vs. 88.9%) and to have prior bDMARDs use (24.3% vs. 42.4%).

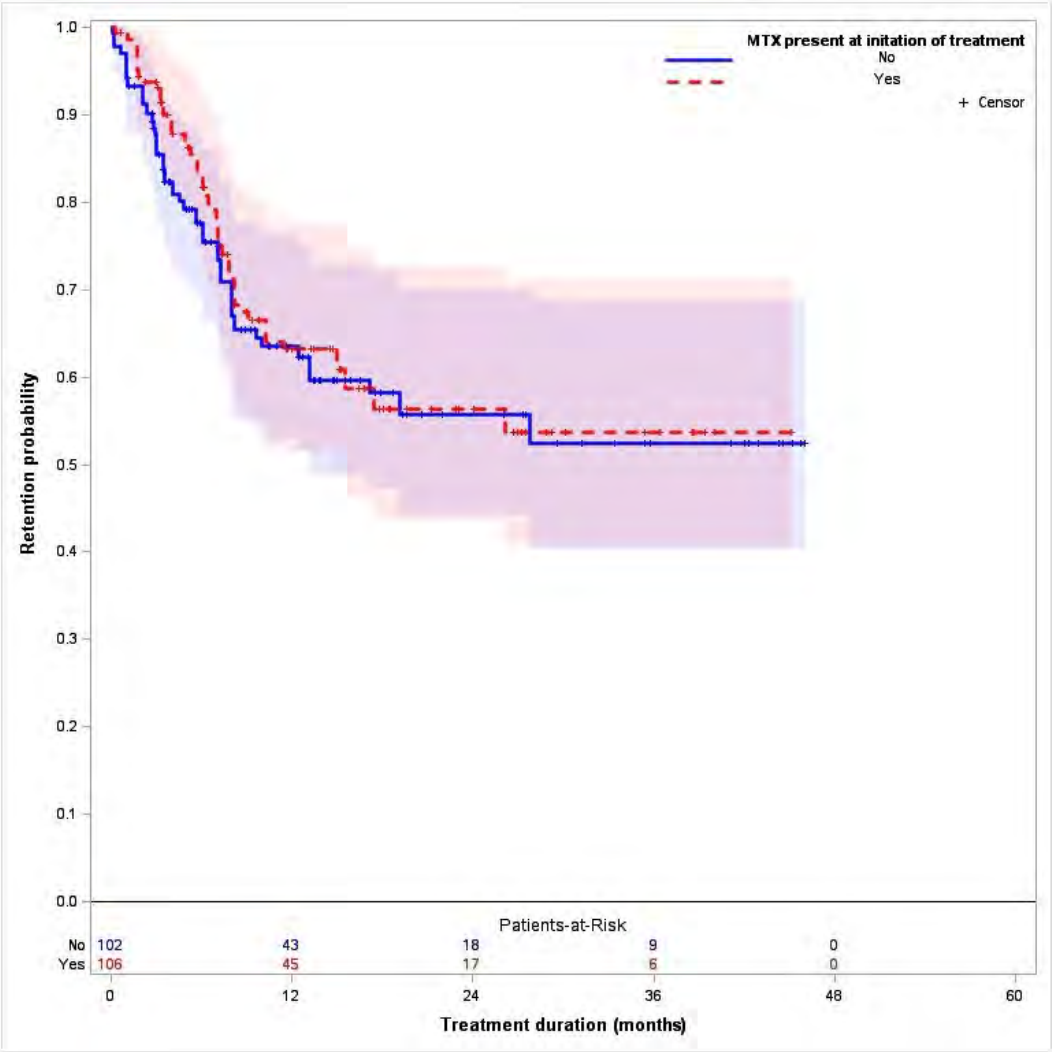

Figure 1. Drug discontinuation TNFi and TOFA; with and without MTX B. TOFA

Over a mean of 17.3 month follow-up, discontinuation was reported in 75 (36%) and 103 (29%) of all TOFA and TNFi patients, respectively. After adjusting for propensity score, patients treated with TNFi and MTX remained on treatment longer than those treated without MTX (Logrank p=0.002) (Figure 1A) while there was no significant difference in TOFA discontinuation in patients with and without MTX (Logrank p=0.31) (Figure 1B).

Conclusion: In this real world data study, we found that TOFA retention is similar in patients with and without MTX, while patients treated with TNFi and MTX remained on treatment longer than those treated without MTX. Merging data with other RA registries in Canada is proposed to increase study power and to provide more robust results.

Disclosure: M. Movahedi, None; **A. Cesta**, None; **X. Li**, None; **E. Keystone**, AbbVie, 2, 5, 8, Celltrion, 2, 5, 8, Eli Lilly, 2, 5, 8, Pfizer Inc, 2, 5, 8, Merck, 2, 5, 8, Sandoz, 2, 5, 8, Samsung Bioepsis, 2, 5, 8, Myriad Autoimmune, 2, 5, 8, Purapharm, 2, 5, 8, Janssen, 2, 5, 8, Sanofi-Genzyme, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, F. Hoffman-La Roche Ltd., 2, 5, 8, Genentech, 2, 5, 8, Gilead, 2, 5, 8, UCB, 2, 5, 8; **C. Bombardier**, CIHR, 2, MOHLTC, 2, Abbvie, 2, Amgen, 2, Janssen, 2, Medexus, 2, Merck, 2, 5, Novartis, 2, Pfizer, 2.

Abstract Number: 0809

Comparative Effectiveness of Intravenous Golimumab vs Dose-Escalated Infliximab in a Real World Population of Rheumatoid Arthritis Patients: 52-Week Data from the AWARE Study

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: AWARE (Comparative and Pragmatic Study of Golimumab IV Versus Infliximab in Rheumatoid Arthritis) is a Phase 4, prospective, noninterventional, observational, multicenter (88 sites), 3-year US study providing real-world assessment of intravenous golimumab (GLM) and infliximab (IFX) in patients with rheumatoid arthritis. Treatment decisions, including prescribed dose and dosing interval, are made by the treating rheumatologists. This analysis of 52-week results from AWARE explored patterns of dose escalation among IFX patients and compared changes in Clinical Disease Activity Index (CDAI), comparing IFX and GLM.

Table. Change from Baseline in CDAI Among Bionaïve Patients at Month 6 and Month 12 for GLM, Dose-Escalated IFX, and Non-Dose Escalated IFX – Comparison of Change in CDAI of Imputed Propensity Balanced vs. Observed Completer Analyses

Imputed and Propensity Balanced Analysis				Observed Completer Analysis			
	Baseline CDAI	Change from Baseline			Baseline CDAI	Change from Baseline	
	Mean (SD)	Month 6 (IPTW Mean Change	Month 12 IPTW Mean Change		Mean (SD)	Month 6 Mean (SD)	Month 12 Mean (SD)
GLM	n=215	n=215	n=215	GLM	n=110	n=97	n=110
	30.27 (14.91)	-10.73	-11.00		29.06 (14.43)	-15.72 (13.43)	-15.50 (13.78)
DE IFX	n=172	n=172	n=172	DE IFX	n=106	n=92	n=106
	31.19 (14.88)	-10.39	-10.66		31.92 (14.32)	-13.39 (13.85)	-13.50 (14.28)
Non-DE IFX	n=50	n=50	n=50	Non-DE IFX	n=32	n=27	n=32
	29.19 (15.64)	-8.06	-8.65		22.38 (12.86)	-10.20 (9.62)	-11.08 (15.21)

CDAI=clinical disease activity index, DE=dose escalation, GLM=IV golimumab, IFX=infliximab, IPTW=Inverse probability of treatment weighted, SD=standard deviation.
Change from baseline in CDAI is based on imputed data using Last Observation Carried Forward for missing data and/or treatment failure rules. Mean changes in CDAI were controlled for baseline values using inverse probability of treatment weighted (IPTW) propensity score. DE (observed completer analysis) = Any patient with at least one normalized prescribed dose > baseline dose and the first dose escalation date was at least 30 days prior to CDAI collection date at Month 12.

Methods: AWARE enrolled patients initiating GLM or IFX treatment. Prescribed dose was recorded at the time of infusion. IFX patients had dose-escalation when ≥1 normalized prescribed dose exceeded the baseline dose. Normalized prescribed dose = ([prescribed dose] x [scheduled time interval] / [actual time interval]). CDAI was determined at baseline and Months 3, 6, and 12. See Table for statistical methods.

Results: Baseline demographics were generally similar between 685 GLM and 585 IFX patients (including 425 dose-escalated IFX patients), although mean ± SD disease duration was 9.20 ± 9.97 years for GLM and 6.87 ± 9.28 years for dose-escalated IFX patients. Among bionaïve and non-bionaïve GLM patients with an imputed CDAI measure, the mean prescribed dose was 2.0 mg/kg from infusion 1 through 9. The mean normalized prescribed dose among bionaïve dose-escalated IFX patients with CDAI data as 3.25 mg/kg and increased at each infusion through infusion 9 (5.14 mg/kg). The mean normalized prescribed dose among non-bionaïve dose-escalated IFX patients with CDAI data was 3.29 mg/kg and increased at each infusion through infusion 9 (5.48 mg/kg). Based on the definition of normalized dose, 75.9% of all IFX patients were dose-escalated (72.4% of bionaïve IFX and 78.7% of non-bionaïve IFX patients). The percent of bionaïve IFX patients prescribed at least 1 dose ≥8 mg/kg increased with each infusion through infusion 12. At the 10^{th} and 12^{th} infusions, respectively, 15.1% (39/258) and 19.1% (36/188) of IFX patients had received at least 1 IFX dose ≥8 mg/kg. Mean changes from baseline in CDAI for GLM, dose-escalated IFX, and non-dose-escalated IFX patients at Months 6 and 12 are shown in the Table.

Conclusion: The majority of IFX patients were dose-escalated, evident in the increasing mean normalized dose and the proportion of patients prescribed at least 1 IFX dose ≥8 mg/kg. The mean changes from baseline in CDAI scores were similar between GLM patients and dose-escalated IFX patients, although numerically lower for non-dose-escalated IFX patients.

Disclosure: S. Schwartzman, Janssen, 5, 8, AbbVie, 5, 8, Genentech, 8, Eli Lilly, 5, 8, Novartis, 5, 8, Pfizer, 1, 8, UCB, 5, 8, Amgen, 1, Boston Scientific, 1, Gilead, 1, 5, Medtronic, 1, Myriad, 5, 6, National Psoriasis Foundation, 6; **S. Kafka**, Janssen Scientific Affairs, LLC, 1, 3; **D. Conaway**, Amgen, 1, Janssen, 1, 2, 3, Pfizer, 1; **A. Broadwell**, Janssen, 1, 2, 3, Amgen, 1, 2, Novartis, 1, UCB, 1, Pfizer, 1, Sanofi, 1, GSK, 1, Eli Lilly, 1, 2, GSK, 1, Sandoz, 1, Radius, 1, Mallinckrodt, 1, Celgene, 1; **S. Black**, Janssen Scientific Affairs, LLC, 1, 3; **S. Xu**, Janssen Research & Development, LLC, 1, 2; **W. Langholff**, Janssen Research & Development, LLC, 1, 2; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5.

Abstract Number: 0810

Long Term Remission Rates from a Biologic Clinic: 12 Year Real World Data

Kieran Murray[1], Matthew Turk[2], Yousef Alammari[2], Francis Young[3], Phil Gallagher[4], Tajvur Saber[5], Sinead Maguire[6], Finbar O'Shea[6], Ursula Fearon[7] and Douglas Veale[8], [1]Saint Vincent's University Hospital, Dublin 4, Dublin, Ireland, [2]Saint Vincent's University Hospital, Dublin 4, Ireland, [3]Saint Vincent's University Hospital, Dublin 4, [4]St Vincents University Hospital, UCD, Dublin, Ireland, [5]Peshawar Rheumatology Clinic, Dabgari Garden, Northern Areas, Pakistan, [6]St James' Hospital, Dublin, Ireland, [7]Molecular Rheumatology, Trinity College Dublin, Dublin, Dublin, Ireland, [8]EULAR Centre for Arthritis and Rheumatic Diseases, St Vincents University Hospital, UCD, Dublin, Dublin, Ireland

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

	RA (n=274)	PsA (n=129)	p
Age	55±11.9	44.8±12.2	<0.001
Female	207 (75.5%)	69 (53.5%)	<0.001
Disease Duration (years)	9 (0-51)	8 (0-40)	0.030
Highest level of education			<0.001
Primary School	70 (25.5%)	8 (8.2%)	0.003
Secondary School	120 (48.8%)	31 (31.6%)	0.004
University	56 (22.6%)	59 (60.2%)	<0.001
Employment			0.014
Employed	37 (66.1%)	31 (91.2%)	0.008
Unemployed	8 (14.3%)	1 (2.9%)	NS
Student	0	1 (2.9%)	NS
Other	11 (19.6%)	1 (2.9%)	0.027
Hours worked (weekly)	37.2 (11.7)	41.1 (9.1)	NS
Smoking status			NS
Never	89 (35.6%)	50 (45.5%)	NS
Ex	94 (37.1%)	35 (31.8%)	NS
Current	67 (26.8%)	25 (22.7%)	NS
Alcohol (units per week)	2 (0-20)	4 (0-40)	0.033
HAQ	1.3 (0.64)	0.89 (0.64)	<0.001
Early morning stiffness (minutes)	30 (0-1440)	30 (0-1440)	NS
RF positive	195 (77.1%)	2 (2.2%)	<0.001
Anti-CCP positive	31 (79.5%)	0 (0%)	<0.001
Erosions	90 (47.1%)	28 (31.5%)	0.013

Table 1. Baseline demographics

Background/Purpose: Biologic therapies are widely used and greatly improve outcomes in RA and PsA. Yet, our ability to predict long-term remission and persistence remains limited. This study explores predictors of remission and persistence in patients 12 years after commencing biologic therapy.

Methods: RA (ACR criteria) and PsA (CASPAR criteria) patients were prospectively enrolled into a specific biologic clinic. Outcomes at the beginning of biologic therapy, at one year and at 12 years were reviewed. Predictors of biologic persistence and remission by EULAR criteria (DAS28-CRP < 2.6) were identified with univariate and multivariate analysis.

Results: RA patients tended to be older, predominantly female and have more severe disease at baseline (Table 1). When looking at disease activity, both groups showed significant clinical improvement (Table 2). DAS28-CRP remission was 91.3% in PsA and 60.6% in RA patients at 12 years (Figure 1). PsA patients had significantly better outcomes than RA patients, despite lower levels of methotrexate use. Multivariate analysis showed 12-year initial biologic persistence [OR 4.98 (95% CI 1.83-13.56)] and male gender [OR 4.48 (95% CI 1.25-16.01)] were predictors of remission. When looking for predictors of long-term persistence, one-year persistence [OR 4.28 (1.28-14.38)] and one-year low disease activity [OR 3.90 (95% CI 1.05-14.53)] were most predictive.

Conclusion: This is the first study to show better long term (12 year) outcomes with biologic therapy in PsA compared to RA. Persistence with initial biologic agent was high and predicted outcome. Persistence and low disease activity at one year predicted long term biologic persistence. Interestingly, PsA patients had higher levels of employment, educational attainment, alcohol use and long term remission rates.

	Baseline			1 Year Review (1.04±0.15 years)			Most Recent Review (11.76±2.69 years)		
	RA (n=274)	PsA (n=129)	p	RA (n=203)	PsA (n=96)	p	RA (n=179	PsA (n=87)	p
Biologic									
Adalimumab	144 (52.6%)	47 (36.4%)	0.002	76 (44.7%)	27 (31.0%)	0.034	43 (25.6%)	28 (33.3%)	NS
Etanercept	100 (36.5%)	68 (52.7%)	0.002	62 (36.5%)	45 (51.7%)	0.019	48 (28.6%)	30 (35.7%)	NS
Infliximab	18 (6.6%)	14 (10.9%)	NS	13 (7.6%)	11 (12.6%)	NS	3 (1.8%)	8 (9.5%)	0.004
Rituximab	12 (4.4%)	0 (0%)	0.011	4 (2.4%)	0 (0%)	NS	16 (9.5%)	0 (0%)	0.004
Other	0 (0%)	0 (0%)	NS	1 (0.6%)	0 (0%)	NS	24 (14.3%)	8 (9.5%)	NS
None	0 (0%)	0 (0%)	NS	14 (5.1%)	4 (3.1%)	NS	34 (20.2%)	10 (11.9%)	NS
Biologic Persistence	n/a	n/a	n/a	136 (49.6%)	76 (58.9%)	NS	66 (38.2%)	45 (52.3%)	NS
Any csDMARD	193 (70.4%)	41 (32%)	<0.001	111 (70.8%)	21 (24.4%)	<0.001	108 (64.3%)	28 (32.9%)	<0.001
Methotrexate	176 (64.2%)	35 (27.3%)	<0.001	108 (64.8%)	21 (24.4%)	<0.001	72 (42.2%)	22 (25.9%)	0.008
Patient global VAS(mm)	60 (0-100)	50 (0-100)	NS	30 (0-100)	20 (0-90)	<0.001	50 (0-100)	5 (0-100)	<0.001
TJC28	9 (0-28)	6 (0-28)	<0.001	1 (0-28)	0 (0-20)	<0.001	0 (0-19)	0 (0-2)	0.019
SJC28	9 (0-28)	5 (0-28)	<0.001	1 (0-28)	0 (0-25)	<0.001	0 (0-15)	0 (0-2)	<0.001
CRP	16 (2-158)	9 (0-108)	<0.001	4 (1-138)	4 (0-41)	0.034	3 (1-65)	2 (1-46)	<0.001
Disease Activity									
Remission	2 (0.8%)	6 (5.1%)	0.013	57 (34.5%)	44 (60.3%)	<0.001	63 (60.6%)	21 (47.7%)	0.005
Low Activity	9 (3.5%)	13 (11.1%)	0.003	91 (55.2%)	60 (55.2%)	<0.001	83 (79.8%)	22 (50%)	NS
Moderate Activity	89 (34.4%)	65 (55.6%)	<0.001	58 (35.2%)	10 (13.7%)	0.001	20 (19.2%)	1 (2.2%)	0.012
High Activity	160 (61.8%)	39 (33.3%)	NS	16 (9.7%)	3 (4.1%)	NS	1 (1%)	0 (0%)	NS
Progression of erosions	N/A	N/A	N/A	36 (28.1%)	5 (8.6%)	0.003	51 (31.9%)	12 (15%)	0.005

Table 2. Medications and outcomes

Figure 1A

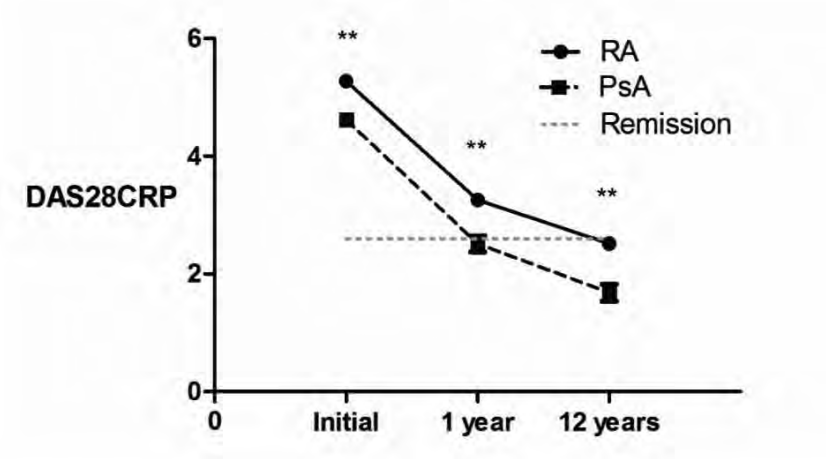

Figure 1B

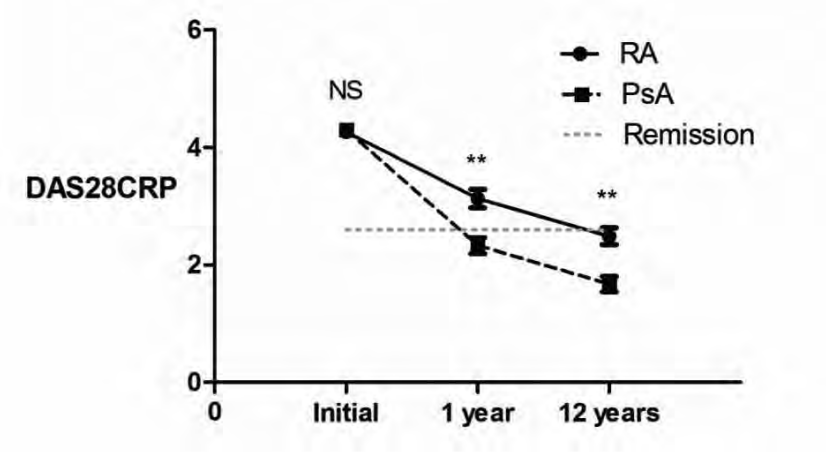

Figure 1. A comparison of mean DAS28-CRP by diagnosis in all patients (Figure 1A) and a cohort matched for baseline disease activity (moderate disease activity) (Figure 1B) (**p<0.001)

Disclosure: K. Murray, None; **M. Turk**, None; **Y. Alammari**, None; **F. Young**, None; **P. Gallagher**, None; **T. Saber**, None; **S. Maguire**, None; **F. O'Shea**, None; **U. Fearon**, None; **D. Veale**, AbbVie, 2, Health Beacon, 1, Janssen, 2, 8, Pfizer, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5.

Abstract Number: 0811

Long-term Opioid Use in Patients with Rheumatoid Arthritis Treated with Sarilumab

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

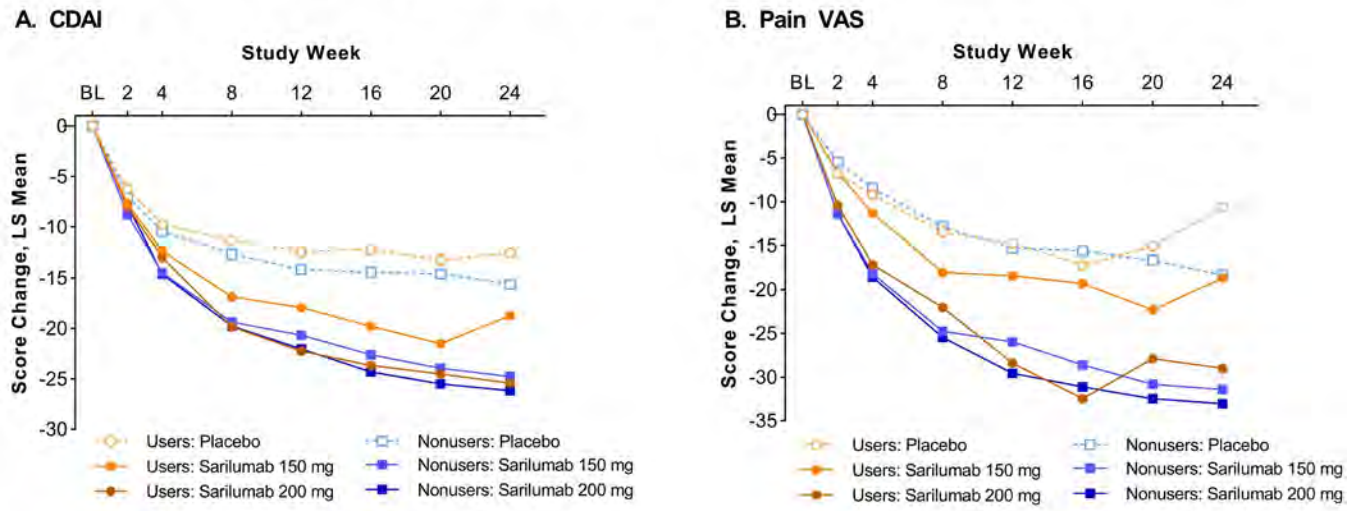
Session Time: 9:00AM–11:00AM

Background/Purpose: Prescription opioids are routinely used in patients with RA. However, use of opioids should be minimized to prevent abuse and addiction. Chronic opioid use doubled from 2002 to 2015 among patients with RA, with severe pain being a strong predictor of use (Lee YC, et al. *Arthritis Rheumatol.* 2019;71:670-677). This post hoc analysis investigated the association between the effect of treatment with sarilumab, an IL-6 receptor antagonist, and opioid use in patients with RA using clinical trial data.

Methods: Data were collected from placebo-controlled, randomized controlled trials (RCTs) MOBILITY (NCT01061736) and TARGET (NCT01709578) (pooled analysis), and from the adalimumab-controlled RCT MONARCH (NCT02332590). Patients received sarilumab (doses of 150 mg or 200 mg) or placebo once every 2 weeks (q2w) in MOBILITY and TARGET, and sarilumab 200 mg or adalimumab 40 mg q2w in MONARCH. Patients could then enroll in the open-label extension (OLE) studies wherein they received sarilumab 200 mg q2w. Change in concomitant medications, including opioids, was not permitted in the RCTs, but was permitted in the OLEs. Outcomes included evaluation of baseline characteristics associated with higher opioid use, efficacy in both RCTs and OLEs based on opioid use, and the rate of opioid discontinuation in OLEs. Data were analyzed using descriptive statistics and logistic regression.

Results: At baseline, 13% (234/1743) of patients in MOBILITY and TARGET, and 10% (38/369) of patients in MONARCH used opioids. Baseline characteristics were consistent among patients with higher opioid use across all trials. Compared with opioid nonusers, opioid users across all trials had higher mean BMI (MOBILITY-TARGET: 32 vs 28 kg/m^2; MONARCH: 30 vs 27 kg/m^2), longer mean disease duration (MOBILITY-TARGET: 12 vs 10 years; MONARCH: 9 vs 7 years), and higher mean Clinical Disease Activity Index score (MOBILITY-TARGET: 46 vs 41; MONARCH: 46 vs 43). In MOBILITY and TARGET, in both opioid users and nonusers, the reduction in disease activity and pain was numerically greater in sarilumab-treated patients versus placebo, but opioid users treated with sarilumab 200 mg showed

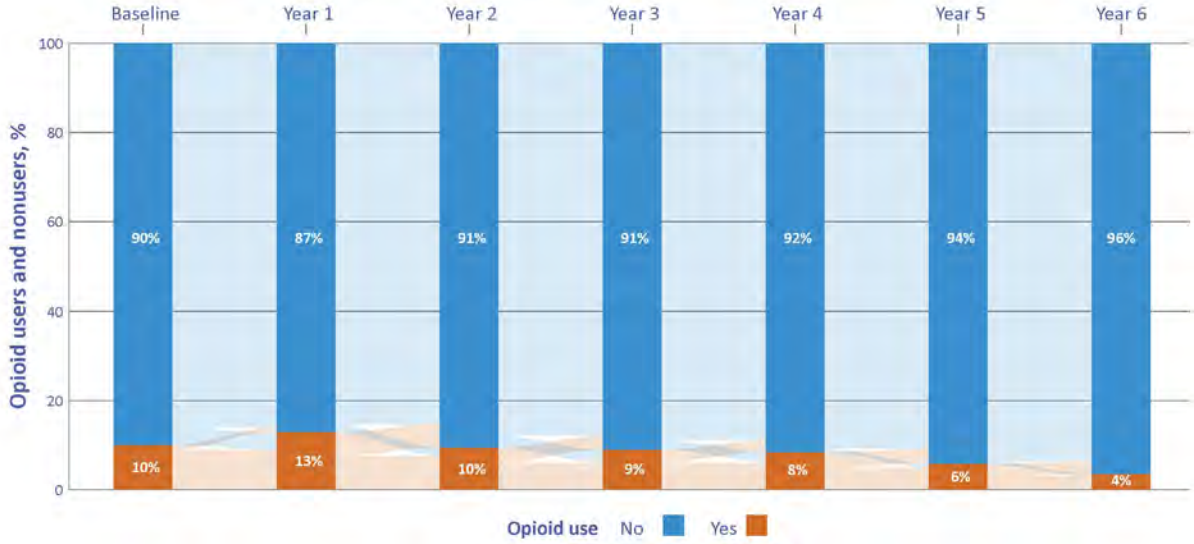
Figure 1. Score changes in CDAI (A) and pain VAS (B) in opioid users and nonusers in the RCTs MOBILITYand TARGET (pooled analysis)



CDAI=Clinical Disease Activity Index; RCT=randomized controlled trial; VAS=visual analog scale.

Figure 1

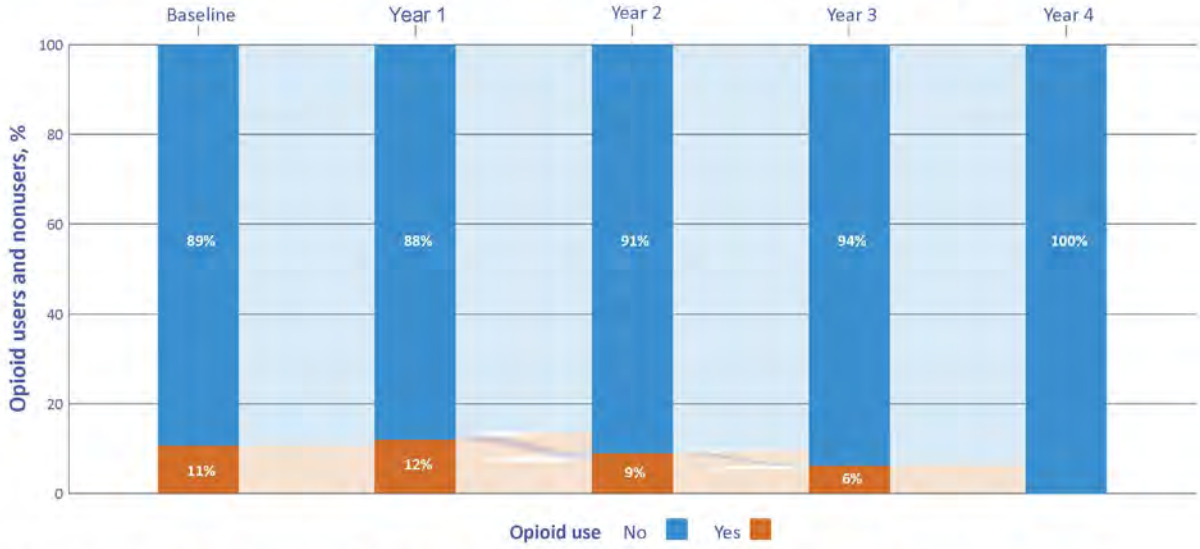
Figure 2: Prevalence of opioid use in the MOBILITY and TARGET OLE studies (pooled analysis, N=1353, ITT)



The bands between the bars indicate the % of patients who switched between opioid users and nonusers.
ITT=intent to treat; OLE=open-label extension.

Figure 2

Figure 3: Prevalence of opioid use in the MONARCH OLE study (N=320, ITT)



The bands between the bars indicate the % of patients who switched between opioid users and nonusers.
ITT=intent to treat; OLE=open-label extension.

Figure 3

greater improvements than those treated with 150 mg (Figure 1). In MONARCH, sarilumab 200 mg was numerically superior to adalimumab 40 mg in reducing both disease activity and pain, regardless of opioid use. After 4 to 6 years of treatment with sarilumab 200 mg in the OLE, efficacy was maintained in patients who were treated with sarilumab in the RCTs, and improved among patients treated with placebo in the RCTs, with those treated with placebo during the RCTs achieving approximately the same level of disease activity as those treated with sarilumab (data not shown). In MOBILITY-TARGET, the proportion of patients using opioids decreased from 10% at OLE baseline to 4% by Year 6 (Figure 2); in MONARCH, the proportion of opioid users decreased from 11% at OLE baseline to 0 at Year 4 (Figure 3).

Conclusion: In this post hoc analysis of long-term data in patients with RA, the efficacy of sarilumab was maintained in both opioid users and nonusers. In addition, the use of opioids decreased over time in patients treated with sarilumab.

Disclosure: J. Pope, AbbVie, 2, 5, Amgen, 5, 8, Lilly, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 5, 8, Sandoz, 5, 8, Roche, 2, 5, 8, Pfizer, 5, 8, Novartis, 5, 8, Merck, 2, 5, 8, Janssen, 5, 8, Gilead Sciences, Inc., 2, 5, BMS, 2, 5, 8, Abbott, 5, Actelion, 5, AstraZeneca, 5, Bayer, 5, Boehringer Ingelheim, 5, EICOS, 5, Emerald, 5, GlaxoSmithKline, 5, Medexus, 5, Seattle Genetics, 2; **A. Praestgaard**, Sanofi, 3; **H. van Hoogstraten**, Sanofi, 1, 3, 4; **M. Iglesias-Rodriguez**, Sanofi, 3; **S. Perrot**, Pfizer, 8, Grunenthal, 8, MSD, 8, UPSA, 8, Menarini, 8; **Y. Lee**, Highland Instruments, Inc., 1, 2, Pfizer, 1, 2, Cigna-Express Scripts, 1; **A. Sebba**, Eli Lilly and Company, 5, 8; **E. Choy**, Abbvie, 2, 8, Amgen, 2, 8, AstraZeneca, 2, 8, Biogen, 2, 8, Bio-Cancer, 2, 8, Boehringer Ingelheim, 2, 8, Bristol-Myers Squibb, 2, 8, Celgene, 2, 8, Chugai Pharma, 2, 8, Eli Lilly, 2, 8, Ferring Pharmaceuticals, 2, 8, GlaxoSmithKline, 2, 8, Janssen, 2, 8, Novartis, 2, 8, Novimmune, 2, 8, ObsEva, 2, 8, Pfizer, 2, 8, R-Pharm, 2, 8, Roche, 2, 8, SynAct Pharma, 2, 8, Tonix, 2, 8, UCB, 2, 8, Synovate, 2, 8, Sanofi, 2, 8, Regeneron, 2, 8, Napp, 2, 8, Hospira, 2, 8, Merck Sharp & Dohme, 2, 8.

Abstract Number: 0812

Real-World Utilization of Infliximab (IFX) and Its Biosimilars in Patients (Pts) with Rheumatoid Arthritis (RA) Since the First Biosimilar Approval in the US

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Biologics have revolutionized the treatment of autoimmune diseases, though costs and payer restrictions have limited who are treated and when these agents are used. Potentially lower cost biosimilars have been developed and FDA-approved, although only 2 TNF inhibitors have been made available to pts. Here, we describe utilization and characteristics of pts receiving IFX and its biosimilars in US community rheumatology practices.

Methods: Electronic medical records data from the American Rheumatology Network (ARN) - Trio Health Rheumatology registry was used for the study. The ARN is a physician-led and owned organization with over 200 practicing rheumatologists that supports some of the largest independent practices in the US. Pts with RA diagnosis who initiat-

P-values <0.05 are shown	A: IFX N=1972	B: Infliximab-dyyb n=574	C: Infliximab-abda n=260	P-value A vs B	P-value A vs C	P-value B vs C
Age, mean (SD)	62.4 (14.1)	63.4 (13.2)	63.7 (13.5)			
Follow-up - months, mean (SD)	19.5 (9.3)	13.1 (8.7)	6.3 (3.8)	<0.001	<0.001	<0.001
Female gender, n (%)	1525 (77)	454 (79)	211 (81)			
White race, n (%)	1064 (54)	289 (50)	128 (49)			
Black or African American	60 (3)	31 (5)	10 (4)	0.007		
Other race	27 (1)	7 (1)	7 (3)			
Unknown race	821 (42)	247 (43)	115 (44)			
Commercial payer, n (%)	943 (48)	189 (33)	59 (23)		<0.001	0.003
Medicare	857 (43)	284 (49)	123 (47)			
Medicare Advantage	62 (3)	15 (3)	11 (4)			
Medicaid	82 (4)	47 (8)	63 (24)		<0.001	<0.001
Other payer	23 (1)	39 (7)	4 (2)			
Unknown payer	5 (0)	189 (33)	59 (23)			0.001
South region, n (%)	671 (34)	341 (59)	46 (18)	<0.001	<0.001	<0.001
Central region	280 (14)	5 (1)	7 (3)	<0.001	<0.001	0.041
West region	1021 (52)	228 (40)	207 (80)	<0.001	<0.001	<0.001
Treatment characteristics						
Prior regimens, mean (SD)	1.4 (1.8)	2.2 (1.9)	2 (1.6)	<0.001	<0.001	0.006
On steroids, n (%)	845 (43)	238 (41)	93 (36)		0.030	
On methotrexate, n (%)	843 (43)	265 (46)	116 (45)			
Baseline Rapid3, mean (SD)	4.1 (2.3) n=562	3.9 (2.4) n=294	3.2 (2.6) n=72		0.005	0.040
Baseline CDAI	12.2 (12.2) n=494	17.4 (12.5) n=324	16.1 (12.4) n=184	<0.001	<0.001	
Baseline DAS28	2.8 (1.4) n=77	4.2 (1.4) n=12	4.5 (1.7) n=20	0.003	<0.001	
Baseline remission or low disease activity (by Rapid3, CDAI or DAS28)	591 (66) n=889	180 (43) n=417	87 (43) n=204	<0.001	<0.001	
Outcomes at 6 months						
CDAI improvement at 6 months	-1.6 (7.9) n=330	-4.9 (11.2) n=185	-4.9 (12.7) n=60	<0.001	0.007	
Rapid 3 improvement at 6 months	-0.4 (2) n=294	-0.4 (2) n=151	-0.6 (1.4) n=15			
DAS28 improvement at 6 months	0.3 (1.1) n=56	-0.7 (1.6) n=6	-0.6 (0.8) n=5	0.048		
6-Month measurement remission or low disease activity	761 (75) n=1021	169 (60) n=284	46 (56) n=82	<0.001	<0.001	

Table 1. Demographic and clinical characteristics

Treatment group	Mean			Median			Log Rank p-value		
	Estimate	95% CI		Estimate	95% CI				
		Lower	Upper		Lower	Upper	vs Infliximab-abda	vs Infliximab-dyyb	vs Infliximab
Infliximab-abda	13.1	11.8	14.4	median not reached			vs Infliximab-abda	vs Infliximab-dyyb	vs Infliximab
Infliximab-dyyb	15.4	14.0	16.7	10.4	8.2	12.6	N/A	0.633	0.695
Infliximab	17.4	16.6	18.2	12.0	11.1	12.9	0.633	N/A	0.296

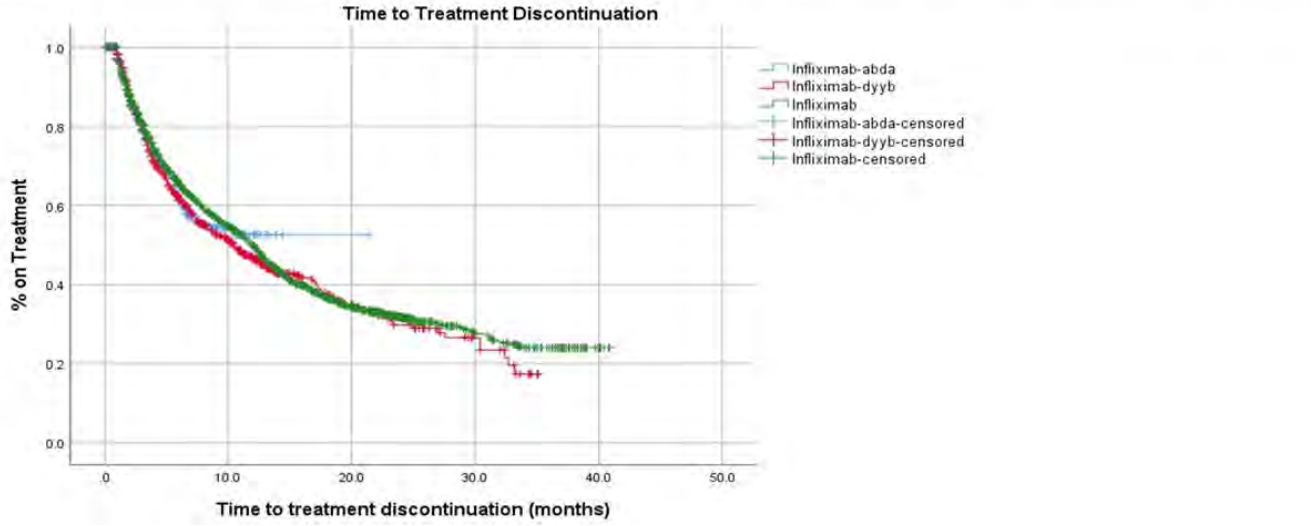

Figure 1. Time to Treatment Discontinuation (months)

	P-value	Adjusted Odds Ratio (aOR)	95% CI	
			Lower	Upper
Baseline disease activity moderate or high vs remission/low	**<0.001**	0.11	0.07	0.15
Age 60 and older vs <60	0.267	1.29	0.82	2.02
On corticosteroids	**<0.001**	0.50	0.35	0.71
Payer	0.329			
Medicare vs commercial	0.569	0.87	0.55	1.39
Medicaid vs commercial	0.109	0.54	0.25	1.15
Other payer vs commercial	0.274	0.63	0.27	1.44
Infliximab group	0.883			
Infliximab-abda vs infliximab	0.952	1.02	0.54	1.91
Infliximab-dyyb vs infliximab	0.620	1.11	0.74	1.65
Number of prior regimens	0.101	0.93	0.86	1.01
Duration of current therapy (months)	**0.001**	1.04	1.01	1.06

Table 2. Logistic regression results: outcome remission/low disease activity at 6 months since regimen initiation

ed or switched to IFX or biosimilars since December 2016 were selected for analysis. Differences between treatment groups were assessed using t-test for continuous variables and chi-square test for categorical variables. Logistic regression model was used to evaluate outcome remission/low disease activity at 6 mo accounting for demographic and treatment characteristics. Time to treatment discontinuation was assessed using Kaplan-Meier method.

Results: 3156 pts met study criteria; 1972 (62%) were on IFX (775 [39%] as monotherapy) and 1184 (38%) received biosimilars (306 [26%] as monotherapy). Of pts on biosimilars, 350 (30%) switched between different biosimilars or IFX and were removed from the analysis. The remaining 834 pts were treated with infliximab-dyyb (574 [69%]) or infliximab-abda (260 [31%]).

There were no differences by age and gender between IFX and each biosimilar group [Table 1]. Compared to pts on biosimilars, pts receiving IFX had longer follow-up, fewer prior DMARD or biologic regimens, and longer duration of treatment with IFX. Pts on biosimilars were less likely to be commercially insured and more likely to be on Medicaid compared to IFX. IFX pts were more likely to be in remission/low disease activity at treatment initiation and at 6 mo since treatment initiation compared to pts on biosimilars; there were no differences between biosimilar groups. IFX pts had smaller improvement from baseline (BSL) to 6-mo CDAI compared to pts on biosimilars.

Accounting for age, payer, regimen, steroid use, duration of therapy, number of prior regimens, and BSL disease activity status, variables significantly impacting the outcome were BSL disease activity, regimen duration, and use of steroids but not choice of a biologic [Table 2].

Median time to treatment discontinuation was not statistically different among groups [Figure 1].

Conclusion: Among RA pts treated with IFX and its biosimilars there were differences in demographic and BSL clinical characteristics. IFX was used earlier in the treatment journey than biosimilars with higher proportion of pts in remission at BSL and last observation. Time to treatment discontinuation was similar among groups. After accounting

for other pt and treatment characteristics, regimen choice (use of a particular biosimilar vs IFX) was not significantly associated with treatment success at 6 mo since regimen initiation.

Disclosure: S. Helfgott, Abbvie, 5; **J. Radtchenko**, Gilead, 2, ViiV, 2; **N. Soloman**, Horizon, 5, 8, Amgen, 2, 8, Abbvie, 2, 5, 8, UCB, 2, 5, 8, Novartis, 5, 8, Jannsen, 2, 8, Pfizer, 8, Lilly, 2, GSK, 2, 5, 8; **K. Huston**, None; **J. Singh**, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **C. Edgerton**, Sandoz, 5.

Abstract Number: 0813

Treatment Outcomes in Patients with Seropositive versus Seronegative Rheumatoid Arthritis in Czech Registry ATTRA Treated with JAK Inhibitors

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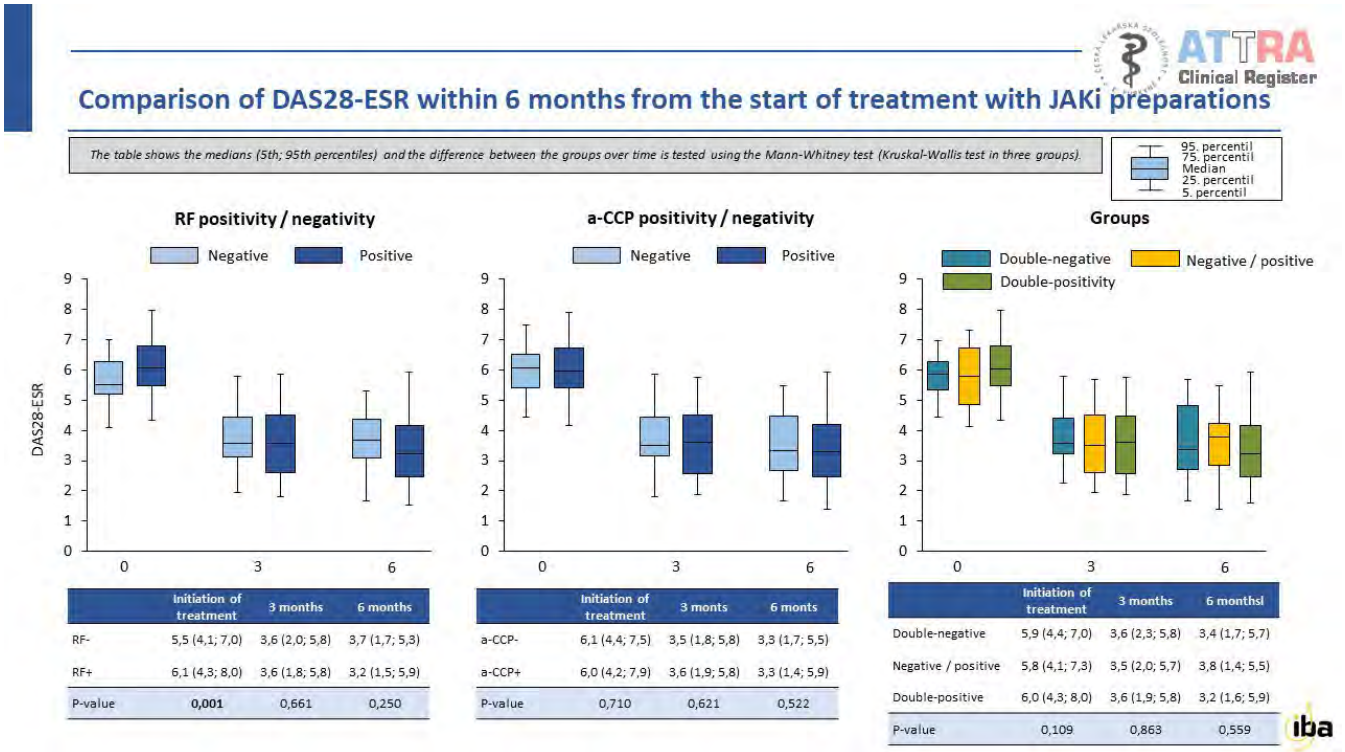
SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM



Background/Purpose: Seropositivity / seronegativity in RA may have influence on response to bDMARDs or tsDMARDs. There is incomplete knowledge of differences in efficacy of JAK inhibitors in different subgroups of patients in real clinical practice. We aimed to compare treatment response between seropositive and seronegative RA patients in the Czech National Registry ATTRA.

Methods: We included patients with moderate to severe RA, who failed in the past MTX or bDMARDs. Primary outcome measure was change(Δ) in DAS28 btw start of therapy and 6 months. Secondary outcomes measures were ΔSDAI and survival on therapy.

Results: We have included 263 patients treated with JAK inhibitors (130 tofacitinib, 133 baricitinib). Mean age at baseline was 55 ± 10 years, disease duration 13 ± 9 years, mean CRP in seropositive group was 25 mg/l and seronegative 21 mg/l ($p = 0,012$), mean DAS 28 ESR was 6.0 in seropositive and 5.6 in seronegative groups ($p < 0.001$). About 60 % patients have concomitant steroids. Concomitant treatment with MTX had 39 % in seronegative and 57 % in seropositive group ($p = 0.028$).

DAS 28 improved in both groups significantly. There were no differences between patients with double positivity (RF, anti CCP), single positivity or double negativity (Figure 1). There were no significant changes in SDAI as well. Adherence to therapy was very good, with no differences in seropositive and seronegative groups (68 % vs. 72 %).

Tolerance on therapy was good with no new signals and no differences between seropositive and seronegative groups.

Conclusion: There were no differences in efficacy of JAK inhibitors between seropositive and seronegative patients in Czech National Registry ATTRA. Double seropositive patients had more severe disease at baseline.

Funding: Supported by MHCR00023728

Disclosure: K. Pavelka, AbbVie, 8, Merck Sharp & Dohme, 8, Bristol-Myers Squibb Company, 8, Roche, 8, Amgen, 8, Pfizer, 8, Novartis, 8, Egis, 8, Biogen, 8, UCB, 8; **Z. Křístková**, None.

Abstract Number: 0814

"I Want to Switch Back": Real-world Experience of Switching Intravenous Abatacept and Tocilizumab to Subcutaneous Injection During the COVID-19 Pandemic

Rishi Gupta[1], Muhammad Shipa[2], Su-Ann Yeoh[2], Pauline Buck[1] and Michael Ehrenstein[2], [1]University College London Hospital, London, United Kingdom, [2]University College London, LONDON, United Kingdom

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: During the COVID-19 pandemic, rapid guidelines by the National Institute for Health and Care Excellence (NICE) in the United Kingdom[1] recommended consideration of switching from intravenous (IV) treat-

ment to subcutaneous (SQ) form to minimise the risk of exposure. The aim of this study is to assess patient-reported outcomes of those who have been switched to SQ form from IV abatacept (ABT) and tocilizumab (TCZ).

Methods: We analysed RA patients at a large rheumatology centre fulfilling the 2010 ACR/EULAR classification criteria who were switched from IV to SQ ABT and TCZ. Patients who have not responded to the SQ form in the past were not switched. We compared Multi-Dimensional Health Assessment Questionnaire (MD-HAQ) scores immediately before and 3 months after the IV to SQ switch. RAPID3 was calculated using three components of MD-HAQ (functional status, pain, and global health). Patients were also asked whether they would prefer their current SQ regimen to continue or whether they would like to revert to IV. Reasons for patient preference to revert to IV were also captured.

Results: 32 patients were switched from IV to SQ [14 (43.7%) ABT and 18 (56.3%) TCZ]. Of the 32 patients who switched, 29 responded to our questionnaires. The majority of patients were in DAS28-ESR clinical remission or low disease activity prior to the switch (mean DAS28-ESR 3.00 for ABT, 2.15 for TCZ).

Unexpectedly, 77% (10/13) in the ABT group and 88% (14/16) in the TCZ group, expressed a preference to return to their IV regimen **(Fig. 1).** In the ABT group, patient preference to revert to IV was primarily due to worsening symptoms of joint pain/stiffness since the switch to SQ (symptom recurrence described in the last 2 days of weekly injection) **(Table 1)**. This, in turn, is associated with a negative impact on function, represented by the statistically significant increase in MD-HAQ functional status score from 3.662 to 4.408 (p= 0.042), with higher values reflecting negative

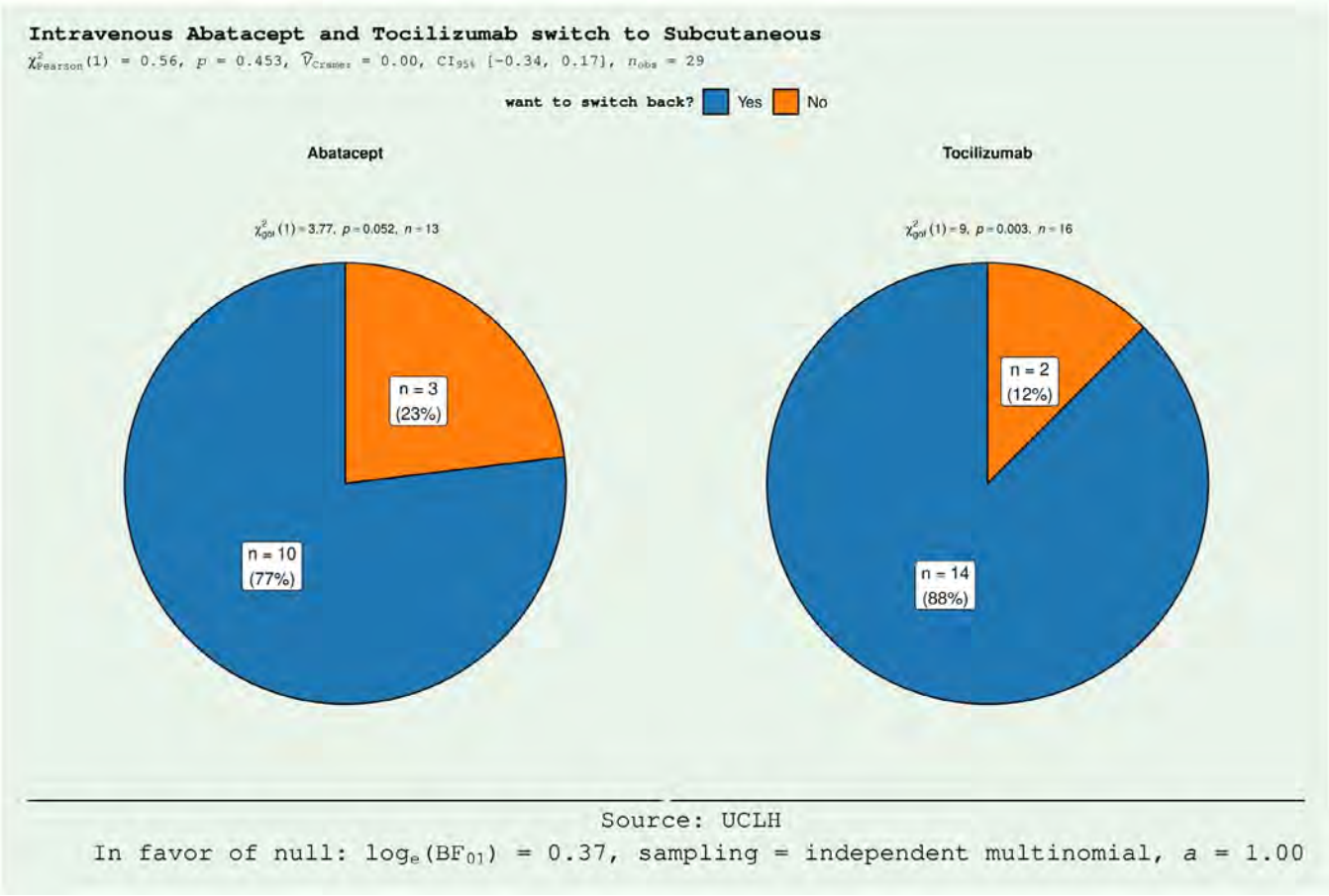


Figure 1. The majority of the patients in the abatacept (ABT) and tocilizumab (TCZ) groups preferred to switch back from subcutaneous (SQ) to intravenous (IV) form. In ABT group, 10/13 wanted to switch back (χ2 3.77, p = 0.052). In the TCZ group, 14/16 would like to switch (χ2 9, p = 0.003).

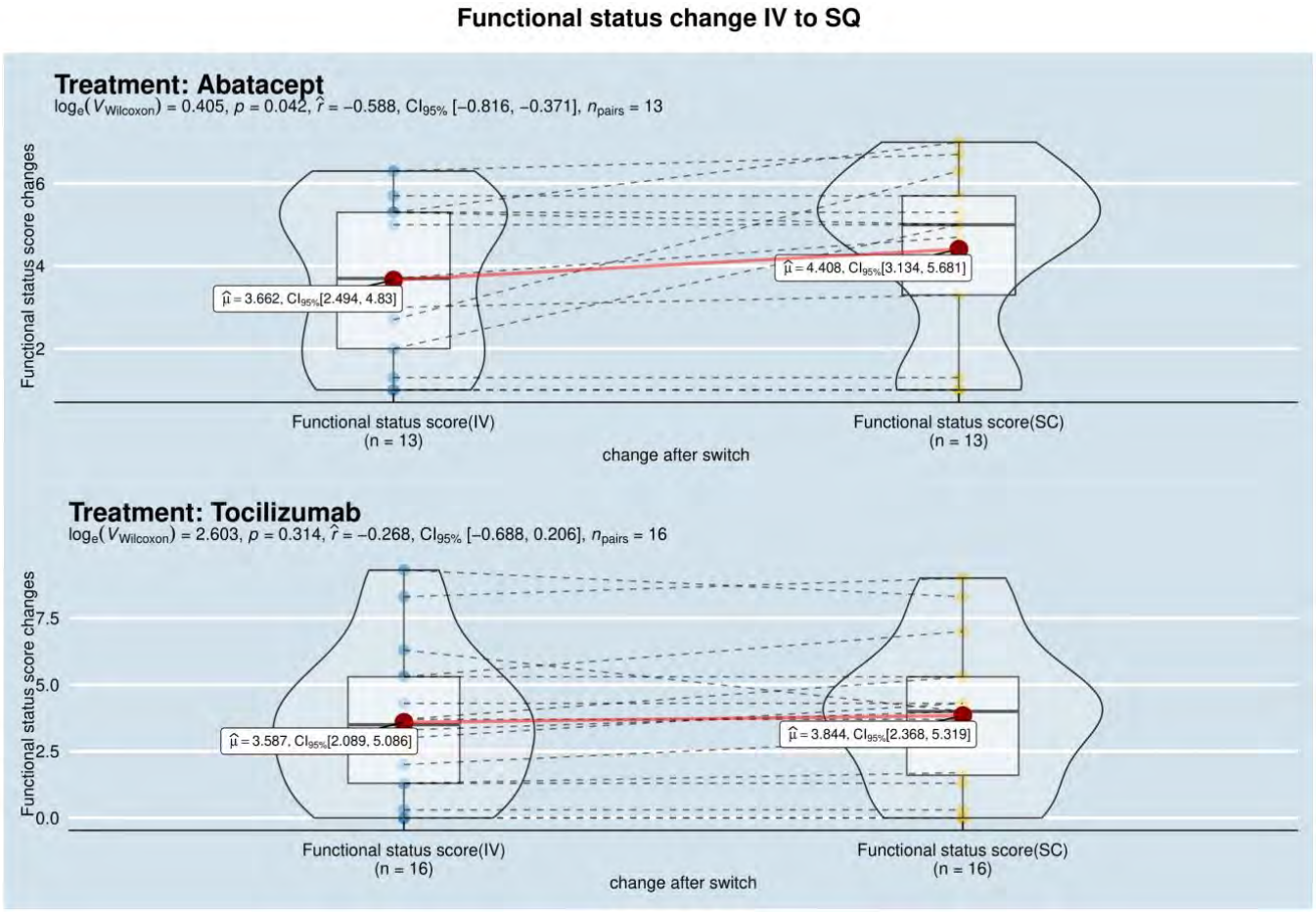


Figure 2. Switching Abatacept (ABT) to subcutaneous (SQ) form, resulted increase in mean score to 4.408 from 3.66 (p = 0.042).

Reason for wanting to switch back from SQ to IV	Abatacept (N = 10), n (%)	Tocilizumab (N = 14), n (%)	p value
Worsening symptoms	6 (60%)	7 (50%)	0.69
Preferred monthly administration over weekly	1 (10%)	2 (14%)	1.00
Preferred seeing healthcare professional in hospital	2 (20%)	5 (36%)	0.65
Preferred not to self-administer own medication	1 (10%)	0 (0%)	0.41

Table 1. Reasons for wanting to switch back from SQ to IV.

patient experiences **(Fig. 2)**. We did not find any significant differences in the other 2 components of MD-HAQ and RAPID3.

In the TCZ group however, although the majority expressed a preference to revert to IV, no statistically significant differences were noted in MD-HAQ and RAPID3. 50% (7/14) preferred to revert to IV due to worsening of symptoms,

whilst 35.7% (5/14) requested to revert to IV as they preferred the face-to-face interaction with a healthcare professional.

Conclusion: This was a small study but nevertheless indicates that the vast majority of RA patients who switched from IV to SQ ABT and TCZ expressed a preference to switch back. For ABT, this decision was associated with worsening of their functional status whereas for TCZ, although we did not find any statistical significant difference in MD-HAQ and RAPID3, the most commonly reported reasons for request to revert to IV were either worsening of symptoms or the benefit of interaction with a healthcare professional with the IV route of administration. These results suggest that IV and SQ formulations should not be considered as equivalent medications for RA.

1. COVID-19 rapid guideline: rheumatological autoimmune, inflammatory and metabolic bone disorders. Published: 3 April 2020 www.nice.org.uk/guidance/ng167.

Disclosure: R. Gupta, None; **M. Shipa**, None; **S. Yeoh**, None; **P. Buck**, None; **M. Ehrenstein**, None.

Abstract Number: 0815

Initial Pharmaceutical Management in a National Cohort of Elderly-Onset Rheumatoid Arthritis Patients

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Methotrexate is the preferred initial drug for treatment of rheumatoid arthritis (RA) per American College of Rheumatology guidelines (2015). People with elderly-onset RA, classified as onset of disease after 60-65 years of age, are frequently undertreated with biologic disease modifying agents (bDMARDs) farther along the course of disease. However, little is known is about the initial management of RA in older patients. Using Medicare data, we examine the pattern in initial drug therapy in elderly onset RA patients.

Methods: We used Medicare claims from the years 2012 - 2016 to identify older adults (>65 years) with RA defined on the basis of a single ICD9/ICD10 claim in hospital claims, two or more ICD9/ICD10 claims in outpatient claims (7 days apart but within 365 days), or single ICD9/ICD10 claim in outpatient claim plus a prescription or outpatient claim for a disease modifying agents (DMARDs). Study subjects were enrolled in Medicare fee-for-service for at least 12 months prior to case ascertainment. We excluded patients with any prior RA claim or DMARD claims in the prior 12 months to establish an incident RA cohort. Measures included baseline demographics and comorbidities, initial DMARDs used after diagnosis of RA along with their initial average daily dose prescribed and average steroids dose used in the first 90 days after first diagnosis.

Results: We identified 99,491 incident cases of RA (see Table 1 for baseline characteristics). The average time from first claim for RA to the first prescription of DMARD was 28.6 days. Conventional DMARDs (cDMARD) were used as an initial drug in 13.9% patients as compared to bDMARDs in 0.3% patients; 45.9% of patients received steroids within the first 3 months. Of all patients starting a cDMARD, hydroxychloroquine (41.04%) and methotrexate (35.72%)

Table 1: Baseline demographics of the incident, older RA cohort

		Incident RA cohort	
		(n=99,441)	(Percent)
Age	65-69	22,002	22.1
	70-74	22,540	22.7
	75-79	20,007	20.1
	80-84	16,476	16.6
	>85	18,416	18.5
Sex	Male	27,349	27.5
	Female	72,092	72.5
Race	Whites	78,383	78.8
	African Americans	9,197	9.3
	Asian/Pacific Islanders	2,197	2.2
	Hispanics	7,914	8
	Others	1,750	1.8
Acute Myocardial Infraction		8,488	8.5%
Ischemic Heart Disease		67,301	67.7%
CHF		47,226	47.5%
Atrial Fibrillation		25,483	25.6%
Stroke or TIA		25,059	25.2%
Hypertension		99,441	100.0%
Hyperlipidemia		87,811	88.3%
Diabetes		50,516	50.8%
Hypothyroid		43,766	44.0%
Cancers	Breast Cancer	8,017	8.1%
	Colorectal Cancer	3,992	4.0%
	Endometrial Cancer	1,493	1.5%
	Lung Cancer	3,060	3.1%
	Prostate Cancer	4,980	5.0%
Chronic Kidney Diease		49,694	50.0%
COPD		44,456	44.7%
Depression		50,289	50.6%
Alzheimers/Related or Senile Dementia		28,208	28.4%
Hip/Pelvic Fracture		8,606	8.7%
Osteoporosis		43,264	43.5%
Chronic Pain/Fatigue		54,099	54.4%

Table 1. Baseline demographics of the incident, older RA cohort

Table 2: Initial DMARD amongst elderly onset RA patients

	Incident RA Cohort	65-69 years	70-74 years	75-79 years	80-84 years	>=85 years
Average time from first diagnosis to 1st DMARD (days)	28.60	31.65	28.47	26.62	27.12	25.09
cDMARDs	13815	4181	3897	2834	1785	1118
Hydroxychloroquine (%)	5670 (41.04)	1786 (42.72)	1577 (40.47)	1168 (41.21)	696 (38.99)	443 (39.62)
Daily Dose (mg)*						
- Mean	350.95	362.1	352.49	349.6	335.47	328.37
- SD	92.82	88.21	90.53	88.09	105.07	103.04
Methotrexate* (%)	4935 (35.72)	1514 (36.21)	1455 (37.34)	1003 (35.39)	619 (34.68)	344 (30.77)
Daily Dose (mg)*						
-Mean	1.91	2.05	1.93	1.82	1.78	1.7
-SD	1.47	1.80	1.25	1.13	1.48	1.49
Sulfasalazine (%)	792 (5.73)	247 (5.91)	221 (5.67)	159 (5.61)	106 (5.94)	59 (5.28)
Daily Dose (mg)						
-Mean	1545.55	1617.52	1580.12	1377.85	1602.14	1465.09
-SD	963.62	663.19	773.63	636.54	1939.99	730.37
Leflunomide (%)	575 (4.16)	157 (3.76)	161 (4.13)	128 (4.52)	77 (4.31)	52 (4.65)
Daily Dose (mg)*						
-Mean	16.07	18.14	15.99	14.9	15.08	14.38
-SD	8.49	11.84	8.52	5.15	5.24	5.13
Minocycline* (%)	1489 (10.77)	368 (8.8)	380 (9.75)	303 (10.69)	244 (13.69)	194 (17.35)
Daily Dose (mg)						
-Mean	169.49	168.07	170.64	167.04	168.16	174.45
-SD	72.5	53.92	109.15	55.77	55.25	53.24
Others	354	109	103	73	43	26
(%)	(2.5)	(2.6)	(2.64)	(2.57)	(2.4)	(2.32)
bDMARDs	330	131	90	66	24	19
Etanercept	64 (19.39)	34 (25.95)	19 (21.11)	NR	NR	NR
Adalimumab	85 (25.76)	32 (24.43)	22 (24.44)	19 (28.79)	NR	NR
Infliximab	85 (25.76)	35 (26.72)	27 (30.00)	14 (21.21)	NR	NR
Certolizumab	15 (4.55)	NR	NR	NR	NR	NR
Golimumab	NR	NR	NR	NR	NR	NR
Abatacept	22 (6.67)	NR	NR	NR	NR	NR
Tocilizumab	11 (3.33)	NR	NR	NR	NR	NR
Tofacitinib	NR	NR	NR	NR	NR	NR
Rituximab	31 (9.39)	NR	NR	12 (18.18)	NR	NR
Steroids within first 3 months	45,612	10,596	11,557	9,727	7,336	6,396
Avg. Daily Dose (mg)*	16.18	17.18	16.41	16.34	14.83	15.38
SD	(35.94)	(18.5)	(16.40)	(19.59)	(15.21)	(85.47)

* denote p<0.05

Table 2 Initial DMARD therapy amongst elderly onset RA patients

were the most common initial cDMARDs. Methotrexate initiation declined with increasing age (36.2% in 65-69-year age group v. 30.77% in >85-year age group). As the age of onset increased, doses of hydroxychloroquine, methotrexate, leflunomide and steroids decreased. Adalimumab and infliximab were the most prescribed bDMARDs.

Conclusion: In a national of elderly-onset RA patients, hydroxychloroquine instead of methotrexate was the preferred initial cDMARD, which could lead to inadequate control of disease. Further, with increasing age, the doses of cDMARDs prescribed reduced which could further contribute to reduced control of early disease.

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Abstract Number: 0816

Treat-to-target Strategy in Patients with Rheumatoid Arthritis in Daily Clinical Practice -still Underused, but Superior to Routine Care: A Propensity Score Matched Analysis from the ATTRA Registry

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Treat-to-target (T2T) is a widely accepted management strategy for RA. It recommends attaining a goal of at least low disease activity (LDA) within 6 months, otherwise the current therapy should be modified. We assessed the compliance with and effectiveness of the T2T principles in real clinical practice using data in the Czech biologics register ATTRA. The ATTRA registry captures more than 95% of patients with RA treated with bDMARDs/tsDMARDs (or Targeted Therapies, TTs) in the Czech Republic (CZ). In CZ, TTs is reimbursed for RA if DAS28 >5.1 despite therapy with csDMARDs. We aimed to investigate whether switching the first-line targeted drug in pts not reaching LDA within the 6 months since baseline leads to a higher probability of meeting LDA at 12-month visit.

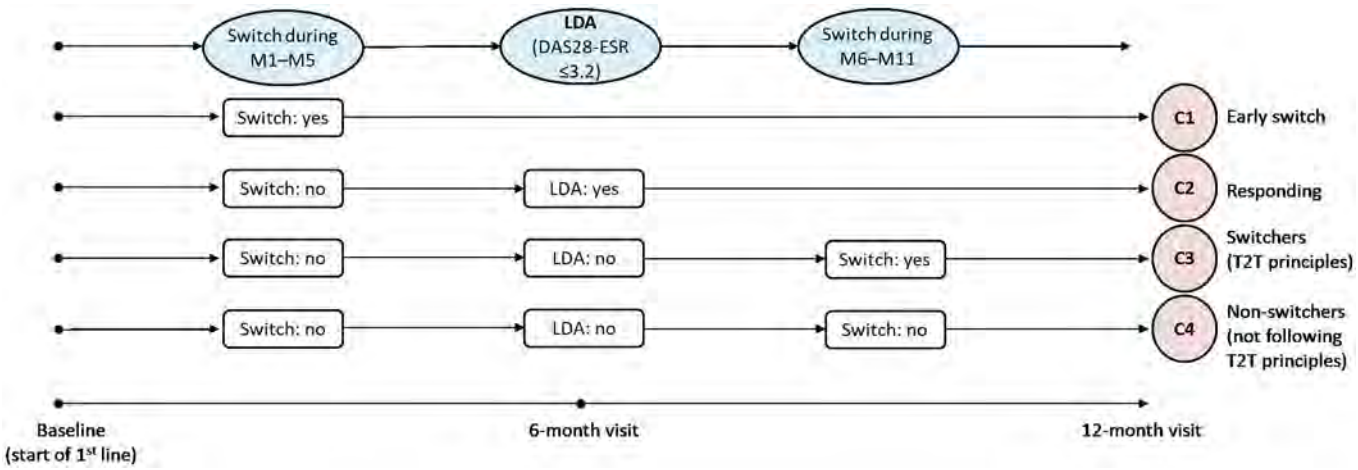

Figure 1. Definition of studied cohorts (C1–C4)

	6 months			12 months		
	C3 (*n*=124)	C4 (*n*=491)	P-value	C3 (*n*=124)	C4 (*n*=491)	P-value
DAS28-ESR (0–10)	5.4 (4.6–6.3)	4.0 (3.5–4.5)	**<0.001**	3.7 (2.6–4.7)	3.7 (3.0–4.4)	0.710
TJC (28 joints)	9.0 (4.0–14.0)	3.0 (2.0–5.0)	**<0.001**	3.0 (1.0–7.0)	2.0 (1.0–5.0)	0.490
SJC (28 joints)	6.0 (2.0–9.5)	2.0 (1.0–4.0)	**<0.001**	2.0 (0.0–4.0)	2.0 (0.0–3.0)	0.498
ESR (mm/h)	28.0 (16.5–46.5)	22.0 (13.0–33.0)	**<0.001**	16.5 (6.5–32.0)	19.0 (11.0–30.5)	0.052
CRP (mg/l)	15.0 (7.9–28.9)	5.7 (2.5–13.7)	**<0.001**	4.7 (1.6–17.0)	5.0 (2.3–11.3)	0.766
SDAI (0–86)	30.2 (19.7–39.5)	13.9 (10.7–18.3)	**<0.001**	13.8 (8.0–20.9)	11.3 (7.7–17.4)	0.093
PTGA (0–100)	61.0 (50.0–75.0)	40.0 (26.0–50.0)	**<0.001**	36.0 (25.0–60.0)	33.0 (20.0–50.0)	**0.044**
MDGA (0–100)	58.0 (40.0–70.0)	30.0 (20.0–40.0)	**<0.001**	25.0 (15.0–45.0)	25.0 (15.0–40.0)	0.812
HAQ-DI (0–3)	1.5 (1.1–1.9)	1.3 (0.9–1.6)	**<0.001**	1.3 (0.9–1.9)	1.3 (0.9–1.6)	0.140
EQ-5D (-0.59–1)	0.2 (0.1–0.7)	0.7 (0.5–0.7)	**<0.001**	0.6 (0.1–0.7)	0.7 (0.5–0.8)	**0.017**
Concomitant csDMARDs	98 (79.0%)	414 (84.3%)	0.159	94 (75.8%)	407 (82.9%)	0.070
Concomitant MTX	79 (63.7%)	341 (69.5%)	0.220	77 (62.1%)	332 (67.6%)	0.245
Concomitant GCs	95 (76.6%)	374 (76.2%)	0.918	92 (74.2%)	370 (75.4%)	0.789

Table 1. Comparison of parameters related to disease activity, quality of life and concomitant therapy between C3 and C4 cohort at the 6-month and 12-month visit (before PS matching)

Methods: We included all adult RA patients starting first-line TT from 1 January 2012 to 31 January 2017 with at least one-year follow-up (FUP), and available DAS28-ESR at baseline, 6- and 12-month visits. We created four mutually exclusive cohorts C1-4 based on 1) switching (and its timing) to another TT within the first year, and 2) reaching LDA (DAS28-ESR ≤ 3.2) at 6-month visit (Fig). The primary outcome was the comparison of odds for reaching LDA at the 12-month visit between patients switching and not switching TT after not reaching LDA at 6 months. Before using logistic regression to estimate the odds ratio, we employed the propensity score (PS) to match patients and make them comparable in characteristics related to disease activity and quality of life at the 6-month visit.

Results: 1275 patients were eligible for the analysis. 62 patients switched within the first 1-5 months of the treatment before evaluating treatment response at the 6-month visit (C1). 598 patients reached LDA within six months of therapy (C2), 124 patients did not reach LDA at 6-month visit and switched to another therapy (C3), and 491 patients continued with the same treatment despite not reaching LDA at the 6-month visit (C4). Clinical cahracteristics of cohorts C3 and C4 at 6 and 12 months are shown in Table 1.75 patients from cohort C3 and 75 patients belonging to a cohort C4 were matched using the PS (Table 2). After PS matching, patients following T2T principle (C3) showed 2.8 (95% CI 1.4–5.8; p=0.005) times increased likelihood of achieving LDA at 12-month visit compared to patients not following T2T strategy (C4).

Conclusion: In daily clinical practice, application of T2T strategy is underused. Switching to another TT after not reaching LDA within the first six months leads to a higher probability of achieving LDA in RA patients at the 12-month visit.

Acknowledgements: Supported by project 00023728 of Ministry of Health, CZ.

	C3 (*n*=75)	C4 (*n*=75)	P-value
Female, *n* (%)*	60 (80.0%)	61 (81.3%)	0.836
Age at diagnosis, years, median (IQR)	45.0 (36.0–53.0)	45.0 (37.0–53.0)	0.678
Age at start of 1st line, years, median (IQR)*	52.0 (45.0–61.0)	55.0 (44.0–61.0)	0.811
Disease duration, years, median (IQR)*	5.0 (2.4–12.7)	5.8 (3.0–13.1)	0.937
RF positive, *n* (%)*	60 (80.0%)	54 (72.0%)	0.251
Presence of comorbidities, *n* (%)*	54 (72.0%)	55 (73.3%)	0.855
Currently smoking, *n* (%)*	21 (28.0%)	21 (28.0%)	1.000
Number of previous csDMARDs, *n* (%)*			
0	2 (2.7%)	0 (0.0%)	0.230
1	16 (21.3%)	15 (20.0%)	
2	20 (26.7%)	28 (37.3%)	
3	17 (22.7%)	20 (26.7%)	
4+	20 (26.7%)	12 (16.0%)	
Glucocorticoids in previous history, *n* (%)*	67 (89.3%)	66 (88.0%)	0.797
Concomitant csDMARDs, *n* (%)*	61 (81.3%)	63 (84.0%)	0.666
Concomitant GCs, *n* (%)*	56 (74.7%)	55 (73.3%)	0.852
DAS28-ESR (0–10), median (IQR)	5.0 (4.2–5.9)	5.0 (4.1–5.7)	0.717
TJC (28 joints), median (IQR)*	8.0 (4.0–12.0)	6.0 (3.0–11.0)	0.677
SJC (28 joints), median (IQR)*	4.0 (2.0–8.0)	4.0 (2.0–7.0)	0.973
ESR (mm/h), median (IQR)*	27.0 (15.0–37.0)	25.0 (12.0–41.0)	0.844
CRP (mg/l), median (IQR)*	15.0 (8.0–22.2)	8.4 (3.5–25.7)	0.090
SDAI (0–86), median (IQR)	25.5 (15.6–34.9)	22.7 (16.1–30.9)	0.531
PTGA (0–100), median (IQR)*	60.0 (40.0–71.0)	50.0 (40.0–71.0)	0.519
MDGA (0–100), median (IQR)	55.0 (35.0–70.0)	45.0 (30.0–60.0)	0.059
HAQ-DI (0–3), median (IQR)*	1.5 (1.1–1.9)	1.5 (1.1–1.9)	0.877
EQ-5D (-0.59–1), median (IQR)[a]	0.2 (0.1–0.7)	0.6 (0.1–0.7)	0.290

Table 2. Description of patients from C3 and C4 cohort at 6-month visit after applying propensity score matching

Disclosure: J. Závada, None; **L. Nekvindova**, None.

Abstract Number: 0817

Uptake of Janus Kinase Inhibitors for Management of Rheumatoid Arthritis in Australia

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: JAK inhibitors (JAKi) are targeted synthetic DMARDs (tsDMARDs) with a different mode of action (MOA) to conventional synthetic and biologic DMARDs (cs and bDMARDs). In Australia the cost of b/tsDMARDs for treatment of RA is subsidized if the patient has high levels of clinical/laboratory disease activity and has not responded to a pre-specified combination of csDMARDs, including methotrexate. Once eligible for subsidy the clinician can prescribe the b/tsDMARD deemed most clinically appropriate until the desired level of disease control has been reached. The aim of this analysis was to determine the patterns of use and reasons for initiation and discontinuation of JAKi in real-world practice in Australia.

Methods: Deidentified clinical data were sourced from the OPAL dataset, which is collected in a custom-built electronic medical record at the time of the consultation. Data from RA patients 18 years and older who commenced a b/tsDMARD between Jan-2007 and Mar-2020 were included in the analysis. The software program Tableau® was used to display data on medication initiation and cessation dates, and reasons for starting and stopping b/tsDMARDs, which is recorded at the time of the decision.

Results: At Mar 2020, there were 47,455 patients with RA in the data set; 27% prescribed b/tsDMARDs. Of patients on treatment at Mar 2020, 51% were receiving a TNF inhibitor (TNFi) and 23% a JAK inhibitor (JAKi), with the remainder receiving tocilizumab, abatacept or rituximab. Of patients who commenced their treatment after JAKi's become available in Sept 2015, 45% were treated with a TNFi, and 32% were treated with a JAKi. Tofacitinib (TOF) has been the most prescribed b/tsDMARD since Sept 2015 with 21% of all initiations; however, since baricitinib (BARI) became available in Sept 2018, it has taken over as the preferred JAKi with 23% of new initiations compared to 14% for TOF. From Sept 2018-Mar 2020 etanercept and adalimumab were the most commonly prescribed first line agents, followed by BARI then TOF; however, BARI was the most prescribed agent in lines 2-6+. The main clinician-listed reason for choice of TOF was MOA in 58%, efficacy compared with alternatives in 21%, mode of administration in 11%, efficacy as monotherapy in 7%, and safety in 1%. BARI was chosen for MOA in 28%, efficacy compared with alternatives in 42%, mode of administration in 19%, efficacy as monotherapy in 8%, and safety in 1%. The main reasons for stopping TOF were lack of efficacy (34%), better alternative (25%), and adverse reaction (14%); those for BARI were lack of efficacy (35%), adverse reaction (25%), and better alternative (12%). Patient non-adherence was listed in 1% and 2% of cessations for TOF and BARI, respectively. 49% of patients discontinuing a JAKi in first line switched to a TNFi in second line, and 34% switched to another JAKi, citing lack of efficacy, adverse reaction, and better alternative as the reason for switching.

Conclusion: There has been significant and sustained uptake of JAKi for the management of RA in Australia. MOA and perceived efficacy rate much higher than mode of administration for clinicians when selecting a JAKi. Clinical outcomes and persistence following JAKi cycling requires further investigation.

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Abstract Number: 0818

Efficacy and Safety of Switching Jakinibs in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Different jakinibs have shown efficacy in rheumatoid arthritis (RA) but in an important proportion of patients, insufficient response leads to therapy withdrawal. The different jakinibs show variable selectivity for the four Jak isoforms (Jak1,2,3 y Tyk2) but there are no clinical trials analyzing the response to a jakinib after the suspension of another jakinib and therefore, observational data may be useful in this regard. The aim of this study is to describe efficacy and safety of the second jakinib in patients with suspension of the first due to failure or side effects.

Methods: Spanish observational multicentric study. Data were retrospectively obtained from medical records of 31 patients with RA sequentially treated with baricitinib or tofacitinib in any order.

Results: We identified 31 patients with RA, median age 62 years (IQR 51-67), 80.6% female (Table 1). Rheumatoid factor and anti-CCP was positive in 80.6% and 71% of the patients . Most of the patients (87%) had received previously treatment with bDMARD, median number of previous bDMARDs 4 (IQR 2-5). Half of the patients received Tofacitinib first, and the other half Baricitinib as the first Jakinib. Median survival for the first Jakinib was 5 months (IQR 3-8) and the reason for withdrawal was inefficacy in 19 cases (61.3%) and adverse effects in 12 (38.7%). Median DAS28CPR in the beginning of the second jakinib was 5.3 (IQR 5-5.9), 9 patients were treated in monotherapy and 26 used glucocorticoids.

9 patients discontinued the second Jakinib, in all of them the reason was inefficacy. The treatment suspension rate was similar among patients discontinuing the first Jakinib for inefficacy (5/19, 26.3%) or for adverse effects (3/12; 25%). Median follow-up of patients who didn't discontinue the second Jakinib was 19.5 (IQR 12-24) months. Disease activity data along this follow-up are depicted in Figure 1 and 2.

	N 31
Clinical characteristics	
Female	25 (80.6%)
Age*	62 (IQR 51-67)
Years since diagnosis*	11 (IQR 6-18)
Rheumatoid Factor (+)	25 (80.6%)
Anti-CCP (+)	22 (71%)
Erosions	16 (51.6%)
Extra-articular manifestations	10 (32.3%)
Rheumatoid nodules	6 (19.4%)
Secondary Sjögren's syndrome	4 (12.9%)
Previous treatment	
bDMARD	27 (87%)
N° of previous bDMARDs *	4 (IQR 2-5)
TNFi	24 (77.4%)
Non-TNFi	22 (70.9%)
Baseline characteristics at the start of the second Jakinib	
Tender joint count (TJC)*	10 (IQR 7.24-14.3)
Swollen joint count (SJC) *	6 (IQR 4-10)
DAS28CPR*	5.3 (IQR 5-5.9)
High disease activity	71%
Moderate disease activity	24%
Low disease activity	5%
Concomitant treatment	
Corticosteroids	26 (84%)
Prednisone mg or eq*	7.5 (IRQ 5-10)
csDMARD	
None	9 (29%)
Methotrexate	17 (54.8%)
Leflunomide	5 (16.2%)

*Data are offered as median (IQR)

Table 1. Characteristics of 31 patients with RA treated sequentially with two jakinibs

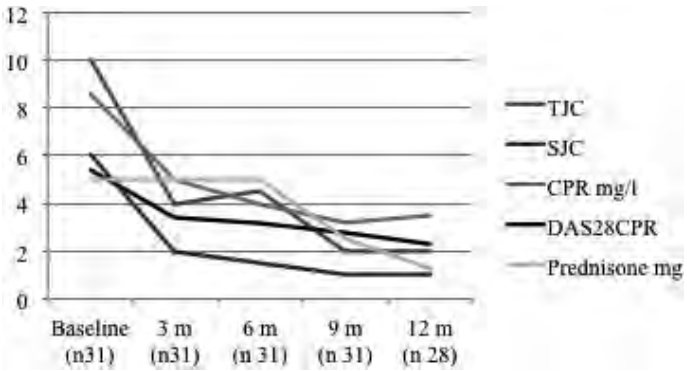

Figure 1. Second jakinib treatment results during the follow-up period (median).

Conclusion: Our data show that therapy with a second jakinib is a safe and efficacious option after discontinuation of the first jakinib due to either inefficacy or side effects. The response rate to the second jakinib is similar in patients with inefficacy or side effects which suggests that failure to the first does not reduce the chance of response to the second.

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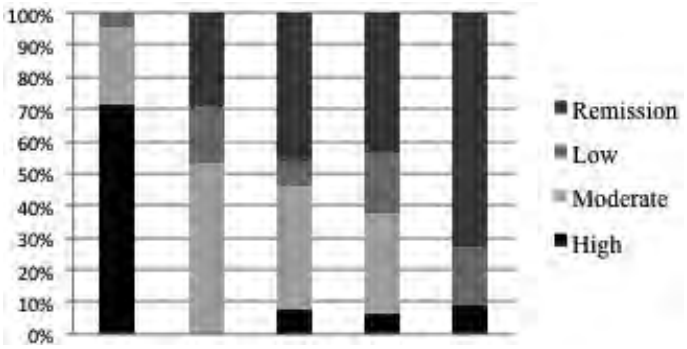

Figure 2. Second jakinib activity development.

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Abstract Number: 0819

The Adherence Patterns Among Patients Using Infliximab Bio-originator and Biosimilar

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

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Background/Purpose: Infliximab (INF) biosimilar was approved for multiple indications in U.S. in 2016. Although clinical trials have demonstrated that switching from infliximab bio-originator to its biosimilar is safe with no significant loss of efficacy, there are limited real-world data comparing their utilization and adherence patterns. Thus, we evaluated medication adherence among INF biosimilar users and compared them to INF bio-originator users using national administrative data, 2014-2018.

Methods: We established 4 cohorts among patients who had at least one administration or pharmacy claim for INF bio-originator or biosimilar in 2017 Truven Marketscan data, including INF biosimilar naïve users, INF biosimilar prevalent users, INF bio-originator naïve users, and INF bio-originator prevalent users. We evaluate the prior use of INF and other biologics using all available data in 2014-2017 prior to the first INF administration in 2017 (index date).The INF naïve users were defined as no prior use of INF bio-originator or INF biosimilar, whereas prevalent users had any prior use of bio-originator INF but no prior INF biosimilar use. Eligible patients were ≥18 years of age, continuously enrolled with full coverage from 2014 and through follow up. Follow-up started on the index date and ended on the earliest date of death, loss of coverage, or 12/31/2018. For patients who had at least 12 or 18 months of follow-up time, we calculated their proportion of days covered (PDC) at 12 or 18 months. Ongoing analyses are adjusting for important patient characteristics that differ across cohorts.

Table. Proportion of days covered calculated at months of 12 and 18 during following up

Cohorts	12 Months Follow-Up Adherence (365 days)			18 Months Follow-Up Adherence (548 days)		
Inflectra (N = 319)	**<50%**	**50 – 80%**	**>80%**	**<50%**	**50 – 80%**	**>80%**
Naïve Inflectra without Past use of Infliximab (N = 96)	27 (40.30)	11 (16.42)	29 (43.28)	9 (39.13)	3 (13.04)	11 (47.83)
Naïve Inflectra with Past use of Infliximab (N = 223)	61 (41.50)	19 (12.93)	67 (45.58)	28 (50.00)	8 (14.29)	20 (35.71)
Infliximab (N = 13, 119)	**< 50%**	**50 – 80%**	**>80%**	**< 50%**	**50 – 80%**	**>80%**
Naïve Infliximab without Past use of Inflectra (N = 2,149)	485 (30.72)	276 (17.48)	818 (51.80)	350 (42.42)	135 (16.36)	340 (41.21)
Prevalent Infliximab Users (N = 10, 970)	1,069 (13.46)	1,082 (13.62)	5,793 (72.92)	1,262 (17.06)	1,381 (18.67)	4,754 (64.27)

Results: We identified 96 INF biosimilar naïve users, 223 INF biosimilar prevalent users, 2,149 INF bio-originator naïve users, and 10,970 INF bio-originator prevalent users. The proportion of other biologic use prior to index date and demographic characteristics are similar across different cohorts with mean age of 45 and 60% females. Among patients who had >=12m of follow-up, 43% INF biosimilar naive users, 41.5% INF biosimilar prevalent users, 52% INF bio-originator naïve users and 73% INF bio-originator prevalent users continued to be adherent (>80%) at 12 months. Among patients who had >=18m of follow-up, 48%, 36%, 41%, and 64% user continued to be adherent at 18 months respectively (Table).

Conclusion: The adherence patterns were similar among INF biosimilar naïve, INF biosimilar prevalent, and INF bio-originator naïve users. We found the INF bio-originator prevalent users had the highest adherence within 12 or 18 months of follow-up. However, further studies with large sample size are needed to evaluate the adherence of INF biosimilar users.

Disclosure: J. Alanaeme, None; **S. Sarvesh**, None; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **H. Yun**, Pfizer, 2.

Abstract Number: 0820

High Remission Rates in RA – Real Life Data from Bariticinib

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Recent developments of targeted treatments such as targeted synthetic DMARDs (tsDMARDs) increase the chances of a sustained low disease activity (LDA) or remission state for patients suffering rheumatoid arthritis (RA). tsDMARDs such as baricitinib, an oral inhibitor of the Janus Kinases (JAK1/JAK2) was recently approved for the treatment of RA with an inadequate response to conventional (cDMARD) and biological (bDMARD) therapy (1, 2).

Aim of this study is to analyze the effect of baricitinb on disease activity (DAS28, LDA) in patients with RA in real life, to analyze drug persistance and associate these effects with various baseline characteristics.

Methods: All RA patients were seen in our outpatient clinic. If a patient was switched to a baricitinib due to medical reasons, these patients were included in our prospective, observational study which started in April 2017. Clinical scores (SJC/TJC 76/78), composite scores (DAS28), PROs (HAQ-DI; RAID; FACIT), safety parameters (not reported in this abstract) as well as laboratory biomarkers were collected at each visit every three months. Linear mixed effects models for repeated measurements were used to analyze the time course of disease activity, patient reported outcomes and laboratory results. We estimated the probabilities of continued baricitinib treatment and the probabilities of LDA and remission by DAS-28 as well as Boolean remission up to one year using survival analysis and explored

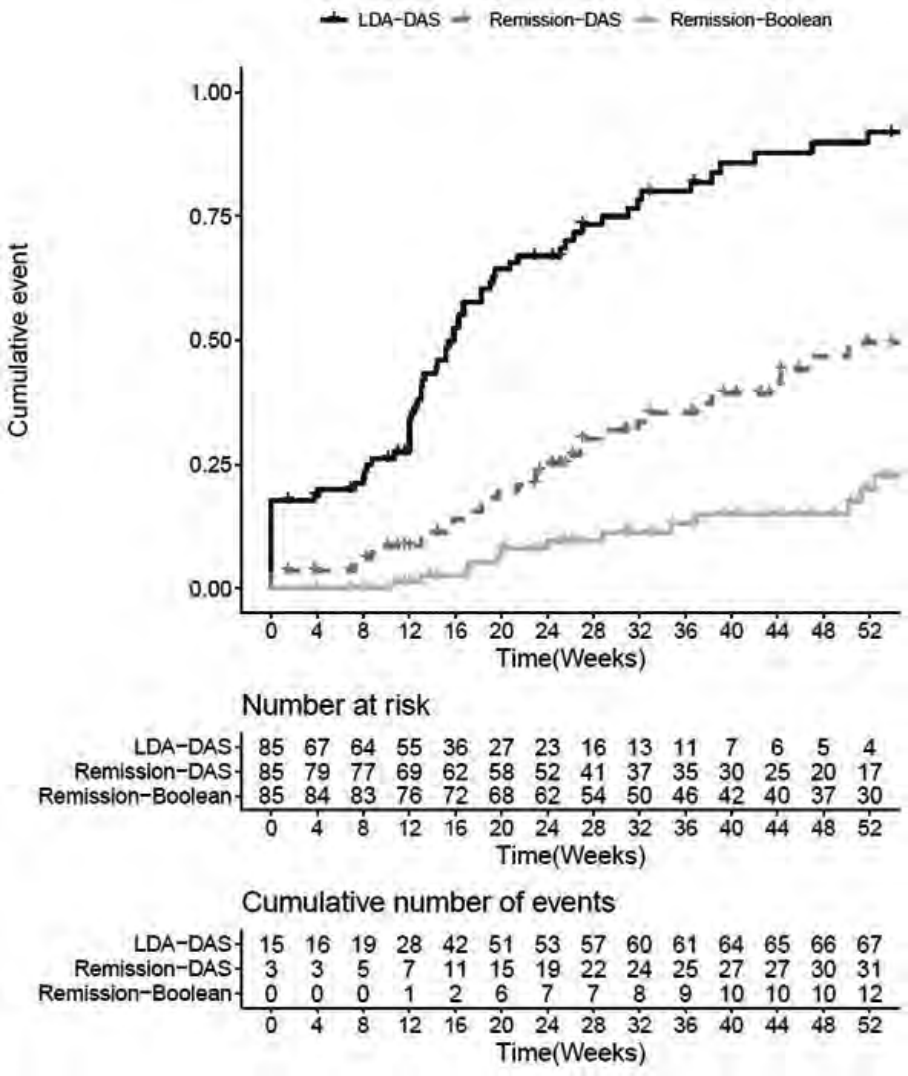

Figure-1. Cumulative probability of low disease activity or remission under treatment with baricitinib.

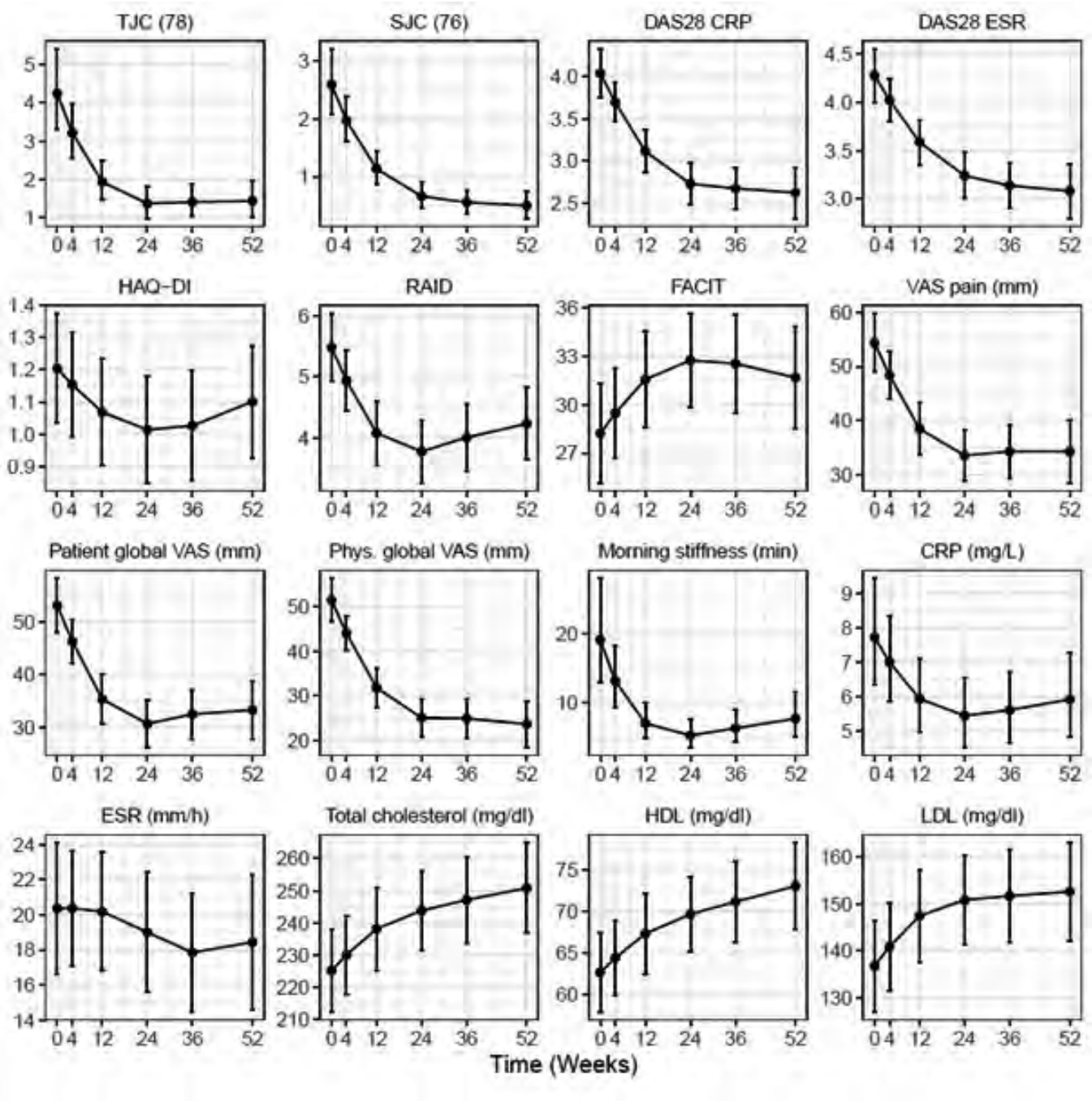

Figure-2. Course of disease activity measures, patient reported outcome measures, acute phase response and cholesterol levels over treatment course in baricitinib users.

their association with disease characteristics using multivariable Cox regression. All patients gave informed consent. The study is approved by the local ethics.

Results: 95 patients were included and 85 analyzed with available follow-up data until November 2019. Demographics are shown in Table 1. Mean follow-up duration after starting baricitinib was 49.3 (28.9) weeks. 51 patients (60%) were on monotherapy. Baricitinib survival (95%CI) was 82% (73% to 91%) at one year. Cumulative number (%probability, 95%CI) of patients that attained DAS-28 LDA at least once up to one year was 67 (92%, 80% to 97%) and the number of patients attaining DAS-28 and Boolean remission were 31 (50%, 34% to 61%) and 12(20%, 9% to

Table-1 Baseline patient characteristics

Age, yr, mean (SD)		57.8 (12.1)
Sex, n(%)	Male	23 (27.1)
	Female	62 (72.9)
Disease duration, yr, mean (SD)		8.5 (8.2)
RF status, n(%)	Negative	16 (18.8)
	Positive	69 (81.2)
ACPA status, n(%)	Negative	19 (22.4)
	Positive	66 (77.6)
anti-MCV status, n(%)	Negative	40 (47.1)
	Positive	45 (52.9)
Followup, weeks, mean (SD)		49.3 (28.9)
Baricitinib use	Monotherapy	51 (60.0)
	Combination	34 (40.0)
TJC (78), mean (SD)		6.6 (6.6)
SJC (76), mean (SD)		4.3 (5.5)
ESR, mm/h, mean (SD)		20.5 (16.4)
CRP, mg/L, mean (SD)		11.7 (12.7)
DAS-28, mean (SD)		4.4 (1.2)
HAQ-DI, mean (SD)		1.2 (0.7)
No. of previous csDMARDs	0	1 (1.2)
	1	27 (31.8)
	2	31 (36.5)
	3	17 (20.0)
	4	8 (9.4)
	6	1 (1.2)
No. of previous bDMARDs	0	28 (32.9)
	1	16 (18.8)
	2	19 (22.4)
	3	8 (9.4)
	4	8 (9.4)
	5	6 (7.1)

30%) respectively. Median time to DAS-28 LDA was 16 weeks (Figure-1). Cox regression analyses did not show any sufficiently precise association of remission or LDA with age, gender, seropositivity, disease duration, concomitant DMARD use and number of previous bDMARDs. Increasing number of previous bDMARDs was associated with poor baricitinib survival (HR=1.5, 95%CI 1.1 to 2.2) while this association was not robust to adjustment for baseline disease activity. Favorable changes were observed in tender and swollen joint counts, pain-VAS, patient and physician disease assessment scores, RAID, FACIT and the acute phase Response.

Conclusion: In this prospective observational study, we observed high rates of LDA and DAS-28 remission and significant improvements in disease activity and patient reported outcome measurements over time.

Disclosure: S. Bayat, Novartis, 8; **K. Tascilar**, None; **A. Kleyer**, Lilly, 8, Novartis, 8, BMS, 8, Sanofi, 8, Gilead, 8; **D. Simon**, Novartis, 8, Lilly, 5, 8, Janssen, 8, AbbVie, 5; **A. Hueber**, None; **G. Schett**, None.

Abstract Number: 0821

Gender and Discontinuation of Biologic DMARDs in Patients with Rheumatoid Arthritis: Data from the Mexican Biologics Registry

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

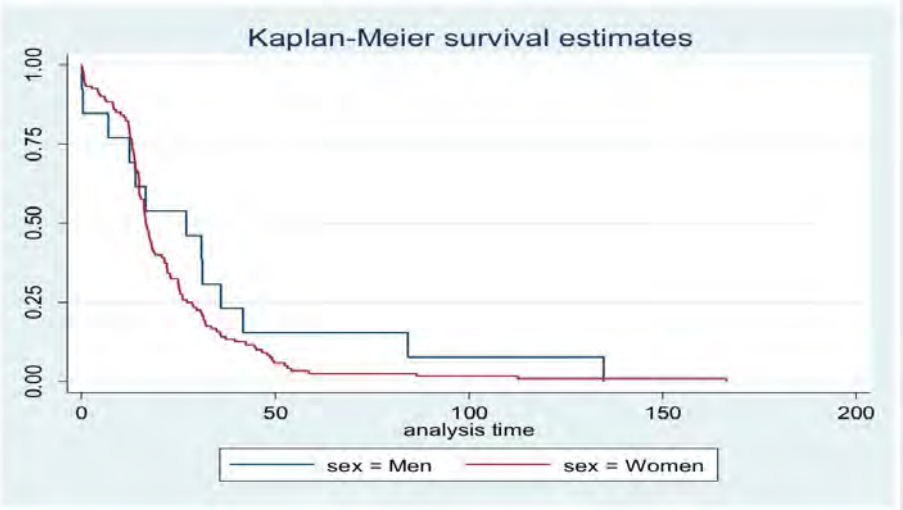
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is the most common autoimmune disease and is more frequent and severe in women than in men. Symptom severity, disease progression, response to therapy and overall survival differ between males and females with AR.

Determine if drug discontinuation of biologic DMARDs (bDMARDs) differs by gender in patients with rheumatoid arthritis in the Mexican Adverse Events Registry (BIOBADAMEX).

Methods: BIOBADAMEX is a Mexican ongoing cohort of patients using bDMARDs since 2016. In this analysis we included all patients with diagnosis of RA with at least two assessments. Survival on bDMARDs was estimated using Kaplan-Meier analysis. Predictors of discontinuation, including gender were investigated by Cox regression analyses. This analysis did not show a sex role on discontinuation of bDMARDs in Mexican RA patients, however we found high DAS28 had a protective role. Further longitudinal analyses will be performed including more patients to assess retention rate of bDMARDs and identify predictive variables of discontinuation.

Results: Among 727 RA patients in the cohort, 134 patients had at least two assessments, from which 121 (90%) were women. At baseline, patients had a median (IQR) disease duration of 11 (5-18) months and 55.2 (45-61) years old of age, with a median DAS28 of 5.2 (4-6). Conventional DMARDS were used by 116 (87%) patients and 53 (40%) used corticosteroids. Comorbidities were present in 66 (50%). The most common bDMARDs received at baseline were tocilizumab 31 (23%), abatacept 29(22%), adalimumab 22 (16%) and certolizumab 20 (15%). At the time of analysis, the median bDMARDs treatment duration was 17 (13-29) months, 59 (44%) had discontinued treatment, 24 for inefficacy, 17 for adverse events and 18 for other reasons. Fig shows discontinuation rate curves by sex. Cox proportional-hazards demonstrated that high DAS28 >5.1 (HR 0.5, 95% CI 0.4-0.9, p=0.01) had a protective role on bDMARD discontinuation that remained in the multivariable analysis (p=0.02), while no significant differences were found regarding female sex (HR 1.4, 95% CI 0.8-2.5, p=0.26), use of corticosteroids (HR 1.3, 95% CI 0.9-1.8, p=0.20), comorbidities (HR 1.0, 95% 0.7-1.5, p=0.82) or other factors, such as age, obesity, tobacco smoking or use of conventional DMARDs.



Discontinuation rate curves by sex

Baseline characteristics	Women 120 (90%)	Men 14 (10%)	Univariable [a]
Age, median (IQR)	55.4 (45.3 – 61.4)	51.5 (45.7 – 64.4)	0.08
Disease duration, median (IQR)	11.5 (4.8 – 17.8)	8.4 (5.2 – 12.7)	0.48
DAS 28, median (IQR)	5.1 (3.78 – 5.9)	5.2 (4.4 – 5.9)	0.04
Body Mass Index, median (IQR)	27.8 (25.4 – 30.8)	28.9 (25.3 – 29.8)	0.00
Smoking, n(%)	10 (8.5)	3 (25)	0.06
Use of DMARD, n(%):	104 (86.7)	13 (92.9)	0.5
Use of steroids, n(%):	47 (39.2)	6 (42.8)	0.7
Use of previous biologic, n(%):	117 (97.5)	14 (100)	0.5
Any comorbidities, n(%):	61 (50.8)	6 (42.9)	0.5
[a] Chi^2test or Kwallis			

Baseline Characteristics

Conclusion: This analysis did not show a sex role on discontinuation of bDMARDs in Mexican RA patients, however we found high DAS28 had a protective role. Further longitudinal analyses will be performed including more patients to assess retention rate of bDMARDs and identify predictive variables of discontinuation.

Disclosure: V. Rivera, None; **S. Sicsik Ayala**, None; **D. Vega Morales**, None; **F. Irazoque-Palazuelos**, Pfizer, 5, 8, Bristol-Myers Squibb, 5, 8, Janssen, 5, 8, Takeda, 5, 8, Roche, 5, 8; **D. Miranda Hernández**, None; **J. Casasola Vargas**, None; **S. Carrillo Vázquez**, None; **A. Peña Ayala**, None; **A. Castillo Ortiz**, None; **O. Muñoz Monroy**, None; **S. Durán Barragán**, None; **A. Paz Viscarra**, None; **E. Torres Valdez**, None; **D. Xibille Friedmann**, None; **E. Zamora Tehozol**, None; **L. Valdés Corona**, None; **A. Ramos Sánchez**, None; **N. Santana Portillo**, None; **F. Guerrero Díaz**, None; **M. Vazquez Zaragoza**, None; **C. Zepeda Moreno**, None; **K. Alvarado Sánchez**, None; **M. Rivera Valencia**, None; **C. Pacheco Tena**, None; **D. Alpizar-Rodriguez**, None.

Abstract Number: 0822

Effectiveness After Transition to SB4 (Brenzys, Etanercept Biosimilar) versus Continuation of Etanercept (ETN) Originator (Enbrel) Among Rheumatoid Arthritis (RA) Patients in Low Disease Activity: A Prospective Multinational Multicenter Observational Study

Janet Pope[1], Stephen Hall[2], Claire Bombardier[3], Edward C Keystone[4], Boulos Haraoui[5], Graeme Jones[6], Latha Naik[7], Wei David Wu[8], Dena Ramey[9], Ricardo Infante[10] and Carol Etzel[11], [1]Department of Medicine, University of Western Ontario, St. Joseph's Health Centre, London, ON, Canada, [2]Emeritus Research, Camberwall, Victoria, Australia, [3]Institute for Work and Health, Toronto, ON, Canada, [4]Mount Sinai Hospital, Toronto, ON, Canada, [5]Rheumatology Institute of Montréal, Montreal, Canada, [6]Menzies Institute for Medical Research, Hobart, Tasmania, Australia, [7]University of Saskatchewan, Saskatoon, SK, Canada, [8]Merck & Co., Rahway, NJ, [9]Merck & Co., West Point, PA, [10]Merck & Co., Kenilworth, NJ, [11]Corrona, LLC, Southborough, MA

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: COMPANION-B was a prospective real-world observational study designed to provide evidence on the effectiveness of SB4, a biosimilar of ETN compared to ETN originator in rheumatoid arthritis (RA) pa-

Table 1 RA Disease Activity at Baseline (Mean, Standard Deviation)

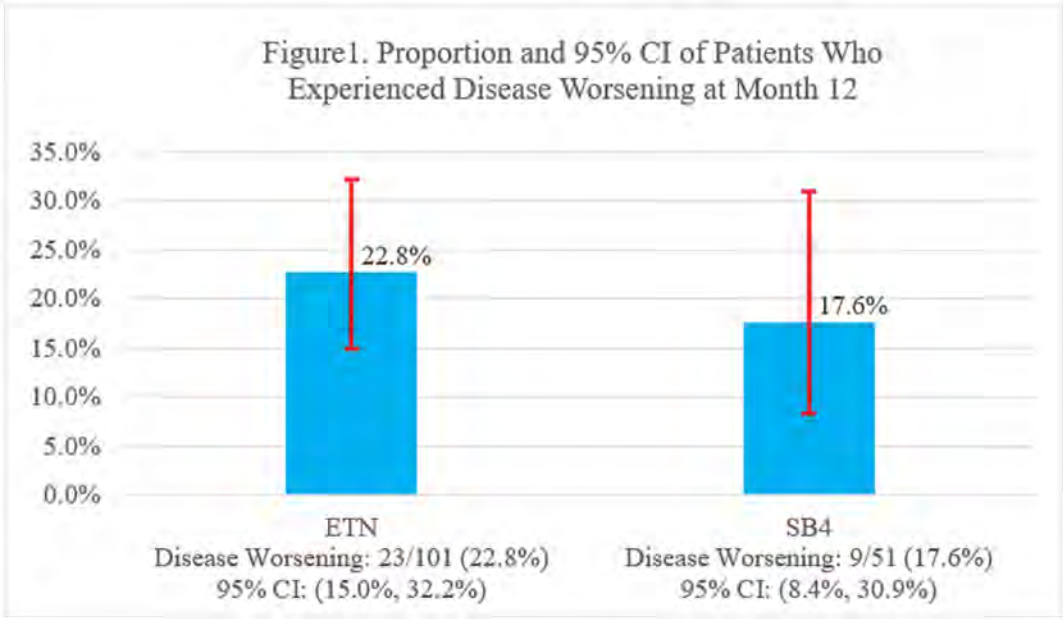
	SB4 (N=51)	ETN (N=101)
Erythrocyte Sedimentation Rate (mm/hr)	11.3 (10.2)	14.5 (13.1)
DAS28-ESR	2.0 (0.7)	2.1 (0.8)
Clinical Disease Activity Index	3.6 (2.7)	3.4 (2.9)
HAQ-DI Score	0.7 (0.7)	0.6 (0.7)
Tender Joint Count	0.5 (1.3)	0.8 (1.7)
Swollen Joint Count	0.4 (1.0)	0.5 (1.3)
Patient Global Assessment	22.3 (19.7)	15.3 (14.5)
Physician's Global Assessment	5.7 (7.9)	6.3 (7.5)

RA Disease Activity at Baseline (Mean, Standard Deviation)

Table 2 RA Disease Activity at 12 Months (Mean, Standard Deviation)

	SB4 (N=51)	ETN (N=101)
Erythrocyte Sedimentation Rate (mm/hr)	13.5 (11.5)	17.1 (14.9)
DAS28-ESR	2.1 (1.0)	2.6 (1.2)
Clinical Disease Activity Index	3.71 (3.7)	5.8 (6.9)
HAQ-DI Score	0.7 (0.8)	0.7 (0.7)
Tender Joint Count	0.6 (2.1)	1.3 (2.8)
Swollen Joint Count	0.1 (0.3)	1.0 (1.8)
Patient Global Assessment	24.8 (25.5)	25.3 (22.2)
Physician's Global Assessment	5.0 (7.1)	10.8 (16.8)

RA Disease Activity at 12 Months (Mean, Standard Deviation)



Proportion and 95% CI of Patients Who Experienced Disease Worsening at Month 12

tients in routine care. The goal was to evaluate whether sTable RA patients with low disease activity or in remission who elected to transition to SB4 had a similar rate of disease worsening over 12 months vs. patients who continued with ETN. Due to insufficient enrollment, the decision was made to conduct only descriptive analyses. Disease worsening (study endpoint) was defined as a composite of occurrence of anyone of the following: 1) A DAS28-ESR increase of ≥1.2 from baseline and minimum score of ≥3.2; 2) increase dose/frequency of treatment due to disease worsening; 3) discontinuation of SB4 or ETN due to disease worsening.

Methods: The study was conducted in 14 sites in Canada and 5 sites in Australia. Patients were ≥18 years old, diagnosed with RA by 2010 American College of Rheumatology (ACR) criteria, with treatment with ETN as their first or second biologic for at least 6 months. Patients needed to have sTable disease defined by DAS28-ESR < 3.2 at enrollment with no evidence of flare within the previous 3 months. Use of background disease modifying antirheumatic drugs (DMARDs) was allowed if patients had taken the same combination for ≥12 weeks and the same dose and frequency of each DMARD for the last 6 weeks.

Results: Of the 163 patients enrolled, 109 patients elected to continue to receive ETN and 54 patients transitioned to SB4. Mean (SD) age was 60.4 (12.7) for ETN and 61.1 (13.6) for SB4. 71.3% of ETN and 66.7% of SB4 patients were female. Approximately 90% of both groups were Caucasian. The mean (SD) duration of RA was 17.2 (10.4) and 18.6 (10.8) years for ETN and SB4 respectively. Approximately half of both groups used concomitant methotrexate. Baseline RA Disease Activity (Table 1) was similar for the two groups.

83.5% of ETN patients and 75.9% of SB4 patients completed the study. The majority of patients (94.1% in ETN group and 84.3% in SB4 group) received ≥36 weeks of study treatment.

RA disease activity at Month 12 was similar between groups (Table 2). Occurrence of adverse events was low and similar between groups.

The primary study endpoint of proportion of disease worsening at Month 12 is 17.6% (95% CI [8.4%, 30.9%]) for SB4 and 22.8% (95% CI [15.5%, 32.2%]) for ETN (Figure 1).

Conclusion: The biosimilar SB4 was shown to have similar efficacy over 12 months compared to originator ETN in this prospective observational study in well-controlled RA patients with sTable disease in a real-world setting. There did not seem to be evidence of a nocebo effect as there was no difference in worsening between groups. This study adds to the accumulating evidence that transitioning patients from originator ETN to biosimilar SB4 offers effective treatment in people willing to switch to a biosimilar and may allow for a reduction in costs.

Disclosure: J. Pope, AbbVie, 2, 5, Amgen, 5, 8, Lilly, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 5, 8, Sandoz, 5, 8, Roche, 2, 5, 8, Pfizer, 5, 8, Novartis, 5, 8, Merck, 2, 5, 8, Janssen, 5, 8, Gilead Sciences, Inc., 2, 5, BMS, 2, 5, 8, Abbott, 5, Actelion, 5, AstraZeneca, 5, Bayer, 5, Boehringer Ingelheim, 5, EICOS, 5, Emerald, 5, GlaxoSmithKline, 5, Medexus, 5, Seattle Genetics, 2; **S. Hall**, Merck, 5; **C. Bombardier**, CIHR, 2, MOHLTC, 2, Abbvie, 2, Amgen, 2, Janssen, 2, Medexus, 2, Merck, 2, 5, Novartis, 2, Pfizer, 2; **E. Keystone**, AbbVie, 2, 5, 8, Celltrion, 2, 5, 8, Eli Lilly, 2, 5, 8, Pfizer Inc, 2, 5, 8, Merck, 2, 5, 8, Sandoz, 2, 5, 8, Samsung Bioepsis, 2, 5, 8, Myriad Autoimmune, 2, 5, 8, Purapharm, 2, 5, 8, Janssen, 2, 5, 8, Sanofi-Genzyme, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, F. Hoffman-La Roche Ltd., 2, 5, 8, Genentech, 2, 5, 8, Gilead, 2, 5, 8, UCB, 2, 5, 8; **B. Haraoui**, Pfizer Canada, 5, 8, UCB Canada, 5, 8, AbbVie Canada, 5, 8, Amgen Canada, 5, Bristol-Myers-Squibb Canada, 5, Eli Lilly Canada, 5, Merck, 5, Roche Canada, 5, Sanofi-Genzyme Canada, 5, Sandoz Canada, 5, Janssen Canada, 8, Celgene Canada, 8; **G. Jones**, Merck, 5; **L. Naik**, Merck, 5; **W. Wu**, Merck & Co., 3; **D. Ramey**, Merck, 3; **R. Infante**, Merck, 3; **C. Etzel**, Merck, 5.

Abstract Number: 0823

Identifying Physician-Perceived Barriers to a Pragmatic Treatment Trial in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this qualitative research was to identify physician-perceived patient and clinic barriers to patient recruitment in a RA pragmatic trial of anti-TNF biologic vs. non-TNF biologic/Janus-Kinase inhibitor initiation after an inadequate response to methotrexate (MTX-IR).

Methods: Semi-structured telephone interviews were conducted with 26 rheumatologists in March 2019. An exploratory thematic analysis approach was used to analyze the interview data.

Results: Physician perceived patient barriers to the implementation of a RA pragmatic trial.

Two main themes were coded, consistent with the research questions identified and included patient barriers, and clinic barriers (**Figure 1).** This theme covers three sub-themes: 1) patients' personal barriers, 2) patients' treatment-related factors, and 3) trial-related factors (e.g., patient recruitment, side effects, mode of use, etc.). Patients' personal factors, the largest sub-theme, included insurance status, language barriers, and travel-related factors. Insurance status and plan was the biggest factor thought to influence patients' medication affordability and thus, trial participation. Seventeen out of 26 (65%) physicians mentioned health insurance as one of the top three patient barriers. The second sub-theme was treatment-related factors, including patients' medical condition and complexity,

Figure 1: Patient Barriers and Clinic Barriers

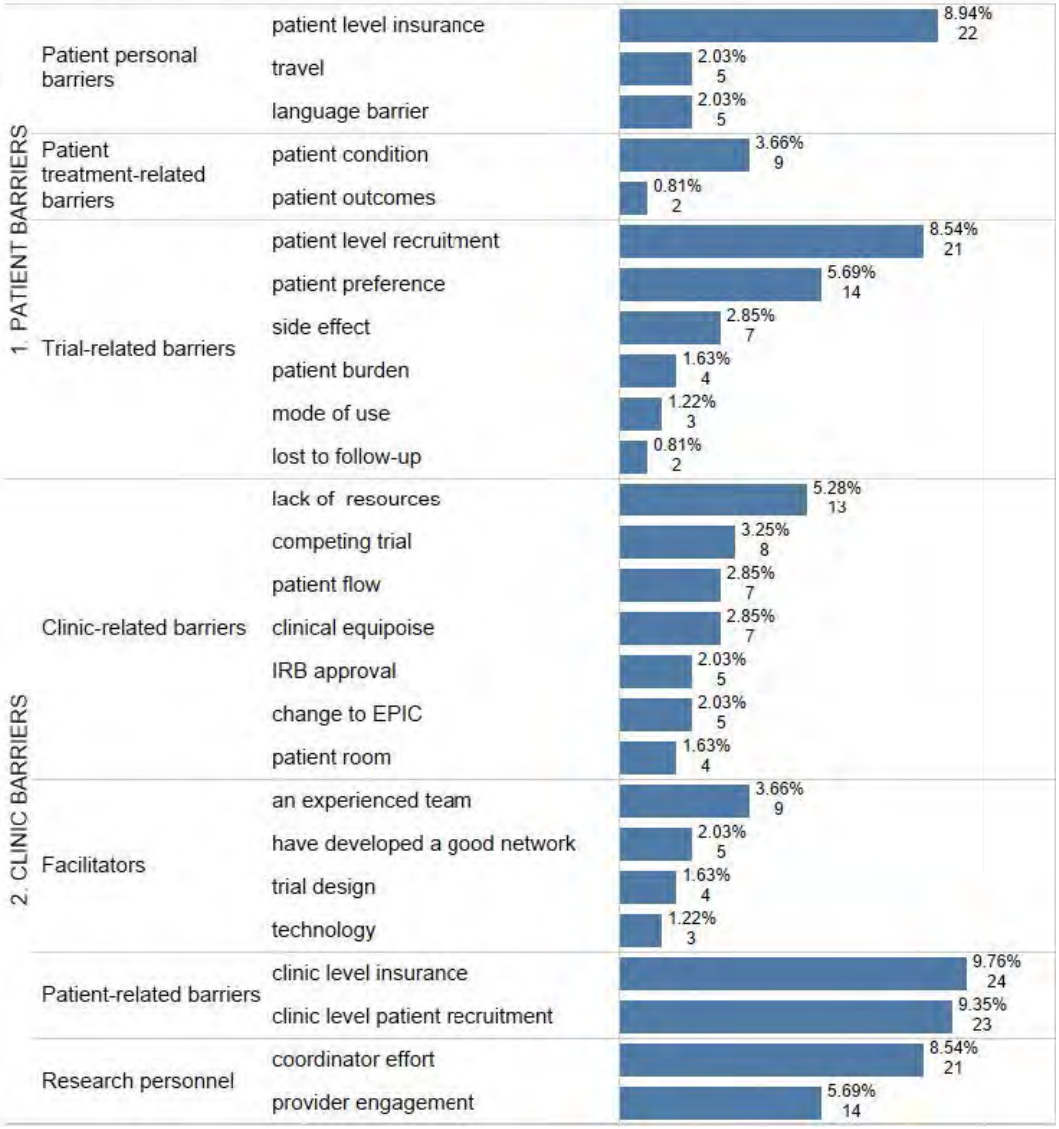

Figure 1. Patient Barriers and Clinic Barriers

comorbidities, treatment, and patient outcomes. The third large sub-theme was trial-related factors, and included patient recruitment, preferences, burden, and side effects (Figure 1).

Physicians perceived clinic barriers interfered with the pragmatic trial enrollment from the clinic or the healthcare system perspective. This theme covered four sub-themes (Figure 1): 1) clinic-related factors, 2) patient-related factors, 3) research personnel, and 4) facilitators (positive factors of the clinic). The clinic-related factors include patient/clinic flow, lack of resources (e.g., patient room, infrastructure, and time), ethics committee approval, competing trial/studies, clinical equipoise, and recent changes to a new health care record system (e.g., EPIC). Among all patient-related factors, insurance was considered as the key clinic barrier by 12 (46%) participants, including 7 participants who thought that insurance was a barrier for both clinic and patients. Research personnel was the third sub-theme under clinic barrier theme, including coordinator efforts and provider engagement.

Conclusion: Our results from the inductive thematic analysis will help researchers understand the key patient and clinic/system factors/barriers that may influence pragmatic RA trial implementation. The themes suggest there are

factors that can be modified (e.g., coordinator effort needed, effective patient recruitment during clinic visits, provider engagement) and challenges to overcome (patient insurance status, busy clinic flow, and space issues including limited number of patient rooms). In summary, these themes provide a basis for our and other research teams to develop clinic-centered and patient-centered strategies to implement a pragmatic RA trial.

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Abstract Number: 0824

The Comparative Effectiveness of Abatacept versus Tofacitinib After 6 Months of Treatment in Patients with RA Who Were Anti-citrullinated Protein Antibody Positive at Baseline: Results from a US National Observational Study

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Previous data from the Corrona RA registry, conducted in a US clinical practice setting, demonstrated that patients (pts) with RA who were ACPA+ had a greater clinical response to abatacept than ACPA– pts, a relationship not observed with TNF inhibitors or tofacitinib.[1,2] This comparative study evaluated the effectiveness of abatacept vs tofacitinib in pts with RA (ACR 1987 criteria) who were ACPA+.

Methods: Pts from the Corrona RA registry who were aged ≥18 years and were anti-CCP+ (≥20 U/mL) before starting treatment, initiated abatacept or tofacitinib from Dec 2012 onwards, had 6-month follow-up data (including CDAI score at initiation and 6 months) and were not in remission at index date were included. Pts were frequency matched 1:1 based on the number of prior biologics (0, 1, ≥2) before 1:1 propensity score matching (PSM) based on: duration of RA, education, number of prior biologics, time on therapy, baseline CDAI, current smoker, history of malignancy and BMI. Primary (mean change in CDAI score) and secondary outcomes 6 months after index date were compared using mixed-effects models. Variables that remained unbalanced after PSM were used as covariates in adjusted multivariable models, including age, sex, race, work status, BMI, systolic blood pressure, history of non-TNF inhibitor biologic (b)DMARD use, history of cardiovascular (CV) disease, baseline CDAI and modified HAQ score. Standardized difference >0.1 indicates a meaningful difference between treatments.

Results: Following PSM, most baseline characteristics for the 276 pt pairs included in the abatacept and tofacitinib groups were well balanced with a standardized difference ≤0.1 (**Table 1**). Compared with those initiating tofacitinib, fewer pts initiating abatacept had received prior treatment with non-TNF bDMARDs, were on monotherapy or had CV disease or chronic obstructive pulmonary disorder, and more had a dose of prednisone >7.5 mg/day (**Table 1**). In the adjusted analyses, there was not a significant difference in mean change from baseline in CDAI score at 6 months in pts initiating treatment with abatacept vs tofacitinib (p=0.400; **Table 2**). Among pts stratified by prior b/targeted syn-

thetic (ts)DMARD use, those who were b/tsDMARD-naïve at baseline had a numerically greater mean change in CDAI at 6 months in the abatacept vs tofacitinib group, although this difference was not statistically significant (p=0.170; **Table 2**). There were no significant differences between abatacept and tofacitinib for any of the secondary outcomes,

Table 1. Demographics and baseline characteristics of anti-CCP+ patients initiating treatment with abatacept or tofacitinib after propensity score matching

	Anti-CCP+ abatacept initiators (n=276)	Anti-CCP+ tofacitinib initiators (n=276)	Standardized difference
Female, n (%)	223 (80.8)	221 (80.1)	0.018
Age, years	60.78 (12.00)	61.39 (11.73)	0.051
RA duration, years	12.04 (10.15)	12.00 (9.65)	0.003
Race, White, n (%)	235 (85.1)	234 (86.0)[a]	0.025
Education (college), n (%)	148 (53.6)	152 (55.1)	0.029
Current smoker, n (%)	60 (21.7)	56 (20.3)	0.036
BMI, kg/m^2	29.84 (7.07)	29.40 (7.22)	0.062
Co-morbid conditions, n (%)			
Hypertension	109 (39.5)	100 (36.2)	0.067
Malignancy[b]	18 (6.5)	22 (8.0)	0.056
Diabetes	29 (10.5)	30 (10.9)	0.012
CV disease[c]	40 (14.5)	53 (19.2)	0.126
Serious infection[d]	36 (13.0)	40 (14.5)	0.042
COPD	6 (2.2)	11 (4.0)	0.105
ILD/pulmonary fibrosis	4 (1.4)	3 (1.1)	0.032
Asthma	17 (6.2)	21 (7.6)	0.057
Number of prior TNF inhibitors, n (%)			
0	46 (16.7)	52 (18.8)	0.057
1	87 (31.5)	90 (32.6)	0.023
≥2	143 (51.8)	134 (48.6)	0.065
Number of prior non-TNF bDMARDs or tsDMARD, n (%)			
0	214 (77.5)	156 (56.5)	0.459
1	45 (16.3)	73 (26.4)	0.249
≥2	17 (6.2)	47 (17.0)	0.345
Current therapy, n (%)			
Monotherapy	76 (27.5)	111 (40.2)	0.270
Prednisone value >7.5 mg/day[e]	29 (32.6)	18 (22.2)	0.234
Disease activity			
CDAI	20.14 (11.67)	20.72 (13.09)	0.047
Patient pain assessment	52.45 (27.57)	53.00 (29.13)	0.020
Patient fatigue assessment	53.26 (29.61)	52.60 (30.06)	0.022
Patient global assessment	49.14 (26.20)	50.33 (27.74)	0.044

Data are mean (SD) unless stated otherwise.

[a]n=272.

[b]History of lung cancer, breast cancer, lymphoma, skin cancer or other cancer.

[c]History of CV disease: cardiac revascularization procedure (coronary artery bypass graft, stent, angioplasty), ventricular arrythmia, cardiac arrest, myocardial infarction, acute coronary syndrome, unstable angina, other coronary artery disease, congestive heart failure (with and without hospitalization), stroke, transient ischemic attack, deep vein thrombosis, peripheral arterial disease, pulmonary embolism, carotid artery disease or other CV disease.

[d]Infection needed hospitalization or IV antibiotics.

[e]n=89 for abatacept and n=81 for tofacitinib.

bDMARD=biologic DMARD; COPD=chronic obstructive pulmonary disease; CV=cardiovascular; ILD=interstitial lung disease; tsDMARD=targeted synthetic DMARD.

Table 2. Adjusted mean change in CDAI score (primary outcome) and in patient-reported outcomes from baseline to 6 months and adjusted achievement of CDAI low disease activity or remission and mACR20/50/70 at 6 months[a]

	Anti-CCP+ abatacept initiators (n=276)	Anti-CCP+ tofacitinib initiators (n=276)	p value[b]
Primary outcome: change from baseline to 6 months in CDAI score, mean ± SE (95% CI)	−5.03 ± 0.49 (−5.99, −4.07)	−3.78 ± 0.54 (−4.85, −2.71)	0.400
Change from baseline to 6 months in CDAI score by prior b/tsDMARD use, mean ± SE (95% CI)			
0	−8.33 ± 2.13, (n=43) (−12.50, −4.16)	−4.32 ± 1.98, (n=45) (−8.20, −0.44)	0.170
1	−4.23 ± 1.57 (n=69) (−7.31, −1.15)	−6.22 ± 1.69 (n=67) (−9.53, −2.91)	0.390
≥2	−4.37 ± 0.95 (n=164) (−6.23, −2.51)	−3.20 ± 1.06 (n=164) (−5.28, −1.12)	0.415
Binary outcomes measured at 6 months, predicted probabilities (95% CI)			
Achievement of low disease activity[c]	0.37 (0.34, 0.39)	0.35 (0.32, 0.37)	0.781
Achievement of remission[d]	0.08 (0.07, 0.09)	0.09 (0.08, 0.10)	0.750
mACR20[e]	0.24 (0.22, 0.26)	0.24 (0.22, 0.26)	0.884
mACR50[e]	0.13 (0.11, 0.14)	0.12 (0.11, 0.13)	0.700
mACR70[e]	0.05 (0.04, 0.06)	0.05 (0.04, 0.06)	0.803

[a]Outcomes adjusted for: age, sex, race, work status, BMI, systolic blood pressure, history of non-TNF inhibitor biologic DMARD use, history of CV disease, baseline CDAI and modified HAQ score.
[b]For the difference between the anti-CCP+ patients initiating abatacept and tofacitinib according to the primary outcome.
[c]CDAI ≤10 among those with moderate or high disease activity.
[d]CDAI ≤2.8 among those with low disease activity or higher.
[e]mACR was based on 2 out of 4 measures (not using ESR or CRP).
b/tsDMARD=biologic/targeted synthetic DMARD; CV=cardiovascular; mACR=modified ACR criteria.

although improvements in mean change in pain and fatigue at 6 months were numerically greater in pts receiving abatacept vs tofacitinib (**Figure 1**).

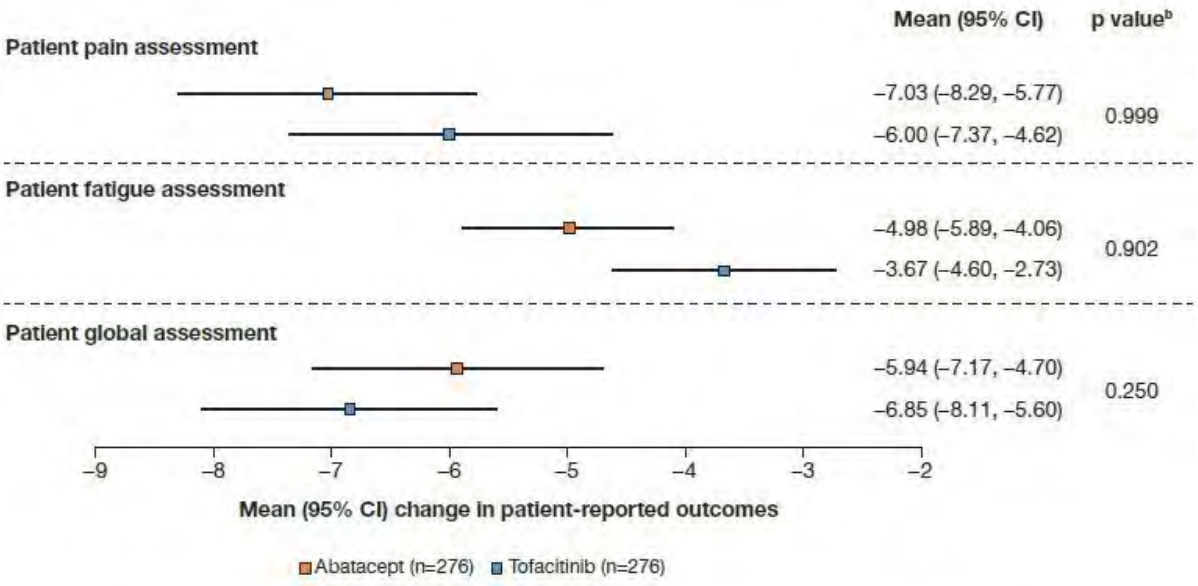
Conclusion: In adjusted analyses, ACPA+ pts with RA treated with abatacept vs those treated with tofacitinib did not have statistically significant differences in reduction of disease activity and pt-reported outcomes. Additional studies to explore these findings in a larger population would be of interest.

References:

1. Harrold LR, et al. J Rheumatol 2018;45;32–39.
2. Harrold LR, et al. Arthritis Rheumatol 2019;71(suppl 10):2415–2416 [abstract 1386].

Medical writing: Catriona McKay, PhD (Caudex)

Figure 1. Adjusted mean (95% CI) change in patient-reported outcomes from baseline to 6 months[a]



[a]Outcomes adjusted for: age, sex, race, work status, BMI, systolic blood pressure, history of non-TNF inhibitor biologic DMARD use, history of CV disease, baseline CDAI and modified HAQ.

[b]For the difference between the anti-CCP+ patients initiating abatacept and tofacitinib according to the primary outcome.

CV=cardiovascular.

Disclosure: L. Harrold, Bristol-Myers Squibb Company, 5; **K. Wittstock**, Bristol-Myers Squibb Company, 3; **S. Kelly**, Bristol-Myers Squibb Company, 1, 3, 4; **X. Han**, Bristol-Myers Squibb Company, 3; **Y. Shan**, Corrona LLC, 3; **P. Moore**, Corrona LLC, 3; **L. Guo**, None; **V. Khaychuk**, Bristol-Myers Squibb Company, 3.

Abstract Number: 0825

Sex Differences in the Efficacy and Safety of Tofacitinib in Rheumatoid Arthritis Patients: A Post Hoc Analysis of Phase 3 and Long-Term Extension Trials

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

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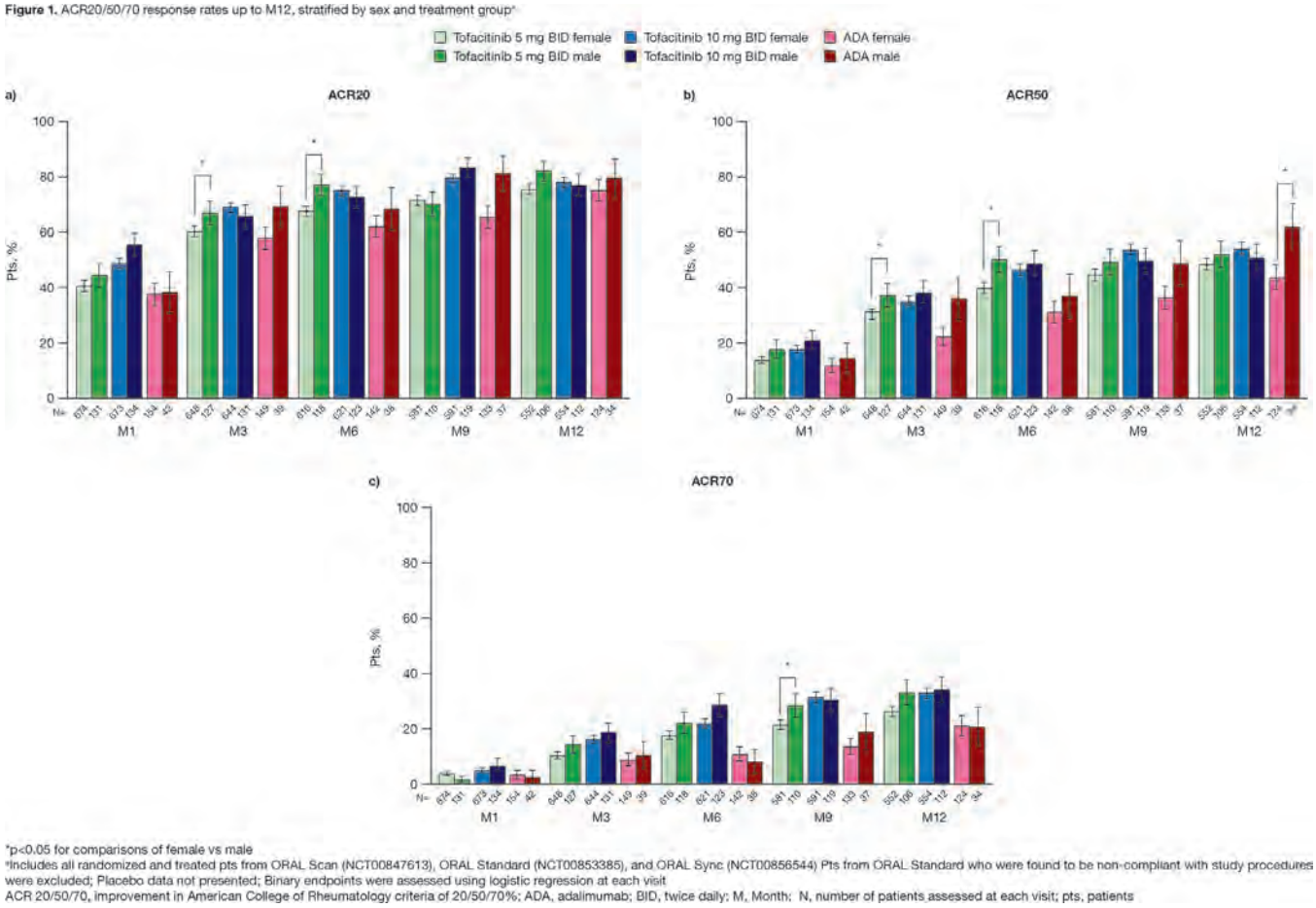
Session Time: 9:00AM–11:00AM



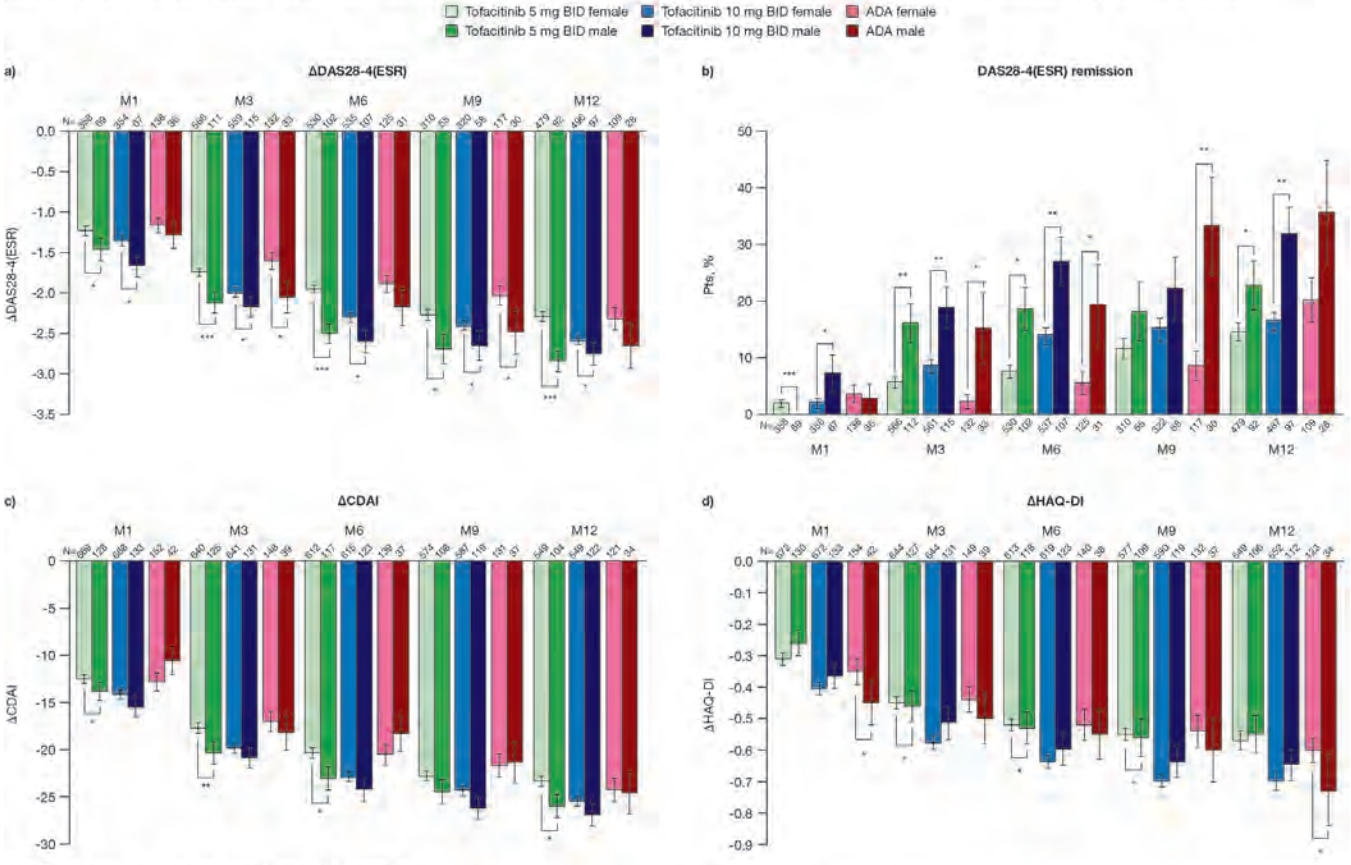
*p<0.05 for comparisons of female vs male
*Includes all randomized and treated pts from ORAL Scan (NCT00847613), ORAL Standard (NCT00853385), and ORAL Sync (NCT00856544) Pts from ORAL Standard who were found to be non-compliant with study procedures were excluded; Placebo data not presented; Binary endpoints were assessed using logistic regression at each visit
ACR 20/50/70, improvement in American College of Rheumatology criteria of 20/50/70%; ADA, adalimumab; BID, twice daily; M, Month; N, number of patients assessed at each visit; pts, patients

Background/Purpose: Differences in efficacy outcomes favoring male vs female patients (pts) with RA have been reported with csDMARDs[1] and TNF inhibitors;[2] results with JAK inhibitors are less clear.[3] Here, we assess the impact of sex on efficacy, safety, and persistence in clinical trials of tofacitinib in RA.

Methods: Efficacy and safety were assessed using data from pooled Phase (P)3 RCTs of pts with RA and an inadequate response to MTX (NCT00847613; NCT00853385) or ≥1 DMARD (NCT00856544) who received tofacitinib 5 or 10 mg BID, adalimumab (ADA) 40 mg Q2W, or placebo (PBO; advancing to tofacitinib at Month [M]3/6) + csDMARDs. Persistence was assessed in pts receiving tofacitinib 5 or 10 mg BID ± csDMARDs using data pooled from two LTE trials (NCT00661661; NCT00413699). Efficacy outcomes (to M12): ACR20/50/70 responses, changes (Δ) from baseline (BL) in DAS28-4(ESR), CDAI, CRP, and HAQ-DI, and DAS28-4(ESR) remission (< 2.6). Safety outcomes (to M24) for tofacitinib and ADA: adverse events (AEs), serious AEs (SAEs), severe AEs, discontinuations due to AEs, and AEs of special interest (AESIs). Kaplan-Meier persistence analysis estimated 2- and 5-year drug survival rates with tofacitinib.

Results: 2,265 pts were included from the P3 RCTs. Demographics and BL characteristics were comparable across sexes and treatments. Tofacitinib or ADA vs PBO generally led to significantly higher ACR20/50/70 responses in both sexes through M6 (data not shown). Up to M12, ACR20/50/70 responses were broadly comparable across active treatments and between sexes, with significant differences favoring males observed at some timepoints (Figure 1). Statistically significant differences favoring males vs females were observed in ΔDAS28-4(ESR) and DAS28-4(ESR) remission rates at most timepoints across treatment groups (Figure 2a,b). Differences in ΔCDAI, ΔCRP (data not shown), and ΔHAQ-DI tended to favor males (except ΔHAQ-DI with tofacitinib 10 mg BID, which was numerically greater in females) (Figure 2c,d). Rates of AEs, SAEs, severe AEs, and discontinuations due to AEs were slightly high-

Figure 2. a) Change from baseline in DAS28-4(ESR), b) DAS28-4(ESR) remission rates, c) change from baseline in CDAI, and d) change from baseline in HAQ-DI up to M12, stratified by sex and treatment group[a]



*p<0.05, **p<0.001, ***p<0.0001 for comparisons of female vs male

[a]Includes all randomized and treated pts from ORAL Scan (NCT00847613), ORAL Standard (NCT00853385), and ORAL Sync (NCT00856544) Pts from ORAL Standard who were found to be non-compliant with study procedures were excluded; Placebo data not presented; Binary endpoints were compared using logistic regression at each visit; Continuous endpoints were compared using a longitudinal mixed-effects linear regression model

Δ, change from baseline; ADA, adalimumab; BID, twice daily; CDAI, Clinical Disease Activity Index; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; M, Month; N, number of patients assessed at each visit; pts, patients

er in females vs males with tofacitinib 5 mg BID (Table 1a); with tofacitinib 10 mg BID and ADA, this trend was generally reversed. AESIs were comparable between sexes with tofacitinib and ADA, although event numbers were low and results should be interpreted with caution. 2- and 5-year tofacitinib survival rates were mostly similar between sexes, with some numerical, non-significant differences favoring females (Table 1b).

Conclusion: In this post hoc analysis, efficacy outcomes with tofacitinib and ADA were generally higher in males and comparable in females vs previously reported mixed population response rates for advanced therapies.[4,5] Safety findings did not reveal a consistent pattern between sexes. Tofacitinib persistence was similar between sexes.

1. Bergstra SA et al. J Rheumatol 2018; 45: 1361-1366.
2. Jawaheer D et al. J Rheumatol 2012; 39: 46-53.
3. Spinelli FR et al. Ann Rheum Dis 2020; 79: 1016-1017.
4. Bird P et al. J Clin Rheumatol 2019; 25: 115-126.
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Table 1. a) Summary of safety up to M24 in pts receiving tofacitinib 5 or 10 mg BID or ADA in pooled csDMARD-IR Phase 3 RCTs,[a] and b) Kaplan-Meier estimates of persistence[b] in pts (months) receiving average tofacitinib 5 or 10 mg BID[c] in pooled LTE studies,[d] stratified by sex

a)

Pts with events, n (%)	Tofacitinib 5 mg BID		Tofacitinib 10 mg BID		ADA	
	Females (N=707)	Males (N=133)	Females (N=698)	Males (N=137)	Females (N=162)	Males (N=42)
Treatment-emergent AEs	562 (79.5)	85 (63.9)	529 (75.8)	107 (78.1)	119 (73.5)	30 (71.4)
SAEs	107 (15.1)	17 (12.8)	71 (10.2)	24 (17.5)	13 (8.0)	6 (14.3)
Severe AEs	86 (12.2)	12 (9.0)	55 (7.9)	22 (16.1)	14 (8.6)	5 (11.9)
Discontinuations due to AEs	87 (12.3)	10 (7.5)	88 (12.6)	10 (7.3)	17 (10.5)	5 (11.9)
AESIs						
Death	6 (0.8)	4 (3.0)	0	3 (2.2)	1 (0.6)	2 (4.8)
Serious infections	28 (4.0)	6 (4.5)	27 (3.9)	6 (4.4)	2 (1.2)	1 (2.4)
All HZ (non-serious and serious)[e]	35 (5.0)	7 (5.3)	43 (6.2)	5 (3.6)	2 (1.2)	3 (7.1)
Tuberculosis	0	0	4 (0.6)	2 (1.5)	0	0
Opportunistic infections (excl. tuberculosis)	3 (0.4)	0	5 (0.7)	0	0	0
MACE	5 (0.7)	0	2 (0.3)	3 (2.2)	0	3 (7.1)
Malignancies (excl. NMSC)	7 (1.0)	1 (0.8)	9 (1.3)	1 (0.7)	0	1 (2.4)
NMSC	2 (0.3)	5 (3.8)	4 (0.6)	2 (1.5)	1 (0.6)	1 (2.4)
Lymphoma	0	0	2 (0.3)	0	0	0
Gastrointestinal perforation	0	0	2 (0.3)	0	0	0
Venous thromboembolism	3 (0.4)	0	3 (0.4)	1 (0.7)	0	0

b)

Survival rate, % (95% CI)	Average tofacitinib 5 mg BID		Average tofacitinib 10 mg BID	
	Females (N=492)	Males (N=101)	Females (N=2122)	Males (N=445)
All-cause discontinuation				
2-year survival	81.7 (78.3, 85.1)	84.2 (77.0, 91.3)	88.3 (86.9, 89.7)	87.2 (84.1, 90.3)
5-year survival	44.2 (39.6, 48.7)	38.8 (28.9, 48.8)	60.3 (58.2, 62.4)	58.1 (53.5, 62.8)
Discontinuation due to lack of efficacy				
2-year survival	98.7 (97.7, 99.7)	96.9 (93.4, 100.0)	98.7 (98.2, 99.2)	99.1 (98.1, 100.0)
5-year survival	96.9 (94.8, 99.0)	95.5 (91.0, 99.9)	96.6 (95.7, 97.5)	97.5 (95.9, 99.2)
Discontinuation due to AEs				
2-year survival	90.9 (88.3, 93.6)	90.6 (84.7, 96.4)	94.2 (93.2, 95.2)	91.9 (89.3, 94.5)
5-year survival	66.8 (61.9, 71.7)	58.9 (47.8, 70.0)	79.8 (78.0, 81.7)	73.2 (68.8, 77.6)

[a]Includes all randomized pts from ORAL Scan (NCT00847613), ORAL Standard (NCT00853385), and ORAL Sync (NCT00856544); [b]Persistence defined as the difference between the end-of-study date and first tofacitinib dose date +1 day. Ongoing pts were censored at the cut-off date; [c]Pts receiving an average dose of tofacitinib 5 mg BID (total daily dose of tofacitinib <15 mg) and average dose of tofacitinib 10 mg BID (total daily dose of tofacitinib ≥15 mg); [d]A3921041 (NCT00661661) and ORAL Sequel (NCT00413699); not all pts from the Phase 3 RCTs enrolled in the LTE studies, thus the population for the persistence analysis was not the same as the population for the efficacy and safety analyses'; [e]Of the 35 HZ cases in females receiving tofacitinib, 4 were serious. Of the 7 HZ cases in males receiving tofacitinib, 0 were serious. Of the 2 HZ cases in females receiving ADA, 0 were serious. Of the 3 HZ cases in females receiving ADA, 0 were serious.

ADA, adalimumab; AE, adverse event; AESI, AE of special interest; BID, twice daily; CI, confidence interval; csDMARD, conventional synthetic disease-modifying antirheumatic drug; HZ, herpes zoster; IR, inadequate response; LTE, long-term extension; M, Month; MACE, major adverse cardiovascular event; N, number of patients randomized, and number of patients included in Kaplan-Meier persistence analysis; n, number of patients with ≥1 event; NMSC, non-melanoma skin cancer; pts, patients; RCT, randomized controlled trial; SAE, serious AE

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Abstract Number: 0826

Clinical Responses and Patient Flow over 2 Years of Treatment with Abatacept, Including Dose De-Escalation, in Patients with Early, MTX-Naïve, ACPA+ RA: Results from a Phase IIIb Study

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SESSION INFORMATION

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Session Type: Poster Session B

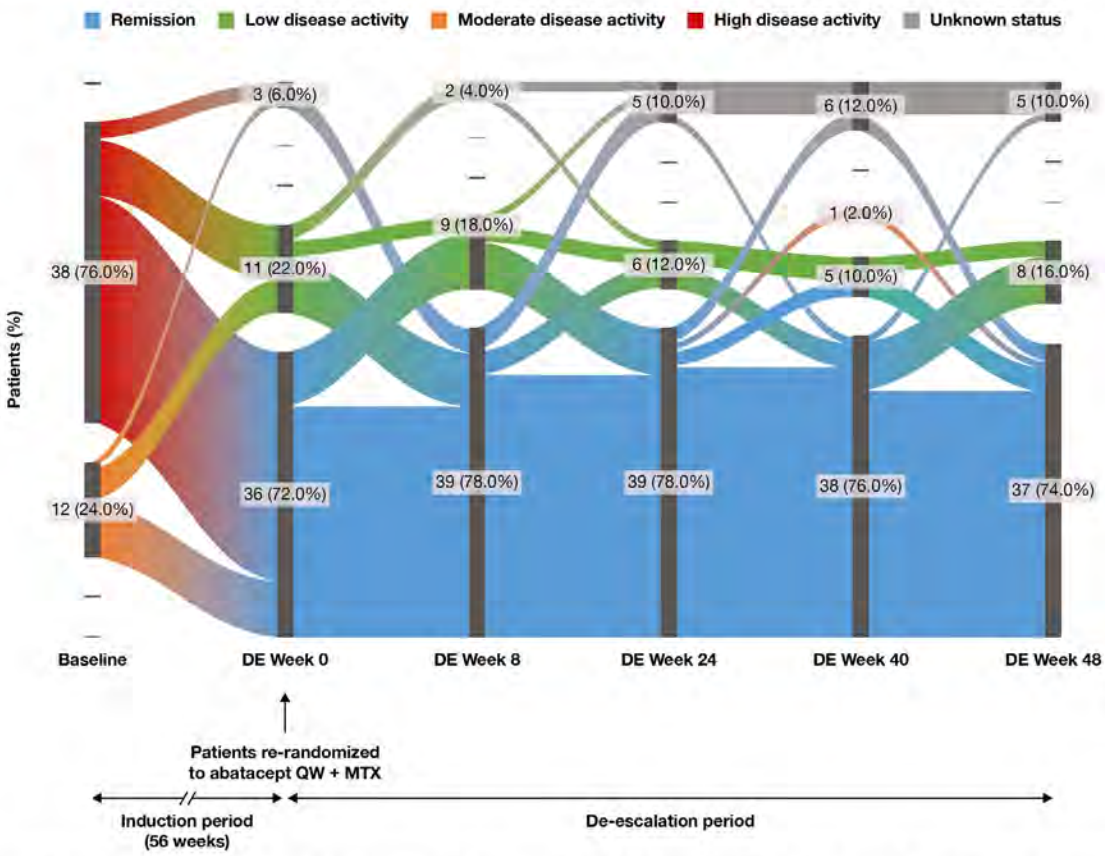
Session Time: 9:00AM–11:00AM

Background/Purpose: In the 56-week (wk) induction period (IP) of the Phase IIIb Assessing Very Early RA Treatment (AVERT)-2 trial (NCT02504268), a greater proportion of patients (pts) achieved SDAI remission (≤3.3) with SC abatacept (ABA) 125 mg once weekly (QW) + MTX vs ABA placebo (PBO) + MTX.[1] Of pts who achieved sustained SDAI remission in the IP and completed a subsequent 48-wk de-escalation (DE) period, ~50% had maintained remission at DE Wk 48.[2] However, whether pts were in sustained remission throughout the DE period is not known. This analysis evaluated pt flow during the DE period.

Methods: Pts who met the inclusion criteria (age ≥18 years [yrs]; RA diagnosis [ACR/EULAR 2010 criteria]; RA duration ≤6 months; SDAI >11; ACPA+; elevated CRP >3 mg/L or ESR ≥28 mm/h; TJC ≥3 and SJC ≥3; DMARD naïve) were enrolled in the 56-wk IP of AVERT-2 and received 1 yr of blinded treatment with ABA QW + MTX or ABA PBO + MTX. Pts who completed induction with ABA + MTX and had sustained SDAI remission (≤3.3 at both Wks 40 and 52 of the 56-wk IP) entered the DE phase and were re-randomized 1:1:1 to ABA QW + MTX for 48 wks (ABA continuation), ABA every other wk (EOW) + MTX for 24 wks then ABA PBO + MTX for 24 wks (DE/withdrawal), or ABA QW + MTX PBO for 48 wks (ABA monotherapy). Pts in sustained SDAI remission on ABA PBO + MTX during the IP were not re-randomized and continued the same blinded treatment in the DE phase (MTX monotherapy). MTX and oral CS doses were maintained in the DE period. Proportion of pts in each SDAI disease activity category (remission, low, moderate, high) was assessed over time (intent-to-treat analysis). Flow of disease activity to DE Wk 48, among re-randomized patients, was plotted using Sankey diagrams.

Results: The proportion of pts with high disease activity at IP baseline, by DE treatment arm, ranged from 72% to 76% for ABA + MTX-treated pts (DE re-randomization). Among pts who had achieved sustained SDAI remission in the IP, at the start of the DE period, 147 ABA + MTX-treated pts were re-randomized to ABA continuation (n=50), DE/withdrawal (n=50) or ABA monotherapy (n=47), and 37 pts assigned MTX monotherapy during the IP continued

Figure 1. Proportion of patients per SDAI disease activity category over time: abatacept continuation arm (n=50)



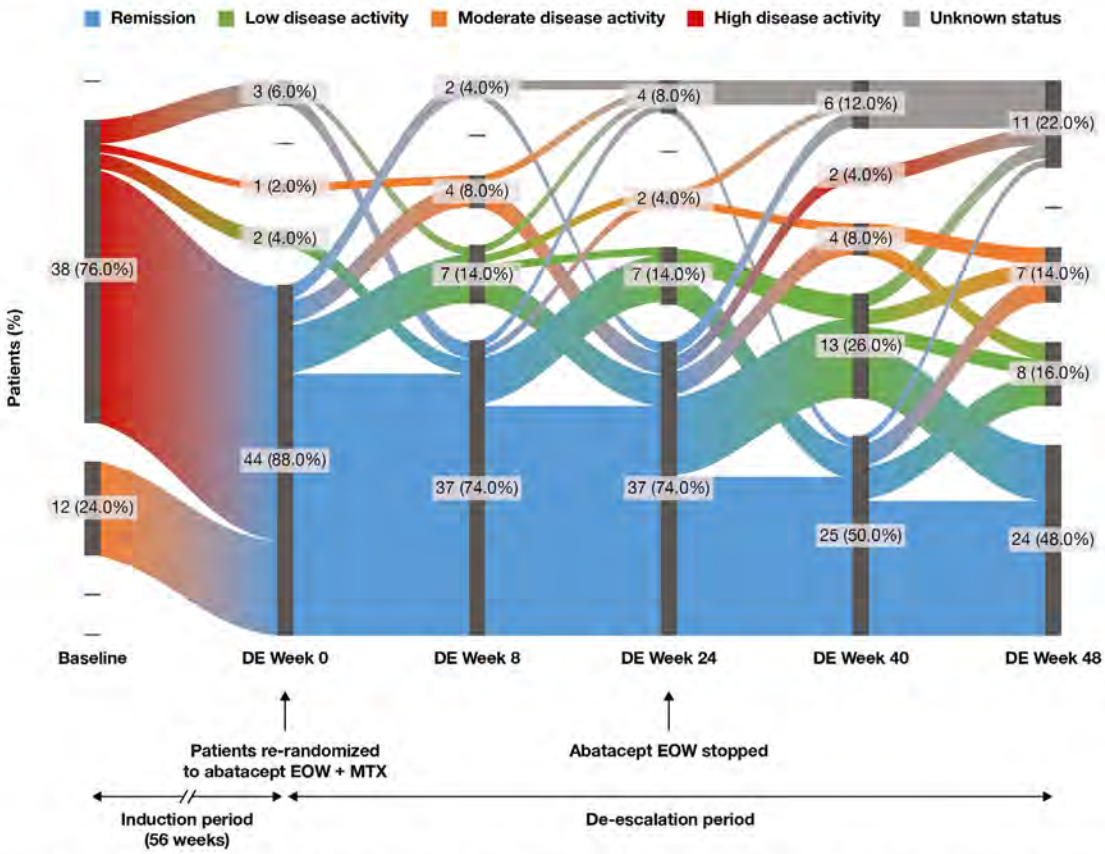
	Baseline	DE Week 0	DE Week 8	DE Week 24	DE Week 40	DE Week 48
Unknown[a]	0	3 (6.0)	2 (4.0)	5 (10.0)	6 (12.0)	5 (10.0)
High disease activity (SDAI 26.1–86)	38 (76.0)	0	0	0	0	0
Moderate disease activity (SDAI 11–26)	12 (24.0)	0	0	0	1 (2.0)	0
Low disease activity (SDAI 3.4–11)	0	11 (22.0)	9 (18.0)	6 (12.0)	5 (10.0)	8 (16.0)
Remission (SDAI ≤3.3)	0	36 (72.0)	39 (78.0)	39 (78.0)	38 (76.0)	37 (74.0)

[a]For patients who did not have data available at all time points, the status was recorded as unknown.
DE=de-escalation; QW=once weekly.

treatment in the DE period. During the DE period, fewer changes in disease activity were seen with ABA continuation versus DE/withdrawal or ABA monotherapy. The proportions of patients in SDAI remission were: ABA continuation: 72% at Wk 0, 74% at Wk 48 (**Figure 1**); ABA DE/withdrawal: 88% at Wk 0, 74% at Wk 24 for ABA EOW + MTX and 48% at Wk 48 after ABA withdrawal (**Figure 2**); ABA monotherapy: 77% at Wk 0, 57% at Wk 48 (**Figure 3**).

Conclusion: Fewer changes in disease activity were observed when IP treatment was maintained during the DE period. Most pts with high disease activity at IP baseline who achieved SDAI remission sustained remission during the DE period, suggesting that DE is possible once sustained remission has been achieved. Continued treatment with abatacept QW + MTX provided the best outcome.

Figure 2. Proportion of patients per SDAI disease activity category over time: DE/withdrawal arm (n=50)



	Baseline	DE Week 0	DE Week 8	DE Week 24	DE Week 40	DE Week 48
Unknown[a]	0	3 (6.0)	2 (4.0)	4 (8.0)	6 (12.0)	11 (22.0)
High disease activity (SDAI 26.1–86)	38 (76.0)	0	0	0	2 (4.0)	0
Moderate disease activity (SDAI 11–26)	12 (24.0)	1 (2.0)	4 (8.0)	2 (4.0)	4 (8.0)	7 (14.0)
Low disease activity (SDAI 3.4–11)	0	2 (4.0)	7 (14.0)	7 (14.0)	13 (26.0)	8 (16.0)
Remission (SDAI ≤3.3)	0	44 (88.0)	37 (74.0)	37 (74.0)	25 (50.0)	24 (48.0)

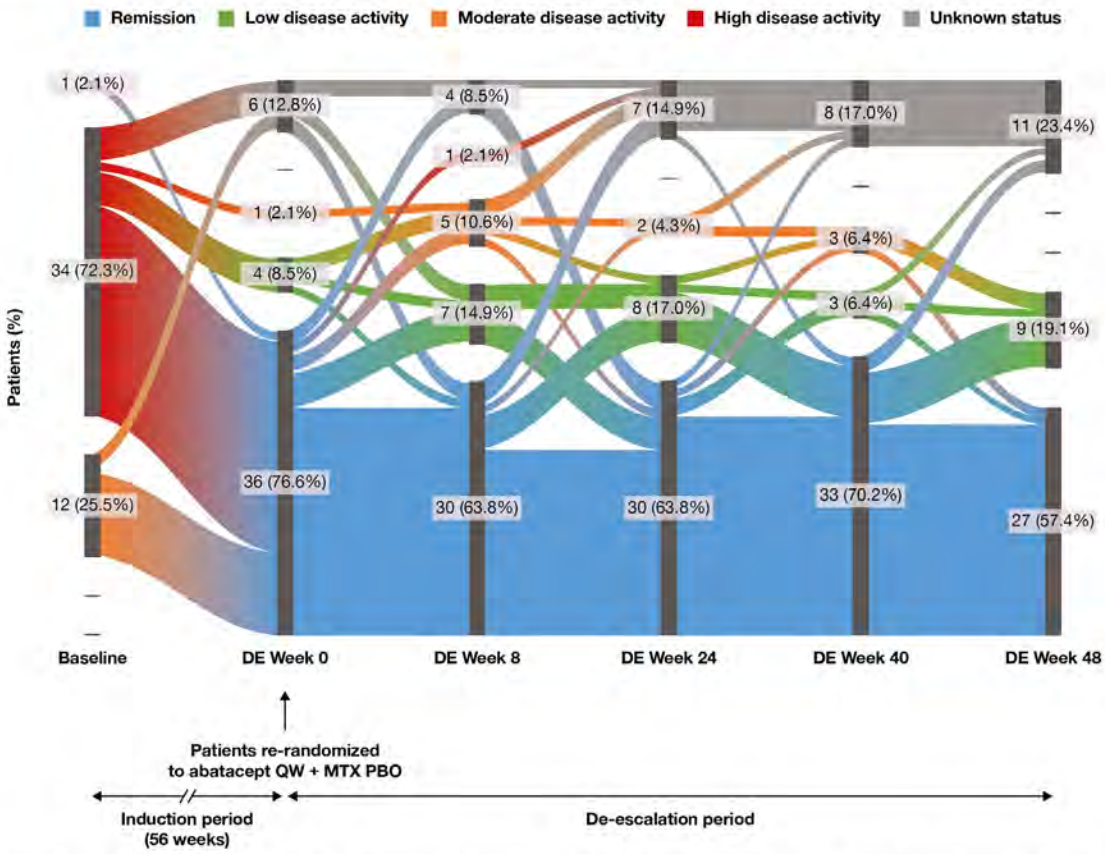
Patients received abatacept EOW + MTX from DE Week 0 to DE Week 24 and then abatacept PBO + MTX from DE Week 24 to DE Week 48.
[a]For patients who did not have data available at all time points, the status was recorded as unknown.
DE=de-escalation; EOW=every other week; PBO=placebo.

References

1. Emery P, et al. *Arthritis Rheumatol* 2018;70(suppl 10):602–604.
2. Emery P, et al. *Arthritis Rheumatol* 2019;71(suppl 10):5241–5242.

Medical writing: Lola Parfitt (Caudex)

Figure 3. Proportion of patients per SDAI disease activity category over time: abatacept monotherapy arm (n=47)



	Baseline	DE Week 0	DE Week 8	DE Week 24	DE Week 40	DE Week 48
Unknown[a]	1 (2.1)	6 (12.8)	4 (8.5)	7 (14.9)	8 (17.0)	11 (23.4)
High disease activity (SDAI 26.1–86)	34 (72.3)	0	1 (2.1)	0	0	0
Moderate disease activity (SDAI 11–26)	12 (25.5)	1 (2.1)	5 (10.6)	2 (4.3)	3 (6.4)	0
Low disease activity (SDAI 3.4–11)	0	4 (8.5)	7 (14.9)	8 (17.0)	3 (6.4)	9 (19.1)
Remission (SDAI ≤3.3)	0	36 (76.6)	30 (63.8)	30 (63.8)	33 (70.2)	27 (57.4)

[a]For patients who did not have data available at all time points, the status was recorded as unknown.
PBO=placebo; QW=once weekly.

Disclosure: P. Emery, AbbVie, 2, 8, Bristol-Myers Squibb Company, 2, 8, Pfizer, 8, Roche, 2, 8, Celltrion, 8, Eli Lilly, 8, Gilead, 8, Novartis, 2, 8, Samsung, 8; **Y. Tanaka**, AbbVie, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 2, 5, 8, Asahi-kasei, 2, 5, 8, Novartis, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Astellas, 2, 5, 8, Chugai, 2, 5, 8, Daiichi-Sankyo, 2, 5, 8, Eisai, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Janssen, 2, 5, 8, Mitsubishi-Tanabe, 2, 5, 8, Pfizer, 2, 5, 8, Takeda, 2, 5, 8, YL Biologics, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8; **V. Bykerk**, Amgen, 2, 5, UCB, 5, National Institute of Health, 2, 9, Bristol-Myers Squibb Company, 2, 5, Gilead, 5, Pfizer, 5, Brainstorm Therapeutics, 1, 3; **C. Bingham III**, Bristol-Myers Squibb, 2, 5, 8, Genetech, 5, 8, Sanofi, 5, 8, AbbVie, 5, Eli Lilly, 5, Pfizer, 5, Gilead Sciences, Inc., 5, Regeneron, 5; **T. Huizinga**, Bristol-Myers Squibb Company, 2, 8, Pfizer, 2, 8, Eli Lilly, 2, 8, LUMC, 9; **G. Citera**, AbbVie, 5, 8, Eli Lilly, 5, 8, Bristol-Myers Squibb Company, 5, 8, Gema, 5, 8, Pfizer, 5, 8, Janssen, 5, 8; **K. Huang**, Bristol-Myers Squibb Company, 1, 3, 4; **S. Connolly**, Bristol-Myers Squibb Company, 1, 3, 4; **Y. Elbez**, Bristol-Myers Squibb Company, 9;

R. Wong, Bristol-Myers Squibb Company, 1, 3, 4; **K. Lozenski**, Bristol-Myers Squibb Company, 3; **R. Fleischmann**, Pfizer, 2, 5.

Abstract Number: 0827

Comparative Clinical Efficacy of Sarilumab versus Upadacitinib over 12 Weeks: Matching-Adjusted Indirect Comparison Analysis

Thomas Huizinga[1], Ernest Choy[2], Amy Praestgaard[3], Hubert van Hoogstraten[4], Patrick R LaFontaine[3], Patricia Guyot[5], Daniel Aletaha[6], Ulf Müller-Ladner[7], Yoshiya Tanaka[8], Jeffrey R Curtis[9] and Roy Fleischmann[10], [1]Leiden University Medical Center, Leiden, Netherlands, [2]CREATE Centre, Cardiff University, Cardiff, Wales, United Kingdom, [3]Sanofi, Cambridge, MA, [4]Sanofi, Bridgewater, NJ, [5]Sanofi, Chilly-Mazarin, France, [6]Division of Rheumatology, Department of Medicine III, Medical University of Vienna,, Vienna, Austria, [7]Department of Rheumatology and Clinical Immunology, Justus-Liebig University, Campus Kerckhoff, Bad Nauheim, Germany, [8]The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, [9]Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, [10]Southwestern Medical Center, Metroplex Clinical Research Center, Dallas, TX

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Sarilumab, an IL-6 receptor inhibitor, and upadacitinib, a Janus kinase (JAK) 1 inhibitor, are both approved for the treatment of patients with moderately to severely active RA. In the absence of head-to-head trials, it has been suggested that treatments can be indirectly compared using the matching-adjusted indirect comparison (MAIC) method, in which patient-level data from one trial can be weighted for preselected patient characteristics to match against aggregated data from a comparator trial. Here, we report an MAIC comparison of sarilumab and upadacitinib outcomes using data from 2 phase 3 trials in patients with RA who were refractive to previous treatment with biologic DMARDs, including TNF inhibitors.

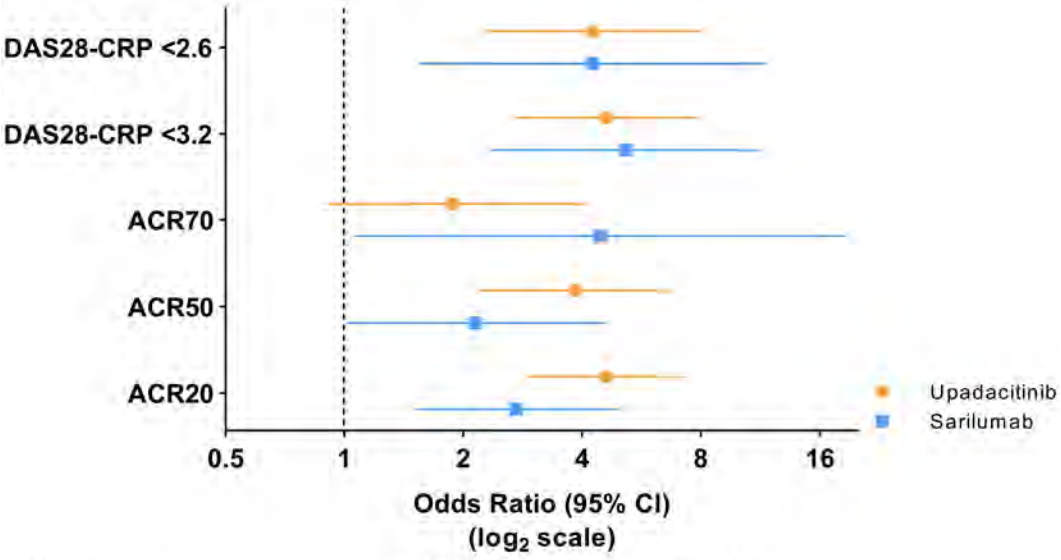
Methods: TARGET (NCT01709578) and SELECT-BEYOND (NCT02706847) were randomized, placebo-controlled trials, and included adults with active RA who had received synthetic DMARDs and had an inadequate response or intolerance to ≥1 biologic DMARD. Patient-level data of participants from TARGET treated with subcutaneous placebo or sarilumab (200 mg once every 2 weeks), and aggregated data of patients from SELECT-BEYOND treated with placebo or oral upadacitinib (15 mg/day) were analyzed. Baseline characteristics with noTable differences between the 2 trials that were potential treatment effect modifiers were identified. They included age, tender joint count (TJC) of 68 counts, swollen joint count (SJC) of 68 counts, and CRP concentration. Individual patients from the TARGET trial were assigned weights such that weighted mean baseline characteristics of the treatment effect modifiers matched those from SELECT-BEYOND. Treatment effects for the adjusted TARGET population at Week 12 were compared with published aggregate data from SELECT-BEYOND. Endpoints evaluated included the proportions of patients achieving ACR20, ACR50, ACR70, DAS28-CRP < 3.2 (low disease activity), and DAS28-CRP < 2.6 (remission).

Results: The analysis included 365 patients from TARGET (sarilumab, n=184; placebo, n=181) and 333 patients from SELECT-BEYOND (upadacitinib, n=164; placebo, n=169). After weighting, the 2 trials were matched for the treatment effect modifiers, which resulted in the decline of the effective sample size of TARGET population to 185 (sarilumab, n=89; placebo, n=96) (Table). After MAIC, the odds of achieving various clinical outcomes versus placebo were similar for sarilumab and upadacitinib for all evaluated clinical outcomes (all nominal p >0.05; Figure). A nonadjusted analysis yielded similar results (data not shown).

Table. Baseline characteristics from TARGET and SELECT-BEYOND before and after matching, mean ± SD				
	TARGET		SELECT-BEYOND	
Before matching				
	Sarilumab n=184	Placebo n=181	Upadacitinib n=164	Placebo n=169
Age, years	52.9 ± 12.9	51.9 ± 12.4	56.3 ± 11.3	57.6 ± 11.4
TJC	29.6 ± 15.5	29.4 ± 14.5	27.8 ± 16.3	28.5 ± 15.3
SJC	20.0 ± 11.9	20.2 ± 11.3	17.0 ± 10.8	16.3 ± 9.6
CRP, mg/L	30.8 ± 28.4	26.0 ± 25.2	16.2 ± 18.6	16.3 ± 21.1
After matching				
	Sarilumab ESS=89	Placebo ESS=96	Upadacitinib n=164	Placebo n=169
Age, years	56.3 ± 11.3	57.6 ± 11.4	56.3 ± 11.3	57.6 ± 11.4
TJC	27.8 ± 16.3	28.5 ± 15.3	27.8 ± 16.3	28.5 ± 15.3
SJC	17.0 ± 10.8	16.3 ± 9.6	17.0 ± 10.8	16.3 ± 9.6
CRP, mg/L	16.2 ± 18.6	16.3 ± 21.1	16.2 ± 18.6	16.3 ± 21.1
ESS=effective sample size; SJC=swollen joint count; TJC=tender joint count				

Table 1

Figure. Odds ratio of achieving clinical endpoints vs placebo, MAIC



DAS28-CRP=disease activity score with CRP; MAIC=matching-adjusted indirect comparison

Figure 1

Conclusion: In this MAIC analysis of patients from the TARGET and SELECT-BEYOND trials matched for several key baseline characteristics, efficacy of sarilumab was statistically similar to upadacitinib when comparing ACR20/50/70 and DAS28-CRP low disease activity/remission outcomes in patients with active RA who had an inadequate response to biologic DMARDs. Prospective head-to-head comparisons are needed to confirm these findings.

Disclosure: T. Huizinga, Bristol-Myers Squibb Company, 2, 8, Pfizer, 2, 8, Eli Lilly, 2, 8, LUMC, 9; **E. Choy**, Abbvie, 2, 8, Amgen, 2, 8, AstraZeneca, 2, 8, Biogen, 2, 8, Bio-Cancer, 2, 8, Boehringer Ingelheim, 2, 8, Bristol-Myers Squibb, 2, 8, Celgene, 2, 8, Chugai Pharma, 2, 8, Eli Lilly, 2, 8, Ferring Pharmaceuticals, 2, 8, GlaxoSmithKline, 2, 8, Janssen, 2, 8, Novartis, 2, 8, Novimmune, 2, 8, ObsEva, 2, 8, Pfizer, 2, 8, R-Pharm, 2, 8, Roche, 2, 8, SynAct Pharma, 2, 8, Tonix, 2, 8, UCB, 2, 8, Synovate, 2, 8, Sanofi, 2, 8, Regeneron, 2, 8, Napp, 2, 8, Hospira, 2, 8, Merck Sharp & Dohme, 2, 8; **A. Praestgaard**, Sanofi, 3; **H. van Hoogstraten**, Sanofi, 1, 3, 4; **P. LaFontaine**, Sanofi, 3; **P. Guyot**, Sanofi, 3, 4; **D. Aletaha**, UCB, 5, 8, Eli Lilly, 5, 8, Gilead Sciences, Inc., 2, 5, Janssen, 5, Sanofi/Genzyme, 5, 8, AbbVie, 2, 5, 8, Amgen, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, Roche, 2, 5, 8, Merck Sharp & Dohme, 2, 5, 8, Bristol-Myers Squibb, 8, Celgene, 5, 8, Medac, 5, 8, Sandoz, 5, 8; **U. Müller-Ladner**, Sanofi, 5, 8, Abbvie, 5, 8; **Y. Tanaka**, AbbVie, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 2, 5, 8, Asahi-kasei, 2, 5, 8, Novartis, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Astellas, 2, 5, 8, Chugai, 2, 5, 8, Daiichi-Sankyo, 2, 5, 8, Eisai, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Janssen, 2, 5, 8, Mitsubishi-Tanabe, 2, 5, 8, Pfizer, 2, 5, 8, Takeda, 2, 5, 8, YL Biologics, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **R. Fleischmann**, Pfizer, 2, 5.

Abstract Number: 0828

Clinical and Functional Response to Tofacitinib in Patients with Rheumatoid Arthritis: Probability Plot Analysis of Results from a Phase 3b/4 Methotrexate Withdrawal Study

Stanley B Cohen[1], Yi-Hsing Chen[2], Naonobu Sugiyama[3], Jose L Rivas[4], Annette Diehl[5], Tatjana Lukic[6], Jerome Paulissen[7], Haiyun Fan[5], Tomohiro Hirose[3] and Edward C Keystone[8], [1]Metroplex Clinical Research Center, Dallas, TX, [2]Taichung Veterans General Hospital, Taichung, Taiwan (Republic of China), [3]Pfizer Japan Inc, Tokyo, Japan, [4]Pfizer SLU, Madrid, Spain, [5]Pfizer Inc, Collegeville, PA, [6]Pfizer Inc, New York, NY, [7]Syneos Health, Morrisville, NC, [8]Mount Sinai Hospital, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

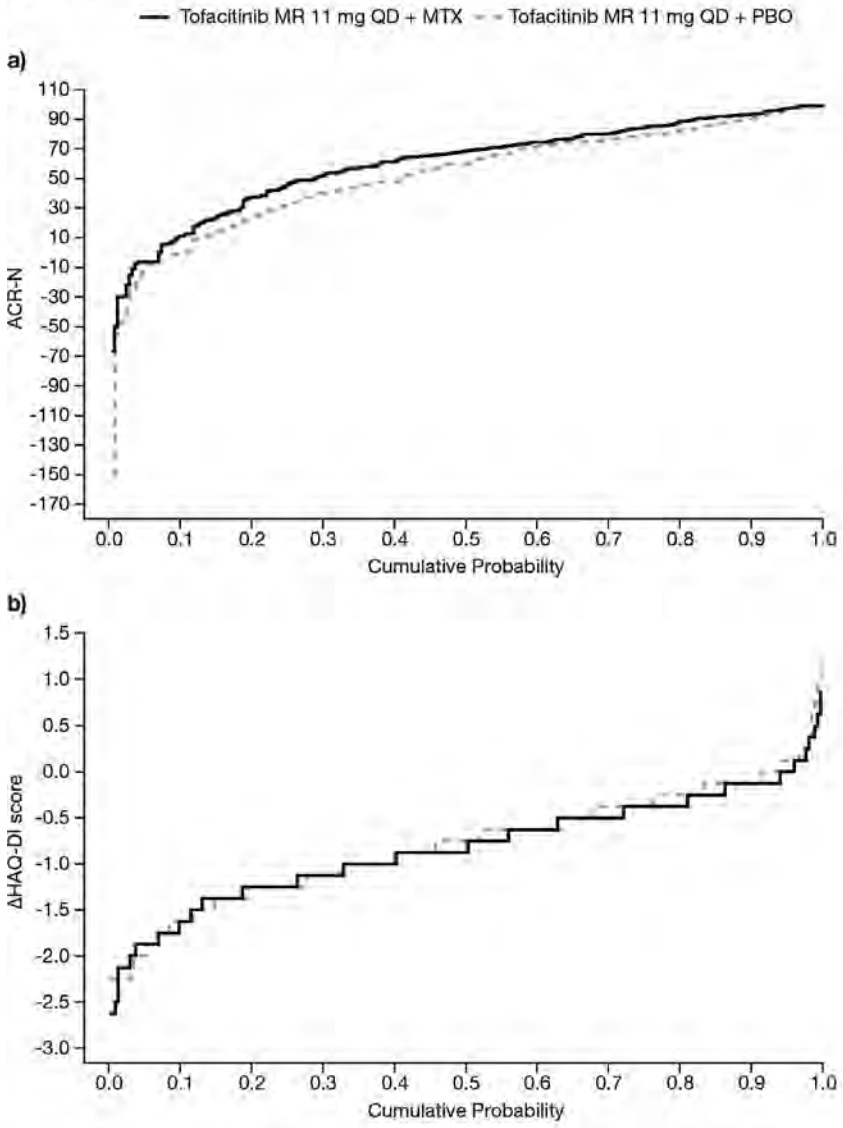
Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: ORAL Shift (NCT02831855) was a 48-week Phase 3b/4 study, which demonstrated sustained efficacy/safety of tofacitinib modified release 11 mg once daily (QD) following MTX withdrawal, that was non-inferior to continued use of tofacitinib + MTX, in patients (pts) with moderate to severe RA who achieved low disease activity (LDA) with tofacitinib + MTX at Week (W)24.[1] This post hoc analysis of data from ORAL Shift assessed the differences and similarities in clinical/functional responses in pts receiving tofacitinib ± MTX.

Methods: Clinical efficacy endpoints included ACR-N (minimum percentage change from baseline [Δ] at W48 achieved by each pt in three efficacy measures), ΔDisease Activity Score in 28 joints, erythrocyte sedimentation rate (DAS28-4[ESR]), and DAS28-4(ESR)-defined clinical remission/LDA and moderate/high disease activity (defined as DAS28-4[ESR] ≤ 3.2 and > 3.2, respectively). Functional efficacy endpoints included ΔHAQ-Disability Index (HAQ-DI) score and clinically relevant functional progression (CRFP) status at W48, defined as failure to achieve an improvement in HAQ-DI score ≥ minimum clinically important difference (MCID; defined as ≥ 0.22 decrease from baseline in HAQ-DI). Consequently, CRFP was defined as < 0.22 decrease, no change, or increase from baseline in HAQ-DI at W48. Cumulative probability plots of ACR-N and HAQ-DI at W48 were used to evaluate tofacitinib ± MTX efficacy. Descriptive statistics were produced for all efficacy endpoints; median of mean CRP values from > baseline–W24 and > W24–W48 were assessed by response subgroups.

Figure 1. Cumulative probability plot at W48 for a) ACR-N; b) ΔHAQ-DI score



In ORAL Shift (NCT02831855), pts received open-label tofacitinib + MTX to W24; Pts who achieved CDAI-defined LDA at W24 were randomized to receive tofacitinib + MTX or tofacitinib + PBO until W48. Endpoints were assessed using the full analysis set (defined as all pts receiving ≥1 dose of study drug with ≥1 value post-baseline), with no imputation for missing values

Δ, change from baseline; ACR-N, American College of Rheumatology response, where N represents the minimum amount of improvement expressed by each pt in % ΔTJC28, % ΔSJC28, and the median of % Δ in PtGA, PGA, Pain, HAQ-DI, and CRP; CDAI, CDAI, clinical disease activity index; CRP, C-reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDA, low disease activity; MR, modified release; MTX, methotrexate; PBO, placebo; PGA, Physician Global Assessment; pt, patient; PtGA, Patient Global Assessment; SJC28, swollen joint count in 28 joints; TJC28, tender joint count in 28 joints; W, week

Results: The analysis included 266 and 264 pts receiving tofacitinib + MTX and tofacitinib + placebo (PBO), respectively, from W24–W48. Cumulative probability plots and descriptive statistics suggested that overall ACR-N responses and mean ACR-N at W48 were numerically greater in pts receiving tofacitinib + MTX vs tofacitinib + PBO (Figure 1a, Table 1); ΔHAQ-DI at W48 was generally similar between groups (Figure 1b; Table 1). ΔDAS28-4(ESR) was numerically greater in pts receiving tofacitinib + MTX vs tofacitinib + PBO (Table 1). A lower proportion of pts receiving tofacitinib + MTX vs tofacitinib + PBO had CRFP; CRFP rates were numerically lower in pts with remission/LDA vs moderate/high disease activity (Table 1). Median of mean CRP over time was generally numerically lower in pts with CRFP vs non-CRFP in pts with DAS28-4(ESR)-defined remission/LDA vs moderate/high disease activity, and in pts receiving tofacitinib + PBO vs tofacitinib + MTX, irrespective of CRFP or DAS28-4(ESR) disease status (Table 2).

Table 1. ACR-N, ΔHAQ-DI, and ΔDAS28-4(ESR) scores at W48, and proportion of pts with HAQ-DI CRFP by DAS28-4(ESR) disease status, at W48

	Tofacitinib 11 mg QD + MTX (N=266)	Tofacitinib 11 mg QD + PBO (N=264)
ACR-N, mean (95% CI)	60.8 (56.8, 64.9)	53.1 (48.5, 57.7)
ΔHAQ-DI, mean (95% CI)	-0.71 (-0.78, -0.63)	-0.67 (-0.75, -0.59)
ΔDAS28-4(ESR) score, mean (95% CI)	-2.95 (-3.12, -2.79)	-2.68 (-2.84, -2.52)
HAQ-DI CRFP, n/N1 (%), *[95% CI]*	46/246 (18.7) *[14.0, 24.1]*	56/238 (23.5) *[18.3, 29.4]*
DAS28-4(ESR) remission/LDA	16/132 (12.1) *[7.1, 18.9]*	20/119 (16.8) *[10.6, 24.8]*
DAS28-4(ESR) moderate/high disease activity	28/107 (26.2) *[18.2, 35.6]*	36/117 (30.8) *[22.6, 40.0]*

In ORAL Shift (NCT02831855), pts received open-label tofacitinib + MTX to W24; Pts who achieved CDAI-defined LDA at W24 were randomized to receive tofacitinib + MTX or tofacitinib + PBO until W48; CRFP was defined as failure to achieve an improvement in HAQ-DI score ≥MCID at W48, with MCID defined as ≥0.22 decrease from baseline in HAQ-DI; consequently, CRFP was defined as <0.22 decrease, no change, or increase from baseline in HAQ-DI score at W48; DAS28-4(ESR) remission/LDA and moderate/high disease activity were defined as DAS28-4(ESR)≤3.2 and DAS28-4(ESR)>3.2, respectively

Δ, change from baseline; ACR-N, American College of Rheumatology response, where N represents the minimum amount of improvement expressed by each pt in % ΔTJC28, % ΔSJC28, and the median of % Δ in PtGA, PGA, Pain, HAQ-DI & CRP; CDAI, CDAI, clinical disease activity index; CI, confidence intervals; CRFP, clinically relevant functional progression; CRP, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDA, low disease activity; MCID, minimum clinically important difference; MTX, methotrexate; n, number of pts meeting assessment criteria at W48; N, total number of pts included in the analysis, the number of pts assessed for each endpoint may be fewer than N; N1, number of pts with non-missing data for HAQ-DI CRFP status and DAS28-4(ESR) disease status at W48; PBO, placebo; PGA, Physician Global Assessment; pt, patient; PtGA, Patient Global Assessment; QD, once daily; SJC28, swollen joint count in 28 joints; TJC28, tender joint count in 28 joints; W, week

Table 2. Median of mean CRP[a] up to W48 by HAQ-DI CRFP status, and by DAS28-4(ESR) disease status

	Tofacitinib 11 mg QD + MTX	Tofacitinib 11 mg QD + PBO
HAQ-DI CRFP	(n=45)	(n=56)
Mean CRP, median (IQR)		
>Baseline–W24	2.84 (1.15–7.30)	1.45 (0.77–4.42)
>W24–W48[b]	2.30 (0.82–4.75)	2.28 (0.53–7.28)
HAQ-DI non-CRFP (HAQ-DI score ≥MCID)	(n=195)	(n=176)
Mean CRP, median (IQR)		
>Baseline –W24	2.81 (1.09–6.19)	2.26 (0.98–4.63)
>W24–W48[c]	2.91 (1.19–5.84)	2.47 (1.13–5.53)
DAS28-4(ESR) remission/LDA	(n=126)	(n=115)
Mean CRP, median (IQR)		
>Baseline –W24	2.48 (1.05–4.95)	1.70 (0.89–4.14)
>W24–W48[d]	2.46 (1.07–4.76)	1.95 (0.81–3.82)
DAS28-4(ESR) moderate/high disease activity	(n=107)	(n=115)
Mean CRP, median (IQR)		
>Baseline –W24	3.56 (1.17–7.13)	2.60 (0.87–5.16)
>W24–W48	3.58 (1.36–8.33)	2.68 (1.34–8.23)

[a]Mean CRP was calculated as the average CRP value during each time period (>baseline–W24 or >W24–W48); [b]At >W24–W48, n=46 for tofacitinib 11 mg QD + MTX; [c]At >W24–W48, n=178 for tofacitinib 11 mg QD + PBO; [d]At >W24–W48, n=127 and n=117 for tofacitinib 11 mg QD + MTX and tofacitinib 11 mg QD + PBO, respectively. In ORAL Shift (NCT02831855), pts received tofacitinib + MTX to W24; Pts who achieved CDAI-defined LDA at W24 were randomized to receive tofacitinib + MTX or tofacitinib + PBO until W48; CRFP was defined as failure to achieve an improvement in HAQ-DI score ≥MCID at W48, with MCID defined as ≥0.22 decrease from baseline in HAQ-DI; consequently, CRFP was defined as <0.22 decrease, no change, or increase from baseline in HAQ-DI score at W48; DAS28-4(ESR) remission/LDA and moderate/high disease activity were defined as DAS28-4(ESR)≤3.2 and DAS28-4(ESR)>3.2, respectively

CDAI, CDAI, clinical disease activity index; CRFP, clinically relevant functional progression; CRP, C-reactive protein; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; HAQ-DI, Health Assessment Questionnaire-Disability Index; IQR, interquartile range; LDA, low disease activity; MCID, minimum clinically important difference; MTX, methotrexate; n, number of pts included in the analysis; PBO, placebo; QD, once daily; pt, patient; W, week

Conclusion: Although clinical and functional responses were generally similar between treatment groups overall, numerical improvements were observed in some efficacy endpoints with tofacitinib + MTX, compared with tofacitinib + PBO. A numerically higher rate of CRFP may be associated with higher DAS28-4(ESR) disease activity. Changes in CRP up to W48 may not trend with CRFP status.

1. Cohen SB et al. Lancet Rheumatol 2019; 1: e23-e34.

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International Comparison of Japanese and US Cross Country Utilization of RA Medications

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Little is known regarding differences in DMARD utilization across countries. A better understanding is needed to contextualize findings from different countries.[1] Using the same type of registry and design approach, our study describes baseline characteristics and clinical measures among rheumatoid arthritis (RA) patients who initiated a disease-modifying anti-rheumatic drug (DMARD) in Japan and the US.

Methods: We identified RA patients in the Corrona RA Japan (RA-J) and Corrona RA US (RA-US) Registries who initiated a DMARD (methotrexate, TNF, nonTNF, Janus kinase inhibitor (JAKi)) between 01/March/2016 to 31/January/2020. We compared cohorts overall and by drug group for sociodemographics, disease characteristics, comorbidities, patient-reported outcome measures (PROMs), and medications (current and prior). Of note, 2nd, 3rd, and 4th DMARDs were initiated later in RA-J in terms of disease duration. Descriptive statistics were provided; t-tests were

used for continuous variables, chi-squared tests for categorical or dichotomous variables, and Fisher's exact tests for categorical/dichotomous variables with a category size smaller than five.

Characteristics	RA Japan N=1996	RA US N=6846	P-value*
Demographic and socioeconomic characteristics			
Age, n Mean(SD)	1996 62.55(14.02)	6827 59.67(13.04)	<0.001
Gender, n Female, n(%)	1568(78.60)	5369(78.61)	>0.99
Lifestyle characteristics			
Smoking, n Never smoker, n(%) Former smoker, n(%) Current smoker, n(%)	 1311(66.35) 405(20.50) 260(13.16)	 3409(50.39) 2170(32.08) 1186(17.53)	<0.001
Alcohol use in the past year, n(%)	846(42.38)	3038(45.73)	0.008
BMI, n Mean(SD)	1662 22.40(3.96)	6624 30.06(6.63)	<0.001
History of Comorbidities, N (%)			
CVD, n(%)	218(10.92)	933(13.63)	0.002
Past serious infections, n(%)	237(11.87)	601(8.78)	<0.001
Prior Herpes zoster, n(%)	235(11.77)	184(2.69)	<0.001
Malignancy**, n(%)	185(9.27)	563(8.22)	0.14
Disease Characteristics			
Duration of RA (yrs), n Mean(SD)	1988 8.13(10.07)	6812 10.36(10.44)	<0.001
RF positive ever (among those with test results available), n(%)	1239(67.56)	2655(62.43)	<0.001
Disease Activity			
CDAI(0-76), n Mean(SD)	1929 22.49(12.62)	6808 18.83(13.81)	<0.001
Swollen Joint Count(28), n Mean(SD)	1979 6.19(5.22)	6839 4.58(5.36)	<0.001
Tender Joint Count(28), n Mean(SD)	1980 6.70(6.17)	6838 6.47(7.07)	0.18
Physician global assessment (VAS 0-100), n Mean(SD)	1948 45.46(22.43)	6834 31.71(23.41)	<0.001
Patient-Reported Outcome Measures			
Pain (VAS 0-100), n Mean(SD)	1980 50.66(27.20)	6829 49.47(28.97)	0.10
Fatigue (VAS 0-100), n Mean(SD)	1968 44.92(27.77)	6803 49.00(30.23)	<0.001
Morning stiffness, n(%)	1464(73.94)	5869(86.16)	<0.001
Duration of morning stiffness (hours), n Mean(SD)	1274 2.93(5.34)	5838 2.09(3.73)	<0.001

BMI: Body Mass Index kg/m^2; CVD: Includes cardiac arrest, myocardial infarction, acute coronary syndrome, unstable angina, coronary artery disease, ventricular arrhythmia, congestive heart failure, cardiac revascularization procedure, other cardiovascular event, stroke, transient ischemic attack, deep vein thrombosis, peripheral arterial disease, pulmonary embolism, carotid artery disease; CDAI, Clinical Disease Activity Index; VAS: visual analog scale; *: Two-sample t-tests are used for continuous variables, chi-squared independence tests for categorical or dichotomous variables; Fisher's exact tests are used for categorical/dichotomous variables with category size smaller than 5; **: Excluding non-melanoma skin cancer

Table 1. Baseline Characteristics of RA Japan and RA US Drug Initiators, Overall

Variable	MTX			TNFi			nonTNFi			JAKi		
	RA Japan N=315	RA US N=1027	P-value*	RA Japan N=576	RA US N=3095	P-Value*	RA Japan N=708	RA US N=1492	P-Value*	RA Japan N=397	RA US N=1226	P-Value*
Demographic and socioeconomic characteristics												
Age, n Mean(SD)	315 60.04(14.10)	1026 59.97(13.52)	0.94	576 60.57(15.04)	3087 59.34(13.15)	0.045	708 65.98(12.80)	1492 60.25(12.93)	<0.001	397 61.30(13.38)	1222 59.55(12.46)	0.017
Gender, n Female, n(%)	231(73.33)	747(72.81)	0.85	470(81.74)	2417(78.22)	0.058	539(76.13)	1218(81.64)	0.003	328(82.62)	987(80.77)	0.41
History of Comorbidities, N (%)												
CVD, n(%)	25(7.94)	147(14.31)	0.003	56(9.72)	403(13.02)	0.028	92(12.99)	211(14.09)	0.49	45(11.34)	172(14.03)	0.17
Past serious infections, n(%)	26(8.25)	62(6.04)	0.16	51(8.85)	228(7.37)	0.22	105(14.83)	174(11.62)	0.034	55(13.85)	137(11.17)	0.15
Prior Herpes zoster, n(%)	36(11.43)	9(0.88)	<0.001	58(10.07)	77(2.49)	<0.001	92(12.99)	50(3.34)	<0.001	49(12.34)	48(3.92)	<0.001
Malignancy**, n(%)	24(7.62)	105(10.22)	0.17	36(6.25)	246(7.95)	0.16	102(14.41)	123(8.21)	<0.001	23(5.79)	89(7.26)	0.32
Disease Characteristics												
Duration of RA (yrs), n Mean(SD)	314 2.52(5.99)	1019 3.30(6.94)	0.073	574 7.35(9.46)	3083 10.43(10.23)	<0.001	705 9.61(10.81)	1489 12.70(10.61)	<0.001	395 11.10(10.29)	1221 13.21(10.51)	<0.001
RF positive ever, n(%)	175(58.72)	441(60.41)	0.62	337(63.47)	1160(62.60)	0.72	470(72.76)	550(60.98)	<0.001	257(71.59)	504(65.63)	0.046
Disease Activity												
CDAI(0-76), n Mean(SD)	305 19.07(11.59)	1021 21.17(15.62)	0.030	558 23.81(13.34)	3079 17.75(13.59)	<0.001	687 22.51(12.02)	1491 19.36(13.15)	<0.001	379 23.24(12.95)	1217 18.98(13.22)	<0.001
Patient-Reported Outcome Measures												
Pain (VAS 0-100), n Mean(SD)	312 46.26(28.13)	1025 49.36(29.51)	0.10	571 50.15(26.76)	3088 47.94(29.25)	0.093	703 51.60(27.13)	1495 51.63(27.99)	0.98	394 53.19(26.88)	1221 50.77(28.77)	0.14
Fatigue (VAS 0-100), n Mean(SD)	312 38.69(27.39)	1024 44.51(31.96)	0.004	562 44.27(27.68)	3076 48.50(29.86)	0.002	700 45.83(27.75)	1489 52.19(29.09)	<0.001	394 49.14(27.51)	1214 50.11(30.55)	0.57
Morning stiffness, n(%)	233(74.68)	882(86.22)	<0.001	428(74.83)	2612(84.89)	<0.001	524(74.22)	1308(87.79)	<0.001	279(71.54)	1067(87.32)	<0.001
Duration of morning stiffness (hours), n Mean(SD)	223 1.83(3.44)	881 2.64(4.86)	0.019	383 2.67(5.00)	2594 2.04(3.64)	0.003	442 3.54(6.17)	1300 1.99(3.44)	<0.001	226 3.27(5.52)	1063 1.89(3.14)	<0.001
Current medications												
Prednisolone/Prednisone use, n(%)	53(16.83)	383(37.29)	<0.001	188(32.64)	895(28.92)	0.072	241(34.04)	462(30.84)	0.13	112(28.21)	369(30.10)	0.47
MTX, n(%)	315(100.00)	1027(100.00)	NA	439(76.22)	1564(50.53)	<0.001	350(49.44)	610(40.72)	<0.001	258(64.99)	434(35.40)	<0.001
Non-MTX csDMARD, n(%)	40(12.70)	206(20.06)	0.003	168(29.17)	903(29.18)	>0.99	263(37.15)	406(27.10)	<0.001	85(21.41)	298(24.31)	0.24
TNFi, n(%)	0(0.00)	0(0.00)	NA	576(100.00)	3095(100.00)	NA	17(2.40)	21(1.40)	0.092	11(2.77)	27(2.20)	0.52
nonTNFi, n(%)	0(0.00)	0(0.00)	NA	7(1.22)	26(0.84)	0.38	708(100.00)	1498(100.00)	NA	5(1.26)	31(2.53)	0.14
JAKi, n(%)	0(0.00)	9(0.88)	0.096	6(1.04)	25(0.81)	0.57	8(1.13)	19(1.27)	0.78	397(100.00)	1226(100.00)	NA
Mono vs. combination therapy(N,%)												
Combine with any csDMARD, n(%)	-	-	-	492(85.42)	2175(70.27)	<0.001	531(75.00)	905(60.41)	<0.001	301(75.82)	667(54.40)	<0.001

CVD: Includes cardiac arrest, myocardial infarction, acute coronary syndrome, unstable angina, coronary artery disease, ventricular arrhythmia, congestive heart failure, cardiac revascularization procedure, other cardiovascular event, stroke, transient ischemic attack, deep vein thrombosis, peripheral arterial disease, pulmonary embolism, carotid artery disease; CDAI, Clinical Disease Activity Index; MTX: methotrexate; csDMARDs: conventional synthetic DMARD; JAKi: Janus Kinase inhibitor; *: Two-sample t-tests are used for continuous variables, chi-squared independence tests for categorical or dichotomous variables; Fisher's exact tests are used for categorical/dichotomous variables with category size smaller than 5; **: Excluding non-melanoma skin cancer; NA: Test was not conducted because of no variation across subgroups.

Table 2. Baseline characteristics of RA Japan and RA US, by drug class

Results: Baseline data were available for 1996 RA-J and 6846 RA-US drug initiators. Overall, the two cohorts differed in most of the variables except that both groups were 79% female. At baseline, RA-J vs RA-US had a shorter mean duration of RA disease (8.1 yrs vs 10.4 yrs), higher percentage of history of serious infections (12% vs 9%), higher level of disease activity (CDAI: 22.5 vs 18.8), swollen joint count (6.2 vs 4.6), and physician global assessment (45.5 vs 31.7), but a lower percentage of history of cardiovascular disease (11% vs 14%) (Table 1).

When RA-J vs RA-US were stratified by drug class, the pattern of the differences between the two cohorts was mostly consistent with the overall analysis, except that the RA-J MTX initiators had a lower level of CDAI (19.1 vs 21.2) and prednisone use (17% vs 37%) than RA-US MTX initiators, while among the other groups (TNFi, nonTNFi, and JAKi) the pattern was reverse for CDAI or not present for prednisone use (Table 2).

Disease activity, PROMs, and current medication use was different between the two cohorts by line of therapy. Among RA-J vs RA-US, mean pain scores were higher (52.9 vs 45.9) in the 3rd line of therapy, and mean CDAI scores were higher [(21.8 vs 17.7), (22.3 vs 16.1), (25.1 vs 19.8)] and more prednisone use occurred [(30% vs 26%), (33% vs 26%), (37% vs 33%)] in the 2nd, 3rd, and 4th lines of therapy, respectively. A greater percentage of RA-J vs RA-US used nonTNFi in the 1st (12% vs 3%), 2nd (41% vs 10%), and 3rd line (40% vs 22%) of therapy. By contrast in RA-J vs

Variable	1st line			2nd line			3rd line			4th or higher line		
	RA Japan N=310	RA US N=785	P-Value[a]	RA Japan N=922	RA US N=1710	P-Value[a]	RA Japan N=420	RA US N=1493	P-Value[a]	RA Japan N=344	RA US N=2858	P-Value[a]
Demographic and socioeconomic characteristics												
Age, n Mean(SD)	310 60.60(14.73)	784 60.14(14.19)	0.64	922 62.42(14.36)	1704 58.85(13.66)	<0.001	420 63.48(13.76)	1491 60.50(12.79)	<0.001	344 63.51(12.55)	2848 59.60(12.42)	<0.001
Gender, n Female, n(%)	226(72.90)	547(69.77)	0.31	723(78.50)	1300(76.25)	0.19	329(78.33)	1170(78.47)	0.95	290(84.30)	2352(82.53)	0.41
History of Comorbidities, N (%)												
CVD, n(%)	25(8.06)	106(13.50)	0.012	97(10.52)	218(12.75)	0.093	51(12.14)	184(12.32)	0.92	45(13.08)	425(14.87)	0.38
Past serious infections, n(%)	22(7.10)	41(5.22)	0.23	98(10.63)	97(5.67)	<0.001	62(14.76)	122(8.17)	<0.001	55(15.99)	341(11.93)	0.031
Prior Herpes zoster, n(%)	33(10.65)	5(0.64)	<0.001	81(8.79)	27(1.58)	<0.001	47(11.19)	45(3.01)	<0.001	74(21.51)	107(3.74)	<0.001
Malignancy**, n(%)	20(6.45)	71(9.04)	0.16	90(9.76)	139(8.13)	0.16	46(10.95)	120(8.04)	0.061	29(8.43)	233(8.15)	0.86
Disease Characteristics												
Duration of RA (yrs), n Mean(SD)	309 2.19(6.36)	782 2.97(7.11)	0.092	920 7.01(9.28)	1702 6.18(8.32)	0.018	418 9.96(10.33)	1488 11.25(10.02)	0.021	341 14.29(10.73)	2840 14.44(10.54)	0.81
RF positive ever, n(%)	157(53.95)	359(66.60)	<0.001	569(67.42)	597(56.43)	<0.001	271(69.85)	590(64.91)	0.085	242(77.61)	1109(63.48)	<0.001
Disease Activity												
CDAI(0-76), n Mean(SD)	302 21.76(13.34)	779 23.18(16.45)	0.18	894 21.83(12.05)	1698 17.65(13.08)	<0.001	402 22.31(12.27)	1487 16.12(13.02)	<0.001	331 25.13(13.58)	2844 19.77(13.45)	<0.001
Patient-Reported Outcome Measures												
Pain (VAS 0-100), n Mean(SD)	307 48.93(28.44)	784 50.72(30.16)	0.37	912 48.47(27.15)	1703 45.89(28.76)	0.026	418 52.88(26.66)	1488 45.66(29.11)	<0.001	343 55.33(26.18)	2854 53.13(28.21)	0.17
Fatigue (VAS 0-100), n Mean(SD)	306 41.54(27.99)	782 45.41(32.76)	0.069	910 42.74(27.83)	1698 45.25(28.94)	0.036	414 47.39(27.95)	1483 46.69(29.79)	0.67	338 50.79(26.10)	2840 53.43(29.34)	0.11
Morning stiffness, n(%)	236(76.62)	676(86.56)	<0.001	677(73.91)	1422(83.75)	<0.001	300(71.94)	1254(84.56)	<0.001	251(74.04)	2517(88.32)	<0.001
Duration of morning stiffness (hours), n Mean(SD)	221 2.10(4.02)	674 2.84(4.99)	0.048	584 2.47(4.62)	1419 1.98(3.67)	0.013	258 3.60(6.12)	1245 1.79(3.18)	<0.001	211 4.26(6.86)	2500 2.11(3.60)	<0.001
Current medications												
Prednisolone/Prednisone use, n(%)	55(17.74)	341(43.44)	<0.001	276(29.93)	445(26.02)	0.032	137(32.62)	385(25.79)	0.005	126(36.63)	938(32.82)	0.16
MTX, n(%)	257(82.90)	685(87.26)	0.081	668(72.45)	1147(67.08)	0.004	243(57.86)	708(47.42)	<0.001	193(56.10)	1079(37.75)	<0.001
Non-MTX csDMARD, n(%)	1(0.32)	29(3.69)	0.002	359(38.94)	591(34.56)	0.026	120(28.57)	377(25.25)	0.17	76(22.09)	816(28.55)	0.012
TNFi, n(%)	12(3.87)	65(8.28)	0.010	366(39.70)	1075(62.87)	<0.001	136(32.38)	890(59.61)	<0.001	80(23.26)	1029(36.00)	<0.001
nonTNFi, n(%)	38(12.26)	22(2.80)	<0.001	378(41.00)	167(9.77)	<0.001	166(39.52)	333(22.30)	<0.001	133(38.66)	990(34.64)	0.14
JAKi, n(%)	6(1.94)	18(2.29)	0.72	120(13.02)	176(10.29)	0.035	123(29.29)	237(15.87)	<0.001	161(46.80)	795(27.82)	<0.001
Mono vs. combination therapy(N,%)												
Combine with any csDMARD, n(%)	257(82.90)	694(88.41)	0.015	831(90.13)	1409(82.40)	<0.001	319(75.95)	983(65.84)	<0.001	232(67.44)	1684(58.92)	0.002

Line of Therapy: number of disease-modifying anti-rheumatic drug (DMARD): 1st line: no prior use of any DMARD at time of initiation; 2nd line: prior use of at least one csDMARD and no prior use of any biologic/JAKi; 3rd line: prior use of at least one csDMARD and/or prior use of 1 biologic/JAKi; 4th line+: prior use of at least one csDMARD and/or prior use of 2+ biologics/JAKi; CVD: includes cardiac arrest, myocardial infarction, acute coronary syndrome, unstable angina, coronary artery disease, ventricular arrhythmia, congestive heart failure, cardiac revascularization procedure, other cardiovascular event, stroke, transient ischemic attack, deep vein thrombosis, peripheral arterial disease, pulmonary embolism, carotid artery disease; CDAI, Clinical Disease Activity Index; MTX: methotrexate; csDMARDs: conventional synthetic DMARD; JAKi: Janus Kinase inhibitor; [a]: Two-sample t-tests are used for continuous variables, chi-squared independence tests for categorical or dichotomous variables; Fisher's exact tests are used for categorical/dichotomous variables with category size smaller than 5; [**]: Excluding non-melanoma skin cancer; NA: Test was not conducted because of no variation across subgroups.

Table 3. Baseline characteristics of RA Japan and RA US drug initiators, stratified by line of therapy

RA-US, TNFi use was lower in the 1st (4% vs 8%), 2nd (40% vs. 63%), 3rd (32% vs 60%) and 4th line (23% vs 36%) of therapy.

Conclusion: Patients in RA Japan and RA US Registries differed in many aspects of demographics, comorbidity histories, clinical measures, and the utilization of DMARDs. Understanding cross-cultural differences in RA management is essential when interpreting results of studies from different countries.

Verstappen SM, et al. *Arthritis Care Res* (Hoboken). 2015 Dec;67(12):1637-45.

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8, Tanabe Mitsubishi Pharma, 8, Pfizer Japan, 8, Gilead, 5; **A. Sagawa**, None; **N. Koido**, AbbVie, 8, Bristol-Myers, 8, Celltrion, 8, Chugai, 8, Daiichi Sankyo, 8, Eisai, 8, Jansssen, 8, Ono, 8, Novartis, 8, Mitsubishi-Tanabe, 8; **C. Consortium**, None; **L. Harrold**, Bristol-Myers Squibb Company, 5; **T. Lin**, Corrona, LLC, 3; **J. Greenberg**, Corrona, LLC, 1, 3; **Y. Tanaka**, AbbVie, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 2, 5, 8, Asahi-kasei, 2, 5, 8, Novartis, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Astellas, 2, 5, 8, Chugai, 2, 5, 8, Daiichi-Sankyo, 2, 5, 8, Eisai, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Janssen, 2, 5, 8, Mitsubishi-Tanabe, 2, 5, 8, Pfizer, 2, 5, 8, Takeda, 2, 5, 8, YL Biologics, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8.

Abstract Number: 0830

Discontinuation Rate of Tofacitinib Is Similar When Compared to TNF Inhibitors in Rheumatoid Arthritis Patients: Real World Results from a Rheumatoid Arthritis Cohort

Mohammad Movahedi[1], Angela Cesta[2], Xiuying Li[3], Edward C Keystone[4] and Claire Bombardier[5], [1]Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada, [2]Toronto General Hospital Research Institute, Toronto, ON, Canada, [3]Toronto General Hospital Research Institute, Toronto, Canada, [4]Mount Sinai Hospital, Toronto, ON, Canada, [5]Institute for Work and Health, Toronto, ON, Canada

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Tofacitinib (TOFA) is an oral, small molecule drug used for rheumatoid arthritis (RA) treatment and is prescribed alone or with methotrexate (MTX). TOFA can be used as an alternative to biologic disease modifying antirheumatic drugs (bDMARDs) including tumor necrosis factor inhibitors (TNFi). We aimed to evaluate the discontinuation rate of TNFi compared to TOFA, in patients with RA in the Ontario Best Practices Research Initiative (OBRI).

Methods: RA patients enrolled in the OBRI initiating their TOFA or TNFi (adalimumab, certolizumab, etancercept, golimumab, and infliximab) between 1st June 2014 (TOFA approval date in Canada) and 31st Dec 2019 were included. Time to discontinuation were assessed using adjusted Kaplan-Meier (KM) survival and Cox regression models. To deal with confounding by indication, we estimated propensity scores for selected covariates with a standard difference greater than 0.1. We then adjusted models by applying stratification and inverse probability of treatment weight (IPTW) methods to compare discontinuation of TNFi versus TOFA. Multiple imputation (N=20) was used to deal with missing data for covaraites at treatment initiation.

Results: A total of 721 patients initiated TNFi (n=417) or TOFA (n=304) with mean (SD) disease duration of 8.9 (9.0) and 13.6 (9.6) years, respectively. In the TNFi group 82% were female and mean age (SD) at treatment initation was 57.0 (13) years. In the TOFA group, 85% were female and mean (SD) age at treatment initation was 60.7 (11) years. The TNFi group was less likely to have prior biologic use (22%) compared with the TOFA group (66%). At treatment initiation, the mean (SD) 28-swollen joint counts was siginificantly lower in the TNFi group [4.8 (4.0)] compared to the TOFA group [5.7 (4.4)]. Physical function measured by HAQ-DI was also significantly lower in TNFi compared to the TOFA group (1.1 vs.1.3).

Over a mean of 20.3 month follow-up, discontinuation was reported in 134 (32.1%) and 108 (35.5%) of all TNFi and TOFA patients, respectively. After adjusting for propensity score across 20 imputated datasets, there was no significant difference in discontinuation between treatment groups (adjusted HRs: 0.80, 95% CI: 0.60-1.05; p=0.11). The

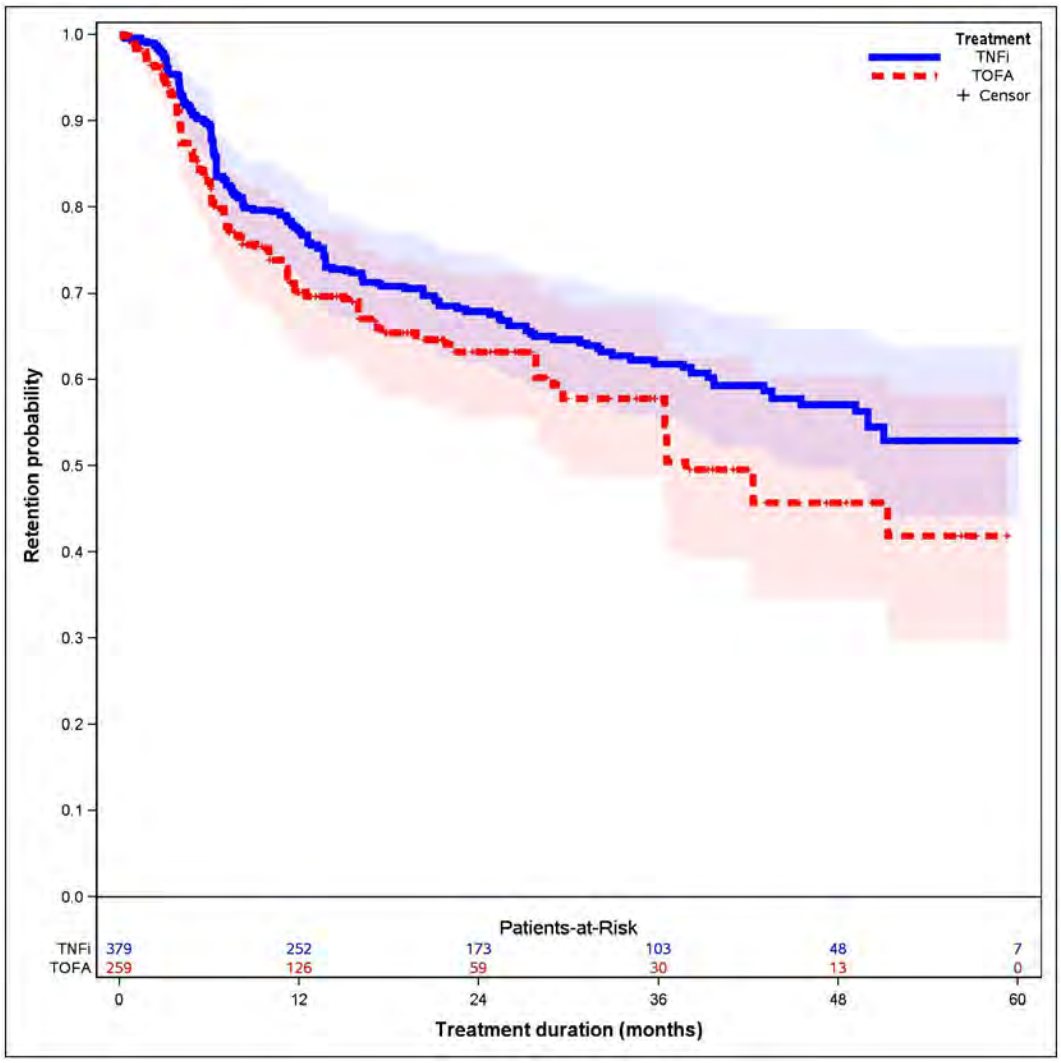

Figure 1. IPTW adjusted KM survival curves comparing discontinuation rates in patients treated with TNFi and TOFA.

results were similar for two propensity adjustment methods. Figure 1 shows IPTW adjusted KM survival curves comparing discontinuation rates in patients treated with TNFi and TOFA.

Conclusion: In this real world data study, we found that TNFi and TOFA retention is similar in patients with RA. Merging data with other RA registries in Canada is proposed to increase study power and to provide more robust results.

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Abstract Number: 0831

Sociodemographic, Disease, and Medication Profile of RA Patients Under 65 Years Compared with 65 Years or Older at Registry Enrollment: Real World Results from a Rheumatoid Arthritis Cohort

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Age is an important factor that can affect disease course, physical function and treat to target strategy for patients with rheumatoid arthritis (RA). We aimed to describe sociodemographic, disease and medication profile of patients with RA in the Ontario Best Practices Research Initiative (OBRI) by their assigned age group at time of their enrollment.

Methods: RA patients enrolled in the OBRI between 1st Jan 2008 and 31st Dec 2019 were included. Patients were allocated into two age groups, under 65 years and 65 years or older. Descriptive cross sectional analysis was used to compare sociodemographic characteristics (gender, ethnicity, spoken language, education, health insurance, and smoking status), disease activity [28 tender and swollen joint count (28SJC and 28TJC), physician global assessment (PhGA), clinical disease activity index (CDAI)], patient report outcomes (PROs) including patient global assessment (PtGA), fatigue score, global pain, and HAQ-DI, and medication profile (prior use of csDMARDs, prior use of bDMARDs, using new bDMARDs or csDMARDs) between the two age groups at enrollment. We calculated the standardized difference as the difference in means or proportions divided by the standard error. A significant difference between the two groups was defined as an absolute value greater than 0.10.

Results: A total of 3,734 patients were included; 2562 (68.5%) were under 65 yeras old and 1172 (31.5%) were 65 years or older.

Sociodemographic profile: Patients under 65 years were significantly more likely to be female (79.7 vs. 73.5%), non-caucasian (14.4 vs. 7.4%), current smokers (18.8 vs 9.3%) and have post-secondary education (62.6 vs. 44.6%), and more likely to have private health insurance (75 vs. 49%) and report English as their spoken language (7.0 vs 9.8%).

Disease activity and PROs profile: Patients under 65 years were significantly more likely to be antiCCP positive (63.0 vs. 57.5%), report higher PtGA (mean: 4.8 vs. 4.5), higher global pain (mean 4.8 vs. 4.4), higher fatigue score (mean 5.0 vs. 4.6), and lower HAQ-DI (mean 1.1 vs. 1.2). No other significant differences were found between the two age groups.

In terms of presence of comorbidities, patients under 65 years had significantly lower proportions of hypertension, cardiovascular disease, diabetes mellitus, lung disease, gastrointestinal disease and malignancy. However, interestingly this group of patients had a higher proportion of depression (17.8% vs 13.3%).

Medication profile: At enrollment, patients under 65 years were significantly more likely to have used prior bDMARDs (31.4 vs.26.1%), and were more likely to be starting a new bDMARD (17.1 vs. 12.8%), or csDMARDs (38.6 vs. 35.6%). No difference in prior use of csDMARDs was found between the two groups.

Conclusion: In this real world data descriptive study, we found that disease activity measures were similar in patients under 65 years compared to those 65 years or older. However, sociodemographics, PROs , comorbidities, and medication profiles were different between two groups. These differences should be taken into account for any clinical decision toward outcome improvement in patients.

Disclosure: M. Movahedi, None; **A. Cesta**, None; **X. Li**, None; **C. Bombardier**, CIHR, 2, MOHLTC, 2, Abbvie, 2, Amgen, 2, Janssen, 2, Medexus, 2, Merck, 2, 5, Novartis, 2, Pfizer, 2.

Abstract Number: 0832

PROSARA - A Prospective, Multicenter, Noninterventional Study to Evaluate the Safety and Effectiveness of Sarilumab for the Treatment of Active Rheumatoid Arthritis in Regular Care in Germany

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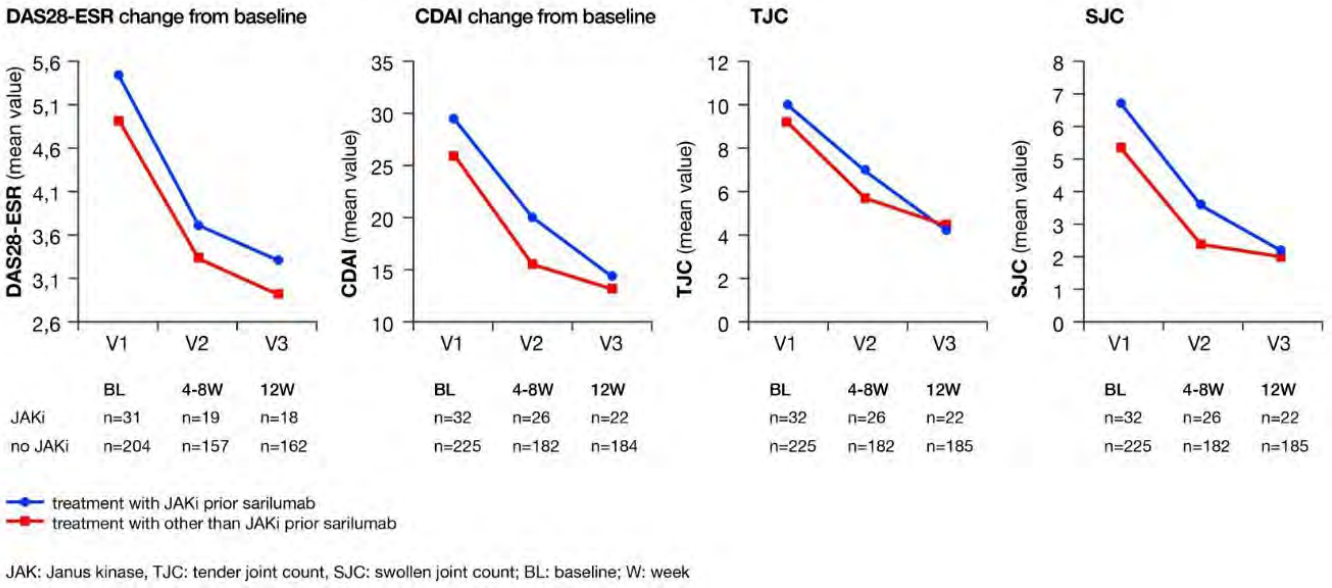
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Blockade of IL-6 signaling by sarilumab has been demonstrated to be an effective treatment approach for RA. Due to strict inclusion and exclusion criteria, randomized controlled trials may not represent the heterogeneous RA patient population encountered in regular care. Here we investigated the safety and effectiveness of sarilumab in the treatment of RA in regular care in Germany.

Methods: The prospective, observational, single-arm, 24-month PROSARA study (SARILL08661) is currently under way in Germany at 79 sites, aiming to include up to 750 patients with RA treated with sarilumab. Patients are selected at physician discretion and treated according to label. Study objectives include documentation of safety and various effectiveness outcomes. This interim analysis included patients with data available up to 12 weeks. All analyses are descriptive only.

Results: To date 348 patients were included in the study, 304 had baseline data, and 265 also had postbaseline data. The mean age was 59 years (range, 24–83 years); 76% (232/304) were women. Mean disease duration was 10 years; 81% (242/300) of patients had comorbidities. At baseline, 32% (86/265) of patients were biologic- and targeted synthetic DMARD (tsDMARD)-naive. Prior treatments with biologic or tsDMARDs included TNF inhibitors (TNFi; 56% [149/265]), non-TNFi biologics (29% [77/265]), and Janus kinase inhibitors (JAKi, 17% [46/265]). At baseline,

Figure 1. Effectiveness of sarilumab in patients switched from JAKi vs. patients switched from other DMARDs.



JAK: Janus kinase, TJC: tender joint count, SJC: swollen joint count; BL: baseline; W: week

Figure 1

49% (149/304) received sarilumab as monotherapy and 29% (88/304) in combination with conventional DMARDs; combination treatment status was not specified for 22% (67/304) of patients. After 12 weeks of sarilumab treatment, the mean ± SD DAS28-ESR score decreased from 5.0 ± 1.5 to 3.0 ± 1.4 and Clinical Disease Activity Index (CDAI) from 26.7 ± 13.8 to 13.6 ± 11.4. DAS28-ESR remission and low disease activity (LDA) were achieved in 43% (77/180) and 59% (107/180) of patients, respectively; 14% (28/206) and 49% (101/206) reached CDAI remission and LDA. At Week 12, 9% (19/201) of patients had Boolean remission. HAQ-disability index improved from 1.3 at baseline to 1.1 at Week 12 (n=195). Mean CDAI improvement at Week 12 was similar for autoantibody (RF or anticitrullinated protein antibody)-positive and -negative patients (–12.5 vs –15.4, respectively). Patients switching from JAKi to sarilumab (n=32) had longer disease duration than patients who switched from another compound. Of note, similar efficacy was observed between patients who switched from JAKi to sarilumab and those who switched from other DMARDs; disease activity measures (DAS28, CDAI, tender joint count, and swollen joint count) and global assessments improved consistently (Figure 1). Safety was consistent with the anticipated profile of IL-6 receptor inhibition and no new safety signals were observed. Adverse events (AEs) and serious AEs were reported in 34% and 6% of patients, respectively.

Conclusion: Sarilumab administered in regular care was associated with rapid and clinically meaningful improvements in a general RA population, including patients switching from JAKi. The safety profile was consistent with data reported from controlled clinical trials.

Disclosure: E. Feist, AbbVie, 5, 8, BMS, 5, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8, Sobi, 5, 8; **P. Aries**, Sanofi, 5, 8; **S. Zinke**, None; **H. Burkhardt**, AbbVie, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Boehringer Ingelheim, 5, 8, Bristol Myer Scripps, 5, 8, Chugai, 5, 8, Eli Lilly, 5, 8, Janssen, 5, 8, Novartis, 5, 8, Sanofi, 5, 8, UCB, 5, 8; **I. Albrecht**, Sanofi, 3; **O. Bley**, Sanofi, 3; **M. Obermeier**, None; **P. Sternad**, None; **M. Welcker**, AbbVie, 2, 8, Amgen, 8, BMS, 2, Celgene, 2, 8, Hexal, 2, 8, Lilly, 2, 8, MSD, 8, Novartis, 2, 8, Roche, 2, Sanofi, 2, 8, UCB, 2, 8; **C. Kühne**, None; **A. Holst**, None; **N. Baerlecken**, None; **H. Tony**, AbbVie, 5, Astra-Zeneca, 5, BMS, 5, Chugai, 5, Janssen, 5, Lilly, 5, MSD, 5, Novartis, 5, Pfizer, 5, Roche, 5, Sanofi, 5.

Abstract Number: 0833

Optimized Treatment of Biological Disease Modifying Drugs in Routine Clinical Practice: Survival Study and Analysis of Patient Characteristics

Andrea De Diego Sola[1], César Antonio Egües Dubuc[2], Nerea Alcorta Lorenzo[1], Jesús Alejandro Valero Jaimes[2], Olga Maíz Alonso[3], Luis Maria Lopez Dominguez[1], Esther Uriarte Isacelaya[4], Jorge Cancio Fanlo[5], María Asunción Aranguren Redondo[6], María Belén Irastorza Larburu[7] and Joaquín María Belzunegui Otano[3], [1]Rheumatology Service, Hospital Universitario Donostia. San Sebastián, Spain, San Sebastian, Pais Vasco, Spain, [2]Hospital Universitario Donostia, San Sebastián, Spain, [3]Rheumatology Service, Hospital Universitario Donostia. San Sebastián, Spain, San Sebastian, Spain, [4]Hospital Universitario Donostia, San Sebastian, Spain, [5]Hospital Universitario Donostia, San Sebastian, Pais Vasco, Spain, [6]Pharmacology Service, Hospital Universitario Donostia. San Sebastián, Spain, San Sebastian, Spain, [7]Pharmacology Service, Hospital Universitario Donostia. San Sebastián, Spain, San Sebastián, Spain

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

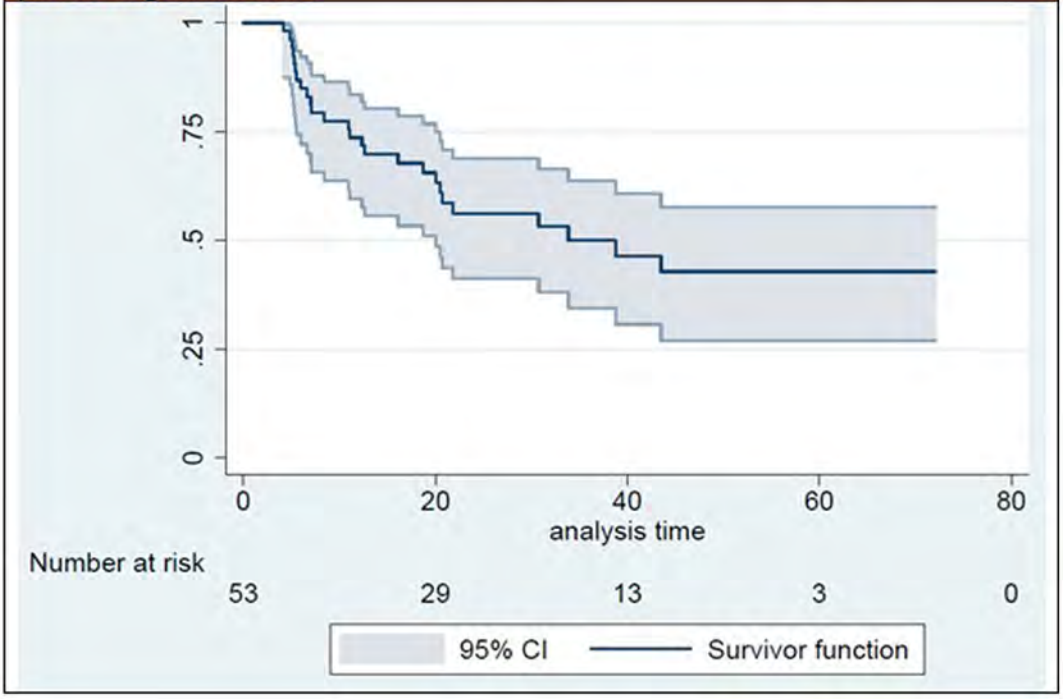
Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: The emergence of biological disease modifying drugs (bDMARD) has allowed a targeted approach to rheumatoid arthritis (RA) (“treat-to-treat” strategy). Once sustained remission is achieved, optimized treatment of bDMARD (OT) is considered: using drugs at lower doses than indicated in data sheets. Studies show that 33-64.2% of patients on OT lose remission in the first 6 months. Still, it is a feasible practice in selected patients and so, it is of interest to study the situation of optimized patients to improve our practice. Our objectives were to describe

Image 1: Kaplan-Meier survival estimate of optimized treatment of biological DMARDs in patients diagnosed with RA.



Time is expressed in months.

Table 1: Characteristics of the sample (N = 53)	
Female	40 (75.47%)
Age at diagnosis (years)	49.54 (11.68)
Active smoker	15 (33.33%)
ACPA positive*	36 (67.92%)
mRF positive*	44 (83.02%)
Nodules	11 (20.75%)
Extra-articular disease	11 (20.75%)
Erosions*	35 (74.47%)
Monotherapy at optimization	23 (43.4%)
bDMARD* previous to OT	0.71 (0.97)
Optimized bDMARD: • ETN • ADA • ABA • TCZ • GOL • CERT	 20 (37.74%) 16 (30.19%) 7 (13.21%) 7 (13.21%) 2 (3.77%) 1 (1.89%)
DAS28 at • Diagnosis • Beginning -1st sDMARD • Beginning -1st bDMARD • Beginning -Opt bDMARD • Optimization	 4.88 (1.25) 4.62 (1.6) 4.98 (1.06) 4.67 (1.17) 1.88 (0.65)
Months from diagnosis to introduction of 1st sDMARD*	19.67 (35.01)
Months from disease debut to low activity*	38.75 (30.34)
Months in low activity until start of OT	23.73 (22.47)

ACPA: anti-citrullinated protein antibodies; mRF: monoclonal rheumatoid factor; Erosions: presence of erosions at Optimization; bDMARD: biological DMARD; ETN: Etanercept; ADA: Adalimumab; ABA: Abatacept; TCZ: Tocilizumab; GOL: Golimumab; CERT: Certolizumab; Opt bDMARD: bDMARD optimized; csDMARD: conventional synthetic DMARD; Low activity: DAS28 < 3.2

demographic, clinical, analytical and therapeutic characteristics of RA patients on OT in our hospital. Secondly, to study the survival of OT and to compare patients with survival longer or shorter to one year.

Methods: We did a retrospective review of the medical records of RA patients who began bDMARD OT [Abatacept (ABA), anti-TNF drugs and Tocilizumab (TCZ)] between January 2014 and December 2018. We defined the end of OT as the restart of the usual dose. Continuous variables are described with mean and standard deviation (SD) and qualitative variables are shown in absolute value and percentage. We divided the sample into patients with OT survival greater than or equal to one year and patients with OT survival less than one year, after which the characteristics of both populations were compared. Categorical variables were analyzed using Pearsons chi^2 and quantitative variables using Student's t-test. Survival analysis was performed using a Kaplan-Meier estimator.

Results: We identified 234 RA patients on bDMARD at our hospital, of which 53 (22.6%) had been optimized between January 2014 and December 2018: 39 (73.6%) with anti-TNF, 7 (13.2) with ABA and 7 (13.2%) with TCZ. Their characteristics are shown in Table 1. It is worth mentioning the rate of monotherapy (43.3%) and the low number of bDMARD prior to optimization (median 0.71, SD 0.97). The median survival of OT was 33.8 months (Image 1) and thirty-nine patients (73.6%) maintained OT for at least one year (95% confidence interval, 0.59 to 0.83). When comparing patients with survival greater/equal versus shorter to one year (Table 2), the only variable showing significant differences was

Table 2: Comparison according to OT survival time			
	OT survival <1 year (N=14)	OT survival ≥1 year (N=39)	p Value
Female	12 (85.71%)	28 (71.79%)	0.299
Age at diagnosis (years)	50.25 (SD 11.87)	49.33 (SD 11.77)	0.815
ACPA positive	10 (71.43)	27 (69.23%)	0.918
mRF positive	13 (92.86%)	31 (84.62%)	0.480
Nodules	5 (35.71%)	6 (15.79)	0.119
Extra-articular disease	5 (35.71%)	6 (15.79)	0.108
Erosions	7 (50%)	28 (84.85%)	0.012
Months from debut to 1st csDMARD	34.67 (SD 55.25)	14.09 (SD 22.41)	0.0701
Months from Opt bDMARD start to OT	49.8 (SD 36.32)	40.78 (SD 34.62)	0.414
Months from debut to remission	31.38 (SD 20.61)	41.45 (SD 33.1)	0.3526
Months from remission to optimization	20.75 (SD 23.02)	24.72 (SD 22.50)	0.587
Monotherapy at optimization	6 (42.86%)	17 (43.59)	0.962
bDMARD* previous to OT	0.64 (SD 0.93)	0.74 (SD 0.99)	0.742
DAS28 at diagnosis	4.84 (SD 1.69)	4.89 (SD 1.12)	0.922
DAS28 at beginning -1st csDMARD	4.31 (SD 1.77)	4.73 (SD 1.54)	0.517
DAS28 at beginning -1st bDMARD	4.64 (SD 1.07)	5.1 (SD 0.18)	0.2001
DAS28 at beginning -Opt bDMARD	4.56 (SD 1.49)	4.72 (SD 1.06)	0.701
DAS28 Optimization	2.06 (SD 0.69)	1.82 (SD 0.64)	0.241

the presence of erosions at beginning of OT (28 patients in the >1 year group vs 7 in the < 1 year group; p=0.012). Although the difference is not significant (p = 0.07), patients with a survival of less than one year have more time between the debut and the beginning of the first conventional synthetic DMARD (csDMARD).

Conclusion: Two limitations should be noted: the sample size and the lack of a homogeneous optimization schedule among rheumatologists. More studies are needed to define the characteristics of patients who can safely benefit from OT.

Disclosure: A. De Diego Sola, None; **C. Egües Dubuc**, None; **N. Alcorta Lorenzo**, None; **J. Valero Jaimes**, None; **O. Maíz Alonso**, None; **L. Lopez Dominguez**, MSD, Pfizer, Lilly, Gebro Pharma, 1; **E. Uriarte Isacelaya**, None; **J. Cancio Fanlo**, None; **M. Aranguren Redondo**, None; **M. Irastorza Larburu**, None; **J. Belzunegui Otano**, None.

Abstract Number: 0834

Is Disease Severity Greater Among Patients with Rheumatoid Arthritis Who Receive a Newly Approved Biologic? Real-world US Experience with Sarilumab from the ACR RISE Registry

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Treatments Poster II: Comparative Effectiveness, Biosimilars, Adherence & the Real World

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with RA who have received multiple biologics or targeted therapies over time tend to have more refractory and more severe disease, which may lead to worse clinical response to treatment. We examined characteristics of sarilumab-treated patients with RA in order to evaluate the hypothesis that disease severity was greater in those who received sarilumab shortly after its Food and Drug Administration (FDA) approval (May 2017) than in subsequent time periods.

Methods: Patients with RA who initiated sarilumab treatment from May 2017 to June 2019 were identified in the American College of Rheumatology's Rheumatology Informatics System for Effectiveness (RISE) registry. They were

Figure. Patient selection flow

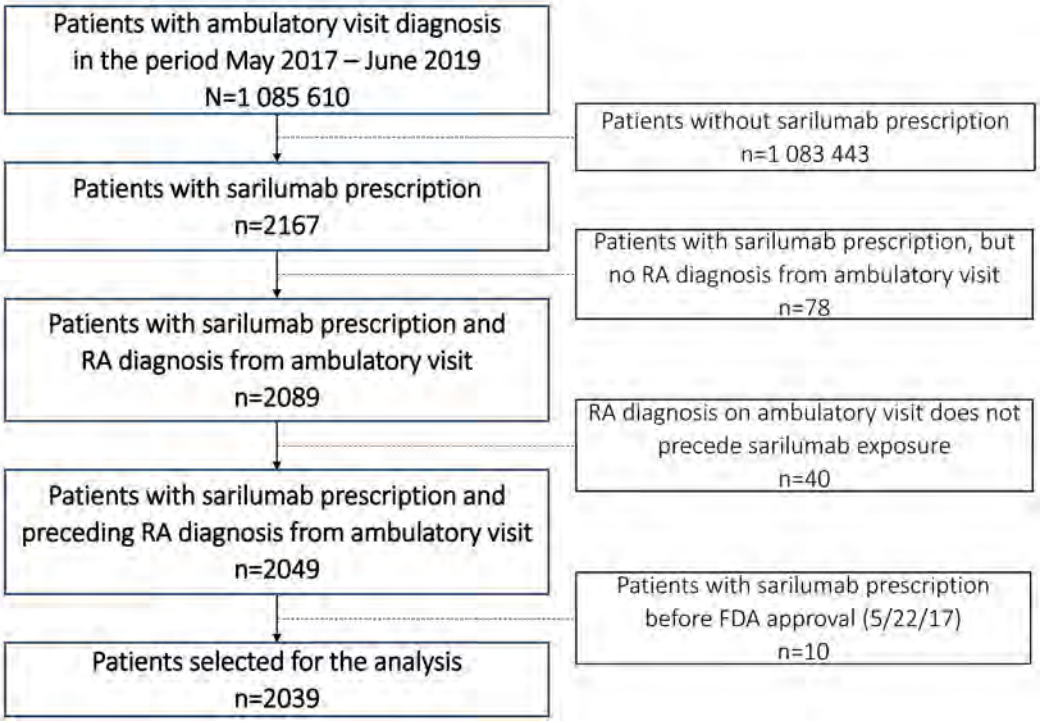

Figure 1

Table. Characteristics of patients with RA who initiated treatment with sarilumab at different time points relative to FDA approval

	Cohort 1 (May 2017–Mar 2018)	Cohort 2 (Apr 2018–Dec 2018)	Cohort 3 (Jan 2019–Jun 2019)	*P*-value
N	495	911	633	
Age, years, mean ± SD	56 ± 11	55 ± 12	55 ± 12	0.61
Women, n (%)	402 (81)	755 (83)	513 (81)	0.43
Race, n (%)				
White	354 (72)	638 (70)	443 (70)	
Black or African American	30 (6)	87 (10)	61 (10)	0.35
Other	24 (5)	37 (4)	23 (4)	
Missing	87 (18)	149 (16)	106 (17)	
Ethnicity (n=1560), n (%)				
Hispanic	28 (6)	55 (6)	37 (6)	0.40
Ambulatory visits, mean ± SD[a]	4.4 ± 3.3	3.9 ± 2.6	3.6 ± 2.2	**0.004**
CDAI score (n=661), mean ± SD	19.7 ± 13.0	18.5 ± 12.5	18.9 ± 13.5	0.64
CDAI category (n=673), n (%)				
High	52 (33)	107 (35)	66 (32)	
Moderate	72 (46)	70 (23)	76 (36)	0.26
Low	28 (18)	108 (35)	52 (25)	
Remission	6 (4)	21 (7)	15 (7)	
RAPID3 score (n=1045), mean ± SD[a]	13.5 ± 6.9	13.9 ± 7.2	13.8 ± 6.8	0.65
RAPID3 category (n=1058), n (%)[a]				
High	122 (54)	304 (61)	204 (61)	
Moderate	68 (30	105 (21)	78 (23)	0.22
Low	20 (9)	55 (11)	32 (10)	
Remission	14 (6)	36 (7)	20 (6)	
RA-related parameters				
Current/recent MTX use, n (%)[a]	134 (27)	251 (28)	148 (23)	0.16
History of MTX use, n (%)	302 (61)	569 (62)	407 (64)	0.52
csDMARD count, mean ± SD	1.5 ± 1.1	1.4 ± 1.0	1.5 ± 1.0	0.11
TNFi use, n (%)	344 (70)	646 (71)	440 (70)	0.79
Non-TNFi count, mean ± SD	0.9 ± 1.0	0.8 ± 0.9	0.7 ± 0.8	**0.002**
Tocilizumab use, n (%)	204 (41)	285 (31)	175 (28)	**<0.0001**
Non-TNFi or JAKi count, mean ± SD	1.4 ± 1.2	1.2 ± 1.1	1.1 ± 1.0	**0.02**
Biologics count, mean ± SD	2.6 ± 1.9	2.4 ± 1.7	2.3 ± 1.7	0.26
Current/recent oral steroid use, n	278 (56)	452 (50)	320 (61)	**0.05**
(%)[a]	118 (58)	235 (56)	162 (56)	0.94
Seropositive (n=911), n (%)	0.5 ± 0.6	0.7 ± 0.5	0.7 ± 0.6	0.06
HAQ-DI score (n=224), mean ± SD	0.3 ± 0.4	0.4 ± 0.4	0.4 ± 0.4	0.36
MDHAQ score (n=427), mean ± SD				
Current/recent opioid use, n (%)[a]	101 (20)	178 (20)	86 (14)	**0.003**
CRP, mg/L (n=1189), mean ± SD[a]	10.4 ± 15.5	11.3 ± 22.8	11.2 ± 20.3	0.39
Comorbidities and indices				
Diabetes, n (%)	24 (5)	39 (4)	30 (5)	0.86
COPD, n (%)	8 (2)	16 (2)	8 (1)	0.74
Hypertension, n (%)	57 (12)	92 (10)	63 (10)	0.64
RDCI, mean ± SD	0.5 ± 1.0	0.4 ± 0.9	0.4 ± 0.9	0.78
RxRisk count, mean ± SD[b]	2.2 ± 4.0	1.5 ± 3.4	1.5 ± 3.3	**0.002**
Elixhauser, mean ± SD	1.6 ± 1.1	1.5 ± 1.0	1.5 ± 1.0	0.48

Characteristics reported using all available prior data unless otherwise indicated. Bolded P-values are ≤0.05.
[a] Measured at the 12-month period prior to sarilumab initiation; [b]Comorbidity based on prescription use
CDAI=Clinical Disease Activity Index; COPD=chronic obstructive pulmonary disease; csDMARD=conventional synthetic DMARD; HAQ-DI=HAQ-Disease Index; FDA=Food and Drug Administration; JAKi=Janus kinase inhibitor; MDHAQ=multidimensional HAQ; RAPID=routine assessment of patient index data; RDCI=Rheumatic Disease Comorbidity Index; TNFi=TNF inhibitor

Table 1

divided into 3 cohorts based on time since FDA approval, with the overall period divided into tertiles rounded to the nearest calendar quarter (Cohort 1: May 2017 to March 2018; Cohort 2: April 2018 to December 2018; Cohort 3: January 2019 to June 2019). Patient characteristics reflecting demographics, RA-related features, and comorbidities (measured based on prescriptions, using the RxRisk score) were evaluated using all available data prior to sarilumab initiation. Between-cohort comparisons were made using chi-square test for categorical variables and a nonparametric test for continuous variables.

Results: A total of 2039 patients, treated by 585 rheumatologists, initiated sarilumab treatment in the period May 2017–June 2019 (Figure). Cohort comparison showed relative similarity over the 3 time periods in terms of patients' age, sex, race, and most clinical characteristics (Table). However, patients receiving sarilumab shortly after FDA ap-

proval (Cohort 1) had more ambulatory visits, a greater number of previously used non-TNF inhibitor (TNFi) biologics (particularly tocilizumab), a higher comorbidity burden, and were more likely to be current users of glucocorticoids or opioids than patients in Cohorts 2 and 3. Ongoing work is evaluating comparative response to therapy in the 3 cohorts.

Conclusion: We observed modest evidence for channeling of patients with greater RA severity and greater prior exposure to non-TNFi biologics to a newly introduced biologic, although disease activity at time of initiation was comparable over the 3 time periods. For real-world evidence generation, considerations should include cohort effects related to the timing of new drug approval in order to make valid inferences resulting from comparative effectiveness research.

Disclosure: S. Fiore, Sanofi, 1, 3; **L. Chen**, None; **C. Clinton**, None; **H. Yun**, Pfizer, 2; **A. Praestgaard**, Sanofi, 3; **K. Ford**, Sanofi Genzyme, 1, 2; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5.

Abstract Number: 0835

Pathogenic Effect of Chronic Stress-induced interleukin-12/23p40 on Neuropsychiatric System in Lupus-prone Mouse

Nobuya Abe[1], Kenji Oku[1], Yuichiro Fujieda[1], Nobuhiko Takahashi[2], Kohei Karino[1], Michihito Kono[1], Masaru Kato[1], Yuki Tanaka[3], Rie Hasebe[4], Olga Amengual[1], Miwako Yamasaki[5], Masahiko Watanabe[5], Masaaki Murakami[3] and Tatsuya Atsumi[6], [1]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Hokkaido, Japan, [2]Division of Molecular Psychoimmunology, Institute for Genetic Medicine, Graduate School of Medicine, Hokkaido University, Sapporo, Japan, [3]Division of Molecular Psychoimmunology, Institute for Genetic Medicine, Graduate School of Medicine, Hokkaido University, Sapporo, Hokkaido, Japan, [4]Biomedical Animal Research Laboratory, Institute for Genetic Medicine, Hokkaido University, Sapporo, Hokkaido, Japan, [5]Department of Anatomy, Faculty of Medicine, Hokkaido University, Sapporo, Hokkaido, Japan, [6]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine, Hokkaido University, Sapparo, Hokkaido, Japan

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

Background/Purpose: Neuropsychiatric system is one of the major organs affected in systemic lupus erythematosus (SLE). However, the pathogenesis of neuropsychiatric SLE (NPSLE) has not been fully established due to a variety of pathogenic pathways including thrombosis, autoantibodies, cytokines, and microglial activation leading to neuronal damage. Physiopsychological stress affects immune responses, putatively being a risk factor for the development of autoimmune diseases. Therefore, we have hypothesized an impact of physiopsychological stress on the pathogenesis of NPSLE, and analyzed stress-induced neuropsychiatric impairment in a murine model of lupus with the aim of establishing a novel therapeutic approach for NPSLE.

Methods: We placed chronic sleep disturbance (SD) stress for 2 weeks on 6-8-week-aged female MRL/lpr lupus prone mice and MRL/MpJ control mice using SD cage (Melquest, Japan). Open field (OF) test and elevated plus maze (EPM) test were used to assess anxiety-like behavior. We performed immunohistochemistry to evaluate neuronal and microglial activation, and Golgi-Cox staining to assess dendric morphological changes of neurons. Gene expression was comprehensively analyzed using RNA sequencing, and enzyme-linked immunoassay was used to evaluate in-

terested protein level in cerebrospinal fluids (CSF) of the mice and of human including healthy controls and NPSLE patients.

Results: SD-subjected MRL/lpr exhibited less anxiety-like behavior than their counterparts in OF and EPM test, while control mice showed more anxiety when stressed. Stress activates ventral tegmental area, projecting medial prefrontal cortex (mPFC) and nucleus accumbens (NAcc). In the mPFC, SD-subjected MRL/lpr demonstrated significant numbers of phospho-cFos positive activated neuronal cells whereas both SD-subjected MRL/lpr and control mice contains higher number of such than SD-free mice in NAcc. Differential gene expressions of mPFC analyzed via RNA sequencing revealed that Il12b expression level was prominent in SD-subjected MRL/lpr. Il12b is reportedly expressed in microglia. We found that SD-subjected MRL/lpr had the highest numbers of activated microglia regarding the morphology and CD68 aggregation. The CSF level of interleukin (IL)-12/23p40 encoded by Il12b was the highest in SD-subjected MRL/lpr. Furthermore, NPSLE patients also showed higher CSF IL-12/23p40 levels than healthy controls and SLE patients without neuropsychiatric symptoms. In Golgi-Cox staining, the increased numbers of dendric spines in mPFC pyramidal neurons were observed only in SD-subjected MRL/lpr.

Conclusion: Physiopsychological stress induced abnormal behavior, microglial activation and elevated level of IL-12/23p40 in lupus model mice. Moreover, IL-12/23p40 in CSF was increased in NPSLE patients, possibly associated with the development of NPSLE. Our data indicates that IL-12/23p40 is a potential therapeutic target for NPSLE.

Disclosure: N. Abe, None; **K. Oku**, None; **Y. Fujieda**, None; **N. Takahashi**, None; **K. Karino**, None; **M. Kono**, GlaxoSmithKline K.K., 2; **M. Kato**, None; **Y. Tanaka**, None; **R. Hasebe**, None; **O. Amengual**, None; **M. Yamasaki**, None; **M. Watanabe**, None; **M. Murakami**, None; **T. Atsumi**, AbbVie Inc., 5, 8, 9, UCB Japan Co.,Ltd., 5, 8, Eisai Co., Ltd., 8, Gilead Sciences, Inc., 5, 8, Bristol Myers Squibb Co., 2, 8, Chugai Pharmaceutical Co., Ltd., 2, 8, 9, Mitsubishi Tanabe Pharma Corporation, 8, 9, Eli Lilly Japan K.K., 2, 5, 8, Astellas Pharma Inc., 8, 9, Pfizer Inc., 2, 8, 9, Daiichi Sankyo Company, Limited, 5, 8, 9.

Abstract Number: 0836

SH3BP2 Deficiency Ameliorates Murine Systemic Lupus Erythematosus

Tomoyuki Mukai[1], Kyoko Kawahara[1], Masanori Iseki[2], Akiko Nagasu[1], Hajime Nagasu[3], Takahiko Akagi[1], Shoko Tsuji[1], Yasuyoshi Ueki[4], Katsuhiko Ishihara[2], Naoki Kashihara[3] and Yoshitaka Morita[1], [1]Department of Rheumatology, Kawasaki Medical School, Kurashiki, Okayama, Japan, [2]Department of Immunology and Molecular Genetics, Kawasaki Medical School, Kurashiki, Okayama, Japan, [3]Department of Nephrology and Hypertension, Kawasaki Medical School, Kurashiki, Okayama, Japan, [4]Department of Biomedical Sciences and Comprehensive Care, Indiana University School of Dentistry, Indianapolis, IN

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Background/Purpose: The adaptor protein, Src homology 3 domain-binding protein 2 (SH3BP2), is widely expressed in immune cells, such as myeloid cells, B cells, and T cells. It controls intracellular signaling pathways such as Syk and Src. The present study was undertaken to investigate the role of SH3BP2 in a murine systemic lupus erythematosus model and to explore differential phenotypes in immune cell sub-populations isolated from SH3BP2-deficient mice.

Methods: For the lupus model, we used *Fas*^{lpr} mice (C57BL/6 background). Clinical and immunological phenotypes were compared between *Fas*^{lpr} and SH3BP2-deficient *Fas*^{lpr} mice. Splenomegaly and renal involvement were assessed in 35-week-old mice. Serum levels of anti-dsDNA antibody and rheumatoid factor were determined using ELISA. Lymphocyte subsets in spleen and lymph nodes were analyzed by flow cytometry. To examine the role of SH3BP2 in specific cells, B cell-specific SH3BP2-deficient lupus mice were generated and analyzed; differentiation of bone marrow-derived dendritic cell and activation of T cells and macrophages were determined in vitro.

Results: SH3BP2 deficiency significantly reduced lupus-like phenotypes, such as splenomegaly, renal involvement, elevated serum dsDNA antibody and rheumatoid factor, and increased splenic $B220^{+}CD4^{-}CD8^{-}$ T cells. Notably, SH3BP2 deficiency in B cells did not rescue the lupus-like phenotypes. Interestingly, SH3BP2 deficiency suppressed the differentiation of dendritic cells but it did not affect the functions of T cells and macrophages in vitro.

Conclusion: SH3BP2 deficiency ameliorated clinical and immunological manifestations in lupus-prone mice, possibly via targeting dendritic cells differentiation. Modulating SH3BP2 expression could thus provide a novel therapeutic approach to autoimmune diseases.

Disclosure: T. Mukai, Chugai Pharmaceutical Co., 2, AYUMI Pharmaceutical Co., 2; **K. Kawahara**, Chugai Pharmaceutical Co., 2, AYUMI Pharmaceutical Co., 2; **M. Iseki**, None; **A. Nagasu**, Chugai Pharmaceutical Co., 2, AYUMI Pharmaceutical Co., 2; **H. Nagasu**, None; **T. Akagi**, Chugai Pharmaceutical Co., 2, AYUMI Pharmaceutical Co., 2; **S. Tsuji**, Chugai Pharmaceutical Co., 2, AYUMI Pharmaceutical Co., 2; **Y. Ueki**, None; **K. Ishihara**, None; **N. Kashihara**, None; **Y. Morita**, Chugai Pharmaceutical Co., 2, AYUMI Pharmaceutical Co., 2.

Abstract Number: 0837

Deletion of miR-223 Exacerbates Lupus Nephritis by Targeting S1pr1 in *Fas*$^{lpr/lpr}$ Mice

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: To identify new candidate genes regulated by micro RNAs (miRNAs) and involved in the pathogenesis of systemic lupus erythematosus (SLE), we integrated miRNA and messenger RNA (mRNA) expression profiling data in $CD4^{+}$ splenic T cells derived from lupus-prone MRL/MpJ-*Fas*^{lpr} /J (MRL/lpr) mice and C57BL6/J (B6) mice. The reduction of sphingosine-1-phosphate receptor 1 (*S1pr1*) and upregulation of miR-223-3p in the splenic T cells in MRL/lpr was identified and we investigated the role of *S1pr1* as a predicted target of miR-223 (Mir223) in SLE.

Methods: L transduction particles containing luciferase reporter and *S1pr1*-3'UTR region was infected into human umbilical vein endothelial cells (HUVECs) for luciferase miRNA target screening. Luciferase reporter assay following co-transfection of lentiviral particles containing reporter vector with miR-223-3p mimic or nontargeting miRNA into HUVECs was performed. To further confirm that *S1pr1* is a target of miR-223-3p, miR-223-3p mimic or nontargeting miRNA was transfected into EL4 mouse T cell lines by lipofection. The transfection efficacy of miR-223-3p was con-

firmed by quantitative PCR (qPCR). The endogenous *S1pr1* mRNA and protein levels were detected by qPCR and Western blot analysis. To explore the involvement of miR-223-3p in SLE pathogenesis, we generated and analyzed *Mir223* knockout lupus-prone B6.MRL-*Fas*^{lpr} mice (*Mir223*$^{-/-}$*Fas*$^{lpr/lpr}$) until 44 weeks of age. The total IgG and titer of anti-ds-DNA antibodies in serum were measured by ELISA. Histopathological grading of glomerular, renal vascular and tubulointerstitial lesions were performed and the glomerular immune complex deposition was assessed by C3 and IgG staining. To clarify the cell types which infiltrates in glomerular lesion, immunofluorescence staining with CD4, CD8 and S1PR1 antibodies was performed. The cell population including apoptotic cells and S1PR1 positive cells in the lymph nodes and spleen were analyzed by flow cytometry. We also investigated the expression levels of *S1pr1* mRNA and miR-223-3p in circulating CD4$^+$ T cells isolated from SLE patients and healthy subjects.

Results: Transfection of HUVEC with mimic miR-223-3p significantly suppressed a luciferase-reporter containing the *S1pr1*-3'UTR. The mRNA levels of *S1pr1* was significantly decreased after miR-223-3p overexpression. *Mir223* deficiency increased the production of serum IgG2b and the proportion of CD3$^+$ T cells, CD3$^+$CD4$^-$CD8$^-$ T cells, CD19$^+$ B cells, CD19$^-$CD138$^+$ cells (Plasma cells), CD3$^+$S1PR1$^+$ T cells and CD3$^+$CD4$^+$S1PR1$^+$ T cells in spleen and the proportion of early apoptotic cells in CD4$^+$ and CD8$^+$ T cells in lymph nodes. Lupus nephritis in *Mir223* knockout mice was exacerbated accompanied with glomerulonephritis with infiltration of CD4$^+$S1PR1$^+$ T cells in glomerulus. *S1pr1* mRNA was significantly decreased in CD4$^+$ T cells from the patients with SLE. miR-223-3p tended to upregulate in lupus patients than healthy control. There was significant correlation between miR-223-3p and serum IgM titer.

Conclusion: Deletion of *Mir223* exacerbated the lupus phenotypes associated with increasing *S1pr1* expression in CD4$^+$T cells and their enhanced infiltration in inflamed kidney tissues.

Disclosure: S. Hiramatsu Asano, None; **T. Mukai**, None; **Y. Morita**, None; **J. Wada**, None.

Abstract Number: 0838

T Cell–Specific CaMKIV Deficiency Protects Mice from Imiquimod-induced Glomerulonephritis

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SESSION INFORMATION
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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease characterized by autoantibody production, immune complex deposition and multisystem involvement. Calcium/calmodulin-dependent protein kinase type IV (CaMK4) is serine-threonine kinase overexpressed in SLE CD4 T cells. Global CaMK4 deficiency or inhibition with a small drug in MRL/lpr mice resulted in prolonged survival, significant suppression of proteinuria, severity of glomerulonephritis and autoantibody production. Here, we hypothesized that targeted T cell specific deletion of CaMK4 will protect mice from the development of systemic autoimmune disease induced by application of imiquimod, a toll-like receptor agonist.

Methods: We generated T cell specific CaMK4 conditionally deficient mice on C57BL/6 background by using *Cre-loxP* system. Mice harboring loxP sites of *Camk4* gene (*Camk4* $^{flox/flox}$) were crossed with Cre transgenic mice driven by distal *Lck* promoter. Female mice were genotyped and 12 weeks old *Lck-Cre* positive and negative *Camk4* $^{flox/flox}$ littermates were used for the experiment. Mice were treated with imiquimod applied to the ears 3 times weekly for 8 weeks. Serum, urine, kidneys and other organs were collected for the analysis. Levels of dsDNA were measured by ELISA. Proteinuria was assessed by measuring albumin to creatinine ratio. Kidney sections were scored for damage in a blinded manner by using the renal activity index. T- test was used for statistical analysis and data are expressed as mean±SEM.

Results: *Lck-Cre+ Camk4* $^{flox/flox}$ mice had normal development and lifespan. We had 4 *Lck-Cre Camk4* $^{flox/flox}$ negative and positive mice per group. After 8 weeks of imiquimod treatment elevated levels of autoantibodies to double-stranded DNA were similar between the groups (*Lck-Cre +/ Camk4* $^{flox/flox}$:18.68±1.72 vs. *Lck-Cre -/ Camk4* $^{flox/flox}$ 21.73± 3.34 IU /ml). Spleen sizes were similar between the groups. Excitingly, proteinuria was significantly decreased in *Lck-Cre +/ Camk4* $^{flox/flox}$ mice compared to *Lck-Cre* negative (871.94±227.24 vs. 1437.9±275.56 mg/gr; p= 0.0023). Histopathologic examination of the kidneys showed that T cell specific CaMK4 deficiency in *LcK-Cre* positive animals significantly decreased infiltration in the kidney parenchima.

Conclusion: We have generated evidence that specific deletion of CaMKIV in T cells ameliorates severity of glomerulonephritis after the administration of the TLR7 agonist without affecting the production of antibodies to dsDNA. Our data support the development targeted delivery of a CaMK4 inhibitors to T cells for the treatment of patients with SLE.

Disclosure: M. Vukelic, None; **M. Umeda**, None; **A. Ferretti**, None; **R. Bhargava**, None; **N. Yoshida**, None; **G. Tsokos**, None.

Abstract Number: 0839

Single-Cell Transcriptomics of Mouse and Human Lupus Nephritis Identifies Conserved Myeloid Populations Across Species

Paul Hoover[1], Michael Peters[2], David Lieb[3], Rakesh Mishra[4], Nir Hacohen[2] and Anne Davidson[5], [1]Brigham and Women's Hospital, Boston, MA, [2]Broad Institute, Boston, [3]Broad Institute, Boston, MA, [4]Feinstein Institute, Manhasset, NY, [5]Northwell Health, New York

SESSION INFORMATION
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Background/Purpose: We recently identified novel immune cell states in the kidneys of lupus nephritis patients (Arazi et al, Nature Immunology 2019). To determine the similarities with lupus mouse models, we compared human immune cell transcriptomes to those from Sle1.Yaa and NZBW mouse kidneys. We focused on macrophages and DCs since intrarenal myeloid abundance may drive tissue damage in lupus patients.

Methods: We collected myeloid cells from dissociated kidneys from pre- and post-nephritic Sle1.Yaa and NZBW mice (3-4 mice per group). Using 10x Genomics we performed single cell transcriptomic profiling and analyzed droplets that contained >500 genes and UMIs after doublet removal. To identify intrarenal mouse immune cells equivalent to those in humans, we leveraged immune cell transcriptomes collected from the kidneys of lupus patients in AMP

Phase 1 to generate state-specific gene signatures from each human myeloid cell cluster composed of: (i) the top 10 to 40 most highly and ubiquitously differentially expressed (DE) genes, (ii) the top 4-10 DE transcription factors, or (iii) modules of co-varying genes from non-negative matrix factorization. After clustering mouse myeloid cells (Seurat v3.0), we calculated the average of the scaled expression for each human signature across mouse clusters to identify those most similar to human. We also calculated the Pearson correlation coefficient between human and mouse clusters using homologous genes with identical names between species.

Results: We mapped gene signatures from the human myeloid states: 'inflammatory' macrophages (CM0) that likely enter from blood and transition to 'phagocytic' (CM1) and 'reparative' (CM4) states; resident macrophages (CM2); dendritic cells (CM3). We identified the human CM0 signature in clusters from NZBW (and weakly in Sle1.Yaa) post-nephritic pro-inflammatory macrophage/DC clusters that infiltrate from blood, similar to CM0 cells in humans. The human CM1 signature mapped to clusters in both mouse models that resembled DCs and that were enriched for transendothelial migration. We identified in both models the CM4 signature in pre- and post-nephritic mouse clusters that resembled resident macrophages and were enriched for antigen presentation and lysosomal processing. Like humans, the post-nephritic CM4 mouse equivalent cluster exclusively expressed Ccl8, a leukocyte chemoattractant and activator, and Gas6, a mediator of apoptotic cell clearance and was skewed towards an alternative phenotype. Finally, we mapped the human CM3 signature to mouse CD103+ DCs and identified gene programs shared with humans for immunoregulation and antigen presentation.

Conclusion: From the kidneys of Sle1.Yaa and NZBW mice we identified human myeloid gene signatures: 'inflammatory' macrophages (CM0), 'phagocytic' (CM1), 'reparative' (CM4) states; dendritic cells (CM3); we did not find the human resident macrophage (CM2) signature. We identified putative functions shared between mouse and human clusters including antigen presentation, phagocytosis, Ccl8 expression. These analyses indicate that we may be able to study in mice some of the myeloid subsets and genes that are highly relevant to human disease.

Disclosure: P. Hoover, None; **M. Peters**, None; **D. Lieb**, None; **R. Mishra**, None; **N. Hacohen**, None; **A. Davidson**, None.

Abstract Number: 0840

Amelioration of Immune Complex-Mediated Glomerulonephritis via CD6 Modulation

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SESSION INFORMATION
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Background/Purpose: CD6 is a co-stimulatory receptor, predominantly expressed on T cells, that binds to activated leukocyte cell adhesion molecule (ALCAM), a ligand expressed on antigen-presenting cells and various epithelial and endothelial tissues. T cells are important contributors to the pathogenesis of SLE, especially in the development of kidney disease (lupus nephritis, LN). The CD6-ALCAM pathway plays an integral role in T cell activation, differentiation, proliferation, and trafficking, and increased levels of CD6 are associated with pathogenic T cell responses.

Thus, the CD6-ALCAM pathway is a potential contributor to disease pathogenesis and presents itself as a potential therapeutic target.

Methods: Nephrotoxic serum nephritis (NTN) is a validated, short-term model of LN. Disease was induced in two separate cohorts of female 129/svJ mice, both aged to 10 weeks. Mice were immunized with rabbit IgG and complete Freund's adjuvant on day 0, followed by passive transfer of pre-formed rabbit anti-mouse glomerular antibodies intravenously (i.e. nephrotoxic serum) given on day 5, causing an antibody-mediated nephritis similar in pathology to LN. One group of mice was treated 3x per week with anti-CD6 monoclonal antibody (10D12) (60ug/dose, n=23), while control mice were treated with either vehicle control (n=23) or isotype control (cohort 2 only, n=12). Healthy mice (immunized with rabbit IgG, but not given nephrotoxic serum) were also included as a control (n=12). We monitored the progress of kidney disease to assess the effect of the anti-CD6 treatment on both cohorts, and completed flow cytometry, RT-PCR, immunofluorescent staining, and multiplexed gene expression analysis to assess the effect of treatment on kidney disease development.

Results: Mice treated with anti-CD6 displayed decreased levels of proteinuria as measured by uristix and albumin:creatine ratios compared to vehicle control ($p < 0.0001$, $p < 0.0001$, respectively) and isotype control treated mice ($p < 0.05$, $p < 0.0001$, respectively). Blood urea nitrogen (BUN) levels were also significantly improved when comparing anti-CD6 to vehicle control treated mice ($p < 0.05$). Anti-CD6 treatment ameliorated glomerular histopathology, and had a near significant improvement in tubular histology. Flow cytometric analysis of kidney tissue indicated decreased numbers of activated T cells (CD4+CD25+CD69+, $p < 0.01$) as well as decreased inflammatory macrophages ($p < 0.05$). Finally, we performed a PCR array to assess expression of a number of inflammatory genes. When comparing anti-CD6 treated mice to both the vehicle and isotype control groups, 13 genes were significantly decreased in both comparisons, including *C3, CCL1, CCL2, CCL5, CCL7, CCL20, CSF1, CXCL3, CXCL2, CD14, CD40, CXCL5,* and *IL1rn*.

Conclusion: Anti-CD6 treatment is beneficial in ameliorating the nephritis associated with nephrotoxic antibody administration, an inducible model of lupus nephritis. These results suggest a promising therapeutic option that is more selective than the immunosuppressive therapies currently offered.

Disclosure: S. Chalmers, None; **S. Garcia**, None; **L. Herlitz**, None; **J. Ampudia**, Equillium, Inc, 3; **C. Ng**, Equillium, Inc, 3; **S. Connelly**, Equillium, Inc, 3; **C. Putterman**, Equillium, 1, 2.

Abstract Number: 0841

CD6 Modulation Ameliorates Kidney and Skin Disease in a Spontaneous Murine Lupus Model

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: T cells are an important contributor to the pathogenesis of SLE and lupus nephritis, and thus present themselves as interesting therapeutic targets. CD6 is a co-stimulatory receptor, predominantly expressed on T cells, that binds to activated leukocyte cell adhesion molecule (ALCAM), a ligand expressed on antigen-presenting cells and various epithelial and endothelial tissues. The CD6-ALCAM pathway plays an integral role in modulating T cell activation and trafficking, and could potentially be targeted within the context of SLE and LN as a therapeutic avenue. In this study, we assessed the expression of CD6 and ALCAM within the context of a murine model of SLE, and then targeted this signaling axis to determine its role in the pathogenesis of disease.

Methods: The MRL/lpr mouse is a spontaneous murine model of SLE, which exhibits systemic autoimmunity, nephritis, and skin disease. In an initial experiment, kidneys from 6-month old MRL/lpr and B6 mice were analyzed for the presence of both ALCAM and CD6. Following the initial experiment, two separate cohorts of female MRL/lpr mice were aged to 9-10 weeks of age, at which point treatment was begun with either anti-CD6 monoclonal antibody (60 ug/dose, intraperitoneally twice per week), isotype control (60 ug/dose, twice per week), or cyclophosphamide (25 mg/kg, once per week). We also included a no treatment group, and a group of MRL/MpJ mice, a congenic control strain. Baseline levels of anti-DNA antibodies, weight, and proteinuria in the MRL/lpr groups were similar. Mice were monitored weekly for proteinuria, lymph node swelling, and macroscopic skin lesions.

Results: At 6 months, when disease is advanced, analysis of ALCAM and CD6 expression by both flow cytometry and immunofluorescence revealed increased levels of ALCAM in renal myeloid cell populations and within the glomeruli and tubules, and increased expression of CD6 on renal T cell subsets, in MRL/lpr compared to B6 healthy control mice. Subsequently, we blocked this signaling axis in MRL/lpr mice using a monoclonal antibody against CD6. Anti-CD6 treatment significantly improved proteinuria levels as measured by uristix and albumin:creatine ratios compared to isotype control treated mice. Blood urea nitrogen levels were also significantly improved ($p< 0.05$), and survival of anti-CD6 treated mice was significantly better than isotype control mice ($p=0.05$). Histology of renal tissue revealed an improvement with anti-CD6 treatment and immunofluorescence staining showed decreased accumulation of renal T cells and myeloid cells. Flow cytometry confirmed decreased renal infiltration T cells and myeloid cells, specifically activated and memory CD4+ T cells and memory CD8+ T cells. Interestingly, anti-CD6 treatment also decreased lymph node size and improved macroscopic skin lesions. The results were confirmed in two separate cohorts.

Conclusion: In a spontaneous model of SLE, anti-CD6 treatment ameliorated pathology in multiple end organs, namely the kidney and skin. Overall, these results indicate that targeting CD6-ALCAM interactions may have promising therapeutic potential within the context of different end organ pathologies of SLE.

Disclosure: S. Chalmers, None; **S. Garcia**, None; **R. Ayilam Ramachandran**, None; **C. Mohan**, Equillium, Inc, 6; **L. Herlitz**, None; **D. Chu**, Equillium, Inc, 3; **J. Ampudia**, Equillium, Inc, 3; **C. Ng**, Equillium, Inc, 3; **S. Connelly**, Equillium, Inc, 3; **C. Putterman**, Equillium, 1, 2.

Abstract Number: 0842

mTOR Signaling Pathway Blockade and Rab4 Expression Affects Metabolism of Lupus T Cells

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Background/Purpose: Pro-inflammatory T-cell development underlies the pathogenesis of systemic lupus erythematosus (SLE). Activation of the mechanistic target of rapamycin (mTOR) plays a central role in T-cell lineage specification both under physiological conditions and during inflammation in SLE. Persistent mitochondrial hyperpolarization (MHP) and the accumulation of mitochondria underlie mTOR activation which serves as a biomarker of pathogenesis and target for treatment in SLE (Nat Rev Rheumatol 2016; 12: 169-82). HRES-1/Rab4, a small GTPase enzyme regulating endosomal trafficking, is overexpressed in lupus T cells and triggers the accumulation of mitochondrial mass and the activation of mTOR. Therefore, understanding metabolic consequences of HRES-1/Rab4 overexpression is expected to shed light on the mechanisms of proinflammatory T cell lineage development in SLE.

Methods: To study the effects of Rab4A expression and mTOR pathway activity in T cells, a site-specific Cre/Lox recombinase system was used to knock down Rab4A expression in lupus-prone triple congenic SLE 1.2.3 mice. The mice were treated with 3 mg/kg intraperitoneal rapamycin three times weekly or solvent control or 10 g/l N-acetylcysteine (NAC) in the drinking water for 14 weeks starting at 27 weeks of age. The metabolic flux was characterized by feeding ^{13}C-sTable isotope labeled nutrients, such as glucose or glutamine, to cells in culture and subsequently measuring isotope labeled metabolites using liquid chromatography-mass spectrometry (LC-MS) after the preparation of cell extracts.

Results: Activation of Rab4A in triple congenic SLE 1.2.3 (B6.TC/ Rab4A^{Q72L}) mice carrying constitutively active Rab4A^{Q72L} alleles had earlier and more severe onset of glomerulonephritis (GN), ANA production and proteinuria than parental lupus-prone controls (B6.TC). In turn, deletion of Rab4A in T cells blocked GN, ANA production and proteinuria. Rapamycin and NAC reduced disease activity in B6.TC/ Rab4A^{Q72L} mice. Rapamycin decreased metabolic flux in CD8+ T cells from ^{13}C -labeled glutamine into mitochondrial tricarboxylic cycle metabolites, such as alfa-ketoglutarate (38% decrease, p=0.005), citrate (37% decrease, p=0.0018) and malate (20% decrease, p=0.025). NAC increased the metabolic flux derived from ^{13}C-labeled glutamine in CD8+ T cells into alfa-ketoglutarate (66% increase, p=0.046), citrate (53% increase, p=0.048) and malate (51% increase, p=0.032). T cell-specific deletion of Rab4A increased ^{13}C-labeled glucose flux into the non-oxidative pentose phosphate pathway (PPP) metabolite, sedoheptulose-7-phosphate (180% increase, p=0.002) and glycolysis intermediates glucose-6-phosphate/fructose-6-phosphate (61% increase, p=0.034) in CD4+ T cells. Rab4A deletion increased glutathione concentration in CD4+ T cells (101% increase, P=0.014).

Conclusion: mTOR pathway blockade and Rab4A inactivation may provide therapeutic targets for correcting pro-inflammatory metabolic dysfunction of T cells in SLE.

Disclosure: T. Faludi, None; **N. Huang**, None; **M. Duarte**, None; **J. Lewis**, None; **A. Perl**, None.

Abstract Number: 0843

Rab4A Activation Predisposes to Hepatitis in Spontaneous and Pristane-Induced Mouse Models of Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: HRES-1/Rab4 or Rab4A, a GTPase responsible for mitochondrial oxidative stress[1] and activation of the mechanistic target of rapamycin[2], is overexpressed in T cells of systemic lupus erythematosus (SLE) patients[3] and livers of lupus-prone mice[4]. Therefore, we investigated the impact of Rab4A on hepatitis in spontaneous and pristane-induced mouse models of SLE.

Methods: C57Bl/6J wild-type (B6) mice, strains expressing constitutively active Rab4A ($Rab4A^{Q72L}$) in all cells, and strains lacking Rab4A in T cells ($Rab4A^{CD4\text{-}KO}$) were injected intraperitoneally (ip) with pristane (500µL/20g body weight). $Rab4A^{Q72L}$ and $Rab4A^{CD4\text{-}KO}$ mice were generated on both B6 and lupus prone *SLE1.2.3 B6*-triple congenic backgrounds (B6.TC). Rapamycin was administered to 27-week-old B6.TC mice (ip) 3 times weekly at a concentration of 3 µg/g for 14 weeks. The number of inflammatory cells, inflammatory foci, cells/foci, and vasculitic lesions were used to measure inflammation normalized to surface area within mouse livers. Vasculitis was scored as earlier

Rab4 Pristane	C57Bl/6J $Rab4A^{WT}$ (n=5) [A] (Wild Type)	C57Bl/6J $Rab4A^{CD4\text{-}KO}$ (n=5) [B] (T Cell Knock Out)	C57Bl/6J $Rab4A^{Q72L}$ (n=5) [C] (Constitutively Active)	P value: C57Bl/6J $Rab4A^{WT}$ vs C57Bl/6J $Rab4A^{CD4\text{-}KO}$ [A vs B]	P value: C57Bl/6J $Rab4A^{WT}$ vs. C57Bl/6J $Rab4A^{Q72L}$ [A vs. C]	P value: C57Bl/6J $Rab4A^{CD4\text{-}KO}$ vs. C57Bl/6J $Rab4A^{Q72L}$ [B vs C]
Inflammatory Cells/mm²	65.02±16.25	23.51±8.30	27.048±9.15	0.053	**0.076**	0.782
Number of Foci/mm²	1.62±0.44	0.32±0.10	1.01±0.39	**0.042**	0.336	0.157
Number of Cells/Focus/mm²	2.96±0.48	4.76±0.08	3.08±0.48	0.308	0.867	0.338
Number of Vasculitic Lesions/mm²	1.68±0.46	0.22±0.02	0.76±0.42	**0.033**	0.177	0.277
Vasculitis Score	3.070±0.113	2±0.324	2.935±0.182	**0.00161**	0.524	**0.0139**

Table summary of Rab4 effect on Pristane-induced SLE liver disease.

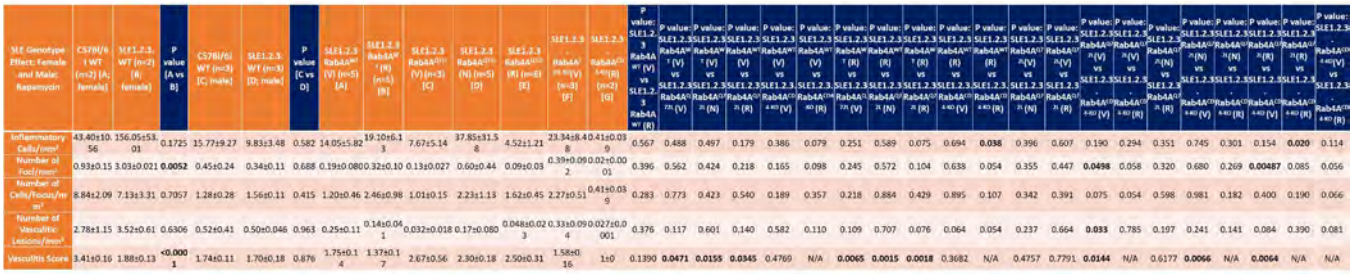

Table. summary of liver disease in the following genotypes: Female SLE1.2.3. vs. female C57Bl/6J; Male SLE1.2.3. vs. male C57Bl/6J; Vehicle/NAC/Rapamycin effects on female SLE1.2.3. mice (30-50 weeks of age) with differential Rab4A expression (Wild Type, Q72L, CD4KO).

SLE Background Female Mice: Rab4A	C57Bl/6J Rab4A^{WT} (n=4) [A]	C57Bl/6J Rab4A^{Q72L} (n=4) [B]	C57Bl/6J Rab4A^{CD4-KO} (n=4) [C]	SLE1.2.3 Rab4A^{WT} (n=4) [D]	SLE1.2.3 Rab4A^{Q72L} (n=3) [E]	SLE1.2.3. Rab4A^{CD4-KO} (n=4) [F]	P value: C57Bl/6J Rab4A^{WT} Vs C57Bl/6J Rab4A^{Q72L}	P value: C57Bl/6J Rab4A^{WT} vs C57Bl/6J Rab4A^{CD4-KO}	P value: C57Bl/6J Rab4A^{WT} vs SLE1.2.3 Rab4A^{WT}	P value: C57Bl/6J Rab4A^{WT} vs SLE1.2.3 Rab4A^{Q72L}	P value: C57Bl/6J Rab4A^{WT} vs SLE1.2.3. Rab4A^{CD4-KO}	P value: C57Bl/6J Rab4A^{Q72L} vs C57Bl/6J Rab4A^{CD4-KO}	P value: C57Bl/6J Rab4A^{Q72L} vs SLE1.2.3 Rab4A^{WT}	P value: C57Bl/6J Rab4A^{Q72L} vs SLE1.2.3 Rab4A^{Q72L}	P value: C57Bl/6J Rab4A^{Q72L} vs SLE1.2.3. Rab4A^{CD4-KO}	P value: C57Bl/6J Rab4A^{CD4-KO} vs SLE1.2.3 Rab4A^{WT}	P value: C57Bl/6J Rab4A^{CD4-KO} vs SLE1.2.3 Rab4A^{Q72L}	P value: C57Bl/6J Rab4A^{CD4-KO} vs SLE1.2.3. Rab4A^{CD4-KO}	P value: SLE1.2.3 Rab4A^{WT} vs SLE1.2.3 Rab4A^{Q72L}	P value: SLE1.2.3 Rab4A^{WT} vs SLE1.2.3. Rab4A^{CD4-KO}	P value: SLE1.2.3 Rab4A^{Q72L} vs SLE1.2.3. Rab4A^{CD4-KO}
Inflammatory Cells/mm^2	22.75±7.78	29.56±7.87	8.36±2.66	27.84±6.18	33.04±6.96	28.30±3.62	0.561	0.131	0.627	0.389	0.542	**0.044**	0.869	0.764	0.889	**0.028**	**0.014**	**0.004**	0.602	0.951	0.541
Number of Foci/mm^2	0.66±0.17	0.72±0.18	0.29±0.10	0.88±0.14	0.90±0.17	77.50±8.16	0.798	0.117	0.381	0.398	0.584	0.074	0.539	0.537	0.820	**0.015**	**0.024**	**0.011**	0.930	0.560	0.514
Number of Cells/Focus/mm^2	0.94±0.32	1.29±0.25	0.87±0.11	1.13±0.31	1.47±0.37	0.86±0.17	0.418	0.840	0.688	0.329	0.828	0.177	0.690	0.701	0.207	0.461	0.138	0.958	0.506	0.476	0.164
Number of Vasculitic Lesions/mm^2	0.66±0.17	0.86±0.10	0.82±0.33	0.77±0.16	1.18±0.30	0.78±0.12	0.345	0.687	0.654	0.166	0.571	0.904	0.630	0.302	0.636	0.896	0.475	0.927	0.241	0.937	0.226
Vasculitis Score	1.87±0.089	1.63±0.080	1.93±0.096	1.82±0.094	2.019±0.100	1.71±0.075	**0.0428**	0.6345	0.6741	0.2809	0.1698	**0.0151**	0.1263	**0.0028**	0.4475	0.3887	0.5521	0.0649	0.1510	0.3813	**0.0135**

Table summary of liver disease in the following genotypes: Female SLE1.2.3. mice (20-40 weeks of age) with differential Rab4A expression (Wild Type, Q72L, CD4KO).

described[5]. Student's t-test was used to test significance; 2-tailed p values < 0.05 were considered significant for hypothesis testing

Results: Following pristane injection, B6/Rab4A^{CD4-KO} mice had fewer inflammatory foci/mm^2 (0.32±0.10 vs 1.62±0.45; p=0.042) and vasculitic lesions (0.22±0.02 vs 1.60±0.46; p=0.033) than WT controls. The average vasculitis score was decreased in B6 Rab4A^{CD4-KO} animals (2±0.324) compared to B6 (3.1±0.11; p=0.0016) and B6 Rab4A^{Q72L} controls (2.9±0.18; p=0.014). Female lupus prone B6.TC mice had more inflammatory foci/mm^2 (3.04±0.2) than B6 controls (0.93±0.15; p=0.0052). Male B6.TC mice did not show differences in liver inflammation relative to B6 controls. Rapamycin reduced the number of inflammatory and vasculitic foci irrespective of genetically enforced changes in expression of Rab4A. Among female B6.TC mice, 30-50 weeks of age, rapamycin-treated B6.TC Rab4A^{CD4-KO} had fewer inflammatory cells/mm^2 (0.41±0.039) compared to rapamycin-treated B6.TC mice (19.10±6.14; p=0.038) and rapamycin-treated B6.TC Rab4A^{Q72L} mice (4.52±1.21; p=0.020). Vehicle treated B6.TC Rab4A^{CD4-KO} also had less severe vasculitis (1.58±0.16) compared to vehicle treated B6.TC Rab4A^{Q72L} (2.67±0.56; p=0.014). Vehicle treated B6.TC Rab4A^{Q72L} had more severe vasculitis (2.67±0.56) compared to vehicle treated B6.TC mice (1.75±0.14; p=0.047). Among 20-40-week-old females, B6 Rab4A^{CD4-KO} mice had fewer inflammatory foci/mm^2 (8.36±2.66) compared to B6 Rab4A^{Q72L} mice (29.56±7.87; p=0.043). B6.TC/Rab4A^{Q72L} mice had moderately increased vasculitis severity (2.019±0.10) compared to B6.TC mice (1.82±0.094; p=0.151). By contrast, vasculitis was reduced in B6.TC/Rab4A^{CD4-KO} mice (1.71±0.075) relative to B6.TC/Rab4A^{Q72L} mice (2.02±0.10; p=0.0428).

Conclusion: Activation of Rab4A predisposes while its T cell-specific deletion protects against inflammation and vasculitis in the livers of mice with spontaneous or pristane-induced SLE. mTOR blockade with rapamycin reduced hepatitis in lupus prone mice.

Disclosure: N. Huang, None; **A. Patel**, None; **Z. Oaks**, None; **A. Perl**, None.

Abstract Number: 0844

Rab4A Regulates Glomerulonephritis and Tryptophan Metabolism in Sle1.2.3. Lupus-prone Mice via Recycling of CD98

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Animal Models Poster
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Session Time: 9:00AM–11:00AM

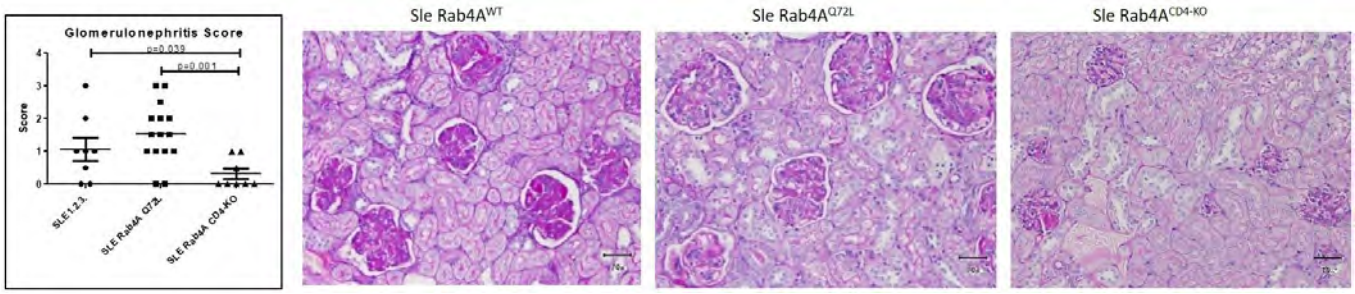

Figure 1. Glomerulonephritis scoring. Kidney sections from Sle Rab4AWT, Sle Rab4AQ72L, and Sle Rab4ACD4-KO mice were scored blind on a 0-4 scale. Left, scores of n=31 mice. Right, representative sections in Sle Rab4AWT, Sle Rab4AQ72L, and Sle Rab4ACD4-KO mice.

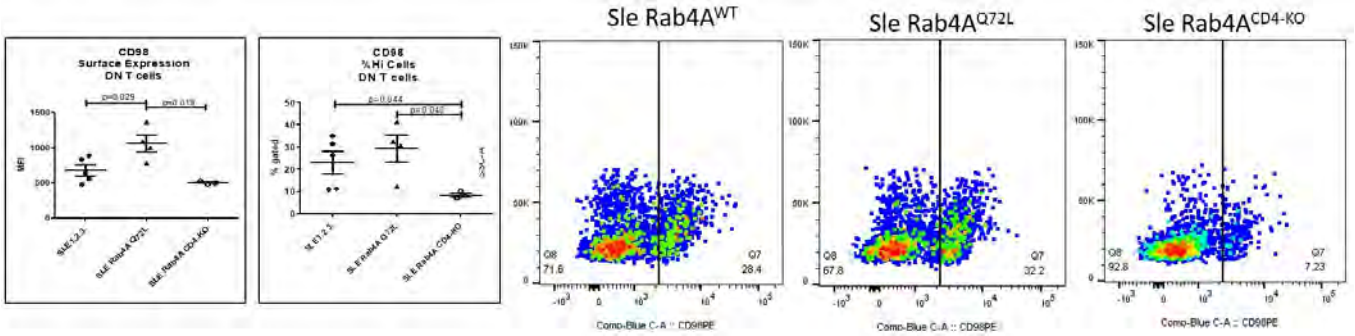

Figure 2. CD98 surface expression in CD4+ T cells and DN T cells. Surface expression was measured by flow cytometry. Left, mean fluorescent intensity and prevalence of CD98hi cells. Right, representative dotplots showing CD98 expression in DN T cells in Sle Rab4AWT, Sle Rab4AQ72L, and Sle Rab4ACD4-KO mice.

Background/Purpose: Systemic Lupus Erythematosus (SLE) is an autoimmune disease with an incompletely understood etiology. Previous work has identified Rab4A, a small GTPase responsible for endosomal recycling, to be a potential pathogenic driver of disease [Caza, et al. *Ann Rheum Dis.* 2014], which involves activation of mTOR that is responsive to accumulation of kynurenine. Here, we investigated whether Rab4A activity controls kynurenine metabolism through regulating surface expression of CD98 via recycling.

Methods: Using the wild-type parental line Sle1.2.3. (Sle Rab4a^{WT}), constitutively active (Sle Rab4A^{Q72L}), or T-cell deleted Rab4A (Sle Rab4A$^{CD4\text{-}KO}$) were generated using a Lox-Cre system. Splenocytes were harvested from the spleens of mice (n=12) and analyzed by flow cytometry using antibodies against CD3, CD4, CD8, CD19 and tryptophan/kynurenine transporter, CD98. Metabolomic data was acquired using a Q-Exactive Hybrid Quadrupole-Orbitrap Mass Spectrometer (ThermoFisher). CD4+ T cells were isolated using a positive selection kit (ThermoFisher), then stimulated for 72hrs with anti-CD3 and anti-CD28 antibodies. The metabolomic profile of Sle Rab4^{Q72L} (n=4) and SLERab-4$^{CD4\text{-}KO}$ (n=4) were compared using Metaboanalyst 3.0. Disease progression was assessed by glomerulonephritis (GN) scoring [1]. Statistical analysis was carried with ANOVA and Student's t-test using GraphPad.

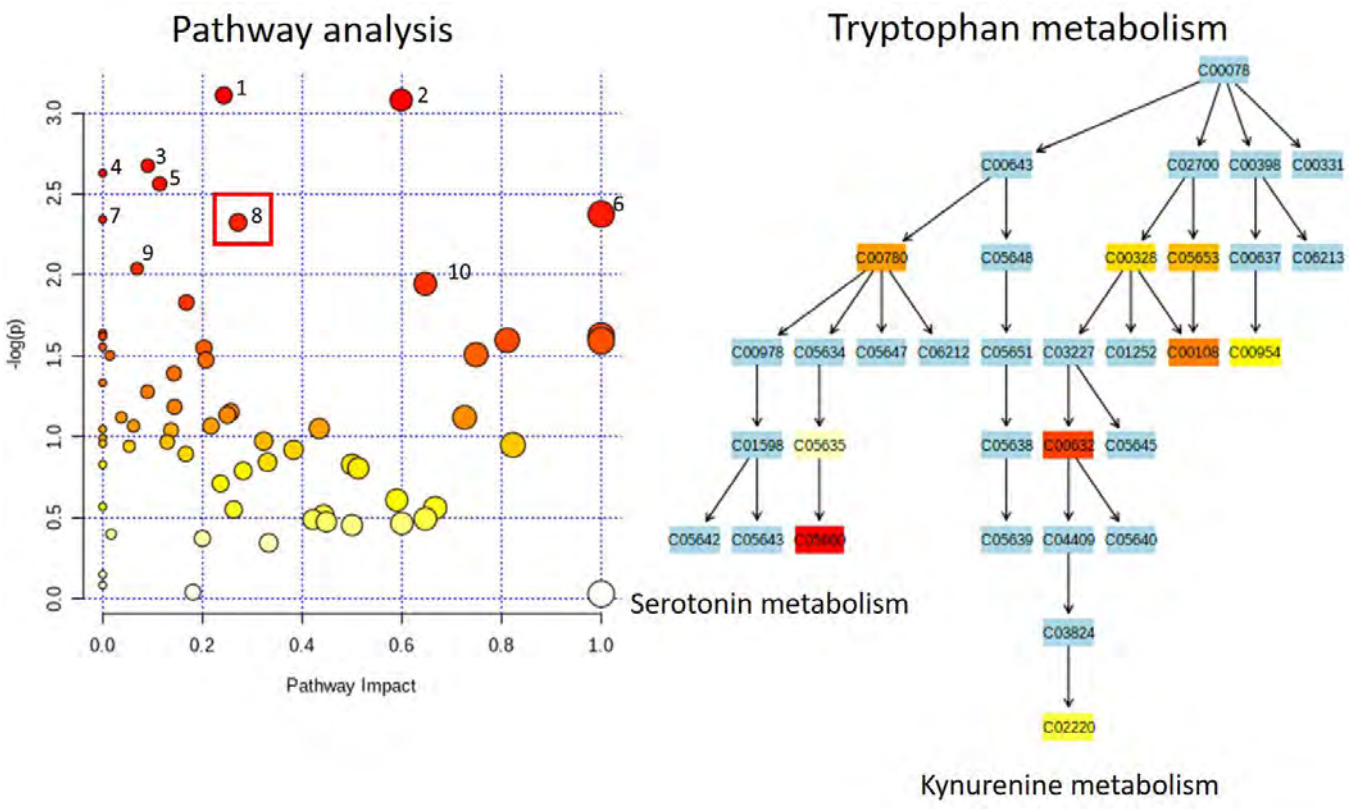

Figure 3. Metabolomic profile of Sle Rab4AQ72L vs. Sle Rab4ACD4-KO mice. CD4+ T cells were measured by mass spectrometry and analyzed by Metaboanalyst to identify discriminating pathways. Left, pathway analysis showing pathways significantly altered between Sle Rab4AQ72L and Sle Rab4ACD4-KO mice (Pathway 8 = Tryptophan). Right, metabolites measured in the tryptophan pathway that are accumulated in Sle Rab4AQ72L mice (increased discrimination colored as yellow -> red).

Results: Mean GN score was significantly reduced in Sle Rab4a$^{CD4\text{-}KO}$ (0.3) compared to Sle Rab4A^{WT} (1.1, p=0.039) and Sle Rab4A^{Q72L} mice (1.5, p=0.001). In pathogenic CD3+CD4-CD8- double-negative (DN) T cells, CD98 expression was significantly increased in Sle Rab4A^{Q72L} compared to Sle Rab4a^{WT} (p=0.029) and Sle Rab4A$^{CD4\text{-}KO}$ mice (p=0.019) (Figure 2). This trend was also seen in CD4+ T cells without reaching significance (Figure 2). CD98^{hi} cells were depleted in Sle Rab4A$^{CD4\text{-}KO}$ compared to Sle Rab4A^{WT} (p=0.044) and Sle Rab4A^{Q72L} mice (p=0.040). The tryptophan metabolomic pathway was measured by mass spectrometry to determine downstream effects of CD98 recycling by Rab4A. In Sle Rab4A^{Q72L} mice, accumulation of several tryptophan metabolites, including kynurenine, anthranilate, and serotonin was seen compared to Sle Rab4A$^{CD4\text{-}KO}$ mice (Figure 3). A global impact on tryptophan metabolism was supported by pathway analysis effectively discriminating between Sle Rab4A^{Q72L} and Sle Rab4A$^{CD4\text{-}KO}$ mice.

Conclusion: Rab4A activity controls the onset and severity of GN Sle1.2.3. lupus-prone mice. Constitutively active Rab4A has increased glomerulonephritis, while deleting Rab4A in T cells ameliorates disease activity. Activation of Rab4A promotes the expression the CD98 and the accumulation of kynurenine and other tryptophan metabolites, suggesting that Rab4A-dependent tryptophan and kynurenine uptake may control mTOR activation seen in human subjects with SLE.

Disclosure: B. Wyman, None; **N. Huang**, None; **Z. Lai**, None; **M. Haas**, None; **M. Duarte**, None; **J. Lewis**, None; **A. Perl**, None.

Abstract Number: 0845

Hematopoietic Specific Deficiency of Rho Kinase Attenuates Neutrophil NETosis and UVB-induced Skin Inflammation

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Neutrophils are the most abundant leukocytes and the first to be recruited to the site of photodamage after ultraviolet B (UVB) exposure. We have shown that UVB induces neutrophil recruitment to the inflamed skin with NET formation and exhibition of NET-associated proinflammatory cytokines. Nuclear envelope rupture is a prerequisite for nuclear DNA release and NET formation. In our latest publication, we have identified that nuclear translocation of PKCα and its mediated lamin B phosphorylation is responsible for nuclear envelope rupture and NETosis. We have shown that application of Rho Kinase (ROCK) inhibitor HA1077 attenuates actin assembly and PKCα nuclear translocation, as well as NETosis in vitro. In our previous work, we found that intraperitoneal application of HA1077 alleviates NETosis in vivo and NET-associated proinflammatory cytokines in skin of the UVB-irradiated C57/BL6 wildtype (WT) mice.

Methods: In the current study, to further investigate the causal role of ROCK in NET formation and UVB-induced skin inflammation, we have generated CD45.1 mice with hematopoietic specific ROCK1 deficiency by bone marrow transplantation (BMT) of hematopoietic stem cells (HSCs) from ROCK1 deficient mice, and following by UVB exposure (150 mJ/cm^2, 5 consecutive days). Then we have examined IFNγ, TNFα, IL-17A expression and exhibition with NETs in skin of the UVB-irradiated skin. We also detected NET formation and cytokine release with NETs in platelet-activating factor (PAF) stimulated neutrophils from different groups of mice.

Results: In results, we found that NET formation in vitro triggered by PAF was significantly decreased in neutrophils isolated from ROCK1 deficient mice as compared to those from WT mice. Most importantly, NET formation and NET-associated IFNγ, TNFα, IL-17A were significantly attenuated in skin of UVB-irradiated CD45.1 BMT mice with ROCK1 deficiency as compared to those transplanted with HSCs from WT mice. To address what we saw in vivo, we conducted ex vivo experiment in which exhibition of neutrophil NET-associated IFNγ, TNFα, IL-17A were reduced in PAF-treated neutrophils from ROCK1 deficient mice as compared to those from WT mice.

Conclusion: In conclusion, using mice with hematopoietic specific ROCK1 deficiency, we demonstrated the role of ROCK1 in neutrophil NET formation and NET-associated proinflammatory cytokine display in UVB-induced skin inflammation. In addition, our study provide insight into a potential therapeutic strategy of targeting on ROCK as a novel potential target treatment of neutrophil NET-associated diseases and UVB-induced skin inflammation and the relevant diseases.

Disclosure: M. Li, None; **X. Lyu**, None; **Y. Li**, None; **J. Liao**, None; **V. Werth**, Corbus Pharmaceuticals, 2, Biogen, 2, 5, Resolve, 2, CSL Behring, 5, Regeneron, 5, Argenx, 5, Viela Bio, 2, 5, Principia, 5, Lilly, 5, Abbvie, 5, AstraZeneca, 2, 5, Amgen, 5, Kyowa Kirin, 5, Glaxo Smith Kline, 5, Cugene, 5, Celgene, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Gilead, 2, 5, Genentech, 2, 5, Syntimmune, 2, MedImmune, 5, Idera, 5, BMS, 5, Medscape, 5, Nektar, 5, Incyte, 5, EMD Sorona, 5, Crisalis, 5, Octapharma, 5, University of Pennsylvania, 9; **M. Liu**, None.

Abstract Number: 0846

MHC Class I Epitopes Derived from Autoantibody Variable Regions, Conjugated to Synthetic Oligodeoxynuleotides, Induce Cytotoxic T Cells That Deplete Autoreactive B Cells and Ameliorate Murine Lupus

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Animal Models Poster
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: B cell depletion or modulation is emerging as a major treatment modality for autoimmune diseases. However, the current treatments to accomplish this non-specifically target pathogenic as well as normal B cells. We previously demonstrated that the heavy chain variable regions of anti-DNA antibodies contain epitopes that can bind MHC class I molecules. Vaccination of lupus-prone mice with plasmid DNA vectors carrying minigenes that encode such epitopes induced CD8+ cytotoxic T lymphocytes (CTL) that killed anti-DNA antibody-producing B cells, reduced serum anti-DNA antibody levels, retarded the development of nephritis, and improved survival (Fan G and Singh RR, J Exp Med 2002). Treatment with peptides alone did not induce such CD8+ T-cells, as we and others have reported impaired CD8+ regulatory and CTL responses in mice and humans (Singh RR, et al, J Immunol 2002; Stohl W, et al, Lupus 1999). Here, we asked if we could overcome such impairment using synthetic oligodeoxynuleotides containing unmethylated cytidine-phosphate-guanosine dinucletides (CpG-ODN) that can enhance innate and adaptive immunity, and whether autoantibody V region epitopes delivered as conjugates with CpG-ODN elicit CTLs that will selectively ablate autoreactive B cells and ameliorate autoimmune disease.

Methods: We compared cytokine responses to CpG-ODN in normal and lupus-prone BWF1 mice, screened and verified BWF1-derived anti-dsDNA antibody VH regions for MHC class I binding epitopes, constructed conjugates of these epitopes with CpG-ODN or a control ODN, immunized BWF1 mice with these conjugates, and assessed CTL responses against anti-dsDNA hybridoma B cells and B cells from nephritic BWF1 mice. We then treated BWF1 mice with selected conjugates and monitored animals for serum anti-dsDNA antibody levels, proteinuria, and survival.

Results: CpG-ODN-induced cytokine responses were lower in BWF1 mice as compared to MHC-matched healthy control animals. BWF1 mice also elicited weak CD8+ T cell responses to immunization with synthetic peptides representing MHC class I binding epitopes from anti-dsDNA VH regions. Immunization with CpG-ODN conjugated to MHC class I-binding, anti-DNA Ab V_H-derived epitopes corrected this impairment in peptide-specific CTL responses in BWF1 mice. Treatment with these conjugates induced strong peptide-specific CTL responses that killed anti-dsDNA hybridoma B cells that carry these epitopes and B cells from diseased lupus-prone mice but not B cells from normal mice, reduced anti-DNA Ab production, retarded the development of lupus nephritis, and improved survival.

Conclusion: CpG-peptides conjugates can be used to elicit a robust CTL response in lupus mice. Immunization with these conjugates carrying autoantibody VH region epitopes can be used to selectively ablate autoreactive B cells. These observations have important implications for developing selective B cell depletion treatments.

Disclosure: R. Singh, None.

Abstract Number: 0847

Impact of Hydroxychloroquine Treatment on Immunologic Markers in SLE Depends on Ethnicity

Laurence Magder[1], Daniel Goldman[2] and Michelle Petri[2], [1]University of Maryland, Baltimore, Baltimore, MD, [2]Johns Hopkins University School of Medicine, Timonium, MD

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE patients with certain immunological markers (i.e., anti-DNA, low complement) are at higher risk of lupus nephritis and those with antiphospholipid antibodies are at higher risk of thrombosis. We explored whether treatment with hydroxychloroquine has an impact on these markers.

Methods: We analyzed data gathered prospectively from quarterly clinic visits from a large American SLE cohort.

Patients visits were classified as "on HCQ" if they reported taking HCQ at that visit and at the previous visit. Patient visits were classified as "off HCQ" if they reported not taking HCQ at that visit and at the previous visit. For a recent subset of visits of patients on HCQ, blood levels of HCQ were also measured.

Table 1: Impact of treatment with HCQ on the odds of being positive for immunologic markers

Clinical marker	All Patients		Number of patients informative about biomarker
	Odds Ratio (95% CI)	P-value	
Confirmed Lupus Anticoagulant	0.58 (0.45, 0.74)	<0.0001	145
antidsDNA	0.81 (0.72, 0.90)	0.0002	356
Low complement	0.72 (0.65, 0.80)	<0.0001	387
aCL IGG>20	0.45 (0.35, 0.58)	<0.0001	123
aCL IGG >40	0.25 (0.16, 0.37)	<0.0001	58
aCL IGM>20	0.42 (0.32, 0.54)	<0.0001	114
aCL IGM >40	0.43 (0.29, 0.65)	<0.0001	55

Table 2: Impact of treatment with HCQ on the odds of being positive for immunologic markers, by race

Clinical marker	Caucasian Americans			African Americans			P-value comparing Caucasians to African Americans
	Odds Ratio (95% CI)	P-value	Number of patients informative about biomarker	Odds Ratio (95% CI)	P-value	Number of patients informative about biomarker	
Confirmed Lupus Anticoagulant	0.31[1] (0.22, 0.45)	<0.0001	66	1.04[1] (0.71, 1.52)	0.82	70	<0.0001
antidsDNA	0.89[1] (0.76, 1.04)	0.14	149	0.66[1] (0.56, 0.78)	<0.0001	182	0.0002
Low complement	0.75 (0.64, 0.87)	<0.0001	177	0.72 (0.62 0.84)	<0.0001	184	0.75
aCL IGG>20	0.41 (0.28, 0.60)	<0.0001	52	0.64 (0.43, 0.93)	0.020	66	0.0053
aCL IGG >40	0.16 (0.09, 0.30)	<0.0001	32	0.54 (0.28, 1.01)	0.055	24	0.0013
aCL IGM>20	0.32 (0.23, 0.45)	<0.0001	60	0.73 (0.48, 1.11)	0.14	46	0.0036
aCL IGM >40	0.16 (0.09, 0.29)	<0.0001	31	2.37[1] (1.08, 5.20)	0.032	18	<0.0001

Table 3: Association between blood levels of HCQ and odds of being positive for various immunologic markers (compared to < 100 ng/mL).

Clinical Marker	100-999 ng/mL		1000-1499 ng/mL		1500+ng/mL		Number of informative patients
	Odds Ratio (vs. <100)	P-value	Odds Ratio (vs. <100)	P-value	Odds Ratio (vs. <100)	P-value	
Confirmed Lupus Anticoagulant	0.76 (0.41, 1.38)	0.36	0.92 (0.47, 1.79)	0.80	0.87 (0.69, 0.42)	0.72	141
antidsDNA	1.05 (0.66, 1.67)	0.85	0.85 (0.52, 1.40)	0.53	0.71 (0.42, 1.22)	0.22	224
Low complement	0.86 (0.61, 1.21)	0.38	0.81 (0.56, 1.17)	0.26	0.71 (0.48, 1.05)	0.08	339
aCL IGG >20	0.46 (0.23, 0.94)	0.034	0.41 (0.18, 0.92)	0.031	0.26 (0.11, 0.64)	0.0035	76
aCL IGG>40	0.43 0.09, 2.00)	0.37	0.61 0.12, 3.21)	0.38	1.18 (0.21, 6.70)	0.40	19
aCL IGM >20	0.89 (0.43, 1.87)	0.76	1.02 (0.46, 2.29)	0.96	0.91 (0.37, 2.23)	0.83	84
aCL IGM>40	0.87 (0.24, 3.22)	0.84	0.95 (0.22, 4.11)	0.94	1.20 (0.25, 5.68)	0.82	28

Serum markers studied included Lupus Anticoagulant (dRVVT, mixing plus confirmatory test), anti-DNA (measured by Crithida), low complement, and anticardiolipin (aCL) IgG and IgM which were considered positive if the titer was greater than 20 or 40.

For each patient, visits on and off HCQ were compared with respect to the rates of immunologic marker positivity. These comparisons were summarized across “informative” patients using conditional logistic regression controlling for age. “Informative” patients were those who sometimes but not always were on HCQ, and sometimes, but not always, were positive for an immunologic marker.

Results: Table 1 shows the overall results of our analyses. While on HCQ, the odds of being positive were significantly reduced for each test. Table 2 shows the same results, stratified by race. There were striking differences between Caucasian and African Americans. Notably, HCQ was associated with a 62% reduction in the odds of lupus anticoagulant among Caucasian Americans, but no association was observed among African Americans. Table 3 shows the relationship between blood concentration of HCQ and immunologic markers among those on HCQ. This analysis (based on a smaller subset with less power) generally showed that those with concentration exceeding 100 ng/ml had lower odds of being positive, but the protective effect was most striking for aCL IgG >20.

Conclusion: These findings suggest that the benefit of HCQ may be mediated by its effects on antiphospholipid antibodies, complement and anti-dsDNA. These findings also highlight the differences between Caucasian Americans and African Americans with respect to these effects of HCQ.

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Abstract Number: 0848

Delineation of a Proinflammatory Cytokine Profile Targeted by Janus Kinase 1/2 Inhibition Using Baricitinib in a Phase 2 Systemic Lupus Erythematosus Trial

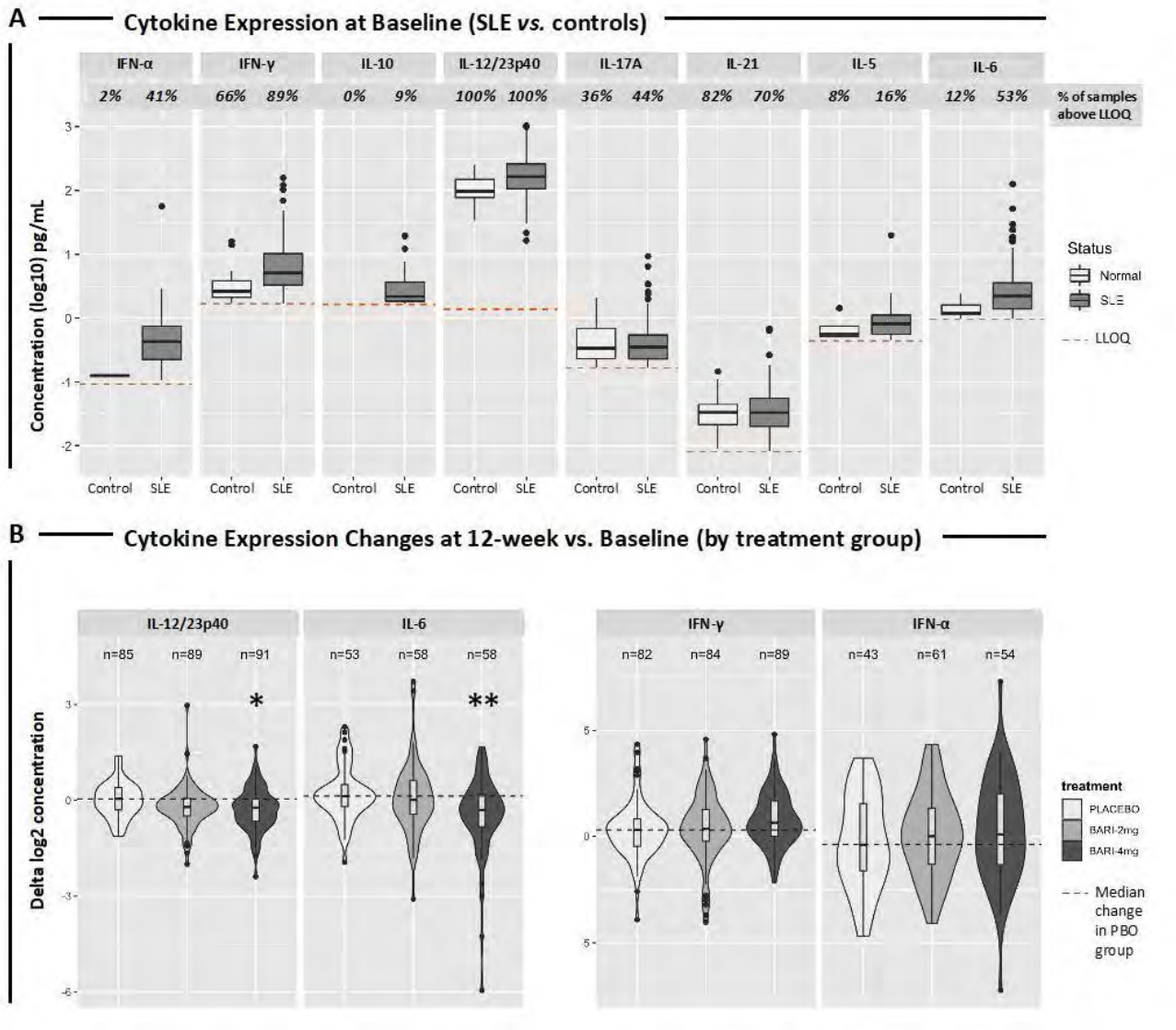
Thomas Dörner[1], Yoshiya Tanaka[2], Michelle Petri[3], Josef Smolen[4], Daniel Wallace[5], Brenda Crowe[6], Ernst Dow[6], Richard Higgs[6], Guilherme Rocha[6], Robert Benschop[6], Maria Silk[6], Stephanie de Bono[6], Robert Hoffman[6] and Damiano Fantini[6], [1]DRFZ and Charité University Hospitals, Berlin, Germany, [2]The First Department of Internal Medicine, University of Occupational and Environmental Health, Kitakyushu, Japan, [3]Johns Hopkins University School of Medicine, Timonium, MD, [4]Division of Rheumatology, Department of Medicine III, Medical University of Vienna, Vienna, Austria, [5]Cedars-Sinai Medical Center/UCLA, Los Angeles, CA, [6]Eli Lilly and Company, Indianapolis, IN

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Given the unmet clinical needs in systemic lupus erythematosus (SLE), including poor disease control and drug toxicities, new therapies are needed. In a phase 2, randomized, placebo-controlled, double-blind study (JAHH), once-daily baricitinib (bari) resulted in significant clinical improvement in patients (pts) with active SLE versus (vs.) placebo (PBO). Bari inhibits Janus Kinase (JAK)1 and JAK2 signaling, and in turn may affect signal transducer and activator of transcription (STAT)1, STAT2 and STAT4 pathways. Therefore, bari has the potential to simultaneously impact several pro-inflammatory immune cytokines implicated in the pathogenesis of SLE, including interferon (IFN)-α, IFN-γ, interleukin (IL)-6, IL-12, and IL-23. The objectives of the current study were: 1) to examine baseline serum cytokines in the JAHH phase 2 clinical trial for correlations with clinical or immunologic assessments; 2) to determine if changes in serum cytokine levels were associated with bari treatment.

Methods: Pts enrolled in the JAHH phase 2 trial received daily treatment with PBO, bari 2 mg, or bari 4 mg through Week 24. Serum samples were collected at baseline (Week [Wk] 0), Wk 12, and Wk 24) from SLE pts (n=270) and 50

Figure 1



*p = 0.015; **p = 0.001; Bari=baricitinib; IFN=interferon; IL=interleukin; LLOQ=lower limit of quantification; PBO=placebo; SLE=systemic lupus erythematosus.

sex- and age-matched controls. Samples were analyzed for: IL-2, IL-3, IL-5, IL-6, IL-10, IL-17A, IL-21, IL-12/23p40, IL-12p70, granulocyte-macrophage colony-stimulating factor (GM-CSF), IFN-α and IFN-γ using ultrasensitive quantitative assays. IFN gene signature, autoantibodies, complement component 3 and 4 (C3 and C4) were measured as previously described.[1]

Results: At Wk 0, serum IL-17A, IL-12/23p40, IL-6, IFN-γ and IFN-α were readily detectable. IL-12/23p40 was detectable in 100% of pts vs. 100% of controls, IFN-γ in 89% of pts vs. 66% of controls, IL-6 in 53% of pts vs. 12% of controls and IFN-α in 41% of pts vs. 2% of controls; detection of serum IL-2, GM-CSF, IL-5, IL-10 and IL-17A was variable (Figure 1). At baseline (Wk 0), IL-12/23p40 was positively correlated with SLE disease activity index and IFN gene signature, and negatively correlated with serum C4. IL-6 was positively correlated with joint swelling, joint tenderness, IFN-γ and C3. Serum IFN-α was positively correlated with serum IFN-γ, antibodies to Smith and ribonucleoprotein antigens (anti-Sm and anti-RNP), and the IFN gene signature (Figure 2). Treatment with bari 4 mg (Figure

Figure 2

Spearman Correlation Coefficients of JAHH Baseline Variables

	IFN-α	IFN-γ	IL-6	IL-12/23p40	IFN Signature	SLEDAI	Swollen Joints	Tender Joints	CLASI	C3	C4	Anti-dsDNA	Anti-Sm
IFN-γ	0.24												
IL-6	0.02	0.28											
IL-12/23p40	0.07	0.34	0.24										
IFN Signature	0.33	0.38	0.06	0.19									
SLEDAI	0.06	0.08	−0.04	0.16	0.21								
Swollen Joints	−0.05	−0.12	0.17	0.07	−0.15	−0.08							
Tender Joints	−0.03	−0.07	0.18	0	−0.13	−0.04	0.64						
CLASI	0.1	0.12	0.01	0.03	0.18	0.41	−0.16	−0.16					
C3	−0.14	−0.2	0.21	−0.08	−0.36	−0.26	0.28	0.26	0				
C4	−0.08	−0.11	0.1	−0.17	−0.35	−0.27	0.13	0.14	0.09	0.65			
Anti-dsDNA	0.1	0.12	0.13	0.06	0.24	0.44	−0.07	−0.02	0.01	−0.38	−0.43		
Anti-Sm	0.16	0.13	0.02	0.12	0.41	0.26	−0.03	−0.05	0.12	−0.31	−0.34	0.29	
Anti-RNP	0.18	0.15	0.1	0.1	0.51	0.24	−0.02	−0.05	0.07	−0.27	−0.3	0.3	0.7

Anti-dsDNA=Anti-double stranded DNA; Anti-RNP=Anti ribonucleoprotein; Anti-Sm=Anti-Smith; CLASI=cutaneous lupus erythematosus disease area and severity index; C3=complement component 3; C4=complement component 4; IFN=interferon; IL=interleukin; SLEDAI=systemic lupus erythematosus disease activity index.

1B) significantly decreased serum IL12/23p40 and IL-6 cytokine levels at Wk 12 ($p< 0.05$) but not serum IFN-α or IFN-γ levels (Figure 1B).

Conclusion: Bari 4 mg treatment was associated with statistically significant decrease of serum IL-12/23p40 and IL-6 at Week 12 which continued through Week 24. Serum IFN-α or IFN-γ were not reduced with bari treatment. Thus, bari 4 mg simultaneously impacted multiple pro-inflammatory cytokines implicated in the pathogenesis of SLE.

Reference:

1. Hoffman RW, et al. *Arthritis Rheumatol*. 2017;69(3):643-654.

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Abstract Number: 0849

Herpes Zoster Events with Anifrolumab in Patients with Active SLE: An Integrated Analysis of Phase 2 and Phase 3 Trials

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: In the phase 2 MUSE and phase 3 TULIP-1 and TULIP-2 trials, treatment with anifrolumab, a monoclonal antibody to the type I interferon receptor, was associated with clinical benefit in patients (pts) with SLE.[1–3] In all 3 trials, herpes zoster (HZ) was observed more frequently with anifrolumab vs placebo. We conducted an integrated analysis to characterize the frequency and nature of HZ events with anifrolumab across the MUSE and TULIP trials.

Methods: MUSE, TULIP-1, and TULIP-2 were randomized, double-blind, 52-wk trials that evaluated anifrolumab 300 mg (IV Q4W for 48 wks) or placebo in pts with moderately to severely active SLE despite SOC.[1–3] MUSE also included a 1000-mg treatment arm, and TULIP-1 included a 150-mg treatment arm; these pts were analyzed separately. We assessed HZ AE incidence, severity, intensity, discontinuation, and time to onset.

Results: In pooled data from MUSE, TULIP-1, and TULIP-2, 459 pts received ≥1 dose of anifrolumab 300 mg and 466 received ≥1 dose of placebo. In addition, 93 pts received anifrolumab 150 mg in TULIP-1 and 105 received 1000 mg in MUSE. HZ occurred in 5.4% (n=5), 6.1% (n=28), and 8.6% (n=9) of pts in the anifrolumab 150-mg, 300-mg, and 1000-mg groups, respectively, and in 1.3% (n=6) of the pooled placebo group (**Table 1**). Forty-four pts had HZ AEs that were mild or moderate, and 4 had events that were severe (anifrolumab 300 mg, n=2; 1000 mg, n=2). Three pts had serious AEs of HZ (anifrolumab 300 mg, n=2; 1000 mg, n=1). Of the 48 pts with HZ AEs, all but 4 continued in the study and all AEs leading to discontinuation were nonserious and moderate (anifrolumab 150 mg, n=1; 300 mg, n=2;

Anifrolumab 300 mg vs placebo	Placebo (n=466)		Anifrolumab 300 mg (n=459)		Difference (anifrolumab 300 mg vs placebo)	
	n (%)	EAIR (per 100 PY)	n (%)	EAIR (per 100 PY)	EAIR (per 100 PY) risk difference (95% CI)	Adjusted difference in cumulative percentage (95% CI)
Any HZ AE	6 (1.3)	1.5	28 (6.1)	6.9		
Any HZ AE with outcome of death	0	0	0	0	0	0
Any HZ SAE	0	0	2 (0.4)	0.5	0.5 (–0.5, 1.7)	0.4 (–1.1, 2.0)
Any HZ DAE	0	0	2 (0.4)	0.5	0.5 (–0.5, 1.7)	0.4 (–1.1, 2.0)
Any HZ AE by maximum reported intensity						
Mild	1 (0.2)	0.3	9 (2.0)	2.2		
Moderate	5 (1.1)	1.2	17 (3.7)	4.1		
Severe	0	0	2 (0.4)	0.5		
Anifrolumab 150 mg vs placebo and anifrolumab 1000 mg vs placebo	Placebo (n=184), n (%)	Anifrolumab 150 mg (n=93), n (%)	EAIR (per 100 PY) risk difference (anifrolumab 150 mg vs placebo) (95% CI)	Placebo (n=101), n (%)	Anifrolumab 1000 mg (n=105), n (%)	EAIR (per 100 PY) risk difference (anifrolumab 1000 mg vs placebo) (95% CI)
Any HZ AE	3 (1.6)	5 (5.4)		1 (1.0)	9 (8.6)	
Any HZ AE with outcome of death	0	0	0	0	0	0
Any HZ SAE	0	0	0	0	1 (1.0)	1.1 (–3.3, 5.9)
Any HZ DAE	0	1 (1.1)	1.2 (–1.1, 6.5)	0	1 (1.0)	1.1 (–3.3, 5.9)
Any HZ AE by maximum reported intensity						
Mild	0	1 (1.1)		1 (1.0)	1 (1.0)	
Moderate	3 (1.6)	4 (4.3)		0	6 (5.7)	
Severe	0	0		0	2 (1.9)	

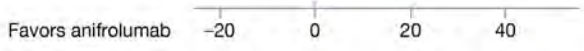
AE, adverse event; DAE, adverse event leading to discontinuation of investigational product; EAIR, exposure-adjusted incidence rate; PY, patient-years; SAE, serious adverse event.
EAIR was reported per 100 PY and defined as the number of patients with the specific event divided by the total exposure time in years and then multiplied by 100. The exposure time was defined as the time from the date of first administration of investigational product to the date of first event, death, end of treatment plus 28 days, or end of study, whatever came first.

Table 1. Herpes Zoster Events During Treatment With Anifrolumab 300 mg vs Placebo in Pooled MUSE, TULIP-1, and TULIP-2 Data, 150 mg vs Placebo in TULIP-1, and 1000 mg vs Placebo in MUSE

1000 mg, n=1). In pooled data available from TULIP-1 and -2, all HZ AEs with anifrolumab 300 mg were cutaneous (21 localized, unilateral; 2 disseminated, unilateral); all 5 HZ AEs with placebo were localized cutaneous. HZ resolved in all cases in MUSE and TULIP; all pts in the anifrolumab group and 4 of 6 pts in the placebo group received antiviral treatment. Using pooled TULIP data, no pattern of HZ event frequency was identified in protocol-defined subgroups. Pts using immunosuppressants (IS; n=349) had a difference in the rate of HZ between anifrolumab vs placebo groups of 8.1% (CI 2.6, 13.7) and those without IS use (n=376) had a difference of 2.2% (CI –1.8, 6.2) (**Figure 1**). Time to first onset of HZ was marginally shorter in the anifrolumab 300-mg vs placebo group (**Figure 2**).

Conclusion: In MUSE and TULIP trials, there appears to be an increased risk of HZ with anifrolumab vs placebo. HZ event characteristics, including duration and severity, were comparable between treatment groups, and most HZ events were mild to moderate, cutaneous, and resolved without discontinuation of study drug.

Subgroup		Placebo n/N (%)	Anifrolumab 300 mg n/N (%)	Treatment difference (95% CI)	Treatment difference (95% CI)
Overall		5/366 (1.4)	23/360 (6.4)		5.0 (1.9, 8.1)
SLEDAI-2K (screening)	<10	2/106 (1.9)	3/109 (2.8)		0.9 (–5.3, 7.0)
	≥10	3/260 (1.2)	20/251 (8.0)		6.8 (2.7, 10.9)
OCS dosage	<10 mg/day	2/180 (1.1)	11/170 (6.5)		5.4 (0.5, 10.3)
	≥10 mg/day	3/185 (1.6)	12/190 (6.3)		4.7 (–0.0, 9.4)
Type I IFNGS status	Test–high	4/301 (1.3)	19/298 (6.4)		5.0 (1.6, 8.5)
	Test–low	1/64 (1.6)	4/62 (6.5)		4.9 (–5.2, 15.0)
Sex	Male	0/25	3/27 (11.0)		11.0 (–8.7, 30.8)
	Female	5/340 (1.5)	20/333 (6.0)		4.5 (1.3, 7.7)
Age	≥18–65 years	5/358 (1.4)	23/344 (6.7)		5.3 (2.1, 8.5)
	≥65 years	0/7	0/16		0
BMI	≤28 kg/m²	3/223 (1.3)	13/205 (6.3)		5.0 (0.7, 9.3)
	>28 kg/m²	2/142 (1.4)	10/155 (6.5)		5.0 (–0.4, 10.5)
Race	White	4/243 (1.6)	13/235 (5.6)		3.9 (–0.0, 7.9)
	Black/African American	1/48 (1.8)	0/46		–1.8 (–12.9, 9.4)
	Asian	0/35	4/41 (9.8)		9.8 (–5.0, 24.6)
	Other	0/31	4/30 (12.6)		12.6 (–5.4, 30.5)
Region	USA/Canada	3/139 (2.1)	9/139 (6.5)		4.3 (–1.6, 10.2)
	Europe	2/122 (1.6)	5/115 (4.4)		2.8 (–3.2, 8.9)
	Latin America	0/57	4/59 (6.7)		6.7 (–3.6, 17.0)
	Asia Pacific	0/32	4/38 (10.7)		10.7 (–5.2, 26.5)
	Rest of world	0/15	1/9 (15.3)		15.3 (–22.8, 53.3)
ADA	Negative	5/330 (1.5)	21/335 (6.3)		4.8 (1.5, 8.0)
	Positive (at any time)	0/35	2/25 (10.4)		10.4 (–8.5, 29.4)
Immunosuppressant	Any use	3/176 (1.7)	17/173 (9.8)		8.1 (2.6, 13.7)
	No use	2/189 (1.1)	6/187 (3.2)		2.2 (–1.8, 6.2)



ADA, antidrug antibody; BMI, body mass index; CI, confidence interval; IFNGS, interferon gene signature; OCS, oral corticosteroid.

Figure 1. Adjusted Difference in Cumulative Proportions of Patients With Herpes Zoster Events With Anifrolumab 300 mg vs Placebo in Pooled TULIP-1 and TULIP-2 Data

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1. Furie R. *Arthritis Rheumatol*. 2017;69:376–86.
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3. Morand EF. *N Engl J Med*. 2020;382:211–21.

Writing assistance by Angela Cimmino, PharmD (JK Associates Inc., a Fishawack Health Company).
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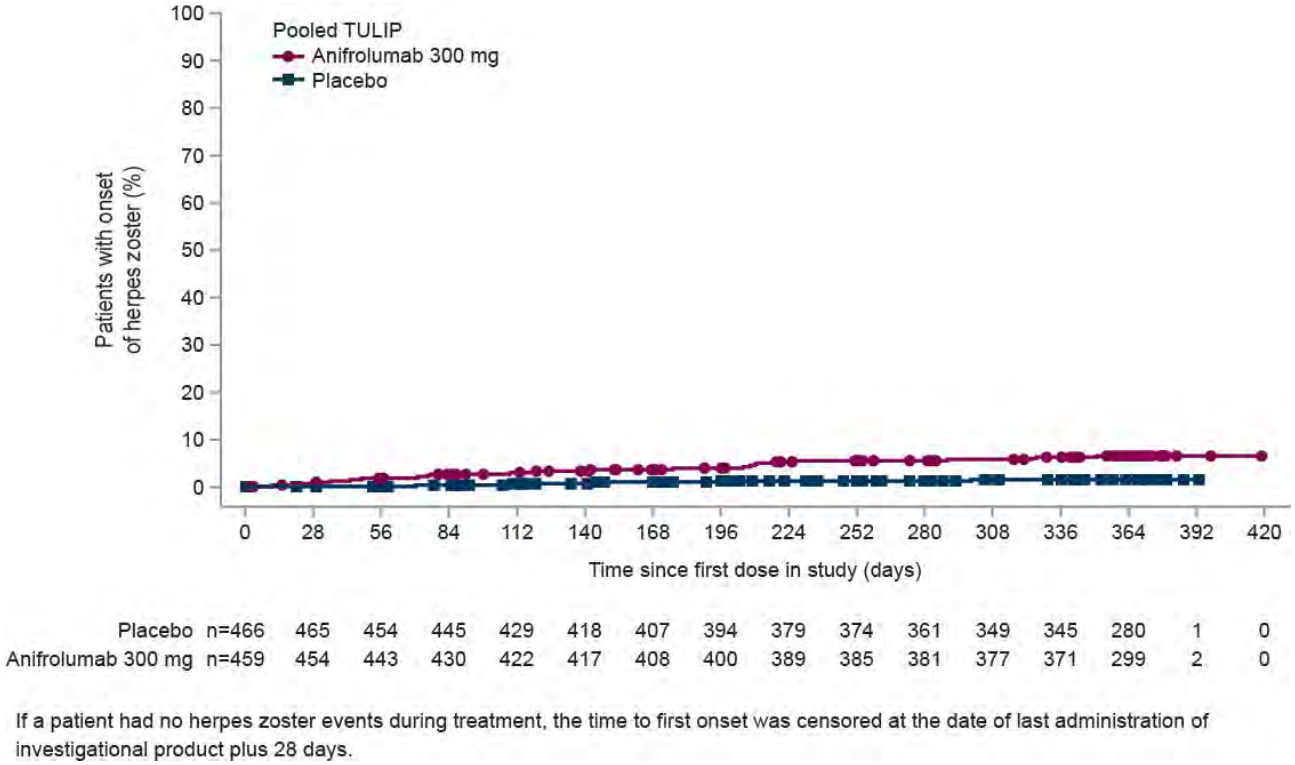

Figure 2. Time to First Onset of Herpes Zoster During Treatment With Anifrolumab 300 mg vs Placebo in Pooled MUSE, TULIP-1, and TULIP-2 Data

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Abstract Number: 0850

What Does It Mean to Be a BICLA (BILAG-Based Composite Lupus Assessment) Responder? Post Hoc Analysis of the Phase 3 TULIP-1 and TULIP-2 Trials

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: SLE – Treatment Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Assessment	BICLA responders[a] at Week 52 (n=318)	BICLA nonresponders[a] at Week 52 (n=501)
Change in SLEDAI-2K from baseline to Week 52		
n	308	352
Mean (SD)	–7.4 (3.64)	–4.2 (4.28)
Change in PGA from baseline to Week 52		
n	309	354
Mean (SD)	–1.28 (0.538)	–0.72 (0.643)
Change in OCS dosage (mg/day) from baseline to Week 52		
n	318	379
Mean (SD)	–5.41 (6.841)	–1.67 (8.081)
OCS AUC (mg) at Week 52		
n	318	501
Mean (SD)	2159.2 (1661.39)	3140.8 (3081.19)
Sustained OCS dosage reduction at Week 52 in patients with OCS ≥10 mg/day at baseline		
≥10 mg/day at baseline, n	165	258
Responders,[a,b] n (%)	130 (79.2)	50 (19.1)
95% CI response rate	72.9, 85.5	14.2, 24.0
Reduction in CLASI activity score (≥50%) at Week 52 in patients with CLASI activity ≥10 at baseline		
≥10 at baseline, n	103	128
Responders,[a,c] n (%)	95 (92.0)	31 (23.2)
95% CI response rate	85.9, 98.1	15.8, 30.6
Change in joint counts from baseline to Week 52		
n	309	355
Tender, mean (SD)	–8.1 (6.81)	–5.3 (7.56)
Swollen, mean (SD)	–5.9 (4.94)	–4.4 (5.51)
Active, mean (SD)	–5.7 (4.96)	–4.4 (5.41)

AUC, area under the curve; BICLA, British Isles Lupus Assessment Group–based Composite Lupus Assessment; CI, confidence interval; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; IFNGS, interferon gene signature; OCS, oral corticosteroid; PGA, Physician's Global Assessment; SD, standard deviation. [a]Responder/nonresponder rates are calculated using a stratified Cochran–Mantel–Haenszel approach, with stratification factors SLEDAI-2K score at screening, Day 1 OCS dosage, and IFNGS status at screening. Patients who prematurely discontinued study drug or received restricted medications were classified as nonresponders; [b]Sustained OCS dosage reduction was defined as OCS dosage ≤7.5 mg/day achieved by Week 40 and sustained through Week 52; [c]CLASI activity score response was defined as ≥50% reduction of CLASI activity score from baseline to Week 52 for patients with CLASI activity ≥10 at baseline.

Table 1. SLE Assessments in BICLA Responders vs Nonresponders in Pooled Data From the Phase 3 TULIP-1 and TULIP-2 Trials

Background/Purpose: BICLA is a validated composite global measure of SLE disease activity that incorporates BILAG, an instrument that distinguishes between partial and complete improvement. BICLA was an endpoint in the phase 3 TULIP-1 and TULIP-2 trials of anifrolumab.[1,2] This study investigated the relationships between BICLA response and SLE clinical and laboratory assessments in TULIP-1 and -2, irrespective of treatment assignment.

Methods: This was a post hoc analysis of pooled data from the 52-week (wk), double-blind TULIP-1 and -2 trials. Patients with moderately to severely active SLE, despite standard of care, were randomized to receive anifrolumab (150 or 300 mg IV Q4W) or placebo for 48 wks. BICLA responses were defined by the following: reduction of all baseline BILAG-2004 A and B domain scores to B/C/D and C/D, respectively, and no worsening in any organ system; no worsening of SLEDAI-2K score; and no worsening ≥0.3 points in Physician's Global Assessment (range 0–3).[3] Attempts to taper oral corticosteroids (OCS) to ≤7.5 mg/day between Wks 8 and 40 were required for patients receiving OCS

Biomarker change from baseline to Week 52	BICLA responders[a] at Week 52 (n=318)	BICLA nonresponders[a] at Week 52 (n=501)
C3[b]		
n	121	127
Mean, g/L (SD)	0.101 (0.1762)	0.078 (0.1889)
C4[b]		
n	70	79
Mean, g/L (SD)	0.016 (0.0284)	0.022 (0.0412)
Anti-dsDNA antibodies[b]		
n	132	147
Mean, U/mL (SD)	−46.1 (335.69)	15.8 (450.92)

BICLA, British Isles Lupus Assessment Group–based Composite Lupus Assessment; IFNGS, interferon gene signature; OCS, oral corticosteroid; SD, standard deviation.
[a]Responder/nonresponder rates are calculated using a stratified Cochran–Mantel–Haenszel approach, with stratification factors SLEDAI-2K score at screening, Day 1 OCS dosage, and IFNGS test status at screening. Patients who prematurely discontinued study drug or received restricted medications were classified as nonresponders; [b]Only patients with baseline positive anti-dsDNA and abnormal complement level are included.

Table 2. Change in Biomarker Levels From Baseline to Week 52 in BICLA Responders vs Nonresponders in Pooled Data From the TULIP Trials

PRO improvement from baseline to Week 52	BICLA responders[a] at Week 52 (n=318)	BICLA nonresponders[a] at Week 52 (n=501)
FACIT-F		
n	318	501
Responders,[a,b] n (%)	176 (55.6)	79 (15.7)
95% CI response rate	50.2, 61.1	12.4, 19.0
SF-36 PCS		
n	318	501
Responders,[a,c] n (%)	183 (57.9)	65 (12.8)
95% CI response rate	52.5, 63.3	9.7, 15.8

BICLA, British Isles Lupus Assessment Group–based Composite Lupus Assessment; IFNGS, interferon gene signature; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; OCS, oral corticosteroid; PCS, physical component summary; PRO, patient-reported outcome; SF-36, Short Form 36 Health Survey.
[a]Responder/nonresponder rates are calculated using a stratified Cochran–Mantel–Haenszel approach, with stratification factors SLEDAI-2K score at screening, Day 1 OCS dosage, and IFNGS test status at screening. Patients who prematurely discontinued study drug or received restricted medications were classified as nonresponders; [b]A response in FACIT-F is defined as an improvement from baseline to Week 52 >3 points; [c]A response in SF-36 is defined as an increase from baseline to Week 52 >3.4 in the PCS domain.

Table 3 Improvement in Patient-Reported Outcome Assessments From Baseline to Week 52 in BICLA Responders vs Nonresponders in Pooled Data From the TULIP Trials

≥10 mg/day at baseline. Sustained OCS dosage reduction was defined as OCS dosage ≤7.5 mg/day achieved by Wk 40 and sustained through Wk 52.

Results: Baseline characteristics were generally similar between BICLA responders (n=318) and nonresponders (n=501). Overall, improved outcomes were observed in BICLA responders vs nonresponders, including numerically greater improvements in SLEDAI-2K (–7.4 [SD: 3.64] vs –4.2 [SD: 4.28]) from baseline to Wk 52 (**Table 1**). Greater mean daily OCS dosage reduction was observed in BICLA responders vs nonresponders (–5.41 [SD: 6.84] vs –1.67 [SD: 8.08] mg/day) from baseline to Wk 52, and sustained OCS dosage reduction was achieved by more BICLA responders vs nonresponders (79.2% vs 19.1%). A ≥50% reduction in Cutaneous Lupus Erythematosus Disease Area and Severity Index activity (CLASI-A) score, for patients with baseline score ≥10, was achieved by more BICLA responders vs nonresponders (92.0% vs 23.2%) at Wk 52. Greater reductions of mean anti-dsDNA antibody levels were observed in BICLA responders vs nonresponders (–46.1 [SD: 335.69] vs 15.8 [SD: 450.92] U/mL) from baseline to Wk 52; numeric improvements were also observed for complement C3 (**Table 2**). More patients who were BICLA responders vs nonresponders reported improved patient-reported outcomes, with greater improvements in the Func-

tional Assessment of Chronic Illness Therapy-Fatigue of >3 points (55.6% vs 15.7%) and the Short Form 36 Health Survey physical component summary of >3.4 (57.9% vs 12.8%) (**Table 3**).

Conclusion: BICLA response was associated with clinical benefit in multiple SLE measures, including SLEDAI-2K, CLASI-A, OCS dosage reduction, and patient-reported outcomes. These data uphold the value of BICLA as an endpoint in SLE trials and also expand its benefit to translating trial data to metrics that are clinically meaningful in everyday practice.

References

1. Morand EF. *N Engl J Med.* 2020;382:211–21.
2. Furie RA. *Lancet Rheumatol*. 2019;1:e208–19.
3. Wallace DJ. *Ann Rheum Dis.* 2014;73:183–90.

Writing assistance by Rosie Butler, PhD (JK Associates Inc., a Fishawack Health Company).
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Disclosure: R. Furie, AstraZeneca/Medimmune, 2, 5; **E. Morand**, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, 5, Merck Serono, 2, 5, Neovacs, 5, Sandoz, 5, Novartis, 8, AbbVie, 5, Amgen, 5, Biogen, 5; **I. Bruce**, Genzyme/Sanofi, 2, GlaxoSmithKline, 2, 5, 8, Roche, 2, UCB, 2, 5, 8, Eli Lilly, 5, Merck Serono, 5, ILTOO, 5, AstraZeneca, 8; **D. Isenberg**, AstraZeneca, 5, Celgene, 5, Merck Serono, 5, UCB, 5, Servier, 5; **R. van Vollenhoven**, BMS, 2, GSK, 2, Lilly, 2, UCB, 2, 5, 8, AbbVie, 5, 8, AstraZeneca, 5, 8, Biogen, 5, Biotest, 5, Celgene, 5, Gilead, 5, Pfizer, 5, 8, Servier, 5, Janssen, 5, 8, Galapagos, 5, 8; **G. Abreu**, AstraZeneca, 3; **L. Pineda**, AstraZeneca, 3; **R. Tummala**, AstraZeneca, 3.

Abstract Number: 0851

Iberdomide Decreases B Cells and Plasmacytoid Dendritic Cells, Increases Regulatory T Cells and IL-2, and Has Enhanced Clinical Efficacy in Active Systemic Lupus Erythematosus Patients with High Aiolos or the IFN Gene Expression Signature

Peter Lipsky[1], Ronald van Vollenhoven[2], Thomas Dörner[3], Victoria Werth[4], Joan Merrill[5], Richard Furie[6], Milan Petronijevic[7], Benito Velasco Zamora[8], Maria Majdan[9], Fedra Irazoque-Palazuelos[10], Robert Terbrueggen[11], Nikolay Delev[12], Michael Weiswasser[12], Shimon Korish[12], Nataliya Agafonova[12], Mark Stern[13], Sarah Hersey[13], Ying Ye[13], Allison Gaudy[12], Zhaohui Liu[12], Shaojun Tang[13] and Peter Schafer[12], [1]RILITE Foundation, Charlottesville, VA, [2]Amsterdam University Medical Centers, Amsterdam, Netherlands, [3]DRFZ and Charité University Hospitals, Berlin, Germany, [4]University of Pennsylvania and the Michael J. Crescenz VA Medical Center, Philadelphia, PA, [5]Oklahoma Medical Research Foundation, Oklahoma City, OK, [6]Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, [7]Military Medical Academy, Belgrade, Serbia, [8]Instituto CER S.A., Buenos Aires, Argentina, [9]Medical University of Lublin and Samodzielny Publicnzy Szpital Kliniczny Nr 4 w Lublinie, Lublin, Poland, [10]Centro de Investigación y Tratamiento Reumatológico S.C, Miguel Hidalgo, Mexico, [11]DxTerity Diagnostics Inc, Rancho Dominguez, [12]Bristol Myers Squibb, Princeton, [13]Bristol-Myers Squibb, Princeton

SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

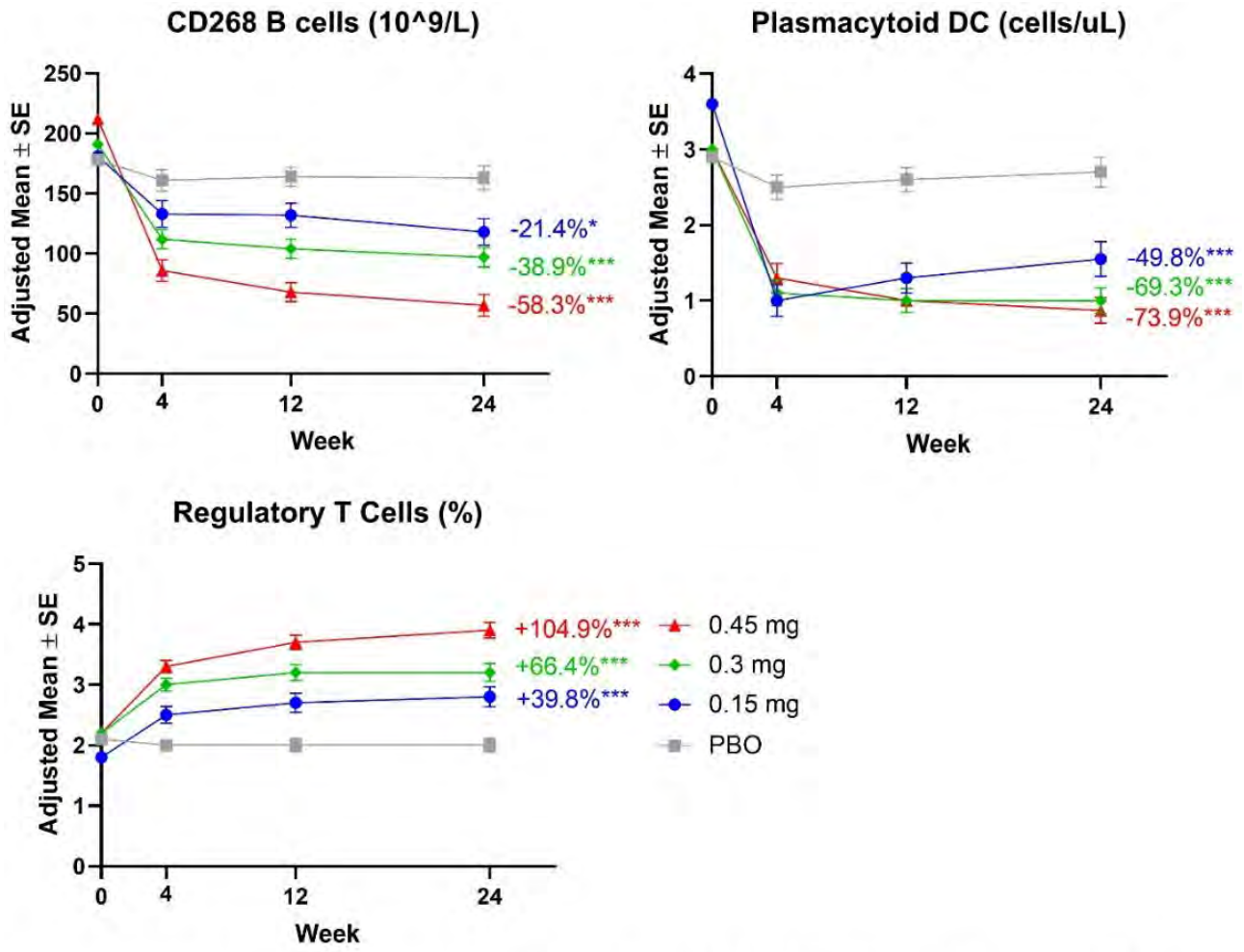

Figure 1. Pharmacodynamic changes in CD268 B cells, plasmacytoid dendritic cells, and regulatory T cells during iberdomide treatment. Values shown are the treatment comparison vs. placebo of adjusted means percent change from baseline (*p≤0.05, **p≤0.01,***p≤0.001).

Background/Purpose: Iberdomide is a high-affinity cereblon ligand that promotes ubiquitination and proteasomal degradation of Ikaros (*IKZF1*) and Aiolos (*IKZF3*), transcription factors linked to the genetic risk for systemic lupus erythematosus (SLE). Ikaros is required for development of B cells and plasmacytoid dendritic cells (pDC) and represses IL-2 transcription. Aiolos is a B-cell modulator and required for maturation of plasma cells. The pharmacokinetics, pharmacodynamics (PD), efficacy, and safety of oral iberdomide were evaluated in a phase 2b study in subjects with active autoantibody-positive SLE (NCT03161483).

Methods: Adult SLE patients (N=288) with a ≥6-month history of SLE and SLE Disease Activity Index (SLEDAI 2K) ≥6 were randomized to placebo (n=83) or iberdomide 0.15 mg QD (n=42), 0.3 mg QD (n=82), or 0.45 mg QD (n=81). Clinical response was determined by the SLE Responder Index 4 (SRI-4) at week 24 for all patients and within prespecified biomarker-enriched subsets based on expression of Ikaros, Aiolos, the Type 1 IFN signature (*IFI27, IFI44, IFI44L, RSAD2*), and other gene modules measured from fingerstick blood collected at baseline (Modular Immune Profile Test, DxTerity Diagnostics, Inc.). PD changes in whole blood leukocytes were measured by flow cytometry (Covance), T regulatory cells (Tregs) by epigenetic assay (EpiontisID, Epiontis GmbH), and plasma cytokines by ul-

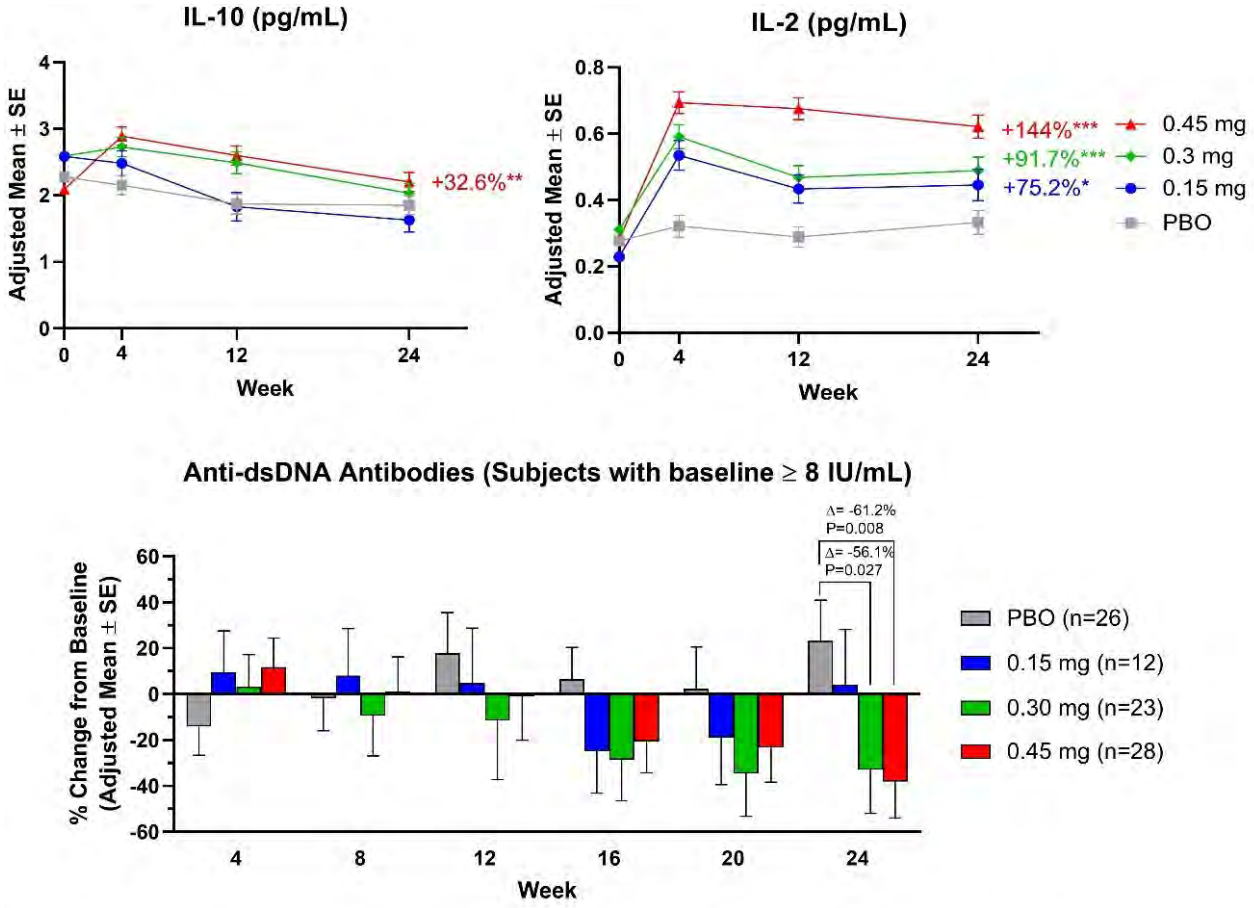

Figure 2. Pharmacodynamic changes in plasma IL-10, IL-2, and anti-dsDNA autoantibodies during iberdomide treatment. Values shown are the treatment comparison vs. placebo of adjusted means percent change from baseline (*p≤0.05, **p≤0.01,***p≤0.001).

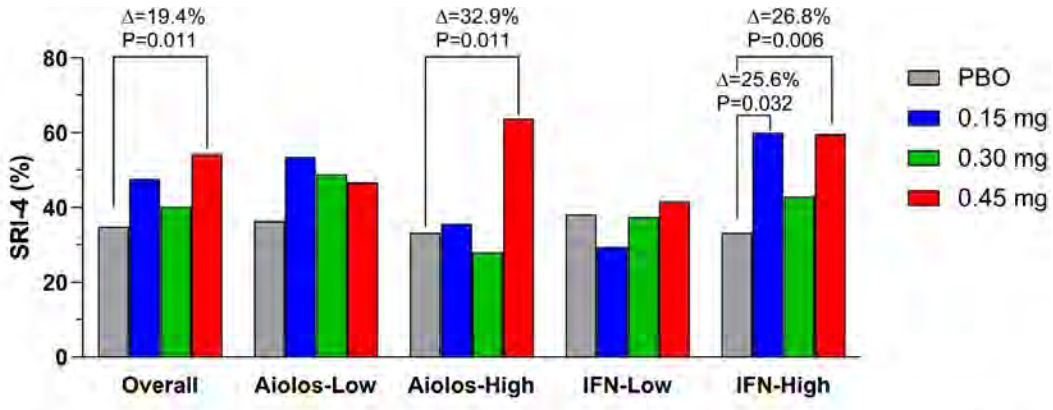

Figure 3. Week 24 SRI-4 clinical response rates in patient subsets defined by Aiolos and Type 1 IFN gene signature status at baseline. Aiolos = IKZF3; Type 1 IFN gene signature= *IFI27, IFI44, IFI44L, RSAD2;* Δ=treatment effect (stratified difference vs. placebo).

tra-sensitive cytokine assays (Erenna, EMD Millipore). PD data were reported as treatment differences from placebo in adjusted mean percent changes from baseline.

Results: Iberdomide pharmacokinetics were linear, with highest mean exposure observed at 0.45 mg. Iberdomide modulated leukocytes and cytokines in a dose-dependent manner, with significant changes at week 24 in the iberdomide 0.45 mg group compared with placebo, including decreased numbers of B cells, including those expressing CD268 (TNFRSF13C) (–58.3%; $P< 0.001$); decreased pDCs (–73.9%; $P< 0.001$); and increased Tregs (+104.9%; $P< 0.001$) (**Figure 1**). At week 24 compared with placebo, iberdomide 0.45 mg increased IL-10 (+32.6%; $P=0.005$) and IL-2 levels (+144.1%; $P< 0.001$) and decreased anti-double stranded (ds) DNA antibodies in patients with ≥8 IU/mL at baseline (–61.2%; $P=0.008$) (**Figure 2**). Iberdomide also decreased expression of the Type 1 IFN gene module. Iberdomide 0.45 mg caused a significant SRI-4 treatment effect versus placebo among patients within the baseline Aiolos-High subset (32.9%; $P=0.011$) and baseline Type 1 IFN-High subset (26.8%; $P=0.006$) (**Figure 3**).

Conclusion: Iberdomide significantly reduced activity of the Type 1 IFN and B cell/plasma cell pathways, including pDCs and Type 1 IFN-inducible genes as well as total B cells and those expressing TNFRSF13C, and anti-dsDNA antibody levels. Increases in Tregs, IL-2, and IL-10 suggest a broad rebalance of immune regulation. Clinical efficacy was noted in the entire cohort receiving 0.45 mg and was greater within the subsets with high expression of Aiolos or the Type 1 IFN gene signature at baseline. If validated, these PD effects may help refine future patient selection and dosing strategies for optimal use of iberdomide in SLE.

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Abstract Number: 0852

How Much Prednisone Is Enough for Remission Induction in Lupus Nephritis? A Propensity Score Matched Analysis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: SLE – Treatment Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Table 1. Baseline characteristics of the patients

	Low-to-medium prednisone (£30mg/day), n=118	High dose prednisone (³40mg/day), n=118	p
Age (y)	34.5 ± 11.0	33.3 ± 11.7	0.436
Caucasian	64 (54.2%)	62 (52.5%)	0.786
Black	18 (15.3%)	30 (25.4%)	0.04
Treatment initiation after 2003	76 (64.4%)	72 (61.0%)	0.662
SLEDAI-2K	13.7 ± 6.5	14.4 ± 6.5	0.395
Class III	14 (11.9%)	17 (14.4%)	0.564
Class IV	33 (28%)	43 (36.4%)	0.140
Class V	42 (35.6%)	27 (22.9%)	0.036
Hypertension*	59 (50%)	57 (48.3%)	0.793
Serum creatinine (mmol/l)	88 ± 39	92 ± 51	0.437
Proteinuria (g/24 hours)	2.7 ± 2.1	2.4 ± 2.0	0.259
Prednisone dose (median, range)	20 (20 - 30)	45 (40 – 80)	0.001
Azathioprine	53 (44.9%)	54 (45.8%)	0.889
Mycophenolate mofetil	56 (47.5%)	51 (43.2%)	0.494
Cyclophosphamide**	9 (7.6%)	13 (11%)	0.727
Antimalarials	69 (58.5%)	67 (56.8%)	0.789
ACEIs/ARBs	50 (42.4%)	48 (40.7%)	0.782

Categorical variables are presented as n (%), continuous as mean±standard deviation

*Defined as BP≥130/90mmHg

**All patients received the Euro-lupus cyclophosphamide protocol (6 intravenous bi-weekly pulses of 500mg each)

SLEDAI-2K: Systemic Lupus Erythematosus Disease Activity Index 2000; SDI: Systemic Lupus International Collaborating Clinics/Damage Index; ACEIs: angiotensin converting enzyme inhibitors; ARBs: angiotensin receptor blockers

Background/Purpose: The existing guidelines for remission induction in lupus nephritis (LN) from both the ACR and the EULAR recommend initial prednisone doses of 0.5-1mg/kg/day. However, recent observational studies reported non-inferior outcomes with significantly lower doses. The aim of this study was to compare the complete renal response rates in LN patients treated initially with £30mg/day or ³40mg/day of prednisone.

Methods: Patients with new-onset LN and standard immunosuppressive treatment with azathioprine or mycophenolate mofetil in standard doses or cyclophosphamide (Euro-lupus protocol) were included and followed for at least 12 months. Subjects were divided into low-to-medium (£30mg/day) and high prednisone groups (³40mg/day) and propensity score-matched based on global and renal disease activity. Complete renal response was defined as pro-

Table 2. Rates of complete renal remission at 12 months for different patient subgroups

	Low-to-medium prednisone (≤30mg/day, n=118)	High dose prednisone (≥40mg/day, n=118)	*p*
Complete remission* (n=236)	45 (38.1%)	68 (57.6%)	**0.003**
Complete and partial remission** (n=236)	64 (57.1%)	76 (66.7%)	0.061
Remission induction with AZA (n=66)	17/33 (51.5%)	19/33 (57.6%)	0.617
Remission induction with MMF or CYC (n=52)	11/26 (42.3%)	18/26 (69.2%)	0.052
Proliferative LN (classes III, IV) (n=66)	12/33 (36.4%)	19/33 (57.6%)	0.127
Non-proliferative LN (classes II, V) (n=26)	2/13 (15.4%)	9/13 (69.2%)	**0.02**
Sub-nephrotic proteinuria (n=86)	19/43 (44.2%)	26/43 (60.5%)	0.144
Treatment initiation before 2003*** (n=40)	10/20 (50%)	12/20 (60%)	0.527
Treatment initiation after 2003*** (n=102)	17/51 (33.3%)	32/51 (62.8%)	**0.004**

AZA: azathioprine, MMF: mycophenolate mofetil, CYC: cyclophosphamide

*Complete remission: proteinuria<0.5g/day and serum creatinine <120% of the baseline value

**Partial remission: proteinuria <50% and serum creatinine <120% of the baseline values

***After 2003, major changes were implemented in the management of LN in the UTLC with more frequent use of MMF and ACEIs/ARBs

teinuria < 0.5g/day and no worsening in renal function (serum creatinine £120% from baseline). Glucocorticoid-related damage was also assessed.

Results: Two hundred and thirty-six patients (118 in each group) were included. Baseline characteristics were well-balanced between groups except Black patients' predominance in the high prednisone group (25.4% vs. 15.3%, p=0.04) and higher frequency of LN class V in the low dose group (35.6% vs. 22.9%, p=0.036), Table 1. Median prednisone doses were 45mg/day and 20mg/day for the high and low-to-medium dose groups respectively. Complete renal response rates at 12 months in the main groups and certain subgroups of patients are shown in Table 2. Complete remission rates were also higher at two [75% vs. 40.3%, p=0.0002] and three years [67.2% vs. 51.7%, p=0.144] after LN diagnosis. Patients in the high dose group received less cumulative glucocorticoids during the 2nd and 3rd year after LN diagnosis and did not accrue more glucocorticoid-related damage, Table 3.

Conclusion: Higher initial prednisone doses (median 45mg/day) achieved significantly better rates of complete renal response at 12 and 24 months in new-onset LN. Findings were similar in different patient subgroups. These patients received less cumulative glucocorticoids in the 2nd and 3rd year and did not accrue more glucocorticoid-related damage. Our findings suggest that the treatment of LN with initially high doses of prednisone leads to improved rates of renal response that, in turn, allows for faster glucocorticoid tapering compared to patients who were treated with lower doses.

Table 3. Yearly cumulative glucocorticoid dose and glucocorticoid related damage accrual over time			
	Low-to-medium prednisone (≤30mg/day)	High dose prednisone (≥40mg/day)	p
At 12 months:	**N=118**	**N=118**	
Cumulative prednisone dose (g)	6.9 ± 3.0	8.9 ± 3.5	0.014
Prednisone dose at 12 months:	16.0 ± 12.4	13.4 ± 9.3	0.101
Cataract (new)	3 (2.5%)	0 (0%)	0.081
Osteoporosis (new)	0 (0%)	1 (0.8%)	0.316
Osteonecrosis (new)	2 (1.7%)	1 (0.8%)	0.561
Diabetes (new)	5 (4.2%)	2 (1.7%)	0.28
At 24 months:	**N=90**	**N=90**	
Cumulative prednisone dose in 12-24 months (g)	6.6 ± 4.0	5.2 ± 4.0	0.034
Prednisone dose at 24 months:	12.5 ± 9.6	8.8 ± 8.6	0.015
Cataract (new)	5 (5.6%)	1 (1.1%)	0.102
Osteoporosis (new)	1 (1.1%)	2 (2.2%)	0.564
Osteonecrosis (new)	4 (4.4%)	4 (4.4%)	1.000
Diabetes (new)	5 (5.6%)	2 (2.2%)	0.257
At 36 months:	**N=65**	**N=65**	
Cumulative prednisone dose in 24-36 months (g)	4.1 ± 3.0	2.7 ± 2.3	0.009
Prednisone dose at 36 months:	10.1 ± 7.8	7.6 ± 7.7	0.079
Cataract (new)	7 (10.8%)	1 (1.5%)	0.034
Osteoporosis (new)	3 (4.6%)	2 (3.1%)	0.655
Osteonecrosis (new)	3 (4.6%)	6 (9.2%)	0.317
Diabetes (new)	4 (6.2%)	2 (3.1%)	0.414

Disclosure: K. Tselios, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **H. Al-Sheikh**, None; **J. Su**, None; **M. Urowitz**, None.

Abstract Number: 0853

Gradual Glucocorticoid Withdrawal Is Safe in Clinically Quiescent Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) patients are usually treated with glucocorticoids even during periods of clinically quiescent disease. A recent study showed that abrupt glucocorticoid withdrawal was associated with increased likelihood of flare in the next 12 months. The aim of the present study was to assess clinical flare rates and damage accrual in patients who tapered glucocorticoids gradually.

Methods: Lupus patients with two consecutive years of clinically quiescent disease were retrieved from our long-term longitudinal cohort. Individuals who maintained a low prednisone dose (5mg/day) comprised the maintenance group whereas patients who tapered prednisone within these two years comprised the withdrawal group. All individuals were followed for two years after discontinuation. Outcomes included clinical flares (any increase in clinical SLEDAI-2K, any increase $^{3}4$ and any increase in clinical SLEDAI-2K plus escalation in systemic therapy (glucocorticoids and/or antimalarials and/or immunosuppressives) as well as damage accrual. A Cox proportional regression analysis was performed for the identification of predictors for clinical flare.

Results: Of 270 eligible patients, 156 maintained low dose prednisone and 114 discontinued gradually (62 within 12 months and 52 in 12-24 months). Demographic, clinical, serological and therapeutic characteristics are shown in Table 1. Patients in the withdrawal group developed significantly less flares by any applied definition at 24 months compared to the maintenance group, Table 2. Flare rates at 12 months were similarly better for withdrawal patients, although insignificantly. Regarding damage, less withdrawal patients accrued new damage at 24 months, Table 2. Further analysis of the slow (within 12-24 months) and fast (within 12 months) withdrawal patients demonstrated that the former group achieved better outcomes both for clinical flares and damage accrual, although insignificantly. Regarding predictors of flares, immunosuppressive therapy at baseline was associated with decreased likelihood of new flare [HR=0.64, 95%CI=0.435-0.943, p=0.024].

Conclusion: Gradual glucocorticoid withdrawal was associated with significantly less clinical flares at 24 months. Damage accrual was significantly less in the withdrawal patients. Immunosuppressive therapy at baseline was protective against new flares. Gradual glucocorticoid withdrawal is safe in clinically quiescent SLE.

Table 1. Demographic, clinical, serological and therapeutic characteristics of the patients at baseline

Variable	Maintenance group (n=156)	Withdrawal group (n=114)	p
Female:	138 (88.5%)	100 (87.7%)	0.852
Caucasians:	102 (65.4%)	79 (69.3%)	0.107
Blacks:	24 (15.4%)	9 (7.9%)	
Others:	30 (19.2%)	26 (22.8%)	
Age (y)	44.7 ± 14.5	41.8 ± 12.9	0.088
Disease duration (y)	15.1 ± 9	11.8 ± 8.5	**0.006**
Duration of clinical remission (y)	3.4 ± 2.3	3.8 ± 2.6	0.125
SLEDAI-2K	1.6 ± 1.5	1.6 ± 1.5	0.827
Adjusted mean SLEDAI-2K for the first 5 years since enrolment	3.2 ± 4.6	3.0 ± 1.9	**<0.001**
History of lupus nephritis*	70 (44.9%)	46 (40.4%)	0.459
History of CNS involvement**	68 (43.6%)	32 (28.1%)	**0.009**
Low C3/C4	64 (41%)	46 (40.4%)	0.866
Anti-dsDNA (+)	61 (39.1%)	43 (37.7%)	0.813
SDI	1.9 ± 2.3	1.0 ± 1.5	**<0.001**
Cumulative glucocorticoid dose*** (g)	47.5 ± 43.8	23.9 ± 22.0	**<0.001**
Antimalarials	97 (62.2%)	76 (66.7%)	0.448
Immunosuppressives	83 (53.2%)	48 (42.1%)	0.071

Categorical variables are presented as n (%), continuous as mean±standard deviation

SLEDAI-2K: SLE Disease Activity Index-2000; SDI: Systemic Lupus International Collaborating Clinics Damage Index

*Based on renal biopsy demonstrating lupus nephritis or abnormal proteinuria (>0.5 g/day) in two consecutive visits treated with glucocorticoids and immunosuppressives by the attending physician

**Based on any central nervous system involvement treated with glucocorticoids and/or immunosuppressives by the attending physician

***From first clinic visit up to the index date (in prednisone equivalent)

Table 2. Flare rates at 12 and 24 months and damage accrual at 24 months			
	Maintenance group (n=156)	**Withdrawal group (n=114)**	***p***
Flares at 12 months			
Flare (1st definition) *	43 (27.6%)	20 (17.5%)	0.055
Flare (2nd definition) **	21 (13.5%)	12 (10.5%)	0.467
Flare (3rd definition) ***	22 (14.1%)	8 (7.0%)	0.067
Flares at 24 months			
Flare (1st definition) *	75 (48.1%)	40 (35.1%)	**0.033**
Flare (2nd definition) **	44 (28.2%)	20 (17.5%)	**0.042**
Flare (3rd definition) ***	43 (27.6%)	16 (14.0%)	**0.008**
Damage accrual at 24 months			
Related to glucocorticoids	12 (7.7%)	3 (2.6%)	0.073
Not related to glucocorticoids	13 (8.3%)	5 (4.4%)	0.199
Increase in SDI	24 (15.4%)	8 (7%)	**0.036**

* Any increase in clinical SLEDAI-2K (excluding serology)

** Any increase in clinical SLEDAI-2K plus treatment escalation (for glucocorticoids, antimalarials or immunosuppressives)

*** Any increase ≥4 in clinical SLEDAI-2K

SDI: Systemic Lupus International Collaborating Clinics Damage Index

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Disclosure: K. Tselios, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **J. Su**, None; **M. Urowitz**, None.

Abstract Number: 0854

Mortality and Adverse Events of Special Interest in Adult Patients with Systemic Lupus Erythematosus Receiving Intravenous Belimumab: A Post Hoc Descriptive Summary of Serious Psychiatric Events

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Table. Key results

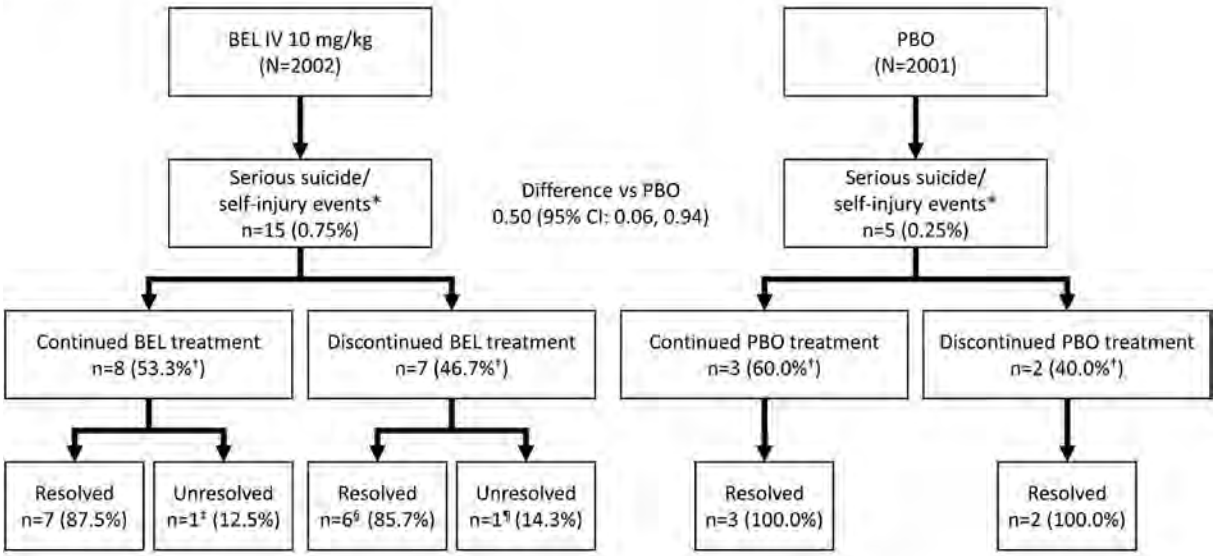
	BEL 10 mg/kg IV N=2002		PBO N=2001	
Number (%) of patients with on-treatment serious suicidal ideation/behavior and self-injury events	15 (0.75)		5 (0.25)	
PMH of psychiatric disorders, n (%)	7 (46.67)		1 (20.00)	
C-SSRS score ≥1 at baseline, n (%)	5 (33.33)		0	
Completed treatment, n (%)	7 (46.67)		1 (20.00)	
Completed study, n (%)	8 (53.33)		2 (40.00)	
	Continued BEL N=8	Discontinued BEL N=7	Continued PBO N=3	Discontinued PBO N=2
On-treatment serious suicidal ideation/behavior and self-injury events				
Median time to recovery,* days (range)	1 (1–919)	3 (1–34)	15 (1–22)	33 (9–56)
C-SSRS score				
Decreased from ≥1 to 0 after event, n/N	7/8†	-	2/3‡	-

*Number of days from onset to documented resolution; †one patient had no further C-SSRS data collected after their event; ‡one patient had a C-SSRS score of 0 throughout.
BEL, belimumab; C-SSRS, Columbia-Suicide Severity Rating Scale; IV, intravenous; PBO, placebo; PMH, prior medical history

Background/Purpose: Intravenous (IV) belimumab (BEL) is approved in patients ≥5 years of age with active systemic lupus erythematosus (SLE). Results of the BASE study (the largest SLE clinical study to date: n=4003), demonstrated similar rates of on-treatment all-cause mortality, infection and malignancy adverse events of special interest (AESI) between BEL and placebo (PBO). However, infrequent but higher incidences of other AESI including serious psychiatric events, fatal infections and hypersensitivity reactions occurred with BEL than PBO.[1] This analysis provides a *post hoc* descriptive summary of the disposition of patients who reported on-treatment serious suicide/self-injury events.

Methods: BASE (GSK Study BEL115467; NCT01705977) randomized adults with SLE (1:1) to receive BEL 10 mg/kg IV or PBO, plus standard SLE therapy, administered on Weeks 0, 2, 4, then monthly until Week 48. Rates of mortality and other pre-specified AESI, including serious psychiatric events and suicidality by Columbia-Suicide Severity Rating Scale (C-SSRS), were assessed on-treatment. The following were summarized *post hoc* for on-treatment serious

Figure. BASE study psychiatric events summary



*On-treatment serious suicidal ideation/behavior and self-injury events per GSK adjudication; †Percentages calculated from patients with serious suicide/self-injury events in each treatment group; ‡Lost to follow up; §One patient considered resolved with sequelae; ¶Withdrew from the study upon experiencing an event of major depression and considered recovering/resolving at follow-up.
BASE, Belimumab Assessment of Safety in SLE; BEL, belimumab; CI, confidence interval; IV, intravenous; PBO, placebo

suicide/self-injury events: time to onset, prior medical history (PMH), treatment completion and study completion, whether investigational product (IP) was taken after these events occurred, time to recovery, the C-SSRS score profile and outcome.

Results: There were 20 on-treatment serious suicidal/self-injury events (per sponsor adjudication), reported in 20 patients: 15 (0.75%) BEL and 5 (0.25%) PBO (*post hoc* difference vs PBO [95% confidence interval] 0.50 [0.06, 0.94]: **Figure**). All patients who experienced an event were female (aged 18–66 years, weight 40.5–99.3 kg, and mainly white [n=9] or black/African American [n=6]); 8/20 patients had a PMH of psychiatric disorder (**Table**). The median time to onset of the event was 205 days for BEL and 204 days for PBO. Approximately half (8/15) of the BEL patients and 3/5 PBO patients continued IP after these events occurred. The median time to recovery (number of days from onset to documented resolution) was shorter in those who did versus did not receive further IP, respectively, and lower in the BEL group vs the PBO group overall (**Table**). For the BEL and PBO groups who received further IP after the event, the C-SSRS score generally fell to 0 after the event (**Table**) and did not rebound, indicating resolution without further suicidal ideation and/or behavior during the study. Overall, 18/20 events were considered resolved and 0 patients experienced a recurrent event (**Figure**). No suicide-related deaths were reported.

Conclusion: An imbalance was observed with higher on-treatment serious suicidal ideation/behavior and self-injury events with BEL than PBO. These results are consistent with previously published data. The median time to onset of these events was similar between BEL and PBO, with the majority resolving with no sequelae, regardless of whether IP was discontinued or not. Overall the benefit:risk profile of belimumab remains positive.

[1]Sheikh S, *et al. Arthritis Rheumatol* 2019;71(S10):Abstract 0858

Disclosure: S. Sheikh, Pfizer, 1, GSK, 1; **R. Acayaba de Toledo**, GSK, 1, AbbVie, 1, 2, Pfizer, 1, Novartis, 1, 2, Janssen, 1, 2, UCB, 1; **L. Geraldino-Pardilla**, Pfizer, 1, BMS, 1; **J. Harris**, GSK, 1, 2, 3; **R. Kurrasch**, GSK, 1, 2, 3; **A. Liu**, GSK, 1, 2, 3; **K. Maksimowicz-McKinnon**, ChemoCentryx, 5, AstraZeneca, 9, Gilead, 9, GSK, 9, Merck, 9; **H. Quasny**, GSK, 1, 2, 3; **D. Roth**, GSK, 1, 2, 3; **L. Soto**, None; **R. Punwaney**, GSK, 1, 2, 3.

Abstract Number: 0855

Treatment of SLE with or Without Nephritis with the Immunoproteasome Inhibitor KZR-616: Updated Results of the MISSION Study

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SESSION INFORMATION
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Background/Purpose: Immunoproteasome inhibition has demonstrated meaningful therapeutic potential in preclinical models of systemic lupus erythematosus (SLE) and lupus nephritis (LN). KZR-616 is a first-in-class selective immunoproteasome inhibitor, which has been shown to have a favorable safety and tolerability profile in early clinical trials. Across 2 healthy volunteer studies, 100 subjects received KZR-616, up to 75 mg subcutaneously (SC), with target levels of immunoproteasome inhibition achieved with doses ≥30 mg. Here we report updated safety, tolerability and exploratory efficacy data from the Phase 1b portion of MISSION (KZR-616-002; NCT: NCT03393013) in which patients with active SLE or LN were treated with KZR-616.

Methods: SLE patients (per Systemic Lupus International Collaboration Criteria [SLICC] Classification Criteria) with SLEDAI ≥4 despite sTable background therapy were enrolled in this open-label dose-escalation study and received KZR-616 at doses of 45 mg (Cohort 1), 60 mg (Cohort 2), 60 mg following a step-up dose (Cohorts 2a, 2b, 2c), or 75 mg (Cohort 3) SC weekly through Week 13 (W13) with 12 weeks of follow-up. Safety, tolerability, PK and PD and early efficacy measures were collected.

Results: Through Cohort 2c, 41 patients with SLE, including 2 patients with active, biopsy-proven proliferative LN, have enrolled in the MISSION Phase 1b study. The majority of TEAEs have been mild or moderate with transient injection-site reactions as the most common TEAE. Improved tolerability was seen with a dose step-up strategy, use of the lyophilized formulation, subsequent doses, and use of pre-medications. To date, no patients have discontinued from later cohorts. All measures of disease activity (SLEDAI, Cutaneous Lupus Erythematosus Disease Area and Severity Index [CLASI], Tender and Swollen Joint Counts using 28 joints, Physician Global Assessment [PhGA], Patient Global Assessment [PtGA], and Patient Assessment of Pain [PtP]) improved from Baseline to W13 and were maintained or improved during the follow-up period compared to baseline. KZR-616 administration resulted in improvements in multiple serologic markers of disease activity as well as reduced expression of inflammatory gene expression modules. Both patients with active proliferative LN showed greater than 50% reductions in urine protein:creatinine ratios (UPCR) from baseline.

Conclusion: KZR-616 demonstrated a favorable safety and tolerability profile at target doses of 45 and 60 mg weekly for 13 weeks. Step-up dosing, use of the lyophilized formulation, subsequent doses, and use of select pre-medications increased tolerability. KZR-616 demonstrated early signals of efficacy as evidenced by improvement in multiple

disease activity and serologic markers, including reduction in proteinuria in 2 of 2 patients with LN. Weekly administration of 75 mg is currently being evaluated in Cohort 3, and a Phase 2 study of KZR-616 in active proliferative LN is open for enrollment.

Disclosure: R. Furie, AstraZeneca/MedImmune, 2, 5; **S. Parikh**, Aurinia Pharmaceuticals, 2, EMD-Serono, 2, Bristol-Meyers Squibb, 5, GlaxoSmithKline, 5; **K. Harvey**, None; **C. Kirk**, Kezar Life Sciences, 1, 3, 4, 6, Kezar Life Sciences, 1, 3, 4, 6; **D. Bomba**, Kezar Life Sciences, 1, 3; **M. Farmer**, Kezar Life Sciences Inc, 1, 3.

Abstract Number: 0856

Time to Renal Insufficiency Based on Prior Hydroxychloroquine Blood Levels

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
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Session Time: 9:00AM–11:00AM

Subgroup	Renal Insuff. events	Person-years of follow up	Rate of events per 1000 person years	Rate ratio (95% CI)	p-value
All	71	2837	25.0		
Sex					
Female	62	2644	23.4	1.00 (Ref)	
Male	9	193	46.7	2 (0.99, 4.02)	0.0531
Ethnicity					
Caucasian	25	1369	18.3	1.00 (Ref)	
African American	39	1214	32.1	1.76 (1.07, 2.91)	0.0272
Other	7	254	27.5	1.51 (0.65, 3.49)	0.3361
Age at person month					
<30	9	291	30.9	1.00 (Ref)	
30-<40	14	698	20.1	0.65 (0.28, 1.5)	0.3126
>=40	48	1848	26.0	0.84 (0.41, 1.71)	0.6324
Smoking					
Never	45	1984	22.7	1.00 (Ref)	
Ever	26	840	31.0	1.37 (0.84, 2.22)	0.2056
BMI					
<20	7	232	30.2	2.02 (0.82, 5.01)	0.1286
20-<25	14	937	14.9	1.00 (ref)	
25-<30	22	777	28.3	1.9 (0.97, 3.71)	0.061
30-<35	13	457	28.5	1.91 (0.9, 4.06)	0.0941
>=35	15	435	34.5	2.31 (1.12, 4.8)	0.0241
Education					
<=12	25	715	34.9	1.00 (ref)	
>12	46	2095	22.0	0.63 (0.39, 1.02)	0.0612
Income					
<$30,000	24	688	34.9	1.00 (ref)	
$30,000-$65,000	23	830	27.7	0.79 (0.45, 1.41)	0.4299
>=$65,000	24	1273	18.8	0.54 (0.31, 0.95)	0.0327

Rates of renal insufficiency events by demographics and patients characteristics

Subgroup	Renal Insuff. events	Person-years of follow up	Rate of events per 1000 person years	Rate ratio (95% CI)	p-value	Adjusted rate ratio[1] (95% CI)	Adjusted p-value[1]
Most recent HCQ blood level tertiles							
0-662	18	946	19.0	1.00 (Ref)		1.00 (Ref)	
663-1171	19	946	20.1	1.06 (0.55, 2.01)	0.87	1.10(0.57, 2.12)	0.7687
1172-5672	34	946	36.0	1.89 (1.07, 3.35)	0.0289	2.03 (1.14, 3.62)	0.0169
Mean prior blood levels tertiles							
3-645	17	946	18.0	1.00 (Ref)		1.00 (Ref)	
645.03-1069	19	946	20.1	1.12 (0.58, 2.15)	0.7376	1.23 (0.63, 2.41)	0.5468
1069.14-3316	35	946	37.0	2.06 (1.16, 3.69)	0.0144	2.19 (1.21, 3.97)	0.0095
Rate ratios and p-values were adjusted for age, sex, race, BMI, education							

Rates of renal insufficiency events by HCQ blood levels

	Unadjusted		Adjusted	
	Rate ratio (95% CI)	p-value	Rate ratio (95% CI)	p-value
Most recent blood levels (per 100 unit difference)	1.05 (1.01, 1.08)	0.0062	1.05 (1.02, 1.08)	0.0037
Mean prior blood levels (per 100 unit difference)	1.06 (1.02, 1.10)	0.0080	1.06 (1.02, 1.10)	0.0051
Rate ratios and p-values were adjusted for age, sex, race, BMI, education				

Association between HCQ levels and renal insufficiency

Background/Purpose: Hydroxychloroquine (HCQ) dosing is reduced in those with renal insufficiency according to guidelines (Marmor MF, et al. Ophthalmology 2016;123:1386–94) as it is partially cleared by the kidneys. Some studies have found that HCQ use might protect against end stage renal disease. We explored these issues using HCQ blood levels.

Methods: Hydroxychloroquine blood levels were measured by liquid chromatography-tandem mass spectrometry as described by Füzéry et al (Clin Chim Acta 2013;421:79–84). Renal insufficiency was defined as GFR < 50% or creatinine > 1.5 mg/mL. At least one HCQ blood level was measured at a clinic visit in 1,066 patients. Excluding patients with prior renal insufficiency (275) and missing information (6), there were 785 patients eligible for analysis, contributing 34,046 person months. There were 71 incident renal insufficiency events after the first HCQ blood level measurement. For this analysis, a dataset with one record for each month of follow up for each person were constructed. Patients were followed from first measure of HCQ blood levels to their first incident renal insufficiency or their last recorded visit with HCQ blood levels. To calculate the rate of renal insufficiency in each demographic or clinical subgroup, the number of renal insufficiency events was divided by the number of person months at risk and then converted to rates per 1,000 person years. Pooled logistic regression was used to assess the relationship between HCQ blood levels and rates of renal insufficiency.

Results: All patients met revised ACR or SLICC classification criteria and were 93.2% female, 41% African-American, and 47.8% Caucasian. Table 1 shows the association between patient characteristics and the rate of renal insufficiency. The categories of HCQ blood levels (mean or most recent) were divided into tertiles, each containing a third

of the person-years, to see if there were any trends of HCQ blood levels in incident renal insufficiency. Table 2 shows the association between HCQ blood levels tertiles and the rate of renal insufficiency. The rate of renal insufficiency increased with HCQ blood levels. Next, the HCQ blood levels were modeled as continuous variables (Table 3). There were significant associations between HCQ blood levels and incident renal insufficiency. The associations persisted after adjustment of covariates.

Conclusion: HCQ blood levels clearly rose in those with renal insufficiency, whether we looked at the most recent level before renal insufficiency or the mean of all prior HCQ blood levels. Disappointingly, HCQ blood levels at the mid or high tertile did not reduce later renal insufficiency. Thus, our data do not support that HCQ would reduce end stage renal disease. Renal insufficiency was associated with higher HCQ blood levels, likely due to reduced HCQ renal clearance, justifying the recommendation to reduce dose in those with chronic kidney disease.

Disclosure: M. Petri, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmithKline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5; **J. Li**, None.

Abstract Number: 0857

Agreement of Hydroxychloroquine Blood Levels Between a University and Commercial Laboratory

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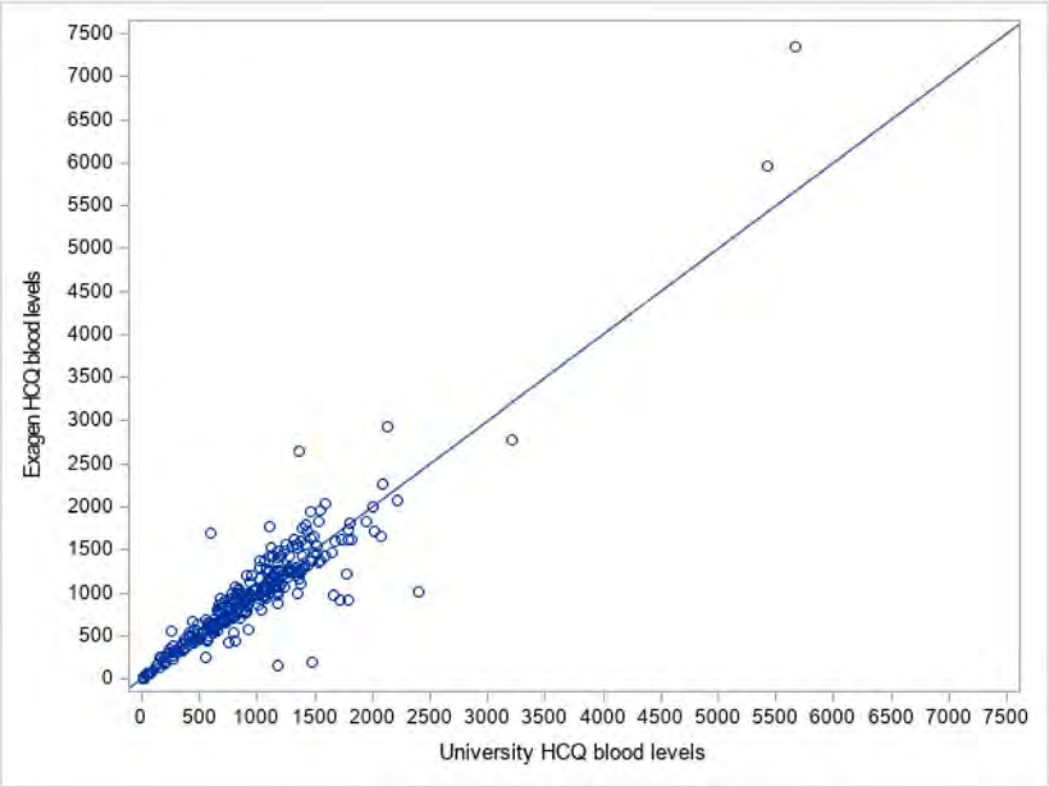
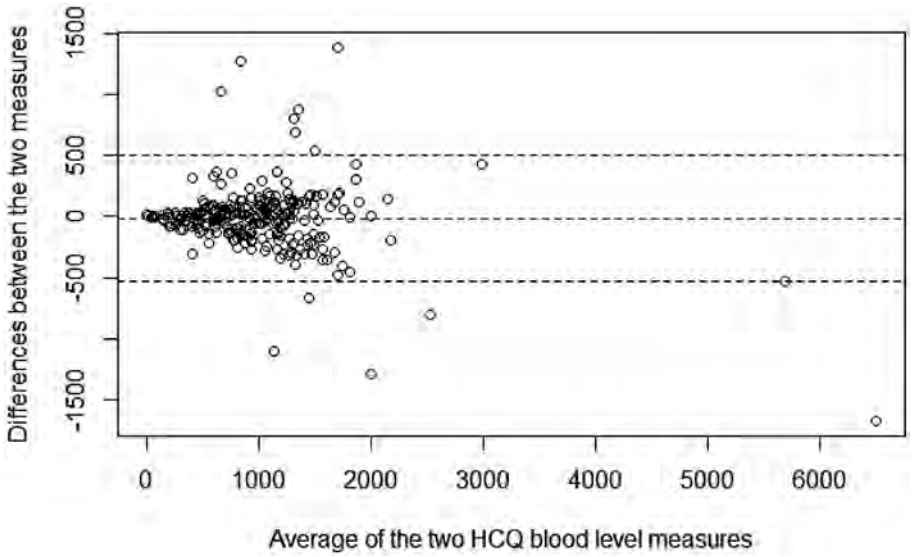
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Therapeutic blood monitoring is not yet an accepted practice in rheumatology. Although hydroxychloroquine (HCQ) blood level monitoring has been utilized in limited pharmacokinetic studies for some time, evidence for the utility of HCQ therapeutic blood monitoring in clinical practice has accumulated in recent years. Blood levels, rather than plasma levels, accurately reflect exposure and measure adherence over the last month. HCQ blood levels predict retinopathy (Arthritis Rheumatol 2020;72:448–53) but also predict benefit, such as prevention of thrombosis (Abstract OP0160, European e-Congress of Rheumatology 2020, June 3-7). We compared HCQ blood levels from the same visit done at two laboratories to ascertain agreement.

Methods: All patients met revised ACR or SLICC classification criteria for SLE. Of the 114 patients included, 15 patients had 1 visit, 27 2 visits, 71 3 visits, and 1 patient 4 visits for a total of 286 visits. Patients were 85% female, 37% African American, and 51% Caucasian. HCQ blood levels were measured using the method of Füzéry et al. (Clin Chim Acta 2013;421:79–84) with a coefficient of variation < 3%, and at Exagen Diagnostics using liquid chromatography coupled to mass spectrometry (AVISE® HCQ). The Bland-Altman plot was generated using R package *BlandAltmanLe*. Intra-class correlation coefficient (ICC) was calculated using *irr* package in R version 3.6.1. Deming regression was performed using mcr package in R. Confidence bounds (95%) were calculated with the bootstrap method.

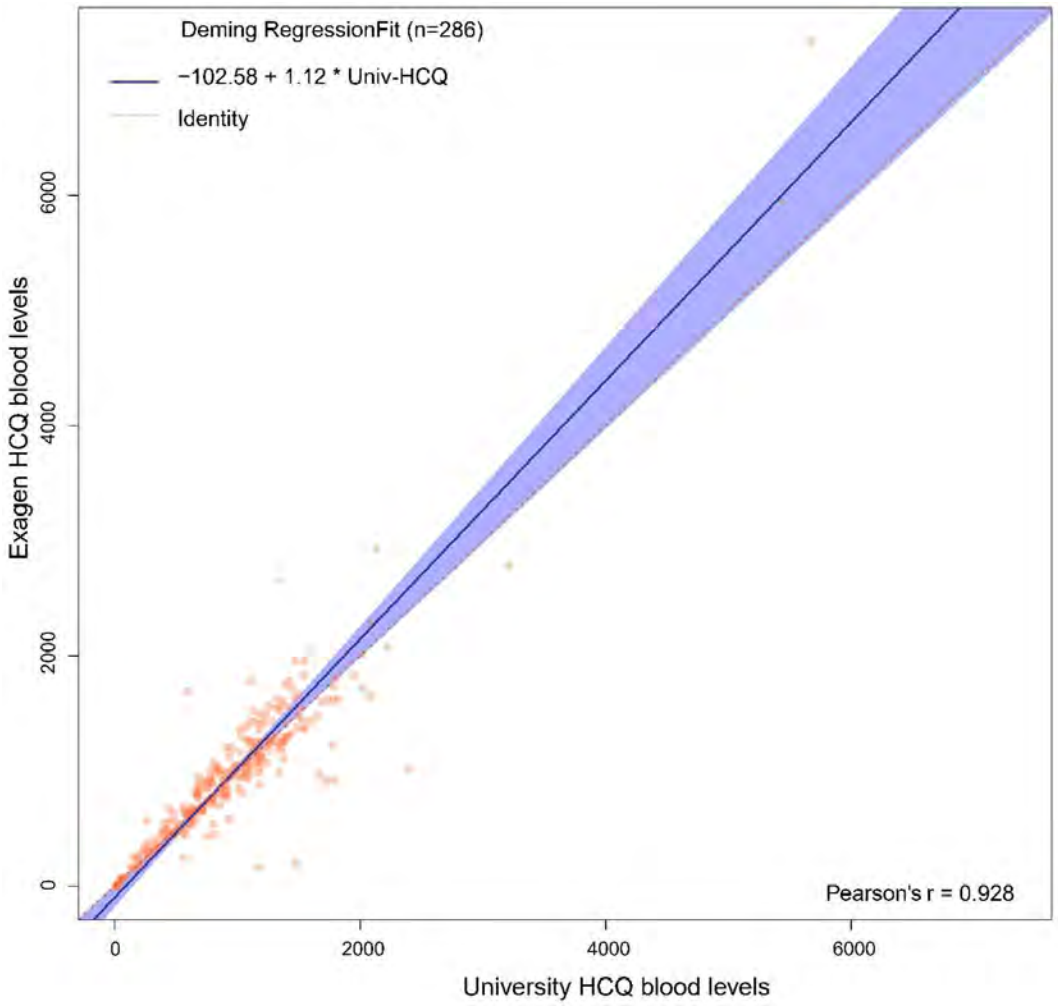


Deming Regression Plot Looking at Systematic Differences Between the Two Hydroxychloroquine Blood Level Measurement Methods



Bland-Altman Plot Showing Differences Between the Two Measures of Hydroxychloroquine Blood Level

Results: Figure 1 shows the comparison of the University HCQ blood levels to the commercial HCQ blood levels. The Bland Altman plot showed the difference between the two measures of HCQ blood level of each patient against the average of the two measures (Figure 2). The mean difference between the two methods was -13.9, 95% limits



Comparison of the University Hydroxychloroquine Blood Levels to the Exagen Hydroxychloroquine Blood Levels

of agreement were (-529.3, 501.5), and 4.2% (n=12) data points fell outside of the confidence limits. Intra-class correlation coefficient was used to calculate an estimate of the overall agreement between the two measurements. The ICC was 0.923 (0.904, 0.938). Deming regression was used to look at systematic differences between the two HCQ blood level measurement methods (Figure 3). The slope of best fit was 1.12 with 95% confidence limits of (0.99, 1.22).

Conclusion: There is excellent agreement between a university and commercial laboratory in measuring HCQ blood levels. Clinicians can be confident in the reliability of the hydroxychloroquine blood level. This should increase acceptance and utilization. Hydroxychloroquine blood levels have proven there is a “therapeutic window” to maintain benefit and still reduce risk of retinopathy.

Disclosure: M. Petri, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmithKline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5; **J. Li**, None; **K. Brady**, Exagen Inc., 1, 3; **J. Conklin**, Exagen, 1, 2; **T. O’Malley**, Exagen, 1, 2; **T. Dervieux**, Exagen, 1.

Abstract Number: 0858

Leflunomide: A Safe and Effective Alternative in Systemic Lupus Erythematosus

Irene Carrión-Barberà[1], Tarek Carlos Salman Monte[1], Luciano Polino[1], Miguel Mejía[1], Manel Ciria[1], Carolina Pérez-García[1], Eva Rodríguez[1] and Jordi Monfort[1], [1]Hospital del Mar, Barcelona, Spain

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Leflunomide (LEF) is a DMARD commonly used safely and effectively in rheumatoid arthritis. The experience with LEF in SLE is mainly based on what has been reported in cases or case series [1], with only one clinical trial evaluating its efficacy in extrarenal manifestations [2].

The purpose of our study is to assess the efficacy and safety of LEF in the treatment of SLE patients as well as to investigate if there are any clinical characteristics that correlate with a better response to treatment and, thus, identify the subgroup of patients that would benefit most from it.

Methods: Retrospective observational study. Medical records of all patients diagnosed with SLE (1997 ACR criteria) were reviewed and those who had received LEF were selected. Patients were evaluated for safety and efficacy after 4.9±3.2 months of therapy. Demographic and clinical data were collected. Variables were analyzed using SPSS 25 (IBM®) by descriptive statistics and cross-tabs if qualitative, the comparison of means by the Student's t-test and correlations by Pearson's correlation coefficient.

Results: Thirty-five patients were included, with a mean age of 52.2±14.7 years and 15.1±13 years since SLE diagnosis. The indication for LEF was arthritis in 34 patients (94.7%), relapsing polychondritis in 1 (2.9%). Age at LEF initiation was 48.3±14.7 years. The dose started was 20mg/day in 20 patients (57.1%), 10mg/day in 13 (37.1%). Seventeen patients (48.7%) went into joint remission after the initiation of LEF, and glucocorticoids (GC) could be withdrawn in 7 (20%). In 7 patients (20%) LEF was withdrawn before the first efficacy evaluation. The different adverse effects, as well as the demographic and clinical data of the patients are detailed in Table 1. We did not find any serious adverse effect or any case of subcutaneous lupus attributed to LEF. Our patients SLE baseline activity was mild–moderate: SLEDAI 6.3±3.1, normal average C3 and C4. Pre-LEF, 10 patients had positive DNA, 7 low C3, and 6 low C4. Failed treatments before LEF and treatments received concomitantly are detailed in Figure 1. In Figure 2, a statistically significant pre- and post-LEF decrease in physician global assessment (PGA), SLEDAI and ESR was observed, a non-significant one in dsDNA and GC values, as well as a non-significant increase in C3 and C4.

No correlation was found between the maximum dose of GC ever used, as an indicator of disease severity, and a better response in any parameters (ESR, CPR, PGA, dsDNA, C3, C4) pre- and post-LEF, or with going or not into joint remission. Neither was found a correlation between achieving remission or not, and the different demographic, clinical or treatment characteristics of patients, which does not allow to discern which subgroup of patients would benefit most from LEF treatment.

Nowadays, 15 patiens continue taking LEF (42.8%), with a mean treatment time of 4.4±3.9 years.

Variables	Number of patients (%)
Sex	
Women	31 (88.6%)
Men	4 (11.4%)
Race	
Caucasians	27 (77.1%)
Hispanics	4 (11.4%)
African-American	1 (2.9%)
Asians	2 (5.7%)
Maghrebi	1 (2.9%)
Reason for LEF withdrawal	
Digestive intolerance	2 (5.7%)
Hypertension	2 (5.7%)
Transient leuko/neutropenia	1 (2.9%)
Transient high liver enzymes	1 (2.9%)
Ineffective	3 (8.6%)
Other active manifestations	3 (8.6%)
Other side effects	6 (17.1%)
dsDNA +	22 (62.9%)
Anti–Ro60 +	12 (34.3%)
Anti–Ro52 +	9 (25.7%)
Anti–Sm +	8 (22.9%)
APS antibodies	10 (28.6%)
RF +	5 (14.3%)
ACPA +	3 (8.6%)
Lupus nephritis	7 (20.0%)
Other autoimmune systemic diseases	15 (42.8%)
Sjögren's syndrome	8 (22.85%)
Rheumatoid arthritis	4 (11.4%)
Antiphospholipid syndrome	3 (8.6%)
Relapsing polychondritis	1 (2.9%)

Table 1. Demographic and clinical characteristics of the 35 included patients.

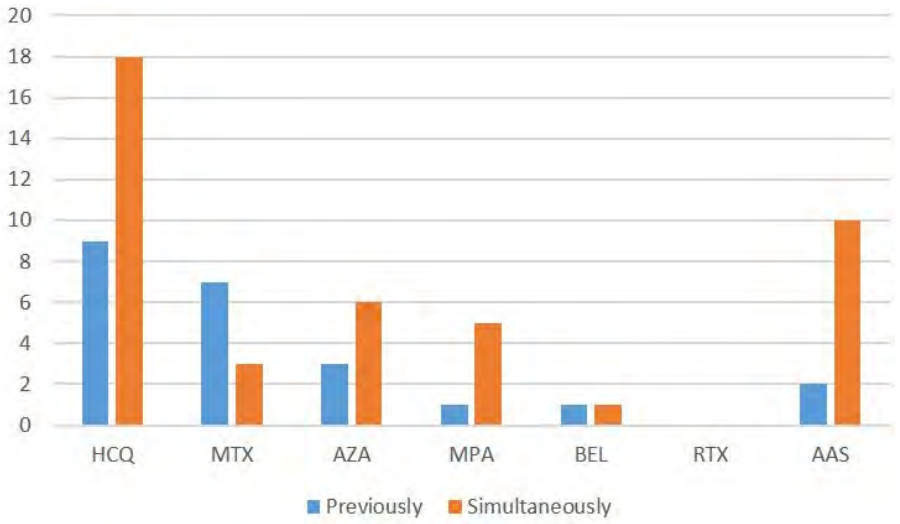


Figure 1. Previous and concomitant treatments to LEF. A treatment is reported as "previously" if it was stopped before LEF was started and "simultaneously" if it was started or maintained at the same time as LEF. HCQ: hydroxychloroquine; MTX: methotrex-ate; AZA: azathioprine; MPA: mycophenolic acid; BEL: belimumab; RTX: rituximab; AAS: acetylsalicylic acid.

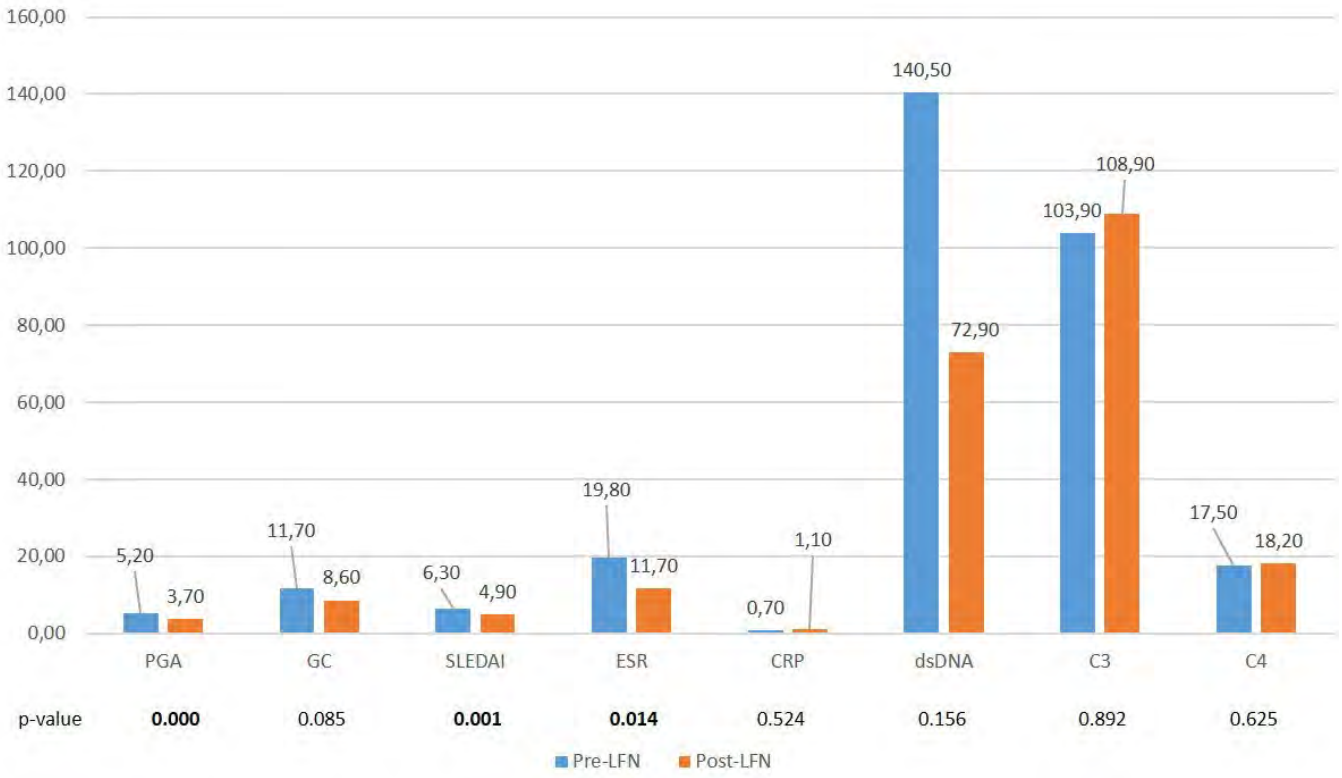


Figure 2. Value changes in different parameters before and after LEF. PGA: physician global assessment, GC: glucocorticoids, SLEDAI: Systemic Lupus Erythematosus Disease Activity Index; ESR: erythrocyte sedimentation rate; CRP: C-Reactive Protein; dsDNA: double-stranded DNA; C3: complement C3; C4; complement C4.

Conclusion: Treatment with LEF in SLE seems to be an effective and safe option, particularly for joint symptoms, with significant improvement observed in PGA, SLEDAI and ESR, as well as a 48.6% of joint remission after its onset.

Disclosure: I. Carrión-Barberà, None; **T. Salman Monte**, None; **L. Polino**, None; **M. Mejía**, None; **M. Ciria**, None; **C. Pérez-García**, None; **E. Rodríguez**, None; **J. Monfort**, None.

Abstract Number: 0859

Biomarkers of B-cell Depletion and Response in a Randomized, Controlled Trial of Obinutuzumab for Proliferative Lupus Nephritis

Ed Vital[1], Philippe Remy[2], Luis Fernando Quintana Porras[3], Laurent Chiche[4], Dominique Chauveau[5], Richard Furie[6], Thomas Schindler[7], Jay Garg[8], Matthew Cascino[8], Zahir Amoura[9], Andrea Doria[10], Cary Looney[8] and Dario Roccatello[11], [1]University of Leeds; NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, [2]APHP Groupe Hospitalier Henri-Mondor, Creteil, France, [3]Hospital Clinic de Barcelona, Barcelona, Catalonia, Spain, [4]Hôpital Européen, Marseille, France, [5]Hôpital Rangueil, Centre Hospitalier Univ de Toulouse, Toulouse, France, [6]Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, [7]F. Hoffmann-La Roche Ltd., Basel, Switzerland, [8]Genentech, Inc., South San Francisco, CA, [9]Hôpital Pitié-Salpêtrière, Paris, [10]University of Padua, Padua, Italy, [11]S Giovanni Hospital, Univ of Turin, Turin, Italy

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Incomplete B-cell and plasmablast depletion, as measured using highly sensitive flow cytometry (HSFC), is associated with lower response rates following rituximab in SLE [1]. Enhanced B-cell depletion with the type II anti-CD20 monoclonal antibody obinutuzumab resulted in increased renal responses in proliferative lupus nephritis (LN) in the NOBILITY trial (NCT02550652) and will be further evaluated in the Phase 3 REGENCY trial (NCT04221477). The objective of this analysis was to measure peripheral B-cells, B-cell subsets (naïve, memory and plasmablast) and B-cell activating factor (BAFF) levels and to assess associations between B-cell depletion and renal response in LN patients in a clinical trial of obinutuzumab.

Methods: 126 patients with active Class III/IV LN were randomized to obinutuzumab or placebo infusions in combination with mycophenolate and glucocorticoids. Peripheral B-cells were measured using a HSFC method with a lower limit of quantitation of 0.441 cells/μL. Serum levels of BAFF were evaluated using ELISA. Sustained depletion was defined by total B-cells below the limit of detection at both weeks 24 and 52. Renal response definitions from Phase 2 NOBILITY and Phase 3 REGENCY trials were used.

Results: Obinutuzumab resulted in rapid depletion of total B-cells, memory and naïve B-cells, and plasmablasts from peripheral blood, with 88% of obinutuzumab patients depleted to < 0.441 total B-cells/μL at week 2 (Figure). Mean serum BAFF increased from 4,585 pg/mL at baseline to 14,601 pg/mL at week 52 in the obinutuzumab group. Sustained B-cell depletion was achieved in 32/52 (62%) of patients with complete data and was associated with a higher renal response rate at week 76 (Table), although patients who achieved sustained depletion also had lower baseline proteinuria and serum creatinine.

Conclusion: Obinutuzumab, a type II anti-CD20 mAb, mediated rapid, complete and sustained depletion of peripheral B-cells and plasmablasts and large increases in serum BAFF. Similar to previous reports, sustained B-cell depletion was associated with increased renal response though there may have been confounding factors. REGENCY is being conducted to further evaluate the therapeutic hypothesis with obinutuzumab in LN.

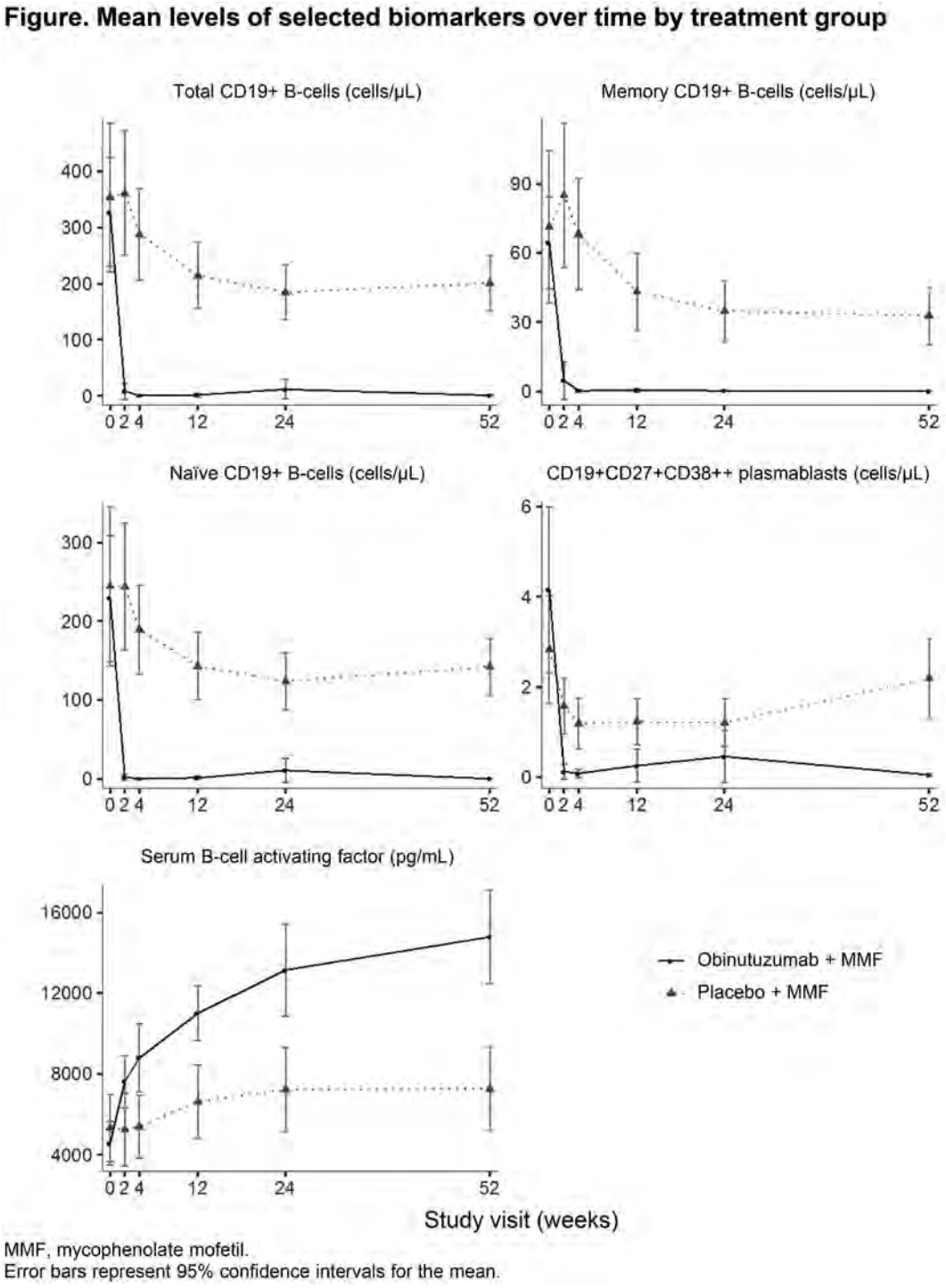


Figure. Mean levels of selected biomarkers over time by treatment group.

References:

1. Md Yusof MY et al. *Ann Rheum Dis*. 2017;76:1829-36.

Definition of response	Obinutuzumab sustained depletion (N = 32)[a]	Obinutuzumab detectable B-cells (N = 20)[a]	Placebo group detectable B-cells (N = 62)
NOBILITY complete response UPCR < 0.5, SCr ≤ ULN and not increased > 15% from baseline SCr, and < 10 RBC/hpf without casts	50%**	35%*	18%
NOBILITY overall response CRR or ≥ 50% reduction in UPCR[b] with SCr not increased > 15% from baseline and urinary RBCs not increased > 50% from baseline	66%***	45%*	29%
REGENCY complete response UPCR < 0.5, SCr ≤ ULN and not increased > 25% from baseline SCr	69%**	45%	31%
REGENCY overall response CRR or ≥ 50% reduction in UPCR[b] with SCr not increased > 25% from baseline	84%***	55%	50%

* P < 0.2 vs. placebo group.
** P < 0.05 vs. placebo group.
*** P < 0.001 vs. placebo group.
[a] Eleven patients in the obinutuzumab group with insufficient data to determine depletion status were excluded.
[b] ≥ 50% reduction in UPCR to a value < 1 (< 3 if the baseline UPCR was ≥ 3).

Table. Data from NOBILITY at week 76 by depletion status at weeks 24 and 52.

Disclosure: E. Vital, Roche/Genentech, 2, 5; **P. Remy**, None; **L. Quintana Porras**, None; **L. Chiche**, None; **D. Chauveau**, None; **R. Furie**, AstraZeneca/MedImmune, 2, 5; **T. Schindler**, Roche, 1, 3; **J. Garg**, Genentech, 1, 3; **M. Cascino**, Genentech, 1, 3; **Z. Amoura**, Roche, 2; **A. Doria**, GlaxoSmithKline, 5, 8, Eli Lilly, 5, 8, Roche, 5, 8, Janssen, 5, 8, Pfizer, 5, 8; **C. Looney**, Genentech, 1, 3; **D. Roccatello**, None.

Abstract Number: 0860

PREVAIL 1: A Multiple Ascending Dose Study in Normal Healthy Volunteers of PRV-3279, a Novel Bispecific DART Molecule Targeting CD32B and CD79B on B Cells, with Potential for Treatment of SLE

Paul Dunford[1], Gail Comer[1], Ralph Raymond[1], Donald Jung[1], Paul Moore[2], Francisco Leon[1] and Joan Merrill[3], [1]Provention Bio, Oldwick, NJ, [2]MacroGenics, Rockville, MD, [3]Oklahoma Medical Research Foundation, Oklahoma City, OK

SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Table 1. Summary of PRV-3279 Safety by System Organ Class/Preferred Term

System Organ Class /Preferred Term	PRV-3279 3 mg/kg (N = 6) n (%) E	PRV-3279 10 mg/kg (N = 6) n (%) E	Pooled Placebo (N = 4) n (%) E
Number of subjects and events with at least 1 TEAE	3 (50.0) 12	5 (83.3) 18	1 (25.0) 4
Number of subjects and events with SAEs	0	0	0
General disorders and administration site conditions	3 (50.0) 6	2 (33.3) 4	1 (25.0) 3
Skin and subcutaneous tissue disorders	1 (16.7) 2	3 (50.0) 6	0
Nervous system disorders	1 (16.7) 1	1 (16.7) 1	1 (25.0) 1
Gastrointestinal disorders	1 (16.7) 1	1 (16.7) 2	0
Respiratory, thoracic and mediastinal disorders	0	2 (33.3) 2	0
Ear and labyrinth disorders	0	1 (16.7) 1	0
Infections and infestations	0	1 (16.7) 1	0
Injury, poisoning and procedural complications	1 (16.7) 1	0	0
Musculoskeletal and connective tissue disorders	1 (16.7) 1	0	0
Reproductive system and breast disorders	0	1 (16.7) 1	0

Table 2. Summary of PRV-3279 Pharmacokinetic Parameters by Dose and Day (Geometric Mean (%CV))

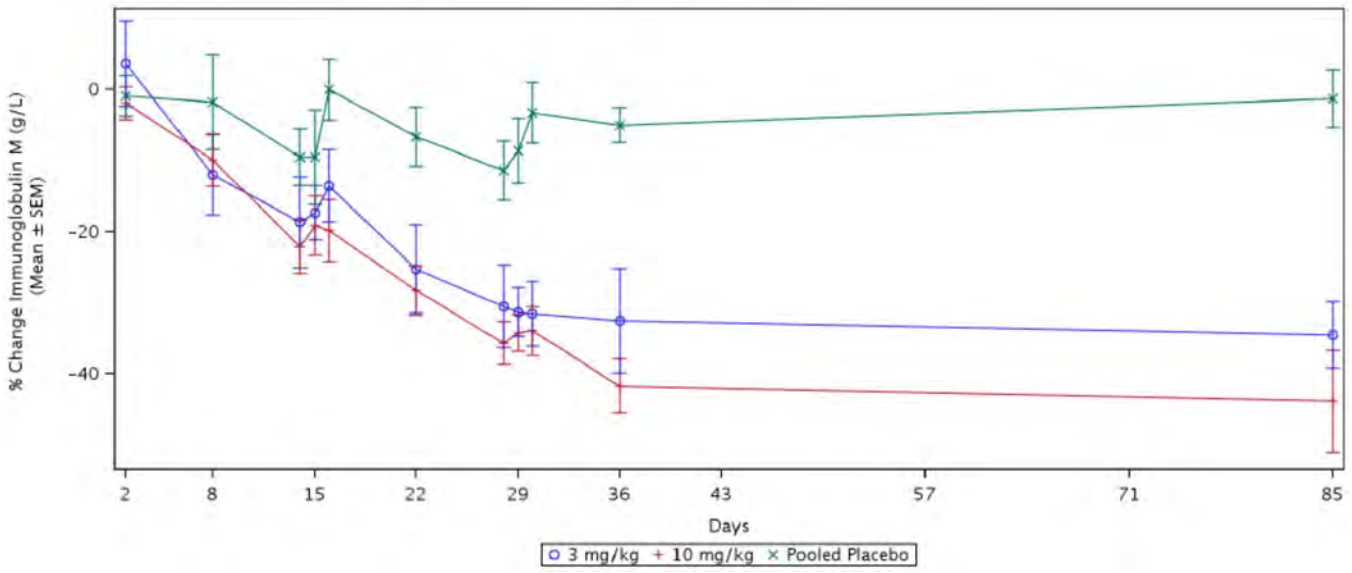
	3 mg/kg (n=6)		10 mg/kg (n=6)	
Parameter	**Day 1**	**Day 29**	**Day 1**	**Day 29***
C_{max} (µg/mL)	90.6 (21.0)	97.9 (14.4)	346 (34.7)	461 (13.6)
$AUC_{0\text{-}336}$ (µg-d/mL)	348 (23.7)	463 (14.3)	1688 (14.2)	2563 (11.5)
Half-Life (d)	3.85 (19.5)	6.54 (18.6)	5.25 (13.8)	7.71 (13.3)
Cl (mL/h/kg)	--	2.71 (14.3)	--	1.63 (11.5)
V_{ss} (L/kg)	--	0.618 (23.6)	--	0.576 (26.8)

*n=5

Background/Purpose: B-cell targeted therapeutics have proven efficacious in the treatment of autoimmune disorders. A desired improvement in efficacy and safety necessitate the development of alternate, fast acting and non-depleting B cell modulators. PRV-3279 (previously MGD010) a bispecific molecule, exploits the inhibitory function of the SLE-associated checkpoint molecule, CD32B, (FcγRIIb) via its simultaneous co-ligation with the BCR component, CD79B. Initial single-dose Phase 1 trials in healthy subjects demonstrated PRV-3279 was well tolerated and modulated B cells without depletion. PREVAIL (PRV-3279 EVAluation In Lupus) 1, a multiple ascending dose study in healthy subjects, was performed to further characterize the safety, PK and PD of PRV-3279 upon repeat administration. In vitro studies on B cells from SLE subjects were also performed to support transition into the planned Phase 2a PREVAIL 2 study in SLE.

Methods: This was a double-blind, placebo-controlled MAD study in healthy volunteers. Subjects (n=8 per group) were randomly assigned to two cohorts to receive an IV administration of 3 bi-weekly infusions of 3 or 10 mg/kg PRV-3279, or placebo (6:2). Safety, PK, binding of PRV-3279 to total and B cell sub-sets, peripheral lymphocyte counts, and determination of serum immunoglobulin levels were assessed for 12 weeks. Additionally, CD32B and CD79B

Figure 1: Effect of PRV-3279 on Circulating IgM Levels



levels on purified B cells from SLE subjects and the effect of PRV-3279 on SLE B cell proliferation was determined, compared with healthy controls.

Results: PRV-3279 was well-tolerated, with no serious adverse events **(Table 1).** Pharmacokinetic **(Table 2)** and pharmacodynamic parameters were dose-dependent with extensive binding to both naïve and memory B cells, and a mean sustained binding of >90% available B cells observed at 10 mg/kg. An extended pharmacodynamic effect was demonstrated by a sustained and maximum mean reduction of 44% in circulating IgM levels at 10 mg/kg, at the final sampling at Week 12 **(Figure 1).** PRV-3279 did not deplete B cells, although there was a mean transient decrease of up to 47% after each infusion, returning to baseline at the next measurement (+1 week). In vitro, expression of CD32B and CD79B on SLE patient B cells was similar to healthy controls, and PRV-3279 inhibition of SLE B cell proliferation (mean 63% reduction) was not significantly different to those from healthy controls.

Conclusion: PRV-3279 was well tolerated after repeat administration with no B cell depletion and dose-dependent PK and PD. Consistent with its mechanism of action, sustained IgM reduction was observed. In vitro studies demonstrated equivalent effects of PRV-3279 on B cells from SLE subjects. These data support further development of PRV-3279 in SLE and other autoimmune disorders**.**

Disclosure: P. Dunford, None; **G. Comer**, ProventionBIo, 5; **R. Raymond**, None; **D. Jung**, ProventionBio, 5; **P. Moore**, None; **F. Leon**, Provention Bio, 1, 3; **J. Merrill**, None.

Abstract Number: 0861

Hydroxychloroquine Use Is Associated with Diminished Type I Interferon-related Pathways in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: SLE – Treatment Poster I

Session Type: Poster Session B

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Background/Purpose: Hydroxychloroquine (HCQ) has been used for decades to treat systemic lupus erythematosus (SLE) and is associated with decreased lupus flares and damage. However, despite reports of an impact on TLR pathways, its mechanism of action remains controversial.

Methods: Whole blood from healthy controls (n=8) and SLE patients taking (n=9) or not taking HCQ (n=9) were stimulated for 15 minutes or 24 hours with either Toll-like receptor (TLR) (for TLR4, TLR7/8 or TLR9), interferon-α (IFNα), T cell (phytohemagglutinin and ionomycin), or cell signaling inducers (phorbol myristate acetate and ionomycin). Cell culture supernatants and phospho-proteins were analyzed. Cytokine levels from patient plasma and culture supernatants were assessed by 37-plex xMAP assays and ELISAs. Alterations in phospho-signaling proteins were assessed by mass cytometry. To determine alterations in phospho-signaling pathways, whole blood from healthy controls were stimulated with IFNα or TLR7/8 or TLR9 agonists with or without HCQ.

Results: We found no differences in plasma IFNα levels of patients taking HCQ versus those not taking it, nor was there altered IFNα production following TLR stimulation. In SLE, persistent activation of T cell, TLR7/8, and TLR9 signaling leads to exhaustion of these pathways. Compared to controls, we confirmed reduced phosphorylation of multiple signaling proteins and reduced cytokines in patients on or off HCQ after stimulation by TLR agonists (Figure 1A and 1B). However, cytokine production following T cell or TLR stimulation was less impaired in patients on HCQ with an increased fold change in IL-10 ($p=0.003$), IFNg ($p=0.011$), IL-18 ($p=0.016$), CXCL13 ($p=0.009$), IL-6 ($p=0.046$), IL-1α ($p=0.036$) and other cytokines that approached healthy controls. The only cytokines that did not exhibit improved production in those on HCQ were IFNα and TNFα following TLR stimulation, where fold change was reduced in all SLE patients compared to healthy controls ($p< 0.01$). In control samples treated with HCQ in vitro, TLR9 induced signaling of p-p38 ($p=0.046$) and pIκBα ($p=0.047$) was reduced in plasmacytoid and myeloid dendritic cells. In SLE samples (where exhaustion of the TLR9 signaling pathway occurs) (Figure 1A and 1B), HCQ use was not associated with any further reduction or rescue of TLR9 signaling. However, IFNα signaling was diminished within the MAPK pathway ($p=0.004$) in SLE patients taking HCQ (Figure 1C), consistent with impeded Type I IFN signaling.

Conclusion: SLE is characterized by diminished cytokine production after prolonged T Cell and TLR stimulation. Once this occurs, HCQ has no observable impact on circulating or TLR-stimulated whole blood IFNα levels. However, rescue of some T Cell and TLR-driven cytokine production, and decreased signaling in the IFNα-induced MAPK pathway occurs in patients on HCQ. This suggests that TLR9 pathway exhaustion circumvents some, but not all, therapeutic activity of HCQ on Type I interferon-mediated pathology.

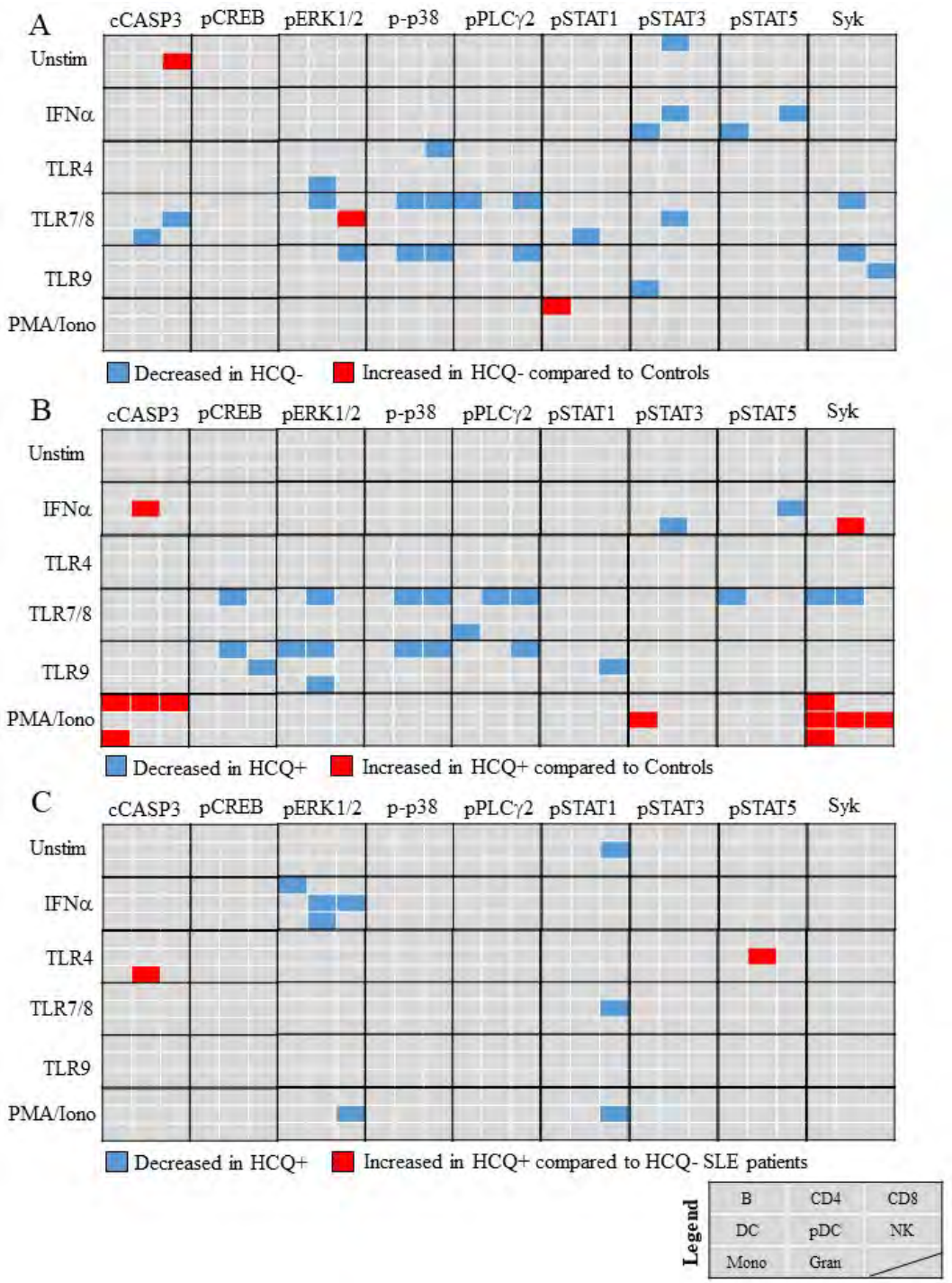

Figure 1. IFN-alpha signaling is diminished in SLE patients taking HCQ. Whole blood from either HCQ+ (SLE patients taking HCQ) or HCQ- SLE patients (SLE patients not taking HCQ) or healthy controls were stimulated for 15 minutes with either no stimuli, IFN-alpha, PMA and ionomycin, or TLR4, TLR7/8, or TLR9 agonists. The median 95th percentile was used to calculate the fold change of (A) HCQ- over controls (B) HCQ+ over controls or (C) HCQ+ over HCQ- in 8 cell populations (B cells, CD4+ T cells, CD8+ T cells, dendritic cells (DCs), plasmacytoid DCs (pDCs), natural killer (NK) cells, monocytes (mono) and granulocytes (gran). Significant increases or decreases in phophorylation following stimulation in a particular signaling molecule are noted by a blue box (decrease) or a red box (increase). The location of the box coincides with significant differences found in a specific cell population (refer to legend). $p<0.05$

Disclosure: S. Slight-Webb, None; **K. Thomas**, None; **R. Lu**, None; **S. Macwana**, None; **J. Merrill**, None; **C. Arriens**, BMS, 1, 2, GSK, 1; **E. Chakravarty**, None; **T. Aberle**, None; **H. Maecker**, None; **P. Utz**, None; **J. Guthridge**, None; **J. James**, Progentec Diagnostics, Inc., 9.

Abstract Number: 0862

Voclosporin Does Not Decrease Mycophenolic Acid Concentrations in Patients with SLE

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SESSION INFORMATION
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Background/Purpose: Voclosporin (VCS) is a novel calcineurin inhibitor, structurally similar to cyclosporine A (CsA). In a Phase 3 clinical trial in patients with active lupus nephritis (AURORA 1), patients treated with VCS in combination with MMF, achieved renal response rates of 40.8% vs. 22.5% for the control arm (OR 2.65; $p < 0.001$). Drug-drug interactions have been demonstrated between CsA and MMF, where CsA interferes with MPA recirculation resulting in up to 50% lower exposure to mycophenolic acid (MPA), the active metabolite of MMF. While VCS did not demonstrate a negative impact on MPA levels in transplantation, the primary objective of this study was to investigate the effect of VCS on MPA levels in subjects with systemic lupus erythematosus (SLE), with or without lupus nephritis.

Methods: Twenty-five subjects with Systemic Lupus Erythematosus, treated with MMF at an oral dose of 1 g BID for at least 28 days prior to screening were enrolled and continued at the same dose throughout the study. Voclosporin was administered at a dose of 23.7 mg BID for seven consecutive days, starting in the evening of Day 1 and ending with the morning dose on Day 7. Blood samples for PK analysis of MPA and mycophenolic acid glucuronide (MPAG) were were collected at pre-am. doses and 0.25, 0.5, 0.75, 1, 1.25, 1.5, 1.75, 2, 3, 4, 5, 6, 8, 10, and 12 hours post-a.m. doses after the morning dose of both drugs on Day 1 and 7. Analyses were performed using Phoenix™ WinNonlin® (Version 6.3)

Results: MPA exposure parameters were similar in the absence and presence of VCS (Cmax: 16.5 µg/mL [Day 1] vs. 15.8 µg/mL [Day 7], AUC0-12: 39.1 µg.h/mL [Day 1] vs. 40.8 µg.h/mL [Day 7]). The median time to Tmax was similar on both days, with comparable ranges of individual values. MPAG exposure showed a small increase in the presence of VCS (12% for Cmax and 27% for AUC0-12). Voclosporin exposure was consistent with previous studies. Administration of VCS with MMF over 7 days was well tolerated

Conclusion: There is no clinically meaningful interaction between voclosporin and MMF. As changes in exposure to MPA may affect its efficacy and safety, these data confirm that VCS and MMF can be given concomitantly without the need to adjust MMF dose

Disclosure: T. van Gelder, Vitaeris, 5, Aurinia Pharmaceuticals, 5, Astellas, 8; **R. Huizinga**, Aurinia Pharmaceuticals Inc., 1, 3; **N. Solomons**, Aurinia Pharmaceuticals, 1, 3; **L. Lisk**, Aurinia Pharmaceuticals, 1, 3.

Abstract Number: 0863

Residual Treatment Burden, Desired Improvement, and Prioritized Treatment Goals in Systemic Lupus Erythematosus (SLE): Results from the SLE-UPDATE (Understanding Preferences, Disease Activity and Treatment Expectations) Survey in the United States

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SESSION INFORMATION
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Background/Purpose: Literature describes a fairly high degree of satisfaction with SLE therapies, despite patients reporting high rates of adverse event (1-2). The objectives of this study were to understand patient satisfaction with their treatment, patient reported treatment burden, desired improvements with therapies, and treatment goal priorities.

Methods: A cross-sectional, non-interventional, online survey was developed based on literature review and expert clinician input. Participants were identified through patient panels and included English-speaking patients ≥18 years old from the United States who self-reported a SLE diagnosis by a physician. For each class of medications used for the treatment of SLE (e.g. anti-malarials (AM), corticosteroids (CS), immunosuppressants (IS), or biologics, patients indicated their level of satisfaction on a 5-point scale ranging from completely satisfied to very unsatisfied, how burdensome each medication was on a 4-point scale (very burdensome to not at all burdensome), reasons it was considered burdensome, and side effects experienced in the past 3 months. Additionally, patients were asked about their desired improvements with treatment and what they considered to be the most important treatment goals. Descriptive data are presented by means (standard deviation [SD]) for continuous measures, and frequency (n, %) for nominal or ordinal measures.

Results: Patients (n=500) were mostly female (75%), Caucasian (76%), with a mean age of 42.6 [12.7] years and mean disease duration of 11.1 [10.6] years. Patient reported current SLE medications included: AM 42%, CS 33%, IS 33%, and biologics 19%. Across medications patients were taking at the time of the survey, 16-38% indicated they were 'completely satisfied', and 41-56% indicated they were 'somewhat satisfied' (Table 1). CS had the highest percentage of 'neutral or not satisfied' responses (35%), while biologics had the largest percentage of 'satisfied' patients (86-94%). However, biologics had the highest percentage of patients rating their medication as 'somewhat' or 'very burdensome' (62-67%). "Reasons for burden" varied by medication, with the most common reported burden being short or long-term side effects, or inconvenient administration. The most common desired improvements to current lupus therapy were keeping lupus disease activity very low (66%), reduction in all symptoms (64%), and reduction in flares (61%). Highest priority lupus treatment goals included reduction in fatigue, pain, and flares. Lower ranked goals were the reduction in use of CS or IS. Over 60% of patients said their physicians did not ask about their most important treatment goals. When they did ask, over 75% of patients felt their goals matched their physician, 16% did not.

Table 1 Patient Reported Treatment Satisfaction, Burden, and Most Common Side Effects

	Corticosteroids (n= 231)	Immunosuppressants (n=163)	Belimumab (n=57)	Rituximab (n=16)	Antimalarials (n=211)
Satisfaction n (%) • Completely satisfied • Somewhat satisfied • Not satisfied*	 36 (15.6%) 115 (49.8%) 80 (34.7%)	 30 (18.4%) 85 (52.1%) 48 (29.4%)	 22 (35.1%) 23 (50.9%) 12 (14.1%)	 6 (37.5%) 9 (56.3%) 1 (6.3%)	 66 (31.3%) 86 (40.8%) 59 (28.0%)
Burden of taking n (%) • Very burdensome • Somewhat burdensome • Only a little burdensome • Not at all burdensome • Unsure	 41 (17.7%) 71 (30.7%) 49 (21.2%) 65 (28.1%) 5 (2.2%)	 27 (16.6%) 53 (32.5%) 34 (20.9%) 45 (27.6%) 4 (2.5%)	 11 (19.3%) 27 (47.4%) 10 (17.5%) 9 (15.8%) n/a	 4 (25.0%) 6 (37.5%) 5 (31.3%) 1 (6.3%) n/a	 12 (5.7%) 32 (15.2%) 52 (24.6%) 108 (51.2%) 7 (3.3%)
Reason for Burden n (%)	• Risk of long-term problems (eg. cataract, osteoporosis): 117 (50.6%) • Experienced side effects: 105 (45.5%) • Have to take pills daily: 104 (45.0%)	• Experienced side effects: 75 (46%) • Risk of organ damage: 60 (36.8%) • Routine lab monitoring: 56 (34.4%) • Have to take pills daily: 55 (33.7%)	• Inconvenience of infusion visits: 24 (42.1%) • Did not start working fast enough: 16 (28.1%) • Experienced side effects: 12 (21.1%)	• Inconvenience of infusion visits: 6 (68.8%) • Routine lab monitoring: 6 (37.5%) • Cost: 5 (31.3%)	• Have to take pills daily: 105 (49.8%) • Routine monitoring for possible eye problems: 94 (44.5%) • Experienced side effects: 49 (23.2%)
Most common side effects n (%)	• Chubby face or cheeks (moon face): 98 (42.4%) • Weight Gain: 97 (42.0%) • Muscle weakness: 75 (32.5%) • Insomnia/sleep difficulty: 72 (31.2%)	• Stomach problems: 77 (47.2%) • Hair loss: 58 (35.6%) • Infections: 40 (24.5%) • Skin or nail changes: 36 (22.1%)	• Depression: 15 (26.3%) • Redness, tenderness, itching at injection site: 15 (26.3%) • Nausea: 12 (21.1%)	• Nausea: 7 (43.8%) • Infections: 5 (31.3%) • Diarrhea: 2 (12.5%)	• Stomach problems: 71 (33.6%) • Headache: 54 (25.6%) • Insomnia/vivid dreams: 51 (24.2%) • Dizziness: 39 (18.5%) • Mood changes: 39 (18.5%)

*Includes: Neither satisfied nor dissatisfied; Somewhat unsatisfied; Very unsatisfied

Conclusion: Patients report relatively high rates of satisfaction with current therapies, despite identifying high levels of treatment burden. From the patient perspective, reduction in fatigue, pain, and flares are the most important treatment goals.

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Abstract Number: 0864

Effect of Cumulative Hydroxychloroquine Dose on Prevention of Damage Progression in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

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Table 1. Correlation between Lifetime Yearly HCQ Dose and SDI

	Correlation	p-value
Baseline	-0.22	p<0.0001
3 Years	-0.18	p=0.008
5 Years	-0.22	p=0.0001

Table 2. Relationship Between Lifetime Yearly HCQ Dose and Disease Damage

	Lifetime Yearly Average HCQ Dose (grams, mean ± SD)		p-value
	SDI = 0	SDI ≥ 1	
Baseline	104.3 ± 52.6 (n=96)	80.9 ± 54.4 (n=146)	p=0.001
3 years	106.2 ± 50.3 (n=69)	81.9 ± 55.5 (n=152)	p=0.006
5 years	113.9 ± 46.9 (n=152)	80.9 ± 54.4 (n=69)	p=0.001

HCQ = hydroxychloroquine; SD = standard deviation; SDI = SLICC/ACR damage index.
Note HCQ 200 mg/day is equivalent to 73 grams/year, HCQ 300 mg/day is equivalent to 110 grams/year, HCQ 400 mg/day is equivalent to 146 grams/year.

Background/Purpose: Hydroxychloroquine (HCQ) has demonstrated a wide array of beneficial effects in patients with systemic lupus erythematosus (SLE), with regard to disease activity, flare rates, organ damage, survival, thrombosis, lipid profile, diabetes mellitus and bone metabolism. Most of the existing data assesses HCQ use as a dichotomous variable at a single time point in a patient's disease process. We looked at lifetime cumulative HCQ doses in a cohort of SLE patients to gain a more comprehensive view of the relationship between HCQ use and damage accrual. It is important to better characterize the benefits and risks of prolonged HCQ use given ongoing concerns about antimalarial-induced retinal toxicity, which is a common reason for HCQ discontinuation.

Table 3. Relationship Between Lifetime Yearly HCQ Dose and Cardiovascular Events

	Lifetime Yearly Average HCQ Dose (grams, mean ± SD)		p-value
	Had Event	No Event	
Any CVE	69.7 ± 54.5 (n=50)	92.5 ± 55.9 (n=194)	p=0.02
Cardiac Event	46.2 ± 48.8 (n=15)	90.6 ± 55.8 (n=229)	p=0.003
Stroke/TIA	67.2 ± 54.6 (n=29)	90.6 ± 56.1 (n=215)	p=0.04

HCQ = hydroxychloroquine; SD = standard deviation; CVE = cardiovascular event; TIA = transient ischemic attack.

Methods: We studied a prospective cohort of 244 adult patients who met the 1997 American College of Rheumatology (ACR) classification criteria for SLE. Patients received care at a university medical center and were followed over at least 10 years. The cumulative HCQ dose from time of enrollment to last known follow-up was calculated for each patient via retrospective chart review. This value was then divided by the number of years since their SLE diagnosis to give a lifetime yearly average HCQ dose. Quinacrine use was accounted for by using a conversation of 300 mg HCQ for every 100 mg quinacrine. Disease damage was assessed using SLICC/ACR Damage Index (SDI) scores at baseline, 3 years, and 5 years after enrollment. We also recorded the incidence of cardiovascular events (CVE), defined as coronary artery disease, myocardial infarction, ischemic stroke, transient ischemic attack (TIA), or peripheral artery disease. Chi-squared test was used for dichotomous variables and Student's t-test for continuous variables. Spearman's test was used to examine correlations between two continuous variables.

Results: The cohort was composed of 99% females, and the mean age of all patients was 40.7 years. There was a statistically significant negative correlation between lifetime yearly average HCQ dose and SDI at baseline, 3 years, and 5 years (Table 1). At all of these time points, patients who had an SDI of zero had a higher lifetime yearly average HCQ dose compared to patients who had an SDI of 1 or greater. These differences were all statistically significant (Table 2). Thirty-six of the 244 patients (18.8%) had at least one CVE during follow-up. Patients who did not have a CVE had a higher lifetime yearly average HCQ dose compared to patients who did have a CVE. The same pattern was seen when looking at cardiac events and ischemic stroke/TIA individually. These differences were all statistically significant (Table 3).

Conclusion: We found an inverse correlation between lifetime yearly HCQ dose and damage accrual in our cohort of patients with SLE. This was seen with regard to overall damage accrual as represented by the SDI, and specifically with cardiovascular damage as represented by CVE incidence. These findings reaffirm existing data on the benefits of HCQ use in SLE, and provide stronger support for the continuous use of HCQ at appropriate dosages over the course of disease unless clearly contraindicated.

Disclosure: L. Zhu, None; **M. Singh**, None; **C. Siegel**, None; **L. Sahakian**, None; **J. Grossman**, Lupus Clinical Trial Consortium, 2, Eli Lilly, 2, Astellas, 2, Astra Zeneca, 2, American Board of Internal Medicine, 5, janssen, 2, rrf, 2, abbvie, 2; **M. McMahon**, None.

Abstract Number: 0865

Efficacy and Safety of Evobrutinib (M2951) in Adult Patients with Systemic Lupus Erythematosus Who Received Standard of Care Therapy: A Phase II, Randomized, Double-blind, Placebo-controlled Dose Ranging Study

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SESSION INFORMATION
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Background/Purpose: Bruton's tyrosine kinase (BTK) is involved in signalling pathways known to be important to the pathogenesis of systemic lupus erythematosus (SLE). Evobrutinib is a highly-selective, oral BTK inhibitor. This global Phase IIb randomized, double-blind, placebo-controlled study evaluated the efficacy, dose response and safety of evobrutinib compared to placebo in adult patients with active autoantibody-positive SLE who received standard of care (SoC) therapy.

Methods: Patients diagnosed with SLE by the SLICC or ACR classification criteria ≥6 months before screening, who had a SLEDAI-2K total score ≥6 at screening, were autoantibody-positive, and on sTable SLE SoC background therapy; were randomized 1:1:1:1 to oral evobrutinib 25 mg once-daily (QD), 75 mg QD, or 50 mg twice-daily (BID), or placebo. Active or severe central nervous system manifestations were exclusionary. The two primary endpoints were the SLE-Responder Index (SRI)-4 at Week 52 in all patients and the SRI-6 response at Week 52 in the subgroup of patients with High Disease Activity (defined as SLEDAI-2K total score ≥10 at screening). Primary safety endpoints included the incidence and severity of treatment-emergent adverse events (TEAEs), and key secondary endpoints were SRI-4 response in the serologically active subgroup, defined as patients with positive anti-dsDNA antibodies and/or low complement levels at screening, and time to first new severe (BILAG A) flare during treatment.

Results: A total of 469 patients were randomized for the study's primary analysis. Age at baseline was 40.7 years ±12.3 (mean ±SD) and 95% were female. Baseline disease characteristics were generally balanced across treatment groups. Median disease duration ranged from 51.6 to 69.2 months across treatment groups. Neither primary endpoints, SRI-4 response at Week 52 or SRI-6 response in patients with High Disease Activity, were met (Table). There was no clinically meaningful treatment difference for SRI-4 response in the serologically active subpopulation (Table). No treatment effect was observed for time to first severe flare. Serious adverse events were infrequently reported in all groups, 8.5% in placebo versus 9.4% in the evobrutinib groups combined. Infections and infestations were the most common treatment-emergent adverse event (TEAE), 42.7% for placebo versus 58.0% for evobrutinib groups combined. Overall, there was no dose effect in TEAEs or SAEs.

Table: Efficacy Results

Endpoints	Placebo N=114	Evobrutinib 25 mg QD N=115	Evobrutinib 75 mg QD N=116	Evobrutinib 50 mg BID N=114
SRI-4 Response Rate in mITT, n (%)	52 (45.6)	64 (55.7)	60 (51.7)	55 (48.2)
Absolute treatment difference of response rate vs Placebo, %		10.0	6.1	2.6
Odds-ratios [95% CI]		1.55 [0.91, 2.64]	1.29 [0.76, 2.18]	1.13 [0.67, 1.93]
P-value before adjustment for multiplicity		0.0522	0.1741	0.3209
	Placebo N=56	**Evobrutinib 25 mg QD N=54**	**Evobrutinib 75 mg QD N=65**	**Evobrutinib 50 mg BID N=55**
SRI-6 Response Rate at Week 52 in HDA, n (%)	22 (39.3)	27 (50.0)	30 (46.2)	24 (43.6)
Absolute treatment difference of response rate vs Placebo, %		10.7	6.9	4.4
Odds-ratios [95% CI]		1.50 [0.69, 3.24]	1.42 [0.68, 2.97]	1.27 [0.59, 2.75]
P-value before adjustment for multiplicity		0.1510	0.1780	0.2731
	Placebo N=59	**Evobrutinib 25 mg QD N=65**	**Evobrutinib 75 mg QD N=60**	**Evobrutinib 50 mg BID N=63**
SRI-4 Response Rate at Week 52 in serologically active patients, n (%)	28 (47.5)	38 (58.5)	29 (48.3)	34 (54.0)
Absolute treatment difference of response rate vs Placebo, %		11.0	0.9	6.5
Odds-ratios [95% CI]		1.52 [0.74, 3.15]	1.03 [0.49, 2.13]	1.35 [0.65, 2.81]
P-value before adjustment for multiplicity		0.1279	0.4729	0.2094
	Placebo N=114	**Evobrutinib 25 mg QD N=115**	**Evobrutinib 75 mg QD N=116**	**Evobrutinib 50 mg BID N=114**
Time to first severe BILAG A flare – mITT Hazard ratios [95% CI]		1.17 [0.57, 2.40]	0.69 [0.31, 1.52]	0.90 [0.42, 1.97]
P-value before adjustment for multiplicity		0.7034	0.5462	0.5462

mITT: modified intent-to-treat; HDA: high disease activity; SRI: SLE-responder index

Conclusion: This Phase IIb dose-ranging study in SLE showed no treatment effect of evobrutinib versus placebo at any dose. Evobrutinib was well tolerated across the overall and high disease activity subgroup populations, and there was no dose effect observed for any adverse events. These results, combined with the negative results of the fenebrutinib SLE study, suggest that BTK inhibition is not an effective therapeutic intervention for patients with SLE.

Disclosure: D. Wallace, Exagen, 1, 2, Exagen, 1, 2; **T. Dörner**, Eli Lilly and Company, 2, 5, Roche, 2, 5, Sanofi, 2, 5, Novartis, 2, 5, Abbvie, 2, 5, Celgene, 5, Pfizer Corporation, 2; **D. Pisetsky**, None; **F. Sanchez-Guerrero**, None; **A. Kao**, EMD Serono (a business of Merck KGaA, Darmstadt, Germany), 1, 3; **D. Parsons-Rich**, EMD Serono, Inc.

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Abstract Number: 0866

Identifying an SLE Patient Cluster with Greater Treatment Effect: Immune Cell Deconvolution of Gene Expression in Two Atacicept Phase II Studies

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

Background/Purpose: Atacicept, a dual inhibitor of the B lymphocyte stimulator and a proliferation-inducing ligand (APRIL), has been associated with a reduction of flares in the Phase II/III APRIL-SLE study (NCT00624338) and disease improvement in a subset of patients (pts) with baseline high disease activity (HDA; SLEDAI-2K ≥10) in the Phase IIb ADDRESS II study (NCT01972568). Using immune cell deconvolution of gene expression data, we previously distinguished two pt clusters in the APRIL-SLE study characterized by different rates of flare in the placebo (PBO) group [1]. We proposed an analysis of ADDRESS II to confirm the differential treatment effect observed using baseline gene expression in the APRIL-SLE study.

Methods: In a prior study of APRIL-SLE samples, a cell deconvolution algorithm [2] was used to assess 17 immune cell subsets in gene expression data from mRNA extracted from whole blood at baseline (N=105). Unsupervised clustering revealed five clusters of pts (P1–P5). In two clusters (P1,3), PBO-treated pts, when compared with atacicept-treated pts, had few new BILAG A or B flares. In the other three clusters (P2,4,5), PBO-treated pts had high flare rates. The P2,4,5 subset includes pts with high plasmablasts, high B cells and low neutrophils, or high activated natural killer cells and high activated dendritic cells. Using the cellular modules that defined these clusters, we developed an algorithm to distinguish P1,3 from P2,4,5 and applied it to the ADDRESS II mITT and HDA populations with gene expression data at baseline. Treatment arms in the two resulting subsets were compared using SLE Responder Index (SRI)-4, SRI-6, BILAG-based Combined Lupus Assessment (BICLA), and low disease activity (SLEDAI-2K ≤2).

Results: In ADDRESS II, 179 pts (58.5%) of the mITT and 93 pts (59%) of the HDA subpopulation had RNAseq expression data; their clinical response rates were similar to the overall mITT and HDA populations. The algorithm assigned 93 mITT pts (52%) to the P1,3 subset and 86 (48%) to the P2,4,5 subset. For HDA pts, 35 (38%) were assigned to P1,3 and 58 (62%) to P2,4,5. The P2,4,5 subset was confirmed to have lower PBO response rates and higher treatment difference for atacicept compared to the P1,3 subset as measured by SRI-4, SRI-6, and BICLA in both mITT and HDA populations. (Table 1).

Conclusion: This exploratory analysis of the ADDRESS II trial demonstrated greater treatment effect of atacicept in a subset of pts identified by an algorithm derived from unsupervised clustering of whole blood gene expression in a

Table 1. SRI-4, SRI-6, BICLA and LDA response rates for the P1,3 and P2,4,5 clusters in the mITT population and HDA subpopulation in ADDRESS II

N, % response Difference vs placebo	mITT			HDA		
	Placebo	Atacicept 75 mg	Atacicept 150 mg	Placebo	Atacicept 75 mg	Atacicept 150 mg
SRI-4: All (P1,2,3,4,5)	60 46.7%	55 54.5% +7.8%	64 48.4% +1.7%	30 46.7%	31 54.8% +8.1%	32 59.4% +12.7%
SRI-4: P1,3	32 53.1%	27 55.6% +2.5%	34 52.9% –0.2%	11 63.6%	11 54.5% –9.1%	13 61.5% –2.5%
SRI-4: P2,4,5	28 39.3%	28 53.6% +14.3%	30 43.3% +4.0%	19 36.8%	20 55.0% +18.2%	19 57.9% +21.1%
SRI-6: All (P1,2,3,4,5)	60 33.3%	55 30.9% –2.4%	64 32.8% –0.5%	30 30.0%	31 41.9% +11.9%	32 53.1% +23.1%
SRI-6: P1,3	32 43.8%	27 29.6% –13.8%	34 35.3% –8.5%	11 54.5%	11 45.5% –9.0%	13 61.5% +7.0%
SRI-6: P2,4,5	28 21.4%	28 32.1% +10.7%	30 30.0% +8.6%	19 15.8%	20 40.0% +24.2%	19 47.4% +31.8%
BICLA: All (P1,2,3,4,5)	60 38.3%	55 43.6% +5.3%	64 42.2% +3.9%	30 20.0%	31 48.4% +28.4%	32 53.1% +33.1%
BICLA: P1,3	32 43.8%	27 33.3% –10.5%	34 38.2% –5.6%	11 27.3%	11 27.3% 0.0	13 46.2% +18.9%
BICLA: P2,4,5	28 32.1%	28 53.6% +21.5%	30 46.7% +14.6%	19 15.8%	20 60.0% +44.2%	19 57.9% +42.1%
LDA: All (P1,2,3,4,5)	60 26.7%	55 25.4% –1.3%	64 29.7% +3.0%	30 10.0%	31 19.4% +9.4%	32 31.3% +21.3%
LDA: P1,3	32 34.4%	27 37.0% +2.6%	34 35.3% +0.9%	11 18.2%	11 36.4% +18.2%	13 30.8% +12.6%
LDA: P2,4,5	28 17.9%	28 14.3% –3.6%	30 23.3% +5.4%	19 5.3%	20 10.0% +4.7%	19 31.6% +26.3%

BICLA, BILAG-based Combined Lupus Assessment; HDA, high disease activity; LDA, low disease activity; mITT, modified intent-to-treat; SRI, SLE Responder Index.

different atacicept study. The observation that better response differences were found in pts with high B cells or high plasmablasts is consistent with atacicept's proposed mechanism of action.

1.Samy *et al.* 2019 Lupus Science & Medicine;6(Suppl 1):A158-A; 2. Abbas *et al.* 2009 PLOS ONE;4(7):e6098

Disclosure: J. Merrill, None; **M. Studham**, EMD Serono (a business of Merck KGaA, Darmstadt, Germany), 3; **E. Morand**, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, 5, Merck Serono, 2, 5, Neovacs, 5, Sandoz, 5, Novartis, 8, AbbVie, 5, Amgen, 5, Biogen, 5; **A. Aydemir**, EMD Serono (a business of Merck KGaA, Darmstadt, Germany), 3; **C. Vazquez Mateo**, EMD Serono (a business of Merck KGaA, Darmstadt, Germany), 3; **A. Rolfe**, EMD Serono (a business of Merck KGaA, Darmstadt, Germany), 3; **A. Kao**, EMD Serono (a business of Merck KGaA, Darmstadt, Germany), 1, 3; **R. Townsend**, EMD Serono (a business of Merck KGaA, Darmstadt, Germany), 3.

Abstract Number: 0867

Hydroxychloroquine Use Predicts Significantly Higher Patient and Graft Survival in Post-Renal Transplant Lupus Nephritis Patients

Shivani Garg[1], Tripti Singh[1], Sarah Panzer[2] and Christie Bartels[3], [1]UW Madison, Madison, WI, [2]UW-Madison, Madison, [3]University of Wisconsin School of Medicine and Public Health, Department of Medicine, Division of Rheumatology, Madison, WI

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is a pivotal therapy for lupus nephritis (LN) as it contributes to 65% lower mortality and 84% lower renal damage compared to HCQ non-users. End-stage renal disease (ESRD) due to LN is a leading cause of renal transplantation and almost 30% of patients suffer from LN recurrence after renal transplant. Yet, the impact of post-transplant HCQ use on LN recurrence, and patient and graft survival has not been elucidated. Therefore, this study aims to examine the role of post-transplant HCQ use on LN recurrence, and patient and renal graft survival. We also examined other predictors of post-transplant patient and graft survival. *We hypothesized that post-transplant HCQ use will predict lower LN recurrence, and better patient and graft survival.*

Methods: Using a comprehensive transplant database, we identified all patients with ESRD due to LN who underwent renal transplant between 1994-2016 at an academic center. Data, including patient, lupus, and transplant characteristics, were extracted from this database. Post-transplant medication HCQ use and biopsy confirmed LN recurrence were abstracted. Primary outcomes were all-cause mortality and graft failure, defined as re-transplant or dialysis. Cox proportional hazards models were used to examine predictors of patient and graft survival. Fisher test was used to examine association between LN recurrence and HCQ use.

Results: Overall, we identified 205 patients undergoing renal transplant for ESRD due to LN. The mean age of 43 years, 78% were white female, and only 34% of the patients were on HCQ after transplant. The post-transplant LN recurrence rate was 14%, with 52% of recurrences occurring in HCQ non-users (p 0.09).

Patient Survival: We identified 47 deaths (23%) during 11-year post-transplant follow up, with 79% of deaths occurring in HCQ non-users. Stratified survival analysis by HCQ use highlighted significantly lower mortality in HCQ users compared to non-users (10/47 vs. 37/47, $p < 0.0001$) (Figure 1). We found that HCQ use predicted 40% lower mortality compared to non-users and a trend was noted on multivariable analysis (*HR 0.6, CI 0.3-1.2, p 0.1*; Table 1). Post-transplant graft failure predicted 51-fold higher mortality risk in our cohort (*HR 51, CI 7-77, p 0.0001*) (Table 1). Age ≥ 45 years predicted 4-fold higher mortality (*HR 3.5, CI 1.8-6.6*), and non-white race predicted 2-fold higher mortality (*HR 2.3, CI 1.1-4.7*).

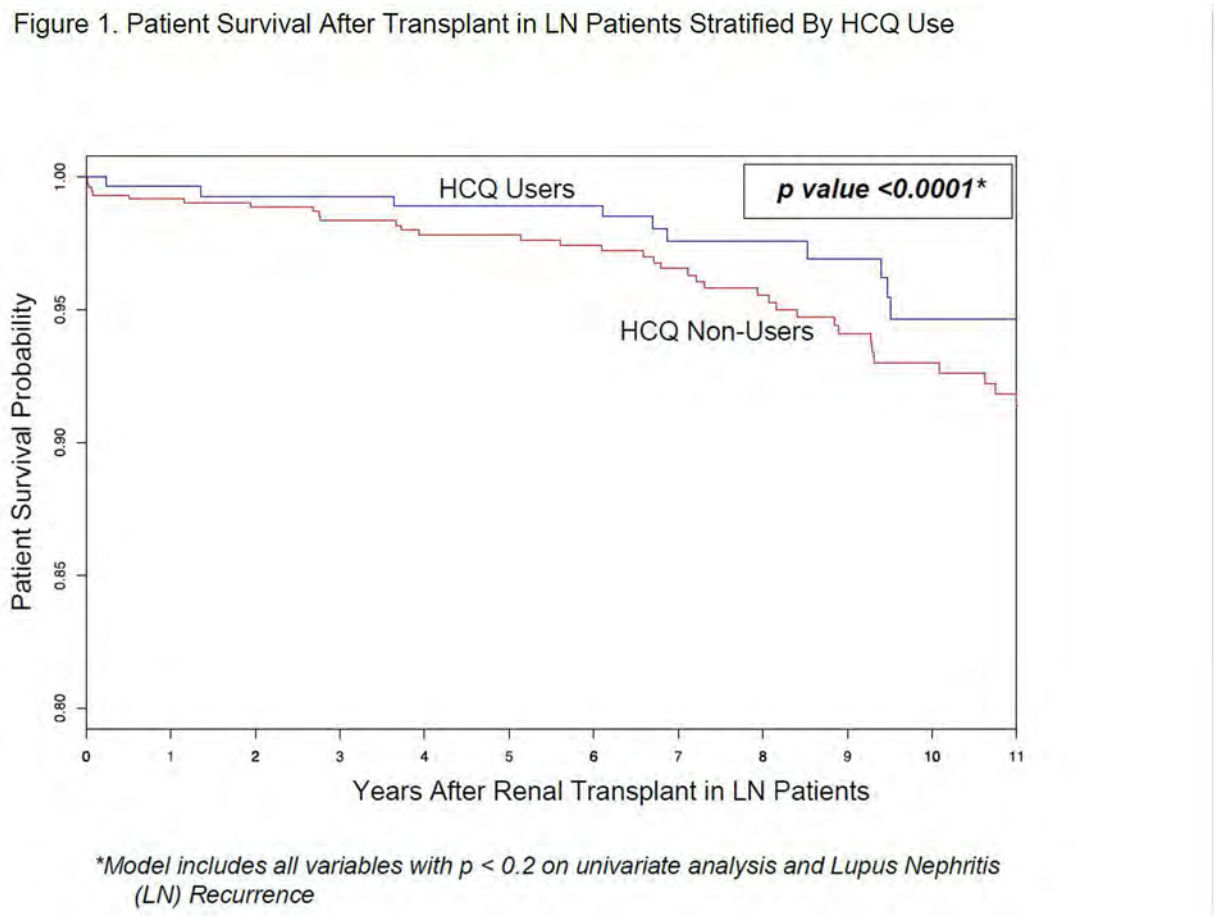

Figure 1. Patient Survival After Transplant in LN Patients Stratified By HCQ Use

Graft Failure: We identified 99 graft failures (48%) during post-transplant follow up. Stratified graft survival analysis revealed significantly lower graft failure in post-transplant HCQ users compared to non-users (29/99 vs 70/99, $p < 0.0001$) (Figure 2). Multivariable analysis showed post-transplant LN recurrence predicted 2-fold higher graft failure risk *(HR 1.7, CI 1.02-3, p 0.04; data not shown)*.

Conclusion: HCQ use predicted higher post-transplant LN patient and renal graft survival. LN recurrence was a strong predictor of graft failure, and renal graft failure predicted 51-fold higher post-transplant mortality. Future efforts should prospectively examine the impact on post-transplant HCQ use on graft and patient outcomes.

Table 1. Cox Proportional Hazards Model to Predict Post-Transplant Survival

Variable	HR (95% CI)	p value
Age at Tx ≥45 years	**3.5 (1.8-6.6)**	**<0.0001**
Non-White Race	**2.3 (1.1-4.7)**	**0.03**
Female	1.2 (0.6-2.3)	0.6
Post-Tx Graft Rejection	**51 (7-77)**	**0.0001**
Live Donor	1.1 (0.5-2.3)	0.8
Pre-Tx HD Duration, 1 year Increments	1.1 (0.98-1.2)	0.09*
Post-Tx LN Recurrence	0.5 (0.2-1.1)	0.08*
HCQ Use	0.61 (0.3-1.2)	0.1*

*Model includes all variables with p < 0.2 on univariate analysis and Lupus Nephritis Recurrence; HCQ Hydroxychloroquine; HD Hemodialysis; LN Lupus Nephritis; Tx Transplant; *indicates a trend; significant p <0.05 are shown in bold*

Table 1. Cox Proportional Hazards Model to Predict Post-Transplant Survival

Figure 2. Graft Survival After Transplant in LN Patients Stratified By HCQ Use

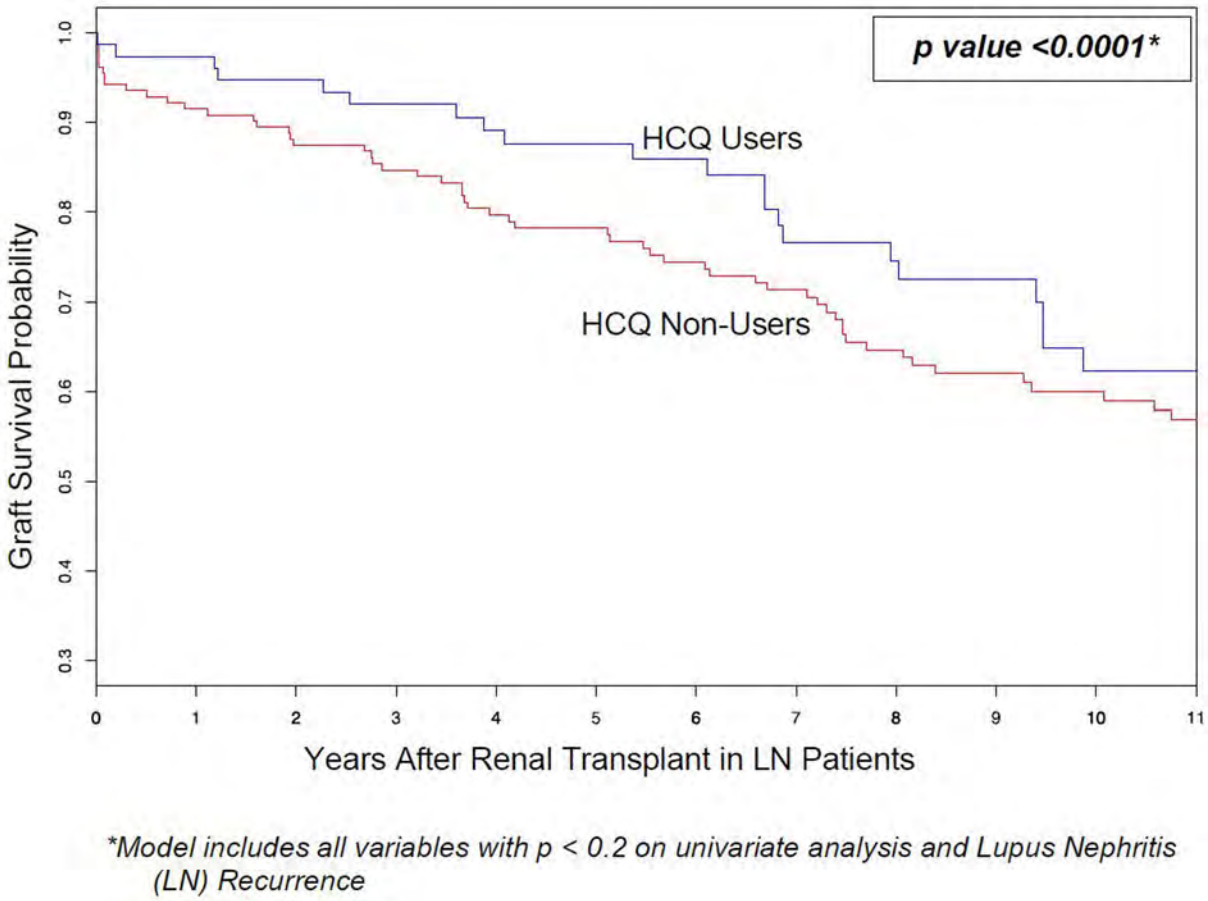

Figure 2. Graft Survival After Transplant in LN Patients Stratified By HCQ Use

Disclosure: S. Garg, None; **T. Singh**, None; **S. Panzer**, None; **C. Bartels**, Independent Grants for Learning and Change (Pfizer), 2.

Abstract Number: 0868

Impact of Proteinuria on the Clearance of Monoclonal Antibodies: Potential Clinical Implications

Justin Penzenstadler[1], Jianmeng Chen[2], Aaron Park[2], Rosemarie Neuner[2], Aliza Thompson[2], Lei He[2], Ping Ji[2], Nikolay Nikolov[2] and Chandrahas Sahajwalla[2], [1]FDA, F, [2]FDA, Silver spring

SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: In general, renal elimination is minimal for therapeutic proteins with a molecular weight more than 69 KDa. However, in patients with proteinuria, there is impaired filtration or insufficiency of absorption of serum protein in the kidney. Proteinuria is commonly seen in a variety of kidney diseases involvement, including lupus ne-

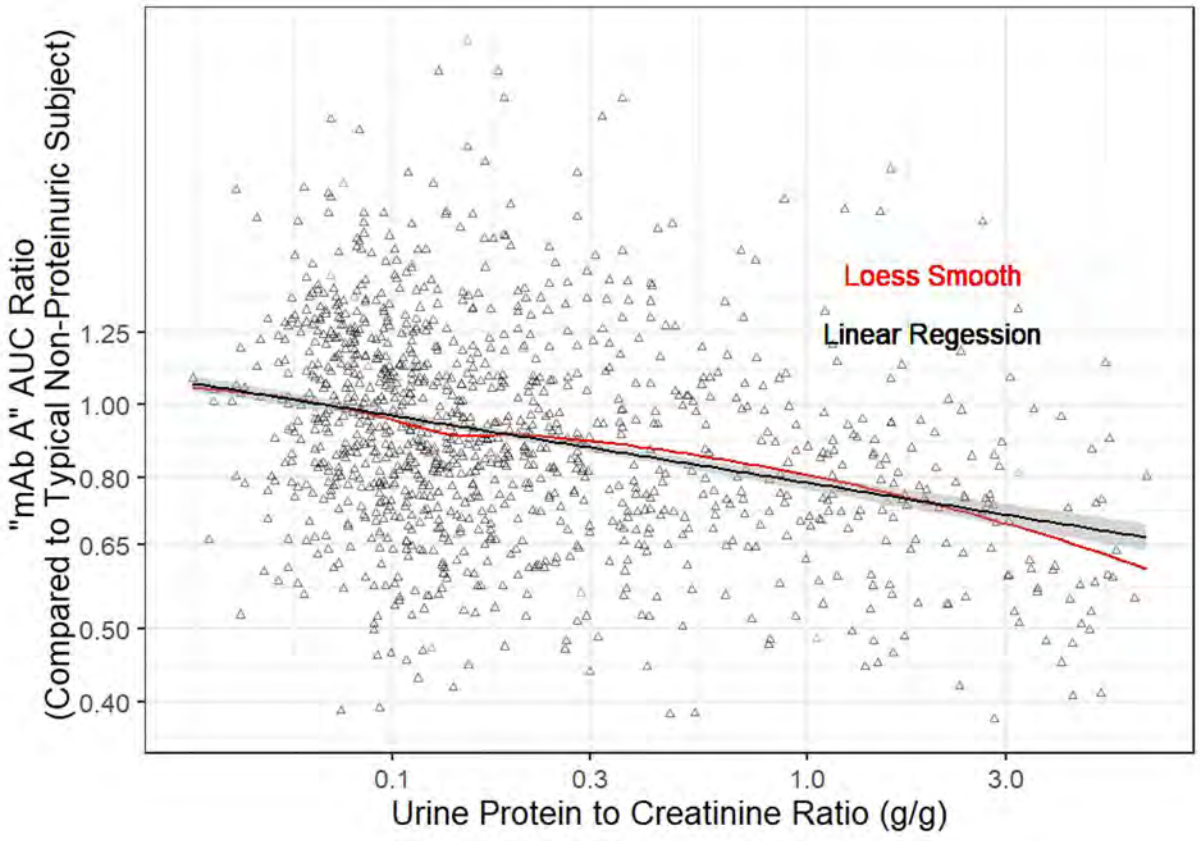

Figure 1. The relationship between baseline urine UPCR and mAb A exposure (AUC) in SLE patients. The black line represents linear regression, and the red line represents Loess smooth fitting.

phritis (LN), nephrotic syndromes, diabetic nephropathy, etc. In these cases, along with the endogenous serum protein, the therapeutic protein such as monoclonal antibody (mAb) is also detected in urine. Additional renal clearance of mAb may lead to a clinically important reduction in serum drug concentration.

Methods: We evaluated longitudinal pharmacokinetic and spot urine protein data for three monoclonal antibodies: mAb A in systemic lupus erythematosus (SLE), mAb B in ANCA-associated vasculitis (AAV), and mAb C in sickle cell disease (SCD). Two studies (in AAV and SCD) collected qualitative urine protein (i.e. dipstick) values, and two studies in SLE collected quantitative urine protein information (i.e., total Urine Protein to Creatinine Ratio, UPCR). The relationship between drug exposure and quantitative UPCR was assessed by fitting a linear model on log-transformed and normalized variables. The assumption of linearity was assessed using a loess-smoothed overlay.

Results: For the SLE studies (mAb A), the median baseline of UPCR (g/g) was 0.144 (IQR: 0.092 – 0.355), and 216 subjects had greater than 500 mg/g (n=1128). In the SCD study (mAb C), a majority of subjects (100/150) had negative protein dipstick readings at baseline, and 50/150 had detectable urine protein. In the AAV study (mAb B), 25/64 had negative protein dipstick readings, and 39/64 were positive for trace to 4+ protein dipstick values.

A statistically persuasive negative correlation between quantitative urine protein with total drug exposure was identified for mAb A in lupus patients ($p < 0.00001$).

The relationship between baseline urine UPCR and drug exposure was well-described by a linear model with logarithmic transformations. This model suggests, on average, a patient with 0.5 g/g UPCR would be expected to have 84% of the exposure (95% CI – 82-86%) of a subject with spot protein of 0.1 g/g or less. Likewise, a subject with 5 g/g would be expected to have 68% (95% CI: 64-73%) of the exposure of a subject with 0.1 g/g or less. Additionally,

preliminary analyses suggest that the pre-dose trough concentration (a key covariate determining adequate dosing interval) may be more affected than overall exposure.

In contrast, no relationship was observed between qualitative urine protein and drug clearance for mAb B in AAV or mAb C in SCD. This may be due to the nature of the disease or the underlying pathophysiology of the kidney involvement, the degree of proteinuria, or other factors.

Conclusion: Overall, different types and severity of proteinuria may have different impact on the clearance of therapeutic proteins. The clinical impact of these observations remains to be determined. These findings may warrant the assessment, during drug development, of the impact of proteinuria on efficacy, safety, or the need for dosing adjustment for biological proteins.

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Abstract Number: 0869

Retinal Toxicity in a Multinational Inception Cohort of Systemic Lupus Patients on Hydroxychloroquine

Celline Almeida-Brasil[1], John Hanly[2], Murray Urowitz[3], Ann Clarke[4], Rosalind Ramsey-Goldman[5], Caroline Gordon[6], Michelle Petri[7], Ellen M Ginzler[8], Daniel J Wallace[9], Sang-Cheol Bae[10], Juanita Romero-Díaz[11], Mary Ann Dooley[12], Christine A. Peschken[13], David Isenberg[14], Anisur Rahman[14], Susan Manzi[15], Søren Jacobsen[16], S. Sam Lim[17], Ronald Van Vollenhoven[18], Ola Nived[19], Andreas Jönsen[19], Diane Kamen[20], Cynthia Aranow[21], Guillermo Ruiz-Irastorza[22], Jorge Sanchez-Guerrero[23], Dafna Gladman[24], Paul Fortin[25], Graciela Alarcón[26], Joan Merrill[27], Kenneth Kalunian[28], Manuel Ramos-Casals[29], Kristjan Steinsson[30], Asad Zoma[31], Anca Askanase[32], Munther Khamashta[33], Ian Bruce[34], Murat Inanc[35] and Sasha Bernatsky[36], [1]McGill University, Montreal, Canada, [2]QEII Health Sciences Centre, Halifax, Canada, [3]University Health Network, University of Toronto, Toronto, ON, Canada, [4]University of Calgary, Calgary, Canada, [5]Division of Rheumatology, Northwestern University Feinberg School of Medicine, Chicago, IL, [6]University of Birmingham, Birmingham, England, United Kingdom, [7]Johns Hopkins University School of Medicine, Baltimore, [8]SUNY Downstate Health Sciences University, Brooklyn, [9]Cedars-Sinai Medical Center, Beverly Hills, CA, [10]Department of Rheumatology, Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [11]Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico, [12]UNC Health, Chapel Hil, [13]University of Manitoba, Winnipeg, Canada, [14]University College London, London, United Kingdom, [15]Temple University, Philadelphia, [16]University of Copenhagen, Copenhagen, Denmark, [17]Emory University, Atlanta, GA, [18]University of Amsterdam, Amsterdam, Netherlands, [19]Lund University, Lund, Sweden, [20]Medical University of South Carolina, Charleston, SC, [21]Feinstein Institutes for Medical Research, Manhasset, NY, [22]Hospital Universitario Cruces, Barakaldo, Spain, [23]University of Toronto, Toronto, Canada, [24]Krembil Research Institute, Toronto Western Hospital, Toronto, ON, Canada, [25]CHU de Quebec - Universite Laval, Quebec, Canada, [26]Division of Clinical Immunology and Rheumatology, Department of Medicine, School of Medicine, The University of Alabama at Birmingham; Department of Medicine, School of Medicine; Universidad Peruana Cayetano, Heredia, Alabama, [27]New York University, New York, [28]University of California San Diego, La Jolla, CA, [29]University of Barcelona, Barcelona, Spain, [30]Reykjavik University, Reykjavik, Iceland, [31]University of Glasgow, Glasgow, United Kingdom, [32]Columbia University College of Physicians & Surgeons, New York, NY, [33]King's College London, London, United Kingdom, [34]The University of Manchester, Manchester, United Kingdom, [35]Department of Rheumatology, Istanbul Faculty of Medicine, Istanbul University, Istanbul, Turkey, [36]The Research Institute of the McGill University Health Centre, Montreal, ON, Canada

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: SLE – Treatment Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite the beneficial effects of hydroxychloroquine (HCQ) in systemic lupus erythematosus (SLE), retinal toxicity is a concern. Factors associated with retinal toxicity have been studied among long-term HCQ

Table 1. Uni and multivariable Cox regression for retinal toxicity in HCQ-exposed SLE patients

Characteristics*	HR (95% CI)	aHR (95% CI)
Male sex	2.18 (0.47, 10.1)	1.73 (0.36, 8.36)
Race/ethnicity		
Caucasian	Reference	-
Black	1.21 (0.25, 5.92)	2.16 (0.37, 12.60)
Others	0.44 (0.09, 2.13)	0.58 (0.11, 2.97)
Age at SLE diagnosis in years	**1.05 (1.01, 1.09)**	1.05 (1.00, 1.09)
HCQ daily dose >5mg/Kg	1.16 (0.35, 3.80)	1.55 (0.46, 5.19)
Overweight (Body mass index≥25)	1.64 (0.44, 6.06)	2.50 (0.54, 11.51)
Smoker	1.23 (0.26, 5.69)	1.26 (0.27, 5.94)

*At baseline, except for age.

Table 1. Uni and multivariable Cox regression for retinal toxicity in HCQ-exposed SLE patients

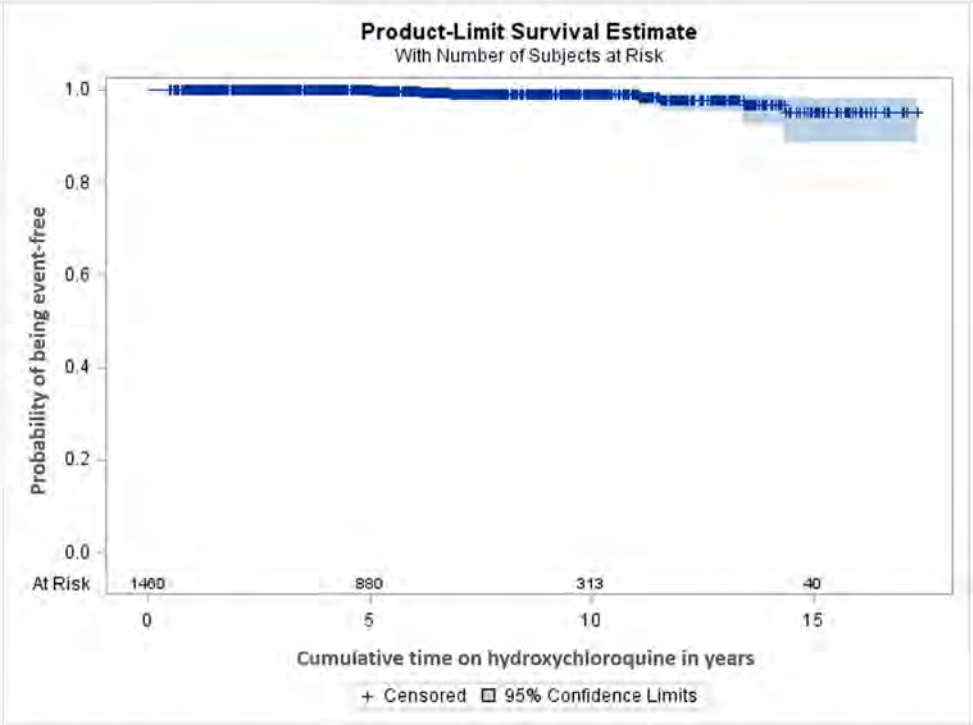

Figure 1. Kaplan-Meier curve for cumulative probability of retinal toxicity. The shaded areas represent pointwise 95% confidence intervals.

Figure 1. Kaplan-Meier curve for cumulative probability of retinal toxicity. The shaded areas represent pointwise 95% confidence intervals.

users but have not been described for incident SLE patients. We evaluated the incidence of HCQ-related retinal toxicity in a large, international, inception cohort of SLE patients, and assessed factors potentially associated with this event.

Methods: We analyzed prospective data from the Systemic Lupus International Collaborating Clinics (SLICC) cohort, that includes SLE patients from 33 sites in Europe, Asia, and North America, enrolled within 15 months of diagnosis.

Using annual study visits between 1999-2019, we followed patients from first visit on HCQ (time zero/baseline) up to the time of retinal toxicity documentation (outcome) or death, loss to follow-up, or censoring at end of study interval. Retinal toxicity was identified based on the SLICC/ACR damage index item for retinal damage and cases were confirmed with chart review. Multivariable Cox regression was used to estimate adjusted hazard ratios (aHRs) and 95% confidence intervals (CIs) for baseline factors potentially associated with retinal toxicity (i.e., sex, race/ethnicity, age at SLE onset, HCQ daily dose/kg, body mass index, and smoking). We also plotted a Kaplan-Meier curve for probability of retinal toxicity related to total duration of HCQ therapy.

Results: A total of 1460 patients (89% female, 52% Caucasian) were included. Mean SLE duration at time zero (HCQ initiation) was 2.4 (standard deviation, SD 2.2) years and patients remained on HCQ an average of 6.4 (SD 4.2) years. Retinal toxicity was confirmed for 11 patients (incidence 1.0 per 1000 person-years) at a mean of 8.8 (SD 4.0) years. Our hazards regression model (Table 1) identified non-significant trends for greater risk in men, black patients, those receiving more than 5 mg per kg at baseline, overweight patients and smokers. In the Kaplan-Meier curve (Figure 1), the crude probability of retinal toxicity was less than 1% until 10 years of cumulative HCQ use, but increased around 1% each year after that, reaching 5% after 14 years.

Conclusion: In recent-onset SLE patients receiving HCQ, the probability of retinal toxicity increases after 10 years of cumulative use. There were non-significant trends for greater risk in men, black patients, those receiving more than 5 mg per kg at baseline, overweight patients and smokers. More sophisticated analyses with time-dependent variables are under way.

Disclosure: C. Almeida-Brasil, None; **J. Hanly**, None; **M. Urowitz**, None; **A. Clarke**, AstraZenca, 5, Exagen Diagnostics, 5; **R. Ramsey-Goldman**, None; **C. Gordon**, UCB, 1, 2, 3, 4, CDC, 1, MGP, 1; **M. Petri**, AbbVie, 5, Amgen, 5, AstraZeneca, 2, 5, BMS, 5, Decision Resources, 5, GSK, 2, 5, INOVA, 5, IQVIA, 5, Janssen, 5, Eli Lilly, 2, 5, Merck EMD Serono, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5, Exagen, 2; **E. Ginzler**, Aurinia Pharmaceuticals, Inc., 2; **D. Wallace**, Exagen, 1, 2, Exagen, 1, 2; **S. Bae**, None; **J. Romero-Díaz**, Biogen, 5; **M. Dooley**, None; **C. A. Peschken**, None; **D. Isenberg**, None; **A. Rahman**, None; **S. Manzi**, None; **S. Jacobsen**, BMS, 2; **S. Lim**, None; **R. Van Vollenhoven**, None; **O. Nived**, None; **A. Jönsen**, None; **D. Kamen**, None; **C. Aranow**, None; **G. Ruiz-Irastorza**, None; **J. Sanchez-Guerrero**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **P. Fortin**, None; **G. Alarcón**, None; **J. Merrill**, None; **K. Kalunian**, Roche, 5, Biogen, 5, Janssen, 5, AstraZeneca, 5, Lupus Research Alliance, 2, Pfizer, 2, Sanford Consortium, 2, Eli Lilly, 5, Genetech, 5, Gilead, 5, ILTOO, 5, Nektar, 5, Viela, 5, Equillium, 5, Bristol-Meyers Squibb, 5; **M. Ramos-Casals**, None; **K. Steinsson**, None; **A. Zoma**, None; **A. Askanase**, Glaxo Smith Kline, 2, Astra Zeneca, 2, Janssen, 2, Eli Lilly and Company, 2, Abbvie, 5, Mallinckrodt, 2, Regeneron, 9, Pfizer, 2, Bristol Myers Squibb, 9; **M. Khamashta**, None; **I. Bruce**, None; **M. Inanc**, None; **S. Bernatsky**, None.

Abstract Number: 0870

Hydroxychloroquine Is Associated with Lower Platelet Activity and Improved Vascular Health in Systemic Lupus Erythematosus

Michael Golpanian[1], **Elliot Luttrell-Williams**[2], MacIntosh Cornwell[2], Khrystyna Myndzar[2], Hanane El Bannoudi[2], Ashira Blazer[2], Stuart Katz[2], Nathaniel Smilowitz[2], Kelly Ruggles[2], Robert Clancy[3], Jill Buyon[4] and Jeffrey Berger[2], [1]New York University, New York, NY, [2]New York University School of Medicine, New York, [3]NYU School of Medicine, New York, [4]Department of Medicine, NYU School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: SLE – Treatment Poster I

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Table 1. Demographics and Clinical Characteristics of Study SLE Cohort			
	All (n=132)	HCQ (n=108)	No HCQ (n=24)
Age, mean (SD)	39.9 (13.0)	39.6 (12.7)	41.25 (14.2)
Female, n (%)	128 (97.0)	104 (96.3)	24 (100.0)
Race, n (%)			
White	60 (45.4)	47 (44.4)	13 (54.2)
Black or African American	40 (30.3)	32 (29.6)	8 (33.3)
Asian	27 (20.4)	25 (23.1)	2 (8.3)
Other/Unknown	5 (3.8)	4 (3.7)	1 (4.2)
Ethnicity, n (%)			
Hispanic	50 (37.9)	38 (35.2)	12 (50.0)
Clinical Characteristics, n (%)			
Malar Rash	66 (50.0)	55 (50.9)	11 (45.8)
Discoid Rash	30 (22.7)	23 (21.3)	7 (29.2)
Photosensitivity	49 (37.1)	39 (36.1)	10 (41.7)
Oral Ulcers	25 (18.9)	18 (16.7)	7 (29.2)
Arthritis	99 (75.0)	80 (74.1)	20 (83.3)
Serositis	35 (26.5)	28 (25.9)	7 (29.2)
Pleuritis	22 (16.7)	16 (14.8)	6 (25.0)
Pericarditis	23 (17.4)	18 (16.8)	5 (20.8)
Renal Disorder	64 (48.5)	53 (49.1)	11 (45.8)
Seizures	4 (3.0)	3 (2.8)	1 (4.2)
Psychosis	3 (2.3)	2 (1.9)	1 (4.2)
Hemolytic Anemia	8 (6.1)	7 (6.5)	1 (4.2)
Leukopenia	57 (43.2)	48 (44.4)	9 (37.5)
Lymphopenia	59 (44.7)	50 (46.3)	9 (37.5)

Background/Purpose: Patients with systemic lupus erythematosus (SLE) are at increased risk of premature atherosclerosis and thrombosis. Hydroxychloroquine (HCQ) is widely used in the treatment of SLE and has been considered of benefit for overall vascular health albeit studies to address this benefit at the cellular level have been limited. Accordingly, this study was initiated to investigate the relationship between HCQ use and dose with platelet activity, the platelet transcriptome, and vascular functional readouts.

Methods: Patients fulfilling ACR or SLICC criteria for SLE were consecutively recruited for platelet evaluation with the only exclusion being on nonsteroidal anti-inflammatory medications, aspirin or anticoagulants. At enrollment, blood was collected for hematology analysis using the Sysmex XN-1000 analyzer, platelet aggregation via the Helena AggRAM™ system, and platelet RNA isolation and storage. Microvascular function was assessed via sublingual sidestream darkfield imaging. Brachial artery reactivity testing was used to evaluate large vessel function. Stored platelet RNA was isolated and analyzed by RNA sequencing (Illumina HiSeq4000 Sequencing).

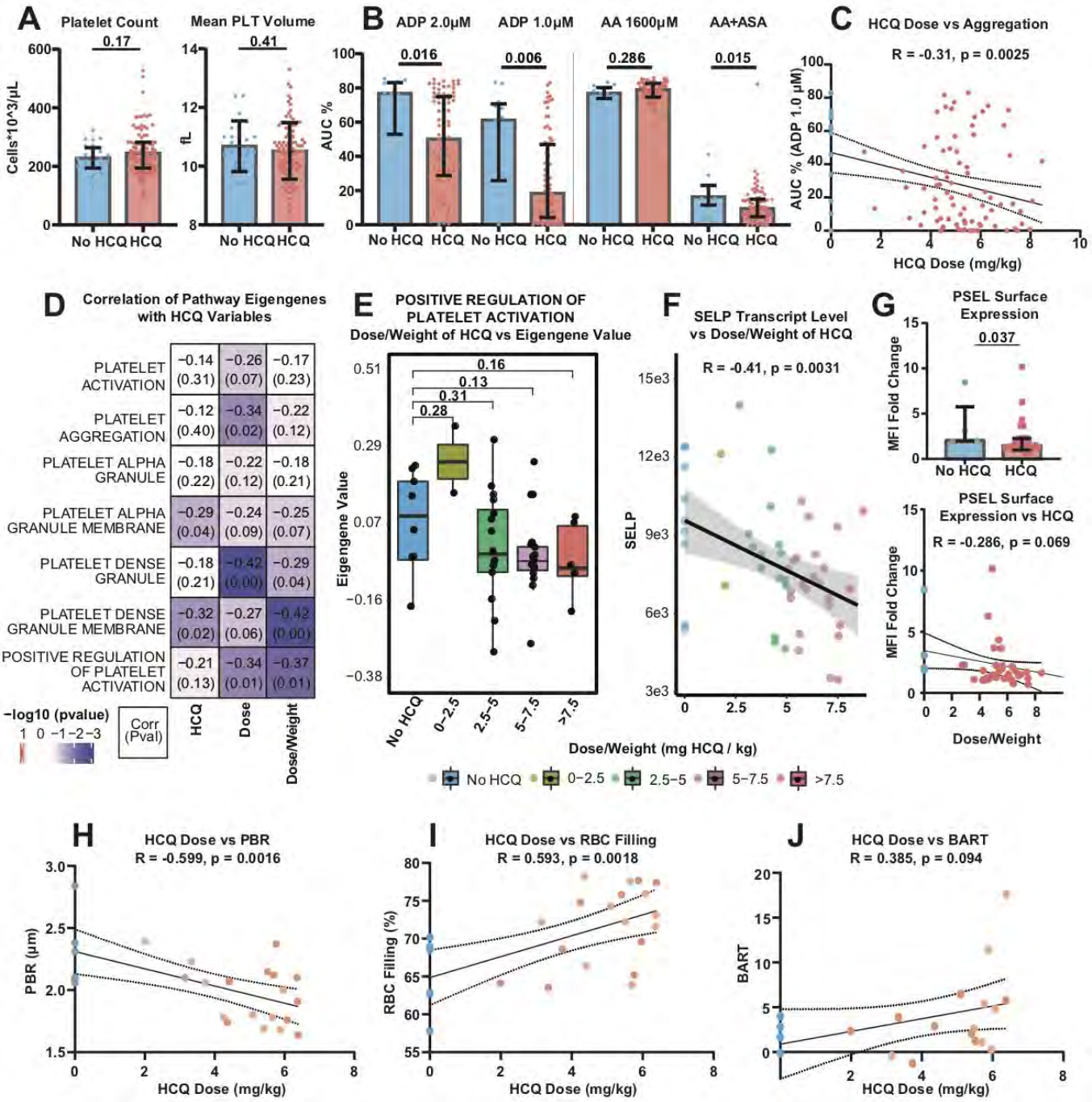

Figure 1. Associations between HCQ use and dose and platelet function, transcriptomics, and vascular function. Comparison of HCQ and non-HCQ groups of SLE subjects examining (A) platelet count and size. (B) Aggregation in response to ADP and AA with and without in vitro aspirin. (C) Pearson correlations of daily HCQ dosing and aggregation in response to 1µM ADP. (D) Heatmap depicting the correlation and p value between the sample eigengene values associated with platelet pathways and HCQ use, dose, and dose adjusted for weight. (E) Boxplots showing the eigengene values for the GO term Positive Regulation of Platelet Activation across different binned ranges of HCQ dose/weight. (F) Scatterplot showing the normalized transcript level of SELP compared against HCQ dose/weight for each patient. (G) Comparison of p-selectin surface expression fold change in subjects on and off HCQ as measured by flow cytometry and a Pearson correlation of HCQ dose and p-selectin fold change. Platelet activity and p-selectin surface expression comparisons made using the Mann-Whitney rank-sum test show median and IQR; for platelet aggregation the HCQ group ranged from 71 to 81 subjects and non-HCQ group ranged from 13 to 15 depending on the measure. For p-selectin, HCQ N=36, No HCQ N=5. Pearson correlations of daily HCQ dosing and PBR (H), RBC Filling (I), and BART (J) were also examined, shown here with 95% CI bands.

Results: Among 132 SLE subjects, 108 were on HCQ. Mean age was 39.9 ± 13.0 and 97% were female. Lupus disease activity at the time of blood draw assessed by the SELENA-SLEDAI activity index was 3.44 (range 0-20). Demographics and SLE disease activity did not differ between those on versus off HCQ (**Table 1**). Platelet count and size were not different between groups (**Figure 1A**). Platelet aggregation in response to submaximal ADP at multiple concentrations was lower in participants on HCQ (**Figure 1B**). Consistently, there was an inverse relationship between HCQ dosing and platelet aggregation in response to ADP (2uM: R=-0.213, P=0.037; 1uM: R=-0.310, P=0.0025; 0.4uM: R=-0.376, P=0.00018; **Figure 1C**). Since no subjects were on aspirin (or any other antiplatelet therapy at enrollment), aggregation in response to arachidonic acid (AA) was robust and similar between groups. However, after incubating platelets with aspirin (3mM) *in vitro*, platelet aggregation in response to AA was lower in the HCQ group compared to non-HCQ group (P=0.035, **Figure 1B**). To investigate the potential mechanisms of HCQ induced lower platelet aggregation, we evaluated platelet RNA sequencing in 49 subjects (8 no HCQ, 41 on HCQ). Positive regulation of pathways related to platelet activation (and in particular, P-selectin expression) was inversely related to HCQ, especially with higher doses (**Figure 1E**). In terms of vascular function, subjects on HCQ had improved microvascular function as noted by an increased proportion of sublingual capillaries filled with RBCs (P=0.011) and smaller perfused boundary region (PBR, P=0.010). HCQ dosing correlated with PBR (R=-0.599, P=0.002, **Figure 1H**) and RBC Filling (R=-0.592, P=0.002, **Figure 1I**). BART also trended positively with HCQ dose (R=0.385, P=0.094; **Figure 1J**).

Conclusion: These findings suggest that HCQ may provide benefit for vascular health in SLE as supported by ex vivo experiments demonstrating decreased platelet aggregation and downregulation of platelet functional pathways as well as improved vascular readouts.

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Abstract Number: 0871

Hydroxychloroquine Dose Reduction and SLE Flares

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: 2016 ophthalmology guidelines recommend using hydroxychloroquine (HCQ) dosages < 5mg/kg/day, which is lower than the traditional 400mg/day for the majority of SLE patients. However, it is unknown whether lower dosages retain efficacy for controlling SLE disease activity. The aim of this study was to determine trends of HCQ dose reduction among SLE patients and identify a potential association with the risk of lupus flares.

Methods: We identified a cohort of patients with SLE from our academic medical center using a previously validated electronic health record SLE phenotype algorithm (PPV 92%) (Jorge A et al. *Semin Arthritis Rheum* 2019) and included patients who met 1997 ACR classification criteria and who had at least two visits in our academic rheumatology practice since 1/1/2016. We excluded patients who did not use HCQ at any time after that date. We obtained

Characteristics at Baseline Visit	Overall	Underwent HCQ Dose Reduction	Remained on 400mg/day	p values
N	216	30	111	
Age (y), mean (SD)	46.2 (15.9)	46.7 (14.7)	44.4 (13.7)	0.42
Female, n (%)	196 (90.3)	27 (90.0)	100 (90.1)	1.00
Race/Ethnicity				
White, n (%)	129 (77.2)	20 (90.9)	64 (72.7)	0.04
Black, n (%)	20 (12.0)	1 (4.5)	14 (15.9)	0.11
Asian, n (%)	10 (6.0)	1 (4.5)	4 (4.5)	0.95
Hispanic, n (%)	8 (4.8)	0	6 (6.8)	0.14
Other/unknown, n (%)	50 (23.0)	8 (26.7)	23 (20.7)	0.58
Body Weight (kg), mean (SD)	75.5 (18.9)	71.7 (17.9)	81.7 (18.4)	<0.01
Body Weight under 80 kg, n (%)	127 (63.4)	22 (73.3)	57 (51.4)	<0.01
SLE Disease Duration (y), median	9.5	11.2	8	0.09
SLE Manifestations, n (%)				
Malar Rash	52 (24)	8 (26.7)	30 (27.0)	0.98
Discoid Rash	17 (7.8)	6 (20)	7 (6.3)	0.05
Arthritis	175 (80.6)	26 (86.7)	98 (88.3)	0.95
Nephritis	42 (19.4)	3 (10.0)	23 (20.7)	0.28

Table 1. Baseline Characteristics of SLE Patients According to Time-Varying Hydroxychloroquine Dose

	Before Dose Reduction			After Dose Reduction			
HCQ Dose-Reduction	Person-time (Y)	Flares (N)	Flare Rate	Person-time (Y)	Flares (N)	Flare Rate	Rate Ratio (95% CI)
Reduction to 200mg	21.3	3	0.14	23.1	7	0.30	2.08 (0.71-6.08)
Reduction to 300mg	15.5	2	0.13	12.3	3	0.24	1.89 (0.32-11.3)

Table 2. Hydroxychloroquine Dose-Reduction and the Incidence of SLE Flares

demographics, anthropometrics, medication use, SLE disease history, and SLE manifestations and disease activity assessed at each rheumatology visit. HCQ dose was assessed as a time-varying exposure, in mg/day as 400, 200, or between 200-400 (typically 300). We identified all dose change events. The primary outcomes were combined mild, moderate, and severe SLE flares defined by the revised SELENA-SLEDAI flare index (rSSFI). The secondary outcome was severe rSSFI flares alone. We determined the rates of SLE flares overall, prior to HCQ dose changes, and following HCQ dose reduction and calculated SLE flare incidence rate ratios.

Results: 216 patients met the inclusion criteria, with a mean 2.6 years of follow up since 2016. Patients were on average 46.2 years of age and were 90.3% female (**Table 1**). A total of 111 patients (51.4%) were treated with a HCQ dose of 400mg/day without a dose change, whereas 33 patients (15.3%) received 200mg/day and 12 (5.6%) received 300mg/day without a dose change during the study period. 30 patients (13.9%) initially received 400mg/day and underwent HCQ dose reduction (n=18 to 200mg/day, n=12 to 300mg/day). A higher proportion of patients who underwent dose reduction had body weight under 80kg (thus 400mg of HCQ would exceed 5mg/kg), but the dose also exceeded 5mg/kg for 51.7% of patients who remained on 400mg/day throughout study follow up. The overall rSSFI flare rates were 0.39 total flares per person-year (PY) and 0.06 severe flares per PY. For patients who received 400mg/day throughout study follow up, the overall flare rate and severe flare rate were 0.48 per PY and 0.08 per PY, respectively. Among patients who underwent HCQ dose reduction, overall SLE flare rates were 0.14 per PY prior to HCQ dose reduction from 400mg to 200mg/day and 0.30 per PY following dose reduction to 200mg. The SLE flare

rates were 0.13 per PY prior to HCQ dose reduction from 400mg to 300mg/day and 0.24 per PY following dose reduction to 300mg (**Table 2**).

Conclusion: In recent years, a minority of patients with SLE underwent HCQ dose reduction. Of those who did, we found a numerically higher incidence of SLE flares following HCQ dose reduction. This finding should be replicated in a larger cohort to clarify a potential loss of benefits associated with lowering the treatment dose.

Disclosure: A. Jorge, None; **G. Ho**, None; **M. Wu**, None; **K. Costenbader**, Glaxo Smith Kline, 5, UpToDate, 7, Lupus Foundation of America, 6, Neutrolis Inc, 5; **H. Choi**, AstraZeneca, 2, Takeda, 5, Selecta, 5, GlaxoSmithKline, 5, Horizon, 5.

Abstract Number: 0872

Usage of Corticosteroids and Hospitalisation Duration in Adult Patients with Systemic Lupus Erythematosus (SLE) in Latvia

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment Poster I
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: To determine the factors influencing hospitalisation duration, re – hospitalisation (more than 1 hospitalisation during the study period), frequency of the usage of corticosteroids (CS) and its correlation with SLEDAI, SLICC/ACR DI of systemic lupus erythematosus (SLE) patients.

Methods: A retrospective study performed from 01 January 2018 till 31 December 2019 analysed the data of 80 SLE patients, including hospitalisation episodes, in Pauls Stradins Clinical University Hospital.

Results: 70 (87.5 %) patients were females and 10 (12.5%) males. 44 (55 %) patients were admitted to the hospital due to SLE flare and 5 (6.3%) patients due to a new onset of SLE. The mean duration of hospitalisation was 6.8 days (SD 4,9). CS (the mean dosage of prednisolone was 12.6 mg (SD 16.1)) was used in 54 (67.5%) patients before hospitalisation. The proportion of re-hospitalised patients was higher among CS users in comparison with CS non-users (61.1% (n = 33) vs. 26.9% (n=7), p = 0.004). CS users were hospitalised due to infection in 9.3% vs. 0.0% in non-users. An overall infection rate as the reason of hospitalisation was increased in 24.4% CS users vs. 3.8% non-users, p< 0.05. The dose of CS correlated with SLICC/ACR DI (r=0.363, p=0.001), but did not correlate with SLEDAI (r=-0.192, p=0.089). Duration of hospitalisation was longer in case of infection (11.4 vs. 5.9 days, p = 0.000), serositis (9.4 vs. 6.2 days, p = 0.018), fever (8.9 vs. 4.7 days, p = 0.004) and neurolupus (7.4 vs. 3.4 days, p = 0.008). Hospitalisation duration had correlation with ESR (r = 0.284, p = 0.012), CRP (r = 0.323, p = 0.003), SLEDAI (r = 0.237, p =0.034), total count of leukocytes (r = -0.317, p = 0.004), and neutrophils (r = -0.287, p = 0.01).

Conclusion: The most common cause of hospitalisation in SLE patients was a flare. More than half of SLE patients in long-term treament received CS with higher rate of hospitalisation and re-hospitalisation within a year due to infection.

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Abstract Number: 0873

Impact of Skin Involvement on Disease Burden Among Patients with Psoriatic Arthritis: Data from the Corrona Psoriatic Arthritis/Spondyloarthritis Registry

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: When deciding to start patients with PsA on biologic therapy, rheumatologists may focus on skin involvement in addition to joint symptoms. The purpose of this study is to investigate the clinical significance of skin involvement in patients with PsA newly initiating an advanced therapy.

Methods: This was a descriptive analysis of adult patients (≥18 years) with PsA enrolled in the Corrona PsA/SpA Registry between March 2013 and March 2020. Patients were included if they initiated an advanced therapy (i.e.,

Table 1. Demographics and Comorbidities of Patients With PsA at Initiation of Advanced Therapy

Characteristic	Body Surface Area (BSA) Category				*P* value[a]
	Overall N=574	Mild BSA ≥0% and ≤3% N=354 (62%)	Moderate BSA >3% and ≤10% N=144 (25%)	Severe BSA >10% N=76 (13%)	
Age (years), mean ± SD	52.0 ± 13.7	51.8 ± 13.9	53.2 ± 13.8	51.0 ± 12.7	0.40
Female, %	320 (56.1)	205 (58.1)	(79) (55.2)	36 (48.7)	0.32
White, n (%)	519 (90.4)	330 (93.2)	126 (87.5)	63 (82.9)	0.008
Work status, n (%)					
Full-time	324 (58.2)	207 (59.7)	74 (52.9)	43 (61.4)	0.55
Part-time	43 (7.7)	N/A[b]	N/A[b]	N/A[b]	
Retired	31 (5.6)	N/A[b]	N/A[b]	N/A[b]	
Other	159 (28.6)	100 (28.8)	41 (29.3)	18 (25.7)	
BMI (kg/m^2), mean ± SD	32.3 ± 8.4	31.9 ± 8.0	32.5 ± 9.3	33.4 ± 8.5	0.34
BMI category, n (%)					
Normal/underweight (<25)	104 (18.4)	71 (20.5)	23 (16.1)	10 (13.3)	0.41
Overweight (≥25 to <30)	144 (25.5)	90 (26.0)	37 (25.9)	17 (22.7)	
Obese (≥30)	316 (56.0)	185 (53.5)	83 (58.0)	48 (64.0)	
Comorbidities, n (%)					
Hypertension	209 (36.4)	122 (34.5)	53 (36.8)	34 (44.7)	0.24
Hyperlipidemia	119 (20.7)	76 (21.5)	31 (21.5)	12 (15.8)	0.52
Metabolic syndrome	93 (16.2)	57 (16.1)	22 (15.3)	14 (18.4)	0.83
Depression	91 (15.9)	61 (17.2)	25 (17.4)	5 (6.6)	0.06
Diabetes	83 (14.5)	46 (13.0)	21 (14.6)	16 (21.1)	0.19
Malignancy	38 (6.6)	24 (6.8)	5 (3.5)	9 (11.8)	0.06
Serious infections	36 (6.3)	23 (6.5)	7 (4.9)	6 (7.9)	0.65
Cerebro-cardiovascular disease	53 (9.2)	32 (9.0)	16 (11.1)	5 (6.6)	0.53

Percentages were calculated for non-missing values. [a]*P* value from two-sample t-tests or Wilcoxon rank sum tests for continuous variables and from chi-square or Fisher exact tests for categorical variables. [b]N/A indicates low counts (<5). BMI, body mass index; BSA, body surface area.

Table 2. Clinical Characteristics, Disease Activity Measures, and Patient-Reported Outcomes of Patients With PsA at Initiation of Advanced Therapy

Characteristic[a]	Body Surface Area (BSA) Category				*P* value[b]
	Overall N=574	Mild BSA ≥0% and ≤3% N=354 (62%)	Moderate BSA >3% and ≤10% N=144 (25%)	Severe BSA >10% N=76 (13%)	
Years since PsA symptom onset	7.0 ± 8.8	7.2 ± 9.3	6.7 ± 7.8	6.6 ± 8.5	0.95
Years since PsA diagnosis	3.6 ± 6.6	3.6 ± 6.9	3.5 ± 5.8	3.7 ± 6.5	0.55
PtGA of PsA	44.2 ± 27.0	42.6 ± 27.8	46.5 ± 25.9	47.0 ± 25.0	0.18
PtGA of PsA and PsO	44.9 ± 26.9	43.0 ± 27.8	47.1 ± 25.7	49.6 ± 24.2	0.06
Tender joint count (28)	4.7 ± 6.0	4.8 ± 6.3	4.4 ± 5.1	5.3 ± 6.1	0.36
Swollen joint count (28)	3.1 ± 4.3	2.9 ± 4.1	3.3 ± 4.5	3.7 ± 5.0	0.40
Dactylitis count	0.56 ± 1.49	0.51 ± 1.33	0.58 ± 1.43	0.76 ± 2.15	0.95
SPARCC enthesitis count	0.97 ± 2.17	1.04 ± 2.27	0.99 ± 2.13	0.66 ± 1.74	0.63
DAS28-ESR	3.7 ± 1.4	3.7 ± 1.5	3.7 ± 1.5	4.0 ± 1.3	0.25
CDAI	15.8 ± 11.5	15.4 ± 11.6	15.9 ± 10.5	17.6 ± 12.7	0.33
PASDAS	4.6 ± 1.5	4.6 ± 1.5	4.8 ± 1.4	4.6 ± 1.4	0.45
ASAS HI	7.6 ± 4.2	7.3 ± 4.5	7.9 ± 4.4	8.2 ± 3.2	0.79
DAPSA	21.7 ± 14.8	21.5 ± 15.1	21.5 ± 14.2	22.9 ± 14.9	0.77
Patient-reported pain (VAS)[c]	49.9 ± 29.3	48.0 ± 29.4	53.6 ± 29.3	51.9 ± 28.5	0.11
Morning stiffness, n (%)[d]	537 (93.6)	329 (92.9)	137 (95.1)	71 (93.4)	0.68
BASDAI	4.8 ± 2.5	4.7 ± 2.5	5.1 ± 2.6	5.1 ± 2.5	0.10
WPAI domains					
% Work time missed	8.8 ± 21.6	8.0 ± 21.9	8.5 ± 18.6	12.8 ± 25.0	0.31
% Impairment while working	28.2 ± 25.8	27.0 ± 26.3	33.1 ± 24.6	25.2 ± 24.7	0.04
% Overall work impairment	32.9 ± 29.3	31.5 ± 30.0	37.3 ± 27.9	32.6 ± 28.1	0.15
% Activity impairment	40.1 ± 29.9	37.9 ± 29.7	44.1 ± 28.9	43.1 ± 32.3	0.08
HAQ-DI	0.82 ± 0.66	0.78 ± 0.65	0.84 ± 0.65	0.96 ± 0.69	0.09

[a]Except where indicated otherwise, values are mean ± SD. [b]*P* value from two-sample t-tests or Wilcoxon rank sum tests. [c]Measured using a 100-point scale. [d]Measured only in patients reporting morning stiffness. ASAS HI, Assessment of SpondyloArthritis international Society Health Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BSA, body surface area; CDAI, Clinical Disease Activity Index; DAPSA, Disease Activity Index in Psoriatic Arthritis; HAQ-DI, Health Assessment Questionnaire-Disability Index; PASDAS, Psoriatic Arthritis Disease Activity Score; PtGA, Patient Global Assessment; PsO, psoriasis; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analog scale; WPAI, Work Productivity and Activity Impairment.

biologic or targeted synthetic disease-modifying antirheumatic drug) at enrollment, had a body surface area (BSA) measurement, and had no prior history of advanced therapy at initiation. Baseline demographics, clinical characteristics, treatment history, disease activity measures, and patient-reported outcome measures were stratified by BSA categories of mild (BSA ≥0 and ≤3%), moderate (BSA >3% and ≤10%), and severe (BSA >10%). Continuous measures were reported using means and standard deviation; means for BSA groups were compared using two-sample t-tests or Wilcoxon rank sum tests. Categorical measures were reported as frequencies and percentages; frequencies in BSA groups were compared using chi-square or Fisher exact tests.

Results: A total of 574 eligible initiators included 354 (61.7%), 144 (25.1%), and 76 (13.2%) with mild, moderate, and severe skin involvement, respectively. Across BSA groups, mean age was 51.0–53.2 years and 48.7–58.1% were female (**Table 1**). TNF inhibitors were the most commonly initiated biologic (77.1–79.0%). Overall, BSA groups were very similar across baseline demographics and comorbidities. Across BSA groups, mean baseline scores were generally similar ($P>0.05$) for musculoskeletal PsA domains (tender/swollen joint, dactylitis, enthesitis counts, and axial involvement), disease activity measures (Clinical Disease Activity Index, Disease Activity in Psoriatic Arthritis, and Psoriatic Arthritis Disease Activity Score), and patient-reported outcomes of pain, Health Assessment Questionnaire-Disability Index, the Assessment of SpondyloArthritis international Society Health Index, and impairment of work productivity and ability to perform daily activities (**Table 2**). BSA groups also did not differ significantly on prior or current therapy at baseline (**Table 3**).

Conclusion: The majority of patients with PsA who initiated an advanced therapy had mild to moderate skin involvement. Moreover, baseline demographics, disease activity in musculoskeletal PsA domains, and patient-reported outcomes were comparable across mild to severe skin involvement. Although rheumatologists' treatment decisions can

Table 3. Treatment History of Patients With PsA at Initiation of Advanced Therapy

	Body Surface Area (BSA) Category				*P* value[a]
	Overall N=574	Mild BSA ≥0% and ≤3% N=354 (62%)	Moderate BSA >3% and ≤10% N=144 (25%)	Severe BSA >10% N=76 (13%)	
Initiated therapy, n (%)					
TNFi	447 (77.9)	276 (78.0)	111 (77.1)	60 (79.0)	0.44
Non-TNFi bDMARD	106 (18.5)	N/A[b]	N/A[b]	N/A[b]	
JAKi	21 (3.7)	N/A[b]	N/A[b]	N/A[b]	
Concomitant therapy, n (%)					
Monotherapy	277 (48.3)	161 (45.5)	74 (51.4)	42 (55.3)	0.21
Combination with MTX	180 (31.4)	114 (32.2)	41 (28.5)	25 (32.9)	0.68
Combination with non-MTX csDMARDs	44 (7.7)	30 (8.5)	9 (6.3)	5 (6.6)	0.65
Prior csDMARD, n (%)					
0	449 (78.2)	273 (77.1)	118 (81.9)	58 (76.3)	0.54
1	105 (18.3)	66 (18.6)	N/A[b]	N/A[b]	
2+	20 (3.5)	15 (4.2)	N/A[b]	N/A[b]	

[a]*P* value from chi-square or Fisher exact tests. [b]N/A indicates low counts (<5).
bDMARD, biologic DMARD; BSA, body surface area; csDMARD, conventional synthetic DMARD; JAKi, Janus kinase inhibitor.

be driven by many factors, severe psoriasis is relatively uncommon in rheumatology practice. Thus, musculoskeletal symptoms are more likely to drive therapeutic decision making when newly initiating advanced therapies for patients with PsA.

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Abstract Number: 0874

A Multi-Center, Randomized, Double-blind, Placebo-controlled Dose-ranging Study Evaluating Efficacy and Safety of SHR-1314 in Subjects with Moderate-to-Severe Plaque Psoriasis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: SHR-1314 is a humanized monoclonal immunoglobulin (IgG1/κ isotype) targeting human interleukin-17A (IL-17A). Preliminary data from phase I study has shown that single dose of SHR-1314 from 8 mg to 240 mg was safe and well-tolerated in healthy subjects (data on file, Hengrui). Here, we report the interim results of a Phase II study (NCT03463187) assessing the efficacy and safety of SHR-1314 in subjects with moderate-to-severe plaque psoriasis after 12-weeks treatment.

Methods: This phase II study was conducted in 20 centers in China, Australia, and the US. Eligible subjects with moderate-to-severe chronic plaque psoriasis were randomized 1:1:1:1:1 into one of five groups to receive SHR-1314 (40 mg, 80 mg, 160 mg, or 240 mg) or placebo subcutaneously at week 0, 4, 8, and 12, followed by unblinding. The date of data cutoff for the present analyses was Dec 18, 2019, although subjects on SHR-1314 received two more drug administration on Week 16 and 20 respectively afterwards. The primary endpoint was the percentage of subjects who achieve at least 75% improvement in the psoriasis area and severity index score (PASI 75) at week 12.

	SHR-1314 40 mg (N=37)	SHR-1314 80 mg (N=38)	SHR-1314 160 mg (N=38)	SHR-1314 240 mg (N=37)	SHR-1314 Total (N=150)	Placebo (N=37)	Total (N=187)
Age, years	39.1±13.0	42.3±13.3	41.6±12.2	42.5±13.9	41.4±13.0	37.7±12.2	40.6±12.9
Male	30 (81.1)	31 (81.6)	26 (68.4)	25 (67.6)	112 (74.7)	28 (75.7)	140 (74.9)
Race							
White	7 (18.9)	7 (18.4)	7 (18.4)	11 (29.7)	32 (21.3)	5 (13.5)	37 (19.8)
Black or African American	0	0	1 (2.6)	1 (2.7)	2 (1.3)	0	2 (1.1)
Asian	30 (81.1)	31 (81.6)	30 (78.9)	25 (67.6)	116 (77.3)	31 (83.8)	147 (78.6)
Other	0	0	0	0	0	1 (2.7)	1 (0.5)
Subjects with any previous psoriasis therapy	28 (75.7)	32 (84.2)	32 (84.2)	31 (83.8)	123 (82.0)	29 (78.4)	152 (81.3)
Duration of psoriasis, (months)	151.0±109.0	150.4±108.2	153.8±111.6	192.1±140.9	161.7±118.2	129.2±78.2	155.3±112.0
Percent of body-surface area involved	42.6±20.6	38.6±19.7	38.4±19.5	36.4±22.2	39.0±20.4	37.5±18.1	/
PASI score	24.0±9.1	22.9±11.0	22.5±11.1	21.6±9.6	22.8±10.2	21.8±8.5	/
sPGA core>=4	21 (56.8)	16 (42.1)	15 (39.5)	14 (37.8)	66 (44.0)	20 (54.0)	/
Weight							
<90kg	31 (83.8)	36 (94.7)	34 (89.5)	31 (83.8)	132 (88.0)	29 (78.4)	/
>=90kg	6 (16.2)	2 (5.3)	4 (10.5)	6 (16.2)	18 (12.0)	8 (21.6)	/

Data are n (%) or mean (SD).

Table 1. Baseline Demographics and Clinical Characteristics.

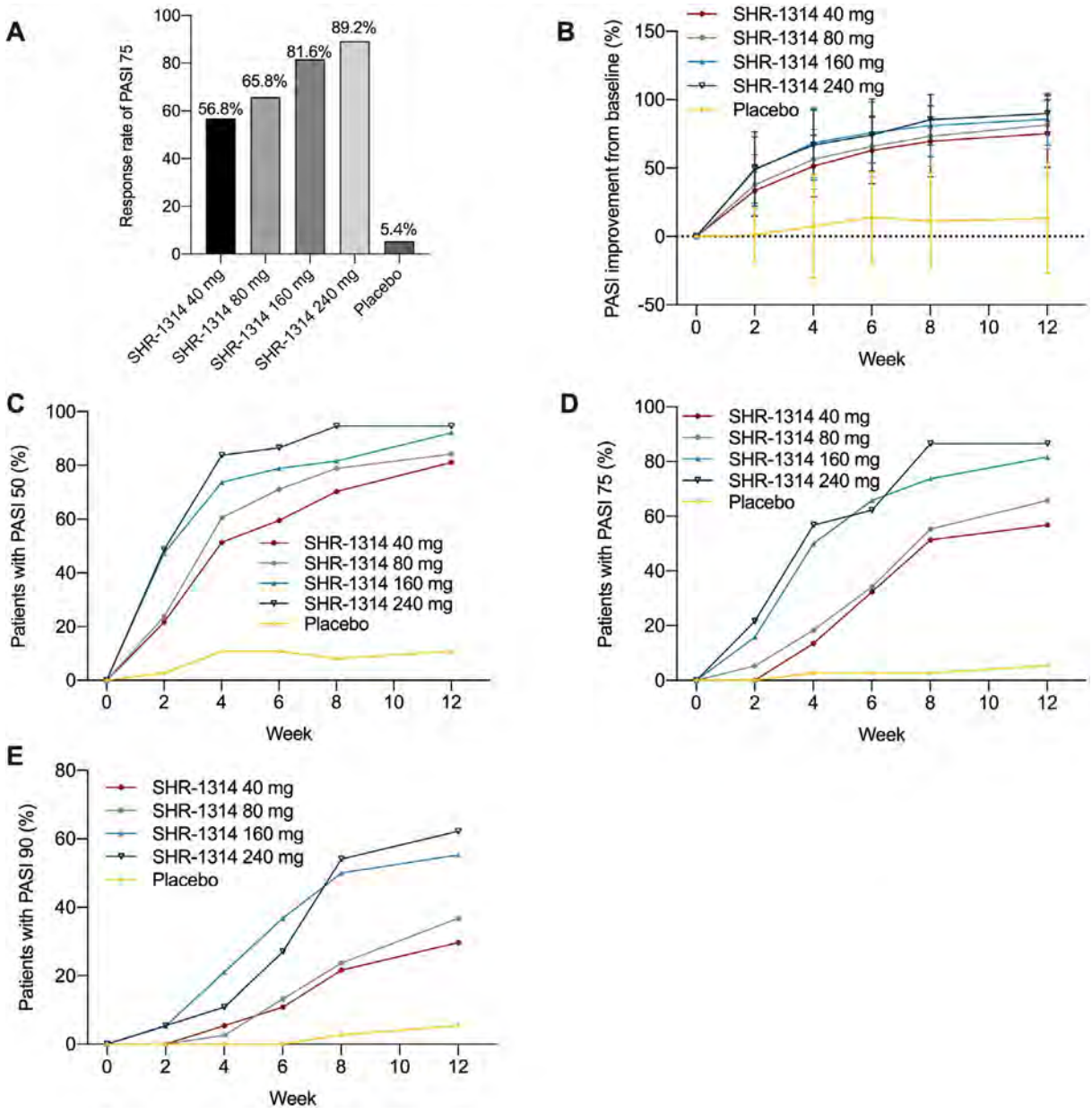

Figure 1. Changes from baseline in PASI score and response rates of PASI 50, PASI 75, and PASI 90. (A) Proportion of PASI 75 responders at week 12. Missing values are handled by LOCF (last observation carried forward). (B) Mean of percent change from baseline in PASI score. (C) Response rate of PASI 50 through Week 12. Missing values are handled by NCF (non-completers considered failure). (D) Response rate of PASI 75 through Week 12. Missing values are handled by NCF. (E) Response rate of PASI 90 through Week 12. Missing values are handled by NCF.

Results: 187 were randomized to receive SHR-1314 at a dose of 40 mg (37 subjects), 80 mg (38 subjects), 160 mg (38 subjects), or 240 mg (37 subjects), or placebo (37 subjects). Baseline demographic and disease characteristics were similar among treatment groups (Table 1). There were significantly greater proportions of PASI 75 responders in all SHR-1314 groups (40, 80, 160, 240 mg: 56.8%, 65.8%, 81.6%, 89.2%; $p< 0.001$ [calculated by Chi-square test] for every SHR-1314 group) compared to placebo (5.4%) at week 12 (Figure 1A). In comparison with placebo, greater improvements over time were observed for subjects with SHR-1314 in percent change from baseline in PASI score (Figure 1B), proportion of subjects with at least 50%, 75%, or 90% improvement from baseline in PASI (PASI 50, PASI 75, or PASI 90, Figure 1C-E), and proportion of subjects achieving physician global assessment (PGA, Figure 2) response of 0 or 1. Treatment-emergent adverse events (TEAEs) were reported in 107 (71.3%) of the 150 subjects with SHR-1314 and 24 (64.9%) of 37 subjects with placebo. The most frequent TEAEs included upper respiratory

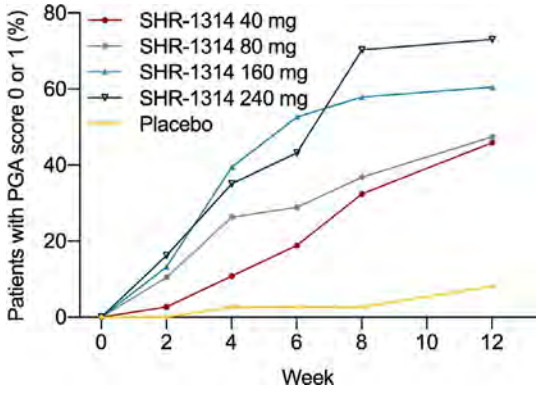

Figure 2. PGA 0 or 1 response rate through Week 12. Missing values are handled by NCF.

tract infection (SHR-1314, 13.3%; placebo, 16.2%) and hyperuricaemia (SHR-1314, 7.3%; placebo, 5.4%). Sixty-five (43.3%) subjects with SHR-1314 and 11 (29.7%) subjects with placebo had treatment-related TEAEs. Most of TEAEs were mild or moderate. Serious TEAEs occurred in one (0.7%) subject with SHR-1314 and two (5.4%) with placebo, none were considered as treatment-related. One (0.7%) subject with SHR-1314 and one (2.7%) with placebo discontinued treatment due to TEAEs. No deaths were reported.

Conclusion: SHR-1314 showed superior efficacy compared to placebo in all groups in subjects with moderate-to-severe plaque psoriasis. 240 mg dosing led to numerically higher PASI 75 responders by week 12 than other doses. SHR-1314 was well-tolerated in the present trial.

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Abstract Number: 0875

Secukinumab Provides Sustained Improvements in Subgroup Analyses of Joint Tenderness and Swelling in Patients with Psoriatic Arthritis: 5-Year Results from the Phase 3 FUTURE 2 Study

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Background/Purpose: Secukinumab, a fully human monoclonal antibody that neutralizes interleukin-17A, has shown long-term efficacy and tolerability in patients with psoriatic arthritis (PsA) in FUTURE 2. Tender joint count (TJC) and swollen joint count (SJC) scores measure synovitis, a key assessment of disease activity. TJC and SJC scores are components of composite measures used to assess joint response to treatment. It is known that response

Table 1: Selected baseline characteristics				
Variable	SEC 300 mg SC (N=100)	SEC 150 mg SC (N=100)	PBO (N=98)	
Mean age, years	46.9	46.5	49.9	
Sex, n (%)				
Male	51 (51.0)	55 (55.0)	39 (39.8)	
Mean weight, kg	85.4	91.2	86.2	
Smoking status, n (%)				
Yes	19 (19.0)	21 (21.0)	17 (17.3)	
Mean time since first diagnosis of PsA, years	7.4	6.5	7.3	
MTX use at randomization, n (%)				
Yes	44 (44.0)	44 (44.0)	50 (51.0)	
Proportion of TNFi-IR patients, n (%)	33 (33.0)	37 (37.0)	35 (37.7)	
Number of prior TNFi therapies, n (%)				
0	67 (67.0)	63 (63.0)	63 (64.3)	
1	16 (16.0)	26 (26.0)	16 (16.3)	
≥2[a]	17 (17.0)	11 (11.0)	19 (19.4)	
Mean adjusted 78 TJC score				
Total population	20.2	24.1	23.4	
Mean adjusted 76 SJC score				
Total population	11.2	11.9	12.1	
Variable	SEC 300 mg SC (N=100)	SEC 150 mg SC (N=100)	PBO–SEC 300 mg SC[b] (N=45)	PBO–SEC 150 mg[b] (N=43)
Mean adjusted 78 TJC score				
TNFi-naive patients	18.9	21.2	22.3	21.7
TNFi-IR patients	23.3	29.1	19.1	25.0
Patients with concomitant MTX use	18.5	23.6	18.3	22.7
Patients without concomitant MTX use	21.9	24.6	24.3	23.0
Mean adjusted 76 SJC score				
TNFi-naive patients	10.2	10.8	12.0	9.5
TNFi-IR patients	13.5	13.9	13.3	13.1
Patients with concomitant MTX use	11.0	12.5	11.0	11.5
Patients without concomitant MTX use	11.5	11.5	14.0	9.7

[a]The maximum number of prior TNFis was three; [b]Mean adjusted 78 TJC/76 SJC scores for placebo are split based on future rerandomization group.

N=number of randomized patients; n=number of evaluable patients.

MTX, methotrexate; PBO, placebo; PsA, psoriatic arthritis; SC, subcutaneous; SEC, secukinumab; SJC, swollen joint count; TJC, tender joint count; TNFi, tumor necrosis factor inhibitor.

Table 1. Selected baseline characteristics

to biologic treatment can be affected by prior and concomitant use of other treatments (e.g. tumor necrosis factor inhibitors [TNFis] or methotrexate [MTX]). Here, we report the 5-year efficacy of secukinumab on reduction of 78 TJC and 76 SJC scores in key FUTURE 2 subgroups: patients naive to or with a prior inadequate response (IR) to TNFis, and patients with and without concomitant MTX use.

Methods: 397 patients with active PsA, who were permitted the use of ≤3 prior TNFis and/or concomitant MTX, were randomized to subcutaneous secukinumab loading dose (300, 150, 75 mg) or placebo at baseline, Weeks 1, 2, 3, and

Table 2: 78 TJC and 76 SJC results at Weeks 24 and 260								
	Week 24				Week 260			
Endpoint	SEC 300 mg SC (N=100)	SEC 150 mg SC (N=100)	PBO–SEC 300 mg SC (N=45)	PBO–SEC 150 mg (N=43)	SEC 300 mg SC (N=100)	SEC 150 mg SC[a] (N=100)	PBO–SEC 300 mg SC (N=45)	PBO–SEC 150 mg[b] (N=43)
Adjusted 78 TJC (total population)								
Change from baseline (SD)	−10.4 (10.8)	−12.1 (16.5)	−10.6 (14.1)	−9.7 (13.6)	−12.8 (10.7)	−15.1 (15.9)	−14.5 (15.4)	−12.5 (10.6)
Adjusted 76 SJC (total population)								
Change from baseline (SD)	−7.2 (5.8)	−6.3 (7.7)	−9.7 (9.5)	−9.6 (10.7)	−9.3 (6.1)	−8.5 (7.9)	−9.5 (8.1)	−8.3 (6.3)
Adjusted 78 TJC (TNF status)								
TNFi-naive								
Change from baseline (SD)	−10.7 (10.8)	−13.0 (16.6)	−3.5 (13.9)	−8.0 (10.7)	−13.1 (11.1)	−15.3 (16.7)	−14.8 (16.0)	−11.5 (10.2)
TNFi-IR								
Change from baseline (SD)	−9.8 (10.9)	−10.3 (16.4)	−11.0 (11.4)	−13.4 (19.5)	−12.0 (9.6)	−14.4 (14.0)	−14.0 (15.1)	−15.7 (12.0)
Adjusted 76 SJC (TNF status)								
TNFi-naive								
Change from baseline (SD)	−6.9 (4.8)	−6.7 (8.2)	−10.5 (11.0)	−6.8 (6.2)	−9.5 (5.7)	−8.8 (8.8)	−9.4 (9.0)	−8.4 (6.9)
TNFi-IR								
Change from baseline (SD)	−7.8 (7.4)	−5.7 (6.5)	−7.8 (5.0)	−15.6 (16.3)	−8.9 (7.4)	−7.9 (5.1)	−9.6 (6.1)	−7.9 (4.6)
Adjusted 78 TJC (MTX use)								
Concomitant MTX use								
Change from baseline (SD)	−10.3 (8.7)	−10.6 (16.7)	−8.7 (13.1)	−7.6 (14.3)	−11.2 (9.1)	−14.7 (14.5)	−12.7 (12.5)	−11.4 (11.4)
No concomitant MTX use								
Change from baseline (SD)	−10.5 (12.3)	−13.3 (16.4)	−15.2 (16.8)	−14.2 (12.0)	−14.4 (12.0)	−15.4 (17.5)	−16.8 (18.6)	−14.1 (9.6)
Adjusted 76 SJC (MTX use)								
Concomitant MTX use								
Change from baseline (SD)	−6.9 (6.1)	−6.0 (8.5)	−8.9 (8.6)	−8.8 (9.7)	−8.9 (6.0)	−9.5 (9.1)	−8.6 (5.3)	−9.4 (7.2)
No concomitant MTX use								
Change from baseline (SD)	−7.4 (5.7)	−6.6 (6.9)	−11.6 (12.4)	−11.2 (13.8)	−9.7 (6.2)	−7.5 (6.5)	−10.6 (10.7)	−6.6 (4.6)

[a]SEC 150 mg arm includes 42 patients who were uptitrated to SEC 300 mg from Week 128.

[b]PBO–SEC 150 mg arm includes 19 patients who were uptitrated to SEC 300 mg from Week 128. Data are reported as observed.

N=number of randomized patients; n=number of patients with evaluation.

IR, inadequate response; MTX, methotrexate; PBO, placebo; PsA, psoriatic arthritis; SC, subcutaneous; SD, standard deviation; SEC, secukinumab; SJC, swollen joint count; TJC, tender joint count; TNFi, tumor necrosis factor inhibitor.

Table 2. 78 TJC and 76 SJC results at Weeks 24 and 260

4, and every 4 weeks thereafter. Patients receiving placebo were re-randomized to secukinumab 300 or 150 mg at Week 16 (non-responders) or 24 (responders). Secukinumab dose could be escalated from 150 to 300 mg or from 75 to 150 or 300 mg starting at Week 128 and maintained thereafter, if active signs of disease were observed based on physician's assessment. ACR20 response and changes in 78 TJC/76 SJC are reported over 5 years (2 years of core study and 3-year extension) for secukinumab 300 and 150 mg (approved PsA doses) in key subgroups: TNFi-naive, TNFi-IR, and with/without concomitant MTX.

Results: Baseline characteristics were similar across treatment arms (Table 1). At baseline, 33.0%, 37.0%, and 35.7% of patients were TNFi-IR, and 44.0%, 44.0%, and 51.0% were using concomitant MTX in the secukinumab 300, 150 mg, and placebo arms, respectively. The primary endpoint, ACR20 response at Week 24, has been reported previously (McInnes, 2015). In subgroup analyses of the secukinumab 300 and 150 mg arms, 79.6% and 77.1% of TNFi-naive patients achieved an ACR20 response versus 56.3% and 66.7% of TNFi-IR patients at Week 260. At the same timepoint, 62.5% and 73.5% of patients with concomitant MTX use achieved an ACR20 response versus

84.8% and 75.0% of patients without concomitant MTX use in the secukinumab 300 and 150 mg arms, respectively. At Week 260, mean change from baseline in adjusted 78 TJC/76 SJC scores for TNFi-naive and TNFi-IR patients was –13.1/–9.5 and –12.0/–8.9 for secukinumab 300 mg, and –15.3/–8.8 and –14.4/–7.9 for secukinumab 150 mg, respectively (Table 2). At Week 260, mean change from baseline in adjusted 78 TJC/76 SJC scores for patients with and without concomitant MTX was –11.2/–8.9 and –14.4/–9.7 for secukinumab 300 mg, and –14.7/–9.5 and –15.4/–7.5 for secukinumab 150 mg, respectively.

Conclusion: Analysis of 78 TJC and 76 SJC scores demonstrated that treatment with secukinumab provided improvements in synovitis at Week 24, which were sustained over 5 years, irrespective of TNFi history and concomitant MTX use.

Disclosure: I. McInnes, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **H. Chinoy**, Novartis, 1; **D. Asquith**, Novartis, 1, 2; **A. White**, Novartis, 1, 2; **C. Gaillez**, Novartis, 1, 3.

Abstract Number: 0876

Gender Differences in Baseline Clinical Characteristics Among Patients with Ankylosing Spondylitis and Non-radiographic Axial Spondyloarthritis: Data from 3 Randomized Ixekizumab Controlled Trials

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
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Background/Purpose: Ixekizumab (IXE), an anti-interleukin-17A monoclonal antibody, has demonstrated superior efficacy to placebo in the treatment of patients with axial spondyloarthritis (axSpA) (Dougados M et al., Ann Rheum Dis, 2020; Deodhar A et al., Lancet, 2020). Previous studies have shown that the clinical presentation of women and men with ankylosing spondylitis (AS) and non-radiographic axSpA (nr-axSpA) may differ and influence treatment response (van der Horst-Bruinsma IE et al., Ann Rheum, 2019; Rusman T et al., Curr Rheumatol Rep, 2018). This analysis explored gender differences in baseline clinical characteristics among patients with AS and nr-axSpA using data from 3 randomized IXE controlled trials.

Methods: Baseline data for patients with AS before IXE treatment were integrated from COAST-V (biologic-naïve; NCT02696785) and COAST-W (prior tumor necrosis factor inhibitor inadequate response; NCT02696798). Baseline data for patients with nr-axSpA before IXE treatment from COAST-X (biologic-naïve; NCT02757352) were analyzed separately. Assessment of SpondyloArthritis International Society (ASAS) criteria was used to classify radiographic axSpA and nr-axSpA. The patients meeting the ASAS criteria for radiographic axSpA also fulfilled modified New York criteria for AS. Descriptive statistics were used to evaluate demographics and baseline clinical characteristics stratified by gender.

Table 1. Demographics and Baseline Clinical Characteristics of Patients with Ankylosing Spondylitis (COAST-V and COAST-W) and Non-radiographic Axial Spondyloarthritis (COAST-X) Stratified by Gender

	Patients with AS (N=376)		Patients with nr-axSpA (N=198)	
Characteristic	**Male (n=298)**	**Female (n=78)**	**Male (n=99)**	**Female (n=99)**
Age (years), mean (SD)	42.8 (12.0)	47.6 (12.6)	37.0 (13.0)	43.9 (12.7)
BMI, kg/m^2, mean (SD)	27.3 (5.6)	27.6 (6.1)	27.2 (4.9)	27.8 (6.2)
Age at AS or nr-axSpA onset (years), mean (SD)	26.5 (8.7)	30.1 (10.1)	27.9 (7.7)	32.0 (10.7)
Duration of symptoms since AS or nr-axSpA onset (years), mean (SD)	16.7 (10.5)	17.8 (12.2)	9.5 (9.2)	12.3 (11.3)
DMARDs use, n (%)[a]	93 (31.2)	23 (29.5)	42 (42.4)	40 (40.4)
HLA-B27 positive, n (%)	259 (86.9)	62 (79.5)	74 (76.3)	70 (70.7)
Anterior uveitis, current or historical, n (%)	71 (23.8)	14 (17.9)	7 (7.1)	15 (15.2)
CRP, mg/L, mean (SD)	17.4 (25.5)	11.2 (12.8)	12.1 (17.4)	12.3 (18.5)
ASDAS, mean (SD)	4.0 (0.8)	3.9 (0.7)	3.7 (0.8)	3.9 (0.8)
BASDAI score				
Mean (SD)	7.1 (1.4)	7.4 (1.5)	6.9 (1.4)	7.4 (1.4)
Median (range)	7.2 (3.3–10.0)	7.6 (2.8–10.0)	7.0 (2.4–10.0)	7.6 (1.4–10.0)
Fatigue/tiredness (BASDAI Q1)				
Mean (SD)	7.4 (1.6)	7.8 (1.5)	7.0 (1.6)	7.9 (1.5)
Median (range)	7.0 (2.0–10.0)	8.0 (2.0–10.0)	7.0 (2.0–10.0)	8.0 (2.0–10.0)
Spinal pain score (BASDAI Q2)				
Mean (SD)	7.9 (1.5)	8.0 (1.5)	7.5 (1.4)	7.9 (1.5)
Median (range)	8.0 (4.0–10.0)	8.0 (5.0–10.0)	7.0 (4.0–10.0)	8.0 (3.0–10.0)
Pain/swelling in joints other than neck, back, or hip (BASDAI Q3)				
Mean (SD)	6.5 (2.1)	6.9 (2.2)	6.6 (2.3)	7.2 (1.9)
Median (range)	7.0 (0–10.0)	7.0 (0–10.0)	7.0 (0–10.0)	7.0 (1.0–10.0)
Discomfort when tender to the touch/pressure (BASDAI Q4)				
Mean (SD)	6.8 (1.8)	7.0 (1.9)	6.6 (1.9)	6.8 (1.8)
Median (range)	7.0 (0–10.0)	7.0 (2.0–10.0)	7.0 (0–10.0)	7.0 (0–10.0)
Morning stiffness (BASDAI Q5)				
Mean (SD)	7.5 (1.6)	7.7 (1.8)	7.3 (1.7)	7.7 (1.9)
Median (range)	8.0 (3.0–10.0)	8.0 (2.0–10.0)	7.0 (2.0–10.0)	8.0 (0–10.0)
Duration of morning stiffness (BASDAI Q6)				
Mean (SD)	6.5 (2.3)	6.5 (2.8)	6.3 (2.3)	6.6 (2.5)
Median (range)	7.0 (1.0–10.0)	7.0 (0–10.0)	6.0 (1.0–10.0)	7.0 (0–10.0)
Spinal pain at night NRS, mean (SD)	7.4 (1.5)	7.8 (1.7)	7.0 (1.8)	7.6 (1.8)
Spinal pain NRS, mean (SD)	7.5 (1.5)	7.8 (1.6)	7.2 (1.5)	7.5 (1.8)
Fatigue Severity NRS, mean (SD)	7.1 (1.7)	7.3 (2.0)	7.0 (1.6)	7.4 (1.7)
BASFI score, mean (SD)	6.8 (1.8)	7.0 (2.0)	6.2 (1.8)	6.7 (2.1)
SF-36 PCS score, mean (SD)	30.9 (8.3)	28.9 (8.2)	33.1 (7.7)	32.1 (7.2)
SF36 MCS score, mean (SD)	47.2 (12.7)	44.4 (12.2)	48.5 (11.3)	46.4 (13.2)

a DMARDs included methotrexate, sulfasalazine, and hydroxychloroquine. Abbreviations: AS, ankylosing spondylitis; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI; Bath Ankylosing Spondylitis Functional Index; BMI, body mass index; CRP, C-reactive protein; DMARD, disease-modifying antirheumatic drug; HLA-B27, human leukocyte antigen B27; nr-axSpA, non-radiographic axial spondyloarthritis; NRS, numeric rating scale; Q, question; SD, standard deviation; SF-36 MCS: Medical Outcomes Study 36-Item Short Form Health Survey Mental Component Score; SF-36 PCS: Medical Outcomes Study 36-Item Short Form Health Survey Physical Component Score

Results: Women were older at disease onset (AS: mean 30.1 [standard deviation 10.1]) vs. 26.5 [8.7] years; nr-axSpA: mean 32.0 [10.7] vs. 27.9 [7.7] years) and had a longer symptom duration (AS: mean 17.8 [12.2] vs. 16.7 [10.5] years; nr-axSpA: 12.3 [11.3] vs. 9.5 [9.2] years) than men. High disease activity, as measured by mean total Bath AS Disease

Activity Index (BASDAI) score, was reported for both women (AS: 7.4 [1.5]; nr-axSpA: 7.4 [1.4]) and men (AS: 7.1 [1.4]; nr-axSpA: 6.9 [1.4]). Women scored higher than men on 5 of the 6 BASDAI questions, indicating that women reported more fatigue, spinal pain, peripheral joint symptoms, discomfort and tenderness, and morning stiffness. Women also reported more spinal pain at night vs. men (AS: 7.8 [1.7] vs. 7.4 [1.5]; nr-axSpA: 7.6 [1.8] vs. 7.0 [1.8]). Anterior uveitis was more common among men than women with AS (23.8% vs. 17.9%) and more common among women than men with nr-axSpA (15.2% vs. 7.1%). The prevalence of human leukocyte antigen B27 (HLA-B27) was higher among men vs. women (AS: 86.9% vs. 79.5%; nr-axSpA: 76.3% vs. 70.7%). C-reactive protein levels were higher in men compared to women with AS (17.4 [25.5] vs. 11.2 [12.8]) but similar in patients with nr-axSpA (men: 12.1 [17.4] vs. women: 12.3 [18.5]).

Conclusion: Baseline clinical characteristics differed between genders in both patients with AS and nr-axSpA. Women were older at disease onset, experienced longer symptom duration, had more peripheral joint symptoms, and had a lower prevalence of HLA-B27 than men.

Disclosure: M. Magrey, Novartis, 5, Eli Lilly, 5, AbbVie, 2, UCB, 2, Amgen, 2, Pfizer, 5, Janssen, 5; **K. de Vlam**, Eli Lilly and Company, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5, 8, Celgene, 2, 5, 8, Pfizer, 2, 5, 8; **R. Bolce**, Eli Lilly and Company, 1, 3; **S. Liu-Leage**, Eli Lilly and Company, 3, 4; **D. Zhu**, Eli Lilly and Company, 1, 2; **T. Hunter**, Eli Lilly and Company, 1, 3; **D. Sandoval**, Eli Lilly and Company, 3; **I. van der Horst-Bruinsma**, AbbVie, 1, 2, 3, UCB Pharma, 2, 5, 8, Merck Sharp & Dohme, 1, 2, 3, Novartis, 1, Pfizer, 1, 2, Bristol-Myers Squibb, 1.

Abstract Number: 0877

Improvements in Global Functioning and Health-related Quality of Life and Their Association with Disease Activity and Functional Improvement in Patients with Active Ankylosing Spondylitis Treated with Upadacitinib

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

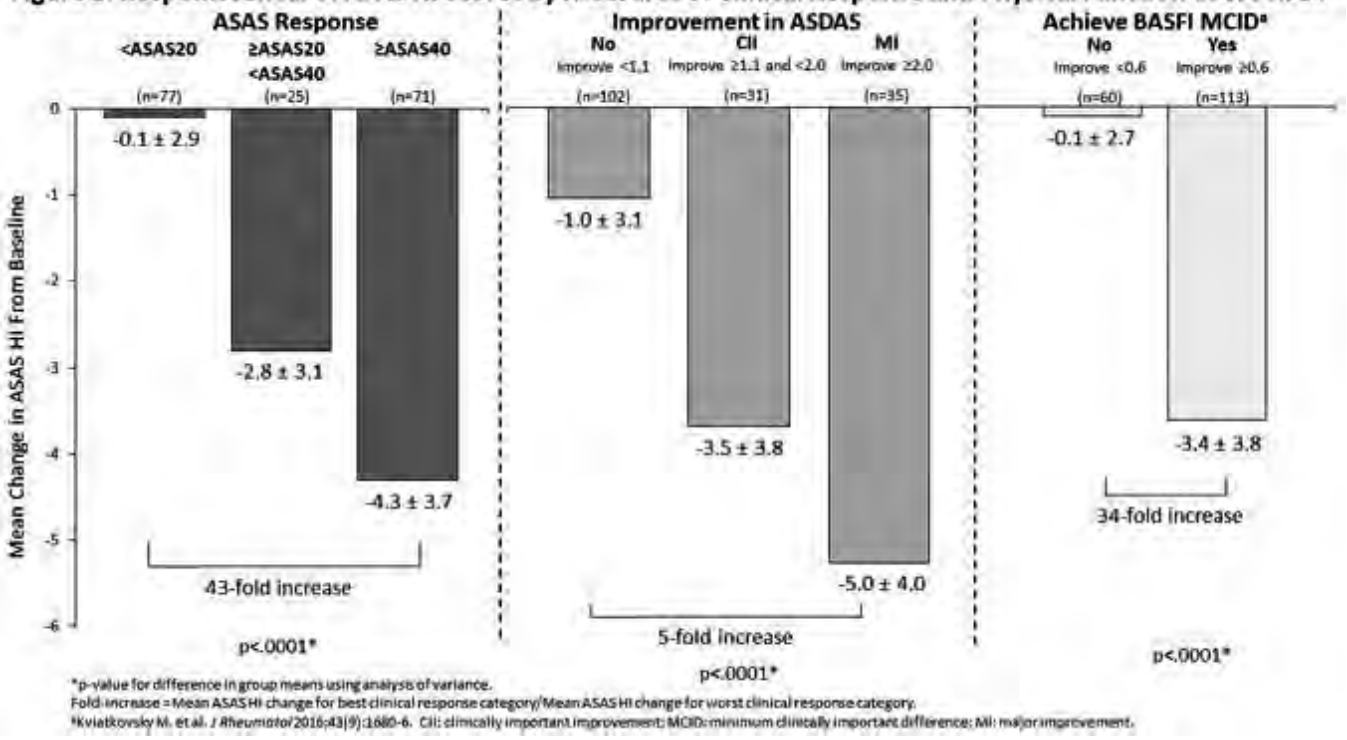
Background/Purpose: Upadacitinib (UPA) has been shown to be effective and well tolerated in patients with active ankylosing spondylitis (AS) [1]. However, improvements in global functioning and health-related quality of life (HRQoL) in patients treated with UPA, and their relationship with established clinical response measures have not been fully characterized. We evaluate the effect of UPA on the Assessment of SpondyloArthritis international Society Health Index (ASAS HI) and Ankylosing Spondylitis Quality of Life (ASQoL) questionnaire and to quantify incremental improvements in ASAS HI and ASQoL response in patients achieving established AS disease activity and physical function improvements at week 14.

Table. ASAS HI and ASQoL Outcomes at Week 14

Outcome	ASAS HI		ASQoL	
	UPA (n=93)	PBO (n=94)	UPA (n=93)	PBO (n=94)
LSM change from baseline	-2.8[a]	-1.4	-4.2[a]	-2.7
Achievement of MCID (≥3-point improvement)[c], n/N (%)	38/85 (44.7)[b]	24/89 (27.0)	51/83 (61.4)[b]	37/86 (43.0)
ASAS HI good health state (ASAS HI score ≤5)[d], n/N (%)	33/74 (44.6)[b]	15/71 (21.1)	NA	NA

[a]p<0.05 vs PBO based on mixed-effects model for repeated measures
[b]p<0.05 vs PBO based on Cochran-Mantel-Haenszel test with non-responder imputation
[c]In patients with ASAS HI/ASQoL score ≥3 at baseline
[d]In patients with ASAS HI >5 at baseline
LSM, least squares mean; NA, not applicable

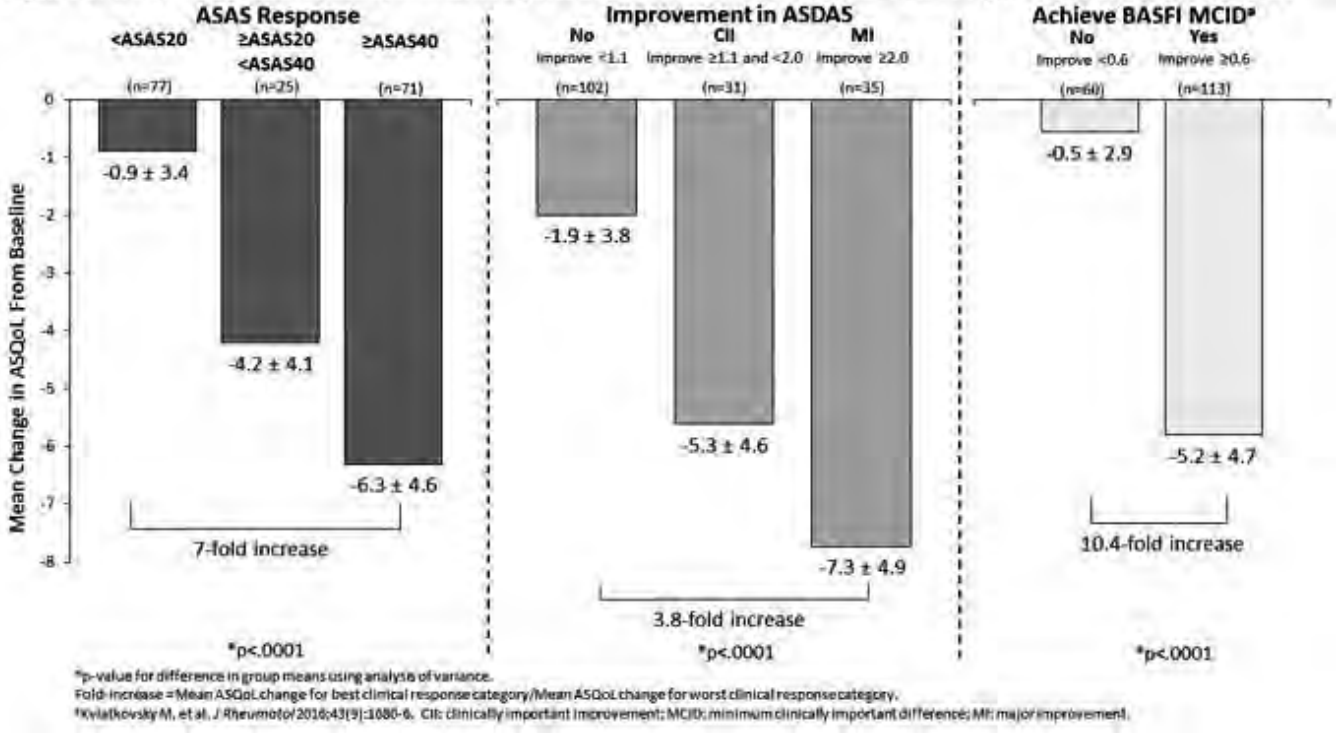
Figure 1. Responsiveness of ASAS HI Scores by Measures of Clinical Response and Physical Function at Week 14



*p-value for difference in group means using analysis of variance.
Fold-increase = Mean ASAS HI change for best clinical response category/Mean ASAS HI change for worst clinical response category.
[a]Kviatkovsky M. et al. *J Rheumatol* 2016;43(9):1680-6. CII: clinically important improvement; MCID: minimum clinically important difference; MI: major improvement.

Methods: This was a post-hoc analysis of the SELECT-AXIS 1 trial [1]. Patients were randomized to either UPA 15 mg once daily or placebo (PBO) for 14 weeks. Mean change in ASAS HI and ASQoL from baseline (BL) to weeks 4, 8 and 14 for UPA and PBO were calculated and UPA vs PBO responses were compared. Achievement of changes in ASAS HI and ASQoL above the minimum clinically important difference (MCID ≥3-point improvement for both measures) and ASAS HI 'good health state' (ASAS HI score ≤5) at week 14 were determined. Changes from BL in ASAS HI and ASQoL were assessed within the combined UPA and PBO group reaching established improvement thresholds across AS clinical response measures at week 14, including ASAS response criteria, ASDAS improvement criteria, and BASFI MCID. Mean ASAS HI and ASQoL changes across groups within each clinical measure and magnitude of ASAS HI and ASQoL change between responders and non-responders were compared.

Figure 2. Responsiveness of ASQoL Scores by Measures of Clinical Response and Physical Function at Week 14



*p-value for difference in group means using analysis of variance.
Fold-increase = Mean ASQoL change for best clinical response category/Mean ASQoL change for worst clinical response category.
[a]Kvien TK, et al. J Rheumatol 2016;43(9):1680-6. CII: clinically important improvement; MCID: minimum clinically important difference; MI: major improvement.

Results: UPA treatment resulted in significant improvement from BL in ASAS HI and ASQoL at week 14 with more patients achieving a MCID and ASAS HI good health state vs PBO (Table). Significant improvements were observed earlier for ASAS HI than for ASQoL, starting at Week 4. At week 14, achievement of clinical improvement thresholds was associated with increasing improvements in both ASAS HI and ASQoL scores (Figures 1 and 2). The magnitude of improvement between the best and worst clinical response categories was greater for ASAS HI than ASQoL: 43-fold vs 7-fold for ASAS response, 5-fold vs 3.8-fold for ASDAS improvement, and 34-fold vs 10.4-fold for BASFI MCID achievement.

Conclusion: UPA treatment in patients with active AS resulted in significant and clinically meaningful improvements compared with PBO in global functioning and HRQoL as measured by ASAS HI and ASQoL, with both measures showing discriminatory ability. Earlier UPA vs PBO response and greater magnitude of change across known clinical response groups suggests that ASAS HI may demonstrate greater responsiveness and ability to capture improvements in AS disease activity and physical function achieved with treatment and translate them to a patient-centric measure.

References:

[1] van der Heijde D, et al. *Lancet* 2019;394:2108–17.

Original abs: *Ann Rheum Dis.* 2020; 79(S1):416.

Disclosure: U. Kiltz, AbbVie, 1, 2, Amgen, 1, 2, Biocad, 1, 2, Biogen, 1, 2, Chugai, 1, 2, Eli Lilly, 1, 2, Grünenthal, 1, 2, Janssen, 1, 2, MSD, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, Roche, 1, 2, UCB, 1, 2; **J. Sieper**, AbbVie, 5, Novartis, 5, 8, Lilly, 8, Janssen, 5, Merck, 5, 8; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **P. Zueger**, AbbVie Inc., 1, 3; **I. Song**, AbbVie, 1, 3; **N. Chen**, AbbVie, 1, 2; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5.

Abstract Number: 0878

Absolute Lymphocyte Count Is Negatively Correlated with Atherosclerotic Cardiovascular Disease Risk Score and Red Cell Distribution Width in Psoriatic Arthritis and Increases with TNF-Inhibitor Therapy

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Absolute lymphocyte count (ALC) is a parameter that represents the number of lymphocytes (B, T, and NK cells) in the blood, and lymphopenia often accompanies rheumatologic disease. Lymphopenia, even in those without rheumatologic disease, has been associated with worse survival due to cardiovascular disease (CVD), especially when accompanied by other pro-inflammatory surrogates, including increased red cell distribution width (RDW). The connection between rheumatic disease and increased risk of atherosclerotic disease has been established, but there is lack of data on ALC levels in patients with psoriatic arthritis. We sought to test the hypothesis that alterations in immunohematologic abnormalities in the setting of psoriatic arthritis may in part reflect traditional cardiovascular risk factors, but are also driven by inflammation.

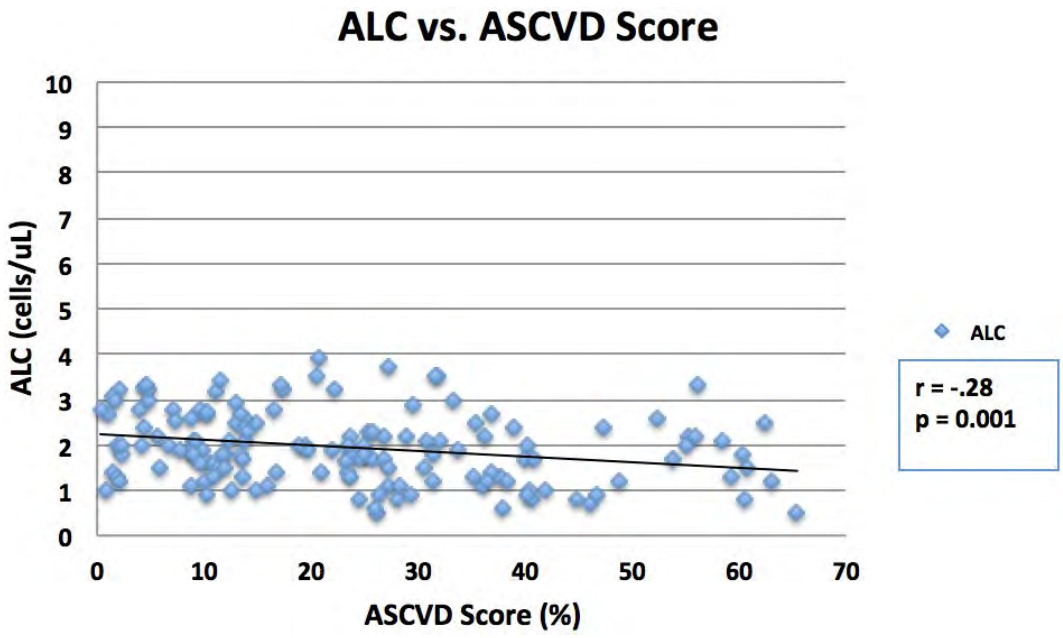

Figure 1 There was a negative, statistically significant, correlation between ALC and ASCVD risk score. As ASCVD score increased, ALC value decreased.

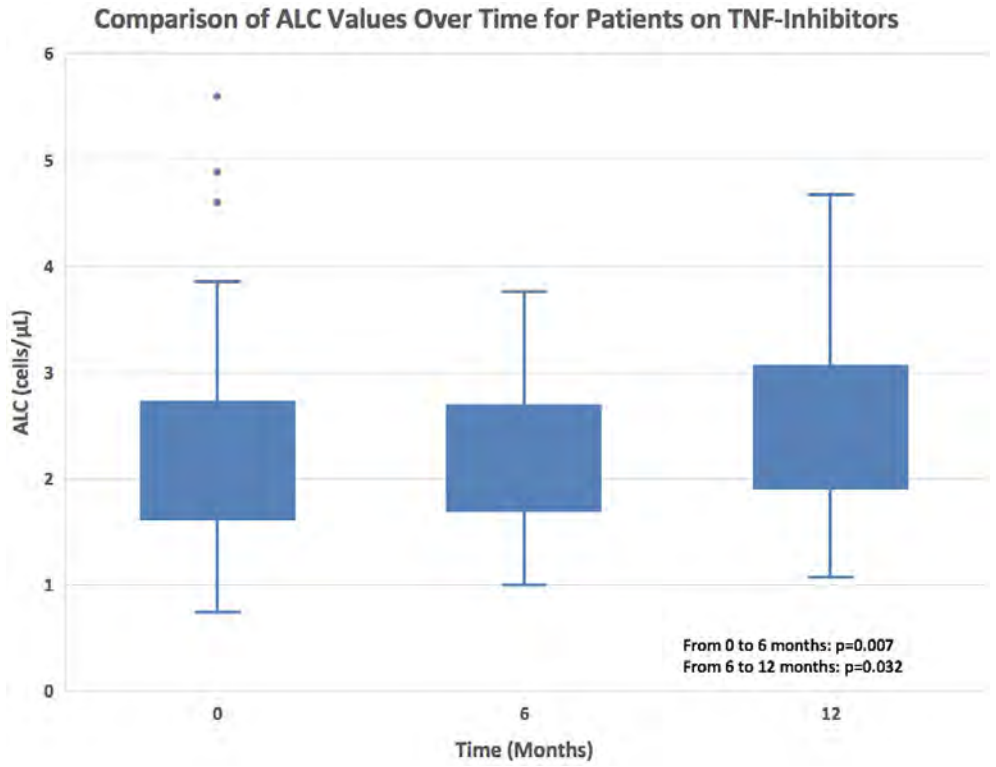

Figure 2. Patients on TNF-inhibitor therapy exhibited a statistically significant increase in ALC over the course of 12 months.

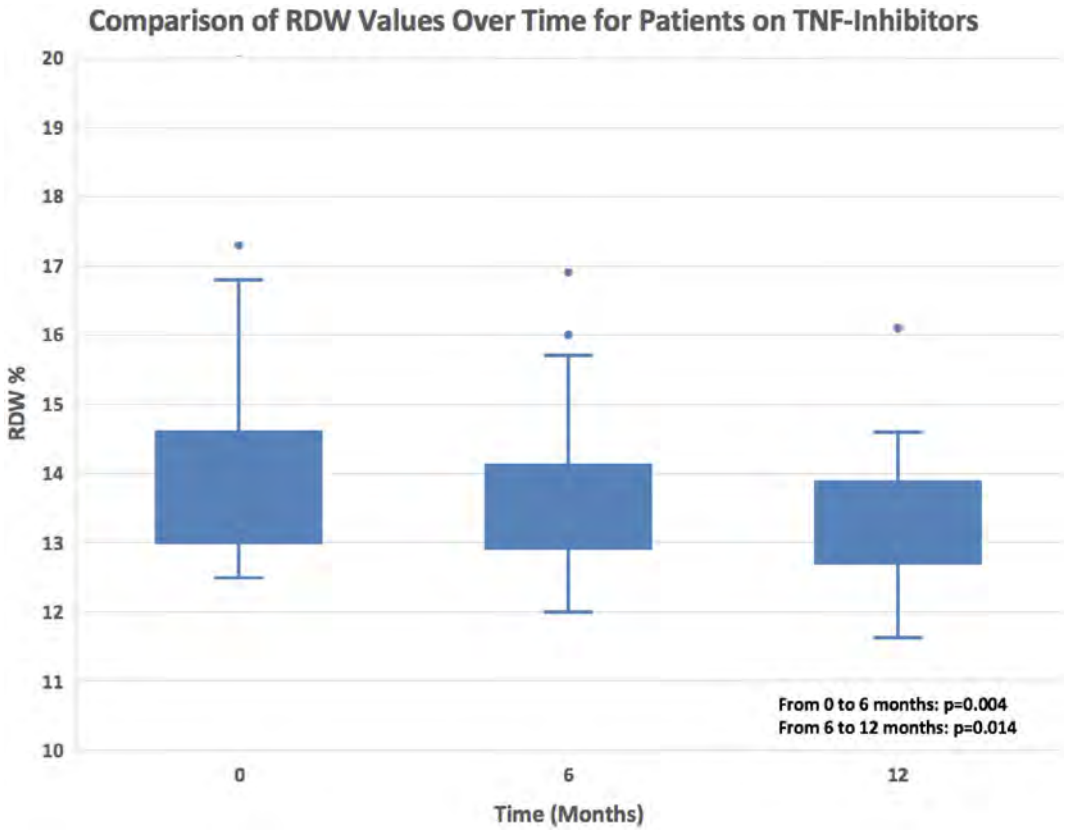

Figure 3. Patients on TNF-inhibitor therapy exhibited a statistically significant decline in RDW over the course of 12 months.

Methods: We performed a retrospective chart review study examining the relationship between ALC, RDW, and traditional atherosclerotic cardiovascular disease (ASCVD) risk in a cohort (n=170) of patients with psoriatic arthritis at the Louis Stokes Cleveland VA Medical Center. All patients had an ICD-10 diagnosis of psoriatic arthritis and either a rheumatologist confirmed diagnosis of psoriatic arthritis or met CASPAR criteria. ASCVD risk was quantified using the pooled cohort equation risk model (based on age, gender, race, presence of hypertension or diabetes, lipid profile, and smoking status). We examined patient treatment history and recorded laboratory values in relation to treatment to understand the effect of immunomodulation on these parameters. The Wilcoxon signed-rank test was used for statistical analysis.

Results: ALC was negatively correlated with ASCVD score (r=-0.28, p=0.001) (Figure 1). Positive correlations were observed between ASCVD score and RDW (r= 0.339, p=0.01), ASCVD score and ESR (r=0.20, p=.02), and negative correlations were observed between ASCVD score and albumin (r=-.20, p=.01), and ASCVD score and hemoglobin (r=-.22, p=.009). When evaluating parameters over the course of therapy, those who were started on TNF-inhibitor therapy (n=60) had an increase in ALC between time 0 and 6 months (p = 0.007), and this was maintained at twelve months (p = 0.032) (Figure 2). Patients on TNF-inhibitor therapy also experienced a decline in RDW at 6 months (p = 0.004) and at 12 months (p = 0.014) (Figure 3).

Conclusion: Our data shows that abnormal lymphocyte levels and RDW are associated with traditional cardiovascular risk factors but also tend to revert with anti-TNF therapy. Thus, correlates of immunohematologic dysfunction relevant to CVD risk may be dynamic and modified by reducing inflammation, at least in psoriatic arthritis. Future studies to define whether trajectories of ALC or RDW can improve cardiovascular disease risk stratification both in psoriatic arthritis and in the general population are warranted.

Disclosure: A. Gupta, None; **S. Damjanovska**, None; **A. Lange**, None; **B. Wilson**, None; **T. Bej**, None; **M. Mattar**, None; **D. Zidar**, None; **D. Anthony**, None.

Abstract Number: 0879

Application of Treat-to-Target in Axial Spondyloarthritis in Daily Practice

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Treat-to-target (T2T) management strategies in inflammatory rheumatic diseases aim to prevent damage and improve overall functioning and health by treating patients towards a predefined target reflecting inactive disease/low disease activity (ID/LDA). An international task force recommended to apply this strategy also in patients with SpA (1). T2T requires regular monitoring of disease activity. Currently, it is unknown what the uptake of these recommendations is in clinical practice. The objective of this study is to evaluate the extent to which T2T is applied in daily practice in patients with axial SpA (axSpA).

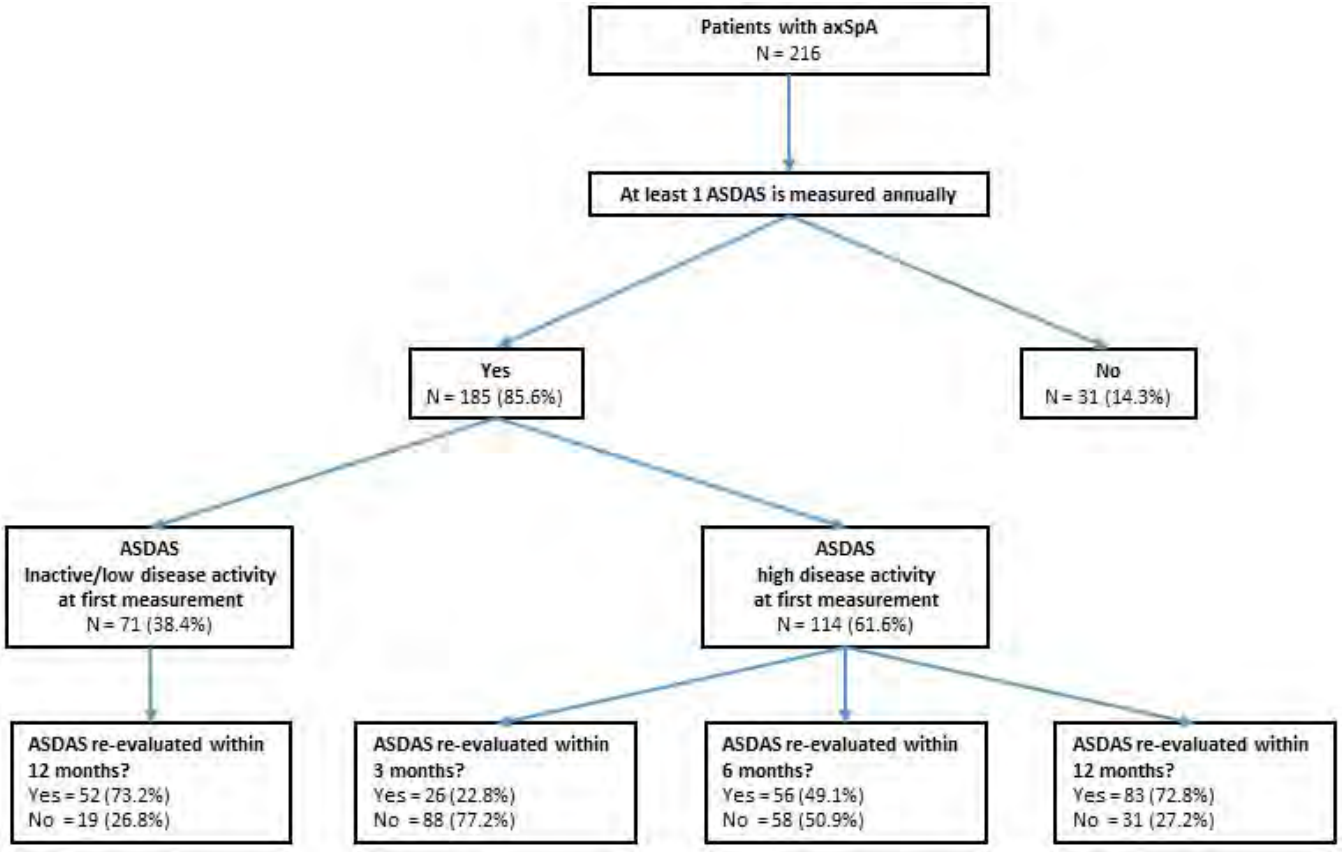

Figure 1 Flowchart of patients with axSpA and measurements of ASDAS within the study period in SpA-Net

Methods: Data were used from three rheumatology centers participating in a quality registry for SpA in the Netherlands (SpA-Net) in which patient and physician relevant outcomes are collected electronically in daily practice (2). Patients were selected if diagnosed with axSpA before July 2017, enrolled in SpA-Net before 2018 and had ≥1 patient or physician reported outcome measure available throughout 2018 (January to December). The extent to which the T2T recommendations were followed was evaluated through four endpoints: First, in which proportion of patients disease activity was measured with ≥1 Ankylosing Spondylitis Disease Activity Score (ASDAS) annually. Second, in which proportion of patients with ≥1 measurement the target of ASDAS< 2.1 was achieved. Third, in which proportion of patients with high disease activity (=ASDAS≥2.1) the ASDAS was re-evaluated within 3, 6 or 12 months, and in patients with ID/LDA (=ASDAS< 2.1) within 6 or 12 months. Fourth, in which proportion of patients pharmacological treatment for SpA was adapted within 6 weeks after obtaining ASDAS≥2.1. The clinical characteristics of patients with high disease activity in whom treatment was adapted or not adapted were compared.

Results: In 185 out of 216 patients (86%) disease activity was measured with ≥1 annual ASDAS and in 71 out of these 185 (38%) patients the target was achieved at the first measurement. In patients with high disease activity, the score was re-evaluated within 3, 6 or 12 months in 26, 56 and 83 out of 114 patients (23%, 49% and 73%, respectively, Figure 1). The proportion of patients in whom disease activity was re-evaluated within 12 months was the same in patients with ID/LDA and with high disease activity (73% and 73%, respectively). In 24 out of 114 (21%) patients with high disease activity at first measurement, treatment was adapted (Figure 2). In this group, the ASDAS and physician global assessment were significantly higher compared to patients in whom treatment was not adapted (3.3 (SD 0.7) versus 3.0 (SD 0.6), p-value< 0.05 and 3.4 (SD 2.1) versus 1.6 (SD 1.1), p-value< 0.01, respectively, Table 1).

Conclusion: Most patients with axSpA had ≥1 annual ASDAS recorded, but the target of ID/LDA was achieved in only one third of the patients at the first measurement. Subsequently, the scores do not seem to be used explicitly, as in

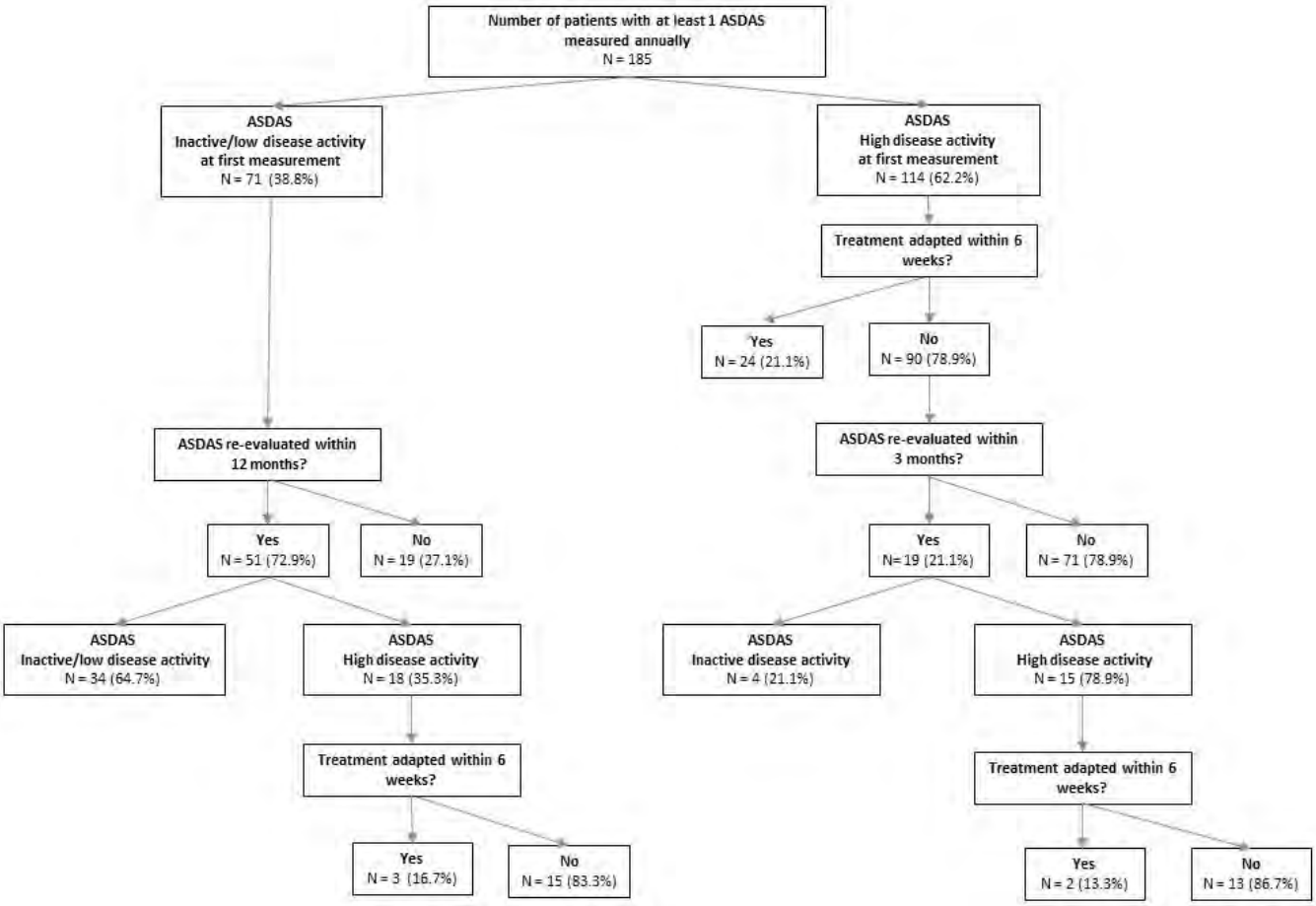

Figure 2. Flowchart of patients, re-evaluation and treatment adaptations based on ASDAS scores

patients with high disease activity re-evaluation of disease activity within recommended time periods and treatment adaptions occur only in a small proportion of patients. We conclude that T2T is applied only to a limited extent in clinical practice in patients with axSpA.

	ASDAS ≥2.1		
Patient and disease characteristics	**No adapted treatment** n = 88	**Adapted treatment** n = 26	**p-value**
Female, n (%)	41 (46.6%)	12 (46.2%)	0.97
Age, years	51.7 (13.5)	50.5 (11.9)	0.67
Symptom duration , years	24.3 (13.9)	23.8 (12.8)	0.85
Disease duration, years	16.7 (13.2)	15.4 (11.4)	0.83
Current use of NSAIDs, n (%)	55 (61.1%)	16 (61.5%)	0.93
Current use of bDMARDs, n (%)	42 (47.7%)	18 (69.2%)	0.05
Sum of current and previous used bDMARDs (%)			0.12
None	38 (42.2%)	5 (19.2%)	
1	23 (25.6%)	10 (38.5%)	
2	12 (13.3%)	6 (23.1%)	
≥3	17 (18.9%)	5 (19.2%)	
Active peripheral arthritis (SJC66>=1)	4 (4.5%)	2 (6.7%)	0.94
Active psoriasis (BSA >=3%)	1 (2.3%)	0 (0.0%)	0.34
ASDAS (0-∞)	3.0 (0.6)	3.3 (0.7)	<0.05
BASDAI (0-10)	5.7 (1.6)	5.9 (1.6)	0.61
PGA (0-10)	5.6 (2.2)	6.3 (1.6)	0.14
CRP, mg/L (0-∞)	6.0 (8.0)	8.6 (9.6)	0.07
VAS pain (0-10)	5.6 (2.1)	6.4 (1.7)	0.26
PhGA (0-10)	1.6 (1.1)	3.4 (2.1)	<0.01
ASAS-HI (0-17)	7.8 (2.7)	7.0 (3.8)	0.46
HAQ-S (0-3)	1.0 (0.5)	1.1 (0.5)	0.36
BASFI (0-10)	4.9 (2.3)	5.0 (2.3)	0.90
EQ-5D (0-1)	0.70 (0.21)	0.74 (0.12)	0.94
SF36 MCS (0-100)	44.9 (12.5)	41.1 (10.4)	0.35
SF36 PCS (0-100)	35.1 (8.7)	35.0 (8.6)	0.84

Values are expressed as mean (SD), unless stated otherwise, Included number of patients might be lower due to missing outcome measures, Correlations are statistically significant at the 0.05 level (two-tailed).
ASDAS = Ankylosing Spondylitis Disease Activity Score, BASDAI = Bath Ankylosing Spondylitis Disease Activity Index, N = Number, NSAIDs = Non-Steroid Anti-Inflammatory Drugs, bDMARDs = biological Disease Modifying Antirheumatic drugs, SJC66 = Swollen Joint Count of 66 joints, BSA = Body Surface Area, PGA = Patient Global Assessment, CRP = C-Reactive Protein, VAS= Visual Analog Scale, PhGA = Physician Global Assessment, ASAS-HI = Assessment of SpondyloArthritis international Society Health Index, HAQ-S = Health Assessment Questionnaire for Spondyloarthritis, BASFI = Bath Ankylosing Spondylitis Functional Index, EQ-5D = EuroQol 5D, SF36 = Medical Outcomes Study 36-Question Short Form, MCS = Mental Component Score, PCS = Physical Component Score

Table 1 Characteristics of patients with high disease activity in whom treatment was adapted or not

Disclosure: E. Beckers, None; **A. Boonen**, AbbVie, 2, Galapagos, 5, Lilly, 5, Celgene, 2, UC, 5; **C. Webers**, None; **P. Ten Klooster**, None; **H. Vonkeman**, None; **M. Efde**, None; **A. van Tubergen**, The Netherlands Organisation for Health Research and Development, 2, Dutch Arthritis Society, 2, Abbvie, 2, Biogen, 2, Celgene, 2, Janssen-Cilag, 2, MSD, 2, Novartis, 2, Pfizer, 2, UCB, 2.

Abstract Number: 0880

Ixekizumab Improves Signs and Symptoms of Patients with Radiographic and Non-radiographic Axial Spondyloarthritis and Extra-articular Manifestation of Enthesitis Through 16 Weeks

Georg Schett[1], Filip Van den Bosch[2], Xenofon Baraliakos[3], David Sandoval[4], Vladimir Geneus[4], Rebecca Bolce[4], Soyi Liu-Leage[5], Andris Kronbergs[4] and Philip Mease[6], [1]Friedrich-Alexander-Universität Erlangen- Nuremberg, Erlangen, Germany, [2]Ghent University Hospital, Ghent, Belgium, [3]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Bochum, Germany, [4]Eli Lilly and Company, Indianapolis, [5]Eli Lilly and Company, Indianapolis, IN, [6]Seattle Rheumatology Associates, P.L.L.C., Seattle, WA

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Table 1. ASAS40, ASDAS-LDA and BASDAI50 responses in all patients, patients with remission of peripheral enthesitis (SPARCC=0) or patients with no remission of peripheral enthesitis (SPARCC>0) at Week 16

	COAST-V and W Integrated			COAST-X		
	Placebo (N=101)	IXE80Q4W (N=118)	IXE80Q2W (N=99)	Placebo (N=86)	IXE80Q4W (N=65)	IXE80Q2W (N=74)
All patients with non-missing SPARCC at Week 16						
ASAS40 Ns	95	105	91	83	65	71
n (%)	12 (12.6%)	35 (33.3%)	37 (40.7%)	17 (20.5%)	25 (38.5%)	27 (38.0%)
†p-value		<0.001	<0.001		0.018	0.020
ASDAS <2.1 Ns	95	105	91	83	65	71
n (%)	4 (4.2%)	28 (26.7%)	20 (22.0%)	11 (13.3%)	17 (26.2%)	19 (26.8%)
†p-value		<0.001	<0.001		0.058	0.042
BASDAI50 Ns	95	105	91	83	65	71
n (%)	10 (10.5%)	32 (30.5%)	27 (29.7%)	11 (13.3%)	20 (30.8%)	22 (31.0%)
†p-value		<0.001	<0.002		0.014	0.010
Patients with SPARCC=0 at Week 16						
ASAS40 Ns	35	37	34	32	23	26
n (%)	8 (22.9%)	18 (48.6%)	23 (67.6%)	10 (31.3%)	12 (52.2%)	15 (57.7%)
ASDAS <2.1 Ns	35	37	34	32	23	26
n (%)	3 (8.6%)	15 (40.5%)	15 (44.1%)	6 (18.8%)	8 (34.8%)	11 (42.3%)
BASDAI50 Ns	35	37	34	32	23	26
n (%)	7 (20.0%)	14 (37.8%)	17 (50.0%)	7 (21.9%)	11 (47.8%)	14 (53.8%)
Patients with SPARCC >0 at Week 16						
ASAS40 Ns	60	68	57	51	42	45
n (%)	4 (6.7%)	17 (25.0%)	14 (24.6%)	7 (13.7%)	13 (31.0%)	12 (26.7%)
ASDAS <2.1 Ns	60	68	57	51	42	45
n (%)	1 (1.7%)	13 (19.1%)	5 (8.8%)	5 (9.8%)	9 (21.4%)	8 (17.8%)
BASDAI50 Ns	60	68	57	51	42	45
n (%)	3 (5.0%)	18 (26.5%)	10 (17.5%)	4 (7.8%)	9 (21.4%)	8 (17.8%)

Abbreviations: ASAS40 = Assessment of Spondyloarthritis International Society 40; ASDAS = Ankylosing Spondylitis Disease Activity Score; BASDAI50 = Bath Ankylosing Spondylitis Disease Activity Index; IXE80Q4W = Ixekizumab 80 mg every 4 weeks; IXE80Q2W = Ixekizumab 80 mg every 2 weeks; N = number of patients in the analysis population; n = number of responders; Ns = number of patients in the enthesitis cohort defined at Week 16; SPARCC = Spondyloarthritis Research Consortium of Canada.

†p-values are from the Fisher's exact test, compared to placebo.

Table 1. ASAS40, ASDAS-LDA and BASDAI50 responses in all patients, patients with remission of peripheral enthesitis (SPARCC=0) or patients with no remission of peripheral enthesitis (SPARCC>0) at Week 16

Table 2. BASFI and SF-36 responses in all patients, patients with remission of peripheral enthesitis (SPARCC=0) or patients with no remission of peripheral enthesitis (SPARCC>0) at Week 16

	COAST-V and W Integrated			COAST-X		
	Placebo (N=101)	IXE80Q4W (N=118)	IXE80Q2W (N=99)	Placebo (N=86)	IXE80Q4W (N=65)	IXE80Q2W (N=74)
All patients at Week 16						
CFB BASFI Ns	95	105	91	83	65	71
LSMean (SE)	-0.90 (0.18)	-2.10 (0.20)	-2.38 (0.24)	-1.38 (0.24)	-2.24 (0.26)	-2.28 (0.28)
†P-value		<0.001	<0.001		0.049	0.017
CFB SF36-PCS Ns	95	105	91	83	65	71
LSMean (SE)	3.02 (0.62)	7.37 (0.74)	7.45 (0.82)	5.46 (0.83)	9.05 (1.03)	8.08 (0.96)
†P-value		<0.001	<0.001		0.013	0.068
Patients with SPARCC =0 at Week 16						
CFB BASFI Ns	35	37	34	32	23	26
LSMean (SE)	-1.48 (0.30)	-2.69 (0.34)	-3.35 (0.40)	-2.04 (0.39)	-2.83 (0.44)	-3.43 (0.46)
CFB SF36-PCS Ns	35	37	34	32	23	26
LSMean (SE)	5.24 (1.03)	7.83 (1.25)	11.0 (1.33)	8.09 (1.38)	13.1 (1.75)	10.9 (1.61)
Patients with SPARCC >0 at Week 16						
CFB BASFI Ns	60	68	57	51	42	45
LSMean (SE)	-0.56 (0.23)	-1.78 (0.25)	-1.81(0.31)	-0.95 (0.30)	-1.91 (0.32)	-1.60 (0.35)
CFB SF36-PCS Ns	60	68	57	51	42	45
LSMean (SE)	1.73 (0.79)	7.12 (0.93)	5.30 (1.03)	3.78 (1.07)	6.85 (1.28)	6.42 (1.22)

BASFI = Bath Ankylosing Spondylitis Functional Index; CFB = Change from baseline; IXE80Q4W = Ixekizumab 80 mg every 4 weeks; IXE80Q2W = Ixekizumab 80 mg every 2 weeks; LSMean = least squares mean; mBOCF=modified baseline observation carried forward; N = number of patients in the analysis population; Ns = number of patients in the enthesitis cohort defined at Week 16. SE = standard error; SF36-PCS = Short form – 36; SPARCC = Spondyloarthritis Research Consortium of Canada.

†P-values vs. placebo are based on an analysis of covariance model including baseline SPARCC, BASFI or SF36-PCS score, treatment, subgroup, and treatment-by-subgroup interaction.

Table 2. BASFI and SF-36 responses in all patients, patients with remission of peripheral enthesitis (SPARCC=0) or patients with no remission of peripheral enthesitis (SPARCC>0) at Week 16

Background/Purpose: Axial SpA (axSpA) is a chronic inflammatory disease affecting the spine and sacroiliac (SI) joints and has two subtypes that represent the spectrum of disease: radiographic axSpA (r-axSpA) and non-radiographic axSpA (nr-axSpA). The distinction between the two is defined by the presence or absence of radiographic changes at the SI joints. Both subtypes may have extra-articular manifestations such as peripheral enthesitis, increasing the disease burden and decreasing quality of life (QoL). Ixekizumab is a high-affinity monoclonal antibody that selectively targets IL-17A. It has shown efficacy in clinical trials for r- and nr-axSpA as well as psoriasis and PsA. This *post-hoc* analysis explores the efficacy of ixekizumab in improving enthesitis, overall disease activity and QoL in patients with r-axSpA, who are biologic DMARD-naïve (COAST-V) or previously exposed to TNF inhibitors (COAST-W), or patients with nr-axSpA (COAST-X).

Methods: Patients with enthesitis at baseline from three Phase 3, randomized, double-blind, placebo (PBO)-controlled studies [COAST-V (NCT02696785), COAST-W (NCT02696798), and COAST-X (NCT02757352)] examining the efficacy and safety of ixekizumab in patients with r-axSpA or nr-axSpA. Ixekizumab (80 mg) or PBO were given SC every 2 (Q2W) or 4 (Q4W) weeks during a double-blind 16-week treatment period, with a starting dose of 80 mg or 160 mg at Week 0. Here, we explore the efficacy of ixekizumab at week 16 in resolving peripheral enthesitis in patients as assessed by Spondyloarthritis Research Consortium of Canada (SPARCC). We also compare the % patients achieving Assessment of Spondyloarthritis International Society 40 (ASAS40), Ankylosing Spondylitis Disease Activity Score (ASDAS) < 2.1 and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI50), change from baseline (CFB) in BASFI and 36-Item Short Form Health Survey (SF36-PCS) in patients achieving and not achieving

SPARCC=0. Missing data were imputed using non-responder imputation for categorical data and modified baseline observation carried forward for continuous data.

Results: 543 Patients had enthesitis at baseline. In patients with r-axSpA, 48.6% and 67.6% achieved resolution of peripheral enthesitis (SPARCC=0) at week 16 in the IXE80Q4W and IXE80Q2W groups, respectively, compared to only 22.9% in the PBO group. For the patients with nr-axSpA, resolution of peripheral enthesitis at week 16 was observed in 52.2% and 57.7% in the IXE80Q4W and IXE80Q2W groups, respectively, while enthesitis resolved in 31.3% of PBO patients. The % of patients achieving ASDAS < 2.1 and BASDAI50 were also greater for the IXE80Q4W and IXE80Q2W groups vs PBO for both r-axSpA and nr-axSpA (Table 2). Patients with enthesitis resolution with ixekizumab showed improvements in BASFI and SF36-PCS compared to PBO for both r-axSpA and nr-axSpA (Table 3). Improvements were also seen in patients with SPARCC >0 at week 16.

Conclusion: Ixekizumab is effective in resolving enthesitis and improvements in overall disease activity and QoL in patients with r-axSpA and nr-axSpA.

Disclosure: G. Schett, None; **F. Van den Bosch**, AbbVie, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Gilead, 5, Merck, 5, 8; **X. Baraliakos**, AbbVie, 2, 5, 8, Novartis, 2, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Pfizer, 5, 8, UCB, 5, 8, BMS, 5, 8, Merck, 5, 8, Galapagos, 5; **D. Sandoval**, Eli Lilly and Company, 3; **V. Geneus**, Eli Lilly and Company, 3, 4; **R. Bolce**, Eli Lilly and Company, 1, 3; **S. Liu-Leage**, Eli Lilly and Company, 3, 4; **A. Kronbergs**, Eli Lilly and Company, 1, 3; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5.

Abstract Number: 0881

Reduction of Anterior Uveitis Flares in Patients with Axial Spondyloarthritis During Certolizumab Pegol Treatment: 96-Week Results from the C-VIEW Study

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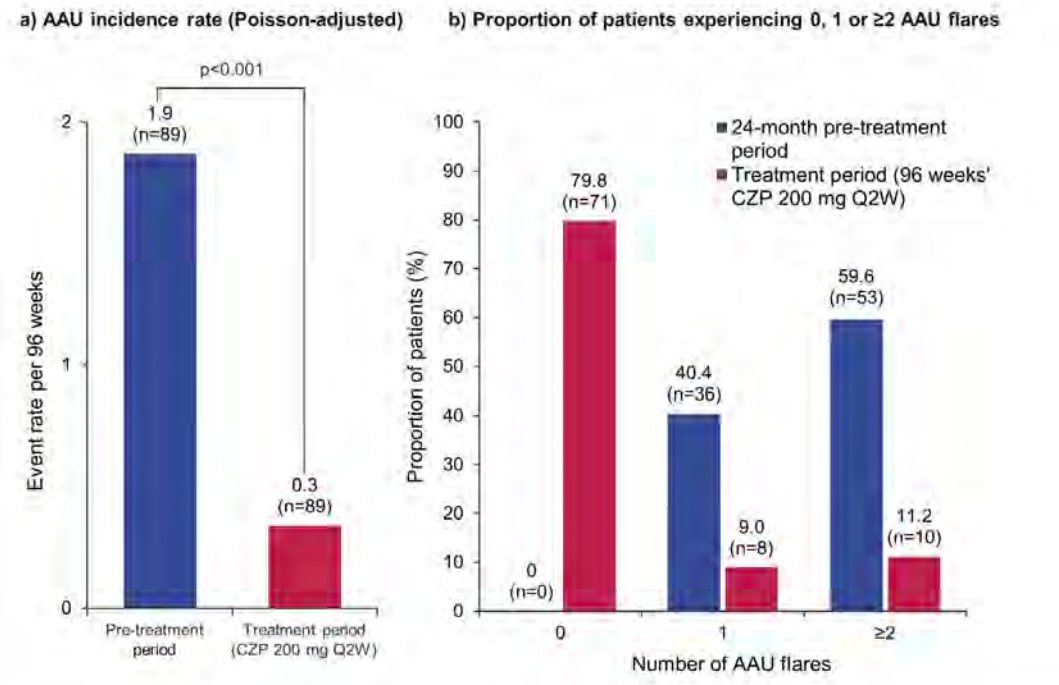
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Acute anterior uveitis (AAU) is the most common extra-articular manifestation in axial spondyloarthritis (axSpA), affecting up to 40% of patients and causing significant burden.[1] Previous studies have shown that tumor necrosis factor inhibitors (TNFi) can reduce the incidence of AAU flares in patients with radiographic axSpA (ankylosing spondylitis),[2-4] but few have focused on patients across the full axSpA spectrum. We report 2-year outcomes from the phase 4, open-label C-VIEW study (NCT03020992), which investigated the impact of certolizumab pegol (CZP) treatment on AAU in patients with active axSpA and a recent history of AAU.

Figure 1: Summary of AAU flares (observed data)



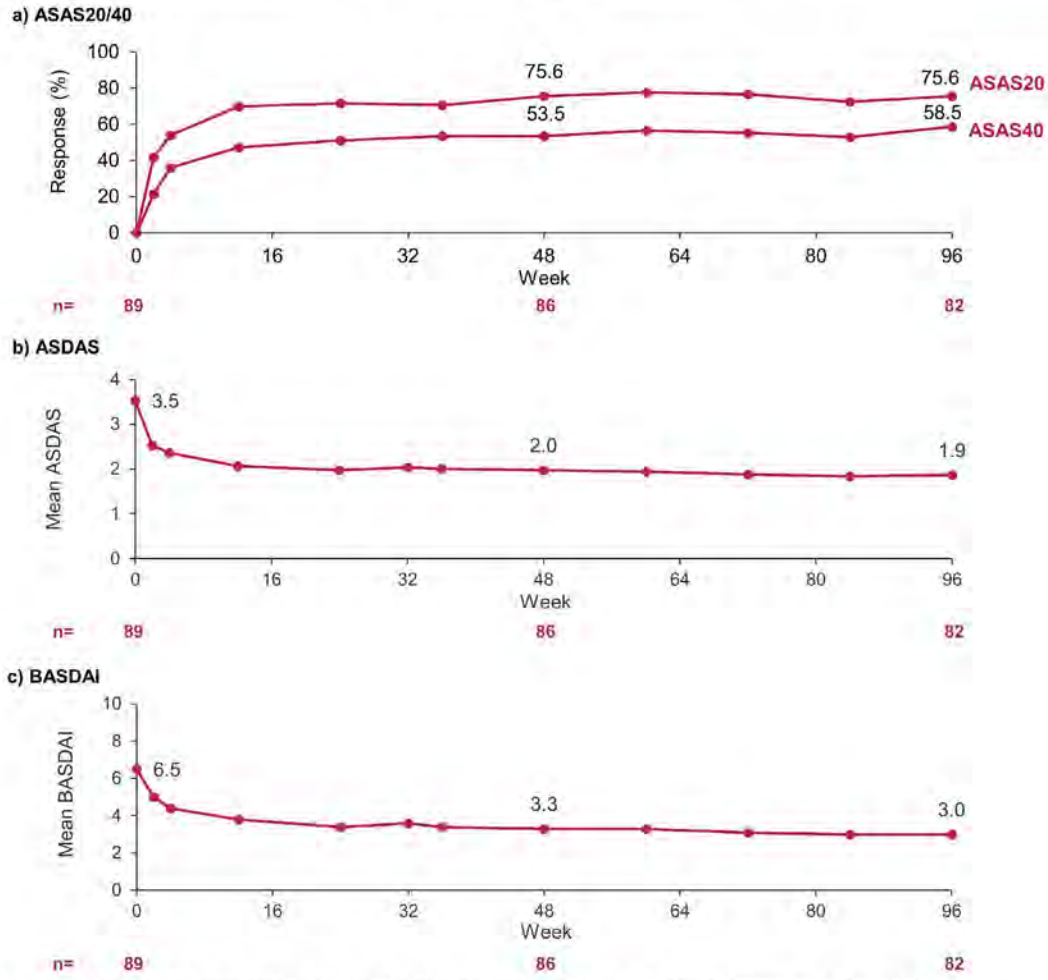
Treatment period: after start of study medication until Week 96 or discontinuation visit. Pre-treatment period: 24 months prior to treatment start. Flares on the same eye are combined and counted as one flare if the time interval between two subsequent flares is <3 months (90 days). Patients received CZP 400 mg at Weeks 0/2/4, then 200 mg Q2W through 96 weeks. a) Poisson regression analysis, with period (pre-/post-baseline) and axSpA disease duration as covariates and adjusting for the length of time in the pre- and post-baseline periods. AAU: acute anterior uveitis; CZP: certolizumab pegol; Q2W: every 2 weeks.

Methods: C-VIEW prospectively investigated patients with active axSpA who were HLA-B27 positive and had recurrent AAU, with a history of ≥1 AAU flare in the year prior to baseline (additional study criteria and study design are described elsewhere[5]). The primary efficacy variable was the incidence of AAU flares during 96 weeks of CZP treatment versus the 2-year pre-baseline period. AAU incidence was evaluated using Poisson regression adjusted for duration of time in each period, with period (pre- and post-baseline) and axSpA disease duration as covariates. Secondary efficacy variables were Assessment of SpondyloArthritis international Society 20%/40% (ASAS20/40) response rates, as well as mean Ankylosing Spondylitis Disease Activity Score (ASDAS) and mean Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) to Week 96.

Results: Of 115 enrolled patients, 89 initiated CZP treatment; 83 completed Week 96. The primary analysis revealed an 82% reduction in the incidence of AAU flares during CZP treatment compared with pre-baseline (**Figure 1**; rate ratio [95% CI]: 0.18 [0.12, 0.28], p< 0.001). The percentage of patients experiencing ≥1 and ≥2 AAU flares reduced from 100% and 59.6% pre-baseline to 20.2% and 11.2% during treatment. There were also improvements in axSpA disease activity (**Figure 2**): by Week 96, 75.6% and 58.5% of patients had achieved ASAS20 and ASAS40 responses, respectively. ASDAS and BASDAI also improved substantially over the 96-week treatment period. No new safety signal was identified, compared to previous reports.[5]

Conclusion: These data support the use of CZP for the treatment of patients with axSpA and a history of recurrent AAU. During 96 weeks' CZP treatment, there was a significant reduction of 82% in the AAU flare rate compared to pre-baseline. There were also substantial improvements in patients' axSpA disease activity.

Figure 2: Changes in axSpA disease activity to Week 96 (observed data)



Patients received CZP 400 mg at Weeks 0/2/4, then 200 mg Q2W through 96 weeks. ASAS20/40: Assessment of SpondyloArthritis international Society 20%/40% response; ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CZP: certolizumab pegol; Q2W: every 2 weeks.

References: 1. Martin TM. Curr Opin Rheumatol 2002;14:337–41; **2.** van der Heijde D. Rheumatology (Oxford) 2017;56:1498–1509; **3.** van Bentum RE. J Rheumatol 2019;46:153–9; **4.** van Denderen JC. J Rheumatol 2014;41:1843–8; **5.** van der Horst-Bruinsma I. RMD Open 2020;6:e001161.

Disclosure: I. van der Horst-Bruinsma, AbbVie, 1, 2, 3, UCB Pharma, 2, 5, 8, Merck Sharp & Dohme, 1, 2, 3, Novartis, 1, Pfizer, 1, 2, Bristol-Myers Squibb, 1; **R. van Bentum**, None; **F. Verbraak**, Bayer, 2, 5, 8, Novartis, 2, 5, 8, IDxDR, 2, 5, 8, UCB Pharma, 2, 5, 8; **T. Rath**, Abbvie, 5, 8, Bristol-Myers Squibb, 5, 8, Chugai, 5, 8, Eli Lilly, 5, 8, Merck Sharp & Dohme, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB Pharma, 5, 8; **J. Rosenbaum**, Gilead, 1, Eli Lilly, 1, Abbvie, 5, UCB Pharma, 5, Roche, 1, Santen, 1, Corvus, 1, Celldex, 1, Horizon, 1, Novartis, 1, Eyevensys, 5, Janssen, 5, UpToDate, 7; **B. Hoepken**, UCB Pharma, 1, 3; **O. Irvin-Sellers**, UCB Pharma, 1, 3; **T. Kumke**, UCB Pharma, 1, 3; **L. Bauer**, UCB Pharma, 1, 3; **M. Rudwaleit**, Bristol-Myers Squibb, 5, 8, Chugai Pharmaceutical Co., Ltd., 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Novartis, 5, 8, UCB Pharma, 5, 8, AbbVie, 5, 8, Pfizer, 5, 8, Celgene, 8, Roche, 5, 8, Merck Sharp & Dohme, 5, 8.

Abstract Number: 0882

Efficacy and Safety of Secukinumab in Patients with Spondyloarthritis and Enthesitis at the Achilles Tendon: 52-weeks Results from a Randomized, Placebo-controlled Phase 3b Trial

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Enthesitis is a key feature of all types of spondyloarthritis (SpA) that substantially contributes to the overall burden of disease. Inhibition of the key effector cytokines of enthesitis, IL-17, IL-23, and TNF, has proved effective in resolution of PsA and axial (ax)SpA.[1] Secukinumab (SEC) is a fully human monoclonal antibody that directly inhibits IL-17A and significantly reduces entheseal inflammation in patients (pts) with PsA.[2] The clinical efficacy and safety outcomes from the ACHILLES trial in a heterogeneous SpA population (PsA and axSpA pts) with enthesitis at the Achilles tendon treated with SEC are presented.

Methods: ACHILLES study included pts (≥18 years) with a diagnosis of active PsA (CASPAR criteria and ≥1 TJC and SJC) or axSpA (ASAS axSpA criteria and total BASDAI ≥4) and MRI-positive heel enthesitis (according to the investigator's judgement) refractory to standard treatment. Pts were randomized to receive s.c. SEC 150 mg, 300 mg or placebo (PBO) at baseline, Weeks (Wks) 1, 2, 3 and 4, followed by once every 4 wks. At Wk 24, pts on PBO were switched to SEC 150 or 300 mg. The primary endpoint was the proportion of pts achieving resolution of Achilles tendon enthesitis at the affected foot (assessed by the respective subcomponent of Leeds Enthesitis Index, LEI) with SEC vs PBO at Wk 24. Assessments at Wks 24 and 52 included LEI, heel pain (by NRS [0-10]), physician's and pt's heel enthesopathy activity and global assessment of disease activities (by VAS [0–100]), and quality of life (QoL, SF-36 v2). Analysis comparing treatments with respect to the primary efficacy variable used a logistic regression model and continuous variables were analyzed using an Analysis of covariance model. Missing values were handled using mixed-effects model repeated measures and last observation carry forward method.

Results: A total of 204 pts (128 PsA, 76 axSpA) were included (SEC, N=102; PBO, N=102; **Table 1**). A numerically higher percentage of SEC-treated pts, though not statistically significant vs PBO, reported resolution of Achilles tendon enthesitis at the affected foot (42.2% vs 31.4%) and in LEI (33.3% vs 23.5%) at Wk 24 (**Table 2**); statistically significant LEI improvement was achieved in PsA pts treated with SEC vs PBO (35.9% vs 18.8%, p=0.025). Pts with a BMI < 30 kg/m^2 improved considerably with SEC vs PBO (49.2% vs 24.6%). Heel pain significantly improved in SEC-treated pts vs PBO (**Table 2**). Significant improvements in physician and pt reported heel enthesopathy activity along with physician and pt global assessment of disease activity were observed in SEC-treated pts vs PBO. SEC

Variables Mean (SD) unless otherwise specified	SEC 150 or 300 mg s.c. N=102	Placebo N=102
Age (years)	47.8 (11.3)	47.7 (11.0)
Male, n (%)	44 (43.1)	47 (46.1)
BMI (kg/m^2), n (%)	29.0 (6.3)	29.7 (6.3)
BMI <30 kg/m^2	61 (59.8)	61 (59.8)
BMI ≥30 kg/m^2	41 (40.2)	41 (40.2)
Time since diagnosis of (months)		
PsA	52.1 (58.6)	75.8 (92.1)
axSpA	49.7 (66.7)	56.2 (74.0)
Time since diagnosis of Enthesitis (months)		
PsA	33.9 (51.8)	33.7 (62.2)
axSpA	39.3 (73.0)	28.9 (51.9)
TNF-naïve, n (%)	92 (90.2)	93 (91.2)
Number of LEI counts present	2.6 (1.6)	2.5 (1.6)
TJC, PsA pts (78 joints)	16.2 (15.9)	13.5 (13.7)
SJC, PsA pts (76 joints)	7.8 (9.4)	5.8 (6.4)
BASDAI, axSpA pts	7.1 (1.1)	7.1 (1.2)
NSAID use at randomization, n (%)	79 (77.5)	72 (70.6)
DMARD use at randomization, n (%)	41 (40.2)	25 (24.5)
Oral corticosteroid use at randomization, n (%)	14 (13.7)	17 (16.7)

N, total number of patients in a group.
BASDAI, Bath ankylosing spondylitis disease activity index; BMI, body mass index; LEI, Leeds Enthesitis Index; SEC, secukinumab; SJC, swollen joint count score; TJC, total joint count score; TNF, tumor necrosis factor

Table 1. Demographics and Baseline Characteristics

provided sustained improvements in all efficacy endpoints through Wk 52. The safety profile of SEC was consistent with previous studies.

Conclusion: Although SEC was not significantly superior to PBO in the resolution of Achilles tendon enthesitis as assessed by the LEI subcomponent at the affected foot, it significantly improved the burden of heel enthesitis, global disease activity, and QoL in pts with active SpA refractory to standard treatment.

References:

1. Schett G, et al. *Nat Rev Rheumatol*. 2017;13:731–741.
2. Coates LC, et al. *Arthritis Res Ther*. 2019;21:266.

Efficacy Endpoint	Week 24 (Imputed)			Week 52 (Observed)	
	SEC 150 or 300 mg	PBO	P value vs PBO	SEC 150 or 300 mg	PBO → SEC
Resolution of Enthesitis					
Patients, N	102	102	-	84	79
Achilles tendon enthesitis (study foot), n (%)	43 (42.2)	32 (31.4)	0.136	59 (57.8)	47 (46.1)
LEI, n (%)	34 (33.3)	24 (23.5)	0.148	49 (48.0)	35 (34.3)
Disease Activity: Heel Enthesitis, Mean change ± SD					
Patients, N	101	100	-	84	78
Heel pain (0-10 NRS)	−2.7 ± 3.0	−1.9 ± 2.8	0.027	−3.6 ± 3.1	−3.3 ± 2.8
Patients, N	101	100	-	84	78
Physician's Heel enthesopathy (0-100 VAS)	−35.8 ± 26.3	−24.9 ± 27.2	0.004	−49.0 ± 24.1	−44.0 ± 24.6
Patients, N	101	99	-	84	76
Patient's Heel enthesopathy (0-100 VAS)	−30.0 ± 30.5	−20.6 ± 31.0	0.049	−38.9 ± 30.9	−35.9 ± 30.0
Disease Activity: Global, Mean change ± SD					
Patients, N	101	100	-	84	78
Physician's global assessment of disease activity (0-100 VAS)	−32.4 ± 27.0	−17.3 ± 26.2	<0.001	−45.4 ± 24.7	−37.8 ± 26.6
Patients, N	98	95	-	82	72
Patient's global assessment of disease activity (0-100 VAS)	−25.6 ± 30.3	−14.7 ± 29.6	0.011	−32.9 ± 32.0	−28.8 ± 30.9
Patients, N	101	100	-	84	78
SF-36 v2	8.5 ± 9.4	4.7 ± 8.9	0.009	8.9 ± 9.8	7.9 ± 7.5

N, total number of patients in a group. Imputation at Week 24 for Resolution of Enthesitis: A patient with a missing assessment will be considered as a responder if he/she has met the response criterion at the time of last assessment. Imputation at Week 24 for Heel pain based on mixed-effect model repeated measures. Imputation at Week 24 for all other questionnaires based on last observation carried forward. Data presented as observed at Week 52 for all outcome parameters.
LEI, Leeds Enthesitis Index; NRS, numeric rating scale; PBO, placebo; SEC, secukinumab; SF-36 v2, Short Form-36 version 2; VAS, visual analog scale

Table 2. Clinical Efficacy Endpoints up to Week 52

Disclosure: F. Behrens, AbbVie, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Chugai, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, UCB, 5, 8, BMS, 5, 8, Celgene, 5, 8, MSD, 5, 8, Biotest, 5, 8, Sanofi, 5, 8, Genzyme, 5, 8, Lilly, 5, 8, Boehringer, 5, 8, Galapagos, 5, 8; **P. Sewerin**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Chugai, 2, 5, 8, Janssen-Cilag, 2, 8, Lilly, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8, Biogen, 5, 8, BMS, 5, 8, Hexal, 5, 8, Roche, 5, 8, Sanofi-Genzyme, 5, 8, Swedish Orphan Biovitrum, 5, 8; **E. De Miguel**, AbbVie, 2, 5, 8, BMS, 8, MSD, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 8, UCB, 8; **Y. Patel**, None; **A. Batalov**, AbbVie, 5, Amgen, 5, MSD, 5, Myland, 5, Novartis, 5, Pfizer, 5, Roche, 5, Sandoz, 5, UCB, 5; **E. Dokoupilova**, Samsung Bioepis, 2; **C. Kleinmond**, Novartis, 5; **E. Pournara**, Novartis, 1, 3; **A. Shekhawat**, Novartis, 3; **C. Jentzsch**, Novartis, 3; **A. Wiedon**, Novartis, 3; **X. Baraliakos**, AbbVie, 2, 5, Celgene, 2, 5, Galapagos, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 2, 5, Chugai, 2, 5, MSD, 2, 5, Sandoz, 2, 5, Hexal, 2, 5.

Abstract Number: 0883

Network Meta-Analysis of Long-Term Efficacy (ASAS40) of Biologic Disease-Modifying Anti-Rheumatic Drugs (bDMARDs) in bDMARD-Naïve Patients with Non-Radiographic Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Biologic disease-modifying anti-rheumatic drugs (bDMARDs) have demonstrated large clinical improvements in patients with non-radiographic axial spondyloarthritis (nr-axSpA), with patients naïve to bDMARDs experiencing substantial benefits; additional treatments are also becoming available. The aim of this network meta-analysis (NMA) was to compare efficacy of various bDMARDs in bDMARD-naïve adult patients with nr-axSpA.

Methods: A systematic literature review (SLR) identified randomized controlled trials (RCTs) published on bDMARDs in adult patients with axSpA who failed at least one non-steroidal anti-inflammatory drug. RAPID-axSpA (NCT01087762) and C-axSpAnd (NCT02552212) clinical study reports informed clinical efficacy of certolizumab pegol (CZP). After evaluation of the evidence, trials assessing the efficacy of bDMARDs in initially bDMARD-naïve nr-axSpA populations/subpopulations were analyzed. Fixed-effects Bayesian NMAs were conducted to compare treatments of interest; fixed-effects models were employed due to limited data. At 12–16 and 52 weeks, the Assessment of SpondyloArthritis international Society 40% response (ASAS40) was evaluated with odds ratios (ORs) and 95% credible intervals (CrIs).

Results: The SLR identified 10 trials evaluating nr-axSpA patients, of which seven were considered comparable for the NMA. Trials primarily evaluated bDMARD-naïve patients, while others reported data for bDMARD-naïve subgroups. Identified bDMARDs included adalimumab (ADA), CZP, etanercept (ETN), golimumab (GOL), ixekizumab (IXE), and secukinumab (SEC), encompassing tumor necrosis factor inhibitors (TNFi) and anti-interleukin (anti-IL) agents. From these trials, RAPID-axSpA (CZP), ABILITY-1 (ADA), EMBARK (ETN), and GO-AHEAD (GOL) reported

Table: NMA results for CZP vs other bDMARDs in bDMARD-naïve Patients

Comparison	ASAS40 OR (95% CrI)	
	12–16 weeks	52 weeks
CZP pooled vs ADA 40 mg	2.14 [0.87, 5.18]	NA
CZP pooled vs ETN 50 mg	2.75 [1.17, 6.37]	NA
CZP pooled vs GOL 50 mg	1.60 [0.71, 3.55]	NA
CZP pooled vs SEC 150 mg	4.07 [2.13, 7.95]	2.94 [1.45, 5.92]
CZP pooled vs IXE 80 mg Q2W	2.45 [1.06, 5.54]	2.35 [0.96, 5.75]
CZP pooled vs IXE 80 mg Q4W	3.01 [1.30, 6.83]	2.50 [1.01, 6.09]

CZP pooled includes both 200 mg Q2W and 400 mg Q4W. SEC 150 mg includes regimens with and without loading dose. ADA: adalimumab; ASAS40: Assessment of SpondyloArthritis international Society 40% response; bDMARD: biologic disease-modifying anti-rheumatic drug; CrI: credible interval; CZP: certolizumab pegol; ETN: etanercept; GOL: golimumab; IXE: ixekizumab; NA: not applicable; OR: odds ratio; Q2W: every two weeks; Q4W: every four weeks; SEC: secukinumab

data only at 12–16 weeks; C-axSpAnd (CZP), PREVENT (SEC), and COAST-X (IXE) reported data at both 12–16 and 52 weeks. At 12–16 weeks (**Table**), CZP demonstrated the greatest odds of ASAS40 compared with SEC (OR [95% CrI]: 4.07 [2.13, 7.95]), with significantly greater odds of response vs ETN or IXE every two weeks (Q2W), and IXE every four weeks (Q4W). Treatment advantage for CZP vs ADA and GOL in ASAS40, while numerically greater, did not reach statistical significance. At 52 weeks (**Table**), CZP demonstrated significantly greater odds of ASAS40 response compared to SEC (2.94 [1.45, 5.92]) and IXE Q4W (2.50 [1.01, 6.09]); advantages for CZP compared to IXE Q2W for ASAS40 did not reach statistical significance. Exploration of statistical heterogeneity was limited by the fact that only one study per treatment was identified for all treatments but CZP.

Conclusion: In bDMARD-naïve patients with nr-axSpA, CZP showed increased odds of an ASAS40 response vs most bDMARDS investigated at 12–16 weeks, and vs anti-IL agents investigated at 52 weeks.

Disclosure: S. Kiri, UCB Pharma, 3; **M. Kim**, UCB Pharma, 3; **M. Betts**, UCB Pharma, 2; **M. Chitnis**, UCB Pharma, 2; **K. Fahrbach**, UCB Pharma, 2; **J. Tarpey**, UCB Pharma, 2; **M. Turner**, UCB Pharma, 2.

Abstract Number: 0884

Comparison of Disease Control Thresholds in Psoriatic Arthritis: Results from the Corrona Psoriatic Arthritis/Spondyloarthritis Registry

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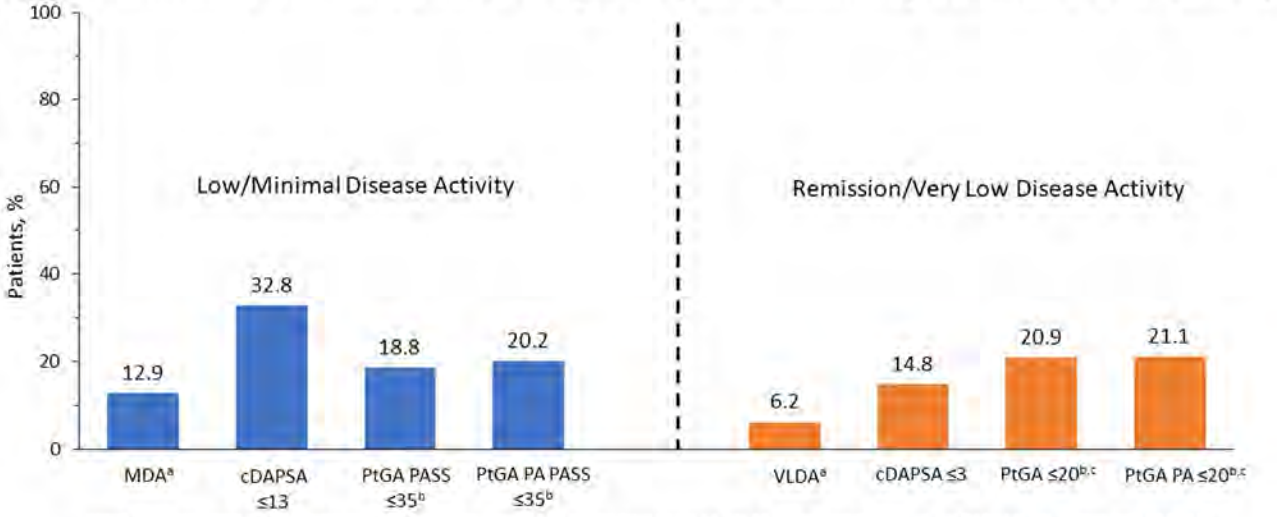
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: There is no single accepted measure of low/minimal disease activity (LDA/MDA) for patients with PsA; thus, describing the characteristics of real-world patients meeting different criteria will provide insight as to the most appropriate criteria for assessing disease control. The aim of this study was to identify and characterize patients with PsA who met LDA/MDA and remission/very low disease activity (VLDA) criteria by multiple measures of PsA disease severity.

Methods: This was a cohort study of patients (≥18 years) who enrolled in the Corrona PsA/SpA Registry between March 2013 and March 2020. Patients who received a biologic DMARD or Janus kinase inhibitor at enrollment, had a 6-month follow-up visit, and were not in a state of LDA/MDA at baseline were included. Percentages of patients who achieved LDA/MDA, remission/VLDA, and Clinical Disease Activity Index for Psoriatic Arthritis (cDAPSA) thresholds at 6-month follow-up were identified. We also examined the patient accepTable symptom state (PASS) for Patient Global Assessment (PtGA) and PtGA of Psoriasis and Arthritis (PtGA PA) using published cutoffs and examined how these exploratory thresholds compared with MDA, VLDA, and cDAPSA thresholds at 6 months. Clinical characteristics were assessed in patients who met disease thresholds at 6 months. Continuous measures were reported as means and standard deviations and categorical measures as frequencies and percentages.

Results: A total of 287 and 569 patients were eligible for the LDA/MDA and remission/VLDA analyses, respectively. Most patients were taking a TNF inhibitor at baseline. The proportion of patients who achieved LDA/MDA at 6 months differed across the LDA/MDA measures (**Figure 1**). MDA had the lowest rate (12.9%) of achievement vs cDAPSA

Figure 1. Achievement of Various Low Disease Activity and Very Low Disease Activity Measures at 6-Month Follow-up



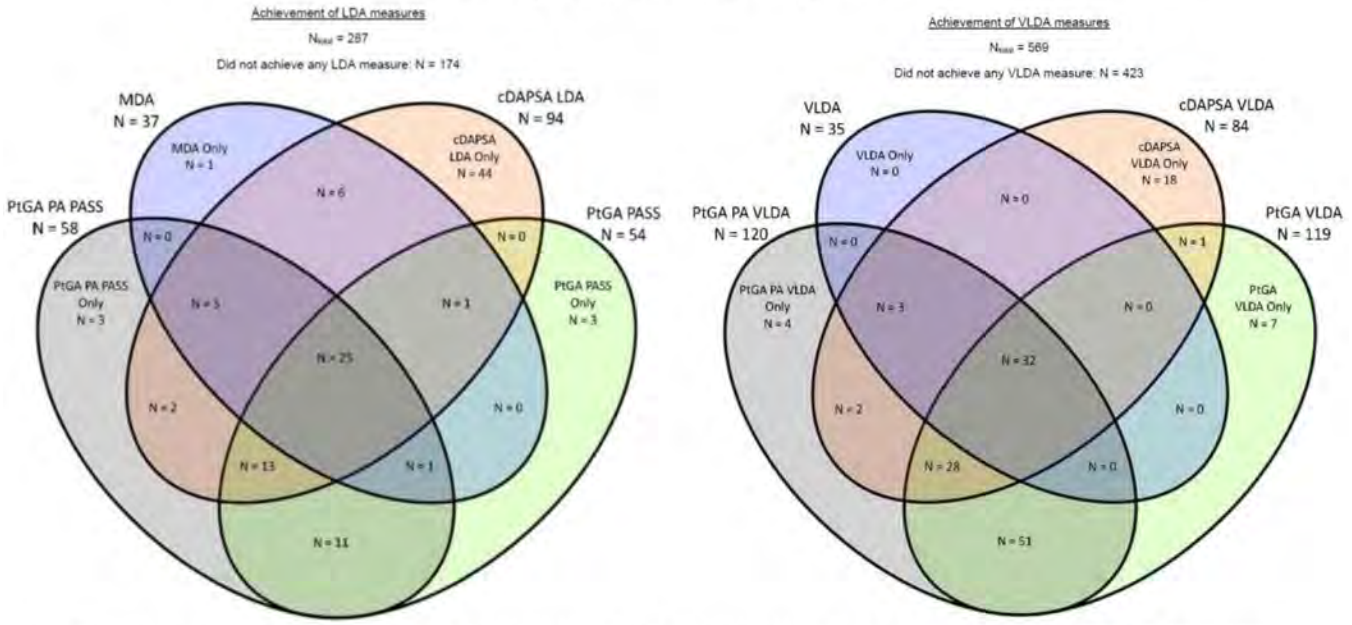
[a]MDA was achieved if 5 of the following 7 criteria were met: (1) 68 tender joint count ≤1, (2) 66 swollen joint count ≤1, (3) BSA ≤3%, (4) patient pain VAS ≤15, (5) PtGA PA VAS ≤20, (6) HAQ-DI ≤0.5, (7) SPARCC enthesitis count ≤1. VLDA was achieved if all 7 of the preceding criteria were met. [b]Measured on a 0–100 numeric scale. [c]There is no established cut-off point for 'very low symptom state' for PtGA PASS or PtGA PA PASS; thus, these cut-off points are considered exploratory. There are more patients in the Remission/VLDA group than in the MDA/LDA group (569 vs 287), so the percentage of patients achieving more stringent conditions appears artificially greater than those achieving less stringent conditions. BSA, body surface area; cDAPSA, Clinical Disease Activity Index for Psoriatic Arthritis; HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; PASS, patient acceptable symptom state; PtGA, Patient Global Assessment; PtGA PA, Patient Global Assessment of Psoriasis and Arthritis; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analog scale; VLDA, very low disease activity.

Table 1. Disease Activity and Patient-Reported Outcomes in Patients Achieving Various Low Disease Activity/Very Low Disease Activity Measures at 6-Month Follow-up

Low Disease Activity	**MDA[a] N=37**	**cDAPSA ≤13 N=94**	**PtGA PASS ≤35[b] N=54**	**PtGA PA PASS ≤35[b] N=58**
Tender joint count (68), mean ± SD	0.6 ± 1.8	0.8 ± 1.4	3.7 ± 7.2	3.3 ± 6.6
Swollen joint count (66), mean ± SD	1.0 ± 2.7	0.4 ± 0.9	2.3 ± 4.4	1.9 ± 4.0
Dactylitis count, mean ± SD	0.1 ± 0.7	0.0 ± 0.4	0.1 ± 0.6	0.0 ± 0.0
Enthesitis count (LEI), mean ± SD	0.0 ± 0.0	0.1 ± 0.6	0.2 ± 0.7	0.2 ± 0.7
PASDAS, mean ± SD	2.2 ± 0.8	2.9 ± 1.0	2.4 ± 0.9	2.6 ± 1.0
Patient-reported pain VAS[b], mean ± SD	23.0 ± 18.5	34.8 ± 23.1	36.4 ± 26.5	36.8 ± 26.0
Morning stiffness, n (%)	32 (86.5)	87 (92.6)	48 (88.9)	51 (87.9)
BASDAI, mean ± SD	2.4 ± 1.7	3.5 ± 2.0	3.4 ± 2.3	3.4 ± 2.2
HAQ-DI, mean ± SD	0.3 ± 0.4	0.6 ± 0.6	0.7 ± 0.6	0.7 ± 0.5
BSA (%), mean ± SD	0.9 ± 1.3	3.7 ± 11.2	5.6 ± 14.2	4.1 ± 11.8
Very Low Disease Activity	**VLDA[a] N=35**	**cDAPSA ≤3 N=84**	**PtGA ≤20[b,c] N=119**	**PtGA PA ≤20[b,c] N=120**
Tender joint count (68), mean ± SD	0.1 ± 0.2	0.1 ± 0.4	2.1 ± 5.3	2.0 ± 5.2
Swollen joint count (66), mean ± SD	0.1 ± 0.3	0.2 ± 0.5	1.1 ± 2.7	1.1 ± 2.7
Dactylitis count, mean ± SD	0.0 ± 0.0	0.0 ± 0.2	0.1 ± 0.3	0.1 ± 0.3
Enthesitis count (LEI), mean ± SD	0.0 ± 0.2	0.0 ± 0.3	0.1 ± 0.4	0.1 ± 0.4
PASDAS, mean ± SD	1.4 ± 0.8	1.7 ± 0.7	2.1 ± 0.9	2.1 ± 0.9
Patient-reported pain VAS[b], mean ± SD	7.3 ± 5.8	10.3 ± 8.5	22.4 ± 21.5	22.0 ± 21.5
Morning stiffness, n (%)	20 (57.1)	60 (71.4)	95 (79.8)	96 (80.0)
BASDAI, mean ± SD	1.0 ± 1.1	1.5 ± 1.4	2.2 ± 1.9	2.1 ± 1.8
HAQ-DI, mean ± SD	0.1 ± 0.1	0.2 ± 0.4	0.4 ± 0.5	0.3 ± 0.4
BSA (%), mean ± SD	0.6 ± 0.7	1.6 ± 2.5	2.2 ± 5.3	2.3 ± 8.1

[a]MDA was achieved if 5 of the following 7 criteria were met: (1) 68 tender joint count ≤1, (2) 66 swollen joint count ≤1, (3) body surface area (BSA) ≤3%, (4) patient pain VAS ≤15, (5) PtGA PA VAS ≤20, (6) HAQ-DI ≤0.5, (7) SPARCC enthesitis count ≤1. VLDA was achieved if all 7 of the preceding criteria were met. [b]Measured on a 0–100 numeric scale. [c]There is no established cutoff point for 'very low symptom state' for PtGA or PtGA PA; thus, these cutoff points are considered exploratory. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BSA, body surface area; cDAPSA, Clinical Disease Activity Index for Psoriatic Arthritis; HAQ-DI, Health Assessment Questionnaire-Disability Index; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; PASS, patient acceptable symptom state; PtGA, Patient Global Assessment of Arthritis; PtGA PA, Patient Global Assessment of Psoriasis and Arthritis; SD, standard deviation; SPARCC, Spondyloarthritis Research Consortium of Canada; VAS, visual analog scale; VLDA, very low disease activity.

Figure 2. Venn Diagrams Showing Achievement of Low Disease Activity/Minimal Disease Activity and Remission/Very Low Disease Activity Measures



cDAPSA, Clinical Disease Activity Index for Psoriatic Arthritis; LDA, low disease activity; MDA, minimal disease activity; PASS, patient acceptable symptom state; PtGA, Patient Global Assessment; PtGA PA, Patient Global Assessment of Psoriasis and Arthritis; VLDA, very low disease activity.

(32.8%) which had the highest rate. At 6 months, patients who achieved MDA reported less pain, lower tender joint, dactylitis, and enthesitis counts, less axial symptoms, and better physical function than those who met the cDAPSA, PtGA PASS, and PtGA PA PASS thresholds for LDA (**Table 1**). Percentages of patients who achieved remission/VLDA differed across remission/VLDA measures. VLDA had the lowest rate (6.2%) of achievement vs PtGA PA (21.1%) which had the highest rate at 6-month follow-up. Patients achieving VLDA reported less pain and axial involvement, and better physical function than patients achieving less stringent remission/VLDA thresholds for cDAPSA, PtGA PASS, and PtGA PA PASS (**Table 1**). Relationships among and between measures of PsA disease severity are illustrated in **Figure 2**.

Conclusion: MDA and VLDA were the most stringent disease activity measures of the respective criteria in patients with PsA and resulted in overall lower disease activity in all of the domains compared with patients who met cDAPSA, PtGA PASS, and PtGA PA PASS thresholds. Rheumatologists should be encouraged to use MDA and/or VLDA to assess disease control in their patients with PsA.

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Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **R. McLean**, Corrona, 3; **T. Blachley**, Corrona, LLC, 3; **L. Anatale-Tardiff**, Corrona, 3; **C. Saffore**, AbbVie, 1, 3; **P. Zueger**, AbbVie Inc., 1, 3; **A. Ogdie**, Lilly, 5, Amgen, 5, AbbVie, 5, BMS, 5, Celgene, 5, Janssen, 5, Norvatis, 2, 5, Pfizer, 2, 5, Takeda, 5.

Abstract Number: 0885

Impact of HLA-B27 Status on Clinical Outcomes in Patients with Ankylosing Spondylitis Treated with Secukinumab

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

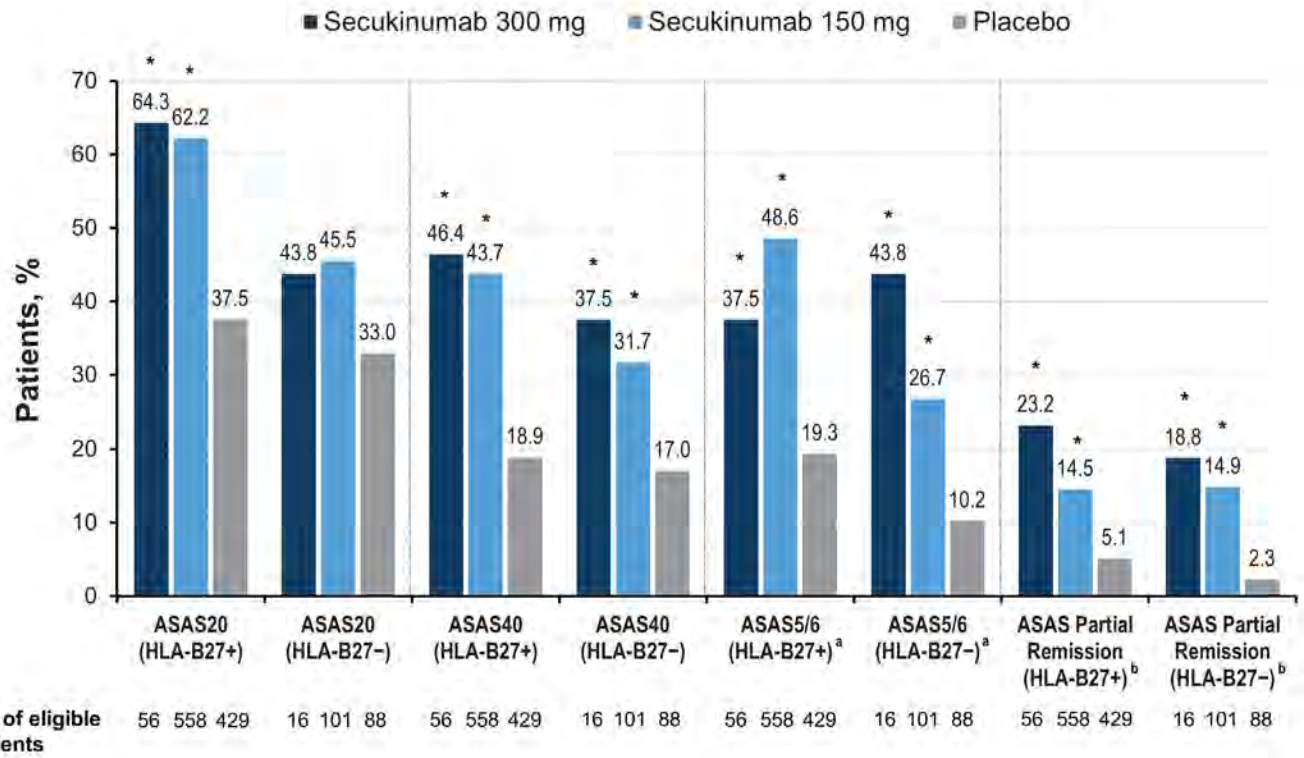
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

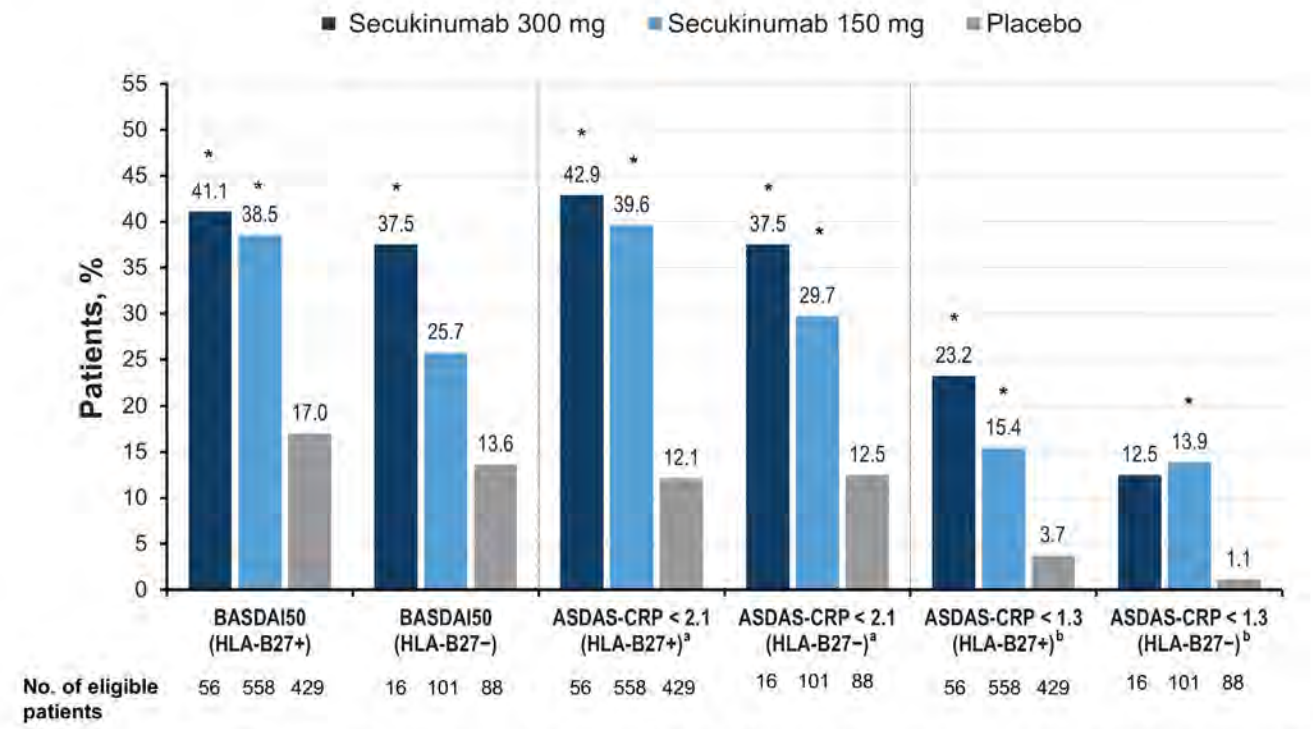
Background/Purpose: Ankylosing spondylitis (AS) is strongly associated with the genetic marker HLA-B27. In patients with AS, negative HLA-B27 status is a predictor of worse response to tumor necrosis factor inhibitors.[1] Approximately 80%-90% of Caucasian patients with AS express HLA-B27 compared with < 8% of the Caucasian pop-

Figure 1. Percentage of Patients With AS Achieving ASAS Responses at Week 16 (nonresponder imputation)



AS, ankylosing spondylitis; ASAS, Assessment in SpondyloArthritis international Society; TNF-α, tumor necrosis factor α.
Logistic regression analysis used treatment and TNF-α inhibitor status as factors and baseline weight as a covariate.
* $P < .05$ compared with placebo.
[a] 20% improvement in ≥ 5 ASAS domains.
[b] Score of ≤ 2 in the patient global, pain, function, and inflammation domains.

Figure 2. Percentage of Patients With AS Achieving BASDAI50 and ASDAS-CRP Responses at Week 16 (nonresponder imputation)



AS, ankylosing spondylitis; ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CRP, C-reactive protein; TNF-α, tumor necrosis factor α.
Logistic regression analysis used treatment and TNF-α inhibitor status as factors and baseline weight as a covariate.
* $P < .05$ compared with placebo.
[a] All patients had ASDAS-CRP of > 2.1 at baseline.
[b] All patients had ASDAS-CRP of > 1.3 at baseline.

ulation; these trends are similar in Chinese patients. The objective of this study is to analyze the impact of HLA-B27 status on clinical outcomes at Week 16 in a racially diverse population of patients with AS treated with secukinumab vs placebo.

Methods: Patients with AS were pooled from the MEASURE 1-5 studies (NCT01358175, NCT01649375, NCT02008916, NCT02159053, and NCT02896127) and stratified by HLA-B27 status. All trials included patients who received secukinumab 150 mg every 4 weeks with or without an initial loading dose (10 mg/kg IV at Weeks 0, 2, and 4 or 150 mg SC at Weeks 0, 1, 2, and 3) or placebo control. MEASURE 3 included patients receiving secukinumab 300 mg every 4 weeks following the initial IV loading dose. A large proportion of patients enrolled in MEASURE 5 were from China. Efficacy at Week 16 was determined by the proportion of patients reporting 20% improvement in Assessment of SpondyloArthritis international Society (ASAS20), ASAS40, ASAS5/6, ASAS partial remission, 50% improvement in the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI50), and Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS-CRP) of < 2.1 or < 1.3. All outcomes were compared within HLA-B27 strata for secukinumab vs placebo using logistic regression at Week 16 with nonresponder imputation for missing data. All analyses were for hypothesis generation, without adjustment for multiple comparisons.

Results: Of 1248 patients included in this pooled analysis, 1043 (83.6%) were HLA-B27+ and 205 (16.4%) were HLA-B27−. Compared with HLA-B27− patients, HLA-B27+ patients were younger (38.6 vs 45.0 years) and more frequently male (77.1% vs 48.8%). Regardless of HLA-B27 status, patients receiving any dose of secukinumab were significantly more likely to report ASAS40, ASAS5/6, ASAS partial remission (**Figure 1**) and ASDAS-CRP of < 2.1 (**Fig-**

ure 2) than those receiving placebo ($P < .05$ for all comparisons). HLA-B27+ patients receiving any dose of secukinumab were also significantly more likely to report ASAS20, BASDAI50, and ASDAS-CRP responses vs those receiving placebo ($P < .05$) (**Figures 1 and 2**), although HLA-B27– patients experienced at least numerical improvements vs placebo in these measures. Among HLA-B27– patients, only those receiving secukinumab 300 mg were significantly more likely to report BASDAI50 response vs those receiving placebo, and only patients receiving secukinumab 150 mg were significantly more likely to have ASDAS-CRP of < 1.3 vs placebo ($P < .05$ for all comparisons) (**Figure 2**).

Conclusion: In a large pooled population of patients with AS including patients from China, secukinumab was effective regardless of HLA-B27 status, although HLA-B27+ patients experienced increased therapeutic benefit compared with HLA-B27– patients.

Reference:

1. Alazmi M, et al. *Arthritis Care Res (Hoboken)*. 2018;70:1393-1399.

Disclosure: A. Deodhar, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8; **V. Strand**, AbbVie, 5, Amgen, 5, Celltrion, 5, Janssen, 5, Merck, 5, Novartis, 5, Regeneron, 5, Sanofi, 5, UCB, 5, Genentech/Roche, 5, GSK, 5, Pfizer, 5, Bayer, 5, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, Galapagos, 5, Lilly, 5, Gilead, 5, Samsung, 5, Servier, 5, Setpoint, 5, Arena, 5, AstraZeneca, 5, Horizon, 5, Ichnos, 5, Inmedix, 5, Sandoz, 5; **P. Machado**, Novartis, 1, 3; **A. Shete**, Novartis, 1, 3; **X. Meng**, Novartis, 1, 3; **M. Magrey**, Novartis, 5, Eli Lilly, 5, AbbVie, 2, UCB, 2, Amgen, 2, Pfizer, 5, Janssen, 5.

Abstract Number: 0886

Achievement of Partial Remission and Inactive Disease in Upadacitinib-Treated Patients with Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

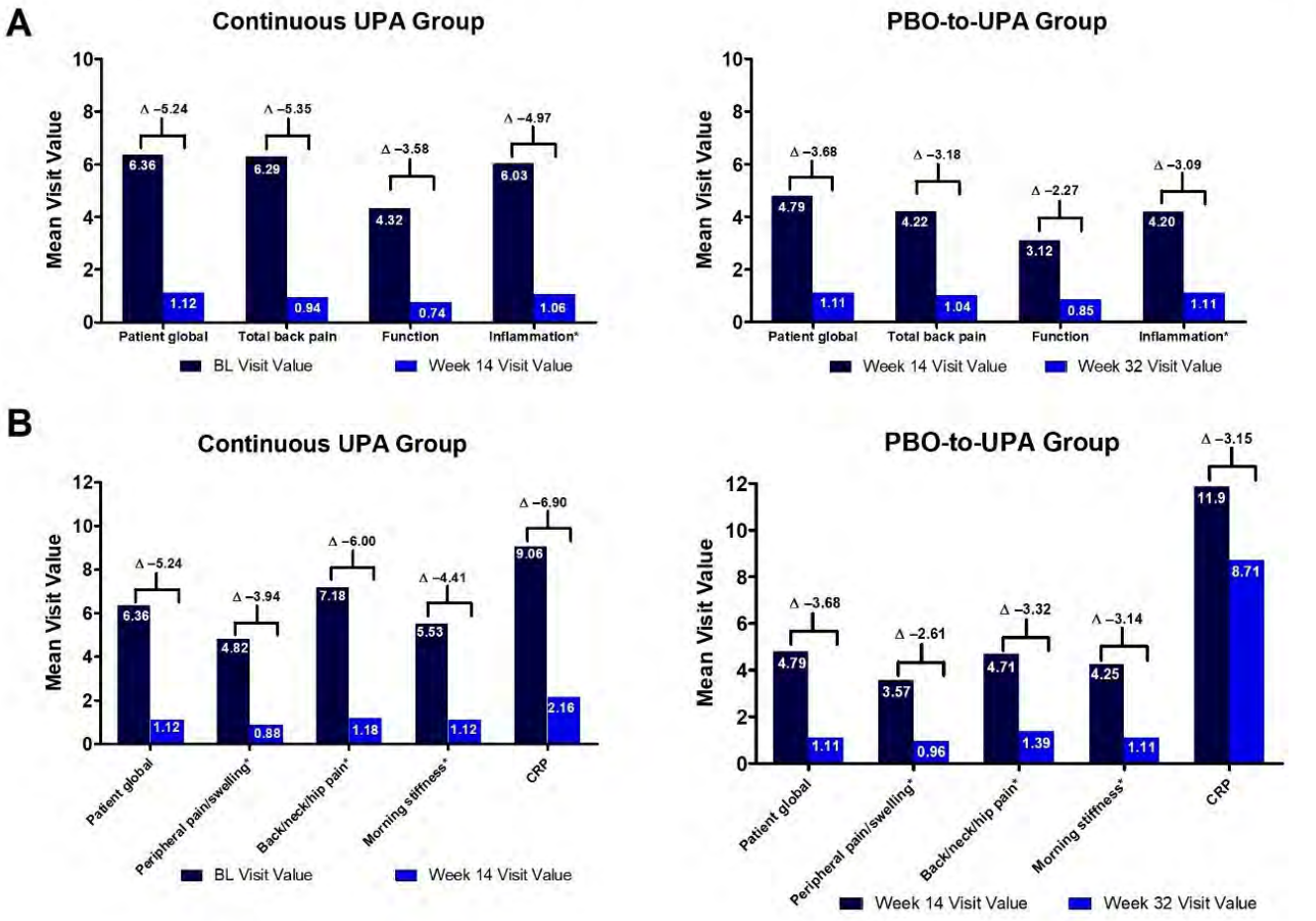
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Assessment of SpondyloArthritis international Society (ASAS) response criteria and AS Disease Activity Score (ASDAS) are both commonly used, rigorous composite indices consisting of components with relevance to patients. Clinically meaningful thresholds for these measures have been defined to reflect partial remission (PR), inactive disease (ID), and low disease activity (LDA). The objective of this analysis was to study the association of ASAS PR and ordinal ASDAS disease categories (including ASDAS ID, which is the most stringent category of this composite score) in upadacitinib (UPA)-treated patients with AS.

Figure. Core ASAS (A) and ASDAS (B) Components Among Patients Who Achieved ASAS PR



*Inflammation based on mean of BASDAI question 5 and 6; peripheral pain/swelling based on BASDAI question 3; Back/neck/hip pain based on BASDAI question 2; duration of morning stiffness based on BASDAI question 6.
ASAS, Assessment of SpondyloArthritis international Society response criteria; ASDAS, AS Disease Activity Score; PBO, placebo; PR, partial remission; UPA, upadacitinib.

Figure

Methods: In the SELECT-AXIS 1 (NCT03178487) study, biologic DMARD naïve-patients (pts; ≥18 y) with active AS and intolerance/contraindication or inadequate response to ≥2 NSAIDs were randomized 1:1 to UPA 15 mg once daily (QD) or placebo (PBO).[1] At wk 14, pts entered an open-label extension (OLE) of UPA 15 mg QD; pts randomized to PBO were switched to UPA. This post hoc analysis assessed the responsiveness of individual ASAS and ASDAS core components among pts who achieved ASAS PR. The association of ASAS PR with achievement of ASDAS ID (ASDAS < 1.3), ASDAS LDA (ASDAS < 2.1 but ≥1.3) or ASDAS high disease activity (HDA)/very HDA (VHDA) (ASDAS ≥2.1 for HDA/VHDA) was also assessed by measures including Youden index, distance to perfect point, and sensitivity/specificity equality. These evaluations were performed in pts randomized to UPA from baseline (BL; continuous UPA, assessed at wk 14) and those who were randomized to PBO and switched to UPA upon entry in the OLE (PBO to UPA; re-baselined at wk 14 and assessed at wk 32, representing 18 wks of UPA exposure).

Results: At wk 14, for the continuous UPA group, 16 pts (19%) achieved ASAS PR. At wk 32, following 18 wks of UPA exposure for the PBO-to-UPA group, 28 pts (33%) achieved ASAS PR. Among both groups (continuous UPA

Table. Association Between ASAS PR and ASDAS Clinical Thresholds (ID/LDA/HDA or VHDA)

	ASDAS ID (<1.3)	ASDAS LDA (1.3 to <2.1)	ASDAS HDA or VHDA (≥2.1)
Continuous UPA Group	n=15	n=31	n=39
ASAS PR Responders (n=16)	11	5	0
ASAS PR Non-responders (n=69)	4	26	39
PBO-to-UPA Group	n=25	n=35	n=25
ASAS PR Responders (n=28)	16	8	4
ASAS PR Non-responders (n=57)	9	27	21

P<0.001 for association of ASAS PR with the ordered ASDAS categories of ID-LDA-HDA, for both Continuous UPA Group and PBO-to-UPA Group.
P value calculated from Cochran-Armitage trend test for association of ordinal categories.
ASAS, Assessment of SpondyloArthritis international Society response criteria; ASDAS, AS Disease Activity Score; HDA, high disease activity; ID, inactive disease; LDA, low disease activity; PBO, placebo; PR, partial remission; UPA, upadacitinib; VHDA, very high disease activity.

Table

and PBO-to-UPA), improvements were seen across all core components (**Figure**). Of the 44 total pts who achieved ASAS PR, 91% achieved either ASDAS ID or LDA. The majority of patients who achieved ASAS PR achieved ASDAS ID in the continuous UPA and PBO-to-UPA groups: 11/16 (69%) and 16/28 (57%), respectively. For the continuous UPA group, the remaining 5 pts who achieved ASAS PR also achieved ASDAS LDA (**Table**). ASAS PR was associated with ASDAS categories in the following manner: the highest rate of ASAS PR was achieved for ASDAS ID followed by ASDAS LDA followed by ASDAS HDA/VHDA. The cutoff of 1.3 (the upper threshold for ASDAS ID) was a better discrimination threshold for ASAS PR than the cutoff of 2.1 (the upper threshold for ASDAS LDA).

Conclusion: Nineteen percent of pts receiving UPA from BL achieved ASAS PR after 14 wks of treatment, with similar results seen in pts who were originally randomized to PBO and switched to UPA at wk 14. A consistent improvement was seen across all core components of ASAS among those who achieved ASAS PR with UPA treatment. The achievement of ASAS PR was most closely associated with the achievement of ASDAS ID, providing further clarity on the reduction of disease activity in AS pts treated with UPA.

References:

1. van der Heijde, et al. *Lancet*. 2019;394(10214):2108-2117.

Disclosure: A. Deodhar, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **A. Östör**, AbbVie, 5, Roche, 5, Janssen, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, Gilead, 5, Paradigm, 5, UCB Pharma, 5, Bristol-Myers Squibb, 5; **A. Maniccia**, AbbVie Inc., 1, 3, 4; **F. Ganz**, AbbVie Inc., 1, 3, 4; **T. Gao**, AbbVie Inc., 1, 3, 4; **A. Chu**, AbbVie Inc., 1, 3, 4; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8.

Abstract Number: 0887

Increasing Use of Biologics in Treatment of Systemic Lupus Erythematosus Patients in US Clinical Practice: Real-World Observations from Trio Health and the American Rheumatology Network

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) treatments include steroids, antimalarials, immunosuppressants and/or biologics, though the use of biologics has been reported as minimal in claim-based studies examining real-world treatment patterns between 2006 to 2016. Here, we examine choice of treatments in the last three years within community rheumatology practices to understand current use of biologics. In addition, we examine persistence to belimumab, the most commonly used biologic for SLE, and association with different treatment and patient characteristics.

Figure 1: Percentage of patient starts by drug class

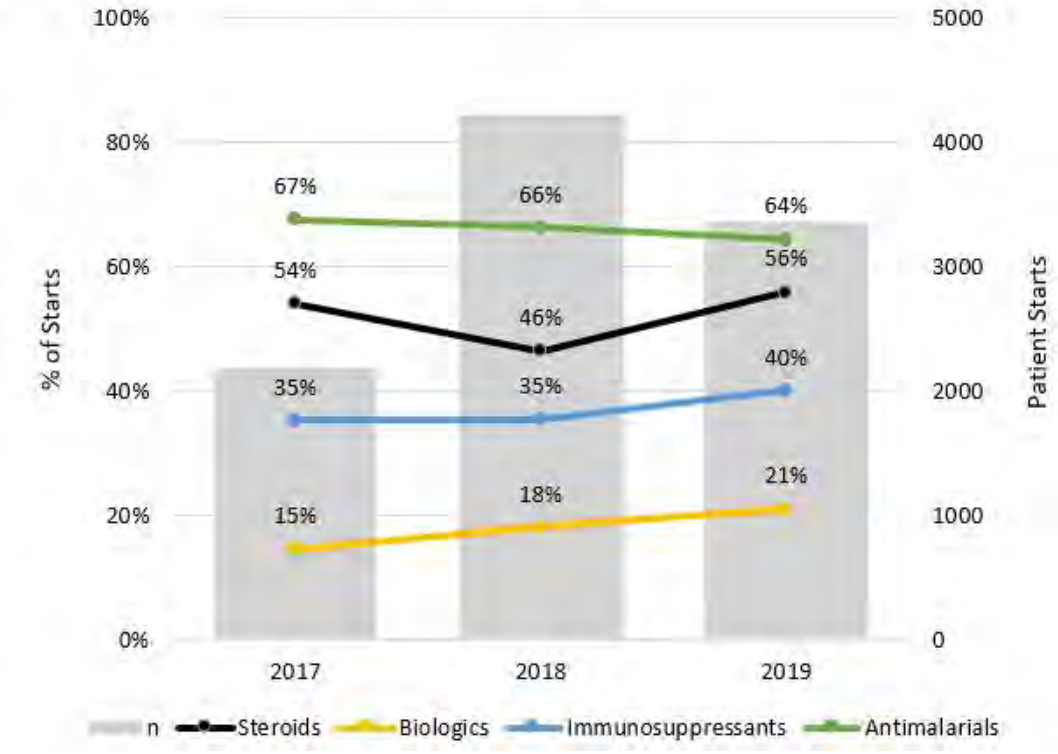

Figure 1. Percentage of patient starts by drug class

Methods: The ARN-TRIO Rheumatology registry contains EMR (fielded and open text), lab, procedure, infusion, medical claims, and specialty pharmacy data generated in care of >75,000 patients by ARN, a network of independent practices with >200 rheumatologists across the US. Data for adult (18+) patients with SLE who initiated or switched to a new treatment (starts) from Jan 2017 to May 2020 were included in this study. Comparisons between groups were made using t-test for continuous variables and chi-square or Fischer's exact tests for categorical variables. Time to events analyses were conducted by Kaplan-Meier and subsequent log-rank test.

Results: A total of 5,797 SLE patients started 10,913 distinct treatments in the observation window. Comparing starts by drug class between 2017 to 2019 indicated annualized growth rates of 20% for biologics, 7% for immunosuppressants, 2% for steroids, and -2% for antimalarials, with significant differences ($p< 0.050$) between 2019 and 2017 start percentages for all drug classes except steroids. [FIGURE 1] To compare populations receiving different drug classes, patients were classified into biologic or non-biologic groups based on initial treatment (index). [TABLE 1] At index, 91% (5,272) received non-biologic therapy; 67% (3,884) received antimalarials, 36% (2,098) steroids, and 22% (1,287) immunosuppressants. Patients treated with biologic therapies at index mostly received belimumab (66%, 347/525); rituximab was used for 11% (60/525) of patients. Compared to the non-biologic group, the biologics group differed in use of other drug classes and payer, but not in age, gender, or race. For patients receiving belimumab, the mean time to discontinuation was 838 days (25th percentile = 620 days, median not reached). Time to belimumab discontinuation differed by concomitant use of steroids, antimalarials, or immunosuppressants and these individual

n (%) unless specified	All Patients	(1) Not on biologics				(2) On biologics	p-value (1) vs (2)
		All not on biologics	On antimalarials*	On steroids*	On immuno-suppressants*		
Study Population	(n=5797)	(n=5272)	(n=3884)	(n=2098)	(n=1287)	(n=525)	
Age, mean (SD)	51.3 (15.3)	51.4 (15.4)	50.6 (15.4)	51.7 (15.7)	50.1 (15.3)	50.8 (14.4)	0.344
Female	5210 (90%)	4729 (90%)	3474 (89%)	1870 (89%)	1136 (88%)	481 (92%)	0.138
Race							
White	2497 (43%)	2242 (43%)	1623 (42%)	905 (43%)	557 (43%)	255 (49%)	0.838
Black	779 (13%)	702 (13%)	496 (13%)	351 (17%)	202 (16%)	77 (15%)	
Asian	42 (<1%)	40 (<1%)	27 (1%)	18 (1%)	18 (1%)	2 (<1 %)	
Other	25 (<1%)	19 (<1%)	12 (<1%)	10 (<1%)	9 (1%)	6 (1%)	
Unknown	2454 (42%)	2269 (43%)	1726 (44%)	814 (39%)	501 (39%)	185 (35%)	
Payer							
Commercial	3652 (63%)	3301 (63%)	2530 (65%)	1228 (59%)	772 (60%)	351 (67%)	0.002
Medicare	1450 (25%)	1336 (25%)	904 (23%)	606 (29%)	347 (27%)	114 (22%)	
Medicaid	488 (8%)	452 (9%)	320 (8%)	184 (9%)	120 (9%)	36 (7%)	
Other	115 (2%)	95 (2%)	59 (2%)	46 (2%)	27 (2%)	20 (4%)	
Unknown	92 (2%)	88 (2%)	71 (2%)	34 (2%)	21 (2%)	4 (1%)	
Concurrent drug class							
+steroids	2331 (40%)	2098 (40%)	1124 (29%)	–	543 (42%)	233 (44%)	0.041
+antimalarials	4091 (71%)	3884 (74%)	–	1124 (54%)	614 (48%)	207 (39%)	<0.001
+immunosuppressants	1440 (25%)	1287 (24%)	614 (16%)	543 (26%)	–	153 (29%)	0.017
+biologics	525 (9%)	–	–	–	–	–	

*overlapping subsets within the "not on biologics" group

Table 1 Patient Characteristics at index

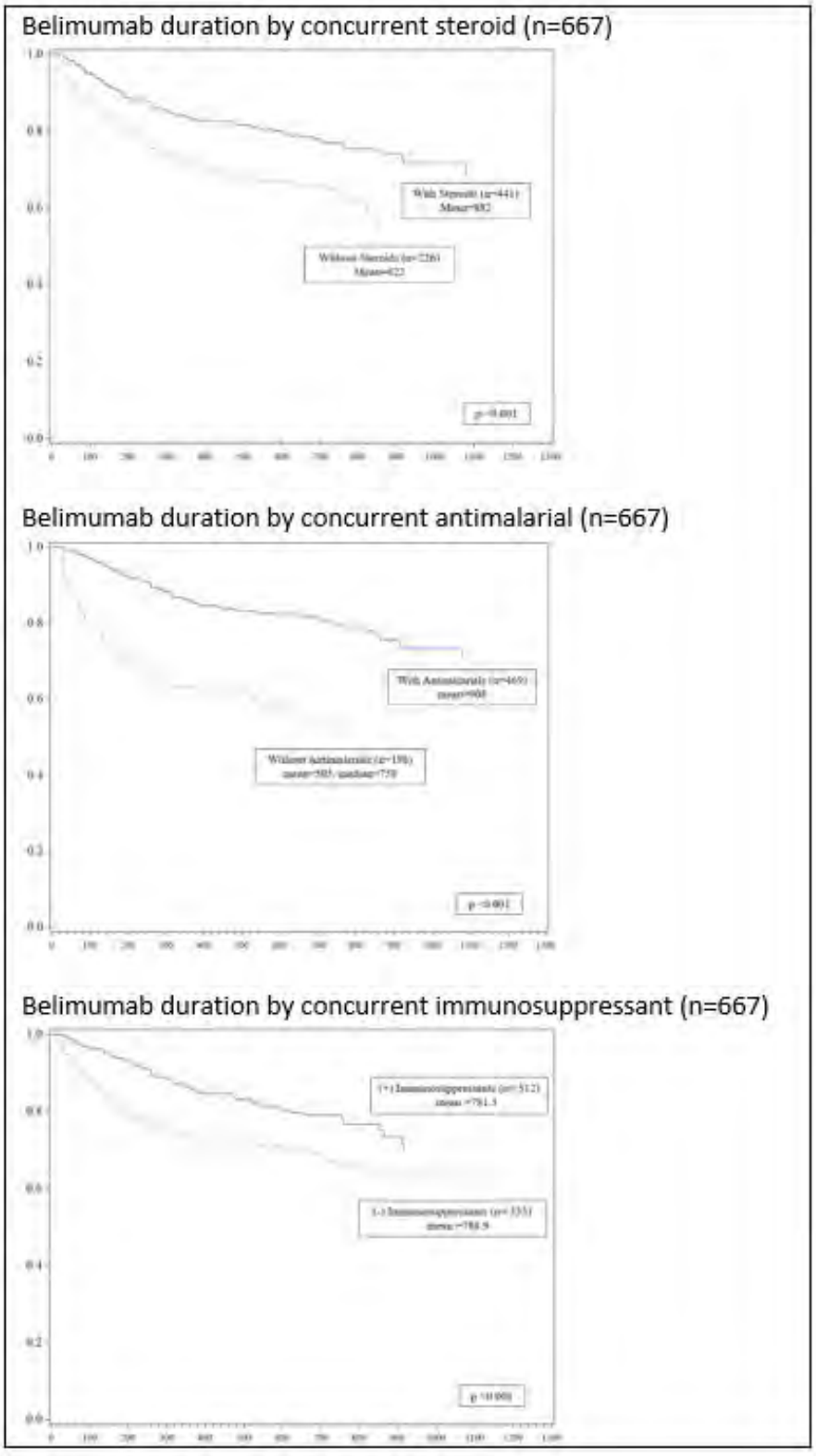

Figure 2. Days to belimumab discontinuation by concurrent drug class

associations persisted regardless of the presence of other drug classes. [FIGURE 2] Time to belimumab discontinuation was not associated with age, gender, race, or payer.

Conclusion: The use of biologics has increased considerably since 2017 though these agents are still limited to a fifth of treatment starts. Aside from a slight but significantly higher percentage with commercial coverage, the group initiating biologics was similar to the non-biologic group for patient characteristics. For patients that received belimumab, persistence on therapy was considerable and increased in populations receiving concomitant steroids, antimalarials, or immunosuppressants.

Disclosure: S. Helfgott, Abbvie, 5; **J. Broestl**, None; **K. Huston**, None; **D. Rane**, None; **J. Singh**, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **N. Soloman**, Horizon, 5, 8, Amgen, 2, 8, Abbvie, 2, 5, 8, UCB, 2, 5, 8, Novartis, 5, 8, Jannsen, 2, 8, Pfizer, 8, Lilly, 2, GSK, 2, 5, 8; **C. Edgerton**, Sandoz, 5.

Abstract Number: 0888

Guselkumab Efficacy and Safety in TNF-Inhibitor-Experienced and TNF-Inhibitor-Naïve Patients with Active PsA: 1-Year Results of a Phase 3, Randomized, Controlled Study

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Guselkumab (GUS), a novel anti-IL-23 monoclonal antibody specific to the IL-23p19-subunit, is approved to treat psoriasis. Through week (W) 24 of the Phase 3, double-blind, placebo (PBO)-controlled DISCOVER-1 trial in patients (pts) with active psoriatic arthritis (PsA), significantly more pts receiving GUS 100 mg every 4 weeks (Q4W) or every 8 weeks (Q8W) vs PBO achieved ACR20 response. 31% of pts previously received 1-2 TNFα inhibitors (TNFi), and ACR20 response patterns through W24 were comparable in TNFi-naïve vs. experienced pts.[1] Here we assess GUS efficacy and safety through 1-year by prior TNFi use.

Methods: Adults with active PsA (≥3 swollen+≥3 tender joints; CRP ≥0.3mg/dL) despite standard therapies were eligible. Pts were randomized 1:1:1, stratified by W0 DMARD use [Y/N] and prior TNFi use (Y/N), to GUS 100 mg Q4W; GUS 100 mg at W0, W4, then Q8W through W48; or PBO and then GUS 100 mg Q4W from W24-W48 (PBO→Q4W).

Table. Summary of Prior TNFi Exposure and Clinical Response by Prior TNFi Exposure Through Week 52 of DISCOVER-1 (Missing Data Imputed as Nonresponse).

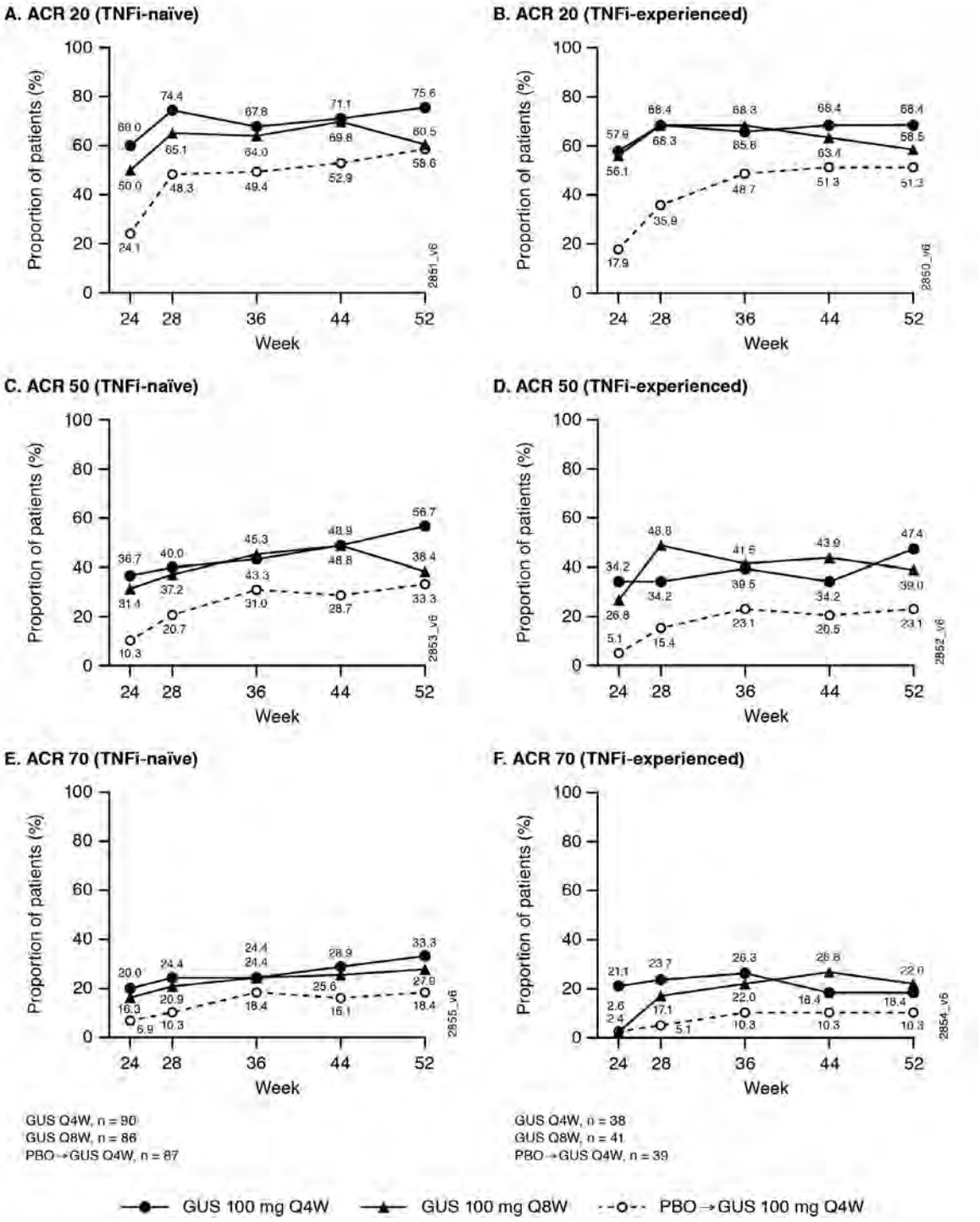
	Guselkumab Q4W		Guselkumab Q8W		Placebo (Week0-24) → Guselkumab Q4W (Week24-52)	
Randomized & treated pts, N	**128**		**127**		**126**	
Prior TNFi Use						
No	90 (70.3)		86 (67.7)		87 (69.0)	
Yes	38 (29.7)		41 (32.3)		39 (31.0)	
Number of Prior TNFi						
1	*33 (86.8)*		*34 (82.9)*		*35 (89.7)*	
2	*5 (13.2)*		*7 (17.1)*		*4 (10.3)*	
Skin, Physical Function, and Composite Endpoint Responses in TNFi-Naive Pts						
	Week24	**Week52**	**Week24**	**Week52**	**Week24**	**Week52**
≥3% BSA psoriasis & IGA ≥2 at W0, N	61		53		52	
IGA 0	35 (57.4)	41 (67.2)	24 (45.3)	29 (54.7)	6 (11.5)	33 (63.5)
PASI75	55 (90.2)	58 (95.1)	39 (73.6)	40 (75.5)	9 (17.3%)	39 (75.0)
HAQ-DI ≥0.35 at W0, N	77		73		74	
≥0.35 improvement	43 (55.8)	53 (68.8)	37 (50.7)	37 (50.7)	22 (29.7)	33 (44.6)
Randomized & treated, N	90		86		87	
MDA	29 (32.2)	39 (43.3)	22 (25.6)	29 (33.7)	13 (14.9)	27 (31.0)
Skin, Physical Function, and Composite Endpoint Responses in TNFi-Experienced Pts						
	Week24	**Week52**	**Week24**	**Week52**	**Week24**	**Week52**
≥3% BSA psoriasis & IGA ≥2 at W0, N	28		29		26	
IGA 0	13 (46.4)	18 (64.3)	7 (24.1)	11 (37.9)	0	10 (38.5)
PASI75	22 (78.6)	25 (89.3)	23 (79.3)	20 (69.0)	2 (7.7)	17 (65.4)
HAQ-DI ≥0.35 at W0, N	33		39		36	
≥0.35 improvement	20 (60.6)	21 (63.6)	20 (51.3)	21 (53.8)	10 (27.8)	17 (47.2)
Randomized & treated, N	38		41		39	
MDA	10 (26.3)	11 (28.9)	7 (17.1)	9 (22.0)	1 (2.6)	5 (12.8)

Data are n (%) unless otherwise noted.

Effects of GUS on joint (ACR20/50/70), skin (Investigator's Global Assessment response [IGA=0/1 + ≥2-grade reduction from W0], IGA=0, and Psoriasis Area Severity Index [PASI] 75/90/100 responses, all in pts with ≥3% BSA psoriasis and IGA ≥2 at W0), physical function (HAQ-disability index [HAQ-DI] ≥0.35 improvement in pts with HAQ-DI ≥0.35 at W0), and composite disease state (minimal disease activity [MDA]) were assessed through W52 using non-responder imputation (NRI) for missing data and summarized by prior TNFi use. Adverse events (AEs) through study completion (W60) were summarized by prior TNFi use.

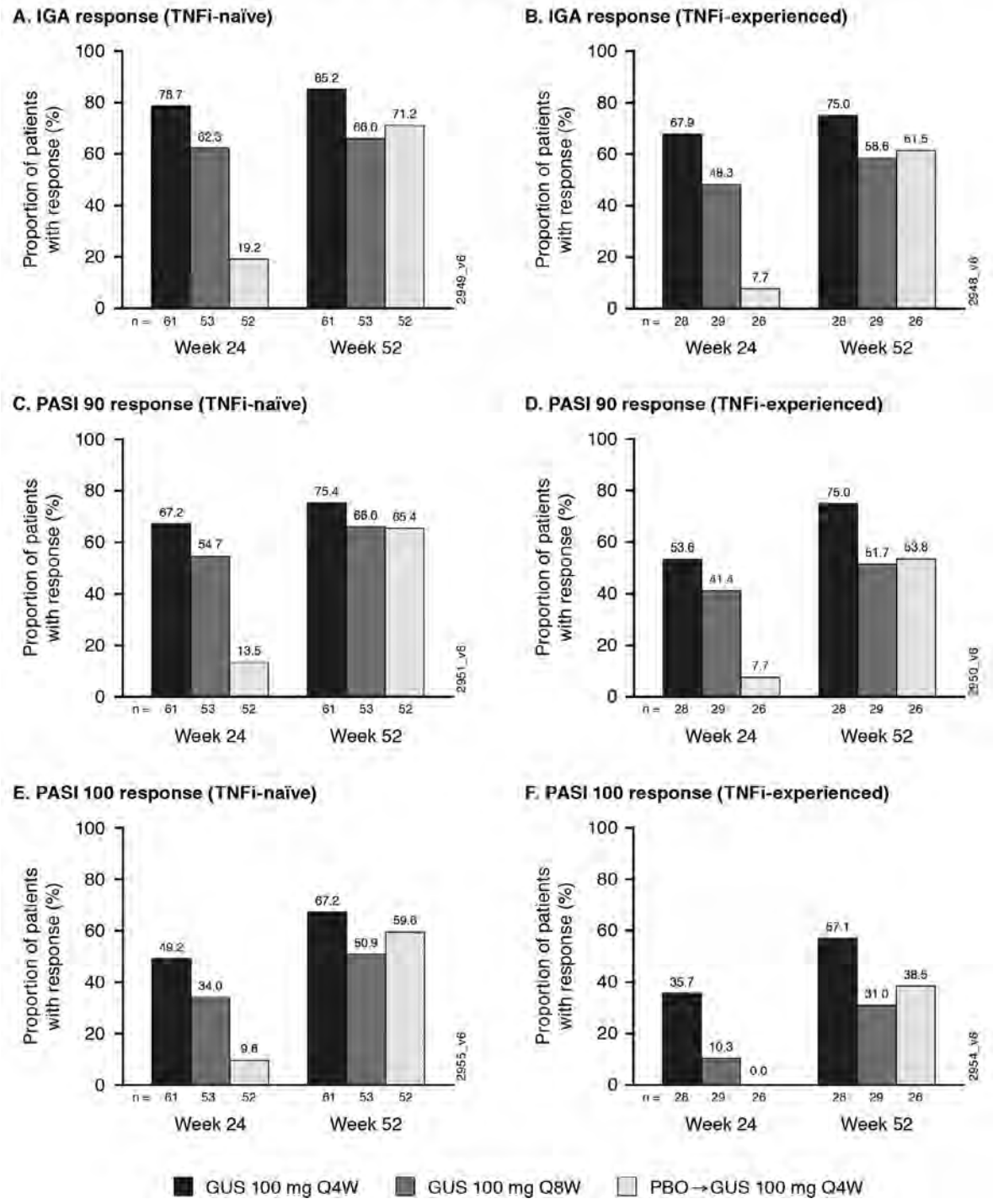
Results: Of 381 treated PsA pts, 362 continued at W24, and 347 completed treatment through W48. 65% of pts were receiving DMARDs at W0; 31% previously received TNFi (**Table**). In both TNFi-naïve and experienced pts, proportions of GUS-treated pts achieving ACR20/50/70 and HAQ-DI ≥0.35 improvement were maintained from W24-W52 (**Fig**). Consistent joint response patterns were seen even in the smaller number of pts who discontinued (d/c) prior TNFi use due to inadequate response, e.g., Q4W and Q8W W52 response rates were 82% (14/17) and 60% (9/15) for ACR20 and 47% (8/17) and 40% (6/15) for ACR50. Robust skin response (IGA/PASI) rates were also maintained at W52 in both TNFi exposure subgroups. Most joint and skin response rates continued to increase over time through W52 regardless of prior TNFi use (**Table, Fig**). Through W60 in GUS-treated TNFi-naïve (n=258) and experienced (n=111) pts, 62% and 64%, respectively, reported ≥1 AE, 3% and 6% had serious AEs, 0.4% and 3% had serious infections, 3% and 2% had AEs lead to treatment d/c, and 7%/7% and 4%/3% had increased ALT/AST levels.

Figure 1. Proportions of randomized and treated patients achieving ACR20, ACR50, and ACR70 responses (NRI) from W24–W52 by prior TNFi use. Among 87 TNF-naïve and 39 TNFi-experienced patients randomized to receive PBO, 82 and 32, respectively, crossed over to GUS Q4W at W24 (after the W24 response assessments); the remaining pts (5 TNFi-naïve, 7 TNFi-experienced), who received PBO only and discontinued from the study, were included as nonresponders over time through W52.



Conclusion: Through 1 year, GUS 100 mg Q4W and Q8W provided robust and sustained improvements in joint symptoms and physical function in both TNFi-naïve and TNFi-experienced pts with active PsA. Meaningful improvements in skin psoriasis and composite disease state were observed, and GUS appeared to be well tolerated in PsA pts, regardless of prior TNFi status.

Figure 2. Proportions of randomized and treated patients with ≥3% BSA psoriasis and IGA ≥2 at Wk0 achieving IGA (IGA 0/1 + ≥2-grade decrease from W0 IGA), PASI90, and PASI100 responses (NRI) from W24–W52 by prior TNFi use. Among 52 TNFi-naive and 26 TNFi-experienced patients randomized to receive PBO, 47 and 21, respectively, crossed over to GUS Q4W at W24 (after the W24 response assessments); the remaining pts (5 in each TNFi subgroup), who received PBO only and discontinued from the study, were included as nonresponders over time at W52.



Reference: [1]Deodhar A, et al. Lancet 2020;395:1115-25.

Disclosure: C. Ritchlin, None; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers

Squibb, 2; **W. Boehncke**, Janssen Research & Development, LLC, 2, 5; **E. Soriano**, AbbVie Inc., 2, 5, 8, Amgen, 2, 5, 8, Bristol Myers, 2, 5, 8, Celgene, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8; **E. Hsia**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **A. Kollmeier**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **X. Xu**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **F. Zazzetti**, Janssen, 3; **M. Shawi**, Janssen Global Services, LLC, 3, Johnson & Johnson, 1; **Y. Jiang**, None; **S. Sheng**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **P. Agarwal**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **P. Helliwell**, AbbVie, 2, 8, Janssen, 2, Pfizer Inc, 8, Celgene, 8, Galapagos, 8, Amgen, 8, Novartis, 2, UCB, 8.

Abstract Number: 0889

Efficacy of Secukinumab Treatment in Patients with Early Psoriatic Arthritis: A Pooled Analysis of 4 Phase 3 Studies

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

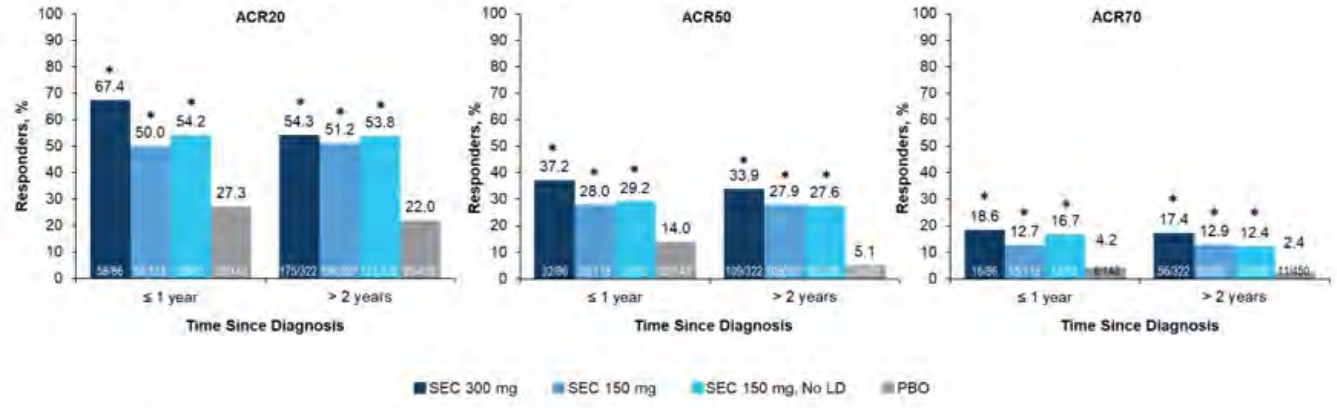
Session Type: Poster Session B

Table 1. Patient Characteristics at Baseline

	Time Since PsA Diagnosis ≤ 1 year				Time Since PsA Diagnosis > 2 years			
Variable	SEC 300 mg (n = 86)	SEC 150 mg (n = 118)	SEC 150 mg, No LD (n = 72)	Placebo (n = 143)	SEC 300 mg (n = 322)	SEC 150 mg (n = 387)	SEC 150 mg, No LD (n = 225)	Placebo (n = 450)
Age, mean (SD), years	46.1 (12.6)	45.4 (14.0)	45.9 (13.2)	47.4 (13.0)	49.3 (12.8)	49.7 (11.5)	50.8 (11.1)	50.2 (11.9)
Male, n (%)	52 (60.5)	51 (43.2)	42 (58.3)	74 (51.7)	148 (46.0)	187 (48.3)	113 (50.2)	188 (41.8)
Prior TNFi therapies, n (%)								
0	74 (86.0)	104 (88.1)	61 (84.7)	133 (93.0)	198 (61.5)	242 (62.5)	155 (68.9)	275 (61.1)
1	8 (9.3)	9 (7.6)	11 (15.3)	9 (6.3)	67 (20.8)	83 (21.4)	42 (18.7)	89 (19.8)
≥ 2	4 (4.7)	5 (4.2)	0	1 (0.7)	57 (17.7)	62 (16.0)	28 (12.4)	86 (19.1)
Time since first diagnosis of PsA, mean (SD), year	0.4 (0.4)	0.5 (0.3)	0.5 (0.3)	0.5 (0.3)	10.1 (8.7)	9.5 (8.0)	8.6 (6.8)	9.8 (7.5)
Patients with specific disease characteristics, n (%)								
Enthesitis	49 (57.0)	79 (66.9)	46 (63.9)	86 (60.1)	205 (63.7)	254 (65.6)	130 (57.8)	292 (64.9)
Dactylitis	26 (30.2)	32 (27.1)	26 (36.1)	47 (32.9)	128 (39.8)	136 (35.1)	96 (42.7)	161 (35.8)
Psoriasis affecting ≥ 3% of BSA	42 (48.8)	57 (48.3)	37 (51.4)	70 (49.0)	148 (46.0)	210 (54.3)	116 (51.6)	209 (46.4)
Nail Psoriasis	60 (69.8)	75 (63.6)	47 (65.3)	99 (69.2)	201 (62.4)	262 (67.7)	152 (67.6)	300 (66.7)
Disease and QOL scores, mean (SD)								
TJC68	16.1 (12.2)	18.0 (13.6)	20.7 (16.4)	18.5 (14.4)	19.4 (13.2)	21.0 (15.3)	18.6 (13.9)	21.0 (14.8)
SJC66	8.5 (5.6)	9.3 (8.0)	10.6 (9.7)	10.4 (9.2)	9.4 (7.0)	10.9 (9.0)	10.4 (8.6)	10.6 (9.0)
DAS28-CRP	4.4 (1.1)	4.5 (1.1)	4.6 (1.1)	4.5 (1.1)	4.6 (1.0)	4.8 (1.1)	4.5 (1.1)	4.7 (1.1)
HAQ-DI	1.0 (0.6)	1.1 (0.6)	1.1 (0.7)	1.2 (0.6)	1.3 (0.6)	1.3 (0.6)	1.2 (0.7)	1.3 (0.6)
Patient global assessment, VAS 0-100 mm	55.7 (20.2)	56.1 (22.3)	55.5 (23.5)	54.7 (20.6)	59.1 (21.4)	58.8 (21.6)	55.9 (22.4)	57.5 (21.7)
Physician global assessment, VAS 0-100 mm	53.6 (17.4)	53.6 (17.2)	54.9 (18.7)	53.4 (18.9)	54.8 (18.1)	57.6 (17.1)	55.7 (19.0)	54.4 (19.0)

BMI, body mass index; BSA, body surface area; DAS-28-CRP, Disease Activity Score in 28 joints-C-reactive protein; HAQ-DI, Health Assessment Questionnaire-Disability Index, LD, loading dose; PsA, psoriatic arthritis; QOL, quality of life; SEC, secukinumab; SJC66, swollen joint count assessed in 66 joints; TJC68, tender joint count assessed in 68 joints; TNFi, tumor necrosis factor alpha inhibitor; VAS, visual analog scale.

Figure 1. ACR Response at Week 16 by Treatment and Time Since Diagnosis



* *P* < .05 vs placebo. LD, loading dose; PBO, placebo; SEC, secukinumab

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) can progress quickly and lead to irreversible damage within 2 years of initial assessment if not treated.[1] Secukinumab (SEC), a selective interleukin 17A inhibitor, demonstrated rapid and sustained improvement in the signs and symptoms of PsA in the phase 3 FUTURE 1-5 studies; the mean time since PsA diagnosis (TSD) was 6 to 7 years in these studies.[2-6] To better understand the effect of earlier treatment in patients (pts) with PsA, we evaluated SEC treatment in pts with a TSD of ≤ 1 year or > 2 years.

Methods: Data from pts enrolled in FUTURE 2 (NCT01752634), 3 (NCT01989468), 4 (NCT02294227), and 5 (NCT02404350) were pooled and included in this hypothesis-generating analysis (N = 1803). Pts received SEC 300 or 150 mg with subcutaneous loading dose (LD), 150 mg without LD, or placebo (PBO). Pts were classified into 2 groups according to TSD: ≤ 1 year or > 2 years. Response to treatment was assessed using multiple outcome measures, including ACR20/50/70, PASI75/90/100, and additional disease activity and quality of life (QOL) measures at week 16. Responses were calculated using nonresponder imputation. No adjustment was made for multiple comparisons.

Results: Overall, 419 pts (23.2%) had a TSD ≤ 1 year; 1384 (76.8%) had a TSD > 2 years. At baseline, most pt characteristics were comparable between the 2 TSD groups (**Table 1**). Dactylitis and prior treatment with TNF inhibitors were more common in pts with a TSD > 2 years at baseline; the mean tender joint count (TJC) was also higher in these pts. At week 16, ACR20/50/70 response rates were higher with SEC than with PBO, regardless of TSD (**Figure 1**). SEC 300 mg was associated with higher ACR response rates than SEC 150 mg. In general, ACR response rates were slightly numerically higher in pts with a TSD ≤ 1 year, especially in those treated with SEC 300 mg. SEC also led to higher response rates in other efficacy outcomes compared with PBO, including resolution of enthesitis and dactylitis and improvement of skin and nail psoriasis (**Table 2**). In SEC-treated pts, the proportion of pts with swollen joint count = 0, TJC = 0, CRP ≤ 10 mg/L, and improved SF-36 mental component score were numerically higher in pts with a TSD ≤ 1 year vs those with a TSD > 2 years. Common adverse events in SEC-treated pts (TSD ≤ 1 year/ > 2 years) were nasopharyngitis (8.3%/6.1%), headache (6.2%/3.6%), and upper respiratory tract infection (5.1%/4.7%). Inflammatory bowel disease was reported in 4 pts (SEC, n = 3; PBO, n = 1), all in pts with a TSD > 2 years. Major adverse cardiovascular events occurred in 2 pts (SEC 300 mg, TSD > 2 years). No tuberculosis events were reported.

Conclusion: SEC treatment led to improvement in clinical outcomes and QOL measures in pts with PsA regardless of TSD. Pts with a TSD of ≤ 1 year had higher clinical response rates in some outcome measures, suggesting that earlier treatment may lead to better outcomes in pts with PsA.

Table 2. Response in Additional Outcomes at Week 16[a]

Responders, n/n (%)	Time Since Diagnosis ≤ 1 Year				Time Since Diagnosis > 2 Years			
	SEC 300 mg (n = 86)	SEC 150 mg (n = 118)	SEC 150 mg, No LD (n = 72)	Placebo (n = 143)	SEC 300 mg (n = 322)	SEC 150 mg (n = 387)	SEC 150 mg, No LD (n = 225)	Placebo (n = 450)
Leeds enthesitis index, complete resolution	**29/49 (59.2)**	37/79 (46.8)	20/46 (43.5)	28/86 (32.6)	**108/205 (52.7)**	**114/254 (44.9)**	**51/130 (39.2)**	83/292 (28.4)
Leeds dactylitis index, complete resolution	**14/26 (53.8)**	11/32 (34.4)	13/26 (50.0)	13/47 (27.7)	**73/128 (57.0)**	**70/136 (51.5)**	**43/96 (44.8)**	49/161 (30.4)
TJC68 = 0	**23/86 (26.7)**	**20/118 (16.9)**	8/72 (11.1)	8/143 (5.6)	**56/322 (17.4)**	**53/387 (13.7)**	22/225 (9.8)	26/450 (5.8)
SJC66 = 0	**39/86 (45.3)**	**40/118 (33.9)**	16/72 (22.2)	21/143 (14.7)	**95/322 (29.5)**	**95/387 (24.5)**	**59/225 (26.2)**	68/450 (15.1)
CRP ≤ 10 mg/L	**18/18 (100.0)**	17/27 (63.0)	11/15 (73.3)	18/38 (47.4)	**58/85 (68.2)**	**60/100 (60.0)**	**34/54 (63.0)**	34/115 (29.6)
PASI90	**22/42 (52.4)**	**26/57 (45.6)**	**12/37 (32.4)**	8/70 (11.4)	**73/148 (49.3)**	**68/210 (32.4)**	**32/116 (27.6)**	14/209 (6.7)
PASI100	**15/42 (35.7)**	**13/57 (22.8)**	8/37 (21.6)	7/70 (10.0)	**50/148 (33.8)**	**43/210 (20.5)**	**15/116 (12.9)**	11/209 (5.3)
mNAPSI75	14/55 (25.5)	**28/70 (40.0)**	11/47 (23.4)	14/95 (14.7)	**59/194 (30.4)**	**68/252 (27.0)**	**33/147 (22.4)**	36/293 (12.3)
HAQ-DI, MCID ≥ 0.35	**49/86 (57.0)**	54/118 (45.8)	34/72 (47.2)	55/143 (38.5)	**177/320 (55.3)**	**189/386 (49.0)**	**123/225 (54.7)**	151/450 (33.6)
SF-36 MCS, MCID ≥ 2.5	45/86 (52.3)	**64/118 (54.2)**	**42/72 (58.3)**	57/143 (39.9)	149/322 (46.3)	**182/387 (47.0)**	**110/225 (48.9)**	181/450 (40.2)

CRP, C-reactive protein; HAQ-DI, Health Assessment Questionnaire–Disability Index; LD, loading dose; MCID, minimal clinically important difference; mNAPSI75, ≥ 75% improvement in the modified Nail Psoriasis Severity Index; PASI75, -90, and -100, ≥ 75%, ≥ 90%, and 100% improvement in the Psoriasis Area and Severity Index; PsA, psoriatic arthritis; SEC, secukinumab; SF-36 MCS, 36-Item Short Form Survey Mental Component Score; SJC66, swollen joint count assessed in 66 joints; TJC68, tender joint count assessed in 68 joints; VAS, visual analog scale.

[a] Bold response rates indicate statistical significance ($P < .05$) vs placebo

References

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2. Mease PJ, et al. *RMD Open*. 2018;4:e000723.
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6. Mease PJ, et al. *Ann Rheum Dis*. 2018;77:890-897.

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Abstract Number: 0890

Ixekizumab Treatment Improves Fatigue, Spinal Pain, Stiffness, and Sleep in Patients with Nonradiographic Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

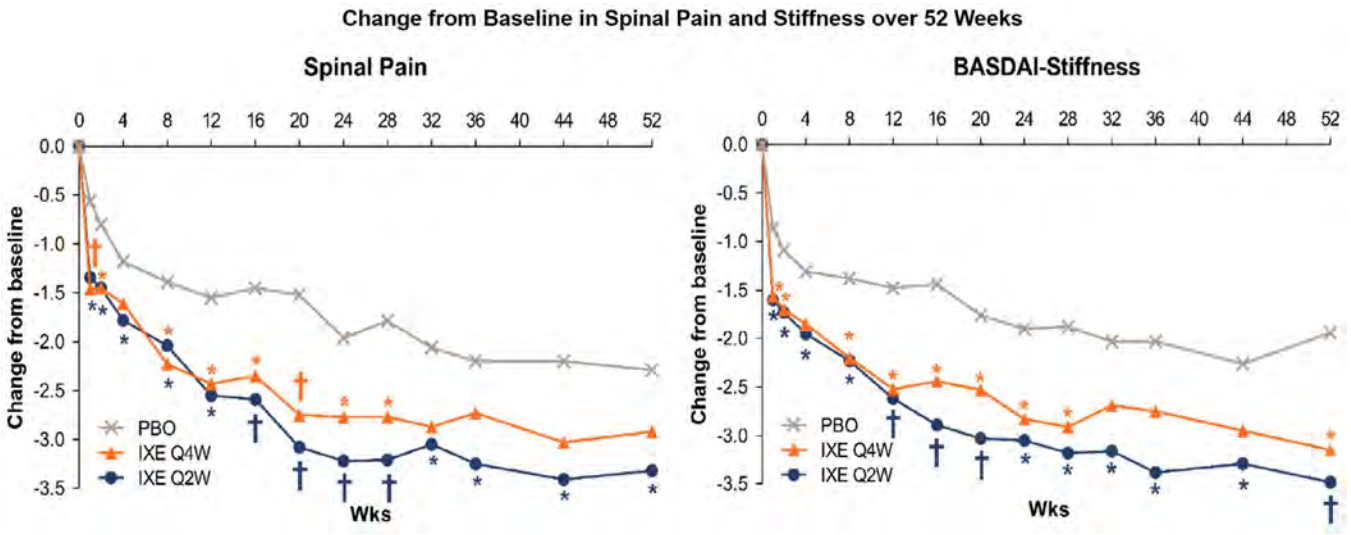
Session Time: 9:00AM–11:00AM

Background/Purpose: Common symptoms of axial spondyloarthritis (axSpA) include fatigue, spinal pain, stiffness, and sleep problems, which can impair health-related quality of life. Ixekizumab (IXE) treatment shows efficacy in active non-radiographic axSpA (nr-axSpA).[1] The objective of this study was to assess fatigue, spinal pain, stiffness, and sleep with IXE treatment versus placebo in patients (pts) with active nr-axSpA up to 16 and 52 weeks.

Table: Least squares mean (standard error) change from baseline-ITT population (mixed-effect model of repeated measures)

Measure	Timepoint	PBO N=105	IXE Q4W N=96	IXE Q2W N=102
Spinal pain[a]	Week 16	-1.45 (0.244)	-2.35 (0.248)*	-2.59 (0.244)†
	Week 52	-2.29 (0.350)	-2.92 (0.305)	-3.32 (0.304)*
Spinal pain at night[a]	Week 16	-1.71 (0.262)	-2.43 (0.267)	-2.79 (0.263)*
	Week 52	-2.25 (0.358)	-3.04 (0.312)	-3.58 (0.311)*
BASDAI-stiffness[b,c]	Week 16	-1.44 (0.242)	-2.44 (0.246)*	-2.89 (0.242)†
	Week 52	-1.94 (0.332)	-3.15 (0.290)*	-3.48 (0.289)†
Fatigue severity NRS[d]	Week 16	-1.4 (0.24)	-2.1 (0.24)*	-1.9 (0.24)
	Week 52	-2.1 (0.38)	-2.6 (0.32)	-2.7 (0.32)
Sleep disturbance[e]	Week 16	-2.3 (0.45)	-2.0 (0.45)	-2.5 (0.45)
	Week 52	-2.9 (0.63)	-3.6 (0.52)	-3.6 (0.53)
Patient Global Assessment of Disease Activity[f]	Week 16	-1.30 (0.246)	-2.32 (0.251)*	-2.64 (0.247)†
	Week 52	-1.81 (0.378)	-2.77 (0.320)	-3.30 (0.321)*

*P<.05 vs PBO; †P≤.001 vs PBO. ITT population: all randomized pts. Pts needing rescue treatment after Week 16 per investigator could switch to open-label IXE Q2W; observations at visits thereafter not included in analyses. Baseline values similar across treatments. Numerical improvements in BASDAI-fatigue not significant vs PBO. [a]Scored 0 (no pain) to 10 (most severe pain) on NRS [b]Mean score BASDAI questions 5 (intensity) and 6 (duration) [c]Scored 1–10 on NRS [d]Scored 0 (no fatigue) to 10 (as bad as you can imagine) [e]Jenkins Sleep Evaluation Questionnaire scored 0 to 20: each of 4 items scored 0 (0 days) to 5 (22–30 days) [f]Scored 0 (not active) to 10 (very active) on NRS BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; BL=baseline; ITT=intent-to-treat IXE=Ixekizumab; N=number of pts in ITT population; NRS=numeric rating scale; PBO=placebo; pt=patient; Q2W=every 2 weeks; Q4W=every 4 weeks; vs=versus; wk=week.



*P<.05 vs PBO; †P≤.001 vs PBO. Significant differences between placebo and IXE Q4W and IXE Q2W are shown by orange and blue symbols, respectively. Changes from BL (Least squares mean) up to Wk 52 were analysed using MMRM analysis in the ITT population, which included all randomized pts. BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; BL=baseline; ITT=intent-to-treat IXE=Ixekizumab; MMRM=mixed-effects model of repeated measures; PBO=placebo; pt=patient; Q2W=every 2 weeks; Q4W=every 4 weeks; vs=versus; wk=week

Methods: In COAST-X, pts with active nr-axSpA were randomized to 52 weeks of double-blind IXE 80 mg once every 4 weeks (Q4W) or every 2 weeks (Q2W), or placebo. Data were collected from baseline to Week 52.

Results: At Week 16, IXE Q4W significantly improved fatigue, spinal pain, and stiffness, and IXE Q2W improved spinal pain, spinal pain at night, and stiffness vs placebo (Table). At Week 52, IXE Q4W significantly improved stiffness, and IXE Q2W improved spinal pain, spinal pain at night, and stiffness vs placebo. Numeric improvements in sleep were not significant vs placebo. Week 1, and up to Week 16, IXE Q4W and Q2W significantly reduced spinal pain and stiffness vs PBO; stiffness was significantly reduced vs placebo up to Week 52 (Figure).

Conclusion: IXE Q4W and/or Q2W significantly improved spinal pain, spinal pain at night, and stiffness vs placebo at 16 and 52 weeks in pts with nr-axSpA. IXE Q4W also improved fatigue at 16 weeks in these pts. Numerical improvements in sleep were not significant vs placebo.

Reference:

1. Deodhar A, et al. *Lancet.* 2020;395(10217):53-64.

Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **P. Rahman**, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5; **H. Marzo-Ortega**, Novartis, 2, 5, 8, Janssen, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, UCB, 5, 8, AbbVie Inc., 5, 8, Celgene, 5, 8, Takeda Pharmaceutical Company, 5, 8; **V. Strand**, AbbVie, 5, Amgen, 5, Celltrion, 5, Janssen, 5, Merck, 5, Novartis, 5, Regeneron, 5, Sanofi, 5, UCB, 5, Genentech/Roche, 5, GSK, 5, Pfizer, 5, Bayer, 5, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, Galapagos, 5, Lilly, 5, Gilead, 5, Samsung, 5, Servier, 5,

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Abstract Number: 0891

Four-Year Efficacy and Safety of Guselkumab in Psoriasis Patients with and Without Psoriatic Arthritis: A Pooled Analysis from VOYAGE 1 and VOYAGE 2

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Guselkumab (GUS), a fully human monoclonal antibody, selectively binds and blocks IL-23. VOYAGE 1 and VOYAGE 2 are two ongoing Phase 3, randomized, double-blind, placebo (PBO)/active comparator-controlled clinical trials of GUS in patients with moderate-to-severe psoriasis (PsO). This post-hoc analysis reported pooled results through 4 years among a subgroup of moderate-to-severe PsO patients with self-reported PsA at baseline.

Methods: 1829 patients were randomized to GUS 100 mg at Weeks 0, 4, and 12, then every 8 weeks (q8wk); PBO at Weeks 0, 4, and 12, GUS at Weeks 16 and 20 then q8wk; or adalimumab (ADA) 80 mg at Week 0, 40 mg at Week 1, then 40 mg q2wk until Week 47 (VOYAGE 1) or Week 23 (VOYAGE 2). In VOYAGE 1, all patients received open-label GUS 100 mg q8wk during Weeks 52-204. VOYAGE 2 incorporated a randomized withdrawal study design, followed by open-label GUS during Weeks 76-204. Pooled subgroup analyses using the combined GUS group were conducted based on self-reported PsA status at baseline. Efficacy based on Investigator Global Assessment (IGA) score and Psoriasis Area and Severity Index (PASI) response was assessed using prespecified treatment failure rules (nonresponder status for all time points after discontinuing due to lack of efficacy, worsening of PsO, or use of a prohibited treatment).

Results: For pooled VOYAGE 1 and VOYAGE 2 patients (N=1721), combined GUS and ADA→GUS response rates at Weeks 100, 156, and 204 were: PASI 90 80.6%, 80.0%, and 80.4%; PASI 100 50.1%, 49.9%, and 52.2%; IGA 0/1 83.6%, 83.3%, and 81.7%; and IGA 0 54.3%, 52.9%, and 53.9, respectively. In the pooled subgroup analysis of patients with and without PsA, response rates were similar across the Week 100, Week 156, and Week 204 evaluations (Table). Rates of adverse events through Week 204 were comparable for patients with PsA vs those without PsA at baseline.

Table: Pooled Guselkumab Response Rates

	Without PsA at Baseline			With PsA at Baseline		
	Wk 100	**Wk 156**	**Wk 204**	**Wk 100**	**Wk 156**	**Wk 204**
	N=1301	N=1239	N=1191	N=289	N=276	N=264
PASI 90	1049 (80.6%)	1001 (80.8%)	964 (80.9%)	233 (80.6%)	211 (76.4%)	206 (78.0%)
PASI 100	648 (49.8%)	631 (50.9%)	635 (53.3%)	149 (51.6%)	125 (45.3%)	125 (47.3%)
	N=1300	N=1235	N=1189	N=288	N=276	N=264
IGA 0/1	1086 (83.5%)	1042 (84.4%)	979 (82.3%)	241 (83.7%)	217 (78.6%)	208 (78.8%)
IGA 0	702 (54.0%)	664 (53.8%)	649 (54.6%)	160 (55.6%)	135 (48.9%)	134 (50.8%)

IGA, Investigator Global Assessment; PASI, Psoriasis Area and Severity Index; Wk, week

Table. Pooled Guselkumab Response Rates

Conclusion: Among GUS-treated patients with moderate-to-severe PsO with and without self-reported PsA at baseline, sTable, durable, and high levels of skin responses, as well as comparable safety outcomes, through 4 years were observed.

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Abstract Number: 0892

Long-Term Safety Profile of Ixekizumab Treatment in Patients with Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Ixekizumab, a high-affinity monoclonal antibody that selectively targets interleukin-17A, has demonstrated efficacy in the treatment of the axial spondyloarthritis (axSpA) spectrum (ankylosing spondylitis and non-radiographic axSpA) in patients who are naive to biologic treatments and in those with an inadequate response or intolerance to a tumor necrosis factor (TNF) inhibitor. The objective of this study was to report the long-term safety profile for ixekizumab in patients with axSpA, using integrated safety data from the COAST clinical trial program.

Methods: Safety data from 3 clinical studies and long-term extensions were integrated. Study populations were composed of patients naïve to biological disease-modifying rheumatic disease treatment (bDMARD-naïve) or TNF-experienced, including patients who had intolerance to bDMARDs. The integrated safety population included all patients with axSpA who received ≥1 dose of ixekizumab. Incidence rates (IR) per 100 person-years with 95% confidence interval (CI) and the number of patients were reported. Adverse event (AE) terms were derived from MedDRA (v221.0).

Results: The integrated safety population consisted of 932 patients with a total of 1849 person-years. Among 932 patients with ≥1 TEAE, 775 (IR 41.9, 95% CI 39.1–45.0) TEAEs were reported, of which 95 (IR 5.1, 95% CI 4.2–6.3) were severe (Table). Nasopharyngitis (IR 8.8, 95% CI 7.5–10.2) and upper respiratory infections (IR 6.0, 95% CI 5.0–7.2) were the most commonly reported TEAEs. A total of 90 (IR 4.9, 95% CI 4.0–6.0) SAEs occurred, and 62 AEs led to treatment discontinuation (IR 3.4, 95% CI 2.6–4.3). Injection site reactions occurred in 155 patients (IR 8.4, 95% CI 7.2–9.8). The IR of SAEs declined from year 1 (IR 6.3, 95% CI 4.9–8.3) through 2 years of follow up (IR 4.5, 95% CI 2.8–7.3), as did discontinuations due to AEs (year 1: IR 5.1, 95% CI 3.7–6.8; year ≥2: IR 1.9, 95% CI 0.9–3.9). Allergic reactions/hypersensitivity occurred in 86 patients and decreased slightly from year 1 (IR 6.6, 95% CI 5.1–8.5) through year 3 (IR 3.5, 95% CI 2.0–6.0). The IR of neutropenia (grade 1 or worse) was 8.4 (95% CI 7.2–9.9, and candidiasis (invasive and oral) was 1.4 (95% CI 1.0–2.1). A total of 20 serious infections, 17 reports of adjudicated inflammatory bowel disease, and 1 incidence of potential (unconfirmed) anaphylaxis occurred. No tuberculosis was reported (Table).

Conclusion: This integrated safety analysis demonstrates the overall safety profile of ixekizumab for treatment of axSpA, shows no new signals, and is consistent with that previously reported in previous studies including psoriasis and psoriatic arthritis indications.

Table. Integrated Safety Outcomes

	Pooled Ixekizumab (N=932) n (IR[a])	95% CI
Total patient years	1849.0	
TEAEs[b]	775 (41.9)	39.1 – 45.0
Nasopharyngitis	162 (8.8)	7.5 – 10.2
Upper respiratory tract infection	111 (6.0)	5.0 – 7.2
SAEs[b]	90 (4.9)	4.0 – 6.0
Discontinuations due to AEs	62 (3.4)	2.6 – 4.3
Deaths[c]	3 (0.2)	0.1 – 0.5
Major adverse cardiac events	4 (0.2)	0.1 – 0.6
Infections	511 (27.6)	25.3 – 30.1
Candida[d]	26 (1.4)	1.0 – 2.1
Serious infections	20 (1.1)	0.7 – 1.7
Opportunistic infections[e]	17 (0.9)	0.6 – 1.5
Injection site reactions	155 (8.4)	7.2 – 9.8
Iridocyclitis	52 (2.8)	2.1 – 3.7
Depression	19 (1.0)	0.7 – 1.6
Inflammatory bowel disease[f]	17 (0.9)	0.6 – 1.5
Ulcerative colitis	10 (0.5)	0.3 – 1.0
Crohn's disease	7 (0.4)	0.2 – 0.8

AE=adverse event; CI=confidence interval; IR=incidence rate; SAE=serious adverse event; TEAE=treatment-emergent adverse event

[a]Incidence rate per 100 patient-years

[b]Deaths due to suicide (1), sepsis (1), and general disorders (1)

[c]Patients with ≥1 event

[d]Candida infections included oral Candida, oral candidiasis, oral fungal infection, esophageal candidiasis, fungal esophagitis, genital Candida, and skin Candida

[e]Opportunistic infections included oral candidiasis, hepatitis B reactivation, herpes simplex (invasive), and herpes zoster

[f]Confirmed by adjudication

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Abstract Number: 0893

Is It Feasible to Achieve Recommended Therapeutic Target Objective in Patients with Axial Spondyloarthritis in Clinical Practice? Data from the SpA-paz Cohort

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

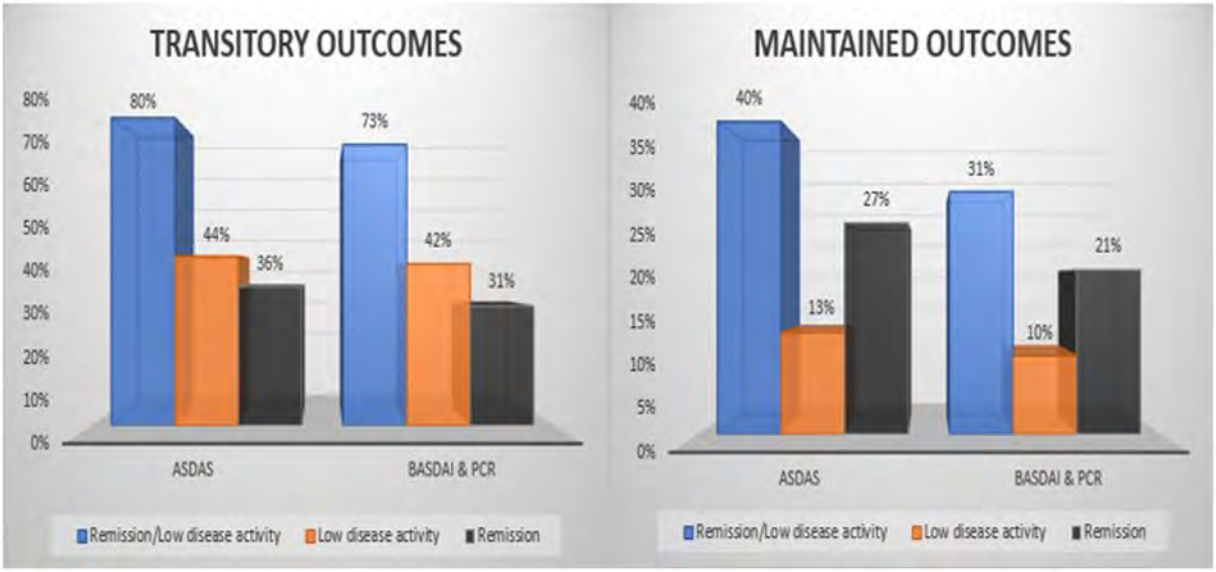
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: to analyze the frequency of patients with axSpA achieving maintained remission (R) or low disease activity (LDA) after receiving biological therapy. Secondary objectives included: i) to assess if the activity index used influences the frequency of maintained R/LDA, ii) analyze the prognostic factors for achieving maintained R/LDA.

Methods: an observational, longitudinal study of a prospective cohort (SpA-Paz) including all patients with axSpA who initiated biological treatment between the years 2003-2017. Demographic, clinical and analytical data were collected at the beginning of treatment and clinical disease activity measured by BASDAI&CRP and ASDAS every 6 months for at least 2 years. Maintained R was defined as (BASDAI < 2 & normal CRP and / or ASDAS < 1.3) and maintained LDA (BASDAI < 4 & normal CRP and / or ASDAS < 2.1) on at least 3 consecutive visits. Statistical analysis: i) measures of central tendency and dispersion for quantitative variables and frequencies for qualitative variables; ii) univariate and multivariate analysis of binomial logistic regression model and calculation of OR and 95% CI.



Graphics

Results: Out of 186 patients with axSpA who initiated their first biological therapy during the study period, 63% were men with a mean age of 54 ± 14.1 years. 75.3% of the patients had radiographic axSpA and 74.7% were HLA-B27 positive. Other baseline characteristics are shown in *Table 1*. Overall, 80% of the patients achieved ASDAS R/LDA (R36%/LDA44%) in at least one of the visits after 2 years of follow-up, but only 40% (R27%/LDA13%) of the patients fulfilled the maintained ASDAS R/LDA state. On the other hand, 73% of patients were classified as BASDAI&CRP R/LDA (R31%/LDA42%) in at least one of the visits, but only 31% (R21%/LDA10%) of the patients obtained the maintained BASDAI&CRP R/LDA state. In the multivariate analysis, we observed an independent statistically significant association with male sex (OR=3.19; 95% CI=1.46-6.99), being younger at the beginning of the biological treatment (OR= 0.97; 95% CI=0.95-0.99) and the use of methotrexate (OR=3.07; 95% CI =1.39-6.78) in patients who achieved maintained BASDAI&CRP R/LDA and with male sex (OR=4.01; 95% CI=1.83-8.77), younger age at the beginning of the biological therapy (OR=0.96; 95% CI=0.94-0.99) and B27 positive (OR=4.30; 95% CI=1.68-11.01) in patients who achieved maintained ASDAS R/LDA.

Conclusion: Although most patients with axSpA who initiate biological therapy achieve the recommended therapeutic goal in the first two years of biological treatment, the percentage of patients who manage to maintain the R/LDA status is limited. In our study, maintained R was more frequent than maintained LDA, being somewhat higher when measured by ASDAS. This fact may suggest that patients who achieve maintained R have a greater inhibition of their inflammatory activity and, therefore, it remains in time. Male sex and younger age at the beginning of the biological therapy were the main baseline predictors for achieving maintained R /LDA.

Disclosure: K. Franco Gomez, None; **C. Plasencia-Rodriguez**, None; **M. Novella Navarro**, None; **D. Benavent Nunez**, Abbvie, 8, Roche, 8; **P. Bogas**, None; **R. Nieto**, None; **I. Monjo**, None; **L. Nuño**, None; **A. Villalba**, None; **D. Peiteado**, None; **A. Balsa-Criado**, None; **V. Navarro-Compán**, Novartis Pharma, 1, 5, 8, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, UCB, 5, 8.

Abstract Number: 0894

Efficacy and Safety of Neihulizumab (AbGn-168H) in Patients with Active Psoriatic Arthritis: 24-week Results from a Phase II Open Label Study

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Neihulizumab is a novel immune checkpoint agonistic antibody that binds to human CD162 (PSGL-1), thereby preferentially inducing apoptosis in late stage activated T cells. It is being tested in putative T-cell mediated inflammatory diseases including ulcerative colitis and graft versus host disease. To assess the efficacy and safety of Neihulizumab in patients with active psoriatic arthritis (PsA) in an open-label 24-week Phase II POC study.

Table 1. Demographic and Baseline Characteristics

Female, n (%)	12 (60%)
Age (years), median (min, max)	55.5 (42, 72)
BMI (kg/m^2), median (min, max)	33.06 (24.50, 42.50)
Race, n (%)	
White	18 (90%)
African American	0
American Indian or Alaska native	0
Asian	0
Others	2 (10%)
Duration of psoriatic arthritis (years), median (min, max)	4.5 (0.7, 30)
Duration of psoriasis (years), median (min, max)	25 (1.9, 47)
Methotrexate current use, n (%)	11 (55%)
Prior exposure to biologics, n (%)	10 (50%)
Disease-related assessment-Baseline values, median (min, max)	
Swollen joint count (SJC)	16.5 (3, 57)
Tender joint count (TJC)	31.5 (5, 65)
Patient's assessment of Pain (VAS)	63.5 (18, 96)
Patient's global assessment of disease activity (VAS)	55.0 (10, 96)
Physician's global assessment of disease activity (VAS)	64.5 (38, 87)
HAQ-DI	1.4375 (0.25, 2.125)
C-reactive protein (mg/L)	0.608 (0.021, 4.346)
DAS28 (CRP), median (min, max)	5.588 (3.249, 7.585)
Static physician's global assessment (sPGA), n (%)	
Clear	0
Almost clear	2 (12.5%)
Mild	7 (43.8%)
Moderate	7 (43.8%)
Severe	0
Target Lesion Psoriasis Severity Score (TLPSS), median (min, max)	5.5 (2, 9)

Methods: Twenty (20) patients with active PsA fulfilling Classification Criteria for Psoriatic Arthritis (CASPAR) were treated with 3 weekly doses plus 4 bi-weekly doses of 9 mg/kg IV Neihulizumab with follow-up at weeks 12, 16, 20, and 24. The primary endpoint was the proportion of patients achieving an ACR 20 response at Week 12. Safety was assessed throughout the study period.

Results: Twenty patients (20) were enrolled. The majority of the patients were female (12/20, 60.0%) and white (18/20, 90.0%). The median age was 55.5(42-72) years. The median duration of psoriatic arthritis was 4.5 (0.7-30) years. The median duration of psoriasis was 25 (1.9-47) years. Forty (40.0) % (8/20) of patients achieved ACR20 responder

Table 2. Summary of Efficacy Results at Week 12 and Week 24

Primary Endpoint	Week 12	Week 24*
ACR 20 (%)	40%	25%
Secondary Endpoints	Week 12	Week 24
ACR 50 (%)	30%	20%
ACR 70 (%)	10%	10%
ΔDAS28(CRP)#	-1.0	-0.7
ΔPain-VAS#	-8.0	-4.0
ΔHAQ-DI#	-0.2	-0.2
ΔTLPSS#	-2.4	-2.5
sPGA (clear or almost clear) (%)	53%	47%

*Last treatment at W10 #Mean change from baseline

Table 3. Overview of Adverse Events

Characteristics of Adverse Event (AE)	Treatment Emergent (N = 20)	Post-Treatment (N = 20)	Overall (N = 20)
With at least 1 AE	13 (65%)	5 (25%)	13 (65%)
With ≥ Grade 3 AEs	0	0	0
With at least 1 treatment-related AEs	7 (35%)	0	7 (35%)
With SAE	0	0	0
With AE leading to discontinuation of treatment*	1 (5%)	0	1 (5%)
With AE leading to discontinuation of study*#	1 (5%)	0	1 (5%)

*Foreign body reaction and #gout.

status at Week 12 in ITT population by Non-Responder Imputation. At week 12 the ACR50 and 70 response rates were 30%, and 10%, respectively. Analysis by DAS28(CRP) showed concordant result. Durability of ACR20/50/70 was maintained through week 24 for at least 50% of responders after the last treatment at Week 10. Neihulizumab treatment was well tolerated with no deaths, no serious AEs, and no severe AEs observed. The most frequent TEAEs overall (including the treatment period and follow-up period) were urinary tract infection (15.0%), psoriatic arthropathy (15.0%), headache (10.0%), sinus congestion (10.0%), and hematoma (10.0%).

Conclusion: Overall treatment of Neihulizumab was well tolerated in this study. Improvement was seen in efficacy parameters, suggesting there may be clinical utility with this novel agent for the treatment of psoriatic arthritis. Controlled studies are indicated

ClinicalTrials.gov Identifier: NCT02267642

Disclosure: S. Cohen, Abbvie, 2, 5, Pfizer, 2, 5, Gilead, 2, 5, Lilly, 2, 5; **J. Fiechtner**, None; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **J. Kaine**, None; **A. Kavanaugh**, Eli Lilly and Company, 5; **Y. Cheng**, None; **C. Chou**, AltruBio Inc., 3; **T. Cheng**, None; **S. Lin**, AltruBio, 1, 3; **M. Genovese**, Abbvie, 2, 5, Eli Lilly and Company, 2, 5, Galapagos, 2, 5, Gilead Sciences Inc., 2, 5, Pfizer, 2, 5, EMD Merck Serono, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, RPharm, 2, 5, Sanofi-Genzyme, 2, UCB, 5, Amgen, 5.

Abstract Number: 0895

Effects of Guselkumab, a Monoclonal Antibody That Specifically Binds to the p19-Subunit of Interleukin-23, on Dactylitis and Enthesitis in Patients with Active Psoriatic Arthritis: Pooled Results Through Week 24 from Two Phase 3 Studies

Dennis McGonagle[1], Iain McInnes[2], Atul Deodhar[3], Georg Schett[4], Philip Mease[5], May Shawi[6], Shelly Kafka[7], Chetan Karyekar[8], Alexa Kollmeier[9], Elizabeth Hsia[10], Xie Xu[11], Shihong Sheng[12], Prasheen Agarwal[12], Bei Zhou[12], Christopher Ritchlin[13] and Proton Rahman[14], [1]The University of Leeds, Leeds Institute for Rheumatic and Musculoskeletal Medicine, NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals Trust, Leeds, UK, Leeds, United Kingdom, [2]Institute of Infection, Immunity, and Inflammation, University of Glasgow, Glasgow, United Kingdom, [3]Oregon Health & Science University, Portland, OR, [4]Friedrich-Alexander-Universität Erlangen- Nuremberg, Erlangen, Germany, [5]Seattle Rheumatology Associates, P.L.L.C., Seattle, WA, [6]Janssen Global Services, LLC, Toronto, ON, Canada, [7]Janssen Scientific Affairs, LLC, Horsham, PA, [8]Janssen Global Services, LLC, Horsham, PA, [9]Janssen Research & Development, LLC, La Jolla, CA, [10]Janssen Research & Development, LLC and University of Pennsylvania Medical Center, Spring House, PA, [11]Janssen Research & Development, LLC, San Marcos, CA, [12]Janssen Research & Development, LLC, Spring House, PA, [13]Department of Medicine, University of Rochester Medical Center, Rochester, NY, [14]Memorial University of Newfoundland, Department of Medicine, St John's, Canada

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Guselkumab (GUS), a novel monoclonal antibody that specifically binds to the p19-subunit of IL-23, demonstrated efficacy in the Ph 3 DISCOVER-1 (D1) & DISCOVER-2 (D2) trials of patients (pts) with

Table. Pooled DISCOVER-1&2: associations resolution between dactylitis/enthesitis and joint/skin response

		ACR20	ACR50	ACR70		PASI75[a]	PASI90[a]
Dactylitis resolution[b]	**N**	**%pts**	**%pts**	**%pts**	**N**	**%pts**	**%pts**
Q4W	**373**	55*	34*	16*	**121**	78*	55*
Q8W	**375**	53*	31*	16*	**116**	80*	65*
PBO	**372**	26*	12*	5*	**115**	19*	10*
Enthesitis resolution[c]							
Q4W	**243**	34*	31*	11*	**187**	82*	63*
Q8W	**230**	40*	7*	12*	**162**	77*	62*
PBO	**255**	14*	13*	5*	**182**	19*	9*

* $p < 0.001$ (Chi-square)
[a] In pts with ≥3% BSA psoriasis & IGA ≥2 at W0
[b] In pts with D at W0
[c] In pts with E at W0

Table. Pooled DISCOVER-1&2: associations between dactylitis/enthesitis resolution and joint/skin response

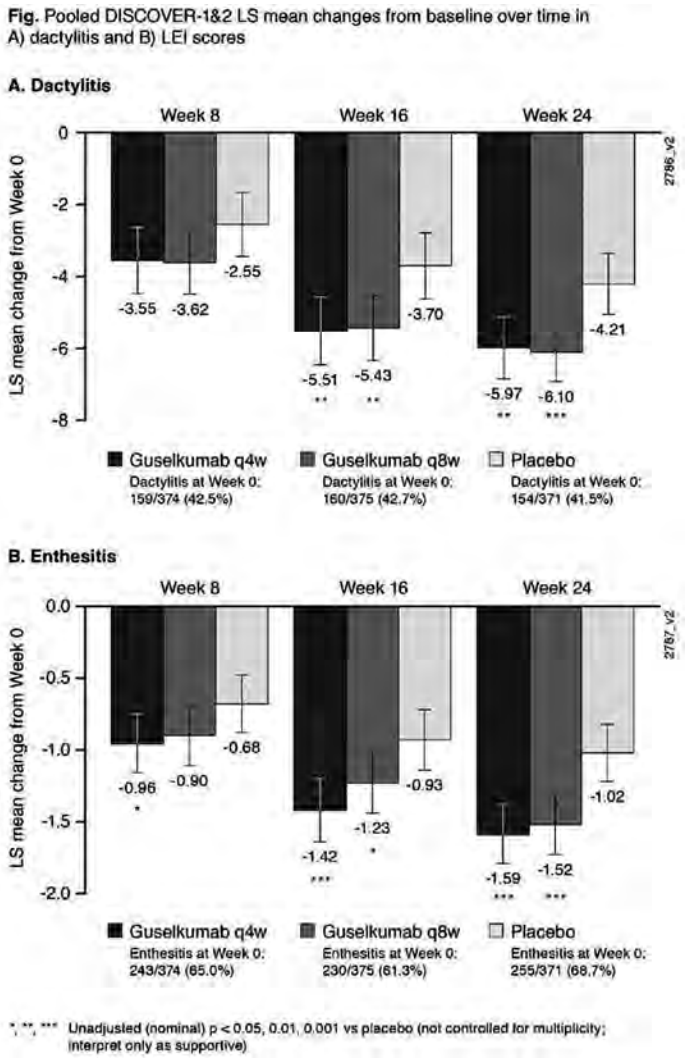

Figure. Pooled DISCOVER 1&2 LS Mean changes from baseline over time

active PsA.[1,2] Dactylitis & enthesitis, key PsA clinical manifestations, can be difficult to treat and may portend more significant disease burden.[3,4] This study assessed 1) changes in symptoms over time and 2) relationships between improvements in dactylitis or enthesitis and other PsA domains in pts with dactylitis or enthesitis at baseline.

Methods: Adults with active PsA despite standard therapies were eligible for D1 & D2. Approx. 30% of D1 pts previously received 1-2 TNF inhibitors; D2 pts were biologic-naïve. Pts were randomized 1:1:1 to GUS 100mg Q4W; GUS 100mg at W0, W4, Q8W; or PBO. Independent assessors evaluated dactylitis (total score: 0-60) & enthesitis (Leeds Enthesitis Index [LEI]; total score 0-6). Dactylitis and enthesitis findings through W24 were prespecified to be pooled across D1 & D2. P-values are unadjusted. We assessed changes in dactylitis and LEI scores over time (ANCOVA); associations between dactylitis or enthesitis resolution and ACR/PASI responses at W24 (Chi-square); and correlations between dactylitis or LEI and HAQ-DI/SF-36 change scores at W24 (Spearman's correlation). AEs through W24 were reported.[1,2]

Results: At W0, 42% of pooled D1+D2 pts had dactylitis; 65% had enthesitis. GUS improved dactylitis and LEI scores vs PBO at W8, W16, W24. GUS vs PBO differences were significant for dactylitis changes at W16 & W24 and LEI changes at W8 (Q4W only), W16 & W24; no dose response was observed (Fig). Rates of dactylitis or enthesitis

resolution by W24 were consistently significantly (p< 0.001) associated with ACR20/50/70 and PASI75/90 response (Table). In GUS-treated pts at W24, significant correlations were observed between dactylitis change scores and PASI (p< 0.001 Q4W; p=0.006 Q8W) and SF-36 MCS (p=0.038 Q4W; p=0.003 Q8W) changes, and between LEI and HAQ-DI change scores (p< 0.001 Q4W; p=0.005 Q8W). No consistent correlations/associations were observed between dactylitis or LEI scores and other clinical outcomes.

Conclusion: In PsA pts with dactylitis or enthesitis at W0, GUS improved dactylitis or LEI scores vs PBO by W8; treatment differences were significant at W16 & W24. Resolution of dactylitis or enthesitis was significantly associated with clinically meaningful improvements in PsA joint & skin symptoms. Improved dactylitis scores correlated with improved skin symptoms and mental health; improved LEI scores correlated with improved physical function.

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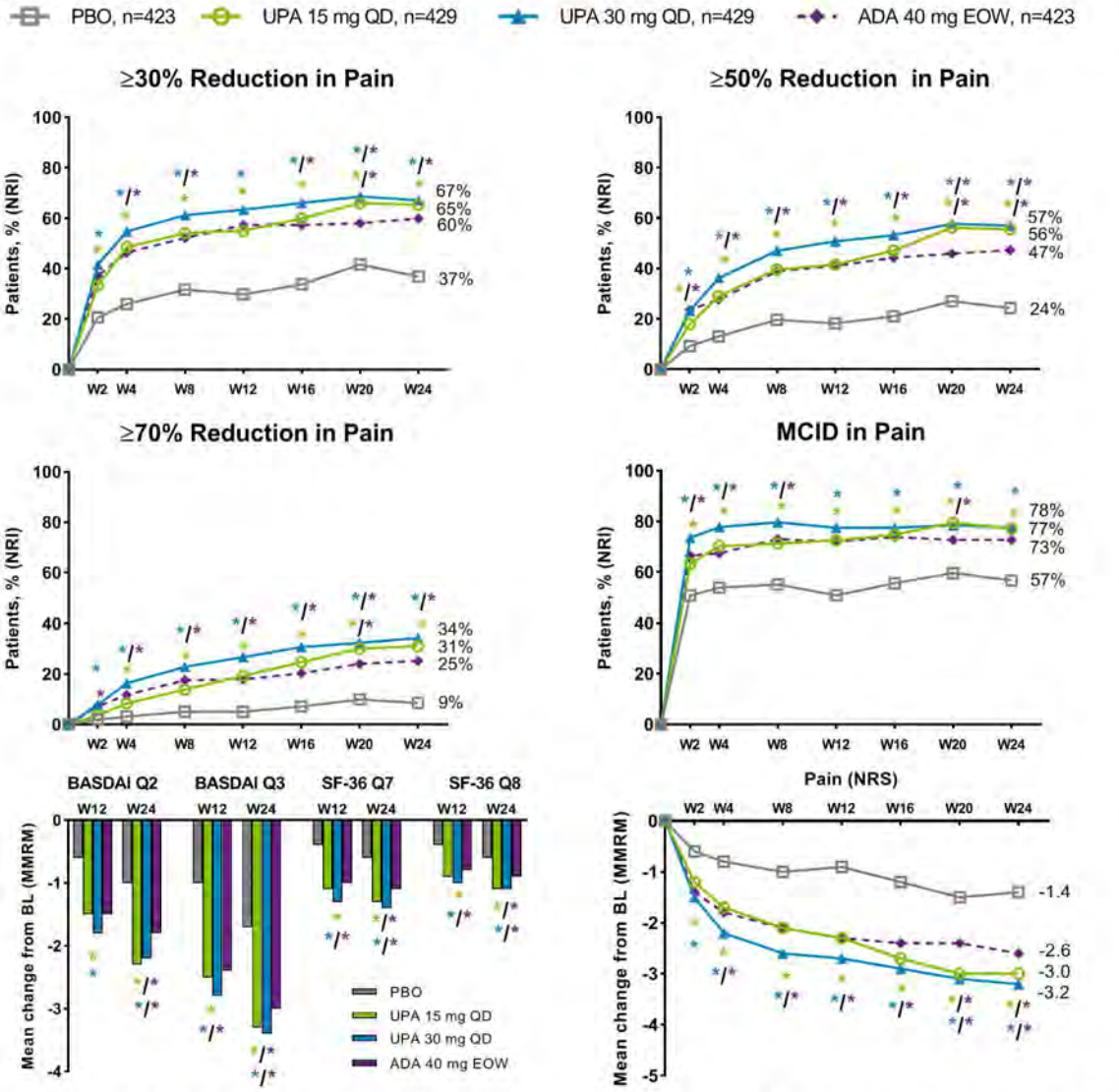
Disclosure: D. McGonagle, AbbVie Inc., 2, 8, Janssen Research & Development, LLC, 2; **I. McInnes**, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **G. Schett**, None; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **M. Shawi**, Janssen Global Services, LLC, 3, Johnson & Johnson, 1; **S. Kafka**, Janssen Scientific Affairs, LLC, 1, 3; **C. Karyekar**, Janssen Global Services, LLC, 3, Johnson & Johnson, 1, Janssen, 5; **A. Kollmeier**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **E. Hsia**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **X. Xu**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **S. Sheng**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **P. Agarwal**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **B. Zhou**, Janssen Reserach & Development, LLC, 3, Johnson & Johnson, 1; **C. Ritchlin**, None; **P. Rahman**, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5.

Abstract Number: 0896

Impact of Upadacitinib on Reducing Pain in Patients with Active Psoriatic Arthritis: Results from Two Phase 3 Trials in Patients with Inadequate Response to Non-biologic or Biologic DMARDs

Iain McInnes[1], William Tillett[2], Philip Mease[3], Kurt de Vlam[4], Louis Bessette[5], Ralph Lippe[6], Anna Maniccia[7], Patrick Zueger[7], Dai Feng[7], Koji Kato[8] and Andrew Östör[9], [1]Institute of Infection, Immunity, and Inflammation, University of Glasgow, Glasgow, United Kingdom, [2]Royal National Hospital for Rheumatic Diseases, Bath, UK; Department of Pharmacy and Pharmacology, University of Bath, Bath, UK, Bath, United Kingdom, [3]Seattle Rheumatology Associates, P.L.L.C., Seattle, WA, [4]Department of Rheumatology, University of Leuven, Belgium, Leuven, Belgium, [5]Laval University, Quebec, Canada, [6]AbbVie Deutschland GmbH & Co. KG, Wiesbaden, Germany, [7]AbbVie Inc., North Chicago, IL, [8]AbbVie Inc, North Chicago, IL, [9]Cabrini Medical Center, Monash University, Malvern, Victoria, Australia

Figure 1. PGA of Pain and BASDAI and SF-36 Pain Assessments in SELECT- PsA 1 Over 24 Weeks



ADA, adalimumab; MCID, minimal clinically important difference; MMRM, mixed-effects model for repeated measurements; NRI, non-responder imputation; NRS, numeric rating scale; PBO, placebo; PGA, patient's global assessment; SF-36, 36-item Short Form; UPA, upadacitinib.
All pain assessments evaluated in overall study population. N's for NRI analysis; nominal *P* value for a binary endpoint was constructed using the Cochran-Mantel-Haenszel test adjusting for the main stratification factor of current DMARD use (yes/no). In the MMRM, the within-subject dependence was modelled by an unstructured variance-covariance matrix. The fixed effects included the continuous baseline measurement, and treatment, visit, treatment-by-visit interaction and the stratification factor of current DMARD use (yes/no) as fixed factors
Blue asterisks: UPA 30 mg vs PBO; green asterisks: UPA 15 mg vs PBO; purple asterisks: UPA vs ADA. *Statistically significant at 0.05 level.

Figure 1

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

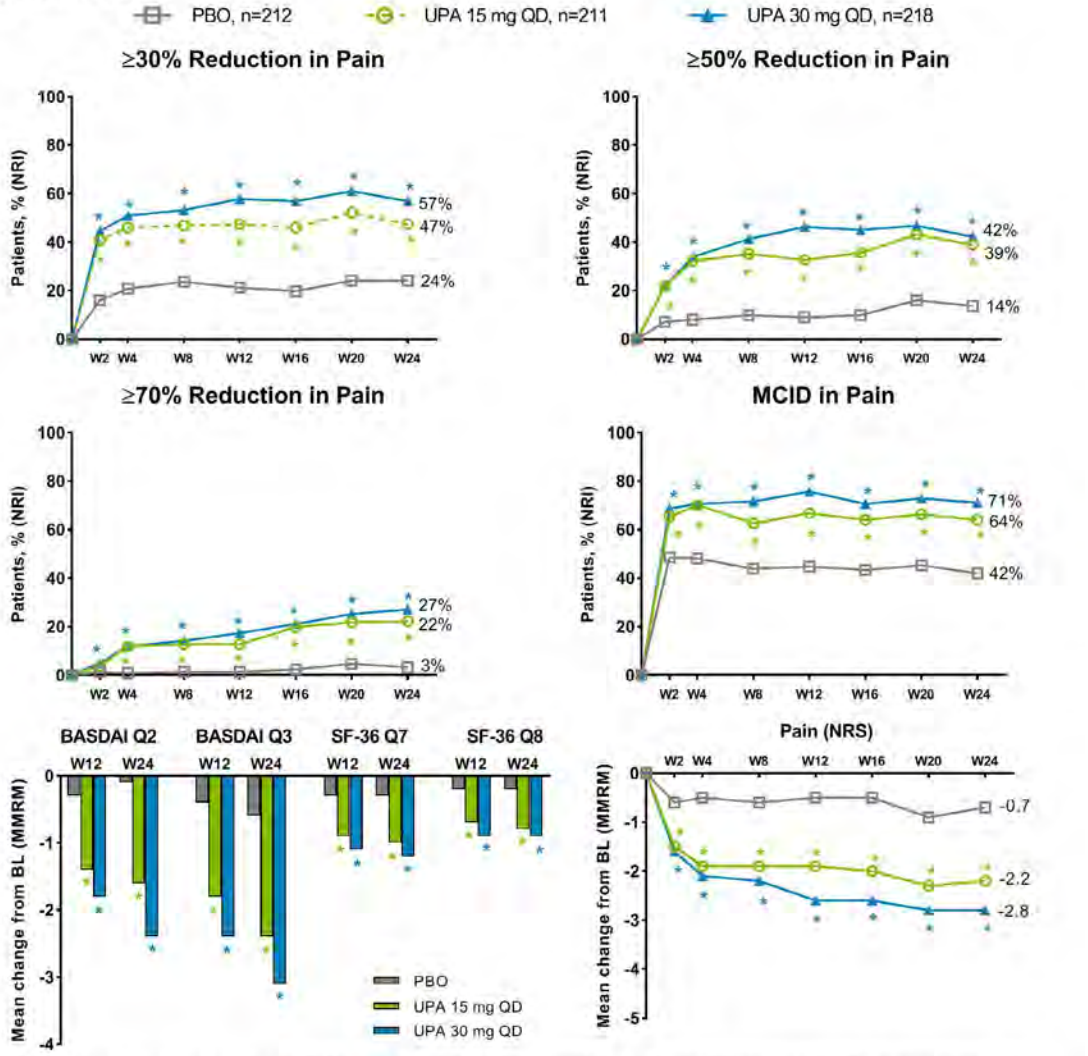
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Pain is a dominant symptom of psoriatic arthritis (PsA), and pain reduction is a priority for patients (pts) that is often assessed in clinical trials. Upadacitinib (UPA), a Janus kinase (JAK) inhibitor engineered for increased selectivity for JAK1 over JAK2, JAK3, and tyrosine kinase2, has demonstrated safety and efficacy in pts

Figure 2. PGA of Pain and BASDAI and SF-36 Pain Assessments in SELECT-PsA 2 Over 24 Weeks



MCID, minimal clinically important difference; MMRM, mixed-effects model for repeated measurements; NRI, non-responder imputation; NRS, numeric rating scale; PBO, placebo; PGA, patient's global assessment; SF-36, 36-item Short Form; UPA, upadacitinib.
All pain assessments evaluated in overall study population. N's for NRI analysis; nominal *P* value for a binary endpoint was constructed using the Cochran-Mantel-Haenszel test adjusting for the main stratification factor of current DMARD use (yes/no). In the MMRM, the within-subject dependence was modelled by an unstructured variance-covariance matrix. The fixed effects included the continuous baseline measurement, and treatment, visit, treatment-by-visit interaction and the stratification factor of current DMARD use (yes/no) as fixed factors.
Blue asterisks: UPA 30 mg vs PBO; green asterisks: UPA 15 mg vs PBO. *Statistically significant at 0.05 level.

Figure 2

with active PsA in the SELECT-PsA 1 and 2 studies.[1,2] The objective of this analysis was to compare the efficacy of UPA vs placebo (PBO) and adalimumab (ADA) on pain using different assessments through 24 weeks (wks).

Methods: The SELECT-PsA program enrolled adult pts with active PsA with prior inadequate response (IR) or intolerance to ≥1 non-biologic DMARD (SELECT-PsA 1; NCT03104400) or prior IR or intolerance to ≥1 biologic DMARD (SELECT-PsA 2; NCT03104374). Concomitant background therapy with ≤2 non-biologic DMARDs was allowed but not required. Pts were randomized to UPA 15 mg or UPA 30 mg once daily (QD) or PBO (both studies), or ADA 40 mg every other week (EOW; SELECT-PsA 1 only). Pain was assessed as proportion of pts achieving ≥30%, ≥50%, or ≥70% reduction from baseline (BL) in Pt's global assessment (PGA) of pain numeric rating scale (NRS) score (0–10), proportion of pts achieving minimal clinically important difference (MCID) in pain (defined as ≥1 point reduction or 15% reduction from BL on a 0–10 NRS)[3,4] and change from baseline in pain NRS (0–10) at all time points. In addition,

change from BL in BASDAI questions 2 (spinal pain) and 3 (joint pain/swelling) and 36-Item Short Form Survey (SF-36) questions 7 (bodily pain) and 8 (pain interference) at weeks 12 and 24 were assessed. Non-responder imputation was used for binary endpoints and mixed-effects model for repeated measurements for continuous endpoints. The statistical significance defined as $P< 0.05$ was exploratory in nature.

Results: In both studies, a significantly higher proportion of pts receiving UPA 15 mg QD and UPA 30 mg QD vs PBO achieved improvements in most pain endpoints as early as wk 2, and improvements were generally either sustained or increased through wk 24 (nominal $P<0.05$; **Figure 1** and **2**). A significant improvement with UPA vs PBO was also observed for change from BL in PGA of pain NRS scores over time, as well as in BASDAI spinal pain and joint pain/swelling and SF-36 bodily pain and pain interference at weeks 12 and 24 (**Figure 1** and **2**). In SELECT-PsA 1 significantly higher proportions of pts receiving UPA 30 mg QD vs ADA 40 mg EOW achieved improvements in most pain assessments as early as wk 2 which were sustained through wk 24; improvements in several assessments were also significantly greater with UPA 15 mg QD vs ADA 40 mg EOW at wk 24 (nominal $P < 0.05$; **Figure 1**).

Conclusion: In pts with active PsA who had inadequate response to non-biologic or biologic DMARDs, a greater proportion of pts treated with UPA vs PBO achieved rapid, significant, and clinically meaningful reductions in pain across multiple pain assessments. The reductions in pain were sustained over 24 wks.

1. McInnes I. et al. *Ann Rheum Dis*. 2020;79(Suppl 1):12-13.
2. Genovese M.C. et al. *Ann Rheum Dis.* 2020;79(Suppl 1):139.
3. Dworkin, R.H. et al. *J Pain.* 2008;9(2):105-121.
4. Salaffi F. et al. *Eur J Pain*. 2004;8:283–291.

Disclosure: I. McInnes, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **W. Tillett**, AbbVie, 5, 8, Amgen, 5, 8, Eli Lilly, 5, 8, Janssen, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB Pharma, 5, 8; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **K. de Vlam**, Eli Lilly and Company, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5, 8, Celgene, 2, 5, 8, Pfizer, 2, 5, 8; **L. Bessette**, Amgen, 1, 2, 3, BMS, 1, 2, 3, Janssen, 1, 2, 3, UCB, 1, 2, 3, AbbVie, 1, 2, 3, Pfizer, 1, 2, 3, Merck, 1, 2, 3, Celgene, 1, 2, 3, Sanofi, 1, 2, 3, Lilly, 1, 2, 3, Novartis, 1, 2, 3, Gilead, 2, 6, 8; **R. Lippe**, AbbVie Inc., 1, 3; **A. Maniccia**, AbbVie Inc., 1, 3, 4; **P. Zueger**, AbbVie Inc., 1, 3; **D. Feng**, AbbVie Inc., 1, 2; **K. Kato**, AbbVie Inc., 1, 3, 4; **A. Östör**, AbbVie, 5, Roche, 5, Janssen, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, Gilead, 5, Paradigm, 5, UCB Pharma, 5, Bristol-Myers Squibb, 5.

Abstract Number: 0897

Temporal Achievement of Clinical Response and Inactive Disease Status in Patients with Axial Spondyloarthritis Treated with Etanercept

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SESSION INFORMATION

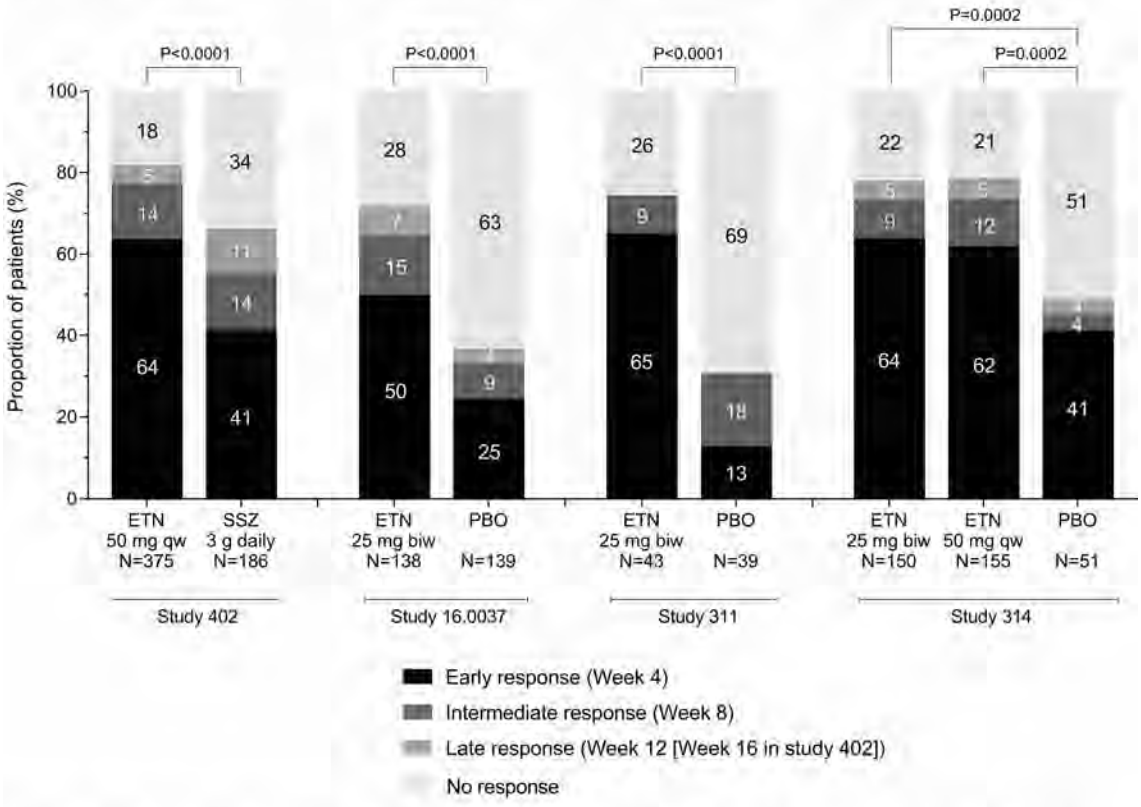
Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Figure 1. Proportions of patients achieving an early, intermediate, or late ASAS20 response



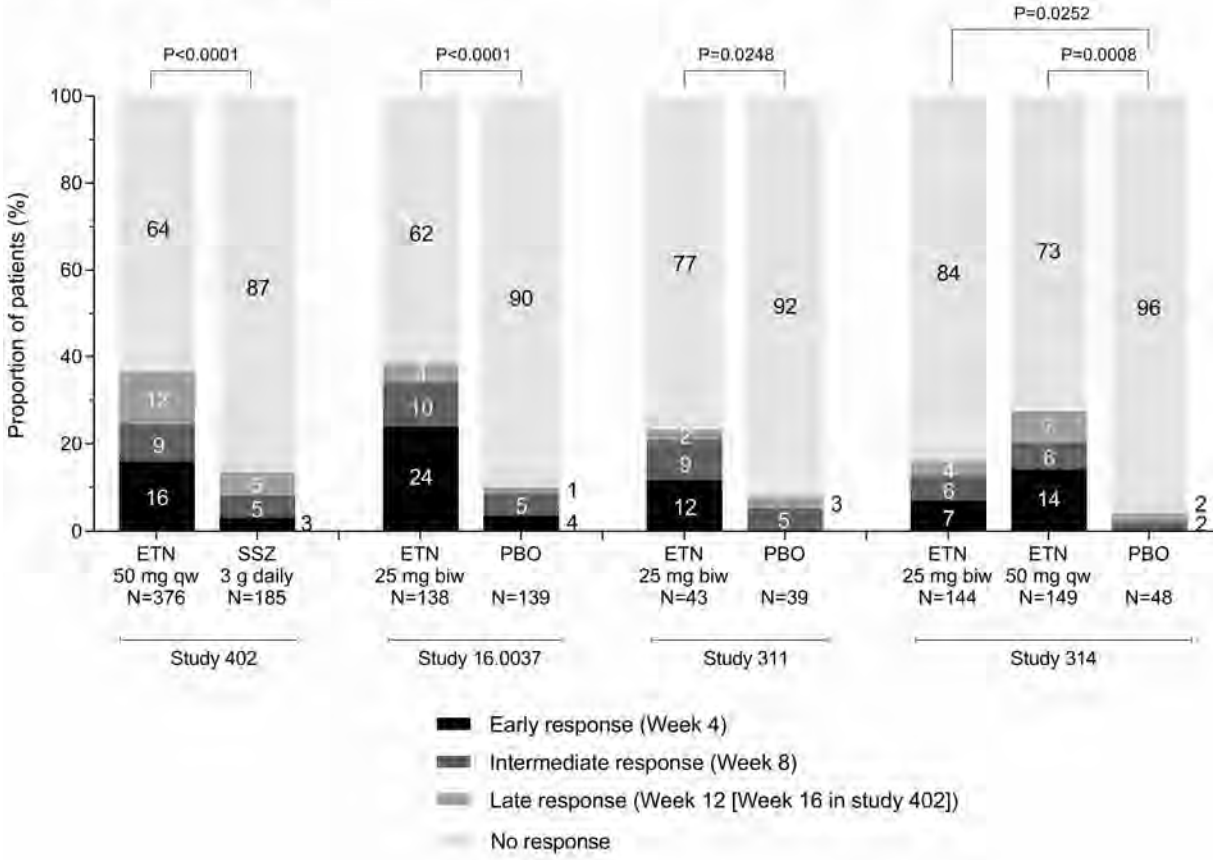
N.B. In all 4 studies, patients could receive optional background therapy with stable doses of NSAIDs and/or hydroxychloroquine, sulfasalazine, or methotrexate (sulfasalazine was not permitted in Study 402 and no NSAIDs were used in Study 16.0037)

ASAS20: Assessment in SpondyloArthritis International Society 20; biw: twice weekly; ETN: etanercept; NSAID: non-steroidal anti-inflammatory drug; PBO: placebo; qw: once weekly; SSZ: sulfasalazine.

Background/Purpose: Treatment with etanercept (ETN) is effective and well tolerated in patients with axial spondyloarthritis (AS), but the time frames within which patients tend to achieve clinical responses have not been well characterized. The aim of this post hoc analysis was to compare the temporal achievement of initial Assessment in SpondyloArthritis International Society 20 (ASAS20) response or initial inactive disease (ID) status in patients randomized to the ETN or control arms of clinical trials.

Methods: Data from 4 multicenter, double-blind, randomized, placebo- or sulfasalazine-controlled trials evaluating the safety and efficacy of ETN in patients with AS were included: Study 402 (phase 4, N=566; NCT00247962), Study 16.0037 (phase 3, N=277; NCT00356356), Study 311 (phase 3, N=84; NCT00421915), and Study 314 (phase 3, N=350; NCT00418548). The proportion of patients achieving ASAS20 response was the primary endpoint in all 4 studies and each study involved patients receiving ≥12 weeks of ETN treatment. In all 4 studies, patients could receive optional background therapy with sTable doses of NSAIDs and/or DMARDs. Analyses were based on observed cases, with the first incidence of each patient achieving an ASAS20 response or ID status (Ankylosing Spondylitis Disease Activity Score with C-reactive protein [ASDAS-CRP] < 1.3) categorized as early, intermediate, or late depending on whether it occurred at Week 4, Week 8, or Week 12 (Week 16 for Study 402), respectively. Patients not achieving ASAS20 response or ID status by Week 12/Week 16 were categorized as “no response”. Proportions of patients achieving early, intermediate, late, or no response in the different treatment arms within each study were compared using Cochran–Mantel–Haenszel tests without adjustment for multiplicity.

Figure 2. Proportions of patients achieving an early, intermediate, or late inactive disease status (ASDAS-CRP <1.3)



N.B. In all 4 studies, patients could receive optional background therapy with stable doses of NSAIDs and/or hydroxychloroquine, sulfasalazine, or methotrexate (sulfasalazine was not permitted in Study 402 and no NSAIDs were used in Study 16.0037)

ASDAS-CRP: Ankylosing Spondylitis Disease Activity Score with C-reactive protein; biw: twice weekly; NSAID: non-steroidal anti-inflammatory drug; ETN: etanercept; PBO: placebo; qw: once weekly; SSZ: sulfasalazine.

Results: Overall, analyses of ASAS20 response and ID status included data from 1276 and 1261 patients, respectively. Within each of the 4 studies, the proportion of patients who achieved either early ASAS20 response (**Figure 1**) or early ID status (**Figure 2**) was significantly greater in the ETN arm compared with the control arm. Across the 4 studies, 50–65% of patients in the ETN arms and 13–41% of patients in the control arms had an early ASAS20 response, with smaller proportions achieving intermediate or late ASAS20 responses. For the analysis of ID status, 7–24% of patients in the ETN arms and ≤4% of patients in the control arms achieved early ID status across the 4 studies, with similar proportions achieving intermediate or late ID status.

Conclusion: The proportion of patients with no response to treatment was smaller in the ETN arms than the control arms throughout all 4 studies analyzed, with the superior clinical response to ETN predominantly driven by significantly greater proportions of the ETN-treated patients achieving an early ASAS20 response or early ID status. The achievement of ASAS20 response showed a different temporal pattern to the achievement of ID status. The majority of ASAS20 responses were categorized as early whereas similar proportions achieved ID status categorized as early, intermediate, or late.

Disclosure: X. Baraliakos, AbbVie, 1, 2, BMS, 1, 2, Chugai, 1, 2, MSD, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, UCB, 1, 2; **A. Szumski**, Syneos Health, 1; **K. Kwok**, Pfizer, 1, 2; **B. Vlahos**, Pfizer, 1, 2.

Abstract Number: 0898

Inadequate Response Among Psoriatic Arthritis Patients Prescribed Advanced Therapy in a Real-world US Commercially Insured Population

Julie Birt[1], **Michael Grabner**[2], Keith Isenberg[3], Theresa Hunter[4], Chia-Chen Teng[2], Mingyang Shan[1], Jeffrey Lisse[1], Jianmin Wu[1], Kirstin Griffing[1] and Jeffrey R Curtis[5], [1]Eli Lilly and Company, Indianapolis, IN, [2]Healthcore, Inc, Wilmington, DE, [3]Anthem, Inc, Indianapolis, IN, [4]Eli Lilly and Company, Indianapolis, [5]Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The purpose of this analysis was to assess the frequency of inadequate response (IR) over 1 year associated with advanced therapy (AT) initiation among psoriatic arthritis (PsA) patients in the US using a claims-based algorithm that was originally developed and validated for rheumatoid arthritis[1]. Baseline factors associated with IR to AT were also analyzed.

Methods: This was a retrospective cohort study using claims data from the HealthCore Integrated Research Database®. Adult patients with PsA who initiated an AT (TNFi: adalimumab, certolizumab, etanercept, golimumab, infliximab; non-TNFi biologic: abatacept, ixekizumab, secukinumab, ustekinumab; other: apremilast, tofacitinib) from 7/1/2016 to 8/31/2018 and had continuous enrollment ≥6 months before and ≥12 months after index date (date of first biologic claim) were included. The index AT was defined as the first AT prescribed during the study time period. Patients were identified as having IR to their index AT if during the 12 months after index date (defined as date of first AT claim) they had one or more of the following: low adherence (defined as proportion of days covered (PDC)< 80%), switched/added a new AT, added a new conventional synthetic immunomodulator (e.g. methotrexate), increased dose/frequency of AT, had >1 glucocorticoid injection/infusion, addition or dose increase of oral glucocorticoids, used a new topical treatment, actinotherapy, or retinoids, or used a new pain medication. Baseline characteristics were compared between responders and IRs using Chi-squared tests for categorical variables and t-tests for continuous variables. A multivariable logistic regression model was constructed to identify baseline characteristics associated with IR to index AT.

Results: A total of 1,433 PsA patients were included in this analysis. Mean age was 49 years, 47% were male, 67% initiated a TNFi, 22% initiated other ATs, and 11% initiated a non-TNFi biologic (Table 1). Over the 1-year follow-up period, 77% of PsA patients had IR to their index AT: 63% of patients had low adherence, 21% switched/added a new AT, 9% added a new conventional synthetic immunomodulator, 3% had a dose/frequency increase of their index AT, 11% had >1 glucocorticoid injection/infusion, 7% had an addition/dose increase of oral glucocorticoids, 3% used a new topical treatment, actinotherapy or retinoids, and 12% used a new pain medication (Table 2). Inadequate responders were more likely to be female (odds ratio (OR)=1.37; p=0.017), have anxiety or depression (OR=1.80; p=0.002), and have a higher baseline Quan-Charlson Comorbidity Index (QCI) score (OR=1.21; p=0.036); while patients with baseline use of methotrexate were more likely to be responders (OR=0.72; p=0.015) (Table 3). Prior exposure to TNFi was associated with a 2.14-fold greater odds of non-response (p=0.003).

Table 1. Demographic and Baseline Characteristics of PsA Patients at Advanced Therapy Index Date

	PsA Patients N=1,433	Responders N=336	Inadequate Responders N=1,097	p-value
Sex, n (%)				
Female	755 (52.7%)	150 (44.6%)	605 (55.2%)	<0.001
Age, continuous				
mean (SD)	49.19 (11.15)	49.45 (11.50)	49.11 (11.04)	0.374
Age, categorical, n (%)				
18-39	278 (19.4%)	60 (17.9%)	218 (19.9%)	0.414
40-64	1047 (73.1%)	250 (74.4%)	797 (72.7%)	0.527
65-74	95 (6.6%)	23 (6.9%)	72 (6.6%)	0.856
≥ 75	13 (0.9%)	<10*	10 (0.9%)	0.975
Health plan type, n (%)				
HMO[1]	241 (16.8%)	57 (17.0%)	184 (16.8%)	0.935
PPO[2]	842 (58.8%)	203 (60.4%)	639 (58.3%)	0.480
CDHP[3]	350 (24.4%)	76 (22.6%)	274 (25.0%)	0.379
Geographic region[5], n (%)				
Northeast	268 (18.7%)	64 (19.1%)	204 (18.6%)	0.853
Midwest	315 (22.0%)	70 (20.8%)	245 (22.3%)	0.561
South	491 (34.3%)	111 (33.0%)	380 (34.6%)	0.588
West	276 (19.3%)	73 (21.7%)	203 (18.5%)	0.190
Other/Unknown	83 (5.8%)	18 (5.4%)	65 (5.9%)	0.697
Index year, n (%)				
2016	443 (30.9%)	98 (29.2%)	345 (31.5%)	0.428
2017	591 (41.2%)	133 (39.6%)	458 (41.8%)	0.480
2018	399 (27.8%)	105 (31.3%)	294 (26.8%)	0.111
Quan-Charlson Comorbidity Index[6]				
Mean (SD)	0.38 (0.82)	0.28 (0.71)	0.41 (0.85)	0.008
0	1,101 (76.8%)	275 (81.9%)	826 (75.3%)	0.013
1	194 (13.5%)	41 (12.2%)	153 (14.0%)	0.413
2	87 (6.1%)	13 (3.9%)	74 (6.8%)	0.053
3+	51 (3.6%)	<10*	44 (4.0%)	0.095
Comorbid conditions[6], n (%)				
Anemia	92 (6.4%)	19 (5.7%)	73 (6.7%)	0.513
Dyslipidemia	116 (8.1%)	23 (6.9%)	93 (8.5%)	0.337
Fibromyalgia	94 (6.6%)	12 (3.6%)	82 (7.5%)	0.011
Hypertension	455 (31.8%)	97 (28.9%)	358 (32.6%)	0.195
Infections	498 (34.8%)	101 (30.1%)	397 (36.2%)	0.039
Low-back pain	324 (22.6%)	65 (19.4%)	259 (23.6%)	0.102
Anxiety or depression	281 (19.6%)	40 (11.9%)	241 (22.0%)	<0.001
Other mental health issue (ex. anxiety/depression)	161 (11.2%)	25 (7.4%)	136 (12.4%)	0.012
Osteoarthritis	436 (30.4%)	92 (27.4%)	344 (31.4%)	0.166
Osteoporosis	48 (3.4%)	10 (3.0%)	38 (3.5%)	0.664
Index advanced therapy, n (%)				
Biologic/TNFi agents	963 (67.2%)	231 (68.8%)	732 (66.7%)	0.490
Adalimumab	532 (37.1%)	121 (36.0%)	411 (37.5%)	0.629
Certolizumab	29 (2.0%)	<10*	23 (2.1%)	0.481
Etanercept	339 (23.7%)	82 (24.4%)	257 (23.4%)	0.712
Golimumab	25 (1.7%)	<10	18 (1.6%)	0.588
Infliximab	39 (2.7%)	16 (4.8%)	23 (2.1%)	0.009
Biologic/Non-TNFi agents	151 (10.5%)	36 (10.7%)	115 (10.5%)	0.904
Abatacept	<10*	0	6 (0.6%)	0.174
Ixekizumab	<10*	<10*	<10*	0.855
Secukinumab	81 (5.7%)	17 (5.1%)	64 (5.8%)	0.591
Ustekinumab	59 (4.1%)	18 (5.4%)	41 (3.7%)	0.191
Other Advanced Therapies	319 (22.3%)	69 (20.5%)	250 (22.79%)	0.385
Apremilast	316 (22.1%)	69 (20.5%)	247 (22.5%)	0.444
Tofacitinib	<10*	0	<10*	0.337

[1]HMO=health management organization; [2]PPO=preferred provider organization; [3]CDHP=consumer-driven health plan; [4]Commercial plan is reference group on index date; [5]Based on US census regions; [6]6-months prior to index date; * denotes n < 10, which was blinded for privacy

Conclusion: Over 75% of PsA patients had an IR to their index AT 1 year after initiation, mostly driven by low adherence and switching to or adding on a new treatment. Health plan claims data appears useful to classify inadequate responders in PsA, and additional research should be done to further validate this claims-based algorithm in a clinical setting.

Table 2. Criteria Classifying PsA Patients as Inadequate Responders 1-year from initiation of an Advanced Therapy

	All PsA Patients N=1,433	TNFi Biologic N=963	Non-TNFi Biologic N=151	Other Advanced Therapy N=319
Inadequate Response (IR) n (%)	1,097 (76.6%)	732 (76.0%)	115 (76.2%)	250 (78.4%)
Criteria for IR, n (%)				
Low adherence to index advanced therapy (PDC[1]<80%)	904 (63.1%)	602 (62.5%)	83 (55.0%)	219 (68.7%)
Switch/add new advanced therapy (on-label)	300 (20.9%)	206 (21.4%)	19 (12.6%)	75 (23.5%)
Add new conventional synthetic immunomodulator therapy[2]	129 (9.0%)	86 (8.9%)	11 (7.3%)	32 (10.0%)
Dose or frequency increase of index advanced therapy	49 (3.4%)	30 (3.1%)	19 (12.6%)	0 (0%)
>1 glucocorticoid injection/IV	158 (11.0%)	98 (10.2%)	23 (15.2%)	37 (11.6%)
Addition or dose increase of oral glucocorticoid	105 (7.3%)	67 (7.0%)	<10*	31 (9.7%)
Use of new topical treatment, actinotherapy, or retinoids not observed at baseline	43 (3.0%)	30 (3.1%)	<10*	<10*
Use of new pain medication not observed at baseline	178 (12.4%)	120 (12.5%)	17 (11.3%)	41 (12.9%)

[1]PDC= proportion of days covered; [2]Conventional synthetic immunomodulator therapy includes methotrexate, sulfasalazine, azathioprine, chloroquine, cyclosporine, hydroxychloroquine, leflunomide, or mercaptopurine; *denotes n < 10, which was blinded for privacy

Table 3. Association between Baseline Patient Characteristics and Inadequate Response to a new PsA Advanced Therapy

Number of patients	N			
Responders, n	336			
Inadequate Responders, n	1,097			
	Adjusted Odds Ratio[1]	**95% CL**		**p-value[4]**
		LCL[2]	**UCL[3]**	
Covariates				
Sex (Female vs. Male)	1.37	1.06	1.78	**0.017**
Age (65 above vs. others)	0.96	0.60	1.55	0.879
Index Rx (Biologic/TNFi vs. Biologic/Non-TNFi)	1.09	0.72	1.65	0.679
Index Rx (Others vs. Biologic/Non-TNFi)	1.16	0.73	1.86	0.533
Prior TNFi exposure[5]	2.14	1.29	3.55	**0.003**
Baseline use of methotrexate	0.72	0.56	0.94	**0.015**
Baseline Quan-Charlson Comorbidity Index score	1.21	1.01	1.45	**0.036**
Baseline fibromyalgia	1.65	0.87	3.13	0.127
Baseline anxiety or depression	1.80	1.24	2.60	**0.002**

[1] Odds ratio was from logistic regression model constructed using forward and backward stepwise selection with entrance and exit p-value cut-offs of 0.15; [2] Lower Confidence Limits; [3]Upper Confidence Limits; [4]p-values obtained from logistic regression model // Model C-statistic=0.6238; Hosmer-Lemeshow test (based on 9 groups) p-value= 0.6609; [5]Prior TNFi exposure= use of TNFi at any time prior to the 6-month baseline period

Disclosure: J. Birt, Eli Lilly and Company, 1, 3; **M. Grabner**, None; **K. Isenberg**, Anthem, 1, 3, Anthem, 1, 3; **T. Hunter**, Eli Lilly and Company, 1, 3; **C. Teng**, None; **M. Shan**, Eli Lilly and Company, 3; **J. Lisse**, Eli Lilly and Company,

1, 3; **J. Wu**, Eli Lilly and Company, 1, 3; **K. Griffing**, Eli Lilly and Company, 1, 3; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5.

Abstract Number: 0899

Secukinumab Provides Significant Improvement of Spinal Pain and Lowers Disease Activity in Patients with Axial Spondyloarthritis: 24-week Results from a Randomized Controlled Phase 3b Trial

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: SKIPPAIN (NCT03136861) is the first randomized controlled study involving a biological disease modifying antirheumatic drug, with spinal pain as the primary endpoint as early as Week (Wk) 8 in a broad population of patients (pts) with axial spondyloarthritis (axSpA; ankylosing spondylitis [AS] and non-radiographic [nr]-axSpA). Clinical studies in axSpA routinely use composite measures of disease activity to assess treatment effect, despite pain being the most troubling symptom for pts[1–2]. Here we present the 24-wk results from the SKIPPAIN study that evaluated the efficacy and safety of secukinumab (SEC) in reducing spinal pain and disease activity following a step-up dosing approach.

Methods: SKIPPAIN was a 24-wk, randomized, double-blind, multicenter, placebo (PBO)-controlled phase 3b study. Pts (aged ≥18 years) diagnosed with active disease defined by Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) score ≥4 and average spinal pain numerical rating scale (NRS) score >4 at baseline and inadequate response to ≥2 NSAIDs ≥4 wks were enrolled. Pts were randomized (3:1) to receive subcutaneous SEC 150 mg or PBO wkly followed by every 4 wks (q4w) starting at Wk 4. At Wk 8, PBO pts were re-randomized to SEC 150 or 300 mg q4w up to Wk 24. Pts originally randomized to SEC 150 mg, were further classified as responders (spinal pain NRS score < 4) or non-responders (spinal pain NRS score ≥4) at Wk 8. Responders were re-assigned to continue double-blind treatment with 150 mg q4w up to Wk 24 (Arm A1). Non-responders were re-randomized to receive double-blind treatment with either 150 (Arm A2) or a step-up dose of 300 mg (Arm A3) q4w up to Wk 24. Primary endpoint was the proportion of pts achieving an average spinal pain score < 4 on a 0–10 NRS with SEC vs PBO at Wk 8. Change in spinal pain NRS and Ankylosing Spondylitis Disease Activity Score using C-reactive protein (ASDAS-CRP) scores at Wk 24 were exploratory endpoints.

Results: A total of 380 axSpA pts (269 [70.8%] AS and 111 [29.2%] nr-axSpA) were randomized to SEC 150 mg (N=285) or placebo (N=95). Primary endpoint of the study was met (proportion of spinal pain NRS (average) score responders: 32% vs 20% with an odds ratio [95% CI] of 1.9 [1.1, 3.3] favoring SEC vs PBO; $P < 0.05$). At Wk 24, further reductions in spinal pain were observed across treatment groups especially in those initially randomized to

Wk 8					
	SEC 150 N = 285			**Placebo N = 95**	
Change from Baseline in Spinal pain NRS score (total), mean (SD) [n]	–2.6 (2.5) [279]			–1.5 (2.2) [92]	
Change from Baseline in ASDAS-CRP score, mean (SD) [n]	–1.2 (1.0) [271]			–0.5 (0.8) [89]	
Wk 24					
	Active treatment group (SEC treatment starting Baseline)			**Placebo switchers group** (SEC treatment starting Wk 8)	
	Arm A1 (SEC 150 R – 150) **N = 90**	**Arm A2** (SEC 150 NR – 150) **N = 94**	**Arm A3** (SEC 150 NR – 300) **N = 94**	**Arm B1** (PBO - SEC 150) **N = 45**	**Arm B2** (PBO - SEC 300) **N = 44**
Change from Week 8 in Spinal pain NRS score (total), mean (SD) [n]	–0.4 (1.5) [88]	–2.1 (2.2) [93]	–1.9 (2.2) [91]	–2.5 (2.6) [45]	–2.9 (2.6) [43]
Change from Baseline in ASDAS-CRP score, mean (SD) [n]	–2.2 (1.0) [86]	–1.2 (1.0) [93]	–1.5 (1.0) [92]	–1.5 (1.1) [44]	–1.8 (0.9) [43]
Arm A1 = SEC responder to SEC 150 mg at Wk 8 (SEC 150 R - 150); Arm A2 = SEC non-responder to SEC 150 mg at Wk 8 (SEC 150 NR - 150); Arm A3 = SEC non-responder to SEC 300 mg at Wk 8 (SEC 150 NR - 300); Arm B1 = Placebo pts to SEC 150 mg (PBO - SEC 150); Arm B2 = Placebo pts to SEC 300 mg (PBO - SEC 300) ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score using C-reactive protein; N, Total number of patients randomized; n, number of evaluable patients; NR, nonresponders; NRS, numerical rating scale; PBO, placebo; pts, patients; R, responders; SEC, secukinumab; Wk, week					

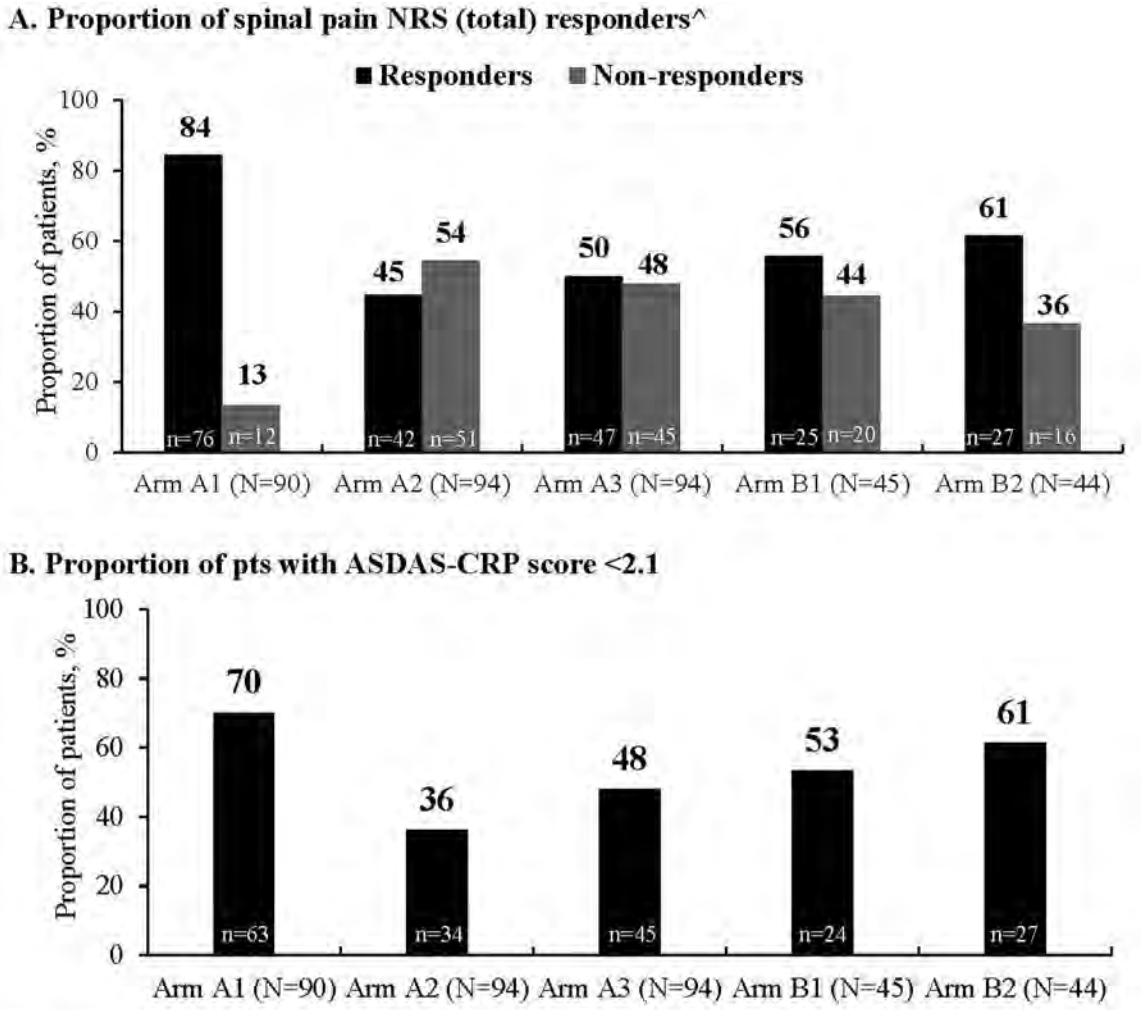
Table. Spinal pain and ASDAS-CRP scores at Wks 8 and 24

placebo and switched to active drug at Wk 8. Pronounced improvements were also observed in other disease activity measurements such as ASDAS-CRP score (**Table** and **Figure**). Of note, a numerically higher proportion of pts achieved ASDAS low disease activity at Wk 24 after SEC dose escalation at Wk 8 (Arm A3) as compared to those who remained on the same dose (Arm A2). No new or unexpected safety signals were reported.

Conclusion: Conclusion: SEC provided rapid, significant improvement in spinal pain and led to low disease activity in pts with axSpA. SEC dose escalation might be beneficial for pts not responding fully to the starting dose.

References:

1. Danve A & Deodhar A. *Clin Rheumatol*. 2019; 38:625-34.
2. Strand V, Singh JA. *J Clin Rheumatol*. 2017;23:383-391.



Arm A1 = SEC responder to SEC 150 mg at Wk 8 (SEC 150 R - 150); Arm A2 = SEC non-responder to SEC 150 mg at Wk 8 (SEC 150 NR - 150); Arm A3 = SEC non-responder to SEC 300 mg at Wk 8 (SEC 150 NR - 300); Arm B1 = Placebo pts to SEC 150 mg (PBO - SEC 150); Arm B2 = Placebo pts to SEC 300 mg (PBO - SEC 300)

^Spinal pain responders were pts with spinal pain NRS score <4

ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score using C-reactive protein; N, Total number of patients randomized; n, number of evaluable patients; NR, nonresponders; NRS, numerical rating scale; PBO, placebo; pts, patients; R, responders; SEC, secukinumab, Wk, week

Figure. Efficacy results at Wk 24

Disclosure: D. Poddubnyy, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Bio-Cad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8; **E. Pournara**, Novartis, 1, 3; **A. Zielinska**, Novartis, 5, Pfizer, 5; **A. Baranauskaite**, AbbVie, 5, 8, Novartis, 8, Amgen, 8, Roche, 8, KRKA, 8; **A. Jiménez**, None; **S. Sadhu**, Novartis, 3; **B. Schulz**, Novartis, 3; **M. Rissler**, Novartis, 1, 3; **C. Perella**, Novartis, 1, 3; **H. Marzo-Ortega**, Novartis, 2, 5, 8, Janssen, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, UCB, 5, 8, AbbVie Inc., 5, 8, Celgene, 5, 8, Takeda Pharmaceutical Company, 5, 8.

Abstract Number: 0900

Achievement of Low Disease Activity According to BASDAI with Ixekizumab in Patients with Axial Spondyloarthritis: 16-Week Results from the COAST Trials

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: The efficacy of ixekizumab (IXE), a selective interleukin-17A antagonist, was assessed in patients (pts) with axial SpA (axSpA) in three Phase 3, randomized, double-blind, placebo (PBO)-controlled trials, COAST-V, COAST-W and COAST-X. The BASDAI is frequently used by clinicians to measure disease activity and response to treatment in pts with axSpA, and when considering starting biologic DMARD therapy[1,2]. We present BASDAI and quality of life (QoL) outcomes at 16 weeks from the COAST trials.

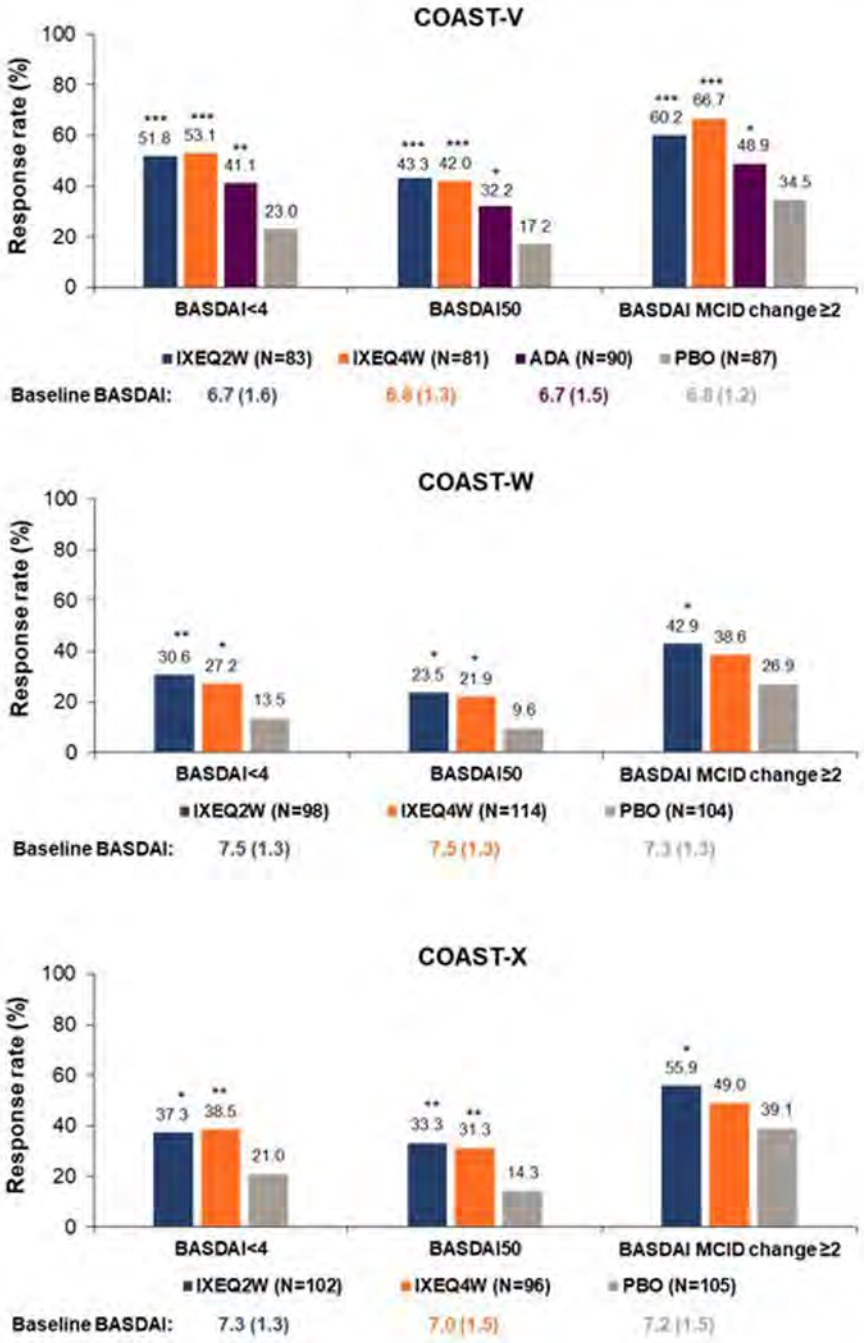
Methods: COAST-V (NCT02696785) and COAST-W (NCT02696798) assessed pts with radiographic axSpA, and COAST-X (NCT02757352) assessed pts with non-radiographic axSpA. All pts fulfilled Assessment of Spondyloarthritis International Society (ASAS) classification criteria for axSpA. Pts were either biologic-naive (COAST-V, COAST-X) or TNFα inhibitor-experienced (COAST-W) and were randomized to IXE (80 or 160 mg at week 0 then 80 mg every 2 or 4 weeks [Q2W, Q4W]) or PBO or adalimumab (ADA, 40 mg Q2W; COAST-V only). Treatment response at week 16 was assessed by the proportion of patients achieving BASDAI< 4, 50% reduction from baseline in BASDAI (BASDAI50), and a clinically meaningful change from baseline in BASDAI of at least 2 units (ΔBASDAI≥2)[1,2]. Categorical variables were analyzed by logistic regression with non-responder imputation (NRI) for missing data. QoL was assessed by change from baseline in Short Form (SF)-36 Physical Component Summary (PCS) scores according to BASDAI< 4 response status at week 16; missing data were imputed using modified baseline observation carried forward (mBOCF).

Results: In total, 341 pts from COAST-V, 316 from COAST-W, and 303 from COAST-X were included in this analysis. At week 16, a greater proportion of pts treated with IXE achieved BASDAI< 4, BASDAI50, and ΔBASDAI≥2 (Figure 1) compared to PBO across all three trials, and the difference was statistically significant for the majority of endpoints. Furthermore, pts achieving BASDAI< 4 showed greater improvements in SF-36 PCS scores (Figure 2).

Conclusion: In the COAST trials, IXE delivered clinically meaningful improvements in pts with axSpA after 16 weeks of treatment. Low disease activity (BASDAI< 4) was achieved with IXE regardless of axSpA type (radiographic or non-radiographic) or prior use of TNFα inhibitors. Achieving BASDAI< 4 was associated with greater improvements in physical QoL.

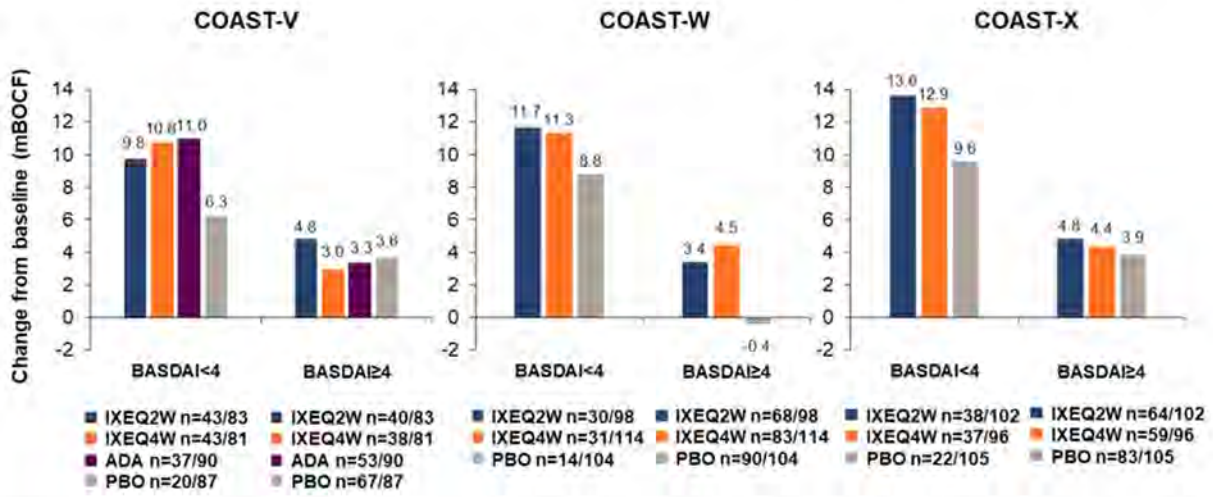
1. Magrey MN, Kiltz U. Chapter 9 in Axial Spondyloarthritis. Elsevier, 2019:121-133.
2. van der Heijde D, et al. Ann Rheum Dis 2017;76:978-991.

Figure 1: BASDAI outcomes with IXE at week 16 in pts with axSpA from the COAST clinical trials



*p≤0.05, **p≤0.01, ***p≤0.001 vs PBO. Nominal P-value from logistic regression with adjustment for covariates (COAST-V: treatment, geographic region and baseline CRP status; COAST-W: treatment, geographic region, baseline CRP status and number of prior TNF inhibitors; COAST-X: treatment, geographic region and baseline MRI/CRP status). Baseline BASDAI values are presented as mean (SD). ADA, adalimumab; axSpA, axial spondyloarthritis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASDAI50, 50% reduction in BASDAI; IXE, ixekizumab; MCID, minimal clinically important difference; PBO, placebo; pts, patients; Q2W, every 2 weeks; Q4W, every 4 weeks; SD, standard deviation.

Figure 2: Change from baseline in SF-36 PCS scores by BASDAI<4 response status at week 16 in pts from the COAST clinical trials



No formal statistical comparisons were performed. ADA, adalimumab; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASDAI<4, BASDAI score <4; BASDAI≥4, BASDAI score ≥4; IXE, ixekizumab; LSM, least squares mean; n, number of patients achieving BASDAI<4; PBO, placebo; Q2W, every 2 weeks; Q4W, every 4 weeks; SF-36 PCS, Short Form-36 Physical Component Summary.

Disclosure: D. Poddubnyy, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8; **X. Juanola**, None; **C. Prati**, AbbVie, 2, Chugai Pharmaceutical Co, 2, Eli Lilly and Company, 2, Novartis, 2, Pfizer, 2, UCB, 2; **H. Russ**, Eli Lilly and Company, 3; **Y. Schymura**, Eli Lilly and Company, 3; **S. Liu-Leage**, Eli Lilly and Company, 3, 4; **M. Haschemi Nassab**, Eli Lilly and Company, 3; **J. Dudler**, None.

Abstract Number: 0901

Proinflammatory Neutrophil Function Is Modulated During Secukinumab Therapy in Psoriatic Arthritis Without Compromising Host Defence

Robert Moots[1], Andy Cross[2], Helen Wright[2], Steven Edwards[2], Nicola Goodson[3], Jenny Hawkes[3], Ayren Mediana[1] and Helen Frankland[1], [1]Liverpool University Hospitals, Liverpool, United Kingdom, [2]University of Liverpool, Liverpool, United Kingdom, [3]University of Liverpool, Liverpool

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
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Background/Purpose: Secukinumab is a monoclonal antibody that neutralises IL-17A, which plays a key role in the IL-23/17A axis underlying the pathophysiology of psoriatic arthritis (PsA). In this disease, Th17 cells produce IL-17A to trigger the release of chemoattractants such as CXCL8 and CCL20, leading to the infiltration of other immune cells including neutrophils. Activated neutrophils can themselves generate numerous chemokines and cytokines that can amplify and sustain inflammation. Therapeutic targeting of IL-17 with biologics such as secukinumab in PsA may

block this inflammatory cycle, but such inhibition should not have deleterious effects on other aspects of immunity associated with host defence.

This study measured changes in the functions of circulating neutrophils in PsA patients pre-therapy, compared to age- and sex-matched healthy controls, and determined if these functions changed in PsA patients prior to and during secukinumab therapy.

Methods: Neutrophils were isolated from venous blood of 20 PsA patients due to start secukinumab and 10 healthy controls. Key neutrophil functions such as: reactive oxygen species (ROS) production; phagocytosis; apoptosis (+/- TNF and GM-CSF); receptor expression and chemotaxis, were measured at baseline and 12 weeks. Changes in gene expression pre- and 12-weeks post-therapy (n=5 PsA) were measured by RNAseq, and pre-treatment PsA neutrophil transcriptomes were also compared to healthy controls.

Results: There were no significant differences in ROS production, phagocytosis or chemotaxis in PsA patients at baseline (compared to healthy controls) or during therapy. RNA-seq analysis revealed many genes with altered expression between PsA neutrophils at baseline and healthy controls. For example, up-stream cytokines predicted to be regulating neutrophil gene expression in PsA included CSF2 (G-CSF), CD40LG, oncostatin M, interferons-a and -g, and TNFa. Ingenuity analysis revealed that signalling pathways associated with IL-8 signalling, toll-like receptor signalling and apoptosis signalling were among those significantly down-regulated by secukinumab. Of note, none of the patients treated with secukinumab contracted Covid-19.

Conclusion: Selective up- and down-regulation of neutrophil transcription was observed in PsA neutrophils compared to healthy controls, and in PSA neutrophils post treatment with secukinumab. However, while these changes may alter the pro-inflammatory function of neutrophils in PsA in response to IL-17A blockade, they did not adversely affect the ability of these neutrophils to carry out their role in host defence against infections.

Disclosure: R. Moots, Novartis, 2, 5; **A. Cross**, None; **H. Wright**, Novartis, 2; **S. Edwards**, Novartis, 2; **N. Goodson**, Novartis, 2, 8; **J. Hawkes**, None; **A. Mediana**, None; **H. Frankland**, None.

Abstract Number: 0902

Impact of Dose Escalation of Secukinumab in Patients with Psoriatic Arthritis in Real-World Setting

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
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Background/Purpose: Secukinumab (SEC) has provided efficacy in clinical trials in patients with psoriatic arthritis (PsA). In PsA patients, a gain in response has been suggested by dose escalation from 150 to 300 mg in the open phase of the FUTURE study[1]. We analyze the usefulness of dose escalation of SEC from 150 to 300 in patients with non-responding PsA to 150 mg in real-world setting.

TABLE 1. Characteristics of the PsA patients according to the SEC dose

	SEC150 (n=58)	SEC300 (n=12)	SEC150-300 (n=28)
n previous biological therapy			
0	24 (41%)	2 (17%)	11 (39%)
1	16 (28%)	1 (8%)	7 (25%)
2	8(14%)	3 (25%)	2 (7%)
3 or more	10 (17%)	6 (50%)	8 (29%)
Survival of SEC (years)	1,3±1	1,6±1,3	1,6±0,9
n SEC discontinuation	24 (41%)	8 (67%)	13 (46%)
Causes of SEC discontinuation			
Primary failure	9 (37%)	2 (25%)	-
Secondary failure	10 (42%)	5 (63%)	13 (100%)
Adverse events	4 (17%)	-	-
Allergy to latex	1 (4%)	-	-
Remission	-	1 (12%)	-

SEC: secukinumab. n: number. PsA: psoriatic arthritis

Methods: Unicentric observational, longitudinal, retrospective study conducted in a tertiary hospital between January 2016 and December 2019. Patients with PsA (CASPAR criteria) receiving at least one dose of SEC were included. Medical records were reviewed to collect demographic and clinical data related to PsA (including activity assessment and treatment).

Descriptive statistics and a comparative analysis of the efficacy of SEC by the Student *t* test in the different dose groups and by the ANOVA test to compare the response between the three dose groups were performed.

Results: 98 PsA patients treated with SEC, of which 69 (70%) female, were included. Mean age was 54 y.o (SD12) and average duration of the disease was 9 (SD 7) years. Three groups were performed according to the dose received, SEC150, SEC300 and SEC150-300 (non-responders after SEC150 onset increasing to 300 mg). *Characteristics are detailed on Table 1.* The SEC150 group includes 58 (59%) patients, SEC300 12 (12%) and SEC150-300 28 (29%) patients.

In the SEC150-300 group, 54% of the patients maintains SEC after responding to the dose increase. The average time of dose increase to 300 mg was 9 (SD6) months in this group.

At 6 months of SEC therapy, a significant decrease in CRP, ASDAS-CRP and DAPSA values was observed in the three treatment groups *(Table 2).* However, when comparing the difference of means obtained during follow-up (ΔCRP, ΔASDAS-CRP and ΔDAPSA) between the 3 dose groups, no significant differences were found (p=0.76 for CRP, p=0.86 for ASDAS-CRP and p=0.35 for DAPSA).

TABLE 2. Disease activity assessment at 6 months of SEC therapy

	Baseline	6 months after SEC	Mean difference	*p* value
CRP_{300} (mg/L)	9±8,3	4,7±3,7	-4,3 (IC95% -8,9 a 0,2)	p=0,06
CRP_{150} (mg/L)	7,3±9,1	4,0±4,7	-2,9 (IC95% -4,7 a -1,3)	p=0,0009
$CRP_{150\text{-}300}$ (mg/L)	9,9±11	6,0±7,4	-3,9 (IC95% -6,9 a -8,5)	p=0,0142
ASDAS-CRP_{300}	2,3±0,7	1,6±0,6	-0,6 (IC95% -0,9 a -0,3)	p=0,0014
ASDAS-CRP_{150}	2,3±0,6	1,6±0,7	-0,7 (IC95% -0,8 a -0,5)	p<0,0001
ASDAS-$CRP_{150\text{-}300}$	2,2±0,6	1,6±0,7	-0,6 (IC95% -0,8 a -0,4)	p<0,0001
$DAPSA_{300}$	33,7±19,3	16,9±10,6	-16,8 (IC95% -29,6 a -3,9)	p=0,01
$DAPSA_{150}$	27,4±11,4	15,4±10,4	-11 (IC95% -14,4 a -7,6)	p<0,0001
$DAPSA_{150\text{-}300}$	28±9,9	15,8±8,7	-12,2 (IC95% -15,3 a -9,1)	p<0,0001

CRP_{300}: C-reactive protein in patients with SCK 300 mg, CRP_{150}: in patients with SCK 150, $CRP_{150\text{-}300}$: in patients with dose escalation from 150 to 300 (same for ASDAS-CRP and DAPSA), SEC: secukinumab

Conclusion: There are no significant differences in the response evaluated by CRP, ASDAS-CRP and DAPSA between the dose of 150 and 300 mg of SEC. However, both doses of treatment provided efficacy in clinical practice with significant reduction of activity parameters.

In patients with non-responding PsA to SEC150 mg and prior failure to TNFi, increasing the dose to 300 mg could be an effective option.

Disclosure: M. Martin-Lopez, None; **B. Joven**, None; **J. Pablos**, None.

Abstract Number: 0903

Changing Patterns of Use of Biologic/Targeted Synthetic DMARDs in Psoriatic Arthritis: An Analysis of the OPAL Dataset

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
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Background/Purpose: In Australia the cost of biologic/targeted synthetic DMARDs (b/tsDMARDs) for treatment of PsA is subsidized if the patient has documented high levels of clinical/laboratory disease activity and has not responded to a pre-specified combination of conventional synthetic DMARDs, including methotrexate. Once eligible for subsidy the clinician can then prescribe the b/tsDMARD deemed most clinically appropriate until the desired level of disease control is reached, with the available options being adalimumab, etanercept, certolizumab pegol, golimumab, infliximab, secukinumab, ixekizumab, ustekinumab and tofacitinib. The aim of this analysis was to determine the patterns of use and reasons for initiation and discontinuation of b/tsDMARDs for PsA in real-world rheumatology practice in Australia.

Methods: Deidentified clinical data were sourced from the OPAL dataset, which is collected in a custom-built electronic medical record at the time of the consultation[1] by 110 rheumatologists in Australia. Prescribing data for patients >18 years with PsA treated with a b/tsDMARD between Jan 2007-Mar 2020 was included in the analysis. The software program Tableau® was used to display data on medication initiation and cessation dates, and reasons for starting and stopping b/tsDMARDs, which is recorded at the time of the decision.

Results: At Mar 2020, there were 13,767 PsA patients in the dataset, with 35% (4,854) prescribed b/ts DMARDs. 67% of patients were receiving a TNF inhibitor (TNFi), 22% an IL-17 inhibitor (IL-17i), 7% a JAK inhibitor (JAKi) and 4% an IL-12/IL-23 inhibitor. In the prior 12 months (April 2019-Mar 2020) TNFi was the preferred 1st line treatment (66%) with adalimumab taking 31% of all initiations, followed by secukinumab and golimumab (16% of initiations each). Secukinumab was the most prescribed bDMARD in 2nd line (23%) followed by tofacitinib (21%), and tofacitinib was the most prescribed 3rd line agent (31%) followed by secukinumab (20%). Mode of action (MOA) was selected as the most common reason for choosing a drug (48%), followed by efficacy compared to alternatives (34%) and efficacy as monotherapy (11%). Mode of administration was considered the driver for 17% of tofacitinib initiations compared to 5% overall. The main reasons for stopping treatment were lack of efficacy (40%), better alternative (25%) and adverse reaction (12%). 42% of patients who switched from a TNFi in 1st line received a TNFi in 2nd line, 33% switched to an IL-17i, and 23% switched to a JAKi. 43% of patients that switched from an IL-17i switched to a TNFi, 33% switched to a JAKi, and 24% switched to an alternative IL-17i.

Conclusion: Clinicians appraise different characteristics of each drug when choosing interventions for their patients. MOA is rated highly which is reflected in the rapid uptake of IL-17i and JAKi in early lines of therapy for patients with PsA. Clinical outcomes following in-class switching versus switching to an agent with a different MOA requires further investigation.

References: [1] Littlejohn GO, Tymms KE, Smith T, Griffiths HT. Using big data from real-world Australian rheumatology encounters to enhance clinical care and research. Clin Exp Rheum Nov 2019.

Disclosure: S. Ciciriello, Gilead, 8; **T. Smith**, OPAL Rheumatology, 9; **G. Littlejohn**, MSD, 5, AbbVie, 5, Roche, 5, BMS, 5, Janssen, 5, Pfizer, 5, Seqirus, 5; **K. Tymms**, None; **D. Mathers**, None; **H. Cooley**, Novartis, 5, UCB, 8, Janssen, 9; **H. Griffiths**, Janssen, 5, Novartis, 5, Roche, 5, UCB, 5; **C. OSullivan**, Janssen, 3, OPAL Rheumatology, 9; **P. Youssef**, Gilead, 2.

Abstract Number: 0904

Response to Ixekizumab by C-reactive Protein Level in Patients with Radiographic Axial Spondyloarthritis: Results from the COAST-V (Biological-Naïve) and COAST-W (TNF Inhibitor-Experienced) Trials at 52 Weeks

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor necrosis factor inhibitors (TNFis) are effective treatments for radiographic axial spondyloarthritis (r-axSpA), but may be less effective in patients (pts) without elevated C-reactive protein (CRP). This study evaluated the efficacy of ixekizumab (IXE), a high-affinity monoclonal antibody selectively targeting interleukin-17A, in pts with r-axSpA at 52 weeks (wks) with nonelevated (≤5 mg/L) and elevated (>5 mg/L) baseline (BL) CRP. Week 16 Assessment of Spondyloarthritis International Society 40% response rate (ASAS40) results comparing IXE to placebo (PBO) stratified by CRP are published.[1]

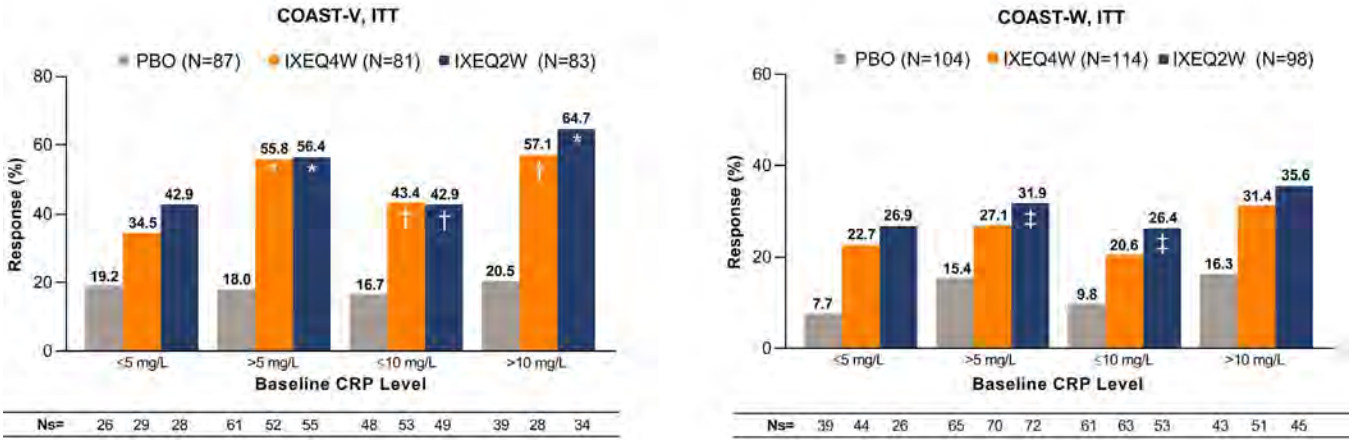
Methods: COAST-V (NCT02696785) and COAST-W (NCT02696798) were phase 3, multicenter, randomized, double-blind, PBO-controlled trials investigating efficacy of 80-mg IXE every 4 wks and every 2 wks in pts who met ASAS criteria for r-axSpA, had radiographic sacroiliitis according to mNY criteria, and were biological disease-modifying antirheumatic drug (bDMARDs)-naïve (COAST-V) or TNFi-experienced (COAST-W). Data from 157 COAST-V pts and 188 COAST-W pts treated with IXE from Wk 0 to Wk 52 were analyzed. Patients were stratified based on nonelevated (≤5 mg/L) vs elevated (>5 mg/L) BL CRP. Additional analysis was done with BL CRP ≤10.0 mg/L vs >10.0 mg/L. Efficacy was assessed by ASAS40, ≥50% improvement in Bath Ankylosing Spondylitis Disease Activity Index (BASDAI50), and change in Short Form 36 physical component summary (SF-36 PCS) score. Missing data were imputed by non-responder imputation for binary measures and modified BL observation carried forward for continuous measure. Week 16 data are presented for comparison.[1]

Results: Of pts treated with IXE through Wk 52, 34.4% had CRP ≤5.0 mg/L, 65.6% had CRP >5.0 mg/L, 61.8% had CRP ≤10.0 mg/L, and 38.2% had CRP >10.0 mg/L at BL in COAST-V and 33.0% had CRP ≤5.0 mg/L, 67.0% had CRP >5.0 mg/L, 55.9% had CRP ≤10.0 mg/L, and 44.1% had CRP >10.0 mg/L at BL in COAST-W.

At Wk 16, the proportion of pts achieving ASAS40 in COAST-V was numerically higher with IXE in the ≤5 mg/L group and significantly higher with IXE in the >5 mg/L group vs PBO, as previously shown [1], and was significantly higher with IXE in the ≤10 mg/L and >10 mg/L groups vs PBO (Fig. 1). Results were similar in COAST-W and significant in the >5 mg/L and ≤10 mg/L groups vs PBO (Fig. 1).

At Wk 52, greater than 45% of COAST-V pts and greater than 35% of COAST-W pts treated with IXE achieved an ASAS40 response, greater than 40% of COAST-V pts and greater than 25% of COAST-W pts treated with IXE

Figure 1. COAST-V and COAST-W ASAS40 Response at Week 16, NRI[a]



a. Week 16 data for the CRP ≤5 mg/L and >5 mg/L groups were previously published in a COAST V/COAST-W integrated dataset.[1] *p<0.001, †p<0.01, ‡p<0.05 vs PBO, ASAS40=Assessment of Spondyloarthritis International Society 40% response rate; CRP=C-reactive protein; ITT=intent-to-treat; IXE=ixekizumab; N=number of patients in the treatment group; Ns=number of patients in each subgroup; NRI=non-responder imputation; PBO=placebo; Q2W=every 2 weeks; Q4W=every 4 weeks.

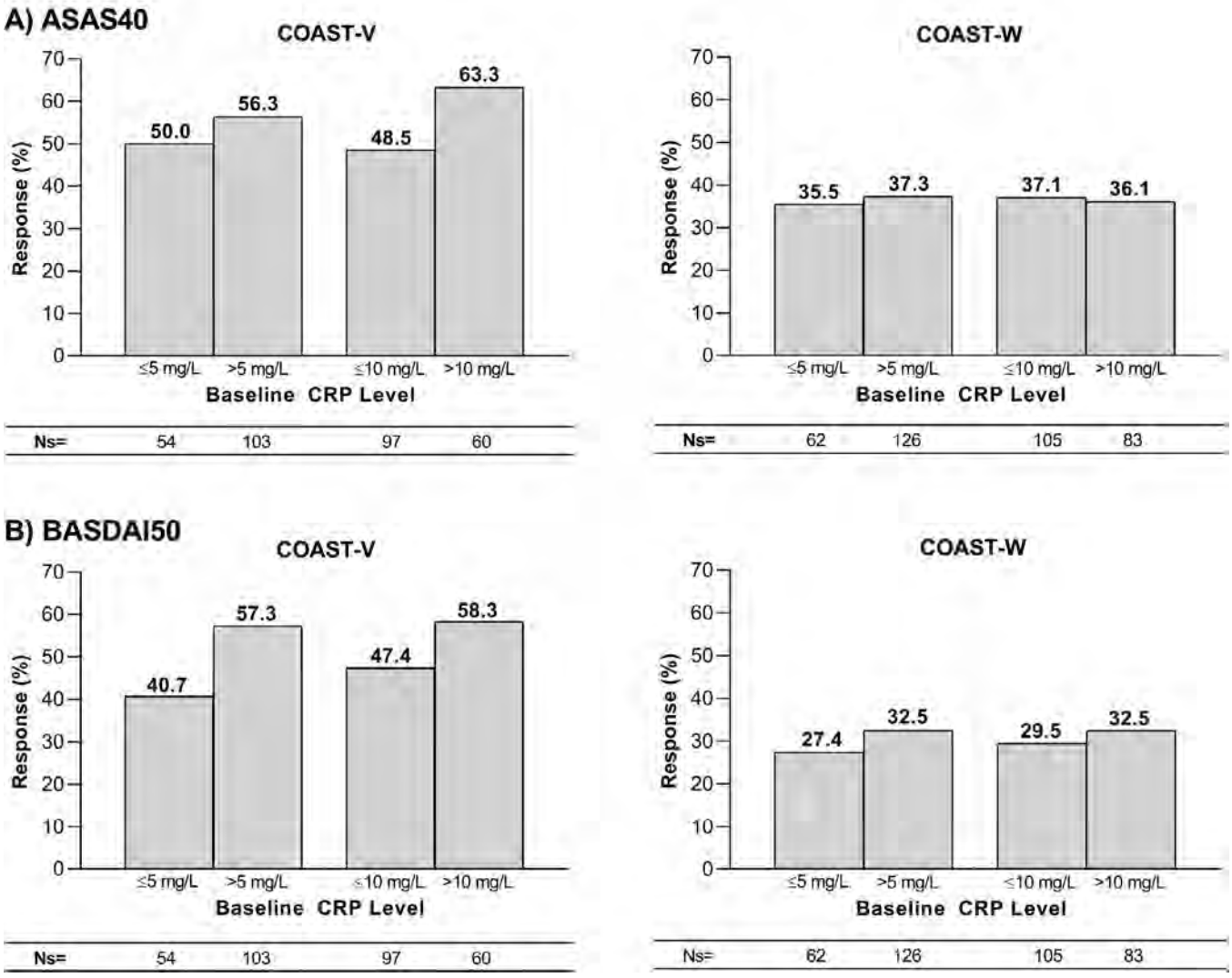
achieved a BASDAI50 response, and change from baseline in SF-36 PCS score in pts treated with IXE was greater than 5 points in both studies regardless of the BL CRP cutoffs evaluated (Figs. 2 and 3).

Conclusion: A higher proportion of ASAS40 responders was observed in IXE treated arms versus PBO among bDMARD-naïve and TNFi-experienced pts with r-axSpA when the CRP cutoff of 10 mg/L was evaluated, and the responses were consistent through Wk 52. Furthermore, similar proportions of pts achieved BASDAI50 and SF-36 responses within each patient population regardless of the BL CRP cutoff evaluated.

Reference:

1. Maksymowych et al. 2019

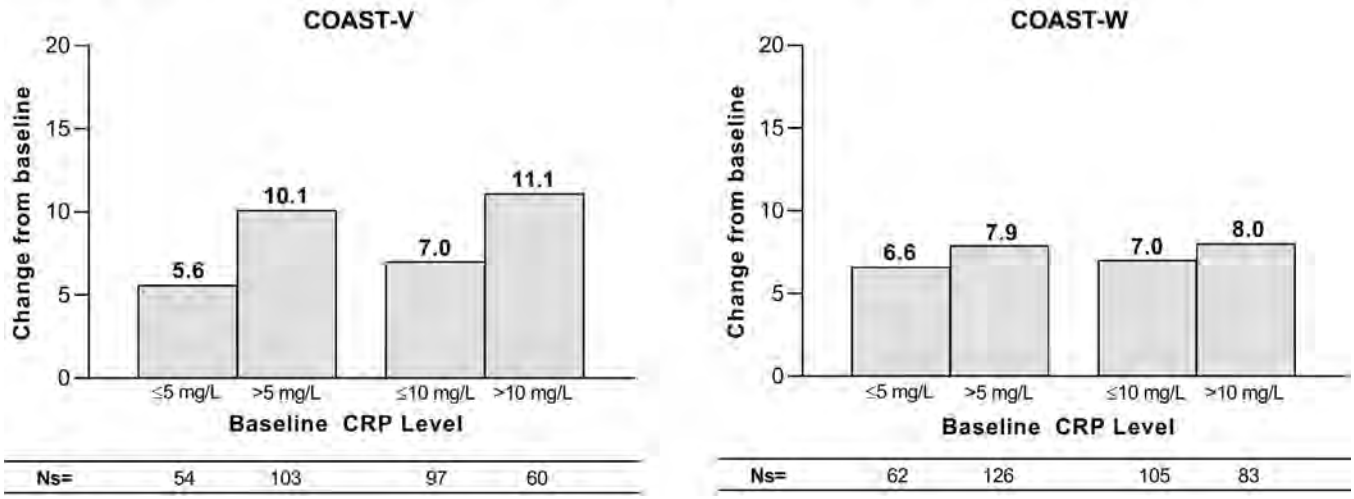
Figure 2. (A) ASAS40 and (B) BASDAI50 Responses at Week 52, NRI



Patients in these analyses received at least one dose of IXE Q4W or Q2W through Week 52. Descriptive statistics are provided without inferential testing. ASAS40=Assessment of Spondyloarthritis International Society 40% response rate; BASDAI50=≥50% improvement in Bath Ankylosing Spondylitis Disease Activity Index; CRP=C-reactive protein; IXE=ixekizumab; NRI=non-responder imputation; Ns=number of patients in each subgroup; Q2W=every 2 weeks; Q4W=every 4 weeks.

Disclosure: J. Reveille, Eli Lilly, 2, UCB, 5, Janssen, 2; **P. Rahman**, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5; **D. Sandoval**, Eli Lilly and Company, 3; **T. Muran**, Eli Lilly and Company, 1, 3; **A. Kronbergs**, Eli Lilly and Company, 1, 3; **R. Bolce**, Eli Lilly and Company, 1, 3; **V. Geneus**, Eli Lilly and Company, 3, 4; **T. Hunter**, Eli Lilly and Company, 1, 3; **S. Liu-Leage**, Eli Lilly and Company, 3, 4; **M. Rudwaleit**, Bristol-Myers Squibb, 5, 8, Chugai Pharmaceutical Co., Ltd., 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Novartis, 5, 8, UCB Pharma, 5, 8, AbbVie, 5, 8, Pfizer, 5, 8, Celgene, 8, Roche, 5, 8, Merck Sharp & Dohme, 5, 8; **J. Maldonado-Cocco**, Pfizer, 2, 5, 8, Merck Sharp Dohme, 2, 5, 8, Novartis, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Roche, 2, 5, 8,

Figure 3. SF-36 PCS Mean Change from Baseline at Week 52, mBOCF



Patients in this analysis received at least one dose of IXE Q4W or Q2W through Week 52. Descriptive statistics are provided without inferential testing. CRP=C reactive protein; IXE=ixekizumab; mBOCF=modified baseline observation carried forward; Ns=number of patients in each subgroup; SF-36 PCS=Short Form 36 Physical Component Score; Q2W=every 2 weeks; Q4W=every 4 weeks.

Boehringer Ingelheim, 2, 5, 8, Schering-Plough, 2, 5, 8, Abbott, 2, 5, 8, UCB, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Gilead, 2, 5, 8; **F. Van den Bosch**, AbbVie, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Gilead, 5, Merck, 5, 8.

Abstract Number: 0905

Probability of Achieving Low Disease Activity or Remission with Apremilast Treatment Among DMARD-Naive Subjects with Active Psoriatic Arthritis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Apremilast (APR) is associated with comparable ACR response rates in DMARD-naive vs DMARD-experienced patients (pts) with PsA (Wells AF, et al. *Rheumatology*. 2018;57:1253-63; Kavanaugh A, et al. *Arthritis Res Ther.* 2019;21:118). A question that remains is if DMARD-naive pts treated with APR have greater chances of achieving treatment targets than DMARD-experienced pts. cDAPSA is a commonly used treatment target. We assessed the predictive value of baseline (BL) clinical disease status on achieving long-term cDAPSA treatment

Probability of Achieving cDAPSA Treatment Targets at Week 52 by Baseline cDAPSA Category

cDAPSA Categories at Baseline*	HDA	Mod	LDA	REM	LDA/REM
LDA	0.0%	0.0%	50.0%	50.0%	100.0%
Mod	9.1%	29.2%	39.8%	21.9%	61.7%
HDA	27.1%	44.7%	24.3%	3.9%	28.2%

cDAPSA Categories at Week 52

- Subjects achieving treatment targets
- Subjects with ≥1 disease activity category improvement
- Subjects with no change in disease activity category
- Subjects with ≥1 disease activity category worsening

*Subjects randomized to APR 30 mg twice daily with cDAPSA scores available at baseline (n = 175). Percentage represents the proportion of subjects in each cDAPSA category at baseline (from left to right, HDA, Mod, LDA, and REM at Week 52 = 100%). Multiple imputation. REM, cDAPSA ≤4; LDA, cDAPSA >4 to ≤13; Mod, cDAPSA >13 to ≤27; HDA, cDAPSA >27. Mod = moderate disease activity.

targets at Week 52 among DMARD-naive subjects in PALACE 4; compared these findings vs those recently reported from PALACE 1-3 in subjects with prior exposure to DMARDs; and provided further evidence that at a group level, achievement of cDAPSA disease targets with APR is associated with no or mild articular and extra-articular disease activity by Week 52.

Methods: This post hoc analysis included subjects assigned to APR 30 mg BID at BL who had available cDAPSA data at BL. We calculated the probabilities of shifting across different cDAPSA categories (remission [REM]: ≤4; low disease activity [LDA]: >4 to ≤13; moderate disease activity [Mod]: >13 to ≤27; high disease activity [HDA]: >27 [Machado PM. *Ann Rheum Dis*. 2016;75:787-790]) from BL to Week 52. Mean values of articular and non-articular variables (PASI, SJC/TJC, MASES, dactylitis) from BL to Week 52 were assessed by cDAPSA category achieved at Week 52 to determine the association between achievement of targets and control of articular and non-articular manifestations. Results from the current analyses were compared with the previously reported results from PALACE 1-3.

Results: A total of 175 subjects receiving APR were included; at BL, 66.3% were in HDA, 31.4% in Mod, and 2.3% were in LDA. Overall, subjects who achieved treatment targets (LDA or REM) by Week 52 had lower levels of disease activity at BL, as shown by a lower number of swollen and tender joints and lower presence of enthesitis and dactylitis. Higher prevalence of psoriasis-involved body surface area ≥3% at BL was observed. Subjects in Mod at BL were estimated to be more than twice as likely to achieve REM or LDA at Week 52 vs subjects in HDA at BL; for subjects in LDA at BL, the estimated probability of achieving cDAPSA treatment targets was 100% (Figure). PALACE 4 subjects with LDA and Mod at BL exhibited higher estimated probabilities of achieving treatment targets (100.0% and 61.7%, respectively) than those observed in the DMARD-experienced population of PALACE 1-3 (71.1% and 46.9%). Subjects in PALACE 4 who achieved REM or LDA by Week 52 showed no or mild articular and extra-articular disease activity by Week 52, similar to what was observed in the PALACE 1-3 population (Mease PJ, et al. *Arthritis Care Res.* 2020 Jan 7. Epub).

Conclusion: DMARD-naive subjects in PALACE 4 who had LDA or Mod at BL had the highest likelihood of achieving treatment targets (cDAPSA REM or LDA) by Week 52 with continued APR treatment. Results from the current probability analyses revealed higher probability rates than those observed in the DMARD-experienced PALACE 1-3 population; control of articular and extra-articular manifestations was observed in the DMARD-naive and DMARD-experienced populations.

Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **A. Kavanaugh**, Eli Lilly and Company, 5; **A. Ogdie**, AbbVie, 5, Amgen, 2, 5, BMS, 1, Celgene, 1, Corrona, 1, Janssen, 1, Eli

Lilly, 1, Novartis, 2, 5, Pfizer, 2, 5, National Institutes of Health/National Institute of Arthritis and Musculoskeletal and Skin Diseases, 2, Rheumatology Research Foundation, 2, National Psoriasis Foundation, 2; **A. Wells**, Abbvie, 1, 2, Eli Lilly & Co., 1, 2; **M. Bergman**, AbbVie, 5, 8, Amgen, 5, 8, Bristol-Myers Squibb, 5, 8, Genentech/Roche, 5, 8, Gilead, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Regeneron, 5, 8, Sanofi, 5, 8, Sandoz, 5, 8, JNJ (parent of Janssen), 1; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **F. Behrens**, Pfizer, 2, 5, 8, Janssen, 2, 5, 8, Chugai, 2, 5, 8, Celgene, 2, 5, 8, Bionorica, 2, Roche, 2, 5, 8, Abbvie, 5, 8, Sanofi, 5, 8, Lilly, 5, 8, Novartis, 5, 8, Genzyme, 5, 8, Boehringer, 5, 8, MSD, 5, 8, Amgen, 5, 8, UCB, 5, 8, Gilead, 5, 8, Sandoz, 5, 8; **S. Richter**, Amgen Inc., 1; **M. Brunori**, Amgen Europe GmbH, 1; **L. Teng**, Amgen Inc., 1; **B. Guerette**, Amgen Inc., 1; **J. Smolen**, AbbVie, 2, 5, 8, AstraZeneca, 2, 5, 8, Eli Lilly, 2, 5, 8, Celgene, 5, 8, Celltrion, 5, 8, Chugai, 5, 8, Gilead, 5, 8, ILTOO, 5, 8, Janssen, 5, 8, Kabi, 5, 8, Novartis-Sandoz, 5, 8, Pfizer Inc, 5, 8, Samsung, 5, 8, Sanofi, 5, 8.

Abstract Number: 0906

Bimekizumab Treatment Is Associated with Improvements in Back Pain and Fatigue in Patients with Active Psoriatic Arthritis: 48-Week Results from a Phase 2b Study

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients (pts) with psoriatic arthritis (PsA) require effective treatment across all symptoms. Bimekizumab (BKZ) is a humanized IgG1 monoclonal antibody which selectively neutralizes interleukin (IL)-17A and IL-17F. During BE ACTIVE (NCT02969525), a phase 2b dose-ranging study in pts with PsA, BKZ demonstrated improved peripheral joint, skin, and extra-articular outcomes over 48 weeks (wks).[1] The Bath Ankylosing Spondylitis Disease Activity Index (BASDAI)[2] is a validated instrument for evaluating disease activity and symptoms in pts with axial spondyloarthritis. We use the BASDAI to assess the effect of BKZ treatment on fatigue and pain in pts with PsA.

Methods: In this randomized controlled trial, pts received BKZ or placebo (PBO).[1] This post hoc analysis focuses on BASDAI over 48 wks. BASDAI data were collected prospectively from all pts as an efficacy variable. We report BASDAI50 (a 50% improvement on baseline [BL] BASDAI score), and mean change from BL (CfB) in BASDAI question scores (higher scores denote worse symptoms), for all BASDAI questions, with a focus on Question 1 (Q1; fatigue) and Question 2 (Q2; neck/hip/back pain). We also report the percentage (%) of pts who had a CfB in BASDAI Q1 or Q2 scores of ≥2 points.[3,4] Observed data are reported for the Full Analysis Set (FAS) in pt subsets with a baseline (BL) BASDAI score of ≥4, and ≥4 for all individual questions. Treatment-emergent adverse event (TEAE) rates are reported per 100 pt-years (PY) for the Safety Set (SS; pts who received ≥1 dose BKZ).

Results: 206 pts were randomized at BL (42 to PBO every 4 weeks [Q4W], 41 to each BKZ Q4W arm: 16 mg, 160 mg, 160 mg+320 mg loading dose [LD] and 320 mg). 152 pts had BASDAI ≥4 at BL (**Table**). 93 of these pts were in the 160–320 mg pool. Their mean (SD) BASDAI at BL was 6.20 (±1.42), and the BASDAI50 response rate was 43% (9%

Table: Mean change from baseline in BASDAI individual question scores at Week 12

Patients with BASDAI score ≥4 at BL (n=152), FAS, OC	PBO (n=32)	16 mg (n=27)	160 mg (n=30)	160 mg LD (n=31)	320 mg (n=32)	160–320 mg dose pool [a] (n=93)
All questions	−0.44	−1.84	−2.57	−3.15	−2.21	−2.63
Q1 (Fatigue)	0.19	−1.67	−2.17	−2.24	−1.44	−1.93
Q2 (Neck/back/hip pain)	−0.66	−1.56	−2.00	−3.07	−2.31	−2.45
Q3 (Peripheral joint pain/swelling)	−0.56	−2.07	−3.37	−3.62	−2.53	−3.15
Q4 (Areas tender to touch or pressure)	−0.78	−1.78	−2.40	−3.17	−2.16	−2.56
Mean of Q5 + Q6 (Morning stiffness intensity and duration)	−0.39	−2.11	−2.93	−3.64	−2.63	−3.05
Patients with BL score ≥4 for each BASDAI question, FAS, OC	**PBO**	**16 mg**	**160 mg**	**160 mg LD**	**320 mg**	**160–320 mg dose pool [a]**
Q1 (Fatigue) (n)	−0.56 (27)	−1.66 (29)	−2.88 (24)	−2.59 (30)	−1.57 (30)	−2.30 (84)
Q2 (Neck/back/hip pain) (n)	−1.00 (30)	−1.69 (29)	−2.21 (29)	−3.07 (29)	−2.55 (29)	−2.60 (87)
Q3 (Peripheral joint pain/swelling) (n)	−0.53 (36)	−2.10 (31)	−3.33 (36)	−3.93 (31)	−2.50 (34)	−3.21 (101)
Q4 (Areas tender to touch or pressure) (n)	−1.00 (33)	−2.10 (29)	−3.00 (29)	−3.34 (31)	−2.27 (33)	−2.85 (93)
Mean of Q5 + Q6 (Morning stiffness intensity and duration) (n)	−0.63 (27)	−2.35 (26)	−3.13 (30)	−3.98 (27)	−2.66 (32)	−3.21 (89)

[a] Patients on bimekizumab 160 mg, 160 mg LD or 320 mg. Dosing frequency was every 4 weeks. Patients in the 160 mg LD arm received a 320 mg dose at baseline and then 160 mg every 4 weeks from Week 4. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BL: baseline; FAS: Full Analysis Set; LD: loading dose; OC: observed case; PBO: placebo.

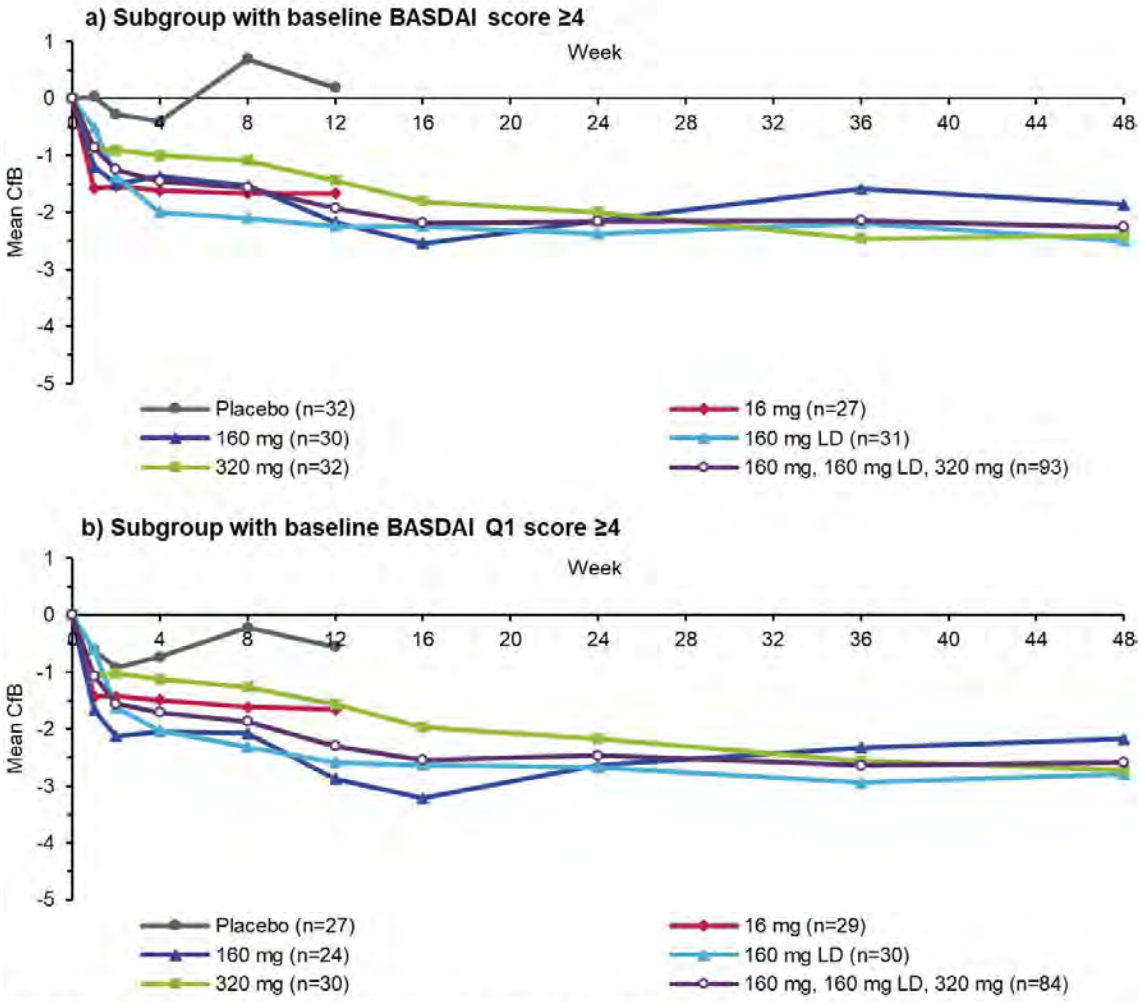
for PBO), and 56% at Wk 12 and Wk 48, respectively. 84 pts in the 160–320 mg pool scored ≥4 for BASDAI Q1 (mean at BL: 6.19 [±1.59]; Wk 48: 3.58 [±2.67], a mean CfB of –2.59). 87 pts in this BKZ pool scored ≥4 for BASDAI Q2 at BL (mean 6.47 [±1.66]; Wk 48: 3.49 [±2.56], a mean CfB of –2.99). Across all 160–320 mg doses, clear improvements in BASDAI Q1 and Q2 scores were seen by Wk 12, continuing to Wk 48. This was also shown for pts with BASDAI Q1 and Q2 scores ≥4 at BL (**Figures 1 and 2**).

For pts in the 160–320 mg pool with a BASDAI Q1 or Q2 score ≥4 at BL, 58–66% and 63–68% had a ≥2-point reduction in their Q1 and Q2 scores, respectively, across Wks 12, 24, and 48. For the same pts on PBO, 26% and 43% had a ≥2-point reduction in their Q1 and Q2 scores at Wk 12, respectively. TEAEs were reported in 74% of BKZ-treated pts (exposure-adjusted event rate [EAER]: 294/100 PY). Serious TEAEs were reported for 3.9% (EAER: 4.52/100 PY).

Conclusion: In this exploratory analysis, BKZ treatment was associated with improvements in BASDAI total and single question scores related to fatigue and neck, back and hip pain in pts with PsA.

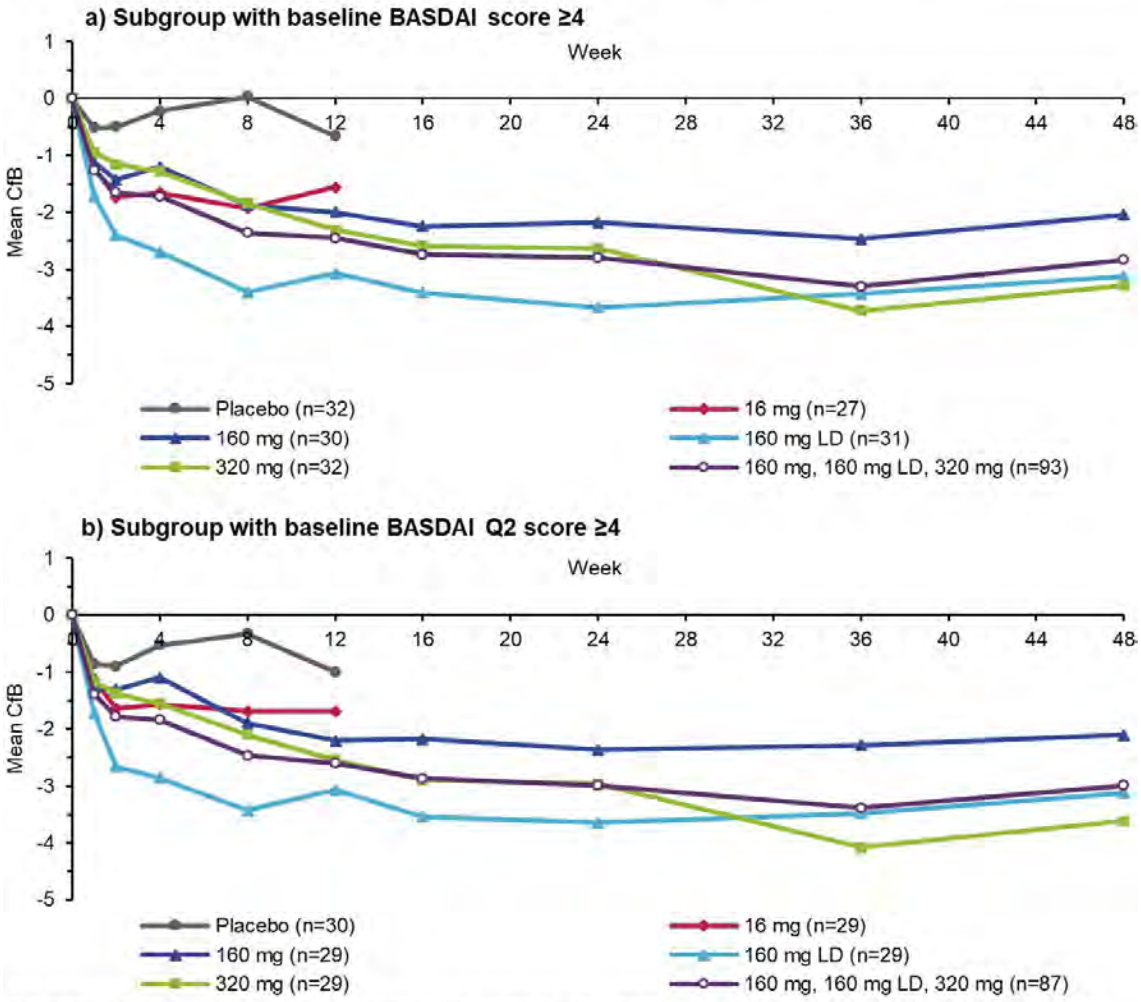
References: 1. Ritchlin C. Lancet 2020;395:427–40; **2.** Garrett S. J Rheumatol 1994;21:2286–91; **3.** Reilly M. Rheumatol 2010;49:812–9; **4.** Braun J. ARD 2006;65:316–20.

Figure 1: Mean change from baseline in BASDAI Question 1 (fatigue)



Full Analysis Set, observed cases. Dosing frequency was every 4 weeks. Patients in the 160 mg LD arm received a 320 mg dose at baseline and then 160 mg every 4 weeks from Week 4. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CfB: change from baseline; LD: loading dose.

Figure 2: Mean change from baseline in BASDAI Question 2 (neck/back/hip pain)



Full Analysis Set, observed cases. Dosing frequency was every 4 weeks. Patients in the 160 mg LD arm received a 320 mg dose at baseline and then 160 mg every 4 weeks from Week 4. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; CfB: change from baseline; LD: loading dose.

Disclosure: A. Deodhar, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **L. Gossec**, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **J. Coarse**, UCB Pharma, 3; **H. Edens**, UCB Pharma, 1, 3; **N. de Peyrecave**, UCB Pharma, 3; **D. Assudani**, UCB Pharma, 3; **B. Ink**, UCB Pharma, 3; **C. Ritchlin**, None.

Abstract Number: 0907

Long-term Outcomes with Filgotinib, an Oral Selective Janus Kinase 1 Inhibitor: 100-week Data from an Open-label Extension (OLE) Study in Patients with Active Psoriatic Arthritis (PsA)

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

	Rate per 100 PYE (number of events) at Week 52 (PYE=160)	Rate per 100 PYE (number of events) at Week 100 (PYE=262)
TEAE	213.9 (342)	191.8 (502)
Serious TEAE	5.6 (9)	5.3 (14)
Serious AE leading to death	0.6 (1)	0.4 (1)
Severe TEAE*	10.0 (16)	9.2 (24)
TEAE leading to permanent discontinuation of study drug†	3.1 (5)	2.7 (7)
TEAE of special interest		
All infections	62.5 (100)	52.7 (138)
All serious infections	1.9 (3)	1.5 (4)
Opportunistic infections	0	0
Herpes zoster	0.6 (1)	0.8 (2)
Active tuberculosis	0	0
Urinary tract infections	3.8 (6)	3.1 (8)
RTI	46.2 (74)	29.7 (78)
Upper RTIs	37.5 (60)	27.5 (72)
Pneumonia	0.6 (1)	0.4 (1)
Malignancies	0.6 (1)	0.4 (1)
Lymphoma	0	0
Non-melanoma skin cancer	0	0
Deep vein thrombosis	0	0
Pulmonary embolism	0	0
Major adverse cardiac events (adjudicated)	0.6 (1)	0.4 (1)
Death	0.6 (1)	0.4 (1)
Anemia	0	0
Neutropenia	1.3 (2)	0.8 (2)
Lymphopenia	0	0
Gastrointestinal perforation	0	0

Table 1. Overview of safety with FIL 200 mg QD at Week 52 and Week 100 of the EQUATOR2 OLE. *Defined as Grade ≥3. †Excludes deaths. AE, adverse event; FIL, filgotinib; OLE, open-label extension; PYE, patient-years of exposure; QD, once daily; RTI, respiratory tract infection; TEAE, treatment-emergent adverse event

Background/Purpose: EQUATOR (NCT03101670) was a randomized, 16-week, Phase 2, multicenter, double-blind, placebo (PBO)-controlled trial of filgotinib (FIL) in patients with active PsA (Mease P, et al. *Lancet* 2018;392:2367–77) . In EQUATOR, FIL was well tolerated and was efficacious vs PBO for the primary endpoint of Week 16 ACR20 response. Patients completing EQUATOR could join an ongoing 304-week OLE (EQUATOR2; NCT03320876). We report the findings of an interim analysis of EQUATOR2 at Week 100. Primary and secondary objectives were to assess safety/tolerability and efficacy, respectively.

Methods: In EQUATOR, patients with active moderate-to-severe PsA (≥5 swollen joints and ≥5 tender joints, fulfilling Classification for PsA [CASPAR] criteria) were randomized 1:1 to receive oral FIL 200 mg or PBO once daily (QD) for 16 weeks. At Week 16, patients could continue into the OLE, receiving FIL 200 mg QD. For this interim analysis, patients were followed for efficacy until the last patient completed their Week 100 visit; safety data were collected up to April 8, 2020. Efficacy measures included minimal disease activity (MDA; meeting 5/7 MDA criteria), MDA/very low disease activity (VLDA; meeting 7/7 MDA criteria), Psoriatic Arthritis Disease Activity Score (PASDAS) low disease activity (score ≤3.2) and VLDA (score ≤1.9), ACR20/50/70, and Psoriasis Area and Severity Index (PASI) 75/90/100. The number and proportion of patients achieving each endpoint were calculated using observed case (OC) and non-re-

	n/N (%)
MDA*	41/131 (31.3)
MDA VLDA†	13/131 (9.9)
PASDAS LDA‡	57/131 (43.5)
PASDAS VLDA§	23/131 (17.6)
ACR20	79/131 (60.3)
ACR50	57/131 (43.5)
ACR70	38/131 (29.0)
PASI 75¶	32/82 (39.0)
PASI 90¶	20/82 (24.4)
PASI 100¶	11/82 (13.4)

Table 2. Responders at Week 100 of the OLE (NRI). *Defined as meeting 5 out of 7 of the MDA criteria. †Defined as meeting 7 out of 7 of the MDA criteria. ‡Defined as a PASDAS score of ≤3.2. §Defined as a PASDAS score of ≤1.9. ¶PASI was only measured in patients with ≥3% of their body surface area affected by psoriasis. ACR, American College Rheumatology; LDA, low disease activity; MDA, minimal disease activity; NRI, non-responder imputation; OLE, open-label extension; PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriasis Area and Severity Index; VLDA, very low disease activity

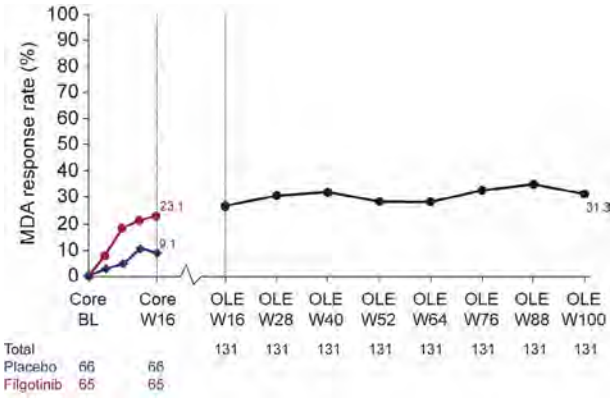

Figure 1. MDA response rate over time (NRI). BL, baseline; MDA, minimal disease activity; NRI, non-responder imputation; OLE, open-label extension; W, Week

sponder imputation (NRI) approaches. Adverse events (AEs) per 100 patient-years of exposure (from first exposure to FIL) are summarized.

Results: Of 131 randomized patients, 124 (95%) completed EQUATOR and 122 (93%) were enrolled in the OLE, of whom 104 patients (85%) remained in the study at Week 100. Safety and tolerability were similar at Week 100 to a previous analysis conducted at Week 52 (**Table 1**). No unexpected safety issues were identified. By Week 100, 1 death (bilateral pneumonia, leading to toxic shock with multi-organ failure) and 1 adjudicated major adverse cardiac event had occurred (both prior to Week 52). Five additional serious treatment-emergent AEs occurred from Week 52 to 100, including 1 serious infection (COVID-19). No deep vein thromboses or pulmonary embolisms occurred up to Week 100. Efficacy was sustained at Week 100 (**Table 2**). The response rate at Week 100 for all patients (regardless of original randomization to PBO or FIL) was 31.3% for MDA (NRI; 42.3% for OC; **Figure**), and 60.3%/43.5%/29.0% for ACR20/50/70 (NRI; 81.4%/58.8%/39.2% for OC). Of 15 patients originally randomized to FIL who were MDA responders at Week 16, 73.3% also had an MDA response at Week 100 (NRI). Sustained responses were observed at ≥3 consecutive visits (each of which was 12 weeks apart) for MDA in 34.4% of patients (NRI).

Conclusion: This interim analysis of long-term extension data from the PsA EQUATOR2 study found FIL 200 mg QD to be generally well tolerated up to Week 100 with a safety profile comparable to that seen up to Week 52. Response rates at Week 100 to FIL 200 mg QD were sTable and comparable to those reported at Week 52. In most patients who were MDA responders at Week 16, responses were also seen at Week 100.

Disclosure: L. Coates, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **F. Van den Bosch**, AbbVie, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Gilead, 5, Merck, 5, 8; **P. Helliwell**, AbbVie, 2, 8, Janssen, 2, Pfizer Inc, 8, Celgene, 8, Galapagos, 8, Amgen, 8, Novartis, 2, UCB, 8; **A. Rychlewska-Hańczewska**, Galapagos, 2, Gilead Sciences, 2; **M. Stanislavchuk**, AstraZeneca, 2, Celltrion, 2, Eli Lilly, 2, Galapagos, 2, Genentech, 2, GlaxoSmithKline, 2, Human Genome, 2, MedImmune, 2, Pfizer, 2, Roche, 2, UCB, 2; **L. Gilles**, Galapagos, 3; **L. Gheyle**, Galapagos, 1, 3; **K. Liu**, Gilead Sciences, 1, 3; **M. Trivedi**, Gilead Sciences, 1, 3, Amgen, 1; **M. Alani**, Gilead Sciences, 3; **R. Besuyen**, Galapagos, 1, 3; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5.

Abstract Number: 0908

Guselkumab Efficacy in Adult Patients with Active Psoriatic Arthritis by Baseline Demographic and Disease Characteristics: Pooled Results of Two Phase 3, Randomized, Placebo-Controlled Studies

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

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Background/Purpose: Guselkumab (GUS), a human monoclonal antibody targeting the IL-23p19-subunit, has shown consistent efficacy in psoriasis pts regardless of body weight/body mass index (BMI).[1] GUS has also shown efficacy across joint and skin endpoints at Week 24 (W24) of the Phase 3 DISCOVER-1[2] and DISCOVER-2 PsA[3] trials. We assessed GUS efficacy at W24 across baseline demographic and disease characteristics subgroups by pooling data across the 2 trials.

Figure 1. ACR50 Response at Week 24 by Select Baseline Characteristics: Pooled Results of DISCOVER-1 and DISCOVER-2

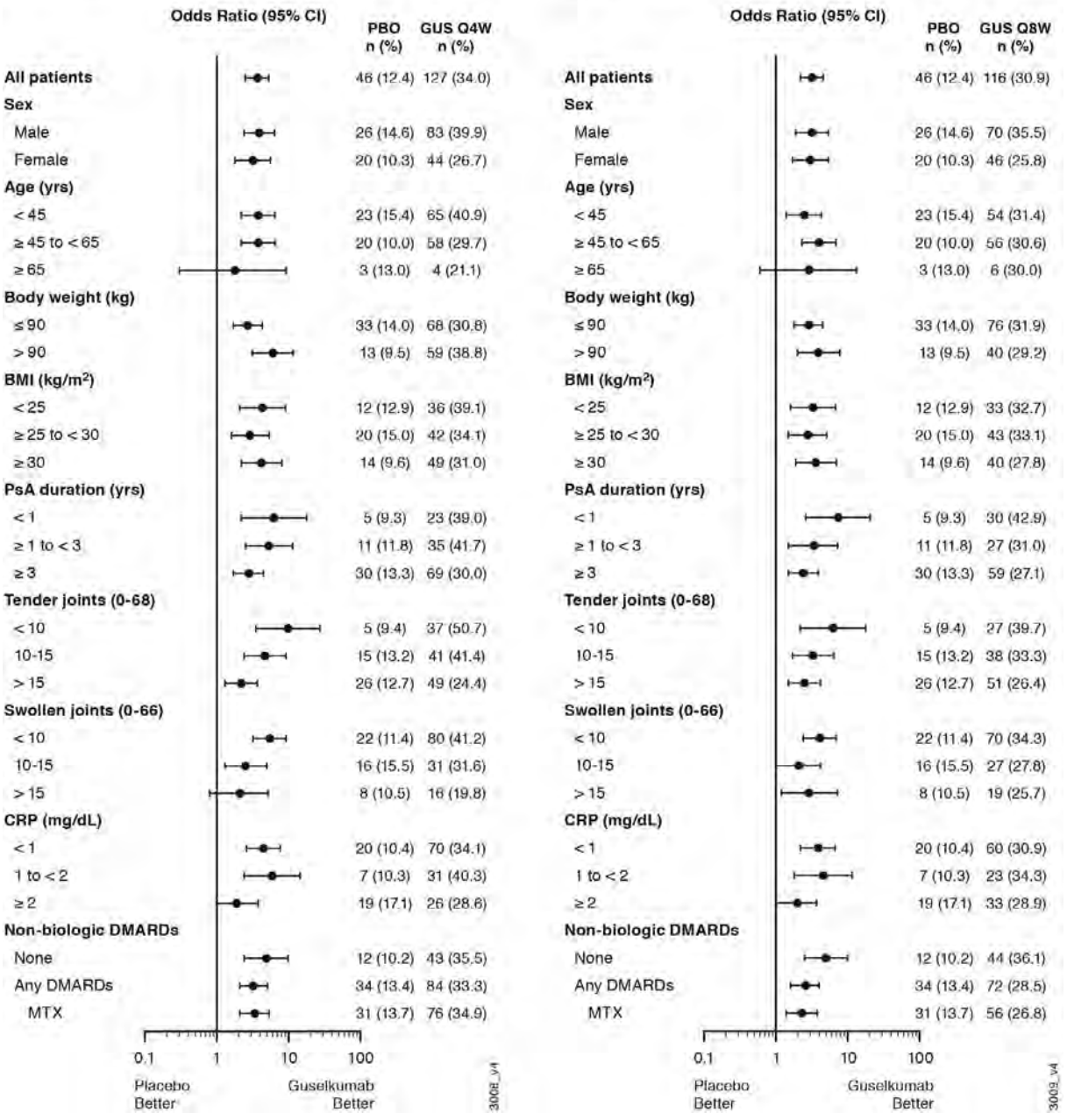
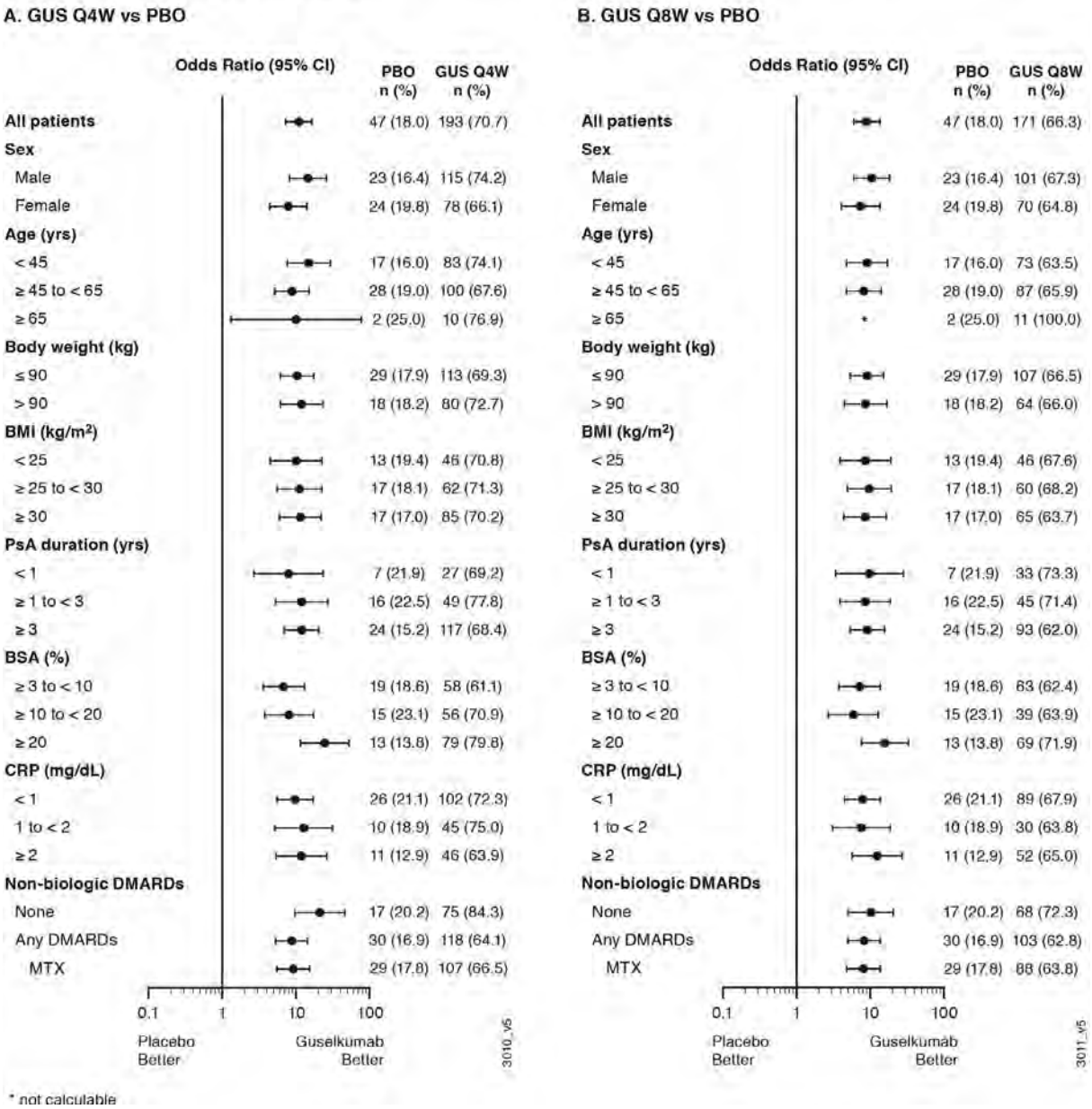


Figure 2. IGA 0/1 Response at Week 24 by Select Baseline Characteristics: Pooled DISCOVER-1 and DISCOVER-2 Patients with ≥3% BSA psoriasis and IGA ≥2 at W0



Methods: Adults with active PsA despite standard therapies were enrolled in DISCOVER-1 (≥3 swollen & ≥3 tender joints; CRP ≥0.3 mg/dL) and DISCOVER-2 (≥5 swollen & ≥5 tender joints; CRP ≥0.6 mg/dL). 31% of DISCOVER-1 pts had received 1-2 prior TNF inhibitors; DISCOVER-2 pts were biologic-naïve. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then every 8 weeks (Q8W); or placebo (PBO). GUS effects on joint (ACR50) and skin (Investigator's Global Assessment [IGA=0/1 + ≥2-grade reduction from W0] in pts with ≥3% body surface area [BSA] psoriasis and IGA ≥2 at W0) responses were evaluated by pt sex, age, body weight, BMI, PsA duration, tender/swollen joint counts (ACR50 only), % BSA (IGA 0/1 only), CRP, and non-biologic (nb) DMARD/methotrexate (MTX) use at W0. Missing data were imputed as nonresponse. Logistic regression compared GUS vs PBO; odds ratios (ORs) and 95% confidence intervals (CIs) are shown on a logarithmic scale.

Results: Baseline characteristics of randomized and treated pts in DISCOVER-1 (N=381) and DISCOVER-2 (N=739) were generally well-balanced across groups.[1,2] On average, the 1120 pooled pts were 47 yrs and 85 kg at W0; 52%

were male; 96% were white. At W24, 34% (127/373) and 31% (116/375), respectively, of pooled GUS Q4W- and Q8W-treated pts achieved ACR50 vs 12% (46/372) for PBO; respective ORs (95% CIs) were 3.7 (2, 5) and 3.2 (2, 5). In subgroups with sufficient sample size, the benefit of GUS Q4W and Q8W over PBO in substantially improving joint signs and symptoms was seen regardless of sex (ORs 3–4), age (2–4), body weight/BMI (3–6), PsA duration (2–7), swollen/tender joint count (2–10), CRP (2–6), or nbDMARD/MTX use (2–5) at baseline. In pooled pts with ≥3% BSA psoriasis and IGA ≥2 at W0, 71% (193/273) and 66% (171/258), respectively, of GUS Q4W- and Q8W-treated pts, vs 18% (47/261) for PBO, had an IGA 0/1 response at W24; respective ORs (95% CIs) were 11 (7, 16) and 9 (6, 14). The benefit of GUS in achieving clear or almost clear skin was seen regardless of sex (ORs 7-15), age (8-15), body weight/BMI (9-12), PsA duration (8-12), % BSA (7-25), CRP (8-13), or nbDMARD/MTX use (8–21) at baseline. Note that small sample sizes in several pt subgroups (eg, pts >65 years, swollen joint count >15) limit their data interpretation. Consistent results were seen for other joint (ACR20/70), skin (PASI90/100), and soft tissue (enthesitis) outcomes.

Conclusion: Conclusions: The benefits of guselkumab 100 mg Q4W and Q8W in substantially improving signs and symptoms of active PsA appeared to be consistent irrespective of the baseline characteristics assessed.

References: [1]Armstrong A, et al. World Congress of Dermatology 2019; Poster P524; [2]Deodhar A, et al. Lancet 2020;395:1115-25; [3]Mease P, et al. Lancet 2020;395:1126-36.

Disclosure: A. Deodhar, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **W. Boehncke**, Janssen Research & Development, LLC, 2, 5; **J. Tesser**, Janssen, 1, 2, 3, Abbvie, 1, 2, 3, Sun Pharma, 1, 2, 3, Novartis, 1, 2, Lilly, 1, 2, 3, BMS, 1, 2, 3, Pfizer, 1, 2, 3, Amgen, 1; **E. Schiopu**, Octapharma, 2; **S. Chakravarty**, Janssen Scientific Affairs, LLC, 1, 3; **A. Kollmeier**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **E. Hsia**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **X. Xu**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **M. Shawi**, Janssen Global Services, LLC, 3, Johnson & Johnson, 1; **Y. Jiang**, None; **S. Sheng**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **P. Agarwal**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **J. Merola**, AbbVie, 9, Merck, 9, Dermavant, 9, Eli Lilly, 9, Novartis, 9, Janssen, 9, UCB, 9, Samumed, 9, Celgene, 9, Sanofi, 9, Regeneron, 9, GlaxoSmithKline, 9, Sun Pharmaceutical, 9, Almirall, 9, Biogen, 9, Pfizer, 9, Incyte, 9, Aclaris, 9, LEO Pharma, 9; **I. McInnes**, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **C. Ritchlin**, None.

Abstract Number: 0909

Residual Disease Activity in Psoriatic Arthritis Patients Treated with Secukinumab and Adalimumab Who Achieved Remission or Low Disease Activity: Results from a Phase 3b, Randomized, Double-blinded, Active-controlled, Head-to-head Study

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Recent EULAR recommendations propose that treatment of psoriatic arthritis (PsA) should seek remission (REM) or alternatively low disease activity (LDA) by regular disease activity assessments using composite indices targeting one or several key manifestations in PsA.[1,2] The EXCEED study compared secukinumab (SEC) and adalimumab (ADA) monotherapy in patients with active PsA with inadequate response/intolerance to csDMARDs. We present a *post hoc* analysis of patients who achieved LDA and/or REM at Week 24 and 52 with their respective levels of residual disease activity (RDA) in the core components of the various composite indices.

Methods: Head-to-head, phase-3b, randomized, double-blind trial: biologic naïve active PsA patients were randomized to receive SEC 300 mg subcutaneous at baseline, Week 1-4, and then every 4wks (q4w) until Week 48 or ADA 40 mg subcutaneous at baseline and then q2w until Week 50. The primary and key secondary endpoints at Week 52 were previously reported.[3] LDA and REM were assessed using MDA, VLDA, DAPSA REM/LDA and PASDAS REM/LDA. The proportions of RDA were established for clinical domains of PsA (articular, enthesitis, and psoriasis), HAQ, VAS pain, patient global assessment (PtGA) and Physician's global assessment (PhGA) of disease activity. The composite indices were analyzed using logistic regression and missing data was handled using multiple imputation. RDA levels are presented in patients who achieved either LDA and/or REM.

Results: A similar proportion of patients receiving SEC and ADA achieved LDA and REM at Week 24. Further increase from Week 24 in LDA/REM was observed in both treatment groups through Week 52. VLDA was achieved by a lower proportion of patients than PASDAS LDA+REM/REM and DAPSA LDA+REM/REM at Week 24 and 52 (Table 1). The proportion of patients achieving VLDA, PASDAS REM and DAPSA REM in the treatment groups at Week 24 had low RDA (10%-19%) across core components except for PhGA and PASI ≤1 (Table 2). At least 66%, 59% and 49% of the patients achieving MDA, PASDAS LDA+REM and DAPSA LDA+REM, respectively, across both treatment groups had no RDA at Week 24 suggesting that MDA was the most stringent composite index. Further decrease in RDA was observed among patients who achieved either REM or LDA at Week 52 across all composite indices in both treatment groups (Table 2 and 3).

Conclusion: A comparable proportion of patients achieved LDA and/or REM at Week 24 across the two treatment groups with further improvements in response/targets at Week 52. Patients who achieved VLDA or MDA tended to

Outcomes, data is presented as % response unless specified otherwise	Week 24			Week 52		
	SEC 300 mg (N=426)	ADA 40 mg (N=427)	P value*	SEC 300 mg (N=426)	ADA 40 mg (N=427)	P value*
MDA	34.5	33.0	0.7084	43.4	37.9	0.1141
VLDA	10.3	11.2	0.6579	18.1	16.9	0.6755
PASDAS based REM	10.7	11.8	0.5553	21.9	18.0	0·1708
PASDAS based LDA and REM	45.8	38.1	0.0322	51.1	44.1	0·0557
DAPSA based REM	16.0	16.6	0.6767	25.4	24.2	0·8252
DAPSA LDA and REM	57.5	51.1	0.1061	61.7	53.1	0·0178

*P values versus adalimumab; unadjusted P values are reported

ADA, adalimumab; DAPSA, disease activity in psoriatic arthritis; LDA, low disease activity; MDA, minimal disease activity (66/68 SJC/TJC); PASDAS, psoriatic arthritis disease activity score; REM, remission; SEC, secukinumab; VLDA, very low disease activity (66/68 SJC/TJC)

Table 1. Proportion of patients achieving LDA and/or REM at Week 24 and 52

Components, %	MDA		VLDA		PASDAS REM		PASDAS LDA+REM		DAPSA REM		DAPSA LDA+REM	
	SEC (N=146)	ADA (N=141)	SEC (N=44)	ADA (N=48)	SEC (N=43)	ADA (N=50)	SEC (N=185)	ADA (N=158)	SEC (N=66)	ADA (N=70)	SEC (N=235)	ADA (N=214)
TJC≤ 1 (68TJC)	69	77	100	100	81	86	59	70	92	91	55	63
SJC≤ 1 (66SJC)	90	89	100	100	93	98	85	87	97	97	88	86
LEI=0	87	89	93	100	95	94	84	90	86	93	82	81
LDI= 0	97	99	98	100	100	100	99	99	97	100	97	98
HAQ-DI ≤0.5	87	87	100	100	93	94	77	76	86	90	63	67
Pt VAS Pain ≤ 1.5 cm	75	84	100	100	86	96	60	73	88	96	51	56
Pt GA ≤20 mm	80	74	100	100	95	94	63	68	97	97	51	49
Ph GA ≤10 mm	66	69	82	90	100	100	70	73	80	81	55	55
PASI score ≤1	98	92	93	85	91	74	85	79	89	74	80	70

N, number of responders at Week 24
ADA, adalimumab; DAPSA, disease activity in psoriatic arthritis; GA, global assessment; LDA, low disease activity; LDI, Leeds dactylitis index; LEI, Leeds enthesitis index; HAQ-DI, health assessment questionnaire-disability index; MDA, minimal disease activity (66/68 SJC/TJC); PASDAS, psoriatic arthritis disease activity score; PASI, psoriasis area severity index; Ph/Pt, physician/patient; REM, remission; SEC, secukinumab; TJC, tender joint count; VLDA, very low disease activity (66/68 SJC/TJC); SJC, swollen joint counts; VAS, visual analogue index

Table 2. Proportion of patients with no residual disease activity levels at Week 24

Components, %	MDA		VLDA		PASDAS REM		PASDAS LDA+REM		DAPSA REM		DAPSA LDA+REM	
	SEC (N=185)	ADA (N=162)	SEC (N=77)	ADA (N=72)	SEC (N=93)	ADA (N=76)	SEC (N=216)	ADA (N=186)	SEC (N=108)	ADA (N=103)	SEC (N=262)	ADA (N=224)
TJC≤ 1 (68TJC)	74	81	100	100	83	88	66	75	91	92	62	69
SJC≤ 1 (66SJC)	93	90	100	100	97	93	88	86	100	100	89	89
LEI=0	94	90	97	96	98	96	91	90	96	94	89	87
LDI= 0	100	99	100	100	99	100	99	100	100	99	99	100
HAQ-DI ≤0.5	90	85	100	100	96	90	81	76	93	83	70	67
Pt VAS Pain ≤ 1.5 cm	80	82	100	100	89	93	72	71	94	93	58	60
PGA ≤20 mm	80	82	100	100	96	95	70	72	94	93	58	61
Ph GA ≤10 mm	77	78	88	92	98	99	80	81	86	88	69	67
PASI score ≤1	97	97	91	89	91	95	89	84	88	86	85	77

N, number of responders at Week 52
ADA, adalimumab; DAPSA, disease activity in psoriatic arthritis; GA, global assessment; LDA, low disease activity; LDI, Leeds dactylitis index; LEI, Leeds enthesitis index; HAQ-DI, health assessment questionnaire-disability index; MDA, minimal disease activity (66/68 SJC/TJC); PASDAS, psoriatic arthritis disease activity score; PASI, psoriasis area severity index; Ph/Pt, physician/patient; REM, remission; SEC, secukinumab; TJC, tender joint count; VLDA, very low disease activity (66/68 SJC/TJC); SJC, swollen joint counts; VAS, visual analogue index

Table 3. Proportion of patients with no residual disease activity levels at Week 52

have a lower residual disease activity than those who achieved PASDAS REM/LDA+REM or DAPSA REM/LDA+REM. Residual disease activity was lower in patients reaching REM than LDA and somewhat lower in patients who achieved VLDA than PASDAS REM or DAPSA REM.

References:

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2. Coates LC, et al. *Rheumatology (Oxford).* 2017;56:1251-1253.
3. McInnes IB, et al. *LANCET.* 2020;395:1496-1505.

Disclosure: I. McInnes, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **L. Coates**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5; **P. Nash**, AbbVie, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8; **A. Ogdie**, Lilly, 5, Amgen, 5, AbbVie, 5, BMS, 5, Celgene, 5, Janssen, 5, Norvatis, 2, 5, Pfizer, 2, 5, Takeda, 5; **F. Behrens**, Pfizer, 2, 5, 8, Janssen, 2, 5, 8, Chugai, 2, 5, 8, Celgene, 2, 5, 8, Bionorica, 2, Roche, 2, 5, 8, Abbvie, 5, 8, Sanofi, 5, 8, Lilly, 5, 8, Novartis, 5, 8, Genzyme, 5, 8, Boehringer, 5, 8, MSD, 5, 8, Amgen, 5, 8, UCB, 5, 8, Gilead, 5, 8, Sandoz, 5, 8; **P. Goupille**, MSD France, 1, 2, Abbvie, 1, Amgen, 1, Biogaran, 1, 2, BMS, 1, Celgene, 1, Chugai, 1, Lilly, 1, Hospira, 1, Janssen, 1, Medac, 1, Nordic Pharma, 1, Novartis, 1, Sanofi-Genzyme, 1, Pfizer, 1, UCB Pharma, 1; **A. Kavanaugh**, AbbVie, 2, 9, Amgen, 2, 9, AstraZeneca, 2, 9, Bristol-Myers Squibb, 2, 9, Celgene, 2, 9, Janssen, 2, 9, Pfizer, 2, 9, Roche, 2, 9, UCB, 2, 9; **R. Martin**, Novartis, 1, 3; **E. Quebe-Fehling**, Novartis, 1, 3; **C. Gaillez**, Novartis, 1, 3.

Abstract Number: 0910

Effect of Filgotinib on the Complete Resolution of Enthesitis in Psoriatic Arthritis (PsA) Patients: 52-week Results from EQUATOR2

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: EQUATOR (NCT03101670) was a 16-week, Phase 2, double-blind, randomized placebo-controlled trial of filgotinib for PsA. At Week 16, placebo-treated patients could switch to filgotinib and those on filgotinib could continue treatment for up to an additional 304 weeks in an open-label extension (OLE) study (EQUATOR2; NCT03320876). This prespecified analysis at Week 52 of the OLE assessed the effect of filgotinib on clinical enthesitis after 52 weeks of treatment in the OLE.

Methods: In EQUATOR, patients with active moderate-to-severe PsA (≥5 swollen joints and ≥5 tender joints, fulfilling Classification for PsA [CASPAR] criteria) were randomized 1:1 to receive oral filgotinib 200 mg or placebo once daily (QD) for 16 weeks. At Week 16, patients could continue into the OLE, receiving filgotinib 200 mg QD. The effects on Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index and Leeds Enthesitis Index (LEI) resolution were assessed in patients with core baseline enthesitis (SPARCC or LEI >0) up to and including Week 52 of EQUATOR2 (≤68 weeks in total), using observed case (OC) and non-responder imputation (NRI) analyses.

	Responder at OLE Week 52 n/N (%)					
	NRI			Observed cases		
	Filgotinib → filgotinib	Placebo → filgotinib	Total	Filgotinib → filgotinib	Placebo → filgotinib	Total
LEI resolution						
Core Week 16 responder	13/17 (76.5)	8/11 (72.7)	21/28 (75.0)	13/15 (86.7)	8/10 (80.0)	21/25 (84.0)
Core Week 16 non-responder	10/13 (76.9)	20/32 (62.5)	30/45 (66.7)	10/12 (83.3)	20/27 (74.1)	30/39 (76.9)
SPARCC Enthesitis Index resolution						
Core Week 16 responder	10/13 (76.9)	8/11 (72.7)	18/24 (75.0)	10/11 (90.9)	8/10 (80.0)	18/21 (85.7)
Core Week 16 non-responder	17/21 (81.0)	20/36 (55.6)	37/57 (64.9)	17/20 (85.0)	20/31 (64.5)	37/51 (72.5)

Table. Number of patients who achieved or maintained their LEI and SPARCC resolution of enthesitis at OLE Week 52. Only subjects with enthesitis (LEI >0 or SPARCC Enthesitis Index >0) at core baseline were considered. LEI, Leeds Enthesitis Index; NRI, non-responder imputation; OLE, open-label extension; SPARCC, Spondyloarthritis Research Consortium of Canada

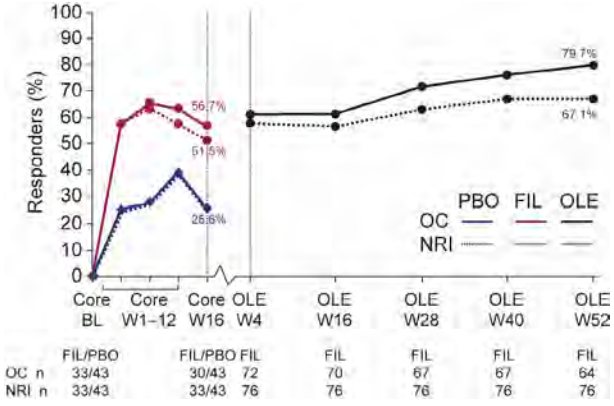

Figure 1. Proportion of LEI responders over time. BL, baseline; FIL, filgotinib; LEI, Leeds Enthesitis Index; NRI, non-responder imputation; OC, observed cases; OLE, open-label extension; PBO, placebo; W, week. Note: The percentage of responders in the placebo group up to core Week 16 was the same in the OC and NRI analyses

Results: In EQUATOR, 131 patients were randomized, of which 76 and 85 had LEI >0 and SPARCC >0 at baseline, respectively. At OLE Week 52, 79.7% and 67.1% of all patients with LEI >0 at baseline (regardless of treatment in the core 16-week trial) achieved LEI resolution (i.e. LEI=0) in the OC and NRI analyses, respectively (Figure 1), and 76.4% and 64.7% of those with SPARCC >0 at baseline, achieved SPARCC Enthesitis Index resolution (i.e. SPARCC=0) in the OC and NRI analyses, respectively (Figure 2). Comparing patients originally assigned filgotinib versus placebo, the proportion of patients with clinical resolution at Week 16 of the core EQUATOR trial was 51.5% and 25.6%, respectively, for LEI, and 35.1% and 22.9%, respectively, for SPARCC (NRI analysis; Figures 1 and 2). At OLE Week 52, the proportion of patients with clinical resolution had increased in both the filgotinib and placebo groups from core

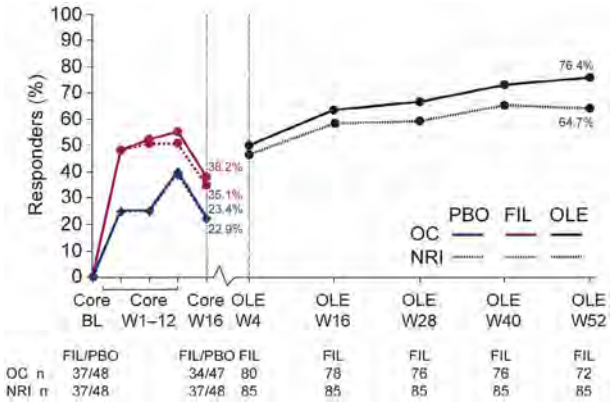

Figure 2. Proportion of SPARCC responders over time. BL, baseline; FIL, filgotinib; NRI, non-responder imputation; OC, observed cases; OLE, open-label extension; PBO, placebo; SPARCC, Spondyloarthritis Research Consortium of Canada; W, week

Week 16 (Figures 1 and 2). Of filgotinib-treated patients who achieved clinical resolution of enthesitis (LEI or SPARCC) at core Week 16 of EQUATOR, 76.5% (13 out of 17) and 76.9% (10 out of 13) also achieved responses at Week 52 of the OLE for LEI and SPARCC, respectively, in the NRI analysis (Table). Of filgotinib-treated patients who did not achieve clinical resolution of enthesitis (LEI or SPARCC) at core Week 16, 76.9% (10 out of 13) and 81.0% (17 out of 21) had responded by Week 52 for LEI and SPARCC, respectively, in the NRI analysis (Table).

Conclusion: Data from this 52-week OLE interim analysis suggest that further improvement in enthesitis can be expected with filgotinib 200 mg QD beyond 16 weeks of treatment in patients with pre-existing enthesitis. The majority of patients were able to maintain and/or achieve clinical resolution of enthesitis by Week 52. These findings should be confirmed in the further extension of this trial and in future Phase 3 trials.

Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **L. Coates**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5; **F. Van den Bosch**, AbbVie, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Gilead, 5, Merck, 5, 8; **P. Helliwell**, AbbVie, 2, 8, Janssen, 2, Pfizer Inc, 8, Celgene, 8, Galapagos, 8, Amgen, 8, Novartis, 2, UCB, 8; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **L. Gilles**, Galapagos, 3; **L. Gheyle**, Galapagos, 1, 3; **M. Trivedi**, Gilead Sciences, 1, 3, Amgen, 1; **M. Alani**, Gilead Sciences, 3; **R. Besuyen**, Galapagos, 1, 3.

Abstract Number: 0911

Impact of Filgotinib on Structural Lesions in the Sacroiliac Joints at 12 Weeks in Patients with Active Ankylosing Spondylitis: Correlation with Clinical Endpoints

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: In the Phase 2 TORTUGA trial (NCT03117270), the oral, selective Janus kinase 1 inhibitor filgotinib reduced inflammation in patients with active ankylosing spondylitis (AS), as measured by Spondyloarthritis Research Consortium of Canada (SPARCC) MRI scores (van der Heijde D, et al. *Lancet* 2018;392:2378–87). In this post hoc analysis, we compared the effects of filgotinib on MRI measures of structural change in the sacroiliac joint (SIJ) with effects on clinical parameters.

Methods: TORTUGA was a randomized trial of 116 patients with active AS (as per modified New York classification criteria, with sacroiliiitis confirmed by central reading) treated with filgotinib 200 mg (n=58) or placebo (n=58) once daily for 12 weeks. MRI scans at baseline and Week 12 (or early discontinuation) were re-evaluated post hoc in a blinded fashion by 2 experts to determine SPARCC SIJ Structural Scores (SSS); erosion, backfill, ankylosis, and fat lesion scores. Observed changes from baseline in the SPARCC SSS measures were evaluated using analysis of covariance with factors for treatment, baseline value, and randomization stratification. Least squares mean changes from baseline and between-group differences with 95% confidence intervals were calculated; p values were nominal. Data were then compared with clinical outcomes. Pearson correlations to assess intra-subject relationships were determined for changes in structural lesions from baseline to Week 12 versus changes in C-reactive protein, Ankylosing Spondylitis Disease Activity Score, Bath Ankylosing Spondylitis Disease Activity Index, Bath Ankylosing Spondylitis Functional Index, and SPARCC MRI SIJ and spine inflammation scores.

Results: Evaluable MRI scans (baseline and Week 12) were obtained from 87 patients (48 filgotinib, 39 placebo). At baseline, there were no noTable differences in MRI structural lesions (erosion, backfill, ankylosis, or fat lesion scores) between filgotinib and placebo (**Table 1**). From baseline to Week 12, erosion scores decreased with filgotinib and

Score	Mean (SD) baseline score	LSM change from baseline (95% CI) at Week 12	LSM group difference at Week 12 (95% CI)
Erosion			
Filgotinib	3.38 (5.34)	−0.46 (−1.31, 0.40)	−1.01 (−1.87, −0.16) p=0.02
Placebo	2.62 (3.76)	0.56 (−0.31, 1.42)	
Backfill			
Filgotinib	1.02 (1.99)	0.76 (0.07, 1.45)	1.02 (0.32, 1.72)
Placebo	1.35 (2.59)	−0.26 (−0.97, 0.45)	p=0.005
Ankylosis			
Filgotinib	9.58 (8.15)	0.14 (−0.02, 0.30)	0.06 (−0.10, 0.22)
Placebo	9.83 (8.45)	0.08 (−0.08, 0.25)	p=0.46
Fat lesions			
Filgotinib	4.19 (6.06)	0.37 (−0.23, 0.97)	0.43 (−0.18, 1.03)
Placebo	4.35 (5.44)	−0.06 (−0.67, 0.56)	p=0.17

Table 1. SPARCC SIJ SSS. CI, confidence interval; LSM, least squares mean; SD, standard deviation; SIJ, sacroiliac joint; SPARCC, Spondyloarthritis Research Consortium of Canada; SSS, SIJ structural scores

	Treatment	Erosion		Backfill		Ankylosis		Fat lesions	
		R	p value	R	p value	R	p value	R	P value
CRP	Filgotinib (n=47)	0.03271	0.8272	–0.10905	0.4656	0.04849	0.7462	–0.03012	0.8407
	Placebo (n=39)	–0.13964	0.3965	–0.04245	0.7975	–0.01842	0.9114	–0.17774	0.2790
ASDAS	Filgotinib (n=47)	0.04626	0.7575	–0.14865	0.3187	0.08502	0.5699	0.00796	0.9577
	Placebo (n=39)	–0.09851	0.5508	0.24511	0.1326	0.31840	0.0482	0.09311	0.5729
BASDAI	Filgotinib (n=47)	0.13275	0.3737	–0.16219	0.2760	0.03497	0.8155	–0.06120	0.6828
	Placebo (n=39)	–0.03679	0.8240	0.34156	0.0333	0.29057	0.0727	0.21383	0.1912
BASFI	Filgotinib (n=47)	0.01148	0.9389	–0.05060	0.7355	–0.03208	0.8305	–0.10663	0.4756
	Placebo (n=39)	0.15751	0.3383	0.13100	0.4267	0.35698	0.0257	0.00908	0.9563
SPARCC MRI inflammation SIJ	Filgotinib (n=47)	0.35921	0.0132	–0.41479	0.0037	0.01711	0.9091	–0.16252	0.2751
	Placebo (n=39)	0.56043	0.0002	–0.37483	0.0187	–0.05163	0.7549	–0.04282	0.7958
SPARCC MRI inflammation spine	Filgotinib (n=47)	0.20778	0.1611	–0.26756	0.0690	–0.01311	0.9303	0.11490	0.4418
	Placebo (n=39)	–0.06349	0.7010	–0.06885	0.6770	–0.06645	0.6878	–0.02965	0.8578

Table 2. Pearson correlations between change from baseline to Week 12 in clinical and MRI inflammation endpoints and MRI structural lesions. ASDAS, Ankylosing Spondylitis Disease Activity Score; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; CRP, C-reactive protein; MRI, magnetic resonance imaging; R, Pearson correlation; SIJ, sacroiliac joint; SPARCC, Spondyloarthritis Research Consortium of Canada

increased with placebo (p=0.02 for between-group difference; **Table 1**). Backfill scores increased with filgotinib but not placebo (p=0.005). There were no significant between-group differences in the change from baseline to Week 12 for ankylosis (p=0.46) or fat lesions (p=0.17) (**Table 1**). At Week 12, changes in erosion scores were positively correlated with changes in SPARCC MRI SIJ inflammation scores (filgotinib: r=0.35921, p=0.0132; placebo: r=0.56043, p=0.0002; **Table 2**), indicating that changes in inflammation and structural scores occur together in the same individual. A negative correlation was observed for backfill (filgotinib: r=–0.41479, p=0.0037; placebo: r=–0.37483, p=0.0187; **Table 2**). All observed correlations were moderate. Overall, significant correlations with erosion and backfill scores were not observed for other clinical endpoints, or for any clinical endpoint with ankylosis or fat lesion scores (**Table 2**).

Conclusion: In the 12-week TORTUGA trial, filgotinib was associated with a decrease in SIJ inflammation compared with placebo—as assessed by MRI—that correlated with a decrease in SIJ erosions and an increase in backfill.

Disclosure: W. Maksymowych, CARE Arthritis Limited, 9, AbbVie, 2, 5, 8, Boehringer Ingelheim, 5, Celgene, 5, Eli Lilly, 5, Galapagos, 5, Janssen, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8; **M. Østergaard**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Hospira, 5, 8, Janssen, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Novo Nordisk, 5, Orion, 5, 8, Regeneron, 5, Roche, 5, 8, UCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, Boehringer Ingelheim, 5, 8, Sandoz, 5, 8, Sanofi, 5, 8; **R. Landewé**, AbbVie, 2, 5, 8, AstraZeneca, 5, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, Galapagos, 5, Novartis, 5, Pfizer Inc, 2, 5, 8, UCB, 2, 5, 8, GlaxoSmithKline, 5, Janssen, 2, 5, 8, Merck, 5, 8, Rheumatology Consultancy BV, 1, Ablynx, 5, Amgen, 2, 5, 8, Celgene, 5, Gilead, 5, Novo Nordisk, 5, Roche, 2, 5, 8, Schering, 2, 5, 8, TiGenix, 5; **W. Barchuk**, Gilead Sciences, 1, 3, AbbVie, 9, Eli Lilly, 9, Johnson & Johnson, 9; **K. Liu**, Gilead Sciences, 1, 3; **C. Tasset**, Galapagos, 1, 3; **L. Gilles**, Galapagos, 3; **T. Hendrikx**, Galapagos, 1, 3; **R. Besuyen**, Galapagos, 1, 3; **X. Baraliakos**, AbbVie, 2, 5, Celgene, 2, 5, Galapagos, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 2, 5, Chugai, 2, 5, MSD, 2, 5, Sandoz, 2, 5, Hexal, 2, 5.

Abstract Number: 0912

Effectiveness of DETECT Algorithm in Japanese Systemic Sclerosis Patients with Old or New Hemodynamic Definition of Pulmonary Arterial Hypertension

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

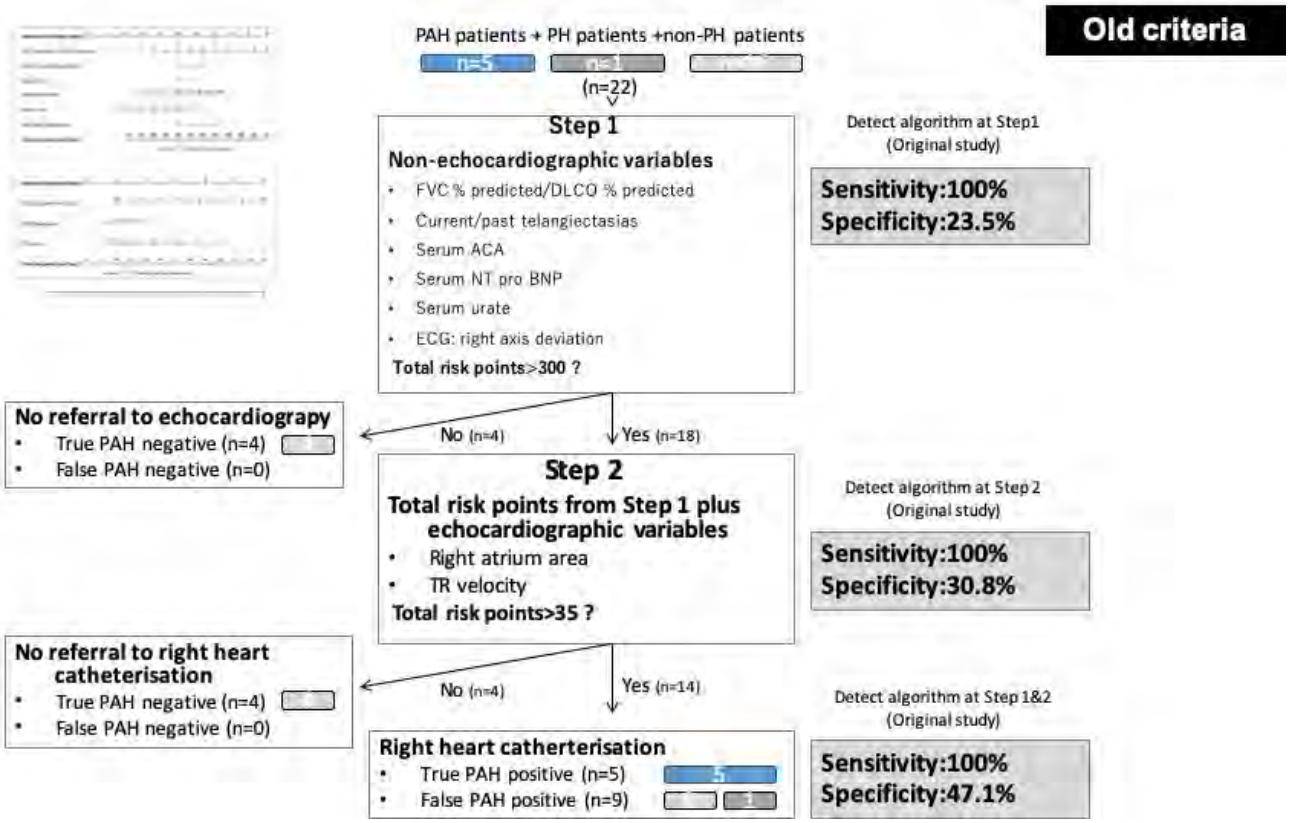
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

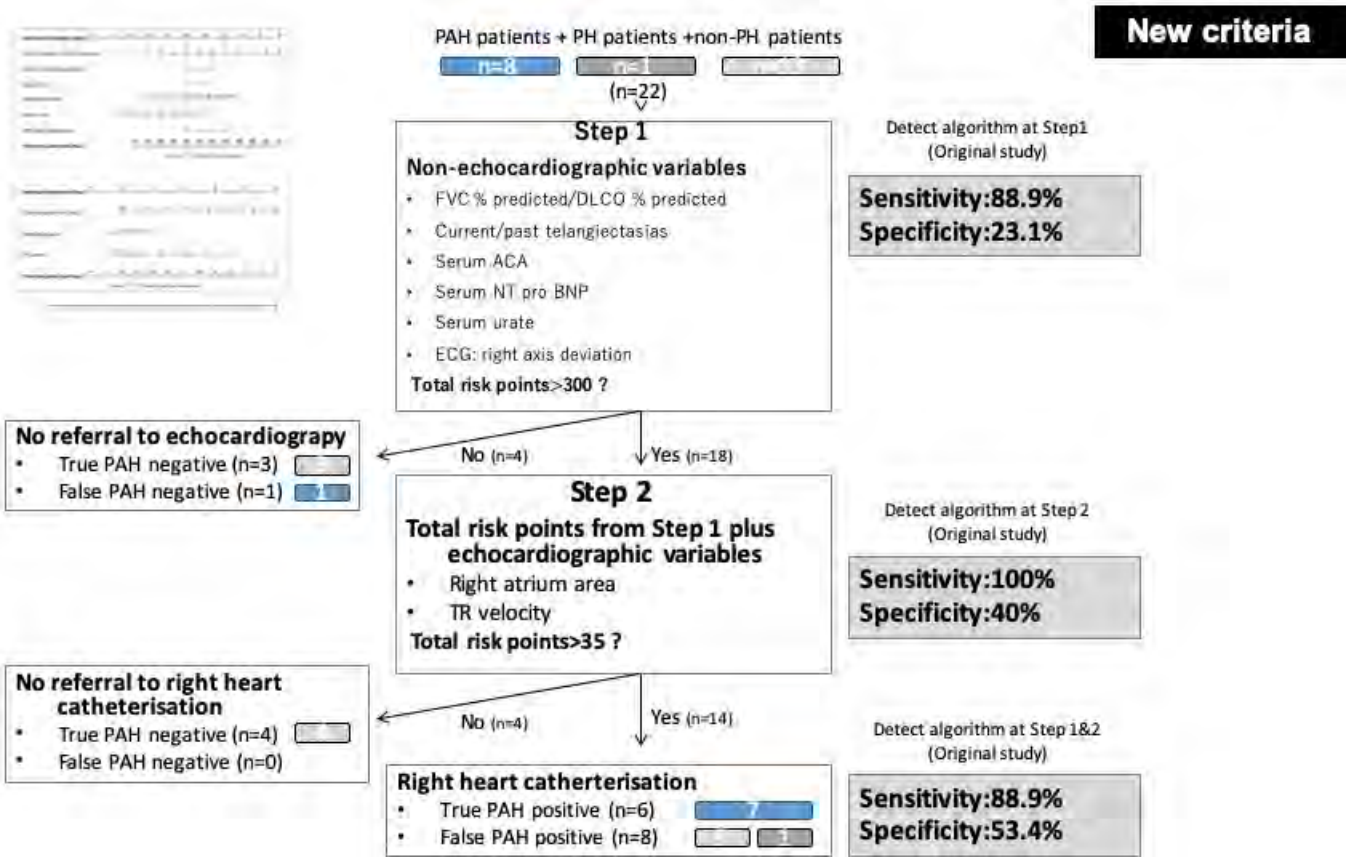
Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis-associated pulmonary arterial hypertension (SSc-PAH) has been known as a life-threatening manifestation in SSc. Earlier detection and subsequent interventions are important to improve the prognosis. DETECT algorithm was established in 2013, however Japanese patients were not included in the original study. The objective of this study was to verify the effectiveness of this algorithm in Japanese with old and new hemodynamic definition of PAH.

Methods: In this retrospective, single-center study, patients with SSc who fulfilled American College of Rheumatology criteria and underwent right heart catheterization (RHC) for the diagnosis of PAH from 2004 to 2019 were included.





We analyzed their results of DETECT algorithm in old and new hemodynamic definition of PAH (Mean pulmonary pressure (mPAP) ≧25 mmHg in old definition and >20 mmHg in new definition, with mean pulmonary capillary wedge pressure ≦15 mmHg).

Results: Twenty-two patients were analyzed in this study. The mean age of enrolled patients was 59 years. The female patients were 73% and limited cutaneous SSc patients were 68%. Five and eight patients were diagnosed as PAH with old and new definition respectively. Overall sensitivity and specificity of DETECT algorithm to PAH in old criteria was 100% and 47.1% (Figure 1). On the other hand, 88.9% and 53.4% in new definition (Figure 2).

Conclusion: The DETECT algorithm was confirmed to be very sensitive and safely used in Japanese patients with SSc as a screening before RHC to minimize missed diagnosis of PAH. However, the algorithm should be used with caution, considering sensitivity was slightly lower with new PAH criteria.

Disclosure: T. Ito, None; **T. Nakai**, None; **G. Kidoguchi**, None; **S. Fukui**, None; **H. Ozawa**, None; **S. Kawaai**, None; **Y. Ikeda**, None; **H. Shimizu**, None; **Y. Suyama**, None; **A. Nomura**, None; **H. Tamaki**, None; **K. Yamaguchi**, None; **M. Okada**, None.

Abstract Number: 0913

Systemic Sclerosis Portends a Higher Risk of Conduction and Rhythm Disorders at Diagnosis and During Disease Course: Results from a US Population Based Study

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiac involvement, including electrocardiogram (ECG) abnormalities, is associated with worse prognosis in systemic sclerosis (SSc). We studied the incidence, risk factors and outcomes of conduction and rhythm disorders in a population-based cohort of patients with SSc and non-SSc comparators from the same geographic area.

Methods: A previously identified incident cohort of SSc patients (1980-2016) in a well-defined geographic area was compared to a randomly selected 2:1 cohort of age- and sex-matched non-SSc subjects from the same population base. Demographics, disease characteristics, cardiovascular risk factors and laboratory tests were abstracted by manual record review. ECGs and Holter ECGs were reviewed to determine the occurrence of any conduction or rhythm abnormalities. The need for cardiac interventions was also abstracted.

Results: 78 incident SSc cases and 156 non-SSc comparators were identified [age 56 years± 15.7, 91% female]. Prevalence of any conduction disorders before SSc diagnosis compared to non-SSc comparators was 15% vs. 7% (p=0.06), and any rhythm disorder was 18% vs. 13% (p=0.33). During a median follow up of 10.5 years in patients with SSc and 13.0 years in non-SSc comparators, conduction disorders developed in 25 SSc patients with a cumulative incidence (ci) of 20.5% (95% CI: 12.4-34.1%) compared to 28 non-SSc patients with ci of 10.4% (95% CI: 6.2-

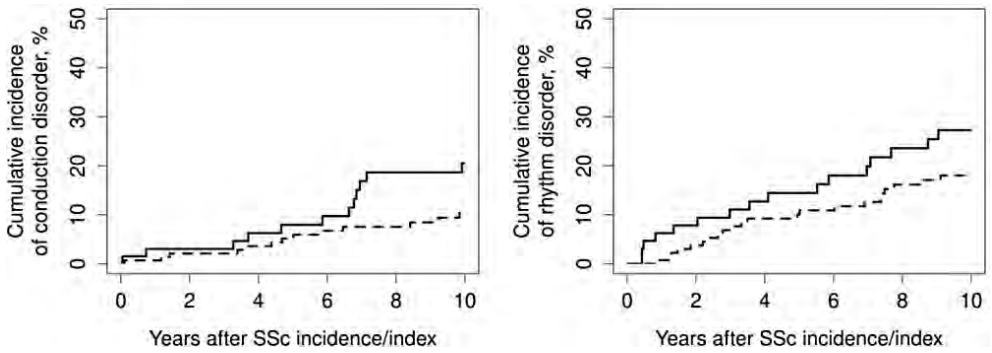

Figure 1. Cumulative incidence of any conduction or any rhythm disorder in systemic sclerosis (SSc) (solid line) vs non-SSc comparators (dashed line).

Outcome	Prior to incidence/index in SSc / non-SSc	After incidence/index in SSc / non-SSc	Cumulative incidence at 10 years for SSc patients (95% CI)*	Cumulative incidence at 10 years for non- SSc subjects (95% CI)*	Hazard ratio (95% CI)**
Surveillance					
Any Holter	6 / 7	18 / 30	19.7 (12.0 , 32.1)	12.0 (7.4 , 19.3)	1.78 (0.98 , 3.25)
Any ECG	42 / 65	30 / 30	57.0 (42.7 , 76.0)	27.6 (19.2 , 39.5)	4.86 (2.81 , 8.40)
Disorders					
Any conduction disorder	12 / 11	25 / 28	20.5 (12.4 , 34.1)	10.4 (6.2 , 17.4)	2.57 (1.48 , 4.45)
Any rhythm disorder	14 / 20	27 / 43	27.3 (17.9 , 41.6)	18.0 (12.3 , 26.4)	1.62 (1.00 , 2.64)
Outcomes					
Cardioversion	2 / 0	3 / 5	2.9 (0.7 , 11.5)	1.3 (0.3 , 5.3)	1.52 (0.35 , 6.47)
Ablation	0 / 0	2 / 2	1.3 (0.2 , 9.0)	0.7 (0.1 , 4.8)	2.13 (0.29 , 5.44)
Pacemaker	0 / 0	4 / 6	4.1 (1.4 , 12.5)	2.1 (0.7 , 6.4)	1.53 (0.42 , 5.60)
CRT	0 / 0	1 / 0	0.0	0.0	--
Defibrillator	0 / 0	4 / 1	4.1 (1.4 , 12.5)	0.0	17.56 (1.44, 214.37)

*Cumulative incidence is adjusted for the competing risk of death.
**adjusted for age, sex and calendar year of SSc/index date
Abbreviation: SSc=Systemic Sclerosis, CI=Confidence Interval, CRT= Cardiac resynchronization therapy

Table 1. Cumulative incidence of conduction and rhythm disorders in 78 patients with systemic sclerosis (SSc) compared with 156 non-SSc comparators

17.4%) (HR: 2.57; 95% CI: 1.48-4.45), while rhythm disorders developed in 27 SSc patients with ci of 27.3% (95% CI: 17.9-41.6%) vs 43 non-SSc patients with ci of 18.0% (95% CI: 12.3-26.4%) (HR: 1.62; 95% CI: 1.00-2.64). (**Figure 1**)

Conduction disorders in patients with SSc during follow up included: 1st-degree atrioventricular block (AVB) (n=12), 2nd-degree AVB (n=1), 3rd-degree AVB (n=1), right bundle branch block (n=10), left bundle branch block (n=4), bifascicular block (n=6), and prolonged-QT (n=13). Rhythm disorders included: atrial fibrillation (n=10), atrial flutter (n=4), supraventricular tachycardia (n=4), ventricular tachycardia (n=1), and premature ventricular contractions (n=16).

ECG, Holter ECG, and cardiac interventions are presented in **Table 1**. Pulmonary hypertension (PHT) was the only significant risk factor identified for development of both conduction and rhythm disorders, while current smoking was a significant risk factor for development of rhythm disorders only (**Table 2**). Conduction and rhythm disorders were associated with increased mortality among patients with SSc (HR=7.60, 95% CI: 3.49-16.55 and HR=4.87, 95% CI: 2.28-10.42, respectively, after adjusting for age, sex and calendar year of diagnosis).

Conclusion: Patients with SSc have a significantly higher prevalence of conduction disorders at disease onset than non-SSc comparators. During the course of their disease, their risk of developing conduction disorders is 2.6-fold, and risk of rhythm disorders is 1.6-fold increased, compared to non-SSc subjects. Our study findings warrant increased vigilance and screening for ECG abnormalities in patients with SSc who have PHT. Underlying mechanisms for this association require further elucidation.

Characteristic	Conduction disorder Hazard ratio[a] (95% CI)	Rhythm disorder Hazard ratio[a] (95% CI)
Age, years	1.74* (1.22, 2.48)	1.24* (0.94, 1.65)
Sex, male	0.41 (0.05, 3.19)	0.85 (0.20, 3.69)
Calendar year of diagnosis	1.03 (0.97, 1.09)	1.05 (0.99, 1.11)
Coronary artery disease at SSc diagnosis	2.32 (0.23, 23.56)	0.70 (0.09, 5.31)
Hypertension	0.61 (0.23, 1.67)	1.34 (0.55, 3.29)
Hyperlipidemia	0.72 (0.27, 1.94)	1.41 (0.60, 3.30)
Ever smoker	1.59 (0.72, 3.55)	1.90 (0.88, 4.08)
Current smoker	1.02 (0.30, 3.47)	2.91 (1.19, 7.12)
Body mass index, kg/m^2	1.00 (0.92, 1.08)	1.05 (0.98, 1.12)
Obesity (BMI≥30 kg/m^2)	1.19 (0.43, 3.31)	1.91 (0.79, 4.62)
Diffuse vs limited/sine	1.26 (0.42, 3.74)	0.55 (0.12, 2.44)
Anti-centromere antibody	0.48 (0.12, 1.96)	0.98 (0.30, 3.21)
Anti-Scl70 antibody	1.22 (0.24, 6.17)	1.13 (0.35, 3.65)
Telangiectasia	1.53 (0.65, 3.61)	1.38 (0.61, 3.13)
Calcinosis	0.68 (0.26, 1.79)	1.28 (0.56, 2.91)
Digital ulcers	0.52 (0.12, 2.25)	1.18 (0.33, 4.18)
Renal involvement[b]	0.56 (0.07, 4.23)	16.89 (1.12, 254.0)
Gastrointestinal involvement[b]	1.01 (0.45, 2.26)	1.25 (0.58, 2.70
Pulmonary artery hypertension	8.38 (1.32, 53.40)	8.07 (1.60, 40.74)
Interstitial lung disease	1.74 (0.34, 9.01)	0.43 (0.05, 3.84)
Raynaud's	0.26 (0.03, 2.14)	0.53 (0.07, 4.09)

*per 10 years
[a]Age-adjusted univariable models
[b]time-dependent covariates

Table 2. Risk factors at systemic sclerosis (SSc) diagnosis for conduction and rhythm disorders in 64 SSc patients without these disorders at disease onset

Disclosure: Y. Radwan, None; **R. Kurmann**, None; **A. Sandhu**, None; **E. El-Am**, None; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1; **E. Matteson**, Boehringer Ingelheim, 5, Gilead, 5, TympoBio, 5, Arena Pharmaceuticals, 5, Up-to-date, 7, Simply Speaking, 8; **T. Osborn**, None; **K. Warrington**, Lilly, 2, Kiniksa, 2; **R. Mankad**, None; **A. Makol**, None.

Abstract Number: 0914

Serious Infections in People with Systemic Sclerosis: A National U.S. Study

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: To study incidence, time-trends and outcomes of serious infections in systemic sclerosis (SSc).

Methods: We used the 1998-2016 U.S. National Inpatient Sample data. We examined the epidemiology, time-trends and outcomes of five serious infections (opportunistic infections (OI), skin and soft tissue infections (SSTI), urinary tract infection (UTI), pneumonia, and sepsis/bacteremia) in hospitalized people with SSc. We performed multivariable-adjusted logistic regression analyses to analyze independent association of factors with healthcare utilization (hospital charges, length of hospital stay, discharge to non-home setting), and in-hospital mortality.

Results: There were 49,904,955 hospitalizations with serious infections in people without SSc and 61,615 in those with SSc. The average age of patients with SSc with a serious infection was 61.4 years (median of 61.7 years; **Table 1**), similar to all SSc hospitalizations.

Compared to patients admitted with serious infection without SSc, people with SSc were younger (median age, 65 vs. 62 years), and were more likely to be female (52% vs. 84%), or have Deyo-Charlson score of 2 or more (42% vs. 64%; **Table 1**).

During 1998-2016, the most common serious infections in SSc were pneumonia (45%), sepsis (32%), SSTI (19%), UTI (3%) and OI (3%). In 2013-14, sepsis surpassed pneumonia as the most common serious infection; by 2015-16, sepsis was 1.8-times more common than pneumonia (**Figure 1**). Over the study period, hospital charges increased, while length of hospital stay and in-hospital mortality decreased, overall and for each serious infection.

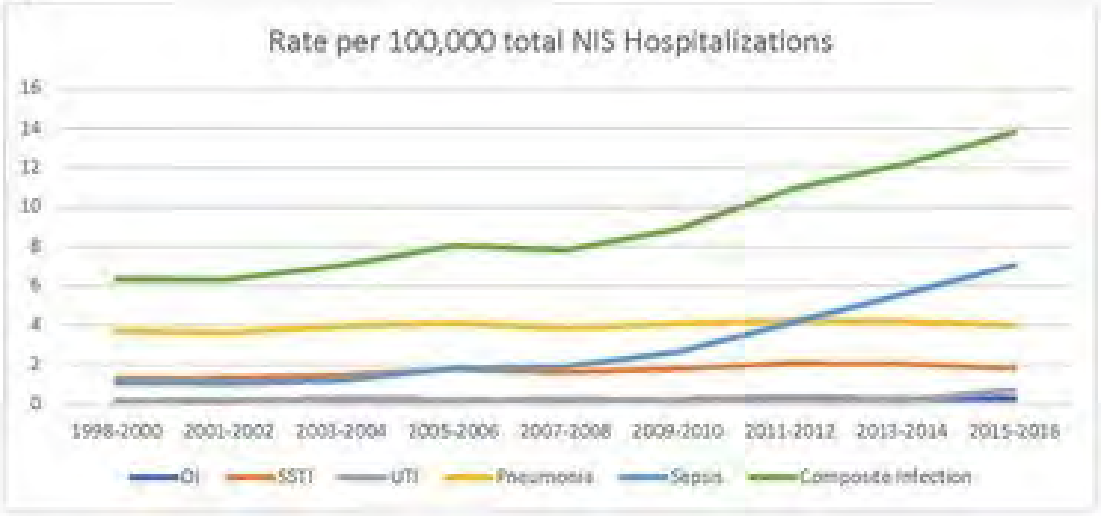
Multivariable-adjusted analyses showed that sepsis, age ≥80 years and Deyo-Charlson score ≥2 were associated with significantly higher odds of healthcare utilization and in-hospital mortality; and Medicare or Medicaid insurance payer, Northeast location, urban teaching or non-teaching hospital, and medium or large hospital bed size with significantly higher odds of healthcare utilization (**Table 2**).

Conclusion: Outcomes in people with SSc hospitalized with serious infections have improved over time, except higher hospital charges. Identification of factors associated with higher healthcare utilization and in-hospital mortality allows for developing interventions to further improve these outcomes.

FIGURES

Figure 1. Rate of hospitalized infection in people with scleroderma per 100,000 total NIS claims (1A) and per 100,000 overall scleroderma claims (1B)

1A.



1B.

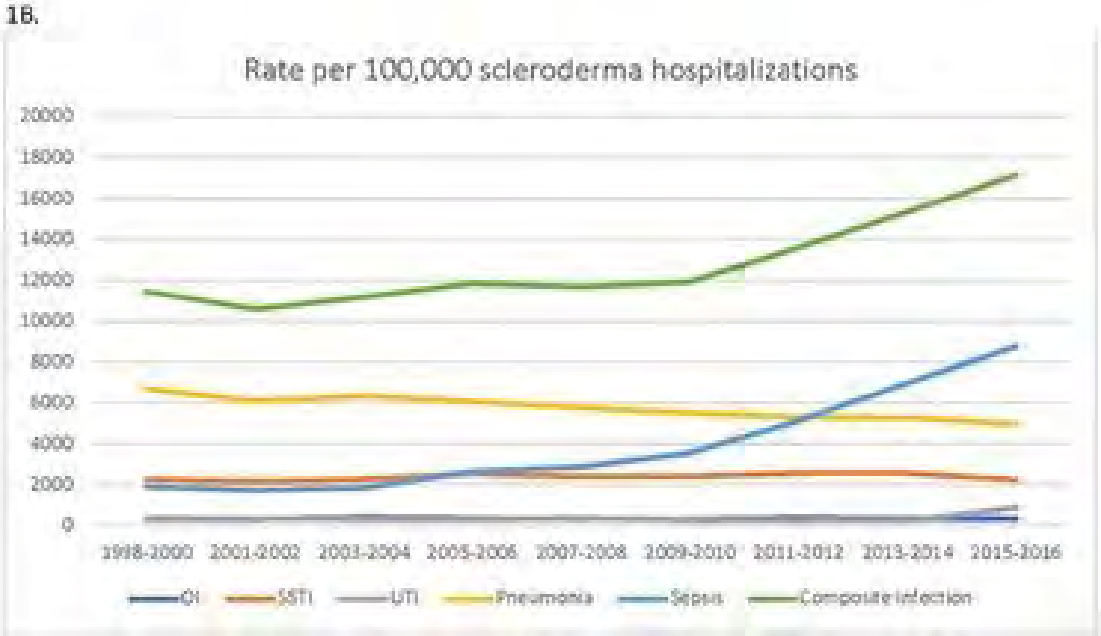


Figure 1. Rate of hospitalized infection in people with scleroderma per 100,000 total NIS claims (1A) and per 100,000 overall scleroderma claims (1B)

Table 1. Characteristics of people with serious infection in cohorts with versus without systemic sclerosis

	All hospitalization claims with a non-primary Systemic sclerosis diagnosis (n= 478,319)	Hospitalized infection in people without Systemic sclerosis (n=49,904,955)	Hospitalized infection in people with Systemic sclerosis (n=61,615)
Age, Mean (Std error); Median	61.5 (0.08); 62.1	59.8 (0.08); 65.0	61.4 (0.15); 61.7
Age category			
<50 years	94,673 (20.84%)	14,069,367 (28.41%)	13,304 (21.66%)
50 - <65 years	151,691 (33.39%)	9,975,198 (20.14%)	20,813 (33.88%)
65 - 79 years	158,140 (34.81%)	13,267,620 (26.79%)	20,364 (33.15%)
≥80 years	49,739 (10.95%)	12,218,686 (24.67%)	6,948 (11.31%)
Female **Sex**	384,898 (84.75%)	26,055,087 (52.63%)	51,601 (83.99%)
Race			
White	273,140 (60.13%)	29,722,254 (59.99%)	36,617 (59.59%)
Black	54,835 (12.07%)	5,335,803 (10.77%)	7,275 (11.84%)
Hispanic	35,376 (7.79%)	4,215,778 (8.51%)	6,098 (9.92%)
Other/Missing	90,923 (20.01%)	10,274,741 (20.74%)	11,454 (18.64%)
Deyo-Charlson Index Score			
0	0 (0%)	15,683,828 (31.65%)	0 (0%)
1	151,810 (33.42%)	12,915,197 (26.06%)	22,179 (36.10%)
≥2	302,469 (66.58%)	20,954,335 (42.29%)	39,266 (63.90%)
Income Category			
0-25th percentile	93,602 (21.03%)	12,965,763 (26.80%)	13,914 (23.13%)
25-50th percentile	110,597 (24.85%)	13,290,261 (27.47%)	15,047 (25.01%)
50-75th percentile	113,958 (25.61%)	11,602,568 (23.98%)	15,000 (24.93%)
75-100th percentile	126,868 (28.51%)	10,518,900 (21.74%)	16,206 (26.93%)
Insurance			
Private	127,345 (28.08%)	10,940,543 (22.13%)	16,348 (26.65%)
Medicare	268,822 (59.27%)	27,438,957 (55.49%)	36,620 (59.70%)
Medicaid	40,457 (8.92%)	7,081,259 (14.32%)	6,184 (10.08%)
Other	9,147 (2.02%)	1,501,315 (3.04%)	1,196 (1.95%)
Self	7,802 (1.72%)	2,484,821 (5.03%)	995 (1.62%)
Hospital Location/Teaching			
Rural	48,537 (10.72%)	7,025,707 (14.93%)	6,989 (11.69%)
Urban	163,400 (36.08%)	19,233,904 (40.88%)	22,105 (36.98%)
Urban Teaching	240,910 (53.20%)	20,791,119 (44.19%)	30,687 (51.33%)
Discharge to Rehabilitation or skilled nursing facility (SNF)	84,801 (19.78%)	11,655,682 (25.42%)	11,875 (21.40%)
Length of Stay in >3 **days**	259,818 (57.19%)	29,452,234 (59.44%)	40,841 (66.47%)
Died during hospitalization	22,276 (4.91%)	3,073,566 (6.21%)	5,503 (8.96%)
Length of Stay in days: Mean (Std error); median	6.1 (0.03); 3.6	6.0 (0.01); 3.7	6.7 (0.07); 4.4
Total hospital charges (US $) >median	307,221 (67.63%)	28,418,604 (57.35%)	40,879 (66.53%)
Total hospital charges1 in US $: mean (SE); median	39,101 (458); 20,880	34,615 (166); 16,832	44,121 (875); 22,105

[1] Median total charges by year: 1998, $5,775; 1999, $6,060; 2000, $6,723; 2001, $7,504; 2002, $8,601; 2003, $9,732; 2004, $9918; 2005, $10,816; 2006, $12,078; 2007, $13,001; 2008, $13,983; 2009, $14,814; 2010, $15,560; 2011, $17,815; 2012, $19,654; 2013, $21,166; 2014, $22,343; 2015, $23,678; 2016, $25,261

Table 1. Characteristics of people with serious infection in cohorts with versus without scleroderma

Table 2. Multivariable-adjusted correlates of healthcare utilization and mortality for serious infections in scleroderma

	Hospital charges >median	Discharge to care facility	Length of Hospital Stay >3 days	In-hospital Mortality
	Adjusted odds ratio (95% Confidence Interval)			
Age category				
<50 years	**Ref**	**Ref**	**Ref**	**Ref**
50 - <65 years	1.06 (0.95 ,1.19)	**1.39 (1.19 ,1.62)**	1.10 (0.99 ,1.22)	**1.54 (1.24 ,1.90)**
65 - 79 years	0.96 (0.85 ,1.09)	**2.01 (1.70 ,2.38)**	1.12 (0.99 ,1.27)	**2.08 (1.65 ,2.63)**
≥80 years	**0.79 (0.68 ,0.93)**	**4.17 (3.43 ,5.08)**	**1.23 (1.05 ,1.44)**	**3.23 (2.46 ,4.24)**
Female **Sex (Ref: Male)**	0.99 (0.89 ,1.11)	0.98 (0.85 ,1.11)	1.03 (0.93 ,1.14)	0.93 (0.78 ,1.10)
Race/ethnicity				
White	**Ref**	**Ref**	**Ref**	**Ref**
Black	1.10 (0.96 ,1.26)	1.13 (0.96 ,1.33)	1.07 (0.94 ,1.22)	1.15 (0.93 ,1.43)
Hispanic	**1.20 (1.03 ,1.39)**	**0.79 (0.65 ,0.96)**	0.95 (0.83 ,1.09)	1.15 (0.92 ,1.44)
Other/missing	1.09 (0.98 ,1.21)	0.98 (0.86 ,1.12)	**1.14 (1.03 ,1.27)**	1.20 (1.00 ,1.44)
Deyo-Charlson index[1] score				
0	Not Est	Not Est	Not Est	Not Est
1	**Ref**	**Ref**	**Ref**	**Ref**
≥2	**1.54 (1.42 ,1.68)**	**1.37 (1.23 ,1.53)**	**1.44 (1.33 ,1.57)**	**1.49 (1.28 ,1.74)**
Income category				
0-25th percentile	**0.81 (0.71 ,0.91)**	0.94 (0.81 ,1.09)	1.00 (0.89 ,1.13)	0.82 (0.68 ,1.00)
25-50th percentile	**0.83 (0.74 ,0.93)**	0.90 (0.78 ,1.04)	1.01 (0.91 ,1.13)	1.03 (0.86 ,1.24)
50-75th percentile	**0.85 (0.76 ,0.96)**	0.96 (0.84 ,1.10)	1.00 (0.90 ,1.12)	0.95 (0.80 ,1.13)
75-100th percentile	**Ref**	**Ref**	**Ref**	**Ref**
Primary Infection Diagnosis				
Sepsis	**Ref**	**Ref**	**Ref**	**Ref**
OI	0.87 (0.66 ,1.15)	**0.38 (0.27 ,0.54)**	**1.48 (1.11 ,1.97)**	**0.46 (0.30 ,0.70)**
SSTI	**0.42 (0.37 ,0.47)**	**0.34 (0.29 ,0.40)**	**0.65 (0.58 ,0.73)**	**0.06 (0.04 ,0.09)**
UTI	**0.28 (0.23 ,0.36)**	**0.34 (0.25 ,0.46)**	**0.32 (0.26 ,0.41)**	**0.02 (0.00 ,0.11)**
Pneumonia	**0.64 (0.58 ,0.70)**	**0.38 (0.34 ,0.43)**	**0.72 (0.66 ,0.79)**	**0.29 (0.25 ,0.34)**
Insurance payer				
Medicare	**1.16 (1.05 ,1.30)**	**1.76 (1.52 ,2.03)**	**1.21 (1.10 ,1.35)**	**0.80 (0.67 ,0.95)**
Medicaid	**1.22 (1.05 ,1.42)**	**1.48 (1.20 ,1.82)**	1.12 (0.97 ,1.29)	0.90 (0.68 ,1.18)
Other	0.92 (0.69 ,1.21)	1.29 (0.86 ,1.93)	0.93 (0.71 ,1.22)	1.46 (0.95 ,2.25)
Private	**Ref**	**Ref**	**Ref**	**Ref**
Self	1.28 (0.93 ,1.77)	0.79 (0.46 ,1.38)	1.06 (0.78 ,1.43)	1.08 (0.60 ,1.94)
Hospital Region				
Northeast	**Ref**	**Ref**	**Ref**	**Ref**
Midwest	**0.75 (0.66 ,0.85)**	1.00 (0.86 ,1.16)	**0.83 (0.73 ,0.94)**	**0.66 (0.53 ,0.81)**
South	0.92 (0.82 ,1.03)	**0.83 (0.72 ,0.95)**	0.95 (0.85 ,1.07)	0.86 (0.71 ,1.03)
West	0.89 (0.78 ,1.02)	0.85 (0.73 ,1.00)	**0.68 (0.60 ,0.77)**	0.83 (0.68 ,1.01)
Hospital Location/Teaching				
Rural	**Ref**	**Ref**	**Ref**	**Ref**
Urban Non-teaching	**2.57 (2.26 ,2.92)**	**0.74 (0.63 ,0.87)**	**1.38 (1.21 ,1.57)**	1.18 (0.93 ,1.49)
Urban Teaching	**2.25 (1.99 ,2.54)**	**0.63 (0.54 ,0.74)**	**1.31 (1.15 ,1.48)**	1.15 (0.91 ,1.45)
Hospital Bed size				
Small	**Ref**	**Ref**	**Ref**	**Ref**
Medium	**1.46 (1.29 ,1.65)**	1.05 (0.90 ,1.23)	**1.20 (1.06 ,1.36)**	1.23 (0.99 ,1.55)
Large	**2.10 (1.89 ,2.35)**	1.01 (0.88 ,1.16)	**1.36 (1.22 ,1.52)**	**1.35 (1.10 ,1.66)**

Table 2. Multivariable-adjusted correlates of healthcare utilization and mortality for serious infections in scleroderma

Disclosure: J. Singh, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **J. Cleveland**, None.

Abstract Number: 0915

Clinical Bedside Tools to Assess Systemic Sclerosis Vasculopathy: Can Digital Thermal Monitoring and Sublingual Microscopy Identify Patients with Current or past Digital Ulcers?

Tracy Frech[1], Zhining Ou[2], Julie Thomas[2] and Angela Presson[2], [1]University of Utah and Salt Lake Veterans Affair Medical Center, Salt Lake City, UT, [2]University of Utah, Salt Lake City, UT

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Sublingual microscopy is reported as a useful tool for vasculopathy assessment in SSc. Digital thermal monitoring (DTM) correlates with flow-mediated dilatation, and may identify patients at risk for digital ulcer (DU). The purpose of this analysis was to assess sublingual microscopy and DTM in SSc patients with and without digital ulcers in order to determine the utility of these clinical tools for end-stage vasculopathy assessment.

Methods: Consented SSc registry patients that presented for routine clinical care and had both DTM and sublingual microscopy on the same day were included in this cross-sectional analysis. Measurements were performed in a quiet room at a controlled ambient temperature. DTM records a temperature rebound in the fingertip after blood pressure cuff occlusion, and is provided as a single, automated vascular reactivity index (VRI) value. Sublingual microscopy provides an automated measure of microvascular perfusion (longitudinal red blood cell fraction, RBC fract) and glycocalyx penetrability (perfused barrier region, PBR). We summarized demographics and clinical outcomes of interest using median, interquartile range (IQR) and range for skew continuous variables; we reported counts and percentages for categorical variables. Exact Wilcoxon rank sum test and Fisher's exact test were used to compare variable between DU groups. We evaluated the pairwise association between VRI, RBCfract and PBR in a monotonic relationship using Spearman's rank correlation in the DU subset. We reported the correlation coefficients (r-s) and their 95% confidence intervals (CIs). We also reported the asymptotic p-values. Statistical significance was assessed at the 0.05 level.

Results: Of the 90 patients that met inclusion criteria, 29 had digitals pits and/or active DU and 61 never had a DU (Table 1). These patients were 76% female, 83% white, 11% current smoker, and 87% SSc-specific autoantibody positive. At the time of assessment, 91% were on vasodilators for Raynaud's phenomenon. The only significant clinical feature associated with the presence of DU was modified Rodnan skin score (p=0.003). The VRI captured by DTM was lower in patients with DU (p=0.01). The sublingual microscopy RBCfract and PBR were monotonic associated ($p < 0.001$) with monotone decreasing with the higher RBCfract the lower PBR (r¬s=-0.71, 95% CI: -0.86, -0.47). VRI was not associated with RBCfract or PBR (p=0.24 or 0.55, respectively) in the small group DU patients (Table 2).

Conclusion: DTM, which captures damage as a vasculopathy feature, is a potentially useful tool for assessing DU risk in the SSc population. In this cross-sectional analysis, sublingual microscopy measurements of perfusion and

Variable	Total (N=90)	Digital Ulcer (N=29)	Not digital ulcer (N=61)	P-value
Age at baseline (yr):	54.5 (13.7)	52.1 (15.0)	55.5 (13.1)	-
• Median (IQR)	55.0 (46.0, 67.0)	53.5 (45.8, 62.2)	57.0 (46.0, 67.0)	0.35*
• Range	(0.0, 78.0)	(0.0, 70.0)	(25.0, 78.0)	-
Gender: Female	76 (84.4%)	22 (75.9%)	54 (88.5%)	0.13†
Male	14 (15.6%)	7 (24.1%)	7 (11.5%)	-
Modified Rodnan Skin Score:	6.0 (6.2)	7.3 (4.9)	5.3 (6.8)	-
• Median (IQR)	4.0 (2.0, 8.0)	7.0 (4.0, 9.0)	3.5 (2.0, 6.2)	0.003*
• Range	(0.0, 33.0)	(1.0, 22.0)	(0.0, 33.0)	-
Race				
• American Indian/Alaskan Native	3 (3.3%)	1 (3.4%)	2 (3.3%)	0.18†
• Black or African American	1 (1.1%)	1 (3.4%)	0 (0%)	-
• More than One Race	1 (1.1%)	1 (3.4%)	0 (0%)	-
• Native Hawaiian or Other Pacific Islander	1 (1.1%)	1 (3.4%)	0 (0%)	-
• Unknown or Not Reported	1 (1.1%)	0 (0%)	1 (1.6%)	-
• White	83 (92.2%)	25 (86.2%)	58 (95.1%)	-
Smoking habit				
• I am a current smoker	9 (11.2%)	4 (16%)	5 (9.1%)	0.43†
• I have never smoked	50 (62.5%)	13 (52%)	37 (67.3%)	-
• I have smoked in the past but do not smoke now	21 (26.2%)	8 (32%)	13 (23.6%)	-
Vascular Reactivity Index (VRI):	0.9 (0.6)	0.7 (0.5)	1.0 (0.6)	-
Median (IQR)	0.9 (0.5, 1.2)	0.6 (0.2, 1.0)	0.9 (0.6, 1.2)	0.010*
Range	(0.0, 3.5)	(0.0, 1.9)	(0.0, 3.5)	-
Red blood cell fraction (RBCfract):	72.3 (10.6)	73.6 (5.1)	71.7 (12.3)	-
Median (IQR)	73.5 (70.0, 78.3)	73.9 (71.8, 75.2)	72.6 (68.9, 79.1)	0.84*
Range	(22.0, 91.4)	(60.5, 83.3)	(22.0, 91.4)	-
Perfused boundary region (PBR):	2.0 (0.4)	2.0 (0.2)	2.0 (0.4)	-
Median (IQR)	2.0 (1.7, 2.2)	2.0 (1.8, 2.1)	2.0 (1.7, 2.2)	0.60*
Range	(1.4, 2.9)	(1.5, 2.4)	(1.4, 2.9)	-

Missing values: Age at baseline (yr)=1, Modified Rudman Skin Score=1, Smoking habit=10
* Exact wilcoxon rank sum test, † Fisher's exact test.

Clinical Features of 90 SSc patients assessed with Digital Thermal Monitoring and Sublingual Microscopy

glycocalyx penetrability did not significantly correlate to VRI in DU patients' assessment. However, a longitudinal study of these sublingual microscopy parameters may be more helpful in capturing vasculopathy activity prior to the possibly irreversible damage that is captured by DTM.

	vascular reactivity index (VRI)	Red blood cell fraction (RBCfract)	Perfused boundary region (PBR)
vascular reactivity index (VRI)	-	0.23 (-0.15, 0.55)	0.12 (-0.26,0.46)
Red blood cell fraction (RBCfract)	0.24	-	-0.71 (-0.86, -0.47)
Perfused boundary region (PBR)	0.55	<0.001	-

Spearman's rank correlation and 95% CI for 29 DU patients.

Disclosure: T. Frech, None; **Z. Ou**, None; **J. Thomas**, None; **A. Presson**, None.

Abstract Number: 0916

Validating Autoantibody Associations and Clinical Impact of Severe Gastrointestinal Involvement in Systemic Sclerosis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic sclerosis (SSc) frequently experience gastrointestinal (GI) symptoms, ranging from mild to debilitating in severity. Better prediction of those most at risk of developing severe GI disease would be helpful for clinical trials and practice.

Previously, we identified demographic factors and serological markers associated with certain gastrointestinal symptoms, in a cohort (n=214) of consecutive SSc patients. Here, we have validated and extended our work in a second independent cohort.

Methods: SSc patients attending our centre between December 2019 and March 2020 completed the UCLA SCTC GIT 2.0 questionnaire, encompassing various domains of SSc-associated GI disease (reflux, distension/bloating, diarrhoea, soilage, constipation, social functioning and emotional wellbeing). Higher domain scores correspond with greater GI disease severity (domain scores range from 0 to 3). Analysis of associations was undertaken using appropriate non-parametric tests. Subgroups on basis of antibodies included ACA, ATA, ARA, U3RNP, nRNP, PmScl and other antibodies. Double autoantibodies were present in 10 subjects and those were classified into the group of the more SSc-specific antibody.

Results: 314 patients completed UCLA GIT 2.0. Mean (SD) age was 55.2 (14.5) and 85.7% were female. The mean number of years since SSc onset was 12.9 (10.0). Limited cutaneous SSc was present in 66.6%, and disease overlap syndromes were present in 25.4%. The most common autoantibody was anti-centromere (ACA, 28.0%), followed by anti-topoisomerase (ATA, 24.2%), anti-RNA polymerase III (ARA, 9.9%), Ro (8.9%), anti-PMScl (6.1%) and anti-nRNP (5.7%). The mean (SD) total GIT score was 0.70 (0.58) and 56.4% patients reported moderate-severe symptoms (Table 1). There was a positive correlation between total GIT score and patient visual analogue scale (VAS) self-reported GI disease burden (Spearman's Rho = 0.68, $p < 0.0001$). There was no association between GI symptoms and disease subset or duration. Gender was only associated with emotional wellbeing, which was more severely affected in

	No/mild symptoms (<0.5)	Moderate symptoms (0.5-1.0)	Severe symptoms (>1.0)
Total GI score	137 (43.6)	93 (29.6)	84 (26.8)
Reflux	141 (44.9)	80 (25.5)	93 (29.6)
Distension/bloating	78 (24.8)	86 (27.4)	150 (47.8)
Faecal soilage	202 (64.3)	62 (19.7)	50 (15.9)
Diarrhoea	158 (50.3)	68 (21.7)	88 (28.0)
Constipation	173 (55.1)	81 (25.8)	60 (19.1)
Social functioning	190 (60.5)	71 (22.6)	53 (16.9)
Emotional wellbeing	181 (57.6)	58 (18.5)	75 (23.9)

Table 1. Distribution of severity of GI symptoms in SSc cohort (n=314), based on total GI score and individual domain scores for patients fully completing the UCLA SCTC GIT 2.0 questionnaire. Total GI score excludes constipation score. Total score and individual domain score frequencies are represented as n (%).

Table 2. Comparison between autoantibody subgroups in terms of GIT symptoms. Comparisons were undertaken using the Kruskal-Wallis test. Cells represent mean/median, Q2-Q3

Antibodies	N	Total GIT 2.0 score	Reflux	Distension/ bloating	Diarrhoea	Constipation	Faecal soilage	Social functioning	Emotional wellbeing
ACA	88	0.81/0.69, 0.31-1.21	0.87/0.63, 0.25-1.44	1.12/1, 0.5-1.63	0.61/0.5, 0-1	0.47/0.25, 0-0.75	0.86/1, 0-1	0.59/0.33, 0-0.92	0.84/0.56 0.11-1.33
ATA	76	0.56/0.41, 0.13-0.93	0.63/0.5, 0.06-0.88	1.05/0.75, 0.25-1.75	0.45/0, 0-1	0.32/0, 0-0.5	0.39/0, 0-0	0.37/0, 0-0.67	0.44/0, 0-0.78
ARA	31	0.87/0.7, 0.36-1.25	0.96/0.63, 0.25-1.75	1.46/1.5, 0.5-2.25	0.5/0.5, 0-1	0.73/0.75, 0.25-1	0.84/0, 0-2	0.63/0.67, 0-1.17	0.86/0.67, 0.22-1.22
U3RNP	7	0.55/0.27, 0.15-1.26	0.95/0.38, 0.25-1.88	0.93/0.5, 0.5-2	0.36/0, 0-1	0.39/0, 0-0.5	0.29/0, 0-0	0.43/0, 0-0.83	0.38/0, 0-0.44
nRNP	13	0.47/0.41, 0.1-0.72	0.72/0.25, 0.13-1	0.94/0.75, 0.5-1.75	0.38/0, 0-0.5	0.5/0.25, 0-0.75	0.15/0, 0-0	0.38/0, 0-0.5	0.21/0, 0-0.11
PmScl	14	0.38/0.23, 0.17-0.49	0.28/0, 0-0.38	0.73/0.5, 0-1	0.39/0, 0-1	0.32/0.13, 0-0.75	0.29/0, 0-1	0.24/0, 0-0.33	0.38/0, 0-0.56
Other	84	0.73/0.66, 0.27-1.02	0.85/0.75, 0.25-1.31	1.35/1.25, 0.63-2.25	0.57/0.5, 0-1	0.48/0.25, 0-0.88	0.48/0, 0-1	0.48/0.17, 0-0.67	0.67/0.33, 0-0.94
p-value		0.0054	0.0153	0.0602	0.5591	0.0463	0.0092	0.0821	0.0001

Table 2. Comparison between autoantibody subgroups in terms of GIT symptoms. Comparisons were undertaken using the Kruskal-Wallis test. Cells represent mean/median, Q2-Q3.

females compared to males (score 0.68 v 0.42, p=0.0339). There were significant differences between the antibody subgroups in terms of GI symptoms (Table 2). Of the SSc-specific antibodies, ARA and ACA appeared to convey increased risk overall and throughout the domains, demonstrating the highest scores. Mean/median total GIT scores and scores for reflux, distension/bloating, constipation, social functioning and emotional wellbeing were highest among ARA+, while scores for diarrhoea and faecal soilage were highest among ACA+ subjects. On the other hand, anti-PmScl+ patients had the lowest scores in most domains, including total GIT 2.0 score.

Conclusion: We have validated our previous results in a second SSc cohort. Higher GIT scores were associated with significantly worse self-reported impact on quality of life. In addition, in this cohort, ARA and ACA positivity appeared to be associated with more severe GI disease. Future studies should explore whether ANA reactivity may identify cases at risk of severe GI manifestations.

Disclosure: F. Ahmed, None; **S. Nihtyanova**, GlaxoSmithKline, 3; **S. Chatzinikolaou**, None; **V. Ong**, None; **C. Murray**, None; **C. Denton**, Janssen, 1, GlaxoSmithKline, 1, 2, Bayer, 1, Sanofi, 1, Inventiva, 1, 2, Boehringer Ingelheim, 1, Roche, 1, Bristol-Myers Squibb, 1, CSL Behring, 1, 2, UCB, 1, Leadiant Biosciences, 1, Corbus Pharmaceuticals, 1, Acceleron Pharma, 1, Horizon Therapeutics, 1, Forbius, 1, Servier, 1.

Abstract Number: 0917

Drug-Drug Interaction Study of Nintedanib (Ofev®) and the Combination of Ethinylestradiol and Levonorgestrel (Microgynon®) in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD)

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

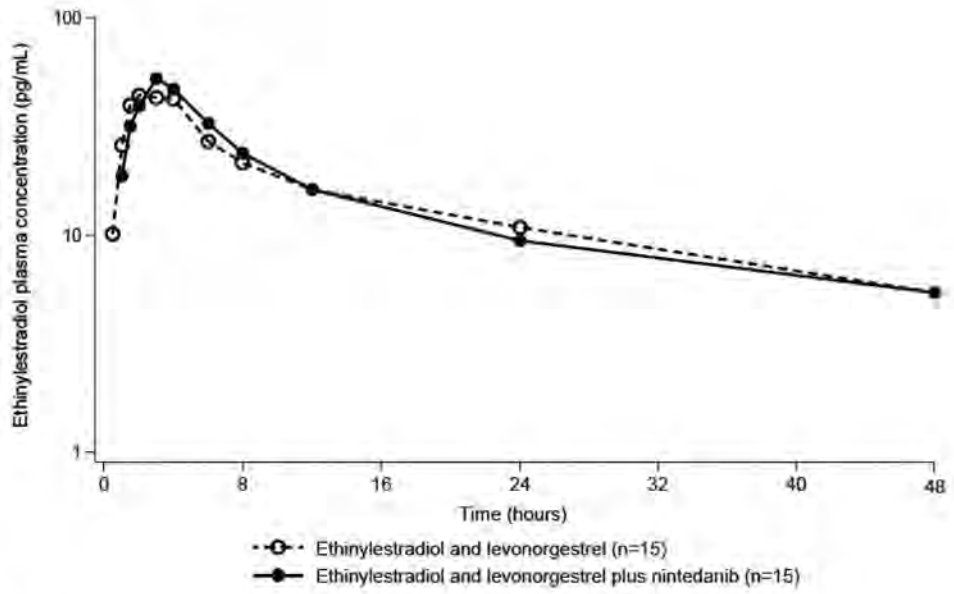
Background/Purpose: Nintedanib is a tyrosine kinase inhibitor that has been approved for the treatment of SSc-ILD. As nintedanib may cause fetal harm, patients taking nintedanib should avoid pregnancy. The combination of ethinylestradiol and levonorgestrel is a commonly used oral contraceptive. We investigated the pharmacokinetics (PK) of the combination of ethinylestradiol and levonorgestrel alone and with nintedanib at steady-state in female patients with SSc-ILD.

Methods: We conducted an open-label, two-period, fixed-sequence, drug–drug interaction study (NCT03675581). Female patients aged ≥18 years, with SSc (based on 2013 ACR/EULAR criteria) and ≥10% extent of fibrotic ILD on a high-resolution computed tomography (HRCT) scan were eligible to participate. In Period 1, patients received a single Tablet containing 30 μg ethinylestradiol and 150 μg levonorgestrel (reference treatment) ≥3 days before the first administration of nintedanib in Period 2. In Period 2, patients received a second Tablet containing 30 μg ethinylestradiol and 150 μg levonorgestrel after continuous intake of nintedanib 150 mg bid for ≥10 consecutive days (test treatment). The primary PK endpoints were the areas under the concentration–time curve of ethinylestradiol and levonorgestrel in plasma over the time interval from 0 to the last quantifiable data point (AUC_{0-tz}) and the maximum measured concentrations of ethinylestradiol and levonorgestrel in plasma (C_{max}). The areas under the concentration–time curve of ethinylestradiol and levonorgestrel in plasma over the time interval from 0 extrapolated to infinity ($AUC_{0-\infty}$) were secondary PK endpoints. The relative exposure to ethinylestradiol and levonorgestrel when administered alone versus in combination with nintedanib was assessed using an ANOVA model.

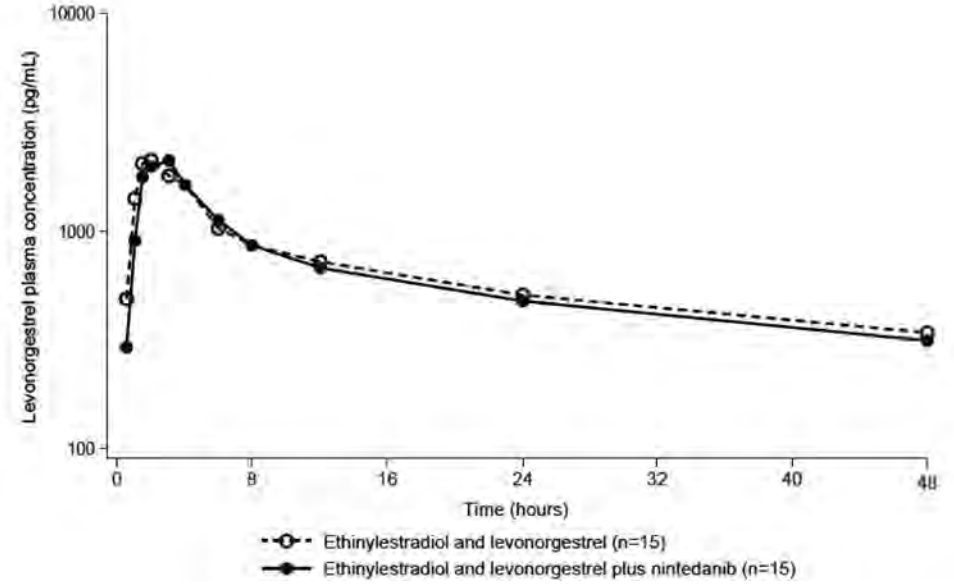
Results: PK data were analyzed from 15 treated patients. Plasma concentration–time profiles of ethinylestradiol and levonorgestrel were similar after administration alone or after administration of nintedanib 150 mg bid for ≥10

Figure. Geometric mean plasma concentration–time profiles on a semi-logarithmic scale of a) ethinylestradiol and b) levonorgestrel after a single oral administration of ethinylestradiol and levonorgestrel alone (Period 1) or after a single oral administration of ethinylestradiol and levonorgestrel after multiple oral administrations of nintedanib 150 mg bid for ≥10 days (Period 2).

a)



b)



consecutive days (Figure). Total exposure to ethinylestradiol ($AUC_{0\text{-}tz}$ and $AUC_{0\text{-}\infty}$) was similar when ethinylestradiol and levonorgestrel were administered alone or after multiple administrations of nintedanib and peak exposure to ethinylestradiol (C_{max}) slightly increased (by approximately 16%) after multiple administrations of nintedanib (Table).

Table. Adjusted gMean comparisons of exposure to ethinylestradiol and levonorgestrel after single oral administration alone (Period 1) and after multiple oral administrations of nintedanib 150 mg bid for ≥10 days (Period 2)

Parameter	Adjusted gMean (gSE)		Adjusted gMean ratio, % (90% confidence interval)
	Ethinylestradiol and levonorgestrel with nintedanib (n=15)	Ethinylestradiol and levonorgestrel alone (n=15)	
Ethinylestradiol			
AUC_{0-tz}, [pg·h/mL]	618.3 (1.2)	610.0 (1.2)	101.4 (92.8, 110.7)
C_{max}, [pg/mL]	63.9 (1.1)	54.8 (1.1)	116.7 (107.6, 126.5)
$AUC_{0-\infty}$, [pg·h/mL]	759.0 (1.1)	749.7 (1.1)	101.2 (94.0, 109.1)
Levonorgestrel			
AUC_{0-tz}, [pg·h/mL]	31872.5 (1.2)	33062.7 (1.2)	96.4 (91.5, 101.6)
C_{max}, [pg/mL]	3152.4 (1.1)	3124.5 (1.1)	100.9 (89.9, 113.2)
$AUC_{0-\infty}$, [pg·h/mL]	49605.4 (1.2)	56311.7 (1.2)	88.1 (80.0, 97.0)

No differences in total or peak exposure to levonorgestrel (AUC_{0-tz} or C_{max}) were observed when ethinylestradiol and levonorgestrel were administered alone or after multiple administrations of nintedanib (Table).

Conclusion: PK results indicate that there is no relevant effect of nintedanib 150 mg bid on the plasma exposure to ethinylestradiol and levonorgestrel in female patients with SSc-ILD.

Disclosure: M. Vonk, Actelion Pharmaceuticals, 1, 2, 3, Boehringer Ingelheim, 1, 2, Roche, 1, 2, GlaxoSmithKline, 1, 2, Ferrer, 1; **M. Avis**, Boehringer Ingelheim, 1; **K. Marzin**, Boehringer Ingelheim, 1; **S. Mack**, Boehringer Ingelheim, 1; **S. Wind**, Boehringer Ingelheim, 1; **M. Gahlemann**, Boehringer Ingelheim, 1.

Abstract Number: 0918

Decline in Forced Vital Capacity in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD) with and Without Gastroesophageal Reflux Disease: Further Analyses of the SENSCIS Trial

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

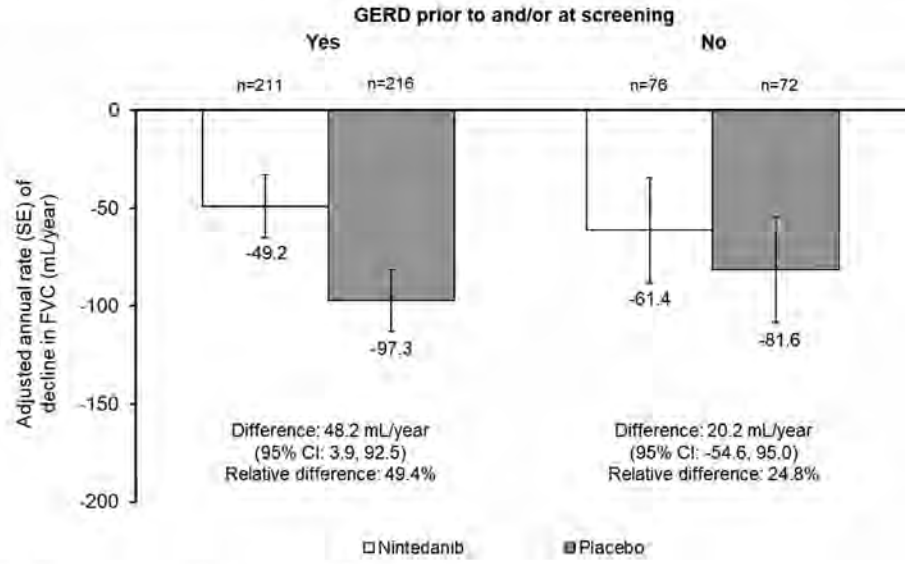
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Gastroesophageal reflux disease (GERD) is a common comorbidity in patients with SSc-ILD and may be associated with progression of SSc-ILD. In the SENSCIS trial in patients with SSc-ILD, nintedanib

Figure. Annual rate of decline in FVC (mL/year) over 52 weeks in the SENSCIS trial in subgroups by presence of GERD prior to and/or at screening.



Treatment-by-time-by-subgroup interaction p=0.53

Table. Most frequent adverse events in the SENSCIS trial in subgroups by presence of GERD prior to and/or at screening.

	With GERD prior to and/or at screening		Without GERD prior to and/or at screening	
	Nintedanib (n=212)	Placebo (n=216)	Nintedanib (n=76)	Placebo (n=72)
Any adverse event	208 (98.1)	208 (96.3)	75 (98.7)	68 (94.4)
Most frequent adverse events*				
Diarrhea	163 (76.9)	74 (34.3)	55 (72.4)	17 (23.6)
Nausea	64 (30.2)	31 (14.4)	27 (35.5)	8 (11.1)
Vomiting	55 (25.9)	25 (11.6)	16 (21.1)	5 (6.9)
Skin ulcers	41 (19.3)	35 (16.2)	12 (15.8)	15 (20.8)
Cough	29 (13.7)	45 (20.8)	5 (6.6)	7 (9.7)
Nasopharyngitis	23 (10.8)	36 (16.7)	13 (17.1)	13 (18.1)
Upper respiratory tract infection	25 (11.8)	27 (12.5)	8 (10.5)	8 (11.1)
Abdominal pain	27 (12.7)	15 (6.9)	6 (7.9)	6 (8.3)
Fatigue	24 (11.3)	17 (7.9)	7 (9.2)	3 (4.2)
Weight decreased	28 (13.2)	10 (4.6)	6 (7.9)	2 (2.8)

Adverse events were reported irrespective of causality and coded using preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). Data are n (%) of patients with ≥1 such event, reported over 52 weeks (or until 28 days after last trial drug intake in patients who discontinued trial drug before week 52). *Adverse events reported in >10% of patients in either treatment group in either subgroup.

reduced the rate of decline in forced vital capacity (FVC) over 52 weeks by 44% versus placebo, with an adverse event profile characterized mainly by gastrointestinal events. We investigated the efficacy and safety of nintedanib in subgroups by presence of GERD at baseline.

Methods: In the SENSCIS trial, patients with SSc-ILD with first non-Raynaud symptom ≤7 years before screening, extent of fibrotic ILD ≥10% on HRCT and FVC ≥40% predicted were randomized to receive nintedanib or placebo until the last patient had reached week 52 but for ≤100 weeks. In post-hoc analyses, we analysed the annual rate of decline in FVC (mL/year) over 52 weeks and adverse events in subgroups by presence of GERD prior to and/or at screening. GERD was defined as present if it was noted as a present or past comorbidity on the SSc-related medical history page of the case report form.

Results: Of 576 patients who received ≥1 dose of trial medication, 74.3% had GERD prior to and/or at screening. At baseline, in patients with and without GERD, respectively, mean (SD) FVC was 2532 (787) and 2405 (744) mL and 72.3 (16.7) and 73.1 (16.7) % predicted; 88.8% and 52.0% of patients were taking anti-acid therapy. In the placebo group, the adjusted annual rate of FVC decline was numerically more pronounced in patients with than without GERD (-97.3 vs -81.6 mL/year). The effect of nintedanib versus placebo on reducing the rate of FVC decline (mL/year) was numerically more pronounced in patients with than without GERD (difference: 48.2 [95% CI: 3.9, 92.5] vs 20.2 [-54.6, 95.0]), but the exploratory interaction p-value did not indicate heterogeneity in the treatment effect of nintedanib between these subgroups (p=0.53) (Figure). The most frequent adverse event reported in all the subgroups was diarrhea (Table). In the nintedanib and placebo groups, respectively, the proportions of patients who had adverse events leading to treatment discontinuation were 14.6% and 9.7% in patients with GERD and 19.7% and 5.6% in patients without GERD.

Conclusion: In the SENSCIS trial in patients with SSc-ILD, nintedanib slowed the rate of FVC decline versus placebo both in patients with and without GERD. The adverse event profile of nintedanib was similar in patients with and without GERD.

Disclosure: K. Highland, Actelion Pharmaceuticals, 1, 2, 3, Bayer, 1, 2, Boehringer Ingelheim, 1, 2, 3, Eiger BioPharmaceuticals, 1, Genentech, 1, Gilead Sciences, 1, Gossamer Bio, 1, Reata Pharmaceuticals, 1, United Therapeutics, 1, 2, 3, Viela Bio, 1; **G. Criner**, Amgen, 1, AstraZeneca, 1, Boehringer Ingelheim, 1, Broncus Medical, 1, CSA Medical, 1, Eolo Medical, 1, Gala Therapeutics, 1, GlaxoSmithKline, 1, HGE Health Care Solutions, 1, Helios Medical, 1, Merck, 1, Medtronic, 1, Mereo BioPharma, 1, NGM Biopharmaceuticals, 1, Novartis, 1, Olympus, 1, PulmonX, 1, Philips Respironics, 1, Respivant Sciences, 1, The Implementation Group, 1, Verona Pharma, 1; **P. Sfikakis**, Abbvie, 2, 5, Amgen, 2, 5, Boehringer Inglheim, 2, 5, Celgene, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5; **H. Nunes**, Boehringer Ingelheim, 1, 2, 3, Roche, 1, 2, 3, Galapagos, 1; **W. Stevens**, Janssen, 5, 8, Boehringer Ingelheim, 5, Actelion Pharmaceuticals, 2; **C. Miede**, Boehringer Ingelheim, 9; **M. Alves**, Boehringer Ingelheim, 3; **M. Kreuter**, Boehringer Ingelheim, 1, 2, Galapagos, 1, Roche, 1, 2.

Abstract Number: 0919

Determinants of Health-related Quality of Life in Systemic Sclerosis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Sclerosis (SSc) is a heterogeneous disease, in which multiple manifestations are associated with considerable morbidity and mortality. Cross sectional studies have shown that compared to patients

Table 1. Baseline characteristics of the included patients

	N=492
Female, n(%)	390 (79)
Age, mean (SD)	55 (14)
Current smoker, n(%)	79 (16)
Disease duration since NR, median (IQR)	3.2 (0.8-10.3)
Follow-up duration, median (IQR)	3.4 (2.0-6.2)
Disease characteristics	
Diffuse cutaneous subset, n(%)	118 (24)
Anti-centromere positive, n(%)	194 (29)
Anti-topoisomerase positive, n(%)	116 (24)
Digital Ulcers, n(%)	62 (13)
Modified Rodnan Skin score, median (IQR)	4 (0-6)
Organ involvement	
Interstitial lung disease, n(%)	183 (37)
Pulmonary arterial hypertension, n(%)	26 (5)
LVEF < 50%, n(%)	31 (6)
Renal crisis, n(%)	14 (3)
Severe GI disease based on UCLA GIT	75 (15)
Myositis, n(%)	8 (2)
Functional impairment	
Six minute walking test (m), mean (SD)	395 (259)
Mouth opening (mm), mean (SD)	31 (37)
Grip strength (kg), mean (SD)	13 (36)
Fingertip to palm (cm), mean (SD)	9.7 (22)

FVC= forced vital capacity, DLCO= diffusing capacity for carbon monoxide, pred=predicted, LVEF= left ventricular ejection fraction, GI=gastro-intestinal

Table 1. Baseline characteristics of the included patients

with other rheumatic diseases, health-related quality of life (HRQoL) is significantly more affected in SSc. How disease specific determinants influence HRQoL over time has not been described thus far.

We aim 1) to evaluate if and how HRQoL changes over time, and 2) to assess how different SSc domains contribute to variations in HRQoL measured over time.

Methods: All SSc patients of the Leiden Combined Care in SSc cohort who fulfilled the ACR/EULAR 2013 criteria for SSc and had at least two visits were included. HRQoL was annually assessed using the EuroQol (EQ5D) and the 36-Item Short Form Health Survey (SF36): mental component score (MCS), and physical component score (PCS). Longitudinal data on clinical characteristics including organ involvement, organ progression and functional assessments were collected. Firstly, we evaluated the mean scores of the EQ5D, MCS and PCS over time and compared these between disease progressors and non-progressors. Secondly, linear mixed-effect regression models were applied to assess changes in HRQoL during the observation time, to control for repeated measurements, and to identify predictive factors. Separate models with the primary outcomes EQ5D, MCS and PCS were applied, first with the independent variables of organ involvement and second with the independent variables of the functional assessments, all adjusted for confounders.

Results: Four-hundred-ninety-two SSc patients were included, with a median follow-up duration of 3.4 years (range 2-6). Over time, both the MCS and PCS worsened with respectively 1.32 points and 1.30 points per year ($p < 0.001$

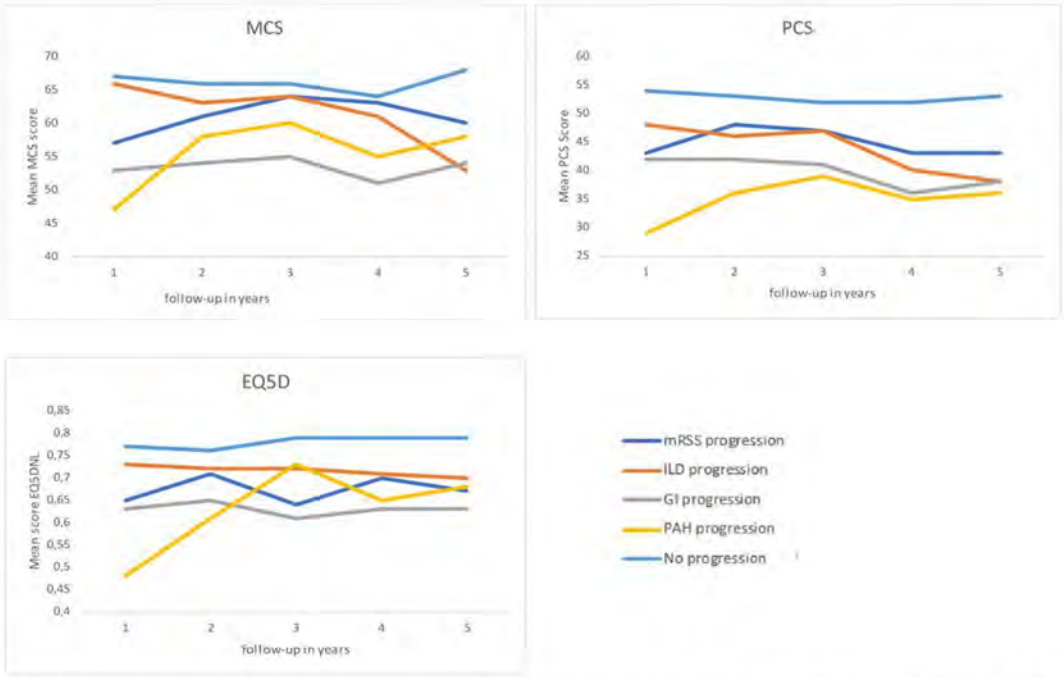

Figure 1. Mean scores of the MCS, PCS and EQ5D for progressors versus never progressors over the follow-up period. Patients who never show progression show higher scores on the PCS, MCS and EQ5D indicating better HRQoL.

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scale 0-100), while the EQ5D showed slight improvement (0.01 points per year, on a scale of -0.57-1, $p< 0.001$). Progression of organ involvement was numerically associated with lower HRQoL scores, indicating a worse HRQol in progressors (Figure 1). The results of the linear mixed model showed that over time the clinical characteristics with the highest impact on deterioration of HRQoL were: digital ulcers (DU) (on the PCS β-3.36), modified Rodnan Skin Score (mRSS) > 15 (PCS β -3.8 and EQ5D β -0.06), Raynaud VAS (on the MCS β-0.10, PCS β-0.12 and EQ5D β-0.002), and severe gastro-intestinal involvement (GI) (EQ5D β-0.05). A worse score on any of the functional assessments, including the six-minute walking test (MCS β 0.007, PCS β 0.009), mouth opening distance (MCS β 0.03, PCS β 0.02) fingertip-to palm distance (MCS β -0.07, PCS β -0.05) and grip strength (MCS β 0.05, PCS β 0.03) was associated with deterioration in HRQoL over time as measured by SF36 ($p< 0.001$).

Conclusion: Over time, HRQoL in patients with SSc slightly worsens and is mainly determined by skin problems including DU, Raynaud and mRSS, and by GI affection. More severe functional impairments also contribute to worsening in HRQoL over time, while impact of ILD seems smaller. These observations underline the heterogeneous nature of SSc and can contribute to interpretation of changes in HRQoL reported in clinical trials.

Disclosure: N. van Leeuwen, None; **J. Ciaffi**, None; **S. Liem**, None; **T. Huizinga**, Bristol-Myers Squibb Company, 2, 8, Pfizer, 2, 8, Eli Lilly, 2, 8, LUMC, 9; **J. de Vries-Bouwstra**, None.

Abstract Number: 0920

Machine Learning Assisted Prediction of Progression in Systemic Sclerosis Patients: An Approach to Concise, Tailored Model Construction Using Outpatient Clinical Data

Nina van Leeuwen[1], Marc Maurits[2], Sophie Liem[2], Jacopo Ciaffi[2], Nina Ajmone Marsan[2], Maarten Ninaber[2], Thomas Huizinga[2] and Jeska de Vries-Bouwstra[2], [1]LUMC, Leiden, Netherlands, [2]Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Sclerosis (SSc) disease course can range from mild, to very severe with progressive organ involvement within months. Guidelines for follow-up are mainly based on expert consensus, and advocate annual assessment. So far, no data driven guidelines exist that describe tailormade systematic assessments for individual patients in line with individual disease course.

Baseline characteristics	n=492
Demographics	
Female, n(%)	389 (79)
Age, mean(SD)	55 (14)
Disease duration nonRP, median (IQR)	3.2 (0.9-10.3)
Organ involvement	
DcSSc, n(%)	118 (24)
mRSS, median (IQR)	4 (0-6)
DU, n(%)	62 (13)
DLCO% of pred, mean (SD)	61 (31)
FVC% of pred, mean (SD)	97 (23)
ILD on HRCT, n(%)	183 (37)
PAH, n(%)	26 (5)
GAVE, n(%)	9 (2)
Myocardial involvement, n(%)	28 (6)
Myositis, n(%)	8 (2)
Renal crisis, n(%)	14 (3)
Autoantibodies	
Anti-centromere, n(%)	194 (39)
Anti-topoisomerase, n(%)	116 (24)
Medication	
Corticosteroids, n(%)	42 (9)
Methotrexate, n(%)	68 (14)
Mycophenolate mofetil, n(%)	19 (4)
Hydroxycholoquine, n(%)	22 (5)
Cyclofosfamide, n(%)	11 (2)
Azathioprine, n(%)	14 (3)
ASCT, n(%)	4 (1)

RP=raynaud phenomenon, dcSSc= diffuse cutaneous systemic sclerosis, mRSS=modified rodnan skin score, DU=digital ulcera, DLCO= single-breath diffusing capacity for carbon monoxide, FVC= forced vital capacity, ILD=interstitial lung disease, HRCT= high resolution computed tomography, PAH= pulmonary arterial hypertension, GAVE= gastric antral vascular extasia, ASCT= autologous stem cell transplantation.

Baseline characteristics

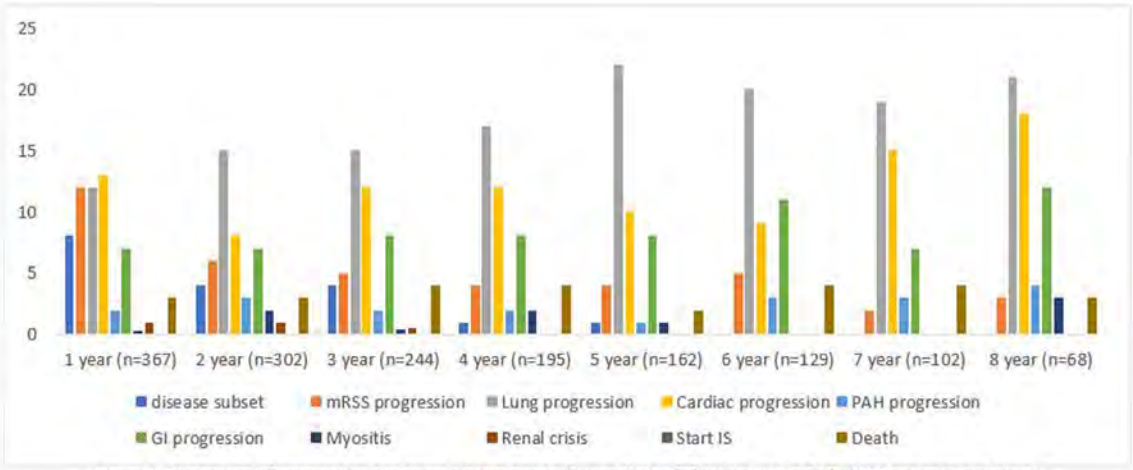

Figure 1. Percentage of progression per organ system per each year during follow-up. We included 492 patients, not every patient had annual complete assessments. Therefore, the n. at visit 1 is not equal to 492.

Figure 1. Percentage of progression per organ system per each year during follow-up. We included 492 patients, not every patient had annual complete assessments. Therefore, the n. at visit 1 is not equal to 492.

In this study we aim to develop a tailormade model to guide annual assessment in individual SSc patients. To address this we 1) determined disease progression in all SSc patients participating in the prospective Leiden SSc cohort with ≥ two visits and 2) applied machine learning to predict progression in patients with complete data available at ≥ 3 time points to determine the outcome.

Methods: Disease progression, evaluated in all SSc patients, was defined per organ system: skin (based on modified Rodnan Skin Score (mRSS) and disease subset), lung (interstitial lung disease and pulmonary function test), myocardial (ejection fraction, arrhythmias, cardiac events), gastro-intestinal (GI) (GAVE, weight loss AND anemia), pulmonary arterial hypertension (PAH), renal crisis, and myositis. The primary endpoint in the prediction model was defined as progression in ≥ 1 organ system, and/or start of immunosuppression (IS) or death between the two most recent visits. To identify patients at risk, we used a machine learning approach known as elastic net regularization using 90 independent patient variables (100% complete) to predict progression. The patients with complete data available at 3 time points were randomly divided over a training (75%) and test (25%) set in order to perform internal validation of the final model. By expert assessment of the test characteristics, including swarm plots of the probability scores, cut-offs were identified for low, intermediate and high risk for disease progression.

Results: In 492 SSc patients (range of follow-up 2-10 years), disease progression during total follow-up was observed in 52% after median 4 years (range 1-8), including myocardial progression in 29%, lung progression in 23%, skin progression in 16%, and death in 12%. Complete data of ≥3 visits were available in n=248. The primary endpoint, i.e. progression at most recent visit, occurred in 24% (median follow-up duration 5 years (range 3-10)). Identified predictors included: previous IS treatment, previous GI or heart progression, previous cardiac event (heart attack, pacemaker), PAH, mRSS, creatinine kinase and diffusing capacity for carbon monoxide. Performance of the model in the test set showed a ROC AUC of 0.66. With the aim to optimize negative predictive value (NPV) cut-offs of probability scores were determined: low risk for disease progression (< 0.197, NPV 1.0; 29% of patients), intermediate risk (0.197-0.223, NPV 0.82; 27%) and high risk (> 0.223, NPV 0.78; 44%).

Conclusion: Our data confirm the severe nature of SSc with cumulative progression in 52%. Although precise risk stratification for the individual patient is difficult, a machine learning approach enabled us to classify 29% of patients as 'low risk'. In this group annual assessment programs might be less extensive.

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Abstract Number: 0921

The Hospital Anxiety and Depression Scale in Patients with Systemic Sclerosis - A Psychometric and Factor Analysis in a Monocentric Cohort

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Session Time: 9:00AM–11:00AM

Background/Purpose: The Hospital Anxiety and Depression Scale (HADS) is a screening tool used in patients with different medical conditions. However, its validity, reliability and responsiveness to change in systemic sclerosis (SSc) patients have not been evaluated yet.

Our objectives were to evaluate the feasibility, validity, reliability, and responsiveness of the Hospital Anxiety and Depression Scale (HADS) and to analyse its model structure in patients with systemic sclerosis (SSc).

Methods: In this study, 307 systemic sclerosis patients were included, of these, 90 participated in the responsiveness analysis. Psychometric properties were tested in analogy to the Outcome Measures in Rheumatology (OMERACT) filter and an exploratory and confirmatory factor analysis was performed to examine the structure of HADS.

Results: The HADS showed adequate feasibility, validity, reliability, and responsiveness to clinically relevant worsening of the disease (Table 1). For our population of SSc patients, the HADS model with two sub-scales, HADS-A and HADS-D, and a general scale HADS-S, measuring anxiety, depression, and distress, respectively, was most appropriate (Figure 1). The rates of anxiety, depression, mixed anxiety-depressive disorder (MADD) and distress identified by HADS in our cohort were 32.7%, 26.1%, 18.6%, and 49.7%, respectively (Figure 2).

Conclusion: The psychometric properties of the HADS make it useful for screening in SSc, where anxiety, depression, MADD, and distress represent a significant burden to patients.Table 1: HADS assessed by OMERACT filter criteria

Pillar	HADS-A	HADS-D	HADS-S
Truth			
Face validity	adequate	adequate	adequate
Content validity	adequate	adequate	adequate
Missing answers	max: 2.22% -item 1 min: 1.05% - item 10	max: 1.75% - item 4 min: 0.93% - item 14	overall missing percentage: 1.41%
Floor and ceiling effect	absent ceiling (%) = 0.3 floor (%) = 9	absent ceiling (%) = 0.3 floor (%) = 9	absent ceiling (%) = 0.6 floor (%) = 3
Construct validity (Spearman's correlations with SOC-13, SF-36-MH, SF-36-MCS, and SHAQ)	strong, very strong, strong, moderate	strong, strong, strong, strong	strong, very strong strong, moderate
Internal consistency reliability (Cronbach's α, split-half reliability)	very good, very good	very good, excellent	excellent, excellent
Discrimination			
sensitivity to change (effect size)	large to very large for ILD and EScSG-A, large for PH events	large for PH, mRSS and EScSG-A events	large for mRSS events
Feasibility			
Applicability	good	good	good

Table 1. HADS assessed by OMERACT filter criteria

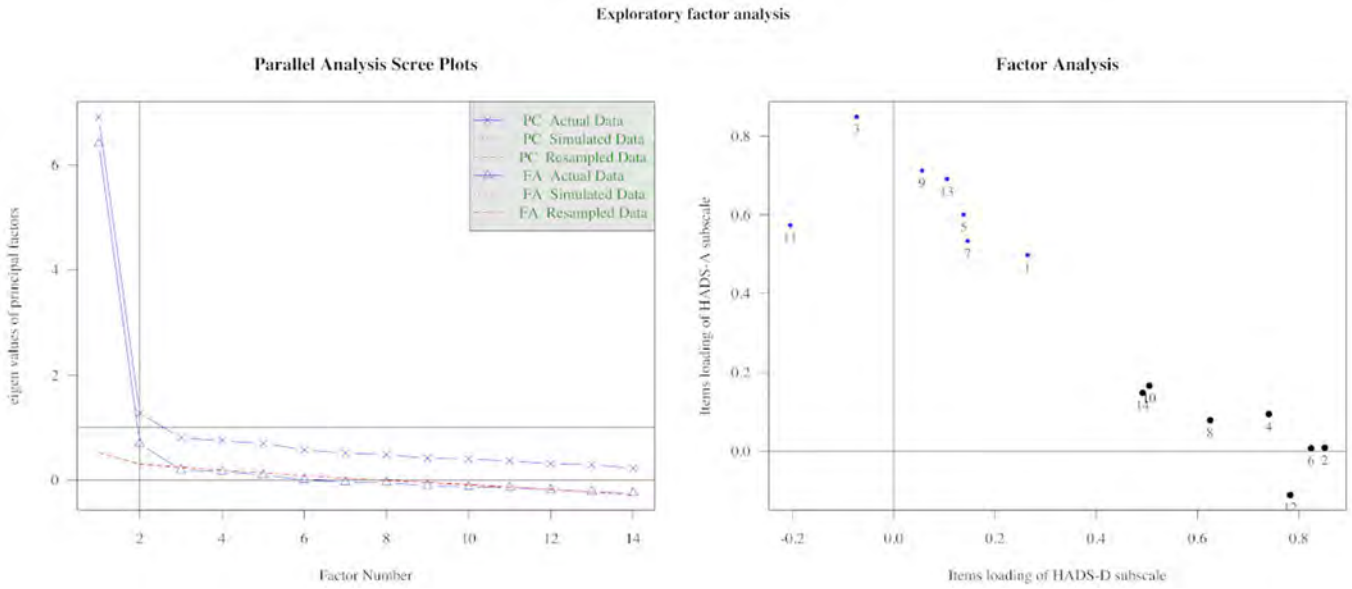

Figure 1. Exploratory Factor Analysis. Parallel analysis scree plot: the solid line shows eigenvalues of actual data, while the dotted and dashed lines (placed on top of each other) show simulated and resampled data. The point of inflection - the point where the gap between simulated data and actual data tends to be minimum - occurs at a number of factors supported by our model (n=2) (left panel); Factor analysis: item loadings of the model sub-scales (right panel).

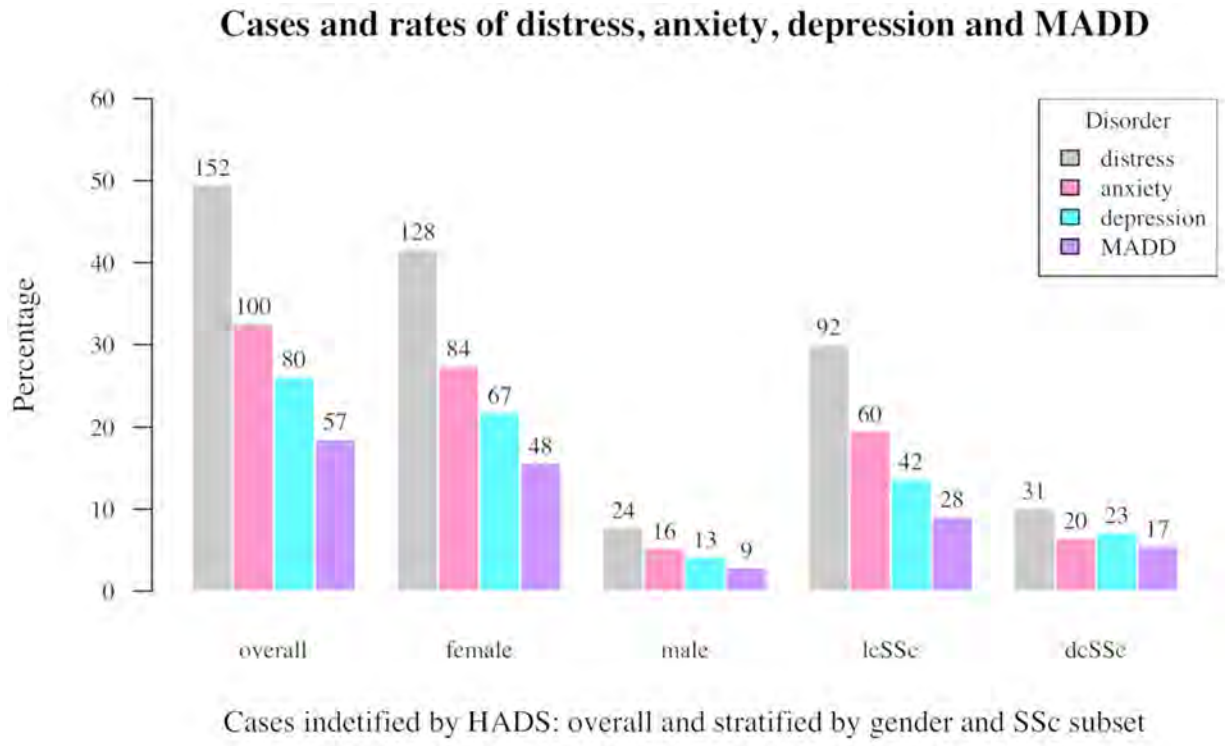

Figure 2 Cases and rates of anxiety, depression, distress and MADD stratified by gender and SSc subset Legend: dcSSc, diffuse cutaneous systemic sclerosis; lcSSc, limited cutaneous systemic sclerosis

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Abstract Number: 0922

Cancer in Systemic Sclerosis: Analysis of Antibodies Against Components of the Th/To Complex

Christopher Mecoli[1], Brittany Adler[2], Qingyuan Yang[2], Laura Hummers[3], Antony Rosen[2], Livia Casciola-Rosen[4] and Ami Shah[5], [1]Johns Hopkins University School of Medicine, Baltimore, MD, [2]Johns Hopkins University, Baltimore, MD, [3]Johns Hopkins Univerisity, Ellicott City, MD, [4]Johns Hopkins University, Johns Hopkins University, MD, [5]Johns Hopkins University School of Medicine, Ellicott City, MD

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study is to describe four of the most common autoantibodies against components of the Th/To complex: hPOP1, RPP25, RPP30, and RPP40. We report their prevalence and clinical characteristics in a systemic sclerosis (SSc) population, and determine whether these specificities associate with cancer.

Methods: A case control study was performed utilizing data from the Johns Hopkins Scleroderma Center Cohort. A total of 804 adult patients with SSc were included; 401 SSc patients with no history of cancer after at least 5 years of disease were compared to 403 SSc patients who ever had a history of cancer. Antibodies against hPOP1, RPP25, RPP30, and RPP40 were assayed by immunoprecipitation of ^{35}S-methionine-labeled proteins generated by in vitro transcription/translation. Demographic and clinical characteristics were compared between groups.

Results: 67/804 (8.3%) of patients had antibodies against any component of the Th/To complex. Patients with antibodies to any component were significantly more likely to have limited cutaneous disease, less likely to have tendon friction rubs, and more likely to have findings consistent with interstitial lung disease or pulmonary hypertension. Patients with antibodies against hPOP1, RPP25, RPP30, and/or RPP40 were significantly less likely to develop cancer within 2 years of SSc-onset (0% vs 11%, p=0.016).

Conclusion: The majority of SSc patients produce autoantibodies to multiple components of the Th/To complex, and have a clinical phenotype characterized by limited cutaneous disease and pulmonary involvement. Our findings show that the presence of any Th/To autoantibody may have a protective effect against contemporaneous cancer.

Disclosure: C. Mecoli, None; **B. Adler**, None; **Q. Yang**, None; **L. Hummers**, Corbus Pharmaceuticals, 1, 2, Boehringer Ingelheim, 1, 2, CSL Behring, 1, 2, Cumberland Pharmaceuticals, 1, Medpace, 1, Glaxo Smith Kline, 1, Kadmon Corporation, 1; **A. Rosen**, Inova, 7, Celgene, 7; **L. Casciola-Rosen**, None; **A. Shah**, None.

Abstract Number: 0923

Criteria for the Diagnosis of Raynaud's Phenomenon – Do They Recognize the Same Patients?

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Background/Purpose: Different criteria aiding the diagnosis of Raynaud's phenomenon (RP) have been proposed. Wigley's "RP criteria 2002", defined RP by history of cold sensitivity, accompanied by pallor and/or cyanosis, and a 3-item questionnaire[1]. International Consensus Criteria proposed criteria ("RP criteria 2014") take a three-step conditional approach (i.e. a screening question, assessment of colour changes and a disease score calculation[2]. As the latter criteria seem more stringent for RP, we aimed to compare the agreement between the two criteria sets and their correlation with nailfold capillaroscopy (NFC) findings and results of immunoserological tests.

Methods: This cross-sectional study was performed between January 2018 and December 2019 at our secondary/tertiary rheumatology centre. Both RP criteria questionnaires were applied by the rheumatologist to all patients and the same day the NFC was done. The agreement between the criteria was determined by the Cohen κ-test. The

Table 1. Comparison between Raynaud's phenomenon criteria

Characteristic	RP Criteria 2014*	RP Criteria 2002*
ANA ≥1:160	0.130 (0.045 – 0.213) p=0.003	0.004 (-0.082 – 0.089) p=0.931
Scleroderma specific Ab$	0.155 (0.069 – 0.237) p <0.001	0.039 (-0.047 – 0.5) p=0.374
ANA ≥1:160 or any Ab against ENA	0.115 (0.029 – 0.199) P=0.009	0.019 (-0.067 – 0.105) P=0.662
Pathologic NFC#	0.135 (0.053 – 0.215) p=0.001	0.163 (0.082 – 0.243) p <0.001
NFC scleroderma pattern	0.175 (0.094 – 0.254) p <0.001	0.098 (0.016 – 0.179) p=0.020
NFC nonspecific pattern	< 0.001 (-0.082 – 0.083) p=0.991	0.094 (0.011 – 0.175) p=0.026

Legend: * Pearson correlation coefficient (95%CI) and p value; ANA antinuclear antibody; Ab antibody; ENA extractable nuclear antigen; $ ACmA or anti-Scl70; # any type of pathological result; NFC nailfold capillaroscopy;

Legend: * Pearson correlation coefficient (95%CI) and p value; ANA antinuclear antibody; Ab antibody; ENA extractable nuclear antigen; $ ACmA or anti-Scl70; # any type of pathological result; NFC nailfold capillaroscopy;

correlation between the two criteria sets, NFC and immunoserological tests (antinuclear antibodies and scleroderma specific antibodies) was calculated with the Pearson correlation test.

Results: We included 565 consecutive patients referred for NFC (84.1% female, median age (IQR) 51.1 (40.1–61.6) years). "RP criteria 2002" and "RP criteria 2014" were fulfilled in 485/565 (85.8%) and 248/565 (43.9%) patients, respectively. The κ-coefficient of agreement between the criteria was 0.22 (95% CI 0.11-0.26). Table 1 shows the correlations between RP criteria and results of NFC and immunoserology.

Conclusion: We found a low level of agreement between the two criteria sets. "RP criteria 2014" correlated better than "RP criteria 2002" with scleroderma specific immunoserology and the scleroderma pattern at NFC, albeit the correlation was low for both criteria.

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Abstract Number: 0924

Towards Systemic Sclerosis Rehabilitation via Videogames

Marica Doveri[1], Marco Trombini[2], Federica Ferraro[3], Rossana Galli[1], Anna Laura Bargeri[4], Simone Rando[1], SIlvana Dellepiane[2] and Gerolamo Bianchi[1], [1]Hospital La colletta Arenzano(Genoa), Arenzano, Liguria, Italy, [2]Department of Electrical, Electronics and Telecommunication Engineering and Naval Architecture (DITEN), University of Genoa, GENOVA, Liguria, Italy, [3]Department of Electrical, Electronics and Telecommunication Engineering and Naval Architecture (DITEN), University of Genoa, Ponsacco, Liguria, Italy, [4]Hospital La colletta Arenzano(Genoa), Arenzano, Italy

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Background/Purpose: The excessive production and accumulation of collagen in systemic sclerosis (SSc) leads to the gradual loss of mobility which affects the quality of life of patients [Parisi, S., et al. 2017]. Hand disabilities in SSc are frequent and contribute to the manifestation of several diseases e.g. reduced mobility, dexterity, and grip strength. Recognizing such symptoms is essential, however no definitive medical treatment is yet available [Young, A., et al. 2016]. The rehabilitation is crucial, and it involves a multidisciplinary team, and aims at improving hand mobility, functionality, and strength [Parisi, S., et al. 2017].

Repetitive movements, typically involved in rehabilitative exercises, can be executed as videogame goal to keep the patient's engagement high. Several studies which make use of videogames can be found in literature, however, very few, and with a limited number of games, refer to the SSc [Eusterwiemann, E., et al. 2019].

The aim of this study was to compare the use of videogames in the assessment phase, in order to address the coherence between the outcome from the digital support, and the standard ones.

Methods: ReMoVES is a telerehabilitation system which provides a support for recovery through videogames, carried out via Leap Motion [Morando, M., et al. 2018].

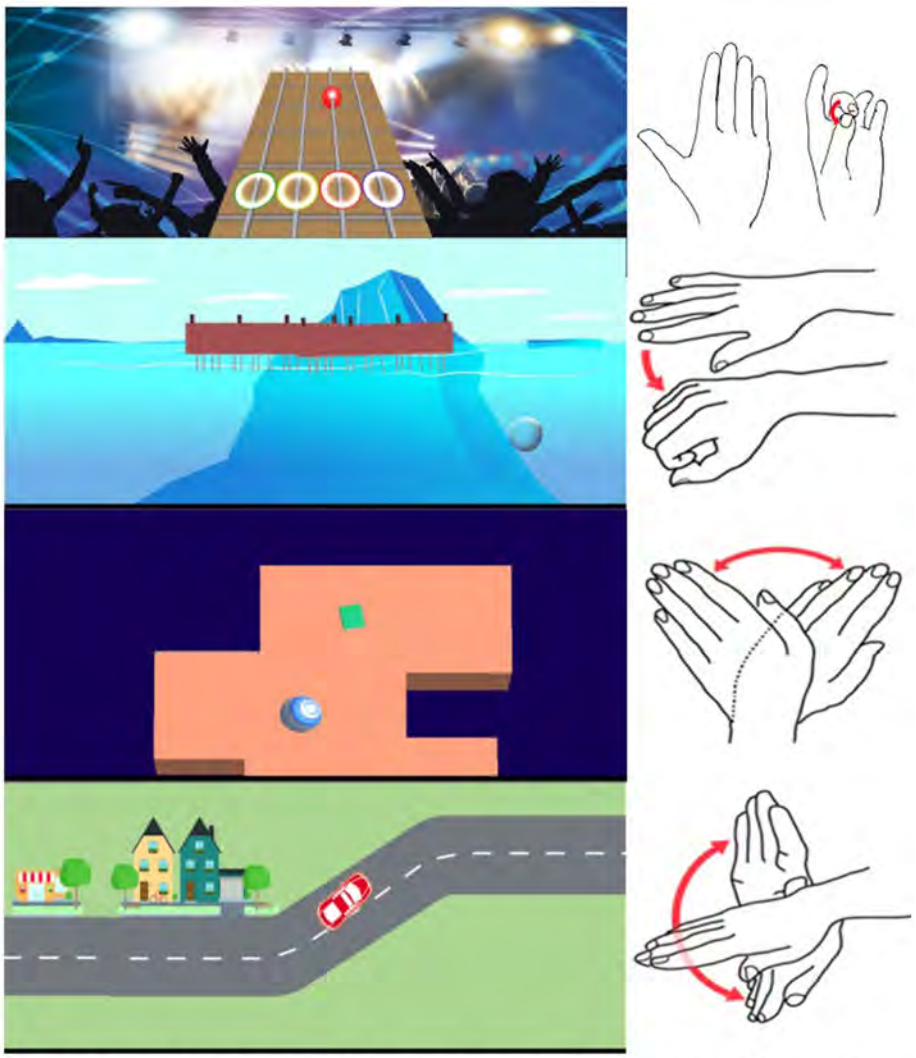

Figure 1: screenshot captured during activity and corresponding thumb opposition, finger flexion-extension, radial-ulnar deviation, and wrist flexion-extension movements respectively.

Four games for hand and wrist movements stimulation were analyzed. They enable the practicing of movements that are typically impaired for SSc patients, i.e. thumb opposition, finger flexion-extension, radial-ulnar deviation, and wrist flexion-extension (Figure 1).

The first purpose was to distinguish patients and control group, based on the ReMoVES feedback. For each activity, the available population is specified in Table 1. The Kruskal-Wallis test was used to this purpose. Then, the correlation between the outcomes deriving from ReMoVES and the score from items 3,6, and 8 from the HAMIS test [Del Rosso, A., et al. 2010], was studied on a population of 12 patients with SSc.

Results: The resulting p-values from the test ($p = 0.0001$ for thumb opposition, $p = 0.0019$ for finger flexion-extension, $p = 0.0028$ for radial-ulnar deviation, and $p = 0.0011$ for wrist flexion-extension) confirmed that the features from ReMoVES are significantly different between patients and control group. Also, the correlation coefficient considering the ReMoVES outcomes and the HAMIS questions proved the coherence between the standard and digital assess-

Activity	Group
Thumb opposition	Patients: 19
	Control: 16
Finger flexion-extension	Patients: 19
	Control: 16
Radial-ulnar deviation	Patients: 18
	Control: 15
Wrist flexion-extension	Patients: 18
	Control: 14

Table 1: Number of participants for each activity.

ment. Such values are: 0.756 for thumb opposition and item 3, 0.767 for finger flexion-extension and item 6, 0.764 for wrist flexion-extension and item 8, 0.788 for radial-ulnar deviation and item 3, and 0.754 for wrist flexion-extension and item 6

Conclusion: Physicians involved in the treatment of SSc need to consider rehabilitation, and skilled physiotherapists and occupational therapists also play a crucial role in evaluating and treating SSc patients. Movements that are typically impaired for SSc patients are stimulated by ReMoVES videogames, which help to entice patients in practicing the rehabilitation activity. The feedback from ReMoVES on the population who participated to the trial is reliable and coherent with the standard outcomes

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Abstract Number: 0925

Early Hydroxychloroquine Use May Reduce Risk for SSc-Associated Pulmonary Hypertension

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Background/Purpose: Systemic sclerosis (SSc) patients are at high risk for pulmonary hypertension (PH), a leading cause of death in this population. Chloroquine is a pulmonary vasodilator shown to attenuate hypoxia-induced PH in mouse models (1). In culture with pulmonary arterial smooth muscle cells (PASMC), chloroquine increases BMPR-II protein expression and inhibits proliferation of PASMC via inhibition of autophagy (2). Our objective was to evaluate whether treatment with hydroxychloroquine (HCQ) was associated with a lower rate or longer time to onset of PH in SSc patients.

Methods: We performed a survival analysis using a prospective, observational SSc cohort from a US SSc Center. We identified SSc patients seen for an initial visit between 1990 and 2015. Individuals exposed to HCQ for a minimum

		HCQ (n=208)	No HCQ (n=976)	p-value
DEMOGRAPHICS				
Age (years) at 1st visit (mean ± SD)		48.9 ± 13.9	52.3 ± 13.3	**< 0.001**
Female		88%	76%	**< 0.001**
Caucasian		85%	91%	**0.006**
SSc PRESENTATION				
Limited cutaneous SSc		67%	50%	**<0.001**
Median mRSS (IQR)		5 (2, 12)	8 (3, 21)	**<0.0001**
Median years of disease at first visit from first SSc symptom (IQR)		3.3 (1.2, 10.4)	2.4 (0.9, 9.0)	**0.05**
First SSc symptom				0.30
Raynaud		55%	55%	
Puffy finger/skin thickening		15%	17%	
Joint symptoms		8%	8%	
Carpal tunnel syndrome		6%	6%	
Dyspnea or cough		2%	2%	
GI		3%	3%	
Other		11%	9%	
ORGAN INVOLVEMENT				
Fibrosis on lung imaging		11%	38%	**< 0.001**
Gastrointestinal		35%	29%	0.09
Renal Crisis		2%	6%	**0.03**
Pulmonary Hypertension				**< 0.0001**
	WHO class 1	10%	12%	
	WHO class 2	--	1%	
	WHO class 3	3%	--	
Joint Involvement	Inflammatory arthralgias	45%	36%	**0.02**
	Joint tenderness on exam	28%	18%	**0.03**
	Joint swelling on exam	19%	9%	**<0.001**
	Joint contractures	35%	43%	**0.03**
	Tendon friction rubs	21%	21%	0.85
SSc-ASSOCIATED AUTOANTIBODY				
Centromere		22%	17%	**0.04**
Scl70		19%	22%	0.43
RNA polymerase 3		20%	26%	0.07
U1-RNP		14%	6%	**<0.001**
Th/To		9%	8%	0.48
PM/Scl		6%	4%	0.10
U3-RNP		4%	4%	0.97
U11-RNP		4%	2%	0.08
RUV-BL/1/2		1%	1%	0.90
Ku		<1%	1%	0.35
Other		9%	12%	0.41

Table 1. Baseline Characteristics

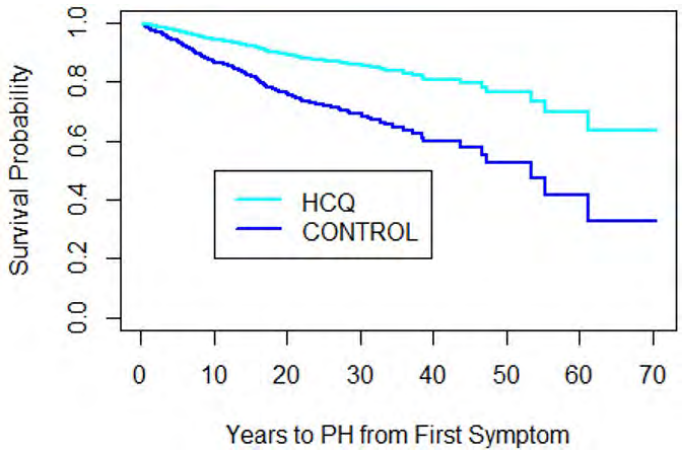

Figure 1. Kaplan-Meier curve of pulmonary hypertension survival probability in SSc patients exposed with HCQ during the first 18 months of disease and SSc patients who were not exposed to HCQ. p=0.04

of 90 days were in the treatment group and all others were controls. Additional chart review and use of electronic medical record coding was performed to confirm HCQ exposure dates and PH evaluations. Descriptive analysis plus Cox Proportional-Hazards modeling with time-dependent covariates to account for duration of HCQ exposure was performed. We analyzed all HCQ exposure, with separate analysis for early (< 18 months of disease) HCQ use.

Results: Eligible were 228 with HCQ exposure and 977 controls; 21 had missing onset of HCQ use, symptoms, or PH diagnosis and were excluded from analysis. Baseline characteristics for the 208 cases and 976 controls are shown in Table 1. HCQ-treated patients were younger, more often female and non-Caucasian. HCQ patients had a higher rate of limited cutaneous disease with more joint involvement at baseline, but lower rates of pulmonary fibrosis, PH and renal crisis. HCQ patients had significantly higher frequencies of anti-centromere (ACA) and anti-U1RNP antibodies, both of which are recognized to be associated with increased risk of PH.

In time to event analysis of the entire group, there was no difference in development of PH between those treated with HCQ, and those not. However, when we evaluated those treated early in their disease, defined as within 18 months of their initial SSc symptom (approximately 25% of HCQ-exposed patients), the time to development of PH was slower (p=0.04), as shown in Figure 1.

Conclusion: Patients with SSc treated with HCQ are younger, more frequently female and more often have limited SSc, joint symptoms and ACA and U1-RNP antibody positivity. Although limited SSc and these antibodies are linked to higher rates of PH, our findings suggest that when HCQ is initiated early in disease (< 18 months) there is a reduced rate of progression to PH. This is in keeping with the plausible biologic actions of HCQ on preventing PH. This early stage of SSc may represent a critical period for therapeutic intervention with HCQ.

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Abstract Number: 0926

Risk Factors for Fractures and Osteoporosis Among Patients with Systemic Sclerosis in a United States Cohort

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic sclerosis (SSc) is associated with several risk factors for osteoporosis and fractures due to malabsorption or malnutrition, physical disability, chronic inflammation, and use of corticosteroid therapy. However, the risks for osteoporosis and fracture in SSc patients in the United States not well-defined. The aim of this study was to examine the relationship between risk factors (e.g. medication use, clinical characteristics of SSc) and the incidence of fractures and osteoporosis (OP) in SSc patients in a large U.S. cohort.

Methods: Patients from 1998 to 2019 in FORWARD, National Databank for Rheumatic Diseases, were screened. Patients with SSc and respective 5:1 age- and gender-matched patients with osteoarthritis (OA) from the same database were included as controls. The primary endpoint was the occurrence of a physician-confirmed diagnosis of OP or an osteoporotic fracture. Single and multivariate Cox proportional hazard models were used to investigate the risk factors for fractures or OP in the SSc and OA cohorts. Models were constructed using stepwise and purposeful selection methods.

Results: The study included 922 patients, 154 with SSc and 768 with OA. For 5046 patient-years (median (IQR) 4.16 (6.2)) of follow-up, 90 patients had either a fracture or incident OP. Univariate analysis (Table 2) showed a significant fracture/OP risk (HR (95% CI)) increase for women (HR 2.49 (1.09 – 5.71)), with being underweight (HR 4.57 (1.56 – 13.4)), higher rheumatic disease comorbidity index (HR 1.10 (1.07 – 1.39)), higher Health Assessment Questionnaire Disability Index (HAQ) (HR 1.60 (1.16 – 2.20)), proton pump inhibitor (PPI) use (HR 1.62 (1.05 – 2.47)), SSRI use (HR 1.91 (1.15 – 3.18)), and OP medication use (HR 2.08 (1.10 – 3.94).

The adjusted model (Table 3) of the combined cohort showed a significant increase in fracture/OP risk with PPI use (HR 1.58 (1.01 – 2.49)), higher HAQ score (HR 1.48 (1.00 – 2.50)), and with being underweight (HR 5.37 (1.69 – 17.0)). However, in the subgroup analysis of SSc patients, PPI use was associated with lower risk (HR 0.81 (0.29 – 2.29)), with the lower risk being significant for those with the highest cumulative omeprazole-equivalent PPI exposure (HR 0.15 (0.03 – 0.85).

Conclusion: Our findings suggest that several risk factors are associated with a higher risk of fractures in SSc. Functional status of SSc and OA patients, as measured by HAQ, is a particularly strong indicator of future fracture/OP risk. Thus, interventions aimed at improving patients' functional status may lead to improved clinical outcomes. Furthermore, while PPIs are often associated with a higher risk of fractures/OP, our findings suggest that such risks may vary across different disease types. Further investigations are necessary to further characterize these relationships.

Clinical Feature	Patients with Scleroderma (n=154)	SD	Patients with Osteoarthritis (n=768)	SD	P value †
Age	57.4	12.6	57.9	11.8	0.323
Age distribution %					0.836
20-50	25.3		23.8		
51-64	46.1		45.3		
≥ 65	28.6		30.9		
Age at diagnosis	44.8	15.3	45.8	13.3	0.206
Disease duration	12.4	10.7	11.7	10.2	0.782
Female %	82.0		87.0		0.991
Post-menopause status %	82.8		79.8		0.412
Non-Hispanic Caucasians %	81.8		84.0		0.507
Education (years)	14.0	2.6	14.2	2.4	0.446
BMI kg/m^2	27.8	6.2	30.8	7.6	†
BMI Categories %					†
Underweight 18.5 ≥	3.25		0.91		
Normal weight < 18.5 – 25 <	33.8		21.1		
Overweight 25-30 <	29.9		28.5		
Obese 30 ≤	33.1		49.6		
Health Insurance %	96.5		96.2		0.796
Ever smoked %	47.4		42.9		0.303
Rheumatic Disease Comorbidity Index (0-9)	2.4	1.8	1.8	1.5	†
HAQ Disability Scale (0-3)	0.9	0.6	0.8	0.3	0.140
Diabetes %	5.2		12.9		0.007
Renal disease %	16.2		7.9		0.004
Osteoporosis %	0.6		0.4		0.656
G.I. disorder %	54.6		41.4		0.007
G.I. scale (0-10)	3.3	3.1	1.9	2.4	†
History of diarrhea	27.3		14.8		0.010
History of irritable bowel syndrome	14.9		8.6		†
History of indigestion	41.5		28.5		0.038
History of vomiting	13.6		3.9		†
History of constipation	29.2		22.5		0.336
History of loss of appetite	18.8		9.6		0.002
History of peptic ulcer disease	31.8		19.8		0.010

* The values are presented as mean (SD) unless indicated otherwise.

† p value < 0.001

Table 1. Baseline characteristic of patients with Systemic Sclerosis and Osteoarthritis

Variable	Unadjusted Hazard Ratio (95% CI)	P value	Unadjusted Hazard Ratio (95% CI)	P value
Demographics	**Whole Cohort**		**Scleroderma Patients Only**	
Scleroderma	1.21 (0.72 – 2.06)	0.474	-	-
Female	2.49 (1.09 – 5.71)	0.031	*	*
Age categories		0.524		
20-50	Ref		Ref	
51-64 years	0.98 (0.46 – 1.79)	0.781	3.43 (0.43 – 27.5)	0.246
≥ 65 years	1.29 (0.67 – 2.48)	0.437	4.11 (0.51 – 33.2)	0.185
Postmenopausal	1.86 (0.81 – 4.33)	0.141	*	*
Non-Hispanic Caucasians	1.20 (0.62 – 2.32)	0.583	*	*
Ever smoked	1.13 (0.74 – 1.73)	0.558	1.00 (0.39 – 2.61)	0.994
Disease duration (years)	1.01 (0.99 – 1.03)	0.199	1.01 (0.97 – 1.06)	0.518
BMI categories (kg/m^2)		0.304		
Underweight 18.5 ≥	4.57 (1.56 – 13.4)	0.006	4.45 (0.86 – 23.1)	0.076
Normal weight <18.5 – 25 <	Ref			
Overweight 25-30 <	1.01 (0.63 – 1.64)	0.631	1.18 (0.36 – 3.88)	0.782
Obese 30 ≤	1.00 (0.58 – 1.72)	0.993	0.73 (0.20 – 2.72)	0.639
Comorbidities				
Rheumatic Disease Comorbidity Index	1.10 (1.07 – 1.39)	< 0.001	1.22 (0.95 – 1.58)	0.123
HAQ disability score	1.60 (1.16 – 2.20)	0.004	2.34 (1.19 – 4.59)	0.014
Diabetes	1.25 (0.75 – 2.08)	0.398	3.27 (0.93 – 11.5)	0.065
Renal disease %	1.15 (0.69 – 1.91)	0.602	2.36 (0.89 – 6.26)	0.083
G.I. disorder %	0.94 (0.61 – 1.46)	0.786	1.46 (0.47 – 4.53)	0.514
G.I. scale (0-10)	0.88 (0.74 – 1.04)	0.144	0.99 (0.75 – 1.30)	0.930
Medications				
Proton pump inhibitors	1.62 (1.05 – 2.47)	0.026	0.78 (0.29 – 2.11)	0.622
PPI cumulative dose (omeprazole equivalent grams)	1.00 (0.97 – 1.04)	0.972	0.94 (0.81 – 1.08)	0.348
Below 50th percentile	Ref		Ref	
Above 50th percentile	0.67 (0.34 – 1.33)	0.255	0.23 (0.04 – 1.28)	0.094
Glucocorticoid use		0.261		
none	Ref		Ref	
Low ≤ 7.5 mg/day	1.44 (0.63 – 3.32)	0.387	1.09 (0.31 – 3.86)	0.888
Medium & High > 7.5 mg/day	2.66 (0.97 – 7.29)	0.058	1.97 (0.25 – 15.4)	0.518
Osteoporosis medications	2.08 (1.10 – 3.94)	0.024	4.23 (1.48 – 12.1)	0.007
SSRI	1.91 (1.15 – 3.18)	0.013	0.36 (0.05 – 2.75)	0.326
Estrogen	0.72 (0.41 – 1.27)	0.257	1.30 (0.37 – 4.55)	0.680
Opioid analgesia	1.38 (0.88 – 2.16)	0.166	0.63 (0.18 – 2.19)	0.464
Nonopioid analgesia	0.77 (0.51 – 1.17)	0.225	1.19 (0.46 – 3.10)	0.720
Anticonvulsants	1.15 (0.66 – 2.01)	0.627	0.65 (0.15 – 2.86)	0.571

Table 2. Univariate Risk Factor Analysis of Fractures and Osteoporosis (OP) in Patients with SSc and OA

Variable	Adjusted Hazard Ratio (95% CI)	P value	Adjusted Hazard Ratio (95% CI)	P value
Demographics	**Whole Cohort**		**Scleroderma Patients Only**	
Scleroderma	0.72 (0.40 – 1.30)	0.274	*	*
HAQ disability score	1.48 (1.00 – 2.50)	0.025	2.59 (1.22 – 5.46)	0.013
Age (years)	1.01 (0.99 – 1.03)	0.270	1.04 (0.99 – 1.09)	0.105
BMI (kg/m²)				
Underweight 18.5 ≥	5.37 (1.69 – 17.0)	0.007	2.19 (0.34 – 14.0)	0.405
Normal weight <18.5 – 25 <	Ref		Ref	
Overweight 25-30 <	1.00 (0.56 – 1.80)	0.964	1.17 (0.34 – 4.07)	0.802
Obese 30 ≤	0.87 (0.48 – 1.56)	0.566	0.46 (0.11 – 1.87)	0.278
PPI use	1.58 (1.01 – 2.49)	0.049	0.81 (0.29 – 2.29)	0.691
PPI cumulative dose (omeprazole equivalent grams)				
Below 50th percentile	Ref		Ref	
Above 50th percentile	0.70 (0.34 – 1.44)	0.338	0.15 (0.03 – 0.85)	0.033

Table 3. Multivariate Risk Factor Analysis of Fractures and Osteoporosis (OP) in Patients with SSc and OA

Disclosure: S. Famenini, None; **J. Perin**, None; **K. Wipfler**, None; **K. Michaud**, Rheumatology Research Foundation, 2; **Z. McMahan**, None.

Abstract Number: 0927

Care Gap in Patients with Systemic Sclerosis with CXR Findings Suggestive of Fibrosis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Lung involvement, including interstitial lung disease (ILD), is the leading cause of death in patients with systemic sclerosis (SSc). High resolution CT (HRCT) is the gold standard for diagnosing SSc-ILD as chest x-rays (CXR) are poorly sensitive for documenting the presence and extent of disease. As such, a CXR suggestive of ILD should warrant the completion of HRCT chest for further characterization. We explored a national patient registry of SSc patients to determine the proportion of patients who receive an HRCT after a CXR suggestive of fibrosis.

Methods: Longitudinal clinical data from patients in the registry collected and contributed by SSc experts between 2004-2018 was reviewed. We included patients at least 18 years of age, with a diagnosis of SSc, and with at least one CXR indicating fibrosis. We excluded patients who had previously known ILD or an abnormal HRCT prior to their first abnormal CXR. Of these patients, we determined the proportion of patients who underwent an HRCT within a year of CXR findings. Using SPSS, descriptive statistics characterized the population and analyses (Pearson's chi-square and T-tests) determined whether there were differences in patient characteristics between those who did and did not receive an HRCT.

Results: Of 1698 SSc patients, we identified 223 who had a positive CXR with no previous abnormal HRCT; Mean (SD) age was 56.6 (12.2) years, 83.9% were female, and 38.1% of patients had diffuse systemic sclerosis. Average FVC and DLCO were 90.4% (SD 18.2%) and 68.8% (SD 23.1%) of predicted, respectively. Only 21.5% (48/223) underwent an HRCT within 12 months following their abnormal CXR. There were no significant group differences in age, sex, smoking history, co-morbidities, subset of disease, autoantibody profile, symptoms, or skin score between those who did and did not undergo an HRCT. Of the patients who had a HRCT, 83.3% had ≥1 abnormality reported.

Conclusion: A large proportion of SSc patients in this study whose CXR suggested fibrosis did not have a HRCT ordered within 1 year of the CXR, suggesting a care gap. A major limitation of this study is that we are unable to account for under-reporting of HRCTs as it may not be available at the time of CSRG data submission; we will examine for this by completing a comprehensive chart review of a smaller cohort of CSRG patients. Other next steps include exploring if HRCT ordering practices evolved over time and how this impacted the proportion of patients who did not undergo HRCT.

Disclosure: S. Dhillon, None; **J. Kapralik**, None; **C. Sobchak**, None; **N. Khalidi**, None; **M. Kolb**, Boehringer Ingelheim, 2, 5, 8, Roche, 2, 5, 8, Pieris, 2, 5, Algernon, 5; **N. Hambly**, None; **G. Cox**, None; **K. Beattie**, None; **M. Larche**, AbbVie, 5, Amgen, 5, Boehringer-Ingelheim, 5, BMS, 5, Celgene, 5, Janssen, 5, Mallinckrodt, 5, Novartis, 5, Pfizer, 5, Roche, 5, Sandoz, 5, UCB, 5.

Abstract Number: 0928

Systemic Sclerosis Progression and Pregnancy: A Hopeful Message from the Canadian Scleroderma Registry Database

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: There is limited guidance for women with systemic sclerosis (SSc) in making decisions about pregnancy and informing them about their disease post-partum. Peripartum maternal and fetal complications have been reported, yet little is known about disease activity *after* pregnancy. We explored the trajectory of disease activity in women who experienced a pregnancy after scleroderma diagnosis and compared it with women who were nulliparous (NP).

Methods: We conducted a retrospective cohort study using data from a national SSc database. We identified two groups of women: those who were NP and those who experienced ≥ one pregnancy after their diagnosis (PAD) of scleroderma. Women with pre-pregnancy cardiac, lung or renal disease were excluded. Of these patients, 97% met ACR classification criteria. Descriptive statistics at the time of entry into the CSRG for each group are shown in Table 1. T-tests compared differences between groups. We used generalized estimating equations to test for the effect of pregnancy on the following outcomes over 8 years: force vital capacity, diffusing capacity of the lungs for carbon monoxide, right ventricular systolic pressure, glomerular filtration rate, antibody-status, active digital ulcers, physician global assessment of activity and physician global assessment of severity. We controlled for age, smoking and time since SSc diagnosis.

Descriptive Table: Nulliparous vs. Pregnancy After a SSc Diagnosis			
	Nulliparous n=152	Pregnancy After Diagnosis n=45	p value
Age, years (mean, SD)	48.42 ± 13.56	44.49 ± 8.04	0.066
Age of Diagnosis, years (mean, SD)	38.77 ± 14.22	22.6 ± 6.79	<0.001
Duration of disease, years (mean, SD)	9.65 ± 8.94	21.89 (9.62)	<0.001
Smoker (n, %)	74 (49.33)	17 (37.78)	0.173
Meets ACR Criteria (n, %)	149 (98)	43 (96)	0.355
Limited SSc (n, %)	94 (61.8)	30 (66.7)	0.556
Diffuse SSc (n, %)	58 (38.2)	15 (33.3)	0.610
Arthritis present (n, %)	41 (28)	22 (49)	0.009
Myositis present (n, %)	17 (11)	7 (16)	0.440
Overlap present (n, %)	31 (20)	7 (16)	0.455
MCTD present (n, %)	8 (5)	3 (7)	0.7262
Raynaud's present (n, %)	150 (99)	44 (98)	0.663
Ulcers present (n, %)	73 (48)	29 (64)	0.053
Scleroderma renal crisis (n, %)	2 (1)	2 (4)	0.194
History of malignancy (n, %)	10 (7)	2 (4)	0.593
CRP, mg/L (mean, SD)	3.65 (1.05-6.2)	2 (1.7-1)	0.375
ESR, mm/hr (mean, SD)	17.5 (8.5-34)	9.5 (4.5-26)	0.311
Centromere + (n, %)	51 (41)	14 (35)	0.514
Topoisomerase + (n, %)	23 (18)	5 (13)	0.387
RNA pol III + (n, %)	16 (13)	1 (3)	0.062
eGFR, mL/min/1.73m^2 (mean, SD)	155.37 ± 48.6	156.98 ± 53.64	0.858
DLCO, mL/min/mmHg (mean, SD)	74.86 ± 22.58	75.88 ± 20.77	0.823
FVC, % predicted (mean, SD)	90.23 ± 19.12	91 ± 18.75	0.837
FEV1/FVC (mean, SD)	79.67 ± 9.9	78.8 ± 8.55	0.658
RVSP, mmHg (mean, SD)	34.47 ± 15.05	31.47 ± 7.03	0.426

Results: At entry into CSRG there were 153 women in the NP group and 45 in the PAD group. After 6 years, n=48 in NP and n=21 in PAD decreased to 18 and 9 patients after 9 years, respectively. Prevalence of anti-topoisomerase positivity was 18.3% in NP and 12.5% in PAD. Differences in baseline characteristics included age of diagnosis (NP 38.8 years, SD 14; PAD 22.6, SD 6.8; p< 0.001), duration of disease (NP 9.6 years, SD 8.9; PAD 21.9, SD 9.6; p< 0.001) and inflammatory arthritis reported by rheumatologists (NP 41, 28%; PAD 22, 49%, p=0.009). Arthritis was not assessed over time.

There were no statistical differences between groups in the change of force vital capacity, diffusing capacity of the lungs for carbon monoxide, right ventricular systolic pressure, glomerular filtration rate, antibody-status, active digital ulcers, physician global assessment of activity and physician global assessment of severity over time.

Conclusion: This retrospective cohort study demonstrated that having ≥1 pregnancy after a diagnosis of systemic sclerosis did not appear to significantly impact renal, respiratory or global function outcomes over 10 years of follow-up. Study limitations include a small cohort size, retrospective data, unknown infertility rates and attrition. While our study offers a hopeful longer-term message for patients with SSc who are planning a pregnancy, physicians and patients should remain vigilant for potential post-partum complications.

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Abstract Number: 0929

The Effect of Mycophenolate Mofetil on Pulmonary Function Tests in Patients with Systemic Sclerosis-associated Interstitial Lung Disease, and the Difference Between the African Americans versus Non-African Americans

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster II

Session Type: Poster Session B

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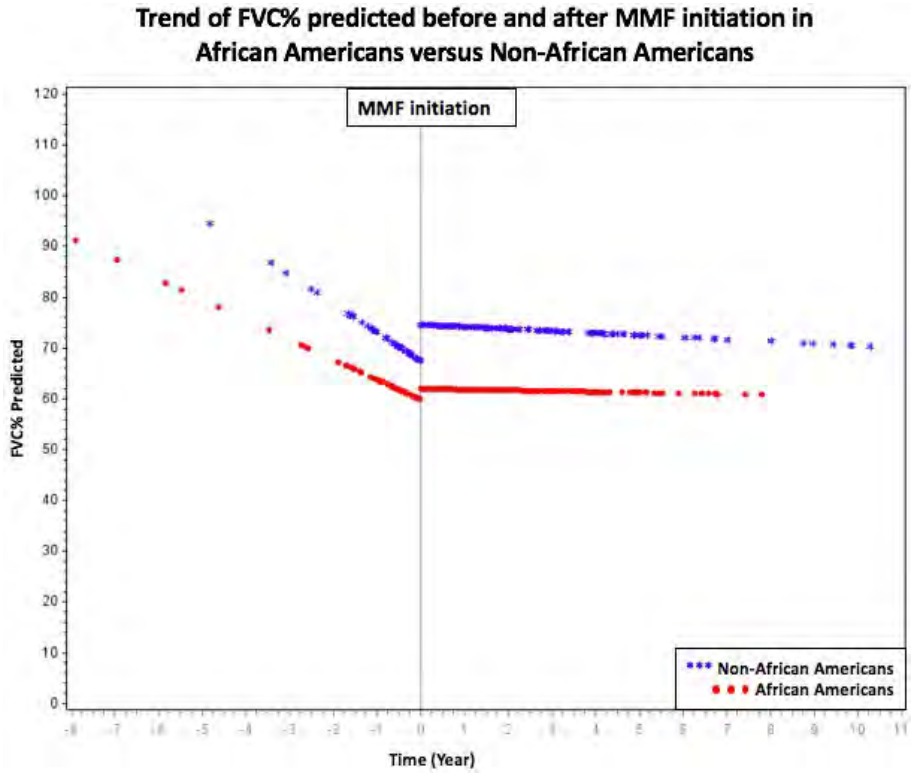
Background/Purpose: Scleroderma-related interstitial lung disease (SSc-ILD) is a pulmonary fibrosing disorder characterized by systemic inflammation and progressive scarring of the lungs that leads to respiratory failure. Previous studies have shown that mycophenolate mofetil (MMF) can be beneficial in SSc-ILD. The majority of studies characterizing patients with ILD and evaluating survival have been conducted in populations with a Caucasian predominance. The objectives of the current study were to explore the role of MMF in the treatment of SSc-ILD, and examine whether racial differences influence response to treatment, specifically between African Americans (AAs) and Non-African Americans (Non-AAs).



Baseline Characteristics	African-American (N=38)	Non-African (N=30)	P- value
Age at first PFTs, median (IQR) years	44 (13.5)	46 (15.1)	0.3192
Female sex -N (%)	35 (92.1)	23 (76.6)	0.0853
Disease duration at first PFTs, median (IQR) years	2.9 (1.4-5.8)	1.3 (0.8-4.6)	0.0725
Disease duration at MMF initiation, median (IQR) years	3.6 (2.0-9.0)	2.3 (1.1-5.5)	0.0647
Scleroderma type -N (%)			
Diffuse	23 (60.5)	19 (63.3)	0.8164
Limited	15 (39.5)	11 (36.7)	0.8164
Pulmonary Function Test mean ± SD			
FVC (% of predicted)	59.8 (2.3)	67.7 (2.7)	0.0228
TLC (% of predicted)	59.5 (2.5)	74.5 (2.9)	0.0001
DLCO (% of predicted)	43.6 (2.8)	56.8703 (3.3)	0.0025
Antinuclear antibodies, N (%)	34/37 (91.9%)	26/27 (96.3%)	0.4801
Anti-centromere	0/22 (0.0%)	0/24 (0.0%)	-
Anti-Scl-70	10/33 (30.3%)	13/28 (46.4%)	0.2016
Anti- RNA polymerase III	1/15 (6.7%)	5/21 (23.8%)	0.1835
Anti-U1 RNP	3/19 (15.8%)	1/21 (4.8%)	0.2569
Isolated nucleolar	10/31 (32.3%)	5/22 (22.7%)	0.4575
Other ANA	1/38 (2.6%)	4/30 (13.3%)	0.3481
Anti-SSA autoantibodies, N (%)	12/27 (44.4%)	4/21 (19.0%)	0.0527
Anti-SSB autoantibodies, N (%)	2/25 (8.0%)	1/21 (4.8%)	0.6662

Methods: We conducted a retrospective study of patients with SSc-ILD that were seen at our institution since 2008, treated with MMF (target dose 1500 mg bid) and had documented PFTs at least once prior to MMF initiation. PFTs at 6, 12, 18, 24, 36, 48 months after initiation of MMF were also documented. Baseline characteristics as well as PFTs were compared using t-test. A regression analysis was used to compare the trend of FVC% predicted, TLC% predicted and DLCO% predicted before and after MMF treatment, as well as to compare AAs and Non-AAs.

Results: Sixty-eight patients were included of which 38 (55.8%) were AAs. The median age in AAs and Non-AAs was 44 (IQR 13.5) and 46 (IQR 15.1), respectively (Table 1). The AA group had a higher female percentage, slightly but not significantly longer disease duration at first PFTs and no significant difference in anti-nuclear antibodies subtypes compared to Non-AA group. Prior to MMF initiation, the average FVC% predicted was 63.2 (± 1.9) for the entire cohort, with AAs having a statistically significant lower baseline than non-AAs (59.8 ± 2.3 vs. 67.7 ± 2.7, p=0.02). The trend change in FVC% predicted pre- and post- treatment was significant in both groups (+3.8 (SE 1.0), p=0.0002 in

AAs and +5.2 (SE 1.1), p < .0001 in non-AAs) with significant stabilization of FVC% predicted after initiation of MMF (Figure 1). The difference in the trend change between the AA and non-AA group was not statistically significant. There was no significant trend change in TLC% predicted and DLCO% predicted, although the AA group showed an insignificant decrease in both values post- MMF compared to non-AA that showed an increase (p >0.05).

Conclusion: MMF can significantly slow the decrease in FVC% predicted in patients with SSc-ILD in both AAs and non-AAs. The main difference in our population was the significantly lower FVC in our AA patients at the start of MMF. It is critical to identify patients with ILD as early as possible to initiate treatment and prevent further deterioration. This is particularly true in AAs.

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Abstract Number: 0930

Sexual Health Impairment in 90 Female Patients with Systemic Sclerosis

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Background/Purpose: Systemic sclerosis (SSc) is a chronic, multisystem, connective tissue disorder characterized by fibrosis of the skin and internal organ involvement. These serious clinical manifestations can be associated with significant impairment of quality of life including sexual life. The aim of this study was to assess sexual functioning in female SSc patients compared to age-/sex-matched healthy controls (HC) and to determine the association between sexual health impairment and physical and psychological aspects of the disease.

Methods: In total, 90 women (70 currently have a partner) with SSc (mean age: 49.1, disease duration: 6.1 years, lcSSc/dcSSc: 62/28, mRSS: 9.3, ESSG activity index: 2.1), who fulfilled the ACR/EULAR 2013 criteria, and 90 healthy controls (82 currently have a partner, mean age: 49.1) without rheumatic diseases filled in 12 well-established and validated questionnaires assessing sexual function [Female sexual function index (FSFI), Sexual function questionnaire (SFQ28), Brief index of sexual function for women (BISF-W)], quality of sexual life [Sexual quality of life questionnaire – female (SQoL-F)], pelvic floor function [Pelvic floor impact questionnaire–short form 7 (PFIQ-7), Pelvic organ prolapse/urinary incontinence sexual questionnaire–short form (PISQ-12)], fatigue [Fatigue impact scale (FIS)], physical activity [Human activity profile (HAP)], depression [Beck's depression inventory II (BDI-II)], quality of life [36-item Short form survey (SF-36)] and disability [Health assessment questionnaire (HAQ), Scleroderma health assessment questionnaire (SHAQ)]. Routine laboratory testing was performed. Data are presented as median (IQR).

Questionnaire: score range (meaning)	SSc (n=90)	HC (n=90)	p-value
FSFI total: 2 (worst)-36 (best)	19.4 (3.9-26.8)	30.1 (23.1-32.9)	p<0.0001
BISF-W total: -16 (worst)-75 (best)	14.3 (2.1-35.1)	38.2 (19.3-46.2)	p<0.0001
SQoL-F: 0 (worst)-100 (best)	61.1 (34.4-81.1)	91.1 (70.0-96.7)	p<0.0001
PISQ–12: 0 (best)-48 (worst)	13.0 (9.0-17.0)	7.0 (5.0-12.0)	p<0.0001
PFIQ-7 total: 0 (best)-300 (worst)	9.5 (0.0-48.8)	0.0 (0.0-8.3)	p<0.0001
SFQ28 desire: 5 (worst)-31 (best)	17.0 (12.0-20.0)	21.0 (17.0-23.0)	p<0.0001
SFQ28 arousal sensation: 4 (worst)-20 (best)	10.0 (8.0-13.0)	12.0 (9.0-15.0)	p=0.0031
SFQ28 arousal lubrication: 2 (worst)-10 (best)	5.0 (4.0-7.0)	8.0 (5.2-9.0)	p<0.0001
SFQ28 arousal cognitive: 2 (worst)-10 (best)	5.0 (4.0-6.0)	7.0 (5.0-8.0)	p<0.0001
SFQ28 orgasm: 1 (worst)-15 (best)	10.0 (6.5-12.0)	12.0 (10.0-13.0)	p<0.0001
SFQ28 pain: 2 (worst)-15 (best)	12.0 (9.5-15.0)	15.0 (13.0-15.0)	p<0.0001
SFQ28 enjoyment: 6 (worst)-30 (best)	19.0 (12.5-24.0)	24.0 (20.0-25.8)	p<0.0001
SFQ28 partner: 2 (worst)-10 (best)	9.0 (8.0-10.0)	10. (9.0-10.0)	p=0.0182
Questionnaire: score range (meaning)	**Sexually active SSc (n=62)**	**Sexually active HC (n=80)**	**p-value**
FSFI total: 2 (worst)-36 (best)	24.0 (16.7-30.2)	30.8 (26.8-33.1)	p<0.0001
BISF-W total: -16 (worst)-75 (best)	30.4 (13.0-38.4)	39.4 (30.3-46.3)	p=0.0006
SQoL-F: 0 (worst)-100 (best)	65.6 (40.3-92.5)	91.1 (78.9-97.0)	p<0.0001
PISQ–12: 0 (best)-48 (worst)	12.0 (9.0-16.5)	7.0 (5.0-11.0)	p<0.0001
PFIQ-7 total: 0 (best)-300 (worst)	4.8 (0.0-34.5)	0.0 (0.0-4.8)	p=0.0019
SFQ28 desire: 5 (worst)-31 (best)	17.0 (12.0-20.0)	21.0 (17.0-23.0)	p=0.0003
SFQ28 arousal sensation: 4 (worst)-20 (best)	10.0 (8.0-13.0)	12.0 (9.0-15.0)	p=0.0048
SFQ28 arousal lubrication: 2 (worst)-10 (best)	6.0 (4.0-7.0)	8.0 (6.0-9.0)	p<0.0001
SFQ28 arousal cognitive: 2 (worst)-10 (best)	5.0 (4.0-6.0)	7.0 (5.0-8.0)	p<0.0001
SFQ28 orgasm: 1 (worst)-15 (best)	10.0 (6.5-12.0)	12.0 (10.0-13.0)	p=0.0002
SFQ28 pain: 2 (worst)-15 (best)	12.0 (10.0-15.0)	15.0 (13.0-15.0)	p<0.0001
SFQ28 enjoyment: 6 (worst)-30 (best)	19.0 (14.0-24.0)	23.0 (20.0-25.0)	p=0.0006
SFQ28 partner: 2 (worst)-10 (best)	9.0 (7.5-10.0)	10. (9.0-10.0)	p=0.0015

Table 1. Sexual function and pelvic floor function in women with SSc and healthy controls

Results: Patients with SSc reported significantly greater prevalence and severity of sexual dysfunction (FSFI, BISF-W, SFQ28 – in all subscales as well as total scores), worse sexual quality of life (SQoL-F) and pelvic floor dysfunction (PISQ-12, PFIQ-7) compared to HC (Table 1). When we analyzed only sexually active patients compared to sexually active HC, the difference between patients and HC remained significant (Table 1). The prevalence of sexual dysfunction in patients with SSc according to the FSFI cut-off score was 77%. Worse scores in SSc patients were associated with disease duration, disease activity, increased inflammation, greater fatigue, severer depression, increased disability, deteriorated quality of life, and worse ability to perform physical activities (Table 2). We did not observe any associations with the current prednisone dose or skin score. Furthermore, no significant differences between lcSSc and dcSSc were found.

Conclusion: Women with SSc reported significantly impaired sexual function and pelvic floor function compared to healthy females with identical age. The prevalence of sexual dysfunction in SSc patients was 77%. Worse scores in SSc were associated with disease duration, disease activity, increased inflammation, severer disability, physical inactivity, fatigue, depression, and decreased quality of life.

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Clinical/laboratory parameter	Sexual function/pelvic floor function parameter	Spearman coefficient	p-value
Disease duration	BISF-W total: -16(worst)-75(best)	-0.243	p=0.026
Disease duration	FSFI lubrication: 0(worst)-6(best)	-0.229	p=0.035
ESSG activity index	FSFI arousal: 0(worst)-6(best)	-0.291	p=0.007
ESSG activity index	BISF-W receptivity/initiation: 0(worst)-15(best)	-0.293	p=0.009
C-reactive protein	BISF-W receptivity/initiation: 0(worst)-15(best)	-0.253	p=0.007
C-reactive protein	BISF-W arousal: 0(worst)-12(best)	-0.301	p=0.024
Erythrocyte sedimentation rate	FSFI arousal: 0(worst)-6(best)	-0.248	p=0.026
Erythrocyte sedimentation rate	BISF-W frequency of sexual activity: 0(worst)-12(best)	-0.244	p=0.031
FIS: 0(best)-160(worst)	FSFI total: 2(worst)-36(best)	-0.496	p<0.0001
FIS: 0(best)-160(worst)	BISF-W total: -16(worst)-75(best)	-0.413	p<0.0001
BDI II: 0(best)-63(worst)	FSFI total: 2(worst)-36(best)	-0.505	p<0.0001
BDI II: 0(best)-63(worst)	SQoL-F: 0(worst)-100(best)	-0.369	p=0.0006
HAQ: 0(best)-3(worst)	FSFI total: 2(worst)-36(best)	-0.394	p<0.0001
HAQ: 0(best)-3(worst)	BISF-W total: -16(worst)-75(best)	-0.359	p=0.0007
HAP: 0(worst)-94(best)	FSFI total: 2(worst)-36(best)	0.535	p<0.0001
HAP: 0(worst)-94(best)	BISF-W total: -16(worst)-75(best)	0.504	p<0.0001
SHAQ: 100(worst)-0(best)	FSFI total: 2(worst)-36(best)	-0.403	p<0.0001
SHAQ: 100(worst)-0(best)	BISF-W total: -16(worst)-75(best)	-0.379	p<0.0001
SF-36 physical functioning: 0(worst)-100(best)	FSFI total: 2(worst)-36(best)	0.428	p<0.0001
SF:36 social functioning: 0(worst)-100(best)	BISF-W total: -16(worst)-75(best)	0.468	p<0.0001

Table 2: Correlation of sexual functioning with clinical/laboratory features

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Oropharyngeal Dysfunction in Patients with Systemic Sclerosis - Results of a Monocentric Clinical Study

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SESSION INFORMATION

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Background/Purpose: Nearly 98% of patients with systemic sclerosis (SSc) are suffering from gastrointestinal involvement (Schmeiser et al. 2012). While in everyday clinical practice screening for reflux and gastrointestinal dysmo-

Testing method	**Type of oropharyngeal dysfunction**		**n**
subjective (anamnesis)			43/55 (78%)
	reflux		29 (67%)
	voice disorder		7 (16%)
	dysphagia		31 (72%)
objective (logopedic examination)			26/26 (100%)
	speech disorder		1 (4%)
	voice disorder		12 (46%)
	breathing disorder		19 (73%)
	dysphagia		15 (58%)
	restriction of oropharyngeal musculature		25 (96 %)
		palate	11 (44 %)
		tongue	19 (76%)
		mimic musculature	13 (52%)

Frequency und type of oropharyngeal dysfunction

	subjectively experiencing oropharyngeal Dysfunction (n=43)	subjectively not experiencing oropharyngeal dysfunction (n=12)	p-values (x^2-test)
dcSSc	9	2	0,86
lcSSc	31	8	0,86
disease duration < 60 months	14	8	0,04
disease duration > 60 months	28	4	0,04
mRSS < 4	15	5	0,66
mRSS >4	28	7	0,66

Influencing factors

tility is part of the routine procedure and evidence-based treatment options exist (Mercado et al. 2005; Boeckxstaens et al. 2002), screening for oropharyngeal dysfunction is rarely done nor adequately treated. In 2012, a study of the German Network of Systemic Scleroderma (DNSS) showed, that about 78% of patients reported hoarseness and/

or chronic cough. As oropharyngeal dysfunction (e.g. voice dysfunction, dysphagia) can significantly affect quality-of-life and lead to social stigmatization, we initiated a study (DRKS00020776) to address this problem.

Methods: We examined patients with systemic sclerosis using a self-constructed questionnaire and a standardized logopedic examination for signs and symptoms of oropharyngeal dysfunction (e.g., speech disorder, voice disorder, reflux, dysphagia), restrictions of the oropharyngeal musculature (palate, tongue, mimic musculature) and breathing disorders. If any of these were positive, oropharyngeal dysfunction was diagnosed. Furthermore, we analysed, if these findings were associated with specific disease characteristics.

Results: Of 55 patients with SSc fulfilling the inclusion criteria, 55 patients agreed to screening for oropharyngeal dysfunction (medical history and physical examination).

43 out of 55 (78%) SSc patients described at least one symptom of oropharyngeal dysfunction: dysphagia (72%), reflux (67%) and/or voice disorder (16%). In physical examination, 43 out of 55 (78%) patients showed also an oropharyngeal dysfunction.

Neither the subtyp of SSc (d/lcSSc) nor the extent of skin fibrosis (mRSS) were significantly associated with the manifestation of oropharyngeal dysfunction. In contrast, a statistically significant relationship between duration of illness and the manifestation of oropharyngeal dysfunction could be found.

26 out 55 patients received an additional logopedic examination. Of these, 26 out of 26 patients (100%) showed to have at least one type of oropharyngeal dysfunction (Table 1). Most striking was the altered function (limitation) of oropharyngeal musculature in 25 out of 26 (96%) cases.

Conclusion: Although it is known that nearly all patients with SSc have an involvement of at least one part of the gastrointestinal tract, examination for oropharyngeal dysfunction is rarely done. The data of our study indicate, that independently of the subtype of SSc, this complication is more frequent than expected, increases with the duration of the disease and should therefore be implemented in the standard routine diagnostics for SSc.

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Skeletal Muscle Involvement in Systemic Sclerosis Predisposes to Severe Gastrointestinal Tract and Cardiac Muscle Disease

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Background/Purpose: Tissues containing muscle cells are affected in systemic sclerosis (SSc) patients in different organ systems: skeletal muscle, cardiac muscle and gastrointestinal (GI) smooth muscle. Prior small cohort studies

	Case (n=101)	Control (n=202)	p-value
Age at first visit	49.9 +/-15.1	54.4 +/-13.6	0.0124
Male gender	18 (17.8%)	43 (21.3%)	0.478
Caucasian ethnicity	77 (76.2%)	187/198 (94.4%)	<.0001
Disease duration at first visit*	0.45 (IQR 0.2, 3.3)	0.27 (IQR 0.8,1.2)	0.0160
Diffuse skin disease	60 (59.4%)	90/200 (45.0%)	0.0183
Fibrosis on chest imaging at first visit	14/32 (43.8%)	33/71 (46.5%)	0.797
Skin score (mRSS) at first visit	12.8+/-12.1	11.8+/-11.0 (n=195)	0.497
CPK level (mg/dL)*	438 (IQR 179-997) (n=46)	74.5 (IQR 41-117) (n=71)	<.0001
Renal crisis	5 (4.9%)	11 (5.5%)	0.856
Tendon friction rub present	12/99 (12.1%)	31/199 (16.3%)	0.342
Joint contractures	61/99 (61.6%)	62/191 (32.5%)	<.0001
Centromere	7 (6.4%)	45 (21.4%)	0.0043
RNA-polymerase 3	13 (11.9%)	52 (24.8%)	0.9101
Scl70	11 (10.0%)	50 (23.8%)	0.0186
PMScl	16 (14.7%)	8 (3.8%)	<.0001
Th/To	1 (0.9%)	18 (8.6%)	0.5169
U11RNP	0	6 (2.9%)	0.5285
U3RNP	5 (4.6%)	1 (0.5%)	<.0001
U1RNP	17 (15.6%)	5 (2.4%)	<.0001
Ku	11 (10.1%)	3 (1.5%)	<.0001
RuvBL1/2	10 (9.1%)	2 (1.4%)	<.0001
Anti-synthetase (EJ, OJ, PL12, PL7)	2 (1.8%)	0 (0%)	<.0001
Other antibody	16 (14.7%)	20 (9.5%)	<.0001

*not normally distributed, statistics reported as median and 25%-75% IQR and Wilcoxon p-value

Baseline Demographics, Disease Characteristics, and Clinical FeaturesT

	Cases (n=101)	Control (n=202)	p-value
MTX Use	49 (48.5%)	26 (12.9%)	<0.0001
MMF Use	28 (27.7%)	61 (30.2%)	0.656
Prednisone Use	84 (83.2%)	97 (48.0%	<0.0001
Highest prednisone dose (mg/day)*	40 (IQR 15-60)	13 (IQR 5-30)	<0.0001
Cancer Frequency (ever)	11 (10.9%)	40 (19.8%)	0.656
Hospitalizations (total)	14 (13.9%)	64 (31.7%)	0.0008

*not normally distributed, statistics reported as median and 25%-75% IQR and Wilcoxon p-value

Table 2. Follow-Up After First Visit

have shown separate associations between skeletal muscle with cardiac and GI involvement. Our objective was to further evaluate the relationship between skeletal muscle involvement and severe or end-stage cardiac and GI involvement in systemic sclerosis (SSc).

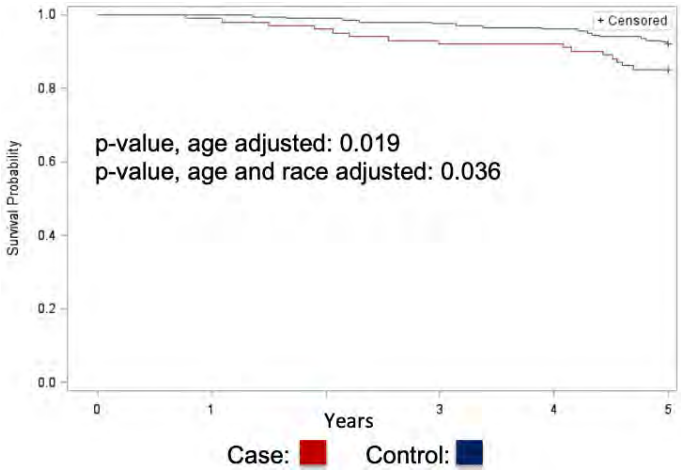

Figure 1. 5-year Survival from First SSc Symptom Onset

Methods: We used an observational SSc cohort from a US Scleroderma Center to perform a case-control study. We included patients seen for an initial visit between 2000-2015 with 2 or more follow up visits at least 4 months apart and continued follow up through at least 3 years after first SSc visit or death. Skeletal muscle cases were identified as those with objective proximal muscle weakness and either CPK level 2 times upper limit of normal, EMG findings of myositis or myopathy, or positive muscle biopsy. Controls included patients that did not meet case identification criteria over a 3-year period. Controls were matched 2:1 with cases and were the next two consecutive SSc initial visits. Disease severity was assessed using the Medsger Severity Scale. Statistical analysis was performed using SAS 9.4 (Cary, NC).

Results: 101 muscle cases and 202 controls were identified. Baseline demographics are shown in Table 1. Cases were significantly younger ($p=0.01$), more frequently non-Caucasian ($p< 0.001$), and had a higher frequency of both diffuse skin disease ($p=0.02$) and joint contractures ($p< 0.001$). As expected, autoantibody profiles were different between cases and controls, with cases having higher frequencies of antibodies associated with myopathy (Table 1): anti-U1RNP, PMScl, Ku, RUV-BL1/2, and U3-RNP antibodies. 23% of cases vs 14% of controls ($p=0.07$) had severe or end-stage GI muscle disease and 18% of cases vs. 13% of controls ($p=0.30$) had severe or end-stage cardiac muscle disease. Cases and controls were treated differently with cases significantly more frequently treated with methotrexate (49% vs 13%, $p< 0.0001$) and prednisone (83% vs 48%, $p< 0.0001$) (Table 2). Overall, cases had a better 5-year survival from first SSc symptom onset when adjusted for age and race (Fig 1).

Conclusion: Severe and end-stage GI and cardiac disease occur at higher frequencies in patients with myopathy, although not statistically significant. Patients with myopathy have a lower rate of 5-year survival. Although the overall frequency of severe and end-stage GI or cardiac disease is low at < 20%, given the poor prognosis of severe GI tract and cardiac involvement, SSc patients with skeletal muscle disease should be followed carefully for these serious complications.

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Advanced Multiparametric Magnetic Resonance Imaging of Muscle for Detection and Quantification of Muscle Disease in Systemic Sclerosis

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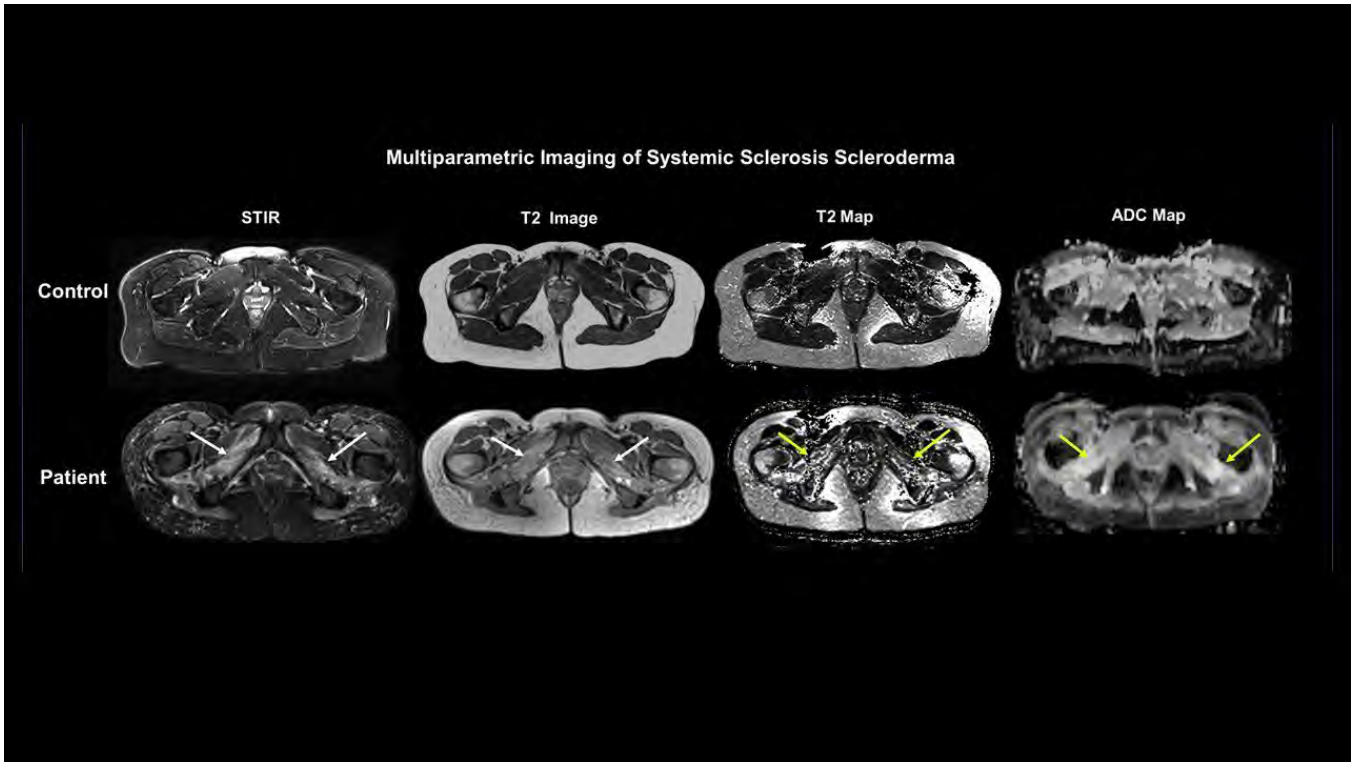
Session Type: Poster Session B
Session Time: 9:00AM–11:00AM

Background/Purpose: Skeletal myopathy in systemic sclerosis (SSc) is underappreciated yet an important manifestation of SSc. While it has been reported that there are distinct histopathologic subsets of myopathy, Multiparametric muscle magnetic resonance imaging (mpMRI) patterns are unknown and the degree of involvement is yet quantified. In order to determine whether unique mpMRI muscle tissue signatures exist in SSc associated myopathy, we implemented advanced mpMRI muscle techniques in the evaluation of SSc in patients with muscle weakness.

Methods: SSc patients were identified as having a skeletal myopathy as defined by proximal weakness and at least one abnormal diagnostic test such as muscle enzymes, EMG, MRI or muscle biopsy. Eligible SSc patients with a myopathy and age matched healthy controls were prospectively recruited. The mpMRI protocol consisted of anatomical and advanced functional sequences that included T_1- and T_2-weighted, T_2 mapping, STIR, Dixon, and diffusion weighted images(DWI) and Apparent Diffusion Coefficient of Water (ADC) maps for detection and quantification the



Representative cases of Multiparametric muscle MRI in a control and SSc patient

burden of muscle involvement in SSc associated myopathy. MpMRI between muscle groups in each cohort were tested using a paired t-test and significance was set at $p< 0.05$.

Results: There were a total of 10 patients, seven who met the 2013 ACR/EULAR criteria for systemic sclerosis and three healthy controls, who underwent the research mpMRI. Six of seven (86%) had diffuse cutaneous SSc. Four of the 7 patients had prior muscle biopsies and demonstrated muscle heterogeneity ranging from a fibrosing myopathy (n=1), necrotizing myopathy (n=2), and dermatomyositis (n=1). Five of the seven were on at least 1 immunosuppressant and/or IVIG for the treatment of myopathy. Mean creatine kinase was 152 ± 111 within 3 months of the mpMRI. There were significant differences between abnormal and normal obturator muscle groups (external and internal) using mpMRI T_2 map values (p=0.02). (Internal Right Side:130±28 versus 87±16 msec and Left Side:138±23 versus 91±16 msec), (External Right Side:157±26 versus 87±16 msec and Left Side:155±26 versus 100±33 msec). Similarly, the ADC values were significantly different in these muscle groups. Figure 1 depicts a representative case where the white arrows show the increased signal intensity in the obturators on the STIR, T_2 maps and ADC maps in a patient compared to a normal control.

Conclusion: In this preliminary study of SSc patients with skeletal myopathy, we demonstrated that by using advanced mpMRI, techniques, the obturator muscles of the pelvis were preferentially affected by SSc compared to healthy controls. Advanced muscle mpMRI could be a useful non-invasive imaging biomarker for muscle disease in SSc associated myopathy that provides new quantifiable metrics.

Disclosure: J. Paik, None; **F. Wigley**, None; **L. Fayad**, None; **L. Hummers**, Corbus Pharmaceuticals, 1, 2, Boehringer Ingelheim, 1, 2, CSL Behring, 1, 2, Cumberland Pharmaceuticals, 1, Medpace, 1, Glaxo Smith Kline, 1, Kadmon Corporation, 1; **M. Jacobs**, None.

Abstract Number: 0934

Warfarin Use and Risk of Knee and Hip Replacements

Priyanka Ballal[1], Christine Peloquin[1], Cindy Boer[2] and Tuhina Neogi[1], [1]Boston University School of Medicine, Boston, MA, [2]Erasmus Medical Center, Rotterdam, Netherlands

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Plenary Session II
Session Type: Plenary Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Vitamin K is an essential co-factor in the post-translational gamma-carboxylation of glutamic acid to form gamma-carboxy-glutamic acid (Gla) residues. This confers functionality to vitamin K-dependent proteins including those in bone and cartilage that play an important role in regulating mineralization. Low vitamin K can lead to under-carboxylation of Gla proteins and thus their dysfunction. Vitamin K deficiency has been associated with OA, and a randomized trial of vitamin K supplementation demonstrated trends towards less OA progression. Studies to date have not evaluated whether vitamin K antagonism with warfarin can be detrimental to OA. We therefore evaluated the relation of warfarin to risk of knee and hip replacements as a reflection of end-stage OA.

Methods: We conducted a nested case-control study using The Health Improvement Network, a general practitioner (GP)-based electronic medical records database from the UK that is representative of the general population. To minimize confounding by indication, we limited our study sample to adults (aged 40-89) with atrial fibrillation, as this diagnosis warrants therapy with anticoagulation. Additionally, we compared warfarin, a vitamin K antagonist, with

	Cases	Controls
Subjects (n)	913	3652
Warfarin use	592 (64.9%)	2057 (56.3%)
Direct oral anticoagulant (DOAC) use	321 (35.1%)	1595 (43.6.%)
Odds Ratio (95% CI), matched for age & gender	1.58 (1.33, 1.87)	
Adjusted* Odds Ratio (95% CI), matched for age & gender	1.57 (1.30, 1.89)	
*adjusted for BMI, factors influencing choice of anticoagulant (CKD 4/5, ESRD, kidney transplant, severe liver disease, mitral stenosis or prosthetic valve, previous intracranial hemorrhage, GI bleed and frequent falls), comorbidities (cancer, congestive heart failure, COPD, dementia, diabetes, hyperlipidemia, hypertension, ischemic heart disease, renal disease, stroke, venous thromboembolism/pulmonary embolus), medications (anti-hypertensives, insulin, oral anti-diabetic drugs, lipid-lowering drugs, NSAIDs, acetaminophen), general practitioner visits, hospitalizations		

Table. Relation of Warfarin versus DOAC use to Risk of Knee or Hip Replacement

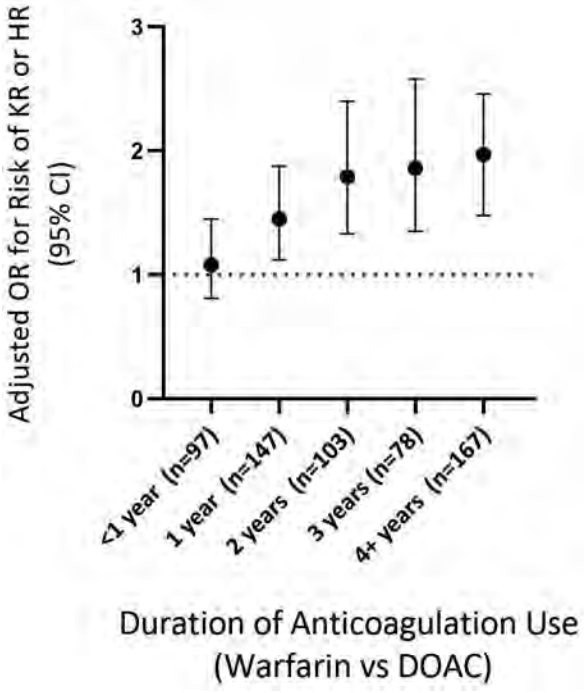


Figure. Relation of Duration of Anti coagulation use (warfarin vs. DOAC) to Risk of KR or HR

direct oral anticoagulants (DOAC), which are not vitamin K antagonists. Because DOACs were first marketed in the UK in 2008, we limited our study to those who had been enrolled for ≥1 year with a GP between 2009 and 2018. We excluded individuals with knee or hip replacement (KR/HR) prior to 2014, severe co-morbidities that would limit surgery, those with warfarin or DOAC use within 1 year prior to our study period, and those who used both drugs during study period. We identified cases as those with KR or HR between 2014-2018, with surgery date being the index date for cases. Each case was matched with up to 4 controls by age and gender. We defined warfarin and DOAC use as having ≥1 prescription after study entry and within 1 year prior to the index date. We assessed the relation of warfarin compared with DOAC use to risk of KR or HR using conditional logistic regression, adjusting for potential confounders.

Results: We identified 913 subjects with KR or HR (cases) who were age and gender-matched 4:1 with 3652 controls (mean age 74, 46% female). Of the 913 cases, 64.9% were warfarin users while 35.1% were DOAC users; in contrast, of the 3652 controls, 56.3% were warfarin users while 43.6% were DOAC users. With adjustment for potential

confounders, warfarin users had 1.57 times higher odds of KR or HR than DOAC users (Adjusted OR 1.57, 95% CI (1.30-1.89)) (Table). When matched by practice ID to account for practice variation, we found a slightly diminished but significant association (Adjusted OR 1.25, 95% CI (1.03-1.52)). There was increasing risk of KR or HR with duration of warfarin vs. DOAC exposure (Figure).

Conclusion: Warfarin use, a vitamin K antagonist, was associated with significantly greater risk of KR or HR (an indicator for end-stage knee OA) than DOAC use, with risk increasing with duration of use. These data add further support to the importance of adequate vitamin K and its dependent proteins in limiting progression of OA and raises the consideration of using DOACs over warfarin when indicated in those with or at risk of OA.

Disclosure: P. Ballal, None; **C. Peloquin**, None; **C. Boer**, None; **T. Neogi**, Lilly, 1, EMD Merck Serono, 1, Novartis, 1, Regeneron, 1, Pfizer/Lilly, 1.

Abstract Number: 0935

Efficacy and Safety Results from a Phase 2, Randomized, Double-Blind Trial of BIIB059, an Anti-Blood Dendritic Cell Antigen 2 Antibody, in SLE

Richard Furie[1], Ronald van Vollenhoven[2], Kenneth Kalunian[3], Sandra Navarra[4], Juanita Romero-Díaz[5], Victoria Werth[6], Xiaobi Huang[7], Hua Carroll[8], Adam Meyers[7], Cristina Musselli[7], Catherine Barbey[9] and Nathalie Franchimont[7], [1]Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, [2]Department of Rheumatology, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands, [3]University of California San Diego, La Jolla, CA, [4]University of Santo Tomas, Manila, Philippines, [5]Instituto Nacional de Ciencias Medicas y Nutricion Salvador Zubiran, Mexico City, Mexico, [6]University of Pennsylvania and the Michael J. Crescenz VA Medical Center, Philadelphia, PA, [7]Biogen, Cambridge, MA, [8]Biogen, Cambridge, [9]Biogen, Baar, Switzerland

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Plenary Session II
Session Type: Plenary Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Type I interferons (IFN-I), inflammatory mediators principally produced by plasmacytoid dendritic cells (pDCs), components of the innate immune system, have been implicated in the pathogenesis of SLE.[1-3] BIIB059 is a humanized IgG1 mAb that binds blood dendritic cell antigen 2 (BDCA2), a pDC-specific receptor, which upon ligation and internalization results in inhibition of the production of IFN-I and other inflammatory cytokines.[4] Administration of BIIB059 in a phase 1 SLE study (NCT02106897) resulted in decreased expression of IFN-response genes in the skin and peripheral blood; reductions of myxovirus resistance protein 1, an IFN-modulated protein, in the skin; reduction in Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity (CLASI-A) scores; and was associated with an accepTable safety profile.[5] LILAC (NCT02847598) is a 2-part, phase 2 study that evaluated the efficacy and safety of BIIB059 in participants with SLE in part A, presented here, and participants with cutaneous lupus erythematosus in part B.

Methods: Enrollment was open to adults fulfilling 4 of 11 1997 revised ACR classification criteria, with ≥4 tender and ≥4 swollen joints (28-joint assessment), active skin disease defined by SLEDAI-2K, and positive ANA and/or elevated anti-dsDNA antibodies. Oral CS doses could not exceed 20 mg/day of prednisone (or equivalent), and mandatory CS tapering was initiated 4 weeks after the first dose of investigational therapy. Concomitant SLE therapy had to be initiated ≥12 weeks and remain sTable ≥4 weeks before randomization and throughout the study. Participants were randomized to BIIB059 450 mg or placebo administered subcutaneously every 4 weeks for 20 weeks (additional dose at week 2). The primary endpoint was the change in total active joint count (sum of tender and swollen joints) from baseline to week 24. Secondary endpoints compared the proportions of participants with 50% improvement from

baseline in CLASI-A score and the proportions of participants who achieved an SRI-4 response at week 24. Safety was assessed.

Results: Of 56 and 64 participants dosed in the placebo and 450 mg BIIB059 groups, respectively, 89.3% and 90.6% completed treatment. The study met its primary endpoint: At week 24, there was a significant difference in least squares mean absolute changes (SE) from baseline in the total active joint count between placebo (-11.6 [1.3]) vs BIIB059 450 mg (-15.0 [1.2], p=0.037). There was a 26-percentage point difference (95% CI: 9.46, 43.24, p=0.003) in the SRI-4 response rate between the BIIB059 450 mg vs placebo group at week 24 (Table 1). Although there was a higher CLASI-50 response rate in the BIIB059 group vs placebo, statistical significance was not attained. The percentages of participants in the placebo and pooled BIIB059 groups that experienced any adverse event were 67.9% and 59.2%, respectively (Table 2).

Table 1. Efficacy endpoints at week 24.

Endpoint	Placebo	BIIB059 450 mg
Primary[a]		
Absolute change from baseline in total active joints[b,c]	n = 46	n = 56
LS mean (SE)	-11.6 (1.3)	-15.0 (1.2)
LS mean diff (95% CI)		-3.4 (-6.7, -0.2)
p value		0.037
Secondary[d]		
CLASI-50 response rate[e]	n = 38	n = 39
LS mean (SE)	49.10 (9.63)	69.10 (8.83)
LS mean diff (95% CI)		20.00 (-1.34, 41.34)
p value		0.064
SRI-4 response rate	n = 56	n = 64
LS mean (SE)	30.42 (7.38)	56.77 (7.36)
LS mean diff (95% CI)		26.35 (9.46, 43.24)
p value		0.003

[a]Post-treatment-failure data were imputed using worse of baseline values or values from the last visit before treatment failure. Data after treatment discontinuation were censored. [b]Total active joints=sum of tender joints and swollen joints (28-joint assessment; maximum score=56). [c]Data from participants enrolled under protocol version 1 were only included in this analysis if they had at least 4 tender joints and 4 swollen joints (28-joint assessment). [d]Participants who failed/discontinued treatment were classified as nonresponders at visits post-treatment failure/discontinuation. Participants who completed treatment but had a missing score at a primary timepoint were classified as nonresponders for that timepoint. [e]Data from participants enrolled under protocol version 2 were only included in this analysis if baseline CLASI-A was ≥8.
CLASI-A = Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity; CLASI-50 = at least 50% improvement from baseline in CLASI-A score; LS mean diff = least squares mean difference from placebo; SRI-4 = SLE Responder Index-4 defined as: reduction from baseline of ≥4 points in the Systemic Lupus Erythematosus Disease Activity Index score 2000, no new British Isles Lupus Activity Group 2004 (BILAG-2004) A domain score or more than 1 new B domain score, no worsening (<10%) from baseline in physician global assessment, and no violations of protocol-specified medication rules.

Table 2. Numbers and percentages of participants with adverse events according to group in LILAC part A.

Event	Placebo (n = 56)	Pooled BIIB059[a] (n = 76)
Any event, n (%)	38 (67.9)	45 (59.2)
Severity, n (%)		
Mild	14 (25.0)	27 (35.5)
Moderate	18 (32.1)	15 (19.7)
Severe	6 (10.7)	3 (3.9)
Related event[b], n (%)	7 (12.5)	15 (19.7)
Serious event, n (%)	6 (10.7)	4 (5.3)
Related serious event[b], n (%)	0	1 (1.3)
Event led to drug withdrawal, n (%)	3 (5.4)	2 (2.6)
Event led to study withdrawal, n (%)	3 (5.4)	0
Deaths, n (%)	3 (5.4)	0

[a]Pooled BIIB059 (n=76): n=6 (50 mg) + 6 (150 mg) + 64 (450 mg). Participants in the BIIB059 50 mg and 150 mg groups were enrolled under protocol version 1. [b]As determined by the investigator.

Conclusion: The LILAC study (part A) met its primary endpoint and a key secondary endpoint (SRI-4). These results, and the observed safety profile, support the continued development of BIIB059 in SLE.

1. *Proc Natl Acad Sci USA* 2003;100:2610; 2. *Lupus* 2008;17:394; 3. *J Exp Med* 2010;207:2053; 4. *EMBO Mol Med.* 2015;7:464; 5. *J Clin Invest.* 2019;129:1359.

Disclosure: R. Furie, AstraZeneca/MedImmune, 2, 5; **R. van Vollenhoven**, AbbVie, 2, 5, Bristol-Meyers Squibb, 2, 5, GlaxoSmithKline, 2, 5, Lilly, 2, 5, Pfizer, 2, 5, UCB, 2, 5, 8, AstraZeneca, 5, 8, Biotest, 2, 5, Celgene, 5, Janssen, 5, 8, Roche, 5, Biogen, 5, Galapagos, 5, 8, Gilead, 5, Servier, 5; **K. Kalunian**, Roche, 5, Biogen, 5, Janssen, 5, Astra-Zeneca, 5, Lupus Research Alliance, 2, Pfizer, 2, Sanford Consortium, 2, Eli Lilly, 5, Genetech, 5, Gilead, 5, ILTOO, 5, Nektar, 5, Viela, 5, Equillium, 5, Bristol-Meyers Squibb, 5; **S. Navarra**, Eli Lilly, 5, 8, Astra-Zeneca, 5, 8, Astellas, 8, Janssen, 5, 8, Novartis, 8, Pfizer, 8, Biogen, 2, 5; **J. Romero-Díaz**, Biogen, 5; **V. Werth**, Biogen, 2, 5; **X. Huang**, Biogen, 1, 3; **H. Carroll**, Biogen, 1, 3; **A. Meyers**, Biogen, 1, 3; **C. Musselli**, Biogen, 1, 3; **C. Barbey**, Biogen, 1, 3; **N. Franchimont**, Biogen, 1, 3.

Abstract Number: 0936

Urine Proteomics and Single Cell Transcriptomics Identify IL-16 as a Biomarker for Lupus Nephritis

Andrea Fava[1], Jill Buyon[2], Chandra Mohan[3], Ting Zhang[3], H. Michael Belmont[4], Peter Izmirly[5], Robert Clancy[6], Jose Monroy-Trujillo[7], Celine Berthier[8], Anne Davidson[9], Nir Hacohen[10], David Wofsy[11], Deepak Rao[12], Soumya Raychaudhuri[13], The Accelerating Medicines Partnership in SLE Network[14], William Apruzzese[15] and Michelle Petri[16], [1]Johns Hopkins University, Baltimore, MD, [2]Department of Medicine, NYU School of Medicine, New York, NY, [3]UT Houston, Houston, [4]New York University, New York, NY, [5]Department of Medicine, New York University School of Medicine, New York, NY, [6]NYU School of Medicine, New York, [7]Johns Hopkins University, Baltimore, [8]University of Michigan, Ann Arbor, [9]Northwell Health, New York, [10]Broad Institute, Boston, [11]University of California San Francisco, San Francisco, CA, [12]Brigham and Women's Hospital, Boston, MA, [13]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [14]Multiple Institutions, Multiple Cities, [15]., Boston, [16]Johns Hopkins University School of Medicine, Timonium, MD

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Plenary Session II
Session Type: Plenary Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Treatment of lupus nephritis relies on renal histopathological features. However, renal biopsies do not capture patient-specific active biological pathways. Urine proteomic biomarkers could revolutionize the diagnosis and management of lupus nephritis by predicting active intrarenal biological pathways and can be noninvasively monitored over time.

Methods: One thousand proteins were quantified (RayBiotech) in a total of 112 longitudinal urine samples from 30 SLE patients with active lupus nephritis and 7 healthy controls (HC). The proteins and molecular pathways detected in the urine proteome at the time of biopsy were then analyzed with respect to lupus nephritis class, response to treatment after 1 year, histopathological features (activity and chronicity indeces), and trajectory over time (baseline and week 12, 26, and 52). The intrarenal expression of candidate biomarkers was evaluated using single cell transcriptomics of renal biopsies from patients with active lupus nephritis.

Results: There were 237 proteins (FDR < 10%) enriched in the urine of patients with lupus nephritis reflecting several molecular pathways involving chemotaxis, extracellular matrix remodeling, and activation of neutrophils and platelets. Hierarchical clustering using urine proteomics segregated SLE patients into 2 groups, with 80% of complete responders clustering together. This finding could not be similarly reproduced using standard features including baseline proteinuria, creatinine, histologic activity or chronicity scores, or class, indicating unique informative features of urine proteomics (**Fig. 1**). Patients

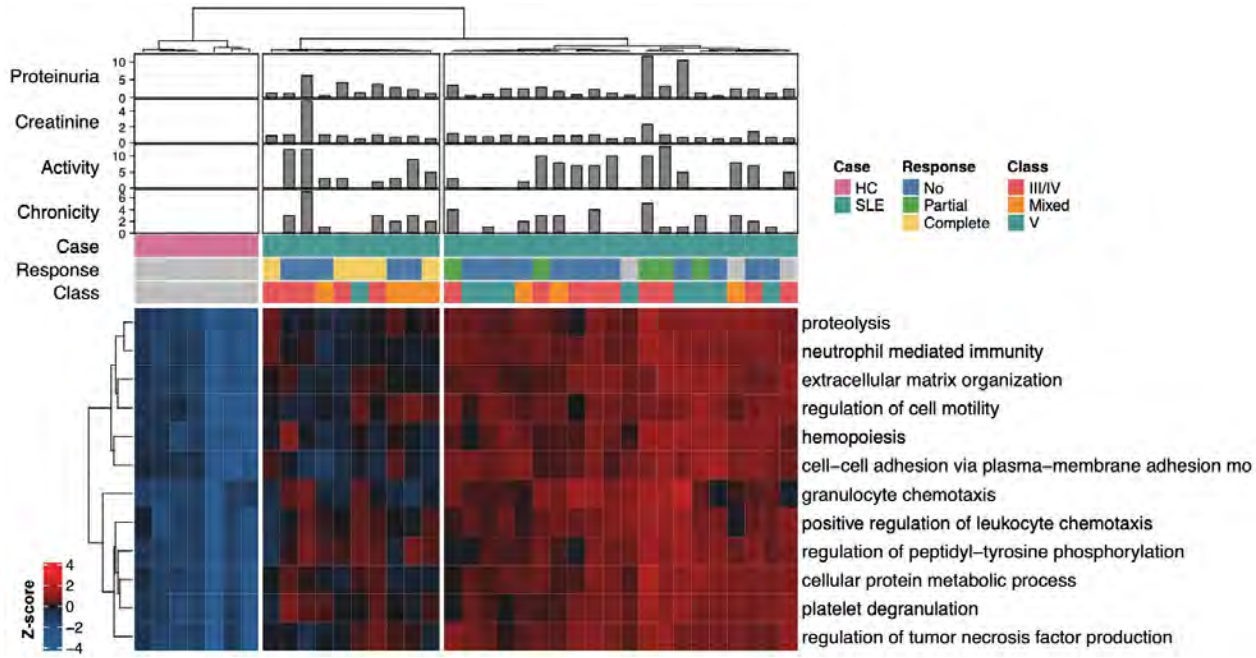


Figure 1. Concentration of enriched proteomic pathways in lupus neprhitis urine. The relative concentration of the 12 non overlapping pathways (GO Biological Process) enriched in the urine of lupus nephritis (LN) patients is reported in this heatmap. Colors represent row-normalized Z-scores. Unsupervised hierarchical clustering identified the healthy controls and two clusters of LN patients. The LN cluster on the left showed overall lower concentration of proteins in the 12 pathways and included 4/5 of complete responders. Figure 1. Concentration of enriched proteomic pathways in lupus neprhitis urine. The relative concentration of the 12 non overlapping pathways (GO Biological Process) enriched in the urine of lupus nephritis (LN) patients is reported in this heatmap. Colors represent row-normalized Z-scores. Unsupervised hierarchical clustering identified the healthy controls and two clusters of LN patients. The LN cluster on the left showed overall lower concentration of proteins in the 12 pathways and included 4/5 of complete responders.

with proliferative lupus nephritis (class III or IV) had stronger activation of chemotaxis pathways. IL-16 was the urinary protein most significantly increased in proliferative disease compared to membranous (FC 6, p=0.002) (**Fig. 2A**). Assessment of urine proteins that correlated with histologic activity kidney highlighted IL-16 as the single most strongly correlated protein with histologic activity (r=0.69, $p=9.5 \cdot 10^{-5}$; **Fig. 2B**). IL-16 concentration was independent of the amount of proteinuria and progressively diminished over time in patients who were responding to immunosuppression (**Fig. 2C**). Single cell RNA sequencing revealed significant intrarenal expression of IL16 by all infiltrating immune cells and highlighted IL16 as the second most expressed cytokine in lupus nephritis kidneys out of a compendium of 236 cytokines (**Fig. 3A-B**).

Conclusion: Urine proteomics can noninvasively identify active and biologically relevant pathways in lupus nephritis. Integrated urine proteomics and renal single cell transcriptomics revealed that IL-16, a CD4 ligand with chemotactic

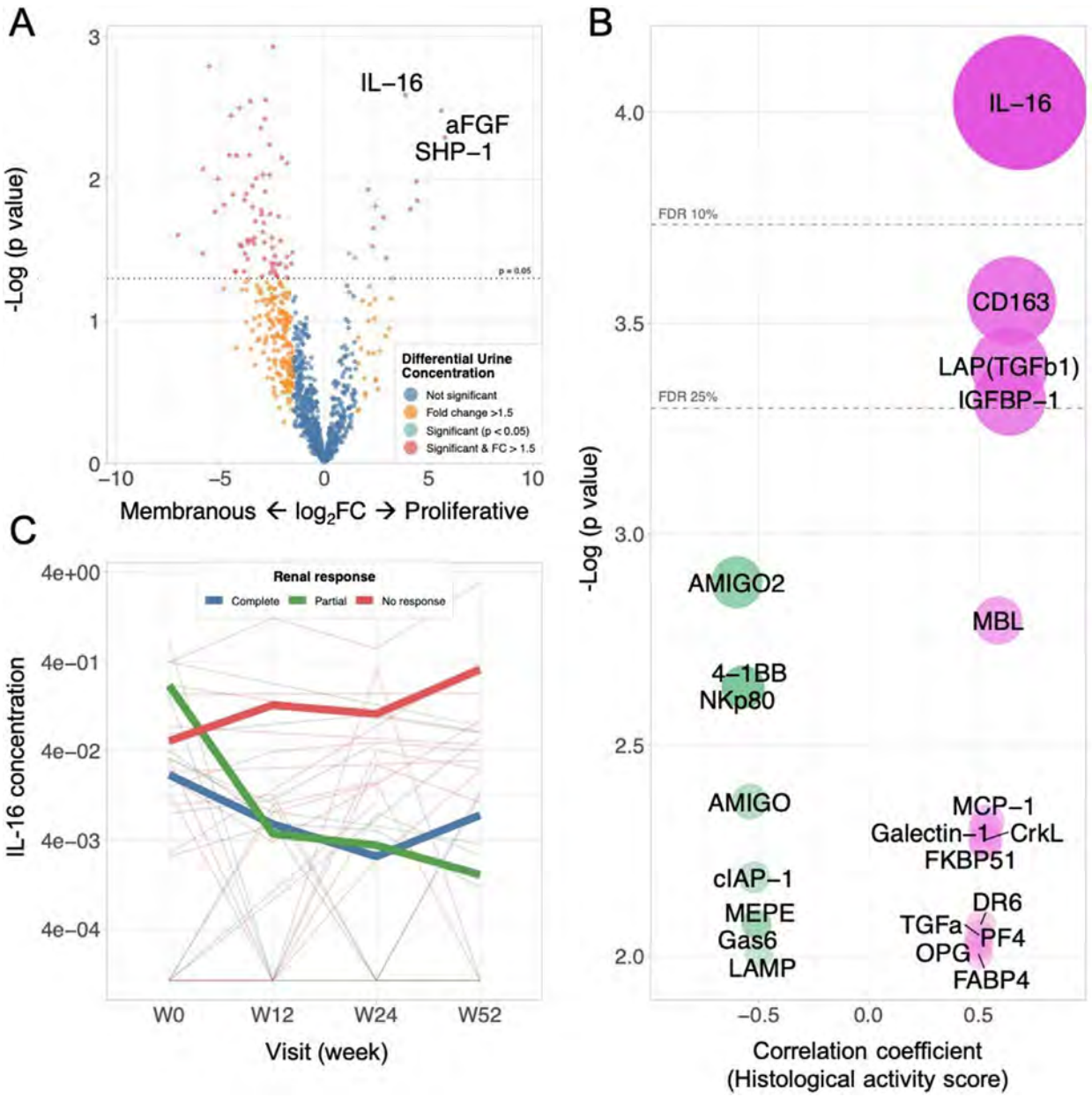


Figure 2. Urinary IL-16 is correlated with renal histological activity and response to treatment. (A) Volcano plot comparing the concentration of 1000 urinary proteins in proliferative vs pure membranous lupus nephritis. (B) Top 20 Pearson's correlations of urinary proteins with renal histological NIH activity index. IL-16 was the only protein with a false discovery rate (FDR) < 10%. Circle areas represent a combination of the absolute correlation coefficient and p value. (C) Longitudinal trends of urinary IL-16 at baseline, week 12, 24 and 52. Thick lines represent the mean concentration according to the response status at week 52.

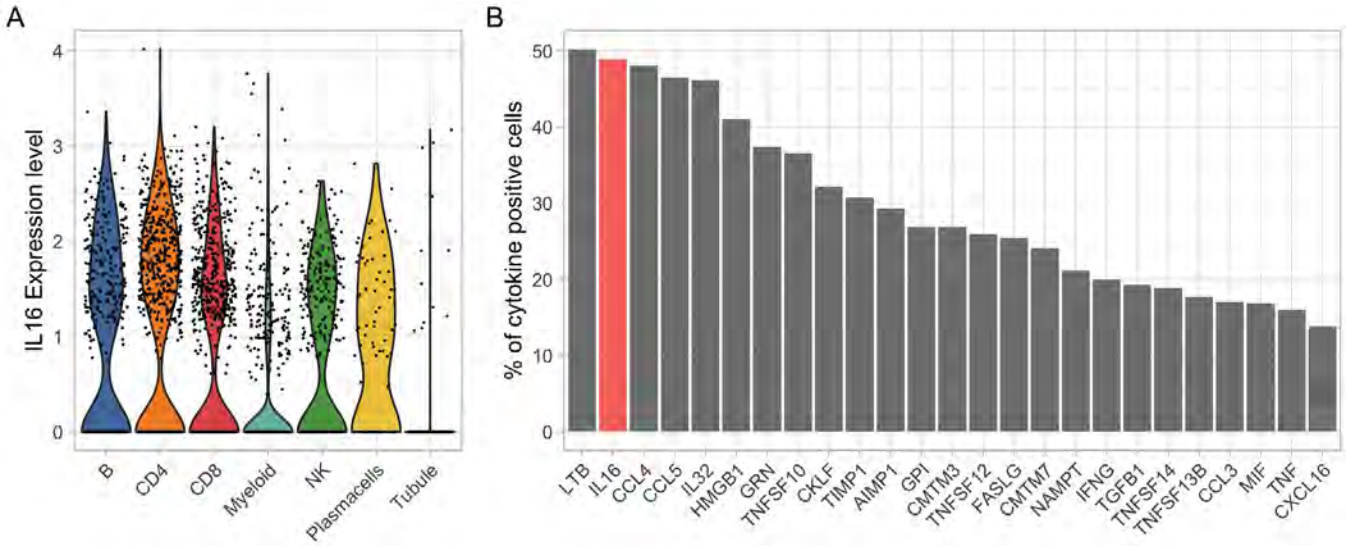


Figure 3. Intrarenal expression of IL16 based on single cell RNA sequencing of lupus nephritis kidney biopsies. (A) Violin plots showing IL16 expression by all kidney infiltrating immune cells. (B) Percentage of cytokine positive cells across all kidney infiltrating immune cells. The bar plot shows the top 25 cytokines out of a comprehensive list of 236 obtained from the "Cytokine Registry" (Immport) and the Gene Ontology database.

and proinflammatory functions, was one of the most expressed cytokine in lupus nephritis. As a urine proteomic biomarker, IL-16 may predict renal histological activity and could be monitored over time to assess response to immunosuppression. Urinary IL-16 is independent of proteinuria thus potentially providing actionable clinical information that is not captured by currently used biomarkers. Further studies are ongoing to validate these findings.

Disclosure: A. Fava, None; **J. Buyon**, None; **C. Mohan**, None; **T. Zhang**, None; **H. Belmont**, Exagen Inc, 8; **P. Izmirly**, GSK, 5; **R. Clancy**, None; **J. Monroy-Trujillo**, None; **C. Berthier**, None; **A. Davidson**, None; **N. Hacohen**, None; **D. Wofsy**, GlaxoSmithKline, 9, Novartis, 9, Principia, 5; **D. Rao**, None; **S. Raychaudhuri**, None; **T. Accelerating Medicines Partnership in SLE Network**, None; **W. Apruzzese**, None; **M. Petri**, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmithKline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5.

Abstract Number: 0937

Late Cardiovascular Outcomes in Children with Kawasaki Disease: A Population-based Cohort Study

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Plenary Session II

Session Type: Plenary Session

Session Time: 11:30AM–1:00PM

Outcome	KD survivors (N=4597)		Non-exposed (N=459,700)		0-1 years		1-5 years		5-10 years		> 10 years	
	n (%)	Incidence (/1000py)	n (%)	Incidence (/1000py)	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Primary outcomes												
Composite cardio-vascular events	746 (16.2)	16.36	23,969 (5.2)	5.13	14.13	12.57 - 15.89	3.56	3.07 – 4.13	1.88	1.54 - 2.29	1.37	1.17 - 1.61
MACE	79 (1.7)	1.53	3,332 (0.7)	0.69	4.63	3.21 - 6.67	1.89	1.21 - 2.94	2.27	1.39 - 3.74	1.14	0.66 - 1.97
Selected cardiovascular outcomes												
MI and ischemic heart disease	247 (5.4)	4.73	3,302 (0.7)	0.75	53.85*	43.16 - 67.19	6.29*	4.67 - 8.48	3.32*	2.24 - 4.91	1.67*	1.17 - 2.40
Arrhythmias (atrial and ventricular)	229 (5.0)	4.53	8,263 (1.8)	1.89	8.92	6.86 - 11.59	3.31	2.54 - 4.31	2.21	1.66 - 2.95	0.90	0.68 - 1.18
Congestive heart failure	49 (1.1)	0.94	741 (0.2)	0.17	14.86	9.58 - 23.05	7.00	3.98 - 12.31	NR†	NR	1.95	0.97 - 3.93
TIA and stroke	61 (1.3)	1.18	2,282 (0.5)	0.52	5.94	3.90 - 9.05	2.15	1.35 - 3.43	2.50	1.47 - 4.25	0.21	0.07 - 0.70
Peripheral vascular disease	107 (2.3)	2.09	863 (0.2)	0.20	153.78	106.59 - 221.87	17.58	11.46 - 26.97	NR	NR	0.49	0.17 - 1.43
Hypertension	159 (3.5)	3.11	9,383 (2.0)	2.15	2.70	1.73 - 4.21	2.08	1.54 - 2.80	1.11	0.75 - 1.63	0.70	0.54 - 0.92

MACE – Major Adverse Cardiac Event, MI – myocardial infarction, TIA – transient ischemic attack
* Hazard ratios for "MI and ischemic heart disease" included angina pectoris, coronary thrombosis, post-myocardial infarction syndrome, and chronic ischemic heart disease. Separate hazard ratios were calculated for acute myocardial infarction but could only be reported between 0-1yr (KD: 7 (0.2%) *vs.* non-exposed: 43 (0.01%), HR 15.88 [7.15-35.31]), due to low event numbers at other time periods.
† NR: not reported as ≤ 5 individuals in one or both groups

Table 1. Incidence and risk of cardiovascular events, comparing KD vs. non-exposed children at 0-1yr, 1-5yr, 5-10yr and >10yr follow-up

Background/Purpose: Kawasaki disease (KD) is a common childhood vasculitis associated with coronary artery aneurysms (CAA). Based on our recent work, the incidence of KD has significantly increased in Ontario over the past two decades. However, the risk of long-term cardiovascular events in children without large CAA remains unknown. Our objectives were to: 1) determine the risk and timing of long-term cardiovascular events (diagnoses and procedures) among KD survivors; and 2) determine the risk of all-cause mortality.

Methods: We identified all children (0-18yr) surviving hospitalization with a KD diagnosis in Ontario between 1995-2018, through validated algorithms using population health administrative databases. We included only the first eligible hospitalization and excluded children previously diagnosed with KD and non-residents. KD cases were matched to 100 non-exposed controls by age, sex and index year. Follow-up continued until death or March 2019 (maximum 24 years). We determined incidence rates (per 1000 person-years (py)) and unadjusted hazard ratios (HR) for cardiovascular events, major adverse cardiac events (MACE; cardiovascular death, myocardial infarction (MI) or stroke composite) and all-cause mortality, comparing KD and non-exposed cohorts during the following time periods: 0-1yr, 1-5yr, 5-10yr and >10yr.

Results: Among 4,597 KD survivors, 746 (16.2%) experienced cardiovascular events, 79 (1.7%) MACE and 9 (0.2%) died during median 11.1-year follow-up (Table 1). The most frequent cardiovascular events among KD survivors were ischemic heart disease (231 children, 4.6 events/1000py), arrhythmias (229, 4.5/1000py), hypertension (159, 3.1/1000py) and peripheral vascular disease (107, 2.1/1000py). KD survivors were at increased risk of cardiovascular events and MACE *vs.* non-exposed children between 0-1yr, 1-5yr and 5-10yr, and cardiovascular events at >10yr

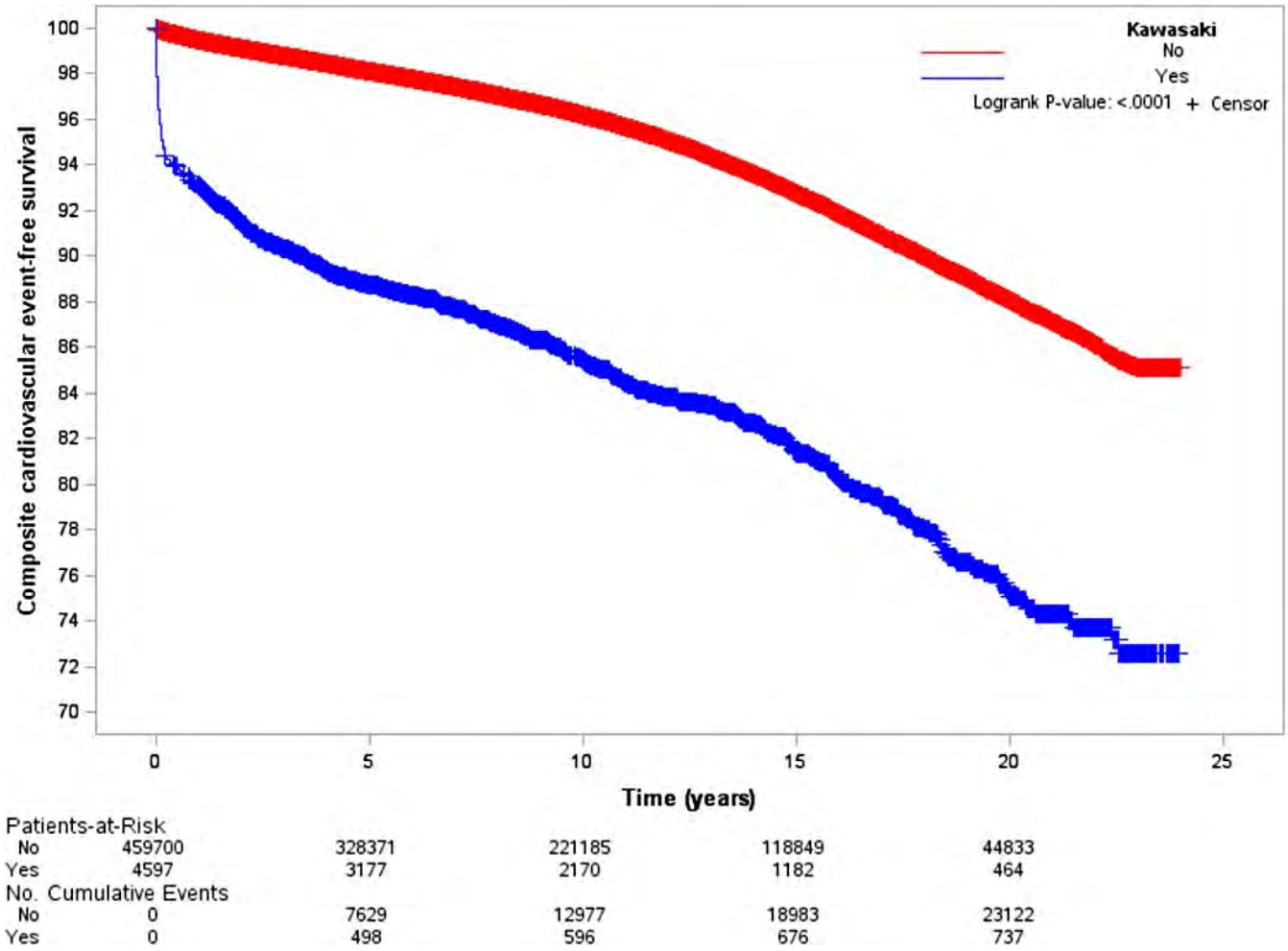

Figure 1. Composite cardiovascular event-free survival among KD survivors vs. non-exposed children

follow-up (Table 1). KD survivors experienced cardiovascular events sooner than non-exposed children (Figure 1; Kaplan-Meier curve, log-rank p< 0.0001). Their risk of cardiovascular events was highest in the first year post-discharge (HR 14.13 [12.57-15.89]). KD survivors were at increased risk of undergoing percutaneous coronary intervention or coronary artery bypass grafting throughout follow-up (KD: 12 (0.3%) *vs.* non-exposed: 63 (0.01%), HR 14.68 [7.73-27.88]). KD survivors were at lower risk of mortality throughout follow-up (KD: 9 (0.2%) *vs.* non-exposed: 2,012 (0.4%), HR 0.42 [0.22-0.81]).

Conclusion: Children diagnosed with KD remain at increased risk of cardiovascular events for >10 years after index hospitalization. Despite the prevalence of cardiovascular disease, they have a lower risk of long-term mortality. Our findings highlight the need for cardiovascular disease surveillance and risk reduction strategies among KD survivors.

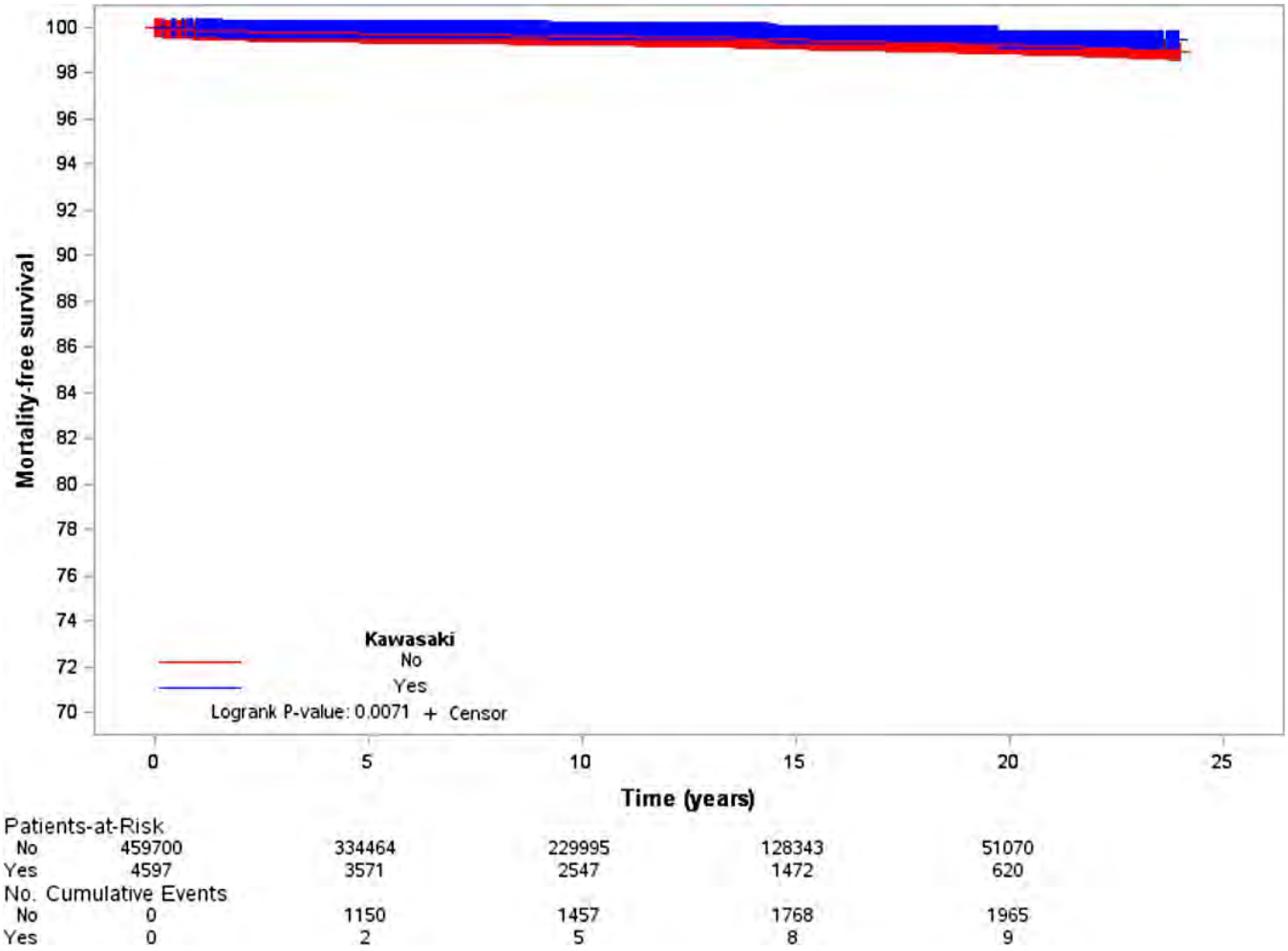

Figure 2. Patient survival among KD survivors vs. non-exposed children

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Disclosure: C. Robinson, None; **R. Chanchlani**, None; **A. Gayowsky**, None; **S. Brar**, None; **E. Darling**, None; **C. Demers**, None; **T. Mondal**, None; **R. Parekh**, None; **H. Seow**, None; **M. Batthish**, Abbvie, 2.

Abstract Number: 0938

Low Preconceptional Complement Level Is Related with an Adverse Obstetric Outcome in a Multicentric Cohort of Pregnancy in Patients with APS and aPL Positivity

Cecilia Nalli[1], Daniele Lini[2], Laura Andreoli[2], Francesca Crisafulli[2], Micaela Fredi[2], Maria Grazia Lazzaroni[2], Victoria Bitsadze[3], Antonia Calligaro[4], Valentina Canti[5], Roberto Caporali[6], Francesco Carubbi[7], Cecilia Chighizola[8], Paola Conigliaro[9], Caterina De Carolis[10], Teresa Del Ross[4], Maria Favaro[4], Maria Gerosa[11], Annamaria Iuliano[12], Jamilya Khizroeva[3], Alexander Makatsariya[3], Pierlugi Meroni[13], Marta Mosca[14], Melissa Padovan[15], Roberto Perricone[9], Patrizia Rovere-Querini[16], Gian Domenico Sebastiani[12], Chiara Tani[14], Marta Tonello[4], Dina Zucchi[14], Franco Franceschini[17] and Angela Tincani[2], [1]Rheumatology and Clinical Immunology Unit, ASST Spedali Civili of Brescia, Brescia, Lombardia, Italy, [2]Rheumatology and Clinical Immunology Unit, Spedali Civili and University of Brescia, Brescia, Lombardia, Italy, [3]Department of Obstetrics and Gynecology of I.M. Sechenov First Moscow State Medical University of the Ministry of Health of the Russian Federation (Sechenov University), Moscow, Russia, [4]Rheumatology Unit, Department of Medicine, University Hospital of Padua, Padua, Italy, [5]Immunology, Rheumatology, Allergology and Rare Disease-IRCCS San Raffaele Hospital, Laboratory of Autoimmunity and vascular inflammation San Raffaele, Milan, Italy, [6]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy, [7]Department of Biotechnological and Applied Clinical Science, Rheumatology Unit, School of Medicine, University of L'Aquila, L'Aquila, Italy, [8]Department of Clinical Sciences and Community Health, University of Milan, Milan, Italy; Experimental Laboratory of Immunorheumatological Researches, Istituto Auxologico Italiano, Milan, Italy, [9]Rheumatology, Allergology and Clinical Immunology, Department of "Medicina dei Sistemi", University of Rome Tor Vergata, Rome, Italy, [10]Polymedical Center for Prevention of Recurrent Spontaneous Abortion, Rome, Italy, [11]Division of Rheumatology, Department of Clinical Sciences and Community Health, Ospedale Gaetano Pini, University of Milan, Milan, Italy, [12]Rheumatology Unit, Azienda Ospedaliera San Camillo-Forlanini, Rome, Italy, [13]Division of Rheumatology, ASST.G Pini, Department of Clinical Sciences and Community Health, University of Milan and Istituto Auxologico Italiano, Milan, Italy, [14]Rheumatology Unit, Department of Clinical and Experimental Medicine, University of Pisa, Pisa, Italy, [15]UO e Sezione di Reumatologia, Dipartimento di Scienze Mediche, Universita' degli Studi di Ferrara, Ferrara, Italy, [16]Unit of Immunology, Rheumatology, Allergy and Rare Diseases, Università Vita-Salute San Raffaele - IRCCS Ospedale San Raffaele, Milan, Italy, [17]Rheumatology and Clinical Immunology, Spedali Civili and University of Brescia, Brescia, Italy

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Plenary Session II

Session Type: Plenary Session

Session Time: 11:30AM–1:00PM

Background/Purpose: The role of complement in the aPL related pathology has been widely studied in animal models. aPL can induce fetal loss in experimental animals but mice deficient in specific complement components (C4, C3, C5) appear somehow protected. In addition, in pregnant mice injected with aPL, antibody deposition has been found at decidual level causing focal necrosis, apoptosis and neutrophil infiltrates and supporting aPL pathogenetic potential. Instead, human studies did find hypocomplementemia associated to pregnancy complications in patients with obstetric APS. These results, however, are not unanimously confirmed and some studies only show increased levels of complement activation products (i.e. Bb) and not decreased levels of C3 and C4. This can be obviously due to methodological problems, challenging also because of the physiological alteration of complement profile during pregnancy. Recently low levels of C3 and/or C4 in early pregnancy and before pregnancy were found to significantly predict pregnancy complications and loss in a large cohort of primary APS. Therefore, we have thought that it would be interesting to investigate if the simple detection of low C3 and/or C4 could be considered a risk factor for adverse pregnancy outcome in obstetric APS and aPL carriers.

Methods: We performed a multicentric study (487 pregnancies from 10 Italian Rheumatology Centers were included) and collected retrospectively data on pregnancies in women with primary APS (n=293) and aPL carriers with persis-

Table 1. Relationship between gestational outcome, maternal pregnancy complications and preconceptional complement levels

	All pregnancies		p	Triple aPL positivity		p	One or double aPL positivity		p
Gestational outcome	**Low C3/C4 (n=97)**	**Normal C3/C4 (n=134)**		**Low C3/C4 (n=32)**	**Normal C3/C4 (n=16)**		**Low C3/C4 (n=65)**	**Normal C3/C4 (n=118)**	
Term live birth (≥37w)	55 (60%)	88 (70%)	ns	16 (50%)	10 (63%)	ns	15 (23%)	20 (17%)	ns
Preterm live birth (<37w)	18 (20%)	25 (20%)	ns	7 (22%)	6 (37%)	ns	11 (17%)	19 (16%)	ns
Pregnancy losses (abortion and miscarriages)	18 (20%)	10 (8%)	0.01	9 (28%)	0 (0%)	0.04	39 (60%)	79 (67%)	ns
Maternal complications									
PE	5 (5%)	4 (3%)	ns	2 (6%)	2 (13%)	ns	4 (6%)	2 (2%)	ns
DVT	1 (1%)	0 (0%)	ns	0 (0%)	0 (0%)	ns	1 (2%)	0 (0%)	ns
thrombocytopenia	1 (1%)	0 (0%)	ns	0 (0%)	0 (0%)	ns	1 (2%)	0 (0%)	ns

Legend: PE, preeclampsia; DVT, deep vein thrombosis.

tent antibody positivity (n=194). Serum C3 and C4 levels were evaluated by nephelometry; hypocomplementemia was defined by local laboratory reference values. Statistical analysis was performed using GraphPad.

Results: Preconceptional complement levels and gestational outcome were available for 96 (49%) aPL carriers pregnancies and 135 (46%) APS pregnancies. In patients with low preconceptional C3 and/or C4, a significantly higher prevalence of pregnancy losses was observed.(p=0.01). A subgroup analysis considered patients with triple aPL positivity. In this subgroup of high risk patients preconceptional low C3 and/or C4 levels were found associated with increased rate of pregnancy loss (p=0.04). On the other hand, in women with single or double aPL positivity, adverse pregnancy outcome was not found related to preconceptional complement levels (Table 1). To note, all pregnancy losses in the subgroup of triple aPL positivity were treated with low dose aspirin and low molecular weight heparin from the pregnancy test positivity. No relationship was found between low preconceptional complement levels and maternal complications (pre-eclampsia, eclampsia, deep vein thrombosis, thrombocytopenia).

Conclusion: Our findings confirm that decreased complement levels before pregnancy are associated with increased risk of adverse outcome in women with aPL, with or without APS. Even in the group of triple aPL positivity, considered *per se* at high risk, the presence of low C3 and/or C4 seems to predict a worse prognosis. Complement levels are cheap and easy to measure, therefore, they could represent a useful aid to identify patients with aPL at increased risk of pregnancy loss.

Disclosure: C. Nalli, None; **D. Lini**, None; **L. Andreoli**, None; **F. Crisafulli**, None; **M. Fredi**, None; **M. Lazzaroni**, None; **V. Bitsadze**, None; **A. Calligaro**, None; **V. Canti**, None; **R. Caporali**, AbbVie, Inc., 5, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, 8, Gilead Sciences, Inc., 5, 8, Merck Sharp & Dohme, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8, Galapagos NV, 5, 8, Celgene, 5, 8; **F. Carubbi**, None; **C. Chighizola**, None; **P. Conigliaro**, None; **C. De Carolis**, None; **T. Del**

Ross, None; **M. Favaro**, None; **M. Gerosa**, None; **A. Iuliano**, None; **J. Khizroeva**, None; **A. Makatsariya**, None; **P. Meroni**, None; **M. Mosca**, None; **M. Padovan**, None; **R. Perricone**, None; **P. Rovere-Querini**, None; **G. Sebastiani**, None; **C. Tani**, None; **M. Tonello**, None; **D. Zucchi**, None; **F. Franceschini**, None; **A. Tincani**, None.

Abstract Number: 0939

Maintenance of Remission After Withdrawal of Etanercept or Methotrexate in Patients with Rheumatoid Arthritis in Sustained Remission on Combination Therapy: Results from a Randomized, Double-blind, Controlled Trial

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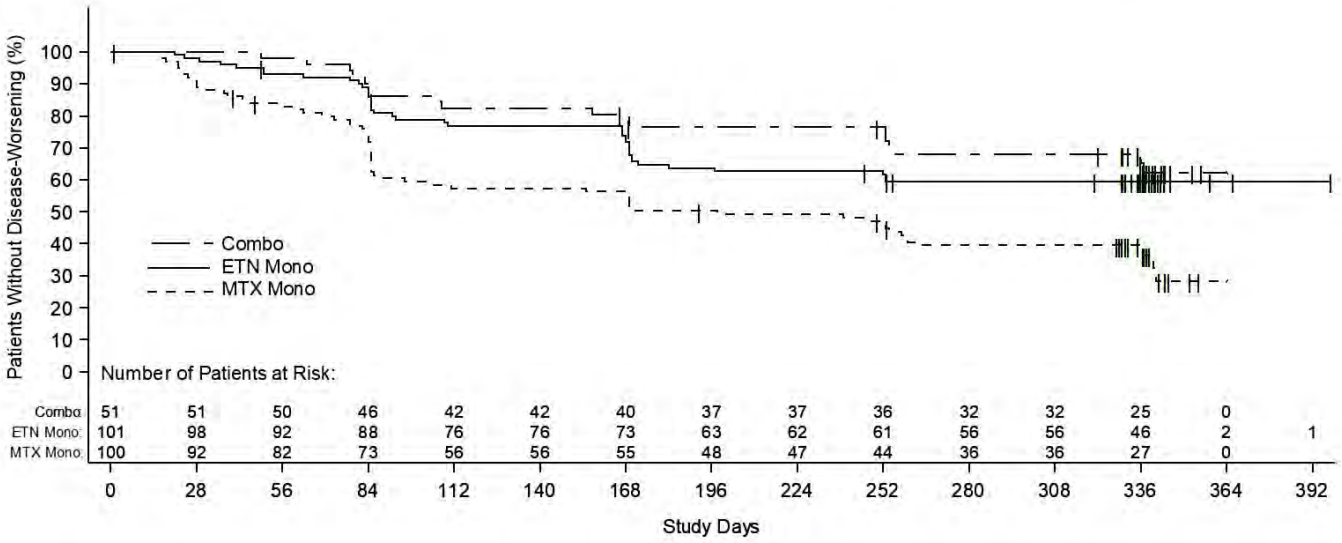
SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Plenary Session II
Session Type: Plenary Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Rheumatoid arthritis (RA) patients (pts) in remission on combination therapy (Combo) of methotrexate (MTX)+etanercept (ETN) face ongoing medication burden and long-term safety/tolerability concerns related to continuing therapies. Reducing therapy has been studied, but whether pts could discontinue either MTX or ETN and maintain remission on monotherapy (mono) has not been rigorously tested. This study compared withdrawing either MTX or ETN on remission maintenance in RA pts who had been in sustained, stringent remission while on Combo.

Methods: The Study of ETN And MTX in RA (SEAM-RA) enrolled adult RA pts on ETN 50 mg/week + MTX 10-25 mg/week who met ACR/EULAR remission criteria (Simplified Disease Activity Index [SDAI] score ≤3.3) in a 24-week, open-label period. After 24 weeks, pts remaining in remission entered a 48-week, double-blind period and were randomized to: (1) withdrawal of ETN (MTX mono); (2) withdrawal of MTX (ETN mono); or (3) continue Combo. Pts with disease-worsening (DW; defined as SDAI >11 at any time or SDAI >3.3 and ≤11 on 2 consecutive visits ≥2 weeks apart or on ≥3 separate visits) received Combo rescue therapy (Combo arm continued Combo therapy) and were considered non-responders. Endpoints included proportion of pts in SDAI remission without DW at week 48 in the ETN mono vs MTX mono arms (primary) and in the Combo vs MTX mono arms (secondary). Other secondary endpoints included time to DW and time to recapture SDAI remission in pts needing rescue therapy. For the primary endpoint, non-responder imputation was used for missing data. The P-value for the primary endpoint was estimated from the Chi-squared test. For secondary endpoints, P-values were not adjusted.

Results: Of 371 pts enrolled in the 24-week, open-label period, 253 (68.2%) remained in remission and were randomized to the double-blind period (101 MTX mono, 101 ETN mono, and 51 Combo). Baseline values were similar across treatment arms: mean (SD) age 55.6 (12.2) years, RA duration 10.3 (7.8) years, MTX dose 16.3 (4.7) mg/week, and SDAI score of 1.3 (1.2). At week 48, SDAI remission was maintained by significantly more pts on ETN mono vs MTX mono (49.5% vs 28.7%; P=0.004) and by more pts on Combo vs MTX mono (52.9% vs 28.7%; P=0.006). Time to DW was shorter with MTX mono compared with ETN mono or Combo (P< 0.001 for both comparisons; Fig. 1). In

Figure 1. Kaplan-Meier Curves of Time to Disease-Worsening (Primary Analysis Set)



	MTX Mono (N = 101)	ETN Mono (N = 101)	Combo (N = 51)
Days to Disease-Worsening, Median (95% CI)	198 (96, 263)	NE (253, NE) P<0.001*	NE (336, NE) P<0.001*

*P-values are nominal and compare the ETN-containing arms with the MTX mono arm using a log-rank test. One patient in the MTX arm discontinued at study day 0, and was thus no longer at risk and was censored.
CI, confidence interval; Combo, combination; ETN, etanercept; mono, monotherapy; MTX, methotrexate; NE, not estimable.

Figure 1. Kaplan-Meier Curves of Time to Disease-Worsening (Primary Analysis Set)

pts with DW treated with Combo rescue therapy, the cumulative percentage who recaptured SDAI remission by end of study was 71%, 75%, and 80% in the MTX mono, ETN mono, and Combo arms, respectively. Time to recapture SDAI remission after initiating rescue therapy was similar in all 3 treatment arms. No new safety signals were reported.

Conclusion: In pts in remission on Combo who then withdrew either MTX or ETN, this study showed that ETN mono was superior to MTX mono in maintaining remission. Similar proportions of pts maintained remission with ETN mono as with Combo. The majority of pts who received rescue therapy recaptured remission. For pts and physicians seeking to reduce treatment burden, these data inform decision-making on therapy withdrawal in well-controlled RA pts.

Disclosure: J. Curtis, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **P. Emery**, AbbVie, 2, 8, Bristol-Myers Squibb Company, 2, 8, Pfizer, 8, Roche, 2, 8, Celltrion, 8, Eli Lilly, 8, Gilead, 8, Novartis, 2, 8, Samsung, 8; **E. Karis**, Amgen, Inc., 1, 2; **B. Haraoui**, Pfizer Canada, 5, 8, UCB Canada, 5, 8, AbbVie Canada, 5, 8, Amgen Canada, 5, Bristol-Myers-Squibb Canada, 5, Eli Lilly Canada, 5, Merck, 5, Roche Canada, 5, Sanofi-Genzyme Canada, 5, Sandoz Canada, 5, Janssen Canada, 8, Celgene Canada, 8; **V. Bykerk**, Amgen, 1, BMS, 1, Gilead, 1, Sanofi-Genzyme/Regeneron, 1, Scipher, 1, Pfizer, 1, UCB, 1, NIH, 1; **P. Yen**, Amgen Inc., 1, 2; **G. Kricorian**, Amgen Inc., 1, 2; **J. Chung**, Amgen Inc., 1, 2.

Abstract Number: 0940

In Patients with Inflammatory Arthritides Central Pain Sensitization Is Strictly Associated with Functional Disability

Giovanni Adami[1], Angelo Fassio[1], Elisabetta Gerratana[2], Alessandro Giollo[1], Camilla Benini[1], Luca Idolazzi[1], Elisabetta Vantaggiato[1], Davide Gatti[1] and Maurizio Rossini[1], [1]Rheumatology Unit, University of Verona, Verona, Italy, [2]Rheumatology Unit, University of Messina, Messina, Italy

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Fibromyalgia & Other Clinical Pain Syndromes
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Long-term nociceptive pain, as in inflammatory arthritides, can cause Central Sensitization (CS) to pain. CS Inventory (CSI) is a validated screening instrument for clinicians to help identifying patients with CS. We sought to investigate the association between CSI score and clinical, demographic and ultrasonographic parameters of patients with rheumatoid arthritis (RA) or psoriatic arthritis (PsA)

Methods: We conducted a cross-sectional analysis on patients with an established diagnosis of RA or polyarticular PsA. Disease activity was measured with SDAI and DAS28-CRP in RA patients and with DAPSA in PsA patients. The presence and severity of synovitis was also measured with the overall ultrasound (US) 7-joints score and its components (gray-scale ultrasound [GSUS], power-Doppler ultrasound [PDUS] and erosions). CSI questionnaire was analyzed either as a continuous variable or as positiveegative (threshold 40 points) or divided in four categories, i.e., subclinical (≤29), mild (30-39), moderate (40-49), severe/extreme (≥50). Exclusion criteria included: diagnosis of PsA with enthesitis predominant and/or spondylitis subtypes.

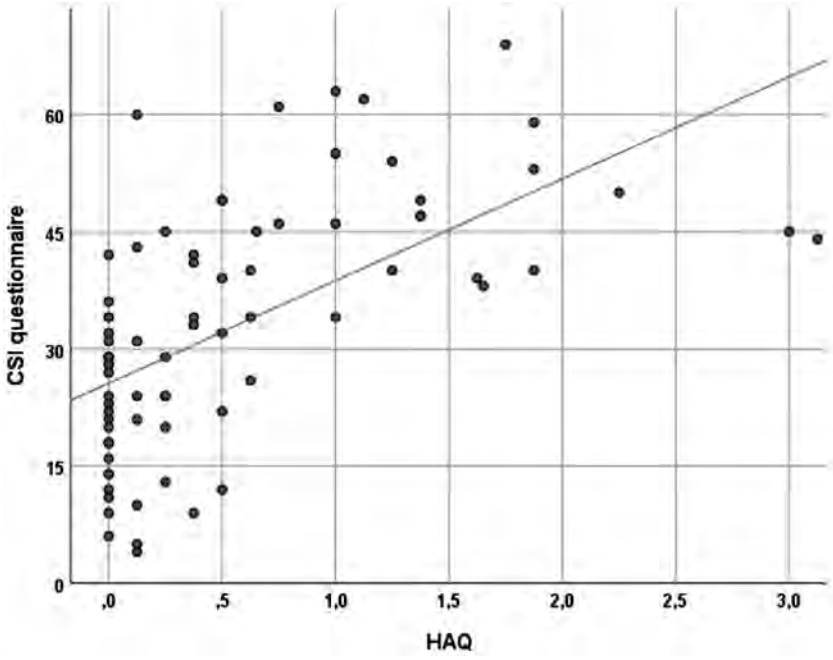


Figure 1. Relationship between HAQ and CSI questionnaire score in patients with inflammatory arthritides. R2 0.361, p <0.0001

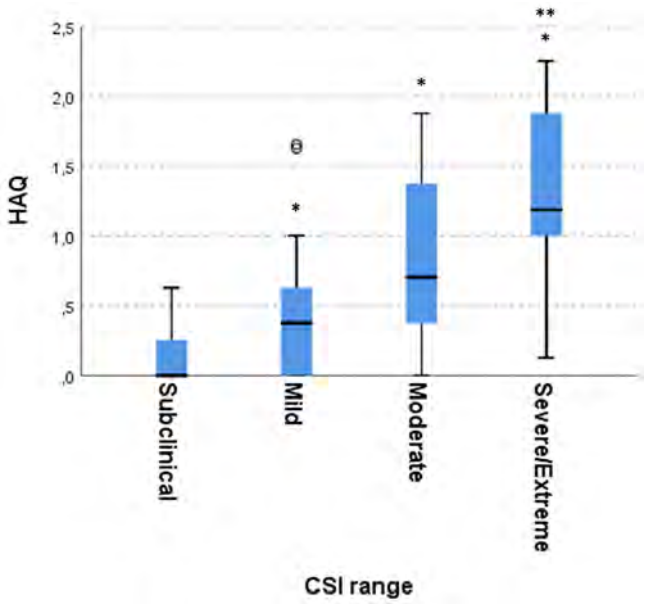


Figure 2. Median HAQ at different CSI questionnaire score ranges

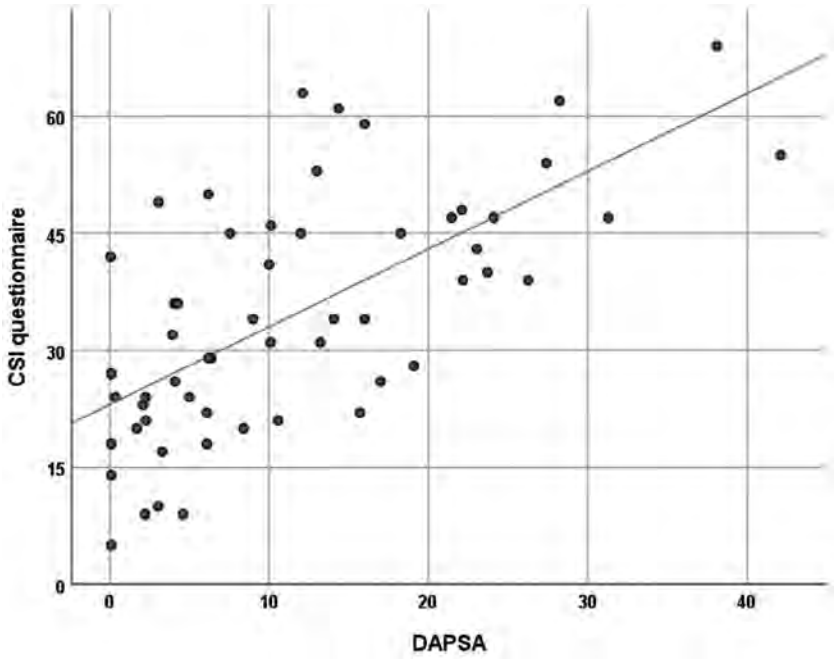


Figure 3. Relationship between DAPSA and CSI questionnaire score in patients with psoriatic arthritis. R2 0.436, p <0.0001

Results: A multiple linear regression analysis was performed to predict CSI score based on clinical and demographic characteristics (age, sex, BMI, disease duration, tender and swollen joints, CRP, 7-joints US score and fibromyalgia diagnosis), including HAQ. HAQ was the only significant predictor of the CSI score (Figure 1 and 2). CSI score increased of 15.3 points for each point of HAQ (95% CI 7.4-23.3, $p < 0.0001$). In PsA patients, but not in RA patients, disease activity was strongly correlated with CSI score (Figure 3).

Overall, we did not find any correlation between 7-joints US score and CSI score. We found a significant association between 7-joints US score (and its components) and disease duration (year to diagnosis r 0.53, $p < 0.0001$), interestingly, only the erosion score correlated significantly with the time from symptoms onset to the diagnosis (0.28, $p < 0.01$). In subgroups analyses, in patients with RA, 7-joints US overall score was positively associated with disease duration (years to onset of symptoms r 0.77, $p < 0.0001$). We found a strong relationship between 7-joints overall, PDUS scores and disease activity scores of RA (r 0.50 p 0.006 for SDAI and PDUS). In PsA patients, we found no association between 7-joints US overall, GSUS, PDUS or erosion score and DAPSA.

Conclusion: In summary, central sensitization assessed with CSI questionnaire was significantly associated with functional disability measured with HAQ independently from age, sex, BMI, concomitant fibromyalgia diagnosis and other clinical parameters (CRP, time to disease onset, tender and swollen joint count). SDAI and DAS28-CRP were significantly associated with ultrasonographic parameters of synovial inflammation.

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Abstract Number: 0941

MDHAQ/RAPID3 (multidimensional Health Assessment Questionnaire/ routine Assessment of Patient Index Data) Levels Are Elevated in Rheumatology Patients Who Meet 2011 Fibromyalgia (FM) or MDHAQ/FAST3 (fibromyalgia Assessment Screening Tool) Criteria

Juan Schmukler[1], Tengfei Li[2], Kyle Schroeder[3] and Theodore Pincus[3], [1]Mount Sinai Hospital Chicago, IL, Chicag, IL, [2]Georgetown University, Washigton, [3]Rush University Medical Center, Chicago, IL

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Fibromyalgia & Other Clinical Pain Syndromes
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: RAPID3 (routine assessment of patient index data) on an MDHAQ (multiple multidimensional health assessment questionnaire) was developed initially to assess patients with rheumatoid arthritis (RA) according to agreement with the DAS28 (disease activity score 28).[1] Routine completion of self-report MDHAQ/RAPID3 by patients with all diagnoses prior to seeing the physician was found to be the most effective strategy for MDHAQ completion by all RA patients in routine care.[2] This led to recognition that RAPID3 was clinically informative to describe clinical status and change in patients with all rheumatic diagnoses,[3] such as evidence of a similar disease burden in osteoarthritis (OA) and RA patients.[4] Another index of MDHAQ scores, FAST3 (fibromyalgia assessment screening tool 3) has been developed to screen for fibromyalgia (FM) on the same MDHAQ that includes RAPID3, with agreement of about 80% with formal 2011 revised FM criteria.[5] We examined RAPID3 levels in patients seen in routine care at one academic site, including all patients and those with OA, RA, systemic lupus erythematosus (SLE), and other diagnoses, in subsets of patients who were FM positive or negative

Methods: All patients with all diagnoses seen at one academic rheumatology site complete an MDHAQ at all visits. The MDHAQ includes 0-10 scores for physical function (FN), pain (PN), patient global assessment (PATGL), fatigue (FT), 0-54 self-report rheumatoid arthritis disease activity index (RADAI) painful joint count, and 0-60 symptom checklist (SX). MDHAQ/RAPID3 (0-30) =FN+PN+PATGL; RAPID3 severity categories include high >12, moderate=6.1-12,

RAPID3 scores according to primary diagnosis by physicians and by FM 2011 and FAST3-P criteria

Primary diagnosis according to physician	Total N (%)	N (%) Diagnosed by physician as having FM	Median RAPID3 (IR) in all patients with this primary diagnosis	Analyses according to FM 2011 fibromyalgia Criteria			Analyses according to FAST3-P fibromyalgia criteria		
				# (%) Positive by these criteria	Median (IR) RAPID3 in FM positive patients	Median (IR) RAPID3 in FM negative patients	# (%) Positive by these criteria	Median (IR) RAPID3 in FM positive patients	Median (IR) RAPID3 in FM negative patients
Total	569 (100%)	121 (21.3%)	12.5 (5.8, 17.7)	146 (25.7%)	19.0 (15.8, 22.5)	9.3 (4.3, 15.3)	188 (33.0%)	19.1 (16.3, 22.5)	8.0 (3.7, 13.2)
Fibromyalgia	49 (8.6%)	49 (100%)	18.5 (15.2, 22.2)	36 (73.5%)	20.0 (16,8, 22.6)	14.8 (9.7, 16.8)	40 (81.6%)	20.0 (16.3, 22.8)	11.3 (8.8, 16.7)
OA	85 (14.9%)	15 (17.7%)	15.2 (10.7, 19.8)	26 (30.6%)	19.8 (16.8, 21.8)	12.5 (8.3, 17.5)	32 (37.6%)	19.8 (15.9, 21.5)	12.1 (7.3, 16.8)
RA	78 (13.7%)	11 (14.1%)	13.3 (5.3, 17.7)	11 (14.1%)	22.3 (14.7, 23.2)	10.1 (4.3, 17.2)	23 (29.5%)	20.0 (17.3, 23.7)	6.8 (3.0, 14.7)
SLE	100 (17.6%)	12 (12.0%)	11.4 (3.8, 16.5)	21 (21.0%)	19.5 (15.5, 21.9)	7.5 (2.3, 13.8)	24 (24.0%)	19.0 (16.2, 21.3)	7.0 (2.3, 13.0)
Other	257 (45.2%)	34 (13.2%)	10.0 (5.0, 16.7)	52 (20.2%)	18.1 (15.2, 22.0)	8.0 (4.0, 13.3)	69 (26.8%)	18.5 (16.5, 22.2)	7.7 (3.5, 11.8)
P value		<0.0001*	<0.0001#	<0.0001*	0.560#	0.0001#	<0.0001*	0.445#	0.0001#

Differences between FM positive and FM negative patients were p<0.001 for 2011 and FAST3-P criteria for all diagnoses

* P-values calculated from Chi-squared test for the comparisons of percentages between different primary diagnoses.

P-values calculated from Kruskal-Wallis test for the comparisons of distributions between different primary diagnoses.

low=3.1-6 and remission≤3. MDHAQ/FAST3-P is a 0-3 cumulative index to screen for FM: 1 point each for PN≥6, RADAI≥16, and SX≥16 (2/3=FM). The 2011 FM criteria are based on 2 questionnaires, somatic symptom scale and widespread pain index, compiled into a polysymptomatic distress scale. RAPID3 scores were classified by severity categories in all patients and in subsets with OA, RA, SLE or other diagnoses, according to positive or negative 2011 FM criteria or MDHAQ FAST3-P FM criteria. Statistical analyses: Chi-square test for comparisons of percentages and Kruskal-Wallis test for RAPID3 distributions between diagnoses

Results: Median RAPID3 was 12.5 (high severity) in all patients, but only 9.3 (moderate severity) in 423 patients (74.3%) who did not meet 2011 FM criteria and 8.7 (moderate severity) in 406 patients (71.4%) who did not meet FAST3-P FM criteria (Table). By contrast, median RAPID3 was 19.0 (high severity) in 146 patients (25.7%) who met 2011 FM criteria and 19.8 in 163 patients (28.9%) who met FAST3-P FM criteria (Table). Similar patterns were seen in patients with OA, RA or SLE or other diagnoses (Table)

Conclusion: Patients who have comorbid FM have substantially elevated scores for RAPID3. Results of treatment in rheumatology clinical trials and clinical care may be underestimated by inclusion of patients with FM; routine FAST3-P screening for FM might be desirable.

References

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2. Clin Exp Rheumatol. 2007;25(6 Suppl 47):69-81
3.Rheum Dis Clin North Am. 2009;35(4):829-42, x-xi
4.RMD Open. 2017;3:e000391
5.ACR Open Rheumatol. 2019;1(8):516-25Table 1. RAPID3 scores according to primary diagnosis by physicians and by FM 2011 and FAST3-P criteria

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Disclosure: J. Schmukler, None; **T. Li**, None; **K. Schroeder**, None; **T. Pincus**, Medical History Services LLC, 9.

Abstract Number: 0942

Use of Medical Cannabis by Patients with Fibromyalgia: A Prospective Cross-sectional Study

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Fibromyalgia & Other Clinical Pain Syndromes
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Treatment strategies for chronic widespread pain (CWP)/fibromyalgia (FM) are imperfect with only a modest effect from medications. Due to the many symptoms experienced by patient, including pain, sleep disturbance and often mental health complaints, an agent that could address multiple symptoms would be ideal. Cannabinoids may have potential to fill this gap. In the setting of recreational legalization of cannabis in Canada, patients now have easier access and may be self-medicating with cannabis. We have examined the prevalence and characteristics of use in FM patients.

Methods: During a two-month period (April-May 2019), consecutive patients attending an academic, community-based rheumatology clinic staffed by 3 rheumatologists participated in an onsite survey comprising 2 questionnaires: 1) demographic and disease information completed by the rheumatologist, 2) patient anonymous questionnaire of health status, cannabis use (recreational and/or medicinal) and characteristics of use.

Results: In a cohort of 1000 rheumatology attendees (73% females; mean age 64 ± 14 yrs), 117 (11.7%) were diagnosed with FM. Medical cannabis (MC) had ever been used by 12.6% (95% CI: 10.7%-14.8%) of the whole cohort, with half continuing use for mostly pain relief. Of the 117 FM patients, 28 (24%) had ever used medical cannabis (95% CI: 16.5%-32.7%), with 16 (57%) continuing use. Users vs. non users were more likely to be younger, 53 vs.58 yrs (p=0.072) and unemployed or disabled 39% vs. 17% (p=0.019), and used more medication types for symptom control (p=0.013), but symptom severity parameters did not differ between groups Table 1. Users were more likely to be past and current cigarette smokers, and previous or current recreational cannabis users. Some comorbid rheumatic condition was present in 82 (70.1%), with 35 (30%) diagnosed with an inflammatory condition. Almost half of patients with FM comorbid with ankylosing spondylitis had used medical cannabis. Symptom relief (VAS, 1-10) was 7.0 ±2.3.

Table 1. Demographic and Disease Related Information for FM Patients

		All patients (n=117)	Never medical cannabis users (n=89)	Ever medical cannabis users (n=28)	p-value
	Age, years, mean (SD)	57.1 (12.2)	58.2 (11.7)	53.4 (13.5)	*0.072*
	Female gender, n (%)	107 (91.5)	79 (88.8%)	28 (100.0%)	0.115
	Employment				
	Full-time, n (%)	39 (33.3%)	30 (33.7%)	9 (32.1%)	
Demo-graphics	*Part-time, n (%)*	9 (7.7%)	6 (6.7%)	3 (10.7%)	
	Unemployed, n (%)	2 (1.7%)	1 (1.1%)	1 (3.6%)	0.109
	Disabled, n (%)	24 (20.5%)	14 (15.7%)	10 (35.7%)	
	Student, n (%)	1 (0.9%)	1 (1.1%)	0 (0.0%)	
	Retired, n (%)	42 (35.9%)	37 (41.6%)	5 (17.9%)	
	Employment: unemployed/disabled, n (%)	26 (22.2%)	15 (16.9%)	11 (39.3%)	**0.019**
	Inflammatory arthritis[1¶], n (%)	35 (29.9%)	25 (28.1%)	10 (35.7%)	0.482
	Rheumatoid arthritis	12 (10.3%)	10 (11.2%)	2 (7.1%)	0.728
	Psoriatic arthritis	6 (5.1%)	5 (5.6%)	1 (3.6%)	>0.999
	Ankylosing Spondylitis	13 (11.1%)	7 (7.9%)	6 (21.4%)	*0.078*
	PMR	3 (2.6%)	2 (2.2%)	1 (3.6%)	0.563
Rheumatic diseases	*SLE*	1 (0.9%)	1 (1.1%)	0 (0.0%)	>0.999
	Other	1 (0.9%)	0 (0.0%)	1 (3.6%)	0.239
	Osteoarthritis§, n (%)	50 (42.7%)	44 (49.4%)	6 (21.4%)	**0.009**
	Small joints, n (%)	23 (19.7%)	23 (25.8%)	0 (0.0%)	**0.002**
	Large joints, n (%)	22 (18.8%)	19 (21.3%)	3 (10.7%)	0.274
	Spine, n (%)	30 (25.6%)	26 (29.2%)	4 (14.3%)	0.141
	Tendonitis / Bursitis, n (%)	11 (9.4%)	9 (10.1%)	2 (7.1%)	>0.999

Table 1. Demographic and Disease Related information for fibromyalgia patients (part 1)

Conclusion: FM patients, including those with comorbid rheumatic conditions, have commonly used medical cannabis, with more than half continuing use. Although symptom severity parameters were similar for users vs. nonusers, symptom relief was reported to be moderately good. Cigarette smoking and recreational cannabis use may play a facilitatory role in medical cannabis use in FM. Adjunctive medical cannabis may be a treatment consideration for patients with CWP, either as a unique diagnosis of FM or comorbid with inflammatory arthritis.

	Other rheumatic condition, n (%)	10 (8.5%)	5 (5.6%)	5 (17.9%)	*0.058*
Comorbid conditions	Cardiovascular, n (%)	30 (25.6%)	22 (24.7%)	8 (28.6%)	0.804
	Pulmonary, n (%)	4 (3.4%)	4 (4.5%)	0 (0.0%)	0.571
	Gastrointestinal, n (%)	31 (26.5%)	24 (27.0%)	7 (25.0%)	>0.999
	Neurological, n (%)	8 (6.8%)	7 (7.9%)	1 (3.6%)	0.678
	Endocrine, n (%)	44 (37.6%)	37 (41.6%)	7 (25.0%)	0.125
	Mood disorder, n (%)	33 (28.2%)	27 (30.3%)	6 (21.4%)	0.472
	Other psychiatric disorder, n (%)	5 (4.3%)	2 (2.2%)	3 (10.7%)	*0.088*
	Other comorbid condition, n (%)	3 (2.6%)	3 (3.4%)	0 (0.0%)	>0.999
Medications for rheumatic diseases	Number of medication types for rheumatic disease, mean (SD)	1.7 (1.3)	1.6 (1.1)	2.3 (1.6)	**0.013**
	Non-steroidal anti-inflammatory drug use, n (%)	40 (34.2%)	29 (32.6%)	11 (39.3%)	0.648
	Disease-modifying anti-rheumatic drug use, n (%)	15 (12.8%)	13 (14.6%)	2 (7.1%)	0.517
	Biologic use, n (%)	14 (12.0%)	7 (7.9%)	7 (25.0%)	**0.039**
	Opioids use, n (%)	19 (16.2%)	14 (15.7%)	5 (17.9%)	0.774
	Tranquilizer use, n (%)	12 (10.3%)	8 (9.0%)	4 (14.3%)	0.478
	Antiepileptic use, n (%)	34 (29.1%)	25 (28.1%)	9 (32.1%)	0.812
	Antidepressant use, n (%)	41 (35.0%)	32 (36.0%)	9 (32.1%)	0.822
	Steroid use, n (%)	4 (3.4%)	3 (3.4%)	1 (3.6%)	>0.999
	Cannabis pharmaceutical	5 (4.3%)	1 (1.1%)	4 (14.3%)	**0.011**
	Cannabis herbal	9 (7.7%)	0 (0.0%)	9 (32.1%)	NA
Disease assessment	Physician Global Assessment (PGA) (0-10), mean (SD)	3.5 (1.9)	3.4 (1.9)	3.7 (1.9)	0.402
	Patient Global Assessment (PtGA) (0-10), mean (SD)	5.5 (2.5)	5.5 (2.6)	5.5 (2.2)	0.945
	Pain, VAS cm, mean (SD)	6.5 (2.2)	6.5 (2.2)	6.6(2.2)	0.806
Cigarette use	Non-smoker n (%)	76 (65.0%)	64 (71.9%)	12 (42.9%)	**0.002**
	Past smoker n (%)	16 (13.7%)	7 (7.9%)	9 (32.1%)	
	Current smoker n (%)	25 (21.4%)	18 (20.2%)	7 (25.0%)	

Table 1. Demographic and Disease Related information for fibromyalgia patients (part 2)

Cannabis use	Recreational	Ever use, n (%)	44 (37.6%)	28 (31.5%)	16 (57.1%)	**0.024**
		Current use, n (%)	7 (6.0%)	2 (2.3%)	5 (17.9%)	**0.009**
	Medical	Ever used >10 times, n (%)	22 (19.5%)	NA	22 (78.6%)	NA
		Current medical use, n (%)	16 (13.7%)	NA	16 (57.1%)	NA
		If never used, consider medical use, n (%)	NA	45 (50.6%)	NA	NA
	Current cannabis use (any reason)§§	Current use, n (%)	19 (16.2%)	2 (2.2%)	17 (60.7%)	**<0.001**
		Method of herbal cannabis use++				
		Smoke, n (%)	9 (47.4%)§§	1 (50.0%)*	8 (47.1%)**	>0.999
		Vaporize, n (%)	8 (42.1%)§§	1 (50.0%)*	7 (41.2%)**	>0.999
		Oil/capsules, n (%)	7 (36.8%)§§	0 (0.0%)*	7 (41.2%)**	0.509
		Edible, n (%)	4 (21.1%)§§	0 (0.0%)*	4 (23.5%)**	>0.999
		Rub, n (%)	0 (0.0%)§§	0 (0.0%)*	0 (0.0%)**	N/A
	Current herbal cannabis use (medical reasons)	Relief of symptoms, mean (0–10) (SD)¥	7.0 (2.3)	NA	7.0 (2.3)	NA

NA, not applicable.

Significant ($p<0.05$) p-values indicated in bold. Missing category is not included in the comparison.

+ Patients may have had more than one type of inflammatory arthritis.

§ Patients may have had more than one type of osteoarthritis.

++ Patients may have used more than one method of herbal cannabis.

§§ Proportions are based on the number of patients currently using herbal cannabis for any reason (All patients: n=19; Current recreational herbal cannabis users: n=2; Current medical herbal cannabis users: n=17).

* Proportions are based on the number of patients in the *'Never medical cannabis users'* group currently using herbal cannabis for recreational purposes (n=2).

** Proportions are based on the number of patients in the *'Ever medical cannabis users'* group currently using herbal cannabis for any reason (All patients n=17).

¥ Among patients using herbal cannabis for medical reasons. Minimum (0) represents 'no relief' and maximum (10) represents 'maximum relief'.

Table 1. Demographic and Disease Related information for fibromyalgia patients (part 3)

Disclosure: M. Fitzcharles, None; **E. Rampakakis**, None; **Y. Shir**, None; **J. Sampalis**, None; **M. Cohen**, None; **M. Starr**, None; **W. Häuser**, None.

Abstract Number: 0943

Reliability and Validity Issues in Fibromyalgia Diagnosis

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Fibromyalgia & Other Clinical Pain Syndromes

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: Fibromyalgia (FM) is a widely recognized and commonly diagnosed disorder that has also been the subject of thousands of research studies. There is no gold standard definition of FM, but well-vetted diagnostic criteria exist. The extent to which these criteria are used for diagnosis by community physicians is uncertain. In 3 large epidemiologic studies, we compared physician diagnosis with diagnosis by published criteria to determine the

Diagnostic category	N	Prevalence	Sens	Specificity	Kappa	Phi	PSD
		(%)	(%)	(%)			Mean (SD)
	Criteria comparisons in research clinical studies						
FM 2016 criteria vs.	4,348	21.4 (20.2, 22,7)		—	—		20.9 (5.5)
London 6 criteria	4,348	26.3 (25.0,27.6)	91.4	91.5	.765	.772	18.9 (6.4)
AAPT criteria	4,348	30.1 (28.7,31.5)	95.6	87.7	.726	.745	16.4 (6.2)
London 4 criteria	4,348	39.1 (37.7,40.6)	98.9	77.2	.586	.640	16.5 (7.0)
	Physician diagnosis in community epidemiologic studies						
FM 2016 criteria vs.	3,276	5.5 (4.8,6.3)					18.4 (4.4)
Primary care practice MDs	3,276	6.1 (5.2,6.9)	35.4	95.6	.296	.297	12.4 (6.9)
FM 2016 criteria vs.	2,531	3.4 (2.7,4.3)					17.7 (3.9)
German population MD Dx	2,531	1.1 (0.6,1.5)	17.3	99.3	.235	.261	11.3 (7.4)
FM 2011 criteria vs.	8,486	2.7 (2.7,2.8)					16.1 (2.9)
US Population MD Dx	8,486	1.8 (1.4, 2.1)	25.7	98.5	.248	.248	9.58 (5.8)

FM 2016 = 2016 revised FM diagnostic criteria; AAPT = AAPT FM diagnostic criteria; London 4 = London 4 quadrant pain FM criteria; London 6 = London 4 + Fatigue score moderate of greater.

Table 1. Characteristics and agreement according to FM diagnostic methods.

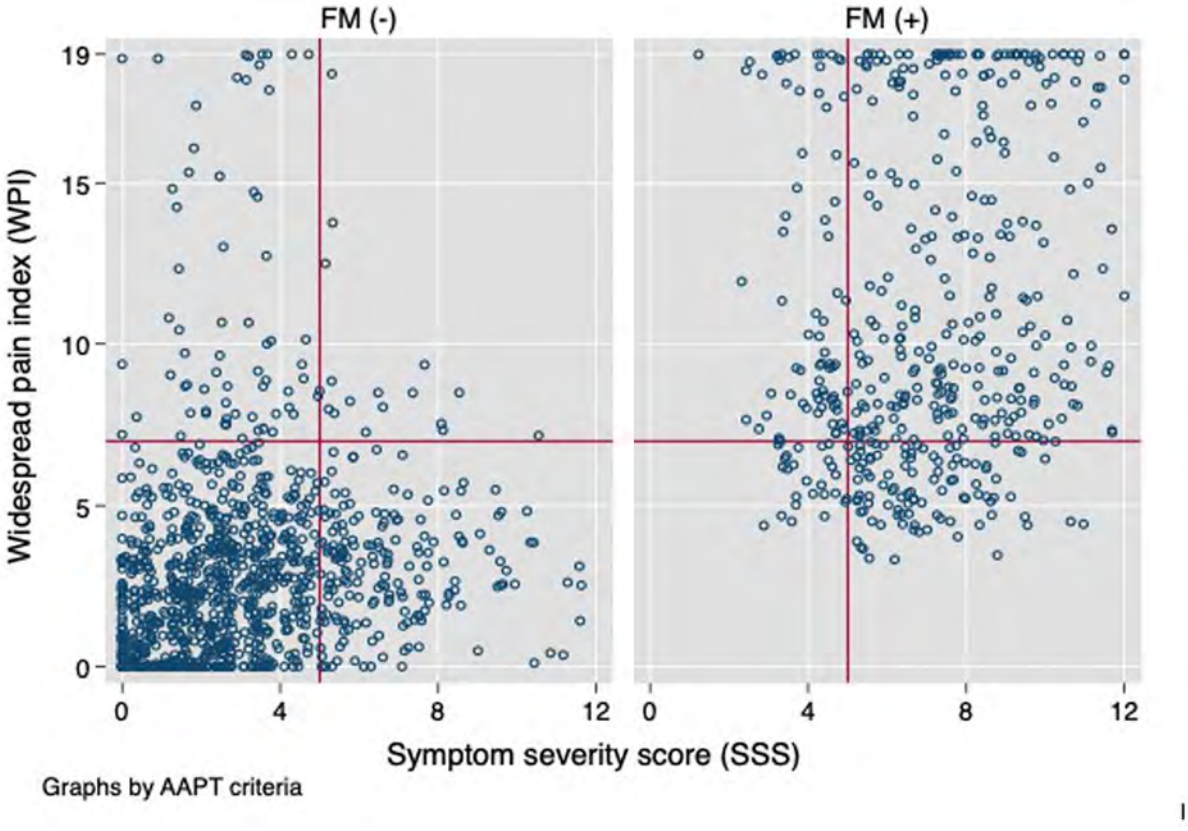

Figure 1. Plot of symptom severity score (SSS) against widespread pain index (WPI) according to AAPT criteria status. Horizontal line at 7 is level of WPI required by FM 2016 criteria. A small amount of random noise is added to each observation so that observations are seen more clearly. Vertical line at 5 is level required by FM 2016 criteria.

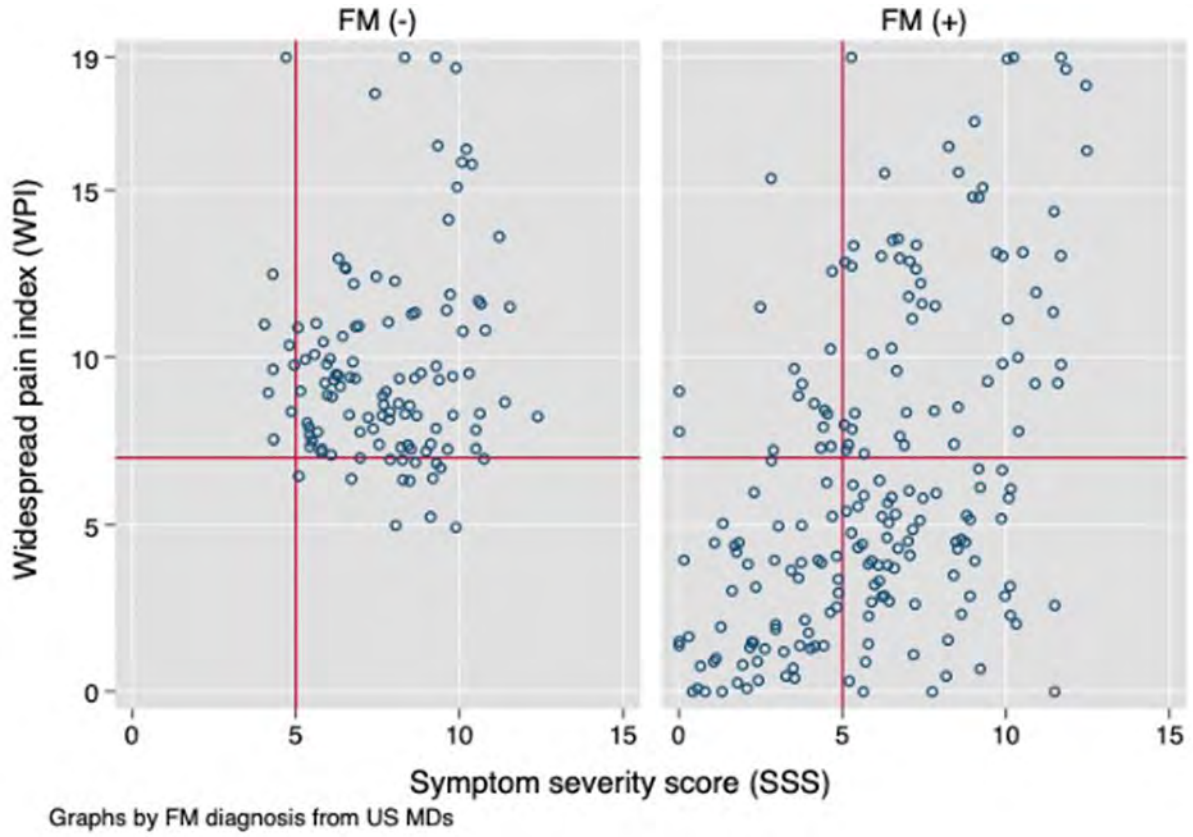

Figure 2. Plot of symptom severity score (SSS) against widespread pain index (WPI) according to reported US primary care physician diagnosis. Horizontal line at 7 is level of WPI required by FM 2016 criteria. Vertical line at 5 is level required by FM 2016 criteria. A small amount of random noise is added to each observation so that observations are seen more clearly. Data include only patients who are FM positive by FM2016 or ad hoc US primary care physician criteria.

level of agreement between criteria and physician diagnosis. We also compared different research criteria in clinical settings to obtain estimates of agreement among competing FM criteria

Methods: We compared 4 sets of published FM diagnostic criteria: The 2016 modification of ACR 2010 criteria (FM 2016), ACTTION-APS Pain Taxonomy criteria (AAPT), London widespread pain criteria (LFESSQ 4), and London widespread pain plus fatigue abnormality (LFESSQ 6) in 4,348 patients using Forward, the National Data Bank for Rheumatic Diseases (NDB) as to agreement with FM 2016. We then compared reported physician (MD) diagnosis of FM with FM 2016 criteria in 3,276 consecutive primary care patients (PC), 2531 persons in a German general population survey (GPS), and 8486 in the US National Health Interview Survey (NHIS). We used Cohen's kappa and the Phi coefficient as measures of agreement, and the polysymptomatic distress (PSD) scale as a measure of FM symptom severity.

Results: As shown in Table 1, FM 2016, LFESSQ 6 and AAPT criteria tapped into similar concepts, yielding kappa and phi coefficients of .726-.752, prevalence values between 21.4-30.1%, and PSD scores between 16.4-20.9. Figure 1 shows increased cases meeting AAPT criteria compared with FM 2016. None of the physician criteria adequately agreed with FM 2016 criteria (all kappa and phi statistics < .300). As shown in Figure 2, many patients who were MD diagnosis positive clearly failed FM 2016 criteria, and many MD classification negative subjects satisfied FM 2016 criteria. The lower the kappa and phi values the less severe were values of PSD (9.6-12.4) among MD diagnosed patients.

Conclusion: Diagnosis by formal criteria had conceptually adequate agreement overall, but at the patient level 34% of positive diagnoses disagreed between FM 2016 and AAPT. Physician diagnosis and formal criteria are in poor agreement. As shown in Figure 2, this is not merely failure to diagnose, but represents incorrect classification. There is not "one" FM. Diagnoses based on physician diagnoses (not formal criteria), such as in hospital and insurance company registries have limited validity and reliability, and kappa and phi values so low as to render diagnosis almost meaningless. FM is a symptom severity-based diagnosis, but until FM care and research rely primarily on reliable continuous severity scales, FM will remain an uncertain diagnosis. Some of the disagreement between MD diagnosis and FM criteria may represent changes in severity over time that are not captured in our data, but also raise the question of the nature of the FM diagnosis.

Disclosure: F. Wolfe, None; **J. Rasker**, None; **B. Walitt**, None.

Abstract Number: 0944

Obstructive Sleep Apnea in Fibromyalgia Patients: A Meta-analysis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Fibromyalgia & Other Clinical Pain Syndromes
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Fibromyalgia is a chronic pain disorder prevalent in about 3% of the population, mostly in females. A common complaint is non-restorative sleep. Obstructive sleep apnea (OSA), the most common sleep related breathing disorder, has an estimated prevalence of 10-15% in females. It is characterized by upper airway collapse during sleep leading to apnea and hypopnea with poor fragmented sleep. Several studies have reported a positive correlation between chronic pain syndromes and sleep disorders. The link between OSA and pain syndromes is still unknown. It has been hypothesized that hyperalgesia occurs because of fragmented sleep and hypoxemia that enhance sensitivity to pain, promote inflammation, and increase spontaneous pain. Our study aimed to determine the incidence and prevalence of OSA in FM patients.

Methods: We comprehensively searched the databases of MEDLINE, EMBASE, and Cochrane from inception to May 2020. Included studies were published observational studies (cohort or case-control) that investigated the incidence of OSA comparing patients with and without FM. We also included studies that reported the prevalence of OSA in FM. Data from each study were combined using the random-effects, generic inverse variance method of DerSimonian and Laird to calculate odd ratio and 95% confidence intervals.

Results: Fifteen studies from 1989 to 2020 were included in this meta-analysis involved ten studies reported prevalence and five case-control studies reported the incidence of OSA in FM patients. Pooled prevalence of OSA was 38.5 per 100 FM patients [95% confidence interval (CI): 24.4-52.6]. Incidence of OSA was significantly higher in patients with FM compared to without FM (pooled odd ratio = 3.51, 95% CI: 1.36-9.05, p = 0.008, I^2=71.3%) (Figure1). There was no publication bias observed in Funnel plot as well as no small-study effect observed in Egger's test (p-value = 0.921)

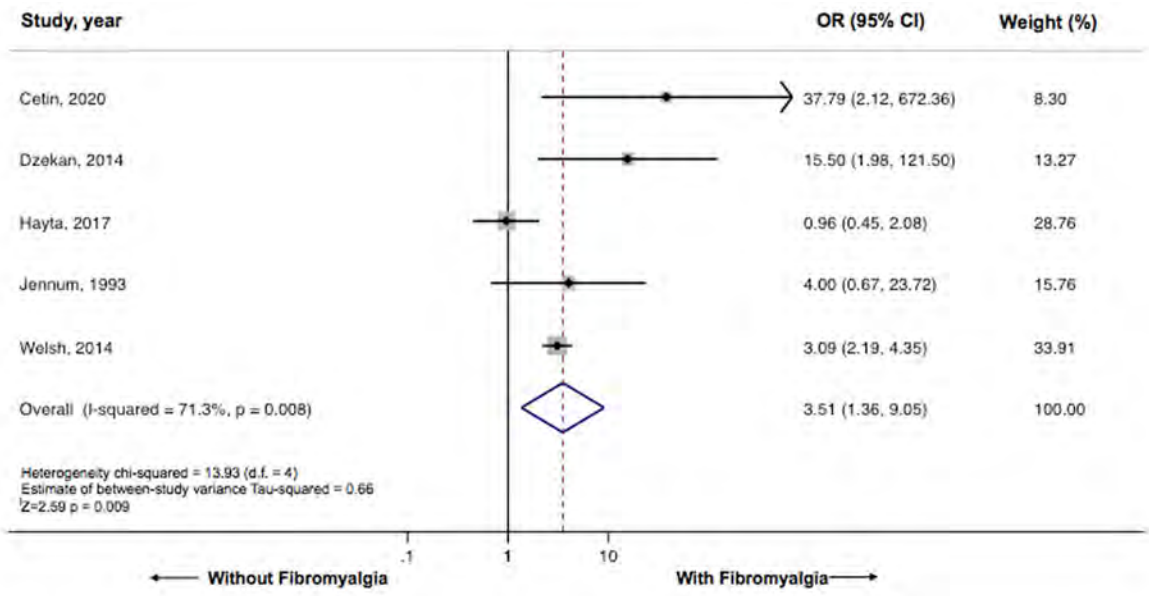

Figure 1. Forest plot demonstrating the association between Fibromyalgia and the Incidence of Obstructive Sleep Apnea

Conclusion: Our study demonstrated that there was a higher incidence and prevalence of OSA among FM patients. Polysomnography should be a standard diagnostic tool in the assessment of FM to unmask underlying treaTable conditions that may contribute to the symptoms. As yet, there is no evidence that the treatment of OSA would lead to amelioration of chronic pain in FM. Further studies are needed to examine whether the treatment of the commonly detected OSA will have a beneficial effect on fibromyalgia symptoms.

Disclosure: N. Eshak, None; **W. Vutthikraivit**, None; **A. Beltagy**, None; **J. Pixley**, None.

Abstract Number: 0945

Neutrophils Mediate Kidney Inflammation Following Acute Skin Exposure to UV Light

Sladjana Skopelja-Gardner[1], Joyce Tai[2], Xizhang Sun[2], Lena Tanaka[2], James Kuchenbecker[2], Tomas Mustelin[1] and Keith Elkon[2], [1]University of Washington, Seattle, WA, [2]University of Washington, Seattle

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Innate Immunity
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Sensitivity to ultraviolet (UV) light affects up to 80% of SLE patients and can exacerbate systemic disease flares, including lupus nephritis (LN). Our findings that neutrophils are the dominant skin infiltrating immune cell after exposure to UV light together with the recent discovery that neutrophil gene signature is the strongest predictor of active SLE prompted the hypothesis that *neutrophils are a key pathogenic link between UV-induced inflammation in the skin and kidney injury in SLE*.

Methods: Mice (C57BL/6J, 3-4mo) were exposed to one dose of UVB (500mJ/cm2). Individual mice were euthanized on 1, 2, or 6 days after UV and perfused with saline; non-irradiated matched mice were used as controls. Immune cells from the skin, bone marrow, blood, lung, and kidney were profiled by flow cytometry (FC). Gene expression was evaluated by QPCR, plasma protein concentration by Legendplex Inflammatory Panel, and proteinuria by Bradford assay. Immunofluorescence staining of fixed kidney tissue was performed. PhotoactivaTable (UBC-PA-GFP) mice were used to photoconvert skin infiltrating neutrophils to GFP+ cells and track them systemically by FC.

Results: Following acute skin exposure to UV light, neutrophils migrate not only to the skin, but also to the kidney, where we observed a 10-fold increase in neutrophil numbers, mainly localized to the tubulointerstitium. Neutralization of IL-17A, which increased 10-100-fold in circulation after exposure to UV light (6-24 hr), inhibited neutrophil migration to the kidney. Relevant to SLE pathogenesis, neutrophil infiltration into the kidney was accompanied by renal inflammatory and injury processes: increased expression of adhesion molecules VCAM-1 and E-Selectin, inflammatory proteins IL1β, s100A8/9, and s100A6, tubular injury markers Ngal and Kim1, as well as elevated urine protein levels. Kidney infiltrating neutrophils produced reactive oxygen species (ROS) and inhibition of neutrophil mobilization by G-CSF neutralization resulted in significant reductions in the expression of adhesion molecules, inflammatory cytokines, and kidney injury markers. Using a mouse model with photoactivaTable immune cells, we observed that a subset of neutrophils found in the kidney had transited through UV light-exposed skin, expressing the pro-inflammatory phenotypes of aged (CXCR4^{hi}) or reverse-transmigrating (ICAM1^{hi}CXCR1^{lo}) cells. We identified elevated levels of CXCR4^{hi} and ICAM1^{hi}CXCR1^{lo} neutrophils in SLE patients particularly within the low-density granulocytes (LDG).

Conclusion: Our study provides several novel findings that could help explain how exposure to sunlight impacts the kidney: i) skin exposure to UV light triggers IL17-A-dependent neutrophil migration to the kidney, accompanied by renal inflammatory and injury responses, ii) neutrophils are directly implicated in subclinical kidney injury as neutralization of G-CSF abrogated renal inflammation and injury, iii) a subset of activated neutrophils has migrated to the kidney via reverse transmigration and is found in SLE patients, suggesting a pathogenic role for these neutrophil populations in lupus.

Disclosure: S. Skopelja-Gardner, None; **J. Tai**, None; **X. Sun**, None; **L. Tanaka**, None; **J. Kuchenbecker**, None; **T. Mustelin**, None; **K. Elkon**, None.

Abstract Number: 0946

ENPP1 Regulates UV Light Triggered Type I Interferon Response in the Skin

Sladjana Skopelja-Gardner[1], Joyce Tai[2], Xizhang Sun[2] and Keith Elkon[2], [1]University of Washington, Seattle, WA, [2]University of Washington, Seattle

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Innate Immunity
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Systemic lupus erythematosus (SLE) patients have a prominent type I interferon (IFN-I) signature in both the lesional and non-lesional skin. We recently showed that exposure to ultraviolet (UV) light triggers cutaneous IFN-I response, in a cGAS-dependent manner. The discovery that ectonucleotide pyrophosphatase/phosphodiesterase 1 (ENPP1) hydrolyzes cGAMP, second messenger of the cGAS-STING DNA sensing pathway, in tumor

immune responses prompted the *question whether ENPP1 regulates UV light stimulated IFN-I signature in the skin.* Since ENPP1 expression has been association with melanogenesis, we also investigated the role of skin pigmentation in IFN-I response and its link with ENPP1 expression.

Methods: Mice (C57BL/6J, *cGAS*-/-, and B6(Cg)-*Tyr*$^{c-2J}$/J Albino, 3mo) were exposed to one dose of UVB light (500mJ/cm^2). Skin biopsies (6mm) were obtained prior to and on days 1 and 2 after UV and tissue digested with DNAse I and Liberase TM, from UV exposed and unexposed skin (< 0.5cm from exposed area) in some experiments. ENPP1 protein expression in non-immune (CD45-) and immune cells (CD45+) was determined by flow cytometry and gene expression by qPCR. Mice were treated intradermally with ENPP1 inhibitor (STF-1084, 0.1mM) or vehicle and expression of interferon stimulated genes (ISG) determined 16hr later by qPCR.

Results: Exposure to a single dose of UV light triggers ISG expression in both the UV-exposed (6hr and 24hr) and non-UV exposed skin (24hr) in B6 mice. This spreading of the IFN-I response 24hr after UV exposure was significantly lower in cGAS-deficient mice. Dermal inhibition of ENPP1, extracellular enzyme that hydrolyzes cGAMP, significantly augmented skin ISG expression after UV light exposure in B6 mice. Interestingly, we observed that ENPP1 expression, found on both CD45- and CD45+ skin cells, was markedly increased in albino CD45- but not B6 mouse skin cells after UV exposure (~60% vs. 5% positive, respectively). This differential ENPP1 response was accompanied by significantly lower ISG expression in albino compared to B6 skin, on day 1 after UV exposure. Dermal inhibition of extracellular ENPP1 in albino mice significantly increased the ISG expression in response to UV light.

Conclusion: Acute skin exposure to UV light triggers spreading of ISG expression in non-UV exposed skin, suggesting that UV light contributes to the IFN-I signature observed in non-lesional skin in SLE. The cGAS requirement for ISG spreading and augmented IFN-I response following ENPP1 inhibition, indicate that extracellular cGAMP amplifies skin ISG induction following UV exposure. The reduced ISG expression in albino compared to B6 mice is likely explained by UV induced ENPP1 expression which reduces extracellular cGAMP. Overall, these findings suggest a role for skin pigmentation in the IFN-I response to UV light that is linked to ENPP1 mediated regulation.

Disclosure: S. Skopelja-Gardner, None; **J. Tai**, None; **X. Sun**, None; **K. Elkon**, None.

Abstract Number: 0947

STING Gain-of-Function in Radio-resistant Cells Supports a Lymphocyte Dependent Auto-inflammatory Lung Disease

Kevin Gao[1], Mona Motwani[1], Ann Marshak-Rothstein[2] and Katherine Fitzgerald[1], [1]University of Massachusetts medical school, worcester, MA, [2]University of Massachusetts medical school, Newton, MA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Innate Immunity
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: cGAS-STING is a cytosolic dsDNA sensing pathway whose regulation is vital to immune homeostasis. Pediatric patients with constitutively active STING mutations develop an autoinflammatory syndrome known as STING Associated Vasculopathy with onset in Infancy (SAVI) and suffer from treatment resistant lung fibrosis. Interestingly, SAVI patients develop immune abnormalities including lymphopenia concomitant with hyperactivation, and lung biopsies from SAVI patients show lymphocyte predominant immune aggregates which strongly

resemble bronchus associated lymphoid tissues (BALT), suggesting a role for lymphocytes in SAVI lung disease. We have genetically engineered a mouse model of SAVI (STING V154M or VM mice) that recapitulates the development of lymphocyte rich BALTs in the lung as early as 6 weeks of age and develops progressive fibrotic disease by 16 weeks. Here, we test our hypothesis that lymphocytes are required for inflammatory lung disease in SAVI mice and use radiation-chimera mice to investigate the mechanism of lymphocyte activation.

Methods: To test the requirement of lymphocytes in SAVI disease, we bred VM Rag1$^{-/-}$ and VM TCR$\beta^{-/-}$ and treated VM mice with αCD20 antibodies. We also generated chimeric mice to test if immune abnormalities were due to hematopoietic or radioresistant cell intrinsic STING Gain-of-Function (GOF) by transferring donor VM bone marrow (BM) into irradiated WT mice or vice versa. We then assessed autoinflammatory disease by body weight, spleen weight, lung histopathology, and performed flow cytometric profiling of central, peripheral, and tissue resident immune cells.

Results: We found that although lymphocytes were required for SAVI inflammatory disease, ablation of only $\alpha\beta$ T cells or B cells failed to rescue disease. These results support the notion that T and B cells could independently contribute to SAVI lung disease. Moreover, we found that VM splenic $\alpha\beta$ T and B cells depended on each other for maximal hyperactivation, suggesting a potential synergistic interaction as well.

Using chimeric mice, we found that BM intrinsic STING GOF was insufficient for lymphocyte activation, and instead, lymphocyte hyperactivation was dependent on STING GOF in radioresistant recipient cells, as donor WT splenic T cells transferred into a VM host developed hyperactivation that phenocopied VM mice. Finally, we found that radio-resistant cell STING GOF was sufficient to perpetuate a progressive SAVI inflammatory lung fibrosis.

Conclusion: Together, these findings suggest that STING GOF in radioresistant cells organizes and activates a profibrotic inflammatory lymphocyte response in the lung. We are currently investigating candidate radioresistant cell populations as initiators of this process including lung epithelium, which is known to robustly express STING, as well as mechanisms by which lymphocytes drive SAVI lung pathology. These findings are clinically relevant for SAVI patients, as well as more broadly for patients suffering from interstitial lung disease associated with rheumatic disease and suggest that lymphocyte depleting therapies may mitigate further lung injury and worsening of fibrosis.

Disclosure: K. Gao, None; **M. Motwani**, None; **A. Marshak-Rothstein**, None; **K. Fitzgerald**, None.

Abstract Number: 0948

Mass Cytometry Reveals Activation Heterogeneity of Circulating Neutrophils in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Innate Immunity
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Neutrophils are important effector cells in systemic immune-mediated diseases. Neutrophil phenotypes vary depending on their age, maturity, activation state, and local environment; however, differences among neutrophils across different inflammatory conditions are poorly understood.

Methods: We analyzed mass cytometry data on blood neutrophils generated in the Accelerating Medicines Partnership RA/SLE Network, which included > 65 million neutrophils from 10 healthy controls, 13 patients with rheumatoid arthritis and 24 patients with biopsy-confirmed lupus nephritis. Neutrophil phenotypes were assessed by dimensional reduction and visualization with UMAP, and subclusters were partitioned by FlowSOM clustering and ConsensusClusterPlus metaclustering.

Results: Using unsupervised dimensionality reduction, we observed that neutrophils clustered by surface phenotype rather than by disease. Comparison of expression levels of surface proteins on neutrophils revealed a significant increase in the expression of Lysosomal-associated membrane protein 1 (LAMP1; CD107a) on neutrophils from SLE patients compared to controls (p=0.022). LAMP-1 expression largely segregated to a subcluster of neutrophils by UMAP visualization, suggesting an increase in a subset of neutrophils with recent de-granulation in SLE patients. SLE patients showed a range of expression of LAMP-1 on neutrophils, and LAMP-1 expression did not correlate with frequencies of PD-1hi CXCR5- T peripheral helper (Tph) cells, PD-1hi CXCR5+ T follicular helper (Tfh) cells, or CD11c+ B cells, which are highly expanded lymphocyte populations in lupus nephritis patients. Hierarchical clustering based solely on neutrophil protein expression distinguished two subgroups of SLE patients. Patients in the SLE1 group had an expanded population of LAMP1+ degranulated neutrophils, and this group also had higher chronicity scores in kidney biopsies. In contrast, patients in SLE2 group displayed an increased frequency of C5aR+ CXCR1+ neutrophils and had higher dsDNA titers and a higher SLEDAI composite score. These two subgroups did not differ in frequencies of Tph cells, Tfh cells, CD11c+ B cells, again suggesting that the neutrophil phenotypes may be independent of activated T/B cell pathways.

Conclusion: This work highlights an altered neutrophil phenotype in patients with lupus nephritis, in particular in a subset of patients associated with increased LAMP-1 expression. Neutrophil surface phenotypes may reveal a unique axis of immune activation in SLE patients.

Disclosure: R. Grieshaber-Bouyer, None; **J. Keegan**, None; **P. Nigrovic**, Novartis, 2, 5, BMS, 2, 5, Pfizer, 2, 5, Sobi, 5, Miach Orthopedics, 5, Simcere, 5, XBiotech, 5, Quench Bio, 5, Siglion, 5, Cerecor, 5, UpToDate, 7, American Academy of Pediatrics, 7, CARRA, 9; **J. Lederer**, None; **D. Rao**, None.

Abstract Number: 0949

SLAMF7 Engagement Drives Monocyte Super-Activation in Acute and Chronic Inflammation

Daimon Simmons[1], Hung Nguyen[2], Emma Gomez-Rivas[3], YunJu Jeong[4], William Apruzzese[5], Edy Kim[6] and Michael Brenner[7], [1]Department of Pathology, Brigham and Women's Hospital, Boston, MA, [2]Division of Rheumatology, Brigham and Women's Hospital,, Boston, MA, [3]Division of Rheumatology, Brigham and Women's Hospital, Boston, MA, [4]Division of Pulmonary and Critical Care, Brigham and Women's Hospital, Boston, MA, [5]., Boston, [6]Brigham and Women's Hospital, Division of Pulmonary and Critical Care Medicine, Boston, MA, [7]Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Innate Immunity
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

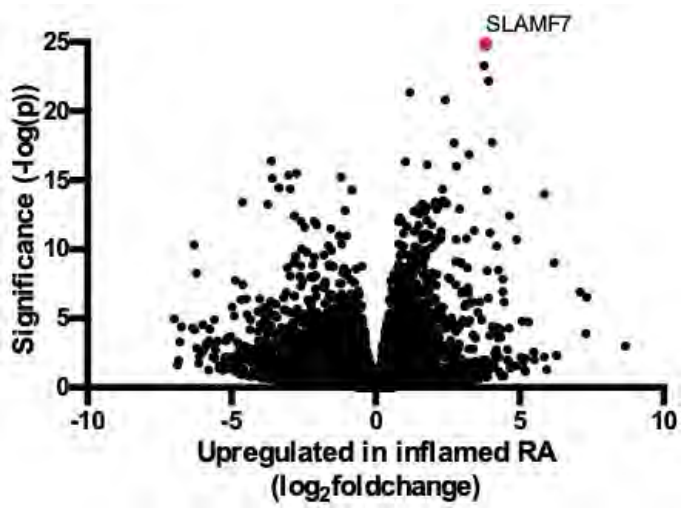


Figure 1. Upregulation of SLAMF7 in inflamed synovial tissues. Differentially expressed genes in synovial monocytes from patients with inflamed RA (n=11) compared to OA (n=10) from AMP Phase 1 bulk RNA-sequencing are shown, with SLAMF7 labeled in red.

Background/Purpose: Monocytes orchestrate immune responses that protect against microbes but can also drive pathological inflammation and autoimmune disease. Monocytes are thought to be activated primarily by cytokines or by microbial molecules, but they express a broad array of receptors allowing them to integrate responses from the environment. We hypothesize that monocytes may be activated by a first, or primary signal, and that a second, booster stimulus can then drive a pathological super-activated state. To address this hypothesis, we analyzed high dimensional transcriptomic data for monocytes from diseased human tissue to identify receptors that might serve as super-activators of these cells, and identified SLAMF7, a receptor that regulates leukocyte activation.

Methods: We analyzed bulk RNA-sequencing (RNA-seq) data from Phase I of the Accelerating Medicines Partnership to identify genes upregulated in monocytes from rheumatoid arthritis synovial tissue compared to osteoarthritis synovial tissue. We used flow cytometry to quantify this receptor on monocytes and sorted monocytes with high versus low SLAMF7 expression for RNA-seq. We used an activating antibody or recombinant SLAMF7 protein to stimulate monocytes *in vitro* and performed ELISA to measured cytokine release and quantitative real-time PCR to quantify gene expression. We also collected RNA-seq data from monocytes after stimulation and identified upregulated genes as the "SLAMF7 Activation Signature." We than analyzed publicly available single cell RNA-seq data from individuals with RA, Crohn's disease and COVID-19 lung infection with the "SLAMF7 Activation Signature."

Results: Through differential gene expression analysis we identified SLAMF7 as a receptor that is profoundly upregulated in monocytes from inflamed synovial tissues (Fig 1). We identified an interferon signature in SLAMF7-high monocytes, and additional *in vitro* stimulation experiments implicated IFN-γ as a key regulator of SLAMF7 expression. Engaging SLAMF7 with an antibody or recombinant protein on monocytes drove profound production of inflammatory cytokines TNF-α, IL-6, and IL-1β, and chemokines CCL3, CXCL1, and CXCL8. We performed transcriptome-wide analysis on these stimulated monocytes to generate a "SLAMF7 Activation Signature". We observed a striking overlap between our experimental signature and the transcriptional signature identified in infiltrating monocytes from RA synovial tissue, bronchoalveolar lavage cells of patients with COVID-19, as well as from ileal tissue of patients with Crohn's disease.

Conclusion: SLAMF7 is a receptor that is massively upregulated on monocytes from inflamed tissues. IFN-γ drives monocytes to express high levels of SLAMF7 but does not drive complete monocyte activation on its own. A second booster activation signal through engagement of SLAMF7 then triggers profound super-activation, resulting in monocyte production of high levels of inflammatory effector molecules. We implicate this pathway as a major contributor

to pathologic inflammation in human diseases. Therapies targeting different steps in monocyte super-activation could have potential for treating diverse human diseases.

Disclosure: D. Simmons, None; **H. Nguyen**, None; **E. Gomez-Rivas**, None; **Y. Jeong**, None; **W. Apruzzese**, None; **E. Kim**, None; **M. Brenner**, None.

Abstract Number: 0950

The Association Between Gout and Cardiovascular Disease Outcomes: Assessment and Recalibration of Individual-level Primary Prevention Risk Prediction Equations in Approximately 450,000 New Zealanders

Ken Cai[1], Billy Wu[2], Nicola Dalbeth[2], Rod Jackson[2] and Katrina Poppe[2], [1]University of Auckland, Sydney, New South Wales, Australia, [2]University of Auckland, Auckland, New Zealand

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Metabolic & Crystal Arthropathies

Session Type: Abstract Session

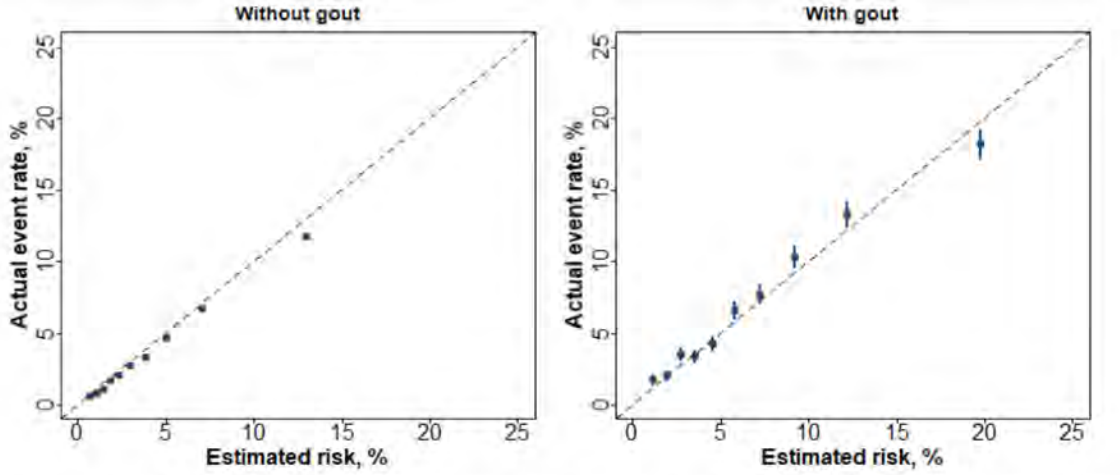
Session Time: 5:00PM–5:50PM

Background/Purpose: Some studies have reported that gout is an independent risk factor for cardiovascular disease (CVD). Individual-level cardiovascular risk prediction equations have been developed and validated for the New Zealand population using a comprehensive primary care dataset (PREDICT-1°) (Pylypchuk, Lancet 2018). We

	Gout		Non-Gout	
	Women	**Men**	**Women**	**Men**
Participants	3325 (14)	19904 (86)	190527 (46)	227967 (54)
Median age (IQR)	59 (52-66)	52 (45-61)	55 (52-66)	50 (45-58)
Urate lowering therapy [a]	2278 (69)	15349 (77)	-	-
Serum urate level monitoring [b]	2585 (78)	15650 (78)	-	-
Estimated CVD risk at enrolment [c]				
<5%	1814 (55)	9526 (48)	159272 (84)	153986 68)
5-10%	969 (29)	5886 (30)	25020 (13)	49965 (22)
10-15%	349 (10)	2687 (13)	4481 (2)	16200 (7)
15-20%	113 (3)	1078 (5)	1146 (0.6)	5169 (2)
>20%	80 (2)	727 (4)	608 (0.3)	2647 (1)
First outcome at 5 years				
Fatal CVD events	30 (0.9)	155 (0.8)	510 (0.3)	960 (0.4)
Total CVD events [d]	215 (6.5)	1290 (6.5)	4998 (2.6)	8190 (3.6)
All deaths	123 (3.7)	530 (2.7)	3017 (1.6)	4054 (1.8)

IQR: interquartile range, CVD: cardiovascular disease. [a] allopurinol, febuxostat or benzbromarone dispensed at least once in the 5 years prior to enrolment. [b] serum urate tested at least once in the 3 years prior to enrolment. [c] Estimated risk of a CVD event in the next 5 years adjusted for age, sex, ethnicity, NZ deprivation quintile, smoking history, family history of premature CVD, atrial fibrillation, diabetes, mesan systolic blood pressure, mean total cholesterol/HDL cholesterol ratio, BMI and baseline dispensing of blood pressure lowering, lipid lowering and antithrombotic medications. [d] includes fatal and non-fatal CVD events.

Table. Participant characteristics (n = 441,723). Data are shown n (%), except age in years.



X-axis represents the 5-year estimated risk of CVD events at the time of risk assessment (enrolment into the PREDICT study) and Y-axis represents the actual CVD event rate after 5 years obtained from linked national ICD-coded hospitalisations and mortality databases. The estimated risk of a CVD event in the next 5 years is adjusted for age, sex, ethnicity, NZ deprivation quintile, smoking history, family history of premature CVD, atrial fibrillation, diabetes, mean systolic blood pressure, mean total cholesterol/HDL cholesterol ratio, BMI and baseline dispensing of blood pressure lowering, lipid lowering and antithrombotic medications.

Figure. Estimated versus actual CVD event rate in people with and without gout.

assessed the performance of these equations in people with gout and recalibrated the primary prevention equation to improve the prediction of CVD events in people with this condition.

Methods: The PREDICT study recruits people in primary care when general practitioners in New Zealand use PREDICT software to routinely assess their patients' risk profile for CVD, which are prospectively linked to national ICD-coded hospitalisation and mortality databases. The study population included men and women (ages 30-74 years) who had no prior CVD, renal disease or congestive heart failure. A validated national health data definition of gout was used to identify those with gout: discharge diagnosis of gout (ICD-9 274, ICD-10 M10) from a public hospital admission or dispensed gout specific medications (Winnard, Rheumatology 2012). Baseline estimates of 5-year CVD risk (of cardiovascular death, non-fatal myocardial infarction, stroke, or other vascular event) were calculated using sex-specific PREDICT-1° risk scores and initially assessed via the slope between estimated and observed risk on the calibration plot ("slope"). Gout was added as a binary predictor to the recalibrated risk models.

Results: From January 1, 2007 to December 31, 2018, 441,723 people (56% men) had a PREDICT-1° risk assessment (**Table**). Of these, 23,229 met the definition of gout (3325 females and 19,904 males). In the whole cohort, 14,693 (3.3%) people had a first CVD event within 5 years of risk assessment. Of these, 1505 occurred in people with gout (6.5% event rate) and 13,188 occurred in people without gout (3.2% event rate). The risk scores underestimated the risk of CVD events in people with gout compared with people without gout (slope = 0.88) (**Figure**). This was more pronounced in women with gout (slope = 0.77) compared with men (slope = 0.96). Adding gout to the recalibrated risk estimates demonstrated that gout was independently associated with an increased risk of CVD events (adj. HR (95% CI) = 1.24 (1.08-1.42) for women; 1.21 (1.14-1.28) for men).

Conclusion: Current cardiovascular risk prediction equations underestimate the risk of CVD in people with gout. Despite adjustment for known CVD risk factors, gout independently increased the hazard ratio for CVD events.

Disclosure: K. Cai, None; **B. Wu**, None; **N. Dalbeth**, AstraZeneca, 1, 2, Abbvie, 1, Arthrosi, 1, Dyve BioSciences, 1, Selecta, 1, Janssen, 1; **R. Jackson**, None; **K. Poppe**, None.

Abstract Number: 0951

The Comparative Effect of Exposure to Various Risk Factors on the Risk of Hyperuricaemia: Diet Has a Weak Causal Effect

Ruth Topless[1], Tanya Major[1], Jose Florez[2], Joel Hirschhorn[3], Murray Cadzow[1], Nicola Dalbeth[4], Lisa Stamp[5], Phillip Wilcox[1], Richard Reynolds[6], Joanne Cole[2] and **Tony Merriman**[1], [1]University of Otago, Dunedin, New Zealand, [2]Massachusetts General Hospital, Boston, [3]Harvard Medical School, Boston, [4]University of Auckland, Auckland, New Zealand, [5]University of Otago Christchurch, Christchurch, New Zealand, [6]University of Alabama Birmingham, Birmingham

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Metabolic & Crystal Arthropathies

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: Prevention of hyperuricaemia (HU) is critical to the prevention of gout. Therefore, understanding the causal relationships and relative contributions of various risk factors to HU is important. Inherited genetic variants have a significant causal role. However, the relative importance of other exposures and questions of causality are still unresolved. Here we use attribuTable fraction to compare the relative contribution of genetic, dietary, urate-lowering therapy (ULT) use and other exposures to HU. We also use Mendelian randomization to evaluate whether diet has a causal role in determining serum urate levels.

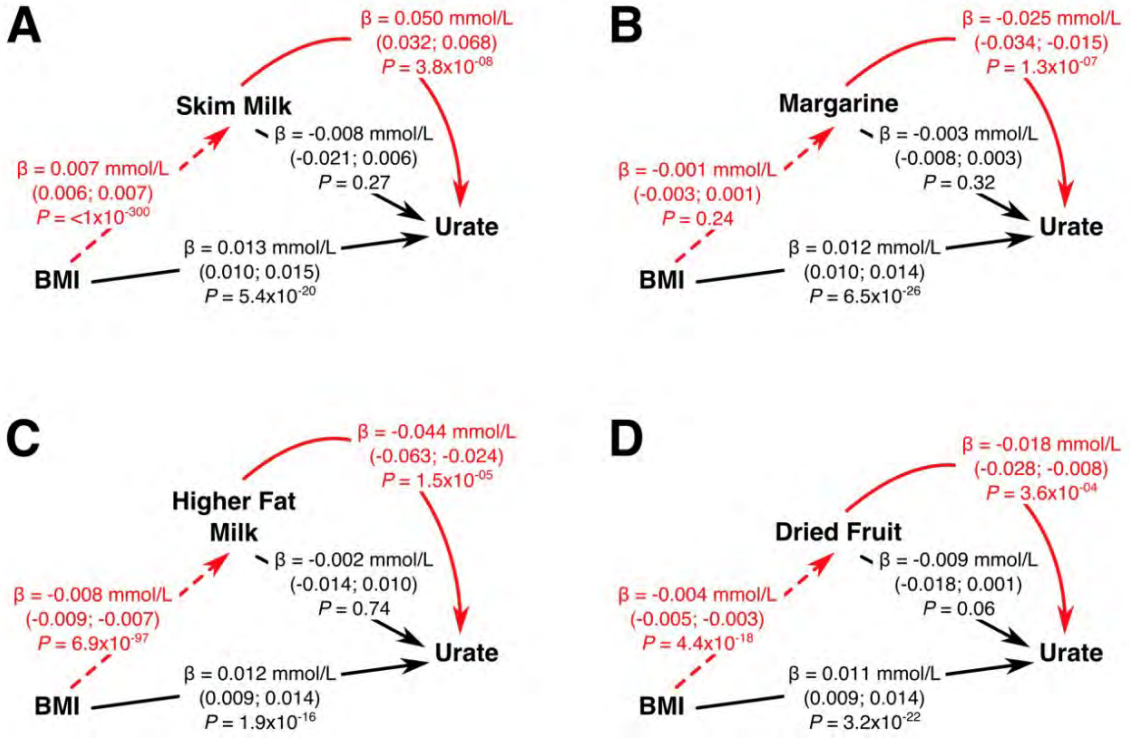
Methods: Four sample sets, three from the general population (n = 419,060) and one of gout patients (n = 6,781), were derived from the Database of Genotypes and Phenotypes (Cohort 1) and the UK Biobank resources (Cohorts 2, 3, and Gout). These sample sets were comprised from individuals of European ancestry with measured serum urate levels and dietary, clinical, and genome-wide genotype information available. Dichotomised exposures to diet, the *SLC2A9 rs12498742* risk variant, BMI, alcohol, diuretic treatment, sex and age were used to calculate adjusted population and average attribuTable fractions for HU (≥0.42 mmol/L in men and women). Exposure to urate-lowering therapy was also assessed in the gout-only cohort. Two sample Mendelian randomization using the UK Biobank cohort was conducted to test for a causal role of dietary habits in determining serum urate levels, using as instruments genetic variants previously reported as associated with dietary patterns (Cole et al. *Nat Comm* 2020;11:1467).

Results: Adherence to dietary recommendations, achieving BMI (< 25 kg/m^2), and absence of the *SLC2A9 rs12498742* urate-raising allele produced population attribuTable fractions for HU of 20 to 24%, 59 to 69%, and 57 to 64%, and average attribuTable fraction estimates of 6 to 7%, 24 to 26%, and 22 to 24%, respectively in the three non-gout cohorts (Table). In the gout cohort, diet, BMI, *SLC2A9 rs12498742,* and urate-lowering treatment population attribuTable fractions for hyperuricaemia were 12%, 47%, 47%, and 62%, and average attribuTable fractions for hyperuricaemia were 3%, 14%, 14%, and 33%, respectively (Table). In the gout cohort ULT explained 34% of variance in serum urate levels, ≥10-fold higher than the other exposures tested. Mendelian randomization (Figure) demonstrated weak causal effects of two dairy-related dietary habits, margarine consumption and dried fruit consumption on serum urate levels (e.g. preferentially drinking skim milk increased urate, β = 0.050 mmol/L, $P = 3.78 \times 10^{-8}$), which were all mediated by BMI, losing significance ($P \geq 0.06$) in multivariate models assessing the BMI-independent effect of diet on urate.

Conclusion: The attribuTable fraction and Mendelian randomization data emphasise the minor role of diet in determining serum urate levels and HU. In gout the use of urate-lowering therapy was the dominant attribuTable fraction tested for serum urate level, with a population attribuTable fraction approximately 6-fold greater and an average attribuTable fraction approximately 10-fold greater than following healthy-eating guidelines.

Table Estimated population and average attributable fractions (PAF / AAF)

Risk Factor	Cohort 1 (US-based)			Cohort 2 (UK-based)			Cohort 3 (UK-based)			Gout Cohort (UK-based)		
	OR (95% CI)	PAF (95% CI)	AAF (95% CI)	OR (95% CI)	PAF (95% CI)	AAF (95% CI)	OR (95% CI)	PAF (95% CI)	AAF (95% CI)	OR (95% CI)	PAF (95% CI)	AAF (95% CI)
Sex - Male	6.2 (5.4; 7.0)	64.3 (64.6; 67.8)	29.8 (29.2; 30.3)	8.2 (7.5; 8.9)	75.6 (74.6; 76.5)	30.9 (30.2; 31.6)	7.5 (7.3; 7.8)	73.4 (73.0; 73.8)	30.8 (30.2; 31.5)	4.6 (3.4; 6.3)	75.5 (68.3; 80.8)	30.2 (29.8; 30.7)
BMI ≥25 kg/m^2	3.4 (3.0; 3.8)	59.2 (55.8; 62.2)	23.5 (23.1; 24.0)	4.2 (3.8; 4.6)	68.6 (66.2; 70.8)	26.2 (25.5; 26.8)	3.8 (3.6; 3.9)	66.4 (65.4; 67.3)	25.8 (25.2; 26.4)	2.0 (1.8; 2.6)	46.7 (33.7; 56.8)	13.8 (13.6; 14.1)
SLC2A9, rs12498742 A allele present	2.4 (1.8; 3.2)	56.6 (43.8; 66.3)	22.0 (21.6; 22.4)	2.9 (2.4; 3.5)	63.8 (56.2; 70.0)	23.5 (22.9; 0.24)	2.7 (2.5; 2.9)	61.7 (58.8; 64.3)	23.1 (22.6; 23.7)	1.9 (1.2; 3.1)	47.3 (15.8; 66.7)	13.7 (13.4; 13.9)
Diet non-adherence	1.3 (0.6; 2.4)[a]	20.3 (54.6; 58.8)[a]	6.3 (6.2; 6.5)[#]	1.3 (1.2; 1.5)[#]	23.6 (12.7; 33.0)[#]	7.1 (6.9; 7.3)[#]	1.3 (1.2; 1.4)*	21.4 (8.2; 24.4)*	6.5 (6.3; 6.7)*	1.2 (0.9; 1.4)*	11.8 (-7.3; 27.1)*	3.1 (3.0; 3.1)*
Alcohol ≥1 drink/week	1.1 (1.0; 1.2)	5.2 (-0.1; 10.0)	1.5 (1.4; 1.5)	1.3 (1.2; 1.4)	19.5 (14.2; 24.3)	5.7 (5.6; 5.9)	1.3 (1.3; 1.4)	19.4 (17.5; 21.2)	5.9 (5.7; 6.0)	1.1 (0.9; 1.4)	10.0 (-5.8; 23.1)	1.9 (1.9; 2.0)
On diuretic therapy	4.8 (4.2; 5.5)	21.1 (20.3; 21.9)	8.7 (8.6; 8.9)	4.2 (3.8; 4.6)	15.1 (14.6; 15.5)	4.8 (4.7; 5.0)	4.3 (4.2; 4.5)	17.1 (16.9; 17.3)	5.8 (5.6; 5.9)	1.8 (1.5; 2.1)	7.0 (5.3; 8.4)	1.8 (1.8; 1.8)
Age ≥50 years	1.3 (1.1; 1.4)	15.1 (8.7; 20.9)	4.7 (4.6; 4.8)	1.0 (0.9; 1.1)	0.4 (-6.4; 6.6)	0.1 (0.1; 0.1)	1.0 (1.0; 1.0)	0.2 (-2.4; 2.7)	0.1 (0.1; 0.1)	0.5 (0.4; 0.6)	^	^
Not treated with urate-lowering therapy	^	^	^	^	^	^	^	^	^	20.9 (18.1; 24.0)	62.1 (61.6; 62.5)	33.0 (32.6; 33.5)



The numbers in red (solid line) derive from the first round of Mendelian randomisation, the estimated causal effect. The numbers in black represent the data from the bivariate MR analysis.

Disclosure: R. Topless, None; **T. Major**, None; **J. Florez**, None; **J. Hirschhorn**, None; **M. Cadzow**, None; **N. Dalbeth**, AstraZeneca, 1, 2, Abbvie, 1, Arthrosi, 1, Dyve BioSciences, 1, Selecta, 1, Janssen, 1; **L. Stamp**, None; **P. Wilcox**, None; **R. Reynolds**, None; **J. Cole**, None; **T. Merriman**, None.

Abstract Number: 0952

Reducing Immunogenicity of Pegloticase (RECIPE) with Concomitant Use of Mycophenolate Mofetil in Patients with Refractory Gout—a Phase II Double Blind Randomized Controlled Trial

Puja Khanna[1], Dinesh Khanna[1], Gary Cutter[2], Jeffrey Foster[2], Joshua Melnick[3], Sara Jaafar[1], Stephanie Biggers[2], AKM Rahman[2], Hui-Chen Kuo[2], Michelle Feese[2] and Kenneth Saag[4], [1]University of Michigan, Ann Arbor, MI, [2]University of Alabama at Birmingham, Birmingham, AL, [3]University of Alabama at Birmingham (UAB), Vestavia Hills, AL, [4]University of Alabama at Birmingham, Division of Clinical Immunology and Rheumatology, Birmingham, AL

SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Metabolic & Crystal Arthropathies

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Characteristics	Pegloticase w/MMF (n = 22)	Pegloticase w/Placebo (n = 10)	P-value
Gender (%)			
Men	19 (86)	9 (90)	0.99
Age in years, mean (SD)	55.0 (9.3)	55.4 (10.6)	0.91
2015 ACR/EULAR criteria points ≥ 8 (%)	22 (100)	10 (100)	N/A
2015 ACR/EULAR criteria points, mean (SD)	13.5 (2.8)	13.8 (2.7)	0.88
Gout flare history			
Flare within last year (%)	15 (68)	5 (50)	0.44
Number of flares last year, median (Q1, Q3)	1 (0, 2)	1 (0, 1)	0.28
Age at diagnosis, years, mean (SD)	40.9 (14.7)	42.1 (12.6)	0.99
Duration of Gout, years, mean (SD)	13.3 (9.8)	13.4 (7.4)	0.82
Gout impact score at screening (range: 0-96)			
Mean (SD)	45.6 (8.1)	44.8 (8.1)	0.79
PROMIS Scores at screening			
Pain intensity T-Score, mean (SD)	54.1 (9.3)	50.6 (10.1)	0.35
Physical function T-Score, mean (SD)	36.1 (7.8)	35.7 (6.5)	0.88
Urate lowering agents			
Allopurinol	13 (59)	6 (60)	0.99
Febuxostat	4 (18)	1 (10)	0.99
Acute gout therapy			
Colchicine	9 (41)	5 (50)	0.71
NSAID	16 (73)	5 (50)	0.44
Corticosteroids	4 (18)	2 (20)	0.99
Alcohol Consumption (number of drinks)			0.62
0	11 (50)	3 (30)	
1-2	7 (32)	4 (40)	
>2	4 (18)	3 (30)	
Pain score History (0 to 10, 10 being the worst), mean (SD)	4.5 (4.0)	2.8 (3.3)	0.36
Serum urate, mg/dL mean (SD)	8.9 (1.8)	9.8 (1.3)	0.15
Serum urate			
≤ 6 mg/dL	2 (9)	0 (0)	0.99
> 6 mg/dL	20 (91)	10 (100)	
eGFR, mean (SD)	82.7 (26.8)	78.0 (17.3)	0.48
< 90 (mL/min/1.73 m^2)	15 (68)	9 (90)	0.38
≥ 90 (mL/min/1.73 m^2)	7 (32)	1 (10)	
BMI (%)			
25 to < 30	3 (14)	1 (10)	0.6316
30 to < 35	8 (36)	6 (60)	
35 to < 40	7 (32)	1 (10)	
40 to < 45	3 (14)	1 (10)	
≥45	1 (4)	1 (10)	
Presence of Tophi	19 (86)	9 (90)	0.99

Table 1. Patient demographics for treatment arms of pegloticase with MMF and pegloticase with placebo

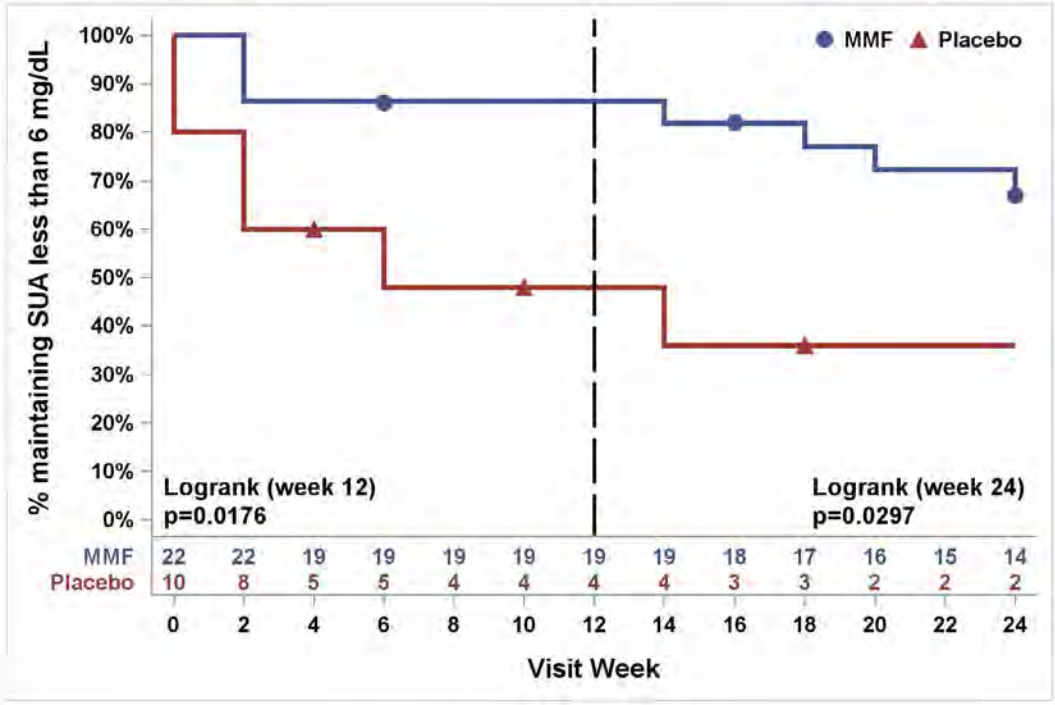


Figure 1. Percentage of subjects maintaining SUA less than 6 mg/dL in MMF/pegloticase vs PBO/pegloticase arms over 24 Weeks (Kaplan-Meier Estimates)

Background/Purpose: Pegloticase, a recombinant, pegylated uricase, is used for treatment of gout in patients who fail oral urate lowering therapy (ULT). Despite successful reduction of urate levels and flares, its use is limited due to immunogenicity leading to infusion reactions.[1] Co-administration of an immunomodulatory agent may mitigate this loss of efficacy and concern for drug-related toxicity.

Methods: Patients from 5 rheumatology practices were recruited over 18 months, and randomized (3:1) by site to either to mycophenolate mofetil (MMF) 1 gram twice a day or placebo (PBO) with a run-in of 2 weeks (wks) prior to intravenous pegloticase at 8 mg every 2 wks (12 infusions). MMF or PBO was given for the first 12 wks. Inclusion criteria were: a) patients ≥ 18 years of age who met 2015 ACR/EULAR gout classification criteria and b) chronic refractory gout defined as symptoms inadequately controlled with ULT or contraindication to ULT. Endpoints included: a) proportion of subjects achieving and maintaining a serum urate (sUA) ≤ 6 mg/dL at 12 wks (primary), b) assess 6-month durability of immune modulation after discontinuation of MMF at 12 wks (secondary), and c) adverse events (AE). Analyses were conducted using SAS (Cary, NC) Version 9.4 with Fisher's exact test for binary outcomes and Wilcoxon two-sample test for continuous outcomes. Kaplan-Meier estimates and log-rank test were performed to compare survival curves between groups. Hypothesis tests were two-tailed and p-value (p) < 0.05 indicated statistical significance.

Results: Of 42 subjects screened, 35 were randomized, and 32 who received at least one dose of pegloticase were included in modified intention to treat analyses (Table 1- demographics). 19 of 22 (86%) in the MMF arm achieved the primary outcome at 12 wks of sUA ≤ 6mg/dL, compared to 4 of 10 (40%) in placebo, p-value 0.01. At wk 24, sUA response was sustained in 68% of MMF arm vs. 30% in placebo. Estimated rates of AEs per month was similar between groups -MMF (0.3) and placebo (0.4). The MMF arm had higher AEs compared to placebo: musculoskeletal (36% vs. 10%), respiratory (18% vs. 0%), and infections (9% vs. 0%). The placebo arm had a greater percentage of infusion reactions (30% vs. 0%). Figure 1 demonstrates that the percentage of subjects maintaining a sUA < 6 mg/dL at 12 wks was significantly higher (p=0.02) in the MMF arm, and a significant difference (p=0.03) at 24 wks indicating sustained benefit from MMF.

Conclusion: Short-term concomitant use of MMF with pegloticase was generally well tolerated in our proof of concept study. It was associated with a statistically significant and clinically meaningful impact on the proportion of subjects achieving and maintaining a sUA ≤6 mg/dL at 24 weeks. To our knowledge, this is the first randomized controlled trial to demonstrate prolonged efficacy of pegloticase with co-administrations of an immunomodulatory agent.

Disclosure: P. Khanna, Selecta, 5, Dyve, 5; **D. Khanna**, Bayer, 2, BMS, 2, Horizon, 2, Pfizer, 2, NIH, 2, Immune Tolerance Network, 2, Eicos Sciences Inc, 4, Acceleron,, 5, Actelion,, 5, Abbvie,, 5, Amgen,, 5, Bayer,, 5, Boehringer Ingelheim, 5, CSL Behring, 5, Corbus,, 5, Galapagos,, 5, Genentech/Roche, 5, GSK, 5, Horizon, 5, Merck,, 5, Mitsubishi Tanabe Pharma, 5, Sanofi-Aventis, 5, United Therapeutics, 5, Impact PH, 9, Scleroderma Development, 6, CiviBioPharma/Eicos Sciences Inc, 6; **G. Cutter**, Horizon Pharmaceuticals, 9, Biogen, 5, Click Therapeutics, 5, Genentech, 5, Gilgamesh Pharmaceuticals, 5, GW Pharmaceuticals, 5, Genzyme, 5, Klein-Buendel Incorporated, 5, Medimmune, 5, Medday, 5, Novartis, 5, Osmotica Pharmaceuticals, 5, Perception Neurosciences, 5, Perception Neurosciences, 5, Recursion Pharmaceuticals, 5, Roche, 5, Somahlution, 5, TG Therapeutics, 5; **J. Foster**, None; **J. Melnick**, None; **S. Jaafar**, None; **S. Biggers**, None; **A. Rahman**, None; **H. Kuo**, None; **M. Feese**, None; **K. Saag**, Arthrosi, 5, Horizon Therapeutics plc, 2, 5, Atom Bioscience, 5, LG Pharma, 5, Takeda, 5, Mallinkrodt, 5, SOBI, 2, 5, Shanton, 2.

Abstract Number: 0953

Long-term Xanthine Oxidase Inhibitor Treat to Target Urate Lowering Therapy Coordinately Re-wires the Mononuclear Leukocyte Mitochondrial and Inflammatory Proteome in Gout

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: In gout, long-term xanthine oxidase inhibitor treat to target urate lowering therapy (XOIT2T) markedly reduces flares and synovitis, despite delayed resolution of tissue crystal deposits. XOI drugs inhibit oxidative stress and the NLRP3 inflammasome in cultured leukocytes, but XOI effects on immune cells *in vivo* are poorly understood. To better define mechanisms and markers of long-term XOIT2T effects on gouty inflammation *in vivo* we curated PBMCs in a sub-cohort (n=32) of allopurinol vs. febuxostat comparative effectiveness trial CSP594 “STOP GOUT”.

Methods: All subjects reported recurrent acute flare activity and poorly controlled serum urate (>6.8 mg/dL) at enrollment. Serum cytokine quantification used mesoscale discovery immunoassay. PBMCs were analyzed by multiplexed, quantitative proteomics. Significantly altered proteins (via *p*-value and fold-change; pi score > 0.6) were subject to K-means clustering, then pathway and network analyses.

Results: At study endpoint (EP: 48 weeks XOIT2T), serum urate dropped by >30% to reach normouricemia, and gout flares dropped by ~50% from baseline (BL)($P < 0.05$ for both). Two subgroups of patients were clearly separable by BL serum IL-8, though indistinguishable by age, comorbidities, and gout flare rates. One subgroup had elevated IL8 at BL that fell until EP (“IL8+” group); the other subgroup had consistently low IL8 (“IL8-” group). To probe for differential responses to XOIT2T, we stratified samples into the 2 subgroups. At study EP, we saw broad PBMC

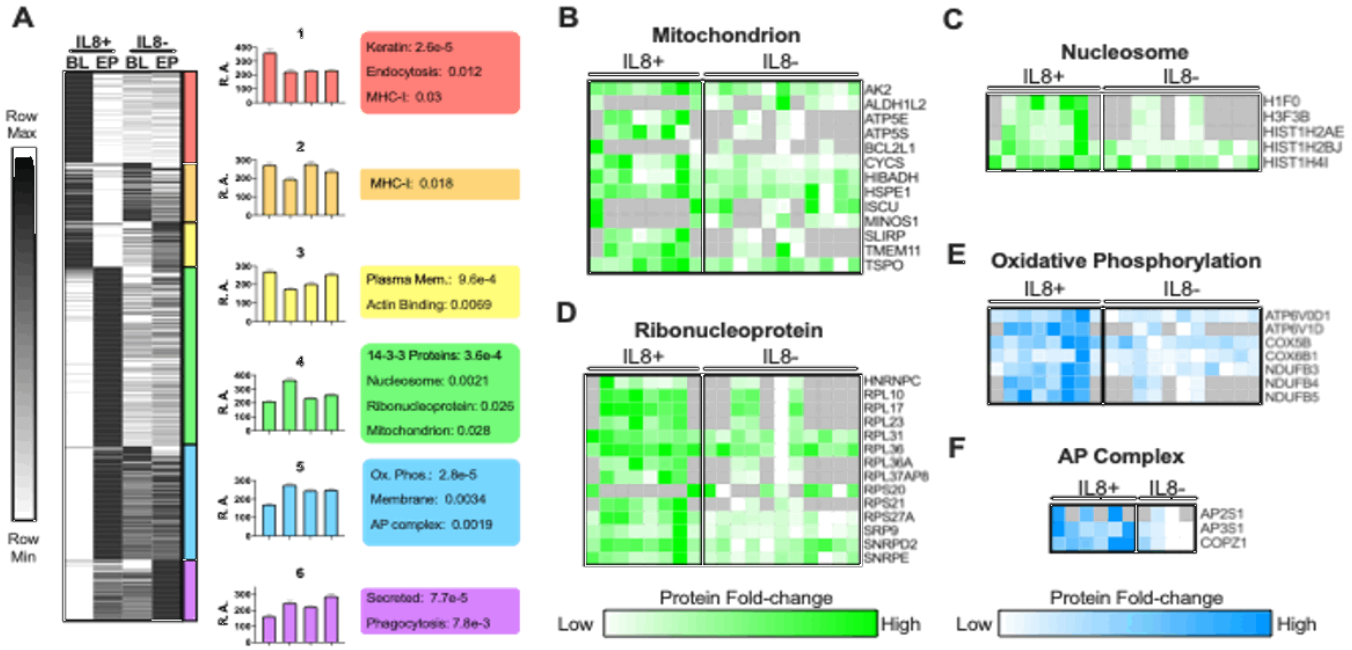

Figure 1. Overview of PBMC Proteomic Response to XOIT2T. (A) K-means clustered heatmap of significantly altered proteins (pi score > 0.6) in response to XOIT2T. Clusters are colored and matched with their respective average profiles and gene ontology analyses. Heatmaps of mitochondrion protein (B), nucleosome protein (C) and ribonucleoprotein (D) fold-changes from cluster 4. Heatmaps of oxidative phosphorylation (E) and AP complex protein (F) fold-changes from cluster 5.

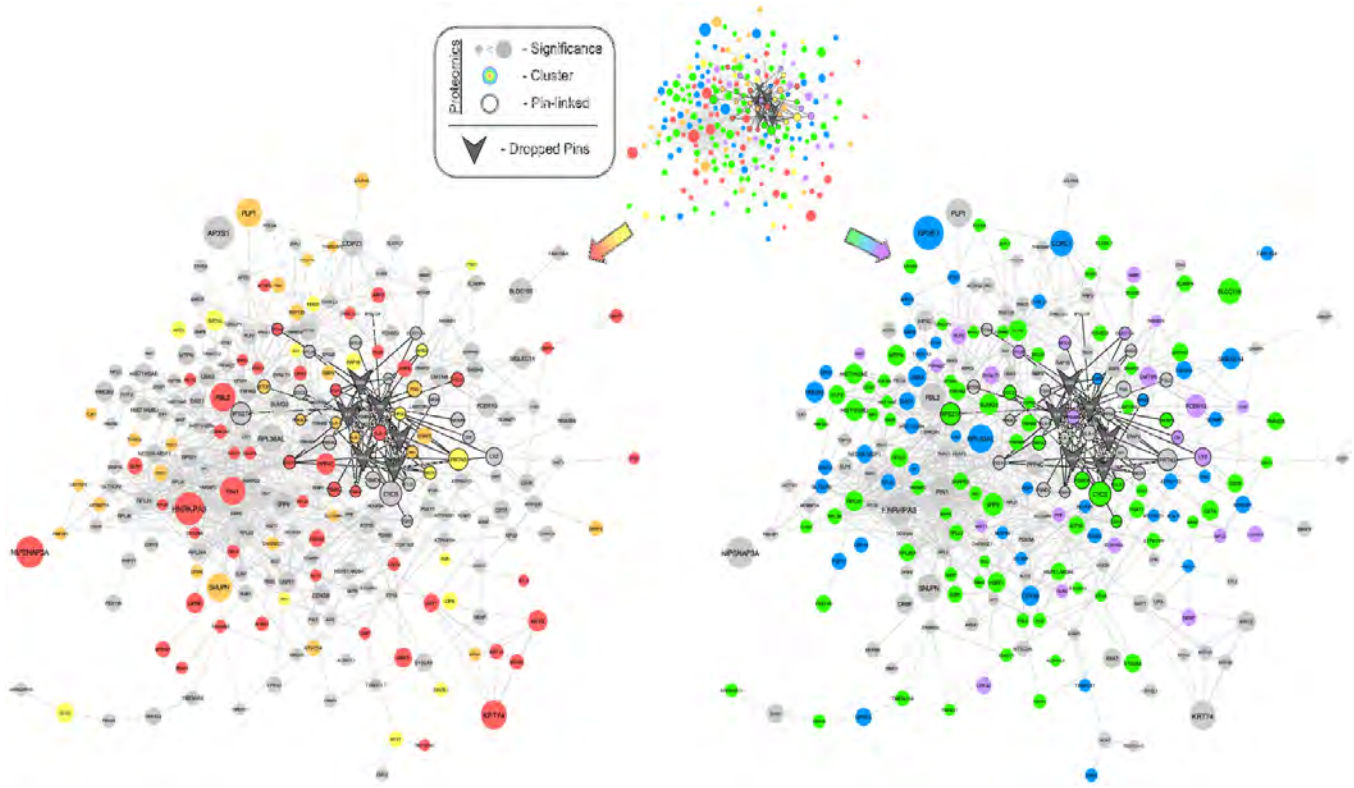

Figure 2. Linkage of Known Gout Mediators to PBMC Proteome Changes Induced by XOIT2T. STRING-db protein association network of significantly altered proteins (pi score > 0.6) and known gout mediators (TNF, IL6, IL1B, IL17A, CXCL8 and CSF2). Proteomic nodes are sized by average significance (ie. pi score) across stratified groups, colored according to K-means clusters in Fig 1 and have black border if directly linked to pin-dropped gout mediators.

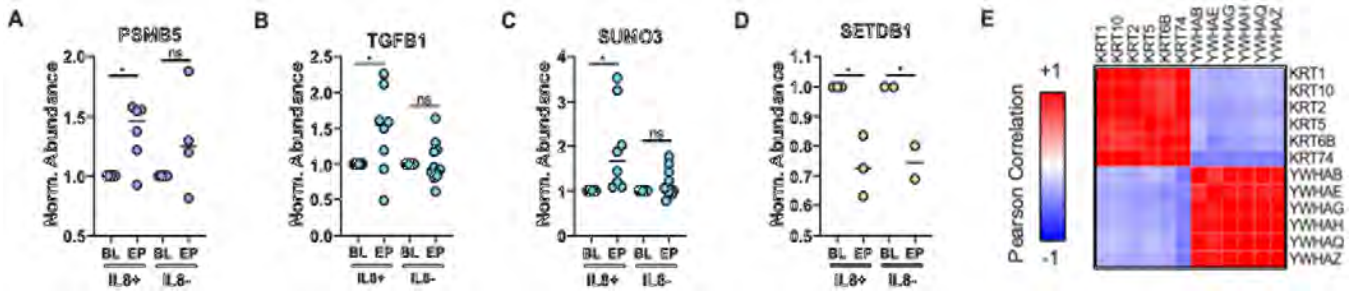

Figure 3. Specific PBMC Proteins of Interest Altered by XOIT2T. Expression of PSMB5 (A), TGFB1 (B), SUMO3 (C) and SETDB1 (D) across all groups normalized to patient BL (*pi score > 0.6; points are colored according to their K-means clusters in Fig 1). (E) Correlation matrix of keratin and 14-3-3 proteins significantly altered by XOIT2T.

proteome changes, with many prominent in the IL8+ subgroup. Specifically, we found increased mitochondrial and oxidative phosphorylation proteins, as well as nucleosome, ribonucleoprotein, and AP protein coat complexes (**Fig 1**). To assess how the proteome changes related to known gout pathways, we "pin-dropped" known central gout signaling molecules into a protein association network derived from the proteomic data (**Fig 2**). From this analysis, we defined a core XOIT2T response linked to known gout mediators (**Fig 2** - black outline), that included increased M2 macrophage markers (TGFB1, PSMB5) and NLRP3 inflammasome inhibition (SUMO3) (**Fig 3**). Differential keratin and 14-3-3 protein expression suggested that XOIT2T alters IL8+ subgroup gout monocytes to limit both a keratinocyte-like subset linked to MMP1 tissue remodeling, and hypermigratory, pro-atherogenic monocytes physiologically suppressed by 14-3-3zeta. However, XOIT2T, which promoted early gout flares, significantly reduced SETDB1, a xanthine oxidase expression regulating histone modifier that also blunts TLR4 inflammatory signaling.

Conclusion: Serum cytokine immunoassays merged with leukocyte quantitative proteomics identified novel markers and mechanisms for gouty arthritis altered by long term flare-reducing XOIT2T. Prior to XOIT2T, gout patients were stratifiable into high and low serum IL8 subgroups. XOIT2T reduced the anti-inflammatory histone H3 modifier SETDB1, a novel potential contributor to early gout flares. However, overall, and especially in IL8+ patients, XOIT2T re-wired the PBMC proteome, promoting mitochondrial function and manifold inflammation resolving mechanisms.

Disclosure: J. Wozniak, None; **R. Bryan**, CymaBay, 2; **D. Gonzalez**, None; **R. Terkeltaub**, Astra-Zeneca, 2, Selecta, 5, Horizon, 5, Genentech, 5, SOBI, 5.

Abstract Number: 0954

Dual-energy CT Predicts Mortality in Gout Patients: A 3-year Follow-up Cohort Study

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020
Session Title: Metabolic & Crystal Arthropathies
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Cardiovascular events, chronic kidney disease and increased mortality are common in gout patients but what links them remains unclear. Tophaceous gout in particular is associated with higher mortality which raised the potential causal role of the monosodium urate (MSU) crystal burden. The volume of MSU crystal depo-

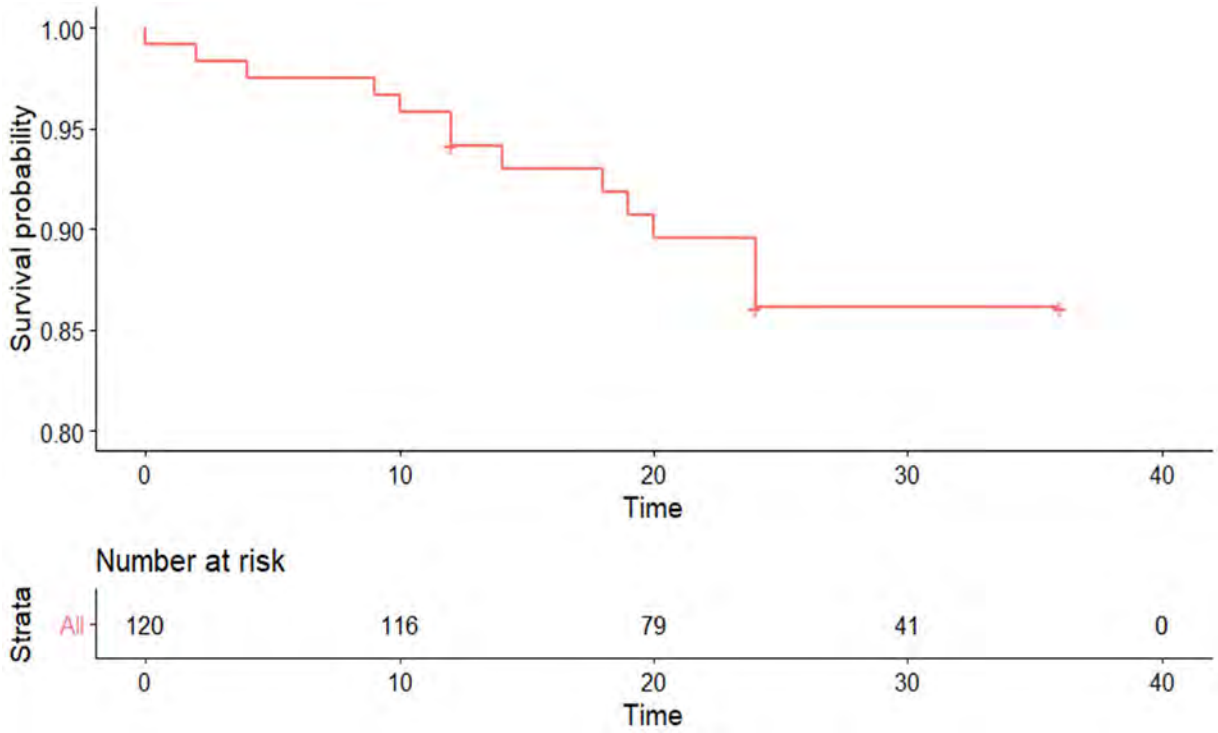

Figure 1. Kaplan-Meyer survival curve.

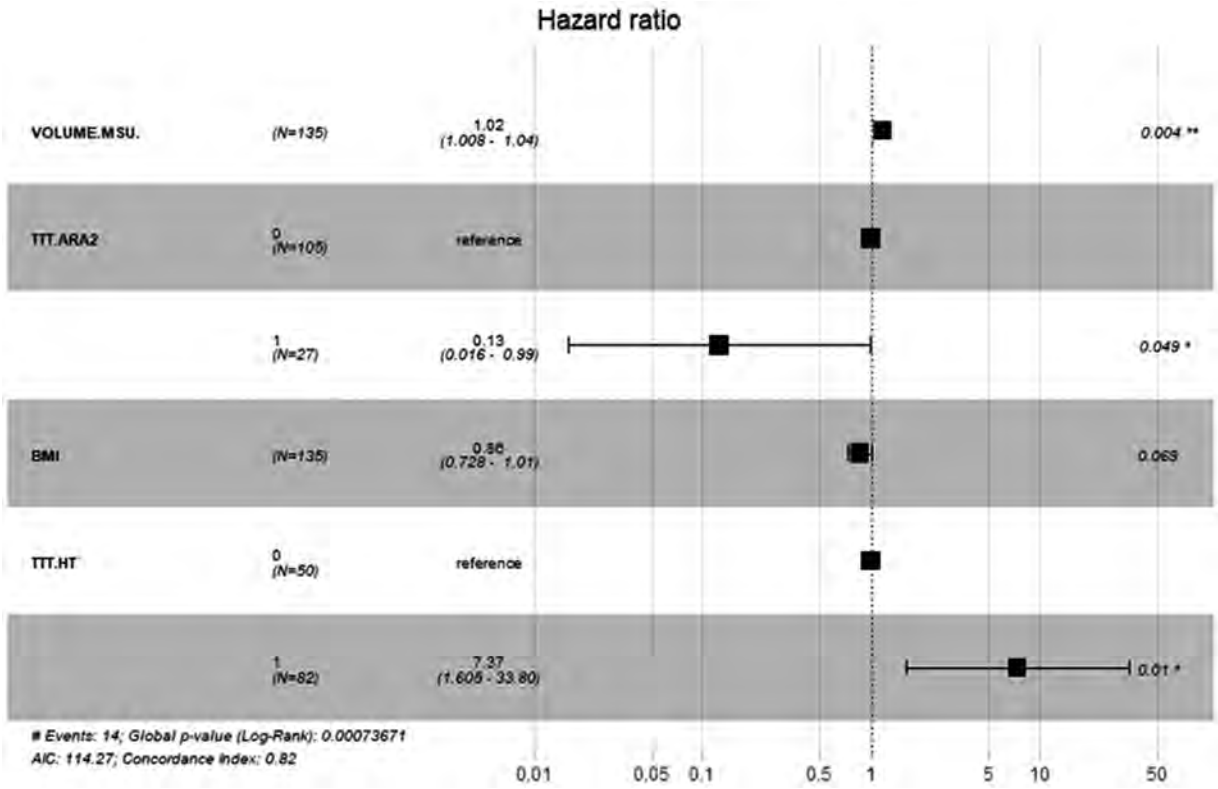

Figure 2. Cox Hazard ratios of factors predictive of short-term mortality in gout patients (within 36 months).

sition in soft tissues measured with dual-energy computed tomography (DECT) is cross-sectionally associated to cardiovascular diseases. The objective of this study was to determine if the initial volume of MSU crystal deposition measured with DECT is predictive of the mortality risk and development of cardiovascular and kidney diseases.

Methods: From April 2016 to May 2019, we prospectively enrolled in the CRYSTALILLE inception cohort of gout patients to undergo baseline DECT scans of both knees and ankles/feet.

Data including disease history and treatment, existing comorbidities, serum urate levels, estimated glomerular filtration rate (eGFR), and volume of MSU crystal deposition measured with DECT at the ankles/feet and knees were assessed at baseline. Data on the onset of major cardiovascular events (MACEs) and mortality, serum urate and eGFR were collected for months 12, 24 and 36. Baseline factors associated with evolution of the eGFR (±5 points of change was considered significant) were studied at months 12, 24 and 36, as well as those associated with MACEs and mortality.

Results: A total of 135 patients were enrolled, they were aged 66 years (±14) years and had a disease duration of 11 years (±10). Patients had baseline serum urate levels of 7.4 mg/dL (±2.2), 62% were naïve of urate lowering therapy and 36% had tophaceous gout. At baseline, 25% of patients had diabetes mellitus, 19% had a history of myocardial infarction, 11% of stroke, and 9% of transient cerebral ischemia.

Follow-up data was available for 123 patients at month 12, 86 at month 24 and 44 at month 36. All-cause mortality was 12% (n=14) during follow-up (Figure 1). In univariate analysis, patients that were deceased during follow-up had a median initial volume of MSU crystal deposition at the knees and feet of 0.4cm^3 [0.2 ; 2.9] and those who survived had a baseline volume of 0.2 cm^3 [0 ; 0.9] (p=0.045). In the multivariate cox model, factors influencing the risk of all-cause mortality were the volume of MSU crystals measured with DECT (HR 1.02 (1.008-1.04) for each additional cm^3), taking with renin-angiotensin inhibitors (HR 0.13 (0.016-0.99)) and taking any anti-hypertensive drugs (HR 7.37 (1.605-33.80)) (Figure 2).

The average serum urate level at months 12 was 5.6 mg/dL (±1.7), 5.9 mg/dL (±2.2) at month 24 and 5.8mg/L (±2.0) at month 36. Overall, at months 12, 24 and 36, 16%, 15% and 21% respectively of patients had improved their eGFR while 36%, 34% and 31% had degraded their eGFR compared to baseline. Neither reaching serum urate levels below 6.0mg/dL nor the initial volume of MSU crystal deposition measured with DECT were predictive of eGFR evolution. A total of 6 (5%) patients presented non-fatal MACE, which was too few to identify predictive factors.

Conclusion: The volume of MSU crystal deposition at the knees and ankles/feet is an independent predictor of short-term mortality in gout patients.

Disclosure: A. Marty-Ané, None; **L. Norberciak**, None; **J. Budzik**, None; **T. Pascart**, Horizon Therapeutics, 2, Novartis, 8.

Abstract Number: 0955

Efficacy and Safety of IVIg (Octagam 10%) in Patients with Active Dermatomyositis. Results of a Randomized, Double-Blind, Placebo-Controlled Phase III Trial (ProDERM Study)

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: Muscle Biology, Myositis & Myopathies

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

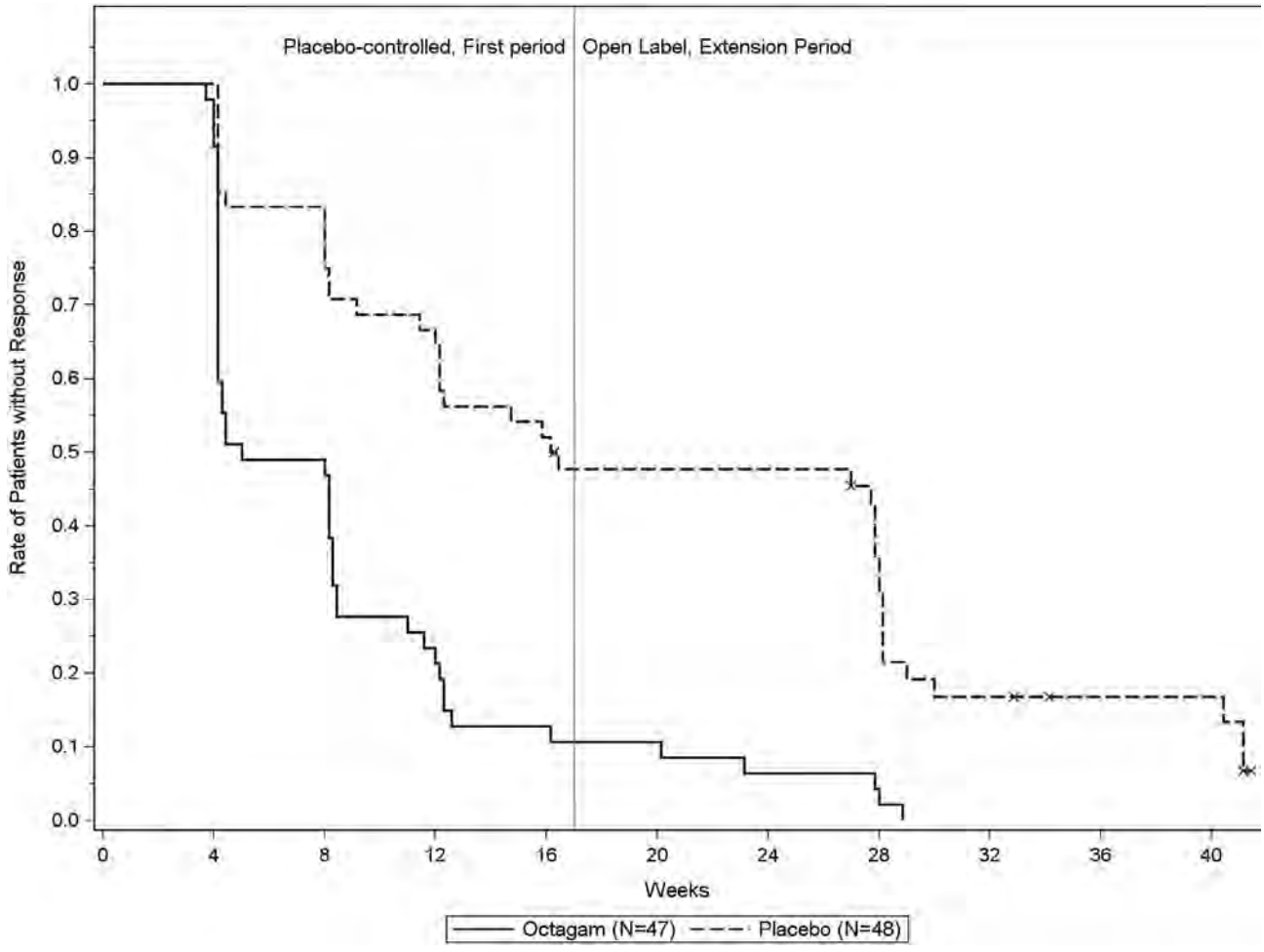

Figure 1. Time to Response (at Least Minimal Improvement; TIS ≥ 20) in both treatment arms

Background/Purpose: Dermatomyositis (DM) is a rare chronic systemic autoimmune disease with characteristic skin rash and progressive proximal muscle weakness. Intravenous immunoglobulin (IVIg) has long been used as adjuvant treatment for DM, but evidence from large randomized clinical trials supporting the efficacy and safety of IVIg in DM is limited.

The ProDERM study aimed to evaluate the efficacy and safety/tolerability of IVIg in DM patients in a double-blind, randomized, placebo-controlled, international multi-centre, phase III clinical trial.

Methods: The trial consisted of 2 periods of 16 and 24 weeks each. In the 1st double-blind, placebo-controlled period, adult patients with definite or probable DM (according to Bohan and Peter criteria) were randomized 1:1 to either high dose IVIg (2g/kg every 4 weeks) or placebo. To be included, subjects must have active disease with a manual muscle testing-8 (MMT-8) score < 142/150. Patients were switched to the alternate treatment arm if they showed clinical worsening (defined according to Oddis *et al*, 2013 - with slight adaptation) between week 8 and week 16. After week 16, all patients on placebo and patients without clinical worsening while on IVIg treatment entered the open label extension period, receiving 2 g/kg IVIg infusions every 4 weeks for 24 weeks. Primary endpoint was the proportion of responders in the IVIg vs. placebo arm at week 16, where response was defined per 2016 ACR/EULAR Myositis response criteria of at least minimal improvement [Total Improvement Score (TIS) ≥ 20 points)] and without clinical worsening at 2 consecutive visits up to week 16.

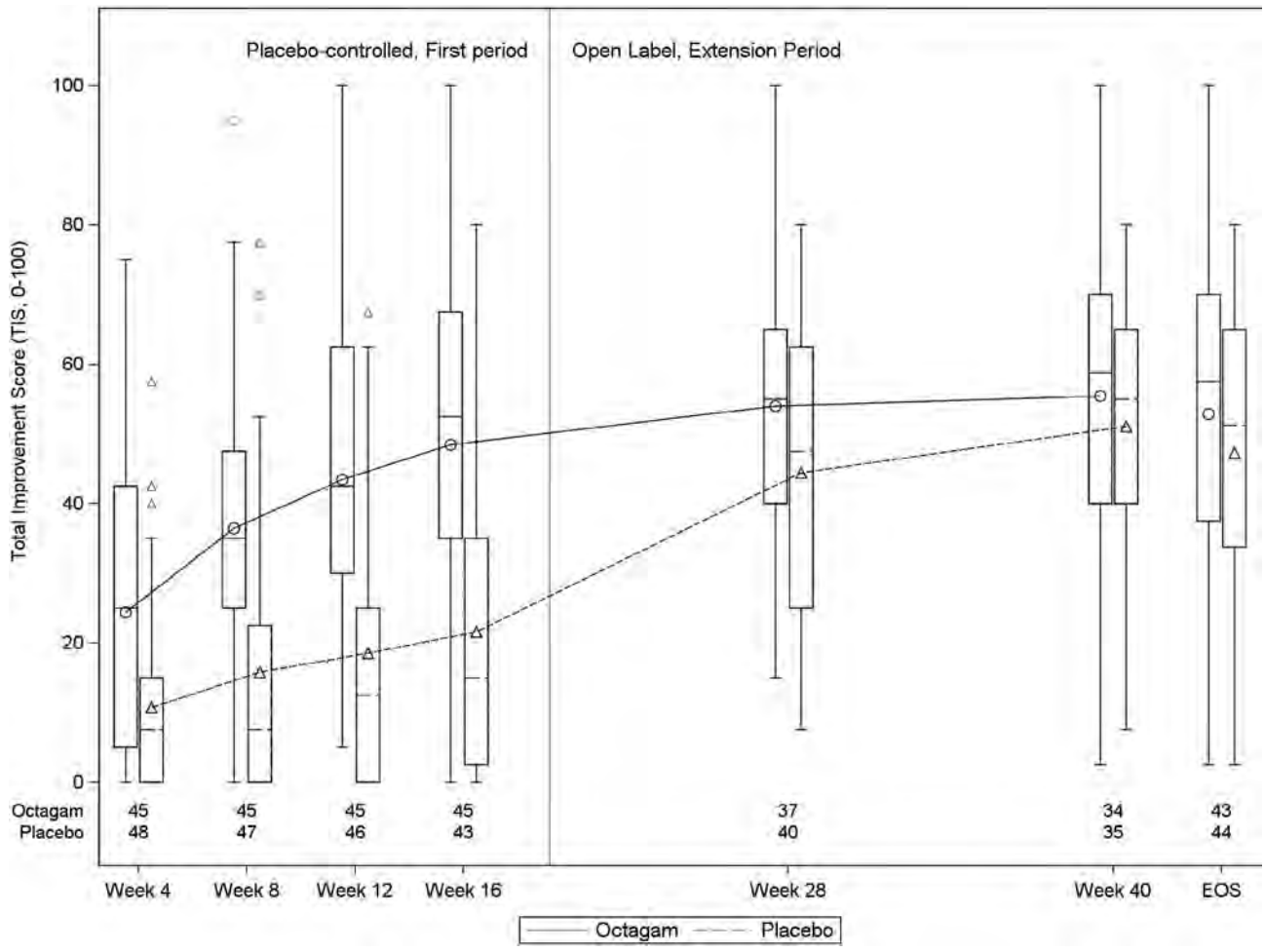

Figure 2. Mean Total Improvement Score (TIS) from week 4 to 40, among the two treatment arms

Results: A total of 95 adult DM patients (mean age: 53 years; 75% females; 92% Caucasian) were enrolled, with 47 and 48 randomized to IVIg and placebo, respectively. Baseline clinical characteristics were balanced between the 2 arms. At week 16, the proportion of responders was significantly higher in the IVIg group (37/47; 78.7%) as compared to the placebo group (21/48; 43.8%; p-value 0.0008) thus meeting the primary endpoint. Only 3 patients worsened in placebo group and none in IVIg group at or before 16 weeks. During the first period time to response was significantly shorter with IVIg (median of 35 days vs. 115 days for placebo; Fig 1).

The difference in response rate was even more marked for at least moderate improvement (TIS $\geq$ 40): 68.1% in the IVIg arm as compared to 22.9% in the placebo arm ($p < 0.0001$).

The mean TIS (SD) was significantly higher in IVIg group [48.4 (24.4)] than in placebo arm [21.6 (20.2)] at week 16 (Fig 2).

The proportion of responders as well as mean TIS at the end of the open-label extension period (week 16 to week 40) was similar in both treatment groups, showing that patients randomized to placebo in the first period improved after switching to IVIg in the extension period (Fig 1,2). Other secondary end points [e.g. MMT-8 and Cutaneous DM Disease Activity Area and Severity index (CDASI)], were also met, further supporting efficacy of IVIg.

The safety and tolerability profile of IVIg was consistent with previously reported safety outcomes.

Conclusion: This is the first large international phase III randomized, placebo-controlled trial demonstrating the efficacy and safety of IVIg as a treatment for patients with DM.

Disclosure: R. Aggarwal, Octapharma, 5, Bristol Myers Squibb, 2, 5, Abbvie, 5, Mallinckrodt, 2, 5, Pfizer, 2, Csl Behring, 5, Kezar, 5; **C. Charles-Schoeman**, AbbVie, 2, 5, Regeneron-Sanofi, 5, Gilead, 5, Bristol-Myers Squibb, 2, Pfizer Inc, 2, 5; **J. Schessl**, Octapharma, 5; **Z. Bata-Csorgo**, None; **M. Dimachkie**, ArgenX, 5, Catalyst, 2, 5, CSL-Behring, 2, 5, Kezar, 5, Momenta, 5, NuFactor, 5, Octapharma, 2, 5, RMS Medical, 5, Sanofi Genzyme, 5, Shire/Takeda, 2, 5, Spark Therapeutics, 2, 5, Alexion, 2, Alnylam Pharmaceuticals, 2, Amicus, 2, Biomarin, 2, Bristol-Myer Squibb, 2, Glaxo Smith Kline, 2, Genentech, 2, Grifols, 2, Mitsubishi Tanabe Pharma, 2, MDA, 2, Novartis, 2, Orphazyme, 2, Sarepta Therapeutics, 2, UCB Biopharma, 2, Viromed&TMA, 2; **Z. Griger**, Octapharma, 5, Abbvie, 8, CSL Behring, 8, Eli Lilly, 8, Novartis, 8, Roche, 8; **S. Moiseev**, None; **C. Oddis**, Genentech, 2; **E. Schiopu**, Octapharma, 2; **J. Vencovský**, Eli Lilly, 5, 8, Abbvie, 5, 8, Boehringer, 5, Octapharma, 5, Sanofi, 8, Merck, 8, Biogen, 8, UCB Biopharma, 8, Roche, 8, Pfizer, 8; **B. Irene**, Octapharma, 3; **C. Elisabeth**, Octapharma, 3; **T. Levine**, Nufactor, 5, Octapharma, 5; **a. ProDERM Investigators**, None.

Abstract Number: 0956

An IL-18-Containing Five-Gene Signature Distinguishes Histologically Identical Dermatomyositis and Lupus Erythematosus Skin Lesions

Alex Tsoi[1], Mehrnaz Gharaee-Kermani[2], Celine Berthier[1], Tori Nault[3], Grace Hile[2], Shannon Estadt[4], Matthew Patrick[1], Rachael Wasikowski[1], Allison Billi[1], Lori Lowe[1], Tamra Reed[1], Johann Gudjonsson[5] and **J. Michelle Kahlenberg**[6], [1]University of Michigan, Ann Arbor, [2]University of Michigan, Ann Arbor, MI, [3]University of Michigan, Canton, MI, [4]University of Michigan, Ypsilanti, MI, [5]University of Michigan, Ann ArborUniversity of Michigan, [6]Division of Rheumatology, University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Muscle Biology, Myositis & Myopathies
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Skin lesions in dermatomyositis (DM) patients are common, frequently refractory, and have prognostic significance. Histologically, DM lesions appear similar to cutaneous lupus erythematosus (CLE) lesions and frequently cannot be differentiated. We thus undertook to examine the transcriptional profile of DM biopsies and compared them to CLE lesions in order to identify unique features.

Methods: For the inquiry cohort, 43 skin biopsies from 36 unique DM patients were identified within the University of Michigan Pathology Database. Comparative cases of 43 subacute cutaneous lupus erythematosus (SCLE) and 47 discoid lupus erythematosus (DLE) biopsies were similarly acquired. RNA was isolated and expression analysis was completed through the University of Michigan Advanced Genomics core using Affymetrix Human Gene ST 2.1 array plates for transcriptional analysis. Following normalization, 5-fold cross-validation was used to train random forest classifiers for genes that are only up-regulated in the control vs DM comparison microarray but not in the control vs CLE comparison (restricted to genes with $p > 0.5$ and $\log_2 FC < |\log_2 1.5|$). A secondary validation cohort was analyzed by real-time quantitative PCR and two additional patients underwent single-cell RNA sequencing. Protein expression was confirmed by immunohistochemistry.

Results: Type I interferon (IFN) signaling, including upregulation of IFN kappa, was a common pathway in both DM and CLE, but CLE also exhibited other inflammatory pathways. Importantly, DM lesions could be distinguished from CLE by a five-gene biomarker panel that included upregulation of *IL18*. Using single-cell RNA-sequencing, we further identified keratinocytes and monocyte/macrophages as the source of increased IL-18 in DM skin.

Conclusion: The novel molecular signature identified in this study has significant clinical implications for differentiating DM from CLE lesions, and we have highlighted the potential role for IL-18 in the pathophysiology of DM skin disease. Further work should examine the potential for anti-IL-18 directed therapies to treat DM skin lesions.

Disclosure: A. Tsoi, None; **M. Gharaee-Kermani**, None; **C. Berthier**, None; **T. Nault**, None; **G. Hile**, None; **S. Estadt**, None; **M. Patrick**, None; **R. Wasikowski**, None; **A. Billi**, None; **L. Lowe**, None; **T. Reed**, None; **J. Gudjonsson**, Celgene, 2; **J. Kahlenberg**, AstraZeneca, 5, Bristol Myers Squibb, 2, 5, Eli Lilly, 5, Avion Pharma, 5, Celgene, 2.

Abstract Number: 0957

Mitochondrial ROS as a Regulator of Calcinosis in Juvenile Dermatomyositis

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Muscle Biology, Myositis & Myopathies
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Calcinosis, the accumulation of calcium crystals in soft tissues, is often a locus of infection and a debilitating manifestation of chronic juvenile dermatomyositis (JDM), contributing to long-term disability and sometimes death. Mechanistic understanding of calcinosis in JDM remains poorly understood, thus impeding therapeutic strategies. Our prior findings that the presence of calcified mitochondria and their remnants in degenerated muscle fibers and blood of JDM associated with calcinosis suggested that mitochondrial calcification plays a central role in JDM calcinosis. In this study, we hypothesized that the pathophysiological process in chronic active JDM contributes to mitochondrial activation and impairment, leading to mitochondrial calcification and extrusion.

Methods: To facilitate mitochondrial calcification, human skeletal muscle cells (RH30 cell line) were incubated in calcium phosphate (Ca-P) solution in the absence or presence of $CoCl_2$ (100 μM) or recombinant interferon-α (IFN-α) to mimic hypoxia and inflammation, respectively. Calcification in cells was assessed using Osteoimage, a stain for hydroxyapatite calcium salt crystals, by flow cytometry and microscopy. The extrusion of calcified mitochondria was determined by fluorescence microscopy. Mitochondrial damage was analyzed by flow cytometric analysis of mitochondrial ROS (mtROS) using fluorescent stain MitoSOX. Inflammation in RH30 cells in response to calcification was quantified by RT-PCR and ELISA.

Results: Hypoxia-mimetic $CoCl_2$ augmented Ca-P media-induced calcification in RH30 cells (% of osteoimage+ cells, 86.85 vs. 52.25; MFI 66929 vs. 12649, $p< 0.05$). Hypoxia caused mitochondrial formation of ROS, a process deemed essential for calcification as mitoTEMPO, a mitochondrial ROS scavenger, completely abrogated mitochondrial calcification. Fluorescent microscopy revealed an extrusion of calcified mitochondria in extracellular vesicles, resembling calcinosis. Muscle cells undergoing mitochondrial calcification demonstrated inflammation characterized by increased expression of interferon-induced genes and secretion of IL-6 in cellular supernatants. Finally, we hypothesized that IFN-α, one of the pathogenic factors of JDM found in muscle tissue, would promote mitochondrial calcification. Accordingly, we found a dose-dependent increase in the calcification of RH30 cells cultured in the Ca-P medium supplemented with IFN-α ($p< 0.05$).

Conclusion: Mitochondrial ROS is a chief regulator of mitochondrial calcification and extrusion in *in vitro* systems, promoting inflammation in muscle cells. Calcinosis associated with JDM is dystrophic, which, by definition, occurs in injured tissues despite the presence of normal systemic levels of calcium and phosphate. Hence, pathologic calcification in JDM does not regress in response to therapy of calcium depletion suggesting a role of local mechanisms in calcium dyshomeostasis. Our findings suggest that therapeutic agents targeting mtROS may prevent mitochondrial impairment and subsequent mitochondrial calcification/extrusion in skeletal muscle cells reducing calcinosis.

Disclosure: B. Duvvuri, None; **L. Pachman**, Reveragen, 2; **R. Moore**, None; **S. Doty**, None; **C. Lood**, Horizon Diagnostic, 2, Exagen, 2, Eli Lilly, 2.

Abstract Number: 0958

Tocilizumab in Myositis: Results of a Phase IIb Double-Blind Randomized Controlled Trial

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Muscle Biology, Myositis & Myopathies
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: To assess the efficacy and tolerability of tocilizumab (anti-IL-6R, TCZ), in a multi-center, randomized, double blind, placebo-controlled trial in refractory adult dermatomyositis (DM) and polymyositis (PM) patients.

Methods: Adult patients with refractory DM and PM were enrolled in a phase IIb double blind; placebo-controlled, clinical trial randomized 1:1 for active drug:placebo for 6 months, with a targeted enrollment of 40 subjects. Inclusion criteria included: (a) probable or definite PM or DM (modified Bohan and Peter criteria), (b) either a classic DM rash, a myositis associated autoAb *or* a PM diagnosis vetted by adjudication, (c) refractory myositis defined by glucocorticoid (GC) failure, or GC/at least one other immunosuppressive failure and (d) active disease defined by at least 3 of 6 abnormal myositis core set measures (CSM) including an MMT< 136/150 or if MMT >136 then the 3 abnormal CSM plus a cutaneous VAS ≥ 3/10 cm. Subjects were randomized to receive either 6 doses of TCZ (8 mg/kg IV) or placebo every 4 weeks for 24 weeks. The primary endpoint compared the Total Improvement Score (TIS; 2016 ACR/EULAR Criteria) between both arms at weeks 4-24, using a GEE model including treatment, diagnosis and time. Secondary outcomes included time to meeting minimal improvement, changes in CSM, steroid-sparing effect, proportion of patients meeting minimal, moderate and major improvement, and safety/tolerability outcomes between both treatment arms.

Results: 36 subjects (23DM, 13PM) were randomized (18 in each arm) and analyzed using intention to treat. All but 4 (2 TCZ/2 placebo) completed 24 weeks of treatment. There was no significant difference (p=0.86) in the TIS (primary outcome) over 24 weeks between TCZ and placebo in the entire cohort or by subgroup (DM alone). There was no significant difference in the mean TIS score over 4-24 weeks between the two arms [mean (SD) all visits: TIS 26.4 (16.75) vs. 29.3 (16.76)] (Figure 1). However, the mean TIS improved significantly (p=0.02) from baseline to the last study visit in both arms. The proportion of patients meeting no, minimal, moderate and major improvement at last study visit, were similar (p=0.22) in both arms [TCZ: 8 (44.4%), 3 (16.7%), 4 (22.2%), and 3 (16.7%); placebo: 5 (27.7%), 5 (27.7%), 6 (33.3%) and 2 (11.1%), (Figure 2)]. The secondary endpoints of time to minimal improvement, CSM change, and steroid-sparing effect were not significantly different between treatment arms. The adverse/serious adverse events (AE/SAE) were not significantly different between both arms [TCZ: 14 events (44.4 % of pts) vs. 9 events (33.3% of pts)]. TCZ was well tolerated and only 4 patients stopped treatment early due to disease worsening (n=3) or SAE (n=1).

Conclusion: TCZ treatment did not meet the primary or secondary efficacy outcomes in refractory DM and PM in this 24-week phase IIb study. TCZ was safe and well tolerated.

Disclosure: R. Aggarwal, Octapharma, 5, Bristol Myers Squibb, 2, 5, Abbvie, 5, Mallinckrodt, 2, 5, Pfizer, 2, Csl Behring, 5, Kezar, 5; **H. Rockette**, None; **S. Venturupalli**, None; **G. Marder**, GSK, 2; **M. Dimachkie**, ArgenX, 5, Catalyst, 2, 5, CSL-Behring, 2, 5, Kezar, 5, Momenta, 5, NuFactor, 5, Octapharma, 2, 5, RMS Medical, 5, Sanofi Genzyme, 5, Shire/Takeda, 2, 5, Spark Therapeutics, 2, 5, Alexion, 2, Alnylam Pharmaceuticals, 2, Amicus, 2, Biomarin, 2, Bristol-Myer Squibb, 2, Glaxo Smith Kline, 2, Genentech, 2, Grifols, 2, Mitsubishi Tanabe Pharma, 2, MDA, 2, Novartis, 2, Orphazyme, 2, Sarepta Therapeutics, 2, UCB Biopharma, 2, Viromed&TMA, 2; **D. Gazeley**, None; **F. Ernste**, None; **L. Crofford**, None; **S. Moghadam-Kia**, None; **D. Koontz**, None; **L. Zhu**, None; **C. Oddis**, Genentech, 2.

Abstract Number: 0959

Altered Gut Microbiome in Dermatomyositis

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SESSION INFORMATION
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Background/Purpose: Dermatomyositis (DM) is an autoimmune myopathy associated with marked microvascular dysfunction and high morbidity and mortality. The gut microbiome has been implicated in the pathogenesis of both vascular and autoimmune disease, however, no studies to date have evaluated whether the gut microbiome is altered in patients with dermatomyositis.

Methods: Fecal samples from DM patients and healthy controls underwent 16S rRNA gene sequencing by Illumina MiSeq. Amplicon sequence variants were identified using DADA2 and the SILVA 132 database. Microbial composition was compared between DM and control groups (beta diversity analysis) using the robust Aitchison distance metric and permutational multivariate analysis of variance controlled for significant differences between groups such as antibiotic use. Alpha diversity was measured by the Shannon Index (reflecting species richness and evenness in each sample) and was compared between groups using analysis of variance. Microbiome diversity and composition were also examined in association with several clinical variables including myositis-specific autoantibodies (MSA). Differentially abundant microbial taxa associated with clinical characteristics were identified using DESeq2.

Results: A total of 36 DM patients and 26 healthy controls (Table 1) were analyzed. Compared with controls, DM patients exhibited a trend towards lower microbial alpha diversity based on the Shannon index (p= 0.08). Higher disease damage (measured by physician global visual analogue scales) in DM patients was significantly correlated with lower microbial diversity (Figure 1-d). When DM patients were analyzed by MSA subgroups (ILD-associated MSA: antisynthetase ab,anti-MDA5 ab, n=12; Cancer-associated: anti-NXP2 ab, anti-TIF1gamma ab, n=13) and compared with controls, there were significant differences in their microbial composition (Figure 2-a). This was also associated with significantly reduced Shannon index in the ILD-associated MSA group compared to controls (Figure 2-b). Differential abundance testing demonstrated that several amplicon sequence variants within the *Firmicutes*, *Actinobacteria*and *Bacteroidetes* phyla were found in greater abundance in ILD-associated and cancer-associated MSA patients compared to controls (Figure 2-d).

Conclusion: DM patients with ILD-associated MSAs have an altered gut microbiome including significantly decreased microbial diversity. Further studies are warranted to determine whether these abnormalities contribute to disease pathogenesis including microvascular damage.

Table 1. Demographics and Clinical Characteristics in DM and healthy controls

	DM (n=36)	Controls (n=26)
Age, years	47±15	47±17
Gender, female	27(75)	17(65)
Ethnicity, hispanic	3(8)	4(15)
Race		
White	23(63)	18(69)
Black	5(14)	1(4)
Asian	8(22)	7(27)
Current use of antibiotics	22(61)*	2(8)
Use of antibiotics within 3 months	22(61)*	3(12)
Current use of probiotic oral supplement	4(11)	3(12)
Hs-CRP, mg/L	2.6±4.6	2.0±3.5
Sedimentation rate, mm/hr	30±25 *	11±8
Disease duration, months	75±95	
Disease specific outcome measures		
Phys global activity VAS 0-100mm	34±26	
Phys global activity Likert, median (IQR)	1.5 (1-2)	
Physician global damage VAS, 0-100mm	26±23	
Physician global damage Likert, median(IQR)	1 (1-2)	
CDASI, activity score	5±5	
CDASI damage score	1±2	
MMT8, 0-150, median (IQR)	148.5 (145-150)	
CPK,U/L	207±299	
LD, U/L	234±137	
Aldolase, U/L	6.0±6.0	
Myositis autoantibodies		
Anti-MDA5 ab	7(19)	
Anti-Jo1 ab	4(11)	
Anti-PL-12 ab	1(3)	
Anti-TIF1gamma ab	8(22)	
Anti-NXP2 ab	6(17)	
Anti-Mi2 ab	3(8)	
Anti-SRP ab	2(6)	
Anti-Ro/SSA ab	2(6)	
Unidentified	1(3)	
No Ab	1(3)	
ILD, yes	14(39)	
Pulmonary function tests		
FVC % predicted	94±22	
FEV1/FVC % predicted	95±10	
TLC % predicted	92±28	
DLCO % predicted	77±21	
Medications		
Methotrexate	3(8)	
Azathioprine	1(3)	
Plaquenil	8(22)	
Mycophenolate Mofetil	21(58)	
Intravenous Immunoglobulin	28(78)	
Rituximab	5(14)	
Cyclophosphamide	3(8)	
Prednisone	28(78)	
Daily prednisone dose, mg/day	15±17	

Values reported as mean ±SD or n(%) unless specified

*p<0.05 in DM vs controls

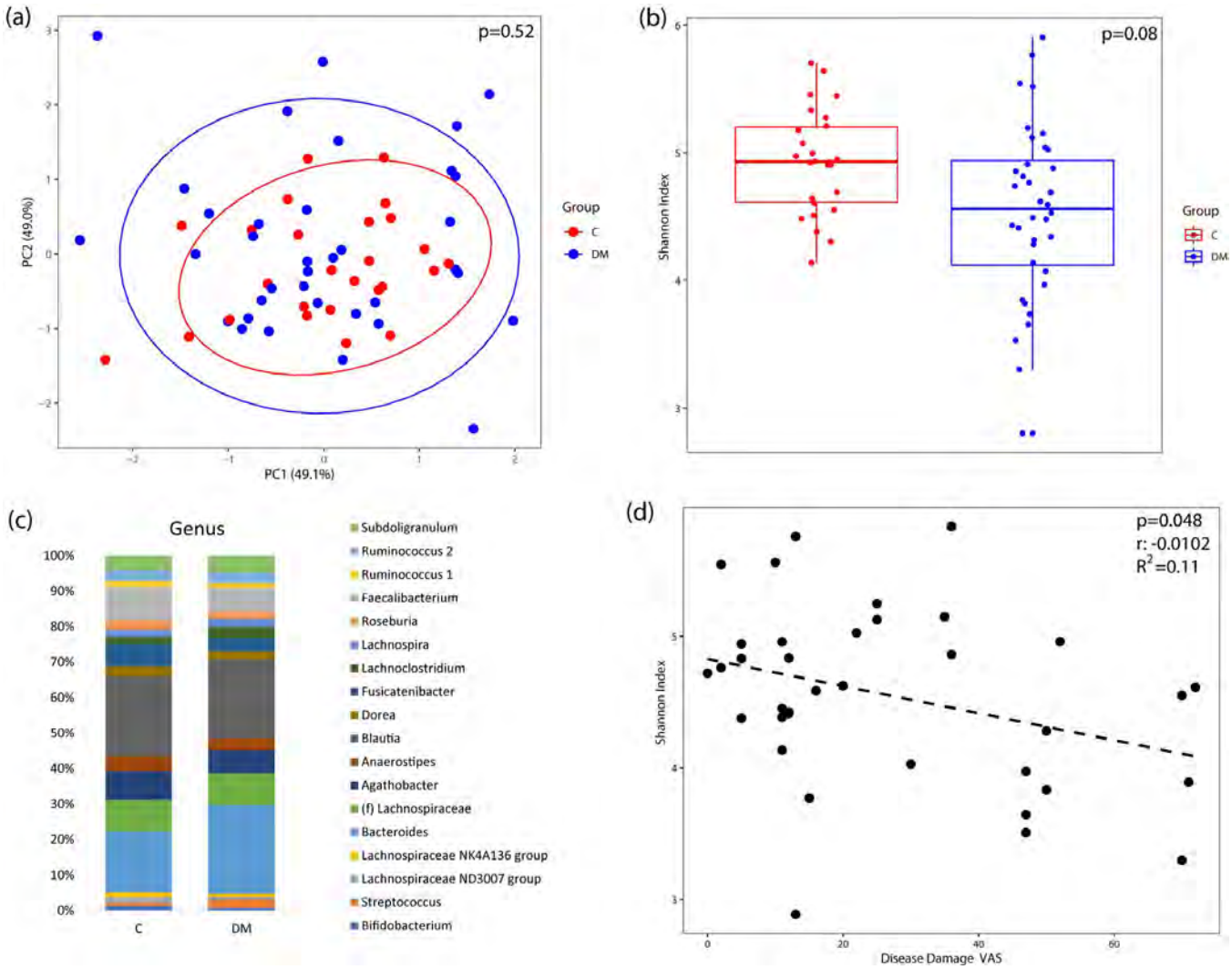

Figure 1. Microbiome diversity in DM patients (n=36) compared to healthy controls (n=26). (a) Comparing the overall microbial composition in DM and healthy control samples by principal components analysis plot using a robust Aitchison distance matrix. Each dot represents a sample from a DM patient (blue) or a healthy control (red). Ellipse represents the 95% confidence interval for each group. (b) Species evenness and richness in DM vs controls by Shannon index adjusted for significant differences in antibiotic use. p value = 0.08 (c) Taxa summary plots between DM and control with only those genera with a relative abundance of ≥ 1%. No genus was differentially abundant in DM compared to controls. (d) Higher disease damage score by visual analog scale in DM patients was significantly correlated with lower evenness and diversity of microbial species.

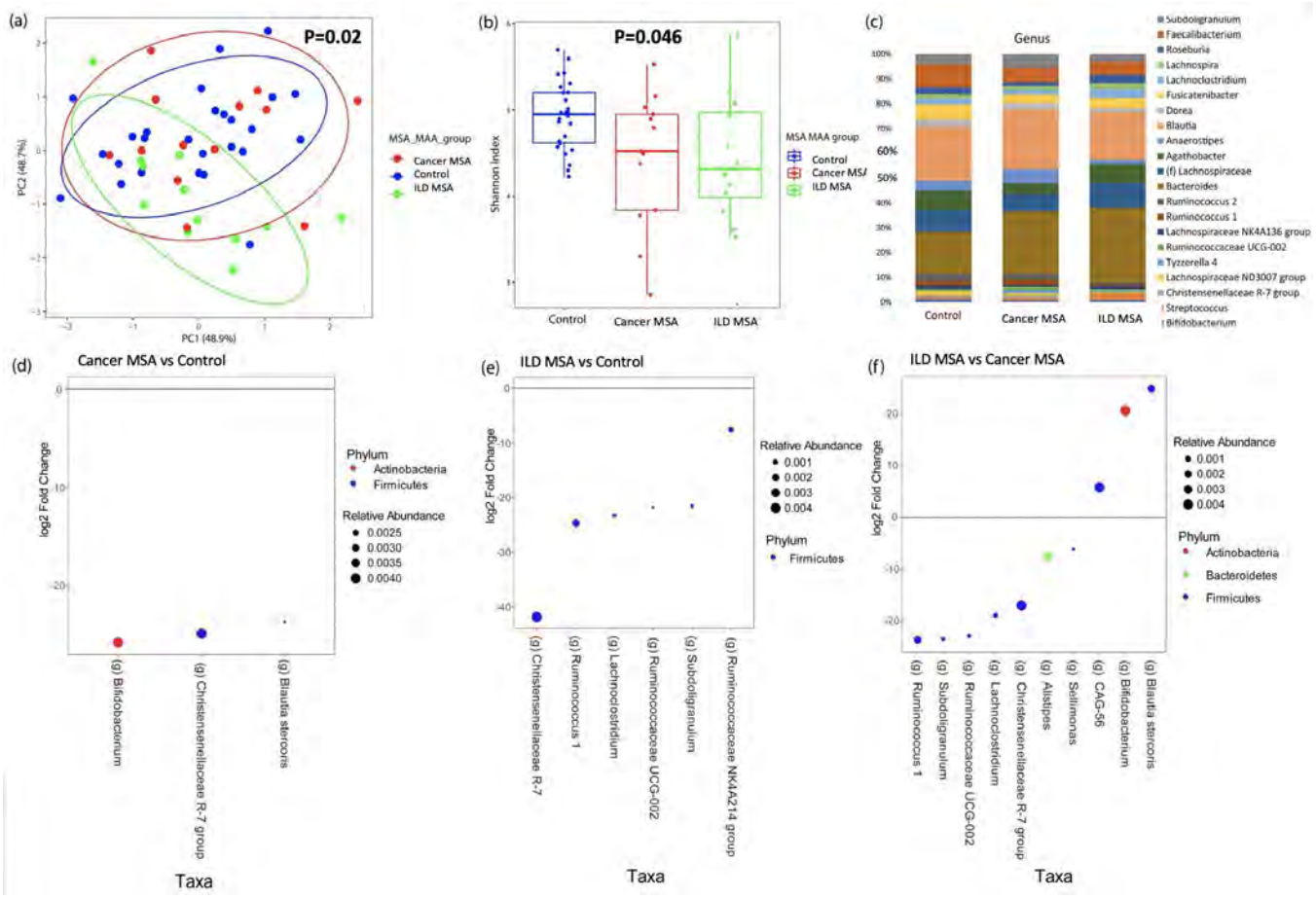

Figure 2. Microbiome diversity in DM patients by MSA subgroups (ILD associated MSA n=12, Cancer associated MSA n=13) compared to healthy controls (n=26). (a) Significant differences in the overall microbial composition between MSA/MAA subgroups of DM and controls. Each dot represents a sample from a DM patient with ILD associated MSA (green), DM patient with cancer associated MSA (red) or healthy control (blue). Ellipse represents the 95% confidence interval for each group. (b) Decreased species evenness and richness in MSA/MAA subgroups of DM compared to controls. (c) Taxonomic summary plots by MSA subgroups, only showing those genera with a relative abundance ≥ 1%. Differential abundance testing at the amplicon sequence variant level between (d) cancer associated MSA patients vs control, (e) ILD associated MSA patients vs control, and (f) ILD associated MSA patients vs Cancer associated MSA patients.

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Abstract Number: 0960

The Risk of Venous Thromboembolism After Septic Total Knee Replacement (TKR) Revision Is Double the Risk After Aseptic TKR Revision: An Analysis of Administrative Discharge Data

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SESSION INFORMATION

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Background/Purpose: Infection can trigger coagulation pathways and increase the risk of thrombosis. However, the impact of infection on postoperative venous thromboembolism (VTE) risk is poorly defined. The aim of this study was to assess the 90-day risk of VTE following total knee replacement (TKR) revision by indication for revision to estimate the impact of infection on postoperative VTE risk.

Table 1: Cohort description of Total Knee Replacement revisions

	Overall	Aseptic	Septic	Fracture	p-value
	25441	17563	7075	803	
	n (%)	n (%)	n (%)	n (%)	
Age - *mean (SD)*	66 (12)	66 (12)	67 (12)	72 (13)	<.001
Sex - Female	15592 (61)	11019 (63)	3962 (56)	611 (76)	<.001
Race White	19025 (75)	13146 (75)	5237 (74)	642 (80)	<.001
Black	3198 (13)	2240 (13)	883 (13)	75 (9)	
Asian	208 (0.8)	118 (0.7)	85 (1.2)	5 (0.6	
Other	2022 (8)	1315 (8)	648 (9)	59 (7)	
Unknown	988 (4)	744 (4)	222 (3)	22 (3)	
Hispanic Yes	1670 (7)	1098 (6)	521 (7)	51 (6)	<.001
No	21701 (85)	14956 (85)	6033 (85)	712 (89)	
Unknown	2070 (8)	1509 (9)	521 (7)	40 (5)	
Smoker	1192 (5)	806 (5)	356 (5)	30 (4)	0.143
Diabetes	5589 (22)	3501 (20)	1875 (27)	213 (27)	<.001
Obesity	4222 (17)	2893 (17)	1201 (17)	128 (16)	0.555
Renal disease	1096 (4)	470 (3)	563 (8)	63 (8)	<.001
COPD	226 (0.9)	148 (0.8)	66 (0.9)	12 (1.5)	0.141
Sleep apnea	1656 (7)	1168 (7)	457 (7)	31 (4)	0.007
Pulmonary hypertension	241 (1)	111 (0.6)	111 (2)	19 (2)	<.001
Cerebrovascular disease	*	101 (0.5)	72 (1)	*	0.001
Heart failure	1169 (5)	513 (3)	581 (8)	75 (9)	<.001
Dementia	*	23 (0.1)	26 (0.4)	*	<.001
Cancer	518 (2)	272 (2)	219 (3)	27 (3)	<.001
Myeloproliferative disorder, polycythemia	*	*	*	*	0.785
Inflammatory bowel disease	*	83 (0.5)	25 (0.4)	*	0.422
Rheumatoid arthritis	1247 (5)	765 (4)	422 (6)	60 (8)	<.001
Psoriatic arthritis	*	38 (0.2)	21 (0.3)	*	0.505
Spondyloarthropathy	*	*	*	*	0.102
SLE	*	95 (0.5)	67 (1.0)	*	0.002
Venous insufficiency, varicose veins	*	113 (0.6)	20 (0.3)	*	0.001
History of prior VTE	889 (4)	572 (3)	288 (4)	29 (4)	0.007
Thrombophilia	*	45 (0.3)	22 (0.3)	*	0.751

We do not report values for cells containing < 11 individuals; COPD = chronic obstructive pulmonary disease; SLE = systemic lupus erythematosus; VTE = venous thromboembolism

Table 1. Cohort description of Total Knee Replacement revisions

Table 2: VTE within 90 days of aseptic, septic and fracture-related TKR revision

	Overall n (%)	Aseptic n (%)	Septic n (%)	Fracture n (%)	p-value
Venous thromboembolism	719 (2.8)	367 (2.1)	305 (4.3)	47 (5.9)	<.001
Pulmonary embolism	203 (0.8)	115 (0.7)	73 (1.0)	15 (1.9)	<.001
Deep vein thrombosis	568 (2.2)	274 (1.6)	258 (3.7)	36 (4.5)	<.001

VTE = venous thromboembolism; TKR = total knee replacement

Table 2. VTE within 90 days of aseptic, septic and fracture-related TKR revision

Methods: We used New York Statewide Planning and Research Cooperative System data to identify all New York

Table 3: Risk of VTE within 90 days of septic and fracture TKR revision in comparison to aseptic TKR revision: results of multivariable logistic regression analysis

	Odds ratio (95% confidence interval)	P value
Septic TKR revision	2.01 (1.72-2.36)	<.001
Fracture TKR revision	2.61 (1.9-3.58)	<.001

VTE = venous thromboembolism; TKR = total knee replacement

Table 3. Risk of VTE within 90 days of septic and fracture TKR revision in comparison to aseptic TKR revision: results of multivariable logistic regression analysis

State residents undergoing TKR revision from 1998 to 2014. Only the first revision was included for patients undergoing multiple revisions. ICD-9-CM codes were used to identify patient comorbidities and classify indication for TKR revision as aseptic, septic or fracture. The primary outcome was any diagnosis code for VTE (pulmonary embolism and/or deep vein thrombosis) recorded for the revision surgery and/or subsequent admissions within 90 days. A multivariable logistic regression analysis adjusting for demographics and comorbidities was performed to estimate the risk of VTE after septic vs aseptic revision TKR, and of fracture-related revision vs. aseptic revision.

Results: This study included 25,441 TKR revision surgeries, 17,563 (69%) of them aseptic, 7075 (28%) septic and 803 (3%) for fracture. Mean (SD) age was 66 (12) years, 15,592 (61%) were female, 3198 (12%) were black, 1192 (5%) were smokers and 4222 (17%) were obese (**Table 1**). A total of 719 (2.8%) patients experienced VTE within 90 days of revision TKR, 387 (1.5%) during the index admission. The 90-day incidence of VTE was 2.1% after aseptic revision, 4.3% after septic revision and 5.9% after revision for fracture (**Table 2**). The 90-day incidence of pulmonary embolism was 0.7% after aseptic revision, 1.0% after septic revision and 1.9% after revision for fracture. The adjusted odds ratio (OR) for VTE relative to aseptic revision was 2.01 (95% CI 1.72-2.36) for septic TKR revision and 2.61 (95% CI 1.9-3.58) for fracture-related TKR revision (**Table 3**). Prior history of VTE was also a risk factor for post revision VTE (OR 2.01, 95% CI 1.48-2.71, p< 0.001).

Conclusion: The risk of VTE after septic TKR revision is double that after aseptic TKR revision. Although fractures account for a small percentage of TKR revisions, the risk of VTE is 2.6-fold higher after those procedures. VTE prophylaxis guidelines should distinguish between the indications for TKR revision, and potent/fast acting VTE prophylaxis should be strongly considered in those with infection or fracture.

Disclosure: A. Bass, None; **B. Mehta**, None; **P. Sculco**, EOS imaging, 1, Intellijoint Surgical, 1, Depuy Synthes, 1, Lima Corporate, 1; **Y. Zhang**, None; **H. Do**, None; **L. Russell**, None; **S. Goodman**, Pfizer, 1, Novartis, 1, UCB, 1, regenosine, 1, 2, Horizon, 1.

Abstract Number: 0961

Development of a Pain Sensitivity Index to Examine the Transition from Intermittent to Constant Pain in Knee Osteoarthritis: The Multicenter Osteoarthritis Study

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SESSION INFORMATION

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Background/Purpose: Alterations in nociceptive signaling, such as pain sensitization, which is an abnormal ascending pain facilitation, and/or inadequate descending pain modulation, are thought to be underlying mechanisms contributing to the transition from intermittent to constant pain in knee osteoarthritis (OA). Studies to date have primarily focused on individual measures of pain sensitivity, which can be assessed by quantitative sensory testing (QST). Whether combining pain sensitivity measures may provide better insights into the transition from intermittent to persistent pain than individual QST measures is not known. We therefore sought to develop a composite pain sensitivity index (PSI) based on QST measures that incorporates multiple aspects of nociceptive alterations and evaluated its relation to development of constant pain in knee OA.

Methods: We included subjects from the Multicenter Osteoarthritis (MOST) Study, a NIH-funded longitudinal cohort study of persons with or at risk of knee OA. We assessed Intermittent and Constant Osteoarthritis Pain (ICOAP) at baseline and two years later, and the following QST measures at baseline: i) pressure pain thresholds (PPT) at the wrist and patellae assessed with an algometer as the point at which pressure changed to slight pain; ii) temporal summation (TS) at the wrist using weighted probes; and iii) conditioned pain modulation (CPM) using PPT at the wrist as the test stimulus pre- and post-conditioning stimulus (forearm ischemia); CPM was computed as the post-PPT: pre-PPT ratio. Each QST measure was standardized and rescaled to 0-100 score, and then the PSI was created by taking the average of the summed scores of the four measures with equal weights, leading to PSI on a 0-100 scale. A lower PSI score represents greater pain sensitivity. Among participants at baseline who had intermittent pain of at

	Development of Constant Pain
Per 10-unit increase	*Odds ratio (95% CI)*
Pain Sensitivity Index	**0.67 (0.49, 0.92)**
PPT, wrist	0.81 (0.67, 0.99)
PPT, patella	0.84 (0.73, 0.97)
TS, wrist	1.00 (0.77, 1.30)
CPM	0.80 (0.44, 1.48)
Analyses were adjusted for age, sex, race, body mass index (BMI), widespread pain, sleep, depressive symptoms, pain catastrophizing, and use of opioids. QST: quantitative sensory testing, PPT: pressure pain threshold, TS: temporal summation, CPM: conditioned pain modulation,	

Table. Relation of PSI Score vs. Individual QST to Developing of Constant Pain Over Two-year Period

least ‘mild’ severity occurring ‘sometimes’, we examined the relation of the PSI to the development of knee-specific constant pain by ICOAP two years later using logistic regression with GEE, adjusting for potential confounders. We repeated analyses for individual QST measures that were also standardized and rescaled to 0-100.

Results: 2737 participants (3031 knees) were included (mean age 64 ± 10, 58% female, mean BMI 29.4 ± 5.7). Over a two-year period, 6.7% developed constant pain. Each 10-unit increase in PSI score (signifying less pain sensitivity) was significantly associated with 33% lower odds of developing constant pain over 2 years (**Table**). In contrast, the magnitude of association for each individual QST measures was either smaller than that of the PSI score, or not associated with developing constant pain (**Table**).

Conclusion: The PSI score was associated with developing constant pain, whereas the individual QST measures had either smaller or null associations. This PSI score highlights the potential clinical relevance of multiple coexisting nociceptive signaling alterations to the pain experience in knee OA, and supports the importance of performing a global assessment of pain sensitization to capture the overall status of the nociceptive system.

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Abstract Number: 0962

Efficacy of Clomipramine for Chronic Lumbar Radicular Pain a Randomized Clinical Trial

Saloua Afilal[1], Safaa Fellous[1], Ilham Aachari[1], Redouane Abouqal[2], Ihsane Hmamouchi[3], Nada Alami[1], Latifa Tahiri[1], Hanan Rkain[1], Najia Hajjaj-Hassouni[4] and Fadoua Allali[1], [1]Rheumatology B Department, El Ayachi Hospital, Faculty of Medicine and Pharmacy of Rabat, Mohammed V University, Rabat, Morocco., Rabat, Morocco, [2]Laboratory of Biostatistics, Clinical Research and Epidemiology (LBRCE), Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco., Rabat, Morocco, [3]Temara Hospital, Laboratory of Biostatistics, Clinical Research and Epidemiology (LBRCE), Faculty of Medicine and Pharmacy, Mohammed V University, Rabat, Morocco, Rabat, Morocco, [4]Health Sciences College, International University of Rabat (UIR), Rabat, Morocco

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Orthopedics, Low Back Pain, & Rehabilitation
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Lumbar radicular pain is the most common chronic neuropathic pain syndrome. Antidepressants are highly recommended for neuropathic pain, but there is no evidence for their efficacy.

The aim of this double-blind, randomised, placebo-controlled trial is to determine whether clomipramine (an antidepressant) is more effective than placebo in reducing pain in individuals with resistant chronic lumbar radicular pain.

Methods: A double-blind, randomized, clinical trial. Sixty-two patients with resistant chronic lumbar radicular pain were included. (The sample size was calculated on the assumption that clomipramine would reduce the incidence of lumbar radicular pain of 35%, compared with placebo, with a two-sided test, an alpha level of 0.05, and a power of 85%). Patients were randomly allocated to receive either Clomipramine by slow intravenous infusion for 10 days in a hospital setting with progressively increasing doses, 25 mg on the first day, 50 mg on the second day and 75 mg on the third day until the tenth day, or placebo (500 ml of physiological serum a day). For both groups, paracetamol

is added intravenously at a dose of 3g per day for ten days, Parecoxib for 3 days and ten sessions of lumbar spine rehabilitation including analgesic massage, muscle strengthening and joint maintenance. At the exit, clomipramine was relayed with 25 mg per day orally until the 90th day for clomipramine group, and paracetamol was authorized in both groups, in case of severe pain. The primary outcome was pain intensity, measured at baseline, 5th day, 10th day and 90th day using VAS pain (10 mm). Secondary outcome included DN4-questionnaire, lumbar radicular discomfort (VAS 10 mm), pain-free perimeter of walking (min), disability assessed using the Roland Morris Disability questionnaire and severity of mood symptoms assessed using the Hospital Anxiety and Depression scale (HAD), measured on days 0, 5, 10 and 90.

Results: 31 patients were assigned to the clomipramine group and 31 to the placebo group. There were no differences between the groups in baseline characteristics. Treatment by clomipramine had a significantly greater reduction in pain, discomfort and DN4 from the 5thday compared to the placebo (3,83 ± 1,63 vs 5,38 ± 1,11, p< 0.0001, 3,90 ± 1,85 vs 5,35 ± 1,45, p= 0.001, 1,87 ± 1,68 vs 3,09 ± 1,49, p= 0.004 respectively) with significant differences maintained until 90th day. There was a statistically significant improvement in pain-free walking distance and disability for the clomipramine group from the 10th day compared to placebo (38 ± 27,04 vs 24,35 ± 17,25, p = 0.02 and 7,61 ± 4,96 vs 11,70 ± 4,51, p=0.001, respectively) and that maintained until 90th day. However, there was no statistically significant differences in HAD between the 2 groups.

Conclusion: This double-blind, randomized, clinical trial shows that clomipramine is quickly effective and maintained over time in the management of resistant chronic lumbar radicular pain. It can therefore be part of the therapeutic arsenal in this sense.

Disclosure: S. Afilal, None; **S. Fellous**, None; **I. Aachari**, None; **R. Abouqal**, None; **I. Hmamouchi**, None; **N. Alami**, None; **L. Tahiri**, None; **H. Rkain**, None; **N. Hajjaj-Hassouni**, None; **F. Allali**, None.

Abstract Number: 0963

Chronic Obstructive Pulmonary Disease Associated with Prolonged Opiate Use, Increased Short-Term Complications and the Need for Revision Surgery Following Total Knee Arthroplasty

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: Orthopedics, Low Back Pain, & Rehabilitation
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Chronic obstructive pulmonary disease (COPD) is a condition which causes a substantial burden to patients, physicians, and the healthcare system at large. Medical comorbidities are commonly associated with adverse health outcomes in the postoperative period. Here, we present a large database review of patients undergoing total knee arthroplasty (TKA) to determine the effect of COPD on patient outcomes.

Methods: The PearlDiver database was queried for all patients who underwent TKA between 2007 and the first quarter of 2017. Medical complications, surgical complications, 30-day readmission rates, revision rates, and opioid utilization were assessed at various intervals following TKA.

Results: 46,769 TKA patients with COPD and 120,177 TKA patients without COPD were studied. TKA patients with COPD experienced increased risk of 30-day readmission (40.8% vs. 32.2%, p< 0.0001), 30-day total medical complications (10.2% vs. 7.0%, p< 0.0001), prosthesis explanation at 6 months (0.4% vs. 0.2, p=0.0130), 1 year (0.6% vs. 0.3%, p=0.0005), and 2 years (0.8% vs. 0.5%, p=0.0003), as well as an increased rate of revision (p< 0.0046) compared to TKA patients without COPD. Opioid utilization of TKA patients with COPD was greater than that of TKA patients without COPD at 3,16 and 12 months.

Conclusion: Patients with COPD have an increased risk for medical and surgical complications, readmission, and prolonged opioid use following TKA. Patients undergoing TKA with a history of COPD represent a high-risk patient population, and it is prudent to ensure that such patients are fully optimized in the perioperative period to reduce complications and minimize health-care costs.

Disclosure: J. Glasser, None; **N. Lemme**, None; **D. Yang**, None; **E. Testa**, None; **A. Daniels**, None; **V. Antoci**, None.

Abstract Number: 0964

Is Meniscal Status in the Anterior Cruciate Ligament Injured Knee Associated with Change in Bone Surface Area? An Exploratory Analysis of Data from the KANON Trial

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SESSION INFORMATION
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Session Title: Orthopedics, Low Back Pain, & Rehabilitation
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Bone shape changes, which may be an important feature of osteoarthritis (OA) development, have been observed to occur early in the knee after anterior cruciate ligament (ACL) injury. The association between co-existing meniscal damage and bone shape changes is unclear. To gain new knowledge of early joint changes post-trauma, we studied the association between meniscal status in the ACL-injured knee and differences in bone surface area.

Methods: We used data from the KANON trial including 121 young ACL-injured adults. We obtained baseline and 2-year follow up knee MRIs read by one musculoskeletal radiologist. Our outcome was bone surface area at 2 years (mean mm^2, log-transformed) in 4 regions (femur, tibia, patella, and trochlea femur) in the medial and lateral compartment. We used data as reported by Bowes et al, who determined bone surfaces of the different areas and their limits with the use of active appearance models, a form of statistical shape model.[1] We defined meniscal damage based on Anterior Cruciate Ligament Osteoarthritis Score (ACLOAS).(Table 1) Meniscal damage was defined as both *present at baseline* and *newly developed*. *Newly developed* meniscal damage includes incident *or* worsening, i.e. pre-existing tears that expanded to another segment, or to extrusion or incident loss of meniscus substance.(Table 1) We used

Table 1. ACLOAS grading system

Type of meniscal damage	*ACLOAS grade*
Normal meniscus with absence of tear, maceration and hypointense signal	0
Intrameniscal hyperintensity not extending to meniscal surface	1
Horizontal tear	2
Radial and vertical tear	3
Bucket-handle tear, displaced tear (including root tears) and complex tears	4
Meniscal repair	5
Partial meniscectomy and partial maceration	6
Progressive partial maceration or re-partial meniscectomy (i.e., loss of morphological substance of the meniscus) as compared to the previous visit	7
Complete maceration or resection	8
Meniscal body extrusion <50%	na
Meniscal body extrusion >50%	na

Meniscal damage was defined as meniscal tear (ACLOAS grade 2 to 4), partial or complete maceration or resection (ACLOAS grade 6 to 8) or meniscal bod extrusion >50%. No tear (0), meniscal extrusion <50%, intrameniscal signal (ACLOAS grade 1) or status post meniscal repair (ACLOAS grade 5) were classified as no meniscal damage. *Worsening of meniscal damage* was defined in a knee with pre-existing meniscal damage in at least one segment as incident meniscal damage in a new segment or new tear, maceration/resection or extrusion >50% in the same segment.

Table 2 Baseline characteristics

	Baseline meniscal damage			Developed (incident/worsening) meniscal damage			Full cohort (N=121)
	MM (N=14)	LM (N=19)	No damage (N=88)	MM (N=24)	LM (N=26)	No damage (N=72)	
Sex, male (N,%)	11 (79)	16 (84)	62 (71)	19 (79)	21 (81)	51 (71)	89 (81)
Age, years (median, range)	25 (20-32)	23 (19-35)	27 (18 – 36)	27 (18 – 35)	25 (18 – 35)	25 (18 – 36)	25 (18 – 36)
BMI, kg/m^2 (median, range)*	23.0 (20.2 – 34.0)	24.8 (21.8 – 39.9)	23.5 (19.4 – 30.8)	24.1 (19.6 – 34.0)	24.2 (21.4 – 39.9)	23.3 (19.4 – 30.8)	23.6 (19.4 – 39.9)

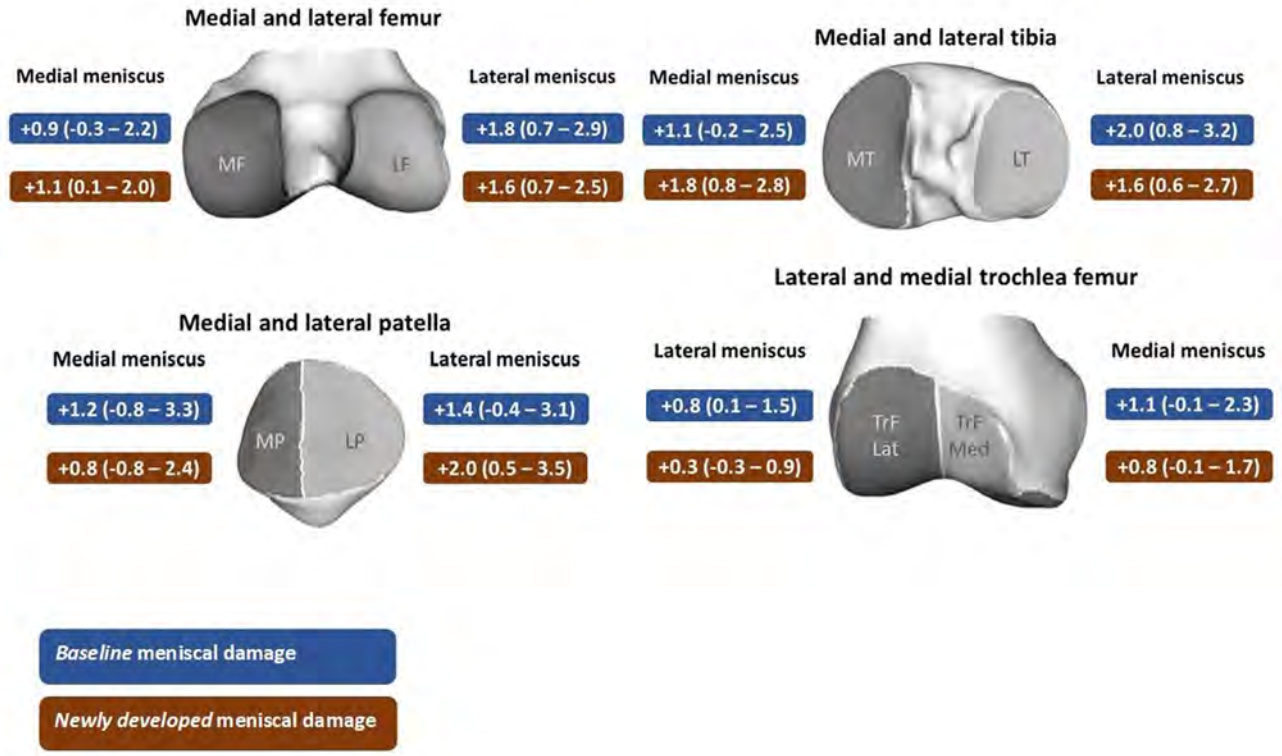
BMI= body mass index, MM=medial meniscus, LM=lateral meniscus, MF=medial femur, LF=lateral femur, TrFMed=medial trochlea femur, TrFLat=lateral trochlea femur, MT=medial tibia, LT=lateral tibia, MP=medial patella, LP=lateral patella. *Baseline meniscal damage* includes every person with a meniscal tear at baseline, irrespective of their meniscal status after two years; *Developed meniscal damage* includes every person that has an incident or progressed meniscal tear after two years of follow-up. Because persons could have both medial and lateral meniscal tears at baseline or developed, the same person could have been included for both medial as well as lateral meniscal tear.
* N=119, because of two missing BMIs at baseline

multilevel linear regression adjusted for baseline bone area, age, sex, body mass index, treatment arm (i.e. early and optional delayed ACL reconstruction), and location. We compared bone area changes in subjects with meniscal damage at baseline or newly developed to those without meniscal damage. We present results as percentage (%) difference in bone area between the groups with 95% confidence intervals (CI).

Results: We included 121 subjects (median age 25 (18-36) years, 81% men). Due to missing MRI information, 109 subjects were analyzed. Baseline bone area in mean mm^2 were similar in those with and without meniscal damage for all four regions (Table 2). In the whole cohort, the bone surface area increased on average by ~2% over 2 years, with ~1% higher increase for *both* subjects with ipsicompartmental meniscal damage at baseline and with newly developed meniscal damage compared to those without meniscal damage during the 2-year follow-up (Figure 1).

Conclusion: In the ACL-injured knee, persons with baseline or newly developed meniscal damage had ~1% increased bone area in the affected compartment compared to persons without such meniscal damage. The clinical relevance of early bone shape changes for future structural and clinical outcomes needs further exploration.

Figure 1 Difference (%) in bone surface area at 2 years of four bone areas in the ACL injured knee between persons with meniscal damage in the same compartment compared to persons without meniscal damage in the same compartment either at baseline or newly developed



Disclosure: B. Snoeker, None; **A. Turkiewicz**, None; **M. Bowes**, Imorphics Ltd, 4; **F. Roemer**, Boston Imaging Core Lab (BICL), LLC, 1, Calibr - California Institute for Biomedical Research, 1; **S. Lohmander**, None; **R. Frobell**, None; **M. Englund**, Pfizer, 5.

Abstract Number: 0965

Repetitive Inhalant Lipopolysaccharide Exposure in the Setting of Arthritis Induction Potentiates Pro-Fibrotic Inflammatory Lung Disease in Mice

Madison Wolfe[1], Ted Mikuls[1], Geoffrey Thiele[1], Amy Nelson[1], Michael Duryee[1], Rohit Gaurav[1], Bryant England[1], Debra Romberger[1] and Jill Poole[1], [1]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Animal Models
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Rheumatoid arthritis (RA) is associated with several lung diseases. Various airborne exposures have been implicated as RA disease risk factors including cigarette smoke and exposures related to pollution, farming, and construction among others. These exposures have also been linked to inflammatory lung disease in RA. A mouse model combining the agriculture organic dust extract-induced airway inflammatory model with collagen induced arthritis (CIA) led to increases in arthritis, autoimmunity, and pro-fibrotic inflammatory lung consequences. Agriculture exposures are complex with lipopolysaccharide (LPS) representing a major component; LPS exposure is

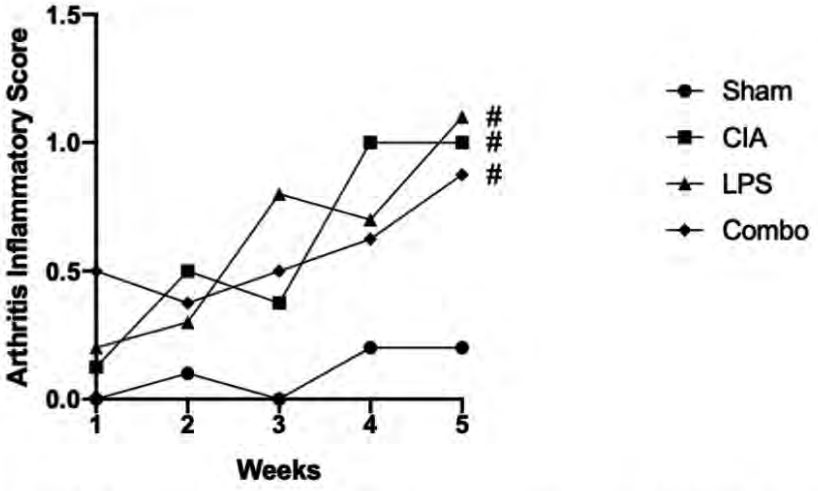


Figure 1. Arthritis inflammatory scores in hind paws increased following repetitive inhalant LPS (100 ng/day) exposure, arthritis induction (CIA), and combination CIA+LPS exposure. There was no difference among CIA, LPS, and combination CIA+LPS. Statistical significance denoted as #p<0.05 vs sham.

commonly found in other pollutant settings. It has been established that systemic LPS potentiates RA joint disease, but it is not known whether repetitive inhalation exposure to a biologically relevant airborne concentration of LPS modulates the RA-lung inflammatory axis.

Methods: DBA1/J male mice (n=5/group) were assigned to either: sham (saline injection/ saline inhalation), CIA (CIA/ saline inhalation), LPS (saline injection/ LPS 100 ng inhalation), or CIA+LPS for 5 weeks. Hind paws were observed weekly and given an arthritis inflammatory score of 0-4 based upon swelling and redness of the hind paws. Bronchoalveolar lavage fluid (BALF) and lung tissues were collected for cell enumeration, flow cytometry and ELISA.

Results: The arthritis inflammatory scores (mean±SEM) for CIA (1.0±0), LPS (1.1±0.24) and CIA+LPS (0.9±0.13) were significantly increased compared to sham (0.2±0.12) (**Figure 1**). **Table 1** depicts lung experimental outcomes. There was profound potentiation in BALF total lung cells ($p< 0.0001$) including neutrophils, macrophages, and lymphocytes in CIA+LPS versus other exposure groups. There was increased lung activated macrophages ($CD11c^{hi}CD11b^{hi}$), neutrophils ($Ly6C^{+}Ly6G^{+}$), monocytes ($CD11c^{-}CD11b^{hi}$) and recruited monocyte/macrophages ($CD11c^{int}CD11b^{+}$) with CIA+LPS exposure. The pro-inflammatory cytokine TNF-α ($p< 0.001$) and neutrophil chemokine (CXCL2) ($p< 0.0001$) were increased in LPS alone, but not LPS+CIA. In contrast, levels of fibronectin and the alarmin IL-33 were increased in the lung homogenates of CIA+LPS versus all other exposure groups. In addition, BALF complement (C5a) and fibronectin were increased in LPS and CIA+LPS and potentiated with combined treatments. As compared to sham, lung IL-33 was increased in LPS alone ($p< 0.01$) and lung fibronectin was increased in CIA alone ($p< 0.05$).

Conclusion: Repetitive LPS inhalation in the setting of arthritis induction induced striking lung inflammatory consequences. This was marked by reduction in classic pro-inflammatory mediators and augmentation of wound repair fibronectin, alarmin IL-33, and C5a with increased recruitment of activated macrophages, recruited/transitional monocyte-macrophages, and monocytes to potentially signify the transition toward pro-fibrotic consequences. These findings would suggest that patients with RA may be more susceptible to developing interstitial lung disease following occupational and environmental exposures enriched in LPS and that interventions to reduce airborne biohazard exposures could be important.

Table 1. Lung experimental outcomes shown as mean (standard error).

	Sham	CIA	LPS	CIA+LPS
BALF total cells (x10^5)	0.574 (0.015)	0.475 (0.115)	**2.66 (0.251)** **	**5.65 (0.716)** ****, ^^^^, ###
BALF neutrophils (x10^5)	0.121 (0.015)	0.133 (0.55)	**2.23 (0.272)** *	**3.98 (0.943)** ***, ^^^
BALF macrophages (x10^5)	0.417 (0.013)	0.333 (0.0922)	0.392 (0.039)	**1.46 (0.306)** **, ^^^, ##
BALF lymphocytes (x10^5)	.0051 (0.0016)	0.0090 (0.0032)	0.0239 (0.0048)	**0.196 (0.041)** ****, ^^^^, ####
BALF TNF-α (pg/ml)	5.78 (1.23)	2.22 (2.22)	**74.4 (9.46)** ***	38.0 (17.3)
BALF CXCL2 (pg/ml)	82.7 (14.3)	72.4 (16.4)	**429.8 (27.6)** ****, ####	94.7 (37.4)
BALF C5a (ng/ml)	8.032 (0.434)	8.70 (0.738)	**12.2 (0.276)** **	**16.9 (1.43)** ****, ^^^^, #
BALF fibronectin (ng/ml)	360.2 (22.3)	334.8 (42.3)	**910 (67.2)** ****	**2552 (213.7)** ****, ^^^^, ####
Lung fibronectin (ng/ml)	248.2 (11.6)	**347.3 (25.4)** *	354.2 (24.9)	**743 (90.1)** ****, ^^^^, ####
Lung IL-33 (ng/ml)	3.88 (0.328)	5.50 (0.679)	**8.86 (1.16)** **	**32.2 (2.21)** ****, ^^^^, ####
Lung total cells (x10^5)	18.5 (1.70)	19.6 (7.82)	15.84 (0.532)	30.2 (3.80)
Lung activated macrophages (x10^5)	0.168 (0.023)	0.363 (0.133)	0.230 (0.030)	**1.67 (0.327)** ****, ^^^, ###
Lung monocytes/macrophages (x10^5)	0.175 (0.0372)	0.379 (0.172)	0.181 (0.0256)	**1.75 (0.359)** ***, ^^^, ###
Lung neutrophils (x10^5)	3.19 (0.381)	2.48 (0.972)	5.16 (0.279)	**7.38 (1.77)** *, ^
Lung resting macrophages (x10^5)	4.32 (0.280)	4.701 (1.72)	2.18 (0.222)	4.71 (0.599)
Lung monocytes (x10^5)	0.110 (0.0151)	**0.556 (0.205)** **	**0.242 (0.0118)** *	**0.568 (0.132)** *

Statistical significance denoted as asterisk (*p<0.05; **p,0.01, ***p<0.001, ****p<0.0001) vs Sham.
Statistical difference of CIA vs CIA+LPS denoted as ^p<0.05; ^^p<0.01, ^^^p<0.001, ^^^^p<0.0001.
Statistical difference of LPS vs CIA+LPS denoted as #p<0.05; ##p<0.01, ###p<0.001, ####p<0.0001. Bold highlights statistical significance.

Disclosure: M. Wolfe, None; **T. Mikuls**, Horizon Therapeutics, 2; **G. Thiele**, None; **A. Nelson**, None; **M. Duryee**, None; **R. Gaurav**, None; **B. England**, None; **D. Romberger**, None; **J. Poole**, None.

Abstract Number: 0966

Decoupling Inflammation and Bone Loss in Rheumatoid Arthritis via Schnurri-3

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Animal Models

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic inflammatory disease that leads to local and systemic bone loss. TNF is a key mediator of bone loss, not only through promotion of osteoclastogenesis, but also through inhibition of osteoblast function. Schnurri3 (*Shn3*) is a large, intracellular zinc-finger adaptor protein and is a suppressor of osteoblast activity, as *Shn3*-deficient mice show a significant increase in bone mass due to augmentation of bone formation. We questioned whether targeting SHN3 in bone cells has therapeutic potential in RA-induced bone loss.

Methods: To investigate the effect of *Shn3* global deletion on bone loss in arthritis, *Shn3*-deficient mice were crossed with SKG mice, a model of IL-17A and TNF-driven RA. SKG or *Shn3*-deficient-SKG mice were injected intraperitoneally with curdlan to synchronize arthritis onset. Mice were scored weekly for peripheral joint inflammation and sacrificed after 7 weeks of inflammation. Micro-computed tomography was used to evaluate joint erosions (ankles) and systemic bone loss (femurs). Histologic sections were scored for inflammation and bone erosion. To test the effect of deletion of *Shn3* in osteoblast precursor cells in the setting of TNF overexpression, $Shn3^{Prx1}$ mice were crossed with TNF-transgenic (TNF-tg) mice. Ankles and femurs were analyzed for inflammation and bone parameters as above. To further determine the effect of *Shn3*-deficient osteoblasts on bone in RA, the serum transfer arthritis (STA) model was employed in $Shn3^{Prx1}$ mice sacrificed at peak inflammation. Mice were again similarly analyzed for inflammation and bone parameters.

Human bone marrow stromal cells (BMSCs) were infected with lentivirus (vector alone (control), SHN3 overexpression, control-shRNA, or SHN3 knockdown) and cultured under osteogenic conditions in the absence or presence of TNF plus IL-17A for 14 days. Mineralization activity was measured by alizarin red staining. Mouse COBs isolated from P5 WT and *Shn3*-deficient pups were cultured in the absence or presence of TNF plus IL-17A and mineralization was measured.

Results: Significant protection from joint erosion and systemic bone loss was noted in *Shn3*-deficient SKG and $Shn3^{Prx1}$;TNF-tg mice, despite similar and ongoing inflammation. In STA, *Shn3*-deficient osteoblasts were present at sites of erosion at the bone-pannus interface where typically few mature osteoblasts are present, indicating that *Shn3*-deficient osteoblasts continue to differentiate and populate eroded bone surfaces despite the presence of inflammation. In parallel with this observation, *Shn3*-deficiency in BMSCs and osteoblasts blocked the inhibitory activity of TNF/IL-17 for differentiation in vitro.

Conclusion: SHN3 acts downstream of and potentiates the negative effects on osteoblasts of TNF/IL-17A. Its inhibition allows for continued bone formation despite the presence of inflammation. Therefore, targeting this pathway provides a potential therapeutic strategy for RA-induced bone loss.

Disclosure: Z. Stavre, None; **J. Kim**, None; **J. Shim**, None; **E. Gravallese**, New England Journal of Medicine, 3, UpToDate, 7, Co-editor of the textbook Rheumatology, 7.

Abstract Number: 0967

Absence of Thy1 Associated with Severe Bone Loss in the TNF-transgenic (TNF-Tg) Mice Arthritis Model

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Animal Models
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Thy1 (CD90) is a glycosylated, glycophosphatidylinositol (GPI)-anchored membrane protein noted to be expressed on many cells including T lymphocytes, stem cells, osteoblasts and fibroblasts. Thy1 is also abundantly expressed by mesenchymal stem cells (MSCs) and we previously demonstrated that it is required for osteoblast differentiation and bone homeostasis. The goal of this study was to examine if knockout of the membrane protein Thy1 (CD90), is associated with increased pathologic bone resorption in a murine model of inflammatory arthritis.

Methods: We performed real-time PCR (RT-PCR) to compare Thy1 mRNA expression levels in mouse bone marrow cells and monocyte-derived dendritic cells (mDCs) of TNF overexpressing (TNF-Tg) and wild type (WT) mice and murine embryonic fibroblasts (MEFs) from (WT) mice. Subsequently, we also investigated the impact of the Thy1 deletion in TNF-Tg (Tg3647) mice, a murine model of inflammatory arthritis. To study the effect of Thy1 depletion on bone erosion, we analyzed bone loss by performing micro-computed tomography (micro-CT) analysis of the long bones, and ankle joints of Thy1$^{-/-}$TNF-Tg, TNF-Tg, Thy1$^{-/-}$ and WT mice.

Results: In vitro assays revealed a significant decrease in Thy1 expression (40% - 65%) in primary bone marrow cells and mDCs of the TNF-Tg mice compared to the WT mice (Figure 1). Thy 1 mRNA levels decreased by more than 25% in murine embryonic fibroblasts following exposure to TNF for 24 hours. Most importantly, micro-CT analysis of the long bone and ankle joints revealed a significant increase in bone loss in the Thy1$^{-/-}$TNF-Tg mice, compared to the TNF-Tg or Thy1$^{-/-}$ mice (Figure 2). In particular, a significant reduction in bone parameters were observed in Thy1$^{-/-}$ TNF-Tg mice compared to the TNF-Tg, Thy1$^{-/-}$ or WT mice. Significant differences were noted in BV/TV (0.003 ± 0.02 in Thy1$^{-/-}$TNF-Tg vs 0.024± 0.01 in TNF-Tg, $p < 0.01$, for tibia), trabecular number (1.57 ± 0.2 in Thy1$^{-/-}$TNF-Tg vs 2.4 ± 0.1 in TNF-Tg, $p < 0.005$, for tibia), and trabecular thickness (0.026 ± 0.002 in Thy1$^{-/-}$TNF-Tg vs 0.032 ± 0.01 in TNF-Tg, $p < 0.01$, for tibia). Similar bone loss was not noted in WT or Thy1 KO mice.

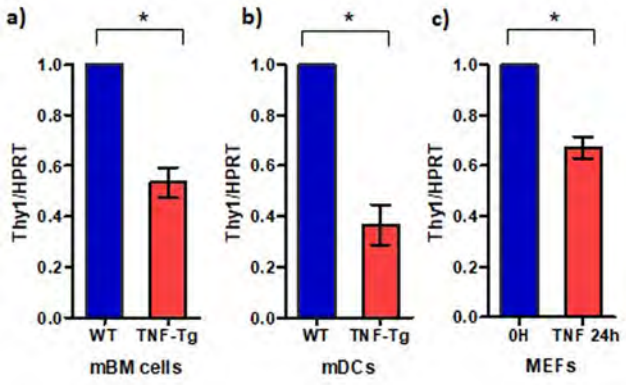


Figure 1. TNF exposure downregulates Thy1 expression in RA SFs, MEFs, BM cells, and mDCs a) Thy1 expression level in SFs from RA patients incubated with or without TNF for 12 hours (microarray data: GSE13837, fold change, n=3); b) MEFs were incubated with or without 5 ng/ml human TNF for 24 hours and thereafter Thy1 expression levels were compared using qPCR (n=3); c) Thy1 expression levels in freshly harvested bone marrow cells from 6 months old male WT and TNF-Tg mice (n=4); d) Thy1 mRNA expression levels in the monocyte-derived DCs of 4-month-old female WT and TNF-Tg mice (n=4). For qPCR data, HPRT1 was used as the housekeeping gene.

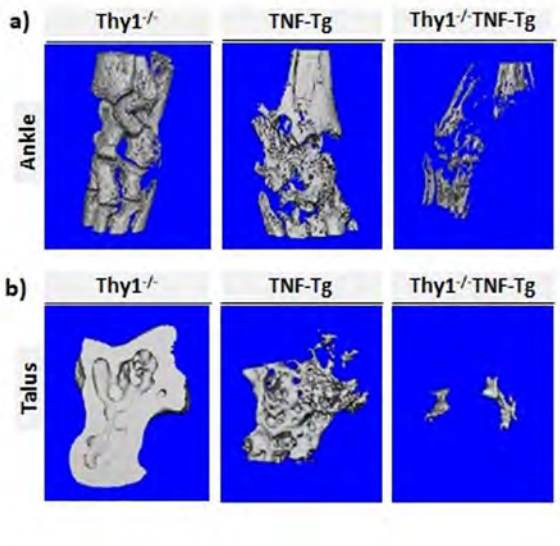


Figure 2. Increased bone loss in Thy1 KO TNF-Tg mice. Long bones from normal diet fed 8 months old male Thy1-/-, TNF-Tg, and Thy1-/-TNF-Tg mice were analyzed with micro-CT to compare changes in bone architecture and structural parameters. Representative micro-CT images of the ankle (a), and talus (b) presented.

Conclusion: We find Thy1 expression significantly decreased in MSCs and myeloid cells following exposure to TNF. Absence of Thy1 was associated with enhanced pathologic bone resorption in murine model of arthritis. Thus, TNF-mediated downregulation of Thy 1 may serve as an important mechanistic link between inflammation and progressive bone loss in inflammatory arthritis.

Disclosure: A. Paine, None; **M. Garcia-Hernandez**, None; **M. Nuzzo**, None; **S. Duemmel**, None; **B. Korman**, None; **C. Ritchlin**, None.

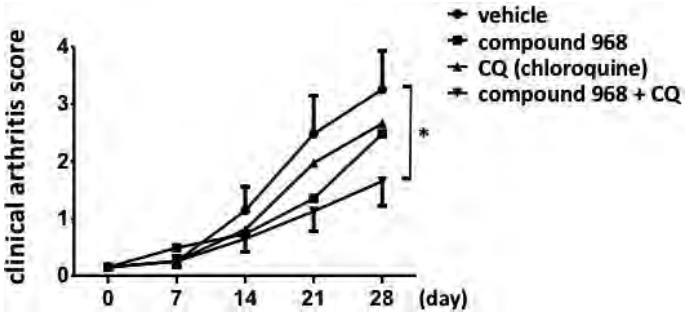
Abstract Number: 0968

Combined Inhibition of Autophagy and Glutamine Metabolism Suppresses Cell Growth of RA Synoviocytes and Ameliorates Arthritis in SKG Mice

Ikuko Naka[1], Jun Saegusa[2], Kenichi Uto[2], Yuzuru Yamamoto[3], Yoshihide Ichise[4], Hirotaka Yamada[4], Yo Ueda[5], Takaichi Okano[4], Soshi Takahashi[6], Sho Sendo[7] and Akio Morinobu[8], [1]Kobe University, Kobe, [2]Department of Clinical Laboratory, Kobe University Hospital, Kobe, Japan, [3]Kobe University, Kobe-city, Japan, [4]Kobe University, Kobe, Japan, [5]Kobe UniversityRheumatology and Clinical Immunology, Kobe University Hospital, Kobe, Japan, [6]Kobe univerity, Kobe, Japan, [7]Kobe university, Kobe city, Japan, [8]Rheumatology and Clinical Immunology, Kobe University Hospital, Kobe, Japan

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Animal Models
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Immunometabolism is now recognaized to be crucial in the pathogenesis of rheumatoid arthritis (RA). We have recently shown that the expression of glutaminase 1 (GLS1), a key enzyme in glutaminolysis,



Combination of C968 and CQ significantly attenuated the degree of arthritis in SKG mice.

is upregulated in fibroblast-like synoviocytes from RA patients (RA-FLS) and that GLS1 inhibition suppresses RA-FLS proliferation (1). However, glutaminolysis has been known to suppress autophagy by activating mTORC1 or counteracting ROS production (2). Given the possibility of autophagy upregulation following glutamiolysis inhibition, therapies targeting both autophagy and glutaminolysis may be more effective in suppressing cell growth of RA-FLS, yet the relation between glutaminolysis and autophagy in RA-FLS has not been investigated. Here we examined the effects of inhibiting both glutaminolysis and autophagy on RA-FLS and autoimmune arthritis in SKG mice.

Methods: GLS1 inhibitor, compound 968 (C968), was used to suppress glutaminolysis, and Chloroquine (CQ) was used to inhibit autophagy. To detect autophagy, the expression of ATG5 and LC3B was measured by real-time PCR and the production of LC3-II was analyzed by Western blotting. The formation of autophagic vacuoles was identified by immunfluorescense. Cell growth was evaluated by BrdU assay. Apoptosis was analyzed by flow cytometry staining with Annexin V-FITC and PI. C968 and CQ were administered subcutaneously to Zymosan A-injected SKG mice.

Results: C968 upregulated the expression of ATG5 and LC3B, and increased the protein level of LC3-II in RA-FLS. C968 also facilitated autophagosome formation. These results suggested that inhibition of glutaminolysis promoted autophagy in RA-FLS. The combined treatment with C968 and CQ significantly suppressed cell proliferation of RA-FLS more strongly than did C968 or CQ alone. In addition, C968 combined with CQ increased the apoptosis rate, whereas either C968 or CQ alone did not. Furthermore, combination of C968 and CQ significantly attenuated the degree of arthritis in SKG mice, while C968 or CQ monotherapy did not (Figure).

Conclusion: The GLS1 inhibitor C968 promotes autophagy in RA-FLS. C968 in combination with CQ reduces proliferation and enhances apoptosis in RA-FLS, and ameliorates the arthritis in SKG mice. Suppressing C968-induced autophagy may be a promising therapy for arthritis.

Disclosure: I. Naka, None; **J. Saegusa**, None; **K. Uto**, None; **Y. Yamamoto**, None; **Y. Ichise**, None; **H. Yamada**, None; **Y. Ueda**, None; **T. Okano**, None; **S. Takahashi**, None; **S. Sendo**, None; **A. Morinobu**, None.

Abstract Number: 0969

Investigating Murine Joint-Draining Lymphatics: Lineage Tracing and Single Cell RNA Sequencing Reveal Evidence That Popliteal Lymphatic Muscle Cells and Their Progenitors Represent Distinct Cell Types Divergent from Striated and Vascular Muscle Cells

H. Mark Kenney[1], Richard Bell[2], Elysia Masters[1], Lianping Xing[1], Christopher Ritchlin[3] and Edward Schwarz[1], [1]University of Rochester Medical Center, Rochester, [2]Hospital for Special Surgery, New York, [3]Department of Medicine, University of Rochester Medical Center, Rochester, NY

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Animal Models
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Previous studies demonstrated that tumor necrosis factor transgenic (TNF-Tg) mice with inflammatory arthritis have damaged lymphatic muscle cells (LMCs) and eventual loss of popliteal lymphatic vessel (PLV) contractions associated with severe joint disease.[1] Anti-TNF therapy in flaring TNF-Tg mice recovers these PLV-LMCs and PLV contractions concomitant with amelioration of arthritis.[1] As this regenerative process is critical for resumption of joint function, knowledge regarding PLV-LMC progenitor origins and physiology is needed. Surprisingly, LMCs express an enigmatic actin profile with co-existing striated and smooth muscle actin isoforms,[2] which is incompatible with the differentiation of known muscle progenitors. To determine PLV-LMC origin, we tested the hypothesis that PLV-LMCs are derived from previously characterized striated or vascular smooth muscle cell (VSMC) progenitors via lineage tracing studies in mice. We also utilized these lineage tracing models to specifically isolate PLV-LMCs and VSMCs for comparative single cell RNA sequencing (scRNAseq) transcriptomic analysis.

1. Bouta et al. 2018. *Nature Reviews Rheumatology*. 14(2):94-106.

2. Muthuchamy et al. 2003. *The FASEB Journal*. 17(8):920-922.

Methods: Constitutive Cre and tamoxifen-inducible CreER models were crossed into Ai9^{tdTomato} reporter lines for lineage tracing of PLV-LMCs during neonatal development. Induction of the CreER was achieved with 0.1 mg/g of tamoxifen administered intraperitoneal on postnatal days 10 – 13 (P10 – 13). All cohorts were sacrificed at both P21 and/or after 6-weeks. Pax7^{Cre} and MyoD^{iCre} animals were used to study striated muscle cell origin, while Prrx1$^{Cre/CreER}$ and NG2$^{Cre/CreER}$ mice were used to trace VSMC progenitors by tdTomato (tdT) expression visualized by ex vivo whole mount immunofluorescent microscopy of PLVs. The NG2^{Cre};tdT model was also utilized for fluorescence activated cell sorting (FACS) of tdT^{+} PLV-LMCs and VSMCs with downstream scRNAseq analysis on a 10X genomics platform.

Genes: Pax7 = Paired Box Protein 7; MyoD = Myogenic Differentiation Protein 1; Prrx1 = Paired Related Homeobox 1; Neural Glial Antigen 2 = NG2

Results: We demonstrate that PLV-LMCs originate from Pax7^{-}/MyoD^{-}/Prrx1^{+}/NG2^{+} progenitors prior to P10, and from previously unknown Pax7^{-}/MyoD^{-}/Prrx1^{+}/NG2^{-} progenitors during development after P10 **(Figure 1)**. In addition, our preliminary scRNAseq results suggest that mature PLV-LMCs are transcriptionally distinct muscle cells **(Figure 2)**.

Conclusion: This is the first study to describe the unique origin of PLV-LMC progenitors and to assess the distinct characterization of mature PLV-LMCs using a scRNAseq approach. Our analysis suggests that PLV-LMCs do not derive from striated muscle progenitors with Pax7- and MyoD-negativity. In addition, PLV-LMCs appear to originate from similar Prrx1^{+}/NG2^{+} progenitors to VSMCs, but derive from distinct Prrx1^{+}/NG2^{-} progenitors prior to P10 to become transcriptionally unique muscle cells. Thus, future work elucidating the PLV-LMC lineage, and defining specific markers of PLV-LMCs, will catalyze the development of LMC targeted therapies for diseases with lymphatic involvement, such as inflammatory arthritis.

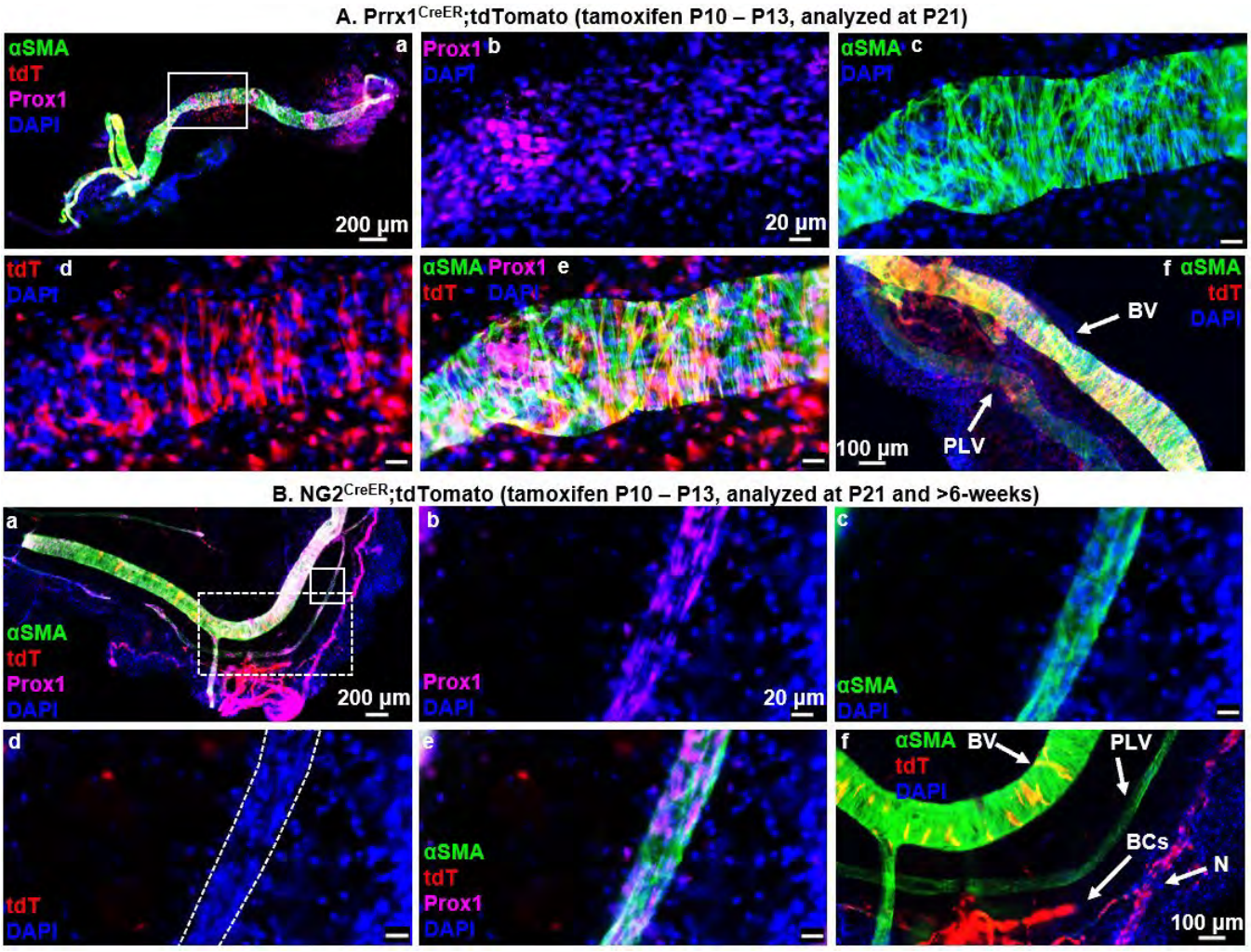


Figure 1. LMCs derive from a unique Prrx1+ and NG2- progenitor cell incorporated onto PLVs between P10 and P21. Multicolor fluorescent microscopy was performed on whole mount immunostained PLVs and adjacent blood vessels (BVs) from tamoxifen-inducible Prrx1CreER (n = 6, P21 depicted), and NG2CreER (n = 5, P90 depicted) reporter mice as described in Fig. 1. Representative low-magnification overlay images of all channels show the PLVs with a highlighted region of interest (white boxes) (A.a, B.a). High-magnification images of the region of interest show Prox1 immunostain of LECs (A.b, B.b), αSMA immunostain of LMCs (A.c, B.c), Cre-driven tdT expression (A.d,.d), overlay of all channels (A.e, B.e), and positive control BV VSMCs (A.f, B.f), blood capillary (BC) pericytes, and peripheral nerves (N) all directly adjacent to PLVs (B.f). Lineage tracing of Prrx1CreER (A.a-f) mice demonstrates tdT expression in PLVs (A.d) that colocalizes with αSMA+ LMCs (A.e) along with successful Cre-recombination with tdT expression in positive control VSMCs, as expected (A.f). NG2CreER (B.a-f) shows absent tdT expression in PLVs (no red staining in outlined PLV) (B.d) with successful tamoxifen induced NG2-driven Cre-recombination depicted by tdT expression in BV VSMCs, BC pericytes, and peripheral nerves (N), as expected (B.f). Note the few yellow VSMCs on the BV, which indicates that these cells were added to the fully formed BV after tamoxifen treatment.

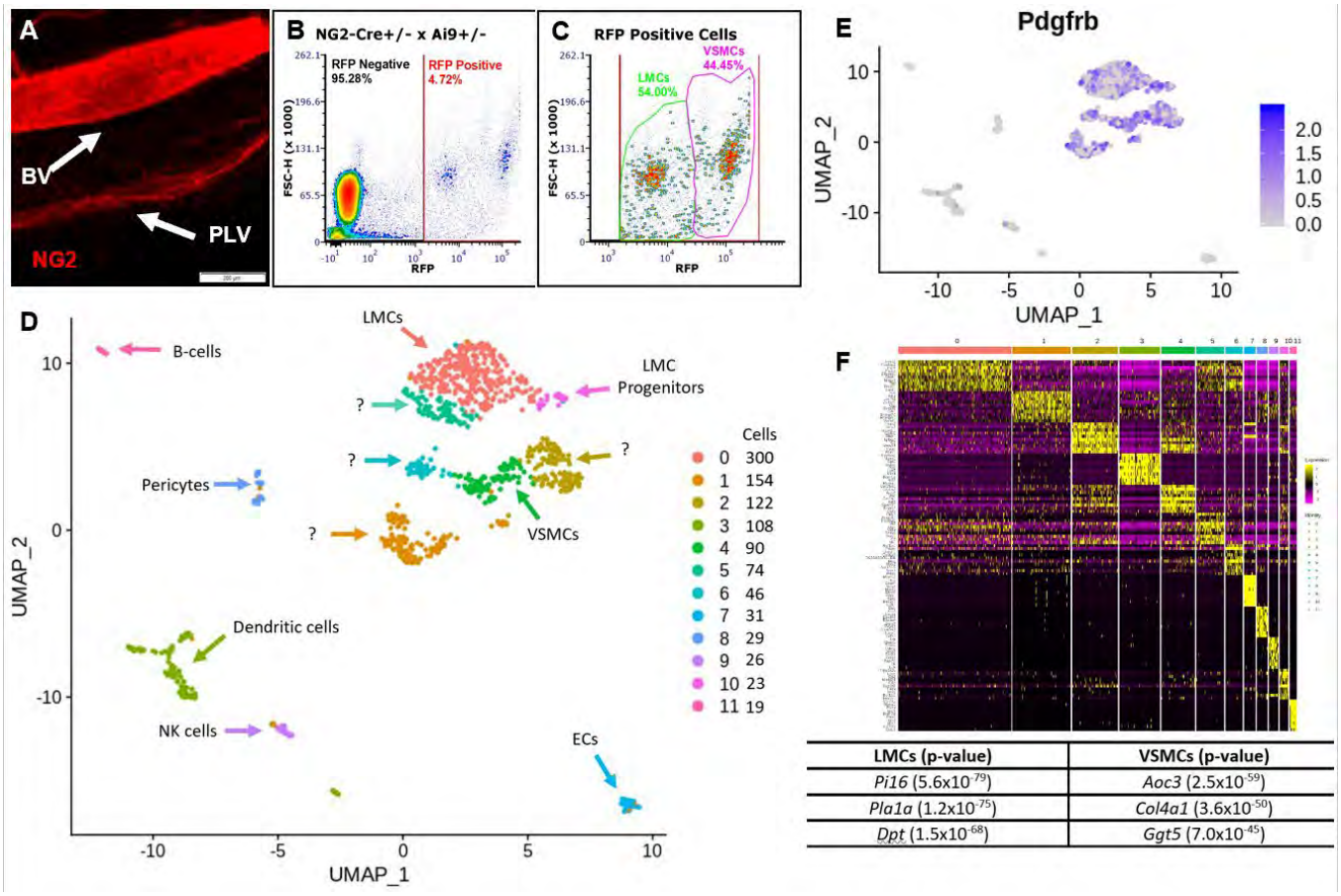


Figure 2. FACS and scRNAseq of tdT+ PLVs and BVs identifies LMC and VSMC populations. Whole mount fluorescent microscopy of PLVs and adjacent BV from NG2-Cre+/- x Ai9+/- mice revealed that both LMCs and VSMCs are RFP+, but VSMCs are much brighter than LMCs (MFI = 63.83 +/- 5.43 vs. 22.28 +/- 5.45 in arbitrary units; p<0.05 n=5 vessels) (A). A single cell suspension was prepared by pooling the lateral saphenous vein and both adjacent PLVs from both hindlegs of 3 NG2-Cre+/- x Ai9+/- mice. The cells were analyzed by FACS with ~6,000 RFP+ events/animal (B), and revealed two distinct populations based on RFP signal intensity (C), presumed to be LMCs and VSMCs based on the whole mount studies. The tdT+ sample contained 1,504 viable cells and was analyzed using scRNAseq (93,099 reads of 2,142 genes/cell with 97.2% barcode validity). UMAP was used to embed the data into 2D space and an sNN clustering algorithm resolved 12 clusters (Clusters 0-11 with cells/cluster, right; Seurat, R). Clusters were annotated using Mouse Gene Atlas, KEGG, Wiki Pathways & GO Biological Process (D). High levels of Pdgfrb expression are seen in the clusters annotated as LMCs and VSMCs validating their identification as mesenchymal muscle cells (E). A heatmap showing the ten most differentially regulated genes between each cluster identified unique muscle-defining genes between LMCs and VSMCs (F).

Disclosure: H. Kenney, None; **R. Bell**, None; **E. Masters**, None; **L. Xing**, None; **C. Ritchlin**, None; **E. Schwarz**, None.

Abstract Number: 0970

Oxylipins Profiles During the Earliest Phases of Rheumatoid Arthritis: Associations with Clinical Stage and Treatment Outcomes

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del Principado de Asturias, Asturias, Spain, Oviedo, [5]Bone and Mineral Research Unit, REDinREN del ISCIII, Hospital Universitario Central de Asturias, Spain, Oviedo, [6]Department of Pharmacology, School of Medicine, University of California, San Diego, USA, San Diego, [7]Division of Rheumatology, University of California San Diego, Department of Medicine, Autonomous University of Barcelona, La Jolla, CA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Altered eicosanoids have been linked to rheumatoid arthritis (RA), suggesting an enhanced metabolization. Eicosanoid metabolism forms a complex network, involving different pathways and mediators, including oxylipins, which are known to modulate inflammation. However, the role of oxylipins in RA is still to be elucidated. This study aims to characterize oxylipins networks during the earliest phases of RA and evaluate their associations with clinical features.

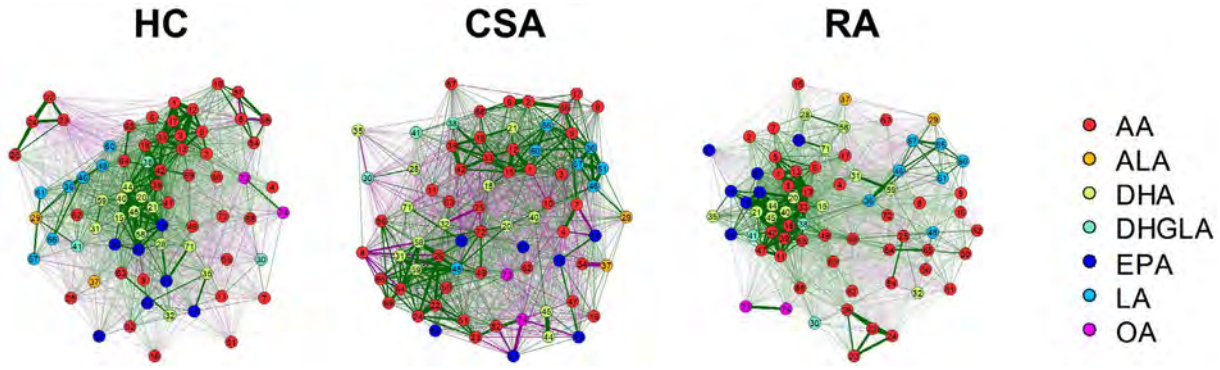

Figure 1. Network analyses based on the concentration of oxylipins in the different study groups. Each node corresponds to a single oxylipin, numbered as per the Figure legend list. Node colours represent the fatty acid precursor as follows: red (AA), green (DHA), dark blue (EPA), light blue (LA), turquoise (DHGLA), orange (ALA) (orange), magenta (OA). The lines between nodes illustrate the strength (width) and type (green: positive, red: negative) of the correlations between each pair of oxylipins. The relative position of the nodes parallels its degree of correlation that is, nodes more closely correlated locate closer to each other.

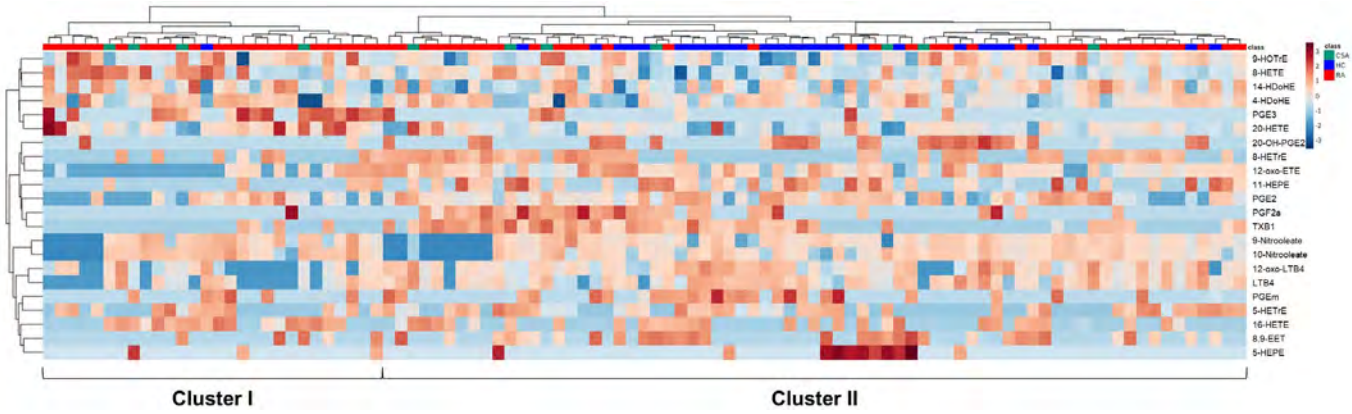

Figure 2. Heatmap and cluster analysis based on oxylipins that best separate the groups. Tiles were coloured based on concentrations, red and blue indicating high and low levels respectively, as indicated in the legend (top right). Upper bar indicates group classes (HC: blue, CSA: green, RA: red). Heatmap allowed the identification of two clusters (bottom).

	Cluster I n=23	Cluster II n=37	p-value
Clinical features			
Tender Joint Count	9.00 (6.00-14.00)	8.00 (4.50-13.00)	0.478
Swollen Joint Count	6.00 (3.00-10.00)	5.00 (3.00-8.50)	0.337
ESR (mm/h)	19.00 (11.00-37.00)	20.00 (7.50-34.00)	0.616
CRP (mg/dl)	0.80 (0.30-3.20)	0.60 (0.20-1.65)	0.256
VAS Global Assessment	70.00 (60.00-90.00)	50.00 (40.00-72.50)	0.016
VAS Pain Assessment	8.00 (7.00-8.00)	6.00 (5.00-8.00)	0.003
DAS28	5.66 (4.68-6.45)	5.05 (3.86-6.07)	0.163
HAQ	1.50 (1.66-0.65)	1.10 (0.60-1.65)	0.432
RF+	16 (69.5)	21 (56.7)	0.321
ACPA+	15 (65.2)	20 (54.0)	0.461
Therapy outcomes			
EULAR good response (6 months)	5/16	21/30	0.012
DAS28 remission (6 months)	4/16	20/30	0.007
EULAR good response (12 months)	4/13	17/27	0.056
DAS28 remission (12 months)	4/13	17/27	0.052

Figure 3. Clinical features of RA patients based on oxylipins clusters. Variables were expressed as median (interquartile range) or n(%), unless otherwise stated. Differences were assessed by Mann-Withney or chi-square tests (or Fisher exact test, when appropriate), according to the distribution of the variables.

Methods: 60 early RA patients (2010 ACR/EULAR criteria), 11 clinically suspect arthralgia (CSA) individuals and 28 control subjects (HC) were recruited. Serum samples were collected at onset, and treatment-naïve patients (n=50) were prospectively followed-up upon csDMARD treatment.

Results: 75 oxylipins, mostly derived from arachidonic, eicosapentanoic and linoleic acids, were identified by LC-MS/MS. Differences in serum levels of 14 oxylipins across HC, CSA and RA were found, exhibiting different trajectories. Network analyses revealed strong differences in the association among oxylipins, with a clear grouping in RA and a fuzzy network with high degree and closeness found in CSA (Figure 1). PLS-DA did not provide a neat separation of groups, but cluster analysis based on oxylipins with VIP scores >1 (n=22) allowed the identification of two clusters. Cluster usage differed among groups (p=0.003) (Figure 2), and showed associations with disease severity and low rates of remission at 6 and 12 months in treatment-naïve RA (Figure 3). Pathway enrichment analyses revealed different precursors and pathways highlighting the relevance of AA and LOX pathway in CSA and RA, respectively.

Conclusion: oxylipins networks differ across stages during earliest phases of RA. Oxylipins can inform on pathways with clinical relevance for disease progression, clinical heterogeneity and treatment response.

Disclosure: R. Coras, None; **J. Rodríguez-Carrio**, None; **M. Alperi-López**, None; **P. López**, None; **C. Ulloa**, None; **F. Ballina-García**, None; **A. Armando**, None; **O. Quehenberger**, None; **M. Guma**, None; **A. Suárez**, None.

Abstract Number: 0971

Single-cell Profiling of Synovial Stromal Cells Reveals an Angiocrine Endothelium in Rheumatoid Arthritis

Kevin Wei[1], Ilya Korsunsky[2], Jennifer Marshall[3], Gerald Watts[4], Triin Major[3], Zhu Zhu[4], Yuhong Li[5], Christopher Buckley[6], Soumya Raychaudhuri[7] and Michael Brenner[1], [1]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Rheumatology Research Group, Institute for Inflammation and Ageing, College of Medical and Dental Sciences, University of Birmingham, Queen Elizabeth Hospital, Birmingham, United Kingdom, [4]Brigam and Women's Hospital, Boston, [5]Brigham and Women's Hospital, Boston, [6]University of Birmingham, Birmingham, United Kingdom, [7]Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Vascular endothelial cells that provide the structure for blood vessels have traditionally been perceived as passive, structural units that provide blood flow. We recently discovered that a key step in synovial sublining fibroblast expansion in rheumatoid arthritis (RA) is driven by endothelial-derived Notch signaling and that Notch3 blockade attenuates arthritis pathology. This observation suggests that synovial endothelial cells, rather than being passive conduits of blood flow, and orchestrate tissue remodeling through secretion of paracrine growth factors, or angiocrine factors. The goal of this study is 1) to define heterogeneity of synovial endothelial cells and 2) to identify novel angiocrine factors involved in the RA pathogenesis.

Methods: Synovial tissues were obtained from RA or osteoarthritis (OA) patients. For scRNAseq analysis, CD45- stromal cells from were subjected to droplet-based scRNAseq (10X Genomics). For bulk RNA-seq analysis of synovial endothelial cells, disaggregated synovial endothelial cells (CD45- PDPN- CD31+ CD146+) from were FACS-sorted and subjected to SMART-seq2. Confocal microscopy imaging analysis were performed to visualize protein expression of endothelial cell subset-specific markers.

Results: Synovial endothelial cell heterogeneity. We identified arterial (*PODXL*+ *NOTCH4*+), venous/capillary (*DARC*+ *CD74*+), and lymphatic (*LYVE1*+) endothelial cells as the major endothelial cell types in synovia. We identified distinct effector modules in venous/capillary and arterial endothelial cells. Whereas venous/capillary endothelial cells are characterized by high expression of genes encoding HLA class II molecules (*CD74*, *HLA-DRA*), arterial endothelial cells are the dominant cellular source of growth factors (*IGF2*, *PDGFB*) and morphogens (*DLL4*, *JAG1*).

Expansion of arterial endothelium in RA synovia. To define transcriptomic changes in RA synovial endothelial cells, we performed deep RNA-seq analysis of CD31+ CD146+ endothelial cells from RA and OA synovia. Differential gene expression analysis revealed striking upregulation of genes involved in cell adhesion (*ICAM2*, *MCAM*) and leukocyte recruitment (*CXCL12*). Interestingly, many endothelial genes upregulated in RA map to the arterial as opposed to

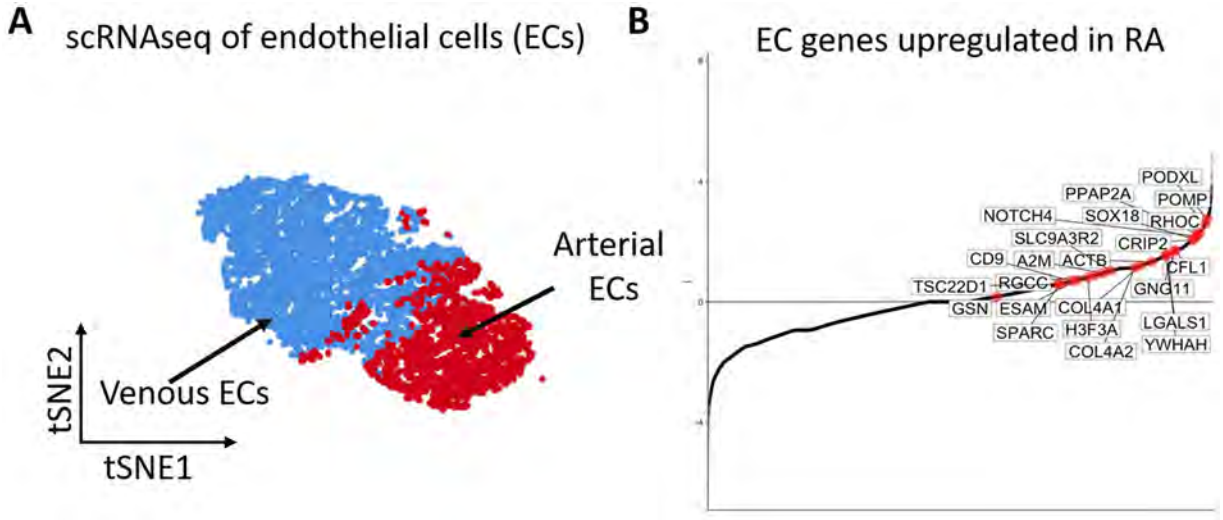

Figure 1. ScRNAseq analysis of synovial endothelial cells. A. Venous (blue) and arterial (red) endothelial cells projected in tsNE space. B. Endothelial genes upregulated in RA synovia.

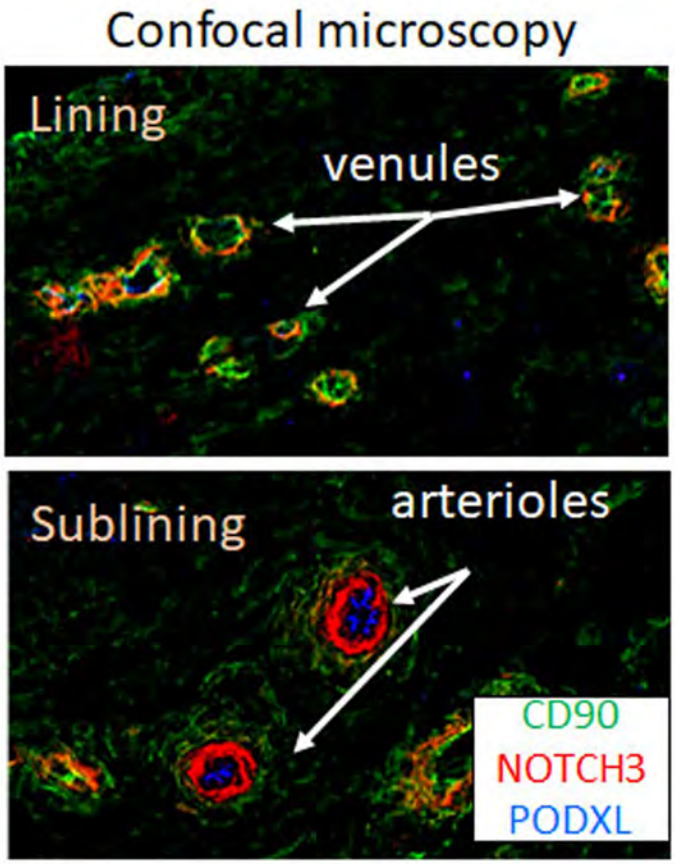

Figure 2. Representative confocal microscopy image of RA synovia endothelium network showing venules near lining and PODXL1+ arterioles in the subliing. Note Notch3 (red)+ cells near arterioles.

venous endothelial cell clusters in our scRNAseq analysis, including *NOTCH4* and *PODXL*, suggesting relative arterialization of endothelial cells in RA synovia (Fig. 1).

Arterial endothelium as the source of Notch gradient in synovial sublining. Using *PODXL* as a marker for arterial endothelial cells, we found PODXL+ endothelial cells are located deep in the synovial sublining. Spatial analysis revealed signification correlation between PODXL+ arterial endothelium and NOTCH3+ fibroblasts, suggesting arterial endothelium is the dominant source of Notch gradient driving sublining expansion in RA (Fig 2).

Conclusion: Single cell profiling of synovial endothelial cells revealed previously underappreciated transcriptomic heterogeneity that reflect distinct lineages and functional states. In RA, synovial endothelium transition towards an arterial state characterized by expression of angiocrine factors that contribute to arthritis pathology.

Disclosure: K. Wei, Gilead, 5; **I. Korsunsky**, Brilyant LLC, 5; **J. Marshall**, None; **G. Watts**, None; **T. Major**, None; **Z. Zhu**, None; **Y. Li**, None; **C. Buckley**, Mestag, 1, GSK, 5, Janssen, 5, Celsius, 2; **S. Raychaudhuri**, None; **M. Brenner**, None.

Abstract Number: 0972

Mapping Oligoclonally Expanded T Cells Within the Peripheral and Synovial Immune Landscape of Untreated ACPA+ Rheumatoid Arthritis Patients at the Single Cell Level

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SESSION INFORMATION
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Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Clonal T cell expansions – some large – have been identified in the peripheral blood (PB) and in synovial tissue (ST) of multiple joints from recently-diagnosed rheumatoid arthritis (RA) patients. As the degree of ST clonal dominance decreased with longer disease duration, new-onset RA presents the ideal opportunity to study the transcriptome and TCRα/β of individual clonotypes. This can be achieved using single-cell RNA-sequencing, which already identified novel T cell subsets in longstanding RA. To elucidate the TCR usage and transcriptome of oligoclonally expanded T cells in the PB and ST compartments in newly-diagnosed RA, we combined TCR repertoire, clonality and transcriptomic analysis of individual ST and paired PB mononuclear cells (PBMC) in untreated HLA-DRB1*0401$^+$ ACPA$^+$ RA patients.

Methods: PBMC and whole cryopreserved ST samples were collected from 4 treatment-naïve RA patients undergoing arthroscopic synovial biopsy. CD45$^+$ leukocytes from cryopreserved PBMC, and CD45$^+$ leukocytes and CD45$^-$ fibroblasts isolated from paired disaggregated ST, by fluorescence-activated cell sorting, were sequenced using 5' RNA/TCR single-cell 10x Genomics kits. Single-cell transcriptomic analysis, using the Seurat package in R, reconstructed the compartment-specific composition of PB and ST.

Results: Myeloid cells were expanded in the ST relative to PB. Myeloid and NK cell expansion was related to arthroscopic synovitis severity. NK and B cell clusters were proportionately smaller among ST than PB leukocytes. Transcriptomics identified 10 unique $CD3^+TCR^+$ populations in PB and ST, including cytotoxic, helper and regulatory T cells. In PB, the most expanded clonotypes were $CD8^+$ and $CD4^+$ cytotoxic T cells. ST expanded clonotypes included $CD8^+$ and $CD4^+$ T cells expressing cytotoxic and multiple cytokine genes, $CD4^+$*ICOS*$^+$ T cells with evidence of IL-6 signalling, and $CD4^+$*GATA3*$^+$ tissue-resident T cells. Shared ST and PB T cell clonotypes were predominantly cytotoxic polyfunctional $CD8^+$ T cells. A proportion of PB cytotoxic clonotypes matched known EBV and CMV-reactive clones, and a proportion of shared PB/ST cytotoxic clonotypes matched CMV-reactive clones.

Conclusion: Similar T cell clusters were identified in ST and PB. Transcriptomes of non-cytotoxic expanded $CD4^+$ T cell clonotypes in the ST of untreated patients suggest B cell interaction and help. The most expanded clonotypes in circulation include T cells with cytotoxic and proinflammatory capability, including known viral-specific clones, some of which reach and expand in RA ST. Antigen derived and presented from persistent viruses may expand responsive clones to be bystander drivers of synovial inflammation.

Disclosure: P. Wehr, None; **H. Nel**, None; **C. Zhou**, None; **A. Mehdi**, None; **A. Christ**, None; **H. Weedon**, None; **M. Wechalekar**, Janssen Research Philadelphia USA, 2; **R. Thomas**, Abbvie, 8, BMS, 5, 8, Janssen-Cilag, 8.

Abstract Number: 0973

Novel Network Tool Highlights Key Features Associated with Disease Pathotypes and Response to Treatment in Early Rheumatoid Arthritis

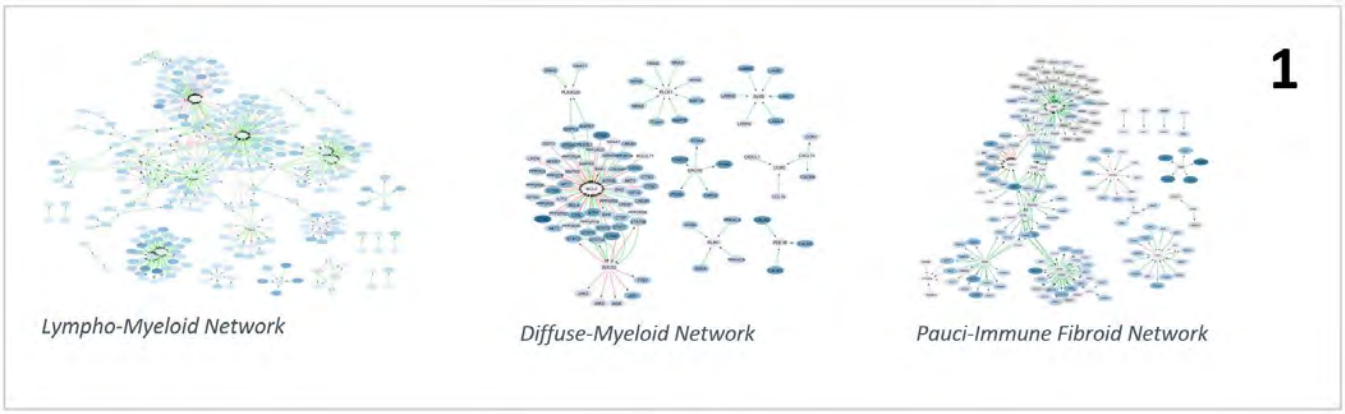
Elisabetta Sciacca[1], Anna Surace[2], Myles Lewis[1], Salvatore Alaimo[3], Vito Latora[4], Felice Rivellese[1], Alfredo Pulvirenti[3], Alfredo Ferro[3] and Costantino Pitzalis[5], [1]Centre for Experimental Medicine and Rheumatology, Queen Mary University of London, London, United Kingdom, [2]Centre for Experimental Medicine and Rheumatology, Queen Mary University of London, Liverpool, United Kingdom, [3]Bioinformatics Unit, Dept of Clinical and Experimental Medicine, University of Catania, Catania, Sicilia, Italy, [4]School of Mathematical Sciences Queen Mary, University of London, London, United Kingdom, [5]Queen Mary University of London, London, United Kingdom

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: RA – Etiology & Pathogenesis
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Biomedical research uses many statistical/bioinformatics tools to find genes or proteins differentially expressed between patient group of interest. However, biological elements are related to one another in a complex network. Understanding those networks is vital to give results meaning in a disease context.

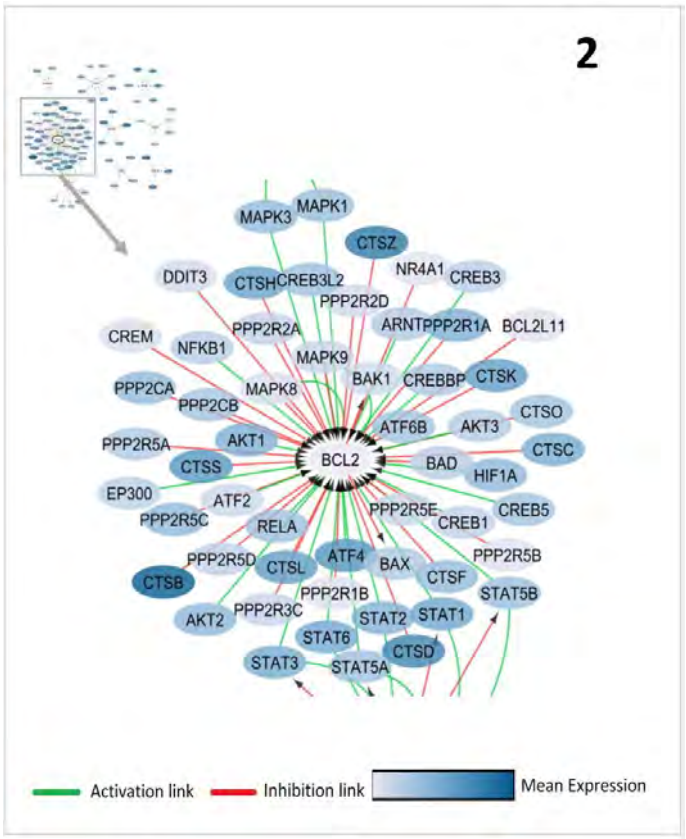
Treatment-naïve early rheumatoid arthritis (RA) patients have been described to have different histological pathotypes (lympho-myeloid, diffuse-myeloid, pauci-immune fibroid), with corresponding molecular signatures, associated with response to conventional synthetic Disease-Modifying Anti-Rheumatic Drugs (csDMARDs) [Lewis et al. 2019, Cell reports]. Purpose of this study was to use a novel pathway analysis approach to determine which gene networks are specifically activated in patients with different pathotypes or different response to csDMARDs.

Methods: We analysed RNA-Sequencing of 90 patients with early treatment-naïve RA fulfilling the 2010 ACR/EULAR Criteria recruited into the Pathobiology of Early Arthritis Cohort (PEAC). A detailed network of biological interactions



Pathotypes networks overview showing different number of nodes, edges and topology across the three groups.

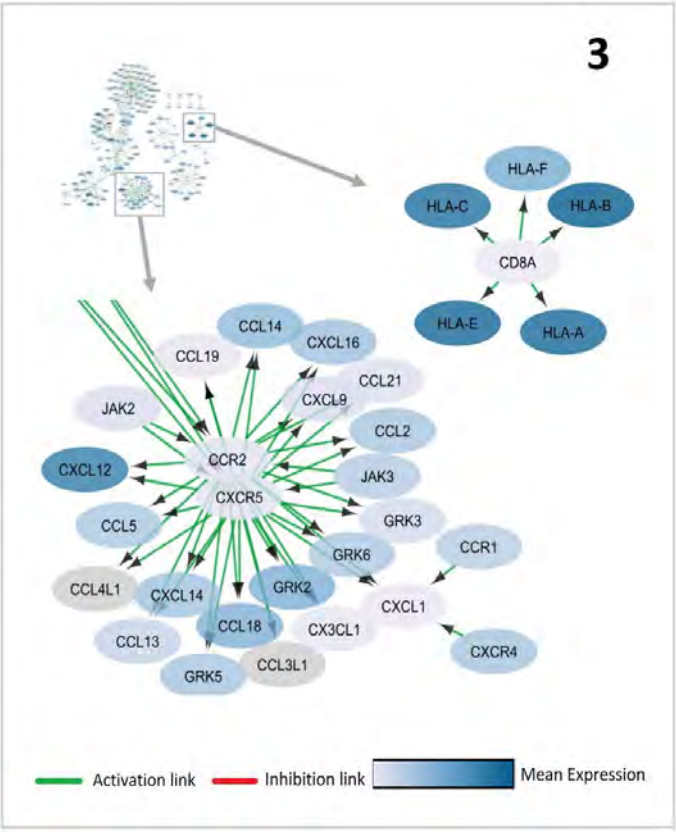
was built starting from the KEGG pathway repository and enriched with miRNA interactions from miRTarBase and



Cell survival genes in patients responding to Disease-modifying anti-rheumatic drug (DMARD) treatment.

miRecords. Interactions between transcription factors (TFs) and miRNAs were added from TransmiR.

For each category, the most active links between genes, protein, metabolites and miRNA were selected based on their RNA-Sequencing expression values. Links redundantly active in two or more categories were removed. The resulting subnetworks show interactions that are active in the selected category only.



Chemokine and T cell cluster genes activated in patients not responding to DMARD treatment.

Results: The interactions networks found for the three pathotypes showed a gene level confirmation of the above taxonomy. The lympho-myeloid pathotype network (373 activator links, 96 inhibitor links) is characterized by lymphocyte activation with NFKB and mTOR signalling and recruitment via chemokines (for example CCL5, CCL2 and CCL19). We found IL3R signalling and cell survival networks to be central in the diffuse-myeloid pathotype (20 activator links, 5 inhibitor links), while in a pauci-immune fibroid environment (430 activator links, 99 inhibitor links) remodelling of the extracellular matrix and vasculature was prominent (Fig. 1).

On one hand, patients who had a good EULAR response to csDMARDs showed cell survival networks with MAP kinase and STAT signalling around BCL2 (Fig. 2). On the other hand, non-response was linked to T cell genes and lymphocyte attraction via chemokine signalling (Fig.3).

Conclusion: Our novel approach of investigating gene networks leads to a deeper understanding of differences in disease pathotypes and response to treatment. Allowing greater insight into underlying mechanisms, it will facilitate more targeted treatment.

Disclosure: E. Sciacca, None; **A. Surace**, None; **M. Lewis**, None; **S. Alaimo**, None; **V. Latora**, None; **F. Rivellese**, None; **A. Pulvirenti**, None; **A. Ferro**, None; **C. Pitzalis**, None.

Abstract Number: 0974

Role of NR4A Nuclear Receptor Family in RA Synovial Ectopic Lymphoid Neogenesis Revealed by Single Cell Profiling

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: RA – Etiology & Pathogenesis

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Ectopic lymphoid structures (ELS) have been observed in synovial tissue of rheumatoid arthritis (RA) patients but their functional relevance in the disease remains unclear. Additionally, little is known about B cell activation pathways during ectopic lymphoid neogenesis (ELN). In this study, we utilized single cell RNA sequencing coupled with B cell repertoire sequencing to characterize B cell subsets that may play a role in ELN in RA synovial tissue and support local B cell activation and development of autoreactive plasma cells.

Methods: Synovial tissue was selected based on the presence of lymphocytic infiltrates by histology (n=4 RA patients). Tissue was disaggregated using protocols established by the Accelerating Medicines Partnership (AMP) consortium. scRNA-seq was performed on sorted tissue B cells using the 10x genomic platform with poly-A selected, 5' initiated expression and V(D)J libraries generated from each single cell. Transcriptomic clusters were compared using supervised classification techniques to AMP phase I RA synovial B cells (n=10), SLE kidney B cells, and blood B cells. Combined single cell repertoire/RNA sequencing from an additional 13 RA synovial samples and 10 matched blood B cells are currently under analysis in AMP phase II. In vitro studies were conducted for elucidation of signals promoting in situ B cell activation, with NR4A detected by qPCR and flow cytometry.

Results: Using single cell RNA sequencing analysis, we identified a unique B cell subset in the RA synovium characterized by high expression of NR4A1-3, a family of orphan nuclear receptors (NUR77, NURR1, and NOR1) that are induced by acute and chronic antigen stimulation in lymphocytes and function as ligand-independent transcription factors. The $NR4A^+$ B cell cluster showed evidence of somatic hypermutation (SHM) and class-switched recombination based on repertoire analysis. The rate of SHM was positively correlated with NR4A1 and NR4A2 gene expression and inversely correlated with IGHD gene expression. Gene Set Enrichment Analysis revealed that the $NR4A^+$ cluster has a transcriptomic profile between naïve and germinal center (GC) B cells sorted from tonsil and differentially expressed genes characteristic of GC centrocytes including CD83 and GPR183. In SLE kidney, and peripheral blood B cells, $NR4A^+$ B cells were reduced to 0.7% and 1.5% abundance, respectively, compared to >40% abundance in synovial tissue from AMP phase I and the 10X platform ($p< 0.001$ under logistic mixed models). NRA4 was upregulated at both the RNA and protein level upon activation through the B cell receptor in vitro. NR4A1 protein was expressed spontaneously in RA tissue B cells by flow cytometric and histologic analysis.

Conclusion: Our data suggest a dynamic progression of B cell activation in RA synovial ectopic lymphoid structures, with NR4A a potential read-out of chronic antigen activation and local adaptive immune responses.

Disclosure: N. Meednu, None; **F. Zhang**, None; **K. Escalera-Rivera**, None; **E. Corsiero**, None; **E. Prediletto**, None; **M. Bombardieri**, None; **E. DiCarlo**, None; **D. Orange**, None; **S. Goodman**, Pfizer, 1, Novartis, 1, UCB, 1, regenosine, 1, 2, Horizon, 1; **L. Donlin**, Stryker, 1, 2; **S. Raychaudhuri**, None; **C. Pitzalis**, None; **A. McDavid**, None; **J. Anolik**, None.

Abstract Number: 0975

Gasdermin D Modulates Murine Lupus and Its Associated Organ Damage

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Animal Models
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Gasdermin D (GSDMD) is the key executioner of the inflammatory cell death mechanism pyroptosis. Recent reports have also implicated GSDMD in other mechanisms of cell death, including apoptosis, necroptosis, and NETosis. Given the role of dysregulated cell death in autoimmune syndromes such as systemic lupus erythematosus (SLE), we hypothesized that GSDMD would play a pathogenic role by promoting inflammatory cell death leading to increased generation of nuclear autoantigens and autoantibodies.

Methods: Methods: The imiquimod-induced model of SLE was tested in Gsdmd-/- and wild-type C57BL/6 (WT) mice. At euthanasia, mice were examined for serum autoantibodies, renal function, immune complex deposition, organ inflammation, immune dysregulation and type I Interferon responses. A pristane-induced lung injury model in Gsdmd-/- and WT C57BL/6 was used to further confirm pulmonary phenotype. Regulation of various mechanisms of cell death was investigated in the mice.

Results: Unexpectedly, Gsdmd-/- mice developed enhanced mortality, more severe renal and pulmonary inflammation, and exacerbated autoantibody production in response to TLR-7 agonists. Pulmonary involvement was also more severe in the short-term pristane model in the absence of GSDMD. Lack of GSDMD was associated with increased levels of circulating nuclear autoantigens, tissue immune complex deposition, significant expansion of myeloid cell subsets, and enhanced B cell activation and differentiation. In the absence of GSDMD, enhanced autoantigen generation was associated with increased local induction of cell death in vivo.

Conclusion: GSDMD negatively regulates autoantigen generation and immune dysregulation in response to tissue injury, and may play previously unappreciated protective roles in systemic autoimmunity.

Disclosure: X. Wang, None; **L. Blanco**, None; **C. Carmona-Rivera**, None; **S. Nakabo**, None; **H. Pedersen**, None; **Z. Yu**, None; **M. Kaplan**, None.

Abstract Number: 0976

Kidney-infiltrating T Cells in Murine Lupus Nephritis Exhibit Transcriptional Heterogeneity and Oligoclonal Expansion

Shuchi Smita[1], Minjung Kim[1], Maria Chikina[1], Mark Shlomchik[1] and **Jeremy Tilstra**[1], [1]University of Pittsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Animal Models
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Lupus nephritis (LN) is a hallmark of SLE, affecting 50-60% of patients within 10 years of diagnosis. Current treatments for LN have suboptimal response rates and considerable side effects. T cells comprise the majority of infiltrating cells in LN kidney biopsies and contribute to end-organ damage in both SLE patients and murine models. Paradoxically, our recent work showed that kidney-infiltrating T cells (KITs) in murine LN exhibit classic features of T cell exhaustion, including expression of inhibitory receptors, suppressed cytokine production, reduced proliferation and altered metabolism. What remains unknown is whether KITs are a heterogenous or homogenous population. Additionally, prior work suggests that KITs are oligoclonal; however, these studies were completed using low resolution methods only assessing β-chain sequences of the T cell receptor (TCR). Thus, in this study using high throughput single cell RNAseq (scRNAseq) and TCR sequencing, we aim to more definitely define KITs in murine lupus nephritis.

Methods: To explore whether there is heterogeneity amongst KITS we performed scRNAseq using the 10X Genomics platform on flow-sorted kidney and splenic CD4 and CD8 T cells from lupus (MRL/lpr) prone mice. We completed two different comparisons in this study: the first comparing splenic T cells and KITs from MRL/lpr mice, with B6 splenocytes used as naïve controls. In the second study we evaluated KITs from 5 MRL/lpr mice using 5' libraries to obtain traditional scRNAseq transcripts along with TCR sequences, and cite-seq for PD-1 and Tim3 expression to better evaluate the exhausted T cell population. In all we obtained reads from nearly 30,000 individual cells.

Results: Despite KITs exhibiting a homogenous functional phenotype in our prior work, we found that there is significant heterogeneity in the transcriptional profile of KITs. CD8 KITs were mainly defined by four subgroups: activated (T_{EM}), exhausted (T_{EX}), tissue resident (T_{RM}), and a transitional group. Interestingly, all of these populations were transcriptionally distinct from splenic T cells. Similarly, CD4 KITs exhibited significant heterogeneity. One specific population of CD4 KITs may represent cytotoxic CD4 T cells defined by granzyme and perforin expression. Similar to the CD8 KITs, the CD4 KITs expressed more exhaustion related genes than did their splenic or naïve CD4 counterparts. Pseudotime trajectory analysis suggested that kidney infiltrating cells and specifically T_{EX} KITs could represent a terminal differentiation state. TCR sequencing analysis confirmed that there is an oligoclonal population of KITs, with single clones representing up to 10% of the CD4 or CD8 T cell compartment in a single mouse. Notably, these clones were more often associated with transcriptional clusters associated with T_{EX}.

Conclusion: These findings will improve our understanding of T cell function in lupus nephritis. We have uncovered that the KIT population is heterogenous, but also oligoclonal in nature. Furthermore, since clonal T cells are associated with an T_{EX} transcriptional profile, this supports the hypothesis that chronic antigen exposure and immune activation in the kidney drives T cell exhaustion.

Disclosure: S. Smita, None; **M. Kim**, None; **M. Chikina**, None; **M. Shlomchik**, None; **J. Tilstra**, None.

Abstract Number: 0977

Expanded T Peripheral Helper Cells and Increased Pathologic B Cell Lung Infiltration in Pristane-induced Murine Lupus in the Absence of BCL6+ Tfh Cells

Runci Wang[1], Pui Lee[2], Peter Nigrovic[3] and Deepak Rao[1], [1]Brigham and Women's Hospital, Boston, MA, [2]1. Boston Children's Hospital;2.Brigham and Women's Hospital;3.Harvard Medical School, Newton, MA, [3]Division of Rheumatology, Inflammation and Immunity, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; Division of Immunology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA, Boston

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Animal Models
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: PD-1^{hi} CXCR5^{-} T peripheral helper (Tph) cells are highly expanded in RA and SLE patients. Like T follicular helper (Tfh) cells, human Tph cells express high levels of ICOS and MAF and secrete IL-21 to facilitate B cell function. While Tfh cells depend on CXCR5 to home to follicles, Tph cells frequently express chemokine receptors that enable migration to inflamed sites. Whether Tph cells expand in murine autoimmunity models, and what the role of Tph cells is in vivo remains unknown. Further, whether Bcl6, a master regulator for Tfh cells, is necessary for Tph cells has not been established. We investigated these questions in pristane-induced lupus.

Methods: We evaluated the cellular and molecular features of Tph cells in the tissues of pristane-treated mice. C57bl6 or CD4^{cre}Bcl6$^{fl/fl}$ mice were injected with 0.4-0.5 ml pristane intraperitoneally once and harvested 2 weeks or >2 months later with age-matched controls. Tissues were processed for flow cytometry and histology.

Results: In pristane-treated mice, PD-1^{hi} CXCR5^{-} CD4^{+} T cells accumulated first in peritoneal fluid and spleen, and later in lung and peritoneal granulomas. These cells in the periphery expressed high levels of ICOS and Maf and produced IL-21, with an intermediate level of Bcl6. While lacking CXCR5, ~40% of PD-1^{hi} CXCR5^{-} T cells in pristane-treated mice expressed CXCR6 across multiple tissues. These results demonstrate that PD-1^{hi} CXCR5^{-} CD4^{+} T cells in this model closely resemble human Tph cells (Fig.1).

Accompanying Tph expansion, B cell responses were seen in pristane-treated mice. In spleen, frequencies of extrafollicular B cells, CD138^{+} plasmablasts, CD11c^{+}CD21^{-} age-associated B cells (ABC), and CD73^{+}IgD^{-} class-switched memory B cells increased, while the proportion of CD23^{hi}CD21^{+} follicular B cells decreased. The frequencies of plasmablasts, ABCs, and memory B cells also increased in lungs (Fig.2). Immunofluorescence microscopy revealed lymphoid aggregates within lungs of pristane-treated mice, which contained clusters of Tph cells and B cells.

To determine the role of Bcl6-dependent Tfh cells in this B cell response, we compared pristane-induced lupus in mice with conditional loss of Bcl6 in CD4^{+} T cells (CD4-Bcl6 KO) and littermate controls (WT). As expected, CD4-Bcl6 KO mice had reduced CXCR5^{+} Tfh cells, and also showed less expansion of extrafollicular, memory and CD138^{+} B cells in spleen, indicating a critical role for Tfh cells in B cell activation in spleen. In contrast, pristane-treated CD4-Bcl6 KO mice had increased frequencies of Tph cells, memory B cells and plasmablasts in lungs, suggesting that Tph accumulation and B cell responses within lungs can occur independently of Bcl6^{+} Tfh cells in pristane-induced lupus.

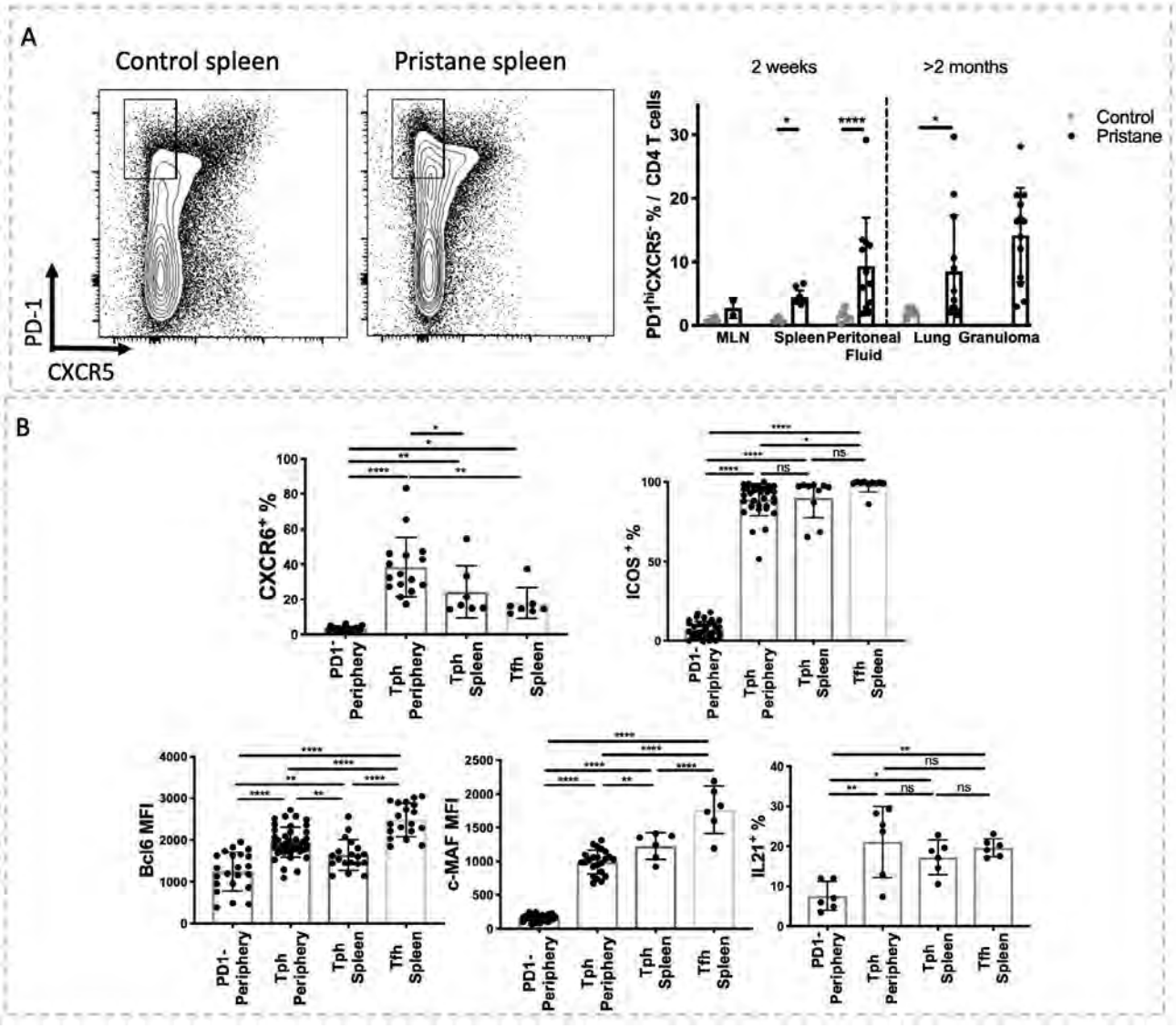

Figure 1. Expanded PD-1hiCXCR5- CD4 Tph cells in murine lupus expressed factors associated with B cell help, including ICOS, Maf and IL-21. A). PD-1hiCXCR5-CD4 T cells expanded in peritoneal fluid and spleen at 2 weeks and were found in lung and granuloma after 2 months in pristane-treated lupus mice (Mann-Whitney test, n= 5 - 13); B). CXCR6 was more frequency expressed on Tph cells in peripheral tissues (PF, lung, and granuloma) than in spleen Tph/Tfh cells and peripheral PD-1- cells; Tph and Tfh cells expressed comparable levels of ICOS, both significantly higher than PD-1-CXCR5- DN cells; Bcl6 and c-Maf were highly expressed by spleen Tfh cells, intermediately expressed by Tph cells in spleen and peripheral tissue, greater than peripheral DN cells; PD-1-, PD1hiCXCR5- Tph, PD1hiCXCR5+ Tfh cells were sorted from pristane-treated mice and stimulated in vitro; Tph and Tfh expressed higher IL-21 than PD1- cells; ordinary ANOVA. Mean±SD shown, , *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

Conclusion: Tph cells are expanded in spleen, target tissues, and ectopic lymphoid structures in pristane-treated mice. Murine Tph cells express molecules involved in B cell activation and migratory receptors distinct from Tfh cells. In the absence of Bcl6 and Tfh cells, pristane-induced lupus mice developed increased Tph cells and B cell activation in lung. These results provide the first in vivo evidence of a role for Tph cells in peripheral B cell responses in autoimmunity.

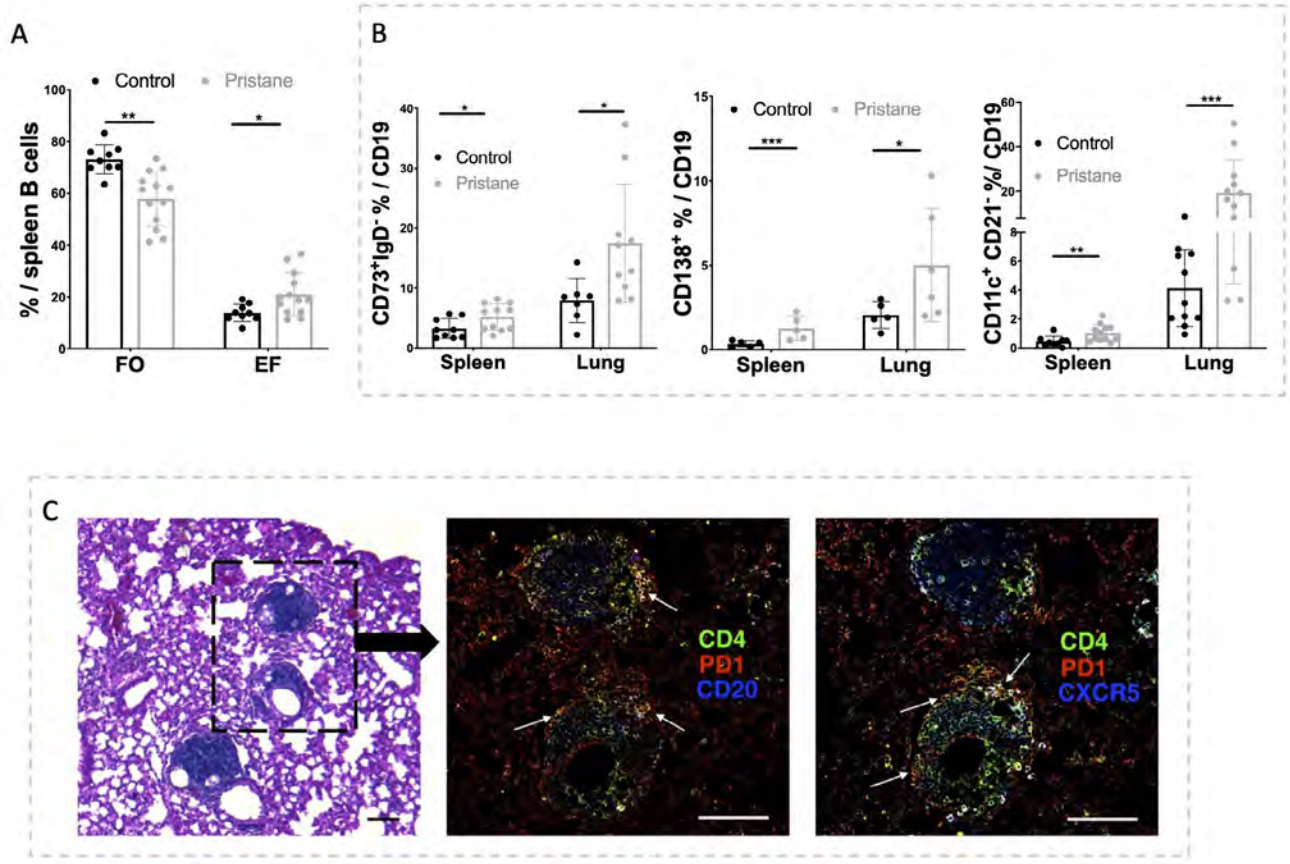

Figure 2. Pathologic B cells expanded in spleen, target organs, and ectopic lymphoid structures in pristane-treated mice. A) Increased extrafollicular B cells (mostly CD23loCD21hi marginal zone B cells) and decreased CD23hiCD21+ follicular B cells were found in the spleen of pristane-treated mice (n=9-13). B) CD11c+CD21- ABCs and CD73+IgD- class-switched memory B cells increased in PF and lung (n=6-12). CD138+ plasmablasts increased in spleen and lung (n=5-6). C) Immunofluorescence images of ectopic lymphoid aggregates in the lung of pristane-treated mice. Mean±SD shown, Mann-Whitney test, *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

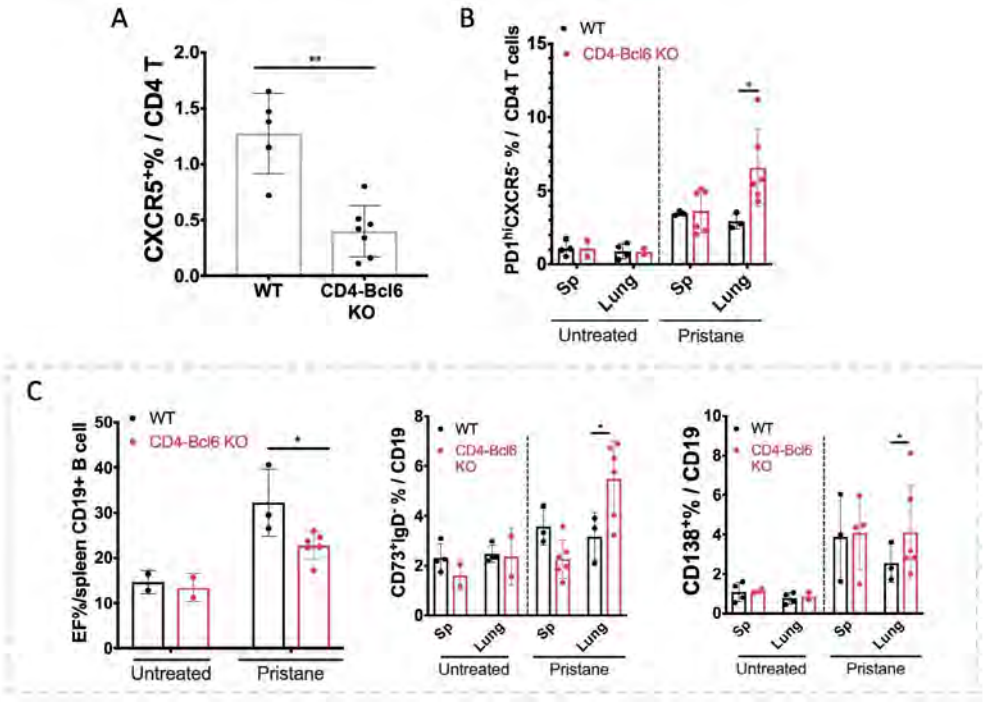

Figure 3. Pristane-treated CD4-Bcl6 KO mice had preferential expansion of Tph in the periphery with pathological B cell changes in the lung. A) Pristane-treated CD4-Bcl6 KO had decreased CXCR5+ CD4 cells compared to littermate controls; B) CD4-Bcl6 KO mice showed increased Tph expansion in lung (6% in CD4-Bcl6 KO and 3% in control) than littermate controls, with comparable Tph frequency in spleen. C) CD4-Bcl6 KO showed less expansion of extrafollicular B cells, class-switched memory B cells and CD138+ B cells in the spleen, while these populations were expanded in the lung compared to WT (n=2-6). Mean±SD shown, Mann-Whitney test, *p<0.05, **p<0.01.

Disclosure: R. Wang, None; **P. Lee**, None; **P. Nigrovic**, Novartis, 2, 5, BMS, 2, 5, Pfizer, 2, 5, Sobi, 5, Miach Orthopedics, 5, Simcere, 5, XBiotech, 5, Quench Bio, 5, Siglion, 5, Cerecor, 5, UpToDate, 7, American Academy of Pediatrics, 7, CARRA, 9; **D. Rao**, None.

Abstract Number: 0978

Border-associated Macrophages Drive Recruitment of Immune Cells into the Choroid Plexus in Mice with Neuropsychiatric Lupus

Erica Moore[1] and Chaim Putterman[1], [1]Albert Einstein College of Medicine, Bronx, NY

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Animal Models
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Neuropsychiatric manifestations are observed in 20-40% of systemic lupus erythematosus patients, including cognitive deficits and affective behaviors such as anxiety and depression. Neuropsychiatric lupus (NPSLE) involves complex mechanisms that are not yet completely understood. Inflammatory mediators such as cytokines and brain-specific autoantibodies, together with compromised brain barriers including the blood brain barrier and the blood-cerebrospinal fluid barrier (formed by the choroid plexus) as the site of entry of these mediators, are thought to play an important pathogenic role. Furthermore, a leukocytic infiltration into the brain is observed in

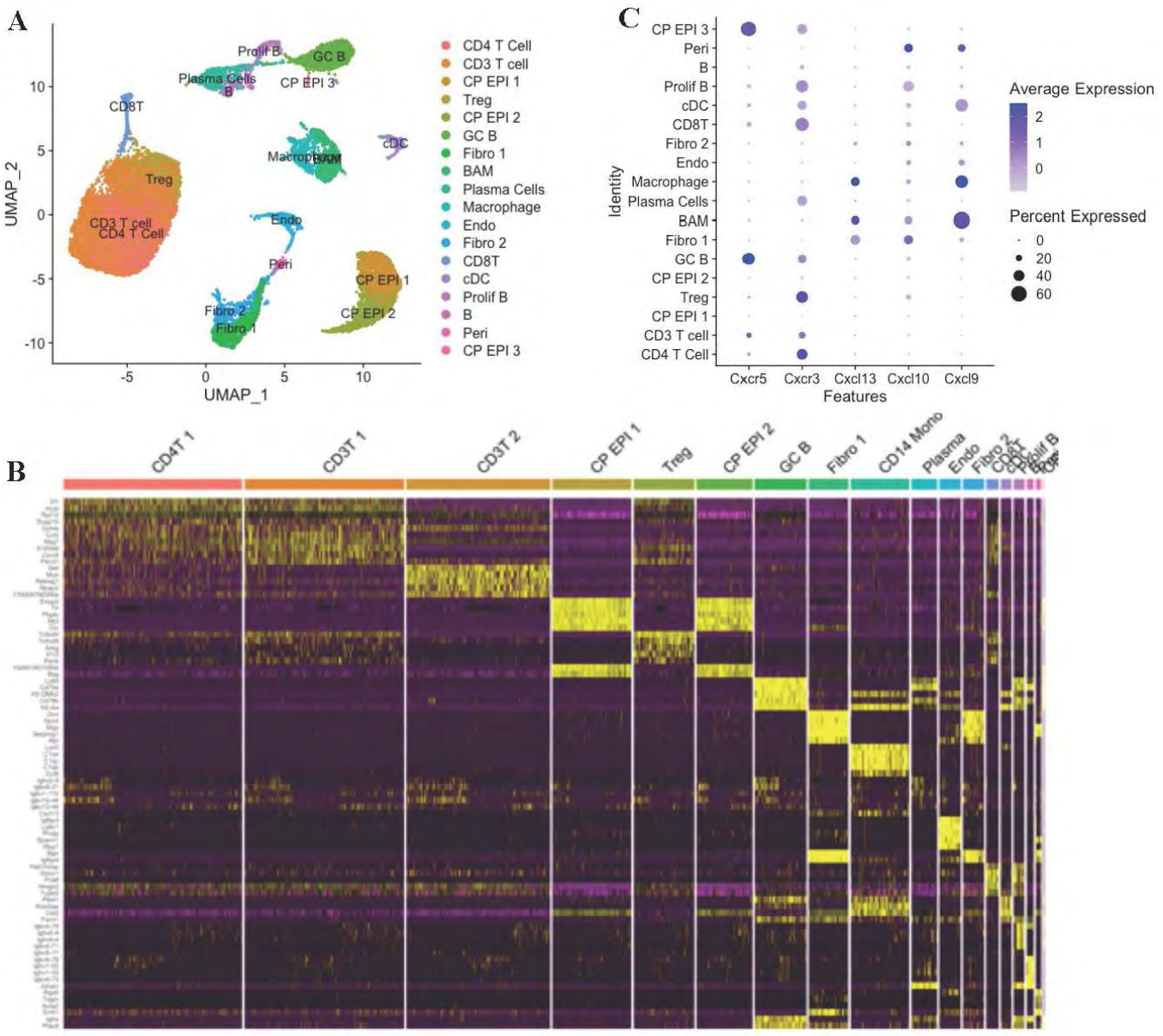

Figure 1. A) Uniformed Manifold Approximation and Projection of three 17 week old MRL/lpr choroid plexuses. B) Heatmap of top 5 significant markers in each cluster. C) Dot plot demonstrating both percentage and average expression of recruiting chemokine and cognate receptor expression. CP EPI = choroid plexus epithelial cells, Treg = T regulatory cells, GC B = germinal center B cells, Fibro = stromal fibroblast-like cells, BAM = border-associated macrophages, Endo = endothelial cells, cDC = circulating dendritic cells, Prolif B = proliferating B cells, Peri = pericytes.

both mouse NPSLE models and in some human NPSLE patients, and the resolution of this infiltration with treatment correlates with improved neuropsychiatric manifestations. Additional characterization of the choroid plexus and its cellular infiltrate was undertaken to better understand the potential contributions of B cells, T cells, and the choroid plexus to NPSLE.

Methods: The choroid plexus from 17-week old MRL/lpr mice (n=3) was excised and digested with 0.5% trypsin-EDTA. The single cell suspension was stained and subsequently sorted for live cells. Single cell immune profiling was performed with the 10X Genomics platform and the reads were sequenced with Illumina High-Seq instrument. The

transcripts were aligned using reference genome, mm10, using the CellRanger pipeline (10X Genomics). The Seurat R package and the 10X Genomics Loupe Browser were used for analysis.

Results: MRL/lpr choroid plexuses clustered into 18 unique cell clusters as depicted in Figure 1A. Preliminary characterization revealed four T cell clusters and multiple B cell subsets including germinal center B and plasma cells. Furthermore, the top 5 significant markers for each cluster is depicted by a heatmap in Figure 1B. Previous bulk RNA-sequencing revealed the upregulation of a number of germinal center-associated genes in the MRL/lpr choroid plexus including chemokines such as Cxcl9, Cxcl10, Cxcl11, and Cxcl13. We found that border-associated macrophages (BAM) and the additional macrophage cluster were the predominant sources of recruiting chemokines, particularly Cxcl9. Correspondingly, immune cells infiltrating the choroid plexus including T cells, B cells, and myeloid cells expressed the cognate receptors, Cxcr3 and Cxcr5. Further profiling of the T and B cells revealed the top BCR and TCR clones in the plasma cell and T cell clusters. The top BCR clones formed IgG2c and IgA antibodies and ranged between 15.3% to 41.1% of all B cells present in the libraries.

Conclusion: The extensive immune infiltration observed in the choroid plexus of neuropsychiatric lupus mice are potential contributors in the pathogenesis of NPSLE. Preliminary analysis reveals that border-associated macrophages contribute to the recruitment of immune cells into the choroid plexus by secreting CxCl9. Understanding the heterogeneity of brain resident and infiltrating immune cells and their transcriptomes may help identify potential therapeutic targets in NPSLE.

Disclosure: E. Moore, None; **C. Putterman**, Equillium, 1, 2.

Abstract Number: 0979

The Identification of Shared and Unique Myeloid Cell States in Pre- and Post-nephritic Lupus Mouse Models, Sle.Yaa1 and NZBW

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Animal Models
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Poor renal prognosis in lupus nephritis (LN) is associated with an abundance of renal macrophages and dendritic cells (DCs) but the role of these cells is not well understood. Because mouse models provide a system for studying the immune response in LN, we characterized the transcriptomes of myeloid cells during pre- and post-nephritic disease in Sle.Yaa1 mice that have an extra copy of TLR7 and NZB/W mice in which an activated adaptive immune system drives disease.

Methods: We sorted PBMCs and dissociated renal cells from pre- and post-nephritic Sle.Yaa1 and NZB/W mice (3-4 per group) using (i) CD45 beads/antibodies to isolate all immune cells or (ii) CD11b/CD11c to enrich for myeloid cells. We performed single cell transcriptomic profiling using 10x genomics and analyzed droplets that contained >500 genes and UMIs after doublet removal. We performed coarse and fine clustering and differential expression

(DE) (Seurat v3.0); gene set enrichment; trajectory (analysis Monocle v2.0 and Velcyto); and integration (Harmony). We identified residential vs. infiltrating cells by co-clustering intrarenal with blood data and by using published residential and infiltration gene signatures. We further identified macrophage and DCs subsets by scoring clusters using gene signatures generated from bulk RNASeq of intrarenal myeloid cells sorted by CD11b/CD11c and F4/80 expression.

Results: Several myeloid clusters were identified using data from >5000 cells from each mouse strain. Several novel subclusters of macrophages and DCs were identified in nephritic mice. Macrophages from pre- and post-nephritic mice clustered separately. Trajectory analysis of these cells indicated the acquisition of activation and inflammatory genes in nephritic mice including IL1b, AP1 (Fos and Jun), chemokines, cytoskeleton remodeling genes and polarization towards an alternative phenotype. Loss of Mmp13 and increased Mmp12 expression further suggests acquisition of a profibrotic phenotype. Fcrl5, Fcrg4 patrolling monocytes were found only in nephritic Sle.Yaa1 mice, confirming their expansion in TLR7 overexpressing models. Putative cluster functions were based on the top DE genes and gene set enrichment: macrophages had characteristics of resident cells and were enriched for phagocytosis, lysosomal function and antigen processing/presentation whereas DCs were enriched for transendothelial migration, chemokine signaling and cell adhesion genes, all characteristics of infiltrating cells. pDCs were enriched in genes in the glycolysis pathway whereas CD103 DCs were highly enriched for genes involved in oxidative phosphorylation.

Conclusion: Resident macrophages are the major myeloid subpopulation in pre-nephritic kidneys in both models and acquire an activated and profibrotic phenotype during nephritis. Post-nephritic kidneys from both models contained novel subclusters of expanded residential and infiltrating macrophages and DCs. Only Sle.Yaa1 kidneys contained patrolling monocytes. These analyses generate new hypotheses about the development of tissue damage in lupus kidney disease and can be used to identify molecular features shared with myeloid cells from human lupus kidneys for targeted follow-up studies.

Disclosure: P. Hoover, None; **M. Peters**, None; **D. Lieb**, None; **H. Geiger**, None; **R. Mishra**, None; **N. Hacohen**, None; **A. Davidson**, None.

Abstract Number: 0980

Hospitalized Infections in Lupus: A Nationwide Study of Types of Infections, Time-trends, Healthcare Utilization and In-Hospital Mortality

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes I: Morbidity
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: To examine the time-trends in hospitalized infections in lupus and the factors associated with healthcare utilization and in-hospital mortality.

Methods: We used the U.S. National Inpatient Sample data from 1998-2016 to examine the epidemiology, time-trends and outcomes of five, common hospitalized infections in people with lupus, namely, pneumonia, sepsis/bacteremia, urinary tract infection (UTI), skin and soft tissue infections (SSTI) and opportunistic infections (OI). Time-trends were compared using the Cochran Armitage test. Multivariable-adjusted logistic regression models examined

Table 1. Demographic characteristics of infection hospitalizations in people with versus without lupus

	Any Hospitalization in people with lupus (n=2,685,628)	Infection hospitalization in people **without** lupus (n=49,637,826)	Infection hospitalization in people **with** lupus (n=328,744)
Age, Mean (Std error); Median	51.7 (0.06); 51.2	59.9 (0.08); 66.1	52.5 (0.09); 51.9
Age category, in years			
<50	1,221,769 (45.5%)	13,940,265 (28.3%)	142,406 (43.4%)
50-64	806,720 (30.0%)	9,896,435 (20.1%)	99,576 (30.4%)
65-79	509,107 (19.0%)	13,221,914 (26.8%)	65,071 (19.8%)
≥80	147,961 (5.5%)	12,304,911 (24.8%)	20,724 (6.3%)
Sex			
Male	294,157 (11.0%)	23,419,036 (47.6%)	40,155 (12.2%)
Female	2,390,778 (89.0%)	25,819,094 (52.4%)	287,594 (87.7%)
Race			
White	1,279,668 (47.6%)	29,602,666 (60.1%)	156,206 (47.7%)
Black	639,196 (23.8%)	5,267,591 (10.7%)	75,487 (23.0%)
Hispanic	258,933 (9.6%)	4,185,067 (8.5%)	36,809 (11.2%)
Other/Missing	507,619 (18.9%)	10,136,912 (20.7%)	59,282 (18.1%)
Deyo-Charlson Score			
0	16 (0%)	15,683,828 (31.8%)	0 (0%)
1	903,434 (33.6%)	12,823,962 (26.0%)	114,414 (34.9%)
≥2	1,782,172 (66.4%)	20,780,211 (42.2%)	213,389 (65.1%)
Income Category			
0-25th percentile	744,212 (28.3%)	12,881,940 (26.8%)	95,737 (29.8%)
25-50th percentile	670,221 (25.5%)	13,221,834 (27.5%)	83,474 (26.0%)
50-75th percentile	618,437 (23.5%)	11,543,240 (24.0%)	74,328 (23.2%)
75-100th percentile	593,719 (22.6%)	10,467,811 (21.7%)	67,294 (21.0%)
Insurance			
Private	811,521 (30.3%)	10,869,686 (22.1%)	87,194 (26.6%)
Medicare	1,260,555 (47.0%)	27,313,205 (55.5%)	162,373 (49.6%)
Medicaid	448,849 (16.7%)	7,029,793 (14.3%)	57,650 (17.6%)
Other	75,012 (2.8%)	1,494,023 (3.0%)	8,488 (2.6%)
Self	85,087 (3.2%)	2,474,225 (5.0%)	11,591 (3.5%)
Hospital Location/Teaching			
Rural	246,012 (9.2%)	7,000,496 (15.0%)	32,201 (10.1%)
Urban	985,319 (36.8%)	19,133,806 (40.9%)	122,203 (38.4%)
Urban Teaching	1,445,881 (54.0%)	20,658,027 (44.1%)	163,779 (51.5%)
Length of hospital stay in days: Mean (SE); median	5.5 (0.01); 3.2	5.9 (0.001); 3.7	6.7 (0.03); 4.3
Length of hospital stay >3 days	1,400,893 (52.2%)	29,381,170 (59.4%)	211,906 (64.6%)
Total hospital charges (US $) >median	1,890,115 (70.4%)	28,243,139 (57.3%)	216,343 (66.0%)
Total hospital charges in US $: mean (SE); median	35,920 (239); 20,769	34,563 (156); 16,805	44,304 (395); 22,319
Discharge to home	2,199,836 (84.9%)	33,997,408 (74.5%)	252,509 (82.4%)
Died during hospitalization	57,191 (2.1%)	3,062,394 (6.2%)	16,675 (5.1%)

Table 1. Demographic characteristics of infection hospitalizations in people with versus without lupus

the factors associated with healthcare utilization (hospital stay >3 days, hospital charges above median, or discharge to non-home setting) and in-hospital mortality.

Results: There were 49,637,826 hospitalizations with infections in people without lupus and 328,744 in those with lupus. The average age of patients with lupus with a primary diagnosis of one of the infections was 52.5 years, with a median of 51.9 years (**Table 1**). Deyo-Charlson score greater than two accounted for 65% of people with lupus and

Table 2. Multivariable-adjusted correlates of utilization and mortality for hospitalized infections in lupus

	Total hospital charges >median	Discharge to Rehabilitation facility	Hospital Stay duration>median	In-hospital Mortality
	Adjusted odds ratio (95% Confidence Interval)			
Age category				
<50 years	Ref	Ref	Ref	Ref
50 - 64 years	**1.09 (1.05, 1.14)**	**1.77 (1.67, 1.88)**	**1.27 (1.22, 1.32)**	**1.47 (1.33, 1.61)**
65 - 79 years	0.98 (0.92, 1.03)	**2.88 (2.68, 3.09)**	**1.35 (1.28, 1.42)**	**2.13 (1.91, 2.39)**
≥80 years	0.92 (0.85, 1.00)	**6.21 (5.67, 6.81)**	**1.60 (1.47, 1.73)**	**2.90 (2.51, 3.34)**
Female Sex	1.00 (0.95, 1.06)	1.06 (0.99, 1.14)	1.04 (0.99, 1.10)	**0.79 (0.72, 0.86)**
Race/ethnicity				
White	Ref	Ref	Ref	Ref
Black	**1.16 (1.10, 1.21)**	**1.17 (1.10, 1.24)**	**1.12 (1.07, 1.17)**	1.06 (0.96, 1.17)
Hispanic	**1.30 (1.22, 1.38)**	**0.76 (0.69, 0.83)**	1.03 (0.97, 1.09)	0.95 (0.84, 1.08)
Other/missing	**1.13 (1.08, 1.19)**	1.00 (0.94, 1.07)	**1.09 (1.04, 1.14)**	**1.26 (1.14, 1.40)**
Deyo-Charlson score				
0	Not estimable*	Not estimable*	Not estimable*	Not estimable*
1	Ref	Ref	Ref	Ref
≥2	**1.34 (1.29, 1.39)**	**1.47 (1.39, 1.55)**	**1.38 (1.33, 1.43)**	**1.40 (1.28, 1.53)**
Primary Infection Diagnosis				
Sepsis	Ref	Ref	Ref	Ref
OI	**0.75 (0.68, 0.83)**	**0.52 (0.45, 0.59)**	1.08 (0.97, 1.20)	**0.50 (0.41, 0.61)**
SSTI	**0.35 (0.33, 0.37)**	**0.34 (0.32, 0.36)**	**0.51 (0.48, 0.53)**	**0.05 (0.04, 0.07)**
UTI	**0.30 (0.28, 0.33)**	**0.27 (0.24, 0.30)**	**0.30 (0.28, 0.32)**	**0.03 (0.02, 0.05)**
Pneumonia	**0.57 (0.54, 0.59)**	**0.35 (0.33, 0.37)**	**0.59 (0.57, 0.62)**	**0.26 (0.24, 0.28)**
Insurance payer				
Medicare	**1.19 (1.14, 1.25)**	**1.67 (1.56, 1.78)**	**1.14 (1.09, 1.19)**	**1.13 (1.01, 1.25)**
Medicaid	**1.11 (1.05, 1.17)**	**1.41 (1.30, 1.53)**	**1.09 (1.03, 1.15)**	**1.14 (1.00, 1.29)**
Other	1.08 (0.97, 1.21)	1.08 (0.90, 1.29)	1.03 (0.91, 1.17)	1.24 (0.97, 1.60)
Private	Ref	Ref	Ref	Ref
Self	1.04 (0.94, 1.14)	**0.68 (0.56, 0.83)**	0.96 (0.87, 1.05)	1.12 (0.88, 1.42)
Hospital Region				
Northeast	Ref	Ref	Ref	Ref
Midwest	**0.69 (0.65, 0.73)**	1.02 (0.95, 1.10)	**0.80 (0.76, 0.85)**	**0.73 (0.64, 0.83)**
South	**0.85 (0.80, 0.89)**	**0.83 (0.78, 0.89)**	0.98 (0.93, 1.03)	1.00 (0.90, 1.12)
West	**1.11 (1.04, 1.18)**	**0.85 (0.77, 0.90)**	0.72 (0.68, 0.77)	0.91 (0.80, 1.03)
Hospital Location/Teaching				
Rural	Ref	Ref	Ref	Ref
Urban	**2.63 (2.47, 2.80)**	**0.86 (0.79, 0.93)**	**1.42 (1.34, 1.51)**	**1.29 (1.11, 1.49)**
Urban Teaching	**2.25 (2.12, 2.39)**	**0.73 (0.67, 0.79)**	**1.36 (1.28, 1.44)**	**1.43 (1.24, 1.65)**
Hospital Bed size				
Small	Ref	Ref	Ref	Ref
Medium	**1.26 (1.19, 1.34)**	**0.89 (0.83, 0.96)**	**1.14 (1.07, 1.20)**	**1.41 (1.23, 1.62)**
Large	**1.72 (1.64, 1.82)**	**0.83 (0.77, 0.89)**	**1.30 (1.23, 1.37)**	**1.56 (1.37, 1.77)**

Not estimable, due to the lack of people in this category; also adjusted for income (not signif); **Bold** indicates a p-value<0.05

Table 2. Multivariable-adjusted correlates of healthcare utilization and mortality for hospitalized infections in lupus

infection, and lowest income quartile for 30% . The lowest income quartile accounted for a third of all lupus and lupus with primary infection hospitalizations.

Hospitalization for any of these 5 infections (composite) increased from 10.7% of all lupus hospitalizations in 1998-2000 to 15.6% in 2015-16 (10,748 vs. 15,645 per 100,000). The corresponding rate of composite infection in the general NIS population increased from 5.8% in 1998-2000 to 10.2% in 2015-16 (5,836 vs. 10,171 per 100,000).

The hospitalization rate /100,000 claims in 1998-2000 versus 2015-2016 (and increase) were as follows: OI, 1.13 vs. 1.61 (1.2-fold); SSTI, 4.78 versus 12.2 (2.5-fold); UTI, 1.94 versus 6.12 (3.2-fold); pneumonia, 15.09 vs. 17.05

Figure 1. Time-trends in the rates of various infections in people with lupus with varying denominator of total NIS claims (A) or total lupus claims (B)

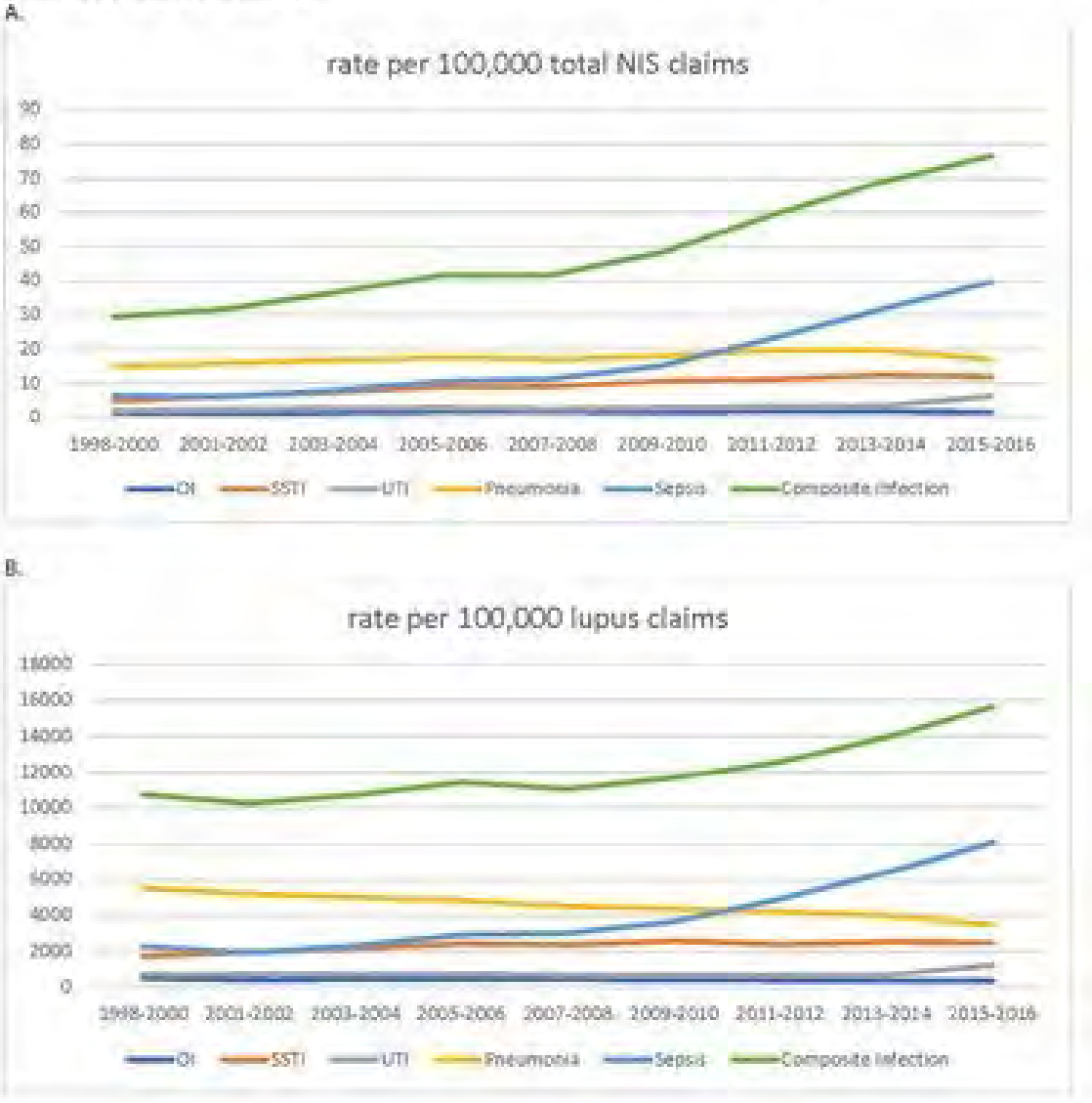

Figure legend
Infection rates are per 100,000 NIS claims (A) and per 100,000 lupus claims (B). The y-axis scales are different for the two panels. The x-axis shows study time-periods from 1998 to 2016

Figure 1. title. Time-trends in the rates of various infections in people with lupus with varying denominator of total National Inpatient Sample claims (A) or total lupus claims (B) Figure 1 legend Infection rates are per 100,000 NIS claims (A) and per 100,000 lupus claims (B). The y-axis scales are different for the two panels. The x-axis shows study time-periods from 1998 to 2016

(1.1-fold); and sepsis, 6.31 vs. 39.64 (6.3-fold; **Figure 1**). In 2011-12, sepsis surpassed pneumonia as the most common hospitalized infection in people with lupus. In multivariable-adjusted models, sepsis diagnosis, older age, Deyo-Charlson score ≥2, Medicare or Medicaid insurance, and urban hospital location were significantly associated with increased odds of in-hospital mortality and all healthcare utilization outcomes; and the black race was significantly associated with increased odds of healthcare utilization (**Table 2**).

Conclusion: Our study found increasing rates of hospitalized infections in lupus over time, and the surpassing of pneumonia by sepsis as the most common infection. We identified risk factors associated with poorer healthcare utilization outcomes and in-hospital mortality. These findings can inform patients, providers and policy-makers regarding lupus infection burden and lead to interventions/pathways to improve outcomes.

Disclosure: J. Singh, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **J. Cleveland**, None.

Abstract Number: 0981

Mortality Among Minority Populations with Systemic Lupus Erythematosus, Including Asian and Hispanic Status: The California Lupus Surveillance Project, 2007-2017

Milena Gianfrancesco[1], Maria Dall'Era[2], Louise Murphy[3], Charles Helmick[3], Jing Li[1], Stephanie Rush[1], Laura Trupin[1] and Jinoos Yazdany[4], [1]University of California, San Francisco, San Francisco, CA, [2]Division of Rheumatology, University of California, San Francisco, CA, [3]Centers for Disease Control and Prevention, Atlanta, GA, [4]UCSF, San Francisco, CA

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes I: Morbidity
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multi-system autoimmune disease with manifestations that vary widely in severity. Contemporary data indicate that minority populations are at higher risk of developing SLE and have more severe outcomes. However, population-based estimates of mortality by race and ethnicity are lacking, particularly for Asians and Hispanics.

Methods: The California Lupus Surveillance Project identified potential SLE cases using community rheumatology and nephrology clinics, community hospitals, and integrated healthcare systems among individuals who were residents of San Francisco County, CA during January 1, 2007 – December 31, 2009. SLE cases were defined as using American College of Rheumatology Classification Criteria (≥4 of the 11 revised criteria as defined in 1982 and updated in 1997) or two alternative definitions: SLE diagnosed by the patient's treating rheumatologist plus 3 ACR criteria; or lupus-related kidney disease (World Health Organization class II-VI lupus nephritis upon biopsy or documented record of SLE diagnosis and dialysis or renal transplantation). Cases were matched to the 2007-2017 National Death Index (NDI) data to measure SLE mortality by age, sex, race and ethnicity. Multivariable risk ratios estimated the association between race and Hispanic/Latino ethnicity with mortality, adjusting for age, sex and years since diagnosis. Standardized mortality ratios (SMRs) estimated observed versus expected deaths by age group, sex, race and Hispanic/Latino ethnicity.

Results: Of the 812 SLE cases analyzed, 90% were female; 38% were white, 20% black, 36% Asian, and 5% mixed/other race; and 17% were Hispanic/Latino. 135 deaths (16.6%) were identified. Mean age at diagnosis among all SLE cases was 34.9 (±15.9) years, and mean age at death was 62.0 (±15.8) years. Mortality increased with older age; among racial/ethnic groups, blacks had the highest percent mortality (25.0%) and a significantly increased risk of mortality after adjusting for age group, sex, ethnicity and disease duration (Table 1). There were no differences in mortality by sex or Hispanic/Latino ethnicity. On average, black individuals died 6.8 years earlier than whites; individuals of Hispanic/Latino ethnicity died 9.5 years earlier than non-Hispanic/Latinos.

Overall, SMRs were three times higher among SLE cases than in the general population of San Francisco County (Table 2). SMRs for those with SLE were four times higher for females, Asians and Hispanic/Latinos, three times higher for males, and two times higher for whites and blacks compared with their non-SLE counterparts. Among females, SMRs were exceptionally high for Asians (4.1) and Hispanic/Latinas (5.8).

Table 1. Factors associated with mortality among cases of systemic lupus erythematosus (SLE) from 2007-2017 – California Lupus Surveillance Project†

Characteristic	No. Deaths / No. SLE Cases	% Mortality	Multivariable-adjusted Risk Ratio (95% CI)
Overall	135/812	16.6	*NA*
Sex			
Female	119/731	16.3	1.0 (0.6, 1.6)
Male	16/81	19.8	*Reference*
Age group (years)			
10-34	11/204	5.4	*Reference*
35-44	15/175	8.6	1.5 (0.7, 3.1)
45-54	26/185	14.1	2.1 (1.1, 4.2)
55-64	33/153	21.6	3.3 (1.8, 6.3)
65-74	35/70	50.0	7.4 (4.0, 14.0)
75+	15/25	60.0	9.3 (4.8, 18.0)
Race			
White	45/312	14.4	*Reference*
Black	41/164	25.0	1.5 (1.1, 2.3)
Asian	45/295	15.3	1.2 (0.8, 1.7)
Other	2/22	9.1	1.3 (0.3, 5.9)
Ethnicity§			
Non-Hispanic/Latino	112/604	18.5	*Reference*
Hispanic/Latino	19/123	15.5	1.1 (0.7, 1.8)

Table 2. Standardized mortality ratios* for cases of systemic lupus erythematosus (SLE) from 2007-2017, age-standardized†, by sex, race§, and Hispanic/Latino ethnicity¶ – California Lupus Surveillance Project

Characteristic	Standardized mortality ratio (95% CI)
Overall	3.0 (2.5, 3.5)
Sex	
Female	3.8 (3.1, 4.5)
Male	2.9 (1.7, 4.7)
Race	
White	2.3 (1.6, 3.0)
Black	2.0 (1.4, 2.7)
Asian	3.8 (2.7, 5.0)
Ethnicity	
Hispanic/Latino	3.9 (2.4, 6.1)
Race for females**	
White females	2.9 (2.1, 3.9)
Black females	2.5 (1.8, 3.4)
Asian females	4.1 (2.9, 5.7)
Ethnicity for females**	
Hispanic/Latina females	5.8 (3.5, 9.2)

Conclusion: These findings provide the first population-based estimates of mortality among Asians and Hispanic/Latinos with SLE and suggest that public health programs and clinical practices targeting the health and maintenance of low disease activity within these populations are needed to reduce mortality.

Disclaimer: The findings and conclusions in this report are those of the authors and do not necessarily represent the official position of the Centers for Disease Control and Prevention.

CI = Confidence Interval * Population estimates by age group, sex, race, and ethnicity for San Francisco County from 2007-2017 were obtained from the CDC Wonder database (https://wonder.cdc.gov): Centers for Disease Control and Prevention, National Center for Health Statistics. Underlying Cause of Death 1999-2018 on CDC WONDER Online Database, released in 2020. Data are from the Multiple Cause of Death Files, 1999-2018, as compiled from data provided by the 57 vital statistics jurisdictions through the Vital Statistics Cooperative Program. Accessed at http://wonder.cdc.gov/ucd-icd10.html on Mar 21, 2020 6:24:20 PM † Risk ratios estimated using a multivariable Poisson model that modeled sex, age category, race (white, black, Asian, other), ethnicity (non-Hispanic/Latino, Hispanic/Latino) simultaneously, adjusting for years since diagnosis. A total of 104 cases were excluded from the multivariable model: 19 cases were missing race information, including two who died, and 85 cases were missing Hispanic/Latino ethnicity status, including four who died. § Hispanic/Latino ethnicity is considered a distinct concept from race, therefore it was collected and reported separately from race.

CI = Confidence Interval * The standardized mortality ratio is a ratio between the observed number of deaths in those with SLE and the number of deaths expected, based on age groups defined in the CDC Wonder Database. Sex, race and Hispanic/Latino ethnicity specific rates in San Francisco County were used, depending on the particular characteristic examined. CIs are calculated for each estimated SMR by assuming a Poisson process. †Age in 2008 was used for adjustment. §Forty-one cases were excluded from race-specific analyses, including four who died: 22 cases had missing race information and 19 cases identified as a race other than white, black or Asian, for which estimates are not available through the CDC Wonder Database. ¶Eighty-five cases who were missing Hispanic/Latino ethnicity status, including four who died, were excluded from ethnicity-specific estimates. ** For female-specific race and ethnicity analyses, crude rates for age group < 15 years were not provided by the CDC Wonder Database or were unreliable and therefore not included in calculations; there was insufficient sample size to generate specific race/ethnic estimates for men.

Disclosure: M. Gianfrancesco, None; **M. Dall'Era**, Janssen, 5, AstraZeneca, 5; **L. Murphy**, None; **C. Helmick**, None; **J. Li**, None; **S. Rush**, None; **L. Trupin**, None; **J. Yazdany**, Eli Lilly, 5, Astra Zeneca, 5.

Abstract Number: 0982

Genetics of Avascular Necrosis in Children and Adults with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes I: Morbidity

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Table. Effect estimates and *p*-values of genome-wide significant SNPs from time-to-AVN GWAS and corresponding values from logistic GWAS

RSID	CHR	BP	Hazard Ratio (95% CI)	Survival *P*-value	Odds Ratio (95% CI)	Logistic *P*-value	MAF
rs34118383	2	175465532	3.0 (2.0,4.4)	$1.9x10^{-8}$	1.1 (1.0,1.1)	0.0002	0.184
rs113585380	4	7403349	18.1 (7.0,46.6)	$1.9x10^{-9}$	1.3 (1.1,1.5)	0.0008	0.013
rs73311970	8	109767335	6.3 (3.4,11.6)	$3.9x10^{-9}$	1.3 (1.1,1.4)	$2.8x10^{-6}$	0.023
rs73311967	8	109765164	6.2 (3.3,11.6)	$4.3x10^{-9}$	1.3 (1.1,1.4)	$2.3x10^{-6}$	0.022
rs73311974	8	109769564	6.2 (3.4,11.4)	$9.6x10^{-9}$	1.3 (1.1,1.4)	$3.9x10^{-6}$	0.023
rs150768740	9	12172252	17.9 (6.7,47.9)	$8.9x10^{-9}$	1.3 (1.2,1.6)	0.0001	0.010
rs117710060	9	12132226	17.1 (6.5,45.3)	$1.1x10^{-8}$	1.3 (1.1,1.5)	0.0005	0.012
rs78353778	11	1949425	26.1 (8.6,79.5)	$9.4x10^{-9}$	1.2 (1.0,1.3)	0.05	0.019
rs114513489	12	77635418	6.2 (3.4,11.3)	$2.5x10^{-9}$	1.2 (1.1,1.2)	0.0003	0.036
rs74492172	12	77634994	6.2 (3.4,11.3)	$2.6x10^{-9}$	1.2 (1.1,1.2)	0.0003	0.036
rs145992614	12	77642670	5.3 (3.0,9.4)	$1.2x10^{-8}$	1.1 (1.1,1.2)	0.0007	0.043

RSID = Rapid Stain Identification; CHR = Chromosome; BP = Base Pair; CI = Confidence Interval; MAF = Minor Allele Frequency

Background/Purpose: Genetics have been shown to contribute to risk of avascular necrosis (AVN), a debilitating complication of systemic lupus erythematosus (SLE). Our aim was to identify genetic risk loci for AVN in people with childhood-onset (cSLE) and adult-onset SLE (aSLE).

Methods: The study consisted of patients with SLE from two tertiary care centres. Participants all met ≥4 of the ACR/SLICC classification criteria for SLE. All participants had prospectively collected clinical data and were genotyped on the Illumina multiethnic array. Ungenotyped SNPs were imputed and ancestry was inferred using principal components (PCs) (1000 Genomes Project reference). The outcome was defined as symptomatic AVN confirmed by imaging (radiograph, CT, bone scan and/or MRI). GWAS of AVN using both time-to-event analysis and logistic regression were conducted with follow-up truncated at 20 years. Models were adjusted for sex, age of SLE diagnosis, cSLE vs. aSLE, PCs, lupus nephritis status, exposure to high dose glucocorticoids, and time from SLE diagnosis to first clinic appointment. High dose glucocorticoids were defined as ≥40 mg/day or ≥2 mg/kg body weight per day (for pediatrics) for at least 30 days. A genome-wide significance threshold ($p< 5x10^{-8}$) was used to indicate statistical significance.

Results: The cohort included 940 individuals with SLE (56% cSLE). The median age of SLE diagnosis was 16.9 years (IQR=15.8) and 87% were female. 71 patients (8%) had imaging-confirmed AVN. Among AVN cases, 82% met the definition for high-dose glucocorticoid exposure compared to 46% of non-AVN patients. In the multivariate time-to-event GWAS, 11 SNPs met the genome-wide significance threshold. The hazard ratios for these significant SNPs ranged from 3.0 (95%CI: 2.4, 4.0) to 26.1 (95% CI: 8.6, 79.5) (Table). These SNPs represented 6 independent loci predictive of earlier AVNinkage disequilibrium < 0.8), with minor allele frequencies (MAF) from 1-18%. Of these SNPs, 3 were linked with genes: *WIPF1*, *TMEM74*, and *LOC105375976*. No SNPs met genome-wide significance in multivariate logistic GWAS with AVN.

Conclusion: Six independent SNPs were found to be significantly associated with decreased time to AVN, in children and adults with SLE. All variants were rare (MAF< 0.05) with the exception of rs34118383 (Chr2), an intronic variant of

the *WIPF1* gene (MAF=0.18). *WIPF1* encodes a protein essential in the formation of podosomes, actin-rich adhesive structures which are necessary for osteoclast-mediated bone resorption. *TMEM74* is involved in the induction of autophagy, a form of programmed cell death, which is necessary for osteoblast and osteoclast homeostasis. These SNPs have not been previously associated with AVN-risk in SLE or non-SLE populations. Future studies are required to replicate these findings in independent cohorts.

Disclosure: D. Webber, None; **J. Cao**, None; **D. Dominguez**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **A. Knight**, None; **D. Levy**, None; **L. Ng**, None; **A. Paterson**, None; **Z. Touma**, None; **M. Urowitz**, None; **J. Wither**, None; **E. Silverman**, None; **L. Hiraki**, None.

Abstract Number: 0983

Outcomes Following Antimalarial Withdrawal in Patients with Quiescent Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes I: Morbidity
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Antimalarial medications (AMs) are central to the management of SLE, affording numerous clinical benefits including the reduction of disease flare. However, little is known about the effects of AM withdrawal in patients who have achieved prolonged disease quiescence. We aimed to investigate the rate of flare in lupus patients who withdrew their AM after achieving clinical remission for at least one year, compared to those who continued therapy. Furthermore, we aimed to compare flare rates in cases who tapered AM versus abruptly withdrew.

Methods: Using the University Lupus Clinic long-term observational cohort study database, we identified 1573 lupus patients ever treated with AM. Cases were defined as those who achieved clinical remission for at least one year then ceased their AM (n = 165). Index date was defined as the date of complete AM cessation. Controls were defined as patients who achieved clinical remission for at least one year and continued AM. Controls were matched according to the duration of antimalarial therapy before the start of clinical remission and the duration of therapy from remission date to case index date (Figure 1). All patients were required to have at least two years of follow up. Of 96 cases with adequate follow up, 88 were successfully matched to one control and 85 to a second control, resulting in a near 1:2 match. In total, there were 88 cases and 173 controls.

Results: Patient characteristics for cases (withdrew AM) and controls (continued AM) are presented in Table 1. Disease flare occurred in 61.4% of cases compared to 45.1% of controls (p = 0.002, Figure 2). The most common types of flare were skin and musculoskeletal flares. Reasons for AM withdrawal included self-cessation (feeling well, pregnancy, medication concerns), toxicity (retinal, mucocutaneous, cardiac), disease quiescence or other reasons such as side effects requiring investigation. Retinal toxicity as defined by the SLICC damage index occurred in 1.9% of patients. Over half of patients who withdrew AM later restarted it, typically due to disease flare. Following recommencement for flare, most patients (88%) recaptured control or improved, while 12% had further flares. Regarding

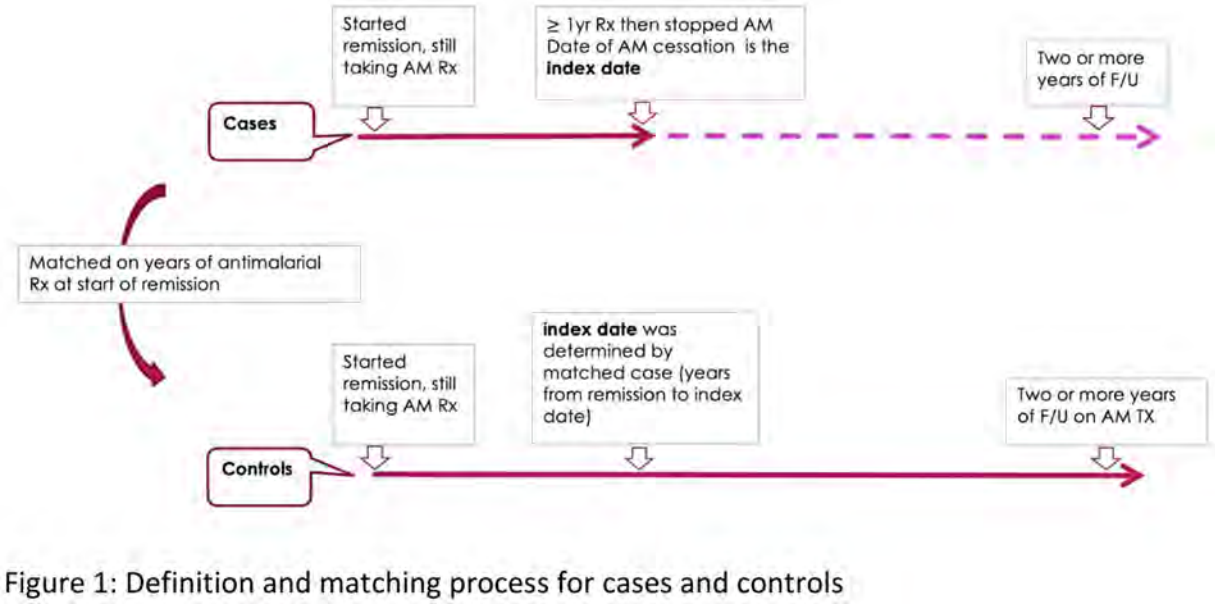

Figure 1. Definition and matching process for cases and controls

patients who withdrew AM, 42% tapered and 58% ceased abruptly (Table 1). The median duration (months) spent on AM from one year after clinical remission to cessation was expectedly longer in the taper group (29.2 months) compared to the abrupt withdrawal group (11.2 months). Patients who tapered had significantly fewer flares (45.9%), similar to the rate for controls (45.1%), when compared to those who withdrew abruptly (72.6%; $p = 0.01$, Figure 2). Additionally, fewer patients in the taper group restarted AM following cessation (37.8%) compared to the abrupt withdrawal group (62.7%; $p = 0.02$).

Conclusion: Antimalarial medications aid in preventing disease flare even in patients who have achieved prolonged clinical remission. For those who withdraw therapy, tapering results in lower rates of disease flare, similar to those seen in patients who continue AMs. Hence, except in the setting of toxicity, cessation of antimalarial therapy in patients with prolonged disease quiescence is feasible using a slow taper.

Table 1: Characteristics of patient population				
VARIABLE		**Cases**	**Controls**	**p value**
Age at index*		44.3 ± 14.9	46.2 ± 15.9	0.1498
Disease duration at index*		14.9 ± 10.4	15.4 ± 10.9	0.4181
Sex**	**F** **N**	81 (92.0% 7 (8.0%)	149 (86.1%) 24 (13.9%)	0.0863
M		7 (8.0%)	24 (13.9%)	
Ethnicity**	**Black** **Caucasian** **Chinese** **Others**	13 (14.8%) 59 (67.0%) 7 (8.0%) 9 (10.2%)	13 (7.5%) 127 (73.4%) 20 (11.6%) 13 (7.5%)	0.0191
Steroids at index**		34 (38.6%)	81 (46.8%)	0.1129
Immunosuppression at index**		16 (18.2%)	50 (28.9%)	0.0364
Reported AM toxicity**		20 (22.7%)	4 (2.3%)	<.0001
Re-started AM after index**		46 (52.3%)	N/A	N/A
Further characteristics of cases: abrupt versus taper withdrawal				
VARIABLE		**Abrupt (N = 51)**	**Taper (N = 37)**	**p value**
Age at index*		41.4 ± 15.6	48.3 ± 13.0	0.031
Sex**	**F** **M**	48 (94.1%) 3 (5.9%)	33 (89.2%) 4 (10.8%)	0.399
Ethnicity**	**Black** **Caucasian** **Chinese** **Others**	6 (11.8%) 39 (76.5%) 1 (2.0%) 5 (9.8%)	7 (18.9%) 20 (54.1%) 6 (16.2%) 4 (10.8%)	0.049
Duration AM from 1yr remission to index***		11.2 (2.9 - 35.4)	29.2 (6.8 - 47.1)	0.003
Steroids at index**		23 (45.1%)	11 (29.7%)	0.1439
Immunosuppression at index**		9 (17.6%)	7 (18.9%)	0.879
Reported AM toxicity**		9 (17.6%)	11 (29.7%)	0.182
Re-started AM after index**		32 (62.7%)	14 (37.8%)	0.021
* Mean ± SD; ** N (%); *** Median months (IQR)				

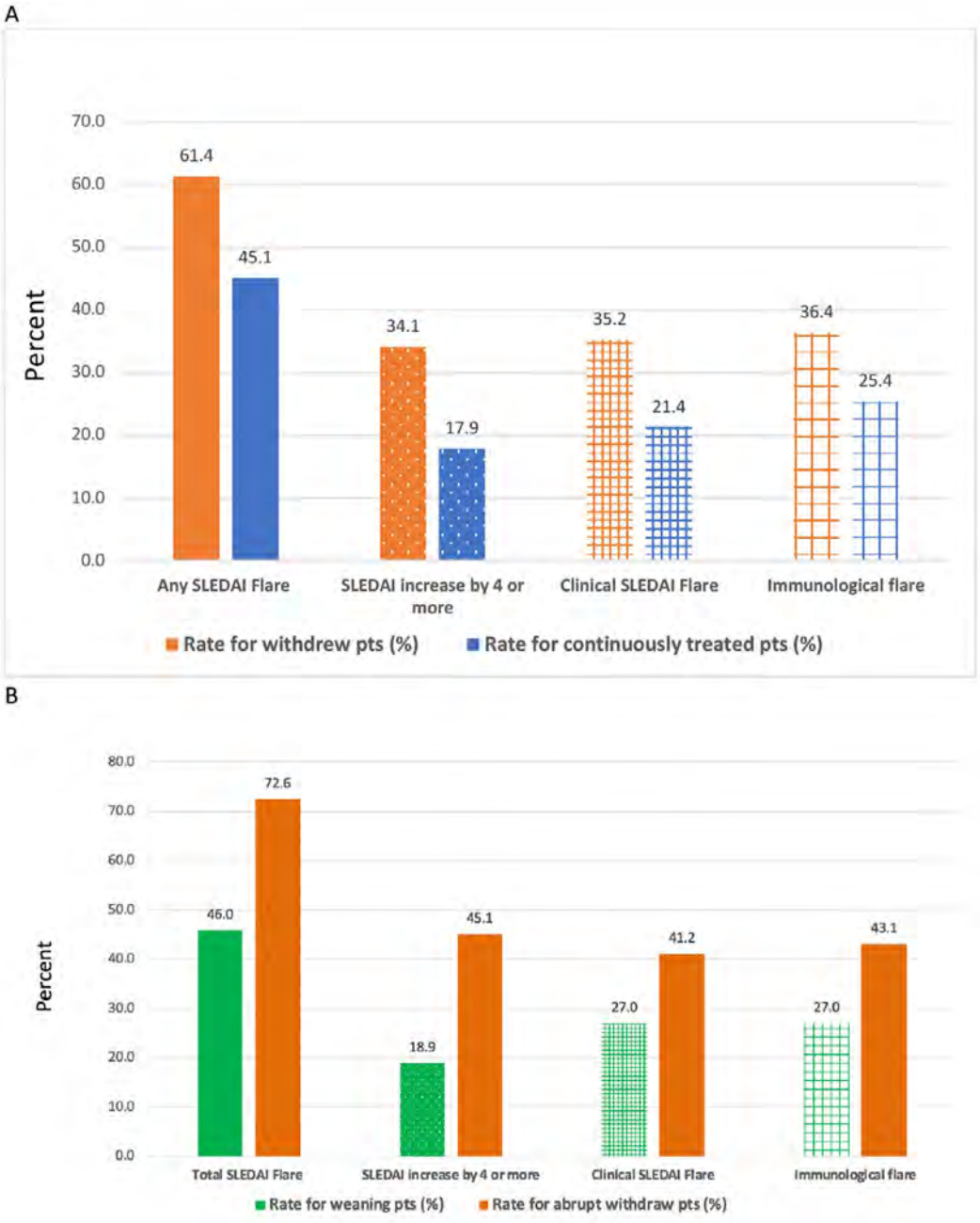

Figure 2: Rates of various flare types (%) including any SLEDAI flare, SLEDAI increase of ≥4, clinical SLEDAI flare and immunological flare in (A) patients who ceased AM compared to patients who continued AM and (B) patients who weaned to AM to cessation compared to patients who abruptly withdrew AM

Figure 2. Rates of various flare types (%) including any SLEDAI flare, SLEDAI increase by 4 or more, clinical SLEDAI flare and immunological flare in (A) patients who ceased AM compared to patients who continued AM and (B) patients who weaned to AM to cessation compared to patients who abruptly withdrew AM

Disclosure: D. Papachristos, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **J. Su**, None; **M. Urowitz**, None.

Abstract Number: 0984

Neighborhood Deprivation and Race/Ethnicity Affects COVID-19 Risk and Severity in SLE

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes I: Morbidity
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Disparities have been reported during the coronavirus disease (COVID-19) outbreak. Systemic lupus erythematosus (SLE) patients represent a unique group that is affected by clinical, treatment, demographic, and socioeconomic (SES) risk factors for severe COVID-19 disease. The Neighborhood Deprivation Index has been associated with non-communicable disease as well as communicable disease outcomes. We conducted this study to identify neighborhood SES factors influencing SLE COVID-19 outcomes.

Methods: Patients with SLE and COVID-19 (confirmed by RT-PCR testing), were identified through a longitudinal survey of an established NYU lupus cohort, query of NYU Langone Health and Bellevue Hospitals systems and referrals from rheumatologists at those institutions. All patients were age 18 or older and met SLE classification criteria or carried a clinical diagnosis of SLE. Baseline characteristics along with zip code neighborhood data including COVID-19 case rates and neighborhood characteristics were obtained using the Hopkins COVID database and the American Community Surveys (ACS 2014-2018) respectively. A principal component analysis was performed to identify contributory neighborhood characteristics. Then a logistic regression analysis identified predictors of testing positive for COVID-19 and COVID-19 hospitalization.

Results: A total of 59 SLE patients (41+ and 18-) were tested for COVID-19 by RT-PCR. The patients were predominantly female, aged 46±16, and racially/ethnically diverse. Roughly 140 neighborhood data points were recorded and categorized as follows: population density, race and ethnicity, household type, household size, education level, employment type and status, income and poverty, transportation method, and insurance status. COVID-19 positive patients tended to live in neighborhoods with more single parent households, households with >4 residents, higher unemployment rate, higher high school dropout rate, more public transit use, and more employment in retail, construction, and personal care services. These variables were directly proportional to principal component 1 (PC1) and accounted for 88% of the variance in neighborhood characteristics. A logistic regression model identified that PC1 (OR= 1.3; 95% CI: 1.0-1.8) and taking immune suppressants (IS) (taking vs not taking OR= 2.1; 95% CI: 1.5 to 23.3) independently correlated with having a positive COVID-19 test when controlling for hydroxychloroquine (HCQ), glucocorticoids (GC), and previous lupus nephritis (LN). Only PC1 independently correlated with COVID-19 hospitalization (OR= 1.4; 95% CI: 1.1-1.9) upon controlling for taking IS, HCQ, GCs, and LN. PC1 associated with African American (AA) or Hispanic patient race/ethnicity (OR= 1.6, 95% CI: 1.2-2.2).

SLE Patients	COVID-19 + (N = 41)	COVID-19- (N = 18)	P-value*
Age	47.0 ± 17.2	45.8 ±12.4	0.78
Gender			0.25
Female	38 (93%)	18 (100%)	
Male	3 (7%)	0 (0%)	
Race			0.48
African American	14 (34.2%)	4 (22.2%)	
White	18 (44%)	8 (44.4%)	
Asian	3 (7.3%)	2 (11.1%)	
Hispanic Ethnicity	15 (37%)	5 (28%)	0.5
SLE Risk Factors			
History of LN	14 (34%)	3 (17%)	0.18
Medications			
Hydroxychloroquine	32 (78.0%)	14 (78.0%)	0.98
Systemic steroids	20 (49%)	5 (28%)	0.25
Immunosuppressants‡	24 (59%)	4 (22%)	0.01

Values are expressed as % (N) for categorical variables and mean ± standard deviation (SD) or median (interquartile range [IQR]) for continuous variables. Categorical variables compared using Fisher's exact test; continuous variables compared using the two-sample T-test or Mann Whitney U Test. Immunosuppressants include non-biologic agents (azathioprine, cyclophosphamide, mycophenolate mofetil, mycophenolic acid, sirolimus, tacrolimus) and biologic agents (anakinra, abatacept, belimumab, rituximab, tocilizumab).

Conclusion: In addition to SLE disease, neighborhood characteristics and SES are important risk factors both for contracting COVID-19 and developing severe disease. Neighborhood deprivation may mediate the reported relationship between AA and Hispanic race/ethnicity and COVID-19. Given that a plurality of SLE patients are of AA and/or Hispanic backgrounds, care teams must formulate strategies to address socioeconomic stress in our patients.

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Abstract Number: 0985

Early and Sustained Reduction in Severity of Skin Disease with Anifrolumab Treatment in Patients with Active SLE Measured by the Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI): Pooled Data from 2 Phase 3 Studies

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SESSION INFORMATION

Session Date: Saturday, November 7, 2020

Session Title: SLE – Treatment

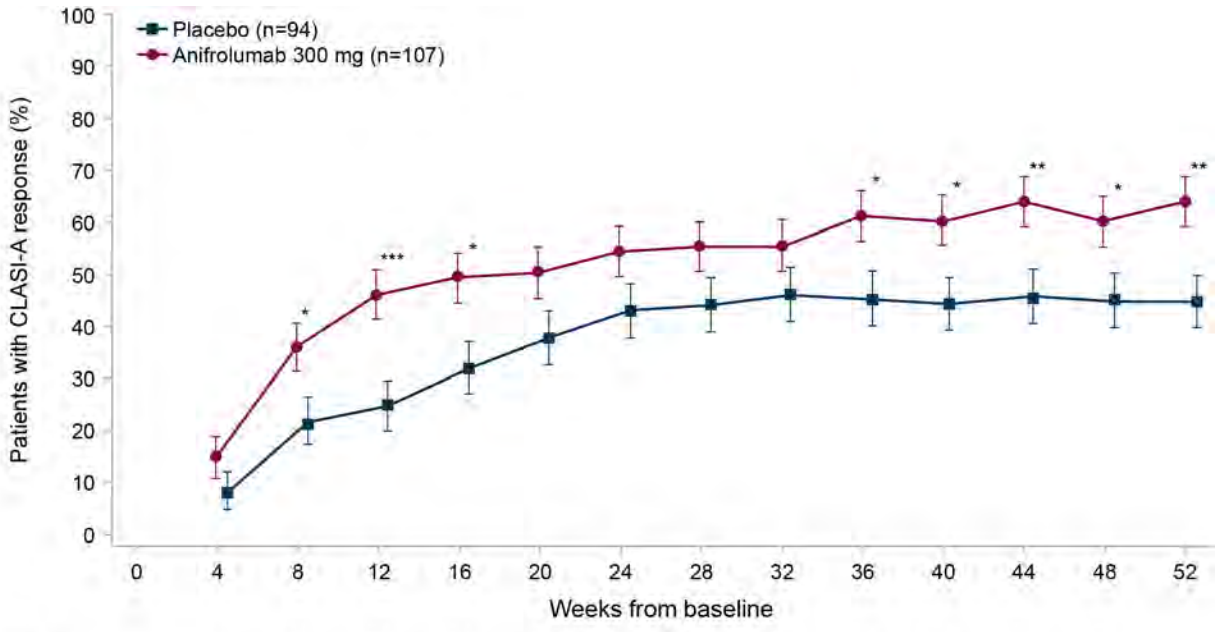
Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Up to 85% of patients with SLE experience skin disease.[1] The Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) is a validated index to measure skin disease severity; activity scores (CLASI-A) range from 0 (mild) to 70 (severe) and include measures for erythema, scale/hypertrophy, mucous membrane lesions, recent hair loss, and nonscarring alopecia. In the phase 3 TULIP-1 and -2 trials of patients with SLE, a greater proportion of patients with CLASI-A ≥10 at baseline achieved ≥50% CLASI-A reduction at Week 12 with anifrolumab compared with placebo.[2,3] We further evaluated the effect of anifrolumab on skin-specific SLE disease activity using data pooled from TULIP-1 and -2.

Methods: TULIP-1 and -2 were 52-week, randomized, double-blind, placebo-controlled trials that evaluated the efficacy and safety of anifrolumab (300 mg IV every 4 weeks for 48 weeks) in patients with moderately to severely active SLE despite standard-of-care treatment. TULIP-1 and -2 were analyzed separately using restricted medication rules per the TULIP-2 protocol, and data from both trials were pooled. We compared skin responses over time in patients receiving anifrolumab vs placebo. A CLASI-A response was defined as ≥50% reduction of CLASI-A from baseline for patients with CLASI-A ≥10. Baseline CLASI-A >0 as well as ≥75% reduction were also evaluated. Time to CLASI-A response sustained to Week 52 was evaluated using a Cox proportional hazards model.

Results: In total, 360 patients received anifrolumab and 366 received placebo. At baseline, 95.9% (696/726) of patients had CLASI-A >0, and 27.7% (201/726) had CLASI-A ≥10 (balanced between groups). In the subgroup of patients with baseline CLASI-A ≥10, CLASI-A response (≥50% reduction) was achieved by Week 12 in 46.0% (49/107) of patients receiving anifrolumab vs 24.9% (24/94) receiving placebo (difference 21.0; 95% CI 8.1%, 34.0%; nominal $P< 0.001$) (**Figure 1**). Separation between treatment groups was observed as early as Week 8 (difference 14.3; 95%



CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-A, CLASI activity score; n, number of patients in analysis; OCS, oral corticosteroids.
Points are estimates and bars are standard errors. A response is defined as ≥50% reduction in CLASI-A from baseline for patients with baseline CLASI-A ≥10. Responder rates are calculated using a stratified Cochran–Mantel–Haenszel approach, with stratification factors SLEDAI-2K score at screening, Day 1 OCS dosage, type I IFN gene signature test result at screening, and study (TULIP-1 and TULIP-2).
Nominal *P*-values are presented,**P*<0.05; ***P*<0.01; ****P*<0.001.

Figure 1. Percentage of Patients With CLASI-A ≥10 at Baseline Achieving ≥50% Reduction in CLASI-A From Baseline Over Time in Pooled Data From the TULIP-1 and TULIP-2 Trials

CI 1.8%, 26.9%; nominal *P*< 0.02) (**Figure 1**). Time to CLASI-A response sustained to Week 52 favored anifrolumab in TULIP-1 (hazard ratio [HR] 1.91; 95% CI 1.14, 3.27) and TULIP-2 (HR 1.55; 95% CI 0.87, 2.85) (**Figure 2**). Of the subgroup of patients with baseline CLASI-A >0, a greater number of patients achieved a CLASI-A response (≥50% reduction) by Week 12 in the anifrolumab vs placebo groups in both TULIP-1 and -2 (nominal *P*< 0.05) (**Figure 3**); similar effects were observed in the subgroup of patients with baseline CLASI-A ≥10 in both TULIP-1 and -2 (nominal *P*< 0.05) (**Figure 3**).

Conclusion: Anifrolumab treatment was associated with rapid and durable improvements in skin-specific SLE disease activity, as assessed by CLASI-A, in subgroups of patients with mild to severe baseline cutaneous disease activity. These findings support the potential of anifrolumab to reduce skin disease activity in patients with moderately to severely active SLE.

References

1. Rothfield N. *Clin Dermatol.* 2006;24:348–62.
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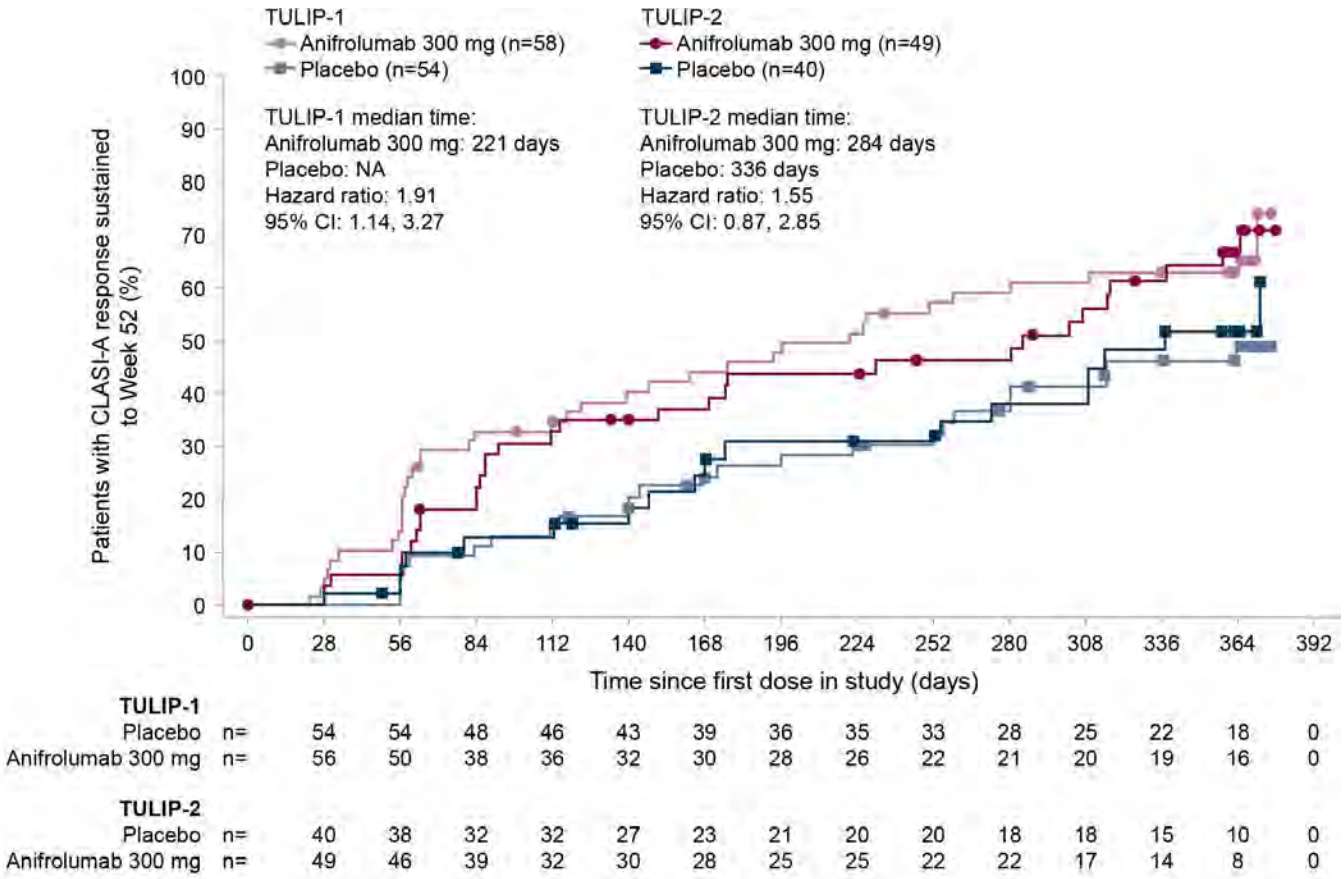
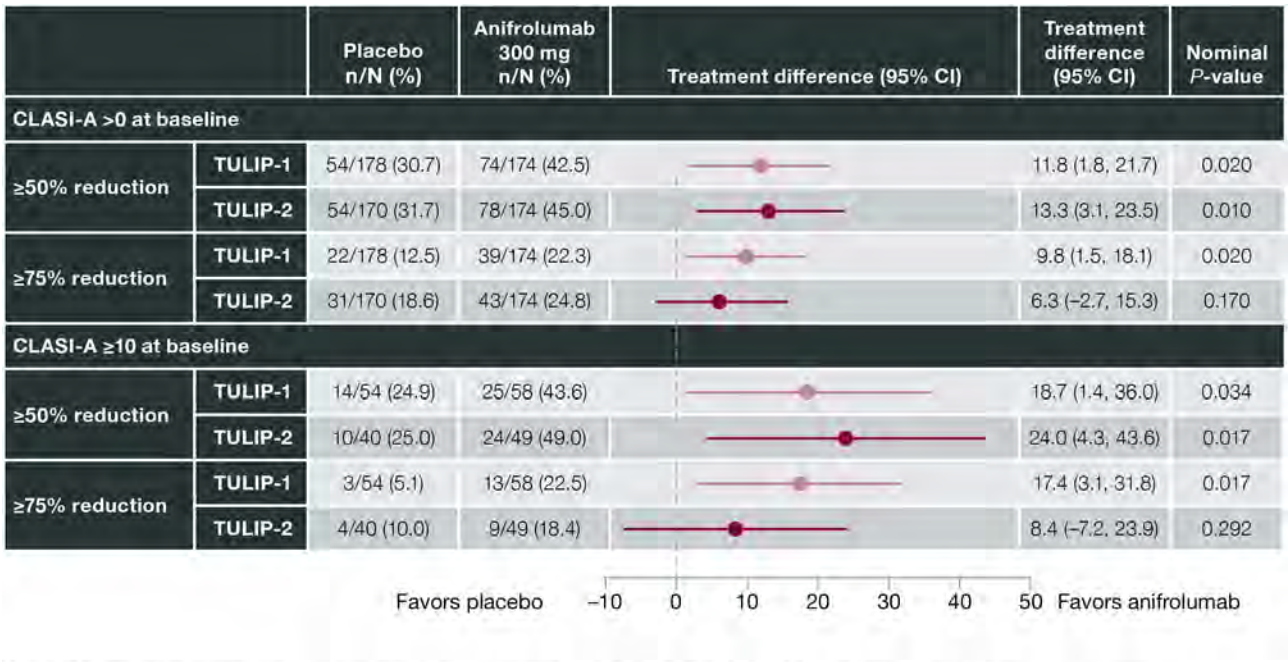


CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-A, CLASI activity score; n, number of patients in analysis; NA, not available; OCS, oral corticosteroids.
A response is defined as ≥50% reduction in CLASI-A from baseline for patients with baseline CLASI-A ≥10. Hazard ratios and 95% CIs were estimated using a Cox regression model with treatment groups and stratification factors (SLEDAI-2K score at screening, Day 1 OCS dosage, and type I IFN gene signature test result at screening) as covariates.

Figure 2. Time to CLASI-A Response (≥50% Reduction From Baseline) Sustained to Week 52 in Patients With CLASI-A ≥10 at Baseline in Data From the TULIP-1 and TULIP-2 Trials



CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; CLASI-A, CLASI activity score.
Baseline is defined as the last measurement before randomization and investigational product dose administration on Day 1.
The difference in estimates and associated 95% CIs are calculated using a stratified Cochran–Mantel–Haenszel approach.
The nominal *P*-values presented are based on this Cochran–Mantel–Haenszel model.

Figure 3. CLASI-A Response at Week 12 by Baseline CLASI-A at 50% and 75% Response Thresholds in Data From the TULIP-1 and TULIP-2 Trials

3. Morand EF. *N Engl J Med.* 2020;382:211–21.

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Abstract Number: 0986

BIIB059, a Humanized Monoclonal Antibody Targeting Blood Dendritic Cell Antigen 2 on Plasmacytoid Dendritic Cells, Shows Dose-Related Efficacy in a Phase 2 Study in Participants with Active Cutaneous Lupus Erythematosus

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: No approved targeted therapies have been developed for cutaneous lupus erythematosus (CLE), a disfiguring autoimmune disease that severely impairs quality of life.[1] BIIB059 is a humanized monoclonal antibody that binds blood dendritic cell antigen 2 (BDCA2), a receptor uniquely expressed on plasmacytoid dendritic cells, leading to BDCA2 internalization and subsequent inhibition of inflammatory mediator production, most notably type I IFNs.[2] LILAC (NCT02847598) was a 2-part, phase 2 study investigating the efficacy and safety of BIIB059. Part A enrolled SLE participants. Part B, presented here, is the largest interventional study to date in CLE participants.

Methods: To be eligible for enrollment, adults with histologically confirmed CLE must have had active CLE defined as a Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity (CLASI-A) score ≥8 despite prior use of or documented intolerance to topical CS and/or antimalarials and ≥1 lesion diagnostic of subacute CLE (CLASI-A erythema score ≥2) and/or chronic CLE (CLASI-A erythema score ≥2 and CLASI-Damage scarring score ≥1); all with or without systemic manifestations. Concomitant CLE/SLE therapy was allowed if doses were initiated ≥12 weeks and kept sTable ≥4 weeks prior to randomization and throughout the treatment period; systemic CS doses could not exceed 15 mg/day of prednisone (or equivalent). BIIB059 (50, 150, 450 mg) or placebo was subcutaneously administered once every 4 weeks, with an additional dose at week 2, for 12 weeks. The primary endpoint was a multiple comparison procedure–modeling test of dose response in % change in CLASI-A score from baseline to week 16. Secondary endpoints included proportion of participants with a 50% improvement in CLASI-A score (CLASI-50 response rate) and ≥7-point reduction in CLASI-A score from baseline over time. Safety was assessed throughout the study.

Results: Of 33, 26, 25, and 48 participants dosed in the placebo and BIIB059 50, 150, and 450 mg groups, respectively, 93.9%, 88.5%, 96.0%, and 87.5% completed treatment. The study met its primary endpoint, demonstrating a dose response (p=0.0005) and statistically significant differences in least squares mean % changes (SE) in CLASI-A score between the placebo vs. BIIB059-treated participants (Table 1). Meaningful clinical improvements in secondary skin-related efficacy endpoints were observed in the BIIB059 groups. AEs and serious AEs (SAEs) for the placebo and pooled BIIB059 groups occurred in 66.7% vs. 71.7% and 9.1% vs. 7.1%, respectively (Table 2). Three (3.0%)

Table 1. Primary and secondary cutaneous efficacy endpoints at week 16.

Endpoint	Placebo n = 33	BIIB059 50 mg n = 26	BIIB059 150 mg n = 25	BIIB059 450 mg n = 48
Primary[a]				
% change in CLASI-A from baseline, LS mean (SE)	-14.49 (6.43)	-38.78 (7.51)	-47.91 (7.47)	-42.48 (5.50)
LS mean diff (95% CI)		-24.29 (-43.70, -4.88)	-33.42 (-52.71, -14.12)	-27.99 (-44.55, -11.42)
p value		0.015	<0.001	0.001
Secondary[b]				
CLASI-50 response rate, LS mean (SE)	25.64 (7.55)	41.44 (9.88)	46.83 (10.47)	48.91 (8.06)
LS mean diff (95% CI)		15.80 (-7.21, 38.80)	21.19 (-2.79, 45.17)	23.28 (2.93, 43.62)
p value		0.133	0.059	0.024
≥ 7-point reduction in CLASI-A from baseline, LS mean (SE)	21.08 (8.33)	31.17 (7.99)	43.85 (9.18)	38.42 (8.92)
LS mean diff (95% CI)		10.08 (-13.00, 33.17)	22.76 (-1.45, 46.98)	17.33 (-6.23, 40.89)
p value		0.366	0.053	0.046

[a]Post-treatment-failure data were imputed using worse of baseline values or values from the last visit before treatment failure. Data after treatment discontinuation were censored. [b]Participants who failed/discontinued treatment were classified as nonresponders at visits post treatment failure/discontinuation. Participants who completed treatment but had a missing score at a primary timepoint were classified as nonresponders for that timepoint. Week 16 response data for participants who completed treatment up to week 12 under protocol version 1 but who could not reconsent to protocol version 2 were derived based on imputed continuous response.
CLASI-A = Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity; CLASI-50 = at least 50% improvement from baseline in CLASI-A score.

Table 2. Numbers and percentages of participants with adverse events according to group in LILAC part B.

Event	Placebo (n = 33)	BIIB059 50 mg (n = 26)	BIIB059 150 mg (n = 25)	BIIB059 450 mg (n = 48)	Pooled BIIB059 (n = 99)
Any event, n (%)	22 (66.7)	18 (69.2)	15 (60.0)	38 (79.2)	71 (71.7)
Severity, n (%)					
Mild	12 (36.4)	7 (26.9)	7 (28.0)	21 (43.8)	35 (35.4)
Moderate	6 (18.2)	11 (42.3)	7 (28.0)	14 (29.2)	32 (32.3)
Severe	4 (12.1)	0	1 (4.0)	3 (6.3)	4 (4.0)
Related event, n (%)[a]	7 (21.2)	11 (42.3)	5 (20.0)	18 (37.5)	34 (34.3)
Serious event, n (%)	3 (9.1)	1 (3.8)	3 (12.0)	3 (6.3)	7 (7.1)
Related serious event[a], n (%)	1 (3.0)	0	1 (4.0)	1 (2.1)	2 (2.0)
Event led to drug withdrawal, n (%)	0	3 (11.5)	1 (4.0)	4 (8.3)	8 (8.1)
Event led to study withdrawal, n (%)	0	0	0	1 (2.1)	1 (1.0)
Deaths, n (%)	0	0	0	0	0

[a]As determined by the investigator.

BIIB059 participants and no placebo participants had AEs of hypersensitivity. Herpes zoster meningitis was observed in 1 participant (BIIB059 50 mg) after study completion.

Conclusion: BIIB059 significantly reduced disease activity in CLE with an accepTable safety profile. Further development of BIIB059 for the treatment of CLE is warranted.

1. Ogunsanya. *Br J Dermatol.* 2017;176:52; 2. Pellerin. *EMBO Mol Med.* 2015;7:464

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Abstract Number: 0987

Efficacy and Safety of Iberdomide in Patients with Active Systemic Lupus Erythematosus: 24-Week Results of a Phase 2, Randomized, Placebo-Controlled Study

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SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Iberdomide is a high-affinity cereblon ligand that promotes ubiquitination and proteasomal degradation of Ikaros (*IKZF1)* and Aiolos (*IKZF3*), transcription factors linked to the genetic risk for systemic lupus erythematosus (SLE). Efficacy, safety, pharmacodynamics (PD), and pharmacokinetics (PK) of iberdomide were evaluated in a phase 2b study in patients (pts) with active SLE (NCT03161483).

Methods: Adults (N=288) with autoantibody-positive SLE by ACR criteria and with SLEDAI 2K score ≥6 were randomized (2:2:1:2) to oral iberdomide (0.45, 0.3, 0.15 mg) or placebo (PBO) daily for 24 wks, on standard background medications. Pts on PBO were re-randomized to iberdomide 0.3 and 0.45 mg at wk 24. Pts were stratified by SLEDAI 2K score (≥10/< 10) and oral corticosteroid (OCS) dose (≥10/< 10 mg/d; max OCS = 20 mg/d prednisone or equivalent). OCS tapering was permitted from wk 8-16. Study duration was 52 wks, and the primary endpoint was

Table 1. Baseline Demographics and Disease Characteristics

	Placebo (n=83)	0.15 mg QD (n=42)	0.30 mg QD (n=82)	0.45 mg QD (n=81)
Age, mean (SD), y	43.4 (13.3)	43.8 (13.0)	44.7 (13.7)	46.4 (11.2)
Female, n (%)	81 (98)	41 (98)	77 (94)	79 (98)
Race n (%)				
Black or African American	7 (8)	3 (7)	6 (7)	5 (6)
White	60 (72)	29 (69)	59 (72)	60 (74)
Other	14 (17)	5 (12)	15 (18)	11 (14)
Hispanic or Latino	41 (49)	21 (50)	46 (56)	33 (41)
Years since SLE diagnosis, mean (SD)	7.7 (7.6)	9.6 (7.8)	9.3 (7.9)	10.4 (7.6)
S2K global score, mean (SD)	9.8 (3.6)	9.5 (2.8)	9.6 (2.7)	9.5 (2.8)
BILAG-2004 1A or ≥2B, n (%)	65 (78)	35 (83)	60 (73)	59 (73)
PGA (0–3), mean (SD)	1.7 (0.4)	1.7 (0.4)	1.7 (0.3)	1.6 (0.5)
CLASI-A activity, mean (SD)	6.3 (6.5)	7.2 (6.1)	7.1 (7.9)	7.2 (7.2)
Swollen joint count, mean (SD)	6.4 (4.7)	7.2 (6.4)	7.2 (6.1)	5.5 (4.0)
Tender joint count, mean (SD)	8.7 (6.1)	8.6 (5.9)	9.8 (7.4)	8.2 (5.8)
Aiolos-High, n (%)	27 (33)	14 (33)	32 (39)	36 (44)
Type 1 IFN-High, n (%)	48 (58)	25 (60)	49 (60)	57 (70)
Elevated anti-ds DNA antibodies, n (%)	27 (33)	13 (31)	23 (28)	29 (36)
Baseline SLE treatments				
OCS, n (%)	64 (77)	31 (74)	64 (78)	153 (75)
OCS dosage ≥ 10 mg/d	31 (37)	17 (41)	30 (37)	32 (40)
Antimalarials, n (%)	66 (80)	28 (67)	63 (77)	50 (62)
Immunosuppressants, n (%)	34 (41)	22 (52)	37 (46)	95 (46)

BILAG, British Isles Lupus Assessment Group; CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity; IFN, interferon; OCS, oral corticosteroid; PGA, Physician's Global Assessment; QD, once daily; SD, standard deviation; SLE, systemic lupus erythematosus; S2K, SLE Disease Activity Index 2000.

American College of Rheumatology (ACR 2020)
Nov 6-11, 2020 • Washington, DC
Submission Deadline: June 16, 2020 (noon ET)

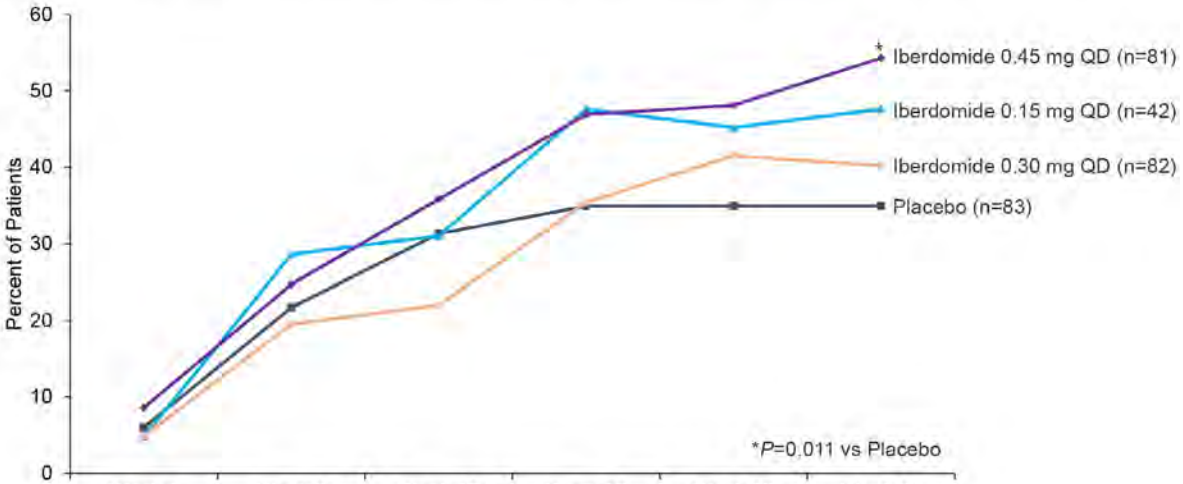
Table 2. Primary and Secondary Efficacy Outcomes at Week 24 (Non-responder Imputation)

	Placebo (N=83)	Iberdomide 0.15 mg QD (N=42)		Iberdomide 0.3 mg QD (N=82)		Iberdomide 0.45 mg QD (N=81)	
	n/N (%)	n/N (%)	Treatment Difference[a] (95% CI) *P* Value	n/N (%)	Treatment Difference[a] (95% CI) *P* Value	n/N (%)	Treatment Difference[a] (95% CI) *P* Value
ITT Population							
SRI-4	29/83 (34.9)	20/42 (47.6)	11.4 (-6.6, 29.0) *P*=0.214	33/82 (40.2)	5.0 (-9.8, 19.5) *P*=0.512	44/81 (54.3)	19.4 (4.1 33.4) ***P*=0.011**
SRI-4 with steroid reduction	19/83 (22.9)	11/42 (26.2)	3.8 (-11.5, 20.7) *P*=0.606	18/82 (22.0)	-1.8 (-14.7, 11.1) *P*=0.768	29/81 (35.8)	13.6 (-0.5, 27.0) ***P*=0.027**
SRI-4 in pts with BL S2K ≥10	16/41 (39.0)	16/22 (72.7)	33.5 (7.6, 53.2) ***P*=0.013**	20/47 (42.6)	3.6 (-16.5, 23.1) *P*=0.732	25/38 (65.8)	27.2 (5.2, 45.9) ***P*=0.016**
S2K ≥4-pt improvement from BL	30/83 (36.1)	20/42 (47.6)	10.3 (-7.7, 28.0) *P*=0.264	35/82 (42.7)	6.5 (-8.5, 21.0) *P*=0.399	45/81 (55.6)	19.3 (4.0, 33.4) ***P*=0.012**
Resolution of S2K arthritis or rash	30/83 (36.1)	21/42 (50.0)	13.4 (-4.8, 30.9) *P*=0.149	33/82 (40.2)	4.6 (-10.2, 19.1) *P*=0.548	43/81 (53.1)	16.7 (1.5, 30.9) ***P*=0.032**
No new BILAG A/2B	65/83 (78.3)	38/42 (90.5)	12.4 (-2.7, 24.1) *P*=0.092	59/82 (72.0)	-5.3 (-18.4, 8.1) *P*=0.434	70/81 (86.4)	8.0 (-3.9, 19.7) *P*=0.182
CLASI-50 (CLASI ≥10 at BL)	8/16 (50.0)	8/11 (72.7)	24.0 (-12.4, 53.1) *P*=0.446	8/18 (44.4)	5.3 (-27.6, 39.4) *P*>0.999	13/19 (68.4)	14.2 (-19.5, 44.5) *P*=0.488
50% improvement in SJC & TJC (SJC/TJC ≥3 at BL)	47/66 (71.2)	20/32 (62.5)	-7.8 (-27.6, 11.1) *P*=0.441	37/64 (57.8)	-13.1 (-28.6, 3.4) *P*=0.120	41/60 (68.3)	-2.3 (-18.0, 13.5) *P*=0.787
BICLA	24/65 (36.9)	13/35 (37.1)	0.3 (-18.4, 20.0) *P*=0.978	20/60 (33.3)	-3.6 (-19.9, 13.1) *P*=0.679	22/59 (37.3)	1.0 (-15.6, 17.7) *P*=0.908
LLDAS	11/83 (13.3)	8/42 (19.0)	6.7 (-6.5, 22.3) *P*=0.311	14/82 (17.1)	5.1 (-6.5, 16.5) *P*=0.357	16/81 (19.8)	6.9 (-4.8, 18.6) *P*=0.221
FACIT Fatigue, adjusted mean CFB, (95% CI)	3.8 (1.6, 6.0)	2.7 (-0.3, 5.6)	-1.1 (-4.7, 2.5) *P*=0.546	3.1 (0.9, 5.4)	-0.6 (-3.7, 2.4) *P*=0.681	5.2 (3.0, 7.4)	1.4 (-1.6, 4.4) *P*=0.350
Aiolos-High Subgroup							
SRI-4	9/27 (33.3)	5/14 (35.7)	2.2 (-24.8, 32.0) *P*>0.999	9/32 (28.1)	-7.1 (-31.1, 16.9) *P*=0.580	23/36 (63.9)	32.9 (7.7, 52.9) ***P*=0.011**
SRI-4 with steroid reduction	7/27 (25.9)	2/14 (14.3)	-10.9 (-32.6, 18.3) *P*=0.683	5/32 (15.6)	-15.2 (-37.1, 8.0) *P*=0.169	16/36 (44.4)	20.4 (-4.1, 40.9) *P*=0.060
BICLA	7/21 (33.3)	5/12 (41.7)	9.9 (-21.3, 40.1) *P*=0.720	6/22 (27.3)	-1.4 (-29.0, 26.0) *P*>0.999	13/25 (52.0)	24.6 (-4.4, 48.8) *P*=0.099
LLDAS	3/27 (11.1)	2/14 (14.3)	3.0 (-18.1, 30.3) *P*>0.999	3/32 (9.4)	-2.2 (-22.9, 17.1) *P*>0.999	10/36 (27.8)	17.5 (-4.5, 35.7) *P*=0.075
Type 1 IFN-High Subgroup							
SRI-4	16/48 (33.3)	15/25 (60.0)	25.6 (1.5, 46.4) ***P*=0.032**	21/49 (42.9)	10.6 (-8.9, 29.1) *P*=0.292	34/57 (59.6)	26.8 (7.5, 43.5) ***P*=0.006**
SRI-4 with steroid reduction	8/48 (16.7)	7/25 (28.0)	11.4 (-7.9, 32.7) *P*=0.217	10/49 (20.4)	2.9 (-13.4, 19.0) *P*=0.705	22/57 (38.6)	17.5 (-0.1, 33.1) ***P*=0.019**
BICLA	15/37 (40.5)	10/20 (50.0)	9.6 (-16.3, 34.4) *P*=0.501	12/37 (32.4)	-6.0 (-27.0, 15.7) *P*=0.594	17/43 (39.5)	-0.4 (-21.7, 20.6) *P*=0.972
LLDAS	4/48 (8.3)	6/25 (24.0)	16.1 (-1.3, 36.3) *P*=0.065	7/49 (14.3)	7.7 (-6.3, 21.6) *P*=0.228	10/57 (17.5)	6.9 (-7.1, 20.2) *P*=0.281

[a]Treatment differences are stratified by randomization factors.; nominal *P* values provided for secondary endpoints.

BICLA, BILAG-based Combined Lupus Assessment: BILAG, British Isles Lupus Assessment Group; BL, baseline; CFB, change from baseline; CI, confidence interval; CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; FACIT, Functional Assessment of Chronic Illness Therapy; IFN, interferon; LLDAS, Lupus Low Disease Activity State; NA, not available; OCS, oral corticosteroid; PGA, Physician's Global Assessment; QD, once daily; SJC, swollen joint count; S2K, Systemic Lupus Erythematosus Disease Activity Index 2000; SRI, SLE Responder Index; TJC, tender joint count

Figure. Time Course of SRI-4 Responses (Non-responder Imputation, Intention-to-Treat Population)



n/N (%)						
Placebo (N=83)	5/83 (6)	18/83 (22)	26/83 (31)	28/83 (35)	28/83 (35)	28/83 (35)
0.15 mg QD (N=42)	2/42 (5)	12/42 (29)	13/42 (31)	20/42 (48)	19/42 (45)	20/42 (48)
0.30 mg QD (N=82)	4/82 (5)	16/82 (20)	18/82 (22)	29/82 (35)	34/82 (42)	33/82 (40)
0.45 mg QD (N=81)	7/81 (9)	20/81 (25)	29/81 (36)	38/81 (47)	39/81 (48)	44/81 (54)

SLE Responder Index (SRI-4) response at wk 24. Efficacy analyses were based on the intent-to-treat population that included all pts who were randomized and received ≥1 dose of investigational product. Pts with missing data and treatment failures were imputed as nonresponders.

Results: Baseline demographic and disease characteristics were balanced between groups (**Table 1**). The primary endpoint at wk 24 was met: 54.3% of pts in iberdomide 0.45-mg group achieved SRI-4 response vs 34.9% in PBO group (stratified difference-19.4%; *P*=0.011). Notably greater SRI-4 responses, vs PBO, were seen starting at wk 16, especially in iberdomide 0.45- and 0.15-mg groups (**Figure**). Several secondary endpoints were also met. In those with SLEDAI 2K score ≥10, a greater proportion receiving iberdomide 0.45 mg also achieved SRI-4 response at wk 24 (66% vs 39%, nominal *P*=0.016). SRI-4 response in the prespecified biomarker-defined subset of baseline Aiolos-High was 64% vs 33% (*P*=0.011) and in pts who were Type 1 IFN-High was 60% vs 33% (*P*=0.006). At wk 24, iberdomide 0.45 mg was superior to PBO for CLASI-50 response in patients with subacute (92% vs 53%, *P*=0.035) and chronic cutaneous lupus (62% vs 28%, *P*=0.029), but not in the overall population. Other endpoints are shown in **Table 2**. Rates of AEs were 77% vs 65% for iberdomide all doses vs PBO; SAEs (6% vs 8%), severe AEs (4% vs 6%), serious infections (1%, both groups) and AEs leading to discontinuation (8% vs 7%) were comparable. The most common AEs with iberdomide (all doses vs PBO) were urinary tract infection (11%, 4%), upper respiratory tract infection (10%, 5%), neutropenia (8%, 2%), influenza (6%, 4%), nasopharyngitis (5%, 1%), and diarrhea (4%, 0%). Rates of neutropenia and infections were dose-dependent. Neutropenia was mostly grade (gr) 1 and 2 (gr 3, 6%; gr 4, 0.5%) and was reversible, not related to infection risk, and rarely led to discontinuation (2%). Neither systemic opportunistic infections nor tuberculosis occurred. There were 2 thromboembolic events observed with iberdomide and 2 with PBO.

Conclusion: Iberdomide showed significant efficacy in the treatment of active SLE and was generally well tolerated. Enhanced effects were observed in 2 biomarker-defined populations (Aiolos-High, Type 1 IFN-High), providing a rationale for this novel mechanism in SLE.

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Abstract Number: 0988

Two-Year Results from a Randomized, Controlled Study of Obinutuzumab for Proliferative Lupus Nephritis

Richard Furie[1], Gustavo Aroca[2], Analia Alvarez[3], Hilda Fragoso-Loyo[4], Elizabeth Zuta Santillan[5], Brad Rovin[6], Paul Brunetta[7], Thomas Schindler[8], Imran Hassan[9], Matthew Cascino[10], Jay Garg[10] and Ana Malvar[11], [1]Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, [2]Simon Bolivar University y Clinica de la Costa, Barranquilla, Colombia, [3]CEMIC, Buenos Aires, Argentina, [4]Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán, Mexico City, Mexico, [5]Instituto de Ginecología y Reproducción, Lima, Peru, [6]The Ohio State University, Columbus, [7]Genentech, Inc., South San Francisco, [8]F. Hoffmann-La Roche Ltd., Basel, Switzerland, [9]Hoffmann-La Roche Ltd, Mississauga, Canada, [10]Genentech, Inc., South San Francisco, CA, [11]Organizacion Medica de Investigacion, Buenos Aires, Argentina

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: NOBILITY demonstrated improved renal responses and complete B-cell depletion with the humanized type II anti-CD20 monoclonal antibody obinutuzumab (OBI) compared with placebo (PBO) through 18 months in patients with proliferative lupus nephritis (LN) when added to standard of care therapies [1]. Two-year results from NOBILITY are reported here.

Methods: Patients with class III/IV LN received mycophenolate and steroids and were randomized to blinded OBI or PBO infusions on weeks 0, 2, 24, and 26. The primary endpoint was complete renal response (CRR) at week 52. Patients were followed through week 104. Secondary endpoints included overall renal response (ORR) and modified CRR (mCRR). The prespecified alpha level was 0.2 and analyses after week 52 were exploratory.

Results: 125 patients were randomized and received blinded infusions; 102 patients (82%) completed 104 weeks of follow up. CRR was greater with OBI than PBO at week 52 (35% vs. 23%, $P = 0.115$), week 76 (40% vs. 18%, $P = 0.007$), and week 104 (41% vs 23%, $P = 0.026$; Table). At week 104, OBI patients had greater improvement in eGFR, UPCR, anti-dsDNA, C3, and C4. Fewer OBI patients required initiation of a new rescue therapy through week 104 (OBI 6, PBO 12). Peripheral B-cells were detected in 92% of OBI patients at week 104. Serious adverse events (OBI 25% vs. PBO 30%), serious infections (8% vs. 18%) and deaths (1 vs. 4) were not increased with OBI.

Conclusion: NOBILITY demonstrated a sustained benefit of OBI through week 104, approximately 18 months after the final OBI infusion. The OBI dosing regimen was associated with a return of peripheral B-cells by week 104. There were no unexpected safety findings. OBI use in LN will be further evaluated in the Phase 3 REGENCY trial.

References:

1. Rovin B, et al. ASN 2019 [abstract].

Table. Week 104 Results.

Week 104 endpoint	OBI (n=63)	PBO (n=62)	Difference (80% CI)	*P* value
CRR	41%	23%	19% (8, 29)	0.026
ORR	54%	29%	25% (14, 36)	0.005
mCRR	56%	33%	22% (11, 33)	0.015
C3 >90 mg/dL	76%	47%	29% (19, 40)	0.008
C4 >10 mg/dL	95%	74%	21% (13, 29)	0.001
Mean change in eGFR from baseline (mL/min/1.73 m^2)	+6.5	-3.2	9.7 (1.7, 18)	0.018
Mean change in UPCR from baseline	-2.3	-1.4	-0.96 (-1.4, -0.57)	0.002

CRR=UPCR <0.5, serum creatinine (SCr) ≤upper limit of normal (ULN) and ≤115% of baseline, <10 red blood cells per high power field (RBCs/HPF), and no RBC casts.
ORR = CRR or partial renal response=UPCR <1 (<3 if baseline UPCR ≥3) and ≤50% of baseline, SCr ≤115% of baseline, and ≤50% increase in urinary RBCs (or <10 RBCs/HPF).
mCRR = UPCR <0.5, SCr ≤ ULN.

Disclosure: R. Furie, AstraZeneca/MedImmune, 2, 5; **G. Aroca**, None; **A. Alvarez**, None; **H. Fragoso-Loyo**, None; **E. Zuta Santillan**, None; **B. Rovin**, GSK, 1, Aurinia, 5, AstraZeneca, 5, Novartis, 5, Alexion, 5, Bristol-Myers Squibb, 5; **P. Brunetta**, Genentech, 9; **T. Schindler**, Roche, 1, 3; **I. Hassan**, Roche, 1, 3; **M. Cascino**, Genentech, 1, 3; **J. Garg**, Genentech, 1, 3; **A. Malvar**, None.

Abstract Number: 0989

Withdrawal of MMF Is Safe in Quiescent Renal and Non-Renal SLE: Results from a Multi-Center Randomized Trial

Eliza Chakravarty[1], Tammy Utset[2], Diane Kamen[3], Gabriel Contreras[4], W. Joseph McCune[5], Kenneth Kalunian[6], Cynthia Aranow[7], Megan Clowse[8], Elena Massarotti[9], Ellen Goldmuntz[10], Jessica Springer[10], Lynette Keyes-Elstein[11], Bill Barry[11], Ashley Pinckney[11] and Judith James[12], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]University of Chicago, Chicago, IN, [3]Medical University of South Carolina, Charleston, SC, [4]University of Miami Miller School of Medicine, Miami, [5]University of Michigan, Ann Arbor, MI, [6]University of California San Diego, La Jolla, CA, [7]Feinstein Institutes for Medical Research, Manhasset, NY, [8]Duke University, Chapel Hill, NC, [9]Brigham and Women's hospital, Boston, MA, [10]NIH/NIAID, Rockville, MD, [11]Rho, Durham, NC, [12]Oklahoma Medical Research Foundation, Oklahoma City

SESSION INFORMATION
Session Date: Saturday, November 7, 2020
Session Title: SLE – Treatment
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Mycophenolate Mofetil (MMF) is standard of care therapy for long term treatment of lupus nephritis and other manifestations of SLE. However, it is associated with adverse effects, pregnancy risks, increased cost, and requirement for routine laboratory monitoring. This randomized, unblinded, study compared the risk of SLE flare in subjects with quiescent disease who withdrew from long-term MMF therapy compared to those continuing maintenance MMF over 60 weeks.

Methods: Adults with quiescent SLE (clinical SLEDAI/cSLEDAI ≤4) on long term MMF therapy (≥ 2 years for nephritis; ≥ 1 year for non-nephritis) were randomized 1:1 to receive unblinded MMF at the baseline dose for 60 weeks (maintenance arm, MA) or to a 12-week structured taper off of MMF (withdrawal arm, WA). All subjects were taking sTable doses of hydroxychloroquine; prednisone ≤ 10 mg daily was permitted. Primary endpoint was the difference between arms in the rate of clinically significant disease reactivation (CSDR) by 60 weeks. CSDR was defined as any SELENA-SLEDAI flare and increased immunosuppression (prolonged corticosteroids, resumption or increased dose of MMF, or addition of other immunosuppressives). Rates of BILAG A and B flares, all SLEDAI flares and adverse events were assessed through 60 weeks. Event rates and time to flare were compared using Kaplan-Meier curves.

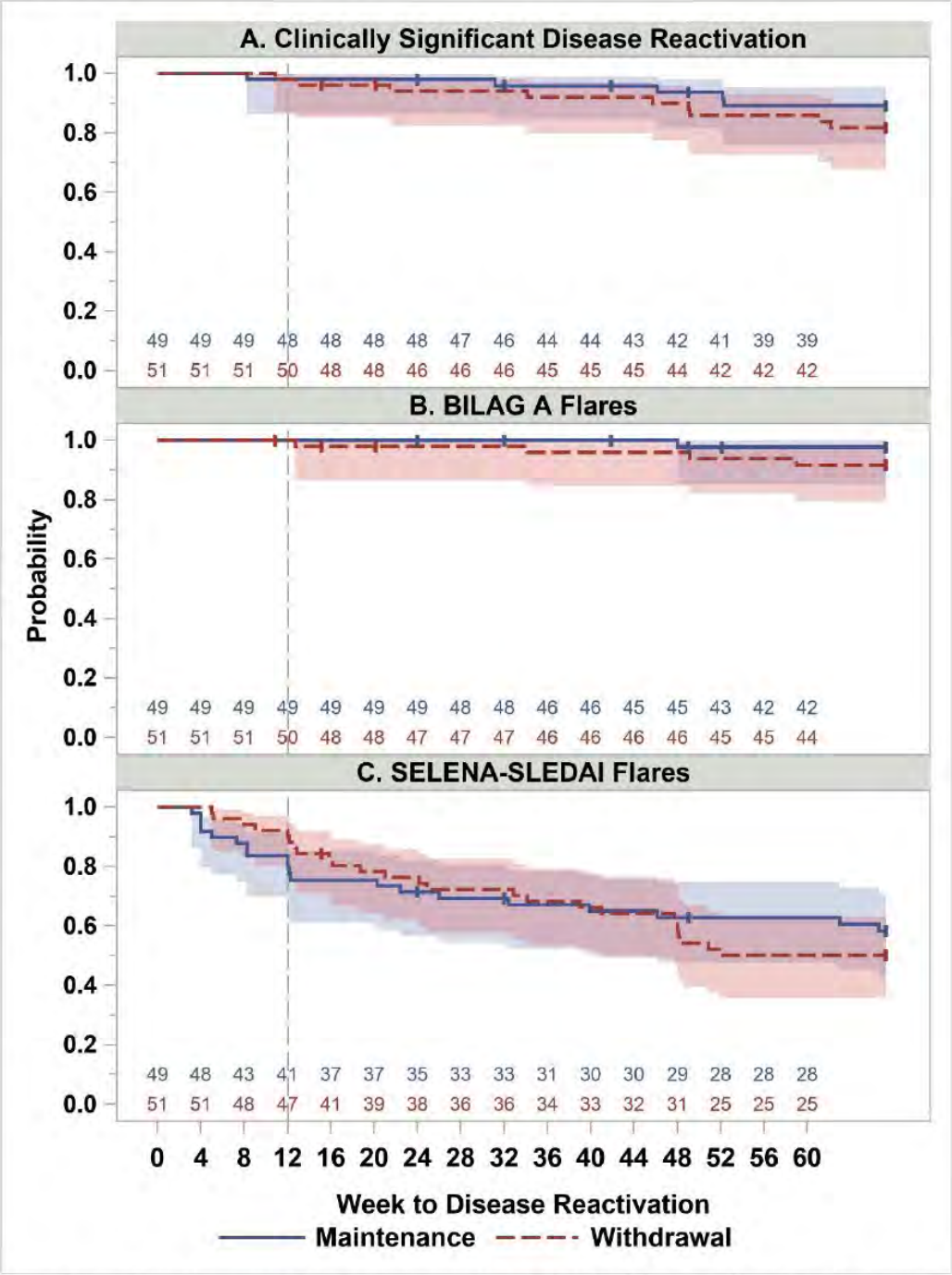
Results: 102 participants were randomized: 50 MA and 52 WA. One subject in each arm was ineligible and 10 subjects terminated early (7 MA, 3 WA). 84% subjects were female, with a mean of 13 years of SLE and 6.6 years of MMF therapy. 76% had a history of lupus nephritis, and mean baseline SLEDAI was 2.2. Five subjects (10%) in the MA experienced a CSDR compared to nine (18%) in the WA with a mean time to CSDR of 38 weeks (median 46 weeks) in both arms. Kaplan Meier estimate of risk difference was 0.07 (95% CI -0.07-0.21). BILAG A disease developed in one subject in the MA (pancreatitis) compared to four in the WA (cranial neuropathy, panniculitis, two renal flares). Kaplan-Meier curves overlapped for CSDR, BILAG A flares, and all SELENA-SLEDAI flares (Figure 1).

Table 1: Baseline and Demographic Characteristics

	Maintenance arm	Withdrawal arm	Total
Randomized	50	52	102
Female, n (%)	39 (78)	47 (90)	86 (84)
White, n (%)	25 (50)	19 (37)	44 (43)
Black, n (%)	19 (38)	22 (42)	41 (40)
Hispanic/Latino, n (%)	10 (20)	12 (23)	22 (22)
Age, Years, mean (SD)	42.4 (12.9)	41.6 (12.5)	42.0 (12.6)
Disease Duration, Years, mean (SD)	13.6 (8.2)	12.2 (7.9)	12.9 (8.0)
H/O Lupus Nephritis, n (%)	40 (80)	38 (73)	78 (76.5)
On Baseline Steroids, n (%)	18 (36)	23 (44)	41 (40)
Prednisone Dose, mg, mean (SD)	4.8 (2.7)	3.3 (1.7)	4.0 (2.3)
MMF Duration, Years, mean (SD)	6.8 (4.3)	6.4 (4.3)	6.6 (4.3)
Baseline MMF Dose, mg, mean	1,612	1,668	1,640
SELENA-SLEDAI, mean (SD)	2.4 (1.76)	1.9 (1.76)	2.2 (1.77)
Positive DsDNA, n (%)	35 (70)	27 (52)	62 (61)
Low C3[1], n (%)	14 (28)	9 (17)	23 (23)
Low C4[1], n (%)	6 (12)	5 (10)	11 (11)

[1]Low C3 and C4 were defined as complement levels below the lower limit of normal.

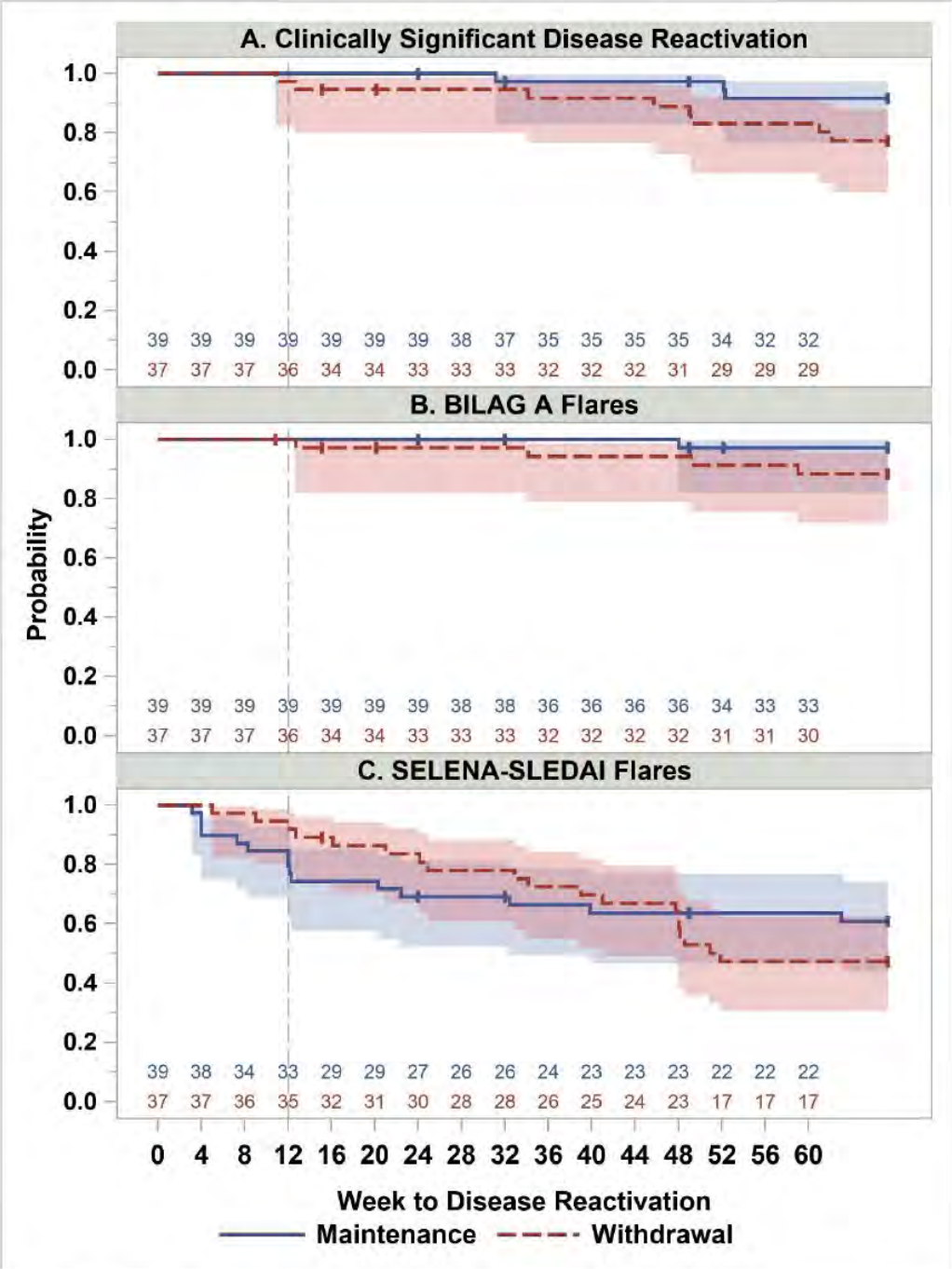
Figure 1: Kaplan-Meier Estimates of A: Clinically Significant Diseases Reactivation, B: BILAG A Flares, C: all SELENA-SLEDAI Flares in the ITT Population



Clinically significant disease reactivation requires a SELENA-SLEDAI defined mild/moderate or severe flare along with increased immunosuppressive therapy on a sustained basis.
The number of subjects at risk in each arm is shown along the bottom of the x-axis, and the vertical dashed line represents the end of the 12 week taper in the withdrawal arm.

In the participants with history of renal disease (76/100 eligible for analysis), demographics were similar to the entire cohort. Three subjects (7.7%) met CSDR criteria in the MA compared to 8 (22%) in the WA. Kaplan-Meier estimate of risk difference between groups was 0.14 (95% CI -0.02-0.31). BILAG A disease occurred in one in the MA compared to four in the WA. Mean time to CSDR was 45 weeks in the MA compared to 41 weeks in WA. BILAG A disease

Figure 2: Kaplan-Meier Estimates of A: Clinically Significant Diseases Reactivation, B: BILAG A Flares, C: all SELENA-SLEDAI Flares in the ITT Lupus Nephritis population.



Clinically significant disease reactivation requires a SELENA-SLEDAI defined mild/moderate or severe flare along with increased immunosuppressive therapy on a sustained basis.
The number of subjects at risk in each arm is shown along the bottom of the x-axis, and the vertical dashed line represents the end of the 12 week taper in the withdrawal arm.

occurred in one in the MA compared to four in the WA. BILAG A flares and all SELENA-SLEDAI flare Kaplan-Meier curves overlapped between arms. (Figure 2).

Adverse events were similar between groups with Grade 2+ infections occurring more commonly in the MA (63 vs. 49).

Conclusion: In this cohort of subjects with quiescent SLE on long-term MMF therapy, few serious flares occurred in the maintenance or withdrawal groups. Flare rates overlapped between groups, and time to flare was similar. The majority of quiescent SLE patients, including those with a history of lupus nephritis, can safely withdraw long-term MMF therapy.

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Abstract Number: 0990

Interferon Lambda Promotes Human Plasma Cell Differentiation in Lupus and Healthy Donors

Jennifer Barnas[1], Jennifer Albrecht[1] and Jennifer Anolik[1], [1]University of Rochester Medical Center, Rochester, NY

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a multisystem autoimmune disease characterized by antinuclear autoantibodies produced by plasma cells. Type I interferon (IFN) are cytokines which promote plasma cell development and are important to lupus pathogenesis. Type III IFN (IFN lambda, IFN-λ) are more recently discovered and not as well-studied with unclear roles in human lupus pathogenesis and the immune system. Because type III IFN utilize a unique receptor from type I IFN, they are not targeted by type I IFN blocking therapies. We have previously shown an expansion of IgD- CD27- CD24- CD21- (DN2) B cells within lupus disease activity. This compartment contains age/autoimmunity-associated B cells (ABC) defined as either CD11c+ T-bet+ or CD11c+CD21-, which are poised for plasma cell differentiation. SLE is associated with an IFN gene signature in many cell types historically attributed to IFN-α. In epithelial cells, IFN-λ generates the same gene transcription profile as IFN-α. Since IFN-α and IFN-λ might induce a similar transcription program in B cells and IFN-α enhances plasma cell formation, we hypothesize that IFN-λ drives plasma cell differentiation.

Methods: Human peripheral blood B cells from healthy donors or SLE patients meeting 1997 ACR classification criteria were isolated for culture and phenotyping by flow cytometry. Dose response to IFN-λ in terms of RNA expression of interferon stimulated genes (ISG) at 4 hours was measured by RT-qPCR via the $2^{\Delta\Delta CT}$ method. B cells were also stimulated with TLR7/8 agonist R848 in the presence of BAFF and IL-21 +/- IFN-λ for flow cytometric analysis on day 7. IgG and IgM levels in culture supernatants at 7 days were quantitated by ELISA.

Results: DN2, T-bet+, and CD11c+CD21- peripheral blood B cells positively correlated with IFN-λ1 serum levels in SLE patients (n=26). IFN-λ1 directly induced IFIT1, IRF7, ISG15 expression at 4 hours *in vitro* confirming IFN-λ receptor functionality in human B cells. A dose response relationship between these ISG and IFN-λ stimulation was observed. When IFN-λ was included with R848 stimulation, CD27+ CD38+ plasmablast percentage increased amongst healthy (n=10, p = 0.002) and lupus B cell (n = 6, p= 0.2) cultures. In TLR7 activated lupus B cells, a higher IgG:IgM ratio was observed compared to cultures from age, sex, and race matched healthy donors. In TLR7 activated healthy

B cell culture supernatants with IFN-λ included, IgM was significantly increased at day 7 (n=8, p=0.02), but not IgG level.

Conclusion: IFN-λ1 stimulation of human B cells induces a gene signature historically attributed to type I IFN. IFN-λ significantly enhances the differentiation of plasmablasts and IgM levels in TLR7-activated B cell cultures from healthy donors with a lesser effect observed among lupus B cells, which may already have been exposed to interferon *in vivo*. IFN-λ could provide explanation for poor clinical response of subsets of patients to type I interferon blockade given type III interferon utilize a different receptor. Studies are ongoing to determine if IFN-λ1 has differential effects on B cell and plasma cell subsets in lupus versus healthy donors.

Disclosure: J. Barnas, None; **J. Albrecht**, None; **J. Anolik**, None.

Abstract Number: 0991

Pathogenic, Glycolytic PD-1^{+} B Cells Accumulate in the Hypoxic RA Joint

Achilleas Floudas[1], Nuno Neto[2], Viviana Marzaioli[3], Kieran Murray[4], Barry Moran[5], Michael Monaghan[6], Candice Low[7], Ronan Mullan[8], Navin Rao[9], Vinod Krishna[9], Sunil Nagpal[10], Douglas Veale[11] and Ursula Fearon[3], [1]Molecular Rheumatology Trinity Biomedical Sciences Institute, Dublin, Dublin, Ireland, [2]Department of Mechanical and Manufacturing Engineering, Dublin, Dublin, Ireland, [3]Molecular Rheumatology, Trinity College Dublin, Dublin, Dublin, Ireland, [4]Saint Vincent's University Hospital, Dublin 4, Dublin, Ireland, [5]Trinity Biomedical Sciences Institute, Dublin, Ireland, [6]Department of Mechanical and Manufacturing Engineering, Dublin, Ireland, [7]EULAR Centre for Arthritis and Rheumatic diseases, St Vincents University Hospital, UCD, Dublin, Ireland, [8]Adelaide and Meath Hospital, Dublin, Dublin, Ireland, [9]Janssen R&D, Spring House, PA, [10]Janssen Research & Development, Collegeville, PA, [11]EULAR Centre for Arthritis and Rheumatic Diseases, St Vincents University Hospital, UCD, Dublin, Dublin, Ireland

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) often has a progressive and debilitating course, with significant impact on the patient's quality of life. Despite the long-known association with autoantibodies, knowledge of the role of B cells and their potential direct contribution to RA pathogenesis remains elusive.

Characterization of B cell subpopulations in the periphery and synovial tissue.

Identification of chemokine receptors responsible for the synovial accumulation of B cells.

Characterization of B cell function and metabolism under the hypoxic conditions of the RA joint.

Methods: Synovial tissue biopsies from RA patients were obtained through key-hole arthroscopy followed by single cell flow cytometric analysis of B cell subpopulations and chemokine receptor expression. SPICE analysis was performed for the chemokine receptor expression of synovial B cells and B cell invasion assays. Functional characterization of sorted RA B cells, cultured *in vitro* under hypoxia, simulating the inflamed joint environment. Characterization of B cell metabolism and transcriptional regulation of pSTAT3 by flow cytometry. Notably, novel, non-invasive Fluorescent Lifetime Imaging Microscopy (FLIM) assay for the characterisation of the metabolic status of sorted RA patient PD-1 B cells coupled with RNAseq analysis was performed.

Results: Extensive flow-cytometric characterisation and SPICE algorithm analyses of single-cell synovial tissue from RA-patients revealed the accumulation of switched and double negative memory PD-1 expressing B cells at the site of inflammation. Accumulation of memory B cells is mediated by CXCR3, evident by the observed increase in CXCR3 expressing synovial B cells compared to the periphery, differential regulation by key synovial cytokines, and restricted B cell invasion demonstrated in response to CXCR3 blockade. Notably, under 3% O_2 hypoxic conditions that mimic the joint-microenvironment, RA B cells maintain marked expression of MMP-9,-TNF and IL-6, with PD-1^+ B-cells demonstrating higher expression of CXCR3, CD80, CD86, IL-1β and GMCSF than their PD-1^- counterparts. Following functional analysis and flow cell sorting of RA PD-1^+ vs PD-1^- B-cells, we demonstrate using RNAseq and novel FLIM visualisation of cellular NADH, a significant shift in metabolism of RA PD-1^+ B-cells towards glycolysis, associated with an increased transcriptional signature of key cytokines and chemokines that are strongly implicated in RA pathogenesis.

Conclusion: Highly polyfunctional pro-inflammatory T cell responses pre-date disease onset as demonstrated by the accumulation of polyfunctional T cells in the synovial tissue of pre-RA arthralgia subjects. These data highlight a key early pathogenic role for T cell plasticity and specific synovial T cell clusters including, DP T cells in RA.

Disclosure: A. Floudas, None; **N. Neto**, None; **V. Marzaioli**, None; **K. Murray**, None; **B. Moran**, None; **M. Monaghan**, None; **C. Low**, None; **R. Mullan**, None; **N. Rao**, Janssen R&D, 1; **V. Krishna**, None; **S. Nagpal**, None; **D. Veale**, AbbVie, 2, Health Beacon, 1, Janssen, 2, 8, Pfizer, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5; **U. Fearon**, None.

Abstract Number: 0992

Impact of Selective Inhibitors of Nuclear Export on SLE Plasma Cells Is Modulated by the BM Microenvironment

Neha Nandedkar-Kulkarni[1], Nida Meednu[2], Jennifer Albrecht[2], Jennifer Barnas[2], Douglas Widman[3] and Jennifer Anolik[2], [1]University of Rochester, Rochester, NY, [2]University of Rochester Medical center, Rochester, NY, [3]Karyopharm Therapeutics, Newton, MA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematous (SLE) is a complex autoimmune disorder with heterogeneous disease presentation and a multi-pronged pathogenesis. Although autoreactive plasma cells play a key role in SLE, they are still elusive targets. Selective inhibitors of nuclear export (SINE) were recently approved by the FDA for treatment of refractory multiple myeloma (selinexor). Our lab has demonstrated that SINE abrogate lupus nephritis and significantly reduce autoreactive plasma cells in lupus prone NZBW/F1 mice. Here we investigated the impact of SINE on *In vitro* survival and antibody secretion of human plasma cells (PC) and how these classic PC functions are modulated by the bone marrow (BM) microenvironment.

Methods: Peripheral blood mononuclear cells (PBMCs) and bone marrow mononuclear cells (BMMCs) from healthy (n = 4) and SLE donors (n = 4), cultured in the presence of mesenchymal stromal cell secretome, were treated with KPT-335 for different periods of time. Number of antibody secreting cells (ASC) and PC survival were assessed by IgG ELISPOT and annexin V-propidium iodide flow based apoptosis assay, respectively. $CD19^+CD27^{hi}CD38^{hi}$ blood plasmablasts, $CD19^+CD27^{hi}CD38^{hi}CD138^+$ BM mature PCs and $CD19^-CD27^{hi}CD38^{hi}CD138^+$ BM long-lived PCs were sorted for transcriptomic analysis (controls: n = 7 and SLE: n = 9).

Results: Blood ASC were significantly reduced (IC50= 0.1uM) compared to BM ASC (IC50 = 10uM) after short-term *ex vivo* treatment with KPT-335 (24 hours). In long-term cultures (120 hours), there was a greater impact on BM PCs (IC50=0.1uM). We also examined the capacity of SINEs to induce apoptosis in different PC subsets. Blood plasmablasts from both healthy and SLE donors were reduced by 30-70% after SINE treatment for 48 hours. Of note, SINE treatment did not affect BM mature and long-lived PC. In transcriptomic analysis, BM PCs showed up-regulation of NFkB signaling and extra-cellular matrix receptor interactions (gene pathway analysis), and experienced down-regulation of cell cycle signaling pathways, compared to blood PC. Mature and long-lived PC in lupus BM had a prominent interferon (IFN) signature compared to controls. We are currently investigating the impact of type I IFN on PC survival and function.

Conclusion: SINEs represent a novel treatment approach for SLE. These results support the hypothesis that the effect of SINEs on PC depends upon the dose and duration of treatment, and is modulated by BM microenvironmental signals that orchestrate PC survival.

Disclosure: N. Nandedkar-Kulkarni, None; **N. Meednu**, None; **J. Albrecht**, None; **J. Barnas**, None; **D. Widman**, Karyopharm Therapeutics, 3; **J. Anolik**, None.

Abstract Number: 0993

N-linked Glycosylation of the Immunoglobulin Variable Domain Affects Antigen Binding and Autoreactive B Cell Activation

Theresa Kissel[1], Changrong Ge[2], Lise Hafkenscheid[1], Linda Slot[1], Marco Cavallari[3], Joanneke Kwekkeboom[4], Manfred Wuhrer[1], Thomas Huizinga[1], Hans Scherer[1], Michael Reth[3], Rikard Holmdahl[2] and René Toes[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]Karolinska Institutet, Solna, Sweden, [3]University Freiburg, Freiburg, Germany, [4]Leiden Univeristy Medical Center, Leiden, Netherlands

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-citrullinated protein antibodies, the hallmarking autoantibodies in Rheumatoid Arthritis (RA), are characterized by *N*-linked glycans in the variable domain (V-domain). The occurrence of these glycans results from the selective introduction of *N*-glycosylation sites during somatic hypermutation and their presence is predictive for the transition from pre-disease autoimmunity towards RA. We have now determined the biological implication of V-domain glycans on antigen-binding and B-cell activation.

Methods: ACPA crystal structures, including the starting monosaccharides of the V-domain glycans, were generated. These crystal structures were used as a basic framework and the complete glycan structure modelled onto the V-domain. Fab crystal structures with modelled V-domain glycans were subsequently used for molecular dynamics simulations. Antigen binding assays using monoclonal ACPA IgG including V-domain glycans and their non-glycosylated counterparts were performed. Further, we generated human Ramos B cells lines including V-domain glycosylated and non-glycosylated mIgG B cell receptors and identified their activation upon stimulation.

Results: Autoantibody crystal structures show that V-domain glycans are positioned in the vicinity of the binding-pocket and dynamic modelling shows their potential to interact with antigen-binding, which is confirmed by bind-

ing assays. Noteworthy, human Ramos B cells carrying V-domain glycosylated B cell receptors undergo increased signalling after stimulation compared to their non-glycosylated counterparts.

Conclusion: Our data indicate that autoreactive B cells in RA are selected for the presence of V-domain glycans that convey a signalling advantage, potentially explaining the outgrowth of autoreactive B cells and the increase of autoantibody levels towards disease-onset. These findings are relevant for the understanding of how autoreactive B cells escape immune checkpoints in humans and indicate that the introduction of V-domain glycans enables B cells to breach tolerance in the prominent autoimmune disease RA.

Disclosure: T. Kissel, None; **C. Ge**, None; **L. Hafkenscheid**, None; **L. Slot**, None; **M. Cavallari**, None; **J. Kwekkeboom**, None; **M. Wuhrer**, None; **T. Huizinga**, Bristol-Myers Squibb Company, 2, 8, Pfizer, 2, 8, Eli Lilly, 2, 8, LUMC, 9; **H. Scherer**, LUMC, 9; **M. Reth**, None; **R. Holmdahl**, None; **R. Toes**, LUMC, 9.

Abstract Number: 0994

Does Tofacitinib Impact B Cell Functions?

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Tofacitinib (tofa) inhibits cytokine signaling mediated by JAK1 JAK3 pathways leading therefore to a decrease in Th17 and an increase of Treg cells. The effect of tofa on B cell profile has been poorly explored. We aimed at studying the *in vitro* effect of tofa on B cell cytokine production (pro and anti-inflammatory) and plasmablast differentiation in the context of JAK-dependent and independent stimuli. The *in vivo* effect of tofa on B cell cytokine production was also assessed in mice.

Methods: Isolated B cells were cultured *in vitro* for 4 to 8 days in absence or presence of tofa and with JAK-dependent (CD40L, IL-2 and IL-21) or JAK-independent (CpG, a TLR9 ligand) stimuli. Cytokine production was assessed by flow cytometry and ELISA. Plasmablasts were defined as $CD19^{+}CD27^{+}CD38^{+}$ cells. p-STAT-3 was quantified by western blot at 30,120 and 240 minutes. IL-6, IL-10 and IFN-γ neutralizing antibodies were added in some experiments. *In vivo*, mice were treated with tofa or placebo for 8 days and B cells were analyzed in inguinal lymph nodes and peritoneal fluid.

Results: In presence of JAK-dependent IL-2/IL-21 stimuli, tofa (1 μM) decreased the levels of IL-6 (2.7%[1.0-7.6] vs 8.9%[7.1-18.1], n=7, p=0.01 for tofa and control respectively), IFN-γ, IL-10 (0.8%[0.5-1.4] vs 2.6%[0.7-3.3], p=0.04), IL-35 (Mean Fluorescence Intensity [MFI] =89.5[56.1-99.6] vs 163[125-239], p=0.01) produced by B cells.

In presence of the JAK-independent stimulation CpG, tofa also decreased IL-6 (30.2%[20.4-48.2] vs 35.5%[27.3-59.0], n=9, p=0.05), IFN-γ, IL-10 (1.9%[0.6-2.5] vs 2.5%[0.9-5.1], p=0.02) and IL-35 (MFI: 129.4[85.2-354.6] vs 177.7[132.5-566.8], p=0.001) in B cells. Whereas IL-2/IL-21 induced a phosphorylation of STAT3 at 30 min, CpG induced a delayed activation of JAK/STAT pathway, suggesting that cytokines produced in response to CpG have an autocrine effect with a secondary activation of JAK/STAT pathway which can be blocked by tofa. To confirm this

hypothesis, we cultured CpG activated B cells in the presence of cytokine-neutralizing antibodies and found that anti-IL-10 antibodies decreased the effect of CpG on IL-6 and IL-10 secretion and that tofa had then a decreased effect on those cytokines. In addition, tofa inhibited the plasmablasts differentiation in IL-2/IL-21 conditions (0.09%[0.05-0.17] vs 2.4%[1.4-3.3], n=6, p=0.03), but not with CpG (3.27%[0.57-4.97] vs 3.94%[0.73-8.41], p=0.15). *In vivo*, tofa decreased the frequency of IL-35 secreting B cells (0.8%[0.42-0.97] vs 1.6%[0.7-2.4, p=0.05] in peritoneal fluid but not IL-10 and TGF-β.

Conclusion: In addition to blocking cytokine pathways, tofa had a cellular impact on B cells, modifying their ability to produce pro- and anti-inflammatory cytokines both in JAK dependent and independent conditions. In JAK independent conditions, this effect of tofa was at least partly explained by the inhibition of an autocrine loop. Moreover, tofa decreased the differentiation of B cells into plasmablasts under conditions mimicking an interaction with T cells but not with TLR activation only, suggesting that tofa might have a lower impact on T-independent humoral immunity. We are currently evaluating the impact of tofa on B cells in tofa-treated rheumatoid arthritis patients.

Disclosure: G. Decarriere, None; **J. Mielle**, None; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **J. Morel**, AbbVie, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Novartis, 5, Pfizer Inc, 2, 5, Sanofi, 5; **R. Audo**, None; **C. Daien**, None.

Abstract Number: 0995

Jo-1-Binding B Cells Undergo Limited Class-Switching but Are Biased Towards Autoreactive-Prone and Memory B Cell Subsets in Anti-histidyl-tRNA Synthetase Syndrome

Jennifer Young-Glazer[1], Alberto Cisneros[2], Erin Wilfong[1], Scott Smith[1], Leslie J. Crofford[1] and Rachel Bonami[1], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbit University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are systemic autoimmune diseases traditionally classified as dermatomyositis or polymyositis, but these disorders are increasingly defined by the presence of specific autoantibodies. Anti-Jo-1 autoantibodies recognize histidyl tRNA synthetase and are found in a subset of these patients, but anti-Jo-1 B cells have not been previously characterized. To target these antigen-presenting cells in anti-histidyl-tRNA synthetase syndrome (HARS), we must first understand how they expand in the repertoire. In this study, we aimed to characterize Jo-1-binding B cells in HARS.

Methods: We enrolled 10 patients diagnosed with HARS, 4 patients with non-Jo-1 IIM, and 8 age and sex-matched healthy controls. We performed flow cytometry to phenotype peripheral blood mononuclear cells (PBMCs) and define the B cell subsets in which Jo-1-binding B cells reside. We polyclonally stimulated PBMCs from HARS subjects to drive *in vitro* B cell differentiation into antibody-secreting cells, and phenotypically compared Jo-1-binding versus non-Jo-1 binding B cells from the same subjects.

Results: On average, 65% of Jo-1-binding B cells were IgM+ (not class-switched). Compared to other B cells from the same donor, anti-Jo-1 B cells contained a higher percentage of autoimmune-prone $CD21^{lo}$ cells, increased

$CD38^{+}CD27^{+}$ memory cells, but fewer $CD38^{hi}CD24^{-}$ plasmablasts. Consistent with phenotypic data, anti-Jo-1 B cells were less likely to differentiate into $CD38^{hi}24^{-}$ plasmablasts following *in vitro* stimulation.

Conclusion: Jo-1-binding B cells were identified in the peripheral blood of all HARS patients assessed, suggesting they can be tracked as biomarkers to assess whether experimental therapies limit their expansion and activation. These data suggest complex B cell biology exists beyond class-switched cells that differentiate to secrete anti-Jo-1 autoantibody, and provide an important advance towards defining antigen-specific B cells and developing novel B cell-directed therapies for HARS patients.

Disclosure: J. Young-Glazer, None; **A. Cisneros**, None; **E. Wilfong**, None; **S. Smith**, None; **L. Crofford**, None; **R. Bonami**, None.

Abstract Number: 0996

Bacteria-Derived Indole Drives Autoimmune Arthritis by Altering B Cell Glycosylation of Autoantibodies

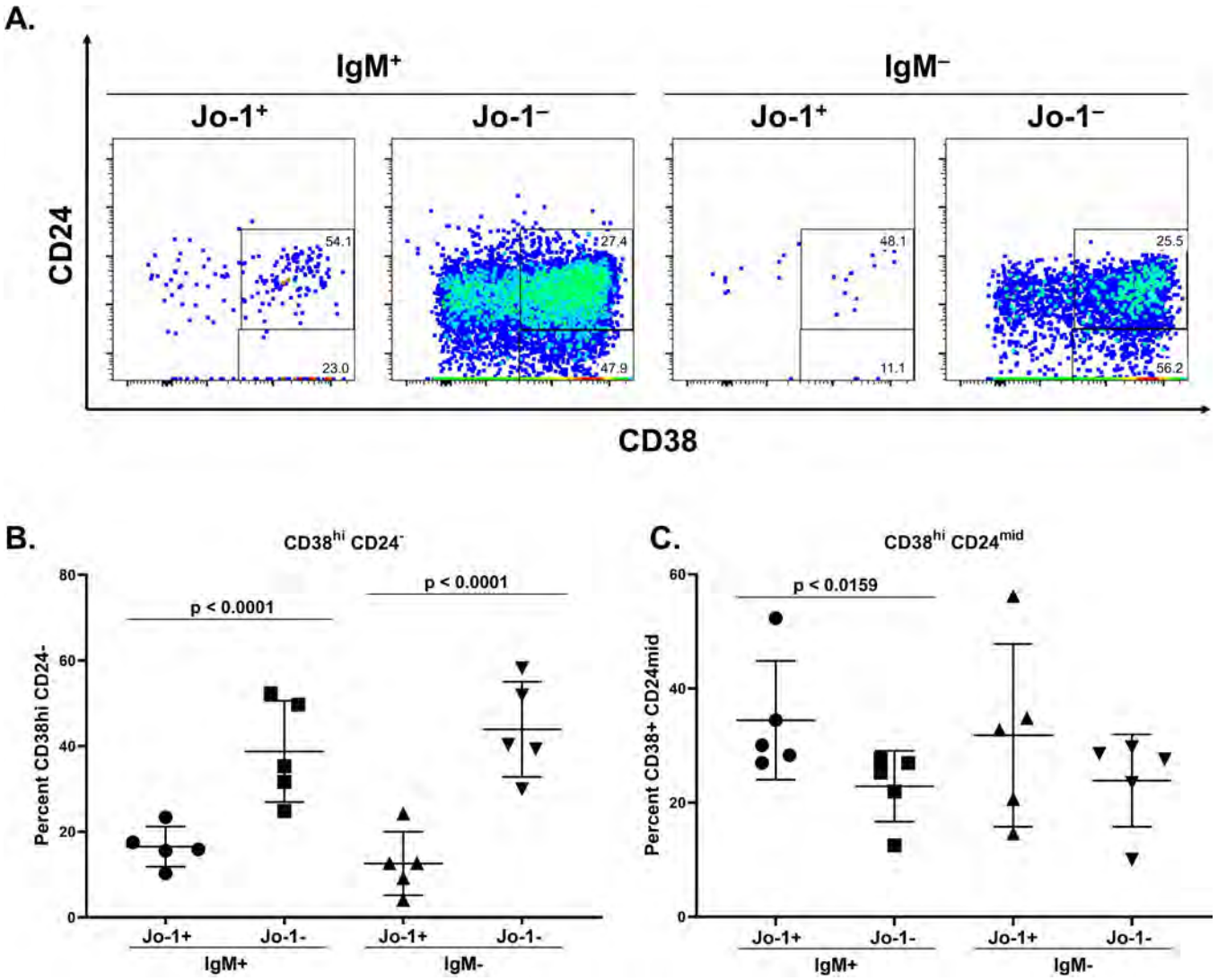
Brandon Trent[1], Meagan Chriswell[2], Widian Jubair[3] and Kristine Kuhn[1], [1]University of Colorado Anschutz Medical Campus, Aurora, CO, [2]UC Denver SOM, Denver, CO, [3]University of Colorado Denver, Denver, CO

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Background: Dysbiosis of gut bacterial communities in rheumatoid arthritis (RA) is a noted phenomenon in both murine models and human patients; however, the mechanisms from dysbiosis that promote RA pathogenesis remain unclear. Our lab previously demonstrated that administration of antibiotics to deplete the microbiota late in the course of murine collagen-induced arthritis (CIA) significantly ameliorated disease and correlated with changes in total antibody glycosylation patterns, known to occur in RA patients and affect complement fixation and FC receptor engagement. We hypothesized that the microbiota mediated antibody glycosylation via production of bacteria-specific metabolites.

Methods: Methods: CIA was induced by immunization of male 6-8 week-old DBA/1 mice with bovine type II collagen emulsified in complete Freund's adjuvant on days 0 and 21. To understand the mechanisms by which late micriobiota depletion would significantly decrease CIA, we analyzed concentrations of cecal metabolites by LC-MS during CIA and after antibiotic treatment (1 mg/ml each ampicillin, neomycin, metronidazole and 0.5 mg/ml vancomycin). 10 mM indole or vehicle was then added to the drinking water containing antibiotics. Arthritis was evaluated based on a score of 0 (no swelling) to 4 (ankylosis) for each paw and summed for the mouse. Assessment of cell populations was performed by flow cytometry. Splenic B cells were evaluated *ex vivo* after stimulation with LPS (5μg/mL) and/or anti-IgM (10μg/mL) and total RNA was collected and analyzed via qRT-PCR.

Results: Results: Metabolomic profiling demonstrated a significant increase in bacteria-produced indole, a byproduct of tryptophan metabolism, in mice with CIA compared to unimmunized controls and those with CIA treated with antibiotics. Interestingly, administration of indole after antibiotic treatment resulted in a partial restoration of a CIA phenotype. Indole administration also resulted in increased T follicular helper cell (Tfh) and B cell populations in the Peyer's patches and mesenteric lymph nodes in mice, but not the spleen. Furthermore, *ex vivo* stimulation of murine



A lower frequency of Jo-1-binding B cells acquire a plasmablast phenotype following stimulation in vitro compared to non-Jo-1-binding B cells from the same IIM patients. PBMCs from n=5 HARS patients with active disease were polyclonally stimulated as in Methods. Cultured cells from 40-60 wells per patient were harvested on day 6 and stained for flow cytometry analysis. A) CD24 and CD38 expression is shown in representative flow plots derived from a single well of stimulated PBMCs. Comparison of relative frequencies for B) CD38 hi CD24 - B lymphocytes or C) CD38 + CD24 mid B lymphocytes between Jo-1 specific and Jo- 1 non-specific populations. Significant differences between IgM + Jo-1 + and IgM + Jo-1 – or IgM – Jo- 1 + and IgM – Jo-1 – populations as calculated using Mann-Whitney U test are indicated. The data are represented as the mean for each population within a given stimulation, the bars indicate the mean ± SD.

splenic B cells with indole induced gene expression of the B4Galt and Fut8 genes, transferases critical in antibody glycosylation.

Conclusion: Conclusions: Our results suggest that gut dysbiosis due to RA results in bacterial production of indole, which promotes RA pathogenesis via activation of B cell populations and altered antibody glycosylation patterns. Precise understanding of which indole metabolites are involved and how they engage cellular receptors will help elucidate the role of intestinal dysbiosis in RA development.

Table 1. Study Participant Characteristics

	Healthy Controls (n=8)	Non-Jo-1 IIM * (n=4)	Stable Jo-1+ Disease ** (n=5)	Active Jo-1 Disease *** (n=5)
Age (years)	48.2 (42.1 - 52.0)	58.2 (50.9 - 63.2)	57.1 (43.4 - 57.4)	53.8 (46.2 - 56.1)
Sex (female)	5 (63)	3 (75)	5 (100)	3 (60)
Race				
Caucasian	6 (75)	4 (100)	5 (100)	3 (60)
African American	1 (13)	0	0	1 (20)
Other Ethnicity	1 (13)		0	0
Disease Duration (years)	-	2 (0.5 – 2.7)	13.8 (4.6-14.5)	1.0 (0.8-4.0)
Daily Steroid Dose ≥ 20mg	-	3 (75)	0	4 (80)
Other Immunosuppressant Use	-	2 (50) †	5 (100) ‡	1 (20) §

Data are presented as medians (interquartile ranges) and counts and percentages for continuous and categorical data, respectively.

* Anti-PL-7, anti-EJ with anti-Ro52, anti-Mi-2, and anti-TIF1-γ

** Stable Jo-1+ antisynthetase syndrome defined as having no medication changes discussed, and current medications either continued or deescalated at the time of blood draw.

*** Active Jo-1+ antisynthetase syndrome defined as either immunosuppression increased during outpatient visit, or patient hospitalized with life-threatening disease at the time of blood draw.

† IVIG (1), Methotrexate (1)

‡ Azathioprine (3), Hydroxychloroquine (1), Leflunomide (1)

§ IVIG (1)

Disclosure: B. Trent, None; **M. Chriswell**, None; **W. Jubair**, None; **K. Kuhn**, None.

Abstract Number: 0997

Novel Shared Antibody Specificities in Ro Antibody Negative Sjögren's Syndrome

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's syndrome (SS) is a rheumatic autoimmune disease characterized by focal lymphocytic infiltrates in the lacrimal and salivary glands, severe dry mouth and eyes, pain and debilitation. Diagnosis requires autoantibodies to ubiquitous Ro antigens or a lip biopsy positive for focal lymphocytic infiltrates. Here we used human proteome arrays to identify novel antibodies in plasma from Ro antibody positive and Ro antibody negative SS patients compared with healthy controls.

Methods: Anti-Ro positive (n=15) and anti-Ro negative (n=15) cases meeting 2016 ACR/EULAR classification criteria for SS were age, race, and sex matched with each other and healthy controls (n=15). Plasma IgG binding to human proteome arrays containing >19,500 recombinant human proteins representing >80% of the human proteome

(HuProt v3.2 arrays, CDI Laboratories) was assessed. Data were normalized by the Robust Linear Model using the PAA Bioconductor Package in R and log intensity values for each protein generated. Thresholds of mean + 3SD were established using the controls. Antigens bound by IgG in at least 4 cases compared to controls were considered significant ($p< 0.05$, one-tailed Fisher's exact test).

Results: IgG from Ro positive SS cases significantly bound 42 proteins, including the canonical SS antigens Ro60, Ro52, and La, with an average of 15 specificities per individual. IgG from Ro negative SS cases significantly bound 24 proteins compared to controls, with an average of 7 specificities per individual. Of the antigens identified, 8 were shared in both the Ro positive and Ro negative groups. Binding to at least one of these 8 proteins identified 93% of the Ro positive cases and 87% of the Ro negative cases.

Conclusion: A set of 8 novel antigens were bound by plasma IgG in both Ro positive and Ro negative cases. These antigens may be useful for diagnosing SS without a lip biopsy.

Disclosure: S. Longobardi, None; **C. Georgescu**, None; **C. Lawrence**, None; **C. Moya**, None; **J. Wren**, None; **J. James**, None; **K. Sivils**, None; **A. Farris**, None.

Abstract Number: 0998

Differential Roles of TNFRI and TNFRII in the Morphology of Secondary Lymphoid Organs

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SESSION INFORMATION
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Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Tumour necrosis factor (TNF) induced signaling events are important in lymphoid organ development and function, both in health and in immune-mediated inflammatory diseases such as arthritis. Important receptors involved in this process include TNF receptors (R) I and II that exert distinct functions. Mice overexpressing transmembrane (tm)TNF develop various features of chronic inflammation, including arthritis, that are mediated via TNFRI and/or TNFRII. In this study we investigated the contribution of TNFRI and TNFRII in spleen and peripheral lymph node (PLN) morphology in transgenic mice overexpressing tmTNF (tmTNF-tg).

Methods: Spleen and PLN were collected from wild type (wt) and heterozygous tmTNF-tg mice, with were either on a normal or TNFRI or TNFRII deficient background. Spleens were stained by immunofluorescence for B and T cell markers, imaged by confocal microscopy and analyzed using FIJI software. PLN were used for whole mount tissue staining for B and T cell markers, cleared, 3D imaged by light sheet microscopy and analyzed using Imaris software.

Results: TmTNF-tg mice exhibited an altered spleen morphology characterized by smaller follicles (tmTNF-tg 69.73 ± 72.25 μm^2; wt 139.3 ± 71.36 μm^2), and a reduced proportion of follicle T cell area (tmTNF-tg 15.22 ± 9.69%; wt 26.60

± 10.46%). Spleen morphology of TNFRI$^{-/-}$ and TNFRII$^{-/-}$ mice was similar to wt mice. TmTNF-tg x TNFRI$^{-/-}$ exhibited a normal spleen architecture (follicle size: 239.2 ± 250.5 μm^2; T cell area: 29.92 ± 11.46%). In contrast, spleen follicles of tmTNF-tg x TNFRII$^{-/-}$ mice had T cell areas (17.31 ± 8.88%) comparable to tmTNF-tg mice. PLNs of tmTNF-tg mice were increased in size (tmTNF-tg 3.74 ± 1.31 mm^3; wt 2.41 ± 0.60 mm^3), also in combination with deficiency of TNFRI (3.98 ± 2.07 mm^3) or TNFRII (4.01 ± 1.96 mm^3). TmTNF-tg PLNs had an increase in absolute B cell volume (tmTNF-tg 0.86 ± 0.33 mm^3; wt 0.51 ± 0.07 mm^3), but no change in B cell area as proportion of total PLN volume. The increased B cell volume was critically dependent on TNFRII. Interestingly, TNFRI deficiency caused profound alterations B cell area morphology that appeared as one peripheral layer of B cells covering a central T cell area rather than properly developed follicles.

Conclusion: This study demonstrates that overexpression of tmTNF leads to an aberrant spleen architecture, characterized by smaller follicles and reduced central T cell areas, which is critically dependent on TNFRI. In addition, overexpression of tmTNF results in enlarged PLN and increased total B cell volume, which is dependent on TNFRII, whereas TNFRI is more important in the proper organization of B cell follicles. Overall, this study employing different state-of-the-art (3D) imaging techniques highlights the importance of tmTNF-TNFR-induced signaling events in secondary lymphoid organ morphology and function, and reveals distinct roles for TNFRI and II. Advancing our knowledge in this field might provide a better understanding of the pathophysiology of TNF-associated diseases such as arthritis, which may be important to develop new or improved treatment strategies.

Disclosure: K. Jeucken, None; **J. van Hamburg**, None; **S. Tas**, None.

Abstract Number: 0999

CXCL13 Is a Key Driver for Migration and Differentiation of Regulatory B Cells

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
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Background/Purpose: Human regulatory B cells still need to be characterized. Given the absence of phenotypical definition, a functional definition based on their ability to secrete IL-10 is often used (corresponding to B10$^+$ cells). Chemokine receptors (CKR) profiles are useful to characterize some populations of T cells but have never been explored among B10$^+$ cells. Moreover, very little is known about B10$^+$ cell migration. Chemokines (CK) have also been implicated in the differentiation of naïve T cells towards regulatory T cells. Therefore, the aims of our study were to characterize the profile of CKR on B10$^+$ cells and also to investigate CK implicated in their migration and differentiation both in control (CTL) and in rheumatoid arthritis (RA) patients.

Methods: B cells were isolated with Rosette Sep Human B cells enrichment followed by Ficoll separation. B cells were activated 24 hours with CpG and CD40L to generate B10$^+$ cells. For RNA sequencing and migration assay, B10$^+$ and IL-10^{neg} B cells (B10^{neg}) cells were then sorted using IL-10 secretion assay. IL-10 secretion from B cells was assessed by FACS and ELISA. For migration assay, ability to migrate in response to CCL21, CCL22, CXCL11, CXCL12

or CXCL13 or synovial fluid (SF) from RA or osteoarthritis (OA), were evaluated by migration assay in 5μM Transwell chambers and expressed as fold increase compare to basal migration towards control media.

Results: Transcriptomic analysis was done on $B10^{+}$ and $B10^{neg}$ from 5 CTL and 4 RA patients. 335 genes were found differentially regulated (DEG) in control $B10^{+}$ cells compared to $B10^{neg}$ in CTL and 188 in RA patients. Of note, only 159 DEG were shared by both groups, while 29 were specific to RA. Gene ontology classification of DEG revealed that genes from CKs pathways were highly enriched in $B10^{+}$ from CTL and to a lesser extend in $B10^{+}$ from RA patients. Among all CK tested, only CXCL13, attracted significantly more $B10^{+}$ than $B10^{neg}$ from CTL (12.4 ± 10.0-fold increased migration of B10+ vs 6.0 ± 3.4-fold increased migration of B10neg, n=21). This was also true in RA patients (18.7 ± 22.8-fold increased migration for $B10^{+}$ vs 6.4 ± 5.3-fold increased migration for $B10^{neg}$, n=13). SF from RA induced a significant migration of $B10^{+}$ cells in CTL (9.6 ± 12.0-fold increased migration, $p< 0.0001$, n=22) and RA patients (7.1 ± 9.7-fold increased migration, p=0.0002, n=13), higher than those induced by SF from OA. CXCL13 was significantly higher in SF from RA than in SF from OA (685.5 ± 135.1 pg/mL vs 122.8 ± 186.7 pg/mL, p=0.03). Importantly, $B10^{+}$ migration towards SF was significantly correlated with the levels of CXCL13 in these SF in CTL (r=0.62, p=0.007, n=17) and with a trend in RA patients (r=0.45, p=0.07, n=17). Lastly, CXCL13 was also found to increase IL-10 secretion in B cells stimulated with CpG in CTL (1.4 ± 0.3-fold increase, $p< 0.0001$, n=20) and in RA patients (1.2 ± 0.2-fold increase, p=0.01, n=13).

Conclusion: We showed that CXCL13 is a key driver for migration and differentiation of $B10^{+}$ cells in CTL and in RA patients.

Disclosure: C. Rempenault, None; **J. Mielle**, None; **K. Schreiber**, None; **P. Corbeau**, None; **J. Morel**, AbbVie, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Novartis, 5, Pfizer Inc, 2, 5, Sanofi, 5; **C. Daien**, None; **R. Audo**, None.

Abstract Number: 1000

Passive Smoking Throughout the Life Course and the Risk of Incident Rheumatoid Arthritis in Adulthood Among Women

Kazuki Yoshida[1], Jiaqi Wang[2], Susan Malspeis[3], Bing Lu[4], Lauren C. Prisco[3], Lily Martin[3], Julia Ford[2], Karen Costenbader[5], Elizabeth Karlson[2] and Jeffrey Sparks[6], [1]Brigham & Women's Hospital and Harvard Medical School, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston, [4]Brigham and Women's Hospital and Harvard Medical School, Newton, MA, [5]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [6]Division of Rheumatology, Inflammation, and Immunity; Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Personal cigarette smoking has been strongly associated with the risk for developing seropositive RA. Previous studies concerning passive smoking conflict; some suggested that childhood passive smoking confers RA risk but not all. No studies have investigated passive smoking throughout the life course and the risk of RA, while also accounting for the possible mediation of personal smoking.

Methods: We conducted a cohort study utilizing the Nurses' Health Study II, an ongoing prospective cohort of female registered nurses. Biennial questionnaires collected information on items such as sociodemographics, anthropomet-

	RA cases/Person-years	Base model*	+Confounders (**main model**)**	+Future adult personal smoking pack-years (possible mediator)†
All RA				
No maternal smoking	325/1,524,943	1.00 (ref)	1.00 (ref)	1.00 (ref)
Maternal smoking	153/578,919	**1.23 (1.02-1.49)**	**1.25 (1.03-1.52)**	1.18 (0.97-1.44)
Don't know/Missing	54/236,574	1.03 (0.77-1.37)	1.04 (0.78-1.39)	1.00 (0.75-1.34)
Seropositive RA				
No maternal smoking	209/1,523,208	1.00 (ref)	1.00 (ref)	1.00 (ref)
Maternal smoking	104/578,203	**1.31 (1.03-1.66)**	**1.34 (1.06-1.70)**	1.26 (0.99-1.61)
Don't know/Missing	39/236,359	1.16 (0.82-1.64)	1.21 (0.86-1.70)	1.16 (0.82-1.64)
Seronegative RA				
No maternal smoking	116/1,521,486	1.00 (ref)	1.00 (ref)	1.00 (ref)
Maternal smoking	49/577,290	1.09 (0.78-1.53)	1.10 (0.79-1.56)	1.05 (0.75-1.48)
Don't know/Missing	15/235,910	0.79 (0.46-1.35)	0.75 (0.44-1.30)	0.73 (0.42-1.26)

* Adjusted for age and questionnaire cycle.
** Additionally adjusted for race/ethnicity, maternal and paternal education, maternal and paternal occupations, home ownership, state born, and family history of RA (pre-exposure confounders for this analysis).
† Additionally adjusted for post-birth variables: birthweight, preterm birth, breastfeeding, and adult personal smoking pack-years (possible mediators).

Table 1. Hazard ratios for rheumatoid arthritis, overall and by serologic phenotype, according to maternal smoking during pregnancy (in utero exposure) (n=90,923).

	RA cases/Person-year	Base model*	+Confounders (**main model**)**	+Future adult personal smoking pack-years (possible mediator)†
All RA				
No parent smoked	160/829,960	1.00 (ref)	1.00 (ref)	1.00 (ref)
Any parent smoked	372/1,510,476	**1.24 (1.03-1.49)**	1.18 (0.96-1.46)	1.13 (0.93-1.42)
Seropositive RA				
No parent smoked	95/829,064	1.00 (ref)	1.00 (ref)	1.00 (ref)
Any parent smoked	257/1,508,706	**1.46 (1.15-1.84)**	**1.41 (1.08-1.83)**	**1.34 (1.03-1.75)**
Seronegative RA				
No parent smoked	65/828,444	1.00 (ref)	1.00 (ref)	1.00 (ref)
Any parent smoked	115/1,506,242	0.93 (0.68-1.26)	0.86 (0.60-1.22)	0.83 (0.58-1.18)

* Adjusted for age and questionnaire cycle.
** Additionally adjusted for race/ethnicity, maternal and paternal education, maternal and paternal occupations, home ownership, state born, family history of RA, birthweight, preterm birth, breastfeeding, and maternal smoking during pregnancy (pre-exposure confounders for this analysis).
† Additionally adjusted for adult personal smoking pack-years (possible mediator).

Table 2. Hazard ratios for rheumatoid arthritis, overall and by serologic phenotype, according to childhood parental smoking at home (n=90,923).

rics, dietary intake, and health conditions. Incident RA and date of diagnosis were determined by medical record review (all meeting 1987 ACR or 2010 ACR/EULAR classification criteria). Serostatus for RA was determined by positive result for RF or anti-CCP protein antibody in medical records. Three passive smoking exposures spanning the life course were assessed: maternal smoking during pregnancy (In utero exposure), parental smoking at home during childhood, and years spent living with a smoker since age 18. Covariates included early life (e.g., parental education, parental occupation, birthweight) and time-updated adult (e.g., personal smoking pack-years, dietary intake, BMI, menopause) factors. Parental smoking behavior could have influenced participants' uptake of late adolescent and adult smoking, making the latter a possible mediator between early life passive smoking and adult-onset RA. We examined the association between each passive smoking exposure and incident RA risk using Cox regression models.

	RA cases/Person-years	Base model*	+Confounders**	+Adult pack-year smoking (confounder, **main model**)†
All RA				
None	267/1,314,984	1.00 (ref)	1.00 (ref)	1.00 (ref)
1-19 years	194/821,720	1.12 (0.93-1.35)	0.97 (0.79-1.19)	0.95 (0.77-1.17)
20+ years	71/203,731	**1.59 (1.22-2.08)**	1.24 (0.92-1.66)	1.02 (0.74-1.40)
Trend p		**p = 0.0008**	p = 0.20	p = 0.97
Seropositive RA				
None	169/1,313,553	1.00 (ref)	1.00 (ref)	1.00 (ref)
1-19 years	136/820,904	**1.26 (1.00-1.58)**	1.04 (0.81-1.33)	1.01 (0.79-1.30)
20+ years	47/203,314	**1.74 (1.25-2.42)**	1.27 (0.88-1.83)	1.05 (0.71-1.55)
Trend p		**p = 0.0006**	p = 0.21	p = 0.81
Seronegative RA				
None	98/1,312,221	1.00 (ref)	1.00 (ref)	1.00 (ref)
1-19 years	58/819,441	0.89 (0.65-1.24)	0.85 (0.60-1.22)	0.83 (0.58-1.19)
20+ years	24/203,024	1.36 (0.86-2.14)	1.19 (0.72-1.98)	1.02 (0.59-1.77)
Trend p		p = 0.32	p = 0.60	p = 0.81

* Stratified for age and questionnaire cycle.
** Additionally adjusted for race/ethnicity, maternal and paternal education, maternal and paternal occupations, home ownership, state born, family history of RA, birthweight, preterm birth, breastfeeding, maternal smoking during pregnancy, childhood parental smoking, childhood personal smoking, age at menarche, BMI at age 18, and adult confounders (menopause and hormone use, parity/breastfeeding, BMI, physical activity, Alternative Healthy Eating Index, residence, census tract income)
† Additionally adjusted for adult personal smoking pack-years (confounder in this analysis).

Table 3. Hazard ratios for rheumatoid arthritis, overall and by serologic phenotype, according to years lived with a smoker since age 18 (n=90,923).

Results: Among 90,923 women (mean age at baseline 34 years), we identified 532 incident RA cases (352 seropositive; 180 seronegative) during 2,340,436 person-years of follow-up (mean 25 years/participant). In the sample, 25% had in utero exposure to maternal smoking during pregnancy; 64% reported childhood home exposure to parental smoking; and 44% reported living with a smoker as an adult (35% with ≤20 years, 9% with 20+ years). Maternal smoking during pregnancy was associated with incident RA after confounding adjustment (HR 1.25 [95% CI 1.03, 1.52]). This finding was stronger for seropositive RA (HR 1.34 [1.06, 1.70]). Childhood parental smoking was associated with seropositive incident RA after adjusting for confounders including maternal smoking during pregnancy (HR 1.41 [1.08, 1.83]). This association was present even after adjusting for a potential mediator, adult personal smoking (HR 1.34 [1.03, 1.75]). After adjustment for confounders including personal smoking, there was no association of adult passive smoking with RA (20+ years lived smoker: HR 1.02 [0.74, 1.40] vs. none).

Conclusion: In this analysis spanning the life course, early life passive smoking exposures were associated with incident seropositive RA in adulthood. Childhood parental smoking was associated with incident seropositive RA even after adjustment for adult personal smoking, suggesting an important influence of early-life inhalant exposures on adult-onset RA. The possible association of adult passive smoking with RA was completely explained by confounders including personal smoking.

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Abstract Number: 1001

Risk of Malignant Melanoma and Nonmelanoma Skin Cancer in Rheumatoid Arthritis Patients Initiating Methotrexate versus Hydroxychloroquine

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SESSION INFORMATION
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Background/Purpose: Previous randomized clinical trials and observational studies have signaled an increased risk of skin cancer in rheumatoid arthritis (RA) patients treated with immunosuppressants such as methotrexate (MTX). The objective of this study was to compare the incidence rates of malignant melanoma and nonmelanoma skin cancer (NMSC) in RA patients initiating MTX versus hydroxychloroquine (HCQ) using real-world data.

Methods: Using Medicare claims data (Parts A/B/D 2006-2017), we conducted a cohort study of RA patients who were 65 years or older and initiators of MTX or HCQ as their first DMARD. Cohort entry date was the date of the first dispensing for either MTX or HCQ. At least 365 days of continuous enrollment in Medicare parts A, B, and D was required. We excluded patients who used any disease-modifying antirheumatic drugs (DMARDs), chloroquine, other immunosuppressants, or had a history of malignancy including skin cancer, immunosuppression, psoriatic arthritis, or systemic lupus erythematosus. The primary outcome was a composite of malignant melanoma and NMSC. Malignant melanoma was defined based on a validated algorithm requiring two International Classification of Diseases (ICD) 9 or 10 diagnosis codes separated by 1-60 days (PPV 83%). NMSC was also defined based on a validated algorithm using one ICD 9 or 10 diagnosis code followed by a NMSC-related procedural code occurring within 60 days (PPV 84%). Secondary outcomes were components of the primary outcome: malignant melanoma, NMSC, basal cell carcinoma (BCC), and squamous cell carcinoma (SCC). To control for confounding, we conducted one-to-one propensity score (PS) matching using more than 60 covariates assessed during a 365-day baseline period. We calculated the incidence rates (IRs), hazard ratios (HRs), and corresponding 95% confidence intervals (CIs) for each outcome.

Results: A total of 24,611 PS-matched pairs of MTX and HCQ initiators were identified. The mean (SD) age was 73.8 (6.6) years and 78% were female. Patient demographics, dermatologic conditions, comorbidities, medication use, and healthcare utilization were well-balanced between the two treatment groups at baseline (**Table 1**). During a total person-years of 52,836, we observed 693 (MTX) and 612 (HCQ) cases of malignant melanoma or NMSC. The IR per 1,000 person-year for the primary outcome was 24.57 (MTX) versus 24.85 (HCQ), and the HR comparing MTX with HCQ was 0.97 (95%CI 0.87-1.09). For secondary outcomes, MTX was associated with an elevated risk of BCC (HR 1.32, 95%CI 1.08-1.60) but a decreased risk of SCC (HR 0.77, 95%CI 0.61-0.97) compared with HCQ (**Table 2**).

Conclusion: In this large cohort of older RA patients initiating MTX or HCQ as their first DMARD, we found no difference in the risk of skin cancer including malignant melanoma and NMSC. However, for individual subsets of NMSC, the risk of BCC was higher in the MTX group compared with HCQ initiators while the risk of SCC was lower.

Table 1. Selected Baseline Characteristics of MTX and HCQ Initiators in the 1:1 Propensity Score Matched Cohort

Characteristics	MTX (N = 24, 611)	HCQ (N = 24, 611)	Standardized difference
Demographics			
Age in years, mean (SD)	73.78 (6.57)	73.80 (6.54)	0.003
Female	19,557 (79.5%)	19,496 (79.2%)	0.006
Dermatologic Conditions			
Actinic keratosis	1,671 (6.8%)	1,676 (6.8%)	0.001
Procedures for benign or premalignant lesions	2,075 (8.4%)	2,065 (8.4%)	0.001
Photodynamic therapy	19 (0.1%)	20 (0.1%)	0.001
Burn and sunburn	97 (0.4%)	85 (0.3%)	0.008
Comorbidities			
Coronary artery disease	5,814 (23.6%)	5,828 (23.7%)	0.001
Stroke or TIA	1,447 (5.9%)	1,467 (6.0%)	0.003
Combined comorbidity index (SD)	1.20 (2.09)	1.22 (2.09)	0.008
Medication Use			
Anticoagulant	2,255 (9.2%)	2,274 (9.2%)	0.003
NSAIDS/Coxibs	11,440 (46.5%)	11,426 (46.4%)	0.001
Statins	11,880 (48.3%)	11,891 (48.3%)	0.001
Insulin	1,452 (5.9%)	1,463 (5.9%)	0.002
Non-insulin diabetes medications	4,419 (18.0%)	4,559 (18.5%)	0.015
Oral steroid use	15,881 (64.5%)	15,913 (64.7%)	0.003
Healthcare Utilization			
Dermatologist visit	3,260 (13.2%)	3,316 (13.5%)	0.007
Rheumatologist visit	19,422 (78.9%)	19,407 (78.9%)	0.001
Emergency department visit	8,320 (33.8%)	8,386 (34.1%)	0.006
Recent hospitalization	1,052 (4.3%)	1,070 (4.3%)	0.004
Skin biopsy	326 (1.3%)	310 (1.3%)	0.006

Abbreviations: MTX, methotrexate; HCQ, hydroxychloroquine; SD, standard deviation; TIA, transient ischemic attack; NSAIDs, Nonsteroidal anti-inflammatory drugs; Coxibs, cyclooxygenase inhibitors

Variables with the standardized difference <0.1 are considered well-balanced between the two groups.

Table 2. Incidence rates (IR) and Hazard Ratios (HR) of Primary and Secondary Outcomes in the 1:1 Propensity Score Matched Cohort

Outcome	Exposure Group	Number of Events	Total Person Years	IR in 1000 Person-Years (95% CI)	HR (95% CI)
Primary Outcome					
Malignant Melanoma* and NMSC†	MTX	693	28205	24.57 (22.79,26.44)	0.97 (0.87, 1.09)
	HCQ	612	24631	24.85 (22.93,26.87)	Ref.
Secondary Outcomes					
Malignant Melanoma	MTX	47	29,345	1.60 (1.18, 2.13)	1.38 (0.87, 2.20)
	HCQ	29	25,564	1.13 (0.76,1.63)	Ref.
NMSC	MTX	668	28,235	23.66 (21.91,25.50)	0.96 (0.86, 1.07)
	HCQ	598	24,646	24.26 (22.38,26.26)	Ref.
Basal cell carcinoma	MTX	258	28,948	8.91 (7.86, 10.06)	1.32 (1.08, 1.60)
	HCQ	167	25,327	6.59 (5.63, 7.67)	Ref.
Squamous cell carcinoma	MTX	139	29,145	4.77 (4.01, 5.63)	0.77 (0.61, 0.97)
	HCQ	151	25,331	5.96 (5.05, 6.99)	Ref.

Abbreviations: NMSC, Nonmelanoma skin cancer; MTX, methotrexate; HCQ, hydroxychloroquine; Ref., reference

* Defined as 2 International Classification of Diseases (ICD) 9 or 10 diagnosis codes for malignant melanoma separated by 1 -60 days

† Defined as 1 ICD 9 or 10 diagnosis code for NMSC followed by a procedural code for NMSC treatment within 60 days

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Abstract Number: 1002

Prostate Cancer Risk Is Not Increased in Rheumatoid Arthritis After Accounting for Retention in a Health Care System

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SESSION INFORMATION
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Background/Purpose: Patients with rheumatoid arthritis (RA) may have up to a 15% increased risk of prostate cancer per a recent meta-analysis (Simon et al. *Arthritis Research & Therapy,* 2015). Previously, we found similar rates of prostate cancer in U.S. Veterans with RA as in individuals from the general population via indirect standardization using the Surveillance, Epidemiology, and End Results (SEER) Program (Brittan et al, Abstract #943, 2018). Recognizing the potential for bias based on the referent population and differences in cancer surveillance, we compared the risk of prostate cancer among RA and non-RA patients in the Veterans Health Administration (VHA; direct standardization).

Methods: We performed a retrospective, matched cohort study in the VHA from 2000 to 2018. We identified male patients with RA using a validated administrative algorithm and matched them to male patients without RA (no RA diagnostic codes or DMARDs) on age and enrollment year (up to 1:5). RA and non-RA patients with prior prostate cancer or prostatectomy were excluded. Prostate cancer and prostate cancer death were identified from the VA oncology domain within the Corporate Data Warehouse and the National Death Index. Multivariable Cox models compared prostate cancer risk after adjusting for race, smoking status, body mass index, Agent Orange exposure, Rheumatic Disease Comorbidity Index score, prostate-specific antigen testing, and health care utilization. Subjects were clustered by the matched RA/non-RA groups. Recognizing the potential for greater retention in the healthcare system and premature mortality among RA patients to influence results, we tested additional models censoring for a gap of >365 days between VA visits and censoring the matched patients at the time of death (in cases unrelated to prostate cancer) in RA patients.

Results: We included 56,514 Veterans with RA and 227,343 Veterans without RA. Mean (SD) age was 64 (11) years and the majority (74% RA, 88% non-RA) were Caucasian. There were 6,550 incident prostate cancers during 2,337,104 patient-years of follow-up. Prostate cancer incidence rates (per 1,000 patient-years) were 3.5 (95% CI 3.3-3.7) in RA and 2.7 (95% CI 2.6-2.7) in non-RA. There was a 28% increased risk of prostate cancer in RA (Model A; Table) that was attenuated to 15% after multivariable adjustment (Model B). Accounting for premature mortality in RA from other causes did not meaningfully affect results (Model C). However, after censoring for a gap of >365 days between VA visits, RA was not significantly associated with prostate cancer risk (Model D: HR 1.07; 95% CI 0.98-1.18; p=0.13). Several sensitivity analyses produced results consistent with the primary results.

Table. Risk of Prostate Cancer in U.S. Veterans with (n=56,514) and without (n=227,343) RA

Model	Hazard Ratio RA vs non-RA	95% Confidence Interval	P value
A. Unadjusted	1.28	(1.20, 1.36)	<0.001
B. Adjusted*	1.14	(1.07, 1.22)	<0.001
C. Adjusted* + Censor matched patients for RA death	1.15	(1.07, 1.23)	<0.001
D. Adjusted* + Censor for gap >365 days between VHA visits	1.07	(0.98, 1.18)	0.13
All models matched RA and non-RA for age and VA enrollment year *Adjusted for race, smoking status; Agent Orange exposure; number of outpatient visits; PSA testing; body mass index; Rheumatic Disease Comorbidity Index score			

Conclusion: Using direct standardization and accounting for relevant confounders and causes of potential bias, we did not find RA to be associated with an increased risk of prostate cancer. These findings highlight the importance of accounting for healthcare system retention when studying cancer risk in rheumatic diseases to prevent detection bias.

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Abstract Number: 1003

Long-term Weight Changes and Risk of Rheumatoid Arthritis Among Women in a Prospective Cohort: A Marginal Structural Model Approach

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SESSION INFORMATION

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Background/Purpose: The risk of rheumatoid arthritis (RA) has been shown to be elevated among overweight and obese women in several studies, but whether weight gain or weight loss are associated with RA risk has been studied less. To address time-dependent confounding and allow for a causal interpretation of the data, we used Marginal Structural Models (MSM) to examine the effect of long-term weight changes on the risk of RA in women using data from the Nurses' Health Study (NHS) II.

Methods: The NHS II prospective cohort study started in 1989 (baseline). We followed up 114,946 women aged from 25 to 42 years and without RA at baseline until 2017 (up to 28 years). We obtained information on lifestyle and health using validated biennial questionnaires. We investigated two time-varying exposures: weight changes from

Table 1. Associations between weight change from baseline and rheumatoid arthritis in the Nurses' Health Study II (1989-2017)

	Categories of time-updated weight change from baseline				
	Loss (<-2 kg)	Stable (-2 - <2 kg)	Gain (2 - <10 kg)	Gain (10 - <20 kg)	Gain (20+ kg)
All RA					
No. of cases/ person-yrs	48/197,984	51/450,712	193/974,788	131/453,192	69/201,566
RR (95% CI) Unadjusted	**2.10 (1.42, 3.12)**	Ref	**1.71 (1.26, 2.33)**	**2.46 (1.78, 3.40)**	**2.88 (2.01, 4.14)**
RR (95% CI) MSM*	**2.00 (1.22, 3.27)**	Ref	**1.87 (1.29, 2.73)**	**3.08 (2.03, 4.65)**	**3.48 (2.13, 5.68)**
Seropositive RA					
No. of cases/ person-yrs	35/197,778	38/450,190	116/973,710	91/452,792	48/201,404
RR (95% CI) MSM*	**1.94 (1.11, 3.38)**	Ref	**1.57 (1.01, 2.44)**	**2.94 (1.81, 4.77)**	**3.20 (1.78, 5.74)**
Seronegative RA					
No. of cases/ person-yrs	13/197,425	13/449,678	77/972,561	40/452,145	21/201,117
RR (95% CI) MSM*	2.17 (0.75, 6.27)	Ref	**2.83 (1.34, 5.97)**	**3.50 (1.56, 7.86)**	**4.35(1.73, 10.94)**

*Adjusted for previous questionnaire cycle weight change, baseline weight, age (years, continuous), smoking (never smoker, 12 months breastfeeding), menopausal status and hormone use (pre-menopausal, post-menopausal with never use, current use and past use), census tract median family income (quartiles), physical activity (0–2.9, 3–8.9, 9–17.9, ≥18 METs/week), alcohol intake (0-<5, 5-<15, ≥15 grams/day).

Table 2. Associations between weight change since age 18 and rheumatoid arthritis in the Nurses' Health Study II (1989-2017)

	categories of Time-updated weight change since age 18				
	Loss (<-2 kg)	Stable (-2 - <2 kg)	Gain (2 - <10 kg)	Gain (10 - <20 kg)	Gain (20+ kg)
All RA					
No. of cases/ person-yrs	32/174,225	27/210,913	111/801,307	168/676,627	201/698,871
RR (95% CI) Unadjusted	1.43 (0.85, 2.38)	Ref	1.08 (0.71, 1.65)	**1.94 (1.29, 2.91)**	**2.23 (1.49, 3.33)**
RR (95% CI) MSM*	1.23 (0.72, 2,12)	Ref	1.17 (0.75, 1.82)	**2.12 (1.38, 3.27)**	**2.40 (1.55, 3.71)**
Seropositive RA					
No. of cases/ person-yrs	26/174,065	19/210,693	68/800,407	104/675,826	140/698,123
RR (95% CI) MSM*	1.34 (0.72, 2.49)	Ref	0.98 (0.58, 1.66)	**1.88 (1.12, 3.15)**	**2.31 (1.38, 3.66)**
Seronegative RA					
No. of cases/ person-yrs	6/173,867	8/210,494	43/799,612	64/674,884	61/696,922
RR (95% CI) MSM*	0.96 (0.32, 2.89)	Ref	1.66 (0.72, 3.79)	**2.76 (1.24, 6.13)**	**2.65 (1.17, 5.97)**

*Adjusted for previous questionnaire cycle weight change, baseline weight, age (years, continuous), smoking (never smoker, 12 months breastfeeding), menopausal status and hormone use (pre-menopausal, post-menopausal with never use, current use and past use), census tract median family income (quartiles), physical activity (0–2.9, 3–8.9, 9–17.9, ≥18 METs/week), alcohol intake (0-<5, 5-<15, ≥15 grams/day).

study baseline) and weight changes from age 18. After calculating weight changes every two years, these continuous variables were then divided into 5 categories: 1) weight loss of < -2 kilograms (kg); 2) weight sTable -2 to < 2 kg

(reference); 3) weight gain of 5 to < 10; 4) weight gain of 10 to < 20; and 5) weight gain of 20+ kg. We used MSMs with inverse-probability-of-censoring and exposure weights that allowed us to create stabilized weights incorporating previous questionnaire cycle weight change, as well as baseline and time-varying covariates. These included baseline weight, age, smoking, parity and breastfeeding status, menopausal status and hormone use, census tract median family income, physical activity, and alcohol intake. Such an approach created a pseudo-population in which the final analyses were performed by pooled logistic regression to approximately calculate risk ratios (RR) and 95% confidence intervals (CI) for the effect of long-term weight gain on the risk of RA in women. Analyses were stratified by serostatus, as risk factors and disease prognosis and severity may differ between these two types of RA.

Results: Over 2,583,266 person-years, we identified 541 women who developed RA. Women who gained 2 kg or more over the study period were at a significantly increased risk of RA. Compared to sTable weight, weight gain from baseline of 2 to < 10, 10 to < 20 and 20+ kg was associated with an increased risk of all RA (RR = 1.87, 95% CI 1.29-2.73; 3.08 95% CI 2.03-4.65; 3.48, 95% CI 2.13-5.68, respectively) (**Table 1**). Weight loss (< -2 kg) was also associated with increased RA risk (RR=2.00, 95% CI 1.22- 3.27) (**Table 1**). Furthermore, weight gain was significantly associated with an increased risk of both seropositive and seronegative RA. Consistently, weight gain of 10 to < 20 and 20 kg or more from age 18 years was associated with an increased risk of RA (RR = 2.12, 95% CI 1.38-3.27; 2.40, 95% CI 1.55-3.71, respectively) (**Table 2**).

Conclusion: Long-term weight gain was associated with an increased risk of RA in women. Maintenance of healthy weight may be a potential strategy for the delay or prevention of developing RA.

Disclosure: N. Marchand, Pritikin Longevity Center, 9; **J. Sparks**, Optum, 1, Janssen, 1, Inova, 1, Gilead, 1, Amgen, 1, Bristol-Myers Squibb, 1, 2; **K. Yoshida**, OM1, 1, Corrona, 1; **S. Malspeis**, None; **X. Zhang**, None; **K. Costenbader**, Glaxo Smith Kline, 5, UpToDate, 7, Lupus Foundation of America, 6, Neutrolis Inc, 5; **E. Karlson**, None; **B. Lu**, None.

Abstract Number: 1004

The Incidence, Mortality, and Economic Burden of Potentially PrevenTable Infections in Rheumatoid Arthritis Patients

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SESSION INFORMATION
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Background/Purpose: *Streptococcus pneumoniae*, Herpes zoster, and influenza infections are common and potentially prevenTable causes of morbidity and mortality. Vaccinations have been shown to reduce infection rates. Unfortunately, some patients are not offered or refuse these vaccinations. Additionally, younger patients are not eligible for pneumococcal and zoster vaccines based on the current age recommendations. In this, study we aimed to determine incidence, mortality, and national costs of hospital admissions for *Streptococcus pneumoniae (Strep pneumo)*, Herpes Zoster, and influenza infections in patients with rheumatoid arthritis (RA).

Methods: Data were abstracted from the National Inpatient Sample (NIS) Database. This database is the largest collection of inpatient admission data in the USA. It is a nationally representative sample of 20% of hospitalizations from

Table 1

	Influenza	*Strep pneumo*	Zoster
# of Hospitalizations	1,120	785	640
Mean age (yrs)	68	66	70
Female (%)	76%	71%	84%
Mean LOS	4.85 days	7 days	5.6 days
Aggregate LOS	10,725 days	5,020 days	3,610 days
Mortality	2.7% (30/1,120)	8.3% (65/785)	2.3% (15/640)
Mean Hospital Charges	$46,087	$67,001	$42,909
Aggregate Hospital Charges	$50,696,057	$52,595,942	$26,818,325

approximately 1000 hospitals. The numbers in the databases are weighted to optimize national estimates. The NIS was searched for hospitalizations in 2016 containing ICD-10 RA codes M05 and M06 as the principal or secondary diagnosis. We further limited the RA cohort to hospitalizations with a principal discharge diagnosis of *Strep pneumo* infection (ICD 10 codes J13, M00.1x, A40.3, B95.3, or G00.1), Herpes Zoster (ICD-10 codes B02), and influenza (ICD 10 codes J09 or J10). The total number of discharges, age, race, length of stay (LOS), mortality and total hospital charges were recorded.

Results: Adult RA patients had 564,835 hospitalizations in 2016. Among the RA patients, there were 1,120 hospitalizations for influenza, 640 hospitalizations for zoster, and 785 hospitalizations for *Strep pneumo* (Table 1).

Of the RA patients hospitalized for influenza, mean age was 68 years, 76% were female, the mean LOS was 4.85 days, aggregate LOS 10,725 days, 2.7% (30/1,120) had in hospital mortality, the mean hospital charges were $46,087 and aggregate hospital charges were $50,696,057.

Of the RA patients hospitalized for zoster, mean age was 70 years, 84% were female, the mean LOS was 5.6 days, aggregate LOS 3,610 days, 2.3% (15/640) had in hospital mortality, the mean hospital charges were $42.909. and aggregate hospital charges were $26,818,325.

Of the RA patients hospitalized for *Strep pneumo* infections, the mean age was 66 years, 71% were female, the mean LOS was 7 days, aggregate LOS 5,020 days, 8.3% (65/785) had in hospital mortality, the mean hospital charges were $67,001, and the aggregate hospital charges were $52,595,942. These numbers do not account for outpatient or emergency department visits. Additionally, hospital charges are known to be higher than allowed or real charges.

Conclusion: Our analysis shows influenza, zoster, and *Strep pneumo* infections constituted only 0.5% of RA hospitalizations but in-hospital mortality was high. Additionally, the economic burden of these infections was large with aggregate national hospital charges totaling over $130 million and an aggregate LOS of 19,355 days. Universal vaccinations programs in RA patients should be studied to reduce hospitalizations, cost, morbidity, and mortality.

Disclosure: S. Kambhatla, None; **E. Gauto-Mariotti**, None; **A. Manadan**, None.

Abstract Number: 1005

Risk of Non-vertebral Fractures Among Rheumatoid Arthritis Patients Treated with Biologic or Targeted-Synthetic DMARDs: A Multi-Database Comparative Safety Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) increases risk of osteoporosis and fractures. However, limited head-to-head comparative data exists on the risk of non-vertebral osteoporotic fractures (NVFs) among biologic (b) or targeted-synthetic (ts) disease-modifying antirheumatic drugs (b/tsDMARDs). The primary objective of this study was to compare the incidence rate of NVFs in RA patients initiating one of the 9 b/tsDMARDs: abatacept (ABA), adalimumab (ADA), certolizumab (CER), etanercept (ETA), golimumab (GOL), infliximab (INF), rituximab (RIT), tocilizumab (TCZ) or tofacitinib (TOF).

Methods: We analyzed 3 U.S. healthcare claims databases [Optum (2008-03/19), Medicare and MarketScan (2008-17)]. RA patients aged≥18 years who newly started b/tsDMARDs without any use in the prior year were identified. Patients with previous fracture or malignancy were excluded. ADA was the most frequently used drug and selected as a common reference. The primary outcome was a composite endpoint of incident NVFs that included hip, humerus, pelvis and wrist fracture requiring intervention (except pelvis). Secondary outcomes were specific subtypes of fractures. We adjusted for >70 potential confounders including demographics, comorbidities, osteoporotic diagnosis and medication use, prior DMARD use, other medications, and healthcare utilization in each database through propensity score (PS)-based inverse probability treatment weighting. For the as-treated analysis, follow-up time started the day after cohort entry until the first occurrence of: outcome, treatment discontinuation, switching to other b/tsDMARD, nursing home admission, death, disenrollment, or the end of study period. For each drug-comparison, weighted Cox proportional hazards models estimated the hazard ratios (HRs) with 95% CIs, and provided pooled estimates after data source level stratification. Secondary analyses were conducted in patients switching from a tumor necrosis factor inhibitor to a b/tsDMARD.

Results: A total of 134,693 b/tsDMARD initiators were identified across 3 databases, of which 26% were ADA initiators. Mean age was 72 years in Medicare, 54 in Optum and 52 in MarketScan. During the 365-day baseline period, 39-65% patients used methotrexate, 64-71% used corticosteroids, and 13-30% had osteoporosis. After PS-weighting, majority of the covariates were well balanced. The average follow-up time (days) ranged from 384 (Optum) to 490 (Medicare). A total of 1,234 NVF events occurred (incidence rate/1,000 person-years: 7.8). The adjusted HRs showed similar risk of composite NVFs in all b/tsDMARD exposures compared to ADA: ABA (HR 1.04, 95% CI 0.82-1.30), CER (1.08, 0.79-1.49), ETA (1.11, 0.88-1.39), GOL (0.90, 0.59-1.39), INF (1.04, 0.84-1.28), RIT (1.07, 0.74-1.55), TCZ

Table. Risk of non-vertebral fractures associated with initiating b/tsDMARDs vs. adalimumab: a propensity score–based inverse probability treatment weighting (IPTW) as-treated analysis

	Exposures								Common reference
	Abatacept (n= 13,753)	Certolizumab (n= 7,864)	Etanercept (n= 34,661)	Golimumab (n= 6,836)	Infliximab (n= 21,408)	Rituximab (n= 7,195)	Tocilizumab (n= 3,499)	Tofacitinib (n= 4,172)	Adalimumab (n= 35,305)
Outcome	Weighted Hazard Ratio (95%CI)								
Primary									
Composite non-vertebral fracture	1.04 (0.82-1.30)	1.08 (0.79-1.49)	1.11 (0.88-1.39)	0.90 (0.59-1.39)	1.04 (0.84-1.28)	1.07 (0.74-1.55)	1.22 (0.69-2.13)	1.07 (0.70-1.65)	ref
Secondary									
Hip fracture	0.96 (0.65-1.41)	1.00 (0.61-1.65)	1.27 (0.85-1.89)	1.47 (0.78-2.78)	1.20 (0.84-1.70)	1.31 (0.71-2.39)	1.05 (0.35-3.10)	1.02 (0.48-2.17)	ref
Humerus fracture	1.60 (0.95-2.70)	1.59 (0.81-3.11)	1.54 (0.94-2.52)	0.73 (0.31-1.71)	1.27 (0.79-2.03)	1.04 (0.49-2.21)	2.03 (0.78-5.31)	1.09 (0.51-2.31)	ref
Pelvis fracture	0.85 (0.39-1.86)	0.59 (0.12-2.76)	0.78 (0.30-2.04)	0.08 (0.01-0.67)	0.71 (0.33-1.52)	0.47 (0.15-1.47)	0.21 (0.03-1.64)	1.58 (0.38-6.52)	ref
Wrist fracture	0.93 (0.65-1.33)	1.05 (0.62-1.78)	0.84 (0.61-1.16)	0.55 (0.33-0.92)	0.89 (0.64-1.24)	1.01 (0.56-1.82)	1.84 (0.77-4.38)	0.95 (0.47-1.93)	ref

Notes: 1. For the primary as-treated analysis, follow-up time started the day after cohort entry and ended on the first occurrence of: outcome, treatment discontinuation, switching to other b/tsDMARD, nursing home admission, death, disenrollment, or the end of study period.
2. Hazard ratios (HR) from the 3 PS-weighted cohorts were combined using weighted Cox models stratified by the data source.

(1.22, 0.69-2.13) and TOF (1.07, 0.70-1.65). Consistent findings were observed in the secondary analyses (not shown) and subtypes of NVFs (Table).

Conclusion: This large multi-database cohort study of RA patients found no differences in the risk of composite endpoint of NVFs or specific NVFs after starting ABA, CER, ETA, GOL, INF, RIT, TCZ or TOF versus starting ADA as their first or second b/tsDMARD therapy.

Disclosure: A. Pawar, None; **R. Desai**, Bayer, 2, Vertex, 2, Novartis, 2; **M. He**, None; **L. Bessette**, None; **S. Kim**, Pfizer, 1, Roche, 1, AbbVie, 1, Bristol-Myers Squibb, 1.

Abstract Number: 1006

Post-menopausal Rheumatoid Arthritis Is Inversely Associated with Lifetime High Level of Estrogen Exposure in the French E3N Cohort

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The involvement of female hormones in the pathogenesis of Rheumatoid Arthritis (RA) is supported by numerous observations: a female predominance, an increased incidence in the post-partum, and around the age of menopause. In the literature, findings on the association between reproductive and hormonal factors, taken individually, and RA are conflicting. Our objectives were to assess the relationships between lifetime durations/level of female hormonal exposures and the risk of RA.

Methods: E3N is an ongoing French prospective cohort of 98,995 women since 1990 aged 40-65 years at enrolment. Validation of RA cases among the cohort has been previously published [Nguyen *et al.* BMJ Open 2019]. Lifetime female hormonal exposures were defined as follows:
-Reproductive span (in years) = duration from menarche to menopause
-Total ovulatory years (in years, time-dependent) = Reproductive span – (number of full-term pregnancies x 0.75 + number of miscarriages x 0.25 + total duration of breast feeding + total duration of oral contraception)
-Lifetime hormonal exposure (in years, time-dependent) = Reproductive span + total duration of menopausal hormonal therapy
-Composite Estrogen Score (CES, range = 0–5, time-dependent), calculated by point assignment for early menarche (≤10 years), high parity (>3 pregnancies), history of hysterectomy, use of hormone therapy (oral contraception and/or menopausal hormonal therapy, ever) and late menopause (≥53 years).

Hazard ratios (HRs) and 95% confidence intervals (CIs) for the risk of incident RA were estimated using Cox proportional hazards regression models with age as the time scale.

Table: Hazard ratios (95% confidence intervals) for rheumatoid arthritis (RA) among 78,391 postmenopausal women by composite oestrogen score (CES) for 2 adjusted models (with stratification for year of birth)

		RA	Non-cases	HRs (95%CI), *p-value*	
				Age adjusted Model	Multi-adjusted Model
CES (0-5)					
	0	36	4173	1.03 (0.8–1.4)	1.04 (0.8–1.4)
	1	345	42,132	1	1
	2	225	26,719	1.02 (0.8–1.2)	1.01 (0.8–1.2)
	3	29	4428	0.70 (0.4–1.0), *p*=0.0705	**0.64 (0.4–0.9), *p*=0.0475**
	4	2	300	1.0 (0.2–3.9)	0.91 (0.2–3.7)
	5	0	2	-	-
Estrogen exposure levels					
	Low [CES =0–1]	381	46,305	1	1
	Moderate [CES=2]	225	26,719	1.01 (0.8–1.2), *p= 0.8631*	1.0 (0.8–1.2), *p=0.9921*
	High [CES=3–5]	21	4730	0.70 (0.4–1.0), *p=0.0738*	**0.65 (0.4–0.9), *p=0.0477***

HRs (95% CI): Hazard ratios (95% Confidence Intervals).
Multi-adjusted Model: adjustment for age, smoking (past/current/never), passive smoking during childhood (ever/never), educational level (<high-school, up to 2 years of University, ≥3 years of university), Body Mass Index (<18.5; 18.5–25; 25–30; >30kg/m²), duration of premenopausal progestogen (0;]0–24]; >24 months), age at the first pregnancy (<22, [22–27[, ≥27 years) and type of menopause (natural/artificial).

Models were adjusted for age (age-adjusted model) and additionally for smoking, passive smoking during childhood, educational level, body mass index , duration of premenopausal progestogen, age at the first pregnancy and type of menopause (multi-adjusted model).

Results: A total of 637 incident RA cases occurred among 78,391 post-menopausal women with a total of 1,864,915 women-years from baseline.

Reproductive span, total ovulatory years and lifetime hormonal exposure were not significantly associated with incident RA in postmenopausal women in age adjusted models (*p for trend*=0.2479, *p for trend*=0.4343, *p for trend*=0.9216 , respectively).

In multivariable-adjusted Cox regression models, high level of estrogen exposure (CES=3-5) was inversely associated with the risk of RA in post-menopausal women: HR=0.65 (95%CI 0.4–0.9), *p*=0.04, taking low level (CES=0-1) as reference (Table).

Interestingly, in a recent publication, high level of CES was associated with a reduced risk of primary Sjögren, but not cumulative menstrual cycling (reproductive span minus time to pregnant) [McCoy *et al.* Arthritis Care Res 2019]. RA and primary Sjögren share a marked female predominance with a peak onset around menopause and the participation of B lymphocytes in this physiopathology.

Conclusion: In E3N cohort, a high CES which reflects lifetime exposure to estrogen was associated with a decreased risk of RA in postmenopausal women.

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Abstract Number: 1007

Atopic Dermatitis and Risk of Incident Rheumatoid Arthritis: A Systematic Review and Meta-analysis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

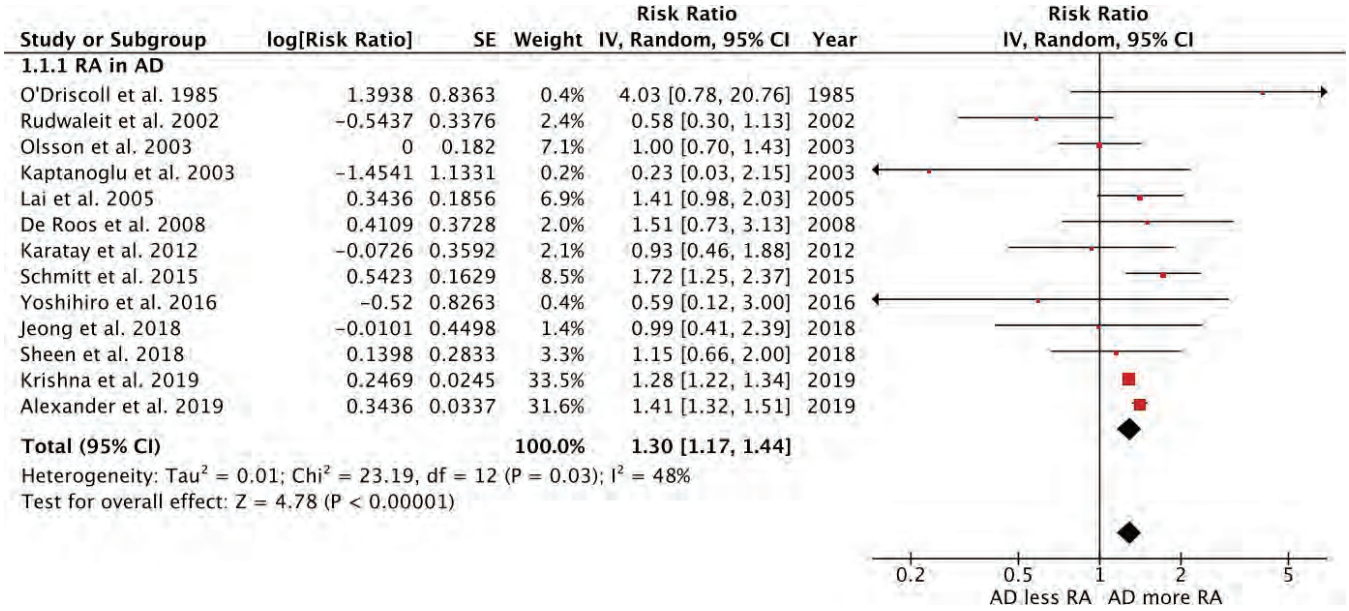
Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Recent observational studies have suggested that patients with atopic dermatitis (AD) may have a higher risk of several non IgE-mediated inflammatory disorders, such as inflammatory bowel disease, systemic lupus erythematosus and Sjogren syndrome. The association between AD and rheumatoid arthritis (RA) is also described although results from previously published studies are conflicting. The current study aimed to combine all available data to investigate whether patients with AD had a higher risk of developing RA using systematic review and meta-analysis technique.

Methods: Systematic review was conducted using Medline and EMBASE database up to November 2019 using search strategy that comprised of terms for "atopic dermatitis" and "rheumatoid arthritis". Eligible cohort study must consist of one cohort of patients with AD and another cohort of comparators without AD. Then, the study must follow participants in both groups for incident RA and must report relative risk (RR), incidence rate ratio (IRR), hazard risk ratio (HR) or standardized incidence ratio (SIR) with 95% confidence intervals (CIs), comparing the incidence of RA between the groups. Eligible case-control study must recruit cases with RA and controls without RA. Then, the study must explore the prior history of AD of both groups and report odds ratio (OR) with 95% CIs comparing the prevalence of prior history of AD between the groups. Point estimates with standard errors were retrieved from each study and were combined together using the generic inverse variance method.



Results: The electronic search identified 21,824 records from the two databases. After two rounds of review, a total of 13 studies (four cohort studies and nine case-control studies) met the eligibility criteria and were included into the meta-analysis. The meta-analysis found that patients with AD had a significantly higher risk of incident RA than individuals without AD with the pooled RR of 1.30 (95% CI 1.17 to 1.44; I^2 48%).

Conclusion: The current systematic review and meta-analysis found a significantly higher risk of incident RA among patients with AD.

Forest plot of the meta-analysis of risk of incident rheumatoid arthritis in atopic dermatitis patients

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Abstract Number: 1008

Assessing Improved Risk Prediction of Seropositive Rheumatoid Arthritis by Environmental, Genetic, and Preclinical Plasma Metabolite Factors

Karen Costenbader[1], Jeffrey Sparks[2], Elizabeth Karlson[3], Kazuki Yoshida[4], Jing Cui[5], Susan Malspeis[6] and **Lilia Bouzit**[7], [1]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [2]Division of Rheumatology, Inflammation, and Immunity; Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [3]Brigham and Women's Hospital, Boston, MA, [4]Brigham & Women's Hospital and Harvard Medical School, Boston, MA, [5]Brigham Women's Hospital, Boston, MA, [6]Brigham and Women's Hospital, Boston, [7]Harvard Chan School of Public Health, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent research has advanced the understanding of associations between environmental, genetic, and metabolic factors and rheumatoid arthritis (RA), introducing potential to improve risk prediction. A novel weighted genetic risk scored (wGRS) was generated from 90 non-*HLA* RA-associated risk alleles and five RA-associated amino acid positions of *HLA-DRB1* haplotypes. Additionally, several preclinical plasma metabolites were recently associated with seropositive RA. This study investigated whether the addition of variables representing the wGRS and preclinical metabolite levels increased the performance of seropositive RA risk prediction models compared to previously validated models in the Nurses' Health Studies (NHS).

Methods: This nested case-control study involved individuals with drawn plasma samples from the NHS prior to RA diagnosis or matched date for controls. Incident seropositive RA cases, based on the ACR 1987 criteria and ACR/EULAR 2010 criteria, were matched to two controls on age, blood collection features, and menstrual patterns at time of blood draw. Environmental variables, including age, smoking, alcohol use, socioeconomic status, region, reproductive factors, and BMI, were measured at the questionnaire cycle preceding the blood draw, corresponding to pre-diagnosis exposures. Four models were generated using logistic regression: a) base model with environmental factors (E), b) environmental and genetic and gene-environment interaction factors (E +G+GEI), c) environmental and pre-diagnosis metabolite factors (E+M), and d) all factors (E+G+GEI+M). Matching factors were included in the models to adjust for selection bias due to the matched case-control design. Model fit was assessed using Nagelkerke's R^2 and the Hosmer-Lemeshow test. The area under the receiver operating characteristic curve (AUC) was measured

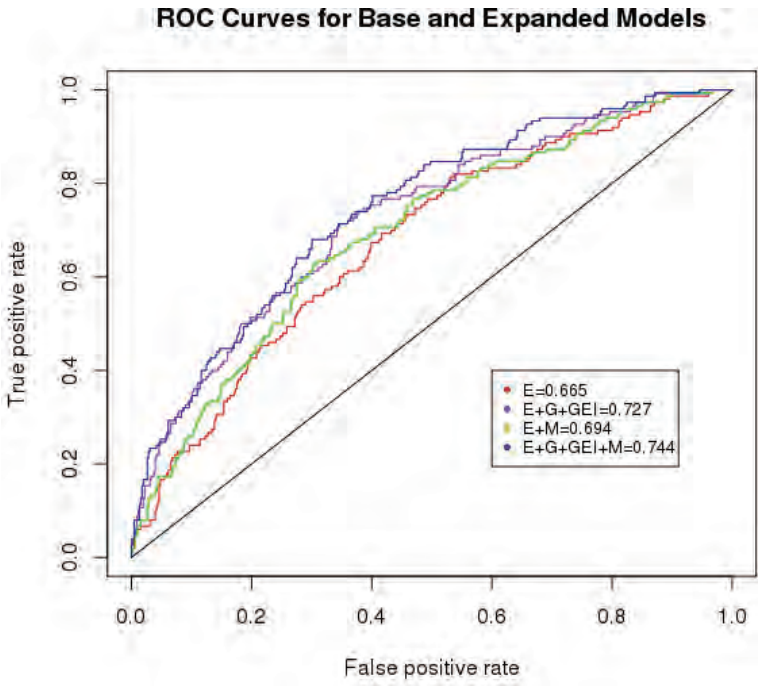
Table 1. Characteristics of Seropositive RA NHS* Sample Participants		
	Cases	Controls
N	150	456
Years prior to RA diagnosis or matched date (mean (SD))	10.09 (5.90)	10.04 (5.51)
Age at blood draw (mean (SD))◊	51.23 (7.79)	51.84 (7.81)
Post-menopausal hormone use (%)◊	61 (40.7)	190 (41.7)
Smoking in pack-years (mean (SD))	12.83 (15.97)	9.44 (16.07)
BMI (mean (SD))	26.01 (5.19)	25.04 (4.53)
Parity/breastfeeding (%)		
Nulliparous/Parous <1 month	62 (41.4)	191 (41.9)
Parous/1-11 months	62 (41.4)	146 (32)
Parous/12+ months	26 (17.3)	119 (26.1)
Cumulative alcohol use (mean (SD))	4.50 (6.12)	5.66 (8.90)
Region (%)		
West	67 (44.7)	184 (40.4)
Midwest	14 (9.3)	62 (13.6)
Mid-Atlantic	18 (12.0)	62 (13.6)
New England	28 (18.7)	81 (17.8)
Southeast	23 (15.3)	61 (13.4)
Irregular menses (%)	22 (14.7)	48 (10.5)
Menstruation before age 12 years (%)	26 (17.3)	105 (23.0)
Husband's education up to high school/vocational (%)	39 (26.0)	98 (21.5)
Median income quantile (%)		
1 – low income	31 (20.7)	80 (17.5)
2	26 (17.3)	94 (20.6)
3	38 (25.3)	86 (18.9)
4	29 (19.3)	98 (21.5)
5 – high income	26 (17.3)	98 (21.5)

*NHS=Nurses' Health Studies ◊Matching factors

to compare performance of expanded vs. base model. Models were internally validated using a bootstrapped estimate of optimism of the AUC. This measure of overfitting is based on the average difference between the predictive ability of the model built using the original sample, and the predictive ability of the models built using each bootstrap sample.

Results: 150 seropositive RA cases and 456 controls were included in the study. The E model yielded an AUC of 0.665 (95% CI 0.616, 0.714). The E model yielded an AUC of 0.665 (95% CI: 0.616, 0.714). The expanded model including genetic factors presented a strong improvement in discrimination; producing AUCs of 0.727 (95% CI: 0.676-0.770) in E+G+GEI model. The E+M model including preclinical metabolite factors produced a modest improvement in discrimination (AUC 0.694, 95% CI: 0.640, 0.736). The full E+G+GEI+M model yielded the highest AUC of 0.744 (95% CI: 0.697, 0.788). Optimism corrected models yielded an AUC of 0.596 for the E model, 0.666 for E+G+GEI, 0.606 for E+M, and 0.672 for E+G+GEI+M.

Conclusion: The addition of the wGRS and HLA haplotype-smoking interaction improve discrimination of the RA risk prediction model compared to models without genetic factors. However, recently reported preclinical metabolite levels do not appear to significantly contribute to prediction.



E: environmental- age, smoking pack-years, cumulative alcohol use, husband's education, income quintile, parity/ breastfeeding, early menses, menstrual irregularity, menopausal status, region, BMI.
E+G+GEI: environmental and genetic- all environmental variables, 90 SNP wGRS, HLA Haplotype GRS, HLA Haplotype GRS*Smoking.
E+M: environmental and metabolite1- all environmental variables, C5 carnitine, 4-acetamidobutanoate, C5:1 carnitine, 3-dehydroxycarnitine, C7 carnitine, N-acetylputrescine, 3-oxooctadecanoate, C3 carnitine, C16:1 CE, C35:0 PE.
E+G+GEI+M: environmental, genetic, metabolite- all variables.

1. Chu, S. H. et al. Circulating plasma metabolites and risk of rheumatoid arthritis in the Nurses' Health Study. Rheumatology (Oxford) (2020) https://doi.org/10.1093/rheumatology/keaa125.

Table 2. Results of Base and Expanded Models

Statistical Parameters	E	E+G+GEI	E+M	E+G+GEI+M
Nagelkerke's R^2 (%)	10.72	18.37	13.11	20.98
Hosmer-Lemeshow χ^2 (p)	7.46 (p=0.49)	7.77 (p=0.46)	3.35 (p=0.91)	3.34 (p=0.91)
AUC (95% CI)	0.665 (0.616, 0.714)	0.727 (0.676-0.770)	0.694 (0.640, 0.736)	0.744 (0.697, 0.788)
Optimism*	0.069	0.061	0.088	0.072
Optimism-adjusted AUC	0.596	0.666	0.606	0.672

AUC = area under the ROC *Optimism calculated using the Harrell method with 200 bootstrap replications using the 632+ rule.

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Abstract Number: 1009

Missing Data and Multiple Imputation in Rheumatoid Arthritis Registries Using Sequential Random Forest Method

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SESSION INFORMATION

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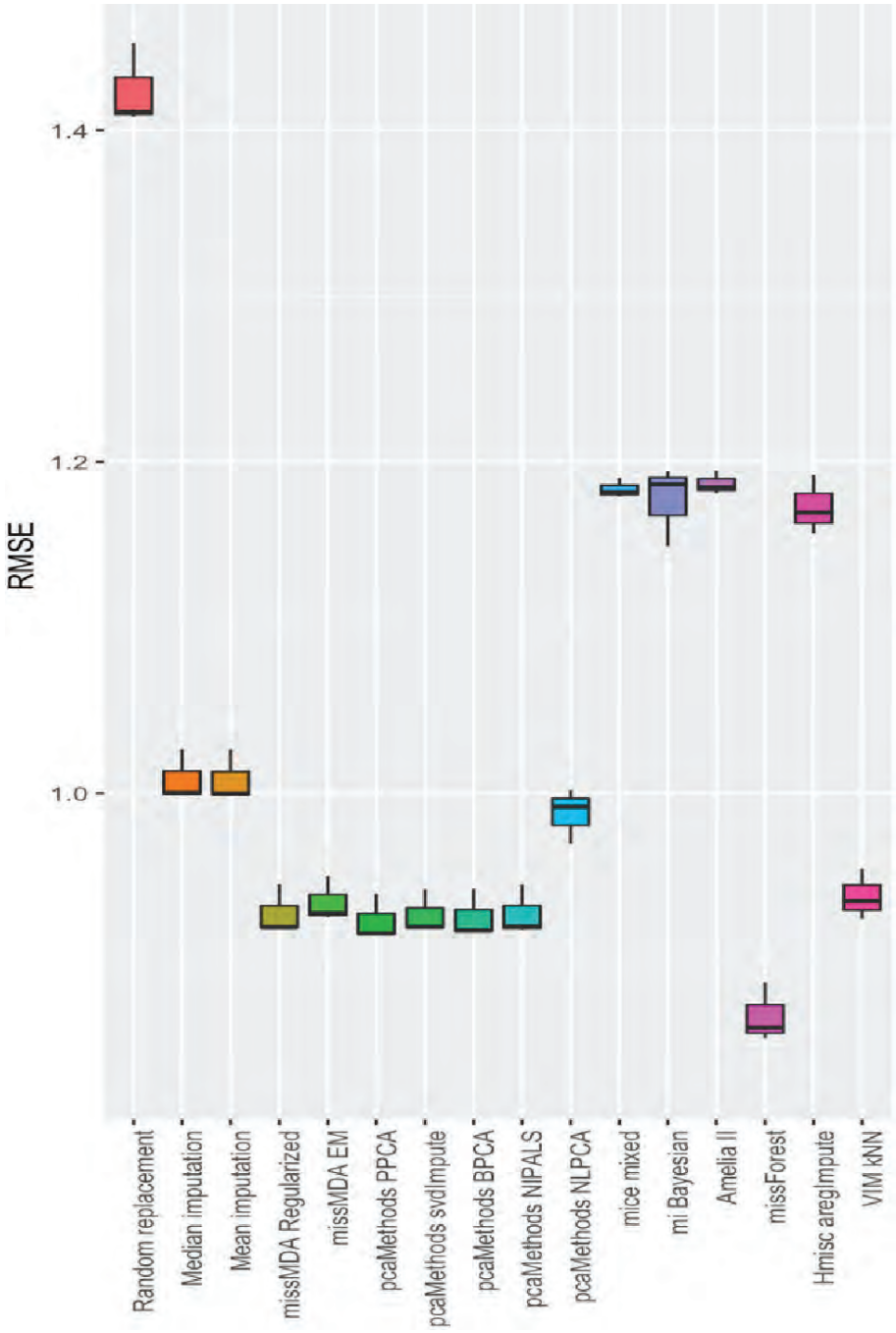
Background/Purpose: Missing data in clinical epidemiological researches violate the intention to treat principle, reduce statistical power and can induce bias if they are related to patient's response to treatment. In multiple imputation (MI), covariates are included in the imputation equation to predict the values of missing data. The purpose of this study is to find the best approach to estimate and impute the missing values in Kuwait Registry for Rheumatic Diseases (KRRD) patients data.

Methods: A number of methods were implemented for dealing with missing data. These included *Multivariate imputation by chained equations* (MICE), *K-Nearest Neighbors* (KNN), *Bayesian Principal Component Analysis* (BPCA), *EM with Bootstrapping* (Amelia II), *Sequential Random Forest* (MissForest) and mean imputation. Choosing the best imputation method was judged by the minimum scores of *Root Mean Square Error* (RMSE), *Mean Absolute Error* (MAE) and *Kolmogorov–Smirnov D test statistic* (KS) between the imputed datapoints and the original datapoints that were subsequently sat to missing.

Results: A total of 1,685 rheumatoid arthritis (RA) patients and 10,613 hospital visits were included in the registry. Among them, we found a number of variables that had missing values exceeding 5% of the total values. These included duration of RA (13.0%), smoking history (26.3%), rheumatoid factor (7.93%), anti-citrullinated peptide antibodies (20.5%), anti-nuclear antibodies (20.4%), sicca symptoms (19.2%), family history of a rheumatic disease (28.5%), steroid therapy (5.94%), ESR (5.16%), CRP (22.9%) and SDAI (38.0%), The results showed that among the methods used, MissForest gave the highest level of accuracy to estimate the missing values. It had the least imputation errors for both continuous and categorical variables at each frequency of missingness and it had the smallest prediction differences when the models used imputed laboratory values. In both data sets, MICE had the second least imputation errors and prediction differences, followed by KNN and mean imputation.

Conclusion: MissForest is a highly accurate method of imputation for missing data in KRRD and outperforms other common imputation techniques in terms of imputation error and maintenance of predictive ability with imputed values in clinical predictive models. This approach can be used in registries to improve the accuracy of data, including the ones for rheumatoid arthritis patients.



Root mean square error (RMSE) of various missing data imputation methods, showing that MissForest method has the lowest error to predict the missing information in KRRD data

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Abstract Number: 1010

Infection and Malignancy Outcomes in Patients with RA Treated with Abatacept: Results from a Multinational Surveillance Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Compared with the general population, patients with RA are at an increased risk of infection and certain malignancies, which may be increased further with the use of DMARDs.[1,2] The abatacept global post-marketing epidemiology program included observational studies based on disease registries and healthcare claims databases. Reports from the core post-marketing epidemiology program on pre-specified outcomes associated with abatacept compared with other DMARD treatments in routine clinical practice showed no increase in the risk of infections requiring hospitalization or overall malignancies.[3,4] The aim of this supplemental post-marketing abatacept only study was to evaluate the incidence of infections and pre-specified malignancies in patients from several countries with RA who were treated with abatacept.

Methods: Data were analyzed from seven RA registries: Anti-TNF Therapy in Rheumatoid Arthritis (ATTRA, Czech Republic), Danish Database for Biologic Therapies (DANBIO), National Registry of Biological Treatment in Finland (ROB-FIN), Swiss Clinical Quality Management (SCQM), Orencia and Rheumatoid Arthritis (ORA, France), The Italian Group for the Study of Early Arthritis (GISEA) and Spanish Registry of Adverse Events of Biological Therapies in Rheumatic Diseases (BIOBADASER). The first day of abatacept treatment was considered the index date and exposure was measured in patient-years (p-y). Incidence rates (IRs) with 95% CIs were calculated for each pre-specified outcome.

Results: Patients treated with abatacept (>5000) were mostly female (78–85%), with a mean age ranging from 52–58 years. Baseline characteristics were largely consistent across the registries, except for longer disease duration in the ORA registry (mean [SD]: 20.4 [9.5] years; range across other registries: 8.1–13.3 years). In abatacept-treated patients, IRs for hospitalized infections across the registries varied, ranging from 0.4 to 10 per 100 p-y (**Table 1**). The IR for overall malignancies in abatacept-treated patients was low and ranged from 0.3 to 1.9 per 100 p-y (**Table 2**).

Table 1. Incidence rates per 100 p-y (95% CI), number of events and p-y of exposure for infections

	ATTRA (n=335)	DANBIO (n=1213)	ROB-FIN (n=362)	ORA[a] (n=1024)	GISEA (n=433)	BIOBADASER (n=350)	SCQM[b] (n=959/974)	Reference range[c,1,2]
Hospitalized infections	0.6	10.0	8.4	4.2	4.3[d]	1.5	0.4	1.9–14.2
	(0.0, 1.2)	(8.7, 11.5)	(6.2, 11.0)	(NR)	(NR)	(0.8, 2.9)	(0.2, 0.8)	
# of events (p-y)	5 (NR)	196 (1955)	49 (NR)	107 (NR)	NA	NA	7 (1902)	
Opportunistic	0	0.1	NR	NR	NR	1.4	NR	
infections		(0.0, 0.3)				(0.7, 2.7)		
# of events (p-y)	0 (0)	2 (2233)	NR (NR)	NR (NR)	NR	NA	NR (NR)	
Tuberculosis	0.6	0.1	0	NR	NR	0	0.2	
	(0.0, 1.2)	(0.0, 0.3)	(0.0, 0.6)				(0.1, 0.5)	
# of events (p-y)	5 (NR)	2 (2230)	0 (0)	NR (NR)	NR (NR)	0 (0)	3 (1939)	

[a]No CIs were provided in the French report submitted by the French Society of Rheumatology to health authorities.

[b]The sample size for hospitalized infections was 959; for tuberculosis the sample size was 974. Incidence rates are by exposure group with mid-imputed dates of occurrence.

[c]TNF versus DMARD in 130 Turkish patients with RA in clinic setting;[1] large US database study TNF vs DMARD in patients with RA.[2]

[d]Calculated incidence rate from the French Society of Rheumatology (FSR) data from GISEA. For ORA, NR means not reported in the French report submitted to the French Health Authorities by the FSR.

ATTRA=Anti-TNF Therapy in Rheumatoid Arthritis; BIOBADASER=Spanish Registry of Adverse Events of Biological Therapies in Rheumatic Diseases; DANBIO=Danish Database for Biologic Therapies; GISEA=The Italian Group for the Study of Early Arthritis; NA=not available; NR=not reported; ORA=Orencia and Rheumatoid Arthritis Registry; p-y=patient-years; ROB-FIN=National Registry of Biological Treatment in Finland; SCQM=Swiss Clinical Quality Management.

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Conclusion: Despite the heterogeneity of the registries and possibility of under-reporting adverse events in observational studies, the safety profile of abatacept in this real-world observational study showed consistent findings in patients with RA treated with abatacept, with no new or increased risks of infection or malignancy identified.

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Medical writing: Fiona Boswell (Caudex).
Contributor: Myriam Riek (SCQM Foundation, Zürich, Switzerland).

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Table 2. Incidence rates per 100 p-y (95% CI), number of events and p-y of exposure for malignancies

	ATTRA (n=335)	DANBIO (n=1213)	ROB-FIN (n=362)	ORA (n=1024)	GISEA (n=433)	BIOBADASER (n=350)	SCQM[a] (n=1053)	Reference range[b,1,2]
# of events (p-y)	8 (NR)	70 (3642)	6 (NR)	65 (NR)	NA	NA	32 (3683)	
Overall	0.9 (0.3, 1.6)	1.9 (1.5, 2.4)	0.73 (0.27, 1.6)	1.33 (NR)	0.32[c] (NR)	1.36 (0.68, 2.72)	0.87 (0.61, 1.23)	0–5.4
Breast	0.2 (0.0, 0.9)	0.2 (0.1, 0.4)	0.24 (0.0, 0.88)	0.1 (NR)[d]	NR	0.17 (0.02, 1.21)	NR	
Lung	0.1 (0.0, 0.8)	0.2 (0.1, 0.4)	0.12 (0.0, 0.68)	NR	NR	0.17 (0.02, 1.21)	NR	
Lymphoma	0.1 (0.0, 0.8)	0.1 (0.0, 0.2)	0 (0.0, 0.45)	NR[d]	NR	0	NR	

[a]Incidence rate is by exposure group with mid-imputed dates of occurrence.

[b]TNF versus non-biologic DMARD in large Taiwanese database of patients with RA;[1] UK registry study DMARD in patients with RA with prior malignancy.[2]

[c]Calculated incidence rate using first- and second-line abatacept counts from November 2015.

[d]ORA computed incidence rate for breast and incidence rate of 0.18 for all malignant hemopathies including lymphoma also includes 1 acute leukemia, 1 chronic lymphoid leukemia, 4 myelomas, 1 refractory anemia with excess blasts, and 1 large granular lymphocyte.

ATTRA=Anti-TNF Therapy in Rheumatoid Arthritis; BIOBADASER=Spanish Registry of Adverse Events of Biological Therapies in Rheumatic Diseases; DANBIO=Danish Database for Biologic Therapies; GISEA=The Italian Group for the Study of Early Arthritis; NA=not available; NR=not reported; ORA=Orencia and Rheumatoid Arthritis; ROB-FIN=National Registry of Biological Treatment in Finland; SCQM=Swiss Clinical Quality Management.

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None; **K. Pavelka**, AbbVie, 8, Merck Sharp & Dohme, 8, Bristol-Myers Squibb Company, 8, Roche, 8, Amgen, 8, Pfizer, 8, Novartis, 8, Egis, 8, Biogen, 8, UCB, 8; **Z. Křístková**, None; **T. Simon**, Bristol Myers Squibb, 5, Lexicon, 5.

Abstract Number: 1011

Effectiveness, Safety and Quality of Life with Tofacitinib Treatment in Adult Patients with Rheumatoid Arthritis Under Routine Clinical Care: First Interim Results from a German Non-Interventional, Prospective, Multi-Center Study

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SESSION INFORMATION

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Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Tofacitinib is an orally applied Janus kinase inhibitor, which is approved for rheumatoid arthritis (RA) treatment in the USA since 2012, so that 'real world data' are already available there for many years. The prospective study ESCALATE-RA is the first non-interventional study with tofacitinib in Germany (ClinicalTrials.gov; NCT03387423). The first patient was enrolled in November 2017, the year of tofacitinib EMA-approval.

Methods: This 5-year study will enroll about 1500 patients at 200 centers in Germany. Adult patients eligible for tofacitinib therapy are documented in a standardized manner from the first tofacitinib intake for 24 months. According to standard clinical practice, patient documentation is expected quarterly and includes data on demographics, effectiveness, adverse events (AEs), and patient-reported outcomes. The present interim analysis (cut-off date January 31st, 2020) describes the patients in two subgroups (tofacitinib treatment without concomitant methotrexate treatment (mono-group); tofacitinib in combination with methotrexate (combi-group)), who reached the visit M12 after 12 months of treatment. In this non-interventional study, all analyses were based on observed data as reported by the site investigators with no imputation for missing data. Since this is an ongoing study, small changes in numbers may occur after the final data quality checks.

Results: In the M12-population (n=548), the mean age was 59 years, the majority of patients were female, had moderate to severe RA at baseline (BL), and were seropositive. 300 patients (54.7%) were treated with a bDMARD

Table 1. Demographics and Clinical Data at Baseline (M12-population)

	Monotherapy at M12 (N=332)[a]	Combination Therapy at M12 (N=216)[b]
Mean Age in years (SD)	60.04 (12.88)	57.93 (11.22)
	n/n_{tot} (%)	n/n_{tot} (%)
Gender		
Female	271/332 (81.6%)	148/216 (68.5%)
Smoking status		
Non-smoker	188/326 (57.7%)	119/205 (58.0%)
Prognostic factors		
Moderate to severe RA	314/332 (94.6%)	209/216 (96.8%)
ACPA positive	167/331 (50.5%)	118/216 (54.6%)
Rheumatoid factor positive	190/332 (57.2%)	141/216 (65.3%)
bDMARD premedication (prior tofacitinib treatment)	176/332 (53.0%)	124/216 (57.4%)
RA co-medication		
Glucocorticoids	212/332 (63.9%)	158/216 (73.1%)
Methotrexate	43/332 (13.0%)	182/216 (84.3%)

ACPA, Anti-citrullinated protein antibodies; bDMARD, biologic disease-modifying antirheumatic drug; M12, visit after 12 months of treatment; N, Number of patients with M12 visit; n_{tot}, Number of patients with available data; RA, rheumatoid arthritis; SD, standard deviation

[a] Includes 44 patients who switched from combination therapy to monotherapy.

[b] Includes 33 patients who switched from monotherapy to combination therapy.

Table 2. Treatment Escalation, Disease Activity, Functional Ability, Health-related Quality of Life and Safety (M12-population)

	Monotherapy at M12 (N=332)[a]	Combination Therapy at M12 (N=216)[b]
Mean Time to 1st Treatment Escalation	301 days	289 days
Treatment persistence after 1 year	0.72 (95% CI: 0.67; 0.76)	0.64 (95% CI: 0.57; 0.70)
Disease Activity		
DAS28-4 (ESR)		
BL Mean (SD), (n_{tot})	4.76 (1.34), (174)	4.61 (1.11), (119)
M12 Mean (SD), (n_{tot})	2.96 (1.13), (182)	3.04 (1.26), (115)
Mean change BL to M12 (SD), (n_{tot})	-1.71 (1.50), (150)	-1.63 (1.40), (97)
DAS28-4 (CRP)		
BL Mean (SD), (n_{tot})	4.37 (1.24), (181)	4.27 (1.03), (119)
M12 Mean (SD), (n_{tot})	2.54 (1.00), (185)	2.74 (1.10), (108)
Mean change BL to M12 (SD), (n_{tot})	-1.80 (1.45), (160)	-1.61 (1.40), (96)
Functional Ability		
Morning Stiffness [min]		
BL Mean (SD), (n_{tot})	75.21 (75.49), (189)	59.96 (54.06), (125)
M12 Mean (SD), (n_{tot})	42.50 (35.08), (119)	41.83 (41.85), (75)
Mean change BL to M12 (SD), (n_{tot})	-45.36 (152.06), (106)	-18.88 (50.32), (67)
Functional Ability Questionnaire Hannover (FFbH)		
BL Mean (SD), (n_{tot})	60.91 (23.04), (228)	65.12 (21.36), (155)
M12 Mean (SD), (n_{tot})	68.16 (23.71), (218)	75.50 (21.65), (128)
Mean change BL to M12 (SD), (n_{tot})	8.61 (16.27), (217)	5.24 (14.13), (127)
FFbH Remission Rate (FFbH >83%)		
n/n_{tot} (%)	72/218 (33.0%)	57/128 (44.5%)
Health-related Quality of Life		
EuroQoL EQ-5D-3L Total Score		
BL Mean (SD), (n_{tot})	0.55 (0.19), (226)	0.59 (0.19), (154)
M12 Mean (SD), (n_{tot})	0.68 (0.17), (215)	0.70 (0.18), (128)
Mean change BL to M12 (SD), (n_{tot})	0.14 (0.19), (214)	0.08 (0.21), (127)
FACIT Fatigue Scale		
BL Mean (SD), (n_{tot})	28.97 (11.40), (224)	31.37 (10.63), (152)
M12 Mean (SD), (n_{tot})	34.69 (11.59), (212)	37.38 (10.30), (123)
Mean change BL to M12 (SD), (n_{tot})	5.25 (10.48), (210)	4.49 (8.87), (123)
	n/n_{tot} (%)	n/n_{tot} (%)
Safety (Patients)		
with tofacitinib related AE	127/332 (38.3%)	92/216 (42.6%)
discontinued study due to AE	0/332 (0.0%)	1/216 (0.5%)
discontinued study drug due to AE but continued study	78/332 (23.5%)	70/216 (32.4%)
with dose reduced or temporary discontinuation due to AE	49/332 (14.8%)	25/216 (11.6%)

AE, adverse event; BL, baseline; CI, confidence interval; CRP, C-reactive protein; DAS28-4, disease activity score in 28 joints based on 4 variables; ESR, erythrocyte sedimentation rate; FACIT, Functional Assessment of Chronic Illness Therapy; FFbH, Functional Ability Questionnaire Hannover; M12, visit after 12 months of treatment; N, Number of patients with M12 visit; n_{tot}, Number of patients with available data; SD, standard deviation

[a] Includes 44 patients who switched from combination therapy to monotherapy.
[b] Includes 33 patients who switched from monotherapy to combination therapy.

immediately prior to enrollment. 332 patients were in the mono-group and 216 patients in the combi-group at M12 (Table 1).

Average time to first treatment escalation was 301 days for patients with monotherapy and 289 days for patients with combination therapy. The treatment persistence after 1 year was 72% (mono-group) and 64% (combi-group) respectively. A considerable reduction of disease activity and morning stiffness was observed in both groups over time while functional ability according to FFbH (Functional Ability Questionnaire Hannover) and self-reported quality of life increased in both groups. The mean change from BL of disease activity and morning stiffness as well as functional ability was greater in mono-group compared to combi-group. Furthermore, patients in mono-group showed a greater improvement in self-reported quality of life than patients in combi-group. However, functional remission was achieved by more patients in the combi-group (44.5%) than in the mono-group (33.0%). An AE (adverse event) related to tofacitinib occurred in 38.3% of mono-group and 42.6% of combi-group (Table 2).

Conclusion: This interim analysis shows a good effectiveness profile and an increased quality of life with tofacitinib therapy. There were no unexpected AEs observed.

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Abstract Number: 1012

The Global Prevalence of Rheumatoid Arthritis: A Meta-Analysis

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SESSION INFORMATION
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Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: To determine the global population prevalence of rheumatoid arthritis (RA) based on published studies and assess factors that influence RA prevalence estimates.

Methods: Four electronic databases were searched (ProQuest, MEDLINE, Web of Science, and EMBASE) for publications that reporting prevalence estimates of RA from 1980 and 2019. A random-effect meta-analysis model was used to produce the pooled prevalence estimates. The potential between-study heterogeneity was identified using sensitivity analysis, sub-group and meta-regression analyses.

Results: A total of 67 studies were included in the meta-analysis, containing 742,246 RA patients and 211,592,925 healthy controls. The global RA prevalence estimate was 0.46% (95% confidence interval (CI): 0.39-0.54; I^2=99.9%) with a 95% prediction interval (0.06–1.27). The RA point-prevalence was 0.45% (95% CI: 0.38- 0.53%) between 1986 and 2014, while the pooled period-prevalence was 0.46% (95% CI: 0.36% and 0.57%) from 1955 to 2015. The highest RA pooled prevalence (0.69%; 95% CI: 0.47–0.95) was derived from linked data sources studies. Based on meta-regression, the factors that explain the studies' heterogeneity of RA prevalence, including geographical location, the risk bias assessment of studies and sample size.

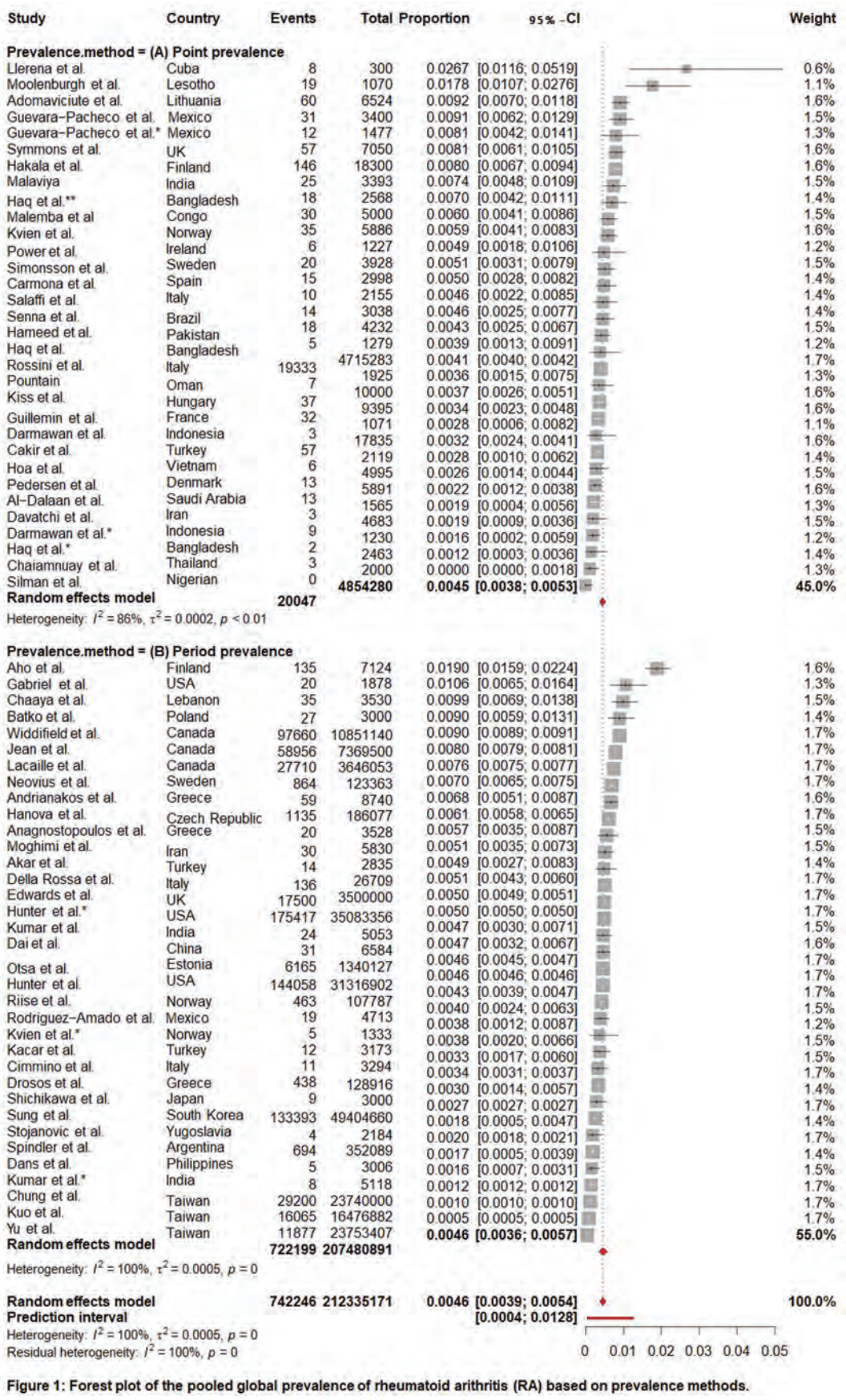

Figure 1. Forest plot of the pooled global prevalence of Rheumatoid Arthritis (RA) based on prevalence methods.

Table 1: The 95% prediction intervals for future RA prevalence estimates of different sub-groups category.

Sub-groups category	n	Lower predication interval	Upper predication interval
Geographical location			
North America	10	0.29%	1.29%
Europe	26	0.38%	0.73%
Asia	26	0.05%	0.73%
Africa	3	*	*
South America	2	*	*
RA classification criteria			
Clinical diagnosis by a doctor	19	0.17%	1.15%
Revised ARA criteria 1987	37	0.17%	0.73%
Modified ARA criteria 1987	7	0.18%	0.71%
ARA criteria 1956	3	*	*
Rome criteria 1961	1	*	*
Types of data sources.			
Admin Data	14	0.03%	1.11%
Population based survey	46	0.05%	1.26
Linked Data	4	*	*
Registry Data	3	*	*
Population based survey			
Participation rate = 75%	15	0.11%	1.20%
Participation rate <75%	31	0.02%	1.35%
COPCORD studies	17	0.00%	1.94%
Other survey method	29	0.11%	1.01%
Geographic population settings			
Urban populations	25	0.21%	0.87%
Mixed populations	30	0.08%	1.21%
Rural populations	12	0.00%	1.21%
Country income levels			
High income countries	39	0.05%	1.33%
Upper middle-income	14	0.08%	1.14%
Lower middle-income	13	0.00%	1.24%
Low income	1	*	*

*=Unavailable due to the limited number of cohort studies; RA= Rheumatoid Arthritis.

Table 1. The 95% prediction intervals for future RA prevalence estimates of different sub-groups category.

Conclusion: The global prevalence of RA between 1980 and 2019 was 460 per 100,000 population, with variations due to geographical location and study methodology. Linked data are the preferred method to estimate RA population prevalence as they provide the best case-ascertainment.

Disclosure: K. Almutairi, None; **J. Nossent**, None; **D. Preen**, None; **H. Keen**, Pfizer Australia, 8, Abbvie Australia, 8; **C. Inderjeeth**, Novartis Australia, 8, Amgen, 5, 8, Kiniksa, 2, Paradigm, 2, BMS, 2.

Abstract Number: 1013

National Burden of RA in Canada 1990-2017: Findings from the Global Burden of Disease Study 2017

Nejat Hassen[1], Diane Lacaille[2], Nizal Sarrafzadegan[3], Alice Xu[4], Sophia Sidi[4], Amani Alandejani[4], Marjan Mansourian[5] and Jacek Kopec[1], [1]University of British Columbia, Arthritis Research Canada, Richmond, BC, Canada, [2]University of British Columbia / Arthritis Research Canada, Richmond, BC, Canada, [3]Isfahan University of Medical Sciences, University of British Columbia, Isfahan, Esfahan, Iran, [4]University of British Columbia, Vancouver, BC, Canada, [5]Isfahan University of Medical Sciences, Isfahan, Iran

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: It is estimated that over 120,000 individuals currently have rheumatoid arthritis (RA) in Canada, yet a comprehensive study summarizing the epidemiology of RA burden in the country is lacking. We used data from the Global Burden of Diseases, Injuries, and Risk Factors (GBD) Study 2017 to evaluate the level, and trends over time, of disease burden indicators prevalence, mortality, years of life lost (YLLs), years lived with disability (YLDs), and disability adjusted life years (DALYs) for RA in Canada by age, sex, and socio-demographic index (SDI), from 1990 to 2017.

Methods: We obtained publicly available data from GBD Study 2017 from the Institute for Health Metrics and Evaluation interactive visualization tool (http://vizhub.healthdata.org/gbd-compare). Estimates were calculated as non-age standardized and age standardized rates per 100,000 population. GBD estimated mortality and prevalence rates based on published literature, survey data, patient records, and health insurance claims. YLLs measure years lost due to premature death calculated as the number of deaths multiplied by the standard life expectancy at each age. YLDs measure the amount of time in a year an individual lives with a short- or long-term health condition, calculated by multiplying RA prevalence with disability weights for that condition, for each age, sex, and year. DALYs was calculated as the sum of YLLs and YLDs for each age group, sex, and year. SDI combines income per capita, average educational attainment, and fertility rates. Canadian DALYs were compared to DALYs of countries with similar SDI

Indicator	Standardization	ALL (Female & Male)			FEMALE			MALE		
		YEAR		Change	YEAR		Change	YEAR		Change
		1990	2017		1990	2017		1990	2017	
Prevalence	Non age standardized	170.3	352.2	107%	241.5	494.7	105%	97.1	205.1	111%
	Age standardized	144.7	223.7	55%	195.5	308.4	58%	87.6	133.1	52%
Mortality	Non age standardized	0.7	0.9	26%	1.0	1.2	21%	0.4	0.5	38%
	Age standardized	0.6	0.4	-22%	0.7	0.5	-23%	0.4	0.3	-18%
YLLs	Non age standardized	12.4	13.0	5%	17.4	17.0	-3%	7.3	8.9	22%
	Age standardized	10.0	7.1	-29%	12.8	8.8	-31%	6.6	5.2	-21%
YLDs	Non age standardized	22.5	46.0	105%	31.7	64.4	103%	13.0	26.9	108%
	Age standardized	19.1	29.5	54%	25.8	40.7	57%	11.7	17.7	51%
DALYs	Non age standardized	34.9	59.0	41%	49.2	81.4	66%	20.2	35.8	77%
	Age standardized	29.2	36.7	20%	38.6	49.4	28%	18.3	22.9	25%

Table 1. Time Trends for Non Age Standardized and Age Standardized RA Burden of Disease Indicators per 100,000, Canada, 1990-2017

values. All extracted data was analysed by DisMod-MR 2.1, a Bayesian meta-regression tool. All Canadian estimates were compared to global estimates.

Results: Time trends were evaluated over the study period 1990-2017. In Canada, the prevalence rate of RA increased by 55%, mortality rate decreased by 22%, YLL rate decreased by 29%, YLD rate increased by 54%, and DALY rate increased by 26%, all age-standardized. The age-standardized prevalence, mortality, YLL, YLD and DALY rates were higher in females. The Canadian prevalence rate increased at a greater rate than the global prevalence rate. The Canadian age-standardized mortality and YLL rates significantly declined after the year 2002. The global age-standardized mortality and YLLs rates declined at a slower rate than Canada. The DALY rate peaked at 70-74 and 75-78 age groups for both females and males. In 2017, YLDs contributed to 81% of the proportion of DALYs. Canada had lower age-standardized DALYs than countries of similar SDI. A weak association was found between age-standardized DALYs and SDI.

Conclusion: RA is a major public health challenge. The age-standardized prevalence, YLDs, and DALYs are increasing while mortality and YLLs are decreasing. Canada fairs better than other high SDI countries with regards to national RA burden. Early identification and management of RA is crucial to reducing the overall burden of RA in Canada, especially in women, who experience a higher burden of disease. Greater availability of data from multiple provincial RA databases would increase the accuracy and generalizability of our estimates for Canada.

Disclosure: N. Hassen, None; **D. Lacaille**, None; **N. Sarrafzadegan**, None; **A. Xu**, None; **S. Sidi**, None; **A. Alandejani**, None; **M. Mansourian**, None; **J. Kopec**, None.

Abstract Number: 1014

Disease Modifying Anti-rheumatic Drugs, Biologics and Corticosteroid Use in Older Patients with Rheumatoid Arthritis over 20 Years

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The objective of the current study was to examine the change in prescribing patterns for older adults with RA over a 20 year period using a validated health administrative database. Specifically we wished to determine if the anticipated changes in prescribing over 2 decades had occurred in the broader population of RA patients and, in particular, if the use of corticosteroids fell over this time.

Methods: This was a secondary analysis of health administrative data using a previously validated dataset and case definition for RA. Cases were matched 1:4 by age and sex to controls within a population of approximately 1 million inhabitants with access to universal health care. Longitudinal data for incident and prevalent RA cases were studied between 1997 and 2017. Statistical analyses included descriptive statistics and linear regression.

Results: There were 8240 RA cases (all ≥ 65 years) with a mean (SD) age 72.2 (7.5) years and 70.6% were female. Over 20 years, annual utilization of coxibs in prevalent RA cases fell with a concomitant increase in disease modifying anti-rheumatic drugs (DMARDs) and biologics. Over the same period corticosteroid use was largely unchanged. Ap-

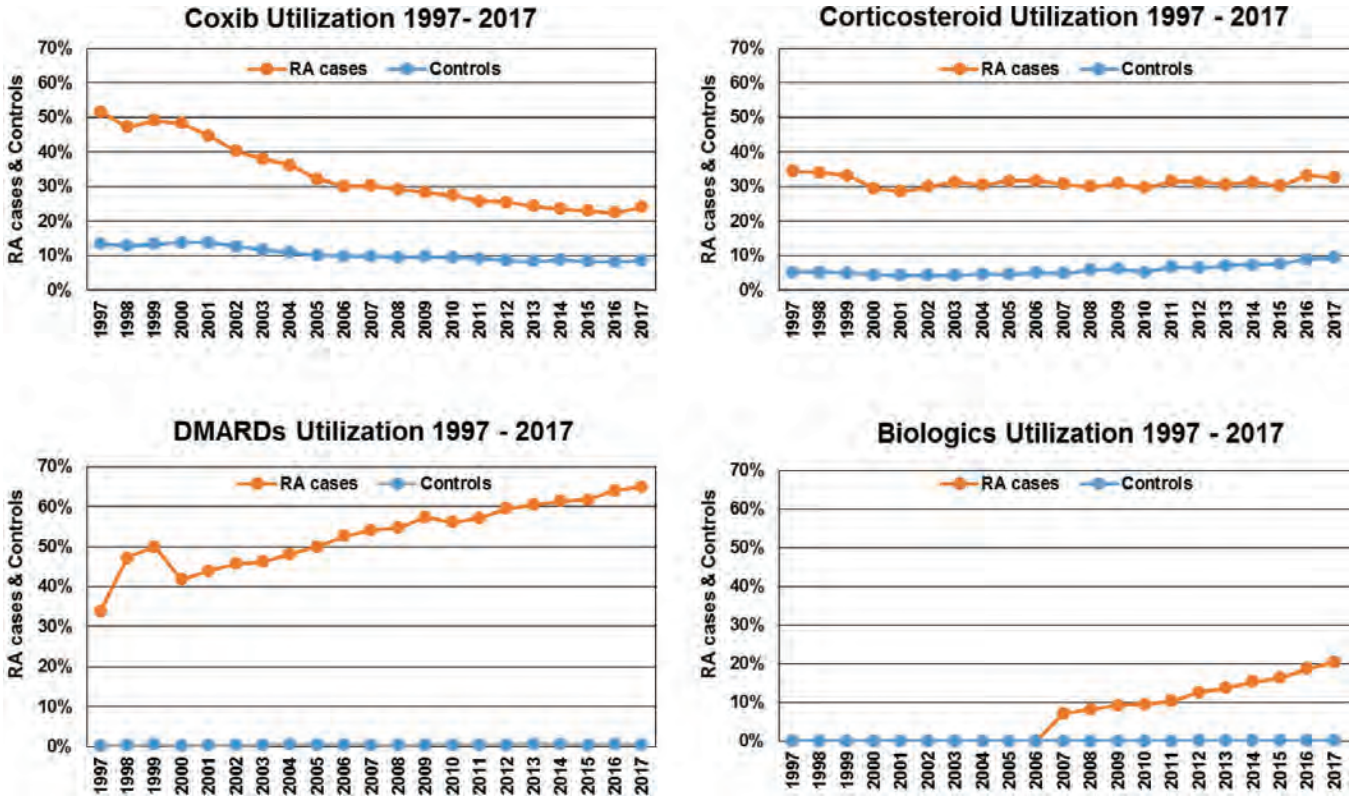

Figure 1. Annual utilization of coxibs, corticosteroids, disease modifying anti-rheumatic drugs (DMARDs) and biologics over 20 years as indicated by the proportion of RA cases and controls who received one or more prescriptions per year.

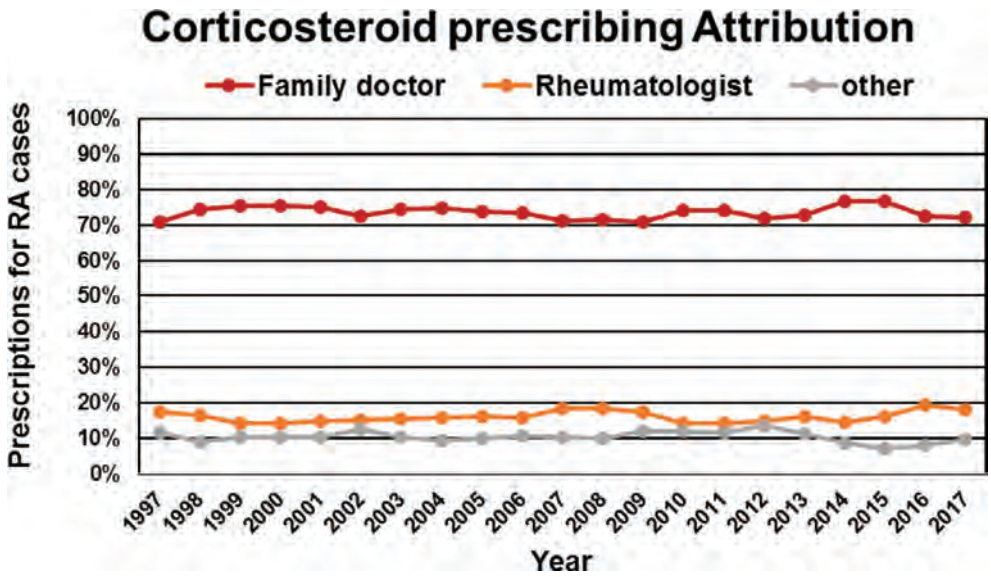

Figure 2. The annual proportion of total corticosteroid prescriptions for RA cases provided by family physicians and non-family physicians over 20 years.

proximately one third of patients had at least one annual prescription for corticosteroid, most frequently prednisone. The mean annual dose showed a modest reduction and the duration of utilization in each year shortened. Rheumatologists prescribed corticosteroids less frequently and in lower doses than other physician groups. For incident RA cases there was a significant fall in annual prescribed dose of prednisone by rheumatologists over time.

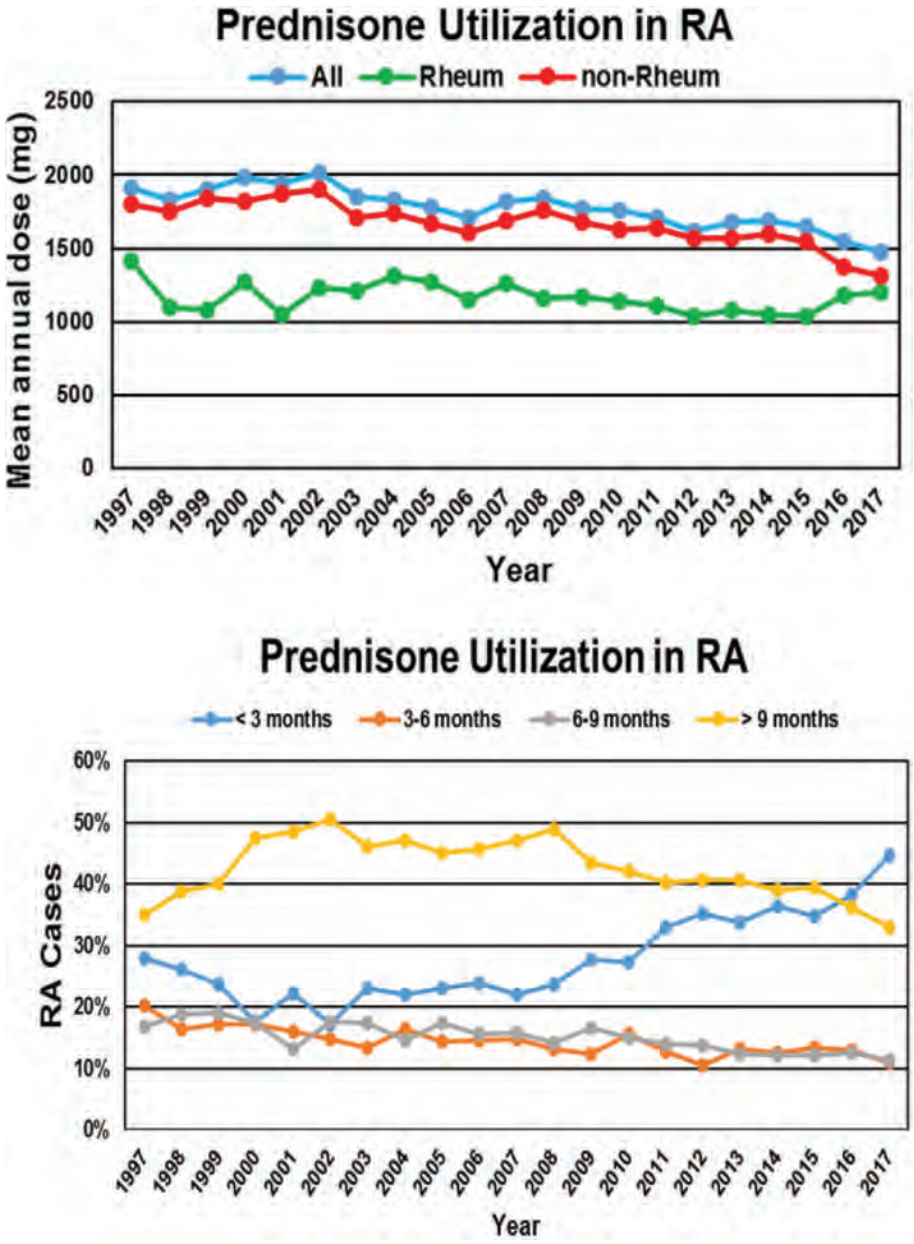

Figure 3. The change in annual utilization of prednisone in RA cases over 20 years. Top panel: change in mean annual dose of prednisone in RA cases and the attribution of prescriptions to rheumatologists (Rheum) and other physician groups (non-Rheum). Some patients received prescriptions from both rheumatologists and other physicians in the same year. Bottom panel: change in the annual duration of exposure to prednisone in RA cases as assessed by one or more prescriptions in each 3 month interval.

Conclusion: In older adults with RA the utilization of DMARDs and biologics has increased over the past 20 years. However, the use of corticosteroids has persisted. Renewed efforts are required to minimize their use in the long-term pharmacological management of RA.

Disclosure: J. Hanly, None; **L. Lethbridge**, None.

Abstract Number: 1015

The Prevalence and Risk Factors for Liver Fibrosis Among Rheumatoid Arthritis (RA) Patients on Disease-Modifying Anti-rheumatic Drugs (DMARDs)

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SESSION INFORMATION
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Background/Purpose: Majority of DMARDs, including methotrexate (MTX), leflunomide (LEF) and sulfasalazine (SSZ) are believed to be hepatotoxic, causing liver fibrosis. However, the clinical findings were inconsistent. An ultrasound(US)-based transient elastography (TE) and shear-wave elastography (SWE) has become a promising tool in detecting liver fibrosis and fatty liver. Our study aims to determine the risk factors of liver fibrosis and fatty liver among RA patients on DMARDs.

Methods: Our cross-sectional cohort study recruited adult RA patients, who fulfilled ACR 1987 or EULAR-ACR 2010 classification criteria, from the rheumatology clinic at Sultanah Bahiyah Hospital, Malaysia. Liver fibrosis and fatty liver score were detected using US TE/SWE. Patient's demographic, disease activity (DAS28 score) and relevant blood parameter were recorded. Data were analysed using Spearman correlation, One-way Anova and Kruskal-Wallis Test.

Results: A total of 43 patients were recruited; the majority were female 38 (88%). The mean age of patients was 51.6± 10.5 years. The cumulative dose of each DMARDs: MTX 1572.5mg (IQR 762.5-2490.0), SSZ 1330g (IQR 685- 2607), LEF 19621± 19719 mg and HCQ of 193.5g (IQR 66.3- 283.6). Our study showed a positive correlation between triglyceride level and SWE (r_s= 0.476, p= 0.002), negative correlation of high-density lipoprotein and SWE (r_s= -0.474, p= 0.002). Whereas there was a negative correlation between albumin level and TE (r_s= -0.312, p= 0.044). High BMI was associated with an increased fatty liver score (r_s= 0.372, p= 0.033). Interestingly, our study demonstrated a negative correlation between the cumulative dose of HCQ and the fatty liver score (r_s= -0.782, p= 0.004). There were no significant differences between monotherapy and combination therapy on the fatty liver score (F(3,37)= 0.892, p= 0.454), SWE (H(3)= 3.687, p= 0.297) and TE (H(3)= 0.693, p= 0.875).

Conclusion: Our study demonstrated that DMARDs were generally safe with low risk of liver fibrosis. Dyslipidemia and obesity should be optimized in order to the reduce risk of liver fibrosis. Hydroxychloroquine administration may be a protective factor against fatty liver.

Disclosure: C. Tan, None; **B. Ng**, None; **N. Ahmad**, None; **S. Soelar**, None; **M. Jazlan**, None; **M. Md Mansor**, None; **M. Mohd Suan**, None; **K. Kiew**, None; **Z. Zainuddin**, None; **M. Abu Hassan**, None; **C. Lim**, None.

Abstract Number: 1016

Annual Cardiac or Orthopedic Procedure Volume in Gout versus Rheumatoid Arthritis: A National Time-trends Study

Jasvinder Singh[1] and John Cleveland[1], [1]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
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Background/Purpose: The hospitalization rate for gout has been increasing in recent years with a reduction in people with RA. To our knowledge, there are no studies of time-trends in U.S. national estimates of cardiac versus orthopedic procedures in people with gout compared to RA. Our study objective was to compare time-trends in cardiac versus orthopedic procedures in people with gout versus RA. We hypothesized that (1) RA would be associated with higher annual volume and rates of both procedures at the beginning and the end of our study period, but the gout-RA gap will narrow over time, (2) increase in the annual volume of orthopedic procedures will be higher than cardiac procedures in both, and (3) increase in their annual volume in gout or RA will outpace that in the general U.S. population.

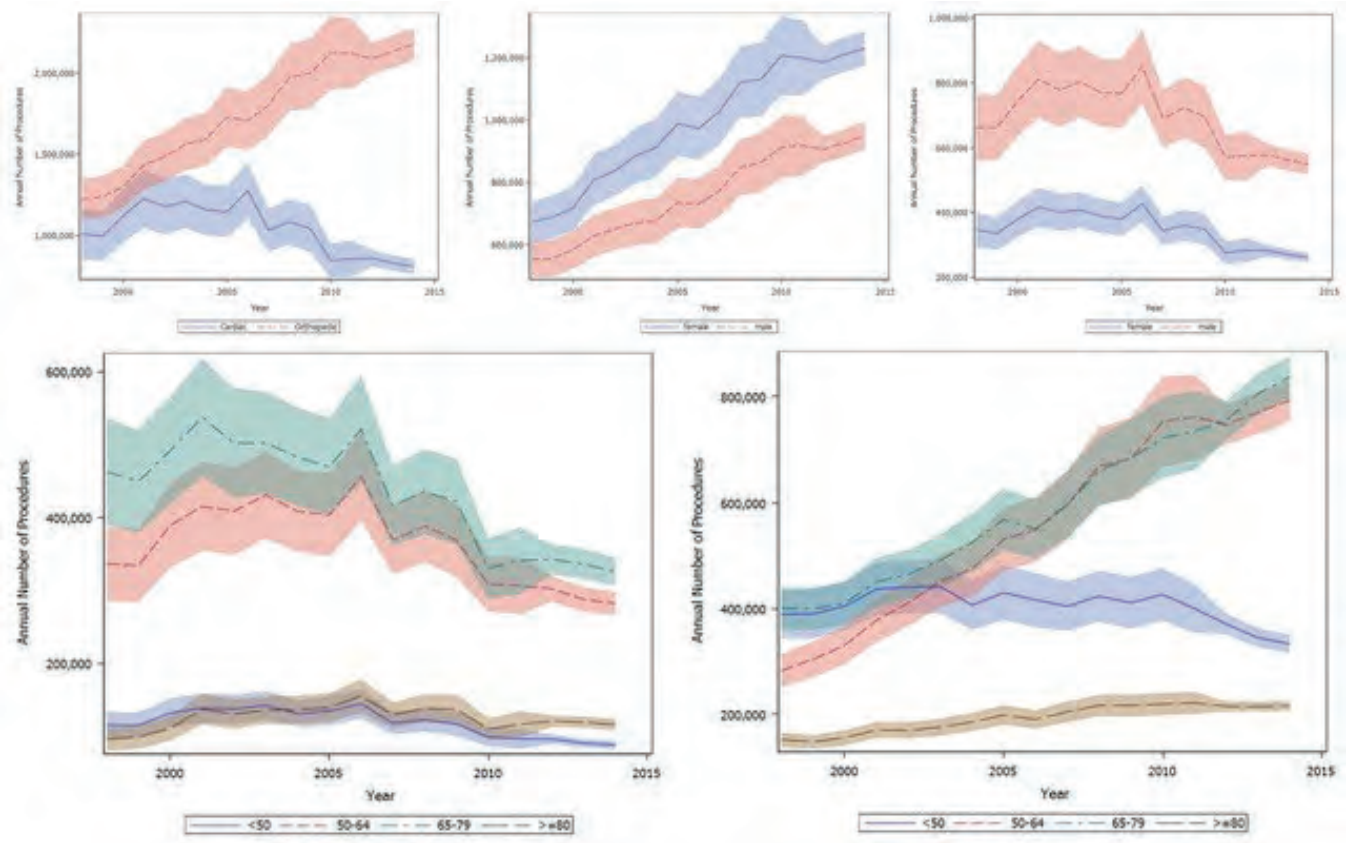

Figure 1. Time-trends in cardiac and orthopedic procedures in the U.S. general population during the study period 1998-2014 showing the overall trend (A), cardiac procedures by sex (B), orthopedic procedures by sex (C), cardiac procedures by age groups (D) and orthopedic procedures by age groups (E) Figure 1 legend: X-axis represents the study year and Y-axis shows the number of annual procedures. Estimates over time are shown with the line and the shaded area represents the upper and lower 95% confidence intervals. The Y-axis scales differs between panels.

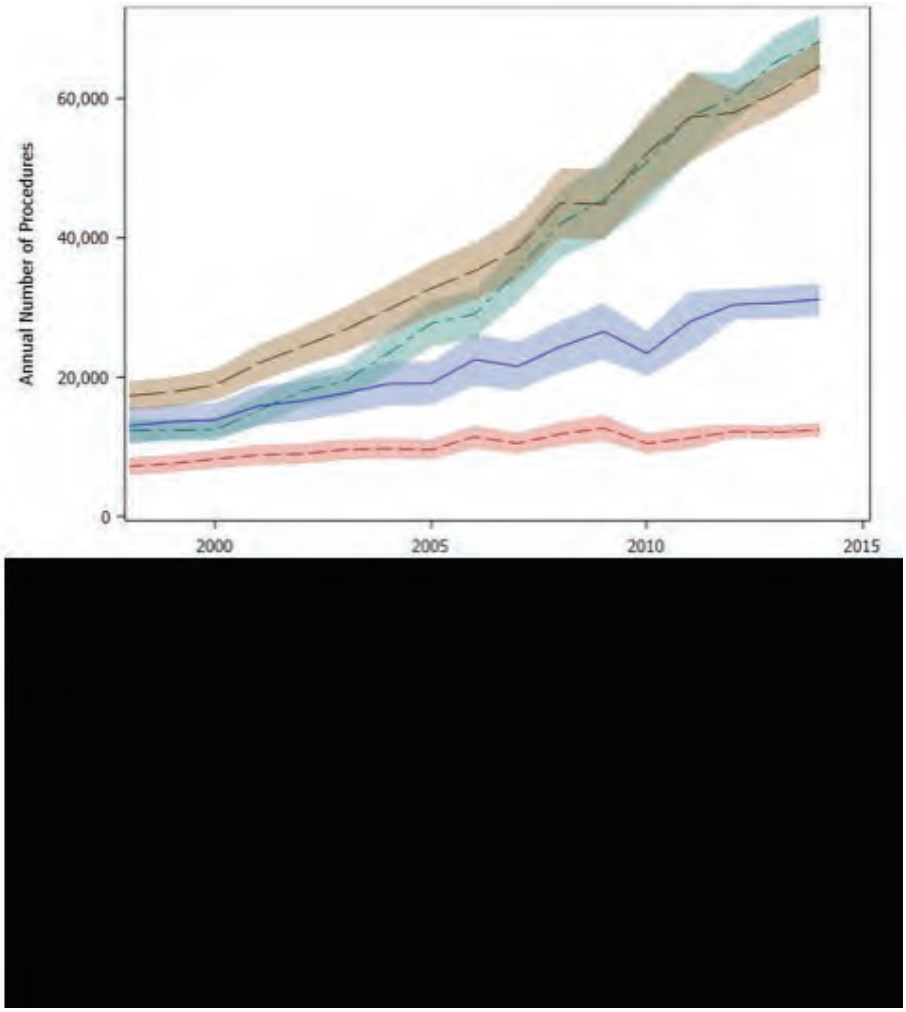

Figure 2. Time-trends in cardiac and orthopedic procedures from 1998-2014 in people with gout or rheumatoid arthritis (RA) during the study period showing the overall trends Figure 2 legend: X-axis represents the study year and Y-axis shows the number of annual procedures. Estimates over time are shown with the line and the shaded area represents the upper and lower 95% confidence intervals. The Y-axis scales differs between panels.

Methods: We examined the frequency of 7 common cardiac and orthopedic procedures in hospitalized people with gout or RA (or the general population) using the 1998-2014 U.S. National Inpatient Sample (NIS). Poisson regression evaluated the statistical significance of the differences in frequencies in 1998 versus 2014, between gout and RA, and within each cohort.

Results: The rate of cardiac procedures per 100,000 NIS claims decreased from 2,977 in 1998 to 2,292 in 2014; the rate of orthopedic procedures increased from 3,609 in 1998 to 6,160 in 2014 in the U.S. general population (**Figure 1**).

Both in-hospital cardiac and orthopedic procedures increased in gout and RA with time, in contrast to declining numbers in the general U.S. population; orthopedic procedures became more common than cardiac procedures in gout and RA. The corresponding increase in in-hospital cardiac and orthopedic procedure rates per 100,000 NIS claims in two populations were as follows: (1) gout, 2.3 (36.6 to 82.8) and 5.1-fold (34.2 to 174.6); and (2) RA, 1.6 (20.1 to 33.1) and 2.4-fold (70.2 to 170.8), respectively (**Figure 2**). In RA, the cardiac-orthopedic procedure volume difference was significant in 1998 and 2014. We noted no significant difference between cardiac versus orthopedic procedures in 1998 in gout, but the difference was significant in 2014. Cardiac procedures were significantly higher in gout versus RA in 1998 (59% higher) and 2014 (92% higher; **Figure 2**).

Table 1. Rate per 100,000 NIS population hospitalization for cardiac or orthopedic procedures or all hospitalizations in people with a concomitant diagnosis of gout or rheumatoid arthritis (RA) from 1998 to 2014

	Cardiac Procedure hospitalizations	Orthopedic Procedure hospitalizations	Cardiac Procedure hospitalizations	Orthopedic Procedure hospitalizations	Any hospitalization	Any hospitalization
	Gout- Primary or secondary	Gout- Primary or secondary	RA- Primary or secondary	RA- Primary or secondary	Gout- Primary or secondary	RA- Primary or secondary
1998	36.6	34.2	20.1	70.2	749.9	763.5
1999	37.4	34.1	21.1	68.4	775.9	791.0
2000	37.6	33.2	22.5	69.4	769.9	800.8
2001	42.3	39.2	23.4	75.3	825.6	834.9
2002	43.4	46.0	23.6	80.9	933.1	863.0
2003	45.8	48.6	24.9	82.5	991.4	889.1
2004	48.5	58.0	24.9	89.6	1071.6	920.3
2005	48.2	67.9	24.4	94.7	1137.7	961.5
2006	56.5	70.7	29.0	98.3	1253.7	1003.2
2007	53.5	85.1	26.3	104.6	1369.5	1034.9
2008	60.7	101.6	29.4	119.6	1556.9	1150.0
2009	66.3	110.5	31.9	118.2	1725.2	1215.3
2010	58.7	124.0	26.7	134.9	1906.3	1279.0
2011	70.8	141.1	28.9	147.3	2221.1	1433.9
2012	77.8	149.5	31.7	150.8	2280.7	1431.1
2013	80.8	166.2	31.7	160.8	2362.4	1471.9
2014	82.8	174.6	33.1	170.8	2416.6	1515.4
Trends were similar for RA or gout as primary diagnosis for cardiac and orthopedic procedure hospitalizations, where estimable						

Table 1. Rate per 100,000 NIS population hospitalization for cardiac or orthopedic procedures or all hospitalizations in people with a concomitant diagnosis of gout or rheumatoid arthritis (RA) from 1998 to 2014

The orthopedic procedures in gout were significantly lower than RA in 1998 (33% lower), but were significantly higher than RA in 2014 (5% higher; **Figure 2**). Of all hospitalizations with cardiac/orthopedic procedures, the proportion of people with each as primary or secondary diagnosis increased from 1998 to 2014: (1) in-hospital cardiac procedures: 1.2% to 3.6% with gout; 0.7% to 1.4% with RA; and (2) in-hospital orthopedic procedures: 0.9% to 2.8% with gout; 1.9% to 2.8% with RA

Conclusion: Cardiac and orthopedic procedures increased in gout and RA 1998-2014 versus decline in the general population. Cardiac procedure volumes and rates were higher in gout versus RA in 1998 and 2014. Increasing in-hospital cardiac procedures in gout and RA contrasting with declining rates in the general U.S. population indicated that early diagnosis of gout and RA, and management of systemic inflammation are needed. Orthopedic procedures were more in 1998, but fewer in 2014 in RA versus gout.

Disclosure: J. Singh, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **J. Cleveland**, None.

Abstract Number: 1017

Racial and Ethnic Disparities in the Risk of Preterm Birth Among Women with Systemic Lupus Erythematosus or Rheumatoid Arthritis with Varying Reference Groups

Lena Sabih[1], Jennifer Strouse[1], Gretchen Bandoli[2], Rebecca Baer[3], Laura Jelliffe-Pawlowski[3], Christina Chambers[2], Namrata Singh[4] and Kelli Ryckman[5], [1]University of Iowa Hospitals and Clinics, Iowa City, IA, [2]University of California San Diego, La Jolla, CA, [3]University of California San Francisco, San Francisco, [4]University of Washington, Bellevue, WA, [5]University of Iowa, Iowa City

SESSION INFORMATION

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Session Type: Poster Session C

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Background/Purpose: Systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) are independently associated with preterm birth (PTB). Black women have higher risk of both ARD and PTB; however, few studies have examined race/ethnic disparities in PTB risk among women with SLE or RA. In a large multiethnic cohort of women, we examined race/ethnic disparities in PTB risk stratified by ARD type (SLE or RA) as well as the interaction between race/ethnicity and ARD type.

Methods: Birth records linked to hospital discharge data of singleton births in California from 2007 to 2012 were leveraged for a retrospective cohort study including women at least 18 years old diagnosed with either SLE or RA identified by the international classification of diseases (ICD), ninth revision. 222 women with both SLE and RA were excluded from analysis. Race/ethnicity (Asian, Black, Hispanic, and White) was abstracted from the birth certificate. The relative risk of PTB (< 37 weeks versus ≥37 weeks gestation) was compared among race/ethnicity and stratified by ARD type (RA or SLE). Results were adjusted for relevant covariates including maternal age, pre-pregnancy body mass index (BMI), insurance, education, country of origin, parity and smoking using Poisson regression with the log link function. In the model we examined all possible combinations of comparisons by race and ethnicity by altering the referent group in the model. Additionally, we identified differences in the racial/ethnic disparities in PTB risk between RA and SLE by including an interaction term to the model between race/ethnicity and ARD (RA versus SLE).

Results: A total of 2,309 with RA and 2,874 women with SLE were included in the analysis. In women with SLE, Black, Hispanic, and Asian women were ~1.3 to 1.5 times more likely to have PTB compared to White women (Table 1). Black, Hispanic, and Asian women with SLE did not significantly differ from each other in PTB risk. Black women with RA were ~1.6 to 2.4 times more likely to have PTB compared to either Asian, Hispanic, or White women. Asian, Hispanic, and White women with RA did not significantly differ from each other in PTB risk. When examining the interaction between race and ARD (RA versus SLE) the Black-White PTB risk disparity in women with RA was 1.5 times higher compared to the Black-White PTB risk disparity in women with SLE (Table 1). The Black-Hispanic PTB risk disparity in women with RA was 2.1 times higher compared to the Black-Hispanic PTB risk disparity in women with SLE. The Black-Asian PTB risk disparity in women with RA was 1.5 times higher compared to the Black-Asian PTB risk disparity in women with SLE, but this did not quite reach statistical significance ($p< 0.05$).

Conclusion: Our findings in this large multiethnic cohort of women are consistent with prior work demonstrating that race/ethnicity is associated with increased relative risk of PTB but indicate that some disparities differ between RA and SLE. Black-White, Black-Hispanic, and Black-Asian disparities in PTB risk were greater in women with RA

Table 1: Association of race with preterm birth stratified by ARD diagnosis.

Comparison	Model	Preterm (<37 vs. ≥37)		Interaction
		RA	SLE	RA vs. SLE
Black vs. White	Unadjusted	**2.22 (1.61, 3.05)**	**1.47 (1.16, 1.85)**	**1.51 (1.02, 2.25)**
	Adjusted	**2.44 (1.73, 3.43)**	**1.33 (1.04, 1.71)**	**1.55 (1.03, 2.33)**
Black vs. Hispanic	Unadjusted	**2.32 (1.69, 3.18)**	1.07 (0.87, 1.32)	**2.17 (1.48, 3.17)**
	Adjusted	**2.31 (1.65, 3.23)**	0.99 (0.75, 1.25)	**2.07 (1.40, 3.06)**
Black vs. Asian	Unadjusted	**1.60 (1.05, 2.46)**	1.04 (0.81, 1.33)	1.54 (0.94, 2.53)
	Adjusted	**1.99 (1.22, 3.24)**	0.90 (0.67 1.20)	1.60 (0.96, 2.67)
Hispanic vs. White	Unadjusted	0.96 (0.75, 1.22)	**1.37 (1.15, 1.63)**	**0.70 (0.52, 0.94)**
	Adjusted	1.06 (0.80, 1.40)	**1.34 (1.10, 1.63)**	0.75 (0.55, 1.02)
Hispanic vs. Asian	Unadjusted	0.69 (0.48, 1.00)	0.97 (0.80, 1.18)	0.71 (0.47, 1.08)
	Adjusted	0.86 (0.57, 1.30)	0.90 (0.72, 1.13)	0.77 (0.50, 1.20)
Asian vs. White	Unadjusted	1.38 (0.95, 2.02)	**1.41 (1.13, 1.76)**	0.98 (0.63, 1.52)
	Adjusted	1.23 (0.80, 1.88)	**1.48 (1.16, 1.90)**	0.97 (0.61, 1.53)

Model adjusted for maternal age, pre-pregnancy body mass index (BMI), insurance, education, country of origin, parity and smoking

ARD = autoimmune rheumatic disease, RR = relative risk, SLE = systemic lupus erythematous, RA = rheumatoid arthritis

Association of race with preterm birth stratified by ARD diagnosis

compared to women with SLE. This information may provide important public health information for addressing racial disparities, particularly in women with RA.

Disclosure: L. Sabih, None; **J. Strouse**, None; **G. Bandoli**, None; **R. Baer**, None; **L. Jelliffe-Pawlowski**, None; **C. Chambers**, Amgen, Inc, 1, AstraZeneca, 1, Celgene, 1, GlaxoSmithKline, 1, Janssen Pharmaceuticals, 1, Pfizer, Inc, 1, Regeneron, 1, Hoffman La-Roche-Genentech, 1, Genzyme Sanofi-Aventis, 1, Takeda Pharmaceutical Company Limited, 1, Sanofi, 1, UCB Pharma, USA, 1, Sun Pharma Global FZE, 1, Gerber Foundation, 1; **N. Singh**, Rheumatology Research Foundation, 2, American Heart Association, 2; **K. Ryckman**, None.

Abstract Number: 1018

Seasonal Variation in the Treat-to-Target Rate of Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE): A Cohort Study on Self-reported Data from Smart System of Disease Management (SSDM)

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SESSION INFORMATION

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Background/Purpose: Treat-to-Target(T2T) is the main therapeutic strategy for patients with RA and SLE. There has been no report on comparation of seasonal variations on T2T rates in patients with RA and SLE.

Smart System of Disease Management (SSDM) is a smart phone-based mobile disease management tool, equipped with two apps, one for doctors and one for patients. After training by health care professionals, rheumatic patients will download and use SSDM for DAS28 or SLEDAI-2000 self-assessment, and upload clinical data (including disease activity, medication status and laboratory test results) to SSDM cloud, meanwhile the data will be synchronized to authorized physicians. Based on the clinical data submitted by the patient, the doctor can respond to the patient's request of consultation and refill the medication.

The purpose of this study was to outline and compare the effect of seasonal variations in the T2T rates through analysis of self-reported disease activity data in patients with RA and SLE from the SSDM system.

Methods: Seasons were designed as following: Spring is from March to May, summer from June to August, autumn from September to November, and winter from December to February.

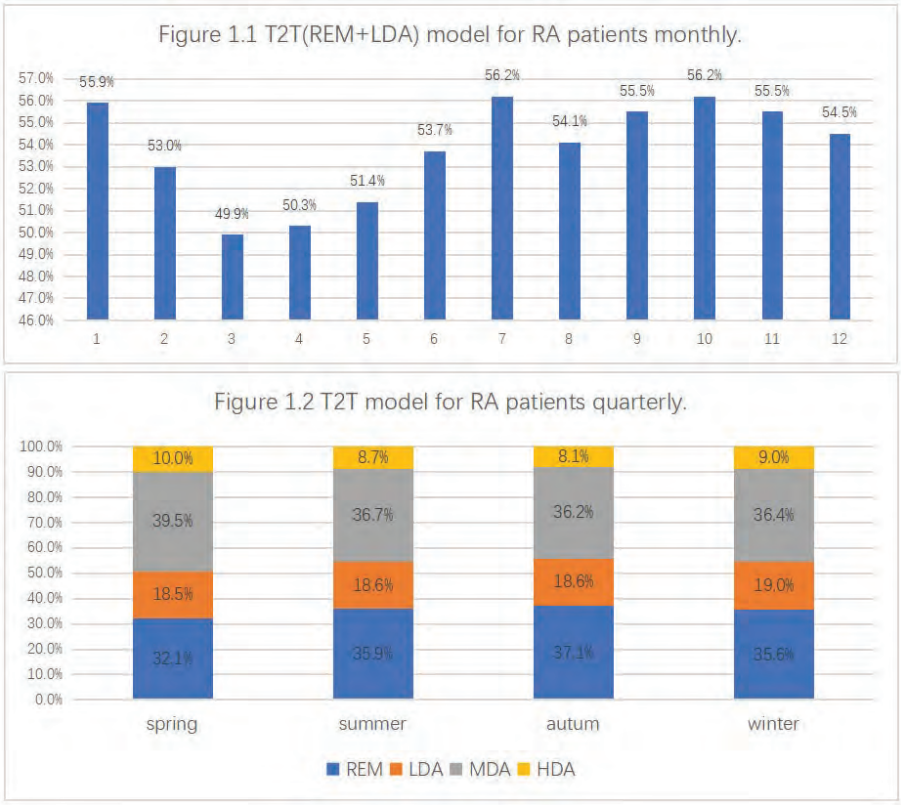


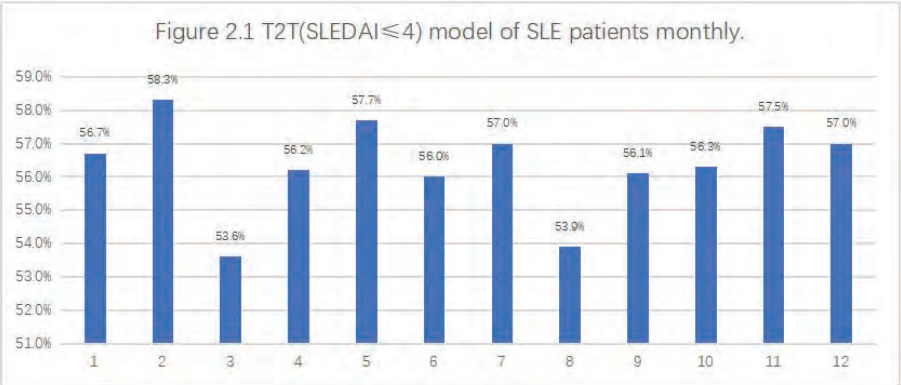
Figure 1. T2T model for RA patients (1.1 monthly;1.2 Quarterly)

DAS28 and SLEDAI-2000 data from each individual patient was extracted from cloud, and then pooled for analysis according to seasonal definition. DAS28≤3.2 and SLEDAI-2000≤4 are considered to be the criteria for achieving "T2T" for patients with RA and SLE, respectively.

Results: Between June 2014 and June 2020, 1,944 doctors from 632 hospitals in China joined the study, and 127,316 DAS28 assessments were conducted by 56,546 (male 10,260, female 46,286) RA patients (mean age 51.35 ±14.13 years, median course of disease 45.97 months), and 42,593 SLEDAI-2000 assessments were conducted by 19,629 (male 1,419, female 18,210) SLE patients (mean age 37.45 ±12.34 years, median course of disease 48.73 months)

The T2T rate of RA patients in spring is the lowest among four seasons in consecutive 5 years (mean rate of T2T is 50.5%, with 49.9% in March, 50.3% in April, and51.4% in May), while the average T2T rate in summer, autumn, and winter is 54.6%, 55.7%, and 54.5% respectively, with a U-shaped distribution from January to July. There is no significant difference in the overall distribution for SLE T2T rates among the four seasons. The T2T rates in spring, summer, autumn and winter were 55.8%, 55.5% ,56.7% and 57.3% respectively. However, there were two significant monthly drops on T2T rates in March (53.6%) and August (53.9%).

Conclusion: To our knowledge, this is the first study of outlining and comparing seasonal variation of T2T rates in patients with RA and SLE. Self-reported clinical data in SSDM for consecutive 5 years showed that RA patients have the lowest T2T rate in the spring season, which corelated with super long holiday of Chinese New Year, while SLE patients have the lowest T2T rate in March and August, which matched with holiday and strong UV light irradiation, respectively.



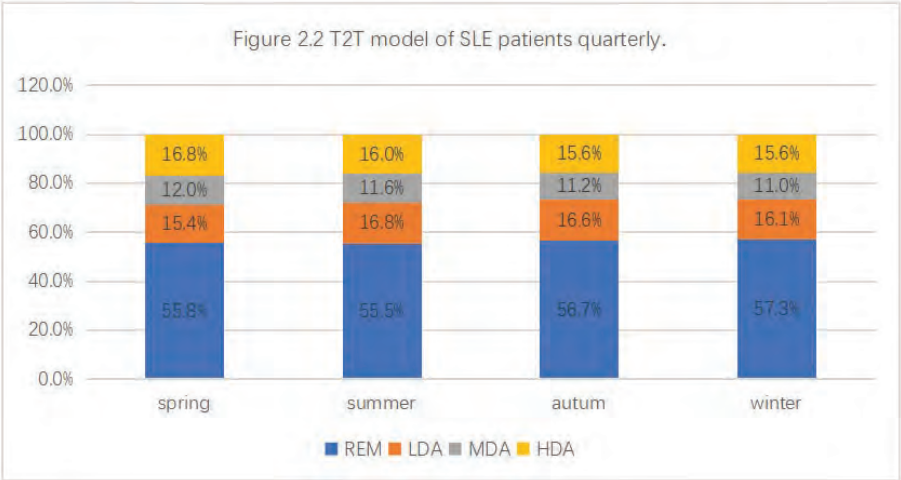


Figure 2. T2T model of SLE patients (2.1 monthly; 2.2 Quarterly)

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Abstract Number: 1019

Outdoor Air Pollution and Systemic Lupus Erythematosus

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Background/Purpose: Understanding the role of environmental exposures in the development of SLE and their association with SLE activity may help identify modifiable risk factors and potential etiological mechanisms. We hypoth-

esized that changes in coarse particulate matter (PM10, < 10 micrometers in size), sulfur dioxide, carbon monoxide, lead, and nitrogen dioxide are predictive of organ specific flares in lupus.

Methods: 1628 patients who fulfill 4 of the 11 ACR or SLICC classification criteria for SLE were included in the analysis. The data ranged from 1999 to 2017. Maximum distance between visits was 110 days with 1-month time aggregation units. Disease activity was expressed as Physician Global Estimate (PGA), taken at every patient visit. A flare was defined as a PGA score increase of 1 point or more compared to the previous visit. Environmental and atmospheric data was obtained from the EPA, including PM10, sulfur dioxide, carbon monoxide, lead, and nitrogen dioxide. The average values of each factor 10 days prior to patient visit was calculated. Univariate and multivariate models were built in order to study the association of these variables with lupus disease activity. The models were adjusted for age, sex, income, county racial distribution, rural vs. urban patient residence, distance to highways, distance to airports, PM2.5, PM10, sulfur dioxide, carbon monoxide, lead, and nitrogen dioxide concentrations, temperature, humidity, barometric pressure, ozone concentration, and residual wind. Univariate and stepwise multivariate logistic regression was used to identify significant determinants associated with lupus flares. Regression was performed for each organ flare outcome. Regression inference was based on generalized estimating equations (GEE) to account for the time repeated outcomes.

Results: Increases in sulfur dioxide concentration were directly associated with rash ($p< 0.01$), joints ($p< 0.001$), and neurologic flares ($p< 0.001$), and inversely associated with renal flares ($p< 0.001$) in multivariate analyses. Lead concentration was directly associated with neurologic ($p< 0.001$) and pulmonary flares ($p< 0.001$), and indirectly associated with serositis ($p< 0.001$) and renal flares ($p< 0.001$) in multivariate analysis. Nitrogen dioxide was directly associated with rash ($p< 0.001$), joints ($p< 0.001$), serositis ($p< 0.001$), hematologic ($p< 0.001$), pulmonary ($p< 0.001$), and renal flares ($p< 0.001$) in multivariate analysis. PM10 and carbon monoxide had no significant associations in multivariate analysis.

Conclusion: There is a strong association between changes in nitrogen dioxide, sulfur dioxide, and lead concentrations 10 days prior to patient visit and organ specific lupus activity at the visit. Nitrogen dioxide is the only pollutant with a general association with all organ specific lupus flares.

Disclosure: G. Stojan, None; **A. Kvit**, None; **F. Curriero**, None; **M. Petri**, AbbVie, 5, Amgen, 5, AstraZeneca, 2, 5, BMS, 5, Decision Resources, 5, GSK, 2, 5, INOVA, 5, IQVIA, 5, Janssen, 5, Eli Lilly, 2, 5, Merck EMD Serono, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5, Exagen, 2.

Abstract Number: 1020

Relationship Between Skin-related Quality of Life, Psychosocial Stress, and Race in Cutaneous Lupus Erythematosus

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SESSION INFORMATION
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Table. Multiple Regression Analysis of Three Quality of Life Skin-Related Domains (Emotions, Functioning, and Symptoms) among Patients with Cutaneous Lupus Erythematosus, by Psychosocial Stressors, Demographics, and Disease Characteristics

QoL Domain: Emotions*				
Category	**Factor**	Model 1 b (95% CI)	Model 2 b (95% CI)	Model 3 b (95% CI)
Psychosocial stressors	Stigma	**1.8 (1.5 to 2.2)**	**1.7 (1.4 to 2.1)**	**1.8 (1.4 to 2.1)**
	Perceived stress	**3.4 (2.3 to 4.6)**	**3.3 (2.1 to 4.5)**	**3.1 (1.9 to 4.3)**
Demographics	African American race (ref: white)		**12.8 (4.3 to 21.4)**	**13.2 (4.8 to 21.7)**
	Age at survey		0.04 (-0.2 to 0.3)	0.02 (-0.3 to 0.3)
	Female sex (ref: male)		5.1 (-3.7 to 13.9)	4.9 (-4.1 to 13.8)
	Education (ref: college or above)			
	High school or less		0.6 (-7.8 to 9.1)	1.1 (-7.4 to 9.5)
	Some college		-5.6 (-14.0 to 2.9)	-4.3 (-12.8 to 4.2)
	Marital Status (ref: married)			
	Widowed, separated, or divorced		-2.5 (-10.4 to 5.4)	-3.2 (-11.2 to 4.7)
	Single		-2.3 (-10.2 to 5.5)	-3.2 (-11.0 to 4.7)
	Work status (ref: out of the labor force†)		7.6 (-2.0 to 17.1)	6.83 (-2.89 to 16.55)
	Employed			
	Unemployed or disabled		**11.3 (1.6 to 21.1)**	**11.2 (1.4 to 21.0)**
Disease	Disease duration (years)			-0.1 (-0.5to 0.2)
	Diagnosis of SLE			-6.3 (-12.6 to 0.1)
QoL Domain: Functioning*				
Category	**Factor**	Model 1 b (95% CI)	Model 2 b (95% CI)	Model 3 b (95% CI)
Social	Stigma	**1.9 (1.6 to 2.2)**	**1.8 (1.5 to 2.0)**	**1.8 (1.5 to 2.1)**
	Perceived stress	**3.3 (2.3 to 4.3)**	**3.3 (2.3 to 4.3)**	**3.2 (2.1 to 4.2)**
Demographics	African American race (ref: white)		6.1 (-1.2 to 13.4)	6.4 (-1.0 to 13.7)
	Age at survey		0.08 (-0.2 to 0.3)	0.1 (-0.1 to 0.4)
	Female sex (ref: male)		2.3 (-5.2 to 9.9)	1.9 (-5.9 to 9.7)
	Education (ref: college or above)		**8.2 (0.9 to 15.5)**	**8.2 (0.9 to 15.6)**
	High school or less			
	Some college		-0.5 (-7.8 to 6.7)	-0.2 (-7.6 to 7.2)
	Marital Status (ref: married)		-0.5 (-7.3 to 6.3)	-0.7 (-7.6 to 6.2)
	Widowed, separated, or divorced			
	Single		-3.7 (-10.4 to 3.0)	-3.9 (-10.7 to 3.0)
	Work status (ref: out of the labor force†)		2.1 (-6.1 to 10.3)	2.5 (-6.0 to 10.9)
	Employed			
	Unemployed or disabled		6.5 (-1.8 to 14.9)	7.1 (-1.5 to 15.6)
Disease	Disease duration (years)			-0.2 (-0.5 to 0.1)
	Diagnosis of SLE			-1.2 (-6.8 to 4.4)
QoL Domain: Symptoms*				
Category	**Factor**	Model 1 b (95% CI)	Model 2 b (95% CI)	Model 3 b (95% CI)
Social	Stigma	**1.2 (1.0 to 1.5)**	**1.1 (0.8 to 1.4)**	**1.1 (0.8 to 1.4)**
	Perceived stress	**2.2 (1.2 to 3.2)**	**2.2 (1.1 to 3.2)**	**2.1 (1.0 to 3.2)**
Demographics	African American race (ref: white)		3.2 (-4.4 to 10.7)	3.3 (-4.3 to 11.0)
	Age at survey		0.03 (-0.2 to 0.3)	0.05 (-0.2 to 0.3)
	Female sex (ref: male)		3.8 (-4.0 to 11.5)	3.5 (-4.6 to 11.6)
	Education (ref: college or above)		4.1 (-3.4 to 11.6)	4.1 (-3.5 to 11.7)
	High school or less			
	Some college		-2.9 (-10.4 to 4.6)	-2.7 (-10.3 to 4.9)
	Marital Status (ref: married)		-0.9 (-8.0 to 6.1)	-1.0 (-8.1 to 6.1)
	Widowed, separated, or divorced			
	Single		-1.7 (-8.7 to 5.2)	-1.9 (-8.9 to 5.2)
	Work status (ref: out of the labor force†)			
	Employed		-2.3 (-10.8 to 6.2)	-2.1 (-10.8 to 6.7)
	Unemployed or disabled		3.8 (-4.8 to 12.5)	4.2 (-4.6 to 13.1)
Disease	Disease duration (years)			-0.1 (-0.4 to 0.2)
	Diagnosis of SLE			-0.7 (-6.4 to 5.0)

*Skin-related quality of life (QoL) domains: Emotions (e.g., depression, embarrassment, anger), Functioning (e.g. sleep, social, work), Symptoms (itching, burning, bleeding) were measured with Skindex-29; Skindex-29 subscale scores range 0-100; a higher score indicates worse QoL). † Includes retirees, students and homemakers. Boldface values indicate a statistically significant association. Abbreviations: b= unstandardized beta (slope of the line between the independent and the dependent variable); CI=confidence interval

Table

Background/Purpose: Chronic stress may trigger or exacerbate physiologic pathways that worsen individual health and wellbeing. Stress is associated with the development and progression of skin conditions; however, little is known about its role in the quality of life (QoL) of people with cutaneous lupus erythematosus (CLE). African American (AA)

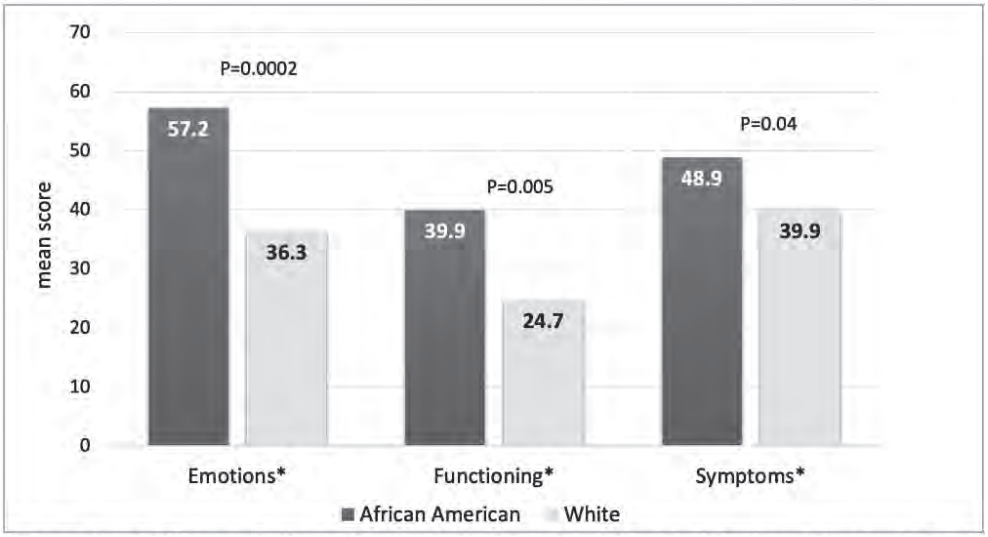

Figure. Racial Differences of Three Quality of Life Skin-related Domains (Emotions, Functioning and Symptoms) among Patients with Cutaneous Lupus Erythematosus. *Skin-related quality of life (QoL) Emotions (e.g., depression, embarrassment, anger), Functioning (e.g. sleep, social, work), and Symptoms (itching, burning, bleeding) were measured with Skindex-29; scores range 0-100; a higher score indicates worse QoL.

Figure

patients with CLE are more likely to be exposed to psychosocial stressors and may have worse QoL than whites. We examined racial differences in three skin-related QoL domains and explored the relationship between QoL, psychosocial stress, and race in patients with CLE.

Methods: We conducted a cross-sectional assessment among AA and white patients with a dermatologist-validated diagnosis of chronic or subacute CLE consented into the Georgians Organized Against Lupus (GOAL) study, a population-based cohort of individuals with lupus in the Southeastern U.S. The Skindex-29, a 5-point Likert scale was used to assess three skin-related QoL domains (emotions [e.g. depression, embarrassment, anger], functioning [e.g. sleep, social, work] and symptoms [e.g. itching, burning, bleeding]), with a higher score (range 0-100) indicating worse QoL of the domain being measured. Psychosocial stress was measured using validated patient-reported tools for disease-related stigma (PROMIS Stigma Short Form) and stress (Cohen self-perceived stress scale). For each skin-related QoL domain, three iterative multiple regression models were built to examine 1) stigma and stress, 2) these relationships controlling for demographic factors, and 3) with the addition of 2 disease-related factors.

Results: We examined 238 patients with CLE (chronic CLE (n=229); subacute CLE (n=9)), of whom 139 (58.4%) lacked systemic manifestations, and 99 (41.6%) had an associated diagnosis of systhemic lupus erythematosus (SLE). The large majority were females (n=208, 87.4%) and AAs (201, 84.5%). Mean age and disease duration were 48.5 and 11.6 years, respectively. AAs had significantly worse QoL (emotions, functioning and symptom scores) compared with whites **(Figure)**. Multivariable models revealed that both stigma and stress were independently associated with worse QoL in each domain, with little attenuation after controlling for race, other demographics, disease duration, and diagnosis of SLE **(Table).** AA race and unemployment were additional significant characteristics in the final two models for the emotions domain; for functioning lower education was significant after adjustment.

Conclusion: Our findings underscore significant racial disparities in three major domains of skin-related QoL among people with chronic or subacute CLE. We also highlighted a substantial role of stigma and stress on skin-related emotions, functioning and symptoms in this population. After controlling for multiple factors, skin-related emotions remained substantially worse in AAs, suggesting more susceptibility to psychological stress than whites. Our findings

suggest that interventions aimed at reducing stigma and managing stress may be helpful in improving the QoL of individuals with CLE and may ultimately contribute to reduced racial disparities in this population.

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Abstract Number: 1021

Organ Damage in Systemic Lupus Erythematosus Is AttribuTable More to Comorbidity (Hypertension) and Less to Socioeconomic Status

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SESSION INFORMATION
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Background/Purpose: Multiple variables are known to contribute to development of organ damage in SLE patients, including prednisone use and ethnicity. The aim of this study was to evaluate the attribuTable risk due to comorbidities (hypertension, obesity, smoking), and socioeconomic factors on the total SLICC/ACR Damage Index (DI) and its sub-items in a large longitudinal prospective SLE cohort.

Methods: We analyzed data from a longitudinal cohort of 2,436 SLE patients who met the revised ACR or SLICC classification criteria (43% African-American, 57% Caucasian and 92% female). The SLICC/ACR DI was calculated based on organ damage that occurred after the diagnosis with SLE until the last visit. The outcome variable was the total damage score and that of each organ system at the last available cohort visit. We calculated the population attribuTable risk (PAR) for the total and each organ damage. Person month files since SLE diagnosis were created. At each month, variables were created to identify if patients had damage accrual. We analyzed the data using pooled logistic regression where the outcome was binary for each organ (accrual of damage). To account for the fact that some patients could contribute multiple damage events in the analysis, the GEE approach was used in fitting the model. Each model was adjusted for sex and age at the person month. Regression coefficients from the model were then used to calculate PAR.

Results: The mean total SLICC/ACR DI was 1.9 (SD=2.3). Hypertension was the strongest contributor to damage accrual, after adjusting for age and sex (Table 1 and 2). Hypertension was responsible for 30% of total damage: 70% of renal damage and 40% of cardiovascular damage was attributed to hypertension. The importance of hypertension was true regardless of ethnicity. Obesity was a strong contributor to neuro-psychiatric (23%) and renal (15.4) damage in Caucasians. It played a less important role in African-American patients, contributing only 3% and 0.8% to neuro-psychiatric and renal damage, respectively. Obesity was protective against skin damage in both African-Americans and Caucasians. Smoking contributed mostly to cardiovascular (13%) and skin (32%) damage. (Table 1). Only about 10% of any organ damage was accounted for by socioeconomic status. The 3 socioeconomic measures, education, low income, and insurance, contributed equally to total damage in patients with SLE. Socioeconomic status played a greater role in skin (28.3%) and peripheral vascular damage (21.5%), compared to damage in the other organ systems (Table 2).

Table 1: Population attributable risk estimates for hypertension, obesity, and smoking of each organ damage accrual in all patients, African-American, and Caucasian patients, adjusting for sex and age at the person month in each model

	PAR(%) for hypertension			PAR(%) for obesity			PAR(%) for smoking		
Damage	All	African-American	Caucasian	All	African-American	Caucasian	All	African-American	Caucasian
Total	28.4	29.1	24.1	10.8	7.3	10.9	3.0	1.9	4.4
Ocular	21.7	27.0	19.1	9.5	17.3	5.3	1.7	6.3	-1.6
Neuro-psychiatric	26.1	21.8	29.4	15.4	3.0	22.9	0.5	-10.6	6.8
Renal	69.3	66.7	66.7	11.8	0.8	15.4	-0.7	1.2	-3.8
Pulmonary	22.7	18.9	15.8	15.4	17.3	8.7	-1.4	-4.5	1.4
Cardiovascular	42.4	44.0	34.3	15.0	15.5	10.6	13.2	10.8	16.0
Peripheral-vascular	31.1	43.7	23.6	3.1	2.2	2.0	4.5	4.7	4.0
Gastrointestinal	8.6	4.05	13.1	16.9	13.0	20.6	8.9	3.5	13.0
Musculoskeletal	14.3	7.9	14.2	11.2	9.5	11.2	2.5	3.4	2.4
Skin	35.2	19.9	34.7	-4.9	-15.2	-12.6	32.0	30.8	36.2
Other	9.2	8.5	7.6	13.0	16.1	10.2	0.5	2.3	-1.0

Abbreviations:
PAR=population attributable risk
*Data restricted to the period of patient's cohort participation since no BMI information were available between SLE diagnosis and cohort entry

Table 2: Population attributable risk estimates for socioeconomic factor of total and each organ system damage accrual in all patients, African-American, and Caucasian patients, adjusting for sex and age at the person month in each model

	PAR(%) for education<=12 years			PAR(%) for low income (<30,000)			PAR (%) for medical assistance insurance		
Damage	All	African American	Caucasian	All	African American	Caucasian	All	African American	Caucasian
Any	8.0	9.3	4.8	12.4	12.6	8.4	7.2	9.1	3.3
Ocular	4.1	1.7	4.7	5.4	0.7	6.4	1.9	1.5	1.2
Neuro-psychiatric	1.7	6.6	-0.6	12.6	15.9	12.0	7.0	12.4	4.3
Renal	12.0	13.0	4.1	18.8	13.2	10.8	10.7	12.2	1.3
Pulmonary	6.6	5.9	2.2	13.6	10.8	7.1	5.3	3.8	1.0
Cardiovascular	8.7	2.0	10.3	12.3	-3.4	14.2	8.3	11.1	1.5
Peripheral-vascular	21.5	20.0	21.7	15.8	18.2	13.4	15.9	19.1	13.2
Gastrointestinal	13.6	17.8	13.0	5.6	3.8	9.0	-0.7	-3.2	2.2
Musculoskeletal	9.2	13.3	3.7	13.9	17.3	8.6	10.0	10.2	7.1
Skin	28.3	25.6	18.5	29.2	12.4	26.7	25.6	19.6	19.7
Other	3.2	7.1	-0.2	10.5	28.8	2.3	4.8	11.6	-0.3

Abbreviations:
PAR=population attributable risk

Conclusion: Of the three comorbidities, hypertension had the highest PAR for total, renal and cardiovascular damage, regardless of ethnicity. Obesity had a protective effect for skin damage. The three measures of socioeconomic status were less important than hypertension. Low income appeared to attribute more PAR than education or type of insurance. The Eight Americas Study found that ethnicity, rather than socioeconomic status, explained the ethnic differences in mortality. Our study suggests that ethnicity and hypertension are the most important contributors to organ damage (the strongest predictor of mortality).

Disclosure: R. Kallas, None; **J. Li**, None; **D. Goldman**, None; **M. Petri**, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmith-Kline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark

Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5.

Abstract Number: 1022

Declining In-hospital Mortality Gap in Lupus Compared to Non-lupus Hospitalizations: A National Study

Jasvinder Singh[1] and John Cleveland[1], [1]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus is a serious, multi-system autoimmune disease that affects young people. Mortality is increased by over 2-3 fold compared to the general population. Time-trends showed a reduction in mortality in a multicentric lupus cohort from 1970 to 2001 and in a U.S. population-based lupus cohort from 1950 to 1992. In contrast, in a study using the U.S. National center for Health Statistics and National Inpatient Sample (NIS) data, in-hospital mortality was 2.9% and it increased from 1978 to 1998. Given these contradictory time-trends and the lack of contemporary data in lupus, an updated study of mortality are needed. Our objective was to assess the time-trends in in-hospital mortality rates in people with lupus hospitalized in the U.S. from 1998 to 2014, and compare it to people without lupus.

Methods: We included discharges from the Healthcare Cost and Utilization Project (HCUP) National Inpatient Sample (NIS) for 1998 through 2014, the last year of the use of the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM). The NIS is a 20% stratified sample of hospital discharges which is designed for creating national estimates.

We identified primary lupus hospitalizations based on the presence of an ICD-9-CM code of 710.0x in the primary position; this diagnostic code approach has a sensitivity of 98% and specificity of 72%.

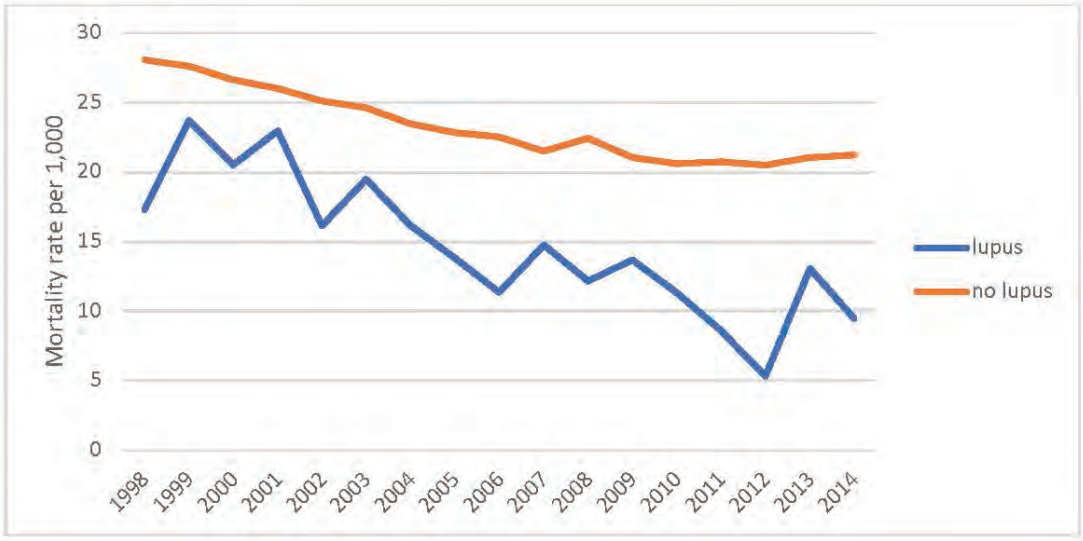
We calculated the unadjusted in-hospital mortality rates per 1,000 hospitalizations for people with versus without primary lupus hospitalizations, with the respective denominators. Rates were adjusted by age, grouped in quintiles (< 20, 20-39, 40-59, 60-79, >79) then by age and sex. We analyzed for time-trends in rates over time using Cochran Armitage test, weighted by the number of hospitalizations in each year.

Results: The 241,130 primary lupus hospitalizations in 1998-2014 included predominantly black (34.3%), young (45% were 20-39 years; mean age, 36 years) and female (86.9%) patients. Deyo-Charlson comorbidity score was ≥2 for 47%, approximately 1/3rd were receiving Medicaid and 1.5% died during the index hospitalization (**Table 1**).

Unadjusted mortality in primary lupus hospitalizations decreased by 45.2% from 17.9 in 1998 to 9.5 per 1,000 in 2014, versus a 25.9% reduction in non-lupus (28.1 to 21.2 per 1,000; **Figure 1**). Age and sex-adjusted mortality gap by lupus also decreased: primary lupus hospitalization, 17.6 per 1,000 claims in 1998 to 13.8 in 2014 (21.5% reduction), versus 15.1 per 1,000 claims in 1998 to 13.2 in 2014 in non-lupus (12.5% reduction; **Figure 1**; **Table 2**). This caused the line of mortality rates for those with primary lupus hospitalization to overlap with that of the rest of the population. The number of primary lupus hospitalizations remained fairly constant at 12-15,000 per year 1998-2014

Figure 1. Time-trends in unadjusted (A) and age- and sex-adjusted (B) in-hospital mortality rates per 1,000 population of hospitalizations in people with lupus compared to people without lupus

A. Unadjusted



B. Age- and sex- adjusted

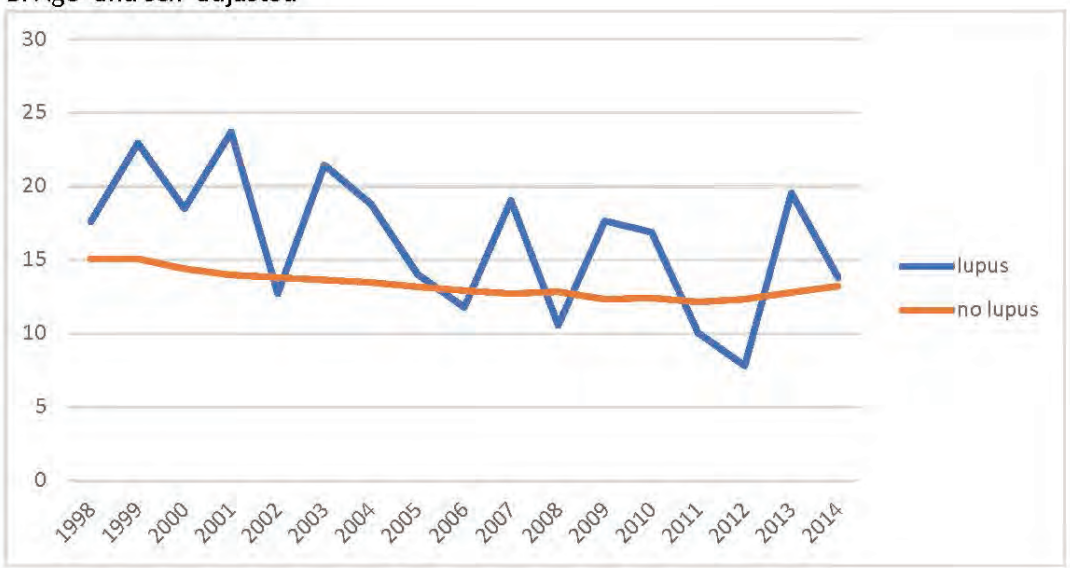


Figure legend

X-axis shows the calendar year. Y-axis shows the mortality rate per 1,000 hospitalizations with the respective denominators of primary lupus diagnosis hospitalizations for lupus and all other hospitalizations for non- lupus

Figure 1. Time-trends in unadjusted (A) and age- and sex-adjusted (B) in-hospital mortality rates per 1,000 population of hospitalizations in people with lupus compared to people without lupus A. Unadjusted B. Age- and sex- adjusted Figure legend X-axis shows the calendar year. Y-axis shows the mortality rate per 1,000 hospitalizations with the respective denominators of primary lupus diagnosis hospitalizations for lupus and all other hospitalizations for non- lupus

Table 1. Characteristics of hospitalizations in people with lupus

	People with lupus N (%), unless specified otherwise
Age in years, Mean (std error); median	36.15 (0.18); 33.8
Age category, in years	
<50 years	192,251 (79.76%)
50 – <65 years	34,660 (14.38%)
65 - <80 years	11,673 (4.84%)
≥80 years	2,464 (1.02%)
Sex	
Male	31,477 (13.06%)
Female	209,458 (86.94%)
Race	
White	61,201 (25.38%)
Black	82,667 (34.29%)
Hispanic	37,979 (15.75%)
Other/Missing	59,266 (24.58%)
Deyo-Charlson Index Score	
0	0 (0.0%)
1	128,510 (53.29%)
≥2	112,620 (46.71%)
Income Category	
0-25th percentile	66,760 (28.43%)
25-50th percentile	58,832 (25.05%)
50-75th percentile	53,690 (22.86%)
75-100th percentile	55,556 (23.66%)
Insurance	
Medicare	51,983 (21.61%)
Medicaid	68,681 (28.55%)
Private	91,736 (38.14%)
Self	16,343 (6.79%)
Other	11,803 (4.91%)
Hospital Bed size	
Small	22,226 (9.25%)
Medium	54,693 (22.76%)
Large	163,345 (67.99%)
Hospital Region	
Northeast	48,566 (20.14%)
Midwest	42,510 (17.63%)
South	100,208 (41.56%)
West	49,846 (20.67%)
Hospital Location/Teaching	
Rural	13,447 (5.60%)
Urban	66,476 (27.67%)
Urban Teaching	160,342 (66.74%)
Died during hospitalization	3,559 (1.48%)

Table 1. Characteristics of hospitalizations in people with lupus

Table 2. Comparison of Mortality rates per 1,000 hospitalized people between lupus vs. non-lupus: unadjusted based on the NIS sample; age- and age- and sex-adjusted rates based on the NIS sample and the census data

	No Lupus			Lupus		
Year	Unadjusted	Age-adjusted	Age- and sex-adjusted	Unadjusted	Age-adjusted	Age- and sex-adjusted
1998	28.1	14.4	15.1	17.3	17.3	17.6
1999	27.6	14.5	15.1	23.7	23.7	22.9
2000	26.7	13.8	14.4	20.5	19.4	18.5
2001	26.0	13.4	14.0	23.0	23.7	23.7
2002	25.1	13.2	13.8	16.1	16.1	12.7
2003	24.6	13.0	13.6	19.5	20.6	21.5
2004	23.5	12.8	13.5	16.2	17.7	18.8
2005	22.9	12.5	13.2	13.8	14.1	14.0
2006	22.5	12.3	12.9	11.4	13.2	11.8
2007	21.5	12.1	12.7	14.8	18.3	19.0
2008	22.4	12.3	12.9	12.2	12.0	10.6
2009	21.0	11.8	12.3	13.7	14.3	17.7
2010	20.6	11.9	12.4	11.3	15.9	16.9
2011	20.7	11.7	12.2	8.6	9.9	10.1
2012	20.5	11.9	12.4	5.3	6.3	7.8
2013	21.1	12.3	12.8	13.0	15.8	19.6
2014	21.2	12.7	13.2	9.5	12.4	13.8
% reduction - 1998 to 2014	24.3%	12.1%	12.5%	45.2%	28.4%	21.5%

Table 2. Comparison of Mortality rates per 1,000 hospitalized people between lupus vs. non-lupus: unadjusted based on the NIS sample; age- and age- and sex-adjusted rates based on the NIS sample and the census data

(i.e., 0.04% of all NIS claims), and the rate per 100,000 NIS claims was 40.3 in 1998-2000 versus 34.9 in 2013-2014; the annual rates of total NIS hospitalizations were also sTable 1998-2014.

The lupus to non-lupus mortality rate ratio was 1.17 in 1998 and 1.04 in 2014.

Conclusion: The reduction in in-hospital mortality in people with lupus exceeded than in non-lupus, including age- and sex-adjusted. The improved in-hospital mortality in lupus is encouraging.

Disclosure: J. Singh, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **J. Cleveland**, None.

Abstract Number: 1023

Epidemiology and Sociodemographic Distribution of Upper Gastrointestinal Bleeding Among Medicaid Beneficiaries with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Individuals with systemic lupus erythematosus (SLE) have multiple risk factors for upper gastrointestinal bleeding (UGIB), including heightened susceptibility to infection and glucocorticoid, NSAID and anticoagulant use. We aimed to examine the epidemiology and sociodemographic distribution of UGIB in a population-based SLE cohort enrolled in Medicaid, the largest U.S. insurance for low income individuals.

Methods: Using Medicaid claims data from 47 states (2000-2006) and from 29 states (2007-2010), we identified individuals 18-65 years with SLE (≥3 ICD-9 codes of 710.0 ≥30 days apart), with ≥12 months of continuous enrollment (baseline period) prior to the third SLE code (index date). Our outcome was UGIB (ED visit or hospitalization discharge diagnosis codes beginning the day following the index date). We assessed demographic factors, medication use, and comorbidities during the 12-month baseline period prior to and including the index date and determined the incidence rates (IR, 95% CI) of UGIB overall and by sociodemographics, medications and comorbidities. We used Cox regression models to compare risk (HR, 95% CI) of first UGIB by these factors. We age, sex and index date-matched SLE patients to the general Medicaid population (1:4, 2007-2010) and compared the HRs of UGIB adjusted

Table 1: Incidence rates and adjusted hazard ratios of UGIB among Medicaid beneficiaries with SLE, 2000-2010

	N	Cases	Person-years	IR (95% CI) per 1,000 person-years	HR* (95% CI)
Overall	49,489	378	169,829	2.23 (2.22, 2.24)	-
Sex					
Male	3,477	31	10,830	2.86 (2.85, 2.88)	1.21 (0.83, 1.76)
Female	46,012	347	158,999	2.18 (2.17, 2.19)	Ref
Race/Ethnicity**					
Black	19,687	186	67,066	2.77 (2.76, 2.79)	**1.43 (1.12, 1.81)**
White	18,866	122	64,496	1.89 (1.88, 1.90)	Ref
Hispanic	7,613	37	25,681	1.44 (1.44, 1.44)	0.86 (0.59, 1.26)
Other	1,576	21	6,354	3.31 (3.28, 3.33)	**1.83 (1.14, 2.92)**
Geographic Region					
Northeast	10,241	57	36,138	1.58 (1.57, 1.58)	Ref
South	19,176	183	63,297	2.89 (2.87, 2.91)	**1.58 (1.16, 2.14)**
Midwest	9,956	72	33,382	2.16 (2.15, 2.17)	1.19 (0.84, 1.70)
West	10,116	66	37,011	1.78 (1.78, 1.79)	1.16 (0.81, 1.67)
Baseline Medication Use					
Glucocorticoids	21531	216	86,173	2.51 (2.49, 2.52)	**1.34 (1.07, 1.69)**
Hydroxychloroquine	16811	119	68,824	1.73 (1.72, 1.73)	**0.69 (0.55, 0.86)**
PPI/H2 blocker	16,041	172	68,597	2.51 (2.50, 2.52)	0.95 (0.75, 1.19)
Baseline Comorbidities					
Cerebrovascular disease	3,649	46	11756	3.91 (3.88, 3.94)	**1.37 (1.00, 1.90)**
Gastritis/duodenitis	3,943	69	13423	5.14 (5.09, 5.19)	**1.89 (1.41, 2.52)**
Peptic ulcer disease/H.pylori	1,130	29	4237	6.84 (6.75, 6.94)	**1.92 (1.26, 2.91)**
Renal disease	2,909	31	7370	4.21 (4.17, 4.24)	**1.54 (1.05, 2.26)**
Alcohol use disorder	1,145	29	5120	5.66 (5.60, 5.73)	**2.21 (1.49, 3.27)**
Thromboembolic disease	2,890	39	9,338	4.18 (4.14, 4.21)	**1.54 (1.05, 2.27)**

*Multivariable Cox regression model adjusted for age, sex, race/ethnicity, region, index year, medication use (including glucocorticoids, NSAIDs, aspirin, anticoagulation, PPI/H2 blocker, SSRIs, opioids, hydroxychloroquine, and immunosuppressives), and presence of comorbidities (cardiovascular disease, cerebrovascular disease, chronic pain, diabetes mellitus, depression, GERD, gastritis/duodenitis, prior UGIB, Peptic ulcer disease/H.pylori infection, hepatitis, renal disease, venous thromboembolism, and alcohol use disorder).

**Asian and American Indian/Alaska Native race/ethnicity and UGIB history results are not shown according to CMS regulations to suppress cell sizes <11.

for sociodemographic factors, medications and comorbidities. In sensitivity analyses we excluded individuals with UGIB during the baseline period.

Results: Among 49,489 Medicaid beneficiaries with SLE, the mean (SD) age was 42.2 (11.7) years, 93% were female, 40% black, 38% white, 15% Hispanic, and 39% were from the South. The mean (SD) follow-up was 3.4 (3) years. There were 378 ED visits or hospitalizations for UGIB (IR 2.23/1000 person-years) (**Table 1**). In adjusted models, the risk of UGIB was higher among blacks compared to whites (HR 1.43, 95% CI 1.12-1.81), and in the South compared to the Northeast (HR 1.58, 95% CI 1.16-2.14). Baseline UGIB, cerebrovascular disease, gastritis/duodenitis, peptic ulcer disease/H.pylori infection, renal disease, alcohol use disorder, and glucocorticoid use were associated with higher risk, while hydroxychloroquine was associated with lower risk (HR 0.69, 95% CI 0.55-0.86). Proton pump inhibitors (PPIs) and H2 blockers were not associated with lower UGIB risk (HR 0.95, 95% CI 0.75-1.19). In medication and comorbidity-adjusted age and sex matched analyses (2007-2010), individuals with SLE had 4.28 times higher risk of UGIB (95% CI 2.39-7.68) compared to the general Medicaid population. After excluding patients with UGIB at baseline, IRs and risk factors were similar.

Conclusion: Among Medicaid beneficiaries, individuals with SLE had >4 times higher risk of UGIB compared to the general population. Black race, residence in the South, related comorbidities and glucocorticoid use were associated with higher risk. Baseline hydroxychloroquine use was associated with reduced risk of UGIB, perhaps a marker of higher quality care, while PPIs and H2 blockers were not, likely because they were prescribed to higher risk individuals. Further studies are needed to understand the efficacy of prevention strategies given this significant burden of UGIB among individuals with SLE.

Disclosure: C. Xu, None; **M. Perencevich**, None; **S. Kim**, Pfizer, 1, Roche, 1, AbbVie, 1, Bristol-Myers Squibb, 1; **K. Costenbader**, Glaxo Smith Kline, 5, UpToDate, 7, Lupus Foundation of America, 6, Neutrolis Inc, 5; **C. Feldman**, Merck, 5, Voyager Therapeutics, 5, Biogen, 8.

Abstract Number: 1024

Time Trends in the Incidence of Systemic Lupus Erythematosus: A 40-Year Study

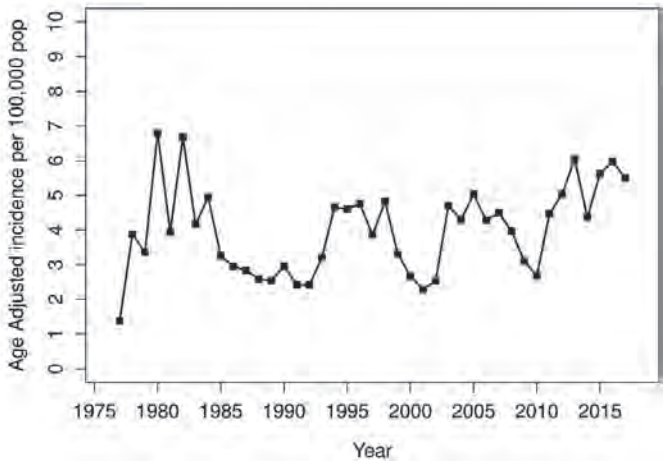
Ali Duarte-Garcia[1], Mehmet Hocaoglu[2], Shirley-Ann Osei-Onomah[3], Jesse Dabit[1], Rachel Giblon[1] and Cynthia Crowson[4], [1]Mayo Clinic, Rochester, MN, [2]University of Maryland Medical Center Midtown Campus, Baltimore, MD, [3]Mayo Clinic, Rochester, [4]Mayo Clinic, Rochester, Minnesota, USA, Rochester, MN

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Changes over time in the incidence of Systemic Lupus Erythematosus (SLE) remain uncertain. It is unclear if the variations in established SLE risk factors, such as the decline in smoking over time or the trend towards use of low-dose oral contraceptives, has had an impact in SLE incidence. We aimed to investigate secular trends in the incidence of SLE in adults from 1976-2018.

Methods: Using established population-based research infrastructure that links the medical records of all the individuals in a geographically well-defined population, we identified all the incident SLE cases from 1976-2018 using diagnostic codes for cutaneous and systemic lupus and the following laboratory measures: anti-nuclear antibodies, anti-double

Figure 1 Trends in age- adjusted systemic lupus erythematosus from 1976-2018



Trends in age- adjusted systemic lupus erythematosus from 1976-2018

Table 1. Demographics

	1976 to 1988 (N=29)	1989 to 1998 (N=30)	1999 to 2008 (N=40)	2009 to 2018 (N=53)	Total (N=152)	P-value
Age (yrs), mean (SD)	46.8 (16.70)	42.2 (15.32)	45.1 (16.80)	49.3 (16.54)	46.3 (16.45)	0.27
Female Sex, n (%)	26 (90%)	28 (93%)	30 (75%)	43 (81%)	127 (84%)	0.16
Race, n (%)						0.10
Asian	0 (0%)	1 (3%)	5 (12%)	10 (19%)	16 (11%)	
Black/African American	0 (0%)	1 (3%)	2 (5%)	5 (9%)	8 (5%)	
Caucasian/White	25 (100%)	26 (90%)	33 (82%)	37 (70%)	121 (82%)	
Other	0 (0%)	1 (3%)	0 (0%)	1 (2%)	2 (1%)	
Missing	4	1	0	0	5	
Hispanic Ethnicity, n (%)	0 (0%)	0 (0%)	2 (5%)	6 (11%)	8 (5%)	0.07

Table 1. Demographics

Table 2 Incidence rates of systemic lupus erythematosus from 1976-2018

	Female		Male		Total	
Calendar years	N	Rate* per 100,000	N	Rate* per 100,000	N	Rate** Per 100,000
1976-2018	127	6.2 (5.1, 7.3)	25	1.6 (0.9, 2.2)	152	3.9 (3.2, 4.5)
1976-1988	26	6.1 (3.5, 8.6)	3	0.9 (0.0, 1.9)	29	3.5 (2.1, 4.9)
1989-1998	28	6.4 (3.9, 8.9)	2	0.6 (0.0, 1.5)	30	3.5 (2.2, 4.9)
1999-2008	30	5.3 (3.4, 7.3)	10	2.4 (0.8, 3.9)	40	3.8 (2.6, 5.0)
2009-2018	43	7.0 (4.9, 9.1)	10	2.0 (0.8, 3.2)	53	4.5 (3.3, 5.7)

*Age-adjusted to the US White 2010 population
**Age- and sex- adjusted to the US White 2010 population

Table 2. Incidence rates of systemic lupus erythematosus from 1976-2018

stranded DNA, anti-Sm, anti-cardiolipin, anti-beta 2 glycoprotein 1 antibodies, complement, coombs and lupus anticoagulant. After an extensive medical record review, cases were classified based on the 1982 or 1997 American College of Rheumatology classification criteria, and we considered the date of meeting classification as the incidence date. Incidence rates were age- and/or sex-adjusted to the estimated 2010 white population of the US. To compute 95% confidence intervals for incidence rates, it was assumed that the number of incident cases followed a Poisson distribution.

Results: We identified 152 incident SLE cases between the years 1976 and 2018. As detailed in Table 1, the mean age was 46.3 years (SD16.4), 84% were female. The racial distribution was 5% Black, 12% Asian, 82% Caucasian while 5% were Hispanic.

The overall SLE incidence was 3.9 (95%CI: 3.2, 4.5) per 100,000. The incidence rate in females was 6.2 (95%CI: 5.1, 7.3) while in males was 1.6 (95%CI: 0.9, 2.2) per 100,000. Age- and sex- specific incidence peaked at 40-49 years for females. In males there was an upward trend in the incidence after age 50. There was an increase over the years in the proportion of incident SLE cases in minorities.

The incidence of SLE increased 29% from 3.5 (95%CI: 2.1, 4.9) in 1976-1988 to 4.5 (95%CI: 3.3, 5.7) in 2009-2018 per 100,000 (Table 2). This increase in incidence was more pronounced in males with an increase of 0.9 to 2 per 100,000. The incidence of SLE seemed to have a 10-year cyclical pattern (Figure 1).

Conclusion: Our 40-year population-based study suggests that the SLE incidence in adults had an overall 29% increase and has doubled in males over the last four decades. SLE has a cyclical pattern similar to other autoimmune diseases. It's unclear if the increase in incidence is due to improvement in awareness and detection of SLE, changes in the racial make-up of the population, changes in lupus-related risk factors or a combination thereof.

Disclosure: A. Duarte-Garcia, None; **M. Hocaoglu**, None; **S. Osei-Onomah**, None; **J. Dabit**, None; **R. Giblon**, None; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1.

Abstract Number: 1025

Prevalence Estimates for Systemic Lupus Erythematosus over Four Decades

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SESSION INFORMATION
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Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Prevalence estimates of disease are important for public health planning. The available prevalence estimates of systemic lupus erythematosus (SLE) do not account for changes in exposures or survival that may contribute to prevalence changes over time. We aimed to estimate the prevalence of SLE over four decades.

Methods: Using established population-based research infrastructure that links the medical records of all the individuals in a geographically well-defined population, we identified all the prevalent SLE cases from 1976 through 2018 using diagnostic codes for cutaneous and systemic lupus and the following laboratory measures: anti-nuclear antibodies, anti-double stranded DNA, anti-Sm, anti-cardiolipin, anti-beta 2 glycoprotein 1antibodies, complement levels, coombs and lupus anticoagulant. Given that patients may migrate to our region after the diagnosis of SLE and might had longstanding disease, we classified prevalent cases if the treating rheumatologist or nephrologist had a statement confirming SLE diagnosis in the medical record.

We estimated point prevalence for January 1 of the years 1985, 1995, 2005 and 2015. Only individuals who were residents of our region for at least a year were included in the analysis.

Table 1. Prevalence Cohorts of Lupus on January 1
Patients can be in multiple cohorts

	1985 (N=46)	1995 (N=63)	2005 (N=92)	2015 (N=131)
Age (yrs) on prevalence date, mean (SD)	47.3 (17.6)	47.1 (17.2)	48.6 (16.2)	54.6 (15.7)
Female sex	42 (91%)	58 (92%)	82 (89%)	109 (83%)
Race				
Black	0 (0%)	1 (2%)	5 (5%)	7 (5%)
Asian	0 (0%)	2 (3%)	7 (8%)	10 (8%)
Am. Indian	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Other/Mixed	0 (0%)	0 (0%)	2 (2%)	6 (5%)
White	41 (100%)	58 (95%)	77 (85%)	107 (82%)
Unknown	5	2	1	0
Hispanic Ethnicity	0 (0%)	1 (2%)	1 (1%)	8 (6%)
Years from SLE clinical dx to prevalence date, mean (SD)	9.6 (8.2)	11.6 (9.1)	12.4 (11.1)	15.1 (11.9)

Table 1. Prevalence Cohorts of Lupus Demographic Characteristics

Table 2 Prevalence rates of systemic lupus erythematosus over four decades

	Female		Male		Total	
Date (D/M/Y)	**N**	**Rate* per 100,000 (95%CI)**	**N**	**Rate* per 100,000 (95%CI)**	**N**	**Rate** per 100,000 (95%CI)**
1-1-1985	42	100.6 (68.0-133.2)	4	7.3 (0-14.8)	46	55.2 (38.1-72.4)
1-1-1995	58	109.8 (79.9-139.7)	5	10.9 (1.1-20.8)	63	61.4 (45.3-77.5)
1-1-2005	82	121.4 (94.5-148.3)	10	17.3 (6.1-28.6)	92	70.3 (55.5-85.1)
1-1-2015	109	144.9 (117.5-172.3)	22	33.6 (19.5-47.7)	131	90.8 (75.1-106.4)

*Age-adjusted to the US White 2010 population
**Age- and sex- adjusted to the US White 2010 population

Table 2. Prevalence rates of systemic lupus erythematosus over four decades

Prevalence rates were age- and/or sex-adjusted to the estimated 2010 white population of the US. To compute 95% confidence intervals for prevalence rates, it was assumed that the number of prevalent cases followed a Poisson distribution.

Results: We identified 46 prevalent cases in 1985, 63 in 1995, 92 in 2005 and 131 in 2015. As detailed in Table 1 the mean age of prevalent cases over four decades increased from 47.3 years in 1985 to 54.6 years in 2015. Race was reported consistently from 1995 onwards, the proportion of whites decreased from 95% to 82% while the proportion of males increased from 9% to 17%.

Overall, from 1985 to 2015 the prevalence increased by 64%; 55.2 per 100,000 in 1985 to 90.8 per 100,000 in 2015. In females the prevalence increased by 44% from 100.6 to 144.9 per 100,000, while in males it increased 360% from 7.3 to 33.6 per 100,000 (Table 2).

Conclusion: Results from the study show a dramatic increase in prevalence of SLE in the last four decades. These trends likely reflect improvements in survival. The biggest gains have been on the male SLE patients. It is unclear if other factors, such as an increase in SLE incidence or changes in the racial composition of the population are influencing these epidemiologic changes.

Disclosure: A. Duarte-Garcia, None; **M. Hocaoglu**, None; **S. Osei-Onomah**, None; **J. Dabit**, None; **S. Achenbach**, None; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1.

Abstract Number: 1026

The Incidence, Mortality, and Economic Burden of Potentially PrevenTable Infections in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: *Streptococcus pneumoniae*, Herpes zoster, and influenza infections are common and potentially prevenTable causes of morbidity and mortality. Vaccinations have been shown to reduce infection rates. Unfortunately, some patients are not offered or refuse these vaccinations. Additionally, younger patients are not eligible for pneumococcal and zoster vaccines based on the current age recommendations. In this, study we aimed to determine incidence, mortality, and national costs of hospital admissions for *Streptococcus pneumoniae (Strep pneumo)*, Herpes Zoster, and influenza infections in patients with systemic lupus erythematosus (SLE).

Methods: Data were abstracted from the National Inpatient Sample (NIS) Database. This database is the largest collection of inpatient admission data in the USA. It is a nationally representative sample of 20% of hospitalizations from approximately 1000 hospitals. The numbers in the databases are weighted to optimize national estimates. The NIS was searched for hospitalizations in 2016 containing ICD-10 SLE codes (M32, M32.1, M32.10, M32.11, M32.12, M32.13, M32.14, M32.15, M32.19, M32.8, and M32.9) as the principal or secondary diagnosis. We further limited the SLE cohort to hospitalizations with a principal discharge diagnosis of *Strep pneumo* infection (ICD-10 codes J13, M00.1x, A40.3, B95.3, or G00.1), Herpes Zoster (ICD 10 codes B02), and influenza (ICD 10 codes J09 or J10). The total number of discharges, age, race, length of stay (LOS), mortality and total hospital charges were recorded.

Results: Adult SLE patients had 173,765 hospitalizations in 2016. Among the SLE patients, there were 340 hospitalizations for influenza, 260 hospitalizations for zoster, and 315 hospitalizations for *Streptococcus pneumoniae* (see Table 1).

Of the SLE patients hospitalized for influenza, mean age was 56 years, 87% were female, the mean LOS was 3.6 days, aggregate LOS 1,230 days, 3% (10/340) had in hospital mortality, the mean hospital charges were $32,265 and aggregate hospital charges were $10,647,531.

Of the SLE patients hospitalized for zoster, mean age was 47 years, 77% were female, the mean LOS was 7 days, aggregate LOS 1,820 days, 0% (0/260) had in hospital mortality, the mean hospital charges were $53,988. and aggregate hospital charges were $ 14,036,866.

Of the SLE patients hospitalized for *Strep pneumo* infections, the mean age was 49 years, 87% were female, the mean LOS was 7.3 days, aggregate LOS 2,315 days, 9.5% (30/315) had in hospital mortality, the mean hospital charges were $ 87,893, and the aggregate hospital charges were $27,246,719. These numbers do not account for

Table 1

	Influenza	*Strep pneumo*	Zoster
# of Hospitalizations	340	315	260
Mean age (yrs)	56	49	47
Female (%)	87%	87%	77%
Mean LOS	3.6 days	7.3 days	7 days
Aggregate LOS	1,230 days	2,315 days	1,820 days
Mortality	3% (10/340)	9.5% (30/315)	0%
Mean Hospital Charges	$32,265	$87,893	$53,988
Aggregate Hospital Charges	$10,647,531	$27,246,719	$14,036,866

outpatient or emergency department visits. Additionally, hospital charges are known to be higher than allowed or real charges.

Conclusion: Our analysis shows influenza, zoster, and *Strep pneumo* infections constituted only 0.5% of SLE hospitalizations but in-hospital mortality was high. Additionally, the economic burden of these infections was large with aggregate national hospital charges totaling over $51,931,116 and an aggregate LOS of 5,365 days. Universal vaccinations programs in SLE patients should be studied to reduce hospitalizations, cost, morbidity, and mortality.

Disclosure: E. Gauto-Mariotti, None; **S. Kambhatla**, None; **A. Manadan**, None.

Abstract Number: 1027

The National Prevalence of Clinically Diagnosed Psoriatic Arthritis in Sweden 2017

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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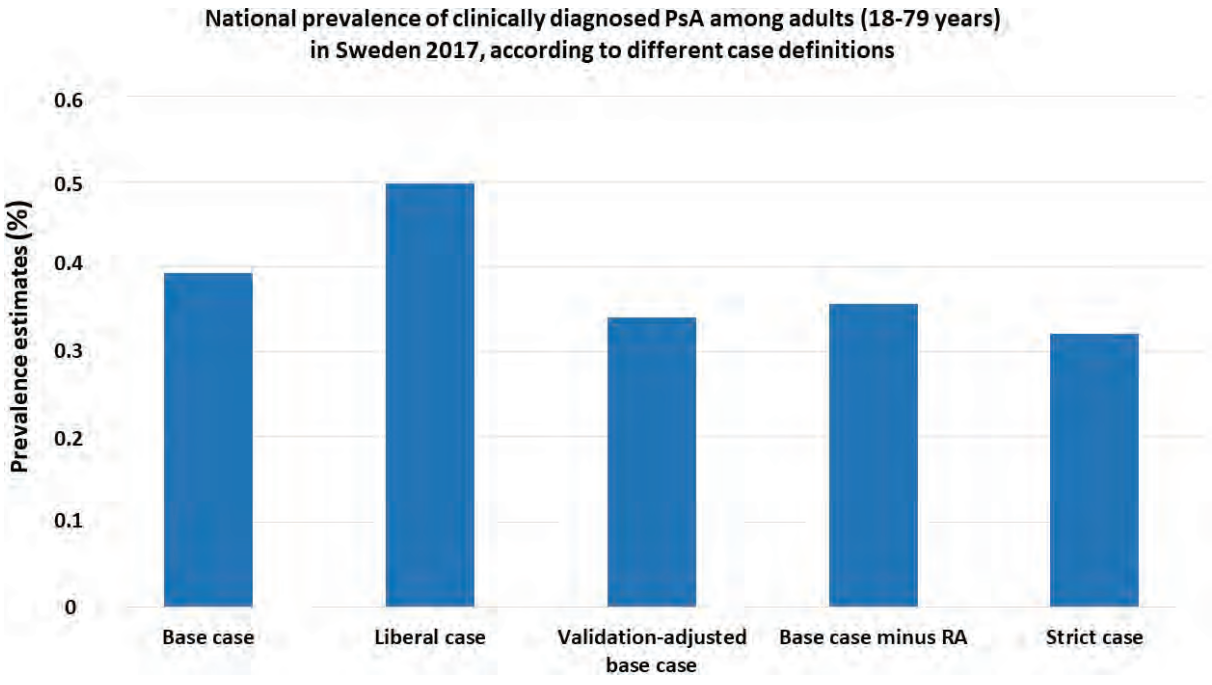
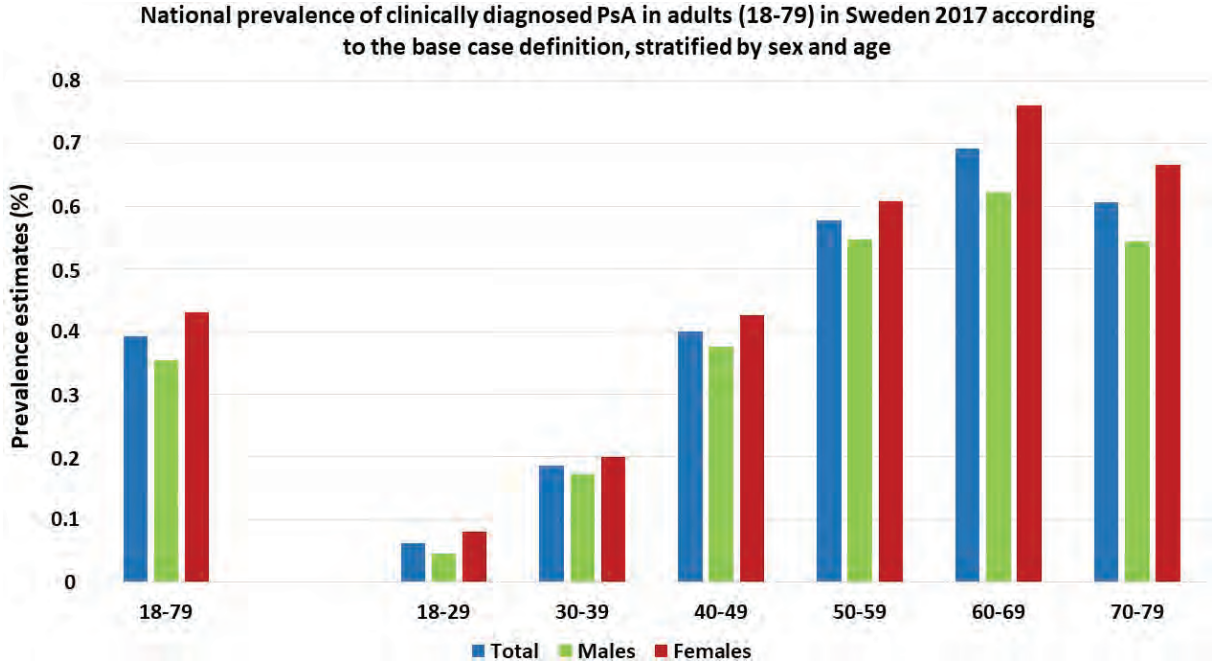
Session Time: 9:00AM–11:00AM

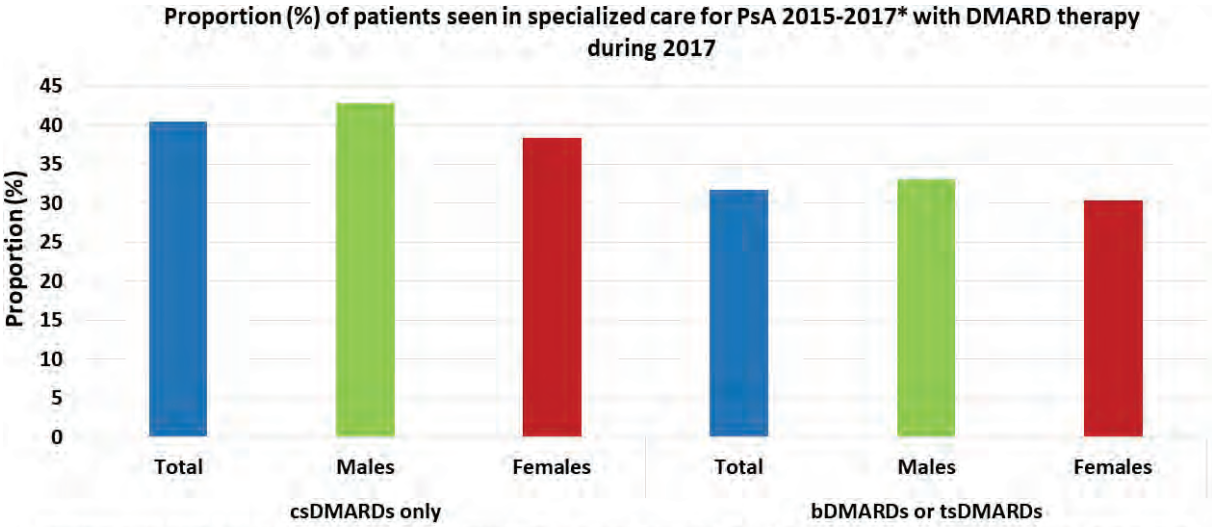
Background/Purpose: Reported prevalence estimates of psoriatic arthritis (PsA) vary considerably, with few nationwide Figures. This study aimed to estimate the prevalence of PsA among adults (18-79 years (y)) in Sweden 2017, overall, stratified by sex/age/education, and with contemporary need of specialized care, respectively. In the latter group, the proportion treated with disease-modifying anti-rheumatic drugs (DMARDs) was also assessed.

Methods: All individuals, 18-79y, alive and residing in Sweden on December 31, 2017, who had been seen in specialized care for clinically diagnosed PsA 1964-2017 were identified from 2 separate, overlapping sources: 1) individuals with ≥1 registered ICD diagnosis of PsA from out-/inpatient visits in the Swedish National Patient Register (NPR); 2) individuals registered with PsA in the Swedish Rheumatology Quality Register (SRQ). Data on the total Swedish population 2017, demographics, education (for individuals ≥30y), and treatments were retrieved from other registers. The base case (BC) PsA definition for prevalence estimation was ≥1 main ICD diagnosis of PsA (ICD-8:696.00; ICD-9:696A; ICD-10:L40.5/M07.0-M07.3) from a department of rheumatology or internal medicine (IM) in NPR, or a PsA diagnosis in SRQ. Sensitivity analysis definitions were: A) Liberal: ≥1 main or secondary ICD diagnosis of PsA from any department in NPR, or a PsA diagnosis in SRQ; B) As BC, but reducing the number of cases in line with a prior validation of the BC definition in which 86% of 400 cases fulfilled PsA classification criteria; C) As BC, but excluding cases with ≥1 main ICD diagnosis of rheumatoid arthritis from rheumatology or IM in NPR; D) Strict: ≥2 ICD diagnoses of PsA in NPR, of which ≥1 as main diagnosis from rheumatology or IM. Furthermore, the prevalence of PsA with contemporary need of specialized care was estimated by restricting the BC definition to 2015-2017 (≥1 main ICD diagnosis of PsA from rheumatology or IM in NPR or ≥1 visit in SRQ 2015-2017), and the proportion of this population with DMARD therapy in 2017 was assessed.

Results: A total of 29 359 cases, 18-79y, alive and residing in Sweden on December 31, 2017, with clinically diagnosed PsA according to the BC definition were identified, resulting in a national, prevalence of PsA in the adult (18-79y) population of 0.39%. Corresponding sensitivity analysis estimates ranged from 0.32-0.50%, with a validation-adjusted BC prevalence of 0.34% (**Figure 1**). Irrespective of age group, the PsA prevalence was numerically higher among females (**Figure 2**). Higher education was associated with numerically lower PsA prevalence (>12y education: 0.38%; 10-12y:0.58%; ≤9y:0.54%, in adults ≥30y; BC PsA definition). The prevalence of PsA seen in







*Defined as ≥1 main ICD diagnosis of PsA from rheumatology or internal medicine in NPR or ≥1 visit in SRQ 2015-2017; constituting 62% of all prevalent PsA patients according to the base case definition.
csDMARDs: Sulfasalazine, Leflunomide, Ciclosporine, Azathioprine, Methotrexate, Sodium aurothiomalate, Auranofin, Chloroquine, Hydroxychloroquine
bDMARDs: Adalimumab, Certolizumab pegol, Etanercept, Golimumab, Infliximab, Abatacept, Secukinumab, Ustekinumab
tsDMARDs: Apremilast.

specialized care 2015-2017 was estimated at 0.24%. In this population, 32% received biologic or targeted synthetic DMARDs, and 41% conventional synthetic DMARDs only, during 2017 (**Figure 3**).

Conclusion: The national prevalence of clinically diagnosed PsA in the adult (18-79y) Swedish population in 2017 was estimated at around 0.35% (0.32-0.39% across most definitions). Among the 62% of these patients who were seen in specialized care for PsA during the last 3 years of our study period, almost 3/4 received DMARD therapy in 2017.

Disclosure: S. Exarchou, Novartis, 1; **J. K. Wallman**, Abbvie, 5, Celgene, 5, Eli Lilly, 5, Novartis, 5, UCB Pharma, 5; **D. Di Giuseppe**, None; **G. Alenius**, None; **E. Klingberg**, Roche, 1, Novartis, 1, Eli Lilly, 1; **V. Sigurdardottir**, Novartis, 1; **S. Wedrén**, None; **U. Lindström**, None; **C. Turesson**, Roche, 1, 2, Abbvie, 1, Pfizer, 1, Bristol-Myers Squibb, 1, 2; **L. Jacobsson**, Abbvie, 1, Eli Lilly, 1, Janssen, 1, Novartis, 1, Pfizer, 1; **J. Askling**, Abbvie, 1, BMS, 1, Eli Lilly, 1, Merck, 1, Pfizer, 1, Roche, 1, Samsung Bioepis, 1, Sanofi, 1, UCB Pharma, 1.

Abstract Number: 1028

Probabilistic Linkage of a Cohort of Individuals with Symptoms Suggestive of Early Spondyloarthritis and the French National Healthcare Database

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SESSION INFORMATION

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Background/Purpose: DESIR is the French cohort of patients with symptoms suggestive of early axial Spondyloarthritis (axSpA). Our objective was to enrich this cohort with claims and hospitalization data from the French national healthcare database (Système National des Données de Santé, SNDS) in order to provide opportunities to answer new research questions related to care consumption, the occurrence of health outcomes and costs and enhance data completeness.

Methods: We carried out a probabilistic linkage of the DESIR cohort database (N=703) and the SNDS (N= 387,463 individuals, sharing the same sex, birth month and year with DESIR patients). DESIR is a cohort of 708 individuals aged 18 to 60 years, included from 2007 to 2010 in 25 centers in France, of whom 703 were not opposed to this linkage. The probabilistic linkage was performed with the Fellegi and Sunter method, using 29 variables collected between baseline and the 24th month of follow-up. Matching variables included area of residence, attending physician, sacroiliac radiographs and MRI dates, blood test dates and treatment by a Disease Modifying Anti-Rheumatic Drug. We calculated for each DESIR-SNDS potential pair of patients a matching score that summed the matching probabilities calculated across all selected variables. Distributions of the highest matching scores for each DESIR patient and for other matching scores were displayed graphically and a cutoff was chosen visually. Pairs with highest matching score for each individual were matched if they exceed this cutoff. To assess the quality of the linkage we compared individuals' characteristics between matched and unmatched individuals. P values were computed with T.test, Chi-square test, Wilcoxon test or Fisher exact test.

Table 1. Characteristics of matched and unmatched individuals

N(%) mean ± SD N= 703	Unmatched N=109 (15,5)	Matched N=594 (84,5)	P-value
Age	31,1 ± 8,32	34,2 ± 8,61	0,0005 †
Men	46 (12,2)	330 (87,8)	0,0137§
BASDAI (/100)	44,6 ± 19,4	44,7 ± 20,1	0,9495*
BASFI (/ 100)	28,7 ± 22,0	30,7 ± 22,9	0,4359*
HLA-B27 positivity	74 (18,2)	333 (81,8)	0,0296§
MRI sacroiliac joint inflammation (ASAS criteria)	39 (16,7)	195 (83,3)	0,4896§
Radiographic sacroiliitis (mNY criteria)	18 (16,2)	93 (83,8)	0,7554§
Loss of follow up by year 5	32 (15,9)	169 (84,1)	0,9384§
Exit from study due to other diagnosis by year 5	2 (8)	23 (92)	0,4044**
TNF treatment by year 5	38 (14,8)	218 (85,2)	0,7962§

P value are computed with T.test (†), Chi-square test (§), Wilcoxon test (*) or Fisher exact test (**)

Results: A total of 594 (84%) were matched. They were, on average, 3 years older than unmatched individuals, were more likely men, and less likely to be HLA-B27 positive. No significant difference was observed between matched and unmatched on baseline clinical or radiographic characteristics: BASDAI and BASFI scores, MRI sacroiliac joint inflammation (ASAS criteria) neither among anti-TNF treatment during the first 5 years of follow-up. Finally, rate of loss to follow up by year 5 were similar in both groups while rate of exit from the DESIR cohort due to other diagnosis than axSpA was slightly higher but not significantly so, among matched vs. unmatched.

Conclusion: It was possible to perform a matching for 84% of patients. No difference was observed on clinical or radiographic characteristics nor treatment between matched and unmatched individuals, thus this cohort issued from the linkage can be used to study outcomes among patients with symptoms suggestive of early axSpA. A possible bias related to both male, older and HLA-B27 positivity over-representation should be discussed in any future study using this linked cohort. In a next step, a deterministic linkage will be performed using a unique individual identifier to validate this linkage and capture remaining unmatched individuals.

Disclosure: A. Ajrouche, None; **C. Estellat**, None; **C. Lopez-Medina**, None; **A. Molto**, ABBVIE, 5, BMS, 5, 8, LILLY, 5, NOVARTIS, 5, 8, UCB, 5, 8, GILEAD, 5; **A. Ruyssen Witrand**, None; **P. Claudepierre**, Abbvie, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Merk, 5, 8, novartis, 5, 8, Lilly, 5, 8, Janssen, 5, 8, BMS, 5, 8; **F. Tubach**, None; **L. Gossec**, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8; **M. Dougados**, Pfizer, 5, 8, AbbVie, 5, 8, Roche, 5, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, 8, Novartis, 5, 8, Sanofi, 5, 8, Biogen, 5, 8, Merck Sharp & Dohme, 5, 8, UCB Pharma, 5, 8.

Abstract Number: 1029

Clinical Characteristics of Patients with Axial Spondyloarthritis in China: Results from the ChinaAS Registry

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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Background/Purpose: The ChinaAS is a nationwide, multicenter registry of patients with axial spondyloarthritis (SpA) in China to facilitate research in epidemiology, pathogenesis, diagnosis and treatment of Chinese patients with axial SpA. The objective of this study is to describe the clinical manifestation of patients registered between July 11th, 2018 and July 10th, 2019, and compare the characteristics of patients who fulfill ASAS criteria and patients who fulfill modified New York criteria for ankylosing spondylitis (AS).

Methods: Patients with a clinical diagnosis of AS or axial SpA were enrolled into the registry from 31 provinces in China. Demographics, clinical manifestations, HLA-B27 status, acute phase reactants, pelvis imagings, patient reported outcomes, medication use, and comorbidities were collected at baseline. Patients, who were enrolled between July 11th,2018 and July 10th, 2019, and fulfilled either ASAS axial SpA criteria or modified New York criteria for AS, were included in the study. Disease duration was defined as the difference between age of diagnosis and age of onset. Early axial SpA was defined as disease duration of less than 3 years. Descriptive statistics were used to described clinical characteristics of enrolled patients.

Results: A total of 3806 patients were included in the current analysis, including 3545 patients who fulfill modified New York criteria for AS, 3241 patients who fulfill ASAS criteria for axial SpA, and 3116 patients who fulfill ASAS criteria for axial SpA imaging arm. Mean age at enrollment was 33 years, 73% were male, about 80% were HLA-B27 positive, and median disease duration was 4 years (Table 1). Among these patients, 2384 patients had complete set of HLA-B27, baseline pelvis radiograph or CT, and baseline pelvis MRI. Nineteen hundred and forty two patients had radiographic axial SpA, with 98% also fulfilled AS criteria (Figure 1). In patients with early SpA (N = 924), majority (N=861, 93.2%) had sacroiliitis on pelvis radiograph or CT, 37 patients (4.0%) had sacroiliitis on MRI but not on pelvis radiograph or CT, and 26 patients (2.8%) were in the clinical arm without sacroiliitis on imaging studies.

Conclusion: In the ChinaAS registry, 3806 axial SpA patients were enrolled from July 11th, 2018 and July 10th, 2019. Majority of patients (98%) with radiographic axial SpA also fulfilled modified New York criteria for AS. In early axial SpA patients, more than 90% of them had a sacroiliitis on pelvis radiograph or CT.

	Ankylosing spondylitis (N = 3545)	Axial spondyloarthritis **(N = 3241)**	**Axial SpA imaging arm (N = 3116)**
Age, years, mean (SD)	33.94(11.54)	33.30(10.89)	33.36(10.84)
Male, n (%)	2552(71.99)	2366(73.00)	2281(73.20)
Age at onset, years, mean (SD)	27.49(10.96)	26.63(9.89)	26.65(9.89)
Age at diagnosis, years, mean (SD)	30.59(11.59)	29.82(10.75)	29.87(10.75)
Disease duration, years, median (Q1, Q3)	4.00(1.00, 10.00)	4.00(1.00, 10.00)	4.00(2.00, 10.00)
Peripheral arthritis, n (%)	1138(32.10)	1019(31.44)	975(31.29)
Enthesitis, n (%)	2439(68.84)	2213(68.30)	2144(68.83)
Extra-articular manifestations, n (%)	435(12.27)	403(12.43)	386(12.39)
• Psoriasis, n (%)	40(1.13)	35(1.08)	35(1.12)
• Uveitis, n (%)	359(10.13)	337(10.40)	321(10.30)
• IBD, n (%)	70(1.97)	61(1.88)	60(1.93)
HLA-B27 positivity, n (%)	2835(79.97)	2672(82.44)	2547(81.74)
hsCRP, mg/L, median (Q1, Q3)	10.00(3.10, 23.36)	9.84(3.03, 23.11)	9.93(3.13, 23.38)
BASDAI (0-10), mean (SD)	3.79(2.20)	3.76(2.21)	3.78(2.21)
BASFI (0-10), median (Q1, Q3)	2.30(0.70, 4.50)	2.10(0.60, 4.30)	2.00(0.60, 4.30)
Total back pain (0-10), mean (SD)	3.90(2.59)	3.89(2.59)	3.92(2.60)
Patient Global Assessment (0-10), mean (SD)	4.21(2.54)	4.19(2.55)	4.22(2.55)
ASDAS-CRP, mean (SD)	2.70(1.21)	2.69(1.23)	2.71(1.23)

Table 1. Baseline characteristics of patients in the ChinaAS registry. SD: standard deviation; IBD: inflammatory bowel disease; hsCRP: high sensitivity C-reactive protein; BASDAI: Bath ankylosing spondylitis disease activity index; BASFI: Bath ankylosing spondylitis functional index; ASDAS: ankylosing spondylitis disease activity score.

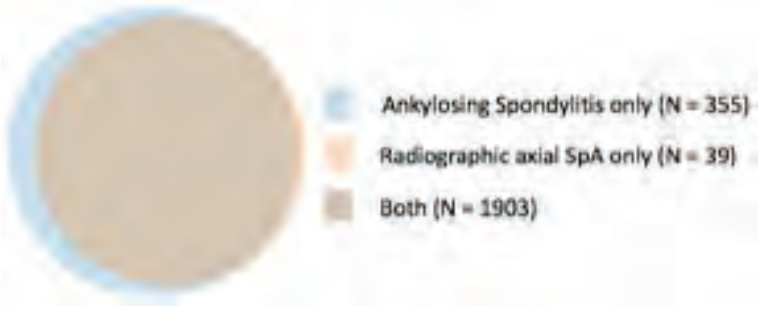

Figure 1. Venn diagram of ankylosing spondylitis and radiographic axial spondyloarthritis in patients with complete sets of HLA-B27, pelvis radiograph/CT and pelvis MRI.

Disclosure: J. Su, None; **R. Wang**, Eli Lilly, 1, Novartis, 1; **P. Zhu**, None; **Y. Wang**, None; **S. Zhang**, None; **L. Peng**, None; **M. Yang**, None; **L. Lei**, None; **L. Qin**, None; **M. Li**, None; **X. Zeng**, None.

Abstract Number: 1030

Pain Medication Use Among Ankylosing Spondylitis and Psoriatic Arthritis Patients Before and After Initiation of Biologic Therapy

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Background/Purpose: Pain is a common symptom among ankylosing spondylitis (AS) and psoriatic arthritis (PsA) patients and can be debilitating, making pain management an integral part of caring for these patients. The purpose of this analysis was to describe pain medication utilization of patients with AS and PsA over 12-months before and after initiation of a biologic.

Methods: This is a retrospective observational cohort study using administrative claims from the HealthCore Integrated Research Database (HIRD®). Patients newly diagnosed with AS or PsA who initiated a biologic from 1/1/2014 to 7/31/2017 were included. Medications that could be used for pain were assessed 12-months prior and 12-months after biologic initiation. Demographics, baseline clinical characteristics, and pain medication use were described using descriptive statistics. Frequencies and percentages were provided for categorical variables and means, standard deviations, and medians were presented for continuous measures. The differences in pain medication use were assessed using McNemar's Test for categorical variables or Wilcoxon signed-rank test for continuous variables as appropriate for comparing before and after biologic initiation.

Results: 188 AS patients and 921 PsA patients were included in this analysis. AS patients had a mean age of 41.6 years, 55.3% were male, and the mean time from diagnosis to biologic initiation was 4.0 months. PsA patients had a mean age of 48.0 years, 49.3% were male, and the mean time from diagnosis to biologic initiation was 6.6 months. Prior to biologic initiation, 68.1% of AS patients were prescribed NSAIDs, 56.4% glucocorticoids, 42.6% opioids, and 41.0% neuromodulators. Similarly, prior to biologic initiation, 51.1% of PsA patients were receiving NSAIDs, 57.4% glucocorticoids, 38.1% opioids, 38.9% neuromodulators, and 4.3% topical pain medication. Twelve months after biologic initiation, use of NSAIDs (AS: 68.1% vs. 51.1%; PsA: 51.1% vs. 42.5%) and glucocorticoids (AS: 56.4% vs. 41.5%; PsA: 57.4% vs. 46.9%) and opioids (AS: 42.6% vs. 36.2%; PsA: 38.1% vs. 33.8%) significantly decreased among AS and PsA patients. Use of neuromodulators did not significantly change from the 12-months prior to the 12-months after biologic initiation among AS (41.0% vs. 40.4%) and PsA (38.9% vs. 39.8%) patients.

Conclusion: Use of pain medications such as NSAIDs, glucocorticoids, opioids, and neuromodulators are common among AS and PsA patients. Though rates of NSAIDs and glucocorticoids decreased after the initiation of biologics, over 40% of AS and PsA patients were still receiving these medications 12-months after initiation of a biologic. In addition, over 30% of AS and PsA patients were still receiving opioids 12-months after initiation of a biologic. The results suggest that AS and PsA patients still require pain medication even after initiating biologics.

Table 1. Demographic Characteristics at Diagnosis Index Date

	AS	PsA
Number of patients, n	188	921
Age on index date (years)		
Mean (SD)	41.6 (13.19)	48.0 (11.87)
Median (IQR)	41.5 (18.0)	49.0 (17.0)
Age categories, n (%)		
18-34	62 (33.0)	140 (15.2)
35-44	49 (26.1)	192 (20.8)
45-54	41 (21.8)	296 (32.1)
55-64	30 (16.0)	233 (25.3)
≥ 65	*	60 (6.5)
Sex, n (%)		
Male	104 (55.3)	454 (49.3)
Female	84 (44.7)	467 (50.7)
Residence Region, n (%)		
Northeast	27 (14.4)	161 (17.5)
Midwest	46 (24.5)	220 (23.9)
South	73 (38.8)	348 (37.8)
West	42 (22.3)	189 (20.5)
Other	0 (0)	*
Plan type, n (%)		
HMO	47 (25.0)	184 (20.0)
PPO	102 (54.3)	594 (64.5)
CDHP	39 (20.7)	143 (15.5)
Medicare Advantage or Supplement coverage, n (%)		
Yes	*	49 (5.3)
Index diagnosis, n (%)		
2014	48 (25.5)	238 (25.8)
2015	70 (37.2)	284 (30.8)
2016	50 (26.6)	248 (26.9)
2017	20 (10.6)	151 (16.4)
Time from index diagnosis to advanced therapy initiation date (months)		
Mean (SD)	4.0 (7.28)	6.6 (8.22)
Median (IQR)	1.3 (3.2)	3.4 (8.2)
Provider specialty on index date, n (%)		
Rheumatologist	102 (54.3)	401 (43.5)
Nephrologist	*	*
Dermatologist	0 (0)	127 (13.8)
Primary care physician	14 (7.4)	97 (10.5)
Others	71 (37.8)	295 (32.0)

* denotes n ≤ 10, which was blinded for privacy

Acronyms: SD: standard deviation; IQR: interquartile range; HMO: Health Maintenance Organization; PPO: Provider Preferred Organization; CDHP: Consumer Driven Health Products

Table 2. Pain medication use 12-months before and 12-months after biologic initiation

	AS		p-value	PsA		p-value
	12M before biologic therapy initiation	12M after biologic therapy initiation		12M before biologic therapy initiation	12M after biologic therapy initiation	
Number of patients, n	188	188		921	921	
Nonsteroidal anti-inflammatory drugs (NSAIDs)						
NSAIDs use, n (%)	128 (68.1)	96 (51.1)	<0.001	471 (51.1)	391 (42.5)	<0.001
NSAIDs fills, mean (SD)	2.7 (3.35)	2.3 (3.31)	0.084	2.0 (3.15)	1.8 (3.30)	0.003
PDC* of all NSAIDs, mean (SD)	0.39 (0.378)	0.24 (0.327)	<0.001	0.26 (0.349)	0.19 (0.311)	<0.001
Glucocorticoids steroids						
Glucocorticoids steroids use, n (%)	106 (56.4)	78 (41.5)	0.001	529 (57.4)	432 (46.9)	<0.001
Glucocorticoids steroids fills, mean (SD)	1.5 (1.99)	1.0 (1.69)	<0.001	1.7 (2.36)	1.3 (2.06)	<0.001
Route of administration						
Oral, n (%)	83 (44.1)	51 (27.1)	<0.001	391 (42.5)	299 (32.5)	<0.001
Intravenous, n (%)	58 (30.9)	48 (25.5)	0.174	307 (33.3)	255 (27.7)	0.001
PDC of all steroids, mean (SD)	0.16 (0.259)	0.07 (0.151)	<0.001	0.15 (0.239)	0.10 (0.194)	<0.001
Non-narcotic analgesics						
Non-narcotic analgesics use, n (%)	*	*	0.317	23 (2.5)	21 (2.3)	0.705
Non-narcotic analgesics fills, mean (SD)	0.0 (0.31)	0.0 (0.66)	0.750	0.1 (1.11)	0.1 (0.92)	0.664
Opioids						
Opioids use, n (%)	80 (42.6)	68 (36.2)	0.052	351 (38.1)	311 (33.8)	0.013
Opioids fills, mean (SD)	2.3 (4.77)	2.3 (5.22)	0.550	1.7 (3.70)	1.6 (3.65)	0.058
Chronic opioid use (≥ 180 days), n (%)	13 (6.9)	19 (10.1)	0.034	61 (6.6)	65 (7.1)	0.465
PDC of all opioids, mean (SD)	0.13 (0.260)	0.13 (0.275)	0.794	0.11 (0.243)	0.09 (0.229)	<0.001
Neuromodulators (anti-depressants, anticonvulsants, muscle relaxants)						
Neuromodulators use, n (%)	77 (41.0)	76 (40.4)	0.881	358 (38.9)	367 (39.8)	0.475
Neuromodulators fills, mean (SD)	2.7 (5.68)	3.0 (6.50)	0.461	3.0 (5.78)	3.3 (6.15)	0.035
Topical pain medications (diclofenac, capsaicin)						
Topical medication use, n (%)	*	*	1.000	40 (4.3)	46 (5.0)	0.467
Topical medication fills, mean (SD)	0.1 (0.75)	0.1 (1.00)	0.235	0.1 (0.52)	0.1 (0.61)	0.216

* denotes n ≤ 10, which was blinded for privacy

PDC= proportion of days covered measured by the number of days with drug on-hand divided by the number of days in the specified time period.

Disclosure: T. Hunter, Eli Lilly and Company, 1, 3; **C. Nguyen**, None; **J. Birt**, Eli Lilly and Company, 1, 3; **J. Smith**, HealthCore, Inc., 3; **M. Shan**, Eli Lilly and Company, 3; **H. Tan**, None; **J. Lisse**, Eli Lilly and Company, 1, 3; **K. Isenberg**, Anthem, 1, 3, Anthem, 1, 3.

Abstract Number: 1031

Real World Treatment Patterns Among Patients with Psoriatic Arthritis Treated with Ixekizumab

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a systemic condition estimated to affect 0.05%-0.25% of the United States (US)[1] population. With approval of ixekizumab (a selectively binding IL-17 inhibitor biologic) for treatment of PsA, there is need to understand its treatment patterns in the real world. The current study aimed to describe adherence, persistence, discontinuation, switching, and dosing among patients with PsA newly initiating ixekizumab (IXE).

Methods: The IBM MarketScan administrative claims databases were used to select adults (≥18 years) initiating IXE between 1/1/2016- 7/31/2019 for this retrospective study (earliest IXE claim = index). Eligible patients had ≥1 PsA diagnosis (ICD-9 696.0x or ICD-10 L40.50-L4.059) during the 12 months preceding index and remained continuously enrolled for 12 months following (follow-up period) index. Adherence (measured by proportion of days covered [PDC]) to IXE, persistence on IXE (< 60 day gap with sensitivity analysis using a < 45 and < 90 day gap), discontinuation of IXE (≥90 day gap), and switching (discontinuation of IXE followed by a claim of a different biologic or targeted synthetic disease-modifying anti-rheumatic drug [tsDMARD] with ≥30 as monotherapy) patterns were reported over the

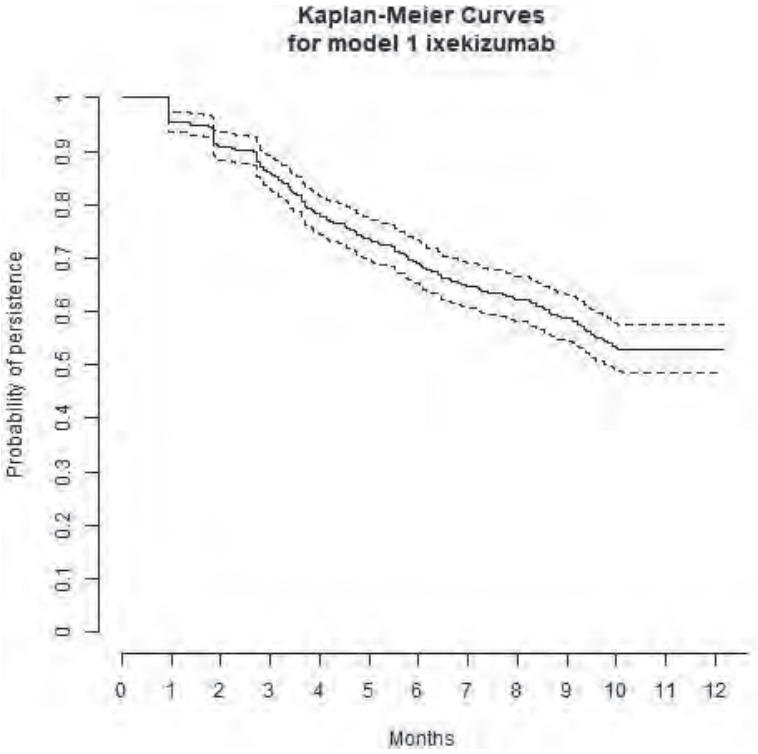

Figure 1. Time to Non-Persistence (60-day gap)

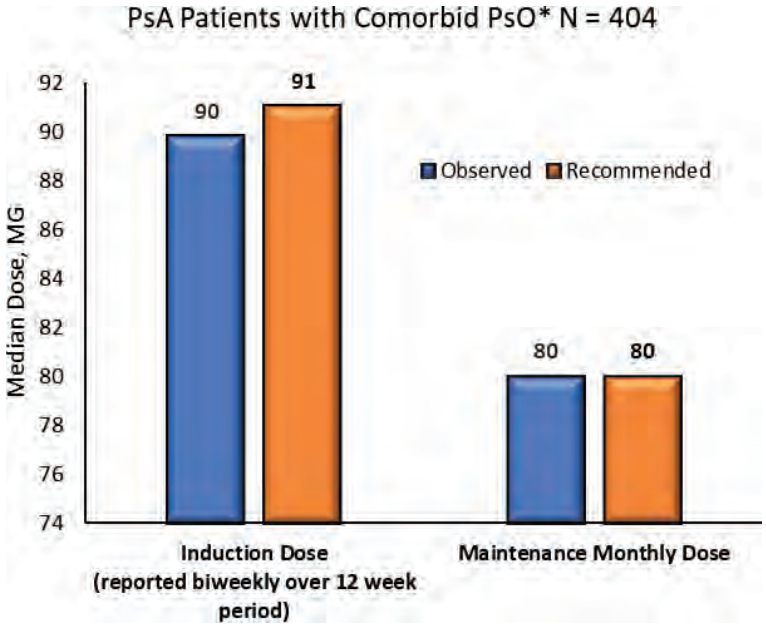

Figure 2a. IXE Dose* Observed in Real World Setting versus Recommended (based on prescribing information for FDA approved dose) Over 12 Months Following Initiation *For patients with comorbid PsO, dose was measured during an induction period of 12 weeks and then during maintenance starting at week 14 and continuing until discontinuation or end of the 12-month follow-up period. Recommended dose based on prescribing information for the FDA approved dose was defined as 160mg at week zero followed by 80mg at weeks 2,4,5,8,10 and 12 (which was equivalent to a dose of 91mg biweekly over the entire induction period).

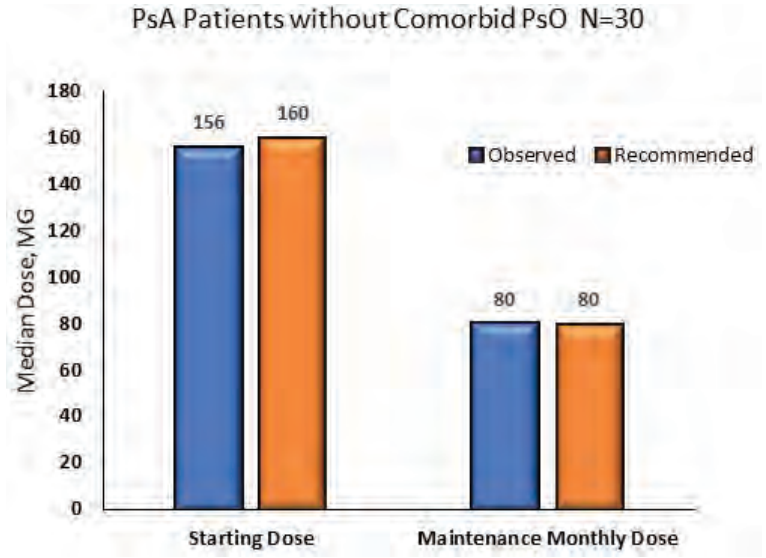

Figure 2b. IXE Dose* Observed in Real World Setting versus Recommended (based on prescribing information for FDA approved dose) Over 12 Months Following Initiation

12-month follow-up period. IXE dose (calculated by multiplying the drug strength by the quantity and dividing by the days of supply for each claim) was reported during the starting/induction and maintenance phase for patients eligible for dosing calculations with and without comorbid psoriasis (PSO).

Results: There were 496 PsA patients initiating IXE eligible for analysis. Mean age was 51.1 (SD 9.8) years, 50.4% were female, and 93.4% had comorbid PsO. Most patients (91.9%) were biologic or tsDMARD experienced, and the

average number of different biologic or tsDMARDs prior to starting IXE was 1.4 (SD 0.06). The most common drugs used prior to IXE were secukinumab, adalimumab, and ustekinumab (34.9%, 28.8%, and 21.4% respectively). Over the 12-month follow-up, 52.8% (using < 60-day gap) remained persistent (47.0% using < 45 day gap and 61.3% using < 90 day gap) on IXE (average of 262 days [SD 123] of persistence; Figure 1). Of all 496 IXE patients, 38.7% discontinued (≥90 day gap), 13.5% had no other treatment, 4.6% restarted IXE, and 20.6% switched to a new biologic/tsDMARD within the 12-month follow-up period.

Adherence to IXE prior to discontinuation was high (mean PDC 0.85 [SD 0.12]) with 70.6% of patients identified as highly adherent (i.e. PDC ≥0.80) to therapy. Dose values during the starting/induction and maintenance periods were consistent with prescribing information for patients with and without comorbid PsO (Figure 2).

Conclusion: Results from this real-world analysis suggest that among PsA patients treated with ixekizumab, 91.9% had previously experienced inefficacy or intolerance to different biologics including other IL-17A and tsDMARD. 52.8% remained persistent and 20.6% switched to a new agent over 12 months of follow-up. Dosing is consistent with prescribing recommendations for patients with and without comorbid PsO.

Disclosure: M. Murage, Eli Lilly and Company, 1, 2; **N. Princic**, IBM Watson Health, 3; **J. Park**, IBM Watson Health, 1; **W. Malatestinic**, Eli Lilly and Company, 1, 2; **B. Zhu**, Eli Lilly and Company, 1, 3; **B. Atiya**, Eli Lilly and Company, 1, 2; **S. Kern**, Eli Lilly and Company, 1, 2; **K. Stenger**, Eli Lilly and Company, 1, 2; **A. Sprabery**, Eli Lilly and Company, 1, 3, Johnson and Johnson, 1; **A. Ogdie**, Lilly, 5, Amgen, 5, AbbVie, 5, BMS, 5, Celgene, 5, Janssen, 5, Norvatis, 2, 5, Pfizer, 2, 5, Takeda, 5.

Abstract Number: 1032

Epidemiology and Geographic Evaluation of ANCA-associated Vasculitis (AAV) at a Rural Academic Health Center Utilizing an Electronic Health Record (EHR)

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health Poster III: Inflammatory Rheumatic Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis has a reported prevalence ranging from 3.2 to 9.1 cases per 100,000 individuals, but little is known of geographic variations. The aim of this study is to observe the prevalence of AAV in a rural based health system using updated ACR/EULAR Diagnostic and Classification Criteria for Primary Systemic Vasculitis (DCVAS). The study also provides geographic mapping of cases to investigate potential environmental factors.

Methods: We reviewed patients with potential AAV through use of EHR from 1/1/2003-6/30/2018 with ICD 9/10 codes consistent with AAV, granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA), or eosinophilic granulomatosis with polyangiitis (EGPA). We conducted a manual chart review of cases that satisfy ACR/EULAR DCVAS. Each case was independently confirmed by a rheumatologist, pulmonologist and nephrologist. The de-

Figure 1: Overall ANCA Vasculitis Prevalence and Patient Demographics

5-Year Point Prevalence	Geisinger Patients	Confirmed ANCA Patients	Prevalence Per 100,000	95% CI
ANCA 2018 Prevalence	465,588	54	11.60	(8.40, 14.80)
Age, mean (S.D.)	50.7 (19.1)	60.8 (16.5)		
Female, n (%)	256,138 (55.0%)	27 (50.0%)		
American Indian or Alaska Native, n (%)	718 (0.2%)	0 (0.0%)		
Asian, n (%)	5320 (1.1%)	0 (0.0%)		
Black or African American, n (%)	18,270 (3.9%)	1 (1.9%)		
Native Hawaiian or Other Pacific Islander, n (%)	2410 (0.5%)	0 (0.0%)		
White, n (%)	437,379 (93.9%)	52 (96.3%)		
Unknown, n (%)	1491 (0.3%)	1 (1.9%)		

nominator for a 5-year point prevalence estimate was calculated by identifying patients > 18 years old with a PCP encounter between 1/1/2003-6/30/2018 who had at least one outpatient encounter between 1/1/2014-12/31/2018. The numerator was calculated by identifying AAV cases within the denominator population. The prevalence estimate was calculated using a simple binomial proportion and the simple asymptotic continuity corrected 95% confidence interval. Prevalence estimates for GPA, MPA, and EGPA were calculated using similar methods as for overall AAV prevalence. Because of the rarity, the 95% confidence interval for the EGPA is reported using a Clopper-Pearson exact method. Statistical analysis was completed using SAS 9.4. All confirmed cases of AAV were plotted along a map to evaluate geographic distribution.

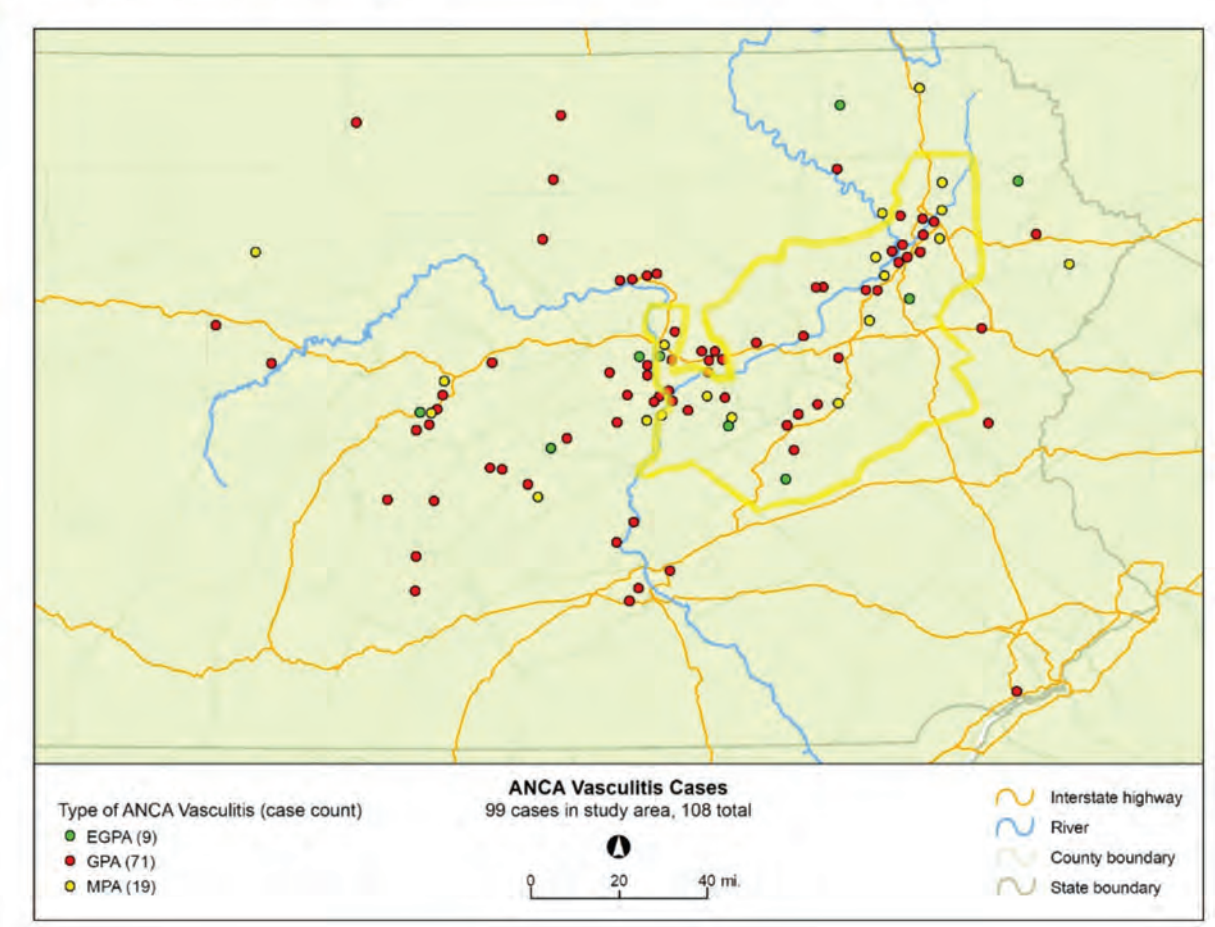
Results: Out of 2983 cases screened by ICD codes, 108 cases satisfied DCVAS. For prevalence criteria, there were 54 confirmed cases out of a denominator population of 458,588. The prevalence estimate for AAV is 11.6/ 100,000 (95% CI: 8.4, 14.8). The total population mean age was 50.7, 55.0% were female and 93.9% were Caucasian. Among the 54 AAV patients, the mean age was 60.8, 50.0% were female, and 96.3% were Caucasian. There were 38 patients with GPA, 13 with MPA, and 3 with EGPA. Prevalence estimates and demographic characteristics are shown in Figure 1 and Figure 2. The prevalence estimates for AAV and GPA is observed to be above the reported national average range. Our geographic mapping shows correlation of cases in counties deemed as Coal Region, following along a major interstate, a regional river, and primary medical service area (Figure 3).

Conclusion: Our prevalence estimates for AAV and GPA is observed to be higher than average, but MPA and EGPA has insufficient U.S. epidemiology to compare. Our health system captures a large region of predominantly Caucasian patients in a rural population so it is of interest to compare to national averages. Mapping suggests a correlation of AAV cases in Coal Region counties and along a major river, suggesting a possible environmental factor. We hope to explore potential environmental-gene interactions and compare epidemiology with an urban system in the future

Figure 2: Prevalence of GPA, MPA and EGPA and Patient Demographics

5-Year Point Prevalence	Geisinger Patients	Confirmed ANCA Patients	Prevalence Per 100,000	95% CI
GPA 2018 Prevalence	**465,588**	**38**	**8.16**	**(5.46, 10.86)**
Age, mean (S.D.)	50.7 (19.1)	59.1 (18.0)		
Female, n (%)	256,138 (55.0%)	19 (50.0%)		
American Indian or Alaska Native, n (%)	718 (0.2%)	0 (0.0%)		
Asian, n (%)	5320 (1.1%)	0 (0.0%)		
Black or African American, n (%)	18,270 (3.9%)	1 (2.6%)		
Native Hawaiian or Other Pacific Islander, n (%)	2410 (0.5%)	0 (0.0%)		
White, n (%)	437,379 (93.9%)	36 (94.7%)		
Unknown, n (%)	1491 (0.3%)	1 (2.6%)		
MPA 2018 Prevalence	**465,588**	**13**	**2.79**	**(1.17, 4.42)**
Age, mean (S.D.)	50.7 (19.1)	68.4 (7.4)		
Female, n (%)	256,138 (55.0%)	7 (53.8%)		
American Indian or Alaska Native, n (%)	718 (0.2%)	0 (0.0%)		
Asian, n (%)	5320 (1.1%)	0 (0.0%)		
Black or African American, n (%)	18,270 (3.9%)	0 (0.0%)		
Native Hawaiian or Other Pacific Islander, n (%)	2410 (0.5%)	0 (0.0%)		
White, n (%)	437,379 (93.9%)	13 (100.0%)		
Unknown, n (%)	1491 (0.3%)	0 (0.0%)		
EGPA 2018 Prevalence	**465,588**	**3**	**0.64**	**(0.13, 1.88)**
Age, mean (S.D.)	50.7 (19.1)	46.6 (11.4)		
Female, n (%)	256,138 (55.0%)	1 (33.3%)		
American Indian or Alaska Native, n (%)	718 (0.2%)	0 (0.0%)		
Asian, n (%)	5320 (1.1%)	0 (0.0%)		
Black or African American, n (%)	18,270 (3.9%)	0 (0.0%)		
Native Hawaiian or Other Pacific Islander, n (%)	2410 (0.5%)	0 (0.0%)		
White, n (%)	437,379 (93.9%)	3 (100.0%)		
Unknown, n (%)	1491 (0.3%)	0 (0.0%)		

Figure 3: Distribution of ANCA vasculitis cases broken down into GPA, MPA and EGPA. The yellow outline is surrounding "Coal Region."



Disclosure: E. Rottmann, None; **J. Bankert**, None; **A. Berger**, None; **L. Kirchner**, None; **J. Dewalle**, None; **M. Meissner**, None; **J. George**, None; **I. Bucaloiu**, None; **J. Sugunaraj**, None; **S. Penupolu**, None; **D. Bulbin**, Novartis, 5, 8, Alexion, 8.

Abstract Number: 1033

Systemic Treatment in Sarcoidosis. Study of 377 Patients from a Single University Hospital

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcoidosis is a multisystemic disease characterized by the formation of non-necrotizing granulomas. The most frequently affected organs are the lungs, skin and eyes. Systemic corticosteroids are the most used drugs in the treatment of this disease. Conventional and biological immunosuppressants may also be used.

Objectives: To evaluate the systemic treatment of sarcoidosis according to clinical domains.

Methods: Study of all consecutive patients diagnosed with sarcoidosis between 1/1/1999 and 1/1/2019 in a tertiary university hospital. The diagnosis was established following the ATS/ERS/WASOG criteria *(Eur Respir J. 1999;14(4):735-737):* compatible clinical and radiological presentation, evidence of non-caseifying granulomas and exclusion of other granulomatous diseases.

Results: We studied 377 patients (188 men/189 women), mean age at diagnosis of 46.0±14.8 years. After a mean follow-up of 13.0±9.3 years, 161 (42.7%) patients did not require treatment. The remaining 216 (57.3%) received oral glucocorticoids (206, 54.6%) with a maximum mean dose of 43.2±19.0 mg/day, conventional immunosuppressants (60, 16.2%), biological therapy (28, 7.4%) and/or endovenous methylprednisolone (15, 4.0%). Biological therapy was indicated by pulmonary (9, 32.1%), ocular (9, 32.1%), neurological (3, 10.7%), muskuloeskeletal (3, 10.7%), cutane-

Table 1: Organ involvement of sarcoidosis and treatment with corticosteroids and conventional immunosuppressants.

ORGAN INVOLVEMENT	Cases n, (%)	NT	OCS	MD of OCS (mg/d)*	IVMP	MTX	AZA	CFM	MMF
Pulmonary	319 (84.6%)	128 (40.1%)	185 (58%)	43.6 (±18.8)	13 (4.1%)	46 (14.4%)	13 (4.1%)	2 (0.6%)	3 (0.9%)
Cutaneous	124 (32.9%)	50 (40.3%)	66 (53.2%)	38.0 (±20.2)	4 (3.2%)	18 (14.5%)	4 (3.2%)	1 (0.8%)	0
Ocular	48 (12.7%)	5 (10.4%)	38 (79.2%)	41.5 (±17.6)	10 (20.8%)	23 (47.9%)	8 (16.7%)	1 (2.1%)	1 (2.1%)
Musculoeskeletal	108 (28.6%)	41 (38%)	65 (60.2%)	39.2 (±18.7)	5 (4.6%)	26 (24.1%)	6 (5.6%)	0	0
Hepatic	41 (10,9%)	12 (29.3%)	27 (65,9%)	43.8 (±15.2)	3 (7.3%)	6 (14.6%)	1 (2.4%)	1 (2.4%)	0
Neurological	27 (7.2%)	4 (14.8%)	23 (85,2%)	50.9 (±20.2)	5 (18.5%)	14 (51.9%)	5 (18.5%)	0	0
Cardiac	8 (2.1%)	4 (50%)	4 (50%)	40.0 (±28.3)	1 (12.5%)	2 (25%)	1 (12.5%)	1 (12.5%)	0
Renal	22 (5.8%)	2 (9.1%)	20 (90,9%)	47.1 (±13.8)	1 (4.5%)	6 (27.3%	2 (9.1%)	0	0
Löfgren's syndrome	44 (11.7%)	18 (40.9%)	24 (54,5%)	29.8 (±15.3)	0	3 (6.8%)	1 (2.3%)	0	0
Heerfordt's syndrome	2 (0.5%)	0	2 (100%)	57.5 (±17.7)	2 (100%)	2 (100%)	1 (50%)	0	0
TOTAL	377	161 (42.7%)	206 (54.6%)	48.2 (±19.0)	15 (4.0%)	53 (14.1%)	16 (4.2%)	2 (0.5%)	3 (0.8%)

NT: no treatment; MD: maxim dose; OCS: oral corticosteroids; IVMP: intravenous methylprednisolone; MTX: methotrexate; AZA: azathioprine; CFM: cyclophosphamide; MMF: mycophenolate mofetil;
* Mean (±SD)

Table 2: Organ involvement of sarcoidosis and treatment with biological immunosuppressants.

ORGAN INVOLVEMENT	Biologic Therapy	IFX	ADA	ETN	GLM	TCZ	RTX	Complete response
Pulmonary	21 (6.6%)	12 (3.8%)	16 (5.0%)	0	1 (0.3%)	2 (0.6%)	3 (0.9%)	64 (33.5%)
Cutaneous	9 (7.3%)	5 (4%)	9 (7.3%)	1 (0.8%)	2 (4.2%)	0	1 (0.8%)	29 (39.2%)
Ocular	13 (27.1%)	5 (10.4%)	11 (22.9%)	1 (2.1%)	2 (4.2%)	2 (4.2%)	0	10 (23.3%)
Musculoeskeletal	12 (11.1%)	8 (7.4%)	8(7.4%)	1 (0.7%)	2 (1.9%)	0	1 (0.9%)	24 (35.8%)
Hepatic	1 (2.4%)	1 (2.4%)	1 (2.4%)	0	0	0	0	6 (20.7%)
Neurological	9 (33.3%)	7 (25.9%)	5 (18.5%)	1 (3.7%)	2 (7.4%)	1 (3.7%)	1 (3.7%)	6 (26.1%)
Cardiac	2 (25%)	2 (25%)	2 (25%)	0	0	0	0	1 (25%)
Renal	2 (9.1%)	1 (4.5%)	2 (9.1%)	0	0	0	0	3 (15%)
Löfgren's syndrome	2 (4.5%)	1 (2.3%)	2 (4.5%)	0	0	0	1 (2.3%)	19 (69.2%)
Heerfordt's syndrome	2 (100%)	2 (100 %)	2 (100 %)	0	0	0	0	0
TOTAL	28 (7.4%)	15 (4.0%)	20 (5.3%)	1 (0.3%)	2 (0.5%)	3 (0.8%)	3 (0.8%)	72 (33.3%)

BT: biologic therapy; IFX: infliximab; ADA: adalimumab; ETN:etanercept; GLM: golimumab; TCZ: tocilizumab; RTX: rituximab

ous (2, 7.1%), nephrological involvement (1, 3.6%); and Heerfordt's syndrome (1, 3.6%). Adalimumab and Infliximab were the biologics used more frequently (**Table 1-2**).

Conclusion: Compared to other studies, the high percentage of patients who required systemic treatment is remarkable. It also highlights the frequency of the use of biological drugs in more severe organ involvement (ocular and neurological), which is consistent with the trend in recent years.

Disclosure: D. Martinez-Lopez, Lilly, 2; **R. Fernandez-Ramon**, None; **J. Martín-Varillas**, None; **L. Sanchez-Bilbao**, None; **I. Gonzalez-Mazon**, None; **J. Gaitan-Valdizan**, None; **R. Demetrio-Pablo**, None; **M. González-Gay**, None; **R. Blanco**, None.

Abstract Number: 1034

Trend of Treatment Plans, and Outcomes of Therapy in Cardiac Sarcoidosis via Analysis of Standardized Uptake Values Score and Ejection Fraction Using a Cardiac PET-CT

Rabia Gill[1], Martin Lavellee[1], Michael Petrides[1], Sarah Ford[1], Gurukripa Kowlgi[2], Huzaefah Syed[3] and Adam Sima[3], [1]Virginia Commonwealth University, Richmond, VA, [2]Mayo Clinic, Rochester, MN, [3]VCU Health, Richmond, VA

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Table 1	no.	%	mean	SD
Mean Age			52	10
Male sex	16	48		
Race				
White	19	61		
Black	11	35		
Other	1	3		
New diagnosis sarcoidosis with cardiac involvement	17	55		
Interval between extra-cardiac diagnosis and cardiac diagnosis (concurrent diagnosis excluded) – yrs.			10.9	9.6
Organ involvement				
Isolated cardiac sarcoidosis	4	13		
Pulmonary	26	84		
Other	22	72		
Presenting symptoms of cardiac sarcoidosis				
Palpitations	23	74		
Shortness of breath	22	71		
Near syncope	20	64		
Syncope	11	35		
Chest pain	6	20		
Lower extremity edema	4	13		
Biopsy				
Endomyocardial site	4	13		
Extra-cardiac site	25	83		
Lung	16	52		
Lymph node	6	19		
Skin	3	10		
Mean ACE level, U/L (n=18)			50.7	29.5
Mean soluble IL2 receptor alpha, U/mL (n=15)			549.5	294.2
Mean CRP, mg/dL (n=20)			0.7	1.4
Baseline cardiac PET-CT				
Mean SUV max (n=21)			9.5	3.5
Mean SUV max MTX group (n=16)			9.2	3.3
Mean SUV max OT group (n=5)			10.4	4.6
Baseline EF				
Mean EF (n=21)			50%	16%
Mean EF MTX group (n=16)			52%	16%
Mean EF OT group (n=5)			46%	14%
Comparison of pre-initial treatment and post-initial treatment cardiac PET- CT				
Mean SUV max difference (n=21)			-4.0	6.0
Mean SUV max difference MTX group (n=16)			-3.5	6.1
Mean SUV max difference other treatment group (n=5)			-5.6	6.2
Comparison of pre-initial treatment and post-initial treatment EF				
Mean change in EF (n=21)			0%	0%
Mean change in EF MTX group (n=16)			2%	10%
Mean change in EF OT group (n=5)			-3%	7%
Time from initial therapy start to post-treatment cardiac PET-CT (months)				
Mean time interval (n=21)			18	15
Mean time interval MTX group (n=16)			19	16
Mean time interval OT group(n=5)			12	8
ACE normal range 14-82 U/L Soluble IL2 receptor alpha normal range 223-710 U/ml CRP normal range 0.0-0.5 mg/dL				

Background/Purpose: Pharmacological management of cardiac sarcoidosis (CS) includes immunosuppressive therapy for active lesions, guideline-directed medical therapy for heart failure, and antiarrhythmics. Our goal was to observe the various clinical characteristics of CS patients, choice of treatment plans, and outcomes of therapy via analysis of standardized uptake values (SUV) and ejection fraction (EF) using pre- and post-treatment cardiac PET-CT.

Figure 1. Box Plot of SUV uptake values pre- and post-initiation of therapy

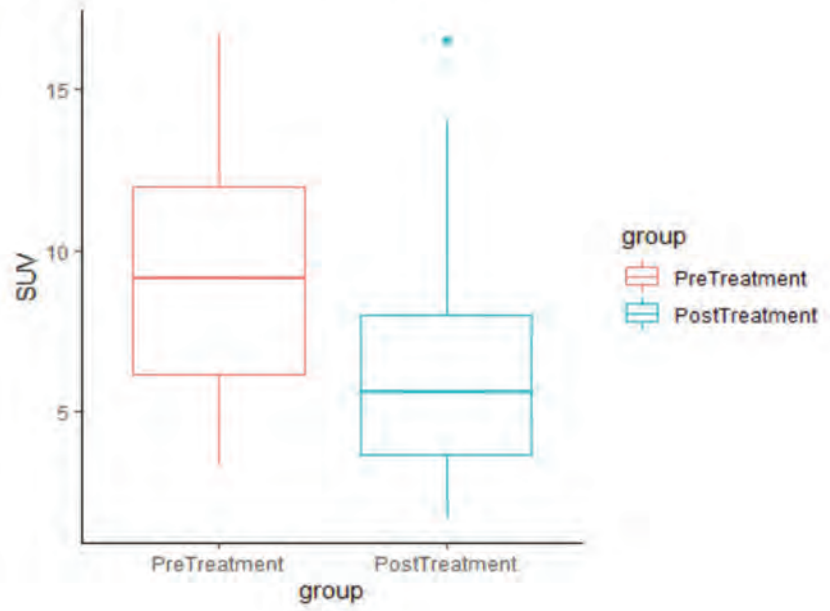

Figure 2. Sunburst plot of the sequence of medications used in cardiac sarcoidosis patients

Methods: The data was gathered by retrospective chart review of 31 patients treated at our institute with a diagnosis of CS (as defined by the Heart Rhythm Society diagnostic criteria). Patients having at least two PET scans spaced at least 6 months apart were included, and they had to be on a sTable treatment regimen for at least 6 months prior to their follow up PET-CT. Changes in medications were noted.

Results: Table 1 summarizes patient's baseline clinical characteristics, diagnostic workup, treatments and the changes in SUV and EF using pre- and post-treatment PET-CT. The average time between first PET-CT and therapy initiation was 4.3 months and the average time between therapy initiation and follow-up PET-CT was 14.5 months. The average SUV uptake before starting any therapy was 9.2 ± 3.64, which decreased to 5.98 ± 3.67 on follow-up assessment (Figure 1). The average difference between pre- and post-treatment SUV was -3.22 (SD=5.39, 95% CI: -5.23, -1.21) with paired t-test (p-value=0.002) suggesting improvement in mean SUV with therapy. The average difference between pre- and post-treatment ejection fraction was 0.13% (95%CI: -3.5%, 3.8%) with paired t-test (p=0.94) suggesting no difference.

MTX was used most commonly as initial therapy followed by AZA, HCQ, LEF and MMF. Many treatment combinations also used background therapy with prednisone. The most common biologic used was infliximab followed by adalimumab. A sunburst plot provides a representation of the sequence of medications use in this cohort of CS patients (Figure 2). Patients were divided into a MTX treatment group (n=16) where MTX formed the backbone of therapy with or without HCQ (n=2) or prednisone (n=10). A second group termed the 'Other treatment group' (OT group) was formed for analysis consisting of: AZA monotherapy (n=1), AZA in combination with prednisone (n=1), prednisone monotherapy (n=1) and MMF in combination with prednisone (n=2). The baseline SUV max was similar in the MTX and OT groups (9.2 vs 10.4) as was the EF (52% vs 46%). There was a difference in the interval between the baseline cardiac PET-CT and the initiation of medical therapy in the MTX group vs the OT group (4 months vs 0.5 months). The change in SUV max was slightly greater in the OT group when compared to the MTX group (-5.6 vs -3.5), though the change in EF was similar (-3% vs 2%).

Conclusion: We described the clinical characteristics and treatment patterns of 31 patients with CS. We did not observe a pronounced difference between the MTX and the OT group with respect to SUV patterns and EF before and after initiating therapy. Further large-scale prospective studies are required to identify the most effective treatment regimen in the management of CS.

Disclosure: R. Gill, None; **M. Lavellee**, None; **M. Petrides**, None; **S. Ford**, None; **G. Kowlgi**, None; **H. Syed**, None; **A. Sima**, None.

Abstract Number: 1035

Study of Ocular Sarcoidosis and Clusters of Clinical Associations in a Series of 383 Patients with Systemic Sarcoidosis from a Single Hospital

Inigo Gonzalez-Mazon[1], Carmen Alvarez-Reguera[2], Lara Sanchez-Bilbao[2], David Martinez-Lopez[3], Alba Herrero Morant[2], Jorge Javier Gaitan-Valdizan[4], Raul Fernandez-Ramon[2], Rosalia Demetrio-Pablo[2] and Ricardo Blanco[2], [1]Hospital Universitario Marques de Valdecilla, Bezana, Spain, [2]Hospital Universitario Marques de Valdecilla, Santander, Spain, [3]Hospital Universitario Marques de Valdecilla, Santander (SPAIN), Spain, [4]Hospital Universitario Marqués de Valdecilla, Santander, Spain

SESSION INFORMATION

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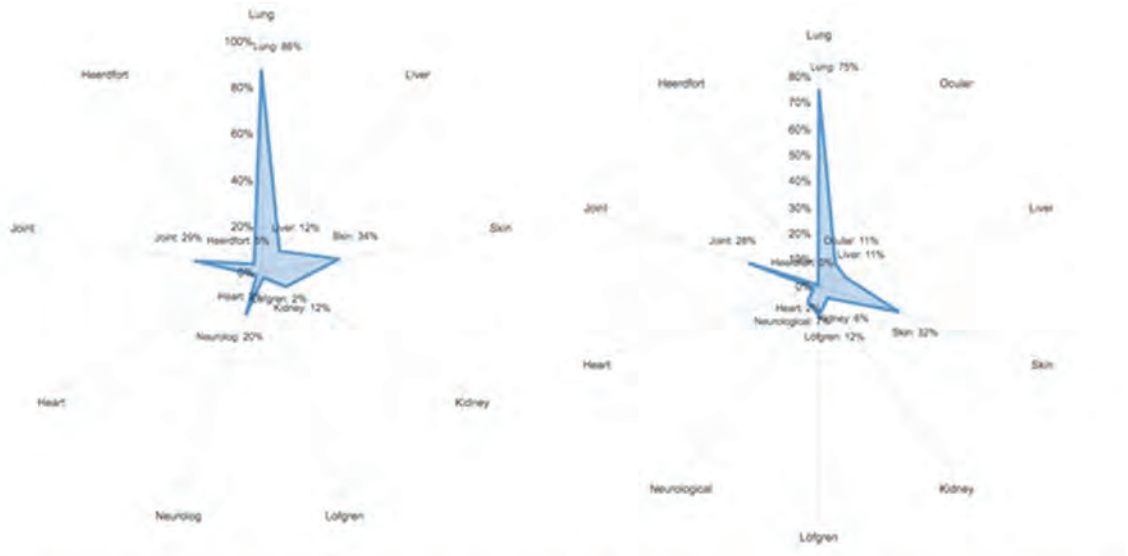

FIGURE: Comparison between distribution of organs affected in ocular sarcoidosis (left) and distribution of organs affected in general sarcoidosis (right).

Background/Purpose: Sarcoidosis is an inflammatory disease which can affect multiple organs. The most frequent affected organs are lungs, skin and eyes. Ocular involvement is a severe complication. The objective of this study was to assess the association of ocular sarcoidosis with other clinical domains.

Methods: Study of a large cohort of systemic sarcoidosis from a single tertiary university hospital. All consecutive patients were diagnosed with systemic sarcoidosis from January 1, 1999 to January 1, 2019 according the ATS/ERS/WASOG criteria.

Results: 41 (22 women/19 men) of 383 (10.7%) patients had ocular involvement, mean age 44.8±16 years. Lung was the most common affected organ associated with ocular sarcoidosis (n=36; 87.8%) followed by skin (n=14; 34.1%), joints (n=12; 29.3%) and neurological affection (n=8; 19.5%).

Ocular sarcoidosis presents a higher percentage of renal and neurological affection compared to organs affected in general sarcoidosis of our larger cohort (12% vs 6% and 19.5 vs 7%; respectively). In **Figure** is shown comparison between distribution of organs affected in ocular sarcoidosis.

Conclusion: The proportion of clinical domains affected in ocular sarcoidosis is mostly similar to global sarcoidosis, except the neurological (which almost is threefold) and renal (which doubles) affection. Hence, the importance of being aware of neurological and renal complications when ocular affection is present.

Disclosure: I. Gonzalez-Mazon, None; **C. Alvarez-Reguera**, None; **L. Sanchez-Bilbao**, None; **D. Martinez-Lopez**, Lilly, 2; **A. Herrero Morant**, None; **J. Gaitan-Valdizan**, None; **R. Fernandez-Ramon**, None; **R. Demetrio-Pablo**, None; **R. Blanco**, None.

Abstract Number: 1036

Ocular Involvement and Treatment in Sarcodosis. Study of 41 Patients of a Series of 383 Patients from a Single University Hospital

David Martinez-Lopez[1], Jorge Javier Gaitan-Valdizan[2], Raul Fernandez-Ramon[3], Rosalia Demetrio-Pablo[3], Lara Sanchez-Bilbao[3], Inigo Gonzalez-Mazon[4], José Luis Martín-Varillas[5], Miguel Ángel González-Gay[6] and Ricardo Blanco[3], [1]Hospital Universitario Marques de Valdecilla, Santander (SPAIN), Spain, [2]Hospital Universitario Marqués de Valdecilla, Santander, Spain, [3]Hospital Universitario Marques de Valdecilla, Santander, Spain, [4]Hospital Universitario Marques de Valdecilla, Bezana, Spain, [5]Hospital Sierrallana, Torrelavega, Spain, [6]Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain

SESSION INFORMATION

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Background/Purpose: Background: The eye is a common and potential severe complication of sarcoidosis. Topical and systemic corticosteroids are the first-line treatment. Conventional and biological immunosuppressants are frequently needed.

Objectives: To assess the frequency, clinical and treatment of ocular involvement of sarcoidosis.

Methods: Study of a large cohort (n=383) of systemic sarcoidosis from a single university hospital. All consecutive patients diagnosed with sarcoidosis from January 1, 1999 to January 1, 2019 according the ATS/ERS/WASOG criteria *(Eur Respir J 1999;14:735–737)* were included.

Results: 41 (22 women/19 men) of 383 (10.7%) patients had ocular involvement, mean age 44.8±16 years. Uveitis (n=34; 82.9%) was the most common ocular manifestation, especially anterior uveitis (n=18; 52.9%). Ocular surface and eye orbit may also be affected **(Table 1)**.

In addition to topical and systemic corticosteroids, conventional (n=23; 56.1%) and biologic (n=14; 34.1%) immunosuppressive drugs were required. Adalimumab and Infliximab were the most used biologic treatments **(Table 2).**

Cystoid macular edema (CME) and Retinal Vasculitis was observed in both cases in 3 (7.3%) patients, 2 of them (66.7%) required biological treatment. Papilitis appeared in 7 (17.1%) cases, biological treatment was needed in 3 (42.9%) patients.

The most frequent sequels were cataract (n=9, 21.9%), intraocular hypertension (n=5; 12.2%) and pupil alterations (n=4; 9.7%). The average of the best corrected visual acuity was 0.6±0.3 at diagnosis and 0.7±0.3 after one year follow up.

Conclusion: Ocular involvement of sarcoidosis is a relative frequent and potential severe complication, especially if panuveitis is presented.

Table 1: Ocular manifestations of sarcoidosis and treatment with corticosteroids and conventional immunosuppressants

OCULAR INVOLVEMENT	Cases	Bilateral	TCS	OCS	MD of OCS (mg/d)	IVMP	Conventional IS	MTX	AZA	CFM	MMF
SURFACE	**3 (7.3%)**	**0 (0%)**	**2 (66.7%)**	**2 (66.7%)**		**2 (66.7%)**	**2 66.7%)**	**2 (66.7%)**	**2 (66.7%)**	**1 (33.3%)**	**0 (0%)**
- CG/N	1 (33.3%)	0 (0%)	1 (100%)	0 (0%)	-	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
- PUK	2 (66.7%)	0 (0%)	1 (50%)	2 (100%)	60	2 (100%)	2 (100%)	2 (100%)	2 (100%)	1 (50%)	0 (0%)
UVEITIS	**34 (82.9%)**	**8 (23.5%)**	**25 (73.5%)**	**28 (82.3%)**		**10 (29.4%)**	**19 (55.6%)**	**18 (52.9%)**	**7 (20.6%)**	**1 (2.9%)**	**1 (2.9%)**
- Anterior uveitis	18 (52.9%)	6 (33.3%)	11 (61.1%)	13 (72.2%)	30	1 (5.5%)	5 (27.8%)	5 (27.8%)	1 (5.5%)	0 (0%)	0 (0%)
- Posterior uveitis	4 (11.7%)	1 (25%)	2 (50%)	3 (75%)	60	1 (25%)	3 (75%)	2 (50%)	2 (50%)	0 (0%)	0 (0%)
- Panuveitis	12 (35.3%)	1 (8.3%)	12 (100%)	12 (100%)	60	8 (66.7%)	11 (91.7%)	11 (91.7%)	4 (33.3%)	1 (8.3%)	1 (8.3%)
EYE ORBIT	**4 (9.7%)**	**0 (0%)**	**2 (50%)**	**3 (75%)**		**2 (50%)**	**2 (50%)**	**2 (50%)**	**2 (50%)**	**0 (0%)**	**0 (0%)**
- Proptosis	2 (50%)	0 (0%)	1 (50%)	1 (50%)	30	1 (50%)	1 (50%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)
- Strabismus	2 (50%)	0 (0%)	1 (50%)	2 (100%)	60	1 (50%)	1 (50%)	1 (50%)	1 (50%)	0 (0%)	0 (0%)
TOTAL	**41 (100%)**	**8 (19.5%)**	**29 (70.7%)**	**33 (80.5%)**	**50 ±15.5**	**14 (34.1%)**	**23 (56.1%)**	**22 (53.7%)**	**11 (26.9%)**	**2 (4.9%)**	**1 (2.4%)**

TCS: topical corticosteroids; **OCS:** oral corticosteroids; **MD:** maximum dose; **IVMP:** intravenous methylprednisolone; **Conventional IS**: conventional immunossupresors; **MTX:** methotrexate; **AZA:** azathioprine; **CFM:** cyclophosphamide; **MMF:** mycophenolate mofetil; **CG/N:** conjunctival granuloma/nodule; **PUK:** peripheral ulcerative keratitis

Table 2: Ocular manifestations of sarcoidosis and treatment with biological immunosuppressants.

OCULAR INVOLVEMENT	Cases	BT	ADA	IFX	TCZ	GLM	ETN
SURFACE	**3 (7.3%)**	**2 (66.7%)**	**2 (66.7%)**	**2 (66.7%)**	**0 (0%)**	**0 (0%)**	**0 (0%)**
- CG/N	1 (2.4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
- PUK	2 (4.9%)	2 (100%)	2 (100%)	2 (100%)	0 (0%)	0 (0%)	0 (0%)
UVEITIS	**34 (82.9%)**	**12 (35.3%)**	**11 (32.3%)**	**4 (11.8%)**	**3 (8.8%)**	**2 (5.9%)**	**1 (2.9%)**
- Anterior uveitis	18 (43.9%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
- Posterior uveitis	4 (9.7%)	2 (50%)	1 (25%)	0 (0%)	0 (0%)	1 (25%)	0 (0%)
- Panuveitis	12 (29.3%)	10 (83.3%)	10 (83.3%)	4 (33.3%)	3 (25%)	1 (8.3%)	1 (8.3%)
EYE ORBIT	**4 (9.7%)**	**2 (50%)**	**1 (25%)**	**1 (25%)**	**1 (25%)**	**0 (0%)**	**0 (0%)**
- Proptosis	2 (4.9%)	1 (50%)	1 (50%)	0 (0%)	1 (50%)	0 (0%)	0 (0%)
- Strabismus	2 (4.9%)	1 (33.3%)	0 (0%)	1 (33.3%)	0 (0%)	0 (0%)	0 (0%)
TOTAL	**41 (100%)**	**14 (34.1%)**	**14 (34.1%)**	**7 (17.5%)**	**3 (7.3%)**	**2 (4.9%)**	**1 (2.4%)**

BT: biologic therapy; **IFX:** infliximab; **ADA:** adalimumab; **ETN:** etanercept; GLM: golimumab; **TCZ:** tocilizumab; **RTX:** rituximab; **CG/N:** conjunctival granuloma/nodule; **PUK:** peripheral ulcerative keratitis

Disclosure: D. Martinez-Lopez, Lilly, 2; **J. Gaitan-Valdizan**, None; **R. Fernandez-Ramon**, None; **R. Demetrio-Pablo**, None; **L. Sanchez-Bilbao**, None; **I. Gonzalez-Mazon**, None; **J. Martín-Varillas**, None; **M. González-Gay**, None; **R. Blanco**, None.

Abstract Number: 1037

Relationship Between Air Quality and Sarcoidosis Inflammatory Activity

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SESSION INFORMATION

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Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

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Background/Purpose: African Americans [AA] and minorities in the lower socioeconomic strata of Chicago are disproportionately affected by pulmonary sarcoidosis, and regularly exposed to poorer air quality than Caucasians [C]. Histopathologically, sarcoidosis is characterized by granulomatous inflammation, and elevated serum angiotensin converting enzyme (sACE) are observed in about 75% of untreated patients with sarcoidosis, in part due to macrophage activation. Though the etiology remains unknown, exposure via antigen inhalation has been posited to evoke this inflammatory immune response. In this study, we examine the relationship between particulate matter air pollution and sarcoidosis inflammation and hypothesize that poor air quality indices are associated with sACE.

Methods: A cohort of female patients from the University of Illinois at Chicago lung disease registry residing in the Chicago area with sarcoidosis and documented sACE levels (2010-2015) was evaluated retrospectively. Demographic and clinical variables were abstracted from the medical record. ACE levels ≥ 50 U/L were considered elevated and inflammatory. Daily AQI measurements were obtained from the USA EPA database during a 6-month interval prior to ACE level measurement. Residential AQI levels were interpolated from the 5 nearest pollution monitors to a patient's residence by inverse distance weighting with a power of 2 (R-package "*phylin"*) and maximum average AQI levels at 10-day intervals were calculated. Demographic/clinical parameters were compared among AA and C groups and the risk of elevated sACE at the end of the 6-month interval was estimated by Cox proportional hazard ratio models (R-package "*survival"*).

Results: We identified 32 female patients (AA=21, C =11) in the study period. sACE levels between AA and C and baseline demographics were similar at the time of sACE measurement (*MWU-test p-val >0.05*). Evaluation of environmental factors, AQI and smoking history on ACE level, adjusted for time from sarcoidosis diagnosis, revealed a significant hazard reduction of elevated sACE levels by 2% for every unit increase in AQI in AA (*Figure 1A, Log-Rank p-val=0.002*). Contrastingly, in C, current or former smoking history, not AQI, was associated with reduced risk of elevated ACE levels (*Figure 1B, Log-Rank p-val=0.005*). At time of ACE level measurements, a trend of increased utilization of systemic immunosuppressive therapy was observed in AA (χ*2 p-val=0.053, odds ratio=5*).

Conclusion: A paradoxical association between inflammatory activity in sarcoidosis and environmental factors that may increase antigenic exposure was identified. It is possible that AA and C females show different phenotypes of sarcoidosis and respond distinctly to inhaled antigens. In AA females, a higher AQI was linked to lower ACE levels while in C, current or former smoking status was linked with lower ACE levels. Further studies are needed to expound underlying mechanisms of these associations; however, our data supports the idea that inhaled antigenic stimuli are directly related with sarcoidosis inflammatory activity and suggest that some antigens may downregulate granulomatous inflammation.

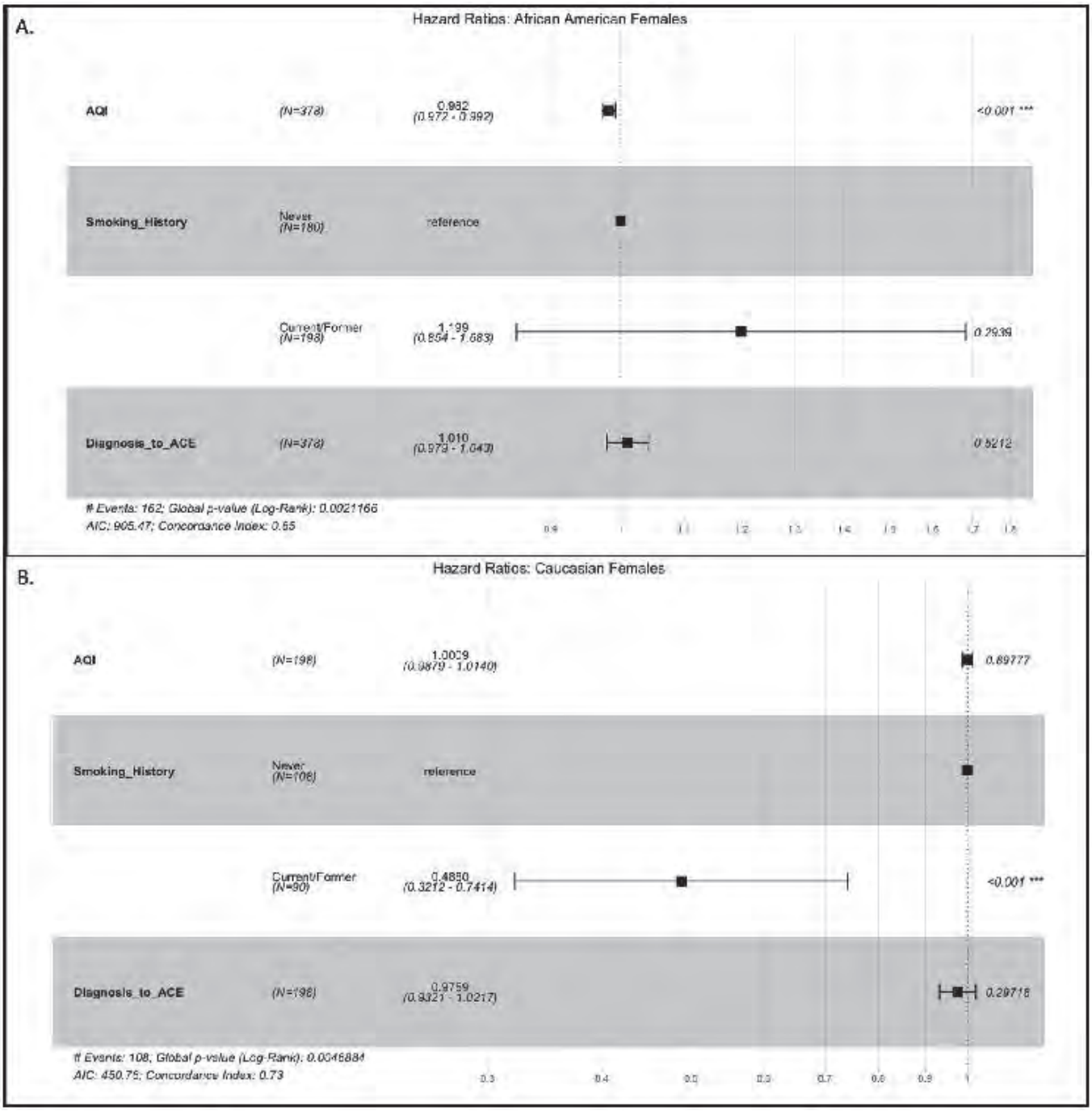

Figure 1. Forest plot demonstrating the Cox proportional hazard ratio and 95% confidence intervals associated with risk of angiotensin converting enzyme (ACE) levels over 50 U/L in (A) African American and (B) Caucasian females. In African American females, unit increments in air quality index (AQI) are associated with a 2% hazard reduction of elevated ACE levels at 6 months. In African Americans, smoking history and time from diagnosis of sarcoidosis (in years) to ACE level are not associated with increased ACE levels. Contrastingly, in Caucasian females, current or former smoking history is associated with a hazard reduction of 51% of elevated ACE levels. In Caucasians, AQI and time from years from diagnosis of sarcoidosis to ACE are not associated with ACE levels.

Disclosure: A. Case, None; **D. Fraidenburg**, None; **I. Rubinstein**, None; **C. Ascoli**, None.

Abstract Number: 1038

STAT1 and JAK2 Are the Most Appropriate Targets of JAK-inhibitor Therapy for Sarcoidosis: An In-silico Meta-nalysis

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Background/Purpose: Our group was the first to contend that STAT1 mediated genes were expressed in sarcoidosis. Since that time, several other groups have found similar results. In a direct extension of these data, JAK-inhibitors have shown benefit in treating sarcoidosis. There are now numerous JAK inhibitors approved to treat inflammatory and hematologic diseases, with varying specificity for JAK molecules. To design more robust clinical studies, we need to determine which JAK-inhibitors are most likely to work in sarcoidosis.

Methods: All publicly available gene expression microarray data from the Gene Ontology Omnibus (GEO) was queried. GEO was queried using the search terms “sarcoidosis” or “sarcoid”, and all human datasets which compared sarcoidosis to healthy controls were included. Microarray data were evaluated for differential expression using GEO2R, a limma based public access software. We analyzed the differential expression of the 4 JAK and 7 STAT genes in all sarcoidosis datasets to date. Significant differential expression was defined as a FC >1.5 or < -1.5, and an adjusted p-value or FDR p-value of < 0.05.

Microarray data were evaluated for differential expression using GEO2R, a limma based public access software available as part of the GEO database. For each dataset, sarcoidosis samples were compared to healthy controls. When sarcoid activity vs inactivity was reported (2 datasets), only active sarcoid samples were included. We analyzed the differential expression of the 4 JAK and 7 STAT genes in all sarcoidosis datasets to date. Significant differential expression was defined as a log2FC >0.585 or < -0.585 (corresponding to a FC >1.5 or < -1.5), and an adjusted p-value or FDR p-value of < 0.05.

Microarray data were evaluated for differential expression using GEO2R, a limma based public access software available as part of the GEO database. For each dataset, sarcoidosis samples were compared to healthy controls. When sarcoid activity vs inactivity was reported (2 datasets), only active sarcoid samples were included. Two analyses were planned. The first was an analysis of differential expression of the 4 JAK and 7 STAT genes. The second was a pathway-based analysis of all pathways known to signal through JAK-STAT. Pathways were evaluated using Gene Set Enrichment Analysis (GSEA).

Results: 12 datasets were included: 6 whole blood, 1 peripheral blood mononuclear cells, and 1 each of anterior orbit, lacrimal gland , bronchoalveolar lavage fluid, lung biopsy, and skin. STAT1 and JAK2 were the most commonly differentially expressed JAK-STAT genes. STAT1 was significantly differentially expressed in 85% of sarcoid datasets; the average FC was 2.6 compared to healthy controls. JAK2 was differentially expressed in 62% of datasets; the average FC was 1.7 compared to healthy controls.

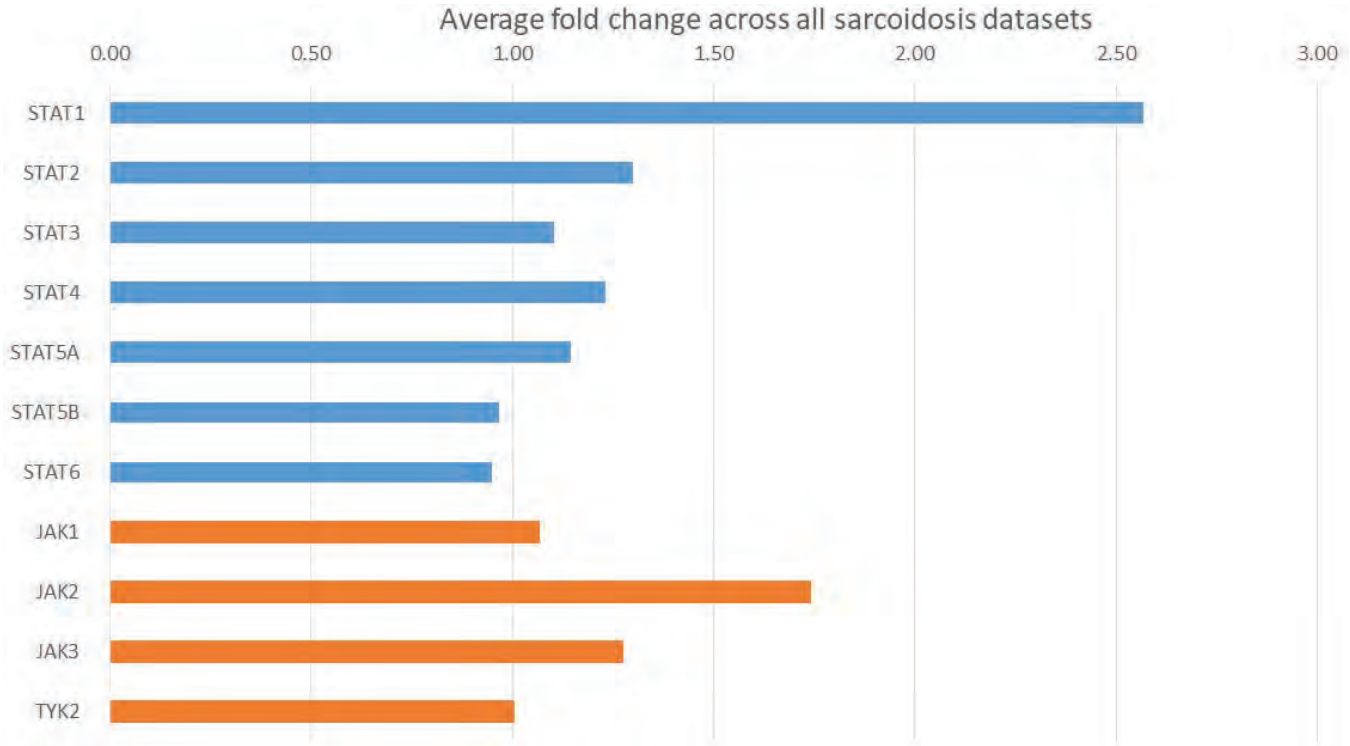

Figure 1. Average fold change of JAK-STAT genes across all sarcoidosis datasets.

Conclusion: This in-silico meta-analysis found that STAT1 and JAK2 are the most significantly expressed JAK-STAT genes in sarcoidosis tissues. We hypothesize that JAK-inhibitors targeting JAK2 are the most likely to be useful in sarcoidosis. Potential JAK inhibitor candidates for clinical trials include tofacitinib, ruxolitinib, baricitinib and peficitinib. We would not suggest trialing JAK1-specific inhibitors in sarcoidosis.

Disclosure: M. Friedman, None; **B. Le**, None; **D. Choi**, None; **J. Rosenbaum**, Gilead, 1, Eli Lilly, 1, Abbvie, 5, UCB Pharma, 5, Roche, 1, Santen, 1, Corvus, 1, Celldex, 1, Horizon, 1, Novartis, 1, Eyevensys, 5, Janssen, 5, UpToDate, 7.

Abstract Number: 1039

Tofacitinib as a Steroid-sparing Therapy in Pulmonary Sarcoidosis: Two Prospective Cases and Molecular Analysis

Marcia Friedman[1], Stevens Janelle[2], Julianna Desmarais[3], Daniel Seifer[3], Brian Le[3], Kimberly Ogle[3], Christina Harrington[3], Peter Jackson[4], Dongseok Choi[3] and James Rosenbaum[3], [1]Oregon Health and Science University, Portland, OR, [2]Tuality Healthcare, Hillsboro, OR, [3]Oregon Health & Science University, Portland, OR, [4]Johns Hopkins University, Baltimore, MD

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

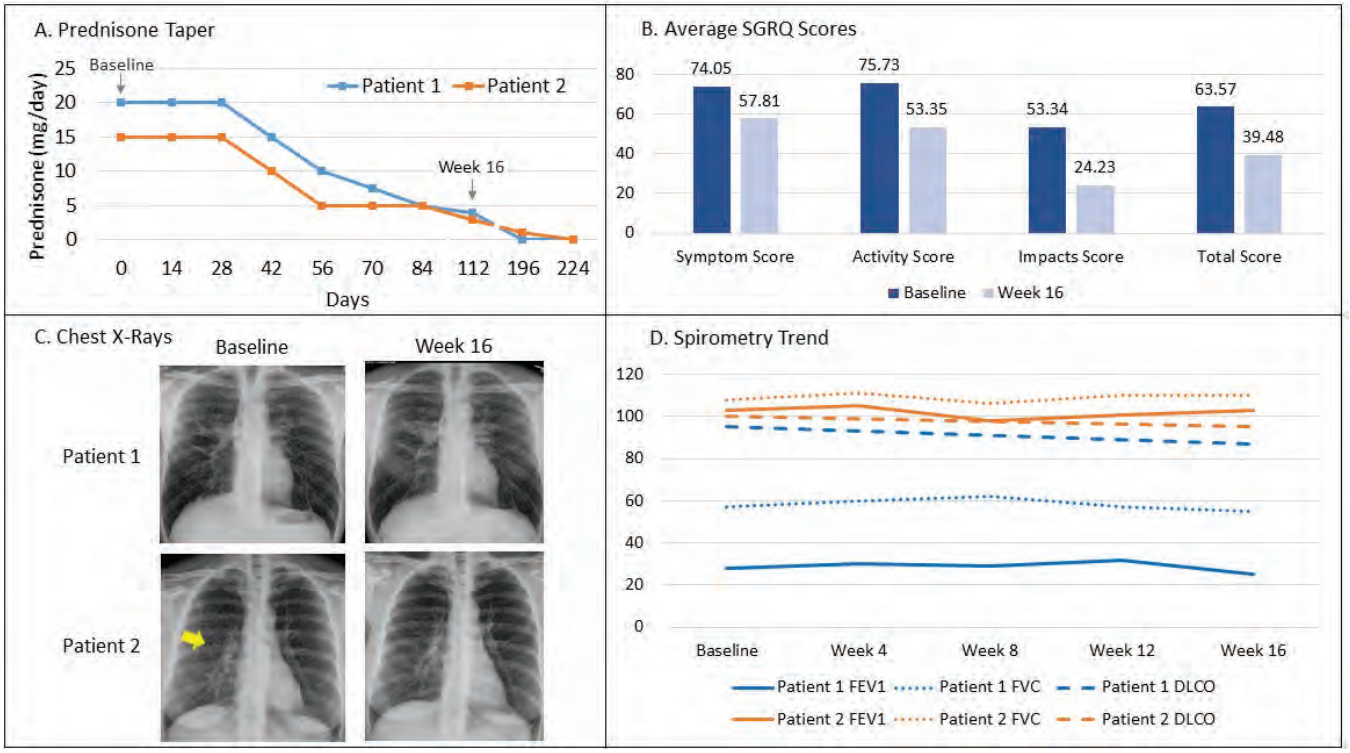

Figure 1. Changes in clinical data from baseline to week 16: A) Prednisone was tapered according to a specified protocol; there were no deviations from the planned taper. Both patients tapered prednisone to <5mg by week 16 and continued to taper during 1-year extension. B) Saint George Respiratory Questionnaire (SGRQ) scores all improved during the trial; a clinically significant difference for SGRQ is 4 units, thus all SGRQ changes were clinically significant. C) The chest x-ray for patient 1 remained sTable over 16 weeks, the chest x-ray for patient 2 showed improvement in mild bronchovascular nodularity (arrow indicates area of improved nodularity). D) Pulmonary function was sTable for both patients given established 10% between-test margin of variability for spirometry measurement.

Background/Purpose: Patients with pulmonary sarcoidosis often require prolonged corticosteroids to treat their disease. There are currently no FDA approved steroid-sparing therapies for sarcoidosis. We report here on the first two patients who have completed a prospective open-label study evaluating tofacitinib as a steroid-sparing therapy in pulmonary sarcoidosis.

Methods: Patients with pulmonary sarcoidosis who were unable to taper below 15-30mg/day of prednisone were invited to participate in this open-label proof of concept study. Patients were started on tofacitinib 5mg twice daily. After 4 weeks, prednisone was tapered according to a specified protocol. The primary endpoint was a ≥ 50% reduction in corticosteroids at week 16 with no worsening of respiratory symptoms by Saint George Respiratory Questionnaire (SGRQ) or pulmonary function; patients who met the primary endpoint were invited to enroll in a one-year extension study.

Results: The first two patients have completed this open-label study. By week 16 each had tapered to ≤ 5mg/day prednisone and thus met the primary endpoint. During the one-year extension study, both patients tapered fully off prednisone. There was no significant change in spirometry. Respiratory symptoms improved (average total SGRQ score change of -24.1 points). Chest imaging was sTable or mildly improved.

Conclusion: We report here the first two patients enrolled as part of an open-label prospective pilot study of tofacitinib as a steroid-sparing agent in pulmonary sarcoidosis. Both patients were able to taper steroids successfully with no disease worsening or significant adverse events. Tofacitinib is a promising therapy for pulmonary sarcoidosis.

Upregulated genes		
Gene Name	Fold Change	FDR p-value
IGLV3-25	4.7	0.0000
TMIGD3	3.4	0.0188
ADGRE4P	3.3	0.0006
AC240565.2	3.3	0.0006
NPIPB3	3.1	0.0127
IL5RA	3.0	0.0038
SAP30	2.8	0.0015
IGKV3-15	2.6	0.0104
PER1	2.5	0.0000
CXCL8	2.5	0.0409
EPN2	2.4	0.0156
PDK4	2.3	0.0226
MS4A7	2.2	0.0053
SAMSN1	2.2	0.0073
TOB1	2.2	0.0123
SMPD3	2.2	0.0392
PHACTR1	2.2	0.0228
ZBTB16	2.1	0.0123
C2CD5	2.1	0.0226
FKBP5	2.0	0.0032
IRS2	1.9	0.0218
TP53INP2	1.9	0.0441
CLEC4E	1.8	0.0394

Downregulated genes		
Gene Name	Fold Change	FDR p-value
MALAT1	-1.8	0.0383
NKG7	-1.8	0.0232
GZMA	-1.9	0.0343
CTSW	-1.9	0.0127
COL9A2	-2.0	0.0052
SLPI	-2.1	0.0034
C1QA	-2.2	0.0439
CST7	-2.3	0.0000
FCGR1A	-2.3	0.0006
ALPL	-2.4	0.0000
GALNT14	-2.5	0.0055
PDGFRB	-3.0	0.0127
AC073172.1	-3.2	0.0019
RN7SL1	-3.6	0.0000
ADAMTS2	-5.8	0.0000
IGLC7	-8.3	0.0017
AC018607.1	-19.7	0.0180
SCARNA7	-26.9	0.0252

Pathways associated with differentially expressed genes	
Pathway	P-value
Hedgehog signaling pathway	0.0070
RIG-I-like receptor signaling pathway	0.0185
Glutamatergic synapse	0.0231
Adipocytokine signaling pathway	0.0231
Thyroid hormone synthesis	0.0251
Olfactory transduction	0.0254
Morphine addiction	0.0322
Sphingolipid signaling pathway	0.0333
IL-17 signaling pathway	0.0345
TNF signaling pathway	0.0345
NF-kappa B signaling pathway	0.0356
Apoptosis	0.0412
Hepatitis C	0.0479

Table 1. Differentially expressed genes in whole blood RNA at week 16 (on tofacitinib) compared to baseline (on higher dose prednisone): A total of 41 genes (23 upregulated and 18 downregulated) were differentially expressed, each with a fold change (FC) >1.5 and a false discovery rate (FDR) p-value <0.05. A Kyoto Encyclopedia of Genes and Genomes (KEGG) pathway analysis revealed 13 pathways significantly associated with differentially expressed genes.

Disclosure: M. Friedman, None; **S. Janelle**, None; **J. Desmarais**, None; **D. Seifer**, None; **B. Le**, None; **K. Ogle**, None; **C. Harrington**, None; **P. Jackson**, None; **D. Choi**, None; **J. Rosenbaum**, Gilead, 1, Eli Lilly, 1, Abbvie, 5, UCB Pharma, 5, Roche, 1, Santen, 1, Corvus, 1, Celldex, 1, Horizon, 1, Novartis, 1, Eyevensys, 5, Janssen, 5, UpToDate, 7.

Abstract Number: 1040

Clinical Characteristics of Sarcoidosis in Asian Population: A 14-year Single Center Retrospective Cohort Study from Thailand

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Data on clinical manifestations of Asians with sarcoidosis are still relatively limited and most of the previously published studies are from East Asia. This study aimed to examine the epidemiology and clinical characteristics of Thai patients with sarcoidosis, using databases of a tertiary care medical center.

	Mean or proportion (N = 89)
Intrathoracic disease	
Intrathoracic involvement	81 (91.0%)
-Stage I	43 (53.1%)
-Stage II	32 (39.5%)
-Stage III	5 (6.2%)
-Stage IV	1 (1.2%)
Pulmonary symptoms	34 (41.9%)
-Dyspnea	21 (25.9%)
-Cough	18 (22.2%)
-Chest pain	2 (2.5%)
Extrathoracic disease	
Uveitis	35 (39.3%)
Skin	24 (26.9%)
Joint	4 (4.5%)
Nervous system	3 (3.4%)
Kidney	3 (3.4%)
Parotid gland	3 (3.4%)
Liver	2 (2.2%)
Spleen	2 (2.2%)
Heart	2 (2.2%)
Bone	1 (1.1%)
Extrathoracic lymph node	18 (22.5%)
Hypercalcemia	9 out of 56 patients who had at least one calcium level checked (16.1%)
Biopsy (positive for non-caseous granuloma / number performed)	
Intrathoracic	53/68 (77.9%)
Skin	21/22 (95.5%)
Extrathoracic lymph node	8/8 (100.0%)
Parotid gland	1/1 (100.0%)
Kidney	1/1 (100.0%)
Treatment	
Oral prednisolone	46 (51.7%)
Methotrexate	16 (17.9%)
Azathioprine	8 (9.0%)
Chloroquine	3 (3.4%)
Leflunomide	1 (1.1%)
Sulfasalazine	1 (1.1%)
Inhaled corticosteroids	6 (6.7%)
Topical corticosteroids	28 (31.5%)

Table 1. Characteristics of patient with sarcoidosis in the current study

Methods: Potential cases of sarcoidosis were identified from two sources, the medical record-linkage system and the pathology database of Siriraj Hospital, Mahidol University in Bangkok, Thailand. Patients with ICD-10-CM codes for sarcoidosis were identified and retrieved from the medical record-linkage system from 2005 to 2018. Patients

with histopathology positive for non-caseating granuloma were identified and retrieved from the pathology database from the same time period. All potential cases underwent individual medical record review to confirm the diagnosis of sarcoidosis which required compatible clinical pictures supported by presence of non-caseating granuloma after exclusion of other granulomatous diseases. A standardized case record form was used to record demographics, clinical manifestations and treatment of confirmed sarcoidosis cases.

Results: From 2005 to 2018, 89 confirmed cases of sarcoidosis were identified. There was female predominance (80.9%) with mean age at diagnosis of 46.8 years (standard deviation [SD] 13.9 years) and mean follow-up time of 5.4 years (SD 4.5 years). The majority of patients with sarcoidosis in this cohort had intrathoracic disease (81 cases; 91.0%). About half of them had stage I pulmonary sarcoidosis (43 cases; 53.1%) followed by stage II (32 cases; 39.5%), III (5 cases; 6.2%) and IV (1 case; 1.2%). However, less than half of patients with intrathoracic disease were symptomatic (34 cases; 41.9%) with dyspnea and cough being the most common symptoms (25.9% and 22.2%, respectively). The yield of intrathoracic biopsy was fair that histopathology was positive for non-caseating granuloma in 53 of 68 patients (77.9%) who underwent biopsy.

Extrathoracic disease was common in this cohort that pulmonary sarcoidosis was accompanied by extrathoracic involvement in 53 patients (65.4%). Isolated extrathoracic disease was observed in 8 patients. Sarcoid uveitis was the most common extrathoracic disease (35 cases; 39.3%; 4 males and 31 females) followed by cutaneous sarcoidosis (24 cases; 26.9%). Calcium was tested in 56 patients and hypercalcemia was seen in 9 of them (16.1%). Biopsy of extrathoracic organs appeared to have a high sensitivity with 21 of 22 skin biopsies and all 8 extrathoracic lymph node biopsies showed evidence of non-caseating granuloma.

A total of 48 patients (53.9%) received at least one systemic treatment during the course of their illness. The most commonly prescribed systemic treatment was oral prednisolone (46 cases; 51.7%) followed by methotrexate (16 cases; 17.9%), azathioprine (8 cases; 9.0%) and chloroquine (3 cases; 3.4%) (**Table 1**).

Conclusion: The current study described clinical characteristics of sarcoidosis in an Asian population. The most prominent findings that are different from sarcoidosis in other ethnic groups included the high prevalence of uveitis and the marked female predominance.

Disclosure: A. Tripipitsiriwat, None; **C. Komoltri**, None; **R. Ruangchira-Urai**, None; **P. Ungprasert**, None.

Abstract Number: 1041

Pharmaco-epidemiology of Non-infectious Ocular Inflammatory Disease in a Tertiary Academic Center

Sanjeev Patil[1], Justine Cheng[2], Lorraine Provencher[3] and Scott Vogelgesang[4], [1]University of Vermont Medical Center, Essex Junction, VT, [2]University of Iowa Hospitals and Clinics, Iowa City, IA, [3]Cincinnati Eye Institute, Cincinnati, OH, [4]University of Iowa Hospitals and Clinics, Iowa City, IA

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

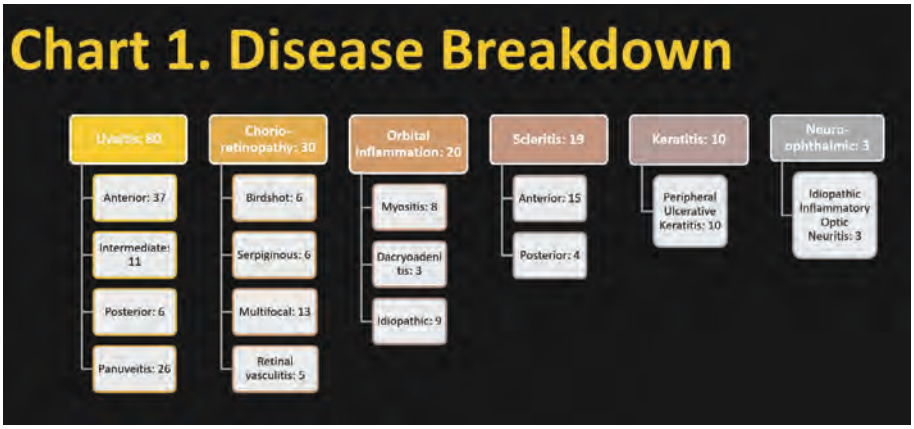
Background/Purpose: Non-Infectious Ocular inflammatory disease (OID) is a group of immune-mediated diseases involving the ocular surface, uveal tract, retina, optic nerve, and peri-orbital tissue. Patients are often referred to rheumatology for assistance with Disease-Modifying Anti-Rheumatic Drug (DMARD) therapy, when topical or systemic corticosteroids have not been completely effective. Real-world rheumatology practice of DMARD therapy selection to treat OID remains undescribed. We aim to describe the current DMARD prescribing practice at a tertiary academic center and identify effectiveness of these DMARDs.

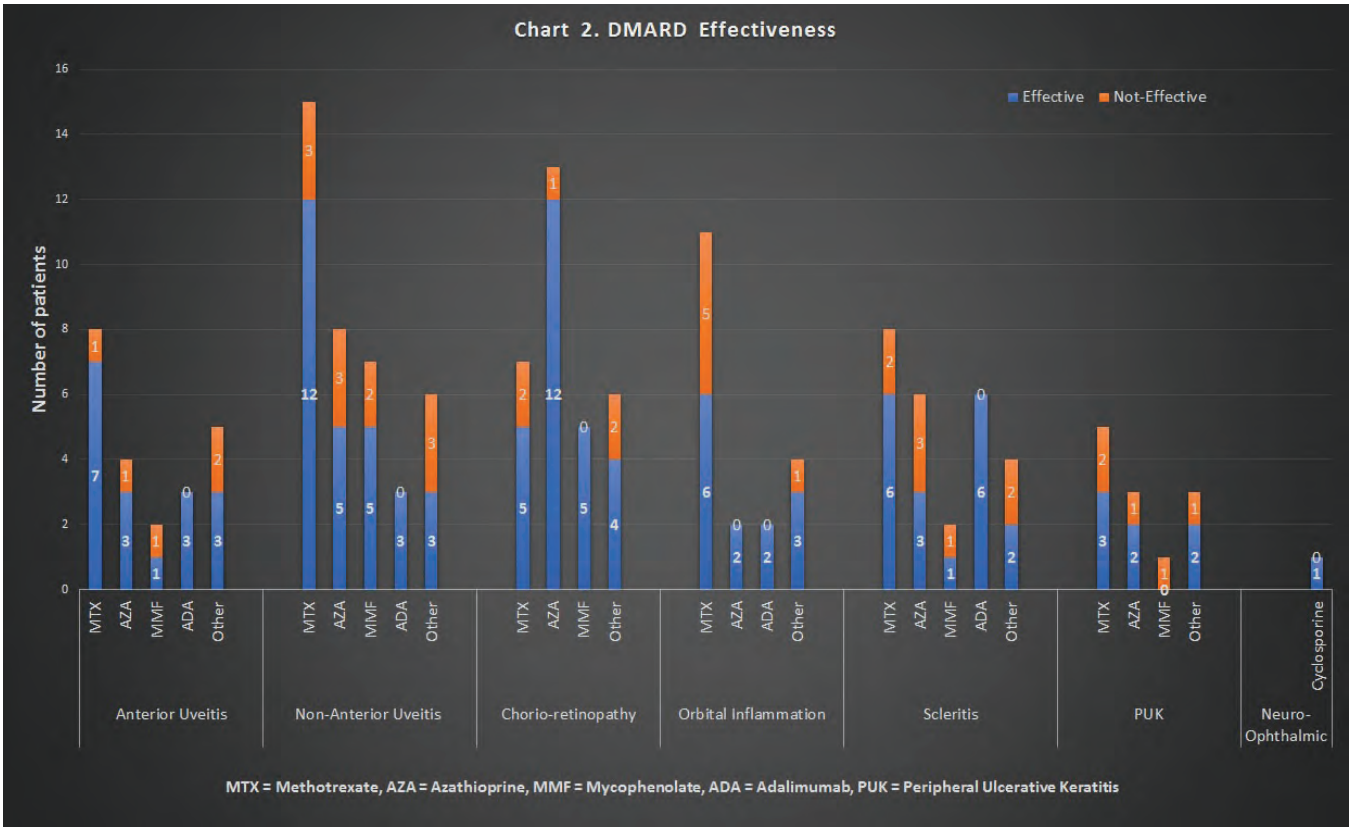
Methods: Retrospective descriptive cohort study of patients with OID treated at an academic tertiary center from 2000 to 2017. Inclusion criteria: age > 18 years, use of DMARDs, ≥ 2 visits with a rheumatologist, treatment with oral corticosteroid (≥10mg). Exclusion criteria: DMARD use for a systemic autoimmune disease and not particularly for OID.

DMARD effectiveness was defined as disease control, as determined by the ophthalmologist, and the ability to taper oral prednisone to ≤ 10mg. DMARD therapy was considered not effective when oral prednisone could not be tapered

Table 1. Patient characteristics

		Number of patients (N=162)	Percentage
Age	Median 42 years [IQR 29 - 56 years]		
Gender	Male	67	41.4%
	Female	95	58.6%
Race	African American	5	3.0%
	Asian	22	13.6%
	Caucasian	102	63.0%
	Hispanic	7	4.3%
	Native American	3	1.8%
	South Asian	2	1.2%
	Unspecified	19	11.7%
Smoking status	Ever smoker	76	47.0%
	Never smoker	77	47.5%
	Unknown	9	5.5%
Systemic Associations: 61 (37.2%)	Ankylosing spondylitis	13	7.9%
	RA	7	4.3%
	GPA	7	4.3%
	Sarcoidosis	7	4.3%
	Behcet's	5	3.0%
	JIA	4	2.4%
	Inflammatory arthritis	3	1.8%
	IBD (UC/Crohn's)	2	1.2%
	Multiple sclerosis	2	1.2%
	SLE	2	1.2%
	Psoriatic arthritis	2	1.2%
	Sjogren's	1	0.6%
	TINU	1	0.6%
	VKH	1	0.6%
	EGPA (Churg Strauss)	1	0.6%
	Relapsing polychondritis	1	0.6%
		Range	
Average Follow-up	7 years	0 to 18 years	





≤10mg due to active disease, active ocular disease as evaluated by the ophthalmologist despite the DMARD, or the need to discontinue the DMARD due to adverse effects.

Proportions were used to describe demographic characteristics, diagnoses, DMARDs prescription trends and effectiveness.

Results: A total of 369 patients were identified and 162 met the inclusion criteria. Median age was 42 years [Interquartile Range (IQR) 29 - 56 years]. The majority were Caucasian (63.0%) and female (58.6%). The most common OID was uveitis (49.4%), followed by chorioretinopathy (18.5%), orbital inflammation (12.3%), scleritis (11.7%), keratitis (6.2%), and neuro-ophthalmic (1.9%) (Chart 1).

With the exception of chorioretinopathy, methotrexate was the most common initial DMARD used in all forms of OID, ranging from 29% in chorioretinopathy to 63.2% in orbital inflammation. Mycophenolate followed by adalimumab were the most common subsequent DMARDs chosen. Other anti-TNF biologics were not used as often.

Chart 2 shows effectiveness of DMARDs in the different forms of OID. Methotrexate was found to be more effective in uveitis (around 80%), scleritis and chorioretinopathy, as compared to in orbital inflammation and keratitis. Adalimumab was found to be highly effective in uveitis, orbital inflammation and scleritis.

Conclusion: Our data suggests that the most common OID rheumatologists at our center treat is Uveitis, while most common DMARD used is methotrexate. Methotrexate and adalimumab were more commonly noted to be effective in treating some forms of OID.

Some of the limitations of our study are that this is a single institutional study, with small cohort when broken down into various subgroups of OID diagnoses, many patients lost to follow up which led to their exclusion, and lack of standardized practice patterns and steroid tapering schedule.

While there are RCTs on treatment of anterior uveitis, there is a need for multicenter RCTs for difficult to treat anterior uveitis and other OIDs.

Disclosure: S. Patil, None; **J. Cheng**, None; **L. Provencher**, None; **S. Vogelgesang**, None.

Abstract Number: 1042

Building LSU Uveitis Registry (BLUR) Study – a Review of an Academic Rheumatology Center's Experience and Approach to Uveitis

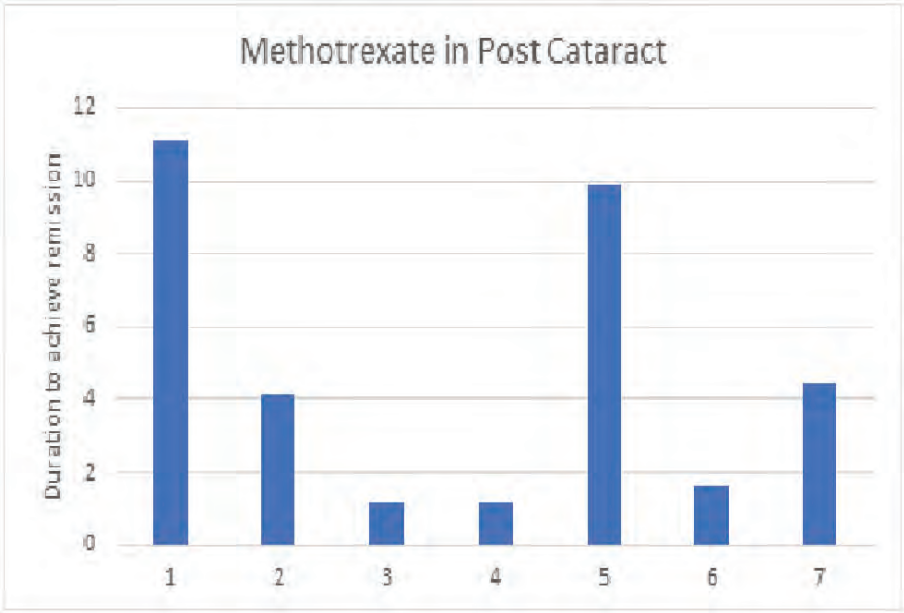
Anusha Vuppala[1], Kinza Muzzafar[1], Swathi Chalasani[1], Sibile Pardue[2], Samina Hayat[3] and Sarwat Umer[3], [1]LSUHSC Shreveport, Shreveport, LA, [2]LSUHSC Shreveport, Shreveport, [3]LSU Shreveport, Shreveport, LA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

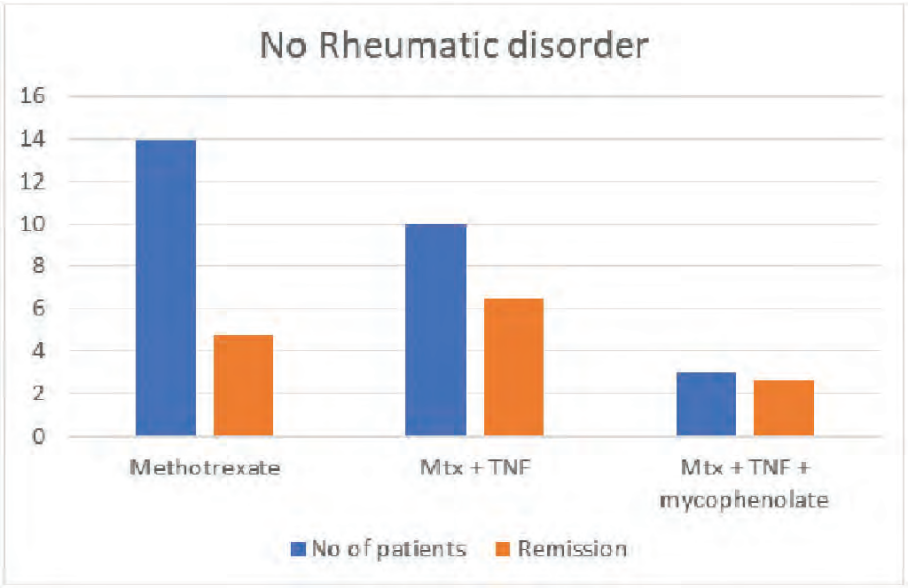
Background/Purpose: Uveitis is the most common ophthalmological finding seen by Rheumatologists. Ocular inflammation commonly presents as a manifestation of underlying rheumatic disorder. Local and systemic glucocorticoid therapies remain mainstay for initial therapy and various steroid sparing agents are being used to achieve disease stability. This study was performed in our Academic Center to identify the steroid sparing drugs with best efficacy to achieve remission in our patient population.

Methods: This is a retrospective analysis of 96 patients seen in our clinic with the diagnosis of Uveitis. Data analysis was done by student t test.

Results: Uveitis in our population is seen from ages 12 – 80 yrs with mean age of 51 yrs. 82% of our patients are African American and 17% are Caucasian. Patients with Sarcoidosis constituted about 23.9% and post cataract constituted 7%. The remaining 20% included RA, SLE, Scleroderma, JIA and ANCA vasculitis. 72% of our patients presented with Anterior uveitis, 14% with posterior uveitis and 10% with pan uveitis. Methotrexate was used most



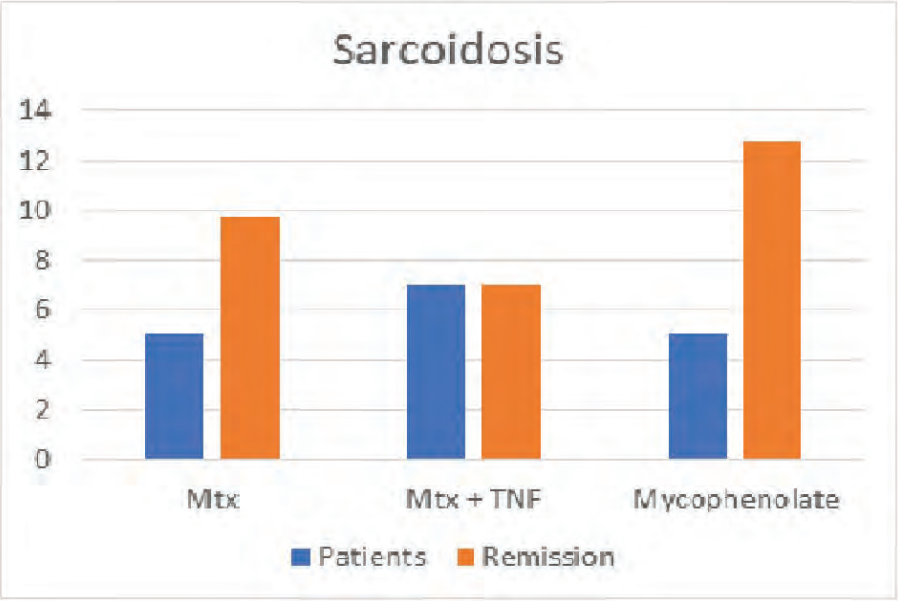
Methotrexate for remission induction in Post cataract patients



Medications for patients with no rheumatic disorder

frequently with 62% of our patient population. It was followed by TNF alpha inhibitors with frequency of 39%. 100% of our post cataract patients achieved remission just with methotrexate with mean remission duration of 4 months. Of the patients with no associated rheumatic disorder, methotrexate is associated with lowest duration to achieve remission – 4.8 months. Patients with Sarcoidosis achieved remission with methotrexate and TNF alpha inhibitors in mean of 7.8 months

Conclusion: Uveitis in our patients is associated with Sarcoidosis, post cataract and few patients with RA, Scleroderma, SLE, JIA, ANCA Vasculitis. 39% of our patients have no associated autoimmune disorder. Stability of disease was able to be achieved in 4 months with use of methotrexate in almost half of our population. 37% of patients required to be placed on combination methotrexate and TNF alpha inhibitors. Remission in these patients was achieved in 6.8



Medications for remission induction in sarcoid

months. Uveitis due to post cataract attained remission solely with the use of methotrexate. Whereas patient with Sarcoidosis responded well to combination of TNF alpha inhibitors and methotrexate rather than methotrexate alone. Mycophenolate was used in few patients with Sarcoidosis who were intolerant to methotrexate, thus confounding the duration for remission. Rituximab was added for refractory uveitis unresponsive to other therapies. Duration for remission with Rituximab appears shorter mainly due to low sample size. More studies are needed to further tailor the treatment regimen for Uveitis associated with various autoimmune rheumatic disorders.

Disclosure: A. Vuppala, None; **K. Muzzafar**, None; **S. Chalasani**, None; **S. Pardue**, None; **S. Hayat**, None; **S. Umer**, None.

Abstract Number: 1043

Ocular Scleral Pathology and Immune-Mediated Inflammatory Diseases. Study of 170 Patients from a Single Universitary Center

Lara Sanchez-Bilbao[1], Inigo Gonzalez-Mazon[2], José Luis Martín-Varillas[3], David Martinez-Lopez[4], Carmen Alvarez-Reguera[1], Alba Herrero Morant[1], Rosalia Demetrio-Pablo[1], Vanesa Calvo-Río[1], Miguel Ángel González-Gay[5] and Ricardo Blanco[1], [1]Hospital Universitario Marques de Valdecilla, Santander, Spain, [2]Hospital Universitario Marques de Valdecilla, Bezana, Spain, [3]Hospital Sierrallana, Torrelavega, Spain, [4]Hospital Universitario Marques de Valdecilla, Santander (SPAIN), Spain, [5]Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

TABLE 1. General features and etiology, n (%)

Episcleritis (n=132): Simple / Nodular	115 (87.1%) / 17 (12.9%)
Scleritis (n=38): Diffuse anterior / Nodular anterior	23 (60.5%) / 15 (39.5%)
Complications	30 (17.7)
- Uveitis	10 (5.9)
- Keratitis	7 (4.6)
- Glaucoma	9 (3.9)
- Cataract	4 (2.6)
ETIOLOGY	
Idiopathic	**85 (50)**
Infectious	**11 (6.5)**
Herpes simplex virus / Varicella zoster virus	9 (5.3) / 2 (1.2)
IMID*	**74 (43.5)**
- Spondyloarthritis	19 (11.2)
- Crohn's disease	16 (9.4)
- Rheumatoid Arthritis	12 (7.1)
- Granulomatosis with polyangiits	7 (4.1)
- Relapsing polychondritis	6 (3.5)
- Systemic lupus	4 (2.4)
- Ulcerative colitis	3 (1.8)
- Psoriasis	2 (1.2)

***Behçet, Sarcoidosis, Leucocytoclastic vasculitis, Thyroiditis, Celiac disease, was observed 1 case of each.**

TABLE 2. Treatment, n (%)

Systemic	
- NSAIDs	119 (70)
- Prednisone	63 (37.1)
- Bolus MTP	6 (3.5)
Conventional immunosupressants	
- Methotrexate	39 (22.9)
- Azathioprine	16 (9.4)
- Salazopyrine	6 (3.5)
- Hydroxychloroquine	6 (3.5)
- Cyclophosphamide	3 (1.8)
- Mycophenolate mofetil	2 (1.2)
Biological agents	
- Infliximab	13 (7.7)
- Adalimumab	11 (6.5)
- Etanercept	3 (1.8)
- Golimumab	5 (2.9)
- Secukinumab	5 (2.9)
- Abatacept	2 (1.8)

Background/Purpose: Ocular scleral pathology (OSP) includes episcleritis and scleritis. Episcleritis is generally a benign disease with a self-limited course, while scleritis is a more severe ocular condition. Both may be associated

with immune-mediated inflammatory diseases (IMID).

In a wide series with OSP our aim was to assess the **a)** epidemiological and clinical features and **b)** relationship with IMID.

Methods: Study of all consecutive patients studied in a single Universitary Hospital during the last ten years with**: a)** episcleritis and **b)** scleritis diagnosed by clinical features and slit-lamp (Watson and Hayreh criteria).

Results: We studied 170 patients (101 women/ 69 men) / 340 affected eyes with OSP (episcleritis=132; scleritis=38); mean age at diagnosis 49.03±14.11 years.

OSP was unilateral in 138 (81.2%), recurrent in 70 (41.2%) and chronic in 21 (12.4%). Most of them were idiopathic (n=85, 50%) while associated IMID were 43.5% (**TABLE 1)**.

Topical treatment was used in all patients. In addition to systemic corticosteroids, conventional immunosuppressive and biological drugs were required in 52 cases (30.6%) and 20 (11.8%), respectively (**TABLE 2)**. The main indication for biological therapy was the presence of underlying IMID.

Conclusion: Scleral pathology is a relatively frequent entity and it is necessary to exclude an underlying systemic disease.

Disclosure: L. Sanchez-Bilbao, None; **I. Gonzalez-Mazon**, None; **J. Martín-Varillas**, None; **D. Martinez-Lopez**, Lilly, 2; **C. Alvarez-Reguera**, None; **A. Herrero Morant**, None; **R. Demetrio-Pablo**, None; **V. Calvo-Río**, None; **M. González-Gay**, None; **R. Blanco**, None.

Abstract Number: 1044

Ocular Manifestations in Inflammatory Bowel Disease. Study of 1442 Patients from a Single Referral Center

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory bowel disease (IBD), which includes Crohn's disease (CD), and Ulcerative colitis (UC) are related to Spondyloarthritis (SpA). Ocular manifestations (OM) are well-stablished in SpA but not in IBD. It has been classically reported that whereas uveitis with SpA is predominantly anterior, unilateral, sudden, and limited; in IBD it is bilateral, posterior, insidious, and chronic *(Lyons & Rosenbaum JT. Arch Ophthalmol 1997; 115:61-4).*

TABLE.

	Uveitis (n= 23)	Epi/scleritis (n=19)	p
DEMOGRAPHIC PARAMETERS			
Sex, n (%)	6 ♂ / 17 ♀	11 ♂ / 8 ♀	**p= 0.04***
Age at diagnosis (years) mean ± SD	49.13±14.64	47.63±12.48	p= 0.415
INTESTINAL AFFECTION			
CD, n (%)	12 (52.17)	16 (84.21)	**p= 0.02***
UC, n (%)	11 47,83)	3 (15,74)	p= 0.16
EXTRAINTESTINAL AFFECTION			
Cutaneous manifestations			
Erythema nodosum, n (%)	6 (26.09)	2 (10.53)	p= 0.30
Pyoderma gangrenosum, n (%)	1 (4.35)	0 (0)	p= 0.92
Psoriasis, n (%)	1 (4.35)	4 (21.01)	p= 0.23
Joint involvement	10 (43.50)	6 (31.60)	p= 0.38
Psoriatic arthritis, n (%)	1 (4.35)	3 (15.80)	p= 0.47
Enteropathic Spondyloarthritis, n (%)	6 (26.09)	3 (15.80)	p= 0.66
Ankylosing Spondylitis, n (%)	3 (13.04	0 (0)	p= 0.28
Digestive manifestations			
NASH, n (%)	4 (17.39)	6 (31.58)	p= 0.28

***p value < 0.05. SD:** standard deviation; **CD:** Crohn's disease; **UC:** ulcerative colitis; **NASH:** non-alcoholic steatohepatitis.

In a large unselected series of IBD, we study the OM and assess; **a)** epidemiological, clinical features, **b)** the relationship with extraintestinal manifestations

Methods: Study of all consecutive patients from a single University Hospital during the last 40 years with**: a)** IBD (CD and UC), and **b)** OM: uveitis and scleral pathology diagnosed by clinical features and slit-lamp.

Results: OM were present in 42 (2.9%) (25 women/17 men) (84 eyes) of 1442 IBD patients; OM included the uveitis group (UG) (n=23; 1.6%) and the scleral pathology group (SG) (n=19, 1.32%) (**TABLE)**.

The most common pattern in SG was episcleritis (n=16; 84.21%) and scleritis (n=3). In UG, uveitis was typically anterior (n=18; 78.3%), unilateral (n=19; 82.6%), sudden (n=19; 82.6%), and limited (n=12; 52.2%).

The comparative study between SG vs UG showed in UG a significant predominance of women and UC. Also, a non-significative higher frequency in Pyoderma gangrenosum, erythema nodosum and joint involvement was observed in UG.

After a mean follow-up of 15.2±9.97 years, extraintestinal manifestations were observed in 100% of patients, being articular forms (n=16; 38.10%) the most common type. In addition, joint/axial flare is more related to the presence of uveitis (p=0.038).

Conclusion: Both uveitis and episcleritis are equally frequent OM in IBD. Although uveitis is more infrequent in IBD than in SpA, it is also anterior, unilateral, sudden and limited in contrast with published data from selected series.

Disclosure: L. Sanchez-Bilbao, None; **D. Martinez-Lopez**, Lilly, 2; **I. Gonzalez-Mazon**, None; **M. García-García**, None; **M. Rivero-Tirado**, None; **B. Castro**, None; **J. Crespo**, None; **M. González-Gay**, None; **R. Blanco**, None.

Abstract Number: 1045

Biological therapy in atypical optic neuritis refractory to conventional treatment. A multicenter study with 19 patients.

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Optic Neuritis (ON) is an inflammation of the optic nerve. Its most common presentation is demyelinating typical ON. Atypical ON is rare, severe, non-demyelinating and can be isolated or associated to different diseases including autoimmune diseases. If it is not treated, it can lead to devastating visual results. Conventional treatment includes systemic corticosteroids and conventional immunosuppressants (CIS). Our aim was to assess the efficacy of biological therapy in atypical ON refractory to conventional treatment.

Methods: Open-label multicenter study including 19 patients diagnosed with atypical ON refractory to systemic corticosteroids and at least one CIS. The main outcomes assessed were Best Corrected Visual Acuity (BCVA) and optic nerve and ganglionar cells Optical Coherence Tomography (OCT). These outcome variables were recorded at baseline, 1 week, 2 weeks, 1 month, 3 months and 6 months and 1 year after biological therapy onset.

Results: We studied 19 patients (12 women/7 men); mean age of 34.8 ± 13.9 years. The underlying diseases were idiopathic (n=7), Behçet´s disease (n=5), systemic lupus erythematosus (n=2), neuromyelitis optica (n=3), sarcoidosis (n=1) and relapsing polychondritis (n=1) **(TABLE).** Before biological therapy and besides systemic corticosteroids, patients had received different CIS. Biological therapy was adalimumab (n=6), rituximab (n=6), infliximab (n=5) and tocilizumab (n=4). After biological therapy, an improvement in ocular parameters was observed: BCVA [0.7±0.3 to 0.8±0.3; p= 0.03], optic nerve OCT [123.2±58.3 to 190.5±175.4; p= 0.11], and ganglionar cells OCT [369.6±137.4

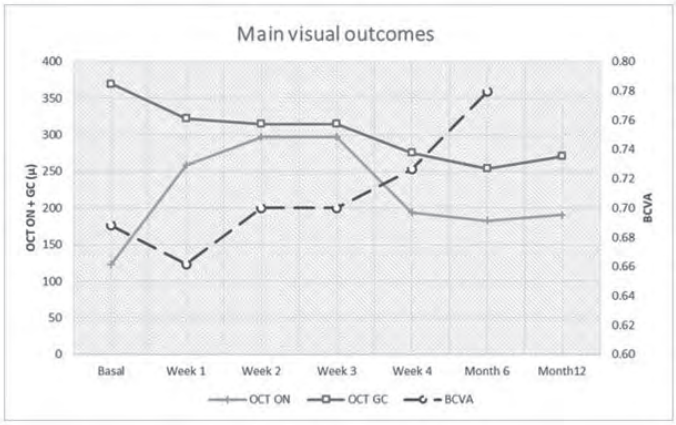
TABLE

Case	Gender/ Age	Underlying disease	Laterality	IV steroids dose (g)	Maximum prednisone oral dose (g)	Conventional immunosuppressants	Biological therapy	Adverse effects
1	F/29	Idiopathic	Unilateral	4	60	AZA	TCZ	No
2	F/26	Idiopathic	Bilateral	5.5	30	AZA	TCZ	No
3	F/13	Idiopathic	Bilateral	-	10	MTX	ADA	No
4	F/25	Idiopathic	Bilateral	4	60	MTX	IFX, TCZ	No
5	F/24	Idiopathic	Bilateral	0.5	60	MTX, AZA	ADA	No
6	M/14	Idiopathic	Bilateral	-	10	MTX	ADA	No
7	F/30	Vasculitis ANCA+	Unilateral	3	60	AZA, MMF, LFM, CFM	RTX	Yes
8	M/21	Behçet	Bilateral	-	60	MTX, AZA	ADA	Nausea Vomits
9	M/25	Behçet	Unilateral	0.5	60	MTX, CyA	ADA	No
10	M/39	Behçet	Unilateral	3	80	MTX, MMF	IFX	No
11	M/40	Behçet	Unilateral	-	80	MMF	IFX	No
12	M/37	Behçet	Unilateral	-	60	CyA	IFX	No
13	F/68	NMO	Unilateral	2.5	30	CFM, AZA	RTX	No
14	F/41	NMO	Unilateral	3	60	CFM	RTX	Infection
15	F/43	NMO	Bilateral	5	60	AZA	RTX	Infusion reaction
16	F/56	SLE	Unilateral	-	60	HCQ, MMF, CFM	RTX	No
17	F/47	SLE	Unilateral	5	60	HCQ, MMF	RTX	No
18	F/43	Relapsing polychondritis	Bilateral	3	60	MTX, CFM	IFX, TCZ	No
19	M/41	Sarcoidosis	Bilateral	3	40	AZA	ADA	No

to 270.7±23.2; p= 0.03] at one year **(FIGURE)**. After a mean follow-up of 29.1 ±19.2 months, there were no severe adverse effects observed.

Conclusion: Biological therapy may be effective in patients with refractory atypical ON.

FIGURE



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Abstract Number: 1046

Risk Factors Associated with Interstitial Lung Disease in Patients with RA: Findings from a Retrospective Healthcare Database Analysis

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SESSION INFORMATION

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Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a frequent complication of RA and is associated with increased morbidity and mortality.[1] Previous studies have shown variability in risk factors for RA-associated ILD (RA-ILD).[1,2] The objective of this analysis was to systematically evaluate the risk factors of RA-ILD in a real-world population of patients with RA.

Methods: Patient demographic and disease characteristics were retrospectively analyzed following data extraction from the Discus Analytics JointMan database, a large US electronic medical records-based dataset. Adults with an RA diagnosis (International Classification of Disease, Ninth Revision, Clinical Modification [ICD-9-CM] code: 714.0; ICD, Tenth Revision, CM [ICD-10-CM] codes: M05, M06) between January 1, 2009 and September 20, 2019, ≥1 visit after the initial visit date, no diagnosis code for ILD prior to RA diagnosis and no diagnosis code for drug-induced ILD at any time during the study period were included in the analysis. Patients with ILD were identified by ICD diagnosis

Table 1. Baseline characteristics of patients with RA and RA-ILD

	RA only (n=5612)	RA-ILD (n=205)	p value
Age, years[a]	59.1 (14.2)	65.8 (11.8)	<0.001*
Age category, years			
18–54	1938 (34.5)	39 (14.1)	<0.001*
55–64	1550 (27.6)	60 (29.3)	0.604
65–74	1360 (24.2)	72 (35.1)	<0.001*
75–79	412 (7.3)	20 (9.8)	0.195
≥80	352 (6.3)	24 (11.7)	0.002*
Sex, male	1375 (24.5)	72 (35.1)	<0.001*
Race			
Black/African American	365 (6.5)	9 (4.4)	0.226
White	4014 (71.5)	165 (80.5)	0.005*
Other/missing	1233 (22.0)	31 (15.1)	0.020*
Primary insurance category			
Commercial	2407 (42.9)	51 (24.9)	<0.001*
Medicare (alone or with other)	1596 (28.4)	97 (47.3)	<0.001*
Medicaid (alone or with commercial)	132 (2.4)	4 (2.0)	0.709
No insurance	410 (7.3)	20 (9.8)	0.223
Missing	1058 (18.9)	33 (16.1)	0.321
CCI score[a]	0.2 (0.6)	0.2 (0.4)	0.963
Co-morbidities			
History of COPD[b]	102 (2.7)	5 (7.0)	0.008*
Diabetes[b]	341 (8.9)	9 (7.8)	0.699
Hyperlipidemia[b]	461 (12.5)	14 (12.2)	0.915
Hypertension[b]	900 (23.4)	23 (20.0)	0.395
Serious infection[b]	38 (1.0)	3 (2.6)	0.091
Coronary artery disease	28 (0.5)	1 (0.5)	0.982
GERD	251 (4.5)	3 (1.5)	0.038*
Obesity[c]	1688 (30.0)	50 (24.4)	0.002*
Smoking status: yes[d]	205 (4.9)	10 (8.5)	0.082
RA characteristics[b]			
RF positive	1388 (36.1)	89 (60.0)	<0.001*
Joint stiffness	1092 (28.4)	39 (33.9)	0.197
Rheumatoid nodules	153 (4.0)	17 (14.8)	<0.001*
Erosions	459 (11.9)	23 (20.0)	0.009*
Extra-articular disease[e]	487 (12.7)	29 (25.2)	<0.001*
Anti-CCP antibodies[f]	1505 (27.1)	94 (45.9)	<0.001*
Joint evaluation[g]			
Swelling	2861 (56.0)	123 (68.0)	0.008*
Tenderness	3729 (75.6)	138 (76.2)	0.951
Laboratory tests[a,g]			
ESR, mm/h	22.0 (22.6)	30.1 (25.5)	<0.001*
CRP, mg/L	22.5 (13.0)	60.6 (25.0)	0.086
CDAI score[a,g]	16.4 (12.7)	16.9 (15.7)	0.049*
Disease activity category			
Remission	342 (7.5)	16 (10.1)	0.205
Low	1387 (30.5)	44 (27.7)	0.128
Moderate	1644 (36.1)	45 (28.3)	0.361
High	1175 (25.8)	54 (34.0)	0.073
SDAI score[a,g]	20.2 (23.9)	28.6 (47.3)	0.031*
Disease activity category			
Remission	152 (6.2)	7 (7.4)	0.995
Low	668 (27.2)	16 (16.8)	0.020*
Moderate	1025 (41.8)	33 (34.7)	0.426
High	607 (24.8)	39 (41.1)	0.002*
DAS28 (CRP) score[a,g]	2.6 (1.2)	3.1 (1.4)	0.004*
Disease activity category			
Remission	1152 (46.5)	31 (32.0)	0.048*
Low	291 (11.8)	11 (11.3)	0.447
Moderate	750 (30.3)	33 (34.0)	0.953
High	283 (11.4)	22 (22.7)	0.001*
DAS28 (ESR) score[a,g]	3.3 (1.4)	3.9 (1.5)	<0.001*
Disease activity category			
Remission	873 (35.1)	20 (21.1)	0.021*
Low	394 (15.9)	11 (11.6)	0.600
Moderate	960 (38.6)	41 (43.2)	0.647
High	257 (10.3)	23 (24.2)	<0.001*
RAPID3 score[a,g]	12.2 (6.4)	12.3 (6.6)	0.482
Disease activity category			
Remission	486 (9.9)	18 (10.3)	0.073
Low	531 (10.8)	12 (6.9)	0.071
Moderate	1331 (27.2)	56 (32.0)	0.206
High	2549 (52.1)	89 (50.9)	0.999

Data are n (%) unless stated otherwise.

*p values are significant (p<0.05).

[a]Mean (SD).

[b]Among patients with non-missing RA characteristics data: RA-only cohort, n=3846; RA-ILD cohort, n=115.

[c]Diagnosis code or BMI ≥30 kg/m².

[d]Among patients with non-missing RA characteristics data: RA-only cohort, n=4102; RA-ILD cohort, n=118.

[e]Including nodules, sicca, uveitis, vasculitis and Felty's syndrome.

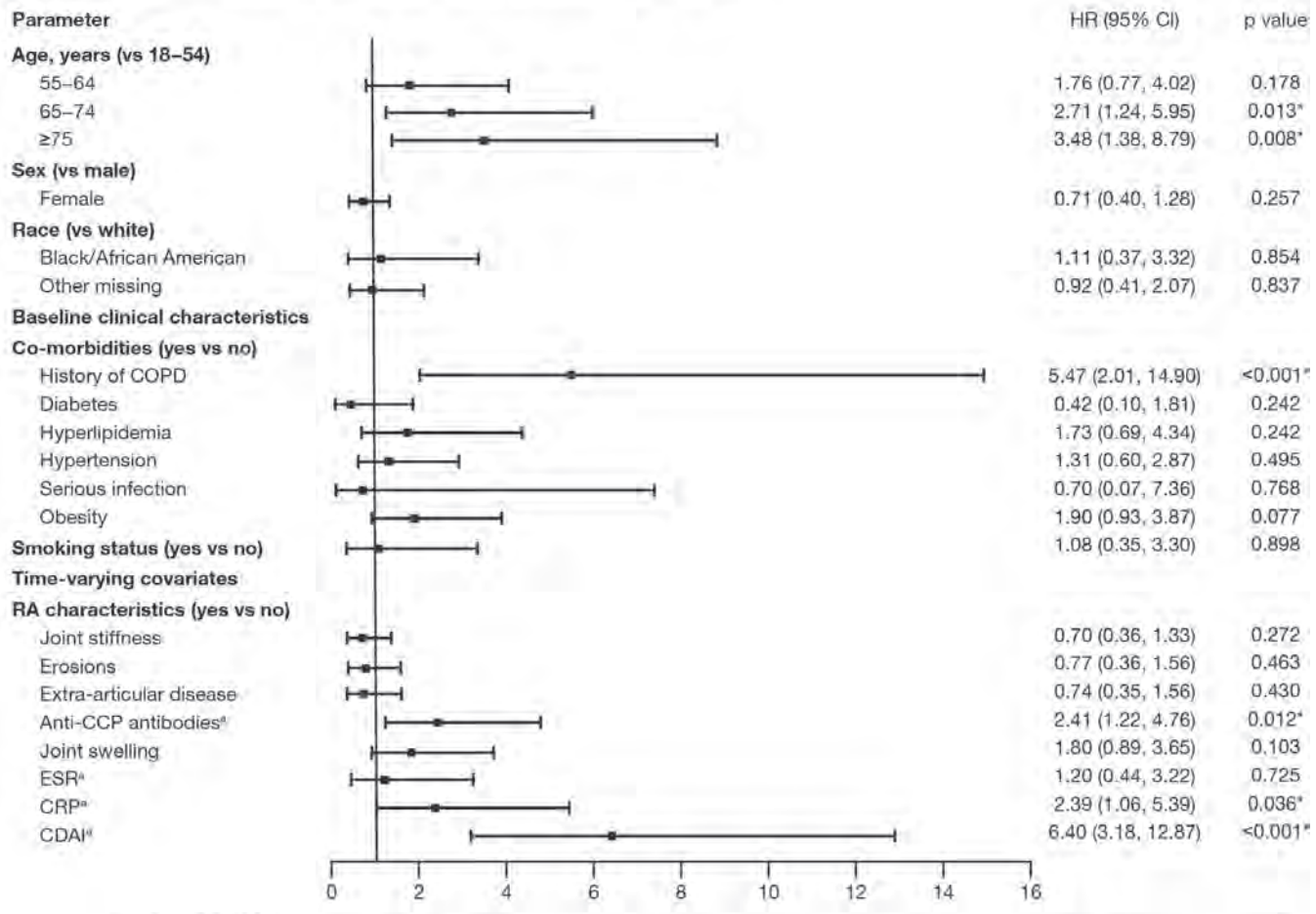
[f]Binary (anti-CCP >20 U/mL considered positive) plus continuous: RA-only cohort, n=5552; RA-ILD cohort, n=115.

[g]Non-missing values: joint evaluation RA-only cohort, n=4929; RA-ILD cohort, n=181; ESR RA-only cohort, n=2952; RA-ILD cohort, n=128; CRP RA-only cohort, n=2997; RA-ILD cohort, n=132; CDAI RA-only cohort, n=4548; RA-ILD cohort, n=159; SDAI RA-only cohort, n=2452; RA-ILD cohort, n=95; DAS28 (CRP) RA-only cohort, n=2476; RA-ILD cohort, n=97; DAS28 (ESR) RA-only cohort, n=2484; RA-ILD cohort, n=98; RAPID3 RA-only cohort, n=4897; RA-ILD cohort, n=175.

CCI=Charlson Comorbidity Index; COPD=chronic obstructive pulmonary disease; GERD=gastroesophageal reflux disease; ILD=interstitial lung disease; RA-ILD=RA-associated interstitial lung disease; RAPID3=Routine Assessment of Patient Index Data 3.

codes (ICD-9-CM codes: 516.0, 516.2, 516.3, 516.4, 516.5, 516.8, 516.9; ICD-10-CM codes: J84.0, J84.1, J84.2, J84.81, J84.82, J84.83, J84.89, J84.9) or by provider indication. Potential predictors of RA-ILD were analyzed by Cox regression model. Patient demographic and co-morbid conditions were collected at baseline (defined as 6 months

Figure 1. Covariates potentially predictive of RA-ILD diagnosis



*p values are significant (p<0.05).

[a]Binary cut-offs were anti-CCP antibodies: >20 (anti-CCP+) = 1, ≤20 (anti-CCP–) and missing = 0; ESR: >28 mm/hr = 1, ≤28 mm/hr and missing = 0; CRP: >5 mg/L or >0.5 mg/dL = 1, ≤5 mg/L or ≤0.5 mg/dL and missing = 0; CDAI: moderate/high CDAI = 1, remission/low/missing CDAI = 0.

COPD=chronic obstructive pulmonary disease; HR=hazard ratio; ILD=interstitial lung disease; RA-ILD=RA-associated interstitial lung disease.

prior to or on date of initial RA diagnosis). RA characteristics were identified during and after the initial RA diagnosis and were controlled as time-varying covariates in the Cox model. Significance was set at $p< 0.05$.

Results: Of the 5817 patients included, 5612 had RA only and 205 had RA-ILD. Several baseline differences between patients with and without ILD were identified: a greater proportion of patients with RA-ILD vs RA only were older, male, of white race, had a history of chronic obstructive pulmonary disease (COPD) and had more severe and more active RA than did patients with RA only (**Table 1**).[3] Cox multivariate regression analysis showed older age (>65 years old) and a history of COPD at baseline to be risk factors for developing ILD (**Figure 1**). Additionally, several time-varying covariates (anti-CCP positivity, CRP >5 mg/L and a moderate-to-high CDAI score) were also shown to be predictive of developing ILD.

Conclusion: In this large, real-world analysis of patients with RA, several risk factors for RA-ILD were identified: age, COPD, anti-CCP+, CRP and CDAI score. Recognition of these risk factors may lead to improved identification and a tailored approach to treatment of RA-ILD.

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2. Kiely P, et al. BMJ Open 2019:9:e028466.
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Medical writing: Rachel Rankin (Caudex).

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Abstract Number: 1047

Prospective Analysis of a Cohort of Patients with Interstitial Lung Disease Associated with Connective Tissue Disease and Their Response to Immunosuppression with Mycophenolate Mofetil and Rituximab

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Connective tissue diseases (CTDs) are commonly identified causes for interstitial lung disease (ILD). Compared with idiopathic interstitial pneumonias, patients with CTD-ILD and interstitial pneumonia with autoimmune features (IPAF) are more likely to respond to immunosuppression with a better prognosis. We aim to investigate use of mycophenolate (MMF) and rituximab (RTX) in a mixed cohort of patients with CTD-ILD, prospectively followed up for one year in a single academic center.

Methods: Patients with CTD and ILD were identified based on electronic medical records from Mayo Clinic Jacksonville and Rochester campuses from 2009 - 2019. Chart review was conducted in 413 patients, with 138 confirmed cases of CTD-ILD or IPAF based on multidisciplinary evaluation. 91 were further excluded due to post transplant status, mild disease only on observation, treatment with agents other than MMF and RTX, or incomplete data. Eventually, 47 patients with CTD-ILD or IPAF, treated with MMF and / or RTX, were included. Demographics, pertinent clinical symptoms, pulmonary function test (PFT) and treatment were collected at baseline, 6-month and 12-month follow up.

MMF and RTX doses and treatment track were analyzed individually with improvement in PFT. Multivariable linear regression models were used to assess baseline and 6-month treatment doses of MMF and RTX, with changes in outcomes during 12-month follow-up. All models were adjusted for age, sex, and prednisone dose at corresponding follow-ups.

Results: Baseline characteristics of the 47 patients are summarized in Table 1. Forty (85%) patients were diagnosed with CTD-ILD, with 19 (40%) as Antisynthetase Syndrome, and 7 (15%) had IPAF. Six (13%) patients were on RTX only, 28 (60%) on MMF only, and the remaining 13 (28%) were on combined therapy with MMF and RTX or switched from MMF to RTX due to lack of response or intolerance to MMF.

PFT outcomes in association with medication dose are summarized in Table 2. Throughout the 12-month study period, forced vital capacity (FVC) and FVC% remained sTable with each treatment dose or track. Patients on higher doses of MMF were associated with an average increase of 1.34 (95% CI: 0.38, 2.29) units in diffusing capacity for carbon monoxide (DLCO) for every 1-gram increase in MMF, from baseline to 6-month (P=0.01), which stabilized from 6 to 12-month follow-up. Patients on RTX monotherapy had significantly worsening in DLCO by 7.21 (95% CI: 4.08, 10.33) units (P< 0.001) from baseline to 12-month.

Ten patients received MMF and RTX combined therapy during study period, with clinical features summarized in Table 3. Although pulmonary function was severely compromised at baseline, these patients acquired sustained improvement from baseline to 12-month. In all cases, prednisone was decreased to a maintenance average dose of 8 mg/day at 12-month follow up.

Table 1. Demographic features

	Overall (N=47)
Age (median)	57 (range: 32, 79)
Females, n (%)	34 (72.3%)
Race, n (%)	
White	36 (76.6%)
Asian	2 (4.3%)
Black or African American	4 (8.5%)
Hispanic or Latino	2 (4.3%)
Smoker	
Former	18 (38.3%)
Never	29 (61.7%)
CTD-ILD	40 (75.0%)
IPAF	7 (25.0%)
CTD diagnosis	
Antisynthetase Syndrome	19 (40.4%)
Seropositive Rheumatoid arthritis	5 (10.6%)
Mixed Connective Tissue Disease	5 (10.6%)
Overlap syndrome	3 (6.4%)
Dermatomyositis	2 (4.3%)
Polymyositis	1 (2.1%)
Amyopathic Dermatomyositis	2 (4.3%)
Limited Scleroderma	1 (2.1%)
Systemic Scleroderma	1 (2.1%)
Unspecified Inflammatory Arthritis	1 (2.1%)
CT diagnosis	
NSIP/OP overlap	21 (44.7%)
NSIP	12 (25.5%)
UIP	4 (8.5%)
COP	4 (8.5%)
Probable or Indeterminate UIP	3 (6.4%)
Others	3 (6.4%)

NSIP, non-specific interstitial pneumonia non-specific, OP, organizing pneumonia, UIP, usual interstitial pneumonia, COP, cryptogenic organizing pneumonia

Table 1. Demographic features

Table 2. Summary of treatment with PFT outcomes

	Unadjusted				Adjusted			
	Baseline to 6-Month		6-Month to 12-Month		Baseline to 6-Month		6-Month to 12-Month	
	Beta (95% CI)	P-value	Beta (95% CI)	P-value	Beta (95% CI)	P-value	Beta (95% CI)	P-value
FVC								
Rituximab	0.28 (-0.08, 0.64)	0.12	0.09 (-0.04, 0.22)	0.16	0.23 (-0.12, 0.57)	0.19	0.09 (-0.03, 0.22)	0.15
Mycophenolate	0.09 (-0.03, 0.22)	0.13	0.04 (-0.01, 0.09)	0.15	0.10 (-0.01, 0.21)	0.07	0.03 (-0.02, 0.09)	0.23
FVC%								
Rituximab	5.19 (-6.17, 16.54)	0.36	2.58 (-1.04, 6.20)	0.16	5.02 (-5.82, 15.86)	0.36	2.86 (-0.81, 6.53)	0.12
Mycophenolate	1.90 (-1.94, 5.75)	0.32	1.27 (-0.29, 2.83)	0.11	2.21 (-1.33, 5.76)	0.21	1.06 (-0.50, 2.63)	0.18
FEV1								
Rituximab	0.24 (-0.05, 0.52)	0.10	0.12 (-0.01, 0.25)	0.07	0.15 (-0.12, 0.42)	0.28	**0.15 (0.03, 0.28)**	**0.02**
Mycophenolate	0.09 (0.00, 0.19)	0.05	0.03 (-0.02, 0.09)	0.24	**0.10 (0.01, 0.18)**	**0.03**	0.03 (-0.02, 0.09)	0.21
FEV1%								
Rituximab	5.74 (-4.78, 16.26)	0.28	**5.30 (0.30, 10.30)**	**0.04**	3.61 (-6.56, 13.77)	0.48	**6.85 (1.88, 11.81)**	**0.01**
Mycophenolate	2.74 (-0.81, 6.30)	0.13	1.61 (-0.53, 3.75)	0.14	2.81 (-0.51, 6.13)	0.10	1.60 (-0.52, 3.71)	0.13
DLCO								
Rituximab	**3.36 (0.63, 6.10)**	**0.02**	0.38 (-1.76, 2.51)	0.72	2.56 (-0.48, 5.60)	0.10	0.41 (-1.99, 2.82)	0.73
Mycophenolate	**1.16 (0.25, 2.07)**	**0.01**	**0.98 (0.10, 1.86)**	**0.03**	**1.34 (0.38, 2.29)**	**0.01**	0.95 (-0.02, 1.93)	0.05
DLCO%								
Rituximab	8.38 (-4.00, 20.76)	0.18	3.41 (-1.33, 8.15)	0.15	7.35 (-6.84, 21.54)	0.30	3.14 (-2.20, 8.48)	0.24
Mycophenolate	2.76 (-1.18, 6.71)	0.16	1.79 (-0.18, 3.76)	0.07	3.32 (-0.78, 7.43)	0.11	1.89 (-0.26, 4.05)	0.08

Table 2. Summary of treatment with PFT outcomes

Conclusion: Through the study period, patients with CTD-ILD or IPAF, treated with MMF, presented with stability of FVC and significant improvement in DLCO; while RTX monotherapy was associated with worsening DLCO. Combination of both medications was related with sustained improvement in PFT and gradual decrease in concurrent steroids doses.

Table 3. Clinical characteristics of patients on MMF and RTX combined therapy at baseline

	Overall (N=10)	P-value
Age (median)	59 (range: 34, 74)	
Females, n (%)	7 (70%)	
Smoker		
Former, n (%)	4 (40%)	
Never, n (%)	6 (60%)	
Clinical presentations		
Mechanic hands, n (%)	8 (80%)	
Proximal weakness, n (%)	4 (40%)	
Synovitis, n (%)	0 (0)	
mMRC 3-4, n (%)	9 (90%)	
CTD diagnosis		
Antisynthetase Syndrome, n (%)	3 (30%)	
MCTD, n (%)	2 (20%)	
Seropositive RA, n (%)	2 (20%)	
PM/DM, n (%)	3 (30%)	
Change in PFT from baseline to 12-month		
FVC (median, L)	0.19 (Range: -0.17, 0.93)	0.06
FVC (median, %)	4.50 (Range: -6.00, 19.00)	0.09
DLCO (median)	1.10 (Range: -1.40, 4.90)	0.08
DLCO (median, %)	7.00 (Range: -5.00, 23.00)	0.03
No. patients on corticosteroids	9	
Dose (mg/day), mean±sd	26.0 ± 16.5	

mMRC, modified medical research council (dyspnea scale), MCTD, mixed connective tissue disease, RA, rheumatoid arthritis, PM, polymyositis, DM, dermatomyositis

Table 3. Clinical characteristics of patients on MMF and RTX combined therapy at baseline

Disclosure: Y. Li, None; **H. Baig**, None; **C. Rojas**, None; **J. Stowell**, None; **E. Lesser**, None; **S. Borkar**, None; **A. Abril**, None; **I. Mira-Avendano**, None.

Abstract Number: 1048

Reduced Decline in Forced Vital Capacity in Patients with Progressive Fibrosing Autoimmune Disease-Related Interstitial Lung Diseases (ILDs) Treated with Nintedanib

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: In the randomized placebo-controlled INBUILD trial in patients with chronic fibrosing ILDs with a progressive phenotype, nintedanib reduced the rate of decline in forced vital capacity (FVC) over 52 weeks, with an adverse event profile characterized mainly by gastrointestinal events. We analyzed the effects of nintedanib on categorical changes in FVC in the subgroup of patients with autoimmune disease-related ILDs.

Methods: The INBUILD trial enrolled patients with a fibrosing ILD other than idiopathic pulmonary fibrosis, reticular abnormality with traction bronchiectasis (with or without honeycombing) of >10% extent on high-resolution computed tomography (HRCT), FVC ≥45% predicted, and DLco ≥30%–< 80% predicted. To be eligible to participate, patients had to meet protocol-specified criteria for progression of ILD within the 24 months before screening despite management as deemed appropriate in clinical practice. In the subgroup of patients with autoimmune disease-related ILDs, we analyzed absolute changes from baseline in FVC (mL) and FVC % predicted at week 52, and the proportions of patients with categorical declines in FVC % predicted at week 52 (analyzed using a worst observation carried forward approach).

Results: The subgroup with autoimmune disease-related ILDs comprised 170 patients (Table 1). At baseline, mean (SD) FVC was 69.6 (15.1) % predicted in the nintedanib group and 72.1 (14.6) % predicted in the placebo group. Mean (SE) absolute changes from baseline in FVC were -92.7 (29.1) mL in the nintedanib group and -185.7 (27.3) mL in the placebo group (difference 93.0 [95% CI 14.1, 172.0]). Mean (SE) absolute changes from baseline in FVC % predicted were -2.7 (0.9) in the nintedanib group and -6.0 (0.8) in the placebo group (difference 3.3 [95% CI 0.9, 5.6]). The proportions of patients with absolute and relative declines in FVC >5% predicted or >10% predicted at week 52 were numerically lower in the nintedanib group than in the placebo group (Table 2).

Conclusion: In patients with progressive fibrosing autoimmune disease-related ILDs, the proportions of patients with categorical declines in FVC % predicted supported an effect of nintedanib in slowing the progression of ILD.

Table 1. ILD diagnoses in patients with autoimmune disease-related ILDs in the INBUILD trial

	Nintedanib (n=82)	Placebo (n=88)
Rheumatoid arthritis-ILD	42 (51.2)	47 (53.4)
Systemic sclerosis-ILD	23 (28.0)	16 (18.2)
Mixed connective tissue disease-ILD	7 (8.5)	12 (13.6)
Other autoimmune disease-related ILDs*	10 (12.2)	13 (14.8)

Data are n(% of patients in that treatment group).

*Other autoimmune disease noted in the "Other fibrosing ILDs" category of the case report form, including Sjogren's disease-related ILD, interstitial pneumonia with autoimmune features (IPAF), and undifferentiated autoimmune disease-related ILD.

Table 2. Proportions of patients with categorical changes in FVC % predicted at week 52 in patients with autoimmune disease-related ILDs in the INBUILD trial

	Nintedanib (n=82)	Placebo (n=88)
Relative decline from baseline in FVC >5% predicted at week 52, n (%)	42 (51.2)	57 (64.8)
Odds ratio (95% CI)	0.56 (0.30, 1.04)	
Nominal p-value	0.07	
Relative decline from baseline in FVC >10% predicted at week 52, n (%)	32 (39.0)	44 (50.0)
Odds ratio (95% CI)	0.63 (0.34, 1.16)	
Nominal p-value	0.14	
Absolute decline from baseline in FVC >5% predicted at week 52, n (%)	35 (42.7)	51 (58.0)
Odds ratio (95% CI)	0.55 (0.30, 1.01)	
Nominal p-value	0.05	
Absolute decline from baseline in FVC >10% predicted at week 52, n (%)	25 (30.5)	37 (42.0)
Odds ratio (95% CI)	0.60 (0.32, 1.15)	
Nominal p-value	0.12	

Analyzed using a worst observation carried forward approach.

Disclosure: E. Matteson, Boehringer Ingelheim, 5, Gilead, 5, TympoBio, 5, Arena Pharmaceuticals, 5, Up-to-date, 7, Simply Speaking, 8; **O. Distler**, Actelion, 2, 5, 8, Bayer, 2, 5, 8, Boehringer Ingelheim, 2, 5, 8, Medscape, 5, 8, Novartis, 8, Roche, 5, 8, Menarini, 8, Mepha, 8, MSD, 5, 8, iQone, 8, Pfizer, 5, 8, AbbVie, 5, Acceleron Pharma, 5, Amgen, 5, AnaMar, 5, Arxx Therapeutics, 5, Beacon Discovery, 5, Blade Therapeutics, 5, CSL Behring, 5, ChemomAb, 5, Corpus Pharma, 5, Curzion Pharmaceuticals, 5, Ergonex Pharma, 5, Mitsubishi Tanabe Pharma, 2, 5, Kymera Therapeutics, 2, 5, Catenion, 5, Galapagos NV, 5, GlaxoSmithKline, 5, Glenmark Pharmaceuticals, 5, Inventiva, 5, Italfarmaco, 5, Lilly, 5, Sanofi, 5, UCB, 5, IQVIA, 5, Medac, 5, Target BioScience, 5, Patent issued, 9; **J. Distler**, Actelion, 5, Active Biotech, 2, 5, AnaMar, 2, 5, UCB, 2, 5, Boehringer Ingelheim, 2, 5, Novartis, 2, GlaxoSmithKline, 2, 5, RuiYi, 5, Galapagos, 2, 5, Medac, 5, Celgene, 2, 5, Inventiva, 2, 5, Redx Pharma, 2, Bayer, 2, 5, JB Therapeutics, 5, Bristol-Myers Squibb, 2, Array BioPharma, 2, Pfizer, 5, Sanofi-Aventis, 2, Arxx Therapeutics, 2, 5, 4D Science, 1, aTyr Pharma, 2; **M. Kuwana**, Ono Pharmaceutical, 2, 8, Chugai, 2, 8, Astellas, 8, Mitsubishi Tanabe Pharma Corporation, 2, 8, AbbVie Inc., 8, Eisai Co., Ltd., 8; **J. Pope**, AbbVie, 2, 5, Amgen, 5, 8, Lilly, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 5, 8, Sandoz, 5, 8, Roche, 2, 5, 8, Pfizer, 5, 8, Novartis, 5, 8, Merck, 2, 5, 8, Janssen, 5, 8, Gilead Sciences, Inc., 2, 5, BMS, 2, 5, 8, Abbott, 5, Actelion, 5, AstraZeneca, 5, Bayer, 5, Boehringer Ingelheim, 5, EICOS, 5, Emerald, 5, GlaxoSmithKline, 5, Medexus, 5, Seattle Genetics, 2; **J. Seibold**, Atlantic, 5, Boehringer Ingelheim, 5, 8, Blade Therapeutics, 5, Corbus Pharmaceuticals, 5, Camurus, 5, Guidepoint, 5, Xenikos, 5, BriaCell, 1, Pacific Therapeutics, 1, Indalo Therapeutics, 5; **A. James**, Boehringer Ingelheim, 3; **R. Schlenker-Herceg**, Boehringer Ingelheim, 3; **K. Rohr**, Boehringer Ingelheim, 3; **K. Flaherty**, Boehringer Ingelheim, 5, Respivant Sciences, 5, Bellerophon Therapeutics, 5, Blade Therapeutics, 5.

Abstract Number: 1049

Effects of Nintedanib in Patients with Progressive Fibrosing Autoimmune Disease-related Interstitial Lung Diseases (ILDs) in the INBUILD Trial: Subgroups by HRCT Pattern

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

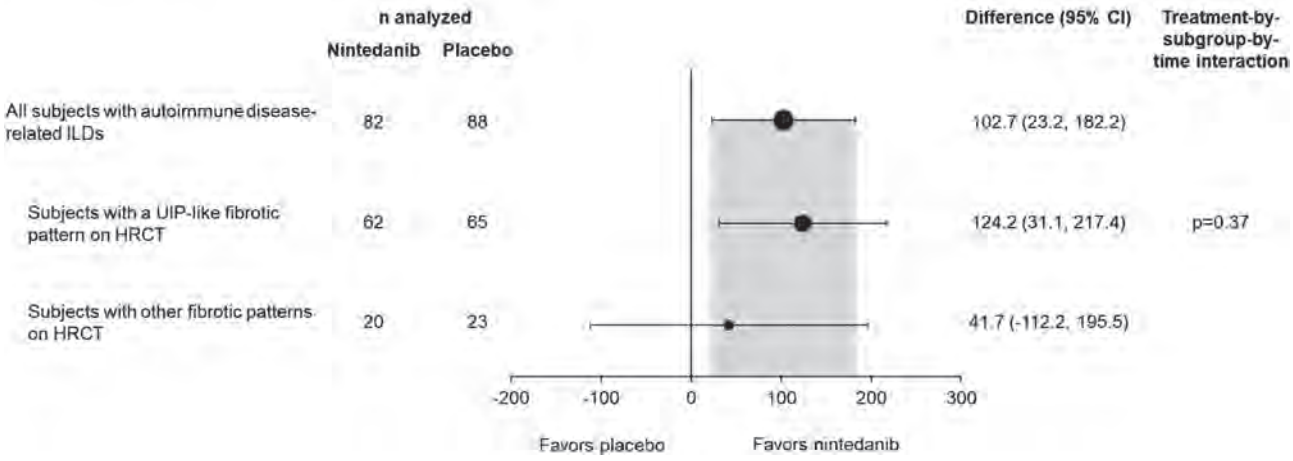
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: In the INBUILD trial, nintedanib reduced the rate of decline in forced vital capacity (FVC) over 52 weeks compared with placebo in patients with chronic fibrosing ILDs with a progressive phenotype. Several studies have suggested that a usual interstitial pneumonia (UIP) pattern on high-resolution computed tomography (HRCT) is associated with faster progression of ILD. We assessed the effect of nintedanib on FVC decline in patients with autoimmune disease-related ILDs in the INBUILD trial in subgroups by fibrotic pattern on HRCT at baseline.

Methods: The INBUILD trial enrolled patients with a fibrosing ILD other than idiopathic pulmonary fibrosis, reticular abnormality with traction bronchiectasis (with or without honeycombing) of >10% extent on HRCT, FVC ≥45%

Figure. Rate of decline in FVC (mL/year) over 52 weeks in subjects with autoimmune disease-related ILDs treated with nintedanib versus placebo in the INBUILD trial by fibrotic pattern on HRCT.



predicted, and DLco ≥30%–< 80% predicted. To be eligible to participate, patients had to meet protocol-specified criteria for progression of ILD within the 24 months before screening despite management as deemed appropriate in clinical practice. Patients were randomized to receive nintedanib or placebo, stratified by fibrotic pattern on HRCT (UIP-like fibrotic pattern or other fibrotic patterns) based on central review. In a post-hoc analysis, we analyzed the rate of decline in FVC over 52 weeks in patients with autoimmune disease-related ILDs in subgroups by UIP-like fibrotic pattern on HRCT and other fibrotic patterns on HRCT.

Results: The subgroup with autoimmune disease-related ILDs comprised 170 patients (89 rheumatoid arthritis-ILD, 39 systemic sclerosis-ILD, 19 mixed connective tissue disease-ILD, 23 other autoimmune disease-related ILDs), of whom 127 (74.7%) had a UIP-like fibrotic pattern on HRCT and 43 (25.3%) had other fibrotic patterns on HRCT. In the placebo group, the rate of decline in FVC over 52 weeks was similar in patients with a UIP-like fibrotic pattern on HRCT (n=65) and with other fibrotic patterns on HRCT (n=23) (-182.8 [SE 32.6] vs -168.1 [51.8] mL/year). The effect of nintedanib versus placebo on reducing the rate of decline in FVC was numerically greater in subjects with a UIP-like fibrotic pattern on HRCT than in those with other fibrotic patterns on HRCT (difference 124.2 mL/year [95% CI 31.1, 217.4] vs 41.7 mL/year [95% CI -112.2, 195.5]) but the interaction p-value did not indicate heterogeneity in the treatment effect between the subgroups by HRCT pattern (p=0.37) (Figure).

Conclusion: In patients with progressive fibrosing autoimmune disease-related ILDs in the INBUILD trial, nintedanib slowed the rate of FVC decline both in patients with a UIP-like fibrotic pattern on HRCT and in patients with other fibrotic patterns on HRCT, with a numerically greater effect in patients with a UIP-like fibrotic pattern on HRCT.

Disclosure: P. Dellaripa, Genentech, 1, Bristol Myers Squibb, 1; **M. Aringer**, Boehringer Ingelheim, 1, 2, Roche, 1, 2, Bristol Myers Squibb, 1, 2, Chugai, 1, 2, Sanofi, 1, 2, AbbVie, 1, 2, AstraZeneca, 1, 2, Lilly, 1, 2, MSD, 1, 2, Novartis, 1, Pfizer, 1, UCB, 1; **A. Hoffmann-Vold**, Boehringer Ingelheim, 1, 2, 3, Actelion Pharmaceuticals, 1, 2, Roche, 1, Bayer, 1; **C. Kelly**, Boehringer Ingelheim, 1; **S. Mittoo**, None; **A. James**, Boehringer Ingelheim, 3; **K. Rohr**, Boehringer Ingelheim, 3; **S. Stowasser**, Boehringer Ingelheim, 1; **Y. Inoue**, Boehringer Ingelheim, 1, 2, 3.

Abstract Number: 1050

Rituximab in the Treatment of Interstitial Lung Disease Associated with Autoimmune Diseases: Experience from a Single Referral Center

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Table 1. Demographic and clinical characteristics of 26 AD-ILD patients included in this study.

Sex (women/men), n (%)	13/13 (50.0/50.0)
Age at ILD diagnosis, years, mean ± SD	58.3 ± 11.1
Age at RTX onset, years, mean ± SD	58.9 ± 10.2
Rheumatic autoimmune disease, n (%)	
Systemic sclerosis	7 (26.9)
Idiopathic inflammatory myositis	6 (23.1)
Rheumatoid arthritis	5 (19.3)
Interstitial pneumonia with autoimmune features	3 (11.5)
Primary Sjögren's syndrome	3 (11.5)
MPO-ANCA positive	2 (7.7)
High-resolution computed tomography pattern, n (%)	
UIP pattern	11 (42.4)
Probable UIP pattern	1 (3.8)
Indeterminate for UIP pattern	1 (3.8)
Features most consistent with an alternative diagnosis	
NSIP pattern	12 (46.2)
Non-NSIP pattern	1 (3.8)
IS treatment at RTX indication, n (%)	
Glucocorticoids	18 (69.2)
Hydroxychloroquine	5 (19.3)
Mycophenolate mofetil	4 (15.4)
Azathioprine	3 (11.5)
Methotrexate	1 (3.8)
Sulfasalazine	1 (3.8)
Tacrolimus	1 (3.8)
Tocilizumab	1 (3.8)
Abatacept	1 (3.8)
Concomitant treatment, n (%)	
Glucocorticoids	21 (80.7)
Hydroxychloroquine	8 (30.7)
Mycophenolate mofetil	7 (26.9)
Azathioprine	3 (11.5)
Sulfasalazine	1 (3.8)
Tacrolimus	1 (3.8)
I.V. immunoglobulins	1 (3.8)

AD: autoimmune disease; ILD: interstitial lung disease; IS: immunosuppressive; NSIP: nonspecific interstitial pneumonia; RTX: rituximab; SD: standard deviation; UIP: unusual interstitial pneumonia.

Table 1. Demographic and clinical characteristics of 26 AD-ILD patients included in this study.

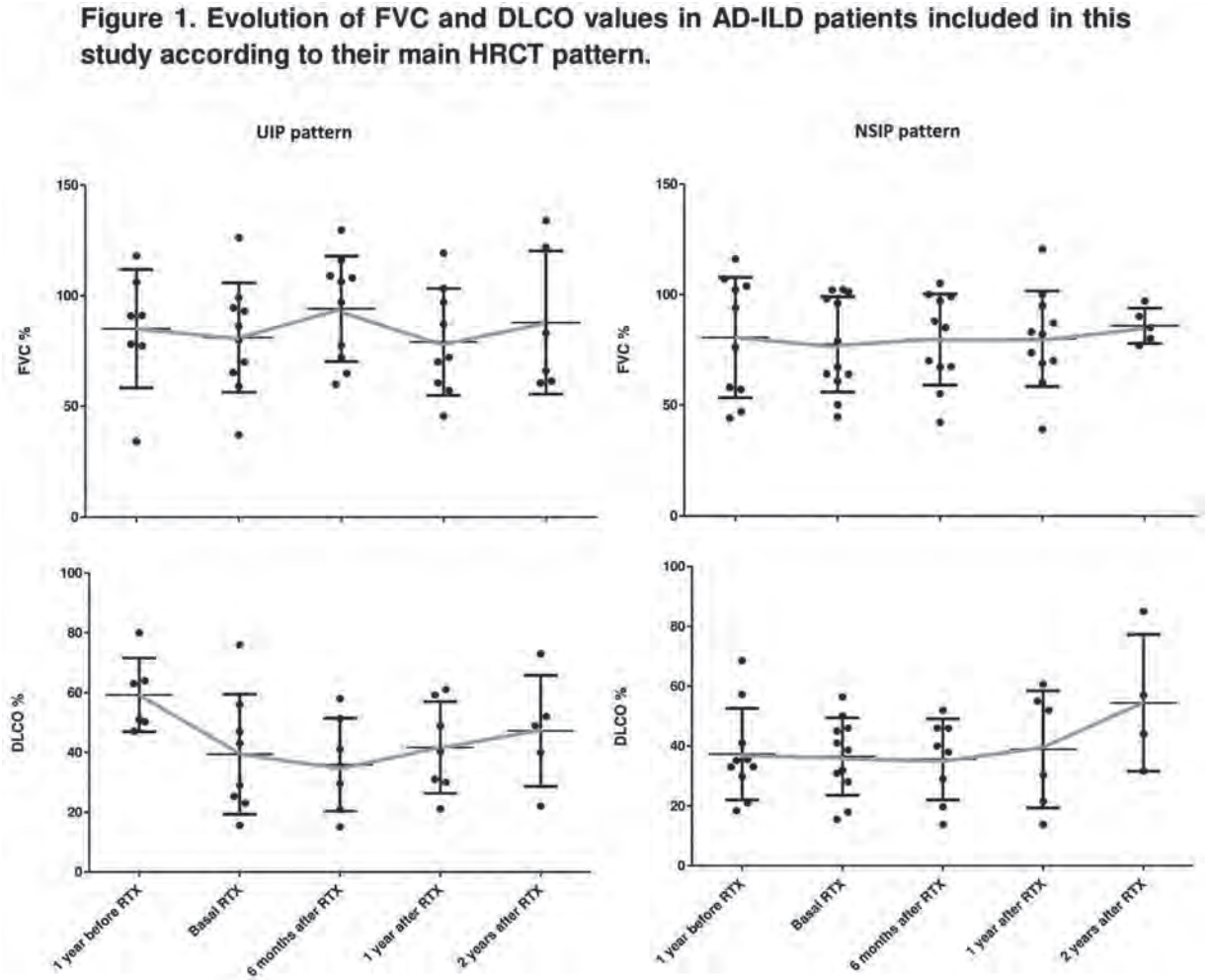

Figure 1. Evolution of FVC and DLCO values in AD-ILD patients included in this study according to their main HRCT pattern.

Background/Purpose: The presence of interstitial lung disease (ILD) in patients with autoimmune diseases (AD)s influences significantly on their morbidity and mortality [1]. Different treatment strategies have been proposed, including lung transplantation as the last alternative [2]. Corticosteroids, cyclophosphamide and mycophenolate mofetil are the most widely used conventional immunosuppressive drugs [3]. Rituximab (RTX), a chimeric (human/ murine) monoclonal antibody against the surface antigen CD20 expressed on pre-B and B lymphocytes, has shown efficacy in the treatment of patients with ILD associated with AD (AD-ILD), even as a rescue alternative in severe and refractory cases [4]. In the present study, we aimed to report our experience with RTX in the treatment of patients with AD-ILD.

Methods: We performed a retrospective study of patients assessed from May 2016 until March 2020 in a referral clinic of ILD and lung transplantation (Hospital Universitario Marqués de Valdecilla, Santander, Spain). Patients with a diagnosis of AD-ILD who received RTX were assessed. The main indications for RTX administration were the presence of a significant ILD in the setting of AD or the identification of an AD in the course of an established ILD. Clinical characteristics, radiological findings and pulmonary function tests (PFTs) were evaluated. PFTs were collected at baseline (RTX onset), at 6 months and annually until 2 years with RTX therapy.

Results: A total of 26 patients were included, with a mean age of 58.3 ± 11.1 years at ILD diagnosis. The most frequent ADs related to ILD were systemic sclerosis, idiopathic inflammatory myositis (including anti-synthetase syn-

drome) and rheumatoid arthritis. Non-specific interstitial pneumonia and usual interstitial pneumonia were the predominant radiological patterns. Demographic and clinical characteristics of the AD-ILD patients are shown in Table 1. A sustained improvement of PFTs was observed from the initiation of RTX, with a statistically significant increase of DLCO from basal to one year after RTX (mean + 4.2%, p = 0.024). Overall, no differences were found comparing PFT's outcomes according to the radiological pattern (Figure 1) or the specific type of AD.

Conclusion: RTX constitutes a good therapeutic option to preserve lung function in patients with AD-ILD, regardless of the radiological pattern or the underlying AD.

Disclosure: B. Atienza-Mateo, None; **S. Remuzgo-Martínez**, None; **D. Prieto-Peña**, None; **V. Mora Cuesta**, None; **D. Iturbe-Fernández**, None; **S. Fernández Rozas**, None; **A. Corrales**, None; **J. Cifrián**, None; **M. González-Gay**, None.

Abstract Number: 1051

Rituximab for Interstitial Pneumonia with Autoimmune Features at Two Academic Medical Centers

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Many patients with interstitial lung disease (ILD) have autoimmune features without a distinct rheumatic disease and are thus designated as having interstitial pneumonia with autoimmune features (IPAF). Rituximab (RTX) may be effective in IPAF, but relevant data are scarce. We describe 50 patients with IPAF treated with RTX at 2 large academic medical centers.

Methods: Patients age ≥18 years meeting the 2015 IPAF classification criteria and treated with rituximab were identified at two large academic medical centers, Mass General Brigham (MGB) and University of Chicago Medicine (UCM). At MGB, patients were identified using an institution-wide data repository of patients seen from 2000-2018. At UCM, patients were identified from an ILD registry between 2006-2019. Patients were excluded if they received RTX for a classifiable autoimmune disease or malignancy or if they had < 1 year of follow-up available. Clinical improvement was defined as meeting all 4 clinical domains at 1 year after RTX initiation: improvement in clinician assessment, decreased oxygen requirement, no hospitalization, and survival. Only those subjects with PFTs within 3 months prior to or 1 month after RTX initiation and 6-18 months after RTX initiation were included in the PFT analysis. PFT improvement was defined as ≥10% increase in forced vital capacity (FVC).

Results: At MGB, 36 IPAF patients (mean age 61 years, 44% female) were treated with RTX, with an average of 2.4 ± 1.3 cycles of RTX and 1.7 ± 0.6 doses per cycle (**Table 1**). At one year, 18 (50%) were clinically improved, 12 (33%) were sTable, and 6 (17%) died from progressive respiratory failure (**Table 2**). Of 32 patients with PFTs available, the

Table 1. Baseline characteristics of patients with interstitial pneumonia with autoimmune features (IPAF) treated with rituximab at two academic medical centers.

	Mass General Brigham (N = 36)	University of Chicago (N = 14)
Age at diagnosis, years, mean (SD)	61 ± 11	53 ± 11
Female sex, N (%)	16 (44)	10 (71)
Race/ethnicity, N (%)		
White	29 (81)	6 (43)
Black	4 (11)	8 (57)
Asian	3 (8)	0
Latinx	1 (3)	2 (14)
Smoking status, N (%)		
Current	1 (3)	0
Past	15 (42)	4 (29)
Never	20 (55)	10 (71)
Prior diagnosis of, N (%)		
Coronary artery disease	2 (6)	4 (29)
Heart failure	3 (8)	7 (50)
Chronic obstructive pulmonary disease	2 (6)	4 (29)
Obstructive sleep apnea	6 (17)	4 (29)
Pulmonary hypertension	2 (6)	7 (50)
Required hospital admission, N (%)	10 (28)	1 (7)
Required mechanical ventilation, N (%)	6 (17)	1 (7)
Required extracorporeal membrane oxygenation, N (%)	2 (6)	0
Radiographic pattern, N (%)		
Nonspecific interstitial pneumonia (NSIP)	9 (25)	8 (57)
Organizing pneumonia (OP)	14 (39)	0
NSIP + OP	8 (22)	3 (21)
Other pattern*	5 (14)	3 (21)
Serologies, N (%)		
Antinuclear antibody (>1:320)	16 (44)	5 (36)
SS-A/Ro-60 kilodalton antibody	3 (8)	6 (43)
SS-A/Ro-52 kilodalton antibody	11 (31)	5 (36)
Rheumatoid factor (>2 times upper limit)	9 (25)	5 (36)
Myositis-specific or associated antibody	8 (22)	5 (36)
Treatments in conjunction with rituximab, N (%)		
Glucocorticoids	32 (89)	14 (100)
Mycophenolate mofetil	11 (31)	2 (14)
Intravenous immune globulin	4 (11)	2 (14)

All values are mean ± SD for continuous variables or number(percentage) for categorical variables.
*Other patterns include non-classifiable, desquamating interstitial pneumonia, hypersensitivity pneumonitis, and diffuse lung injury. No patients had usual interstitial pneumonia (UIP).

mean absolute change in FVC (% predicted) was +9.3% ± 16.4%. At UCM, 14 IPAF patients (mean age 53 years, 71% female) were treated with RTX with an average of 2.9 ± 2.1 cycles and 2.0 ± 0 doses per cycle. Compared to the MGB cohort, the UCM cohort was younger and had more females, Black/African American and Latinx patients, and baseline comorbidities. At the time of IPAF diagnosis, fewer patients at UCM required hospitalization for hypoxemia than at MGB (1 [7%] vs. 10 [28%]). In the UCM cohort at one year, 8 (57%) were improved, 2 (14%) were sTable, and 3 (21%) died from progressive respiratory failure. Of 12 patients with PFTs available, the mean absolute change in FVC (% predicted) was +1.3% ± 6.3%. By one year, 14 (39%) patients in the MGB cohort and 7 (50%) in the UCM cohort had tapered off glucocorticoids completely. Overall at both sites, 9 patients had infections and 2 had minor infusion reactions; only 2 discontinued therapy due to adverse events (infections) during 1 year of therapy.

Table 2. Outcomes at one year after treatment with rituximab in patients with interstitial pneumonia with autoimmune features (IPAF).

	Mass General Brigham (N = 32 with PFTs, 36 total)	University of Chicago (N = 12 with PFTs, 14 total)
Clinically improved, N (%)*	18 (50)	8 (57)
Clinically stable, N (%)	12 (33)	2 (14)
Clinically worsened/died, N (%)	6 (17)	3 (21)
Absolute change in FVC (% predicted), mean % (SD)	+9.3 ± 16.4	+1.3 ± 6.3
Absolute change in DLCO (% predicted), mean % (SD)	+2.0 ± 13.5	+7.0 ± 8.8
FVC improved, N (%)†	15 (47)	7 (58)
FVC stable, N (%)	14 (44)	5 (42)
FVC worsened, N (%)	3 (9)	0
Tapered off corticosteroids completely, N (%)	14 (39)	7 (50)

All values are mean ± SD for continuous variables or number (percentage) for categorical variables. PFTs = pulmonary function tests; FVC = forced vital capacity; DLCO = diffusion capacity of carbon monoxide.
*Improvement defined as positive change in 4 out of 4 domains: clinician assessment, oxygen requirements, need for hospitalization, and survival.
†Improvement defined as ≥10% improvement in forced vital capacity. Stable defined as forced vital capacity within ±10% of prior measurement. Worsening defined as ≥10% decline in forced vital capacity.

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Absolute change in FVC (% predicted), mean % (SD)	+9.3 ± 16.4	+1.3 ± 6.3
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All values are mean ± SD for continuous variables or number (percentage) for categorical variables. PFTs = pulmonary function tests; FVC = forced vital capacity; DLCO = diffusion capacity of carbon monoxide.
*Improvement defined as positive change in 4 out of 4 domains: clinician assessment, oxygen requirements, need for hospitalization, and survival.
†Improvement defined as ≥10% improvement in forced vital capacity. Stable defined as forced vital capacity within ±10% of prior measurement. Worsening defined as ≥10% decline in forced vital capacity.

Conclusion: In 50 patients with IPAF treated with RTX at 2 large academic medical centers, most patients demonstrated improvement or stability at 1 year. These findings call for prospective studies, including randomized controlled trials, to further determine the risks, benefits, optimal timing, and cost effectiveness of RTX use in IPAF.

Disclosure: K. D'Silva, None; **I. Bauer Ventura**, None; **M. Bolster**, Cumberland, 9, Corbus, 9, Gilead, 5, Johnson & Johnson, 1, Abbvie, 2, Pfizer, 2; **F. Castelino**, Boehringer Ingelheim, 5, 8; **A. Sharma**, Hummingbird Diagnostics, 9, Thoracic Imaging: The Requisites, 9; **B. Little**, Elsevier, 9; **A. Adegunsoye**, Genentech, 5, Boehringer-Ingelheim, 5; **M. Strek**, Boehringer-Ingelheim, 2, 9, Galapagos, 9, Novartis, 9; **S. Montesi**, United Therapeutics, 9, Merck, 2, Wolters Kluwer, 7; **H. Choi**, AstraZeneca, 2, Takeda, 5, Selecta, 5, GlaxoSmithKline, 5, Horizon, 5.

Abstract Number: 1052

Connective Tissue Disease-Related Interstitial Lung Disease in American Indian/Alaska Native People in Alaska

Joanna Marco[1] and Elizabeth Ferucci[2], [1]University of Washington, Seattle, WA, [2]Alaska Native Tribal Health Consortium, Anchorage, AK

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Many connective tissue diseases are known to cause interstitial lung disease (ILD). American Indian/Alaska Native (AI/AN) populations have higher prevalence and severity of a number of connective tissue diseases that can be associated with ILD, but no previous studies have examined the clinical characteristics of connective tissue disease-associated ILD (CTD-ILD) in AI/AN populations. We sought to describe the spectrum of CTD-ILD in the AI/AN population in Alaska.

Methods: Through this retrospective chart review conducted at the Alaska Native Medical Center, 45 AI/AN adults with a clinical diagnosis of CTD-ILD were identified. A detailed medical record abstraction was performed for each potential case. Clinical characteristics are reported, including demographics, underlying CTD, ILD subtypes, serologies, pulmonary function tests (PFTs) with changes over time, and medications prescribed.

Results: Underlying connective tissue disease diagnosis was heterogeneous in this population. Rheumatoid arthritis (RA) was the most common (n = 13), followed by systemic sclerosis (SSc, n = 12; limited cutaneous n = 7, diffuse cutaneous n = 5), and mixed connective tissue disease (MCTD, n = 9). The mean age at connective tissue disease diagnosis was 45 (standard deviation (SD) 15), and the mean age at ILD diagnosis was 52 (SD 14), for a mean time from CTD diagnosis to ILD diagnosis of 7 years. Most patients were diagnosed with usual interstitial pneumonia (UIP) by high resolution CT (HRCT) (60%). The baseline forced vital capacity (FVC) was 68 percent predicted, and fell by an average of 1.2 absolute percentage points per year. The baseline diffusing capacity of the lungs for carbon monoxide (DLCO) was 56 percent predicted and fell by an average of 5.1 absolute percentage points per year.

Conclusion: This study is the first to describe patterns of CTD-ILD in any AI/AN population. As in other populations, RA-ILD and SSc-ILD are common, but this population additionally had a high proportion of ILD associated with of MCTD. Understanding the clinical characteristics of CTD-ILD in this population may improve recognition and care of CTD-ILD in AI/AN people.

Disclosure: J. Marco, None; **E. Ferucci**, None.

Abstract Number: 1053

Efficacy of Rituximab for Connective Tissue Disease (CTD) Associated Interstitial Lung Disease (ILD) : A Single Center Study of 47 Patients-Extension Study

Ahmad Qurie[1], Smita Maruvada[1], Sarwat Umer[1], Jerry Mclarty[2] and Samina Hayat[1], [1]LSU Shreveport, Shreveport, LA, [2]LSU Shreveport, Shreveport

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

sex

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	F	39	83.0	83.0	83.0
	M	8	17.0	17.0	100.0
	Total	47	100.0	100.0	

race

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	black	37	78.7	78.7	78.7
	white	10	21.3	21.3	100.0
	Total	47	100.0	100.0	

Descriptive Statistics

	N	Minimum	Maximum	Mean	Std. Deviation
Age	47	25	73	55.40	12.683
CTD_years	47	5	28	4.43	6.014
ILD_years	47	1	13	2.66	2.980
DLCO0	25	.260	.810	.45560	.148551
DLCO6	16	.220	.790	.48688	.168116
DLCO12	12	.249	.790	.52242	.162864
DLCO18_24	15	.28	.93	.5520	.19295
DLCO24_36	21	.23	.93	.5329	.20633
FVC0	39	.290	1.230	.64692	.229498
FVC6	27	.310	.970	.64185	.204902
FVC12	16	.320	1.600	.71694	.293383
FVC18_24	22	.37	.92	.6423	.14402
FVC24_36	25	.10	.96	.6536	.18810

Summary Statistics On Patient Characteristics and Outcomes (N=47)

HRCT0 * HRCT6 Crosstabulation

Count

	HRCT6			
	worsened	stable	improved	Total
Mild	0	4	3	7
Moderate	0	11	0	11
Severe	1	7	2	10
Total	1	22	5	28

Fishers Exact p = 0.04

HRCT0 * HRCT12 Crosstabulation

Count

	HRCT12			
	worsened	stable	improved	Total
Mild	1	4	1	6
Moderate	0	7	0	7
Severe	0	5	1	6
Total	1	16	2	19

Fishers Exact p = 0.42

HRCT0 * HRCT18_24 Crosstabulation

Count

		HRCT18_24		
		stable	improved	Total
	Mild	1	4	5
	Moderate	6	1	7
	Severe	6	3	9
Total		13	8	21

Fishers Exact p = 0.087

HRCT0 * HRCT24_36 Crosstabulation

		HRCT24_36			Total
		worsened	stable	improved	
	Mild	0	7	6	13
	Moderate	1	8	3	12
	Severe	2	5	3	10
Total		3	20	12	35

Fishers Exact p = 0.502

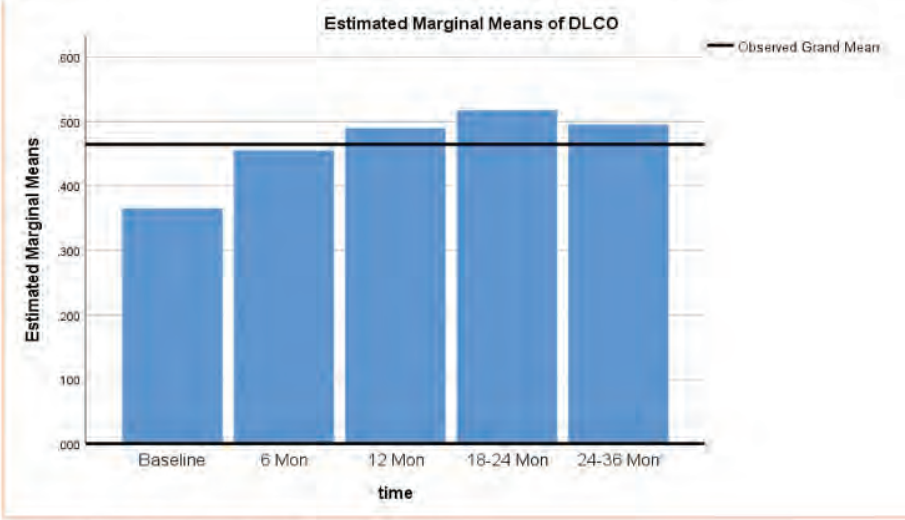
HRTC Changes from Baseline

Background/Purpose: Interstitial lung disease (ILD) is a fatal complication associated with connective tissue diseases (CTDs), often resulting in substantial morbidity and mortality. Despite numerous advances in immunosuppressive agents, there remains limited data on effective treatment for this challenging entity. This study aims to evaluate the efficacy of rituximab (RTX) in patients with CTD-ILD and determine factors correlated with outcomes at 6, 12, 24 and 36 months post-RTX.

Methods: We analyzed data for 47 patients with CTD-ILD, all of whom met ACR classification criteria for a specific CTD. ILD was confirmed by high-resolution CT chest (HRCT) and pulmonary function tests with forced vital capacity (FVC) and diffusion capacity of lung for carbon monoxide (DLCO). We compared HRCT chest findings, FVC and DLCO at time of diagnosis and at 6, 12, 24 and 36 months post-RTX. At diagnosis HRCT chest findings classified into 3 groups (mild, moderate and severe). At 6, 12, 24 and 36 months after RTX, using the same semi-quantitative scoring system, HRCT chest findings were ranked as worsening, sTable or improving.

Multiple patient characteristics (Table 1) were tested for their correlation with each outcome. For some variables, nonparametric statistical methods were used due to a small number of non-missing variables. The Spearman rank

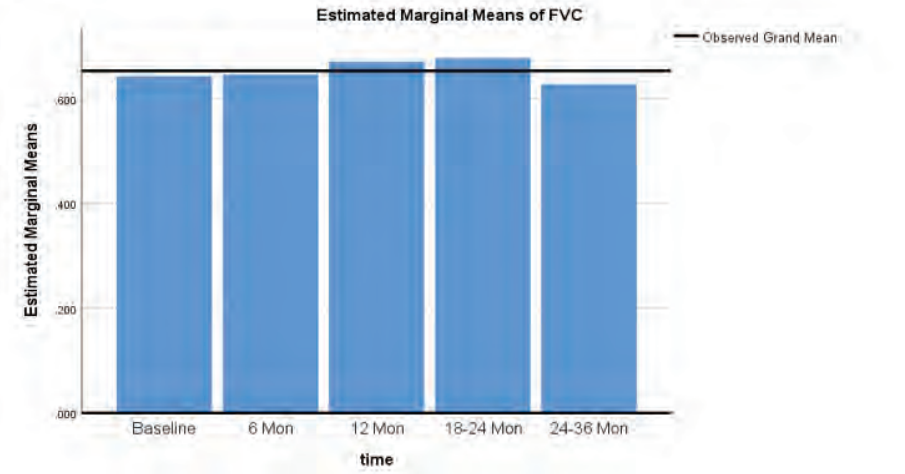
Figure 1A



No significant changes in DLCO over time: $p > 0.12$

No significant differences in DLCO values at any two time points: $p > 0.20$

Figure 1B



No significant changes in FVC over time: $p > 0.7$

No significant differences in FVC values at any two time points: $p > 0.34$

Figure 1A and 1B

correlation and Wilcoxon signed rank test were used to determine changes in FVC and DLCO at 6, 12, 24 and 36 months after RTX treatment.

Results

1. Majority of the patients were female and African American with median age of 60.
2. HRCT Chest findings after RTX showed either improvement or stability at 6, 12, 24 months, 3 cases showed worsening at 36 months, two of them missed one or two doses of Rituxan, and the 3rd cases was a longstanding ILD secondary to Scleroderma

(Table 2).

3. There was no statistical significance at p-value for changes in FVC and DLCO, however observed changes have shown improvement as evidenced by observed grand mean. The largest changes were observed for FVC and DLCO at 1 year and DLCO at 2 years after treatment (Figure 1A, Figure 1B).
4. CTD duration showed negative correlation with FVC change at 1 year post-RTX with estimated 1.1% decrease in FVC for every year increase in CTD. ILD duration showed negative correlation with DLCO change at 2 years post-RTX with estimated 3.9% decrease in DLCO for every year increase in ILD.

Conclusion: Based on this single center retrospective study, RTX appears to be an effective therapy for CTD-ILD. Our observations also suggest using RTX earlier in the disease course of CTD-ILD may have a greater long-term impact. RTX may help to fill an unmet therapeutic need for CTD-ILD but larger randomized clinical trials are needed

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Disclosure: A. Qurie, None; **S. Maruvada**, None; **S. Umer**, None; **J. Mclarty**, None; **S. Hayat**, None.

Abstract Number: 1054

Treatment with Certolizumab Pegol in Refractory Uveitis Secondary to Inmune-Mediated Inflammatory Diseases. Multicenter Study of 39 Patients

José Luis Martín-Varillas[1], Vanesa Calvo-Río[2], Lara Sanchez-Bilbao[2], Inigo Gonzalez-Mazon[3], Ignacio Torre[4], Alvaro García Martos[5], Amalia Sánchez Andrade[6], Angel García Aparicio[7], Juan Ramón De dios[8], Ana Urriticoechea[9], Olga Maiz Alonso[10], Raul Veroz[11], Andrea García Valle[12], Sergio Rodriguez Montero[13], Roberto Miguelez[14], Vega Jovani[15], Marisa Hernandez Garfella[16], Arantxa Conesa[17], Olga Martinez Gonzalez[18], Paula Rubio Muñoz[19], Eva Peña Sainz-Pardo[20], Miguel Ángel González-Gay[21] and Ricardo Blanco[2], [1]Hospital Sierrallana, Torrelavega, Spain, [2]Hospital Universitario Marques de Valdecilla, Santander, Spain, [3]Hospital Universitario Marques de Valdecilla, Bezana, Spain, [4]Hospital Basurto, Bilbao, Spain, [5]Hospital del Tajo, Madrid, Spain, [6]H. Lucus Augusti, Lugo, Spain, [7]H. Mostoles, Madrid, Spain, [8]H. Alava, Alava, Spain, [9]Can Misses, Ibiza, Spain, [10]Hospital Universitario Donostia, San Sebastian, Pais Vasco, Spain, [11]H. Mérida, Mérida, Spain, [12]H. Palencia, Palencia, Spain, [13]H. Virgen de Valme, Sevilla, Spain, [14]Toledo, Toledo, Spain, [15]H. Alicante, Alicante, Spain, [16]H. Valencia, Valencia, Spain, [17]H. Castellón, Castellón, [18]H. Salamanca, Salamanca, [19]H. Esperit Sant, Barcelona, Spain, [20]H. 12 de Octubre, Madrid, Spain, [21]Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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Background/Purpose: Infliximab and adalimumab therapy has significantly improved the prognosis of patients with non-infectious refractory uveitis. However, there is not enough evidence for the use of other anti-TNFs such as Certolizumab Pegol (CZP). Our objective was to evaluate the efficacy and safety of CZP in uveitis due to Immune-Mediated Inflammatory Diseases (IMID).

Methods: Multicenter study of 39 patients with uveitis due to IMID refractory to glucocorticoids and conventional immunosuppressants. The efficacy of CZP was evaluated with the following ocular parameters: best corrected visual acuity (BCVA), anterior chamber cells, macular thickness and presence of retinal vasculitis. Efficacy of CZP was com-

	Baseline	1st week	1st Month	6th Month	1st year	2nd year
BCVA (mean±SD)	0.77±0.29	0.77±0.30*	0.82±0.29*	0.85±0.26*	0.86±0.27*	0.88±0.23*
Tyndall (median [IQR])	0 [0-2]	0 [0-2]	0 [0-1]*	0 [0-0]*	0 [0-0]*	0 [0-0]*
OCT (mean±SD)	355±61.5	-	284.1±40.4*	-	224.8±121.1*	-
Retinal Vasculitis (eyes affected, %)	2 (3.6)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)

*$p<0.05$

pared between baseline, 1st week, 1st and 6th month, and 1st and 2nd year. Statistical analysis was performed with STATISTICA (Statsoft Inc. Tulsa, Oklahoma, USA).

Results: 39 patients/56 affected eyes (18 men/21 women) with a mean age of 40.5±11.9 years were studied. IMIDs included were: spondyloarthritis (n=17), psoriatic arthritis (6), Crohn (3), juvenile idiopathic arthritis (JIA) (2), Behçet (2), reactive arthritis (2), rheumatoid arthritis (1), relapsing polychondritis (1), pars planitis (1), Birdshot (1) and idiopathic uveitis (3). Uveitis pattern was as follows: anterior (n=30), posterior (4), panuveitis (3) and intermediate (2).

Previous CZP, patients received: oral prednisone (n=18) methylprednisolone bolus (1), methotrexate (22), azathioprine (10), cyclosporine (4), leflunomide (2), mycophenolate mofetil (2) and cyclophosphamide (1). 77% of patients had received previous biological therapy, with a mean of 1.6±1.2 biological drugs per patient. Gestational desire was the reason for prescribing CZP in 8 patients. CZP was administered in monotherapy in 16 patients and in the remaining 23 patients combined with conventional immunosuppressants.

After a median follow-up of 24 [6-36] months, most of the ocular variables analysed showed a rapid and significantly sustained improvement (**Table**). CZP was discontinued in 11 patients for the following reasons: remission (n=1), insufficient response of ocular symptoms (n=1) and limited response of extraocular manifestations (n=9). No serious adverse effects were reported.

Conclusion: CZP seems to be effective and safe in patients with refractory uveitis due to IMID.

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Abstract Number: 1055

Myositis and Systemic Sclerosis Spectrum IPAF Patients Are More Likely to Respond Favorably to Immunosuppression

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster II: Sarcoidosis, Interstitial Lung Disease, & Inflammatory Eye Disease

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Classification criteria for interstitial pneumonia with autoimmune features (IPAF) were introduced in 2015 to identify interstitial lung disease (ILD) patients who might benefit from immunosuppression but do not meet classification criteria for a defined connective tissue disease. While many descriptions of IPAF have focused on radiographic and histologic distinctions (e.g. usual interstitial pneumonia v. non-specific interstitial pneumonia), fewer investigations probed whether various autoantibodies correlate with immunosuppression response. We hypothesized that IPAF patients with myositis and systemic sclerosis associated antibodies would have a greater improvement in % predicted forced vital capacity (FVC) and diffusing capacity of the lungs for carbon monoxide (DLCO) compared to other IPAF patients.

Methods: Patients meeting classification criteria for IPAF were enrolled in the longitudinal VUMC Myositis and Scleroderma Treatment Initiative Center Cohort (VUMC IRB 141415). Patients were enrolled from 9/17/2017-3/30/2019). Inclusion criteria included treatment with immunosuppression (e.g. azathioprine, mycophenolate mofetil, or rituximab), complete serologies (RF, CCP, immunofluorescent ANA, and extended myositis panel), and at least 6 months of physiologic follow-up data. Patients with an anti-synthetase antibody, Scl70, Pm/Scl70, or MDA5 antibody were classified as myositis/systemic sclerosis spectrum.

Results: Twenty-eight patients were identified from the MYSTIC cohort who met inclusion criteria. Demographics and pulmonary radiographic and physiologic features are shown in Table 1. There was no difference in age, female gender, or Caucasian race between IPAF and myositis/SSc spectrum patients. There was no difference in the severity of restriction between the groups at baseline, but myositis/SSc spectrum patients had a greater improvement in the % predicted FVC (7.5 ± 2.7% v. -1.7 ± 1.8%, p=0.006) after immunosuppression. At baseline, IPAF patients trended towards a worse % predicted DLCO than myositis SSc spectrum patients at baseline (33.9 ± 4.3 v. 43.5 ± 4.8 %, p=0.06). Myositis/SSc patients also trended towards greater improvement in the % predicted DLCO after immunosuppression (5.6 ± 4.0% v. -2.3 ± 2.2, p=0.13).

Table 1. Demographic and pulmonary characteristics of IPAF patients

	IPAF (n=17)	Myositis/SSc spectrum (n=11)	p value
Age (yrs)	56.0 ± 3.1	55.9 ± 3.1	0.82
Female Gender	10 (58.8%)	7 (63.6%)	1.00
Caucasian Race	12 (70.5%)	8 (72.3%)	1.00
Probable or definite UIP	2 (11.8%)	1 (9.0%)	1.00
Baseline % predicted FVC	59.1 ± 3.6	54.5 ± 7.0	0.17
% Change in FVC at 6 months	-1.7 ± 1.8	7.5 ± 2.7	0.006
Baseline % predicted DLCO	33.9 ± 4.3	43.5 ± 4.8	0.06
% Change in DLCO at 6 months	-2.3 ± 2.2	5.6 ± 4.0	0.13

Conclusion: In this single-center prospective longitudinal study, patients with myositis and SSc specific antibodies derived benefit from immunosuppression and should be immunosuppressed even if they do not meet classification criteria. These findings further highlight the importance of comprehensive serologies in the initial evaluation of ILD.

Disclosure: E. Wilfong, None; **G. Schroeder**, None; **A. Barnado**, Nashville Biosciences, 1; **S. Lord**, None; **N. Annapureddy**, None; **R. Dudenhofer**, None; **L. Crofford**, None.

Abstract Number: 1056

Descriptive Data Analysis of Patients with Anti Jo1 Syndrome (AJS) and Lung Involvement

Mohamed Alalwani[1], Bassam Alhaddad[2], Basem Zraik[3], Christopher O'Rourke[3], Ruchi Yadav[3], Ali Askari[1], Charles Malemud[1] and Soumya Chatterjee[4], [1]Case Western Reserve University / University Hospitals Cleveland Medical Center, Cleveland, OH, [2]MetroHealth Medical Center, Westlake, OH, [3]Cleveland Clinic, Cleveland, OH, [4]Cleveland Clinic, Richmond Heights, OH

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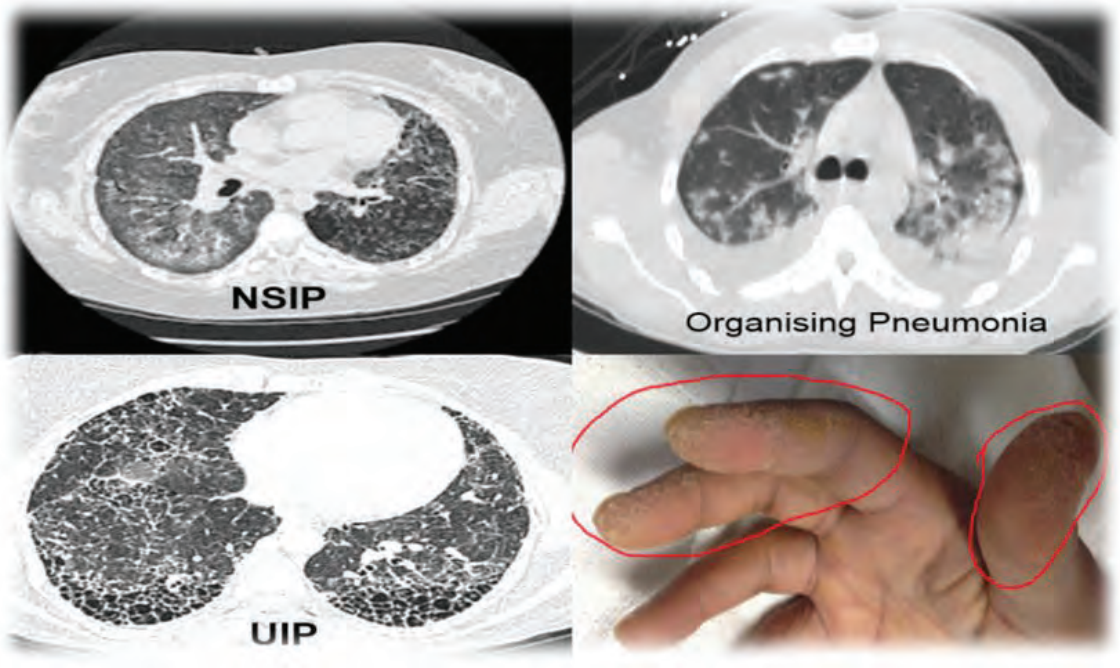
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the patterns, severity and, prognostic parameters of interstitial lung disease (ILD) in Anti Jo1 Syndrome (AJS).

Methods: We identified 51 anti-Jo-1 patients with ILD between 2003 and 2012. Clinical and laboratory data were obtained along with PFTs and pattern/scoring of thoracic HRCT scans based on Ooi scoring system (inflammation and

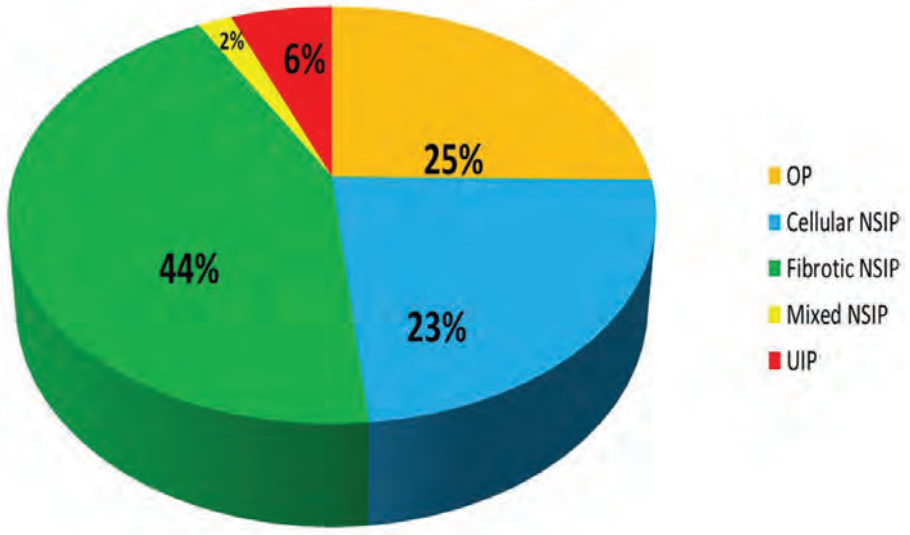


ILD patterns and Mechanic's hands in AJS

		Absent		Present			
Factor	Total	N	Statistics	N	Statistics	Test Statistic	p-value
% change in FVC from Dx [b]	44	22	8.1 (-0.5, 17.8)	22	21.3 (5.3, 39.5)	200	0.33[W]
% change in DLCO from Dx [b]	37	18	1.3 (-13.5, 23.9)	19	16.7 (-0.8, 33.1)	131	0.23[W]
FVC at ILD diagnosis [b]	47	25	71.4 (63.6, 79.6)	22	62.1 (54.5, 69.7)	329.5	0.25[W]
Last FVC [b]	44	22	75.3 (67.5, 83.1)	22	72 (63.1, 81.7)	244	0.97[W]
DLCO at ILD diagnosis [b]	45	23	64.4 (56, 73.1)	22	53.2 (45, 62.1)	329.5	0.084[W]
Last DLCO [b]	38	19	62.7 (51.5, 72.6)	19	62.5 (52.4, 71.2)	187	0.86[W]
Died [a]	49					0.1	0.81[$]
no	42	23	82.1	19	90.5		
yes	7	5	17.9	2	9.5		
Latest Fibrosis Score [b]	45	24	1.6 (0.2, 3.7)	21	2.7 (1.3, 4.1)	187.5	0.089[W]
Latest Inflammation Score [b]	45	24	5.2 (3.9, 6.5)	21	4.4 (2.9, 6)	291.5	0.37[W]
Total Index Change [b]	**31**	**15**	**-0.7 (-1.5, -0.1)**	**16**	**1.1 (0.2, 2.1)**	**57.5**	**0.007[W]**
Fibrosis Change (Last-First) [b]	31	15	0.4 (-0.1, 1.1)	16	2.4 (0.9, 4.2)	80	0.068[W]
Time between AJS and ILD Dx	50	29	-0.5 (-1.7, 0.3)	21	-2.4 (-5.1, -0.4)	343	0.44[W]

[a] Percentage; [b] Mean (95% Bootstrap CI)
C: Pearson's Chi-squared test with Yates' continuity correction
F: Fisher's Exact Test for Count Data
W: Wilcoxon rank sum test
S: Log-rank test for survival data

Table: Comparisons by Esophageal Disorder



Patterns of ILD in AJS at diagnosis

fibrosis indices) [1]. Progression of ILD was defined as follows: a decrease in DLCO and/or FVC (first to last reported) by >15%, an increase in fibrosis index or total HRCT score of ≥2, and death from respiratory failure.

Results: Of 51 patients; 20 were male and 15 had a diagnosis of dermatomyositis (DM). The median age at onset was 47 years, mean follow-up duration was 6.6 years; 3/15 (20%) presented with ILD prior to AJS diagnosis. Arthritis, mechanic's hands, Raynaud phenomenon and fever were reported in 88%, 37%, 31%, and 23% of DM patients, respectively. Four patients had cancer: lung (1), prostate and gallbladder (1) and lymphoma (2). At diagnosis 3 patients had upper respiratory pneumonia, 13 (25%) had organizing pneumonia (3 with non-specific interstitial pneumonia

(NSIP), with 5 developing NSIP later); 36 (70%) had NSIP: 22 fibrotic, 2 mixed and 12 cellular; 75% of cellular NSIP became fibrotic on subsequent imaging. Mean DLCO and FVC at diagnosis were 58.9% and 67%, respectively. The median initial inflammation and fibrosis indices at diagnosis were 5.6, 1.16 and at last follow-up 4.8, 2.1, respectively. Among 45 patients with available follow-up data; 17 had worsening ILD (39%) and 5 (11%) died of respiratory failure. A lower DLCO at diagnosis of DM was a predictor of disease progression [50 vs. 65% (p=0.0290)]. All upper respiratory pneumonia patients progressed during follow-up. Only 7 patients had a late diagnosis of ILD (≥3 years after onset of AJS). Of those, 5 (70%) had a DLCO ≤50% compared to a DLCO of 25% in those with early diagnosis. Sjögren's syndrome antibody (SSA) positivity was detected in 53% of patients; lower initial (53% vs. 62%) and last (56% vs. 67%) DLCO as well as higher fibrosis score at last follow-up [3.5 vs. 0.9 (p=0.089)] were observed in SSA negative group. These differences did not reach statistical significance. Interestingly; 6/7 patients who died were SSA negative. Nine patients who developed pulmonary hypertension had higher median disease duration (10 years) and CT score (12.5) and all of them had DLCO ≤50%. Esophageal disease other than dysphagia was detected in 43% [GERD (33%), abnormal manometry or gastric emptying (15%) and dilatation on chest CT (10%)]. Esophageal disease trended towards lower DLCO at diagnosis [53 vs. 62% (p=0.084)], higher fibrosis score [2.7 vs. 1.6 (p=0.089)] and higher %change of total CT score [1.1 vs. -0.7 (p=0.007)].

Conclusion: Lower DLCO at diagnosis was associated with progression of ILD. The lower DLCO observed in late onset ILD may suggest a silent disease and reemphasizes the role of screening for ILD in AJS. In contrast to previous studies; SSA co-positivity was not associated with an adverse outcome. Esophageal disease seemed to be prevalent in anti-Jo-1 patients with ILD and may predict worsening fibrosis. However, the association of malignancy with anti-Jo1 syndrome (AJS) was not significant.

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Abstract Number: 1057

Earlier Cancer Diagnosis After Idiopathic Inflammatory Myopathy Onset Is Associated with Improved Long Term Survival - Results from Four European Cohorts

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The idiopathic inflammatory myopathies (IIMs) are strongly associated with the development of clinically detecTable cancer. Cancer screening has therefore been advocated in newly diagnosed IIM cases, however no study has investigated if this confers improved long term survival. This study aimed to investigate if a shorter time between IIM onset and cancer diagnosis is associated with improved long term survival.

		Whole cohort N = 248	Female cohort N = 169	Male cohort N = 79
Median follow up time / years (IQR)	Whole cohort	5.1 (1.7, 8.9)	5.0 (1.7, 8.5)	5.5 (1.5, 9.8)
	Alive	5.9 (2.8, 10.3)	5.6 (2.7, 10.2)	6.6 (3.0, 10.3)
	Deceased	2.3 (0.3, 6.1)	2.8 (0.4, 6.4)	1.2 (0.2, 3.8)
Median age at IIM onset / years (IQR)	Whole cohort	56.5 (46.2, 63.7)	56.2 (46.0, 63.6)	56.9 (47.9, 64.0)
	Alive	56.5 (46.0, 63.7)	58.7 (46.0, 63.9)	55.6 (46.8, 62.6)
	Deceased	56.4 (47.6, 63.4)	53.8 (47.2, 62.1)	61.4 (56.1, 67.8)
Median time between IIM onset and cancer diagnosis / years (IQR)	Whole cohort	4.6 (1.2, 10.5)	5.0 (1.3, 11.5)	4.1 (1.0, 9.0)
	Alive	4.5 (1.0, 10.2)	5.0 (1.1, 10.5)	4.1 (1.0, 9.4)
	Deceased	5.5 (1.5, 13.6)	5.5 (1.5, 15.5)	4.9 (1.2, 8.8)
Number of deaths in follow up period (%)		60 (24.2)	44 (26.0)	16 (20.3)
Median time between cancer diagnosis and death / years (IQR)		2.0 (0.3, 5.3)	2.4 (0.4, 5.6)	1.0 (0.2, 3.3)

IQR = inter-quartile range, IIM = idiopathic inflammatory myopathy

Table 1. Time to cancer diagnosis and death for the whole cohort, divided by gender

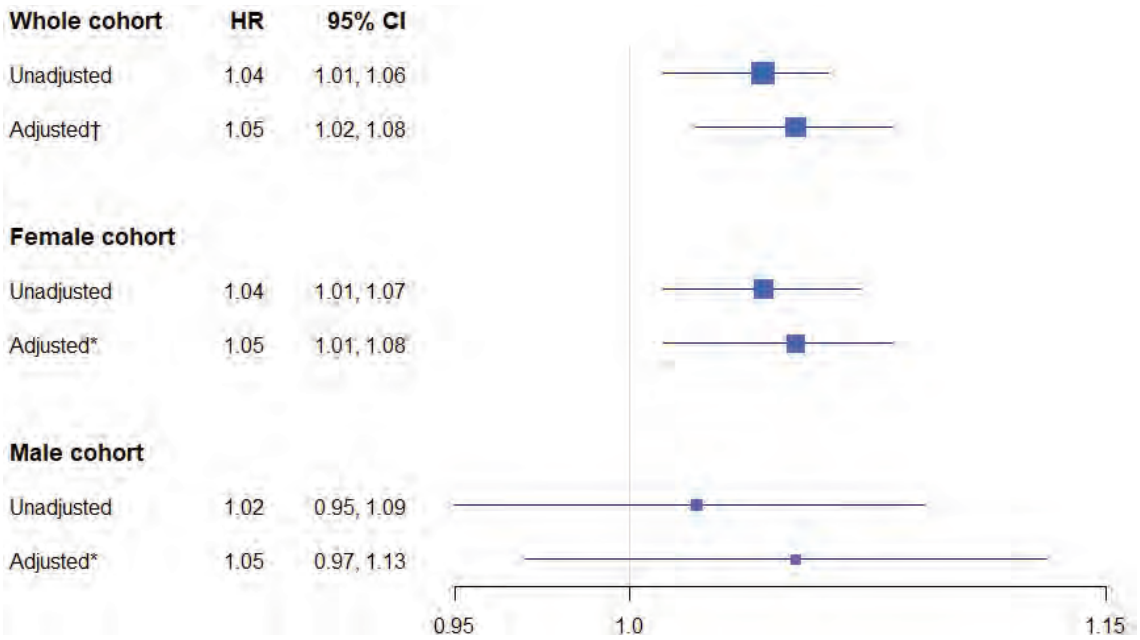

Figure 1. Modelling results of relationship between survival and time between IIM onset and cancer diagnosis, divided by gender.

HR = hazard ratio. CI = confidence interval.
† Hazard ratio for survival - adjusted for age and gender.
* Hazard ratio for survival - adjusted for age.

Methods: Adult IIM cases (dermatomyositis, polymyositis and anti-synthetase syndrome) were recruited from four separate cohort studies from the UK, France, Czechia and Hungary.

Only cases with cancer diagnosis following IIM onset were included in analysis (i.e. synchronous cancer cases were excluded). The time between IIM onset and cancer diagnosis was calculated for each case. Where death occurred, the time between cancer diagnosis and death was calculated and employed as follow up time. Where death did not occur, the time between cancer diagnosis and their follow up cut-off date was calculated. Cases were censored at the end of their follow up period if death did not occur. The relationship between survival at the end of follow up and

time between IIM onset and cancer diagnosis was quantified via calculation of hazard ratios using a Cox-proportional hazard model adjusted for age and gender.

Results: A total of 248 (68% female) verified IIM cases with a total of 1,601 person-years follow up (median 5.1 years [IQR 1.7, 8.9]) were included in the analysis (Table 1).

Sixty deaths occurred within the follow up period in the whole cohort. The median time between cancer diagnosis and death was 2 years (IQR 0.3, 5.3). The IIM to cancer diagnosis time was shorter for those that survived at the end of follow up, compared to those that died: 4.5 years (IQR 1.0, 10.2), 5.5 years (IQR 1.5, 13.6), respectively. Deaths in the male cohort occurred earlier after cancer diagnosis than in the female cohort: 1 year vs 2.4 years.

Cox-proportional hazard modelling indicated that a longer IIM onset to cancer diagnosis time was significantly associated with death for the whole cohort (HR 1.04 [95% CI 1.01, 1.06], p-value < 0.01) (Figure 1). This relationship persisted after adjustment for age and gender (HR 1.05 [95% CI 1.01, 1.08], p-value < 0.01). However, this relationship was observed in the female cohort only (HR 1.05 [95% CI 1.01, 1.08], p-value < 0.01) and not the male cohort (HR 1.05 [95% CI 0.97, 1.13], p-value 0.26).

Conclusion: This is the first study to identify that earlier cancer diagnosis after IIM onset is associated with improved long term survival in a large cohort, comprising UK, French, Czechia and Hungarian cases. However, this relationship was only significant for the female cohort. These findings indicate that cancer screening in newly diagnosed IIM cases may confer improved survival, especially in female cases.

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Abstract Number: 1058

The Relationship of Different Muscle Enzymes in Adult Myositis Patients

Rohit Aggarwal[1] and **Tanya Chandra**[2], [1]University of Pittsburgh, Pittsburgh, PA, [2]University of Connecticut, HARTFORD, CT

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Muscle Biology, Myositis & Myopathies Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Muscle enzymes are a core set measure (CSM) in clinical trials. The 2016 ACR/EULAR myositis response criteria and the IMACS definition of improvement recommend using the most abnormal muscle enzyme at trial entry among the following five, creatine kinase (CK), aldolase, AST, ALT, and LDH. However, there is limited data on their relationship when assessed at the same time and which muscle enzyme should be followed as the CSM

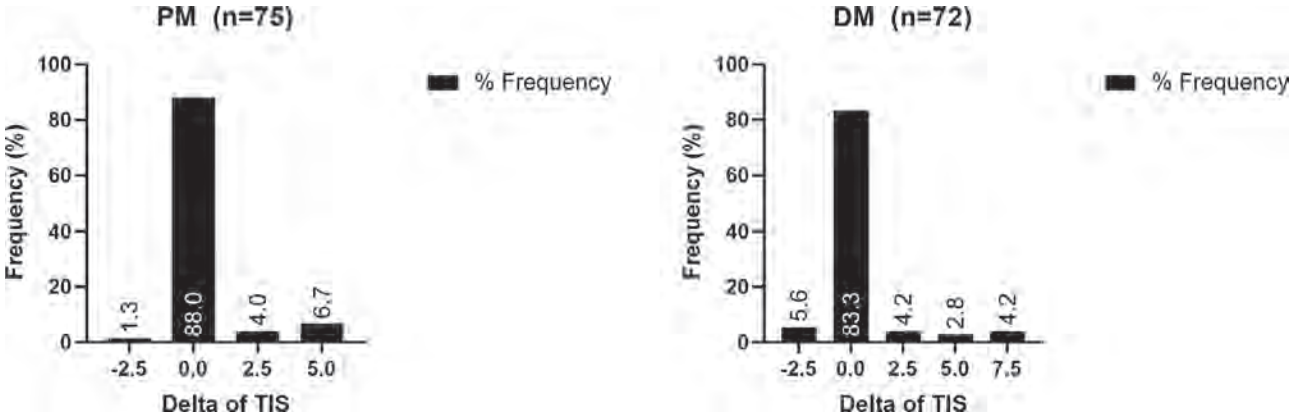

Figure 1. TIS change when CK is substituted for the most abnormal muscle enzyme in PM and DM subjects

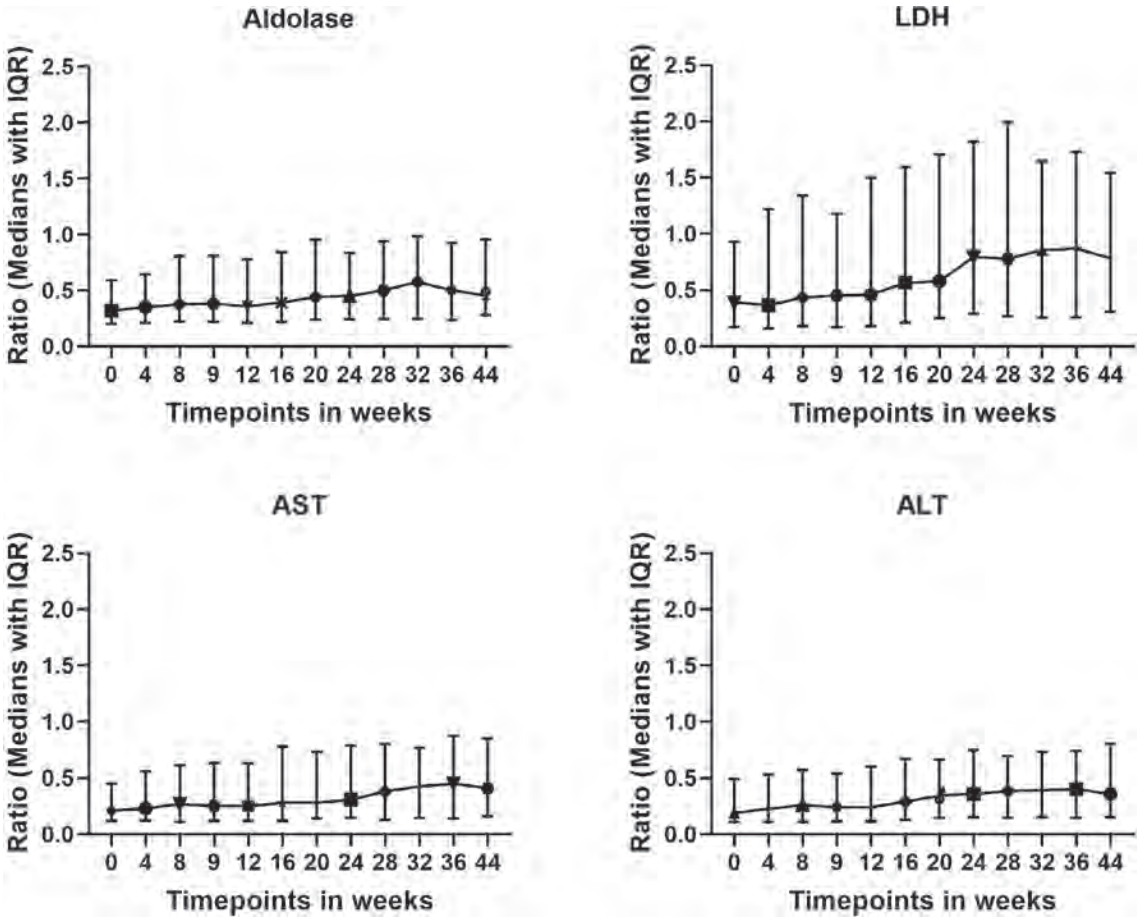

Figure 2. Ratios of the different muscle enzymes related to serum CK (all expressed as xULN)

in adult myositis clinical trials. We aimed to evaluate the relationship of the aforementioned muscle enzymes in the Rituximab in Myositis (RIM) trial.

Methods: All five muscle enzymes and their summary statistics were analyzed at baseline and longitudinally in 75 adult polymyositis (PM) and 72 adult dermatomyositis (DM) subjects enrolled in the RIM Trial. Their respective values

were incorporated into the published Total Improvement Score (TIS) of the 2016 ACR/EULAR Myositis Response Criteria at weeks 24 and 44. All muscle enzymes were reported as the times of upper limit of normal (xULN).

Results: At baseline, the CK was the most abnormal enzyme in adult PM and DM (81.3%, 55.6 %) followed by LDH (10.7%, 25%), aldolase (5.3%, 6.9%), AST (0%, 8.3 %) and ALT (2.7%, 4.2%). The CK was elevated in 86.7% of PM and 63.9 % of DM patients respectively, followed by LDH (89.3%, 62.5%), aldolase (68%, 51.4%), AST (65.3%, 45.8%) and ALT (65.3%, 47.2%). Similar results were seen across gender, race, age groups as well as different autoantibody subsets . Even when CK was not the most abnormal muscle enzyme in PM and DM (18.7%, 44.4%), the frequency of abnormal enzymes was: CK (5.3% PM, 9.7% DM), Aldolase (6.7% PM, 11.11%DM), LDH (12%PM, 16.7%DM), AST (4%PM, 6.9%), ALT (6.7%PM, 9.7%) and the CK levels were only marginally lower than the levels of the most abnormal enzyme. The median difference between the CK and most abnormal enzyme was only 0.03% at 24 weeks. Thus, when the CK was substituted as the most abnormal muscle enzyme in calculating the TIS, most (85.7%) adult myositis subjects (88% PM, 83.3% DM) had no change in the TIS at week 24. In the approximately 15% of subjects demonstrating a change in the TIS score, the mean (SD) change was quite small at 4.05 (1.8) for all subjects [3.89 (1.24) for PM and 4.17 (2.12) for DM (Figure 1)]. Only 1 adult PM patient had a change in the TIS score that translated to a shift from a 'minimal' clinical response to 'no' response. Similar results were observed at week 44.

The ratios between the different enzymes (expressed as xULN) across all the time points throughout the RIM Trial were relatively well preserved with median (IQR) ratios of CK with aldolase, LDH, AST, ALT of 0.41(0.12), 0.57 (0.35), 0.28 (0.15) and 0.32 (0.14) respectively (Figure 2).

Conclusion: The serum CK is most frequently elevated in adult PM and DM, followed by the LDH especially in DM, and can be used as the single muscle enzyme for published myositis response criteria without significant change in the outcome analysis. This is particularly important when other muscle enzyme levels may not be feasible for the determination of outcome given the adverse effect of many drugs. Muscle enzyme ratios are well-preserved over time, such that AST and ALT elevations outside of these ratios should prompt evaluation for other causes.

Disclosure: R. Aggarwal, Octapharma, 5, Bristol Myers Squibb, 2, 5, Abbvie, 5, Mallinckrodt, 2, 5, Pfizer, 2, Csl Behring, 5, Kezar, 5; **T. Chandra**, None.

Abstract Number: 1059

Anti-mitochondrial Autoantibodies Are Associated with Cardiomyopathy, Dysphagia, and Features of More Severe Disease in Adult-onset Myositis

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SESSION INFORMATION

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Background/Purpose: We examined the prevalence of anti-mitochondrial autoantibodies (AMA) in adult- and juvenile-onset myositis longitudinal cohorts and investigated phenotypic differences between myositis patients with or without AMA.

Methods: We screened sera from myositis patients who were classified as adult- or juvenile-onset dermatomyositis (DM, JDM), polymyositis (PM, JPM), inclusion body myositis (IBM), or amyopathic DM, including 619 adults and 371 children, compared to healthy controls (64 adults and 92 children), for AMA by ELISA. Clinical characteristics were compared between myositis patients with and without AMA.

Results: AMA were present in 5% of adult myositis patients (16 DM, 10 PM, 4 IBM, 1 amyopathic DM), 1% of juvenile myositis patients (3 JDM, 1 JPM), and 1% of adult and juvenile healthy control subjects. In patients with adult-onset myositis, AMA were associated with persistent muscle weakness (90% vs 62%, p=0.005), DM-specific rashes (60% vs 41%, p=0.04), Raynaud's phenomenon (43% vs 14%, p< 0.001), dysphagia (63% vs 36%, p=0.003), and cardiomyopathy (16% vs 5%, p=0.01). Adult myositis patients with AMA may have more severe or treatment refractory disease, as they more frequently received glucocorticoids (90% vs 67%, p=0.04), intravenous immunoglobulin (IVIG) (60% vs 29%, p=0.003), and overall received a higher total number of medications, including glucocorticoids, mycophenolate mofetil, methotrexate, IVIG, azathioprine, rituximab and cyclophosphamide, (2.8 vs 2.0, p=0.002) than those who were AMA negative. In juvenile myositis, children with AMA often had falling episodes (4/4) and dysphagia (3/4), but no other clinical features or medication usage were significantly associated with AMA.

Conclusion: AMA are present in 5% of adult myositis patients and associated with cardiomyopathy, dysphagia, persistent weakness, vasomotor instability, and additional therapy. The prevalence of AMA is not increased in patients with juvenile myositis compared to age-matched controls. These data suggest that the presence of AMA in adult myositis patients should prompt screening for cardiac and swallowing involvement.

Disclosure: S. Sabbagh, None; **I. Pinal-Fernandez**, None; **M. Casal-Dominguez**, None; **J. Albayda**, None; **J. Paik**, None; **F. Miller**, None; **L. Rider**, NIEHS, NIH, 2, Cure JM Foundation, 2, Bristol Myers Squibb, 2, Hope Pharmaceuticals, 2, Eli Lilly and Company, 9, MedImmune/AstraZeneca, 9; **A. Mammen**, None; **L. Christopher-Stine**, None.

Abstract Number: 1060

B-cell-rich Inflammatory Myopathies in Adults: Striking Association with Connective Tissue Diseases

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

Background/Purpose: Myositis with significant B-cell infiltrates on muscle biopsy has scarcely been described in adults. Radke (2018) found B cells in adult dermatomyositis (DM) and stratified them as classic, B-cell-rich and follicle-like DM. In patients without DM, three neuropathology studies described myositis with significant B-cell infiltrates. De Bleeker (1996) reported 7 patients with biopsies showing nodules resembling lymph nodes, i.e. a B-cell-rich center surrounded by CD4+ T-cell-rich peripheral zone; noTable findings were cervical muscle weakness and the presence of a connective tissue disease (CTD). Pestronk (2006) described 9 patients with prominent perimysial and perivascular B-cell infiltrates, cervical muscle weakness and either myasthenia gravis or a CTD. Espitia-Thibault (2017) studied 4 patients with primary Sjögren syndrome (SS) and myositis; and found germinal centre-like structures composed predominantly of CD4+ T cells and B cells. The aim of the present study was to describe the clinicoserological findings of patients with B-cell-rich infiltrates on muscle biopsy, and no DM.

Methods: Muscle biopsies with significant B-cell infiltrates (≥ 30 CD20+ cells/aggregate) were identified from 2 neuropathology centers. All cases were reviewed in multidisciplinary meetings. Clinical, serological, pathological features and classification criteria for inclusion body myositis (IBM) were recorded. Patterns of muscle involvement were noted, including cervical, finger flexor and quadriceps weakness. The presence of a CTD and cancer within 3 years of myositis diagnosis was also recorded. Patients with a DM rash were excluded.

Results: Ten patients with myositis, no DM rash, and significant B-cell infiltrates on muscle biopsy were included. Nine were female; median age at myositis diagnosis was 66.5 years (range 51-85). Median CK level was 291 UI/L (range 98–4372). Two patients with normal strength, but myalgias (n=1) or cervical muscle edema (n=1), had imaging suggestive of myositis. All remaining patients had cervical muscle weakness (n=8), and 3 had objective oropharyngeal dysphagia. Quadriceps (n=6) and finger flexor (n=3) weakness was noted, and 4 patients met the Lloyd IBM classification criteria. Associated diseases included anti-CCP positive RA (n=3), systemic sclerosis (SSc) (n=3), primary SS (n=1), systemic lupus erythematosus (n=1) and lung cancer (n=1). Serologically, all patients but one were tested: none had myositis-specific autoantibodies (aAbs) and 2 patients with SSc had anti-Th/To (n=1) and anti-PM-Scl (n=1) aAbs. Anti-Ro52/TRIM21 (n=4), anti-SSA/Ro60(n=3), anti-SSB/La (n=2) were present. Anti-NT5c1A aAbs were present in 1 of 3 tested patients.

Conclusion: Myositis and significant B-cell infiltrates were associated, as in previous studies, with various CTDs, and not only with SS. Cervical weakness and features of IBM were frequent in this subset of patients. CD20 stains were listed as optional in the 205th European Neuromuscular Centre international workshop. Routine CD20 staining should be considered in patients with cervical muscle weakness and suspected myositis in the setting of an associated CTD.

Disclosure: P. Korathanakhun, None; **O. Landon-Cardinal**, None; **V. Leclair**, None; **B. Ellezam**, None; **A. Meyer**, None; **J. Bourré-Tessier**, None; **A. Mansour**, None; **S. Larue**, None; **F. Grand'Maison**, None; **R. Massie**, None; **M. Le Page**, None; **C. Isabelle**, None; **N. Routhier**, None; **F. Roy**, None; **M. Satoh**, None; **M. Fritzler**, Inova Diagnostics Inc, 5, 8, Werfen International, 5, 8; **J. Senécal**, None; **Y. Troyanov**, None; **M. Hudson**, None; **J. Karamchandani**, None; **E. O'Ferrall**, Sanofi Genzyme, 2, Acceleron, 2, Biogen, 8.

Abstract Number: 1061

Daily Myositis Symptom Changes Collected via a Smartphone-Based App Are Associated with Flare Occurrence - Providing Evidence of Potential Digital Biomarkers

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Muscle Biology, Myositis & Myopathies Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The concept of idiopathic inflammatory myopathy (IIM) flare is widely used, although no consensus definition exists. Studies have demonstrated the feasibility and utility of using tailor-made smartphone apps to collect daily symptom patient-reported outcome measurements (PROMs). This methodology allows researchers to investigate relationships between events, such as a flare, with changes of daily symptoms. Delineation of patterns of symptom changes associated with flares may provide a preliminary patient definition of an IIM flare and identify "digital biomarker" candidates.

This study aimed to use daily smartphone app-collected data to:

	Variable	Flare occurrence	No flare occurrence	p-value†	Modelling results*		
					OR	95% CI	p-value
Mean symptom score 7 days prior to flare reporting (SD)	Participant global activity	39.0 (19.7)	30.8 (21.6)	<0.01	1.09	1.03, 1.15	<0.01
	Fatigue	43.1 (19.4)	35.2 (22.5)	<0.01	1.05	1.02, 1.09	<0.01
	Overall pain	36.1 (21.0)	26.4 (18.5)	<0.01	1.10	1.04, 1.16	<0.01
	Myalgia	34.5 (22.0)	23.5 (16.8)	<0.01	1.09	1.04, 1.15	<0.01
	Weakness	38.5 (20.0)	32.1 (24.1)	0.03	1.07	1.01, 1.13	0.02
Mean magnitude of day to day change 7 days prior to flare reporting (SD)	Participant global activity	9.3 (5.5)	7.6 (5.9)	0.03	1.07	1.01, 1.14	0.04
	Fatigue	11.7 (6.8)	10.8 (7.6)	0.33	1.01	1.01, 1.01	<0.01
	Overall pain	9.2 (6.4)	8.2 (5.8)	0.25	1.03	0.97, 1.10	0.33
	Myalgia	8.6 (6.2)	7.4 (5.6)	0.13	1.05	0.99, 1.13	0.12
	Weakness	10.1 (5.8)	7.8 (5.9)	<0.01	1.09	1.01, 1.16	0.02
Mean entropy 7 days prior to flare reporting (SD)	Participant global activity	7.5 (0.1)	7.5 (0.1)	0.36	8.60	0.12, 38.47	0.27
	Fatigue	7.5 (0.1)	7.5 (0.1)	0.52	4.25	0.13, 13.63	0.42
	Overall pain	7.5 (0.1)	7.5 (0.1)	0.38	4.95	0.15, 16.03	0.37
	Myalgia	7.5 (0.1)	7.5 (0.1)	0.44	7.58	0.11, 54.50	0.35
	Weakness	7.5 (0.1)	7.5 (0.1)	0.69	0.57	0.02, 14.65	0.74

† Variables were compared between flare and non-flare weeks using the independent 2 group t-test

* Odds ratio for flare occurrence - multi-level mixed effects logistic regression modelling, adjusted for age and gender

OR = odds ratio, CI = confidence interval, SD = standard deviation

Table 1. Summary and modelling results of daily symptom scores, day to day change and entropy, divided by flare occurrence

1. Characterise the pattern of patient-reported flares in an IIM cohort
2. Identify changes of daily symptoms associated with flares
3. Identify IIM flare digital biomarker candidate variables

Methods: Data was collected via the Myositis Physical Activity Device (MyoPAD) study. Recruited participants (UK adult participants with a verified IIM diagnosis) answered PROMs every day of the 91 day study period via an IIM-tailored smartphone-based app. Daily symptom PROMs addressed 1) global activity, 2) overall pain, 3) myalgia, 4) fatigue and 5) weakness (0-100 visual analogue scale). Every 7 days, participants were also asked whether or not they suffered a flare (present/absent) via the app. To illustrate the daily symptom and weekly flare reporting, Figure 1 shows a single participant's data over a 3 week period.

The following were calculated for each 7 day period prior to each flare question:

1. Mean score of each daily PROM
2. Mean magnitude of day-to-day change of each daily PROM (i.e. negative differences were multiplied by -1)
3. Entropy (measure of variability) of each daily PROM

Multi-level mixed effects logistic regression models tested the relationships between flare occurrence and each above calculated measurement. This was subsequently adjusted for age and gender.

Results: 21 participants (67% female) took part in the study. The median age of the cohort was 50 years (IQR 43, 56) and median disease duration 3 years (IQR 2, 5). Engagement was high - a total of 22880 PROMs, 88% of a potential total 25977, were entered. Participants reported experiencing flares on a median of 3 weeks (IQR 2, 5) per participant, out of a possible 13. A total of 81 (31%) flares were reported across the cohort from 261 answered flare questions (4% questions not answered).

Modelling revealed that a higher score of each daily symptom PROM was significantly associated with flare occurrence (Table 1 and Figure 2). Higher magnitude of day-to-day change of participant global activity, fatigue and weakness were also significantly associated with flare occurrence. Flare occurrence was not significantly associated with entropy of any daily symptom.

Conclusion: This study has characterised the frequency of flare occurrence in an IIM cohort - flares were reported to occur one week in four on average. This study has also delineated daily symptoms associated with patient-reported IIM flares - particularly global activity, fatigue and weakness. Smartphone app collected daily symptom data

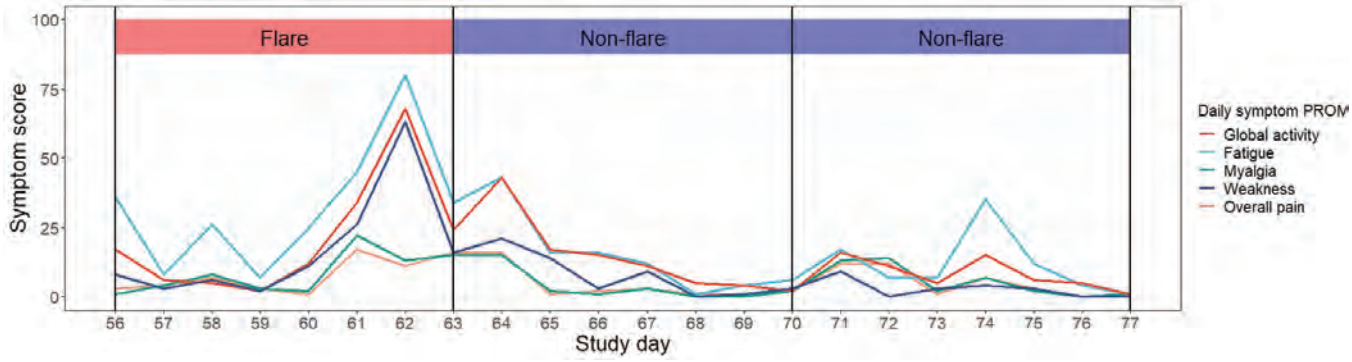

Figure 1. Three week extract (days 56 to 77 of 91 day study period) of single participant's daily symptom PROM scores and flare occurrence. PROM = patient reported outcome measurement

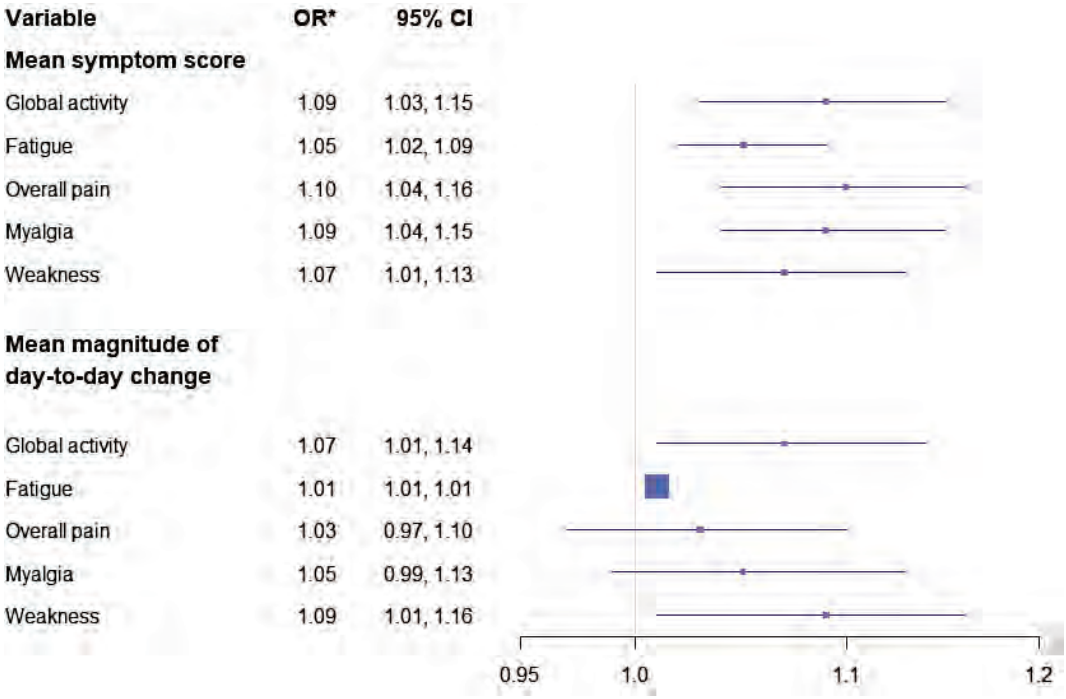

Figure 2. Modelling results of mean symptom score and magnitude of day-to-day change over 7 day period prior to flare occurrence.

may therefore provide digital biomarkers capable of predicting IIM flare occurrence and enable reactive treatment instigation.

OR = odds ratio, CI = confidence interval.
* Odds ratio for flare occurrence - multi-level mixed effects logistic regression modelling, adjusted for age and gender.

Disclosure: A. Oldroyd, None; **B. Yimer**, None; **M. Little**, None; **W. Dixon**, Google, 1, Bayer, 1; **H. Chinoy**, Novartis, 1.

Abstract Number: 1062

Dermatomyositis: A Dermatology-Rheumatology Clinic Retrospective Analysis

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

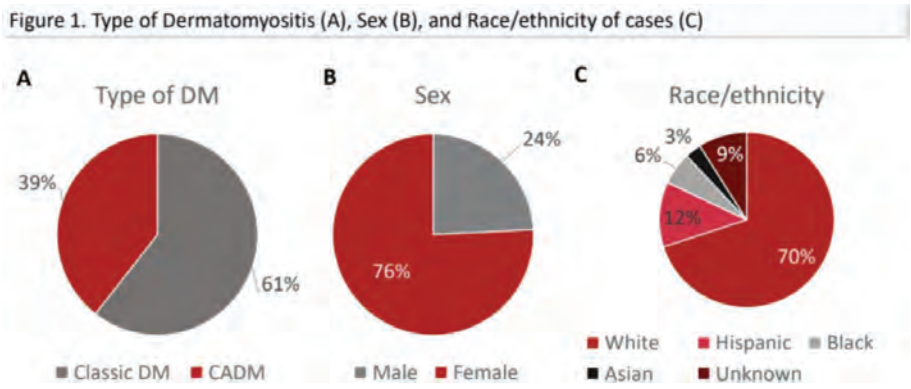

Figure 1. Type of Dermatomyositis (A), Sex (B), and Race/ethnicity of cases (C)

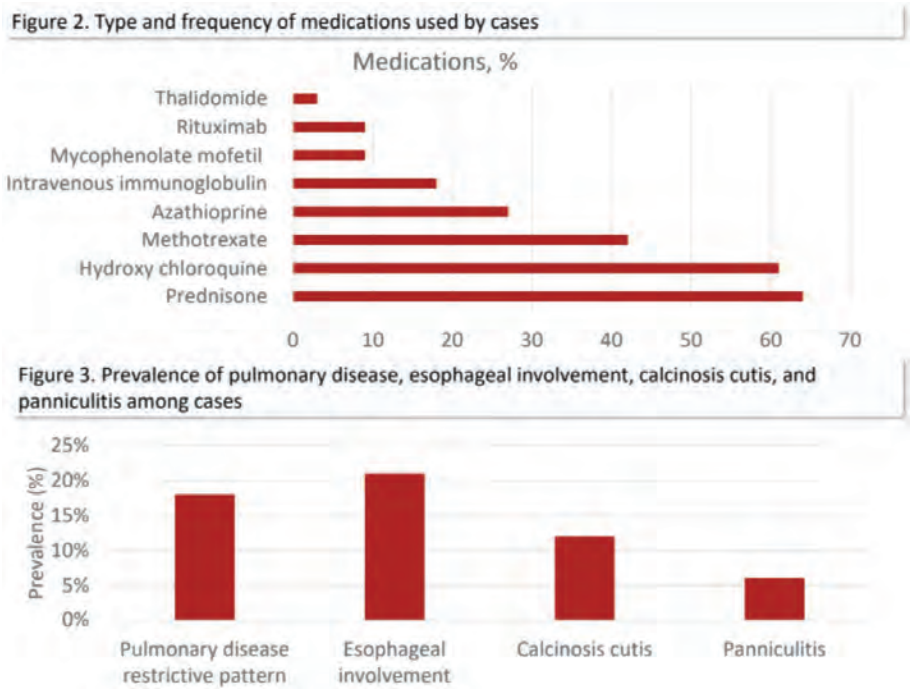

Figure 2. Type and frequency of medications used by cases Figure 3: Prevalence of pulmonary disease, esophageal involvement, calcinosis cutis, and panniculitis

Background/Purpose: Dermatomyositis (DM) can be categorized into two major subtypes: clinically amyopathic dermatomyositis (CADM) and classic dermatomyositis (CDM). In this study, we aimed to identify characteristics of the patients with DM evaluated at the combined Dermatology-Rheumatology clinic.

Methods: We used ICD-9/10 codes to identify patients with DM. Demographics, clinical features, laboratory values, type cancer diagnosis (if any) was obtained by electronic medical records. We used descriptive statistics to present characteristics of patients. The association between a variety of factors and risk of cancer was examined using logistic regression.

Results: 33 patients with DM were identified. 8 (24%) were male and 25 (76%) were female. The average age at diagnosis was 50 (SD:17). 61% had CDM, 39% had CADM. 70% White, 12% Hispanic, 6% Black, 3% Asian and 9% unknown (Figure 1). Medications used by patients for DM in order of frequency (n, %) include prednisone (21, 64 %), hydroxychloroquine (20, 61 %), methotrexate (14, 42%), azathioprine (9, 27%), intravenous immunoglobulin (6,

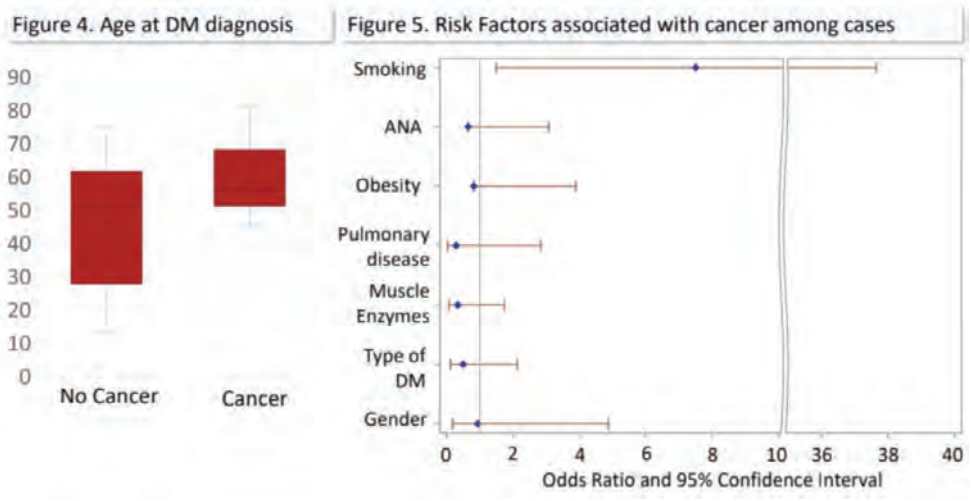

Figure 4. Age at DM diagnosis Figure 5: Risk Factors associated with cancer among cases

18%), mycophenolate mofetil (3, 9%), rituximab (3, 9%), and thalidomide (1, 3%) (Figure 2). Pulmonary disease with restrictive pattern 6 (18%), esophageal involvement 7 (21%), calcinosis cutis 4 (12%) and panniculitis were reported in 2 (6%) of the patients (Figure 3). Muscle enzymes were high in 20 (61%), normal in 9 (27%) and unknown in 4 (12%). Positive antinuclear antibodies were reported in 52%, majority with speckled pattern. One patient had juvenile DM. 36% (n=12) had a history of cancer, including breast 12%, prostate 6%, T-cell lymphoma, gastric lymphoma, non-small cell lung cancer, cervix, squamous cell carcinoma (SCC) of the tonsil and invasive skin SCC, each one 3%. Three cancer cases occurred within 1 year, 5 cases within 5 years and 4 cases more than 5 years before/after the diagnosis of DM. Average age at diagnosis for patients with cancer was 57 (SD: 12) and for patients without cancer was 45 (SD: 19) (Figure 4). We found no evidence of an association between gender, type of DM, enzyme level, pulmonary involvement, obesity, positive ANA and cancer. History of current or former smoking was strongly associated with increased risk of cancer (OR: 7.50, 95% CI: 1.49-37.66) (Figure 5).

Conclusion: Our results show a higher prevalence of cancer among DM patients compared to the general population. The average age at diagnosis of DM was higher in patients with cancer. We found no association between gender and cancer which is in contrast to previous studies that reported higher risk of malignancy in males compared to females. Smoking (ever versus never) was strongly associated with cancer. This can be explained by the synergistic effect of smoking in patients with DM. No association between pulmonary involvement and cancer was found. Limitations include small sample size and retrospective study design.

Disclosure: B. Elkiran, None; **M. Tajalli**, None; **T. Vance**, None; **A. Qureshi**, None; **A. Reginato**, None.

Abstract Number: 1063

Spirulina Stimulates Inflammatory Cytokine Production Through the STING and TLR Pathways in Dermatomyositis in Vitro

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Muscle Biology, Myositis & Myopathies Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Spirulina, a popular herbal supplement, stimulates the immune system, as determined by in vitro and in vivo studies. Our recent epidemiologic data suggest that Spirulina is associated with the onset or exacerbation of pre-existing autoimmune skin diseases, such as DM. The purpose of this study was to investigate the immunostimulatory effects of Spirulina and characterize the role of the Stimulator of interferon genes (STING) and Toll-like Receptor (TLR) pathways.

Methods: PBMCs were isolated from DM and normal controls and stimulated with increasing concentrations of pure Spirulina supernatant (0, 0.3, and 1 mg/ml). All DM patients met the EULAR/ACR definition of DM or amyopathic DM. PBMCs were also pre-treated for 1 hour with the following inhibitors: STING inhibitor, H-151; TLR4 inhibitor, TAK 242; TLR2 and TLR4 inhibitor, Sparstolonin B; and TBK1 inhibitor, MRT67307. Cells were incubated for 18 hours before supernatant was collected for ELISA.

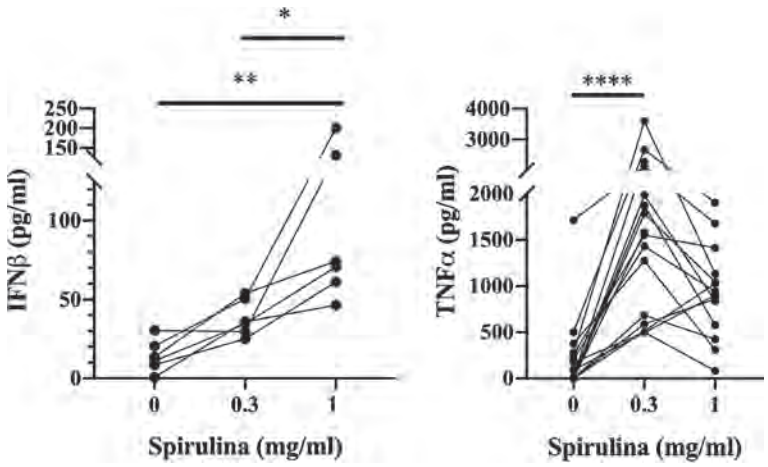

Figure 1. (a) DM PBMCs secreted mean (standard error of mean) IFN**β** of 14.18 (4.18), 38.26 (4.69), and 97.42 (23.76) pg/ml, at 0, 0.3, and 1 mg/ml Spirulina concentrations, respectively (n=6). (b) DM PBMCs secreted mean (standard error of mean) TNF**α** of 213.03 (101.08), 1718.94 (208.95), and 938.36 (134.72) pg/ml at 0, 0.3, and 1 mg/ml Spirulina concentrations, respectively (n=17). Bars show * p<0.05, ** p<0.01, **** p<0.0001. Line represents the median.

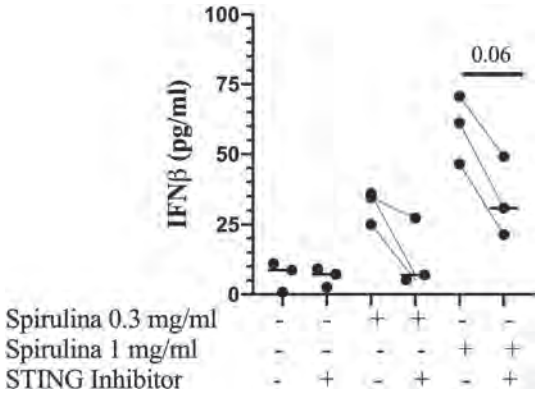

Figure 2. Effects of STING inhibitor versus sham on secretion of IFN**β** from unstimulated and Spirulina-stimulated PBMCs in "Good Responders." Line represents the median. (n=3)

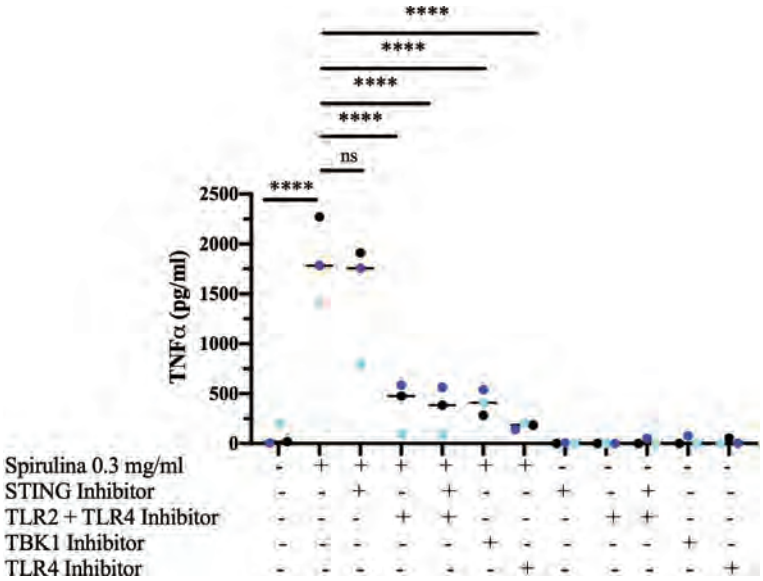

Figure 3. Effects of STING, TLR2 + TLR4, TLR2 + TLR4 + STING, TBK1, or TLR4 inhibition versus sham on secretion of TNF**α** from unstimulated and Spirulina-stimulated PBMCs (n=3). Bars show **** p<0.0001. Line represents the median.

Results: Spirulina dose-dependently increases PBMC production of IFNβ in DM patients (Figure 1a). Spirulina also increases PBMC production of TNFα, with peak levels when stimulated with 0.3 mg/ml Spirulina (Figure 1b).

In the presence of Spirulina, STING inhibitor suppressed secretion of IFNβ in all five DM patients. "Good Responders," defined as subjects with >20% decrease in cytokine levels with STING inhibitor and stimulation at both Spirulina concentrations had mean (standard error of mean) IFNβ levels of 33.78 (1.51) pg/ml pre-antagonist and 13.19 (7.11) post-antagonist when stimulated with Spirulina 0.3 mg/ml and IFNβ levels of 59.47 (7.04) pg/ml pre-antagonist and 33.81 (8.17) post-antagonist when stimulated with Spirulina 1 mg/ml (p=0.06) (Figure 2).

With Spirulina stimulation, STING inhibitor only suppressed secretion of TNFα in 6/15 subjects and these results were not statistically significant. A second experiment using 3 subjects further examined the effects of TLR2 and TLR4, TLR2 and TLR4 and STING, TBK1, or TLR4 inhibition on PBMC production of TNFα. In the presence of 0.3 mg/ml Spirulina stimulation, these four inhibitors significantly decreased TNFα levels (Figure 3) with TNFα decreasing from mean (standard error of mean) 1829 (243.47) pg/ml to 384.6 (149.27), 346.0 (138.11) 410.7 (73.43), and 175.7 (17.68) pg/ml when TLR2 and TLR4, TLR2 and TLR4 and STING, TBK1, or TLR4 inhibitors were added, respectively (n=3) (p< 0.0001). STING inhibition decreased TNFα production from 1829 pg/ml to 1488 pg/ml (n=3) (p=0.84).

Conclusion: Our preliminary results show that Spirulina increases production of key inflammatory cytokines TNFα and IFNβ. For TNFα production, Spirulina's immunostimulatory effects appear to be primarily mediated via the TLR4 pathway. Inhibition of TBK1, an important kinase in the innate immune system active in both the STING and NF-kappa B pathways, also significantly decreases TNFα production. For IFNβ production, Spirulina's immunostimulatory effects appear to be partially mediated by the STING pathway. Our findings provide a potential mechanism by which Spirulina use may lead to disease onset or flare in susceptible patients.

Disclosure: C. Bax, National Center for Advancing Translational Sciences of the National Institutes of Health, 2; **Y. Li**, None; **S. Maddukuri**, None; **A. Ravishankar**, None; **J. Patel**, None; **D. Yan**, None; **J. Concha**, None; **V. Werth**, Biogen, 2, 5.

Abstract Number: 1064

Anti-SMN Autoantibodies Are Associated with Systemic Sclerosis Small Bowel Involvement in anti-U1RNP Positive Autoimmune Myositis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Muscle Biology, Myositis & Myopathies Poster

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Session Time: 9:00AM–11:00AM

Background/Purpose: The survival of motor neuron (SMN)/gemin proteins are components of a multifunctional protein complex that plays an essential role in RNA metabolism. SMN is present in Cajal bodies, i.e. nuclear structures that play an essential role in the assembly of small nuclear RNPs. Deletion or mutation of the SMN gene is associated with spinal muscular atrophy. Autoantibodies (aAbs) to SMN (anti-SMN) have not been thoroughly studied. Anti-SMN have been associated with scleromyositis (SM), originally in a cohort of 163 autoimmune myositis (AIM) (n=3, 1.8%) patients, and recently in a cohort of 20 seronegative SM (n=5, 25%). In another report, a single patient with anti-U1RNP and anti-SMN aAbs had a necrotizing autoimmune myopathy. The aim of this study was to evaluate the prevalence of anti-SMN aAbs in patients with anti-U1RNP+ AIM, and compare phenotypic differences in patients with and without anti-SMN aAbs.

Methods: All patients with a diagnosis of AIM associated with anti-U1RNP were identified from a clinically and serologically described retrospective cohort of 100 AIM patients. Sera were analyzed for anti-SMN by addressable laser bead immunoassay with results expressed as median fluorescence units (MFU) and positivity defined as 3 SD above the mean of normal and unrelated disease controls (>900 MFU), as previously validated by protein A-assisted immunoprecipitation. Clinical features were collected to assess the presence of ACR/EULAR and non ACR/EULAR features of systemic sclerosis (SSc), systemic lupus erythematosus (SLE) and Sjögren syndrome (SS).

Results: Of 9 AIM patients with anti-U1RNP+, 8 (88.9%) were females and median age at myositis diagnosis was 45 years old (range 24–61). At presentation, clinical features included Raynaud phenomenon (100% of patients), sclerodactyly (100%), lower esophageal dysmotility (88%), arthritis (78%) and proximal weakness (100%). Mean serum CK level was 2601 IU/L (range 329–6000). At myositis diagnosis, 88%, 22% and 22% of 9 patients fulfilled the ACR/EULAR criteria for SSc, SLE and SS, respectively. Five of 9 patients (55.6%) had anti-SMN aAbs (median 15952 MFU, range 4321–18848). These patients had a higher proportion of neck flexor weakness (60% vs 0%), bilateral trigeminal neuropathy (40% vs 25%), interstitial lung disease (40% vs 0%), acute lupus rash (80% vs 25%) and leucopenia

(80% vs 25%) compared to patients without anti-SMN aAbs. Strikingly, only patients with anti-SMN aAbs had SSc small-bowel involvement (n=4/5, 80% vs n=0/4, 0%, P=0.048 by Fisher's exact test) that included pneumatosis intestinalis (n=2/4), small intestine bacterial overgrowth (n=3/4) and pseudo-obstruction (n=4/4). One of these patients required parenteral nutrition whereas 3 others presented severe pseudo-obstruction necessitating hospitalization. At last follow-up (mean duration 12 years), 100%, 22% and 67% of 9 patients fulfilled the ACR/EULAR criteria for SSc, SLE and SS, respectively.

Conclusion: More than 50% of patients with anti-U1RNP+ AIM and SSc also have high titers of anti-SMN aAbs. The presence of anti-SMN aAbs may be predictive of severe SSc small bowel involvement compared to patients without anti-SMN aAbs.

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Abstract Number: 1065

Immunostimulatory Herbal Supplement Use Is More Common Among Patients with Dermatomyositis

Adarsh Ravishankar[1], Daisy Yan[2], Christina Bax[3], Josef Symon Concha[2], Bridget Shields[4], Lisa Pappas-Taffer[4], Rui Feng[5], Joyce Okawa[4] and Victoria Werth[2], [1]University of Pennsylvania and the Michael J. Crescenz VA Medical Center, Philadelphia, [2]University of Pennsylvania and the Michael J. Crescenz VA Medical Center, Philadelphia, PA, [3]University of Pennsylvania, Department of Dermatology, Philadelphia, [4]Department of Dermatology, University of Pennsylvania, Philadelphia, PA, [5]University of Pennsylvania, Philadelphia

SESSION INFORMATION
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Session Title: Muscle Biology, Myositis & Myopathies Poster
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Background/Purpose: The use of complementary and alternative medicine (CAM) is prevalent in dermatology. Certain CAMs, including Spirulina, Alfalfa, Chlorella, Echinacea, and Blue-Green Algae have been reported to incite an immune response or induce dermatomyositis (DM), cutaneous lupus erythematosus (CLE) or autoimmune blistering diseases (AIBD). Given these potential effects, there is a need to characterize CAM usage in patients.

Methods: We performed a retrospective chart review of prospectively-collected data at the University of Pennsylvania to characterize CAM usage among patients with DM, CLE, AIBD (including pemphigus vulgaris and bullous pemphigoid), and controls without autoimmune disease. Information gathered included demographic information, disease history, and CAM usage and duration (Spirulina, Chlorella, Alfalfa, Green Algae, Echinacea, or other). CAM use was elicited in a stepwise manner, starting with asking patients open-ended questions about CAM use, followed by handing a flyer that lists herbal supplements to aid with recall. Statistical analysis was performed using logistic regression to calculate odds ratios (OR), accounting for race and sex as covariates, at a significance level of 0.05.

Results: 372 patients were enrolled, including 158 DM (42.5%), 122 CLE (32.8%), 31 AIBD (8.3%), and 61 controls (16.4%). All cohorts were predominantly female and Caucasian. DM had the greatest proportion of Caucasians (81.6%), followed by controls (78.7%), AIBD (61.3%), and CLE (52.5%). CAM use was reported in 12.1% of all patients

Total # of patients	Any Herbal	Spirulina	Echinacea	Blue-Green Algae	Chlorella	Alfalfa
Dermatomyositis (n = 158)	31 (19.6)	23 (14.6)	4 (2.5)	4 (2.5)	12 (7.6)	3 (1.9)
Lupus (n = 122)	7 (5.7)	5 (4.1)	2 (1.6)	0 (0)	2 (1.6)	2 (1.6)
AIBD (n = 31)	2 (6.5)	0 (0)	1 (3.2)	2 (6.5)	1 (3.2)	0 (0)
Control (n = 61)	5 (8.2)	4 (6.6)	1 (1.6)	1 (1.6)	3 (4.9)	2 (3.3)
Total (n = 372)	44 (11.8)	32 (8.6)	8 (2.2)	7 (1.9)	18 (4.8)	7 (1.9)

Patient Demographics (%)

Cohort	Sex		Age at Visit	Race	
	Male	Female		Caucasian	Non-Caucasian
Dermatomyositis (n = 158)	20 (12.7)	138 (87.3)	56.3 ± 14.2	129 (81.6)	29 (18.4)
Lupus (n = 122)	20 (16.4)	102 (83.6)	51.5 ± 15.1	64 (52.5)	58 (47.5)
AIBD (n = 31)	9 (29.0)	22 (71)	66.0 ± 13.7	19 (61.3)	12 (38.7)
Control (n = 61)	15 (24.6)	42 (75.4)	51.4 ± 15.9	48 (78.7)	13 (21.3)
Total (n = 372)	64 (17.2)	304 (81.7)	54.7 ± 15.3	260 (69.9)	112 (30.1)

Herbal supplement use for each cohort (%)

Cohort Comparisons	Any Herbal		Spirulina	
	Odds Ratio (95% CI)	p-value	Odds Ratio (95% CI)	p-value
Dermatomyositis vs. Controls	2.37 (0.94, 7.30)	0.0919	2.34 (0.85, 8.29)	0.1345
Dermatomyositis vs. non-DM Autoimmune	3.47 (1.57, 8.33)	0.0032*	4.92 (1.87, 15.53)	0.0027*
Non-DM Autoimmune vs. Controls	0.82 (0.26, 2.86)	0.7477	0.56 (0.14, 2.39)	0.4084

Logistic regression comparison of herbal and spirulina use between cohorts

(19.6% of DM, 5.7% of CLE, 6.5% of AIBD, and 8.2% of controls). Spirulina was the most frequently-used herbal supplement for DM (14.6%), CLE (4.1%), and controls (5.7%), while blue-green algae was the most frequently-used CAM for AIBD (3.2%). Herbal use in DM was greater compared to controls (OR = 2.37, p = 0.0919), and compared to other autoimmune cohorts (OR = 3.47, p = 0.0032). Spirulina use was greater among DM patients compared to both controls (OR = 2.34, p = 0.1345) and to other autoimmune cohorts (OR = 4.92, p = 0.0027). Herbal and spirulina use were not significantly associated with non-DM autoimmune diseases compared to controls.

Conclusion: Our study demonstrates that CAM use, in particular spirulina, is greater among patients with DM. This association is statistically significant for DM compared to CLE or AIBD. This study demonstrates that the use of CAM is of concern among the patients with a history of DM. Patients with DM should be educated regarding the risk of onset or flare from using immunostimulatory CAM such as Spirulina.

Disclosure: A. Ravishankar, None; **D. Yan**, None; **C. Bax**, None; **J. Concha**, None; **B. Shields**, None; **L. Pappas-Taffer**, None; **R. Feng**, None; **J. Okawa**, None; **V. Werth**, Biogen, 2, 5.

Abstract Number: 1066

Prevalence of Cervical Dysplasia in Women with Antisynthetase Syndrome

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
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Background/Purpose: Increased risk of cervical dysplasia and cervical cancer have been reported in patients with systemic lupus erythematosus (SLE). However, the reason for this increased risk is not known but may be related to chronic inflammation or immunosuppressive medications. We hypothesize that patients with Antisynthetase Syndrome (ASS), which is also an inflammatory disease treated with immunosuppression, will have an increased risk of cervical abnormalities. There has not previously been a study evaluating the risk of cervical dysplasia or cervical cancer in ASS patients.

Methods: Clinical data were obtained by retrospective review of EMR at Cleveland Clinic (CC) from 2000-2020. Female patients, over the age of eighteen, diagnosed with ASS by a CC rheumatologist and with the presence of one of the ASS specific autoantibodies (Ab): Jo-1, PL-7, PL-12, EJ, or OJ, were selected. Patients with SLE diagnosed by a CC rheumatologist were age-matched to the ASS patient cohort. An age-matched control population without any known autoimmune rheumatic disease was obtained through the Medicine Institute Value-Based Care Research Registry. In addition to the above criteria, the patients were also required to have Pap smear data available in the EMR. Patients who carried concurrent diagnoses of ASS and SLE were excluded from the study.

Variables	Odds Ratio (95% CI)	P-value
Group:		
Control	ref	ref
Antisynthetase	0.43 (0.11, 1.74)	0.24
SLE	0.48 (0.14, 1.62)	0.24
Immunosuppression:		
No	ref	ref
Yes	1.36 (0.4, 4.69)	0.63
HPV Positive:		
No	ref	ref
Yes	6.26 (2.1, 18.63)	<0.001
Smoking:		
No	ref	ref
Yes	1.1 (0.51, 2.39)	0.81
OCP:		
No	ref	ref
Yes	2.21 (0.99, 4.96)	0.054

Table 1. Multivariable Logistic Regression

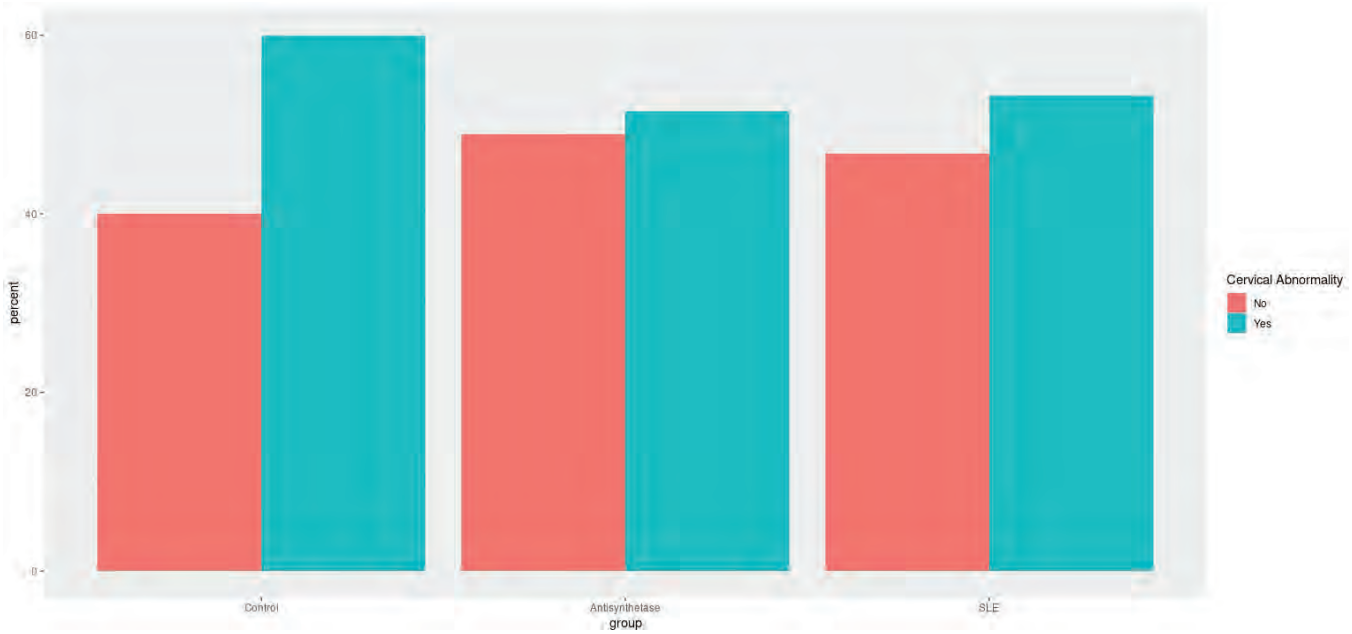

Figure 1. Comparison of the Presence of Cervical Abnormalities by Group

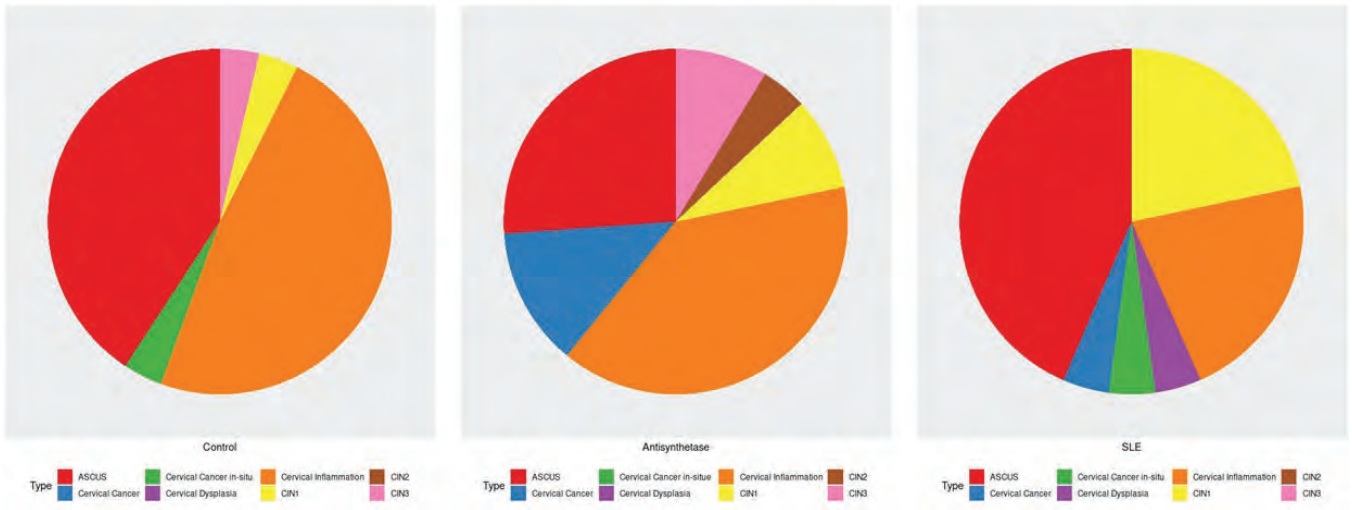

Figure 2. Comparison of Cervical Abnormality Type by Group

Results: A total of 135 patients were included in our analysis with 45 patients in each subgroup: ASS, SLE, or controls. The median age was 52 years. Cervical abnormalities, including cervical inflammation, cervical dysplasia, and cervical cancer, were compared between groups. More than half (53.3%) of all patients had some degree of cervical abnormality, most commonly cervical inflammation (27/74, 37%) and atypical squamous cells of undetermined significance (ASCUS) (27/74, 37%). There were no statistically significant differences in the presence of cervical abnormalities between the three groups. Cervical cancer was present in 6 patients. HPV infections were documented in 23% of patients (31/135), and even after multivariable analysis HPV remained a strong predictor of cervical abnormalities (p= < 0.001). There was also a trend towards use of oral contraceptive pills (OCPs) predicting cervical abnormalities, but this did not reach statistical significance once multivariable logistic regression was completed (p=0.054).

Conclusion: In our cohort, there was no statistically significant difference in the prevalence of cervical dysplasia and cervical cancer in the three groups. This is an interesting finding as numerous studies have reported an increased prevalence of cervical abnormalities in SLE patients, but this was not found in our cohort. The reason for this is unclear but may be related to the small number of ASS patients available for review. Additionally, there may be selection bias towards sicker patients who are more likely to be encouraged to have age-appropriate cancer screening. Our study was limited by being a single-center retrospective analysis of a relatively small cohort. Further studies, with larger sample sizes, maybe helpful to fully understand the underlying risk factors contributing to the prevalence of HPV, cervical dysplasia, and cervical cancer in SLE and ASS patients.

Disclosure: A. Katz, None; **Y. Jin**, None; **S. Chatterjee**, None.

Abstract Number: 1067

Anti-Viral Proinflammatory Phenotype in Circulating Monocytes from Patients with Anti-Melanoma Differentiation-Associated Gene 5 Antibody-Associated Interstitial Lung Disease

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SESSION INFORMATION
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Session Title: Muscle Biology, Myositis & Myopathies Poster
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Background/Purpose: Anti-melanoma differentiation-associated gene 5 (MDA5) antibody is associated with interstitial lung disease (ILD), which often represents rapidly progressive course and fatal outcomes. Circulating levels of ferritin were remarkably increased in patients with anti-MDA5-associated ILD, especially in those with rapidly progressive ILD, suggesting involvement of monocyte/macrophage activation in the pathogenic process. However, stimuli that trigger activation of monocytes/macrophages in anti-MDA5-associated ILD still remain unknown. In this study, we investigated molecules and pathways involved in activated monocytes in circulation from patients with anti-MDA5-associated ILD, using microarray expression profiling combined with the integrated miRNA-mRNA association analysis.

Methods: We first examined comprehensive expression profiling of mRNA and miRNA by a microarray system using circulating $CD14^+$ monocytes from 3 untreated patients with anti-MDA5-associated ILD and 3 healthy controls (HCs). Then, integrated miRNA-mRNA association analysis was conducted to identify molecules related to disease pathways and their regulator effect networks using Ingenuity Pathway Analysis (IPA) system. The relevant gene expression levels were validated by real-time PCR using additional circulating monocyte samples obtained from 5 untreated patients with anti-MDA5-associated ILD, 5 patients with anti-aminoacyl tRNA synthetase (ARS)-associated ILD, and 5 HCs.

Results: Twenty-six significant matched pairs of differentially down-regulated miRNA and up-regulated mRNA were identified by IPA, and 6 relevant genes associated with disease pathways included IFIT2, IFIT3, MX1, IRF7, CCL2 and CLU. The major relevant genes of our dataset were type 1 interferon (IFN)-inducible genes. The regulator effect network analysis identified 5 predicted upstream regulators, including IFN-β, toll-like receptor (TLR) 3, TLR7, TLR9, and

SPI1. Anti-viral infection pathway was identified as the predicted downstream effect involved with those 6 relevant genes. The mRNA expressions levels of 6 genes associated with disease pathways were confirmed to be higher in patients with anti-MDA5-associated ILD than in those with anti-ARS-associated ILD or HCs, and were declined after immunosuppressive treatment in patients with anti-MDA5-associated ILD.

Conclusion: Anti-viral proinflammatory pathways are activated in circulating monocytes from patients with anti-MDA5-associated ILD, suggesting roles of viral infection in triggering this devastating condition.

Disclosure: T. Gono, Bristol Myers Squibb, 1, Chugai pharmaceutical, 1, Ono pharmaceutical, 1, Boehringer Ingelheim, 1, Janssen, 1; **Y. Okazaki**, None; **M. Kuwana**, Ono Pharmaceutical, 2, 8, Chugai, 2, 8, Astellas, 8, Mitsubishi Tanabe Pharma Corporation, 2, 8, AbbVie Inc., 8, Eisai Co., Ltd., 8.

Abstract Number: 1068

Efficacy of Early Initiation of Plasma Exchange Therapy for a Patient with Anti-MDA5 Autoantibody-Positive Dermatomyositis Developing Refractory Rapidly Progressive Interstitial Lung Disease

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SESSION INFORMATION
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Background/Purpose: Dermatomyositis (DM), and particularly the subtype clinically amyopathic DM (CADM), is often associated with fatal rapidly progressive interstitial lung disease (RP-ILD) when anti-melanoma differentiation-associated gene 5 (MDA5) antibody is present, especially in Eastern Asian populations. There is no evidence-based strategy for treating this disease, but intensive treatment with high-dose corticosteroid and multiple immunosuppressants may be effective. However, RP-ILD often fails to respond to such intensive treatment regimens, and still has a very poor prognosis. Here, we report the efficacy of early initiation of plasma exchange (PE) therapy in addition to high-dose corticosteroid and multiple immunosuppressants.

Methods: Retrospective study of DM patients who satisfied the ACR/EULAR classification criteria attending Tokai University Hospital between 2010 and 2019, screened for autoantibodies, and with RP-ILD diagnosed based on the clinical course of respiratory symptoms, function and computed tomography. A model combining 4 serum biomarkers (ferritin ≥ 500 ng/mL, CRP ≥1 mg/dL, KL-6 ≥1,000 U/mL and anti-MDA5 antibody positivity) was used for predicting poor prognosis. All patients received intensive immunosuppressive therapy (high-dose prednisolone (PSL) including methyl-PSL pulse therapy, calcineurin inhibitor and/or intermittent intravenous cyclophosphamide). In addition to this, one group of patients also underwent PE. Comparisons of treatment response and prognosis between the two groups were assessed using Fisher's exact test and paired or unpaired t-test.

Results: Fifteen DM/CADM patients with RP-ILD and at least 3 factors predicting poor prognosis were identified, 7 of whom had classic DM and 8 had CADM. Of these 15 patients, 11 (5 female, 6 male, mean age 57 ± 12 SD, range 38-75 years) received intensive immunosuppressive therapy (IS group) and 4 received PE therapy in addition to im-

munosuppressive therapy (PE group, 2 female, 2 male, mean age 56 ± 14 SD, range 40-70 years). PE therapy was started at the same time as immunosuppressive therapy in 3 of 4 these patients. Respiratory symptoms improved in all 4 patients receiving PE, who were still alive at the end of the study, whereas only 3 of 11 patients receiving immunosuppression alone survived (100% vs. 27%, P= 0.026). Three patients in the PE group and 3 of 11 in the IS group exhibited all 4 indicators of poor prognosis conferring the highest risk of death. Notably, of these 6 patients, all 3 in the PE group but none in the IS group survived. Serum ferritin levels were significantly reduced in the PE group (1459 ng/mL vs. 57 ng/mL, P= 0.043), with decreasing to within the normal range in all 4 patients. Moreover, the mean ferritin level in the PE group after remission was significantly lower than in the IS group (57 vs. 3450 ng/mL; P= 0.037).

Conclusion: PE therapy, especially its early initiation in addition to intensive immunosuppressive therapy, is effective in patients with DM and severe refractory RP-ILD.

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Abstract Number: 1069

Scleromyositis Is Associated with Nailfold Capillary Abnormalities Compared to Immune-Mediated Necrotizing Myopathy

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Muscle Biology, Myositis & Myopathies Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Scleromyositis (SM) is an emerging subgroup of autoimmune myositis associated with features of systemic sclerosis (SSc) and characterized by prominent vasculopathic features on ultrastructural evaluation of muscle capillaries. Yet, SM is also a frequent mimicker of immune-mediated necrotizing myopathy (IMNM) on muscle biopsy. Therefore, the aim of this study was to explore whether nailfold videocapillaroscopy (NVC) patterns in SM were distinct from IMNM.

Methods: A systematic review of NVCs from SM patients and IMNM controls was performed. In the absence of a gold standard or classification criteria, the clinical diagnosis of SM was based on expert opinion (consensus of ≥2 experts). Clinical, serological and pathological data were collected using a standardized protocol. NVC images were acquired using the DS MEDICA Videocap (200X magnification). Nailfolds of the 2nd, 3rd, 4th and 5th fingers of both

hands were photographed by two experienced physicians (GG and MK) and scored by one of them (GG). Microhemorrhages, giant capillaries, ectasias and ramified capillaries were scored using a standardized semi-quantitative scale (0 = no, 1 = ≤33%, 2 = 33–66%, and 3 = ≥66% abnormalities/linear mm). Capillary density was scored both semi-quantitatively (0 if ≥7, 1 if 4–6, or 2 if ≤3 capillaries/mm) and quantitatively (mean number of capillaries/mm). Patterns were classified as SSc-active, SSc-like, non-specific abnormalities or normal. Each NVC parameter and the different NVC patterns were compared between SM and IMNM.

Results: 20 SM cases and 5 IMNM comparators (4 anti-HMGCR positive, 1 anti-HMGCR/anti-SRP negative) were included. SM patients were predominantly females (80%), mean duration from myositis diagnosis to NVC was 2±17 months and vasculopathic features included: Raynaud in 18/20 (90%), history of digital ulcers in 4/20 (20%) and pulmonary arterial hypertension in 1/20 (5%) patient. Sixty-five percent of SM patients fulfilled the ACR/EULAR SSc criteria at myositis diagnosis. SSc features leading to the diagnosis of SM in the remaining 7 patients included: positive ANAs and/or SSc-associated autoantibodies (n=7/7, 100%), Raynaud (n=5/7, 71%), interstitial lung disease (n=5/7, 71%), sclerodactyly (n=1/7, 14%) and SSc calcinosis (n=1/7, 14%). Giant capillaries, ramified capillaries and ectasia were present in 65%, 75% and 80% of SM subjects (median scores 0.16; 0.24 and 0.63, all $p< 0.05$ by Wilcoxon-Mann Whitney U test), respectively, and none of the IMNM controls. Capillary density was lower than normal (7.0-11.0/mm) in SM (median 4.9/mm) and significantly lower compared to IMNM controls (median 8.5/mm, $p=0.012$ by Wilcoxon-Mann Whitney U test). Seventy percent of SM patients had an SSc-active or an SSc-like NVC pattern (35% each), 15% had non-specific abnormalities and 15% were normal. Using the European NeuroMuscular Center pathological criteria, 29% of the SM muscle biopsies were classified as IMNM and 100% of these patients had an abnormal NVC whereas all NVCs were normal in IMNM controls.

Conclusion: An abnormal NVC may serve as a clue to support the diagnosis of SM in anti-SRP or anti-HMGCR negative patients presenting with histologic features of IMNM.

Disclosure: O. Landon-Cardinal, None; **V. Leclair**, None; **Y. Troyanov**, None; **M. Koenig**, None; **A. Meyer**, None; **S. Hoa**, None; **J. Bourré-Tessier**, None; **I. Ferdinand**, Pfizer Canada, 5, 8, AbbVie Canada, 5, Amgen Canada, 5, 8, Novartis Canada, 5; **J. Karamchandani**, None; **E. O'Ferrall**, Sanofi Genzyme, 2, Acceleron, 2, Biogen, 8; **M. Satoh**, None; **M. Fritzler**, Inova Diagnostics Inc, 5, 8, Werfen International, 5, 8; **B. Ellezam**, None; **J. Senécal**, None; **M. Hudson**, None; **G. Gyger**, None.

Abstract Number: 1070

Scleromyositis Is Associated with Distinct Muscle Vasculopathic Features

Océane Landon-Cardinal[1], Valérie Leclair[2], Yves Troyanov[3], Alain Meyer[4], Sabrina Hoa[1], Josiane Bourré-Tessier[1], Valérie Nadon[5], Julie Drouin[6], Jason Karamchandani[7], Erin O'Ferrall[8], Minoru Satoh[9], Marvin Fritzler[10], Jean-Luc Senécal[1], Marie Hudson[2] and Benjamin Ellezam[11], [1]Division of Rheumatology, Centre hospitalier de l'Université de Montréal, Montréal, QC, Canada, [2]Division of Rheumatology, Jewish General Hospital, Montréal, QC, Canada, [3]Division of Rheumatology, Hôpital du Sacré-Coeur, Montréal, QC, Canada, [4]Service de rhumatologie et Centre de références des maladies autoimmunes rares, Hôpitaux universitaires de Strasbourg, Strasbourg, Alsace, France, [5]Division of Rheumatology, Hôpital Notre-Dame, Montreal, Québec, Canada, Montréal, QC, Canada, [6]Division of Rheumatology, Centre hospitalier régional de Trois-Rivières, Trois-Rivières, QC, Canada, [7]Department of Pathology, Montreal Neurological Institute and Hospital, Montreal, QC, Canada, [8]Department of Neurology and Neurosurgery, Montreal Neurological Institute and Hospital, Montreal, QC, Canada, [9]Department of Clinical Nursing, University of Occupational and Environmental Health, Kitakyushu, Japan, [10]Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, [11]Division of Pathology, Centre hospitalier universitaire Sainte-Justine, Montréal, QC, Canada

SESSION INFORMATION
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Session Title: Muscle Biology, Myositis & Myopathies Poster
Session Type: Poster Session C
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Background/Purpose: Scleromyositis (SM) is an emerging subgroup of autoimmune myositis (AIM) associated with features of systemic sclerosis (SSc). Muscle biopsy studies are sparse and have suggested that SM is heterogeneous. Whether there is a distinct pathological signature remains uncertain. SSc is associated with a prominent vasculopathy. The aim of this study was to explore whether a distinct vasculopathic pattern is associated with SM as compared to other AIM.

Methods: A systematic review of SM muscle biopsies and AIM controls was performed by 2 reviewers. In the absence of gold standard, SM clinical diagnosis was based on expert opinion (consensus of ≥2 experts). Reviewers were blinded to the clinical diagnosis/serological status and used a pre-specified protocol including all stains recommended by the ENMC for the pathological diagnosis of AIM, and collagen IV immunofluorescence for endomysial capillary abnormalities (dropout and/or mural thickening and/or luminal dilation). Examination of capillaries was also done by electron microscopy (EM) for the presence of marked basement membrane (BM) reduplication (≥5 layers) and endothelial abnormalities.

Results: 31 SM cases and 18 AIM controls (4 dermatomyositis, 5 immune-mediated necrotizing myopathies (IMNM, all anti-HMGCR+), 5 inclusion body myositis (IBM), and 4 antisynthetase syndrome) were included. SM patients were predominantly females (86%) and mean age at muscle biopsy was 55.6±13.1 years. Myopathic features at presentation were: proximal weakness in 86% of patients and mean CK elevation of 1596±1510 IU/L. 71% of patients fulfilled the ACR/EULAR SSc criteria at myositis diagnosis. SSc features leading to the diagnosis of SM in the remaining 8 patients included: Raynaud phenomenon (n=7), positive ANAs and/or SSc-associated autoantibodies (n=7), interstitial lung disease (n=5), SSc nailfold capillaroscopy (n=3), sclerodactyly (n=1) and puffy fingers (n=1). Capillary BM reduplication was observed in 68% (n=21) of SM muscle biopsies compared to 11% of AIM controls (mildly observed in 2 IBM) ($p < 0.001$). Marked capillary BM reduplication was only observed in SM biopsies (55%, n=17). Of the SM patients without BM reduplication, all but one presented capillary abnormalities on immunofluorescence and/or endothelial abnormalities on EM. Using the ENMC pathological criteria for AIM, our SM cases would have been most frequently classified as IMNM (32%) or non-specific myositis (32%). In the subset of SM cases with an IMNM-like phenotype, marked BM reduplication and/or other ultrastructural capillary abnormalities were observed in all SM cases and none of the IMNM controls. No cases of dermatomyositis showed marked BM reduplication.

Conclusion: SM is associated with endomysial capillary BM reduplication, a distinct ultrastructural vasculopathic feature compared to other AIM. SM is a frequent mimicker of IMNM on muscle biopsy and should be ruled out by ultrastructural examination of capillaries in patients negative for anti-SRP or anti-HMGCR autoantibodies. The identification of marked BM reduplication may improve early identification of SM, especially in those presenting without SSc skin involvement.

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Abstract Number: 1071

Characteristics of Anti-Transcription Intermediary Factor 1-gamma Autoantibody Positive Dermatomyositis Patients in Singapore

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Background/Purpose: Anti-transcription intermediary factor 1-gamma autoantibody (anti-TIF-1y Ab) associated dermatomyositis (DM) is strongly associated with the occurrence of malignancies. Patients may develop cancers prior to, concurrent with, or at a period after the diagnosis of DM. Close surveillance for cancer has been advocated for this group to allow early detection and cure of the underlying malignancy. The objective of this study was to determine the clinical profile and outcomes of anti-TIF-1y positive DM patients in Singapore.

Methods: A chart review was undertaken of 79 DM patients with positive myositis specific antibodies diagnosed between January 2015 and July 2019 at a major tertiary hospital in Singapore. All patients included fulfilled the Bohan/

Table : Demographics and clinical characteristics of anti-TIF1- γ Ab-positive and negative DM groups

	Total Cohort N=79	Anti-TIF1-γ Ab positive N=33	Anti-TIF1- γ Ab negative N=46
Female, n (%)	51 (64.6%)	23 (69.7%)	28 (60.9%)
Smokers, n (%)	10 (12.7%)	5 (15.2%)	5 (10.9%)
Age of DM onset, years, median (range)	58 (7-96)	61 (29-96)	56 (7-76)
Patients with cancer, total, n (%)	23 (29.1%)	19 (57.6%)	4 (8.7%)
Sequence of DM and cancer diagnosis, patients with cancer			
DM diagnosed first, subsequent cancer, n (%)	7 (30.4%)	5 (26.4%)	2 (50%)
Cancer diagnosed first, subsequent DM, n (%)	7 (30.4%)	7 (36.8%)	0 (0.0%)
Cancer and DM diagnosed at same time, n (%)	9 (39.2%)	7 (36.8%)	2 (50%)
Time from DM to cancer onset, months, median (range)	4 (1-22)	4 (1-22)	3 (2-4)
Time from cancer to DM onset, months, median (range)	12 (288-6)	12 (288-6)	n/a
Patient outcomes, with cancer			
Died, n (%)	8 (34.8%)	7 (36.8%)	1 (25.0%)
Improved and stable, n (%)	14 (60.9%)	11 (57.9%)	3 (75.0%)
Relapse, n (%)	1 (4.3%)	1 (5.3%)	0 (0.0%)
Sites of cancer			
Nasopharyngeal (NPC), n (%)	7 (30.4%)	6 (31.6%)	1 (25.0%)
Breast, n (%)	5 (21.7%)	4 (21.1%)	1 (25.0%)
Bowel (intestine), n (%)	3 (13.0%)	3 (15.8%)	0 (0.0%)
Lung, n (%)	2 (8.7%)	2 (10.5%)	0 (0.0%)
Cervical/Ovarian, n (%)	1 (4.3%)	1 (5.3%)	0 (0.0%)
Lymphoma, n (%)	1 (4.3%)	1 (5.3%)	0 (0.0%)
Thyroid, n (%)	1 (4.3%)	1 (5.3%)	0 (0.0%)
Kidney, n (%)	1 (4.3%)	1 (5.3%)	0 (0.0%)
Prostate, n (%)	1 (4.3%)	0 (0.0%)	1 (25.0%)

Peter criteria for probable/ definite DM and had International Myositis Classification Criteria scores of at least 55% consistent with probable idiopathic inflammatory DM.

Results: Of the 79 patients diagnosed with DM, 33 were found to be anti-TIF-1y Ab positive. In the anti-TIF-1y Ab positive group, 69.7% were female, 15.2% were smokers, and the median age of DM diagnosis was 61 years. A higher proportion of the anti-TIF-1y Ab positive group (57.6%) developed cancer compared to the anti-TIF-1y Ab negative group (8.7%).

The median time interval to diagnosis of malignancy in the cancer associated anti-TIF-1y Ab positive DM group was 12 months prior to or 12 months following the onset of DM. In the cancer associated anti-TIF-1y Ab positive group, DM was diagnosed before cancer in 26.3 % of patients, cancer before DM in 36.8 % and both cancer and DM diagnosed at the same time in 36.8 %. In those anti-TIF-1y Ab negative DM patients that developed cancer, the cancer was either diagnosed prior or concurrently with DM.

Nasopharyngeal carcinoma (NPC) was the commonest cancer (31.6%) in the anti-TIF-1y Ab positive DM group, followed by breast (21.1%), bowel (15.8%), lung (10.5%), cervical/ovarian (5.3%), lymphoma (5.3%), thyroid (5.3%), and kidney (5.3%). Of these patients 35% died, 60% improved and remained sTable, and 5% sustained a relapse. Of those anti-TIF-1y Ab positive NPC, 66.6% presented with advanced stage (Stage III or more) and all had undifferentiated histology.

Conclusion: Our results show the strong association of anti-TIF-1y Ab DM and increased risk of malignancy, particularly nasopharyngeal cancer in our Singaporean population. The cancer associated anti-TIF-1y Ab DM patients developed cancer within a year prior to or following the onset of DM and had a worse prognosis than the anti-TIF-1y Ab negative group. The clinical profile revealed in this review will be useful in guiding the targeted cancer surveillance needed for this group of patients to reduce morbidity and mortality.

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Sexual Health Impairment in 62 Female Patients with Idiopathic Inflammatory Myopathies

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Questionnaire: score range (meaning)	IIM (n=62)	HC (n=62)	p-value
FSFI: Female Sexual Function Index: 2(worst)-36(best)	18.2 (3.2-28.5)	28.4 (14.4-32.1)	p=0.006
BISF-W: Brief Index of Sexual Function for Women: -16(worst)-75(best)	18.6 (2.7-32.3)	34.0 (8.0-44.7)	p=0.004
SQoL-F: Sexual Quality of Life Questionnaire – Female: 0(worst)-100(best)	60.0 (41.4-83.6)	86.7 (70.8-95.6)	p<0.0001
PISQ–12: Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form: 0(best)-48(worst)	14.5 (9.0-18.0)	8.0 (5.0-12.0)	p<0.0001
PFIQ7: Pelvic Floor Impact Questionnaire – short form 7: 0(best)-300(worst)	4.8 (0.0-23.8)	0.0 (0.0-4.8)	p=0.052
SFQ28: Sexual Function Questionnaire – 28, subscale pain: 2 (worst)-15 (best)	12.0 (10.0-15.0)	15.0 (12.3-15.0)	p=0.005
SFQ28: Sexual Function Questionnaire – 28, subscale enjoyment: 6 (worst)-30 (best)	18.5 (14.0-22.0)	23.0 (18.3-25.0)	p=0.026
Questionnaire: score range (meaning)	**Sexually active IIM (n=33)**	**Sexually active HC (n=43)**	**p-value**
FSFI: Female Sexual Function Index: 2(worst)-36(best)	27.4 (19.7-32.5)	31.3 (27.4-32.6)	p=0.029
BISF-W: Brief Index of Sexual Function for Women: -16(worst)-75(best)	29.8 (20.5-37.5)	39.5 (33.3-46.2)	p=0.002
SQoL-F: Sexual Quality of Life Questionnaire – Female: 0(worst)-100(best)	78.4 (47.2-89.4)	93.3 (81.1-96.7)	p=0.0005
PISQ–12: Pelvic Organ Prolapse/Urinary Incontinence Sexual Questionnaire short form: 0(best)-48(worst)	11.0 (8.0-14.8)	7.0 (5.0-12.0)	p=0.0003
SFQ28: Sexual Function Questionnaire – 28, subscale pain: 2 (worst)-15 (best)	12.5 (10.0-15.0)	15.0 (13.0-15.0)	p=0.011
SFQ28: Sexual Function Questionnaire – 28, subscale enjoyment: 6 (worst)-30 (best)	19.0 (14.5-23.5)	23.0 (19.0-25.0)	p=0.023

Table. Sexual function and pelvic floor function in women with IIM and healthy controls

Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of rare diseases characterized by chronic muscle inflammation and multiple organ involvement. These serious clinical manifestations can be associated with significant impairment of quality of life including sexual life. The aim of this study was to assess sexual functioning in female IIM patients compared to age-/sex-matched healthy controls (HC) and to determine the association between sexual health impairment and physical and psychological aspects of the disease.

Methods: In total, 62 women (45 currently have a partner) with IIM [mean age: 53.1, disease duration: 5.2 years, dermatomyositis (DM, 29)/ polymyositis (PM, 27)/ necrotizing myopathy (IMNM, 5)/ inclusion body myositis (IBM, 1)], who fulfilled the Bohan/Peter 1975 criteria for DM/PM, or ENMC criteria for IMNM or IBM, and 62 healthy controls (HC) (51 currently have a partner, mean age: 53.1) without rheumatic diseases filled in 11 well-established and validated questionnaires assessing sexual function (FSFI, SFQ28, BISF-W), quality of sexual life (SQoL-F), pelvic floor function (PFIQ-7, PISQ-12), fatigue [Fatigue impact scale (FIS)], physical activity [Human activity profile (HAP)], depression [Beck's depression inventory II (BDI-II)], quality of life [36-item Short form survey (SF-36)], and disability [Health assessment questionnaire (HAQ)]. A routine laboratory testing was performed. Data are presented as median (IQR).

Results: Patients with IIMs reported significantly greater prevalence and severity of sexual dysfunction (FSFI, BISF-W, SFQ28, SQoL-F) and pelvic floor dysfunction (PISQ-12) compared to HC (Table). When we analyzed only sexually active patients compared to sexually active HC, the difference between patients and HC remained significant (Table). The prevalence of sexual dysfunction in patients with IIM according to the FSFI cut-off score was 59%. Worse scores in IIM patients were associated with greater muscle weakness of m. gluteus maximus [MMT8: FSFI (r=0.289, p=0.035), PFIQ-7 (r=-0.407, p=0.003)], m. gluteus medius [MMT8: PFIQ-7 (r=-0.381, p=0.005)], greater fatigue [FIF: FSFI arousal subscale (r=-0.343, p=0.007), SQoL-F (r=-0.412, p=0.003)], severer depression [BDI-II: SQoL-F (r=-

0.459, p=0.0007)], increased disability and deteriorated quality of life [HAQ: FSFI (r=-0.436, p=0.005); SF-36 D1: BISF-W (0.449, p=0.0005), SF-36 D5: SQoL-F (0.428, p=0.002], and worse ability to perform physical activities [HAP: FSFI (r=0.403, p=0.001), SQoL-F (r=0.368, p=0.007)]. We did not observe any associations with disease duration, current prednisone dose, or serum levels of muscle enzymes. Furthermore, no significant differences between DM and PM were found.

Conclusion: Women with IIM reported significantly impaired sexual function and pelvic floor function compared to healthy females with identical age. The prevalence of sexual dysfunction in IIM patients was 59%. Worse scores in IIM were associated with muscle weakness, decreased physical activity, greater fatigue, severer depression, increased disability and deteriorated quality of life.

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Anti Melanoma Differentiation-associated Protein Gene 5 Antibody Titer Monitoring Is a Useful Indicator for Early Detection of Recurrence in Rapidly Progressive Interstitial Lung Disease Associated with Dermatomyositis

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Background/Purpose: Anti melanoma differentiation-associated gene 5 (MDA5) antibody (Ab) positive dermatomyositis (DM) often complicates rapidly progressive interstitial lung disease (RP-ILD), which shows fatal prognosis at early phase from the onset in spite of intensive immunosuppressive therapies. Although relapse of RP-ILD after remission with initial treatment is relatively rare in this condition, its long-term clinical course still remains unclear. Therefore, we investigated clinical characteristics and possible indicators for early detection of recurrence in patients with anti-MDA5 Ab positive DM and RP-ILD.

Methods: Adult Japanese DM patients who were treated at Tokai University Hospital from 2012 to 2019 were screened. Anti-MDA5 Ab was identified by immunoprecipitation with [35S] methionine-labeled HeLa cells, and anti-MDA5 Ab titers were measured using anti-MDA5 enzyme-linked immunoabsorbent assay. Patients who showed the exacerbation of RP-ILD and/or DM symptom after stabilized for more than a year were considered as recurrence.

Clinical and immunological features were retrospectively collected. Statistical analyses were performed using the Fisher's exact test.

Results: Thirty patients were diagnosed as DM with anti-MDA5 Ab. All had ILD and required hospitalization for intensive treatment. Seventeen of 30 (57%) achieved an improvement in respiratory function in response to their initial treatment and were discharged from the hospital. During their disease courses in outpatient care, 3 (18%) of 17 patients experienced recurrence and required re-hospitalization. Among 3 relapsed cases, 2 (67%) showed exacerbation of RP-ILD and remaining 1 (33%) revealed muscle weakness. Although all 3 relapsed patients showed anti-MDA5 Ab titer elevation at the time of relapse, no increase in the titer was seen in 14 non-relapsed patients (100% vs. 0%, P=0.002) Interestingly, marked increase of anti-MDA5 Ab titers preceded appearance of recurrent symptoms in all relapsed cases, whereas ferritin levels were within normal range at the recurrence (38-120 ng/dl) and gradually increased after readmission.

Conclusion: These results suggest that continuous measurement of anti-MDA5 Ab titer as well as careful observation of physical and imaging findings is crucial for monitoring disease activity and early detection of relapse in patients with anti-MDA5 Ab positive DM.

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Abstract Number: 1074

A Novel Autoantibody Recognizing a 65-kDa Protein Is Associated with Scleromyositis with Head Drop and/or Bent Spine

Karel Venne[1], Valérie Leclair[2], Julie D'Aoust[1], Océane Landon-Cardinal[3], Alexandra Albert[4], Julie Beauchemin[5], Denis Brunet[6], Lucie Roy[7], Benjamin Ellezam[8], Jason Karamchandani[9], Rami Massie[10], Erin O'Ferrall[10], Alain Meyer[11], Yves Troyanov[12], Minoru Satoh[13], Marvin Fritzler[14] and Marie Hudson[2], [1]Division of Rheumatology, Rheumatology Fellow, McGill University,, Montreal, QC, Canada, [2]Division of Rheumatology, Jewish General Hospital, Montréal, QC, Canada, [3]Division of Rheumatology, Centre hospitalier de l'Université de Montréal, Montréal, QC, Canada, [4]Division of Rheumatology, Centre Hospitalier de l'Université Laval, Québec, QC, Canada, [5]Division of Rheumatology, Hôpital Charles-Lemoyne, Longueuil, QC, Canada, [6]Division of Neurology, Centre Hospitalier de l'Université Laval, Quebec, QC, Canada, [7]Division of Rheumatology, CIUSSS du Saguenay Lac-Saint-Jean, Saguenay, Canada, [8]Division of Pathology, CHU Sainte-Justine, Montreal, QC, Canada, [9]Department of Pathology, Montreal Neurological Institute and Hospital, Montreal, QC, Canada, [10]Department of Neurology and Neurosurgery, Montreal Neurological Institute and Hospital, Montreal, QC, Canada, [11]Service de rhumatologie et Centre de références des maladies autoimmunes rares, Hôpitaux universitaires de Strasbourg, Strasbourg, France, [12]Division of Rheumatology, Hôpital du Sacré-Coeur, Montréal, QC, Canada, [13]Department of Clinical Nursing, University of Occupational and Environmental Health, Kitakyushu, Japan, [14]Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada

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Background/Purpose: Scleromyositis (SM) is an emerging subgroup of autoimmune myositis associated with features of systemic sclerosis (SSc). There is a paucity of data on scleromyositis associated with head drop and/or bent spine. The aim of this study was therefore to describe the clinical and serological features of scleromyositis patients presenting with head drop and/or bent spine as the dominant myopathic feature.

Table 1. Comparison of scleromyositis subjects based on the presence and the absence of dropped head and/or bent spine

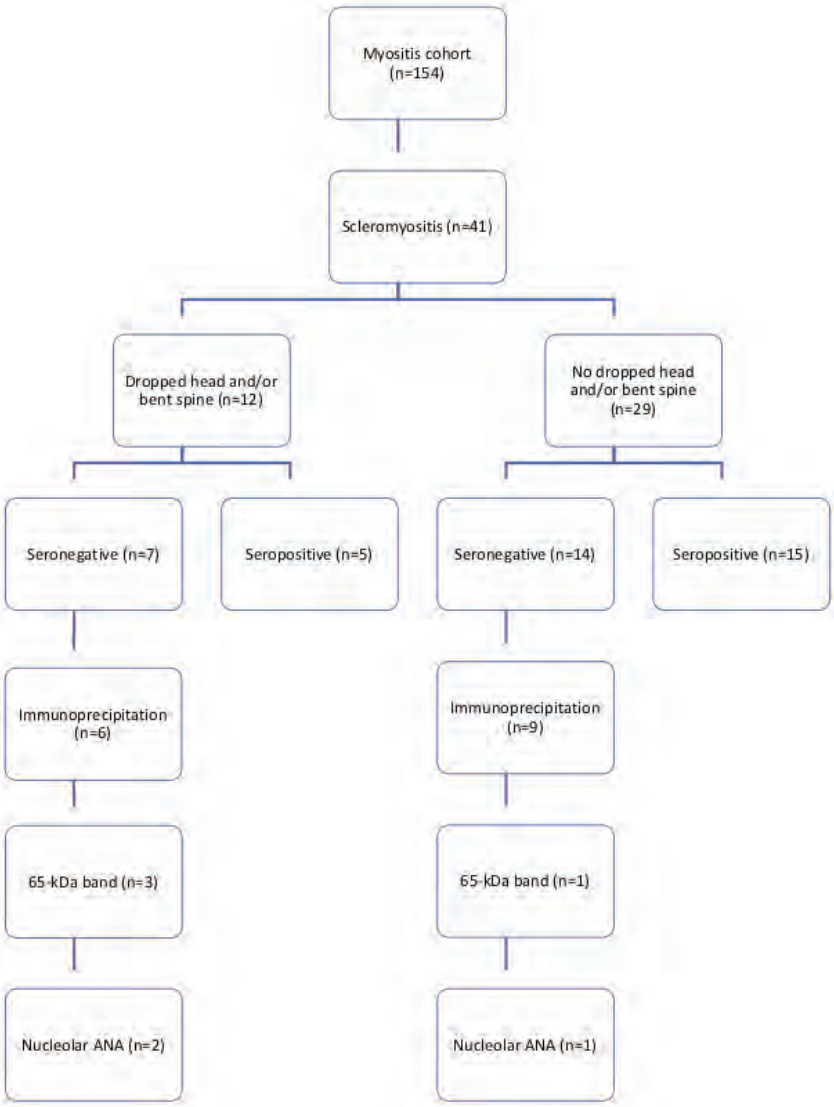
	Dropped head and/or bent spine (n = 12)	**No** dropped head and/or bent spine **(n = 29)**
Female n,%	11 (92)	22 (76)
Age at diagnosis mean, range	55 (38-79)	55 (20-81)
Autoantibody profiles		
Centromere	0	1 (3)
Topoisomerase	0	0
RNA polymerase III	2 (17)	2 (7)
Th/To	1 (8)	0
Fibrillarin	0	2 (7)
PM/Scl	2 (17)	7 (24)
Ku	0	0
U1-ribonucleoprotein (RNP)	0	4 (14)
Ro52	2 (17)	7 (24)
Skin thickening		
Diffuse	5 (42)	9 (31)
Limited	5 (42)	8 (28)
Sine	2 (17)	12 (41)
Raynaud	9 (75)	26 (90)
Pitting scars	1/10 (10)	4/27 (15)
Digital ulcers	1/11 (9)	6/28 (21)
Telangiectasias	8 (67)	9 (31)
Abnormal nailfold capillaroscopy	5/5	18/23 (78)
Calcinosis	1 (8)	3 (10)
Muscle weakness		
Proximal weakness	11 (92)	24 (83)
Distal weakness	8 (67)	14/28 (50)
Diaphragmatic weakness	1 (8)	1 (3)
Dysphagia	4 (33)	13 (45)
Classic dermatomyositis rash	2 (17)	7 (24)
Mechanics' hands	0	1 (3)
Elevated creatine kinase	8 (67)	26 (90)
Peak creatine kinase median, range	283 (84-1488)	877 (48-5075)
Myopathic electromyography	9/10 (90)	23/25 (92)
Arthritis	2 (17)	9 (31)
Interstitial lung disease on HRCT	1 (8)	16 (55)
Pulmonary hypertension*	0	1 (3)
Trigeminal neuropathy	1 (8)	2 (7)

Abbreviations: HRCT, high resolution computed tomography; PM/Scl, antibodies to polymyositis/scleroderma exosome antigen; Th/To, mitochondrial RNA processing (MRP) complex (note LIA detects only anti-hPOP1).

* Right heart catheterization was available for 7 patients of which one had pulmonary arterial hypertension. The rest of the cohort was screened by cardiac echocardiography and none had signs of pulmonary hypertension.

Methods: All patients with a diagnosis of SM were identified from a research cohort of 154 autoimmune myositis patients. In the absence of a gold standard, the clinical diagnosis of SM was based on expert opinion (consensus of ≥2 experts). SM patients were grouped according to the presence or absence of dropped head and/or bent spine. Clinical and serological data were collected and stored using a standardized protocol. Sera from patients with no known SSc-specific (anti-centromere (ACA), -topoisomerase I (Scl-70) (ATA), RNA polymerase III (RNApol), -Th/To, -fibrillarin) or SSc-associated (anti-PM/Scl), -Ku, -U1RNP) were tested by immunoprecipitation (IP) of ^{35}S-methionine-labeled cell extracts. Descriptive statistics were used to summarize the data.

Figure1. Flowchart



Results: Forty-one SM subjects were identified (Table 1). The majority were female (80%) and mean age at diagnosis was 55 years (range: 20-81). Most of the SM subjects had Raynaud's phenomenon (85%) and all had abnormal nailfold videocapillaroscopies. Although the majority had proximal weakness (85%), more than 50% also had distal weakness. Head drop and/or bent spine was the dominant myopathic feature in 12 (29%) SM patients. In those with head drop and/or bent spine compared to those without, SSc skin involvement was more common (84% vs 59%), interstitial lung disease (ILD) was less frequent (8% vs 55%), and peak creatine kinase level was lower (median 283 IU/L (range: 84-1488) vs 877 IU/L (range: 48-5075)). Only 5 of 12 patients (42%) with dropped head and/or bent spine had SSc-specific or -associated antibodies, including -RNApol III (n=2), Th/To (n=1) and PM/Scl (n=2). Among patients without known antibodies, IP was performed in 15 subjects: 6 of 7 subjects with and 9 of 14 subjects without dropped head and/or bent spine (Figure 1). Among these 15 patients, a 65- kiloDalton (kDa) band was identified in 3 subjects with, and 1 subject without, dropped head and/or bent spine. Three of the four patients with a 65-kDa band had a nucleolar pattern on HEp-2 indirect immunofluorescence staining. The subjects with a 65-kDa band had limited

skin disease (3/4) and dysphagia (3/4) but no ILD or arthritis. The subject with a 65-kDa band without dropped head and/or bent spine had a nucleolar IIF and predominantly distal weakness.

Conclusion: Dropped head and/or bent spine was a dominant myopathic feature in a third of our scleromyositis patients. An autoantibody recognizing a 65-kDa protein represents a novel autoantibody associated with scleromyositis presenting with dropped head and/or bent spine. Further studies to identify the 65-kDa autoantibody target are underway.

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Diagnostic Utility of Myositis Antibodies in HyperCKemia: A University Affiliated Single Center Retrospective Study

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Session Time: 9:00AM–11:00AM

Background/Purpose: Myositis specific and associated autoantibodies are now being used more frequently in the diagnosis of idiopathic inflammatory myositis. However there is a no study looking at the utility of antibody testing in subjects presenting with HyperCKemia during routine clinical practice. We aimed to determine the usefulness of antibody testing in subjects with both symptomatic and asymptomatic hyperCKemia referred to a university affiliated practice.

Methods: This was a retrospective chart review of electronic health records of subjects in whom antibody testing was performed between January 2013 till December 2018. The autoantibody testing were performed using myomarker panel 3® (Anti-Jo-1 Ab, Anti-Mi-2 Ab, Anti-PL-12 Ab, Anti-PL-7 Ab, Anti-EJ Ab, Anti-OJ Ab, Anti-SRP Ab, Anti-Ku Ab, Anti-U2 RNP, Anti-PM/Scl-100 Ab, Anti-MDA5 Ab, Anti-NXP2 Ab, Anti-TIF-1γ Ab, Anti-SSA 52 kD IgG Ab, Anti-U1 RNP Ab, Anti-Fibrillarin U3 RNP Ab), [RDL Reference Laboratory, Los Angeles, CA], Anti-cN-1A (NT5c1A)and Anti-HMGCR Ab IgG . Baseline demographics, reason for referral, presenting symptoms, muscle enzymes (CPK, Aldolase, ALT, AST), autoantibody results, electromyography and nerve conduction studies (EMG & NCS), muscle biopsies and final clinical diagnosis were extracted from the records.

Only HyperCKemia with and without symptoms were considered for the study. We used Stat view version 5.01 (SAS Institute Inc. Cary, NC) for analysis

Results: There were 138 subjects for whom antibody testing were performed. 47 subjects met our inclusion criteria. 9 subjects were excluded from final analysis as their final diagnosis was not classified. 38 subjects included in final analysis. Baseline demographics, presenting symptoms and muscle enzyme levels are presented in Table 1. Results

Table 1. Baseline Characteristics of study population(N = 47)

Age (Mean ± SD)	58 ± 12 years
Gender (%)	
Male	32 (68%)
Female	15 (32%)
Ethnicity (%)	
Caucasian	22 (47%)
African American	20 (43%)
Other	5 (2%)
Asymptomatic hyperCKemia	12(26%)
*Symptomatic w/o weakness	18(38%)
*Symptomatic w/ weakness	15 (32%)
CPK (Mean ± SD)	1147 ± 1245 (24-204 U/L)
AST (Mean ± SD)	44 ±23 (0-40 IU/L)
ALT (Mean ± SD)	47 ± 45(0-44 IU/L)
Aldolase (Mean ± SD)	9.5 (<8 U/L)

Symptomatic = Myalgia, muscle cramps, decrease exercise tolerance, unsteady gait, paresthesia, muscle stiffness.

Table 1. Baseline Characteristics of study population(N = 47)

of EMG & NCS, myositis antibody and final clinical diagnosis details are presented in Table 2. The relationship between CPK, final diagnosis and myositis antibodies are shown in Figure 1. Subjects with moderate elevation of CPK and positive antibody are more likely to have polymyositis. Subjects with mild elevation of CPK and positive antibody are more likely to have inclusion body myositis. Negative antibody subjects are more likely to be diagnosed with idiopathic hyperCKemia and metabolic myopathy.

Antibody positive was statistically associated with polymyositis, inclusion body myositis with a chi square of 25.94 with p value 0.002 with 9 degree of freedom.

Antibody positivity was statistically associated with inflammatory myositis on muscle biopsy with a chi square of 16.37 p value 0.01 with 6 degree of freedom.

Metabolic myopathy will likely have negative myositis antibody test.

Conclusion: Subjects presenting with asymptomatic or symptomatic hyperCKemia and having positive antibody, are more likely to have positive muscle biopsy and final diagnosis of inflammatory myositis. Therefore, performing initial antibody testing in such cases would help clinicians in pursuing these cases with EMG & muscle biopsy.

Table 2. Muscle biopsy, EMG & NCS, Myositis antibody and Final clinical diagnosis

Muscle biopsy (N=29)	
Normal biopsy	1 (3 %)
Neurogenic atrophy	6 (21%)
necrotizing myopathy without inflammation	1(3%)
Inclusion body myositis	5 (17%)
Metabolic myopathy	4 (14%)
Polymyositis	5 (17%)
Non diagnostic	7 (24%)
Electromyography/Nerve conduction study (N=38)	
Brief polyphasic motor units	17 (44%)
Myopathy	9 (24%)
Myositis antibody positive (N=47)	**12 (26%)**
Anti-cN-1A (NT5c1A) IBM (N=15)	4 (27%)
Anti-HMGCR Ab IgG (N=19)	1 (5%)
Anti-Jo-1 Ab (N=42)	2 (5%)
Anti-Ku Ab(N=42)	1(2%)
Anti-TIF-1γ Ab(N=42)	1(2%)
Anti-SSA 52 kD IgG Ab(N=42)	4(10%)
Anti-PM/Scl-100 Ab(N=42)	2(5%)
Anti-U1 RNP Ab(N=42)	2(5%)
Anti-U2 RNP(N=42)	1(2%)
Final Clinical Diagnosis (N =47)	
Idiopathic HyperCKemia	16 (34%)
Polymyositis	7 (15%)
Inclusion body myositis	4 (9%)
Metabolic myopathy	4 (9%)
Not classified	9 (19%)
Others*	7 (15%)

(*IgM Monoclonal gammopathy of unknown significance, chronic inflammatory demyelinating polyneuropathy, Rhabdomyolysis, HIV infection/Highly active antiretroviral therapy (HAART) related, Movement disorder/amyotrophic lateral sclerosis)

Table 2. Muscle biopsy, EMG & NCS, Myositis antibody and Final clinical diagnosis

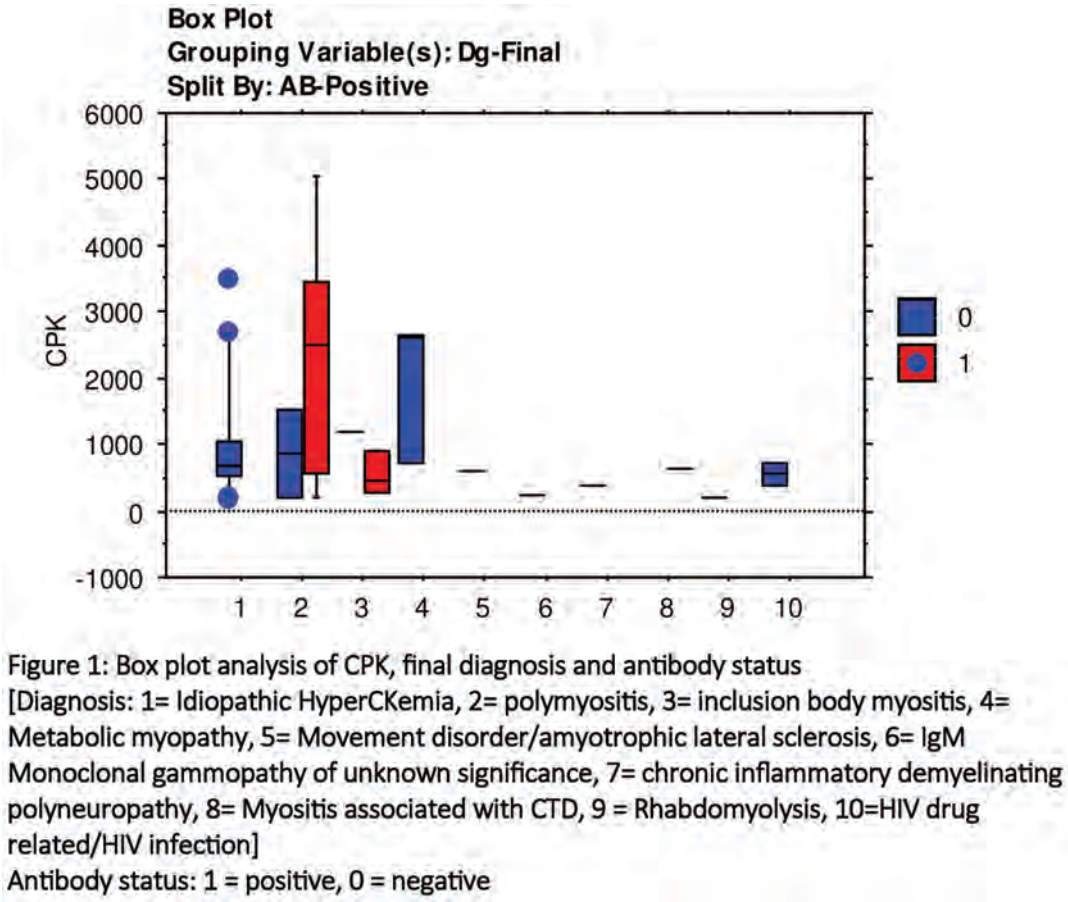

Figure 1. Box plot analysis of CPK, final diagnosis and antibody status

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Disclosure: S. Gupta, None; **D. Pattanaik**, None; **T. Bertorini**, None; **A. Afreire**, None.

Abstract Number: 1076

Anti-Jo1 Antibody Quantification Serve as a Prognostic Factor in Anti-synthetase Syndrom

Lois Bolko[1], Kevin Didier[2], Jean-Hugues Salmon[1], Makoto Miyara[3], Segolene Toquet[2], Amelie Servettaz[2], Yves Allenbach[3], Olivier Benveniste[4] and Baptiste Hervier[5], [1]Maison Blanche Hospital, Reims, Champagne-Ardenne, France, [2]Robert Debre Hospital, Reims, Champagne-Ardenne, France, [3]Sorbonne Université, Paris, Ile-de-France, France, [4]Sorbonne Université, paris, France, [5]Saint-Louis Hospital, Paris, Ile-de-France, France

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Muscle Biology, Myositis & Myopathies Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-Synthetase Syndrome (ASyS) is a rare systemic autoimmune disease defined by a combination of pulmonary, muscle, joint, and skin manifestations and the presence of antibodies (Aab) targeting a tRNA t-synthetase. The anti-Jo1 (Histidyl-t-RNA-synthetase) antibody is the most commonly found and can be quantified

by Luminex® technology. The aim of this study was therefore to evaluate the value of indirect quantification by LUMINEX® technology of anti-Jo1 Aab as a prognostic factor and biomarker of activity.

Methods: We conduct a retrospective, bi-centric study beetween the Pitié Salpêtrière Hospitals and Reims University Hospital Centre. ASyS diagnostic was defined by the presence of at least 2 clinical manifestations associated with this Aab.

Severity was defined by the need for mechanical intubation-ventilation, hypoxemia < 60 mmHg PaO2, the presence of proven cardiac injury, severe muscle injury with bed confinement, diaphragmatic injury, or the presence of swallowing difficulties. Activity assessment was rated using the tools recommended by IMACS and ACR/EULAR and was represented on a numerical scale summarizing the practitioner's overall assessment. Quantification of Anti-Jo1 Aab was performed using a Luminex® approach (Euroline Myositis Profile 3: Euroimmun).

Results: Among the 99 patients followed for SAS, 27 were excluded for lack of information. Patients from sub-Saharan Africa and the Caribbean were more represented in the group with a complication at diagnosis (23% vs. 9%, p=0.04). The anti-Jo1 Aab titer (209 [176.8-257.3] vs 128 [89.5-169]; p< 0.001), as well as the CK level (3350 [1486-15000] vs 1078 [246-4125] p< 0.05) were higher in the severe event group. For the 37 patients whose titer was available at diagnosis, one or more controls were available for 24 patients. The median titre of Jo1 antibody was higher at diagnosis compared to the corresponding assay at the time of clinical remission (171.5 [113.3-232.3] vs 137 [90-160.3] p=0.02). The maximum anti-Jo1 antibody titer was significantly higher in the patient with severe event than the no severe event group (229.5 [182-272.3] vs 149.5 [118.8-184.3] p< 0.001). The ROC curve produced had an area under the curve of 0.81 IC95(0.71-0.91) p< 0.001. A value of anti-Jo1 Ac > 186 had a sensitivity of 74% and a specificity of 79% to predict the risk of a serious event.

Of the 33 patients with a titer > 186, 70% had a serious event in follow-up, of which 50%, the vast majority, occurred within the first 30 days of follow-up. Conversely, only 21% of patients with a titer < 186 had an event during follow-up.

Conclusion: Indirect quantification of Ac anti-Jo1 by fluorescence intensity using the Luminex technology was correlated with the occurrence of serious events in the monitoring of ASyS. It was a reliable, reproducible and automated technique that could be used to assist in patient follow-up and treatment monitoring. The validation of these results on independent cohorts is nevertheless necessary.

Disclosure: L. Bolko, None; **K. Didier**, None; **J. Salmon**, None; **M. Miyara**, None; **S. Toquet**, None; **A. Servettaz**, None; **Y. Allenbach**, None; **O. Benveniste**, None; **B. Hervier**, None.

Abstract Number: 1077

Glucagon-like Peptide-1 Receptor Agonist Suppresses Muscle Inflammation and Muscle Fiber Death, and Ameliorates Muscle Weakness in Experimental Polymyositis

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SESSION INFORMATION
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Session Title: Muscle Biology, Myositis & Myopathies Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoids (GC) are the cornerstone of the treatment for polymyositis (PM). However, the treatment with GC causes GC-induced myopathy, which further deteriorates the muscle weakness. Therefore, new therapeutic strategy that not only suppresses muscle inflammation but also improves muscle strength is needed. Glucagon-like peptide-1 receptor (GLP-1R) agonists, which have been developed as an anti-diabetic therapy, have pleiotropic actions including anti-inflammatory effects, suppression of muscle wasting, and inhibition of cell death. We hypothesized that GLP-1R agonists have beneficial effects on PM to recover muscle strength and to suppress muscle inflammation. The aim of this study is to examine the effect of a GLP-1R agonist on in vitro and in vivo models of PM.

Methods: Muscle specimens of PM patients and C protein-induced myositis (CIM), a murine model of polymyositis, were examined with immunohistological staining for the expression of GLP-1R. The effect of PF1801 (ImmunoForge, Seaul, South Korea), a GLP-1R agonist, on CIM was examined in monotherapy (5 mg/kg body weight (BW)/day) or in combination with prednisolone (PSL, 20 mg/kg BW/day). The levels of HMGB1, TNF-α and IL-6 in the serum and the muscle were measured by ELISA. C2C12-derived myotubes were treated with FAS ligand (FASLG) to induce the myotube death. The effect of PF1801 on the myotube death was examined.

Results: Histological analysis of muscle specimens of PM patients and CIM revealed that GLP-1R was expressed on the plasma membrane of muscle fibers. The expression level of GLP-1R on the muscle fibers was high in the area where inflammatory infiltrates were observed. The treatment of CIM with PSL ameliorated CIM histologically in the levels of inflammatory infiltrate and the necrotic area, but did not ameliorate the muscle weakness nor muscle weight loss. The treatment with PF1801 in monotherapy (PF) or in combination with PSL (PF+PSL) suppressed CIM-induced muscle weakness (grip strength, mean ± SD ($\times 10^3$ g/kg BW); PF 12.2 ± 1.0 ($p< 0.0001$), PF+PSL 12.7 ± 1.7 ($p< 0.0001$), Vehicle 8.4 ± 1.0) and the muscle weight loss (wet weight of quadriceps, mean ± SD (mg/g BW); PF 6.35 ± 0.72 ($p< 0.01$), PF+PSL 7.02 ± 0.42 ($p< 0.001$), Vehicle 5.16 ± 0.80) as well as the severity of histological myositis (histological score, median (interquartile range); PF 0.0 (0.0 to 0.5) ($p< 0.05$), PF+PSL 0.0 (0.0 to 0.0) ($p< 0.001$), Vehicle 1.9 (1.3 to 3.3)). The levels of HMGB1, TNF-α and IL-6 in the serum and the muscle were lower in PF1801-treated CIM mice than the mice treated with the vehicle control. In vitro, PF1801 inhibited FASLG-induced myotube death.

Conclusion: GLP-1R agonist could be a novel therapy to recover muscle weakness and to suppress muscle inflammation in PM.

Disclosure: M. Kamiya, None; **S. Kim**, None; **J. Yeon Kim**, None; **S. Yasuda**, Chugai Pharmaceutical Co., Ltd., 1, 2, GlaxoSmithKline Pharmaceuticals Ltd., 1, Mitsubishi Tanabe Pharma Co., 1, Astellas Pharma Inc., 1, Ono Pharmaceutical Co., Ltd., 1, Asahi Kasei Corporation, 1, 2, Bristol Myers Squibb, 1, 2; **E. Lee**, None; **F. Mizoguchi**, AbbVie, 2, 8, Astellas Pharma, 2, Bristol-Myers Squibb, 2, 8, Chugai Pharmaceutical, 2, 8, Daiichi Sankyo Company, 2, 8, Eisai, 2, 8, Eli Lilly and Company, 2, 8, ImmunoForge, 2, 5, Japan Blood Products Oraganization, 2, Mitsubishi Tanabe Pharma, 2, Novartis Pharma Japan, 2, Ono Pharmaceutical, 2, 8, Otsuka Pharmaceutical Factory, 2, Pfizer, 2, 8, Sanofi, 2, Takeda Pharmaceutical Company, 2, Teijin, 2, Asahi Kasei Pharma, 5, 8, Glaxo Smith Kline, 8.

Abstract Number: 1078

Highly Reactive anti-Jo1 Autoantibodies to Distinct HisRS Variants and Domains Associate with Lung and Joint Involvement in Patients with Myositis

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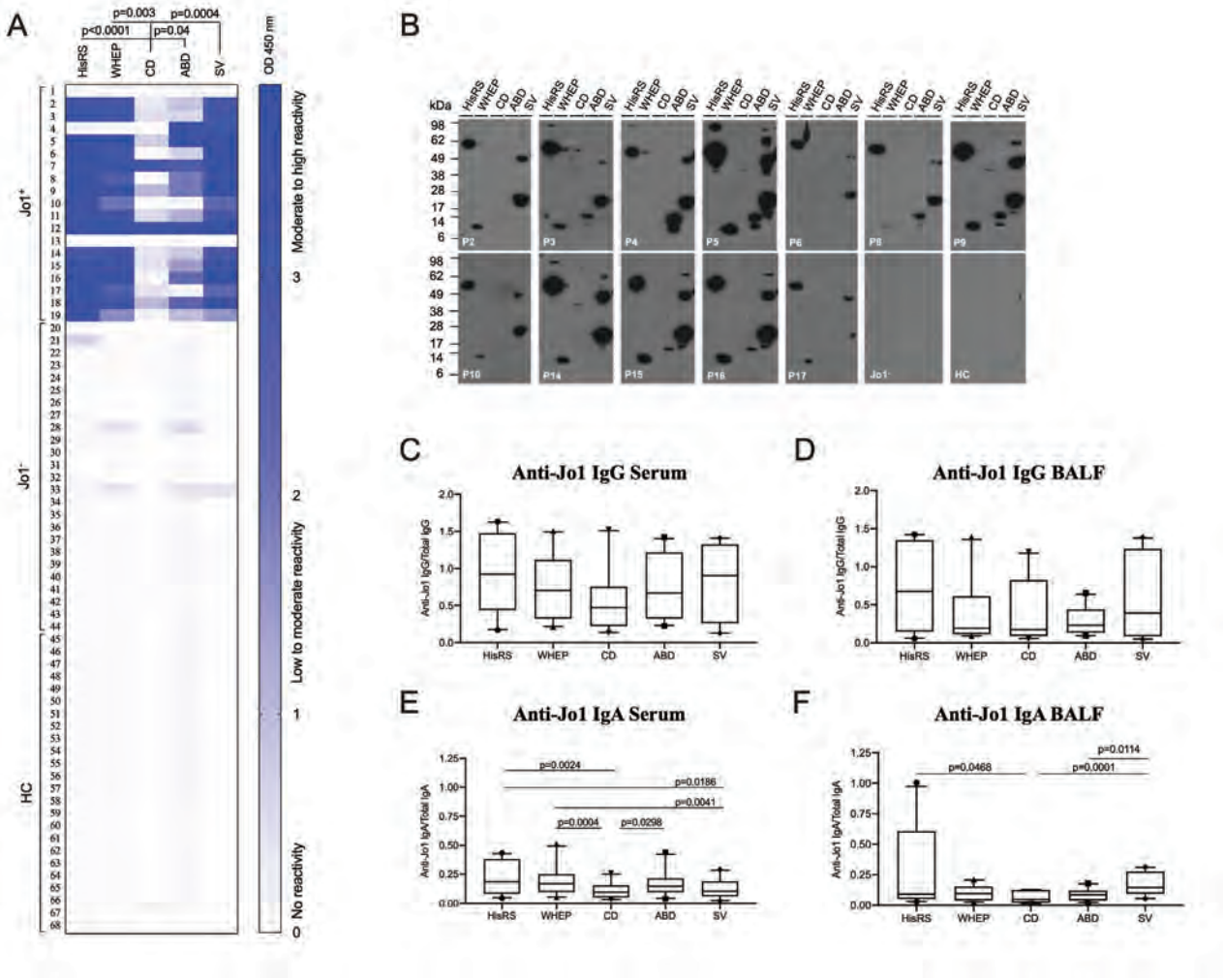
SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Muscle Biology, Myositis & Myopathies Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM



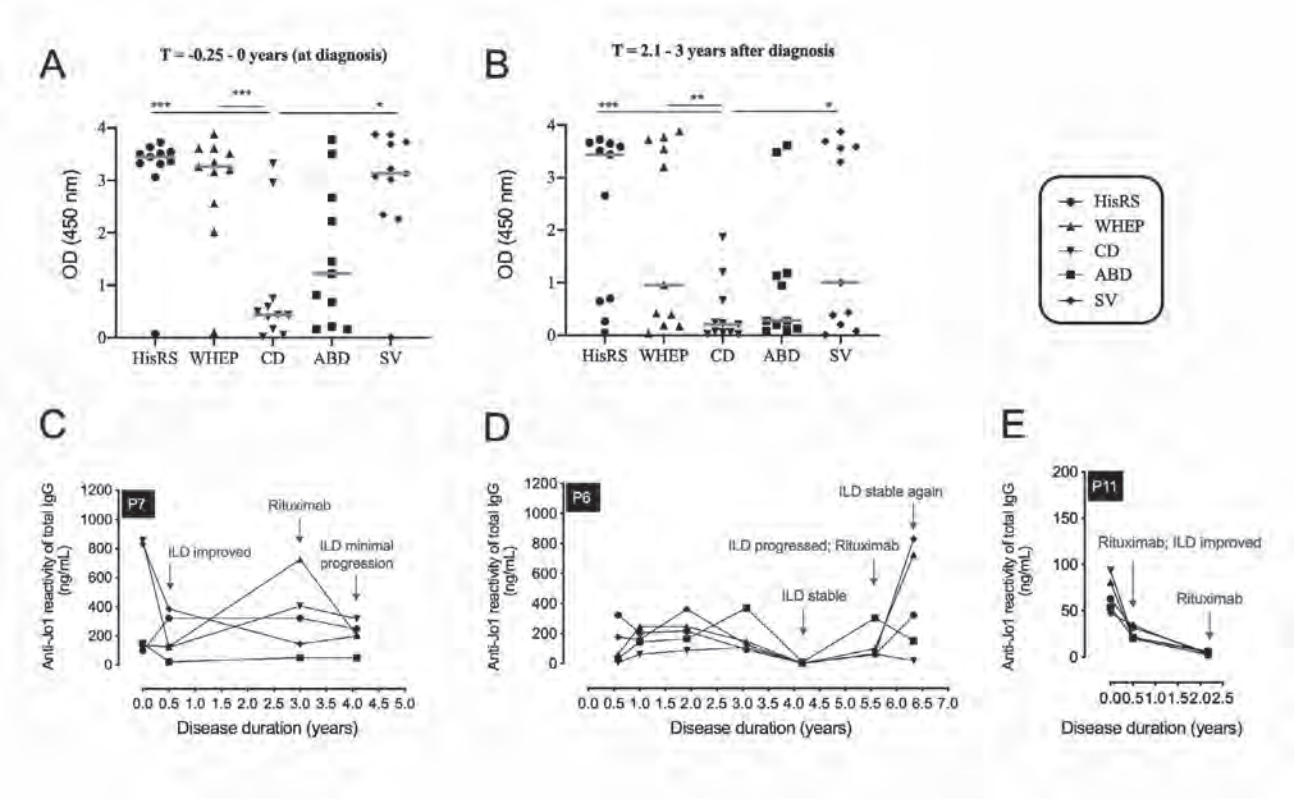
Background/Purpose: To address the reactivity and affinity against histidyl-transfer RNA synthetase (HisRS) autoantigen of anti-Jo1 autoantibodies from serum and bronchoalveolar lavage fluid (BALF) and associations with clinical data in patients with idiopathic inflammatory myopathies/anti-synthetase syndrome (IIM/ASS).

Methods: Samples and clinical data were obtained from: i) 25 anti-Jo1^{+} (19 sera and 6 BALF/matching sera at diagnosis, 16/19 sera at follow-up); ii) 29 anti-Jo1^{-} (25 sera and 4 BALF/matching sera at diagnosis) patients; iii) 24 age/gender matched healthy controls. Reactivity towards HisRS full-length (HisRS-FL), two HisRS domains, and two HisRS splice variants (WHEP and SV) was tested. Anti-Jo1 IgG reactivity was evaluated by ELISA and western blot in IgG purified from serum by affinity chromatography. In paired serum-BALF, anti-Jo1 IgG and IgA reactivity was analyzed by ELISA. Autoantibodies affinity was measured by surface plasmon resonance. Correlations between autoantibody reactivity and clinical data were evaluated.

Results: Anti-Jo1 IgG from serum and BALF bound HisRS-FL, WHEP and SV with high reactivity, already at diagnosis and recognized both conformation-dependent and -independent HisRS epitopes (Figure 1). Levels of autoantibodies (against HisRS-FL, -domains and -splice variants) generally decreased over time (Figure 2). Individuals with interstitial lung disease, arthritis and less skin involvement presented higher autoantibody levels against HisRS-FL (Figure 3). IgG with anti-WHEP reactivity in BALF correlated with poor pulmonary function. Anti-HisRS-FL IgG displayed high affinity early in the disease.

Conclusion: High levels and high affinity of anti-Jo1 autoantibodies towards HisRS early in disease in sera and BALF support the hypothesis that autoimmunity against HisRS is most likely initiated before IIM/ASS diagnosis.

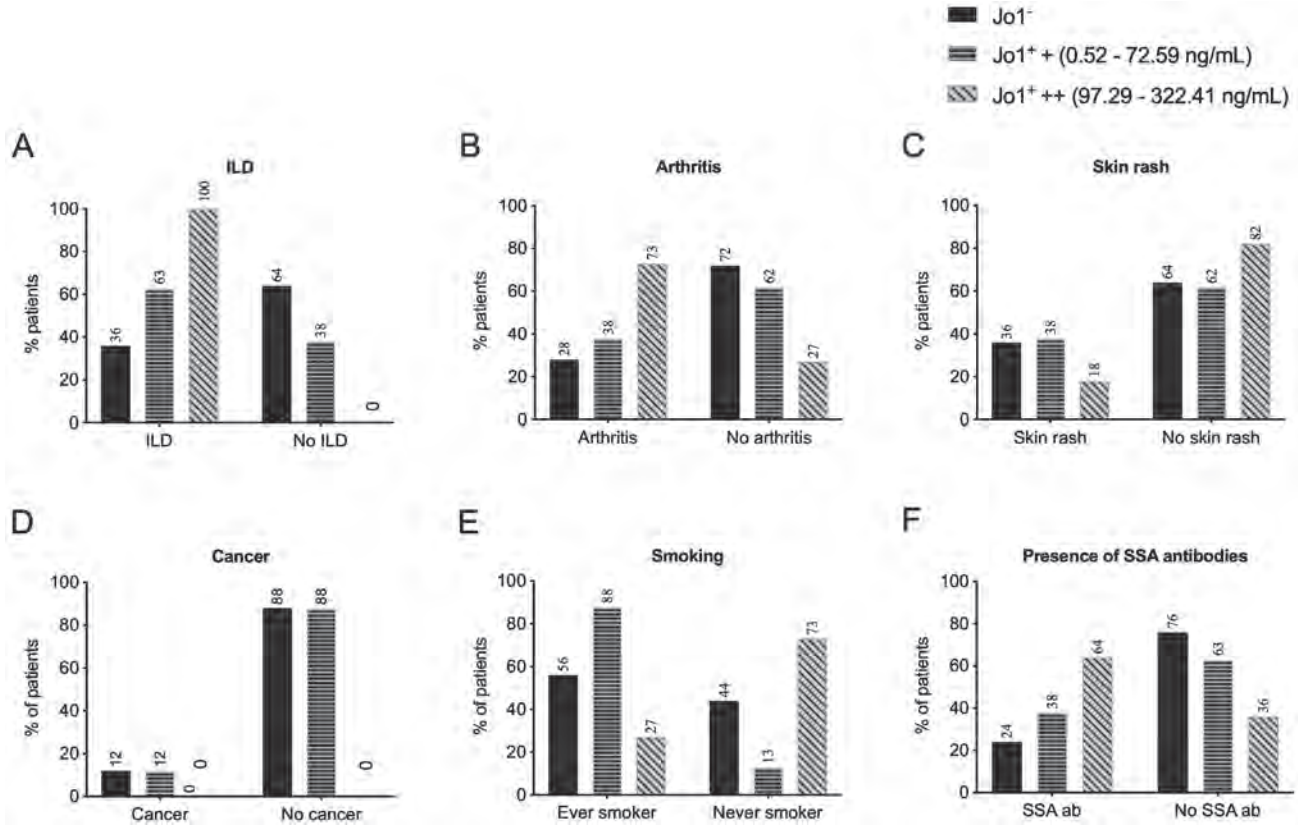
Serum and BALF-derived anti-Jo1 autoantibodies display high reactivity against HisRS variants/domains already at IIM/ASS diagnosis. (A) The reactivity towards HisRS-FL, WHEP, CD, ABD, and SV as conformational epitopes was



measured by ELISA in IgG purified from serum of 19 anti-Jo1+, 25 anti-Jo1-, and 24 healthy controls (HC). Higher reactivity corresponds to stronger blue color. (B) Anti-Jo1 reactivity against linear HisRS antigens was addressed by WB in IgG purified from serum of 12 anti-Jo1+, 1 anti-Jo1-, and 1 HC. Stronger band intensity denotes higher anti-Jo1 reactivity. Some patients also showed an additional band, correspondent to HisRS dimer. (C-D-E-F) Anti-Jo1 IgG and IgA reactivity in BALF and paired serum was measured by ELISA in 6 anti-Jo1+. Autoantibody levels were normalized to total values of IgG and IgA (Y-axis). Kruskal-Wallis (A) and Friedman's tests (C-D-E-F) corrected for multiple comparisons by Dunn's test was applied. $P<0.05$ was assumed as significantly different.

Reactivity of anti-Jo1 autoantibodies towards HisRS variants decreases over time but remains high against HisRS-FL. (A-B) Reactivity against HisRS-FL, -splice variants (WHEP and SV), and -domains (CD and ABD) displayed by total IgG purified from the first available anti-Jo1+ sera close to diagnosis (T = -0.25 – 0 years) and 2.1 – 3 years after diagnosis. (C-D-E) Anti-Jo1 reactivity of 3 anti-Jo1+ patients (P7, P6, P11) displayed by total IgG purified from sera collected longitudinally. Y-axis represents anti-Jo1 antibody levels against HisRS, measured in the total IgG isolated from anti-Jo1+ IIM/ASS sera. X-axis represents disease duration in years. Dark grey sentences provide information on rituximab introduction and/or follow-up on interstitial lung disease/arthritis. Concentration (ng/mL) of anti-Jo1 antibodies was calculated based on a standard curve derived from anti-Jo1 IgG isolated from a sera pool of 38 anti-Jo1+ IIM/ASS individuals. Total anti-Jo1+ IgG from different patients present distinct binding capacity to HisRS proteins (note the different scale which goes from 100, 200, 400 up to 1200 ng/mL). The letter P (Patient) followed by a number in each graph represents an anti-Jo1+ IIM/ASS individual.

IIM/ASS patients diagnosed with ILD and arthritis and less skin involvement harbor more reactive anti-Jo1 autoantibodies. (A-B-C-D-E-F) Percentage of IIM/ASS patients distributed according to anti-HisRS full-length (HisRS-FL) reactivity levels, clinical diagnosis and clinical manifestations. The anti-HisRS-FL reactivity displayed was measured in total anti-Jo1+ IgG purified from serum. Numbers on top of the bars represent the percentage of patients in the group. Jo1-, anti-Jo1 IIM/ASS negative patients; Jo1+ +, anti-Jo1 IIM/ASS positive patients with low to moderate



reactivity (0.52 – 72.59 ng/mL); Jo1+ ++, anti-Jo1 IIM/ASS positive patients with moderate to high HisRS reactivity (97.29 – 322.41 ng/mL). IIM, idiopathic inflammatory myopathies. ILD, interstitial lung disease; ASS, anti-synthetase syndrome.

Disclosure: A. Notarnicola, None; **C. Preger**, None; **S. Lundström**, None; **N. Renard**, None; **E. Wigren**, None; **E. Van Gompel**, None; **A. Galindo-Feria**, None; **H. Persson**, None; **M. Fathi**, None; **J. Grunewald**, None; **P. Jakobsson**, None; **S. Gräslund**, None; **I. Lundberg**, Bristol Myers Squibb, 2, Astra Zeneca, 2; **C. Fernandes-Cerqueira**, None.

Abstract Number: 1079

Sex Differences in Antibody Profile, Phenotype, and Treatment Response in a Racially Diverse Population with Idiopathic Inflammatory Myopathies

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Session Type: Poster Session C
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Background/Purpose: It is established that autoimmune diseases are more common in females than males. Large scale idiopathic inflammatory myopathy (IIM) registries have shown a similar pattern of female predominance. However, inflammatory myopathies have a wide variability of clinical manifestations and it remains unclear if differences in prevalence leads to different phenotypes and thus, a different medication response, between males and females. We aim to compare differences in antibody profile, organ involvement, frequency of comorbidities, and treatment response between male and female patients with IIM.

Methods: A registry was created of Montefiore Medical Center patients that met 2017 EULAR/ACR classification criteria for IIM. Demographics, IIM subtype, clinical manifestations, comorbidities, and treatment history were documented. Interstitial lung disease (ILD) presence, progression, and severity were determined by CT and pulmonary function tests. Medication failure was defined by rheumatologist, discontinuation due to adverse effects, or medication change within 3 months. Medication control was defined by documented clinical improvement. Statistical analyses included Chi-square and Fisher's Exact test.

Results: The cohort consisted of 152 patients, of which 114 (75%) were women and 38 (25%) were men. 25% of cohort was of Latin ethnicity and races represented included African American (53%), Caucasian (34%), Asian (4%), and American Indian (2%).

The distribution of myositis exhibited was predominantly female, as expected, except IBM was more prevalent in males (27% vs 7%, p=0.008). Antibody profiles revealed men had increased frequency of NXP2 (21% vs 2%, p= 0.0443) while the rest of antibodies were similarly distributed between the sexes.

		Female (n=114)	Male (n=38)	P-Value
Demographics	Latin Ethnicity	20%	38%	0.05
	American Indian	2%	0%	0.40
	Asian	2%	0%	0.40
	Black	46%	45%	0.74
	White	30%	29%	0.81
Clinical Diagnosis / Phenotype	PM	36 (32%)	9 (24%)	0.44
	DM	69 (60%)	20 (53%)	0.70
	- CADM	9/60 (15%)	2/20 (20%)	0.60
	MCTD (Overlap)	12 (11%)	3 (8%)	
	Nec (Statin-associated)	1 (1%)	0 (0%)	
	IBM	8 (7%)	9 (24%)	0.008
Antibody Profile	dsDNA	2/89 (2.2%)	1/22 (4.5%)	0.56
	RNP	15/90 (16.7%)	3/24 (12.5%)	0.65
	SSA	36/99 (36.4%)	6/26 (23.1%)	0.29
	SSB	6/97 (6.2%)	1/24 (4.2%)	0.71
	Jo-1	24/105 (22.9%)	4/32 (12.5%)	0.27
	Centromere	2/74 (2.7%)	0/16 (0%)	0.51
	Smith	4/89 (4.5%)	1/24 (4.2%)	0.96
	Ribosomal P	1/58 (1.7%)	1/14 (7.1%)	0.26
	HMG CR	1/12 (8.3%)	0/3 (0%)	0.62
	Mi-2	7/55 (12.7%)	3/18 (16.7%)	0.72
	PL-12	0/53 (0%)	0/16 (0%)	-----
	PL-7	2/53 (3.8%)	0/16 (0%)	0.44
	EJ	2/53 (3.8%)	0/16 (0%)	0.44
	OJ	0/53 (0%)	1/16 (6.3%)	0.067
	SRP	2/54 (3.7%)	0/16 (0%)	0.44
	Ku	4/53 (7.5%)	0/16 (0%)	0.27
	U2 RNP	0/44 (0%)	0/164(0%)	-----
	PM	1/45 (2.2%)	1/14 (7.1%)	0.39
	MDA5	3/42 (7.1%)	2/14 (14.3%)	0.44
	NXP2	1/42 (2.4%)	3/14 (21.4%)	0.044
	TIF1 gamma	2/44 (4.5%)	0/14 (0%)	0.43
	SSA 52 kD	16/44 (36.4%)	6/14 (42.9%)	0.72
	U1 RNP	4/46 (8.7%)	0/14 (0%)	0.27
	U3 RNP	1/45 (2.2%)	0/14 (0%)	0.57
	c1Na	1/1 (100%)	2/3 (66.7%)	0.74
ILD	Total	44/114 (39%)	10/38 (47%)	0.46
	Mild	26/44 (59%)	11/18 (61%)	0.92
	Moderate	5/44 (11%)	3/18 (17%)	0.60
	Severe	12/44 (27%)	4/18 (22%)	0.72
	Progressive	28/44 (64%)	11/ 18 (61%)	0.18
Skin Manifestations	Heliotrope rash	44 (39%)	12 (32%)	0.54
	Gottron sign or papules	46 (40%)	15 (39%)	0.94
	Shawl sign	22 (19%)	3 (8%)	0.13
	V sign	15 (13%)	4 (11%)	0.69
	Holster sign	4 (4%)	0 (0%)	0.25
	Mechanic hands	19 (17%)	7 (18%)	0.79
	Periungal erythema	21 (18%)	3 (8%)	0.16
	Raynaud with ulceration	19 (17%)	5 (13%)	0.64
	Telangiectasia	23 (20%)	3 (8%)	0.11
	Calcinosis	8 (7%)	3 (8%)	0.86

Table 1. Similarities in demographics, antibody profile, and clinical manifestations among men and women with IIM.

		Female (n=114)	Male (n=38)	P-value
MTX	Failure	30/49 (61%)	9/9 (100%)	0.10
	Control	19/49 (39%)	0/9 (0%)	0.08
AZA	Failure	31/53 (58%)	11/16 (69%)	0.62
	Control	22/53 (42%)	5/11 (31%)	0.58
MMF	Failure	15/40 (38%)	6/14 (43%)	0.79
	Control	25/40 (62%)	8/14 (57%)	0.82
Rituximab	Failure	8/20 (40%)	5/10 (50%)	0.47
	Control	12/20 (60%)	5/10 (50%)	0.69
IVIG	Failure	14/35 (40%)	12/18 (67%)	0.19
	Control	21/35 (60%)	6/18 (33%)	0.20
HCQ	Failure	12/44 (27%)	4/5 (80%)	0.034
	Control	32/44 (73%)	1/5 (20%)	0.034
Steroids	<2 years, <20 mg	35 (31%)	0 (0%)	0.0006
	<2 years, >20 mg	32 (28%)	9(24%)	0.65
	>2 years, <20 mg	36 (32%)	16 (42%)	0.34
	>2 years, >20 mg	4 (3%)	7 (18%)	0.003
	Never	6% (6%)	6 (16%)	0.08

Table 2. Differences in medication response and steroid exposure between males and females with IIM.

There were no significant sex differences in frequencies of DM skin manifestations, except the holster sign was not documented in men. Prevalence, severity, and progression of ILD were similar (Table 1). The frequency of neoplasms, HTN, HLD, and GERD were evenly distributed. However, 17 (19%) females patients had osteoporosis while only 1 (3%) male patient was had osteoporosis (p= 0.039). 29% of women had a single secondary autoimmune condition in comparison to 10% of men (p value = 0.0279).

Comparison of treatments revealed patients, regardless of sex, had less disease control with AZA and MTX, yet MMF and Rituximab had increase rates of control (Table 2). Men achieved less disease control with HCQ in comparison to women (p value =0.034). 35 (31%) of women had limited, low dose exposure to steroids while 0 (0%) of men were exposed to similar length and dosing of steroids (p value =0.0006). Yet, 18% of men had increased exposure to chronic, high dose steroids in comparison to 3% of women (p value= 0.003).

Conclusion: Although antibody profiles and clinical presentations between the sexes were similar, men had less disease control with MTX and were exposed to increased dose and length of steroid treatment. Women had shorter time and smaller dose exposure to steroids, yet steroid damage was still evident. This retrospective chart review was limited by small sample sizes but differing medication responses and prescriber patterns between sexes in IIM warrants further investigation.

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Abstract Number: 1080

Sensitivity and Specificity of the 2017 EULAR/ACR Criteria for Idiopathic Inflammatory Myopathies in a Cohort of Patients from Latin America

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SESSION INFORMATION
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Background/Purpose: Idiopathic inflammatory myopathies (IIM) are a heterogeneous group of diseases characterized by muscle inflammation and internal organ involvement. The Bohan & Peter (B&P) criteria (1) have been widely used for both, diagnostic and classification criteria for IIM, up until recently, when newer classification criteria were developed by the European League Against Rheumatism/American College of Rheumatology (EULAR/ACR) (2). These criteria are based on data from children and adults with different ethnicities from Europe, America and Asia, but the original study did not include patients from Latin America. We sought to determine the performance of the 2017 EULAR/ACR classification criteria for IIM in a cohort of Chilean patients in Latin America.

Methods: We performed a retrospective study of all patients from a tertiary referral medical center in Chile from 2014 to 2019 who had an associated ICD-10 code of M33 (dermatomyositis (DM)/polymyositis(PM)), M60.9 (myositis), and G72.4 (inflammatory myopathy). Demographic data, clinical and serological features were collected from medical records according to a pre-defined protocol in REDCap.(3) Patients were classified according to B&P criteria and 2017 EULAR/ACR classification criteria for IIM. Sensitivity, specificity, and Cohen's Kappa coefficient of agreement (κ) were calculated to assess the performance of the 2017 EULAR/ACR classification criteria when compared to B&P criteria.

Results: 150 patients were included in the study. Our cohort was 77% female, mean age was 43.2±22.6 years, 61% presented with heliotrope rash, 53% with Gottron papules, 61% with proximal muscle weakness, 64% patients had elevated CK (mean CK 3386±9391 U/L), 60% had positive ANA, 5% had a positive Jo-1 antibody. 42 patients had myositis-associated antibodies (MAA) and 37 patients had at least one myositis-specific antibody (ASM). Muscle biopsy was available in 58 patients, electromyography was available in 76 patients, and was suggestive of myositis in 38 patients. 139 patients met B&P criteria; 34 (24.5%) were classifiable as PM (12 patients definite, 9 probable, 13 possible) and 105 (75.5%) as DM (30 definite, 48 probable, 27 possible). 134 patients (89.3%) met EULAR/ACR criteria; 105 (78.4%) patients were classifiable as definite IIM, 27 (20.2%) patients as probable IIM, and 2 (1.5%) as possible. Subclassification of IIM was as follows: 22 (16.4%) patients were classified as juvenile DM, 51 (38%) as adult DM, 32 (23.9%) as amyopathic DM, 28 (21%) as PM, and 1 (0.75%) as inclusion body myositis. Sensitivity of EULAR/ACR criteria to detect IIM was 0.92, and specificity was 0.53 when compared to B&P criteria. Kappa coefficient of agreement was weak between the two classification criteria (0.39, SD 0.15-0.64). Sensitivity and specificity of

	Patients (N)	Sensitivity	Specificity
IIM	134	0.92	0.53
Dermatomyositis	105	0.92	0.82
Polymyositis	27	0.85	0.90

IIM= Idiopathic inflammatory myopathy

Table 1. Sensitivity and specificity of 2017 ACR/EULAR criteria for IIM

ACR/EULAR criteria to diagnose DM was 0.92 and 0.82, respectively. Sensitivity of ACR/EULAR criteria for PM was 0.85 and specificity was 0.9 (Table 1).

Conclusion: The current most accepted classification criteria for IIM have good sensitivity but low specificity in a Latin American cohort of patients. The new EULAR/ACR criteria performed well in this cohort to classify DM and PM correctly.

Disclosure: A. Valenzuela Vergara, None; **M. Torres**, None; **A. Deves**, None.

Abstract Number: 1081

Patient-reported Outcomes in Early Autoimmune Inflammatory Myopathies

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SESSION INFORMATION

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Table 1. Baseline characteristics of the cohort

Clinical features	n=72	Missing
Female, n (%)	51 (71)	
Age at diagnosis, mean (SD)	53 (15)	
Disease duration in years, median (IQR)	0.8 (0.4-1.2)	
Subset, n (%)		
Dermatomyositis	35 (49)	
Overlap myositis	34 (47)	
Immune-mediated necrotizing myopathy	3 (4)	
Antibodies		
MSA positive	33 (46)	1
MSA negative, MAA positive	9 (13)	
Seronegative	21 (29)	
Corticosteroids, n (%)	56 (78)	
MMT8 (0-150), median (IQR)	148 (142-150)	3
Dysphagia, n (%)	21 (29)	
NRS skin activity (0-10), median (IQR)	1.5 (0-3)	
Interstitial lung disease, n (%)	36 (50)	
Arthritis, n (%)	14 (19)	
NRS global activity (0-10), median (IQR)	3 (2-5)	3

Legend: MSA, myositis-specific antibodies; MAA, myositis-associated antibodies; MMT8, manual muscle testing; IQR, interquartile range; SD, standard deviation, NRS numerical rating scale.

Table 2. Baseline patient-reported outcomes

	n=72	Missing
Physical disability		
HAQ, median (IQR)	1 (0.3-1.6)	1
Fatigue		
FACIT, median (IQR)	28 (19-40)	2
Sleep quality		
PROMIS, median (IQR)	24 (18-31)	1
PROMIS, mean t-score (SD)	57 (10)	1
Depression		
PHQ-9, median (IQR)	10 (6-16)	1
Health-related quality of life		
Physical component summary, mean (SD)	35 (11)	5
Mental component summary, mean (SD)	42 (15)	5

Legend: HAQ, Health Assessment Questionnaire; IQR, interquartile range; FACIT, Functional Assessment of Chronic Illness Therapy; PHQ-9, Patient Health Questionnaire; SD, standard deviation; VAS, visual analog scale.

Background/Purpose: Patient-reported outcomes (PROs) are increasingly used in rheumatology. Such outcomes are under-reported in autoimmune inflammatory myopathies (AIM) especially in incident cohorts. The objective of this study was to explore physical function, fatigue, depressive symptoms, sleep quality and health-related quality of life (HRQoL) in early AIM, and the effect of disease activity on those domains.

Methods: Cross-sectional study of adult AIM subjects with disease duration of ≤2 years enrolled in a multicenter research cohort. Standardized clinical histories, medical examinations, and self-administered questionnaires were collected at baseline visit. Physical functioning was assessed using the Health Assessment Questionnaire (HAQ; scores from 0 (no disability) to 3 (severe disability)). Fatigue was measured using the Functional Assessment of Chronic Illness Therapy (FACIT; scores from 0-52, lower scores representing more fatigue). Depressive symptoms were assessed using the Patient Health Questionnaire (PHQ-9; scores from 0-27, higher scores representing worse symptoms). The PROMIS Short Form v1.0 – Fatigue 8a and the Medical Outcomes Trust Short Form-36 (SF-36) were used to assess sleep quality and HRQoL, respectively. Both are norm based, with mean scores of 50 and standard deviations (SD) of 10 (PROMIS, higher scores representing worse sleep quality; SF-36, lower scores representing worse HRQoL). Disease activity was measured by the recruiting physician using a numerical rating scale ranging from 0 (no activity) to 10 (maximum severity). Multivariate linear regression models were generated to determine the association between disease activity and PROs.

Results: The study included 72 AIM subjects (71% female, mean age 53 years, mean disease duration 0.8 years) with dermatomyositis (49%), overlap myositis (47%) and immune-mediated necrotizing myopathies (4%) (Table 1). Half of the subjects had interstitial lung disease, 29% dysphagia and 19% arthritis. Baseline median (IQR) disease activity was 3 (2-5).

PRO results are presented in Table 2. Median (IQR) HAQ score was 1 (0.3-1.6) indicating moderate disability. Median (IQR) FACIT scores was 28 (19-40). Mean (SD) PROMIS score was 57 (10), indicating substantially worse sleep quality compared with the general population. Median (IQR) PHQ-9 score was 10 (6-16). The mean (SD) SF-36 physical and mental component summary scores were 1.5 SD (35 (11)) and almost 1 SD (42 (15)) below that of the general population, respectively. Multivariate linear regression analyses (Table 3) showed a statistically significant association between disease activity and worse physical functioning measured with the HAQ (β 0.17, 95%CI 0.09, 0.26), more

Table 3. Multivariate linear regression showing the effect of selected clinical variables on patient-reported outcomes in early disease

	Estimate (β)	95% CI	p-value
Physical disability (HAQ, median)			
Age	-0.0008	-0.01, 0.01	0.90
Female	0.33	-0.08, 0.73	0.12
Disease activity	0.17	0.09, 0.26	<0.001
Fatigue (FACIT, median)			
Age	0.18	-0.02, 0.39	0.08
Female	-1.98	-8.31, 4.35	0.53
Disease activity	-2.41	-3.81, -1.01	0.001
Sleep quality (PROMIS, mean t-score)			
Age	-0.12	-0.30, 0.05	0.15
Female	2.80	-2.49, 8.10	0.29
Disease activity	0.91	-0.24, 2.06	0.12
Depression (PHQ-9, median)			
Age	0.03	-0.11, 0.17	0.70
Female	2.60	-1.63, 6.78	0.23
Disease activity	-0.03	-0.95, 0.89	0.95
HRQoL – physical component (PCS, mean)			
Age	0.11	-0.09, 0.30	0.27
Female	-2.85	-8.62, 2.92	0.33
Disease activity	-1.77	-3.05, -0.48	0.008
HRQoL – mental component (MCS, mean)			
Age	0.22	-0.03, 0.48	0.08
Female	-3.60	-11.2, 4.01	0.35
Disease activity	-1.42	-3.11, 0.28	0.10

Legend: HAQ, Health Assessment Questionnaire; FACIT, Functional Assessment of Chronic Illness Therapy; PHQ-9, Patient Health Questionnaire, HRQoL, health-related quality of life; PCS, physical component summary; MCS, mental component summary; CI, confidence interval.

fatigue measured with the FACIT (β -2.41, 95%CI -3.81, -1.01) and impaired physical HRQoL measured with the SF-36 PCS (β -1.77, 95%CI -3.05, -0.48).

Conclusion: Early AIM subjects feel and function poorly. Impairments in PROs for which standards exist, in particular function, sleep quality and HRQoL, are large, in some cases exceeding 1 SD. There is a need to standardize fatigue and depressive measures to better understand those results. Further research into correlates of and trajectories in PROs in AIM are urgently needed.

Disclosure: V. Leclair, None; **B. Thombs**, None; **M. Wang**, None; **E. Vinet**, None; **A. Albert**, None; **M. Hudson**, None.

Abstract Number: 1082

The Presence of Anti-Jo1, anti-PL7, And/or anti-MDA5 Antibodies in Idiopathic Inflammatory Myopathy Confers an Increased Risk of a Significant Restrictive Pulmonary Defect

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Background/Purpose: A subset of patients with idiopathic inflammatory myopathy develop significant restrictive lung disease, although risk factors for this are poorly defined. Autoantibodies may be important in defining risk. The primary purpose of this study is to identify clinical and serologic risk factors for development of significant restrictive pulmonary defects on pulmonary function testing in patients with idiopathic inflammatory myopathy.

Methods: We conducted a retrospective chart review of patients with diagnoses of dermatomyositis, polymyositis, and/or anti-synthetase syndrome with at least one pulmonary function test seen at Rush University Medical Center between January 1, 2010, and October 6th, 2019. We used ICD-9 and ICD-10 codes to identify study patients and confirmed the diagnoses via chart review. We extracted baseline demographic data, relevant disease features, smoking history, serologic data (hemoglobin, muscle enzymes, autoantibody profiles), chest CT reports, and pulmonary function data from the medical record. We compared patients with forced vital capacity (FVC) % predicted < 70 at any time during their clinical course to patients with FVC % predicted ≥ 70, using this cut point to define a significant restrictive defect. We used two-tailed Student's T-tests to compare continuous variables and Chi square tests (or Fisher's exact tests) for categorical variables. We used the exploratory analyses to select factors to include in a multivariable logistic regression to model the outcome of FVC% predicted < 70.

Table 2. Univariate and Multivariable Regression of Factors Predictive of FVC ever <70%

	Univariate Regression[1]		Multivariable Regression[2]	
Factor	OR (95% CI)	p-value	OR (95% CI)	p-value
Female sex	1.33 (0.48-3.67)	0.578	5.73 (0.68-8.64)	0.110
Age at first symptom, y	1.00 (1.00-1.00)	0.465	1.00 (0.99-1.01)	0.921
Disease duration since first symptom, y	0.95 (0.88-1.03)	0.204	0.88 (0.76-1.01)	0.075
Baseline CK	1.00 (1.00-1.00)	0.080	1.00 (1.00-1.00)	0.178
Ever smoker	1.00 (0.38-2.64)	1.00	0.48 (0.06-3.77)	0.487
Presence of: Jo1, MDA5, or PL7 antibodies	7.15 (1.93-26.5)	0.003	18.49 (2.13-160.76)	0.008

Abbreviation: CK = creatine kinase

1. Logistic regression was used with each individual factor as the predictor and FVC status as the outcome.
2. Significant factors were included in a multivariable logistic regression model as the predictors of FVC status.

Univariate and Multivariable Regression of Factors Predictive of FVC Ever <70%

Results: Eighty-eight patients met the inclusion/exclusion criteria. Of these, 50/88 (56.8%) patients had FVC% predicted ≥ 70 and 38/88 (43.2%) patients had FVC% predicted < 70. Patients' ages ranged from 28.0 to 56.7 years, 48/85 (56.5%) were African-American, and 45/88 (51.1%) had a primary diagnosis of dermatomyositis. Patients with FVC% predicted < 70 had a greater mean CK (4264.3 units/L vs. 1461.0 units/L; p= 0.0412) and were more likely to be positive for anti-Jo1 (4/35 [32.4%] vs. 4/35 [11.4%]; p=0.044), anti-MDA5 (7/17 [41.2%] vs. 3/19 [15.8%]; p=0.139), and anti-PL7 (4/17 [23.5%] vs. 1/20 [5.0%]; p= 0.159) antibodies. Multivariable logistic regression demonstrated that the presence of anti-Jo-1, anti-MDA5, and/or anti-PL-7 antibodies was independently associated with a significant restrictive pulmonary defect (OR 18.49 95% CI 2.13-160.76; p = 0.008).

Conclusion: The presence of anti-PL-7, anti-Jo1, and/or anti-MDA5 antibodies was associated with a nearly 19-fold increased risk of significant restrictive pulmonary defect in this cohort of patients with dermatomyositis and polymyositis. Patients with a significant restrictive defect had greater mean CK levels, but CK level was not an independent risk factor for a significant restrictive defect in multivariable analyses. Future studies should be conducted to validate these findings in an external cohort and to differentiate between restrictive pathology due to ILD and restrictive pathology due to muscle weakness.

Disclosure: D. Cherny, None; **C. Richardson**, None.

Abstract Number: 1083

Alterations of Lipid Profile in IIM Patients Are Associated with Disease Activity, Duration, and Glucocorticoid Treatment

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Background/Purpose: Idiopathic inflammatory myopathies (IIM) are characterized by skeletal muscle and organ involvement and chronic course. Systemic inflammation, limited mobility, and glucocorticoid treatment can have a negative impact on intermediate metabolic pathways, especially on lipid metabolism. The aim of this study was to assess the differences in the lipid profile of IIM patients and healthy controls (HC) and the association with disease-specific features.

Methods: 133 patients with IIM (106 females; mean age 60.3; disease duration 2.2 years; DM 47 / PM 41 / IMNM 45) and 133 age-/sex-matched HC (106 females, mean age 60.2) without rheumatic diseases were included. Patients with DM and PM fulfilled the Bohan/Peter criteria for PM/DM and patients with IMNM fulfilled the ENMC criteria.

Table 1

Table 1: Baseline characteristics					
	IIM (n = 133)	DM (n = 47)	PM (n = 41)	IMNM (n = 45)	HC (n = 133)
Gender, n (%): female / male	106 (80) / 27 (20)	37 (79) / 10 (21)	34 (83) / 7 (17)	34 (76) / 11 (24)	106 (80) / 27 (20)
Age (years): median (IQR)	60.0 (49.3 – 69.3)	56.4 (49.7 – 65.8)	58.3 (43.7 – 65.4)	68.8 (57.6 – 72.8)	IIM-HC 60.2; DM-HC 56.5; PM-HC 58.4; IMNM-HC 68.3
BMI (kg/m²): median (IQR)	26.7 (23.4 – 30.5)	27.4 (23.6 – 32.5)	24.7 (21.1 – 28.1)	27.4 (25.2 – 31.5)	-
Disease duration (years): median (IQR)	2.2 (0.7 – 6.9)	2.8 (1.4 – 7.8)	5.0 (1.6 -9.4)	0.7 (0.4 – 3.2)	
Disease activity (MITAX): median (IQR)	0.11 (0.05 – 0.21)	0.15 (0.07 – 0.28)	0.11 (0.08 – 0.2)	0.07 (0.04 – 0.18)	
MDI: median (IQR)	0.05 (0.02 – 0.1)	0.08 (0.03 – 0.11)	0.05 (0.03 – 0.11)	0.06 (0.03 – 0.14)	
MMT-8: median (IQR)	62 (54 – 72)	65 (55 – 74)	62 (56 – 73)	58 (49.5 – 68.5)	
CRP (mg/L): median (IQR)	3.0 (1.8 – 5.9)	3.0 (2.0 – 6.5)	2.8 (1.6 – 5.6)	3.2 (1.7 – 6.0)	
ESR (mm/h): median (IQR)	14 (8 – 26)	13 (8.3 – 19.8)	20 (8 – 33)	11 (5 – 24)	
CK (µkat/L): median (IQR)	3.8 (1.0 – 20.7)	1.2 (0.7 – 2.8)	3.6 (0.9 – 9.5)	40.1 (7.7 – 73.5)	
LD (µkat/L): median (IQR)	4.6 (3.5 – 7.2)	3.7 (3.1 – 5.0)	3.8 (2.9 – 5.0)	8.9 (5.7 – 16.4)	
Myoglobin (µg/L): median (IQR)	179.2 (71.2 – 940.5)	99.9 (59.9 – 172.5)	141.7 (51.3 – 326.9)	1374 (537.1 – 2227)	
Glycemia (mmol/L): median (IQR)	5.3 (4.6 – 6)	5.2 (4.4 – 5.8)	5.1 (4.7 – 5.7)	5.7 (4.8 – 7.0)	
Prednisolone equivalent dose (mg/day): median (IQR)	15 (5 – 30)	15 (5 – 30)	7.5 (2.5 – 20)	27.5 (2.19 – 58.75)	
IIM-associated clinical manifestations, n (%): MW / OD / SR / MH / RP / A / ILD / CI	109 (82) / 39 (29) / 18 (14) / 16 (12) / 25 (19) / 17 (13) / 37 (29) / 15 (11)	38 (81) / 18 (38) / 16 (34) / 11 (23) / 11 (23) / 2 (4) / 15 (32) / 7 (15)	33 (81) / 10 (24) / 0 (0) / 5 (12) / 11 (27) / 14 (34) / 19 (46) / 6 (15)	38 (84) / 11 (24) / 2 (4) / 0 (0) / 3 (7) / 1 (2) / 3 (7) / 2 (5)	
Autoantibodies (positive), n (%): ANA / Mi-2 / p155-140 / CADM-140 / SAE / p140 / SRP / Jo-1 / PM-Scl / RNP / Ku / Ro / HMGCR	36 (27) / 8 (6) / 3 (3) / 4 (3) / 1 (1) / 4 (3) / 7 (6) / 21 (16) / 10 (8) / 4 (3) / 4 (3) / 25 (20) / 27 (21)	15 (32) / 6 (13) / 3 (6) / 3 (6) / 1 (2) / 4 (9) / 1 (2) / 5 (11) / 7 (15) / 1 (2) / 1 (2) / 6 (13) / 1 (2)	12 (29) / 1 (2) / 0 (0) / 1 (2) / 0 (0) / 0 (0) / 0 (0) / 0 (0) / 14 (34) / 2 (5) / 2 (5) / 2 (5) / 14 (34) / 0 (0)	9 (20) / 1 (2) / 0 (0) / 0 (0) / 0 (0) / 0 (0) / 0 (0) / 6 (13) / 2 (4) / 1 (2) / 1 (2) / 1 (2) / 5 (11) / 26 (58)	
Treatment, n (%): GC / MTX / AZA / CSA / CPA / LEF / MMF	112 (84) / 40 (30) / 14 (11) / 8 (6) / 3 (2) / 1 (1) / 2 (2)	42 (89) / 14 (30) / 5 (11) / / 4 (9) / 2 (4) / 0 (0) / 0 (0)	37 (90) / 11 (27) / 5 (12) / 2 (5) / 1 (2) / 1 (2) / 2 (5)	33 (73) / 15 (33) / 4 (9) / 2 (4) / 0 (0) / 0 (0) / 0 (0)	
Arterial hypertension (treated), n (%)	65 (50)	18 (38)	18 (44)	29 (64)	
Diabetes mellitus, n (%): Untreated / PAD / Insuline treatment	15 (12) / 18 (14) / 11 (9)	6 (13) / 1 (2) / 1 (2)	3 (7) / 4 (10) / 5 (12)	6 (13) / 13 (30) / 5 (11)	
Statin use, n (%): Current / Previous / Other current hypolipidemic drugs	3 (2) / 37 (28) / 3 (2)	2 (4) / 4 (8) / 1 (2)	1 (2) / 3 (7) / 2 (5)	0 (0) / 45 (67) / 0 (0)	
Smoking (current), n (%)	4 (3)	0 (0)	0 (0)	4 (9)	

Acronyms: IIM, idiopathic inflammatory myopathies; DM, dermatomyositis; PM, polymyositis; IMNM, immune mediated necrotising myopathy; HC, healthy controls; MITAX, Myositis Intention to Treat Activity Index; MMT-8, manual Muscle Testing-8; CRP, C-reactive protein; ESR, erythrocyte sedimentation rate; CK, creatine kinase; LD, lactate dehydrogenase; MW, muscle weakness; OD, oesophageal motility disorder; SR, skin rash; MH, mechanic's hands; RP, Raynaud's phenomenon; A, arthritis; ILD, interstitial lung disease; CI, cardiac involvement ANA, antinuclear antibodies; Mi-2, anti-nuclear helicase 218/240 kDa; p155-140, anti-TIF1 (transcription factor-1); CADM-140, anti-MDA5 (antigen associated with melanoma differentiation); SAE, anti-SUMO1 (small ubiquitin-like activating enzyme); p140, anti-NXP2 (nuclear matrix protein); SRP, anti-signal recognition particles; Jo-1, ami-histidyl-tRNA synthetase; PM-Scl, anti-Pm-Scl (anti-core complex 11-16 proteins); RNP, anti-ribonucleoprotein; Ku, anti-Ku (against the nuclear DNA-protein kinase subunit); Ro, anti-Ro (52 / 60kDa against cytoplasmic RNA and associated peptides); GC, glucocorticoids; MTX, methotrexate; AZA, azathioprine; CSA, cyclosporin A; CPA, cyclophosphamide; LEF, leflunomide; MFF, mycophenolate mofetil; PAD, peroral antidiabetic drugs.

Table 1. Baseline characteristics

Levels of selected parameters of lipid metabolism were measured in sera drawn after 8 hours of fasting by routine analytic methods. In IIM patients, disease activity, and damage were evaluated by MITAX and MDI, muscle involvement by manual muscle testing (MMT-8), and comorbidities of interest and current treatment were recorded. Data are presented as median (IQR).

Table 2

Table 2: Lipidogram in IIM patients compared to healthy controls						
Parameter of lipidogram	IIM (n = 133)	DM (n = 47)	PM (n = 41)	IMNM (n = 45)	HC (n = 133)	p-value IM-HC; DM-HC; PM-HC; IMNM-HC
TC (mmol/L); median (IQR)	5.79 (4.95 – 6.81)	5.36 (4.87 – 6.17)	5.65 (4.52 – 6.68)	6.3 (5.42 – 7.18)	5.14 (4.42 – 5.79)	**<0.001**; 0.135; **0.040**; **<0.001**
TG (mmol/L); median (IQR)	2.02 (1.36 – 2.80)	1.91 (1.32 – 2.71)	1.88 (1.27 – 2.75)	2.27 (1.59 – 2.97)	1.28 (0.93 – 1.65)	**<0.001**; **<0.001**; **0.002**; **<0.001**
LDL-C (mmol/L); median (IQR)	3.13 (2.54 – 3.98)	2.95 (2.30 – 3.33)	3.12 (2.33 – 3.91)	3.58 (3.03 – 4.36)	2.82 (2.09 – 3.66)	**0.005**; 0.436; 0.131; **<0.001**
Apo-B (g/L); median (IQR)	1.06 (0.87 – 1.33)	1.02 (0.82 – 1.14)	0.98 (0.76 – 1.35)	1.26 (1 – 1.47)	0.91 (0.71 – 1.08)	**<0.001**; 0.16; **0.017**; **<0.001**
Non-HDL-C (mmol/L); median (IQR)	4.4 (3.40 – 5.20)	4.25 (3.60 – 4.76)	4.15 (3.40 – 5.50)	5.1 (4.10 – 5.85)	3.9 (3.18 – 4.50)	**<0.001**; 0.262; **0.040**; **<0.001**
Lp(a) (g/L); median (IQR)	0.1 (0.04 – 0.26)	0.1 (0.05 – 0.30)	0.1 (0.02 – 0.28)	0.12 (0.04 – 0.31)	0.15 (0.04 – 0.49)	0.098; 0.733; 0.242; **0.032**
HDL-C (mmol/L); median (IQR)	1.122 (0.96 – 1.55)	1.13 (0.87 – 1.53)	1.18 (0.94 – 1.48)	1.36 (0.99 – 1.63)	1.2 (0.95 – 1.55)	0.913; 0.917; 0.503; 0.928
Apo-A (g/L); median (IQR)	1.7 (1.49 – 2.06)	1.76 (1.52 – 2.14)	1.75 (1.50 – 2.12)	1.68 (1.41 – 1.97)	1.8 (1.60 – 2.06)	0.073; 0.782; 0.267; **0.025**
AI (log(TG/ HDL-C); median (IQR)	3.85 (2.73 – 5.05)	3.9 (2.58 – 4.95)	3.85 (2.50 – 5.20)	3.7 (3.00 – 5.10)	3.15 (2.20 – 4.43)	**0.003**; 0.425; 0.071; **0.002**

Acronyms: TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein; Apo-B, apolipoprotein B; non-HDL-C, non-high-density lipoprotein (TC minus measured HDL-C); Lp(a), lipoprotein A; HDL-C, high-density lipoprotein; Apo-A, apolipoprotein A; AI, atherogenic index of plasma = log(TG/ HD-CL)

Table 2. Lipidogram in IIM patients compared to healthy controls

Table 3

Table 3: Correlation of lipid profile parameters and disease-specific features in all IIM patients (n=133)		
Correlated parameters	Spearman's r	p-value
TC: Disease duration; LD; PED; Age; CK; Myoglobin	-0.322; 0.343; 0.292; 0.193; 0.198; 0.249	<0.001; <0.001; <0.001; 0.027; 0.025; 0.007
TG: Disease duration; PED; BMI	-0.326; 0.316; 0.271	<0.001; <0.001; 0.003
LDL-: Disease duration; LD; Age; CK; Myoglobin;	-0.310; 0.359; 0.212; 0.257; 0.289	<0.001; <0.001; 0.015; 0.003; 0.002
Apo-B: Disease duration; LD; PED; Age; BMI; MMT-8; CK; Myoglobin; Glycemia	-0.311; 0.348; 0.307; 0.220; 0.239; -0.214; 0.256; 0.307; 0.201	<0.001; <0.001; <0.001; 0.012; 0.009; 0.017; 0.004; <0.001; 0.031
non-HDL-C: Disease duration; LD; BMI; CK; Myoglobin; PED	-0.303; 0.322; 0.202; 0.214; 0.270; 0.275	<0.001; <0.001; 0.027; 0.015; 0.003; 0.002
HDL-C: CRP	-0.230	0.010
Apo-A: CRP; CK; Myoglobin	-0.293; -0.214; -0.258	<0.001; 0.016; 0.005
AI: BMI	0.209	0.021

Acronyms: TC, total cholesterol; TG, triglycerides; LDL-C, low-density lipoprotein; Apo-B, apolipoprotein B; non-HDL-C, non-high-density lipoprotein (TC minus measured HDL-C); HDL-C, high-density lipoprotein; Apo-A, apolipoprotein A; AI, atherogenic index of plasma = log(TG/ HDL-C); LD, lactate dehydrogenase; PED, current prednisolone equivalent dose; CK, creatine kinase; BMI, body mass index; MMT-8, manual muscle testing-8; CRP, C-reactive protein

Table 3. Correlation of lipid profile parameters and disease-specific features in all IIM patients (n=133)

Results: Several differences in disease activity, the dose of glucocorticoids, prevalence of comorbidities, and serum lipid levels were observed among the three subtypes of IIM (Table 1). Lipid profile parameters, especially levels of negative cardiovascular predictive markers such as TC, TG, LDL-C, Apo-B, and the atherogenic index, were significantly higher compared to healthy controls. The most significant changes were observed in the IMNM group (compared to the corresponding age-/sex-matched HC) (Table 2). Levels of TC, TG, LDL-C, apo-B and nonHDL negatively correlated with disease duration, but positively with laboratory markers of disease activity and the current prednisolone equivalent dose. Higher levels of HDL-C were associated with decreased levels of CRP, which is in line with the negative correlation of apo-A levels with CRP, CK, and myoglobin (Table 3).

Conclusion: We have observed significant alterations in serum lipid parameters in our IIM patients compared to healthy age-/sex-matched individuals. Differences were also found among the three subtypes of IIM. These alterations were associated with laboratory parameters of disease activity and the current dose of corticosteroids. **Acknowledgement:** Supported by AZV NV18-01-00161A, MHCR-00023728, SVV-260373, and GAUK-312218.

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Abstract Number: 1084

Consumer-based Activity Trackers in Evaluation of Physical Function in Myositis Patients

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Muscle Biology, Myositis & Myopathies Poster
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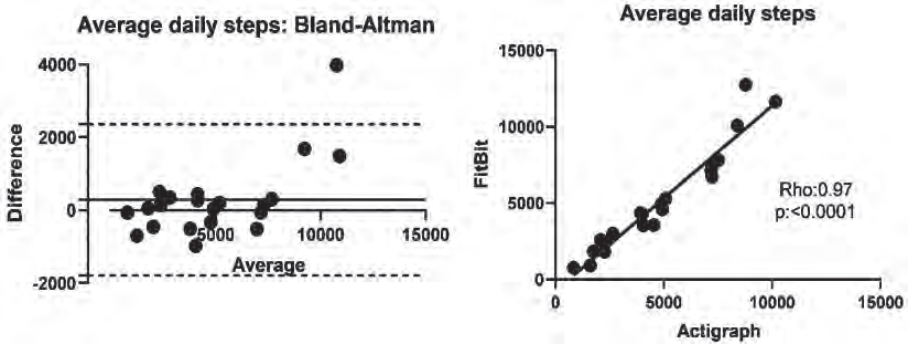
Background/Purpose: Idiopathic inflammatory myopathies are systemic inflammatory conditions characterized by muscle weakness and reduced muscle endurance that limit activities of daily living. Daily step count is an accepted metric of physical activity used in many population studies. Wearable technologies enable tracking of daily step counts longitudinally. The Actigraph is an FDA-approved triaxial accelerometer and tracks step count with high accuracy. It is used for research and not commercially available. Fitbit also measures step counts and is the most widely used consumer-based activity tracker with nearly 30 million users and many studies have validated Fitbit step counts compared to accelerometers. Given the need for objective measures of physical activity in myositis patients and broad availability of Fitbit, we assessed the reliability, validity and responsiveness of Fitbit in evaluating physical function in myositis patients and compared the accuracy of Fitbit step counts to the Actigraph.

Methods: This was a prospective longitudinal observational study with 3-visits at 0, 3-, and 6-months in polymyositis (PM), dermatomyositis (DM), necrotizing myopathy (NM) or anti-synthetase syndrome (AS) subjects. Six myositis core set measures [manual muscle testing (MMT), physician global disease activity (MD-GDA), patient global disease activity (PT-GDA), extra-muscular global disease activity (EM-GDA), HAQ-DI and creatine kinase (CK)], three functional measures [six-minute walk (6MWD), timed up-and-go (TUG) and sit-to-stand tests (STS)] and SF-36 physical function-10 (PF10) were collected at each visit. Total improvement score (TIS) was used as a measure of clinical response. Patients used a waist-worn Fitbit One and ActiGraph T3X-BT concurrently for 7 days/month for 6 consecutive months with a "valid day" defined as requiring ≥1500 steps.

Results: Twenty-four (10 DM, 8 PM/NM and 6 AS without myositis) patients (17 females/7 males; 91% Caucasian) were enrolled. Test-retest reliability of daily step count was strong in patients who had 1-month follow-up (r:0.84, ICC 0.89). Daily step count showed moderate-strong correlations with MD-GDA, PT-GDA, HAQ-DI, SF-36 PF10 and all

	Average daily step count	
	Rho	*p* value
Demographics		
Age at enrollment	-0.06	0.7
Disease duration	0.27	0.1
BMI	-0.36	0.07
Myositis outcome measures		
Extra-muscular global disease activity	-0.07	0.7
Creatine kinase level	-0.32	0.1
Physician-reported disease activity	-0.39	0.05*
MMT score	0.41	0.04*
Patient-reported disease activity	-0.45	0.02*
HAQ-DI	-0.52	0.008*
SF-36 PF10	0.57	0.004*
Pain	-0.53	0.007*
Fatigue	-0.58	0.002*
PROMIS PF-20	0.56	0.003*
Task-oriented functional tests		
Sit-to-stand	0.44	0.03*
Timed-up and go	-0.40	0.04*
Six-minute walk distance	0.66	0.0004*

Correlations of Fitbit average daily steps and demographics, myositis outcome measures, and task-oriented functional tests.



Agreement (Bland-Altman plot) and correlation (scatter plot) between FitBit and Actigraph measured average daily steps in patients wearing both devices at the same time for the same duration.

three functional tests supporting convergent validity (Table 1). Patients with inactive muscle disease had 49% higher daily step count than patients with active myositis. Fitbit and Actigraph demonstrated excellent agreement and strong correlation (Rho:0.97, ICC 0.96; Figure 1). Fitbit overestimated the daily step count in two-thirds of the patients with a median of 6.8% (3.8-14.6). The absolute change in daily steps at 6 months correlated moderately-strongly with absolute changes in MD-GDA, TIS and 6MWD.

Conclusion: Fitbit measured daily step counts are a reliable and valid measure of physical activity in a cohort of myositis patients. Daily step counts measured by Fitbit and Actigraph are in strong agreement with a slight overestimation by Fitbit. This pilot data suggests that Fitbit daily step counts have a potential to be used in clinical practice and trials to monitor physical activity in myositis patients, but larger studies are needed for further validation.

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Abstract Number: 1085

Pain in Myositis Is Associated with the Disease Activity

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SESSION INFORMATION

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Session Title: Muscle Biology, Myositis & Myopathies Poster

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Session Time: 9:00AM–11:00AM

	Pain VAS Baseline		Pain VAS Relative % change	
	Rho	*p* value	*Rho*	*p value*
Myositis disease activity measures				
Cutaneous disease activity	-0.09	0.51	0.18	0.55
Pulmonary disease activity	0.26	0.06	-0.37	0.36
Extra-muscular global disease activity	0.25	0.07	0.22	0.26
Creatine kinase	0.23	0.13	0.21	0.35
Muscle disease activity	0.31	0.02	0.52	0.006
Physician Global disease activity	0.37	0.007	0.37	0.05
MMT-9 score	-0.36	0.009	-0.26	0.18
Patient-reported disease activity	0.58	<0.0001	0.51	0.006
Fatigue 10 cm VAS	0.70	<0.0001	0.62	0.0008
Physical reported measures				
PROMIS PF	- 0.56	<0.0001	0.15	0.44
HAQ-DI	0.54	<0.0001	0.27	0.17
SF36 PCS	-0.61	<.0001	-0.53	0.008
SF36 MCS	-0.71	<.0001	-0.51	0.01
Task oriented functional measures				
Sit-to-stand (STS)	-0.21	0.14	-0.37	0.07
Timed-up and go (TUG)	0.08	0.54	0.42	0.02
Six-minute walk distance (6MWD)	-0.30	0.03	-0.31	0.13
Other measures				
Aldolase	0.60	0.0003	0.44	0.09

Table 1. Correlation of pain by VAS with myositis disease activity, functional and patient-reported outcomes at baseline and longitudinal change at 6 months.

Background/Purpose: Pain in myositis is poorly studied and multifactorial relating to muscle weakness, arthritis, myofasciitis, fibromyalgia or other co-morbidities. We sought to prospectively evaluate patient-reported pain, cross-sectionally and longitudinally in association with the collection of myositis core set measures of disease activity, patient reported and functional measures.

Methods: In a prospective, longitudinal observational study, we enrolled 50 myositis patients [dermatomyositis (DM), polymyositis (PM), necrotizing myositis (NM), and anti-synthetase syndrome (AS)] from February 2016 to April 2018. Patients with fibromyalgia and severe arthritis (except from myositis) were excluded. All subjects had a baseline and 6-month visit, where all myositis core set measures (CSM) [muscle enzymes, manual muscle testing (MMT-9), patient and physician (MD) global disease activity, extra-muscular disease activity and HAQ-DI], functional measures [Timed up and go (TUS), Sit to Stand (STS), 6 Minute Walk Distance (6-MWD)] and patient-reported outcomes [PROMIS-physical function (PF) and SF-36] were evaluated. Further, a standard 10 cm visual analogue scale(VAS) for pain and fatigue were recorded at both visits. A score between 0-3 was considered mild, >3-7 moderate, and >7-10 as severe pain. The phenotypic and disease activity measures of the cohort were correlated with pain (Spearman) at baseline visit. Longitudinal changes in pain at 6 months were correlated with the CSM and the functional and patient-reported outcomes. The change in pain was also evaluated if it improves with the published 2016 ACR/EULAR myositis response criteria graded as no, minimal, moderate or major improvement and the MD and patient global assessment of change. Strength of correlation was defined as weak (0.1-0.29), moderate (0.3-0.49) or strong (≥0.5).

Results: Twenty-four patients had DM, 9 NM, 6 PM and 11 AS with a mean age, 51.6 (±14.9) with 60% (n=30) females. The mean (SD) of pain was 2.7 (2.6), with 55.1% having mild pain, 40.8 % moderate pain and 4.08% severe pain at baseline. There was no significant difference in pain by disease subsets (DM vs. non-DM), autoantibody status, age at diagnosis or enrollment, or BMI. Pain was associated with having muscle weakness (MMT), disease duration and showed trends for association with active disease (as per MD) and female gender. At baseline, pain showed a strong correlation with fatigue, patient-reported disease activity, HAQ-DI, PROMIS PF, SF36 and aldolase and a moderate correlation with muscle weakness (MMT), MD global disease activity and 6MWD. Longitudinal analyses suggested that changes in pain showed a moderate to strong correlation with MD global disease activity, patient-reported disease activity, fatigue, SF36 and functional measures (TUG and STS). Pain improved significantly

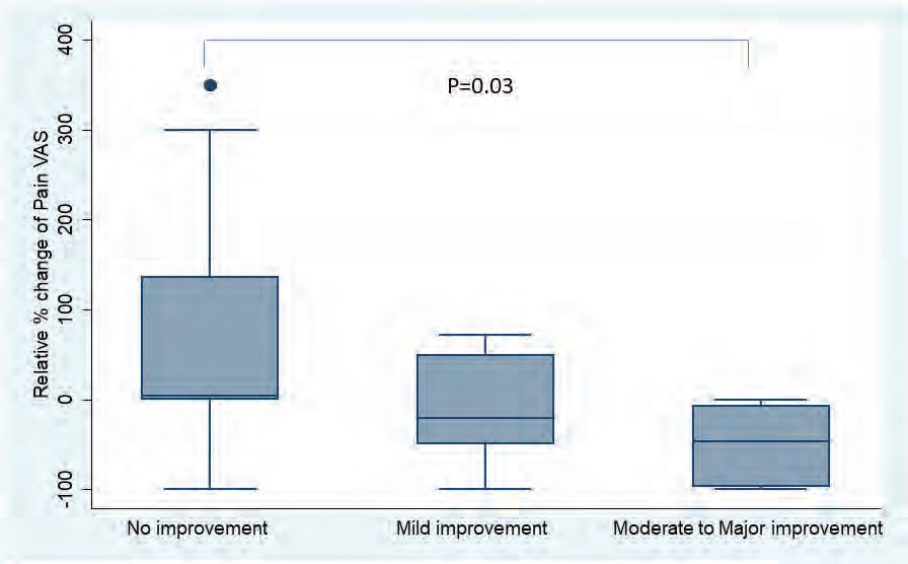

Figure 1. Relative percent change in VAS pain scores related to the ACR-EULAR myositis response criteria.

in patients with a moderate to major improvement, and similar non-significant trends were seen for the physician and patient reported change.

Conclusion: Pain in myositis is typically of mild to moderate severity and is moderately associated with the CSM and improves over time particularly in subjects demonstrating a moderate to major clinical response in published outcome metrics.

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Abstract Number: 1086

The Diagnostic Value and Clinical Significance of Myositis-Specific Antibodies in Patients Suspected to Have Autoimmune Myopathies and/or Autoimmune Rheumatic Diseases

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SESSION INFORMATION
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Background/Purpose: Myositis-specific antibodies (MSA) are thought to be highly specific in patients with idiopathic inflammatory myopathies.[1] However, in clinical practice these antibodies are frequently found in the absence of autoimmune myopathy which may lead at times to unnecessary interventions and treatments. We sought to determine the frequency of final clinical diagnoses, including autoimmune myopathy, in patients tested positive for one or more MSA.

Methods: We conducted a retrospective chart review on patients with documentation of MSA testing from November 1, 2007 to December 31, 2019 in our academic center.

Data extracted included clinical variables (myalgias, muscle weakness, interstitial lung disease (ILD) and history of malignancy within 3 years of positive antibody test) and laboratory tests including anti-nuclear antibodies and creatine kinase. Electromyographic testing and skeletal muscle biopsy studies were reviewed. Patients with a neuromuscular or autoimmune rheumatologic diagnosis were identified. A neuromuscular specialist determined the presence or absence of an autoimmune myopathy based on CK level, weakness, EMG and muscle biopsy findings when available. Frequency of associated clinical diagnoses in patients with positive MSA were calculated. In addition, we reviewed the frequency of certain clinical diagnoses specifically with anti-synthetase antibodies.

Results: We identified 47 subjects with positive MSA. Thirty-three (70%) were females. Thirty-four (72%) were Caucasian. Only 16 out of 47 subjects (34%) with positive MSA had an autoimmune myopathy. Among subjects with positive MSA but no autoimmune myopathy (n=31), 26 (83.8%) had ILD and/or a rheumatologic diagnosis and 5 (16.1%) had neither. In patients with autoimmune myopathy (n=16), there was an overlap with ILD and/or rheumatologic diagnosis in 5 patients (31.25%). Of all subjects with positive MSA (n=47), 31 (65.9%) had a rheumatologic diagnosis

Positive myositis specific antibody	Number of patients (n = 47)
With autoimmune myopathy n= 16	
Autoimmune myopathy alone	11 (68.75)
Autoimmune myopathy + ILD	2 (12.5%)
Autoimmune myopathy + Rheumatologic diagnosis	1 (6.25%)
Autoimmune myopathy + both ILD and rheumatologic diagnosis	2 (12.5%)
Without autoimmune myopathy n= 31	
ILD alone	5 (16.1%)
Rheumatologic diagnosis alone	7 (22.5%)
Both ILD and Rheumatologic diagnosis	14 (45.1%)
Patient with no ILD or rheumatologic diagnosis	5 (16.1%)

Positive myositis-specific antibodies in comparison to clinical diagnoses

and/or ILD. Five (10.6%) did not have a rheumatologic diagnosis, autoimmune myopathy or ILD. Anti-synthetase antibodies were found in 19 subjects. These antibodies were associated with autoimmune myopathy in 7 subjects (36.8%). Anti-synthetase syndrome was diagnosed in only 5 (26.3%) with positive anti-synthetase antibodies while a rheumatologic diagnosis was present in 12 (63.1%). Among patients with positive anti-synthetase antibodies and autoimmune myopathy (n=7), perimysial pathology on muscle biopsy was found in 4 (57.1%).

Conclusion: Despite the reported specificity of MSA for the diagnosis of autoimmune myopathy, we observed that most MSA positive subjects in our cohort did not have this diagnosis. We also found that rheumatologic diagnoses and ILD were frequently found in patients with positive MSA with or without autoimmune myopathy. Similarly, anti-synthetase antibodies did not necessarily indicate the presence of anti-synthetase syndrome or autoimmune myopathy.

Disclosure: S. El Chami, None; **C. Williams**, None; **G. Noaiseh**, None; **A. Bath**, None; **D. Jabari**, None.

Abstract Number: 1087

Plasma-derived Extracellular Vesicles Induced STING-mediated Proinflammatory Effects in Dermatomyositis

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Background/Purpose: Dermatomyositis (DM) is an acquired inflammatory myopathy characterized by chronic skin inflammation. The pathogenesis of DM is still unclear. Extracellular vesicles (EVs) are lipid bilayer membrane vesicles existing in various bodily fluids and implicated in the pathogenesis of autoimmune diseases. As type I interferons, specifically IFN-b, are uniquely elevated in DM, and Stimulator of interferon genes (STING) works as a critical sensor and adaptor in type I IFN signaling, we hypothesized that EVs derived from DM patients' plasma might trigger STING-mediated proinflammatory effects.

Methods: DM patients were recruited in the dermatology clinic at University of Pennsylvania. Peripheral blood mononuclear cells (PBMCs) were isolated by Ficoll gradient. EVs derived from plasma were isolated via ultracentrifugation. The supernatant was harvested for ELISA and the lysed cells were collected for Western blot after HC-derived PBMCs were stimulated by EVs.

Results: Here we found that DM patients' plasma derived EVs triggered cytokine release (IFNb: (30.24±0.65) vs control (2.683±0.35); TNFα: (1451±98.40) vs control (16.75±1.407); IL6: (945.0±57.40) vs control (0.0±0.0)pg/mL; n=6) with STING phosphorylation. Inhibition of STING significantly attenuated DM patients' plasma-derived EVs-triggered cytokine production (IFNb: (21.58±2.22) vs (28.34±1.73); TNFα: (434.8±94.50) vs (919.1±133.0); IL6: (611.5±54.22) vs (844.2±73.60)pg/mL; n=6) via suppressing STING and its down-stream signal TBK1, IRF3, and NFκB phosphorylation. Besides, TBK1 inhibitors Amlexanox and MRT67307 also suppressed DM patients' plasma derived EVs-induced IFNb release by inhibiting TBK1 phosphorylation. To further explore whether STING signaling pathway activation and the proinflammatory effects were caused by EVs-captured dsDNA, EVs were pretreated with Triton X-100 and DNase I to digest DNA. Triton X-100 and DNase pretreatment decreased EVs-triggered cytokine release (IFNb: (4.113±2.08) vs (28.94±5.473); TNFα: (19.00±19.00) vs (1361±293.6); IL6: (210.7±103.6) vs (1020±43.86)pg/mL; n=3-6) and STING activation. To specifically digest dsDNA, EVs were also pretreated with dsDNase. Triton X-100 and dsDNase pretreatment also decreased EVs-triggered cytokine release (IFNb: (1.893±1.893) vs (28.94±5.473); TNFα: (290.3±57.03) vs (1361±293.6); IL6: (617.6±127.4) vs (1020±43.86)pg/mL; n=3-6) and STING activation..

Conclusion: EVs derived from plasma trigger STING-mediated proinflammatory effects in DM. The STING signaling pathway is activated during EVs triggering of proinflammatory effects and was at least partially mediated by dsDNA captured by EVs. Targeting STING pathway might provide insight into a potential therapeutic approach for DM.

Disclosure: Y. Li, None; **C. Bax**, None; **J. Patel**, None; **A. Ravishankar**, None; **K. Desai**, None; **M. Zeidi**, None; **M. Bashir**, None; **V. Werth**, Biogen, 2, 5.

Abstract Number: 1088

Recruitment Rates of Virtual Remote Research (Tele-Research) in Myositis

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: There is a paucity of randomized, controlled clinical trials in myositis. Subject enrollment and retention in clinical trials for this rare, heterogeneous disease has always been a major challenge. There is an urgent need for innovative recruitment and clinical trial strategies including a virtual and remote approach. Our aim was to compare the effectiveness of recruitment, enrollment and retention of a traditional center-based cohort (CBC) to a novel remote tele-research cohort (TRC) using state-of-the-art tele-medicine, wearable devices and mobile app.

Methods: The TRC was recruited remotely across the U.S. using a mobile app/website while the CBC was derived from two myositis centers in a prospective observational myositis study. Subjects in both cohorts were followed concurrently and longitudinally for 6 months using the same protocol including inclusion criteria, study visits and data collection. However, the TRC and CBC had 2 different recruitment methodologies: online/social media recruitment in the TRC with the help of myositis patient support organizations (The Myositis Association, Myositis Support & Understanding) vs. traditional clinic-based recruitment in the CBC which included directly approaching myositis clinic patients or traditional advertisement to local/regional subspecialists. Study visits included a baseline and 6-month physician evaluation conducted through telemedicine in the TRC with monthly patient-driven data collection through a mobile app/website. Conversely, the CBC utilized conventional in person clinic visits and monthly data collection on

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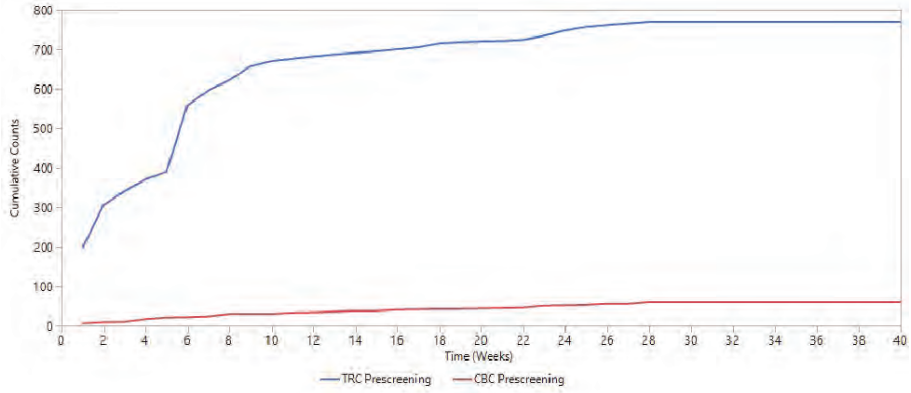

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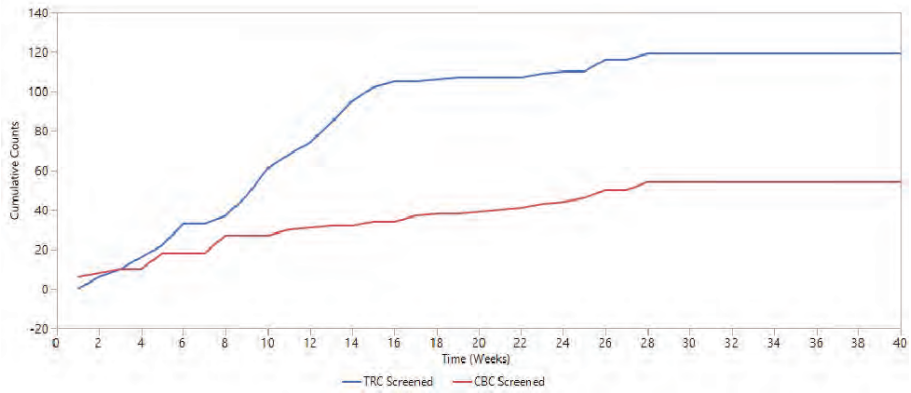

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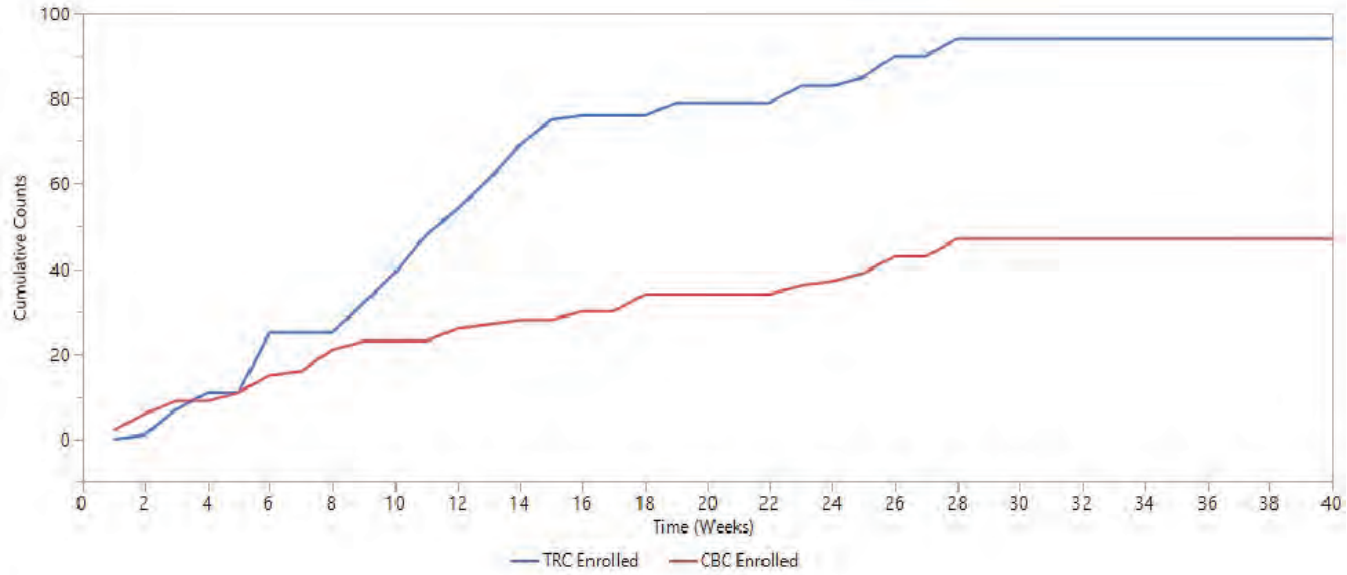

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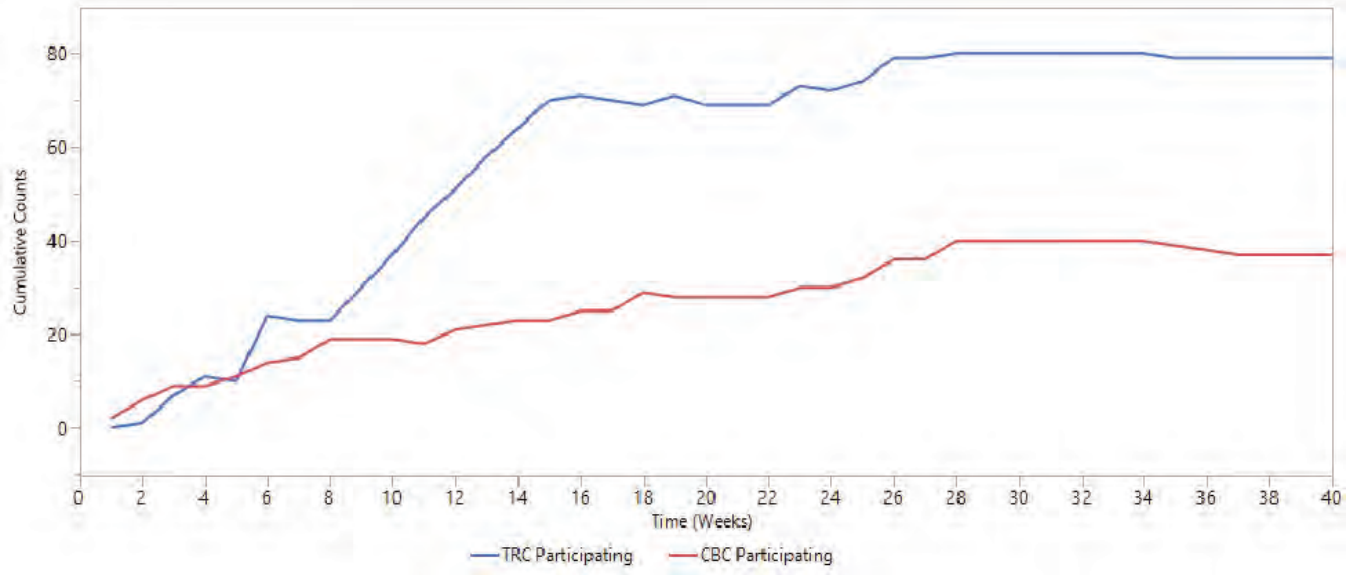

(A) Pre-screening, (B) screen, (C) enrollment, and (D) active participation rates in the TRC vs. CBC

paper forms or Tablets. The rates and success of prescreening, screening, enrollment and retention were compared between 2 parallel cohorts with competitive enrollment using time to event, t-test and Chi-square analysis.

Results: The TRC enrolled 94 subjects compared to only 47 in the CBC during the recruitment period of 40 weeks. Demographics and disease in both cohorts were similar (Table 1). In the TRC, 700 subjects completed prescreening on the app or website, and 626 (81%) met preliminary eligibility. In comparison, 205 patients were approached for prescreening in the CBC but only 60 agreed to undergo prescreening of which 56 (93.3%) met preliminary eligibility. During the enrollment process, 120 TRC participants were screened by physician review of medical records lead-

Demographics and Disease subsets	Tele-Research Cohort (TRC)	Center Based Cohort (CBC)
Gender (Female %)	76%	70%
Race (Caucasians %)	87%	79%
Age range	25-78	25-80
Mean (SD) age	54.5 (13.9)	56.9 (12.5)
Disease subset		
Dermatomyositis	52.3%	53.8%
Polymyositis	39.8%	35.8%
Necrotizing Myopathy	7.9%	10.3%

Table 1. Demographics and disease subsets in both tele-research cohort (TRC) and center based cohort (CBC).

ing to 94 (78%) being enrolled, while only 54 CBC subjects underwent screening and 47 (87%) were enrolled. The cumulative number and rate of prescreening, screening and enrollment was faster and 2-3 folds higher in the TRC compared to CBC over the same recruitment period (Figure 1). Prescreen to preliminary eligibility as well as screen failure rates were similar in both cohorts. Retention rates were similar in both cohorts, with only 14 (15%) drop outs in the TRC vs. 7 (15%) in the CBC.

Conclusion: Recruitment and enrollment for a virtual TRC was far superior to a traditional center-based approach, with similar screen failure and retention rates in this observational study. Further, the TRC recruitment techniques using social media and online approaches for a virtual TRC were surprisingly efficient and should be considered for rare diseases such as myositis.

Disclosure: S. Moghadam-Kia, None; **C. Oddis**, Genentech, 2; **S. Venturupalli**, None; **S. Mahajan**, None; **D. Scaramangas Plumley**, None; **D. Ascherman**, None; **N. Neiman**, None; **F. Onelangsy**, None; **D. Koontz**, None; **K. Goldby-Reffner**, None; **S. Dzanco**, None; **L. Zhu**, None; **R. Aggarwal**, Octapharma, 5, Bristol Myers Squibb, 2, 5, Abbvie, 5, Mallinckrodt, 2, 5, Pfizer, 2, Csl Behring, 5, Kezar, 5.

Abstract Number: 1089

Intermuscular Adipose Tissue in Patients with Systemic Lupus Erythematosus

Jorge Gamboa[1], Daniel Carranza Leon[1], Rachelle Crescenzi[1], Adriana Marton[2], Annette Oeser[1], Cecilia Chung[1], Jens Titze[2], Michelle Ormseth[1] and C. Michael Stein[1], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Duke NUS Medical School, Singapore, Singapore

SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Muscle Biology, Myositis & Myopathies Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic lupus erythematosus (SLE) have reduced physical activity and frequently complain of fatigue. Exercise reduces fatigue in patients with SLE; however, the mechanism of the exercise-induced reduction in fatigue is unknown. Exercise also improves muscle quality, particularly by reducing intermuscular adipose tissue (IMAT). To date, no study has evaluated the presence of IMAT in patients with SLE. Thus,

Table 1.

Participant Characteristics

Parameter	Controls	SLE	p-value
Age	35 (26, 58)	38 (31, 54)	0.78
Sex (Female), N (%)	24 (85.7)	20 (87)	0.61
Race (African American), N (%)	6 (21.4)	5 (21.7)	0.52
BMI	22.7 (22.4, 23.8)	26.2 (22.9, 31.7)	0.16
Creatinine	0.74 (0.65, 0.81)	0.79 (0.63, 0.93)	0.99
History of hypertension, N (%)	2 (7.1)	8 (34.8)	0.02
History of diabetes, N (%)	0 (0)	1 (2)	0.45
Glucose	86 (75, 95)	83 (78, 98)	0.74
Corticosteroid use, N (%)	1 (3.7)	13 (56.5)	<0.001
PR-Fatigue	2 (0,5)	48.5 (28, 62.5)	<0.001
PR-physical activity (miles)	5.0 (3.0, 5.0)	1.1 (0.2, 2.0)	<0.001

BMI, body mass index; PR, patient-reported

Table 1

in this study, we hypothesize that IMAT is increased in patients with SLE, and it is associated with patient-reported physical activity and fatigue.

Methods: In a cross-sectional study, we evaluated 51 participants (23 patients with SLE and 28 controls). IMAT was evaluated in the calf muscles using sequential T1-weighted and Dixon magnetic resonance images (MRI). Patient-reported physical activity and fatigue were evaluated using visual analog scales.

Results: Patients with SLE and controls were similar in terms of age, sex, race, body mass index (BMI), and renal function (Table 1). Corticosteroid and antihypertensive medication use was higher in patients with SLE than in controls. IMAT accumulation, expressed as the ratio of IMAT area to total muscle size, was significantly higher in patients with SLE than in controls (7.92%, 4.51-13.39%, *vs.* 2.65%, 1.15-4.61%, median, IQR, p< 0.001, Figure 1). These differences between the groups remained significant after adjustment for age, race, and BMI. Corticosteroid use may affect the accumulation of IMAT, however, in patients with SLE IMAT accumulation did not differ significantly among corticosteroid users and non users p=0.48. Patient-reported fatigue and physical activity were higher and lower, respectively, in patients with SLE than in controls (Table 1). IMAT was positively correlated with patient-reported fatigue (rho=0.52, p< 0.001) and inversely correlated with patient-reported walking distance (rho=-0.60, p< 0.001). Physical

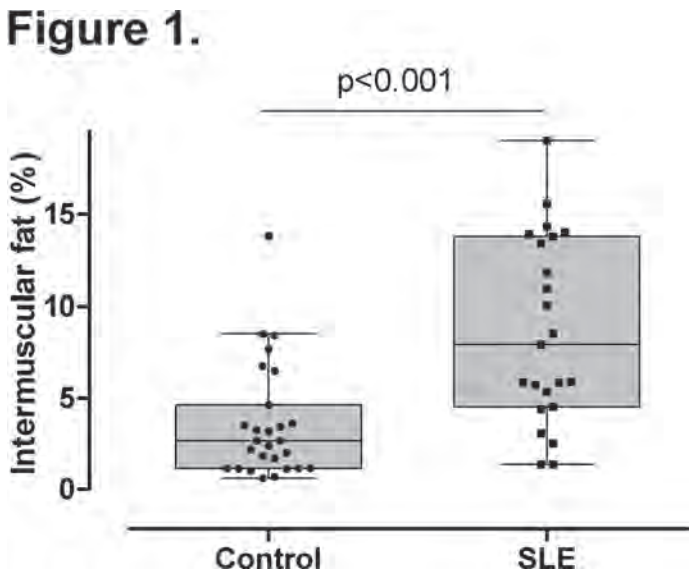

Figure 1

activity may affect IMAT accumulation, however, the difference in IMAT between controls and patients with SLE remains significant after adjusting for the reported physical activity (p=0.015).

Conclusion: Patients with SLE have greater IMAT accumulation than controls. Increased IMAT is associated with greater fatigue and lower physical activity. Future studies should evaluate the effectiveness of interventions that improve muscle quality to alleviate fatigue in patients with SLE.

Disclosure: J. Gamboa, None; **D. Carranza Leon**, None; **R. Crescenzi**, None; **A. Marton**, None; **A. Oeser**, None; **C. Chung**, None; **J. Titze**, None; **M. Ormseth**, None; **C. Stein**, None.

Abstract Number: 1090

Abnormal HDL Antioxidant Function Is Associated with Longitudinal Change in Lung Physiology in Dermatomyositis/Polymyositis Associated Lung Disease

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Muscle Biology, Myositis & Myopathies Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a leading cause of death in patients with dermatomyositis (DM) and polymyositis (PM). We previously reported abnormal anti-oxidant function of HDL in DM/PM patients with ILD, which was associated with higher levels of oxidized fatty acids in HDL and worse lung function. The current project aimed to evaluate the predictive value of baseline HDL antioxidant function for change in lung physiology on longitudinal follow-up in DM/PM patients.

Methods: To determine the anti-oxidant capacity of HDL, the change in fluorescence intensity as a result of the oxidation of 2',7'-dichlorodihydrofluorescein diacetate to 2',7'-dichlorofluorescein in incubations with a standard LDL in the absence or presence of the patient HDL was assessed and the HDL inflammatory index (HII) calculated (*Arthritis Rheum 60(10):2870-9,2009*). Change in forced vital capacity (Δ FVC) at the follow-up visit was calculated as the difference between most recent and baseline FVC divided by baseline FVC. Linear regression models of baseline DM/PM clinical characteristics with ΔFVC as the outcomewere constructed in the total DM/PM group and in patients only with DM/PM-ILD; all models were adjusted for time between baseline and follow-up FVC assessment. Multivariate linear regression analysis examining an association of HII with ΔFVC included other clinical variables that were significantly associated with ΔFVC in univariate analysis.

Results: A total of 45 DM/PM patients with baseline HII assessments and follow-up FVC measurements were included in the study (Table 1). Mean (SD) follow up time between PFTs was 37(31) months. In univariate analysis, a higher baseline HII consistent with worse antioxidant function of HDL was associated with improvement in FVC over the follow-up period. In addition, baseline higher daily prednisone dose, fewer steroid sparing agents, the absence of mycophenolate use, and lower FVC and TLC were associated with greater improvement in FVC (Table 1). Higher baseline HII remained significantly associated with greater ΔFVC over time after multivariate adjustment.

Table 1. Association between baseline predictors and change in FVC adjusted for time between PFTs using linear regression

	DM/PM total (n=45)			DM/PM-ILD (n=34)		
Baseline predictors	**Mean(SD) or N(%)**	**β**	**P**	**Mean(SD) or N(%)**	**β**	**P**
Demographics						
Age, years	51(13)	-0.13	0.76	51(12)	-0.23	0.68
Sex, Female	25(56)	-6.87	0.53	20(57)	-9.49	0.50
Race, White	19(43)	7.25	0.52	11(32)	12.20	0.42
Ethnicity, hispanic	6(14)	-7.17	0.65	5(13)	-4.92	0.81
Other Clinical variables						
Ever smoker, yes	9(20)	5.06	0.70	7(20)	7.48	0.94
BMI, kg/m²	27(6)	-1.68	0.06	28(6)	-2.00	0.05
History of MI	2(4)	-0.07	0.99	2(5)	-4.38	0.85
Hypertension	6(13)	-4.92	0.75	5(14)	-9.27	0.63
Diabetes	4(9)	-15.99	0.39	3(9)	-14.13	0.56
IIM variables						
IIM type, DM	34(76)	11.59	0.34	26(74)	12.74	0.45
Disease duration, months, median (IQR)	10(1-44)	-0.08	0.25	14(1-59)	-0.09	0.24
MD global disease activity VAS, 0-100mm	43(23)	0.08	0.74	42(24)	0.11	0.69
MD global disease activity Likert, 0-4, median (IQR)	2(1-3)	2.44	0.71	2(1-3)	2.83	0.73
MD global disease damage VAS, 0-100mm	40(21)	0.06	0.81	46(17)	-0.17	0.68
MD global disease damage Likert, 0-4 median (IQR)	2(1-2)	1.59	0.81	2(2-2)	-6.63	0.57
CPK, 10U/L	547(1215)	-0.01	0.80	350(518)	0.06	0.65
Aldolase, U/L	13(15)	0.17	0.71	11(10)	1.31	0.20
Sedimentation rate, 10mm/hr	32(26)	-0.11	0.61	34(28)	-0.14	0.59
Hs-CRP,mg/L	6.9(10.4)	0.33	0.52	7.8(11.5)	0.27	0.66
Myositis Autoantibodies						
Antisynthetase ab	19(42)	10.55	0.38	18(51)	13.50	0.30
Anti-MDA5 ab	7(16)	5.95	0.70	6(17)	12.53	0.44
Other MSA/MAA†	11(24)	ref		6(17)	ref	
Unidentified ab	6(13)	3.59	0.82	4(11)	8.37	0.64
Medications						
IVIG	10(22)	-9.44	0.46	7(20)	-15.13	0.37
Mycophenolate Mofetil	18(40)	**-20.79**	**0.04**	14(40)	**-27.69**	**0.04**
Azathioprine	4(9)	-11.70	0.53	4(11)	-14.39	0.50
Methotrexate	4(9)	-7.90	0.67	2(6)	-15.04	0.61
Plaquenil	8(18)	-10.54	0.45	6(17)	-14.13	0.43
Cyclophosphamide	2(4)	-11.34	0.66	2(6)	-13.79	0.64
Rituximab	2(4)	-8.27	0.75	1(3)	-12.41	0.76
Prednisone dose, mg/day	21(24)	**0.46**	**0.04**	22(25)	0.54	0.06
Number of steroid sparing agents, median (IQR)	1(0-2)	**-12.21**	**0.03**	1(0-2)	**-16.04**	**0.02**
Statin	5(11)	-15.21	0.36	4(11)	-20.37	0.32
ILD variables						
ILD, yes	34(76)	10.11	0.43	34(100)	-	-
FVC % predicted	71(21)	**-0.71**	**0.01**	65(18)	**-1.04**	**0.01**
TLC % predicted	76(23)	**-0.38**	**0.045**	67(20)	-0.49	0.10
DLCO Hg % predicted	63(24)	-0.12	0.60	57(22)	-0.01	0.95
Lipid measures						
Total cholesterol, 10mg/dl	217(56)	-0.23	0.84	218(51)	0.28	0.88
LDL-C, 10 mg/dl	136(52)	-0.06	0.95	129(51)	0.23	0.86
HDL-C, 10 mg/dl	61(27)	0.07	0.97	64(26)	-0.32	0.91
Triglycerides, 10 mg/dl	183(142)	0.23	0.58	181(142)	-0.31	0.57
HDL Inflammatory Index (HII)	0.76(0.60)	12.39	0.14	0.74(0.50)	**29.78**	**0.03**

† Myositis specific autoantibody testing available in 68/72 patients, other MSA/MAA includes Mi2 n=6, MJ n=5, Ro n=4, SRP n=4, HMGCR n=3, Ku n=1, RNP n=1, SAE n=1

Table 2. Multivariate linear regression models for change in FVC % predicted in IIM cohort (n=45)

Variables	Regression Coefficient (95% CI)	P value
Time between PFTs	0.14 (-0.15,0.44)	0.33
Prednisone dose	**0.44(0.08,0.79)**	**0.02**
# of steroid sparing agents	**-14.20(-23.28,-5.12)**	**0.003**
Baseline FVC	**-0.74(-1.17,-0.31)**	**0.001**
HDL Inflammatory Index	**16.20(2.55,29/84)**	**0.02**

TLC was not included as it was colinear with FVC, Mycophenolate use was not included as it was colinear with # of steroid sparing agents

Conclusion: Abnormal antioxidant function of HDL is associated with changes in lung physiology over time. We hypothesize that a higher baseline HII may identify patients with active, reversible lung disease that may be more likely to improve with treatment over time. Further studies are needed to determine the consequences of abnormal antioxidant function of HDL to the progression of DM/PM associated lung disease.

Disclosure: S. Bae, None; **J. Wang**, None; **A. Shahbazian**, None; **C. Charles-Schoeman**, AbbVie, 2, 5, Regeneron-Sanofi, 5, Gilead, 5, Bristol-Myers Squibb, 2, Pfizer Inc, 2, 5.

Abstract Number: 1091

A Computer-Aided Diagnostic System for Quantitative Scoring of Extent of Interstitial Lung Disease (ILD) in Dermatomyositis/Polymyositis Associated ILD

Sangmee Bae[1], Andrea Oh[2], Grace Kim[3], Jonathan Goldin[3] and Christina Charles-Schoeman[4], [1]University of California Los Angeles, Los Angeles, CA, [2]National Jewish Health, Denver, CO, [3]University of California, Los Angeles, Los Angeles, [4]University of California, Los Angeles, Los Angeles, CA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Muscle Biology, Myositis & Myopathies Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) occurs in up to 80% of patients with dermatomyositis (DM) and polymyositis (PM), and is a leading cause of morbidity and mortality (Lung. 2016;194(5):733-737). The current study validates the use of a computer aided diagnostic system to quantitatively score ILD on high-resolution computed tomography (HRCT) scans (Clin Exp Rheumatol 2010;28, S26-35) in a cohort of DM/PM patients. The predictive value of the baseline quantitative ILD score on change in lung function at follow-up is also examined.

Methods: HRCT images were retrospectively analyzed from DM/PM patients in our longitudinal myositis cohort who had thin-section, full inspiration images available for review. The QILD is the sum of all abnormally classified scores, which include quantitative scores for reticulations/fibrosis (QLF) and ground glass opacity (QGG). Quantitative ILD scores (QGG, QLF, QILD) were assessed for whole lung, and for zone of maximum involvement. Linear regression models were constructed in patients with DM/PM associated ILD, as well as in total DM/PM patients with QILD scores to evaluate the association between baseline variables including QILD scores and the relative change in forced vital capacity (FVC) at the follow-up visit. Change in FVC was calculated as the difference between most recent and baseline FVC divided by baseline FVC. Mean (SD) follow-up time between PFTs was 37(31) months.

Results: A total of 72 DM/PM patients with baseline and follow-up HRCT scans were included in the analysis. Quantitative ILD scores showed predominance of ground glass rather than fibrosis with most of the involvement in lower lung zones, consistent with nonspecific interstitial pneumonia (NSIP) pattern. The quantitative ILD scores (QGG, QLF, QILD) demonstrated good concordance with lung physiology (FVC, TLC and DLCO) (correlation coefficient between -0.41 to -0.70, $p < 0.001$ for all). When analyzed by myositis autoantibody subgroups, patients with antisynthetase and anti-MDA5 antibodies had the highest fibrosis score (QLF) and total ILD score (QILD) (Table 1).

Linear regression models demonstrated that higher baseline quantitative ILD scores were associated with greater improvement in FVC at follow-up (Table 2). These relationships remained strong after multivariate adjustment of oth-

Table 1. Quantitative ILD scores of whole lung in myositis autoantibody groups

Ab group	N	QGG whole lung	QLF whole lung	QILD whole lung
ASS	22	14.3(6.5)*	8.8(7.4)*	23.3(13.0)*
Anti-MDA5 ab	11	14.5(10.9)	8.2(7.9)*	22.9(14.5)*
Other MSA/MAA	26	10.6(7.7)	2.2(4.1)	13.3(11.0)
Unidentified ab	7	14.9(11.2)	6.5(7.2)	21.5(17.2)
No ab	2	13.9(16.8)	2.2(2.8)	16.1(19.6)

*P<0.05 compared to other MSA/MAA group by Wilcoxon
ASS, Antisynthetase antibodies; other MSA/MAA, other myositis specific associated antibodies and myositis associated antibodies (anti-Mi2, anti-MJ, anti-Ro, anti-SRP, anti-HMGCR, anti-Ku, anti-RNP, anti-SAE)

Table 2. Association between baseline predictors and change in FVC using linear regression adjusted for time between PFT

Baseline Predictors	Mean (SD) or N(%)	Change in FVC	
		DM/PM-ILD (n=44)	Total (n=72)
		β (95% CI)	β (95% CI)
Age, years	51(14)	-0.26(-1.29,0.75)	-0.16(-0.92,0.60)
Sex, Female	45(63)	-7.68(-34.46,19.10)	-5.55(-26.58,15.48)
Race, White	33(47)	10.04(-18.70,38.79)	5.88(-15.57,27.33)
Ethnicity, hispanic, n(%)	11(16)	-5.07(-44.61,34.46)	-7.38(-38.7,23.95)
Ever smoker, n(%)	12(17)	7.48(-24.56,39.51)	6.41(-18.48,31.31)
Body mass index, kg/m2	27(6)	-2.00(-4.01,0.01)	-1.71(-3.44,0.02)
Hypertension, n(%)	12(17)	-9.66(-44.64,25.33)	-5.40(-33.74,23.04)
Diabetes, n(%)	10(14)	-14.22(-61.97,33.52)	-16.15(-52.50,20.19)
IIM variables			
IIM type, DM	54(75)	12.74(-17.36,42.85)	11.74(-11.99,35.47)
Disease duration, years, median(IQR) †	0.8(0.1-2.8)	-0.09(-0.25,0.06)	-0.08(-0.21,0.05)
MD global activity VAS (0-100mm)	43(23)	0.13(-0.42,0.68)	0.10(-0.35,0.54)
MD global disease activity Likert (0-4), median(IQR)	2(1-3)	1.49(-13.34,16.32)	1.16(-11.05,13.37)
MD global damage VAS (0-100mm)	35(23)	-0.12(-0.87,0.63)	0.08(-0.43,0.58)
MD global disease damage Likert, median(IQR)	2(1-2)	-5.52(-27.77,16.72)	1.70(-11.60, 15.00)
Laboratory variables			
CPK, U/L	600(1656)	0.01(-0.02,0.03)	-0.001(-0.01,0.01)
Aldolase, U/L	13(24)	1.27(-0.67,3.21)	0.16(0.77,1.10)
ESR, mm/hr	33(28)	-0.14(-0.64,0.35)	-0.12(-0.53,0.29)
hsCRP,mg/L	6.8(10.6)	0.25(-0.93,1.42)	0.32(-0.70,1.33)
Myositis autoantibodies			
Antisynthetase antibody	22(31)	-5.28(-34.28,23.72)	0.68(-23.17,21.81)
Anti-MDA5 antibody	11(15)	-9.45(-49.17,30.27)	-6.46(-36.25,23.33)
Other¶	34(47)	ref	ref
Medications			
Prednisone dose, median(IQR)	7.5(0-40)	0.51(-0.00,1.04)	**0.45(0.03,0.86)***
# of steroid sparing agents, median(IQR)	1(0-2)	**-15.29(-28.14,2.43)***	**-11.75(-22.15,1.34)***
IVIG	10(23)	-15.11(-48.03,17.81)	-9.64(-34.29,5.01)
Mycophenolate Mofetil	17(39)	-24.82(-49.74,0.10)	-18.79(-38.64,1.05)
Azathioprine	7(16)	-14.48(-56.07,27.11)	-11.89(-48.24,24.46)
Methotrexate	2(5)	-15.20(72.92, 42.52)	-8.15(-44.49,28.18)
Plaquenil	7(16)	-14.13(-50.05,21.80)	-10.72(-37.73,16.28)
Cyclophosphamide	2(5)	-13.92(-70.97,43.12)	-11.55(-61.67,38.57)
Rituximab	1(2)	-12.62(-92.94,67.70)	-8.63(-59.88,42.62)
Pulmonary function test			
FVC, %predicted	77(22)	**-0.87(-1.50,-0.23)****	**-0.66(-1.12,-0.21)****
TLC, %predicted	82(23)	-0.50(-1.07,0.07)	**-0.39(-0.74,-0.02)***
DLCOHg, %predicted	70(23)	-0.01(-0.65,0.63)	-0.12(0.58,0.34)
Quantitative ILD scores			
GG, whole lung	13.4(9.0)	**1.69(0.20,3.18)***	**1.49(0.36,2.62)***
GG, zone of maximum involvement	19.4(11.9)	**1.38(0.22,2.48)***	**1.10(0.28,1.93)***
QLF, whole lung	6.0(7.1)	**2.50(0.81,4.20)****	**2.23(0.91,3.55)****
QLF, zone of maximum involvement	16.5(17.2)	-0.14(-0.92,0.64)	0.03(-0.55,.61)
QILD, whole lung	19.6(14.4)	**1.33(0.45,.22)****	**1.11(.44,1.77)****
QILD, zone of maximum involvement	36.3(24.8)	0.24(-0.38,0.86)	0.25(0.16,0.66)

*p<0.05 **p<0.01 †DM/PM or ILD duration, whichever that started first ¶ MSA testing in 68/72 patients, other includes other MSA/MAA (Mi2 n=6, MJ n=5, Ro n=4, SRP n=4, HMGCR n=3, Ku n=1, RNP n=1, SAE n=1), unidentified ab (n=7) and no autoab (n=2)

Table 3. Multivariate linear regression models for change in FVC % predicted in IIM cohort (n=72)

Variables	β	P	β	P	β	P	β	P
Time between PFTs	**0.34**	**0.04**	0.23	0.09	**0.31**	**0.04**	0.14	0.35
Prednisone dose	0.36	0.06	**0.57**	**0.001**	**0.42**	**0.02**	**0.43**	**0.02**
# of steroid sparing agents	**-10.78**	**0.04**	-8.69	0.06	**-9.59**	**0.047**	**-12.75**	**0.01**
QGG	1.12	0.05	-	-	-	-	-	-
QLF	-	-	**2.50**	**<0.001**	-	-	-	-
QILD	-	-	-	-	**1.00**	**0.003**	-	-
Baseline FVC	-	-	-	-	-	-	**-0.70**	**0.001**
R^2	0.33		0.48		0.41		0.43	

er baseline variables including baseline daily prednisone dose and number of steroid sparing agents (Table 3). The predictive value of QLF, QILD models assessed by R^2 was comparable to the model using baseline FVC, suggesting quantitative ILD scores may be used as a quantitative outcome measure for DM/PM-ILD severity.

Conclusion: Quantitative ILD scores can provide an objective quantitative tool for assessing ILD severity in DM/PM-ILD and are associated with clinically meaningful longitudinal outcomes.

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Abstract Number: 1092

NMR-Based Serum Metabolomics, Is It Different in Clinico-Serological Clusters of Idiopathic Inflammatory Myositis?

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Muscle Biology, Myositis & Myopathies Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic inflammatory myositis (IIM) are rare and heterogenous. Myositis specific antibodies (MSA) show mutual exclusivity and identify specific clinical phenotypes[1]. Most biomarker studies are limited by the number of patients of individual phenotypes. Since serum metabolomics can distinguish active from inactive myositis[2,3], we determined if the serum metabolomic profile is distinctive in clinical and antibody-based phenotypes.

Methods: Sera (n=116) from IIM (ACR-EULAR criteria, 34 years (23.5 - 50.5 IQR), M/F 28:88] were compared with healthy controls [n=18, age= 44 (35-50) years, M/F-8:10]. Clinical phenotypes were defined as previously described[4] and antibody by presence of MSA and MAAs. In addition, those with 3 of 5 ASSD features were labelled as clinical ASSD for analysis.

Metabolic profiles were obtained at 800 MHZ NMR spectrometer and compared using multivariate partial least-squares discriminant analysis (PLS-DA). The discriminatory metabolites were identified based on variable importance in projection (VIP) statistics and further evaluated for statistical significance (p-value < 0.05). Metaboanalyst® was used for analysis.

Results: Serum metabolites were no different based on clinical diagnosis (Figure 1a) or in those with ILD, arthritis, bulbar weakness, amyopathic presentation and skin rashes (Gottron's, heliotrope, mechanic's hands, cutaneous ulcers and photosensitivity,) than individuals without these (Figure 1b-e). IIM with a clinical ASSD without ARS was similar to ARS group (Figure 1f). Metabolome clusters defined by distinct MSAs also exhibited significant overlap (Figure 2a-e). The presence and absence of MAA (Figure 2f) and ANA (Figure 2b) were not discriminative in the metabolome.

Conclusion: Serum metabolome does not reflect change with clinico-serologic phenotype in IIM, suggesting distinctive value as biomarker of disease activity uninfluenced by heterogeneity.

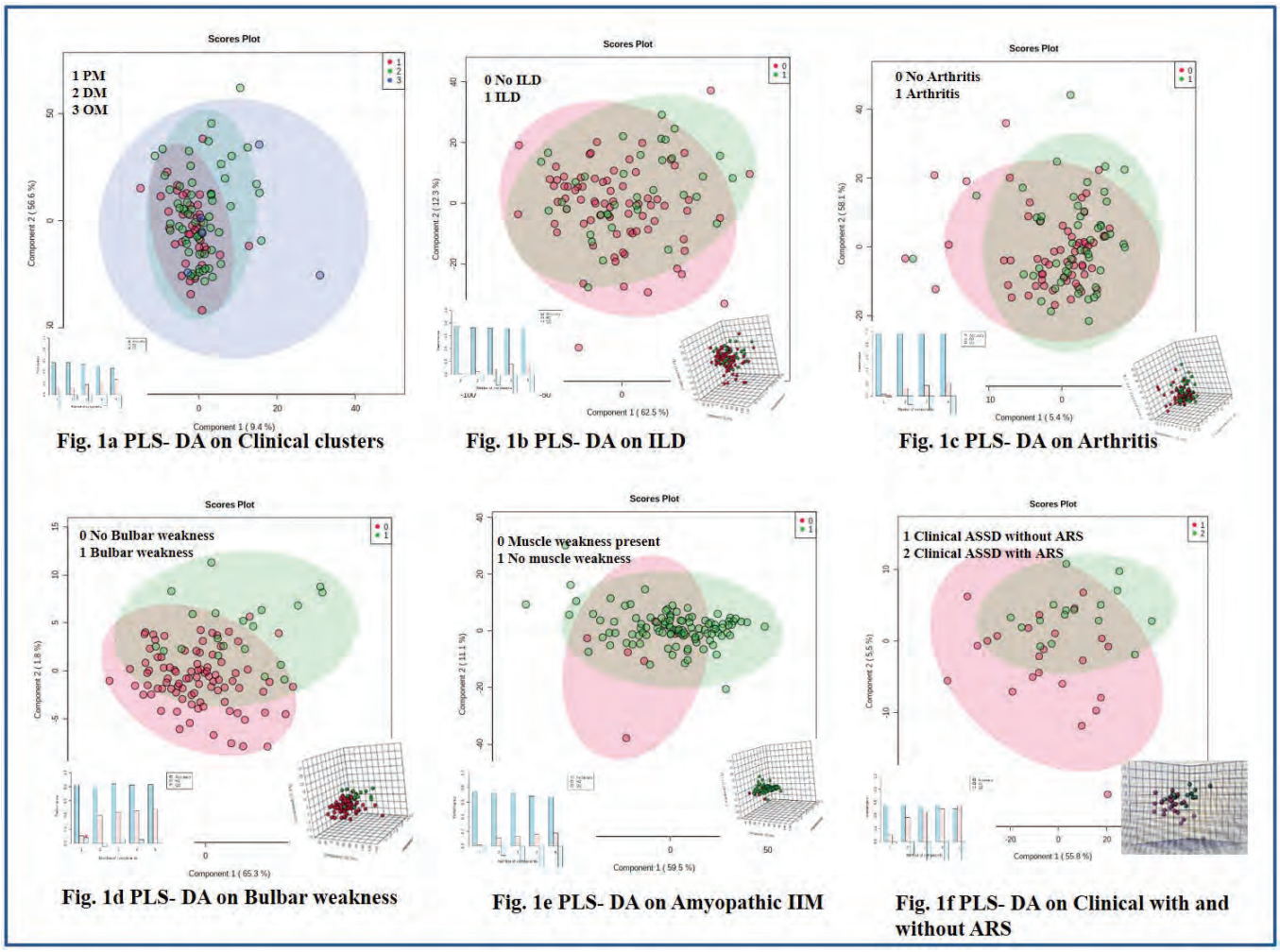

Figure 1. PLS-DA on Clinical Clusters of IIM

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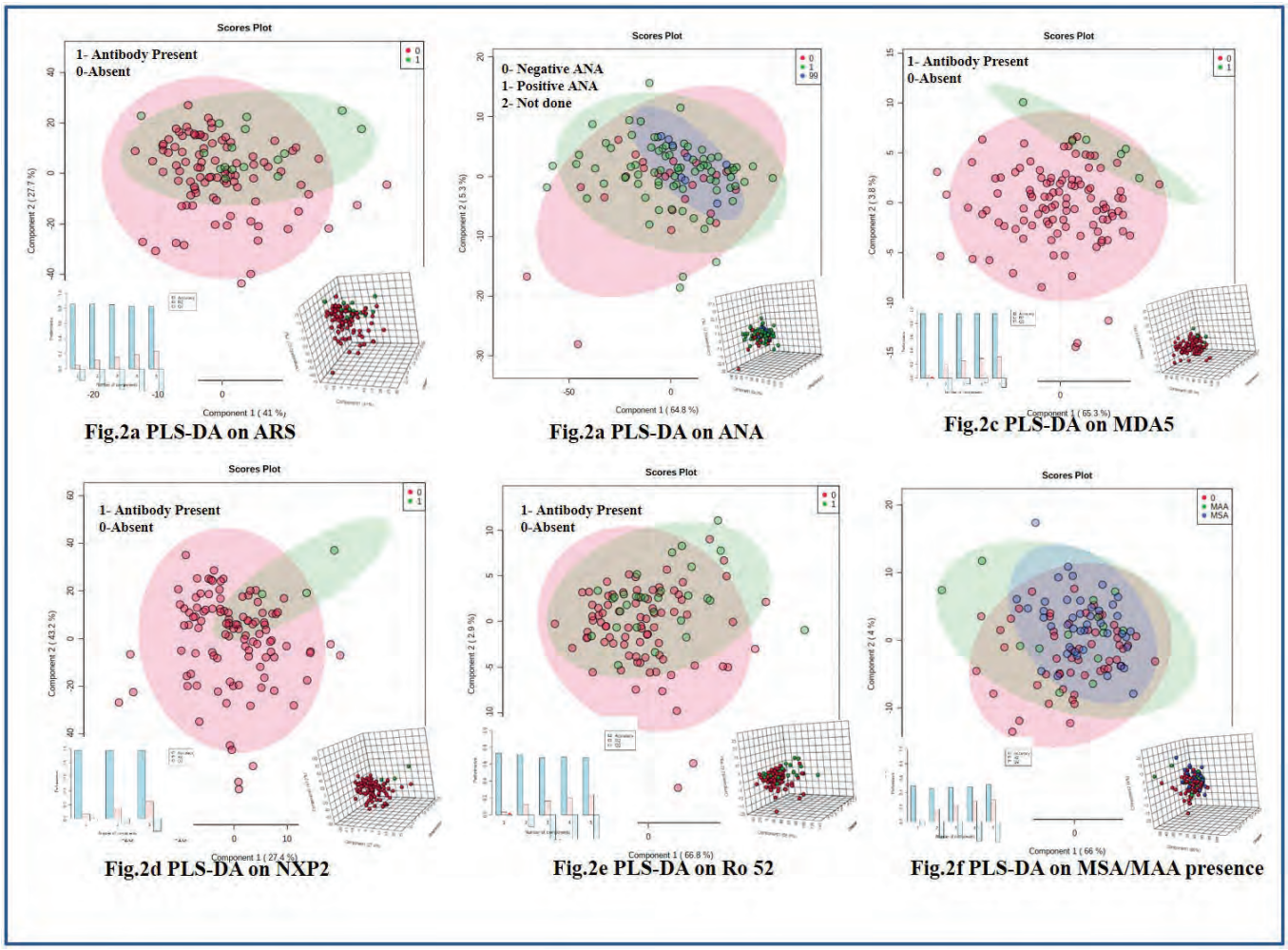

Figure 2. PLS-DA on Antibody Based Clusters of IIM

Disclosure: N. R, None; **A. Guleria**, None; **D. Kumar**, None; **U. Kumar**, None; **A. Anuja**, None; **V. Agarwal**, None; **L. Gupta**, None.

Abstract Number: 1093

Impact of Blood Flow Restricted Strength Training on Myogenic Stem Cells and Myofiber Hypertrophy in Sporadic Inclusion Body Myositis Patients

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SESSION INFORMATION

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Background/Purpose: Sporadic inclusion body myositis (sIBM) is clinically characterised by marked progressive muscle weakness and impaired physical function. Physical training has become an area of interest with the aim of mitigating or circumventing the progressive decline in functional capacity, as immunosuppressive medication has shown little effect in sIBM patients. Low-load blood flow restricted (BFR) exercise has been shown to upregulate skeletal muscle stem cells (satellite cells) and evoke gains in myofiber cross sectional area. In addition, satellite cells appear to play an important role supporting myofiber hypertrophy through myonuclei addition and myofiber regeneration.

Consequently, the present study aimed to investigate the effect of BFR strength training on satellite cell content, myofiber hypertrophy and myogenic signalling markers in lower limb skeletal muscle of sIBM patients.

Methods: Muscle biopsies from a previous randomised control trial (NCT02317094) in sIBM patients performing 12-weeks of low-load blood flow restricted exercise were used. 11 patients (age: 67.5 + 6.5, months from diagnosis: 57.8 + 87.7) were included from the exercise group (BFRE) and 10 patients (age: 69.2 + 4.6, months from diagnosis: 46.6 + 27.2) from the control group (CON). Muscle biopsies were obtained from either the m. tibialis anterior or the m. vastus lateralis and were stained for Pax7, CD31, SIX1, KI67 and DAPI, which were visualized by using three-color immunofluorescence microscopy. Visiopharm-based image analysis quantification was used for assessing the amount of Pax7, CD31, SIX1, KI67 and DAPI positive cells. Myofiber cross sectional area was assessed in a separate analysis. A linear mixed model was used for the statistical analysis.

Results: Satellite cells ($Pax7^+$) including newly proliferated satellite cells ($Ki67^+/Pax7^+$) remained unaltered following the intervention period in both BFRE and CON. Likewise, total myonuclei content ($SIX1^+DAPI^+$) and capillaries ($CD31^+$) did not change in BFRE or CON. A group (intervention) by time interaction was observed in type 2 fibre cross-sectional area (CSA) ($p=0.04$). Notably, type 1 fibres demonstrated a larger CSA than type 2 fibres both pre and post intervention and irrespective of group ($p\leq0.05$).

Conclusion: 12 weeks of low-load blood flow restricted exercise training did not upregulate satellite cells, myogenic markers nor increase myofiber area in the present group of sIBM patients. These findings suggest that satellite cell function and myogenic capacity are impaired in long-term sIBM.

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Abstract Number: 1094

Long Term Open Label Extension of Study of Tofacitinib in Refractory Dermatomyositis

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SESSION INFORMATION
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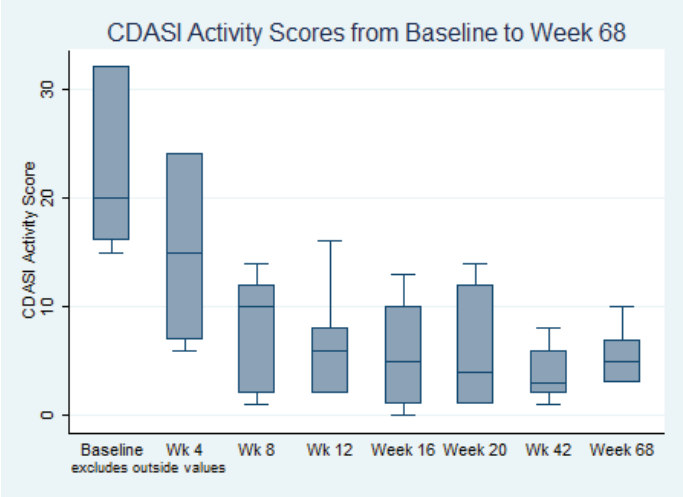

CDASI Activity Scores from Baseline to Week 68

Background/Purpose: Tofacitinib is a pan-JAK inhibitor that demonstrated safety and efficacy in a 12 week open label trial of 10 subjects with refractory dermatomyositis (NCT03002649). Long term disease activity and safety is unknown in subjects receiving tofacitinib.

Methods: To provide long-term safety and efficacy data in dermatomyositis subjects in the study, subjects who completed up to week 12 were eligible to receive tofacitinib XR 11mg daily in a long term study extension. Safety and efficacy using the validated ACR/EULAR Myositis Response Criteria, as measured by the Total Improvement Score (TIS) and Cutaneous Dermatomyositis Activity and Severity Index (CDASI) was assessed every 4 weeks until 20 weeks. Following this, subjects remained on drug and returned for a 42 week and 68 week visit.

Results: 7 of 10 (70%) of patients entered the long term extension of the study drug. There were no serious adverse events to date. 6 of 7 (86%) continued to meet the IMACS DOI at 68 weeks. The median Total Improvement Score (TIS) was 37.5 [30, 37.5] at 42 weeks, and 25 [22.5, 37.5] at 68 weeks. There continued to be a statistically significant change in mean CDASI when compared to baseline at all time points during the extension period. The mean baseline CDASI was 25.4 ± 15 which dropped to 3.85 ± 2.41 (p=0.008) by week 42, and 5.43 ± 2.51 by week 68 (p=0.01). Two subjects required additional immunosuppression with low dose methotrexate during the long term extension period. No patients required any high dose steroid therapy or admission to the hospital for a flare.

Conclusion: Tofacitinib continues to be safe and well tolerated in the long term open label extension of the study. There were no serious adverse events or study discontinuation related to tofacitinib. These data support further investigation of JAK inhibitors in dermatomyositis in a randomized placebo controlled study.

Disclosure: J. Paik, None; **J. Albayda**, None; **E. Tiniakou**, None; **G. Purwin**, None; **A. Koenig**, Pfizer Inc, 1, CSL Behring, 1; **L. Christopher-Stine**, None.

Abstract Number: 1095

Avascular Necrosis in the Hopkins Myositis Cohort: A Single Center Experience

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SESSION INFORMATION
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Background/Purpose: To assess the prevalence of avascular necrosis (AVN) in a large cohort of patients with idiopathic inflammatory myopathies (IIM) and define the major associated risk factors.

Methods: We retrospectively reviewed the electronic medical records of all patients with a definitive diagnosis of IIM in our cohort, querying for keywords ("avascular necrosis", "AVN", "osteonecrosis"). Pertinent demographic, clinical (including major risk factors for AVN), serologic and imaging data were collected. A matched group of patients without AVN was then selected for comparison (matched for sex, age at IIM diagnosis ± 2 years, and duration of IIM ± 1 year).

Table 1. Demographic and clinical characteristics of patients with AVN and myositis

		Myositis with AVN
Number of patients		53
Gender	Men	16 (30)
	Women	37 (70)
Race	White	30 (57)
	Black	16 (30)
	Asian	1 (2)
	Hispanic	2 (4)
	Other	4 (7)
Age at Myositis diagnosis, years		44.5±12.4
Diagnosis	DM	31 (59)
	PM	15 (28)
	IBM	2 (4)
	AD	2 (4)
	HMGCR related	3 (6)
Site of AVN	Hip joint	44 (77)
	Knee joint	9 (16)
	Shoulder joint	4 (7)
Symptomatic AVN		10 (18)
Recurrent AVN		5 (9)
OR for AVN		10 (18)
Age at AVN diagnosis, years		47.2±12.6
Time Myositis to AVN, months		46 [-338, 384]

Data are expressed in number of cases (%), mean ± SD or median [min, max]. *Abbreviations:* **DM** dermatomyositis, **PM** polymyositis, **IBM** inclusion body myositis, **AD** amyopathic dermatomyositis, **HMGCR** 3-hydroxy-3-methylglutaryl-CoA reductase antibody, **OR** surgical correction.

Table 2. Risk factors and serology in myositis with AVN vs myositis without AVN

		Myositis with AVN	Myositis without AVN	p-value
AVN risk factors	History of Cancer, yes	4 (7)	5 (11)	NS
	History of Hyperlipidemia, yes	11 (21)	4 (9)	NS
	History of tobacco use, yes	13 (24)	15 (34)	NS
	History of HIV, yes	2 (4)	1 (2)	NS
	History of Alcohol use, yes	19 (36)	6 (13)	0.01
	History of Steroid use, yes	46 (87)	38 (86)	NS
	Prednisone equivalent dose used, mg	17 [0, 100]	15 [0, 60]	NS
Serology	Seronegative, yes	9 (17)	5 (11)	NS
	Anti-PL12, positive	5 (9)	1 (2)	NS
	Anti-Ro52, positive	19 (36)	16 (37)	NS
	Anti-Ro, positive	6 (11)	4 (9)	NS
	Anti-Jo1, positive	5 (9)	12 (27)	0.03
	Anti-PL7, positive	5 (9)	2 (4)	NS
	Anti-EJ, positive	0 (0)	1 (2)	NS
	Anti-OJ, positive	1 (2)	0 (0)	NS
	Anti-T1F1g, positive	10 (19)	9 (20)	NS
	Anti-MDA5, positive	5 (9)	1 (2)	NS
	Anti-NXP2, positive	3 (6)	5 (11)	NS
	Anti-Ku, positive	2 (4)	0 (0)	NS
	Anti-SRP, positive	4 (7)	1 (2)	NS
	Anti-PM75, positive	4 (7)	5 (11)	NS
	Anti-PM100, positive	2 (4)	2 (4)	NS
	Anti-Mi2b, positive	6 (11)	3 (7)	NS
	Anti-Mi2a, positive	3 (6)	3 (7)	NS
	Anti-SAE1, positive	0 (0)	0 (0)	NS
	RF, positive	0 (0)	3 (7)	0.08
	Anti-CCP, positive	1 (2)	2 (4)	NS
	ANA, positive	10 (19)	24 (54)	0.001
	Anti-U1RNP, positive	1 (2)	1 (2)	NS
	Anti-HMG, positive	2 (4)	1 (2)	NS
	Anti-PMSCL, positive	1 (2)	2 (4)	NS

Data are expressed in number of cases (%) or median [min, max].

Table 3. Multivariate logistic regression analysis models, predictors of developing AVN in myositis population

	Variable	OR	95% CI [min-max]	P value
Model 1	History of Cancer, yes	0.47	[0.09-2.33]	0.3
	History of Hyperlipidemia, yes	2.55	[0.66-9.86]	0.1
	History of HIV, yes	2.20	[0.16-30.0]	0.5
	History of Alcohol abuse, yes	**3.98**	[1.31-12.0]	**0.01**
	History of tobacco abuse, yes	0.51	[0.19-1.37]	0.1
	History of Steroid use, yes	1.88	[0.46-7.55]	0.3
Model 2	History of Alcohol abuse, yes	2.81	[0.92-8.56]	0.06
	ANA, positive	**0.22**	[0.08-0.58]	**<0.01**
	Anti-Jo1, positive	0.42	[0.12-1.44]	0.1

Abbreviations: **OR** odds ratio, **CI** confidence interval. **Model 1** included the following variables (history of Cancer, history of hyperlipidemia, history of HIV, history of tobacco use, history of alcohol use, history of steroid use). **Model 2** included the following variables (history of alcohol use, ANA positivity, Anti-Jo1 positivity).

Results: A total of 1680 patients were diagnosed with IIM between 2003 and 2017. Fifty-three patients developed AVN, with a global prevalence of 3.1% (53/1680). Musculoskeletal magnetic resonance imaging (MSK MRI) was available for 1085 patients and AVN was present in 48 patients, with a relative prevalence of 4.4% (48/1085). The majority of patients were Caucasian females (57%) with a mean age at diagnosis of 44.5□12.4 years. 59% had dermatomyositis (DM), 28% had polymyositis (PM). The median time from diagnosis of IIM to diagnosis of AVN was 46 months. Only 18 % were symptomatic. Hip joint was involved in 77%, Knee joint in 16% and Shoulder joint in 7%. A history of alcohol use was the only risk factor that was statistically associated with AVN (36% vs 13%; OR=3.98, CI [1.31-12.0], p=0.01). Corticosteroid use was not associated with an increased risk of AVN.

Conclusion: Although mostly asymptomatic, the global prevalence of AVN in IIM was 3.1% but the prevalence on MSK MRI was 4.4% and alcohol use was the only risk factor for AVN development.

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Abstract Number: 1096

Assessing Interstitial Lung Disease in a Racially Diverse Population with Idiopathic Inflammatory Myositis

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SESSION INFORMATION
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Background/Purpose: Interstitial lung disease (ILD) is a common extra-muscular manifestation of Idiopathic Inflammatory Myositis (IIM) and increases risk of mortality. Prior studies and registries have focused on either smaller cohorts or predominantly Caucasian/European populations. Our aim was to better characterize the clinical disease manifestations of ILD in racially diverse population of IIM patients in the Bronx, NY, particularly to describe the associated phenotypes and antibody profiles, clinical skin manifestations, and autoimmune co-morbidities.

Methods: Montefiore Medical Center patients that met 2017 EULAR/ACR classification criteria for IIM were included. The presence of ILD, as well as the radiographic pattern, severity, and progression were determined using available pulmonary function testing and CT of the chest. Statistical analyses included Chi-Square test and Fisher's test.

Results: There were 152 myositis patients in this cohort, of which 62 patients had evidence of ILD (41%). Among the 62 patients with ILD, 71% were women and 29% were men. Patients with ILD were 44% Latin ethnicity and consisted of 56% Black, 24% White, 3% American Indian, 3% Asian (Table 1). Patients with ILD were radiographically classified as follows: 18 (29%) with ground glass opacities without specific pattern, 6 (10%) with usual interstitial pneumonia (UIP), 21 (34%) with nonspecific interstitial pneumonia (NSIP), and 17 (27%) with other patterns of ILD (Table 2).

		ILD (N=62)	No ILD (N=90)	P-value
Demographics:	Female (%)	44 (71)	70 (78)	0.63
	Male (%)	18 (29)	20 (22)	0.41
	Latin Ethnicity (%)	27 (44)	33 (39)	0.61
	American Indian (%)	2 (3)	0 (0)	0.11
	Asian (%)	2 (3)	4 (4)	0.60
	Black (%)	35 (56)	35 (39)	0.30
	White (%)	15 (24)	30 (33)	0.15

Table 1. Patient Demographics

		Incidence Rate
Based on CT Chest	NSIP (%)	21/62 (34)
	GGO (%)	18/62 (29)
	UIP (%)	6/62 (10)
	Other ILD (%)	17/62 (27)
Based on CT and or PFTs	Mild (%)	38/62 (61)
	Moderate (%)	8/62 (13)
	Severe (%)	16/62 (26)
Based on 2 consecutive studies	Progressive (%)	27/62 (44)
	Non-Progressive (%)	35/62 (56)

Table 2. Incidence of ILD subtypes in IIM patients

Among patients with ILD, 22 (35%) had PM, 38 (61%) had DM with 7 of those patients having CADM, 2 (3%) had IBM, and 1 (2%) patient had necrotizing (statin-induced) myopathy. Of the PM/DM patients, 14 (23%) qualified as having anti-synthetase syndrome and 13 (21%) had MCTD, UCTD, or an overlap syndrome, both of which had higher ILD prevalences (p=0.0002 and p=0.0001). There was no statistical associated between IBM and ILD (p value = 0.01) but there were 2 cases of IBM with ILD. Patients with ILD had higher prevalence of Jo-1 and SSA antibodies (p=0.002, p=0.003). Dermatomyositis patients with Mi-2 antibody had no prevalence of ILD in this cohort (p=0.03) (Table 3). Majority of these findings are similar to larger, predominant Caucasian studies of IIM.

While IIM patients with ILD showed varying skin manifestations, there were no particular skin manifestations that were significantly more prevalent in patients with ILD in this racially diverse cohort. Patients with ILD also had a higher prevalence of one or more autoimmune comorbidities (p=0.01). Conversely, patients without ILD had higher prevalence of no autoimmune co-morbidities (p=0.04).

		ILD (N=62)	No ILD (N=90)	P-Value
Clinical Diagnosis / Phenotype	Polymyositis (%)	22 (35)	23 (26)	0.27
	Dermatomyositis (%)	38 (61)	51 (57)	0.85
	-Amyopathic (%)	7/38 (18)	4/51 (8)	0.12
	IBM (%)	2 (3)	15 (17)	0.01
	MCTD/UCTD/Overlap (%)	13 (21)	2 (2)	0.0002
	Necrotizing (Statin - associated) (%)	1 (2)	0 (0)	0.23
Antibody Profiles	dsDNA (%)	3/52 (5.8)	0/59 (0)	0.07
	RNP (%)	12/53 (22.6)	6/61 (9.8)	0.09
	SSA/Ro (%)	28/55 (50.9)	14/70 (20)	0.003
	SSB/La (%)	4/53 (7.5)	3/68 (4.4)	0.48
	Jo-1 (%)	20/59 (33.9)	8/78 (10.3)	0.002
	Centromere (%)	1/47 (2.1)	1/42 (2.4)	0.94
	Smith (%)	4/53 (7.5)	1/60 (1.7)	0.14
	Ribosomal P (%)	2/37 (5.4)	0/35 (0)	0.17
	HMGCR (%)	1/5 (20)	0/10 (0)	0.16
	Mi-2 (%)	2/34 (5.9)	8/39 (20.5)	0.09
	PL-12 (%)	0/32 (0)	0/37 (0)	
	PL-7 (%)	0/32 (0)	2/37 (5.4)	0.19
	EJ (%)	1/32 (3.1)	1/37 (2.7)	0.92
	OJ (%)	1/32 (3.1)	0/37 (0)	0.28
	SRP (%)	0/32 (0)	2/38 (5.3)	0.19
	Ku (%)	2/32 (6.3)	2/37 (5.4)	0.88
	U2 RNP (%)	0/28 (0)	0/30 (0)	
	PM/Scl-100 (%)	1/29 (3.4)	1/30 (3.3)	0.98
	MDA5 (%)	4/27 (14.8)	1/29 (3.4)	0.16
	NXP-2 (%)	2/27 (7.4)	2/29 (6.9)	0.94
	TIF1 Gamma (%)	0/28 (0)	2/30 (6.7)	0.17
	SSA 52 (%)	12/28 (42.9)	10/30 (33.3)	0.56
	U1 RNP (%)	2/31 (6.5)	2/29 (6.9)	0.95
	U3 RNP (%)	1/29 (3.4)	0/29 (0)	0.32
	CN1A (%)	0/0 (0)	3/4 (75)	
Skin Manifestations:	Heliotrope (%)	26 (42)	30 (33)	0.39
	Gottron sign/papules (%)	25 (40)	35 (39)	0.89
	Periungal Erythema (%)	7 (11)	17 (19)	0.25
	Raynaud's with ulceration (%)	11 (18)	7 (8)	0.08
	Telangiectasia (%)	9 (15)	17 (19)	0.52
	Calcinosis (%)	7 (11)	4 (4)	0.12
	Mechanic's hands (%)	14 (23)	12 (13)	0.18
	V sign (%)	7 (11)	13 (14)	0.60
	Shawl sign (%)	12 (19)	12 (13)	0.36
	Holster Sign (%)	4 (6)	4 (4)	0.60
Number of secondary autoimmune Comorbidities	0 (%)	25 (40)	59 (66)	0.04
	1 (%)	16 (26)	19 (21)	0.55
	1+ (%)	21 (34)	12 (13)	0.01
Types of Autoimmune Comorbidities	Anti-synthetase syndrome (%)	14 (23)	2 (2)	0.0001
	Raynaud syndrome (%)	16 (26)	12 (13)	0.08
	Sjogren (%)	7 (11)	5 (6)	0.22
	Autoimmune Thyroiditis (%)	10 (16)	8 (9)	0.20
	SLE (%)	6 (10)	5 (6)	0.35
	Scleroderma (%)	7 (11)	0 (0)	0.002
	Rheumatoid Arthritis (%)	1 (2)	6 (7)	0.15

Table 3. Antibody profiles, clinical manifestations, and autoimmune co-morbidities in IIM Patients with ILD

Conclusion: ILD in this racially diverse population with IIM is a significant manifestation of disease that presents heterogeneously. This study serves to confirm that certain myositis phenotypes, associated antibody profiles, and autoimmune comorbidities are associated with ILD, even in a racially diverse urban population. Limitations include

a small sample size of antibody profiles for study. Future direction will include further stratifying patients with ILD in this diverse population by radiographic patterns to assess if response to medications is similar to more homogenous cohorts.

Disclosure: J. Law, None; **A. Valle**, None; **K. Mullins**, None; **S. Mahmood**, None.

Abstract Number: 1097

Immunophenotypic Characterization of Myeloid Derived Supressor Cells (MDSCs) and Their Relationship to the Clinical Characteristics of Patients with Inflammatory Myopathies

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Muscle Biology, Myositis & Myopathies Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Myeloid derived suppressor cells (MDSCs) including their granulocyte (Gr-MDSCs) and monocyte (Mo-MDSCs) subtypes constitute a cellular subset with potent immune regulatory capacity. An augmented proportion of MDSCs has been described in patients with cancer, infections and autoimmune diseases, nevertheless the presence of MDSCs in Idiopathic inflammatory myopathies (IIM) has not been explored. The aim of this study is to evaluate the proportion of myeloid derived suppressor cells and their relationship with clinical characteristics of patients with IIM.

Methods: Twenty-two adult patients with the diagnosis of IIM according to the ACR/EULAR criteria and active disease were recruited. The disease activity, damage accrual and disability were evaluated with the myositis disease activity assessment tool (MDAAT), the manual muscle test 8 (MMT8), the myositis damage index (MDI) and the health assessment questionnaire (HAQ). MDSCs were measured by flow cytometry in the peripheral blood mononuclear cell (PBMC) fraction after separation of blood with density gradients. Gr-MDSCs were defined as those $CD33^{dim}$, $CD11b^{+}$, $CD66b^{+}$, $HLA\text{-}DR^{-}$. Gr-MDSCs were classified as mature if they expressed CD16 ($CD16^{+}$) and immature if they were $CD16^{-}$. Mo-MDSCs were defined as those $CD33^{+}$, $HLA\text{-}DR^{-}$ and $CD14^{+}$. Also, the proportion and expression of arginase 1^{+} and $PDL1^{+}$ in MDSCs was evaluated by their mean fluorescence intensity. The proportion of MDSCs and their expression of arginase 1 and PDL1 was compared with 14 healthy donors. Quantitative variables were expressed as medians and interquartile range (IQR). The difference between independent medians was assessed with the Mann-Whitney U test and the correlation between variables was evaluated with the Spearman Rho.

Results: Twelve patients with IIM were women (54.5%). The median of age was 40 (26-42.5) years and patients had a time since diagnosis of 6 (4.5-9.75) months. The most frequent diagnosis was dermatomyositis (72.7%) and most patients had positive anti-Ro52 (36.4%), anti-MDA5 and anti-Mi2 (18.2% each) antibodies. At the time of evaluation 68.2% of patients were taking prednisone, 31.8% methotrexate, 9.1% azathioprine, 18.2% mycophenolate mofetil and 31.8% hydroxychloroquine. Sixteen patients (76.2%) had cutaneous manifestations, 47.6% had dysphagia and 23.8% had interstitial lung disease. Five healthy donors were women (35.7%). The median of age was 27.5 (25-33) years. There was not a statistically significant difference in the age and gender of the study groups.

Table 1. Proportion of MDSCs and their expression of arginase 1 and PDL1 in IIM patients and healthy donors.

Variable	IIM N=22 Median (IQR)	Healthy donor N=14 Median (IQR)	P
% of Gr-MDSCs	0.73 (0.21-2.15)	0.037 (0.009-0.17)	<0.0001
% of immature Gr-MDSCs	89 (33-97.1)	28.3 (15.8-37)	0.003
% of mature Gr-MDSCs	10.2 (2.95-67.00)	71.7 (63.00-84.20)	0.003
% of Arg1+ Gr-MDSCs	0.62 (0.24-4.27)	0.007 (0.000-0.060)	0.016
Mean fluorescence intensity of Arg1 in Gr-MDSCs	4743 (2515-7618)	1556 (955-2593)	0.005
% of PDL1+ Gr-MDSCs	0.29 (0.07-0.67)	0.01 (0.0005-0.044)	0.022
Mean fluorescence intensity of PDL1+ in Gr-MDSCs	3517 (1669-3971)	1627 (1450-1797)	0.05
% of Mo-MDSCs	1.11 (0.07-2.93)	0.11 (0.01-2.99)	0.23
% of Arg1+ Mo-MDSCs	0.84 (0.15-1.38)	0.14 (0.003-0.47)	0.16
Mean fluorescence intensity of Arg1 in Mo-MDSCs	3507 (3339-5483)	1967 (1540-2849)	0.028
%of PDL1+ Mo-MDSCs	0.8 (0.13-2)	0.002 (0.000-0.031)	0.006
Mean fluorescence intensity of PDL1+ in Mo-MDSCs	2169 (1882-12857)	4445 (2216-6295)	0.89

Table 1. Proportion of MDSCs and their expression of arginase 1 and PDL1 in IIM patients and healthy donors.

As shown in Table 1, the proportion of MDSCs and their expression of arginase 1 and PDL1 was higher in patients with IIM, except for the proportion of Mo-MDSCs. The proportion of immature Gr-MDSCs was correlated with the cutaneous damage (Rho=0.486, P=0.048). There was not a relationship between immunosuppressive therapy and MDSCs.

Conclusion: Patients with IIM have a higher proportion of Gr-MDSCs with an immature phenotype and a higher expression of arginase 1 and PDL1+. Further studies are required to evaluate their suppressor capacity and their relationship with other clinical features including the presence of neoplasia.

Disclosure: H. Culebro, None; **J. Torres-Ruiz**, None; **F. Cassiano Quezada**, None; **A. Perez Fragoso**, None.

Abstract Number: 1098

Anti-cortactin Autoantibodies Are Associated with Key Clinical Features in Adult Myositis but Are Rarely Present in Juvenile Myositis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Muscle Biology, Myositis & Myopathies Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: To define the prevalence and clinical phenotype of anti-cortactin autoantibodies in adult and juvenile myositis.

Methods: In this longitudinal cohort study, anti-cortactin autoantibody tiers were assessed by ELISA in 670 adults and 343 juvenile myositis patients as well as 202 adult and 90 juvenile healthy controls. The prevalence of anti-cortactin autoantibodies was compared among groups. The clinical features of patients with and without anti-cortactin autoantibodies were also compared.

Results: The prevalence of anti-cortactin autoantibodies was not different between all adult myositis patients compared to adult healthy controls (11% vs. 8%; p=0.2). However, compared to adult healthy controls, anti-cortactin autoantibodies were more common in adult dermatomyositis (DM) patients (15%, p=0.005), particularly those with co-existing anti-Mi2 (24%, p=0.03) or anti-NXP2 (23%, p=0.04) autoantibodies. In adult myositis, anti-cortactin was associated with DM-skin involvement (62% vs. 38%, p=0.03), dysphagia (36% vs. 17%, p=0.02) and co-existing anti-Ro52 (47% vs. 26%, p=0.001) or anti-NT5C1a autoantibodies (59% vs. 33%, p=0.001). Moreover, the titers of anti-cortactin antibodies were higher in patients with interstitial lung disease (0.15 vs. 0.12 arbitrary units, p=0.03). The prevalence of anti-cortactin autoantibodies was no different in juvenile myositis (2%) or any juvenile myositis subgroup compared to juvenile healthy controls (4%). Nonetheless, juvenile myositis patients with these autoantibodies had a higher prevalence of mechanic's hands (25% vs. 7%; p=0.03), a higher number of hospitalizations (2.9 vs. 1.3, p=0.04) and lower peak CK values (368 vs. 818 IU/L, p=0.02).

Conclusion: The prevalence of anti-cortactin autoantibodies is only increased in adult DM patients with co-existing anti-Mi2 or anti-NXP2 autoantibodies. In adults, anti-cortactin autoantibodies are associated with dysphagia and interstitial lung disease.

Disclosure: I. Pinal-Fernandez, None; **K. Pak**, None; **A. Gil-Vila**, None; **A. Baucells**, None; **B. Plotz**, None; **M. Casal-Dominguez**, None; **A. Derfoul**, None; **M. Martinez**, None; **A. Selva-O'Callaghan**, None; **S. Sabbagh**, None; **F. Miller**, None; **L. Rider**, NIEHS, NIH, 2, Cure JM Foundation, 2, Bristol Myers Squibb, 2, Hope Pharmaceuticals, 2, Eli Lilly and Company, 9, MedImmune/AstraZeneca, 9; **L. Christopher-Stine**, None; **A. Mammen**, None.

Abstract Number: 1099

High Burden of Infections in Indian Patients with Idiopathic Inflammatory Myopathy: Validation of Observations from the MyoCite Dataset

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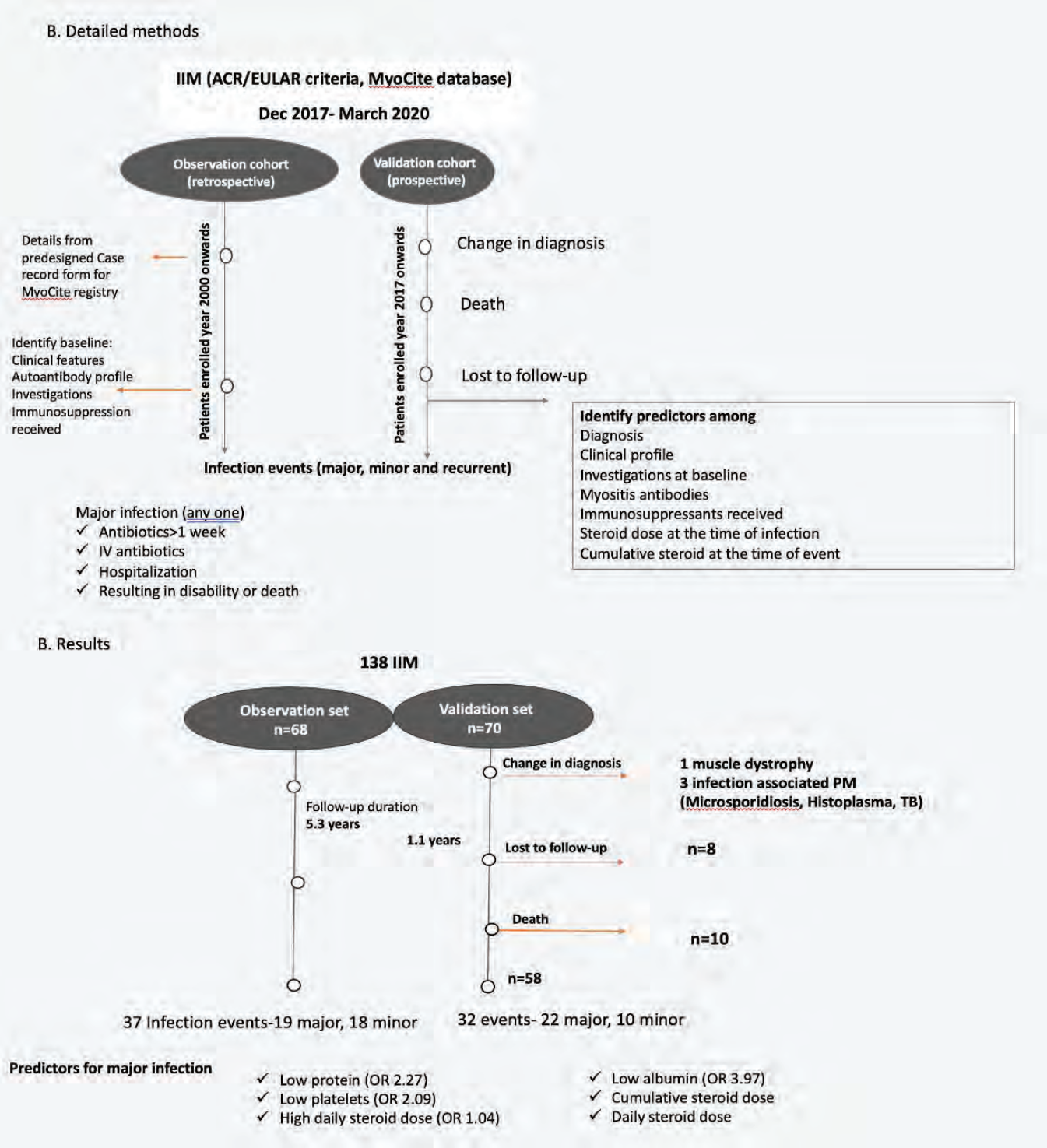
SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Muscle Biology, Myositis & Myopathies Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Infections are a major cause of morbidity and mortality in idiopathic inflammatory myopathy (IIM), more so in India.[1-3] The objective of this study was to characterize the profile and predictors of infections in IIM.



Methods: Details of IIM from the MyoCite database (Dec 2017- March 2020) were retrieved and characterised as the observation cohort.[4-6] The patients enrolled at inception during this period were followed up as the validation cohort to confirm findings from the observation cohort. Definitions and statistical analysis are detailed in Figure 1A. Descriptive data is expressed as median/mean (IQR/SD). Multivariate analysis was done using logistic regression. Missing values imputed using predictive means modelling. Statistical analysis was carried out on Rstudio version 1.2.5033.

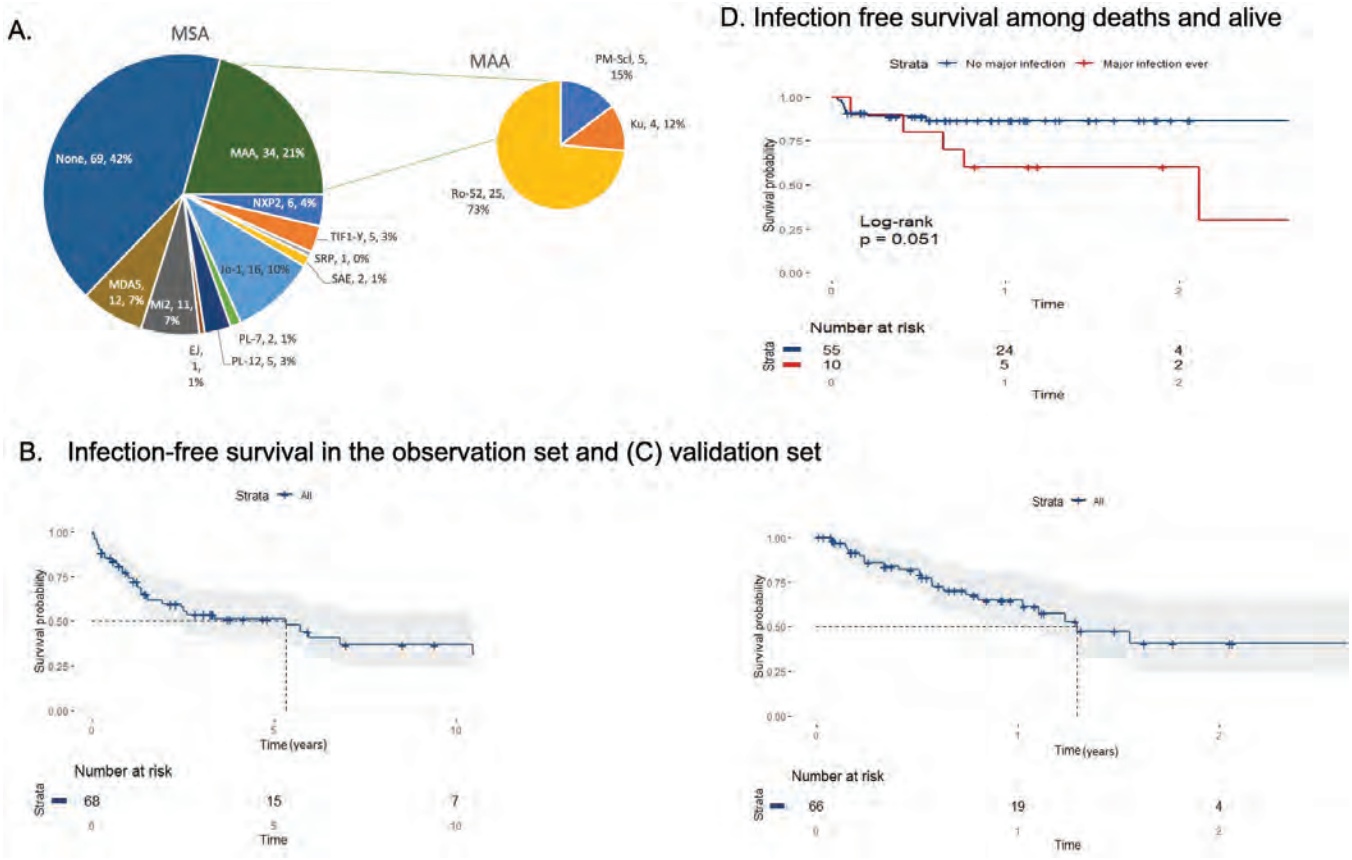


Table 1. Profile of infections in the observational and validation cohorts.

	Observational cohort (n=68)		Validation cohort (n=66)	
All infections	Influenza like illness	8	Influenza like illness	5
	Mucocutaneous	7	Mucocutaneous	
	Herpes zoster	4	Herpes zoster	8
	Pneumonia	6	Pneumonia	1
	Tuberculosis	11	Tuberculosis	4
	Gastrointestinal	2	Gastrointestinal	2
	Urinary tract infection	1	Urinary tract infection	4
			Dengue haemorrhagic fever	1
				1
Major infections	Tuberculosis		Pulmonary tuberculosis	2
	Pulmonary	6	Pneumonia	
	Tuberculous brain abscess	1	*Klebsiella*	2
	Cutaneous	1	*Streptococcus*	2
	Gastrointestinal	1	Cause undetermined	2
	Osteomyelitis	1	Sepsis	
	Pleural effusion	1	Mucocutaneous (MRSA)	1
	Pneumonia			1
	Streptococcus	1		
	Citrobacter	1		
	Cytomegalovirus	3		
	Cause undetermined	1		
	Urinary tract infection (E.Coli)	1		
	Pelvic inflammatory disease	1		

Results: A total 138 individuals (59 DM, 23 PM, 15 JDM, 34 OM, 3 CAM) were enrolled. Of these, 68 were in the retrospective observation cohort with median age 32 (25.5-42.4. F:M 4.2:1), and 66 prospectively enrolled at inception formed the validation cohort with median age 37 (21-47.7, F:M 3.7:1). Myositis antibodies are detailed in Figure 2 A.

Observation cohort.

Over a mean follow up of 64 months, 37 patients had infections (Table 1), of which 19 (51.3%) were major. 11 (29%) had recurrent infections. Tuberculosis was the most common infection (29% of all infections; 57% of major infections), with 45% being extra-pulmonary. On multivariate logistic regression low protein (OR 2.27), low platelets (OR 2.09) and high daily steroid dose (OR 1.04) were predictors of major infections, with a model accuracy of 79%. Median infection free survival was 64.9 months (Figure 2B).

Validation cohort.

Over a mean follow up of 13.6 months, 4 patients were reclassified as non-IIM, of which 3 had atypical infections of the muscle tissue. Among those with IIM, 22 developed had infections, of which 10(45.4%) were major. Four (18%) had recurrent infections. Median infection free survival was 22.7 months. Mots common infection was community acquired pneumonia. On multivariate logistic regression, low albumin (OR 3.97) was a predictor of major infections, with a model accuracy of 90%.

There were 10 deaths, 1 of them as a direct result of infection. Any major infection in the disease course was associated with overall deaths (p=0.013, Figure 2D).

Conclusion: Infections are common and predispose to mortality in Indian patients with IIM. Tuberculosis is the leading case of infections in North India with a higher incidence of extrapulmonary forms, in early as well as established disease.

Disclosure: R. Chatterjee, None; **P. Mehta**, None; **V. Agarwal**, None; **L. Gupta**, None.

Abstract Number: 1100

The Hand Osteoarthritis Registry of New York University: Impacts of Gender and Obesity

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Hand osteoarthritis (HOA) data is often obtained from large knee OA cohorts. Targeted HOA cohorts in Europe have shed light on this disease, but the etiologies and pathophysiology remain less defined than other sites of OA. Some studies suggest a metabolic role of adiposity in OA (beyond mechanical load), as evidenced by prevalent HOA in obese patients, while other reports link hormonal status to HOA pain. Our dedicated cohort of HOA patients aims to study factors that contribute to its prevalence and severity.

Methods: From 2016 to 2020, we enrolled patients with interphalangeal (IP) OA, regardless of 1st carpometacarpal (CMC) involvement. Patients with rheumatoid arthritis, psoriatic arthritis or lupus were excluded. Demographic and relevant history data were collected. Participants completed adapted versions of the Michigan Hand Outcomes

Covariates	Age (years)	P value	BMI (kg/m^2)	P value	Adapted MHQ Pain Score (0-100 scale)	P value	QuickDASH Disability Score (0-100 scale)	P value	# of hand joints affected (by X-ray)	P value
Gender:										
Male (n=36)	67.1	0.166	27.5	0.143	29.9	**0.035***	21.8	**0.004***	8.5	**0.020***
Female (n=134)	66.1		25.9		39.0		32.8		10.5	
BMI (kg/m^2)										
<25 (n=79)	65.9		22.0		34.2		27.3		10	
25-30 (n=57)	67.6	0.480	27.2	**<0.001***	35.4	**0.029†**	30.0	**0.027‡**	11.1	0.455
> 30 "obese" (n=34)	65.2		34.1		46.4		38.6		9.6	
Tobacco Use										
Current (n=4)	70.2		25.6		47.2		38.1		7.7	
Past (n=50)	67.0	0.492	26.8	0.520	34.5	0.430	27.9	0.441	10.5	0.600
Never (n=106)	65.8		25.9		37.7		31.4		10.4	
Additional Sites of OA										
Yes (n=132)	67.3	**0.010***	26.5	0.159	39.5	**0.018***	33.0	**0.005***	10.4	0.881
No (n=38)	62.9		25.2		29.2		21.9		10.2	
Erosive OA										
Yes (n=62)	65.0	0.236	25.8	0.192	39.2	0.323	33.1	0.535	12.6	**<0.001***
No (n=87)	66.9		26.9		34.4		30.9		9.1	
Female Age Groups (years)										
<48 (n=5)	45.0		27.6		32.5		26.8		4.2	
48 - 54 (n=12)	51.0	**<0.001***	24.3	0.464	46.5	0.397	36.2	0.669	8.4	**0.002***
>54 (n=117)	68.5		26.0		38.5		32.7		11.4	

MHQ: Michigan Hand Outcomes Questionnaire (0=no pain, 100 = worst pain); QuickDASH: Disabilities of the Arm, Shoulder and Hand Score (0= no disability, 100 = worst disability)

*indicates significant results for alpha set to 0.05

† indicates a post-hoc LSD subgroup ANOVA revealed significant differences in pain (p=0.046) between healthy weight (<25 kg/m^2) and obese (>30 kg/m^2) subjects at alpha set to 0.05

‡ indicates a post-hoc LSD subgroup ANOVA revealed significant differences in disability (p=0.020) between healthy weight (<25 kg/m^2) and obese (>30 kg/m^2) subjects at alpha set to 0.05

Table 1. Covariates affecting hand osteoarthritis symptoms.

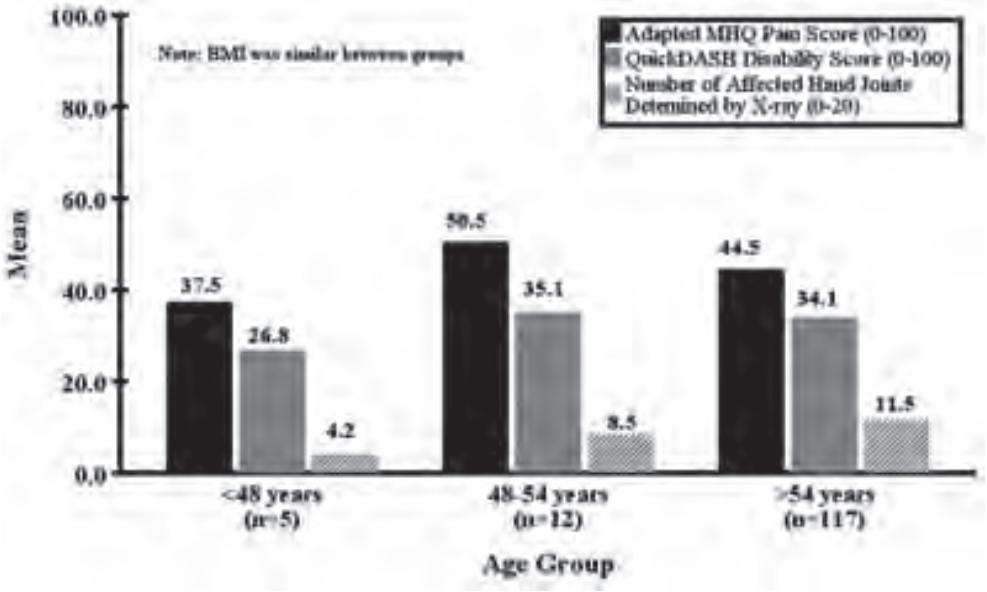

Figure 1. Women ages 48-54 demonstrated more severe hand OA pain and disability.

(MHQ) and QuickDASH Outcome questionnaires to assess pain, stiffness, and function. The semi-quantitative scores were aggregated and normalized to a 0-100 scale. Hand x-rays, if available, were scored in binary fashion for joint narrowing, osteophytes, and central erosions in all 20 joints (18 IPs, 2 1st CMCs). Blood and urine were banked for future assays.

Results: We screened 337 patients and found 170 to be eligible and willing to enroll. The present cohort is 80.0% Caucasian and 78.8% female with an average age of 66.3±9.5 years (range 42-90) and BMI of 26.2±5.0 kg/m^2 (range 16.4-42.1). Bilateral hand x-rays, available for 149 patients, involved 10.5±5.1 joints with OA on average, with 102 (68.4%) having concurrent IP and CMC OA. Radiographs revealed central erosive changes in ≥1 joint in 36.5% of patients, with this subset also reporting a higher number of affected joints (12.5 vs. 9.1, p=< 0.001). Patients with BMI > 30 kg/m^2 had significantly more hand pain (p=0.022) and stiffness (p=0.047) by the adapted MHQ, and more disability (p=0.025) by the QuickDASH, compared to those with BMI < 25 despite similar ages and joint burden by x-ray (**Table 1**). Patients reporting OA in additional sites also reported more hand pain (p=0.018) and more disability (p=0.003), though this signal could be confounded by this subgroup's advanced age (67.7 vs. 62.3 years, p=0.01). Women reported significantly more pain (p=0.035), disability (p=0.004), and a higher average number of joints affected (p=0.02) than men with similar ages and BMI. A small subgroup of likely perimenopausal women (ages 48-54) reported more pain and disability than their older counterparts, despite a lower mean BMI and fewer hand joints affected by OA. (**Figure. 1**). Our analyses did not reveal any association between hand symptoms and tobacco use, comorbidities, or prior hand trauma.

Conclusion: We have established the only registry and biorepository in North America focused on hand OA, which could enhance progress made by existing cohorts. HOA pain and disability independently associated with adiposity, and was more severe in women. We postulate that hormonal influences during the perimenopausal state may increase HOA symptoms during those years. As we run assays on stored biospecimens, we anticipate the HONEY cohort will further our understanding of HOA etiologies and pathophysiology while facilitating future clinical trials.

Disclosure: F. Bomfim, None; **S. Chen**, None; **S. Zak**, None; **T. Jazrawi**, None; **V. Qie**, None; **B. Plotz**, None; **J. Samuels**, None.

Abstract Number: 1101

Effect of Transcutaneous Vagal Nerve Stimulation in Erosive Hand Osteoarthritis: Results from an Open-label Non-randomized Pilot Trial

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Beyond classical effect on vegetative functions, the activation of the vagus nerve inhibits inflammation and reduces the pain signal. Vagus nerve stimulation (VNS) can be performed using transcutaneous VNS (tVNS) of the ascendant auricular branch of the VN that selectively innervates the cutaneous zone of cymba conchae

Figure 1. tVNS device kit.

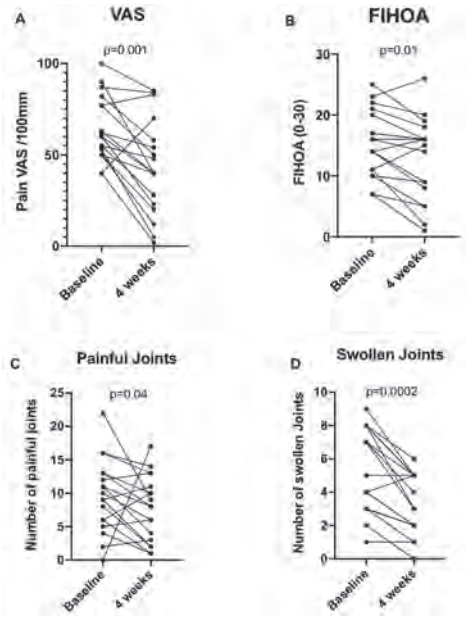

Figure 2. Effect of tVNS on EHOA symptoms. Evolution of (A) VAS hand pain on a 0-100mm scale, (B) function evaluated by FIHOA, (C) number of painful joints (0-30), (D) number of swollen joints (0-30) of the EHOA for each of the eighteen patients. Paired, non-parametric Wilcoxon t-test was used.

(1). Erosive hand osteoarthritis (EHOA) is the most severe HOA subtype characterized by a higher level of pain, a higher inflammation and functional disability than its non-erosive counterpart. The aim of this open-label pilot study was to determine the tolerance and the short-term efficacy of tVNS on EHOA symptoms (NCT03919279).

Methods: Symptomatic EHOA patients, defined by at least one erosive joint (phase E or R of the Verbruggen phase score) with a pain VAS ≥40/100mm and ≥ 1 interphalangeal swollen joint were included. The tVNS was performed using an auricular electrode applied one hour/day on the left ear, connected to a TENS device for 4 weeks (**Figure** 1). The TENS was set up at 25Hz frequency and 50 microseconds pulse width while the intensity was gradually increased to 15mA or below in case of ear discomfort on the stimulation zone (tingling, dysesthesia). Clinical efficacy was evaluated by hand pain VAS on a 0-100mm scale, the functional FIHOA score, the number of tender and swollen joints. Changes in EHOA symptoms between baseline and 4 weeks were evaluated using a Wilcoxon t-test. The proportion of patients that reached the Patient AccepTable Symptom State (PASS), defined by a VAS£40mm, and the minimum clinically important improvement (MCII), defined by an absolute decreased of 15mm or a relative improvement of 20% of their hand pain VAS, were calculated. Tolerance was also reported.

Results: Twenty patients were included but the analysis was performed on eighteen patients (median age 69 years-old [IQR 66.7;73.2], 83% women), two patients being lost to follow-up after the first session. At baseline, hand pain VAS was 60mm [50;78.2] and FIHOA score 15 [10.7;20.2], median number of tender and swollen joints was 9.5 [5.7;13] and 4.5 [3;8] respectively .After 4 weeks, tVNS significantly reduced pain, with a median decrease of 23.5mm

[7.7;37.2], p=0.001 and FIHOA by 2 points [0.75;5.2], p=0.01. Ten of the 18 patients (55%; CI95%: 0.33-0.75) reached the PASS and 13 the MCII (72%; CI95%: 0.49-0.87) (**Figure 2**). tVNS also induced a decrease of 3 [1;5.2] painful joints and 2 [1;3] swollen joints/patient. No serious adverse events were reported. One patient stopped tVNS because of an auricular discomfort.

Conclusion: This first proof-of-concept trial indicated that targeting the vagus nerve using tVNS stimulation may decrease joint inflammation and clinical symptoms in painful EHOA without major safety concern. A randomized controlled study versus sham stimulation is now necessary to confirm these results.

References:

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Abstract Number: 1102

Neuropathic Pain in Inflammatory Hand Osteoarthritis(OA) Lowers Quality of Life and May Require Another Approach Than Anti-inflammatory Treatment

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate whether neuropathic pain is present in patients with inflammatory hand OA, to investigate characteristics of those patients and the impact of neuropathic pain on quality of life (QoL), and whether neuropathic pain is influenced by anti-inflammatory treatment.

Methods: Data from a randomized, double-blind, placebo-controlled trial in which 92 patients with hand OA fulfilling ACR criteria were treated with prednisolone, has been analysed. Patients had signs of synovial inflammation, a VAS finger pain of ≥30 and showed flaring ≥20 upon NSAID washout. The primary endpoint of this trial was VAS finger pain (0-100) at week 6.

Neuropathic pain was measured at baseline and after treatment by the painDETECT questionnaire, consisting of questions on pain quality, pain intensity over time and radiating pain. Total score: -1 to 38. Scores< 12 unlikely, scores 13-18 undetermined, scores >18 likely neuropathic pain. QoL was measured with physical component scale (PCS) of Short-Form 36 (SF36; 0-100), comorbidities with the Self-administered Comorbidities Questionnaire (SCQ; 0-45);

Table 1. Multivariate Multinomial logistic regression with painDETECT categories as dependent variable

		PainDETECT		
Variables	All N=91 (100%)	Score <13 N=48 (53%) Reference group	Score 13-18 N=28 (31%)	Score >18 N=15 (16%)
Age	64 (9)	1	0.91 (0.83 to 0.98)*	0.97 (0.90 to 1.08)
Female sex	72 (79%)	1	3.20 (0.78 to 13.13)	9.50 (0.81 to 111.7)
BMI	27 (24 to 29)	1	1.06 (0.94 to 1.19)	0.96 (0.83 to 1.12)
SCQ score	2 (1 to 5)	1	1.13 (0.96 to 1.35)	1.30 (1.05 to 1.60)*
VAS finger pain	53.8 (2.1)	1	1.01 (0.99 to 1.04)	1.03 (0.99 to 1.07)
KL sumscore	37 (16)	1	0.99 (0.95 to 1.04)	0.94 (0.89 to 1.00)*

Table 1. Data are mean (SD), number (%) or median (IQR) in the first column. Data are relative risk ratios (95% Confidence Interval) in the second through fourth column. * Indicates a $p<0.05$. SCQ = Self-administered comorbidities questionnaire. BMI = body mass index. VAS = visual analog scale. KL= Kellgren-Lawrence.

Figure 1

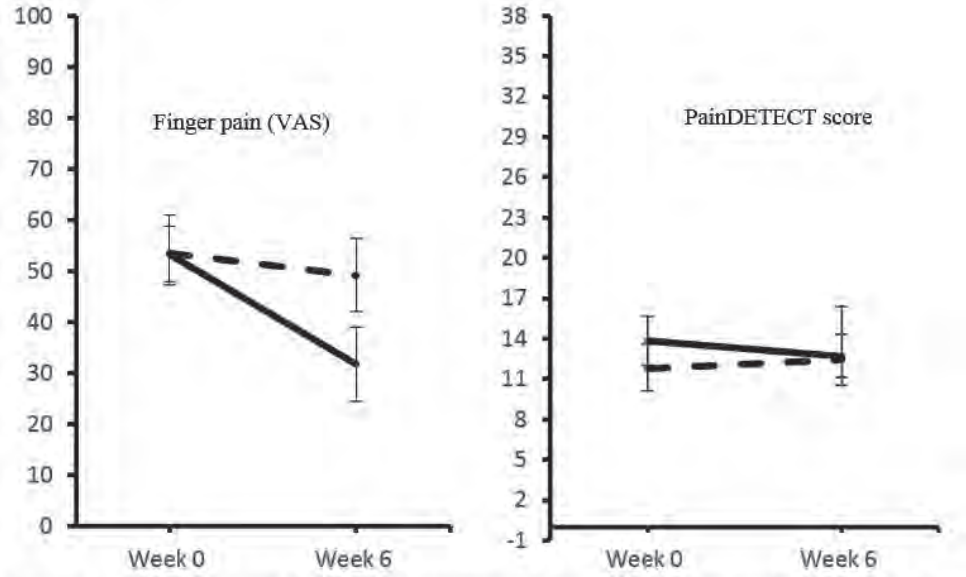

Figure 1. Mean pain at week 0 and week 6, per treatment arm, for VAS finger pain and PainDETECT. Placebo shown in dashed line, prednisolone 10 mg daily in solid line. Whiskers indicate 95% CI.

radiographic severity with Kellgren-Lawrence (KL) sumscore (0-120). OMERACT-OARSI responder criteria were used to determine response on prednisolone.

Association of patient characteristics with neuropathic pain was analysed with multivariate multinominal logistic regression with painDETECT categories as dependent variable. Association of neuropathic pain with QoL was analysed with multivariate linear regression, adjusted for age, sex, BMI, VAS finger pain, SCQ score and KL sumscore, with PCS as dependent variable. Response of neuropathic pain to prednisolone was analysed with generalised estimating equations. Association of neuropathic pain at baseline with response to treatment were analysed using chi-squared tests.

Results: 91 Patients had complete painDETECT data at baseline (mean 12.8 (SD 5.9)). Of these, 53% had no neuropathic pain, 31% were undetermined and 16% had neuropathic pain. Higher painDETECT scores at baseline were associated with lower age, female sex, less radiographic damage and more comorbidities in multivariate analysis (Table 1).

Patients with likely neuropathic pain had a lower QoL (PCS -6.5 (95%CI -10.4 to -2.6), than those without (painDETECT < 13). Neuropathic pain did not change during the trial in both treatment groups, and there was no difference in painDETECT scores between the groups (between group difference mean -1.7 (95%CI -3.9 to 0.4)). VAS pain improved more in the prednisolone group than in the placebo group (between group difference mean -16.5 (95%CI -26.1 to -6.9)) (Figure 1). In this study we could not show an association between the presence of neuropathic pain at baseline and OMERACT-OARSI response to treatment (data not shown).

Conclusion: Patients with inflammatory hand OA and additional neuropathic pain are more often female and have more comorbidities, and report a lower QoL, than those without. Neuropathic pain seems unresponsive to anti-inflammatory therapy. Clinicians should be aware of the presence of neuropathic pain in their patients as these findings might implicate that this kind of pain should be specifically targeted.

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Abstract Number: 1103

Metacarpo-phalangeal Osteoarthritis Is Not Rare and Is Associated with Mechanical Rather Than Systemic Factors in Hand Osteoarthritis: An Observational Study from a Large Hospital-based Cohort

Inès Kouki[1], Sophie Tuffet[2], Michel Crema[3], Alexandra Rousseau[2], Pascal Richette[4], Maxime Dougados[5], Francis Berenbaum[6], Jeremie Sellam[6] and Alice Courties[6], [1]AP-HP, Sorbonne Université, Service de rhumatologie, Hôpital Saint-Antoine, Paris,, Paris, France, [2]AP-HP, Hôpital Saint-Antoine, Unité de Recherche Clinique de l'Est Parisien (URC-Est), Paris, 75012,, Paris, France, [3]Boston University School of Medicine, Paris, France, [4]Department of Rheumatology, Lariboisière Hospital, AP-HP Université de Paris, INSERM U1132, Paris, [5]Department of Rheumatology, Hopital Cochin, Université de Paris, Paris, France, [6]AP-HP, Hôpital Saint-Antoine, Service de Rhumatologie, Centre de Recherche Saint-Antoine, INSERM UMR_S 938,Sorbonne Université, Paris, 75012, France, Paris, France

SESSION INFORMATION
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Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Proximal and distal inter-phalangeal (PIP, DIP) and thumb base joints are the most common sites affected in hand osteoarthritis (HOA), while involvement of metacarpo-phalangeal (MCP) joints is considered as uncommon and rather related to chondrocalcinosis, haemochromatosis or chronic inflammatory arthritis. The aim of this study was to assess the prevalence of radiographic MCP OA in a large cohort of HOA patients and to determine the factors associated with radiographic MCP OA.

	Univariate analysis		Multivariate analysis	
	OR [IC à 95%]	p-value	OR [IC à 95%]	p-value
Age	1.09 [1.05-1.13]	<.0001	1.05 [1.01-1.10]	0.0194
Sex		0.2947		0.2505
Men	1	.	1	.
Women	1.40 [0.74-2.65]	.	1.59 [0.72-3.48]	.
Body mass index	1.00 [0.95-1.05]	0.9912	0.99 [0.93-1.05]	0.7547
Family history of osteoarthritis		0.7893		0.8558
No	1	.	1	.
Yes	0.94 [0.58-1.51]	.	1.05 [0.59-1.87]	.
Socio-professional category		0.0114		0.0158
Intellectual professions	1	.	1	.
Farmers, craftsmen, traders and workers	3.16 [1.31-7.62]	0.0104	3.74 [1.21-11.54]	0.0218
Intermediate professions and employees	1.67 [1.05-2.68]	0.0320	1.85 [1.07-3.21]	0.0280
Dominant hand		0.0727		
Right	1	.		
Left	0.32 [0.09-1.11]	.		
Time of evolution of hand osteoarthritis (years)		<.0001		
< 5 years	1	.		
5-15 years	4.64 [1.32-16.39]	0.0170		
> 15 years	9.67 [2.91-32.14]	0.0002		
Number of erosive joints among PIP and DIP (0-18)		0.0027		
0	1	.		
1-3	1.58 [0.94-2.64]	0.0815		
4 and +	2.94 [1.57-5.52]	0.0008		
Number of DIP KL ≥ 2 (0-8)		<.0001		
0-3	1	.		
4-6	3.37 [1.11-10.25]	0.0323		
7-8	9.02 [3.16-25.77]	<.0001		
Number of PIP KL ≥ 2 (0-8)		<.0001		<.0001
0-4	1	.	1	.
5-8	6.78 [3.23-14.23]	<.0001	7.83 [3.58-17.16]	<.0001
9-10	15.34 [7.22-32.59]	<.0001	14.29 [6.46-31.64]	<.0001
Number of ST KL ≥ 2 (0-2)		<.0001		0.0045
0	1	.	1	.
1-2	2.60 [1.64-4.12]	.	2.18 [1.27-3.72]	.
Number of TMC KL ≥ 2 (0-2)		0.0430		
0-1	1	.		
2	1.59 [1.01-2.51]	.		
Painful joints on pressure (0-30)		0.0232		
0-1	1	.		
2-3	0.45 [0.24-0.82]	0.0097		
4-6	0.48 [0.25-0.93]	0.0289		
7 and +	0.86 [0.47-1.59]	0.6319		
Swelling joints (0-30)		0.0013		
0-2	1	.		
3 and +	2.49 [1.43-4.35]	.		
Joints with nodes (0-30)		0.0010		
0-3	1	.		
4-10	2.12 [1.07-4.16]	0.0301		
11 and +	3.77 [1.84-7.69]	0.0003		
Grip strength on dominant hand		0.0143		
> 30kg	1			
≤ 30kg	2.12 [1.16-3.87]	.		

Table. Univariate and multivariate analysis. * Systematic adjustment on age, sex, BMI and family history of osteoarthritis

Methods: Using the data from DIGital Cohort Osteoarthritis Design (NCT01831570), a French hospital-based observational cohort including patients of >35 years-old with symptomatic HOA, we evaluated the prevalence of radiographic MCP HOA defined by at least two MCP joints with a Kellgren Lawrence (KL) score ≥ 2. This cohort includes patients who have symptomatic HOA according to one of the following definitions: i) symptomatic HOA fulfilling American College of Rheumatology (ACR) criteria on at least 2 joints among proximal or distal interphalangeal (PIP/DIP) joints or first IP joint with KL ^{3} 2, or ii) symptomatic thumb base OA with KL ^{3} 2. Patients with chondrocalcinosis or other inflammatory rheumatic diseases (such as psoriatic arthritis or rheumatoid arthritis) were not included. We

compared the prevalence of MCP HOA between dominant and non-dominant hands (McNemar test). Associations between radiographic MCP OA and patients characteristics (general and HOA characteristics) were studied using logistic regression. Adjustment was made on age, gender, Body mass index (BMI) and family history of HOA and factors selected in unadjusted analysis ($p \leq 0.20$). Odds ratios and their 95% confidence intervals were reported.

Results: 425 patients were included of whom 45.6% had erosive HOA. Radiographic MCP OA was present in 138 patients (32.5%), and 139 (32.8%) patients had at least one painful MCP on pressure. Only two patients (0.5%) had an erosive MCP joint. MCP OA patients had a mean±SD age of 69.2±6.9 years-old, a BMI of 25±4.2kg/m2, 119 patients (86.2%) were women and 89 (66.9%) had a family history of HOA. MCP OA was more frequent at the dominant hand (40.6% vs 34.7%, p=0.01) and predominated at the 1st and 2nd MCP joints.

In multivariate analysis, radiographic MCP OA was associated with older age (OR 1.05; CI95% [1.01-1.10] for each year), manual occupations (OR 3.74, CI95% [1.21-11.54]), the presence of scapho-trapezial OA (OR 2.18, CI95% [1.27-3.72]) and with a higher number of radiographic PIP OA joints (OR 14.29, CI 95% [6.46-31.64]) (**Table**). No association with obesity or metabolic syndrome (ATPIII criteria), HOA symptoms (pain, stiffness, or function), hyperferritinemia or elevated transferrin saturation coefficient were found.

Conclusion: In this hospital-based HOA cohort, radiographic MCP OA was frequent (32.5%) and associated with structure rather than symptom severity. Our results strongly suggest that the involvement of MCP joints in HOA is predominantly related to mechanical rather than systemic factors.

Disclosure: I. Kouki, None; **S. Tuffet**, None; **M. Crema**, Boston Imaging Core Lab, 1; **A. Rousseau**, None; **P. Richette**, None; **M. Dougados**, Pfizer, 1, 2, Abbvie, 1, 2, UCB, 1, 2, Merck, 1, 2, Lilly, 1, 2, BMS, 1, 2, Roche, 1, 2, Novartis, 1, 2; **F. Berenbaum**, Pfizer, 1, Eli Lilly, 1; **J. Sellam**, None; **A. Courties**, None.

Abstract Number: 1104

The Disability Associated with Hand Osteoarthritis Is Substantial in a Cohort of Post-menopausal Women : The QUALYOR Study

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SESSION INFORMATION
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Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a highly prevalent disease, affecting more than 400 millions individuals around the world. Hand osteoarthritis (HOA) is the most frequent form of OA. The prevalence is variable depending on the definition used and the population studied. It has been suggested in a few studies that disability may be comparable to that seen in rheumatoid arthritis (RA). As HOA is more frequent than RA, the burden of disease is greater. The aim of this study was to systematically assess the disability associated with HOA, along with its correlates, in a cohort of post-menopausal women, the QUALYOR study (QUalité Osseuse Lyon Orléans).

Methods: At the 72 months follow-up visit of the study, we performed, radiographs using a High-resolution direct digital X-ray device (BMA®, D3A Medical Imaging), clinical examination assessing pain, nodes and deformations, grip

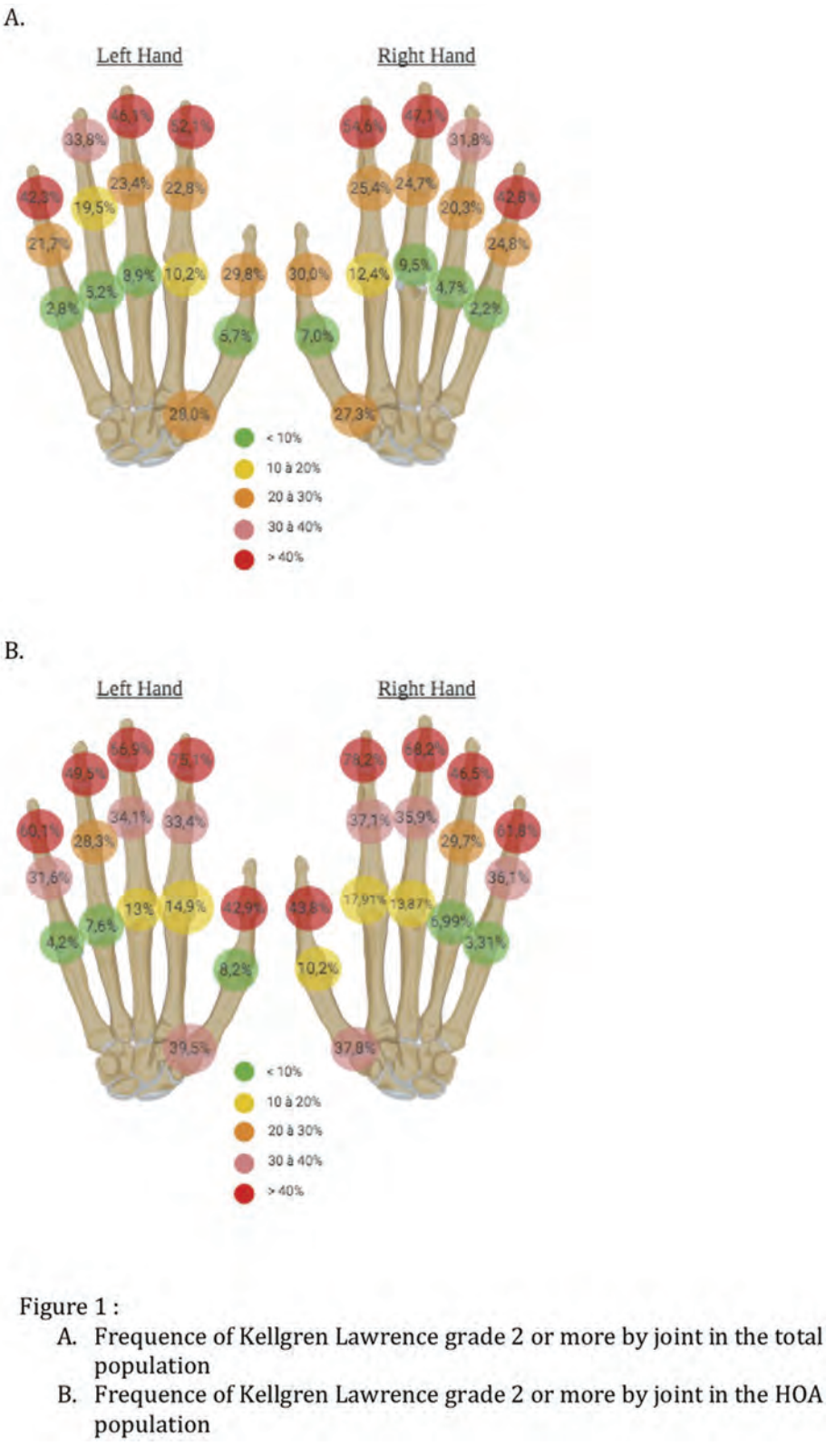

Figure 1 :

A. Frequence of Kellgren Lawrence grade 2 or more by joint in the total population
B. Frequence of Kellgren Lawrence grade 2 or more by joint in the HOA population

Figure 1

strength, AUSCAN and COCHIN questionnaires and a bone densitometry (DXA Hologic Discovery A). At baseline, a HRpQCT (XtremeCT, Scanco Medical), a DXA and a blood sample to assess bone turnover markers (CTX, PINP) were performed. Radiographic hand OA (RHOA) was defined as at least 2 over 30 articulations grading 2 or more using the

Kellgren Lawrence score. Moderate to severe symptomatic HOA was defined as radiographic hand OA and AUSCAN total score > 43/100 (threshold previously identified as the level of non accepTable disability in HOA(1)). T-tests were used to compare continuous variables, Spearman correlations were performed to explore the association of these parameters with HOA and a multivariate analysis including age using logistic regression models was made.

Results: We included 1189 patients, aged at least 55. The mean age was 71.7 years. Inter-reader reliability was good (ICC = 0.86) and intra-reader reliability was excellent (ICC = 0.97). RHOA was rare before age 60. Among 1189 women, 815 (68.5%) had RHOA. They were older than those without RHOA and grip strength was significantly lower in this group. No significant difference was noted on bone microarchitecture, bone turnover markers and clinical characteristics especially BMI. Figure 1 presents RHOA prevalence by joint in the total population and in the RHOA population. Of note, 194 patients with RHOA had erosions on radiographs (23.8%). 86 patients over 815 (10.5%) had moderate to severe symptomatic HOA. BMI at the time of osteoarthritis evaluation was significantly higher in this group. Grip strength was significantly lower in those with symptomatic RHOA. No significant difference was seen in bone microarchitecture, bone mineral density and bone turnover markers in RHOA.

Conclusion: In our cohort of post-menopausal women aged at least 55, 68.5% had RHOA and 10.5% of them had a moderate to severe HOA related disability. BMI was associated with symptomatic RHOA.

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Disclosure: M. Auroux, None; **B. Merle**, None; **E. Lespessailles**, MSD, 2, 5, 8, Amgen, 2, 5, 8, Lilly, 2, 5, 8, UCB, 2, Expanscience, 5, 8, Abbvie, 2; **R. Chapurlat**, Pfizer, 5.

Abstract Number: 1105

RANK-L Activity: Understanding the Pathogenesis of Erosive Osteoarthritis

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SESSION INFORMATION
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Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Erosive osteoarthritis (EOA) is characterized by osteoarthritic findings with central erosions and collapse of the interphalangeal joint subchondral bone plate. A number of studies indicate that there is an inflammatory component but the pathophysiology of the erosions is not known. Receptor activator of nuclear factor kappa-B ligand (RANK-L) is involved in the erosive process of inflammatory arthritides and we hypothesized that it would be involved in the erosive process of EOA. We therefore compared the RANK-L levels in histological specimens of EOA with non-erosive hand OA specimens and compared the bone mineral densities (BMDs) of a cohort of EOA patients with those of OA patients.

	OA (n=60)		EOA (n=20)		Significance
	Mean	SD	Mean	SD	P value
RANK-L$^+$ Area (microns^2)	1102.32	606.91	3773.24	2372.35	p<0.0001

Table 1. RANK-L signal area per 200x field of synovial tissue

	OA		EOA	
	Fields (n)	Mean number of cells	Fields (n)	Mean number of cells
Reader 1	61	1.80	30	5.4
Reader 2 (1st pass)	61	1.64	30	5.07
Reader 2 (2nd pass)	61	1.61	30	4.8

Table 2. RANK-L+ cells counted per 200x field of synovial tissue

Methods: This was a single center retrospective, observational study. Histological tissue from EOA (n=8) and hand OA (n=15) patients who underwent surgery between 2005 and 2015 were retrieved and stained with an antibody to RANK-L. The diagnosis of EOA was defined by OA based on American College of Rheumatology (ACR) clinical criteria with erosions in at least two interphalangeal joints, as well as a negative rheumatoid factor, anti-citrullinated antibody, and anti-nuclear antigen without personal or family history of psoriatic arthritis or crystal-induced arthritis.

RANK-L$^+$ cells were counted in two to five random 200x fields and RANK-L area was measured in 200X pictures with Image J NIH software. Morphometric analysis was performed in a blinded fashion by two independent evaluators.

A retrospective chart review, of diagnostic codes for EOA and OA from 7/1/2009-7/1/2019 was conducted. EOA diagnosis was confirmed either by radiologic evidence of characteristic erosions in at least two interphalangeal joints or diagnosis by a rheumatologist. Patients with crystalline arthritis, rheumatoid arthritis, psoriasis, and psoriatic arthritis

	OA (n=50)	EOA (n=23)
Median T-score [a]	-1.35	-1.5
Median BMD (g/cm^2) [a]	0.85	0.79
Median Height (in.)	63.1	64
Median Weight (lbs.)	148	142
Median Age	67	63
Sex	45 F (90%), 5 M (10%)	22 F (95.65%), 1 M (4%)
Race	46 C (92%), 3 B (6%), 1 H (2%)	21 C (91.30%), 2 B (8.70%)
Patients on osteoporotic meds [b]	9 (18%)	3 (13.04%)
Smoking status	29 non (58%), 18 former (36%), 2 current (4%), 1 unknown (2%)	10 non (43.48%), 10 former (43.48%), 2 current (8.70%), 1 unknown (former or current) (4.34%)

[a] Left total femur [b] bisphosphonates, denosumab, and PTH analogues/PTHrP analogues
F = female, M = male, C= caucasian, B = black, H = hispanic

Table 3. DEXA measurements with group demographics

diagnoses as well as those with a family history of psoriasis were excluded. Dual energy x-ray absorptiometry (DEXA) scans for 23 EOA and 50 randomly selected OA patients from the University of Rochester Medical Center were reviewed. Data on age, sex, race, smoking history, height, weight, and osteoporotic medication use was collected. Patients on high doses of steroids were excluded.

Results: There was a significantly larger area of RANK-L staining found with Image J NIH software area calculations for EOA (3773.24 ± 2372.35 microns^2, p< 0.0001) compared to OA (1102.32 ± 606.91 microns^2, p< 0.0001) (Table 1). There was also a higher number of RANK-L$^+$ cells in the EOA samples compared to the OA samples (Table 2).

DEXA comparison between OA and EOA patients showed a lower median BMD and T-score in the EOA group (0.79 g/cm^2, -1.5) compared with the OA group (0.85 g/cm^2, -1.35). Demographics between these groups were also compared and were relatively unremarkable (Table 3).

Conclusion: Our study demonstrated that EOA patients had higher levels of RANK-L in synovial tissue and were with lower BMD scores than patients with OA. We therefore propose that RANK-L activity promotes the osteoclastic driven erosive changes in EOA and also results in systemic bone loss.

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Abstract Number: 1106

MMP Mediated Type I Collagen Degradation Is Associated with Erosive Hand Osteoarthritis in a Hospital-based Observational Cohort – the NOR-HAND Study

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SESSION INFORMATION
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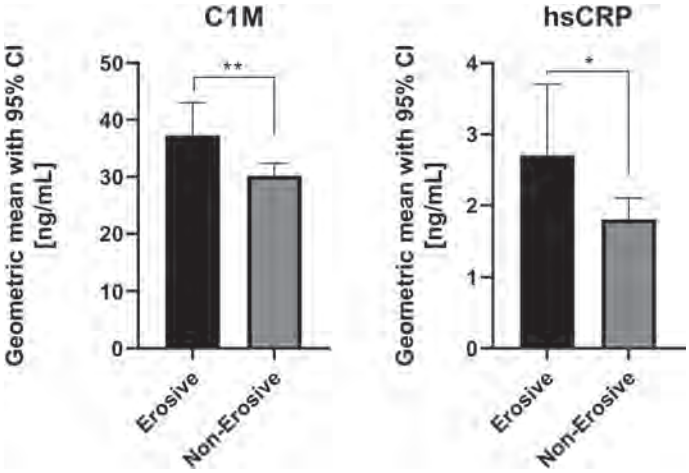
Session Time: 9:00AM–11:00AM

Background/Purpose: Hand osteoarthritis (OA) is a common degenerative joint disease affecting mainly the interphalangeal and first carpometacarpal joints. The disease manifests as inflammation and deterioration of joint structure leading to pain, loss of function, and reduced quality of life. Hand OA presents as different subtypes, where the erosive type is considered a more severe phenotype with more pronounced symptoms, more inflammation and a faster disease progression. The erosive suptype is associatedwith the development of joint erosions followed by characteristic repair and remodeling of the joint plate. Type I collagen turnover, measured by MMP generated type I collagen neo-epitope C1M in serum have previously been associated with synovial inflammation, disease activity and structural progression in rheumatoid arthritis (RA). The aim of this study was to investigate the association between erosive hand OA and systemic levels of C1M.

Methods: Serum was collected from 291 hand OA patients in the Nor-Hand study, a hospital based cohort study exploring the validity of imaging modalities and disease processes in hand OA. C1M, a measure of MMP mediated type I collagen tissue degradation and the acute phase reactant hsCRP reflecting inflammation was measured at baseline.



Bilateral hand radiographs were evaluated by an experienced reader (IKH)(n=287). Erosive hand OA was defined as at least one distal or proximal interphalangeal joint with erosions (defined as E or R stage according to the Verbruggen Veys anatomical phase scoring system). Logistic regression was used to model the odds of having erosive hand OA as function of C1M. C1M was log transformed before entering the model(s). Similar analysis was performed for hsCRP as comparison. All analyses were corrected for age, sex, BMI, and grey scale synovitis of the knee (0-3 scale) or hip (capsule thickness in millimeters) measured by ultrasound.

Results: The greater part of patients were women (n=256, 89%) with a mean (SD) age of 60.8 (6.2) years. 58 (20 %) patients were identified with erosive hand OA. These patients had higher levels of both C1M and hsCRP than patients with non-erosive disease (Table). A 10% increase in C1M was associated with an increase in the odds of having erosion by 1.069 (95% CI 1.016 – 1.126). The estimated odds ratio was similar after adjustment for clinical and demographic covariates (OR = 1.072; 95% CI 1,014 – 1.134). In comparison, a 10% increase in hsCRP was associated with an increase in odds by 1.027 (95% CI 1.016-1.051). The association remained after adjustment for covariates (OR=1.031; 95%CI 1.004-1.059).

Conclusion: MMP driven turnover of type I collagen measured by C1M, is associated with the presence of erosive hand OA, which is considered a more inflammatory phenotype. These findings suggest that systemic C1M levels may reflect specific pathological joint tissue alterations, and may be a potential biomarker in hand OA studies. Future studies are needed to explore the associations with synovitis and the sensitivity to change.

Disclosure: C. Thudium, Nordic Bioscience, 3; **N. Sharma**, None; **M. Gløersen**, None; **P. Frederiksen**, None; **A. Bay-Jensen**, Nordic Bioscience, 1; **I. Haugen**, None.

Abstract Number: 1107

IL1RN Polymorphism Predicts Weight Loss, Inflammatory Biomarker Changes and Knee Osteoarthritis Pain Relief After Bariatric Surgery

Jonathan Samuels[1], Fernando Bomfim[2], Mukundan Attur[3], Christine Ren-Fielding[4], Manish Parikh[5], Renata La Rocca-Vieira[6] and Steven B. Abramson[7], [1]NYU Langone, Rye Brook, NY, [2]New York University, Department of Medicine, Division of Rheumatology, Millburn, NJ, [3]NYU Langone Health, New York, NY, [4]NYU Langone Health, New YOrk, [5]Bellevue Hospital, New York, NY, [6]NYU, New YOrk, [7]New York University School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Symptomatic knee osteoarthritis (SKOA) patients with obesity who undergo bariatric surgery experience knee pain relief, though the reduced mechanical load explains only part of the improvement. A reduction in inflammatory biomarkers from adipose tissue may also impact pain. We previously identified an *IL1RN* haplotype (TTG; rs419598, rs315952, and rs9005) that associates with OA severity and inflammatory markers. We aimed to determine whether TTG distinguishes patients who lose more weight and have more significant decreases in inflammation with greater knee OA pain relief.

Methods: From 2013-2019 we enrolled patients ≥30 years old with BMI ≥30 kg/m^2 and painful knee OA who planned surgical (sleeve gastrectomy, gastric bypass, or laparoscopic band) or medical weight loss (MWL) at Bellevue Hospital or NYU Langone Health. Patients with lupus, rheumatoid arthritis, or psoriatic arthritis were excluded. Weight-bearing knee x-rays assessed OA severity to confirm a Kellgren-Lawrence grade of at least 1 (scale 0-4). Participants completed the Knee Injury and Osteoarthritis Outcomes (KOOS) questionnaire and provided blood at baseline and 1, 3, 6, and 12 months. Patients were genotyped to determine whether they carried 1 or 2 copies of the TTG haplotype (TTG-1/2) or none (TTG-0). Sleeve was the most common weight loss intervention, therefore our analysis is focused on this surgical subset to minimize variable effects on weight and biomarkers.

Results: We enrolled 113 patients (95 F, 18 M) with painful knee OA prior to their weight loss intervention. The mean age, BMI, and KOOS pain at baseline were 50.3 ± 12.0 years, 44.8 ± 8.9 kg/m^2, and 48.4 ± 18.2 (0-100, with 100 = no pain). Of 113 patients, 48 underwent sleeve, 20 bypass, 9 laparoscopic banding, 12 did not have the surgery, and 24 pursued medical weight loss. The 77 who completed surgery had a mean % excess weight loss (%EWL) of 51.7 after 6 months, with significant decreases in hsCRP (4.4 mg/L) and leptin (32.8 ng/dL), and mean KOOS pain improvement of 22.4 (MCID= 16.7). The corresponding changes for patients who tried various MWL regimens were modest at best. We obtained the *IL1RN* haplotype for 45 of the 48 sleeve patients, and found 34 (70.8%) carried the TTG-1 or TTG-

	Baseline	1 Month	3 Month	6 Month	
	mean (n)	mean (n)	mean (n)	mean (n)	p-value
% excess weight loss					
TTG-0 (n=11)	N/A	33.3 (9)	53.5 (7)	70.0 (7)	**0.005***
TTG-1/2 (n=34)	N/A	24.3 (26)	42.1 (26)	53.8 (24)	
KOOS Pain					
TTG-0 (n=11)	52.3 (11)	79.9 (9)	79.4 (7)	82.5 (7)	**0.021***
TTG-1/2 (n=34)	46.3 (34)	65.2 (26)	75.6 (26)	77.4 (24)	
hsCRP (mg/L)					
TTG-0 (n=11)	6.2 (10)	2.3 (5)	2.1 (6)	1.9 (6)	0.36
TTG-1/2 (n=34)	7.8 (34)	6.1 (18)	5.1 (25)	4.9 (21)	
Leptin (ng/mL)					
TTG-0 (n=11)	105.3 (10)	36.8 (8)	17.5 (6)	16.5 (6)	**0.006***
TTG-1/2 (n=34)	94.7 (33)	46.8 (23)	38.6 (25)	31.6 (19)	

Table 1

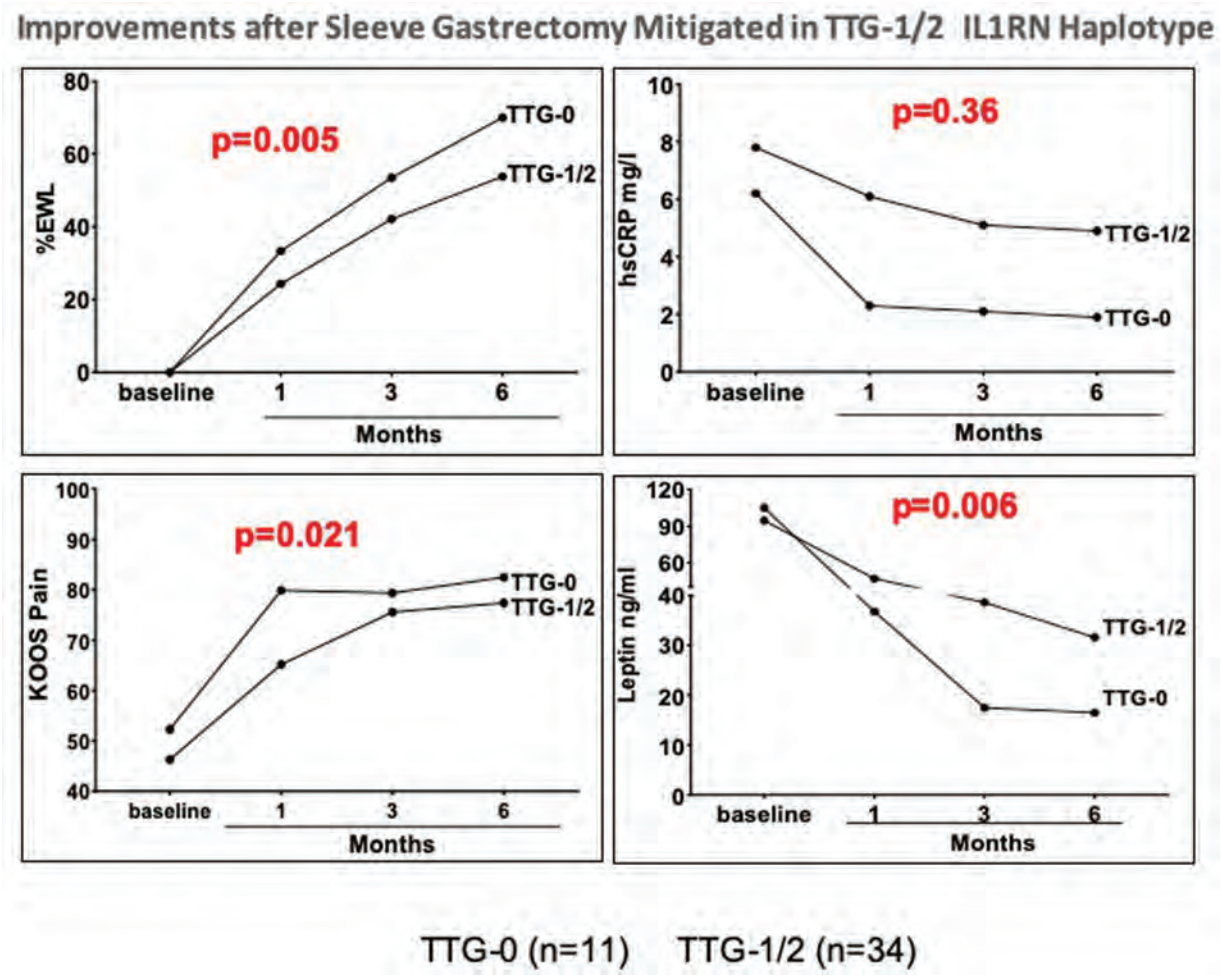


Figure 1

2 haplotype while 11 were TTG-0 (with similar baseline age, BMI, and KOOS for the two groups). At each follow-up time point through 6 months (Figure 1), TTG-1/2 patients had more difficulty losing weight than the TTG-0 group ($p< 0.005$ by ANOVA), with corresponding smaller reductions in *hs*CRP ($p=0.36$) and leptin ($p=0.006$). TTG-1/2 carriers also reported less KOOS pain relief relative to the TTG-0 group ($p=0.021$), markedly at 1 and 3 months with some improvement later (Table 1). All of these findings held true when only plotting data only from the 23 patients (18 TTG-1/2, 5 TTG-0) who completed each of the followup visits.

Conclusion: SKOA patients with obesity achieve marked excess weight loss, reductions in inflammatory mediators, and knee pain relief with bariatric surgery. The subset of patients with the TTG-0 *IL1RN* haplotype demonstrated more significant and/or rapid improvement in each of these outcomes, suggesting a potential predictor of which OA patients will have a more successful response to bariatric surgery.

Disclosure: J. Samuels, None; **F. Bomfim**, None; **M. Attur**, NYU School of Medicine, 4; **C. Ren-Fielding**, Covidien LP, 1, Ethicon Inc., 1, Intuitive Surgical, Inc., 1, Levita Magnetics International Corp, 1, W. L. Gore & Associates, Inc., 1, Allergan Inc., 1, Nalpropion Pharmaceuticals LLC, 1; **M. Parikh**, None; **R. La Rocca-Vieira**, None; **S. Abramson**, NYU Grossman School of Medicine, 9.

Abstract Number: 1108

Cartilage Biomarkers s-Coll2-1 and s-Coll2-1NO2 Are Associated with Knee Osteoarthritis MRI Features and Predict Disease Worsening

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Osteoarthritis – Clinical Poster I

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: To identify if biochemical markers s-Coll2-1, a peptide of type collagen and its nitrated from, s-Coll2-1NO2 are associated to knee osteoarthritis (OA), focusing on pain, function as well as structural features assessed by MRI and to assess their ability at predicting knee OA worsening.

Methods: 116 subjects with knee OA were followed during one year with pain, function and MRI evaluation (PRODIGE study, NCT02070224). Type II collagen-specific biomarker Coll2-1 and its nitrated form Coll2-1NO2 were directly measured in serum using immunoassays at baseline and after three, six and twelve months follow-up.

Results: S-Coll2-1 was significantly correlated with bursitis (r=0.29, P< 0.01), bone attrition (r=0.25, P=0.01), cysts (r=0.24, P=0.02) and cartilage (r=0.23, P=0.03) WORMS sub-scores for the whole joint as well as with the medial femorotibial joint sum score (r=0.26, P=0.01) and medial femorotibial joint cartilage (r=0.23, P=0.02). s-Coll2-1NO2 was correlated with WORMS total score (r=0.23, P=0.02), WORMS scores in the patellofemoral (r=0.23, P=0.02) and medial femorotibial compartments (r=0.21, P=0.03) and with osteophytes scores (r=0.27, P< 0.01). Baseline s-Coll2-1NO2 was higher in subjects with a pain worsening (426.4 pg/mL [278.04-566.95]) as compared to non-progressors (306.84 [200.37-427.84]) over one year (AUC=0.655, P=0.015).

Conclusion: Cartilage biomarkers s-Coll2-1 and s-Coll2-1NO2 are associated to several knee OA features quantified with WORMS scoring system on MRI. Serum values of Coll2-1NO2 are also associated to a worsening of target knee pain over one year. Coll2-1 and Coll2-1NO2, in association with other structural features, pain and function, could help at identifying OA phenotypes and patients at risk of OA worsening.

Disclosure: Y. Henrotin, Artialis SA, 1; **A. Hick**, Artialis SA, 3; **B. Costes**, Artialis SA, 3; **A. Labasse**, Artialis SA, 3; **T. Conrozier**, LABHRA, 2, 5; **M. Malaise**, None; **Y. Maugars**, None; **F. Pelousse**, SODIRAY, 1, 5; **J. Lemaire**, Sodiray, 3; **C. Tits**, DNAlytics, 3; **T. Helleputte**, DNAlytics, 1, 3; **D. Loeuille**, None.

Abstract Number: 1109

Pain in Women with Knee and/or Hip Osteoarthritis Is Related to Systemic Inflammation and to Adipose Tissue Dysfunction and Distribution: A Cross-sectional Metabolic Biomarkers Cohort Study

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
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Background/Purpose: Beyond the link between metabolic diseases and osteoarthritis (OA) risk, some studies have suggested an association between metabolic syndrome or visceral obesity and OA-related pain (1,2). Here, we investigated whether biomarkers of adipose tissue dysfunction and distribution could be associated with OA-related pain.

Methods: We cross-sectionally analyzed patients with knee and/or hip OA at inclusion in the 863 patients included in the national multicentric KHOALA cohort (NCT00481338). We used visual analogic scale (VAS) for pain, the Western Ontario and McMaster Universities Arthritis Index (WOMAC) and Osteoarthritis Knee and Hip Quality of Life (OAKHQOL) pain subscores. For WOMAC and VAS pain, higher scores reflects more symptoms, while it is the opposite for OAKHQOL.

At inclusion, we measured in the serum ultra-sensitive C reactive protein (usCRP), leptin and total adiponectin for calculation of leptin:adiponectin ratio (LAR), a marker of adipose tissue dysfunction associated with truncal obesity, high-molecular-weight adiponectin, visfatin and apolipoproteins (apoA1, apoB100). Univariate and multivariate analyses using stepwise linear regression models were performed to search for correlation between pain assessments and these biomarkers, with adjustment on age and Kellgren-Lawrence score and with stratification by sex since gender interacts with pain intensityand with adipokines level.

Results: In 596 women with hip and/or knee OA, multivariate analyses indicated that higher pain intensity was associated with higher LAR (VAS pain: b=0.48; p=0.0001, OAKHQOL pain: b=-0.45; p=0.0002, WOMAC pain: b=0.29; p=0.002) in the whole group. Analyzing knee and hip OA populations separately, these correlations were found for both joints in multivariate analyses (knee OA: VAS pain b = 0.52 p = 0.0001; OAKHQOL pain: b = -0.48 p = 0.0002; WOMAC pain b = 0.28 p = 0.006; hip OA: VAS pain b = 0.64 p = 0.03; OAKHQOL pain: b = -0.55 p = 0.04). Pain intensity correlated also with usCRP level (VAS pain: b= 0.27; p=0.02, OAKHQOL pain: b =-0.31; p=0.01) and Kellgren-Lawrence score. Serum visfatin, high-molecular-weight adiponectin, Apo A1 and Apo B100 levels were not related to pain level, whatever the score used. In 267 men, no correlation between biomarkers and pain was found.

Conclusion: Serum LAR and usCRP level are associated with pain level, independently of radiographic structural severity in women with hip and/or knee OA, emphasizing the role of adipose tissue dysfunction, truncal fat repartition and meta-inflammation in pain experience in this population.

1. Pan F et al Osteoarthr Cartilage 2020;28:45–52. 2. Li S, et al. Arthritis & Rheumatology (Hoboken, NJ) 2020.

Disclosure: J. Sellam, None; **A. Rat**, Sanofi Genzyme, 5; **S. Fellahi**, None; **J. Bastard**, None; **W. NGUEYON SIME**, None; **H. EA**, None; **P. Richette**, AbbVie Inc., 1, Biogen, 1, Janssen, 1, BMS, 1, Roche, 1, Pfizer, 1, Amgen, 1, Sanofi-Aventis, 1, UCB, 1, Lilly, 1, Novartis, 1, Celgene, 1; **J. Capeau**, None; **F. Guillemin**, Expanscience, 2; **F. Berenbaum**, Pfizer, 1, Eli Lilly, 1.

Abstract Number: 1110

Osteoarthritis-Related Knee Inflammation Measured by Ultrasound Is Associated with Performance-Based Measures of Function

Holly Philpott[1], Trevor Birmingham[2], Ryan Pinto[2], Dominique Arsenault[2], Codie Primeau[2], Edward Vasarhelyi[3], Steven MacDonald[3], Brent Lanting[3] and Tom Appleton[4], [1]Western University, London, ON, Canada, [2]Western University, London, Canada, [3]London Health Sciences Centre, London, Canada, [4]The University of Western Ontario, LONDON, ON, Canada

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Signs of inflammation in knee osteoarthritis (OA), including synovitis, are associated with worse clinical outcomes such as increased pain, risk of progression, and future need for knee replacement surgery. To date, no studies have examined the association between ultrasound (US) features of OA and performance-based

Table 1. Demographic characteristics for n=183 patients.

Age, mean ± SD [range]	64.9 ± 9.0 [37-85]
Sex, n (%)	
Male	74 (40.4%)
Female	109 (59.6%)
BMI (kg/m^2), mean ± SD [range]	31.8 ± 6.6 [20.2-54.1]
Radiographic Severity, n (%)	
Early (KL ≤ 2)	67 (36.6%)
Late (KL ≥ 3)	116 (63.4%)
Synovitis, n (%)	
0 (none)	39 (21.3%)
1 (mild)	74 (40.4%)
2 (moderate)	58 (31.7%)
3 (severe)	12 (6.6%)
KOOS Pain, mean ± SD [range]	53.2 ± 18.3 [0-100]
Chair-sit-stand, mean ± SD [range]	10.1 ± 3.8 [0-20]
40-meter walk (s), mean ± SD [range]	36.3 ± 12.4 [19.3-109.9]
6-minute walk test (m), mean ± SD [range]	379.0 ± 103.8 [90.2-698.6]
Flexion (Nm), mean ± SD [range]	35.2 ± 19.9 [5.1-106.9]
Extension (Nm), mean ± SD [range]	76.6 ± 36.9 [12.9-217.1]

Table 2. Multivariate linear regression model estimates			
Variable	**β coefficient**	**Robust Standard Errors**	**95% CIs**
Model 1: 40-meter walk test (s)			
Synovitis			
0 vs 1	**-5.02***	2.19	-9.35 to -0.69
0 vs 2	-1.53	2.13	-5.73 to 2.67
0 vs 3	**-7.11***	2.85	-12.73 to -1.50
Age	**0.28***	0.08	0.13 to 0.43
Sex	**4.35***	1.60	1.19 to 7.51
BMI	**0.47***	0.20	0.07 to 0.86
KOOS Pain	**-0.20***	0.06	-0.32 to -0.08
KL (early/late)	1.39	1.95	-2.47 to 5.24
Model 2: 6-minute walk test (m)			
Synovitis			
0 vs 1	33.21	19.34	-4.96 to 71.38
0 vs 2	-1.72	20.26	-41.70 to 38.27
0 vs 3	32.64	24.49	-15.70 to 80.99
Age	**-3.88***	0.78	-5.42 to -2.33
Sex	**-31.23***	12.85	-56.60 to -5.86
BMI	**-5.58***	1.08	-7.70 to -3.46
KOOS Pain	**1.77***	13.43	1.12 to 2.41
KL (early/late)	-19.30	0.33	-45.81 to 7.21
Model 3: Chair-sit-stand (#)			
Synovitis			
0 vs 1	0.99	0.63	-0.26 to 2.24
0 vs 2	0.17	0.63	-1.08 to 1.42
0 vs 3	1.39	0.98	-0.54 to 3.32
Age	**-0.11***	0.03	-0.16 to -0.06
Sex	-0.53	0.50	-1.51 to 0.45
BMI	**-0.15***	0.05	-0.24 to -0.06
KOOS Pain	**0.07***	0.01	0.04 to0.09
KL (early/late)	0.53	0.54	-0.54 to 1.61
Model 4: Isokinetic extension (quadriceps strength) (Nm)			
Synovitis			
0 vs 1	**12.31***	5.73	1.00 to 23.62
0 vs 2	6.51	6.03	-5.40 to 18.41
0 vs 3	-2.71	9.63	-21.71 to 16.30
Age	**-1.27***	0.31	-1.88 to -0.66
Sex	**-42.34***	5.24	-52.68 to -32.00
BMI	0.40	0.41	-0.40 to 1.21
KOOS Pain	**0.36***	0.14	0.08 to 0.63
KL (early/late)	2.26	5.20	-8.00 to 12.53
Model 5: Isokinetic flexion (hamstring strength) (Nm)			
Synovitis			
0 vs 1	**7.65***	3.19	1.35 to 13.95
0 vs 2	3.20	3.29	-3.30 to 9.70
0 vs 3	0.31	4.87	-9.31 to 9.92
Age	**-0.77***	0.14	-1.04 to -0.50
Sex	**-22.05***	2.86	-27.68 to -16.41
BMI	-0.26	0.18	-0.61 to 0.09
KOOS Pain	0.14	0.07	-0.004 to 0.29
KL (early/late)	3.49	3.00	-2.43 to 9.41

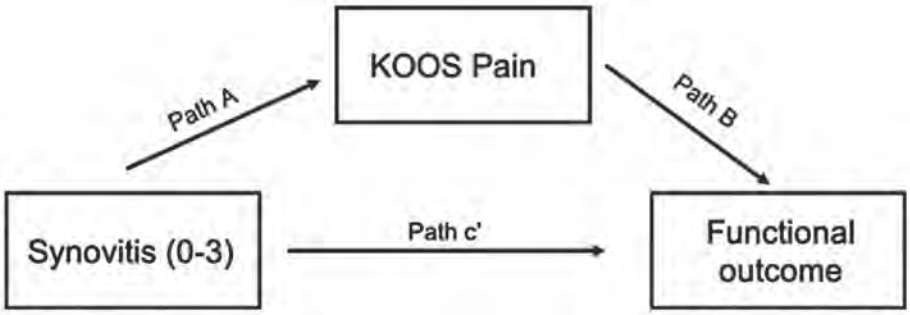

Figure 1. Diagram of each path in mediation analysis.

measures of function or muscle strength in patients with knee OA. Understanding the relationship between imaging features of knee OA and functional limitations, may help guide treatment algorithms and assessment of disease burden. The aim of this study was to assess the association of US-synovitis with performance-based measures of function and muscle strength in patients with knee OA.

Methods: Patients diagnosed with clinical knee OA based on the American College of Rheumatology (ACR) criteria were included in this cross-sectional analysis. Patients completed the Knee injury and Osteoarthritis Outcome Score (KOOS) questionnaire (0-100; lower scores indicate more pain) and a series of performance-based measures of function including the chair-sit-stand test, 40-meter walk test, 6-minute walk test, and quadriceps and hamstring strength (knee extension and flexion peak torque assessed using isokinetic dynamometry). Musculoskeletal-US was used to measure synovitis in the suprapatellar region (0-3; None-Severe). Radiographs were used to obtain Kellgren-Lawrence (KL) grades of OA severity. We fitted a series of multivariate linear regression models to evaluate the association between synovitis (predictor of interest) and performance-based measures of function (outcome), adjusting for age, sex, body mass index (BMI), KL grade, and KOOS Pain. Model outcome measures were 1) 40-meter walk test 2) 6-minute walk test 3) chair-sit-stand test, 4) extension (quadriceps strength), and 5) flexion (hamstring strength). Robust sandwich estimators were used. We reported results as unstandardized β coefficients with 95% confidence intervals (CIs), and robust standard errors. We evaluated for confounding and completed mediation analyses using PROCESS macro v3.5. Mediation results are reported as indirect effect estimates, standard error, and 95% CIs.

Results: Analyses included 183 patients (Table1). Greater synovitis was associated with decreased time for the 40-meter walk test, and increased quadriceps and hamstrings muscle strength, only when adjusting for age, sex, BMI, KL grade, and KOOS Pain (Table 2). Mediation analyses (Figure 1) for each model show that the effect of synovitis (0 vs 3) on performance-based functional outcomes and muscle strength is mediated by KOOS Pain. Indirect effects for 40-meter walk (3.30; SE:1.50; 95%CI: 0.86-6.75), chair-sit-stand (-1.08; SE:0.41; 95%CI: -19.6- -0.36), 6-minute walk test (-29.61; SE: 10.59; 95%CI: -52.67- -10.50), and extension (-5.97; SE: 2.98; 95%CI: -12.43- -0.80) indicate significant mediation.

Conclusion: Important factors such as pain, age, sex, and body size are known to be related to function in knee OA. We demonstrated that US-synovitis is another important factor that should be considered. Moreover, our findings suggest that a complex relationship exists between knee synovitis and physical function that is mediated by pain.

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Arthritis, 2, Gilead, 2, 5, 8, Pfizer, 2, 5, 8, Servier/Galapagos, 2, Amgen, 5, 8, BMS, 5, 8, Celgene, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Hoffman LaRO=oche, 5, 8, Sandoz, 5, 8, Sanofi-Genzyme, 5, 8, UCB, 5, 8, Ontario Rheumatology Association, 6, Canadian Rheumatology Association, 6, American College of Rheumatology, 6.

Abstract Number: 1111

Intra-Articular Mineralization on Knee CT Increases Risk of Knee Pain: The Multicenter Osteoarthritis Study

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Intra-articular (i.a.) calcium crystal deposition is common in knee osteoarthritis (OA). Low-grade inflammation related to crystals may contribute to knee pain, including pain fluctuation. Chondrocalcinosis has been measured primarily on radiographs to date, which have low sensitivity. We used CT to identify i.a. mineralization to overcome this limitation, and used longitudinal data to examine the relation of i.a. mineralization to the development of knee pain.

Methods: We used data from the Multicenter Osteoarthritis (MOST) Study, a NIH-funded longitudinal cohort of people with or at risk of knee OA. The 12th-year visit was the baseline for this analysis as this was the first study visit at which CTs were obtained, and a new cohort was recruited (age 45-69) who had KL ≤2 in both knees, and either no knee pain or if they had knee pain, it could not be severe, constant pain. All participants had pain questionnaires, knee radiographs, and bilateral knee CTs at baseline, and assessed for pain outcomes every 8 months x3. A musculoskeletal radiologist scored multiplanar CT images (axial native images with coronal and sagittal 2D reformats)

Location/Extent of Intra-articular Mineralization	Odds Ratio (95% CI)		
	Incident Frequent Knee Pain	Incident Frequent Intermittent or Constant Pain	WOMAC Pain Worsening
Any mineralization in the knee	1.18 (0.76, 1.83)	1.37 (0.86, 2.18)	1.36 (0.98, 1.90)
Any cartilage mineralization	1.44 (0.88, 2.36)	**1.72 (1.04, 2.84)**	**1.48 (1.03, 2.14)**
Any meniscal mineralization	1.37 (0.89, 2.11)	1.55 (0.94, 2.56)	1.27 (0.88, 1.83)
Mineralization in >5 regions vs. 0 regions	**1.95 (1.12, 3.40)**	**1.97 (1.06, 3.66)**	1.54 (0.99, 2.40)

Relation of Intra-Articular Mineralization to Risk of Developing Knee Pain or Knee Pain Worsening Over Two Years

using the Boston University Calcium Knee Score (BUCKS). Mineralization in each of WORMS-defined subregions of cartilage and menisci was scored on a 0-3 scale. Ligament and joint capsule mineralization were scored as present or absent. We examined presence of any i.a. mineralization, any cartilage mineralization, and any meniscal mineralization to the risk of development of: frequent knee pain (FKP) among those free of FKP at baseline, development of more frequent intermittent knee pain (indicated as at least "often") or constant pain among those with no constant pain or only infrequent intermittent pain (occurring no more than "sometimes" based on the ICOAP) at baseline, and WOMAC worsening of ≥2/20 (MCID) over 2 years. We carried out knee-specific analyses using logistic regression with GEE and adjusting for age, sex, BMI, race, and KL grade.

Results: A total of 2090 participants were included (mean age 61, mean BMI 28.8, 57% female). Overall, 10.2% of knees had i.a. mineralization, 7.3% had any cartilage, and 8.2% had meniscal mineralization. Presence of i.a. mineralization in a greater number of regions was associated with risk of developing FKP (OR 1.95, 95% CI 1.12-3.40), more frequent intermittent or constant pain (OR 1.97 (95% CI 1.06-3.66), and a trend towards more severe pain (OR 1.54, 95% CI 0.99-2.40) (**Table**). In addition, cartilage mineralization was significantly associated with developing more frequent intermittent and constant pain as well as developing more severe knee pain, while the association of meniscal mineralization with these pain outcomes did not reach statistical significance, though there were trends towards increased risk.

Conclusion: Intra-articular mineralization was associated with risk of developing knee pain and worsening pain over two years. This first report of CT-based i.a. mineralization on risk of knee pain highlights the important role crystals play in the knee pain experience. These findings implicate crystal deposition in changing pain patterns over time in knee OA, and point to need for research at therapy directed towards crystal disease in OA.

Disclosure: T. Neogi, Lilly, 1, EMD Merck Serono, 1, Novartis, 1, Regeneron, 1, Pfizer/Lilly, 1; **J. Lynch**, None; **M. Jarraya**, None; **D. Felson**, None; **N. Wang**, None; **J. Torner**, None; **C. Lewis**, None; **M. Nevitt**, None; **A. Guermazi**, AstraZeneca, 1, Pfizer, 1, MerckSerono, 1, Galapagos, 1, Roche, 1, TissueGene, 1, Boston Imaging Core Lab, 1.

Abstract Number: 1112

Relationship of Depth-Specific Subchondral Bone Mineral Density and Pain in Knee Osteoarthritis: The Multicenter Osteoarthritis Study

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SESSION INFORMATION
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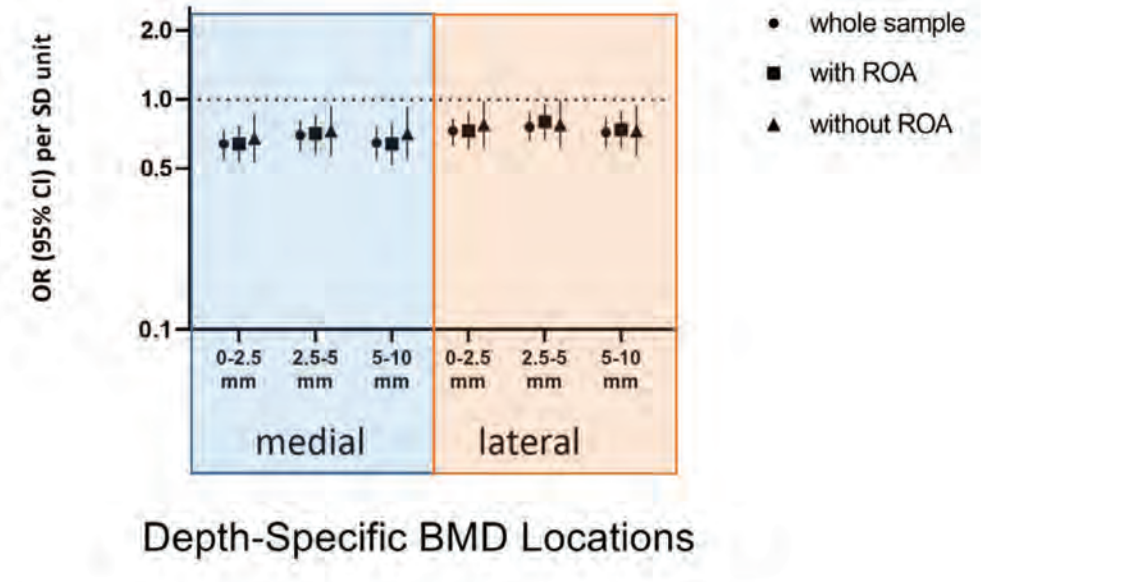
Background/Purpose: OA has traditionally been considered a disease of cartilage but early OA changes in subchondral bone may precede cartilage abnormalities. Altered subchondral bone mineral density (BMD) is thought to lead to cartilage pathology through abnormal force transfer. This in turn may contribute to pain in OA. It is unclear whether BMD increases or decreases with OA, and/or what effect these changes may have on pain. CT topographic mapping of subchondral density (CT-TOMASD) is a 3D imaging tool that precisely measures subchondral cortical and trabec-

Figure 1. Relation of subchondral tibial BMD to knee pain, by compartment and depth, with stratification by ROA status



All models adjusted for age, sex, and BMI. Adjusted ORs are reported for a SD-unit difference in subchondral BMD.

Abbreviations: BMD, bone mineral density; BMI, body mass index; OR, odds ratio; ROA, radiographic osteoarthritis; SD, standard deviation

Figure 1.

ular BMD in relation to depth from the subchondral surface. The aim of this study was to evaluate compartment- and depth-specific subchondral BMD in relation to knee pain.

Methods: Participants from the Multicenter Osteoarthritis (MOST) study, a NIH-funded longitudinal prospective cohort of older adults with or at risk of knee OA, who had knee CTs and knee pain assessed were included in this cross-sectional analysis. Knee pain was measured as the mean pain in the past 30 days, scored on a visual analog scale (VAS) (range 0-100), and dichotomized at 40/100. CT-TOMASD was used to assess tibial subchondral BMD at depths of 0-2.5 mm, 2.5-5.0 mm, and 5-10 mm relative to the subchondral surface. Regional analyses of each medial and lateral plateau, at each depth were performed to calculate average BMD. We evaluated the relation of subchondral BMD to presence of knee pain using logistic regression with generalized estimating equations to account for 2 knees within individuals, for each compartment and depth in separate models, and adjusted for age, sex, and body mass index (BMI). We additionally adjusted for, and stratified by, radiographic OA (ROA) status in separate models.

Results: 2082 subjects were included (mean age 61.1±9.7, 56.5% female, mean BMI 28.8±5.2 kg/m^2). The odds of having a VAS knee pain of ≥40/100 was significantly lower for a SD-unit increase in average subchondral BMD, after adjustment for age, sex, and BMI. This association was seen in both medial and lateral compartments though more marked within the medial compartment. The magnitude of association did not differ for increasing depths beneath the subchondral surface. Analyses adjusting for, or stratifying by, ROA status did not differ substantially from the main results.

Conclusion: Lower subchondral tibial BMD measures were associated with higher knee pain scores in individuals with or at risk for knee OA. There were no clear differences noted with increasing depths beneath the subchondral surface that would support differential depth-specific contributions from subchondral BMD involved in the pathogenesis of pain in knee OA. These findings may reflect the stage of OA at which there may be high bone remodeling in response to abnormal joint loading, impact or injury, and may be worth exploring as a more timely stage of intervening for targeting OA-related pain. Further studies using CT-TOMASD will evaluate the association of these subchondral BMD measures, including effects of stress-shielding, and structural changes seen on MRI.

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Abstract Number: 1113

Intrameniscal Signal Alterations Strongly Predict Destabilizing Meniscal Tears and Accelerated Knee Osteoarthritis: Data from the Osteoarthritis Initiative

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Background/Purpose: It is unknown whether early changes in the menisci (e.g., intrameniscal signal alterations) have long-term consequences. We conducted a study to assess the prognostic potential of intrameniscal signal alterations with incident destabilizing meniscal tears (radial or complex tears or macerated menisci) or accelerated knee osteoarthritis (KOA).

Methods: We used existing magnetic resonance (MR)-based data from a sex-matched nested case-control study of 3 groups from the Osteoarthritis Initiative without radiographic KOA at baseline (Kellgren-Lawrence [KL] < 2): 1) accelerated KOA: developed KL 3 or 4 within 48 months; 2) typical KOA: increased in KL grade within 48 months (excluding accelerated KOA); 3) no KOA: no change in KL grade within 48 months. From the original groups (n = 375), we included people with intact medial and lateral menisci at baseline (n = 226) and 48-month meniscal data (n = 221). Two readers read annual intermediate-weighted MR sequences with and without fat-suppression from baseline to the 48-month visit using a modified version of the International Society of Arthroscopy, Knee Surgery, and Orthopaedic Sports Medicine meniscal tear classification. The readers assessed 3 regions (anterior, body, posterior) of the medial and lateral menisci. Baseline meniscal status was operationally defined: 1) normal (intact with no signal intensity abnormalities) and 2) intrameniscal signal alteration (intrameniscal increased signal on a fluid-sensitive sequence that does not extend to an articular surface). We defined an incident destabilizing meniscal tear as the emergence of a radial (including root tears) or complex tear or maceration. Our readers had good inter-reader agreement (medial meniscal interobserver kappa = 0.90; lateral meniscal kappa = 0.63). We used 2 logistic regression models to assess

Table. The Presence of Baseline Intrameniscal Signal Alterations Predicts Future Destabilizing Meniscal Tears and Incident Accelerated Knee Osteoarthritis (KOA)				
Outcome	**Predictor**	**Outcome Presence**		
		Absent	**Present**	**Odds Ratio (95% CI)**
Incident Medial Destabilizing Meniscal Tear	No medial intrameniscal signal alterations	122 (91%)	12 (9%)	Reference
	Medial intrameniscal signal alterations	67 (77%)	20 (23%)	3.03 (1.40 to 6.59)
Incident accelerated KOA (reference= typical KOA)	No medial or lateral intrameniscal signal alterations	34 (71%)	14 (29%)	Reference
	Medial or lateral intrameniscal signal alterations	31 (40%)	47 (60%)	3.68 (1.71 to 7.95)
Note. 95% CI = 95% confidence interval				

1) whether the presence of medial intrameniscal signal alteration (predictor) was associated with an incident medial destabilizing meniscal tear versus no incident medial destabilizing meniscal tear (reference group), and 2) if the presence of intrameniscal alterations in either meniscus predicted incident accelerated versus typical KOA (reference group) over the next 4 years.

Results: We analyzed 221 knees with intact medial and lateral menisci at baseline. Overall, the study sample was mostly female (68%), with an average age of 58 (8) years, and an average body mass index of 28.1 (4.8) kg/m^2. The presence of medial intrameniscal signal alterations was strongly associated with incident medial destabilizing meniscal tears (odds ratio = 3.0 [95% CI = 1.4 to 6.6]; Table). Though numbers were small, 8 out of 9 incident lateral destabilizing meniscal tears had lateral intrameniscal signal alterations at baseline. The presence of baseline intrameniscal signal alteration in a knee strongly predicted the onset of accelerated versus typical KOA (odds ratio = 3.7 [95% CI = 1.7 to 8.0]; Table).

Conclusion: Intrameniscal signal alterations on intermediate-weighted fat-suppressed images may be clinically meaningful as they relate to future outcomes. Intrameniscal signal alterations may be a potential therapeutic target and warrant further study.

Disclosure: J. Driban, Pfizer, Inc., 1, 2, Eli Lilly and Company, 1; **J. MacKay**, None; **T. McAlindon**, Pfizer, 1, Sanofi Aventis US, 1, Kolon Tissuegene, 1, Samumed, 1, Seikagaku, 1, Kiniksa Pharmaceuticals, 1, Anika Therapeutics, 1; **M. Harkey**, Pfizer, Inc., 1; **B. Lu**, None; **C. Eaton**, None; **G. Lo**, Takeda Pharmaceuticals, 1, Taro Pharmaceuticals, 1, Teva Pharmaceuticals, 1, XBI Biotech Co, 1; **M. Barbe**, None; **R. Ward**, None.

Abstract Number: 1114

Longitudinally Assessed Structural Abnormalities on MRI and Relative Contributions to Risk of Incident Radiographic Knee Osteoarthritis over 10 Years of Follow-up

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Background/Purpose: MRI has identified joint tissues affected during knee OA development, though the relative importance of structures in the pathogenic process is unknown. Our objective was to estimate relative contributions of structural abnormalities to risk of incident radiographic knee OA (iRKOA), with assessment of longitudinal MRI during 10 year follow-up.

Methods: We conducted a case-cohort study with 10 year follow-up. The parent cohort included 2,987 Osteoarthritis Initiative participants with at least one knee at risk of developing iRKOA (i.e., Kellgren-Lawrence [KL] 0 or 1 at baseline). Within the parent cohort, participants who developed iRKOA (cases, n=844) and a random sample of the parent cohort (subcohort, n=868) were identified for MRI readings, a total of 1,455 participants (Figure 1). If a participant had two knees at risk, we selected the first knee to develop iRKOA or otherwise selected a knee at random (one knee per person).

Participants underwent bilateral posteroanterior fixed-flexion weight-bearing x-ray at baseline and annually through year 4, and then every two years until year 10; x-rays were centrally read for KL grade. 3T MRI was acquired at clinic visits up to year 8; longitudinal structural abnormalities in knees identified as cases and/or in the subcohort were graded using the MRI Osteoarthritis Knee Score (MOAKS).

We fit Cox models for time to iRKOA, with subcohort controls weighted inversely proportional to the sampling fraction; longitudinal structural features were included as time-varying predictors, lagged from the visit prior to each x-ray to establish temporality. We fit feature-specific models for bone marrow lesions (BML), cartilage damage, and meniscal damage with maximum scores in each compartment (i.e., medial tibiofemoral [TF], lateral TF, patellofemoral

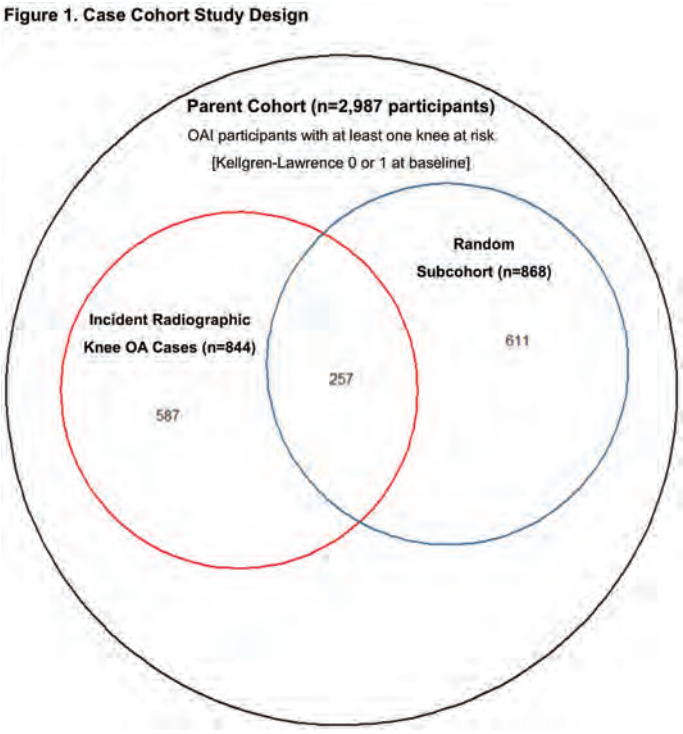

Figure 1.

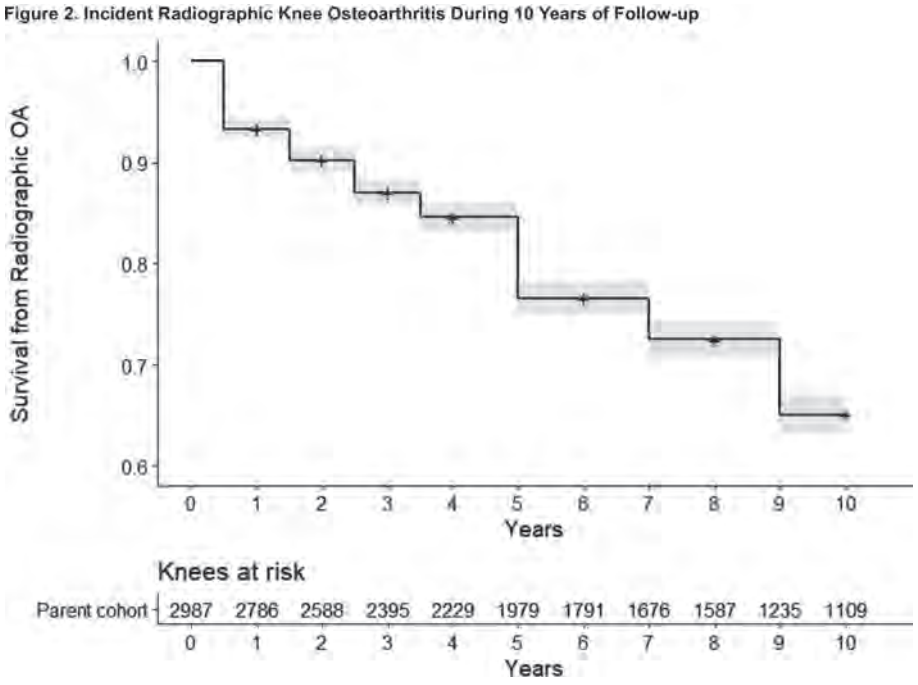

Figure 2.

[PF]), as well as an inflammation model for whole-knee effusion-synovitis (ES) and Hoffa-synovitis (HS). We also fit a full model with all features.

Results: Time to iRKOA is shown in Figure 2. The subcohort reflected the parent cohort, with a mean age of 60 years (SD 9), 55% female, 84% white and 14% African American, and predominately overweight (40%) or obese (32%).

In feature-specific models, all structural abnormalities were associated with iRKOA, and in nearly every compartment. The magnitude of association for specific abnormalities attenuated in the full model that included all features, though medium/large ES and PF cartilage damage of >10% surface area with >10% full-thickness or >75% surface area was associated with at least a two-fold increase in risk of iRKOA (based on lower bounds of the 95%CIs). Small ES, large medial TF BMLs, and PFJ cartilage damage of 10-75% surface area with any full-thickness, and lateral meniscus maceration were estimated to increase risk by at least 50% (Table 1).

Conclusion: While all structural abnormalities were associated with iRKOA in at least one compartment, our findings suggest that ES, PF cartilage damage, large medial TF BMLs, and lateral meniscus maceration are particularly indicative of increased risk of iRKOA. Varied structural abnormalities associated with knee OA development suggests heterogenous disease pathology that may require custom multifaceted treatment approaches.

Table 1. MRI-detected abnormalities and Incident Radiographic Knee Osteoarthritis

MRI-detected abnormalities			Time points	HR (95%CI)* (feature-specific models)	Wald X^2 p-value*	HR (95%CI)** (full model with all features)	Wald X^2 p-value**
Inflammation model	Effusion-Synovitis	Physiologic amount	4,205	1.00 (reference)		1.00 (reference)	
		Small	1,291	2.91 (2.40, 3.53)	194.8	2.07 (1.70, 2.51)	90.4
		Medium	232	4.84 (3.42, 6.84)	<.0001	2.80 (1.99, 3.93)	<.0001
		Large	30	13.71 (7.96, 23.62)		6.62 (3.80, 11.53)	
	Hoffa-Synovitis	Normal	3,633	1.00 (reference)		1.00 (reference)	
		Mild	1,921	1.99 (1.62, 2.44)	63.3	1.52 (1.23, 1.88)	24.2
		Moderate	191	2.75 (1.78, 4.24)	<.0001	2.01 (1.38, 2.94)	<.0001
		Severe	11	5.14 (2.63, 10.02)		2.74 (1.17, 6.40)	
Bone Marrow Lesion model	Medial	0: none	4,742	1.00 (reference)		1.00 (reference)	
		1: <33%	841	1.90 (1.50, 2.41)	108.5	1.33 (1.03, 1.71)	18.3
		2: 33-66%	142	3.23 (2.20, 4.76)	<.0001	1.53 (1.00, 2.34)	<.001
		3: >66%	30	10.49 (6.14, 17.92)		3.13 (1.77, 5.53)	
	Lateral	0: none	5,139	1.00 (reference)		1.00 (reference)	
		1: <33%	480	1.34 (0.99, 1.81)	11.1	1.04 (0.76, 1.41)	2.0
		2: 33-66%	114	1.89 (1.18, 3.01)	0.01	1.30 (0.79, 2.15)	0.58
		3: >66%	23	2.41 (0.83, 6.96)		1.63 (0.64, 4.17)	
	PFJ	0: none	2,317	1.00 (reference)		1.00 (reference)	
		1: <33%	2,102	1.10 (0.90, 1.36)	34.2	0.76 (0.59, 0.97)	8.2
		2: 33-66%	970	1.85 (1.47, 2.34)	<.0001	0.96 (0.71, 1.29)	0.04
		3: >66%	367	1.86 (1.30, 2.67)		1.01 (0.69, 1.49)	
Cartilage model	Medial	0: Normal	3,351	1.00 (reference)		1.00 (reference)	
		1: 1-10% SA, no FT	925	1.26 (0.96, 1.66)	83.8	1.11 (0.83, 1.49)	9.5
		1.1: 1-10% SA, 1-10% FT	240	1.87 (1.27, 2.76)	<.0001	1.41 (0.95, 2.09)	0.09
		2: 10-75% SA, no FT	1,027	2.30 (1.80, 2.94)		1.38 (1.03, 1.84)	
		2.1: 10-75% SA, 1-10% FT	150	3.81 (2.32, 6.25)		1.77 (1.08, 2.91)	
		2.2+ >10% SA with >10% FT, or >75% SA	64	5.07 (2.91, 8.84)		1.86 (1.02, 3.38)	
	Lateral	0: Normal	3,530	1.00 (reference)		1.00 (reference)	
		1: 1-10% SA, no FT	962	0.75 (0.56, 1.02)	45.3	0.66 (0.49, 0.90)	15.4
		1.1: 1-10% SA, 1-10% FT	332	1.19 (0.80, 1.76)	<.0001	1.11 (0.77, 1.60)	<.01
		2: 10-75% SA, no FT	566	1.90 (1.40, 2.58)		1.33 (0.99, 1.78)	
		2.1: 10-75% SA, 1-10% FT	185	2.49 (1.59, 3.90)		1.26 (0.83, 1.91)	
		2.2+ >10% SA with >10% FT, or >75% SA	182	2.12 (1.39, 3.26)		1.11 (0.68, 1.80)	
	PFJ	0: Normal	1,370	1.00 (reference)		1.00 (reference)	
		1: 1-10% SA, no FT	928	0.91 (0.64, 1.29)	104.1	0.98 (0.68, 1.42)	59.3
		1.1: 1-10% SA, 1-10% FT	330	0.98 (0.61, 1.59)	<.0001	1.11 (0.66, 1.89)	<.0001
		2: 10-75% SA, no FT	1,198	2.12 (1.58, 2.85)		1.98 (1.41, 2.79)	
		2.1: 10-75% SA, 1-10% FT	797	2.05 (1.47, 2.87)		2.23 (1.52, 3.28)	
		2.2+ >10% SA with >10% FT, or >75% SA	1,134	3.47 (2.59, 4.64)		3.05 (2.14, 4.36)	
Meniscus model	Morphology, medial	Normal	2,258	1.00 (reference)		1.00 (reference)	
		Signal	1,901	1.53 (1.20, 1.96)	24.6	1.22 (0.94, 1.58)	13.3
		Tear	1,175	1.86 (1.42, 2.43)	<.0001	1.68 (1.26, 2.25)	<.01
		Maceration	422	1.16 (0.78, 1.73)		1.25 (0.84, 1.86)	
	Morphology, lateral	Normal	4,415	1.00 (reference)		1.00 (reference)	
		Signal	655	1.68 (1.26, 2.24)	30.5	1.28 (0.96, 1.73)	14.1
		Tear	597	1.77 (1.31, 2.40)	<.0001	1.37 (1.00, 1.88)	<.01
		Maceration	90	3.50 (1.85, 6.61)		2.58 (1.50, 4.44)	
	Extrusion, medial	<2 mm	3,974	1.00 (reference)		1.00 (reference)	
		2.0-2.9mm	1,165	2.54 (2.00, 3.21)	85.4	1.52 (1.18, 1.96)	13.0
		3.0-4.9mm	541	2.76 (2.02, 3.77)	<.0001	1.36 (0.98, 1.88)	<.005
		>= 5.0mm	78	5.15 (2.70, 9.82)		2.08 (1.16, 3.73)	
	Extrusion, lateral	<2 mm	5,616	1.00 (reference)		1.00 (reference)	
		2.0-2.9mm	96	1.71 (0.90, 3.26)	3.6	1.41 (0.78, 2.54)	1.7
		3.0-4.9mm	46	1.84 (0.81, 4.22)	0.17	1.39 (0.68, 2.81)	0.43

* Hazard ratios and Wald Chi-square tests from from feature-specific models (e.g., the inflammation model includes ES and HS; the BML model includes medial, lateral, and PFJ BMLs)

** Hazard ratios and Wald Chi-square tests from the full model with all features included.

Table 1

Disclosure: C. Kwoh, Abbvie, 2, Merck KGaA, 2, 5, Fidia, 5, Thusane Astellas, 5, Regulus, 5, Taiwan Liposome, 5, Regeneron, 5, EMD Serono, 5, Express Scripts, 5, Kolon Tissue Gene, 5, Pfizer, 2, UCB, 2, Novartis, 2, Eli Lilly, 2, GSK, 2; **A. Guermazi**, AstraZeneca, 1, Pfizer, 1, MerckSerono, 1, Galapagos, 1, Roche, 1, TissueGene, 1, Boston Im-

aging Core Lab, 1; **E. Ashbeck**, EMD Serono, 5; **C. Hu**, None; **E. Bedrick**, None; **L. Sharma**, None; **C. Eaton**, None; **M. Hochberg**, Bone Therapeutics, 5, Bristol Myers Squibb, 5, Eli Lilly, 5, EMD Serono, 5, Gilead, 5, GlaxoSmithKline, 5, IBSA Institut Biochimique SA, 5, Novartis Pharma AG, 5, Noven Pharmaceuticals Inc., 5, Pfizer Inc., 5, Regenosine, 5, Samumed LLC, 5, Theralogix LLC, 5, Vizuri Health Sciences, 5, ACI Clinical, 5, Covance Inc., 5, Galapagos, 5, ICON plc, 5, IQVIA, 5, Elsevier, 7, Wolters Kluwer, 7, BriOri Biotech, 1, Theralogix LLC., 1, Rheumcon, Inc., 6; **R. Jackson**, None; **T. McAlindon**, Pfizer, 1, Sanofi Aventis US, 1, Kolon Tissuegene, 1, Samumed, 1, Seikagaku, 1, Kiniksa Pharmaceuticals, 1, Anika Therapeutics, 1; **M. Nevitt**, None; **J. Cauley**, None; **F. Roemer**, Boston Imaging Core Lab (BICL), LLC, 1, Calibr - California Institute for Biomedical Research, 1.

Abstract Number: 1115

The Relation of MRI-Based Cartilage Lesions to Knee Replacement and Knee Pain Severity in Osteoarthritis: The Multicenter Osteoarthritis Study

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SESSION INFORMATION
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Session Title: Osteoarthritis – Clinical Poster I
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Background/Purpose: Recently, the FDA has indicated that data supporting imaging biomarkers of relevance to clinically important outcomes, such as knee replacement (KR) may be considered as an endpoint for OA RCTs, including MRI-based cartilage evaluations. We therefore evaluated the relation of MRI-based cartilage lesions to knee replacement and knee pain severity, short-term change in cartilage lesions, which is of relevance for drug development programs so that insights can be gained regarding likelihood of clinically important outcomes after a shorter term RCT based on a surrogate.

Methods: We used data from the Multicenter Osteoarthritis (MOST) Study, a NIH-funded longitudinal cohort of persons with or at risk of knee OA. All participants had knee MRIs and WOMAC pain obtained at baseline, 30-, 60-, and 84-months. Cartilage lesions were scored from 1.0 T knee MRIs using WORMS. To replicate eligibility for trials, we excluded knees with KL=4 or malalignment >5 degrees. We evaluated the relation of baseline and 2.5-year changes in cartilage lesions to subsequent risk of KR and WOMAC knee pain severity over 7 years. Baseline cartilage lesions were analyzed as: 1) maximal score across all subregions (0-6); 2) sum of scores across all subregions (0-84). Change over 2.5 years were analyzed as: 1) change in sum of scores; 2) proportion of subregions with worsening lesions. We evaluated the sample as a whole, as well as limited to those with JSN=2 (~ JSW=1.5-3.5mm), a group demonstrating more responsiveness in recent RCTs, and to those with WOMAC pain 8-18 (out of 20), a typical pain range for entry into RCTs. For the relation of cartilage lesions to KR, we used a mixed-effects Cox proportional hazards model with a random-intercept for subjects. For WOMAC pain, we used linear mixed-effects model with a random-intercept for subjects and a nested random-intercept for knees within subjects. For analyses of change in cartilage score from baseline to 2.5 years later, we evaluated outcomes occurring at time-points after 2.5 years.

Results: Overall, 1755 subjects (2554 knees) met inclusion criteria (mean age 62, 64% female, 86.5% White, mean WOMAC pain 2.7). 113 knees underwent KR overall (4.4%); of knees that were JSN=2 at baseline, 19.8% (41/258)

Knee Replacement		**Worst cartilage score across all subregions at baseline**		
		Whole Sample (N=2554)	Among JSN=2 (N=258)	Among WOMAC pain 8-18/20 (N=244)
	% with event	4.4%	19.8%	10.2%
	Hazard Ratio* (95% CI) (per unit increase** in score)	**1.71 (1.38, 2.12)**	**1.78 (1.04, 3.04)**	**3.17 (1.33, 7.53)**
		Change in sum of WORMS cartilage score across all subregions over 2.5 years		
		Whole Sample (N=1721)	Among JSN=2 (N=196)	Among WOMAC pain 8-18/20 (N =172)
	% with event	5.7%	24.0%	12.2%
	Hazard Ratio* (95% CI) (per unit increase** in sum)	**1.19 (1.13, 1.24)**	**1.16 (1.04, 1.29)**	**1.16 (1.05, 1.29)**
WOMAC Pain Severity		**Worst cartilage score across all subregions at baseline**		
		Whole Sample (N=2554)	Among JSN=2 (N=258)	Among WOMAC pain 8-18/20 (N=244)
	Beta Coefficient* (95% CI) (per unit increase** in score)	**0.19 (0.13, 0.24)**	**0.54 (0.17, 0.91)**	0.06 (-0.18, 0.29)
		Change in sum of WORMS cartilage score across all subregions over 2.5 years		
		Whole Sample (N=1721)	Among JSN=2 (N=196)	Among WOMAC pain 8-18/20 (N=172)
	Beta Coefficient* (95% CI) (per unit increase** in sum)	**0.08 (0.04, 0.11)**	0.07 (-0.10, 0.23)	-0.04 (-0.15, 0.07)

*adjusted for age, sex, BMI, race, education, employment status, insurance status, maximum joint-space narrowing grade, alignment

**each unit increase in score for worst cartilage score (0-6) is not the same as the increment for each increase in sum for change in sum of WORMS cartilage score (-17 to +26.5)

Relation of Baseline & 2.5-year Change in Cartilage Morphology to Risk of Knee Replacement and to Knee Pain Severity

underwent KR and of knees with WOMAC 8-18 at baseline, 10.2% (25/244) underwent KR. Overall, both severity and extent of baseline cartilage lesions as well as change in cartilage lesions over 2.5 years were significantly associated with risk of KR (**Table**). In contrast, while cartilage lesions were significantly associated with WOMAC pain severity, the relationship was weak (**Table**).

Conclusion: These findings support the clinical relevance of cartilage lesions to the clinically important endpoint of KR. Relatively short-term changes in cartilage lesions over 2.5 years may be potentially useful as a prognostic marker for later clinical endpoints such as KR. However, the magnitude may not be sufficient for validation as an imaging

biomarker. In contrast, cartilage lesions were not strongly associated with WOMAC pain, potentially partly reflecting the uncertainty in utility of WOMAC pain to detect long-term change in pain over several years.

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Abstract Number: 1116

Magnetic Resonance Imaging Structural Changes Correlated with Knee Extension: Data from the Osteoarthritis Initiative

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SESSION INFORMATION
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Background/Purpose: Knee OA is often accompanied by loss of passive extension, termed a flexion contracture (FC), resulting in worse clinical outcomes. To our knowledge, MRI-based studies examining OA-related changes associated with knee FC have not been performed. Our objective was to study associations between knee FC and MRI-based OA-related structural changes. We hypothesized: 1) knee FC would be associated with cartilage lesions and bone marrow lesions (BMLs) in the patellofemoral (PF) joint, as well as osteophytes and meniscal alterations, and 2) normal knee extension would have high negative predictability for PF cartilage lesions and BMLs. We tested our hypotheses using data from the Osteoarthritis Initiative (OAI).

Methods: The OAI (NCT00080171, ethics approval #10-00532) is a National Institutes of Health (NIH)-funded, multi-center, prospective cohort study focusing on knee OA. For this study, 596 knees with knee extension data from the Foundation for the NIH nested case-control study were included. Knee extension was measured with a goniometer using a method with high inter-rater reliability. Inability to extend the knee to 0° constituted a FC.

Enrolment 3-Tesla MRI images were scored with the MRI Osteoarthritis knee score (MOAKS) system with assessors blinded to participant ID. Structural changes (cartilage lesions, BMLs, osteophytes, meniscal alterations, effusion, synovitis) within MOAKS-based regions of the knee that could biomechanically obstruct extension were analyzed (Figure 1A). Multivariable linear regression models evaluated for effect size of MRI outcomes on knee extension. Sensitivity, specificity, positive predictive value (PPV) and negative predictive value (NPV) were calculated based on presence or absence of FC. Area under the curve (AUC) was calculated using knee extension as a continuous variable for all participants and those without radiographic OA [Kellgren-Lawrence (KL) scores 0-1] or knee hyperextension.

Results: Of 596 participants, 72 (12.1%) had KL scores 0-1 (3.9% FC, 8.2% no FC). Knee alignment was overall 0.3±3.7° valgus. Higher lateral femoral cartilage scores (indicating greater size and depth of cartilage lesions on the femoral side of the lateral PF joint) and BML number scores were associated with lost knee extension (Table 1). Higher osteophyte scores in multiple regions correlated with lost knee extension (Table 1). Worse meniscal score in the medial meniscal body and posterior horn and a worse effusion score correlated with lost knee extension (Table 1). A representative image of a knee with FC is shown in Figure 1B.

Table 1. Multivariable linear regression showing effect size of OA-related structural changes on knee extension loss

Structural feature	Beta	95% C.I.	p-value
Cartilage morphology			
Femur lateral anterior	0.709	0.399-1.019	<0.001
BML Number			
Femur lateral anterior	0.666	0.211-1.122	<0.001
Osteophytes			
Femur medial anterior	0.649	0.533-0.765	<0.001
Femur lateral anterior	1.145	1.044-1.245	<0.001
Tibia medial	0.883	0.755-1.011	<0.001
Tibia lateral	1.031	0.901-1.160	<0.001
Patella superior	0.634	0.528-0.741	<0.001
Patella inferior	0.814	0.687-0.942	<0.001
Patella medial	0.608	0.481-0.736	<0.001
Patella lateral	0.598	0.486-0.709	<0.001
Meniscus			
MM morphology - body	0.164	0.007-0.321	0.040
MM morphology – posterior horn	0.400	0.229-0.570	<0.001
Whole Joint effusion	0.711	0.324-1.098	<0.001

Linear regression model adjusting for age, BMI, gender, KL grade, knee laterality, knee alignment, WOMAC pain.
C.I.: confidence interval; MM: medial meniscus.

Table 2. Sensitivity, specificity, positive and negative predictive values of knee extension loss for the detection of an anterior lateral cartilage and BML number

	All participants	KL 0-1, no hypertextension
	Value (%) [95% C.I.]	Value (%) [95% C.I.]
Presence of cartilage lesion		
Sensitivity	43.1 [36.7-49.6]	54.5 [26.5-80.6]
Specificity	72.5 [67.8-76.9]	55.3 [39.5-70.3]
PPV	48.7 [41.8-55.7]	26.1 [11.3-45.9]
NPV	67.8 [63.1-72.2]	80.8 [63.1-92.6]
Presence of BML		
Sensitivity	41.5% [34.3-49.0]	83.3 [44.6-99.0]
Specificity	69.9 [65.4-74.1]	58.1 [43.2-72.1]
PPV	35.7 [29.2-42.5]	21.7 [8.4-41.0]
NPV	74.8 [70.4-78.9]	96.2 [84.1-99.8]

BML: bone marrow lesion; C.I.: confidence interval; NPV: negative predictive value; PPV: positive predictive value.

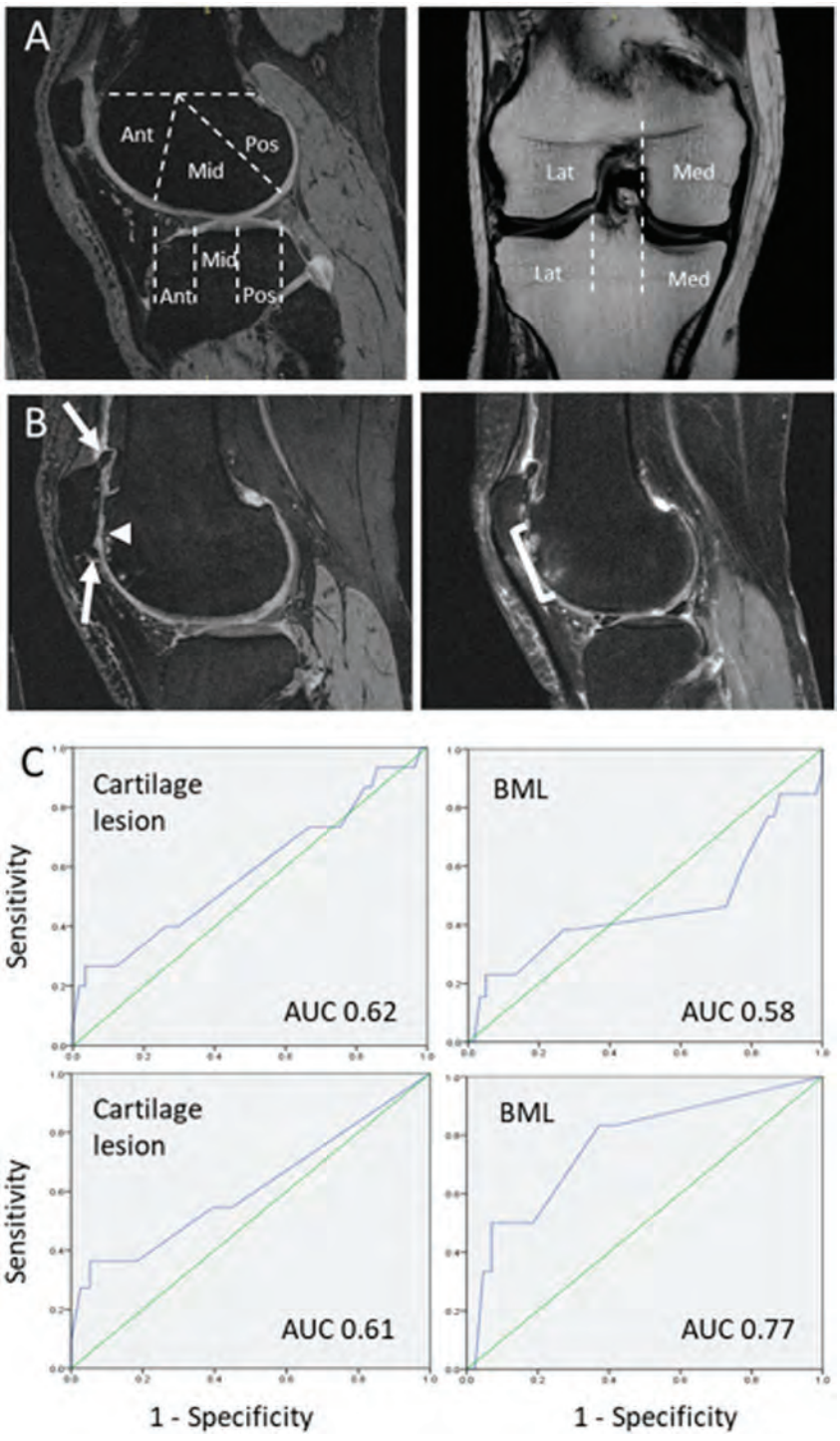

Figure 1. Structural changes associated with knee extension loss. (A) Left: Regional knee division of the MRI Osteoarthritis Knee Scoring system. Cartilage and bone marrow lesions were evaluated in the patellar, anterior (ant) and middle (mid) femoral, and anterior tibial regions where they could limit knee extension via pain inhibition. Osteophytes were evaluated in the patellar, anterior and middle femoral and anterior tibial regions where they could mechanically limit knee extension. Meniscal lesions were evaluated in all regions, as any "locking" from meniscal tears could limit knee extension. Right: Corresponding coronal sections where medial and lateral regions were investigated. (B) MRI of a participant with knee flexion contracture Left: Dual echo steady state sequence showing thinner articular cartilage in the antero-lateral femur making up the femoral side of the patellofemoral joint (arrowhead) and patellar osteophytes (arrows). Right: T2-weighted image with bracket showing large BML in the antero-lateral femur. (C) Receiver-operator curves for the presence of cartilage lesion (left) and bone marrow lesion (BML, right). Top: All participants KL 0-1 (n=596). Bottom: KL 0-1, excluding knees with hyperextension (n=49). Ant: anterior; AUC: Area under the curve; Med: medial; Lat: lateral; Mid: middle; Pos: posterior.

Sensitivity, specificity, PPV and NPV for presence/absence of knee FC are summarized in Table 2. For those with KL score 0-1 without hyperextension AUC was 0.77 (95% C.I. 0.55-0.98; Figure 1C).

Conclusion: Knee extension loss was associated with widespread degenerative changes, including those not visible on knee x-ray, and appears to be linked to global severity of disease. Precisely measuring knee extension may help predict knee OA progression, obviating the need for MRI and reducing health care costs. Longitudinal studies evaluating knee extension as a biomarker for MRI-related structural changes are needed.

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Abstract Number: 1117

Prediction Model for Progression to Different Find-Grained MRI-Based Osteoarthritis Severity States: The Vancouver Longitudinal Study of Early Knee Osteoarthritis (VALSEKO)

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Background/Purpose: To develop a novel, fine-grained MRI osteoarthritis (OA) severity score, based on cartilage, osteophytes and meniscus (OA-COM) scores and to predict the progression to different OA severity states using OA-COM scores as the outcome and clinical variables as predictors in a population-based 7-year longitudinal cohort study.

Methods: A population-based cohort, age 40-79, was assessed at baseline, 3- and 7-year follow-up using clinical assessments, x-ray and MRI. MRI OA severity score was based on the sum of scores for cartilage, osteophytes and menisci, measured semi-quantitatively at 6, 8 and 6 sites, respectively, using 0-3 grading for cartilage and osteophytes and 0-2 grading for menisci, for a total score ranging from 0-54, where 0 = no MRI OA and 54 = severe MRI OA. In order to anchor the OA-COM score at interpreTable points representing different levels of disease severity, we fit logistic regression models using baseline OA-COM score to predict each baseline Kellgren Lawrence (KL) grade in a subset of data including only KL grades at or one point below the predicted grade. For each model, we produced ROC curves and for each cut point we computed sensitivity, specificity, positive and negative predictive values and sum of squares (SS) of those statistics. The optimal threshold for OA-COM scores in predicting a given KL grade was selected using the cut points with the highest SS, adjusted to attain equal spacing between cut points. To predict progression to different OA severity states, we developed logistic regression models for progression at or above the given OA-COM score cut point from baseline to 7-year follow-up, using the subset of data of patients who could progress; that is, with OA-COM score below the given cut point at baseline. Predictors in multivariable models were selected using forward selection based on best AIC at each step. In order to obtain results that were population-representative, sample weights were used for all analyses.

OA-COM cut-point	Predictor variable	OR (95% CI)	AUC (95% CI)
12	Age (per 10 years) BMI Female Effusion	1.34 (0.57, 3.13) 1.19 (1.00, 1.41) 6.82 (1.40, 33.3) 8.74 (0.62, 123.5)	0.793 (0.658, 0.929)
18	Age (per 10 years) BMI Female Effusion	1.13 (0.61, 2.07) 1.11 (0.99, 1.25) 2.11 (0.75, 5.94) 8.43 (2.20, 32.38)	0.719 (0.602, 0.837)
24	Age (per 10 years) BMI Crepitus (fine) Crepitus (coarse) Malalignment Effusion	1.82 (0.99, 3.35) 1.03 (0.89, 1.19) 0.94 (0.24, 3.64) 3.63 (0.80, 16.35) 4.68 (1.08, 20.25) 3.56 (0.99, 12.86)	0.823 (0.730, 0.916)
30	Age (per 10 years) BMI Female Crepitus (fine) Crepitus (coarse)	1.77 (0.99, 3.17) 1.07 (0.92, 1.23) 0.51 (0.17, 1.54) 4.55 (0.77, 26.86) 6.48 (0.94, 44.50)	0.768 (0.660, 0.876)

Logistic regression analysis to predict progression to OA-COM states, using cut-points 12, 18, 24 and 30 as outcomes.

Results: Of 122 subjects, at baseline, 39.6% had radiographic OA (KL grade ≥2), mean age 55.5, female sex 55.7%. OA-COM score cut points were 12, 18, 24 and 30 for KL grades 1 to 4, respectively. Clinical predictor variables and odds ratios for each OA-COM cut point are shown in the Table 1. BMI was predictive of progression to all OA-COM scores over 7 years. Effusion was a strong predictor for progression to an OA-COM score of 12, 18 and 24, while malalignment and coarse crepitus predicted progression to higher OA-COM scores of 24 and 30.

Conclusion: We have developed a novel MRI OA severity score, the OA-COM score, using cartilage, osteophytes and menisci. OA-COM scores of 12, 18, 24 and 30 represent an MRI score that is equivalent to KL grades 1 to 4, while offering fine-grain differentiation of OA states between KL grades. In prediction modeling, we found that effusion, malalignment and crepitus, as well as age, sex and BMI, were predictive of progression to different states of OA severity over 7 years in this population-based cohort.

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Abstract Number: 1118

Bone Marrow Lesion Scores in Patients with Knee Osteoarthritis Undergoing Tibial Osteotomy: Reliability and Concurrent Validity of the Knee Inflammation MRI Scoring System (KIMRISS)

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Bone marrow lesions (BMLs) commonly occur in knee osteoarthritis (OA) and are associated with increased risk of cartilage damage and pain. The Knee Inflammation MRI Scoring System (KIMRISS) is a semi-quantitative (score range 0-500) grading tool designed to evaluate features of inflammation in patients with knee OA. Therefore, we assessed 1) inter-rater reliability of KIMRISS BML scores between expert readers and a trainee reader before and 1-year BML scores before and 1-year after medial opening wedge HTO and 2) concurrent validity of semi-quantitative (KIMRISS) and quantitative (manual segmentation) measures of BMLs at baseline.

Methods: Thirty-four patients with varus alignment and medial compartment knee OA undergoing unilateral HTO were included. 3-Tesla MRIs were acquired of both knees pre and 1-year post HTO, after surgical removal of hardware. Femoral BML scores in the medial and lateral compartments were assessed on images blinded to limb and time by masking evidence of surgery. Three raters independently scored the same 136 scans (two limbs at two time points

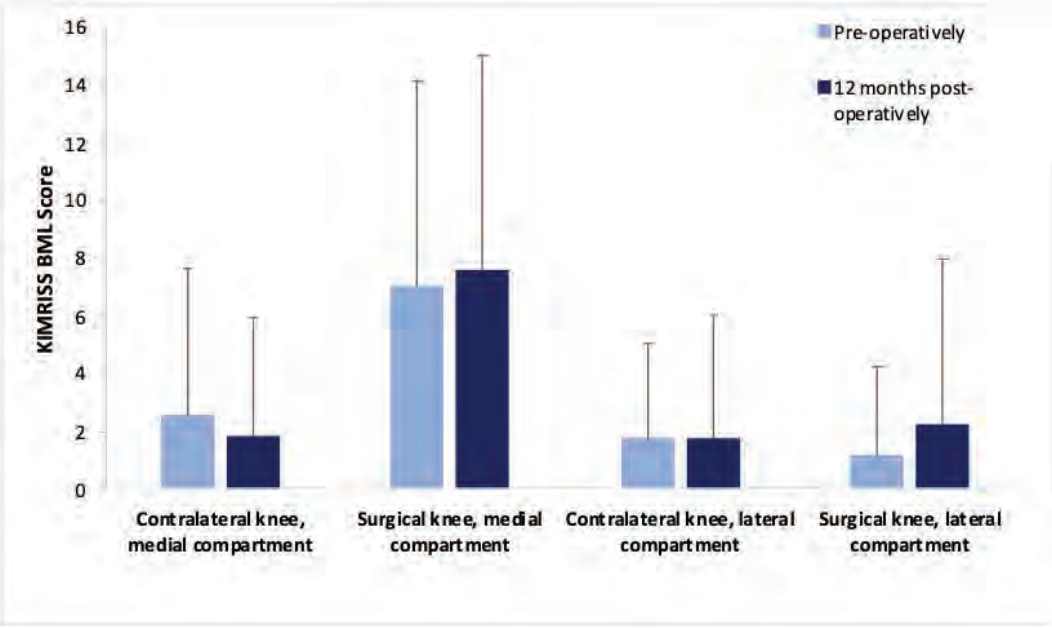

Figure 1. Means and standard deviations for KIMRISS femoral BML scores in the medial and lateral compartments for surgical and contralateral knees.

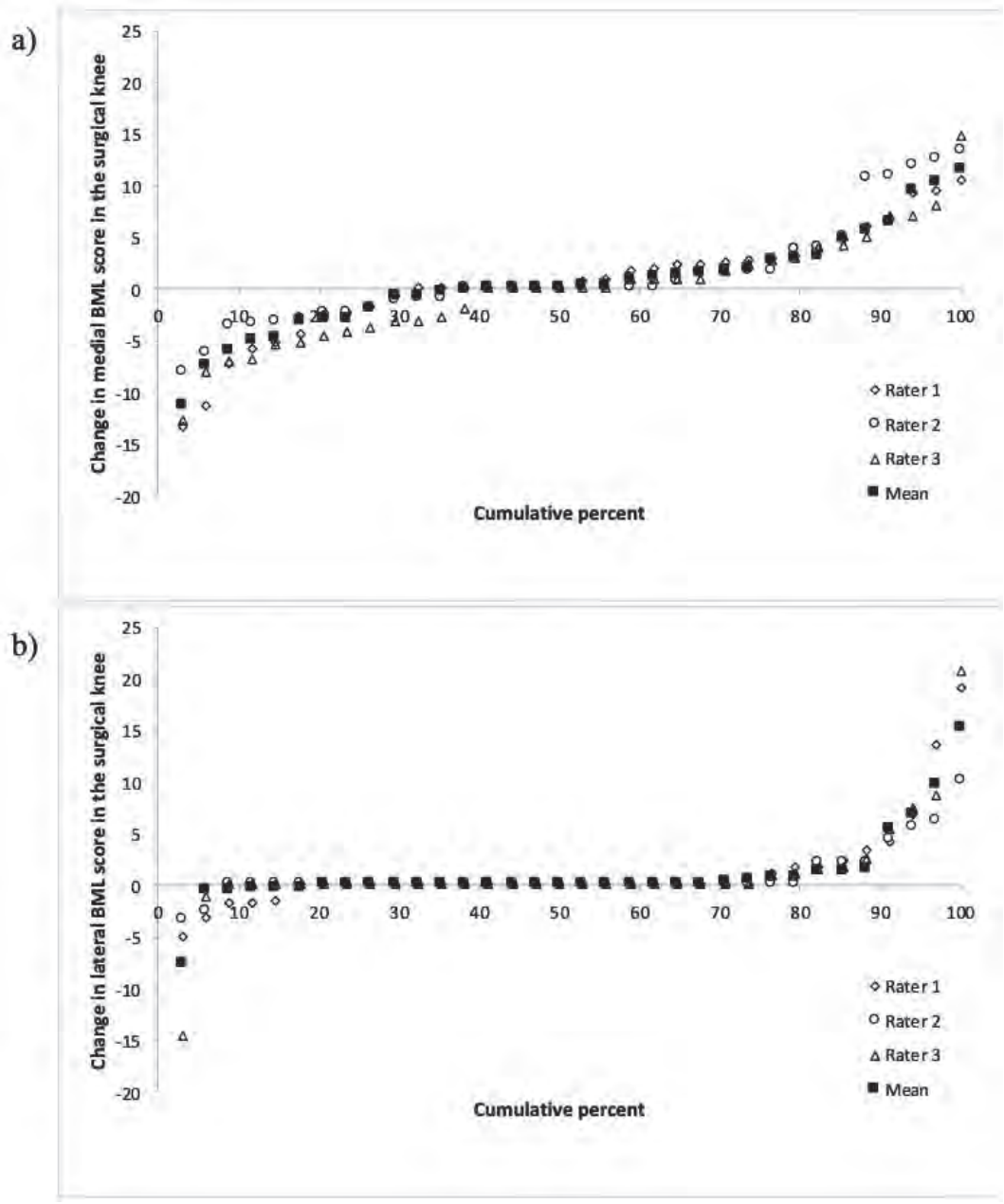

Figure 2. Change after surgery in the femoral BML score in both the medial (a) and lateral (b) compartments of the surgical knee for all three raters individually, as well as the average.

for each patient) using the KIMRISS. Additionally, one rater manually segmented femoral BMLs. Reliability of BML change scores in the medial and lateral compartment of the surgical limb were evaluated by calculating intraclass correlation coefficients (ICC) and Bland-Altman plots with 80% Limits of Agreement (LoA). Correlations between KIMRISS and manual segmentation values on the pre-operative surgical limb were evaluated using Pearson's correlation coefficients (r).

Results: Descriptive statistics for KIMRISS scores are reported in Figure 1. The mean change in the surgical limb (± SD) was 0.54 ± 4.78 in the medial compartment and 1.00 ± 3.62 in the lateral compartment. Changes following surgery varied considerably but were detected by all three raters (Figure 2). When combining all three raters, the ICC

a) Medial compartment		c) Medial compartment	
Rater pair	**ICC (95% CI)**	**Rater pair**	**80% LoA**
1 vs 2	0.77 (0.59, 0.89)	1 vs 2	-4.68, 7.51
1 vs 3	0.76 (0.57, 0.87)	1 vs 3	-5.07, 6.55
2 vs 3	0.69 (0.45, 0.83)	2 vs 3	-5.03, 7.13
Combined	0.74 (0.59, 0.85)	Combined	-3.57, 5.44
b) Lateral compartment		**d) Lateral compartment**	
Rater pair	**ICC (95% CI)**	**Rater pair**	**80% LoA**
1 vs 2	0.68 (0.45, 0.83)	1 vs 2	-3.31, 5.89
1 vs 3	0.83 (0.68, 0.91)	1 vs 3	-4.92, 7.70
2 vs 3	0.56 (0.28, 0.76)	2 vs 3	-3.75, 5.96
Combined	0.71 (0.55, 0.83)	Combined	-1.57, 3.47

Table 1. Intraclass correlations (95% Confidence Intervals) (a,b) and 80% Limits of Agreement (c,d) for change in BML scores in the surgical knee in the medial and lateral compartments. Rater 1 = trainee, raters 2-3 = experts (one MSK radiologist and one rheumatologist).

(95% confidence interval) was 0.74 (0.59, 0.85) for the medial compartment and 0.71 (0.55, 0.83) for the lateral compartment. Paired rater ICCs ranged from 0.56-0.83. The 80% LoA was -3.57 to 5.44 for the medial compartment and -1.57 to 3.47 for the lateral compartment (Table 1). Paired rater LoA ranged from -5.07 to 7.70. Semi-quantitative and quantitative BML measures were positively correlated for the medial (r=0.54) and the lateral (r=0.39) compartments.

Conclusion: The KIMRISS can reliably detect small differences between femoral BML scores after HTO and can be learned by a trainee reader both efficiently and effectively. The KIMRISS BML scores are moderately correlated with scores from manual segmentation. These findings support the inter-rater reliability, concurrent validity and feasibility of KIMRISS compartment-specific BML scoring

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Abstract Number: 1119

Association of Primary Insurance Status on Bilateral Knee Arthroplasty Utilization and Complications: A United States Nationwide Analysis

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with end-stage bilateral knee osteoarthritis, treatment options include either a staged total knee arthroplasty (TKA) procedure, often with a few months in between surgeries, or a simultaneous bilateral TKA (BTKA) procedure during the same anesthetic session. The choice in treatment strategy largely depends on patient and surgeon preferences, and guidelines vary per institution. Our objective was to assess if variations in utilization and in-hospital complications in BTKA are associated with primary insurance.

Methods: Using the National Inpatient Sample (NIS)- Healthcare Cost and Utilization Project (HCUP) database (2007-2016) we sought to examine BTKA utilization and in-hospital complications comparing those with Medicare/Medicaid (CMS) vs those with private insurance (Pvt) in a retrospective analysis. All patients ≥ 50 years who underwent elective primary TKA were included. We computed differences in temporal trends in proportional utilization and in-hospital complications after BTKA comparing those with CMS vs Pvt insurance. Next, we performed multivariable logistic regression models to assess insurance differences in temporal trends adjusting for individual (age, sex, Elixhauser comorbidity index, and morbid obesity), hospital level (hospital volume, bed size, region and teaching status) and community level (median household income) variables. Discharge weights were used for nationwide estimates.

Results: An estimated 132,400 (49.5%) CMS patients and 135,046 (50.5%) privately insured patients underwent BTKA from 2007-2016. (Table 1) Amongst UTKA patients, 62.7% had CMS insurance and 37.3% had Pvt. While in both UTKA and BTKA, patients with private insurance were more likely to be younger and had a higher proportion of females. In univariate analysis, hospital mortality, length of stay and complications were significantly higher in those with CMS compared to private insurance ($p < 0.001$). After adjusting for covariates, CMS was associated with higher odds of in-hospital BTKA and UTKA complications compared to Pvt (Bilateral aOR: 1.10, 95% CI: 1.05–1.15, P = < 0.0001; Unilateral aOR: 1.32, 95% CI: 1.10–1.59, P = 0.003). BTKA in-hospital complications remained higher in CMS group throughout the study period (1.23% in Pvt vs 1.36% in CMS in 2007-08, whereas 0.54% in Pvt vs 1.14% in CMS in 2015-16), though the trend difference was not statistically significant (Figure 1). Proportional utilization of BTKA amongst private insurance was higher than CMS throughout the study period even after adjusting for covariates (7.18% in Pvt vs 4.59% in CMS in 2007-08, whereas 5.63% in Pvt vs 3.13% in CMS in 2015-16, P < .0001) (Figure 2).

Conclusion: In this nationwide study of BTKA patients from 2007 to 2016, we found that the utilization of BTKA is higher in those who are privately insured compared to those who have Medicare/Medicare insurance. Further privately insured patients have lower in-hospital complication rates compared to those with government insurance. There can be many factors explaining these findings such as working status and patient preference which may play a role in BTKA decisions and thus further research in this area need to be done to understand these differences.

Variable	Unilateral[a]			Bilateral[b]		
	Medicare/Medicaid	Private	P[c]	Medicare/Medicaid	Private	P[c]
	N = 3,334,412 (62.7%)	N = 1,987,693 (37.3 %)		N = 132,400 (49.5%)	N = 135,046 (50.5%)	
Patient characteristics						
Age, mean (SE)	71.7 (0.03)	60.7 (0.04)	***	70.6 (0.07)	59.7 (0.05)	***
Sex: Female, n(%)	2,151,721 (64.57)	1,172,586 (59.03)	***	76,931 (58.12)	73,061 (54.12)	***
Race, n(%):			***			
Black	203,455 (6.88)	128,893 (7.46)		6816 (5.82)	6806 (5.74)	
White	2,466,140 (83.36)	1,448,700 (83.87)		102,350 (87.32)	104,024 (87.74)	
Other	288,797 (9.76)	149,769 (8.67)		8041 (6.86)	7731 (6.52)	
Median Household Income (by patient's zip code), n(%):			***			***
0-25th percentile	777,239 (23.70)	369,236 (18.88)		29,240 (22.48)	23,433 (17.62)	
26th to 50th percentile (median)	899,829 (27.44)	503,248 (25.73)		34,714 (26.69)	33,542 (25.23)	
51st to 75th percentile	852,728 (26.01)	545,996 (27.91)		33,251 (25.57)	37,260 (28.02)	
76th to 100th percentile	749,252 (22.85)	537,456 (27.48)		32,845 (25.26)	38,727 (29.13)	
Morbid Obesity, n(%)	200,461 (6.01)	185,279 (9.32)	***	7517 (5.68)	12,188 (9.02)	***
Elixhauser Index[d], n(%):			***			***
0	345,397 (10.36)	336,632 (16.94)		16,023 (12.10)	24,038 (17.80)	
1-4	2,746,567 (82.37)	1,575,281 (79.25)		107,583 (81.26)	106,141 (78.60)	
≥ 5	242,448 (7.27)	75,779 (3.81)		8794 (6.64)	4867 (3.60)	
Hospital characteristics						
Hospital Region, n(%):			***			***
Northeast	548,916 (16.46)	331,976 (16.70)		31,365 (23.69)	33,337 (24.69)	
Midwest	894,031 (26.81)	575,407 (28.95)		35,438 (26.77)	39,676 (29.38)	
South	1,235,751 (37.06)	701,138 (35.27)		46,556 (35.16)	43,384 (32.13)	
West	655,714 (19.67)	379,171 (19.08)		19,040 (14.38)	18,650 (13.81)	
Hospital Bedsize, n(%):			***			***
Small	696,868 (20.96)	455,460 (22.98)		24,054 (18.24)	28,797 (21.42)	
Medium	895,491 (26.94)	530,732 (26.77)		36,632 (27.78)	36,715 (27.31)	
Large	1,731,687 (52.10)	996,037 (50.25)		71,159 (53.97)	68,947 (51.28)	
Hospital Volume (cases per year), n(%):			***			*
<100	1,276,836 (38.29)	681,665 (34.29)		42,390 (32.02)	40,868 (30.26)	
100-200	764,637 (22.93)	457,631 (23.02)		28,973 (21.88)	29,930 (22.16)	
>200	1,292,939 (38.78)	848,396 (42.68)		61,036 (46.10)	64,247 (47.57)	
Hospital Location/Teaching status, n(%)			***			***
Rural	408253 (12.28)	194,572 (9.82)		20,238 (15.35)	16,446 (12.23)	
Urban nonteaching	1,401,475 (42.16)	819,832 (41.36)		48,175 (36.54)	49,990 (37.18)	
Urban teaching	1,514,318 (45.56)	967,825 (48.83)		63,431 (48.11)	68,023 (50.59)	
Outcomes						
Died during hospitalization	2458 (0.07)	451 (0.02)	***	289 (0.22)	29 (0.02)	***
LOS, mean (SE)	3.13 (0.01)	2.84 (0.01)	***	3.81 (0.03)	3.68 (0.04)	***
In-Hospital Complications:	38068 (1.14)	19635 (0.99)	***	1600 (1.21)	1151 (0.85)	***
AMI	7290 (0.22)	1585 (0.08)	***	558 (0.42)	208 (0.15)	***
VT	2920 (0.43)	1616 (0.39)	*	138 (0.51)	125 (0.45)	
Device complications	10381 (0.31)	6700 (0.34)	*	40 (0.15)	37 (0.13)	

All values were estimated using sampling weights and hospital clusters.

[a] Unilateral unweighted frequencies: N = 681,965 for Medicaid/Medicare; N = 407,172 for Private

[b] Bilateral unweighted frequencies: N = 27,192 for Medicaid/Medicare; N = 27,687 for Private

[c] P-values are calculated based on the Rao-Scott chi-square test is a design-adjusted version of the Pearson chi-square test. Significance levels: * = p<0.05, ** = p<0.01, *** = p<0.001.

[d] Clinical comorbidities were identified based on coding algorithms developed by Quan and colleagues (enhanced Elixhauser version), using either ICD-9-CM or ICD-10 codes, as appropriate. The Elixhauser co-morbidity index score is calculated based on the cumulative number of comorbidity conditions.

Table1. Baseline characteristics and outcomes by TKA type and Insurance

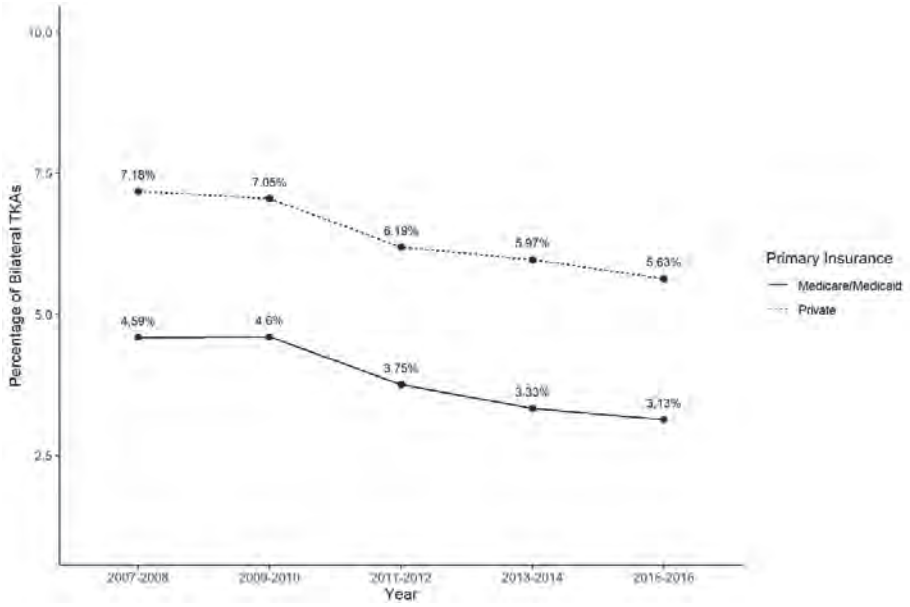

Figure 1. Bilateral Complications by Primary Insurance

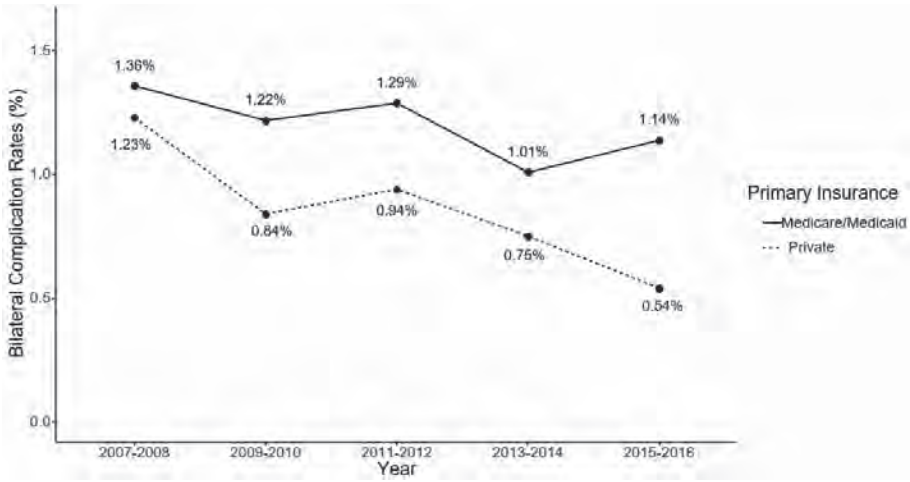

Figure 2. Percentage of Bilateral TKAs by Primary Insurance

Disclosure: B. Mehta, Novartis, 1; **K. Ho**, None; **J. Bido**, None; **S. Memtsoudis**, Teikoku, 1, Sandoz Inco, 1, HATH, 1; **M. Parks**, ZimmerBiomet, 1; **L. Russell**, None; **S. Goodman**, Pfizer, 1, Novartis, 1, UCB, 1, regenosine, 1, 2, Horizon, 1; **S. Ibrahim**, None.

Abstract Number: 1120

A Comparison of Opioid-Related Outcomes Among Commercially-Insured Osteoarthritis Patients Treated with Tramadol vs. Non-Tramadol Opioids

Stuart Silverman[1], James Rice[2], Alan White[2], Catherine Fernan[2], Michael Somma[2], Craig Beck[3], Rebecca Robinson[4] and Patricia Schepman[5], [1]Cedars-Sinai Medical Center, Los Angeles, CA, [2]Analysis Group, Boston, MA, [3]Pfizer, London, [4]Eli Lilly and Company, Indanapolis, IN, [5]Pfizer, New York City, NY

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In 2019, the American College of Rheumatology conditionally recommended tramadol for patients with hip and knee osteoarthritis (OA). While tramadol is known to be less prone to opioid use disorders, little is known about the degree to which the magnitude of these disorders differ among patients receiving tramadol relative to other non-tramadol opioids, and also the degree to which other opioid-related outcomes are lower among those receiving tramadol. The goal of this research is to compare the clinical burden of commercially-insured patients diagnosed with OA of the hip and/or knee among patients initiated on treatment with tramadol relative to those receiving non-tramadol opioids, using a large, national database in recent years.

Methods: The Optum Healthcare Solutions, Inc. data (1/2012-3/2017) were used to identify patients ≥18 years old with ≥2 diagnoses of hip and/or knee OA, and ≥90 days supply of tramadol or non-tramadol opioids during the three-year period from first prescription (*index date*) after their first OA diagnosis. Patients were required to be continuously-enrolled during the six months before (baseline) and 36 months after (follow-up) the index date. Selected clinical outcomes including rates of opioid use disorders, opioid dependence medications, constipation, fatigue, nausea, falls, and fractures. Patients in each cohort were matched 1:1 using a propensity score model accounting for baseline characteristics that included demographics, underlying comorbid conditions, medical resource use, and direct medical costs prior to initiation of treatment.

Results: Data for 14,491 patients were analyzed: 4,048 (28%) were initiated on tramadol, and 10,443 (72%) were initiated on non-tramadol opioids. After matching, 4,048 patients in each cohort were analyzed. Tramadol patients had elevated risk of opioid use disorders (1.2% of patients with opioid use disorder diagnoses), however risk of opioid use disorders was almost 3-fold higher in the non-tramadol cohort (4.2%) ($p< 0.01$). Consistent with those findings, rates of methadone and buprenorphine were also elevated in the non-tramadol cohort relative to the non-tramadol cohort (1.9% vs. 0.5% ($p< 0.01$); 3.2% vs. 1.4% ($p< 0.01$) respectively). Rates of other opioid-related outcomes were also lower, although quantitatively similar among the tramadol cohort vs. non-tramadol cohort, with rates of falls of 7.9% and 9.2% ($p=0.03$); fractures of 15.6% and 17.9% ($p< 0.01$); nausea of 17.4% and 20.0% ($p< 0.01$); fatigue of 33.5% and 37.1% ($p< 0.01$); and constipation of 12.9% and 15.0% ($p< 0.01$), respectively. Total 3-year healthcare costs of the tramadol cohort were lower than the non-tramadol cohort ($54,122 vs. $60,303 ($p< 0.01$), or avg. annual costs of $18,040 vs. $20,101).

Conclusion: This study reinforces that rates of opioid use disorders among OA patients initiated on tramadol are lower than those initiated on non-tramadol opioids; other negative events commonly associated with opioid treatment are lower but quantitatively similar among patients receiving tramadol and non-tramadol opioids.

Disclosure: S. Silverman, Pfizer, 1; **J. Rice**, None; **A. White**, None; **C. Fernan**, None; **M. Somma**, None; **C. Beck**, Pfizer, 1, 2; **R. Robinson**, Eli Lilly, 1, 2; **P. Schepman**, Pfizer, 1, 2.

Abstract Number: 1121

Osteoarthritis in the Million Veterans Program: Integrating the Electronic Medical Record with Precision Medicine

Merry-Lynn McDonald[1], Preeti Lakshman Kumar[1], Vinod Srinivasasainagendra[1], Joshua Richman[1], Sarah Pinson[1], Alison Rocco[1], Dennis Richard[2], Vivek Jagadale[2], Cynthia Brown[1], Hemant Tiwari[1], Jasvinder Singh[3] and Marcas Bamman[1], [1]University of Alabama at Birmingham, Birmingham, [2]Central Arkansas Veterans Healthcare System, Little Rock, [3]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Osteoarthritis – Clinical Poster I

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) had profound impacts on societal and patient-centered outcomes, including disability. As the first step to leverage the rich resource of the Million Veterans Program (MVP) to examine genetic variants for OA in a large, ethnically diverse cohort, we implemented to characterize OA using data collected from the electronic health record (EHR).

Methods: OA cases and controls were identified using ICD9 and ICD10 codes, using data from 1990-2019. For OA case identification, lists of codes were provided for a general OA category and overlapping lists for specific subtypes of OA (Hip, Knee, Spine, Hand, Finger, and Thumb). Inclusion and exclusion lists were adapted from Zengini et al. 2018 (PMC5896734). Exclusion criteria for controls included a wide range of non-OA arthropathies. We further identified a list of codes for traumatic and post-traumatic arthropathy by examining ICD9 and ICD10 code descriptions for the string 'trauma' and identifying those denoting traumatic or post-traumatic arthropathy. To further increase specificity, a Veteran OA case was defined as having at least two ICD codes within an OA category at least 30 days

		Sex			Age			BMI		
Ethnicity	OA Type	Males	Females	Total	(<=65)	(>65)	Total	(<=30)	(>30)	Total
European	Hip	8627 (7.57%)	681 (9.42%)	9308	4304 (6.11%)	5004 (7.10%)	9308	4459 (6.53%)	4807 (9.07%)	9266
European	Knee	27051 (23.74%)	2417 (33.43%)	29468	14806 (21.01%)	14662 (20.81%)	29468	12480 (18.28%)	16882 (31.87%)	29362
European	Hand	3847 (3.38%)	543 (7.51%)	4390	2266 (3.22%)	2124 (3.01%)	4390	2472 (3.62%)	1898 (3.58%)	4370
European	Spine	10828 (9.50%)	1048 (14.49%)	11876	7070 (10.03%)	4806 (6.82%)	11876	5944 (8.71%)	5847 (11.04%)	11791
Total		**113958**	**7231**		**70464**	**70464**		**68260**	**52970**	
African	Hip	2654 (10.21%)	283 (8.75%)	2937	2099 (9.76%)	838 (10.86%)	2937	1456 (9.66%)	1474 (10.42%)	2930
African	Knee	8421 (32.40%)	1436 (44.40%)	9857	7400 (34.41%)	2457 (31.83%)	9857	3957 (26.25%)	5851 (41.35%)	9808
African	Hand	642 (19.85%)	134 (4.14%)	776	530 (2.46%)	246 (3.19%)	776	388 (2.57%)	381 (2.69%)	769
African	Spine	3234 (12.44%)	528 (16.33%)	3762	2968 (13.80%)	794 (10.29%)	3762	1813 (12.03%)	1913 (13.52%)	3726
Total		**25991**	**3234**		**21508**	**7718**		**15075**	**14151**	
Hispanic	Hip	602 (6.03%)	34 (5.35%)	636	406 (5.78%)	230 (6.40%)	636	291 (5.38%)	339 (6.51%)	630
Hispanic	Knee	2996 (30.03%)	234 (36.79%)	3230	2143 (30.53%)	1087 (30.24%)	3230	1292 (23.89%)	1915 (36.78%)	3207
Hispanic	Hand	321 (3.22%)	45 (7.08%)	366	234 (3.33%)	132 (3.67%)	366	190 (3.51%)	170 (3.26%)	360
Hispanic	Spine	1168 (11.71%)	90 (14.15%)	1258	937 (13.35%)	321 (8.93%)	1258	594 (10.99%)	649 (12.46%)	1243
Total		**9977**	**636**		**7019**	**3595**		**5407**	**5207**	
Asian	Hip	42 (3.14%)	6 (9.84%)	48	30 (3.30%)	18 (3.67%)	48	34 (3.30%)	14 (3.79%)	48
Asian	Knee	240 (17.94%)	16 (26.23%)	256	164 (18.04%)	92 (18.74%)	256	169 (16.39%)	82 (22.22%)	251
Asian	Hand	32 (2.39%)	6 (9.84%)	38	24 (2.64%)	14 (2.85%)	38	27 (2.62%)	11 (2.98%)	38
Asian	Spine	108 (8.07%)	10 (16.39%)	118	88 (9.68%)	30 (6.11%)	118	89 (8.63%)	26 (7.05%)	115
Total		**1338**	**61**		**909**	**491**		**1031**	**369**	

Prevalence of OA at each site by ancestry and key biological variables

apart, within the general OA category and/or within a subtype (e.g. Spine). Controls were identified as participants who were not OA cases and who had no codes in the exclusions list.

Results: A total of 121,229 Veterans of European, 29,225 Veterans of African, 10,613 Veterans of Hispanic and 1,399 Veterans of Asian descent had complete phenotypic and genotypic data for analyses. Using the above inclusion and exclusion criteria, the frequency of OA was 47% among Veterans of Europen descent, 58.1% among Veterans of African descent, 52.8% among Veterans of Hispanic descent and 33.1% among Veterans of Asian descent.

We found differences in prevalence of OA at various sites by sex, age and obesity (BMI >=30 kg/m^2) within different ancestaries (**Table 1**).

Conclusion: Overall OA burden was higher in non-Caucasian Veterans, except in Asian descent, where it was lower. OA prevalence by joint varied by biological factors.

Disclosure: M. McDonald, None; **P. Lakshman Kumar**, None; **V. Srinivasasainagendra**, None; **J. Richman**, None; **S. Pinson**, None; **A. Rocco**, None; **D. Richard**, None; **V. Jagadale**, None; **C. Brown**, None; **H. Tiwari**, None; **J. Singh**, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **M. Bamman**, None.

Abstract Number: 1122

Osteoarthritis in a Large Integrated Health System Population: 18-Year Retrospective Review

Jove Graham[1], Tonia Novosat[1], Haiyan Sun[1], Brian Piper[2], Joseph Boscarino[1], Melissa Kern[1], Vanessa Duboski[3], Eric Wright[3], Patricia Schepman[4], Rebecca Robinson[5], Edward Casey[6], Craig Beck[7] and Jerry Hall[8], [1]Geisinger, Danville, [2]Geisinger, Scranton, [3]Geisinger, Forty Fort, [4]Pfizer, New York City, NY, [5]Eli Lilly and Company, Indianapolis, [6]Pfizer, New York, [7]Pfizer, London, [8]Eli Lilly and Company, Indianapolis, IN

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is a mechanically and immunologically mediated common disease with a complex pathogenesis. Despite epidemiologic studies proving increasing age, obesity and female gender as risk factors, many individuals are unable to manage OA symptoms and optimal treatment strategies at a population health level remain a challenge. Our aim was to determine prevalence, incidence and characteristics of OA patients over an 18-year timeframe to provide insight into what treatments and preventative strategies would maximize impact.

Methods: This was a retrospective descriptive study reviewing electronic health records and billing data at Geisinger, an integrated health system in central and northeastern Pennsylvania serving over 500,000 patients per year. Patients were included if they had at least two outpatient encounters at age 18 or greater and defined as having OA after having at least one diagnosis code for OA (ICD-9: 715.*, ICD-10 M15-19) on a problem list or encounter diagnosis or had an OA-related procedure (hip or knee replacement, arthroscopy or injection). Patients with total knee replacement (TKR) were also examined separately as a subset. For each year from 2001-2018, we calculated OA prevalence

	Patients with OA (n=271,126)	Patients with OA and total knee replacement (n=10,788)
Age at first visit, in years, N (%)		
<45	109,754 (40.5%)	1,013 (9.4%)
45-65	100,469 (37.1%)	5,681 (52.7%)
65-79	49,384 (18.2%)	3,668 (34.0%)
80+	11,519 (4.3%)	426 (4.0%)
Sex, N (%)		
Males	113,013 (41.7%)	4,308 (39.9%)
Females	158,086 (58.3%)	6,480 (60.1%)
Not documented	7 (<0.1%)	0 (0%)
Body mass index, in kg/m^3, N (% with measure available)		
<30	123,964 (51.7%)	2,669 (29.4%)
30-35	64,066 (26.7%)	3,140 (34.6%)
>35	51,680 (21.6%)	3,271 (36.0%)
Patients with medication at any time, N (%)		
Acetaminophen	170,384 (62.8%)	9,668 (89.6%)
Duloxetine	15,348 (5.7%)	897 (8.3%)
Homeopathic medication	3,346 (1.2%)	333 (3.1%)
Injectable OA medication	2,786 (1.0%)	316 (2.9%)
Oral NSAID or Continuous NSAID	162,288 (59.9%)	8,446 (78.3%)
Opioid (non-tramadol)	221,201 (81.6%)	10,316 (95.6%)
Salicylates	31,284 (11.5%)	4,472 (41.5%)
Topical OA medication	25,066 (9.3%)	1,669 (15.5%)
Tramadol	95,957 (35.4%)	8,006 (74.2%)
Patients with comorbidities at any time, N (%)		
Chronic pulmonary disease	56,522 (20.9%)	2,349 (21.8%)
Diabetes without complications	52,565 (19.4%)	3,142 (29.1%)
Any tumor	37,870 (14.0%)	1,267 (11.7%)
Hypertension	114,020 (42.1%)	6.983 (64.7%)
Chronic kidney disease	35,630 (13.1%)	2,520 (23.4%)
Gastroesophageal reflux disease	57,999 (21.4%)	3,045 (28.2%)
Depression	45,739 (16.9%)	1,904 (17.7%)
Anxiety disorders	53,50 (19.8%)	1,905 (17.7%)

Demographics, Medications, and Comorbidities Table

(percent of patients seen with OA) and incidence (percent of patients newly diagnosed with OA that year). We also examined baseline demographics, OA-related prescription medication use, and comorbidities at any time during the study period.

Results: We identified 271,126 patients with encounters in the health system and evidence of OA, representing 32% of the total patient population in 2018. Yearly incidence remained steady over the past 10 years at between 4 and 5 newly diagnosed per 100 and was similar between males and females. The cohort remained steady at approximately 60% female, and consistent with the geographic region, was 98% Caucasian and non-Hispanic. The largest segment of the OA population was in the range of 45 to 64 years old at first encounter, but the youngest age segment (18-45 years old) increased from 20% to 25% of the OA population over the study period. Over half (54%) of OA patients had a BMI over 30 and this percentage increased by 7% since 2001. Non-tramadol opioids were the most commonly prescribed pain medications, followed by acetaminophen (prescription or over-the-counter) and oral non-steroidal anti-inflammatory drugs. Depression and anxiety disorders were diagnosed in 17% and 20% of the OA population, respectively, 20% reported chronic obstructive pulmonary disease, and 46% reported current or past tobacco smok-

ing. Approximately 4% of patients underwent TKR; this subgroup was more likely to use prescription pain medication and had higher rates of several chronic diseases including congestive heart failure, hypertension and chronic kidney disease.

Conclusion: Osteoarthritis affected a large, increasing segment of a large health system population, with higher rates among females and the proportion of younger individuals increasing over time. The treatment of these patients may have been further complicated by comorbidities including obesity, depression, anxiety and multiple chronic disease states.

Disclosure: J. Graham, None; **T. Novosat**, Pfizer, 2; **H. Sun**, None; **B. Piper**, Pfizer, 2, 9; **J. Boscarino**, None; **M. Kern**, None; **V. Duboski**, None; **E. Wright**, None; **P. Schepman**, Pfizer, 1, 2; **R. Robinson**, Eli Lilly and Company, 1, 3; **E. Casey**, Pfizer, Inc., 1, 3; **C. Beck**, Pfizer, 1, 2; **J. Hall**, Eli Lilly & Company, 1, 3.

Abstract Number: 1123

The Patient Journey in Knee OA: Variations in Patient Characteristics and Treatment by Physician Specialty

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Knee osteoarthritis (OA) affects 32.5 million US adults and is typically treated by primary care physicians, rheumatologists (RH), orthopedists (OS), sports medicine (SM) physicians, and pain specialists (PS). Treatment is multimodal and comprises conservative and pharmacological therapies, intra-articular injections, and

Table 1: Demographics

	Total *N=854*	Orthopedist (OS) *n=352*	Rheumatologist (RH) *n=250*	Sports Medicine (SM) *n=152*	Pain Specialist (PS) *n=100*
Mean age	65.15	65.46[C]	65.36[C]	63.34	66.33[C]
65 years of age or older (total)	476	198	145	71	62
	56%	56%[C]	58%[C]	47%	62%[C]
Mean age when symptoms started	55.13	56.78[BCD]	54.75	53.48	52.59
Male	419	185	106	77	51
	49%	53%[B]	42%	51%	51%
Female	435	167	144	75	49
	51%	47%	58%[A]	49%	49%
Mean BMI	30.74	30.19	29.80	32.96[AB]	31.64[AB]
BMI ≥35	22%	18%	17%	32%[AB]	34%[AB]
Not currently employed (total) due to inability to perform function	59%	57%	67%	52%	73%[ABC]
	7%	5%	7%	5%	15%[ABC]
Bilateral OA (total)	428	146	96	77	49
	50%	41%	62%[ACD]	49%	51%

Key: Statistical significance, $P<0.1$; A: versus orthopedist, B: versus rheumatologist, C: versus sports medicine physician, D: versus pain specialist

Table 2: Reasons for discontinuation†

Therapy (are using or have used); n (%)	Duration (mean)	DC'd % (n)	Top reasons for discontinuation†
OTC NSAIDs, patches, or creams; n=660 (73%)	4.4 years	27% (177)	48% (n=85) lack of efficacy 19% (n=33) unknown 37% (n=66) worsening of symptoms 15% (n=26) residual symptoms
Acetaminophen; n=606 (71%)	4.8 years	28.5% (173)	57% (n=98) lack of efficacy 20% (n=35) unknown 25% (n=44) worsening of symptoms 13% (n=23) residual symptoms
Prescription NSAIDs (oral or topical); n=561 (66%)	3.7 years	31.5% (177)	38% (n=67) lack of efficacy 14% (n=24) unknown 27% (n=47) safety concerns 19% (n=33) side effects
Celecoxib; n=261 (31%)	2.6 years	49.4% (129)	41% (n=53) lack of efficacy 13% (n=17) unknown 21% (n=27) safety concerns 18% (n=23) cost
Opioid; n=173 (20%)	3.2 years	32% (55)	51% (n=28) safety concerns 18% (n=10) unknown 36% (n=20) side effects 16% (n=9) lack of efficacy
Prescription antidepressant; n=89 (10%)	3.0 years	25% (22)	36% (n=8) lack of efficacy 36% (n=8) unknown 18% (n=4) side effects
Injectables	**Duration (mean)**		
Intra-articular corticosteroid; n=512 (60%)	1.4 years	82.4% (422)	17% (n=73) lack of efficacy 48% (n=201) unknown 14% (n=59) cost of medication 12% (n=50) worsening of symptoms
Single-injection hyaluronic acid; n=187 (22%)	2.0 years	52.4% (98)	61% (n=60) lack of efficacy 10% (n=10) unknown 22% (n=22) worsening of symptoms 12% (n=12) residual symptoms 9% (n=9) cost

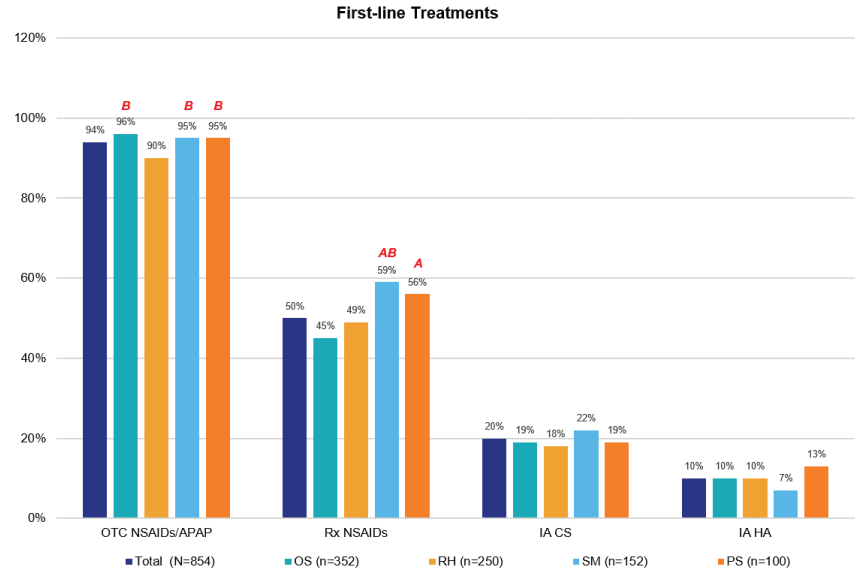
†Reasons for discontinuation are not mutually exclusive.

surgery. Guidelines provide recommendations in idealized settings, but little documentation exists in real world settings; hence, we aimed to assess patient characteristics and treatment patterns across 4 specialties.

Methods: This project was exempt from IRB review and HIPAA consent. Physicians with >2 years in practice and >10 knee OA patients per week were interviewed about their 2 most recent knee OA patients. Interviews (structured questions and answers) assessed demographics, referrals, comorbidities, time to treatment, and lines of therapy. As this study was designed to assess effect modifications, a confidence level of 90% was used.

Results: Patient demographics are shown in Table 1. Participating physicians included 125 RH, 176 OS, 76 SM, and 50 PS. Overall, 854 patients were included in the chart review. Patients were mean age 65 years, mean BMI 30.7, and 51% were female. First-line treatments are shown in Figure 1. Mean time between symptom onset and diagnosis was 3.4 years. Over 90% of patients used over-the-counter (OTC) nonsteroidal anti-inflammatory drugs (NSAIDs) and acetaminophen (APAP), with lowest use in RH patients. IA corticosteroids (CS) were used in ~20% of patients and hyaluronic acid (HA) in ~10% of patients, with similar use across specialties. Reasons for therapy discontinuation (DC) included lack of efficacy, AE/safety, and formulary/cost (Table 2). DC for lack of efficacy was 61% for single-injection HA. AE/safety concerns were reasons for DC of prescription (Rx) NSAIDs and opioids. Second-line treatments included CS >OTC Rx NSAIDs/APAP >HA. Third-line treatments were HA >CS >OTC Rx NSAIDs/APAP.

Figure 1: First-line treatments



Key: Statistical significance, *P*<0.1; A: versus orthopedist, B: versus rheumatologist, C: versus sports medicine physician, D: versus pain specialist

Mean BMI was significantly higher in SM (33) and PS (32) patients compared with OS (30) and RH (30) patients. There were significantly more female RH patients (56%) than OS patients (47%). PS patients had significantly higher current unemployment (73%) due to an inability to perform function (15%) than patients treated by other specialties. RH, SM, and PS patients had significantly more comorbidities than OS patients. Overall, mean pain (NRS 0–10) was 5.6 and KL grade was 3. PS patients had significantly higher pain scores (6.5) than patients treated by other specialties. Limitations included selection bias, confounding, small N, and missing data.

Conclusion: PS see more patients with pain syndromes and higher BMIs. RH see more patients with rheumatoid conditions. OS patients used significantly more OTC NSAIDs/APAP than RH patients and were less likely than SM and PS patients to use Rx NSAIDs. Lack of efficacy drove most therapy changes. Of HA patients, 61% discontinued due to lack of efficacy. These data suggested that treatment patterns for knee OA were similar across physician types, and new therapies can provide additional options to currently available treatments that may have efficacy or safety concerns.

Disclosure: A. Bedenbaugh, Samumed, 3; **V. Lee**, Samumed, 5; **G. Oderda**, Samumed, LLC, 5; **S. Kennedy**, Samumed, LLC, 1, 3; **D. Brixner**, Samumed, 5; **J. Tambiah**, Samumed, LLC, 1, 3; **T. McAlindon**, Pfizer, 1, Sanofi Aventis US, 1, Kolon Tissuegene, 1, Samumed, 1, Seikagaku, 1, Kiniksa Pharmaceuticals, 1, Anika Therapeutics, 1.

Abstract Number: 1124

Improving Documentation Rates of Non-Pharmacologic Therapies for Knee Osteoarthritis

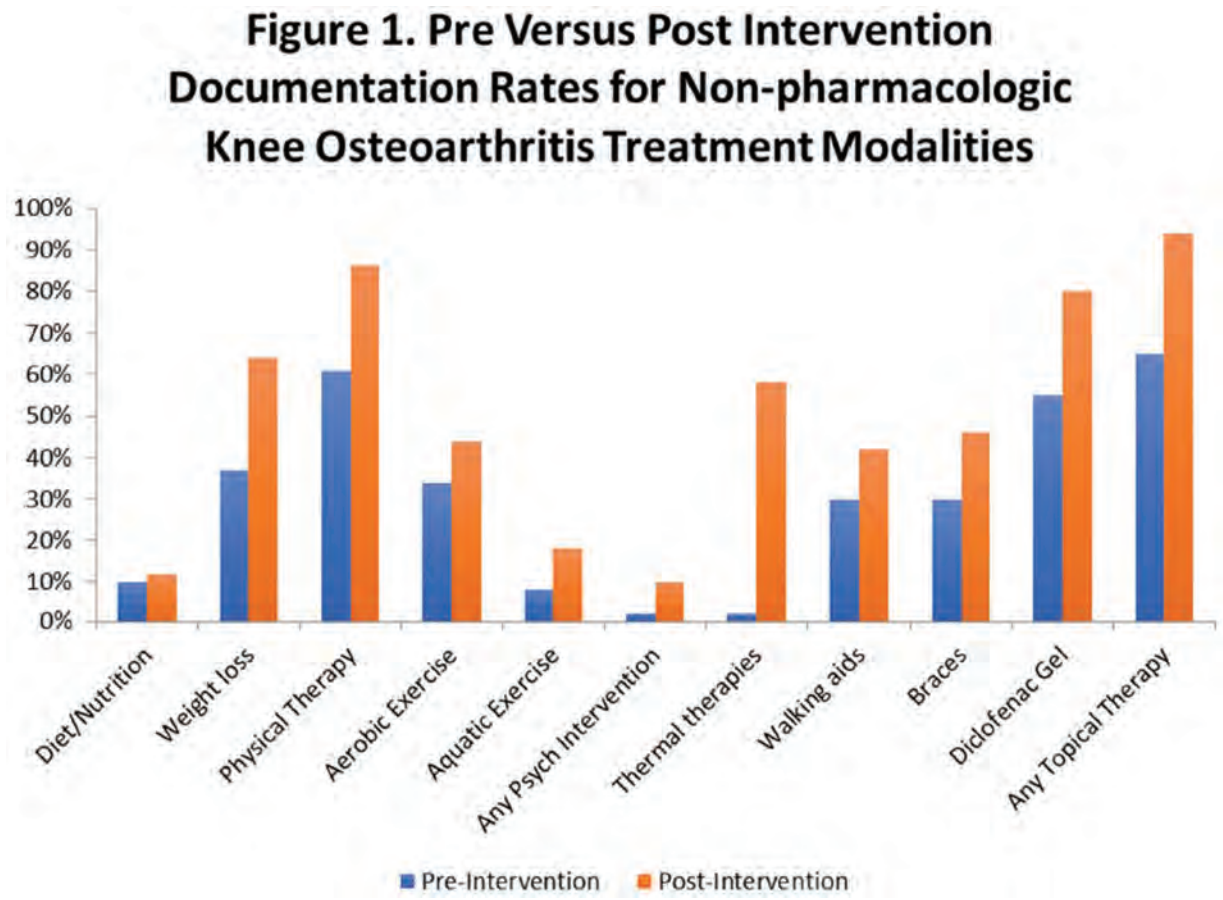
Megan Milne[1], Travis Welsh[1] and Una Makris[2], [1]University of Texas Southwestern, Dallas, TX, [2]UT Southwestern Medical Center, Dallas, TX

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis – Clinical Poster I
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Musculoskeletal (MSK) pain is the leading cause of disability in older adults. Specifically, knee osteoarthritis (OA) accounts for a large burden of MSK disability worldwide. A multi-modal approach is necessary to treat this common disease. Current guidelines recommend a combination of pharmacologic and non-pharmacologic treatments. A multi-phase quality improvement project was conducted at the Dallas VAMC Rheumatology clinic to improve documentation of non-pharmacologic therapies offered to older veterans with knee OA. The VA is an ideal location to conduct a quality improvement project to enhance MSK pain care as many of the guideline-concordant referrals are readily available, accessible and integrated into the care for Veterans.

Methods: Fifty charts from a VA rheumatology clinic were reviewed for documentation of non-pharmacologic knee OA therapies during outpatient office visits in May 2018. Then, a new note template dedicated to MSK pain management was developed and implemented in August 2019. The Assessment and Plan utilized pre-written management options for specific non-pharmacologic modalities: aerobic exercise, aquatic exercise, weight loss, nutrition counseling, physical therapy referral, use of assistive devices, Yoga/Tai Chi, thermal therapies, and psychological interventions. The pre-written plans permitted editing by the note author. Next, a rheumatology grand rounds presentation emphasized the importance of non-pharmacologic interventions for knee OA to both trainees and faculty. A post-intervention chart review was conducted on a subsequent 50 charts in November 2019.

Results: The majority of patients were men aged 65 years or older. All patients had a documented history of knee OA in a rheumatology clinic note. Therapies with the most improvement in documentation rates were: thermal therapies (2% to 58%), use of topical therapies (66% to 94%), weight loss (36% to 64%), physical therapy (60% to 86%), and



Pre-intervention versus post-intervention rates of documentation for non-pharmacologic knee osteoarthritis treatment modalities

exercise regimens (42% to 62%) (Figure 1). Psychological therapies were the least documented therapy and had the lowest rate of improvement (2% to 8%) as seen in Figure 1.

Conclusion: A dedicated MSK pain template note and departmental presentation on OA management improved documentation rates of non-pharmacologic therapies for knee OA. Further improvement is needed, as important modalities, specifically mental health interventions, remain under-utilized. Documentation is important for continuity of care for this clinic. Many medical trainees rotate through the clinic, and a patient is unlikely to have the same provider on subsequent visits, making the note a vital tool of care continuity. Future providers now have access to all prior treatment strategies and the current treatment plan in one well-organized location –the clinic note. The next step in this quality improvement project is to assess if increasing documentation rates of non-pharmacologic modalities is associated with increased referral rates for these interventions, followed by an increased use of non-pharmacologic therapies by patients, and ultimately improved patient outcomes.

Disclosure: M. Milne, None; **T. Welsh**, None; **U. Makris**, None.

Abstract Number: 1125

Patient Reported Impact of Lupus on Quality of Life

Beth Schneider[1], [1]MyHealthTeams, San Francisco, CA

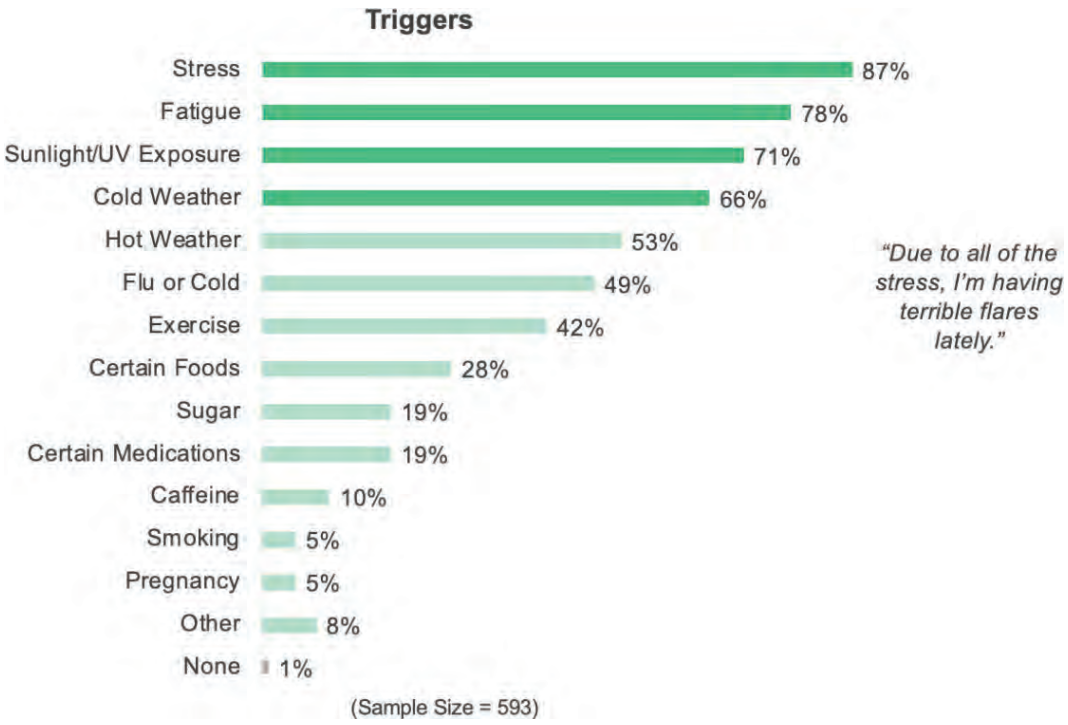
SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Research was undertaken to better understand how people living with lupus describe its sum total impact on their lives including work, challenges with relationships and its toll on mental health.

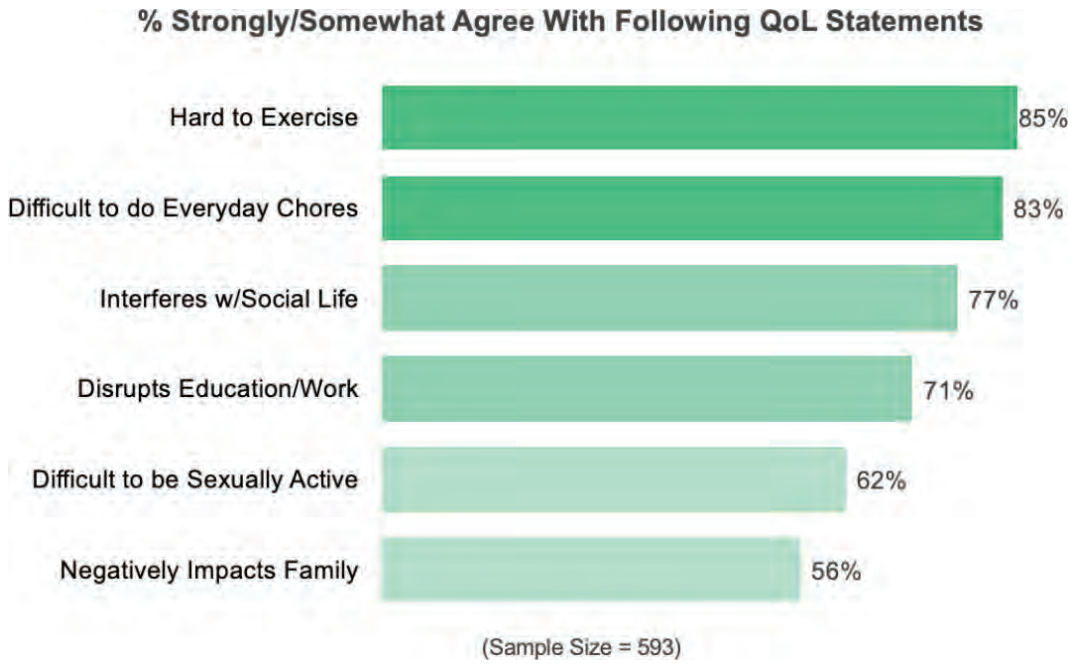
Methods: In January 2020 an email invitation to an online survey was sent to US members of MyLupusTeam, a social network of over 171,000 members. In total, 593 members completed the 21-question survey regarding experiences with lupus and impact of the disease on everyday life.

Results: The far-reaching impact on quality of life was evident in that most reported that they found it hard to exercise (85%) and do everyday chores (83%). They also felt that lupus interferes with social life (77%) and disrupts education/work (71%). The emotional toll of lupus manifested in anxiety (72%), depression (70%), feeling isolated/alone (66%) and ensuing challenges in sleeping (79%). Patients reported that the biggest triggers exacerbating lupus symptoms were stress (87%), fatigue (78%), UV exposure (71%) and cold weather (66%). Top two symptoms reported were joint pain/swelling (93%) and fatigue (92%) and these symptoms were considered to be the biggest obstacles to managing lupus (82% pain and 76% fatigue). While lupus patients had a good understanding of potential lupus symptoms they might experience (75%) and potential triggers (68%), they were less clear on types of medications (58%), exercises (54%) and foods to eat/avoid (48%). The sum total impact of lupus is that only 49% reported that they are able to lead a full life.

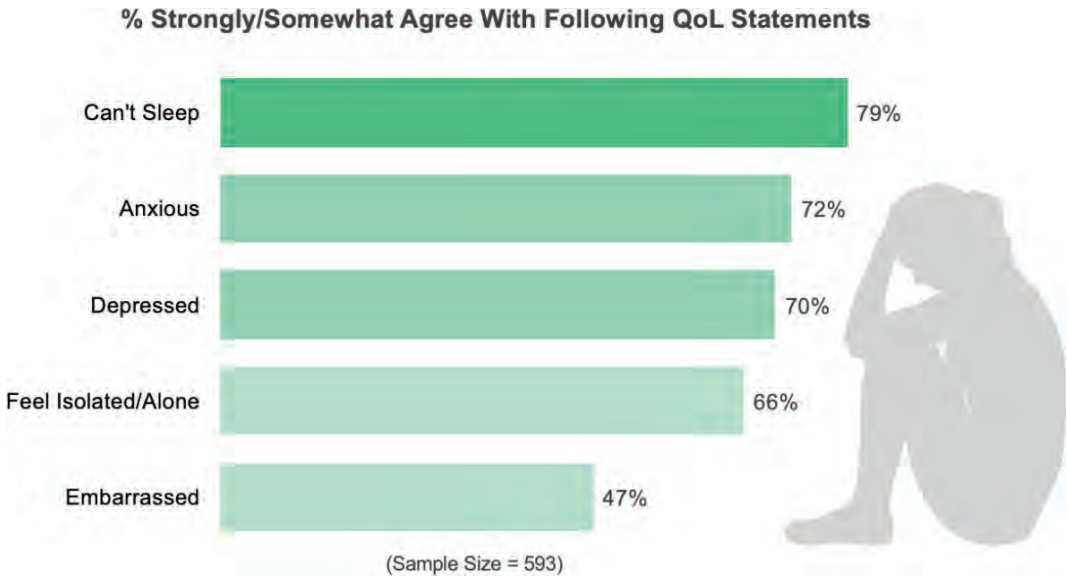
Conclusion: Understanding the physical, emotional and quality of life impact of lupus, can help rheumatologists provide a more holistic approach to treating lupus patients. Importantly, by addressing the mental health aspects of lupus, HCPs can help create better health outcomes, including treatment adherence and effective self-care regimens.



Triggers That Worsen Lupus Symptoms



Impact of Lupus on Quality of Life



Emotional Toll of Lupus

Disclosure: B. Schneider, None.

Abstract Number: 1126

A Mobile Mindfulness Meditation Program May Improve Health-Related Quality of Life for Patients with Rheumatic Disease, a Pilot Study

Dana DiRenzo[1], Carly Hunt[2], Erica Sibinga[2], Neda Gould[2], Ami Shah[3], Susan Bartlett[4] and Clifton Bingham III[1], [1]Johns Hopkins University, Baltimore, MD, [2]Johns Hopkins University, Baltimore, [3]Johns Hopkins University School of Medicine, Ellicott City, MD, [4]McGill University, Montreal, Canada

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Mindfulness Based Interventions (MBIs) are well-established self-management programs shown to be beneficial for pain, depression, and anxiety that focus on learning how to respond to bodily sensations and emotions through guided meditative practices. However, due to time constraints, scheduling, and physical limitations, we found it difficult for patients to attend in-person MBIs; we therefore implemented a mobile MBI, using the commercially available smartphone application, Calm©.

Methods: Established patients with rheumatic disease in our Rheumatology Division at a tertiary referral center were eligible for inclusion. Participants were asked to engage in the app for a minimum of 5 minutes/day for 30 days, provide baseline clinical and demographic information, and complete baseline and 30-day questionnaires pertaining to health-related quality of life (HRQL). Questionnaires included the Patient Reported Outcome Measurement Information System (PROMIS) (v2.0) 4a short forms (physical function, social participation, fatigue, sleep disturbance, pain interference), computer adaptive tests (CATS) (v1.0) for anxiety, depression, self-efficacy for managing emotions, and for managing symptoms and the NIH Toolbox Perceived Stress FF v2.0. Demographics, clinical characteristics, and

Patient Characteristic	Completers	Non-Completers	p-value
n	18	17	
Age, mean (SD)	49 (13)	52 (12)	0.38
Sex, n (%) female	16 (89%)	16 (94%)	0.58
Race, n (%)			
White	14 (78%)	12 (71%)	0.77
Black	3 (17%)	3 (18%)	
Asian	1 (6%)	1 (6%)	
Other	0 (0%)	1 (6%)	
Education, n (%)			0.12
High School	0 (0%)	3 (18%)	
Some College	5 (28%)	4 (24%)	
College	5 (28%)	5 (29%)	
Masters	8 (44%)	3 (18%)	
PhD	0 (0%)	2 (12%)	
Employment, n (%)			0.70
Not Working	1 (6%)	1 (6%)	
Part Time	3 (18%)	2 (12%)	
Full Time	8 (47%)	11 (65%)	
Disabled	1 (6%)	2 (12%)	
Retired	3 (18%)	1 (6%)	
Homemaker	1 (6%)	0 (0%)	
Diagnosis, n (%)			
Inflammatory Arthritis	12 (67%)	11 (50%)	**0.063**
Lupus	2 (11%)	7 (32%)	
Sjogren's Syndrome	3 (17%)	0 (0%)	
Scleroderma	1 (6%)	4 (18%)	
Disease Duration (years), mean (SD)	8 (10)	14 (10)	0.12
Current Medications, n (%)			
Antidepressants	8 (50%)	6 (35%)	0.38
Anxiolytics	8 (44%)	3 (18%)	0.09
Sleep Aids	5 (29%)	4 (24%)	0.70
Opioids	3 (17%)	1 (6%)	0.32
Prednisone >5 mg/day	1 (6%)	1 (6%)	0.96
Perceived Stress T-Score, mean (SD)	63.1 (12.5)	50.8 (14.9)	**0.012**
Self-Efficacy T-Score, mean (SD)			
Managing Symptoms	40.3 (5.7)	47.9 (10.1)	**0.009**
Managing Emotions	42.1 (8.7)	47.6 (11.3)	0.12
Anxiety T-Score, mean (SD)	62.1 (8.8)	55.4 (11.1)	0.054
PGA, median (IQR)	59.2 (28.4)	35.4 (30.1)	**0.024**
Pain VAS, median (IQR)	61.2 (17.9)	38.6 (29.6)	**0.010**

Table 1. Baseline patient characteristics comparing those who completed the full program compared to those lost to follow up.

mean T-scores were compared between groups using t-tests or chi-square. A sensitivity analysis was performed for participants who fully completed the program.

Results: 40 participants consented, 35 participants completed baseline questionnaires, 17 participants completed post survey questionnaires and used Calm, 17 participants completed baseline questionnaires but were lost to follow up, and 1 participant completed both surveys but did not use Calm. Participants had a mean age (SD) of 50 years (13), were mostly female (91%), white (74%), well-educated (66% with a college degree or greater) and working full time (56%). Most participants had inflammatory arthritis (60%); patients with lupus (17%), Sjogren's syndrome (9%), and scleroderma (14%) were also included. Compared to non-completers, full completers had similar demographics and use of medications that could potentially impact mood. However, full completers had higher patient

HRQL Domain	Day 0	Day 30	Mean Difference	p-value
Fatigue T-Score (SD) *	62.9 (9.7)	55.4 (8.3)	7.6	**0.017**
Sleep Disturbance T-Score (SD) *	56.3 (8.8)	52.8 (5.3)	3.5	0.15
Pain Interference T-Score (SD) *	60.0 (5.0)	57.3 (7.4)	2.7	0.21
Anxiety T-Score (SD) **	62.1 (8.8)	57.9 (8.1)	4.2	0.14
Depression T-Score (SD) **	56.6 (8.4)	54.6 (9.2)	2.0	0.50
Self-Efficacy, Emotions T-Score (SD) **	42.1 (8.7)	45.3 (6.9)	-3.2	0.23
Self-Efficacy, Symptoms T-Score (SD) **	40.3 (5.7)	43.9 (7.1)	-3.6	0.10
Perceived Stress T-Score (SD) ***	63.1 (12.5)	55.4 (10.7)	7.7	0.055
Pain VAS, mean (SD)	61 (18)	51 (21)	10.0	0.14
PGA, mean (SD)	59 (28)	52 (27)	7.0	0.47

Table 2. HRQL domains pre/post 30-day mobile, mindfulness meditation trial for participants who completed pre/post questionnaires (n=18). * Derived from PROMIS 4a form extracted from Global-29 collection of surveys; **CATs, ***NIH Fixed Form.

global assessment of disease activity (PGA) scores, more pain (VAS), higher perceived stress, and more anxiety at baseline (Table 1). Full completers meditated on average for 302 minutes (SD 254; n=15). For completers, significant improvements were noted in fatigue by course end with trends for improvement in perceived stress, anxiety, sleep disturbance, and self-efficacy (Table 2).

Conclusion: Results from a pilot study on use of a 30-day smartphone mindfulness meditation application for patients with rheumatic disease revealed that this is a feasible and accepTable non-pharmacologic modality to target HRQL. Participants with higher baseline stress, anxiety, pain, and PGA scores were more likely to complete the mobile MBI program. Among completers, preliminary results showed improvements in fatigue and perceived stress. More rigorous study on mindfulness application use and barriers, as well as potential effect on HRQL, is needed.

Disclosure: D. DiRenzo, None; **C. Hunt**, None; **E. Sibinga**, None; **N. Gould**, None; **A. Shah**, None; **S. Bartlett**, Pfizer, 1, UCB, 1, Lily, 1, Novartis, 1, Merck, 1, Janssen, 1, Abbvie, 1; **C. Bingham III**, Bristol-Myers Squibb, 2, 5, 8, Genetech, 5, 8, Sanofi, 5, 8, AbbVie, 5, Eli Lilly, 5, Pfizer, 5, Gilead Sciences, Inc., 5, Regeneron, 5.

Abstract Number: 1127

Association of Health Literacy and Numeracy with Patient Reported Psychological Outcomes

Mithu Maheswaranathan[1], Jennifer Rogers[2], Amanda Eudy[1], Kai Sun[1], Stacy Bailey[3], S. Nicole Hastings[1] and Megan Clowse[4], [1]Duke University, Durham, NC, [2]Duke, Durham, NC, [3]Northwestern University, Chapel Hill, NC, [4]Duke University, Chapel Hill, NC

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Over 33 percent of American adults have low health literacy, which limits their ability to understand basic health information and make healthcare decisions. A component of health literacy is health numeracy (quantitative skills). Low health literacy has been associated with negative psychological and patient reported outcomes in other disease states including lower self-efficacy, reduced quality of life, and higher rates of depression.

Table 1: Demographic Differences between Patients with Low/Adequate Health Literacy and Numeracy

	Health Literacy by BHLS		
	Adequate	Low (Limited)	p-value
	n=148	n=24	
Demographics			
Age [Mean (SD)]	43.2 (13.4)	44.2 (17.2)	0.8
Female	140 (95%)	22 (92%)	0.6
African American (n=169)	90 (62%)	16 (65%)	0.8
College Graduate (n=165)	86 (60%)	9 (43%)	0.2
Income <$50,000 (n=159)	74 (54%)	15 (71%)	0.2
Medicaid Insurance (n=164)	64 (45%)	13 (62%)	0.2
Disability (n=158)	42 (31%)	11 (52%)	0.08
	Numeracy by SNS3		
	Adequate	Low (Limited)	p-value
	n=88	n=82	
Demographics			
Age [Mean (SD)]	43.5 (14.1)	43.0 (13.7)	0.8
Female	81 (92%)	79 (96%)	0.3
African American (n=167)	47 (54%)	56 (70%)	0.04*
College Graduate (n=163)	58 (68%)	36 (46%)	0.007*
Income <$50,000 (n=158)	38 (46%)	50 (66%)	0.02*
Medicaid Insurance (n=162)	32 (38%)	43 (55%)	0.04*
Disability (n=156)	21 (26%)	31 (42%)	0.04*

*$p \leq 0.05$

However, the relationship between health literacy and psychological outcomes has not been evaluated in SLE. The objective of this study was to assess the relationship of health literacy with psychological and patient-reported outcomes in SLE.

Methods: SLE patients meeting SLICC criteria were recruited from an academic university clinic from March 2019 through January 2020. Self-reported health literacy and numeracy were assessed using the Basic Health Literacy Screen (BHLS) and the 3-item Subjective Numeracy Scale (SNS-3). Low health literacy was defined as BHLS < 12 and low numeracy as SNS3 ≤ 14. Patients completed assessments for depression (Patient Health Questionnaire, PHQ9), fibromyalgia severity score (FSS), and self-reported cognitive dysfunction. Additionally, PROMIS Short-Forms for General Self-Efficacy and for Managing Treatments and Medications were obtained. We evaluated relationships between health literacy, self-efficacy and psychological covariates using descriptive statistics. Fisher's exact testing was performed for categorical measures and two-sample t-tests were performed for continuous measures.

Results: The study included 172 patients with SLE with average age 41 years, 94% female, and 61% African American. Mean clinical SLEDAI was 3.17. We found 14% of patients had low health literacy, while 45% of patients had low numeracy.

Health Literacy:

There were no differences in demographics or patient-reported outcomes between patients with low versus adequate health literacy (**Tables 1-2**).

Table 2: Association of Health Literacy with Patient-Reported Psychological Outcomes and Self-Efficacy

	Health Literacy by BHLS		
	Adequate	Low (Limited)	p-value
	n=148	n=24	
Psychosocial			
PHQ-9 Depression (n=156)	20 (15%)	5 (24%)	0.3
Cognitive Dysfunction	84 (57%)	14 (58%)	1.0
Fibromyalgia Severity Score	7.4 (5.7)	7.6 (5.3)	0.9
Self-Efficacy	n=115	n=20	
PROMIS Self-Efficacy General (n=87)	53.1 (10.2)	54.8 (10.6)	0.7
PROMIS Self-Efficacy for Managing Chronic Conditions (Manage Meds/Treatments) (n=87)	50.3 (8.6)	48.6 (7.6)	0.6

	Numeracy by SNS3		
	Adequate	Low (Limited)	p-value
	n=88	n=82	
Psychosocial			
PHQ-9 Depression (n=154)	5 (6%)	20 (27%)	0.0004*
Cognitive Dysfunction	43 (49%)	54 (66%)	0.03*
Fibromyalgia Severity Score	6.3 (5.0)	8.6 (6.1)	0.01*
Self-Efficacy	n=68	n=65	
PROMIS Self-Efficacy General (n=87)	55.3 (8.0)	50.6 (11.9)	0.04*
PROMIS Self-Efficacy for Managing Chronic Conditions (Manage Meds/Treatments) (n=87)	51.7 (7.9)	48.2 (8.9)	0.06

*$p \leq 0.05$

Numeracy:

Patients with lower numeracy were more likely to be African American, less likely to be a college graduate, more likely to have income < $50,000 annually, and more likely to be on Medicaid insurance or disability (**Table 1**). Those with lower numeracy were more likely to have depression, higher fibromyalgia severity scores, and cognitive dysfunction (**Table 2**). Additionally, patients with lower numeracy had worse self-efficacy by PROMIS Self-Efficacy (50.6 vs 55.3, p=0.04).

Conclusion: Lower numeracy was associated with higher rates of depression, higher fibromyalgia severity, lower self-efficacy and lower socioeconomic status factors. This data suggests numeracy may be an important factor to consider in patient counseling, particularly patients with concomitant depression or other psychiatric comorbidities. Future studies should evaluate the role of health literacy with other lupus outcomes.

Disclosure: M. Maheswaranathan, None; **J. Rogers**, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 2, Pfizer, 2; **K. Sun**, None; **S. Bailey**, Pfizer, 2, 5, Sanofi, 5, Merck, 2, Eli Lilly, 2; **S. Hastings**, RelyMD, 3, 4, 6; **M. Clowse**, UCB, 5, GSK, 2, 5, Astra Zeneca, 5, Pfizer, 2.

Abstract Number: 1128

The Diagnosis of Systemic Sclerosis as a Traumatic Experience: Patients' Reactions to the Diagnostic Process

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Background/Purpose: Both the process of being diagnosed with a chronic illness and the illness itself can be a traumatizing experience (1). The current study examined the diagnosis of a chronic illness, systemic sclerosis (SSc), as a potentially traumatic experience. We examined SSc patients' perceptions of the process of getting diagnosed and their reactions to this diagnosis. Our research question was, "What do patients report experiencing regarding the process of being diagnosed with SSc?"

Methods: Patients with SSc were approached to participate by their rheumatologist (specializing in SSc) during an office visit. Sixty-four patients completed the study (42% diffuse, 45% limited, 13% unknown type of SSc). All patients included met ACR-Eular criteria for diagnosis of SSc. Most respondents were female (85%), white (95%), and had an average age of 61 years.

Patients completed open-ended questions (e.g., what prompted you to first go to the doctor, what occurred through the time you were diagnosed with SSc, how did you react to the diagnosis). Two researchers independently categorized responses. Discrepancies were resolved by discussion. Additionally, one researcher retrieved demographic and disease information from patients' records.

Reaction to SSc Diagnosis	Percent of Patients Reported Reaction
Fear (all types)	78%
Fear of future	48%
Fear of dying	30%
Fear of falling apart	11%
Fear, unspecified	31%
Upset (previously) about not having a diagnosis	20%
Concerned due to disease progression in others	17%
Grief or anticipatory grief	14%
Sad	13%
Questioning ability to cope	11%
Shock	11%

Table 1. Reactions to Being Diagnosed With SSc and Percent of Patients Who Reported Each Reaction

Results: Seventeen percent of the sample received a potentially traumatic message from a health professional during the diagnostic process. For example, one patient reported learning there was no treatment for SSc and it would continue to get worse, one reported being told she was dying (before SSc was diagnosed), and another reported physicians involved in the diagnostic process were dismissive of independent and seemingly unrelated symptoms.

As can be seen in Table 1, fear was the most common patient reaction, especially fear of the future and fear of dying. Other reactions were feeling upset about not having a diagnosis (before SSc was diagnosed), feeling concern because of the disease progression they witnessed in others, feeling anticipatory grief, feeling sad or shock, and questioning their ability to cope.

Conclusion: Diagnosing and treating chronic illness can be a difficult process for both patients and practitioners (1). Consistent with past research, reactions to the diagnostic process showed patients did not self-label their reactions as depression (2). In the current study, few patients even reported sadness; fear was the overwhelmingly common reaction.

The current data emphasize the importance of physicians attending to the way information regarding SSc is conveyed to patients. Although a majority did not report receiving traumatic messages from a health care professional during the diagnostic process, over 1 in 6 patients did. Given the diagnostic process for SSc can be lengthy, patients may be feeling distressed for years. Health providers working with SSc patients should address patients' emotions and the causes of them (e.g., internet, statement by health provider) and know that their conversations with patients can make a difference.

References:

1. Fennell PA Managing chronic illness using the Four-Phase Treatment Approach. Wiley; 2003
2. Newton EG, Thombs BD, Groleau D. The experience of emotional distress among women living with scleroderma. Qual Health Res 2012; 22: 1195-1206.

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Discordance in Patient and Physician Assessment of Disease Activity in Relapsing Polychondritis

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Background/Purpose: Relapsing polychondritis (RP) is a rare chronic disabling inflammatory condition primarily affecting cartilage tissue. Self-reported patient outcome measures, which have not been evaluated in RP, are necessary to understand how RP disease manifestations affects patients. The objective of this study was to compare patient and physician assessment of disease activity in a cohort of patients with RP to determine the need for multimodal response criteria in RP.

Methods: Adult patients who fulfilled diagnostic criteria for RP were recruited into a prospective, observational cohort. Patients underwent a standardized comprehensive evaluation at six-month interval visits that included a clinical evaluation by rheumatology and otolaryngology, laboratory studies, audiology, and chest imaging. From this information, physicians rated the Physician Global Assessment (PhGA) on a scale of 0 to 10. Patients simultaneously completed four patient-reported outcome questionnaires: Patient Global Assessment (PtGA), SF-36 Health Survey, Brief Illness Perception Questionnaire (BIPQ), and Multidimensional Fatigue Inventory (MFI). The intraclass correlation coefficient (ICC) (2, 1) was calculated to determine the agreement between physicians and patients. Patient – Physician discordance was defined as a difference (PtGA-PhGA). Visit characteristics were compared between the positive discordant group and the concordant group using Mann Whitney or Fisher's exact test. Response to treatment was analyzed in all patients who had at least two study visits.

Results: A total of 154 visits from 76 patients were analyzed. The median PhGA was 3 (interquartile range 2-3) and median PtGA was 5 (interquartile range 4-7). The ICC was low (0.14; 95% confidence interval -0.06 to 0.334, *p=0.10)*. PtGA and PhGA were concordant in 66 visits (42.6%). In a total of 84 visits (54.2%), patients scored disease activity 3 or more points higher than physicians (positive discordance), whereas in only 4 visits (2.6%) PtGA was 3 or more points less than PhGA (negative discordance). Compared to visits with concordance, visits with positive discordance were associated significantly with worse scores on the MFI, BIPQ, SF 36 Physical component score (PCS), and SF 25 Mental component score (MCS). There were no differences in demographics, medication use, clinical symptoms, or objective measures of airway inflammation between the concordant and positively discordant groups. Treatment was increased over 52 visit intervals in 36 patients. Whereas PhGA scores significantly improved in response to increased treatment from a median 3 (interquartile range 2-4) to 2 (interquartile range 2-3) (P< 0.01), there was no significant change in PtGA. (Figure 1)

Conclusion: Patients with RP typically self-report higher disease activity than their physician counterparts and do not necessarily perceive similar improvement in response to treatment. Discordance is possibly due to the psychological

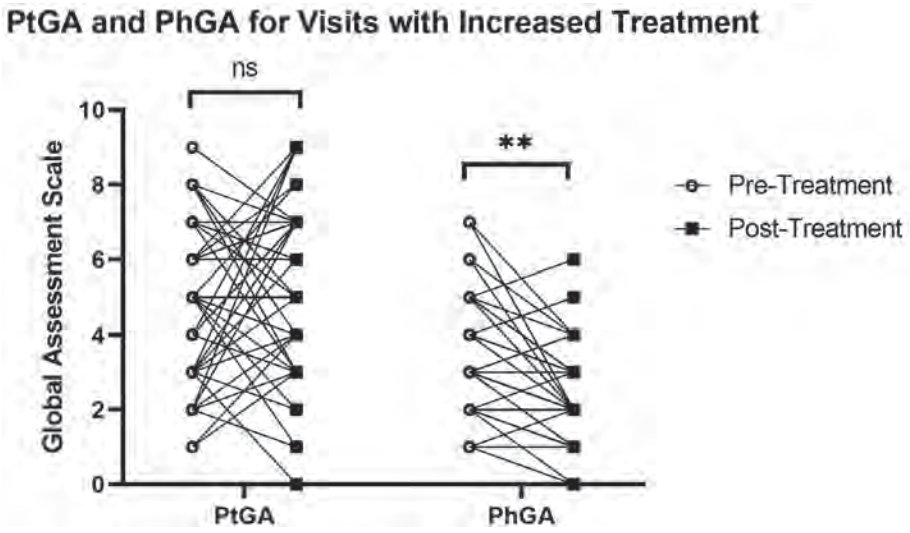

Figure 1. Increased treatment improves disease activity from physician (median change PhGA=-1 , IQR= -2-0) but not patient perspective (median change PtGA=0 , IQR= -1-1)

burden of illness experienced by patients. Future disease activity assessment instruments in RP should consider the utilization of composite response criteria that incorporate patient-reported outcome measures.

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Abstract Number: 1130

Patient Perspectives on Biobanking and Data-linkage for Rheumatic Disease Research

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Table 1. Participant characteristics

Age, (yrs)	Gender	Condition	Condition duration, (yrs)	Country of birth	Cultural heritage	Level of education
60	Female	Rheumatoid arthritis	6	New Zealand	Maori / German	Year 8
61	Male	Rheumatoid arthritis	11	Poland	Polish	Year 14
65	Female	Undifferentiated		Australia	Scottish	Tertiary
49	Female/Non-binary	Reactive arthritis	0.33	USA	Australian	Tertiary
89	Female	Rheumatoid arthritis	62	-	Australian	Year 12
73	Male	Rheumatoid arthritis	0.5	Australia	Australian	Year 10
72	Female	Rheumatoid arthritis	18	Australia	Australian	TAFE
71	Female	Rheumatoid/Psoriatic arthritis	20	Australia	Aboriginal	Year 10
64	Female	Rheumatoid arthritis	30	Australia	Australian	Diploma
29	Female	Juvenile rheumatoid arthritis	13	Australia	Australian	Adv. Diploma
45	Male	Ankylosing spondylitis	25	Australia	Asian/Australian	Tertiary
30	Female	Rheumatoid arthritis	2	Saudi Arabia	Sri Lankan/Australian	Tertiary
45	Female	Rheumatoid arthritis	8.5	Australia	Australian	Year 12
27	Male	Psoriatic arthritis	5	Australia	Australian	Year 12
76	Male	Rheumatoid arthritis	10	Australia	Australian	Year 10

Table 1. Participant characteristics

Background/Purpose: The causes of arthritis and autoimmune conditions remain unknown. A complex interplay of genetic and environmental factors is thought to underlie these diseases. Prospective collection of blood, saliva and

Table 2. Illustrative quotes

Theme	Illustrative quotes
Knowledge of biobanking and data-linkage	
	"One of the things I have not given any thought to" (60s female)
	"It's personalised medicine and I think that's the future. And that's right. And so again, the more the data is linked to our specific profile, the more personalized medicine can grow." (40s female)
	"I just have a vision of a huge big fridge with loads of test tubes in it" (70s female) "storing biological material… keeping like a safe of someone's biological material.. keeping like a database but a physical database.. (30s female)
Perceived barriers	
Privacy protection	"It's a bit like the whole having my health record, isn't it?...But do you ever get that a biobank like that sort of information could get into the wrong hands and then adversely affect you." (60s female)
	"you need good data governance. But I think that that good data, data governance should be openness to all kinds of researchers to do all kinds of things with the data and how it's linked to me in my personal records. Yeah, there's a little bit more risk there, but I'm also willing for that to happen as an ongoing flow of information. I'm willing to take that risk." (40s female)
	"I think those are things that we really do need to consider because there's all this discussion about, you know, lack of privacy and the impact it could have on things like health insurance, super and work, employment. So I think it is important…some sort of guarantee that would be necessary." (60s female)
Data-sharing	
Fears of data being used for secondary purposes	"Abused" (70s male)
	"Unless you're going to make cyborgs' out of them?" (70s female)
	"I guess the only thing which is, which I'd be concerned about is if someone decides to take some and then clone me, but hopefully that won't happen." (40s male)
	"Those kinds of things where they can just look you up and be like, you're not fit to drive anymore even though you're perfectly able.." (20s female)
Fears of data being manipulated	"we can manipulate the samples right" (60s male)
	"I would like to figure it out that there are some preventive methods … to… prevent any undue influence.. on the data and how it's used to come up with certain specific results..." (60s male)
Cost and funding	
Time consuming	"It probably sounds terrible, but just the time factor involved… I am very interested. But if it's going to take out a huge chunk of my time, I just don't have it because of what's going on in my life at the moment. And the other thing is you know, blood tests and things like that, stool samples, et cetera, they're all very easy. If it was anything more, which would take like a few hours, then I'd have to really consider how would I make that fit in" (40s female)
Frequency of samples	"But if someone was to turn around and say for the next 12 months, you need to give me a stool sample every two weeks, I think I'd be like, no, not interested. If it was once every six months, depends on the consistency. And then again, same with the needle side of things. Once a month. Yes. Once every two, three days, no." (20s female)
Funding	"Funding is shocking." (70s female)
Fear of discomfort	"Nothing too invasive." (20s female)
	"Would patients go through any pain when they're giving these samples."(30s female)
Perceived benefits	
Personal benefit	"What you really want is your condition to be improved." (60s female)
Helping science or society	"that could impact me personally. But I also think that it's you know contributing to the collective is really important …especially now that statistics can do so much calculation so quickly with stuff like all of the different genes in our gut. That's not something we could have parsed before, but now we can. And we need more data to get the best results." (40s female)
	I think it's the way we improve the health of the human race…I think the faster the better and you know, let the machine learning out on the data. Let's see what happens. (40s female)
	"A: Well, I think any research is tremendously important because I don't think it's going to go away. And future generations they, what can you say, you just hope that something's going to turn up. To make their lives easier? "(70s female) "B: I think it's very important. I've got my son, my nephew, who are looking very much, they are seeing rheumatologists already." (60s female)
Giving back	"I got really excellent medical care and that was given to me by this hospital and by a researcher here. And you know, that's something that I can give back." (40s female)
Attitudes towards participation	
General support	"No ! don't have any concerns. I came here with two hands up with bells on." (70s male)
Concerns about privacy do not influence willingness to participate	"I know a lot of people are very picky about things, such as privacy, but I think people are generally overly protective over that kind of stuff…unless you know, unless you've done something illegal (40s male)
	"I'm trusting that the data governance" (40s female)
	"When it comes to health and medicine, it doesn't worry me no." (20s male)
Positive relationship with healthcare providers	"I know this organization, I trust this organization." (60s female)
	"I got really excellent medical care and that was given to me by this hospital and by a researcher here" (40s female)
COVID19 and timing of participation	"So if the covid19 thing didn't exist, what sort of timeframe were you're looking at to sort of get the ball rolling?" (40s female)

Table 2. Illustrative quotes for the identified themes

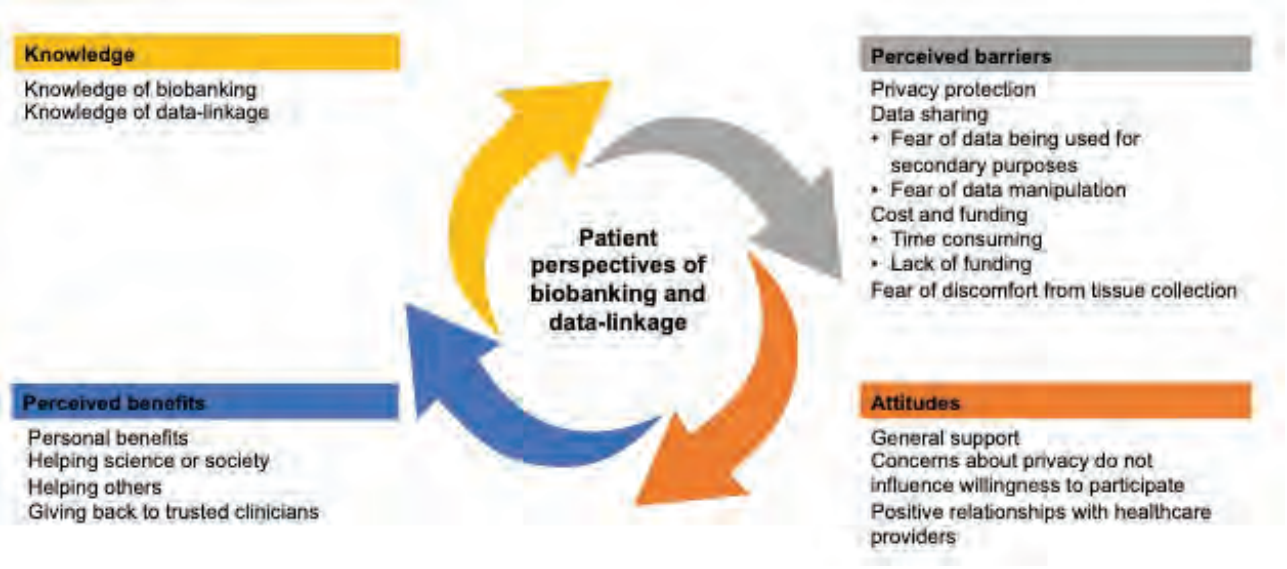

Figure 1. Thematic schema Our participants had varied knowledge of biobanking and data-linkage. Although there were many perceived barriers, as illustrated in the schema, participants' attitudes towards participations were generally supportive and we hypothesise this is likely due to the perceived benefits of helping themselves, their families, society and giving back to their clinicians.

stool samples from patients will be necessary for identifying biomarkers which may play critical roles in predicting, managing and preventing arthritis and autoimmune conditions.

Biobanking refers to the collection, storage and distribution of human biospecimens and linked health data for research. Engagement with patients and the public is required for the success of biobanking endeavours.

To our knowledge there are no qualitative studies investigating the attitudes of patients with rheumatic conditions towards biobanking and data-linkage. This is of importance for us as we, like a growing number of countries globally, develop a national biobank for rheumatic conditions in Australia. Our aim is to explore participants' knowledge, attitudes, perspectives and beliefs regarding the process of biobanking and data-linkage to national health statistics in the context of their illness.

Methods: This qualitative study was conducted between October 2019 and April 2020. Ethics approval was granted by Northern Sydney Local Health District Ethics Committee (2019/ETH11659). Adult patients with rheumatic conditions were invited to participate in focus groups or semi-structured phone interviews. Patients were recruited via rheumatology clinics from a tertiary hospital in Sydney, Australia.

Focus groups and semi-structured interviews were moderated according to a question guide which was informed by current literature. Recruitment ceased when no new themes emerged.

The collection, analysis and interpretation of data was an iterative process using grounded theory underpinned by the health belief model. Data was entered into computerised data management program (NVivo 12) where further refinement occurred.

Results: There were fifteen participants, their characteristics are summarised in Table 1, nine of fifteen were women, the mean age was 55.7years (range 27 – 76), majority of patients had rheumatoid arthritis (11/15) and the average disease duration was 15.1years (range 0.33 – 62 years). Four main themes arose including knowledge of biobanking

and data-linkage, perceived barriers, perceived benefits and attitudes towards biobanking. Table 2 shows illustrative quotes from the interviews and Figure 1 provides a diagrammatic representation of the identified themes.

Conclusion: Knowledge of biobanking varied significantly amongst Australian patients with rheumatic conditions. Although there were many perceived risks to participation, the majority of participants in this study were willing to accept these risks and engage with biobanking research. We hypothesise that this willingness to participate was influenced by the relevance of the biobank's objective to their own condition, perceived benefits in helping themselves, their families, future generations and their trusted clinicians. This study should inform patient information and frequently asked questions when developing recruitment strategies for rheumatic disease biobanks.

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Abstract Number: 1131

Patient Perspective of Helpfulness of Lupus Medications: A Qualitative Study of Medication Use Within the Type 1 and 2 SLE Model

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Background/Purpose: Medication management in systemic lupus erythematosus (SLE) is particularly complex given the clinical heterogeneity of symptoms and a wide range of medications used. We developed a conceptual model that characterizes symptoms and corresponding medications into two categories: Type 1 medications are used for Type 1 SLE symptoms or inflammatory manifestations (such as arthritis, nephritis, rashes) while Type 2 medications are used for Type 2 SLE symptoms of fatigue, myalgia, anxiety/depression and cognitive dysfunction. Type 1 medications included antimalarials, oral immunosuppressants, biologics and steroids. Type 2 medications included pain medications, muscle relaxants, sleep medications, and antidepressants. We conducted a qualitative descriptive study to assess perceived helpfulness (benefits and drawbacks) of Type 1 and Type 2 medications and describe disease experiences in patients with SLE.

Methods: We conducted semi-structured qualitative interviews among purposefully selected adult patients meeting SLICC criteria for SLE from an academic medical center. We asked patients to describe the helpfulness of medications, including whether they believed their symptoms had improved. All interviews were audio-recorded and transcribed, and we used applied thematic analysis to analyze the data.

Results: We interviewed 37 patients (12 with Type 1 SLE, 12 with Type 2 SLE, and 13 with Mixed SLE); 73% were age ≤55 years, 84% had disease duration ≥5 years, 49% were black or African American, and 35% had a history of nephritis.

Medication Helpfulness: The majority of patients endorsed benefit from at least one Type 1 or Type 2 medication. More patients reported at least one Type 2 medication as not helpful (n=24) compared to those reporting at least one Type 1 medication as not helpful (n=18).

Table 1: Themes Observed and Selected Quotes, by Medication Class

	Medication Class	Themes	Selected Patient Quotes
TYPE 1 Medications	**ANTIMALARIAL** • hydroxychloroquine	• mild or delayed benefit, often minimal improvement of symptoms • uncertainty regarding helpfulness or indication	*"Like, if I were taking it, it would probably be a 1 on the side of the pain, but like if I weren't taking it, it would be like a 2 or a 3." [**HCQ**]*
	ORAL IMMUNOSUPPRESSANTS • azathioprine • methotrexate • mycophenolate	• varying degrees of helpfulness • no change in symptoms observed • uncertainty regarding helpfulness	*"They don't change them or improve them [symptoms]... I just don't see where any of it is doing anything"*
		• uncertainty regarding indication	*"That's the hard part. I really can't tell you. Besides it helped my lupus." [**methotrexate**]*
		• medication concerns re pill burden or medication management • side effects often limiting benefit	*"The one thing I do not like... is that the pills are humongous, and you have to take six a day... That can be difficult" [**mycophenolate mofetil**]*
	BIOLOGICS/ IV INFUSION • belimumab • Rituximab • cyclophosphamide • IVIg	• varying degrees of helpfulness (more dramatic benefit noted)	*"I nicknamed that one my Super Woman drug" [**cyclophosphamide**]*
		• initially felt worse followed by a delayed response	*"I felt sicker... I was constantly nauseous... I actually felt worse on Benlysta than I felt before. Now that I've been on it about a year, I do notice a difference... my joint pain has improved. [**belimumab**]*
		• more certainty re helpfulness or indication	
	STEROIDS • oral prednisone • intramuscular • intravenous (methylprednisolone)	• majority noted helpfulness (rapid improvement or dramatic benefit) • no uncertainty regarding the helpfulness or indication • concerns regarding long-term side effects	*It's one of those love-hate relationships... because you know it works and I think that's a lot of the issue as far as a lot of the lupus medications that we don't see it. We can't tell. [**prednisone**]*
TYPE 2 Medications	**NERVE and PAIN MEDICATIONS** • gabapentin, pregabalin • opioids, Tramadol • topiramate	• helpful but often with associated side effects influencing adherence • no change or improvement in symptoms in some patients	*"Thank God for Gabapentin. Gabapentin is a wonder drug... like if miss a dose or something, you can tell right away. It comes right back – that tingling feeling"*
	MUSCLE RELAXANTS • cyclobenzaprine • tizanidine	• helpful with improved symptoms (muscle pain and insomnia) • side effects (drowsiness) noted, sometimes influenced adherence	*"It does help with pain... But at the same time, it also makes me really drowsy so it's not something I can take and...work." [**cyclobenzaprine**]*
	SLEEP MEDICATIONS • melatonin • zolpidem, eszopiclone • trazodone	• helpful in some patients, although side effects (psychological or cognitive) sometimes precluded use	*"It will definitely mellow you out. It will definitely make you tired... I found it a lot more mentally and cognitively dampering" [**trazodone**]*
	ANTI-DEPRESSANTS • SSRI medications • SNRI medications • TCA (amitriptyline) • benzodiazepines	• helped with depression and anxiety symptoms in a subset • some with no benefit or psychological SE limiting use	*"It did suppress some of those feelings of sadness, and loneliness... but I wasn't myself. It wasn't my personality. It was augmenting the happiness that really wasn't there" [**alprazolam**]*

Unable to Assess Helpfulness: More patients were unable to assess the helpfulness of Type 1 medications (~50%, n=19) compared to Type 2 medications (~20%, n=7). Inability to determine helpfulness was often due to no change in symptoms or uncertainty of symptoms the medication was supposed to improve.

We categorized participant experiences with Type 1 and Type 2 medications by class of medication thematically (Table 1). For example, patients viewed hydroxychloroquine as minimally beneficial compared to the dramatic improvements they noted on biologics and IV infusions. Patients also had less certainty regarding the helpfulness and indication for antimalarials and oral immunosuppressants compared to biologics, steroids, and Type 2 medications.

Conclusion: For both Type 1 and 2 medications, the vast majority of patients reported at least some benefit in helping symptoms. However, substantially more patients were unable to assess the helpfulness of Type 1 medications compared to Type 2, most often due to uncertainty regarding helpfulness or lack of awareness of indication. These findings suggest physician/patient discussion about specific indications for which medications are prescribed and potential side effects may increase patient understanding and expectations regarding medication use.

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Abstract Number: 1132

Reliability of Virtual Sources of Education for Patients with Vasculitis

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Background/Purpose: Vasculitides are defined as inflammation of the vessel wall of different organ systems with reactive damage of mural structures. Patient education in understanding the pathophysiology of the disease and its treatments can be challenging and affects medication compliance and disease outcomes. YouTube (YT) is one of the most popular websites with visual representations of healthcare topics recorded by a diverse group of people including patients, healthcare providers, organizations, universities, etc. There have been multiple studies done investigating the quality and reliability of information available on multiple diseases on YT. However, investigation of videos pertaining to vasculitis education is not known. Our objective was to review the quality of videos on vasculitis education and compare them to the popularity of each video.

Methods: A search was performed on YT using the term "vasculitis education." A total of 30 videos were reviewed. Duration of the video, number of viewers, time since video, likes, and dislikes were recorded. The video power index (VPI) and view ratio (VR) were used to determine video popularity. The DISCERN instrument, a questionnaire developed for judgement of the quality of consumer health information, was used to determine quality and reliability of each video. We further collapsed the DISCERN summated score into two categories, Excellent (EQ) or Good (GQ) Quality (51-80) and Fair (FQ) or Poor Quality (PQ) (7-50) according to the standard score ranges. The Mann-Whitney U test was done to determine video quality categories resulted in differences in the VR and VPI outcomes. Fisher's Exact test was done to determine if there were proportional differences in video quality based on publisher. We set alpha equal to 0.05 for statistical significance.

Results: A total of 30 videos were analyzed. The individuals who recorded these videos included 23 physicians, 4 allied health professionals, 1 commercial company, and 2 patients. On average, duration of each video was 14:25. The average time since upload was 40 months. The average DISCERN score was 52 (SD 13). Out of the 30 videos, the DISCERN score showed 8 EQ videos (63-80), 8 GQ (51-62), 9 FQ (39-50), 5 PQ(27-38 points), and no videos were very poor quality (16-26 points). According to the DISCERN quality labels, videos that were either EQ or GQ (n=16), had an average VR of 373.9 ± 607.2 and an average VPI score of 359.8 ± 595.3. Videos that were either FQ or PQ in quality (n=14), had an average VR of 1588.9 ± 2081.9 and average VPI score of 1550.8 ± 2077.9. These mean ranking differences were statistically significant for VR and VPI (p= 0.04 and p= 0.03, respectively). Most videos were published by physicians (77%). Of those videos, 65% were rated as EQ or GQ. Of the videos published by others (n=7), only 1 (14%) was rated as EQ or GQ and this proportional difference was statistically significant (p= 0.03).

Conclusion: Videos that were rated as Fair or Poor in quality tended to be more popular on YT compared to the videos that were rated as EQ or GQ. In addition, physician recorded videos had better quality. Further larger scale studies are required to determine the utility of YT as an educational tool for patients with vasculitis.

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Abstract Number: 1133

Patient Perceptions of Diagnosis, Tests, Treatments, Adherence and the Impact on Their Disease Understanding and Participation in Research Studies

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Session Time: 9:00AM–11:00AM

Background/Purpose: The diagnosis and treatment of inflammatory arthritis has been transformed largely by the development of drugs that target specific molecules of the immune system. However, these changes have increased the complexity of the mechanisms of disease, its treatment and patients understanding. Patient education is needed in this area to facilitate decision making.

Methods: An online anonymous survey of 27 questions addressed patient understanding of their diagnosis, diagnostic tests performed at outpatient clinics, their treatments and how they worked. Questions also addressed adherence and disease flare, issues of heredity and pregnancy, and patient involvement in research.

Results: The survey was completed by 1,873 patients, 1607 had an inflammatory arthritis RA (62.29%), SpA (41.88%) and JIA (2.92%). Respondents were predominantly female (83.77%). Most patients understood the difference between inflammatory arthritis and osteoarthritis (68.12% vs 31.88%), and 76.48% were concerned it was hereditary. Patients were asked to indicate their understanding of diagnostics tests performed at out-patient clinics (Scale 1-10; 1=don't understand at all, 10=understand very clearly). For all diagnostic tests < 25% of patients had an understanding of what was measured and the implication for disease, including ESR, CRP, RF, anti-CCP, VAS and Das28. Significantly, 72% understood how specific medications treat inflammatory arthritis, while 27.97% had no understanding. Adherence was strong with >87% vs 12% adhering to their medication. Of those stopping medication, without the advice of their doctor, the main reasons were 'feeling better', 'don't think it works' and 'side effects', however 68.43% of these patients also reported disease flare following cessation of medication. Patients of childbearing age (31%) worried that inflammatory arthritis reduced their chances of getting pregnant, and 79% believed arthritis medications are not safe to take during pregnancy. Finally, only 9% of patients had ever been asked to participate in a research study by their doctor.

Conclusion: This patient awareness survey demonstrates that patients have an understanding of their diagnosis, but little understanding of the diagnostic tests performed, their implication for disease progression and response. Furthermore patients concerns regarding heredity and pregnancy need to be addressed more thoroughly. Patients reported significant medication adherence, with those non-adherent experiencing flares. Finally, very few patients had been asked to participate in a research study.

Disclosure: V. Marzaioli, None; **M. Canavan**, None; **S. Wade**, None; **A. Fraser**, None; **S. Harney**, None; **A. Donnelly**, None; **A. Charity**, None; **D. Veale**, AbbVie, 2, Health Beacon, 1, Janssen, 2, 8, Pfizer, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5; **U. Fearon**, None.

Abstract Number: 1134

Prevalence of Frailty and Associated Factors in a National Observational Cohort of Rheumatic Diseases

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Frailty is associated with poor health outcomes in the general population, and recent studies have highlighted its importance in rheumatic musculoskeletal diseases (RMDs). Prior studies have found associations between frailty and low bone mineral density and fractures in RA and mortality in SLE and OA. These studies used performance or comorbidity-based measures of frailty which may not be feasible to collect in routine clinical care. Self-reported measures of frailty are validated in the general population but have not been widely studied in RMDs. We aimed to describe the prevalence of self-reported frailty across RMDs and to determine factors associated with frailty in a large observational cohort.

Methods: Data were from participants in FORWARD, The National Databank for Rheumatic Diseases, an observational longitudinal US-cohort registry with biannual patient questionnaires since 1998. The most recent wave of questionnaires, released in January 2020, included a 5-item validated patient-reported frailty index[1]. Participants were asked to report levels of fatigue, ability to walk several blocks, ability to climb ten stairs, weight loss, and presence of 11 comorbidities. Those meeting ≥3 of 5 criteria were categorized as frail. This analysis included all responses collected as of June 5, 2020. Multivariable logistic regression analysis was performed to identify factors independently associated with frailty.

Results: 1423 responses were included in this analysis, 63% with RA, 15% with OA, 7% with SLE, 4% with FM and 11% with other/unknown RMDs. Those categorized as frail (N=420, 30%) were older, had longer disease duration, greater pain, and were more likely to be obese (Table 1). The frail group reported a higher frequency of prednisone use in the last year as compared to the non-frail group (26% vs. 16%) but reported similar ever and never use of prednisone. The frail group reported more historical fractures than those who were not frail. SLE had the highest proportion of frailty (39%) despite being the youngest group (61±12 years). The top three factors contributing to frailty scores were inability to walk several blocks, inability to climb 10 stairs, and [3]5/11 comorbidities (Table 1). In the multivariable model, age, disease duration, pain scale, prednisone use within the last year, and prior fracture were associated with elevated odds ratios of frailty (ORs 1.04, 1.01, 1.23, 1.58 and 2.02 respectively, all $p< 0.05$) (Table 2). Within RMDs, using OA as the reference group, SLE was associated with 2.39-fold greater odds of frailty ($p=0.008$). Using normal weight as the referent, overweight and obesity were also associated with a greater odds of frailty (ORs 2.02 and 4.99, $p< 0.0001$).

Table 1- Cohort characteristics as a whole and by frailty status determined by a five question, patient-reported index. Frailty index range 0-5 and frailty defined as ≥3/5 criteria. Reported as N (%) or mean (SD).

	Overall (N=1423)	Not Frail (N=1003, 70%)	Frail (N=420, 30%)
Age (years)	65.4 (11.3)	64.6 (11.5)	67.4 (10.4)
Female	1230 (86.5%)	857 (85.9%)	373 (88.8%)
White Race	1292 (90.8%)	918 (91.5%)	374 (89.0%)
Disease Duration (years)	23.7 (12.3)	22.8 (12.0)	25.9 (12.8)
Primary Diagnosis			
-Osteoarthritis	213 (15.0%)	147 (14.7%)	66 (15.7%)
-RA	901 (63.3%)	643 (64.1%)	258 (61.4%)
-SLE	92 (6.5%)	56 (5.6%)	36 (8.6%)
-Fibromyalgia	63 (4.4%)	40 (4.0%)	23 (5.5%)
-Other or missing[a]	154 (10.8%)	117 (11.7%)	37 (8.8%)
Pain Scale[b]	3.26 (2.59)	2.79 (2.43)	4.42 (2.62)
Body Mass Index[c]			
-Underweight	22 (1.6%)	18 (1.8%)	4 (1.0%)
-Normal	447 (31.4%)	378 (37.7%)	69 (16.4%)
-Overweight	419 (29.4%)	308 (30.7%)	111 (26.4%)
-Obese	535 (37.6%)	299 (29.8%)	236 (56.2%)
Prior Fracture	426 (29.9%)	246 (24.5%)	180 (42.9%)
Prednisone Use			
-Never	786 (55.2%)	587 (58.5%)	199 (47.4%)
-Ever (not last year)	371 (26.1%)	258 (25.7%)	113 (26.9%)
-Within the last year	266 (18.7%)	158 (15.8%)	108 (25.7%)
Frailty Categories[d]			
-Fatigue	818 (57.4%)	579 (57.7%)	238 (56.7%)
-Stair Climb	464 (32.6%)	131 (13.1%)	333 (79.3%)
-Walking	632 (44.4%)	249 (24.9%)	383 (91.2%)
-Illnesses	534 (37.5%)	244 (24.3%)	290 (69.1%)
-Weight Loss	233 (16.4%)	92 (9.2%)	141 (33.6%)

-RA: rheumatoid arthritis; SLE: systemic lupus erythematosus.
[a]-Other category comprised of >20 primary rheumatic disorders other autoimmune and musculoskeletal syndromes or those missing a primary diagnosis.
[b]-Pain by visual analog scale. Range 0 (no pain at all) to 10 (worst pain imaginable).
[c]-Based on World Health Organization Body Mass Index categories: Underweight (<18.5 kg/m^2), Normal (18.5-24.9 kg/m^2), Overweight (25-29.9 kg/m^2) and Obese (>30 kg/m^2).
[d]-FRAIL scale frailty categories: self-reported fatigue, inability to climb 10 stairs, inability to walk several blocks, ≥5/11 comorbidities, ≥5% weight loss in the last year. Morley JE et al. *J Nutr Health Aging*. 2012; 16(7):601–608.
-Missing >5% data: Disease Duration (N=242) and Primary Diagnosis (N=110).

Conclusion: Self-reported frailty was prevalent in a third of participants with RMDs, with the highest rate in those with SLE despite that group having the lowest age. SLE, prior fracture, prednisone use within the last year, and obesity had the greatest odds of frailty in the multivariable model. Future longitudinal analyses to determine factors associated with incident frailty and its sequelae are needed in this high-risk population.

1. Morley et al, J Nutr Health Aging. 2012;16(7):601

Table 2- Multivariable logistic regression showing the independent associations between rheumatic musculoskeletal diseases and patient characteristics with frailty status determined by a five question, patient-reported index. Frailty range 0-5 and frailty defined as ≥3/5 criteria.

	Odds Ratio	95%CI	p-value
Age (years)	1.04	1.03-1.06	<0.0001
Female	1.32	0.87-2.02	0.198
Disease Duration (years)	1.01	1.00-1.02	0.040
Primary Diagnosis			
-Osteoarthritis	ref	--	--
-RA	1.16	0.78-1.73	0.452
-SLE	2.39	1.26-4.55	0.008
-Fibromyalgia	1.01	0.52-1.98	0.977
-Other or missing[a]	1.11	0.57-2.14	0.762
Pain Scale[b]	1.23	1.16-1.29	<0.0001
Body Mass Index[c]			
-Underweight	1.22	0.36-4.10	0.745
-Normal	ref	--	--
-Overweight	2.02	1.37-2.98	<0.0001
-Obese	4.99	3.47-7.19	<0.0001
Prior Fracture	2.00	1.51-2.66	<0.0001
Prednisone Use			
-Never	ref	--	--
-Ever (not last year)	1.10	0.79-1.52	0.564
-Within the last year	1.58	1.11-2.26	0.012

-RA: rheumatoid arthritis; SLE: systemic lupus erythematosus.
[a]-Other category comprised of >20 primary rheumatic disorders other autoimmune and musculoskeletal syndromes or those missing a primary diagnosis.
[b]-Pain by visual analog scale. Range 0 (no pain at all) to 10 (worst pain imaginable).
[c]-Based on World Health Organization Body Mass Index categories: Underweight (<18.5 kg/m^2), Normal (18.5-24.9 kg/m^2), Overweight (25-29.9 kg/m^2) and Obese (>30 kg/m^2).

Disclosure: K. Wysham, None; **J. Baker**, None; **K. Wipfler**, None; **S. Lieber**, None; **S. Sattui**, None; **P. Katz**, None; **K. Michaud**, Rheumatology Research Foundation, 2.

Abstract Number: 1135

Barriers to Influenza Vaccination in Patients at a Tertiary Care Rheumatology Clinic

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatologic conditions are at high risk of hospitalization, ICU admission, and death related to influenza infection due to their underlying diseases and associated treatments. The influenza vaccination rate for the Stanford Rheumatology Clinic during the 2019/2020 influenza season was 61%, leaving a significant number of patients without this protection. We sought to investigate the personal and environmental factors that prevented patients from receiving the influenza vaccine.

Methods: During each clinic visit, patients were asked if they received, plan to receive, or decline the influenza vaccination. At the end of the influenza season, the demographics of patients who received and did not receive the influenza vaccine were compared. Those who did not have a confirmed vaccination in the electronic medical record (EMR) were contacted by secure message or phone and asked open-ended questions regarding their reasoning for not receiving the influenza vaccine in the past year. These responses were recorded and categorized, allowing for multiple responses if given.

Results: Demographic analysis found that patients aged 18-29 were less likely to be vaccinated compared to those aged 50-64 (p=0.018) and those aged 65-79 (p=0.014). No significant difference in vaccination status was found based on sex, race, or health insurance provider (Table 1). Five hundred and ninety two (592) patients without a recorded vaccine at the end of the influenza season were contacted to date and 368 responded (Figure 1). Of those who "Planned To", 50.3% reported being vaccinated, although this had not been captured in the EMR. The most common barriers cited by this group were lack of time (25.2%) and access (19.4%). In the "Decline" group, patients

	Unvaccinated Group (N=698)	Vaccinated Group (N=594)	P-value	Overall (N=1292)
Age				
18 to 29	100 (14.3%)	54 (9.1%)	<0.001	154 (11.9%)
30 to 39	121 (17.3%)	86 (14.5%)		207 (16.0%)
40 to 49	114 (16.3%)	93 (15.7%)		207 (16.0%)
50 to 64	211 (30.2%)	180 (30.3%)		391 (30.3%)
65 to 79	125 (17.9%)	146 (24.6%)		271 (21.0%)
80 and older	27 (3.9%)	35 (5.9%)		62 (4.8%)
Sex at Birth				
Female	498 (71.3%)	417 (70.2%)	0.859	915 (70.8%)
Male	200 (28.7%)	177 (29.8%)		377 (29.2%)
Race				
White	332 (47.6%)	293 (49.3%)	0.126	625 (48.4%)
Black or African American	22 (3.2%)	16 (2.7%)		38 (2.9%)
Hispanic/Latino	109 (15.6%)	74 (12.5%)		183 (14.2%)
Asian	114 (16.3%)	132 (22.2%)		246 (19.0%)
American Indian or Alaska Native	3 (0.4%)	2 (0.3%)		5 (0.4%)
Native Hawaiian or Other Pacific Islander	9 (1.3%)	5 (0.8%)		14 (1.1%)
Other	69 (9.9%)	44 (7.4%)		113 (8.7%)
Unknown	24 (3.4%)	16 (2.7%)		40 (3.1%)
Patient Refused	16 (2.3%)	12 (2.0%)		28 (2.2%)
Health Insurance				
Blue Cross	170 (24.4%)	124 (20.9%)	0.0594	294 (22.8%)
Blue Shield	66 (9.5%)	49 (8.2%)		115 (8.9%)
Managed Care	177 (25.4%)	139 (23.4%)		316 (24.5%)
Medi-Cal	86 (12.3%)	62 (10.4%)		148 (11.5%)
Medicare	181 (25.9%)	206 (34.7%)		387 (30.0%)
Other	18 (2.6%)	14 (2.4%)		32 (2.5%)

Table 1. Demographics of patients who were vaccinated for influenza during the 2019/2020 influenza season compared to those who remained unvaccinated.

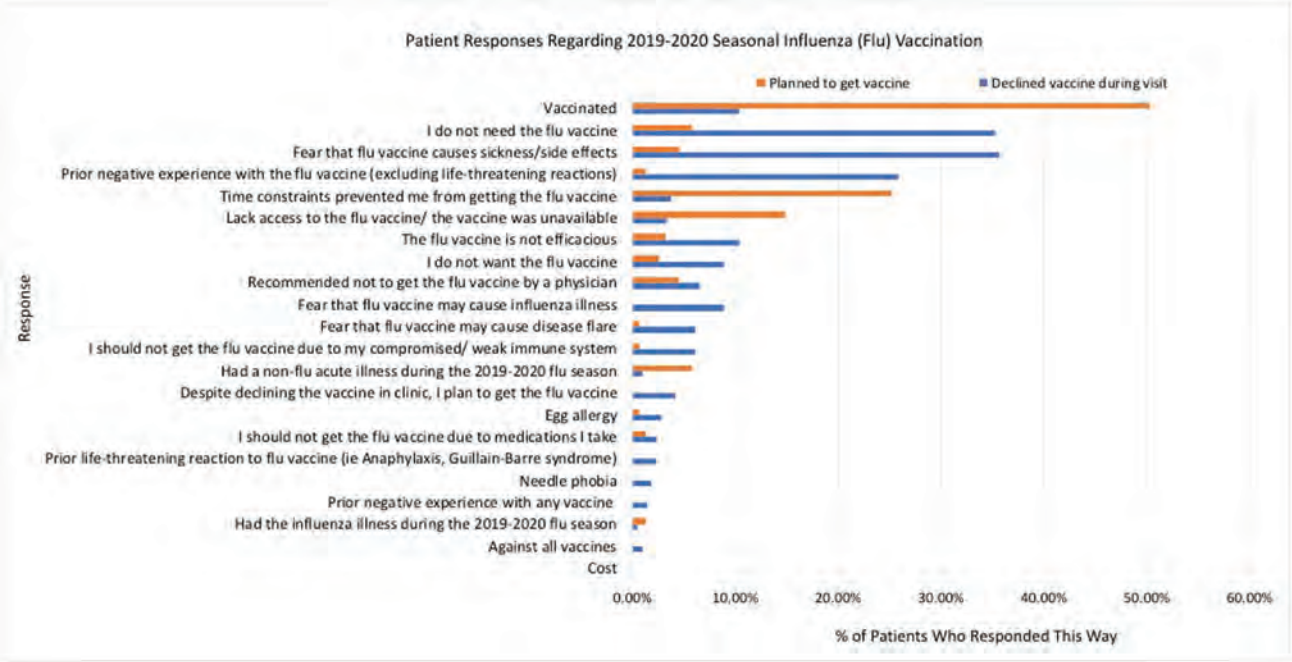

Figure 1. Patient reasons for not obtaining the influenza vaccination during the 2019/2020 influenza season separated into groups of patients who initially planned to get vaccinated (orange, n=155) and declined vaccination (blue, n=213).

reported fear of getting sick or side effects (35.6%), belief that they did not need the vaccine (35.2%), and prior negative influenza vaccine experience (25.8%) as reasons for not pursuing vaccination. Only a small proportion reported concerns related to their rheumatologic disease such as prompting a flare (6.1%), a weakened immune system (6.1%), and medication concerns (2.3%). No patient reported cost as a significant barrier.

Conclusion: In patients who desired influenza vaccination, time and vaccine availability were significant barriers. Fear of adverse reaction and prior negative experiences with the influenza vaccine were the primary reasons for active avoidance, although a significant percentage generally did not feel it was necessary. The results of this project can be used for targeted patient education to help improve vaccination rates in the future.

Disclosure: A. Horomanski, None; **G. Triant**, None; **K. Kolstad**, None; **M. Dymock**, None; **J. Lin**, None.

Abstract Number: 1136

Survey of Medical Cannabis Use in Lupus and Scleroderma

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases
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Background/Purpose: Despite the lack of research regarding medical cannabis, marijuana and its by-products have gained popularity over the last decades. A 2019 Statistics Canada report revealed that approximately 16% of Cana-

dians used marijuana in the last year. A Canadian study also revealed that 80% of rheumatologist participants were questioned by their patients weekly regarding medical marijuana; and in a similar study, 75% of participants were not comforTable prescribing medical marijuana. Despite being a common and debilitating feature in rheumatic diseases, there is little attention given to the study of medical options for the management of pain. The effects, both positive or negative of medical marijuana in patients suffering from lupus or scleroderma, is still unclear. We conducted a survey amongst patient diagnosed with lupus or scleroderma to evaluate their beliefs, concerns and personal experience if any with medical cannabis.

Methods: Patients with diagnosed lupus or scleroderma were recruited from the Ottawa Hospital division of Rheumatology. Consent was implied with completion of the survey and answers remained anonymous. Inclusion criteria: age >18, diagnosis of systemic lupus or scleroderma and able to complete survey in English or French. Data analysis of the results of the survey are qualitative.

Results: On preliminary results, 20% of participants are actively using medical cannabis, primarily in the form of CBD oil or inhaled. In those patients taking medical cannabis, they reported no significant side effects. Of those not using cannabis, 49% of participants considered using it, and 62% would like further discussion with their rheumatologist regarding pros and cons of medical cannabis. Among our participants, the most common reasons for use of medical cannabis were insomnia, anxiety, and pain. The majority (97%) were aware that there can be side effects, and this was often the reason for wanting more information. The main elements important to the discussion was trust in their treating physician, having a non-judgemental approach, the degree of uncontrolled pain/symptoms and need for alternatives as well as receiving reliable information.

Conclusion: Our survey results suggest that a proportion of our patients have already tried medical cannabis, and most have an interest in the use of cannabis to help with symptoms not relieved by standard therapies to date. We need to be prepared to better guide our patients with respect to medical cannabis. These results will highlight common reasons/indications for medical cannabis use in this patient population. This study will ultimately assist with broadening patient perspective on medical cannabis, its impact on our patients and guide us in elaborating new strategies when discussing medical cannabis.

Disclosure: W. Karkache, None; **C. Ivory**, None.

Abstract Number: 1137

Access to Digital Health in an Urban Rheumatology Population

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Advances in treatment of rheumatologic diseases have increased emphasis on physician and patient use of health information technologies (HIT). While studies indicate that e-health platforms can improve rheumatology outcomes, patients with rheumatologic disease are at risk for being caught on the wrong side of the digital divide. However, despite this potential disconnect, few studies have examined barriers to e-communication and preferences in rheumatology.

Table 1. Demographic of patient survey respondents.

Characteristic	Mean (SD) or n (%)		
	Clinic Population	Clinic Low SES	Clinic Non-Low SES
Age in years, mean (SD)	53 (14)	57 (13)	47 (14)
Male, n (%)	31 (19%)	12 (24%)	9 (35%)
Female, n (%)	129 (81%)	38 (76%)	17 (65%)
Household income in US Dollars, n (%)			
<$20,000	50 (31%)	50 (100%)	0 (0%)
$20,000—49,999	43 (27%)	0 (0%)	0 (0%)
$50,000—100,000	18 (11%)	0 (0%)	18 (69%)
>$100,000	8 (5%)	0 (0%)	8 (31%)
I don't know or I don't want to answer	29 (18%)	0 (0%)	0 (0%)
Highest Education Completed, n (%)			
Some High School	33 (21%)	15 (30%)	0 (0%)
Completed High School	72 (45%)	25 (50%)	7 (27%)
Completed college or graduate school	53 (33%)	10 (20%)	19 (73%)

Methods: We investigated preferences regarding e-communications in an urban rheumatology clinic using a patient survey to quantify HIT access, identify barriers to HIT access, and evaluate HIT preferences. We used a cross-sectional survey design to study patients from our rheumatology clinic (n=160, 81% female, 19% male, average age 53, SD 14 years).

Results: Demographic characteristics are shown in Table 1. The high percentage of female respondents is in accordance with the institutional analysis of all patients visiting the Drexel Rheumatology Clinic for the duration of the study (82% female and 18% male, average age 54 years old with SD of 14, n=687).

Patients reported their preferred method of contacting physicians as being the phone (74%) followed by email (29%), online patient portal (17%), mail (11%), and other, such as in person (3%) (Table 2). The general population of rheumatology patients does not use patient portals. Specifically, only 21% of survey participants reported using Drexel's online patient portal, FollowMyHealth, while 14% reported using external electronic patient portals.

A large percentage of patients reported believing that it is very important or absolutely necessary to contact physicians electronically (40%) (Table 3). Respondents reported their main preferred method of internet access as being a mobile device (64%) followed by home computer (44%), Tablet (23%), outside computer (8%).

Cross-tabulation analyses indicate that the rate of internet access for an urban rheumatology clinic is similar to that of the general population. Within the clinic, higher SES demographic is significantly associated with higher internet access ($\chi 21$, N=76=28.27, P< 0.01), utilization of internet for health purposes ($\chi 21$, N=76=7.82, P< 0.01), use of smartphones ($\chi 21$, N=76=8.55, P< 0.005) and laptops ($\chi 21$, N=76=3.85, P< 0.05) for HIT access, and rating of the importance of contacting physicians electronically ($\chi 21$, N=76=4.45, P< 0.05).

Conclusion: Our institutional experience confirms that the rheumatology clinic population faces a digital divide. As expected, individuals of low SES in comparison to higher SES exhibit differences in access to, use of, and perception of HIT. We also note a low adoption rate of e-health platforms, suggesting that despite the development and promo-

Table 2. Patient consumption behavior for health information technology.

Patient Consumption Behavior for HIT	n (%)
Contacting physicians outside appointments	
Talk on the phone (landline, regular cell phone, or smart phone)	118 (74%)
Email	46 (29%)
Online patient communication portal	27 (17%)
Through the mail	17 (11%)
Other	5 (3%)
Utilization of patient portal access	
Uses the Drexel online patient portal usage (Follow my Health)	34 (21%)
Unfamiliarity with this particular patient portal	14 (9%)
Uses other electronic patient portals outside of Drexel	23 (14%)
Unfamiliarity with patient portals	9 (6%)
Internet access at home via mobile device or personal computer or laptop	129 (81%)
Utilization of electronic devices at least once a week	
Smartphone with internet access	120 (75%)
Traditional mobile device without internet access	32 (20%)
Landline phone	50 (31%)
Desktop Computer	41 (26%)
Laptop Computer	57 (36%)
Tablet	50 (31%)
Frequency of internet access for health purposes	
At least few times a week	33 (21%)
A few times a month	26 (16%)
Once a month	10 (6%)
Once every few months	29 (18%)
None	60 (38%)

tion e-communication, mobile health applications, and tele-health technologies, further effort is required to improve access to and comfort with HIT for rheumatology patients. Physician and patient education, intervention programs, and technology improvements should be explored to narrow this observed digital divide for rheumatology patients, inclusive of and tailored for low SES patient populations.

Table 3. Patient preferences for health information technology.

Patient Preference Categories for HIT	n (%)
Preference for contacting physicians electronically	
Very important or absolutely necessary	64 (40%)
Somewhat important but necessary	55 (34%)
Not important at all or don't care	39 (24%)
Preferred method of internet access	
Home Computer	71 (44%)
Outside Computer	13 (8%)
Mobile Device	102 (64%)
Tablet	37 (23%)
I don't go on to the internet regularly	27 (17%)
Importance of reviewing test results online	
Very important or absolutely necessary	79 (49%)
Somewhat important, but not necessary	47 (29%)
Not important at all or don't care	28 (18%)
Importance of learning more about health or tracking health online	
Very interested	60 (38%)
Somewhat interested	49 (31%)
Not very interested	18 (11%)
Not interested at all	32 (20%)

Disclosure: B. Youm, None; **A. Jayatilleke**, None.

Abstract Number: 1138

Estimation of Clinically Important Differences in Patient-Reported Outcomes Measurement Information System (PROMIS) Measures in Juvenile Myositis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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Background/Purpose: Juvenile myositis (JM) causes weakness, rashes, pain, and fatigue, thereby impacting health-related quality of life (HRQoL). Patient-Reported Outcomes Measurement Information System (PROMIS®) measures have undergone initial validation in JM, but clinical interpretability is limited. Estimates of clinically important differences (CIDs) have not yet been determined for PROMIS measures in JM. This study estimates CIDs of PROMIS fixed short forms in JM.

Table 1. Descriptive Statistics	
Diagnosis	n (%) / median (IQR)
Juvenile Dermatomyositis	71 (94.7)
Juvenile Polymyositis	1 (1.3)
Mixed Connective Tissue Disease	1 (1.3)
Overlap Syndrome	1 (1.3)
Autoimmune Necrotizing Myopathy	1 (1.3)
Female Gender	59 (78.7)
Race (White)	59 (78.7)
Age at Onset (years)	5.3 (3.6, 6.9)
Age at First Visit (years)	11.7 (8.1, 14.3)
Clinical Anchor Variables	
Physician's Global Assessment - Disease Activity	1.0 (0.0, 3.0)
Disease Activity Score (DAS) - Total	3.0 (0.0, 6.0)
DAS - Muscle	0.0 (0.0, 2.0)
DAS - Skin	1.5 (0.0, 5.0)
Childhood Myositis Assessment Scale (CMAS)	52 (47, 52)
Any Muscle Enzymes Elevated	22 (29.3)
Patient/Parent-Reported Outcomes	
PROMIS (child report)	
Anxiety	38.8 (33.5, 47.4)
Depression	35.2 (35.2, 50.9)
Fatigue	34.2 (30.3, 48.1)
Mobility	58.5 (46.9, 58.5)
Pain Interference	39.4 (34.0, 50.2)
Upper Extremity	56.7 (54.9, 56.7)
PROMIS (parent report)	
Anxiety	47.2 (34.6, 56.8)
Depression	42.2 (36.2, 54.6)
Fatigue	44.3 (34.1, 54.3)
Mobility	46.8 (39.9, 56.5)
Pain Interference	38.1 (37.8, 59.4)
Upper Extremity	54.8 (40.2, 54.8)
PedsQL-GC (child report)	
Total	90.2 (78.5, 97.8)
Physical	93.3 (81.2, 100.0)
Psychological	90.0 (80.0, 98.3)
Emotional	95.0 (81.2, 100.0)
Social	100.0 (85.0, 100.0)
PedsQL-GC (parent report)	
Total	83.7 (73.1, 95.7)
Physical	87.5 (75.0, 100.0)
Psychological	83.3 (72.9, 96.7)
Emotional	87.5 (70.0, 100.0)
Social	95.0 (75.0, 100.0)
PedsQL-RM (child report)	
Pain and Hurt	100.0 (81.2, 100.0)
Daily Activities	100.0 (100.0, 100.0)
Treatment	92.9 (67.9, 100.0)
Worry	91.7 (75.0, 100.0)
Communication	91.7 (75.0, 100.0)
PedsQL-RM (parent report)	
Pain and Hurt	87.5 (68.8, 100.0)
Daily Activities	100.0 (95.0, 100.0)
Treatment	78.6 (60.0, 100.0)
Worry	100.0 (79.2, 100.0)
Communication	91.7 (66.7, 100.0)

Table 1. Descriptive Statistics

Methods: JM patients (5-17 yo) and their parents were recruited at routine clinic visits. Clinical/demographic data were collected. Patients (8-17 yo) and parents (5-17 yo) completed PROMIS pediatric fixed short forms for Anxiety, Depressive Symptoms, Mobility, Upper Extremity Function, Fatigue, and Pain Interference domains. Distribution-based estimates (i.e. 0.5 standard deviation) of CIDs were calculated. Cross-sectional and longitudinal anchor-based estimation of CIDs was performed. Longitudinal anchor-based CID estimates (i.e. change in PROMIS score associated with change in anchor variable) were calculated for patient-parent dyads with data collected at 2

Table 2. Cross-Sectional Anchor-Based Clinically Important Differences (CIDs)

Child Report

PROMIS Measure	# CID Estimates	CID Range (min-max)	Effect Size (min-max)
Anxiety	6	6.2 - 12.1	0.53 - 1.0
Depression	7	7.1 - 12.6	0.67 - 1.2
Fatigue	7	5.9 - 17.6	0.49 - 1.4
Mobility	9	5.5 - 11.7	0.72-1.5
Pain Interference	6	7.6 - 16.0	0.73-1.5
Upper Extremity Function	1	12.5*	1.8*

Parent Report

PROMIS Measure	# CID Estimates	CID Range (min-max)	Effect Size (min-max)
Anxiety	7	5.8 - 14.0	0.46 - 1.1
Depression	7	5.7 - 12.4	0.54 - 1.2
Fatigue	14	3.9 - 17.3	0.32 - 1.4
Mobility	12	4.7 - 13.9	0.50 - 1.5
Pain Interference	7	5.9 - 13.8	0.53 - 1.2
Upper Extremity Function	11	5.9 - 14.8	0.6 - 1.5

*A single value, rather than a range, is provided if there is only one CID estimate for a given PROMIS measure.

Table 2. Cross-Sectional Anchor-Based Clinically Important Differences (CIDs)

Table 3. Longitudinal Anchor-Based Clinically Important Differences (CIDs)

*Child Report**

PROMIS Measure	# CID Estimates	CID Range (min-max)	Effect Size (min-max)
Anxiety	1	8.3**	0.73**
Depression	1	4.9**	0.49**
Fatigue	5	7.2 - 16.0	0.51 - 1.1
Mobility	5	6.1 - 14.3	0.57 - 1.33
Pain Interference	1	9.3**	1.0**

Parent Report

PROMIS Measure	# CID Estimates	CID Range (min-max)	Effect Size (min-max)
Anxiety	3	5.9 - 11.5	0.59 - 1.2
Depression	4	5.5 - 11.3	0.64 - 1.3
Fatigue	12	4.0 - 17.3	0.31 - 1.3
Mobility	13	4.6 - 12.4	0.45 - 1.2
Pain Interference	5	8.4 - 11.2	0.74 - 0.98
Upper Extremity Function	10	5.7 - 13.1	0.53 - 1.2

*Upper Extremity Function (child report) did not have any eligible longitudinal CID estimates.

**A single value, rather than a range, is provided if there is only one CID estimate for a given PROMIS measure.

Table 3. Longitudinal Anchor-Based Clinically Important Differences (CIDs)

study visits. Anchor variables collected at study visits included: Physician's Global Assessment of Disease Activity (PGA), muscle enzymes, Disease Activity Score Muscle and Skin Domains (MDAS, SDAS), Childhood Myositis Assessment Scale (CMAS), PedsQL Generic Core Scales (PedsQL-GC) and PedsQL Rheumatology Modules (PedsQL-RM). Anchor variables were grouped into clinically distinct categories based on published score cutoffs. Criteria for reporting anchor-based CID estimates included: 1) Spearman's correlation ≥0.3; 2) n ≥5 per clinically distinct anchor variable category; 3) effect size (i.e. Cohen's D) > 0.2. Differences in mean PROMIS scores across adjacent clinically distinct anchor variable categories were reported as CID estimates. Mean standard error of measurement (SEM) for each PROMIS domain served as the lower bound for CID estimates.

Results: Seventy-five patient-parent dyads enrolled, with descriptive data in Table 1. Mean SEM for PROMIS child report and parent report were respectively: Anxiety (4.7; 3.9), Depressive Symptoms (4.7; 4.5), Fatigue (4.6; 3.5), Mobility (5.3; 4.6), Pain Interference (4.4; 3.9), Upper Extremity Function (6.5; 5.7). Distribution-based PROMIS CID estimates ranged 3.4-6.1 and 4.7-6.3 for child report and parent report respectively. Cross-sectional anchor-based CID estimates are shown in Table 2. Longitudinal anchor-based CID estimates are presented in Table 3.

Conclusion: Our CID estimates enhance interpretability of PROMIS measures in JM by linking differences in PROMIS measures with relevant clinical and patient-reported anchors. CIDs can support the design and power calculations for future studies (e.g. clinical trials). Future multicenter studies should enhance precision and generalizability of CID estimates and assess differences in CIDs by disease status (e.g. high vs low disease activity).

Disclosure: M. Wolfe, None; **A. Robinson**, None; **J. Lai**, None; **T. Coles**, None; **E. Gray**, None; **R. Chang**, None; **D. Cella**, None; **K. Ardalan**, None.

Abstract Number: 1139

Primary Non-adherence in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Up to 50% of patients with systemic lupus erythematosus (SLE) are nonadherent to their medications, which increases the risk of renal failure and death (1). SLE is a particularly challenging disease because it primarily affects young, black women who are less likely to be insured, potentially making adherence more of a challenge. While some factors like depression, polypharmacy, low socioeconomic status, and education level may contribute to nonadherence, factors that can reliably predict nonadherence have not been thoroughly identified. We evaluated the rates of primary nonadherence (defined as patient not filling a medication at the pharmacy) in our population of patients with SLE. We also evaluated demographics and other variables that may be associated with primary nonadherence

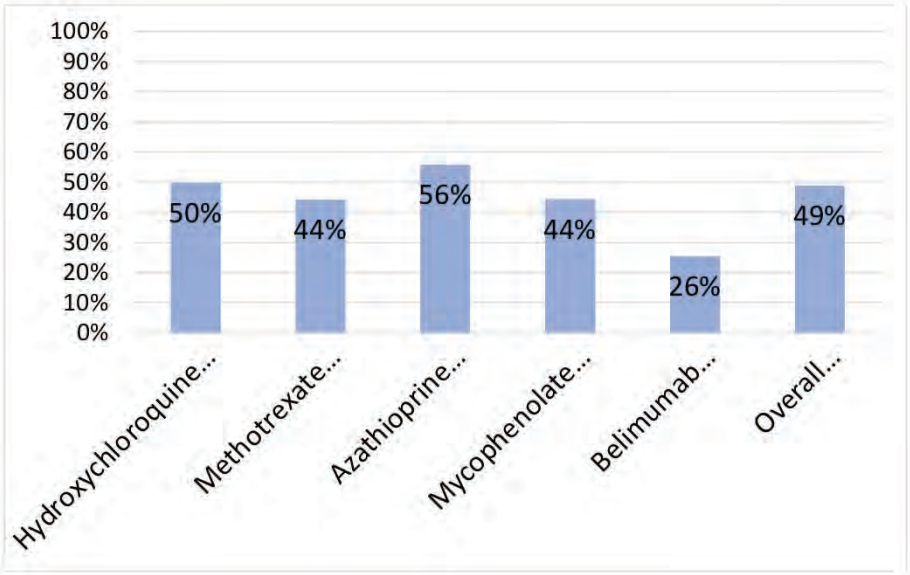
1. Feldman CH Arth and Rheum 2016 68(6): 1323-6

Methods: Prescription fill data and medication orders were extracted from the electronic medical record (EMR) between 1/1/2018 and 12/31/2018 for 181 patients who were enrolled in an SLE or pregnancy-rheumatology registries. Prescription fill data is automatically entered into the EMR through a vendor (Surescripts) that pulls this information from pharmacies and prescription benefit managers. Specifically, we evaluated 5 medications for adherence: hydroxychloroquine, methotrexate, azathioprine, mycophenolate mofetil and belimumab. We compared prescription fill data to medication orders during this time period and measured the percentage of medications that were filled within 30 days of a medication order or expected refill. We also calculated the medication possession ratio (MPR) during this time frame. We designated a patient as adherent if they had an MPR of Finally, we evaluated several demographic and patient variables that may serve as predictors of non-adherence.

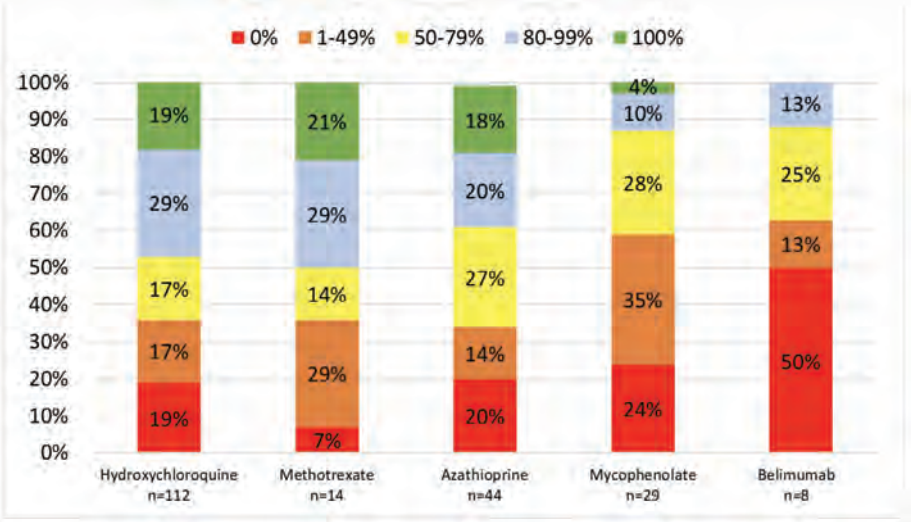
Characteristic	
Gender (Female)	174 (96.1%)
Age, median (quartiles)	36 (29 – 47)
Race	
Caucasian/White	56 (31.1)
Black or African American	105 (58.3)
Other	19 (10.6)
Missing	1
Hispanic	10 / 181 (5.5)
Education	
High school graduate/GED or less	18 (10.6%)
Some college but no degree	56 (33.1%)
College graduate and some graduate education	63 (37.3%)
Graduate education	32 (18.9%)
Missing	12
Income	
Up to $15,000	29 (18.6%)
$15,001 - $50,000	52 (33.3%)
$50,001 - $100,000	38 (24.4%)
$100,001 or more	37 (23.7%)
Missing	25
Insurance	
Government	78 (44.1%)
Commercial	99 (55.9%)
Missing	4
Marital Status	
Single, never married	50 (29.8%)
Living with partner	16 (9.5%)
Married	73 (43.5%)
Divorced	21 (12.5%)
Separated	5 (3.0%)
Widowed	3 (1.8%)
Number of concomitant medications, median (quartiles)	10 (6 – 16)
Registry	
Duke Autoimmunity in Pregnancy Registry	26 (14.4%)
Duke Lupus Registry	138 (76.2%)
Maternal Autoimmune Disease Research Alliance	17 (9.4%)

Characteristics of patients entered into analysis

Results: Study population characteristics are presented in Table 1. At total of 181 patients were evaluated. 49% of prescription orders were filled within 30 days (Figure 1). Azathioprine was filled most often (56%) while belimumab the least (26%). Only 40-50% of patients had an MPR of at least 80% to hydroxychloroquine, azathioprine and meth-



Medication fills within 30 days of order



Medication possession ratio

otrexate. Less than 15% had an MPR of 80% to mycophenolate mofetil and belimumab. When evaluating predictors of non-adherence only age (less than 30 years old) was a significant predictor of non-adherence to all prescribed medications. Additionally, Caucasian patients had greater adherence to all medications compared to those identified as “Black” or “other”. Gender, level of education, income, insurance type and marital status were not significant predictors.

Conclusion: By using a methodology that allows for data supplied by Surescripts to be easily and directly extracTable from an EMR, we were able to identify that nearly 50% of patients were non-adherent in terms of filling prescriptions at a pharmacy, particularly for mycophenolate mofetil and belimumab. This correlates with other studies of adherence (both primary and secondary) using different methodology. Specifically, younger, non-white patients may be at the largest risk for primary non-adherence and may serve as a target population for intervention.

Disclosure: A. Shah, Boehringer-Ingleheim, 2, Reata Inc., 2, Bristol-Myers Squibb, 2, Affinergy Inc, 2; **M. Clowse**, UCB, 5, GSK, 2, 5, Astra Zeneca, 5, Pfizer, 2; **D. Wojdyla**, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 2, Pfizer, 2.

Abstract Number: 1140

How Did SARS-CoV2/COVID-19 Pandemic Affected Patients with Rheumatic Diseases in Latin America? A Regional Survey from PANLAR

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Social isolation during SARS-CoV-2/COVID-19 pandemic has undermined follow-up of patients with rheumatic diseases. These patients face a critical dilemma between the risk of exposure as a vulnerable population and the need of medical attention. During previous pandemics, factors associated with differential behaviors have been identified, including lack of knowledge and perception of risk. Knowledge, attitudes, and behaviors studies are used to investigate patterns of community reactions to a disease. The aim of this study was to explore the knowledge, attitudes, and behaviors of patients with rheumatic diseases in Latin America during the COVID-19 pandemic.

Methods: We performed a cross-sectional observational study by means of a digital anonymous survey (RedCap®). We included patients over 18 years old from Spanish-speaking PANLAR countries with at least one rheumatic disease (self-reported). We retrieved demographics, comorbidities, rheumatic disease treatment, adherence and self-reported activity prior and during the pandemic, COVID-19 basic knowledge, diagnosis and risk perception, information sources, adherence to precaution measures, impact on daily living, attitudes and behaviors regarding telehealth. We calculated median and interquartile range for quantitative variables and frequencies and percentages for qualitative variables.

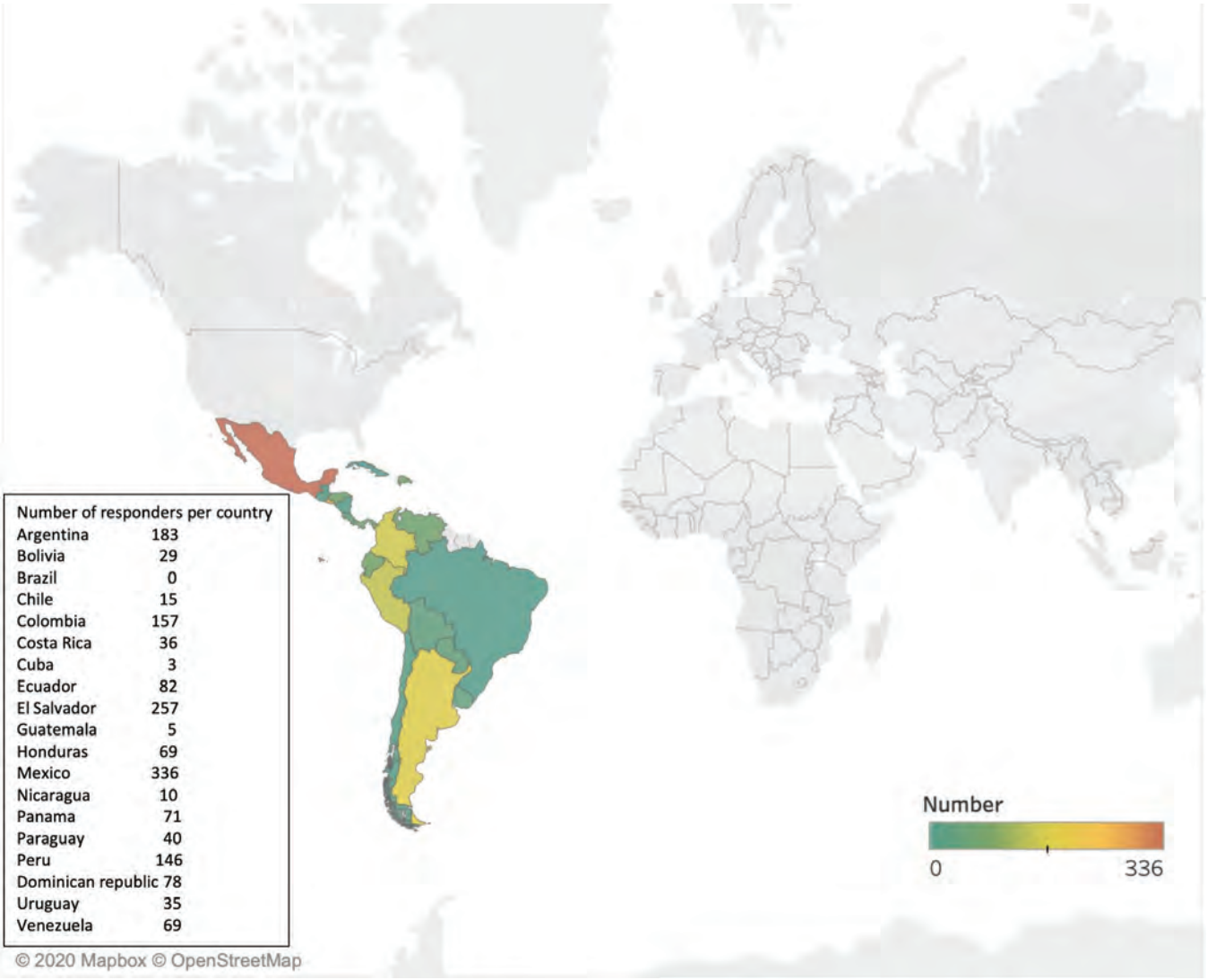

Figure 1. Number of patients filling the survey per country

Results: Our interim results include 1621 patients from 19 countries. The median age is 46 (37-56), most of them are women (92.4%). The most frequent rheumatic diseases were RA (54%) and SLE (26%). Self-reported disease activity increased during the pandemic (35% [8-60] vs 50% [13.5-70]). Twenty-seven (1.7%) responders were diagnosed with COVID-19. Twenty-three percent suspended at least 1 antirheumatic drug, particularly due to unavailability in pharmacies (34.7%); antimalarials were suspended by 22.2% of patients, mainly for the same reason (60.5%). Almost half reported that their follow-up appointments were cancelled and only 29% were offered an alternative. Twelve percent received telehealth, mainly via telephone (58%) and video call (34%), with a median satisfaction of 90% (62.5-100). Although 84% of responders consider telehealth as a valid strategy during the pandemic, this proportion reduces to 53.9% as a hypothetical alternative after the pandemic. An adequate knowledge on COVID-19 was found in 46%. The most frequent sources of information were television and social networks. Most patients reported a disruption in daily living due to social restrictions. Most responders reported an adequate adherence to general precautions.

Conclusion: Patients with rheumatic diseases in Latin America were negatively affected by the SARS-CoV2/COVID-19 pandemic. An increase in self-reported disease activity, a reduction in medication adherence and hurdles for medical follow-up were reported. Telehealth is perceived as a valid alternative to in-person consults during the pan-

Variable n (%)	n= 1621
Demographics	
Age in years (IQR)	46 (37-56)
Women	1498 (92.4)
Civil status	
Married	725 (44.7)
Single	575 (35.5)
Living with partner – not married	138 (8.5)
Widow	72 (4.4)
Other	111 (6.8)
Education	
Elementary	109 (6.7)
High school	360 (22.2)
Technician	218 (13.5)
Graduate	673 (41.5)
Postgraduate	183 (11.3)
Other	78 (4.8)
Occupation	
Student	59 (3.6)
Office (mostly intellectual)	235 (14.5)
Mostly manual chores	65 (4)
Both manual an intellectual	177 (10.9)
Health worker	180 (11.1)
Unemployed	254 (15.7)
Retired	235 (14.5)
Other	416 (25.7)
Children in charge (Yes)	831 (51.7)
Tobacco use	
Active	61 (3.9)
Previous	218 (13.8)
No tobacco use	1297 (82.3)
Most frequent self – reported rheumatic diseases	
Rheumatoid arthritis	877 (54.1)
Systemic lupus erythematosus	428 (26.4)
Sjögren's syndrome	164 (10.1)
Ankylosing spondylitis	62 (3.8)
Miscellaneous inflammatory arthritis	62 (3.8)
Median self-reported rheumatic disease activity (prior/during the pandemic, IQR)	35 (8-60) / 50 (13.5-70)
Patients that suspended at least one medication for rheumatic disease	372 (23)
Antimalarials	129 / 526 (24.5)
Comorbidities (at least one)	854 (54)
Most frequent comorbidities	
Hypertension	308 (19)
Depression/Anxiety disorder	189 (11.7)
Osteoporosis	105 (6.5)
Diabetes mellitus	90 (5.5)
Cardiac dysrhythmia	69 (4.3)
Rheumatology appointments	
Cancelled on self-choice	513 (31.6)
Were cancelled	719 (44.3)
Were offered an alternative	213 (29.6)
Accepted telehealth	200 (12.3)
Telephone call	116 (58)
Video call	69 (34.5)
Other	38 (19)
Home medical consultation	5 (2.5)
Median percentage of satisfaction (IQR)	90 (62.5-100)
Telehealth	
Agree is valid during the pandemic	1360 (84)
Agree is valid after the pandemic	874 (53.9)
Knowledge on COVID-19	
Adequate (modes of transmission, lethality, lack of treatment)	747 (46.1)
Source of information	
Television	1086 (67)
Social networks (Facebook, Twitter)	906 (55.9)
Official websites (CDC, WHO)	823 (50.8)
Health worker	501 (30.9)
Radio	273 (16.8)
Internet videos (Youtube)	262 (16.2)
Newspaper	241 (14.9)
Friends and family	251 (15.5)
Non-official websites	154 (9.5)
Other	38 (2.3)
Adherence to precaution measures	
Adequate (avoid public gatherings, use of face mask, frequent hand wash)	1566 (96.6)
Disruption of daily living	1350 (83.3)
High or very-high perceived risk of being infected with SARS-CoV-2/COVID19 during the pandemic (IQR)	
Self-risk	405 (25)
Family risk	283 (17.5)

Table 1. Demographics, attitudes and practices prior and during COVID-19 pandemic of patients in Spanish-speaking PANLAR countries.

demic. Attitudes and behaviors towards general precautions in this vulnerable population are reassuring. Our study is still ongoing and we present interim results; it is planned to collect data until July 31th, 2020.

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Abstract Number: 1141

Reversing Seasonal Decline of T2T Outcome in RA Patients Under Double Hits by Chinese New Year and COVID-19 Epidemic via Online Interaction with SSDM

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases

Session Type: Poster Session C

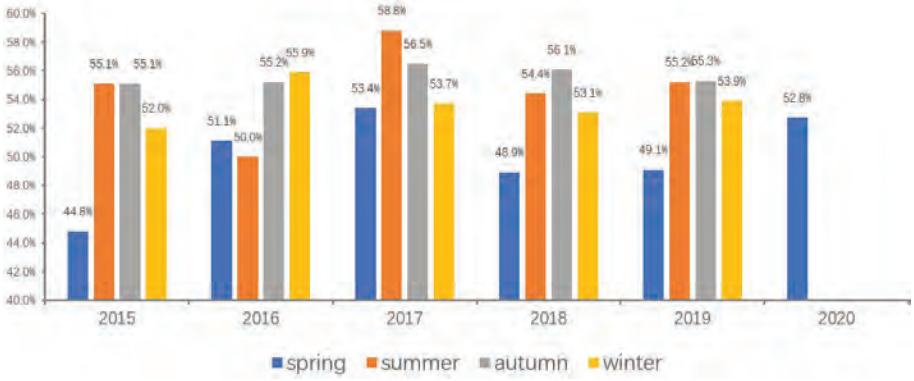
Session Time: 9:00AM–11:00AM

Background/Purpose: Treat-to-target (T2T), achieving a DAS28 below 3.2 is the main management strategy for RA. The Chinese New Year is a long holiday started in Jan. or Feb. based on the lunar calendar. Few clinics were available and most of the patients could returned to their hometown for over a month. The Chinese New Year of 2020 initiated at the end of January, which was overlapped with the quarantine of the COVID-19 epidemic. The whole country was locked down till late of April.

The purpose of this study was to evaluate T2T status of RA patients under double hits by long holiday and COVID-19 lockdown via the Smart System of Disease Management (SSDM).

Figure 1. T2T model of RA patients(monthly) 2015-2019 and 2020

Figure 2. The T2T rate of every season



Methods: SSDM is an interactive mobile disease management tool, including two application systems (APPs) for both doctors and patients. From Jun. 2014 to Jun. 2020, more than 180,000 patients with rheumatic diseases were trained to use SSDM. After executing DAS28 assessment, inputting treatment regiments and lab test records by patients themselves, all data can be synchronized automatically to the authorized physicians' tool. The doctors can practice online consultation and continue or adjust treatment regiments based on patients' profile.

Data were extracted from SSDM cloud to develop data analysis model by python software based on data mining since January 2015 to June 10, 2020, and monthly distribution models of the T2T rate were structured. Changes in SSDM online services such as consultation and refilling/adjusting medicines before and during the outbreak were evaluated. Calculations of the monthly average T2T from 2015 to 2019 in spring season, and comparations with the rate of the T2T rate in 2020 were performed.

Results: From June 2014 to June 2019, 56,546 adult RA patients (mean age was 51.35±14.13 years, and median disease duration was 45.97 months) performed self-assessment of DAS28 totally for 127,316 times via SSDM. The T2T rates were the lowest in the year during consecutive 3 months after Chinese New Year eve throughout 2015-2019. In 2020, the country was locked down on January 23, the New Year Eve. Compared with 2019, the T2T rates of RA patients increased significantly by 11.3%, 15.8%, 12.0% and 10.4% from January to April 2020, and was also significantly higher than monthly average rate in same period of 2016-2019. ($p < 0.01$) Fig 1.

During the COVID-19 epidemic, the interactions between doctors and patients via SSDM was increased significantly. SSDM data in holiday-epidemic season showed 628 rheumatologists from 277 hospitals provided 9,924 consultations for 6,041 RA patients. And 407 rheumatologists in 192 hospitals conducted 3,493 refilling/adjusting medications for 2,233 patients. Compared with 2019, the number of consultations has increased by 2.85 times, and the number of medication refill/adjustment had increased by 4.29 times.

Conclusion: The T2T rate of RA patients was lowest in every past Chinese New Year season. During the COVID-19 epidemic, the trend of decline at T2T rates were reversed by strengthen SSDM's online consultation and continued medication services. Through active interactions between rheumatologists and patients via SSDM, the outcomes were improved and the double hits of Chinese New Year-Epidemic turned out to be a happy accident for Chinese RA patients.

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Abstract Number: 1142

Implementation of an Evidence-based Transition Clinic in a Pediatric Rheumatology Academic Institution

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Transition from pediatric to adult rheumatology care is more likely to be successful if a transition program is in place. Previously successful interventions to improve transition outcomes have included integrating an adult subspecialist in the pediatric clinic setting. We hypothesize that we will improve transition outcomes by implementing a transition clinic which includes an adult rheumatologist providing care within a pediatric rheumatology clinic.

Methods: We initiated a weekly transition clinic in November 2018 called ACCORD (Adult Center for Childhood Onset Rheumatic Disease). This clinic is staffed by 1 adult rheumatologist (board certified in internal medicine and pediatrics), 2 pediatric nurses, and 2 research coordinators. Patients can be seen if they are ≥ 16 years old with known rheumatic disease or suspicion for rheumatic disease. All patients (and legal guardians) receive education and monitoring of transition readiness. We provide transition readiness education and feedback in 6 discrete modules adapted from Got Transition $_{Tm}$ (Table 1). All patients (and legal guardians) complete patient reported outcome measures (PRO's). We maximize continuity of care in several ways: our adult rheumatologist meets pediatric patients who anticipate transfer to the transition clinic, she manages all transition clinic visits and education, and when possible she migrates care to our institution's associated adult rheumatology clinic. Demographics, PRO's, transition readiness measures, and clinical outcomes are collected in a prospective longitudinal registry.

Results: 35 patients have now participated in our transition clinic and been enrolled in our registry (Table 2). 9 patients (25.7%) thus far have decided, with the adult rheumatologist, to attempt to transition to an adult provider. 1 of the 9 transitioned to a provider other than the adult rheumatologist. 8 of the 9 transitioned to the adult clinic of the adult rheumatologist. Of the 9, all have had at least one follow up appointment with their new adult provider. 5 of the 9 (55.6%) had gaps of ≤ 4 months between their last pediatric rheumatology clinic visit and their first adult rheumatology clinic visit. The longest gap between visits was 8 months. Of the 4 in whom subsequent follow up appointments have been indicated with their adult rheumatologist, all 4 have successfully kept these appointments on time. 1 of 35 (2.9%) has been lost to follow up (gap > 3 months past scheduled/recommended visit without subsequent successful contact).

Conclusion: Our unique transition clinic is in its early stages of development. However, this research shows that our interventions including a dedicated transition education and planning in the clinical setting as well as the integration of a Med/Peds trained adult rheumatologist can improve the chance of a successful clinical transition from pediatric to adult sub-specialty care.

Table 1. Transition Education and Research Metrics

Module	Target age	Patient materials and data*	Parent materials and data*
1	(12-14 yo)	• Introductory sheet (patient version) • Transition policy (one for patient)	• Introductory sheet (parent version) • Transition policy (one for parent)
2	(14-18 yo)	• Plan of care • **Transition readiness assessment (patient version)**	• **Transition readiness assessment (parent version)**
3	(14-18 yo)	• Medical summary and emergency care plan • Medication list	
4	(18-21 yo)	• "10 things to know" • **HAQ** • **Mind the Gap (patient)** • **PHQ 9** • **SF 36**	• **Mind the Gap (parent)**
5	(18-26 yo)	• Medical summary and emergency care plan • Medication list • Plan of care • **Transition readiness assessment (patient)**	• **Transition readiness assessment (parent)**
6	≤ 12 months following 1st adult rheumatology visit	• **Transition feedback survey (patient)** • **PROMIS Self-Efficacy Manage Medications and Treatments**	• **Transition feedback survey (parent)**

*Bold = research data collected

Table 2. Demographics of Transition Clinic *

	Sex		Mean Age (years)		Race					
	Male n (%)	*Female n (%)*	*Male/ Female*		*White n (%)*	*Black n (%)*	*Asian n (%)*	*American Indian or Alaskan Native n (%)*	*Native Hawaiian or Pacific Islander n (%)*	*Unknown/Not Reported/Other n (%)*	*Total*
Juvenile Idiopathic Arthritis or Rheumatoid Arthritis	4 (11.4)	19 (54.3)	22.1	19.7	17 (48.6)	1 (2.9)	1 (2.9)	0	1 (2.9)	3 (8.6)	23
SLE (or other CTD)	1 (2.9)	8 (22.9)	18.5	19.9	5 (14.3)	0	2 (5.7)	1 (2.9)	0	1 (2.9)	9
Other	0	3 (8.6)	N/A	18.4	3 (8.6)	0	0	0	0	0	3
Total											35

*All percentages are of entire cohort (n = 35)

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Abstract Number: 1143

The Influence of YouTube on Spreading Awareness and Patient Education Regarding Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases
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Session Time: 9:00AM–11:00AM

Background/Purpose: A large global survey released by the World Lupus Federation showed that the awareness of SLE is low and many individuals have never heard of the disease. Amongst the patients diagnosed with SLE, most of the patients were noted to have poor insight. Therefore, it is essential to have good patient education in order to improve the overall outcomes. Most of the patients with SLE are young and are known to use the internet as a source of information to learn about their disease. As of May 2020, YouTube is the most popular website with monthly traffic of 1.62 billion in the world. YouTube being the most popular website, we have analyzed the source, content, quality, and association between several variables of the videos.

Methods: We searched YouTube using the keywords Systemic Lupus Erythematosus. The resulting search feed of the top 100 videos was arranged in descending order of the number of views which was then analyzed. We included

Global Quality Score :
1.Definition (1 point):
Systemic lupus erythematosus (SLE) is a chronic autoimmune disease of unknown cause that can affect virtually any organ of the body
2.Etiology (2 points; 1 point for 1-3, 2 points for >4)
Autoimmune, Genetic, Environmental, Drugs, Hormonal, Infectious
3.Symptoms (3 points; 1 point for 1- 3 systems, 2 points for 4-6 systems, 3 points for >7 systems)
Constitutional symptoms, Dermatological and Mucosal, Musculoskeletal, Renal, Pulmonary, Neurologic symptom, Hematological, Gastrointestinal involvement, Gynecological involvement.
4.Diagnosis: (3 points;1 point for each of the following)
Signs and symptoms, Appropriate laboratory workup, Imaging, Histopathology
5.Disease complications(2 points; 1 point for each)
Medication toxicity, Related to disease process
6.Prognosis (Max 1 point)
Survival rate with and without treatment
7.Preventative interventions (Max 2 points, 1 point for 1-2, 2 points for >3)
Photoprotection, Lifestyle- diet, exercise, smoking cessation, Compliance with medications
8.Treatment (Max 3 points, 1 p, point for 1-2, 2 points for 3-4, 3 points for >4)
NSAIDs, Corticosteroids, DMARDS - Nonbiologic and Biologic, IVIG, Plasmapheresis.
Scoring system: Total: 17 points

Figure 1. Global Scoring System

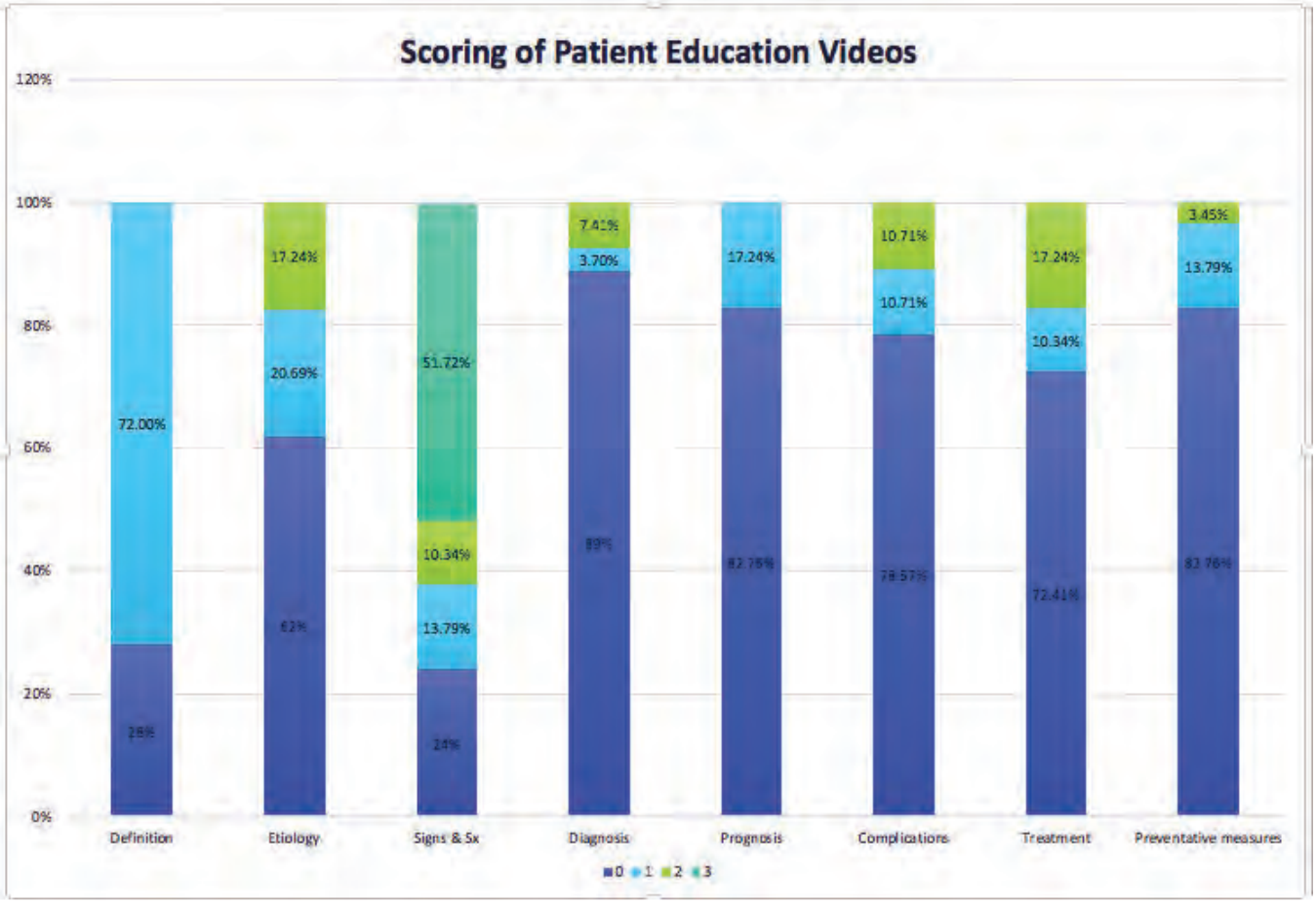

Figure 2. Scoring of Patient Education Videos

Video source	Mean	Standard Deviation	Minimum	Maximum
Healthcare Providers				
Number of Views	99873.36	249491.55	2302	1500000
Likes	901.12	2471.2	0	15000
Dislikes	25.58	47.4	0	270
Media				
Number of Views	151811.18	310125.27	7528	1292133
Likes	959.18	1883.13	0	7100
Dislikes	28.43	40.05	0	158
Patients				
Number of Views	13808.92	765058	5498	31704
Likes	207.38	163.35	14	556
Dislikes	5.23	4.51	0	14
Professional Societies				
Number of Views	64897.84	191243.05	2624	1040094
Likes	797.27	2760.88	7	15000
Dislikes	19.62	49.32	0	264

Figure 3. Video source and number of views, likes, and dislikes.

videos that are less than 30 minutes in length and only in the English language. These following variables and their combinations thereof were analyzed:-

1. Content of the video: Patient experience, Advertisement, Patient education, and Medical professional education
2. Source of the video: Professional Societies, Health care providers, Patients, and Media
3. Duration
4. The number of views likes and dislikes
5. Quality of patient education videos

The quality of these videos was rated using a Global Quality Score system(Figure 1) which is derived from the following- definition, etiology, signs and symptoms, diagnosis, prognosis, complications, and treatment measures. This scoring system has a minimum of 0 points and a maximum of 17 points. This statistical data were analyzed using the SAS system.

Results: The top 100 viewed videos were classified based on the content of the video. Medical professional education contributed to 46 videos(46%), whereas 29 videos (29%) were related to patient education and 20 videos (20%) were based on personal experience and 5% on advertisements. Of the 29 patient education videos analyzed 22 videos defined Systemic Lupus Erythematosus,11 videos out of 29 discussed etiology, 4 videos of 29 discussed the signs and symptoms, 5 videos of 29 discussed prognosis, 6 videos of 29 discussed the complications of the disease, 8 videos of 29 discussed treatment modalities and 3 videos of 29 discussed preventative measures. The results of the Global Scoring System is further analyzed in Figure 2. Further analysis regarding the association of the video source and Number of views, likes, and dislikes was made. Of all the video sources, media (tv shows, news, social media received the most number of views, likes, and dislikes. (Figure 3)

Conclusion: Based on the information obtained, these videos are very popular but a poor source of educating people regarding the disease. There is a clear need to increase the understanding and awareness of systemic lupus erythematosus and highlight the prognosis, treatment options, and preventative measures. Healthcare providers should emphasize the impact lupus has on people living with lupus and provide more insight into the disease and spread education materials and videos. We should also advise the patients to obtain information from reputed sources.

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Abstract Number: 1144

Concerns and Behaviors of Patients with Common Autoimmune Rheumatic Diseases in the United States Early in the COVID-19 Pandemic

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SESSION INFORMATION
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Background/Purpose: Patients with autoimmune rheumatic diseases may be particularly concerned about COVID-19. We aimed to assess concerns and associated health behaviors of patients with autoimmune rheumatic diseases during the COVID-19 pandemic and evaluate geographic differences within the United States.

Methods: Members of the ArthritisPower research registry and CreakyJoints patient community were invited to complete a baseline survey online with plans for follow-up surveys every 2 weeks for 8 weeks and then at 6 and 12 months. Reponses to the baseline surveys in adults from the United States with self-reported physician diagnoses of rheumatoid arthritis (RA), psoriatic arthritis (PsA), ankylosing spondylitis (AS), and systemic lupus erythematosus (SLE) were analyzed. Differences in patient concerns, avoidance of office visits and testing, use of telehealth, and interruptions in medications were assessed, comparing patients with different autoimmune conditions, immunosuppression use, and residing in different geographies, using zip code-based measures of income, education, rural residence, and COVID-19 activity. Patient concerns (5-point Likert scale) were compared with Kruskal-Wallis tests and other outcomes with univariate logistic regression.

Results: Among 1517 participants (925 RA, 299 PsA, 185 AS, 108 SLE) the mean age was 55.1, 88.3% were female, and 89.5% white (Table 1). 243 participants (13.9%) reported a respiratory illness but were not diagnosed with COVID-19, 47.9% of whom wanted to be tested but were not. 11 patients reported a physician diagnosis of COVID-19. Participants reported substantial concerns about COVID-19 and that their autoimmune disease affected these concerns, with greater concerns among those on biologics/Janus kinase inhibitors (JAKi) (both $p < 0.01$) (Figure 1). There were no significant differences in concern geographically (census bureau divisions) or in urban versus rural areas. Use of telemedicine (29.5%) and avoidance of doctor's office visits (56.6%), laboratory testing (42.3%), and other testing (36.0%) were more common in participants from urban areas and counties with more COVID-19 cases per capita (Table 2). Among participants on DMARDs who did not report a respiratory illness or COVID-19 diagnosis, 14.9% stopped one of their medications, more commonly those receiving biologics and with greater COVID-19 concerns (Table 2). Most medication interruptions (78.7%) were not recommended by a physician. Patients who reported that telemedicine was not available were more likely to stop medications (25.4% versus 13.1%, $p < 0.01$).

Conclusion: In the early months of the COVID-19 pandemic, patients with RA, PsA, AS, and SLE frequently avoided office visits and laboratory testing. Patient behavior was associated more with urban status and geographic variation

Table 1: Participant demographic and clinical characteristics

	No reported respiratory illness	Reported a respiratory illness but not COVID-19	Reported a physician diagnosis of COVID-19
Sample size, N	1,295	211	11
Age (years)	55.4 +/- 11.8	53.5 +/- 11.9	46.9 +/- 8.8
Female	1,140 (88.0%)	191 (90.5%)	9 (81.8%)
Caucasian	1,169 (90.3%)	179 (84.8%)	10 (90.9%)
Hispanic	60 (4.6%)	15 (7.1%)	0 (0.0%)
Rural	183/1,245 (14.1%)	31/198 (14.7%)	0/11 (0.0%)
County cases of COVID-19 per capita*			
Lowest tertile	421 (32.5%)	75 (35.5%)	1 (9.1%)
Middle tertile	560 (43.2%)	91 (43.1%)	3 (27.3%)
Highest tertile	259 (20.0%)	32 (15.2%)	7 (63.6%)
Autoimmune condition			
Rheumatoid arthritis	806 (62.2%)	113 (53.6%)	6 (54.5%)
Psoriatic arthritis	246 (19.0%)	52 (24.6%)	1 (9.1%)
Ankylosing spondylitis	158 (12.2%)	26 (12.3%)	1 (9.1%)
Systemic lupus erythematosus	85 (6.6%)	20 (9.5%)	3 (27.3%)
Medications			
Biologic DMARD	681 (52.6%)	99 (46.9%)	10 (90.9%)
JAKi	144 (11.1%)	14 (6.6%)	0 (0.0%)
Methotrexate	471 (36.4%)	62 (29.4%)	4 (36.4%)
Hydroxychloroquine	342 (26.4%)	58 (27.5%)	2 (18.2%)
Glucocorticoids	311 (24.0%)	57 (27.0%)	5 (45.5%)
NSAIDs	525 (40.5%)	96 (45.5%)	5 (45.5%)
SARS-CoV-2 Testing			
Tested for SARS-CoV-2	18 (1.4%)	26 (12.3%)	3 (27.3%)
Wanted testing but was not tested for SARS-CoV-2	308 (23.8%)	101 (47.9%)	7 (63.6%)

Number (%) and mean +/- standard deviation shown

*Cumulative COVID-19 cases per capita on the date the participants filled out the survey, divided into tertiles of activity in the United States over the time period of the study

DMARD: disease modifying anti-rheumatic drug; JAKi: Janus kinase inhibitor; NSAIDs: non-steroidal anti-inflammatory drugs

in COVID-19 activity than with measures of socioeconomic status. Participants often stopped medications without the advice of a physician, and medication interruptions were more common in participants without access to telehe alth.

Table 2: Impact of the COVID-19 pandemic on patient concerns and behavior

	N	Avoid going to the doctor's office	Avoid getting laboratory tests	Avoid other tests (e.g. x-ray)	Had a telehealth visit	Stopped medications**
All patients	1,517	858 (56.6%)	641 (42.3%)	546 (36.0%)	448 (29.5%)	169/1,132 (14.9%)
Rheumatoid arthritis	925	515 (55.7%)	377 (40.8%)	314 (33.9%)	263 (28.4%)	97/733 (13.2%)
Psoriatic arthritis	299	168 (56.2%)	124 (41.5%)	113 (37.8%)	95 (31.8%)	**41/213 (19.2%)***
Ankylosing spondylitis	185	104 (56.2%)	82 (44.3%)	68 (36.8%)	54 (29.2%)	22/115 (19.1%)
SLE	108	**71 (65.7%)***	**58 (53.7%)***	**51 (47.2%)***	36 (33.3%)	9/71 (12.7%)
No biologic/JAKi	569	344 (60.5%)	261 (45.9%)	207 (36.4%)	162 (28.5%)	33/307 (10.7%)
Biologic or JAKi	948	**514 (54.2%)***	**380 (40.1%)***	339 (35.8%)	286 (30.2%)	**136/825 (16.5%)***
Urban county	1,240	718 (57.9%)	543 (43.8%)	453 (36.5%)	381 (30.7%)	146/933 (15.6%)
Rural county	214	**108 (50.5%)***	**73 (34.1%)***	68 (31.8%)	**48 (22.4%)***	19/156 (12.2%)
Median household income of zip code						
Lowest tertile	274	147 (53.6%)	112 (40.9%)	105 (38.3%)	77 (28.1%)	35/200 (17.5%)
Middle tertile	483	273 (56.5%)	200 (41.4%)	152 (31.5%)	134 (27.7%)	**39/360 (10.8%)***
Highest tertile	703	410 (58.3%)	308 (43.8%)	267 (38.0%)	222 (31.6%)	92/533 (17.3%)
Education of zip code (% greater than high school)						
Lowest tertile	168	93 (55.4%)	73 (43.5%)	69 (41.1%)	51 (30.4%)	25/117 (21.4%)
Middle tertile	445	253 (56.9%)	189 (42.5%)	155 (34.8%)	117 (26.3%)	**44/328 (13.4%)***
Highest tertile	850	486 (57.2%)	359 (42.2%)	301 (35.4%)	265 (31.2%)	97/650 (14.9%)
County COVID-19 cases per capita						
Lowest tertile	497	268 (53.9%)	186 (37.4%)	173 (34.8%)	126 (25.4%)	49/370 (13.2%)
Middle tertile	654	376 (57.5%)	**283 (43.3%)***	216 (33.0%)	188 (28.7%)	75/486 (15.4%)
Highest tertile	298	179 (60.1%)	**144 (48.3%)***	**129 (43.3%)***	**112 (37.6%)***	40/228 (17.5%)
Concerned about COVID-19						
Not at all, slightly, or somewhat concerned	304	117 (38.5%)	86 (28.3%)	74 (24.3%)	78 (25.7%)	19/218 (8.7%)
Moderately or extremely concerned	1,213	**741 (61.1%)***	**555 (45.8%)***	**472 (38.9%)***	370 (30.5%)	**150/914 (16.4%)***

* $p < 0.05$ vs. the reference groups (rheumatoid arthritis, no biologic/JAKi, urban residence, lowest tertile of median household income, greater than high school education, or COVID-19 cases per capita) from univariate logistic regression models

** Proportion stopping medications is among patients who were on immunosuppression/immunomodulatory therapy and did not report a respiratory illness or diagnosis of COVID-19

SLE: systemic lupus erythematosus; JAKi: janus kinase inhibitor

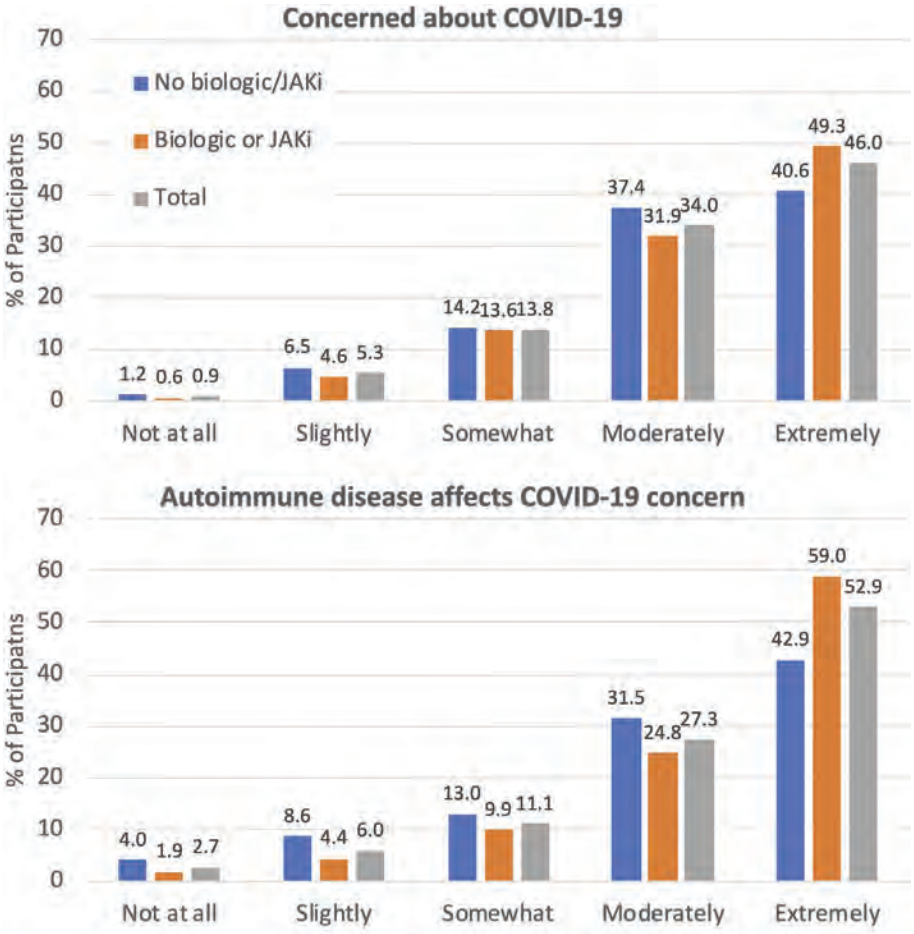

Figure 1: Participant concerns about COVID-19

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Abstract Number: 1145

Implementation of Web-Based Patient-Reported Outcome Measures (PROMs) in SLE Clinical Care: A Multi-Center Prospective Cohort Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases

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Session Time: 9:00AM–11:00AM

Background/Purpose: Patient-reported outcome measures (PROMs) are powerful tools which can highlight the patient experience of illness. Although PROMs are standard metrics in SLE clinical research, they are not routinely integrated in clinical care. Individuals with SLE are enthusiastic about the potential of PROMs to facilitate patient-centered care, but little is known about the utility and burden of implementing PROMs in SLE clinical encounters. The aim of this study was to assess the feasibility and impact of implementing web-based PROMs in the routine clinical care of outpatients with SLE.

Methods: Outpatients fulfilling 1997 ACR SLE classification criteria were enrolled in this longitudinal cohort study at two academic medical centers. Subjects completed PROMIS computerized adaptive tests at enrollment and prior to two consecutive routinely scheduled rheumatology visits using the ArthritisPower research registry mobile or web-based application. Score reports were shared with patients and providers before the visits. Patients and rheumatologists completed post-visit surveys evaluating the utility of PROMs in the clinical encounters.

Table 1. Characteristics of Participants

Patient Characteristics (n = 105)	**Value**
Age, median [25th, 75th percentiles] years	39 [32, 51]
Disease duration, median [25th, 75th percentiles] years	8 [4, 15]
Sex, n (%)	
Male	3 (2.9)
Female	102 (97.1)
Race, n (%)	
White	47 (44.8)
Black or African-American	25 (23.8)
Asian	16 (15.2)
More than one	9 (8.6)
Not Reported	8 (7.6)
Ethnicity, n (%)	
Hispanic or Latino	20 (19)
Insurance, n (%)	
Medicaid	25 (23.8)
Medicare	14 (13.3)
Commercial/private	64 (61.0)
None	2 (1.9)
Baseline SELENA-SLEDAI, mean [SD]	3.8 [3.8]
Baseline SLICC-ACR Damage Index, mean [SD]	1.1 [1.8]
Provider Characteristics (n = 16)	**Value**
Years in practice, median [25th, 75th percentiles]	5.5 [1.75, 15.75]
SLE patients seen/week, median [25th, 75th percentiles]	3.5 [3, 5]

SELENA-SLEDAI = Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index
SD = Standard deviation
SLICC-ACR Damage Index = Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index

Table 1. Characteristics of Participants

Table 2. Post-Visit Survey Results (n = 159 visits)

Question	"Yes" Patient Responses (n = 157)	"Yes" Physician Responses (n = 159)
Did you review PROM scores?	**73%** (95% CI 66, 80)	**92%** (95% CI 86, 96)
Were PROMs discussed during the visit?	**60%** (95% CI 52, 68)	**65%** (95% CI 57, 72)
Were PROMs useful?	**91%** (95% CI 85, 95)	**83%** (95% CI 76, 89)
Did PROMs help communication?	**86%** (95% CI 80, 91)	**72%** (95% CI 64, 79)
Did PROMs identify issues for discussion?	**44%** (95% CI 36, 52)	**36%** (95% CI 28, 44)
Did PROMs impact treatment plan/management?	**43%** (95% CI 35, 51)	**51%** (95% CI 43, 59)

PROM = Patient-reported outcome measure
CI = Confidence interval

Table 2. Benefits, Challenges, and Ideal Use of Patient-Reported Outcome Measures in Clinical Care

PROMs in 159 of 184 eligible encounters (86%, 95% CI 81 – 91) prior to study suspension due to the COVID-19 pandemic. Following baseline surveys, PROMs were completed for 90% (95% CI 82 – 95) of visit 1's and 82% (95% CI 72 – 90) of visit 2's. Nearly all PROMs (93%) were completed remotely. Patients and rheumatologists found that PROMs were useful (91% and 83% of encounters respectively) and improved communication (86% and 72%) (Table 2). Rheumatologists reported that PROMs impacted patient management in 51% of visits, primarily by guiding conversations (84%), but also by influencing medication changes (15%) and prompting referrals (10%). There was no statistically significant difference in visit length before (mean=19.5 minutes) and after (mean=20.4 minutes) implementation of PROMs (p=0.52).

Conclusion: The remote capture and subsequent integration of PROMs into clinical care was feasible in this diverse cohort of SLE outpatients. PROMs were useful to both patients and rheumatologists, promoting patient-centered care primarily by facilitating communication. The implementation of PROMs was not significantly associated with an increase in length of visits.

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Abstract Number: 1146

Pilot Study of an Internet-Based Pain Coping Skills Training Program for Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with Systemic Lupus Erythematosus (SLE) have increased symptoms of fatigue, chronic pain, depression and anxiety, which are associated with negative impacts on quality of life. Interventions that enhance the use and effectiveness of coping strategies may lead to better physical and psychological outcomes among patients with SLE. Pain coping skills training (PCST) programs have been shown to improve outcomes among patients with other rheumatic conditions, but there have been no trials of PCST among patients with SLE. This study was a preliminary assessment of the feasibility and efficacy of painTRAINER (formerly PainCOACH), an automated, internet-based PCST program, among patients with SLE.

Methods: Participants were 60 individuals with a diagnosis of SLE, identified from electronic medical records of one health care system. Participants were randomly assigned with equal allocation to painTRAINER or a wait list control group. PainTRAINER involves 8 modules; participants were instructed to complete one module weekly, along with practice activities for each cognitive or behavioral coping skill. Outcomes were assessed at baseline and 9-week follow-up, including the Pain Catastrophizing Scale, PROMIS Subscales (Pain Interference, Physical Function, Sleep Disturbance, Anxiety, Depression, Fatigue and Participation), and the LupusPRO quality of life questionnaire. Baseline characteristics and changes in outcomes from baseline to follow up (mean, standard deviation and Cohen's d effect sizes) were computed for painTRAINER and wait-list control groups.

Results: Participant characteristics are shown in Table 1. Among those randomized to the painTRAINER group, 53% accessed the program ("painTRAINER users"). Most of those who did not access the program stated that they did not receive instructions via email. Table 2 shows changes in study outcomes for the wait list and painTRAINER groups, as well as participants randomized to painTRAINER who did access the program. PainTRAINER users had a small decrease in Pain Catastrophizing (the tendency to ruminate about pain and feel helpless in dealing with it), while participants in the other groups had increases in scores. Participants in the painTRAINER group had greater improvement in PROMIS Pain Interference than the wait list group, with painTRAINER users having the greatest improvement. PainTRAINER users also had more favorable responses than the other groups with respect to PROMIS sleep disturbance, fatigue, and the LuposPRO Health-Related Quality of Life Score.

Table 1. Participant Characteristics

	Wait List (N=30)	painTRAINER (N=30)
Mean Age (SD)	47 (12)	51 (14)
% Female	93%	97%
% Caucasian	37%	33%
% With Some College Education	87%	77%
% Married / Living with Partner	50%	40%
% With "Adequate" Income	83%	70%
% Working	37%	23%

Table 1

Table 2. Mean Changes (SD), Follow-up minus Baseline, and Effect Sizes Compared to Wait List					
	Wait List (N=30)	painTRAINER (N=30)		painTRAINER Users (N=16)	
	Mean (SD) Change	Mean (SD) Change	Effect Size	Mean (SD) Change	Effect Size
Pain Catastrophizing†	3.6 (6.5)	2.3 (9.6)	-0.16	-0.4 (8.8)	-0.53
PROMIS Pain Interference†	-1.7 (790)	-2.6 (6.6)	-0.12	-4.2 (6.4)	-0.33
PROMIS Physical Function*	-0.6 (7.0)	-3.8 (4.1)	-0.56	-3.8 (4.4)	-0.51
PROMIS Participation*	0.5 (6.8)	0.7 (6.5)	0.03	1.0 (7.4)	0.08
PROMIS Sleep Disturbance†	0.4 (9.3)	0.6 (9.4)	0.02	-2.1 (7.5)	-0.27
PROMIS Anxiety†	0.4 (11.2)	1.4 (9.3)	0.09	0.2 (8.6)	-0.03
PROMIS Depression†	-0.6 (9.0)	-3.4 (8.6)	-0.32	-3.3 (5.8)	-0.34
PROMIS Fatigue†	-3.5 (7.1)	-2.2 (8.2)	0.17	-4.5 (6.4)	-0.14
LupusPRO Health-Related Quality of Life Score‡	1.4 (12.0)	2.0 (13.3)	0.04	4.8 (10.7)	0.29
LupusPRO Non-Health-Related Quality of Life Score§	3.7 (13.4)	3.9 (13.3)	0.02	2.9 (14.3)	-0.06
*Positive score indicates improvement; †Negative score indicates improvement; ‡Includes physical health, pain, symptoms, cognition, medications and procreation; §Includes satisfaction with care, coping, desires-goals, and social support					

Table 2

Conclusion: PainTRAINER users reported meaningful improvements in multiple physical and psychological outcomes, supporting the promise of this program for patients with SLE. Future research in a larger study needs to address tailoring of the content to patients with SLE and improved strategies for patient recruitment, engagement and retention.

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Abstract Number: 1147

Development of a Digital Toolkit to Improve Quality of Life of Patients with Systemic Lupus Erythematosus: A Pilot Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes Poster II: Miscellaneous Rheumatic Diseases

Session Type: Poster Session C

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Background/Purpose: Individuals living with systemic lupus erythematosus (SLE) face a number of challenges in managing their condition. Initial interviews and community forums with SLE patients suggested that unpredictability and variability of symptoms contribute to the erosion of formal and informal social support and highlighted the need for information and skills to adapt to symptom fluctuations. Patients suggested that digital tools may be particularly well suited to addressing these unmet needs because symptom unpredictability reduces the ability to reliably attend in-person interventions. The purpose of this project was to use patient-centered outcomes research (PCOR) and community-based participatory research (CBPR) principles of practice to engage stakeholders including SLE patients, patient advocacy organizations, and providers to prioritize unmet needs and to develop resources to address those needs.

Methods: Initial recommendations for content priorities and methods of delivery were developed through a series of stakeholder meetings (patients, health care providers, representatives from community-based organizations) and a mixed-methods survey of SLE patients evaluating internet usage and access. A clickable prototype of the digital toolkit was then developed incorporating priority content areas. Alpha (individuals with no affiliation with SLE clinic) and beta (patients and family members, health care providers, clinical staff) usability assessments of the clickable prototype were conducted through semi-structured interviews.

Results: Content areas identified as priorities included: nutrition, improving communication (family/friends and health care providers), physical activity, and self-management. Respondents provided a number of suggestions based on their review of our toolkit and experiences with existing SLE resources. Respondents emphasized the benefits of digital access to this content (website, smartphone application). Given the variability of SLE experiences, respondents desired the ability to regularly visit the platform, to receive tailored messages which would guide them to relevant information, and to conduct open searches of the material. Key suggestions for improving the platform included a sign-in for users to track activity, a live chat with SLE experts, a variety of static and dynamic virtual tools, and an ability to connect with other SLE patients.

Conclusion: Individuals living with SLE have dynamic needs that change over time. Digital platforms were identified by stakeholders as a viable way to respond to these dynamic needs since they can be easily accessed and tailored to individuals. Community-based/patient-centered approaches ensure that the perspectives of those who are affected most by a problem are included in intervention design.

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Abstract Number: 1148

The SHARE Recommendations on Diagnosis and Treatment of Systemic JIA

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

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Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) is a rare, complex auto-inflammatory disease with significant morbidity including fever, rash, serositis and articular problems. With the availability of interleukin-1 (IL-1) and IL-6 inhibitor treatment, morbidity has significantly reduced and the (long term) outcome for sJIA patients has improved over the last decade. However, differences in access to care and differences in treatment strategies between countries in and outside of Europe remain a concern.

The Single Hub and Access point for paediatric Rheumatology in Europe (SHARE) consortium aimed to develop best practices for paediatric rheumatic diseases in order to decrease differences in care between European countries. Here, we present the final results of the literature review and a series of consensus meetings on defining overarching, diagnostic and therapeutic recommendations for diagnosis and treatment of systemic JIA.

Methods: The SHARE methodology concerning consensus-based principles and guidelines has been previously published, including the use of the EULAR standardized operating procedure for developing best practice recommendations(1). As per these guidelines, a methodologist provided supervision during the process and consensus meetings.

A systematic literature search of the Medline, Embase and Cochrane databases was performed in June 2013 and this was updated in November 2019. Results were used to develop and support recommendations on diagnosis, treatment and complications of systemic JIA. These recommendations were pre-tested in an online survey to a task-force of expert paediatric rheumatologists to assess potential agreement and enable rewording. The participating experts convened in 3 consensus meetings (Genua 2014, Barcelona 2015 and Utrecht 2020) to develop the best practices.

Table 1	Principles for systemic juvenile idiopathic arthritis (sJIA)		
Overarching principles	**L**	**S**	**A (%)**
Systemic JIA is a systemic auto-inflammatory disease.	1B	B	96
Systemic JIA and Adult Onset Still's Disease (AOSD) represent a single disease entity with different age at onset.	5	D	100
In patients with suspicion of MAS, even without fulfilling the EULAR/ACR/PRINTO 2016 MAS classification criteria, MAS specific treatment should not be delayed.	3	B	100
Treating physicians should be aware of the rare risk of sJIA patients developing associated interstitial lung disease (sJIA-ILD).	4	C	100
Diagnostic principles			
Important differential diagnoses for sJIA include: infections, malignancies, vasculitides and other auto-inflammatory syndromes. If suspected, these diagnoses should be actively excluded by appropriate diagnostic procedures upon indication.	3-4	C	96
Arthritis can be an important feature but may not be present at the early stage of the disease.	3	C	91
Although several diagnostic biomarkers have been shown to be promising in case control and cohort studies, so far no single biomarker has been validated to help diagnosing sJIA with sufficient specificity and sensitivity.	2B-4	C-D	100
Treatment principles			
High-dose glucocorticoids are effective in sJIA, but their use is limited by glucocorticoid toxicity. Therefore their use and duration should be minimized where possible.	2B	B	100
IL-1 blocking agents (both anakinra and canakinumab) are an effective treatment option in glucocorticoid resistant or glucocorticoid dependent sJIA.	1	A	91
Anakinra is an effective treatment option early in the disease course of sJIA, including in glucocorticoid naïve patients.	3	C	96
Tocilizumab, an IL-6 blocking agent, is an effective treatment option in glucocorticoid resistant or glucocorticoid dependent sJIA.	1	A	96
Tocilizumab may prevent radiological damage of the joints in sJIA.	3	C	91
Methotrexate can be of some benefit in the treatment of arthritis in sJIA, but has no proven benefit in the treatment of systemic features.	1B	A	86
Overall, TNF blockade is of less benefit for the treatment of sJIA compared to IL-1 or IL-6 blockade, but may be useful for the treatment of some patients with persistent arthritis.	2	B	100
So far, no evidence-based recommendations can be made on how and when to stop biologicals for sJIA.	4	D	100

Making use of the Nominal Group Technique, recommendations were proposed, discussed and voted on. Recommendations that reached ≥80% were accepted in this guideline.

Results: The 2-step systematic literature review finally included 98 papers on sJIA. Quality and grade of evidence was assessed and a categorized overview was used as backbone and reference during the consensus meeting. In total, 15 recommendations were developed and accepted in the final consensus meeting: 4 overarching principles, 3 diagnostic recommendations and 8 recommendations on treatment of sJIA and its complications. Recommendations are presented with accompanying level of evidence (LoE), strength of recommendation (SoR) and percentage of agreement (PoA). In addition, adherence to the 2018 EULAR Treat-to-Target principles on JIA was confirmed by the expert panel.

Conclusion: These SHARE best practices on sJIA are based on the best available evidence and expert opinion, and provide recommendations for the diagnosis and treatment of patients with sJIA, aiming to improve the outcome for all sJIA patients in Europe and beyond.

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Abstract Number: 1149

Risk Score of Macrophage Activation Syndrome (MAS) in Patients with Systemic Juvenile Idiopathic Arthritis (sJIA)

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Macrophage Activation Syndrome (MAS) is a severe, life-threatening, complication of Systemic Juvenile Idiopathic Arthritis (sJIA) with a significant mortality. A score that identify sJIA patients with high risk to develop MAS would be useful in clinical practice.

Table 1. Laboratory parameters and cut-off used to create the MAS risk score in sJIA patients.

Laboratory parameters	Cut-off	Score
Ferritin (ng/ml)	>750	3.5
LDH (UI/L)	>540	2.5
AST (UI/l)	>30	2
Triglycerides (mg/dl)	>100	1.5

Table 2. Sensitivity, Specificity, Positive predictive value and Negative predictive value in the construction and validation cohorts.

	Construction cohort	Validation cohort
Sensitivity (Se)	96.4	81.3
Specificity (Sp)	80.5	60.0
Positive predictive value (PPV)	77.1	39.4
Negative predictive value (NPV)	97.1	90.9

Methods: We evaluated whether routine laboratory parameters at disease onset may predict the development of MAS in patients with sJIA and we defined a risk score of MAS using these parameters. Then, we validated the score in a second population. Laboratory parameters of disease activity and severity were retrospectively evaluated in 99 sJIA patients referred to Bambino Gesù Hospital in the last 10 years with at least 2 years of follow-up. Laboratory parameters were evaluated during active sJIA, without MAS, at disease onset or disease flare, immediately before treatment for sJIA was started or modified. Patients were divided in two groups: sJIA patients without MAS in the 2 years of follow-up and sJIA patients with at least one MAS episode. To create the MAS risk score, laboratory parameters with a statistically significant difference between the 2 groups were selected.

Results: Thirty patients, that fulfilled the 2016 classification criteria for MAS [1] at time of sampling, were excluded from the analysis. Therefore, we analysed laboratory parameters of 69 sJIA patients, 41 without MAS in the follow-up and 28 with at least one episode of MAS. Levels of ferritin, AST, LDH and triglycerides were significantly higher in patients with MAS during follow-up compared to those without. Their respective cut-off were computed by means of ROC curve analysis. A regression coefficient-based scoring system was used to assign weights to the risk index and the optimal score cut-off was defined by ROC curve analysis (Table 1). A MAS risk score ≥5 identified 27 out of 28 sJIA patients with MAS during the follow-up and 8 out of 41 sJIA patients without MAS. Sensitivity (Se), specificity (Sp), positive predictive value (PPV) and negative predictive value (NPV) of the score are detailed in Table 2. In order to validate the MAS risk score on a different population, we applied the score on 132 sJIA patients from other pediatric rheumatology centers, 100 without history of MAS and 32 with at least one episode of MAS. Se, Sp, PPV and NPV of the score are reported in Table 2.

Conclusion: In conclusion we developed a MAS risk score based on routine laboratory parameters, available worldwide, that can help clinicians to identify early in the disease course sJIA patients with high risk to develop MAS.

Reference:

1. Ravelli A et al. Ann Rheum Dis. 2016 Mar;75(3):481-9.

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Abstract Number: 1150

Traditional Laboratory Parameters and New Biomarkers in Macrophage Activation Syndrome and Secondary Hemophagocytic Lymphohistiocytosis

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

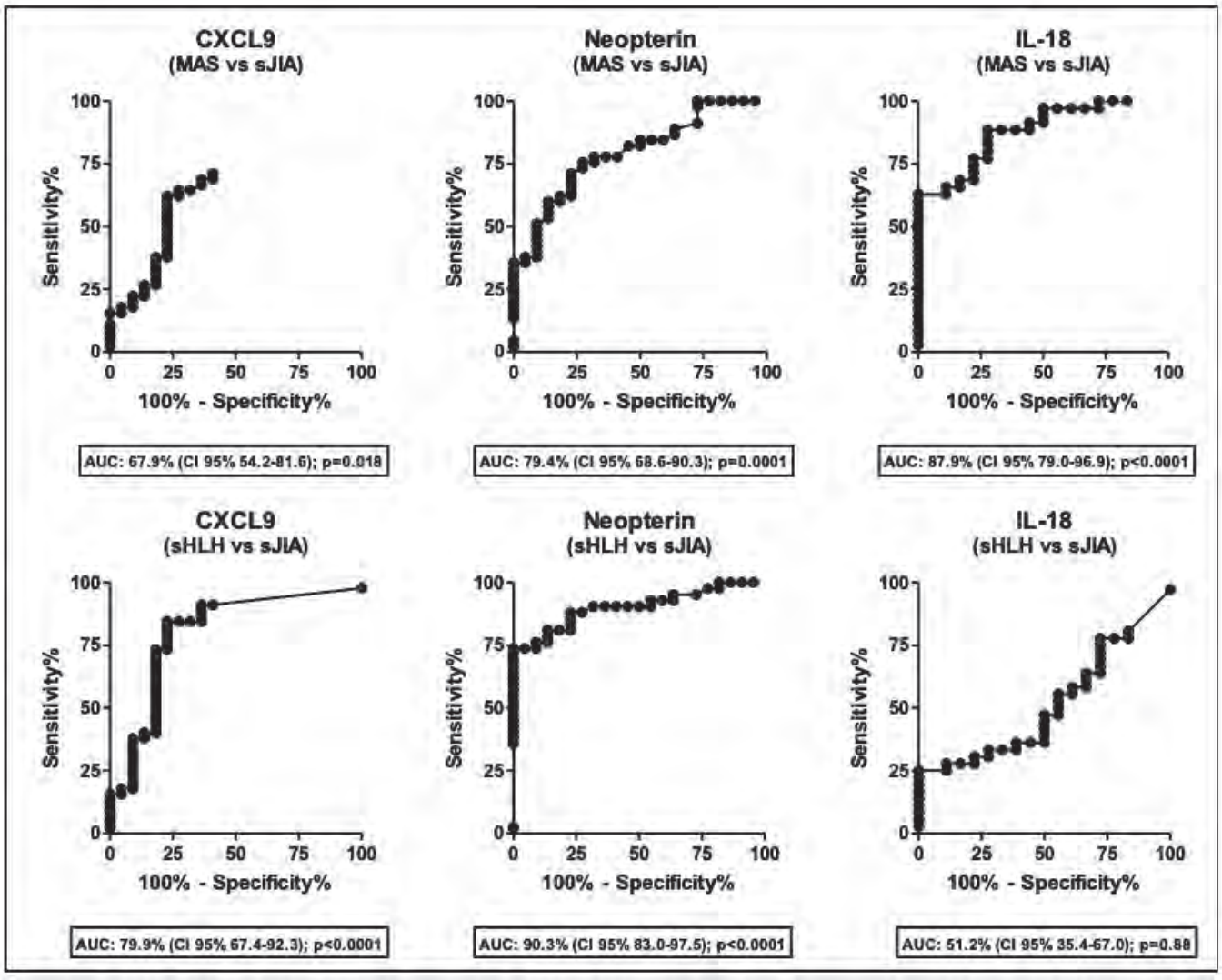
Background/Purpose: Macrophage Activation Syndrome (MAS) and secondary Hemophagocytic Lymphohistiocytosis (sHLH) are hyperinflammatory conditions caused by a cytokine storm, in which IFNγ plays a pivotal role. In this study we aimed to evaluate clinical characteristics of sHLH, MAS and systemic Juvenile Idiopathic Arthritis (sJIA) patients at disease onset. We compared laboratory parameters of hyperinflammation (platelet count, ferritin, AST, triglycerides, fibrinogen) and IFNγ related biomarkers in samples collected in three different time points: active disease (T0), 7-10 days from starting therapy (T1) and in clinical inactive disease (from 1 to 3 months from onset) (T2).

Methods: Routine laboratory parameters of disease activity and severity were collected from a cohort of 82 patients with sHLH (38), MAS in the context of sJIA (26), and sJIA (18) at T0, T1 and T2. Serum levels of the IFNγ related biomarkers (CXCL9, CXCL10, neopterin and IL-18) were measured at each time points by ELISA.

Results: A total of 306 samples were collected. Fever was present in the majority of patients (95%), while splenomegaly was more frequently in MAS (65%) and sHLH (63%) compared to sJIA (17%). Laboratory characteristics at T0 are detailed in Table 1. Using the 2016 classification criteria for MAS [1], we found that platelet count is a specific parameter, any patient with sJIA had a value < $181x10^9$/liter; while ferritin is a sensitive one, 94% of patients with MAS had ferritin > 684 mg/ml. CXCL9, CXCL10 and neopterin levels in T0 were significantly higher in MAS and in sHLH compared to sJIA, while IL-18 was significantly higher only in MAS group (Table 2). The ROC curves performed for each biomarker in MAS showed a statistically significant AUCs ($p< 0.05$). In sHLH the AUCs was significant for CXCL9, CXCL10 and Neopterin ($p< 0.0001$), while for IL-18 was not ($p= 0.9$) (Figure 1). In MAS CXCL9 and neopterin were significantly correlated to laboratory parameters of hyperinflammation as well as IL-18, except for ferritin. In sHLH only neopterin was significantly correlated to platelet count and triglycerides. CXCL9, CXCL10, neopterin and IL-18 levels progressively lowered at T1 and normalized in T2. CXCL9 decreased faster compared to neopterin, with a similar trend of laboratory parameters.

Conclusion: Our results confirme that platelet counts and ferritin have and high specificity and sensitivity, respectively, to diagnose MAS in the context of sJIA. Moreover, our results confirmed that IFNγ related biomarkers are significantly high in patients with MAS and sHLH and could be useful for diagnosis in addition to traditional laboratory

Figure 1. ROC curve of IFNγ related biomarkers at T0 in patients with MAS and sHLH.



parameters. CXCL9 seems to be more related to active disease, while neopterin seems to be more useful to follow the disease course. As already known, IL-18 is a specific biomarker for MAS.

Reference

1. Ravelli A et al. Ann Rheum Dis. 2016 Mar;75(3):481-9.

Table 1. Laboratory results of events in T0. [1]Number (%) - Chi-square test[C]/Fisher's exact test[F]; [2]Median (1st-3rd quartile) - Mann-Whitney U test

	sJIA	MAS	sHLH	*p-value*		
N. of samples	N=22	N=47	N= 45	MAS vs sJIA	MAS vs sHLH	sJIA vs sHLH
White blood cell count (x10^9/liter)[2]	13.20 (8.40-20.38)	11.32 (6.33-16.36)	3.90 (2.18-6.57)	0.20	**<0.0001**	**<0.0001**
Neutrophil count (x10^9/liter)[2]	9.97 (4.54-16.68)	8.13 (4.05-13.01)	2.03 (0.82-3.18)	0.34	**<0.0001**	**<0.0001**
Lymphocyte count (x10^9/liter)[2]	2.09 (1.53-3.65)	1.52 (1.16-2.11)	1.32 (0.47-2.39)	**0.0093**	0.24	**0.004**
Hemoglobin (g/dl)[2]	10.25 (9.60-11.30)	10.70 (9.50-11.50)	9.30 (8.10-10.70)	0.61	**0.0045**	**0.05**
Platelet count (x10^9/liter)[2]	454.5 (349.0-540.0)	237.0 (168.0-455.0)	95.0 (42.0-178.0)	**0.0010**	**<0.0001**	**<0.0001**
PLT <= 181x10^9/liter[1]	0 (0.0)	12 (25.5)	34 (50.8)	**0.007**	**<0.0001**	**<0.0001**
Ferritin (ng/ml)[2]	457.5 (323.0-738.0)	3143 (1473-5573)	5215 (2220-17271)	**<0.0001**	0.06	**<0.0001**
Ferritin >684[1]	7 (31.8)	44 (93.6)	48 (71.6)	**<0.0001**	0.71	**<0.0001**
AST (U/L)[2]	28 (19-43)	64 (39-114)	136 (51-324)	**<0.0001**	**0.003**	**<0.0001**
AST>48[1]	0 (0.0)	30 (63.8)	35 (52.2)	**<0.0001**	0.14	**<0.0001**
ALT (U/L)[2]	19 (11-49)	39 (17-141)	97 (29-275)	**0.0375**	**0.01**	**<0.0001**
LDH (U/L)[2]	474 (287-620)	1038 (679-1446)	1370 (757-2862)	**<0.0001**	0.1	**<0.0001**
Triglycerides (mg/dl)[2]	83.5 (67.0-104.0)	166.0 (136.0-216.0)	222.0 (159.0-367.0)	**<0.0001**	**0.04**	**<0.0001**
Trig > 156[1]	0 (0.0)	28 (59.6)	34 (50.8)	**<0.0001**	0.10	**<0.0001**
Fibrinogen (mg/dl)[2]	640.5 (492.0-696.0)	392.0 (251.0-583.0)	236.0 (137.0-317.0)	**0.0001**	**<0.0001**	**<0.0001**
Fibr <=360[1]	2 (9.1)	20 (42.6)	38 (56.7)	**0.005**	**<0.0001**	**<0.0001**
D-dimer (ng/ml)[2]	2.16 (1.03-5.82)	2.80 (1.79-5.62)	5.42 (2.83-17.3)	**0.24**	**0.03**	**0.01**
ESR (mm/h)[2]	53 (32-75)	40 (19-65)	28 (14-59)	0.15	0.30	0.06
CRP (mg/dl)[2]	10.27 (4.57-16.45)	6.31 (2.98-13.09)	3.39 (0.62-11.61)	0.12	0.08	**0.004**

Table 2. IFNγ related biomarkers at the onset of symptoms. * Number of samples (number of samples for IL-18).

	sJIA	MAS	sHLH	*P-value*		
	N*= 22 (18)	N*= 45 (35)	N*= 45 (35)	MAS vs sJIA	sJIA vs sHLH	MAS vs sHLH
CXCL9 (pg/ml)	300 (300-838)	1258 (300-6063)	4180 (1836-10038)	**0.0146**	**0.0001**	**0.01**
CXCL10 (pg/ml)	150 (150-269)	452 (150-1161)	717 (198-3048)	**0.0017**	**0.0001**	0.30
Neopterin (ng/ml)	3.93 (2.66-4.86)	8.74 (4.75-14.39)	23.1 (8.6-35.0)	**0.0001**	**<0.0001**	**0.001**
IL-18 (pg/ml)	17923.5 (2171.0-36764.0)	150577.0 (60667.0-219466.0)	14429.0 (2635.0-103022.0)	**<0.0001**	0.75	**<0.001**

Disclosure: A. De Matteis, None; **D. Pires Marafon**, None; **I. Caiello**, None; **M. Pardeo**, None; **G. Marucci**, None; **E. Sacco**, None; **G. Prencipe**, None; **F. De Benedetti**, Novartis, 2, 8, Novimmune, 2, 9, Sobi, 2, 8, 9, Roche, 2, 8, Pfizer, 2, Sanofi, 2, AbbVie, 8; **C. Bracaglia**, SOBI, 8.

Abstract Number: 1151

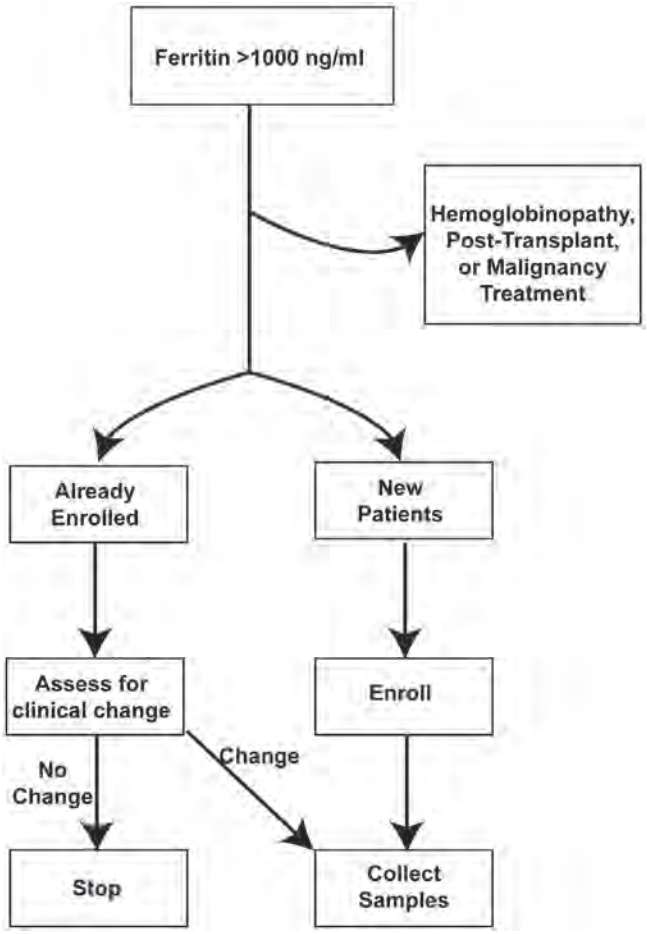
Implementation and Initial Experience with a Screening Protocol for Inflammatory Hyperferritinemia

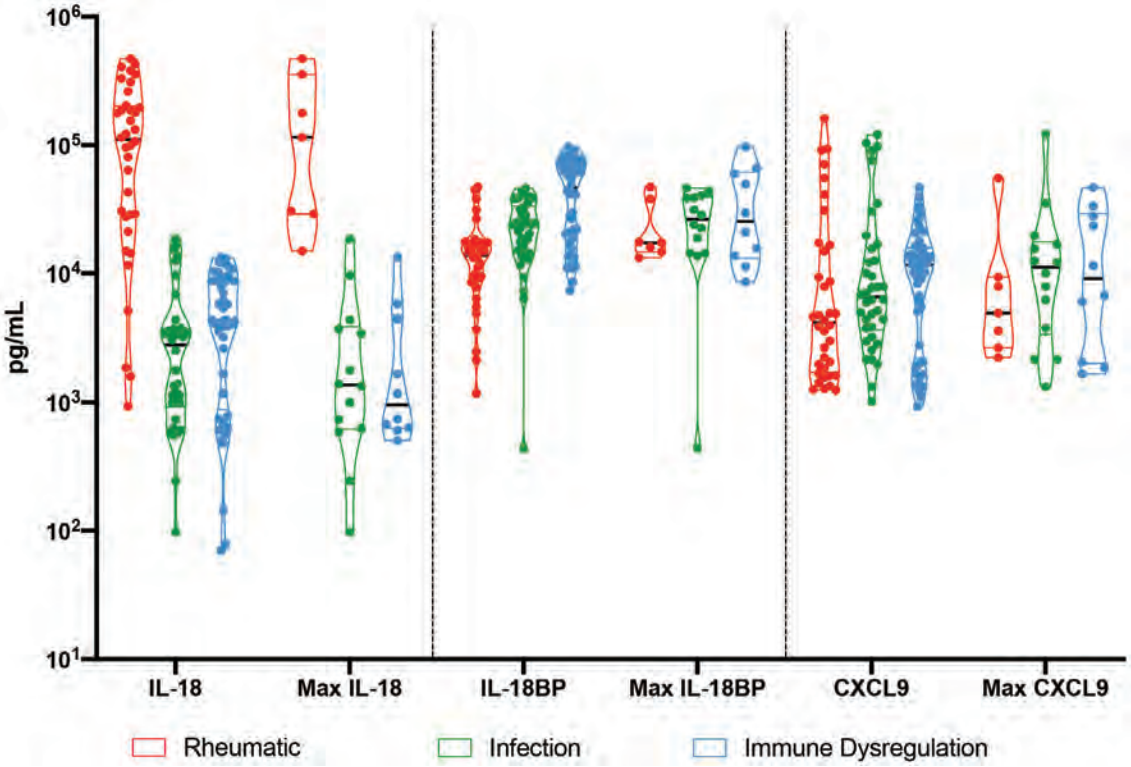
Michael Zhang[1], Corinne Schneider[2], Vinh Dang[2] and Scott Canna[3], [1]Children's Hospital UPMC, Pittsburgh, PA, [2]University of Pittsburgh, Pittsburgh, [3]University of PIttsburgh, Pittsburgh, PA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Macrophage activation syndrome (MAS) and hemophagocytic lymphohistiocytosis (HLH) epitomize a diverse and deadly group of inflammatory hyperferritinemic syndromes. Early biomarkers distinguishing these syndromes, especially those indicating specific treatments, are lacking.

Methods: .Between 6/2017 to 6/2019, we instituted a hyperferritinemic alert system for serum ferritin >1000ng/mL (Figure 1). Positive alerts were screened via real-time chart review and categorized into inflammatory hyperferritinemia, hemoglobinopathy (e.g. sickle cell disease), malignancy, post-transplant (solid organ and hematopoietic), and miscellaneous. The earliest available leftover serum samples from inflammatory hyperferritinemia alerts were set aside by and frozen in our clinical laboratory. Such patients were contacted for enrollment into an ongoing natural history protocol, and samples from patients able to be (or previously) enrolled were collected and tested. Longitudinal samples were obtained when possible focusing on changes in clinical status. Subsequently, we divided the inflammatory hyperferritinemia patients into infectious, rheumatic (all of whom were systemic JIA, or SJIA, during this period), or immune dysregulation. We extracted laboratory elements of MAS/HLH from enrolled patients' electronic medical record (AST, CRP, platelets) and measured IL-18, IL-18 binding protein (IL-18BP), and CXCL9 on stored samples. All procedures were approved by the University of Pittsburgh Institutional Review Board (STUDY20010099).


Ferritin >1000 ng/ml
Hemoglobinopathy, Post-Transplant, or Malignancy Treatment
Already Enrolled
New Patients
Assess for clinical change
Enroll
No Change
Change
Stop
Collect Samples


pg/mL
10^6
10^5
10^4
10^3
10^2
10^1
IL-18
Max IL-18
IL-18BP
Max IL-18BP
CXCL9
Max CXCL9
Rheumatic
Infection
Immune Dysregulation

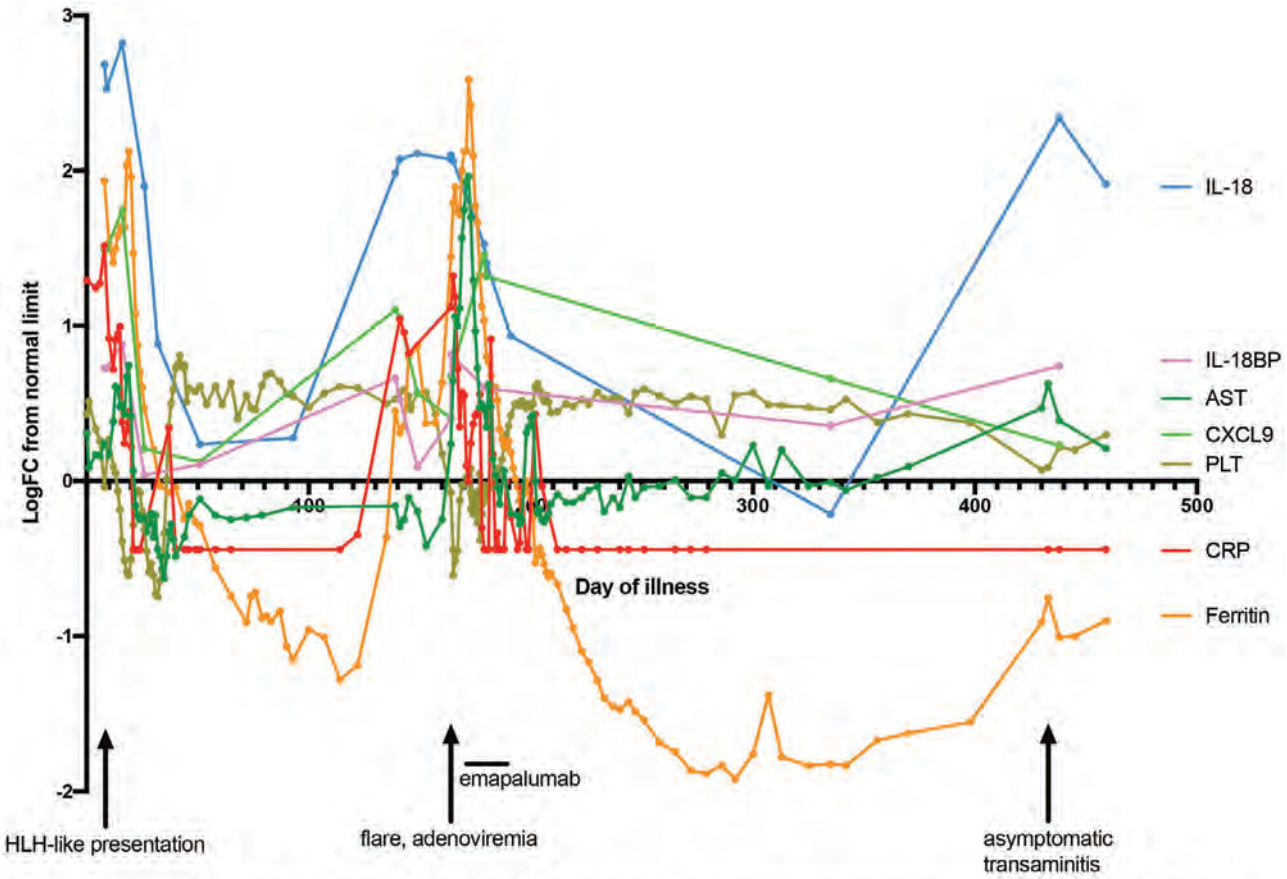


Figure 3: Course of a patient with mixed MAS/HLH picture. LogFC=Log10 Fold Change from normal limit: AST/55, Ferritin/300, PLT=Platelets/150, CRP/0.8, IL-18/540, IL-18BP/5000, CXCL9/1000.

Results: We screened 931 alerts from 180 unique patients. Inflammatory hyperferritinemia was adjudicated as the cause of 40.3% of screened ferritin levels from 30.5% of distinct patients. Maximum ferritin levels were higher in patients with inflammatory hyperferritinemia compared to hemoglobinopathies, malignancies, post-transplant, and miscellaneous diseases. Among the inflammatory hyperferritinemia group, the highest AST levels were observed in patients with "immune dysregulation", whereas maximum CRP levels were higher in infectious and SJIA-associated hyperinflammatory states. Platelets were less-consistently depressed in SJIA-associated hyperferritinemia. Consistent with previous findings, highly elevated IL-18 was uniquely observed in samples from patients with SJIA/MAS, whereas this group showed slightly less IL-18BP and CXCL9 elevation (Figure 2). Longitudinal analysis showed that IL-18 correlated with active or "smoldering" MAS activity (Figure 3).

Conclusion: Prospective screening based on hyperferritinemia is a feasible way to identify patients and collect early samples. Extremely elevated serum IL-18 was consistently observed in patients with SJIA, and improved pathophysiologic understanding in patients with unclear diagnoses (e.g. Figure 3). This protocol would be amenable to lower triggering thresholds and expanded biomarker screening to further optimize identification, diagnosis, and treatment of MAS/HLH and related diseases.

Disclosure: M. Zhang, None; **C. Schneider**, None; **V. Dang**, None; **S. Canna**, AB2Bio, Ltd, 2.

Abstract Number: 1152

IL-18: A Biomarker That Reflects Disease Activity, Could It Be the Next Disease Activity Measure in Systemic Juvenile Idiopathic Arthritis?

Shima Yasin[1], Thuy Do[2], Sanjeev Dhakal[2], Elizabeth Baker[2], Alexei Grom[3] and Grant Schulert[4], [1]Cincinnati Children's Hospital Medical Center, Liberty twp, OH, [2]Cincinnati Children's Hospital Medical Center, Cincinnati, [3]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [4]PRCSG, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

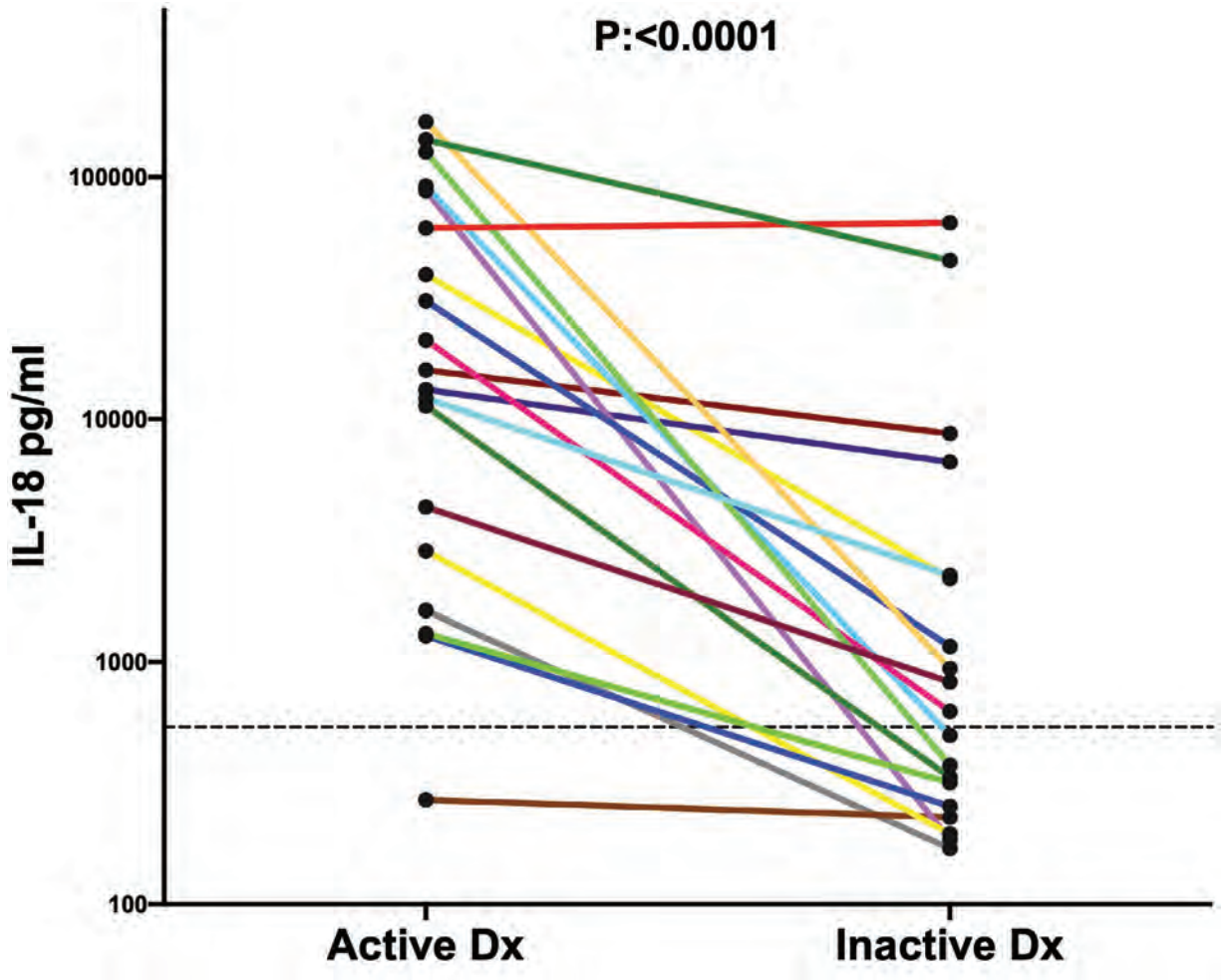


Figure 1: Total IL-18 levels for each individual patient at active disease and inactive disease status and different time points. Each line represents an individual patient. Horizontal dotted line represents upper limit of normal of total IL-18 (540 pg/ml).

Background/Purpose: Systemic juvenile idiopathic arthritis (sJIA) is a childhood arthritis with prominent innate immune activity. Disease presentation and flares could largely mimic infections with fever being a prominent feature. sJIA is associated with production of inflammatory cytokines including IL-18. IL-18 plays a key role in the pathogenies, with high levels in patients with active disease. To date, there are no specific reliable biomarkers for disease activity in sJIA. IL-18 may be a useful biomarker for diagnosis and more importantly monitoring disease activity and flares. Our objective is to quantify change in serum IL-18 levels in response to change in clinical disease activity in patients with sJIA.

Methods: This is a prospective longitudinal study. Serial serum levels of total IL-18 (pg/ml), CXCL9, and S100 proteins were obtained from 30 sJIA patients aged 1-19 at time of sampling. Clinical data was abstracted from medical records. Levels were compared within and between individual patients with regards to clinical and laboratory features. This study was approved by CCHMC Institutional Review Board, and informed consent was obtained.

Results: IL-18 was significantly higher in active disease (median 13279 pg/ml (IQR: 2496-61638), N=35) in comparison to clinically inactive disease (CID) (median 810 (326.5-4471), N=25). The median difference (12469 pg/ml) was statistically significant ($p < 0.0001$). IL-18 correlated with S100 A8/9 ($r=0.49$, $p=0.0008$) and CXCL9 ($r=0.55$, $p=0.0004$) regardless of clinical disease activity.

IL-18 was significantly different between patients with CID, active disease due to arthritis only, active disease due to systemic features only or active disease due to both ($p< 0.0001$). Post-hoc analysis showed that there is no difference between CID and active disease due to arthritis only ($p >0.999$). The difference was significant between those with systemic features only or systemic features combined with arthritis compared to CID ($p=0.0012$ and 0.0002, respectively). Also, IL-18 correlated strongly with systemic manifestation score of systemic JADAS ($r=0.67$, $p< 0.0001$).

19 patients had paired samples captured at both CID and active disease status, while 8 had samples at only active disease and 3 only at CID. Median time difference between samples for each patient was 10.5 months. Comparing paired samples, median difference in IL-18 was not significant (455.5 pg/ml, $p=0.855$). Interestingly however, median decline in IL-18 between paired samples of patients changing status from active to inactive approached 90% (median decrease 9963 pg/ml, $p< 0.0001$). The difference was minimal (343 pg/ml) and not significant with no status change ($p=0.7002$). For paired samples with changing disease status, IL-18 performed well with AUC of 84% ($p=0.0002$).

Conclusion: Capturing within individual changes, IL-18 drops significantly with disease control and decreased clinical disease activity, but change is minimal for those with unchanged activity. IL-18 is significantly higher in patients with systemically active disease. This report raises optimism about the use of IL-18 as a biomarker of disease activity change and to guide initiation, continuation, escalation and cessation of therapy.

Disclosure: S. Yasin, None; **T. Do**, None; **S. Dhakal**, None; **E. Baker**, None; **A. Grom**, Sobi, Novartis and AB2Bio, 5; **G. Schulert**, Novartis, 5, Sobi, 5.

Abstract Number: 1153

Trends in Timing of Biologic Use for Treatment of Systemic Juvenile Idiopathic Arthritis in the CARRA Registry

Ginger Janow[1], Timothy Beukelman[2], Yukiko Kimura[3], Rayfel Schneider[4], Shalini Mohan[5], Gail Rodich[6] and Mary Beth Son[7], [1]Joseph M. Sanzari Children's Hospital at Hackensack Meridian Health, Hackensack, NJ, [2]University of Alabama at Birmingham, Birmingham, AL, [3]Hackensack Meridian School of Medicine, Hackensack, NJ, [4]University of Toronto, The Hospital for Sick Children, Toronto, Canada, [5]Genentech, Inc., South San Francisco, CA, [6]Genentech, Mill Valley, CA, [7]Boston Children's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The treatment of systemic juvenile idiopathic arthritis (SJIA) has changed dramatically over the past decade, associated with overall improvement in functional outcomes. There may be an early "window of opportunity" where biologic therapies provide maximal benefit while decreasing morbidity associated with glucocorticoids (GC). The Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry has enrolled more than 10,000 patients with pediatric rheumatic diseases. Our aim was to (1) assess temporal trends in the timing of non-biologic and biologic medication use in the first year after diagnosis of SJIA with an emphasis on early initiation of biologics, and (2) determine if demographic factors impact timing of biologic introduction.

Methods: Patients with SJIA enrolled in the CARRA registry between 2015 and 2018 were included. Medication information was collected retrospectively for all patients at enrollment in the Registry and prospectively after enrollment. Patients with missing month of diagnosis or medication start date were excluded. Medications were grouped by mechanism of action, and temporal trends in medication class usage were assessed using frequencies. Timing of initiation of IL-1 inhibition (IL-1i) and IL-6 inhibition (IL-6i) were assessed by year of diagnosis. Patients were grouped into one of three categories: (1) initiated IL-1i or IL-6i in first 91 days, (2) initiated on day 92-364, and (3) no use in first year. Sub-analysis was performed looking at the timing of IL-1/6i initiation (0-3, 3-6, 6-12 months after diagnosis) was analyzed to determine if demographic factors contribute to timing of medication start.

Results: 561 patients were included in the analysis. There was an upward trend in IL-1/6i usage during the first year of treatment over time (Figure 1), with a concurrent decline in tumor necrosis factor inhibitor (TNFi) use. Nearly half of patients (46%) were treated with IL1/6i in the first 3 months and 59.4% were treated with IL-1/6i in the first year. Initiation of IL-1i and IL-6i in the first 91 days following diagnosis appears to have increased over time (Figure 2). No significant differences were found in timing of introduction of IL-1/6i based on age, sex, race, or median time from symptom onset to diagnosis. Timing of IL-1/6i introduction did not affect frequency of DMARD use in the first 12 months (Table 1).

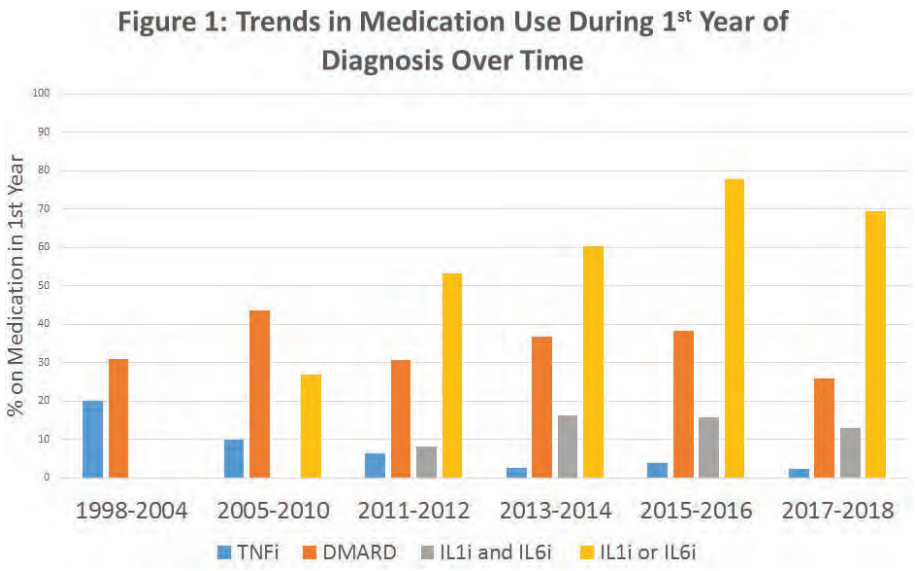


Fig 2: Timing of IL1i or IL6i initiation from 1998-2018

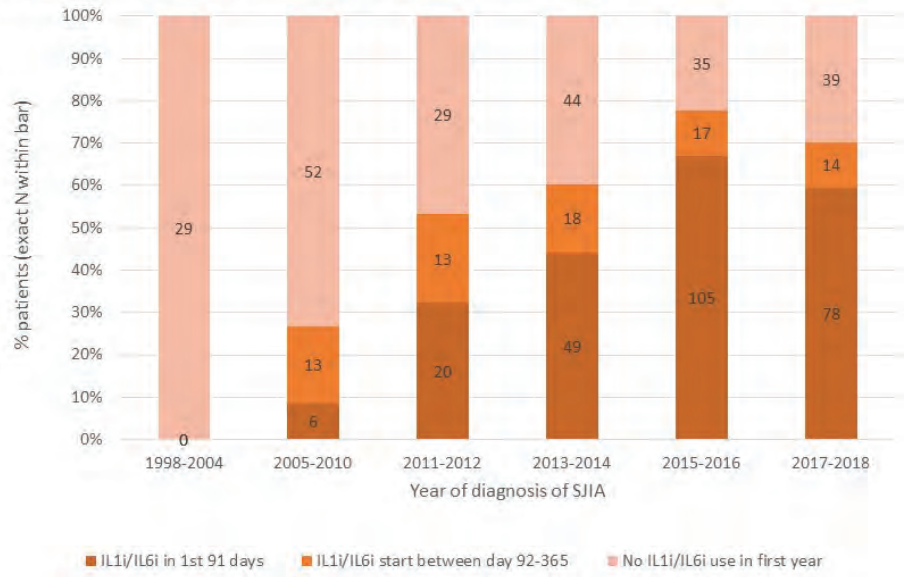


Table 1: Demographics by timing of IL-1 Inhibition or IL-6 Inhibition

	Entire Cohort	First IL-1 or IL-6 inhibition within 91 days after diagnosis	First IL-1 or IL-6 inhibition between 92-183 days after diagnosis	First IL-1 or IL-6 inhibition between 184-365 days after diagnosis	No IL-1 or IL-6 inhibition in first 365 days after diagnosis	p-value
N	561	258	36	39	228	
Sex (% female)	245 (43.7)	115 (44.6)	16 (44.4)	18 (46.2)	96 (42.1)	0.94
Age at diagnosis (median [IQR])	5.9 (4.26)	6.38 (4.5)	5.28 (4.6)	4.8 (4.1)	5.6 (3.9)	0.05
Race						
-White	379 (70.8)	187 (72.5)	26 (72.2)	27 (69.2)	157 (68.9)	0.84
-Black	79 (14.1)	34 (13.2)	4 (11.1)	5 (12.8)	36 (15.8)	0.79
-Hispanic	60 (10.7)	31 (12.0)	2 (5.6)	3 (7.7)	24 (10.5)	0.61
Average (SD) time from symptom onset to diagnosis (mean [SD])	117.5 (293.9)	83.1 (134.1)	130.5 (264.6)	127.5 (185.7)	152.6 (416)	0.08
Median (IQR) time from symptom onset to diagnosis	45 (22, 95.5)	37 (21, 83)	62.5 (26.8, 116.8)	48 (28.5, 132.5)	49.5 (21, 105.3)	0.09
Use of non-biologic DMARD in first 12 months	194 (34.6)	87 (33.7)	16 (44.4)	16 (41.0)	75 (32.9)	0.5

Conclusion: In SJIA patients in the CARRA Registry enrolled over a 3-year period, there has been an increase in IL-1/6i usage. Of those prescribed IL-1/6i, the majority began treatment in the first three months of disease. This does not appear to vary by age of diagnosis, time from symptom onset to diagnosis, race/ethnicity, or methotrexate use. Our data suggests that there may be an increase in "early" use of IL-1i and IL-6i, possibly due to increasing provider comfort, experience, and availability, as well as the perceived potential for a "window of opportunity" in treatment and desire to decrease GC use in these patients. Whether these changes result in improved disease outcomes requires further study.

Disclosure: G. Janow, None; **T. Beukelman**, Novartis, 5, UCB, 5; **Y. Kimura**, CARRA, 9, Up to Date, 7, Genentech, 2; **R. Schneider**, Novartis, 5, Sobi, 5, Novimmune, 5, Roche, 5; **S. Mohan**, Genentech, Inc, 1, 3; **G. Rodich**, Genentech, 3; **M. Son**, None.

Abstract Number: 1154

Distinct Gene Signature Predicts Strong Clinical Responses to Canakinumab in Children with Systemic Juvenile Idiopathic Arthritis

Emely Verweyen[1], Alex Pickering[2], Alexei Grom[3] and Grant Schulert[4], [1]Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [2]Harvard Medical School, Boston, MA, [3]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [4]PRCSG, Cincinnati Children's Hospital Medical Center, Cincinnati, OH

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Canakinumab is a human anti-IL1β blocking agent that effectively neutralizes IL1β mediated signaling and is used to treat diseases such as systemic juvenile idiopathic arthritis (sJIA). To date there is no predictive analysis that can identify patients that respond to canakinumab or those that do not respond, requiring alternative treatments. Here, we investigate and characterize a potentially predictive gene signature for treatment response to canakinumab in sJIA patients.

Methods: Whole blood gene expression of healthy controls and patients with sJIA during baseline (day 0, before treatment) and day 3 after treatment onset was previously measured by Affymetrix DNA microarrays [GEO:GSE80060]. Strong responders were based on the JIA American College of Rheumatology (aACR) response criteria and defined as >90, while non-responders were defined as < 30. A random effects model with patient identity as the random variable was used for differential expression analysis.

Results: We identified a distinct gene expression signature in patients with strong clinical response to canakinumab treatment vs non-responders. This signature was characterized by a severely dysregulated gene profile at baseline, and the degree of clinical response (ACR 90/100 vs 50/70 vs 30/0) correlated with upregulation of this signature. The gene profile of responders was mediated by significant (adj. P-val ≤0.05) upregulation of neutrophil and IL1β related genes, as well as Toll-like-receptor and inflammasome associated genes. In line with this, GO pathway analysis top upregulated pathway was ficolin-1-rich granule membrane (P-val 5.74E-13), representing neutrophil activation. Interestingly, while there was no direct upregulation of IL-6 or of IFNγ, SOCS3 was upregulated. Upon treatment initiation, early changes by day 3 in the gene expression profile of the responders were highlighted by significantly decreased expression of these above noted genes and pathways. Interestingly, CD163, a marker for polarization of haemophagocytic macrophages that is upregulated in sJIA-MAS (Macrophage activation syndrome) and sJIA-LD

(lung disease), was among the genes upregulated in non-responders, and was not affected by treatment, suggesting IL-1-independent gene pathways in these patients.

Conclusion: Here, we identify several genes and gene pathways whose expression levels distinguish high clinical responders to IL-1 blockade from non-responders before treatment onset. Further study is needed to assess this potentially valuable tool aiding treatment decisions in sJIA.

Disclosure: E. Verweyen, None; **A. Pickering**, None; **A. Grom**, Sobi, Novartis and AB2Bio, 5; **G. Schulert**, Novartis, 5, Sobi, 5.

Abstract Number: 1155

Long-term Safety Profile of Anakinra in Patients with Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the long-term safety profile of anakinra in patients with systemic juvenile idiopathic arthritis (sJIA)

Characteristics	Complete set	Long-term treatment set-12	Long-term treatment set-18	Long-term treatment set-24
N, (%)	**306**	**141 (46.1)**	**104 (34.0)**	**86 (28.1)**
Female, n (%)	154 (50.3)	60 (42.6)	45 (43.3)	37 (43.0)
Median age (years; q1,q3)	8.0 (4.0, 11.8)	8.5 (4.6, 11.9)	8.5 (4.9, 11.4)	8.5 (4.9, 11.1)
Infant (<2 years), n (%)	22 (7.2)	7 (5.0)	2 (1.9)	1 (1.2)
Child (2-<12 years), n (%)	210 (68.6)	100 (70.9)	81 (77.9)	68 (79.1)
Adolescent (12-<18 years), n (%)	69 (22.6)	31 (22.0)	19 (18.3)	16 (18.6)
Adult (≥ 18 years),n (%)	5 (1.6)	3 (2.1)	2 (1.9)	1 (1.2)
Time since sJIA onset (years), median (q1,q3)	0.6 (0.2, 2.2)	1.1 (0.4, 3.4)	1.5 (0.6, 4.3)	1.5 (0.6, 4.3)
Time since sJIA diagnosis (years), median (q1,q3)	0.3 (0.0, 1.9)	0.8 (0.1, 3.0)	1.1 (0.2, 3.8)	1.3 (0.2, 4.0)
Patients with prior history of MAS, n (%)	10 (3.3)	6 (4.2)	5 (4.8)	4 (4.6)

Table 1. Demographics of the study patient population.

Time window from anakinra start	1-6 months		7-12 months		13-18 months		19-24 months		>24 months		Overall	
N of patients	**306**		**194**		**144**		**106**		**104**		**306**	
Patient-time (years)	**117.3**		**80.2**		**58.1**		**47.0**		**206.7**		**509.3**	
System organ class	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
All	**71**	**23.2**	**19**	**9.8**	**11**	**7.6**	**5**	**4.7**	**20**	**19.2**	**99**	**32.4**
Infections and infestations	20	6.5	9	4.6	5	3.5	-	-	7	6.7	36	11.8
Skin and subcutaneous tissue disorders	17	5.6	3	1.5	1	0.7	-	-	3	2.9	23	7.5
General disorders and administration site conditions	15	4.9	3	1.5	1	0.7	1	0.9	2	1.9	21	6.9
Gastrointestinal disorders	11	3.6	1	0.5	-	-	1	0.9	3	2.9	16	5.2
Injury, poisoning and procedural complications	10	3.3	1	0.5	2	1.4	1	0.9	2	1.9	16	5.2
Immune system disorders	7	2.3	1	0.5	2	1.4	-	-	3	2.9	12	3.9
Investigations	6	2.0	1	0.5	-	-	-	-	1	1.0	7	2.3
Endocrine disorders	5	1.6	-	-	-	-	-	-	-	-	5	1.6
Blood and lymphatic system disorders	3	1.0	2	1.0	-	-	-	-	3	2.9	8	2.6
Hepatobiliary disorders	3	1.0	-	-	-	-	-	-	1	1.0	4	1.3
Metabolism and nutrition disorders	3	1.0	-	-	1	0.7	-	-	-	-	4	1.3
Nervous system disorders	2	0.7	-	-	-	-	3	2.8	-	-	4	1.3
Ear and labyrinth disorders	1	0.3	-	-	-	-	-	-	-	-	1	0.3
Musculoskeletal and connective tissue disorders	1	0.3	1	0.5	1	0.7	-	-	1	1.0	4	1.3
Renal and urinary disorders	1	0.3	-	-	-	-	1	0.9	-	-	2	0.7
Reproductive system and breast disorders	1	0.3	-	-	-	-	-	-	-	-	1	0.3
Respiratory, thoracic and mediastinal disorders	1	0.3	-	-	-	-	-	-	1	1.0	2	0.7
Surgical and medical procedures	1	0.3	-	-	-	-	-	-	1	1.0	2	0.7
Vascular disorders	1	0.3	-	-	-	-	-	-	-	-	1	0.3
Eye disorders	0	0	1	0.5	1	0.7	-	-	1	1.0	3	1.0

Table 2. Number of AEs and SAEs by time window.

All the study patient population	**N of MAS events**	306 (total number of patients)		
	MAS event	**n**	**Patient-time (years)**	**Rate (95% CI)**
	1st occurrence	11	497.5	2.2 (1.2-4.1)
	2nd occurrence	1	6.2	16.1 (2.6-97.7)
	3rd occurrence	0	5.6	0
History of MAS at baseline	**N of MAS events**	10		
	MAS event	**n**	**Patient-time (years)**	**Rate (95% CI)**
	1st occurrence	1	18.0	5.6 (0.7-42.9)
	2nd occurrence	1	1.0	100
	3rd occurrence	0	5.6	0
No History of MAS recorded at baseline	**N of MAS events**	296		
	MAS event	**n**	**Patient-time (years)**	**Rate (95% CI)**
	1st occurrence	10	479.5	2.1 (1.1-3.9)
	2nd occurrence	0	5.2	0
	3rd occurrence	0	-	-

Table 3. Overall MAS events and by history of MAS.

Methods: Data from patients with sJIA according to the ILAR classification criteria, treated with anakinra and enrolled in the Pharmachild registry before 30 September 2018 were analyzed (EUPAS28378). The study endpoints were: the occurrence of non-serious adverse events of at least moderate severity (AEs), serious AEs (SAEs), and events of special interest (ESI) including macrophage activation syndrome (MAS) according to MedDRA version 21.1; the duration of anakinra treatment and the reasons for discontinuation. All endpoints were analyzed overall and stratified by 6 months time windows.

Results: 306 patients were enrolled with both genders equally represented (Table 1). Almost half of the patients (n=146; 46%) were continuously treated with anakinra for at least 12 months, 34.0% for at least 18 months and 28.1% for at least 24 months. A total of 201 AEs was reported during a total of 509.3 patient years (py) of treatment with an overall incidence rate (IR) of 39.5 (95% CI 30.8-50.6) per 100 py , mostly represented by infections (52 events, 25.9%; IR 10.2/100 py). 56 SAEs were reported (IR 11.0/100 py; 95% CI 7.9-15.2), whereof 13 infections (23.2%; IR 2.6/100 py), and 11 MAS episodes (19.6%; IR 2.2/100 py).The proportion of patients experiencing AEs was highest during the first 6 months of treatment and did gradually decrease over time (Table 2). Ten patients (3.3%) had a history of MAS before anakinra start, 9 of these patients did not experience any new MAS episode after anakinra start. 8 patients developed MAS several months after anakinra discontinuation (Table 3). Discontinuation of treatment occurred at least once in 233 patients (76%), more often during the first 6 months, then decreasing over time, and was overall secondary to inefficacy (43%), remission (31%) or AEs and intolerance (15.0%). No deaths occurred during anakinra treatment while 3 deaths occurred after anakinra discontinuation (5 months, 3 years, and 5 years after discontinuation, respectively). No malignancies were reported neither during treatment with anakinra nor after discontinuation .

Conclusion: The results of the present study confirm the long-term safety profile of anakinra in sJIA patients without any new safety findings. Long-term treatment with anakinra in sJIA patients was well tolerated, with a decreasing overall incidence rate of AEs over time.

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Abstract Number: 1156

Comparison of Immunological Biomarkers and Lung Histology in Patients with Elevated IL18 - Pulmonary Alveolar Proteinosis and Recurrent Macrophage Activation Syndrome (IL-18PAP-MAS) and Other Inflammatory Lung Diseases

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Recently, pulmonary alveolar proteinosis (PAP) and recurrent macrophage activation syndrome (MAS) have been reported in rare patients (pts) with systemic juvenile idiopathic arthritis (SJIA) like disease. The pathomechanisms of lung disease remain elusive. We aimed to characterize genetic and immunological biomarkers IL-18PAP-MAS pts. We sought to understand pathophysiology by comparison of blood and lung biopsy markers to other inflammatory diseases.

Methods: Eight patients with IL-18PAP-MAS were enrolled in an IRB approved protocol (NCT02974595). Serum (n=8), whole blood RNA (n=8) bronchoalveolar lavage (BAL, n=2) samples and lung biopsies (n=3) from IL-18PAP-MAS pts were compared to samples from pts with NLRC4-MAS (n=4), Interferon (IFN) mediated diseases (n=10), including pts with STING associated vasculopathy with onset in infancy (SAVI, n=7), neonatal onset multisystem inflammatory disease (NOMID, n=4), sarcoidosis (n=10) and healthy controls (HC, n=3). Cytokines were measured by Luminex assay in serum and BAL, *CXCL9* and *CXCL10* transcript levels were quantified by Nanostring. Lung biopsies were scored for inflammatory features, including cell infiltrate, lymphoid aggregates, type 2 pneumocyte hyperplasia and cholesterol crystals and damage (emphysema, consolidation, vascular damage, fibrosis, neovascularization, thrombosis). Radiographs were scored by one radiologist.

Results: Of 8 pts with IL-18PAP-MAS and nail clubbing, 2 pts (25%) met the ILAR SJIA criteria. All patients had high elevation of serum IL-18 levels similar to patients with NLRC4-MAS. *CXCL9* and *CXCL9*/*CXCL10* ratio (IFN gamma response markers) were higher in IL-18PAP-MAS compared to interferonopathy and controls (Fig.1A). BAL fluid from IL-18PAP-MAS pts had higher expression of IL-18 and free IL-18, which were solely detected in IL18 PAP-MAS in contrast to SAVI and sarcoidosis (Fig.1B). Histologic features showed innate immune cells including high expression of neutrophils, histiocytes and alveolar macrophages with fewer lymphocytes and B cell infiltrates compared to SAVI, and low numbers of parenchymal and peribronchial lymphoid aggregates (Fig.2A). Cholesterol clefts and mucous plugging were cardinal features in IL18 PAP-MAS (Fig.2B). Distinctive radiological features suggestive of active in-

Figure 1

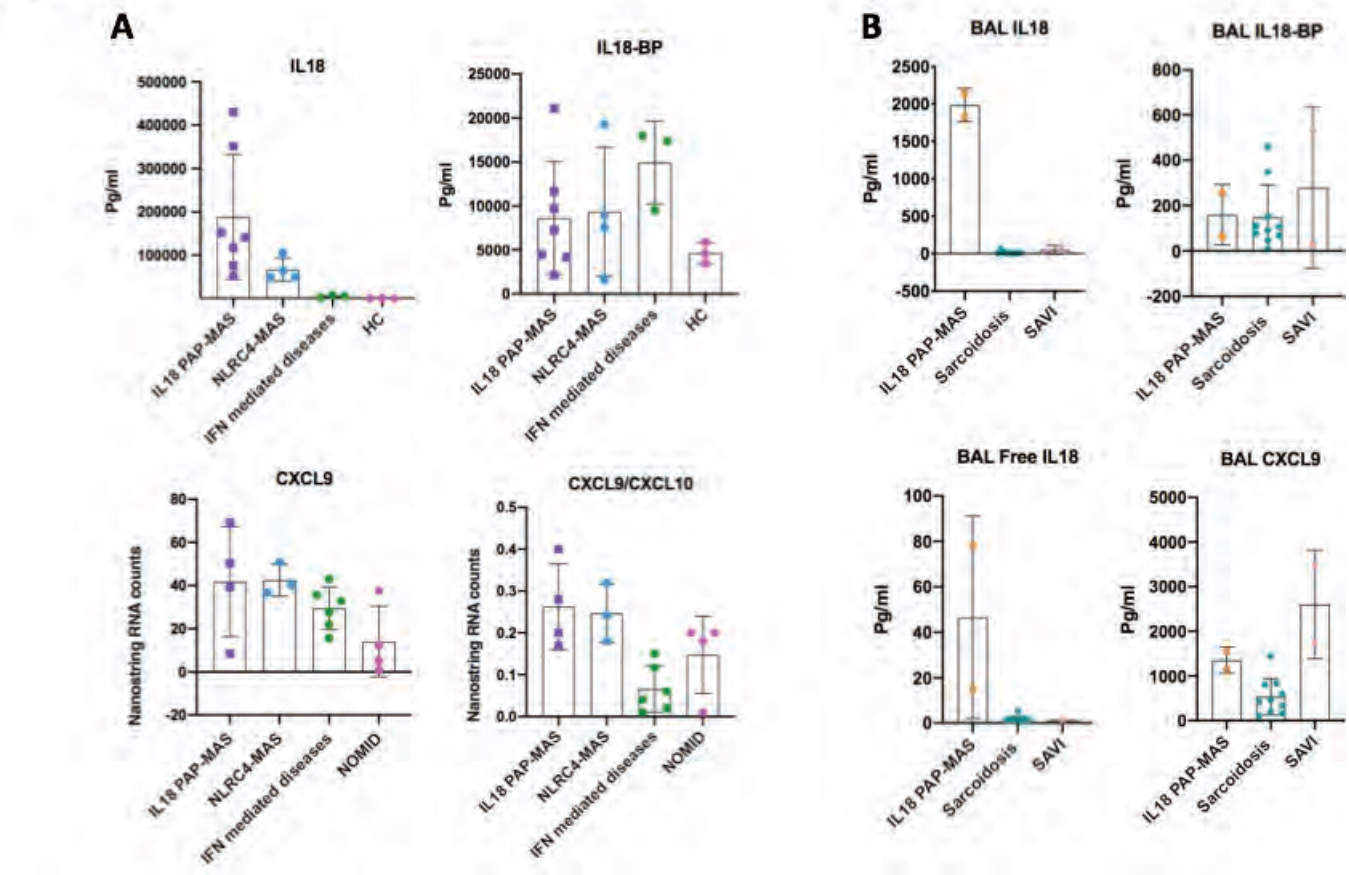

Figure 1. Assessment of total IL18, IL18-BP, CXCL9 and CXCL9/CXCL10 ratio (Higher ratio likely indicate IFN gamma response). A. Serum (upper panel) and whole blood RNA (lower panel) and B. BAL (bronchoalveolar lavage).

flammation included consolidation most prominent in the lower lobes, intralobular septal thickening, and pulmonary nodules, with higher inflammatory vs damage scores in contrast to SAVI (Fig. 3A, B).

Conclusion: IL-18PAP-MAS/SJIA like lung disease is a recently characterized, not yet genetically defined clinical syndrome. Histological pulmonary features of IL18 PAP-MAS differ from lung manifestations of SAVI and sarcoidosis, which includes recruitment of innate immune cells, predominantly neutrophils and alveolar macrophages. BAL fluid shows high expression of total and free IL-18 compartmentalized in the BAL of IL-18 PAP-MAS but not in SAVI and sarcoidosis pts suggesting a role of free IL-18 in the distinct pathogenesis of PAP in IL-18PAP-MAS.

Funding: This work was supported by the NIH IRP of NIAID

Figure 2

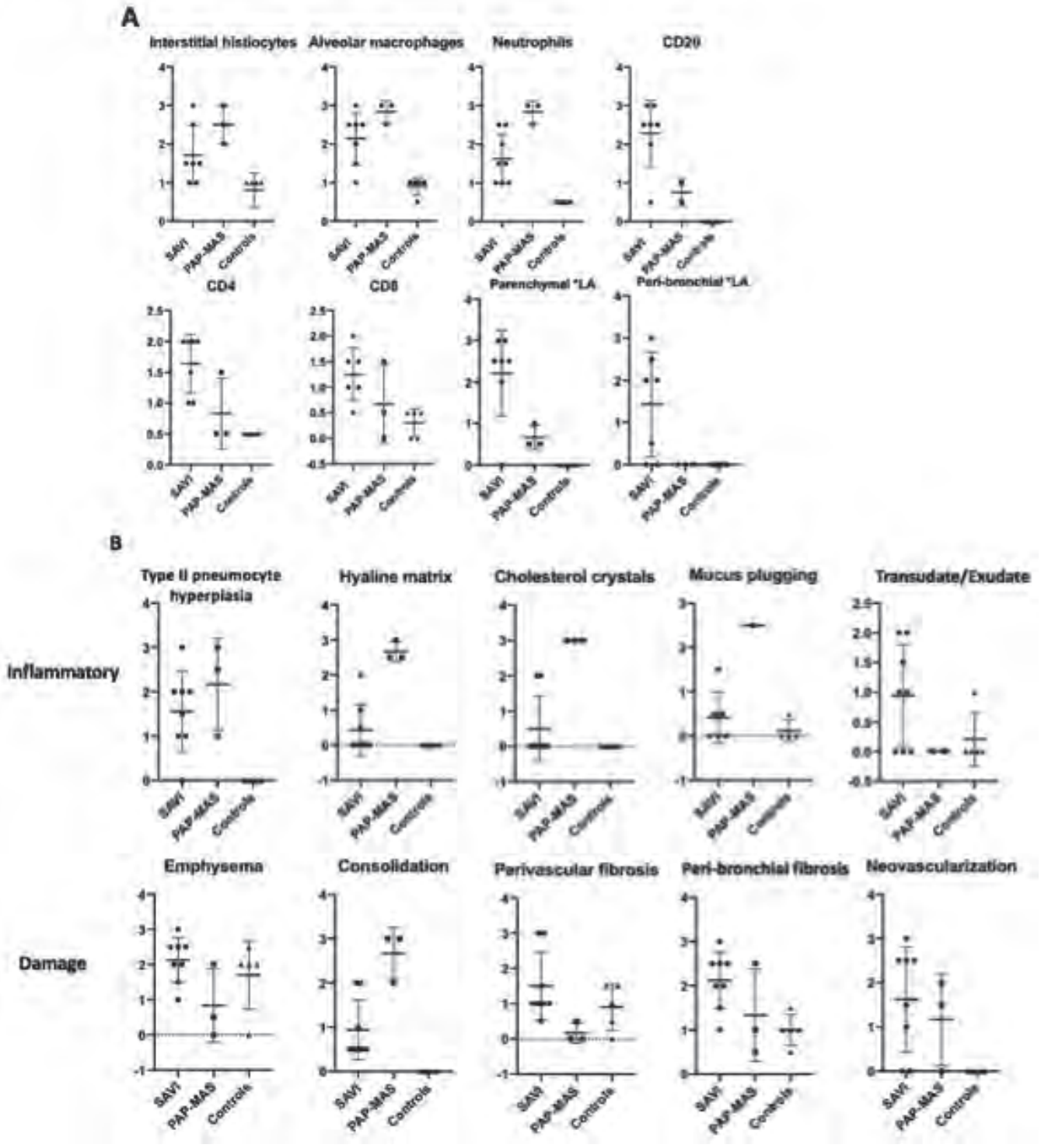

Figure 2. A. Cellular infiltrates in lung biopsies of IL-18PAP-MAS vs. SAVI and normal controls. B. Comparison of histological features in IL-18PAP-MAS and SAVI. * LA: Lymphocyte aggregate.

Figure 3

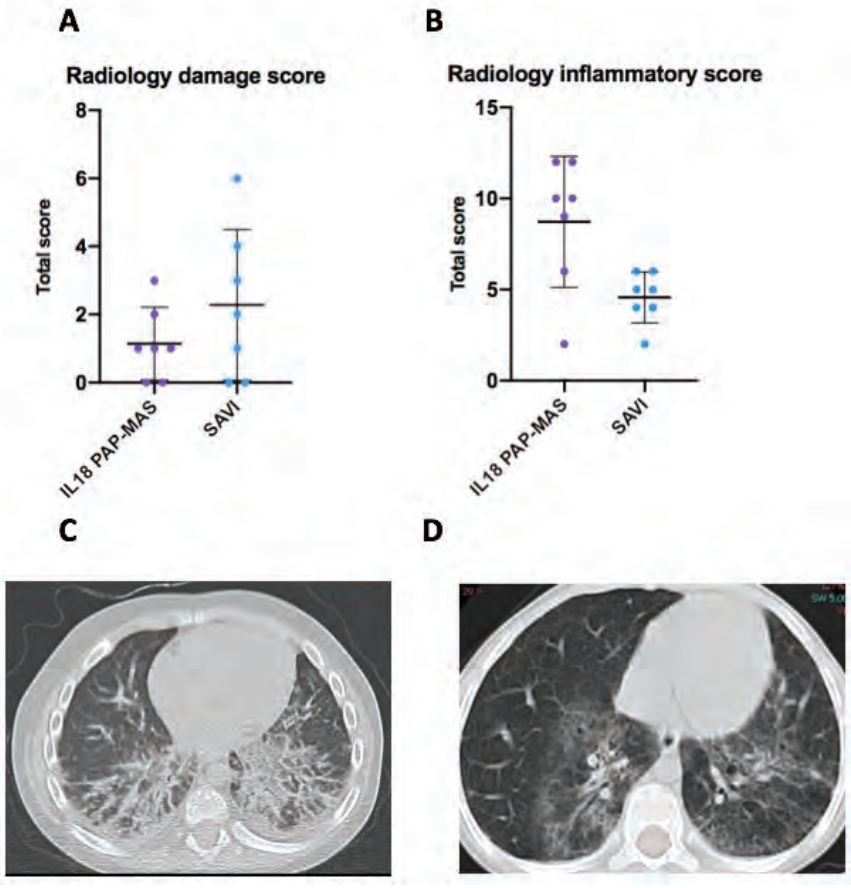

Figure 3. A, B. Radiological characteristics with damage (A) and inflammatory (B) score in IL18 PAP-MAS and SAVI. C, D. Severe bilateral infiltrates predominantly in the lower lobes and volume loss in IL-18PAP-MAS (A) and ground-glass opacities with emphysematous changes in SAVI (B)

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Abstract Number: 1157

Health and Socioeconomic Outcomes in a Neonatal-Onset Multisystem Inflammatory Disease (NOMID) Cohort Followed for a Median of Fifteen Years

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients (pts) with NOMID have systemic inflammation and organ damage such as sensorineural hearing loss, hydrocephalus, optic nerve atrophy and growth plate defects. IL-1 blocking agents are approved for the treatment of NOMID[1,2]. This study is reporting the long-term health and socioeconomic outcomes in NOMID patients on treatment.

Methods: We followed 41 NOMID patients (Female n=24, White n=27), median age 21 years (range 9-57) who were treated with IL-1 blockade (anakinra n=35, canakinumab n=6) for the median of 15 years (range 7-18). All were enrolled in an IRB-approved natural history protocol. Disease remission, organ damage, incidence of medical and psychological diagnoses and socioeconomic status were evaluated.

Results: Sustained remission and normalization of inflammatory markers was achieved in 38 pts (93%) with continued dose adjustment for weight and temporary dose increase during stress. 1 patient is non-compliant, 1 has recurrent uveitis and 1 has aseptic meningitis. 23 pts required at least 5 mg/kg of anakinra (or equivalent canakinumab) to achieve remission (56%). In 11 pts anakinra was switched to canakinumab, 6 switched back to anakinra because of worsened headache (55%)[2]. Bone age and mineral density normalized in all children on treatment. 20 pts (49%) have moderate to severe hearing loss, from those 16 use hearing aids, 2 have cochlear implants. 7 pts (17%) are legally blind and 5 (12%) are wheelchair bound . All but 2 pts attended school, 14 out of the remaining 39 (36%) required individualized education plans; speech therapy is the most common service received. 10 pts (24%) have neurocognitive delay, 8 (20%) have anxiety or mood disorders and 1 has schizophrenia. 16 out of 22 adults (72%) hold a high school diploma or college degree. 10 (45%) are either full time students or have a job. 10 pts (24%) are obese, 8 (20%) have hypertension, dyslipidemia or both. 12 pts (30%) developed skin abscess, cellulitis, or pustular acne on treatment. A 57 years old man developed a Hurtle cell thyroid dysplasia, a 44 years old woman was diagnosed with EBV negative large diffuse B-cell lymphoma of the liver and completed chemotherapy.

Conclusion: IL-1 inhibition provides sustained efficacy in the treatment of NOMID with the requirement for dose adjustment based on weight and intermittent dose escalation during stress or infections. Hearing loss is the leading cause of disability. Most can walk without assistive devices but challenges with mobility are not uncommon. Skin infections are common on treatment. Headache with or without low grade CSF leukocytosis was the most common reason for switching from canakinumab to anakinra. Anakinra allowed normalization of growth and bone health, but obesity and hypertension in adults were similar to reports in the general population. No obvious malignancy signals were detected; however, long term follow-up in a larger cohort of the entire CAPS spectrum are needed to estimate the effect on the development of hematologic and solid malignancies.

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[1]Sibley et al. Arthritis Rheum 2012

[2]Sibley et al. Ann Rheum Dis. 2015

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Abstract Number: 1158

Clinical Features and Outcomes in STING-Associated Vasculopathy with Onset in Infancy (SAVI)

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: STING-Associated Vasculopathy with Onset in Infancy (SAVI) is an autoinflammatory interferonopathy caused by gain-of-function mutations in *STING1*, characterized by peripheral vasculopathy and interstitial lung disease. Our aim is to describe the clinical and immunological manifestations of SAVI.

Methods: Clinical information on 33 patients with SAVI, based on NIH evaluation (n=15) or on records and samples provided by collaborators (n=18), were retrospectively reviewed. Patients were enrolled in an IRB-approved natural history protocol. The IFN score was calculated as previously described [1]. Features of lung inflammation and damage on Computed Tomography (CT) were scored by a single radiologist (LF). Severe lung disease was defined as presence of at least one characteristic: lung fibrosis, respiratory insufficiency, pulmonary hypertension, or digital clubbing associated with interstitial lung disease on chest CT.

Results: 13/33 (39.4%) patients were female. SAVI was sporadic in 73% and familial in 27%. Heterozygous mutations were disease-causing in 81.8%, however, a p.R281W mutation, present in 6 patients from 4 families, required homozygosity (additive gain-of-function). The p.N154S and p.V155M mutations were most common (27.3% and 24.2% respectively, see Table 1). Disease symptoms presented in the first year of life (75%), with rash (18/31), respira-

Table 1. Genetic features in 33 patients with SAVI

Nucleotide change	Amino acid change	Inheritance	Exon	Number of patients	%	Number of families
c.463G >A	**p.V155M**	Heterozygous	5	8	24.24	-
c.461A>G	**p.N154S**	Heterozygous	5	9	27.27	-
c.841C>T[1]	**p.R281W[1]**	Homozygous	7	6	18.18	4 families
c.214 C>A[1]	**p.H72N[1]**	Heterozygous	3	3	9.09	1 family of 3
c.842G>A	**p.R281Q**	Heterozygous	7	2	6.06	1 family of 2
c.439G>C	**p.V147L**	Heterozygous	5	2	6.06	-
c.439G>A	**p.V147M**	Heterozygous	5	1	3.03	-
c.457T>G[1]	**p.F153V[1]**	Heterozygous	5	1	3.03	-
c.473G>C[1]	**p.G158A[1]**	Heterozygous	5	1	3.03	-

[1]Novel mutations, Lin et al. submitted

Table 2. Clinical and laboratory features in 33 patients with SAVI

Clinical features	n (%)	Laboratory features	n (%)	Outcomes and complications	n (%)
Cutaneous manifestations	29/32 (90.6%)	Elevated inflammatory markers	26/31 (83.9%)	Premature death	7/33 (21.2%)
Vasculopathy	22/31 (71.0%)	Anemia	22/28 (78.6%)	Lung fibrosis	15/27 (55.5%)
Lung disease	28/33 (84.9%) (severe disease in 22/33 (66.7%)	Thrombocytosis	16/24 (66.7%)	Respiratory insufficiency	11/31 (35.5%)
Failure to thrive	25/33 (75.8%)	Lymphopenia	12/25 (48%)	Pulmonary hypertension	4/30 (13.3%)
Fever	22/29 (75.9%)	Elevated IgG	20/28 (71.4%)	Nasal septum perforation	7/31 (22.6%)
Clubbing	12/24 (50%)	Elevated IgA	16/26 (61.5%)	Amputations	7/32 (21.9%)
Arthralgia/arthritis	12/31 (38.7%)	Autoantibodies	28/31 (90.3%)	Osteoporotic fractures	4/16 (25%)
Myositis	5/32 (15.6%)				
Basal ganglia calcifications	2/12 (16.7%)	Elevated IFN Score	17/17 (100%)*	Short stature	16/27 (59.3%)

* In 4 patients the IFN score was positive only inPBMCs

tory symptoms (13/31) and fever (11/31). Table 2 lists clinical and laboratory features in SAVI. The p.N154S mutation is associated with vasculopathy (p=0.03); patients with the p.V155M mutation tend to have more severe lung disease (p=0.2). Median age at last evaluation was 12 years (range 0.4-54.1). 7 patients died at a mean age of 7 years (range 0.4-15); due to respiratory failure n=4, multiorgan failure n=1, sepsis n=1, unknown n=1. In 4/17 the IFN score was negative in whole blood, but positive in PBMCs. Patients failed a mean of 2.1 DMARDs or biologics, 76.6% received steroids. 25 patients were treated with a JAK-inhibitor (baricitinib n=14, tofacitinib n=7, ruxolitinib n=7), for an average of 2.1 years (range 0-5.7). Skin ulcers improved in 10/10, but recurred. Over an average of 2.6 years (range 1.1-3.9), on chest CT, features of inflammation improved in 6/7, with sTable/improved damage in 6/7.

Conclusion: SAVI is a severe early-onset interferonopathy, that can lead to amputations, respiratory insufficiency and premature death. SAVI is sporadic in 73%. Most pathogenic *STING1* mutations are heterozygous, except for

p.R281W, which is disease-causing in homozygosity. With the absence of peripheral disease in 9.4%, SAVI should be suspected in any patient with interstitial lung disease even in the absence of vasculopathy. The p.N154S mutation is associated with vasculopathy, and the p.V155M with more severe lung disease. Rarely, the IFN score can be negative in whole blood and positive in PBMCs. Treatment with JAK inhibitors halted progression of lung damage over an average of 2.3 years, but only partially controlled peripheral vasculopathy and did not normalize the IFN score.

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1. Kim et al. J Interferon Cytokine Res 2018;38:171–85

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Abstract Number: 1159

Novel *STING1* Mutations Including in the Transmembrane Linker Region Cause STING-associated Vasculopathy with Onset in Infancy (SAVI)

Bin Lin[1], **Dana Kahle**[1], Adriana Almeida de Jesus[1], Sofia Torreggiani[2], Jacob Mitchell[2], Alexander Aue[1], Zheng Ji[3], Tengchuan Jin[3] and Raphaela Goldbach-Mansky[4], [1]Translational Autoinflammatory Disease Section (TADS)/NIAID/NIH, Bethesda, [2]Translational Autoinflammatory Disease Section (TADS)/NIAID/NIH, Bethesda, MD, [3]University of Science and Technology of China, Hefei, China (People's Republic), [4]Translational Autoinflammatory Disease Section (TADS)/NIAID/NIH, Potomac, MD

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: STING-associated vasculopathy with onset in infancy (SAVI) is an autoinflammatory disease caused by gain-of-function (GOF) mutations in *STING1*/*TMEM173* that encodes stimulator of interferon genes, STING, a key mediator in the cytosolic DNA sensing pathway that drives the synthesis of type-I interferons. We report 3 novel SAVI-causing mutations that all lead to STING auto-activation in heterozygosity; 2 mutations occurred de novo and are located in the connector loop domain of STING, and one SAVI-causing mutation was present in 3 affected family members (autosomal-dominant transmission by mother) and is located in the transmembrane linker region.

Methods: All patients were clinically evaluated and studied under an institutional review board (IRB) approved protocol (NCT02974595). To investigate the autoactivating potential of these novel mutations, mutant STING constructs with the respective mutations were transfected into HEK293T cells. *IFNB1* reporter activation was measured, and interferon-response gene signatures were measured from whole blood and peripheral blood mononuclear cells (PBMC) RNA samples from patients and their family members.

Results: We identified 3 novel SAVI-causing mutations, p.G158A, or p.F153V occurred de novo and p.H72N was present in 3 symptomatic family members. All patients developed disease in childhood (age at onset 2 months-4 years) and experienced peripheral vasculopathy with chilblains in 4 and erythematous-purple discoloration of the extremities and nasal septal perforation in one; mild lung disease was present only in two patients (p.H72N and p.G158A). None of the patients received chronic steroid treatment or DMARDs, 3 were treated with baricitinib. In an *IFNB1* luciferase reporter assay all 3 mutant STING constructs were auto-activating in the absence of cGAMP ligand consistent with previously reported SAVI-causing GOF mutations. Additional mutations of H72 into K, R, D, L, Q, or F, all lead to loss-of-function or partial loss-of-function, indicating the importance of H72 in maintaining the STING structure. Structural modeling reveals that H72 lies in the "arm" restraining the ligand-binding domain, and the H72N mutation partly relieves this restrain and allows the ligand-biding domain to rotate, thus leading to auto-activation. The other 6 mutations on the H72 residue may strongly destabilize this supporting arm and lead to an ill-structured STING dimer, which results in loss-of-function. In contrast to previously reported SAVI patients, patients with the H72N and G158A mutations had a normal interferon scores in the whole blood RNA samples but were positive in PBMC samples.

Conclusion: We identified 3 novel SAVI-causing variants, that all confer a GOF in an *IFNB1* luciferase reporter assay. Two mutations, p.F153V and p.G158A, in the connector loop were predicted to be activating by a recent STING Cryo-EM structural model. The H72N is the first mutation in the transmembrane linker region, thus revealing a novel important region that controls STING activation. The absence of an elevated interferon signature in whole blood but presence in PBMCs needs further investigation, but points to the need to evaluate PBMCs in some patients.

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Abstract Number: 1160

Treatment Intensity and Impact on Bone Lesion Evolution and Distribution Patterns in Severe Chronic Recurrent Multifocal Osteomyelitis

Aleksander Lenert[1], T. Shawn Sato[2], Sedat G Kandemirli[1], Patrick Ten Eyck[1] and Polly Ferguson[3], [1]University of Iowa, Iowa City, IA, [2]University of Iowa, Iowa City, [3]University of Iowa Carver College of Medicine, Iowa City, IA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: To compare bone lesion evolution and bone lesion distribution patterns identified by whole body magnetic resonance imaging (WB-MRI) by treatment intensity in patients with chronic recurrent multifocal osteomyelitis (CRMO).

Methods: We performed an IRB-approved observational study of previously collected data from a large longitudinal CRMO cohort at the University of Iowa. We extracted detailed demographic, clinical, treatment and imaging data in patients with biopsy-proven CRMO who have undergone ≥2 serial WB-MRIs between 2014-2019. WB-MRIs were reviewed by two pediatric radiologists with expertise in imaging of CRMO. Bone lesions were characterized for anatomic location and lesion evolution on serial scans; specifically, we identified the total number of unique lesions on

Table 1. Comparison of Patient Characteristics and Bone Lesion Evolution by Treatment Intensity in Chronic Recurrent Multifocal Osteomyelitis

	Bisphosphonate group	NSAID group	Biologic DMARD group	Synthetic DMARD group
Patients, n	28	10	8	5
Age (years), mean (SD)	11.6 (3.7)	13.1 (3.3)	13.9 (4.0)	9.7 (1.8)
Sex (female), n (%)	18 (64.3)	5 (50)	5 (62.5)	4 (80)
Prior GC use, n (%)	13 (46.4)	1 (10)	3 (37.5)	2 (40)
Follow-up time (years), mean (SD)	2.6 (1.5)	2.2 (1.8)	2.1 (1.7)	2.1 (1.5)
Unique Bone Lesions (total), n	505	51	55	30
Unique Bone Lesions on Initial Imaging, n (%)	198 (39)	26 (51)	34 (62)	26 (87)
Unique Bone Lesions on Initial Imaging, mean (SD)	4.1 (11)	0.9 (1.7)	1.4 (4.6)	1.0 (2.7)
Unique Bone Lesions on Follow-up Imaging, n (%)	307 (61)	25 (49)	21 (38)	4 (13)
Unique Bone Lesions on Follow-up Imaging, mean (SD)	4.3 (14)	0.5 (1.6)	0.4 (1.7)	0.1 (0.4)
Resolved Bone Lesions on Follow-up Imaging, n (%)	406 (80)	35 (69)	43 (78)	18 (60)
Resolved Bone Lesions on Follow-up Imaging, mean (SD)	6.4 (20)	0.7 (2.2)	1.0 (3.4)	0.4 (1.6)

NSAID: non-steroidal anti-inflammatory drug, DMARD: disease-modifying antirheumatic drug, SD: standard deviation, GC: glucocorticoid.

initial and follow-up scans, as well as fully resolved lesions at the final scan. We stratified our CRMO cohort into four treatment groups based on a hierarchical therapy approach reflective of clinical practice at our institution. We defined the active treatment groups at the time of the initial WB-MRI scan. The four groups were: non-steroidal anti-inflammatory (NSAID) group (defined as active NSAID use only); synthetic disease-modifying antirheumatic drug (DMARD) group (defined as active sDMARD ± NSAID); biological DMARD group (defined as active bDMARD ± sDMARD ± NSAID); and bisphosphonate group (defined as active bisphosphonate use ± bDMARD ± sDMARD ± NSAID). Descriptive statistics were used to compare the 4 treatment intensity groups.

Results: The findings of our study are summarized in Tables 1 and 2. In our CRMO cohort (n=51), the majority of patients belonged to the bisphosphonate group (n=28), followed by NSAID (n=10), bDMARD (n=8) and sDMARD (n=5) groups respectively (Table 1). Mean age, sex distribution and mean follow-up time were overall similar across groups, except for younger age and higher proportion of females in the sDMARD group. Prior systemic glucocorticoid use was similar, except less frequent in the NSAID group. Patients in the bisphosphonate group had the highest total and mean (per patient) number of bone lesions identified on WB-MRI (Table 1). Additionally, the mean number of bone lesions per patient was ~4x higher on initial and ~8x higher on follow-up imaging in the bisphosphonate group compared to the three non-bisphosphonate groups. The bone lesion distribution pattern in the bisphosphonate group most frequently involved the lower extremity (LE), spine and pelvis; this group had the highest spine burden compared

Table 2. Comparison of Bone Lesion Distribution by Treatment Intensity in Chronic Recurrent Multifocal Osteomyelitis

	Bisphosphonate group	NSAID group	Biologic DMARD group	Synthetic DMARD group
Unique Bone Lesions (total), n	505	51	55	30
Spine, n (%)	177 (35)	3 (5.9)	1 (1.8)	3 (10)
Mandible, n (%)	1 (0.2)	0 (0)	0 (0)	0 (0)
Medial clavicle, n (%)	9 (1.8)	3 (5.9)	0 (0)	0 (0)
UE, n (%)	19 (3.8)	2 (3.9)	20 (36.4)	0 (0)
LE, n (%)	259 (51.3)	41 (80.4)	28 (50.9)	25 (83.3)
Anterior chest, n (%)	8 (1.6)	0 (0)	0 (0)	0 (0)
Pelvis, n (%)	27 (5.3)	2 (3.9)	6 (10.9)	2 (6.7)
Ribs, n (%)	5 (1)	0 (0)	0 (0)	0 (0)

NSAID: non-steroidal anti-inflammatory drug, DMARD: disease-modifying antirheumatic drug, UE: upper extremity, LE: lower extremity.

to other groups (Table 2). Peripheral (upper extremity and LE), medial clavicular and pelvic bone lesions, without spine involvement, were a common pattern observed in the NSAID, bDMARD and sDMARD groups. The proportion of resolved bone lesions on follow-up imaging was highest in the bisphosphonate group, followed by bDMARD group.

Conclusion: Treatment-stratified bone lesion evolution and distribution patterns reflect the severity of CRMO and current management strategies. Further study to elucidate differential treatment effects on individual bone lesions is needed to individualize therapeutic approaches in patients with severe CRMO.

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Abstract Number: 1161

Perspectives of Radiologist Physicians in the Imaging of Chronic Nonbacterial Osteomyelitis

Farzana Nuruzzaman[1], Mingqian Huang[2], Christian Hedrich[3], Hermann Girschick[4], Julie Cherian[5], T. Shawn Sato[6], Karen Onel[7], Polly Ferguson[8] and Yongdong Zhao[9], [1]Stony Brook Children's Hospital, Stony Brook, NY, [2]Mount Sinai Hospital, 10003, NY, [3]University of Liverpool, Liverpool, United Kingdom, [4]Vivantes Children's Hospital, Wuerzburg, Germany, [5]Stony Brook Children's Hospital, Stony Brook, NY, [6]University of Iowa, Iowa City, [7]Pediatric Rheumatology, Hospital for Special Surgery, New York, NY, [8]University of Iowa Carver College of Medicine, Iowa City, IA, [9]University of Washington, Seattle, WA

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Radiological imaging is integral to the diagnosis of chronic nonbacterial osteomyelitis (CNO) and has been included as a central component in suggested diagnostic criteria [1,2]. Objectives of this study were: 1) to determine imaging modalities and features deemed important by radiologists in the diagnostic workup of suspected CNO cases; 2) to generate input from radiologists regarding monitoring of patients with CNO.

Methods: Population targeted were active attending radiologist physician members of the Society of Skeletal Radiology email list serve. The survey was administered online through RedCap. Descriptive statistics were conducted with continuous variables reported as medians/means and categorical variables as frequencies/percentages.

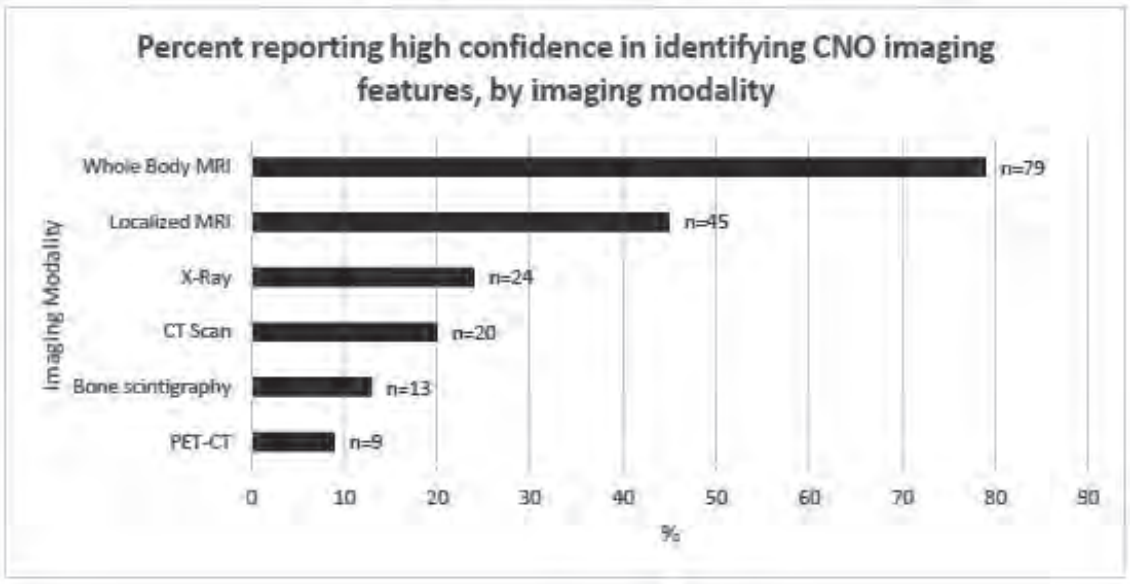
Results: A total of 66 respondents (5%) consented and completed the survey. The majority were pediatric radiologists, subspecializing in musculoskeletal radiology, with >10 years of experience (Table 1). Radiologists consider CNO in the radiological imaging interpretation differential diagnosis an average of 10 cases per year. 79% and 45% of respondents reported high confidence in identifying imaging features of CNO on whole body MRI (WBMRI) and localized MRI, respectively. The level of confidence drops to 24% and 19% when interpreting X-rays (XRs) and

Baseline Characteristics and Demographics

Characteristics	N* (%)
Subspecialty	
Pediatric Musculoskeletal Radiology	34 (64)
Pediatric General Radiology	19 (36)
Adult Musculoskeletal Radiology	13 (25)
Location of Professional Institution	
North America	36 (68)
Asia	8 (15)
Europe	7 (13)
Year of Attending Physician/Consultant Experiences	
>10 years	28 (54)
5-10 years	15 (29)
<5 years	9 (17)
Time Spent on MSK Imaging	
>50% of time	18 (34)
20-50%	19 (36)
<20%	16 (30)
New Cases per year CNO considered in Imaging	
>=10	17 (32)
5-9	18 (34)
1-4	18 (34)
Established CNO Cases per year followed by Imaging	
>20	4 (9)
10-19	15 (33)
<10	26 (58)

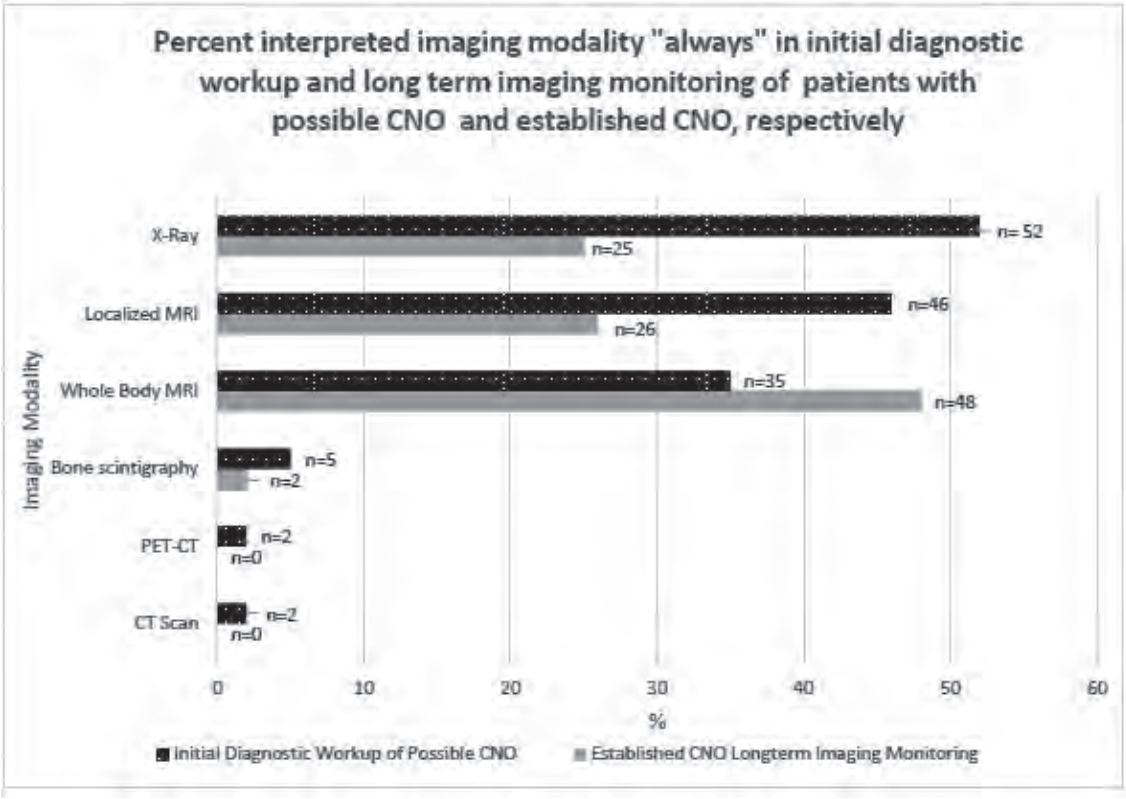
*= number of participants who responded to survey question

Baseline characteristics and demographics of survey respondents



Percent reporting high confidence in identifying CNO imaging features, by imaging modality

bone scintigraphy, respectively (Figure 1). Among all imaging modalities interpreted "always" in the initial diagnostic workup of potential cases of CNO, XRs (52%) were most commonly interpreted, followed by localized MRI (46%) and WBMRI (35%), which suggested the sequence of utilization of these three imaging modalities in new cases. In estab-



Percent interpreted imaging modality "always" initial diagnostic workup and longterm imaging monitoring of patients with possible CNO and established CNO, respectively

lished cases of CNO, wherein WBMRI was the most frequently interpreted (48%), followed by localized MRI (26%) and XRs (25%) (Figure 2). Most common imaging features that led respondents to suggest a bone biopsy included disorganized bone formation (64%/56%), moth-eaten appearance (61%/56%), and lytic lesions (50%/44%) on XRs/CTs, respectively as well as the presence of soft tissue mass/swelling(68%/44%) and MRI signal hyperintensity of bone marrow at unifocal site (24%). A majority of respondents preferred a combination of short tau inverse recovery (STIR), T1 and diffusion weighted imaging (DWI) sequences in the MRI images of potential CNO cases. 46% of respondents reported using an established WBMRI protocol at their institutions.

Conclusion: WBMRI is considered the most useful imaging modality for initial diagnosis and monitoring of CNO by radiologists. Certain morphological features including disorganized bone structure, moth-eaten appearance, lytic lesions, soft tissue mass/swelling and unifocal signal hyperintensity of bone marrow may result in increased chance of bone biopsy to exclude differential diagnoses. Findings from this survey will promote discussion within a focused group to develop imaging guidelines for the diagnostic workup and disease monitoring in CNO and contribute to earlier diagnosis and individualized care.

[1] Jansson, A et al. "Classification of nonbacterial osteitis." *Rheumatology (Oxford)* 46, 1 (2007)

[2] Roderick, MR,*et al.* "Chronic recurrent multifocal osteomyelitis (CRMO)." *Pediatric Rheumatology* 14, 47 (2016)

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Abstract Number: 1162

Comparison of Clinicopathologic and Imaging Features Between Chronic Nonbacterial Osteomyelitis and Its Mimickers: A Multi-national 450 Case-Control Study

Yongdong Zhao[1], Raymond Naden[2], Melissa Oliver[3], Zhaoyi Wang[4], Eveline Wu[5], Cassyanne Aguiar[6], Jonathan Akikusa[7], Ozge Basaran[8], Kevin Cain[1], Martina Capponi[9], Nathan Donaldson[10], Emily Fox[11], Antonella Insalaco[12], Annette Jansson[13], Ummusen Kaya Akca[14], Tzielan Lee[15], Edoardo Marrani[16], Kamran Mahmood[17], Elizabeth Murray[18], Farzana Nuruzzaman[19], Karen Onel[20], Manuela Pardeo[12], Lauren Potts[21], Nathan Rogers[10], Anja Schnabel[22], Gabriele Simonini[23], Jennifer Soep[10], Sara Stern[24], Alexander Theos[25], Yujuan Zhang[26], Polly Ferguson[27], Christian Hedrich[28], Fatma Dedeoglu[29], Hermann Girschick[30], Ronald Laxer[31] and Seza Ozen[32], [1]University of Washington, Seattle, WA, [2]Department of Medicine, Middlemore Hospital, Auckland, Auckland, New Zealand, [3]Department of Pediatric Rheumatology, Riley Children's Hospital, Carmel, IN, [4]University of Washington, Bothell, WA, [5]UNC Chapel Hill, Chapel Hill, NC, [6]Children's Hospital of the King's Daughters/EVMS, Norfolk, VA, [7]PRINTO, Istituto Giannina Gaslini, Genova, Italy, [8]Hospital for Special Surgery, New York City, NY, [9]IRCCS Ospedale Pediatrico Bambino Gesu', Rome, Italy, [10]Children's Hospital Colorado, Aurora, CO, [11]Children's Mercy Kansas City, Kansas City, MO, [12]Division of Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, Rome, Italy, [13]Dr. von Hauner Children's Hospital, Munich, Germany, [14]Hacettepe University, Division of Pediatric Rheumatology, Department of Pediatrics, Faculty of Medicine, Ankara, Turkey, [15]Stanford University School of Medicine, Palo Alto, CA, [16]University of Florence, Firenze, Italy, [17]Alder Hey Children's NHS Foundation Trust Hospital, Liverpool, England, United Kingdom, [18]CRMO Patient Partner, New York, NY, [19]Stony Brook Children's Hospital, Stony Brook, NY, [20]Pediatric Rheumatology, Hospital for Special Surgery, New York, NY, [21]CRMO Patient Partner, Fort Collins, CO, [22]Universitätsklinikum Carl Gustav Carus, Technische Universität Dresden, Dresden, Germany, [23]Anna Meyer Children's Hospital, Firenze, Italy, [24]University of Utah and Primary Children's Hospital, Salt Lake City, UT, [25]Georgetown University, DERWOOD, MD, [26]Tufts Medical Center, Boston, MA, [27]University of Iowa Carver College of Medicine, Iowa City, IA, [28]University of Liverpool, Liverpool, United Kingdom, [29]Boston Children's Hospital, Boston, MA, [30]Vivantes Children's Hospital, Wuerzburg, Germany, [31]The Hospital for Sick Children, Toronto, ON, Canada, [32]Department of Pediatric Rheumatology, Hacettepe University, Ankara, Turkey, Ankara, Turkey

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic nonbacterial osteomyelitis (CNO)/chronic recurrent multifocal osteomyelitis (CRMO) predominantly affects children and young adults. Classification criteria are not available and diagnostic criteria that have been suggested have not been validated. We previously identified candidate items for the development of classification criteria.

Methods: We aimed to refine candidate items for pediatric classification criteria for CNO by comparing clinical, laboratory and imaging features of CNO against mimicking conditions. International multicentre collection of clinical and investigational features of cases with CNO or mimicker diseases with at least 12 months follow-up was conducted through a REDCap online database. Prevalence ratios of each collected item between CNO and mimickers were calculated. A p value of <.05 was considered significant.

Results: 450 cases were collected from 20 centers in 7 countries and 4 continents. Cases were filtered based on indicated confidence levels of diagnosis for CNO or mimickers using a cut-off of +/- 2 (moderately confident). 264 (59%) CNO cases and 145 (32%) mimicker controls were used for analysis. 41 (9%) cases were excluded. Key findings are summarized in Table 1.

When compared to mimicker diagnoses, CNO patients were predominantly female, more frequently exhibited intermittent versus continued pain (especially of neck, back and upper torso), but less commonly had fever. Clavicular swelling was more common in CNO, while active arthritis was less common as compared to controls. CNO patients more frequently had whole body imaging (usually whole-body MRI). Symmetric patterns of bone lesions were more common in CNO. CNO frequently involved the thoracic spine, clavicle, sternum/manubrium, pelvic bones, bilateral femur, bilateral tibia, unilateral fibula, and foot bones. Imaging features that are concerning for infection or malignancy (including cortical bone disruption, disorganized bone formation, mass structure, marrow infiltrate, abscess or geographic appearance) were less common in CNO. Lastly, complete and sustained response to antibiotic treatment was less frequent in CNO patients.

Conclusion: Using a case-based approach, key features of CNO were identified to support the development of classification criteria. Next steps will include expert panel discussions and a 1000Minds exercise.

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Abstract Number: 1163

Predictors of Colchicine Response in Patients with Undefined Systemic Autoinflammatory Diseases

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic autoinflammatory diseases (SAIDs) result from dysregulation of the innate immune system. Many patients with SAIDs have specific mutations that lead to the release of inflammatory cytokines that can be targeted with anti-inflammatory drugs or cytokine blockers. However, up to half of the patients with SAIDs do not have symptoms or mutations indicative of a specific SAID and are diagnosed with undefined (uSAIDs). Little is known about therapeutic options for these patients. The goal of this single-center study was to evaluate predictors of colchicine response among patients with uSAIDs in an American cohort.

Methods: We conducted a retrospective chart review of patients with clinical diagnoses of uSAIDs who tolerated colchicine for at least 3 months, followed at a large pediatric rheumatology clinic. "Complete colchicine response" was defined as having a complete resolution of the episodes and not requiring additional therapy for the treatment of flares (e.g. NSAIDs, acetaminophen, prednisone, tonsillectomy). "Partial colchicine response" was defined as a decrease in the frequency, severity, or length of episodes, without complete resolution of symptoms or the requirement of additional therapy to achieve full response. "No colchicine response" was defined as no change in the clinical and laboratory features in response to colchicine. For statistical analyses, "partial" and "no colchicine response" were combined into a single category.

Table 1. Patient characteristics

	Partial and non-colchicine responders n= 42	Complete colchicine responders n= 33	P-value
Age of onset in months - median (IQR)	18 (9-72)	35 (13-63)	0.469
Duration of fever (days)	4.5 (3-6)	4 (3.5-7)	0.845
interval between flares (days)	30 (21-49)	30 (22-37.5)	0.708
Female Sex	30 (71%)	16 (48%)	**0.043***
Family history of recurrent fevers	11 (26%)	9 (27%)	1.0
Genetic test sent	36 (86%)	23 (70%)	0.154
Heterozygous MEFV mutation (n=59)	7/36 (19%)	6/23 (26%)	0.748
Regular interval between episodes n= 57	10 (29%)	11 (48%)	0.175
Region of ancestry			
America	15 (36%)	10 (30%)	0.806
Europe	32 (76%)	22 (67%)	0.440
Eastern Mediterranean	0 (0%)	7 (21%)	**0.002***
South-East Asia	0 (0%)	0 (0%)	N/A
Western Pacific	3 (7%)	3 (9%)	1.0
Africa	1 (2%)	1 (3%)	1.0

Table 2. Clinical features

	Partial and non-colchicine responders n= 42	Complete colchicine responders n= 33	P value
Oral ulcers	19 (45%)	7 (21%)	**0.049***
Genital ulcers	3 (7%)	0 (0%)	0.251
Oral herpetic-like lesions	1 (2%)	5 (15%)	0.081
Maculo-papular rash	6 (14%)	7 (21%)	0.543
Urticarial rash	4 (10%)	4 (12%)	0.725
Thoracic pain	0 (0%)	3 (9%)	0.080
Vomiting	7 (17%)	13 (39%)	**0.036***
Abdominal pain	17 (40%)	16 (48%)	0.640
Myalgia	13 (31%)	10 (30%)	1.0
Arthralgia	16 (38%)	10 (30%)	0.626
Lymphadenopathy	10 (24%)	10 (30%)	0.603

Results: Of the 75 patients identified, 33 (44%) were complete colchicine responders, 35 (47%) were partial responders, and seven patients (9%) did not respond. Patient characteristics are shown in Table 1 and clinical features of disease flares are in Table 2. Eastern Mediterranean ancestry and the presence of vomiting were predictive of a complete colchicine response, whereas oral ulcers and female sex were associated with partial or no colchicine response.

Conclusion: Many patients with uSAIDs had a complete response to colhicine. Confirming results of our previous preliminary study (1), the presence of oral ulcers remained as a predictor of partial response and vomiting was a predictor of complete response. Unlike a similar study conducted in a European cohort (2), short episode duration, and the regular interval between episodes were not associated with good response to colchicine in this American cohort. Limitations of this study include its retrospective nature and potential physician selection bias of patients to start on cochineal. Prospective studies would help better identify patients who could benefit the most from this therapy.

References:

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(2) Ter Haar NM, Eijkelboom C, Cantarini L, et al. Clinical characteristics and genetic analyses of 187 patients with undefined autoinflammatory diseases. Ann Rheum Dis 2019;78:1405–1411

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Abstract Number: 1164

Frequency of Genetic Diagnosis in an Autoinflammatory Disease Natural History Protocol Cohort of Patients

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SESSION INFORMATION

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Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Monogenic autoinflammatory diseases (AID) are caused by innate immune dysregulation resulting in systemic inflammation and variable organ-specific clinical manifestations. The Translational Autoinflammatory Disease Section (TADS) studies patients with rare and early-onset AIDs, such as the IL-1 mediated diseases neonatal onset multisystem inflammatory disease (NOMID) and deficiency of IL-1 receptor antagonist (DIRA), the interferon (IFN) mediated diseases chronic atypical neutrophilic dermatosis with lipodystrophy and elevated temperature (CANDLE) and STING associated vasculopathy with onset in infancy (SAVI), and patient with yet undifferentiated

Diagnosis	Number of Patients	Male|Female	Ethnicity ratio[1]	Mean age (σ)	Median age (range)	Mortality
CANDLE	n=17	9|8	8|4|5|0|0	14.0 (7.8)	13 (1-27)	2/17 11.8%
SAVI	n=24	15|9	17|1|2|0|4	14.8 (11.9)	11.5 (2-55)	5/24 20.9%
DIRA	n=9	4|5	3|0|2|1|3	12.4 (4.5)	11 (6-21)	0/9 0%
NOMID/CAPS	n=60	25|35	37|2|4|5|12	23.7 (14.1)	22.5 (2-79)	0/60 0%
IL-18PAP-MAS[2]	n=8	4|4	3|1|1|2|1	19.6 (16.5)	12 (6-64)	2/10 20%
AGS	n=7	3|4	6|0|1|0|0	16.4 (4.0)	16 (9-21)	0/7 0%
NEMO-NDAS	n=10	3|7	3|2|3|0|2	8.4 (5.0)	8 (1-19)	0/10 0%
SAMD9L-SAAD	n=6	2|4	3|0|2|0|1	7.8 (3.3)	6.5 (5-13)	2/6 33.3%
Other genetic diagnosis	n=64	31|33	47|3|5|1|8	22.5 (16.1)	17 (3-64)	2/64 3.1%
Clinical diagnosis[3]	n=84	26|58	62|8|4|3|7	33.2 (19.8)	27 (4-83)	0/84 0%
Undiff. no genetic and no clinical diagnosis	n=182	72|110	118|12|5|5|42	19.3 (15.9)	15 (0-87)	5/182 2.7%
All Patients	n=471	194|277	302|32|34|16|87	21.7 (16.8)	16 (0-87)	18/471 3.8%

[1]Ethnicity Ratio = White|Black|Hispanic, Latino|Asian|Unknown, Other, Mixed

[2]No single gene defect was detected in patients with IL-18PAP-MAS.

[3]Clinical diagnoses include: juvenile dermatomyositis (JDM, n=30), pustular psoriasis (n=19), chronic recurrent multifocal osteomyelitis (CRMO, n=16), adult-onset Still's disease (AOSD, n=14), others (n=5)

Table 1. Demographic Features of Patients Enrolled in an Autoinflammatory Disease Natural History Protocol

AIDs. We aim to identify the frequency of genetically defined diagnoses, demographic information and mortality rates in patients enrolled in TADS Natural History Protocol.

Methods: All patients were consented to an IRB-approved natural history protocol (NCT02974595) and underwent a standard procedure of clinical and laboratory evaluation. For genetic investigation, most patients had Sanger sequencing, whole exome (WES) or genome sequencing (WGS) performed. Patients with IFN-mediated diseases had whole blood interferon scores performed to assess disease-associated flare status. Patient information was compiled into a clinical database that includes variables such as demographic features, diagnosis, clinical manifestations, disease outcome and gene affected.

Results: Since 2003, 471 patients have been enrolled in the AID natural history protocol. Genetic diagnoses were assigned to 197/471 (41.8%). The cohort consists of 194 males (41.1%), 277 females (58.8%). Demographics and outcomes of genetic diagnoses with more than 3 confirmed patients are depicted in Table 1. These included patients with CANDLE (n=17), SAVI (n=24), DIRA (n=9), NOMID (n=60), IL-18 pulmonary alveolar proteinosis and macrophage activation syndrome (IL-18PAP-MAS, n=8), Aicardi-Goutières syndrome (AGS, n=7), NEMO-deleted exon 5 autoinflammatory syndrome (NEMO-NDAS, n=10), and SAMD9L-associated autoinflammatory disease (SAMD9L-SAAD, n=6). Among patients with undifferentiated AID and genetic diagnoses with less than 3 confirmed cases (Other genetic diagnosis)(Table 1), we have identified two patients with LYN-kinase associated AID, two with dysferlin associated AID, one patient with Majeed syndrome and another with CARD14-mediated psoriasis (CAMPS). We have also identified 5 patients with monogenic forms of MAS, including 3 patients with NLRC4-MAS and 2 with CDC42-AID. Interestingly, 7 patients had 2 genetic diagnoses, including one patient with NEMO-NDAS and LRBA-deficiency. Diseases showing the highest mortality in our cohort were SAMD9L-SAAD (33.3%), SAVI (21%), IL-18PAP-MAS (20%), and CANDLE (11.8%).

Conclusion: A comprehensive characterization of an AID cohort revealed a variety of monogenic AIDs in 42% of the patients. Future studies to assess response to treatment, end organ damage and disease progression are needed.

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Abstract Number: 1165

Validation of Healthcare Claims Algorithms for Identification of Herpes Zoster Among Children with Autoimmune/Autoinflammatory Disease

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Herpes zoster (HZ) is a known serious infectious complication in children with autoimmune/autoinflammatory disease and potentially exacerbated by immunomodulatory medications. Information on HZ burden is especially pertinent as JAK-STAT inhibitors have been recently FDA approved for use in children and are known to reactive latent VZV infection. However, our knowledge of HZ prevalence among children is limited. Because of its relative rarity, validating the diagnosis of HZ in healthcare claims and electronic medical record (EMR) databases is a critical first step. This study aimed to evaluate the validity of International Classification of Diseases, 10th Revision, (ICD-10) code-based algorithms for identification of HZ.

Methods: We identified all patients with ICD-10 for HZ (B02.xx) as their primary or secondary diagnosis in the EMR of a large, integrated pediatric healthcare network including 31 primary care practices, 4 urgent care centers, 19

Table 1. Demographics and Clinical Characteristics of Subjects with HZ ICD-10 code (B02). All ICD-10 codes corresponding to HZ infection (B02.xx) were used for inclusion into cohort. Rash defined as pruritic and/or painful dermatomal rash documented by treating physician. Antiviral prescription defined as prescription for any oral and/or IV antiviral treatment, including IV acyclovir, oral acyclovir, and valacyclovir.

	Definitive HZ	*Possible HZ*	*False HZ*
Number	47	18	7
Female, N (%)	20 (43%)	8 (44%)	4 (57%)
Age Mean at diagnosis (SD)	12.2 (6.3)	11.9 (7.12)	8.9 (5.1)
Positive VZV PCR, N (%)	16 (34%)	1 (6%)	0 (0%)
Dermatomal Rash, N (%)	46 (98%)	11 (61%)	4 (57%)
Antiviral Rx, N (%)	40 (85%)	7 (39%)	5 (71%)
Inpatient treatment, N (%)	10 (21.3%)	0 (0%)	0 (0%)
Immunomodulatory Rx, N (%)	9 (12.8%)	0 (0%)	0 (0%)
Chronic disease, N (%)	14 (29.8%)	1 (5.6%)	2 (28.6%)
*Autoimmune/autoinflammatory**	6 (12.8%)	1 (5.6%)	1 (14.3%)
*Heme/onc***	6 (12/8%)	0 (0%)	0 (0%)
*Genetic/congenital****	2 (4.3%)	0 (0%)	1 (14.3%)

Abbreviations: VZV = Varicella Zoster Virus, HZ = Herpes Zoster; Rx = prescription, Heme/onc = hematologic/oncologic
*Autoimmune/autoinflammatory group included the following diagnoses: multiple sclerosis (1), autoimmune thyroiditis (1), systemic lupus erythematosus (2), inflammatory bowel disease (2), Type 1 diabetes mellitus (1), HIV (1)
**Heme/onc group included the following diagnoses: solid tumors (3), leukemia (2), aplastic anemia (1)
***Genetic/congenital group included the following diagnoses: Xp22 deletion/MIDAS syndrome (1), spina bifida (1), congenital cranial vascular abnormalities (1)

Table 2. Alternative Algorithms for Defining HZ Infection

	Total	Definitive	Possible	Definitive only* PPV % (95% CI)	Combined** PPV % (95% CI)
One ICD-10 Code	72	47	18	65.3 (53.4-75.5)	90.3 (80.8 – 95.4)
ICD-10 + Rash	61	46	11	75.4 (62.9-84.8)	93.4 (83.5 – 97.6)
ICD-10 + Antiviral Rx	52	40	7	76.9 (63.3-86.6)	90.4 (78.5 – 96.0)
ICD-10 + Rash + Antiviral Rx	46	39	4	84.8 (70.9-92.7)	93.5 (81.2 – 97.9)

Abbreviations: HZ = Herpes Zoster; Rx = prescription
*PPVs calculated using only those with definitive/confirmed HZ diagnosis
**PPVs calculated using those with both definitive/confirmed and possible HZ diagnosis

subspecialty divisions, and a 600-bed tertiary care hospital from January 2010 – March 2019. Both ambulatory and inpatient databases were queried. Electronic charts were reviewed to adjudicate diagnostic code-based algorithms for true HZ infection. Positive predictive values (PPVs) for confirmed HZ as well as those with confirmed or possible HZ were calculated for each algorithm.

Results: A total of 72 unique individuals were identified as having at least one physician-entered ICD-10 corresponding to HZ (B02). The PPV for a single ICD-10 code was 90.3% (95% CI 80.8-95.4) for definitive and/or possible cases of HZ and 65.3% (95% CI 53.4-75.5%) for definitive cases alone. Adding a prescription for an antiviral did not improve the PPV (90.4%; 78.5-96.0), while adding documentation of pruritic and/or painful dermatomal rash increased the PPV to 93.4 (95% CI 83.5-97.6). The combination of diagnostic code, antiviral prescription and documentation of rash had the highest PPV of 93.5% (95% CI 81.2-97.3) but with substantial loss in sample size. Seventeen of the 72 patients identified (23.6%) had underlying chronic conditions (excluding asthma) requiring frequent follow-up with a sub-specialist. Eight patients (11.1%) had autoimmune/autoinflammatory diagnoses, 6 (8.3%) had oncologic/hematologic diagnoses requiring systemic therapy and 3 (4.2%) had genetic/congenital disease. Out of the 47 cases of definitive HZ, 10 (21.3%) required inpatient hospitalization for IV antiviral therapy, 7 (70%) of which had underlying chronic disease and 5 (50%) of which were on systemic immunomodulatory therapy. Seven out of the 17 patients (41.7%) with chronic disease required inpatient admission for HZ treatment, and 5 of these 7 (71.4%) were on systemic immunomodulatory therapy.

Conclusion: HZ can be identified with a high PPV in electronic medical records of children. There were modest improvements in PPV with the addition of characteristic rash. These findings can be employed in pharmacoepidemiologic research to better understand risk factors for HZ infection, which is especially important as new immunomodulatory medications come to market.

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Abstract Number: 1166

Use of Rituximab to Treat COPA Syndrome: A Multi-Institutional Cohort

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Coatomer protein complex subunit α (COPA) syndrome is a rare genetic multisystem autoimmune disorder inherited in an autosomal dominant manner. Onset typically occurs in childhood, including pulmonary, musculoskeletal, and renal manifestations. Pulmonary features include cough, dyspnea, and life-threatening diffuse alveolar hemorrhage. Lung involvement is a key negative prognostic factor. Musculoskeletal and renal manifestations

can include arthralgias, polyarticular arthritis, and glomerulonephritis. Patients are usually diagnosed with other rheumatologic conditions prior to the discovery of COPA syndrome and are often treatment refractory. Therefore, it remains unclear which immunomodulating drugs are the most beneficial for these patients. We report the demographics, clinical findings, prior medications, and current outcomes for COPA syndrome patients treated with rituximab, including 3 patients not previously reported.

Methods: A retrospective chart review was performed for 11 COPA syndrome patients who were treated with rituximab.

Results: The mean age of symptom onset was 8 years (range 0.5-18). The mean current age is 25 years (range 4-55), with a mean of 16 years (range 2-54) since illness onset. There was a female majority (55%), and patients were white non-Hispanic (55%), white Hispanic (27%), and black (18%). Diagnoses given prior to the discovery of COPA syndrome included mixed connective tissue disease, juvenile idiopathic arthritis, ANCA-associated vasculitis, rheumatoid arthritis, and idiopathic pulmonary hemosiderosis. Patients predominantly carried the p.R233H mutation (82%). The majority of patients presented with pulmonary symptoms (55%), but some presented with arthritis (27%), renal (9%), and neurologic (9%) manifestations. All patients had interstitial lung disease by chest CT. Other features included pulmonary hemorrhage (27%), arthritis (55%), and renal disease (36%). Laboratory results revealed elevated ESR (82%) and the presence of ANA (82%), ANCA (73%), RF (82%), and ACPA (50%). Prior to rituximab, the majority of patients (55%) failed 5 or more immunomodulatory drugs (mean: 4.5, range 1-9), and 3 patients (27%) were on oxygen therapy at rest. Patients had been treated with corticosteroids (100%), hydroxychloroquine (82%), methotrexate (45%), TNF-inhibitors (45%), azathioprine (36%), mycophenolate mofetil (36%), cyclophosphamide (27%), sulfasalazine (27%), tofacitinib (9%), and anti-IL-6R (9%). At last follow-up after rituximab (mean 2 years, range 1-5), no patients were on oxygen at rest. Chest CT results remained sTable or showed improvement of nodules and ground glass opacities. The majority of patients (90%) reported symptomatic respiratory improvement; one patient had an arthritis flare. No patients have required listing for lung or renal transplants. These COPA patients tolerated rituximab without serious adverse events, specifically there were no infectious complications.

Conclusion: The COPA syndrome patients in our cohort had symptomatic improvement, sTable or improving chest CT results, and decreased oxygen requirements after rituximab. Rituximab is a potentially promising therapy for patients with COPA syndrome.

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Abstract Number: 1167

Capturing the Range of Disease Involvement in Localized Scleroderma: The Total Morbidity Score

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Background/Purpose: Localized scleroderma (LS) is a chronic inflammatory and fibrosing disease that causes both cutaneous and extracutaneous (EC) damage. EC involvement (ECI) is common in juvenile LS (jLS), and includes joints, bones, eye, and nervous system. A measure that captures the full spectrum of morbidity would improve disease assessment. The CARRA LS group generated a measure, the Total Morbidity score (TMS), for this purpose. We report on its performance in a prospective cohort of jLS patients beginning methotrexate (MTX) treatment.

Methods: The TMS specifies that items should only be scored if considered related to LS, not to treatment or other factor. TMS items were generated based upon literature review and expert group discussion. A modular design was used, with modules of cutaneous features (i.e., dyspigmentation, subcutaneous atrophy) and extent, musculoskeletal (MSK, i.e., arthritis, myositis), growth difference of body (i.e., limb girth or length difference), head/neuro (i.e., facial hemiatrophy, brain involvement), other organ (i.e., vasculopathy). The weighting of scored items was determined by surveys, 1000Minds software, and iterative cycles of testing and discussion.

We evaluated the TMS in a prospective cohort of jLS patients followed for 12 months after starting MTX treatment (jLS consensus treatment plan pilot study). Clinical assessments included skin scores, physician global assessment of disease damage (PGA-D), and ECI scoring. Data was analyzed by descriptive statistics, Wilcoxon sign rank test, Spearman's rho. p values < 0.05 were considered to be significant.

Results: Fourty-eight patients had TMS scores at baseline, 43 at 12 months. There were 33 females, 44 Caucasian, median age of LS onset 9.6 years, median disease duration 12.5 months. The most common LS subtype was linear scleroderma. Baseline median TMS was 7, range 0-40. Patients with ECI had higher scores than those without ($p < 0.001$, Table 1), and there was a trend towards higher scores in patients with disease duration > 2 years ($p = 0.086$,

	# Patients	Median score (IQR)	Scoring Range	P value
All patients	48	7 (4, 13)	0-40	
EC involvement	34	10.5 (6, 15)	3-40	<0.001
No-EC involvement	14	4 (2.5, 6)	0-10	
Disease duration ≤ 2 years	30	6.5 (5, 10)	0-20	0.086
Disease duration > 2 years	18	11.5 (4.3, 15.8)	2-40	
Linear scleroderma	28	9 (6, 15)	0-20	NS
Non-linear subtypes	20	6.5 (4, 10.5)	2-40	
Mixed morphea	10	10.5 (9.3, 12.8)	5-40	NS
Non-mixed subtype	38	6.5 (4, 13.3)	0-20	

Table 1. Total Morbidity Scores at the Baseline Visit of 48 jLS patients beginning methotrexate-based treatment. The number of patient in each category, their median TMS, and the range of scores is shown. P-values were calculated by t-test, $p < 0.05$ considered to be significant. EC: extracutaneous; IQR: interquartile range; jLS: juvenile localized scleroderma.

Table 1). Higher scores were seen in linear scleroderma and mixed morphea subtype patients, but these differences were not significant (Table 1).

The most commonly scored TMS module was Cutaneous, followed by MSK, Growth differences, and Head/Neuro modules, which were each scored in >30% of patients at baseline (Figure 1). From 0 to 12 months, scores changed in 31 patients (72%), with change most often occurring in the Cutaneous and MSK modules (Figure 2). Patients with

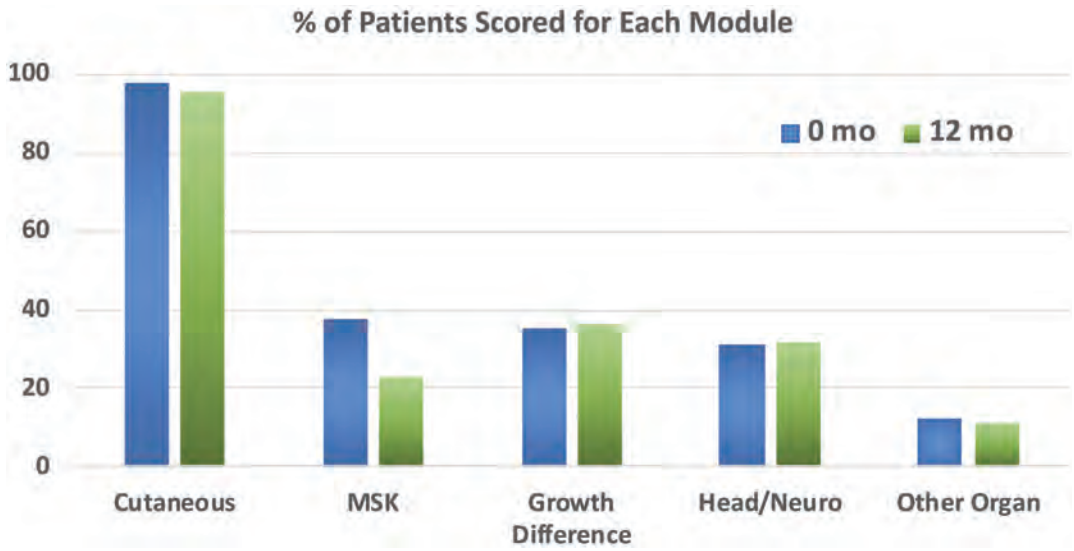
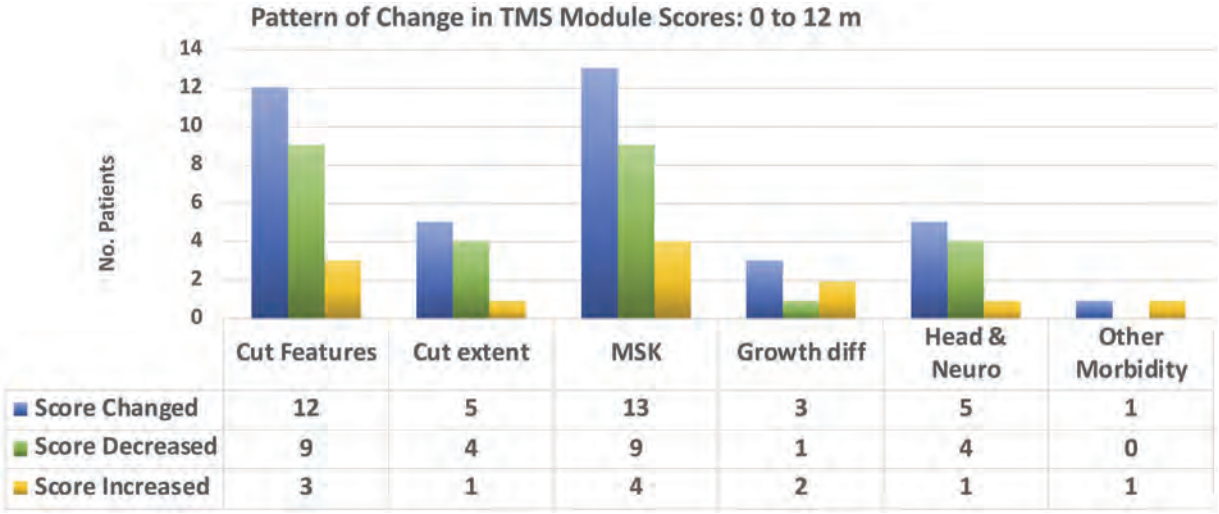


Figure 1. Percent of patients that were scored for each of the modules of the Total Morbidity Score at start of treatment (0 months) and after 12 months of methotrexate treatment. 48 jLS patients were assessed at 0 months, 43 at 12 months. Cutaneous refers to skin features (dyspigmentation, dermal atrophy, and skin thickening), subcutaneous tissue atrophy, and extent of these features in affected anatomic sites. Musculoskeletal (MSK) includes arthritis, joint contractures, myositis, fasciitis. Growth difference includes girth hemiatrophy, limb length differences, and breast, trunk, or buttock hemiatrophy. Head/Neuro includes hair loss, facial disFigurement, seizures, peripheral neuropathy, brain imagining abnormalities, and ocular or oral involvement. Other organ includes gastroesophageal reflux, Raynauds phenomenon, and other miscellaneous morbidities.



	Cut Features	Cut extent	MSK	Growth diff	Head & Neuro	Other Morbidity
Score Changed	12	5	13	3	5	1
Score Decreased	9	4	9	1	4	0
Score Increased	3	1	4	2	1	1

Figure 2. Change in TMS modules from 0 to 12 months. JLS patients were followed for 12 months after beginning methotrexate treatment. The columns show the percent of patients that had a change in their score of each TMS module from 0 to 12 months. 31 patients had a change in their TMS score, and 12 had sTable scores. Cut. Extent (cutaneous extent) refers to estimate of surface area of involvement of skin and subcutaneous damage features in each affected anatomic site. Growth diff = growth difference module.

linear scleroderma had a decrease in TMS scores from 0 (9, IQR 6-15) to 12 months (6, IQR 5-12, p =0.028). Good correlation was found between TMS and PGA-D at 0 and 12 months (rho = 0.778, p < 0.001; 0.756, p < 0.001, respectively), higher than that found for the localized scleroderma skin damage index (0.629 at 0 months, 0.713 at 12 months).

Conclusion: The Total Morbidity Score was developed to capture the range of, and quantify, LS morbidity. Scores were found to reflect a range of damage levels and morbidities in jLS patients, and vary over time. The TMS showed good correlation with PGA-D. Our findings suggest the TMS could aid tracking of clinical status and response. More study is needed to further assess its performance.

Disclosure: S. Li, Merck, 3, CARRA, 9, UpToDate, 7, Arthritis Foundation, 2, Scleroderma Foundation, 2; **A. Patel**, None; **E. Pope**, None; **T. Mason**, None; **V. Sivaraman**, None; **F. Dedeoglu**, Novartis, 1; **K. Torok**, None; **K. Stewart**, None; **G. Higgins**, None; **C. Rabinovich**, AbbVie, 2, CARRA, 2, UCB Pharma, 2, Janssen Research & Development, 2; **R. Fuhlbrigge**, None; **M. Ibarra**, None; **S. Hong**, None; **P. Ferguson**, NIH/NIAMS R01AR059703, 1, Novartis, 1; **M. Becker**, CARRA, 9; **B. Feldman**, Pfizer, 1, AB2-Bio, 1, Optum, 1, Novartis, 1; **R. Laxer**, Eli Lilly Canada, 1, Novartis, 1, Sanofi, 1; **C. Investigators**, None.

Abstract Number: 1168

Reliability and Validity of a New Skin Activity Measure for Localized Scleroderma

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile localized scleroderma (jLS) is a chronic inflammatory and fibrosing disease. Treatment is directed towards controlling disease activity to minimize risk for functional impairment and severe damage. To work towards identifying optimal therapy, sensitive disease measures are needed to allow for comparative effectiveness studies.

A prior study identified several lesion features specific to and/or tracking with disease activity. These features were used to generate a new skin activity measure, LS Cutaneous Activity Measure (LSCAM), by LS Childhood Arthritis and Rheumatology Research Alliance (CARRA) group. We report its performance in two prospective cohorts.

Methods: The LSCAM was modelled after the modified Localized Scleroderma Scoring Index (mLoSSI). Both measures score and sum disease extension, erythema, and skin thickening across affected sites; mLoSSI weighs extension more. LSCAM also scores violaceous color, tactile warmth, and waxy white/yellow, weighing variables equally.

	W Round 1	W Round 2	Intra-rater	Average score
LSCAM	0.594	0.661	0.730	2.21
mLoSSI	0.5401	0.670	0.678	1.12
PGA-A	0.645	0.667	0.724	19.1
LSCAM variables				
-Erythema	0.437	0.536	0.626	0.87
-Violaceous/Blue	0.473	0.431	0.710	0.10
-Waxy/white/yellow	0.398	0.502	0.754	0.30
-Lesion Warmth	0.257	0.288	0.448	0.13
-Skin Thickening	0.494	0.460	0.620	0.46

Table 1. Reliability of Localized Scleroderma Cutaneous Activity Measure scoring from one day meeting. Thirteen jLS patient volunteers were evaluated two times in a one day meeting by 14 raters: 13 pediatric rheumatologists, 1 pediatric dermatologist. Patients were evaluated in a different random order by each rater in the two rounds. A maximum of two anatomic sites were evaluated per patient, with these sites identified in advance by one of the investigators (K. Torok). PGA-A was scored from 0-100. The average score of each measure and feature is shown; Erythema and skin thickening were scored from 0-3, other variables were scored from 0-1. For inter-rater reliability, Kendall's coefficient of concordance (W) were calculated. For Intra-rater reliability, Spearman's correlation were calculated for each rater. All reliability values shown were found significant, p <0.0001. LSCAM: Localized scleroderma cutaneous activity measure = disease extension + erythema + skin thickening + violaceous color + waxy white or yellow + tactile warmth. mLoSSI: modified localized scleroderma severity index= 3*disease extension + erythema + skin thickening. PGA-A = Physician global assessment of disease activity

	LSCAM	mLoSSI
Convergent validity: comparison to PGA-A		
-1 day meeting	0.951[1]	0.7765[1]
-12 month CTP pilot study	0.7487[1]	0.7268[1]
Divergent validity: comparison to PGA-D		
-1 day meeting	-0.137	-0.0261
-12 month CTP pilot study	0.4326[1]	0.3495[1]

Table 2. Construct validity of Localized Scleroderma Cutaneous Activity Measure. LSCAM and mLoSSI scores were analyzed in comparison to PGA-A for convergent validity, and to PGA-D for divergent validity in the two prospective jLS cohorts: 13 patient volunteers in a one day meeting, and 44 jLS patients initiating methotrexate treatment in the jLS CTP pilot study. Spearman's rho correlation coefficients are shown. 1p < 0.001. CTP: consensus treatment plan; LSCAM: Localized scleroderma cutaneous activity measure; jLS: juvenile localized scleroderma; mLoSSI: modified localized scleroderma severity index; PGA-A = Physician global assessment of disease activity; PGA-D = Physician global assessment of disease damage

Reliaibity of LSCAM scoring was evaluated in a 1-day meeting where, following a training session, 14 physicians scored 13 jLS patient volunteers twice. Each scorer was given a photo scoring atlas to aid scoring standardization.

Construct validity was determined by comparison to Physician Global Assessment of disease activity (PGA-A) and disease damage (PGA-D) in two cohorts: The patient volunteers as described, and a cohort of jLS patients followed for 12 months on methotrexate treatment (consensus treatment plan (CTP) pilot study). We calculated Kendall's coefficient of concordance to assess inter-rater reliability, and Spearman's rho to assess intra-rater reliability and validity. Levels of 0.2 to < 0.4 were considered poor, 0.4 to < 0.6 moderate, 0.6 to 0.8 good, >0.8 excellent.

Results: A moderate to good level of inter-rater reliability of scoring of LSCAM and mLoSSI was found in both rounds at the meeting (Table 1). A good level of intra-rater reliabiilty of scoring was found for LSCAM, mLoSSI, and PGA-A.

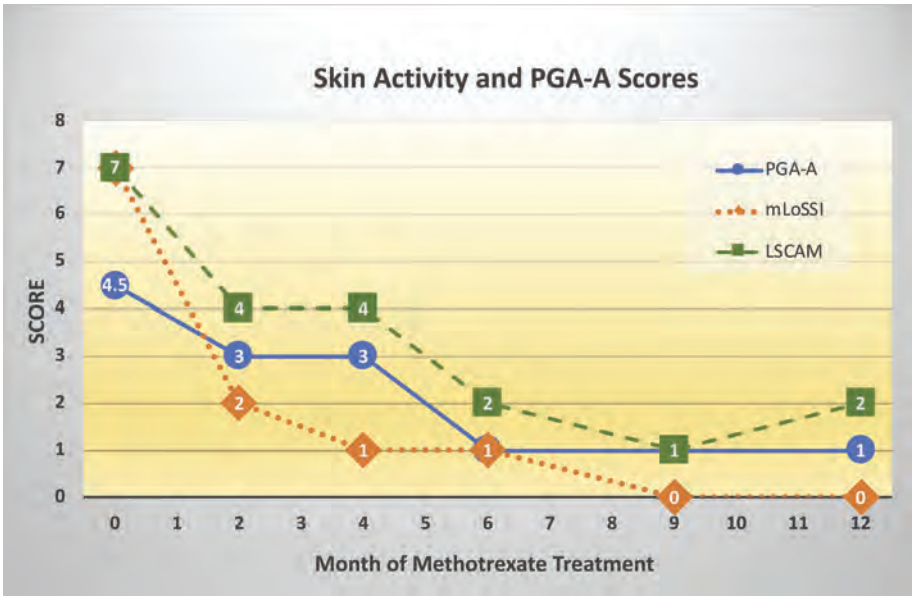

Figure 1. Change in scores for Skin Activity measures and PGA-A over 12 months of methotrexate treatment (jLS CTP Pilot study). Fourty-four jLS patients were monitored for 12 months after initiating methotrexate treatment (one of three methotrexate-based consensus treatment plans). The median LSCAM, mLoSSI, and PGA-A scores at each visit is shown. CTP: consensus treatment plan; LSCAM: Localized scleroderma cutaneous activity measure; mLoSSI: modified localized scleroderma severity index; PGA-A: physician global assessment of disease activity.

Among the individual variables, all except waxy white or yellow and tactile warmth had moderate reliability in both rounds (Table 1). Intra-rater was higher than inter-rater reliabiity (Table 1).

Excellent convergent construct validity was found between LSCAM and PGA-A, and good between mLoSSI and PGA-A in the 1-day meeting (Table 2). Good construct validity was found for LSCAM and mLoSSI in the CTP Pilot (Table 2). Divergent construct validity with PGA-D was shown between LSCAM and mLoSSI in the meeting, but not in the CTP Pilot (LSCAM 0.433, mLoSSI 0.350, Table 2). Scores for LSCAM, mLoSSI, and PGA-A decreased over time in the CTP study, with LSCAM appearing to more closely mirror changes in PGA-A score than mLoSSI (Figure 1).

Conclusion: LSCAM is a reliable and valid measure for assessing cutaneous activity in jLS. The level of inter- and intra-rater reliability of LSCAM was similar to greater than mLoSSI. A similar to higher level of convergent construct validity with PGA-A was found for LSCAM compared to mLoSSI, with LSCAM appearing to track better with PGA-A scores in the 12 month study. Our findings suggest the LSCAM will aid monitoring of LS activity, and facilitate conducting comparative treatment studies.

Disclosure: S. Li, Merck, 3, CARRA, 9, UpToDate, 7, Arthritis Foundation, 2, Scleroderma Foundation, 2; **M. Becker**, CARRA, 9; **S. Hong**, None; **P. Ferguson**, NIH/NIAMS R01AR059703, 1, Novartis, 1; **T. Nyrienda**, None; **T. Andrews**, None; **K. Stewart**, None; **C. Rabinovich**, AbbVie, 2, CARRA, 2, UCB Pharma, 2, Janssen Research & Development, 2; **R. Fuhlbrigge**, None; **T. Mason**, None; **E. Pope**, None; **M. Ibarra**, None; **F. Dedeoglu**, Novartis, 1; **G. Higgins**, None; **R. Laxer**, Eli Lilly Canada, 1, Novartis, 1, Sanofi, 1; **M. Punaro**, None; **K. Torok**, None; **C. Investigators**, None.

Abstract Number: 1169

Three-Dimensional Analysis of Facial Asymmetry in Craniofacial Scleroderma

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Localized scleroderma (LS) is a rare, progressive autoimmune disease of the skin and underlying connective tissue that can result in devastating functional impairment and cosmetic damage in children. Approximately 25% of patients with pediatric-onset LS have the craniofacial (Cf-LS) subtype, with scalp and face involvement known as *en coup de sabre* or Parry Romberg Syndrome. Standardized cutaneous evaluations may be limited for monitoring craniofacial lesions due to deeper tissue involvement. Advanced stereophotogrammetrical imagers create high-resolution 3D craniofacial models that can be manipulated and analyzed to identify degree and location of facial asymmetry, such as seen in Cf-LS. Normative measurements of asymmetry have been suggested. (*Taylor HO, et al. Quantitative facial asymmetry: using three-dimensional photogrammetry to measure baseline facial surface symmetry. J Craniofac Surg. 2014;25(1):124-128*)

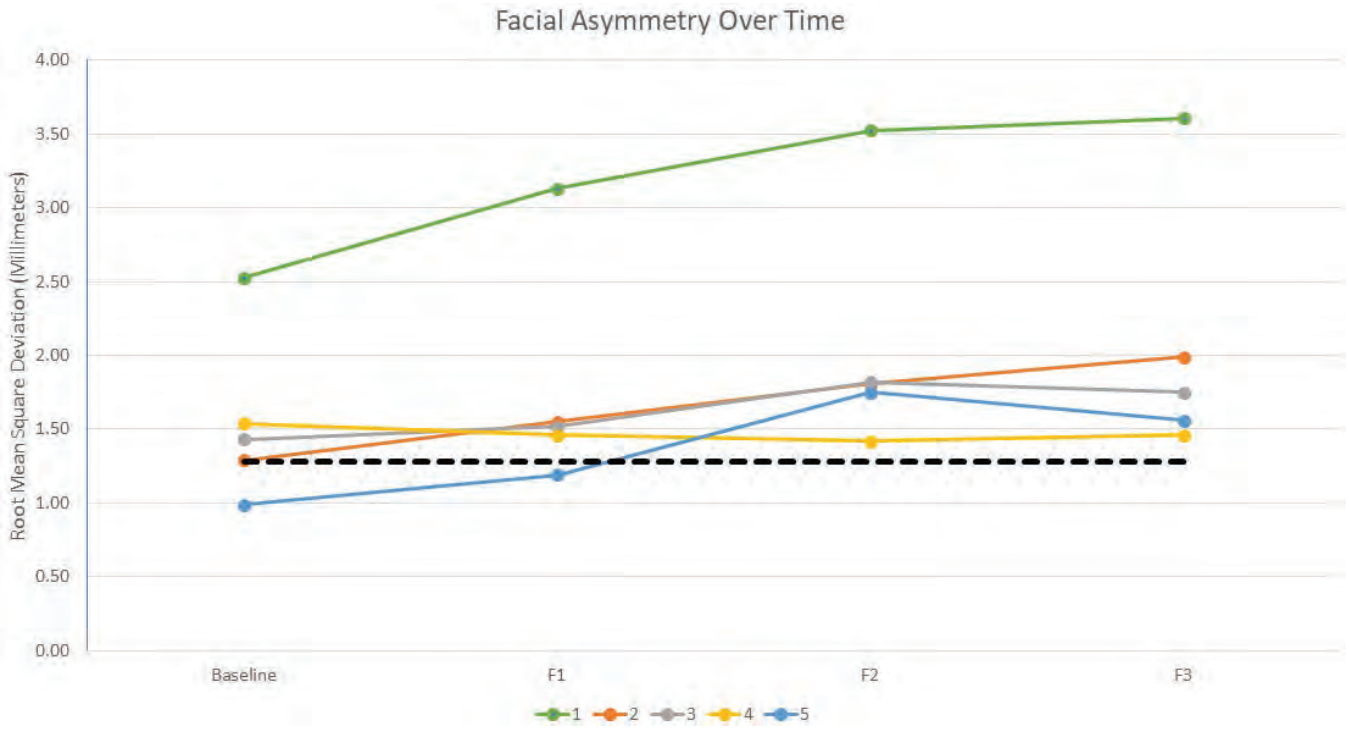

Figure 1. Longitudinal facial asymmetry root mean square deviation (RMSD) values. Baseline and four follow up time points are denoted. The dashed line represents the upper limit of normal RMSD values (1.28mm), defined as 2 standard deviations (0.24mm) above the normative mean (0.80mm) per Taylor et al 2014.

Table 1 Demographics (n=5)

Age (years), mean (range)	
Baseline	14.9 (12.1 - 16.2)
Onset of disease	6.2 (1.2 – 11.2)
Sex	
Female	5
Race/Ethnicity	
White	5
Clinical Diagnosis	
Parry-Romberg Syndrome (PRS)	2
En coup de sabre (ECDS)	2
PRS + ECDS	1
Follow up (months), mean (range)	
Total time	28.6 (17.9 – 35.7)
Between images	9.5 (4.1 – 13.6)
Body Mass Index, mean (range)	
Baseline	27.7 (23.0 – 36.6)
End	28.7 (23.7 – 39.2)
LoSAI, median (range)	
Baseline	2 (0 – 8)
End	0 (0 – 3)
mLoSDI, median (range)	
Baseline	10 (5 – 105)
End	10 (5 – 107)
Treatment#	
Corticosteroids (oral, IV)	(4, 2)
Methotrexate	4
Mycophenolate Mofetil	3
Topicals	3
Abatacept	1
Infliximab	1
Plaquenil	1

#Received at any time point during follow-up

LoSAI, Localized scleroderma activity index; *mLoSDI*, modified localized scleroderma damage index

Table 1 Demographics (n=5)

Our goal was to longitudinally assess patients with Cf-LS to determine the course of facial asymmetry over time. We hypothesize that patients with Cf-LS have facial asymmetry beyond normative data which is maintained that can reliably be detected and tracked longitudinally via computerized stereophotogrammetrical measurements.

Methods: Patients (N=5) with craniofacial scleroderma (*en coup de sabre* and/or Parry Romberg Syndrome) were retrospectively identified in the National Registry for Childhood Onset Scleroderma (NRCOS). Demographic data, medication use, and standardized cutaneous outcomes were extracted from the NRCOS database. This data was paired with clinical 3D facial maps collected via Canfield VECTRA M3 or 3dMD.head.t imaging systems. Image surfaces were analyzed in Vectra Analysis Module. Trimmed and registered images were divided along the plane of maximal symmetry utilizing VAM automated alignment. The hemi-face was then reflected about this plane to superimpose the affected and unaffected sides. Root mean square deviation (RMSD) in millimeters was calculated for each reflection as the main outcome measure. Descriptive statistics were applied.

Results: Patients were followed for a mean of 28.6 months (Table 1). Body-mass index (BMI) was relatively sTable across the follow up period. All patients received systemic immunomodulation during the follow-up period. Stand-

Table 2 Individual longitudinal Root Mean Square Difference values

Patient	Diagnosis	Root Mean Square Difference# (millimeters)			
		Baseline	F1	F2	F3
1	PRS	2.53&	3.13&	3.53&	3.61&
2	PRS	1.29*	1.55&	1.81&	1.99&
3	PRS+ECDS	1.43*	1.52&	1.82&	1.75&
4	ECDS	1.54&	1.46*	1.42*	1.46*
5	ECDS	0.99	1.19	1.75&	1.56&

#Normative mean RMSD = 0.80mm, standard deviation = 0.24mm per *Taylor et al. 2014*

* ≥2 SDs above the normative mean

& ≥ 3 SDs above the normative mean

PRS, Parry Romberg Syndrome; *ECDS*, en coup de sabre

Table 2 Individual longitudinal root mean square difference values

ardized cutaneous activity measurements decreased at follow up, though damage measures were unchanged (Table 1). At baseline, 4/5 patients had facial asymmetry RMSD exceeding 2 standard deviations (SD) of normal and 2/5 exceeded 3 SDs. All patients had facial asymmetry RMSD >2SD at the end of the follow-up period (28 months), and 4/5 exceeded 3 SDs. Asymmetry increased in 80% (4/5) compared to baseline (Table 2, Figure 1).

Conclusion: Facial asymmetry in patients with craniofacial scleroderma is reliably detecTable by 3D stereophotogrammetry. Asymmetry generally worsens over time. BMI and age-related skeletal growth do not appear to influence asymmetry. Conventional cutaneous scoring may fail to detect relevant changes in damage the lead to progressive asymmetry.

Disclosure: D. Glaser, None; **C. Liu**, None; **K. Torok**, None.

Abstract Number: 1170

Exploring the Use of Von Willebrand Factor as a Disease Biomarker in a Cohort of Patients with Juvenile Scleroderma: A Pilot Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile Scleroderma (JScl) is a heterogenous disease characterized by autoimmunity, vasculopathy, and fibrosis. Morbidity and mortality remain high in part due to the continuing limited understanding of disease pathogenesis, and in part due to the lack of validated biomarkers. Von Willebrand Factor (VWF) is a multimeric glycoprotein synthesized in endothelial cells (ECs) with high prothrombotic properties. In Scl, VWF has emerged as a potential biomarker based on evidence indicating that EC injury might be central to the pathogenesis. Cross-sectional studies in adults with Scl indicate: 1) levels of VWF antigen (Ag) in plasma are found elevated compared to healthy controls, 2) baseline levels can predict death and future development of pulmonary hypertension, and 3) presence of high-molecular weight multimers (HMWM), being the most active forms of VWF, may contribute to the significant microangiopathy. Longitudinal studies exploring the role of VWF as a disease biomarker in Scl are lacking and there

Table 1.
Demographic and Clinical Characteristics at Study Entry by Disease Type

	Total N=24	JSSc N=12	JLS N=12	p**
Characteristic				
Age (years)	14.4 [9.4; 16]	15.2 [9.4; 16.9]	13.4 [9.4; 15.4]	0.6
Female	20 (83.3)	11 (91.7)	9 (75)	0.6
Ethnicity†				**0.02**
Hispanic	11 (47.8)	3 (25)	7 (70)	
Non-Hispanic	12 (52.2)	9 (75)	3 (30)	
Body Mass Index (Kg/m^2) †	20.2 [16.6; 24.2]	20.1 [17.6; 24]	22.1 [16.6; 24.3]	0.9
Disease duration (years) †‡	2.0 [1.0; 6.0]	2.3 [1.4; 3.8]	1.0 [0.75; 6.5]	0.38
Time to diagnosis (years)†§	1.2 [0.75; 3.6]	2.0 [0.93; 3.6]	1.0 [0.67; 5.0]	0.5
Follow up time (years) *	0.9 [0.3; 2.3]	2.3 [1.0; 3]	0.5 [0.1; 0.8]	**<0.01**
Off systemic steroids	22 (91.7)	11 (91.7)	11 (91.7)	0.99
Off DMARD	19 (79.2)	9 (75)	10 (83.3)	0.99
VWF antigen (%)	121.5 [88.5; 201]	169 [106; 223]	105 [79; 168]	0.16
ESR (mm/hr)†	17 [11; 27]	22 [15; 30]	12 [4; 27]	0.24
CRP (mg/dL)†	0.5 [0; 0.5]	0.2 [0; 0.5]	0.5 [0.1; 0.5]	0.14
Hemoglobin (g/dL)†	12.5 ± 1.27	12.2 ± 1.25	12.6 ± 1.31	0.41
Albumin (g/dL)	4.5 ± 0.38	4.37 ± 0.24	4.6 ± 0.48	0.11
CPK (U/L)	139 [76; 586]	152 [84; 924]	96 [67; 167]	0.23
LDH (U/L)	233 [184; 268]	254 [214; 283]	206 [173; 228.5]	0.09
ANA positive†	17 (74)	11 (91.7)	6 (54.5)	0.07

JSSc= Juvenile Systemic Sclerosis, JLS= Juvenile Localized Scleroderma, DMARD= disease modifying anti-rheumatic drug, VWF= Von Willebrand Factor, ESR= erythrocyte sedimentation rate, CRP= C-reactive protein; CPK= creatine phosphokinase, LDH= lactate dehydrogenase ANA= antinuclear antibody
Categorical values are represented as n (%) and continuous values as mean ± SD or as median [25;75 percentiles]
**Two-tailed P-values are reported with P<0.05 having statistical significance
†Missing values= 1 for ethnicity, BMI, disease duration, hemoglobin, and ANA; 2 for time to diagnosis; 3 for ESR; 5 for CRP
‡ From date of first presenting symptom to date of study entry
§ From date of first presenting symptom to date diagnosis was made by a rheumatologist

is limited understanding of its use in patients with childhood-onset disease. We aim to describe trajectories of VWF Ag levels over time in patients with JScI and its association with disease type. We also investigate for predictors of persistently elevated levels of VWF Ag, and for the presence of HMWM

Methods: Data of children ages < 18 years, fulfilling the 2007 Pediatric Rheumatology Provisional Classification Criteria for Juvenile Systemic Sclerosis (JSSc) and the Padua Criteria for Juvenile Localized Scleroderma (JLS) were reviewed between 2009-2020. Trends in VWF Ag levels were explored using time series plot. Cross-sectional and longitudinal analysis using linear and logistic regression models with GEE were performed to look for: 1) association of VWF Ag levels with disease type, and 2) independent predictors of persistently elevated levels of VWF Ag defined as a value of >150% in ≥75% of the visits. Leftover samples kept frozen for quality control studies were extracted for VWF multimeric analysis to study the presence of HMWM, and for the Ristocetin Cofactor assay to assess VWF activity [expressed as VWF Activity (Act): VWF Ag ratio]

Results: Twenty-four patients with JScI (50% jSSc, 50% JLS) were studied (Table 1). A negative trend in VWF Ag levels with different patterns in JSSc vs. JLS patients was seen (Figure 1). No statistically significant association was found between VWF Ag levels and disease type. Disease severity was an independent predictor of VWF Ag levels

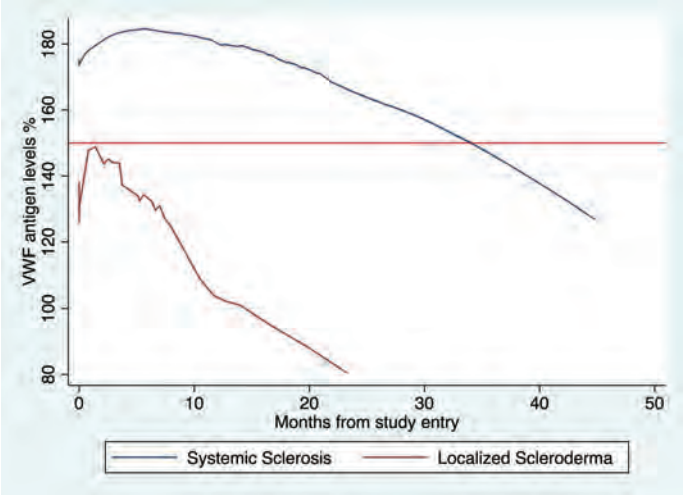

Figure 1. Lowess smoothed time series plot of Von Willebrand Factor antigen levels versus time by disease type. The normal upper cutoff value of VWF is represented by the horizontal red line (=150%). There is a negative trend of VWF antigen levels over time in both groups. Patients with systemic sclerosis have higher and more chronically elevated levels of VWF antigen compared to those with localized scleroderma. VWF=Von Willebrand Factor.

when adjusting for disease type (52.6% ± 23.7%, p=0.03). Skin ulcers (OR 0.25, p=0.01), exposure to DMARDs (OR 0.27, p=0.008), and Non-Hispanic ethnicity (OR 4.0, p=0.04) are independent predictors of persistently elevated levels of VWF Ag. In 8/15 samples (53%), HMWM of VWF were found elevated while median VWF Act: VWF Ag ratio was decreased [0.44 (IQR 0.21; 0.55)]

Conclusion: Consistent with literature in adults, in patients with childhood-onset disease: 1) elevated levels of VWF Ag are found in plasma, 2) higher levels of VWF Ag predict disease severity, and 3) a high proportion of individuals have circulating levels of HMWM of VWF. Larger prospective studies are needed to further characterize VWF and its potential use as a disease biomarker in JScl

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Disclosure: N. Vasquez-Canizares, None; **B. Agarwal**, None; **T. Rubinstein**, None; **D. Wahezi**, None; **M. Reyes-Gil**, None.

Abstract Number: 1171

Under Detection of Interstitial Lung Disease in Juvenile Systemic Sclerosis (jSSc) Utilizing Pulmonary Function Tests. Results from the Juvenile Scleroderma Inception Cohort

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

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Background/Purpose: Juvenile systemic sclerosis (jSSc) has a prevalence in around 3 in a million children. Pulmonary involvement occurs in approximately 40 % in the international juvenile systemic scleroderma cohort (JSScC). Traditionally in jSSc, pulmonary function testing (PFT) with FVC and DLCO are used for screening and computed tomography (HRCT) was more reserved for those with abnormal PFTs. More recently, it has become apparent that PFTs might not be sensitive enough for detecting interstitial lung disease (ILD) in children.

Methods: JSScC database was queried for available patients with recorded PFT parameters and HRCT performed to determine sensitivity of PFTs detecting disease process.

Results: Of 129 patients in the jSScC, 67 patients had both CT imaging and an FVC reading from PFTs for direct comparison. DLCO readings were also captured but not in as many patients with tandem HRCT (n =55 DCLO and HRCT scan). Therefore, initial analyses focused on the sensitivity, specificity and accuracy of the FVC value from the PFTs to capture the diagnosis of interstitial lung disease as determined by HRCT.

Overall, 49% of the patients had ILD determined by HRCT, with 60% of patients having normal FVC (>80%) with positive HRCT findings, and 24% of patients having normal DLCO (> 80%) with positive HRCT findings. Fourteen percent (n = 3/21) of patients with both FVC and DLCO values within the normal range had a positive HRCT finding.

Conclusion: The sensitivity of the FVC in the JSScC cohort in detecting ILD was only 39%. Relying on PFTs alone for screening for ILD in juvenile systemic sclerosis would have missed the detection of ILD in almost 2/3 of the cohort, supporting the use of HRCT for detection of ILD. The cut off utilized, of less than 80% of predicted FVC or DLCO could be too low to exclude beginning ILD.

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Cardiovascular involvement as a clue for diagnosis of Juvenile Systemic Sclerosis *sine scleroderma*

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Background/Purpose: Juvenile Systemic Sclerosis (JSSc) is a rare condition in childhood and its variety with no skin involvement, systemic sclerosis *sine scleroderma* (JSSSS) is anecdotal as only two cases have been reported to date[1,2]. We describe a series of four patients from our Center and compare these six patients with a cohort of patients with standard JSSc.

Methods: Unselected consecutive patients with Juvenile Systemic Sclerosis (JSSc), diagnosed according with the PRES/EULAR/ACR criteria[3] were retrospectively evaluated. For every patient, we collected demographic, clinical and laboratory data, autoantibody profile and treatment. The following clinical-instrumental parameters were considered: skin involvement by the mRodnan Skin Score, Raynaud's phenomenon (RP), chest x-ray, high-resolution computed tomography (HRCT), diffusing capacity for carbon monoxide (DLCO), forced vital capacity (FVC), musculoskeletal involvement, esophageal scintiscan or 24-hour pH-metry, and malabsorption test. Cardiac investigations included

at rest electrocardiography (EKG), cEcho and cMRI. Patients without skin involvement at onset were compared with those with standard JSSc. The association between categorical variables has been investigated with Fisher's exact test. Student T test or Mann Whitnet U test was used to compare numerical variables between the two groups, as appropriate.

Results: Among 47 patients with JSSc, 4 (8.5%) presented with systemic sclerosis *sine scleroderma (JSSSS).* The clinical features of these four patients and of other two, reported in the literature[1,2], were compared with a group of 30 JSSc patients with complete clinical data available. All JSSSS patients, 3 male and 3 female, had cardiovascular involvement as presenting feature, 3 primary myocarditis, 3 secondary to pulmonary arterial hypertension (PAH) and two (33.3%) died after a brief disease course. ANA was positive in all except one reported in 1993[2]. Scleroderma specific antibodies were present in Patient 4/5 tested patients (2 anti-topoisomerase, 1 anti-centromere, 1 anti-RNA polymerase I and III). Altered EKG and cMRI were present in all tested patients; cEcho parameter ejection fraction (EF) was reduced in 4/6 patients. The comparison between the two cohort of patients, JSSSS and JSSc, revealed a significant higher cardiac involvement in JSSSS (100% vs 16.7%, $p< 0.0001$), higher prevalence of EKG, cEcho and MRI abnormalities ($p< 0.001$). All the other clinical and laboratory parameters, including age at onset, sex and delay in diagnosis, were not significantly different in the two groups.

Conclusion: To the best of our knowledge, this is the first case series of patients JSSSS. Cardiovascular involvement represents the most important clinical feature of this subtype and still carries a very high morbidity and mortality rate[4]. Our experience, although in a small cohort, confirms the crucial role of complete rheumatologic work-up in pediatric patients with isolated myocardiopathy or PAH.

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Abstract Number: 1173

No Disease Progression After 36 Months Follow up in the Juvenile Systemic Scleroderma Inception Cohort

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SESSION INFORMATION
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Background/Purpose: Juvenile systemic scleroderma (jSSc) is an orphan disease with a prevalence of 3 in 1 000 000 children. Longitudinal prospective follow up data of patients with jSSc is rare. In the international juvenile systemic scleroderma cohort (jSScC) patients are followed with a standardized assessment prospectively.

Methods: Patients diagnosed according the ACR 2013 criteria for systemic sclerosis were included, if they developed the first non-Raynaud symptom before the age of 16 and were under the age of 18 at the time of inclusion. Patients were followed prospectively every 6 months with a standardized assessment.

Results: 39 patients in the JSScC had 36 months follow up. 80% had a diffuse subtype. 95% of the patients were Caucasian origin and 80% female. Mean disease duration at time of inclusion was 3.5 years. Mean age onset of Raynaud's was 8.8 years and mean age of onset at the first non-Raynaud´s was 9.5 years. The MRSS dropped from the time point of the inclusion into the cohort from 13.9 to 11.8 after 36 months. Pattern of organ involvement did not show any significant change, beside the increase of the nailfold capillary changes from 49% to 73% (p=0.037). No renal crisis occurred. No mortality was observed.

They were positive significant changes in the patient related outcomes assessed on a VAS scale of 0 to 100. The physician global disease activity decreased from 40.0 to 22.1 ($p < 0.001$).

Patients global disease activity decreased from 43.3 to 20.4 and patients global disease damage from 45.0 to 21.7 ($p< 0.001$).

Conclusion: After 36 months follow up, we could observe a significant improvement of patient related outcomes and only one significant change in organ pattern involvement. In a mostly diffuse subset patient population this is a very promising result regarding outcome.

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HEADSS and Shoulders, Knees and Toes: Improving Sexual Orientation and Gender Identity Screening in the Pediatric Rheumatology Clinic

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Background/Purpose: Adolescence is an especially vulnerable time when many rheumatologic conditions first present for diagnosis and management. Adolescence brings unique challenges including those relating to body image, schooling, complexities of interpersonal relationships, compliance with medications, and independence with healthcare needs. Within this population, LGBTQ spectrum adolescents are a population with known health disparities and psychosocial stressors. It is of the utmost importance that providers for adolescent patients conduct appropriate

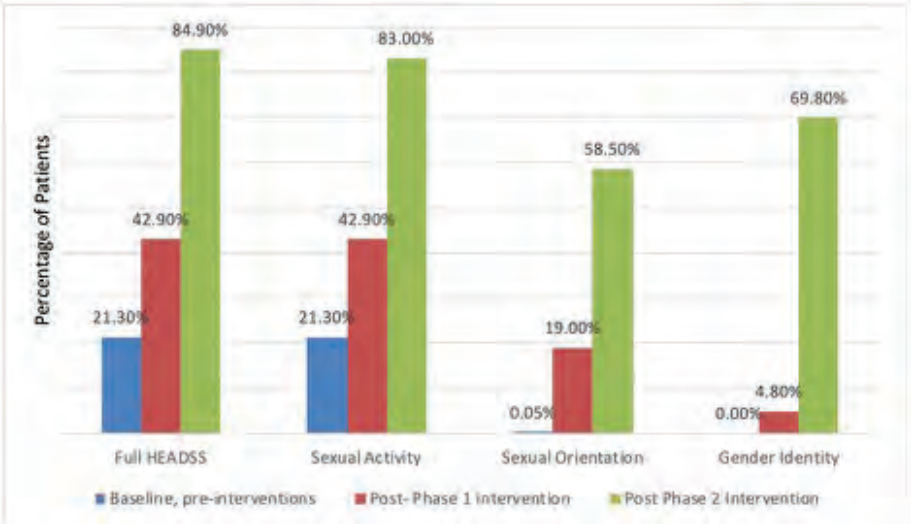

Figure 1. Comparison of Documentation Status Pre- and Post- Phase 1 and 2 Intervention

	Pre-Intervention	Post Phase 1 Intervention	P Value	Post Phase 2 Intervention	P Value
Full HEADSS	16/75 (21.3%)	18/42 (42.9%)	0.0194	45/53 (84.9%)	0.0001, <0.0001
Sexual Activity	16/75 (21.3%)	18/42 (42.9%)	0.0194	45/53 (84.9%)	0.0001, <0.0001
Sexual Orientation	4/75 (0.05%)	8/42 (42.9%)	0.0266	31/53 (58.5%)	0.0001, <0.0001
Gender Identity	0/75 (0%)	2/42 (4.8%)	0.1269	37/53 (69.8%)	0.0001, <0.0001

Table 1. Documentation Status Pre- and Post- Phase 1 and 2 of Intervention

psychosocial screenings to better identify these patients and address their unique healthcare needs. The HEADSS assessment (home, education/employment, activities, drugs, sexuality, suicide/depression) is a validated tool developed to provide a comprehensive psychosocial assessment of adolescent patients. Sexual orientation and gender identity (SOGI) screening can be incorporated within the HEADSS framework. We conducted a quality improvement (QI) project aimed to increase provider screening and appropriate documentation of SOGI data for adolescent patients seen for initial evaluation in pediatric rheumatology clinics at an academic medical center.

Methods: This QI initiative consisted of two phases: 1) a short lecture illustrating the components of the HEADSS assessment, highlighting the importance of SOGI screening, and discussing strategies to incorporate them into routine clinic visits and 2) an electronic note template to be utilized for HEADSS/SOGI documentation. Charts of all patients age 12 and older seen for initial evaluation in pediatric rheumatology clinic were reviewed during a two month window prior to interventions and one month after Phases 1 and 2 for documentation of a full HEADSS assessment, sexual activity and health assessment, sexual orientation, and gender identity. Documentation of HEADSS assessment and SOGI information prior to and after each phase were compared using Fisher's exact test. For all statistical analyses a two-tailed p-value < 0.05 was considered significant.

Results: Chart review included 75 patients pre- intervention for assessment of baseline information, 42 patients post-phase 1 intervention, and 53 patients post- phase 2 intervention (Table 1). There was a statistically significant increase in assessment of all measures in the period immediately following the interventions. The phase 2 intervention not only showed a statistically significant increase from the phase 1 intervention but also from baseline.

Conclusion: Provider education and introduction of an electronic note template greatly enhanced screening and documentation of SOGI data for adolescent patients seen in pediatric rheumatology clinics at an academic medical center. Further studies are needed to assess whether these findings are sustainable and reproducible between other centers.

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Using a Patient-Engaged Approach to Identify Cross-Cutting Disease Factors Impacting Mental Health in Youth with Rheumatologic Disease

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Background/Purpose: Mental health problems are common and often untreated in youth with rheumatologic disease, yet their relationship with disease features is poorly understood. We engaged patients and parents on the research team to identify cross-cutting disease factors impacting mental health in this population.

Methods: An anonymous cross-sectional online survey examined mental health experiences of patients with juvenile arthritis, juvenile dermatomyositis, or systemic lupus erythematous. Youth ages 14-24 years and parents of youth 8-24 years were eligible. The survey was developed with patient and parent advisors, the Childhood Arthritis & Rheumatology Research Alliance (CARRA), and the Patients, Advocates, and Rheumatology Teams Network for Research and Service (PARTNERS). Participants were recruited through the Arthritis Foundation, Lupus Foundation of America, and Cure JM Foundation. Primary outcome was the presence of any clinician or self-diagnosed mental health problem. Exposures of interest included several cross-cutting disease factors: disease duration, active disease status, current steroid medication, history of disease flare following remission, and appearance-altering comorbidities (psoriasis, stretch marks, alopecia, skin ulceration, visible scarring). We used logistic regression models to examine

Table 1. Demographic and disease characteristics of youth with rheumatologic disease

Demographic or Disease Characteristic	All Respondents (n=447)	Any self-reported mental health problem (n=293)	No mental health problem (n=154)	*p*
Age group				
8-17 years	303 (68%)	191 (65%)	112 (73%)	.105
18-24 years	144 (32%)	102 (35%)	42 (27%)	
Female gender (n, %)	350 (78%)	228 (78%)	122 (79%)	.739
Race (n, %)				
White	360 (80%)	234 (80%)	126 (82%)	.470
American Indian/Alaska Native	5 (1%)	3 (1%)	2 (1%)	
Asian	18 (4%)	12 (4%)	6 (4%)	
Black/African American	18 (4%)	9 (3%)	9 (6%)	
Native Hawaiian/Other Pacific Islander	1 (0.2%)	1 (<1%)	0 (0%)	
Other	45 (10%)	34 (12%)	11 (7%)	
Hispanic ethnicity (n, %)	52 (12%)	33 (11%)	19 (12%)	.824
Highest household education level (n, %)				
Less than High School	10 (2%)	8 (3%)	2 (1%)	.640
High School	13 (3%)	8 (3%)	5 (3%)	
Some College	74 (17%)	42 (14%)	32 (21%)	
Associate Degree	45 (10%)	30 (10%)	15 (10%)	
Bachelor Degree	147 (33%)	98 (34%)	49 (32%)	
Advanced Degree	156 (35%)	106 (36%)	50 (33%)	
Household income above federal poverty line (n, %)	387 (87%)	251 (86%)	136 (88%)	.540
Rheumatologic diagnosis				
Juvenile arthritis (n, %)	210 (47%)	135 (46%)	75 (48%)	.130
Juvenile dermatomyositis (n, %)	173 (39%)	109 (37%)	64 (42%)	
Systemic lupus erythematosus (n, %)	64 (14%)	49 (17%)	15 (10%)	
Disease characteristics				
Age at diagnosis in years (mean, SD)	8.88 (4.64)	8.38 (4.89)	9.14 (4.48)	.100
Disease duration in years (mean, SD)	6.40 (4.66)	6.03 (4.76)	6.59 (4.61)	.230
Current active disease (n, %)	235 (53%)	163 (56%)	72 (47%)	.200
Current steroid medication (n, %)	129 (29%)	40 (26%)	89 (30%)	.329
Flare following remission (n, %)	105 (23%)	33 (21%)	72 (25%)	.456
Appearance-altering co-morbidity (n, %)	206 (46%)	150 (51%)	56 (36%)	.003

the association between any clinician or self-diagnosed mental health problems and disease factors for the combined youth/parent sample, and for youth and parents separately. Secondarily, we examined results by mental health problem (depression, anxiety, self-harm/suicidal ideation). Alpha values < .05 were considered significant.

Results: See Table 1 for sample characteristics. 447 respondents included 123 youth and 324 parents; they were not required to be dyads. Combining youth and parent responses, 210 had juvenile arthritis, 173 had juvenile dermatomyositis, and 64 had systemic lupus erythematosus. Those with and without mental health problems were comparable on many demographic and disease factors, although patients with appearance altering comorbidities were more

Table 2. Estimates for regression models predicting clinician or self-diagnosed mental health problems

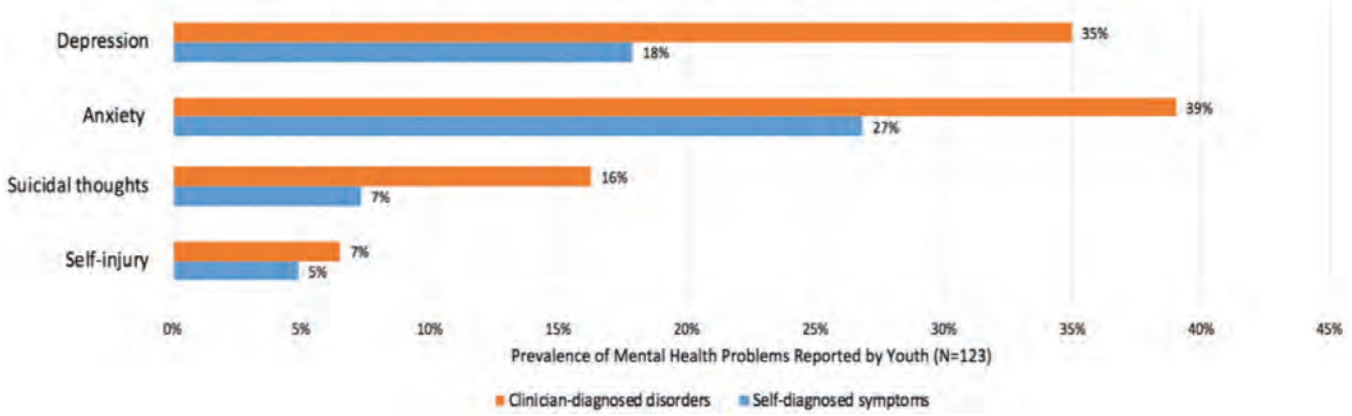
Outcome	Predictor	Odds Ratio, 95% CI *Youth & Parents* n=447	*Parents only* n=386	*Youth only* n=123
Any clinician or self-diagnosed mental health problem	Disease duration	1.03 [.98, 1.08]	1.02 [.97, 1.09]	.99 [.90, 1.08]
	Active disease	1.10 [.75, 1.61]	1.34 [.86, 2.10]	.53 [.24, 1.17]
	Current steroid medication	1.23 [.77, 1.97]	1.15 [.66, 2.01]	1.17 [.46, 2.97]
	Flare following remission	1.10 [.64, 1.89]	.88 [.45, 1.72]	1.61 [.59, 4.38]
	Appearance altering comorbidities	**1.76** [1.18, 2.64]**	**1.83* [1.13, 2.97]**	1.11 [.47, 2.60]
	Gender	.96 [.64, 1.46]	.74 [.44, 1.25]	1.45 [.41, 5.15]
Clinician or self-diagnosed depression	Disease duration	**1.07** [1.02, 1.13]**	1.05 [.99, 1.12]	1.06 [.97, 1.17]
	Active disease	1.25 [.84, 1.88]	1.42 [.88, 2.30]	.78 [.34, 1.80]
	Current steroid medication	1.46 [.90, 2.37]	1.05 [.58, 1.91]	2.57 [.99, 6.70]
	Flare following remission	1.11 [.63, 1.93]	1.07 [.53, 2.16]	.90 [.32, 2.49]
	Appearance altering comorbidities	**1.79** [1.18, 2.73]**	**2.10 **[1.26, 3.53]**	.87 [.37, 2.05]
	Gender	1.56 [.96, 2.53]	1.34 [.76, 2.37]	1.36 [.42, 4.43]
Clinician or self-diagnosed anxiety	Disease duration	1.02 [.97, 1.07]	1.01 [.95, 1.08]	.94 [.84, 1.06]
	Active disease	1.32 [.86, 2.03]	1.57 [.96, 2.59]	.56 [.22, 1.47]
	Current steroid medication	1.35 [.80, 2.28]	1.23 [.67, 2.27]	1.24 [.41, 3.77]
	Flare following remission	.76 [.42, 1.36]	.65 [.32, 1.32]	.83 [.25, 2.72]
	Appearance altering comorbidities	**2.19** [1.39, 3.43]**	**2.24** [1.31, 3.82]**	1.12 [.40, 3.11]
	Gender	1.58 [.98, 2.57]	1.23 [.71, 2.12]	4.86 [.87, 27.03]
Reported suicidal ideation or history of self-harm	Disease duration	1.05 [.99, 1.11]	1.02 [.95, 1.10]	1.05 [.95, 1.15]
	Active disease	.81 [.48, 1.36]	.57 [.29, 1.14]	1.35 [.57, 3.20]
	Current steroid medication	1.42 [.80, 2.53]	1.24 [.58, 2.68]	1.40 [.54, 3.62]
	Flare following remission	**2.46** [1.28, 4.71]**	2.28 [.91, 5.71]	2.02 [.74, 5.52]
	Appearance altering comorbidities	1.11 [.67, 1.86]	1.29 [.66, 2.51]	.89 [.37, 2.11]
	Gender	1.63 [.93, 2.86]	1.04 [.50, 2.14]	N/A[1]

*$p<.05$
**$p<.01$
[1]Gender was omitted from the model as all youth who endorsed reported suicidal ideation or self-harm were female

likely to report mental health problems. Rates of clinician and self-diagnosed depression, anxiety, suicidal thoughts, and self-harm are shown in Figure 1.

Adjusted logistic regression models (Table 2) indicate that having appearance altering comorbidities predicted the presence of a mental health problem in the combined youth/parent sample and in the parent-only sample. In the combined sample, appearance altering comorbidities also predicted depression and anxiety problems, whereas history of flare following remission predicted reported suicidal ideation or self-harm. Within the youth responses, reported depression trended to be more likely among those taking steroids ($p=.053$).

Figure 1. Prevalence of Mental Health Problems for Youth with Rheumatologic Disease



Conclusion: Certain cross-cutting rheumatologic disease factors such as appearance-altering comorbidities are predictive of mental health problems such as depression or anxiety. These findings are helpful for identifying targets for mental health screening in youth with rheumatologic disease, and should be addressed in screening recommendati ons.

Disclosure: A. Danguecan, None; **O. Fawole**, None; **M. Reed**, None; **J. Harris**, None; **A. Hersh**, None; **M. Rodriguez**, None; **K. Onel**, None; **E. Lawson**, None; **T. Rubinstein**, None; **K. Ardalan**, None; **E. Morgan**, None; **A. Paul**, None; **J. Barlin**, None; **R. Daly**, None; **M. Dave**, None; **S. Malloy**, None; **S. Hume**, None; **S. Schrandt**, None; **L. Marrow**, None; **A. Chapson**, None; **D. Napoli**, None; **M. Napoli**, None; **M. Moyer**, None; **V. Delgaizo**, None; **E. von Scheven**, None; **A. Knight**, None.

Abstract Number: 1176

Identifying Targets to Improve the Assessment of Psychosocial Risk Factors in Adolescent Patients: Perspectives from Pediatric Rheumatology Fellows in the United States and Canada

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Adolescent patients cared for in the pediatric rheumatology clinic balance challenges related to psychosocial stressors and physical growth with the complexities of living with a chronic medical condition. Due to the interplay between these factors, it is important that all providers for adolescent patients conduct appropriate psychosocial screenings to better identify at risk patients and address their unique healthcare needs. The HEADSS assessment (home, education/employment, activities, drugs, sexuality, suicide/depression) is a validated tool that provides a framework to comprehensively screen for psychosocial risk factors. The objective of this study was to identify targets to improve psychosocial screening of adolescent patients presenting to the pediatric rheumatology clinic by assessing current practice patterns and perceived barriers to screening by pediatric rheumatology fellows.

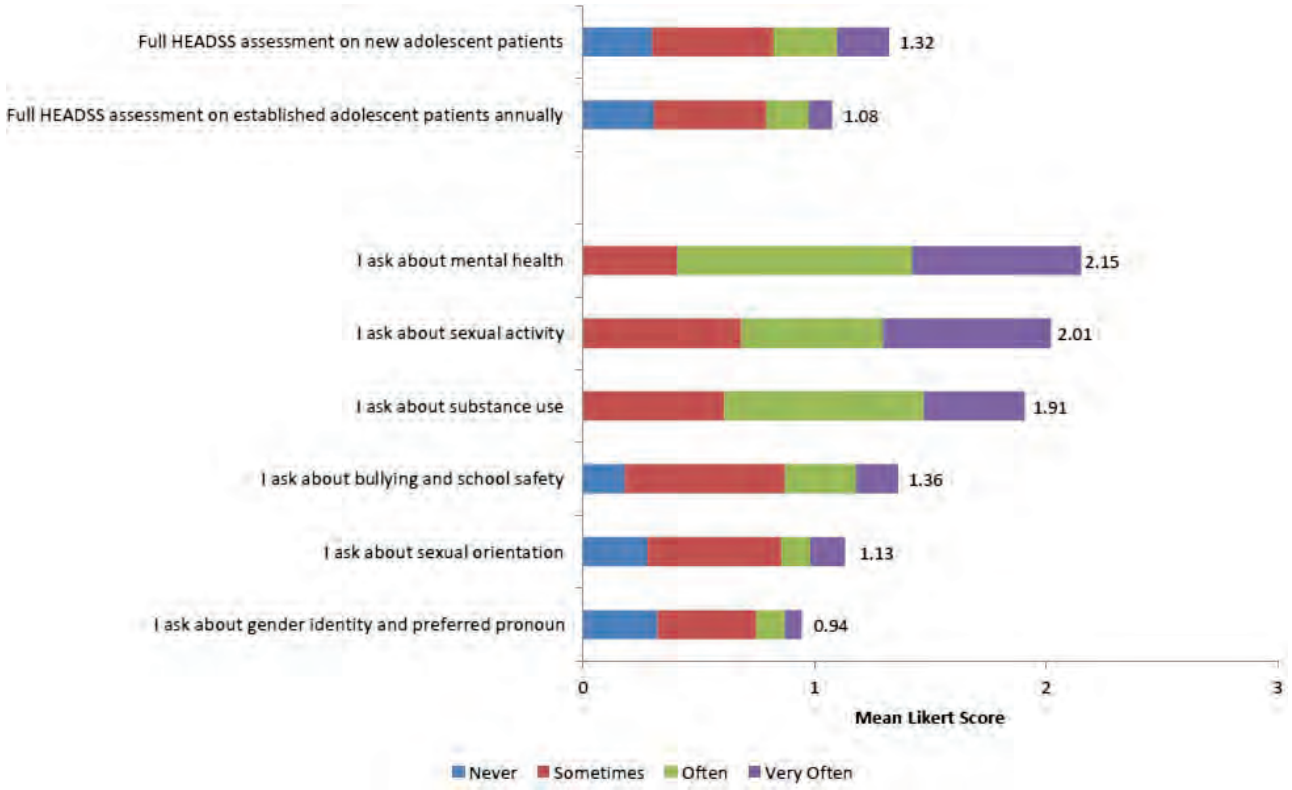

Figure 1. Frequency of pediatric rheumatology fellows performing a full HEADSS assessment and individual components of the HEADSS assessment on adolescent patients. Components of the HEADSS assessment are ranked by mean Likert score for frequency (range 0-3), as well as the proportion of responses for each frequency rating (0 = never, 1 = sometimes, 2 = often, 3 = very often).

Methods: This is a descriptive survey-based study sent to active fellow-in-training members of the Childhood Arthritis and Rheumatology Research Alliance (CARRA). Responders completed a secure web-based survey using REDCap (Research Electronic Data Capture) to assess current practices, beliefs, and barriers regarding the utilization of the HEADSS assessment.

Results: Of the 99 eligible CARRA fellow members, 57 responded (58%) and 53 completed the survey in its entirety. All but two responders are currently training in the United States, and the majority (81%) reported practicing in an urban setting. Sixty-one percent agreed or strongly agreed that a full comprehensive HEADSS assessment should be completed on all adolescent patients seen in the pediatric rheumatology clinic; however, only 38% reported often conducting a full HEADSS assessment on new adolescent patients, and 26% often conducted a full HEADSS assessment on established adolescent patients annually. Frequencies of conducting individual components of the HEADSS assessment are summarized in Figure 1. Of these, sexual orientation and gender identity (SOGI) data were cited as being the least frequently collected information. Barriers to screening are summarized and ranked in Figure 2. The most commonly cited barriers to screening were lack of time and providers not knowing what to do with positive screens. Fifty-seven percent of responders cited interest in receiving additional training in application of the HEADSS assessment. Sixty-five percent cited interest in receiving additional training in collecting SOGI information.

Conclusion: Pediatric rheumatology fellows perceive the importance of assessing psychosocial risk factors in adolescent rheumatology patients but have difficulty completing a full assessment due to lack of time and uncertainty of what to do with a positive screen. In particular, fellows are least likely to ask patients about SOGI information. Potential strategies to overcome barriers include enhanced adolescent and LGBTQ health-related training for pediatric

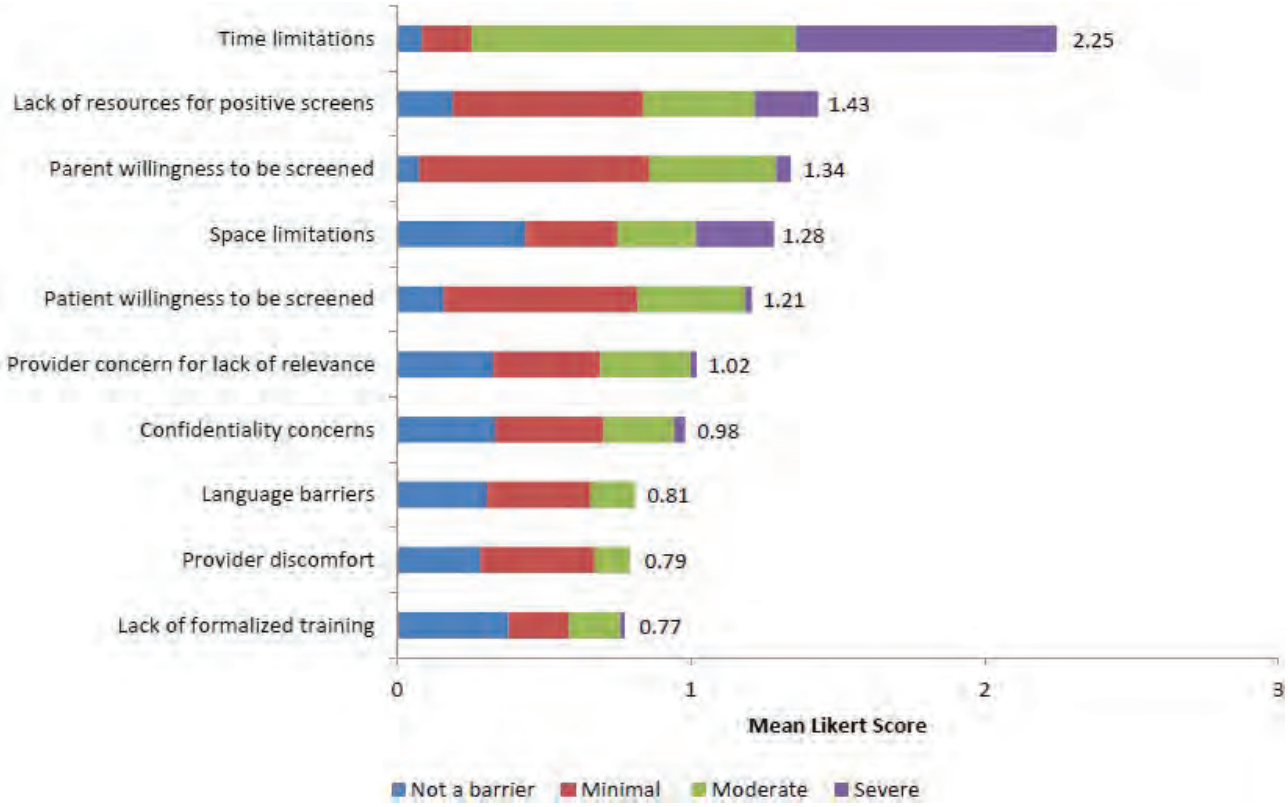

Figure 2. Barriers to performing a HEADSS assessment and collecting SOGI data as perceived by pediatric rheumatology fellows. Perceived barriers are ranked by mean Likert score for degree of perceived barrier (range 0-3), as well as the proportion of responses for each degree of perceived barrier rating (0 = not a barrier, 1 = minimal barrier, 2 = moderate barrier, 3 = severe barrier).

rheumatologists, standardized screening practices, and integration of multidisciplinary teams to develop an algorithm for referral services for positive screens.

Disclosure: J. Spitznagle, None; **N. Balmuri**, None; **A. Adams**, None; **K. Onel**, None; **S. Taber**, None; **N. Pan**, None.

Abstract Number: 1177

Rheumatic Diseases in Mexican Children and Their Psychosocial and Economic Impact on Caregivers

Fernando García Rodríguez[1], Brenda de Jesús Fortuna[2], Ingris Pelaez-Ballestas[3], Enrique Faugier Fuentes[4], Samara Mendieta Zerón[5], Greta Reyes Cordero[6], Sol Jiménez Hernández[7], Ana Villarreal Treviño[8], Jessica Guadarrama[9], Sara Rosiles de la Garza[8], Manuel de la O Cavazos[8] and Nadina Rubio Pérez[10], [1]Hospital Universitario "Dr. José E. González", Mexico City, Nuevo Leon, Mexico, [2]Hospital Infantil De México Federico Gómez, Monterrey, Nuevo Leon, Mexico, [3]Hospital General de Mexico, Mexico, Distrito Federal, Mexico, [4]Hospital Infantil de México Federico Gómez, CDMX, Distrito Federal, Mexico, [5]ISSEMYM Toluca, Estado de México, Distrito Federal, Mexico, [6]Hospital Infantil de Especialidades de Chihuahua, Chihuahua, Chihuahua, Mexico, [7]Hospital Universitario "Dr. José E. González", Monterrey, Mexico, [8]Hospital Universitario "Dr.José E. González", Monterrey, Nuevo Leon, Mexico, [9]Hospital Infantil de México Federico Gómez, CDMX, Distrito Federal, Mexico, [10]Hospital Universitario "Dr. José E. González", Monterrey, Nuevo Leon, Mexico

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical Poster II: Systemic JIA, Autoinflammatory, & Scleroderma

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Pediatric rheumatic diseases (PRD) are a heterogeneous group of disorders. PRD patients and their caregivers face a number of challenges, these include the consequences of the PRD in patients and the impact on multiple dimensions of the caregiver's daily life. Our group developed and validated the CAREGIVERS questionnaire to measure the impact on caregivers of children with PRD.

The objective of this study was to measure the economic, psychological and social impact that PRD has on the caregivers of Mexican children and the factors associated with these impacts.

Methods: This is a cross-sectional study in which primary caregivers were prospectively included between April and November 2019 in four public hospitals of specialized care. Descriptive statistics used used to the sociodemographic characteristics of the participants and the patients' clinics, a univariate analysis was performed with the interview

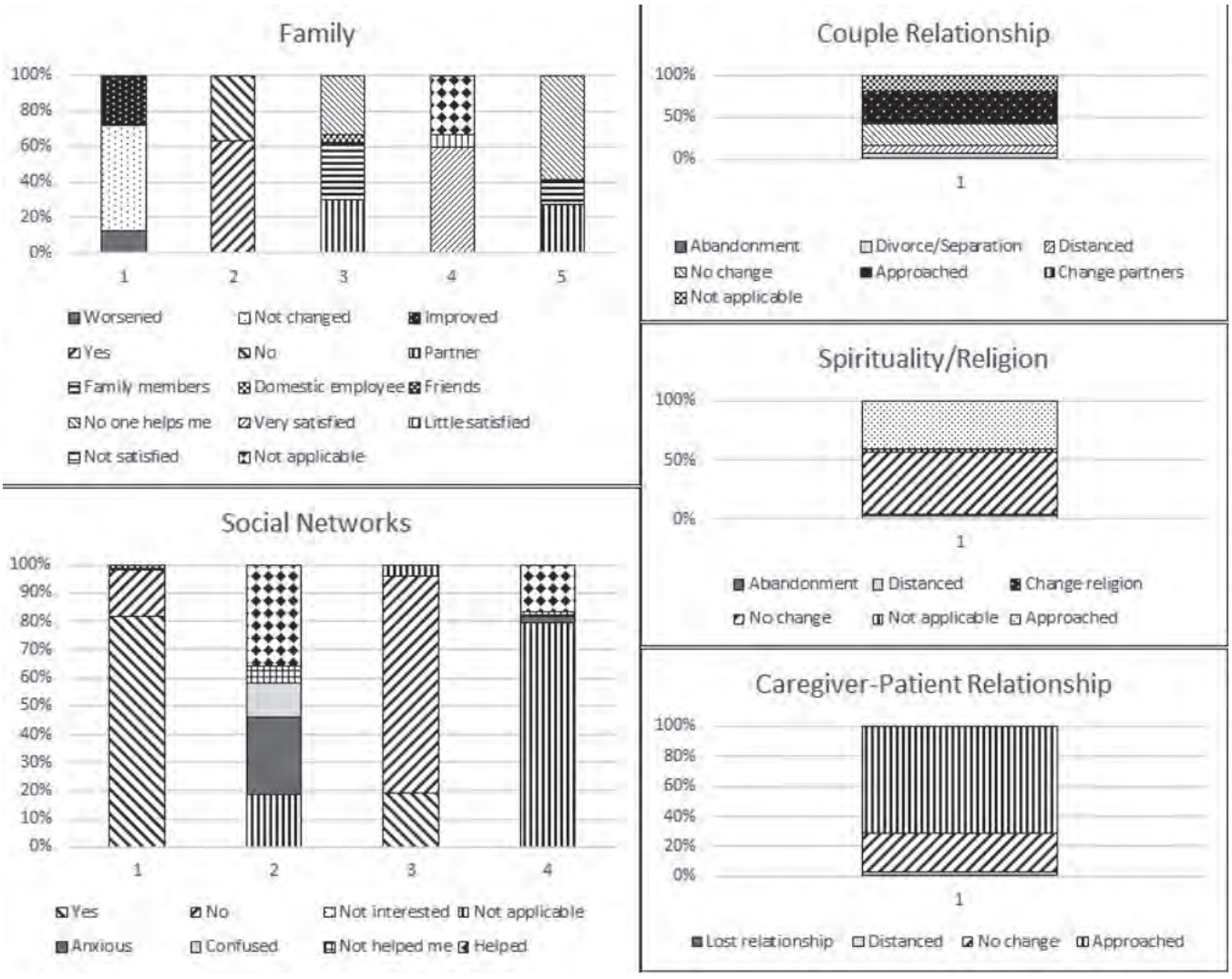

Figure.1 Socio-economic impact in caregivers

responses of the CAREGIVERS questionnaire and the sociodemographic, clinical, and health system variables using the Chi square, Mann-Whitney U, and Kruskal-Wallis tests ($p < 0.05$).

Results: 200 participants were included, women (84.5%) with median age of 38 years; 54.5% cared for patients with JIA, 14% with JDM and 31.5% with JSLE. Most of the caregivers felt concern (42.5%) when learning about the diagnosis, which then was modified by tranquility (44%) when the current feeling was questioned; however, 40 expressed sadness when sharing the patient's PRD (20%) and 39 do not like to do so (19.5%).The main cause of concern is pain (41.5%), followed by difficulty in movement (28.5%) and covering the costs of treatment (25%). Social impact: In 99 caregivers (49.5%), the use of their time changed a lot upon learning the PRD. Social life varied according to the PRD, in JSLE it had a significant change (39.6%), but it did not change in JIA (44%) and it slightly changed in JDM (53.5%, $p < 0.01$).Financial impact: the family financial situation worsened upon diagnosis of the patient in most cases (JIA 63 [57.8%], JSLE 19 [69.8%] and JDM 44 [67.8%], $p = 0.27$). Almost two thirds had had to borrow money, more frequently in JSLE (48 [76.1%] vs JIA 62 [56.8%] and JDM 19 [67.8%], $p = 0.03$); 63 stopped buying medicines due to lack of money (31.5%) and 86 received additional financial support for the treatment (43%).The emotional impact increased in caregivers of male patients. Social dimension showed significant differences regarding PRD, healthcare system, time to reach the center, presence of disability, active disease, cutaneous and systemic manifestations and treatment.

Conclusion: This study highlights a series of lessons learned and the most important is the need to improve opportunities for support, especially regarding financial support, for caregivers of patients with PRD. The study has shown that social status can be devastating in the impact that PRD can have on families. We feel confident that, although all the participants are Mexican, the findings can be generalized to populations with similar characteristics in other regions

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Disclosure: F. García Rodríguez, None; **B. Fortuna**, None; **I. Pelaez-Ballestas**, None; **E. Faugier Fuentes**, None; **S. Mendieta Zerón**, None; **G. Reyes Cordero**, None; **S. Jiménez Hernández**, None; **A. Villarreal Treviño**, None; **J. Guadarrama**, None; **S. Rosiles de la Garza**, None; **M. de la O Cavazos**, None; **N. Rubio Pérez**, None.

Abstract Number: 1178

Associations of Walking Endurance and Speed with Multiple Measures of Subclinical Cardiovascular Disease in Rheumatoid Arthritis

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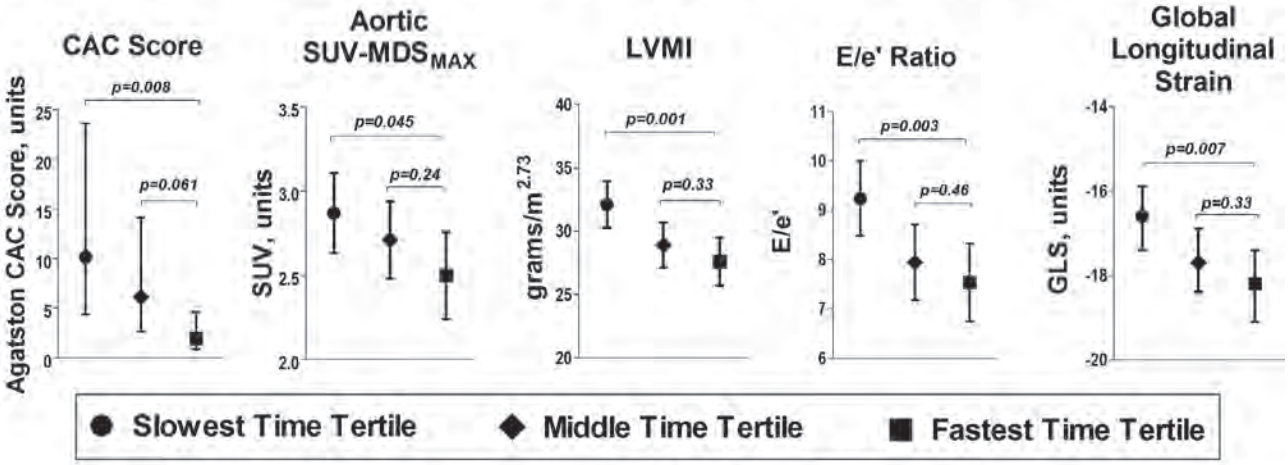
SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The 400 meter timed walk test has been studied as a simple summary measure of fitness that is predictive of mobility limitation and incident cardiovascular disease (CVD) events in older individuals. However, it has not been studied in the context of CVD in RA, a disease associated with physical disability, a heightened risk of atherosclerosis and myocardial dysfunction.

Figure. Association of 400m Walk Completion Time with Coronary Calcium, Arterial Inflammation, and Myocardial Structure and Function



Means and 95% CIs shown. CAC=coronary artery calcium; SUV=standardized uptake variable; MDS=most diseases segment; LVMI=left ventricular mass index; GLS=global longitudinal strain

Methods: RA participants in a study of subclinical CVD underwent cardiac computed tomography (CT) for assessment of coronary artery calcification (CAC), 18-flourodeoxyglucose (FDG) positron emission tomography (PET) CT for assessment of aortic FDG uptake (a measure of atherosclerotic plaque inflammation) and myocardial FDG uptake (a measure of myocarditis), stressed N-13 ammonia PET for assessment of coronary microvascular dysfunction (CMD) and 3D echocardiography for assessment of left ventricular structure and function. Patients also underwent the 400m timed walk test. Generalized linear models were used to model walking endurance (i.e. total walking time) and walking speed with CVD outcomes, adjusting for potential confounders. We explored whether self-reported disability—as captured by the Health Assessment Questionnaire (HAQ)—recreated the same associations as the walk test.

Results: A total of 119 RA patients were studied [mean age=54 ± 13 years; 82% female; 74% seropositive for RF or anti-CCP; median RA duration=7 years; median DAS28-CRP=3.9]. Among these, 103 (87%) completed the walk test. Nine (8%) started but could not complete the walk, and 7 (6%) did not initiate the test. Among completers, those in the slowest time tertile were significantly older, had higher BMIs and more traditional CVD risk factors. RA duration, DAS28-CRP, tender joint count, CRP and HAQ scores were significantly higher in the slower tertile compared with the faster, but DMARD treatment did not differ. Slower completion time was associated with significantly higher CAC, aortic FDG uptake, left ventricular mass index and echocardiographic measures consistent with diastolic dysfunction (i.e. higher E/e' ratio) (Figure). Although ejection fraction did not differ according to walk time, global longitudinal strain was worst in the slower group (Figure). Neither walk time nor walk speed was associated with myocardial FDG uptake or CMD. Modeling HAQ for walk time and walk speed did not recreate the associations. However, modeling potential confounders eliminated the associations of walk time and walk speed with all of the CVD outcomes except walk time with aortic FDG uptake, which remained significantly associated with slower walk time after adjustment for relevant confounders.

Conclusion: Although not independently associated with all CVD outcomes, walking endurance and speed is a potential summary measure of CVD risk that is a composite of multiple traditional and inflammatory risk factors for atherosclerosis and myocardial dysfunction in RA.

Association of 400m Walk Completion Time with Coronary Calcium, Arterial Inflammation, and Myocardial Structure and Function

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Disclosure: G. Braverman, None; **S. Bokhari**, None; **K. Ito**, None; **J. Bathon**, None; **J. Giles**, AbbVie, 5, Bristol-Myers Squibb, 5, Eli Lilly, 5, Gilead, 5, Pfizer, 2.

Abstract Number: 1179

Cardiovascular Risk Assessment with Carotid Ultrasonography in Addition to the Traditional Cardiovascular Risk Factor in Rheumatoid Arthritis: A Case Control Study

Roxana Gonzalez Mazario[1], Jorge Juan Fragio Gil[1], Marta De la Rubia Navarro[1], Cristobal Pavez Perales[1], Samuel Leal Rodriguez[2], Jose Ivorra Cortes[1], Luis Gonzalez Puig[3], Elena Grau Garcia[2], Elvira Vicens Bernabeu[1], F Ortiz-Sanjuan[1], Rosa Negueroles Albuixech[1], Cristina Alcañiz Escandell[2], Jose Eloy Oller Rodriguez[1], Inmaculada Chalmeta Verdejo[1], Isabel Martinez Cordellat[1], Carmen Najera Herranz[1], Ines Canovas Olmos[1], Antonio Cañada Martínez[4] and Jose Andres Roman Ivorra[1], [1]Rheumatology Department. HUP La Fe, Valencia, Spain, [2]Rheumatology Department. HUP La Fe, Valencia, Comunidad Valenciana, Spain, [3]Rheumatology Department. HUP La Fe, Torrente (Valencia), Spain, [4]HUP La Fe, Valencia, Spain

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Characteristic	RA cases n=200	Healthy controls n=111
Age - years	60.56 (10.71)	56.79 (12.15)
Female sex – number (%)	163 (81.5)	73 (65.77)
BMI – value (ds)	26.38 (5.03)	26.2 (5.19)
Daily physical activity	138 (69%)	64 (57.66%)
Smoking habit		
Never Smoked	107 (53.5%)	71 (63.96%)
Ex-smoker	51 (25.5%)	20 (18.02%)
Active smoker	42 (21%)	20 (18.2%)
Race – number (%)		
Caucasian	186 (93)	62 (93.94)
Asian	1 (0.5)	1 (0.9)
Latin	3 (6.5)	9 (8.11)
Comorbidities – number (%)		
High blood pressure	83 (41.5%)	34 (30.63%)
Dyslipidemia	93 (46.5%)	39 (35.14%)
Diabetes Mellitus	16 (8%)	9 (8.1%)
Family history of early CV disease	26 (13%)	9 (8.11%)
Osteoporosis	61 (30.5%)	13 (1.71%)
Gout	1 (0.5%)	6 (5.41%)
Use of Statin	85 (42.5%)	35 (31.53%)
Blood pressure – mmHg	127.2(18.36)/78.67(10.21)	127.77(19.42)/78.28 (10.59)

Table 1. Demographic and clinical characteristics of patients and controls.

Characteristic	RA cases n=200
Disease duration --years	16.98 (11.38)
Erosions (X-Ray of hands/feet)	163 (81.5%)
Seropositive (RF/anti-CCP)	146 (73%)
Extra-articular symptoms	44 (22%)
Intersticial difusse lung disease	10 (5%)
Rheumatoid nodules	14 (7%)
Prednisone use --mg	103 (51.5%)
Median dose of Prednisone last year --mg	2.34 (2.84)
sDMARDs	
Methotrexate	104 (52%)
Leflunomide	29 (14.5%)
Hydroxychloroquine	9 (4.5%)
bDMARDs	89 (44.5%)
TNFi	41 (20.5%)
Abatacept	15 (7.5%)
IL6i (Tocilizumab or Sarilumab)	22 (11%)
Rituximab	11 (5.5%)
JAKi	26 (13%)
Baricitinib	11 (5.5%)
Tofacitinib	15 (7.5%)
Prior bDMARD	68 (34%)
1 bDMARD failure	31 (15.5%)
2 bDMARD failure	17 (8.5%)
3 bDMARD failure	20 (10%)
DAS 28-ESR	3.1 (2.3, 3.9)
SDAI	7.85 (4.04, 13.41)
HAQ	0.88 (0.22, 1.5)
RF (U/mL)	51 (15, 164.5)
Anti-CCP (U/mL)	173 (22, 340)

Table 2. Rheumatoid Arthritis disease characteristics among patients included.

Background/Purpose: To assess the Cardiovascular Risk (CV) in Rheumatoid Arthritis (RA) patients using carotid ultasonography additionally to the traditional CV risk factors.

Methods: A single center cross-sectional case control study was performed. Inclusion criteria were adult patients who fulfilled the ACR/EULAR 2010 RA criteria (cases) and matched healthy adults in terms of age, sex and CV risk factors (controls). Population over 75 years old, patients with established CV disease and/or chronic kidney disease (from III Stage) were excluded. Controls with other inflammatory diseases, pregnant women or any malignancy were also excluded. This study was performed from July-2019 to January-2020.

CV risk assessment included risk factors collection such as serum biomarkers (glucose, total cholesterol, HDL cholesterol, LDL cholesterol, Triglycerides, Creatinine, Glomerular filtrate [CKD-EPI], uric acid, C reactive protein [CRP], Erythrocyte Sedimentation Rate [ESR]), Body Mass Index, life style habits, family history of early CV disease.

The US evaluator was blinded to the case/control condition and evaluated the carotid artery by using B-mode imaging of the arterial wall, color doppler flow analysis, presence of plaques, plaque number and measured the intima-media thickness in both right and left carotid.

Characteristic	RA cases n=200	Healthy controls n=111
Blood test		
Fasting plasma glucose –mg/dL	92.14 (14.98)	93.31 (15.22)
Estimated glomerular filtration rate	84.36 (17.49)	89.41 (15.37)
Uric acid – mg/dL	4.46 (1.2)	4.82 (1.33)
Total cholesterol –mg/dL	197.88 (37.17)	194.77 (35.79)
cLDL –mg/dL	108.79 (34.48)	114.44 (30.93)
cHDL –mg/dL	63.72 (15.66)	56.99 (15.1)
CT/cHDL	3.28 (0.97)	3.77 (1.05)
Tryglicerides –mg/dL	119.56 (63.83)	121.58 (75.08)
CRP –mg/dL	5.46 (8.5)	2.31 (2.32)
ESR –mm/h	20.75 (16.58)	11.25 (7.42)
25-hydroxyvitamin D –ng/mL	31.1 (11.78)	26.26 (9.87)
Ultrasound findings		
Right carotid cIMT	0.78 (0.15)	0.62 (0.11)
Left carotid cIMT	0.77 (0.14)	0.64 (0.12)
Plaques	101 (50.5%)	32 (28.83%)
Bilateral	64 (32%)	11 (9.91%)
Right carotid	17 (8.5%)	7 (6.31%)
Left carotid	20 (10%)	14 (12.61%)

Table 3. Blood test and Ultrasound Results in patients and controls.

Statistical analysis was performed with R software (3.6.1 version) and included a multivariate variance analysis (Manova) and a negative binomial regression adjusted by confounding factors.

Results: Overall, a total of 200 cases and 111 healthy controls were included in the study. Demographical and clinical variables were comparable between cases and controls and are shown in Table 1. In both groups a relationship between age, BMI and high blood pressure was detected (p< 0.001). RA disease characteristics are displayed in Table 2.

US study revealed a higher IMT in both right and left carotid arteries with greater presence of plaques in patients than in controls (CI 95% [1.542; 3.436], p< 0.001). Plaques were found in both carotid arteries in the 32% of cases and 9.91% of controls. The longer duration of RA was related to a higher presence of carotid plaques (95% [1.015; 1.056], p< 0.001). The age was also related to plaque development (CI 95% [1.051; 1.094], p< 0.001) as seen with high blood pressure (CI 95% [1.124; 2.27], p=0.012). Female sex protected against carotid plaques presence (CI 95% [0.367; 0.856], p=0-009). US and blood test results are shown in Table 3.

Conclusion: RA leads to a higher intima-media thickness and this is related to the disease duration. Traditional risk factor may explain only partially the global CV risk in RA. These findings might support that RA acts as an independent cardiovascular risk factor.

Disclosure: R. Gonzalez Mazario, None; **J. Fragio Gil**, None; **M. De la Rubia Navarro**, None; **C. Pavez Perales**, None; **S. Leal Rodriguez**, None; **J. Ivorra Cortes**, None; **L. Gonzalez Puig**, None; **E. Grau Garcia**, None; **E. Vicens Bernabeu**, None; **F. Ortiz-Sanjuan**, None; **R. Negueroles Albuixech**, None; **C. Alcañiz Escandell**, None; **J. Oller Rodriguez**, None; **I. Chalmeta Verdejo**, None; **I. Martinez Cordellat**, None; **C. Najera Herranz**, None; **I. Canovas Olmos**, None; **A. Cañada Martínez**, None; **J. Roman Ivorra**, None.

Abstract Number: 1180

External Validation of a Multi-biomarker-Based Cardiovascular Disease Risk Prediction Score for Rheumatoid Arthritis Patients

Jeffrey R Curtis[1], Eric Sasso[2], Elena Hitraya[2], Cheryl Chin[3], Richard Bamford[3], Rotem Ben-Shachar[3], Alexander Gutin[3], Darl Flake[3], Brent Mabey[3] and Jerry Lanchbury[3], [1]Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, [2]Myriad Autoimmune, South San Francisco, CA, [3]Myriad Genetics, Inc., Salt Lake City, UT

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: A novel score for predicting 3-year risk for CVD events in RA patients combines age, four traditional CVD risk factors (diabetes, hypertension, smoking, history of high-risk CVD event), a personalized assessment of RA-related inflammation based on the multi-biomarker disease activity (MBDA) score and, individually, 3 of its 12 biomarkers, TNF-R1, MMP-3 and leptin (log-transformed). This score was developed and internally validated using patient data from the Medicare database. The purpose of this analysis was to externally validate the MBDA-based CVD risk prediction score in a younger cohort from the Symphony claims database.

Methods: A cohort of patients ≥18 years old with RA diagnosis from a rheumatologist and evidence of an RA-specific treatment, excluding patients with malignancy, past myocardial infarction (MI) or stroke, was created by a third party (Symphony) by matching medical and pharmaceutical claims and linking them to MBDA scores from a database of tests done for routine care. Medicare patients were excluded to avoid overlap with the internal validation cohort. Only the first MBDA test was used for each patient. The study endpoint was time from MBDA testing to first CVD event within a 3-year time horizon. CVD event was defined as MI or stroke, based on ICD-9 or ICD-10 diagnosis codes in hospital claims. Analyses focused on relative risk, not absolute risk, because CVD event data in Symphony may be incomplete. A univariate Cox proportional hazards regression model was fit with the MBDA-based CVD risk score as the sole predictor of time to CVD event to obtain a hazard ratio (HR) estimate (95% CI) and p-values from a likelihood ratio test (LRT). Sensitivity analyses determined HR for patient subgroups, with p-values determined for the interaction between subgroups and the MBDA-based CVD risk score. Using a multivariate Cox proportional hazard regres-

Variable	Median (IQR) or N (%)
Total patients	48,868
Age, years	54 (46-60)
Sex, male	8,940 (18.3%)
Diabetes	7,974 (16.3%)
Hypertension	19,132 (39.2%)
History of high-risk CVD event	6,713 (13.7%)
Smoking	7,487 (15.3%)
CRP, mg/L	4.1 (1.4-11.5)
Leptin, ng/mL	24.3 (10.6-47.1)
MMP-3, ng/mL	21.1 (14.3-36.2)
TNF-RI, ng/mL	1.4 (1.1-1.7)
MBDA score	40 (31-48)
MBDA-based CVD risk score	3.3 (2.8-3.8)

Table 1. Cohort characteristics of RA patients with linked biomarker data and at risk for CVD events.

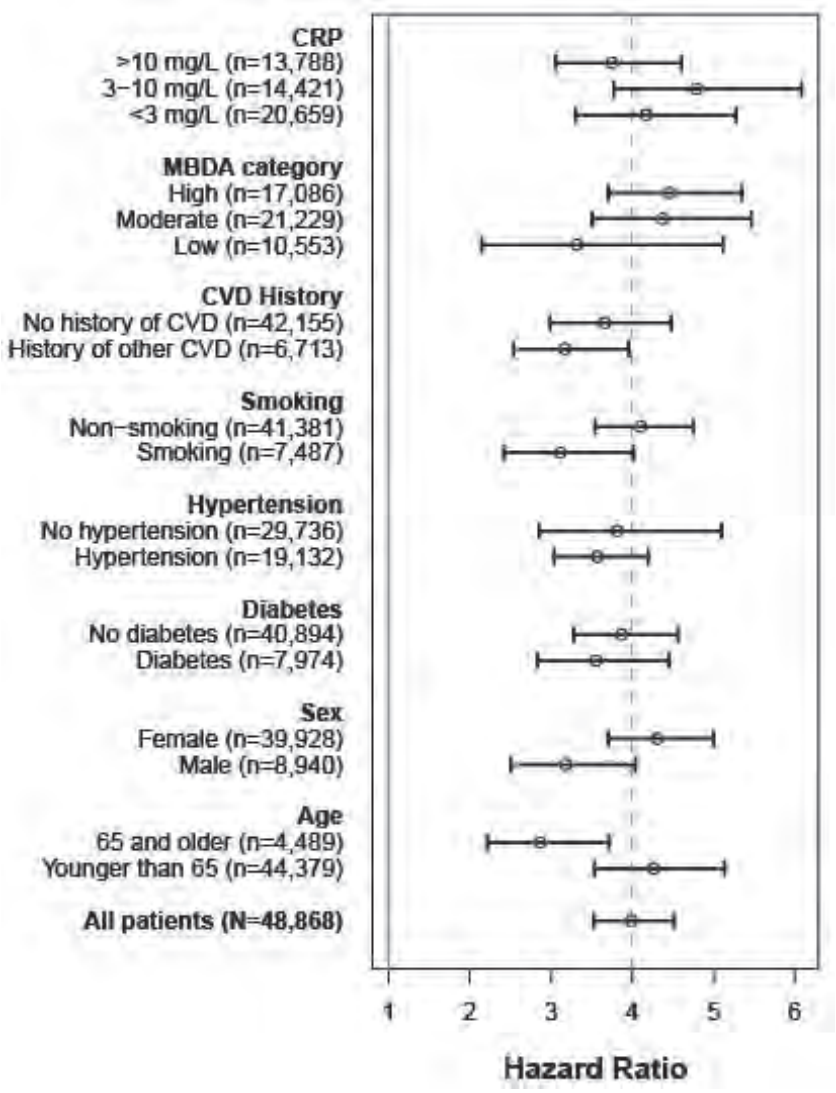

Figure 1. Hazard ratios for CVD event over 3 years in the external validation dataset (N=48,868). Vertical dashed line indicates the hazard ratio for all patients.

sion model, the MBDA-based CVD risk score was compared to a simpler model that included only age, sex, diabetes, hypertension, history of other CVD, smoking and CRP (log-transformed) for ability to predict time to a CVD event.

Results: 48,868 patients with 337 CVD events met eligibility criteria and had linked biomarker data. Mean age was 54.4 years. 81.7% were female (Table 1). Mean follow-up was 24.4 months. The MBDA-based CVD risk score (mean 3.3, IQR 2.8–3.8) was highly significant in univariate analysis, with HR = 3.99 (95% CI: 3.52-4.51, $p = 4.4\times10^{-95}$); i.e., for every 1-unit increase in risk score, the CVD event rate in this cohort was ~4 times as high. Similar results were seen in the subset of 44,379 patients < 65 years old, with HR=4.26 (95% CI: 3.53-5.14, $p = 1.2\times10^{-47}$). In sensitivity analyses, after adjusting for multiple comparisons, there were no significant differences between HR of complementary subgroups (Figure 1). The MBDA-based CVD risk score added significant prognostic information to a simpler, clinical model (HR=2.28 [95% CI: 1.69-3.08, $p = 1.6\times10^{-7}$] after accounting for all other factors).

Conclusion: The MBDA-based CVD risk prediction score has been externally validated in a cohort that is younger than and independent of the Medicare cohort used previously for test development and internal validation.

Disclosure: J. Curtis, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **E. Sasso**, Myriad Genetics, Inc., 1, 3; **E. Hitraya**, Myriad Genetics, Inc., 1, 3; **C. Chin**, Myriad Genetics, Inc., 1, 3; **R. Bamford**, Myriad Genetics, Inc., 1, 3; **R. Ben-Shachar**, Myriad Genetics, Inc., 1, 3; **A. Gutin**, Myriad Genetics, Inc., 1, 3; **D. Flake**, Myriad Genetics, Inc., 1, 3; **B. Mabey**, Myriad Genetics, Inc., 1, 3; **J. Lanchbury**, Myriad Genetics, Inc., 1, 3.

Abstract Number: 1181

Gains in Cardiovascular Risk Knowledge Through Web Based Educational Intervention for Rheumatoid Arthritis Patients

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular disease (CVD) is a leading cause of mortality in rheumatoid arthritis (RA). Ischemic heart disease in RA is often silent and precedes myocardial infarction. Patients' understanding of conventional and RA-specific CVD risks is pivotal to improving CVD mortality in RA. We describe the results evaluating the effectiveness of a web based educational intervention (EI) for RA patients towards improving their CVD risk knowledge.

Methods: 296 consenting RA patients were enrolled through Rush University Rheumatology clinic. All patients completed demographics, Heart Disease Knowledge Questionnaire (HDKQ) and Heart Disease Fact Questionnaire-RA (HDFQ-RA)) at baseline; a higher score on the HDKQ & HDFQ indicates a higher level of knowledge. HDFQ-RA also includes RA specific CVD risk knowledge questions. An educational video was developed specifically for RA patients with emphasis on RA specific CVD risks. Patients in the EI arm (n=150) watched the 28-minute video, followed immediately by HDKQ and HDFQ-RA. All patients (EI and non EI) completed HDKQ and HDFQ-RA at a follow-up visit 3-4 months later. Medical chart reviews were completed for RA and CVD pertinent data. Correct response ratios (CRR) were obtained for both questionnaires. General linear model (GLM) analyses for repeated measure were used to compare within person changes with time and intervention status (EI or non EI) in CVD risk knowledge. Effect sizes (ES) for improvements were calculated.

Results: Mean age was 56.5±13.9 years, and 86% were women. 42% were Caucasians, and 40% were African American. There were no differences in EI or non EI group by age, gender, race, education, smoking, hypertension, dyslipidemia, diabetes, body mass index, disease activity or current use of steroids.

Mean (SD) CRR for HDKQ and HDFA-RA for 296 patients at baseline were 0.59 (0.18) and 0.76 (0.17) respectively. Summary scores for HDKQ and HDFA-RA at baseline, post intervention and 3 month follow up stratified by the study intervention group are shown in Table 1. Patients in the EI arm had significantly higher CRR on HDKQ than those in the non EI at baseline (p 0.007). Improvements in HDKQ were observed at 3 months in both EI (ES 0.35) and non EI (0.25) groups. Only within person changes in HDKQ were observed as significant on GLM. Large improvements were seen in the EI group on HDFQ-RA immediately post EI (ES 0.64), and the improvement in CVD risk knowledge was retained at 3 months post EI follow up (ES 0.48). There were no significant improvements noted in HDFQ-RA in non

Table 1: Correct Response Ratio for CVD risk Knowledge and Effect size as a function of time and intervention status

		Baseline		Post-Intervention				3 month			
	Study Arm	N	Mean ±SD (Median, IQR)	N	Mean ±SD (Median, IQR)	P value*	Effect Size*	N	Mean ±SD (Median, IQR)	P value**	Effect Size**
HDKQ	Non EI	144	0.56±0.20 (0.60, 0.30)		N/A			76	0.63±0.16 (0.67,0.22)	0.03	0.25
	EI	148	0.62±0.16 (0.633, 0.23)	135	0.66±0.17 (0.70, 0.17)	<0.001	0.32	94	0.68±0.15 (0.70,0.17)	0.001	0.35
HDFQ-RA	Non EI	143	0.74±0.20 (0.76,0.15)		N/A			94	0.78±0.15 (0.77,0.23)	0.35	0.09
	EI	147	0.77±0.15 (0.76,0.15)	134	0.88±0.17 (0.92, 0.15)	<0.001	0.64	93	0.85±0.15 (0.92,0.15)	<0.001	0.48
			* Baseline vs Post Intervention								
			** Baseline vs 3 month								

Table 1

Figure 1: Improvement in CVD Knowledge in RA through web based intervention

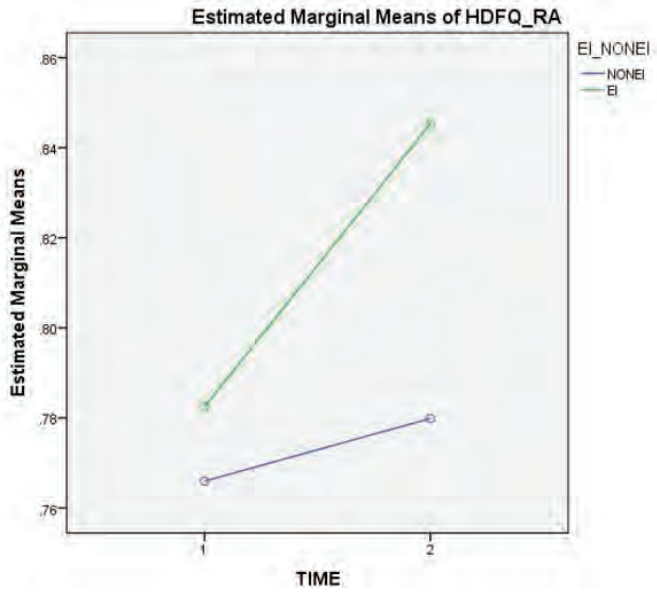

Figure 1

EI group patients at 3 months (ES 0.09). GLM showed both within (time) and between person changes (EI or non EI) to be significant with HDFQ-RA (Figure 1).

Conclusion: Large improvements in CVD risk knowledge (HDFA-RA) were observed among the patients who watched the educational intervention that specifically focused on RA related CVD risks, and the benefits were retained at 3 months. As expected, some improvements in CVD risk knowledge (HDKQ) were observed with time in both groups, as participation in the study and completion of the CVD risk questionnaires alone may have primed the participant's interest in the topic.

Disclosure: M. Jolly, PFIZER, 2, CELGENE, 7, BI, 7, BMS, 7, AURINIA, 7, EVIDERA, 7, LUCIN, 5; **C. O'Brien**, None; **A. Kugasia**, None; **A. Gorfin**, None; **L. Klebek**, None; **J. Fair**, None; **J. Block**, None.

Abstract Number: 1182

Increased Prevalence of Carotid Atherosclerosis in Postmenopausal Women with Rheumatoid Arthritis: A Case Control Study

Dionicio Ángel Galarza-Delgado[1], José Ramón Azpiri López[2], Iris Jazmín Colunga Pedraza[3], **Mayra Alejandra Reyes Soto**[3], Alejandra Pérez Villar[3], Itzel Corina Zárate Salinas[2], Paola Fernanda Frausto Lerma[3] and Salvador Lugo Pérez[2], [1]Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma Nuevo León, Monterrey, Nuevo Leon, Mexico, [2]Cardiology Service, Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma Nuevo León, Monterrey, Mexico, [3]Rheumatology service, Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma Nuevo León, Monterrey, Mexico

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects

Session Type: Poster Session C

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Background/Purpose: Cardiovascular disease (CVD) is the primary cause of mortality in women in developed countries. CVD risk rises with age, yet for women there is a rapid increase in CVD that occurs after the onset of menopause (1). There has been found that there is four to five times atherosclerosis compared to premenopausal women. Adding to traditional CVD risk, subjects with rheumatoid arthritis (RA) have an increased CVD morbimortality because of the inflammatory disorder (2). To detect the burden of CVD, carotid ultrasound has been promoted to identify preclinical atherosclerosis.

Objectives: To determine the prevalence of carotid atherosclerosis and *carotid* intima-media thickness (cIMT) in postmenopausal patients with RA and compare them to matched controls.

Methods: Observational, cross-sectional study. RA patients aged 40 to 75 years that fulfilled 2010 ACR/EULAR criteria with post menopause and matched controls (without RA) were included. Patients with history of previous atherosclerotic CVD, women who undergone menopause due to hysterectomy or cessation of periods other than by a natural cause, women on hormone replacement therapy and having irregular menses were excluded. Clinical history and carotid ultrasound were performed by an expert radiologist. Increased cIMT was defined as ≥0.9 mm and carotid plaque as a focal narrowing ≥0.5 mm of the surrounding lumen. Descriptive analysis was done with frequencies (%), median (q25-q75). Comparisons with Chi-square and Mann Whitney-U test. Binary regression analysis was used to test association an increased cIMT with cardiovascular risk factors and RA diagnosis.

GRAPHIC 1. BASELINE CHARACTERISTICS

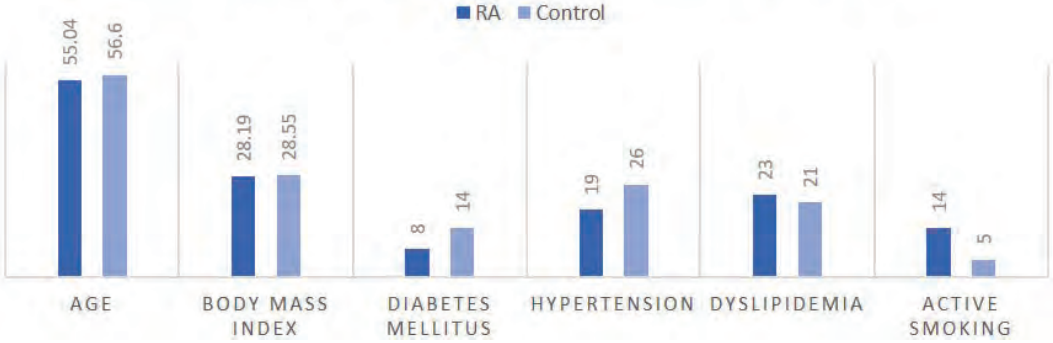

Table 2. Carotid ultrasound findings	RA (N= 70)	Controls (N=69)	p
Any plaque, n (%)	24 (34.3)	17 (24.6)	NS
Right CP, n (%)	19 (27.9)	8 (11.6)	0.01
Left CP, n (%)	17 (25)	13 (18.8)	NS
Any cIMT ≥0.9 mm, n (%)	38 (54.3)	19 (27.5)	0.001
Right carotid cIMT ≥0.9 mm, n (%)	25 (35.7)	10 (14.7	<0.001
Left carotid cIMT ≥0.9 mm, n (%)	31 (44.3)	15 (21.7)	<0.001
CP characteristics:			
Homogeneous n (%)	2 (2.8)	3 (4.3)	NS
Heterogeneous, n (%)	20 (28.6)	16 (23.2)	NS
CP:carotid plaque			

Results: A total of 139 women with established menopause were included. Median of disease duration of RA patients 10.32 (4.5-15.3). Baseline characteristics (Graphic 1). Right carotid atherosclerosis prevalence was found more than twice (19% vs 8%, p=0.01) and an increased cIMT was found higher in postmenopausal RA patients (right 25% vs 10%, p=< 0.001; left 31% vs 15%, p=< 0.001) compared to controls (Table 2). Binary regression showed that the odds of having RA increases three times the risk of having ≥0.9 mm CIMT when adjusted to age, hypertension, dyslipidemia, and active smoking OR 3.0, 95% CI (1.41-6.36) (p=0.004).

Conclusion: Despite the increase in cardiovascular risk in postmenopausal women compared to the general population, women with RA have a higher risk compared to healthy women. Carrying out cardiovascular prevention and management in patients with RA is essential, especially in those who are in a stage of post-menopause.

Disclosure: D. Galarza-Delgado, None; **J. Azpiri López**, None; **I. Colunga Pedraza**, None; **M. Reyes Soto**, None; **A. Pérez Villar**, None; **I. Zárate Salinas**, None; **P. Frausto Lerma**, None; **S. Lugo Pérez**, None.

Abstract Number: 1183

Factors Associated with Incident Heart Failure Subtypes in Patients with Rheumatoid Arthritis Using Electronic Health Record Data

Sicong Huang[1], Tianrun Cai[1], Brittany Weber[1], Zeling He[1], Kumar Dahal[1], Chuan Hong[2], Andrew Cagan[3], Jacob Joseph[4], Seoyoung Kim[1], Daniel H Solomon[1], Tianxi Cai[2] and Katherine Liao[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Harvard Medical School; Harvard T.H. Chan School of Public Health, Boston, MA, [3]Partners Healthcare, Somerville, MA, [4]Brigham and Women's Hospital; Veterans Affairs Boston Healthcare System, Boston, MA

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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Session Time: 9:00AM–11:00AM

Background/Purpose: Heart failure (HF) is a major cause of mortality in rheumatoid arthritis (RA) and is broadly categorized into two subtypes, each with distinct pathophysiology: HF with preserved ejection fraction (HFpEF) and HF with reduced EF (HFrEF). Studies of HF subtypes in RA are limited as the EF data are typically embedded in narrative notes. Natural language processing (NLP) has allowed for efficient extraction of EF data from the electronic health

Table 1. Clinical characteristics of RA patients with HF compared those without evidence of HF. Demographics assessed at RA index date; RA-specific factors assessed between RA index date and end of follow-up; traditional HF factors assessed prior to RA index date.

Clinical characteristics	HF (n=1,007)	No HF (n=7,628)
Age (years, mean, sd)	66.22 (11.92)	54.73 (14.39)
Female gender (%)	69.9	77.8
Caucasian race (%)	81.5	78.2
Seropositive (%)	49.3	58.0
Follow up time (years, mean, sd)	6.29 (5.25)	9.70 (6.55)
RA factors (assessed prior to HF diagnosis date)		
ESR (mm/hr, mean, sd)	42.4 (26.4)	26.1 (20.2)
Methotrexate (%)	26.8	53.3
TNFi (%)	11.8	35.0
Other nbDMARDs (%)	30.6	50.1
Other bDMARDs (%)	2.2	9.6
Corticosteroids (%)	59.2	72.5
Comorbidities associated with HF from general population (assessed prior to RA index date)		
CAD (%)	21.6	7.6
Valvular disease (%)	15.1	6.6
Atrial fibrillation (%)	6.2	1.7
Hypertension (%)	45.1	23.2
Diabetes (%)	4.7	1.3
Dyslipidemia (%)	26.6	17.3
Peripheral vascular disease (%)	6.3	1.7
Stroke (%)	11.9	4.3
CKD (%)	6.8	2.1
Charlson's comorbidity index (mean, sd)	1.19 (2.01)	0.65 (1.46)

CAD, coronary artery disease; CKD, chronic kidney disease; DMARD, disease-modifying anti-rheumatic drug (nbDMARD: non-biologic DMARD, bDMARD: biologic DMARD); EF, ejection fraction; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction;; RA, rheumatoid arthritis; TNFi, tumor necrosis factor alpha inhibitor.

Table 1. Clinical characteristics of RA patients with HF compared those without evidence of HF.

records (EHR) facilitating studies of HF subtypes. The objective of this study was to examine the association between clinical risk factors for incident HF as well as the two subtypes, HFpEF and HFrEF, among RA patients.

Methods: Utilizing a validated EHR-based RA cohort (n=16,248), we identified patients with HF using a published approach (PPV=90%) and extracted EF using NLP from cardiac imaging reports. The RA index date was defined as the first occurrence of RA ICD-9, 10, or NLP code. The HF incident date was the date of the first HF ICD code. patients with HF were classified into HFrEF (EF< 40%) or HFpEF (EF >50%) using the EF value closest to the HF incident date. We excluded patients with < 1-year of EHR data, and those with HF prior to the RA index date. Follow-up started at the RA index date and continued through incident HF or a censoring event (death or last known visit date). Demographics were assessed at the RA index date; known comorbidities associated with HF from the general population were assessed from EHR entry to RA index date; and RA-specific factors were assessed from the RA index date until HF diagnosis or censoring; erythrocyte sedimentation rate (ESR), the most common inflammatory marker avail-

Table 2. Clinical factors associated with incident (a) HF, (b) HFpEF, and (c) HFrEF vs. no HF (reference) among RA patients *.

	All HF		HFpEF		HFrEF	
Clinical factors	**OR**	**95% CI**	**OR**	**95% CI**	**OR**	**95% CI**
Age (years)	1.04	1.03 – 1.05	1.04	1.03 – 1.05	1.04	1.02 – 1.06
Female gender	0.82	0.66 – 1.02	0.97	0.76 – 1.24	**0.43**	**0.26 – 0.70**
RA factors (assessed prior to HF diagnosis date)						
ESR (every 5mm/h)	1.12	1.10 – 1.14	1.12	1.10 – 1.14	1.15	1.10 – 1.20
Methotrexate	0.59	0.48 – 0.73	0.59	0.47 – 0.75	0.48	0.28 – 0.82
TNFi	0.70	0.53 – 0.92	**0.62**	**0.45 – 0.86**	0.93	0.48 – 1.81
Other nbDMARDs	0.72	0.59 – 0.88	**0.69**	**0.55 – 0.86**	0.72	0.43 – 1.21
Comorbidities associated with HF from general population (assessed prior to RA index date)						
CAD	1.61	1.22 – 2.11	1.39	1.02 – 1.88	**3.09**	**1.63 – 5.86**
Valvular disease	1.32	0.98 – 1.77	**1.48**	**1.08 – 2.04**	0.38	0.13 – 1.11
Dyslipidemia	0.78	0.60 – 1.00	0.84	0.64 –1.10	**0.47**	**0.24 – 0.91**
Hypertension	1.45	1.14 – 1.87	**1.52**	**1.17 – 1.99**	1.72	0.95 – 3.11
Diabetes	2.11	1.21 – 3.62	**2.31**	**1.29 – 4.12**	1.71	0.36 – 8.22

* Only variables with significant associations shown. Multivariable logistic regression model adjusted for age, sex, race, RA serostatus, ESR, methotrexate, TNFi, other bDMARD and nbDMARD, corticosteroid, peripheral vascular disease, diabetes, hypertension, valvular disease, CAD, atrial fibrillation, dyslipidemia, chronic kidney disease, stroke, and Charlson's comorbidity index.
CAD, coronary artery disease; DMARD, disease-modifying anti-rheumatic drug (nbDMARD: non-biologic DMARD, bDMARD: biologic DMARD); EF, ejection fraction; HF, heart failure; HFpEF, heart failure with preserved ejection fraction; HFrEF, heart failure with reduced ejection fraction; RA, rheumatoid arthritis; TNFi, tumor necrosis factor alpha inhibitor.

Table 2. Clinical factors associated with incident (a) HF, (b) HFpEF, and (c) HFrEF vs. no HF (reference) among RA patients.

able was averaged from RA index date to either HF event or time of censoring. We tested the association between RA-specific factors with overall HF, HFpEF, and HFrEF using logistic regression adjusting for potential confounders.

Results: We studied 8635 RA patients of which 1007 (11.7%) developed HF during 9.3 (SD 6.5) years follow-up. In this RA cohort, patients with HF were older, more likely to be male, Caucasian, and had more comorbidities compared to those without HF (Table 1).

Higher levels of ESR was associated with a higher overall HF risk and across both subtypes compared to RA patients without HF, while MTX use was associated with a reduced risk in all HF patients, and in HFpEF and HFrEF (Table 2). TNFi and nbDMARD use was associated with a reduced risk of HFpEF but not HFrEF, after adjusting for potential confounders. Comorbidities more strongly associated with HFpEF and not HFrEF included valvular disease, hypertension, and diabetes, consistent with studies from the general population.

Conclusion: In this large cohort of RA patients, we observed differences in risk factors associated with incident HFpEF compared to HFrEF. While TNFi use is not recommended for patients with moderate to severe HF, these data suggest that TNFi's may have a different effect for risk of HF depending on the subtype. Future studies with more detailed drug data are needed to closely examine DMARD use and risk of HFpEF vs HFrEF in RA.

Disclosure: S. Huang, None; **T. Cai**, None; **B. Weber**, None; **Z. He**, None; **K. Dahal**, None; **C. Hong**, None; **A. Cagan**, None; **J. Joseph**, None; **S. Kim**, Pfizer, 1, Roche, 1, AbbVie, 1, Bristol-Myers Squibb, 1; **D. Solomon**, AbbVie, 2, Amgen, 1, Genentech, 1, Janssen, 1, Corrona, 1; **T. Cai**, None; **K. Liao**, None.

Abstract Number: 1184

In a Prospective RA Cohort, Higher Baseline Disease Activity Is an Independent Predictor of Decline in Left Ventricular Diastolic Function

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) patients are at nearly 50% increased risk of heart failure (HF) compared to non-RA patients, despite adjusting for the presence of coronary artery disease, suggesting that RA associated inflammation is an independent contributor to HF. Higher prevalence of diastolic dysfunction as well as significantly higher rate of change in key diastolic parameters (mitral A wave velocity, mitral E/A, and Left Atrial Volume Index (LAVI)) were demonstrated in RA patients without clinical HF vs. controls. While significant associations between baseline patient reported RA characteristics and adverse changes in diastolic parameters have been demonstrated, an association between RA disease activity against baseline and/or change in diastolic function has not yet been elucidated.

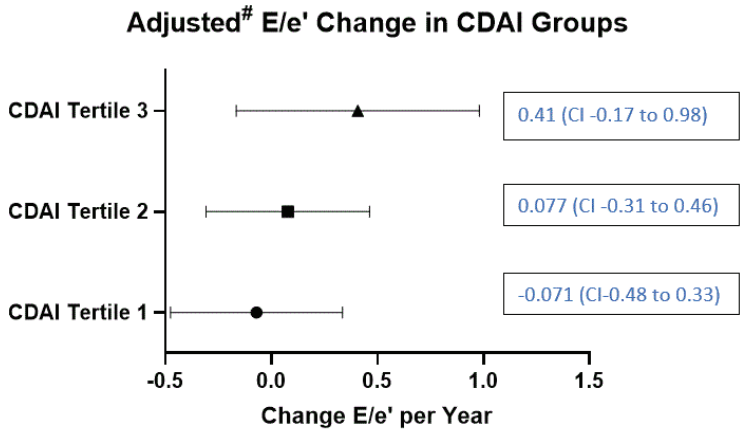
Methods: RA patients (N=163) without clinical cardiovascular disease were enrolled and followed over a 3-to 6-year time period. At baseline, patients underwent echocardiography and assessment of cardiovascular and RA associated disease risk factors. A subset (n=60) underwent repeat echocardiography on a subsequent visit 3-6 years later. Diastolic function was assessed according to 2015 guidelines. Annualized rate of change for each chosen diastolic outcome variable (E/e', E/A, tricuspid regurgitation (TR) velocity, LAVI, Deceleration Time (DT) of E wave) was calculated. Multivariable regression models were used to adjust for biologically plausible confounders identified from univariate regressions.

Table 1. Longitudinal Change in Diastolic Parameters

*Diastolic Parameters	Mean Annualized Rate of Change (SD)	P value
Δ E/e'	0.12 (0.81)	P=0.38#
Δ Septal e' Wave Velocity	-0.11 (0.46)	**P=0.05#**
Δ Lateral e' Wave Velocity	-0.22 (0.47)	**P=0.001##**
Δ E/A	-0.02 (0.07)	**P=0.03##**
Δ E Wave Velocity	-1.05 (3.91)	**P=0.01##**
Δ A Wave Velocity	0.34 (3.67)	P=0.60##
Δ Peak TR Velocity	0.07 (0.24)	P=0.63##
Δ Deceleration Time of E Wave	2.56 (20.22)	P=0.14##
Δ LAVI	0.09 (1.73)	P=0.82#

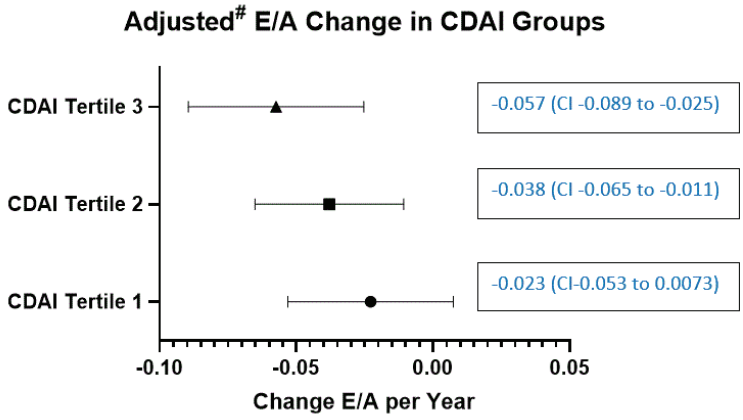
paired t-test; ## Wilcoxon signed rank test

Figure 1A.



#Adjusted for Age, Gender, BMI, SBP, MFR, and Prednisone Use

Figure 1B



#Adjusted for Gender, BMI, Race, LDL, CCP, HCQ use

Results: At least one abnormal diastolic parameter was observed in 59% of the cohort at baseline, and in 69% at follow-up. Significant decline in E velocity (*p=0.01*), lateral and septal e' velocity (*p=0.001 and p=0.05*, respectively) and E/A (*p=0.03*) were observed (*Table 1*). After adjustment for confounders, baseline E/e' was 0.363 units *higher* per square root Clinical Disease Activity Index (CDAI) (*p=0.002*) and 0.539 units *higher* per unit of DAS28CRP (*p=0.005*). Additionally, E/e' *increased* by 0.174 units/year per square root CDAI (*p=0.026)* in adjusted models. As CDAI increased in tertile, greater *increase* in E/e' per year was observed (*See Figure 1A*). Moreover, E/A *decreased* by 0.014 units/year per square root CDAI (*p=0.029*) in a final adjusted model. As CDAI increased in tertile, greater *decline* in E/A per year was observed (*See Figure 1B*).

Conclusion: We report significant adverse changes over time in 2 key diastolic parameters (increasing E/e' and decreasing E/A) in association with higher baseline disease activity, while adjusting for a number of potential confounders. Whether DMARD treatment and subsequent reduction of disease activity impacts baseline and follow up left ventricular structure and function in RA should be elaborated further in prospective/controlled studies.

Disclosure: E. Park, None; **K. Ito**, None; **C. Depender**, None; **J. Giles**, Gilead, 5, Eli Lilly, 5, Bristol Myers Squibb, 5, Pfizer, 2; **J. Bathon**, None.

Abstract Number: 1185

Performance of the MBDA-based CVD Risk Score in RA Patient Groups of Clinical Interest

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SESSION INFORMATION

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Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: A novel risk prediction score combines serum biomarkers from the multi-biomarker disease activity (MBDA) test with clinical information to predict 3-year risk for a cardiovascular disease (CVD) event in RA patients. The CVD risk prediction score was developed and internally validated in a cohort of patients from the Medicare database. We have now examined the performance of the score in subgroups of patients of interest to practicing rheumatologists.

Methods: A cohort of RA patients age ≥40 with ≥1 RA diagnosis from a rheumatologist, without history of malignancy, past myocardial infarction (MI) or stroke was created by linking Medicare administrative data (2006-2016) to MBDA test results obtained during routine care. The cohort was randomly split 2:1 for training/internal validation. The composite CV outcome was MI, stroke or CV death occurring within 3 years. Candidate predictors for inclusion in model training were selected from traditional CV risk factors, RA-related factors and the MBDA score and its 12 biomarkers (log-transformed). Training was conducted using backward elimination. The final risk score algorithm included: age, diabetes, hypertension, smoking, prior history of CV disease, adjusted MBDA score, TNF-R1, MMP-3

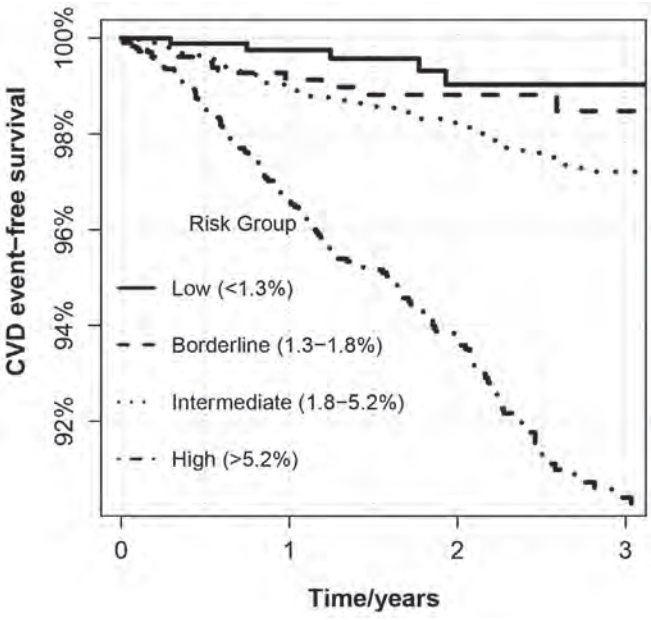

Figure 1. Kaplan-Meier plot for CVD event occurrence by the risk category predicted with the MBDA-based CVD risk score model, validation data (N=10,275)

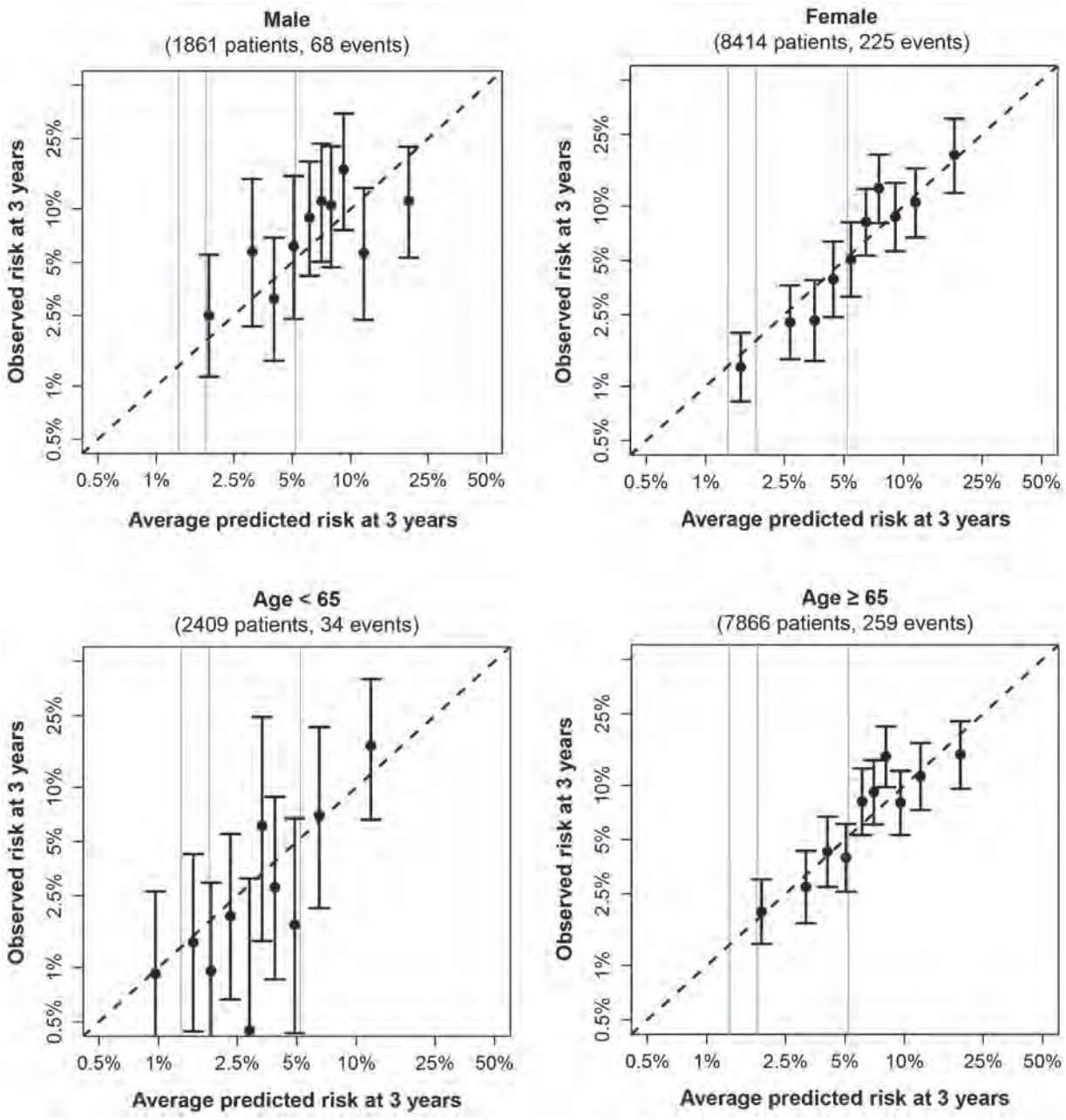

Figure 2. Goodness-of-fit Plots for Demographic Subgroups

and leptin. In the internal validation dataset this MBDA-based CV risk score was evaluated by: 1) Kaplan-Meier (KM) curves of observed event rates over time for patients grouped by the test into the low, borderline, intermediate or high categories of predicted risk and 2) goodness-of-fit plots showing the relationship between observed event rates and predicted risk for patients grouped by CV event-based deciles (based on Kaplan-Meier estimates with 95% CI).

Results: 30,751 RA patients were linked to MBDA test results and eligible for analysis. Mean (SD) age was 68.7 (9.5) years (23.4% < 65 years); 82% were women; mean MBDA score was 41 (14). Comorbidities were frequent (diabetes 39%, hypertension 78%, smoking 24%, history of high-risk CV condition 37%). RA-related features included use of glucocorticoids by 58%, methotrexate 60%, TNFi 33% and other biologics 16%. Median (IQR) 3-year CV risk predicted by the test was 3.4% (2.1%, 5.6%). Based on extrapolation to 10-year risk, 19.6% of patients would be

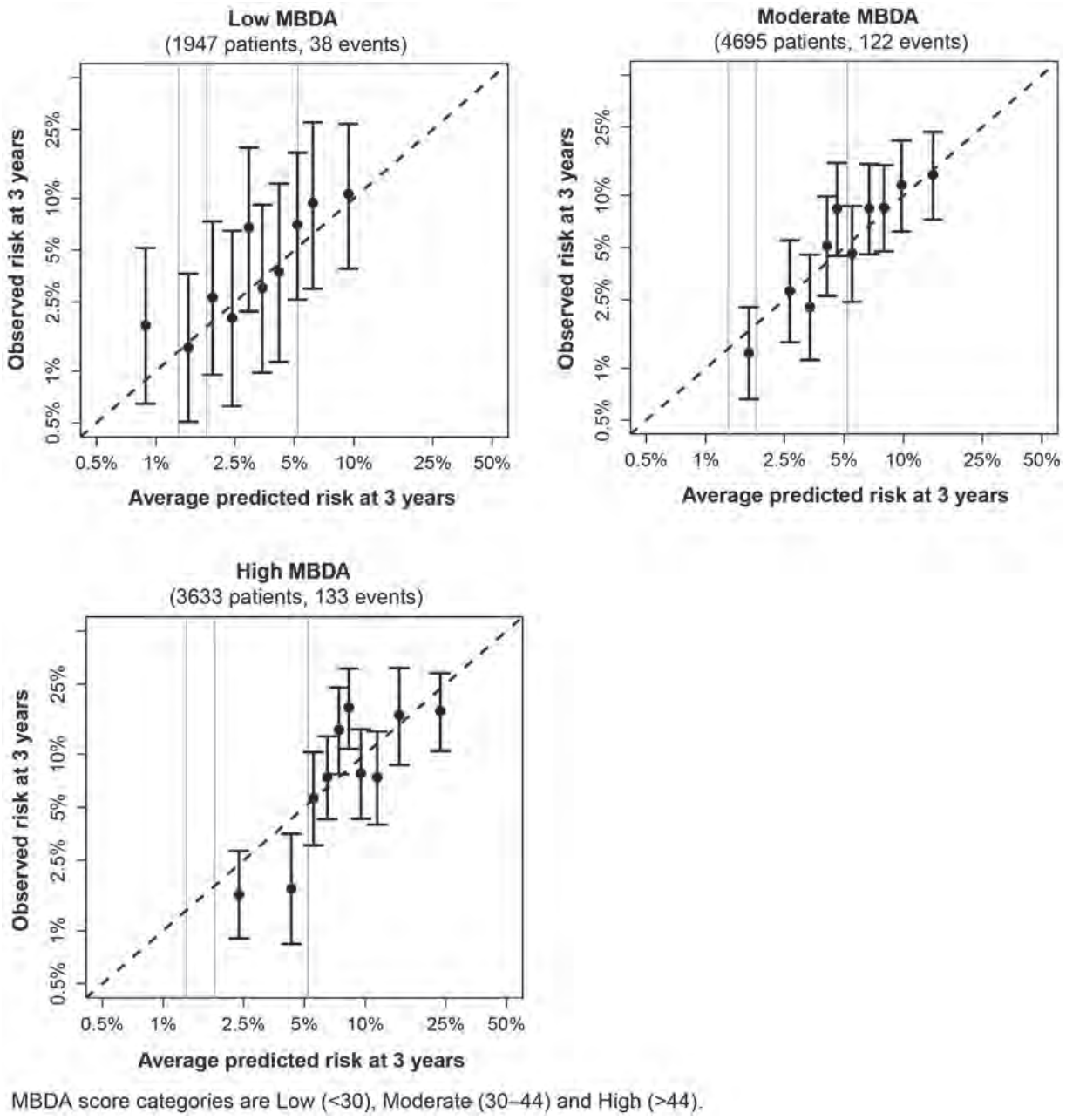

Figure 3. Goodness-of-fit Plots for Disease Activity Subgroups, based on Category of MBDA Score

considered low/borderline, 52.2% intermediate, and 28.2% high risk per ACC/AHA 2018 guidelines. In the validation dataset, CVD event rates increased the most over time for patients assigned by the test to categories of greatest CVD risk (Figure 1). The relationship between predicted CVD risk and observed CVD events demonstrated a good fit in the validation dataset, both overall and among patients grouped by sex, age, diabetes, prior CVD history, statin use, initiation of change of a biologic/targeted therapy and category of MBDA score (Figures 2 and 3).

Conclusion: The MBDA-based CVD risk prediction score, which combines biomarker and clinical variables, discriminated 3-year risk for a CVD event in RA patients. Predicted risk had good fit relative to observed CVD event rates, both overall and in several patient subgroups, including males/females, diabetics, statin users and patients with different levels of disease activity based on the MBDA score.

Disclosure: J. Curtis, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **F. Xie**, None; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1; **E. Sasso**, Myriad Genetics, Inc., 1, 3; **E. Hitraya**, Myriad Genetics, Inc., 1, 3; **C. Chin**, Myriad Genetics, Inc., 1, 3; **R. Bamford**, Myriad Genetics, Inc., 1, 3; **R. Ben-Shachar**, Myriad Genetics, Inc., 1, 3; **A. Gutin**, Myriad Genetics, Inc., 1, 3; **D. Flake**, Myriad Genetics, Inc., 1, 3; **B. Mabey**, Myriad Genetics, Inc., 1, 3; **J. Lanchbury**, Myriad Genetics, Inc., 1, 3.

Abstract Number: 1186

Red Cell Distribution Width and Absolute Lymphocyte Count Associate with Biomarkers of Inflammation and Subsequent Mortality in Rheumatoid Arthritis

Sofi Damjanovska[1], Lenche Kostadinova[2], Ibtissam Gad[3], Sameena Syed[4], Alyssa Lange[5], Corinne Kowal[6], Carey Shive[7], Christopher Burant[8], Brigid Wilson[9], Taissa Bej[9], Nora Singer[10], David Canaday[4], Maya Mattar[11], David Zidar[4] and Donald Anthony[12], [1]Case Western Reserve University/Cleveland VA Medical Center, Cleveland Heights, OH, [2](1) Department of Medicine, VA Medical Center and VA GRECC, Case Western Reserve University, Cleveland OH, Highland Heights, OH, [3]Case Western Reserve/ Cleveland VA Medical Center, Cleveland Heights, OH, [4]Case Western Reserve University/Cleveland VA Medical Center, Cleveland, [5]Cleveland VA Medical Center, Cleveland, [6]Case western reserve university/Cleveland VA Medical Center, ohio, [7](2) Department of Pathology, Case Western Reserve University, ohio, [8]Case Western Reserve University, Cleveland, [9]Department of Medicine, VA Medical Center and VA GRECC, Case Western Reserve University, Cleveland OH, Cleveland, [10]The MetroHealth System, Case Western Reserve University School of Medicine, Cleveland, OH, [11]Department of Medicine, VA Medical Center and VA GRECC, Case Western Reserve University, Cleveland OH, Cleveland, OH, [12]Case Western Reserve University/Cleveland VA Medical Center/ MetroHealth Medical Center, Cleveland, OH

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Peripheral blood red cell distribution width (RDW) and absolute lymphocyte count (ALC) are associated with aging, cardiovascular disease (CVD), and mortality in the general population, and in rheumatoid arthritis (RA) with disease activity. Little is known whether RDW or ALC are associated with specific parameters of inflammation or mortality in the setting of RA. We evaluated relationships between RDW, ALC, CVD, mortality, and plasma markers of systemic inflammation in persons with RA.

Methods: In a retrospective cohort of RA patients treated with methotrexate (MTX) since 2006 at a single VA Rheumatology Clinic with complete blood count lab results available prior to or during treatment (n = 499), we evaluated RDW and ALC prior to and over the course of MTX therapy, with and without the addition of TNF blocker. We further examined the associations between pre-treatment lab values and subsequent mortality. In a subset of these patients (n=64), and in non-RA general medicine clinic controls (n=37) we evaluated relationships between plasma levels of soluble tumor necrosis factor receptor II (sTNF RII), C-reactive protein (CRP), interleukin-6 (IL-6), soluble cluster of differentiation 14 (sCD14), sCD163, Pentraxin 3 (PTX3), Mac-2 binding protein (Mac2BP), and Monocyte Chemoattractant Protein-1 (MCP-1) by ELISA, and RDW and ALC.

Results: High RDW and Low ALC prior to treatment were both associated with increased mortality (log-rank test $p< 0.001$ for RDW > 14; $p=0.018$ for ALC < 1.2). Patients with both low ALC and high RDW had higher mortality than patients with neither or either alone ($p< 0.001$). After adjusting for age and co-morbidities, high RDW remained signif-

icantly associated with mortality (Cox regression model p< 0.001). In the sub-cohort sCD14, sCD163, TNFRII, IL-6, and MCP-1 plasma levels were higher in participants with RA than controls, and RDW levels correlated with PTX3 and MCP-1 levels, while ALC levels negatively correlated with RDW, sCD14, TNF RII, and sCD163 levels. Given these associations between levels of inflammatory markers, ALC and RDW, we evaluated the effect of in vivo MTX and TNF blocker therapy on RDW and ALC levels using longitudinal modelling adjusting for correlated results within patient. We observed MTX to result in increased RDW and lower ALC levels (pre-treatment vs. MTX, p< 0.01 for each), and this was partially reversed by the addition of TNF blocker therapy (MTX vs. MTX + TNFa, p< 0.01 for each).

Conclusion: These findings are consistent with a model wherein inflammatory pathways associated with RA alter erythropoiesis (reflected by RDW) and drive lymphopenia (before and/or after starting DMARD therapy) in association with specific biomarkers of monocyte/macrophage activity. Partial reversal with TNF blockade implies mechanistic/causal linkages. Together, these data suggest immunohematologic dysfunction in the context of RA identifies a poor prognosis, but may be reversible with TNF inhibition.

Disclosure: S. Damjanovska, None; **L. Kostadinova**, None; **I. Gad**, None; **S. Syed**, None; **A. Lange**, None; **C. Kowal**, None; **C. Shive**, None; **C. Burant**, None; **B. Wilson**, None; **T. Bej**, None; **N. Singer**, None; **D. Canaday**, None; **M. Mattar**, None; **D. Zidar**, None; **D. Anthony**, None.

Abstract Number: 1187

Red Cell Distribution Width Is Associated with ASCVD Risk Score and CVD in RA After Initiation of Methotrexate

Ibtissam Gad[1], Sofi Damjanovska[2], Lenche Kostadinova[3], Alyssa Lange[4], Christopher Burant[4], Brigid Wilson[5], Taissa Bej[5], Nora Singer[6], Maya Mattar[7], David Zidar[8] and Donald Anthony[9], [1]Case Western Reserve/ Cleveland VA Medical Center, Cleveland Heights, OH, [2]Case Western Reserve University/Cleveland VA Medical Center, Cleveland Heights, OH, [3](1) Department of Medicine, VA Medical Center and VA GRECC, Case Western Reserve University, Cleveland OH, Highland Heights, OH, [4]Case Western Reserve University, Cleveland, [5]Department of Medicine, VA Medical Center and VA GRECC, Case Western Reserve University, Cleveland OH, Cleveland, [6]The MetroHealth System, Case Western Reserve University School of Medicine, Cleveland, OH, [7]Department of Medicine, VA Medical Center and VA GRECC, Case Western Reserve University, Cleveland OH, Cleveland, OH, [8]Case Western Reserve University/Cleveland VA Medical Center, Cleveland, [9]Case Western Reserve University/Cleveland VA Medical Center/MetroHealth Medical Center, Cleveland, OH

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) has been shown to be associated with increased risk of cardiovascular disease (CVD) and mortality. Red cell distribution width (RDW) represents the variability of red blood cell size. RDW correlates with CVD in the general population as well as in those with spondyloarthritis including psoriatic arthritis. RDW also correlates with RA disease activity as measured by acute phase reactants. We explored the relationship between RDW, CVD and the composite of traditional cardiovascular risk factors, the Atherosclerotic Cardiovascular Disease (ASCVD) risk score, in patients with seropositive RA.

Methods: A retrospective chart review study was conducted at the Cleveland VA Medical Center. Medical records were reviewed for RA ICD10 diagnosis in 2017 in patients being treated with MTX monotherapy for seropositive RA (rheumatoid factor (RF) and/or cyclic citrullinated peptide antibody positive (CCP)). Charts were reviewed for de-

Table 1: Clinical Characersitics		
Race		
African American (%)	20 (21.1%)	
Caucasian (%)	71 (74.7%)	
Hispanic (%)	1 (1%)	
Other (%)	3 (3.2%)	
Sex		
Female (%)	7 (7.4%)	
Male (%)	88 (92.6%)	
	At Start of MTX Treatment	**At Last Available Point**
Age (years) Median	64 (57.5, 70)	73 (69, 80.5)
Years Between MTX Start and Last Available Point Median	9 (6.5, 14)	
Comorbidities		
Coronary Artery Disease (%)	-	30 (31.6%)
Diabetes Mellitus (%)	17 (17.9%)	25 (26.3%)
Hypertension (%)	53 (55.8%)	70 (73.7%)
Smoking History		
None (%)	24 (25.3%)	24 (25.3%)
Prior Smoker but Quit (%)	38 (40%)	39 (41.1%)
Current Smoker (%)	33 (34.7%)	32 (33.7%)
Other CVD Characersitics		
Statin Use (%)	41 (43.2%)	51 (53.7%)
Cholesterol (mg/dL) Median	166.5 (142, 185.5)	156 (132, 187)
LDL (mg/dL) Median	100 (73, 119)	91 (73, 111)
HDL (mg/dL) Median	42 (34, 49)	44 (36, 52)
ASCVD 10- Year Score (%) Median	19.7 (12.6, 28.9)	28.4 (21.3, 38.3)
Seropositivity Titers		
CCP (u/mL) Median	250 (192.3, 250)	-
RF (IU/mL) Median	210 (59.5, 436.5)	-

Table 1 lists the clinical characteristics of the 95 patients at the start of therapy and at the last available time point.

mographic information, concomitant diagnoses of diabetes, hypertension, CVD diagnosis and ASCVD risk factors as calculated by the ASCVD 10-Year Risk Score. RDW, C-Reactive Protein (CRP), hemoglobin, platelet count, and albumin were collected prior to the start of MTX, 6 and 12 months into therapy, and at the last time point available. ASCVD Risk Score was calculated both prior to treatment with MTX and at the last available time point. When calculating ASCVD Risk Score, if age or lipid levels were above or below the limitations of the calculator, either the upper or lower limit values were used, respectively. Correlations were analyzed by Spearman's and differences among groups by Mann-Whitney U (spss v24).

Results: Clinical characteristics of the 95 patients at the start of therapy and at the last available time point are shown in Table 1.

Prior to therapy with MTX: RDW positively correlated with CRP ($r=0.3$, $p=0.007$) and negatively correlated with albumin ($r= -0.4$, $p< 0.0001$), and hemoglobin ($r= -0.4$, $p< 0.0001$), but did not correlate with the ASCVD 10-Year Risk Score ($r=0.2$, $p=0.07$) or CVD at any time point ($p=0.6$).

Table 2: Treatment at the Last Available Time Point	
Treatment	**n**
MTX monotherapy	23
MTX + conventional DMARD (hydroxychloroquine, leflunomide, sulfasalazine)	22
MTX + biologic +/- conventional DMARD	7
Conventional or biologic DMARD, without MTX	27
No TX with DMARD	16
Total	**95**

Table 2 depicts the RA therapy of patients at the last available time point.

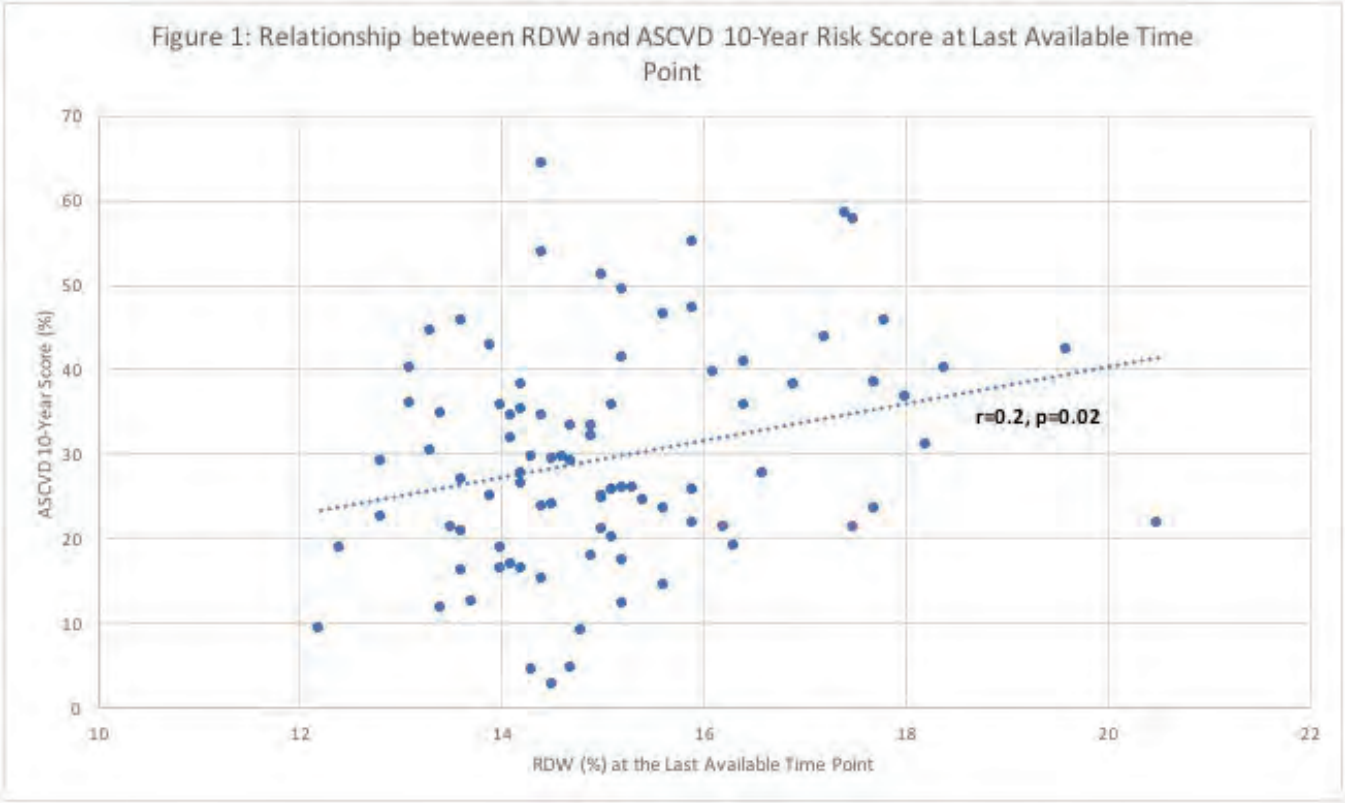

Figure 1 illustrates the linear relationship between RDW and ASCVD 10-Year Risk Score (r=0.2, p=0.02) at the last available time point.

At the last available time point: RA therapy at this time point is shown in Table 2. RA patients with CVD diagnosis had a higher ASCVD Risk Score (p=0.02). Positive correlations were found between RDW and age (r=0.3, p=0.002), and RDW and ASCVD 10-Year Risk Score (r=0.2, p=0.02) (Figure 1). Those RA patients diagnosed with CVD had higher RDW levels at the last endpoint (p=0.01) compared to RA patients without known CVD.

Conclusion: RDW correlates with ASCVD risk score and CVD in other arthropathies. Here we extend this observation to seropositive RA patients during the first year after the introduction of MTX. RDW prior to initiation of MTX associated with parameters of inflammation, including higher CRP, and lower albumin, but not ASCVD risk score or CVD, perhaps making it limited for pre-screening for CVD at the pre-treatment time point. However, at the last available time point post introduction of therapy, RDW correlated with ASCVD Risk Score and was associated with CVD. Fur-

ther study of RDW as a biomarker of CVD in seropositive RA is warranted to help identify those patients who need more CVD risk abatement.

Disclosure: I. Gad, None; **S. Damjanovska**, None; **L. Kostadinova**, None; **A. Lange**, None; **C. Burant**, None; **B. Wilson**, None; **T. Bej**, None; **N. Singer**, None; **M. Mattar**, None; **D. Zidar**, None; **D. Anthony**, None.

Abstract Number: 1188

Serum Anti-malondialdehyde-acetaldehyde IgA Antibody Concentration Improves Prediction of Coronary Atherosclerosis Beyond Traditional Risk Factors in Patients with Rheumatoid Arthritis

Hannah Lomzenski[1], Geoffrey Thiele[2], Michael Duryee[2], Sheau-Chiann Chen[1], Fei Ye[1], Ted Mikuls[2], C. Michael Stein[1] and Michelle Ormseth[1], [1]Vanderbilt University Medical Center, Nashville, TN, [2]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) have increased cardiovascular disease (CVD) independent of traditional risk factors. Oxidative stress is increased in patients with RA and may contribute to CVD. Malondialdehyde-acetaldehyde (MAA) protein adducts are highly immunogenic products of oxidative stress; and anti-MAA antibodies are detecTable in human serum. The aim of this study was to examine the relationship between anti-malondialdehyde-acetaldehyde (MAA) antibody concentrations and CVD risk factors in patients with RA and determine their utility as a predictive biomarker for coronary atherosclerosis.

Methods: In this cross-sectional study, serum concentrations of anti-MAA antibody isotypes (IgA, IgG, and IgM) were measured in 166 patients with RA by ELISA. The relationship between serum anti-MAA antibody concentrations and cardiometabolic measures in RA patients were examined by Spearman correlation. The predictive accuracy of anti-MAA antibodies for presence of any coronary artery calcium (CAC) and high CAC (≥300 Agatston units or ≥75th percentile) were examined by calculating the c-statistic with bootstrapping for internal validation of each fitted logistic regression model.

Results: Serum IgA anti-MAA antibody concentration was modestly associated with increased CAC (Rho=0.18, P=0.02), insulin resistance (Rho=0.18, P=0.03), and decreased high-density lipoprotein (HDL) particle number (Rho=-0.20, P=0.01). Serum IgG and IgM anti-MAA antibodies were not associated with increased CAC. The addition of anti-MAA IgA antibody concentration as an interaction term with ACC/AHA 10-year risk score improved the c-statistic from 0.83 to 0.85 for prediction of presence of CAC and improved the c-statistic from 0.72 to 0.75 for prediction of high CAC.

Conclusion: Anti-MAA IgA concentration is significantly associated with several non-traditional cardiovascular risk factors in patients with RA. Anti-MAA IgA concentration may aid in prediction of elevated atherosclerotic cardiovascular disease and risk stratification when added to standard measures of cardiovascular risk.

Disclosure: H. Lomzenski, None; **G. Thiele**, None; **M. Duryee**, None; **S. Chen**, None; **F. Ye**, None; **T. Mikuls**, Horizon Therapeutics, 2; **C. Stein**, None; **M. Ormseth**, None.

Abstract Number: 1189

Serum High-sensitive Cardiac Troponin at Baseline Predict Cardiovascular Events in Rheumatoid Arthritis and Osteoarthritis

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects
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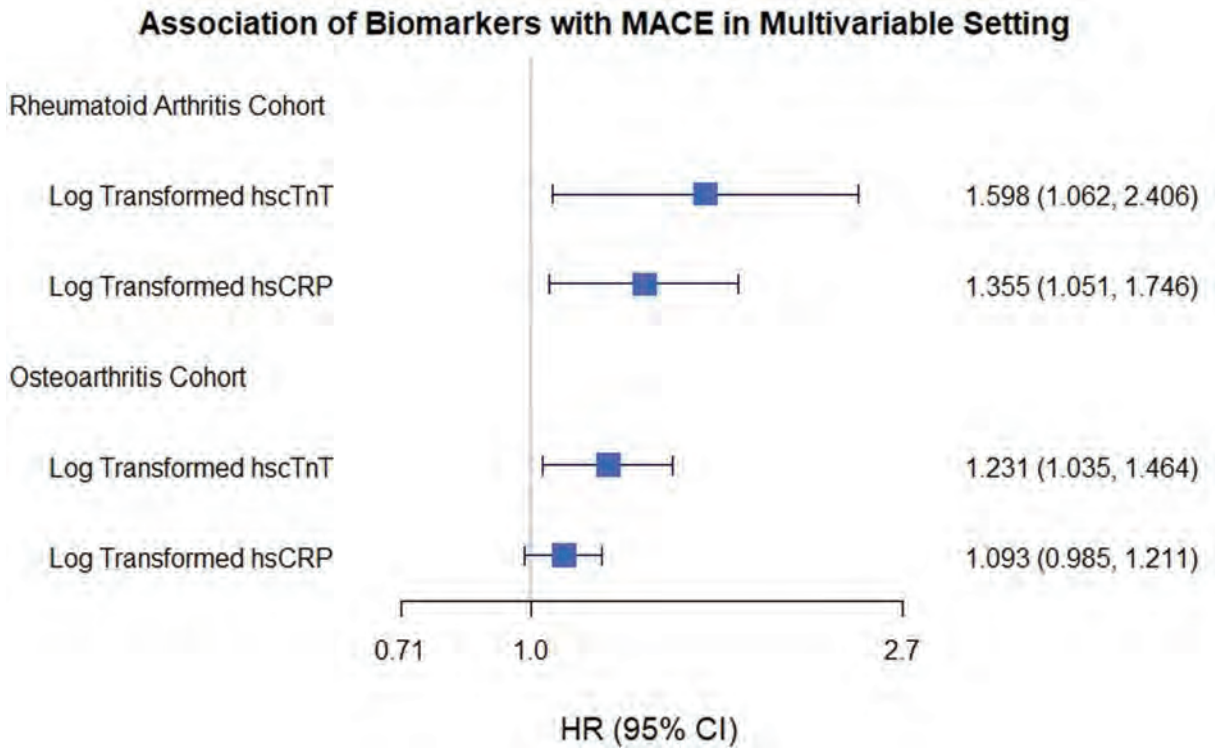
Background/Purpose: In rheumatoid arthritis (RA), excess mortality and inflammation has been attributed to cardiovascular (CV) diseases. High-sensitivity cardiac troponins (hscTnT) allow measurement of cardiac troponin concentrations below conventional levels of detection, and can be used to assess the severity of subclinical myocardial damage. Meanwhile, high-sensitivity C-reactive protein has traditionally been applied for CV risk stratification. We evaluated the prognostic relevance of hscTnT and hsCRP in RA and osteoarthritis (OA) patients enrolled in the PRECISION biomarker sub-study.



Methods: The PRECISION trial was a randomized, controlled non-inferiority clinical trial conducted worldwide involving patients who had RA or OA and with increased CV risk. We measured hscTnT (Roche Gen 5 STAT) and hsCRP (Roche) in a subset of 636 RA and 6,269 OA patients who participated in a biomarker sub-study. The primary CV outcome was major adverse cardiac events (MACE) which is defined as CV death, non-fatal myocardial infarction or non-fatal stroke, re-vascularization, hospitalization for unsTable angina or transient ischemic attack) with at least 18 months of follow-up. Multivariable Cox proportional hazards models were developed with age, gender and baseline status of the following: CAD, diabetes, hypertension, and smoking status as covariates.

Results: In the study cohort, mean age was 63.6±9.4 years, 58% were female, 80% Caucasian, and 32.7% were aCCP positive in the RA cohort. In the total cohort, 17.8% had known coronary artery disease, 36.5% diabetes, and 80% hypertension. The median baseline hscTnT was 6.3ng/L (IQR 3.6, 10.3) and was similar between the cohorts: 5.6ng/L [IQR 3.0, 9.1] in RA and 6.4ng/L [IQR 3.6, 10.3] in OA. We observed that baseline hscTnT was a significant predictor of MACE during follow-up in the RA cohort (HR 1.60, 95%CI 1.06, 2.41), as well as in the OA cohort (HR 1.23, 95%CI 1.04, 1.46, see Figure). In contrast, there was weaker association between baseline hsCRP levels and MACE in RA (HR 1.36, 95% CI 1.05, 1.75) and no significant association in OA (HR 1.09, 95% CI 0.99, 1.21).

Conclusion: In our study cohort, baseline hscTnT was independently associated with major adverse cardiovascular events in both RA and OA. There was a stronger association for both hsCRP and hscTnT in the RA cohort compared to the OA cohort. Further prospective studies addressing the predictive role of hscTnT for CVD events in patients with OA and RA can help expand preventative treatment strategies.

Disclosure: M. Husni, Abbvie, 5, BMS, 5, Janssen, 5, Pfizer, 5, Regeneron, 5, Novartis, 5, Lilly, 5, Pfizer, 2, PASE questionnaire, 7, National Psoriasis Foundation, 6; **D. Solomon**, AbbVie, 2, Amgen, 1, Genentech, 1, Janssen, 1, Corrona, 1; **M. Shao**, None; **K. Wolski**, None; **S. Nissen**, Pfizer, 2, Pfizer, 2; **S. Hazen**, Roche Diagnostics, 2, P&G, 2, 5, 7, Cleveland HeartLab, 7; **W. Tang**, Sequana Medical AG, 5.

Abstract Number: 1190

Sex Differences in Cardiovascular Disease Prevention in Patients with Rheumatoid Arthritis: World-wide Data from the SURF-RA

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects
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Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with 2-fold increase in risk of cardiovascular (CV) disease. Extensive evidence from the general population suggests that control of CV risk factors helps in reducing CV morbidity and mortality. However, CV risk factor screening and management has been suboptimal both in the general population and in patients with RA. We aimed to establish whether there is a difference in CV risk factor screening and control of CV risk factors in RA by sex globally, and whether RA characteristics affect the likelihood of CV screening in women and men.

Table 1. Cardiovascular risk factor measures overall and by sex in patients with RA

Characteristic	Overall	Women	Men	P value[X]
Lipid panel available, n (%)*	9553 (66)	7055 (66)	2444 (67)	0.33
- Total cholesterol <174 mg/dL, n (%)**	3012 (32)	1980 (29)	1015 (42)	<0.0001
- LDL-C < 100 mg/dL, n (%)	3229 (36)	2308 (34)	903 (39)	<0.0001
BP panel available, n (%)*	10857 (75)	8099 (75)	2708 (74)	0.05
BP<140/90 mm/ Hg, n (%)**	7609 (71)	5820 (72)	1752 (65)	<0.0001
HbA1c available, n (%)*	2254 (16)	1679 (16)	571 (16)	1.00
HbA1c < 7.0%, n (%)**	1992 (88)	1499 (89)	489 (86)	0.02
CV Health Index Score, n (%)#				<0.0001
- Poor (<3)	338 (13)	249 (12)	89 (17)	
- Intermediate (3-4)	1516 (59)	1175 (58)	339 (64)	
- Good (>4)	705 (28)	598 (30)	105 (20)	

Abbreviations: TCH=total cholesterol; LDL=low density lipoprotein; BP=blood pressure; HbA1C=hemoglobin A1C; CV=cardiovascular
*n (%) = number (%) of patients with available measures; **n (%) = number (%) of patients with normal measures, among those with available measures; [X]comparison between women and men; #calculated as a sum of controlled CV risk factors out of the following six: smoking, BMI, physical activity, BP, LDL-C and HbA1c

Table 2. Association of RA disease characteristics with cardiovascular risk factor assessment *

Variable	Lipid panel Odds ratio (95%CI)			Blood pressure Odds ratio (95%CI)			HbA1C Odds ratio (95%CI)		
	All	Women	Men	All	Women	Men	All	Women	Men
RA disease duration	1.09 (1.03-1.15)	1.11 (1.05-1.19)	1.02 (0.91-1.14)	1.06 (1-1.12)	1.08 (1.02-1.16)	1 (0.9-1.11)	0.99 (0.91-1.07)	1 (0.91-1.1)	0.92 (0.76-1.11)
RF-positive	1.06 (1.02-1.11)	1.09 (1.03-1.14)	0.99 (0.91-1.09)	1.16 (1.11-1.22)	1.17 (1.11-1.24)	1.12 (1.02-1.23)	0.97 (0.9-1.03)	0.99 (0.92-1.07)	0.9 (0.79-1.03)
ACPA positive	1.12 (1.07-1.18)	1.15 (1.09-1.22)	1.04 (0.95-1.14)	1.2 (1.14-1.27)	1.2 (1.13-1.28)	1.21 (1.1-1.34)	1.04 (0.97-1.11)	1.06 (0.98-1.15)	0.97 (0.85-1.11)
DAS28-CRP	1.13 (1.06-1.21)	1.12 (1.04-1.21)	1.19 (1.05-1.34)	1.52 (1.4-1.65)	1.45 (1.31-1.59)	1.66 (1.42-1.94)	0.99 (0.92-1.06)	1 (0.92-1.08)	0.98 (0.85-1.12)
CRP	0.96 (0.9-1.03)	0.95 (0.88-1.02)	0.99 (0.88-1.12)	1.15 (0.99-1.18)	0.93 (0.87-1.07)	1.4 (1.12-1.74)	0.97 (0.92-1.06)	0.99 (0.94-1.1)	0.88 (0.75-1.03)

* adjusted for age, sex, country and ethnicity
Abbreviations: 95%CI=95% Confidence Interval; HbA1C= Hemoglobin A1C; RF=rheumatoid factor; ACPA=anti-citrullinated protein antibodies; DAS28-CRP=disease activity score with 28 joint count and C-reactive protein (CRP)

Methods: The SUrvey of cardiovascular disease Risk Factor management in Rheumatoid Arthritis (SURF-RA) is an international clinical audit. The data were collected from rheumatology and cardiology clinics in Western and Eastern Europe, North and Latin America and Asia, using a one-page collection sheet. Information on demographics, CV risk factors (i.e. smoking, body mass index [BMI], physical activity, lipid panel, hemoglobin A1c [HbA1c], blood pressure [BP] measurements) and RA disease characteristics (i.e. serologic status, C-reactive protein [CRP], Disease activity score using 28 joints and CRP [DAS28-CRP]) was collected. Lipid panel and HbA1c were required within 1 year of clinic visit. CV Health Index Score was calculated as a sum of controlled CV risk factors out of the following six: smoking, BMI, physical activity, BP, low density lipoprotein cholesterol (LDL-C) and HbA1c. Normal levels were defined as follows: total cholesterol < 4.5 mmol/L (< 174 mg/dL), LDL-C < 2.5 mmol/L (< 100 mg/dL), BP< 140/90 mm/Hg, HbA1c < 7.0%, BMI < 25.0 kg/m^2.

Results: A total of 14,503 patients with RA from 53 centers in 19 countries were included in the study: mean age 60 years, 75% female, 57% rheumatoid factor (RF) positive, 54% positive for antibody to cyclic citrullinated peptide (ACPA), mean DAS28-CRP 3.0. Information on CV risk factor measures by sex is shown in Table 1. No difference was observed in frequency of assessment of lipid measures, BP or HbA1c. Men were more likely to have normal total cholesterol ($p< 0.0001$) and LDL-C than women ($p< 0.0001$). In contrast, women were more likely to have normal BP ($p< 0.0001$) and normal HbA1c ($p=0.02$) than men. Women had overall better CV Health Index Score than men ($p< 0.0001$). Table 2 shows associations of risk factor assessment in patients with RA, adjusting for age, sex, country and ethnicity. Longer RA disease duration, positivity for RF and ACPA, higher DAS28-CRP were associated with higher likelihood of lipid and BP testing, particularly in women, but did not appear to affect the odds of HbA1c assessment.

Conclusion: Women with RA are more likely to have normal BP and HbA1c, resulting in better overall control of CV risk factors, as assessed by CV Health Index Score than men. Patients with RF and/or ACPA, longer RA duration (particularly women), as well as men and women with higher DAS28-CRP are more likely to have lipid panel and BP assessments, suggesting physician awareness of adverse CV risk profile in RA.

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Abstract Number: 1191

Specificity for Inflammatory Pathways Associated with Coronary Microvascular Dysfunction in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Coronary microvascular disease (CMD) is associated with increased mortality in RA independent of traditional cardiovascular (CV) risk factors. Inflammation likely plays an important role the pathogenesis of RA. Studies suggest that higher RA clinical disease activity index (CDAI) is associated with a higher degree of CMD. However, it is not known whether specific inflammatory pathways implicated in RA, including interleukin 6 (IL-6), tumor necrosis factor alpha (TNFα), and interleukin 1 beta (IL-1β), play a stronger role than others in the pathogenesis of CMD in RA. The objective of this study was to identify the associations between inflammatory cytokines and CMD in RA.

Methods: We used baseline data from the first 53 subjects enrolled in the Lipids, Inflammation, and CV Risk (LiiRA, ClinicalTrials.gov: NCT02714881) study. LiiRA enrolls RA patients, age >35, immediately prior to TNF inhibitor initiation. Exclusion criteria include known cardiovascular disease, statin use, prednisone dose >10mg, or biologic DMARD (bDMARD) use in the past 6 months. All subjects underwent a stress myocardial perfusion PET scan (cardiac PET). The cardiac PET quantifies myocardial blood flow at rest and during maximal hyperemia in response to a coronary vasodilator. Coronary flow reserve (CFR) is the ratio of myocardial blood flow during maximal hyperemia over that at rest. A lower CFR in the absence of obstructive coronary artery disease (CAD) is indicative of CMD.

Table 1. Baseline clinical characteristics of LiiRA subjects

Clinical characteristics	All, n= 53
Age, years mean (SD)	54.9 (11.1)
Female (%)	83.0
RA disease duration, years mean (SD)	9.1 (9)
Seropositive (%)	70
CDAI*, mean (SD)	22.2 (13.6)
Low (%)	22.6
Moderate (%)	34.0
High (%)	43.4
ESR mm/h, mean (SD)	29.3 (44)
Baseline RA treatment (%)	
Methotrexate	67.9
Sulfasalazine	1.9
Hydroxychloroquine	22.6
Leflunomide	13.2
No DMARD	17.0
Prednisone (%)	37.7
Prednisone, mean dose (SD)	8.7 (6.8)
Comorbidities (%)	
Hypertension	26.4
Coronary artery disease	0
Diabetes mellitus	0
BMI, mean (SD)	29.4 (6.7)
Family history of CVD (%)	60.4
Ever smoker (%)	43.4
Abnormal stress test, n (%)	3 (5.8)

CDAI=clinical disease activity index, CVD=cardiovascular disease, BMI=body mass index
*CDAI, remission=0-2.8; low activity=2.9-10.0; moderate activity 10.1-22.0; high activity 22.1-76.0

Demographics, RA clinical factors, serum inflammatory markers, and CDAI were collected. Inflammatory markers included high-sensitivity C-reactive protein (hsCRP), IL-6, soluble TNF receptor 2 (sTNFr2), and IL-1β. We tested the association between inflammatory markers and CFR using the Spearman correlation.

Results: The mean age of subjects in LiiRA was 55 years, 83% were female, 70% seropositive, with a mean RA disease duration of 9.1 years (Table 1); per the study protocol, none of the subjects were on a bDMARD. Baseline

Table 2: Correlation between inflammatory markers and coronary flow reserve (CFR)

Inflammatory marker	CFR	
	r	p-value
IL-6	-0.4	0.006
sTNFR2	-0.34	0.02
IL-1β	-0.1	0.5
hsCRP	-0.2	0.2

CFR=coronary flow reserve, IL-6=interleukin 6, sTNFR2=soluble tumor necrosis factor receptor 2, IL-1β= interleukin 1 beta, hsCRP=high sensitivity C reactive protein

cardiac risk factors were uncommon; no patients had diabetes and 26 % had hypertension. IL-6 and sTNFR2 were correlated with a lower CFR. However, no significant associations were observed between IL-1β and hsCRP (Table 2).

Conclusion: Among RA patients with no history of overt CAD and low prevalence of CV risk factors, the severity of CMD was correlated with IL-6 and sTNFR2 but not IL-1β or hsCRP, a general measure of inflammation. These findings provide potential insight into the mechanisms by which inflammation mediates microvascular dysfunction.

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Subclinical Coronary Calcification Associated with Long-term Cardiovascular Outcomes in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

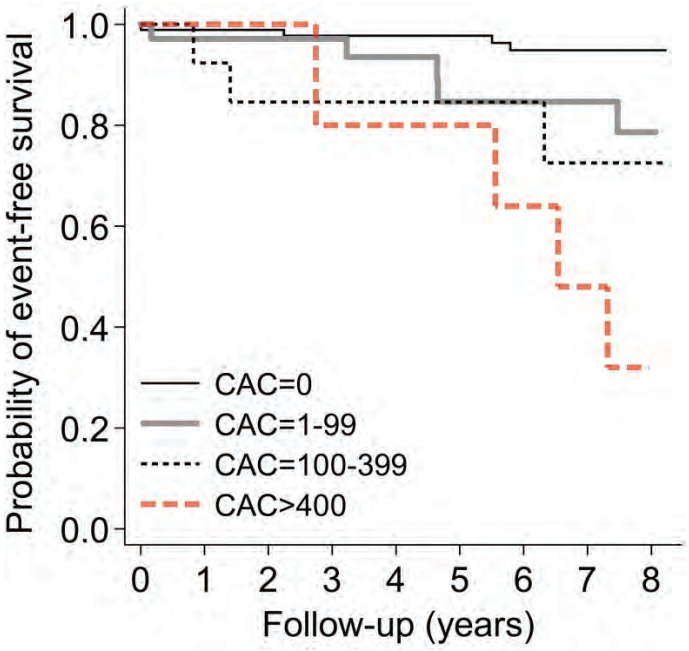

Figure 1. Increasing CAC scores associated with higher cardiovascular event risk in RA

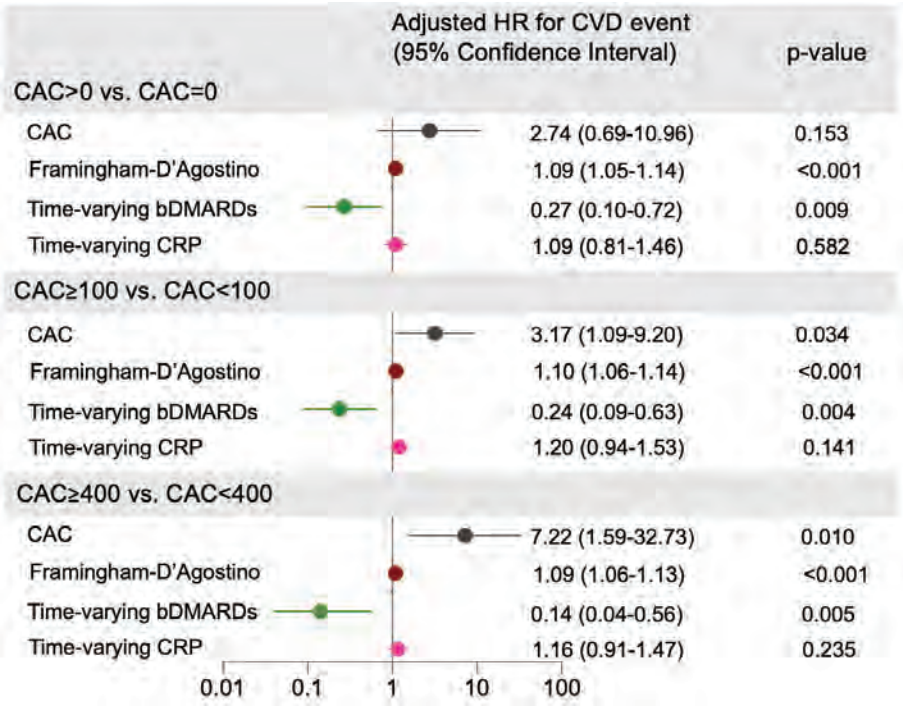

Figure 2. Impact of different CAC thresholds on cardiovascular event risk in RA

Background/Purpose: Large, multicenter studies established the strong prognostic value of coronary artery calcium (CAC) scoring in asymptomatic individuals. Increasing CAC score is an independent predictor of worsening cardiovascular disease event risk in general patients. The prognostic significance of higher CAC score strata in the long-term cardiovascular risk in rheumatoid arthritis (RA) is unknown. We sought to evaluate the long-term cardiovascular event risk across CAC strata in a prospective, single center cohort of established RA patients without symptoms or prior diagnosis of cardiovascular disease

Methods: One hundred-fifty patients underwent computed tomography angiography for coronary atherosclerosis evaluation. CAC score was measured according to Agatston. Cardiovascular disease (CVD) events were prospectively recorded, including cardiac death, myocardial infarction, unsTable angina, revascularization, stroke, claudication, and heart failure hospitalization over 6.0±2.4 years of follow-up. Unadjusted, robust Cox proportional hazards regression models evaluated CVD event risk across higher CAC strata (CAC = 1-99, CAC = 100-399 and CAC ≥ 400) compared to CAC = 0. Additional multivariable robust Cox regression models with time-varying covariates evaluated the impact of log transformed CAC or different CAC thresholds (CAC > 0 vs. CAC = 0, CAC ≥ 100 vs. CAC < 100 and CAC ≥ 400 vs. CAC < 400) on future CVD events. Models were controlled for Framingham-D'Agostino clinical risk score, time-varying current bDMARD use and time-varying CRP.

Results: Sixteen patients incurred 19 events, for a total of 2.1 (95% CI 1.3-3.3) events/100 patient-years. Increasing risk for cardiovascular events was observed across ascending CAC strata; HR 3.87 (95%CI 1.03-14.48), 6.31 (95%CI 1.38-28.91) and 16.98 (95%CI 4.50-64.10) for CAC = 1-99, CAC = 100-399 and CAC ≥ 400 respectively compared to CAC = 0 (Figure 1). In fully adjusted models, CAC score associated with future event risk independently of Framingham D'Agostino score, time-varying bDMARD use and time-varying CRP (HR 1.31 [95%CI 1.04-1.66]). CAC thresholds ≥ 100 (vs. < 100) and CAC ≥ 400 (vs. < 400) in fully adjusted models similarly constituted independent predictors of long-term cardiovascular events (Figure 2).

Conclusion: Increasing CAC scores are strong, independent predictors of long-term cardiovascular events in RA patients without symptoms or prior diagnosis of cardiovascular disease.

Disclosure: G. Karpouzas, Pfizer, 2; **S. Ormseth**, None; **E. Hernandez**, None; **M. Budoff**, None.

Abstract Number: 1193

Unsupervised Molecular Profile Clustering in the Serum of Rheumatoid Arthritis Patients Identifies Groups with Differential CV-risk SCORE: Modulation by Biological Therapies

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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Background/Purpose: To identify specific molecular profiles associated to the enhanced cardiovascular (CV)-risk present in Rheumatoid Arthritis (RA) patients and their modulation by biologic disease modifying anti-rheumatic drugs (b-DMARDs).

Methods: Two hundred and eleven RA patients and 52 healthy donors (HD) were recruited to the study. Serum inflammatory and oxidative stress biomolecules and Netosis-derived products were quantified, and miRNnomes were identified using next-generation sequencing miRNA assay. The CV-risk score was calculated following EULAR recommendations. To evaluate the contribution of molecular profiles to the CV-risk, unsupervised clustering analyses were developed.

In parallel cohorts of 45 and 27 RA patients, respectively, the in vivo effects of biologic drugs [anti-TNFalpha (TNFi) and anti-CD20 (CD20i) inhibitors] were evaluated before and after 6 months of therapy.

Results: A number of circulating biomolecules related to inflammation, NETosis, and oxidative stress were coordinately altered in the serum of RA patients and closely related to the activity of the disease. Besides, more than a hundred circulating miRNAs were found altered in RA patients and linked with the biomolecules found altered.

Unsupervised clustering analyses differentiated 2 clusters representing different molecular profile groups. Clinically, each cluster was characterized by: 1) RA patients with high CV-risk Score (7.01±8.4), medium disease score (DAS28: 3,37±1,4), and positivity for ACPAS and RF near 50%. 2) RA patients with low CV-risk Score (1.6±3.2), medium-high disease score (DAS28: 4.5±1.5) and positivity for ACPAS and RF around 75%. Interestingly, patients belonging to each cluster displayed a distinctive molecular profile in terms of inflammatory molecules deregulated, so that cluster 1 expressed higher levels of cytokines and chemokines related to cell proliferation, chemotaxis and angiogenesis (i.e. IFNg, IL5, IL6, IL10, IL15, VEGF, MCP1, and eotaxin), while in cluster 2 these molecules were reduced and predominated a different set of cytokines (IL1RA, IL1b, IL2, IL7, IL8, IL12, IL13, IL17, FGFb, MIP1b, TNFa). Hence, a different signature of miRNAs regulating these proteins was altered, so that in cluster 1 miR-106a-5p, miR-199a-5p and miR-148b-3p were reduced and miR-346, miR-299-3p, miR-6816 were elevated in relation to cluster 2. Likewise, NETosis derived products and oxidative stress molecules were increased in cluster 2 in comparison with cluster I. I*n vivo* treatments with TNFi and CD20i reduced disease activity and induced the re-establishment of normal levels in these altered biomolecules in an inhibitor-dependent manner.

Conclusion: 1. Extensive molecular profiling of serum in RA patients might help to define precise CV-risk profiles in RA patients. 2. Specific mediators of autoimmunity, inflammation, oxidative damage and Netosis, along with the miRNAs modulating their expression, coordinately determine a higher CV-risk score in RA patients. 3. Biological drugs, such as TNFi and CD20i re-establish normal levels of these circulating biomolecules, thus reducing the CV risk in RA patients.

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Abstract Number: 1194

MUC5B Promoter Variant rs35705950 and Risk Stratification for Rheumatoid Arthritis - Interstitial Lung Disease

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Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is an extra-articular manifestation of rheumatoid arthritis (RA) detected in 20 to 60% of patients with RA on high-resolution computed-tomography (HRCT) chest scan and is clinically significant in near 10%. Despite a high morbi-mortality, a definite strategy for ILD screening in patients with RA remains to be determinate and the identification of markers predictive of the occurrence of ILD is needed. To date, numerous biomarkers have been reported to be associated with ILD among patients with RA but most of them requires validation in a prospective cohort. Recently, in a large international genetic association case-control study, the rs35705950 *MUC5B*promoter variant was identified as the major RA-ILD risk factor. The ESPOIR cohort included patients aged 18 to 70 years who had a definitive or probable diagnosis of RA and included a prospective follow-up. Consequently, we investigated in the ESPOIR cohort, whether the rs35705950 *MUC5B*promoter variant would improve risk stratification at baseline for ILD detection after 13 years of RA duration.

Methods: In this cross-sectional study of the French ESPOIR cohort, an ILD detection by chest HRCT scan was systematically proposed for every patient after 13 year of RA duration. Chest HRCT scans were centrally reviewed by an experienced radiologist and classified according to the presence, the extension and the pattern of ILD. All included patients were genotyped for rs35705950 *MUC5B*promoter variant. Baseline clinical and biological data were collect-

Variable		Odds ratio	p
MUC5Bd	GG	Reference	
	GT/TT	3.84 (1.48, 10.13)	0.006
SEX	F	Reference	
	M	2.56 (0.98, 6.60)	0.051
AGE_	<=49	Reference	
	>49	5.21 (2.03, 15.12)	0.001
SJC	<=9	Reference	
	>9	2.87 (1.17, 7.23)	0.022
Persistent arthritis		Reference	
Migrating arthritis		3.37 (1.37, 8.65)	0.009

Baseline predictors of ILD occurence at 13 years of RA duration

ed. A logistic model was used to identify baseline predictors for the occurrence of ILD on HRCT scans. Confidence intervals were estimated using sampling methods.

Results: Among the 170 patients who were investigated with an HRCT scan (133 women (78.2%), mean RA duration 13.7 ±1.1 years), ILD was detected in 31 patients (18.2%). ILD extension was >10% in 9 patients (5.3%), fibrotic ILD was detected in 16 patients (9.4%). Two additional patients from the ESPOIR cohort that previously died from ILD were included in the analysis. Among European Caucasian patients, *MUC5B*rs35705950 minor allele frequency (MAF) was 26.5% in the RA-ILD population compared to 8.9% in the RA-noILD population (OR=6.0 $CI_{95\%}$(2.0-17.6)). After logistic regression, baseline predictors for ILD were male sex (OR=2.6 $CI_{95\%}$(1.0-6.6)), age at RA onset > 49 y/o (OR=5.2 $CI_{95\%}$(2.0-15.1)), number of swollen joints > 9 (OR=2.9 $CI_{95\%}$(1.2-7.2)), migrating arthritis vs persistent arthritis (OR=3.4 $CI_{95\%}$(1.4-8.7)) and *MUC5B*rs35705950 T risk allele (OR=3.8 $CI_{95\%}$(1.5-10.1)). The logistic model using could predict RA-ILD occurrence after 13 years of RA duration with an AUC=0.80 $CI_{95\%}$(0.72-0.90).

Conclusion: In RA patients, altogether with baseline clinical data, *MUC5B*rs35705950 genotyping could help to improve risk stratification for ILD occurrence at 13 years of RA duration.

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Abstract Number: 1195

MUC5B rs35705950 and Rheumatoid Arthritis Associated Interstitial Lung Disease Progression

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SESSION INFORMATION

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Background/Purpose: Rheumatoid arthritis (RA) associated interstitial lung disease (ILD) and idiopathic pulmonary fibrosis (IPF) sharephenotypic and genotypic similarities. Recently, in a large international genetic association case-control study, the IPF major risk factor, *MUC5B*rs35705950 promoter variant was found to be associated with RA-ILD. Regarding IPF, *MUC5B*rs35705950 T risk allele has been associated with better prognosis. However, the impact of *MUC5B*rs35705950 on RA-ILD prognosis remains to be determined. Our objective was to explore the influence of *MUC5B*rs35705950 on pulmonary function tests (PFTs) evolution in patients with RA-ILD.

Methods: Patients with RA-ILD were included from France, USA, Mexico, Greece andtheNetherlands in this observationalinternational study. Patients were genotyped for *MUC5B*rs35705950 and PFTs data were collected. Longitudinal data up to a 10-year follow-up were considered and analyzed using mixed regression models. We defined a significant deterioration of pulmonary function as an absolute decrease of at least 10% in FVC (expressed in percent

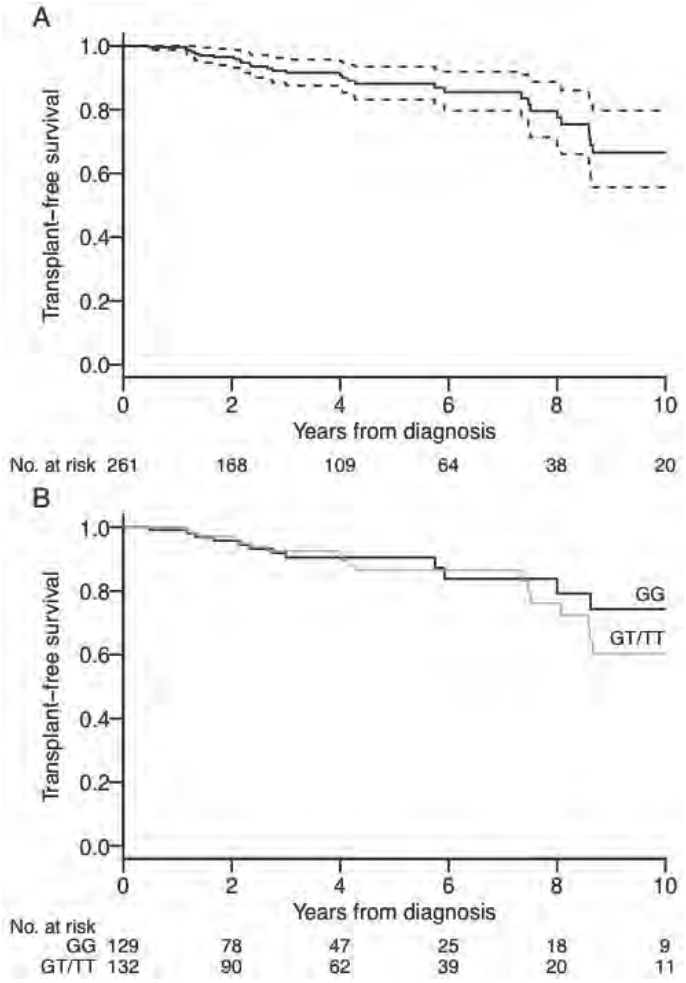

Figure 1. Transplant-free survival of all patients (A) and according to MUC5B rs35705950 polymorphism (B).

of the predicted value) or a relative decrease in FVC of at least 10%, at two years from baseline. Individuals who underwent lung transplantation or who died before 2 years from baseline were considered as experiencing a significant decrease of pulmonary function.

Results: Out of 321 registered patients, 261 could be included in the study: 139 women (53.3%), median age at RA-ILD diagnosis 65 y/o (IQR 57 – 71), 151 ever smokers (59.2%), 128 definite or possible usual interstitial pneumonia (UIP) (53.4%), 74 non-specific interstitial pneumonia (NSIP) (30.8%). Baseline median forced vital capacity (FVC) was 78.2% predicted (IQR 64.2 – 100.7) and Baseline diffusing capacity for carbon monoxide (DLCO) was 56.0% predicted (IQR 46.5 – 72.0). *MUC5B*rs35705950 minor allele frequency was 27.20%. Median follow-up was 3.5 years. Overall, there was a slight trend to decrease of 0.8% per year ($CI_{95\%}$ 0.3 – 1.4). Additionally, an important inter-patient variability of FVC was found at baseline as well as during follow-up. DLOC shows a significant decrease of 1.8% per year on average ($CI_{95\%}$ 1.2 – 2.3). A significant deterioration of PFTs at 2 years was observed for 33 of 256 evaluable patients. No baseline characteristics was associated with a significant deterioration of PFTs at 2 years, including the HRCT UIP pattern (OR=0.7; $CI_{95\%}$ 0.3 – 1.6). *MUC5B*rs35705950 T risk allele was not associated with a better or worse deterioration of PFTs (OR=0.7; $CI_{95\%}$ 0.2 – 2.2). No difference was found between *MUC5B*rs35705950 T risk allele carriers and non-carriers for transplant free survival (Figure 1.).

Conclusion: In this international multiethnicobservational study, PFTs from patients with RA-ILD were relatively sTable over time and*MUC5B*rs35705950 T risk allele was not associated with a better or a worse evolution of PFTs.

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Associations of Biological Sex with Interstitial Lung Disease in Patients with Rheumatoid Arthritis Are Independent of Other Known Risk Factors

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SESSION INFORMATION
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Background/Purpose: Extra-articular manifestations of rheumatoid arthritis (RA), such as nodules and interstitial lung disease (ILD), portend poor outcomes and are more common in men than in women. Whether differences in the risk of RA-ILD between men and women are related to biologic sex or to other known risk factors such as cigarette smoking or increased RA disease activity, which might differ by sex, is unknown. The purpose of this cross-sectional study was to evaluate sex differences in the prevalence of extra-articular manifestations in RA, accounting for known factors that might confound these associations.

Methods: Participants were enrollees in a multicenter, longitudinal observational cohort of US Veterans with RA. A total of 2,691 participants were studied. Baseline demographic, clinical, and treatment variables were collected and compared between men and women using either Student's t-tests or chi-square tests. Participants were categorized by the presence or absence of subcutaneous nodules, chronic lung disease (ILD or chronic obstructive pulmonary disease [COPD] vs. ILD alone) and ILD. Chronic lung diseases were determined from diagnostic codes recorded by treating rheumatologists at enrollment. Associations of sex (male vs. female) with each extra-articular manifestation was assessed using separate multivariable logistic regression models. Covariates included; Model 1: age; Model 2: age, race, body mass index (BMI); Model 3: age, race, BMI, measures of disease activity and RA treatments; Model 4: all aforementioned covariates and HLA-DRB1 shared epitope status, smoking history, and anti-citrullinated protein antibody (ACPA) status.

Results: Baseline characteristics of men and women with RA are shown in (**Table 1)**. Compared to women with RA, men were older, more likely to be Caucasian, smokers, and had greater disease activity, higher autoantibody concentrations and more comorbidity. Men more often had nodules (28% vs. 19%, p = 0.001), COPD (17% vs. 10%, p

Table 1: Demographic, Clinical, and Treatment Variables of VARA Registry at Enrollment

Variables		Cohort				
		N	Total (n=2691)	Men (n= 402)	Women (n=289)	P
Age, mean yrs		2691	64 (11)	65 (10)	55 (12)	<0.001[a]
Disease duration, yrs		2638	12 (11)	12 (11)	10 (10)	0.023[a]
Body Mass Index, kg/m^2		1969	28 (6)	28 (5)	30 (7)	<0.001[a]
Race/Ethnicity, n (%)	Caucasian	2683	2073 (77)	1908 (80)	165 (58)	<0.001
	African American		433 (16)	341 (14)	92 (32)	
	Hispanic		117 (4)	101 (4)	16 (6)	
	Other		60 (2)	47 (2)	13 (5)	
Smoking, ever, n (%)	Current	2623	683 (26)	637 (27)	46 (17)	<0.001
	Former		1404 (54)	1311 (56)	93 (34)	
	Never		536 (20)	405 (17)	131 (49)	
Presence of nodules, n (%)		2691	716 (27)	662 (28)	54 (19)	0.001
RAPID-3		2169	2.5 (1.5)	2.5 (1.4)	2.3 (1.5)	0.016
MD-HAQ		2308	0.9 (0.6)	0.9 (0.6)	0.8 (0.7)	0.001
RDCI		2691	2.0 (1.7)	2.0 (1.7)	1.3 (1.4)	<0.001
	ILD	2691	116 (4.3)	113 (4.7)	3 (1.0)	0.004
	COPD	2691	448 (17)	418 (17)	30 (10)	0.002
HLA-SE positive, n (%)		2474	1692 (68)	1528 (69)	164 (61)	0.010
RF positive, n (%)		2285	1801 (79)	1634 (79)	167 (74)	0.041
RF titer (IU/ml)		2285	329 (689)	340 (706)	230 (499)	0.002
ACPA positive, n, (%)		2282	1777 (78)	1607 (78)	170 (75)	0.254
ACPA titer (units/ml)		2282	234 (386)	240 (397)	177 (266)	0.012
Methotrexate, n (%)		2352	1284 (55)	1160 (55)	124 (53)	0.505
Prednisone, n (%)		2352	973 (41)	897 (42)	76 (32)	0.003
Biologic agent n, (%)		2691	711 (26)	621 (26)	90 (31)	0.054

Tests are chi-square tests except as noted.

a – t-test.

* RAPID-3: Routine Assessment of Patient Index Data; MD-HAQ: Multidimensional Health Assessment Questionnaire; RDCI: rheumatic disease comorbidity index; ILD: interstitial lung disease; COPD: chronic obstructive pulmonary disease; HLA-SE: human leukocyte antigen shared epitope; RF: rheumatoid factor; ACPA: anti-citrullinated peptide antibodies

= 0.004) and ILD (4.7% vs. 1.0%, p = 0.002). In hierarchical regression models, these sex differences all remained following adjustment for age (**Table 2, Model 1**). With progressive adjustments (**Table 2, Models 2 to 4**), associations between sex and nodules or chronic lung disease were attenuated and no longer significant. In contrast, associations of male sex with ILD alone remained following progressive adjustments. Results were unchanged in more parsimonious models including only age, smoking, disease activity and ACPA positivity as covariates (data not shown).

Conclusion: The association between subcutaneous nodules and chronic lung disease with male sex in RA is confounded by other factors, rather than representing true differences arising from biologic sex. In contrast, associations of biologic sex with RA-ILD persist even after adjustment for multiple confounders, including cigarette smoking, RA disease activity and/or severity, and treatments. Our findings suggest that real sex differences drive the marked differences observed in RA-ILD prevalence in men compared to women. Further exploration into mechanisms underpinning the predisposition to RA-ILD among men is needed as this could inform future preventive and/or treatment strategies.

Table 2: Associations of biologic sex (male vs. female) with extra-articular disease manifestations (nodules, chronic lung disease, or ILD)

	Odds Ratio and 95% Confidence Intervals Male vs. Female Sex		
	Nodules	**Chronic Lung Disease (ILD or COPD)**	**ILD**
Model 1	1.58 (1.15, 2.18)	1.62 (1.09, 2.40)	3.95 (1.23, 12.70)
Model 2	1.42 (0.98, 2.06)	1.37 (0.89, 2.13)	4.64 (1.12, 19.19)
Model 3	1.18 (0.78, 1.78)	1.33 (0.81, 2.20)	7.79 (1.06, 57.26)
Model 4	1.13 (0.73, 1.75)	1.19 (0.70, 2.05)	7.37 (0.99, 54.74)

Covariates: Model 1 = age Model 2 = age, race, BMI Model 3 = age, race, BMI, disease duration, RAPID-3, MTX, prednisone, biologic therapy Model 4 = age, sex, race, BMI, disease duration, RAPID-3, MTX, prednisone, biologic therapy, HLA-DRB1 (pos vs. neg), smoking (ever vs. never), ACPA positivity

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Biomarkers for Rheumatoid Arthritis-Associated Interstitial Lung Disease: A Systematic Review

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: RA-associated interstitial lung disease (RA-ILD) is among the most frequent and severe extra-articular manifestations of RA, contributing significantly to the excess mortality among RA patients. Optimal methods to identify RA-ILD and prognosticate its disease course are lacking. Peripheral biomarkers capable of performing these roles would be of great utility in the management of RA-ILD. To summarize this evidence, we performed a systematic review of peripheral biomarkers for the identification and prognosis of RA-ILD.

Methods: We performed a systematic review of published manuscripts investigating peripheral biomarkers in RA-ILD (PROSPERO registration number CRD42019137143) following PRISMA guidelines. We searched MEDLINE, EMBASE, the Cochrane Library, and Scopus from inception to 12/10/2019. We included primary studies evaluating pe-

ripheral biomarker(s) for the identification or prognostication of RA-ILD. We excluded those in non-English language, studies with < 20 RA-ILD patients, published reports prior to 1990 (given advancements in imaging for RA-ILD), and those not reporting results for RA-ILD specifically (e.g. grouped with CTD-ILD). We extracted study characteristics (including study design, method of biomarker measurement), patient characteristics (including demographics, smoking status, RA disease severity, and method of ILD ascertainment), and performance of peripheral biomarkers for identifying RA-ILD (vs. RA without ILD; or vs. other lung diseases) and predicting prognosis. We assessed the quality of studies using modified Quality Assessment of Diagnostic Accuracy Studies-2 (QUADAS-2) and Quality in Prognostic Studies (QUIPS) tools.

Results: Our search identified 1,189 studies, and 43 remained after applying inclusion and exclusion criteria. Study designs were primarily cross-sectional and included patients from the U.S., Japan, and China. Patient characteristics and sample sizes were highly variable across studies. Methods of ILD ascertainment were similar across most studies, typically incorporating imaging criteria (primarily CT) with or without clinical criteria. A total of 71 peripheral biomarkers were identified, with the majority being measured in serum. Peripheral biomarkers associated with the presence of RA-ILD included autoantibodies, lung epithelial/surfactant proteins, tumor markers, cytokines and

Table. Peripheral biomarkers associated with the presence of RA-ILD

Biomarker category	RA-ILD vs. RA without ILD	RA-ILD vs. other lung diseases
Autoantibodies	Anti-aminoacyl-tRNA synthetase antibodies (anti-threonyl tRNA synthetase [anti-PL7] antibody, anti-alanyl-tRNA synthetase [anti-PL-12] antibody), **Anti-citrullinated protein antibodies (anti-citrullinated alpha enolase antibodies***, Anti-citrullinated-heat shock protein 90, **Anti-CCP 1*/2***/3), Anti-IL-1a, **Anti-malondialdehyde acetaldehyde antibodies**, **Anti-peptidyl-arginine deiminase antibodies (Anti-PAD 2**, **Anti-PAD 3/4XR)**, **Rheumatoid factor***	Anti-citrullinated-heat shock protein 90, **Anti-malondialdehyde acetaldehyde antibodies**
Lung epithelial / surfactant proteins	**Krebs von den Lungen-6*, Surfactant protein-D***	Krebs von den Lungen-6*, Surfactant protein-D
Tumor markers	Cancer Antigen (CA) 15-3*, CA 19-9*, **CA 125***	
Cytokines / chemokines	**C-X-C motif chemokine 10(CXCL10)/interferon gamma-induced protein 10(IP-10)**, **chemokine ligand 16 (CXCL16)**, **eotaxin**, **fractalkine/chemokine (C-X3-C motif) ligand 1, growth related oncogene 1/chemokine ligand 1**, **IL-1α, IL-1β, IL-2**, **IL-6**, **IL-7**, **IL-8**, **IL-9**, **IL-12p40**, **IL-12p70**, **IL-15**, **IL-18,** IL-33*, **interferon-α2**, **lipopolysaccharide binding protein, monocyte chemotactic protein 3, macrophage inflammatory protein 1- β, pulmonary and activation-regulated chemokine (PARC)/CC-chemokine ligand-18, tumor necrosis factor α**	
Growth factors	**Fibroblast growth factor 2**, **FMS-related tyrosine kinase 3 ligand**, **granulocyte-macrophage colony-stimulating factor**, **transforming growth factor α**, **vascular endothelial growth factor**	
Extracellular matrix proteins	Lysyl oxidase-like 2, **matrix metalloproteinase (MMP)-1**, **MMP-2**, MMP-3, **MMP-7***, **MMP-9**, **MMP-10**	
Genetic markers	HLA haplotypes: DQB1*04, DQB1*06, **DR2 (*15:01**, ***15:02** and *16:02)*, DR4 (*04:01, *04:03, *04:04, *04:05, *04:06, *04:07, *04:10)*, DRB1*14:06, DRB1*16:02-DQB1*05:02, MUC5b promoter variant rs35705950, microRNA (hsa-miR-7-5p, has-miR-214-5-p), **shared epitope****	**DR2 (*15:01**, ***15:02 only)**, MUC5b promoter variant rs35705950
Other	**25-OH Vitamin D**, C-reactive protein*, erythrocyte sedimentation rate*, gamma-glutamyl transferase, globulin, lactate dehydrogenase, Lysine, **Wnt5a**	leukocyte telomere length, erythrocyte sedimentation rate

Bolded biomarkers were associated with RA-ILD in multivariable adjusted analyses
Underlined biomarkers were negatively associated with RA-ILD
* Biomarkers associated with RA-ILD in ≥ 2 studies
** Biomarker positively and negatively associated with RA-ILD

chemokines, growth factors, extracellular matrix proteins, genetic markers, and other biomarkers (**Table**). The risk of bias pertaining to patient selection, biomarker testing, reference standard assessment, and flow and timing was generally low or unclear. Several studies were determined to have a moderate to high risk of bias related to the statistical analyses due to lack of adjustment for confounding variables. Only 1 study focused on RA-ILD prognostication.

Conclusion: Several peripheral biomarkers have been found to be associated with the presence of RA-ILD, while few have been evaluated for their role in the prognostication of RA-ILD. Further investigation and clinical validation is needed before these candidate biomarkers can be employed in the care of RA and RA-ILD patients.

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Lifestyle and Clinical Risk Factors for Incident Rheumatoid Arthritis-Associated Interstitial Lung Disease Among Patients with Rheumatoid Arthritis

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Background/Purpose: Despite the known excess mortality of rheumatoid arthritis-associated interstitial lung disease (RA-ILD), its association with certain lifestyle factors such as obesity and future prediction have not yet been determined. We aimed to investigate the association between novel lifestyle factors on risk of incident RA-ILD, to define the threshold at which smoking increases risk of RA-ILD, and to calculate the degree to which known clinical risk factors predict RA-ILD.

Methods: This nested case-control study was performed within a prospective RA registry. All participants had RA confirmed by a rheumatologist using ACR/EULAR criteria. Three radiologists/pulmonologists determined incident RA-ILD status based on research review of clinically-obtained chest computed tomography (CT) scans. Controls had RA and no patient/physician report or billing codes for ILD. Index date was the first CT with RA-ILD or matched date. We matched each incident RA-ILD case to three controls on age, sex, RA duration, rheumatoid factor positivity, and time from exposure assessment to index date. Exposures were assessed at the earliest study visit prior to RA-ILD and included education, body mass index (BMI), smoking pack-years, anti-CCP positivity, race, hand bone erosions, rheumatoid nodules, CRP, DAS28-CRP, functional status (multi-dimensional HAQ [MDHAQ]), disease-modifying anti-rheumatic drug use, and glucocorticoid use. Conditional logistic regression models for each exposure determined

Table 1. Association of novel risk factors and smoking pack-years with incident RA-ILD in 84 RA-ILD cases and 243 RA non-ILD controls

Characteristic	OR Conditioned on Matching Factors* (95% CI)	Multivariable** OR (95% CI)
Body Mass Index, kg/m²		
<20	0.98 (0.30-3.21)	1.00 (0.29,3.43)
20-<25	(ref)	(ref)
25-<30	1.35 (0.72-2.52)	1.56 (0.79,3.06)
≥30	**2.05 (1.03-4.07)**	**2.42 (1.11,5.24)**
p for trend	**0.035**	**0.023**
C-Reactive Protein, mg/L		
Normal (<3)	(ref)	(ref)
Low-Positive (3-<10)	**1.86 (1.04-3.34)**	1.67 (0.87,3.20)
High-Positive (≥10)	**2.79 (1.36-5.69)**	**2.61 (1.21,5.64)**
p for trend	**0.008**	**0.021**
MDHAQ Score		
0-<0.2	(ref)	(ref)
0.2<-1.0	1.16 (0.57-2.34)	1.07 (0.50,2.30)
≥1.0	**3.11 (1.48-6.54)**	**3.10 (1.32,7.26)**
p for trend	**<0.001**	**0.004**
Smoking Pack-Years		
Never Smoker	(ref)	(ref)
1-9	0.53 (0.22-1.26)	0.54 (0.22-1.31)
10-19	1.30 (0.59-2.89)	1.42 (0.62-3.24)
20-29	1.16 (0.42-3.19)	1.44 (0.51-4.06)
≥30	**5.34 (2.50-11.5)**	**6.06 (2.72-13.5)**
p for trend	**<0.001**	**<0.001**

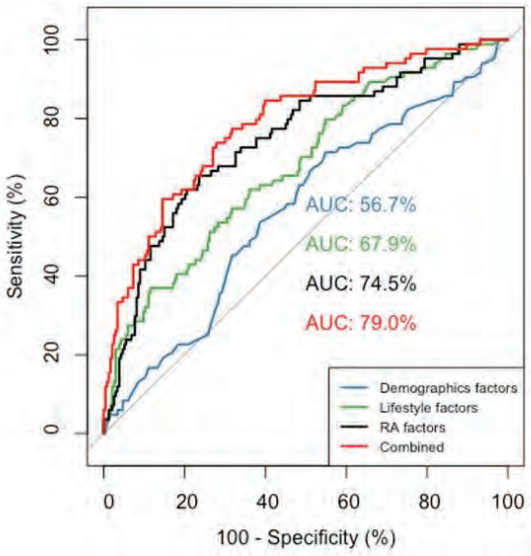
*All models were conditioned on matching factors (age, sex, RA duration, RF status, and time from study visit to index date)

**Also adjusting for anti-CCP, race/ethnicity, education, BMI, and smoking pack-years

odds ratios (OR) for RA-ILD, adjusting for matching factors, anti-CCP, race, education, BMI, and smoking pack-years. Area under the receiver operating characteristic curves (AUROC) were calculated based on lifestyle and clinical exposures.

Results: We identified 84 confirmed incident RA-ILD cases and 243 matched controls. RA-ILD cases had a mean age of 67 (standard deviation 10), and 77% were female. Mean time from exposure assessment to RA-ILD onset was 1.5

Figure 1. Receiver operating characteristic curve for incident RA-ILD risk among the 84 RA-ILD cases and 243 RA non-ILD controls using demographic, lifestyle, and RA clinical risk factors



years. After adjustment, obesity, high-positive CRP (≥10 mg/L), and poor functional status (MDHAQ ≥1) were each associated with increased risk of RA-ILD (Table 1). Smoking pack-year history greater than 30 was associated with a six-fold increased risk of RA-ILD compared to nonsmokers; less than 30 pack-years were not associated with RA-IOLD risk. Together, lifestyle and clinical risk factors for RA-ILD had an AUROC of 0.79 (95% CI 0.73-0.85) (Figure 1).

Conclusion: This study identified obesity, high-positive CRP, poor functional status, and a smoking threshold of 30 pack-years as novel predictors of RA-ILD. The overall ability to predict RA-ILD based on lifestyle and clinical factors was modest. Future studies should investigate whether smoking cessation and weight loss may delay or prevent RA-ILD. Additional factors such as biomarkers may improve prediction of RA-ILD among patients with RA.

Demographic factors: age, sex, race, education Lifestyle factors: BMI, smoking pack-years RA factors: RA duration, RF status, anti-CCP status, hand bone erosions, rheumatoid nodules, biologic DMARD use, methotrexate use, glucocorticoid use, disease activity (DAS28-CRP), functional status (MDHAQ).

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Abstract Number: 1199

Prevalence of Subclinical Interstitial Lung Disease After a Mean Rheumatoid Arthritis Duration of 13 Years: Results from the French ESPOIR Cohort

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a frequent extra-articular manifestation of rheumatoid arthritis (RA). It is associated with a high morbi-mortality. However, the exact prevalence of clinical and subclinical RA-ILD is still unknown as it largely varies between studies, depending on the screening tool and the temporality of the screening. Using a systematic detection by high-resolution computed-tomography (HRCT) chest scan, subclinical ILD has been reported in 20 to 60% of patients with RA. Our objective was to estimate the prevalence of clinical and subclinical ILD in the ESPOIR cohort after 13 years of RA duration.

Methods: In this cross-sectional study of the ESPOIR cohort, a HRCT chest scan was systematically proposed to the patients after a mean RA duration of 13 years. The ESPOIR cohort included patients aged 18 to 70 years who had a definitive or probable diagnosis of RA and included a prospective follow-up. HRCT scans were centrally reviewed by an expert radiologist. ILD presence, extension and characteristics were assessed using the current recommendations for ILD assessment (Raghu *et al*, Am J Respir Crit Care Med, 2011). To note, 2 patients had previously died from clinical ILD and were not included in this analysis.

Results: Within the ESPOIR Cohort, 493 patients had a 10 or more years of follow-up. 175 patients were assessed by HRCT scan. 170 patients (133 women (78.2%), mean age (61.1 ±10.3 y/o), mean RA duration (13.7 ±1.1 years)) had an interpreTable HRCT scans and were included in the analysis. Among them, chest HRCT scan identified subclinical ILD in 31 patients (18.2%): 19 women (61.3%), mean age 67.9 ±8.7 y/o, mean age at RA onset 54.3 ±8.6 y/o. Seventeen patients (54.9%) had a smoking history. Subclinical ILD with a HRCT extension of < 5%, 5-10% and >10% was observed in: 7 (4.1%), 15 (8.8%) and 9 patients (5.3%), respectively. Among the 9 patients with a HRCT extent >10%, 4 had a definite or probable usual interstitial pneumonia pattern, 3 patients had a non-specific interstitial pneumonia pattern and 2 had indeterminate patterns.

Conclusion: In the French ESPOIR Cohort, the prevalence of subclinical ILD after a mean RA duration of 13 years was 18.2%, illustrating that the occurrence of ILD is not a rare event.

Disclosure: P. Juge, Bristol-Myers Squibb Company, 5; **M. Debray**, None; **E. Ebstein**, None; **R. Borie**, None; **A. Constantin**, AbbVie Inc., 5, 8, Amgen, 5, 8, Celltrion, 5, Gilead, 5, 8, Eli Lilly and Company, 5, 8, Novartis, 5, 8, Pfizer Inc., 5, 8, UCB, 5, 8, Janssen, 8; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **B. Fautrel**, MSD France, 1, 2, Abbvie, 1, 2, Pfizer, 1, 2, Biogen, 1, BMS, 1, Boehringer Ingelheim, 1, Celgene, 1, Janssen, 1, Lilly, 1, Medac, 1, Nordic Pharma, 1, Novartis, 1, Roche, 1, Sanofi-Aventis, 1, SOBI, 1, UCB Pharma, 1; **R. Flipo**, MSD France, 1, 2, Sanofi-Aventis, 1; **X. Mariette**, None; **O. Vittecoq**, BMS, 5, Novartis, 8, Pfizer, 8, ABBVIE, 5, 8; **A. Saraux**, AbbVie, 5, 8, Bristol-Myers Squibb, 5, 8, Chugai, 5, 8, Eli Lilly, 5, 8, Nordic, 5, 8, Sanofi, 5, 8, UCB Pharma, 5, 8; **G. Carvajal Alegria**, None; **J. Sibilia**, Roche-Chugaï, 8, BMS, 8, UCB, 8, GSK, 8, LFB, 8, Actelion, 8, Pfizer, 8, MSD, 8, Novartis, 8, Amgen, 8, Abbvie, 8, Sandoz, 8, Gilead, 8, Lilly, 8, Sanofi, 8, Janssen, 8, Mylan, 8; **F. Berenbaum**, Pfizer, 1, Eli Lilly, 1; **B. Crestani**, None; **P. Dieude**, None.

Abstract Number: 1200

Serum Anti-PAD4 and Anti-PAD3/4XR Antibodies in Rheumatoid Arthritis Associated-Interstitial Lung Disease Are Associated with Better Lung Function

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster III: Cardiopulmonary Aspects

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) associated-interstitial lung disease (ILD) affects approximately 10% of RA patients. It is a leading cause of morbidity and mortality, which is more severe in the fibrotic subtype RA-usual interstitial pneumonia (RA-UIP). Serum antibodies to peptidylarginine deiminase type 4 (anti-PAD4), particularly a subset that cross-react with PAD3 (PAD3/4XR), have been associated with imaging evidence of ILD. However, whether anti-PAD4 and anti-PAD3/4XR antibodies are associated with a particular phenotype of RA-ILD is unknown. Importantly, idiopathic pulmonary fibrosis (IPF) shares similar risk factors and clinical features with RA-ILD, and a recently published study by our group found that anti-cyclic citrullinated peptide (anti-CCP) antibodies were present in 25% of IPF patients. As such, in this study, we sought to identify the specificity and lung disease characteristics of anti-PAD4 and anti-PAD3/4XR antibodies in RA-ILD and IPF.

Methods: Our cohort included 48 patients with RA-ILD (confirmed by chest imaging and assessment of a pulmonologist specializing in ILD) and 32 patients with IPF (meeting 2018 diagnostic criteria) who had stored serum in the National Jewish Health Biobank. Forty-six patients with RA-ILD and 28 with IPF performed pulmonary function tests within 3 months of serum collection. Subgroups of RA-ILD were defined by imaging pattern on high-resolution chest computed tomography (HRCT) scan (nonspecific interstitial pneumonia, RA-NSIP; usual interstitial pneumonia, RA-UIP) as determined via consensus reads by a trained radiologist and pulmonologist. Serum was tested for anti-CCP (CCP3.1 IgG/IgA, Inova) and rheumatoid factor (RF-IgA and IgM) by ELISA. Serum anti-PAD4 and anti-PAD3/4XR antibodies were quantified using immunoprecipitation of radiolabeled target protein and gel electrophoresis. Clinical characteristics, measures of lung function (% predicted forced vital capacity, FVC; % predicted diffusion capacity

Table 1. Characteristics, Pulmonary Function and Serum Antibody Testing in RA-ILD and IPF

					P value**			
	RA-ILD* (n=48)	RA-NSIP* (n=11)	RA-UIP* (n=37)	IPF* (n=31)	RA-ILD vs IPF	RA-NSIP vs IPF	RA-UIP vs IPF	RA-UIP vs NSIP
Age	62 ± 12	56 ± 13	64 ± 11	69 ± 8	<0.01	<0.01	0.03	0.05
Female	50%	55%	49%	19%	<0.01	0.05	0.02	NS
Ever Smoker	53%	46%	56%	68%	NS	NS	NS	NS
Smoking Pack years	13 ± 18	10 ± 15	14 ± 19	22 ± 27	NS	NS	NS	NS
% predicted FVC	69 ± 20	68 ± 23	69 ± 19	68 ± 17	NS	NS	NS	NS
% predicted DLCO	47 ± 18	53 ± 22	45 ± 17	44 ± 16	NS	NS	NS	NS
Anti-CCP+	71%	73%	70%	32%	<0.01	0.03	<0.01	NS
RF IgA+	63%	55%	65%	19%	<0.01	0.05	<0.01	NS
RF IgM+	73%	55%	78%	0%	<0.01	<0.01	<0.01	NS
Anti-PAD4+	19%	9%	22%	0%	0.01	NS	<0.01	NS
Anti-PAD3/4+	10%	9%	11%	0%	NS	NS	NS	NS

*Values displayed as mean ± SD or %.
**Based on Chi-square or t-test where appropriate, NS = not significant, P>0.05.
Clinical data was missing for: Ever smoking for 1 RA-ILD; PY for 4 RA-ILD, 1 IPF; FVC% for 2 RA-ILD, 4 IPF; DLCO % for 4 RA-ILD, 6 IPF.

Table 2. Differences in Characteristics and Pulmonary Function Based on Serum Anti-PAD4 and Anti-PAD3/4XR Antibody Positivity in RA-UIP

					P value**	
	PAD4+* (n=8)	PAD4-* (n=29)	PAD3/4XR+* (n=4)	PAD3/4XR-* (n=33)	PAD4+ vs PAD4-	PAD 3/4XR+ vs PAD3/4XR-
Age	62 ± 7	64 ± 12	60 ± 6	64 ± 11	NS	NS
Female	62%	44%	75%	45%	NS	NS
Ever smoker	75%	50%	100%	50%	NS	NS
Smoking Pack years	14 ± 15	14 ± 20	23 ± 14	13 ± 19	NS	NS
Anti-CCP+	75%	69%	100%	67%	NS	NS
% predicted FVC	82 ± 12	65 ± 20	87 ± 16	67 ± 19	0.02	0.05
% predicted DLCO	51 ± 15	43 ± 17	54 ± 19	44 ± 17	NS	NS

*Values displayed as mean ± SD or %.
**Based on Chi-square or t-test where appropriate, NS = not significant, P>0.05.
Clinical data was missing for: Ever smoking for 1 PAD4-, 1 PAD3/4XR-; PY for 1 PAD4+, 3 PAD4-, 4 PAD3/4XR-; FVC % for 2 PAD4-, 2 PAD3/4XR-; DLCO % 4 PAD4-, 4 PAD3/4XR-.

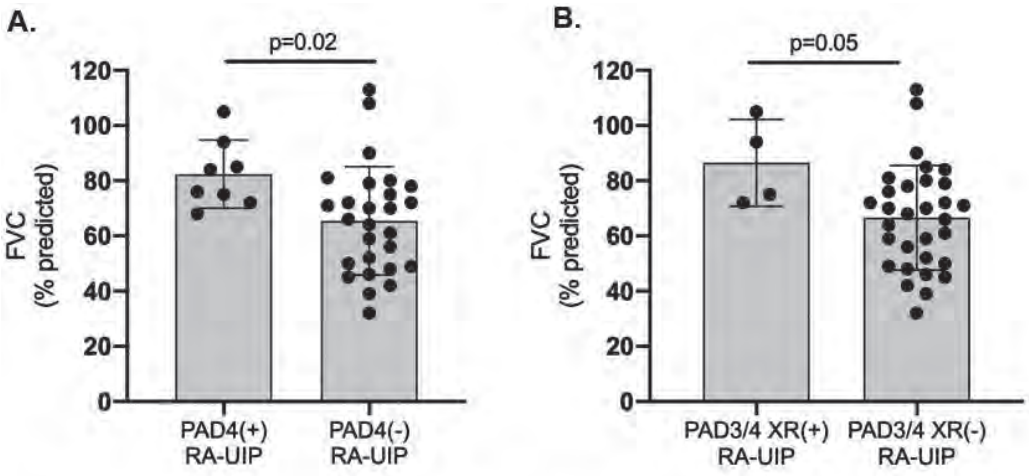

Figure 1. Forced vital capacity (FVC) in anti-PAD4+ and anti-PAD3/4XR+ RA-UIP. Mean FVC (% predicted) +/- SD in individuals with RA-UIP when stratified by anti-PAD4 status (panel A, n=8 anti-PAD4+, n=27 anti-PAD4-) and anti-PAD3/4XR (panel B, n=4 anti-PAD3/4XR+, n=31 anti-PAD3/4XR-) positivity. P-values based on independent samples t-test.

carbon monoxide, DLCO) and prevalence of serum antibodies were compared using Chi-square and t-tests as appropriate.

Results: Compared to IPF, subjects with RA-ILD were younger and more often female, but there were no differences in smoking history or baseline lung function (Table 1). Anti-PAD4 and anti-PAD3/4XR antibodies were present in 9/48 (19%) and 5/48 (10%) subjects with RA-ILD, respectively, and no subjects with IPF (Table 1). Within the RA-ILD group, anti-PAD4 antibodies were associated with better lung function. In particular, within RA-UIP subjects, the % predicted FVC was higher in anti-PAD4(+) and anti-PAD3/4XR(+) RA-UIP subjects (Table 2 and Figure 1).

Conclusion: We demonstrate that serum anti-PAD4 and anti-PAD3/4XR antibodies are highly specific for RA-ILD and associated with better lung function in RA-UIP patients. Because patients with RA-UIP can often have a worse

prognosis compared to RA-NSIP patients, the identification of a biomarker that is associated with better lung function could provide new insights into RA-ILD pathogenesis and may identify a new prognostic biomarker for RA-ILD, although future longitudinal studies are needed.

Disclosure: T. Wilson, None; **J. Solomon**, Pfizer Inc., 2, Boehringer Ingelheim, 2, Roche-Genentech, 9; **J. Swigris**, Gilead, 2, Boehringer Ingelheim, 2; **E. Darrah**, Bristol Myers Squibb, 2, Pfizer, 2, Celgene, 2, Gilead, 5; **M. Demoruelle**, Pfizer Inc., 2.

Abstract Number: 1201

Effect of Filgotinib on Pain in Patients with Rheumatoid Arthritis: Results from Phase 3 Clinical Trials

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: RA patients (pts) often suffer substantial pain despite ongoing treatment (tx) and regard pain control as a top tx goal. Filgotinib (FIL)—a potent, oral Janus kinase-1 selective inhibitor—was efficacious and generally well tolerated in the FINCH phase 3 RA clinical trial program.[1,2] A post hoc analysis of FINCH studies was conducted to assess the impact of FIL on pain.

Methods: All pts met 2010 ACR/EULAR criteria for RA. In FINCH 3 (F3), MTX-naïve RA pts received FIL 200 mg + MTX, FIL 100 mg + MTX, FIL 200 mg monotherapy, or MTX monotherapy for up to 52 weeks (W). Pts in FINCH 1 (F1) had active RA and inadequate response to MTX (MTX-IR) and received FIL 200 mg, FIL 100 mg, adalimumab (ADA) 40 mg, or placebo (PBO) on a background of MTX for up to 52W; at W24, PBO pts were rerandomized to FIL 200 or 100 mg. In FINCH 2 (F2), pts receiving conventional synthetic (cs)DMARDs who had an inadequate response or intolerance to biologic DMARD (bDMARD-IR) received FIL 200 mg, 100 mg, or PBO on a background dose of csDMARD(s) for up to 24W.

Each study was analyzed separately. Pt-reported pain was assessed on a visual analog scale (VAS). Proportions of pts achieving thresholds of 30% (defined as "moderate clinically important differences") and 50% ("substantial improvements")[3] reduction from baseline were analyzed, as were exploratory thresholds of 70% and 90%, and residual VAS pain scores of ≤10/20/40 mm out of 100 mm. P-values were calculated from the logistic regression with tx groups and stratification factors in the model. Comparisons were not adjusted for multiplicity; nominal P values are presented and should be interpreted as exploratory.

Results: Median duration of RA since diagnosis was 0.3–0.4 years (y) in F3, 4.8–5.8y in F1, and 9.8–10.3y in F2. Baseline pain was high among all arms (mean VAS scores of 64–68 mm across studies). Pain improved across pt populations from MTX-naïve to bDMARD-IR during tx. At W2, the percent of pts with pain reduction ≥30%, ≥50%,

Table 1. Achievement of pain ≥30%/50%/70%/90% reduction and residual pain score <10/20/40 mm

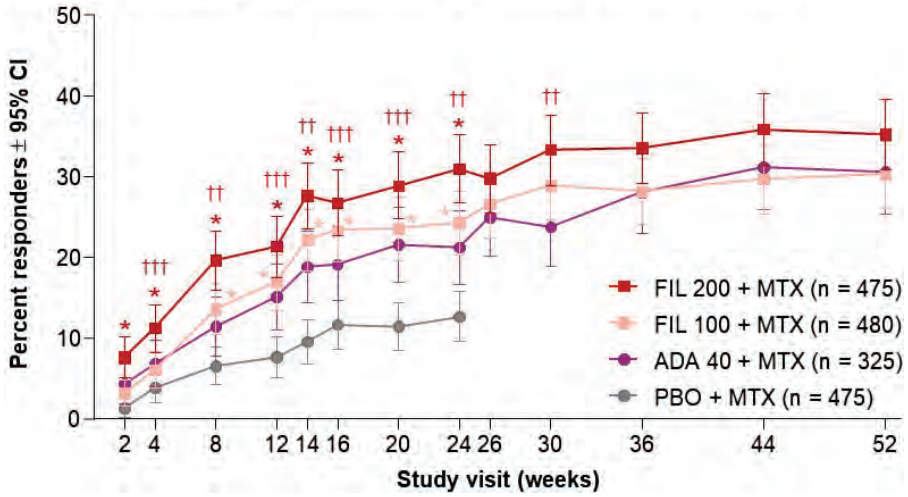
	FINCH 1				FINCH 2			FINCH 3			
	FIL 200 + MTX n = 475	FIL 100 + MTX n = 480	ADA 40 + MTX n = 325	PBO + MTX n = 475	FIL 200 + csDMARD n = 147	FIL 100 + csDMARD n = 153	PBO + csDMARD n = 148	FIL 200 + MTX n = 416	FIL 100 + MTX n =207	FIL 200 n = 210	MTX n = 416
Percent of pts achieving a 30% reduction from baseline											
Week 2	**36.2***	**30.1***	32.9	18.7	**44.2***	**36.6****	21.6	**44.4†**	**34.5†**	**36.2†**	19.2
Week 12	**67.4***	**61.8***	60.9	44.8	**59.9***	**50.3***	27.0	**69.8†**	**62.6†††**	56.7	54.3
Week 24	**67.4***	**68.5***	65.2	50.7	**61.2***	45.8	35.1	**73.4††**	66.5	68.1	63.2
Week 52	69.7	69.1	67.4	—	—	—	—	**66.9†**	**66.0††**	**69.5†**	54.6
Percent of pts achieving a 50% reduction from baseline											
Week 2	**20.0***	**12.9*****	16.0	8.2	**24.5***	**17.0*****	8.8	**24.6†**	**20.4†**	**21.4†**	10.1
Week 12	**50.1*†††**	**45.1***	41.5	28.0	**49.7***	**39.9***	19.6	**59.2†**	**48.5†††**	**47.6†††**	39.2
Week 24	**56.6***	**55.1***	52.0	39.2	**49.7***	**39.9****	25.0	**63.5†**	54.4	**57.1†††**	48.6
Week 52	62.5	58.9	58.8	—	—	—	—	**60.1†**	**57.8†††**	**61.4†**	47.6
Percent of pts achieving a 70% reduction from baseline											
Week 2	**10.9*†††**	4.8	5.8	3.8	**8.8*****	6.5	2.0	**11.8†**	**9.7††**	**10.0††**	3.6
Week 12	**33.9*†**	**26.3***	22.5	13.5	**29.9***	**25.5****	12.2	**42.3†**	**33.5††**	**35.7†**	23.6
Week 24	**40.6*†††**	**35.3***	33.8	23.4	**37.4***	**31.4***	10.8	**50.2†**	40.8	40.5	33.7
Week 52	47.8	43.2	44.0	—	—	—	—	**52.2†**	**45.1†††**	**47.1††**	36.1
Percent of pts achieving a 90% reduction from baseline											
Week 2	**2.1*****	1.3	1.2	0.2	1.4	2.0	0.7	**2.7†††**	**2.9†††**	**3.3†††**	0.2
Week 12	**13.7*††**	**9.8***	7.7	3.4	**10.9*****	8.5	4.1	**20.8†**	**17.5††**	**19.5†**	8.7
Week 24	**20.0*††**	**15.0***	12.9	6.7	**16.3***	**13.7****	4.1	**27.3†**	**21.8††**	**21.9††**	13.7
Week 52	25.1	22.8	21.8	—	—	—	—	**31.6†**	**24.8††**	**26.2††**	15.9
Percent of pts who achieved ≤10 mm residual pain score											
Week 2	**7.6***	3.1	4.3	1.3	4.8	3.9	2.0	**8.2†**	**7.2††**	5.7	2.6
Week 12	**21.3*†††**	**16.9***	15.1	7.6	**19.7***	**13.7****	4.7	**30.8†**	**26.1†**	**26.7†**	13.7
Week 24	**30.9*††**	**24.2***	21.2	12.6	**24.5***	**20.3****	7.4	**39.4†**	**32.9†††**	29.0	24.3
Week 52	35.2	30.2	30.5	—	—	—	—	**43.8†**	31.4	**34.8†††**	26.7
Percent of pts who achieved ≤20 mm residual pain score											
Week 2	**16.4*†††**	8.1	10.2	5.3	**17.0****	12.4	6.8	**16.3†**	**14.0††**	**14.3††**	6.5
Week 12	**37.7*†**	**30.0***	25.5	16.2	**35.4***	**27.5****	14.2	**46.2†**	**35.7††**	**35.7††**	25.0
Week 24	**45.7*†††**	**40.2***	36.9	25.9	**40.1***	**33.3***	13.5	**54.1†**	42.5	42.9	35.8
Week 52	49.7	45.2	47.7	—	—	—	—	**53.4†**	42.5	**48.1†††**	37.7
Percent of pts who achieved ≤40 mm residual pain score											
Week 2	**35.8*†††**	**29.6***	28.9	17.1	**41.5***	**33.3****	18.9	**43.0†**	**32.9††**	**33.8†**	21.2
Week 12	**61.5***	**57.3***	56.0	38.3	**58.5***	**47.1****	29.1	**70.4†**	55.6	53.3	49.8
Week 24	**65.3***	**66.0***	62.8	46.9	**57.8***	**43.8*****	29.7	**70.2†**	63.3	61.4	58.4
Week 52	68.6	66.0	64.6	—	—	—	—	**65.4†**	**61.8†††**	**66.7†**	52.9

***Nominal P <0.05 for FIL arm vs PBO, **nominal P <0.01 for FIL arm vs PBO, *nominal P <0.001 for FIL arm vs PBO; †††nominal P <0.05 for FIL arm vs ADA or MTX, ††nominal P <0.01 for FIL arm vs ADA or MTX, †nominal P <0.001 for FIL arm vs ADA or MTX. P-values were calculated from the logistic regression with treatment groups and stratification factors in the model. Pts with missing outcomes were set as nonresponders for binary response measurements. —, not measured at this time point because in FINCH 1, pts receiving PBO were rerandomized 1:1 to FIL 200 or 100 mg at week 24, and, in FINCH 2, the study period ended at 24 weeks. ADA, adalimumab; csDMARD, conventional synthetic DMARD; FIL, filgotinib; PBO, placebo; pts, patients.

and residual pain ≤40 mm was significantly greater for all FIL arms compared with PBO (F1/F2) or MTX (F3) (nominal P < 0.05; **Table 1**). Pain was reduced by ≥90% by W52 in approximately 25% of pts in F1/F3 (**Table 1**). Except for pts receiving FIL 100 mg in the ≥30% reduction analysis, significantly more bDMARD-IR pts receiving FIL had pain reduction at W24 compared with PBO in all analyses (F2; nominal P < 0.05; **Table 1**). FIL + MTX significantly reduced pain in MTX-naïve pts vs MTX monotherapy (F3; nominal P < 0.05 for FIL 200 for all measures and time points and for FIL 100 for several measures and time points; **Table 1**). Overall, more pts with MTX-IR (F1) receiving FIL had greater pain reduction and lower residual pain vs pts receiving ADA, with significant differences noted for FIL 200 (but not FIL 100) for some measures at W2–W30 (nominal P < 0.05; **Table 1**; **Fig 1**; **Fig 2**).

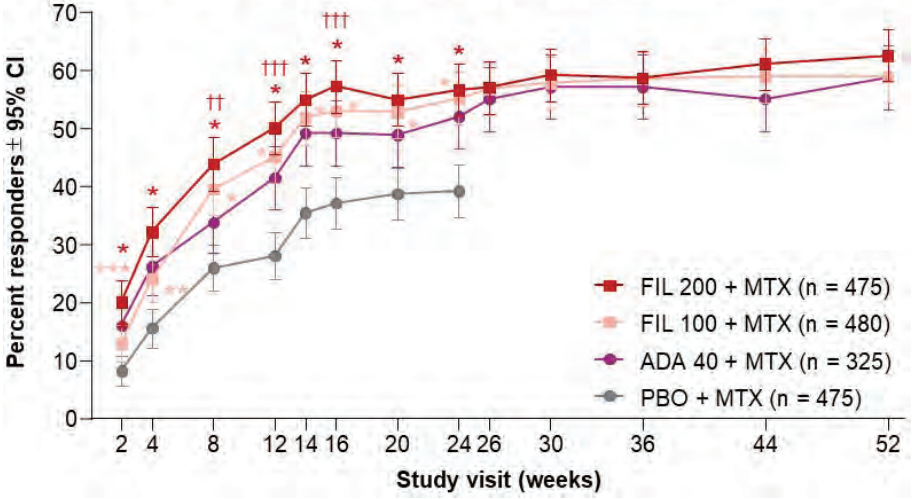
Conclusion: FIL 200 and 100 mg provided rapid, clinically meaningful pain relief among a broad spectrum of RA pts and across several measures. The degree of improvement was substantial for many pts; ≥40% of pts in all studies had a ≥50% reduction in pain.

Figure 1. Percent of patients with residual pain score of ≤10 mm in FINCH 1



Pts receiving PBO were rerandomized 1:1 to FIL 200 or 100 mg at week 24. P-values for FIL vs PBO were assessed for weeks 2—24; P-values for FIL vs ADA were assessed for all visits. *Nominal P <0.001 for FIL 200 or FIL 100 vs PBO; †††nominal P <0.05 for FIL 200 vs ADA, ††nominal P <0.01 for FIL 200 vs ADA. P-values were calculated from the logistic regression with treatment groups and stratification factors in the model. Pts with missing outcomes were set as nonresponders for binary response measurements. ADA, adalimumab; CI, confidence interval; FIL, filgotinib; PBO, placebo; pts, patients.

Figure 2. Percent of patients who achieved a ≥50% reduction of pain in FINCH 1



Pts receiving PBO were rerandomized 1:1 to FIL 200 or 100 mg at week 24. P-values for FIL vs PBO were assessed for weeks 2–24; P-values for FIL vs ADA were assessed for all visits. ***Nominal P <0.05 for FIL 100 vs PBO, **nominal P <0.01 for FIL 100 vs PBO, *nominal P <0.001 for FIL 200 or FIL 100 vs PBO; †††nominal P <0.05 for FIL 200 vs ADA, ††nominal P <0.01 for FIL 200 vs ADA. P-values were calculated from the logistic regression with treatment groups and stratification factors in the model. Pts with missing outcomes were set as nonresponders for binary response measurements. ADA, adalimumab; CI, confidence interval; FIL, filgotinib; PBO, placebo; pts, patients.

References

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2) Westhovens et al. *Arthritis Rheumatol*. 2019;71 [suppl 10]:1606–8.
3) Dworkin et al. *J Pain.* 2008;9:105–21.

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Abstract Number: 1202

Cannabis Use Assessment and Its Impact on Pain in Rheumatic Diseases: A Systematic Review and Meta-analysis

Manon Guillouard[1], Nicolas Authier[1], Bruno Pereira[1], Martin Soubrier[1] and **Sylvain Mathieu**[1], [1]CHU Gabriel Montpied, Clermont-Ferrand, France

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Despite classic analgesic or effective treatments in rheumatic diseases, such as synthetic Disease Modifying Anti-Rheumatic Drugs in rheumatoid arthritis (RA), patients remain in pain and often turn to non-prescribed pharmacological alternatives, such as cannabis self-therapeutic use. However, this medical use of cannabis has not been thoroughly studied.

Methods: We searched PubMed to find reports of interest published since 24 January 2020. The following search terms were used: "(cannabis OR cannabinol OR cannabinoids) and (rheumatoid OR osteoarthritis OR ankylosing OR arthritis OR arthralgia OR pain OR spondylitis)". The incidence of cannabis consumption was calculated by metaproportion. Differences between cannabis users and non-users were expressed as standardized mean differences using the inverse-variance method. We also assessed the effects of cannabis on pain.

Results: A total of 2,807 citations were obtained from the initial search. After reading the title, abstract, and full text, we obtained 13 eligible studies, plus 7 found searching abstract databases, for a total of 13,134 patients with rheumatic diseases. Cannabis consumption. In the 12 studies on rheumatic diseases, a total of 2,666 patients reported cannabis consumption in a sample of 9,665 patients (incidence 40.3% [95%CI 26.2,55.2]), and 16% [95%CI 4.8,32.1] specified that they were currently taking cannabis. Cannabis use was higher in the three fibromyalgia studies (56.3%

[95%CI 0.26,0.84], n=510) compared to five articles concerning RA or lupus (33.6% [95% CI 0.16,0.54], n=7,061). Effects of cannabis on pain over time. Cannabis consumption was associated with a decrease in pain intensity (VAS pain at baseline 8.2±2.9 vs. 5.6±3.5 mm over time; pooled effect size -1.75 [95%CI -2.75,-0.76]). Tolerance was good with mild or moderate side effects. Patients reported red eyes (7 to 90%), dry mouth (7 to 27%), hunger feeling (1 to 15%), sore thorat (10%), nausea (1 to 5%), somnolence (2 to 3%), hyperactivity (1 to 5%) or mood deflection (7%). Comparison of cannabis users and non-users. Cannabis users were younger (58.2±11.1 vs. 63.4±11.9 years; p< 0.001), more often smokers (OR 3.37 [95%CI 1.91,5.92]) or unemployed (OR 2.25 [95%CI 1.09,4.65]), and had higher pain intensity (4.9±2.4 vs. 4.1±2.5 mm; p< 0.001) than non-users. A significant relationship was found, with a three-fold risk of cannabis use among alcohol drinkers (148/304 (48.7%) vs. 382/1581 (24.2%); OR 3.12 [95% CI 2.41,4.04]). The proportion of cannabis users was significantly lower in female patients (OR 0.52 [95% CI 0.28,0.96], p=0.04).

Conclusion: Nearly 20% of patients suffering from rheumatic diseases actively consume cannabis, with an improvement in pain. The issue of cannabis use in the management of these patients should be addressed during medical consultation, essentially with cannabis-based standardized pharmaceutical products.

Disclosure: M. Guillouard, None; **N. Authier**, None; **B. Pereira**, None; **M. Soubrier**, None; **S. Mathieu**, Bristol Myers Squibb, 1, Pfizer, 1, Abbvie, 1, Novartis, 1, Roche and Chugai, 1, Merck Sharp and Dohme, 1.

Abstract Number: 1203

Analysis of the Impact of Tofacitinib Treatment on Weight in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: A prior post hoc analysis of tofacitinib clinical trial data reported improvements in RA outcomes with tofacitinib vs placebo (PBO) through Month (M)6, regardless of baseline (BL) BMI.[1] This post hoc analysis assessed change from BL (Δ) in BMI, and disease activity by BL BMI status, in patients (pts) with moderate/severe RA receiving tofacitinib through M12.

Methods: Data were pooled from Phase 3 and 3b/4 studies of pts who were MTX-naïve (NCT01039688), or inadequate responders to conventional synthetic (cs) or biologic DMARDs (NCT00960440; NCT00847613; NCT00814307; NCT00856544; NCT00853385; NCT02187055; NCT02831855). Pts received ≥ 1 dose of tofacitinib 5 or 10 mg twice daily (BID), or 11 mg once daily (QD), alone or with background csDMARDs, or PBO. Least squares (LS) mean ΔBMI (linear mixed model repeated measures; observed cases) was summarized for all treatment groups at M3/6/12 (M3/6 only for tofacitinib 11 mg QD and PBO). Other assessments at M3/6/12 included ΔBMI +/- BL concomitant glucocor-

Table 1. Patient demographics and baseline characteristics

	Tofacitinib 5 mg BID (N=2,349)	Tofacitinib 10 mg BID (N=1,611)	Tofacitinib 11 mg QD (N=694)	PBO (N=681)
Female, n (%)	1,943 (82.7)	1,357 (84.2)	532 (76.7)	553 (81.2)
Age (years), mean (SD)	51.6 (12.2)	51.7 (12.0)	56.8 (11.8)	52.5 (12.0)
Race, n (%)				
White	1,558 (66.3)	1,007 (62.5)	594 (85.6)	439 (64.5)
Black	88 (3.8)	47 (2.9)	33 (4.8)	24 (3.5)
Asian	474 (20.2)	377 (23.4)	37 (5.3)	166 (24.4)
Other	229 (9.8)	180 (11.2)	30 (4.3)	52 (7.6)
BMI (kg/m^2), mean (SD)	27.3 (6.5)	27.0 (6.3)	28.2 (6.2)	27.2 (6.8)
Smoking status, n (%)				
Smoker	336 (14.3)	282 (17.5)	129 (18.6)	130 (19.1)
Ex-smoker	389 (16.6)	238 (14.8)	163 (23.5)	124 (18.2)
Never smoked	1,624 (69.1)	1,091 (67.7)	402 (57.9)	425 (62.4)
Duration of RA (years), mean (SD)	7.6 (7.7)	7.7 (8.1)	8.8 (8.8)	9.3 (8.5)
DAS28 -4(ESR), mean (SD)	6.5 (1.0)	6.5 (1.0)	6.0 (1.0)	6.4 (1.0)
Treatment history, n (%)				
Prior MTX	1,946 (82.8)	1,183 (73.4)	690 (99.4)	649 (95.3)
Prior non-MTX csDMARD	1,122 (47.8)	908 (56.4)	100 (14.4)	398 (58.4)
Prior TNFi	338 (14.4)	287 (17.8)	95 (13.7)	201 (29.5)
Prior non-TNFi bDMARD	109 (4.6)	72 (4.5)	55 (7.9)	46 (6.8)
Concomitant glucocorticoid use, n (%)	1,348 (57.4)	864 (53.6)	174 (25.1)	396 (58.2)
Concomitant antidepressant use, n (%)	194 (8.3)	125 (7.8)	37 (5.3)	46 (6.8)
Comorbidities at baseline, n (%)				
Diabetes	204 (8.7)	127 (7.9)	74 (10.7)	48 (7.1)
Coronary heart disease	14 (0.6)	5 (0.3)	2 (0.3)	4 (0.6)
Myocardial infarction	25 (1.1)	20 (1.2)	14 (2.0)	7 (1.0)
Hypertension	820 (34.9)	579 (35.9)	299 (43.1)	243 (35.7)

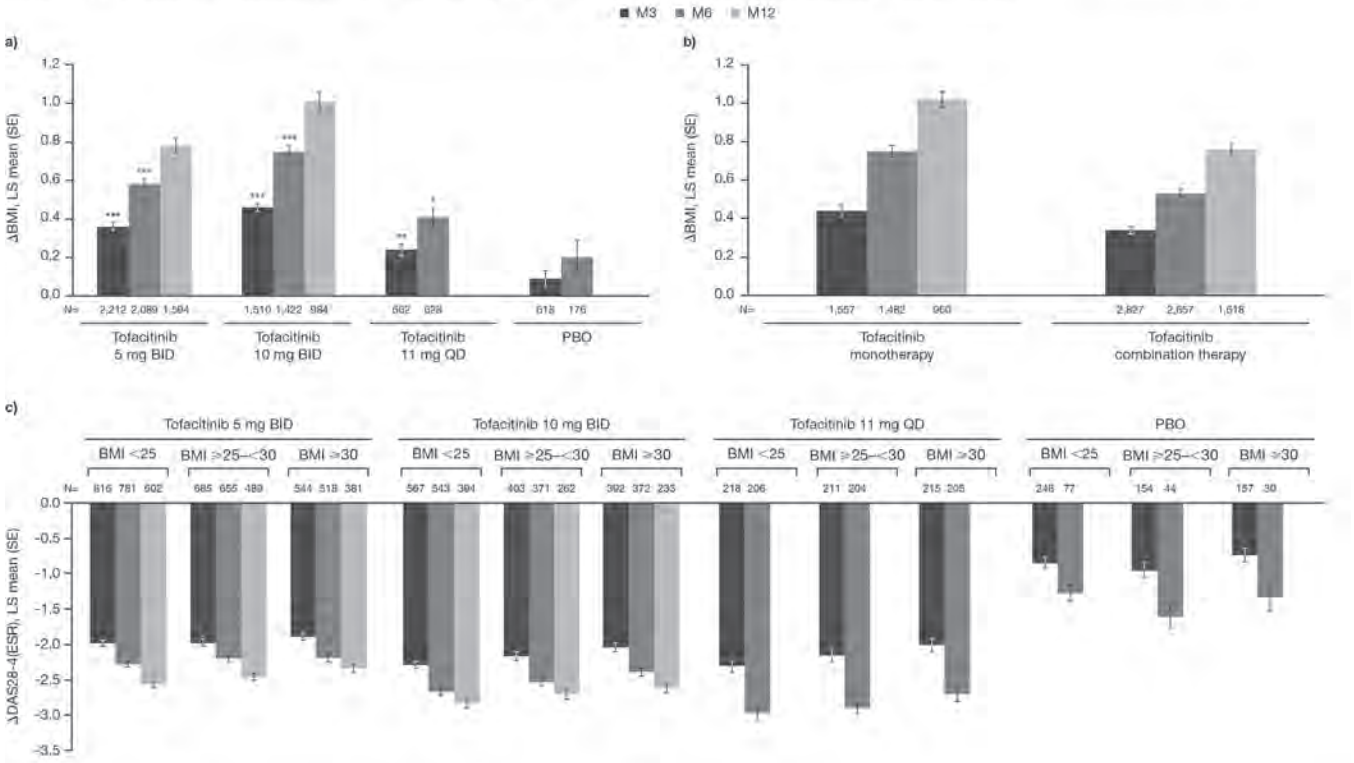
bDMARD, biologic DMARD; BID, twice daily; BMI, body mass index; csDMARD, conventional synthetic DMARD; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; DMARD, disease-modifying antirheumatic drug; MTX, methotrexate; N, number of patients in the analysis; n, number of patients in each category; PBO, placebo; QD, once daily; RA, rheumatoid arthritis; SD, standard deviation; TNFi, tumor necrosis factor inhibitor

ticoids (GC) or antidepressants (descriptive statistics only), LS mean ΔDAS28-4(ESR), stratified by BL BMI status (< 25, ≥ 25 – < 30, ≥ 30), and correlations between LS mean ΔBMI and ΔDAS28-4(ESR).

Results: In total, 2,349, 1,611, 694, and 681 pts received tofacitinib 5 mg BID, 10 mg BID, 11 mg QD, or PBO, respectively. Demographics and baseline characteristics were generally similar across treatment groups, except in pts receiving tofacitinib 11 mg QD, where some differences were observed in gender, race, and concomitant GC use (Table 1). At M3/6, LS mean BMI significantly increased from BL with all tofacitinib doses vs PBO (all $p< 0.05$); ΔBMI was greatest with 10 mg BID, and lowest with 11 mg QD (Figure 1a). LS mean ΔBMI was greater in pts receiving tofacitinib as monotherapy vs combination therapy at M3/6/12 (Figure 1b). ΔBMI was generally similar in pts receiving treatment +/- concomitant GCs or antidepressants (data not shown). Improvements in DAS28-4(ESR) scores were observed in each BL BMI status group at M3/6/12, and were greatest with all tofacitinib doses vs PBO. LS mean ΔDAS28-4(ESR) was generally numerically highest for pts with BMI < 25 and numerically lowest for pts with BMI > 30, for all tofacitinib doses. LS mean ΔDAS28-4(ESR) was also generally greatest with tofacitinib 10 mg BID and 11 mg QD vs 5 mg BID across BL BMI status groups (Figure 1c). Across treatment groups, model-adjusted associations between ΔDAS28-4(ESR) scores and ΔBMI were weak (correlation coefficients all < 0.3; Table 2).

Conclusion: ΔBMI was greater with tofacitinib (all doses) vs PBO at M3/6, and with tofacitinib monotherapy vs combination therapy at M3/6/12. Improvements in DAS28-4(ESR) were seen across all BL BMI status groups. BMI increases with tofacitinib were only weakly associated with DAS28-4(ESR) improvements. The relationship between disease activity and ΔBMI requires further investigation.

Figure 1. a) ΔBMI in patients with RA receiving tofacitinib 5 or 10 mg BID, tofacitinib 11 mg QD or placebo;[a] b) ΔBMI in patients with RA receiving tofacitinib monotherapy or tofacitinib in combination with csDMARDs;[b] c) ΔDAS28-4(ESR) in patients with RA, stratified by BL BMI status[c]



[a]Statistical analyses were performed for comparisons of ΔBMI in patients receiving tofacitinib vs PBO up to M6 only; [b]Descriptive statistics only.
*p<0.05, **p<0.01, ***p<0.001. LS means were calculated using longitudinal linear MMRM (observed cases), with treatment, visit, treatment*visit, BL BMI (panels A and B) or BL DAS28-4(ESR) (panel C), age, gender, race, and RA duration included in the model. For patients receiving tofacitinib 11 mg QD in ORAL Shift (NCT02831855), only data up to M6 were included: Patients who advanced from PBO to tofacitinib at the end of the PBO-controlled period were excluded from the analysis post-advancement
Δ, change from baseline; BID, twice daily; BL, baseline; BMI, body mass index; csDMARDs, conventiona synthetic DMARDs; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; DMARD, disease-modifying antirheumatic drug; LS, least squares; M, month; MMRM, mixed model repeated measures; N, number of patients in the analysis at each time point; PBO, placebo; QD, once daily; RA, rheumatoid arthritis; SE, standard error

Table 2. Correlations between LS mean ΔDAS28-4(ESR) and ΔBMI through M12

Correlation between ΔDAS28-4(ESR) and ΔBMI

	Tofacitinib 5 mg BID		Tofacitinib 10 mg BID		Tofacitinib 11 mg QD		PBO	
	N	Correlation coefficient	N	Correlation coefficient	N	Correlation coefficient	N	Correlation coefficient
M3	2,021	0.1169	1,348	0.1240	641	0.0907	554	0.0783
M6	1,918	0.1305	1,270	0.1397	611	0.0438	150	0.1556
M12	1,455	0.1213	874	0.1826	---	---	---	---

Slopes for associations between ΔBMI and ΔDAS28-4(ESR) were significantly different from 0 at M3/6/12 with tofacitinib 5 and 10 mg BID (all p<0.05); Correlations between ΔBMI and ΔDAS28-4(ESR) were analyzed by a general linear model method, with BL age, race, gender, and RA duration included in the model. For patients receiving tofacitinib 11 mg QD in ORAL Shift (NCT02831855), only data up to M6 were included; Patients who advanced from PBO to tofacitinib at the end of the PBO-controlled period were excluded from the analysis post-advancement
Δ, change from baseline; BID, twice daily; BL, baseline; BMI, body mass index; DAS28-4(ESR), Disease Activity Score in 28 joints, erythrocyte sedimentation rate; LS, least squares; M, month; N, number of patients in the analysis at each time point; PBO, placebo; QD, once daily; RA, rheumatoid arthritis

1. Dikranian A et al. Arthritis Rheumatol 2018; 69 (suppl 10).

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er Inc, 2, Roche-Chugaï, 2, Sandoz, 2; **A. Ruyssen-Witrand**, None; **C. Lukas**, None; **C. Richez**, None; **A. Shapiro**, Pfizer Inc, 1, 3; **D. Chapman**, Pfizer Inc, 1, 3; **M. Cros**, Pfizer Inc, 1, 3; **J. Rivas**, Pfizer Inc, 1, 3; **G. Citera**, AbbVie, 5, 8, Eli Lilly, 5, 8, Bristol-Myers Squibb Company, 5, 8, Gema, 5, 8, Pfizer, 5, 8, Janssen, 5, 8.

Abstract Number: 1204

Use of Multi-Biomarker Disease Activity Scores to Assess Biosimilarity in a Phase 3 Randomized Controlled Trial Comparing Biosimilar Infliximab-qbtx (PF-06438179/GP1111) with EU-Sourced Reference Infliximab in Patients with Active RA

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

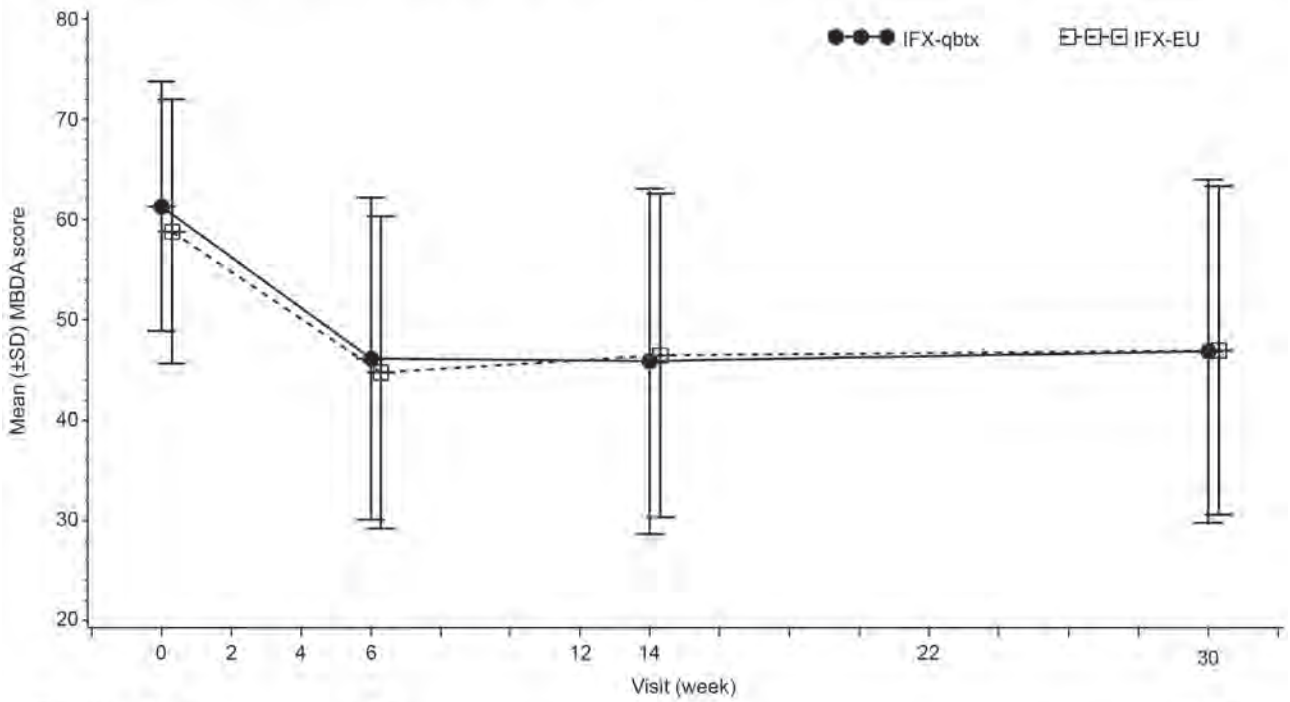
Background/Purpose: The multi-biomarker disease activity (MBDA; Vectra® DA, Myriad Genetics, Inc.) score is calculated from concentrations of 12 serum proteins to assess disease activity (DA) of patients with RA (Centola et al. PLoS One 2013;8(4):e60635). In a phase 3 randomized controlled trial (RCT), efficacy of the infliximab (IFX) biosimilar IFX-qbtx (PF-06438179/GP1111) was equivalent to that of reference IFX sourced from the European Union (IFX-EU; Janssen Biologics B.V., Leiden, The Netherlands) in patients with active, moderate to severe RA (Cohen et al. *Arthritis Res Ther* 2018;20(1):155). In this exploratory analysis, we compared MBDA scores between treatment groups in this RCT to determine the utility of this approach as an assessment of biosimilarity.

Methods: All 650 patients in the study met the 2010 ACR/EULAR classification criteria for RA and had disease duration of ≥4 months. Patients were randomized 1:1 to IFX-qbtx or IFX-EU (3 mg/kg intravenous at weeks 0, 2, 6, and then every 8 weeks), both given with MTX (10-25 mg/week). Mean values of MBDA scores (low: 1 to < 30; moderate: 30 to ≤44; high: >44–100) were calculated at baseline (BL), and at weeks 6, 14, 30, 54, and 78 by combining the concentrations of 12 serum biomarkers using the Vectra® DA algorithm. Mean MBDA scores were compared between treatment groups. Results are reported from treatment period 1 (weeks 0–30). Analyses were performed using the intent-to-treat (ITT) population, without imputation for missing data, and data were summarized using descriptive statistics.

Results: At baseline (BL), mean (± standard deviation [SD]) MBDA scores for IFX-qbtx (n=236) and IFX-EU (n=248) were 61.3 (±12.5) and 58.8 (13.2), respectively. Mean MBDA scores were comparable between IFX-qbtx and IFX-EU at all measured time points through week 30 (**Figure**). Similar proportions in the IFX-qbtx (66.0%) and IFX-EU (66.9%) groups had high (>44) MBDA scores at BL; the proportions of patients with high MBDA scores decreased to 42.3% and 40.2%, respectively, at week 30. Mean MBDA scores decreased by 15.2 and 14.1 from BL to week 6 in the IFX-qbtx and IFX-EU groups, respectively, and remained sTable between weeks 6 and 30. Changes in the concentrations of individual biomarkers over time were generally similar between treatment groups. Changes from BL in MBDA scores correlated positively with changes from BL in high-sensitivity CRP (hs-CRP) results (**Table**).

Conclusion: This RCT of IFX-qbtx and IFX-EU comparing efficacy of a biosimilar and its reference product is the first study that incorporated MBDA score as an assessment of biosimilarity. Changes in MBDA scores over time were similar between IFX-qbtx and IFX-EU groups. Use of an MBDA score based on serum biomarker levels provides a sensitive assessment of biosimilarity that is independent of DA measures, which require physical examination of the patient or subjective patient global assessment.

Figure. Mean MBDA score over time up to week 30 in patients with RA treated with IFX-qbtx or IFX-EU (ITT population)[a]



[a] Baseline was defined as the measurement taken at the week 0 visit. For post-baseline visits, patients with both baseline and post-baseline data at each visit were counted.

Table. Correlations between MBDA scores and hs-CRP (ITT population)[a]

	Pearson's correlation coefficient (r)	
MBDA score vs hs-CRP	**IFX-qbtx**	**IFX-EU**
Baseline	0.742	0.812
Change from baseline to week 6	0.798	0.814
Change from baseline to week 14	0.782	0.802
Change from baseline to week 30	0.814	0.820

[a] Baseline was defined as the measurement taken at the week 0 visit.

Disclosure: J. Kay, Pfizer Inc., 9, Alvotech Suisse AG, 1, Arena Pharmaceuticals, Inc., 1, Boehringer Ingelheim GmbH, 1, Celltrion Healthcare Co. Ltd., 1, Mylan Inc., 5, Novartis AG, 5, Samsung Bioepis, 5, Sandoz Inc., 5, Gilead Sciences, Inc., 9; **D. Alvarez**, Pfizer, 1, 2; **M. Rehman**, Pfizer, 1, 3; **M. Zhang**, Pfizer, 1, 3; **N. Iikuni**, Pfizer, 1, 3.

Abstract Number: 1205

Soluble Vascular Biomarkers in Rheumatoid Arthritis and Ankylosing Spondylitis: Effects of One-year Anti-TNF-α Therapy

Anita Pusztai[1], Attila Hamar[2], Ágnes Horváth[2], Katalin Gulyás[2], Edit Végh[2], Nóra Bodnár[2], György Kerekes[2], Monika Czókolyová[2], Szilvia Szamosi[2], Levente Bodoki[2], Katalin Hodosi[2], Andrea Domján[2], Gábor Nagy[2], Luis Lopez[3], Ejii Matsuura[4], Zoltán Prohászka[5], Sándor Szántó[2], Zoltán Nagy[2], Yehuda Shoenfeld[6], **Zoltán Szekanecz**[2] and Gabriella Szűcs[2], [1]University of Debrecen Faculty of Medicine, Department of Rheumatology, Debrecen, Hungary, [2]University of Debrecen, Debrecen, Hungary, [3]Corgenix Inc., Broomfield, CO, [4]Okayama University, Okayama, Japan, [5]Semmelweis University, Budapest, Hungary, [6]Zabludowicz Center, Tel-Hashomer, Israel

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) and ankylosing spondylitis (AS) have been associated with cardiovascular (CV) disease. The treatment of arthritis by tumour necrosis factor α (TNF-α) inhibitors may decrease the serum concentrations of vascular biomarkers. We determined circulating levels of oxidized LDL (oxLDL)/β2 glycoprotein I (β2GPI) complexes, antibodies to 60 kDa heat shock protein (anti-Hsp60), soluble urokinase plasminogen activator receptor (suPAR) and Brain type natriuretic peptide (BNP) fragment in sera of RA and AS patients undergoing anti-TNF treatment.

Methods: Fifty-three RA/AS patients were treated with etanercept (ETN) or certolizumab pegol (CZP) for one year. Circulating oxLDL/β2GPI complex (AtherOx®), anti-Hsp60 IgG and BNP_{8-29} fragment levels were assessed by ELISA. suPAR levels were determined by suPARnostic® Quick Triage test. Flow-mediated vasodilation (FMD), carotid intima-media thickness (IMT) and arterial pulse-wave velocity (PWV) were determined by ultrasound.

Results: One-year anti-TNF treatment significantly decreased oxLDL/β2GPI levels, as well as suPAR levels in patients with "critically" high suPAR levels at baseline. In RA, BNP levels were higher in seropositive vs seronegative patients. Serum levels of these vascular biomarkers variably correlated with lipids, ACPA, RF and CRP. IMT positively correlated with BNP, PWV with suPAR and anti-Hsp60, while FMD inversely associated with anti-Hsp60. In RM-ANOVA analysis, disease activity supported the effects of anti-TNF treatment on 12-month changes in oxLDL/β2GPI. IMT supported the effects of therapy on changes of anti-Hsp60 and suPAR.

Conclusion: These biomarkers may be involved in the pathogenesis of atherosclerosis underlying RA/AS. TNF inhibition variably affect the serum levels of oxLDL/β2GPI, suPAR and BNP.

Disclosure: A. Pusztai, None; **A. Hamar**, None; **. Horváth**, None; **K. Gulyás**, None; **E. Végh**, None; **N. Bodnár**, None; **G. Kerekes**, None; **M. Czókolyová**, None; **S. Szamosi**, None; **L. Bodoki**, None; **K. Hodosi**, None; **A. Domján**, None; **G. Nagy**, None; **L. Lopez**, Corgenix Inc, 1; **E. Matsuura**, None; **Z. Prohászka**, None; **S. Szántó**, None; **Z. Nagy**, None; **Y. Shoenfeld**, None; **Z. Szekanecz**, Pfizer, 1; **G. Szűcs**, None.

Abstract Number: 1206

Associations of Vascular and Bone Status in Anti-TNF-treated Rheumatoid Arthritis and Ankylosing Spondylitis Patients

Anita Pusztai[1], Attila Hamar[2], Monika Czókolyová[2], Katalin Gulyás[2], Ágnes Horváth[2], Edit Végh[2], Zsófia Pethő[2], Szilvia Szamosi[2], Emese Balogh[2], Nóra Bodnár[2], Ágnes Szentpétery[3], Harjit Bhattoa[2], György Kerekes[2], Balázs Juhász[2], Éva Szekanecz[2], Katalin Hodosi[2], Andrea Domján[2], Sándor Szántó[2], Hennie Raterman[4], Willem Lems[5], **Zoltán Szekanecz**[2] and Gabriella Szűcs[2], [1]University of Debrecen Faculty of Medicine, Department of Rheumatology, Debrecen, Hungary, [2]University of Debrecen, Debrecen, Hungary, [3]Uppsala University Hospital, Uppsala, Sweden, [4]Northwest Clinics, Alkmaar, Netherlands, [5]Amsterdam Rheumatology and Immunology Centre, Amsterdam, Netherlands

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular (CV) disease and osteoporosis (OP) have become increasing challenges in the ageing population, even more in patients with inflammatory rheumatic diseases, such as rheumatoid arthritis (RA) and ankylosing spondylitis (AS). Both diseases have been associated with generalized and localized bone loss, accelerated atherosclerosis, increased CV morbidity and mortality.

Bone and vascular biomarkers and parameters along with the effect of one-year anti-TNF therapy on these markers were assessed in order to determine correlations between vascular pathophysiology and bone metabolism in RA and AS.

Methods: Fifty-three patients including 36 RA patients treated with etanercept (ETN) or certolizumab pegol (CZP) and 17 AS patients treated with ETN were included in a 12-month follow-up study. Bone and vascular markers were assessed by ELISA. Bone density was measured by DXA and quantitative CT (QCT). Flow-mediated vasodilation (FMD), common carotid intima-media thickness (IMT) and pulse-wave velocity (PWV) were assessed by ultrasound. Data on the effects of vascular markers on bone and bone effects on vasculature had undergone statistical analysis.

Results: We found a great number of correlations between vascular and bone surrogate markers. Both univariable and multivariable analyses suggested that osteoprotegerin (OPG) may positively determine FMD, parathyroid hormone (PTH) may be a determinant of PWV and sclerostin (SOST) may influence IMT at different time points. QCT total and trabecular BMD inversely correlated with IMT and IMT was also inversely associated with QCT total BMD. Baseline vitamin D3 (VITD3) inversely affected PWV. Some biomarkers at baseline also significantly determined other parameters at later time points. Moreover, one-year biologic treatment combined with baseline levels of different bone biomarkers may predict changes of IMT upon therapy. According to the multivariate analyses, systemic inflammation (C-reactive protein) or disease activity, as well as their change between baseline and 12 months may significantly influence the interrelationship between certain bone and vascular biomarkers.

Conclusion: In our study of anti-TNF treated RA and AS patients, vascular and bone parameters showed numerous correlations. Some bone markers may predict vascular status after one-year treatment and vice versa. Systemic inflammation and arthritic disease activity may influence the associations between bone and vascular biomarkers.

Bhattoa, None; **G. Kerekes**, None; **B. Juhász**, None; **. Szekanecz**, None; **K. Hodosi**, None; **A. Domján**, None; **S. Szántó**, None; **H. Raterman**, None; **W. Lems**, None; **Z. Szekanecz**, Pfizer, 1; **G. Szűcs**, None.

Abstract Number: 1207

Impact of Body Mass Index on Clinical Responses of Novel Subcutaneous Infliximab (CT-P13 SC) in Patients with Active Rheumatoid Arthritis: 1-Year Results from a Part 2 of Phase I/III Randomized Controlled Trial

DaeHyun Yoo[1], Rene Westhovens[2], Piotr Wiland[3], Marek Zawadzki[4], Delina Ivanova[5], Alfredo Berrocal Kasay[6], Elias Chalouhi[7], Eva Balázs[8], SangJoon Lee[9], SungHyun Kim[9], NooRi Han[9] and YooBin Jung[9], [1]Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [2]University Hospitals Leuven, Belgium, Leuven, Belgium, [3]Medical Univeristy, Wroclaw, Poland, [4]Medical Univeristy, Dpt of Rheumatology , Wroclaw, Wroclaw, Poland, [5]Diagnostic-Consultative Center Aleksandrovska EOOD, Sofia, Bulgaria, [6]ABK Reuma SRL, LIMA, Peru, [7]Clinica Internacional Sede Lima, Lima, Peru, [8]Dr. Bugyi István Hospital, Szentes, Hungary, [9]Celltrion, Inc., Incheon, Republic of Korea

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In the analysis of PLANETRA, a Phase III randomized controlled trial (RCT), no significant association was found between body mass index (BMI) and clinical responses in rheumatoid arthritis (RA) patients using weight-based intravenous (IV) infliximab (3 mg/kg every 8 weeks)[1,2]. Since the subcutaneous (SC) formulation of CT-P13 which was approved from EMA after demonstrating non-inferiority compared to CT-P13 IV is a fixed-dose of 120 mg biweekly, it is meaningful to evaluate the impact of BMI on the clinical response of CT-P13 SC[3,4]. This study is to investigate the impact of BMI on clinical responses of CT-P13 SC 120 mg in Part 2 of Phase I/III RCT in active RA patients throughout the 1-year treatment period.

Methods: A total of 165 patients who received at least one full dose of CT-P13 SC (after IV infusions at Weeks 0 and 2 in the IV dose-loading phase) before Week 30 and who had at least one efficacy evaluation result after Week 6 or thereafter were included in this analysis. Patients were categorized into the three groups; under/normal weight (< 25kg/m^2), overweight (≥25kg/m^2, < 30kg/m^2), and obesity (≥30kg/m^2) based on the WHO BMI classification. Baseline characteristics, mean change from baseline in disease activity by DAS28 (CRP), remission (DAS28 [CRP]≤2.6) and low disease activity (LDA; 2.6< DAS28 [CRP]≤3.2), duration (week) of LDA, EULAR response, and ACR response were evaluated among the three BMI groups.

Results: In the under/normal weight (n=63), overweight (n=61), and obesity (n=41) groups, the mean±SD of age (years) (48.7±14.00, 51.5±10.93, 53.8±10.62) and the mean±SD of RA duration (years) (6.4±6.00, 8.2±9.27, 5.4±4.72) were comparable. At baseline, the rates of high disease activity (90.5%, 90.2%, 87.8%; DAS28 [CRP] >5.1) were similar among the groups. All other baselines and disease characteristics including gender, race, and other disease activity were also comparable among the groups. The rate of remission or LDA (Figure 1), the mean change from baseline of DAS28 (CRP) (-3.3, -3.1, -3.3 at Week 54), duration of LDA up to Week 54 (26.2, 29.2, 27.9 weeks), and the good or moderate EULAR responder rates (84.1%, 80.3%, 90.2% at Week 54) were all comparable among the groups and there were no statistically significant differences (p-value >0.05). The ACR responder rates were also comparable among the groups except for the ACR70 at Weeks 2 and 6 which were obtained following 2 IV infusions in the IV dose-loading phase. The absolute value of Pearson correlation coefficient was below 0.06 between BMI at baseline

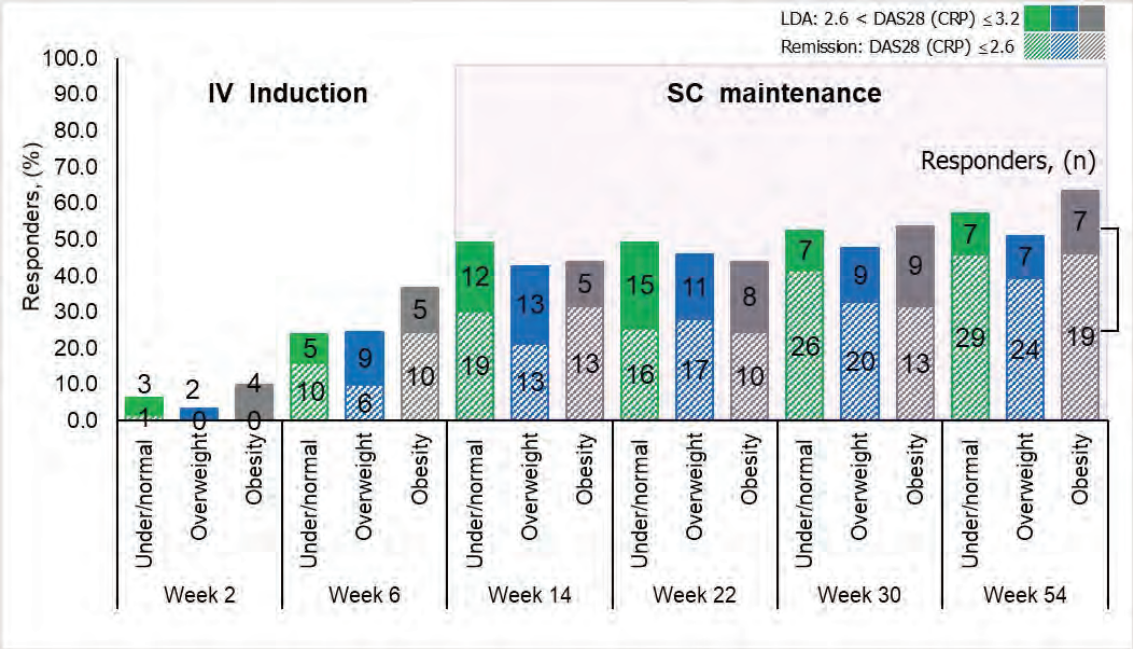


Figure 1. Remission or LDA Based on DAS28 (CRP)

and mean change from baseline in DAS28 (CRP) during the CT-P13 SC treatment from Weeks 14 to 54, indicating that correlation between two measurements was weak and was not statistically significant (p-value >0.05) (Figure 2).

Conclusion: These results showed that there was no impact of BMI on the clinical responses of CT-P13 SC 120 mg biweekly in RA patients. Therefore, CT-P13 SC 120 mg is considered to be a valid therapeutic option regardless of BMI.

References:

1. Yoo D.H., et al. Ann Rheum Dis, 2013;72:1613-20.
2. Yoo D.H., et al. Ann Rheum Dis, 2016;75:1005.
3. Westhovens R., et al. Ann Rheum Dis, 2019;78:A1158
4. Westhovens R., et al. Arthritis Rheumatol. 2019;71 (suppl 10).

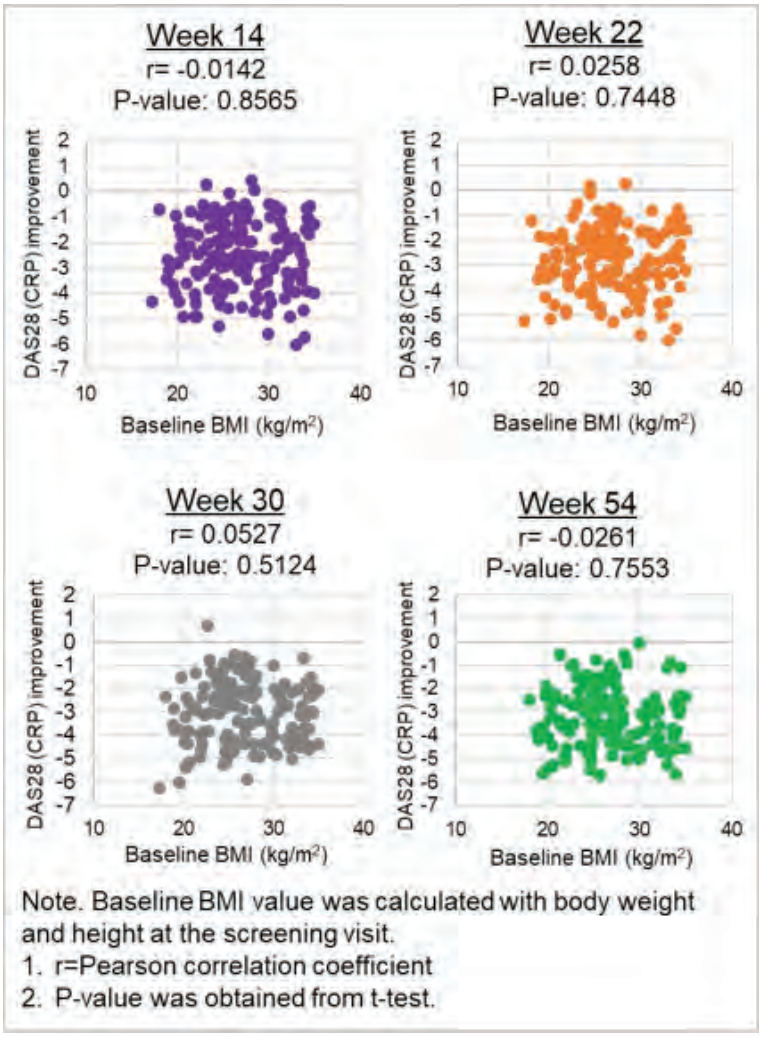


Figure 2 Correlation between BMI at Baseline and Mean Change from Baseline of DAS28 (CRP)

Disclosure: D. Yoo, Celltrion, Inc., 1, 2, Celltrion Healthcare, Inc, 1; **R. Westhovens**, Celltrion, Inc., 2, 5, Galapagos NV, 2, 5, Gilead Sciences, Inc., 2, 5; **P. Wiland**, Celltrion, Inc., 1, Novartis, Pfizer, Abbvie, Gedeon-Richter, Lilly, Roche, Sandoz, 1; **M. Zawadzki**, Celltrion, Inc., 1; **D. Ivanova**, Celltrion, Inc., 1; **A. Berrocal Kasay**, Celltrion, Inc., 1, Pfizer, 1; **E. Chalouhi**, Celltrion, Inc., 1; **E. Balázs**, Celltrion, Inc., 1, Amgen, 1; **S. Lee**, Celltrion, Inc., 1; **S. Kim**, Celltrion, Inc., 1; **N. Han**, Celltrion, Inc., 1; **Y. Jung**, Celltrion, Inc., 1.

Abstract Number: 1208

Utility of Measuring the Immunogenicity to CT-P13 for Subcutaneous Use in Patients with Active Rheumatoid Arthritis: 1-Year Results from a Multicenter, Randomized Controlled Pivotal Trial

Rene Westhovens[1], DaeHyun Yoo[2], Piotr Wiland[3], Marek Zawadzki[4], Delina Ivanova[5], Alfredo Berrocal Kasay[6], Elias Chalouhi[7], Eva Balázs[8], SangJoon Lee[9], SungHyun Kim[9], JeeHye Suh[9], ChanKyoung Hwang[9] and DaeSeok Choi[9], [1]University Hospitals Leuven, Belgium, Leuven, Belgium, [2]Hanyang University Hospital for Rheumatic Diseases, Seoul, Republic of Korea, [3]Medical Univeristy, Wroclaw, Poland, [4]Medical Univeristy, Dpt of Rheumatology , Wroclaw, Wroclaw, Poland, [5]Diagnostic-Consultative Center Aleksandrovska EOOD, Sofia, Bulgaria, [6]ABK Reuma SRL, LIMA, Peru, [7]Clinica Internacional Sede Lima, Lima, Peru, [8]Dr. Bugyi István Hospital, Szentes, Hungary, [9]Celltrion, Inc., Incheon, Republic of Korea

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

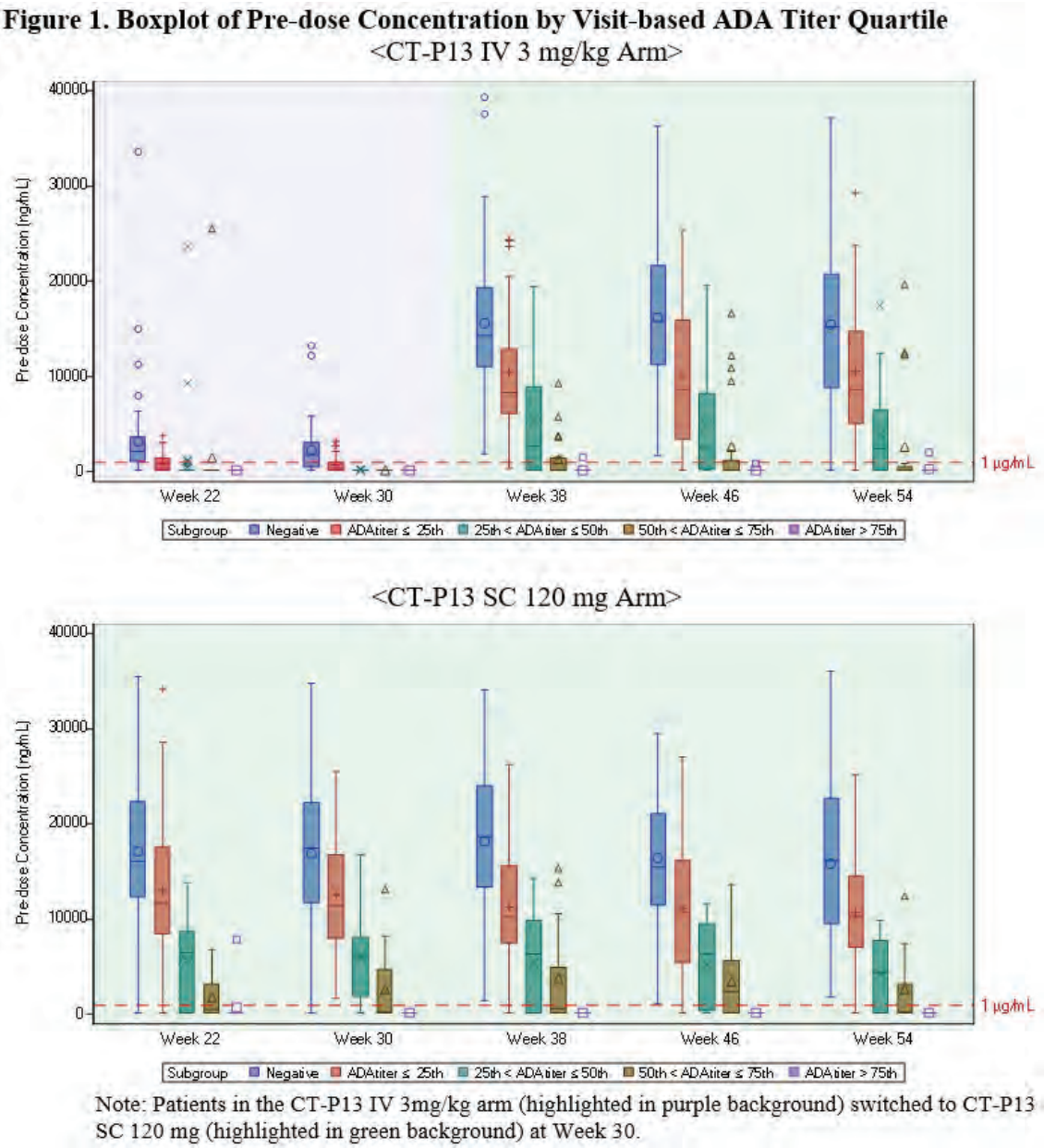
Session Time: 9:00AM–11:00AM

Background/Purpose: Novel subcutaneous infliximab (CT-P13 SC) was developed to augment the flexibility in the therapeutic use of infliximab and non-inferiority (NI) of CT-P13 SC versus CT-P13 intravenous (IV) was demonstrated for efficacy in patients with rheumatoid arthritis (RA)[1]. CT-P13 SC 120 mg biweekly showed relatively high therapeutic trough levels during the treatment period, which consistently helps in maintaining efficacy over time. Since immunogenicity has clinical importance in patients using anti-TNF alpha agents and there is a general presumption that SC route is more immunogenic than IV route, this needs careful assessment. In this report, immunogenicity assessment of CT-P13 SC with further impact analysis was performed on the pivotal data set[1] to determine whether there was any correlation between the magnitude of anti-drug antibody (ADA) positivity and clinical outcomes in RA patients or not.

Methods: The immune response against CT-P13 in human serum was detected using an electrochemiluminescence (ECL) platform with an Affinity Capture Elution (ACE) step. An ADA ECL ACE assay showed the ability to detect ADA at low levels in all samples regardless of residual drug in serum (25 ng/mL ADA in the presence of 80 μg/mL of CT-P13 in RA patient serum). To investigate the impact of ADA titer on PK, efficacy, and safety, key clinical parameters were assessed by visit-based ADA titer quartile. All patients who had 'Positive' ADA status result at each visit were included in the analysis and categorized into 4 groups using the 25th, 50th, 75th percentiles of ADA titer result, respectively.

Results: The 4 subgroups categorized by quartiles at each visit from week 22 to week 54 were: 1st (ADA titer ≤ 3), 2nd (3 < ADA titer ≤ 9), 3rd (9 < ADA titer ≤ 27) and 4th (27 < ADA titer). There was a trend for pre-dose concentration to decrease as ADA titer increases for both CT-P13 SC and CT-P13 IV arms as expected (Figure 1). Patients in the 1st and 2nd subgroup maintained a sufficient therapeutic drug concentration level. Figure 2 shows the correlation between ADA titer and efficacy outcomes where the change from baseline of DAS28 (CRP) and the proportion of patients achieving ACR20 were lower in the 3rd and 4th subgroup than 1st and 2nd subgroup. The ADA impact was especially apparent in the 4th subgroup where the mean pre-dose concentration of the patients was below the therapeutic drug concentration level (1 μg/mL), which led to worse efficacy outcomes in both IV and SC arms than other subgroups. Nevertheless, no impact of ADA on the safety profile in both arms was observed. A neutralizing antibody (NAb) method with enhanced drug tolerance but limited performance was also developed and clinical consequences of NAb titer in terms of PK, efficacy, and safety were not different from the results with ADA.

Figure 1. Boxplot of Pre-dose Concentration by Visit-based ADA Titer Quartile



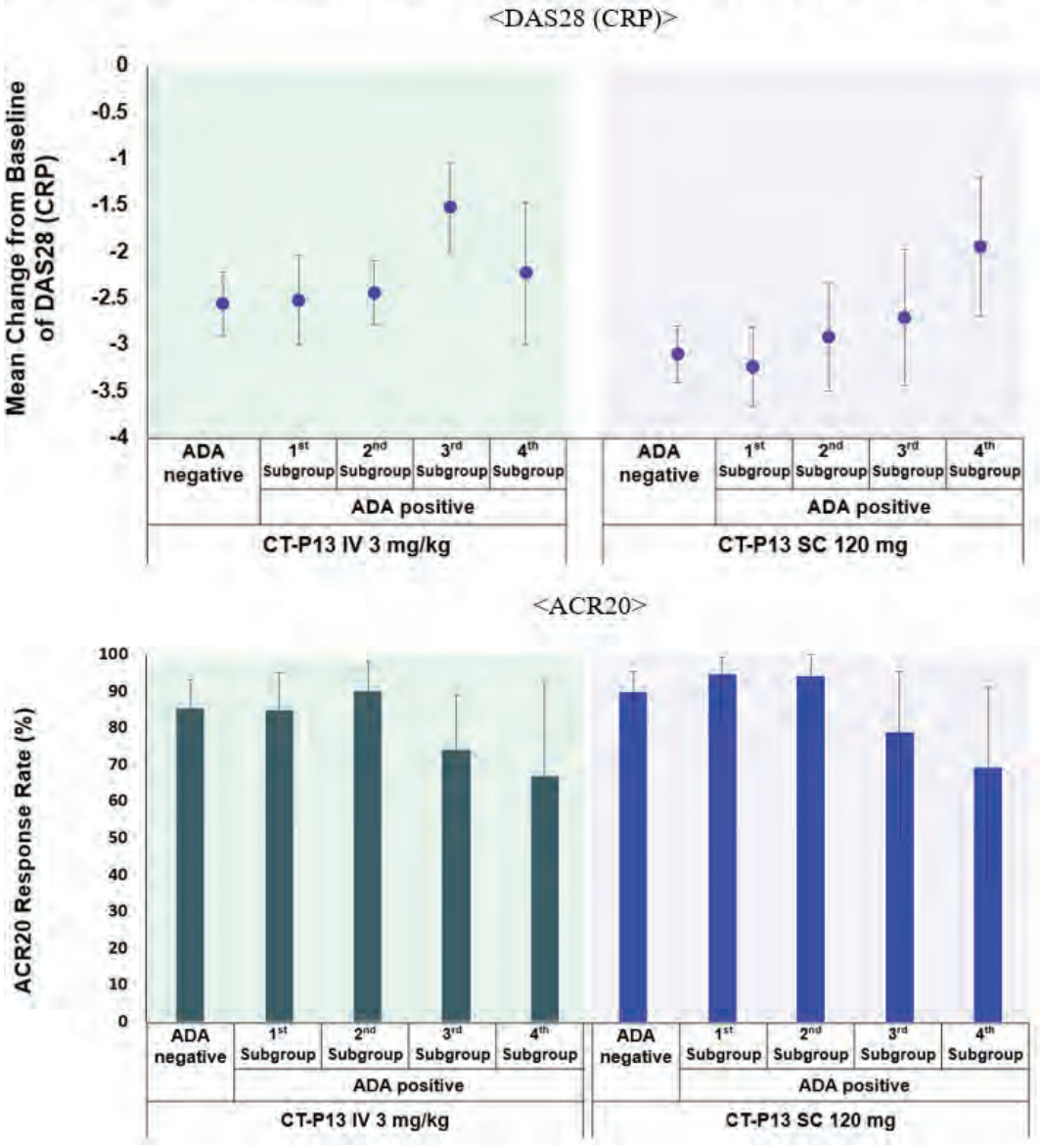
Note: Patients in the CT-P13 IV 3mg/kg arm (highlighted in purple background) switched to CT-P13 SC 120 mg (highlighted in green background) at Week 30.

Conclusion: The analysis of both ADA positivity and titer is clinically meaningful in the prediction of PK profile and clinical response. CT-P13 SC administration did not result in a greater incidence of ADA compared to the CT-P13 IV and there were no clinical differences depending on the formulation.

References:

1. Westhovens R, et al. Annals of the Rheumatic Diseases 2019;78:1158-1159.

Figure 2. Mean Change from Baseline of DAS28 (CRP) and Proportion of ACR20 Responder with 95% Confidence Interval at Week 30 by Visit-based ADA Titer Quartile



Disclosure: R. Westhovens, Celltrion, Inc., 2, 5, Galapagos NV, 2, 5, Gilead Sciences, Inc., 2, 5; **D. Yoo**, Celltrion, Inc., 1, 2, Celltrion Healthcare, Inc, 1; **P. Wiland**, Celltrion, Inc., 1, Novartis, Pfizer, Abbvie, Gedeon-Richter, Lilly, Roche, Sandoz, 1; **M. Zawadzki**, Celltrion, Inc., 1; **D. Ivanova**, Celltrion, Inc., 1; **A. Berrocal Kasay**, Celltrion, Inc., 1, Pfizer, 1; **E. Chalouhi**, Celltrion, Inc., 1; **E. Balázs**, Celltrion, Inc., 1, Amgen, 1; **S. Lee**, Celltrion, Inc., 1; **S. Kim**, Celltrion, Inc., 1; **J. Suh**, Celltrion, Inc., 1; **C. Hwang**, Celltrion, Inc., 3; **D. Choi**, Celltrion, Inc., 3.

Abstract Number: 1209

The Strength of IL-6/STAT3 Signal Inhibition by SAR S.c q2w Showed Significantly Higher Level Than That of TCZ S.c q2w but Lower Than TCZ S.c q1w

Shuntaro Saito[1], Katsuya Suzuki[2], Keiko Yoshimoto[2], Yasushi Kondo[2], Jun Kikuchi[2], Kotaro Otomo[2], Hironari Hanaoka[2], Yuko Kaneko[2] and Tsutomu Takeuchi[3], [1]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Shinjuku-ku, Tokyo, Japan, [2]Division of Rheumatology, Department of Internal Medicine, Keio University School of Medicine, Tokyo, Japan, [3]Division of Rheumatology, Department of internal Medicine, School of Medicine, Keio University, Tokyo, Japan

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

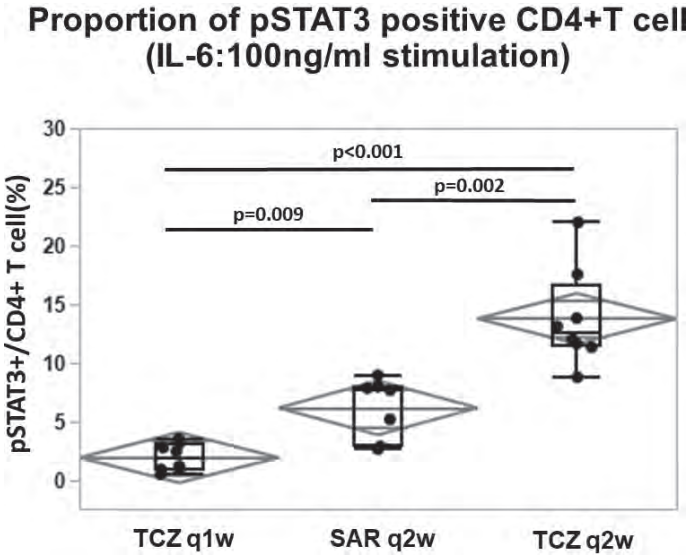
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Interleukin-6 (IL-6) is a key cytokine in the pathogenesis of rheumatoid arthritis (RA). Tocilizumab (TCZ) and Sarilumab (SAR) are monoclonal antibodies that bind to membrane and soluble forms of human IL-6 receptor, efficiently inhibiting IL-6/STAT3 signaling. Our group had previously reported the bioassay for measuring the strength of IL-6/STAT3 signal inhibition by TCZ (Arthritis Research & Therapy 2017.19:231). In this study, we measured phosphorylated STAT3 (pSTAT3) in RA patients treated with subcutaneous (s.c) administration of TCZ and SAR, in order to assess the difference in the strength of IL-6/STAT3 signal inhibition among both medications.

Methods: RA patients who achieved low disease activity (CDAI< =10) by treatment with weekly or biweekly administration of 162 mg s.c of TCZ (TCZ q1w, n = 8, and TCZ q2w group, n = 8), and those with 200 mg s.c of SAR biweekly (SAR q2w group, n = 7) were collected. Whole blood samples from each group were stimulated with each concentration of recombinant human (rh) IL-6 (0, 0.1, 1, 10, 100 ng/ml). The proportion of pSTAT3 positive CD4+ T cells was measured by phosflow cytometric analysis.



Proportion of pSTAT3 positive CD4+T cell

Clinical Characteristics

	A) TCZ q1w (N = 8)	B) SAR q2w (N = 7)	C) TCZ q2w (N =8)	A) VS B), p	B) VS C), p	A) VS C), p
Age (y/o)	66 (47-81)	56 (53-76)	61 (52-71)	0.60	0.95	0.75
Female (n,%))	8/8 (100%)	7/7 (100%)	8/8 (100%)	-	-	-
RA duration (m)	134 (46-190)	103 (18-204)	134 (85-241)	0.60	0.18	0.56
Duration of TCZ/SAR use (m)	12 (10-13)	8 (7-10)	12 (8-18)	0.07	0.27	0.91
RF positive (n,%)	7/8 (88%)	7/7 (100%)	8/8 (100%)	0.33	1.00	0.33
anti-CCP positive (n,%)	7/8 (88%)	6/7 (86%)	7/8 (88%)	0.92	0.92	1.00
MTX dose (mg/week)	0 (0-8)	0 (0-6)	0 (0-8)	1.00	1.00	0.95
PSL dose (mg/day)	0 (0-2)	0 (0-1)	0 (0-0)	0.38	0.09	0.10
CRP (mg/dl)	0.01 (0.00-0.01)	0.01 (0.00-0.02)	0.01 (0.00-0.06)	0.66	0.67	0.53
ESR (mm/hr)	3 (2-7)	5 (2-9)	6 (2-20)	0.37	0.89	0.66
DAS-ESR	1.86 (0.89-2.59)	1.67 (1.04-1.99)	1.36 (0.69-2.96)	0.95	0.95	0.79
CDAI	6 (1.6-8.1)	2 (0.4-6.8)	1.8 (0.3-5.5)	0.33	0.77	0.18
HAQ	0.375 (0.0-1.75)	0.375 (0.0-1.125)	0.125 (0.0-1.00)	0.95	0.44	0.48

Descriptive values are expressed as median (Q1-Q3)

Clinical Characteristics

Results: The clinical characteristics of each group were not different in each group (Table1). Proportion of pSTAT3 positive CD4+ T cells stimulated by 100ng/ml of rhIL-6 showed significant difference in each group (median 1.8 [0.9-3.0]% vs 7.7 [2.9-8.0]% vs 12.5 [11.4-16.6]% in TCZ q1w, SAR q2w, TCZ q2w group, respectively, $p < 0.05$ for all comparisons)(Figure 1).

Conclusion: The strength of IL-6/STAT3 signal inhibition by SAR 200mg q2w showed significantly higher level than that of TCZ s.c q2w but lower than TCZ s.c q1w. The result of this study might be useful in considering the adjustment of the strength of IL-6 blockade treatment in each RA patient.

Disclosure: S. Saito, Chugai Pharmaceutical Co. Ltd., 1, Eisai Co.,Ltd., 1, Pfizer Japan Inc., 1, Asahikasei Pharma Corp., 1, Bristol–Myers Squibb, 1, Mitsubishi Tanabe Pharma Co., 1; **K. Suzuki**, None; **K. Yoshimoto**, None; **Y. Kondo**, None; **J. Kikuchi**, None; **K. Otomo**, None; **H. Hanaoka**, None; **Y. Kaneko**, None; **T. Takeuchi**, Astellas Pharma Inc., 2, 5, 8, Daiichi Sankyo Company, Limited, 2, 5, 8, Takeda Pharmaceutical Company Limited, 2, 5, 8, AbbVie GK., 2, 5, 8, Asahi Kasei Pharma Corporation, 2, 5, 8, Mitsubishi Tanabe Pharma Corporation, 2, 5, 8, Eisai Co., Ltd., 2, 5, 8, Nippon Kayaku Co., Ltd., 2, 5, 8, Chugai Pharmaceutical Co., Ltd., 2, 5, 8, Eli Lily Japan K.K, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Pfizer Japan, Inc., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, AYUMI Pharmaceutical Corporation, 2, 5, 8, Novartis Pharma K.K., 2, 5, 8, UCB, 2, 5, 8, Dainippon Sumitomo Co., 2, 5, 8, Shionogi & Co., Ltd., 2, 5, 8.

Abstract Number: 1210

Patient-Reported Outcomes Measurement Information System (PROMIS) Assessment of Response to Treatment with Golimumab IV or Infliximab in Rheumatoid Arthritis Patients: Results from a Phase 4 Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: AWARE (Comparative & Pragmatic Study of Golimumab [GLM] Intravenous [IV] vs Infliximab [IFX] in RA) is a Phase 4 study designed to provide a real-world assessment of GLM IV and IFX in pts with RA. Patients (pts) with rheumatoid arthritis (RA) experience significant symptoms (eg, pain and fatigue) and impact on physical function. Using the Patient Reported Outcomes Measurement Information System (PROMIS), a validated disease agnostic set of health assessment instruments,[1] we assessed outcomes related to social, mental, and physical well-being through the 8th infusion (≈1 year of treatment).

Methods: AWARE is a prospective, noninterventional, multicenter (88 sites), observational study in the United States (US). A total of 1270 RA pts were enrolled when initiating treatment with GLM or IFX. The 52 Week Analysis Set reported here included pts with ≥1-year treatment or those discontinued for any reason and, while enrolled, completed PROMIS-29 or PROMIS short form (SF) questionnaires. The PROMIS instruments were administered at baseline and prior to infusions 2, 5, and 8. PROMIS-29 consists of 7 domains (Depression, Anxiety, Physical Function, Pain Interference, Fatigue, Sleep Disturbance, and Social Participation) and a pain intensity 0-10 visual analogue scale. The PROMIS SFs Fatigue 7a and Pain Interference 6b were also completed. The raw score of each domain was converted into a standardized T-score with a mean of 50 (general population mean) and a standard deviation (SD) of 10. All PROMIS T-scores are based on observed data without any imputation rules applied. Higher PROMIS scores represent more of the domain concept being measured.

Results: At baseline, treatment groups were balanced based on demographics and medical characteristics. The majority of pts were white (87.0% GLM, 86.2% IFX) and female (83.4% GLM, 82.4% IFX). Mean ages were 58.5 ±12.96 years for GLM and 59.6 ±13.24 years for IFX. Overall, 35.3% GLM and 42.9% IFX pts were bionaïve. The proportion of GLM and IFX pts with prior exposure to 1 or 2 biologics was similar; however, 20.1% GLM pts vs 10.8% IFX pts had exposure to ≥3 biologics. Methotrexate use was similar between GLM (76.4%) and IFX pts (75.0%). Based on mean PROMIS T-scores at baseline (Table), Fatigue, Pain Interference, and Physical Function domains assessed by PROMIS in RA pts indicate that these assessments were worse than those of the general US population. Among all PROMIS domains, mean Depression T-scores were closest compared with the general population (51.9 GLM, 52.5 IFX). Through the 8th infusion, GLM- and IFX-treated pts achieved meaningful improvement based on mean changes from baseline in all PROMIS-29 domains and respective SFs. The percentage of GLM or IFX pts with improvements of ≥3, ≥5, or ≥10 units change in T-scores increased from infusion 2 through infusion 8.

Table. Mean (SD) Change from Baseline PROMIS-29 Domain and Short Form T-Scores: 52 Week Analysis Set			
	GLM	IFX	Least square mean difference (95% CI)*
Anxiety (4-item)	N=674	N=570	
Baseline	53.4 (10.13)	54.6 (10.53)	
Change from baseline at infusion 5	N=435	N=397	-0.41 (-1.40, 0.58)
	-2.0 (7.98)	-2.9 (8.41)	
Change from baseline at infusion 8	N=223	N=286	-0.29 (-1.54, 0.97)
	-2.6 (8.10)	-3.7 (7.86)	
Depression (4-item)	N=674	N=574	
Baseline	51.9 (9.83)	52.5 (10.21)	
Change from baseline at infusion 5	N=434	N=399	0.54 (-0.39, 1.47)
	-1.8 (7.51)	-1.5 (7.98)	
Change from baseline at infusion 8	N=225	N=287	0.49 (-0.72, 1.70)
	-2.1 (7.56)	-2.3 (7.89)	
Fatigue (4-item)	N=671	N=574	
Baseline	58.4 (9.91)	59.4 (9.99)	
Change from baseline at infusion 5	N=435	N=393	-0.26 (-1.24, 0.71)
	-2.0 (7.81)	-2.6 (7.88)	
Change from baseline at infusion 8	N=225	N=281	0.69 (-0.64, 2.03)
	-3.4 (8.72)	-3.1 (7.77)	
Short form Fatigue 7a	N=681	N=576	
Baseline	59.1 (8.51)	59.7 (8.25)	
Change from baseline at infusion 5	N=441	N=400	0.60 (-0.20, 1.40)
	-2.6 (6.74)	-2.4 (6.11)	
Change from baseline at infusion 8	N=228	N=287	1.01 (-0.11, 2.14)
	-3.2 (7.40)	-2.4 (6.35)	
Pain interference (4-item)	N=679	N=574	
Baseline	63.0 (7.56)	63.9 (7.80)	
Change from baseline at infusion 5	N=440	N=398	0.83 (-0.05, 1.71)
	-3.4 (7.02)	-3.1 (6.95)	
Change from baseline at infusion 8	N=227	N=284	1.84 (0.55, 3.13)
	-4.2 (8.23)	-3.1 (7.77)	
Short form Pain interference 6b	N=680	N=576	
Baseline	61.9 (7.45)	62.8 (7.54)	
Change from baseline at infusion 5	N=441	N=400	0.43 (-0.40, 1.26)
	-3.4 (6.66)	-3.3 (6.31)	
Change from baseline at infusion 8	N=228	N=287	1.31 (0.15, 2.48)
	-3.8 (7.88)	-3.2 (6.67)	
Physical function (4-item)	N=678	N=571	
Baseline	38.2 (6.79)	38.0 (6.90)	
Change from baseline at infusion 5	N=435	N=396	-0.31 (-1.01, 0.39)
	1.8 (5.26)	1.8 (5.37)	
Change from baseline at infusion 8	N=224	N=283	-0.76 (-1.73, 0.21)
	2.2 (5.64)	1.9 (5.85)	
Sleep disturbance (4-item)	N=671	N=569	
Baseline	54.6 (8.72)	N=55.5 (8.61)	
Change from baseline at infusion 5	N=428	N=395	-0.04 (-0.95, 0.88)
	-1.7 (7.69)	-2.0 (7.26)	
Change from baseline at infusion 8	N=221	N=281	0.23 (-0.96, 1.42)
	-1.4 (7.45)	-1.7 (7.61)	
Social participation (4-item)	N=673	N=574	
Baseline	43.7 (8.40)	42.9 (8.77)	
Change from baseline at infusion 5	N=437	N=396	-0.27 (-1.15, 0.61)
	2.5 (7.40)	2.5 (6.64)	
Change from baseline at infusion 8	N=225	N=283	-0.10 (-1.36, 1.16)
	3.2 (8.15)	3.4 (7.48)	

*The least square mean difference and confidence interval (CI) are based on analysis of covariance controlling for baseline PROMIS score using inverse probability of treatment weighted propensity score.

Conclusion: RA pts treated with GLM or IFX achieved comparable improvements across social, mental, and physical well-being PROMIS measures. PROMIS-29 was able to detect change to subsequent anti-tumor necrosis factor-α therapies.

Reference:

1. http://www.healthmeasures.net/score-and-interpret/interpret-scores/meaningful-change/165-meaningful-change

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Disclosure: C. Bingham III, Bristol-Myers Squibb, 2, 5, 8, Genetech, 5, 8, Sanofi, 5, 8, AbbVie, 5, Eli Lilly, 5, Pfizer, 5, Gilead Sciences, Inc., 5, Regeneron, 5; **S. Kafka**, Janssen Scientific Affairs, LLC, 1, 3; **S. Black**, Janssen Scientific Affairs, LLC, 1, 3; **S. Xu**, Janssen Research & Development, LLC, 1, 2; **W. Langholff**, Janssen Research & Development, LLC, 1, 2; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5.

Abstract Number: 1211

Relationship Between Changes in Lipid Levels and Improvement in Disease Activity Outcomes in Patients with Rheumatoid Arthritis Receiving Upadacitinib Treatment: Pooled Analysis of Data from Two Phase 3 Studies

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib (UPA) is an oral Janus kinase (JAK) inhibitor engineered to have greater selectivity for JAK1 vs JAK2, JAK3, and tyrosine kinase 2, and is approved for the treatment of RA. Across 2 double-blind, placebo (PBO)-controlled Phase 3 studies of UPA in patients with RA, after an initial increase through Week 8, lipid levels remained sTable up to Week 24.[1,2] Previous studies of JAK or IL-6 receptor inhibitors have reported a negative correlation between changes in lipid levels and RA disease activity.[3,4] The aim of this analysis was to determine the relationship between changes in lipid levels and disease activity outcomes in patients with RA treated with UPA.

Methods: Patients with RA and an inadequate response to conventional synthetic/biologic DMARDs (cs/bDMARD-IR) from SELECT-NEXT/SELECT-BEYOND, respectively, were randomized to receive UPA 15 mg once daily (QD), UPA 30 mg QD, or PBO for 12 weeks followed by an extension of up to 5 years; patients randomized to PBO switched to UPA 15 or 30 mg after 12 weeks. Spearman correlations of maximum changes from baseline (BL) through Week 12 in fasting-state lipid levels (low- and high-density lipoprotein cholesterol [LDL-C; HDL-C], and total cholesterol [TC]) with clinical disease activity outcomes measured by change from BL in Clinical Disease Activity Index (CDAI), DAS of 28 joints using CRP (DAS28[CRP]), tender/swollen joint count in 28 joints (TJC28/SJC28), and pain by visual analog scale (VAS) at Weeks 12 and 24, were determined. Spearman correlations of maximum changes from BL in lipid levels and CRP through Week 12 were also determined.

Table 1. Spearman correlations of maximum changes from BL in lipid levels through Week 12 with disease activity outcomes at Weeks 12 and 24

	Week 12			Week 24	
	UPA 15 mg QD	UPA 30 mg QD	PBO	UPA 15 mg QD	UPA 30 mg QD
Correlation with CDAI change from BL					
LDL-C	−0.117* (n=286)	−0.116 (n=282)	−0.075 (n=281)	−0.124* (n=278)	−0.147* (n=264)
HDL-C	−0.136* (n=288)	−0.022 (n=285)	−0.071 (n=281)	−0.147* (n=280)	−0.054 (n=267)
TC	−0.160** (n=288)	−0.158** (n=285)	−0.076 (n=281)	−0.179** (n=280)	−0.157** (n=267)
Correlation with DAS28(CRP) change from BL					
LDL-C	−0.125* (n=299)	−0.191*** (n=299)	−0.068 (n=301)	−0.151** (n=292)	−0.224*** (n=274)
HDL-C	−0.169** (n=301)	−0.086 (n=301)	−0.074 (n=301)	−0.143* (n=294)	−0.117 (n=276)
TC	−0.195*** (n=301)	−0.249*** (n=301)	−0.110 (n=301)	−0.185** (n=294)	−0.264*** (n=276)
Correlation with TJC28 change from BL					
LDL-C	−0.093 (n=305)	−0.106 (n=303)	−0.060 (n=303)	−0.084 (n=295)	−0.112 (n=277)
HDL-C	−0.066 (n=307)	−0.010 (n=305)	−0.028 (n=303)	−0.062 (n=297)	−0.009 (n=279)
TC	−0.098 (n=307)	−0.128* (n=305)	−0.083 (n=303)	−0.097 (n=297)	−0.098 (n=279)
Correlation with SJC28 change from BL					
LDL-C	−0.116* (n=305)	−0.118* (n=303)	−0.069 (n=303)	−0.166** (n=295)	−0.126* (n=277)
HDL-C	−0.087 (n=307)	−0.023 (n=305)	−0.067 (n=303)	−0.069 (n=297)	−0.043 (n=279)
TC	−0.140* (n=307)	−0.161** (n=305)	−0.109 (n=303)	−0.195*** (n=297)	−0.132* (n=279)
Correlation with pain (VAS) change from BL					
LDL-C	−0.046 (n=302)	−0.118* (n=299)	−0.046 (n=301)	−0.047 (n=292)	−0.164** (n=273)
HDL-C	−0.164** (n=304)	−0.044 (n=301)	−0.093 (n=301)	−0.192*** (n=294)	−0.037 (n=275)
TC	−0.132* (n=304)	−0.169** (n=301)	−0.045 (n=301)	−0.095 (n=294)	−0.208*** (n=275)

*p<0.05, **p<0.01, ***p<0.001. BL, baseline; CDAI, Clinical Disease Activity Index; DAS28(CRP), DAS of 28 joints using CRP; HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PBO, placebo; QD, once daily; SJC28, swollen joint count in 28 joints; TC, total cholesterol; TJC28, total joint count in 28 joints; UPA, upadacitinib; VAS, visual analog scale

Results: Available fasting samples from 1,160 pooled patients (UPA 15 mg, n=386; UPA 30 mg, n=384; PBO, n=390) were included. Modest, but statistically significant, negative correlations were observed between maximum changes from BL in TC through Week 12 and change from BL in CDAI, DAS28(CRP), SJC28, and pain (VAS) at Week 12 with UPA 15 or 30 mg (**Table 1**); similar trends were observed at Week 24. Significant correlations between changes in LDL-C and HDL-C and disease activity outcomes were also observed, but were not consistent across UPA doses and time points. No significant correlations were noted between changes in lipid levels and disease activity outcomes in the PBO group. Statistically significant weak negative relationships were observed between maximum changes from BL in lipid levels and CRP levels through Week 12 with UPA 15 mg (HDL-C and TC) or UPA 30 mg (LDL-C and TC) (**Table 2**).

Conclusion: In this large pooled data set of patients receiving UPA, increases in lipid levels showed modest, but statistically significant, correlations with improvement in clinical disease activity outcomes in patients with cs/bD-

Table 2. Spearman correlation of maximum changes from BL in lipid levels through Week 12 with maximum change from BL in CRP through Week 12

	UPA 15 mg QD	UPA 30 mg QD	PBO
LDL-C	0.099 (n=303)	-0.174** (n=302)	-0.053 (n=303)
HDL-C	-0.184** (n=305)	-0.087 (n=304)	-0.024 (n=303)
TC	-0.189*** (n=305)	-0.236*** (n=304)	-0.056 (n=303)

**p<0.01, ***p<0.001. HDL-C, high-density lipoprotein cholesterol; LDL-C, low-density lipoprotein cholesterol; PBO, placebo; QD, once daily; TC, total cholesterol; UPA, upadacitinib

MARD-IR RA. These results add to evidence suggesting a relationship between systemic inflammation and lipid metabolism in patients with RA, which is modifiable with effective interventions, and reinforce the importance of monitoring for hyperlipidemia in these patients.

1. Burmester GR, et al. Lancet 2018;391:2503–12.

2. Genovese MC, et al. Lancet 2018;391:2513–24.

3. Kremer JM, et al. Arthritis Rheumatol 2017;69:943–52.

4. Cacciapaglia F, et al. Mediators Inflamm 2018;2018:2453265.

Disclosure: C. Charles-Schoeman, AbbVie, 2, 5, Regeneron-Sanofi, 5, Gilead, 5, Bristol-Myers Squibb, 2, Pfizer Inc, 2, 5; **J. Giles**, AbbVie, 5, Bristol-Myers Squibb, 5, Eli Lilly, 5, Gilead, 5, Pfizer, 2; **N. Lane**, Amgen, 5, Mallinckrodt, 5, Pfizer, 5, Roche, 5; **E. Choy**, Abbvie, 2, 8, Amgen, 2, 8, AstraZeneca, 2, 8, Biogen, 2, 8, Bio-Cancer, 2, 8, Boehringer Ingelheim, 2, 8, Bristol-Myers Squibb, 2, 8, Celgene, 2, 8, Chugai Pharma, 2, 8, Eli Lilly, 2, 8, Ferring Pharmaceuticals, 2, 8, GlaxoSmithKline, 2, 8, Janssen, 2, 8, Novartis, 2, 8, Novimmune, 2, 8, ObsEva, 2, 8, Pfizer, 2, 8, R-Pharm, 2, 8, Roche, 2, 8, SynAct Pharma, 2, 8, Tonix, 2, 8, UCB, 2, 8, Synovate, 2, 8, Sanofi, 2, 8, Regeneron, 2, 8, Napp, 2, 8, Hospira, 2, 8, Merck Sharp & Dohme, 2, 8; **H. Camp**, AbbVie, 1, 3; **Y. Song**, AbbVie, 1, 2; **S. Anyanwu**, AbbVie, 1, 3; **I. McInnes**, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9.

Abstract Number: 1212

Whole Blood Transcriptional Changes Following Selective Inhibition of Janus Kinase 1 (JAK1) by Filgotinib in MTX-Naïve Adults with Moderately-to-Severely Active Rheumatoid Arthritis (RA)

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL), a selective, oral JAK1 inhibitor, has shown efficacy and safety in phase 3 studies in adults with moderately-to-severely active RA. Previously, we described molecular response to FIL in large-scale RNA sequencing studies of gene expression in other RA populations[1-3].We conducted a similar study in methotrexate (MTX)-naïve RA patients (pts) (FINCH3; ClinicalTrials.gov NCT02886728) to identify gene transcripts and biological pathways associated with RA and altered in response to FIL.

Methods: MTX-naïve RA pts received sTable dose of MTX+placebo (PBO+MTX), FIL 200mg alone (FIL 200mg), FIL 100mg+MTX, or FIL 200mg+MTX. Whole blood samples were collected using PAXgene tubes at baseline (BL), weeks 4, 12, and 24. RNA was extracted and sequenced on Illumina HiSeq 2500 platform following globin RNA depletion. Correlations between BL gene expression and disease measurements were performed using Spearman's rank partial correlation to account for covariates. Differentially expressed genes (DEGs) were identified using voom-limma. Biological pathway analyses were performed on Molecular Signature Database v6.1 using single sample gene set enrichment analysis with focus on immune signaling pathways from Kyoto Encyclopedia of Genes and Genomes (KEGG). A false-discovery rate of 5% was applied.

Results: Differential gene expression analyses comparing BL samples with after-treatment samples showed rapid onset of transcriptional changes in FIL pts. Fewer DEGs were observed in PBO+MTX patients with peak number at week 24, an observation consistent with MTX clinical response kinetics.[4] Up to 3x as many significant DEGs were observed in FIL 200mg+MTX compared to FIL 100mg+MTX arm, a finding consistent with superior clinical efficacy of FIL 200mg. As with other FIL clinical trial RNA-seq studies and consistent with the selective MoA of FIL, JAK-STAT pathway-induced genes *SOCS2* and *CISH* were significantly downregulated across FIL arms and timepoints, but not PBO+MTX. RA disease activity-associated genes[2-3] *FAM20A* and *METTL7B* were significantly reduced at all timepoints in FIL pts, but only at week 24 in PBO+MTX. While no significant changes in KEGG immune signaling pathways were observed in PBO+MTX arm, a dose-dependent effect on pathway modulation was observed in FIL arms, including reductions in JAK-STAT, toll-like receptor, chemokine, and RIG-I like receptor signaling.

Conclusion: More rapid and sustained changes of transcriptional activity in whole blood transcriptional profile of RA pts after FIL treatment were found compared to PBO+MTX. Dose dependent changes were observed in FIL-treated pts, most notably in KEGG JAK-STAT signaling pathway. These observations confirm an inhibition of JAK-STAT signaling by FIL and are consistent with observed clinical efficacy of FIL in these pts.

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4. Taylor PC, *et al. J Clin Med*. 2019;8(4): pii: E515. https://doi.org/10.3390/jcm8040515

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Abstract Number: 1213

Discrepancy Between the Multi-biomarker Disease Activity Score and Clinical Disease Activity Scores in a 2-Part, Multicenter Study of Repository Corticotropin Injection (Acthar® Gel) for Patients with Persistently Active Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Assessment of disease activity in RA with validated measures, such as the Disease Activity Score with 28 joint count and erythrocyte sedimentation rate (DAS28-ESR) and the Clinical Disease Activity Index (CDAI), is useful in evaluating therapeutic efficacy and guiding treatment. The multi-biomarker disease activity (MBDA) score was developed to provide an objective laboratory assessment of disease activity. We assessed DAS28-ESR, CDAI, and MBDA scores in a multicenter, placebo-controlled, randomized, phase 4 withdrawal study of repository corticotropin injection (RCI, Mallinckrodt Pharmaceuticals), a naturally sourced complex mixture of adrenocorticotropic hormone analogs and other pituitary peptides, in patients with persistently active RA despite treatment with sTable low-dose glucocorticoids and 1 or 2 nonbiologic and/or biologic disease-modifying antirheumatic drugs (ClinicalTrials.gov ID: NCT02919761).

Methods: Patients received 80 U of RCI subcutaneously (SC) twice weekly during a 12-week open-label period; those who achieved low disease activity (LDA; DAS28-ESR < 3.2) were randomly assigned to receive 80 U of RCI or placebo SC twice weekly during a 12-week double-blind period. Disease activity was assessed using the DAS28-ESR, CDAI, and MBDA at baseline (BL), week (W) 12, and W24; changes were evaluated via *t* tests. Correlations for the total MBDA score and its individual components with both DAS28-ESR and CDAI scores at BL, W12, and W24 were assessed via Pearson correlation coefficients for subgroups with/without LDA at W12 or W24. Analyses used the modified intent-to-treat population, defined as patients who received ≥1 dose of study drug and contributed any efficacy data.

Results: RCI therapy was associated with clinically meaningful improvements in disease activity; mean decreases exceeded the minimal clinically important difference thresholds for the DAS28-ESR and CDAI, but not the minimally important difference for the MBDA (**Table 1**). Statistically significant correlations between MBDA and DAS28-ESR scores were seen at BL and W12 in patients with and without LDA at W12, but low correlation coefficients suggested weak relationships (**Table 2**). Low correlation coefficients (most nonsignificant) also suggested weak relationships between MBDA and CDAI scores (**Table 2**). Among individual MBDA components, some significant correlations were

Table 1. Change from BL in DAS28-ESR, CDAI, and MBDA scores at W12 and W24 (mITT population)

Assessment	Part 1: Open-label RCI (N=259)		Part 2: Double-blind						MCID/MID (absolute difference)
			RCI to Placebo (N=76)		RCI to RCI (N=77)				
	Change from BL[a] to W12	*P* value[b]	Change from BL[c] to W12	Change from BL[c] to W24	Change from BL[d] to W12	*P* value[e]	Change from BL[d] to W24	*P* value[e]	
DAS28-ESR	−2.8 (1.5)	**<0.001**	−3.5 (1.0)	−2.8 (1.5)	−3.5 (0.9)	0.723	−3.0 (1.2)	0.285	≥1.2 units[1]
CDAI	−26.6 (14.1)	**<0.001**	−30.5 (12.7)	−26.6 (15.7)	−30.5 (10.9)	0.994	−28.5 (12.8)	0.426	LDA: ≥1 units MDA: ≥6 units HDA: ≥12 units[2]
Total MBDA score	−2.9 (14.3)	**0.002**	−5.9 (13.3)	−1.5 (13.3)	−1.8 (13.6)	0.063	−0.8 (16.2)	0.785	≥8 units[3]

Changes from BL are expressed as mean (SD).

[a]Mean (SD) at BL was 6.3 (1.0) for DAS28-ESR, 38.3 (12.3) for CDAI, and 46.2 (16.7) for MBDA. [b]From 1-sample *t* test. [c]Mean (SD) at BL was 6.2 (1.0) for DAS28-ESR, 36.0 (12.3) for CDAI, and 47.0 (16.5) for MDBA. [d]Mean (SD) at baseline was 6.2 (0.9) for DAS28-ESR, 36.1 (10.6) for CDAI, and 43.4 (16.3) for MBDA. [e]From 2-sample *t* test.

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Abbreviations: BL, baseline; CDAI, Clinical Disease Activity Index; DAS28-ESR, Disease Activity Score with 28 joint count and erythrocyte sedimentation rate; HDA, high disease activity; LDA, low disease activity; MBDA, multi-biomarker disease activity; MCID, minimal clinically important difference; MDA, moderate disease activity; MID, minimally important difference; mITT, modified intent-to-treat; RCI, repository corticotropin injection; SD, standard deviation; W, week.

Table 2. Correlations between MBDA and disease activity scores

	Part 1: Open-label RCI		Part 2: Double-blind			
			Placebo		RCI	
	LDA at W12 (n=163)	No LDA at W12 (n=96)	LDA at W24 (n=32)	No LDA at W24 (n=44)	LDA at W24 (n=47)	No LDA at W24 (n=30)
MBDA and DAS28-ESR correlations						
BL			*BL*			
Pearson correlation coefficient	**0.341**	**0.322**	**0.420**	**0.387**	**0.381**	**0.400**
P value	<0.001	0.002	0.017	0.014	0.008	0.035
W12			*W24*			
Pearson correlation coefficient	**0.339**	**0.217**	**0.293**	**0.078**	**0.107**	**0.033**
P value	<0.001	0.038	0.123	0.666	0.485	0.864
MBDA and CDAI correlations						
BL			*BL*			
Pearson correlation coefficient	**0.206**	**0.001**	**0.202**	**0.233**	**0.335**	**0.158**
P value	0.009	0.996	0.268	0.148	0.020	0.421
W12			*W12*			
Pearson correlation coefficient	**0.114**	**0.036**	**0.063**	**−0.182**	**−0.046**	**−0.225**
P value	0.154	0.737	0.744	0.311	0.764	0.240

LDA was defined as DAS28-ESR <3.2 across all analyses.

P values are from Pearson correlation coefficient test.

Abbreviations: BL, baseline; CDAI, Clinical Disease Activity Index; DAS28-ESR, Disease Activity Score with 28 joint count and erythrocyte sedimentation rate; LDA, low disease activity; MBDA, multi-biomarker disease activity; RCI, repository corticotropin injection; W, week.

noted with both the DAS28-ESR and CDAI scores at BL, W12, and W24; low correlation coefficients suggested weak relationships (data not shown).

Conclusion: In this study of RCI therapy in patients with persistently active RA, clinical disease activity scores were weakly correlated with MBDA total and individual component scores. Similar results have been seen with 3 other agents with different mechanisms of action.[1,2] These findings support the 2019 ACR recommendations against use of MBDA as a preferred measure for disease activity in RA.[3]

References

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Disclosure: R. Fleischmann, Pfizer, 2, 5; **J. Liu**, Mallinckrodt Pharmaceuticals, 3; **J. Zhu**, Mallinckrodt Pharmaceuticals, 3; **O. Segurado**, Mallinckrodt Pharmaceuticals, 9; **D. Furst***, Actelion, 1, 2, Amgen, 1, 2, BMS, 1, Corbus, 1, 2, Galapagos, 1, 2, GSK, 1, NIH, 1, Norvatis, 1, 2, Pfizer, 1, 2, Sanofi, 1, Roche/Genentech, 1, Gilead, 1, Horizon, 1, 2, Kadmon, 1, Talaris, 1, 2, CMC Connect (McCann Health Company), 8, Cytori, 5, AbbVie, 5.

Abstract Number: 1214

Association Between Changes in C-reactive Protein at Week 12 and Patient-Reported Outcomes at Week 24 with Sarilumab Therapy Across Three Pivotal Phase 3 Studies

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SESSION INFORMATION

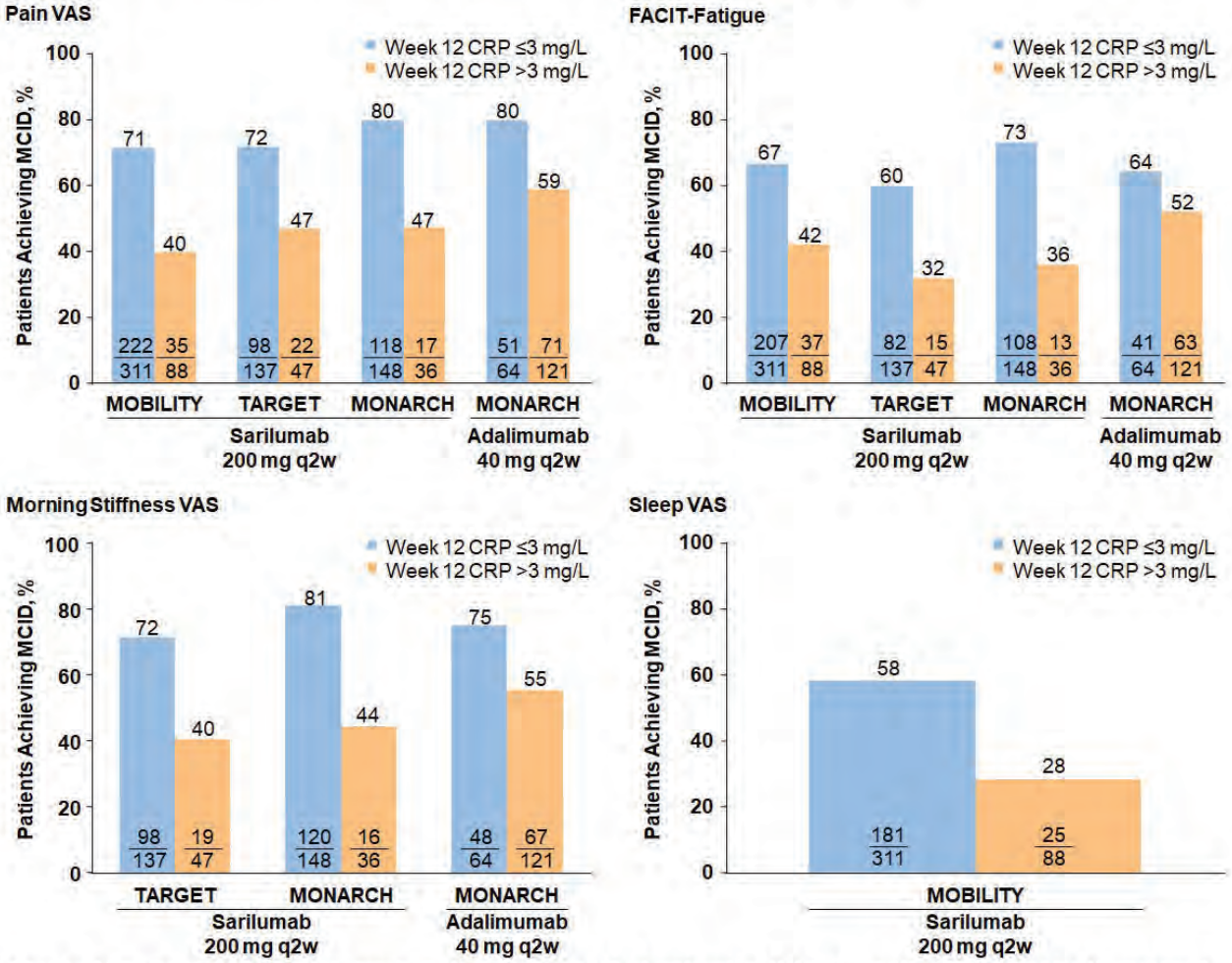
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Evaluation of response to RA therapy at 12 weeks after initiation is recommended in treatment guidelines. CRP response after 12 weeks of therapy may indicate favorable subsequent improvement in patient-reported outcomes (PROs). Here, we describe the association between CRP response to sarilumab at Week 12 and PRO improvements at Week 24, using data from 3 pivotal studies.

Methods: The analysis included patients with RA who took part in MOBILITY (NCT01061736), TARGET (NCT01709578), or MONARCH (NCT02332590) and were treated with sarilumab 200 mg every 2 weeks (q2w) or adalimumab 40 mg q2w (MONARCH only). Patients who achieved a CRP response at Week 12 (defined as serum concentration ≤3 mg/L) were evaluated for PROs at Week 24. Response for PROs was defined as an improvement from baseline in visual analog scale score of ≥10 mm for pain, sleep, and morning stiffness, and an improvement of ≥4 points for the Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue score. Odds ratios (ORs) and 95% confidence intervals (CIs) were generated for the likelihood of achieving PRO responses at Week 24, based on patients' achievement of CRP response at Week 12.

Results: Data for pain and fatigue were available in all 3 trials, for morning stiffness in TARGET and MONARCH only, and for sleep in MOBILITY only. After 12 weeks of treatment with sarilumab 200 mg every 2 weeks, CRP ≤3 mg/L was attained in 74% (137/184), 78% (311/399), and 80% (148/184) of patients from TARGET, MOBILITY, and MONARCH, respectively; in MONARCH, treatment with adalimumab 40 mg q2w was associated with CRP response in 35% (64/185) of patients. Across all 3 trials and all 4 PROs assessed, attainment of CRP ≤3 mg/L at Week 12 was associated with a higher proportion of PRO responders at Week 24 (Figure). These data suggest higher odds of achieving

Figure. Proportions of PRO responders at week 24, by CRP level status at Week 12



Values at the base of each column denote the numbers of patients; CRP=C-reactive protein; MCID=minimal clinically important difference; PRO=patient-reported outcome; q2w=twice weekly; VAS=visual analog scale

Figure

Table. Odds ratios (95% CI) of achieving PRO response at Week 24

	Treatment/Phase 3 Trial			
	Sarilumab 200 mg q2w			Adalimumab 40 mg q2w
	MOBILITY	TARGET	MONARCH	MONARCH
Pain VAS	3.8 (2.3, 6.2)	2.9 (1.4, 5.7)	4.4 (2.0, 9.5)	2.8 (1.4, 5.6)
FACIT-fatigue	2.7 (1.7, 4.5)	3.2 (1.6, 6.4)	4.8 (2.2, 10.3)	1.6 (0.9, 3.1)
Morning stiffness VAS	–	3.7 (1.9, 7.4)	5.4 (2.5, 11.6)	2.4 (1.2, 4.7)
Sleep VAS	3.5 (2.1, 5.9)	–	–	–

FACIT=Functional Assessment of Chronic Illness Therapy; PRO=patient-reported outcome; q2w=every 2 weeks; VAS=visual analog scale

Table

Week 24 PRO response in sarilumab-treated patients who did versus those who did not attain CRP ≤3 mg/L at Week 12 (Table). In MONARCH, sarilumab-treated patients who attained CRP ≤3 mg/L at Week 12 had numerically higher odds of achieving Week 24 PRO response than their adalimumab-treated counterparts (Table).

Conclusion: This post hoc analysis suggests that, in patients with moderate to severe RA treated with sarilumab 200 mg q2w or adalimumab 40 mg q2w, attainment of a CRP level ≤3 mg/L at Week 12 could predict improvements in pain, sleep, morning stiffness, or fatigue at Week 24.

Disclosure: J. Tesser, Janssen, 1, 2, 3, Abbvie, 1, 2, 3, Sun Pharma, 1, 2, 3, Novartis, 1, 2, Lilly, 1, 2, 3, BMS, 1, 2, 3, Pfizer, 1, 2, 3, Amgen, 1; **G. Wright**, Exagen, 5, 8, AbbVie, 5, 8, Amgen, 5, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly and Company, 5, 8, Myriad Autoimmune, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Regeneron Pharmaceuticals, Inc., 5, 8, Sanofi Genzyme, 5, 8, UCB, 5, 8; **V. Strand**, AbbVie, 5, Amgen, 5, Celltrion, 5, Janssen, 5, Merck, 5, Novartis, 5, Regeneron, 5, Sanofi, 5, UCB, 5, Genentech/Roche, 5, GSK, 5, Pfizer, 5, Bayer, 5, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, Galapagos, 5, Lilly, 5, Gilead, 5, Samsung, 5, Servier, 5, Setpoint, 5, Arena, 5, AstraZeneca, 5, Horizon, 5, Ichnos, 5, Inmedix, 5, Sandoz, 5; **J. Kaine**, Eli Lilly, 8, Merck, 8, Sanofi, 8, Regeneron, 8; **K. Maslova**, Sanofi, 1, 3; **G. St John**, Regeneron, 3, Intercept Pharmaceuticals, Inc, 3, 4; **K. Ford**, Sanofi Genzyme, 1, 2; **A. Praestgaard**, Sanofi, 3; **E. Choy**, Abbvie, 2, 8, Amgen, 2, 8, AstraZeneca, 2, 8, Biogen, 2, 8, Bio-Cancer, 2, 8, Boehringer Ingelheim, 2, 8, Bristol-Myers Squibb, 2, 8, Celgene, 2, 8, Chugai Pharma, 2, 8, Eli Lilly, 2, 8, Ferring Pharmaceuticals, 2, 8, GlaxoSmithKline, 2, 8, Janssen, 2, 8, Novartis, 2, 8, Novimmune, 2, 8, ObsEva, 2, 8, Pfizer, 2, 8, R-Pharm, 2, 8, Roche, 2, 8, SynAct Pharma, 2, 8, Tonix, 2, 8, UCB, 2, 8, Synovate, 2, 8, Sanofi, 2, 8, Regeneron, 2, 8, Napp, 2, 8, Hospira, 2, 8, Merck Sharp & Dohme, 2, 8.

Abstract Number: 1215

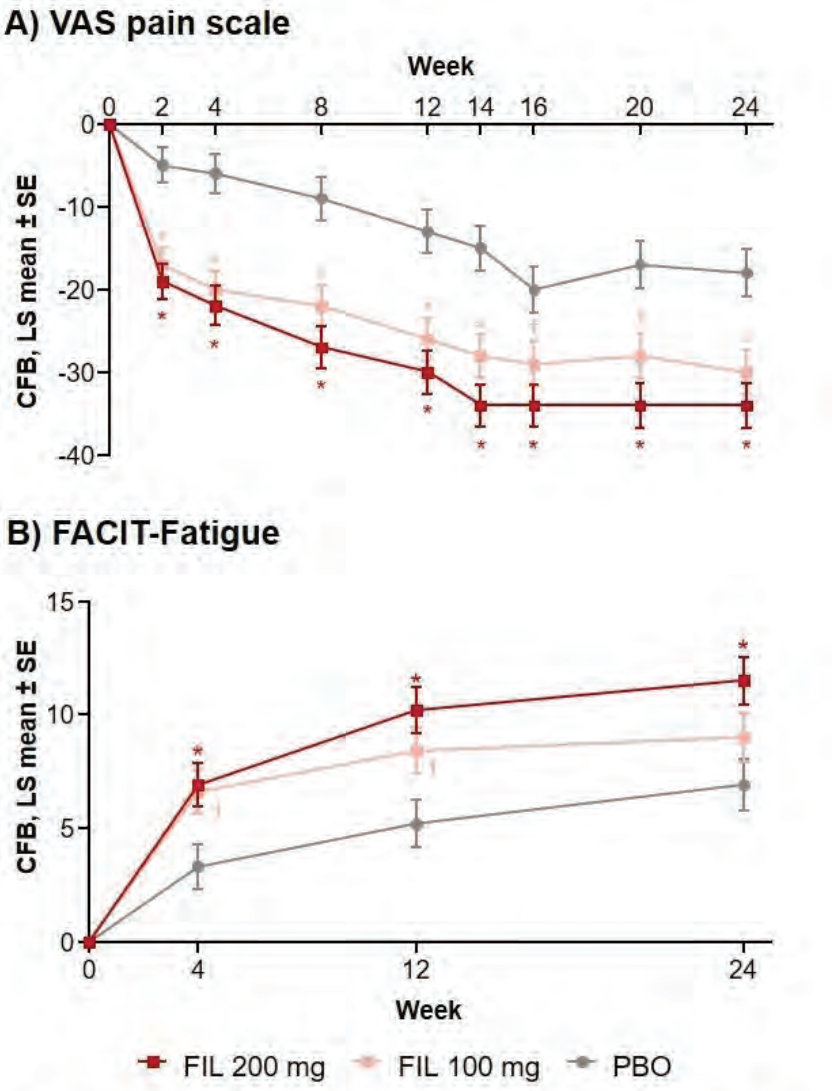
Filgotinib Provided Rapid and Sustained Relief of Pain and Fatigue and Improved Health-Related Quality of Life in Patients with Rheumatoid Arthritis and Inadequate Response to Biologic DMARDs

David Walker[1], Tsutomu Takeuchi[2], Beatrix Bartok[3], Shangbang Rao[3], I-Heng Lee[4], Robin Besuyen[5], Jacques-Eric Gottenberg[6] and Mark Genovese[3], [1]Northumbria Healthcare Trust, North Shields, United Kingdom, [2]Keio Univ School of Medicine, Tokyo, Japan, [3]Gilead Sciences, Inc., Foster City, CA, [4]Gilead Sciences, Foster City, CA, [5]Galapagos BV, Leiden, Netherlands, [6]Strasbourg University Hospital, Strasbourg, France

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: EULAR guidelines recommend a treat-to-target approach focusing on reducing inflammation to prevent joint damage, physical disability, and mortality.[1] However, patients consider reduction in pain and fatigue, along with maintenance of physical function, and improvement in health-related quality of life (HRQoL) important areas for improvement with RA treatment.[2] In the FINCH 2 study, filgotinib (FIL)—a potent, selective, oral small molecule Janus kinase 1 inhibitor—in combination with conventional synthetic (cs)DMARD therapy significantly improved the signs and symptoms of rheumatoid arthritis (RA) in patients with an inadequate response to a biologic (b)DMARD compared with placebo (PBO).[3] In addition, patients experienced significant improvements in HAQ-DI at week (W)12 and W24 with FIL 100 mg ($p < 0.001$, $p = 0.003$) or 200 mg ($p < 0.001$ for both) compared with PBO.[3] The rate and magnitude of change in patient-reported outcomes (PROs) from FINCH 2 assessing pain, HRQoL and fatigue were evaluated.

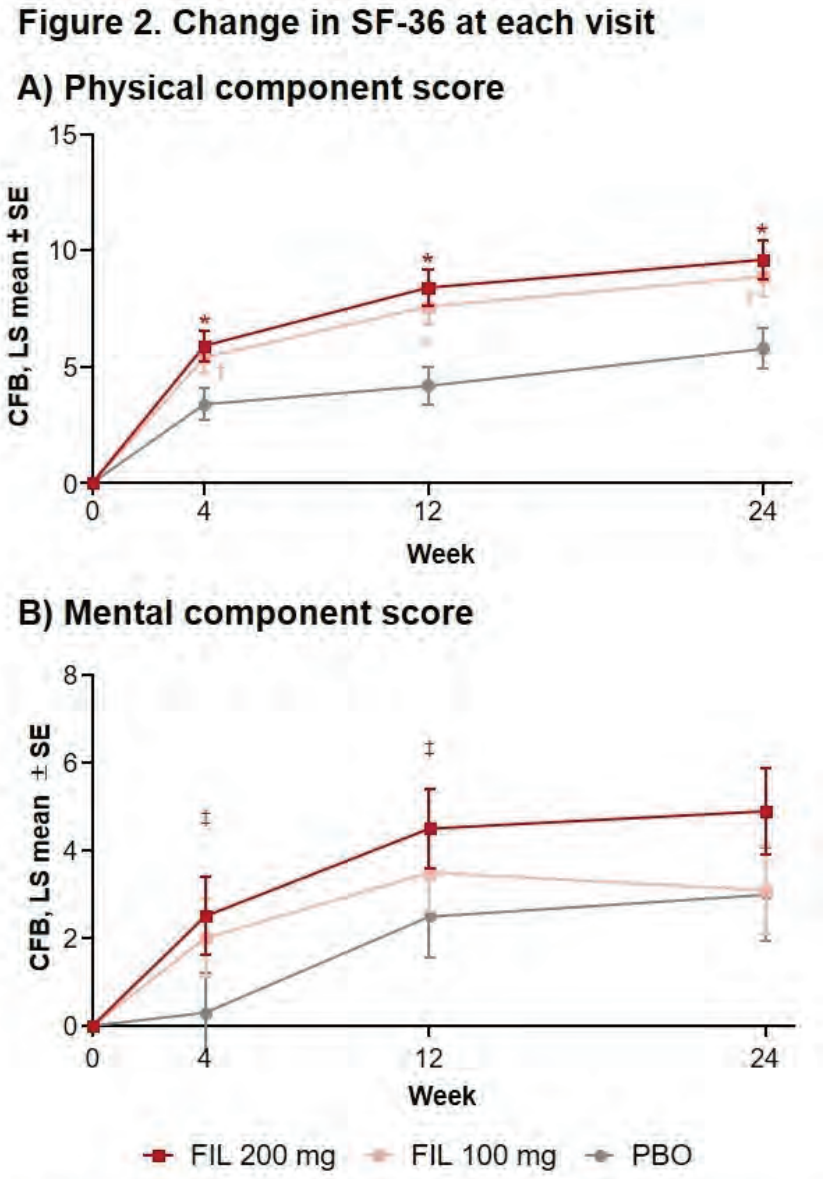
Figure 1. Change in patients' pain and fatigue at each visit



*p ≤0.001, †p <0.01 for LS mean difference between the FIL arm vs PBO.
CFB, change from baseline; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; FIL, filgotinib; LS, least squares; PBO, placebo; SE, standard error; VAS, visual analog scale.

Methods: Patients in this double-blind, randomized study (NCT02873936) received FIL 200 mg, FIL 100 mg, or PBO while continuing csDMARD therapy. PROs were collected prospectively on day 1 and at the W2, W4, W8, W12, W14, W16, W20, and W24 visits for assessment of pain (VAS pain scale]) and on day 1 and at W4, W12, and W24 for assessment of fatigue (FACIT-Fatigue) and HRQoL (SF-36). Changes from baseline for each PRO at each time point up to W24 were analyzed longitudinally using a mixed-effects model for repeated measures. P values for the difference between each FIL arm and PBO at each time point were calculated.

Figure 2. Change in SF-36 at each visit



*p ≤0.001, †p <0.01, ‡p <0.05 for LS mean difference between the FIL arm vs PBO.
CFB, change from baseline; FIL, filgotinib; LS, least squares; PBO, placebo; SE, standard error; SF-36, Short-Form 36.

Results: Among the 448 patients randomized and treated (FIL 200 mg, n = 147; FIL 100 mg, n = 153; PBO, n = 148) 381 (85.0%) completed the study. Baseline mean (SD) VAS pain scale was 67 (21.0), SF-36 physical component summary (PCS) was 31.1 (7.89), SF-36 mental component summary (MCS) was 44.3 (11.6), and FACIT-Fatigue score was 24.4 (11.6); baseline values did not vary between treatment groups. Significantly greater improvements in VAS pain scores began at W2 and were maintained through W24 for patients who received either dose of FIL vs PBO (**Fig 1A**). FIL also significantly improved patients' fatigue at W4, W12, and W24 compared with PBO for those receiving 200 mg doses, and at W4 and W12 for those receiving 100 mg doses (**Fig 1B**). HRQoL related to physical functioning (SF-36 PCS) was significantly enhanced at W4, W12, and W24 with both doses of FIL as compared with PBO (**Fig 2A**). Improvements to mental-health-related QoL (SF-36 MCS) were reported for FIL as early as W4 and maintained through W24, with statistically significant improvements at W4 and W12 for FIL 200 mg vs PBO (**Fig 2B**).

Conclusion: In a patient population with refractory disease that had inadequate response to prior bDMARDs and had significant disease at baseline, FIL treatment—coadministered with csDMARD therapy—was able to provide rapid and sustained improvements in key measures of pain, HRQoL, and fatigue as reported by patients.

References:

1) Smolen, et al. *Ann Rheum Dis*. 2017;76:960–77.
2) Fautrel, *et al*. *Rheumatol Int.* 2018;38:935–47.
3) Genovese, *et al*. *JAMA*. 2019;322(4):315–25.

Disclosure: D. Walker, Gilead, 2, 5, Lilly, 5, 8, Pfizer, 5, 8, Novartis, 5, 8; **T. Takeuchi**, AbbVie, 2, 8, Asahikasei Pharma Corp., 2, 5, Astellas Pharma, Inc., 2, 5, AYUMI Pharmaceutical Corp., 8, Bristol-Myers Squibb, 8, Chugai Pharmaceutical Co, Ltd., 2, 5, 8, Daiichi Sankyo Co., Ltd., 2, 8, Eisai Co., Ltd., 2, 8, Eli Lilly Japan,, 5, 8, Gilead Sciences, Inc., 8, Mitsubishi-Tanabe Pharma Corp., 2, 8, Nipponkayaku Co.Ltd., 2, Novartis Pharma K.K., 8, Pfizer Japan Inc., 8, Sanofi K.K., 8, Shionogi & Co., Ltd., 2, Takeda Pharmaceutical Co., Ltd., 2, UCB Japan, 2, Dainippon Sumitomo Co., Ltd., 8; **B. Bartok**, Gilead Sciences, Inc., 1, 3; **S. Rao**, Gilead Sciences, Inc., 1, 3; **I. Lee**, Gilead Sciences, 1, 2; **R. Besuyen**, Galapagos, 1, 3; **J. Gottenberg**, Bristol-Myers Squibb, 2, 8, Pfizer, 2, 5, UCB, 5, 8, Eli Lilly, 2, 8, AbbVie, 2, 8, Roche, 2, 8, Sanofi-Genzyme, 5, 8; **M. Genovese**, AbbVie, 2, 5, Eli Lily and Co, 2, 5, EMD Merck Serono, 2, 5, Galapagos, 2, Genentech/Roche, 2, 5, Gilead Sciences, Inc., 1, 2, 3, 5, GSK, 2, 5, Novartis, 2, 5, Pfizer, Inc., 2, Rpharm, 2, 5, Sanofi Genzyme, 2, 5.

Abstract Number: 1216

Filgotinib Provided Rapid and Sustained Improvements in Functional Status, Pain, and Health Related Quality of Life, and Reduced Fatigue over Time in Patients with Rheumatoid Arthritis Who Are Methotrexate-Naïve: Results from a Phase 3 Study

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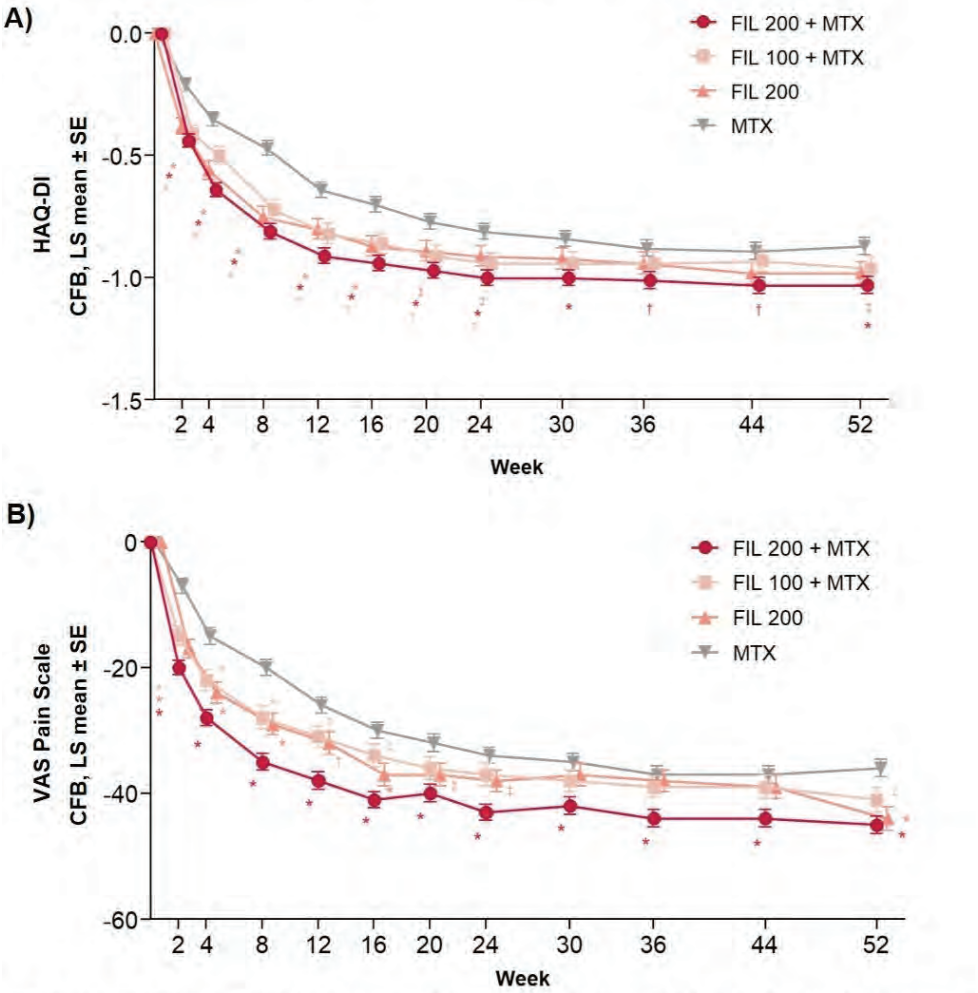
SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In FINCH 3, filgotinib (FIL)—a potent, selective, oral JAK1 inhibitor[1]—in combination with methotrexate (MTX), demonstrated significant improvements in signs and symptoms of rheumatoid arthritis (RA) vs MTX alone in patients (pts) who were MTX-naïve.[2] For pts with RA, rapid control of pain and fatigue along with maintenance of physical function and health-related quality of life (HRQoL) are important outcomes.[3] Patient-reported outcomes (PROs) can provide physicians with evidence to guide treatment decisions beyond guideline-recommended treatment targets of reducing immune inflammation to prevent joint damage, physical disability, and mortality.[4] Here, we evaluated rate and magnitude of change in PROs assessing functional status, pain, HRQoL, and fatigue from FINCH 3 (NCT02886728).

Figure 1. Change in HAQ-DI and VAS pain scale at each visit



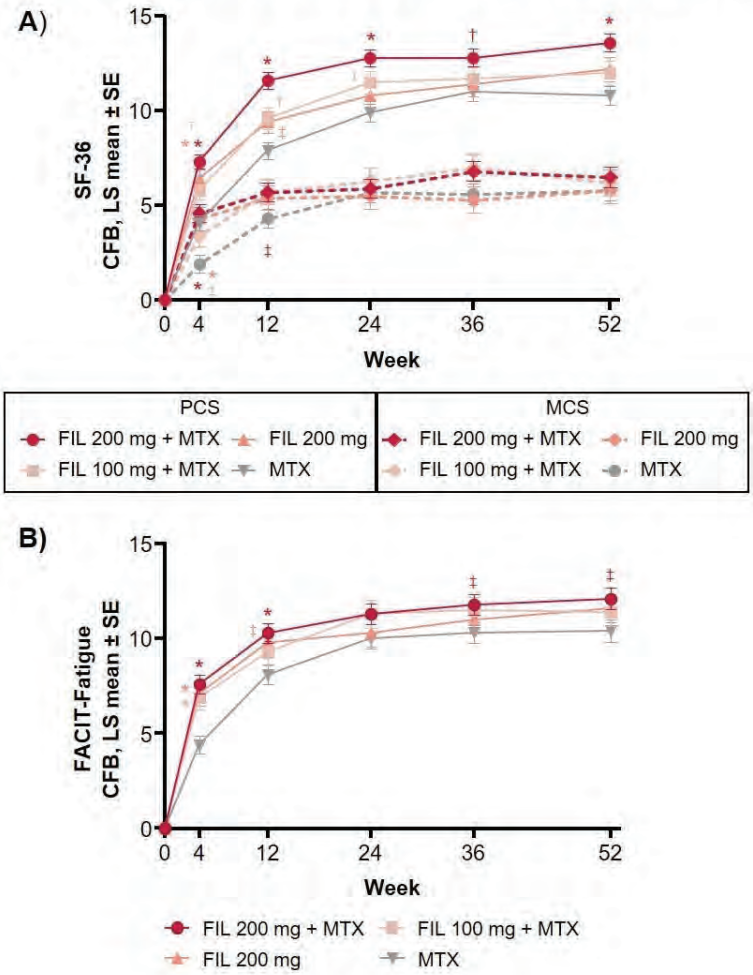
*p <0.001, †p <0.01, ‡p <0.05 for LS mean of the difference between FIL arm vs MTX. P values were not adjusted for multiplicity, except for HAQ-DI CFB at W24 for FIL 200 mg + MTX and FIL 100 mg + MTX vs MTX.
CFB, change from baseline; FIL, filgotinib; LS, least squares; MTX, methotrexate; SE, standard error; VAS, visual analog scale.

Methods: Pts with active RA and MTX-naïve received FIL 200 mg daily+MTX, FIL 100 mg+MTX, FIL 200 mg+placebo (PBO), or MTX+PBO for up to 52 weeks. PROs, recorded prospectively, included HAQ-DI (functional status) and VAS pain scale (day 1, week [W]2, W4, W8, W12, W16, W20, W24, W30, W36, W44, W52), SF-36 (HRQoL), and FACIT-Fatigue (day 1, W4, W12, W24, W36, W52). The least squares mean of the change from baseline (CFB) at each time point up to W52 and p values (each FIL arm vs MTX) were analyzed using mixed-effects model for repeated measures.

For HAQ-DI, proportion of pts who achieved the minimum clinically important difference (MCID; reduction ≥0.22) between each FIL arm and MTX was analyzed using logistic regression analysis. P values for comparisons of PROs were not adjusted for multiplicity, except for HAQ-DI CFB at W24 for FIL 200 mg + MTX and FIL 100 mg + MTX vs MTX.

Results: Of 1249 pts randomized and treated (FIL 200 mg + MTX, n=416; FIL 100mg + MTX, n=207; FIL 200mg, n=210; MTX, n=416), 82.1% completed the study. Compared with MTX alone, a nominally significantly greater CFB

Figure 2. Change in SF-36 and FACIT-Fatigue at each visit



*p <0.001, †p <0.01, ‡p <0.05 for LS mean of the difference between FIL arm vs MTX. P values were not adjusted for multiplicity.
CFB, change from baseline; FIL, filgotinib; LS, least squares; MCS, mental component score; MTX, methotrexate; PCS, physical component score; SE, standard error.

in functional status and pain from W2 to W24 was observed in all FIL arms; the benefit was sustained from W30 to W52 (**Fig 1**). By W2, a nominally significantly greater proportion achieved the HAQ-DI MCID or greater (≥0.22) in all FIL arms (FIL 200 mg + MTX: 61.9%, p < 0.001; FIL 100 mg + MTX: 58.5%, p < 0.001; FIL 200 mg: 53.9%, p=0.004) compared with MTX (42.2%). By W8, ≥72% of pts in all FIL arms vs 63% of pts in the MTX arm achieved the HAQ-DI MCID; a numerically greater proportion of pts in FIL arms vs MTX achieved HAQ-DI MCID through W52. SF-36 physical component summary and FACIT-Fatigue scores were nominally significantly improved with FIL treatment vs MTX alone at various time points (**Fig 2A, B**). Improvements in SF-36 mental component summary scores were nominally significant for pts in all FIL arms vs MTX alone as early as W4, and the CFB reached at W12 for FIL arms was generally sustained up to W52 (**Fig 2A**).

Conclusion: For pts with moderate to severe RA who were MTX-naïve, FIL—with or without concomitant MTX—led to rapid and sustained improvements in functional status, pain, fatigue, and HRQoL, compared with MTX alone.

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Disclosure: R. Alten, Pfizer, 2, 8, Gilead Sciences, Inc., 2, Novartis, 2, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 5, Lilly, 2, 5, UCB, 2, 5; **W. Rigby**, Gilead Sciences, Inc., 5; **A. Pechonkina**, Gilead Sciences, Inc., 1, 3; **Z. Yin**, Gilead Sciences, Inc., 1, 3; **K. Hasegawa**, Gilead Sciences, Inc., 1, 3; **T. Hendrikx**, Galapagos, 1, 3; **T. Atsumi**, AbbVie Inc., 5, 8, 9, UCB Japan Co.,Ltd., 5, 8, Eisai Co., Ltd., 8, Gilead Sciences, Inc., 5, 8, Bristol Myers Squibb Co., 2, 8, Chugai Pharmaceutical Co., Ltd., 2, 8, 9, Mitsubishi Tanabe Pharma Corporation, 8, 9, Eli Lilly Japan K.K., 2, 5, 8, Astellas Pharma Inc., 8, 9, Pfizer Inc., 2, 8, 9, Daiichi Sankyo Company, Limited, 5, 8, 9; **R. Westhovens**, Celltrion, Inc., 2, 5, Galapagos NV, 2, 5, Gilead Sciences, Inc., 2, 5.

Abstract Number: 1217

Effects of JAK Inhibitors Against JAK2-mediated Signaling in Innate Immune Cells

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Janus kinase (JAK) family is comprised of JAK1, JAK2, JAK3 and tyrosine kinase 2 (TYK2). JAKs form homo- or hetero-complexes, the combination of which plays crucial role in various cytokine signaling. JAK inhibitors (JAKis) have been approved for the treatment of RA. Granulocyte Macrophage colony-stimulating Factor (GM-CSF) could be implicated in the pathophysiology of RA by activating innate immune cells. We assessed the effects of isoform-specific JAKis on GM-CSF-primed human innate immune cells.

Methods: Human monocytic cell line, THP-1 cells or primary human neutrophils pretreated with tofacitinib (TOF), baricitinib (BAR) and upadacitinib (UPA) were stimulated with GM-CSF (20 ng/mL). JAK/ signal transducer and activator of transcription (STAT) phosphorylation and subsequent interleukin-1β (IL-1β) production were investigated using western blot and ELISA method.

Results: All JAKis blocked GM-CSF induced JAK2 phosphorylation at high concentration (400 nM) in THP-1 cells. BAR and UPA also inhibited JAK2 phosphorylation at lower concentrations (25 and 100 nM). Similarly, not TOF but BAR and UPA suppressed STAT5 phosphorylation at higher concentrations (100 and 400 nM) in THP-1 cells. BAR

and UPA significantly suppressed the IL-1β at lower concentrations (25 and 100 nM) compared to TOF in THP-1 cells. Consistent with THP-1 cells, all JAKis inhibited IL-1β production at high concentration (400 nM) in human neutrophils. However, BAR significantly suppressed IL-1β at lower concentration (25 nM) compared to TOF in human neutrophils. All JAKis suppressed the expression of NLR family pyrin domain-containing 3 and casepase-1 (p20) release at high concentration (400 nM) whereas only BAR suppressed them even at lower concentration in human neutrophils.

Conclusion: The inhibition of JAK2-dependent cytokine signals varies depending on the type of JAKis. This suggests difference of JAK selectivity among JAKis may affect the modulation of innate immune cell activation.

Disclosure: Y. Fujita, None; **N. Matsuoka**, None; **M. Furuya-Yashiro**, None; **J. Temmoku**, None; **Y. Kuroiwa**, Eli Lilly Japan K.K., 3; **M. Tanaka**, Eli Lilly Japan K.K, 3; **T. Asano**, None; **S. Sato**, None; **H. Matsumoto**, None; **H. Watanabe**, None; **H. Kuzuru**, None; **H. Yatsuhashi**, None; **A. Kawakami**, None; **K. Migita**, Eli Lilly Japan K.K., 2.

Abstract Number: 1218

Filgotinib Provided Rapid and Sustained Improvements in Functional Status, Pain, Health-related Quality of Life, and Fatigue in Patients with Rheumatoid Arthritis and Inadequate Response to Methotrexate

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

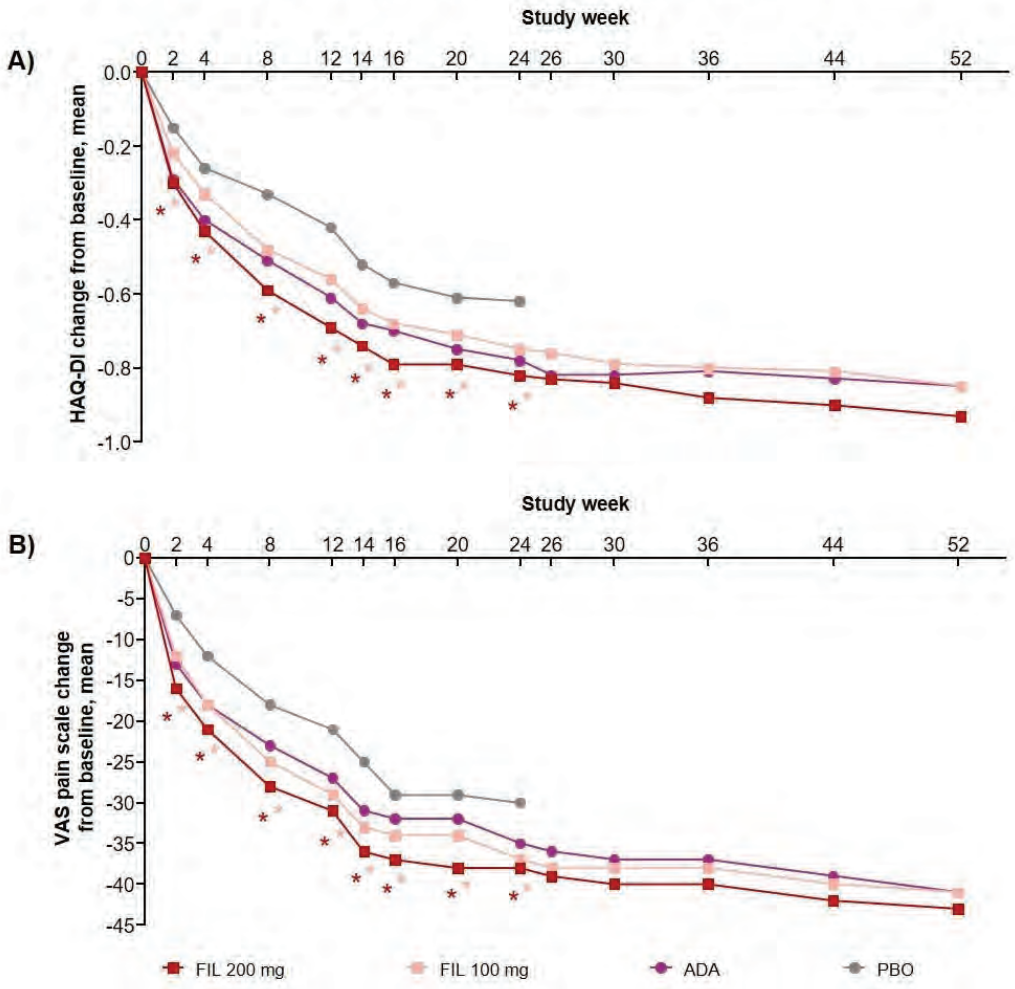
Background/Purpose: In the FINCH 1 study, filgotinib (FIL)—an oral, potent, selective JAK1 inhibitor—plus methotrexate (MTX) provided significant improvements in signs and symptoms of rheumatoid arthritis (RA) in patients (pts) with inadequate response to MTX.[1] EULAR guidelines recommend a treat-to-target approach focused on reducing inflammation to prevent joint damage, physical disability, and mortality, but pts consider pain and fatigue control, and maintenance of physical function and health-related quality of life (HRQoL), to be important aspects of care.[2,3] Here, we present the rate and magnitude of change in PROs from FINCH 1.

Methods: In FINCH 1 (NCT02889796), pts with active RA received oral FIL 200 mg + MTX, FIL 100 mg + MTX, PBO + MTX, or subcutaneous adalimumab (ADA) 40 mg + MTX for up to 52 weeks (W); pts receiving PBO at W24 were rerandomized 1:1 to FIL 100 or 200 mg.

PROs included the HAQ-DI and VAS pain scale, SF-36, and FACIT-Fatigue questionnaire. The change from baseline (CFB) at each time point was assessed up to W52 for each treatment group. Mixed-effects model for repeated measures was used to compare each FIL group with PBO for the CFB at each time point through W24. logistic regression model was used to compare each FIL group with PBO for the proportion of pts achieving the minimum clinically important difference (MCID) of ≥0.22 reduction in CFB in HAQ-DI at each time point through W24.

Results: Of 1755 pts randomized and treated (475 FIL 200 mg + MTX; 480 FIL 100 mg + MTX; 325 ADA + MTX; and 475 PBO + MTX), 1417 (80.7%) received study drug through W52. As early as W2 through W24, pts receiving

Figure 1. Change from baseline in A) HAQ-DI and B) VAS pain scale at each visit

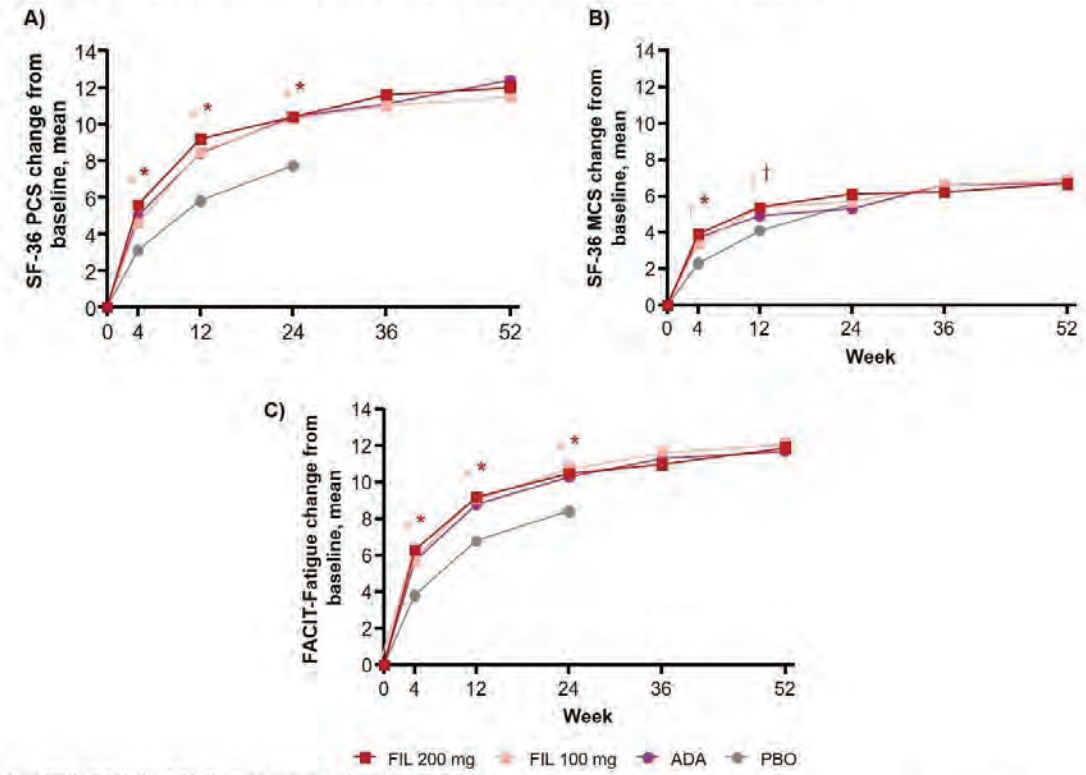


*p vs PBO <0.001, not adjusted for multiplicity except at week 12 for HAQ-DI.
Patients receiving PBO were rerandomized 1:1 to FIL 100 or 200 mg at week 24.
ADA, adalimumab; FIL, filgotinib; HAQ-DI, Health Assessment Questionnaire Disability Index; PBO, placebo; VAS, visual analog scale.

either FIL dose experienced nominally significantly greater ($p < 0.001$) CFB in HAQ-DI and VAS pain scale than those receiving PBO; CFB improvements were maintained through W52 (**Fig 1A, B**). At W2, compared with PBO (40.2%), a nominally significantly greater proportion of pts achieved the HAQ-DI MCID in both the FIL 200 (52.5%; $p < 0.001$) and 100 mg (46.7%; $p = 0.043$) groups. This benefit vs PBO was maintained up to W24 and the proportion of pts who achieved a HAQ-DI reduction ≥0.22 remained ≥75.8% in the FIL 200 mg group and ≥71.5% in the FIL 100 mg group from W12 through W52. FIL provided nominally significantly greater improvement in HRQoL vs PBO at W4 and W12 for both the CFB of the SF-36 Physical Component Summary (PCS; $p < 0.001$) and Mental Component Summary (MCS;$p \leq 0.006$); nominal significance was also seen at W24 for CFB of SF-36 PCS (**Fig 2A, B**). By W4, pts receiving either dose of FIL reported a nominally significantly greater mean CFB in FACIT-Fatigue scores vs PBO ($p < 0.001$); significance was maintained through W24 and improvement in reported fatigue continued through W52 in the FIL groups (**Fig 2C**). In general, CFB for HAQ-DI, VAS pain scale, and FACIT-Fatigue observed for the FIL groups was higher or comparable to ADA at various time points (**Fig 1, 2**).

Conclusion: Both doses of FIL provided rapid and sustained improvements in functional status, pain, HRQoL, and fatigue vs PBO for pts with RA and inadequate response to MTX throughout the 52-week period.

Figure 2. Change from baseline in SF-36 A) PCS and B) MCS and C) FACIT-Fatigue



*p vs PBO ≤0.001; †p ≤0.01. P values were not adjusted for multiplicity.
Patients receiving PBO were rerandomized 1:1 to FIL 100 or 200 mg at week 24.
ADA, adalimumab; FACIT, Functional Assessment of Chronic Illness Therapy; FIL, filgotinib; MCS, mental component summary; PBO, placebo; PCS, physical component summary; SF-36; Short-Form 36.

References:

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2. Fautrel B, *et al. Rheumatol Int.* 2018;38:935–47.
3. Smolen JS, *et al*. *Ann Rheum Dis.* 2017;76:960–77.

Disclosure: A. Kivitz, Sanofi, 1, 5, 8, Amgen, 1, Gilead, 1, AbbVie, 5, Genzyme, 5, 8, Janssen, 5, Novartis, 8, Regeneron, 5, 8, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 8, Horizon, 8, Merck, 8, Pfizer, 1, 5, 8, Sun Pharma, 5, UCB, 5; **Y. Tanaka**, AbbVie, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 2, 5, 8, Asahi-kasei, 2, 5, 8, Novartis, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Astellas, 2, 5, 8, Chugai, 2, 5, 8, Daiichi-Sankyo, 2, 5, 8, Eisai, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Janssen, 2, 5, 8, Mitsubishi-Tanabe, 2, 5, 8, Pfizer, 2, 5, 8, Takeda, 2, 5, 8, YL Biologics, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8; **S. Lee**, Gilead Sciences, Inc., 3; **L. Ye**, Gilead Sciences, Inc., 1, 3; **H. Hu**, Gilead Sciences, Inc., 1, 3; **R. Besuyen**, Galapagos, 1, 3; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8.

Abstract Number: 1219

Reaching Remission by IL-1 Inhibition in Rheumatoid Arthritis Patients with Type 2 Diabetes Improves the Glucose Homeostasis: Long-term Findings from TRACK Study, a Multicentre, Open-label, Randomised, Controlled Trial

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The inflammatory contribution to type 2 diabetes (T2D) has suggested new therapeutic targets by using biologic DMARDs designed for rheumatoid arthritis (RA), and IL-1 would be a common pathogenic mediator, suggesting a possible common therapeutic target. In TRACK study, a multicentre open-label, randomised controlled trial, anakinra, a human interleukin-1-receptor antagonist, showed to induce a significant improvement of metabolic alteration whereas TNFi did not show any significant improvement on that, after 6 months of therapy (crude difference of 0.93 of glycated haemoglobin, HbA1c% between groups). Concerning RA, a progressive reduction of disease activity was observed in both groups.

Since TRACK study has been prematurely stopped for "early benefit" after 6 months of follow-up, in this work, we aimed at investigating how long lasted the improvement of HbA1c% and of RA disease activity, including the rate of reduction and discontinuation of both antidiabetic drugs and glucocorticoids (GCs).

Methods: In this study, participants with RA and T2D, were randomised to anakinra or to a TNFi and the primary endpoint was the change in HbA1c% (EudraCT: 2012-005370-62; ClinicalTrial.gov: NCT02236481). In this further evaluation, we assessed how long lasted the improvement of HbA1c% and of RA disease activity.

Results: In TRACK study, 39 participants with RA and T2D (age 62.72 ± 9.97, 74.4% female gender) were randomised to anakinra or to TNFi; the majority of participants had seropositive RA disease with active disease (DAS28: 5.54 ± 1.03; C-reactive protein 11.84 ±9.67 mg/L) and all participants had T2D (HbA1c%: 7.77 ±0.70, fasting plasma glucose: 139.13 ±42.17 mg). Considering the last available observation, a maintenance of reduced levels of HbA1c% was observed in anakinra-treated participants (Baseline: 7.73% ±0.67; 6 months: 6.70% ±0.67; last follow-up: 6.60% ±0.52). Paralleling with HbA1c%, a significant reduction of dosages of antidiabetic therapies was observed in anakinra-treated participants, with a percentage of participants who discontinued any anti-diabetic therapy. Conversely, an intensification of antidiabetic therapies was reported in TNFi-treated participants. Concerning RA, the clinical response was maintained during the whole follow-up, although a larger percentage of anakinra-treated participants discontinued the concomitant GCs therapy. Analysing the safety profile, as observed in first 6 months of the study, only minor side effects were recorded during the whole follow-up with no difference between groups, except for self-limited urticarial lesions at the injection site which were more frequently in anakinra-treated participants.

Conclusion: Data deriving from the long-term extension of participants with RA and T2D, enrolled in the TRACK study, showed that the benefits of IL-1 inhibition on metabolic and inflammatory parameters lasted longer than the first 6 months of follow-up. Thus, the presence of T2D could identify a subset of RA patients likely benefitting of IL-1

inhibition. Finally, the achievement of optimal therapeutic targets for both RA and T2D might significantly improve the cardiovascular burden of these patients.

Disclosure: P. Ruscitti, BMS, 8, Ely Lilly, 8, MSD, 8, Novartis, 8, Pfizer, 2, SOBI, 8; **O. Berardicurti**, None; **P. Cipriani**, None; **R. Giacomelli**, Abbvie, 8, Actelion, 2, BMS, 8, Ely Lilly, 8, MSD, 8, Novartis, 8, Pfizer, 2, Roche, 8, SOBI, 8.

Abstract Number: 1220

Increased Serum Levels of Circulating Vimentin and Citrullinated Vimentin Are Differently Regulated by Tocilizumab and Methotrexate Monotherapies in Rheumatoid Arthritis

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Presence of citrullinated protein fragments in the circulation of patients with Rheumatoid Arthritis (RA) is a highly disease-specific phenomenon. Vimentin is often a target for citrullination and MMP-mediated degradation as a consequence of disease initiation and progression. Generation of citrullinated or non-citrullinated vimentin fragments (VICM and VIM) are associated with chronic inflammation and can be of high biomarker potential for disease and treatment monitoring. In this study, we aimed to investigate if two different monotherapies, Tocilizumab (TCZ) and Methotrexate (MTX) can differently modulate serum levels of VIM and VICM in RA patients at the early therapy time-point.

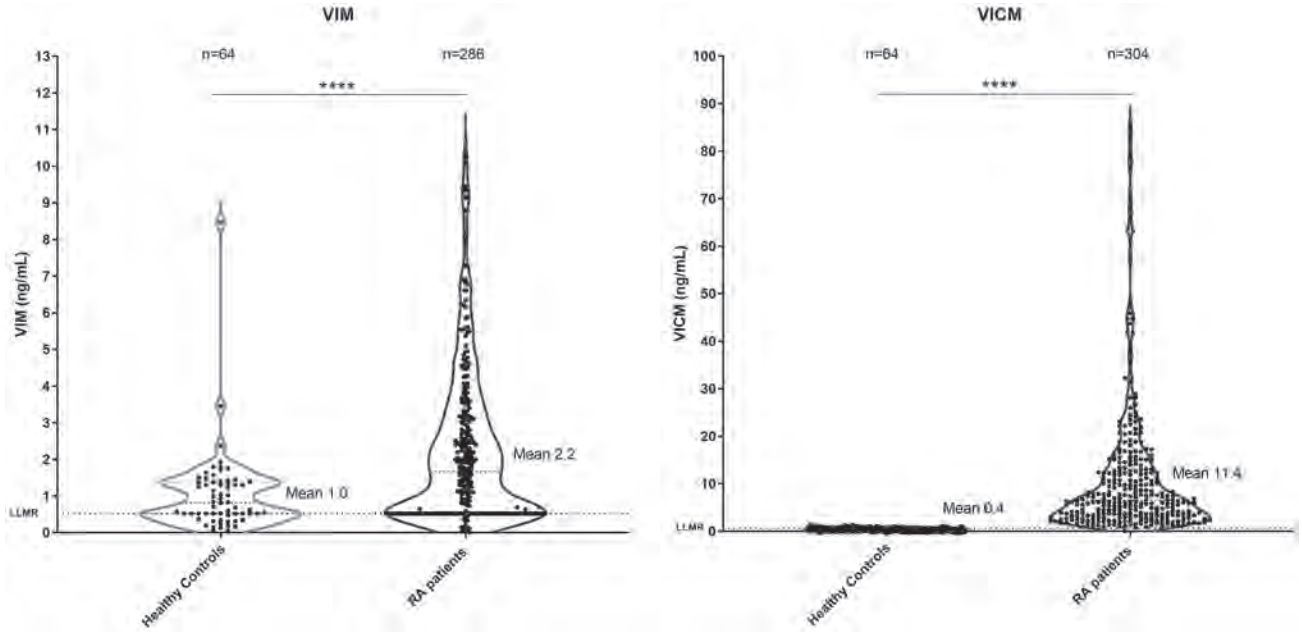

Figure 1. Figures represent differences in serum levels of VIM and VICM biomarker between healthy controls and RA patients at baseline.

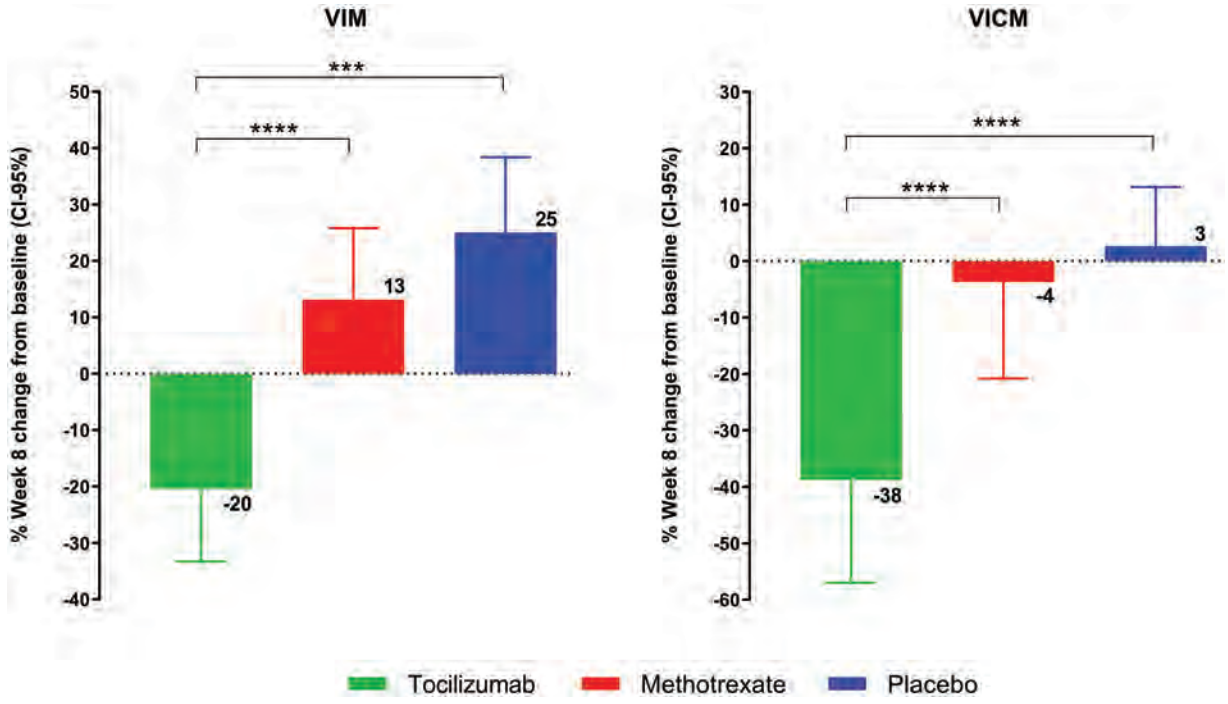

Figure 2. Figures represent differences in modulation of VIM and VICM biomarker levels according to treatment group from baseline to week 8. Data are shown as mean with confidence interval CI-95%.

Methods: Patients with moderate to severe RA in phase III randomized controlled clinical trial were exposed to either TCZ monotherapy (8 mg/kg every 4 weeks) or MTX monotherapy (starting at 7.5 mg/kg and titrated to 20 mg/kg) over 24 weeks. Serum levels of VIM and VICM were measured at baseline and 8-weeks sera from 304 RA patients and 64 healthy controls by validated ELISA assays. We investigated the comparison between treatment and response groups using ANCOVA and correlations using Spearman's rho adjusted for patient demographic characteristics (gender, age, BMI and disease duration).

Results: Serum levels of VIM and VICM were significantly higher in RA patients than in healthy controls ($P < 0.0001$) (Fig. 1). RA patients with the greatest disease activity had the highest serum levels of VICM ($P < 0.01$). VIM and VICM biomarkers were significantly inhibited at week 8 by TCZ compared to placebo patients ($P < 0.001$ and $P < 0.0001$, respectively) (Fig. 2). The inhibition of VIM and VICM levels with TCZ was respectively 33% and 34% greater than that of MTX (both $P < 0.0001$). Biomarker profiles of VIM and VICM revealed a significant inhibition difference in MTX ACR50 treatment responding and non-responding patients ($P < 0.05$ and $P < 0.01$), whereas no statistically significant difference was observed in TCZ ACR50 patients. Change in serum levels of VICM to week 8 in MTX patients correlated significantly with change in disease activity score-28 (DAS28) at week 8, 16 and 24 (rho 0.31 to 0.23, $P = 0.0006$ to 0.01).

Conclusion: Present findings show that patients treated with TCZ for 8 weeks have clearly higher suppression of VIM and VICM biomarkers over patients treated with MTX. The differences in biomarker profiles of ACR50 patients enable for their stratification and identification of those who benefit from the treatment at the early time-point. The correlation of serum VICM with DAS28 at different time-points may suggest its treatment prognostic value in RA.

Disclosure: P. Drobinski, None; **A. Bay-Jensen**, Nordic Bioscience, 1; **A. Siebuhr**, Nordic Bioscience, 3; **M. Karsdal**, None.

Abstract Number: 1221

Evaluation of Methotrexate Efficacy and Exploration of Metabolites Associated with Disease Activity in Collagen-induced Arthritis Mouse Model

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Methotrexate (MTX) is cornerstone of therapy for rheumatoid arthritis. However, response to MTX is variable and unpredicTable among patients. Therefore, there is a critical need to identify potential biomarkers to improve drug response to MTX in arthritis. This study aims to evaluate MTX and circulating folates in the response to MTX treatment, and to explore metabolomic data to identify potential biomarkers associated with disease activity in collagen-induced arthritis (CIA) mouse.

Methods: The study included untreated healthy control group (n=10), MTX treated control group (n=10), untreated CIA group (n=8), and MTX treated CIA group (n=9). As endpoint analysis, disease activity score using an established scoring system were determined and paw volume using limb water volume displacement were measured. Plasma or erythrocyte samples were collected and submitted to the National Institutes of Health West Coase Metabolomics Center to measure intermediates of primary metabolism, biogenic amines, and lipids. Raw peak intensity data was utilized to identify and rank metabolites using MataboAnalyst 4.0. The metabolites with significant fold change and false discovery rate adjusted R values in the induction of disease or in the treatment of MTX were subjected to enrichment analysis using Chemical Similarity Enrichment Analysis for Metabolomics (ChemRich) and mapping data were visualized using Cytoscape 3.7.2.

Results: MTX efficacy in CIA and control mice with or without MTX treatment was evaluated. Compared to control group, CIA mice appeared significant induction in both disease activity scores (Mean±S.E.M., 9 ± 1 vs 0 ± 0, $P < 0.001$) and paw volume (0.48 ± 0.02 ml vs 0.35 ± 0.01 ml, $P < 0.001$). CIA group treated with MTX had reduced disease activity scores (1 ± 0.4 vs 9 ± 1, $P < 0.001$) and paw volume (0.37 ± 0.01 ml vs 0.48 ± 0.02 ml, $P < 0.001$) compared to the CIA untreated group. A concentration of 5mTHF in RBCs was significantly influenced by the induction of disease ($P < 0.05$) and the exposure of MTX ($P < 0.001$). Similarly, a significant diffrence in a concentration of 5mTHF in plasma was observed between untreated CIA group and MTX treated CIA group (9.34 ± 3.18 nM vs 45.03 ± 10.84 nM, $P < 0.01$). RBC 5mTHF was postiviely correlated with disease activity score ($\rho = 0.740$, $P = 0.001$) and paw volume ($\rho = 0.709$, $P = 0.001$) in CIA mice. Metabolomic analysis using ChemRich revealed most significant changes in the unsaturated triglycerides in the induction of disease and unsaturated phosphatidylcholines in the treatment of MTX.

Conclusion: Our study demonstrated that MTX treatment recovered a reduction in arthritis disease activity in the CIA mouse model. Associations of pharmacologic folates level with MTX efficacy suggest that erythrocyte 5mTHF levels as a potential predictor of MTX response. Metabolomic analysis of plasma generated a list of metabolites that significantly correlated with disease activity. The results suggest that metabolomic approach may lead to identify potential biomarkers in MTX response in autoimmune arthritis.

Disclosure: Y. Cho, None; **R. Funk**, None.

Abstract Number: 1222

Iron Management in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a chronic connective tissue disease with immune background, which affects approximately 0.3-2% of the population. Anaemia is the most common hematologic disorder in patients with RA, has a multifactorial origin with the significant contribution of inflammatory processes and the deficiencies of several erythropoiesis modulators. Anaemia occurring in the course of RA intensifies the severity of primary disease and makes favorable conditions for more extensive joint structure damage. There is evidence showing a clinical significance of iron deficiency (ID) seen in inflammatory diseases, regardless of concomitant anaemia. There is no comprehensive analysis of this problem in rheumatological patients.

Aim of the study was to evaluate iron metabolism in patients with RA using standard laboratory parameters. The influence of tocilizumab on iron status parameters and the course of primary disease in patients with RA have been evaluated.

Methods: Sixty-two RA patients hospitalized in the Department of Internal Medicine. The diagnosis of RA was made in accordance of the American Rheumatology Society. The patients were divided: group A - observational and group B -interventional. In the part A, patients with RA and healthy persons were examined. In the part B, patients included in tocilizumab therapy. Patientsfrom B group were examined twice, before and after the 3-month therapy with tocilizumab. Patients with RA were treated with standard disease modifying medications in accordance with recommendations.

Results: ID was found in patients with or without anaemia (66% vs 55%; $p > 0.2$). Patients with RA in comparison to healthy subjects had lower transferrin saturation, lower serum ferritin and hepcidin, and increased serum soluble transferrin receptor ($p < 0.05$). Patients with RA and ID in comparison to those without ID had lower serum hepcidin ($p < 0.05$). In patients with RA there were correlations between lower hemoglobin, lower red cell indices and parameters describing iron status. In univariable models, there were no associations between the prevalence of ID and some inflammatory parameters and those describing immune abnormalities in patients with RA. In multivariable models, two strongest determinants of ID prevalence in patients with RA were identified: lower hemoglobin and higher DAS28 score. In addition the three-month therapy with tocilizumab reduced the severity of RA assessed on the reduction of both CRP level and DAS28 score ($p < 0.05$). The therapy also influenced parameters of iron status: reduced serum ferritin and hepcidin and reduced the magnitude of ID as expressed by the reduction in the percentage of patients with TSAT< 20% and the decrease in serum soluble transferrin receptor.

Conclusion: Among patients with RA iron deficiency is more common than anaemia. Tocilizumab therapy in patients with RA along with the improvement in clinical status and the attenuation of inflammatory processes partially normalizes iron status assessed on circulating biomarkers. The results constitute premises to take into consideration the assessment of iron status parameters in the standard clinical evaluation of patients with RA.

Disclosure: W. Tański, None; **M. Chabowski**, None; **E. Jankowska**, None.

Abstract Number: 1223

Characterizing Rheumatoid Arthritis Patients by Their Biologic DMARD Prescription History

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
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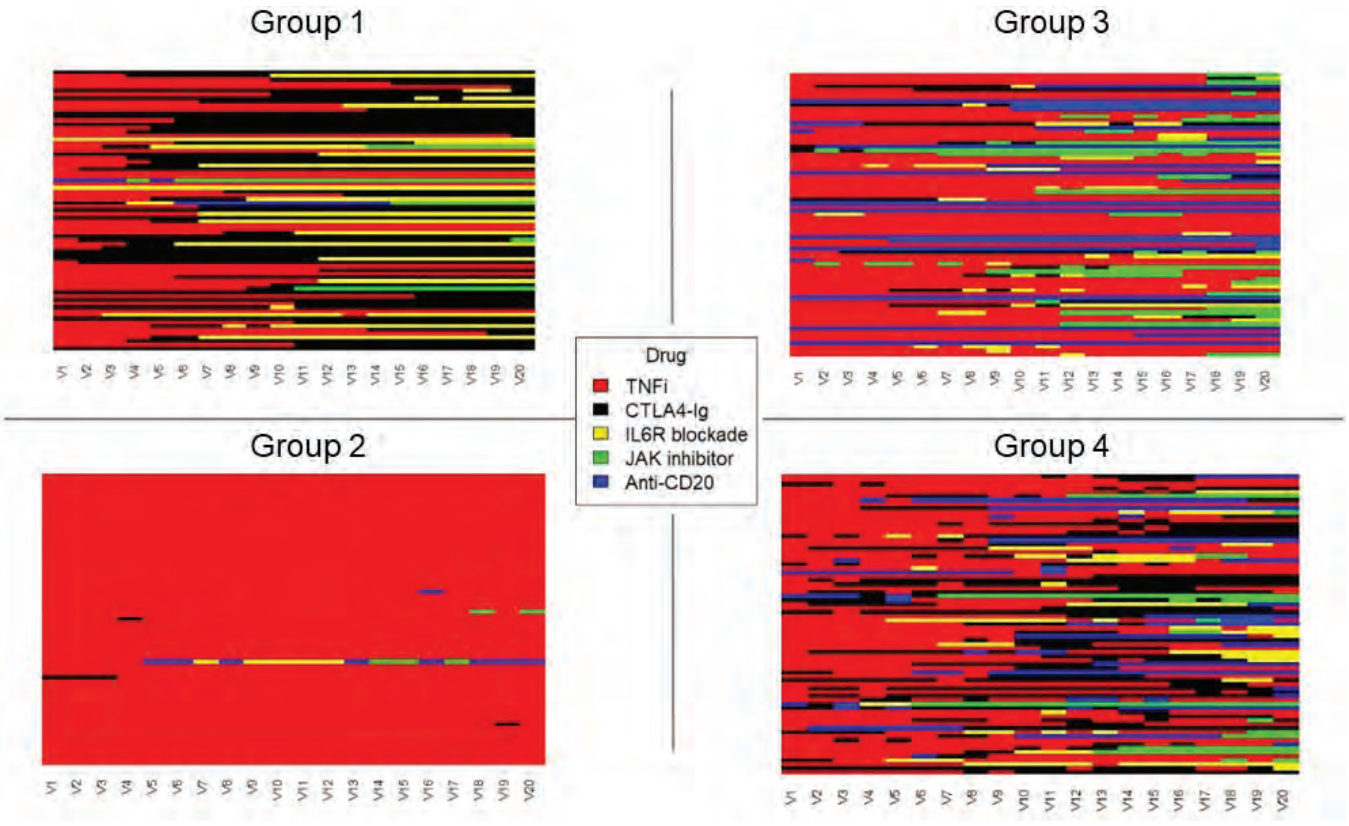
Session Time: 9:00AM–11:00AM

Background/Purpose: IIn rheumatoid arthritis (RA), a patient's biologic disease modifying anti-rheumatic drug (bDMARD) history and the duration of time they remain on each drug may provide an alternative approach to studying treatment efficacy. Due to the complexity of these data, how to determine if patients are similar based on their past bDMARD use is challenging. Bioinformatics methods designed to study genetic sequences are now available that



Visualization of the 4 groups identified from clustering bDMARD sequences. Data from 75 random patients from each group shown with x-axis denoting the first 20 states (V1-V20) for each patient.

Clinical characteristic	Group			
	1	2	3	4
Age, mean (SD)	50.3 (14.7)	47.8 (15.6)	53.7 (16.1)	49.3 (14.6)
% female	83.0	70.6	74.8	83.3
RA follow-up time (months)	94.2	73.5	60.8	71.1
% seropositive	80.5	64.7	70.4	72.1
Charlson comorbidity index, mean	1.7	1.4	2.8	1.6
Short description	Abatacept & tocilizumab	TNFi	Rituximab & TNFi	Multiple bDMARD use

Comparison of clinical characteristics at the time of first bDMARD prescription across the 4 groups.

cluster sequences by similarity. In this proof of concept study, we applied and modified this bioinformatics approach to cluster RA patients by similar sequences of bDMARD prescriptions.

Methods: We studied patients from a validated electronic health record cohort of RA patients from two tertiary care centers and extracted data on all subjects who initiated a bDMARD 1/1/2008 through 07/31/2019. Inclusion criteria included subjects with ≥6 months of data prior to 1/1/2008 and no bDMARD prescription. The sequence of bDMARD for each subject was initiated with the 1st bDMARD prescription. Sequences were defined by 5 bDMARD drug classes: tumor necrosis factor inhibitors (TNFi), CTLA4-Ig/abatacept, IL6R blockade/tocilizumab, JAK inhibitor/tofacitinib (small molecule grouped as bDMARD for this study), and anti-CD20/rituximab. A change in bDMARD was defined as a change in bDMARD therapy ≥3 months from the prior bDMARD prescription. A sequence by drug class was constructed for each subject. The sequences were then analyzed using mixture Markov chain analysis. We consider the transitions of drug classes of a patient over the time as Markov chains where each of the drug classes was considered a state. We clustered the patients based on the sequence of drug classes. We calculated descriptive statistics for demographics, and obtained the Charlson comorbidity index at the time of the 1st bDMARD prescription to compare across clusters.

Results: We studied 8684 RA subjects who initiated a bDMARD after 1/1/2008. The mean age was 48.9 years, 73% female, 82% white, 68% seropositive, with mean follow-up time of 6.2 years; each subject had a unique sequence, thus there were 8684 sequences. The sequences clustered in 4 main groups (Figure). Descriptively, group 1 included patients who persisted on abatacept and tocilizumab therapy. Group 2 contained patients on TNFi for the majority of their follow-up. Group 3 contained a mixture of patients persisting on rituximab and TNFi. Group 4 included patients who tried multiple bDMARDs for variable lengths of time. The lowest % of females was observed in Group 2 (70%) compared to Group 4 (83%) which had the highest ($p< 0.0001$) (Table). The highest % seropositive was observed in group 1 (80.5%) compared with group 2 (65%) which had the lowest ($p< 0.0001$).

Conclusion: Transforming bDMARD prescription histories into a sequence allowed us to cluster RA patients into 4 main groups which demonstrated differing clinical characteristics at the time of the 1st bDMARD prescription. Future studies will examine whether the clinical profiles of patients in these clusters can be used to inform optimal bDMARD choices among RA patients prospectively.

Disclosure: P. Das, None; **S. Huang**, None; **K. Dahal**, None; **H. Zheng**, None; **J. Coblyn**, None; **M. Weinblatt**, Crescendo Bioscience, 1, Bristol Myers Squibb, 1, Sanofi, 2, Lilly, 1, Amgen, 1, AbbVie, 5, Amgen, 2, 5, Arena, 5, Bristol Myers Squibb, 2, 5, Canfite, 1, 5, Corrona, 5, Crescendo, 2, 5, GlaxoSmithKline, 5, Gilead, 9, Horizon, 9, Johnson and Johnson, 9, Lilly, 2, 9, Pfizer, 9, Scipher, 1, 9, Set Point, 9, Roche, 9, Canfite, 1, Inmedix, 1, Lycera, 1, Vorso, 1, Scipher, 1; **T. Cai**, None; **K. Liao**, None.

Abstract Number: 1224

Glucocorticoid Reduction in Different Profiles of Patients with Rheumatoid Arthritis and Treatment with Sarilumab

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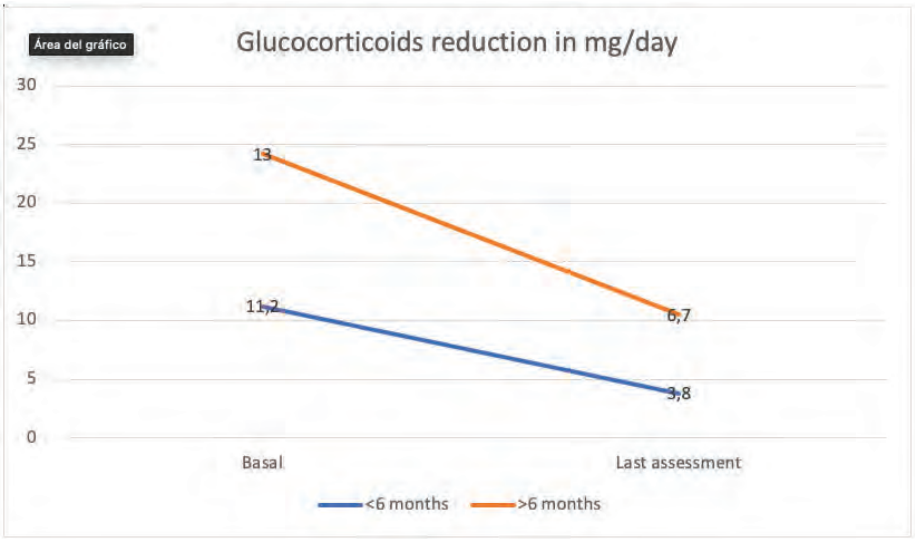
SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Glucocorticoid reduction in different profiles of patients with rheumatoid arthritis and sarilumab treatment. Real clinical practice studies are tasked with providing clinically relevant data that may clarify the benefits of this new IL-6 receptor blocking alternative, with higher affinity and dosing every two weeks. Beyond the magnitude of the effect that a drug can give us in a randomized, double-blind, control group clinical trial, the well-known selection biases of these studies do not always offer a representative picture of reality when using that drug on the day consultation day.

Methods: The data, hereafter commented, is the result of a retrospective analysis carried out in March 2020 on patients who were assigned to Sarilumab from September 2018 to November 2019 and therefore have at least a first clinical evaluation carried out 12 weeks after their Start. This study offers in our opinion several novelties: Firstly, almost two thirds of the analyzed cohort are patients naïve to another biological treatment (58.6%). This fact allows us to assess “the best opportunity” for a drug. We found it interesting to analyze two variables: the reduction of glucocorticoid doses secondary to the use of sarilumab and the efficacy depending on its association or not with a csDMARD.

A descriptive study was carried out; For the parametric distribution numerical variables, the mean and standard deviation are performed, reserving the median for those non-parametric distribution numerical variables. For qualitative variables, a study was carried out using frequency Tables. And for the non-parametric ones, the Wilconxon test was



n=58	Women	Men	Total
N	42 (72.4%)	16 (27.6%)	58
age	53.3± (21-76)	54.0± (23-72)	53.5± (21-76)
RA (years)	¿?	¿?	9 (1-35)
RF+	37 (88%)	16 (100%)	53 (91.4%)
ACPA+	27 (64.3%)	14 (87.5%)	41 (74.1%)
DM	3 (7.1%)	2 (12.5%)	5 (8.6%)
ILD	0	1 (6.2%)	1 (1.7%)
Tobacco	10 (23.8%)	9 (56.2%)	19 (32.7%)
DAS28 base ± sd	4.84± (3.4-5.9)	4.18±(3.2-5.5)	4.54± (3.2-5.9)
Monotherapy	18 (42.8%)	6 (37.5%)	24 (41.3%)
Combination	24 (57.2%)	10 (62.5%)	34 (58,7%)
MTX	17 (38%)	9 (56%)	26 (43%)
ESG basal media, mm/h ± sd	25.5 ± (4-91)	14.3 ± (2-57)	22.4 ±(2-91)
nº biológicos previos			
0 Biological therapies previus	-	-	34 (58.6%)
1 Biological therapies previus	-	-	17 (29.3%)
2 Biological therapies previus	-	-	5(8.6%)
>2 Biological therapies previus	-	-	2 (3.4%)
t Sarilumab time (months) ± sd	8.2± (4-15)	9.9± (5-18)	8.9±3.84(3-18)
DGlucocorticoids dose ± sd	12± (0-40)	13± (5-30)	12.2± (0-40)
DM: Diabetes Mellitus; IDL: Interstitial Lung Disease			

used, which also show values of $p < 0.05$ For inferential studies, a 95% CI was used. All of them analyzed using SPSS 19.

Results: The evolution in prednisone dose for the total of patients was striking and satisfactory. For a variable of temporary drug exposure, such as the one previously mentioned, we went from an average dose of 12mg / day to 5.2mg / day, a dose very close to the dose recommended in EULAR clinical practice guidelines, for the maintenance of a effective therapeutic strategy in an accepTable safety range. As in the case of efficacy assessed by an activity index, we stratified patients between those over 6 months exposed to Sarilumab and those with 6 or less months of treatment duration. In both cases the change had an effect size with clinical significance. In the population 6 months or less from the start of Sarilumab, the prednisone dose went from 11.2mg / day to mean prednisone 3.8mg / day and in patients with more than 6 months of treatment 12.9mg / day. at 6.7 mg / day.

Conclusion: In general, it could be stated that the drug Sarilumab presents in accepTable clinical practice an accepTable and predicTable safety profile. From the point of view of the efficacy variable, we highlight one aspect: A good ability to reduce the steroid dose in a short time.

Disclosure: E. Rubio Romero, None; **A. Jiménez**, None; **R. Martinez Perez**, None; **L. Mendez Diaz**, None.

Abstract Number: 1225

Targeting to IL-6 or Specific JAKs for RA Treatment: Seeking a Rationale for Switching Each Other If One of These Treatments Resulted in Lack of Efficacy

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SESSION INFORMATION
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Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
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Background/Purpose: Inhibition of IL-6 signaling is one of the most established strategies for RA treatment. Tocilizumab (TCZ) is the pioneer which blocks IL-6 signaling by preventing IL-6 from binding to its receptors. Tofacitinib (TOF) inhibits Janus kinase (JAK) 1, JAK3 and, to a lesser extent, JAK2. Recently, Baricitinib (BAR), JAK 1 and JAK2 selective kinase inhibitor, were also approved to treat RA. These JAK inhibitors are known to inhibit cytokine signaling IL-6. It is very important to know whether these treatments affect common biological processes or disparate, because it will provide a rationale for switching each other if one of these treatments resulted in lack of efficacy. In this study, we investigate the gene-expression modification profiles among TOF, BAR and TCZ treatments.

Methods: Total of 38 RA cases were analyzed, including TOF (n=15), BAR (n=10:) and TCZ (n=13) treatment groups. Peripheral blood was drawn at just before (pre) and 3 months after (post) these treatments. Total RNAs were then extracted with using PAXgene miRNA kit. After quantifying the expressions of transcripts by multiplex sequencing, differentially expressed genes (DEGs) were selected by paired comparison (post vs. pre) with using paired T-test. And then, hierarchical clustering analysis and enrichment analysis using gene ontology (GO) terms were performed.

Results: From the comparison of post- vs. pre-treatment of TOF, BAR and TCZ, the 120, 62 and 193 genes were selected as DEGs respectively. It seems to be discrete depending on the treatment, because overlapped genes were only 1.0% in up-regulated and 5.7% in down-regulated genes. The hierarchical clustering with expression profiles of these DEGs showed major 4 clusters. 92.3% of TCZ and 70% of BAR cases were segregated into 1st and 3rd clusters respectively, while those of TOF cases fell into 2nd and 4th clusters. Disparate GO terms were enriched in each DEGs group. For example, genes relevant to viral defense including ‘response to type I interferon (IFN)’ were suppressed in TOF group. Meanwhile, down regulation of genes involved in phosphorylation process including ‘IL-7 signaling’ seemed to be significant in BAR group. It is noteworthy that terms related to wound healing such as ‘platelet activation’ were enriched in the down-regulated genes of TCZ group.

Conclusion: It is speculated that the downstream biological cascade for TOF, BAR and TCZ treatment might be shared, as IL-6 signaling is mediated by JAK1/JAK2/TYK2 activation. However, the influence of these treatments over the transcriptome in the peripheral blood seems to be disparate. Enrichment analysis using GO terms also indicated that different biological processes were involved in the effect of each treatment. Our findings will support a rationale for switching each other if one of these treatments resulted in lack of efficacy. An increased risk of herpes zoster by a treatment with JAK inhibitors has been well recognized. It makes sense because IFN signaling is also mediated by JAK/STAT pathway. On the other hand, we have experienced a case with exacerbation of skin ulcer during TCZ treatment despite the activity of RA was absolutely under control. It is accounted for by the suppression of genes involved in wound healing after TCZ treatment.

Disclosure: Y. Koyama, Eli-Lilly, 2, Mochida, 2, BMS, 8, Ayumi, 8, Chugai, 8, Ono, 8, Mitsubishi Tanabe, 8, Abbvie, 8, Eisai, 8; **Y. Sato**, None; **H. Iijima**, None; **M. Sakamoto**, None; **T. Higuchi**, None.

Abstract Number: 1226

Outcomes and Efficacy of Selective versus Automatic Switching from Etanercept to a Biosimilar in Inflammatory Arthritis Using Electronic Health Records from UK

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Biosimilars have been approved for the treatment of inflammatory arthritis and evidence from randomised controlled trials have demonstrated equivalent efficacy to biologics. Etanercept biosimilar, SB4, is licensed for use to treat inflammatory arthritis. While some patients may selectively switch from reference etanercept (ETN) to SB4 by a rheumatologist or rheumatology nurse specialist, others may be automatically switched, by pharmacy. Currently, it is the policy of one Health Board area in Wales to use SB4 in place of ETN and to automatically switch ETN patients to SB4. While in a neighboring Health Board area, patients are not automatically switched but can selectively switch or commence SB4 treatment.

Methods: Using electronic health records we will investigate the safety and efficacy of switching of ETN to SB4 in one health region (Automatic SB4 area), compared with selective use and switching in a neighboring health region (Selective SB4 area). Data from the Secure Anonymised Information Linkage (SAIL) databank in Wales, United Kingdom was used to create a retrospective cohort study using linked, general practitioner, hospital and rheumatology clinic records. Patients aged 18 years or over with diagnosis codes for Rheumatoid Arthritis (RA), Psoriatic Arthritis (PsA) or Ankylosing spondylitis (AS) and treated with SB4 were included. Data was included from 2014 to 2019 to coincide with the introduction of biosimilar therapies in UK clinical practice.

Table 1: Characteristics and treatment outcomes of SB4 treated patients at selective SB4 area compared to automatic SB4 use area.

	Selective SB4 area (n=55)	Automatic SB4 area (n=184)	Difference 95% (CI)
Female	60% (33)	57.6% (106)	2.4 (-12.5 to 16.3)
Age at diagnosis	38.7 (SD:14.9)	39.7 (SD:12.7)	1 (-5.0 to 3.0)
Disease duration	23.2 (SD:3.5)	23.5 (SD:11.8)	0.3 (-3.5 to 2.9)
BMI	25.6 (SD:5.2)	27.9 (SD:5.8)	2.3 (0.6 to 4.0)*
RA diagnosis	61.8% (34)	70.1% (129)	8.3 (-22.9 to 5.3)
PsA diagnosis	20% (11)	11.4% (21)	8.6 (-1.4 to 21.5)
AS diagnosis	23.6% (13)	19.6% (36)	4.1 (-7.2 to 17.8)
Previous Etanercept	12.7% (7)	33.2% (61)	20.5 (7.5 to 30)*
Previous biologics	18.2% (10)	41.8% (77)	23.6 (9.7 to 34.4)
Mean previous csDMARDs	4.3 (SD: 1.8)	4.0 (SD: 1.7)	0.3 (-0.2 to 0.8)
SB4 treatment failure	No failure	16.8% (31)	-
Time to treatment failure (days)	N/A	515.9 (SD: 319.7)	-
Mean DAS28 pre-SB4	4.4 (SD: 1.1)	4.6 (SD: 1.0)	0.2 (-1.2 to 0.8)
Mean DAS28 post-SB4	2.6 (SD: 1.3)	4.2 (SD: 1.2)	1.6 (0.4 to 2.8)*
Difference in DAS28 score pre-and post-SB4	1.8 (SD: 1.5)	0.4 (SD: 0.8)	1.4 (0.4 to 2.4)*
Mean reduction in GP visits post-SB4	45 (SD: 46.9)	20.8 (SD: 75.5)	24.2 (19.1 to 45.4)*

*p=<0.05

Results: There were 239 patients with inflammatory arthritis treated with SB4 included in the study (Table 1). The majority of the patients had RA. In the automatic switching area, 184 patients were treated with SB4, compared to 55 in selective use area, where most patients were biologic naïve (45/55). Here, 7 of these patients (12.7%) were selectively switched from ETN to SB4 (Table 1). In the automatic switching area, 61 out of 181 (33.2%) were automatically switched; the remaining patients would have automatically commenced SB4 in place of reference ETN. Following treatment with SB4, the DAS28 reduced by 1.8 ± 1.5 in the selective SB4 area compared to a reduction of 0.4 ± 0.8 in the automatic SB4 area. This confirmed patients were switched from sTable disease. The GP visits were reduced in both selective (45 ± 46.9) and the automatic SB4 area (20.8 ± 75.5). The GP visit reduction was significantly larger in patients from the selective area compared to automatic area (difference 24.2 visits, 95% CI: 3.0 to 45.4).

Sensitivity analyses compared changes in DAS28 scores pre- and post-SB4 treatment between biologic naïve and biologic experienced SB4 patients. No significant difference was found in the change in DAS28 scores between biologic naïve and biologic experienced SB4 patients (difference 0.1, 95% CI: -1.2 to 1.4).

Conclusion: SB4 was effective in etanercept naïve patients. Automatically switching did not lead to disease worsening significant. Furthermore, treatment with SB4 reduced healthcare utilisation of patients, as measured by GP visits, whether automatically or selectively treated with the drug.

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Abstract Number: 1227

Reduction in Peripheral CD19^{+} CD27^{-} Naïve B Cells Is Associated with Clinical Remission in Patients with Rheumatoid Arthritis Receiving Combined Treatment with Methotrexate and TNF Inhibitors

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

Background/Purpose: Biological therapies, as TNF inhibitors (TNFi) are increasing remission rates in rheumatoid arthritis (RA) patients although these are still limited. This study aims to explore whether TNFi modulate peripheral blood mononuclear cells (PBMC) after 6 months (m) of treatment and to identify a cellular profile associated with clinical remission (REM) in patients with RA.

Baseline patients' characteristics	Total patients (n=78)	DAS28>2.6 (n=49; 63%)	DAS28≤2.6 (n=29; 37%)	p-value
Age (years)	54±12	55±13	51±11	0.1
Female	67 (86)	43 (88)	24 (83)	0.5
Disease duration (years)	6 (3-11)	8 (4-12)	6 (3-10)	0.7
RF positive	60 (77)	35 (71)	25 (86)	0.1
ACPA positive	65 (83)	38 (78)	27 (93)	0.07
Smoking habit (n=64)				0.4
Non-smokers	29 (45)	19 (50)	10 (38)	
Smoker	35 (55)	19 (50)	16 (62)	
Body mass index (kg/m2)	25.4 (22.8-30.2)	25.6 (23.0-30.2)	24.7 (22.4-30.4)	0.6
DAS28	4.9±1.0	5.3±0.9	4.2±0.9	**<0.001**
Concomitant csDMARDs	75 (96)	48 (98)	27 (93)	0.7
MTX [±OD]	58 (74)	39 (80)	19 (68)	0.2
Only OD	17 (22)	9 (18)	8 (25)	0.2
Prednisone	45 (58)	30 (61)	15 (54)	0.5

Methods: A prospective and observational bi-center study including 78 patients with RA treated with standard doses of their first TNFi and followed-up during 6m was carried out. All included patients fulfilled the ACR/EULAR 2010 classification criteria for RA, were adults, with moderate or high disease activity (DAS28 >3.2). PBMC were analysed by flow-cytometry at the baseline and 6m. Clinical activity at baseline and after 6m was assessed by DAS28, establishing DAS28≤2.6 as the criteria for REM. Depending on data distribution, comparisons were conducted using unpaired t, Mann-Whitney U or Fisher's exact tests. The association between REM and the percentage of change (Δ, 6m-0m) within each PBMC subset was evaluated by uni- and multi-variable logistic regression. The presence of interactions with covariates (age, sex, disease duration, RF, ACPA, smoking habit, body mass index, baseline DAS28 and concomitant methotrexate (MTX)) was tested, stratifying the results if this was significant ($p< 0.05$). In case of no interaction, the model was later adjusted for these covariates.

Results: After 6m of TNFi treatment, 37% patients achieved REM. Univariable analyses (odds ratio; 95% CI; p-value) were performed to investigate the association between REM and the baseline variables. A significant association was found for lower baseline DAS28 (OR: 0.28; 95% CI: 0.19-0.51; $p< 0.001$). Associations of REM with other baseline patients' characteristics, such as for age (OR: 0.97; 95% CI: 0.94-1.01; p=0.1), RF positivity (OR: 2.50; 95% CI: 0.73-8.50; p=0.1) and ACPA positivity (OR: 3.91; 95% CI: 0.80-19.07; p=0.09), were found, although not significant. Therefore, further analyses were adjusted by age, RF, ACPA and baseline DAS28. In addition, a significant association were found for reducing the percentage of naïve B cells (OR: 0.85; 95% CI: 0.73-0.99; p=0.04). A significant interaction between the change in the percentage of naïve B cells and the use of concomitant MTX was identified (Wald chi-square value=4.56; p=0.03), for the outcome of achievement of REM. Therefore, further analyses about the association between the change in the percentage of naïve B cells and REM were stratified according to the use of concomitant MTX. No significant interactions with other variables were found.

A reduction in the percentage of naïve B cells after 6m of TNFi treatment was associated with achieving REM, mainly in patients who received concomitant MTX (OR: 0.58; 95% CI: 0.38-0.90; p=0.015). However, no association was found for patients who did not received concomitant MTX (OR: 0.78; 95% CI: 0.45-1.35; p=0.4).

Conclusion: A reduction of naïve B cells was associated with the achievement of REM by TNFi therapy, mainly in patients who received concomitant methotrexate. Our results suggest that naïve B cells may be useful as a marker of REM in patients with RA cotreated with TNFi and MTX.

Baseline characteristics of patients included in the study, stratified by remission at 6 months of TNFi treatment The Table shows mean±SD, median (IQR) or absolute number (percentage) for all patients included (n=78). RF, rheumatoid factor; ACPA, anti-citrullinated protein antibodies; DAS28, Disease Activity Score-28; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; MTX, methotrexate; OD, other conventional synthetic disease-modifying anti-rheumatic drugs than methotrexate. The differences between groups were analysed considering p-value<0.05 as statistically significant result.

Disclosure: B. Hernandez-Breijo, None; **C. Plasencia**, None; **V. Navarro-Compán**, Novartis Pharma, 1, 5, 8, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, UCB, 5, 8; **I. Nieto-Gañán**, None; **C. Sobrino**, None; **A. Martínez-Feito**, None; **C. García-Hoz**, None; **P. Lapuente-Suanzes**, None; **J. Bachiller-Corral**, None; **G. Bonilla**, None; **C. Pijoán-Moratalla**, None; **G. Roy**, None; **M. Vázquez**, None; **A. Balsa**, BMS, 9; **L. Villar**, None; **D. Pascual-Salcedo**, None; **E. Rodríguez-Martín**, None.

Abstract Number: 1228

Baricitinib 2-mg Provides Greater Improvements in Patient-Reported Outcomes Across All Disease Activity Levels Compared to Placebo: Post-hoc Analyses of RA-BEACON and RA-BUILD Trials

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
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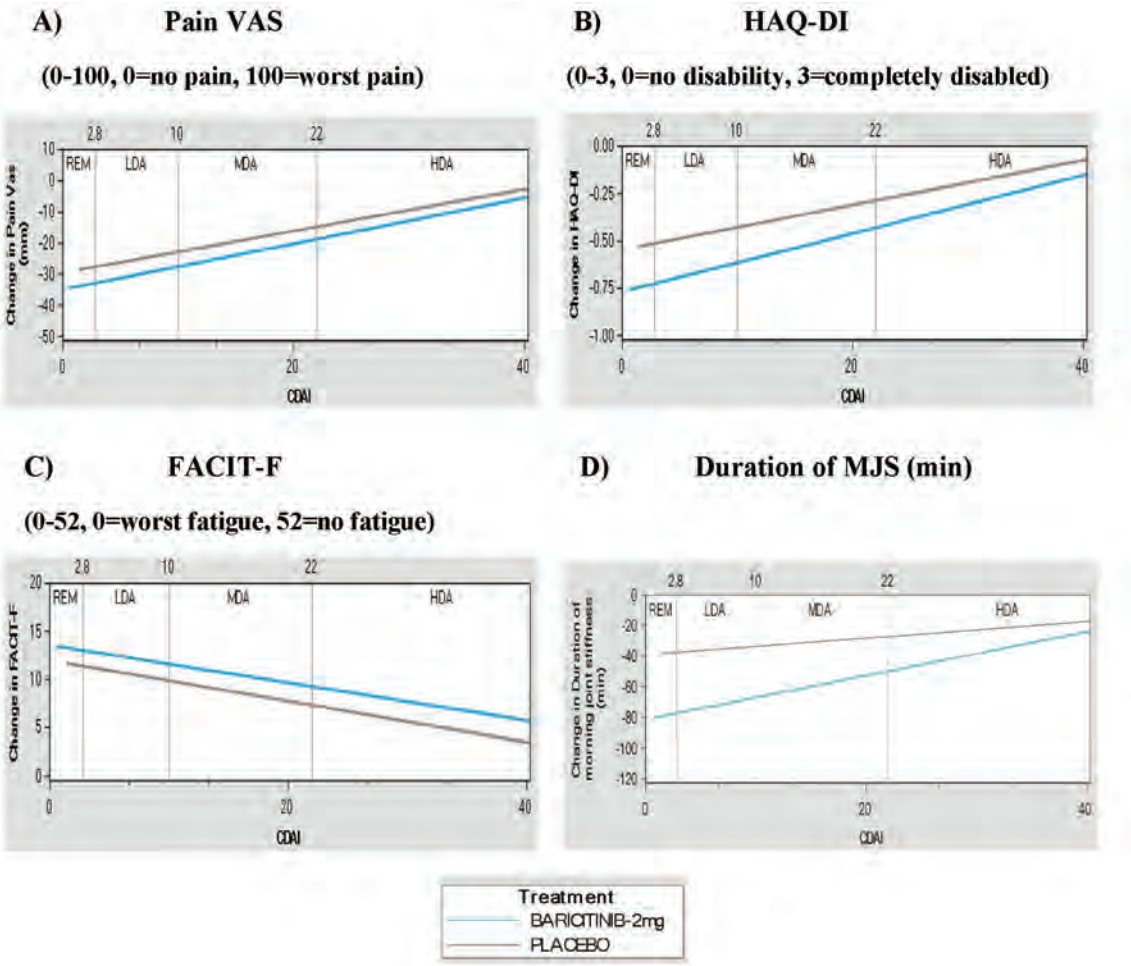
Background/Purpose: Baricitinib (BARI) improved patient-reported outcomes (PROs) in patients with insufficient response or intolerance to ≥1 tumor necrosis factor inhibitors (TNFi) or other biological disease-modifying antirheumatic drugs (bDMARDs) as well as in patients with inadequate response (IR) to conventional synthetic DMARDs (csDMARDs).[1,2] The purpose of this analysis was to determine the association between improvement in PROs (pain, physical function, fatigue, and morning joint stiffness) and disease activity (measured using Clinical Disease Activity Index [CDAI] at 12 weeks. We evaluated whether BARI 2-mg provided greater PRO improvement compared to placebo (PBO), across all levels of disease activity.

Methods: Data for these post-hoc analyses were taken from two phase 3 studies, RA-BEACON (NCT01721044; bDMARD-IR patients) and RA-BUILD (NCT01721057; csDMARD-IR patients). Pain was assessed on a 0-100 mm visual analog scale; physical function was assessed using the Health Assessment Questionnaire-Disability Index (HAQ-DI); and fatigue was measured using the Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) scale. Duration of morning joint stiffness (MJS, minutes) was also reported by the patient. Disease activity was assessed with the Clinical Disease Activity Index (CDAI) and categorized as: remission (≤2.8), low disease activity (LDA; >2.8 to ≤10), moderate disease activity (MDA; >10 to ≤22), high disease activity (HDA; >22). To evaluate the extent of benefit in PROs with BARI across disease activity levels at Week 12 relative to PBO, we used linear regression to model the relationship between change in PROs at Week 12 (response), and CDAI values at Week 12 (primary explanatory variable). Two additional variables included were treatment group and the interaction term between treatment and CDAI. We used last observation carried forward to impute missing values.

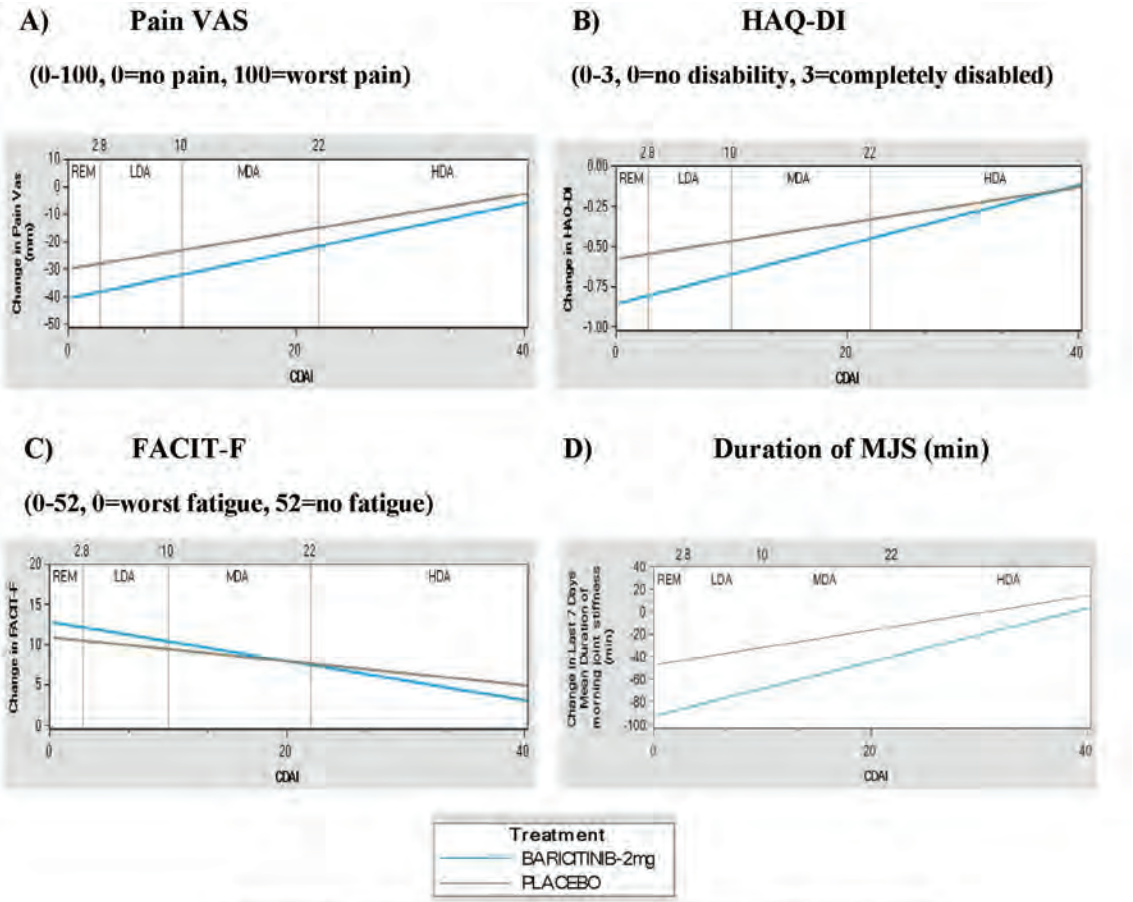


Estimated Changes at Week 12 (Mean)	CDAI=2.8		CDAI=10		CDAI=22	
	PBO	BARI 2-mg	PBO	BARI 2-mg	PBO	BARI 2-mg
Pain-VAS	-27.6	-32.8	-22.7	-27.5	-14.7	-18.7
HAQ-DI	-0.5	-0.7	-0.4	-0.6	-0.3	-0.4
FACIT-F	11.4	13.0	9.9	11.6	7.3	9.3
Duration of MJS (min)	-37.5	-77.6	-33.7	-67.3	-27.2	-50.0

BARI=Baricitinib; bDMARD-IR= biological disease-modifying antirheumatic drugs (bDMARDs)-inadequate response. CDAI=Clinical Disease Activity Index; FACIT-F= Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI=Health Assessment Questionnaire-Disability Index; HDA=High disease activity; LDA=Low disease activity; MDA=Moderate disease activity; MJS=Morning joint stiffness; PBO=Placebo; REM=remission; PROs=patient-reported outcomes; VAS=Visual Analog Scale, min=minutes

Figure 1. Estimated changes in PROs by CDAI disease activity at Week 12 in RA-BEACON (bDMARD-IR) trial. A) Pain VAS, B) HAQ-DI, C) FACIT-F, D) Duration of MJS.

Results: At 12 weeks in bDMARD-IR patients, BARI 2-mg demonstrated greater improvements in pain, physical function, fatigue and MJS duration across all disease activity levels vs. placebo group (Figure 1). In csDMARD-IR patients, BARI 2-mg provided greater improvement in PROs (pain, HAQ-DI, MJS and fatigue) for patients who achieved disease control (remission or LDA) compared to placebo group. Greater reduction in pain and MJS duration were also observed in BARI 2-mg patients with MDA or HDA relative to placebo (Figure 2).



Estimated Changes at Week 12 (Mean)	CDAI=2.8		CDAI=10		CDAI=22	
	PBO	BARI 2-mg	PBO	BARI 2-mg	PBO	BARI 2-mg
Pain-VAS	-28.0	-38.3	-23.1	-32.0	-14.9	-21.6
HAQ-DI	-0.5	-0.8	-0.5	-0.7	-0.3	-0.5
FACIT-F	10.5	12.2	9.4	10.4	7.6	7.5
Duration of MJS (min)	-43.1	-85.7	-32.0	-68.5	-13.6	-39.9

BARI=Baricitinib; CDAI=Clinical Disease Activity Index; csDMARD-IR= conventional synthetic disease-modifying antirheumatic drugs -inadequate response; FACIT-F= Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI=Health Assessment Questionnaire-Disability Index; HDA=High disease activity; LDA=Low disease activity; MDA=Moderate disease activity; MJS=Morning joint stiffness; PBO=Placebo; REM=remission; PROs=patient-reported outcomes; VAS=Visual Analog Scale

Figure 2. Estimated changes in PROs by CDAI disease activity at Week 12 in RA-BUILD (csDMARD-IR) trial. A) Pain VAS, B) HAQ-DI, C) FACIT-F, D) Duration of MJS.

Conclusion: BARI 2-mg provided greater improvements in pain, physical function, fatigue and MJS duration across all levels of disease activity in bDMARD-IR patients and csDMARD-IR patients who achieved remission or LDA. Greater reduction in pain and MJS duration were also observed in csDMARD-IR patients with MDA or HDA at Week 12.

References:

1. Smolen et al. *Ann Rheum Dis.* 2017;76(4):694-700.
2. Emery et al. *RMD Open*. 2017;3(1):e000410.

Disclosure: C. Bingham III, Bristol-Myers Squibb, 2, 5, 8, Genetech, 5, 8, Sanofi, 5, 8, AbbVie, 5, Eli Lilly, 5, Pfizer, 5, Gilead Sciences, Inc., 5, Regeneron, 5; **B. Jia**, Eli Lilly and Company, 1, 3; **J. Wu**, Eli Lilly and Company, 1, 3; **A. Quebe**, Eli Lilly & Co., 1, 2; **C. Kannowski**, Eli Lilly and Company, 1, 3; **S. Otawa**, Eli Lilly and Company, 1, 3; **Y. Chen**, Eli Lilly and Company, 1, 3; **K. Griffing**, Eli Lilly and Company, 1, 3; **D. He**, None; **D. Sholter**, None.

Abstract Number: 1229

Blood Lymphocyte Subsets for Early Identification of Non-Remission to TNF Inhibitors in Rheumatoid Arthritis

Eulalia Rodriguez-Martín[1], Israel Nieto-Gañán[1], Borja Hernández-Breijo[2], Cristina Sobrino[3], Carlota García-Hoz[1], Javier Bachiller-Corral[4], Ana Martínez-Feito[5], Victoria Navarro-Compán[6], Paloma Lapuente-Suanzes[1], Gema Bonilla[7], Dora Pascual-Salcedo[8], Garbiñe Roy[1], Teresa Jurado[2], Pilar Nozal[2], Mónica Vázquez[4], Alejandro Balsa[7], Luisa M Villar[1] and Chamaida Plasencia[7], [1]Hospital Universitario Ramón y Cajal-IRYCIS, Madrid, Spain, [2]Hospital Universitario La Paz-Idipaz, Madrid, Spain, [3]Hospital Ramón y Cajal-IRYCIS, Madrid, Spain, [4]Rheumatology, Hospital Universitario Ramón y Cajal, Madrid, Spain, [5]Hospital Unversitario La Paz- idipaz, Madrid, Spain, [6]Hospital Universitario La Paz IdiPaz, Madrid, Pais Vasco, Spain, [7]Rheumatology, La Paz University Hospital-IdiPAZ, Madrid, Spain, [8]Hospital Universitario La Paz-Idipaz, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: TNF inhibitors (TNFis) are widely used for the treatment of rheumatoid arthritis (RA), although the response rates to this therapy in patients with RA remains heterogeneous and less than 50% achieve remission (REM).

Our aim was to analyze baseline peripheral blood leukocytes profiles in order to search for biomarkers identifying patients who will most likely not achieve REM under TNFi treatment.

Methods: A prospective bi-center pilot study including 98 RA patients treated with TNFis and followed-up during 6 months. Patients were classified according to DAS28 as follows: those who achieved REM (DAS28≤2.6) and those who did not (DAS28 >2.6) at 6 months after starting TNFis. These rates were also assessed by simplified disease activity index (SDAI ≤3.3 and SDAI >3.3, respectively). Peripheral blood immune cells were studied by flow cytometry before treatment initiation.

Results: At 6 months, 61% or 80% of patients did not achieve REM by DAS28 or SDAI, respectively. Basal leukocyte profiles differed between REM versus non-REM patients. Non-REM patients showed lower percentages of total and naïve B cells at baseline than REM subjects. A B lymphocyte/CD4+ lymphocyte ratio (BL/CD4 ratio) < 0.2 clearly associated with a higher probability of non-REM status based on DAS28 at 6 months (OR=9.2, p=0.006). These data were confirmed when patient response was evaluated by SDAI index.

Conclusion: Our results strongly suggest that BL/ CD4 ratio could be considered as a useful biomarker for the early identification of non-remitters to TNFi in clinical practice.

Disclosure: E. Rodriguez-Martín, None; **I. Nieto-Gañán**, None; **B. Hernández-Breijo**, None; **C. Sobrino**, None; **C. García-Hoz**, None; **J. Bachiller-Corral**, None; **A. Martínez-Feito**, None; **V. Navarro-Compán**, Novartis Pharma, 1, 5, 8, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, UCB, 5, 8; **P. Lapuente-Suanzes**, None; **G. Bonilla**,

None; **D. Pascual-Salcedo**, None; **G. Roy**, None; **T. Jurado**, None; **P. Nozal**, None; **M. Vázquez**, None; **A. Balsa**, BMS, 9; **L. Villar**, None; **C. Plasencia**, None.

Abstract Number: 1230

Curcumin: Prevalence and Perceived Efficacy in the Treatment of Rheumatoid and Psoriatic Arthritis

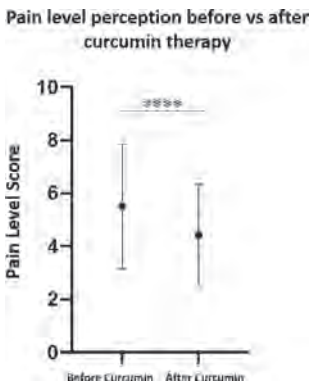
Neha Bhaskar[1], **Lilian Otalora Rojas**[2], Tara Jehu[1], Shazia Beg[1] and Neha Bhanusali[1], [1]University of Central Florida College of Medicine, orlando, [2]University of Central Florida HCA Healthcare GME, Orlando

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Ancient Eastern medicine has valued the Curcuma longa (turmeric) plant for its powerful medicinal properties. Curcumin is suggested to possess potent anti-inflammatory, antioxidant, antimicrobial, anticarcinogenic, and anticoagulant properties. There is currently no research relating symptom exacerbation or alleviation with curcumin therapy in patients with Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA). The focus of this study is on determining the prevalence and perceived efficacy of curcumin in RA and PsA populations.

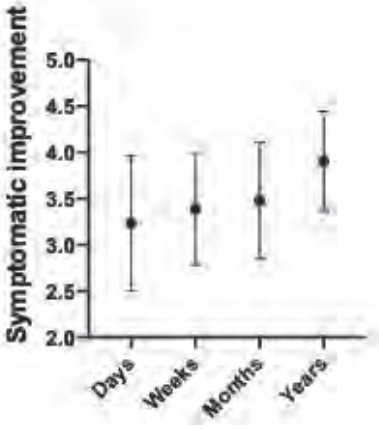
Methods: We conducted an observational, cross-sectional study of patients with active RA and PsA who visited a rheumatology outpatient clinic from October 2019 to March 2020. We used a voluntary, brief and anonymous Qualtrics survey questionnaire of concrete questions regarding curcumin use, source, form, method, and dosage, as well as patient perceptions of efficacy and any experienced side effects. Descriptive and correlation analyses were performed.

Results: A total of 291 patients were included. 84.9% RA, 5.1% PsA. 82.3% women and 17.7% men. 37.2% of patients reported having taken curcumin supplementation. No statistical differences between demographics (age, gender and diagnosis) were found in patients taking vs not taking curcumin. The majority of patients sourced the curcumin from a local store (54.3%), supplemented once a day (53.4%) in the form of capsules (59.2%), and took either 0-200 mg/day or 200-500 mg/day of Curcumin. Amongst those who chose not to supplement, the majority of patients reported potential side effects as being the main deterrent to supplementation.

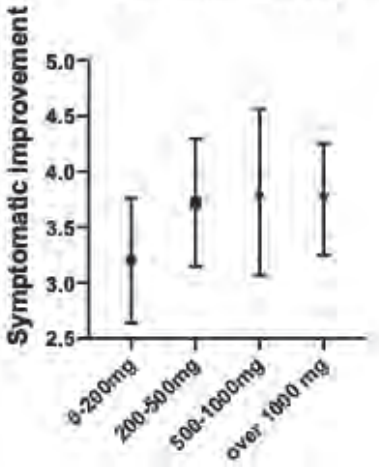


Statistically Significant difference between patient pain perception (scores from 1 to 10) reported before vs after Curcumin therapy. Paired t test (P <0.0001 r2 0.36).

Correlation between symptomatic improvement and duration of curcumin therapy



Correlation between symptomatic improvement and curcumin dosed



Pain scores were significantly decreased after curcumin therapy was started ($P < 0.0001$). Patients who were taking curcumin for years perceived improvement of symptoms (pain, swelling, stiffness, and fatigue) and better symptomatic control when compared with patients taking it for months (P 0.01), weeks (P 0.02) or days (P 0.02). There was a significant difference in symptom improvement in patients taking 200 to 1000 mg when compared with patients taking < 200 mg (P 0.01). Patients taking curcumin once or twice daily reported significant symptom improvement when compared with patients taking it rarely. Symptomatic improvement was reported as follows: pain (35.7%), swelling (25%), stiffness (23.21%) and fatigue (16.07%).

Conclusion: Patients with RA and PsA who were taking curcumin in the study population perceived associated improvement in pain and other symptoms. There is an interesting association between perception of symptomatic improvement in patients taking curcumin and treatment's frequency, dosages (200-1000mg), and length (years). These result suggest curcumin's efficacy for symptom alleviation in patients with RA and PsA.

Disclosure: N. Bhaskar, None; **L. Otalora Rojas**, None; **T. Jehu**, None; **S. Beg**, None; **N. Bhanusali**, None.

Abstract Number: 1231

Radiographic Outcomes in Patients with Rheumatoid Arthritis Receiving Upadacitinib as Monotherapy or in Combination with Methotrexate: Results at 2 Years

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

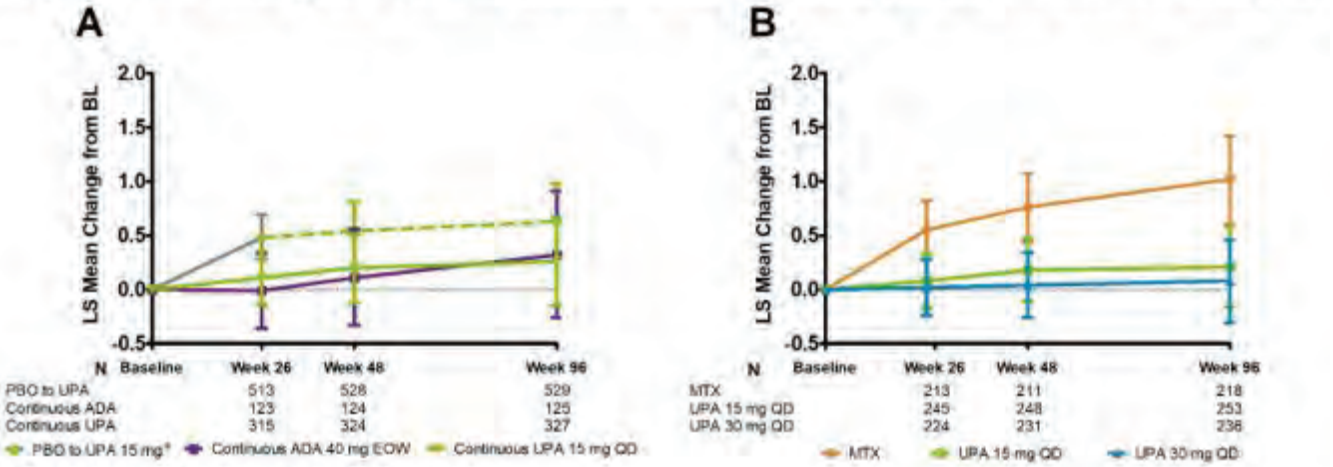
Session Time: 9:00AM–11:00AM

Background/Purpose: For patients with rheumatoid arthritis (RA), long-term prevention of structural joint damage is a key treatment goal.[1] In the SELECT-EARLY and SELECT-COMPARE trials, upadacitinib (UPA), an oral JAK inhibitor, inhibited the progression of structural joint damage at 6 months and 1 year when used either as monotherapy or in combination with methotrexate (MTX) in patients (pts) with active RA.[2] We describe the radiographic progression up to 2 years (96 wks) among pts with RA receiving UPA either as monotherapy or in combination with MTX.

Methods: Both the SELECT-EARLY and SELECT-COMPARE phase 3, randomized controlled trials enrolled pts at high risk for progressive structural damage with baseline (BL) erosive joint damage and/or seropositivity.[3,4] In SELECT-EARLY, MTX-naïve pts (N=945) were randomized to UPA 15 mg or 30 mg once daily (QD) or MTX monotherapy. In SELECT-COMPARE, pts with an inadequate response to MTX (N=1629) were randomized to UPA 15 mg, placebo (PBO), or adalimumab (ADA) 40 mg every other wk, with all pts continuing background MTX; at wk 26, all pts receiving PBO were switched to UPA 15 mg, regardless of response. In both trials, mean changes from BL in modified Total Sharp Score (mTSS), joint space narrowing, and joint erosion as well as the proportion of pts with no radiographic progression (change in mTSS $\leq$0) were evaluated based on X-rays taken at wks 24/26, 48, and 96 for those patients in whom wk 96 X-rays were available. Data are reported as observed (AO).

Results: BL demographics have been reported previously.[3,4] In the SELECT-EARLY study, at wk 96 UPA monotherapy (15 mg and 30 mg doses) significantly inhibited radiographic progression compared with MTX as measured by mean change in mTSS and by the proportion of patients with no radiographic progression (**Figures 1 and 2**). When patients who were rescued (MTX added to UPA or UPA added to MTX) were removed from the analysis, changes in mTSS from baseline remained similar. By the same measures, in SELECT-COMPARE, the degree of inhibition of structural progression observed was comparable between UPA and ADA. Following the switch of all PBO patients to UPA, the rate of progression slowed and was comparable to that observed in pts receiving UPA from BL. Among pts from both studies that had no radiographic progression at wk 24/26, >90% remained without radiographic progression at wk 48 and 96.

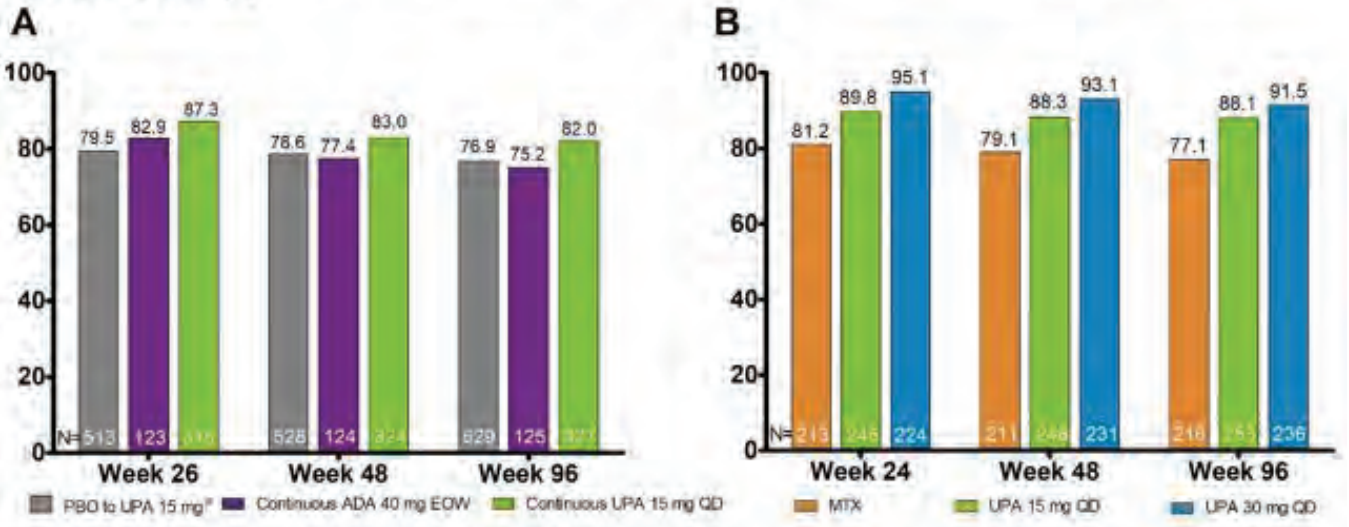
Figure 1. Mean Change in mTSS from Baseline in SELECT-COMPARE (A) and SELECT-EARLY (B)



*Per study design, all patients in the PBO group who were not previously rescued were switched to UPA 15 mg at wk 26.

Least squares mean estimator is based on an ANCOVA model with treatment and prior bDMARD (SELECT-COMPARE) or geographic region (SELECT-EARLY) as fixed factors and baseline value as a covariate. Error bars represent 95% confidence interval.

Figure 2. Proportion of Patients with No Radiographic Progression in SELECT-COMPARE (A) and SELECT-EARLY (B)



*Per study design, all patients in the PBO group who were not previously rescued were switched to UPA 15 mg at wk 26.

Conclusion: UPA was effective in inhibiting the progression of structural joint damage through 2 years both in MTX-naïve patients receiving UPA monotherapy and MTX-inadequate responder patients receiving UPA in combination with MTX.

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1. Smolen, et al. *Ann Rheum Dis* 2017;76(6):960-77.
2. Peterfy, et al. *Ann Rheum Dis* 2019;78(suppl 2):369-370.
3. Fleischmann, et al. *Arthritis Rheumatol* 2019;71(11):1788-1800.

4. van Vollenhoven, et al. *Arthritis Rheumatol* 2018;70(suppl 10).
Original abs: *Ann Rheum Dis.* 2020; 79(S1):326.

Disclosure: C. Peterfy, AbbVie, 1, Acerta, 1, Amgen, 1, 2, Astra Zeneca, 1, Bristol-Myers Squibb, 1, Centrexion, 1, Daiichi Sankyo, 1, Five Prime Therapeutics, 1, Genentech, 1, Gilead, 1, Hoffman-La Roche, 1, Janssen, 1, Lilly, 1, Medimmune, 1, Merck & Co, 1, Myriad, 1, Novartis, 1, Plexxikon, 1, Pfizer, 1, Sanofi, 1, Salix Santarus, 1, Samsung, 1, Samumed, 1, Setpoint, 1, Sorrento, 1, UCB, 1, Vorso, 1, Spire Sciences, 1, 2, 3; **V. Strand**, AbbVie, 5, Amgen, 5, Celltrion, 5, Janssen, 5, Merck, 5, Novartis, 5, Regeneron, 5, Sanofi, 5, UCB, 5, Genentech/Roche, 5, GSK, 5, Pfizer, 5, Bayer, 5, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, Galapagos, 5, Lilly, 5, Gilead, 5, Samsung, 5, Servier, 5, Setpoint, 5, Arena, 5, AstraZeneca, 5, Horizon, 5, Ichnos, 5, Inmedix, 5, Sandoz, 5; **M. Genovese**, Abbvie, 2, 5, Eli Lilly and Company, 2, 5, Galapagos, 2, 5, Gilead Sciences Inc., 2, 5, Pfizer, 2, 5, EMD Merck Serono, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, RPharm, 2, 5, Sanofi-Genzyme, 2, UCB, 5, Amgen, 5; **A. Friedman**, AbbVie, 1, 2; **J. Enejosa**, AbbVie, 1, 2; **S. Hall**, AbbVie, 1, 2, Bristol-Myers Squibb, 1, 2, Lilly, 1, 2, Janssen, 1, 2, Pfizer, 1, 2, UCB Pharma, 1, 2, Novartis, 1, 2; **E. Mysler**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sandoz, 2, 5; **P. Durez**, None; **X. Baraliakos**, AbbVie, 2, 5, Celgene, 2, 5, Galapagos, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 2, 5, Chugai, 2, 5, MSD, 2, 5, Sandoz, 2, 5, Hexal, 2, 5; **T. Shaw**, AbbVie, 1, 2; **Y. Song**, AbbVie, 1, 2; **Y. Li**, AbbVie, 1, 2; **I. Song**, AbbVie, 1, 3.

Abstract Number: 1232

Association of Low Hemoglobin with Efficacy and Patient-reported Outcomes in Three Phase III Studies of Sarilumab (TARGET, MOBILITY and MONARCH)

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Anemia is a common comorbidity in patients (pts) with RA, and changes in hemoglobin (Hb) levels are associated with changes in inflammatory disease activity. Since IL-6 is a central mediator and is known to impact iron metabolism/bioavailability it could contribute to anemia of chronic disease. We hypothesize that if IL-6 inhibition by sarilumab improves Hb levels, resulting in better clinical efficacy and patient-reported outcomes (PROs) in anemic RA pts vs comparators (placebo [PBO]+MTX or adalimumab), it might do so through its effects on Hb. In this *post hoc* analysis we assessed the association of low Hb level with clinical efficacy measures and PROs in 3 sarilumab phase III studies: TARGET (NCT01709578), MOBILITY (NCT01061736), MONARCH (NCT02332590).

Methods: Patients enrolled in MOBILITY and TARGET received either PBO or sarilumab 150 mg or 200 mg subcutaneously (SC) every 2 wks (q2w), in combination with MTX (52 wks) or in combination with weekly csDMARD (24 wks). Analysis used combination therapy pooled data from TARGET and MOBILITY through 24 wks. In MONARCH, pts received either adalimumab 40 mg or sarilumab 200 mg SC q2w monotherapy (24 wks). We evaluated mean changes

Table 1. Baseline demographics and disease characteristics of patients in the TARGET+MOBILITY pooled study group and MONARCH study group

	TARGET and MOBILITY pooled		MONARCH	
	Low Hb (N=600)	Normal Hb (N=1143)	Low Hb (N=92)	Normal Hb (N=277)
Age, years	50.1 (13.1)	52.0 (11.2)	50.0 (13.3)	53.0 (11.9)
Female, n (%)	515 (85.83)	909 (79.53)	78 (84.78)	229 (82.67)
BMI[a], kg/m^2	27.28 (6.53)	29.38 (6.60)	26.23 (7.05)	27.49 (5.66)
Duration of RA since diagnosis years	9.76 (8.69)	10.13 (8.40)	6.28 (7.33)	7.68 (8.18)
TJC28	16.33 (6.96)	15.67 (6.59)	16.70 (6.42)	16.69 (6.20)
SJC28	12.90 (5.97)	12.22 (5.61)	13.33 (5.77)	12.78 (5.50)
HAQ-DI (0-3)	1.76 (0.65)	1.64 (0.63)	1.73 (0.51)	1.61 (0.62)
CRP, mg/L	32.25 (29.28)	18.63 (19.56)	35.01 (35.04)	15.97 (21.46)
CDAI[b]	42.64 (13.08)	40.84 (12.29)	43.60 (12.90)	42.82 (11.75)
DAS28-CRP[c]	6.21 (0.93)	5.93 (0.87)	6.26 (0.94)	5.93 (0.85)
Pain VAS[c], mm	69.23 (20.05)	66.63 (20.71)	71.52 (17.85)	71.51 (19.11)
Morning stiffness VAS[d], mm	72.37 (22.04)	67.70 (23.13)	68.59 (20.54)	69.69 (20.17)
Prior RA medication use				
Opioid use, n (%)	90 (15.00)	144 (12.60)	13 (14.13)	25 (9.03)
Corticosteroid use, n (%)	374 (62.33)	722 (63.17)	52 (56.52)	150 (54.15)
NSAID use, n (%)	433 (72.17)	753 (65.88)	60 (65.22)	181 (65.34)
SSRI use, n (%)	17 (2.83)	52 (4.55)	1 (1.09)	4 (1.44)
Neutrophil count[e], 10^9/L, n (%)	6.25 (2.49)	6.00 (2.43)	5.72 (2.50)	5.62 (2.34)
GABA use, n (%)	10 (1.67)	15 (1.31)	1 (1.09)	2 (0.72)

N = Number of patients with low or normal Hb subgroup. All values are mean (SD), unless specified otherwise.

[a] TARGET+MOBILITY, N= 599 for "Low Hb" and N = 1142 for "Normal Hb"; MONARCH, N = 276 for "Normal Hb" group

[b]TARGET+MOBILITY, N= 599 for "Low Hb" and N = 1142 for "Normal Hb" group

[c]TARGET+MOBILITY, N = 1142 for "Normal Hb" group

[d]TARGET+MOBILITY, N = 186 for "Low Hb" and N=360 for "Normal Hb" group; MONARCH, N = 276 for "Normal Hb" group

[e]TARGET+MOBILITY, N=1137 for "Normal Hb" group; MONARCH, N = 276 for "Normal Hb" group

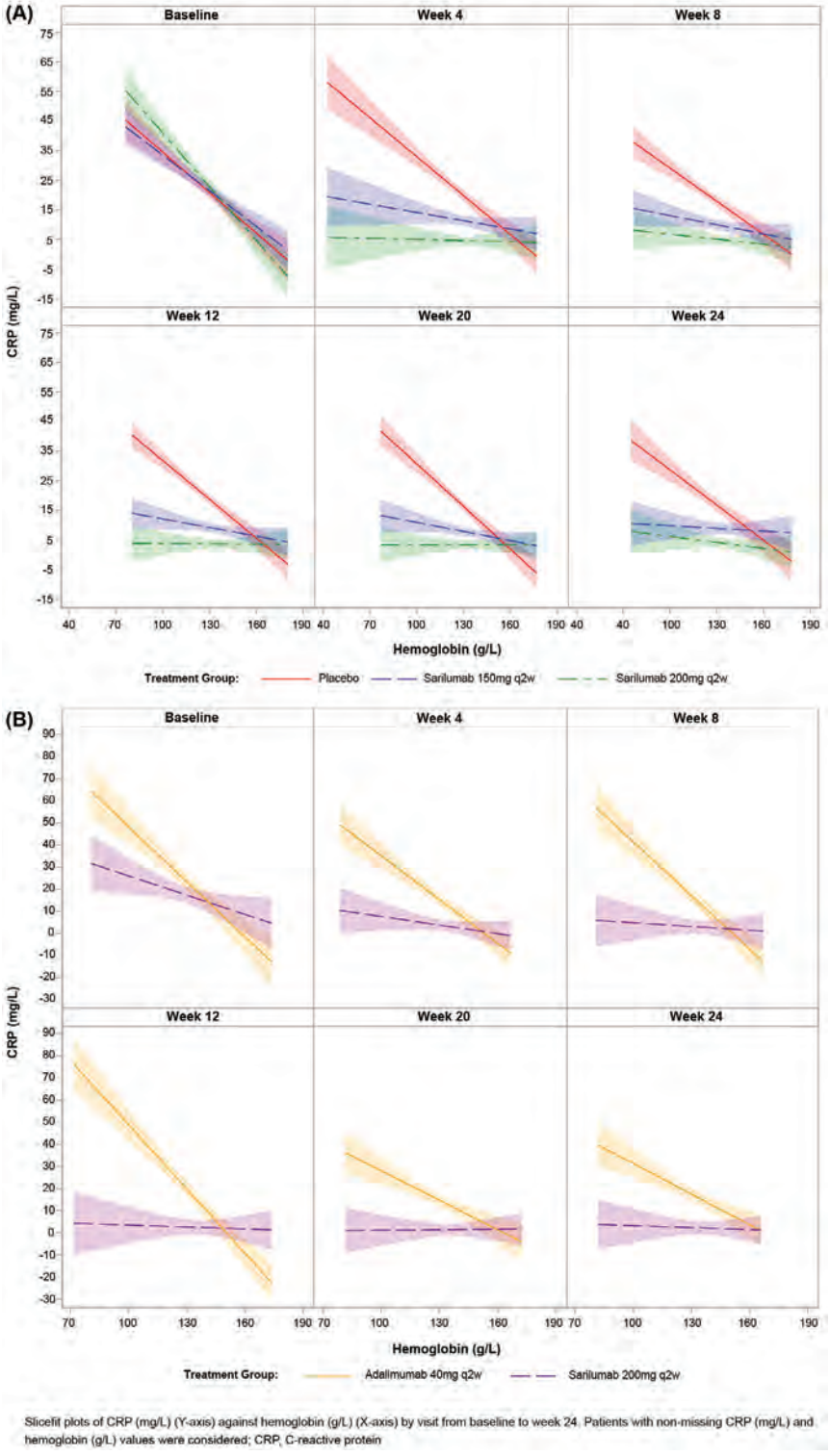
SD: Standard deviation, SE: Standard error, HAQ-DI: Health Assessment Questionnaire-Disability Index, TJC28: Tender joint count based on 28 joints, SJC28: Swollen joint count based on 28 joints, CRP: C-reactive protein, CDAI: Clinical Disease Activity Index, DAS28-CRP: Disease Activity Score 28-C-reactive protein, VAS: Visual analogue scale, NSAID: Nonsteroidal anti-inflammatory drug, SSRI: Selective serotonin reuptake inhibitors, GABA: Gamma-aminobutyric acid

from baseline to Wk 24 in Clinical Disease Activity Index (CDAI), CRP, 28-joint Disease Activity score-CRP (DAS28-CRP), pain visual analogue scale (VAS), patient global assessment (PtGA), stratified by Hb levels as low (Hb< 12.0 g/dL [females]/< 13.0 g/dl [males]) vs normal (Hb 12.0 to 15.5 g/dL[females]/13.5 to 17.5 g/dL [males]). Bivariate linear regression was performed to evaluate relationships between Hb level and outcomes from baseline to Wk 24. Mean change from baseline in efficacy measures and PROs were summarized as mean (SD) values.

Results: Low Hb was observed in 34% of pts in the pooled group (N = 1743, TARGET+MOBILITY) and in 25% of pts in the monotherapy group (N = 369, MONARCH). Baseline characteristics, demographics and concomitant medications were similar between groups (Table 1). Over 24 wks, higher Hb levels were associated with better clinical efficacy/pain outcomes in all evaluated study groups. Fig 1 shows a steady disassociation between Hb level and CRP in sarilumab-treated pts from baseline to Wk 24 in both study groups. A similar trend was also observed for other efficacy measures and PROs (data not shown). Mean change from baseline to Wk 24 in CDAI, DAS28 CRP, Pain VAS, PtGA

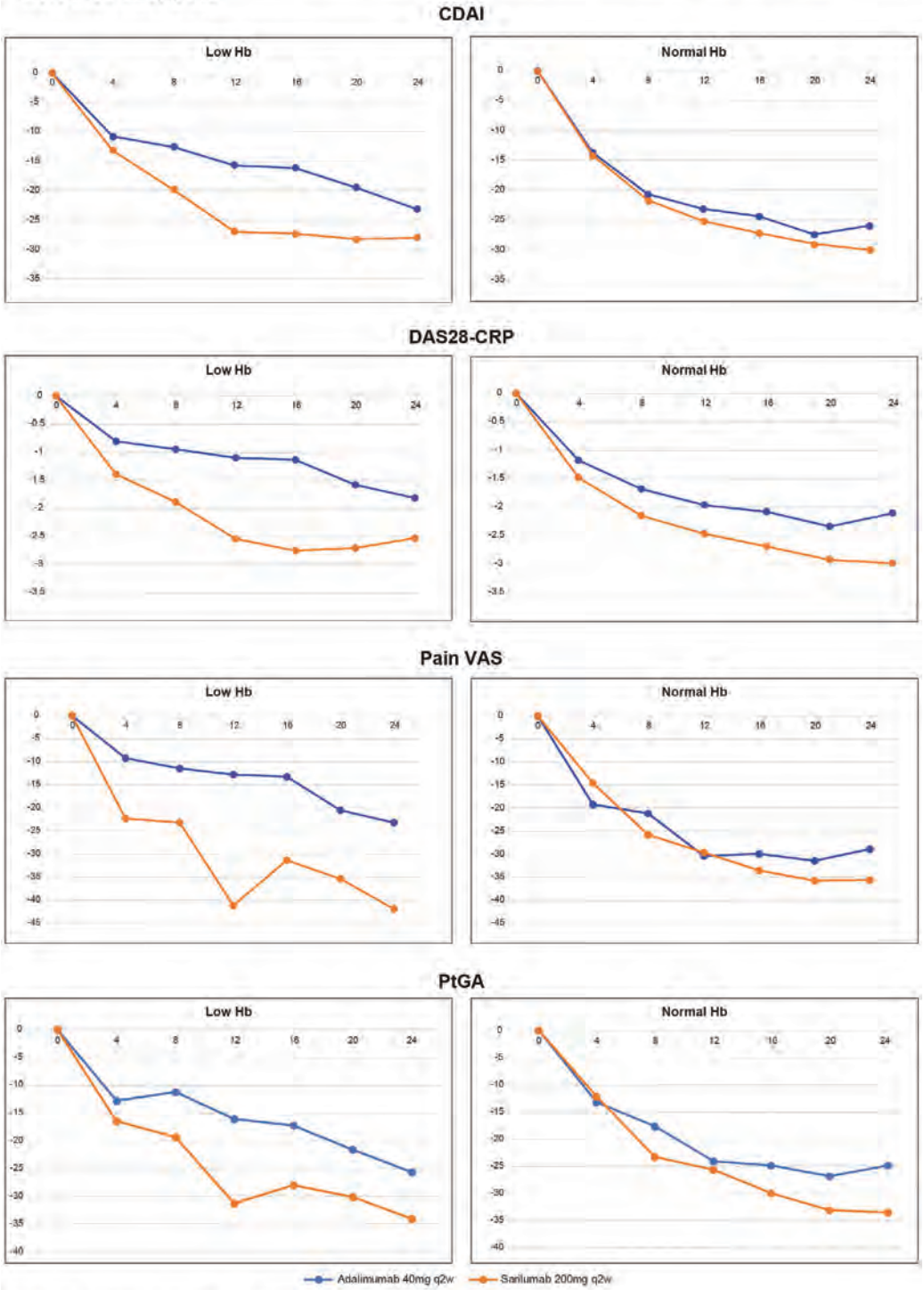
was similar in both groups, irrespective of the baseline Hb levels (low vs normal; Fig 2). Effect size (difference between sarilumab and adalimumab) was larger for low Hb subgroup, especially in MONARCH (Fig 2; combination therapy, data not shown). The safety profile of sarilumab has been previously reported and was not part of this analysis.

Figure 1: Relationship Between Outcomes and Hb Over Time (Baseline to Week 24): CRP **(A)** TARGET+MOBILITY B pooled and **(B)** MONARCH



Slicefit plots of CRP (mg/L) (Y-axis) against hemoglobin (g/L) (X-axis) by visit from baseline to week 24. Patients with non-missing CRP (mg/L) and hemoglobin (g/L) values were considered; CRP, C-reactive protein

Figure 2: Mean Change in Treatment Outcomes from Baseline to Week 24 (Stratified by Hb level at Baseline) - MONARCH study group



All values are represented as mean change from baseline (SD) till Week 24

CDAI, Clinical Disease Activity Index; CRP, C-reactive protein; DAS28-CRP, 28-joint Disease Activity using C reactive protein; Hb, hemoglobin; PtGA, patient-global assessment; SD, standard deviation; VAS, visual analogue scale.

Conclusion: In this analysis, by Week 24, in sarilumab-treated patients with low Hb levels, we observed better clinical efficacy measures and PROs than with adalimumab in the MONARCH Study. Furthermore, the positive effect of sarilumab was independent of the baseline Hb level (low vs normal). The observed dissociation indicates that the drug's efficacy is not 'solely' mediated by its effects on Hb.

Disclosure: A. Rubbert Roth, AbbVie, 1, Bristol-Myers Squibb, 1, Chugai Pharma, 1, 2, Eli Lilly, 1, 2, Hexal, 1, Novartis, 1, Sanofi, 1, 2, Roche, 1, 2, Pfizer, 1, Merck Sharp & Dohme (MSD), 1, Janssen, 1; **D. Furst***, Actelion, 1, 2, Amgen, 1, 2, BMS, 1, Corbus, 1, 2, Galapagos, 1, 2, GSK, 1, NIH, 1, Norvatis, 1, 2, Pfizer, 1, 2, Sanofi, 1, Roche/Genentech, 1, Gilead, 1, Horizon, 1, 2, Kadmon, 1, Talaris, 1, 2, CMC Connect (McCann Health Company), 8, Cytori, 5, AbbVie, 5; **S. Fiore**, Sanofi, 1, 3; **A. Praestgaard**, Sanofi, 3; **V. Bykerk**, Amgen, 2, 5, UCB, 5, National Institute of Health, 2, 9, Bristol-Myers Squibb Company, 2, 5, Gilead, 5, Pfizer, 5, Brainstorm Therapeutics, 1, 3; **C. Bingham III**, Bristol-Myers Squibb, 2, 5, 8, Genetech, 5, 8, Sanofi, 5, 8, AbbVie, 5, Eli Lilly, 5, Pfizer, 5, Gilead Sciences, Inc., 5, Regeneron, 5; **C. Charles-Schoeman**, AbbVie, 2, 5, Regeneron-Sanofi, 5, Gilead, 5, Bristol-Myers Squibb, 2, Pfizer Inc, 2, 5.

Abstract Number: 1233

Use of Multi-Biomarker Disease Activity Scores to Compare Biosimilar Adalimumab-afzb (PF-06410293) with EU-Sourced Reference Adalimumab in a Phase 3, Randomized, Double-Blind Trial in Patients with Active RA

Jonathan Kay[1], Amy Bock[2], Noriko Iikuni[3], Wuyan Zhang[4] and Daniel Alvarez[5], [1]University of Massachusetts Medical School, Worcester, MA, [2]Pfizer, Cambridge, MA, [3]Pfizer, New York, NY, [4]Pfizer, New York, [5]Pfizer, Collegeville, PA

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

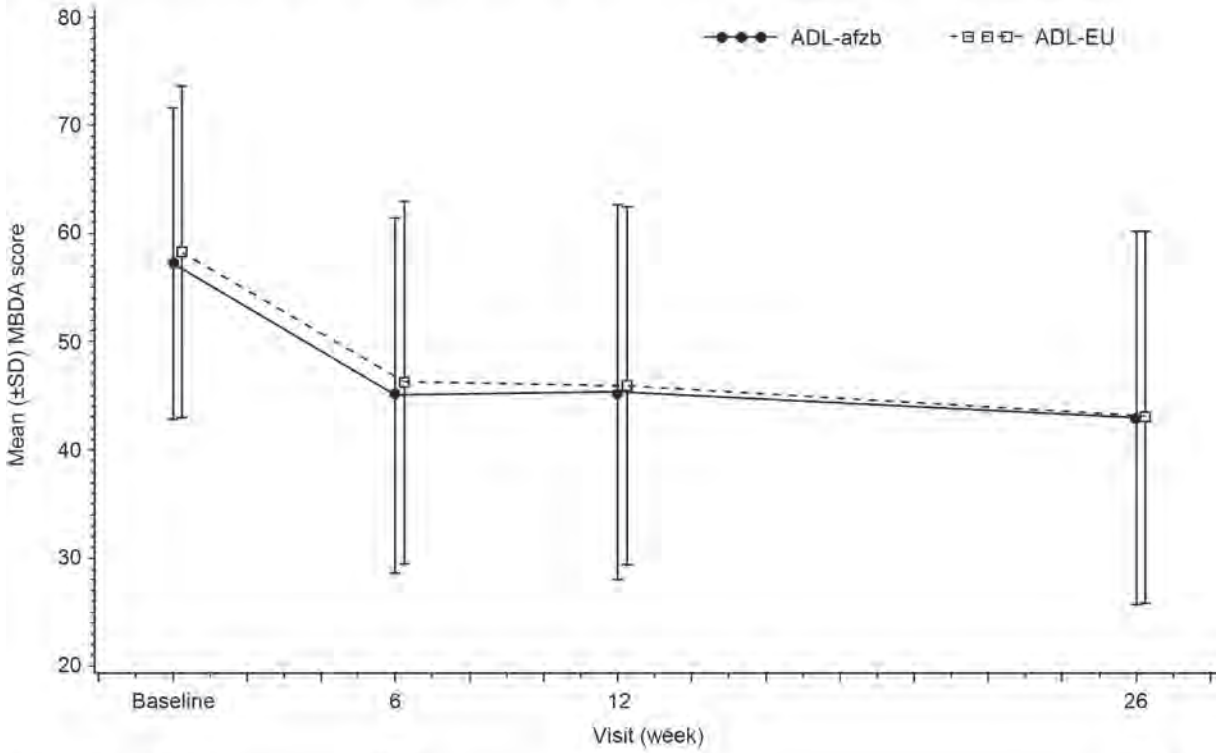
Session Time: 9:00AM–11:00AM

Background/Purpose: Traditional efficacy endpoints of disease activity (DA) in studies of anti-rheumatic drugs can be confounded by subjective (patient-/physician-reported) assessments, comorbidities, and pre-existing joint damage. Limitations of these efficacy endpoints have prompted regulatory authorities to encourage use of biomarkers as endpoints in clinical trials evaluating biosimilars. The multi-biomarker disease activity (MBDA; Vectra® DA, Myriad Genetics, Inc.) score provides a validated, objective, and composite measure of DA in patients with RA based upon concentrations of 12 serum protein biomarkers. An exploratory analysis was performed to compare MBDA scores between treatment groups in a randomized, double-blind trial to determine the utility of this approach as an assessment for biosimilarity. Biosimilar adalimumab-afzb (ADL-afzb; PF-06410293) was compared with reference adalimumab sourced from the European Union (ADL-EU; AbbVie Deutschland GmbH & Co KG, Ludwigshafen, Germany) in adult patients with active moderate to severe RA inadequately responsive to MTX (Fleischmann et al. *Arthritis Res Ther*. 2018;20:178).

Methods: All 597 patients in the study met the 2010 ACR/EULAR classification criteria for RA and had disease duration of ≥4 months. Patients were randomized 1:1 to ADL-afzb (n=297) or ADL-EU (n=300) (40-mg subcutaneously every other week) and continued to receive MTX. The concentrations of 12 biomarkers were measured and combined using the Vectra® DA algorithm. Mean MBDA scores (low, ≤29; moderate, 30–44; high, >44–100) were calculated at baseline and at weeks 6, 12, and 26. Mean MBDA scores were compared between treatment groups. Data were summarized using descriptive statistics in the intent to treat population.

Results: At baseline, mean (± standard deviation [SD]) MBDA scores for ADL-afzb and ADL-EU groups were 57.2 (± 14.44) and 58.3 (± 15.34), respectively. Mean values of MBDA scores were comparable between treatment groups at all measured time points through 26 weeks (**Figure**). Similar proportions of patients in the ADL-afzb (78.5%) and ADL-EU (81.7%) treatment groups had high MBDA scores (>44) at baseline; the proportions of patients with high MBDA scores decreased to 45.5% and 41.7%, respectively, at week 26. Mean MBDA scores decreased from baseline in the ADL-afzb and ADL-EU groups by 11.9 and 12.4 at week 6, by 11.7 and 12.4 at week 12, and by 14.3 and 15.5 at week 26, respectively. Mean log-transformed values for each of the individual 12 biomarkers over time up to week 26

Figure: MBDA scores over time up to week 26 (intent-to-treat population)[a]



[a] Baseline, last non-missing measurement taken on or before study day 1.

Table: Correlations between MBDA scores and hs-CRP (intent-to-treat population).

	Pearson's correlation coefficient (r)		
MBDA score vs hs-CRP[a]	**ADL-afzb**	**ADL-EU**	**Overall**
Baseline[b]	0.782	0.720	0.749
Change from baseline to week 12	0.809	0.733	0.770
Change from baseline to week 26	0.835	0.718	0.776

[a] hs-CRP (mg/L) log-transformed values.
[b] Baseline, last non-missing measurement taken on or before study day 1.

were consistently similar between ADL-afzb and ADL-EU groups. MBDA scores correlated with the high-sensitivity CRP (hs-CRP) assay results (**Table**).

Conclusion: Over 26 weeks, mean values for MBDA scores were similar between the ADL-afzb and ADL-EU groups throughout this randomized, double-blind trial in which the adalimumab biosimilar was compared with its reference product. MBDA score based on 12 serum biomarkers provides a sensitive and objective clinical assessment of biosimilarity that does not require physical examination of the patient or subjective patient global assessment of DA.

Disclosure: J. Kay, Pfizer Inc., 9, Alvotech Suisse AG, 1, Arena Pharmaceuticals, Inc., 1, Boehringer Ingelheim GmbH, 1, Celltrion Healthcare Co. Ltd., 1, Mylan Inc., 5, Novartis AG, 5, Samsung Bioepis, 5, Sandoz Inc., 5, Gilead Sciences, Inc., 9; **A. Bock**, Pfizer, 1, 2; **N. Iikuni**, Pfizer, 1, 3; **W. Zhang**, Pfizer, 1, 2, AbbVie, 1, Abbott, 1; **D. Alvarez**, Pfizer, 1, 2.

Abstract Number: 1234

Noninflammatory Pain Is a Frequent Phenomenon in Rheumatoid Arthritis and Responds Well to Treatment with Sarilumab

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammation is a key driver of pain in rheumatoid arthritis (RA). However, in some patients the level of pain exceeds what would be expected based on the amount of synovitis observed and acute phase reactants, which may indicate the presence of noninflammatory pain (NIP). Interleukin-6 (IL-6) has been shown in animal models to increase sensitization to pain and may play a role in NIP.

Methods: The analysis included data from three Phase 3 studies of sarilumab: MOBILITY (NCT01061736), MONARCH (NCT02332590), and TARGET (NCT01709578). Patients received double-blind placebo or sarilumab 150 mg or 200 mg subcutaneously (SC) every 2 weeks (q2w), plus weekly csDMARD (MOBILITY and TARGET), or adalimumab 40 mg or sarilumab 200 mg SC q2w as monotherapy (MONARCH). This analysis assessed the effect of sarilumab, a human IL-6 receptor inhibitor approved for the treatment of adults with moderate to severely active RA, on NIP and disease activity, stratified by baseline (BL) NIP status.

NIP was defined using an established formula: tender 28-joint count (TJC) – swollen 28-joint count (SJC) ≥7 [1,2]. Patients were assessed for NIP at study BL and for change in NIP status at Weeks 12 and 24. The proportion of patients achieving ACR20/50/70, Clinical Disease Activity Index (CDAI) ≤10, and DAS28-CRP < 3.2 at Week 24 was assessed in patients with and without BL NIP.

No inferential statistics were performed.

Results: Of 2112 patients in the analysis, 490 (23%) met the criteria for NIP at study BL: MOBILITY, n = 294/1197 (25%); MONARCH, n = 90/369 (24%); TARGET, n = 106/546 (19%). BL demographics were similar for patients with or

Table 1. Baseline characteristics

	Patients with TJC – SCJ ≥7	
Mean (SD)	Yes (n = 490)	No (n = 1622)
Duration of RA, years	9.1 (8.6)	9.7 (8.4)
TJC, 0–28	21.7 (4.7)	14.3 (6.2)
SJC, 0–28	10.7 (4.3)	13.1 (6.0)
CRP, mg/L	22.7 (27.0)	22.9 (24.0)
HAQ-DI, 0–3	1.8 (0.6)	1.7 (0.6)
DAS28-CRP	6.4 (0.7)	5.9 (0.9)
CDAI	46.0 (9.4)	40.4 (13.0)
Pain VAS	72.3 (18.2)	67.0 (20.7)

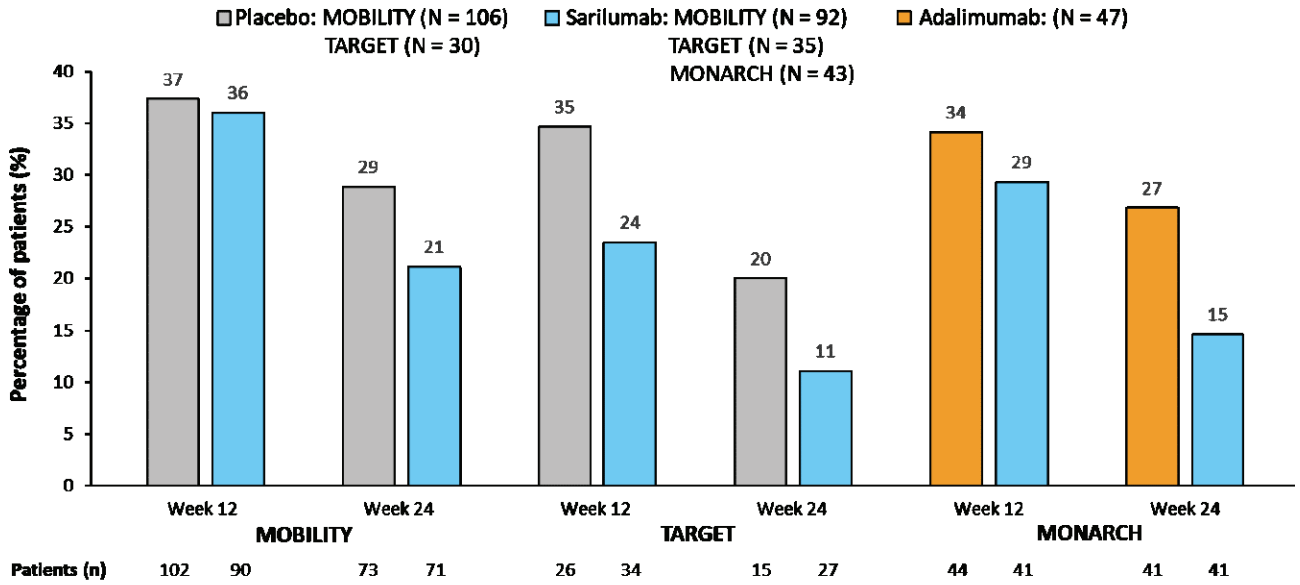

Figure 1 Percentages of patients with baseline noninflammatory pain who had noninflammatory pain at Weeks 12 and 24*

*For MOBILITY and TARGET, data are shown only for patients who received sarilumab 200 mg

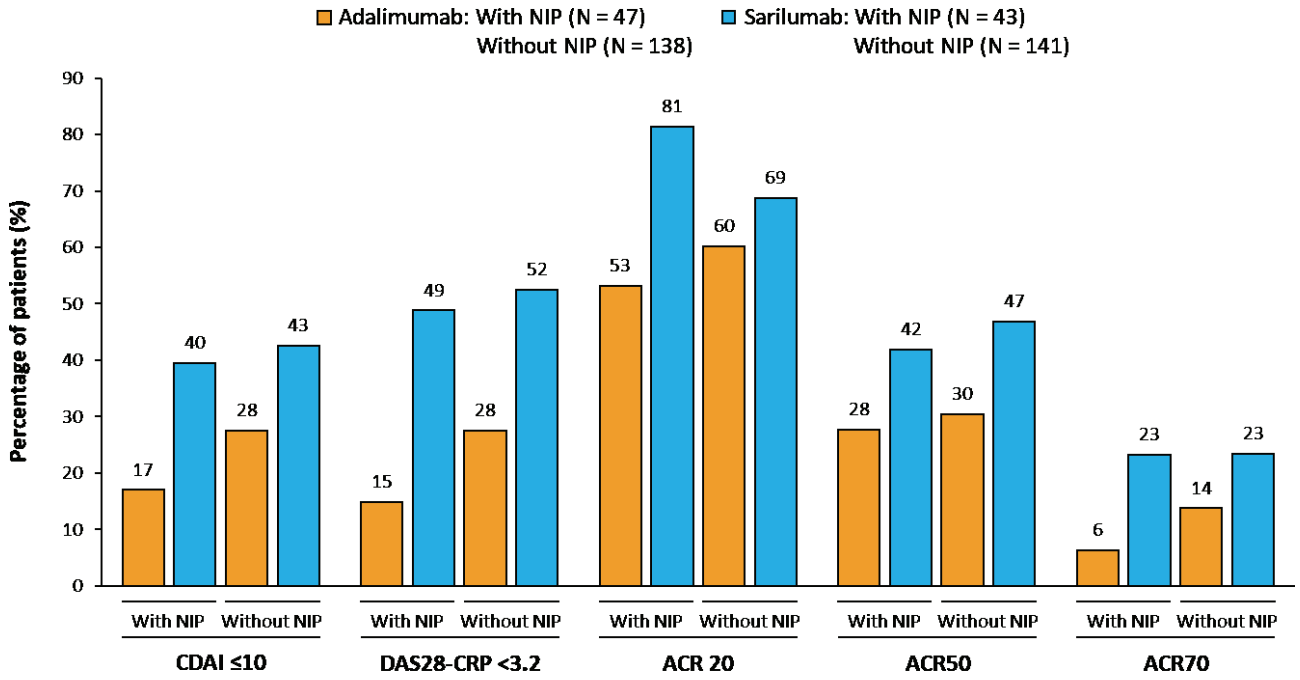

Figure 2 Percentages of sarilumab and adalimumab responders at Week 24 by baseline noninflammatory pain status

without BL NIP: mean age (SD) was 52.6 (10.7) versus 51.2 (12.3) years, and 85% versus 81% were female. Patients with BL NIP had higher CDAI, DAS28-CRP, pain Visual Analog Scale (VAS), and TJC at BL versus patients without NIP (**Table 1**). Of patients with NIP at BL, those who received sarilumab were more likely to have no NIP at Weeks 12 and 24 versus patients who received placebo or adalimumab (**Figure 1**). The percentage of patients achieving improvements in disease activity at Week 24 was greater for sarilumab versus adalimumab among both patients with and without BL NIP, and these differences were larger among patients with BL NIP for all assessments except ACR50 (**Figure 2**).

Conclusion: NIP was prevalent at BL in the patient populations assessed. Among patients with BL NIP, a lower proportion continued to have NIP at Weeks 12 and 24 when treated with sarilumab versus placebo or adalimumab. Patients with and without BL NIP had greater improvements in pain when treated with sarilumab versus adalimumab. The difference in clinical improvement was greater among patients with BL NIP versus without BL NIP for most measures. These trends support the emerging concept that mechanisms other than direct inflammation may contribute to pain in RA, potentially mediated via IL-6 signaling.

References:

1. Durán J et al. *Rheumatology*. 2015;54:2166–70
2. Pollard LC et al. *Rheumatology*. 2010;49:924–8

Disclosure: E. Choy, Abbvie, 2, 8, Amgen, 2, 8, AstraZeneca, 2, 8, Biogen, 2, 8, Bio-Cancer, 2, 8, Boehringer Ingelheim, 2, 8, Bristol-Myers Squibb, 2, 8, Celgene, 2, 8, Chugai Pharma, 2, 8, Eli Lilly, 2, 8, Ferring Pharmaceuticals, 2, 8, GlaxoSmithKline, 2, 8, Janssen, 2, 8, Novartis, 2, 8, Novimmune, 2, 8, ObsEva, 2, 8, Pfizer, 2, 8, R-Pharm, 2, 8, Roche, 2, 8, SynAct Pharma, 2, 8, Tonix, 2, 8, UCB, 2, 8, Synovate, 2, 8, Sanofi, 2, 8, Regeneron, 2, 8, Napp, 2, 8, Hospira, 2, 8, Merck Sharp & Dohme, 2, 8; **V. Bykerk**, Amgen, 1, 2, Bristol-Myers Squibb, 1, Gilead, 1, Pfizer, 1, Regeneron Pharmaceuticals, Inc., 1, Sanofi Genzyme, 1, Scipher, 1, UCB, 1, 2, Novartis, 1, National Institutes of Health (NIH), 1, Genetech, 1, Cedar Hill Foundation, 1; **Y. Lee**, Highland Instruments, Inc., 1, 2, Pfizer, 1, 2, Cigna-Express Scripts, 1; **G. St John**, Regeneron, 3, Intercept Pharmaceuticals, Inc, 3, 4; **H. van Hoogstraten**, Sanofi, 1, 3, 4; **K. Ford**, Sanofi Genzyme, 1, 2; **A. Praestgaard**, Sanofi, 3; **A. Sebba**, Eli Lilly and Company, 5, 8.

Abstract Number: 1235

Radiographic Progression of Structural Joint Damage over 5 Years of Baricitinib Treatment in Patients with Rheumatoid Arthritis: Results from RA-BEYOND

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Baricitinib (BARI) is an oral, reversible and selective Janus kinase 1 and 2 inhibitor. Treatment with once-daily oral BARI resulted in low rates of radiographic progression for up to 2 years in patients with rheumatoid arthritis (RA). The objective of this paper is to evaluate radiographic progression of structural joint damage in patients with RA over 5 years of treatment with BARI.

Methods: This study included patients who completed three phase 3 trials, RA-BEGIN (DMARD-naïve), RA-BUILD (csDMARD-IR) or RA-BEAM (MTX-IR), and enrolled in the long-term extension study, RA-BEYOND. Patients receiving blinded BARI at the conclusion of phase 3 trials remained on that dose (2mg or 4mg, once daily) in RA-BEYOND. At 52 weeks, DMARD-naïve patients receiving methotrexate (MTX) or combination therapy (BARI 4mg + MTX) were

	Baseline, Mean (SD)				Year 3 (Week 148)			Year 4 (Week 196)			Year 5 (Week 244)		
DMARD-naïve	**MTX, N=132**	**BARI 4mg, N=116**	**BARI 4mg + MTX, N=148**	**DMARD-naïve**	**MTX→BARI 4mg mono, N=129**	**BARI 4mg mono, N=113**	**BARI 4mg + MTX→BARI 4mg mono, N=145**	**MTX→BARI 4mg mono, N=125**	**BARI 4mg mono, N=111**	**BARI 4mg + MTX→BARI 4mg mono, N=141**	**MTX→BARI 4mg mono, N=113**	**BARI 4mg mono, N=104**	**BARI 4mg + MTX→BARI 4mg mono, N=133**
mTSS	7.35 (14.12)	8.29 (17.58)	9.09 (17.20)	ΔmTSS	2.22	1.08*	0.65***	2.43	1.21*	0.89**	2.53	1.25*	1.13*
Erosion score	4.67 (7.68)	5.03 (9.74)	5.43 (9.36)	ΔErosion score	1.44	0.71*	0.44***	1.57	0.82*	0.56***	1.64	0.81*	0.71**
Joint space narrowing	2.69 (7.17)	3.26 (8.39)	3.67 (8.68)	ΔJoint space narrowing	0.77	0.37	0.22*	0.86	0.39	0.33*	0.90	0.45	0.42
MTX-IR	**PBO, N=354**	**BARI 4mg, N=371**	**ADA, N=254**	**MTX-IR**	**PBO→BARI 4mg, N=337**	**BARI 4mg, N=363**	**ADA→BARI 4mg, N=243**	**PBO→BARI 4mg, N=346**	**BARI 4mg, N=353**	**ADA→BARI 4mg, N=242**	**PBO→BARI 4mg, N=322**	**BARI 4mg, N=330**	**ADA→BARI 4mg, N=218**
mTSS	35.86 (43.50)	35.48 (45.78)	37.16 (46.07)	ΔmTSS	2.05	1.38*	1.45	2.32	1.75	1.66	2.53	1.97	2.02
Erosion score	20.00 (23.94)	19.49 (25.14)	20.22 (24.05)	ΔErosion score	1.17	0.86	0.66*	1.31	1.06	0.73*	1.40	1.20	0.85*
Joint space narrowing	15.86 (21.11)	15.99 (22.13)	16.94 (23.60)	ΔJoint space narrowing	0.89	0.52*	0.80	1.02	0.70	0.93	1.14	0.77	1.17
	Baseline, Mean (SD)				**Year 3 (Week 144)**			**Year 4 (Week 192)**			**Year 5 (Week 240)**		
csDMARD-IR	**PBO, N=150**	**BARI 2mg, N=161**	**BARI 4mg, N=151**	**csDMARD-IR**	**PBO→BARI 4mg, N=142**	**BARI 2mg, N=152**	**BARI 4mg, N=144**	**PBO→BARI 4mg, N=143**	**BARI 2mg, N=153**	**BARI 4mg, N=147**	**PBO→BARI 4mg, N=130**	**BARI 2mg, N=141**	**BARI 4mg, N=132**
mTSS	14.02 (28.29)	17.65 (32.45)	20.84 (36.88)	ΔmTSS	1.25	1.25	0.88	1.55	1.35	1.08	1.71	1.53	1.27
Erosion score	7.82 (15.54)	9.74 (17.99)	11.80 (20.12)	ΔErosion score	0.78	0.70	0.50	0.99	0.75	0.62	1.09	0.82	0.74
Joint space narrowing	6.19 (13.56)	7.91 (15.84)	9.04 (17.66)	ΔJoint space narrowing	0.47	0.55	0.38	0.57	0.61	0.46	0.62	0.71	0.54

*p≤0.05, **p≤0.01, ***p≤0.001 vs. PBO or MTX. Δ=change from baseline; ADA=adalimumab; BARI=baricitinib; csDMARD=conventional synthetic disease-modifying antirheumatic drug; IR=inadequate response; mono=monotherapy; mTSS=modified Total Sharp Score; MTX=methotrexate; PBO=placebo

Table 1. Changes from baseline in mTSS and its components in different patient populations

switched to BARI 4mg monotherapy; MTX-IR patients receiving adalimumab (ADA) were switched to BARI 4mg on background MTX. At 24 weeks, csDMARD-IR patients receiving placebo (PBO) were switched to BARI 4mg on background csDMARD. Analysis population included patients who had baseline and at least one radiograph collected after 2 years. Radiographic progression of structural joint damage (Years 3-5) was determined by changes from baseline in van der Heijde modified Total Sharp Score (ΔmTSS), erosion score, and joint space narrowing. Proportion of patients showing no progression was assessed based on change from baseline mTSS (Δ mTSS) from the originating study, using thresholds of 0.5 or the smallest detecTable change (SDC). Mixed model repeated measures and logistic regression models were used to analyze continuous variables and categorical variables, respectively; linear extrapolation was used for imputation of missing data (maximum of 1 year).

Results: Overall, 82.6% (2125/2573) of patients entered the long-term extension study. Among DMARD-naïve patients, those on initial BARI monotherapy or in combination with MTX had significantly slower radiographic progression (ΔmTSS) compared to those on initial MTX at years 3, 4, and 5 (Table 1; p≤0.05). These patients also had significantly fewer erosions at these time points (p≤0.05). A greater proportion of patients who had received initial BARI therapy and BARI in combination with MTX had no radiographic progression compared to initial MTX monotherapy using thresholds of 0.5 (Table 2; p≤0.05). Among MTX-IR patients, patients on initial BARI treatment had slower radiographic progression compared to PBO and the results were comparable to those on initial adalimumab treatment at years 3, 4, and 5 (Table 1). A greater proportion of patients who had received initial BARI therapy had no radiographic progression compared to initial PBO using thresholds of SDC (Table 2; p≤0.05). Among csDMARD-IR patients, although differences between groups were small, patients on initial BARI 4mg had slowest radiographic progression

	Year 3 (Week 148)			Year 4 (Week 196)			Year 5 (Week 244)		
DMARD-naïve	**MTX→BARI 4mg mono, N=129**	**BARI 4mg mono, N=113**	**BARI 4mg + MTX→BARI 4mg mono, N=145**	**MTX→BARI 4mg mono, N=125**	**BARI 4mg mono, N=111**	**BARI 4mg + MTX→BARI 4mg mono, N=141**	**MTX→BARI 4mg mono, N=113**	**BARI 4mg mono, N=104**	**BARI 4mg + MTX→BARI 4mg mono, N=133**
ΔmTSS, ≤0.5, n (%)	73 (56.6)	80 (70.8) *	115 (79.3)***	69 (55.2)	76 (68.5) *	102 (72.3)**	62 (54.9)	71 (68.3) *	99 (74.4)**
ΔmTSS, ≤SDC, n (%)	98 (76.0)	90 (79.6)	125 (86.2)*	91 (72.8)	89 (80.2)	118 (83.7)*	81 (71.7)	80 (76.9)	107 (80.5)
MTX-IR	**PBO→BARI 4mg, N=337**	**BARI 4mg, N=363**	**ADA→BARI 4mg, N=243**	**PBO→BARI 4mg, N=346**	**BARI 4mg, N=353**	**ADA→BARI 4mg, N=242**	**PBO→BARI 4mg, N=322**	**BARI 4mg, N=330**	**ADA→BARI 4mg, N=218**
ΔmTSS, ≤0.5, n (%)	205 (60.8)	243 (66.9)	166 (68.3)	208 (60.1)	225 (63.7)	163 (67.4)	190 (59.0)	203 (61.5)	137 (62.8)
ΔmTSS, ≤SDC, n (%)	253 (75.1)	299 (82.4)*	193 (79.4)	251 (72.5)	280 (79.3)*	188 (77.7)	238 (73.9)	269 (81.5)*	167 (76.6)
	Year 3 (Week 144)			Year 4 (Week 192)			Year 5 (Week 240)		
csDMARD-IR	**PBO→BARI 4mg, N=142**	**BARI 2mg, N=152**	**BARI 4mg, N=144**	**PBO→BARI 4mg, N=143**	**BARI 2mg, N=153**	**BARI 4mg, N=147**	**PBO→BARI 4mg, N=130**	**BARI 2mg, N=141**	**BARI 4mg, N=132**
ΔmTSS, ≤0.5, n (%)	102 (71.8)	110 (72.4)	115 (79.9)	101 (70.6)	111 (72.5)	114 (77.6)	87 (66.9)	98 (69.5)	100 (75.8)
ΔmTSS, ≤SDC, n (%)	112 (78.9)	119 (78.3)	122 (84.7)	112 (78.3)	122 (79.7)	124 (84.4)	98 (75.4)	108 (76.6)	106 (80.3)

*p≤0.05, **p≤0.01, ***p≤0.001 vs. PBO or MTX

Δ=change from baseline; ADA=adalimumab; BARI=baricitinib; csDMARD=conventional synthetic disease-modifying antirheumatic drug; IR=inadequate response; mono=monotherapy; mTSS=modified Total Sharp Score; MTX=methotrexate; n=number of patients in each category; PBO=placebo

Table 2. Percentage of patients without structural damage progression in different patient populations

compared to initial PBO and initial BARI 2mg (Table 1). At least 74% of the structure data used in the analyses are based on observed data.

Conclusion: Treatment with once-daily oral BARI maintained low rates of radiographic progression for up to 5 years in different patient populations with RA.

Disclosure: D. van der Heijde, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5; **C. Kartman**, Eli Lilly and Company, 1, 3; **L. Xie**, Eli Lilly and Company, 1, 3; **S. Beattie**, Eli Lilly and Company, 1, 3; **D. Schlichting**, Eli Lilly and Company, 1, 2; **P. Durez**, None; **Y. Tanaka**, AbbVie, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 2, 5, 8, Asahi-kasei, 2, 5, 8, Novartis, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Astellas, 2, 5, 8, Chugai, 2, 5, 8, Daiichi-Sankyo, 2, 5, 8, Eisai, 2, 5, 8, Eli Lilly, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Janssen, 2, 5, 8, Mitsubishi-Tanabe, 2, 5, 8, Pfizer, 2, 5, 8, Takeda, 2, 5, 8, YL Biologics, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8; **R. Fleischmann**, Pfizer, 2, 5.

Abstract Number: 1236

Association Between Change in Health Assessment Questionnaire Disability Index and Treatment Response in Patients with Rheumatoid Arthritis in Tocilizumab Clinical Trials

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

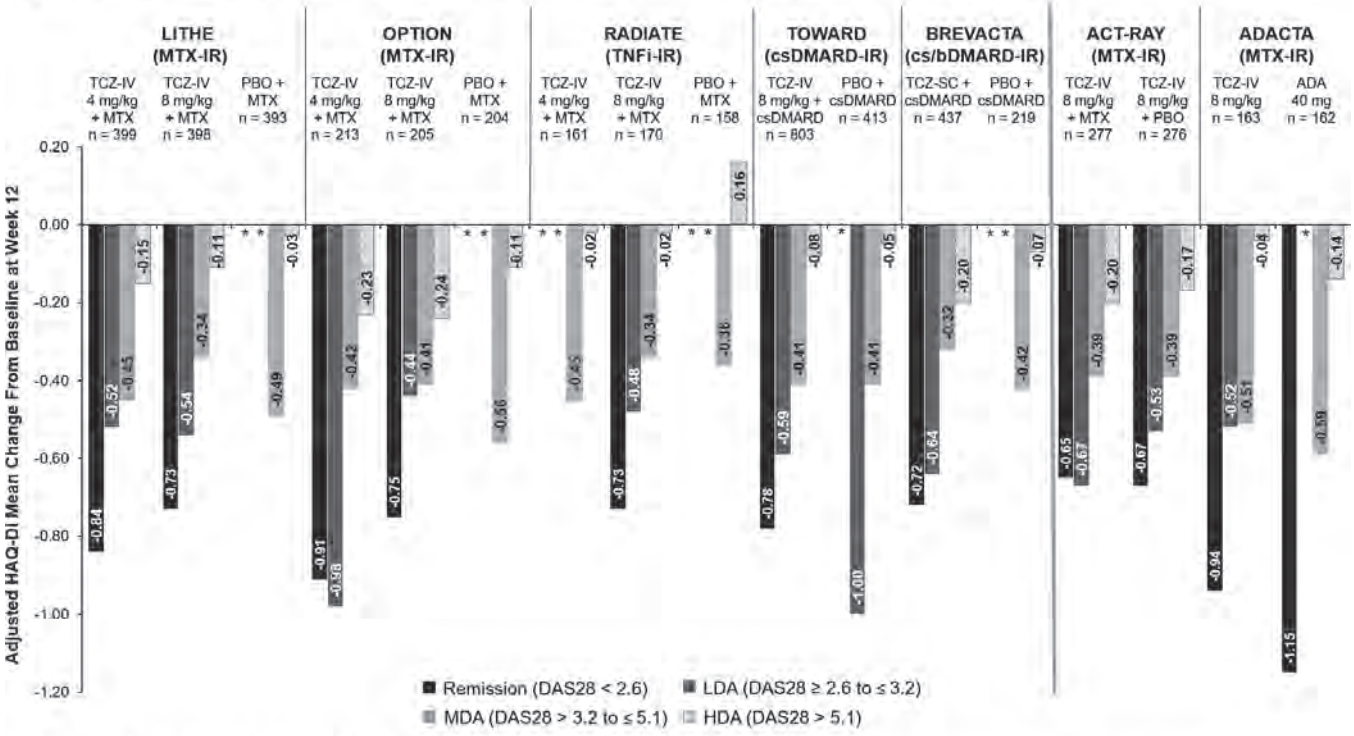
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

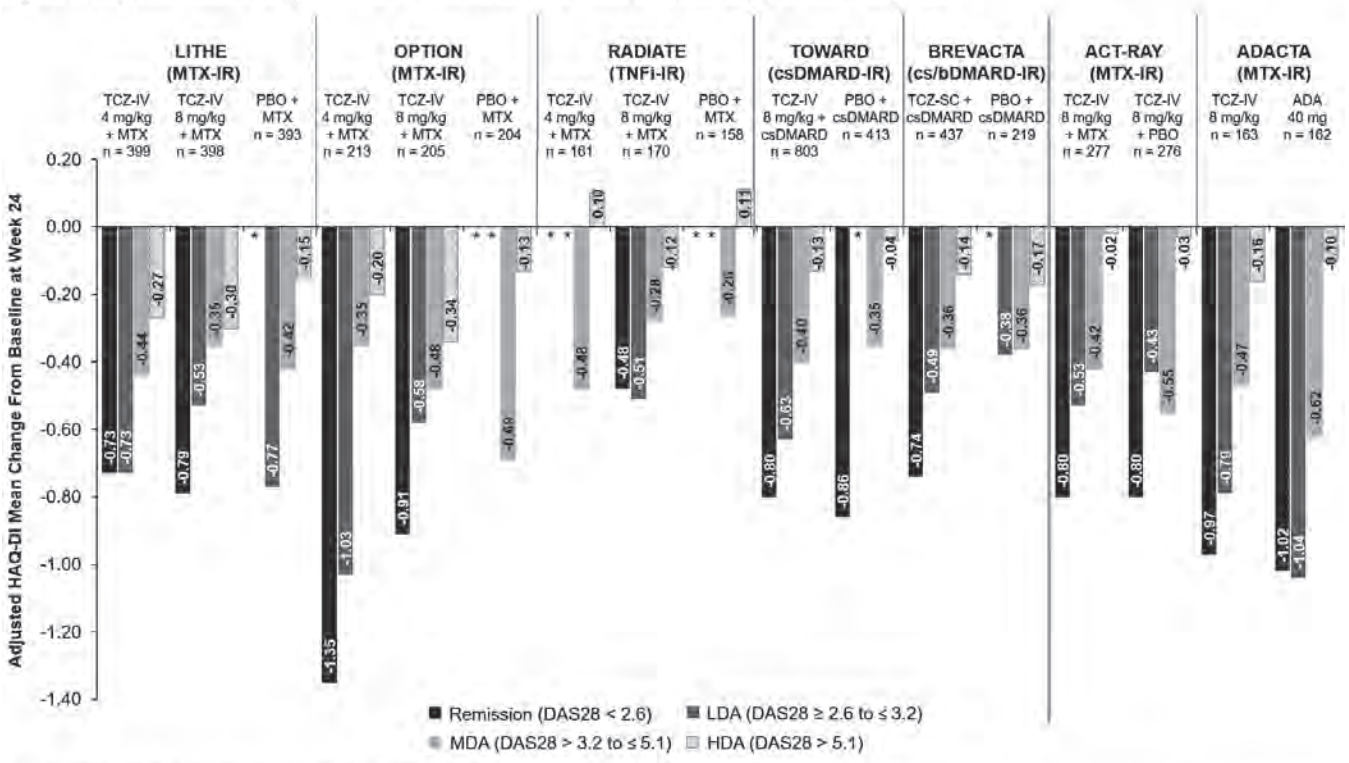
Background/Purpose: The efficacy and safety of intravenous (IV) and subcutaneous (SC) tocilizumab (TCZ) in combination with conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) and as monotherapy in patients with rheumatoid arthritis (RA) has been demonstrated in large clinical trials and real-world data studies. The Health Assessment Questionnaire Disability Index (HAQ-DI) is commonly used to assess physical function in patients with RA. While HAQ-DI outcomes at Week 24 in TCZ clinical trials have been reported, outcomes at Week 12 and results stratified by treatment response categories at Weeks 12 and 24 have not been previously described. The

Figure 1. Adjusted Mean Change in HAQ-DI from Baseline to Week 12 Stratified by DAS28 Disease Activity Level*



*Mean change not shown for groups with ≤ 10 patients in the DAS28 response category.
ADA, adalimumab; bDMARD, biologic disease-modifying antirheumatic drug; csDMARD; conventional synthetic disease-modifying antirheumatic drug; DAS28; disease activity score based on 28 joints; HAQ-DI, Health Assessment Questionnaire Disability Index; HDA, high-disease activity; IR, inadequate response; IV, intravenous; LDA, low-disease activity; MDA, moderate-disease activity; MTX, methotrexate; PBO, placebo; SC, subcutaneous; TCZ, tocilizumab; TNFi; tumor necrosis factor inhibitor.

Figure 2. Adjusted Mean Change in HAQ-DI from Baseline to Week 24 Stratified by DAS28 Response*



*Mean change not shown for groups with ≤ 10 patients in the DAS28 response category.
ADA, adalimumab; bDMARD, biologic disease-modifying antirheumatic drug; csDMARD; conventional synthetic disease-modifying antirheumatic drug; DAS28; disease activity score based on 28 joints; HAQ-DI, Health Assessment Questionnaire Disability Index; HDA, high-disease activity; IR, inadequate response; IV, intravenous; LDA, low-disease activity; MDA, moderate-disease activity; MTX, methotrexate; PBO, placebo; SC, subcutaneous; TCZ, tocilizumab; TNFi; tumor necrosis factor inhibitor.

objective of this study was to report the association between change in HAQ-DI from baseline to Weeks 12 and 24 and Disease Activity Score in 28 joints (DAS28) response categories in patients who received TCZ or comparators in TCZ clinical trials.

Methods: Data from patients with active RA who received TCZ or a comparator from 6 Phase 3 or 4 TCZ-IV studies (OPTION [NCT00106548], RADIATE [NCT00106522], TOWARD [NCT00106574] LITHE [NCT00109408], ACT-RAY [NCT00810199] and ADACTA [NCT01119859]) and 1 Phase 3 TCZ-SC study (BREVACTA [NCT01232569]) were analyzed. Mean change in HAQ-DI score at Weeks 12 and 24 was assessed in patients stratified by DAS28 disease activity level (DAS28 < 2.6 [remission], DAS28 ≥ 2.6 to ≤ 3.2 [low disease activity; LDA], DAS28 > 3.2 to ≤ 5.1 [moderate disease activity; MDA], DAS28 > 5.1 [high disease activity; HDA] at Weeks 12 and 24. The adjusted least squares mean (LSM) change from baseline was estimated using a mixed model with repeated measures, including region (North America vs non-North America), RA duration (> 2 years vs ≤ 2 years), baseline HAQ-DI and DAS28, treatment, visit, visit by treatment and visit by baseline HAQ-DI.

Results: Data from 5051 patients were included. Across all studies, the mean duration of RA ranged from 6.3 to 12.6 years. At baseline, patients had severe RA with a mean DAS28 ≥ 6.3; baseline HAQ-DI was ≥ 1.5. At Week 12, patients who achieved remission or LDA had greater improvements in HAQ-DI than those in MDA or HDA (**Figure 1**). Results were similar at Week 24 (**Figure 2**). Among patients who received TCZ and achieved remission or LDA, mean improvement in HAQ-DI was ≥ 0.65 and ≥ 0.44, respectively, at Week 12 (**Figure 1**) and ≥ 0.48 and ≥ 0.43 at Week 24 (**Figure 2**). Mean changes in HAQ-DI were similar between patients who received TCZ-IV in combination with MTX or as monotherapy (ACT-RAY) and in those who received TCZ-IV or ADA as monotherapy (ADACTA).

Conclusion: Patients with long-standing, severe RA who received IV or SC TCZ as monotherapy or in combination with csDMARDs had improvement in physical function and disease activity at Week 12 that was maintained at Week 24. Overall, across all the trials, response to treatment was associated with improvement in patient-reported physical function.

Disclosure: S. Unizony, Genentech, Inc., 2; **J. Dang**, Genentech, Inc., 1, 2; **J. Han**, Genentech, Inc., 1, 2; **M. Michalska**, Genentech, Inc., 1, 2; **J. Best**, Genentech, Inc., 1, 2.

Abstract Number: 1237

Pain and Other Patient-Reported Outcomes in Patients with Rheumatoid Arthritis Who Did or Did Not Achieve Treatment Response Based on Improvement in Swollen Joints in Tocilizumab Clinical Trials

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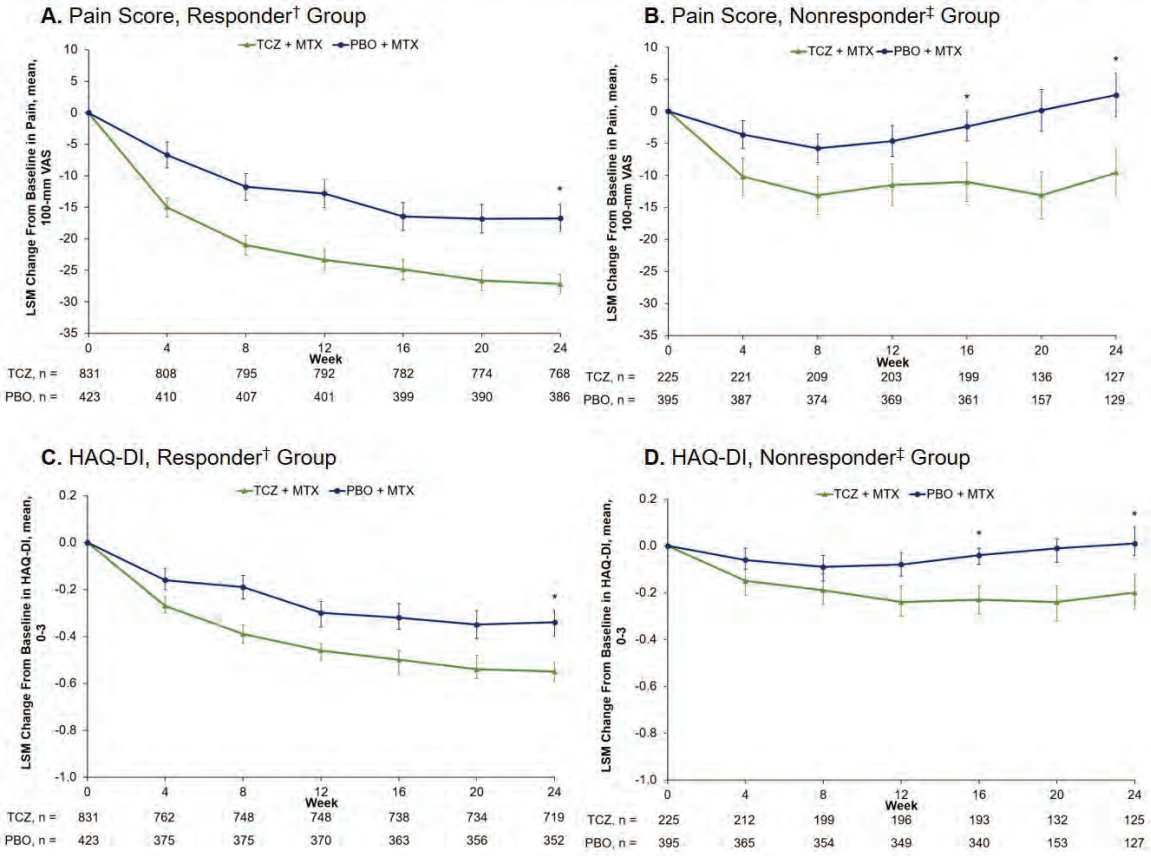
SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent data suggest that rheumatoid arthritis (RA) pain may be noninflammatory and inflammatory, and improvement in pain scores and other patient-reported outcomes (PROs) may be seen in patients who do not respond to treatment based on disease activity measures that evaluate inflammation. This study evaluated changes in pain scores and other PROs in patients with RA who did or did not achieve ≥ 20% improvement in swollen joint count (SJC) in tocilizumab (TCZ) clinical trials.

Methods: Data from patients with active RA who received intravenous TCZ 8 mg/kg + methotrexate (MTX) or placebo (PBO) + MTX in 3 Phase III studies (OPTION [NCT00106548], TOWARD [NCT00106574] and LITHE [NCT00109408]) were included. Changes in pain (visual analog scale [VAS], 0-100 mm), Health Assessment Questionnaire Disability Index (HAQ-DI, 0-3), 36-Item Short Form Survey (SF-36) physical component score (PCS) and mental component score (MCS; 0-50) and Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) score (0-52) from baseline to Week 24 were evaluated. Results were compared between patients receiving TCZ + MTX and those receiving PBO + MTX in both patients who achieved ≥ 20% improvement in SJC (responders) and those who did not (nonresponders). The changes from baseline were analyzed using a mixed model with repeated measures, including the following covariates and interactions: treatment, visit, baseline of endpoint, region, baseline DAS28 and interactions of visit with treatment and baseline of endpoint.

Results: Data from 1254 responders (TCZ + MTX, n = 831; PBO + MTX, n = 423) and 620 nonresponders (TCZ + MTX, n = 225; PBO + MTX, n = 395) were included. Patients receiving TCZ + MTX had significantly greater improvement in pain and HAQ-DI than PBO + MTX in the responder group (–27.19 vs –16.77 and –0.55 vs –0.34, respectively; $P < 0.0001$ for both) and nonresponder group (–9.59 vs 2.53 and –0.20 vs 0.01; $P < 0.0001$ for both) at Week 24 (**Figure 1**). Similar results were seen at Week 16 in the nonresponder group (–11.06 vs –2.38 and –0.23 vs –0.04; $P < 0.0001$ for both). At Week 24 in the responder group, patients receiving TCZ + MTX had significantly greater improvements compared with PBO + MTX in SF-36 PCS and MCS (9.16 vs 5.71 and 6.55 vs 3.79, respectively; $P < 0.0001$ for both) (**Figure 2**) and FACIT-F (8.39 vs 5.11; $P < 0.0001$). In the nonresponder group, patients receiving TCZ + MTX had

Figure 1. LSM Change in Pain Score and HAQ-DI From Baseline to Week 24 in Responder and Nonresponder Groups

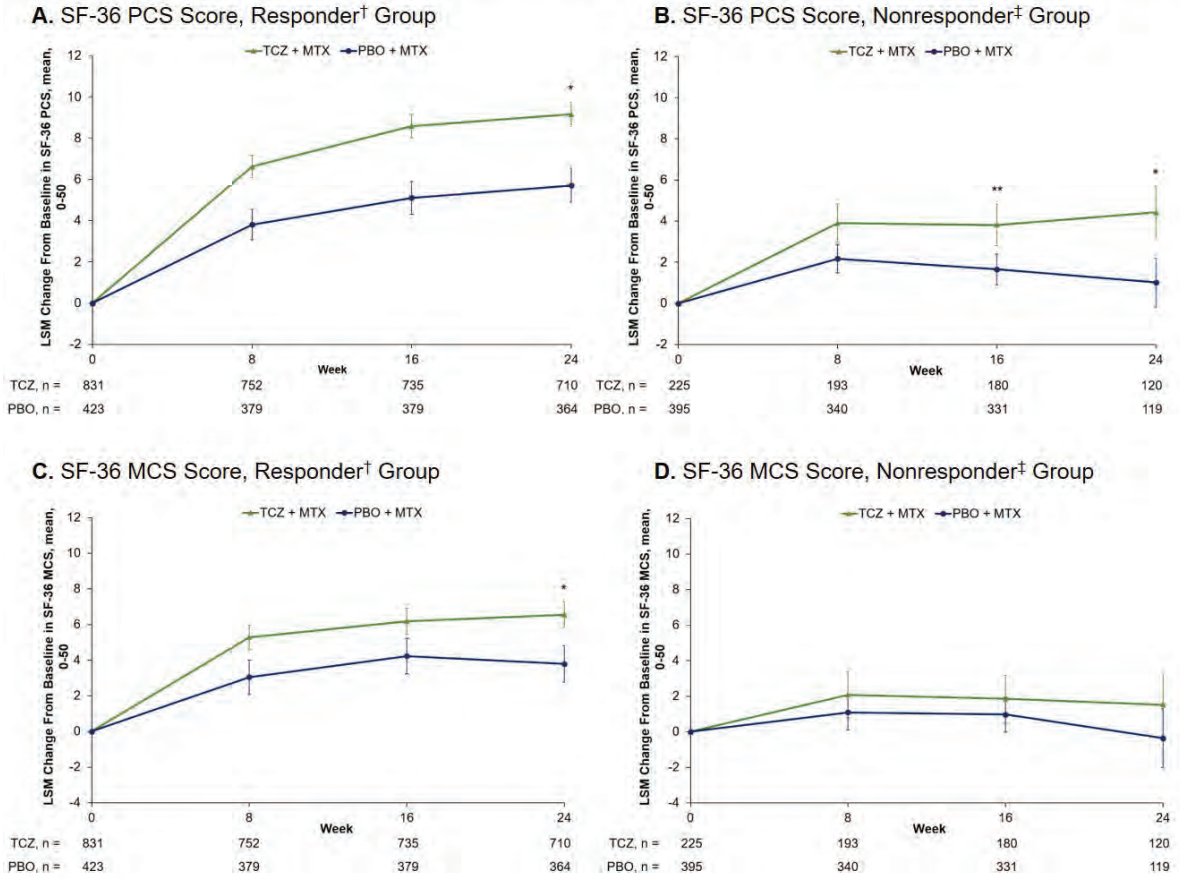


HAQ-DI, Health Assessment Questionnaire Disability Index; LSM, least squares mean; MTX, methotrexate; PBO, placebo; TCZ, tocilizumab; VAS, visual analog scale.
*$P < 0.0001$ for comparison between TCZ + MTX and PBO + MTX.
†Patients who achieved ≥ 20% improvement in swollen joint counts.
‡Patients who did not achieve ≥ 20% improvement in swollen joint counts; at Week, 16 patients were permitted to receive rescue therapy.

significantly greater improvements compared with PBO + MTX in SF-36 PCS at Week 16 (3.81 vs 1.65; $P = 0.0006$) and Week 24 (4.42 vs 1.01; $P < 0.0001$) (**Figure 2**) and FACIT-F at Week 16 (3.82 vs 1.32; $P = 0.0039$) and Week 24 (3.90 vs 1.40; $P = 0.0111$).

Conclusion: Patients with RA who received TCZ + MTX had significantly greater improvements in pain and other PROs than those who received PBO + MTX regardless of whether they achieved ≥ 20% improvement in SJC. Clinical outcome at Week 24 correlated well with PROs, with a relatively larger improvement in PROs in the responder group than in the nonresponder group; relative to PBO + MTX, these improvements appear numerically similar in the responder and nonresponder groups. The consistent effect of TCZ on PROs in responder and nonresponder groups warrants further study on TCZ's impact on pain sources independent of that caused by joint inflammation.

Figure 2. LSM Change in SF-36 PCS and MCS From Baseline to Week 24 in Responder and Nonresponder Groups



LSM, least squares mean; MTX, methotrexate; MCS, mental component score; PCS, physical component score; PBO, placebo; SF-36, 36-Item Short Form Survey; TCZ, tocilizumab.
*P < 0.0001 for comparison between TCZ + MTX and PBO + MTX.
**P < 0.001 for comparison between TCZ + MTX and PBO + MTX.
†Patients who achieved ≥ 20% improvement in swollen joint counts.
‡Patients who did not achieve ≥ 20% improvement in swollen joint counts; at Week 16, patients were permitted to receive rescue therapy.

Disclosure: A. Sebba, Eli Lilly and Company, 5, 8; **J. Han**, Genentech, Inc., 1, 2; **S. Mohan**, Genentech, Inc., 1, 2.

Abstract Number: 1238

Associations Between Rheumatoid Arthritis Disease Activity and Patient-reported Outcomes in Sarilumab Clinical Trials

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Sarilumab is a human IL-6 receptor inhibitor approved for the treatment of adults with moderately to severely active RA. The relationship between disease activity, sarilumab treatment, and improvements in patient-reported outcomes (PROs) has not been well studied. Here, we assess the association between disease activity and PROs in 3 sarilumab phase 3 trials.

Methods: This post hoc analysis included patients from 2 placebo-controlled trials (MOBILITY [NCT01061736] and TARGET [NCT01709578], with sarilumab dose groups of 150 mg and 200 mg every 2 weeks [q2w] combined for this analysis) and the active-controlled MONARCH (NCT02332590; sarilumab 200 mg vs adalimumab 40 mg q2w) trial. Associations between PRO improvement and achievement of low disease activity (LDA) were tested at Week 24. All statistics are descriptive.

Table. Change from baseline in PRO scores, median (Q1–Q3 interquartile range)

	FACIT-fatigue (0–52)		Pain (VAS 0–100)		Sleep (VAS 0–100)	
MOBILITY[a]	Placebo	Sarilumab	Placebo	Sarilumab	Placebo	Sarilumab
DAS28-CRP <3.2	7.3	9.0	–36.0	–41.0	–17.0	–26.0
DAS28-CRP ≥3.2	4.3	7.5	–14.0	–18.5	–12.0	–14.5
CDAI ≤10	7.3	9.0	–37.0	–41.0	–17.0	–26.0
CDAI >10	4.3	8.0	–12.5	–22.0	–12.0	–14.0
SDAI ≤11	8.0	9.0	–37.0	–40.0	–24.0	–26.0
SDAI >11	4.0	8.0	–12.0	–22.0	–10.0	–16.0
TARGET[b]	Placebo	Sarilumab	Placebo	Sarilumab		
DAS28-CRP <3.2	16.0	14.0	–44.5	–53.0		
DAS28-CRP ≥3.2	7.0	8.5	–18.0	–27.5		
CDAI ≤10	14.0	14.0	–42.0	–52.0		
CDAI >10	6.0	9.0	–18.0	–28.0		
SDAI ≤11	15.0	14.0	–45.0	–52.5		
SDAI >11	6.0	8.9	–17.5	–27.0		
MONARCH[c]	Adalimumab	Sarilumab	Adalimumab	Sarilumab		
DAS28-CRP <3.2	10.0	11.0	–45.0	–42.0		
DAS28-CRP ≥3.2	7.0	5.0	–21.0	–20.5		
CDAI ≤10	10.0	11.0	–44.0	–42.0		
CDAI >10	7.0	7.0	–21.0	–28.5		

[a]Placebo n=398, sarilumab n=799; [b]Placebo n=181, sarilumab n=365, sleep not assessed; [c]Adalimumab n=185, sarilumab n=184, SDAI and sleep not assessed. Disease activity thresholds per trial protocols. CDAI=Clinical Disease Activity Index; FACIT=Functional Assessment of Chronic Illness Therapy; Q=quartile; SDAI=Simplified Disease Activity Index; VAS=visual analog scale

Results: Across all trials, PRO improvements were numerically larger in patients who achieved LDA than in those who did not (Table). Sarilumab was associated with numerically larger PRO improvements than placebo, in patients who did and also in those who did not achieve LDA (Table). In the active-comparator trial, improvements in PROs were generally comparable between sarilumab and adalimumab (Table).

Conclusion: In this post hoc analysis, achieving LDA was associated with increased PRO improvements. In patients who did not achieve LDA, the improvements were numerically more favorable with sarilumab than with placebo. There is an emerging concept that changes in PROs may also occur via different mechanisms than just suppression of inflammation, potentially via IL-6 inhibition (Taylor PC, et al. *J Clin Med. 2*019;8[6]:831), which may account for some of the results seen here.

Disclosure: G. Burmester, AbbVie, 5, 8, Pfizer, 5, 8, Gilead Sciences, Inc., 5, 8, Eli Lilly, 5, 8, Novartis, 5, Celgene, 5; **L. Gossec**, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8; **H. van Hoogstraten**, Sanofi, 1, 3, 4; **A. Praestgaard**, Sanofi, 3; **G. St John**, Regeneron, 3, Intercept Pharmaceuticals, Inc, 3, 4; **T. Huizinga**, Bristol-Myers Squibb Company, 2, 8, Pfizer, 2, 8, Eli Lilly, 2, 8, LUMC, 9; **D. Aletaha**, UCB, 5, 8, Eli Lilly, 5, 8, Gilead Sciences, Inc., 2, 5, Janssen, 5, Sanofi/Genzyme, 5, 8, AbbVie, 2, 5, 8, Amgen, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, Roche, 2, 5, 8, Merck Sharp & Dohme, 2, 5, 8, Bristol-Myers Squibb, 8, Celgene, 5, 8, Medac, 5, 8, Sandoz, 5, 8; **R. Fleischmann**, Pfizer, 2, 5.

Abstract Number: 1239

Peripheral Protein Biomarker Changes Following Selective Inhibition of Janus Kinase 1 (JAK1) by Filgotinib in Methotrexate Naïve Adults with Moderately-to-Severely Active Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Filgotinib (FIL), an oral selective JAK1 inhibitor, has shown efficacy and safety in phase 3 studies in adults with moderately-to-severely active rheumatoid arthritis (RA), including those naïve to methotrexate (MTX) (FINCH3;NCT02886728). A longitudinal study of protein biomarkers related to JAK signaling[1], bone biology[2], immune cell migration[2] and inflammation[2] was conducted in FINCH3 patients (pts) to identify disease-relevant biomarkers altered by FIL vs MTX.

Methods: MTX-naive RA pts enrolled in FINCH3 received a sTable dose of MTX (MTX), FIL200mg monotherapy (FIL200mg), FIL100mg+MTX, or FIL200mg+MTX. Up to 27 disease relevant biomarkers were evaluated. Baseline (BL) correlation between biomarkers and clinical response measures were analyzed by Spearman Rank. Multiscale bootstrap resampling was used to evaluate significant intra-cluster biomarker membership. Mean changes from BL to weeks (wks) 4, 12 and 24 were compared using MTX-adjusted estimates from a linear mixed effects model. A false discovery rate of 5% was applied.

Results: At BL, distinct clusters (CL) of biomarkers differentiated by JAK signaling were identified. The strongest intra-group correlations were in biomarkers upstream of JAK2 signaling (CL1; Rho range 0.88–0.98) and cytokines associated with JAK1 signaling (CL2; Rho range 0.72–0.77). Within MTX-naïve RA pts, there were significant BL correlations between 15 biomarkers and clinical measures. The strongest associations observed were between DAS-28CRP and IL6, CXCL10, TNFRI, YKL-40, and CXCL13 (Rho >0.3).

Relative to MTX, 23 biomarkers exhibited significant *early responses* (any arm, wk 4). The strongest treatment effect observed at wk 4 was a reduction for CXCL13 (FIL100mg+MTX: -28.2%; FIL200mg+MTX: -40%; FIL200mg: 34%). This reduction was sustained through 24 wks, with the greatest reduction by FIL200mg+MTX (-37.8%). Dose differences were observed relative to FIL100mg+MTX, where FIL200mg+MTX led to an *early* (wk 4) and significantly greater reduction of 9 biomarkers. There was a significant dose difference as a *delayed* response (wk 24) with a greater reduction by FIL200mg+MTX for 8 biomarkers.

FIL200mg produced a greater effect on 18 biomarkers vs MTX, significant through wk 24. The greatest effects in FIL200mg were reductions by wk 24 in CTX1 (-29.1%), CXCL13 (-33.2%), and IL6 (-29.5%); biomarkers associated with DAS28CRP at BL. Four biomarkers were different between FIL200mg and FIL200mg+MTX arms by wk 24: greater increase of MMP7 and decrease of GMCSF in FIL200mg+MTX; greater decrease of TRACP5B and ICAM1 in FIL200 alone.

Conclusion: Treatment through 24 weeks with FIL200mg ±MTX reduced many disease-relevant biomarkers tested; markers related to JAK signaling[1], bone biology[2], inflammation[2], and immune cell migration[2] in MTX-naïve RA setting. Changes were significantly reduced relative to MTX mono at wk 4, supporting the rapid onset of FIL clinical efficacy. The current study identified significant reductions of RA-associated disease markers unique to FIL mono, supporting the FIL mechanism of action in RA treatment.

1. Front Immunol. 2017;8:29

2. J Clin Invest. 2008;118:3537-45

Disclosure: P. Taylor, Eli Lilly, 2, 5, 8, Celgene, 2, 5, 8, AbbVie, 2, 5, 8, Biogen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celltrion, 2, 5, 8, Fresenius, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Janssen, 2, 5, 8, Nordic Pharma, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8, Pfizer, 2, 5, 8, Gilead, 2, 5, 8, Galapagos, 2, 5, 8; **A. Mirza**, Gilead Sciences, Inc., 3, Gilead Sciences, Inc., 1; **B. Downie**, Gilead Sciences, Inc., 3, Gilead Sciences, Inc., 1; **J. Liu**, Gilead Sciences, Inc., 3, Gilead Sciences, Inc., 1, Roche, 1; **R. Hawtin**, Gilead Sciences, Inc., 3, Gilead Sciences, Inc., 1; **E. Elboudwarej**, Gilead Sciences, Inc., 3, Gilead Sciences, Inc., 1.

Abstract Number: 1240

An Increase in Red Cell Mean Corpuscular Volume by Methotrexate Is Potentiated by Hydroxychloroquine and Predicts Clinical Response in Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Methotrexate (MTX) can result in an increase in mean corpuscular volume (MCV) of red blood cells. The range of MCV change varies between patients on treatment with MTX. We investigated MCV as a biomarker of response to MTX treatment in early rheumatoid arthritis (RA) patients.

Methods: This is a real-world data of biologic-naïve RA patients (as per 2010 ACR/EULAR classification) in a teaching hospital who were started on oral MTX. Results were validated by using a second cohort from a different hospital.

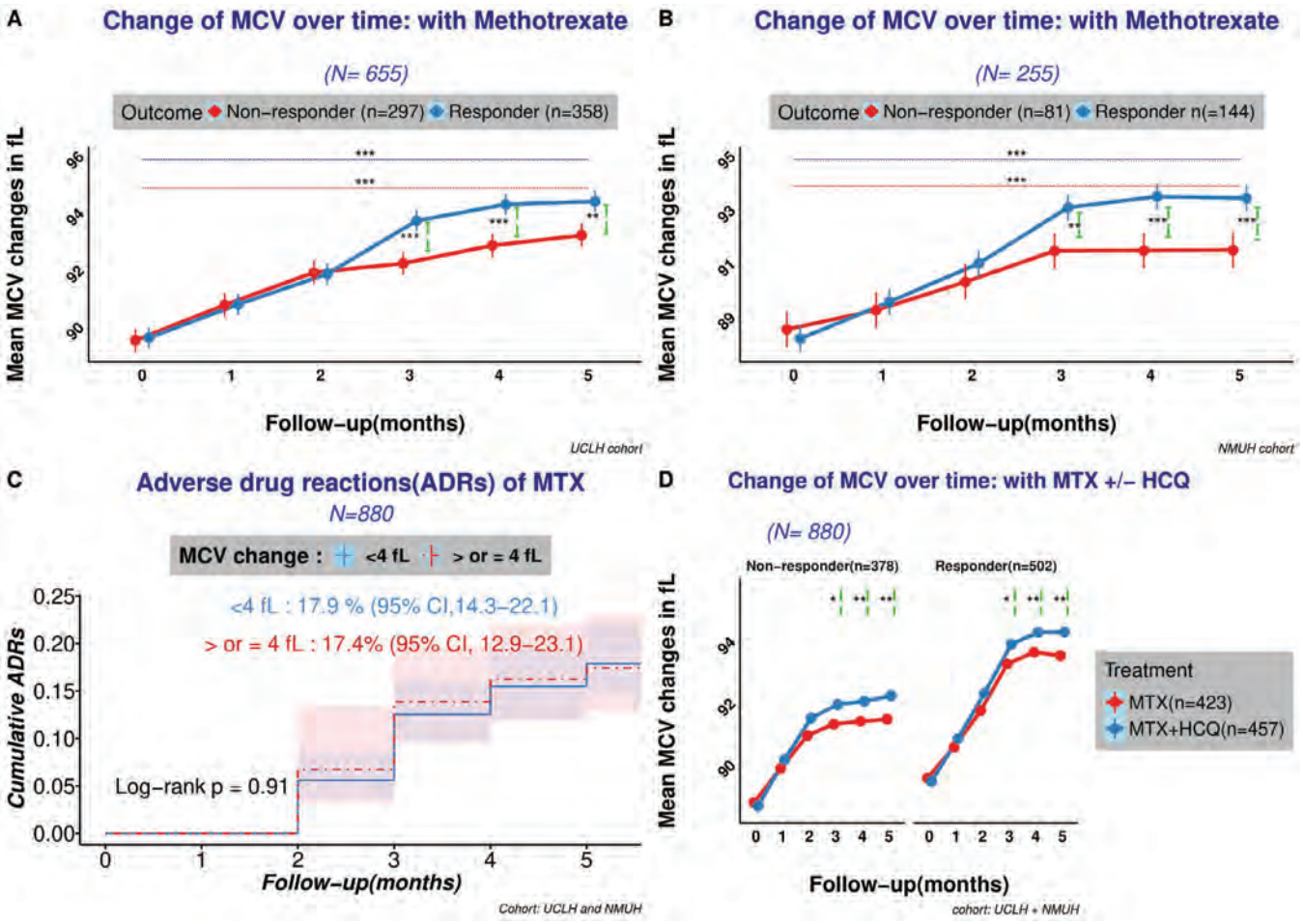

Figure 1 (A-D): A. MCV (mean corpuscular volume) change after initiation of methotrexate (MTX). Overall, MCV increased significantly from baseline for both MTX responder and non-responder groups. A significantly higher increase in MCV is demonstrated in the responder group from month 3 and onwards. B. The changes in MCV seen in 1A were confirmed in a second cohort of patients. C. Kaplan-Meier survival curves of adverse drug reactions (ADRs) event in the first 6 months after initiation of methotrexate (MTX) stratified by mean corpuscular volume (MCV) change (either <4 or ≥ 4 fL) from baseline did not reveal any difference. Overall adverse effect was noted for 17.4% (95% CI 12.9-23.1) of patient who had an MCV increment of ≥ 4 fL, compared to 17.9% who had an MCV increase of <4 (95% CI 14.3-22.1). Both cohorts have been combined for ADRs. ADRs include: MCV change <4: 20 deranged liver function (10 resulting in drug discontinuation), 2 suspected pneumonitis, 2 infections, 1 pancytopenia, 29 gastrointestinal (GI) side effects, 3 other causes. MCV ≥ 4: 31 deranged liver function (13 resulting in drug discontinuation), 33 GI side effects, 2 thrombocytopenia, 1 hypersensitivity reaction, 13 other causes. D. adding hydroxychloroquine (HCQ) to MTX potentiated the MCV changes. Each error bar (lime green) represents the p value between MTX monotherapy patient and MTX+HCQ group each time point.

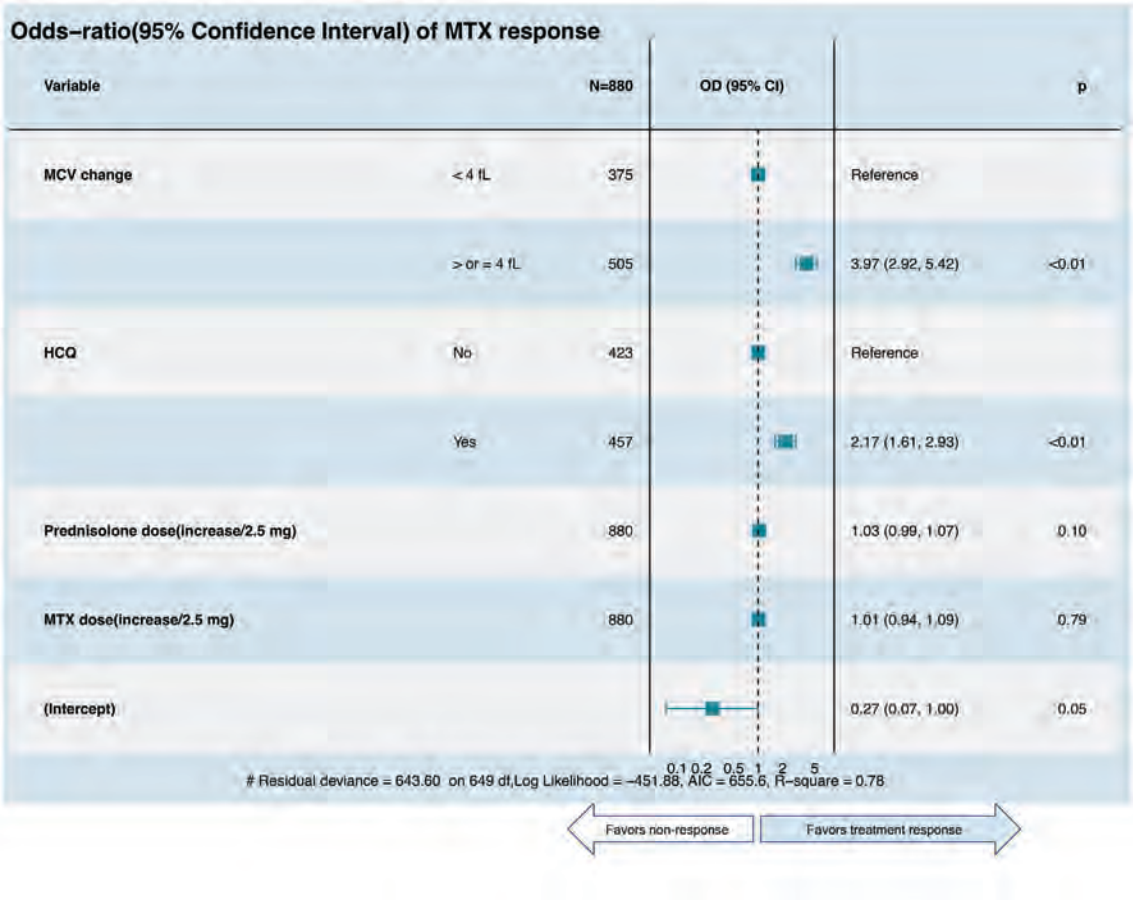

Figure 2. Random- and fixed-effects multivariate logistic regression model of predictors of treatment response of methotrexate (MTX). The final model was selected by stepwise regression using Akaike information criterion (AIC), which included: - Change of MCV (used as categorial variable), disease duration (not shown, not significant in the final model) - Adjusted by concomitant prednisolone (if applicable), MTX dose, and concomitant use of disease-modifying antirheumatic drugs (DMARDs) which includes hydroxychloroquine (HCQ), sulfasalazine (SSZ) or leflunomide (LEF).

Treatment response to oral MTX was defined as at least moderate to good EULAR response and no initiation of additional conventional, synthetic or biologic disease-modifying agents within 6 months. After initiation of MTX, MCV changes were analysed (stratified by responder and non-responder groups), by using linear mixed model analysis. Receiver operating characteristic (ROC) curve analysis (area under the curve [AUC]) was employed to identify the optimal cut-point of MCV change. Kaplan-Meier analysis captured the cumulative adverse drug reactions (ADRs) over 6 months due to MTX. Multivariate logistic regression was applied to identify predictors of treatment response within patient demographics, baseline characteristics, antibody status and concomitant treatment. Latent classes were then identified based on MCV changes.

Results: Although the MCV increased from baseline to 3 months and beyond in both responders and non-responders, MTX-responder showed a significantly greater increase of MCV from 3 months post-MTX compared to non-responders ($p < 0.001$, **Fig. 1A)**. This finding was validated in a second cohort **(Fig. 1B)**. An increase in MCV of 4 femtolitres (fL) at 3 months was associated with better treatment response using a ROC analysis with an AUC of 0.76 (95% CI 0.73- 0.80). AUC was 0.75 (95% CI 0.69- 0.83) for increase in MCV by 4.2 fL in the second cohort. However, a raised MCV ≥ 4 fL was not associated with increased ADRs **(Fig. 1C**). Hydroxychloroquine (HCQ) therapy potentiated the MCV changes when combined with MTX, in both treatment responder and non-responder group **(Fig. 1D)**.

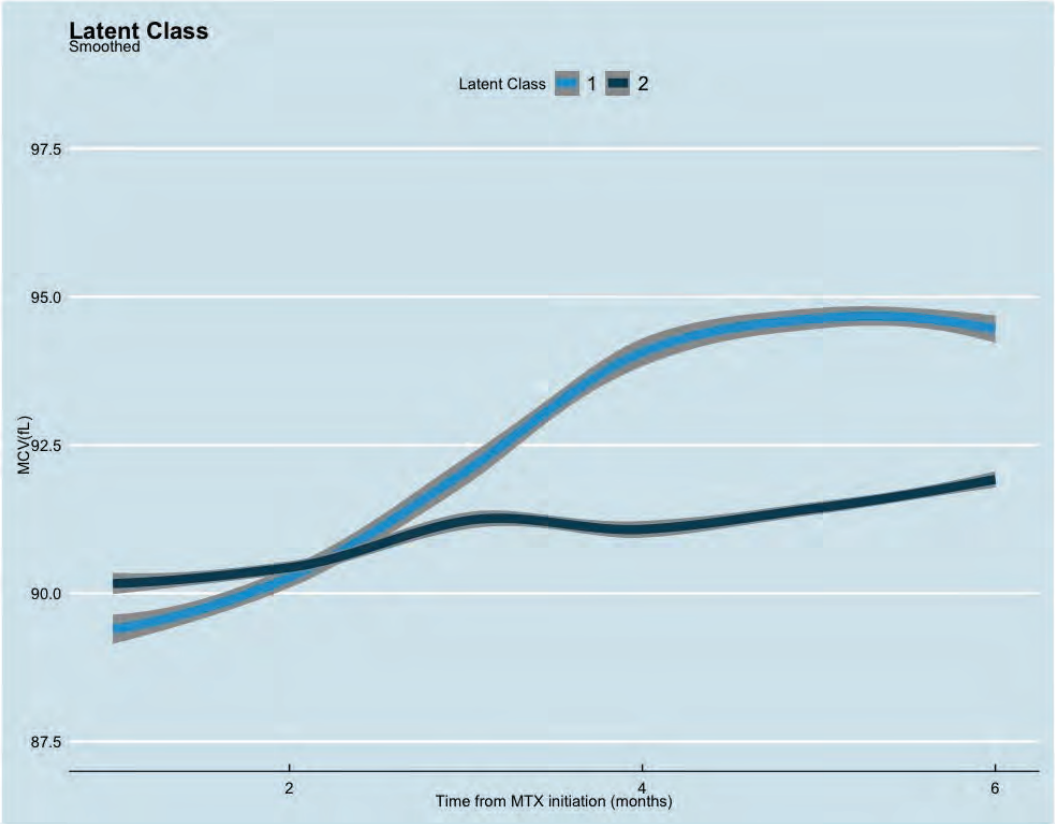

Figure 3. Mean profile change of mean corpuscular volume (MCV) over 6 months from initiation of methotrexate (MTX) after combining both cohorts and stratified by predicted class membership. Class 1: greater increase in MCV (light blue): N=496, 56.64% Class 2: minimal increase in MCV (dark blue): N=384, 43.63%. (entropy - 0.9863)

There was no change in MCV when HCQ was given without methotrexate suggesting a synergistic effect with MTX (data not shown).

Multivariate logistic regression revealed an increment of MCV by ≥ 4 fL [Odds Ratio (OR), 3.97 with 95% CI of 2.92-5.42; p=0.001] and concomitant use of HCQ (OR 2.17 with 95% CI 1.61-2.93; p=0.003) predicted clinical response **(Fig. 2)**.

Two latent classes were identified based on MCV changes **(Fig. 3)**: a greater increase in MCV group (class 1) which was associated with more treatment responders [Log (OR) 5.93, SE 0.85, p=0.001)] compared to the other class (class 2) with minimal increase in MCV. Higher MCV over time in class 1 was associated with lower C-reactive protein (CRP) [Log (OR) 0.97, SE 0.24, p=0.001] and concomitant use of HCQ [Log (OR) 0.28, SE 0.7, p=0.000)]. This effect was in the opposite direction for class 2 [Log (OR) for CRP was 0.33 with SE 0.04, p=0.000 and for HCQ -0.38 with SE 0.07, p=0.000].

Conclusion: Our data suggests that an increase of MCV increase of 4 fL from 3 months predicts response to MTX therapy in biologic-naïve RA patients and that concomitant HCQ potentiates the increase in MCV and the therapeutic effect of MTX.

Disclosure: M. Shipa, None; **S. Yeoh**, None; **D. Mukerjee**, None; **M. Ehrenstein**, None.

Abstract Number: 1241

Patient-Reported Outcomes in Rheumatoid Arthritis Patients Treated with Tofacitinib or Biological DMARDs in Real Life Conditions in Two Latin America Countries

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: RA – Treatments Poster III: PROs, Biomarkers, Systemic Inflammation & Radiographs
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The objective of this study was to describe the efficacy, safety and patient reported outcomes in Latin-American patients with Rheumatoid Arthritis (RA) treated with tofacitinib 5mg (BID) or biological DMARDs (bDMARDs) after failure to respond to conventional DMARDs in real-life conditions. The primary objective of this study was to compare the disease activity measured by RAPID3 at 0- and 6-months follow-up.

Methods: This was a prospective and retrospective non-interventional study (NIS) comparing tofacitinib to bDMARDs treatments in patients with RA after failure of conventional DMARDs; the study was performed in 13 sites from Colombia and Peru between 2017 to 2019. Convenience sampling in the tofacitinib arm and randomized in the bDMARDs arm was performed. Demographic and clinical information was collected at baseline and follow up. The following questionnaires were applied at baseline and Month 6 (±1 month) of follow-up: RAPID3 (Routine Assessment of Patients Index Data) to measure Disease activity; HAQ-DI (Health Assessment Questionnaire) to measure Functional status; EQ-5D-3L (EuroQol Questionnaire) to measure Quality of life. Frequency of Adverse Events (AE) was taken from clinical records retrospectively and collected during visits when spontaneously reported. The clinical outcomes were adjusted through linear regression by demographic, clinical and access variables. Unadjusted and adjusted differences from baseline were reported in Standardized Mean Difference (SMD).

Results: Data from 100 RA patients treated with tofacitinib and 70 RA patients with bDMARDs (85% treated with etanercept, rituximab, tocilizumab and infliximab) was collected and patients were recruited between April 2017 and February 2019. At baseline, patients mean age was 53.53 years (SD 13.77), mean disease duration was 6.31 years (SD 7.01) and mean DAS28 was 5.48 (SD 2.97). There was a significant difference in the following baseline demographic and clinical characteristics of the patients: previous methotrexate therapy, complementary access mechanism and time to supply were higher in the tofacitinib group, while prednisolone treatment and concomitant use of leflunomide were higher in the biologics. At month 6, there was no statistical difference in the adjusted SMD [Standard Error] from baseline for tofacitinib versus bDMARDs for RAPID 3 (-0.20 [0.69] vs. -0.32 [0.71]), HAQ-DI (-0.56 [0.07] vs. -0.50 [0.08]), EQ-5D-3L (0.23 [0.06] vs. 0.29 [0.06]) and DAS28 (-3.86 [0.59] vs. -4.23 [0.61]). Patients with tofacitinib and biologics presented a similar proportion of non-serious AE (30.0% and 28.6%, respectively); there were two serious AE in the tofacitinib group (2.0%) that were not related to the treatment. These results have limitations (heterogeneity among groups, sample size) given the specific characteristics of NIS.

Conclusion: There were no differences between patients with RA treated with tofacitinib and biological DMARDs regarding the disease activity, quality of life and functional status. Tofacitinib had similar safety profile to biological DMARDs in Latin American RA patients.

Disclosure: H. Madariaga, Pfizer, 8; **J. Reyes**, Pfizer, 3; **M. Gutierrez**, Pfizer, 3; **D. Ponce de Leon**, Pfizer, 1; **T. Lukic**, Pfizer Inc, 1, 3; **L. Amador**, Pfizer, 3.

Abstract Number: 1242

Transcranial Direct Current Stimulation for Fatigue in Patients with Sjogren's Syndrome: A Randomized, Double-blind Pilot Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Sjögren's Syndrome Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

	Group	
	Active	Sham
Age (years) - Mean ± SD	55.8 ± 8.5	53.1 ± 10.3
Weight (kg) - Mean + SD	67.2 + 13.7	71.6 + 9.8
Height (meters) - Mean ± SD	1.6 ± 0.1	1.6 ± 0.1
Body Mass Index - Mean ± SD	26.8 ± 5.3	27.5 ± 3.5
Education (years)	11.9 ± 4.1	11.1 ± 3.7
Time since onset of symptoms (years) - Mean + SD	12.3 + 6.9	12.3 + 9.0
Time since diagnosis (years) - Mean ± SD	7.5 ± 5.4	6.4 ± 6.1
Concurrent comorbidities - n (%)	13 (72)	14 (78)
Arterial Hypertension - n (%)	4 (22)	4 (22)
Diabetes Mellitus - n (%)	3 (17)	2 (11)
Hyperlipidaemia - n (%)	1 (6)	2 (11)
Hypothyroidism - n (%)	2 (11)	2 (11)
Hashimoto's Disease - n (%)	2 (11)	0 (0)
Osteoporosis - n (%)	2 (11)	2 (11)
Osteoarthritis - n (%)	0 (0)	1 (6)
Anxiety Disorder - n (%)	2 (11)	0 (0)
Unipolar Depression - n (%)	0 (0)	1 (6)
Bipolar Depression - n (%)	0 (0)	1 (6)
Chronic obstructive pulmonary disease - n (%)	2 (11)	0 (0)
Raynaud Phenomenon - n (%)	1 (6)	1 (6)
Renal Tubular acidosis - n (%)	0 (0)	1 (6)
Arrhythmia - n (%)	0 (0)	1 (6)
Polycystic ovary syndrome n (%)	0 (0)	1 (6)
Taking biologics - n (%)	4 (22)	5 (28)
Number of NSAIDs and Analgesics - n (%)	4 (22)	2 (11)
Number of steroids - n (%)	7 (39)	8 (44)
Number of DMARDs - n (%)	10 (56)	9 (50)
Total taking medication for Sjogren - n (%)	17 (94)	18 (100)

n: number of participants; SD: standard deviation; n: number of participants; NSAIDs: Nonsteroidal anti-inflammatory drugs; DMARDs: Disease-modifying anti-rheumatic drugs. * Oral, patches, or injectables.

Table 1. Baseline demographics and clinical characteristics of participants. Active Group (n=18); Sham Group (n=18)

Primary Outcome		Baseline	T2	Change (T2 - Baseline)	T3	Change (T3 - Baseline)	T4	Change (T4 - Baseline)
Fatigue Severity Scale	Active - Mean ± SD	6.33 ±0.40	5.14 ±1.43	-1.18 ±1.20	5.37 ±1.28	-0.94 ±1.21	4.86 ±1.49	-1.46 ±1.46
Score range (1-7)	Sham - Mean ± SD	6.10 ±0.65	5.76 ±0.78	-0.34 ±0.91	5.25 ±1.47	-0.85 ±1.61	5.57 ±1.11	-0.53 ±1.04
Between-group difference	Mean			-0.85		-0.09		-0.93
	(95% CI)			(-1.57; -0.13)		(-1.07; 0.90)		(-1.79; -0.07)
Effect Size				0.80		0.06		0.73
Secondary Outcomes								
Mental Fatigue (PROFAD)	Active - Mean ± SD	5.40 ±1.27	3.94 ±2.26	-1.46 ±2.75	3.88 ±1.97	-1.54 ±2.48	3.69 ±2.01	-1.71 ±2.18
Score range (0-7)	Sham - Mean ± SD	4.86 ±2.40	4.44 ±1.55	-0.42 ±2.30	4.03 ±2.25	-0.83 ±2.85	4.31 ±2.11	-0.56 ±2.29
Between-group difference	Mean			-1.04		-0.71		-1.15
	(95% CI)			(-2.76; 0.67)		(-2.56; 1.13)		(-2.66; 0.36)
Effect Size				0.41		0.27		0.52
Somatic Fatigue (PROFAD)	Active - Mean ± SD	4.65 ±1.29	4.25 ±1.62	-0.40 ±1.34	3.87 ±1.92	-0.68 ±2.03	3.44 ±1.95	-1.21 ±2.22
Score range (0-7)	Sham - Mean ± SD	4.90 ±1.74	4.89 ±1.33	-0.01 ±2.21	4.58 ±1.66	-0.32 ±1.86	4.56 ±1.79	-0.34 ±1.82
Between-group difference	Mean			-0.39		-0.36		-0.87
	(95% CI)			(-1.63; 0.85)		(-1.69; 0.98)		(-2.24; 0.51)
Effect Size				0.21		0.18		0.43
Patient Reported Fatigue (ESSPRI)	Active - Mean ± SD	7.47 ±1.66	6.23 ±1.44	-1.23 ±1.52	6.29 ±1.45	-1.29 ±1.69	5.50 ±2.50	-2.11 ±1.81
Score range (0-10)	Sham - Mean ± SD	7.08 ±1.88	7.25 ±2.02	0.17 ±1.15	6.58 ±2.66	-0.50 ±2.23	6.44 ±2.15	-0.64 ±1.47
Between-group difference	Mean			-1.40		-0.79		-1.47
	(95% CI)			(-2.33; -0.48)		(-2.16; 0.57)		(-2.59; -0.35)
Effect Size				1.04		0.40		0.89
Patient Reported Dryness (ESSPRI)	Active - Mean ± SD	8.35 ±1.11	6.94 ±1.85	-1.41 ±1.97	6.71 ±2.78	-1.71 ±2.26	6.56 ±3.43	-1.89 ±3.08
Score range (0-10)	Sham - Mean ± SD	7.71 ±1.83	7.33 ±1.49	-0.38 ±1.42	7.00 ±2.11	-0.71 ±2.05	7.06 ±2.36	-0.66 ±1.72
Between-group difference	Mean			-1.03		-0.99		-1.23
	(95% CI)			(-2.21; 0.14)		(-2.47; 0.48)		(-2.94; 0.48)
Effect Size				0.60		0.46		0.49
Patient Reported Pain (ESSPRI)	Active - Mean ± SD	7.71 ±2.20	6.29 ±1.65	-1.41 ±1.94	6.65 ±3.04	-1.06 ±2.79	6.61 ±2.59	-1.22 ±2.71
Score range (0-10)	Sham - Mean ± SD	5.92 ±3.27	5.78 ±2.07	-0.14 ±2.96	5.67 ±2.72	-0.25 ±3.36	6.61 ±2.45	0.69 ±2.64
Between-group difference	Mean			-1.27		-0.81		-1.92
	(95% CI)			(-3.00; 0.46)		(-2.94; 1.32)		(-3.73; -0.10)
Effect Size				0.51		0.26		0.72
HRQoL - Physical Domain (SF-12)	Active - Mean ± SD	34.70 ±7.25	34.20 ±9.16	-0.50 ±6.46	38.54 ±9.61	3.80 ±7.13	39.52 ±9.23	4.82 ±9.66
Score range (0-100)	Sham - Mean ± SD							
Between-group difference	Mean	35.00 ±10.07	36.65 ±7.04	1.65 ±8.58	37.41 ±9.75	2.40 ±10.94	37.26 ±9.92	9.66 ±11.01
	(95% CI)							
Effect Size				-2.14		1.40		2.57
				(-7.29; 3.00)		(-5.00; 7.80)		(-4.44; 9.59)
				0.28		0.15		0.25
HRQoL - Mental Domain (SF-12)	Active - Mean ± SD	43.10 ±12.30	45.98 ±10.09	2.88 ±8.95	48.31 ±9.35	4.64 ±12.32	47.90 ±11.42	4.80 ±12.60
Score range (0-100)	Sham - Mean ± SD							
Between-group difference	Mean	38.67 ±13.05	42.19 ±10.53	3.52 ±6.42	40.06 ±13.85	1.39 ±13.47	40.51 ±11.08	1.84 ±10.39
	(95% CI)							
Effect Size				-0.63		2.88		2.96
				(-5.91; 4.64)		(-6.01; 11.78)		(-4.87; 10.78)
				0.08		0.25		0.26
General Health (VAS)	Active - Mean ± SD	5.56 ±2.81	3.78 ±2.09	-1.78 ±3.06	4.45 ±2.57	-1.13 ±3.88	4.17 ±2.26	-1.39 ±3.96
Score range (0-10)	Sham - Mean ± SD	5.59 ±2.95	3.85 ±2.60	-1.74 ±2.74	5.04 ±1.76	-0.55 ±3.04	5.64 ±1.43	0.050 ±3.38
Between-group difference	Mean			-0.03		-0.58		-1.43
	(95% CI)			(-2.00; 1.93)		(-2.98; 1.81)		(-3.93; 1.06)
Effect Size				0.01		0.17		0.39

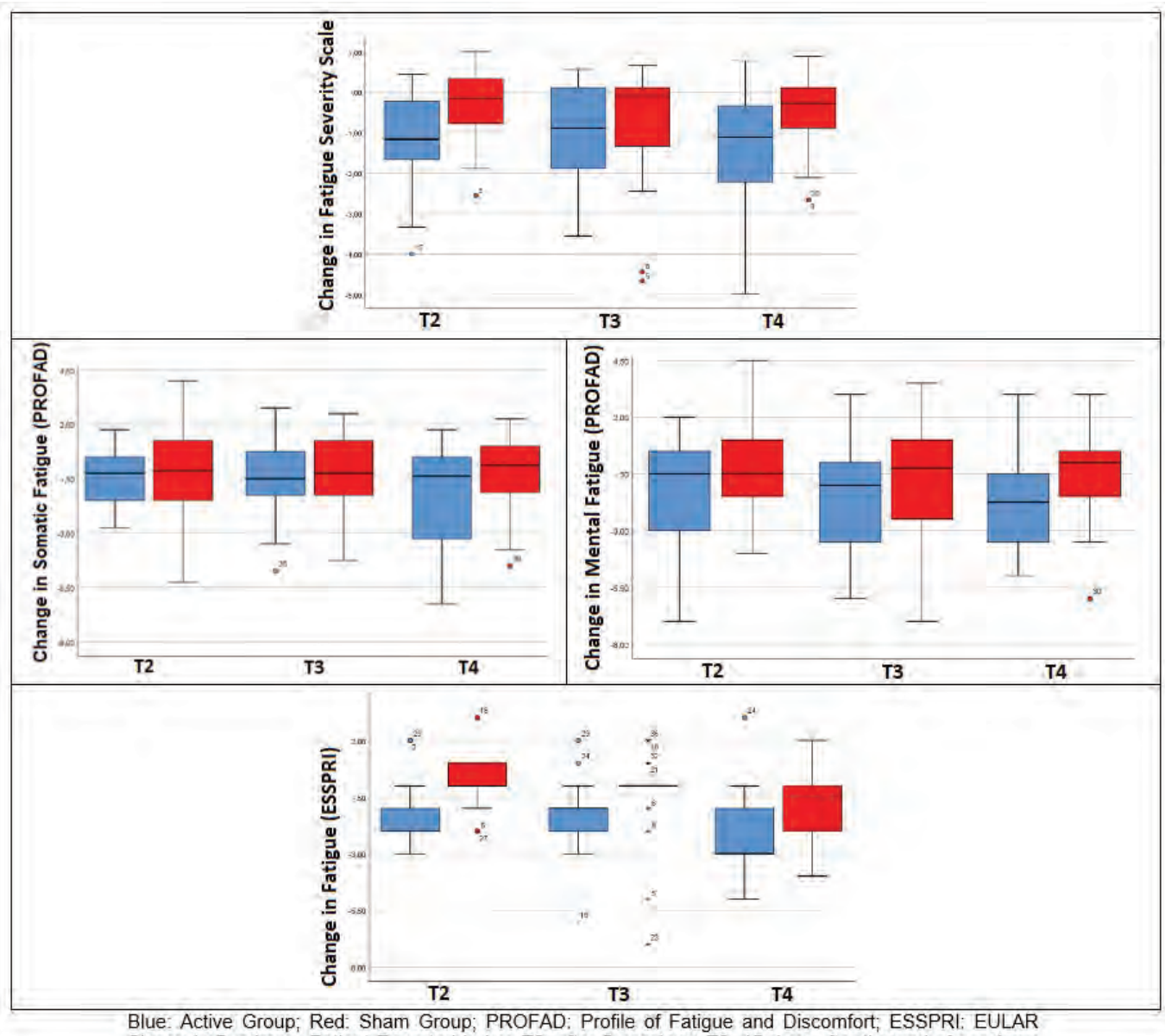
n: number of participants; SD: standard deviation; CI: confidence interval; PROFAD: Profile of Fatigue and Discomfort; ESSPRI: EULAR Sjogren's Syndrome Patient Reported Index; HRQoL: Health-related Quality of Life; SF-12: Short-form 12 Health Survey; VAS; Visual analogue scale; T2: after 5 sessions; T3: 15 days after the end of sessions; T4: 30 days after the end of sessions; Changes were calculated between time points T2, T3 and T4 from baseline values. In FSS, PROFAD, ESSPRI, and VAS assessments, higher values represent worse outcomes; for HRQoL higher values represent better outcomes. **One patient in the active group did not attend their follow-up appointment 15 days after the end of stimulation.

Table 2. Primary and secondary outcomes at each time point, change scores from baseline, and group comparison of change scores at each time point. Active Group (n=18); Sham Group (n=18)

Background/Purpose: Transcranial direct-current stimulation (tDCS) has shown promise to decrease fatigue. However, it has never been examined in primary Sjogren Syndrome (pSS). We aimed to assess the effect of a tDCS protocol on fatigue in patients with pSS.

Methods: This is a parallel, double-blind pilot study (**NCT04119128).** Women aged 18-65 years, with pSS, on sTable pharmacological therapy, with complaints of fatigue for at least three months, and with scores > 5 on Fatigue Severity Scale (FSS) were included. We randomized 36 participants to receive five consecutive or sham tDCS sessions, with an intensity of 2mA, for 20 minutes/day.

Results: After five tDCS sessions, fatigue severity assessed by the FSS (primary outcome) demonstrated a mean group difference of -0.85 [95% confidence interval (CI) -1.57, -0.13; effect size 0.80] favoring the active group. The



Blue: Active Group; Red: Sham Group; PROFAD: Profile of Fatigue and Discomfort; ESSPRI: EULAR Sjogren's Syndrome Patient Reported Index; T2: after 5 sessions; T3: 15 days after the end of sessions; T4: 30 days after the end of sessions; Changes were calculated between time points T2, T3 and T4 from baseline values.

The central box spans the interquartile range (IQR - first to third quartile). The segment inside the box shows the median values. Whiskers sprout from the two ends of the box until they reach the sample maximum and minimum values. Outliers are either 3×IQR or more above the third quartile or 3×IQR or more below the first quartile. Outliers are displayed as dots above and below the whiskers.
**One patient in the active group did not attend their follow-up appointment 15 days after the end of stimulation.

Figure 1. Box-plots presenting changes in Fatigue Severity Scale, somatic fatigue, mental fatigue and patient self-reported fatigue. Active Group (n=18); Sham Group (n=18).

active group presented significantly greater reductions in fatigue as measured by the EULAR Sjögren's Syndrome Patient Reported Index after five tDCS sessions [mean group difference: 1.40; 95%CI -2.33, -0.48; effect size 1.04]. Although there were no between-group differences in the secondary outcomes of sleep, mood and anxiety, within-group comparisons evidenced a small but significant difference in the active group for depression and sleep. There were no significant cortisol changes. All reported adverse events were mild and transitory.

Conclusion: tDCS seems to be safe and reduce fatigue in pSS. Given that tDCS treatment may have a differential effect on mood and sleep but not on cortisol levels, the dorsolateral prefrontal-affective network may mediate tDCS effects on fatigue.

Disclosure: A. Pinto, None; **S. Piva**, None; **A. Vieira**, None; **S. Gomes**, None; **A. Rocha**, None; **D. Tavares**, None; **M. Santana**, None; **C. Carlesso**, None; **A. Andriolo**, None; **F. Santos**, None; **F. Fregni**, None; **V. Trevisani**, None.

Abstract Number: 1243

Self-reported Fatigue in Patients with Primary Sjögren's Syndrome Is Associated with an Objective Decline in Physical Performance and Symptoms of Pain and Depression

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Fatigue is a major complaint in autoimmune diseases including primary Sjögren's syndrome (pSS). For many pSS patients, fatigue is their most dominant and disabling symptom. In a conceptual framework[1], fatigue is defined as a self-reported symptom derived from 2 attributes: 1. performance fatigability, an objective decline in performance, and, 2. changes in anticipated capabilities of the performer (modulated by factors such as pain and depression). In multiple sclerosis, studies have already demonstrated a relation between performance decline and self-reported fatigue[2]. So far, no data are available on performance fatigability in pSS. Our objectives were to assess

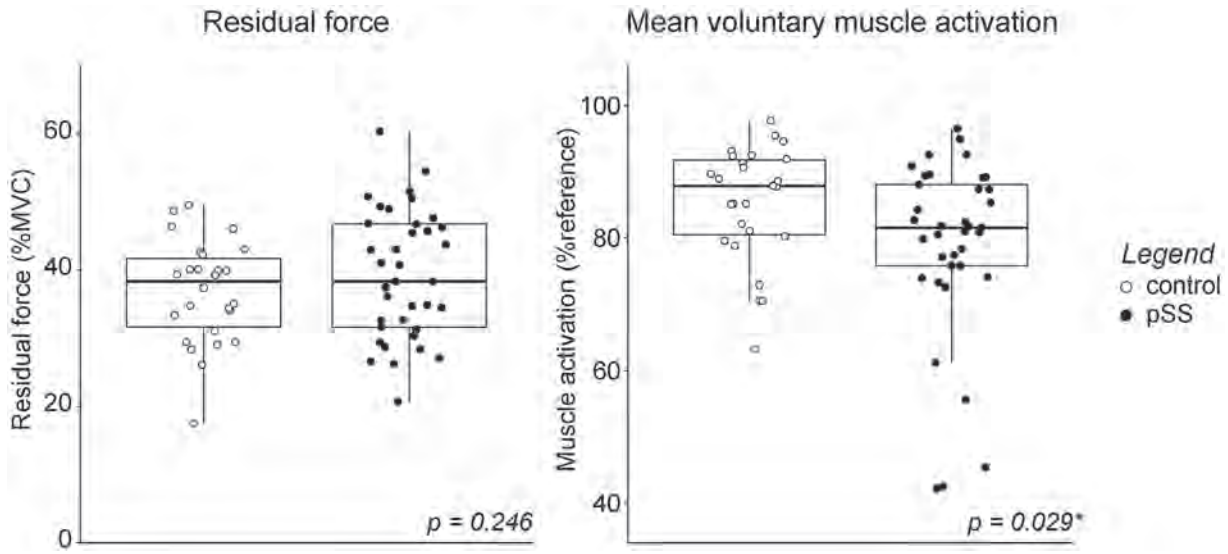
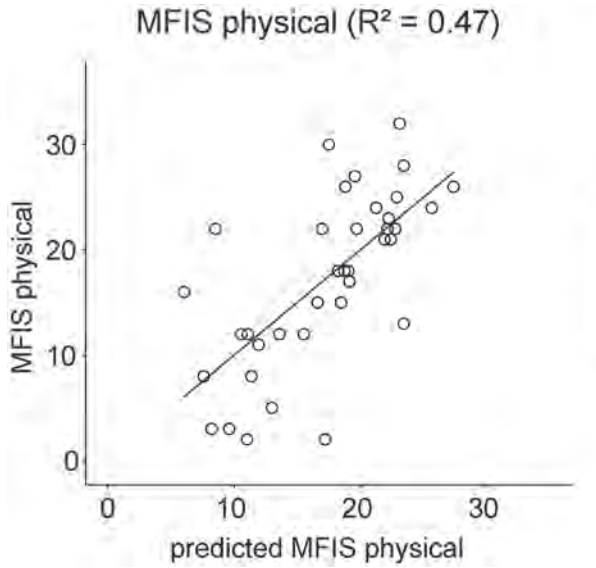


Figure 1. Measures of performance fatigability. A) Residual force following the sustained maximal voluntary contraction, expressed as a percentage of maximal force (MVC). B) Voluntary muscle activation (mean across 7 time-points) during the sustained maximal voluntary contraction. Voluntary muscle activation of 100% indicates that the muscle is firing at its maximal capacity, and that central nervous system drive is optimal. P-values are shown in both graphs.



Predictor	*standardised β*	*p-value*
HADS depression	0.479	0.001
ESSPRI pain	0.343	0.019
Residual force	0.314	0.023

Figure 2. Relationship between self-reported fatigue (MFIS physical) and performance fatigability, pain, and depression. Predicted MFIS physical score is based on results of the multivariable regression. Standardized beta's and p-values of the model predictors are shown on the right. MFIS = Modified Fatigue Impact Scale; HADS = Hospital Anxiety and Depression Scale.

whether performance fatigability is affected in pSS, and to explore its relations with self-reported fatigue, pain, and depression.

Methods: Thirty-nine pSS patients (fulfilling the 2016 ACR-EULAR criteria; 5 males, age 27-65 years) and 27 healthy control participants (5 males, age 27-65 years) were included in the study. To assess performance fatigability, participants generated a sustained (124 s) maximal voluntary contraction (MVC) with the index finger abductor muscle; force was recorded using force-transducers. During the contraction, voluntary muscle activation was indexed by electrical stimulation of the ulnar nerve (for details:[2]). Self-reported fatigue was quantified using questionnaires: Fatigue Severity Scale (FSS) and, in patients only, Modified Fatigue Impact Scale (MFIS). The MFIS distinguishes a physical and cognitive domain. Pain and depression were measured using the EULAR Sjögren's Syndrome Patient Reported Index (ESSPRI pain) and Hospital Anxiety and Depression scale (HADS), respectively. Differences between pSS and controls were assessed using ANOVAs or Mann-Whitney U tests. Linear regression analysis was performed to determine which factors could explain increased levels of self-reported fatigue in pSS.

Results: With regard to performance fatigability, residual force after the sustained MVC did not differ between groups. However, voluntary muscle activation was reduced in pSS ($p = 0.029$, Fig. 1). Self-reported fatigue was significantly higher in pSS than controls (FSS median: 4.8 vs. 2.3, $p< 0.001$), and 67% of the pSS patients reported significant fatigue (FSS >4) versus none of the controls. In pSS, 47% of the variance in MFIS physical could be explained by residual force after the sustained MVC, and partly by pain and depression ($p< 0.001$, Fig. 2). FSS and MFIS cognitive could be best explained by HADS depression scores.

Conclusion: Performance fatigability in pSS was compromised by reduced voluntary muscle activation. Furthermore, self-reported fatigue in pSS was related to objectively measured performance decline (i.e. performance fatigability), as well as symptoms of pain and depression. These findings indicate that performance fatigability should be considered when investigating fatigue, and may serve as an important outcome measure for future clinical trials.

References:

1. Enoka et al., Med Sci Sports Exerc. 2016 Nov 48(11):2228-38.
2. Steens et al., Neurorehabil Neural Repair. 2012 Jan 26(1):48-57.

Disclosure: R. Prak, None; **S. Arends**, Pfizer, 2; **G. van Zuiden**, Roche, 8; **F. Kroese**, Bristol-Myers Squibb, 2, 5, 8, Roche, 8, Janssen-Cilag, 8; **H. Bootsma**, Bristol-Myers Squibb, 2, 5, 8, Roche, 2, 5, Novartis, 5, 8, Medimmune, 5, Union Chimique Belge, 5; **I. Zijdewind**, None.

Abstract Number: 1244

Clinical Characteristics and Outcomes in Patients with Primary Sjögren's Syndrome-Associated Interstitial Lung Disease

Joanna Marco[1], Gregory Gardner[1] and Nishant Gupta[2], [1]University of Washington, Seattle, WA, [2]University of Cincinnati, Cincinnati

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's syndrome (pSS) is a chronic autoimmune exocrinopathy that features interstitial lung disease (ILD) in up to 16% of patients. The clinical characteristics and natural history of pSS-associated ILD (pSS-ILD) are not well defined.

Methods: Patients with pSS-ILD were identified at two academic institutions: University of Cincinnati and University of Washington. Clinical data including demographics, diagnosis dates, serologies, imaging findings, histopathology, pulmonary function testing results, and treatments were abstracted from chart review. ILD patterns were assigned on the basis of histopathology (when available) and radiology characteristics on chest high-resolution CT scans. Categorical variables are summarized as frequencies and percentages, and continuous variables are summarized as median and range. Survival analysis was conducted using Kaplan-Meier method.

Results: There were a total of 81 patients with pSS-ILD in our cohort. The majority of the patients (86%, 70/81) were women. Sjögren's-related antibodies were common. Positive SSA alone was observed in 49%, positive SSB alone was observed in 3%, and both SSA and SSB were observed in 40%. ILD was the presenting manifestation of pSS in 17 (21%) patients. ILD and pSS were diagnosed concurrently in 34 (43%) patients. In the remaining patients (36%, 28/79), the diagnosis of ILD was established after a median of 6 years (range 1-31 years) following the diagnosis of pSS.

The most common ILD pattern in our cohort was usual interstitial pneumonia (UIP) (32%, 25/78), followed by nonspecific interstitial pneumonia (NSIP) (28%, 22/78), lymphocytic interstitial pneumonia (LIP) (21%, 16/78), and organizing pneumonia (OP) (10%, 8/78). Over a median follow-up of 4 years, 70% (46/66) had a sTable or improving functional vital capacity, and 75% (47/63) had a sTable or improving diffusion capacity for carbon monoxide.

The diagnosis of pSS-ILD led to a new immunomodulatory therapy in 54 (67%) patients. The most common steroid-sparing immunomodulatory medications utilized were mycophenolate (49%), hydroxychloroquine (44%), azathioprine (25%), and rituximab (7%). 21 patients (26%) with pSS-ILD died during follow-up. The median survival time after ILD diagnosis was 11 years (95% confidence interval: 6-12 years).

Conclusion: ILD is frequently seen and can be the presenting manifestation in patients with pSS. UIP and NSIP are the most common ILD patterns in patients with pSS-ILD. Although most patients with pSS-ILD have sTable to improving pulmonary function tests over time, approximately one-fourth may continue to decline over time. Close serial monitoring is warranted to identify the subset of patients that are declining and institute timely interventions. The diagnosis of ILD has a substantial impact on pharmacological therapy and overall patient survival.

Disclosure: J. Marco, None; **G. Gardner**, None; **N. Gupta**, None.

Abstract Number: 1245

Smoking Might Reduce Odds of Sjögren's Syndrome Among Rheumatoid Arthritis Patients

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Smoking increases the risk of many rheumatic disease, including rheumatoid arthritis (RA). Previous studies have identified that current smoking might reduce the risk of primary Sjögren's syndrome (SS), but it remains unknown whether smoking is positively or negatively associated with SS among RA patients. The objective of this cross-sectional study was to examine the relationship between smoking and RA-SS overlap in a large RA cohort.

Methods: Electronic health records from a rural, population-based cohort were screened for RA cohort eligibility. Inclusion criteria include age ≥18 years, at least two RA diagnosis codes from a rheumatologist on distinct dates within a two year period or positive rheumatoid factor or ant-CCP antibody between 1/1/2005 and 12/31/2018. Index date was defined by the first RA diagnosis code. The baseline period for evaluation of comorbidities and medication use began twelve months before the index date. The independent variable of smoking status was defined as never, current, or past (quit) smoker at or before the index date. The dependent variable of SS was defined by ICD 9 code 710.2. Descriptive statistics were performed using chi square for categorical and unpaired student's t-test for continuous variables. Multivariable logistic regression was performed to determine odds ratios (ORs) of SS as the primary outcome by smoking status. Models were adjusted for age, sex, and race.

Results: Among 1861 patients with RA identified for cohort inclusion, 1296 patients had a reported smoking status available. Current smokers were younger and had lower female predominance than never and past smokers (Table 1). Fewer current smokers had anemia, congestive heart failure, hypertension, hypothyroidism, and renal disease. Descriptive analysis of RA patients with or without SS revealed that SS patients were more likely to be female and less likely to be anemic or smoke (Table 2). Adjusted OR of female sex was positively associated with SS (OR 2.56 [95% Confidence Interval (CI) 1.48-4.73]; Table 3). Current smoking was negatively associated with SS (OR 0.2 [95% CI 0.06-0.68]). Because data on smoking before cohort entry were missing for 565 patients, we repeated analysis on smoking status of patients captured before cohort exit (38 patients missing) and reproduced these results (data not shown).

Table 1. Demographics of RA Patients by Smoking Status at Cohort Entry (n=1861)

	Never Smoker (n=589)	Past Smoker (n=406)	Current Smoker (n=301)	p
Age mean (SD)	58.7 (16.3)	63.2 (13.4)	53.1 (12.6)	<0.0001
Female n (%)	471 (80)	234 (58)	200 (67)	<0.0001
Race n (%)				0.01
Asian	6 (1)	0	0	
Black	1 (0.2)	1 (0.3)	1 (0.3)	
Caucasian	570 (97)	393 (98)	286 (96)	
Other	5 (1)	5 (1)	11(4)	
Hispanic Ethnicity n (%)	12 (2)	3 (1)	7 (2)	0.25
Payor n (%)				<0.0001
Commercial or Workers Comp n (%)	118 (20)	69 (17)	42 (14)	
Medicaid	68 (12)	41 (10)	76 (25)	
Medicare	143 (24)	126 (31)	55 (18)	
Unknown	260 (44)	179 (42)	128 (43)	
Comorbidities n (%)				
Anemia	80 (14)	58 (14)	23 (8)	0.01
CHF	22(4)	24 (6)	6 (2)	0.03
COPD	77 (13)	84 (21)	55 (18)	0.004
Depression	71 (12)	62 (15)	54 (18)	0.05
DM	71 (12)	74 (18)	39 (13)	0.02
HTN	242 (41)	197 (49)	89 (30)	<0.0001
Hypothyroidism	96 (16)	64 (16)	31 (10)	0.04
Solid Tumor	36 (6)	39 (10)	15 (5)	0.04
Obesity	113 (19)	98 (24)	60 (20)	0.16
Renal Disease	54 (9)	39 (10)	11(4)	0.003
HCQ Use	202 (34)	151 (37)	107 (36)	0.64

CHF=Congestive Heart Failure; COPD=Chronic Obstructive Pulmonary Disease; DM=Diabetes Mellitus; HCQ=Hydroxychloroquine; Missing n=565.

Conclusion: We report for the first time that RA patients who smoke had 80% lower odds of SS. Previously, studies have shown reduced risk of primary SS in current smokers, supporting our findings. We found female sex in RA had a greater than 2.5 fold association with SS. Our data suggest a negative correlation between smoking and SS among RA patients. Our cross-sectional observational study cannot exclude reverse causality of quitting smoking with SS symptoms. Future studies should prospectively examine pack year dose relationships with overlap RA-SS incidence to further examine risk reduction and causality.

Table 2. Demographics and Comorbidities of Sjögren's Syndrome (SS) Among RA Patients (n=1861)

	RA-SS (n=96)	RA No SS (n=1765)	p
Smoking Status at Cohort Entry**			
Current	3 (6)	298 (24)	0.0008
Past	15(29)	391 (31)	
Never	34 (65)	555 (45)	
Age mean (SD)	60.5 (14.5)	57.82 (15.2)	0.09
Female n (%)	82 (85)	1231 (70)	0.0005
Race n (%)*			0.24
Caucasian	94 (98)	1668 (95)	
Other	1 (1)	41 (2)	
Hispanic Ethnicity	0	26 (1)	0.10
Payor			
Commercial or Workers Comp n (%)	10 (10)	219 (12)	0.27
Medicaid	15 (16)	404 (23)	
Medicare	17 (18)	259 (15)	
Unknown	54 (56)	883 (50)	
Comorbidities n (%)			
Alcohol Abuse	1 (1)	31 (2)	0.57
Anemia	17 (18)	189 (11)	0.047
CHF	4 (4)	57 (3)	0.63
COPD	18 (19)	254 (14)	0.25
Depression	13 (14)	233 (13)	0.93
DM	7 (7)	221 (13)	0.10
HTN	35 (37)	635 (36)	0.93
Hypothyroidism	11 (12)	236 (13)	0.58
Solid Tumor	6 (6)	101 (6)	0.87
Obesity	12 (13)	336 (19)	0.09
Renal Disease	8 (8)	105 (6)	0.37

CHF=Congestive Heart Failure; COPD=Chronic Obstructive Pulmonary Disease; DM=Diabetes Mellitus;*Missing Race n=49; **Missing Smoking n=565.

Table 3. Odds of Sjögren's Syndrome Among RA Patients

Explanatory Variable	Unadjusted Odds Ratio (CI)	Adjusted* Odds Ratio (CI)	p
Male	Ref	Ref	
Female	2.54 (1.43-4.52)	2.65 (1.48-4.73)	0.001
Smoking Status at Cohort Entry			
Never	Ref	Ref	
Past	0.63 (0.34-1.17)	0.68 (0.36-1.30)	0.25
Current	0.16 (0.05-0.54)	0.20 (0.06-0.68)	0.01

*Adjusted for age, sex, and race; CI=95% confidence interval

Disclosure: S. McCoy, Bristol-Myers Squibb, 1, Novartis, 1; **C. Bartels**, Independent Grants for Learning and Change (Pfizer), 2.

Abstract Number: 1246

Sjogren's Syndrome and Its Risk of Cervical Lesions

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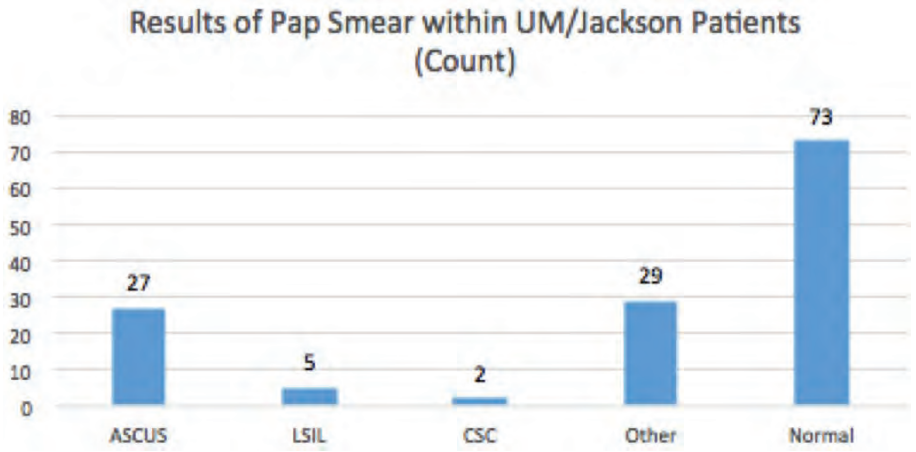
SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjogren's syndrome is chronic inflammatory disease that results in lacrimal and salivary dysfunction and can include extra-glandular manifestations. While it is well established that patients with auto-immune conditions such as systemic erythematous lupus and rheumatoid arthritis have an increased risk of cervical dysplasia, the risk of Sjogren's syndrome and cervical malignancy has not been determined due scarce data. Epidemiological data shows that 5% of all national papanicolaou smears results in atypical squamous cells of undetermined significance (ASCUS), while low-grade squamous intraepithelial lesions (LSIL) is found in 2% of pap smears, and less than 1% result is cervical cancer. Determining the risk of cervical lesions from Sjogren's syndrome, may lead to better understanding of its risk of cervical dysplasia, possibly affecting cervical cancer screening guidelines for these patients.

Methods: Retrospective chart review of women between the age of 21-65 years of age in the Jackson Health care system and University of Miami was performed using ICD 9 and 10 codes for Sjogren's syndrome (710.2, M35.0) between the years 2010 to 2019. Cervical pathology results were recorded for each patient as well as their HPV status, HIV status, immunosuppression history, and other auto-immune diagnoses. Descriptive analysis of these data points was conducted.

Results: We identified 136 women with an ICD 9 or 10 diagnosis of Sjogren's from the Jackson Memorial hospital and University of Miami Health systems. Out of the 136 women, 34 women had abnormal cervical cells, which consisted of 27 pap smear samples resulting with ASCUS, 5 with LSIL, and 2 with cervical squamous carcinoma. This amounted to 25% having concerning pap smears, with 62.3% of these samples infected with high risk HPV strains. Out of the women with reported ASCUS, 16 were positive for high risk HPV, and out of the women with LSIL 1 was



positive for high risk HPV. The rest of the 102 women had pap smears negative for cervical dysplasia, however 29 of those women had pap smears that resulted in inflammatory, reactive, or atrophic changes.

Conclusion: Results revealed that women from our retrospective study diagnosed with Sjogren's syndrome were found to have abnormal cervical cells on pap smears at a rate much higher than the national average. Although 62.3% of these women with ASCUS/dysplasia were also infected with high risk HPV, the increased rate of ASCUS results at 19.9% is significantly higher than the national rate of 5% in U.S women. There was also an increase in pap results yielding in inflammatory and reactive changes. Although there is limited data published on Sjogren's syndrome and cervical dysplasia, our results poses interest in the possibility of Sjogren's leading to increased cervical inflammation, as well as susceptibility to HPV-infections that may lead to cervical dysplasia. These findings suggest we should be vigilant about offering our Sjogren's patients appropriate HPV vaccination and ensure appropriate cervical cancer screening has been done.

Disclosure: K. Corbitt, None; **I. Lopez**, None; **S. Culpepper**, None.

Abstract Number: 1247

Features of Childhood Sjogren's Syndrome: A Literature Review Based Cohort

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjogren's syndrome (SS) is an autoimmune chronic disease characterized by inflammation of exocrine glands, but it can affect other organs as well. This study aims to describe childhood SS (cSS) features by reviewing pediatric published cases with individual data.

Methods: We conducted a literature review of cSS (age < 18 years). Eligible papers were identified through a Medline search of English language articles published in the PubMed database until February 2020. Statistical analysis was performed to detect associations between clinical/laboratory features.

Results: Two-hundred-forty patients were identified (191 female); the median age at disease onset was 10 years (range 3 months-17 years). Main clinical features are shown in Figure 1. The most frequently reported clinical SS-specific feature was parotitis (134/198 patients; bilateral:unilateral=2.5:1); fewer patients had sicca symptoms (89/159 with dry eyes; 85/144 with dry mouth). Arthritis was the most frequent extraglandular manifestation. Renal tubular acidosis represented the typical expression of renal involvement (19 cases). Neuromyelitis optica and aseptic meningoencephalitis (6 and 9 cases, respectively) were the most typical neurologic manifestations. Two cases of interstitial lung disease and one of pulmonary hypertension were reported. Investigations are shown in Figure 2. Almost all patients had autoantibodies, mostly ANA (200/224 patients) and anti- SSA/Ro (170/208 patients). The Schirmer test was per-

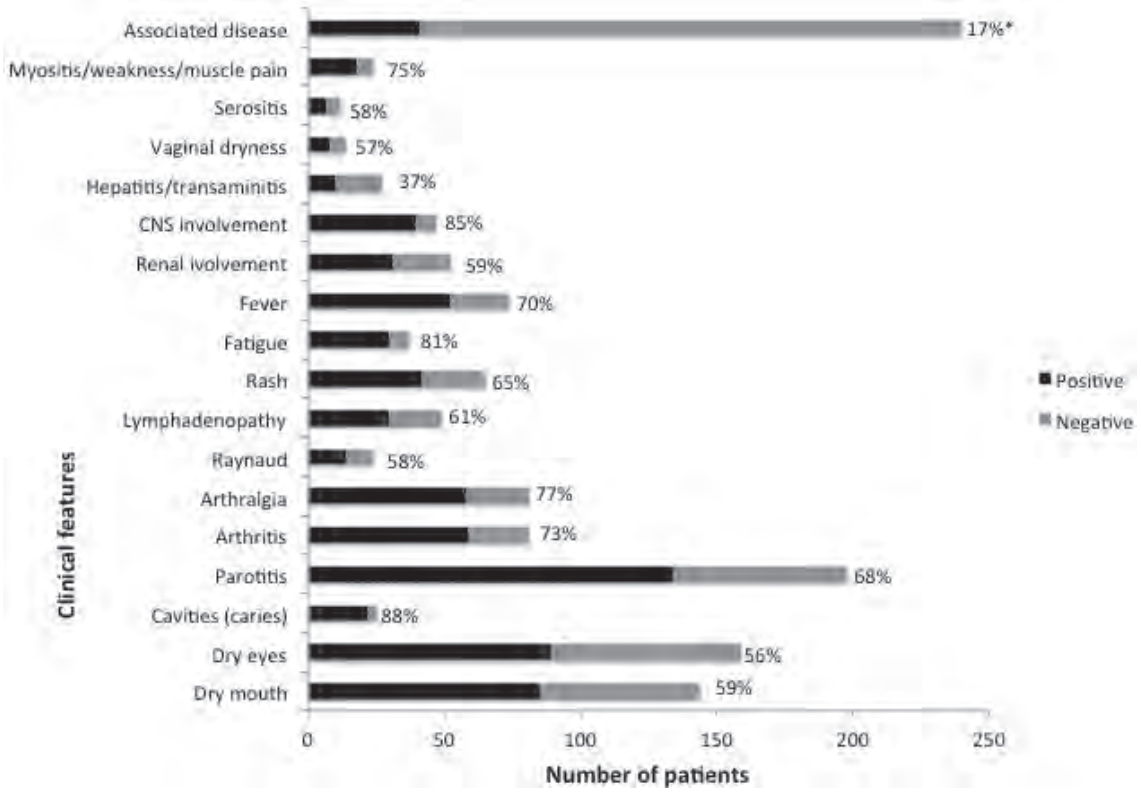

Figure 1. Main clinical features. *Values are the number of patients with positive findings/patients with available information (%). CNS: central nervous system

formed in less than half of the patients, of whom 62% tested positive. A positive result of minor salivary biopsy was reported in 129/140 cases with available data. Juvenile idiopathic arthritis was the most frequently associated disease, followed by systemic lupus erythematosus (16 and 8 cases, respectively). No significant differences between patients with or without parotitis were found except that patients with parotitis showed increased levels of CRP more frequently than those without it (p= 0.00). Patients with anti-SSA/Ro had more frequently a positive Schirmer test (p= 0.04). The presence of RF was significantly associated with dry mouth (p= 0.00), arthritis (p= 0.00), and rash (p= 0.04). A positive minor salivary biopsy was more common in children with dry eyes than in those without this clinical feature (p= 0.02). Arthritis was more frequent in patients with other diseases than in those with primary SS (p= 0.00). We further investigated SS features according to the age groups (≤ 6 years, 7-11 years, ≥ 12 years). Parotid involvement was inversely proportional to the age and occurred more frequently in younger patients (79% of those ≤ 6 years; p= 0.03). Interestingly, the rate of anti-SSA/Ro positivity increased with age (97% of those ≥ 12 years; p= 0.00).

Conclusion: Even though parotitis was the most frequently reported feature, a wide range of clinical manifestations in children with SS has been reported so far. A better knowledge of cSS features will help to pave the way for the development of cSS specific diagnostic criteria.

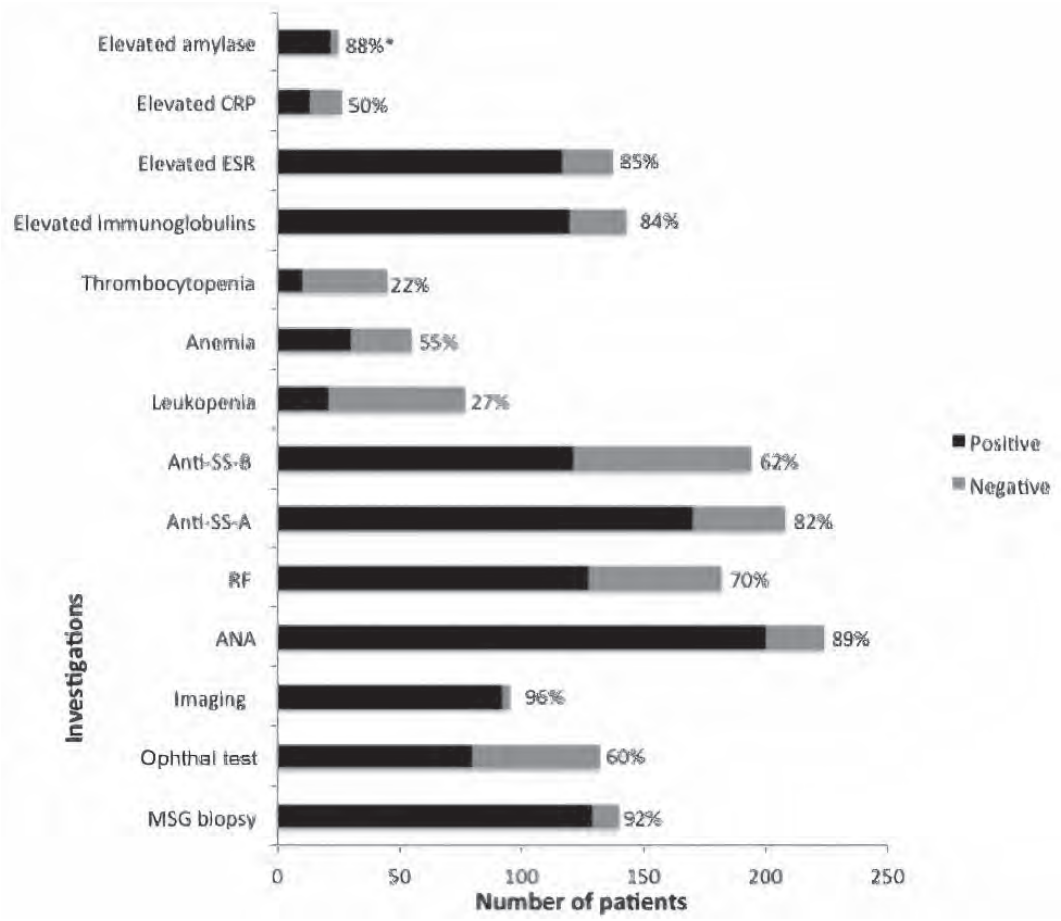

Figure 2. Investigations. *Values are the number of patients with positive findings/patients with available information (%). CRP :C-reactive protein; ESR: erythrocyte sedimentation rate; RF: rheumatoid factor; ANA: antinuclear antibodies; Opthalm test: Ophthalmological test (Schirmer test or Rose Bengal staining); MSG biopsy: minor salivary gland biopsy.Imaging: parotid ultrasound or computed tomography, sialogram, scintigraphy

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Disclosure: A. Marino, None; **M. Romano**, None; **T. Giani**, None; **C. Gaggiano**, None; **S. Costi**, None; **R. Singh**, None; **J. Mehta**, None; **S. Lieberman**, None; **R. Cimaz**, None.

Abstract Number: 1248

Patients Seropositive for La/SSB Without Ro/SSA Differ from Those Displaying La/SSB with Ro/SSA in a Single Center Sjogren's Cohort

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Sjögren's disease (SS) is characterized by the presence of antibodies against protein-small RNP complexes designated Ro/SSA and La/SSB. Both are included in the 2002 American-European Consensus Group Criteria (AECG) for SS, however La/SSB was excluded from the 2016 ACR-EULAR on the basis of findings[1,2] demonstrating that SS patients seropositive for La/SSB without Ro/SSA (La/SSB) lacked an association with the phenotypic features of SS. We examined our single-center rheumatology division based primary SS cohort for the presence of patients SS displaying La/SSB. The phenotypic characteristics of this subset was compared to SS patients seropositive for La/SSB and Ro/SSA.

Methods: We retrospectively reviewed the charts of 318 patients for primary SS to determine the prevalence of La/SSB . Patients suspected of having secondary SS on the basis of the presence of another major connective tissue disorder were excluded. One hundred and twenty-eight fulfilled AECG. La/SSB were matched by age and symptom duration to an equal number of patients who were positive for La/SSB and Ro/SS-A. Groups were examined for sex, race, sicca symptoms, number of extraglandular manifestations (EGM), fulfillment of AECG, presence of ANA, RF, and IgG level at presentation. The difference between continuous variables was determined by the Wilcoxon ranked sign test. Differences in proportions among categorical variables was determined by Fisher's exact test.

Results: Of the 318 evaluated charts, 17 had La/SSB without Ro/SSA (5.3%). When compared to 17 with La/SSB and Ro/SSA, differences in clinical and laboratory characteristics were noted. La/SS-B displayed significantly fewer EGM, fulfilled AECG less often, and had significantly lower levels of RF, ANA and serum IgG. La/SSB were more often Caucasian (NS) (see Table 1 for details). The 5 La/SSB who fulfilled AECG represented 3.9% of the 128 patients fulfilling AECG; all 5 had positive labial salivary gland biopsies.

Conclusion: Consistent with results from the SICCA cohort[1] and the OMRF cohort[2], a small percentage (3.9%) of our rheumatology division based SS cohort who fulfilled SS criteria had La/SSB in the absence of Ro/SSA. In the majority of cases, La/SSB appears to constitute an atypical form of SS or represent a related but distinct autoimmune disorder.

References; [1]Baer A. et al. Ann. Rheum. Dis. 2015:74(8); 1557-1561 [2] Danda D. et al. Clin. Exp. Rheumatol. 2017:35; 438-444

Characteristic	La/SSB only	La/SSB and Ro/SSA	P
Sex (F)	82.3 %	100.0%	0.227
Race (Caucasian)	88.2%	64.7%	0.225
Ocular sicca	82.3%	100.0%	0.102
Oral sicca	100.0%	100.0%	>0.999
Mean EGM	0.94	1.41	**0.002**
Fulfilled AECG	29.4%	100.0%	**<0.0001**
ANA	41.2%	76.5%	**0.0365**
RF	17.6%	47.1%	**0.0283**
IgG elevation	14.2%	56.3%	**0.0173**

Differences between Sjogren's patients displaying La/SSB alone versus La/SSB with Ro/SSA

Disclosure: R. Mongroo, None; **S. Chowdhury**, None; **S. Carsons**, Novartis, 2.

Abstract Number: 1249

The Impact of Anti-Ro Antibodies on the Pregnancy Outcome in Relation to Maternal Disease Presentation: A Descriptive Analysis of 231 Pregnancies

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Anti-Ro antibody positivity is linked to adverse fetal outcomes like congenital heart block CHB (2%) and neonatal lupus. The incidence of CHB increases to 6-13% with subsequent pregnancies.

These antibodies are present in cases of primary Sjogren, SLE, Rheumatoid as well as asymptomatic population. It's unclear if the virulence of these antibodies is linked to the underlying disease.

Many asymptomatic women are identified retrospectively after having a baby with Congenital Heart block.

The purpose of this study is to describe the impact of anti-Ro positivity on the pregnancy outcome and it's relation to the underlying maternal disease.

Methods: We retrospectively collected data from a specialized Pregnancy and Rheumatic Disease clinic at the largest tertiary hospital in Qatar. We targeted this clinic due to the standardized approach and treatment.

All cases with anti-Ro positivity were included and stratified according to the underlying disease. The analysis was performed using SPSS software.

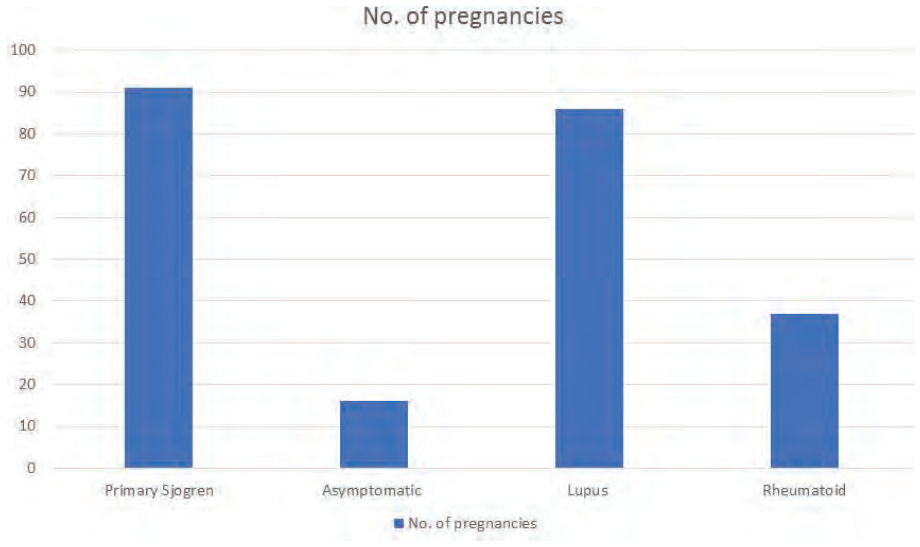

Chart 1. Number of pregnancies per Rheumatic diseases.

Fetal complication	Frequency in Total	Highest rate in:
Miscarriage	25.5%	SLE, Primary Sjogren
Prematurity	14.7 %	SLE, Primary Sjogren
IUFD	3%	Primary Sjogren
Congenital Heart Block	1.2 %	Asymptomatic mothers

Table1. Adverse Fetal Outcomes

Anti Ro titer	Frequency of adverse events (N)
< 50	14
51-100	19
101-200	9
>200	48

Table 2. Anti- Ro titer (u/ml) in relation to the rate of adverse fetal outcomes.

Results: We identified 231 pregnancies of 62 mothers from our records between 2017-2020.

One hundred and sixteen pregnancies occurred after the diagnosis.

Disease Stratification: Primary Sjogren (92 pregnancies), SLE(86 pregnancies), Rheumatoid (37 pregnancies), and Asymptomatic (16 pregnancies). Chart 1.

Adverse outcomes: eleven pregnancies (4.8%) were complicated by pre-eclampsia, while (6.5%) had gestational diabetes.

Fetal adverse events: Miscarriage was the most prominent (25.5%), followed by prematurity (4.7%), then IUFD (3%). These adverse events occurred more frequently in patients with SLE and primary Sjogren (Table 1).

Asymptomatic anti-Ro positivity and congenital heart block: CHB occurred in 3 asymptomatic cases. Two of them required permanent pacemaker and 1 developed transient bradycardia.

These Asymptomatic women had 11 healthy pregnancies in total before this event. And 2 of them had healthy pregnancies on hydroxychloroquine after their babies with CHB.

No cases of CHB were identified among the other diseases.

Hydroxychloroquine role: HCQ was used in 94 pregnancies as treatment of the underlying diagnosis. None of them developed CHB, and it was associated with a lower rate of miscarriages.

Anti-Ro titer (u/ml): Sixty women out of 62 were tested at least once for anti-Ro titer. Fetal adverse events were more frequent in patients with high titers. (Table 2).

Anti-La antibodies tested positive in 12 patients only (titer range: 14-320 u/ml).

Conclusion: In this study, we observed low incidence of congenital heart block in general. Interestingly, it happened only in asymptomatic women with high antibody titer.

Miscarriage and IUFD were more frequent than CHB in patients with Primary Sjogren.

Hydroxychloroquine was associated with a lower frequency of fetal adverse events.

Disclosure: E. Satti, None; **N. Hadwan**, None; **H. Ashour**, None; **R. Saleh**, None; **F. Alam**, None; **O. Alsaed**, None; **S. Al Emadi**, None.

Abstract Number: 1250

Early Sjögren Antibodies: Potential Biomarker for Abnormal Minor Labial Salivary Gland Biopsy in Juvenile Sjögren's Syndrome

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Sjögren's Syndrome Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile Sjögren's Syndrome (jSS) is a perplexing systemic autoimmune disease in children presenting with positive autoantibodies, glandular, and/ or extraglandular symptoms. In pediatric practice, the diagnosis has relied upon the positivity of ANA and SSA/ SSB antibodies, so-called classic Sjögren antibodies (cSjA). Children with negative cSjA autoantibodies or exclusively extraglandular symptoms become a diagnostic challenge. Early Sjögren antibodies (eSjA) including IgG, IgA and IgM autoantibodies to salivary protein 1 (SP-1), carbonic anhydrase 6 (CA6), and parotid secretory protein (PSP), are 9 novel salivary gland autoantibodies. The eSjA were found to be early biomarkers in adults, especially in negative cSjA cases. The roles of ANA, cSjA, and eSjA as biomarkers and predictors for abnormal minor labial salivary gland biopsy (MSGB) have been unknown in jSS. The goal of this study is to determine if ANA, cSjA, and eSjA can serve as biomarkers and predictors for abnormal minor salivary gland biopsy (MSGB) in the University of Florida (UF) cohort with jSS.

Methods: Forty children with a new-onset jSS diagnosed at the UF Health Shands Children's hospital and the UF Health Oral Medicine between January 2017-May 2020 were evaluated retrospectively. Autoantibodies were positive if ANA was 1:160 or higher or one of cSjA and eSjA were higher than normal values. A MSGB was abnormal if the focus score was 1 or more. The sensitivity, specificity, positive predictive value (PPV), negative predictive value (NPV) of ANA, cSjA, and eSjA were analyzed using the MSGB as a gold standard.

Table 1: Comparision of sensitivity, specificity, PPV and NPV of ANA, classic Sjögren antibodies (cSjA), and early Sjögren antibodies (eSjA) in 32 children with jSS based upon the MSGB results

	Sensitivity	Specificity	PPV	NPV
ANA	51.8%	50%	87.5%	11.5%
cSjA	40.7%	60%	84.6%	15.8%
eSjA	74%	60%	90.9%	30%
ANA and cSjA	63%	40%	85%	16.7%
ANA and eSjA	85.2%	20%	85.2%	20%
cSjA and eSjA	88.9%	40%	88.9%	40%
ANA and cSjA and eSjA	89.2%	25%	89.2%	25%

Table 1. Spearman's rho correlation coefficients for salivary gland target lesions scored by ultrasound and MRI.

Results: Thirty-two children 5-17 years of age (mean 12.28, median 14) who underwent testing for ANA, cSjA, eSjA, and MSGB were included. Twenty-three children fulfilled the 2016 ACR/EULAR SS classification criteria. Abnormal MSGB results were found in 5 of 9 children who have not fulfilled the criteria. One child with normal MSGB has fulfilled the criteria. Twelve and five of the children had positive SSA and SSB antibodies respectively. All but 1 of the positive SSB patients were also SSA positive. Twenty-two children had at least one positive eSjA with anti-CA6 IgG, the most prevalent novel antibodies (52%). Abnormal MSGB with a focus score of 1 and more than 1 were found in 2 and 25 children, respectively. Three of the four children with all negative autoantibodies still had abnormal MSGB. The sensitivity, specificity, PPV, and NPV of each autoantibody is shown in Table 1. The eSjA has the highest PPV and NPV. The combination of eSjA and ANA or cSjA or both slightly increased sensitivity, but not specificity, PPV or NPV of eSjA.

Conclusion: eSjA are a potential biomarker and reliable predictor of abnormal MSGB in jSS. Patients with negative autoantibodies did not entirely exclude a diagnosis of jSS since these biomarkers have a low NPV. MSGB should still be considered in any case with a high index of suspicion with negative autoantibodies.

Disclosure: A. Thatayatikom, None; **S. Thatayatikom**, None; **I. Bhattacharyya**, None; **M. Elder**, None; **R. Modica**, None; **S. Cha**, None.

Abstract Number: 1251

Assessing the Construct Validity of the Novel OMERACT Ultrasound Scoring System for Salivary Glands Target Lesions by Comparison with MRI in Patients with Sjögren's Syndrome - An OMERACT Ultrasound Working Group Exercise

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Imaging techniques such as salivary gland ultrasound and magnetic resonance imaging (MRI) are able to diagnose primary Sjögren syndrome (pSS) patients with high sensitivity and specificity. Recently, the OMERACT ultrasound novel scoring system for major salivary gland (SG) lesions in patients with pSS was developed showing good inter-reader and excellent intra-reader reliability. The aim of the OMERACT Sjögren ultrasound subtask group exercise was to assess the validity of the OMERACT ultrasound novel scoring system for major salivary

		r	p
Total MRI Score	Total-OMERACT SGUS Score	0,8	0.002
MRI R PG	US R PG	0,7	0.004
MRI L PG	US L PG	0,9	0.000
MRI R SMG	US R SMG	0,7	0.017
MRI LSMG	US LSMG	0,6	0.046

Table 1. Comparision of sensitivity, specificity, PPV and NPV of ANA, classic Sjögren antibodies (cSjA), and early Sjögren antibodies (eSjA) in 32 children with jSS based upon the MSGB results

	MRI Score					OMERACT SGUS Score				
	TOTAL	R PG	L PG	R SMG	LSMG	TOTAL	R PG	L PG	R SMG	LSMG
Unstimulated SFR	r:-0,8 p: 0.004	r:- -0,8 p: 0.009	r:- -0,8 p: 0.009	r:- -0,9 p: 0.001	r:- -0,9 p: 0.001	r:-0,7 p=0.04	r:- -0,8 p: 0.009	r:- -0,7 p: 0.03	r:- -0,8 p: 0.012	r:- -0,9 p: 0.001
Stimulated SFR	r:-0,8 p: 0.013	r:- -0,7 p: 0.024	r:- -0,7 p: 0.024	r:- -0,8 p: 0.003	r:- -0,8 p: 0.003	r:-0,7 P=0.027	r:- -0,7 p: 0.024	r:- -0,7 p: 0.024	r:- -0,7 p: 0.02	r:- -0,8 p: 0.003

Table 2. Spearman's rho correlation coefficients of MRI and US scores of salivary glands with salivary flow rates (SFR).

gland (SG) lesions compared with MRI of parotid (PGs)/submandibular glands(SMGs) and salivary flow rates (SFRs) in patients with pSS.

Methods: Nine sonographers and two radiologists participated in the validity exercise, evaluating the parenchymal changes of bilateral PGs and SMGs in 11 pSS patients using greyscale ultrasound and MRI. Nine sonographers examined the superficial lobe of the PGs in both longitudinal and transverse plane, while the SMGs were evaluated in longitudinal plane only. Machine settings were not allowed to modify during scanning. The OMERACT novel four grade semiquantitative ultrasound score was applied: Grade 0, normal parenchyma; Grade 1: minimal change: mild inhomogeneity without anechoic/hypoechoic areas; Grade 2: moderate change: moderate inhomogeneity with focal anechoic/hypoechoic areas; Grade 3: severe change: diffuse inhomogeneity with anechoic/hypoechoic areas occupying the entire gland surface or fibrous gland. MRI images were evaluated by two radiologists with at least ten years of expertise in head and neck practice. The PGs parenchyma were graded by modifying the protocol as proposed by Kojima et al., i.e. , grade 0 definitely normal, grade 1 slightly heterogeneous, grade 2 clearly abnormal, and grade 3 severely heterogeneous destroyed parenchyma. Differences in opinion between radiologists, if any, were resolved by reevaluating those cases. Furthermore, both stimulated and unstimulated salivary flow rates (SFRs) were assessed in 11 pSS patients.

Results: OMERACT novel ultrasound score was strongly correlated with MRI score for the PGs and for the SMGs (Table 1). Correlation was similar for both the PGs and the SMGs combined (r:0,8 p=0.002). Moreover, both unstimulated and stimulated SFRs as objective criteria were associated with total OMERACT novel ultrasound score (r:0,7 p=0.04; r: 0,7 p=0.027) and total MRI score (r:0,8 p=0.004; r: 0,8 p=0.013). Similar trend was observed in PGs and SMGs (Table 2).

Conclusion: The OMERACT novel ultrasound scoring system for the evaluation of SG in pSS showed strong correlation with MRI assessment. Furthermore, both imaging methods strongly correlate with unstimulated and stimulated SFRs.

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cevar, None; **S. Finzel**, None; **L. Terslev**, AbbVie, 8, MSD, 8, Novartis, 8, Roche, 8, Pfizer, 8, General Electric (GE), 8, Bristol Myers Squibb (BMS), 8, Janssen, 8; **A. Iagnocco**, None; **P. Hanova**, None; **W. Schmidt**, None; **G. Mumcu**, None; **G. Bruyn**, None.

Abstract Number: 1252

Ultrasound-guided Parotid Gland Biopsy in Cadavers Performed by Rheumatologists – an OMERACT Ultrasound Working Group Study

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: With the diagnostic capability of the parotid gland biopsy similar to minor salivary gland biopsy in Sjögren's syndrome, the parotid gland biopsy may also provide information on treatment response and development of lymphoma. Comparing complications of both procedures, facial nerve damage represents a risk of parotid gland biopsy, while transient numbness of the lower lip incision area may occur after minor salivary gland biopsy. Avoiding the facial nerve during the parotid gland biopsy, therefore, is essential. In recent years, high-frequency (15–25 MHz) ultrasound probes have become available for clinical use, facilitating high-resolution visualization of small nerves or nerve fascicles.

We aimed to evaluate the diagnostic capability and safety of parotid gland biopsy in cadavers avoiding the region of the facial nerve under high-frequency (15–25 MHz) ultrasound guidance.

Methods: Prior to the parotid biopsy ultrasound exercise, an ultrasound training session on healthy subjects was conducted with the aim of assessing the most suitable facial nerve-free area for biopsy was determined in healthy subjects using high-frequency ultrasound (Figure 1). Thereafter, nine rheumatologists with experience in salivary gland ultrasound performed ultrasound-guided biopsies from four parotid glands in two different cadavers with 18 G core biopsy needles (Figure 2).

Results: A total of 36 pathology specimens were evaluated histologically by the expert pathologist for the presence of parotid gland tissue and any vascular and neuronal tissue of the gland. Eighty percent of the 36 pathology prepa-

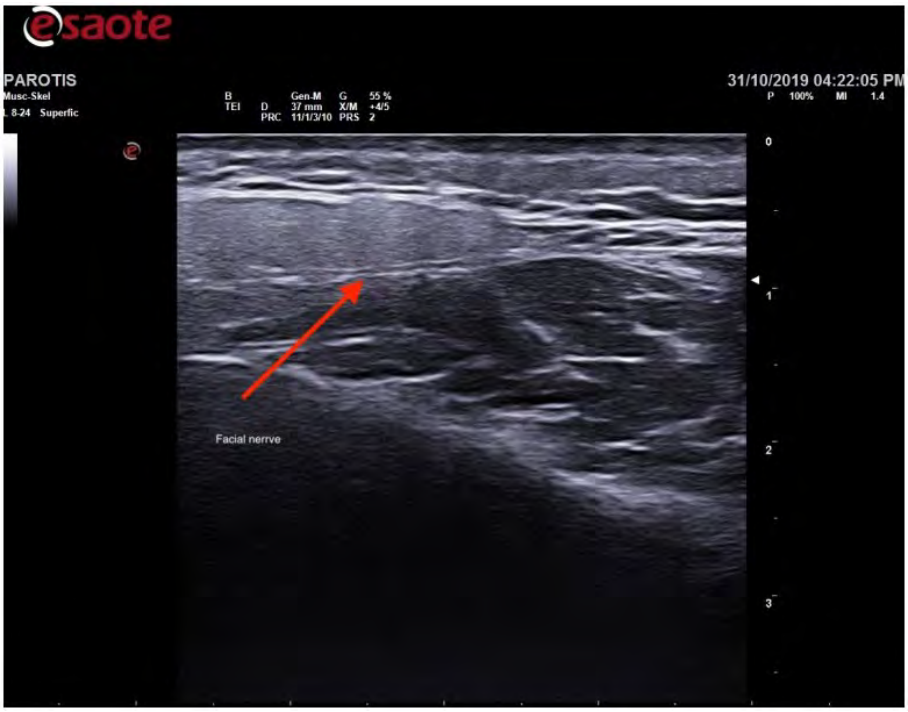

Figure 1. Ultrasound image of a parotid gland. The facial nerve appears as a linear tubular like hypoechoic structure with hyperechoic rim inside the homogenous relatively hyperechoic parotid gland (Esaote MyLab 9 equipped with 6-24 MHz probe).

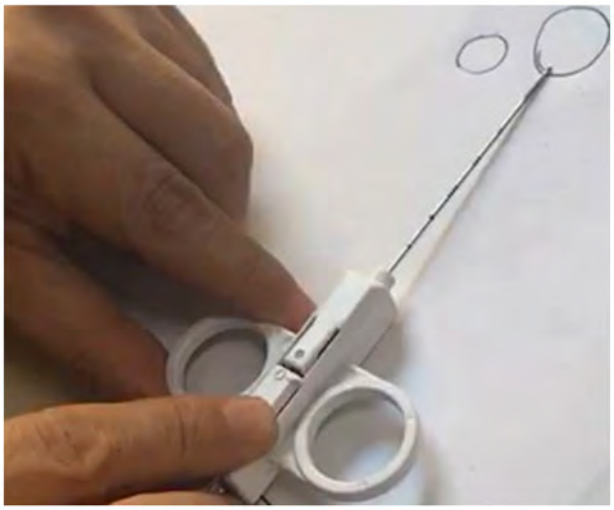

Figure 2. Core biopsy needle.

rations showed evidence of parotid gland tissue. Neuronal tissue was present in 2 specimens (5.5%), one with a very small amount of neuronal tissue. Vascular tissue was found in another 2 specimens (5.5%).

Conclusion: The present study has demonstrated that ultrasound-guided core needle biopsy of the parotid gland allows obtaining salivary gland tissue in the vast majority of cases. Longer procedural training would most likely improve the capability to obtain glandular samples.

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Abstract Number: 1253

Re-evaluation of the Extent of Lymphocytic Infiltration May Improve the Diagnostic Accuracy of Lip Biopsy in Primary Sjögren's Syndrome (pSS)

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Focus score (FS) remains the key element for the histological diagnosis of pSS; nonetheless, additional parameters have been proposed for clinical trials including the analysis of ectopic lymphoid structures (ELS) and the percentage of lymphocytic infiltration. Relatively few information are available regarding the feasibility and the usefulness of these additional histomorphological parameters in improving the diagnostic assessment of pSS in daily clinical practice.

Methods: Consecutive minor salivary gland biopsies (MSGBs) were collected and centralized to the same Pathology Unit from January 1st 2017 to January 1st 2020. An expert pathologist evaluated the samples focusing on: glandular tissue areas, assessment of focal lymphocytic sialoadenitis (FLS) versus non-specific chronic sialoadenitis (NSCS), number of foci, presence of ELS and. the percentage of lymphocytic infiltration (area of lymphocyte infiltration / total assessed surface area).

Results: We collected 267 MSGBs: 79 (29.6%) presenting a FLS with a FS≥1, 50 (18.7%) with a 0< FS< 1 and 114 (42.7.8%) with a NSCS. Moreover, the area of 24/267 (9%) further biopsies was lower than 4 mm2 and those samples were read only according to the Chisolm and Mason grading. The diagnosis of pSS was confirmed in 123 cases (46.1%). A FS≥1 was detected in 76/123 (61.8%) pSS patients and in 3/144 (2.1%) of no-SS patients, a 0< FS< 1 was observed in 13/123 (10.6%) pSS patients and in 37/144 (25.7%) no-SS patients, and a NSCS was found in 14 (11.4%) pSS patients and in 100/144 (69.4%) (p=0.000). Therefore, the FS did not support the diagnosis of pSS in 47/123 (38%) cases. In those samples with a 0< FS< 1 or with an uncertain FS due to an area lower than 4 mm2, the percentage of lymphocytic infiltration appeared significantly higher in pSS patients with respect to patients with no-SS (9.8% ± 4.1% vs 5.2% ± 3.6%, p=0.01) and correlated with anti-Ro/SSA positivity (r=0.443, p=0.02). ELS were present in the 30% samples and correlated with several ESSDAI domains including: lymphadenopathy, glandular, haematological and biological (p< 0.05). ELS correlated with the percentage of infiltration (r=0.733, p=0.001) highlighting the critical role of the size of the foci besides their numbers in determining the complexity of the infiltrate.

Conclusion: The percentage of lymphocytic infiltration and the assessment of ELS may provide complementary information to improve the diagnostic assessment of patients with suspected pSS, particularly in patients with a 0< FS< 1. Moreover, additional histomorphological parameters may also contribute to the identification of patients subgroups with more homogeneous glandular and extra-glandular manifestations.

Disclosure: C. Baldini, None; **F. Ferro**, None; **G. Governato**, None; **G. Fulvio**, None; **E. Elefante**, None; **M. Mosca**, None; **S. Bombardieri**, None; **V. Donati**, None.

Abstract Number: 1254

Lack of Efficacy of Early Treatment with Hydroxychloroquine in a Group of Hispanics with Primary Sjögren's Syndrome

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SESSION INFORMATION
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Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Treatment of primary Sjögren's syndrome (pSS) with hydroxychloroquine (HCQ) has been evaluated in the past but with conflicting results regarding its efficacy. While earlier studies showed its effectiveness on the treatment of sicca symptoms and some extra-glandular manifestations, recent randomized controlled trials have found limited clinical benefit. However, the impact of early treatment with HCQ has not been examined. Thus, we sought to determine the clinical outcome of pSS patients receiving early HCQ therapy.

Methods: A cross-sectional study was performed in a cohort of Hispanics from Puerto Rico with pSS. All patients fulfilled the 2012 American College of Rheumatology classification criteria for pSS. Demographic features, cumulative extra-glandular and comorbidities, disease activity (per EULAR Sjögren's Syndrome Disease Activity Index [ESSDAI]), disease damage (per Sjögren's Syndrome Disease Damage Index [SSDDI]), and pharmacologic profile were assessed. Early treatment was defined using the following cutoff periods: initiation of HCQ < 6 and < 12 months from onset of symptoms attributable to pSS, and < 6 and < 12 months from pSS diagnosis. Statistical analyses were performed using Fisher's exact test, Pearson Chi-squared test, and Wilcoxon rank-sum test, as appropriate.

Results: Of the entire cohort (n=100), 84 were treated with HCQ. Of those who received HCQ, the mean age was 51.9 years and 82.1% were females. Results of the bivariate analysis are depicted in tables 1 and 2. No differences were found for age, gender, extra-glandular manifestations, comorbidities, and disease damage between all study groups. Patients who received HCQ therapy < 6 months from onset of pSS symptoms were more likely to be treated with methotrexate than those who received HCQ ≥6 months after onset of symptoms. Those that had HCQ treatment ≥12 from pSS diagnosis were more likely to have higher mean ESSDAI score when compared to those who received HCQ < 12 months from diagnosis. However, when ESSDAI score was adjusted for disease duration, statistical significance was not retained.

Conclusion: In this group of Hispanics with pSS, no major differences were found for extra-articular manifestations, comorbidities, disease activity, damage accrual, and exposure to immunosuppressive medications. This study suggests that early HCQ has limited effect on the clinical outcome of pSS patients.

Table 1. Demographic, clinical, and pharmacologic features in pSS patients receiving early HCQ treatment <6 and <12 months from onset of pSS symptoms.

Features	< 6 months (n=15)	≥ 6 months (n=69)	p-value	< 12 months (n=24)	≥ 12 months (n=60)	p-value
Age, mean (SD) years	53.5 (11.7)	51.5 (12.8)	0.566	53.6 (10.9)	51.1 (13.2)	0.422
Gender, % female	100	92.6	0.580	95.8	93.3	>0.999
Disease duration, mean (SD) years	7.02 (5.11)	5.38 (4.34)	0.189	5.78 (4.47)	5.64 (4.56)	0.733
Extra-glandular manifestations, %						
Leukocytoclastic vasculitis	13.3	11.6	>0.999	8.3	13.3	0.717
Arthritis	20.0	23.2	>0.999	20.8	23.3	0.805
Interstitial lung disease	6.7	2.9	0.450	4.17	3.3	>0.999
Pure sensory neuropathy	26.7	17.4	0.471	20.8	18.3	0.767
Mixed polyneuropathy	20.0	10.1	0.374	20.8	8.3	0.140
Leukopenia (≤4,000/mm^3)	26.7	29.4	>0.999	33.3	27.1	0.571
Anemia	33.3	37.7	>0.999	37.5	36.7	0.943
Thrombocytopenia (≤100,000/mm^3)	6.7	7.4	>0.999	8.3	6.8	>0.999
ESSDAI score, mean (SD)	1.13 (1.73)	0.59 (0.81)	0.502	0.92 (1.41)	0.6 (0.85)	0.486
SSDDI score, mean (SD)	1.0 (1.85)	0.59 (0.99)	0.524	0.71 (1.52)	0.65 (1.04)	0.750
Comorbidities, %						
Hypertension	33.3	37.7	0.752	29.2	40.0	0.353
Type 2 diabetes mellitus	6.7	11.6	>0.999	12.5	10.0	0.710
Dyslipidemia	26.7	36.2	0.562	37.5	33.3	0.717
Overweight/obesity (BMI ≥ 25.0)	50.0	63.9	0.373	52.3	64.8	0.321
Coronary artery disease	6.67	2.9	0.450	8.3	1.7	0.195
Medications, %						
Prednisone	53.3	29.0	0.070	41.7	30.0	0.306
Methotrexate	20.0	2.9	0.039	12.5	3.4	0.142
Azathioprine	13.3	2.9	0.145	8.3	3.3	0.574
Rituximab	13.3	1.45	0.081	8.3	1.7	0.195

Table 2. Demographic, clinical, and pharmacologic features in pSS patients receiving early HCQ treatment <6 and <12 months from pSS diagnosis.

Features	< 6 months (n=60)	≥ 6 months (n=22)	p-value	< 12 months (n=67)	≥ 12 months (n=15)	p-value
Age, mean (SD) years	52.3 (13.0)	51.2 (12.1)	0.710	52.2 (12.8)	52.3 (12.7)	0.950
Gender, % female	95.0	90.0	0.607	94.0	93.3	0.919
Disease duration, mean (SD) years	5.04 (4.3)	7.56 (4.5)	0.015	4.88 (4.13)	9.42 (4.23)	0.004
Extra-glandular manifestations, %						
Leukocytoclastic vasculitis	10.0	18.2	0.446	9.0	26.7	0.079
Arthritis	21.7	27.3	0.571	23.9	20.0	>0.999
Interstitial lung disease	5.0	0.0	0.560	4.5	0.0	>0.999
Pure sensory neuropathy	20.0	13.3	0.748	19.4	13.3	0.726
Mixed polyneuropathy	11.7	9.1	>0.999	10.5	13.3	0.666
Leukopenia (≤4,000/mm3)	27.1	31.8	0.677	27.3	33.3	0.752
Anemia	33.3	54.6	0.081	34.3	60.0	0.065
Thrombocytopenia (≤100,000/mm3)	8.5	4.6	>0.999	9.0	0.0	0.587
ESSDAI, mean (SD)	0.57 (1.03)	0.95 (1.09)	0.054	0.55 (0.99)	1.2 (1.21)	0.016
SSDDI, mean (SD)	0.58 (1.17)	0.86 (1.25)	0.196	0.58 (1.13)	1.0 (1.41)	0.175
Comorbidities, %						
Hypertension	38.3	36.4	0.871	37.3	40.0	0.846
Type 2 diabetes mellitus	10.0	13.6	0.696	10.5	13.3	0.666
Dyslipidemia	35.0	36.4	0.909	34.3	40.0	0.678
Overweight/obesity (BMI ≥ 25.0)	54.9	68.2	0.315	56.9	66.7	0.493
Coronary artery disease	5.0	0.0	0.560	4.5	0.0	>0.999
Medications, %						
Prednisone	31.7	40.9	0.444	29.9	53.3	0.083
Methotrexate	5.0	14.3	0.177	6.1	13.3	0.307
Azathioprine	6.7	0.0	0.570	6.0	0.0	>0.999
Rituximab	5.0	0.0	0.560	4.5	0.0	>0.999

Disclosure: A. González-Meléndez, None; **P. Jordán-González**, None; **R. Gago-Piñero**, None; **N. Varela-Rosario**, None; **N. Pérez-Ríos**, None; **L. Vilá**, None.

Abstract Number: 1255

Sjögren's Syndrome Minor Salivary Gland Mesenchymal Stromal Cells Derived Deploy Intact Immune Plasticity and Display Myofibroblast-Like Properties

Sara McCoy[1], Jayeeta Giri[1], Rahul Das[1], Pradyut Paul[1], Andrea Pennati[1], Maxwell Parker[1], Yun Liang[1] and Jacques Galipeau[1], [1]University of Wisconsin, Madison

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Primary Sjögren's syndrome (pSS) is the second most common systemic autoimmune disease with hallmark features of severe ocular and oral sicca, leading to reduced quality of life. Minor salivary glands are central to the diagnosis and prognosis of pSS. The exact pathogenesis of pSS remains unclear, but focal lymphocytic infiltrate, and ultimately, increased fibrosis of the minor salivary gland, is a key feature of pSS. Mesenchymal stromal cells (MSCs), a cell type with the potential to abrogate inflammation/fibrosis, have been isolated from human minor salivary glands but little is known of their immunobiology. The objective of this study is to define the immunobiology of culture-adapted MSCs derived from endogenous salivary minor salivary gland (MSG)-MSCs.

Methods: All pSS subjects (N=11) fulfilled ACR/EULAR criteria for pSS. Control subjects (N=12) were referred for minor salivary gland biopsy but did not have features or diagnosis of autoimmune disease. MSG-MSC phenotype was assessed by morphology and flow cytometry using typical MSC surface markers (CD19-,CD45-,HLADR;CD105+,CD90+,CD73+). The immunomodulatory capacity of pSS and control MSG-MSCs was evaluated using flow cytometry for programmed death-ligand 1 (PD-L1), indoleamine 2,3-dioxygenase (IDO), and intercellular adhesion marker (ICAM-1) with and without IFNg pre-treatment. Co-culture of MSCs and peripheral blood mononuclear cells was performed by treating MSG-MSCs with IFNg then culturing MSG-MSCs with PBMCs at ratios of 1:10, 1:50, and 1:500. Co-culture was followed by Ki-67 staining and flow cytometry. RNA-Sequencing was performed on three pSS and control samples with MedGenome. Differentially expressed genes had p-value < 0.1 and log2 fold change >1 for upregulated genes and < -1 for down regulated genes. Gene ontology and pathway analysis was then performed on the differentially expressed genes. Western blot was performed with α smooth muscle actin primary antibody and GAPDH loading control. Immunocytochemistry was performed with anti-αSMA antihuman primary antibody after MSG-MSC fixation. Real-time PCR was performed using primers for COL6A6 and COL22A1.

Results: We found that MSG-MSCs deploy normal immunoregulatory functionality after IFNg stimulation as demonstrated by increased protein level expression of IDO, PD-L1, and ICAM-1 (Figure 1a-c) We also found that MSG-MSCs were able to suppress T cell proliferation in a dose-dependent manner (Figure 1d). Gene ontology and pathway analysis highlighted extracellular matrix deposition as a possible difference between pSS and control MSG-MSCs (Figure 2a-c). MSG-MSCs demonstrated increased αSMA expression. MSCs indicating a partial myofibroblast-like adaptation in MSG-MSC (Figure 3a-d).

Conclusion: These findings establish similar immunoregulatory function of MSG-MSCs in both pSS and control patients that precludes intrinsic MSC immune regulatory defects in pSS. pSS MSG-MSCs show a partial imprinted myofibroblast-like phenotype which may arise in the setting of chronic inflammation and provide a plausible etiology for pSS related mucosal fibrosis.

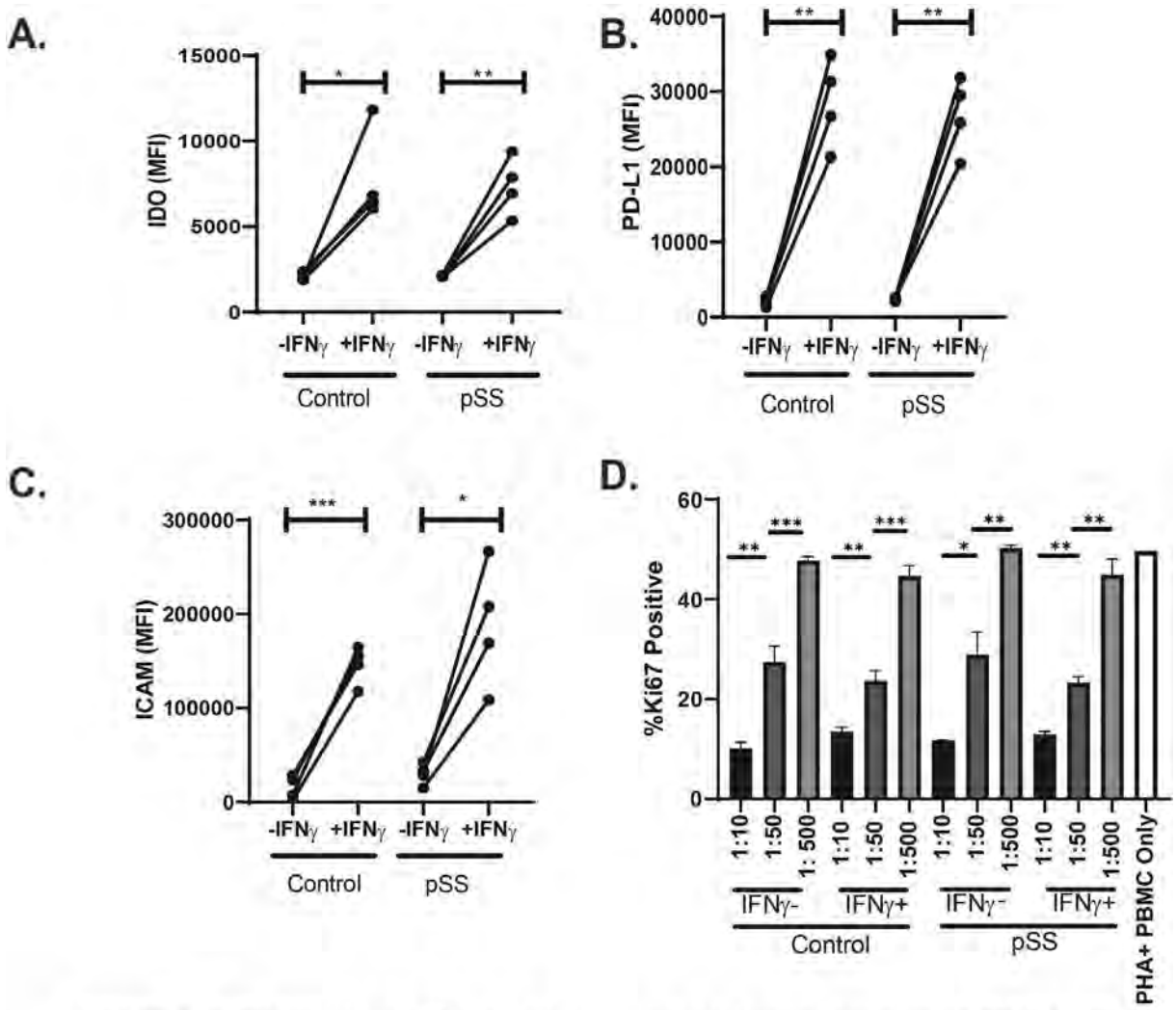

Figure 1. IFNy licensing effects on immunomodulatory properties of MSG-MSCs. pSS (n=3) and control (n=3) MSG-MSCs licensed with IFNγ(25 ng/mL) for 48 hours were harvested and stained with antibodies anti-IDO, PD-L1, and ICAM-1. Flow cytometry was performed after staining. Median fluorescence intensity (MFI) of MSC immunomodulatory markers A) IDO; B) PD-L1; C) ICAM-1; D) T cell suppression assay with MSG-MSCs with Ki-67 on pSS (n=3) and control (n=3). Values are means ± SEM. *=p<0.05, **=p<0.01, ***=p<0.001.

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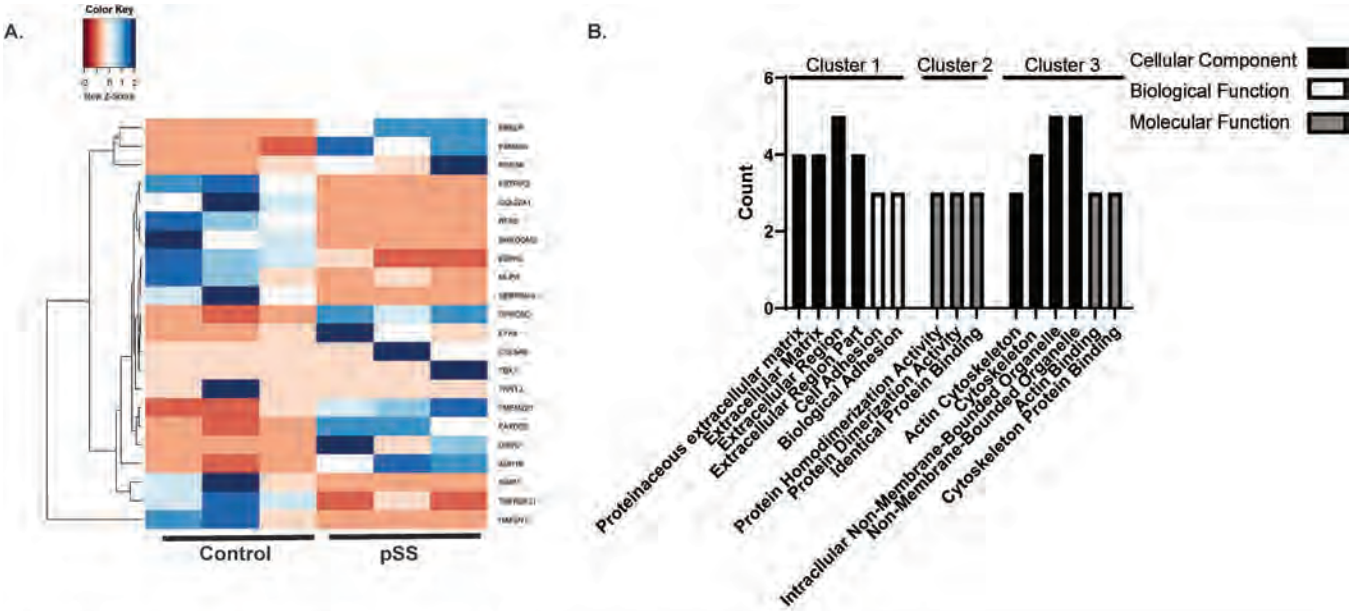

C. Pathways Identified by Signal Pathway Impact Analysis

Database	Pathway	pSize	NDE	pNDE	tA	pPERT	pG	pGFdr	pGFWER	Status
REACTOME	Extracellular matrix organization	90	2	0.0074	-1437	0.386	0.02	0.0918	0.31274	Inhibited
REACTOME	PPARA Activates Gene Expression	106	2	0.0101	0	1	0.057	0.0918	0.90503	Inhibited
REACTOME	Regulation of Lipid Metabolism by Peroxisome proliferator-activated receptor alpha (PPARalpha)	107	2	0.0103	0	1	0.057	0.0918	0.9185	Inhibited

Figure 2. Transcriptomic profiling of pSS and control MSG-MSCs. MSG-MSCs were serum starved for 24 hours in 1% FBS and α-MEM After 24 hours, the cells were trypsinized and frozen. Untreated pSS (n=3) and control (n=3) and estrogen treated pSS (n=3) and control (n=3) MSG-MSC primary cell lines were evaluated. Heat maps displayed differentially regulated genes filtered with an adjusted p-value <0.1 and log2 fold change >1 for upregulated genes and <-1 for down regulated genes. Gene ontology and pathway analysis were performed on genes with an adjusted p-value<0.1. A) The top untreated pSS versus control differentially regulated genes are displayed in the heat map (Figure 4a); B) gene ontology analysis shows recurrent theme of extracellular matrix components to the differentially expressed genes; C) Signal Impact Pathway Analysis shows the only significant pathway to be activated extracellular matrix organization pathways. pSize=number of genes in the pathway; NDE=number of differentially expressed genes in the pathway; pNDE=hypergeometric probability of observing NDE differentially expressed genes in the pathway by chance; tA=observed value of the perturbation score; pPERT=bootstrap probability associated to tA; pG=combined probability of pNDE and pPERT; pGFDR=adjusted pG using False Discovery Rate correction; pGFWER=adjusted pG using Family Wise Error Rate (Bonferroni); Status=Inhibition or Activation according to the negative or positive sign of tA.

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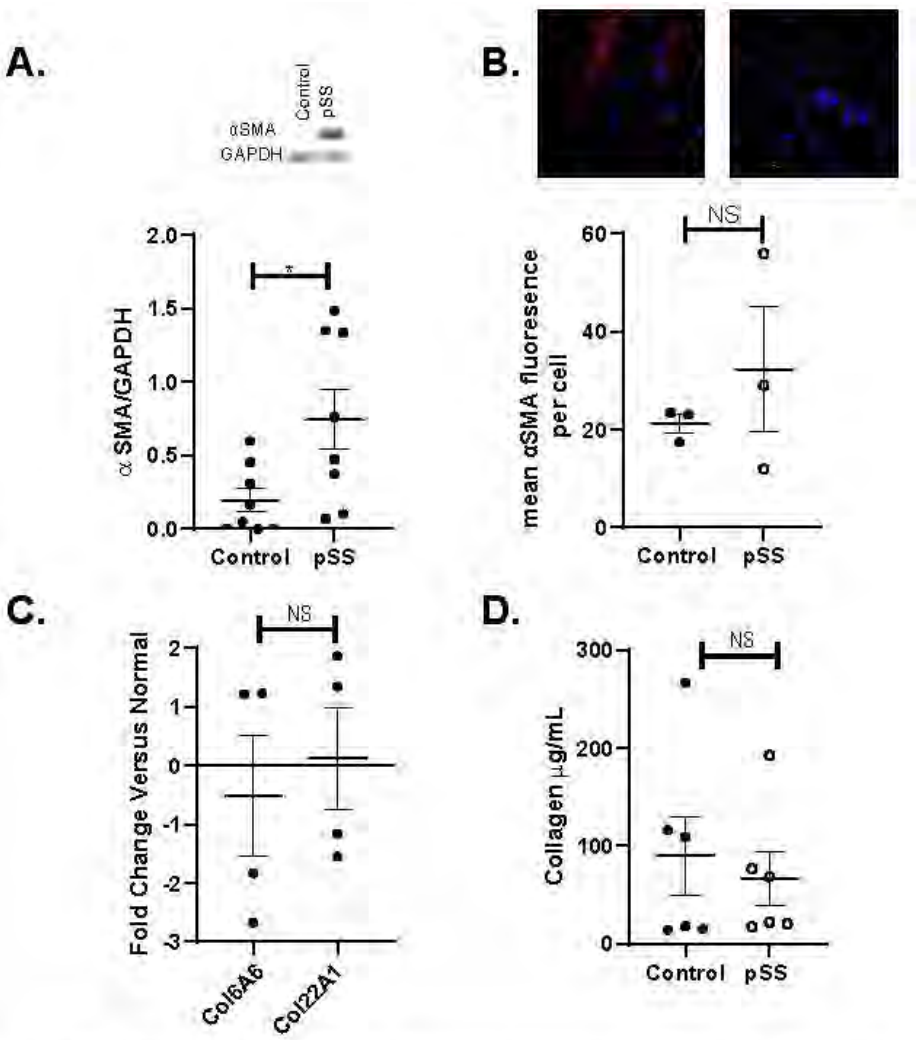

Figure 3. Expression of αSMA and collagen in pSS and control MSG-MSCs. A) Proteins were isolated from MSG MSCs and western blot of eight control and eight pSS MSG-MSC samples was performed. αSMA expression of each sample relative to GAPDH loading control was estimated by densitometry analysis; B) Immunocytochemistry of three control and three pSS MSG-MSC primary cell lines. MSG-MSCs were serum starved in α-MEM and 1% FBS for 24 hours. Then MSG-MSCs were fixed and stained with anti-αSMA unconjugated mouse antihuman primary antibody and microscopy was performed at 60x with at least three images taken per slide. αSMA fluorescence was quantified using NIS elements software; C) Real-time PCR of COL6A6 and COL22A1 MSCs. Four pSS and four control samples were studied in triplicate. Each dot represents the average of the triplicate. Error bars represent standard error of the mean. Values are reported as fold change compared to normal. D) Total collagen µg/mL amounts from conditioned media from 6 pSS and 6 control samples, diluted 50% as per manufacturer's recommendations. Significance was calculated through ΔCT comparison using unpaired Student's t-test. Values are means ± SEM. *=p<0.05, **=p<.01, ***=p<.001, NS=non-significant.

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Disclosure: S. McCoy, Bristol-Myers Squibb, 1, Novartis, 1; **J. Giri**, None; **R. Das**, None; **P. Paul**, None; **A. Pennati**, None; **M. Parker**, None; **Y. Liang**, None; **J. Galipeau**, None.

Abstract Number: 1256

Mast Cells Contribute to the Development of Sialadenitis Associated with Sjögren's Syndrome via Inducing Tissue Fibrosis by TGFβ Production

Shinjiro Kaieda[1], Kyoko Fujimoto[1] and Hiroaki Ida[1], [1]Kurume University School of Medicine, Kurume, Japan

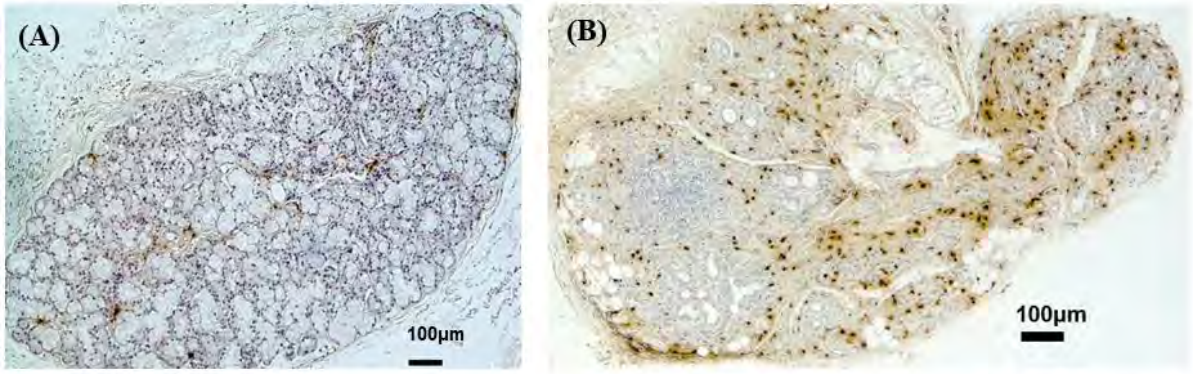
SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Mast cells have been implicated in many immune-inflammatory disorders. They mediate a variety of inflammatory and fibrotic conditions, but their role in sialadenitis in patients with primary Sjögren's syndrome (pSS) is unclear. We examined whether mast cells play a critical role in the pathogenesis of pSS.

Methods: Labial salivary gland samples were collected from 22 individuals with pSS and 10 with sicca syndrome (controls). Saliva production was evaluated by Saxon's test. Mast cell density in minor salivary glands was calculated at 400 magnification. The degree of fibrosis in minor labial salivary gland was graded on a quantitative scale as previously reported (Clin Exp Rheumatol.1998;16:63-65). We used immunohistochemistry to identify and quantify tryptase or TGFβ-positive mast cells and vimentin-positive fibroblasts. Fibrous tissue was identified by using EVG stain. Conditioned medium for fibroblast culture was obtained from human mast cell line-1 (HMC-1)cells stimulated

Figure1

Labial salivary gland biopsy stained with anti-tryptase antibodies



Original magnitude x40

Tryptase immunohistochemistry on labial salivary glands from sicca patients (A) and pSS patients (B).
Immunohistochemistry with an antibody to tryptase revealed the upregulation of mast cells in labial salivary glands .

Figure2

Mast cells contribute to the decreased salivary secretion via inducing tissue fibrosis rather than lymphoid infiltration

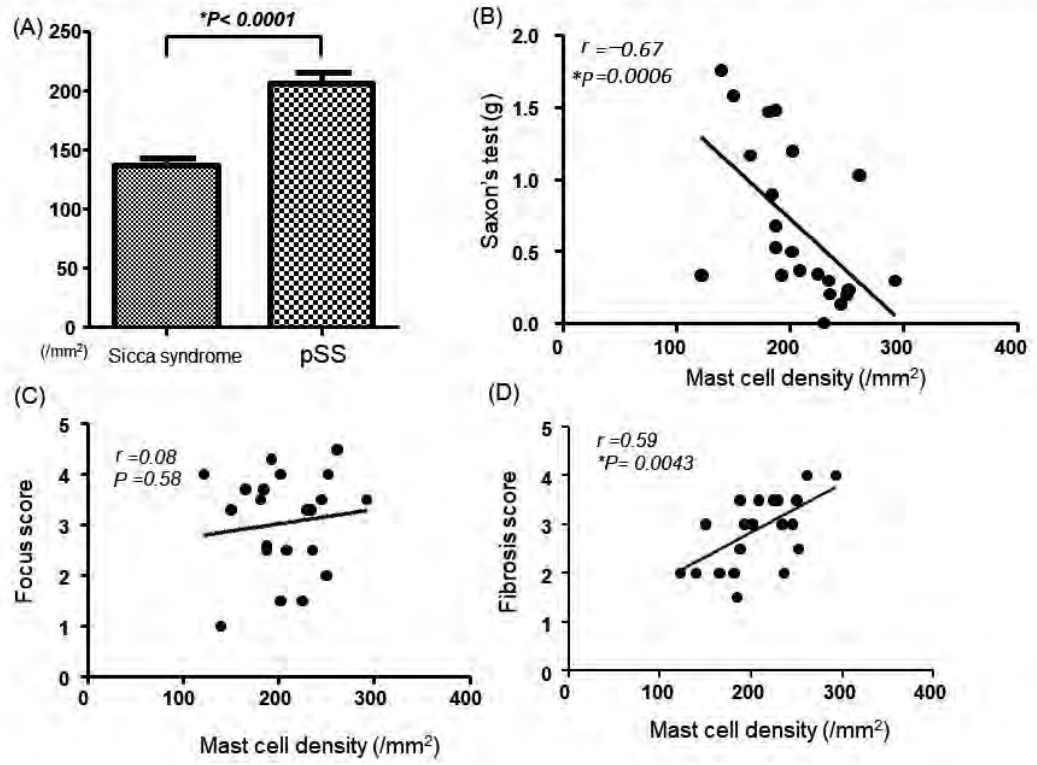
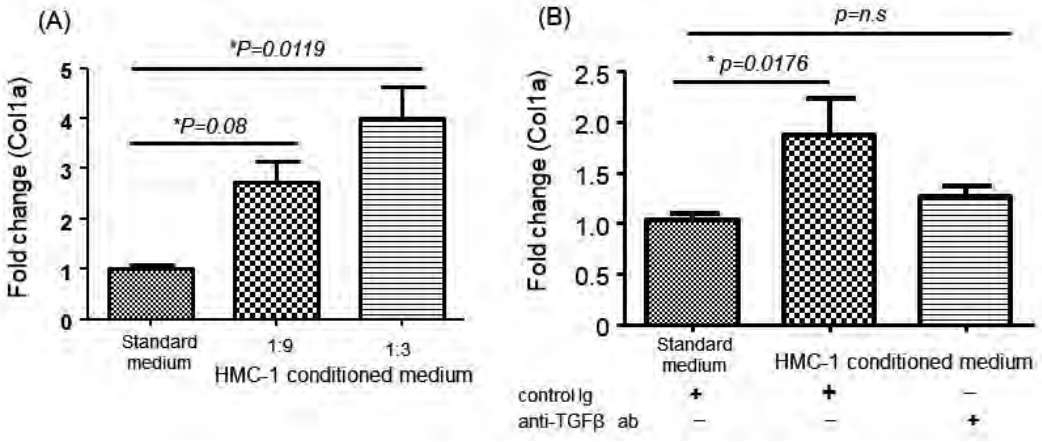


Figure3 **Mast cell-derived TGFβ induces type I collagen synthesis in fibroblasts**



with recombinant human IL-33 and SCF for 24 hours. Fibroblasts were treated with HMC-1 conditioned medium for 24 hours and type I collagen synthesis in fibroblast was evaluated by RT-qPCR. Neutralization antibodies for human TGFβ was utilized during fibroblast culture with HMC-1 conditioned medium or standard culture medium.

Results: We found that the number of mast cells in labial salivary glands of patients with pSS was significantly increased compared to that in control subjects (Figure 1 and Figure 2A). There was a significant negative correlation between the Saxon's test results and the number of mast cells, suggesting the involvement of mast cells in the decreased salivary secretion (Figure 2B). There was no correlation between the intensity of lymphoid infiltration as-

sessed by focus score and the mast cell density (Figure 2C). In contrast, a significant correlation between the number of mast cells and the degree of fibrosis was observed (Figure 2D). Consistent with these findings, mast cells were proximal to EVG-stained fibrous tissue and vimentin-positive fibroblasts. We hypothesized that mast cells were involved in the development of tissue fibrosis via modulation of fibroblast immune function. Significant up-regulation of Col1a mRNA was observed in fibroblast with HMC-1 conditioned medium as inverse proportion to the degree of dilution compared to that of fibroblast with standard culture medium (Figure 3A). Furthermore, neutralization for TGFβ abolished upregulation of Col1a mRNA in fibroblast in HMC-1 conditioned medium, thus suggesting that HMC-1-derived TGFβ contributes to upregulation of type I collagen synthesis (Figure 3B). Immunohistochemistry revealed that tryptase-positive mast cells exhibited positive signal of TGFβ in serial section.

Conclusion: These results suggest a novel role for mast cells in the development of sialadenitis in patients with pSS by induction of tissue fibrosis via fibroblast collagen synthesis by TGFβ production.

Disclosure: S. Kaieda, None; **K. Fujimoto**, None; **H. Ida**, None.

Abstract Number: 1257

Gestational Diabetes Mellitus in Pregnant Women with Systemic Lupus Erythematosus

Sofia Gernaat[1], Julia Simard[2], Elisabet Svenungsson[3] and Elizabeth Arkema[4], [1]Karolinska Institutet, Stockholm, Stockholms Lan, Sweden, [2]Stanford Medicine, Stanford, CA, [3]Karolinska University Hospital, Stockholm, Sweden, [4]Karolinska Institutet, Stockholm, Sweden

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Increased insulin resistance is pivotal in the development of gestational diabetes mellitus (GDM). Women with SLE may be at higher risk of GDM due to their increased risk of insulin resistance and use of glucocorticoids. In contrast, use of hydroxychloroquine may lower the risk of GDM. This study investigated the risk of GDM in women with SLE compared to women from the general population.

Methods: Women with SLE and comparators without SLE from the general population were identified from the Swedish Lupus Linkage (SLINK) cohort. Briefly, SLINK includes all individuals with SLE identified in the Swedish National Patient Register (NPR) and 5 randomly selected individuals without SLE matched on sex, birth year, calendar time, and county of residence between 1964-2013. SLE (International Classification of Diseases (ICD) 10: M32) was defined by ≥2 visits in the NPR and Medical Birth Register (MBR) with ≥1 of these visits preceding pregnancy. Women in the study population with singleton births in the MBR (Nov 2006-2016) were included. GDM (ICD 10: O24.4) was defined by ≥1 visit in the NPR and MBR during pregnancy. Glucocorticoid and hydroxychloroquine dispensations 6 months before and during pregnancy, and anti-diabetic drug dispensations at any time before and during pregnancy were collected from the Prescribed Drug Register. Women with drug-induced SLE (ICD 10: M32.0), diabetes mellitus (ICD 10: E10-E11, H36.0, O24 excluding O24.4) or filling anti-diabetic drugs (Anatomical Therapeutic Chemical (ACT) codes: A10A, A10B) at any time before pregnancy or during the first trimester were excluded. Risk ratio (RR) of GDM associated with SLE comparing SLE pregnancies with non-SLE pregnancies was estimated for first births only and all births using a Modified Poisson Regression model adjusted for age, year of birth and previous GDM.

Results: We identified 695 pregnancies among 502 women with SLE and 4,637 pregnancies among 3,243 women without SLE. Of these, 18 (2.6%) pregnancies among 14 women with SLE and 58 (1.3%) pregnancies among 44 women without SLE were diagnosed with GDM. Among GDM pregnancies, mean age at delivery was higher in women with SLE (35 years) than in women without SLE (33 years). The adjusted RR of GDM associated with SLE was 1.2 (95% Confidence Interval (CI) 0.5-2.9) for first births and 1.8 (95% CI 1.2-2.8) for all births. The proportion of SLE pregnancies without any glucocorticoid or hydroxychloroquine dispensation before or during pregnancy were similar between those with GDM (61.1% or 61.1%, respectively) and those without GDM (55.5% or 58.5%, respectively). In 5 out of 18 SLE pregnancies with GDM (27.7%) and in 207 out of 677 SLE pregnancies without GDM (30.6%), women received ≥1 glucocorticoid dispensation both before and during pregnancy. In 6 SLE pregnancies with GDM (33.3%) and in 184 SLE pregnancies without GDM (27.2%), women received ≥1 hydroxychloroquine dispensation both before and during pregnancy.

Conclusion: Although the number of SLE pregnancies with GDM (2.6%) were small, the RR of GDM was almost 2 times higher in pregnancies with SLE than in pregnancies without SLE. Neither glucocorticoids nor hydroxychloroquine differed by the GDM outcome.

Disclosure: S. Gernaat, None; **J. Simard**, None; **E. Svenungsson**, None; **E. Arkema**, None.

Abstract Number: 1258

Trajectory of Damage Accrual in African-American vs. Caucasian Systemic Lupus Erythematosus

Romy Kallas[1], Jessica Li[2], Daniel Goldman[3] and Michelle Petri[3], [1]Johns Hopkins Medical Institution, Baltimore, MD, [2]Johns Hopkins University, Baltimore, MD, [3]Johns Hopkins University School of Medicine, Timonium, MD

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: African-Americans have a higher incidence/prevalence of SLE, more lupus nephritis, higher rates of end stage renal disease and higher mortality than Caucasians. The aim of this study was to look at the trajectory of cumulative and individual organ damage accrual in a large longitudinal prospective SLE cohort in which African-American and Caucasian ethnicities were well represented, with a mean follow-up time of 13 years.

Methods: We analyzed data on 2,436 patients (43% African-American, 57% Caucasian, and 92% female) until January 2020. Patients met the revised ACR or SLICC classification criteria. The SLICC/ACR Damage Index (DI) was calculated based on organ damage that occurred after diagnosis until the last visit. Poisson regression allowing for overdispersion for each organ system with an offset term accounting for time followed since diagnosis was used. The outcome variable was the damage score of each organ system at the last available cohort visit. The associations were adjusted for sex, age, income, education, and insurance. We used Cox regression model to determine the association between individual damage items and ethnicity. These associations were adjusted for sex, age, and education.

Results: The mean total SLICC/ACR DI was 1.9 (SD=2.3). There was a linear relationship between time since diagnosis and mean DI with no plateau. By 5 years after SLE diagnosis, 44% of African-Americans vs. 36% of Caucasians had accrued damage. The rate of cumulative damage accrual was significantly higher in African-Americans

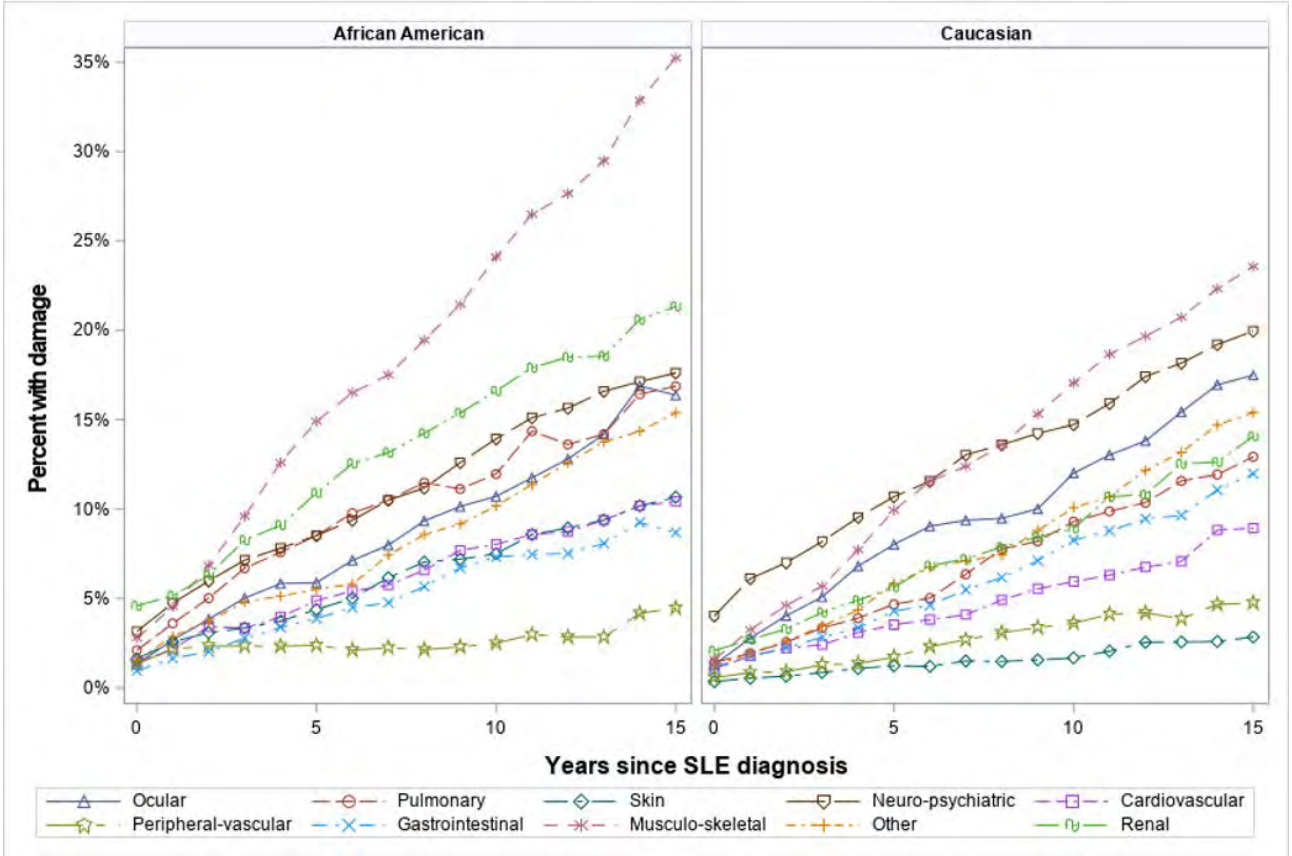


Figure 1. Damage accrual rate of each organ over time in African-American and Caucasian patients

Table 1: Associations between Time to Damage Index Items and Ethnicity (African-American vs. Caucasian)

		African-American vs. Caucasian	
	# of events	HR[1] (95% CI)	p-value[1]
Estimated or measured GFR < 50%	416	1.53 (1.25,1.87)	**<0.0001**
Proteinuria 3.5g/24hrs	156	2.47 (1.76,3.47)	**<0.0001**
End-stage renal disease	112	2.57 (1.72,3.85)	**<0.0001**
Pulmonary hypertension	184	1.93 (1.43,2.61)	**<0.0001**
Pulmonary fibrosis	173	1.57 (1.15,2.14)	**0.0043**
Cardiomyopathy	79	2.39 (1.48,3.84)	**0.0004**
Pericarditis>6 months, OR pericardiectomy	29	2.92 (1.3,6.53)	**0.0091**
Infarction or resection of bowel	204	0.7 (0.53,0.94)	**0.0174**
Deforming or erosive arthritis	219	2.1 (1.59,2.78)	**<0.0001**
Osteoporosis with fracture or vertebral collapse	311	0.51 (0.4,0.66)	**<0.0001**
Avascular necrosis	200	2.12 (1.59,2.84)	**<0.0001**
Scarring chronic alopecia	65	6.3 (3.27,12.14)	**<0.0001**
Extensive scarring or panniculum other than scalp and pulp space	37	2.8 (1.34,5.83)	**0.0060**
Diabetes	130	1.89 (1.32,2.72)	**0.0006**

[1]Adjusted for sex, age at diagnosis, years of education

(p-value 0.01). The mean time to onset of damage was 6.6 (SD 7.1) years from SLE diagnosis in Caucasian and 5.5 (SD 6.3) years in African-Americans. The divergence of the curves started early in the disease course. Renal (p-value < 0.0001), pulmonary (p-value 0.0066), and skin (p-value < 0.0001) damage in African-Americans accumulated at a

higher rate compared to Caucasians (Figure 1). African-Americans had a higher risk of renal insufficiency, proteinuria 3.5g/24hrs, end-stage renal disease, pulmonary hypertension, pulmonary fibrosis, cardiomyopathy, pericardial damage, deforming or erosive arthritis, avascular necrosis, skin damage, and diabetes than Caucasians at any time during follow-up. On the other hand, Caucasian patients were at higher risk for osteoporosis with fracture or vertebral collapse and infarction or resection of bowel (Table 1).

Conclusion: At any point during the disease, the SLICC/ACR DI was higher and accrued at a faster rate in African-American compared to Caucasian SLE. Damage in most organ systems progressed at a faster rate in African-Americans with the exception of osteopenic fracture and bowel infarction/resection. Of particular concern was the linear increase in damage in both ethnicities over time.

Disclosure: R. Kallas, None; **J. Li**, None; **D. Goldman**, None; **M. Petri**, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmithKline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5.

Abstract Number: 1259

The Impact of Antimalarial Agents on Traditional and Non-traditional Cardiovascular Markers in Patients with Systemic Lupus Erythematosus: A Systematic Review and Meta-analysis

Claudia Mendoza-Pinto[1], Mario Garcia-Carrasco[1], Pamela Munguía-Realpozo[2], Ivet Etchegaray-Morales[2] and Socorro Mendez-Martínez[1], [1]Instituto Mexicano del Seguro Social, Puebla, Puebla, Mexico, [2]Facultad de Medicina, Benemérita Universidad Autónoma de Puebla, Puebla, Puebla, Mexico

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular morbidity and mortality is a well-established problem in patients with systemic lupus erythematosus (SLE). Hydroxychloroquine (HCQ) has been seen as a potential atheroprotective agent. The aim of this systematic review was to assess the impact of HQC on traditional and nontraditional cardiovascular markers in patients with SLE.

Methods: A search of MEDLINE, Embase and the Cochrane library for randomized controlled trials (RCTs) or cohort studies evaluating the impact of antimalarials on cardiovascular (CV) markers in patients with SLE was conducted up to January 2020. Data extraction included traditional (lipid profile, diabetes, blood pressure [BP]) and nontraditional CV markers (glycosylated hemoglobin levels, insulin resistance, high sensitivity C-reactive protein, homocystein concentrations, IgG anti-apolipoprotein A1 [anti-apoA1], endothelial function, arterial stiffness, arterial elasticity and coronary artery calcification [CAC]). The methodological quality was assessed using the QUIPS risk of bias tool for observational studies and the Cochrane Risk of Bias Assessment Tool for RCTs. A narrative synthesis of the findings was presented, and a meta-analysis will be conducted if appropriate. The review was registered on PROSPERO (CRD42020162067).

Patients or population: Patients with SLE				
Setting: Hospital				
Prognostic factor: Antimalarial therapy				
Outcomes or subgroup title	**Number of participants**	**Number of studies**	**Mean difference (95% CI)**	**GRADE assessment**
Continuous (with and without antimalarial)				
Total cholesterol	1135	14	-11.12 [-24.71, 2.47]	Very low
LDL cholesterol	891	13	-5.93 [-12.67, 0.80]	Very low
HDL cholesterol	643	11	**3.05 [0.46, 5.61]**	Very low
VLDL cholesterol	258	5	**-10.29[-15.35, -5.24]**	Very low
Triglycerides	395	8	**-15.68 [-27.51, -3.86]**	Very low
HOMA-IR	218	2	-0.09 [-0.75, 0.55]	Very low
Systolic BP	174	3	-3.25 [-12.02, 5.51]	Very low
Diastolic BP	174	3	**-3.42 [-5.62, -1.23]**	Very low
Homocysteine concentrations	134	2	0.06 [-1.05, 1.17]	Very low
Continuous (before and after antimalarial)				
Total cholesterol	211	4	**-14.01 [-21.71, -6.31]**	Very low
LDL cholesterol	30	2	**-13.41 [-26.42, -0.40]**	Very low
HDL cholesterol	30	2	0.58 [-6.15, 7.31]	Very low
Triglycerides	35	2	-3.89 [-23.80, 16.03]	Very low
Dichotomous (with and without antimalarial)			**OR/HR (95% CI)**	
Prevalence of Diabetes	70	2	**0.08 [0.01, 0.41]**	Very low
Prevalence of Hypertension	475	5	0.70 [0.47, 1.04]	Very low
Prevalence of CAC	233	2	1.13 [0.50, 2.54]	Very low
Prevalence of IgG anti-apoA1	583	2	0.85 [0.51, 1.42]	Very low
Incidence of Diabetes	10199	3	**0.44 [0.24, 0.83]**	Low

Table 1. Modified GRADE summary of findings on the influence of antimalarial therapy on cardiovascular outcomes

Results: The search strategy produced 715 articles, of which 24 and 14 were extracted (16,717 SLE patients) for quantitative and qualitative analysis, respectively. Only one RCT and 37 observational studies were included. The follow-up period varied widely in longitudinal studies, ranging from 3 months to 9.3 years. Table 1 shows a summary of findings with mean differences or effect size from pooled studies. The mean differences in VLDL-cholesterol, triglycerides, and diastolic BP were significantly lower in patients on antimalarial therapy compared to those without antimalarial therapy, and HLD-cholesterol was significantly higher in the former group. Within-group analysis showed significantly lower total cholesterol and LDL-cholesterol after antimalarial therapy. Moreover, patients on antimalarials had a lower risk of prevalence and incidence of diabetes than patients not on antimalarials. HCQ use was protective and was associated with lower BP variability. However, the risk of prevalent hypertension or IgG anti-apoA1 was not significantly lower in patients with antimalarial therapy. The benefit of antimalarial therapy on endothelial function and arterial stiffness was unclear. The QUIPS tool showed a low-to-high RoB, and GRADE showed very low to low quality of evidence per outcome.

Conclusion: There is some evidence from observational studies on associations between antimalarial therapy and some CV outcomes. However, the data on which this conclusion was based was of very low to low evidence. This emphasizes the need for higher quality studies to resolve uncertainties.

Disclosure: C. Mendoza-Pinto, None; **M. Garcia-Carrasco**, None; **P. Munguía-Realpozo**, None; **I. Etchegaray-Morales**, None; **S. Mendez-Martínez**, None.

Abstract Number: 1260

Longitudinal Relationships Between Depression, Anxiety and Cognition in Lupus

Kathleen Bingham[1], Juan Pablo Diaz-Martinez[2], Mahta Kakvan[2], Robin Green[3], Dorcas Beaton[4], Lesley Ruttan[3], Carmela Tartaglia[5], Marvin Fritzler[6], May Choi[7], Jiandong Su[2], Denisse Bonilla[8], Nicole Anderson[2], Joan Wither[2], Patricia Katz[9] and Zahi Touma[10], [1]Department of Psychiatry, University of Toronto, Toronto, ON, Canada, [2]University of Toronto Lupus Clinic, Centre for Prognosis Studies in Rheumatic Diseases, Toronto Western Hospital, University Health Network, Toronto, ON, Canada, [3]Toronto Rehabilitation Institute, University Health Network, Toronto, ON, Canada, [4]Institute for Work & Health, Toronto, ON, Canada, [5]University of Toronto, Krembil Neurosciences Centre, Toronto, ON, Canada, [6]Department of Medicine, Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, [7]Brigham and Women's Hospital | Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, [8]University Health Network, Toronto, Canada, [9]University of California, San Francisco, Novato, CA, [10]University of Toronto, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: There is a consistent relationship between cognition and depression and anxiety (affective symptoms) in lupus. Together, affective and cognitive symptoms represent among lupus' most common and disabling neuropsychiatric symptoms. Although the relationship between cognitive and affective symptoms is well established, less is known about i) which cognitive domains are most related to affective symptoms, and ii) the longitudinal relationship between cognitive and affective symptoms. The primary aim of this study is to examine the relationship between cognitive performance across domains and affective symptoms over time in lupus.

Methods: This is an analysis of data from a cohort of 301 lupus patients from the Toronto Lupus Clinic enrolled between Aug 2017 and Jan 2019. Cognition was measured using the ACR battery with tests representing manual dexterity, processing speed, language, memory and executive function. Raw scores were transformed to z-scores using age- and gender-adjusted normative data. Participants were classified as cognitively impaired if they received a z-score of less than or equal to 1.5 on two or more pre-defined domains. Depression and anxiety were measured

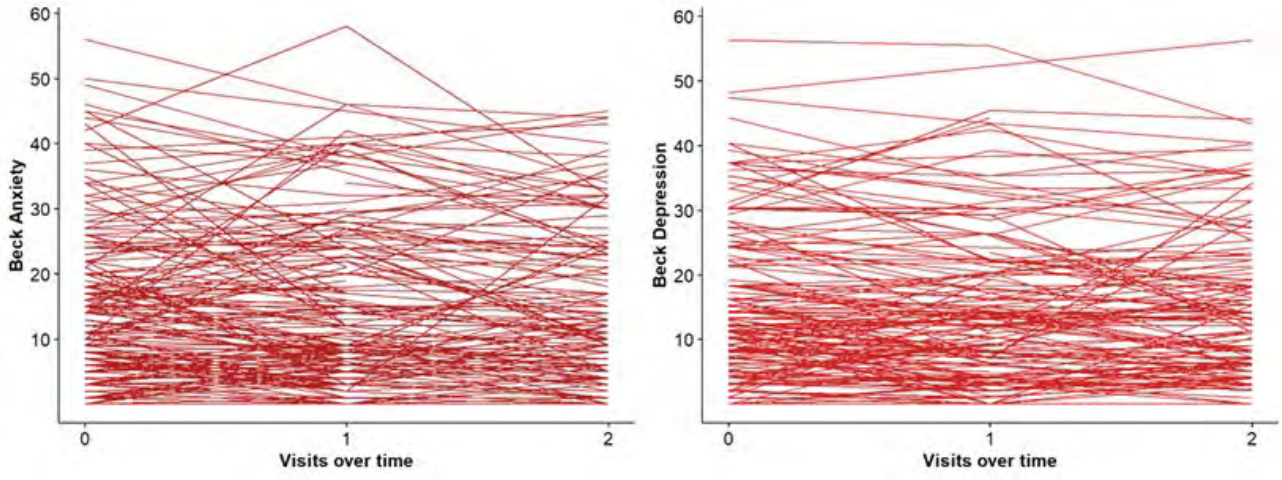


Figure 1. Participants' scores on BAI and BDI-II across three timepoints (baseline, 6 months and 12 months). Mean (SD) baseline BAI scores were 16.6 (13) and mean (SD) baseline BDI-II scores were 15.3 (12.5).

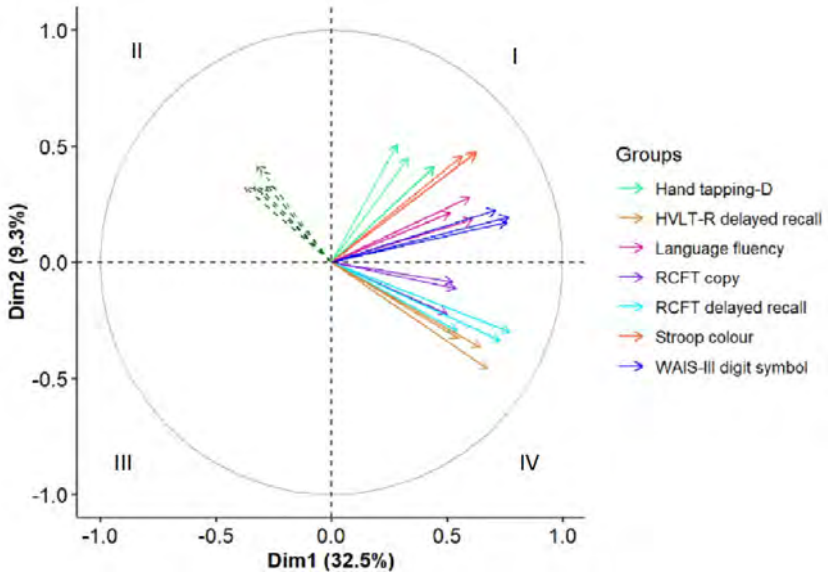


Figure 2. Results of MFA showing representative neuropsychological tests at each timepoint in relation to the two cognitive dimensions. Axis x represents the first dimension explaining 32.5% of the variance in cognition and axis y represents the second dimension. Affective symptoms at each time point are shown as supplementary variables (six dark green, dotted arrows in quadrant II). The length of each arrow represents the strength of the relationship between the variable it represents and the cognitive dimensions. Variables whose representative arrows are close in proximity are more strongly related (e.g. depression and anxiety are highly correlated, and the cognitive tests are highly correlated to each other across timepoints). The closer to 180 degrees the angle between the arrows representing anxiety and depression and those representing the cognitive tests, the stronger the relationship between the variables they represent. For example, affective symptoms are most strongly related to HVLT-R delayed recall and RCFT delayed recall (verbal and visual memory). If the angle between two arrows is 90 degrees, the two variables are independent. Hence, anxiety and depression have no relationship with hand tapping and Stroop color scores (motor dexterity and simple information processing speed).

using the Beck Depression Inventory-II (BDI-II) and Beck Anxiety Inventory (BAI). Participants were classified as having depression if they scored greater than 17 on the BDI-II and anxiety if they scored greater 18 on the BAI. Data was taken from baseline, 6 and 12 months. Data from all neuropsychological tests were entered into multiple factor analysis (MFA) across all three timepoints, for the purposes of item reduction and to explore relationships among cognitive domains and affective symptoms.

Results: Mean (SD) participant age was 41 (12), with 89% women. Mean (SD) disease duration at study entry was 14 (10.1) years. Anxiety and depression scores were stable across time (see Fig 1). Cognitive tests loaded onto two dimensions explaining 41.8% of the variance in neuropsychological performance. The first dimension (32.5%) consisted mainly of more complex cognitive tests and primarily explained the cognitive impairment status of participants. The second dimension (9.3%) was mainly explained by measures of simple information processing or motor speed. Affective symptoms were most strongly negatively related to verbal (r = -0.35) and visual memory domains (r = -0.32) (see Fig 2). The relationships were stable across all timepoints. Fig 3 demonstrates the distribution of participants with cognitive impairment, depression and anxiety. 38.2% of participants were categorized cognitively impaired at baseline, (36.2% were anxious and 33.2% were depressed). There is substantial overlap among these classifications (see quadrant II Fig 3 graphs), though there is a group of participants classified as having cognitive impairment without affective symptoms (quadrant III Fig 3).

Conclusion: Lupus patients exhibit a negative relationship between affective symptoms and cognition, particularly in the memory domains, that is highly stable across time. Future research should examine whether change in affective symptoms results in memory improvement, as well as potential mechanisms underlying this relationship.

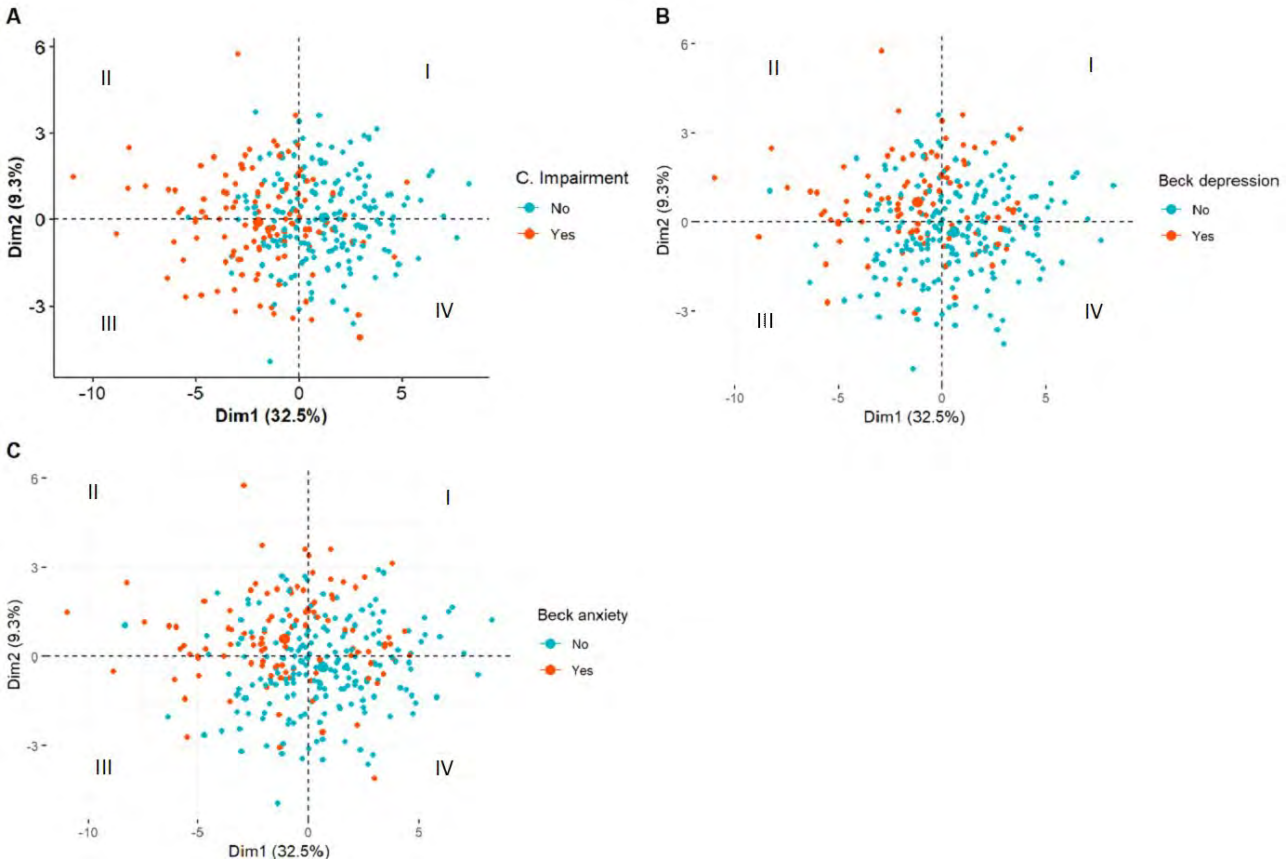


Figure 3. Axis x represents the first cognitive dimension (explaining 32.5% of the variance) and axis y represents the second dimension. Distribution of individual participants in the cohort classified by presence or absence of cognitive impairment (A), depression (B), or anxiety (C). There is substantial overlap in participants classified as having cognitive impairment, depression and anxiety. For example, many participants quadrant II of the graphs demonstrate cognitive impairment plus anxiety and depression. However, there is a subset of participants with cognitive impairment (shown in quadrant III of the graphs) who are classified as having cognitive impairment without anxiety and depression.

Disclosure: K. Bingham, None; **J. Diaz-Martinez**, None; **M. Kakvan**, None; **R. Green**, None; **D. Beaton**, None; **L. Ruttan**, None; **C. Tartaglia**, None; **M. Fritzler**, Inova Diagnostics Inc, 5, 8, Werfen International, 5, 8; **M. Choi**, None; **J. Su**, None; **D. Bonilla**, None; **N. Anderson**, None; **J. Wither**, None; **P. Katz**, None; **Z. Touma**, None.

Abstract Number: 1261

Antiphospholipid Patterns Predict the Risk of Thrombosis in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Table 1. Relationship between any thrombosis and each antiphospholipid antibody						
		No. of any thrombotic events	Person years	Rate per 1000 person years	Age-adj. rate ratio (95% CI)	p value
LAC	(-)	74	5936	12.5	1.00 (ref)	
	(+)	14	318	44.0	**3.56 (2.01, 6.30)**	**<.0001**
aCL-G	(-)	84	5986	14.0	1.00 (ref)	
	(+)	4	268	14.9	1.1 (0.4, 3)	0.859
aCL-M	(-)	85	6000	14.2	1.00 (ref)	
	(+)	3	254	11.8	0.83 (0.26, 2.61)	0.7446
aCL-A	(-)	86	6209	13.9	1.00 (ref)	
	(+)	2	45	44.4	3.08 (0.75, 12.65)	0.1195
aB_2GPI-G	(-)	84	6056	13.9	1.00 (ref)	
	(+)	4	198	20.2	1.48 (0.54, 4.05)	0.4442
aB_2GPI-M	(-)	79	5557	14.2	1.00 (ref)	
	(+)	9	697	12.9	0.91 (0.46, 1.81)	0.7797
aB_2GPI-A	(-)	68	5447	12.5	1.00 (ref)	
	(+)	20	807	24.8	**2.00 (1.22, 3.3)**	**0.0065**

Table 2. Additive effect of other antiphospholipid antibodies adjusting for LAC						
	ANY thrombosis		VENOUS thrombosis		ARTERIAL thrombosis	
	age adjusted RR 95%(CI)	p-value	age adjusted RR 95%(CI)	p-value	age adjusted RR 95%(CI)	p-value
Model 1: LAC + aCL-G						
LAC (+) vs (-)	3.9 (2.14,7.09)	<.0001	5.8 (2.56,13.15)	<.0001	3.11(1.34,7.23)	0.0084
aCL-G (+) vs (-)	0.63 (0.22,1.81)	0.3910	0.47 (0.1,2.13)	0.3289	1.04(0.3,3.62)	0.9449
Model 2: LAC + aCL-M						
LAC (+) vs (-)	3.88 (2.16,6.98)	<.0001	5.09 (2.28,11.36)	<.0001	3.41(1.5,7.78)	0.0035
aCL-M (+) vs (-)	0.53 (0.16,1.73)	0.2938	0.76 (0.17,3.31)	0.7157	0.61(0.14,2.63)	0.5083
Model 3: LAC+ aCL-A						
LAC (+) vs (-)	3.42 (1.9,6.13)	<.0001	4.67 (2.11,10.34)	0.0001	3.06(1.36,6.88)	0.007
aCL-A (+) vs (-)	1.86 (0.44,7.89)	0.3981	2.14 (0.28,16.56)	0.4659	1.57(0.21,11.97)	0.6623
Model 4: LAC+ aB_2GPI-G						
LAC (+) vs (-)	3.68 (2.01,6.71)	<.0001	4.85 (2.09,11.28)	0.0002	3.23(1.41,7.44)	0.0058
aB_2GPI-G (+) vs (-)	0.84 (0.29,2.41)	0.7408	1.03 (0.29,3.73)	0.9617	0.84(0.19,3.69)	0.8172
Model 5: LAC+ aB_2GPI-M						
LAC (+) vs (-)	3.71 (2.08,6.64)	<.0001	4.99 (2.26,11.02)	<.0001	3.32(1.47,7.47)	0.0038
aB_2GPI-M (+) vs (-)	0.76 (0.38,1.52)	0.4341	0.88 (0.34,2.3)	0.8008	0.72(0.28,1.83)	0.4875
Model 6: LAC+ aB_2GPI-A						
LAC (+) vs (-)	3.16 (1.76,5.68)	0.0001	3.95 (1.77,8.83)	0.0008	2.96(1.31,6.68)	0.0091
aB_2GPI-A (+) vs (-)	**1.73 (1.04,2.88)**	**0.0362**	**2.27 (1.13,4.59)**	**0.0218**	1.33(0.64,2.78)	0.4469

Background/Purpose: Antiphospholipid syndrome (APS) has been classified as the development of venous and/or arterial thromboses, and/or pregnancy morbidity, in the presence of persistently raised levels of the circulating antiphospholipid antibodies, namely lupus anticoagulant (LAC), anticardiolipin (aCL) and anti-β2-glycoprotein I. APS is

a significant cause of morbidity and mortality in patients with Systemic Lupus Erythematosus (SLE). It is well known that LAC positivity is more strongly associated with both arterial and venous thrombosis than either aCL or anti-β2glycoprotein I antibodies in SLE. An unanswered question is the contribution of different combinations of positive antiphospholipid antibodies to thrombosis risk. We evaluated which antiphospholipid antibody combinations increased the risk of future thrombosis in patients with SLE.

Methods: This prospective analysis included SLE patients who had been tested for all 7 antiphospholipid antibodies: lupus anticoagulant (LAC), anticardiolipin (aCL) isotypes IgM, IgG, IgA, and anti-β2-glycoprotein I isotypes IgM, IgG, IgA. We excluded RVVT measures if patients were taking anticoagulants (warfarin/ heparin). We constructed a dataset with one record per month of follow up for each patient. Rates of thrombosis for each antiphospholipid or each combination of antiphospholipid antibody were calculated as the number of thromboses divided by the number of person-months at risk and the results are converted to rates per 1000 person-years. To assess the relationship between antiphospholipid antibodies and thrombosis, we used pooled logistic regression.

Results: There were 821 patients with a complete profile of 7 antiphospholipid antibodies with a total of 75048 person-months of follow up. Among these patients, there were 88 incident cases of thrombosis: 48 patients with arterial, 37 patients with venous and three patients both with arterial and venous thrombosis.In individual models; LAC was the most predictive of any [3.56 (2.01, 6.30) p< 0.0001], venous [4.89 (2.25, 10.64) p< 0.0001], and arterial [3.14 (1.41, 6.97) p= 0.005] thrombosis. Anti-β2-glycoprotein I IgA positivity was a significant risk factor for any [2.00 (1.22, 3.3) p=0.0065] and venous [2.8 (1.42, 5.51) p=0.0029] thrombosis. We looked at patients who were LAC positive and asked if having another positive antiphospholipid antibody increased the risk ratio for any, venous, and arterial thrombosis. We found that having anti-β2-glycoprotein I IgA appeared to add significant risk to any [1.73 (1.04, 2.88) p=0.0362], and venous [2.27 (1.13, 4.59) p=0.0218] thrombosis among those with or without LAC.

Conclusion: Our study shows that LAC is still the best predictor of risk of any, arterial and venous thrombosis in SLE. Moreover, anti-β2glycoprotein I IgA positivity appeared to add significant risk for any and venous thrombosis. The clinical significance of IgA anti-β2glycoprotein I deserves further investigation in SLE patients.

Disclosure: S. Demir, None; **J. Li**, None; **L. Magder**, None; **M. Petri**, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmithKline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5.

Abstract Number: 1262

Single LAC Positivity versus Double and Triple Positivity for Thrombosis in SLE

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid syndrome (APS) is classified as the development of venous and/or arterial thromboses, and pregnancy morbidity, in the presence of antiphospholipid antibodies (aPL); lupus anticoagulant, moderate-to-high titer anticardiolipin (aCL) and anti-β2- glycoprotein I. LAC positivity is more strongly associated with both arterial and venous thrombosis than either aCL or anti-β2glycoprotein I antibodies in SLE (1).Some studies found that thromboembolic events were significantly higher in "triple positive" patients. The rate of pregnancy loss was also higher in "double positive" patients (2). In contrast, PROMISSE found only LAC to predict adverse pregnancy outcomes. We investigated the risk of thrombosis in Systemic Lupus Erythematosus patients with single LAC positivity versus double and triple positivity in the Hopkins Lupus Cohort.

Methods: Anticardiolipin and anti-Beta2 glycoprotein I were defined as positive when the antibody titer exceeded 20 units.The lupus anticoagulant was determined by dilute Russell's viper venom time (dRVVT) and confirmatory mixing studies, if prolonged. It was defined as positive if a patient had a dRVVT of 45 or more seconds and a positive confirm ratio of more than 1.4. For each aPL, we defined the patient as positive at a given month of follow up if they ever had a positive value in the previous measures. Logistic regression analysis was used to identify the independent predictive antiphospholipid antibody patterns for risk of lifetime occurrence of any/venous/arterial thrombosis. The odds ratios were adjusted for age. Thrombosis was defined as: arterial thrombosis (C VA, MI, other arterial thrombosis or digital gangrene); and venous thrombosis (D V T, PE or other venous thrombosis)

Results: There were 805 patients with a complete profile of 7 antiphospholipid antibodies, with a total of 73417 person months (6118 person years) of follow up. For any thrombosis when compared to patients with LAC positivity only, double positivity with any isotypes [1.15(0.50, 2.66) p=0.7484] and triple positivity with any isotypes [1.68(0.74, 3.80), p=0.2145] showed higher point estimates but not statistically significant.

Table1. Single, double and triple positive patterns and the risk of any thrombosis.

Pattern	Number of events	Person-years	Rate per 1000 person-years	adjusted RR (95% CI)	p-value
LAC positivity only	10	633	15.8	1.00 (Ref)	
Never any aPL	33	2581	12,8	0.73(0.36, 1.47)	0.3819
any aCL positivity only	6	793	7,6	0.43(0.16, 1.18)	0.1028
any aB2-GPI positivity only	7	517	13,5	0.78(0.30,2.05)	0.6195
any aCL and aB2-GPI positivity only	5	404	12,4	0.71(0.24,2.04)	0.5211
LAC and aCL positivity	7	406	17,3	1.15(0.50,2.66)	0.7484
LAC and aB2-GPI positivity	12	490	24,5		
Triple positivity	0	147	0,0	1.68(0.74,3.80)	0.2145

Conclusion: Triple or double positive aPL profiles are not superior to single LAC positivity in their association with any thrombosis in SLE patients.

Disclosure: S. Demir, None; **J. Li**, None; **L. Magder**, None; **M. Petri**, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmith-Kline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5.

Abstract Number: 1263

Association of the Systemic Lupus International Collaborating Clinics Frailty Index (SLICC-FI) and Damage Accrual in Long Standing Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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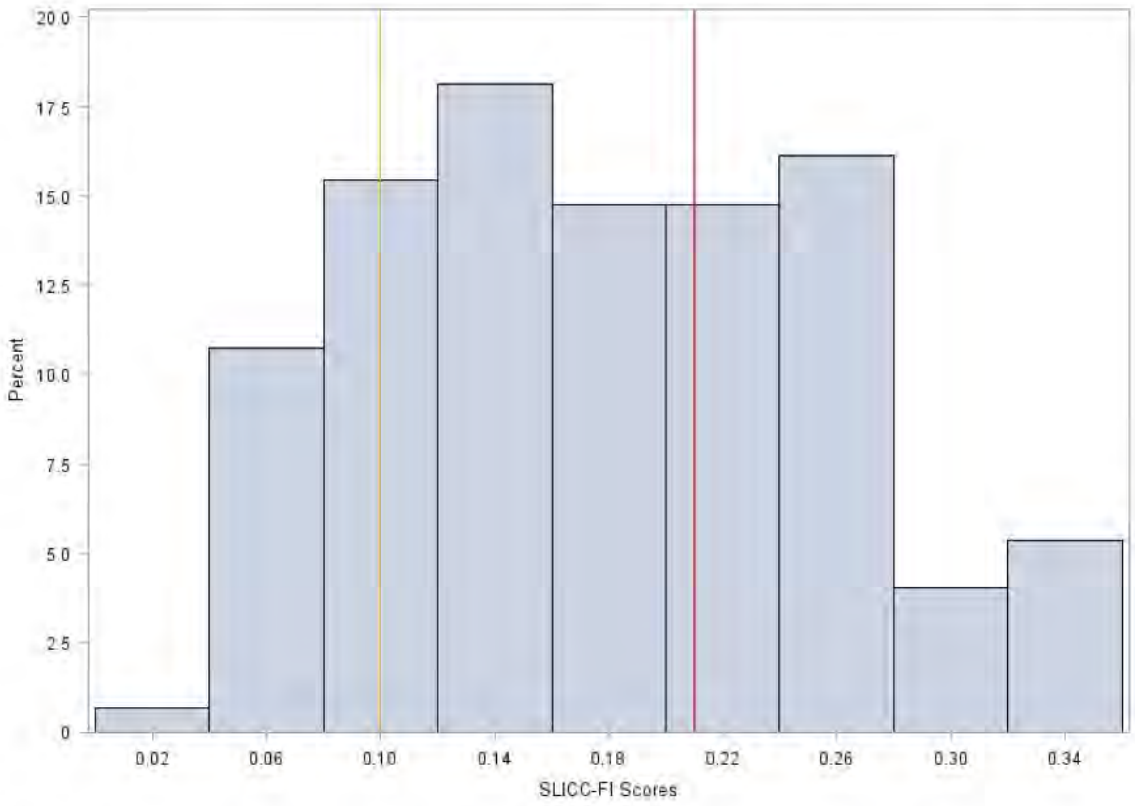
Background/Purpose: The Systemic Lupus International Collaborating Clinics Frailty Index (SLICC-FI) was recently shown to predict mortality and damage accrual in the SLICC inception cohort. The objective of this study was to apply the SLICC-FI to a prevalent SLE cohort and assess the ability of the SLICC-FI to predict damage accrual among individuals with more longstanding SLE.

Table 1: Baseline demographic and clinical characteristics for patients in SOLVABLE cohort *(n=149)

Baseline Characteristics	Mean (SD) or n (%)
Age (yrs), mean (SD)	43.30 (10.15)
Race, n (%)	
White	91 (61.07)
African American	41 (27.52)
Hispanic	8 (5.37)
Asian	9 (6.04)
Education, n (%)	
Less than high school diploma	5 (3.36)
Highschool diploma	44 (29.53)
College graduate	61 (40.94)
Advanced degree	39 (26.17)
Disease duration (yrs), mean (SD)	11.93 (8.46)
SLEDAI-2K score, mean (SD)	3.85 (3.56
SLICC Damage Index score, mean (SD)	1.64 (1.83)
Medication Use, n (%)	
Corticosteroids	59 (39.60)
Plaquenil	114 (76.51)
Immunosuppressants	51 (34.23)

SD=standard deviation, BMI= body mass index, SLEDAI-2K= SLE Disease Activity Index 2000
* Patients with 5-year follow-up

Figure 1: Distribution of Baseline SLICC-FI Scores in SOLVABLE cohort (n=149)



Note: Yellow line represents cut off between relatively fit and least fit, red line represents cut off between least fit and frail

Table 2: Logistic regression models for damage accrual (from baseline to 5 years), n=149

	Unadjusted Model (n =149)		Adjusted model * (n = 149)	
	Odds Ratio (95% CI)	p value	Odds Ratio (95% CI)	p value
Model 1: SLICC-FI cont. (0.05-unit)	1.28 (1.03, 1.60)	0.024	1.28 (1.01, 1.63)	0.042
Model 2: SLICC-DI (1-unit)	1.02 (0.85, 1.22)	0.809	1.02 (0.83, 1.25)	0.856
Model 3: SLICC-FI (0.05-unit)	1.41 (1.08, 1.84)	0.011	1.39 (1.05, 1.85)	0.016
SLICC-DI (1-unit)	0.87 (0.69, 1.09)	0.216	0.88 (0.68, 1.12)	0.291

Notes: SLICC = Systemic Lupus International Collaborating Clinics; FI = Frailty Index; DI=Damage Index

* Model 1 and 2 adjusted for age, race, and disease duration; Model 3 adjusted for age, race, disease duration, and baseline SDI

Methods: This was a secondary analysis of data from the Study of Lupus Vascular and Bone Long-Term Endpoints (SOLVABLE) cohort, which consists of adult women from the Chicago Lupus Database (age >18) who met at least 4 of the 1997 revised ACR classification criteria for definite SLE. A total of 185 SLE patients were enrolled, of which 149 patients were included in a 5-year follow up analysis. Baseline SLICC-FI was adapted based on available data in the SOLVABLE cohort, maintaining 46 health deficits for calculation of SLICC-FI scores. Damage accrual was defined as

Table 2: Logistic regression models for damage accrual (from baseline to 5 years), n=149

	Unadjusted Model (n =149)		Adjusted model * (n = 149)	
	Odds Ratio (95% CI)	p value	Odds Ratio (95% CI)	p value
Model 1: SLICC-FI cont. (0.05-unit)	1.28 (1.03, 1.60)	0.024	1.28 (1.01, 1.63)	0.042
Model 2: SLICC-DI (1-unit)	1.02 (0.85, 1.22)	0.809	1.02 (0.83, 1.25)	0.856
Model 3: SLICC-FI (0.05-unit)	1.41 (1.08, 1.84)	0.011	1.39 (1.05, 1.85)	0.016
SLICC-DI (1-unit)	0.87 (0.69, 1.09)	0.216	0.88 (0.68, 1.12)	0.291

Notes: SLICC = Systemic Lupus International Collaborating Clinics; FI = Frailty Index; DI=Damage Index

* Model 1 and 2 adjusted for age, race, and disease duration; Model 3 adjusted for age, race, disease duration, and baseline SDI

any increase of SLICC-Damage Index (SLICC-DI) at 5-year follow-up. Unadjusted and adjusted logistic regression models were conducted using baseline SLICC-FI (per 0.05 increase) to predict damage accrual.

Results: Among the 149 patients with 5-year follow up data, mean (SD) age was 43.30 (10.15) years, mean (SD) disease duration was 11.93 (8.46) years, and mean (SD) SLICC-DI score was 1.64 (1.83) at baseline. The mean (SD) baseline SLICC-FI score was 0.18 (0.08) with a median (interquartile range) of 0.17 (0.10-0.23). At baseline, 36% (53 out of 149) of participants were categorized as frail, based on SLICC-FI values >0.21. About 40% of these patients (58 out of 149) had damage accrual at 5-year follow-up (minimum-maximum 1-11). In unadjusted analysis, each 0.05-unit increase in baseline SLICC-FI score was associated with a 28% higher odds of subsequent damage accrual (odds ratio [OR]=1.28, 95% CI 1.03-1.60). In the adjusted model (adjusted for age, race, disease duration, and baseline SLICC-DI score), each 0.05-unit increase in baseline SLICC-FI score was associated with a 39% higher odds of subsequent damage accrual (OR=1.39, 95% CI 1.05, 1.85).

Conclusion: In a prevalent SLE cohort, higher baseline SLICC-FI scores were associated with higher risk of subsequent damage accrual at 5-year follow up, after adjusting for age, race, disease duration, and baseline SLICC-DI scores. This demonstrates the utility of the SLICC-FI as a predictive tool for adverse outcomes among individuals with longstanding SLE.

Disclosure: K. Lima, None; **A. Legge**, None; **J. Hanly**, None; **J. Lee**, None; **J. Song**, None; **A. Chung**, None; **R. Ramsey-Goldman**, None.

Abstract Number: 1264

Mortality in Patients with Systemic Lupus Erythematosus and Neuropsychiatric Symptoms

Rory Monahan[1], Rolf Fronczek[1], Jeroen Eikenboom[1], Huub Middelkoop[1], Liesbeth Beaart-van de Voorde[1], Gisela Terwindt[1], Nic van der Wee[1], Frits Rosendaal[1], Thomas Huizinga[1], Margreet Kloppenburg[1] and Margreet Steup-Beekman[1], [1]Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

	NPSLE (n = 149)	Minor/non-NPSLE (n = 202)
Deaths (n, %)	13 (8.7)	17 (8.4)
Age at death (median, range)	49 (32 – 79)	59 (20 – 89)
Follow-up time (years)	906	1047
Crude mortality rate (per 1000 PY)	14.3	16.2
All-cause mortality*		
Female	5.5 (2.8 – 9.6)	3.4 (1.9 – 5.7)
Male	2.3 (0.1 - 12.8)	6.2 (1.3 – 18.2)
Combined	5.0 (2.6 – 8.5)	3.7 (2.2 – 6.0)

**Standardized mortality ratio, ratio of the observed and expected number of deaths*

Background/Purpose: Little is known about mortality in patients with systemic lupus erythematosus (SLE) presenting with neuropsychiatric (NP) symptoms. We aimed to evaluate all-cause and cause-specific mortality in patients with SLE and NP symptoms.

Methods: All patients with the clinical diagnosis of SLE visiting the tertiary referral NPSLE clinic of the LUMC between 2007-2018 were included in this study. Patients were classified as NPSLE if NP symptoms were attributed to SLE (either at current assessment or in the past) and immunosuppressive or anticoagulant therapy was initiated, otherwise patients were classified as minor or non-NPSLE (minor/non-NPSLE). Municipal registries were checked for current status. Electronical medical files were studied for clinical characteristics and cause of death. Standardized mortality ratios (SMRs) and 95% confidence intervals were calculated using data from the general Dutch population. In addition, a rate ratio (RR) was calculated using direct standardization to compare mortality in NPSLE with minor/non-NPSLE patients.

Results: 351 patients with NP symptoms and the clinical diagnosis of SLE were included, of which 149 patients were classified as NPSLE (42.5%). Compared with the general population, mortality was increased five times in NPSLE (SMR 5.0, 95% CI: 2.6-8.5) and nearly four times in minor/non-NPSLE patients (SMR 3.7, 95% CI: 2.2-6.0), as shown in *Table 1*. Risk of death due to cardiovascular disease (CVD) was increased in minor/non-NPSLE patients (SMR 6.2, 95% CI: 2.0-14.6) and an increased risk of death to infections was present in both NPSLE and minor/non-NPSLE patients (SMR 29.9, 95% CI: 3.5 – 105 and SMR 91.3 95% CI: 18.8 – 266) respectively. However, mortality did not differ between NPSLE and minor/non-NPSLE patients (RR 1.0, 95% CI: 0.5 – 2.0).

Conclusion: Mortality was increased in both NPSLE and minor/non-NPSLE patients in comparison with the general population, but there was no difference in mortality between NPSLE and minor/non-NPSLE patients. This is different than expected and might imply that major NPSLE does not influence prognosis when recognized and treated.

Disclosure: R. Monahan, None; **R. Fronczek**, None; **J. Eikenboom**, None; **H. Middelkoop**, None; **L. Beaart-van de Voorde**, None; **G. Terwindt**, None; **N. van der Wee**, None; **F. Rosendaal**, None; **T. Huizinga**, Bristol-Myers Squibb Company, 2, 8, Pfizer, 2, 8, Eli Lilly, 2, 8, LUMC, 9; **M. Kloppenburg**, Dutch Arthritis society, 2; **M. Steup-Beekman**, None.

Abstract Number: 1265

2019 Lupus Classification Criteria Score Predicting Cost of Future Hospitalizations

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
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Background/Purpose: The latest 2019 Lupus Classification criteria score (CCS) is based on weighted criteria and has been shown to predict 10-year mortality[1]. Our previous study also suggests that lupus score greater than 19 increases the risk of future hospitalizations[2]. We attempt to test the hypothesis that 2019 lupus classification criteria score can predict the cost of future hospitalizations.

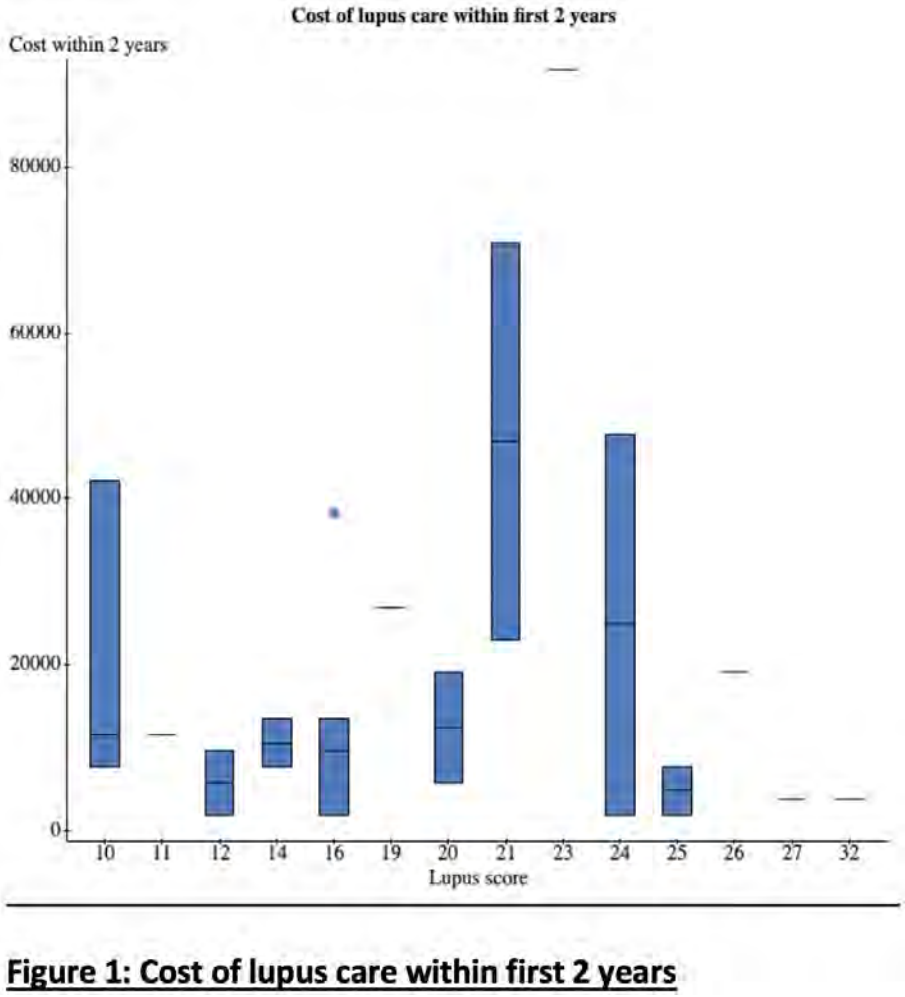

Figure 1. Cost of Lupus Care within first 2 years

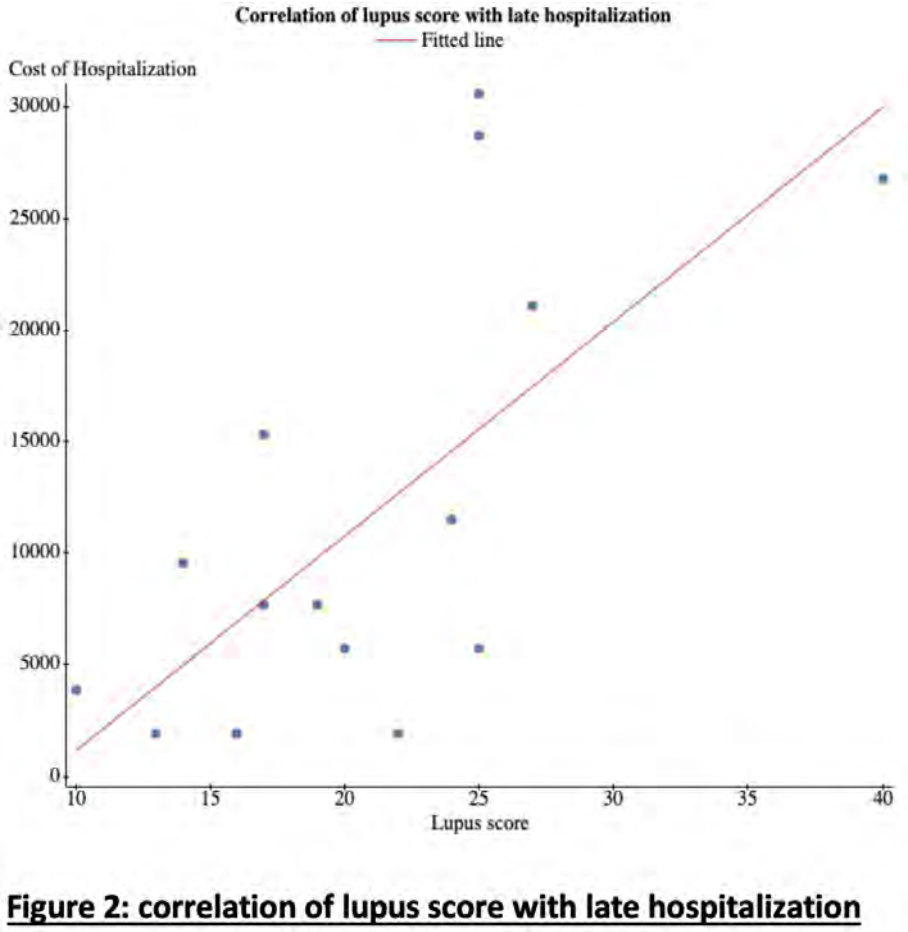

Figure 2. Correlation of Lupus Score with late hospitalization

Methods: Retrospective chart review was done at University of Kentucky (UK) between 2013 – 2019 to ascertain risk factors for hospitalization of lupus patients[2]. Post hoc analysis was applied to calculate cost of care.

Inclusion criteria: At least 3 outpatient rheumatology visits at UK with an ICD 9/10 diagnosis code for Lupus. Total of 217 patients met the inclusion criteria and 42 patients were hospitalized. 2019 Lupus classification score was calculated from first outpatient rheumatology visit. Total hospitalization cost was calculated by using hospital expense data[3]. Hospital expense data avoided variability of charges and reimbursement based on the type of insurance.

Results: Among 42 patients hospitalized, 26 (62%) were hospitalized within 2 years of their index rheumatology visit (Figure 1). Of 26, 15 were hospitalized due to lupus related causes with total mean hospital cost of 20426 usd. 11 patients were hospitalized unrelated to lupus with total mean cost of 17060 usd.

Patients whose 1st hospitalization was after 2 years of their index visit showed a trend toward overall lower mean hospitalization cost: 11370 usd as compared to patients hospitalized earlier than 2 years: 21065 usd (p value: 0.05). In addition, later hospitalization cost showed strong linear correlation with lupus score (r: 0.68, p value: 0.003) (Figure 2).

Patients who scored > 19 on the lupus CCS had almost twice the cost (28725 usd) due to inpatient hospitalization as compared to patients with CCS 19 or less in the subsequent two years of their index visit. In analysis of hospitalization any time after their index visit rather than the initial 2 years, patients with higher lupus score (>19) still incurred higher cost compared to those with a lower CCS score (23841 usd vs 11490 usd, $p < 0.07$) (Table 1).

	Lupus Score (19 or less)	Lupus Score > 19	P value:
Mean Cost of Hospitalization per patient (for 1st 2 years after index rheumatology visit)	14,499 (n: 14)	28725 (n: 12)	0.255
Mean Cost of hospitalization per patient (anytime after index outpatient rheumatology visit)	11490 (n=22)	23841 (n= 20)	0.0761

Table 1: Cost of hospitalization by lupus score (19 or less vs > 19)

Table 1. Cost of Hospitalization by Lupus score (19 or less vs > 19)

Conclusion: Our study found that late first hospitalization expense (1st hospitalization after 2 years of index visit) correlate well with the lupus score (p value: 0.05). In addition, higher lupus score (> 19) increased hospitalization cost almost twofold as compared to lupus score 19 or less. These data could help to create models using 2019 Lupus classification criteria scores as a surrogate to predict future lupus hospitalization and cost of care, supporting Interventions designed to bring the cost down.

References

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3. Trendwatch Chartbook 2018, American Hospital Association

Disclosure: S. Suman, None; **A. Batool**, None; **J. Keller**, None; **W. Roberts**, None.

Abstract Number: 1266

Multivariate Risk Model Shows Different Risk Factors for Myocardial Infarction and Stroke in SLE

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular events remain a major cause of morbidity and mortality in SLE. Accelerated atherosclerosis occurs in SLE and many other inflammatory diseases. In the general population both the Framing-

	MI		Stroke	
	HR (95% CI)	p-value	HR (95% CI)	p-value
African American	1.03 (0.66, 1.61)	0.8930	0.95 (0.7, 1.29)	0.7302
Age at diagnosis	1.02 (1, 1.04)	**0.0200**	1 (0.99, 1.01)	0.9553
Sex: Male	2.24 (1.27, 3.94)	**0.0055**	0.75 (0.42, 1.33)	0.3187
Low C3	1.13 (0.73, 1.75)	0.5890	1.76 (1.27, 2.46)	**0.0007**
Hypertension	1.25 (0.75, 2.09)	0.3892	1.72 (1.19, 2.48)	**0.0037**
Lupus anticoagulant	1.36 (0.85, 2.17)	0.1984	1.54 (1.09, 2.19)	**0.0150**
Cholesterol	2.15 (1.25, 3.7)	**0.0055**	1.8 (1.27, 2.57)	**0.0011**
Diabetes	2.06 (1.12, 3.79)	**0.0203**	2.43 (1.52, 3.86)	**0.0002**
Obesity	1.05 (0.67, 1.67)	0.8193	1.13 (0.82, 1.55)	0.4674
Ever smoking	1.79 (1.17, 2.75)	**0.0072**	1.17 (0.87, 1.58)	0.3026

Relationships Between Predictors and MI/Stroke Based on a Multivariable Model

ham Risk Score and the ACC/AHA Risk Equation combine stroke and myocardial infarction as the outcomes. The prospective SLE Cardiovascular Risk Equation took the same approach. The model found that traditional risk factors (age, sex, ethnicity, systolic blood pressure, total cholesterol, smoking, and diabetes mellitus) and SLE-specific risk factors (low C3 and lupus anticoagulant) were independent predictors of a later cardiovascular event (Lupus Sci Med. 2019;6:e000346). In this study, we took a different approach, and examined risk factors separately for myocardial infarction and for stroke.

Methods: SLE was defined by the revised ACR or SLICC classification criteria. Cardiovascular events were defined as myocardial infarction (MI) or stroke (ACC/AHA definition). In our cohort of 2,398 patients, 1,029 were African-American and 1,369 Caucasian. Nineteen were missing a SLE diagnosis date and 9 had missing data on events. There were 230 strokes and 116 myocardial infarctions.

Results: Table 1 shows the multivariate model of predictors of myocardial infarction and of stroke in SLE. Surprisingly, demographic variables such as age at diagnosis and African-American race were not risk factors. Male gender was a risk factor only for MI. Traditional cardiovascular risk factors were present for both outcomes, but overlapped only for hyperlipidemia and diabetes. Smoking was a risk factor only for MI. Hypertension was a risk factor only for stroke. The lupus-specific risk factors, low C3 and lupus anticoagulant, were only risk factors for stroke.

Conclusion: SLE is different from the general population in the predictive value of traditional cardiovascular risk factors for MI and stroke, with only hyperlipidemia and diabetes being risk factors for both. SLE-specific risk factors, low C3 and lupus anticoagulant, were important only for stroke. Attention to both traditional and SLE-specific risk factors remains paramount to lessen the cardiovascular morbidity of SLE. It is disappointing, however, that we do not have a clinically available SLE measure that predicts MI. We must still depend on non-invasive tests such as coronary CT or CT angiogram to identify patients early with atherosclerotic plaque.

Disclosure: M. Petri, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmithKline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5; **J. Li**, None; **D. Goldman**, None.

Abstract Number: 1267

Perceived Stress During the COVID-19 Pandemic Independently Associates with Worse Patient-Reported Outcomes in Systemic Lupus Erythematosus (SLE)

Sarah Patterson[1], Laura Trupin[2], Kimberly DeQuattro[1], Cristina Lanata[1], Maria Dall'Era[3], Jinoos Yazdany[2] and Patricia Katz[2], [1]UCSF, San Francisco, CA, [2]University of California, San Francisco, San Francisco, CA, [3]Division of Rheumatology, University of California, San Francisco, CA

SESSION INFORMATION
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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
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Background/Purpose: Causes and risk factors for variations in SLE disease activity and symptom severity are incompletely understood. Prior studies suggest a link between stressful life events (e.g. trauma), perceived stress, and greater disease severity. We examined whether (1) high levels of stress during the COVID-19 pandemic—both generalized and attributed to COVID-19—were associated with worse patient-reported outcomes (PROs) among patients with lupus, and (2) increases in perceived stress concurrent with the pandemic associated with increases in symptoms and/or incident SLE flares.

Methods: Participants, drawn from the California Lupus Epidemiology Study (CLUES), were ≥18 years old and met ACR criteria for SLE. Data derive from interviews conducted during the COVID-19 pandemic and study assessments during the prior year. General stress was measured using the 4-item Perceived Stress Scale (PSS, range 0-16). Scores in the top quartile were categorized as high stress. High stress from COVID-19 was assessed by asking whether it had caused "a great deal of stress or worry" and/or "the most stressful situation I have been through". PROs included: self-report disease activity (SLE Activity Questionnaire, SLAQ), pain severity (scale 1-10), fatigue (PROMIS fatigue scale), cognitive function (PROMIS cognitive ability scale), and self-report SLE flares (prior month). Multivariable linear and logistic regression first evaluated associations of generalized and COVID-19-specific stress with PROs during the pandemic while controlling for potential confounders (age, sex, race, education, income, smoking, disease duration, and disease damage), and then modeled changes in PROs from pre-pandemic to during the pandemic as a function of change in perceived stress (by PSS). We calculated adjusted means for each outcome based on the multivariable regression.

Results: The sample (n=201) was 91% female; 36% white, 27% Asian, 24% Hispanic, and 9% African American; mean age 50 (± 14) years; 17% with poverty-level income; and mean disease duration 22 (± 10) years. During the COVID-19 pandemic, 29% reported severe stress related to the health crisis. The mean PSS score in the high stress group was 10.1 (± 1.4), compared with 4.4 (± 2.6) among the rest of the cohort. In the cross-sectional multivariate regression model, high stress by both measures (PSS and COVID-19 stress question) was associated with worse scores for each PRO: greater self-reported disease activity, more pain, more fatigue, lower cognitive function, and higher frequency of flares (Table 1). In the longitudinal analysis, increase in stress independently associated with an increase in disease activity, increase in fatigue, and decrease in cognitive function, but no significant change in pain severity or flares (Table 2).

Conclusion: In a racially diverse SLE cohort, psychological stress during the COVID-19 pandemic independently associated with worse PROs including self-reported disease activity, fatigue, and cognitive dysfunction. Evidence-based

Table 1. Cross-sectional Analysis: Adjusted* Means (95% CI) for Patient Reported Outcomes and Prevalence of Lupus Flares by Perceived Stress During the COVID-19 Pandemic

	High General Perceived Stress**			High COVID-19-Associated Stress***		
Disease Outcomes	Yes**	No***	P	Yes	No	P
Disease Activity (SLAQ)	13.1 (11.1, 15.1)	7.9 (7.0, 8.7)	<0.01	11.2 (9.7, 12.7)	7.7 (6.8, 8.7)	<0.01
Pain (0-10)	4.0 (3.1, 4.9)	2.5 (2.1, 2.9)	0.002	3.6 (3.0, 4.3)	2.4 (2.0, 2.8)	0.002
Fatigue (PROMIS)	61.5 (58.1, 65.0)	50.3 (48.8, 51.9)	<0.01	57.1 (54.3, 59.8)	50.3 (48.6, 52.0)	<0.01
Cognitive Function† (PROMIS)	42.0 (39.2, 44.7)	49.3 (48.2, 50.6)	<0.01	45.5 (43.3, 47.3)	49.2 (47.8, 50.6)	0.005
Self-report SLE Flares, %	52.2 (35.1 - 69.3)	25.6 (18.9, 32.2)	0.005	40.3 (27.8, 53.0)	25.4 (18.1, 32.7)	0.041

*Adjusted means and p-values calculated based on multivariate linear or logistic regression adjusted for age, sex, race, education, income, smoking, disease duration, and disease damage (Brief Index of Lupus Damage score).

**Patients with scores in the top quartile of the 4-item Perceived Stress Scale (PSS)

***Patients who reported that stress caused by the COVID-19 pandemic was "a great deal" or "the most stressful situation I have gone through"

†Higher scores reflect better status (better cognitive function)

SLAQ – Systemic Lupus Activity Questionnaire

PROMIS – Patient Reported Outcomes Measurement Information System

Table 1

Table 2. Longitudinal Associations for Change in Perceived Stress* with Change in PROs During the COVID-19 Pandemic

Change in Disease Outcomes:	Adjusted β/OR**	P-value
Disease Activity (SLAQ)	β = 0.44	<0.01
Pain (0-10)	β = 0.07	0.196
Fatigue (PROMIS)	β = 1.04	<0.01
Cognitive Function† (PROMIS)	β = -0.58	<0.01
Incident self-report SLE Flare	OR = 1.00	0.989

*Difference in Perceived Stress Score from before to during the COVID-19 pandemic.
**Adjusted regression coefficients and p-values calculated based on multivariate linear or logistic regression adjusted for age, sex, race, education, income, smoking, disease duration, and disease damage (Brief Index of Lupus Damage score).
†Higher scores reflect better status (better cognitive function)
SLAQ – Systemic Lupus Activity Questionnaire
PROMIS – Patient Reported Outcomes Measurement Information System

Table 2

non-pharmacologic interventions to bolster stress resiliency are urgently needed to improve outcomes in this patient population during the ongoing health crisis.Table 1

Disclosure: S. Patterson, None; **L. Trupin**, None; **K. DeQuattro**, None; **C. Lanata**, None; **M. Dall'Era**, Janssen, 5, AstraZeneca, 5; **J. Yazdany**, Eli Lilly, 1, Astra Zeneca, 1; **P. Katz**, None.

Abstract Number: 1268

Structural Validity of a Comprehensive Neuropsychological Battery for Assessment of Cognitive Impairment in Systemic Lupus Erythematosus: Exploratory Factor Analysis Confirms Six Cognitive Domains

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) can lead to neuropsychiatric manifestations including cognitive impairment (CI). The gold standard for assessment of SLE cognitive function is the American College of Rheumatology comprehensive neuropsychological battery (NB), which was introduced in 1996 and assesses 6 cognitive domains. COnsensus-based Standards for the selection of health Measurement INstruments (COSMIN) define structural validity as "*the degree to which the scores of an instrument are an adequate reflection of the dimensionality of the construct being measured".* Our primary aims were to explore the number of latent factors encompassed by the NB and assess the battery's structural validity, i.e., determine if identified latent factors can be mapped to NB's intended cognitive domains.

Methods: 300 consecutive consenting SLE patients aged 18-65 years attending a single center, were enrolled (Jul 2016 – Nov 2019) and completed the NB. The NB includes the following tests: Finger tapping, Trail Making Test A and B, Stroop Color and Word Test, Rey-Osterrieth Complex Figure Test (RCFT), Controlled Oral Word Association Test (COWAT), Animal Naming, Hopkins Verbal Learning Test – Revised (HVLT-R), Wechsler Adult Intelligence Scale Digit Symbol Substitution Test (WAIS III), Letter-Number Sequencing, and Consonant Trigrams.Structural validity was examined with exploratory factor analysis (EFA) using squared multiple correlations as prior communality estimates. The maximum likelihood method was used to extract factors, followed by a varimax (orthogonal) rotation. A scree plot was developed to examine the underlying factors of NB. Factors with Eigenvalues of >1 were extracted. The sample size met standards for EFA of more than 100 participants or at least 5 times the number of variables being analyzed. A multiple imputation model was used to account for missing data.

Results: 300 participants entered the cohort (89.0% female, mean age at enrollment 41.1±12.1 years, mean disease duration 14.1±10.0 years) (**Table 1**). 54 (18.0%) of patients had at least one test score missing.

Characteristics	N= 300
Sex (F)	267 (89%)
Age at diagnosis (Mean ± SD)	27.0 ± 10.5
Age at study enrolment (Mean ± SD)	41.1 ± 12.1
Disease Duration at study enrolment (Mean ± SD)	14.1 ± 10.0
Ethnicity	
Black	59 (19.7%)
Caucasian	162 (54.0%)
Asian	52 (17.3%)
Others	27 (9.0%)
Education Level	
High school not completed	9 (3.0%)
High school completed	48 (16.2%)
Post-secondary education (College/University)	239 (80.8%)

Table 1. Patient demographics at enrolment

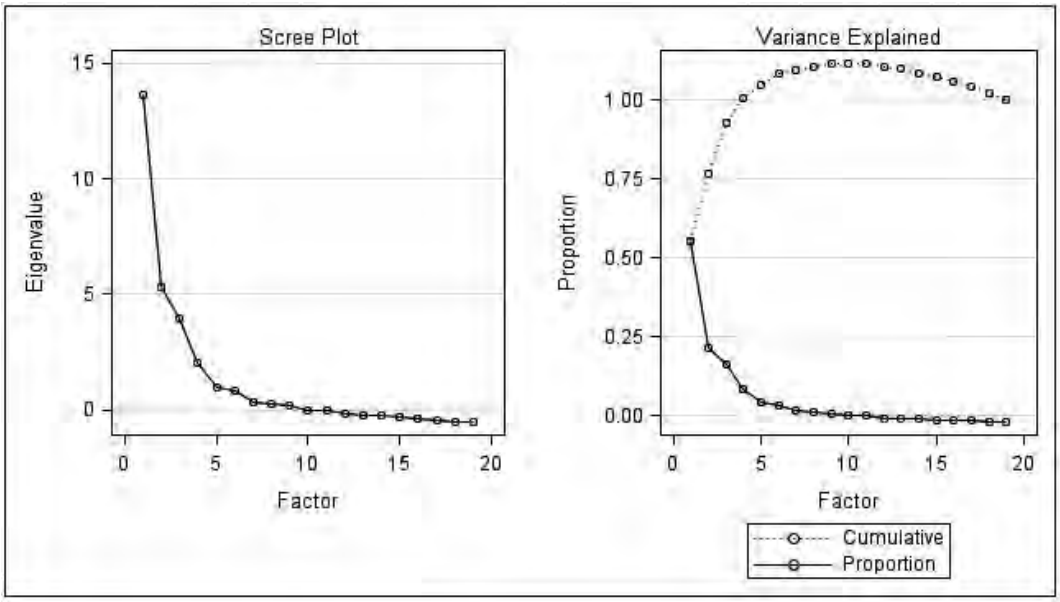

Figure 1. Scree and Variance Plots confirming a 6 factor model

EFA model fitting indicated a six-factor model as the best fit, with Akaike Information Criterion (AIC) -24 and Tucker and Lewis Reliability Coefficient of 95% comparing to models with less or more factors. The choice of model was confirmed with Scree and Variance Explained plots with cumulative variance of 100% explained by six factors (**Figure 1**).

Individual NB tests primarily loaded on the factors representing the intended cognitive domains (**Table 2**), although the strength of weights of individual tests varied within each factor. The one exception was Consonant Trigrams, which loaded on the Memory factor, although its second highest loading was on its intended factor.

Conclusion: EFA indicates that a six-factor model fits the structure of the NB. The factors identified by EFA closely resemble the structure of the 1996 NB and confirms its structural validity. Variations in strength of weights raises the

	Test Name	Factor1	Factor2	Factor3	Factor4	Factor5	Factor6
Visual Spatial Construction	RCFT Recall	0.974	0.089	0.143	0.046	0.060	0.130
	RCFT Delay Recall	0.873	0.100	0.146	0.056	0.043	0.108
	RCFT Copy	0.442	0.374	0.061	0.104	-0.008	0.100
	RCFT Recognition	0.356	0.213	0.103	0.061	-0.010	0.028
Executive function and simple attention	Trails B	0.184	0.679	0.076	0.128	0.122	0.129
	WAIS-III Digit Symbol	0.157	0.632	0.198	0.161	0.308	0.111
	Trails A	0.152	0.545	0.045	0.105	0.213	0.098
	Stroop (interference score)	0.071	0.365	0.184	0.215	-0.039	0.035
Learning and Memory	HVLT-R Delayed Recall	0.139	0.160	0.808	0.080	0.071	-0.006
	HVLT-R Total Recall	0.168	0.222	0.730	0.202	0.014	-0.008
	HVLT-R Recognition	0.046	0.005	0.543	0.065	0.030	-0.046
	Consonant Trigrams	0.082	0.089	0.384	0.317	0.0400	0.015
Language Processing and executive function	COWAT	0.027	0.098	0.125	0.804	0.124	0.078
	ANIMALS	0.066	0.326	0.179	0.542	0.078	0.035
	WAIS Letter-Number	0.173	0.242	0.218	0.408	0.161	0.106
Simple attention	Stroop Word Reading	-0.004	0.169	0.043	0.116	0.967	0.091
	Stroop Colour Naming	0.059	0.382	0.106	0.209	0.522	0.100
Manual Motor Speed	Dominant hand tapping	0.062	0.110	-0.001	0.047	0.042	0.829
	Non-dominant hand tapping	0.163	0.115	-0.058	0.072	0.083	0.333

Table 2. EFA model fitting with 6 factors Abbreviations: Rey-Osterrieth Complex Figure Test (RCFT), Controlled Oral Word Association Test (COWAT), Animal Naming, Hopkins Verbal Learning Test – Revised (HVLT-R), Wechsler Adult Intelligence Scale Digit Symbol Substitution Test (WAIS III)

possibility of reducing the number of tests to those with the highest loadings, which might increase the feasibility of administering the NB.

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Abstract Number: 1269

Evaluation of a Patient-reported Frailty Tool in Women with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Frailty has been associated with increased disability and mortality in SLE. To our knowledge, no patient-reported frailty tool has been evaluated alongside a standard frailty measure in SLE. We aimed to assess 1) the prevalence of frailty according to both the standard Fried phenotype (FP) and a validated self-reported frailty

Table 1. Baseline characteristics by frailty classification

Characteristic (Median and IQR)	Fried phenotype (N=72)			FRAIL scale (N=67)		
	Non-frail (N=61)	Frail (N=11)	p-value	Non-frail (N=49)	Frail (N=18)	p-value
Age (years)	41.0 [31.0, 57.0]	56.0 [51.0, 63.0]	0.08	42.0 [29.0, 56.0]	55.0 [37.0, 64.0]	**0.04**
SLE disease duration (years)	13.0 [6.0, 23.0]	16.0 [12.0, 38.0]	0.15	13.0 [6.0, 19.0]	15.5 [10.0, 32.0]	0.06
Charlson comorbidity index	2.0 [1.0, 3.0]	3.0 [2.0, 6.0]	**0.02**	3.0 [2.0, 3.0]	3.0 [1.0, 5.0]	0.35
SELENA-SLEDAI* score	4.0 [0.0, 4.0]	0.0 [0.0, 8.0]	0.66	2.0 [0.0, 4.0]	4.0 [2.0, 7.0]	0.11
SLICC/ACR Damage Index** score	0.0 [0.0, 2.0]	4.0 [1.0, 5.0]	**0.002**	0.0 [0.0, 1.0]	2.0 [1.0, 4.0]	**0.0006**
Current prednisone dose (mg)	5.0 [4.0, 9.0]	5.0 [5.0, 5.0]	0.81	5.0 [4.0, 8.0	5.0 [4.5, 6.5]	0.88
BMI (kg/m^2)	24.1 [22.1, 30.8]	26.6 [25.2, 35.3]	0.10	24.1 [22.1, 29.7]	28.3 [23.2, 31.2]	0.09
Race, N (%) Asian Black or African American White	 5 (9.1) 15 (27.3) 19 (34.6)	 0 (0) 6 (60.0) 2 (20.0)	0.44	 5 (10.4) 15 (31.3) 15 (31.3)	 0 (0) 7 (38.9) 6 (33.3)	0.70
Ethnicity, N (%) Hispanic Non-Hispanic	 15 (27.8) 39 (72.2)	 4 (40.0) 6 (60.0)	0.47	 11 (23.4) 36 (76.6)	 8 (44.4) 10 (55.6)	0.10
Education, N (%) High school or less Some college College Graduate/professional school	 6 (10.9) 13 (23.6) 22 (40.0) 14 (25.5)	 4 (36.4) 3 (27.3) 2 (18.2) 2 (18.2)	0.18	 2 (4.1) 12 (24.5) 22 (44.9) 13 (26.5)	 8 (44.4) 4 (22.2) 3 (16.7) 3 (16.7)	**0.0009**
Insurance status, N (%) Medicare Medicaid Commercial insurance	 8 (14.6) 15 (27.3) 36 (65.5)	 4 (36.4) 7 (63.6) 3 (27.3)	 0.10 **0.03** **0.04**	 5 (10.2) 13 (26.5) 33 (67.4)	 8 (44.4) 10 (55.6) 6 (33.3)	 **0.004** **0.03** **0.01**
Smoking status, N (%) Ever	 6(10.9)	 5(45.5)	**0.01**	 6(12.2)	 5(27.8)	0.15
Concurrent fibromyalgia, N (%)	8 (14.6)	4 (36.4)	0.10	6 (12.2)	6 (33.3)	0.07

*SELENA-SLEDAI: Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index. Range 0-105; higher is worse.
**SLICC/ACR Damage Index: Systemic Lupus Internal Collaborating Clinics/ACR Damage Index. Range 0-46; higher is worse.

Table 1

instrument, 2) differences between frail and non-frail women according to each definition, 3) the association of each frailty measure with patient-reported disability, and 4) the correlation between frailty definitions.

Methods: Adult women < 70 years old with validated SLE and mild/moderate disease were recruited from a single center. Measures included: frailty (FP and the self-reported FRAIL Scale [FS] [1]); disease activity (SELENA-SLEDAI); disease damage (SLICC/ACR Damage Index); inflammatory/metabolic biomarkers; and patient-reported outcome measures (PROMs), including Valued Life Activities disability. Differences between frail and non-frail participants were evaluated using Fisher's exact or Wilcoxon rank sum tests and the association of frailty with disability using logistic regression. Correlation between the FP and the FS was determined using Spearman's correlation.

Results: 72 women enrolled; 67 (93%) completed the FS. 17% and 27% were frail according to the FP and the FS, respectively. Frail women according to either definition had greater disease damage (FP: p=0.002; FS: p=0.0006),

Table 2. Inflammatory and metabolic biomarkers and patient-reported outcome measures by frailty classification

Biomarker (Median and IQR)	Fried phenotype (N=72)			FRAIL scale (N=67)		
	Non-frail (N=61)	Frail (N=11)	p-value	Non-frail (N=49)	Frail (N=18)	p-value
ESR (mm)	13.0 [8.0, 22.0]	25.0 [20.0, 36.0]	**0.01**	14.0 [8.0, 24.0]	20.0 [13.0, 32.0]	0.06
High-sensitivity CRP (mg/L)	1.6 [0.6, 4.2]	8.1 [2.0, 9.8]	**0.02**	1.4 [0.6, 4.1]	4.6 [2.0, 10.2]	**0.02**
Adiponectin (microg/mL)	22.6 [17.3, 34.0]	15.6 [7.8, 23.9]	0.10	19.8 [15.2, 33.1]	24.6 [15.4, 30.7]	0.96
Insulin-like growth factor 1 (ng/mL)	128.2 [100.0, 206.5]	118.1 [78.3, 174.5]	0.43	137.3 [102.0, 206.6]	107.5 [78.3, 131.1]	0.06
Interleukin 6 (ng/mL)	0.8 [0.4, 1.3]	2.1 [1.4, 3.3]	**0.0005**	0.8 [0.4, 1.3]	1.6 [1.2, 2.2]	**0.003**
Patient-reported outcome measure						
PROMIS domains*						
Mobility	46.4 [40.2, 49.7]	35.2 [31.8, 38.1]	**<.0001**	46.6 [42.0, 49.7]	35.2 [33.0, 37.7]	**<.0001**
Physical function	43.9 [39.8, 48.5]	32.7 [24.5, 37.5]	**<.0001**	44.8 [40.9, 50.1]	32.7 [28.8, 37.5]	**<.0001**
Pain behavior	56.6 [49.7, 59.8]	60.1 [57.4, 64.4]	**0.009**	55.4 [48.5, 59.0]	62.1 [58.5, 63.6]	**<.0001**
Pain interference	54.3 [46.6, 60.1]	65.0 [58.5, 68.2]	**0.0005**	54.3 [46.6, 57.3]	65.7 [58.5, 68.2]	**<.0001**
Fatigue	55.6 [49.1, 62.7]	71.6 [64.0, 73.9]	**0.0004**	55.4 [48.5, 62.4]	65.9 [62.4, 73.9]	**<.0001**
Depression	51.3 [44.7, 57.5]	54.3 [46.3, 69.5]	0.22	51.2 [44.6, 55.0]	56.8 [49.9, 67.6]	**0.02**
Anxiety	54.1 [50.6, 61.5]	58.9 [46.9, 71.3]	0.52	53.7 [49.9, 61.3]	60.2 [52.9, 65.1]	0.17
LupusQOL domains**						
Physical health	71.9 [53.1, 84.4]	31.3 [12.5, 56.3]	**0.0003**	75.0 [56.3, 84.4]	39.1 [25.0, 56.3]	**<.0001**
Pain	75.0 [50.0, 91.7]	41.7 [25.0, 50.0]	**0.0006**	83.3 [50.0, 91.7]	45.8 [25.0, 50.0]	**<.0001**
Planning	75.0 [66.7, 91.7]	41.7 [8.3, 75.0]	**0.01**	75.0 [66.7, 91.7]	50.0 [16.7, 83.3]	**0.00**
Intimate relationships	75.0 [50.0,100.0]	0.0 [0.0, 37.5]	**0.001**	87.5 [75.0, 112.5]	87.5 [0, 125.0]	**0.05**
Burden to others	75.0 [58.3, 88.3]	50.0 [16.7, 83.3]	0.44	75.0 [50.0, 83.3]	62.5 [50.0, 83.3]	0.27
Emotional health	83.3 [58.3, 91.7]	54.2 [33.3, 91.7]	0.30	83.3 [58.3, 91.7]	56.3 [50.0, 83.3]	0.06
Body image	80.0 [50.0, 91.7]	60.0 [37.5, 83.3]	0.15	95.0 [70.0, 105.0]	82.5 [60.0, 95.0]	0.19
Fatigue	56.3 [37.5, 75.0]	43.8 [12.5, 62.5]	0.06	56.3 [37.5, 75.0]	43.8 [18.8, 56.3]	**0.02**
Valued Life Activities†	0.5 [0.2, 0.9]	1.2 [1.1, 1.8]	**0.0001**	0.5 [0.1, 0.8]	1.2 [1.0, 1.7]	**<.0001**
Center for Epidemiologic Studies Depression Scale‡	17.0 [15.0, 22.0]	25.0 [19.0, 35.0]	**0.001**	17.0 [15.0, 22.0]	22.5 [19.0, 28.0]	**0.008**

*PROMIS: Patient Reported Outcome Measurement Information System. Scored using a T score metric, with 50 representing the population mean and a difference of 5 considered clinically significant.
**LupusQOL: Scores range from 0-100, with higher scores indicating higher health-related quality of life.
†Valued Life Activities: Scores range from 0-3, with higher scores indicating greater disability.
‡Center for Epidemiologic Studies Depression Scale: Scores range from 0-60, with high scores indicating greater depression.

Table 2

significantly greater high-sensitivity CRP (FP and FS: p=0.02) and interleukin 6 (FP: p=0.0005; FS: p=0.003), and significantly worse PROMS across multiple domains (Tables 1 and 2). Compared with non-frail women, frail women classified by the FP had greater comorbidity burden (p=0.02), higher prevalence of smoking (p=0.01), and higher ESR (p=0.01); when classified by the FS, frail women were significantly older (p=0.04) with lesser educational attainment (p=0.0009) (Tables 1 and 2). Frailty according to either definition was significantly associated with disability after adjustment for age, comorbidity burden, and disease activity (FP: p=0.02; FS: p=0.0003), but this relationship was attenuated for the FP after adjustment for disease damage (p=0.08) (Table 3). There was moderate correlation between the FS and the FP (r=0.48; p< 0.0001).

Conclusion: The prevalence of patient-reported frailty was high in this cohort of women with SLE. Frail women had generally worse PROMs, providing face validity for both definitions. The FS was strongly associated with disability even after adjustment for multiple confounders. While estimates are imprecise, these data suggest that the FS may be an informative point-of-care tool to identify frail women with SLE.

Table 3. Cross sectional association of frailty with disability by frailty classification

Model	Fried phenotype (N=72)			FRAIL scale (N=67)		
	Odds ratio	95% confidence interval	p-value	Odds ratio	95% confidence interval	p-value
Unadjusted*	7.7	1.9,31.5	**0.005**	17.2	4.5,66.2	**<0.0001**
Adjusted for age	6.0	1.4,25.9	**0.02**	15.1	3.8,59.6	**0.0001**
Adjusted for age and CCI**	6.9	1.4,33.1	**0.02**	16.5	4.0,68.5	**0.0001**
Adjusted for age, CCI**, and disease activity	6.2	1.3,30.1	**0.02**	20.8	4.1,105.8	**0.0003**
Adjusted for age, CCI**, disease activity, and disease damage	4.4	0.9,22.5	0.08	17.8	3.4,94.2	**0.0007**

*Odds of Valued Life Activities score in the top quartile in frail versus non-frail women
**Charlson Comorbidity Index

Table 3

References

1. Morley JE et al. J Nutr Health Aging 2012;16:601-8.

Disclosure: S. Lieber, None; **S. Paget**, None; **J. Berman**, None; **M. Barbhaiya**, None; **L. Sammaritano**, None; **K. Kirou**, None; **J. Carrino**, Covera Health, 5, Image Analysis Group, 5, Image Biopsy Lab, 5, Pfizer, 5, Simplify Medical, 5, Arthritis and Rheumatology journal, 9, Osteoarthritis Imaging journal, 9; **M. Nahid**, None; **M. Rajan**, Veterans Health Administration, 3; **D. Sheira**, None; **L. Mandl**, Annals of Internal Medicine, 9, UpToDate, 7, Regeneron, 2.

Abstract Number: 1270

Trend of Survival of a Cohort of Patients with Systemic Lupus Erythematosus over 25 Years

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose

Background: Few studies of systemic lupus erythematosus (SLE) have a follow-up duration long enough to evaluate the time trend of survival, particularly in Asian countries.

Objectives: To revisit the trend of survival of SLE in a cohort of southern Chinese patients over 25 years.

Methods: Patients who fulfilled the 1997 ACR criteria for SLE and were followed in our hospital since 1995 were included. Patients were stratified into 2 groups according to the year of diagnosis: (1) 1995-2004; and (2) 2005-2018.

Survival of patients was studied by Kaplan Miere's analysis. For those who died or lost to follow-up, data were censored at their last clinic / hospital visits. Organ damage was assessed by the Systemic Lupus International Collaborating Clinics (SLICC) damage index (SDI) and causes of death in the first 10 years of SLE onset were compared between the two groups. Cox regression was used to study factors associated with survival.

Results: A total of 1098 SLE patients were registered in our database. After excluding 157 patients diagnosed outside the time period of 1995-2018, 941 patients were studied (92% women). All were ethnic Chinese. The mean age of SLE onset was 35.1±14.4 years and the mean follow-up duration by the same groups of physicians was 13.1±6.6 years. Seventy-seven patients were lost to follow up. Groups 1 and 2 consisted of 364 and 577 patients, respectively. The mean SDI score at 10 years of disease onset was significantly higher in group 1 than group 2 patients (1.01±1.43 vs 0.57±0.94; p< 0.01), particularly in the neuropsychiatric, musculoskeletal and gonadal domains. The proportion of patients with organ damage in these 3 systems was also significantly higher in this group of patients. Within 10 years of SLE onset, 32 (8.8%) patients in group 1 and 25 (4.3%) patients in group 2 died (p=0.005). The 5- and 10-year cumulative survival rates were 93.6% and 91.0% in group 1; and 96.5% and 94.2% in group 2 patients, respectively (log rank test p=0.048). Infection accounted for more than half of the deaths in both groups. More group 1 than group 2 patients died of vascular events but the difference was not statistically significant. Univariate Cox regression analysis showed that age of onset, male sex and SDI score at 10 years were associated with survival. Group 2 patients showed a better survival than group 1 but statistical significance was borderline (HR 0.61[0.38-1.001]; p=0.05). Multivariate analysis revealed only the age of onset (1.06 [1.04-1.08] per year; p< 0.001) and SDI at 10 years (1.65 [1.47-1.85] per point; p< 0.001) were significantly associated with survival. The period in which SLE was diagnosed was not a significant factor determining survival (HR 0.68[0.41-1.14]; p=0.14).

Conclusion: The survival of our Chinese SLE patients has improved significantly from 1995-2004 to 2005-2018, which is contributed by lower organ damage accrual.

Disclosure: C. Mok, None; **L. Ho**, None; **K. Chan**, None; **S. Tse**, None; **C. To**, None.

Abstract Number: 1271

Post-Traumatic Stress Disorder (PTSD) and Risk of Systemic Lupus Erythematosus (SLE) Among Medicaid Recipients

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Post-traumatic stress disorder (PTSD), the sentinel stress-related mental disorder, may be associated with increased risk of developing autoimmune disease, including systemic lupus erythematosus (SLE). This study aimed to study the relationship between PTSD and risk of SLE in a large, diverse population of Medicaid enrollees. We hypothesized patients with incident SLE would be more likely to have a prior diagnosis of PTSD than those without SLE.

Methods: We performed a case-control study using patients ages 18 to 65 years old in the Medicaid Analytic eXtract (MAX) database between January 1, 2007 and December 31, 2010. Cases of SLE were defined as having ≥3 ICD-9

Table 1. Characteristics of US Medicaid Patients with SLE vs. Matched US Medicaid Patients without SLE (2007-2010), matched at the Index Date for SLE

Characteristic	SLE Cases (n=10,942)	Matched General Medicaid Population Controls (n= 109,420)
Mean age, years (SD)*	40.8 (12.4)	40.8 (12.4)
Female, %*	93.5	93.5
Race, %*		
African American	39.8	39.9
White	37.5	37.5
Asian	2.3	2.3
Hispanic	16.9	16.9
Native American	0.95	0.87
Other	2.5	2.5
Median zip code level income, %		
1st Quartile	25.9	24.8
2nd Quartile	25.8	24.9
3rd Quartile	23.8	25.4
4th Quartile	24.6	25.0
US Region of Residence, %		
South	37.4	38.9
Northeast	21.8	19.4
Midwest	20.4	23.1
West	20.3	18.6
Smoking, %	11.3	7.3
Obesity, %	7.1	4.2
Oral contraceptive use (among women only), %	8.8	10.5

*Matching factor
IQR: interquartile range, SD: Standard deviation

codes for SLE from hospital discharge diagnoses or physician visit claims, occurring at least 30 days apart. Index date was defined as the date of the first code for SLE. Controls were matched to SLE cases for age, sex and race using a 1:10 ratio. Controls were patients without any claims for SLE, but who had another inpatient or outpatient claim in Medicaid on the SLE index date of the matched case. Exclusion criteria included having less than 12 months of continuous Medicaid enrollment prior to the index or matched control date. The exposure was PTSD, defined as having ≥2 ICD-9 codes for PTSD on different dates within 4 months of each other, occurring prior to the index date for SLE (Gravely, 2011; PPV 82%). We used conditional logistic regression to calculate the odds ratio (OR) and 95% confidence interval (CI) for history of PTSD prior to index date in cases vs. controls. Finally, we used multivariable analysis to adjust for variables collected prior to the index date, including area-level socioeconomic status (SES), smoking, obesity, oral contraception use, and time enrolled in Medicaid.

Results: We identified 10,942 cases of incident SLE, who were matched to 109,420 controls. There were significant differences at the index date in several characteristics, including zip code level income as a measure of socioeconomic status (SES), US region of residence, smoking, obesity, and oral contraceptive use (Table 1). 1.46% of Medicaid enrollees with SLE met the definition of PTSD prior to the index date, compared to 0.75% of controls ($p< 0.001$). The OR for PTSD and risk of incident SLE was 1.96 (95% CI 1.66-2.33, $p< 0.001$) in conditional logistic regression, and 2.02 (95% CI 1.65-2.48, $p< 0.001$) after multivariable adjustment (Table 2). Further adjustment for the matching factors did not alter risk estimates.

Conclusion: In this large, racially and sociodemographic diverse US patient population, we found a near doubling of odds of SLE associated with prior PTSD diagnosis. Chronic stress leading to hypothalamic-pituitary axis dysregulation and inflammatory cytokine upregulation are postulated mechanisms. Future studies are needed with longer

Table 2. Conditional logistic regression models for PTSD in relation to incident SLE, comparing PTSD to no PTSD

	Conditional logistic regression			Multivariable-adjusted conditional logistic regression*		
	OR	CI	p-value	OR	CI	p-value
No PTSD	1.00	Ref		1.00	Ref	
PTSD	1.96	1.66-2.33	<0.0001	2.02	1.65, 2.48	<0.0001

*Conditioned on matching factors, age, sex and race/ethnicity. Multivariable conditional logistic regression additionally adjusted for area-level median household income, smoking, obesity, oral contraceptive use, and days enrolled in Medicaid prior to index date.

follow-up time to clarify the underlying pathophysiology and characterize modifying influences in the relationship between PTSD and SLE.

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Abstract Number: 1272

Impact of Remission and Low Disease Activity Status on Hospitalizations Among SLE Patients from the GLADEL Latin American Cohort

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: To determine whether remission and low disease activity state (LDAS) reduce hospitalizations in systemic lupus erythematosus (SLE) patients.

Methods: A multi-ethnic, multi-national Latin-American SLE cohort was studied.

Variable	Univariable HR (95% CI)	p value	Multivariable HR (95% CI)	p value
Disease activity status				
Remission on treatment	0.39 (0.25-0.61)	<0.0001	0.46 (0.29-0.72)	0.001
LDAS	1.19 (0.94-1.51)	0.139	1.20 (0.94-1.53)	0.135
Active	Ref.		Ref.	
Age at diagnosis	0.88 (0.82-0.95)	0.001	0.89 (0.82-0.96)	0.002
Gender, Female	1.02 (0.77-1.34)	0.914	1.11 (0.84-1.46)	0.477
Ethnicity				
Caucasians	Ref.		Ref.	
Mestizo	1.20 (1.00-1.44)	0.051	1.03 (0.85-1.24)	0.771
ALA	1.10 (0.83-1.46)	0.514	0.99 (0.75-1.33)	0.986
Others	1.46 (0.92-2.30)	0.109	1.29 (0.82-2.05)	0.276
Rural residence	0.91 (0.67-1.22)	0.520		
Socioeconomic status				
High	Ref.		Ref.	
Medium	1.90 (1.28-2.84)	0.002	1.81 (1.21-2.71)	0.004
Low	2.52 (1.72-3.67)	<0.0001	2.02 (1.37-2.96)	0.001
Medical insurance, Full coverage	0.91 (0.77-1.08)	0.363		
Previous hospitalization	1.41 (1.20-1.67)	<0.0001	0.99 (0.83-1.20)	0.953
Increase on the SDI, per 1 unit	1.33 (1.26-1.40)	<0.0001	1.27 (1.20-1.35)	<0.0001
Antimalarial use	0.53 (0.44-0.63)	<0.0001	0.61 (0.51-0.72)	<0.0001
Prednisone (highest dose)				
None	Ref			
<7.5mg/d	0.90 (0.51-1.61)	0.730		
7.5-15mg/d	1.00 (0.73-1.37)	0.997		
15-60mg/d	0.97 (0.79-1.20)	0.793		
>=60mg/d	0.99 (0.76-1.28)	0.922		

Table 1. Impact of disease activity status on hospitalization: univariable and multivariable analyses. LDAS: low disease activity status; ALA: Afro-Latin American; SDI: SLICC/ACR damage index; HR: Hazard ratio; 95% CI: 95% confidence interval; Ref: reference group

Visits were performed every six months. Variables were ascertained at each visit. The first hospitalization following cohort entry was evaluated in the interval between two visits. Based on the definitions of remission in SLE (DORIS) framework, for each visit remission on treatment was defined as a SLEDAI of 0, prednisone ≤5 mg/day and maintenance treatment with immunosuppressants. LDAS was defined as a SLEDAI ≤4 with no SLEDAI scores for renal, central nervous system, serositis, vasculitis, and constitutional components, no increase in any SLEDAI component since the previous visit, and prednisone dose ≤7.5 mg/day. Immunosuppressants at maintenance doses were allowed for LDAS. Antimalarial treatment was allowed for both states. Potential confounders of hospitalization included sociodemographic factors, baseline damage (Systemic Lupus International Collaborating Clinics Damage Index or SDI), previous hospitalizations, glucocorticoids and antimalarials (users and non-users). Both, disease activity status and antimalarials were evaluated as time-dependent covariates. Cox regression model was used to evaluate whether remission on treatment and LDAS protected against hospitalizations after controlling for important confounders. A multivariable model was built by selecting covariates using a backward elimination procedure.

Results: One thousand three hundred and forty-one patients were included; 1201 (89.6%) were female. The median (IQR) age at diagnosis was 27 (20-37) years and the median (IQR) follow up time 27.5 (4.7-62.2) months. A total of 508 patients were hospitalized, of those 455 (89.6%) were female.

There were 6,089 intervals for these 1,341 patients. The median number of intervals per patient was 4 (2-7), and the median length of the intervals was 7.1 (5.1-11.7) months. Of the intervals examined, the most frequent status was non-optimally controlled, with 4,269 (75.1%) intervals, followed by remission on treatment 772 (13.6%) and LDAS 643 (11.3%) intervals. In the multivariable analysis, remission on treatment (HR 0.46; 95% CI 0.29–0.72) but not LDAS was found to decrease the hazard ratio of hospitalization, after adjusting for confounders. Of interest, antimalarials were found to be protective (HR: 0.61; 95% CI 0.51-0.72).

Conclusion: In this large Latin American multiethnic, multinational lupus cohort, remission on treatment reduced the risk of hospitalization after adjusting for other well-known risk factors. It is worth pointing out that antimalarial use seemed to protect against the occurrence of hospitalizations, supporting its role as a cornerstone treatment in SLE. Our findings call for seeking remission as a fundamental target in the management of patients with SLE.

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Abstract Number: 1273

The Impact of the COVID-19 Pandemic on the Fibromyalgia Symptoms of SLE Patients

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

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Background/Purpose: Many patients with SLE experience symptoms of chronic pain and fatigue, often meeting criteria for fibromyalgia (FM). In this study, we sought to examine whether FM symptoms improved or worsened following the outset of the COVID-19 pandemic.

Methods: On Maya 6, 2020, 287 patients in the Duke Lupus Registry (DLR) were emailed an invitation to take a survey about the impact of the COVID-19 pandemic. Responses to the ACR 2016 FM diagnostic criteria questions (defined as post-pandemic responses) were compared to the 53 patients' responses to the same questions collected at their most recent clinic visit prior to March 18, 2020 (defined as pre-pandemic responses). Significant clinical improvement was defined as a 3+ decrease in fibromyalgia severity score (FSS), a patient reported outcome scored as 0-31; significant clinical worsening was defined as 3+ increase in FSS. A two-tailed student t-test was used to

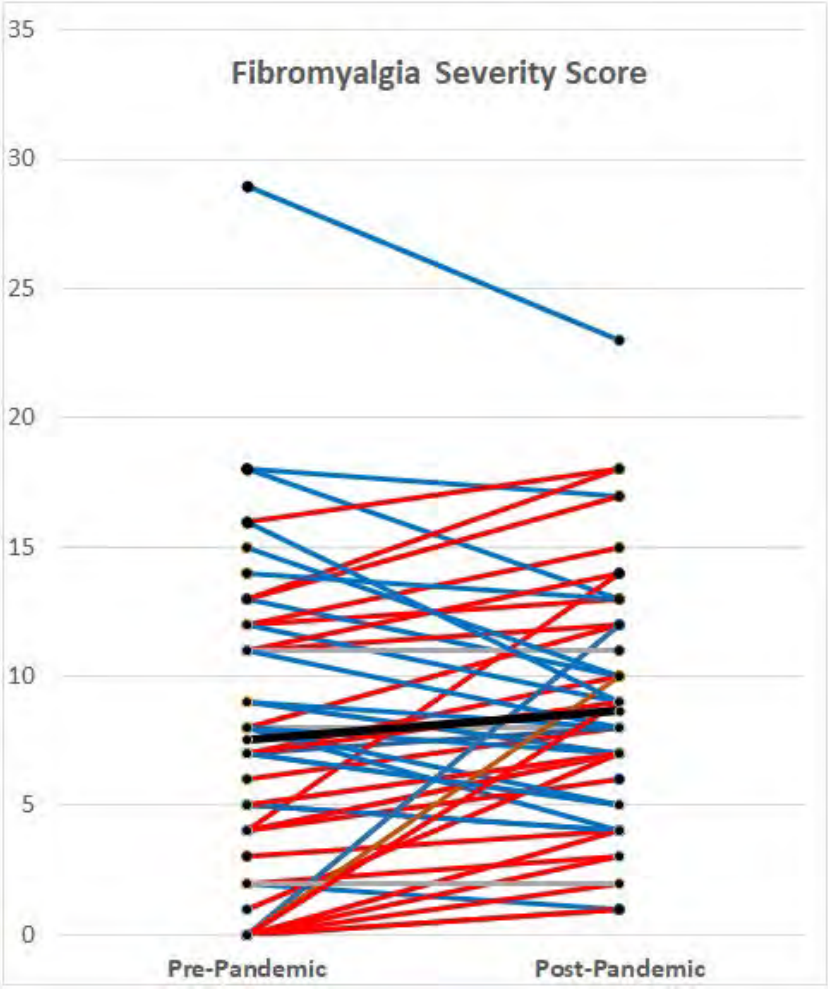

Figure 1. FSS change over time. For each patient participating in the survey, a pre-pandemic FSS (FSS from the most recent clinical visit prior to March 18, 2020) was compared to the post-pandemic FSS (collected from the online survey distributed on May XX, 2020). Red lines indicate patients with worsening FSS; blue lines indicate patients with improving FSS; grey lines indicate patients with unchanged FSS. The thick black line highlights the pre-pandemic mean (7.5) compared to the post-pandemic mean (8.7).

performed a paired analysis of pre-pandemic FSS to post-pandemic FSS. Finally, the polysymptomatic distress scale (PDS) was used to characterize symptoms as mild (0-3), moderate (4-7), or severe (12-19).

Results: Survey responses were received from 53/287 (18%) of the Duke Lupus Registry participants, 92.5% of whom were women, 34% Black, and 60% Caucasian, compared to 93.4%, 53.8%, and 39.4%, respectively, in the registry as a whole. The mean pre-pandemic FSS for these patients was 7.5 ± 0.8 (SEM), compared to 8.7 ± 0.7 (SEM), post-pandemic (p=0.05). Pre-pandemic, 15 patients (28%) met criteria for mild polysymptomatic distress, 12 (23%) moderate, and 7 (13%) severe; post-pandemic, 21 patients (40%) met criteria for mild polysymptomatic distress, 15 (28%) moderate, and 8 (15%) severe (see Figure 1). Of the 53 survey respondents, 8 (15%) demonstrated significant clinical improvement during the pandemic, whereas 14 (26%) experienced significant clinical worsening. Of the 14 patients with worsened FSS, 12 (86%) did not identify any specific pandemic-related stressors or challenges in the domains of physical health, mental health, or personal life (work, family, and finances); the other 2 patients only mentioned worsening symptoms (pain, anxiety, and depression) as challenges. In contrast, of the 8 patients with improving FSS, 4 (50%) did not describe specific challenges, whereas the other 4 patients described symptoms in addition to articulating themes of isolation, missing extended family and family events, struggling with job loss, working to find opportunities for exercise, and grappling with balancing childcare and work responsibilities.

Conclusion: The experience of the COVID-19 pandemic is heterogeneous for SLE patients. In average, patient's FM symptoms worsened following the onset of the pandemic, with 14 patients experiencing significant clinical worsening and only 8 patients experiencing significant clinical improvement in FM symptoms. Interestingly, the patients who improved articulated more pandemic-related challenges, perhaps suggesting that insight into one's challenges is key to healthy coping. Further research is needed to identify risk factors and protective factors for SLE patients in the setting of the COVID-19 pandemic.

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Abstract Number: 1274

COVID-19 in Patients with Systemic Lupus Erythematosus

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Background/Purpose: Patients with systemic lupus erythematosus (SLE) represent a unique population in considering risk for coronavirus disease 2019 (COVID-19) with biologic, genetic, demographic, clinical and treatment issues all at play. By the nature of their chronic inflammatory autoimmune condition and regular use of immunosuppressive medications, these individuals would traditionally be considered at high risk of contracting the severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) and having a worse prognosis. Accordingly, we aimed to characterize

	Hospitalized* N = 24
Details of Hospitalization (N, %)	
Regular Floor	20 (83.3%)
ICU	4 (16.7%)
Oxygen/Ventilation Requirements (N, %)	
Room Air (N = 19)	9 (47.4%)
Supplemental O_2† (N = 19)	7 (36.8%)
Intubation/MV (N = 23)	3 (13.0%)
ECMO (N = 23)	0
Renal Replacement Therapy (N,%)‡	
Required (N = 19)	1 (5.3%)
Not Required (N = 19)	18 (94.7%)
Laboratory Results§ (Median, Range)	
ESR (N = 7)	117 (44 – 168)
CRP (N = 14)	65.4 (1.6 – 250.4)
Ferritin (N = 14)	740 (34.3 – 21845)
D-dimer (N = 13)	648.5 (113 – 27156)
IL-6 (N = 5)	22.5 (<5 – 58.1)
Creatinine‡ (N = 14)	1.7 (0.6 – 5.1)
Chest Imaging (N, %)	
Abnormal Chest Imaging (N = 17)	14 (82.4%)
Normal Chest Imaging (N = 17)	3 (17.6%)
Death¶ (N, %)	4 (16.7%)

Table 1. Characteristics of hospitalized SLE patients with COVID-19. Values are expressed as % (N) for categorical variables and median (range) for continuous variables. * Two patients remained hospitalized as of June 15, 2020 † Supplemental oxygen administered via nasal canula, high-flow nasal canula, simple or Venturi mask. ‡ One patient had end stage renal disease (ESRD) and was on hemodialysis at baseline (not included). § Laboratory results are peak values if >1 available, or only available value. ¶ Three patients were DNR/DNI. CRP, C-Reactive Protein; COVID-19, Coronavirus Disease 2019; DNR/DNI, Do Not Intubate/Do Not Resuscitate; ECMO, Extracorporeal Membrane Oxygenation; ESR, Erythrocyte Sedimentation Rate; ICU, Intensive Care Unit; IL-6, Interleukin-6; MV, Mechanical Ventilation; O2, Oxygen.

patients with SLE affected by COVID-19 in New York City (NYC) and analyze associations of comorbidities and medications on outcomes.

Methods: Patients with SLE and COVID-19 (confirmed by RT-PCR testing), were identified through a longitudinal survey of an established NYU lupus cohort, query of New York University Langone Health and Bellevue Hospitals systems and referrals from rheumatologists at those institutions. All patients were age 18 or older and met SLE classification criteria or carried a rheumatologist's diagnosis of SLE. Only English-, Spanish- or Mandarin-speaking patients were included in the study. Data were prospectively collected via a web-based questionnaire and review of electronic medical records. Baseline characteristics and medications were compared between the hospitalized and ambulatory patients with COVID-19. A logistic regression analysis was performed to identify independent predictors of hospital admission.

Results: A total of 41 SLE patients were confirmed COVID-19 positive by RT-PCR. The patients were predominantly female and encompassed the major racial/ethnic demographics seen in NYC. The most common symptoms of

COVID-19+ Patients	Hospitalized (N = 24)	Ambulatory (N = 17)	P-value*
Age	49.38 ± 17.81	43.65 ±16.26	0.30
Gender			1.00
Female	22 (91.7%)	16 (94.1%)	
Male	2 (8.3%)	1 (5.9%)	
Race			0.15
White	4 (16.7%)	7 (41.2%)	
Non-White	20 (83.3%)	10 (58.8%)	
Hispanic Ethnicity	10 (41.7%)	5 (29.4%)	0.52
BMI†	29.0 (25.7, 37.1)	27.4 (24.7, 30.7)	0.34
SLE Risk Factors			
APLS	3 (12.5%)	0 (0%)	0.25
History of LN	11 (45.8%)	3 (17.7%)	0.10
Medications			
Hydroxychloroquine	18 (75.0%)	14 (82.4%)	0.71
Systemic steroids	13 (54.2%)	5 (29.4%)	0.20
Immunosuppressants‡	15 (62.5%)	9 (52.9%)	0.75
NSAIDs	1 (4.2%)	1 (5.9%)	1.00
Comorbidities (≥1)	15 (62.5%)	5 (29.4%)	0.06

Table 2. Comparison of hospitalized and ambulatory SLE patients with confirmed COVID-19. Values are expressed as % (N) for categorical variables and mean ± standard deviation (SD) or median (interquartile range [IQR]) for continuous variables. * Categorical variables compared using Fisher's exact test; continuous variables compared using the two-sample T-test or Mann Whitney U Test. Age: T-test; BMI: Mann Whitney U Test (chosen by whichever gave more conservative p-value). † Median (IQR); N=23 for Hospitalized group ‡ Immunosuppressants include non-biologic agents (azathioprine, cyclophosphamide, mycophenolate mofetil, mycophenolic acid, sirolimus, tacrolimus) and biologic agents (anakinra, abatacept, belimumab, rituximab, tocilizumab). § Comorbidities refers to at least one of the following: congestive heart failure, active malignancy, pregnancy, diabetes mellitus, asthma, chronic obstructive pulmonary disease. APLS, Antiphospholipid Syndrome; BMI, Body Mass Index; COVID-19, Coronavirus Disease 2019; COVID-19+, positive testing for SARS-CoV-2 by polymerase chain reaction; LN, Lupus Nephritis; SLE, Systemic Lupus Erythematosus.

COVID-19+ patients were cough (78.4%), fever (64.9%), and shortness of breath (64.9%). Of those SLE patients with COVID-19, 24 (59%) were hospitalized, 4 required ICU level of care, and 4 died, all of hypoxic respiratory failure, Table 1. Hospitalized patients tended to be older, non-white, Hispanic, and have higher BMI, antiphospholipid syndrome, a history of lupus nephritis and at least one medical comorbidity, Table 2. There was no difference between the groups in use of hydroxychloroquine, systemic steroids or immunosuppressants. Logistic regression analysis identified the following independent predictors of being hospitalized with COVID-19: race (OR = 7.78 for non-white vs. white; 95% CI: 1.13 to 53.58; p=0.037), the presence of at least one comorbidity (OR=4.66; 95% CI: 1.02 to 21.20; p=0.047), and BMI (OR = 1.08 per increase in kg/m^2; 95% CI: 0.99 to 1.18; p=0.096).

Conclusion: Patients with SLE and COVID-19 have a high rate of hospitalization but similar mortality rate to the general population in NYC. Risk factors such as non-white race, higher BMI, and the presence of one or more comorbidities were identified as independent predictors of hospitalization in SLE patients who develop COVID-19. The use of hydroxychloroquine and immunosuppressants did not appear to influence the outcomes of patients with SLE in the setting of COVID-19. Further studies are needed to understand additional risk factors for poor COVID-19 outcomes in patients with SLE.

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Unexpected Changes in Physical and Psychological Measures Among Georgia Lupus Patients During the Early Weeks of the COVID-19 Pandemic in the United States, March 30–April 21, 2020

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SESSION INFORMATION

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Background/Purpose: An infectious disease outbreak can lead to negative physical and psychological consequences in the general public, as shown by the early COVID-19 pandemic, through significant negative global impacts on depression, anxiety, and stress. These outcomes are also known to be common among people with lupus. To evaluate the early impacts of the COVID-19 pandemic, we examined changes in standardized patient-reported outcomes in a cohort of patients with SLE between 2018–2019 and early 2020 and evaluated how the pandemic's impact on physical and psychological health differed by subgroups, particularly among black persons, who are at higher risk for adverse outcomes from both SLE and COVID-19.

Methods: Georgians Organized Against Lupus (GOAL) is a Centers for Disease Control and Prevention-supported population-based validated cohort of patients with SLE in Atlanta who complete patient-matched annual surveys across multiple domains. We analyzed sociodemographics and validated measures of lupus characteristics and physical and psychological parameters (see table footnotes) from surveys before (2018–2019) and during the pandemic's early onset (March 30–April 21, 2020). The 2020 surveys closely corresponded to the statewide shelter-in-place order in Georgia (April 3–24). We conducted descriptive analyses of prevalence (%) estimates with standard deviations (SD) and temporal changes in scale scores and paired t-tests for statistically significant differences (α=0.05); analyses were examined overall and stratified by sex and race.

Results: Overall, 316 participants had survey data from both time points. Most were black (76.6%) and female (93.4%); more than a quarter live in poverty (28.5%) (Table 1). Compared with before the pandemic, no physical or psychosocial measure worsened during the early onset of the pandemic. Rather, there were small, statistically significant improvements in stress, pain interference, fatigue, depression, anger, everyday discrimination, and emotional support overall, particularly in females and black persons (Table 2). Only Pain Interference improved significantly in males and Discrimination in white respondents (Table 2). No changes were observed in disease activity, disease damage, insurance, or poverty status.

Table 1. Descriptive Characteristics Among Georgians Organized Against Lupus (GOAL) Cohort Patients Before the COVID-19 Pandemic, 2018-2019

Category	Characteristic	Result (n=316)
Demographics	Race, n (%)	
	Black	242 (76.6)
	White	67 (21.2)
	Other	7 (2.2)
	Sex (female), n (%)	295 (93.4)
	Age in years, mean (SD)	47.0 (13.2)
	Disease duration, mean (SD)	15.4 (9.5)
	Marital status, n (%)	
	Single	113 (35.8)
	Married	110 (34.8)
	Separated	13 (4.1)
	Divorced	53 (16.8)
	Widowed	7 (2.2)
	Living with partner	20 (6.3)
	Number of adults in household, mean (SD)	2.1 (0.9)
	Number of children in household, mean (SD)	0.7 (1.1)
Socio-economics	Insurance type, n (%)	
	No insurance	37 (11.7)
	Private insurance	129 (41.0)
	Medicare	71 (22.5)
	Medicaid	40 (12.7)
	Medicare and Medicaid	38 (12.1)
	Employed, n (%)	138 (44.4)
	Poverty, n (%)	87 (28.5)
Lupus Characteristics	Disease activity[2] (SLAQ), mean (SD)	14.1 (8.1)
	Organ damage[3] (SA-BILD), mean (SD)	2.3 (2.5)
Stress	Perceived Stress[4], mean (SD)	17.5 (7.9)
Pain[1]	Pain interference, mean (SD)	57.2 (10.6)
Fatigue[1]	Fatigue, mean (SD)	57.3 (10.7)
Depression[1]	Depression, mean (SD)	50.8 (10.5)
Anxiety[1]	Anxiety, mean (SD)	50.3 (11.3)
Anger[1]	Anger, mean (SD)	50.5 (12.9)
Discrimination	Everyday discrimination[5], mean (SD)	1.6 (0.6)
Physical*	Physical health, mean (SD)	41.4 (8.7)
	Physical function, mean (SD)	42.1 (10.3)
Mental*	Mental health, mean (SD)	44.3 (9.3)
Emotional*	Emotional support, mean (SD)	51.7 (9.7)

[1] PROMIS measure, T-score; [2] SLE Activity Questionnaire (SLAQ), range 0-47; [3] Self Administered Brief Index of Lupus Damage (SA-BILD), range 0-30; [4] Cohen's Perceived Stress Scale, range 0-40; [5] Everyday Discrimination Scale, range 1-4

SD=standard deviation; SLAQ=SLE Activity Questionnaire; SA-BILD=Self Administered Brief Index of Lupus Damage

Table 2. Continuous Measures Prior to (2018-2019) and During the Early Onset (March 30-April 21, 2020) of the Pandemic, Stratified by Sex and Race

Measure	All (n=316)				Female (n=295)				Male (n=21)				Black (n=242)				White (n=67)			
	GOAL Measure, Mean (SD)				GOAL Measure, Mean (SD)				GOAL Measure, Mean (SD)				GOAL Measure, Mean (SD)				GOAL Measure, Mean (SD)			
	Prior to Pandemic	Early Pandemic	Change (Early-Prior)	P value (Paired)	Prior to Pandemic	Early Pandemic	Change (Early-Prior)	P value (Paired)	Prior to Pandemic	Early Pandemic	Change (Early-Prior)	P value (Paired)	Prior to Pandemic	Early Pandemic	Change (Early-Prior)	P value (Paired)	Prior to Pandemic	Early Pandemic	Change (Early-Prior)	P value (Paired)
*Negative measures**																				
Disease activity (SLAQ)[2]	14.1 (8.1)	13.6 (8.4)	-0.5 (6.5)	0.19	14.2 (8.2)	13.7 (8.5)	-0.5 (6.5)	0.18	12.5 (6.4)	12.6 (8.1)	0.1 (5.5)	0.94	14.6 (7.9)	13.9 (8.4)	-0.7 (6.7)	0.1	13.1 (8.7)	13.3 (8.8)	0.2 (5.4)	0.7
Organ damage (SA-BILD)[3]	2.3 (2.5)	2.4 (2.45)	0.1 (1.8)	0.55	2.3 (2.47)	2.4 (2.47)	0.1 (1.8)	0.31	2.3 (2.37)	1.7 (2.08)	-0.6 (1.8)	0.15	2.44 (2.53)	2.46 (2.52)	0.02 (1.9)	0.87	2.0 (2.18)	2.2 (2.21)	0.2 (1.2)	0.21
Perceived stress[4]	17.5 (7.9)	16.5 (8.1)	-1.0 (6.7)	**0.007**	17.5 (8.0)	16.4 (8.2)	-1.1 (6.6)	**0.004**	17.7 (6.6)	18.1 (6.8)	0.4 (8.0)	0.81	17.8 (7.8)	16.6 (8.2)	-1.2 (6.9)	**0.008**	16.8 (8.3)	16.1 (7.7)	-0.7 (5.9)	0.32
Pain interference[1]	57.2 (10.6)	55.4 (10.3)	-1.8 (9.4)	**0.001**	57.1 (10.7)	55.6 (10.4)	-1.5 (9.2)	**0.009**	59.0 (10.2)	52.2 (9.1)	-6.8 (11.6)	**0.015**	57.8 (10.2)	56.0 (9.9)	-1.8 (9.4)	**0.003**	55.9 (11.7)	54.3 (11.4)	-1.6 (9.3)	0.15
Fatigue[1]	57.3 (10.7)	55.0 (11.1)	-2.3 (8.4)	**<0.0001**	57.6 (10.8)	55.3 (10.9)	-2.3 (8.4)	**<0.0001**	53.3 (9.5)	51.2 (12.3)	-2.1 (8.6)	0.27	57.7 (10.4)	55.0 (11.3)	-2.7 (8.5)	**<0.0001**	56.9 (11.6)	55.6 (10.3)	-1.3 (8.3)	0.2
Depression[1]	50.8 (10.5)	49.3 (9.8)	-1.5 (9.2)	**0.005**	50.8 (10.7)	49.3 (9.8)	-1.5 (9.3)	**0.005**	50.7 (8.6)	49.9 (9.7)	-0.8 (8.2)	0.69	50.7 (10.3)	49.0 (9.9)	-1.7 (9.3)	**0.004**	51.2 (11.4)	50.6 (9.6)	-0.6 (9.2)	0.61
Anxiety[1]	50.3 (11.3)	50.3 (11.1)	<0.1 (10.2)	0.92	50.2 (11.5)	50.4 (11.1)	0.2 (10.1)	0.73	50.5 (9.9)	48.6 (11.0)	-1.9 (12.1)	0.47	50.1 (11.3)	49.8 (11.3)	-0.3 (10.3)	0.75	51.3 (11.3)	52.4 (10.8)	1.1 (9.8)	0.37
Anger[1]	50.5 (12.9)	47.7 (11.9)	-2.8 (12.1)	**<0.0001**	50.6 (13.1)	47.6 (11.9)	-3.0 (12.1)	**<0.0001**	49.1 (9.8)	49.3 (12.4)	0.2 (12.1)	0.94	50.6 (13.0)	47.5 (12.2)	-3.1 (12.2)	**<0.0001**	49.8 (11.9)	48.5 (10.9)	-1.3 (11.8)	0.34
Everyday Discrimination[5]	1.6 (0.6)	1.4 (0.6)	-0.2 (0.6)	**<0.0001**	1.6 (0.64)	1.4 (0.60)	-0.2 (0.6)	**<0.0001**	1.5 (0.48)	1.4 (0.75)	-0.1 (0.9)	0.77	1.60 (0.65)	1.4 (0.63)	-0.2 (0.6)	**<0.0001**	1.5 (0.54)	1.3 (0.57)	-0.2 (0.5)	**0.02**
*Positive measures**																				
Physical health[1]	41.4 (8.7)	42.0 (9.0)	0.6 (6.3)	0.12	41.4 (8.8)	41.9 (9.1)	0.5 (6.4)	0.15	42.5 (8.2)	43.3 (7.6)	0.8 (5.0)	0.5	40.7 (8.4)	41.2 (8.6)	0.5 (6.3)	0.21	43.4 (9.4)	43.7 (9.9)	0.3 (6.3)	0.63
Physical function[1]	42.1 (10.3)	42.5 (10.3)	0.4 (7.1)	0.36	41.9 (10.3)	42.3 (10.3)	0.4 (7.0)	0.34	45.9 (9.3)	46.0 (10.0)	0.1 (9.0)	0.97	41.5 (10.2)	41.6 (10.0)	0.1 (7.1)	0.85	43.5 (10.2)	44.9 (10.8)	1.4 (7.3)	0.13
Mental health[1]	44.3 (9.3)	44.5 (8.9)	0.2 (7.4)	0.58	44.3 (9.4)	44.5 (9.0)	0.2 (7.4)	0.62	43.8 (7.0)	44.3 (8.8)	0.5 (9.1)	0.82	43.6 (8.8)	43.8 (8.6)	0.2 (7.5)	0.74	46.6 (10.1)	46.8 (9.5)	0.2 (6.3)	0.75
Emotional Support[1]	51.7 (9.7)	53.6 (8.9)	1.9 (8.3)	**<0.0001**	51.8 (9.6)	53.7 (8.8)	1.9 (7.9)	**<0.0001**	50.7 (10.5)	52.4 (9.7)	1.7 (13.3)	0.56	51.0 (9.8)	53.1 (9.1)	2.1 (8.7)	**<0.0001**	53.9 (9.1)	54.7 (8.1)	0.8 (6.7)	0.36

*Negative measures: a higher score means a worse condition
**Positive measures: a higher score means a better condition
[1] PROMIS measure, T-score; [2] SLE Activity Questionnaire (SLAQ), range 0-47; [3] Self Administered Brief Index of Lupus Damage (SA-BILD), range 0-30; [4] Cohen's Perceived Stress Scale, range 0-40; [5] Everyday Discrimination Scale
SD=standard deviation; P-values in bold are <0.05

Conclusion: We expected to see worsening in most measures among patients with SLE early in the COVID-19 pandemic, so the absence of deterioration and even minor improvements is notable and may be explained by several hypotheses. These findings may reflect baseline severity of many outcomes for people with SLE. The study period was early in the pandemic, so potential negative financial pressures may not have been fully realized and may have been mitigated by economic impact payments from acute policy measures. Many negative consequences of living with SLE (isolation, reduced activity, anxiety, and fear of stigma) became a reality for the general population. This may have made those with SLE feel closer to the norm while limiting opportunities for certain negative experiences, including discrimination. Importantly, longer-term impacts of the pandemic may reverse these findings and ultimately lead to more severe negative outcomes, requiring continued close study.

Disclosure: S. Lim, None; **K. Theis**, None; **C. Dunlop-Thomas**, None; **G. Bao**, None; **C. Helmick**, None; **C. Gordon**, UCB, 1, 2, 3, 4, CDC, 1, MGP, 1; **C. Drenkard**, None.

Abstract Number: 1276

Using Classification and Regression Tree Analysis to Assess the Construct Validity of the Automated Neuropsychological Assessment Metrics in the Assessment of Cognitive Impairment in SLE Compared to the ACR Neuropsychological Battery

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SESSION INFORMATION

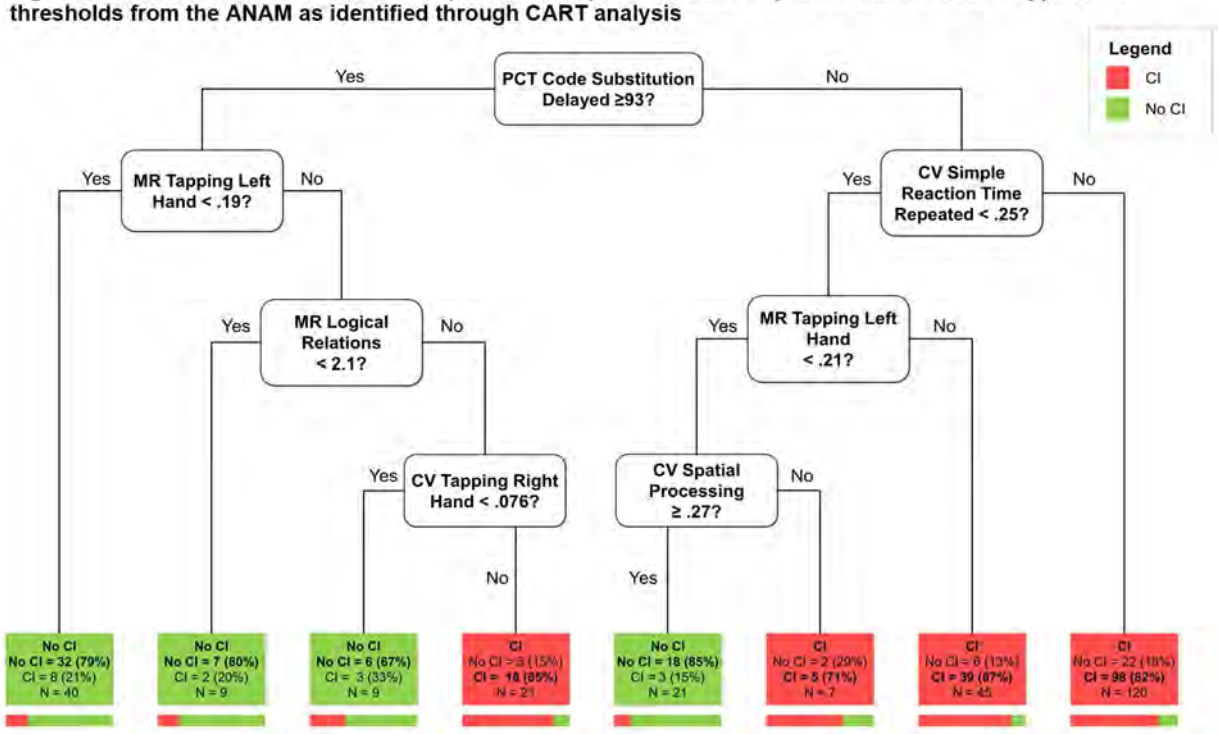
Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Figure 1. Decision tree of the best model (PCT, MR, CV) and the most important subtests, scoretypes and thresholds from the ANAM as identified through CART analysis

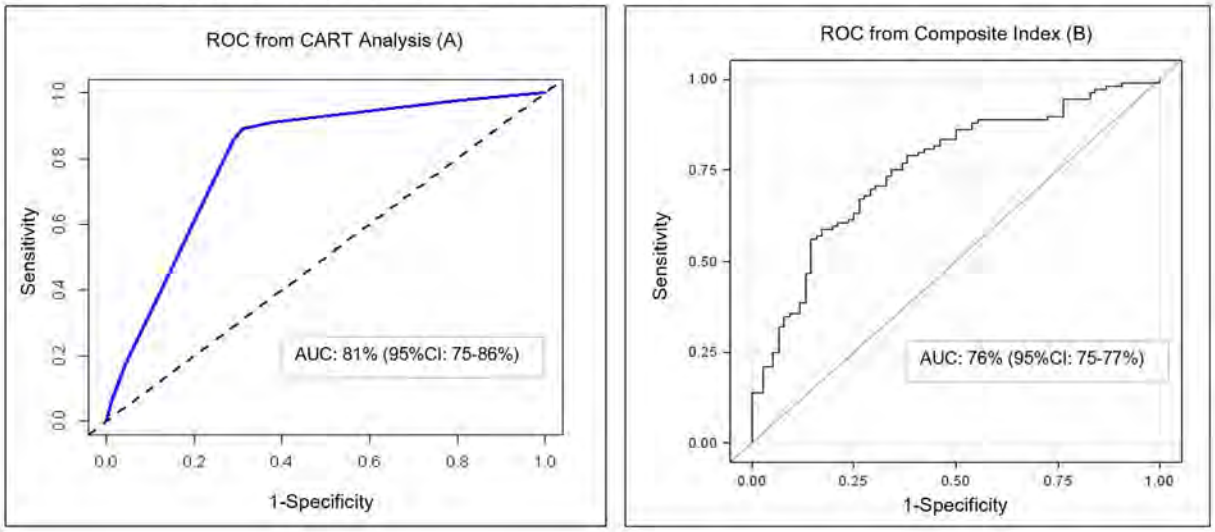


CI: cognitive impairment; PCT: percentage correct responses; MR: mean reaction time; CV: coefficient of variation of mean reaction time; TP: throughput For most of the ANAM tests, there are 4 score types provided. PCT represents accuracy. MR represents the average reaction time. TP is a measure of cognitive efficiency and is derived as the number of correct responses per minute. CV is an index of the patient's consistency of response speed within a given timed subtest. It is a derived score (standard deviation of MR divided by MR). Better cognitive performance is indicated by higher PCT and TP scores, and lower MR and CV scores. Code substitution delayed measures delayed memory and requires the participant to compare a symbol-digit pair with previously defined and memorized symbol-digit pairs. The participant presses designated buttons to indicate whether the pair was correct or incorrect based on their memory. Tapping left hand and tapping right hand measure motor skill and reaction time. The participant is required to press the spacebar with the designated hand as many times as possible in a single trial. Simple reaction time repeated measures reaction time and requires the participant to respond as quickly as possible to a target stimulus. The "repeated" session is administered later in the battery and is also designed to measure fatigue. Logical relations measures abstract reasoning and verbal fluency whereby the participant evaluates the truth of statements and describes the order of two symbols displayed on the screen. Spatial processing measures visual spatial skills whereby the participant compares two histograms displayed side-by-side in different orientations.

Background/Purpose: Cognitive impairment (CI) is common in systemic lupus erythematosus (SLE) patients, however there is no standard screening tool available. The American College of Rheumatology Neuropsychological Battery (ACR-NB) is the gold standard diagnostic tool but requires trained personnel and 1-hour to complete. The Automated Neuropsychological Assessment Metrics (ANAM) is a promising screening tool as it is a shorter, self-administered battery. We previously developed a composite index for interpreting ANAM, and in this study we aimed to provide further evidence on the construct validity of the ANAM as a screening tool for detecting CI in SLE compared to ACR-NB. Objectives: 1) to determine the best subtests and score types of ANAM to predict CI using Classification and Regression Tree (CART) analysis, 2) provide a new approach for interpreting ANAM results, and 3) compare the performance of ANAM composite index to the best CART model.

Methods: 300 consecutive consenting adult SLE patients attending a single center between 2016 and 2019 completed the ANAM and ACR-NB on the same day. Patients were classified CI or non-CI based on ACR-NB. CI was defined by a z-score of ≤-1.5 in ≥ 2 domains; non-CI if no domain had a z-score of ≤-1.5. ANAM has 15 subtests with each test comprising different score types (percentage of correct responses [PCT], mean reaction time [MR],

Figure 2. Receiver operating characteristic (ROC) curve of the best model (PCT, MR, CV) from CART Analysis (A) and Composite Index (B) for identifying cognitive impairment compared to ACR-NB



CART: Classification and Regression Tree; AUC: Area under the curve; PCT: Percentage of correct responses; MR: Mean reaction time; CV: Coefficient of variation The ROC curve of the best model (PCT, MR, CV) from CART analysis reported an AUC of 81% compared to ACR-NB. The composite index formula (which was derived using logistic regression from our previous study) based on the model with PCT, MR, CV was applied to the current dataset and reported an AUC of 76% compared to ACR-NB.

throughput [TP], and coefficient of variation [CV]). We built 6 models including all subtests, but each model included a different set of score types. Each model was run through CART analyses with k-fold cross validation. The data was split into k-subsets (k=10). Each subset randomly selected 90% of patients as training data and 10% as testing data, repeated 3 times. A decision tree was generated for each model separating patients into CI or non-CI based on ANAM subtests, score types, and thresholds that best predict CI. We hypothesized ANAM would identify CI with good Area Under the Receiver Operating Characteristics (ROC) curves (AUC = 0.71-0.80) and a sensitivity ≥ 80%. The performance of the best CART model was compared to ANAM composite index using ROC analysis and kappa statistic. Composite Index: 3.88-0.05*Code Substitution Delayed$_{PCT}$ - 8.4*Spatial Processing$_{CV}$ + 2.44*Code Substitution Learning$_{MR}$ + 9.87*Tapping Left$_{MR.}$

Results: 145 patients were defined as CI and 90 as non-CI based on ACR-NB. The best model included 6 ANAM subtests and PCT, MR, CV score types (**Figure 1**), with 89% sensitivity, 69% specificity, AUC of 81% (95% confidence interval: 75-86%), 81% accuracy, 82% positive predictive value, and 79% negative predictive value compared to ACR-NB. The most important subtests, score types, and thresholds were displayed in a decision tree (**Figure 1**). Concordance between the best CART model and ANAM composite index was 74%, κ = 0.48 (95% confidence interval: 0.37-0.59) (**Figure 2**).

Conclusion: Our findings extend the evidence on the construct validity of the ANAM as a screening tool for CI in SLE patients. Good concordance was found between the ANAM composite index and best CART model. Six most important subtests and scores for detecting CI from the ANAM were identified. A decision tree was generated to simplify the interpretation of ANAM and enhance clinical utility.

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Abstract Number: 1277

Low Cost Composite Markers to Differentiate Infection from Disease Activity in a Febrile Patient with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with Systemic Lupus Erythematosus (SLE) are at an increased risk of infection owing to immunosuppressive therapy along with coexistent immune dysregulation. It is often difficult to differentiate between infection and disease activity in a patient with SLE who presents with fever. Though many markers have been studied, markers like procalcitonin, which has high specificity, are expensive and not available in resource poor countries. Thus, we planned to see if low cost markers can be useful to differentiate infection from disease flare in a patient of SLE with fever.

Methods: Patients with SLE (SLICC criteria) presenting with fever of more than 48 hours duration, from December 2018 to February 2020 were included in the study. Detailed history, clinical examination and investigations were done to assess for infection. In addition, neutrophil to lymphocyte ratio (N/L), neut-x, y, z indices[1], Erythrocyte sedimentation rate (ESR), C-reactive protein (CRP), C3, C4, anti-dsDNA antibodies and procalcitonin levels were measured.

Table 1: Comparative analysis of variables between those with infection and disease activity

	Infection, n= 12	Disease Flare, n= 22	p
Age, years	29.5 (21.5-39.25)	22 (19.5-30)	0.12
Gender, female	11	20	0.7
Disease duration (months)	24(4.5-18.75)	18 (7.5-42)	0.8
Steroids >7.5 mg	8 (66.7%)	10 (45.4%)	0.3
Steroid sparing drug	9 (75%)	6 (27.3%)	0.01* OR8, 95% CI (1.6-39.9)
Duration of fever, days	7.5 (4.5-18.75)	15(6-21)	0.4
SLEDAI 2K	6.5 (2-13.75)	12 (5.5-18)	0.2
N/L ratio	6.8(3.1-11.25)	3.5(2.35-5.27)	0.04*
Neutrophil-x	130.9 (126.9-137.5)	126 (123-129)	0.01*
Neutrophil-y	50.15 (47-52.18)	44.5 (43-49.25)	0.04*
Neutrophil-z	141.5 (136.3-146.8)	134.7 (131.1-139.4)	0.02*
Anti-dsDNA	10 (10-58.5)	232.4 (48.7-300)	0.002*
C3, mg/dl	87 (71.8-128)	53.1 (41.5-95.8)	0.02*
C4, mg/dl	30.8 (15.5-40.6)	11.7 (9.2-16.8)	0.0001*
ESR, mm/hour	102.5(47.8-127.5)	98 (60-125.5)	0.9
CRP, mg/dl	4.1 (2.13-11.5)	0.99 (0.5-3.7)	0.03*
ESR/CRP ratio	26.5 (6.9-38.4)	67.78(24.5-167.4)	0.02*
MRP 8/14, IU/L	72.5 (29.9-121.9)	41.9 917.4-82)	0.12
CD 64 %	95.75 (88.9-99.1)	82.1 (63.2-98.1)	0.2
Procalcitonin, ng/ml	1.3 9 (0.6-6.2)	0.16 (0.04-0.5)	0.0001*

CRP- C Reactive Protein, dsDNA- double stranded Deoxy Ribonucleic Acid, N/L- Neutrophil to Lymphocyte, SLEDAI 2K- Systemic Lupus Erythematosus Disease Activity Index 2000

Table 1. Comparative analysis of variables between those with infection and disease activity

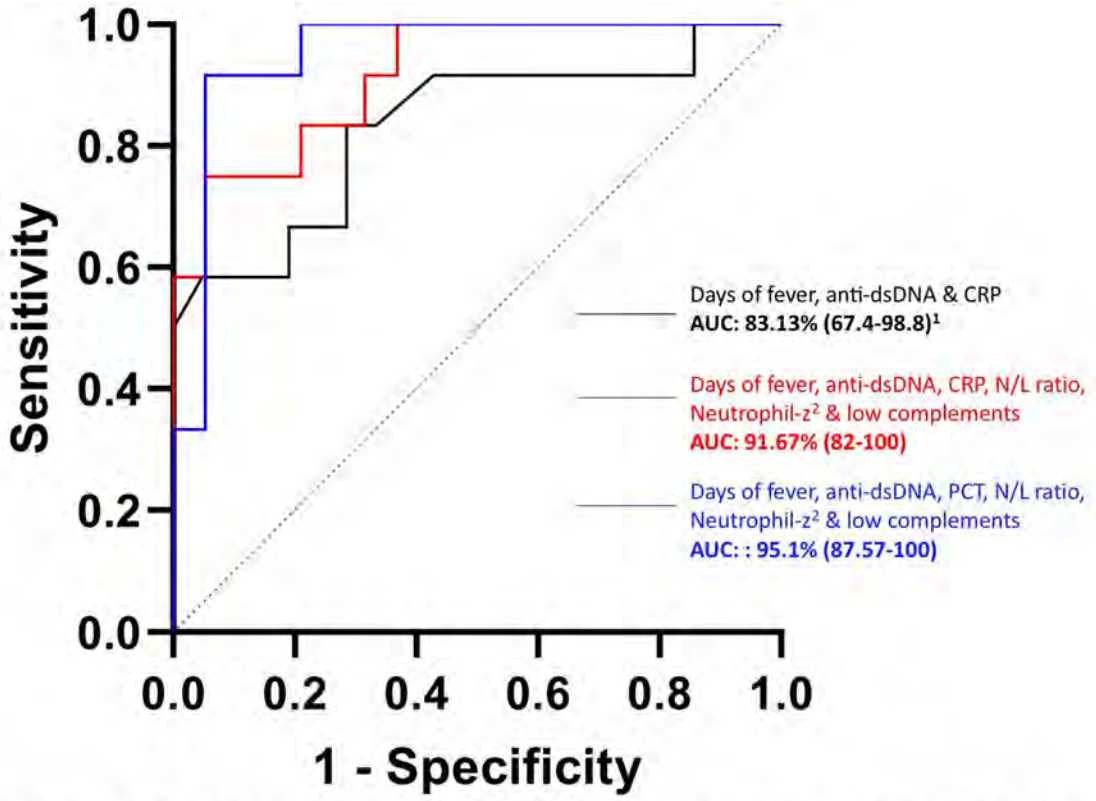

Figure 1: ROC curves demonstrating the composite of various variables used to determine infection

ROC- Receiver Operator Curve, CRP- C Reactive Protein, dsDNA- double stranded Deoxy Ribonucleic Acid, N/L- Neutrophil to Lymphocyte ratio, PCT- Procalcitonin. References, 1. Luo Y, Lin J, Chen H, Zhang J, Peng S, Kuang M. Utility of neut-X, neut-Y and neut-Z parameters for rapidly assessing sepsis in tumor patients. Clinica Chimica Acta. 2013 Jun 25;422:5-9.
2. Beça S, et al, Development and validation of a risk calculator to differentiate flares from infections in systemic lupus erythematosus patients with fever, Autoimmun Rev (2015)

Figure 1. ROC curves demonstrating the composite of various variables used to determine infection

Neut-x and y indices are parameters obtained by objective evaluation of toxic granulation and the nuclear maturity of neutrophils by the Sysmex counter and Neut-z refers to the vector sum of the two.

Based on clinical assessment and laboratory data, fever episode was classified as infection, disease flare or both. The differences in variables between infection episode and disease flare were analyzed using Mann Whitney-U test for continuous and chi-square for categorical variables respectively, Binary logistic regression and ROC for multivariate analysis were used for analysis. In addition, a previously proposed low-cost calculator by Beca etal[2]was also validated and improved upon by addition of other variables.

Results: 42 episodes of fever were seen in 40 patients with SLE, and among these 18 were due to infection, 22 were related to disease activity and in 2 both infection and disease activity contributed to fever. The median age of the patients was 26.5 years with 90% being women. Two-thirds had a major organ involvement, distributed equally across the groups. Six patients with tuberculosis, viral and fungal infection were excluded from further analysis. High anti-dsDNA (p=0.002) and low complements(C3, p=0.02 and C4, p=0.0001) were characteristic of disease flare whereas high N/L ratio (p=0.04), high Neut-x (p=0.01), -y (p=0.04), -z (p=0.02), CRP (p=0.03), low ESR to CRP ratio (p=0.02) and high procalcitonin (p=0.0001) were seen with infection.

Using the 3 variables suggested by Beca etal i.e. days of fever, anti-dsDNA antibody and CRP the ROC curve had an area under curve (AUC) of 0.81 which increased to 0.91 when low complement levels, N/L ratio and Neut-z was added to this model. Replacing CRP with procalcitonin had higher AUC but it increased the cost.

Conclusion: A composite score oflow cost and routinely available parameters like days of fever, anti-dsDNA, low C3/C4, neutrophil to lymphocyte ratio and Neut-z gives a good discrimination between infection and flare in a febrile patient with SLE.

Disclosure: P. Mehta, None; **K. Singh**, None; **A. Aggarwal**, None; **S. Sharma**, None.

Abstract Number: 1278

Does Co-existing Systemic Lupus Erythematosus Affect Outcomes of Hospitalizations for Ischemic Stroke?

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Various studies have shown that individuals with Systemic Lupus Erythematosus (SLE) have a higher risk of stroke and cerebrovascular events than the general population. These events represent a significant cause of death in SLE patients. It is however unclear if SLE patients who develop cerebrovascular events have different outcomes compared to stroke patients without SLE. The aim of this study is to compare the outcomes of patients primarily admitted for ischemic stroke with and without a secondary diagnosis of SLE.

Methods: Data were abstracted from the National Inpatient Sample (NIS) 2016 and 2017 Database. This database is the largest collection of inpatient hospitalization data in the United States (U.S). The NIS was searched for hospitalizations for adult patients with ischemic stroke as principal diagnosis with and without SLE as secondary diagnosis using ICD-10 codes. The primary outcome was inpatient mortality. Hospital length of stay (LOS), total hospital charges, odds of receiving tissue plasminogen activator (TPA), and mechanical thrombectomy were secondary outcomes of interest. Multivariate logistic and linear regression analysis was used accordingly to adjust for confounders. Confounders adjusted for include age, sex, Charleston co-morbidity index, and cardiovascular comorbidities. STATA software was used to analyze the data.

Results: There were over 71 million discharges included in the combined 2016 and 2017 NIS database. Out of 525,570 patients with ischemic stroke, 2,280 (0.43%) had SLE. SLE group was younger (58 vs 70 years, P< 0.0001) and had more females (83% vs 50%, P< 0.0001). The adjusted odds ratio (AOR) for inpatient mortality for ischemic stroke with co-existing SLE compared to without co-existing SLE was 0.95 (95% CI 0.58-1.54, P=0.824). Hospitalizations for ischemic stroke with co-existing SLE had higher mean total hospital charges ($80,306 vs $70,157, P=0.019) and less odds of receiving TPA (OR: 0.61, 95% CI 0.41-0.90, P=0.012) compared to those without co-existing SLE.

Conclusion: Patients admitted primarily for ischemic stroke with a secondary diagnosis of SLE had similar inpatient mortality, more total hospital charges, and less likelihood of receiving TPA compared to those without SLE. LOS and

	Stroke with SLE (n=2,280)	Stroke without SLE (n=523,290)	Adjusted OR	P-value
	% (95% CI)	% (95% CI)	(95% CI)	
Primary outcome				
In-hospital mortality	4.61 (3.03-6.94)	5.53 (5.36-5.70)	0.95 (0.58-1.54)	0.824
Secondary outcomes				
TPA	7.02 (5.02-9.72)	9.30 (9.08-9.54)	0.61 (0.41-0.90)	0.012*
Mechanical thrombectomy	6.14 (4.29-8.71)	5.05 (4.76-5.37)	0.75 (0.49-1.14)	0.179
			Adjusted mean difference	
LOS, mean (SE), days	7.10 ± 0.69	5.68 ± 0.04	0.10 ({-1.25}-1.46)	0.882
Total charges, mean $	$80,306 \pm 5100$	$70,157 \pm 913$	-10,394 (-{19,091-1,697})	0.019*

Abbreviations: SLE: Systemic Lupus Erythematosus, TPA: Tissue Plasminogen Activator, LOS: Hospital length of stay, OR: Odds Ratio; C.I: Confidence Interval, SE: Standard Error, * Statistically significant

Table 1 Clinical outcomes of ischemic stroke hospitalizations with and without SLE

odds of receiving mechanical thrombectomy were similar between both groups. Though SLE is known to increase the risk of cerebrovascular events, SLE does not negatively affect outcomes of patients primarily admitted for ischemic stroke based on this large U.S hospital database.

Disclosure: E. Edigin, None; **P. Eseaton**, None; **P. Ojemolon**, None; **A. Manadan**, None.

Abstract Number: 1279

Clinical Characteristics and Impact of the COVID-19 Pandemic in Systemic Lupus Erythematosus Patients in a Spanish Tertiary Hospital

Andrea Briones-Figueroa[1], María Jesús García-Villanueva[2], África Andreu Suárez[1], Marina Tortosa-Cabañas[2], Ana Corral-Bote[2], Sandra Garrote-Corral[2], Javier Bachiller-Corral[1] and Mónica Vázquez[1], [1]Rheumatology, Hospital Universitario Ramón y Cajal, Madrid, Spain, [2]Hospital Universitario Ramón y Cajal, Madrid, Spain

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Data about incidence, clinical characteristics and outcome of patients with Systemic Lupus Erythematosus (SLE) with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) disease is scarce. We aimed to describe the infection rate, clinical characteristics and course of COVID-19 in patients with SLE.

	Suspected/confirmed COVID-19 (n=33)	No COVID-19 (n=218)	p value
Age, years (mean ±SD)	46,52 ±11,70	48,91 ±13,47	0,266
Body-mass index, kg/m^2 (mean ± SD)	25,55 ±7,19	24,27 ± 5,70	0,918
Female	33 (100%)	201 (92,20%)	0,097
Diabetes	0 (0%)	10 (4,58%)	0,209
Hypertension	9 (27,27%)	48 (22,02%)	0,502
Asthma	3 (9,09%)	4 (1,83%)	0,018
COPD	1 (3,03%)	3 (1,37%)	0,479
Chronic kidney disease	1 (3,03%)	2 (0,92%)	0,298
Hydroxychloroquine	24 (72,72%)	157 (72,69%)	0,996
Prednisone < 10mg per day	12 (36,36%)	77 (35,32%)	0,336
Immunosuppressant therapy	12 (36,36%)	87 (39,91%)	0,698
Cyclophosphamide	0 (0%)	1 (0,46%)	
Azathioprine	4 (12,12%)	21 (9,63%)	
Mycophenolate mofetil	3 (9,09%)	36 (16,51%)	
Methotrexate	4 (12,12%)	28 (12,84%)	
Leflunomide	0 (0%)	1 (0,46%)	
Cyclosporine	0 (0%)	2 (0,92%)	
Tacrolimus	1 (3,03%)	5 (2,29%)	
Everolimus	1 (3,03%)	0 (0%)	
Biological therapy	6 (18,75%)	12 (5,51%)	0,007
Rituximab	2 (6,06%)	5 (2,29%)	
Belimumab	4 (12,12%)	6 (2,75%)	
ACE inhibitors	6 (18,18%)	23 (10,60%)	0,205
Angiotensin II receptor blockers	4 (12,12%)	26 (11,98%)	0,982

Baseline and clinical characteristics of SLE patients with and without COVID-19.

Methods: An observational and descriptive study was conducted, which included patients with SLE from our Rheumatology Department. Clinical data and diagnosis of suspected or confirmed COVID-19 infection were extracted from electronic health records. We registered information about the clinical course of COVID-19 and performed a survey about the impact of the pandemic on the behavior and treatment of our patients.

Results: We included 251 patients with SLE, meeting the SLICC or 2019 ACR/EULAR criteria. 93,2% were women, with a mean age of 48,59 ± 13,25 years. 33 patients (13,1%) were diagnosed with suspected or confirmed COVID-19. Eight patients were confirmed by positive RT-PCR assay in nasopharyngeal swabs or by positive serology tests, while 25 patients were considered suspected cases with compatible clinical findings according to the general practitioner but without microbiological confirmation. The most frequent COVID-19 symptoms were cough (78,8%), fever (51,5%) and diarrhea (36,4%). 3 patients had contact with other SARS-CoV-2 positive individuals. Six patients (18,2%) had high disease activity according to SLEDAI-2K prior to the pandemic. 18,2% had secondary antiphospholipid syndrome. Five subjects (15,2%) attended the emergency department and all of them required hospital admission. One patient was admitted to the intensive care unit. Nine patients (39,4%) received specific treatment for COVID-19. The most frequent antiviral drugs were hydroxychloroquine (24,2%) and azithromycin (21,2%). Three individuals received corticosteroids (9,1%) and one received anti-IL6 (3%). Two patients (6,1%) died due to COVID-19, who were receiving rituximab and mycophenolate mofetil, respectively. We compared the characteristics of SLE patients with and without COVID-19 as shown in the table. The survey was responded by 27 patients. During the current COVID-19

	Suspected/confirmed COVID-19 (n=33)	No COVID-19 (n=218)	p value
Age, years (mean ±SD)	46,52 ±11,70	48,91 ±13,47	0,266
Body-mass index, kg/m^2 (mean ± SD)	25,55 ±7,19	24,27 ± 5,70	0,918
Female	33 (100%)	201 (92,20%)	0,097
Diabetes	0 (0%)	10 (4,58%)	0,209
Hypertension	9 (27,27%)	48 (22,02%)	0,502
Asthma	3 (9,09%)	4 (1,83%)	0,018
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Immunosuppressant therapy	12 (36,36%)	87 (39,91%)	0,698
Cyclophosphamide	0 (0%)	1 (0,46%)	
Azathioprine	4 (12,12%)	21 (9,63%)	
Mycophenolate mofetil	3 (9,09%)	36 (16,51%)	
Methotrexate	4 (12,12%)	28 (12,84%)	
Leflunomide	0 (0%)	1 (0,46%)	
Cyclosporine	0 (0%)	2 (0,92%)	
Tacrolimus	1 (3,03%)	5 (2,29%)	
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Biological therapy	6 (18,75%)	12 (5,51%)	0,007
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Angiotensin II receptor blockers	4 (12,12%)	26 (11,98%)	0,982

Baseline and clinical characteristics of SLE patients with and without COVID-19.

pandemic, 63% lived with their families with a median of 3 people (IQR 2-4), while 18,5% lived alone. 74,1% did complete lockdown and 18,5% occasionally left home interacting with other people. 55,5% had telematic follow-up by our Rheumatology department. Regarding rheumatological therapy, 74,1% maintained their usual treatment, 7,4% discontinued biological therapy and 3,7% completely interrupted their current treatment. 63% defined their rheumatic disease as stable whereas 37% experienced more flares during the period under review.

Conclusion: Despite the limited number of patients in our series, there does not appear to be an increased frequency of SARS-CoV-2 in SLE patients. A higher proportion of patients with biological treatment and a history of asthma was found among those who presented suspicious symptoms of COVID-19. This pandemic has had a major impact on the behavior and treatment of our patients; therefore, we emphasize the importance of encouraging patients to maintain current treatment and reinforce preventive measures.

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Abstract Number: 1280

COVID-19 Infections May Increase the Risk of SLE Flares

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: COVID-19 has overwhelmed the healthcare systems in New York City. Initial data from the Columbia Lupus Cohort suggests that 4% of patients with systemic lupus erythematosus (SLE) developed symptomatic COVID-19 infection, compared to the community transmission of 2% in New York City (Gartshteyn et al., 2020). There is no data about the impact of COVID on disease activity in SLE.

Methods: This study updates the earlier data with newly identified patients with SLE and COVID and describes post infection flares.

Results: From our cohort of 450 patients we identified and treated 27 SLE patients with COVID-19 infections (6%): 8 patients were hospitalized, 8 patients with confirmed infections were treated in an outpatient setting, and 11 patients with symptoms highly suggestive of COVID-19 were also treated as outpatient. Of the 16 confirmed cases, 12 patients had positive SARS-CoV-2 RT-PCR nasopharyngeal swabs and 4 patients had positive anti-SARS-CoV-2 antibodies.

77.8% of patients were female, mean age 40 ±10, 55.6% were Hispanic, 33.3% were Black, 3.7% were Asian, 7.4% were Caucasian, 81.5% of patients were taking antimalarials (hydroxychloroquine or chloroquine), 66.7% were taking non-biologic immunosuppressants, 11.1% had been treated with rituximab in the last 6 months, and 22.2% were either on prednisone or had taken prednisone within a week of their diagnosis. Their COVID-19 symptoms included fever (85.2%), myalgia (22.2%), cough (55.6%), shortness of breath (37%), chest pain (18.5%), and anosmia (7.4%).

Out of the 8 hospitalized patients 3 were critically ill with severe hypoxemic respiratory failure, one required mechanical ventilation. All received empiric antibiotics, 3 received high-dose IV methylprednisolone and tocilizumab. One non-critically ill patient required supplemental oxygen via nasal cannula. All hospitalized patients survived and were discharged (2 to acute rehab). Of the 19 SLE patients treated outpatient, 7 (36.8%) received azithromycin as treatment for COVID-19, 3 were prescribed aspirin for empiric thromboprophylaxis, and one patient not already on HCQ, received a 5 day course of HCQ. All had resolution of symptoms without further escalation of care. Hospitalized patients were less likely to be taking HCQ at the time of COVID diagnosis compared to those treated as outpatient (p=0.04). No other SLE treatment differences were identified between the groups.

Of the 27 patients, 6 (22.2%) experienced an SLE disease activity flare within 22 days post-COVID (range 3-49 days). Of the 6 flares, 5 were mild/moderate and 1 severe using the SELENA Flare Index (SFI) definitions. The flare symptoms included arthritis -5, alopecia -2, low C3/C4 -3, positive dsDNA -2, rash -1 and pleurisy -1.

Table 1. Demographics and Medications for patients with COVID-19 and SLE

	CONFIRMED (N=16)		CLINICALLY SUSPECTED (N=11)
	HOSPITALIZED (N=8)	OUTPATIENT (N=8)	OUTPATIENT (N=11)
Age, years	41±10	41±12	37±10
Female, n(%)	7(87.5%)	7(87.5%)	7(81.8%)
Race/Ethnicity			
Hispanic, n(%)	4 (50%)	2(25%)	9(81.8%)
Black, n(%)	3 (37.5%)	4(50%)	2(18.2%)
Caucasian, n(%)	1 (12.5%)	1(12.5%)	-
Asian	-	1(12.5%)	-
BMI kg/m^2	30±8	25±5	30±7
Ever Smoker, n(%)	1 (12.5%)	1(12.5%)	2(18.2%)
Disease Duration, years	20 [8-36]	9.6 [2-20]	11.5[1-25]
SLEDAI, at last visit	7.3 [2-12]	3.125 [0-14]	4 [0-10]
Lupus Nephritis, n(%)	6 (75%)	4 (50%)	4 (36.4%)
aPL Antibodies, n(%)	4(50%)	-	3(27.3%)
ANA Antibodies, n(%)	8 (100%)	8 (100%)	11 (100%)
Elevated dsDNA (ever), n(%)	5(62.5%)	5(62.5%)	8(72.7%)
Absolute Lymphocytes at last visit (x10^3 cells/μL)	1.52±0.68	1.30±0.71	1.48±0.69
Medications			
Antimalarials, n (%)	4(50%)	7(87.5%)	11 (100%)
Non-biologic immunosuppressants n (%)	7(87.5%)	5(62.5%)	6(75%)
Rituximab, n (%)	0	1 (12.5%)	2 (18.2%)
Prednisone, n (%)	3(37.5%)	0	3 (27.3%)
Mean Prednisone dose	9.3 ± 9.3 mg	0	4.16 ±1.4mg

Conclusion: SLE patients in our cohort experienced COVID infections at a rate similar to that of the general population. Our data suggest that SLE patients may experience disease flares following COVID-19 infections and HCQ may be protective of severe COVID.

Disclosure: L. Khalili, None; **Y. Gartshteyn**, None; **N. Schmidt**, None; **T. Kapoor**, None; **L. Geraldino-Pardilla**, Pfizer, 1, BMS, 1; **A. Askanase**, GlaxoSmithKline, 2, 5, AstraZeneca, 2, 5, AbbVie, 5, Bristol Myers Squibb, 5, Janssen, 2, Eli Lilly, 2, Pfizer, 2, LuCIN, 2, Mallinckrodt Pharmaceuticals, 2.

Abstract Number: 1281

Opioid-Related Encounters as a Predictor of 30-Day Readmissions in Lupus

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: One in four Medicare hospitalizations with systemic lupus erythematosus (SLE) results in readmission within 30 days, with "injuries and poisonings" as the second most common cause. This finding, which could be driven by opioid use, coupled with a recent study reporting that as many as 31% of patients with lupus received at least one opioid prescription in a year (Sommers 2019), raised new questions as to whether a focus on opioids could inform mechanistic-focused readmission reduction strategies. To begin to test the strength of this premise, we examined the extent to which prior opioid-related encounters in the baseline year predicted risk for 30-day readmission.

Methods: One in four Medicare hospitalizations with systemic lupus erythematosus (SLE) results in readmission within 30 days, with "injuries and poisonings" as the second most common cause. This finding, which could be driven by opioid use, coupled with a recent study reporting that as many as 31% of patients with lupus received at least one opioid prescription in a year (Sommers 2019), raised new questions as to whether a focus on opioids could inform mechanistic-focused readmission reduction strategies. To begin to test the strength of this premise, we examined the extent to which prior opioid-related encounters in the baseline year predicted risk for 30-day readmission.

Results: Table 1 shows that compared to the overall Medicare admissions cohort, the SLE cohort (n=23,309) was younger, and more often female, Black, disabled or on Medicaid, or had end stage renal disease (ESRD). In SLE, those with prior opioid-related codes were younger and more often female or receiving Medicaid or disability. Readmissions occurred in 18% of overall Medicare and 24% of SLE admissions. In SLE, observed readmission rates were 10% higher among those with opioid history (33% vs 23%, $p< .001$). The SLE group was over twice as likely as the overall Medicare group to have had opioid-related encounters in the prior year (9.0% vs 4.1%, $p< .001$; Table 2). Opioid-related codes were highest in the youngest SLE group; 25% of admissions of 18-32 year olds had prior opioid-related encounters (vs. 20% in Medicare cohort, $p< .001$).

Adjusted multivariable models showed 20% higher odds of readmission (aOR 1.201 (1.041, 1.384)) with opioid history (Table 3). This was similar in magnitude to an increase in composite comorbidity (HCC aOR 1.199 (1.180, 1.218)), and slightly less than ESRD (ESRD aOR 1.294 (1.122, 1.491)).

Limitations include the absence of Medicare Part D pharmacy claims to further examine opioid history, thus rates may not reflect actual opioid use.

Table 1. Baseline characteristics of Medicare SLE admissions with & without opioid-related code history

		Overall Medicare Cohort n=1,494,396	Overall w/ Opioid History n=61,467	SLE Cohort n = 23,309	SLE with Opioid History n=2,107	SLE without Opioid History n = 21,202	p*
Admit age (mean, [SD])		74, [14]	58, [15]	64, [16]	52, [15]	65, [16]	<.0001
Age group	18-33	1%	7%	6%	16%	5%	<.0001
	34-49	5%	21%	16%	31%	14%	
	50-64	14%	37%	24%	30%	23%	
	65-79	45%	28%	39%	20%	41%	
	≥80	35%	7%	16%	2%	17%	
Sex	Female	56%	55%	84%	89%	84%	<.0001
Race/Ethnicity	White	82%	78%	69%	69%	69%	0.0036
	Black	12%	17%	24%	25%	24%	
	Asian	1%	0.4%	1%	0.3%	1%	
	Native American	1%	2%	1%	1%	1%	
	Other/Unknown	1%	1%	1%	1%	2%	
	Hispanic	1%	2%	4%	3%	4%	
Medicaid ever		30%	60%	42%	64%	40%	<.0001
Disability		32%	77%	57%	82%	54%	<.0001
Index stay days (mean, [SD])		5.0, [5.0]	5.2, [5.5]	5.3, [5.4]	5.4, [5.8]	5.3, [5.4]	0.3532
RUCA	Urban	84%	87%	87%	89%	87%	0.0184
	Large City/Town	8%	7%	7%	6%	7%	
	Small Rural	5%	3%	3%	2%	3%	
	Isolated	4%	2%	3%	2%	3%	
ADI disadvantage Least	1-20	17%	13%	15%	12%	16%	
	21-40	21%	19%	19%	19%	19%	
	41-60	22%	22%	21%	21%	21%	
	61-80	22%	23%	23%	24%	23%	
Most	81-100	18%	23%	22%	24%	21%	
HCC Score (mean, [SD])		2.9, [2.2]	4.2, [2.7]	3.8, [2.5]	5.1, [2.8]	3.7, [2.4]	<.0001
Diabetes mellitus		38%	41%	36%	39%	36%	0.0038
ESRD		3%	5%	11%	11%	11%	0.6023
Discharge volume:	Highest	34%	34%	37%	35%	37%	0.0322
	Middle	33%	33%	34%	36%	34%	
	Lowest	33%	33%	29%	29%	29%	
Medical school affiliation		49%	49%	52%	51%	51%	0.6728
For-profit status		15%	16%	16%	17%	16%	0.0028
30-Day Outcomes							
Readmissions		**18%**	**28%**	**24%**	**33%**	**23%**	**<.0001**
Deaths		6%	2%	4%	2%	4%	<.0001

**P values compared SLE with and without opioid history calculated using t test for numeric variables & chi-square for categorical comparisons. Abbreviations: RUCA = rural urban commuting area, ADI = area deprivation index, HCC= Hierarchical Classification Code, ESRD = end-stage renal disease.*

Table 2. Opioid-related encounter history in Medicare overall and with SLE by age

		Overall Opioid History n (%)	SLE Opioid History n (%)	p
Opioid-related encounter history		61,467 (4.1)	2,107 (9.0)	<.0001
By age group	18-33	4,197 (20.2)	343 (24.5)	<.0001
	34-49	13,068 (37.0)	653 (18.0)	.09
	50-64	22,838 (11.2)	637 (11.6)	.39
	65-79	16,988 (2.5)	415 (4.6)	<.001
	≥80	4,376 (0.8)	59 (1.6)	<.001

Table 3. GEE model odds ratios (OR) of 30-day readmissions in SLE

		Unadjusted OR, 95% CI	Adjusted OR, 95% CI
Opioid-related encounter history		**1.651 (1.367, 1.882)**	**1.201 (1.041, 1.384)**
Age at admission	18-33	**2.235 (1.858, 2.689)**	**1.543 (1.264, 1.883)**
	34-49	**1.423 (1.245, 1.626)**	**1.188 (1.022, 1.323)**
	50-64	1.117 (1.003, 1.244)	0.942 (0.835, 1.064)
	65-79	Ref	Ref
	≥80	0.914 (0.815, 1.025)	0.952 (0.848, 1.026)
Sex	Female	0.913 (0.820, 1.016)	0.925 (0.835, 1.026)
Race/Ethnicity	White	Ref	Ref
	Black	1.538 (1.382, 1.712)	1.103 (0.987, 1.234)
	Asian	**0.682 (0,462, 1.006)**	**0.589 (0.399, 0.869)**
	Native American	1.508 (0.996, 2.282)	1.153 (0.795, 1.671)
	Other/Unknown	1.273 (0.918, 1.765)	1.032 (0.782, 1.363)
	Hispanic	1.314 (1.0651.623)	0.970 (0.797, 1.181)
Medicaid ever		1.461 (1.340, 1.593)	1.051 (0.956, 1.155)
Disability		1.186 (1.087, 1.293)	0.926 (0.832, 1.031)
Length of index stay		**1.039 (1.033, 1.046)**	**1.027 (1.020, 1.034)**
ADI disadvantage	1-20 (least)	Ref	Ref
	21-40	0.924 (0.802, 1.065)	0.893 (0.784, 1.018)
	41-60	1.123 (0.980, 1.287)	1.056 (0.931, 1.198)
	61-80	1.158 (1.005, 1.335)	1.069 (0.939, 1.217)
	81-100 (most)	1.284 (1.112, 1.482)	1.066 (0.931, 1.221)
HCC Comorbidity Score		**1.231 (1.212, 1.249)**	**1.199 (1.180, 1.218)**
Diabetes mellitus		1.377 (1.264, 1.500)	1.018 (0.936, 1.107)
ESRD		**1.993 (1.755, 2.262)**	**1.294 (1.122, 1.492)**
Discharge Volume	Highest	Ref	Ref
	Middle	0.995 (0.906, 1.093)	1.036 (0.938, 1.145)
	Lowest	0.922 (0.836, 1.017)	1.021 (0.931, 1.119)
Medical school affiliation		1.119 (1.034, 1.211)	1.009 (0.930, 1.094)

Conclusion: Hospitalized Medicare beneficiaries with SLE were twice as likely to have prior opioid-related encounters, and exposure to these opioid-related encounters was associated with a substantially increased readmission risk even after adjusting for comorbidities. Future studies should investigate readmission reduction interventions to help SLE patients with opioid histories.

Disclosure: C. Bartels, Independent Grants for Learning and Change (Pfizer), 2; **M. Schletzbaum**, None; **Y. Chen**, None; **A. Kind**, None.

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The Impact of High Disease Activity as Measured by SLEDAI and Drug Burden on Healthcare Utilization, Quality of Life and Work Productivity in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION

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Background/Purpose: Although there is abundant literature on healthcare utilization in SLE patients, the impact of disease activity in SLE patients is not well understood.

To quantify the impact of disease activity, as measured by SLEDAI score and drug burden, in SLE patients on health care resource utilization (HCRU), health related quality of life (HRQoL) and work productivity (WP).

Methods: Data were collected from a cross-sectional survey of 300 rheumatologists completing 752 patient record forms in US and EU5 from the Adelphi Real World 2010 & 2013 Lupus Disease Specific Programmes (DSP). Physicians were asked to complete patient record forms (PRFs) for the next 5 prospectively consulting SLE patients; the same patients were asked to complete patient self-completion (PSC) forms describing how SLE affected them. PRFs collected data pertaining to the patient's diagnosis, disease history, current clinical outcomes, treatment and management history. PSCs focused on similar data collection and included patient reported outcome measures (PROs). Propensity score matching was used to assess differences in HCRU and PRO scores between SLE patients who had a low disease activity and those who had a high disease activity. Low disease activity was defined as a SLEDAI score of ≤4, a steroid dose of < 7.5mg/day, and not on immunosuppressant or biologic. High disease activity was a

Table 1 Demographic data

Variable	Low disease activity	High disease activity
Mean age (years)	38.1	40.0
% Female	90.7	88.2
% White/Caucasian	76.7	67.7
Mean years diagnosed	5.5	5.0

Table 2 Propensity score matching results

Outcome variable	Low activity mean	High activity mean	Coefficient	95% CI	p-value
Flared in the last 12 months	11.63	37.97	-0.26	[-0.38 – -0.14]	<0.001
Number of flares in last 12 months	0.21	0.70	-0.49	[-0.72 – -0.26]	<0.001
Hospitalized in last 12 months	4.65	14.98	-0.10	[-0.17 – -0.04]	0.001
Number of consults in last 12 months	2.84	3.52	-0.68	[-1.19 – -0.17]	0.009
EQ-5D-3L	0.88	0.78	0.10	[0.03 – 0.17]	0.004
FACIT Fatigue	39.86	34.68	5.19	[0.80 – 9.57]	0.02
WPAI overall percentage work impairment	14.42	45.35	-30.93	[-45.32 – -16.54]	<0.001

SLEDAI score of >4, or on an immunosuppressant, biologic, or steroid dose of >7.5mg/day. Patients were matched on age, sex, and ethnicity.

Results: Data was extracted from 752 PRFs, and 388 PSCs. Using the estimated propensity score each low disease activity patient (n=43) was matched with a high disease activity patient (n=709). Using 1:1 matching, with replacement and allowing for ties, matching resulted in 257 high disease activity patients being used as matches for 43 low disease activity patients. Demographic data are reported in Table 1. Patients with a low disease activity were significantly less likely to be currently flaring, lower number of flares in last 12 months, less likely to have been hospitalized in the last 12 months, had fewer consultations in the last 12 months, reported better HrQoL (EQ5D), more favourable levels of fatigue (FACIT), and lower work impairment (WPAI). (Table 2).

Conclusion: Systemic lupus erythematosus patients with lower levels of disease activity are less burdensome to the healthcare system and experience a significantly better HRQoL and lower levels of productivity impairment. There is a need to establish a universal definition of low disease activity as a treatment goal to benefit patient quality of life and reduce HCRU.

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Abstract Number: 1283

Factors Affecting Mortality of Systemic Lupus Erythematosus Patients in Spain in the 21st Century: Data from the RELESSER Registry

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
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Background/Purpose: The mortality in Systemic Lupus Erythematosus (SLE) varies largely across different countries most probably due to social, healthcare and ethnic differences.

To analyze the causes and identify predictive factors of mortality of SLE in Spain in the present century.

Methods: We performed a cross-sectional and retrospective study analyzing data from the RELESSER cohort (Spanish Registry of Systemic Lupus Erythematosus of the Spanish Society of Rheumatology). We included all patients diagnosed with SLE since the year 2000 and recorded sociodemographic, clinical and serological variables, comorbidities and treatments, as well as indicators of disease activity, damage and severity. The characteristics of the deceased patients were compared with those of the survivors, and variables with clinical significance or statistical significance were grouped into multivariate models to determine which ones were independently associated with the outcome of the disease.

Results: A total of 2004 patients were included, 88.6% female, the mean age at diagnosis was 38.3 (± 15.3) years, with a mean delay in diagnosis of 28.9 (± 52.6) months. Up to 2.84% of the individuals had died. The leading cause of death was SLE activity (n=16), followed by infections (n=14), vascular events (n=12) and cancer (n=6). The mean age of death was 54.68 (± 20.13) years, and neither age, sex nor delay in diagnosis was independently associated

MODEL 1: SLE			MODEL 2: Treatment			MODEL 3: Comorbidity		
Variable	p	OR	Variable	p	OR	Variable	p	OR
Cytopenias	0.144	2.1 (0.77-5.92)	**Rituximab**	**0.04**	**2.43 (1.04-5.69)**	**Charlson**	**<0.001**	**1.74 (1.41-2.14)**
APS	0.246	1.66 (0.70-3.95)	**Antimalarial**	**0.001**	**0.34 (0.17-0.65)**	**Serious Infections**	**0.001**	**1.87 (1.27-2.74)**
Nephritis	**0.011**	**2.74 (1.26-5.95)**	**CYC**	**<0.001**	**4.65 (2.24-9.65)**	Mellitus diabetes	0.465	1.71 80.40-7.28)
Serositis	0.885	1.05 (0.50-2.23)	**CC dose**	**0.024**	**2.27 (1.11-4.64)**	**Depression**	**0.048**	**2.87 (1.01-8.17)**
Skin involvement	**0.036**	**0.47 (0.23-0.95)**	**(>60mg/day)**			Valve disease	0.087	3.22 (0.84-12.34)
Anti-Ro	0.177	0.59 (0.27-1.26)						
SLEDAI	**0.006**	**1.11 (1.03-1.19)**				Ischemic disease	0.840	0.85 (0.17-4.11)
SLICC	**<0.001**	**1.79 (1.50-2.14)**						

Table 1. Summary Multivariate Statistical Analysis

with mortality. The presence of nephritis, depression, severe infections, organ damage (SLICC/ACR DI) or disease activity (SLEDAI), as well as the use of cyclophosphamide, rituximab or high doses of corticosteroids, were predictors of mortality in our cohort. Antimalarial treatment and skin manifestations were linked to improved survival.

Conclusion: In the RELESSER cohort, clinical factors, co-morbidities, as well as therapeutic attitudes were associated with a significant increase in mortality in SLE. Interestingly, depression was independently associated to mortality. The activity of the disease and infections continue to be the main causes of death at the beginning of the 21st century amongst our patients.

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Abstract Number: 1284

Application of a Novel Method for Determination of Muscle Mass Relative to Fat Mass in Women with Systemic Lupus Erythematosus and Association with Disability

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
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Background/Purpose: Patients with SLE are at risk for both skeletal muscle loss and increased adiposity, which may predispose to worse health-related quality of life. Decreased skeletal muscle mass, particularly after adjustment for

Table 1. Participant characteristics

N, mean (SD) unless otherwise specified	Combined (N=237)	New York (N=71)	California (N=166)	p-value
Age (years)	47.2 (13.0)	45.2 (14.3)	48.0 (12.3)	0.13
Race, N (%)				<0.001
Asian	32 (13.5)	8 (11.3)	24 (14.5)	
Black or African American	42 (17.7)	22 (31.0)	20 (12.0)	
White	118 (49.8)	19 (26.8)	99 (59.6)	
Other/declined to state	45 (19.9)	22 (31.0)	23 (13.8)	
BMI (kg/m^2)	26.9 (6.4)	26.6 (5.6)	27.1 (6.8)	0.58
ALMI Z-score*	-0.34 (0.86)	-0.55 (0.86)	-0.24 (0.84)	0.01
FMI-Z score**	-0.34 (1.09)	-0.35 (0.79)	-0.33 (1.21)	0.92
$ALMI_{FMI}$ Z-score***	-0.18 (1.22)	-0.36 (1.02)	-0.09 (1.30)	0.13
SLE disease duration (years)	15.8 (10.2)	16.2 (12.2)	15.6 (9.3)	0.70
SELENA-SLEDAI score†	X	1.7 (2.3)	X	Not applicable
SDI score††	X	1.2 (1.6)	X	Not applicable
SLAQ score‡	X	X	12.6 (7.4)	Not applicable
BILD score‡‡	X	X	2.1 (2.0)	Not applicable
High-sensitivity CRP (mg/dl)	6.3 (8.1)	4.7 (8.3)	9.2 (6.9)	0.005
Currently on steroids, N (%)	10 (43.5)	30 (42.3)	73 (44.0)	0.89
Valued Life Activities score****	0.79 (0.57)	0.75 (0.60)	0.80 (0.56)	0.54
Education, N (%)				0.06
High school or less	32 (13.5)	9 (12.7)	23 (13.9)	
Some college	86 (36.3)	17 (23.9)	69 (41.6)	
College	72 (30.4)	26 (36.6)	46 (27.7)	
Graduate/professional school	41 (17.3)	16 (22.5)	25 (15.1)	
Insurance status, N (%)				0.95
Medicare/Medicaid	88 (37.1)	26 (36.6)	62 (37.3)	
Private insurance	135 (57.0)	42 (59.2)	93 (56.0)	
Other	3 (1.3)	1 (1.4)	2 (1.2)	
Current smoking, N (%)	10 (4.2)	4 (5.6)	6 (3.6)	0.47

*ALMI Z-score: Appendicular lean mass index index Z-score. More negative reflects greater muscle mass deficit relative to the general population.
**FMI Z-score: Fat mass index Z-score. More negative reflects greater fat mass deficit relative to the general population.
***$ALMI_{FMI}$ Z-score: Adiposity-adjusted appendicular lean mass index Z-score. More negative reflects greater fat-adjusted muscle mass deficit relative to the general population.
†SELENA-SLEDAI: Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index. Range 0-105; higher is worse.
††SDI: Systemic Lupus Internal Collaborating Clinics/ACR Damage Index. Range 0-46; higher is worse.
‡SLAQ: Systemic Lupus Activity Questionnaire. Range 0-44; higher is worse.
‡‡BILD: Brief Index of Lupus Damage. Range 0-46; higher is worse.
****Valued Life Activities: Scores range from 0-3, with higher scores indicating greater disability.
>5% missing: Race (N=40); education (N=12); insurance status (N=22)

Table 1

fat mass (FM), has been associated with disability in RA, but this relationship is not well understood in SLE. We aimed to determine the range of body composition in women with SLE relative to a national reference population without SLE and the associations of fat-adjusted and unadjusted appendicular lean mass (ALM) with self-reported disability.

Table 2. Cross-sectional associations between body mass Z-scores and natural log of Valued Life Activities disability score

	ß coefficient	95% confidence interval	p-value
*ALMI Z-score**			
Unadjusted	0.21	0.002, 0.42	0.05
Adjusted†	0.11	-0.12, 0.33	0.37
*FMI Z-score***			
Unadjusted	0.49	0.23, 0.74	<0.001
Adjusted†	0.35	0.06, 0.64	0.02
*$ALMI_{FMI}$ Z-score****			
Unadjusted	-0.27	-0.56, 0.03	0.07
Adjusted†	-0.27	-0.60, 0.07	0.12

*ALMI Z-score: Appendicular lean mass index index Z-score. More negative reflects greater muscle mass deficit relative to the general population.
**FMI Z-score: Fat mass index Z-score. More negative reflects greater fat mass deficit relative to the general population.
***$ALMI_{FMI}$ Z-score: Adiposity-adjusted appendicular lean mass index Z-score. More negative reflects greater fat-adjusted muscle mass deficit relative to the general population.
†Adjusted for age, race/ethnicity, natural log of high-sensitivity CRP (hsCRP), and study center.

Table 2

Table 3. Median (IQR) disability scores by body mass Z-score classification

$ALMI_{FMI}$ status	Low ALMI Z-score	Normal ALMI Z-score	Totals	p-value
Low* *$ALMI_{FMI}$ Z-score***	1.00 (0.53, 1.13)	0.80 (0.22, 1.32)	0.86 (0.37, 1.32)	P=0.316†
Normal *$ALMI_{FMI}$ Z-score****	0.71 (0.28, 1.16)	0.73 (0.35, 1.26)	0.71 (0.29, 1.17)	
Totals	0.75 (0.29, 1.16)	0.76 (0.25, 1.27)	0.76 (0.29, 1.17)	
p-value	P=0.682‡			

*Low defined as Z score of -1 or less (<16th percentile for reference data).
**ALMI Z-score: Appendicular lean mass index index Z-score. More negative reflects greater muscle mass deficit relative to the general population.
***$ALMI_{FMI}$ Z-score: Adiposity-adjusted appendicular lean mass index Z-score. More negative reflects greater fat-adjusted muscle mass deficit relative to the general population.
†Wilcoxson rank sum test comparing disability scores by low to normal fat-adjusted ALMZ Z-scores.
‡ Wilcoxon rank sum test comparing disability scores by low to normal ALMI Z-scores.

Table 3

Methods: Cross sectional dual energy x-ray absorptiometry (DXA) data from 2 prospective cohorts of women with validated SLE were analyzed. Age, sex, and race/ethnicity-specific ALM index (ALMI, kg/m^2) and FM index (FMI, kg/m^2) Z-scores, as well as fat-adjusted ALMI Z-scores, reflecting the number of standard deviations from average for a given level of adiposity, were generated using National Health and Nutrition Examination Survey reference ranges. Associations between fat-adjusted and unadjusted ALMI Z-Scores, as well as FMI Z-scores, and natural log of Valued Life Activities disability were determined using univariate and multivariate linear regression models and adjusted for

age, race/ethnicity, natural log of high-sensitivity CRP, and study center. A kappa statistic was calculated to assess concordance between low and normal fat-adjusted and unadjusted ALMI scores, with low lean mass for age defined as fat-adjusted or unadjusted ALMI Z-Score ≤-1 (< 16th percentile for reference data).

Results: In the combined cohort of 237 women with SLE, mean unadjusted ALMI, FMI, and fat-adjusted ALMI Z-scores were -0.34, -0.34, and -0.18, respectively, suggesting modest deficits compared to national reference data (Table 1). Although there were significant associations between ALMI Z-score and disability (p=0.05) and separately FMI Z-score and disability (p< 0.001), fat-adjusted ALMI Z-score was not significantly associated with disability (p=0.07) (Table 2). The association of ALMI Z-score with disability was attenuated after adjustment for multiple covariates (p=0.37) while the association of FMI Z-score with disability remained significant (p=0.02). The correspondence between fat-adjusted and unadjusted ALMI definitions of low lean mass for age was fair (κ 0.28, p< 0.001) (Table 3).

Conclusion: Women with SLE had muscle deficits relative to a national reference population without SLE before and after adjustment for adiposity. However, these muscle deficits, unlike fat mass, were not independently associated with self-reported disability. Further study is needed to determine the association of body composition with additional measures of health-related quality of life.

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Abstract Number: 1285

Association of Frailty with Disability Is Not Attenuated by Lean Body Mass in Women with SLE

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Background/Purpose: Frailty has been associated with disability and mortality in SLE. Whether this association is confounded by sarcopenia, a degenerative loss of muscle mass and quality typically associated with aging, has not been explored. This aim of this study is to evaluate the cross-sectional association of frailty with self-reported disability, adjusting for lean body mass.

Methods: Adult women with validated SLE and mild/moderate disease were recruited from 2 centers. Frailty and pre-frailty were measured according to Fried frailty criteria (unintended weight loss, weakness, slow gait, poor endurance, inactivity) and disability according to Valued Life Activities. Dual energy x-ray absorptiometry was used to compute sarcopenia based on 2 definitions (Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project [1] and European Working Group on Sarcopenia in Older People 2 [2]) incorporating measures of muscle strength and quantity. Associations between frailty and disability were determined using univariate and multivariate linear regression models adjusted for age, race/ethnicity, SLE duration, current steroid use, high-sensitivity CRP (hsCRP), and 2 measures of lean body mass, appendicular lean mass index (ALMI) and adiposity-adjusted ALMI

Table 1. Participant characteristics

N, median (IQR) unless otherwise specified	Robust (N=48)	Pre-frail (N=121)	Frail (N=41)	p-value
Age (years)	47.5 (32.2, 55.6)	47.0 (35.0, 56.0)	53.0 (46.0, 60.0)	0.05
Race, N (%)				0.15
Asian	8 (16.7)	20 (16.5)	3 (7.3)	
Black or African American	3 (6.3)	24 (19.8)	11 (26.8)	
White	27 (56.3)	58 (47.9)	21 (51.2)	
Other/declined to state	10 (20.8)	19 (15.7)	6 (14.6)	
BMI (kg/m^2)	22.4 (20.5, 30.2)	25.9 (22.5, 31.0)	25.6 (22.0, 30.4)	0.12
ALMI*	6.5 (5.7, 7.0)	6.7 (6.0, 7.3)	6.3 (5.5, 7.4)	0.26
ALMI$_{FM}$ Z-score**	-0.4 (-0.7, 0.6)	-0.2 (-1.0, 0.7)	-0.3 (-1.6, 0.4)	0.45
Sarcopenia, N (%)				
FNIH***	0 (0)	4 (3.3)	10 (24.4)	<0.001
EWGSOP 2****	0 (0)	1 (0.8)	9 (22.0)	<0.001
SLE disease duration (years)	12.5 (9.0, 19.0)	13.5 (8.5, 21.5)	14.0 (10.0, 21.0)	0.63
SELENA-SLEDAI score†	1.0 (0, 4.0)	2.0 (0, 6.0)	6.0 (2.0, 8.0)	<0.001
SDI score††	0 (0, 1.0)	0 (0, 2.0)	1.5 (1.0, 4.0)	0.04
SLAQ score‡	6.5 (4.0, 10.0)	12.0 (7.5, 17.0)	16.0 (14.0, 22.0)	<0.001
BILD score‡‡	1.0 (0, 2.0)	1.0 (1.0, 3.0)	3.0 (1.0, 5.0)	<0.001
High-sensitivity CRP (mg/dl)	0.9 (0.4, 2.6)	1.3 (0.6, 4.3)	2.7 (0.8, 8.3)	0.01
Currently on steroids, N (%)	20 (41.7)	47 (38.8)	27 (65.9)	0.01
Valued Life Activities score*****	0.3 (0.1, 0.6)	0.7 (0.3, 1.1)	1.2 (1.0, 1.7)	<0.001
Education, N (%)				0.02
High school or less	2 (4.2)	18 (14.9)	7 (17.1)	
Some college	11 (22.9)	46 (38.0)	19 (46.3)	
College	24 (50.0)	38 (31.4)	8 (19.5)	
Graduate/professional school	11 (22.9)	19 (15.7)	7 (17.1)	
Insurance status, N (%)				0.06
Medicare/Medicaid	12 (25.0)	44 (36.4)	21 (51.2)	
Private insurance	33 (68.8)	73 (60.3)	17 (41.5)	
Other	0 (0)	3 (2.5)	0 (0)	
Current smoking, N (%)	0 (0)	5 (4.1)	5 (12.2)	0.02

*ALMI: Appendicular lean mass index.
**ALMI$_{FM}$ Z-score: Adiposity-adjusted appendicular lean mass index Z-score. More negative reflects greater fat-adjusted muscle mass deficit relative to the general population.
***FNIH: Foundation for the National Institutes of Health Biomarkers Consortium Sarcopenia Project definition.
****EWGSOP 2: European Working Group on Sarcopenia in Older People 2 definition
†SELENA-SLEDAI: Safety of Estrogens in Lupus Erythematosus National Assessment-Systemic Lupus Erythematosus Disease Activity Index. Range 0-105; higher is worse. Available for participants in New York.
††SDI: Systemic Lupus Internal Collaborating Clinics/ACR Damage Index. Range 0-46; higher is worse. Available for participants in New York.
‡SLAQ: Systemic Lupus Activity Questionnaire. Range 0-44; higher is worse. Available for participants in California.
‡‡BILD: Brief Index of Lupus Damage. Range 0-46; higher is worse. Available for participants in California.
*****Valued Life Activities: Scores range from 0-3, with higher scores indicating greater disability.

Table 1

Z-score, reflecting the number of standard deviations from average for a given level of adiposity using National Health and Nutrition Examination Survey reference ranges.

Results: In the combined cohort of 210 women with SLE, 20% of participants were frail and 58% were pre-frail (Table 1). Frail women were significantly older (p=0.05), with lesser educational attainment (p=0.02), greater disease activity (p< 0.001), more damage (p=0.04 for SLICC/ACR Damage Index; p< 0.001 for Brief Index of Lupus Damage), higher hsCRP (p=0.01), and more frequent steroid use (p=0.01) and cigarette smoking (p=0.02). Sarcopenia was more prevalent among frail women with SLE as compared to pre-frail and non-frail women according to both definitions (p<

Table 2. Associations between frailty and disability in unadjusted and adjusted linear regressions

	Frailty classification	ß coefficient	95% confidence interval	p-value
Unadjusted	Frail	0.93	0.72, 1.14	<0.001
	Pre-frail	0.36	0.19, 0.53	<0.001
Adjusted, including for ALMI*	Frail	0.95	0.72, 1.17	<0.001
	Pre-frail	0.40	0.21, 0.60	<0.001
Adjusted, including for $ALMI_{FMI}$ Z-score***	Frail	0.92	0.69, 1.16	<0.001
	Pre-frail	0.43	0.23, 0.63	<0.001

All adjusted models controlled for age, race/ethnicity, disease duration, current steroid usage, and high-sensitivity CRP.
*ALMI Z-score: Appendicular lean mass index.
***$ALMI_{FMI}$ Z-score: Adiposity-adjusted appendicular lean mass index Z-score. More negative reflects greater fat-adjusted muscle mass deficit relative to the general population.

Table 2

0.001). There was a significant dose-dependent association between frailty and pre-frailty and disability ($p< 0.001$), which was not attenuated after adjustment for multiple confounders and either measure of lean body mass (Table 2).

Conclusion: Frailty was significantly associated with disability. Sarcopenia was more common among frail than pre-frail and non-frail women with SLE. The association of frailty with disability was not attenuated by multiple covariates, including lean body mass. These data suggest that frailty is a distinct phenotype not fully described by direct measures of low muscle mass. Further study is needed to determine the relative contributions of frailty and sarcopenia to other adverse health outcomes in SLE.

References

1. Studenski et al. J Gerontol A Biol Sci Med Sci 2014;69:547-8.
2. Cruz-Jentoft et al. Age Ageing 2019;48:16-31.

Disclosure: S. Lieber, None; **P. Katz**, None; **J. Baker**, None; **D. Jannat-Khah**, Astrazeneca, 1, Cytodyn, 1, Walgreens Boots Alliance, 1; **D. Sheira**, None; **L. Mandl**, Annals of Internal Medicine, 9, UpToDate, 7, Regeneron, 2.

Abstract Number: 1286

Personalizing Cardiovascular Risk Prediction for Patients with Systemic Lupus Erythematosus by Physician Global Assessment of Disease Activity

May Choi[1], Emma Stevens[2], Hongshu Guan[2], Daniel Li[3], Jack Ellrodt[4], Benjamin Kargere[4], Tianrun Cai[2], Kazuki Yoshida[5], Brendan Everett[2] and Karen Costenbader[6], [1]Brigham and Women's Hospital | Cumming School of Medicine, University of Calgary, Calgary, AB, Canada, [2]Brigham and Women's Hospital, Boston, MA, [3]Harvard, Columbus, OH, [4]Williams College, Williamstown, [5]Brigham & Women's Hospital and Harvard Medical School, Boston, MA, [6]Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The risk of cardiovascular disease (CVD), including myocardial infarction and stroke, is higher in SLE than in the general population. The excess risk of premature CVD has been attributed to SLE-related systemic inflammation and its treatment. CVD risk prediction algorithms perform poorly in SLE populations because they do not capture SLE-related inflammation. The purpose of this study was to quantify the excess CVD risk, beyond that predicted by a traditional risk calculator, in strata of patients defined as mild/remission, moderate or severe SLE by the Physical Global Assessment (PGA) of disease activity.

Methods: We included SLE patients enrolled in a local SLE cohort and collected their one-year baseline data on traditional CVD risk factors, demographic and clinical features from the electronic medical record (EMR) at cohort enrollment. Subjects were required to have one or more visits for SLE during the baseline period. Their overall disease activity representing all encounters during the entire baseline year was rated independently by two reviewers (KC and MC) using a modified PGA tool (**Table 1**). PGA scores ranged from 1 (remission/mild), 2 (moderate), to 3 (severe). A 10-year follow-up period for CVD events began day +1 at end of baseline period (index date). The first MI or stroke in the follow-up period was identified in the EMR using ICD-9/10 codes and adjudicated by medical record

Table 1. Modified SLE Physician Global Assessment definitions generated using the European League Against Rheumatism (EULAR) SLE management guideline[1] and the SLE disease severity algorithm that was developed for claims data[2]

Score	Disease Activity	Keyword in Visit Notes[2]	EULAR Definition of Disease Activity[1]	Medications
1	Remission or mild	"Remission", "quiescent", "burnt out", "mild", "low activity"	Constitutional symptoms/mild arthritis/rash ≤9% BSA/PLTs 50-100 x $10^3/mm^3$; SLEDAI ≤6; BILAG C or ≤1 BILAG manifestation	No SLE medication or low-dose anti-malarial, low-dose steroids, anti-malarial, NSAID, stable dose of DMARD
2	Moderate	"Moderate"	RA-like arthritis/rash 9-18% BSA/cutaneous vasculitis ≤18% BSA; PLTs 20-50 x $10^3/mm^3$; SLEDAI 7-12; ≥2 BILAG B manifestations	Moderate dose steroids, biologics, multiple/escalating dose of DMARDs
3	Severe	"Severe"	Major organ threatening disease (nephritis, cerebritis, myelitis, pneumonitis, mesenteric vasculitis; PLTs <20 x $10^3/mm^3$, TTP-like disease or acute hemophagocytic syndrome; SLEDAI >12; ≥1 BILAG A manifestations	High dose/pulse steroids, cyclophosphamide, plasmapheresis

[1]Fanouriakis, Antonis, et al. "2019 update of the EULAR recommendations for the management of systemic lupus erythematosus." Annals of the rheumatic diseases 78.6 (2019): 736-745.

[2]Garris C, et al. Healthcare utilization and cost of systemic lupus erythematosus in a US managed care health plan. Journal of medical economics. 2013;16(5):667-77.

Abbreviations: BILAG, British Isles Lupus Assessment Group; BSA, body surface area; DMARD, disease modifying anti-rheumatic drug; NSAIDs, non-steroidal anti-inflammatory drug; PLT, platelets; RA, rheumatoid arthritis; SLEDAI, systemic lupus erythematosus (SLE) disease activity index; TTP, thrombotic thrombocytopenic purpura.

Table 2. Baseline characteristics and cardiovascular disease (CVD) risk factors in patients with SLE with and without CVD outcome events (myocardial infarction or stroke)

Baseline Characteristic	With CVD event n= 212	Without CVD event n=1,031	P*
SLE disease duration in years, mean (SD)	13.8 (10.9)	10.0 (8.3)	<0.0001
Age in years, mean (SD)	47.8 (14.6)	40.3 (12.7)	<0.001
Female, n (%)	196 (92.5)	960 (93.1)	0.73
Treated Systolic BP in mmHg, mean (SD)	131.6 (25.5)	124.4 (17.9)	0.001
Untreated Systolic BP in mmHg, mean (SD)	125.6 (14.9)	118.5 (15.2)	0.0001
Current smoker, n (%)	30 (14.2)	124 (12.0)	0.39
Diabetes mellitus, n (%)	26 (12.3)	60 (5.8)	<0.001
Total cholesterol in mg/dL, mean (SD)	195.2 (91.3)	179.1 (43.1)	0.004
High-density lipoprotein cholesterol in mg/dL, mean (SD)	55.5 (18.3)	55.8 (20.3)	0.90
Physician Global Assessment			
Remission/mild	162 (76.4)	841 (81.6)	0.12
Moderate	23 (10.9)	88 (8.5)	0.72
Severe	27 (12.7)	102 (9.9)	0.67

* Two-tailed P value for t-test and Fisher's exact test, for continuous and binary risk factors, respectively.
Abbreviations: BP, blood pressure; SD, standard deviation

review. We excluded subjects with CVD events prior to the index date. Relative excess risk of CVD event in 10 years was determined by comparing the risk expected according to the 2013 American College of Cardiology (ACC) and the American Heart Association (AHA) risk equation and to the observed outcomes, stratified by PGA. The Greenwood-Nam-D'Agostino calibration test was used to compare observed to expected in each PGA category.

Results: We included 1243 patients; 93.0% female and mean age of 41.6 (SD 13.3) years (**Table 2**). 80.6% patients had remission/mild disease, while 8.9% had moderate and 10.3% had severe disease. Inter-rater agreement of PGA's was substantial with 93.5% agreement corresponding to weighted k of 0.75 (SE 0.08, $p< 0.001$), respectively. There were 212 CVD events, 173 MIs and 64 strokes, over the follow-up period of 8242.92 person-years (PY). The incidence rate (IR) for the entire cohort was 26 [22, 29]/1000 patient PY. When stratified by PGA, the IRs were 24 [21, 28] for remission/mild, 32 [22, 49] for moderate, and 35 [24, 51] for severe. The observed vs expected ratio of CVD events using the ACC/AHA risk equation was highest among patients with severe disease (35.93 [95%CI 8.74,72.86]), followed by moderate (16.03 [95%CI 7.59, 26.02]) and remission/mild disease (12.39 [95%CI 7.88,17.00]) (**Table 3**). All calibrations were $p< 0.01$ meaning the calibration of observed events to risk predicted by the ACC/AHA algorithm was significantly off for all PGA categories.

Conclusion: The excess risk of CVD events in SLE patients is underestimated by traditional cardiovascular prediction tools, although the degree of underestimation may be increased in patients with more severe SLE disease activity over the past year. Therefore, more SLE-specific CVD risk prediction algorithms are needed.

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Table 3. Relative risk of cardiovascular disease (CVD) outcomes in SLE compared with those expected based on 2013 American College of Cardiology (ACC) and the American Heart Association (AHA) risk score for CVD

	Observed : Expected Number of CVD Events Ratio (95%CI)
Entire cohort	15.08 (8.39, 22.46)
Cohort stratified by Physician Global Assessment score	
Remission/Mild	12.39 (7.88, 17.00)
Moderate	16.03 (7.59, 26.02)
Severe	35.93 (8.74, 72.86)

Abbreviations: CI, confidence interval

Abstract Number: 1287

Prevalence of Morbidity Prior to Diagnosis of Incident Systemic Lupus Erythematosus in the Danish Population

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with SLE experience a high burden of various comorbidities at disease onset and during disease progression. Studies of excess morbidity prior to SLE diagnosis are limited. We thus estimated the cumulative prevalence of common comorbidities (defined by validated morbidity indices) in incident SLE patients before SLE diagnosis and compared it with matched population comparators in Denmark.

Methods: Patients ≥18years of age with a first registration of SLE (defined by International Classification of Diseases (ICD) codes) from Jan 1, 1996 to July 31, 2018 in the Danish National Patient Register (DNPR), and who had no SLE ICD codes prior to 1996 were identified. For a registration of SLE to qualify for the case definition, it had to be a primary or secondary SLE ICD code from rheumatology, nephrology or dermatology departments (inpatient or outpatient) or a primary SLE ICD code from any inpatient department. The first-ever SLE registration was set as SLE diagnosis date (the index date), and the case definition fulfillment date was used for matching. Patients with >12 months between these dates were excluded. Up to 19 comparators per SLE case, matched by age and sex, were selected from the general population. ICD-coded diagnoses during outpatient and inpatient care were retrieved from the DNPR and DNPR-Psychiatry. To identify comorbid conditions, the initial date of diagnosis from DNPR based on ICD codes or the date of the first prescription filled for osteoporosis, hypertension, or diabetes, were used. We estimated cumulative prevalence and prevalence ratios (PR) with corresponding 95% confidence intervals (CI) of morbidities as defined by Charlson, Elixhauser, and SLICC-ACR damage indices at 10, 5, 2, and 1 year before and at index date in SLE patients and the population comparators, adjusted for age and sex.

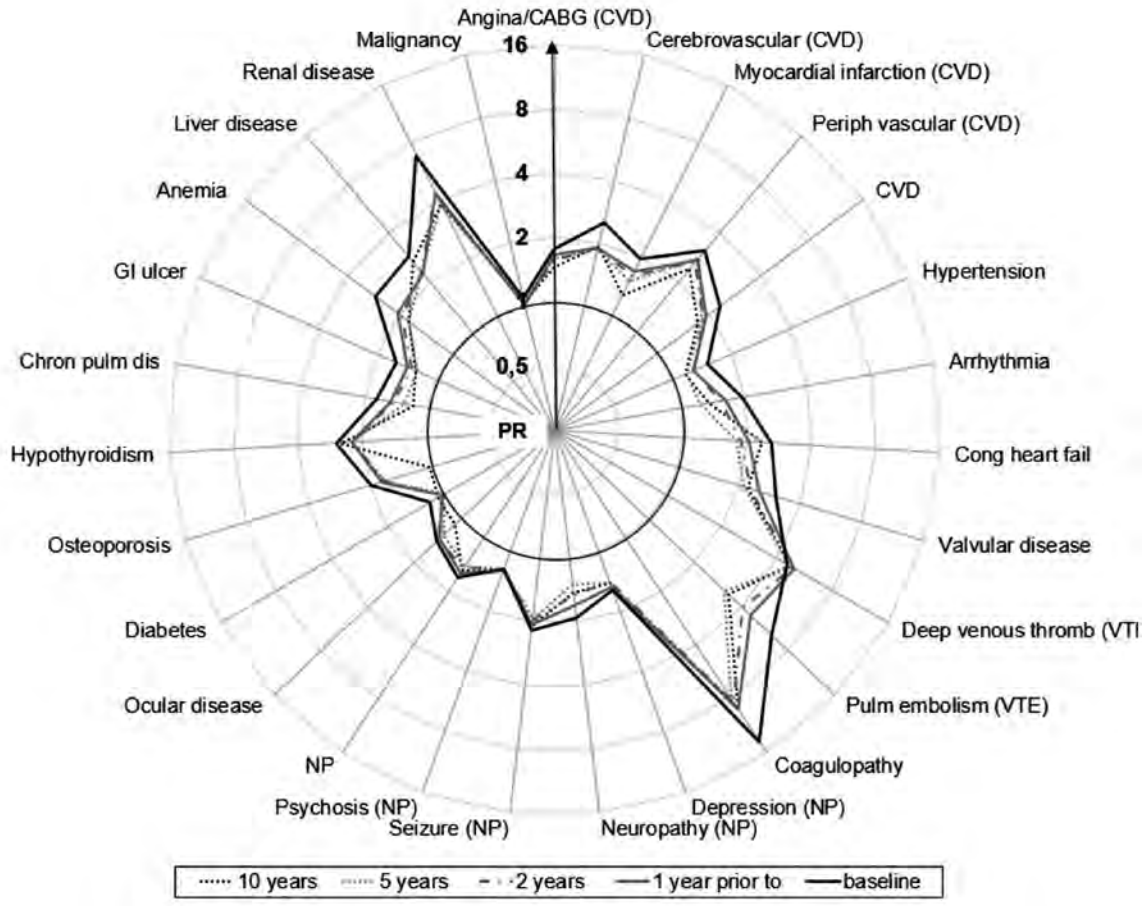
Results: 3,010 patients with incident SLE were matched to 57,046 population comparators. 84% of the subjects were female; the mean age at index date was 47 years. Except for malignancy, all morbidities appeared more prevalent 10 years before index date or at index date compared to the population comparators (Table). The PRs were

Table. Cumulative prevalence and prevalence ratios of comorbidities at 10 years before and at index date in incident SLE (n=3,010) and matched population comparators, non-SLE (n=57,046).

Comorbidity	Prevalence 10 years before index date, n (%)	Prevalence ratio 10 years before index date (95% CI)	Prevalence at index date, n (%)	Prevalence ratio at index date (95% CI)
Myocardial infarction				
SLE	19 (0.6)	1.3	83 (2.8)	**2.0**
Non-SLE	283 (0.5)	(0.8-2.0)	798 (1.4)	**(1.6-2.5)**
Angina or coronary bypass				
SLE	26 (0.9)	**1.4**	92 (3.1)	**1.7**
Non-SLE	340 (0.6)	**(1.0-2.1)**	989 (1.7)	**(1.4-2.2)**
Congestive heart failure				
SLE	12 (0.4)	**2.3**	71 (2.4)	**2.6**
Non-SLE	97 (0.2)	**(1.3-4.2)**	514 (0.9)	**(2.0-3.3)**
Cardiac arrhythmia				
SLE	35 (1.2)	**1.4**	173 (5.7)	**1.9**
Non-SLE	484 (0.8)	**(1.0-1.9)**	1673 (2.9)	**(1.7-2.3)**
Valvular disease				
SLE	11 (0.4)	**2.2**	66 (2.2)	**3.0**
Non-SLE	94 (0.2)	**(1.2-4.1)**	413 (0.7)	**(2.3-3.9)**
Hypertension				
SLE	128 (4.2)	**1.2**	722 (24.0)	**1.5**
Non-SLE	2068 (3.6)	**(1.0-1.4)**	9055 (15.9)	**(1.4-1.6)**
Renal disease				
SLE	21 (0.7)	**3.8**	100 (3.3)	**6.9**
Non-SLE	104 (0.2)	**(2.4-6.1)**	274 (0.5)	**(5.5-8.7)**
Peripheral vascular disease				
SLE	29 (1.0)	**2.4**	123 (4.1)	**3.1**
Non-SLE	227 (0.4)	**(1.6-3.5)**	747 (1.3)	**(2.6-3.7)**
Deep venous thrombosis				
SLE	29 (1.0)	**5.1**	66 (2.2)	**4.9**
Non-SLE	108 (0.2)	**(3.4-7.6)**	257 (0.4)	**(3.7-6.4)**
Cerebrovascular disease				
SLE	40 (1.3)	**1.9**	198 (6.6)	**2.5**
Non-SLE	395 (0.7)	**(1.4-2.6)**	1505 (2.6)	**(2.1-2.9)**
Neuropathy				
SLE	59 (2.0)	**1.5**	209 (6.9)	**1.9**
Non-SLE	759 (1.3)	**(1.1-1.9)**	2061 (3.6)	**(1.7-2.2)**
Other neurologic disease				
SLE	84 (2.8)	**2.0**	147 (4.9)	**2.0**
Non-SLE	803 (1.4)	**(1.6-2.5)**	1361 (2.4)	**(1.7-2.4)**
Epilepsy, seizure				
SLE	69 (2.3)	**2.1**	115 (3.8)	**2.2**

particularly high for venous thromboembolic events, coagulopathy, valvular diseases, and renal diseases with PRs ranging from 3.0 to 14. Also, cardiovascular, neurologic, hematologic, gastrointestinal, and endocrine diseases were significantly overrepresented before the index date. A striking finding is the stability of the overrepresentation for the mentioned morbidities even 10 years before index date among SLE patients as depicted in the Figure.

Figure. Spidergram of comorbidity prevalence ratios (PR) at 10, 5, 2, 1 and 0 years before index date; incident SLE patients (n=3,010) versus matched population comparators (n=57,046).



Conclusion: We found a higher than expected prevalence of multiple morbidities - not only at the time of SLE diagnosis but also during the 10-year pre-diagnosis period among the individuals with incident SLE. These findings may have implications on our understanding of SLE pathogenesis and the subsequent accumulation of morbidity after SLE diagnosis. In a clinical setting, these findings underscore the importance of a broad screening for various comorbidities at SLE diagnosis as early awareness and treatment of multimorbidity is expected to improve outcomes in SLE.

Disclosure: J. Simard, None; **M. Faurschou**, None; **S. Jacobsen**, Soeren Jacobsen, 2; **R. Hansen**, None.

Abstract Number: 1288

Predictors of Frailty Identified by the Short Physical Performance Battery and Associations with Patient-reported Outcomes

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Frailty, defined as a generalized vulnerability to stressors, has emerged as a relevant concept in SLE[1], although its origins are in geriatrics. As defined by the Fried Frailty Phenotype (FFP)[2], frailty is an aggregate of 5 constructs: weight loss, exhaustion, low physical activity, slowness, and weakness. Other means of identifying frailty have been suggested that may be easier to implement in clinical settings, including a shorter performance-based method, the Short Physical Performance Battery (SPPB)[3]. We examined the prevalence of frailty using the SPPB in a well-characterized SLE cohort.

Methods: Data are from the California Lupus Epidemiology Study (CLUES), a longitudinal cohort of individuals with rheumatologist-confirmed SLE. Data are collected annually through in-person research visits and structured interviews. At one visit, the SPPB was administered to a subset of the cohort. SPPB consists of balance tests, time to complete 5 chair stands, and gait speed over 4 meters. Scores range from 0 – 12; a score of < 10 identifies frailty.

Table 1. Differences in characteristics of individuals with SLE classified as frail or not frail

	Not frail (n=78)	Frail (n=72)	p
Age	43.9 ± 13.1	45.5 ± 15.0	.50
Female	85.9 (67)	91.7 (66)	.31
Race/ethnicity			.0003
White, non Hispanic	32.1 (25)	19.4 (14)	
Black	3.9 (3)	12.5 (9)	
Hispanic	12.8 (10)	37.5 (27)	
Asian	51.3 (40)	30.6 (22)	
Income below poverty	11.0 (8)	30.8 (20)	.005
Physical inactivity	29.5 (23)	47.2 (34)	.03
Obese (BMI≥30)	14.1 (11)	26.4 (19)	.07
Disease duration	16.4 ± 10.0	14.1 ± 9.6	.15
SLEDAI	2.9 ± 3.2	3.3 ± 3.2	.57
SDI	1.1 ± 1.6	1.1 ± 1.1	.98
SLAQ	7.5 ± 5.9	10.2 ± 7.4	.01
Glucocorticoid use, current	46.2 (36)	45.8 (33)	.99

p-values from t-tests or chi-square analyses comparing frail and non frail.
SLEDAI = SLE Disease Activity Index; SLAQ = Systemic Lupus Activity Questionnaire; SDI = SLICC Damage Index
SPPB = Short Physical Performance Battery

Table 2. Predictors of frailty, multivariate analysis		
	Model 1	Model 2
Race/ethnicity		
White, non Hispanic	(ref)	(ref)
Black	3.0 (0.6, 14.5)	5.1 (1.0, 26.3)
Hispanic	3.2 (1.1, 9.5)	4.4 (1.4, 14.1)
Asian	0.8 (0.3, 2.0)	1.1 (0.4, 2.8)
Income below poverty	2.0 (0.4, 3.1)	1.4 (0.5, 4.1)
Physical inactivity	1.6 (0.7, 3.6)	0.9 (0.3, 2.6)
Obese (BMI≥30)	1.1 (0.4, 3.2)	0.9 (0.4, 2.7)
SLEDAI	1.0 (0.9, 1.1)	---
SLAQ	---	1.03 (0.97, 1.1)
Results are odds ratio (95% confidence interval) from multiple logistic regression, controlling for variables shown. Model 1 adjusted for SLEDAI, Model 2 for SLAQ SLEDAI = SLE Disease Activity Index; SLAQ = Systemic Lupus Activity Questionnaire SPPB = Short Physical Performance Battery		

Table 3. Association of frailty with patient-reported outcomes		
	Frail	p
PROMIS Physical Function	-5.1	.002
PROMIS Fatigue	0.7	.75
PROMIS Pain interference	4.4	.01
PROMIS Cognitive Ability	-2.2	.19
PROMIS Satisfaction with Social Roles	-5.2	.007
PROMIS Satisfaction with Discretionary Roles	-3.6	.06
Depressive symptoms (PHQ)	1.3	.18
Results from multivariate regression analyses adjusted for race/ethnicity, income, obesity, and SLEDAI. Tables values are beta and p-value from regression analyses. PROMIS = Patient Reported Outcomes Measurement Information System PHQ = Patient Health Questionnaire		

Differences in participant characteristics for frail/not frail were examined using t-tests or chi-square analyses. Multivariate logistic regression analyses identified independent predictors of frailty, including age, sex, race/ethnicity, l, obesity, SLE duration, SLE disease activity, and steroid use. Separate models were constructed to include either physician-assessed (SLE Disease Activity Index, SLEDAI) or patient-reported disease activity (Systemic Lupus Activity Questionnaire). The impact of frailty on patient-reported outcomes (PROs) was examined with multiple regression analyses.

Results: Among the 150 individual who completed the SPPB, mean age was 45 ± 14 years, disease duration 15 ± 10 years, 89% were female, 41% Asian, 25% Hispanic, 26% white non-Hispanic, and 8% African American. The proportion of individuals classified as frail was 48% (Table 1). Factors associated with frailty in bivariate analyses were low income, obesity, physical inactivity, and patient-reported disease activity (Table 1). In multivariate analysis, only race/ethnicity remained a significant independent predictor of frailty (Hispanic only when adjusting for SLEDAI, Hispanic and African America when adjusting for SLAQ). In post-hoc analyses, obesity and inactivity were found to be significantly more common among Hispanics and African Americans ($p < .01$, not shown). Frailty was associated with worse scores on most PROs, even after adjusting for race/ethnicity, income, obesity, and physician-assessed disease activity (Table 3).

Conclusion: Using the SPPB, nearly half of this sample was identified as frail. A previous study using the FFP found 20% prevalence of frailty and 50% pre-frailty. Racial/ethnic differences were noted, but may be due to greater prevalence of obesity and inactivity among Hispanics and African Americans. Patient-reported outcomes were consistently worse among individuals classified as frail, even after adjusting for covariates. Interventions aimed at reducing inactivity may reduce frailty among individuals with SLE.

[1] Katz P. Lupus Sci Med 2017;4:e000186 [2] Fried L. J Gerontol 2001; 56:M146 [3] Guralnik J. J Gerontol 1994; 49:M85

Disclosure: P. Katz, None; **J. Yazdany**, Eli Lilly, 1, Astra Zeneca, 1; **L. Trupin**, None; **S. Rush**, None; **C. Lanata**, None; **L. Criswell**, None; **M. Dall'Era**, Janssen, 5, AstraZeneca, 5.

Abstract Number: 1289

Sex Differences in Mental Health and Quality of Life and Their Impact in the Treatment of Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) predominantly affects young women. It is usually more aggressive in men and carries a worse prognosis. Information about gender differences on psychiatric disorders, quality of life (QoL), patient-doctor relationship and adherence to treatment is limited, as men with SLE are often underrepresented.

Methods: We performed a cross-sectional study in a third-level hospital in Mexico City, from June to December 2019. We included SLE patients who met ACR criteria and recorded demographic and clinical data, including disease activity (*SLEDAI 2K*) and disease damage (*SLICC-DI*). We assessed depression (*CES D-20*) and anxiety (*BAI*), with tools validated to Spanish language. We also evaluated QoL (*LupusPRO*), patient-doctor relationship (*PDRQ-9*) and adherence to treatment (*Morisky-8)*.

Results: A total of 65 men and 140 women with SLE were recruited. There were no differences in demographic and clinical aspects (years from diagnosis, treatment strategies, and damage index), except for disease activity at the time of inclusion; men had higher SLEDAI scores [4(0-5) vs 2 (0-4), p=0.017] (Table 1). Conversely, there was no significant difference between genders in satisfaction with patient-doctor relationship and low adherence to treatment was reported by both groups (Figure 1).

On the other hand, QoL, as measured by LupusPRO, had lower scores in all domains for women, with a global score of 76 (64-83) in women vs 83 (73-88) in men, p=0.003 (Figure 2). Female patients more frequently reported high scores in the depression [46 vs 31%, p=0.042] and anxiety [29 vs 11%, p=0.004] scales than their male counterparts. We found that anxiety had a negative weak correlation with patient-doctor relationship satisfaction (r=-0.179, p=0.010)

	Men (n=65)	Women (n=140)	p
Age (median, p25-p75)	34 (27-44)	36 (26-45)	0.937
With a significant other (n, %)	35 (54.7%)	58 (42.6%)	0.111
Secondary education (n, %)	51 (82.3%)	101 (74.8%)	0.248
Low socioeconomic status (n, %)	32 (49.2%)	78 (55.7%)	0.386
Years from SLE diagnosis (median, P 25-P75)	9 (4-16)	10 (5-16.5)	0.286
Treatment with prednisone (n, %)	40 (62.5%)	75 (53.6%)	0.233
Number of immunosuppressants prescribed (median, p25-p75)	2 (1-2)	2 (1-2)	0.877
SLEDAI 2K (median, p25-p75)	**4 (0-5)**	**2 (0-4)**	**0.017**
SDI (median, p25-p75)	0 (0-1)	0 (0-1)	0.056

Table 1. SLEDAI 2K= Systemic Lupus Erythematosus Disease Activity Index 2000, SDI= Systemic Lupus International Collaborating Clinics/ American College of Rheumatology Damage Index

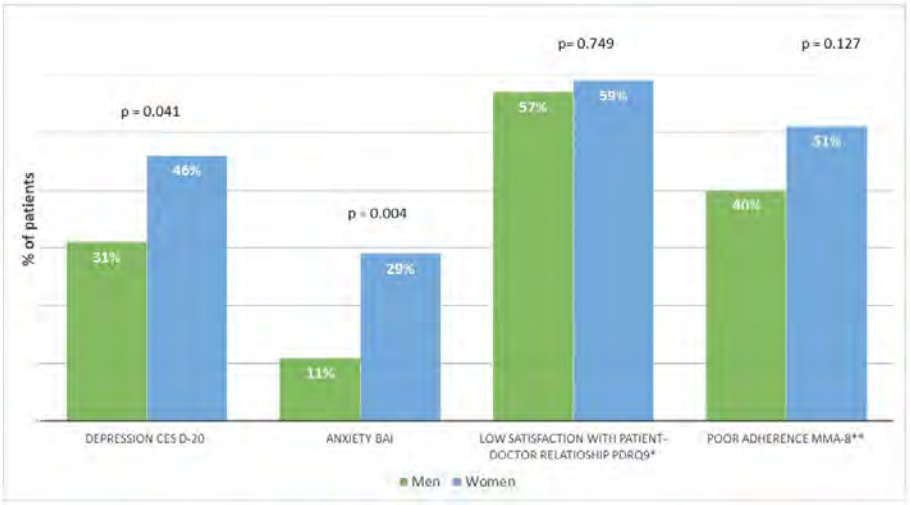

Figure 1. CES D-20= Center for Epidemiologic Studies Depression Scale, BAI= Beck Anxiety Inventory, PDRQ9= 9-item Patient-Doctor Relationship Questionnaire, MMA-8= 8-item Morisky medication adherence. *Patients that reported scores below the threshold for satisfaction in their patient-doctor relationship. **Patients with poor adherence according to the MMA-8 tool, using < 6 to define poor adherence.

and adherence to treatment (r=0.266, p< 0.005) in the whole group. Depression also negatively correlated with these two scores (patient-doctor relationship: r=-0.194, p=0.005; and adherence to treatment: r=-0.206, p=0.003).

In the multinomial logistic regression model, we found that women with SLE had a significantly higher prevalence of anxiety, depression or both (OR 2.57, 95%CI 1.36- 4.8, p=0.004).

Conclusion: This is the first study to demonstrate that being female is an independent risk factor for anxiety, depression, or both, in patients with SLE. It also demonstrates that, even though men have higher disease activity, women have lower scores in QoL and often report more SLE-associated symptoms. It is important that rheumatologists take these findings into account, in order to establish optimal support according to gender.

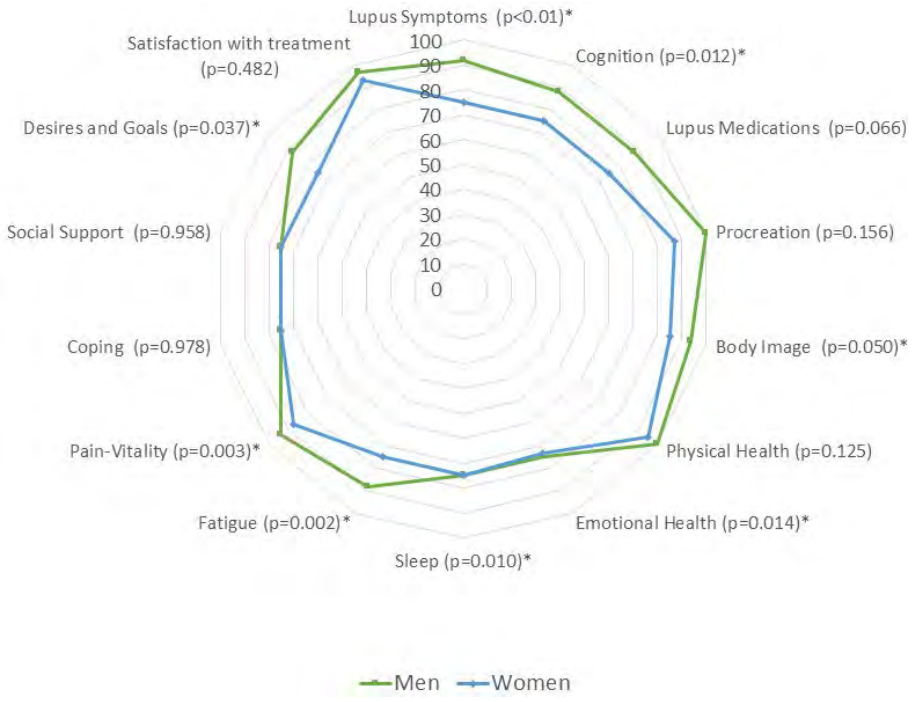

Figure 2. Quality of life spydergram for men and women with systemic lupus erythematosus measured by LupusPRO, * values are statistically significant.

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Abstract Number: 1290

A Multitrait-Multimethod Matrix Approach to the Construct Validity of Patient Reported Outcomes Measurement Information System Computerized (PROMIS) Adaptive Tests (CAT) in Systemic Lupus Erythematous

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SESSION INFORMATION
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Background/Purpose: Use of The Patient Reported Outcomes Measurement Information System computerized adaptive test (PROMIS-CAT) in adults with systemic lupus erythematous (SLE) is an emerging research field. Previous studies showed PROMIS short forms are reliable and valid against the SF-36 in persons with SLE. Our previous

Table 1: Patient characteristics at study enrolment (n=227)

Characteristic	Value (n=227)
Mean age (years)	48.6 ± 14.1
SLE disease duration (years)	18.5 ± 12.4
Sex (Female) (%)	205 (90.3)
Ethnicity (%) Black Caucasian Asian Other	 31 (13.7) 144 (63.4) 25 (11.0) 27 (11.9)
Highest level of education (%) ≤ Grade 8 >Grade 8 High school graduate Post Secondary Degree (College/University)	 1 (0.4) 7 (3.) 42 (18.8) 174 (77.7)
Mean SLEDAI-2K	2.1 ± 2.3
Mean SLICC-ACR Damage Index (SDI)	1.7 ± 1.9

Table 2. Multitrait-Multimethod Matrix of SF-36 and PROMIS-CAT Domain: Spearman correlations results

PROMIS	SF-36 Domains								Average Convergent and Divergent Correlations *	
	Physical Function	Role Physical	Bodily Pain	Vitality	Role Emotional	General Health	Mental Health	Social Function	Convergent	Divergent
Physical Function	**0.87**	**0.76**	0.65	0.61	0.63	0.56	0.41	0.62	0.82	0.58
Mobility	**0.91**	**0.70**	0.62	0.55	0.58	0.50	0.36	0.58	0.81	0.53
Pain Behaviour	0.75	0.72	**0.80**	0.62	0.65	0.55	0.47	0.65	0.80	0.63
Pain Interference	0.71	0.76	**0.82**	0.65	0.68	0.59	0.48	0.68	0.82	0.65
Fatigue	0.61	0.76	0.65	**0.85**	0.67	0.64	0.54	0.73	0.85	0.66
Anger	0.37	0.50	0.46	0.54	**0.55**	0.43	0.64	0.51	0.55	0.49
Anxiety	0.34	0.51	0.40	0.52	**0.61**	0.45	0.78	0.56	0.61	0.51
Depression	0.43	0.58	0.49	0.60	**0.65**	0.47	**0.80**	0.67	0.72	0.54
Ability to participate in social roles	0.76	0.79	0.64	0.68	0.71	0.61	0.47	**0.78**	0.78	0.67
Satisfaction with social roles	0.68	0.74	0.60	0.69	0.70	0.58	0.54	**0.71**	0.71	0.65

In columns of SF-36 domains the **bolded** values represent a priori expected convergent correlations within a domain; unbolded values represent a priori expected divergent correlations. All spearman correlations were statistically significant.
*Average convergent and divergent correlations within a domain were compared using multitrait-multimethod approach

Construct validity was also tested using additional five a priori hypotheses to explore the relationships of PROMIS-CAT domains with corresponding SF-36 domains. We hypothesized that the following associations would be found, with at least moderately positive associations (r >0.3):

1) PROMIS-CAT Physical Function the SF-36 domains of Physical Function and Role Physical.

2) PROMIS-CAT Anger, Anxiety, and Depression with SF-36 Emotional Health scores.

3) PROMIS-CAT Ability to Participate in Social Roles and Satisfaction with SF-36 Social Roles.

4) PROMIS-CAT Fatigue with SF-36 Vitality.

5) PROMIS-CAT Depression with SF-36 Mental Health.

Results: Of the 227participants in the cohort, 90.3% were female, mean age at study enrolment was 48.6 ± 14.1 years, and mean disease duration was 18.5 ± 12.4 years (Table 1). The multitrait-multimethod matrix examining construct validity confirmed that the average convergent correlations were greater than the average divergent correlations for all domains (Table 2). All five a priori hypotheses were satisfied with moderate to strong correlations (Spearman correlation, r=0.55-0.87) between PROMIS-CAT and most SF-36 domains.

Conclusion: Our results provide evidence on the validity of PROMIS-CAT in an SLE Canadian cohort. The use of multi-trait multimethod analyses highlighted the convergent and divergent construct validity compared to legacy instrument. This is the first study to use multitrait-multimethod matrix analysis to establish validity support for the PROMIS-CAT and our results demonstrate encouraging results.

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Abstract Number: 1291

Depressed Symptomatology Persists over Time in the Majority of Systemic Lupus Erythematosus Patients and Is Independent of Disease Activity

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Depression is a prevalent (24-30%) and significant comorbidity in patients with systemic lupus erythematosus (SLE) (1). As the American College of Rheumatology (ACR) classifies depression as a neuropsychiatric manifestation of SLE (2), many clinicians assume that depressed affect fluctuates with SLE disease activity. In the present study, we leveraged the well-characterized longitudinal SLE cohort at Washington University Lupus Clinic to address the following questions: 1) what is the longitudinal course of depressed affect among outpatients with SLE, and 2) what is the relationship between SLE disease activity and depressed affect.

Methods: Longitudinal data from patients with ACR or SLICC-classified SLE managed in the Lupus Clinic were analyzed. Depressed symptoms were assessed at each visit using the Center for Epidemiologic Studies Depression Scale, Revised (CESD-R). Scores were obtained from individual patients over an average of 30.2 months (SD: 13.3; range: 2.6-48.0). Standard CESD-R scores of < 16, 16-21, and >21 were used to define no depression, depressed affect, and major depression. SLE disease activity was measured via the SLEDAI2K Responder Index-50 (S2K RI-50).

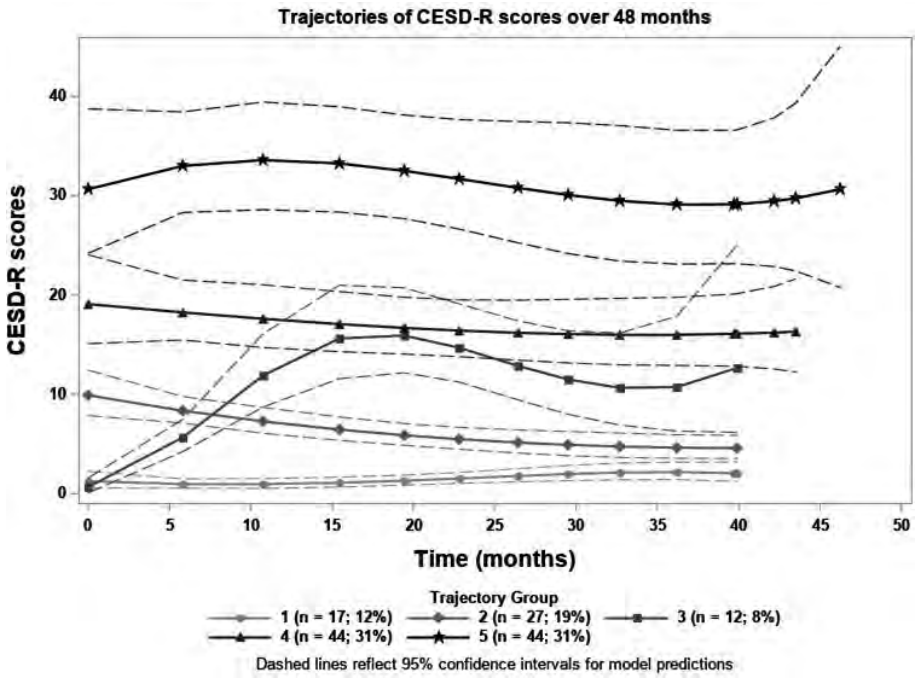

Figure 1. Identified trajectories of depression scores over time

Group-based trajectory modeling (GBTM) was applied to identify groups of patients with similar temporal trajectories of depressed symptoms over time. Baseline characteristics of individuals in each depressed trajectory group were compared using chi-square tests, Fisher's exact tests, or ANOVA. The relationship between disease activity and depression over time was assessed using multilevel linear regression models.

Results: The sample (n=144) was 91.0% female, 56.3% African American, and 38.9% White, with a mean age of 40.4 (SD: 12.6; range: 19-74). GBTM revealed 5 distinct groups of patients who demonstrated consistent trends in depression overtime (Figure 1). Members of groups 1 and 2 (n=17, 11.8%; n=27, 18.8%) had consistently normal CESD-R scores, group 3 (n=12, 8.3%) had rising CESD-R scores over time, and groups 4 (n=44, 30.6%) and 5 (n=44, 30.6%) demonstrated symptom patterns consistent with depressed affect and major depression, respectively. While visit-to-visit scores varied considerably, patterns remained durable over time documenting the prevalence of persistent major depression. Of note, African American patients were much more common in Group 5 (n=32, 72.7%, $p< 0.02$). Analyses did not identify an association between CESD-R and disease activity over time.

Conclusion: 61.2% of patients had scores indicating persistent depressed affect or major depression for up to 4 years. A relatively small group of patients (8.3%) reported CESD-R scores increasing from the 'normal' to depressed during the study. These data reinforce the disquieting pervasiveness of depression in SLE patients. The lack of a relationship of CESD-R to SLE disease activity highlights the need to identify non-clinical factors, particularly race, that contribute to and moderate this co-morbidity.

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2. Aiinala, H., et al., Arthritis Care Res (Hoboken), 2001;45:419-423.

Disclosure: S. Kellahan, None; **X. Huang**, None; **D. Lew**, None; **H. Xian**, None; **S. Eisen**, None; **A. Kim**, Exagen Diagnostics, Inc., 5, 8, GlaxoSmithKline, 2, 5, 8, Alexion Pharmaceuticals, 5, Annexon Biosciences, 5, JPMorgan Chase & Co., 5.

Abstract Number: 1292

Frequency and Predictors of Influenza Vaccine Hesitancy in Systemic Autoimmune Rheumatic Diseases

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SESSION INFORMATION
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Background/Purpose: Patients with systemic autoimmune rheumatic diseases (SARDs) benefit from getting annual inactivated influenza vaccine (IIV). However, vaccine uptake among SARDs is suboptimal. The delay in acceptance or refusal of vaccines despite the availability of vaccine services is known as vaccine hesitancy. This constitutes one of the ten threats to global health (World Health Organization, WHO 2019). In order to promote vaccine uptake in SARDs, it is key to understand the determinants of hesitancy. We assessed the frequency and predictors of influenza vaccine hesitancy in SARDs.

Methods: Between 11/2019 and 03/2020, consecutive SARDs patients presenting to the rheumatology clinics of a large tertiary care center completed an anonymous survey. We collected demographic data, factors reported to affect vaccine uptake (e.g. education, employment), SARDs specific information (e.g. diagnosis, disease duration, treatment), and questions proposed by the WHO to assess causes of vaccine hesitancy. The likelihood of a patient to get the flu vaccine was assessed based on a 10-point scale ('0 = I definitely will not get the flu vaccine' to '10 = I unquestionably will get the flu vaccine'). Patients were classified as (a) likely to refuse IIV (values 0-2); (b) likely to accept IIV (values 8-10), or (c) IIV uncertain (values 3-7). Multivariate logistic regression models were performed to determine predictors of influenza vaccine hesitancy.

Results: A total of 107 SARDs patients completed the survey. Patients' age ranged from 18 to 89 years (mean ± SD: 51.6 ± 17.0), 69.8% were female (n=74), and disease duration was (mean ± SD) 9.8 ± 10.8. Fifty-four patients (52.4%) had a university-level education and almost half were employed (n=51, 48.1%). Patients self-reported diagnoses were: SLE (n=57, 53.3%), vasculitis (n=27, 25.2%) myopathies (n=8, 7.5%), and others (n=15, 14.0%). Seventeen percent of SARDs had never received IIV, and 39% did not receive IIV in the previous season. Over one third of SARDs patients (38%) reported safety concerns about IIV, and 23% were uncertain if the benefits of IIV were larger than its risks. Twenty-three (23.5%) patients were likely to refuse IIV, 55 (56.1%) likely to accept IIV, and 20 (20.4%) were uncertain. Patients 'likely to refuse IIV' had more often rejected IIV (43.5% vs 7.5% of the likely to accept vs 15% of the uncertain). Compared to patients 'likely to accept IIV', those 'likely to refuse IIV' more often had never received IIV (OR 147.4, 95% CI 6.9 - >999). Eighty percent of those 'likely to refuse IIV' feel they should get IIV. Neither demographic data, employment status, disease duration or treatment predicted IIV acceptance. Bad reactions (personal or in known contacts) to IIV predicted vaccine refusal (OR 26.4, 95% CI 2.1 - 324.6).

Conclusion: Vaccine hesitancy in SARDs contributes to reduced IIV uptake. Despite most SARDs patients feel they should receive IIV, a third of them are concerned about the safety of the IIV. Adverse reactions to IIV strongly predict its refusal in SARDs. Reassuring SARDs patients about vaccine safety may enhance IIV uptake.

Disclosure: V. Valerio, None; **M. Useche**, None; **M. Wang**, None; **S. Bernatsky**, None; **C. Pineau**, None; **I. Colmegna**, None.

Abstract Number: 1293

Factors Associated with Early Hospital Readmission in Systemic Lupus Erythematosus: Data from National Readmission Database

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Early hospital readmission is a major healthcare burden. Studies evaluating factors associated with readmissions in rheumatic diseases are sparse. Our aim was to use a large national database to identify rates and the predictors of readmission in SLE as compared to common medical conditions with known high readmission rates including congestive heart failure (CHF) and chronic obstructive pulmonary disease (COPD).

Methods: We used the US nationwide readmission database (NRD, 2010-2014) to identify index adult (≥ 18 years) discharges with SLE, CHF, and COPD using ICD-9 codes in the first 5 diagnosis positions, and assessed their rates of readmission (defined as "early" readmission within 30 days). Index discharges with same-day transfers or those discharged as deceased were excluded. Discharges with the same diagnosis after 30 days from the previous index discharge date could count as another index, thus, allowing one patient to contribute to multiple observations. We performed multivariate regression to identify factors independently associated with early readmission, including demographic, hospital, and clinical factors. Comorbidities that were significant in univariate analysis ($p \leq 0.05$) were included in the multivariate model. We accounted for the clustering of multiple index discharges within the same patient using generalized estimating equations.

Results: In the combined data from 2010-2014, we identified 351,219 index SLE discharges, and compared them to 3,022,240 CHF, and 4,052,574 COPD index discharges. The readmission rate was 16.9% for SLE compared to 21.3% for CHF and 18.4% for COPD. Readmission was higher in males (19.5 %, 21.4 % and 19.4%) compared to females (16.6%, 21.2% and 17.7 %) for SLE, CHF and COPD, respectively.

Some demographic and hospital factors associated with higher odds of readmission in SLE included non-private insurance, longer length-of-stay at index hospitalization, and lowest income quartile. Age >65 and female sex were associated with reduced odds of readmission. Discharges against medical advice (AMA) had a higher odds of readmission in all cohorts (**Table 1**).

Among select diagnoses present in the index SLE discharges, the top 5 comorbid conditions associated with highest odds of readmission were chronic kidney disease (OR: 1.31, 95% CI: 1.23 – 1.39, $p < 0.001$), alcoholic liver disease

Associated factors	SLE	CHF	COPD
	OR (95% CI)	OR (95% CI)	OR (95% CI)
Demographic and socioeconomic characteristics			
Age > 65 (ref: 18-65), years	0.78 (0.75 - 0.82)	0.87 (0.86 - 0.89)	0.94 (0.92 - 0.95)
Female (ref: Male)	0.91 (0.87 - 0.95)	0.99 (0.99 - 1)	0.89 (0.88 - 0.89)
Insurance status (ref: Private)			
Medicare	1.31 (1.26 - 1.37)	1.29 (1.27 - 1.31)	1.36 (1.34 - 1.38)
Medicaid	1.45 (1.39 - 1.51)	1.44 (1.41 - 1.47)	1.55 (1.52 - 1.58)
Self-pay	1.13 (1.04 - 1.22)	0.85 (0.82 - 0.88)	0.92 (0.89 - 0.95)
Others, no charge or missing	1.09 (1 - 1.18)	1.06 (1.02 - 1.09)	1.13 (1.1 - 1.16)
Median household income (ref: 76th-100th), percentile			
51-75	1.04 (1 - 1.09)	1.02 (1.01 - 1.04)	1 (0.98 - 1.01)
26-50	1.05 (1 - 1.09)	1.03 (1.02 - 1.05)	1.02 (1 - 1.03)
0-25	1.09 (1.04 - 1.14)	1.09 (1.07 - 1.1)	1.05 (1.03 - 1.06)
Hospital Characteristics			
Hospital ownership (ref: government, non-federal)			
Private, non-profit	0.93 (0.89 - 0.97)	0.97 (0.95 - 0.98)	0.99 (0.98 - 1)
Private investor owned	1.03 (0.98 - 1.08)	1.02 (1.01 - 1.04)	1.04 (1.02 - 1.05)
Hospital bedsize (ref: small)			
Medium	1.01 (0.95 - 1.07)	1.04 (1.02 - 1.05)	1.03 (1.02 - 1.05)
Large	1.04 (0.99 - 1.1)	1.04 (1.03 - 1.06)	1.05 (1.03 - 1.06)
Hospital teaching status (ref: Non-metropolitan)			
Metropolitan non-teaching	1.11 (1.04 - 1.18)	1.04 (1.03 - 1.06)	1.1 (1.08 - 1.11)
Metropolitan teaching	1.16 (1.09 - 1.23)	1.05 (1.03 - 1.07)	1.11 (1.09 - 1.12)
Clinical characteristics			
Length of Stay (ref: <3), days			
3-5	1.16 (1.12 - 1.2)	1.07 (1.06 - 1.08)	1.07 (1.05 - 1.08)
>5	1.64 (1.57 - 1.71)	1.24 (1.23 - 1.26)	1.26 (1.25 - 1.28)
Discharge disposition (ref: Routine)			
Short term hospital	1.53 (1.32 - 1.77)	1.14 (1.1 - 1.19)	1.16 (1.11 - 1.21)
Skilled nursing, Intermediate care or other facility	1.03 (0.98 - 1.1)	1.18 (1.16 - 1.19)	1.23 (1.22 - 1.25)
Home health care	1.12 (1.07 - 1.17)	1.16 (1.15 - 1.17)	1.27 (1.26 - 1.28)
Against medical advice	1.88 (1.71 - 2.08)	2.11 (2.03 - 2.2)	1.93 (1.87 - 1.98)
Discharged alive, destination unknown or missing	0.68 (0.34 - 1.35)	0.51 (0.43 - 0.61)	0.75 (0.65 - 0.87)
Number of chronic conditions on discharge record	1.02 (1.01 - 1.03)	1.01 (1 - 1.01)	1.02 (1.02 - 1.03)
Number of diagnoses on discharge record	1.01 (1.01 - 1.02)	1 (1 - 1)	1 (1 - 1.01)
Number of procedures on discharge record	0.98 (0.97 - 0.98)	1 (1 - 1)	1.01 (1.01 - 1.02)
Comorbidity index > 5 (ref: ≤ 5)	0.95 (0.9 - 1)	1.05 (1.03 - 1.07)	0.99 (0.97 - 1)

Table 1. Multivariate analysis of demographic, hospital and clinical factors associated with early readmission in systemic lupus erythematosus (SLE), congestive heart failure (CHF) and chronic obstructive pulmonary disease (COPD)

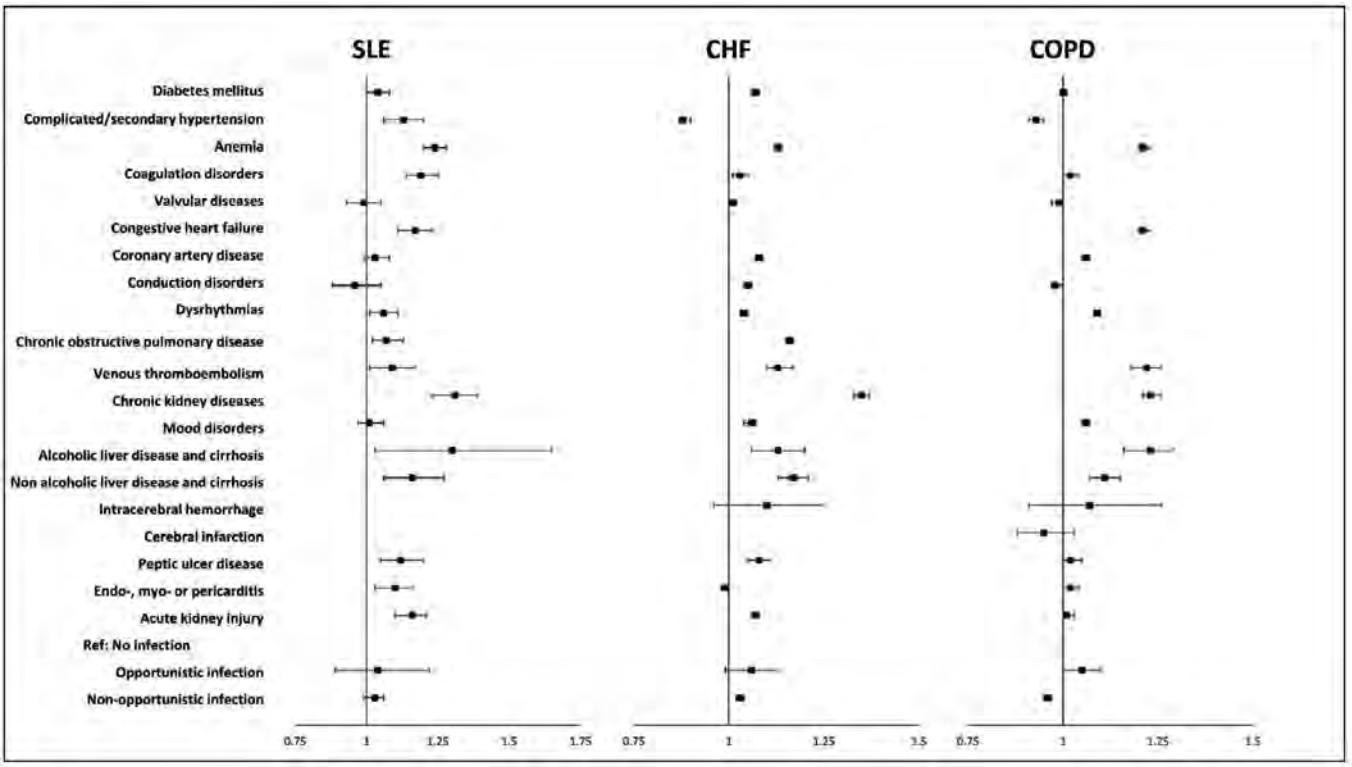

Figure 1. Multivariate analysis of comorbidities present at index discharges associated with early readmission in systemic lupus erythematosus (SLE), congestive heart failure (CHF) and chronic obstructive pulmonary disease (COPD)

(OR: 1.30 , 95% CI: 1.02 -1.65, p=0.03), anemia (OR 1.24, 95% CI: 1.20 – 1.28, p< 0.001) , coagulation disorders (OR: 1.19, 95% CI 1.14 – 1.25, p< 0.001), and CHF (OR: 1.17, 95% CI: 1.11– 1.23, p< 0.001). Acute kidney injury was associated with early readmission in CHF and SLE. Carditis (peri-, myo- and endocarditis) and cardiomyopathy were associated with increased readmission only in SLE (**Fig 1**).

Conclusion: We found readmission in SLE to be comparable to that in CHF and COPD. Higher readmission in younger SLE patients likely reflects the more severe phenotype in this group. Similarly, the presence of anemia, coagulopathy, and myopericarditis conferred higher readmission risk, likely reflecting more severe SLE with organ involvement. Studying the role of various common and unique predictors in a prospective setting could identify avenues for improving inpatient and transitional care in SLE.

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Abstract Number: 1294

Prediction of Damage in SLE Using Unbiased Analysis of Large Datasets

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SESSION INFORMATION
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Background/Purpose: A key goal of treatment of SLE is the prevention of irreversible organ damage. The ability to identify patients at increased risk for damage could select patients for early intervention but is currently lacking. Conventional studies of damage outcomes in SLE utilize composite disease activity scores, and associations with damage are only modest. We evaluated whether using all available data in an unbiased fashion, including continuous laboratory data usually analysed dichotomously in disease activity scores, could give rise to superior predictive algorithms for organ damage in SLE.

Methods: Prospectively collected longitudinal data from a 13-centre multinational cohort were used. Each visit was assigned yes/no as being in a damage-transition period based on whether the nearest subsequent annual measurement of organ damage (SLICC damage index) increased. Candidate variables included demographic (3), baseline serology (4), medication classes (anti-malarial, immunosuppressant, and glucocorticoid), routine clinical laboratory parameters (14) and SLEDAI-2K. Logistic regression models were selected to predict the probability of damage transition using backward, forward, and hybrid stepwise selection methods, either including or excluding SLEDAI-2K. The primary metric evaluating performance was area under the receiver operating characteristic curve (AUC) for association with damage transition.

Results: Data from 15,625 visits of 1,621 patients were split randomly 80:20 into training and test datasets; a separate cohort (2,178 visits, 188 patients) was used for independent validation. As there were only 1,157 damage transition visits in the training dataset, oversampling was used to create a dataset with 23,120 visits with a 'transition visit' ratio of 50%.

Altogether 2^{21} (~ 2 million) models with different combinations of predictors were analysed. After excluding models with >20 variables or training AUC < 0.62 we ranked 43,332 models excluding SLEDAI, and 224,349 models including SLEDAI, according to the mean of the training, test, and validation set AUC.

The highest performing model (mean AUC=0.659) included age, sex, and ethnicity; baseline ANA, anti-Sm, and anti-phospholipid antibody positivity; prednisolone use; and routine clinical lab variables ESR, eGFR, haemoglobin,

platelet & neutrophil count, and urine protein & red cells. All top 20 models included age, sex, ethnicity, some baseline serology, prednisolone use, and both ESR & eGFR, with anti-phospholipid status, haemoglobin, platelet and neutrophil count and urine protein and red cells in most. In this analysis, the inclusion in model selection of clinician measurement of disease activity using SLEDAI2K did not improve performance (highest AUC including SLEDAI2K=0.651).

Conclusion: We have derived algorithms predictive of organ damage, an important clinical outcome in SLE, using an unbiased 'big data' approach. Continuous laboratory variables contributed to damage risk, while clinician measured disease activity did not improve prediction. This suggests continuous laboratory measures should be included in future SLE clinical trial endpoints.

Disclosure: E. Morand, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, 5, Merck Serono, 2, 5, Neovacs, 5, Sandoz, 5, Novartis, 8, AbbVie, 5, Amgen, 5, Biogen, 5; **D. Liyanage**, None; **R. Hoang**, None; **V. Golder**, None; **W. Louthrenoo**, None; **S. Luo**, None; **Y. Wu**, None; **S. Sockalingam**, None; **S. Morton**, None; **S. Navarra**, Eli Lilly, 5, 8, Astra-Zeneca, 5, 8, Astellas, 8, Janssen, 5, 8, Novartis, 8, Pfizer, 8, Biogen, 2, 5; **L. Zamora**, None; **L. Hamijoyo**, None; **Y. Katsumata**, None; **M. Harigai**, AbbVie Japan GK, 1, 2, Asahi Kasei Corp., 1, Astellas Pharma Inc., 1, Ayumi Pharmaceutical Co. Ltd., 1, 2, Bristol Myers Squibb Co., Ltd, 1, 2, 3, Chugai Pharmaceutical Co. Ltd., 1, 2, Daiichi-Sankyo, Inc., 1, Eisai Pharmaceutical, 1, 2, Nippon Kayaku Co. Ltd., 1, Mitsubishi Tanabe Pharma Co., 1, Taisho Pharmaceutical Co. Ltd., 1, Takeda Pharmaceutical Co. Ltd., 1, 2, Eli Lilly Japan K.K, 1, Pfizer Japan Inc, 1, AbbVie, 1; **M. Chan**, None; **S. O'Neill**, None; **F. Goldblatt**, None; **C. Lau**, None; **Z. Li**, None; **J. Bonin**, None; **R. Koelmeyer**, None; **M. Nikpour**, Actelion, 2, 5, 8, GSK, 2, 5, 8, Boehringer Ingelheim, 5; **R. Kandane-Rathnayake**, None; **H. Nim**, None.

Abstract Number: 1295

Disease Activity and Mental Health in SLE Patients: A Cross-section Study with Self-Assessments Based on Smart System of Disease Management (SSDM) Mobile Tools

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SESSION INFORMATION

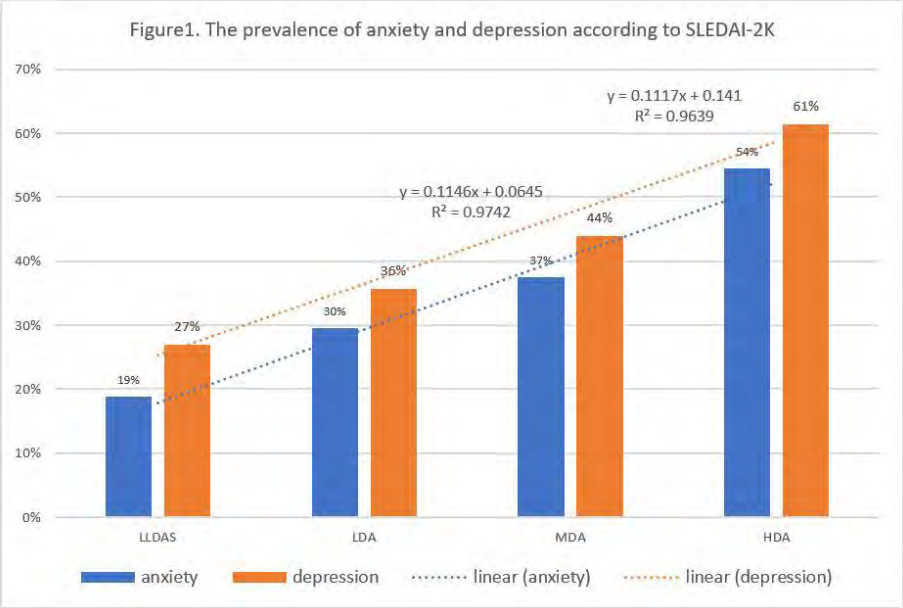
Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Figure 1. ↵



Background/Purpose: WHO survey showed that the prevalence of anxiety and depression in Chinese population and Chinese patients with chronic diseases were between 3.1% - 4.2% and 3.1% - 7.3%, respectively. SLEDAI-2K and Hospital Anxiety and Depression Scale (HADS) are commonly used to evaluate SLE patients' disease activity and mental health. All the Assessments were mainly performed by health professionals (HCPs) with paper questionnaire previously. SSDM is a novel smart disease management tool that allows patients to do self-assessments on SLEDAI-2K and HADS by mobile App.The purpose of this study is to investigate the prevalence of anxiety and depression in Chinese patients with SLE and to analyze the potential association between disease activity of SLE and mental health.

Methods: Under the guidance and training by HCPs, SLE patients downloaded SSDM and performed self-assessments bundle of SLEDAI-2K and HADS with SSDM. SLEDAI-2K < =4, 5-9, 10-14 and >=15 are defined SLE inactive, low (LDA), moderate (MDA) and high (HDA) disease activity, respectively. SLEDAI-2K score < = 4 is set as the main criteria for Lupus Low Disease Activity State (LLDAS) and achievement of T2T. HADS score >=8 can be diagnosed with anxiety or depression.

Results: From June 2016 to Jan 2020, 3,332 SLE patients (199 male, 3,133 female) with a mean age of 36.34 ± 12.80 (10-91) years and the median disease duration of 3.43 years from 216 hospitals performed bundle self-assessments for 4,967 times in total. According to the HADS and SLEDAI-2K Assessment results, the prevalence of anxiety and depression in all patients was 36.7% and 39.3% respectively, which was significantly higher than that in the WHO survey in Chinese population and chronic disease patients. The proportion of patients achieved and failed on LLDAS was 53% and 47%, respectively. The prevalence of anxiety (A) and depression (D) was 19% and 27% among LLDAS achievers; 41% and 47% among LLDAS failures, respectively (pA< 0.01, pD< 0.01).

According to SLEDAI-2K, in LLDAS, LDA, MDA and HDA subgroups, the prevalence of anxiety and depression was 19%, 30%, 37%, 54% and 27%, 36%, 44%, 61%, respectively. The correlation coefficients of anxiety (A) and depression (D) with SLEDAI-2K were rA=0.9957 and rD=0.9819. It suggested that with the increase of disease activity, the proportion of SLE patients with anxiety and depression increased significantly. (Figure 1)

Conclusion: Conclusion: Higher prevalence of anxiety and depression were Associated with higher levels of disease activity in SLE patients. SSDM is an effective mobile interface to monitor and study entanglement of disease activity and mental health in SLE patients, which build a foundation for proactive interventions physically and mentally in future.

Disclosure: Y. Wang, None; **H. Wei**, None; **R. Wu**, None; **J. Wu**, None; **S. Zhang**, None; **Q. Li**, None; **Y. Li**, None; **Y. Sun**, None; **Y. Zhao**, None; **Q. Shu**, None; **L. Kang**, None; **B. Wu**, None; **L. Qin**, None; **F. Jiang**, None; **H. Yang**, None; **J. Zhang**, None; **H. Xiao**, None; **B. Wu**, None; **Y. Jia**, None; **F. Xiao**, None; **L. Sun**, None.

Abstract Number: 1296

Associations of Metabolic Syndrome and Adipokines in SLE

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Metabolic syndrome (MetS) is a chronic pro-inflammatory and pro-thrombotic state associated with increased atherosclerosis, cardiovascular events and type 2 diabetes. It is diagnosed in the presence of at least 3 of 5 metabolic risk factors (obesity, hypertension, hypertriglyceridemia, low high-density lipoproteins (HDL) and insulin resistance [1]). The pathophysiology of MetS remains incompletely understood, but may share mechanisms with inflammatory states such as SLE. Visceral adiposity is known as a source of pro-inflammatory cytokines by adipocytes, the so-called adipokines. The contribution of glucocorticoids to the development of MetS in SLE is not clear, even though their use is associated with cardiovascular comorbidities [2]. We aim to characterize the prevalence and associations of MetS, including serum levels of adipokines, in a multi-ethnic cohort of patients with SLE.

Methods: Using a standardised protocol, baseline demographics, per visit disease activity (SLEDAI2K) and treatment data, and annual recording of organ damage accrual (SLICC damage index (SDI)) were prospectively captured on SLE patients from a single tertiary centre. The presence of MetS,defined using the updated joint consensus criteria [1], was assessed retrospectively at the last recorded visit. Serum levels of adipokines (resistin, lipocalin-2, TNF, MCP-1) and insulin were measured by Quantibody.

Results: 116 patients (median (IQR) age at enrolment 39.5 (31.4-51.1) years, median disease duration 6.1 (1.4-12) years) were followed for a median of 6.7 (4.1-8.1) years. 80% of patients were exposed to glucocorticoids (median time-adjusted mean dose 3.7 (0.5-7.0) mg/day and 50% accrued organ damage during follow-up. The prevalence of MetS in this cohort was 29%. The prevalence of the components of MetS included: hypertension (59%), low-HDL (51%), hypertriglyceridemia (32%), obesity (16%) and hyperglycaemia (22%). In univariable analysis, MetS was associated with baseline organ damage (SDI) (OR 4.34; 95% CI 1.80-10.48; P< 0.01) and organ damage accrual (OR 2.34; 1.02-5.36; P=0.04). The association between MetS and baseline organ damage remained significant in multivariable analysis (adjusted OR 3.36; 95% CI 1.32-8.59; P=0.01). Unexpectedly, glucocorticoid use was not associated with MetS or any of its five components. High serum levels of resistin were significantly negatively associated with MetS (OR 0.17; 95% CI 0.04-0.70; P=0.014); no other adipokine were associated with MetS.

Conclusion: MetS is common in SLE patients, with the most frequent components being hypertension and low-HDL. An independent association was found of MetS with baseline organ damage, and low serum resistin, but not glucocorticoid exposure or disease activity.

Disclosure: D. Apostolopoulos, None; **F. Vincent**, None; **R. Koelmeyer**, None; **A. Hoi**, None; **E. Morand**, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, 5, Merck Serono, 2, 5, Neovacs, 5, Sandoz, 5, Novartis, 8, AbbVie, 5, Amgen, 5, Biogen, 5.

Abstract Number: 1297

Lupus Antibodies in Relation to Malignancy

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic Lupus Erythematosus (SLE) a chronic inflammatory autoimmune disease that has the potential to affect every organ system. Studies have shown increased risk of certain malignancies among patients with SLE, with a potentially decreased risk of breast and prostate cancer related to anti-dsDNA antibodies (abs). This study examines the prevalence of malignancy types and relationships between clinical characteristics, autoantibody positivity and malignancy risk among patients with SLE.

Methods: Data was obtained from an ongoing longitudinal registry of patients with SLE (≥4 ACR classification criteria) and non-SLE population-matched controls. Information on demographics, medical and social history, and SLE characteristics (if applicable) was gathered from in-person interviews and medical record review. Disease damage was determined by SLICC/ACR Damage Index (SDI) with the malignancy item removed from scoring ("any damage present" if score ≥1). Children (age< 18 years) and those missing data on malignancy status were excluded from the study population. Analysis included descriptive statistics, Pearson's chi-squared testing for categorical measures and two-sample t-tests for continuous measures.

Results: A total of 750 SLE patients and 548 controls were included (Table 1). The mean age at SLE diagnosis was 31.1 years (SD ±13.8), mean age of malignancy diagnosis was 37.9 years (SD ±15.3), with mean age at last follow-up of 50.9 years (SD ±16.1). Comparing malignancy types between patients with SLE and controls, there was a higher incidence of gynecologic cancers (1.6% vs. 0.2%, p=0.01) and non-melanoma skin cancers (1.7% vs. 0.2%) among the patients. The 65 malignancies among the 54 patients with SLE are described in Table 2. The data did not show an association between BMI with either SLE or malignancy, but other clinical manifestations were associated with malignancy, as shown in Table 3. SLE patients that were lupus autoantibody negative (defined as being negative for dsDNA, SM, antiphospholipid, SSA and SSB antibodies), were statistically significantly more likely to have a malignancy history.

Conclusion: We found in this population of patients with SLE, that despite an overall increased risk of cancer, especially skin and gynecologic malignancies, compared to population-matched controls, the presence of certain SLE-associated autoantibodies decreased the likelihood of having a cancer history. These results support further studies to examine the relationship of autoantibodies, including anti-SM, anti-SSA and anti-SSB, and malignancy risk.

Table 1:

Characteristics	SLE n=750	Controls n=548	P-Value
Female (%)	92.6	91.1	0.71 (NS)
African American (%)	73.1	87.4	**<0.01**
Ever Smoker (%)	27.3	24.8	0.33 (NS)
Insured, Any (%)	93.9	93.3	0.68 (NS)
High School Graduate (%)	85.7	86.4	0.72 (NS)
Malignancy Diagnosed (%)	7.2	3.8	**0.01**

Table 1

Table 2:

Types of Malignancies in SLE Cohort	N=54
Lymphoma	4
Hematologic, not Lymphoma	2
Breast Cancer	15
Lung	2
Gynecologic	13
Prostate	1
Gastrointestinal	3
Melanoma	5
Skin	14
Other	6

Table 2

Table 3:

Characteristics	SLE Patients with Malignancy n=54	SLE Patients without Malignancy n=696	P-Value
Female (%)	92.6	91.1	0.71 (NS)
African American (%)	44.4	55.6	**<0.01**
Ever Smoked	44.4	55.5	**<0.01**
History of Cutaneous Manifestations (%)	50.0	43.6	0.76 (NS)
History of Photosensitivity (%)	51.8	38.9	0.41 (NS)
History of Alopecia (%)	37.0	40.0	0.66 (NS)
History of Lupus Nephritis (%)	31.5	53.7	**0.02**
History of Hematologic Manifestations (%)	44.4	37.0	0.71 (NS)
Non-Cancer Damage by SLICC-DI (%)	63.0	52.4	0.14 (NS)
Anti-dsDNA Positive (%)	42.6	46.7	0.17 (NS)
Anti-SM Positive (%)	3.70	15.4	**0.02**
Anti-phospholipid (%)	7.41	8.05	0.44 (NS)
Anti-SSA Positive (%)	27.3	49.8	0.14 (NS)
Anti-SSB Positive (%)	10.0	28.5	0.20 NS)
ANA Positive (%)	96.0	97.2	0.64 (NS)
Lupus Autoantibody Negative	21.9	6.21	**<0.01**

Table 3

Disclosure: S. Huse, None; **J. Oates**, None; **G. Gilkeson**, None; **D. Kamen**, None.

Abstract Number: 1298

Lupus Damage Free-Survival by Age at Diagnosis: A Retrospective Incident Lupus Cohort

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: While medical comorbidities increase with age, younger age at onset of Systemic Lupus Erythematosus (SLE) has been associated with greater risk of some types of end-organ damage. Few studies have reported damage-free survival by age at diagnosis which would be useful for prognosis discussions. Using a large single-center retrospective cohort of incident SLE patients, the objectives of this study were to estimate new damage and mortality-free median survival time and 1-, 5-, and 10-year survival probabilities and to compare damage-free survival by age at diagnosis and within organ systems.

Methods: Electronic Health Records (EHR) from a single academic health system were queried for patients with SLE diagnosis codes in 2003-2016 and at least one visit to both a rheumatology and a primary care provider to better capture damage events. Trained abstractors manually validated cases meeting either 1997 ACR or 2012 SLICC SLE criteria and recorded damage event dates, including events pre-EHR. Age at diagnosis used the earliest date of a SLE diagnosis code from a rheumatologist or date of meeting SLE criteria. Patients with less than 30 days of observation after diagnosis were excluded.

All observed events within the post-diagnosis follow-up period were compared by age group at diagnosis (< 30, 30-44, 45-59, and 60+ years). Gross damage rates were calculated using Poisson regression. Kaplan-Meier was used to estimate new damage and mortality-free median survival time and 1-, 5-, and 10-year survival probabilities by age group at diagnosis. Differences in organ-specific damage-free survival by age group at diagnosis were assessed with logrank tests on Kaplan-Meier curves.

Results: The cohort included 462 patients with incident SLE followed for a median of 6 years. There were 86 (19%) patients diagnosed before age 30, and the median diagnosis age was 45 (Table 1). Patients diagnosed before age 30 were more likely to be Asian, Black or to receive Medicaid. Of SLE damage events observed after diagnosis, the most common were neuropsychiatric (18% of events), ocular (17%), and musculoskeletal (14%). Increasing age group correlated with gross damage rate, from 10% per year risk in those < 30, to 39% per year risk in those 60+ (Table 2). Survival until first damage event after diagnosis was similar in patients diagnosed before age 30 and ages 30-44; survival decreased in older age groups. In the first year, patients younger than 30 years experienced damage rates similar to older age groups (45-59 year olds) (Figure 1). For most organ systems, survival without damage negatively correlated with age. However, cardiovascular and pulmonary damage-free survival was similar or shorter in patients diagnosed < 30 compared to those diagnosed decades later in life.

Table 1. Characteristics and Observation Time of Incident SLE Patients by Age at Diagnosis

Characteristic (n (%))		Total Cohort N= 462	Age < 30 N= 86	Age 30-44 N= 149	Age 45-59 N= 145	Age 60+ N= 82	p
Female		416 (90.0)	80 (93.0)	134 (89.9)	134 (92.4)	68 (82.9)	0.09
Race/Ethnicity	White	358 (77.7)	56 (66.8)	108 (72.5)	118 (81.4)	77 (93.9)	**<0.001**
	Black	57 (12.3)	14 (16.3)	27 (18.1)	14 (9.7)	2 (2.4)	
	Asian	20 (4.3)	8 (9.3)	6 (4.0)	5 (3.5)	1 (1.2)	
	Hispanic	19 (4.1)	2 (2.3)	8 (5.4)	7 (4.8)	2 (2.4)	
	Other	7 (1.5)	6 (7.0)	0 (0)	1 (0.7)	0 (0.0)	
Medicaid Ever		109 (23.6)	38 (44.2)	40 (26.9)	25 (17.2)	6 (7.3)	**<0.001**
ACR Criteria at Diagnosis (median, (IQR))		5 (4-6)	5 (4-7)	5 (4-6)	5 (4-6)	5 (4-5)	0.20
Observation Time in Years (median, IQR)		6.0 (3.6-9.3)	6.6 (3.8-10.1)	6.6 (3.8-9.4)	5.9 (3.2-9.5)	5.5 (2.9-7.3)	**0.03**

Table 2. Gross Damage Rates, Median Damage- and Death-Free Survival Time, and 1-, 5-, and 10-year Damage- and Death-Free Survival Probabilities by Age Group at SLE Diagnosis

	Total Cohort N= 462	Age < 30 N=86	Age 30-44 N=149	Age 45-59 N=145	Age 60+ N=82
Total Damage Events	562	60	116	206	180
Observation Time (Years) (median, IQR)	6.0 (3.6-9.3)	6.6 (3.8-10.1)	6.6 (3.8-9.4)	5.9 (3.2-9.5)	5.5 (2.9-7.3)
Gross Damage Rate (% per person-year) (mean (95%CI))	16.2 (14.7, 17.8)	9.8 (7.5, 12.6)	11.1 (9.3, 13.4)	21.8 (19.0, 25.0)	39.4 (34.0, 45.6)
Median Damage & Death-Free Survival Time (median (95%CI))	6.00 (5.30, 6.84)	11.15 (7.06, NE)	8.40 (6.33, 10.51)	4.64 (3.57, 5.79)	1.42 (0.79, 2.41)
1-year Damage & Death-Free Survival Probability (mean % ± SE)	83 ± 2	89 ± 3	93 ± 2	83 ± 3	56 ± 6
5-year Damage & Death-Free	57 ± 3	72 ± 5	70 ± 4	48 ± 5	28 ± 5
10-year Damage & Death Free	31 ± 3	55 ± 7	40 ± 6	13 ± 7	0 ± 0

NE = Not estimable based on data

Conclusion: Younger patients (< 30), who were more likely to be non-White and Medicaid beneficiaries, experienced a relatively high rate of first damage in the first year after diagnosis and similar damage rates to patients decades older within cardiovascular and pulmonary systems. Overall damage rates in SLE correlated with age at diagnosis, with a 30% per year difference in damage risk between the youngest (< 30) and oldest (>60) patients at SLE diagnosis.

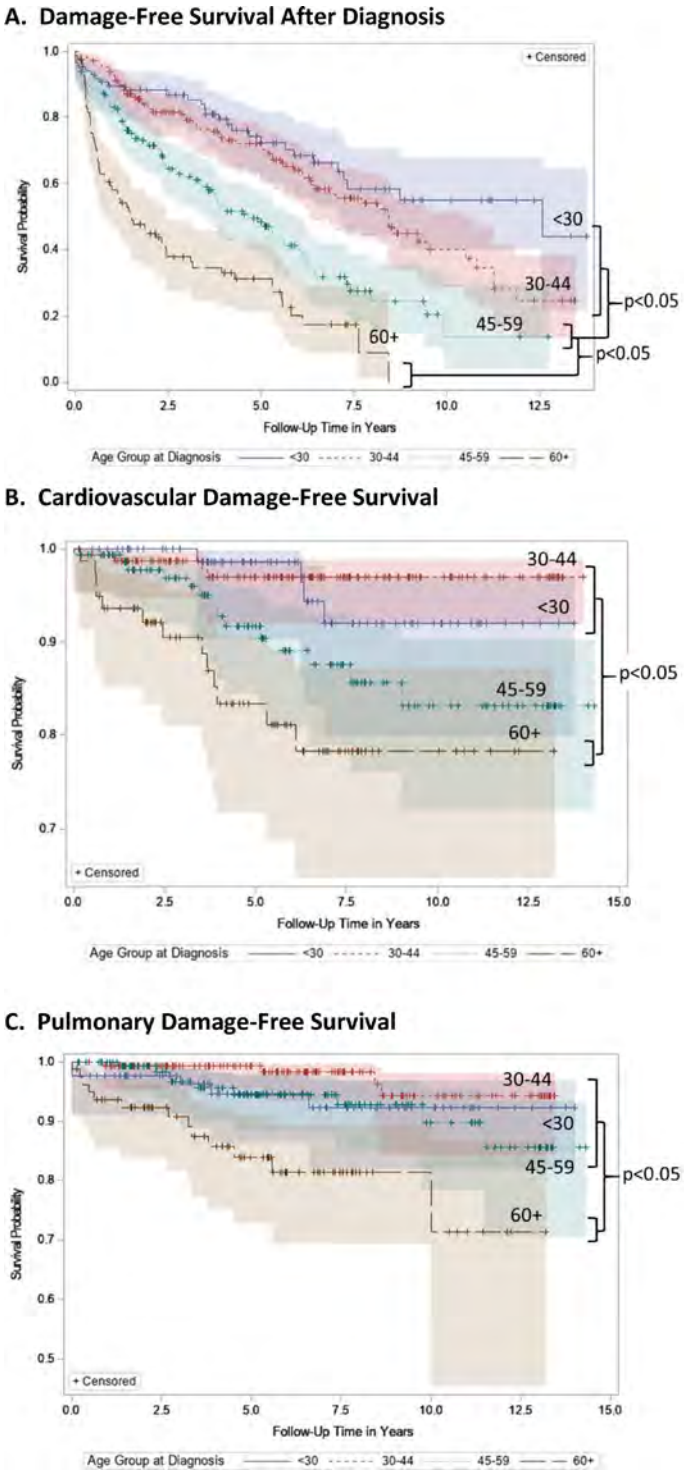

Figure 1. Damage, Cardiovascular, and Pulmonary Damage-Free Survival by Age Group at Diagnosis. Kaplan-Meier survival curves for damage after lupus diagnosis by age group at diagnosis with death as a censoring event for select organ systems. Panel A shows survival until first new damage event after diagnosis. Survival time was longer in patients diagnosed before age 45 and decreased with increasing age group. Panel B shows cardiovascular damage-free survival, which was longer for patients diagnosed before 45 compared to those after age 60. Panel C displays pulmonary damage-free survival which was shorter for patients diagnosed after age 60 than those diagnosed younger.

Disclosure: M. Schletzbaum, None; **N. Ezeh**, None; **T. McKown**, None; **S. Garg**, None; **C. Bartels**, Independent Grants for Learning and Change (Pfizer), 2.

Abstract Number: 1299

Longitudinal Patterns of Anxiety Symptomology Among Patients with Systemic Lupus Erythematosus (SLE) Remain Stable over Time and Do Not Associate with SLE Disease Activity

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Almost 40% of patients with SLE have comorbid mental health conditions.[1] Though depression is most commonly reported (24% to 30%), many SLE patients also experience some form of anxiety disorder.[2] The mechanisms underlying the association of psychiatric disorders with neuropsychiatric SLE are unclear. Moreover, the relationship between the longitudinal course of anxiety symptomology and SLE disease activity remains largely unstudied. Thus, the aims of this study are to identify patterns of anxiety symptomology over time among patients with SLE, and to assess the longitudinal relationship between anxiety symptomology and SLE disease activity.

Methods: Longitudinal data from patients with ACR or SLICC-classified SLE treated in the Washington University Lupus Clinic were analyzed. Anxiety symptomology was assessed at each visit using the validated Patient-Reported Outcomes Measurement Information System (PROMIS) Emotional Distress: Anxiety Short Form 8a. Patients with at

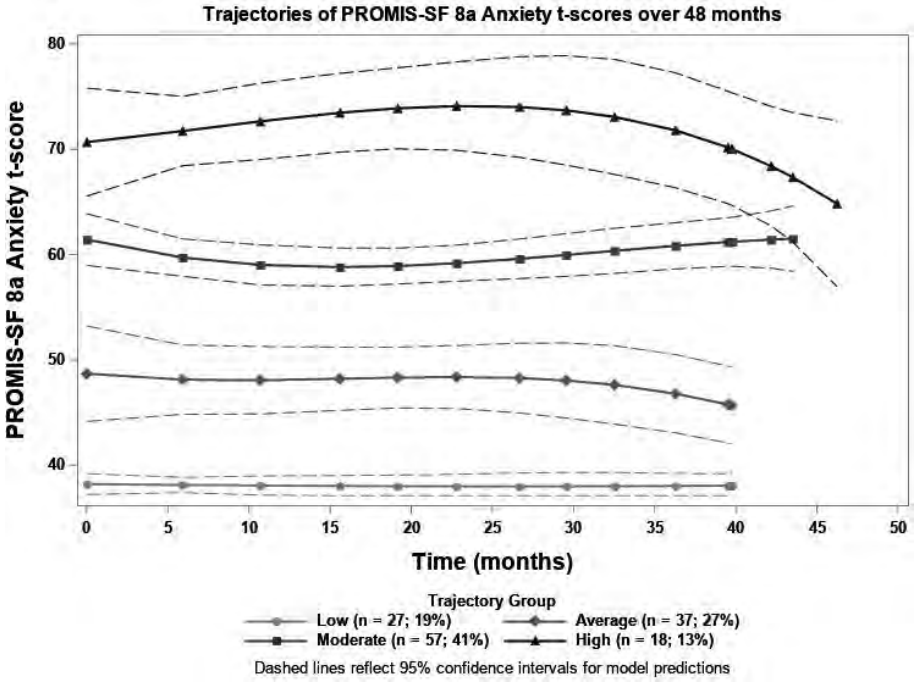

Figure 1. Identified trajectories of anxiety scores over time

Variable	Low (n=27)	Average (n=37)	Moderate (n=57)	High (n=18)	p-value
Age (SD)	37.8 (15.4)	40.2 (12.0)	41.1 (12.3)	40.9 (11.4)	0.732
Sex (% female)	24 (88.9)	34 (91.9)	53 (93.0)	15 (83.3)	0.579
Race					0.008*
White	12 (44.4)	19 (51.4)	21 (36.8)	2 (11.1)	
Black	12 (44.4)	15 (40.5)	35 (61.4)	16 (88.9)	
Other	3 (11.1)	3 (8.1)	1 (1.75)	0 (0)	
Highest Education Attainment					0.656
Unknown	5 (18.5)	10 (27.0)	17 (29.8)	7 (38.9)	
High School or GED/Below	3 (11.1)	6 (16.2)	11 (19.3)	3 (15.8)	
College/Over college	19 (70.4)	21 (56.8)	29 (50.9)	8 (44.4)	
Marital Status					0.848
Unknown	3 (11.1)	4 (10.8)	8 (14.0)	4 (22.2)	
Not married	17 (63.0)	19 (51.4)	32 (56.1)	9 (50.0)	
Married	7 (25.9)	14 (37.8)	17 (29.8)	5 (27.8)	
Employment Status					0.239
Unknown	8 (29.6)	12 (32.4)	18 (31.6)	6 (33.3)	
Employed	14 (51.9)	14 (37.8)	20 (35.1)	2 (11.1)	
Unemployed	0 (0)	2 (5.4)	4 (7.0)	1 (5.6)	
Other	5 (18.5)	9 (24.3)	15 (26.3)	9 (50.0)	

Table 1. Baseline sociodemographic characteristics of patients in each of the identified anxiety trajectory groups * Statistically significant at $p < 0.05$

least 3 PROMIS anxiety and SLEDAI2K Responder Index-50 scores obtained at the same clinic visit over 2 to 48 months were included. The PROMIS anxiety scale scores are converted to t-scores with a mean of 50, reflecting average levels of anxiety in the general adult population, with standard deviation of 10.[3] T-scores between 60-70 and above 70 reflect moderate and severe symptomology, respectively. Group-based trajectory modeling (GBTM) identified groups of patients with similar temporal trajectories of anxiety symptomology. Baseline characteristics of individuals in each anxiety trajectory group were compared using chi-square tests, Fisher's exact tests, or ANOVA. The relationship between disease activity and anxiety over time was assessed using multilevel linear regression models.

Results: 139 patients had at least 3 PROMIS anxiety scores over an average of 30.9 months (SD: 13.0; range: 2.6-48). Mean patient age was 40.2 (SD: 12.7; range: 19-74), 90.1% were female and 56.1% African American. GBTM identified 4 unique temporal trajectories of anxiety symptomology (Figure 1), labeled: low (LA), average (AA), moderate (MA), and high anxiety (HA). Of note, 88.9% of individuals classified in the HA group were African-American, compared to only 44.4% of individuals in the LA group (Table 1). SLEDAI score was not significantly associated with anxiety levels longitudinally (β=0.07, p=0.3).

Conclusion: Anxiety symptomology over time remained relatively stable in this patient cohort. More than 50% of patients experienced persistent moderate or severe anxiety symptomology, and a higher proportion of African-American patients demonstrated moderate or severe anxiety. SLE disease activity was not significantly associated with anxiety symptomology over time. These findings emphasize the importance of better understanding psychosocial factors that contribute to the persistence of anxiety symptomology. Patients with SLE should be regularly screened for mental health conditions and provided access to appropriate mental health resources.

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3 Pilkonis PA, et al. Assessment. 2011;18(3):263-283.

Disclosure: D. Lew, None; **X. Huang**, None; **S. Kellahan**, None; **H. Xian**, None; **S. Eisen**, None; **A. Kim**, Exagen Diagnostics, Inc., 5, 8, GlaxoSmithKline, 2, 5, 8, Alexion Pharmaceuticals, 5, Annexon Biosciences, 5, JPMorgan Chase & Co., 5.

Abstract Number: 1300

Identifying Cognitive Impairment in Patients with Systemic Lupus Erythematosus Using Hidden Markov Models: A Bayesian Approach

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Cognitive impairment (CI) is usually operationalized on the American College of Rheumatology Neuropsychological Battery (ACR-NB) as a z-score of ≤-1.5 on ≥2 domains or z ≤-2 on ≥1 domain.

Given that this binary classification may miss participants who have CI but score just below the cut-off, we explored using continuous z-scores, instead of the binary approach of the ACR-NB, to facilitate the interpretability of the results. This framework is developed based on Hidden Markov Models (HMMs) and on existing data over time.

Methods: 301 consecutive consenting SLE patients aged 18-65 years attending a single center were assessed for CI at baseline using the ACR-NB and 187 patients completed visits at 6 and 12 months.

ACR-NB includes 19 tests and 6 cognitive domains. Age and gender matched normative data were used to obtain z-scores.

The **1st step** of our approach reduces the high-dimensional aspect of the ACR-NB tests using principal component analysis (PCA) to create a single component score which explains the most variance (1st dimension). The **2nd step** builds a 2-state cognitive status based on a discrete-time HMM with the dimensionality reduction gained in the first step. The HMM assumes that the change of the component score over time in patients with SLE can be segmented into 2 distinct cognitive states, where each state captures if a patient is CI or not at time t, using the component score obtained at each time point. We assumed that the component score is Normal with unknown mean and variance, and the mean and variance are different between the two hidden states (CI or non-CI). Additionally, we specified that the mean of the Normal outcome depends linearly on education level; this adjustment means that the hidden states will capture the unobserved heterogeneity not explained after controlling by education level. All the statistical analysis was done from a Bayesian perspective using Stan through R which implements the Hamiltonian Markov Chain Monte Carlo method.

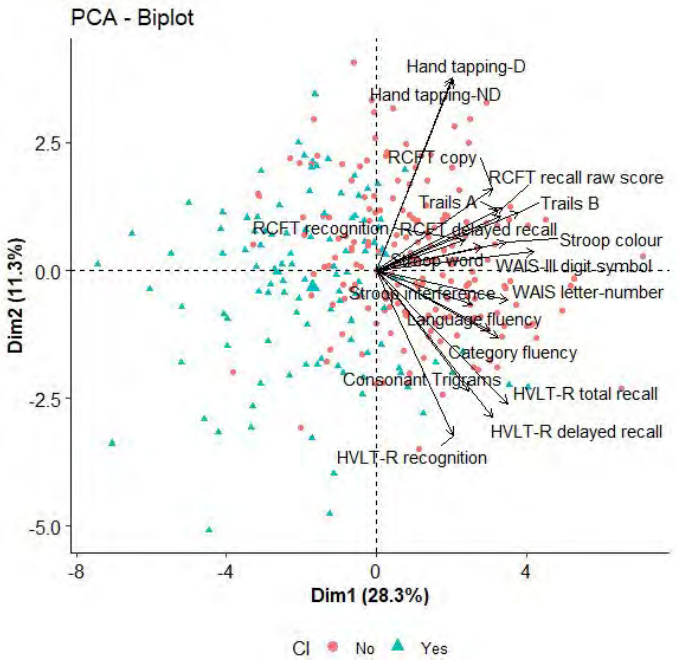

Figure 1. Biplot at baseline. PCA where patients' component scores are colored by ACR-NB CI binary definition (turquoise for CI and orange for non-CI). The 1st dimension separates patients into CI and non-CI at baseline. Axis x represents the first dimension (explaining 28.3% of the variance) and axis y represents the second dimension. The length of each arrow represents the strength of the relationship between the ACR-NB subtests, and the cognitive components found in our PCA. The angle between variables represents the strength of the correlation between them. The ACR-NB included the following domains: Manual motor speed and dexterity, simple attention and processing speed, visual-spatial construction, verbal fluency, learning and memory, executive function.

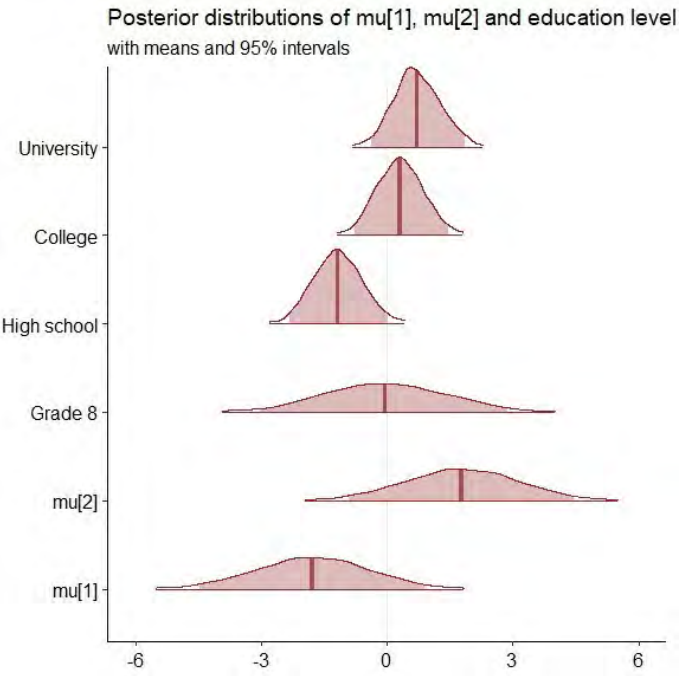

Figure 2. Posterior estimates from the HMM. X axis represents the distribution of the parameters of interest. Y axis represents the parameters where inference is made. The dark shaded region represents the point estimate from a frequentist point of view and the light shaded region represents the 95% uncertainty interval, i.e., with 95% of probability the estimate would lie in that region. As an example mu[1] represents the inference made on the unknown mean of the observed component score given that it comes from the CI state after adjusting for education level. The point estimate is -1.78 with 95 % CrI (-4.47, 0.91).

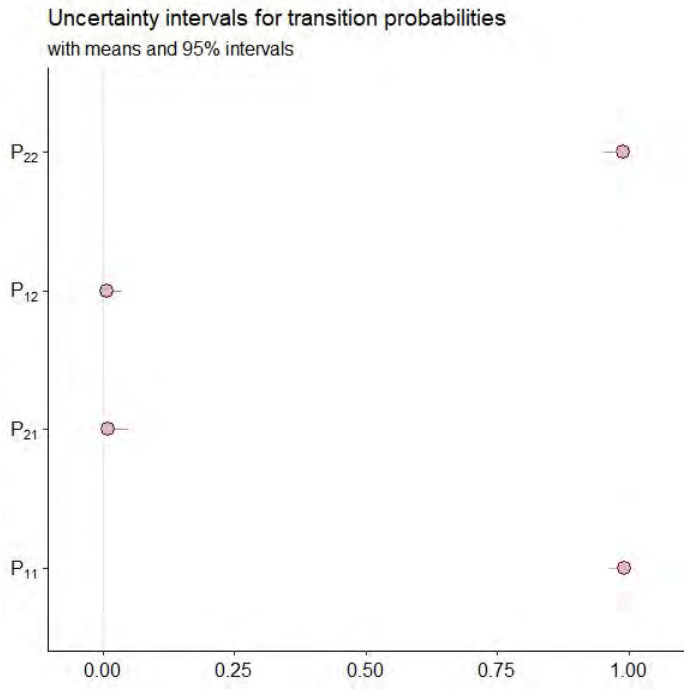

Figure 3. Posterior uncertainty intervals for the transition probabilities in the HMM. X axis represents the transition probability and Y axis represents the parameters where inference is made. We labeled '1' as the CI state and '2' as the non-CI. Therefore, over discrete time points, P11 is the probability of remaining in the CI state, P12 is the probability of moving from the CI state to non-CI state and so on (P21 and P22). The dot on the graph represents the point estimate and the line represents the 95% CrI.

Results: Of 301 patients, 89.0% were women, mean age 40.9 ± 12.1 and mean disease duration 14 ± 10.1 years at study entry. Figure 1 shows the results of the PCA; at baseline, 1st dimension separates patients into CI and non-CI and 2nd dimension was mainly explained by measures of simple information processing or motor speed.

From the HMM analysis, the estimated mean for the CI state was -1.78 (95% Credible Interval [CrI]: -4.47, 0.91) and 1.78 (95% CrI: -0.92, 4.46) for the non-CI state. A patient will be classified as CI if their observed component score lies on the area of mu[1] (Fig. 2) and as non-CI if it lies on the area of mu[2].

We found higher education level associates with an increase mean component score (implies less CI). We also found that patients did not transition between CI and non-CI over time (Fig. 3).

Conclusion: This is the first framework which aimed to classify patients with SLE as CI or not using an unsupervised method. This approach relies on the observed z-scores from the 19 tests on the ACR-NB and not on the binary classification. We found that the probability of changing between CI and non-CI over 1 year is low.

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Abstract Number: 1301

Characterizing How SLE Patients Access Health Information Pre and During COVID-19

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The spread of misinformation related to COVID-19 has been especially acute for SLE patients as unsubstantiated claims regarding the efficacy of antimalarials for COVID-19 first jeopardized drug supplies, and then misinformation regarding toxicity provoked abrupt discontinuation. Conflicting health messages based on unfounded information can contribute to detrimental health decisions, exacerbate stress, and precipitate SLE flares. In attempt to mitigate the adverse consequences of accessing, spreading, and acting on misinformation, we assessed how SLE patients access health information pre and during COVID-19.

Methods: SLE patients fulfilling the ACR or Systemic Lupus International Collaborating Clinics (SLICC) Classification Criteria for SLE from a patient cohort in Alberta, Canada completed an online survey in June 2020 regarding the sources of health information they accessed in the 12 months preceding (pre March 11, 2020) and during the COVID-19 (post March 11, 2020) pandemic. Descriptive statistics were used to calculate the percentage of patients accessing each source of information, their preferred sources, and the level of trust in each source. McNemar tests were used to compare frequencies preceding and during the pandemic.

Table 1: Health Information Source Frequency of Access Pre and Post March 11, 2020

	Health Information Source Accessed [a]		
	Pre 11/03/20	Post 11/03/20	95% CI for Difference
Family Physicians	72.6%	52.8%	-19.8% (-30.3%, -9.3%)
Lupus Specialists (e.g., rheumatologists, nephrologists, hematologists, dermatologists)	66%	48.1%	-17.9% (-27.5%, -8.4)
Pharmacists	57.5%	46.2%	-11.3% (-21.4%, -1.2%)
Alternative Care Providers (e.g., chiropractor, naturopath)	28.3%	14.2%	-14.2% (-21.7%, -6.6%)
Peers (e.g., family, friends, colleagues)	36.8%	36.8%	0.0% (-10.7%, 10.7%)
Advocacy Organizations (e.g., provincial/national lupus organization)	18.9%	20.8%	1.9% (-5.5%, 9.2%)
News Media (e.g., newspaper, online news, radio, television)	38.7%	56.6%	17.9% (7.3%, 28.6%)
Social Media (e.g., Facebook, Instagram, Internet blogs, Twitter)	34%	38.7%	4.7% (-3.8%, 13.2%)

[a] *Respondents who reported health information source access sometimes/often/always*

Table 2: Preferred Health Information Sources Pre and Post March 11, 2020

	Overall Rank	
	Pre 11/03/20	Post 11/03/20
Lupus Specialists	1	1
Family Physicians	2	2
Pharmacists	3	4
Advocacy Organizations	4	6
Peers	5	7
Alternative Care Providers	6	8
News Media	7	3
Social Media	8	5

Table 3: Trustworthiness of Health Information Source Pre and Post March 11, 2020

	Trust in Source [a]		
	Pre 11/03/20	Post 11/03/20	95% CI for Difference
Family Physician	86.8%	80.2%	-6.6% (-14.6%, 1.4%)
Lupus Specialists	90.6%	86.8%	-3.8% (-9.9%, 2.4%)
Pharmacists	77.4%	72.6%	-4.7% (-11.7%, 2.3%)
Alternative Care Providers	36.8%	27.4%	-9.4% (-17.1%, -1.8%)
Peers	24.5%	27.4%	2.8% (-4.8%, 10.4%)
Advocacy Organizations	50.9%	45.3%	-5.7% (-12.4%, 1.0%)
Newspaper	27.4%	23.6%	-3.8% (-11.1%, 3.5%)
Online news media	35.9%	38.7%	2.8% (-4.8%, 10.4%)
Radio	31.1%	29.3%	-1.9% (-7.3%, 3.6%)
Television	38.7%	42.5%	3.8% (-2.4%, 9.9%)
Facebook	10.4%	10.4%	0.0% (-3.6%, 3.6%)
Instagram	5.7%	7.6%	1.9% (-2.7%, 6.5%)
Internet blog	9.4%	7.6%	-1.9% (-7.3%, 3.6%)
LinkedIn	5.7%	5.7%	0.0% (-0.9%, 0.9%)
Pinterest	2.8%	3.8%	0.9% (-1.8%, 3.7%)
Reddit	1.9%	1.9%	0.0% (-0.9%, 0.9%)
TikTok	2.8%	2.8%	0.0% (-0.9%, 0.9%)
Twitter	5.7%	5.7%	0.0% (-3.6%, 3.6%)
YouTube	10.4%	8.5%	-1.9% (-5.4%, 1.6%)
[a] Respondents who reported source as somewhat/very trustworthy			

Results: 106 of 248 patients completed the survey (43% response rate); 91.5% were female, 71.7% Caucasian, and the mean age at diagnosis was 35.9 years (SD 14.0) and mean disease duration was 16.6 years (SD 12.8). 73.6% had completed some form of post-secondary education, and 83% reported taking antimalarials in the past 12 months. No participants reported a doctor diagnosis of COVID-19. Patients accessed news media more frequently during the pandemic (38.7% accessed sometimes/often/always pre vs 56.6% post), while access to family physicians, SLE specialists, pharmacists and alternative care providers decreased during the pandemic (Table 1). Lupus specialists and family physicians were ranked the most preferred (Table 2) and considered the most trustworthy sources (Table 3) pre and during the pandemic. News and social media were ranked more highly as preferred sources post vs pre March 11 (Table 2), but were considered much less trustworthy than physicians (86.8% rated lupus specialists as somewhat/very trustworthy post vs 38.7% for online news media).

Conclusion: Although SLE specialists and family physicians are ranked as the most preferred and trustworthy sources of health information, patients accessed these sources less frequently during the pandemic and accessed news media, a less preferred source, more frequently. This study is currently being expanded to include additional Canadi-

an and international centers to further investigate the sociodemographic and geographic factors influencing access to and use of health information. This research will improve existing information dissemination pathways valued by SLE patients and enhance public health response during the pandemic and beyond.

Disclosure: F. Cardwell, None; **S. Elliott**, None; **M. Choi**, None; **R. Chin**, None; **A. Clarke**, AstraZenca, 5, Exagen Diagnostics, 5.

Abstract Number: 1302

Exploration of Machine Learning Methods in Predicting Systemic Lupus Erythematosus Hospitalizations

April Jorge[1], Zhiyao Wu[2], Tashrif Chowdhury[2] and Yijun Zhao[2], [1]Massachusetts General Hospital, Boston, MA, [2]Fordham University, Computer and Information Sciences Department, New York, NY

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster II: Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Characteristics	Overall	Cluster 1	Cluster 2	Cluster 3	Cluster 4
Number of patients	1996	1104	160	407	325
Hospitalized for SLE in last year of follow-up, n (%)	92 (7.7)	33 (3.0)	15 (9.4)	21 (5.2)	23 (7.1)
Age, mean (SD)	52 (15)	55 (15)	43 (13)	50 (15)	50 (15)
Female, n (%)	1818 (91.1)	1015 (91.9)	146 (91.3)	365 (89.7)	293 (90.2)
Race/Ethnicity, n (%)					
White	1,343 (67.3)	849 (76.9)	61 (38.1)	256 (62.9)	177 (54.5)
Black	267 (13.4)	97 (8.8)	48 (30.0)	63 (15.5)	59 (18.2)
Asian	101 (5.1)	21 (1.9)	21 (13.1)	31 (7.6)	28 (8.6)
Hispanic	131 (6.6)	55 (5.0)	17 (10.6)	23 (5.7)	36 (11.1)
Medication use*, n (%)					
Hydroxychloroquine	1960 (98.2)	1084 (98.2)	159 (99.4)	398 (97.8)	319 (98.2)
Oral corticosteroids	1381 (69.2)	717 (65.0)	141 (88.1)	312 (76.7)	211 (64.9)
Oral immunosuppressant	1,024 (51.3)	441 (40.0)	140 (87.5)	292 (71.7)	151 (46.5)
SLE manifestations, n (%)					
Acute lupus rash	702 (35.2)	314 (28.4)	101 (63.1)	149 (36.6)	138 (42.5)
Lupus nephritis	396 (19.8)	123 (11.0)	78 (48.8)	131 (32.2)	64 (19.7)
SLE serologies, % of the time positive, mean					
dsDNA ab	33	12	54	91	22
SS-A ab	35	16	54	36	96
SS-B ab	15	7	22	9	47
Smith ab	13	5	90	12	6
RNP ab	27	17	94	32	23
B2 glycoprotein 1 ab, IgG	2	1	2	3	1
B2 glycoprotein 1 ab, IgM	1	1	3	1	0

*Prior to last year of follow-up

Table 1. Characteristics of Systemic Lupus Erythematosus Patients Overall and by Serologic Clusters

SLE Patient Subset	Method	Class 1 Acc.	Class 0 Acc.	Overall	class 1_F1	class 0 _F1	AUC
All Data	DT	0.79	0.59	0.60	0.15	0.74	0.74
	RF	0.79	0.61	0.62	0.16	0.75	0.75
	LR	0.67	0.62	0.62	0.14	0.75	0.70
	SVM	0.78	0.59	0.59	0.15	0.73	0.72
Cluster 1	DT	0.78	0.66	0.67	0.12	0.79	0.79
	RF	0.87	0.59	0.60	0.11	0.74	0.81
	LR	0.75	0.64	0.65	0.11	0.78	0.77
	SVM	0.84	0.53	0.53	0.10	0.69	0.77
Cluster 2	DT	0.51	0.76	0.74	0.27	0.84	0.65
	RF	0.49	0.85	0.81	0.33	0.89	0.68
	LR	0.36	0.74	0.70	0.18	0.82	0.55
	SVM	0.04	0.98	0.89	0.07	0.94	0.51
Cluster 3	DT	0.54	0.61	0.61	0.12	0.75	0.57
	RF	0.60	0.56	0.57	0.13	0.71	0.58
	LR	0.62	0.64	0.63	0.15	0.77	0.63
	SVM	0.56	0.62	0.62	0.13	0.75	0.59
Cluster 4	DT	0.54	0.61	0.61	0.16	0.74	0.59
	RF	0.64	0.66	0.66	0.21	0.78	0.65
	LR	0.67	0.65	0.65	0.21	0.77	0.67
	SVM	0.75	0.68	0.69	0.26	0.80	0.73

DT, Decision Tree; RF, Random Forest; LR, Logistic Regression; SVM, Support Vector Machines

Table 2. Performance Characteristics of Four Machine Learning Models in Predicting Hospitalization for Systemic Lupus Erythematosus, Overall and by Cluster

Background/Purpose: Systemic lupus erythematosus (SLE) is a heterogeneous disease associated with increased morbidity and mortality, and severe SLE flares can lead to hospitalizations. Our objective was to apply machine learning methods to predict hospitalizations for SLE from electronic health record (EHR) data.

Methods: We identified 1,996 patients with SLE in a longitudinal academic medical center EHR-based cohort since 2016. Patients were identified with a previously validated SLE phenotype algorithm (PPV 92%) (Jorge A et al. *Semin Arthritis Rheum* 2019). K-means cluster analysis was used to identify groups of SLE patients with similar autoantibody patterns (dsDNA, SSA, SSB, Smith, RNP, and B2 glycoprotein 1 antibodies). The outcome of interest was hospitalization with a discharge diagnosis code of SLE (ICD10 M32, excluding M32.0, or ICD9 710.0) in the most recent year of follow up. We applied multiple machine learning methods to predict hospitalizations for SLE, including decision tree, random forest, logistic regression, and support vector machines. Candidate predictors were derived from coded EHR features and included demographics, laboratory tests, medications, ICD-9/10 codes for SLE manifestations (e.g., nephritis, acute lupus rash, and pericarditis), and healthcare utilization including specialist visits. We applied these methods to the overall SLE cohort and within clusters. The performance of each model was evaluated by sensitivity, specificity, accuracy, the F statistic, and the area under the receiver operator curve (AUC).

Results: Four distinct autoantibody clusters were identified (**Table 1**). SLE patients were 91% female, with mean age 52 years. Overall, 7.7% of patients were hospitalized for SLE in the last year of follow-up. Race/ethnicity and SLE manifestations varied among the clusters as did the proportion of patients with hospitalizations for SLE. Model performance was greatest within cluster 1, the largest cluster (**Table 2**). The most common predictors of SLE hospitalizations overall from the various machine learning methods included age, hemoglobin/hematocrit, ESR, and albumin. Top 5 predictors for SLE hospitalizations varied among clusters of SLE patients (**Table 3**).

SLE Patient Subset	Rank	Decision Tree	Random Forest	Logistic Regression	Support Vector Machines
All data	1	albumin	albumin	age	hemoglobin
	2	hemoglobin	hematocrit	hemoglobin	hematocrit
	3	ESR	ESR	# outpatient clinics*	# outpatient clinics*
	4	dsDNA Ab(binary)	hemoglobin	AST	ESR
	5	age	age	creatinine	age
Cluster 1	1	albumin	albumin	venous thrombosis	albumin
	2	ESR	hematocrit	Albumin	hemoglobin
	3	hemoglobin	ESR	hemoglobin	hematocrit
	4	hematocrit	hemoglobin	hematocrit	ESR
	5	ALT	CRP (mg/L)	ESR	venous thrombosis
Cluster 2	1	hemoglobin	hematocrit	hemoglobin	hemoglobin
	2	hematocrit	hemoglobin	white race	venous thrombosis
	3	CRP (mg/L)	albumin	venous thrombosis	hematocrit
	4	albumin	CRP (mg/L)	chloroquine	white race
	5	ALT	ALT	hematocrit	RBC - UA - 0
Cluster 3	1	SS-A(Ro) Ab(combined)	SS-A(Ro) Ab(combined)	SS-A(Ro) Ab(combined)	SS-A(Ro) Ab(combined)
	2	C4	C4	dsDNA Ab(binary)	C4
	3	C3	age	No urine protein	C3
	4	Rheumatology visits	hematocrit	hematocrit	dsDNA Ab(binary)
	5	age	hemoglobin	Asian race	age
Cluster 4	1	albumin	albumin	age	2+urine protein
	2	creatinine, random urine	# outpatient clinics*	azathioprine	3+ urine protein
	3	WBC	CRP (mg/L)	Protein - UA - 2	2+ urine blood
	4	RNP Ab	creatinine, random urine	methotrexate	RNP Ab
	5	C4	ALT	acute lupus rash	Urine RBCs

*Number of outpatient clinics in addition to 'Rheumatology', 'Nephrology', 'Dermatology' visits

Table 3. Comparison of Top Five Predictive Features of Four Machine Learning Models

Conclusion: We have demonstrated that machine learning methods can be used to predict SLE hospitalizations and to identify predictors of these events. Future work will incorporate natural language processing of narrative text to capture additional predictors of SLE hospitalizations.

Disclosure: A. Jorge, None; **Z. Wu**, None; **T. Chowdhury**, None; **Y. Zhao**, None.

Abstract Number: 1303

Performance of Three Referral Algorithms for Diagnosing Axial Spondyloarthritis: Results from the Screening in Axial Spondyloarthritis for Psoriasis, Iritis, and Colitis Cohort

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients presenting with back pain and psoriasis, acute anterior uveitis (AAU), or inflammatory bowel disease (IBD), represent a high-risk population for the presence of axial spondyloarthritis (axSpA) but may remain undiagnosed for many years. Several referral strategies have been proposed aiming at pre-selecting patients with a high probability of having axSpA among the common condition of non-specific back pain in primary care. The Berlin criteria include inflammatory back pain (IBP), B27 and sacroiliitis by imaging. The ASAS modification excludes IBP as a mandatory entry item. The Dublin Evaluation Tool (DUET) restricted to AAU is based on joint pain, B27 and cutaneous psoriasis, but not on IBP. Validation of these algorithms in inception cohorts is limited.

We aimed to: (1) compare the performance of referral algorithms in an inception cohort of patients with extra-articular manifestations presenting to a rheumatologist with undiagnosed back pain, when tested against the final local rheumatologist; (2) determine whether different IBP criteria impact the performance of the algorithms.

Methods: The multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study at 11 sites is aimed at early detection of axial SpA in consecutive patients presenting with undiagnosed back pain to the rheumatologist. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, AAU, or IBD undergo routine clinical evaluation by a rheumatologist for axSpA. The rheumatologist determines the presence or absence of axSpA at 3 consecutive stages: 1. After the clinical evaluation; 2. After the results of labs (B27, CRP) and radiography; 3. After the results of MRI evaluation. Final diagnosis by the rheumatologist was used as external standard to test the performance of the algorithms. We tested the following criteria for IBP in the algorithm: ASAS, Berlin, rheumatologist global for likelihood of IBP >5 (0-10 scale), and DUET in AAU.

Results: 246 patients were recruited, 73 presented with AAU, 46 with psoriasis, and 127 with IBD. 47.6% were diagnosed with axSpA (68.5% B27-positive). The diagnosis of axSpA was established in 45.7%, 61.6%, and 40.2% of patients with psoriasis, AAU, and IBD, respectively. The performance of the ASAS-modification of the Berlin algorithm was superior to the original algorithm as reported previously[3], primarily for enhanced sensitivity, and this was observed irrespective of the IBP criteria (Table 1). Conversely, the DUET algorithm in the subset of patients with AAU performed worse than previously reported[1].

Algorithm	Sensitivity (%)	Specificity (%)	Correct diagnosis (%)	False negative (%)	False positive (%)
Original Berlin (ASAS criteria for IBP)	65.3	76.6	71.1	16.7	12.2
Original Berlin (Berlin criteria for IBP)	64.4	76.6	70.7	17.1	12.2
Original Berlin (IBP global >5)	67.8	78.1	73.2	15.4	11.4
ASAS Modification 2 of Berlin algorithm (ASAS criteria for IBP)	73.7	75.8	74.8	12.6	12.6
ASAS Modification 2 of Berlin algorithm (Berlin criteria for IBP)	73.7	75.0	74.4	12.6	13.0
ASAS Modification 2 of Berlin algorithm (IBP global >5)	76.3	77.3	76.8	11.4	11.8
DUET	84.4	50.0	71.2	9.6	19.2

Conclusion: The ASAS modification of the Berlin algorithm showed the optimal balance between sensitivity and specificity and represented the preferred referral strategy for patients presenting with undiagnosed back pain and extra-articular features.

1. Haroon M et al. Ann Rheum Dis 2015;74:1990
2. Poddubnyy D et al. J Rheumatol 2011;38: 452
3. Van den Berg R et al. Ann Rheum Dis 2013;72:1646

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Abstract Number: 1304

Uveitis Occurrence in Early Inflammatory Back Pain: Five Years Data from a Prospective French Nationwide Cohort

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Uveitis is the most frequent extra rheumatological manifestation in axial Spondyloarthritis (SpA). DESIR is a prospective multicenter cohort of patients with early inflammatory back pain suggestive of SpA.

We reported previously a 8.5% baseline prevalence of uveitis for the patients included in the cohort; this history of uveitis at the first visit of the cohort was associated with inflammatory bowel disease (IBD) and preceding infection (1).

The aim of the study was to evaluate the prevalence and incidence of uveitis over the first five years of prospective follow-up of the cohort, and to evaluate its associated factors.

Methods: DESIR is a prospective observational cohort of patients with recent onset inflammatory back pain (more than 3 months, less than 3 years), suggestive of axial SpA, All available factors in the database were compared between patients with and without uveitis at 5 years, by uni and then multivariate analysis. Baseline factors associated with new cases of uveitis occurrence over the 5 years were also analyzed. Significance: p less than 0.05.

Results: After 5 years, 91 patients (out of 480 with complete follow-up) had at least one uveitis episode, giving an estimated prevalence of 18.9% [95%CI : 15.4-22.4]. In multivariate analysis, uveitis was associated with dactylitis (OR 2.92 [2.06 – 4.14] ; p=0.002**), ESR > 7mm (median value) (OR 2.19 [1.57 – 3.06] ; p=0.018*).

New incident uveitis occurred in 31 cases over 5 years, giving an estimated incidence rate of 1.29 / 100 patient-years [0.84 – 1.74]. New incidence of uveitis was associated in multivariate analysis with the following baseline factors: diagnosis of SpA (OR 9.65 [3.21 – 28.96] ; p=0.039*), total sacro iliac MRI inflammatory SPARCC score (central reading) over median (OR 3.98 [2.26 – 7] ; p=0.015*), dactylitis (OR 4.7 [2.65 – 8.36] ; p=0.007**), syndesmophyte score over median (central reading) (OR 0.22 [0.1 – 0.45] ; p=0.039*).

No significant association was found with HLA-B27, cs or b DMARDs, BASDAI, ASDAS, BASFI.

Conclusion: Five-years data of the DESIR cohort allowed an estimation of incidence rate of uveitis of 1.3/100p-y; over five years, uveitis was associated with dactylitis, biologic and sacro iliac MRI inflammation.

(1) Wendling D, et al. Arthritis Care Res (Hoboken). 2012 Jul;64(7):1089-93.

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Abstract Number: 1305

Is the Occurrence of Acute Anterior Uveitis Linked Primarily to Ankylosing Spondylitis (AS) or to HLA-B27? Results of a 35-Year Follow-Up Family Study of a Swiss Cohort of Patients with AS

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Background/Purpose: Approximately 30% of HLA-B27(+) patients with ankylosing spondylitis (AS) have one or more episodes of acute anterior uveitis (AAU), a condition that is also seen in HLA-B27(+) individuals without AS. We sought to investigate whether the occurrence of AAU is linked primarily to AS rather than to HLA-B27 allele.

Methods: In 1985 members of the Swiss AS Patient Society who had been diagnosed as having AS by their own physicians, as well as their first degree relatives, were invited to participate in the current study. After obtaining ethical approval and informed consent, 1178 subjects, 363 of them probands, formed our study cohort. They completed questionnaires on disease manifestations, underwent rheumatological examination of axial and peripheral joints, and provided blood samples for genetic studies, including HLA-B27. Probands also provided a recent pelvic radiograph to document presence of sacroiliitis. If their pelvic radiograph was not available, it was performed on-site. Relatives aged ≥18 years underwent pelvic radiography, unless pregnant. Pelvic radiographs were available for 360 probands and 713 relatives. Radiographs were blindly assessed twice by each of 4 readers. The assessment could only be performed once for 164 (46%) of the 360 radiographs of the probands (only available a few hours). The sacroiliitis score for each sacroiliac (SI) joint ranged from 0 (normal) to 4 (ankylosis). Scores were added and then divided by the number of assessments. Scores below bilateral grade 2.0 or grade 3.0 unilaterally were considered not meeting New York (NY) radiographic criteria.

Table. Prevalence of eye symptoms that together suggest acute anterior uveitis (AAU) among HLA-B27 positive probands with ankylosing spondylitis (AS) and their healthy HLA-B27 positive and HLA-B27 negative relatives

Questionnaire item	AS Probands HLA-B27 positive number positive/total (percentage)	Relatives HLA-B27 positive Number positive/total (percentage)	Relatives HLA-B27 negative number positive/total (percentage)	HLA-B27 positive AS Probands *<versus>* HLA-B27 negative Relatives LR+ LR- *(p-value)*	HLA-B27 positive Relatives *<versus>* HLA-B27 negative Relatives LR+ LR- *(p-value)*
Have you *ever* had a painful, red inflamed eye?	49/83 (59.0%)	40/111 (36.0%)	43/129 (33.3%)	1.77 1.63 *(0.00023)*	1.08 1.04 *(0.66)*
If so, how many eyes were affected at the same time?					
• one eye?	30/85 (35.3%)	30/110 (27.3%)	29/130 (22.3%)	1.58 1.20 *(0.03694)*	1.22 1.07 *(0.37)*
• both eyes	20/85 (23.5%)	10/110 (9.1%)	16/130 (12.3%)	1.91 1.15 *(0.03119)*	0.74 0.96 *(0.424)*
Did you have any such eye inflammation more than once?	42/84 (50.0%)	22/111 (19.8%)	24/129 (18.6%)	2.69 1.63 *(0.00000)*	1.07 1.02 *(0.81)*

In 2018 the ethical committee of the Swiss Kanton of Bern approved the follow up study. Many Swiss city and village administrations provided current addresses of former participants and reported the year of death of 182 deceased persons, including 123 AS probands. A total of 462 consenting participants completed a 157 item postal disease related questionnaire that included questions addressing AAU-related symptoms (Table 1). We compared the responses (to our questions suggestive of AAU) by the 85 HLA-B27(+) AS patients meeting the NY radiographic criteria for sacroiliitis with those of the 130 unaffected ("healthy") HLA-B27(-) relatives, and also the responses of the 111 unaffected ("healthy") HLA-B27(+) relatives with those of the 130 HLA-B27(-) "healthy" relatives. Scores were compared by chi-square testing and likelihood ratio analysis.

Results: Eye symptoms that suggested previous occurrence(s) of AAU episode(s) were reported significantly more often by the 85 HLA-B27(+) AS patients fulfilling the NY radiographic criteria than by the 130 HLA-B27(-) relatives (of the HLA-B27(+) AS probands) (Table). Interestingly, we found no differences in responses suggestive of AAU episodes between HLA-B27(+) and HLA-B27(-) relatives.

Conclusion: It should be noted that our questionnaire has not yet been validated. However, although one cannot exclude selection or detection bias (for AS patients), the results support the view that HLA-B27(+) AAU is more closely related to the disease AS/axSpA than to the HLA-B27 allele itself.

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Abstract Number: 1306

High Prevalence of Previously Undiagnosed Axial Spondyloarthritis in Patients Referred with Anterior Uveitis and Chronic Back Pain

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: To reduce the diagnostic delay in axial spondyloarthritis (axSpA), Rheumatology and Ophthalmology guidelines recommend to refer patients with acute anterior uveitis (AAU) and chronic back pain (CBP) to a rheumatologist. The impact of these recommendations in daily practice, has not yet been described. This study evaluated the prevalence of previously unrecognized axSpA in AAU patients with CBP, referred by ophthalmologists following a short instructional course to increase awareness. Secondary aims were to evaluate the timing of onset of AAU and CBP, and gender differences.

Methods: This cross sectional study included AAU patients referred with CBP (≥3 months, started < 45 years of age), from five Ophthalmology clinics. Patients with a previously diagnosed rheumatic disease, or an established other cause of AAU, were excluded. All patients underwent thorough rheumatologic evaluation, including assessment of ASAS inflammatory back pain (IBP), ASAS SpA features, laboratory examination and pelvis radiography (evaluated

Table 1. Patient characteristics at referral, subdivided for the clinical diagnoses.

	Overall	Clinical diagnosis			
		Definite axSpA	Possible axSpA	No axSpA	*Differences between groups p-value**
	(n=81)	(n=19)	(n=33)	(n=29)	
Age, median	41 (33-48)	34 (28-51)	37 (30-48)	42 (39-52)	*0.09*
Gender, men	42 (52)	14 (74)	16 (49)	12 (41)	*0.09*
Ethnicity[1], Caucasian	58 (72)	14 (79)	23 (70)	20 (70)	*0.23*
Body mass index, median	25 (22-28)	24 (21-26)	25 (24-30)	25 (22-28)	*0.51*
Fulfilling ASAS classification criteria[2]	46 (57)	19 (100)	18 (55)	9 (31)	
Radiographic axSpA (ASAS)	11 (24)	10 (53)	1 (3)	0 (0)	
Non-radiographic axSpA (ASAS)	35 (76)	9 (47)	17 (52)	9 (31)	
Anterior uveitis, >1 flare in total	47 (58)	13 (68)	18 (55)	16 (55)	*0.58*
Years since first AAU, median	4 (2-9)	5 (3-21)	5 (2-10)	2 (0-6)	
Number of previous flares, median	3 (2-4)	3 (2-7)	3 (2-7)	3 (2-3)	
Back pain before first AAU	60 (74)	13 (68)	24 (73)	23 (79)	
Back pain					
Currently back pain	70 (86)	17 (90)	27 (82)	26 (90)	*0.61*
Age at onset, years, mean	27 (10)	26 (10)	26 (10)	28 (11)	*0.72*
Years since onset, median	10 (5-24)	10 (4-26)	9 (2-21)	11 (6-28)	*0.36*
Inflammatory back pain[3], ever	43 (53)	15 (79)	20 (61)	8 (28)	*<0.002*
ASAS SpA features, mean number	3 (1)	4 (1)	3 (1)	2 (1)	*<0.001*
HLA-B27 positive	45 (56)	18 (95)	18 (55)	9 (31)	*0.002*
Arthritis history	4 (5)	2 (11)	2 (6)	0 (0)	*0.85*
Enthesitis history	6 (7)	2 (11)	3 (9)	1 (3)	*0.61*
Psoriasis history	7 (9)	3 (16)	2 (6)	2 (7)	*0.47*
Good response to NSAIDs	30 (37)	13 (68)	12 (36)	5 (17)	*0.003*
Family history of SpA	9 (11)	3 (16)	4 (12)	2 (7)	*0.63*
Elevated CRP (>7 mg/L)	17 (21)	8 (42)	5 (15)	4 (14)	*0.006*
CRP level (mg/L), median	13 (11-23)	18 (12-33)	14 (9-20)	11 (8-19)	
Other SpA features					
Morning stiffness >30 minutes	34 (42)	8 (42)	18 (55)	8 (28)	*0.11*
Alternating buttock pain	28 (35)	10 (53)	12 (36)	6 (21)	*0.08*
Artralgia without arthritis	19 (24)	1 (5)	11 (33)	7 (24)	*0.12*
Stemal pain	12 (15)	4 (21)	6 (18)	2 (7)	*0.34*

Legend: Numbers are mostly depicted as number of patients (%), unless stated otherwise (mean (±SD) or median (Q1-Q3). *p-value of <0.002 was regarded statisticall significant, after Bonferroni correction for multiple testing. 1. Caucasian 72%, African 6%, Hindustan 5%, Turkish 5%, Moroccan 4%, Asian 1%, Latin American 3%, mixed ethnicity 4%; 2. Patients fulfilling the ASAS classification criteria for axSpA (radiographic or non-radiographic); 3. IBP according to the ASAS IBP criteria. AAU, acute anterior uveitis; ASAS, Assessment of Spondyloarthritis international Society; axSpA, axial spondyloarthritis; CRP, C-reactive protein; HLA-B27, Human Leukocyte Antigen B27; NSAIDs, nonsteroidal anti-inflammatory drugs.

Table 1. Patient characteristics at referral, subdivided for the clinical diagnoses

based on the modified New York (mNY) criteria for sacroiliitis). The primary endpoint was a clinical axSpA diagnosis (definite/possible/no axSpA), made by the rheumatologist. Patients with a definite- or possible diagnosis were classified according to the ASAS classification criteria for axSpA.

Results: Of the 101 referrals, 81 patients fulfilled the referral criteria (52% male, median age 41 years, median back pain onset 10 years before referral, Table 1). IBP was present in 53%, 56% was HLA-B27 positive, and 32% had some level of radiographic sacroiliac joint abnormalities (of whom 42% fulfilled the mNY criteria). Eventually, 23% (n=19) was clinically diagnosed with definite-axSpA (100% fulfilling the ASAS axSpA criteria; 53% radiographic) and 41% (n=33) with possible-axSpA (55% fulfilling the ASAS axSpA criteria; 6% radiographic). Importantly, of the 47 patients with recurring AAU, 87% had already had CBP during previous AAUs. Men had the same chance of fulfilling

the ASAS axSpA criteria as women (57%, vs 56%), and did not differ in number of SpA features, HLA-B27, back pain duration and IBP. However, men were more likely to be clinically diagnosed with axSpA (33% versus 13% in women).

Conclusion: The referral of AAU patients with CBP resulted in 23% new axSpA diagnoses (more prevalent in men), and another 41% required follow up because of a suspicion of early axSpA. There was a substantial diagnostic delay in the majority of patients with recurring AAU, as many already had back pain during previous AAU. In AAU, screening for CBP and prompt referral has a high diagnostic yield, and should consistently be promoted among ophthalmologists and rheumatologists.

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Abstract Number: 1307

Detecting Subtle Changes in Fundoscopic Retinal Images in Patients with Axial Spondyloarthritis with Deep Learning

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SESSION INFORMATION

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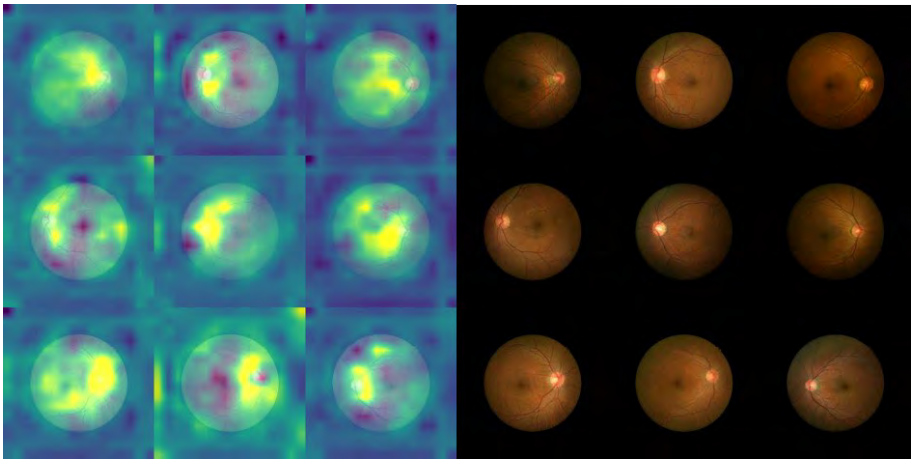
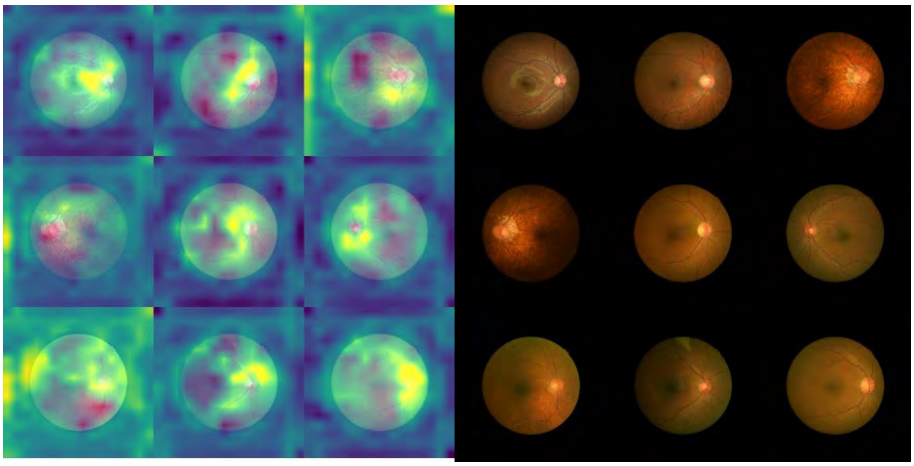
Background/Purpose: Fundoscopy is essential to identify the retinopathy of patients with autoimmune diseases. However, the classification of different autoimmune diseases is difficult by human eyes using traditional fundoscopy. We hypothesized that patients with axial spondyloarthritis (SpA) might have subtle differences in retinal images that are sufficient to classify SpA. We aimed to develop a deep learning model to detect the difference in retinal images between patients with SpA and other autoimmune diseases.

Methods: We prospectively collected 342 retinal images from 218 patients with or without SpA, which diagnosis was based on the Assessment of SpondyloArthritis international Society classification criteria for axial spondyloarthritis. The population was divided into a training group, a validation group and testing group (5:1:1). The retinal images were fed to a model based on the EfficientNet-B1, which was trained to classify SpA. The performance of the model was tested on a hold-out dataset of 31 patients whose retinal images were not used in the model training. The essential pixels that the models used to classify SpA was visualized using the Gradient-weighted Class Activation Mapping (Grad-CAM). Overall model performance was measured by accuracy, sensitivity, specificity, area under the curve of the receiver operator curve (AUROC).

Results: We included 51 women and 93 men with SpA (mean age, 42.9±12.8 years) and 74 non-SpA individuals (F: M, 57:17; mean age, 49.4±13 years). Among them, images from 187 patients were used for training and validation, while 31 of them were used to test the model performance. The overall model performance was 0.735 by AUROC. The sensitivity and specificity to classify SpA was 87% and 62.5%, respectively. Figures 1 and 2 showed the results from Grad-CAM, which highlighted the model interpretability.



Highlighting important regions of fundoscopy localized by Grad-CAM(left) and original fundoscopy(right) in SpA patients.



Highlighting important regions of fundoscopy localized by Grad-CAM(left) and original fundoscopy(right) in non-SpA patients.

Conclusion: This exploratory study indicates that subtle changes in retinal images may be distinctive for SpA which may be detected by deep learning models.

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Abstract Number: 1308

The Presence of Spondyloarthritis Is Associated with Higher Clinical Disease Activity in Patients with Early Crohn's Disease: Results of a Prospective Cohort Study

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Background/Purpose: Inflammatory bowel disease (IBD) and specifically Crohn's disease (CD) is known to be associated with spondyloarthritis (SpA) (1). However, only little is known about factors associated with the development of spondyloarthritis in CD. The purpose of this study is to identify factors associated with the presence of SpA in a cohort of patients with CD.

VARIABLE		TOTAL n=108	SpA n=23	No SpA n=85	p *
Age, years, mean ± SD		36.6 ± 12.7	37.5 ± 11.3	36.3 ± 13.1	0.44
Male sex, n (%)		50 (46.3)	10 (43.5)	40 (47.1)	0.82
CD symptom duration, years, mean ± SD		5.3 ± 7.4	5.4 ± 7.2	5.1 ± 7.5	0.63
HLA-B27 positive, n (%)		13 (12.0)	6 (26.1)	7 (8.2)	0.03
Montreal classification	Location: L1 - ileal	68 (63.0)	13 (56.5)	55 (64.7)	0.48
	L2 - colonic	0	0	0	
	L3 - ileocolonic	39 (36.1)	7 (30.4)	32 (37.6)	0.63
	L4 – isolated upper disease	10 (9.3)	3 (13.0)	7 (8.2)	0.44
	Behavior: B1 – non-stricturing, non-penetrating	69 (63.9)	15 (65.2)	54 (63.5)	1.00
	B2 - stricturing	19 (17.6)	4 (17.4)	15 (17.6)	1.00
	B3 - penetrating	6 (5.6)	0	6 (7.1)	0.34
	Peri-anal disease	7 (6.5)	2 (8.7)	5 (5.9)	0.64
C-reactive protein, mg/l, mean ± SD		10.7 ± 24.8	13.6 ± 23.2	10.0 ± 25.3	0.02
Harvey-Bradshaw Index, mean ± SD		3.6 ± 4.0	5.5 ± 4.7	3.1 ± 3.6	0.01
Fecal calprotectin, mcg/d, mean ± SD		185.9 ± 213.7	211.7 ± 243.8	179.5 ± 207.9	0.43
Treatment of CD	Mesalazine, n (%)	16 (14.8)	9 (39.1)	7 (8.2)	0.001
	Methotrexate, n (%)	27 (25.0)	3 (13.0)	24 (28.2)	0.18
	Azathioprine, n (%)	1 (0.9)	0	1 (1.2)	1.00
	Biologics naive, n (%)	103 (96.3)	22 (95.7)	81 (96.4)	1.00

* U-Mann Whitney test for numerical variables and Fisher's exact test for categorical variables

Table. Baseline demographic and clinical characteristics of the included patients with Crohn's disease with or without spondyloarthritis.

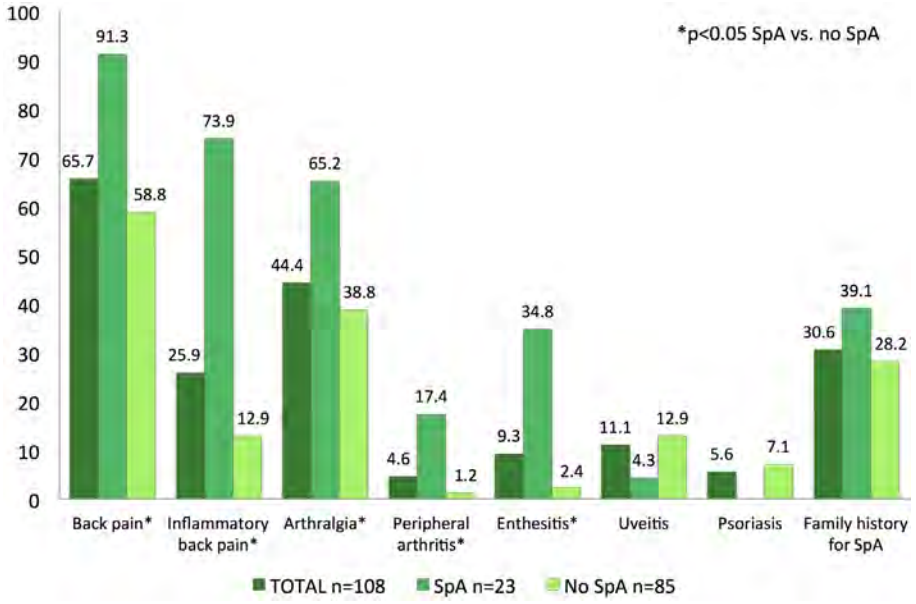

Figure. Spondyloarthritis manifestations in patients with Crohn's disease.

Methods: Patients with a definite diagnosis of CD naïve to or not being treated with biological agents for at least 3 months were included in a CD-arm of the German Spondyloarthritis Inception Cohort (GESPIC-Crohn). Gastroenterologists were encouraged to include consecutively recently diagnosed CD patients. Patients were classified according to the Montreal classification including location and behavior of CD. Patients received a structured assessment of SpA manifestations (including magnetic resonance imaging of sacroiliac joints and spine) by a rheumatologist who was responsible for the final diagnosis of SpA / no SpA. Clinical activity of CD was assessed by the Harvey-Bradshaw Index (HBI). In addition, colonoscopy was performed, Simple endoscopic Score for Crohn's Disease (SES-CD) was determined and fecal calprotectin was measured.

Results: A total of 108 patients with CD were enrolled. The mean (mean ± SD) age was 36.6 ± 12.7 years, and CD symptom duration was 5.3 ± 7.4 years. At baseline, 44 (40.7%) patients were treated with non-biologic immunomodulating drugs: 16 (14.8%) patients received mesalazine, 27 (25.0%) azathioprine, and 1 (0.9%) methotrexate. Oral steroids were given to 38 (35.2%) patients. A total of 103 (96.3%) patients were biologics naïve. SpA was diagnosed in 23 (21.3%) patients: 12 had axial SpA and 11 peripheral SpA. Patients with SpA had higher prevalence of HLA-B27, of clinical SpA features (back pain, inflammatory back pain, peripheral arthritis, enthesitis), higher level of CRP and higher activity of CD as measured by the HBI. There were not substantial differences between SpA vs. non-SpA patients in terms of CD duration, endoscopic activity, disease location or behavior, or treatment, except for mesalazine, which was more frequently administered in patients with SpA than non-SpA (39.1% vs. 8.2%, p=0.001, respectively).

Conclusion: SpA was present in 21% of patients with CD in this early cohort with almost equal proportions of axial and peripheral forms. Presence of HLA-B27 and higher clinical activity of CD were associated with the presence of SpA.

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8, Pfizer, 8, Prometheus, 8, Takeda, 8, CED Service GmbH, 8, Ferring, 8; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8.

Abstract Number: 1309

Prevalence of Undiagnosed Axial Spondyloarthritis Among Patients with Inflammatory Bowel Disease: A Secondary Care Cross-Sectional Study

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (axSpA) is closely related to inflammatory bowel disease (IBD), however contemporary data on the burden of hidden disease in the IBD population is lacking. This is despite significant advances in imaging and improved understanding of the axSpA disease spectrum. Recognition of the association between axSpA and IBD is important in order to bridge the gap of diagnostic delay and streamline referral for treatment. This study aims to elucidate the hidden prevalence of axSpA in IBD patients in secondary care.

Methods: Screening questionnaires were sent to consecutive IBD patients attending routine clinics (September 2017 to February 2019) in a large teaching hospital serving an estimated 3000 IBD patients. Patients fulling the eligibility criteria (gastroenterologist-verified diagnosis, 18 to 80 years old, biologic therapy naïve, no previous diagnosis of axSpA); and a moderate-diagnostic-probability of axSpA (self-reported chronic-back-pain (CBP) onset before 45 years old) were invited for rheumatological assessment. This included a medical interview, physical examination (including joint and tender point count, MASES, dactylitis count, BASMI), patient reported outcomes (BASDAI, BASFI, BASGI, Harvey-Bradshaw-Index, Partial-Mayo-Index), relevant laboratory tests (CRP, ESR, HLA-B27), pelvic radiograph, axSpA protocol MRI, and remote review by a panel of expert axSpA rheumatologists.

Results: The prevalence of rheumatologist-verified diagnosis of axSpA was 5% (95% CI 1.3,12.0) with a mean delay to diagnosis of 12 (S.D. 12.4) years. Using contemporary classification criteria, the prevalence of axSpA was 39% (ESSG), 12% (ASAS), (mNYC) respectively. Of the 470 patients approached, 41% (n=191) responded. Of the 173 valid completed questionnaires, 53% (n=91) had CBP onset < 45 yr and 90% (n=82) attended for clinical assessment. The mean age was 52 yr, 37% male. 74% ulcerative colitis, 26% crohn's disease, 66% disease remission. The prevalence of physician verified inflammatory back pain (IBP) was 20%. However, 38%, 35%% and 29% fulfilled Calin, Berlin and ASAS classification criteria respectively. Previous history of acute anterior uveitis (AAU), skin psoriasis, other peripheral musculoskeletal (MSK) axSpA manifestations were reported by 5%, 7% and 16% respectively. Thirty-five percent (n=29) had a positive family history of axSpA-related conditions (62% IBD, 52% skin psoriasis, 4% axSpA). Mean CRP and ESR were 4.3mg/L and 14mm/h respectively; 7% HLA-B27 positive; 4% ASAS positive MRI (active sacroiliitis); 6% fulfilled mNYC radiological criteria.

Conclusion: The hidden prevalence of rheumatologist-verified diagnosed axSpA in IBD patients seen routinely in a hospital setting with self-reported CBP which started before 45 years old is conservatively estimated at 5%. This

represents a significant hidden disease burden. Greater awareness and education are still needed. We need to get it right first time by appropriate identification and referral from gastroenterology to rheumatology, in order to potentially shorten the delay to diagnosis and allow access to effective therapy.

Disclosure: C. Lim, None; **M. Tremelling**, None; **L. Hamilton**, None; **A. MacGregor**, None; **T. Turmezei**, None; **M. Kim**, None; **K. Gaffney**, Abbvie, 2, 5, 8, Celgene, 2, 5, 8, Lilly, 2, 5, 8, Pfizer, 2, 5, 8, Gilead, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 1310

Gut Microbiome Changes Are Different Between Ankylosing Spondylitis and Inflammatory Bowel Disease, and Correlate with Disease Activity in Both Diseases

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities

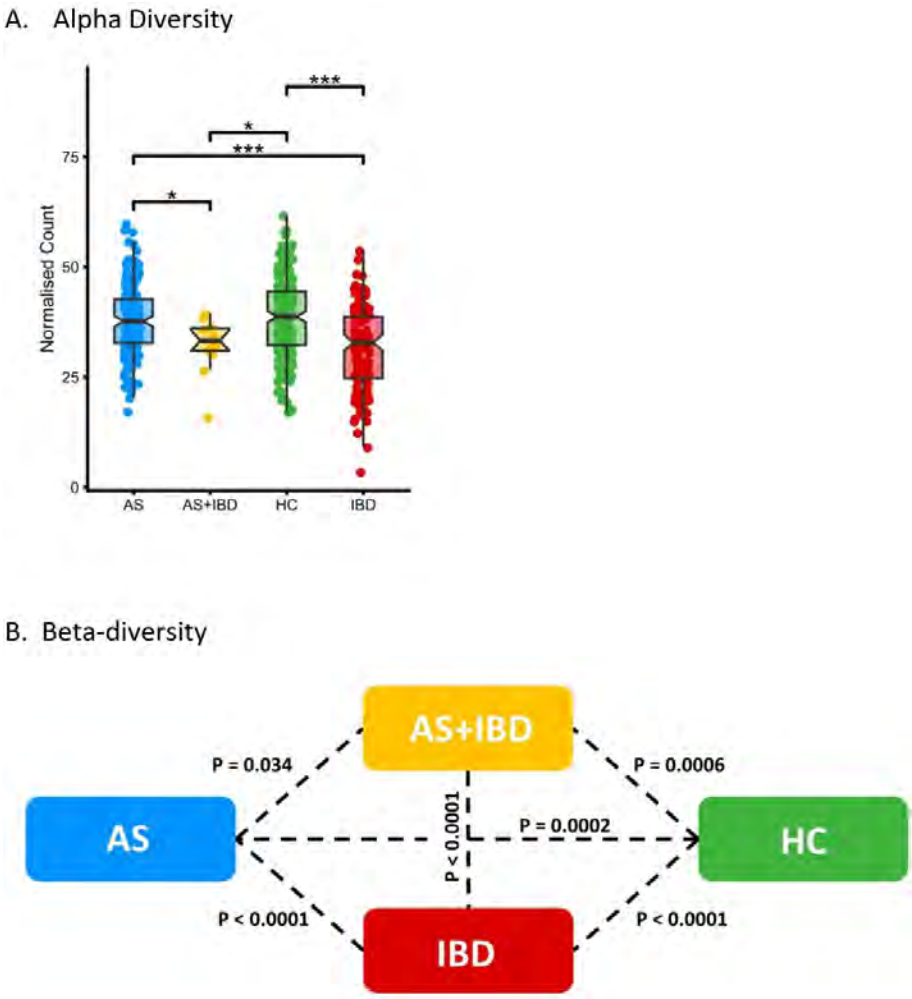
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Multiple studies have confirmed that the gut and stool microbiome in ankylosing spondylitis (AS) and inflammatory bowel disease (IBD) are distinct from healthy controls, and it is known that ~60% of AS cases have subclinical IBD, and 5-10% have clinical IBD. As different microbiome studies of these diseases have used different sequencing and analytic methods, it has not been possible to determine if these diseases have similar or different gut microbiomes. This study aimed to test the hypothesis that the gut microbiome in AS and IBD is different, and whether the gut microbiome in AS correlated with disease activity.

Methods: After ethics approval and written informed consent, stool samples, terminal ileal biopsies, colonic biopsies and/or rectal biopsies were obtained from 192 AS patients (136 Swedish, 33 Australian (5 with concomitant IBD, 'AS-IBD') and 23 Italian), 59 Australian IBD patients, and 112 controls undergoing colon cancer screening studies but with no ill-health (105 Australian and 7 Italian). Metagenomic profiling was performed using 16S rRNA sequencing and processed using Qiime2. Alpha-diversity, beta-diversity and taxonomic comparisons were controlled for age, BMI, country of origin, BMI, smoking status, gender, and TNF-inhibitor usage.

Results: AS, AS-IBD and IBD patients differed from one another and from healthy controls in both alpha and beta-diversity (Figure 1). Considering patients with either fecal calprotectin (FCP)< 100 or >100, AS patients differed in both alpha and beta-diversity from IBD patients (P< 0.01 all comparisons). FCP >100 was also associated with



Comparison of Australian, Swedish and Italian AS patients, Australian IBD patients, and Australian and Italian healthy controls sampled from four body sites: terminal ileum, right colon, rectum, and stool.

microbiome differentiation in AS and IBD patients. AS patients with and without clinical IBD could be distinguished from one another with moderate accuracy using stool microbiome (AUC=0.754), similar to the performance of FCP (AUC=0.752) and better than the Dudley Inflammatory Bowel Symptom Questionnaire (AUC=0.716). Stool microbiome also accurately distinguished IBD patients from healthy controls (AUC=0.757). Amongst AS patients, beta- but not alpha-diversity differed between those with BASDAI 0-2.5, 2.5-5.0, 5.0-7.5 and 7.5-10 (P=0.015). TNFi usage was associated with differentiation of the gut microbiome in IBD patients. Increased *Haemophilus* carriage was observed in AS, AS-IBD, AS patients with elevated BASDAI (7.5+), and IBD patients with FCP >100. Apart from *Streptococcus* and *Haemophilus*, no other indicator taxa were shared between AS and IBD patients.

Conclusion: AS and AS-IBD patients have a distinct gut microbiome compared with IBD patients and healthy controls. This is consistent with immunological and genetic evidence suggesting that the gut plays a different role in driving AS compared with IBD. AS and IBD disease activity is associated with changes in the gut microbiome.

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Abstract Number: 1311

Identification of Clinical Phenotypes in Patients with Axial Spondyloarthritis, Peripheral Spondyloarthritis and Psoriatic Arthritis According to Peripheral Musculoskeletal Manifestations: A Cluster Analysis in the International ASAS-PerSpA Study

Clementina Lopez-Medina[1], Sylvie Chevret[2], Anna Molto[1], Joachim Sieper[3], Mehmet Tuncay Duruöz[4], Uta Kiltz[5], Bassel El-Zorkany[6], Najia Hajjaj-Hassouni[7], Ruben Burgos-Vargas[8], Jose Maldonado-Cocco[9], Nelly Ziade[10], Meghna Gavali[11], Victoria Navarro-Compán[12], Shue Fen Luo[13], Alessandro Biglia[14], Tae-Jong Kim[15], Mitsumasa Kishimoto[16], Fernando Pimentel-Santos[17], Jieruo Gu[18], Laura Muntean[19], Floris van Gaalen[20], Pál Géher[21], Marina Magrey[22], Sebastian Ibanez[23], Wilson Bautista-Molano[24], Walter Maksymowych[25], Pedro M Machado[26], Robert Landewé[27], Désirée van der Heijde[28] and Maxime Dougados[29], [1]Rheumatology Department, Cochin Hospital, Paris, Paris, France, [2]INSERM (U1153): Clinical Epidemiology and Biostatistics, University of Paris, Paris, France, [3]Charité Universitätsmedizin Berlin, Berlin, Germany, [4]Marmara University School of Medicine, PMR Department, Rheumatology Division, Istanbul, Turkey, [5]Rheumazentrum Ruhrgebiet, Ruhr-University Bochum, Herne, Germany, [6]Cairo University, Cairo, Egypt, [7]Health Sciences College, International University of Rabat (UIR), Rabat, Morocco, [8]Department of Rheumatology, General Hospital of Mexico, Ciudad de Mexico, Mexico, [9]Buenos Aires School of Medicine, Buenos Aires, Argentina, [10]Saint-Joseph University, Beirut, Lebanon, Beirut, Lebanon, [11]Nizam's Institute of Medical Sciences, Hyderabad, India, [12]Hospital Universitario La Paz IdiPaz, Madrid, Pais Vasco, Spain, [13]Chang Gung Memorial Hospital-Linkou, Taoyuan, Taipei, Taiwan (Republic of China), [14]Fondazione IRCCS Policlinico S. Matteo, University of Pavia, Pavia, Italy, [15]Department of Rheumatology, Chonnam National University Medical School and Hospital, Gwangju, Republic of Korea, [16]Department Nephrology and Rheumatology, Kyorin University School of Medicine, Tokyo, Japan, [17]3.CEDOC, NOVA Medical School, Faculdade de Ciências Médicas da Universidade NOVA de Lisboa, Lisboa, Portugal; 7.Hospital Egas Moniz (CHLO) (Rheumatology Department), Lisboa, Portugal, Lisbon, Portugal, [18]Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, guangzhou, China (People's Republic), [19]Rheumatology Department, Iuliu Hatieganu University of Medicine and Pharmacy, Cluj-Napoca, Romania, [20]Leiden University Medical Center (LUMC), Leiden, Netherlands, [21]Semmelweis University, Budapest, Budapest, Hungary, [22]Case Western Reserve University School of Medicine, Cleveland, OH, [23]Facultad de Medicina Clínica Alemana – Universidad del Desarrollo, Santiago, Region Metropolitana, Chile, [24]University Hospital Fundación Santa Fé de Bogotá and Universidad El Bosque, Bogotá, Colombia, [25]University of Alberta, Edmonton, AB, Canada, [26]University College London, London, United Kingdom, [27]Amsterdam University Medical Center & Zuyderland Hospital, Amsterdam, Netherlands, [28]Leiden University Medical Center, Leiden, Netherlands, [29]Department of Rheumatology, Hopital Cochin, Université de Paris, Paris, France

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with a clinical diagnosis of Spondyloarthritis (SpA) and Psoriatic Arthritis (PsA) may have predominant axial or predominant peripheral symptoms. However, a huge clinical overlap exists and clear patterns of distribution are lacking. The objective of this study was to identify patterns of peripheral involvement according to the specific location of these symptoms in the whole spectrum of SpA and PsA.

Methods: International, cross-sectional and multicentre study with 24 participating countries. Consecutive patients considered by their treating rheumatologist as suffering from either PsA, axial SpA (axSpA), peripheral SpA (pSpA), inflammatory bowel disease (IBD)-related SpA, reactive arthritis or juvenile SpA were enrolled. A specific cluster analysis for each peripheral musculoskeletal manifestation (i.e., peripheral articular involvement, enthesitis and dactylitis) was conducted using data concerning the specific location of these symptoms at any time during the course of the disease. Multiple correspondence analyses and k-means clustering methods were used. Distribution of peripheral manifestations and clinical characteristics were compared across the different clusters.

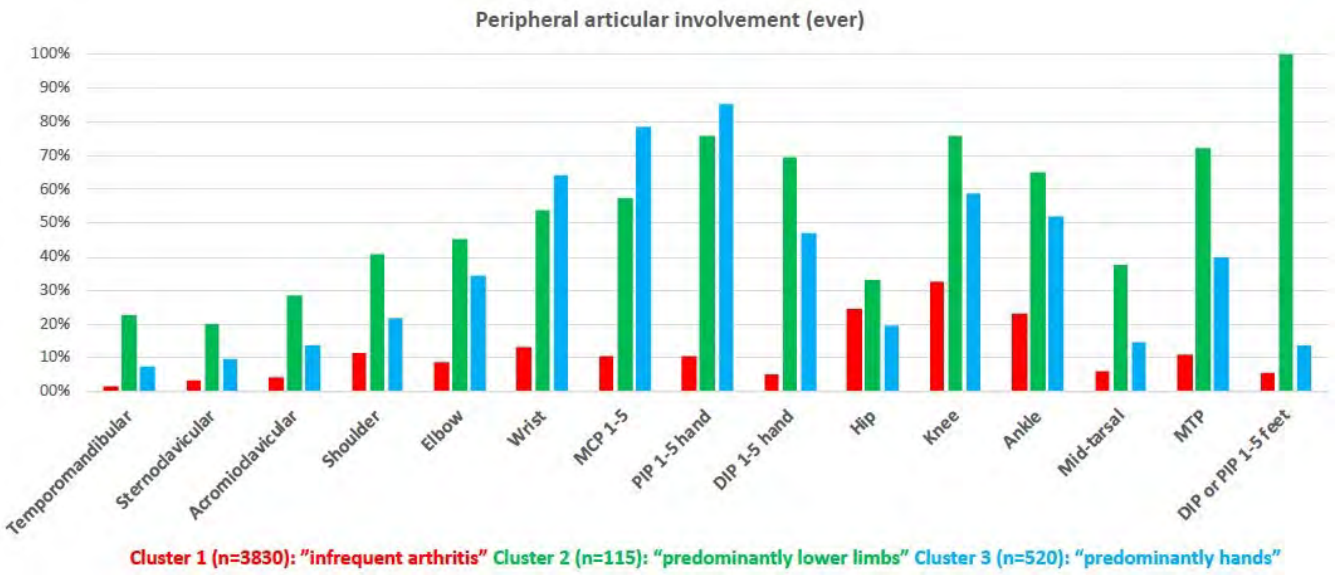

Figure 1. Cluster analysis for peripheral articular involvement: distribution of the affected joints with regard to the cluster.

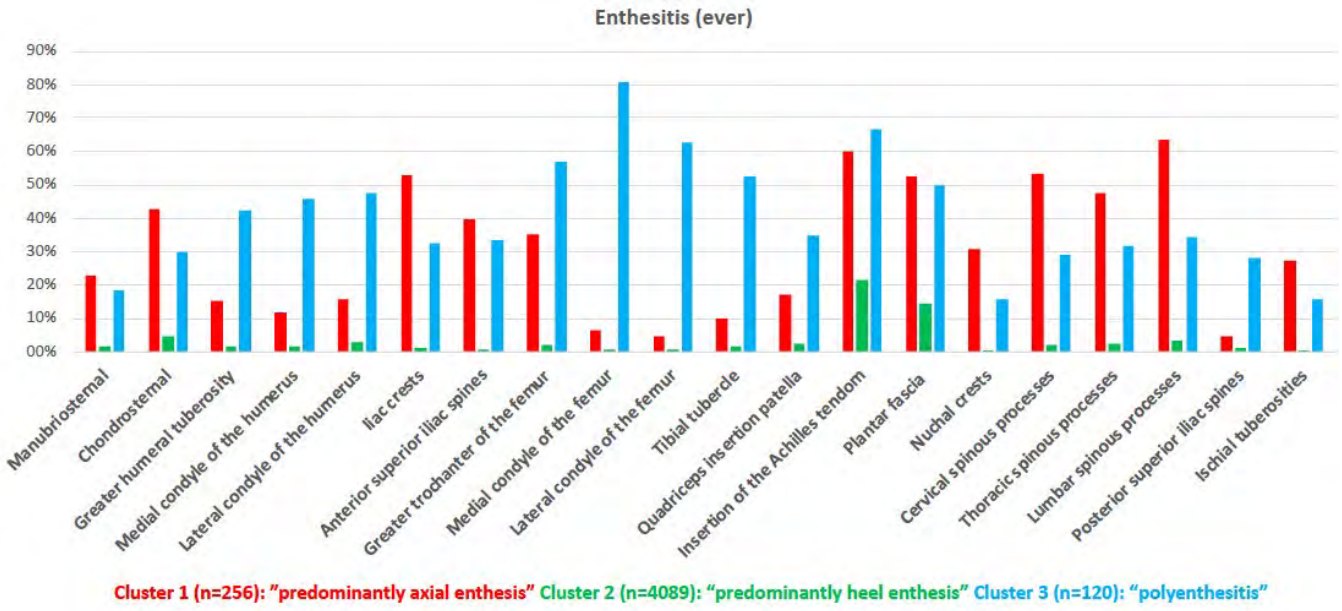

Figure 2. Cluster analysis for enthesitis: distribution of the affected enthesis with regard to the cluster.

Results: A total of 4465 patients were included in the analysis. Three clusters were found with regard to the location of peripheral articular involvement (Fig. 1), labelled as "infrequent arthritis (a)", "predominantly lower limbs (b)" and "predominantly hands (c)". Patients from the "a" group showed, in comparison with "b" and "c" groups, a higher prevalence of males (63.9% vs 51.3% vs 41.5%), HLA-B27 positivity (79.8% vs 48.2% vs 34.8%) and SpA diagnosis (axSpA or pSpA) (76.7% vs 30.6% vs 35.2%), but lower prevalence of psoriasis (23.2% vs 67.8% vs 59.6%) and PsA diagnosis (17.2% vs 61.7% vs 58.5%). Between "b" and "c" clusters, the first one showed a higher prevalence of uveitis (15.7% vs 8.7%), and a lower prevalence of IBD (3.5% vs 6.7%).

With regard to the location of enthesitis (Fig. 2), 3 clusters were also found, labelled as “predominantly heel enthesitis (d)”, “predominantly axial enthesitis (e)” and “polyenthesitis (f)”. Patients from the “f” group showed a higher prevalence of fibromyalgia according to the FiRST questionnaire (41.3% vs 17.4% vs 31.3%), psoriasis (48.3% vs 28.4% vs 23.4%) and PsA diagnosis than in the “d” and “e” groups (40.8% vs 22.7% vs 21.5%), and a lower prevalence of males (40% vs 61.9% vs 56.2%) and SpA diagnosis (52.5% vs 71.0% vs 73.1%).

Finally, 3 clusters were found with regard to the location of dactylitis, labelled as “absence of dactylitis (g)”, “predominantly toes (h)” and “predominantly fingers (i)”. The “g” group showed in comparison with the other two groups, the highest prevalence of males (61.4% vs 51.4% vs 52.9%), HLA-B27+ (66.6% vs 52.5% vs 50.0%) and SpA diagnosis (72.1% vs 30.7% vs 41.2%), and the lowest prevalence of psoriasis (26.9% vs 68.6% vs 79.4%) and PsA diagnosis (21.5% vs 65.7% vs 52.9%).

Conclusion: These results suggest the presence of heterogeneous patterns of peripheral involvement in SpA and PsA patients without clearly defined groups, confirming the clear overlap of these peripheral manifestations across the different underlying rheumatological diseases.

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Abstract Number: 1312

Time-dependent Analysis of Incident Extra-articular Manifestations and Comorbidities in Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (axSpA) patients have higher morbidity and mortality compared to healthy controls. Much of this excess disease burden is related to extra-articular manifestations (EAM) and comorbidities that may develop over time. Knowledge of predictive factors for the development of extra-spinal events in axSpA is limited by a dominance of cross-sectional studies in this area. This study aims to use real-world data to longitudinally analyse the risk factors for the development of extra-spinal events in axSpA.

Methods: This is a longitudinal observational cohort study, consisting of consecutive adult-onset axSpA patients (age of onset of axial symptoms ≥ 16 years) from July 2003 onwards. Patients were reviewed on a standard protocol every six months, with comprehensive documentation of demographics, clinical, laboratory and radiographic data. EAMs were defined as acute anterior uveitis (AAU), psoriasis (PsO) and inflammatory bowel disease (IBD). Time-to-event analysis, with time-weighted covariate exposure lagged by one year, was performed using R statistical package to assess the cumulative burden of extra-spinal events.

Results: Of the 1148 axSpA patients included in the study, 66% (n=757) were male and mean age was 40 (SD 12) years at study entry. AAU was present in 22% (n=246), IBD in 5% (n=55) and PsO in 4% (n=47) at baseline. After excluding these patients in the longitudinal analysis, AAU was the most frequent EAM to develop (see Figure 1) and was associated with the use of DMARDs (HR 2.28, p=0.01; Table 1). There was no impact of sex or disease activity on the development of any EAM. Hypertension was the most prevalent comorbidity at study entry (11%, n=120), followed by peptic ulcer disease (7%), depression (7%) and hyperlipidaemia (6%). The prevalence of ischaemic heart disease (IHD) was low (1.2%). Hypertension was the most frequent comorbidity to develop in follow-up (n=198), followed by depression (n=152) and hyperlipidaemia (n=128). IHD remained low (n=35). Age was the most common predictor for the development of a comorbidity (Table 2). Being male significantly increased the risk of hypertension (HR 2.61) and high cholesterol (HR 2.96), and was protective against fibromyalgia (HR 0.21). Time-averaged exposure analysis of

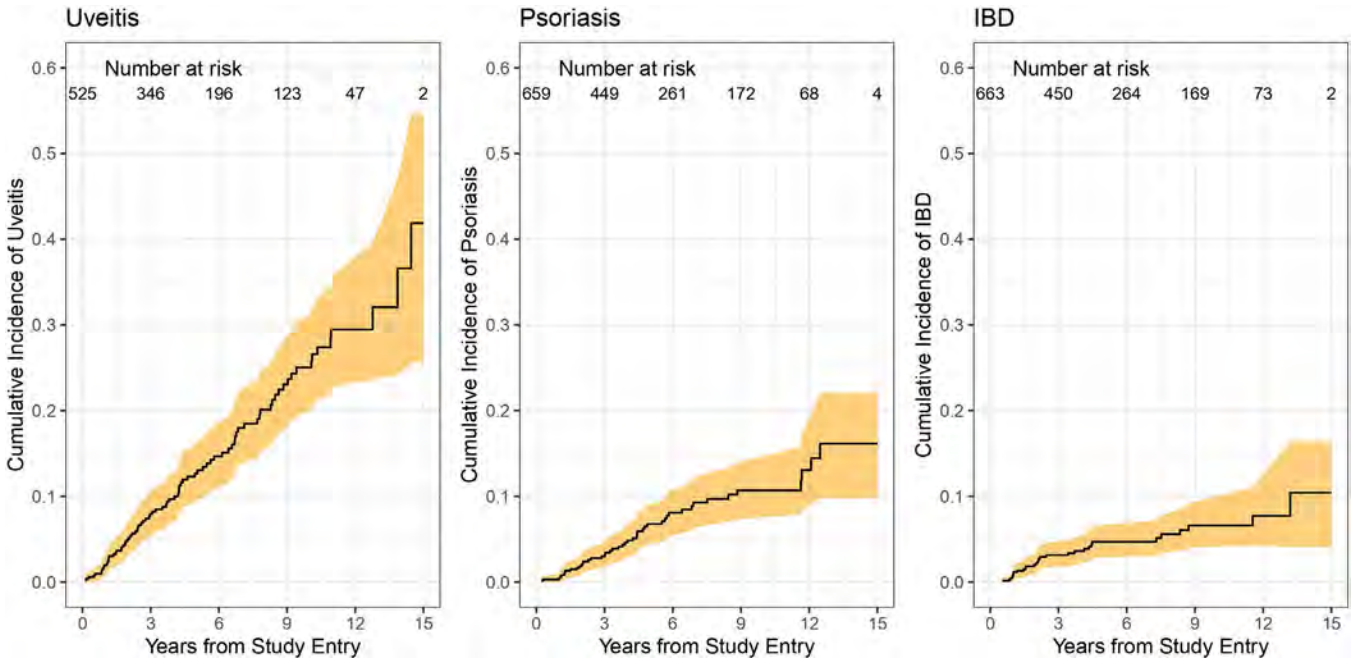

Figure 1. Incidence of Uveitis, Psoriasis and Inflammatory Bowel Disease

	AAU		PsO		IBD	
	HR	*p*	*HR*	*p*	*HR*	*P*
Biologic use	0.83	0.53	1.17	0.70	1.95	0.19
DMARD use	2.33	**0.01**	1.24	0.68	1.89	0.26
NSAID use	1.16	0.59	0.61	0.20	0.78	0.60
HLA-B27 positive	1.64	0.06	1.13	0.72	0.56	0.13
Age	0.99	0.20	0.98	0.12	1.00	0.81
Male	0.84	0.47	0.81	0.48	0.97	0.94
BASDAI	1.00	0.99	1.10	0.19	1.03	0.73

AAU: acute anterior uveitis; BASDAI: Bath Ankylosing Spondylitis disease activity index; HLA: human leucocyte antigen; IBD: inflammatory bowel disease; NSAID: non-steroidal anti-inflammatory disease; PsO: psoriasis.

Table 1. Regression analysis of predictors for the development of extra-articular manifestations over time.

	Hypertension		High cholesterol		IHD		CVD		Depression		Osteoporosis		Fibromyalgia		Sleep apnoea		Cancer	
Number of events	198		128		46		13		152		53		64		51		57	
	HR	*p*	*HR*	*p*	*HR*	*p*	*HR*	*p*	*HR*	*p*	*HR*	*p*	*HR*	*p*	*HR*	*p*	*HR*	*p*
Biologic use	2.35	**0.01**	1.74	0.13	2.13	0.31	1.37	0.61	1.89	0.05	0.85	0.74	6.5	**0.02**	1.10	0.89	1.45	0.46
DMARD use	1.63	0.18	1.72	0.19	0.84	0.87	0.54	0.55	1.07	0.88	1.93	0.24	1.43	0.67	0.22	0.22	0.91	0.89
NSAID use	2.15	**0.01**	0.85	0.66	3.27	0.14	1.11	0.86	1.26	0.47	0.55	0.21	1.20	0.81	1.68	0.45	0.83	0.71
HLA-B27 positive	0.53	**0.01**	0.83	0.54	1.04	0.95	1.90	0.32	0.64	0.07	0.45	0.05	0.54	0.26	0.31	**0.03**	1.47	0.42
Age	1.08	**<0.01**	1.07	**<0.01**	1.07	**0.01**	1.08	**<0.01**	0.99	0.19	1.07	**<0.01**	0.99	0.49	1.02	0.35	1.09	**<0.01**
Male	2.61	**<0.01**	2.96	**0.01**	2.36	0.27	2.19	0.22	0.92	0.74	0.71	0.40	0.21	**0.01**	1.58	0.44	0.91	0.82
BASDAI	1.09	0.11	1.02	0.80	0.94	0.66	1.09	0.48	1.41	**<0.01**	0.92	0.36	1.75	**<0.01**	1.38	**0.01**	0.97	0.79

BASDAI: Bath Ankylosing Spondylitis disease activity index; CVD: cerebrovascular disease; DMARD: disease-modifying anti-rheumatic drug; HLA: human leucocyte antigen; HR: hazard ratio; IHD: ischaemic heart disease; NSAID: non-steroidal anti-inflammatory drug; P: p-value.

Table 2 Regression analysis of predictors for the development of comorbidities over time.

medication usage showed an association between biologics and an increased incidence of hypertension (HR 2.35) and fibromyalgia (HR 6.5). NSAIDs (HR 2.15) were associated with an increased risk of hypertension (HR 2.15). A higher average BASDAI over the preceding five years significantly increased the risk of the development of sleep apnoea, depression and fibromyalgia.

Conclusion: To our knowledge, this is the largest longitudinal analysis of extra-spinal events in a real-world cohort of axSpA patients. Although overt IHD was uncommon, hypertension and high cholesterol were frequent. The traditional non-modifiable risk factors of age and male sex were associated with the development of cardiovascular comorbidity. Depression was associated with a higher average BASDAI in the five years preceding the diagnosis. Contrary to expectations, we saw no interaction between biologics and incidence of EAM.

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Abstract Number: 1313

Prevalence of Extra-Articular Manifestations in Early Ankylosing Spondylitis versus Non-Radiographic Axial Spondyloarthritis: A Systematic Literature Review and Meta-Analysis of 1504 Patients

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Uveitis, psoriasis and inflammatory bowel disease (IBD) are Extra-articular manifestations (EAM) of axial spondyloarthritis (axSpA). A recent meta-analysis comparing EAMs in patients with ankylosing spondylitis (AS) and non-radiographic axial spondyloarthritis (nr-axSpA) (mean symptom duration: 1.2 to 17.7 years in AS, 1.0 to 12.1 years in nr-axSpa) reported higher prevalence of uveitis (23.0% vs. 15.9%, AS vs. nr-axSpA), however, similar prevalences of psoriasis (10.2% vs. 10.9%, AS vs. nr-axSpA) and IBD (4.1% vs 6.4%, AS vs. nr-axSpA) in patients with AS compared to nr-axSpA. Nonetheless, data comparing the prevalence of EAMs in early AS and nr-axSpA patients are lacking.

Methods: A systematic literature review was conducted in Pubmed up to 31.12.2019. Keywords referring to EAMs and early axSpA were used, publications reporting prevalence of at least one of the EAMs in patients with early AS and nr-axSpA (mean symptom duration ≤5 years). For longitudinal studies, article with largest participant number from that cohort was included. Case reports and reviews were excluded. Data were collected according to a pre-defined collection form. Prevalences of each EAM in AS and nr-axSpA were assessed by meta-analysis of proportions, using a random-effects model and the DerSimonian & Laird method. The prevalences were compared between the AS and nr-axSpA populations by calculating a pooled risk difference using R based software (Jamovi version 1.2).

Results: Of 667 articles, 6 were analyzed and all were cohort studies (details in **Table 1**). For uveitis and psoriasis 1504 (577 AS and 927 nr-AxSpA) patients and for IBD 1440 (531 AS and 909 nr-AxSpA) with early SpA were analyzed to compare the prevalence of each EAM in AS and nr-AxSpA patients: weighted mean ages 30.2±8.1 and 31.5±8.4 years (standardized mean difference: 0.6 (0.03, 1.1) years), weighted mean axSpA symptom duration 23.2±22.6 and 16.7±14.3 months (standardized mean difference: 2.9 (0.8, 5.1) months), 74.3% and 56.1% male (pooled risk difference: 16.5% (95% Confidence Interval (CI); 4.3, 28.7)) , 77.9% and 69.8% (pooled risk difference: 7.6% (95% CI; -1.3, 16.5)) carried HLA-B27, for AS and nr-AxSpA, respectively. In pooled analysis uveitis prevalence was 14.9% (95% CI; 9.1, 20.7) in AS and 9.7% (95% CI; 6.0, 13.4) in nr-axSpA, resulting in a difference in pooled prevalence of 3.5% (95% CI; 0.1, 6.8) (p=0.042); psoriasis prevalence was 8.2% (95% CI; 4.0, 12.4) in AS and 8.8% (95% CI; 2.7, 15.0) in nr-axSpA, resulting in a difference in pooled prevalence of -0.1 % (95% CI; -3.0, 2.7) (p=0.92) and IBD prevalence was 4.1 % (95% CI; 0.9, 7.4) in AS and 2.7% (95% CI; 0.8, 4.5) in nr-axSpA, resulting in a difference in pooled prevalence of -0.3 % (95% CI; -0.7, 2.7)(p=0.25) (details in **Figure 1**).

Conclusion: EAMs are frequent in early axSpA either AS or nr-axSpA. Higher prevalence of uveitis in AS patients compared to nr-axSpA patients may suggest the appearance of new cases over follow-up. Physicians need to screen carefully for EAMs at diagnosis and over follow-up especially for uveitis.

Table 1. Cohorts comparing the prevalence of EAMs in AS and nr-AxSpA patients

Cohort or first author's name	Design		n	Age mean (SD), years	Male (%)	Symptom duration mean (SD), month	HLA B27 (%)	% Uve	% PsO	% IBD
SPACE	LOS	AS	22	25.7 (1.5)	58.1	13.1 (1.8)	65.2	13.4	13.4	13.4
		Nr-AxSpA	51	30.5 (1.1)	52.9	13.1 (1.1)	60.8	9.8	7.8	11.8
DESIR	LOS	AS	185	31.3 (8.9)	59.5	19.2 (10.8)	74.0	12.0	15.7	7.6
		Nr-AxSpA	484	34.5 (8.4)	41.7	18.0 (10.8)	53.8	8.3	17.8	4.1
ESPERANZA	LOS	AS	109	32.7 (6.8)	74.3	13.9 (6.4)	67.6	6.4	7.3	5.5
		Nr-AxSpA	85	31.3 (6.7)	54.1	13.0 (6.8)	58.3	4.7	12.9	2.4
GESPIC	LOS	AS	119	36.1 (11.4)	65.6	36 (19.2)	73.1	19.3	9.2	2.5
		Nr-AxSpA	226	36.1 (10.6)	42.9	31.2 (20.4)	74.7	12.4	9.8	1.8
Ki Min	XS	AS	96	21 (1.5)	100	24 (22.2)	88.5	14.6	3.1	0
		Nr-AxSpA	63	21 (0.8)	100	12 (14.8)	77.8	11.1	1.6	0
Hulejova	XS	AS	46	34.8 (7.6)	84.8	60 (62.2) †	91.0	32.0	4.0	-
		Nr-AxSpA	18	36.3 (10.1)	44.4	2.5 (35.6) †	94.0	38.0	0	-
Meta – analysis		AS	577	30.2 (8.1)	74.3	23.2 (22.6)	77.9			
		Nr-AxSpA	927	31.5 (8.4	56.1	16.7 (14.3)	69.8			
Difference (95% CI)				0.6 (0.03;1.1)*	16.5 (4.3;28.7)**	2.9 (0.8;5.1)*	7.6 (-1.3 ; 16.5)**			

CI: Confidence Interval, IBD: Inflammatory bowel disease, LOS: Longitudinal observational study, NS: Not Stated, N/A: Not Applicable, PsO: Psoriasis, Ret: Retrospective, Uve: Uveitis, XS: Cross-sectional. * Standardized mean difference, ** Difference in pooled prevalence †Disease duration

Table 1. Cohorts comparing the prevalence of EAMs in AS and nr-AxSpA patients

Figure 1. Pooled prevalence and prevalence differences of each EAM in patients with AS and nr-AxSpA subgroups

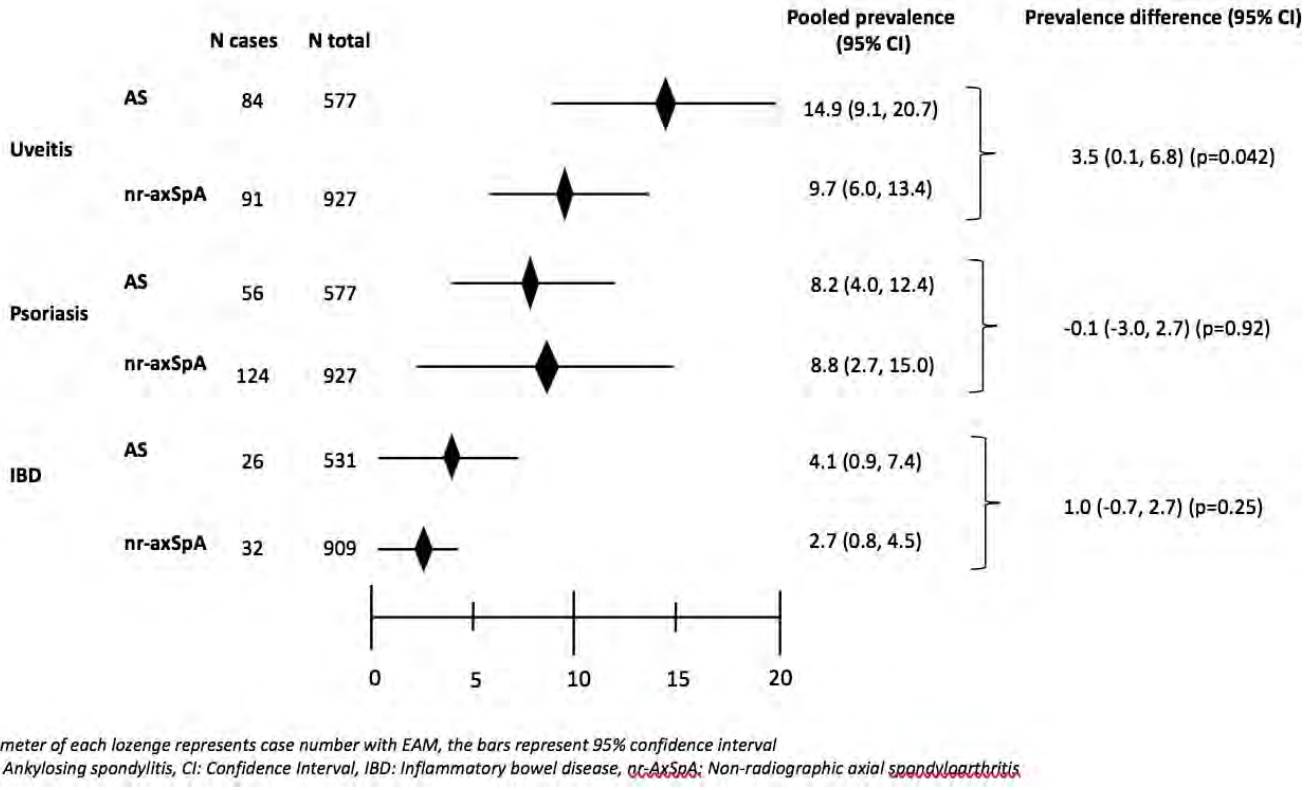

Figure 1. Pooled prevalence and prevalence differences of each EAM in patients with AS and nr-AxSpA

Disclosure: E. Bilgin, None; **U. Kalyoncu**, Abbvie, 1, Amgen, 1, Jannsenn, 1, Lilly, 1, Novartis, 1, UCB, 1; **L. Gossec**, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8.

Abstract Number: 1314

Fatigue in Psoriatic Arthritis (PsA): Prevalence in Patients from the US and Europe, and Impact on Quality of Life and Work Productivity

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

	PsAID12 fatigue score				
	0 (n=180)	1-3 (n=445)	4-7 (n=142)	>7 (n=64)	P value
Demographic characteristics					
Age, mean (SD)	45.3 (13.0)	46.5 (13.7)	51.2 (12.6)	52.5 (12.2)	**<0.01**
Female, n (%)	62 (34.4)	213 (47.9)	78 (54.9)	37 (57.8)	**<0.01**
BMI, mean (SD)	26.8 (5.4)	26.4 (4.8)	27.1 (4.7)	26.9 (4.7)	0.53
Caucasian, n (%)	167 (92.8)	412 (92.6)	130 (91.6)	59 (92.2)	0.23
Working full time, n (%)	125 (71.0)	280 (64.2)	61 (43.6)	23 (38.3)	**<0.01**
Biologic tx, n (%)	91 (50.6)	196 (44.0)	76 (53.5)	37 (57.8)	0.06
Disease characteristics					
Years since diagnosis, mean (SD)	4.8 (2.3)	4.5 (2.2)	6.9 (4.1)	8.0 (5.6)	**<0.01**
Current severity (provider-assessed), n (%) -Mild -Moderate -Severe	 171 (95.0) 9 (5.0) 0 (0.0)	 350 (78.7) 89 (20.0) 6 (1.4)	 76 (53.5) 59 (41.5) 7 (4.9)	 26 (40.6) 32 (50.0) 6 (9.4)	**<0.01**
Current BSA %, mean (SD)	2.2 (3.7)	6.2 (7.7)	9.2 (10.2)	7.6 (10.8)	**<0.01**
*66 swollen joint count, mean (SD)	0.6 (1.8)	2.3 (3.9)	7.1 (11.3)	4.2 (4.8)	**<0.01**
*68 tender joint count, mean (SD)	1.1 (3.2)	2.8 (3.5)	7.6 (7.8)	6.2 (4.3)	**<0.01**

Table 1. Demographic and clinical characteristics by patient reported PsAID12 fatigue score.

	PsAID12 fatigue score	Change in predicted PRO values	P value
EQ5D utility (n=650)	0 (ref)	0.95	
	1-3	-0.07	**<0.01**
	4-7	-0.18	**<0.01**
	>7-10	-0.33	**<0.01**
EQ5D VAS (n=660)	0 (ref)	87.35	
	1-3	-6.04	**<0.01**
	4-7	-18.28	**<0.01**
	>7-10	-24.08	**<0.01**
WPAI % overall work impairment (n=354)	0 (ref)	9.06	
	1-3	+5.17	**0.04**
	4-7	+17.23	**<0.01**
	>7-10	+18.89	**<0.01**
HAQ-DI (n=648)	0 (ref)	0.46	
	1-3	+0.14	**<0.01**
	4-7	+0.46	**<0.01**
	>7-10	+0.96	**<0.01**
PsAID12 (n=652)	0 (ref)	2.36	
	1-3	+1.10	**<0.01**
	4-7	+3.47	**<0.01**
	>7-10	+5.08	**<0.01**

Table 2. Incremental impact of PsAID12 fatigue score on PROs. α PRO key for worse outcome (range): EQ5D utility (0-1.0) = lower; EQ5D VAS (1-100) = lower; WPAI (0-100) = higher; HAQ-DI (0-3) = higher; PsAID12 (0-10) = higher.

Background/Purpose: Fatigue is an important aspect of PsA for patients. Understanding the impact of fatigue on patient reported outcomes is important for effective management of PsA. The objective of this study was to compare clinical and patient-reported outcomes in patients who report fatigue and those who do not, and to describe the prevalence of fatigue in PsA patients from physician and patient perspective.

Methods: Cross-sectional study among patients with PsA recruited by rheumatologists and dermatologists in France, Germany, Italy, Spain, UK, and US. Data were collected from Jun-Aug 2018 via physician-completed patient record forms and patient self-completed forms. Physicians reported patient demographic and disease characteristics, and if patients experienced fatigue (yes/no). Patients also reported fatigue via PsAID12 domain scale (0-10 score, grouped for analysis as 0, 1-3, 4-7, >7), quality of life (EQ5D-5L), work productivity (WPAI), and disability (HAQ-DI). Patients were compared according to grouped fatigue scores using parametric tests and non-parametric tests. Multiple linear regression analyses examined impact of incremental PsAID12 fatigue score on patient reported outcomes (PROs) (EQ5D, HAQ-DI, PsAID12, WPAI). Models controlled for gender, age, BMI, body surface area psoriasis percent, number of joints affected, pain, and Charlson Comorbidity Index score. Regressions were run on patients for whom all variables were available.

Results: Data were collected from 932 physician-patient pairs. Regression analyses showed that patients with increasingly severe fatigue scores reported worse outcomes in terms of quality of life, work impairment, and disability than those with lower fatigue scores. Physicians reported fatigue in 27.5% of patients, while 80.7% of patients reported they experienced fatigue. 44.9% of physician-patient pairs agreed on fatigue presence or absence.

Conclusion: After adjusting for demographic and clinical factors, patients with severe fatigue were found to have worse clinical, quality of life, work productivity, and disability outcomes than those with mild or no fatigue. Differences between patient and physician reports of fatigue suggest that physicians may not be aware of the extent to which patients experience fatigue.

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Abstract Number: 1315

Exploring the Prevalence and Factors Associated with Fatigue in Axial Spondyloarthritis in a Multiethnic Asian Cohort in Singapore

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SESSION INFORMATION

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Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Fatigue is a cardinal symptom of axial spondyloarthritis (axSpA) that poses management challenges. Data on fatigue amongst Asian patients with axSpA is limited. Ethnicity and geographic differences may shape the disease manifestations, severity and comorbidities. In this study, we aim to evaluate the prevalence of fatigue and the factors associated with fatigue among patients with axSpA within a multi-ethnic Asian population.

		BASDAI-F criteria		SF-36 VT criteria	
Characteristics	Total axSpA (n=262)	No severe fatigue (n=117)	Severe fatigue (n=145)	No severe fatigue (n=115)	Severe fatigue (n=52)
Social demographics					
Age, years	41.7 (13.7)	42.4 (15.1)	41.2 (12.5)	41.0 (13.2)	38.6 (11.9)
Men, n (%)	207 (79)	97 (82.9)	110 (75.9)	96 (83.5)	37 (71.2)
Chinese, n (%)	216 (82.4)	92 (78.6)	124 (85.5)	94 (81.7)	43 (82.7)
Secondary education and below, n (%)	52 (26.8)	14 (16.7)	38 (34.5)**	21 (21.6)	13 (31.0)
Public housing, n (%)	150 (78.5)	57 (69.5)	93 (85.3)**	74 (77.9)	35 (83.3)
BMI, kg/m^2	24.6 (6.1)	23.9 (6.1)	25.2 (6.0)*	24.4 (5.4)	24.9 (7.0)
Clinical characteristics					
Duration of disease, years	10.1 (8.3)	10.4 (9.1)	9.9 (7.7)	9.4 (8.7)	9.1 (7.4)
BASMI$_{10}$ (0-10)	3.4 (1.8)	3.2 (1.8)	3.5 (1.8)	3.2 (1.8)	3.6 (1.7)
Tender joint count (0-68)	0.3 (1.8)	0.2 (2.0)	0.4 (1.5)*	0.1 (0.4)	0.8 (2.4)
Swollen joint count (0-66)	0.2 (1.1)	0.1 (0.3)	0.3 (1.5)	0.1 (0.4)	0.7 (2.3)
Clinically damaged joints (0-68)	0.1 (0.8)	0.2 (1.0)	0.1 (0.5)	0.0 (0.0)	0.1 (0.5)**
SPARCC enthesitis index (0-16)	0.4 (1.5)	0.2 (1.0)	0.6 (1.8)*	0.2 (1.1)	0.7 (2.1)*
Patient reported outcomes					
BASDAI (0-10)	3.6 (1.9)	2.4 (1.3)	4.7 (1.7)***	3.1 (1.6)	5.0 (1.8)***
BASDAI-axial pain (0-10)	4.4 (2.5)	3.1 (2.2)	5.5 (2.3)***	4.1 (2.5)	5.7 (2.2)***
BASDAI-peripheral joint pain (0-10)	2.5 (2.8)	1.5 (1.8)	3.3 (3.1)***	1.8 (2.2)	4.5 (3.0)***
BASDAI-morning stiffness (0-10)	3.7 (2.5)	3.0 (2.3)	4.2 (2.5)***	3.3 (2.3)	4.9 (2.6)***
BAS-G (0-100)	40.1 (20.2)	31.9 (18.2)	46.8 (19.3)***	39.2 (17.3)	52.1 (19.0)***
BASFI (0-10)	2.3 (2.1)	1.4 (1.6)	3.0 (2.3)***	1.8 (2.0)	3.4 (2.2)***
ASQoL (0-18)	3.7 (4.2)	2.3 (3.2)	4.9 (4.6)***	3.2 (3.6)	8.2 (3.9)***
SF-36 Domains[¥]					
PF (0-100)	73.7 (22.3)	83.1 (18.5)	66.7 (22.5)***	79.6 (19.7)	60.5 (22.5)***
RP (0-100)	73.5 (24.7)	81.1 (23.1)	67.9 (24.5)***	79.3 (22.6)	60.7 (24.7)***
BP (0-100)	57.0 (21.4)	66.4 (17.6)	50.2 (21.5)***	64.6 (19.0)	40.4 (16.8)***
GH (0-100)	53.7 (20.6)	58.1 (21.0)	50.5 (19.9)*	59.4 (18.8)	41.2 (18.9)***
VT (0-100)	57.4 (18.2)	65.9 (18.1)	51.1 (15.7)***	66.7 (13.2)	36.8 (7.9)***
SF (0-100)	75.8 (22.1)	85.6 (16.9)	68.6 (22.9)***	82.8 (18.2)	60.3 (22.2)***
RE (0-100)	79.4 (23.0)	84.9 (21.5)	75.4 (23.3)**	85.2 (19.7)	66.7 (24.6)***
MH (0-100)	69.9 (19.1)	75.4 (18.1)	65.8 (18.9)**	76.7 (15.4)	54.8 (17.8)***
PCS NBS	41.7 (12.0)	46.1 (10.0)	38.5 (12.4)***	44.6 (10.4)	35.5 (13.1)***
MCS NBS	43.8 (11.3)	47.4 (11.4)	41.1 (10.6)***	48.6 (9.1)	33.2 (8.2)***

Note: All figures are given in mean (SD) unless otherwise specified

Abbreviations: BMI, body mass index; BASMI$_{10}$, Bath Ankylosing Spondylitis Metrology Index; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BAS-G, Bath Ankylosing Spondylitis Global Score; BASFI, Bath Ankylosing Spondylitis Functional Index; ASQoL, Ankylosing Spondylitis Quality of Life; SF-36, Short Form-36; PF, physical function; RP, role-physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role-emotional; MH, mental health; PCS, physical component summary; MCS, mental component summary; NBS, norm-based scoring

[¥] Data available in 167 patients who completed the SF-36; *p<0.05; **p<0.01; ***p<0.001.

Table 1. Baseline characteristics of patients with axSpA

Methods: We used the baseline data from a clinic registry in Singapore General Hospital. All patients fulfilled the 2009 Assessment of SpondyloArthritis international Society (ASAS) classification criteria for axSpA. Fatigue was assessed using the Bath Ankylosing Spondylitis Disease Activity Index fatigue item (BASDAI-fatigue) and the Short Form-36

BASDAI-F			
Variables	*b*	95% CI	*p*-value
BASDAI-axial pain	0.214	0.079, 0.348	0.002
BASFI	0.238	0.077, 0.399	0.004
BAS-G	0.024	0.006, 0.041	0.009
Ethnicity	0.894	0.119, 1.669	0.024
SF-36 VT			
Variables	*b*	95% CI	*p*-value
ASQoL	-2.346	-2.931, -1.760	<0.001
BASDAI-morning stiffness	-1.368	-2.348, -0.388	0.007

Variables entered into both models: gender, ethnicity (chinese/ non-chinese), age, education (1-7), housing type (1-7), BMI, duration of disease, $BASMI_{10}$, SPARCC enthesitis index, swollen joint count, clinically damaged joints, BASDAI-axial pain, BASDAI-peripheral pain, BASDAI-morning stiffness, BAS-G, BASFI and ASQoL.

Table 2. Factors associated with BASDAI-F and SF-36 VT on multiple linear regression

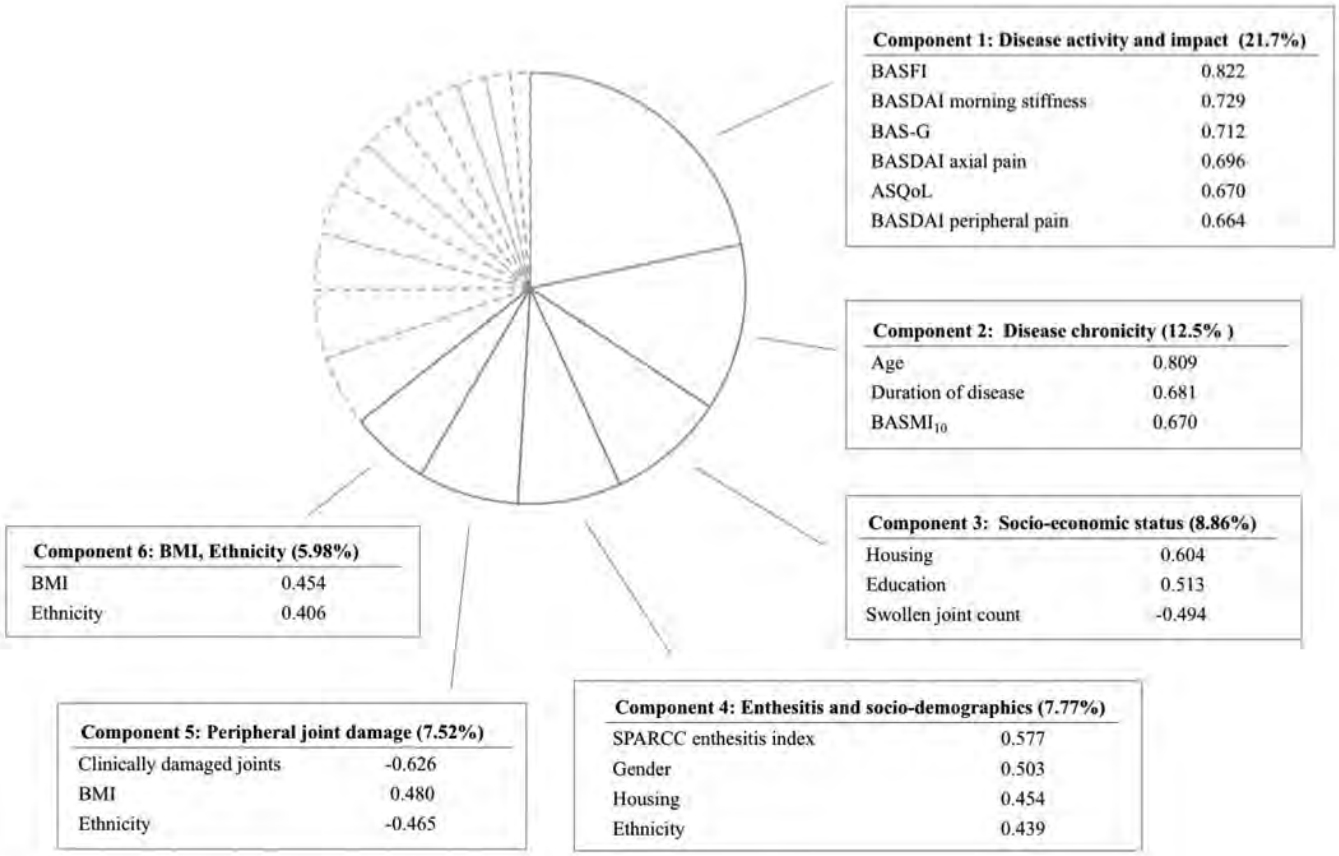

Figure 1. Principal component analysis yielding 6 components with eigenvalue greater than 1

Health Survey vitality domain (SF-36 VT). Severe fatigue was defined as BASDAI-fatigue ≥ 5/10 and SF-36 VT ≤ 10th percentile of the general Singaporean population.

Results: We included 262 consecutive patients with axSpA (79% men, 82.4% Chinese). The mean (standard deviation, SD) age and duration of disease were 41.7 (13.7) and 10.1 (8.3) years respectively. 145 (55.3%) patients reported severe fatigue by the BASDAI-fatigue criteria; 52 (31.1%) patients out of 167 with available SF-36 data had severe fatigue by the VT criteria. Patients with severe fatigue had worse scores across all disease activity assessments: BASDAI-axial pain, peripheral joint pain, morning stiffness and Spondyloarthritis Research Consortium of Canada (SPARCC) enthesitis index; and disease impact measures: Bath Ankylosing Spondylitis Patient Global Score (BAS-G), Bath Ankylosing Spondylitis Functional Index (BASFI), Ankylosing Spondylitis Quality of Life (ASQoL) and all SF-36 domains, compared to those without severe fatigue (Table 1). In the principal component analyses (Figure 1), disease activity and disease impact were statistically significantly associated with BASDAI-fatigue, while disease activity, disease impact and disease chronicity were associated with SF-36 VT. In the univariable analyses, all disease activity assessments and disease impact measures correlated with both BASDAI-fatigue and SF-36 VT; education level correlated with BASDAI-fatigue, while damaged joint count and age correlated with SF-36 VT. In the multivariable analyses, BASDAI-axial pain, BASFI, BAS-G and ethnicity were associated with BASDAI-fatigue, while ASQoL and BASDAI-morning stiffness were associated with SF-36 VT (Table 2).

Conclusion: Fatigue is prevalent amongst patients with axSpA in Asia and is associated with disease activity, disease impact as well as patient related factors including education level and ethnicity.

Disclosure: W. Lim, None; **W. Fong**, None; **Y. Kwan**, None; **Y. Leung**, Novartis, 1, Jassen, 1, AbbVie, 1, Eli Lilly, 1.

Abstract Number: 1316

Patient Perceptions of Fibromyalgia Symptoms and the Overlap with Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities
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Session Time: 9:00AM–11:00AM

Background/Purpose: In clinical practice, it is often challenging to distinguish fibromyalgia syndrome (FMS) from axial spondyloarthritis (axSpA), which includes ankylosing spondylitis and non-radiographic axSpA. Early stages of axSpA may present with an onset similar to FMS, and likewise patients with FMS may have symptoms that are similar to axSpA. Differentiating between axSpA and FMS can also be challenging for patients and can cause confusion about their diagnosis. This study examined the prevalence of axSpA symptoms among patients with FMS and differences in the pathway to diagnosis among patients with and without concomitant axSpA.

Methods: Adult US patients with FMS without concomitant rheumatoid arthritis or psoriatic arthritis in the ArthritisPower registry received email invitations to participate. Participants (pts) were asked whether they had a diagnosis of axSpA or ankylosing spondylitis and completed patient-reported outcome measures including Patient Reported Out-

comes Measurement Information System (PROMIS) measures for Pain Interference, Sleep Disturbance and Fatigue, and the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI). Pts then responded to a 57-item customized survey developed by the researchers in collaboration with patient partners. Results are descriptively reported.

Results: As of March 2020, 301 pts completed the survey; 97% female, 90% White, mean (SD) age of 53 (10). Mean (SD) Pain Interference score was 68 (5); Sleep Disturbance 64 (8); Fatigue 69 (6); and BASDAI 46 (8). Of the pts, 44 (15%) reported concomitant axSpA, 61% osteoarthritis, 6% gout, 5% Crohn's or ulcerative colitis, and 4% lupus. Half (52%) of all pts perceived their FMS to be 'rarely' or 'never' well managed and 80% ever felt that they have had an additional undiagnosed condition. Three-fourths (74%) of pts reported being able to differentiate between their FMS pain and pain from a concomitant disorder. Back pain lasting >3 months was reported by 93% of axSpA pts and 94% of non-axSpA pts; 11% reported all of the symptoms consistent with patient reported versions of the Assessment of SpondyloArthritis International Society (ASAS) criteria (back/buttock pain >3 months; age of symptom onset < 45; sacroiliitis diagnosis; at least one spondyloarthritis feature) (Figure 1), and of these, 32% reported an axSpA diagnosis. More pts with axSpA received their FMS diagnosis by a rheumatologist (45%) than without (41%) (Figure 2). Of the pts without an axSpA diagnosis (n=257), only 7% recalled their provider ever discussing with them the possibility of axSpA, including non-radiographic axSpA. Half (52%) of pts with axSpA believe that their axSpA should have been diagnosed earlier, with 39% reporting one reason for the delay as their doctors' belief that FMS was the cause of any axSpA symptoms.

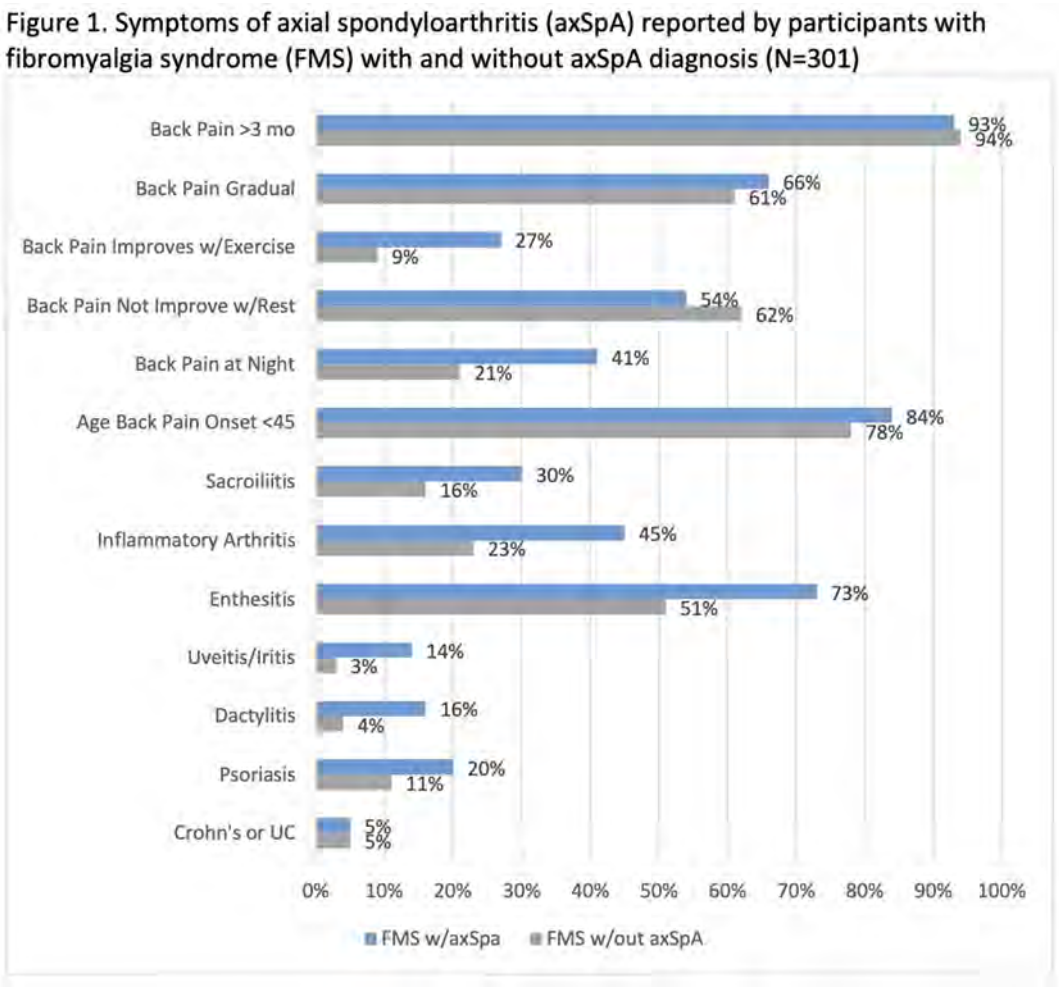

Figure 1. Symptoms of axial spondyloarthritis (axSpA) reported by participants with fibromyalgia syndrome (FMS) with and without axSpA diagnosis (N=301)

Figure 2. Provider giving fibromyalgia (FMS) diagnosis, by axial spondyloarthritis (axSpA) diagnosis status (N=301)

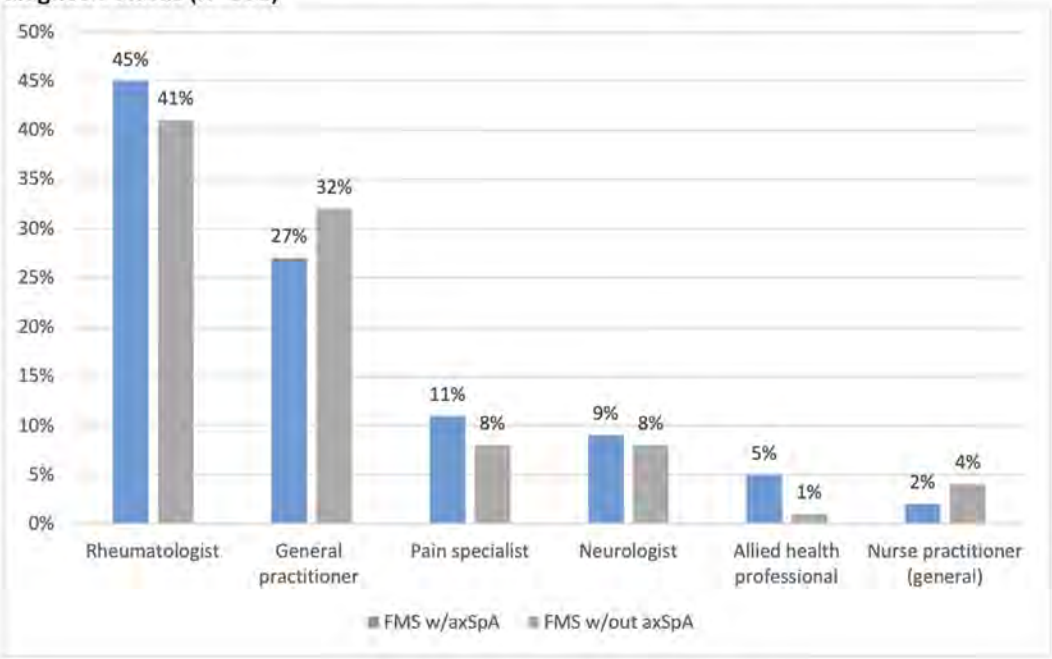

Figure 2. Provider giving fibromyalgia (FMS) diagnosis, by axial spondyloarthritis (axSpA) diagnosis status (N=301)

Conclusion: Patients with FMS often experience symptoms of axSpA and the two conditions can occur concomitantly. Additional research is needed to improve the triage, diagnosis, and education of patients with FMS and symptoms of axSpA.

Disclosure: K. Gavigan, None; **W. Nowell**, None; **R. Reynolds**, None; **L. Stradford**, None; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **A. Ogdie**, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1.

Abstract Number: 1317

A Large Agreement Between the Pain Points of the ACR 1990 Fibromyalgia Criteria and the MASES Enthesitis Score Is Observed in Patients with Axial Spondylitis, Including in Patients Without Concomitant Fibromyalgia

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Enthesitis is the hallmark lesion in Spondyloarthritis (SpA). The Maastricht Ankylosing Spondylitis Enthesitis score (MASES), which assesses 13 enthesitic sites, is the most widely used. Fibromyalgia (FM) is characterized by chronic diffuse musculoskeletal pain and diffuse pain points assessed by the tender points of the ACR 1990 criteria. Coexistence of FM represents a difficulty in the evaluation of enthesitis due to a possible overlap between the tender points of the MASES and the ACR criteria for FM.

To assess the agreement between the MASES and the tender points of the ACR 1990 FM criteria in a population of patients with axial spondyloarthritis (axSpA).

Methods: Ancillary cross-sectional analysis of the French Predict-SpA study. Patients had a diagnosis of axSpA according to their rheumatologist and an indication to start a TNF blocker (TNFb). All patients were screened for FM according to the FiRST questionnaire, and all patients underwent a physical examination : 18 tender points of the ACR 1990 criteria and the 13 enthesitic sites of the MASES were evaluated in a random order. Analysis: the overlap/agreement between the MASES and the ACR/FM tender points was assessed by the intraclass correlation coefficient (ICC). The agreement for "high" values in both scores (i.e. >6 for MASES and >9 for ACR) was evaluated by the PABAK (Prevalence-Adjusted Kappa). The same analysis was performed in the group of patients with and without concomitant FM. The characteristics of patients with high ACR and MASES scores were compared with the rest of the population by univariate and multivariate analyses.

Results: The study involved 526 patients with axSpA diagnosis, and among them, 202 were screened as FM by the FiRST questionnaire (by a score ≥ 5/6) but only 86/526 (16.3%) fulfilled the 1990 ACR FM criteria. Among the 526 patients, 446 (84.8%) had at least one ACR 1990 point, 423 (80.4%) had a MASES ≥1 and 404 (76.8%) had both at least one ACR 1990 point and a MASES ≥1. The ICC between both scores was 0.7 (95%CI [0.6-0.8]). A total of 77/526 (14.6%) patients had high ACR and MASES scores simultaneously. The agreement for high scores, assessed by PABAK, was 0.7 (95%CI [0.6-0.7]).

Among the 202 patients with concomitant FM, 179 (88.6%) had at least one ACR 1990 point and a MASES ≥1, whereas this was the case for 225/324 (69.4%) of patients without FM. The ICC between both scores was 0.6 (95%CI [0.3-0.8]) and 0.7 (95%CI [0.6-0.8]) for patients with and without FM, respectively. The agreement for high scores assessed by PABAK was 0.5 (95%CI [0.4-0.7]) in patients with FM and 0.8 (95%CI [0.7 - 0.8]) in those without.

Patients with concomitantly high ACR and MASES scores were more often HLAB27 negative (OR (95%CI) = 2.4 [1.3-4.4]), had more often a history of talalgia (OR (95%CI) = 1.9 [1.0-3.5]), a BASDAI at inclusion >4 (OR (95%CI) = 4.2 [1.2-26.6]) and a FM (OR (95%CI) = 3.38 [1.87-6.29]).

Conclusion: These results suggest a great overlap between both scores in patients with axSpA, including in those without concomitant FM. However, the coexistence of FM was associated with the presence of many pain points (both in MASES and ACR). Additional studies assessing the metrological performance of MASES in axSpA patients with concomitant FM seem necessary.

Disclosure: F. Hamitouche, None; **C. Lopez-Medina**, None; **L. Gossec**, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5,

8; **S. Perrot**, Pfizer, 8, Grunenthal, 8, MSD, 8, UPSA, 8, Menarini, 8; **M. Dougados**, Pfizer, 5, 8, AbbVie, 5, 8, Roche, 5, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, 8, Novartis, 5, 8, Sanofi, 5, 8, Biogen, 5, 8, Merck Sharp & Dohme, 5, 8, UCB Pharma, 5, 8; **A. Molto**, ABBVIE, 5, BMS, 5, 8, LILLY, 5, NOVARTIS, 5, 8, UCB, 5, 8, GILEAD, 5.

Abstract Number: 1318

Catastrophizing in Patients with Axial Spondyloarthritis and Psoriatic Arthritis

Baptiste Coste[1], Charlotte Traverson[1], Elisabeth Filhol[1], Soraya Benamar[1], Jacques Morel[2], Sabine Laurent-Chabalier[3], Bernard Combe[4], Claire Daien[2], Cédric Lukas[5], Charlotte Hua[1] and Cecile Gaujoux-Viala[6], [1]Department of Rheumatology, CHU Nîmes, University of Montpellier-Nîmes, France, Nimes, France, [2]Rheumatology department, CHU Montpellier and University of Montpellier, Montpellier, France, [3]Department of Biostatistics, Clinical Epidemiology, Public Health and innovation in Methodology, CHU Nîmes, University of Montpellier-Nîmes, France, Nimes, France, [4]University of Montpellier, Montpellier, France, [5]CHU Montpellier and University of Montpellier, Montpellier, France, [6]Department of Rheumatology, CHU Nîmes, University of Montpellier-Nîmes, France, EA2415, University of Montpellier, Montpellier, France, Nîmes, France

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
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Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Catastrophizing is a negative cognitivo-affective response to an anxiety-provoking stimulus, especially to pain. Catastrophism plays a role in maintaining chronic pain and is associated with several pain related outcomes.The objective was to assess catastrophizing prevalence and associated factors in axial spondyloarthritis (SA) and psoriatic arthritis (PsA).

Methods: In rheumatology departments of two hospitals, patients completed clinical and laboratory assessment (pain VAS, global VAS, tender and swollen joints, C-reactive protein, ESR, DAS28) and questionnaires on different outcomes: disease activity (BASDAI), catastrophizing (PCS), coping (CSQ), quality of life (Sf12, Eq5D), functional impact (BASFI, HAQ), fibromyalgia (FiRST), anxiety and depression (HADS, GAD7), and insomnia (ISI). Statistical analysis included samples t-test, one-way analysis of variance, Spearman's correlations, khi-2 test, Fisher's test, Wilcoxon test, linear and logistic regressions.

Results: In all, 253 patients were included (168 SA, 85 PsA). The prevalence of a PCS score ≥20 was 45.6% [95%CI 39.5;51.8]. It was 45.5% [38.0;53.0] in SA and 45.9% [35.3;56.5] in PsA. Median PCS score was 18 [Q1-Q3 6-18] in the global population. It was 18 [7-27] in SA and 16 [6-29] in PsA. Catastrophizing was significantly associated with anxiety, depression and disease activity in SA, and with anxiety, low quality of life and pain in PsA.

Conclusion: Almost half of patients with SA or PsA were high catastrophizers. Catastrophizing has a major impact on patient daily life. It may be interesting to detect catastrophizing in order to improve the management of our patients.

Disclosure: B. Coste, None; **C. Traverson**, None; **E. Filhol**, None; **S. Benamar**, None; **J. Morel**, AbbVie, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 5, Novartis, 5, Pfizer Inc, 2, 5, Sanofi, 5; **S. Laurent-Chabalier**, None; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **C. Daien**, None; **C. Lukas**, None; **C. Hua**, None; **C. Gaujoux-Viala**, AbbVie, 5, Amgen, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Eli Lilly, 5, Gilead Sciences, Inc., 5, Janssen, 5, 8, Medac, 5, Merck-Serono, 5, Mylan, 5, 8, Nordic Pharma, 5, Novartis, 5, 8, Pfizer, 5, Roche, 5, Sandoz, 5, 8, Sanofi, 5, UCB, 5.

Abstract Number: 1319

Disease Activity and Mental Health of as Patients: A Cross-section Study with Self-assessments Based on Smart System of Disease Management (SSDM) Mobile Tools

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

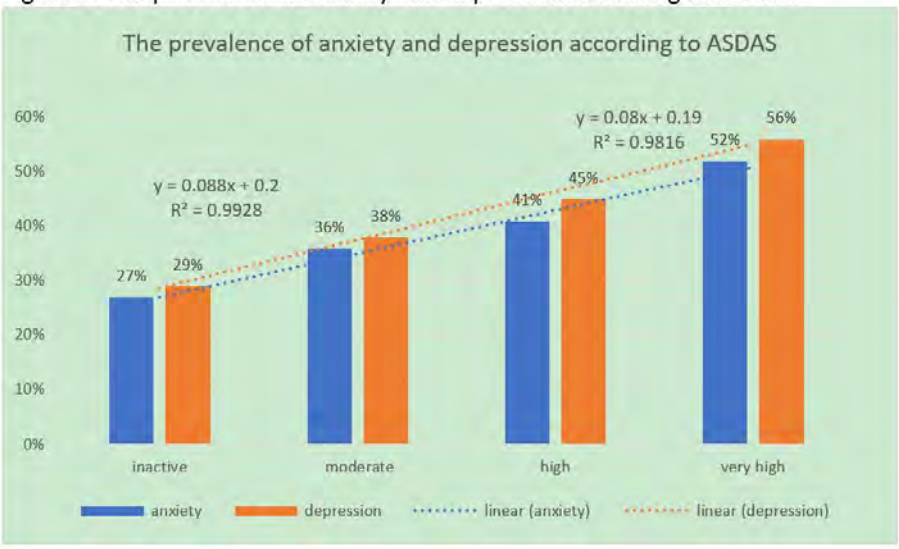
Background/Purpose: WHO survey showed that the prevalence of anxiety and depression in Chinese population and Chinese patients with chronic diseases were between 3.1% - 4.2% and 3.1% - 7.3%, respectively. Ankylosing Spondylitis Disease Activity Score (ASDAS) and Hospital Anxiety and Depression Scale (HADS) are commonly used to evaluate AS patients' disease activity and mental health. All those assessments were mainly performed by health professionals (HCPs) with paper questionnaire previously. SSDM is a novel smart disease management tool that allows patients to do self-assessments on ASDAS and HADS by mobile terminals.The purpose of this study is to estimate the prevalence of anxiety and depression in Chinese patients with AS and to analyze the potential association between disease activity and mental health.

Methods: Under the guidance and training by HCPs, AS patients downloaded SSDM and performed self-assessments bundle of ASDAS and HADS with SSDM. ASDAS< =1.3, 1.3-2.1, 2.1-3.5 and >3.5 are defined as inactive (IDA), moderate (MDA), high (HDA) and very high (VHDA) disease activity, respectively. ASDAS score < =1.3 represents inactive disease status and achievement of T2T. HADS score >=8 can be diagnosed with anxiety or depression.

Results: From June 2016 to Jan 2020, 1,931 AS patients (1,118 male, 813 female) with a mean age of 34.09 ± 11.86 (12-82) years and the median disease duration of 2.61 years from 207 hospitals performed bundle self-assessments for 2,477 times in total. According to the HADS and ASDAS assessment results, the prevalence of anxiety and depression in all patients was 36.7% and 39.3% respectively, which was significantly higher than that in the WHO survey in Chinese population and chronic disease patients. The proportion of patients achieved and failed on T2T was 29% and 71%, respectively. The prevalence of anxiety (A) and depression (D) was 25% and 23% among T2T achievers; and 37% and 32% among T2T failures, respectively (pA< 0.05, pD< 0.05).

According to ASDAS, in IDA, MDA, HDA and VHDA subgroups, the prevalence of anxiety and depression was 27%, 36%, 41%, 52% and 29%, 38%, 45%, 56%, respectively. The correlation coefficients of anxiety (A) and depression

Figure 1. The prevalence of anxiety and depression according to ASDAS.



(D) with ASDAS were rA=0.9908 and rD=0.9964. It suggested that with the increase of disease activity, the proportion of AS patients with anxiety and depression increased significantly. (Figure 1)

Conclusion: The prevalence of anxiety and depression in AS patients was significantly higher than that in the WHO survey in Chinese population and chronic disease patients. Higher prevalence of anxiety and depression were associated with higher levels of disease activity. SSDM is an effective mobile interface to monitor and study entanglement of disease activity and mental health in AS patients, which build a foundation for proactive interventions in future.

Disclosure: H. Song, None; **H. Wei**, None; **M. Zhang**, None; **L. Wu**, None; **Z. Wu**, None; **A. Chu**, None; **B. Wang**, None; **W. Fan**, None; **X. Wang**, None; **X. Chen**, None; **H. Wu**, None; **W. Zhou**, None; **F. Xiao**, None; **H. Xiao**, None; **Y. Jia**, None; **B. Wu**, None; **J. Lu**, None.

Abstract Number: 1320

Are Coping Strategies, Anxiety and Depression Associated with Daily Physical Activity in Patient with Axial SpA?

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Background/Purpose: Background: Patients with axial spondyloarthritis (axSpA) who are more physically active experience less pain and better physical functioning. It is also known that psychological factors such as anxiety and depression are associated with physical functioning and reduction of Quality of Life (QoL). Furthermore, evasive

		Lowest n=27 range 1030-6075	Moderate n=27 range 6210-10370	Highest n=28 range 10725-21585
Age (years)		48.5 ± 14.6	50.8 ± 14.0	46.4 ± 12.8
Gender (male), n (%)		14 (52.0)	15 (55.6)	21 (75.0)
Working status (working), n (%)		9 (35.0)*	15 (55.6)	24 (86.0)
Body Mass Index (kg/m^2)		27.9 (26.3;30.8)*†	26.1(23.7;30.3)	25.7 (22.7;27.8)
BASDAI (0-10)		5.1 (3.4;6.8)*†	3.0 (1.1;4.9)	2.2 (1.4;5.2)
ASDAS		2.6 (1.9;3.1)*†	1.9 (1.0;2.8)	2.1 (1.1;2.7)
CRP (mg/L)		1.8 (0.8;3.2)	2.8 (1.1;10.0)	1.2 (0.7;4.3)
BASFI (0-10)		4.8 (2.6;7.0) *†	2.1 (0.7;4.7)†	2.7 (1.0;4.0)
Disease influence on well-being (0-10)		6.0 (4.0;8.0)*†	3.0 (1.0;5.0)	3.0 (1.0;6.0)
ASQoL (0-18)		9.3 (3.3;13.0)*†	3.6 (0.0;8.1)	4.0 (1.0;6.9)
HADS	Anxiety (0-21)	5.0 (4.0;10.0)*†	4.0(2.0;5.0)	4.0 (2.0;6.0)
	Depression (0-21)	5.0 (3.0;9.0)*†	2.0 (1.0;4.0)	3.0 (2.0;4.3)
CORS	Comforting cognitions	25.5 (22.8;28.0)	26.0 (21.0;28.0)	25.0 (23.0;30.0)
	Decreasing activities	21.0(18.0;23.3)*†	17.0(13.0;20.0)	16.0 (14.0;18.0)
	Diverting attention	19.0 (14.8;21.0)	19.0 (14.0;21.0)	19.0 (16.0;20.0)
	Optimism	15.0 (13.0;16.0)	15.0 (13.5;17.0)	15.5 (13.0;17.0)
	Pacing	27.2 (23.8;30.3)*	22.0 (20.0;28.0)	22.0 (17.0;26.0)
	Creative solution seeking	21.0 (18.0;23.0)	20.0 (15.6;22.0)	19.0 (17.0;24.0)
	Accepting one's dependence	13.5 (11.8;16.0)	11.0 (8.5;14.5)	12.0 (10.0;16.0)
	Showing consideration	16.0 (15.0;18.0)	16.0 (13.0;17.0)	17.0 (14.0;18.0)

Data presented as number of patients (%), mean ± SD or median (IQR)
* P-values≤0.05 for highest group compared to lowest group
† P-values≤0.05 for intermediate PA group compared to lowest PA group
ǂ P-values≤0.05 for intermediate PA group compared to high PA group

Table 1. Differences between the low, intermediate and high physical activity tertiles

coping strategies are commonly used in health-related coping. Our objective was to determine if coping strategies, anxiety and depression are associated with physical activity in patients with axSpA. To our knowledge this has not been studied before

Methods: Consecutive out-patients from the Groningen Leeuwarden AxSpA cohort (GLAS) participated in this study. Additionally to the standardized follow-up assessments, patients completed the axSpA-Short Questionnaire to assess health-enhancing physical activity (axSpA-SQUASH), the Coping with Rheumatic Stressors (CORS) and the Hospital Anxiety and Depression Scale (HADS). Uni- and multivariate linear regression analyses were used to explore associations of copings strategies, anxiety and depression, and patient- and disease related factors with daily physical activity. Patients were stratified into three tertiles of physical activity: low, intermediate and high. To identify group differences, Kruskal-Wallis test or the Chi-Square test were used with post-hoc testing.

Results: In total 85 patients were included; 59% were male, mean age was 49±14, median symptom duration 19.5 years (IQR 12.0-31.0), 71% were HLA-B27 positive and mean ASDAS was 2.1 (SD 1.0). Median axSpA-SQUASH total physical activity score was 9406.3 (IQR 5538.8;12081.3). Scores of HADS-Anxiety (scale 7-28) and HADS-Depression (scale 7-28) had median scores 5.0 (IQR 3.0;7.0) and of 3.0 (IQR 2.0;5.5). The mostly used coping strategies was comforting cognitions (for pain, range 9-36) median of 25.5(IQR 22.0;28.0).

Univariate analysis showed that lower daily physical activity was significantly associated with gender (female), higher disease activity (BASDAI), worse physical function (BASFI), worse quality of life (ASQoL), coping strategies "decreasing activities" and "pacing", higher depression score (HADS). In the multivariate linear regression model the coping strategy "decreasing activities" (β: -376.4; 95%-CI: -621.9; -130.8, p-value: 0.003) and BMI (β: -235.5; 95%-CI:

-450.9; -20.0, p-value: 0.03) were independently associated with physical activity. The multivariate model explained 22% of variance (R2: 0.2197, p-value: 0.001). In the group comparison similar results were seen. (Table 1)

Conclusion: In this cross-sectional study in axSpA patients with established disease, multiple patient and disease related factors were associated with daily physical activity. The evasive coping strategy "decreasing activities" and BMI were independently associated with the level of physical activity. These findings suggest that to improve daily physical activity in axSpA patients attention should be paid not only on targeting disease activity, but also to other patient and disease related aspects especially coping strategies used..

Disclosure: M. Carbo, None; **L. van Overbeeke**, None; **Y. Kamsma**, None; **F. Wink**, Abbvie, 5, Janssen, 5; **S. Arends**, Pfizer, 2; **D. Paap**, None; **A. Spoorenberg**, Pfizer, 1, 2, Novartis, 1, 2, Abbvie pharmaceuticals, 1, 2, MSD, 1, UCB, 1.

Abstract Number: 1321

Central Sensitization, Disease Perception and Obesity Should Be Taken into Account When Interpreting Disease Activity in Patients with Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Up to 40% of ankylosing spondylitis patients report persistently high pain scores of >4 (scale of 0-10) even after responding to long-term TNF-α blocking therapy.[1] In other rheumatic diseases, nociplastic pain (due to altered functioning of the nervous system leading to peripheral and central sensitization) is common.[2] In axial spondyloarthritis (axSpA), patient illness and pain perceptions were shown to influence disease outcome.[3] Therefore, we hypothesized that central sensitization and patients' illness perceptions are associated with persistently high disease activity in axSpA.

Our objective was to investigate to what extent central sensitization, pain catastrophizing and patients' perceptions play a role in axSpA and to explore associations with disease activity.

Methods: Between April and September 2019, consecutive outpatients from the Groningen Leeuwarden axSpA (GLAS) cohort,[4] an ongoing large prospective cohort, were included in this study. Besides the standardized assessments, patients filled out three additional questionnaires: Central Sensitization Inventory (CSI), Pain Catastrophizing Scale (PCS) and Revised Illness Perception Questionnaire (IPQ-R). Univariable and multivariable linear regression analyses were used to investigate the association of CSI, PCS and each of the eight subscales of the IPQ-R, and disease activity assessments $ASDAS_{CRP}$, BASDAI, and CRP. We also tested the following patient characteristics: gender, symptom duration, BMI class, educational level, smoking status and HLA-B27 status.

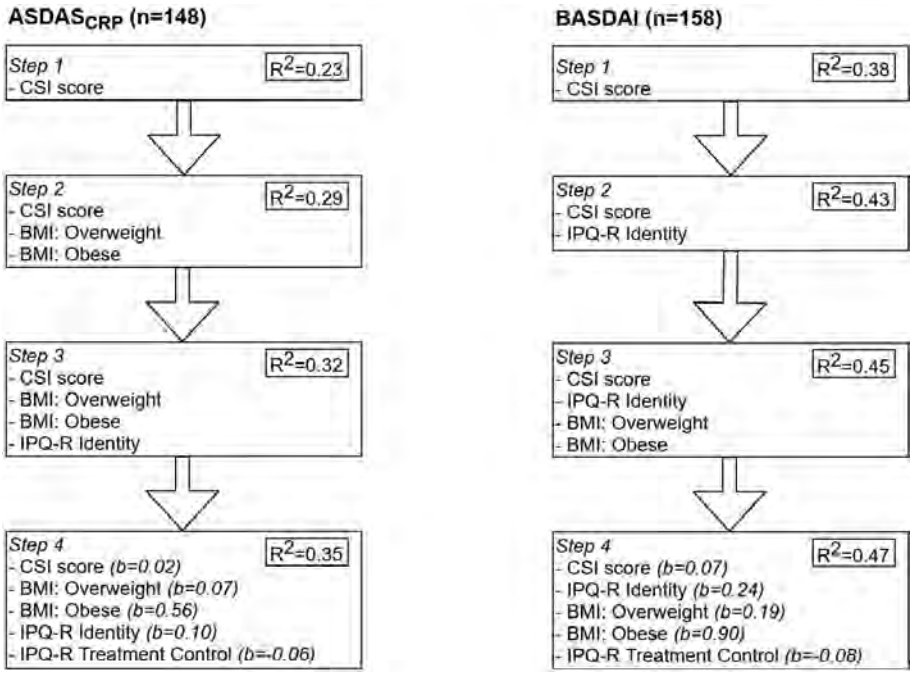

Figure 1. Results of multivariable linear regression analyses for ASDAS and BASDAI. ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Score; CSI: Central Sensitization Inventory; IPQ-R: Revised Illness Perceptino Questionnaire; BMI: Body Mass Index.

Results: Of 182 included patients, 57% were male, 79% were HLA-B27 positive, median symptom duration was 21 (IQR 10-32), mean ASDAS$_{CRP}$ 2.1 ± 1.0, mean BASDAI 3.9 ± 2.2 and median CRP 2.9 (IQR 1.1-7.0). Mean CSI score was 38.0 ± 14.1 (scale of 0-100), and 45% of patients scored ≥40 on the CSI.[5] Median PCS score was 15 (IQR 8-22) (scale of 0-52), median IPQ-R illness identity subscore 3 (IQR 2-4) (scale of 0-14) and median IPQ-R treatment control subscore 18 (IQR 16-20). In univariable regression analysis, CSI, PCS and IPQ-R subscores all showed significant associations with ASDAS$_{CRP}$, and all except the IPQ-R subscale personal control showed significant associations with BASDAI. Only IPQ-R treatment control was significantly associated with CRP. Central sensitization, two IPQ-R subscales (perceived treatment control and the number of symptoms patients attributed to their axSpA: illness identity) and obesity were independently associated with disease activity assessments BASDAI (R^2=0.47) and ASDAS$_{CRP}$ (R^2=0.35) (Figure 1). Only obesity was independently associated with CRP.

Conclusion: In this axSpA population with long-term disease, 45% scored above the CSI cutoff point of 40, indicating a high probability of central sensitization. CSI score, illness identity, perceived treatment control and obesity were independently associated with disease activity assessments ASDAS$_{CRP}$ and BASDAI.

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Abstract Number: 1322

Prevalence and Associated Factors of Sleep Disorders in Patients with Axial Spondyloarthritis. Results from the European Map of Axial Spondyloarthritis (EMAS)

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Sleep is an essential health aspect that is often impacted in patients with axial spondyloarthritis (axSpA). This analysis aims to assess the prevalence and associated factors of sleep disorders in a large sample of European axSpA patients.

Methods: Data were analyzed from 2,846 unselected patients with self-reported clinician-given diagnosis of axSpA of the European Map of Axial Spondyloarthritis (EMAS) through an online survey (2017-2018) across 13 European countries. Socio-demographic data; BASDAI [0-10] scores; engagement in physical activity; axSpA influence on work

	Sleep disorders (yes) n: 1,058 (mean ± SD or %)	Sleep disorders (no) n: 1,655 (mean ± SD or %)	p-value
Patient characteristics			
Age, years	44.0 ± 11.7	44.3. ±12.5	0.644
Gender (female)	723 (68.3)	952 (57.5)	**<0.001**
Educational level (university)	503 (47.5)	806 (48.7)	0.490
Marital status (married)	693 (65.5)	1157 (69.9)	**0.011**
Overweight/Obesity	598 (56.5)	824 (49.8)	**0.001**
Patient-reported outcomes			
Overweight/Obesity	598 (56.5)	824 (49.8)	**0.001**
BASDAI (0-10) N:2503	6.1 ± 1.8	5.0 ± 2.1	**<0.001**
Fatigue/tiredness (0-10)* N:2503	7.0 ± 2.0	5.8 ±2.4	**<0.001**
Morning stiffness severity (0-10)* N:2503	5.8 ± 2.4	4.8 ± 2.4	**<0.001**
Functional limitation (0-54) N:2498	21.9 ±14.6	22.2 ± 16.9	0.310
Reported work impact (yes) N:2430	547 (56.5)	559 (38.2)	**<0.001**
Physical activity (yes)	864 (81.7)	1360 (82.2)	0.735
Anxiety diagnosis (yes)	588 (56.8)	205 (12.5)	**<0.001**
Depression diagnosis (yes)	531 (51.8)	166 (10.1)	**<0.001**
GHQ-12 (0-12)**N:2507	6.4 ±4.0	3.9 ±3.9	**<0.001**

*As measured by the respective item of the BASDAI scale

**12-item General Health Questionnaire. A value of 3 or above indicates a risk of poor mental health

Table 1. Sociodemographic characteristics and patient-reported outcomes by presence of sleep disorders (N = 2713, unless otherwise specified)

	Simple logistic regression			Multivariable logistic regression		
	OR	95% CI	p-value	OR	95% CI	p-value
Gender (female)	1.59	1.36-1.87	**<0.001**	1.40	1.13-1.73	**0.002**
Marital status (married)	1.13	0.99-1.28	0.074	NA	NA	NA
Overweight/Obesity	1.31	1.12-1.53	**0.001**	1.39	1.14-1.71	**0.001**
BASDAI (0-10)	1.33	1.27-1.39	**<0.001**	1.07	0.95-1.21	0.246
Fatigue/Tiredness (0-10)*	1.28	1.23-1.33	**<0.001**	1.04	0.97-1.12	0.271
Morning Stiffness intensity (0-10)*	1.19	1.15-1.23	**<0.001**	1.05	0.98-1.13	0.188
Reported Work impact (yes)	2.10	1.78-2.48	**<0.001**	1.29	1.05-1.58	**0.015**
Anxiety (yes)	9.18	7.58-11.11	**<0.001**	3.84	2.99-4.94	**<0.001**
Depression (yes)	9.53	7.78-11.66	**<0.001**	3.09	2.37-4.02	**<0.001**
GHQ-12 (0-12)**	1.16	1.14-1.19	**<0.001**	1.03	1.00-1.06	**0.029**

*As measured by the respective item of the BASDAI scale
**12-item General Health Questionnaire. A value of 3 or above indicates a risk of poor mental health

Table 2. Regression analysis to predict presence of sleep disorders (N = 2191)

choice (assessed with yes/no question “Was your current or past work choice in any way determined by axSpA?”),; risk of psychological distress (12-item General Health Questionnaire [GHQ-12; 0-12]); functional limitation [0-54] and self-reported anxiety and depression were evaluated. Presence of sleep disorders was assessed by the question: “Please indicate whether you have been diagnosed with any of the following: sleep disorders”. A Mann-Whitney test was used to compare the means of numerical variables between dichotomous variables, the Chi-Square test was used to compare the distribution between the categorical variables. Simple and multivariable logistic regression models were used to identify associations between sleep disorders and disease characteristics, mental health and work-related variables.

Results: Age of respondents was 43.9 years; 61.3% were female; 48.1% had a university degree; 67.9% were married and 71.3% were HLA-B27 positive. The prevalence of sleep disorders was 39.0%. In the bivariate analysis, presence of sleep disorders was associated with female gender (68.3% vs. 31.7%; p< 0.001); overweight/obese (56.5% vs. 49.8%; p< 0.001); increased BASDAI scores (6.1±1.8 vs. 5.0±2.1; p< 0.001); fatigue (7.0±2.0 vs. 5.8±2.4; p< 0.001); morning stiffness (5.8±2.4 vs. 4.8±2.4; p< 0.001), work impact (56.5% vs. 38.2%; p< 0.001); anxiety (56.8% vs. 12.5%; p< 0.001); depression (51.8% vs. 10.1%; p< 0.001) and higher GHQ-12 scores (6.4±4.0 vs. 3.9±3.9; p< 0.001) [Table 1]. However, factors that remained independently associated with sleep disorders in the multivariable analysis were anxiety (OR=3.8 p< 0.001) and depression (OR=3.1 p< 0.001) and female gender (OR=1.4; p=0.002) [Table 2]. According to employment status, the greatest prevalence of sleep disorders was concentrated in those on permanent sick leave (52.3%) and temporary sick leave (50.2%). [Table 3].

Conclusion: Sleep disorders were highly prevalent among axSpA European patients and strongly associated with female gender and reporting worse mental health, and spinal stiffness. Patients on permanent and temporary sick leave were more likely to report sleep disorders. The strong association between sleep disorders with both anxiety

	Sleep disorders		P-value
	Yes	No	
Employed	456 (32.9)	932 (67.1)	**<0.001***
Unemployed	88 (44.0)	112 (56.0)	
Temporary sick leave	144 (50.2)	143 (49.8)	
Permanent sick leave	145 (52.3)	132 (47.7)	
Retired	82 (36.8)	141 (63.2)	
Homemakers	47 (42.7)	63 (57.3)	
Student	20 (37.0)	34 (63.0)	
Early retirement	16 (39.0)	25 (61.0)	

*The association was significant at the 0.05 level (bilateral)

Table 3. Presence of sleep disorders according to employment status categories (N = 2,580)

and depression should encourage rheumatologists to screen their patients with sleep disturbance in case they require additional specialist support.

Disclosure: M. Garrido-Cumbrera, None; **V. Navarro-Compán**, Novartis Pharma, 1, 5, 8, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, UCB, 5, 8; **L. Christen**, Novartis Pharma AG, 3; **C. Bundy**, Abbvie, 8, Celgene, 8, Janssen, 8, Lilly, 8, Novartis, 8, Pfizer, 8; **R. Mahapatra**, None; **S. Makri**, None; **C. Delgado-Domínguez**, None; **J. Correa-Fernández**, None; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8.

Abstract Number: 1323

Pregnancy in Axial Spondyloarthropathy: A Systematic Review & Meta-Analysis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthropathy (axSpA) is an inflammatory arthritis affecting the sacroiliac joints and the spine. Although this chronic condition affects a wide range of ages, many females affected are of childbearing age. At present it is unclear how axSpA affects pregnancy, in terms of prevalence of pregnancy related complications and foetal outcomes. Similarly, studies exploring the effects of pregnancy on axSpA disease activity and medication use have been limited, with divergent conclusions drawn. Studies of women with other forms of inflammatory arthritis have suggested improved disease control during pregnancy with increased risk of postpartum flares. It is unknown if axSpA follows this pattern.

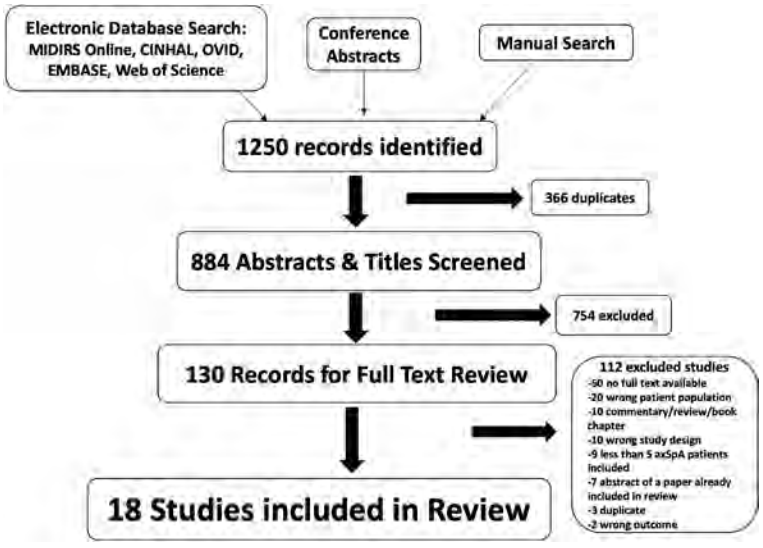

Figure 1. Study Selection

	OR	95% CI	AxSpA Weighted Pooled Mean (%)	Control Weighted Pooled Mean (%)
Cesarean Section	1.85	(1.46, 2.30)	37.3	18.6
Preterm birth	0.84	(0.39, 1.81)	5.5	5.3
Sensitivity Analysis	*1.24*	*(0.94, 1.64)*	8	5.3
Miscarriage	0.75	(0.03, 19.7)	3	3.2
Pre-eclampsia	1.74	(0.85, 3.54)	2.8	2.5
Sensitivity Analysis	*1.3*	*(0.92, 1.82)*	2.1	2.5
Gestational diabetes	0.88	(0.24, 3.21)	4.3	5.7
IUGR	1.17	(0.26, 5.17)	4.3	4.7
PPROM	0.92	(0.2, 4.24)	6.7	N/A
Stillbirth	0.7	(0.26, 1.85)	0.7	1.1

Table 1. Summary of Pregnancy Complications

	OR	95% CI	axSpA Weighted Pooled Mean (%)	Control Weighted Pooled Mean (%)
LBW	1.47	(0.98, 2.21)	6.3	2.9
SGA	1.66	(0.93, 2.95)	8.7	11
Congenital abnormalities	1.34	(0.63, 2.84)	3.4	3
NICU admissions	1.55	(0.96, 2.51)	17.4	11.9

Table 2. Summary of Fetal Complications

Methods: A systematic review of case-controlled trials, observational studies, cross sectional studies and case series (n >5) focusing on axSpA in pregnancy. Studies were compiled by searching EMBASE, Medline (OVID), CINAHL, Maternity and Infant Care (MIDIRS online), and Web of Science from time of inception to September 2019 for key words related to axSpA, pregnancy, and pregnancy complications. Two reviewers independently reviewed articles to determine suitability for inclusion. The Newcastle & Ottawa Scale was used to asses risk of bias. Data extraction was performed using a standardized template to streamline data to allow comparison and meta-analysis. Where suitable data was assessed for suitability for pooling with a random effects model. Statistical heterogeneity was assessed by confidence interval overlap of the odds ratio, chi^2 test output and output of the I^2 statistic. Studies with high heterogeneity were assessed with sensitivity analysis and calculation of a weighted pooled means. The protocol for this review was prospectively registered with an international registry for systematic reviews (PROSPERO, Ref CRD42020147814).

Results: The search strategy returned 884 records. Of these, 130 full text articles were assessed for eligibility. Following assessment by two reviewers, 18 studies with a total of 3,166 axSpA women were eligible for inclusion in this review. There was an increase in the prevalence of pre-eclampsia (OR 1.3, 95% CI 0.92-1.82) and IUGR (OR 1.17, 95% CI 0.26-5.17) and a statistically significant increase in prevalence of cesarean section (OR 1.85, 95% CI: 1.46-2.30) in axSpA females (table 1). Prevalence of all analyzed fetal complications was higher in axSpA pregnancies (table 2), this did not reach significance. Disease activity during pregnancy varied significantly, but overall 47.8% of patients assessed by standardized outcomes reported increased disease activity in pregnancy. Few studies examined medication usage in pregnancy.

Conclusion: Females with axSpA overall have significantly higher prevalence of cesarean section then the general population. This analysis suggests a trend towards higher rates of pre-eclampsia, IUGR and a number of fetal complications, although further research is needed to explore this. There is a risk of active disease in pregnancy for a high proportion of axSpA females. Medication usage varied with time and country. Ongoing development of national registries could help to better understand axSpA in pregnancy.

Disclosure: S. Maguire, None; **T. O'Dwyer**, None; **F. Wilson**, None; **D. Mockler**, None; **F. O'Shea**, None.

Abstract Number: 1324

Risk Factors for Adverse Pregnancy Outcomes in Women with Spondyloarthritis: An Observational Study from Two European Multidisciplinary Pregnancy Clinics

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Women with Spondyloarthritis (SpA) seem at increased risk for adverse pregnancy outcomes (APO), however limited data have been published so far. The aim of this work was to assess pregnancy outcomes and to identify risk factors for APO in SpA pregnancies managed at two high-risk european pregnancy clinics.

Methods: Data on SpA pregnancies prospectively-followed in two centers between 2009-2019 were retrospectively analysed. Pregnancies complicated by APO were compared with uneventful pregnancies for demographic and clinical variables. Active disease was defined as a DAS-28-CRP >3.2 or an ASDAS-CRP > 2.1 according to peripheral or axial dominant disease, respectively.

Results: Ninety-four pregnancies in 82 patients (median age at conception 33 years, IQR 31-37) were analysed: 45 psoriatic arthritis, 23 axial SpA, 18 undifferentiated SpA, 5 enteropathic SpA, 2 reactive arthritis and 1 enthesitis-related juvenile idiopathic arthritis. APO occurred in 39 (41%) pregnancies: 7 (7%) early miscarriages; 6 (7%) preterm births (one < 34 gestational week; four for preterm premature rupture of membranes (PROM)); 2 (2%) PROM; 5 (5%) foetal growth restriction; 2 (2%) malformations – 1 central nervous system malformation leading to medical abortion, 1 case of oesophageal atresia; 14 (17%) small for gestational (SGA) new-borns; and 7 (7%) gestational diabetes. History of inflammatory bowel symptoms (IBS) (p=0.02) and an active disease before conception (OR: 18.3, 1.9-179.9) or during pregnancy (namely at the 2nd and 3rd trimester – OR: 2.7 CI: 1.0-7.2 and OR: 3.2 CI: 1.2-8.5, respectively) were associated with an increased risk for APO (Table 1). Likewise, APO occurred more frequently if a previous use of ≥2 conventional or biological DMARDs (OR: 2.5 CI: 1.05-6.02), suggesting a more aggressive disease phenotype. Although not significant, patients with APO were less often treated with low-dose acetylsalicylic acid (LDASA) during pregnancy. No differences were found regarding maternal age, use of corticosteroids or anti-phospholipid positivity.

Conclusion: The birth of SGA infants was the most frequent APO. History of IBS, a more aggressive disease phenotype and an active disease before conception or during pregnancy increased the risk for APO. Larger studies are warranted to confirm these data and to assess the potential protective role of LDASA.

	Pregnancies with APO N=39	Pregnancies without APO N=55	*p* value
Maternal age at conception, median (IQR), years	34 (32-37)	33 (30-36)	0.2
Axial dominant disease – N, %	10, 26	14, 26	1.0
Peripheral dominant disease – N, %	12, 31	25, 45	0.2
Hx enthesitis – N, %	16, 41	23, 42	0.9
Hx dactylitis– N, %	7, 18	15, 27	0.3
Hx psoriasis– N, %	16, 41	21, 38	0.8
Hx uveitis– N, %	2, 5	7, 13	0.3
Hx IBS – N, %	6, 15	1, 2	**0.02**
Presence of HLA-B27– N, %	14, 50	18, 51	0.9
aPL positivity– N, %	7, 19	8, 15	0.6
Use of ≥2 cs or bDMARDs before conception – N, %	18, 46	14, 25	**0.04**
Ever corticoids in pregnancy – N, %	9, 31	18, 35	0.8
Ever LDASA in pregnancy – N, %	9, 26	21, 41	0.2
Active disease before conception: N, %	11, 92	6, 38	**0.004**
Active disease 1st trimester: N, %	11,33	9, 20	0.2
Active disease 2nd trimester: N, %	15, 58	17, 33	**0.04**
Active disease 3rd trimester: N, %	15, 54	13, 27	**0.02**

Table 1. Differences between patients with and without APO. aPL – antiphospholipid antibodies; APO – adverse pregnancy outcomes; b – biologic; cs – conventional synthetic; DMARDs – disease-modifying anti-rheumatic drugs; Hx – history of; IBS – inflammatory bowel symptoms; LDASA – low-dose acetylsalicylic acid.

Disclosure: A. Cruz-Machado, None; **F. Crisafulli**, None; **S. Barreira**, None; **P. Martins**, None; **M. Gerardi**, None; **M. Filippini**, None; **M. Fredi**, None; **R. Gorla**, None; **M. Lazzaroni**, None; **C. Nalli**, None; **M. Taglietti**, None; **A. Lojacono**, None; **S. Zatti**, None; **M. Centeno**, None; **C. Araújo**, None; **L. Pinto**, None; **F. Franceschini**, None; **A. Tincani**, None; **S. Capela**, None; **L. Andreoli**, None.

Abstract Number: 1325

Monoclonal Gammopathy in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Monoclonal gammopathy of undetermined significance (MGUS) is an asymptomatic premalignant clonal plasma disorder, defined by the **presence of a serum monoclonal protein (M-protein) at a concen-**

Variable	Controls (N=837)	Cases (N=46)	P-value
Gamma	9.79 (3.9)	18.82 (2.3)	**<0.0001**
Age_Psoriasis, mean (SD)	28.53 (14.3	27.04 (15.2)	0.522
Age_PsA, mean (SD)	38.93 (13.7	36.65 (13.8)	0.282
Psoriasis_Duration, mean (SD)	We can not calculate	24.02 (14.6)	We can not calculate
PsA_Duration, mean (SD)		14.41 (10.8)	
Active joint count, median (IQR)	2 (7)	2.5 (7)	0.828
Damage joints #, median (IQR)	4 (10)	7 (24.5)	**0.0343**
ESR(>13 Male; >20 Female) n(%)	247 (29.6)	37 (82.2)	**<0.0001**
Caucasian, n (%)	719 (86.3%)	35 (76.1%)	0.157
Male, n (%)	481 (57.5%)	28 (60.9%)	0.76
Deaths, n(%)	28 (3.3)	3 (6.5)	0.216

Active joint count: Tender +/- Swollen joints *

Table 1.

tration < 30 g/L, a bone marrow (BM) plasma cell percentage < 10%, and absence signs and symptoms related to multiple myeloma (MM). The prevalence of MGUS in psoriatic arthritis (PsA) has been reported to be higher than the general population. However, no follow-up is available to determine whether these patients progress to MM.

Purpose: To determine the current **prevalence of MGUS in the PsA** cohort, evaluate the **outcome** of patients PsA – MGUS and determine any association **of MGUS development and TNF inhibitors**.

Methods: Included were patients followed at the PsA Clinic between January 2008 to January 2018. All patients fulfilled the CLASsification for Psoriatic Arthritis (CASPAR). MGUS was defined as the presence of a discrete band in the gamma- globulin region on at least 2 separate serum protein electrophoresis tests, performed 6 months apart. MM was the outcome of interest. Data extracted from our database included demographic variables, ESR level, use of conventional disease modifying antirheumatic drugs (cDMARD) and Biologic DMARDs (bDMARDs).

Analyses included descriptive statistics [mean (SD) for continuous variables and frequency (percent) for categorical values]. Patients with MGUS were compared to those without using t -test, Wilcoxon test and Fisher test.

Results: Of the 883 patients assessed, **46 (5.3%) had evidence of MGUS on at least 2 separate** blood tests. At the time of diagnosis **55.5%** of patients were already on bDMARDs. Patients with MGUS had mean PsA duration of 14 years, were less likely to use DMARDs (30%), had more damage joints (24%), higher ESR levels (p=0.0001), but equal number of actively inflamed joints compared to the control group. 1 patient evolved to MM. Both groups were similar in gender, race (Caucasian) and ages of PsA and PsO diagnosis.

Conclusion: The prevalence of MGUS among our cohort of patients with PsA was 5.2%, higher than the prevalence in whites (1.5% – 3%), but lower than the 9.7% reported by Eder et al.

Only 1 patient progressed and died of MM, less than that expected in the general population. The presence MGUS was associated with measures of disease activity/severity (higher ESR levels and more damaged joints). There was no relationship to bDMARDs.

Disclosure: V. Ocampo, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5.

Abstract Number: 1326

Malignancy Risk Among Patients with Ankylosing Spondylitis in the United States: A Population-Based National Study

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Increased cancer risk has been reported with Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE), but the correlation is poorly studied in Ankylosing spondylitis (AS).

Objectives: To study the correlation between AS and cancer in the US and to further assess whether the biologic therapy imposes any cancer risk on AS patients.

Methods: This is a retrospective observational study using the IBM Explorys database, a pooled de-identified clinical database of > 60 million unique patients in the US with patient-level data. The Explorys collects aggregated, standardized, and normalized clinical data from different electronic health records automatically updated in near real-time. In Explorys, patient records are mapped into a single set of Unified Medical Language System ontologies to facilitate searching and indexing. Diagnoses, findings, and procedures are mapped into the systematized nomenclature of medicine – clinical terms (SNOMED-CT) hierarchy.

Criteria of AS included at least one visit with a rheumatologist and the diagnosis code of AS (N=14,310) between 2009-2019. We further stratified the cohorts by adding the following variables to the search tool: race, gender, smoking, laboratory data (elevated ESR and CRP, HLA-B27 status), extra-articular manifestations (psoriasis, inflammatory bowel disease or uveitis) and medication use (TNF inhibitors, secukinumab or NSAIDs). The index date was defined as the date of the first-ever malignant neoplastic disease diagnosis occurring after the qualifying AS diagnosis.

The controls group (24,542,770) included adults ≥ 18 years of age with the exclusion of positive ANA, diagnosis of RA, SLE, AS, or vasculitis, and at least one outpatient office visit during the study period. For both groups we excluded the previous diagnosis of cancer prior to 2009. A chi-square test of association was performed between the 2 groups (AS patients and controls) and the odds ratio (OR), its standard error, and the 95% confidence interval (CI) were calculated.

Results: Of the 14,310 patients with AS, only 1300 (9.08%) patients had a cancer diagnosis compared to 2,719,240 controls (11.07%). The AS patients found to have decreased odds of cancer compared to control group (OR 0.9, 95

	AS patients with Cancer (n=1300)	Controls with Cancer (n=2,719,240)
Caucasians	85.38%	82.09%
Males	53.08 %	45.53%
Smokers	30.00%	22.22%
Elevated ESR	44.61%	10.20%
Elevated CRP	44.61%	10.25%
NSAIDs use	76.92%	47.20%

Table 1. Demographics and other features of patients with cancer.

	AS with cancer (n=1300)	AS without cancer (n=11,350)	P value
Male	**690 (53.08%)**	**5690 (50.13%)**	**0.04**
Female	610 (46.92%)	5650 (49.78%)	0.05
Caucasians	**1110 (85.38%)**	**8980 (79.12%)**	**<0.0001**
African American	70 (5.38%)	930 (8.19%)	**0.0004**
Psoriasis	180 (13.85%)	1510 (13.30%)	0.56
IBD	**120 (9.23%)**	**520 (4.58%)**	**<0.0001**
Uveitis	180 (13.85%)	1480 (13.04%)	0.41
Smoking	**390 (30%)**	**2910 (25.64%)**	**0.0007**
Elevated ESR	**580 (44.61%)**	**3490 (30.75%)**	**<0.0001**
Elevated CRP	**580 (44.61%)**	**4240 (37.36%)**	**<0.0001**
HLA B27 positivity	**110 (8.46%)**	**760 (6.7%)**	**0.018**
TNFi	530 (40.77%)	4840 (42.64%)	0.2
Secukinumab	50 (3.85%)	360 (3.17%)	0.19
NSAIDs	**1000 (76.92%)**	**7660 (67.49%)**	**<0.0001**

Table 2. Risk factors for cancer in patients with AS using chi-square test.

% CI: 0.85 to 0.95, P = 0.0003). Demographics and clinical characteristics of AS patients and controls with cancer are shown in table 1. Risk factors for increased cancer risk in AS patients are shown in table 2.

Skin cancers (Squamous cell carcinoma (SCC), malignant melanoma and basal cell carcinoma), and SCC of head and neck were significantly increased in AS patients compared to controls as shown in table 3. Additionally, no significant difference in the skin cancer diagnosis was observed between AS patients who are TNFi-naive and AS patients exposed to TNFi (OR 0.9, 95% CI 0.73 to 1.1, p 0.3).

Conclusion: Our study demonstrated that skin and head neck cancers are more frequently seen in AS patients compared to controls with no rheumatic disease, but the overall cancer risk was found to be lower in the AS patients

Primary malignancy	AS patients with cancer (n=1300)	Controls with cancer (n =2,719,240)	P value
Colon	30 (2.3%)	144,380 (5.31%)	<0.0001
Rectum and anus	10 (0.77%)	74,710 (2.75%)	<0.0001
Intestine	40 (3.08%)	175,880 (6.47%)	<0.0001
Esophagus	10 (0.77%)	20,750 (0.76%)	0.97
Stomach	10 (0.77%)	25,180 (0.92%)	0.57
SCC of head and neck	**50 (3.85%)**	**65,360 (2.40%)**	**0.0006**
Ear, nose and/or throat	10 (0.77%)	57,860 (2.13%)	0.0007
Thyroid	30 (2.3%)	65,550 (2.41%)	0.8
Lung	50 (3.85%)	170,750 (6.28%)	0.0003
Ovary	10 (0.77%)	48,440 (1.78%)	0.006
Uterus	20 (1.54%)	57,150 (2.1%)	0.16
Breast	80 (6.15%)	352,400 (12.96%)	<0.0001
Skin			
Malignant melanoma	**90 (6.92%)**	**133,850 (4.92%)**	**0.0009**
SCC	**110 (8.46%)**	**165,110 (6.07%)**	**0.0003**
BCC	**200 (15.38%)**	**319,480 (11.75%)**	**<0.0001**
Prostate	100 (7.69%)	276,020 (10.15%)	0.003
Bladder	20 (1.54%)	73,900 (2.72%)	0.009
Kidney	40 (3.08%)	68,610 (2.52%)	0.2
Leukemia	20 (1.54%)	81,260 (2.99%)	0.002
Multiple myeloma	20 (1.54%)	37,410 (1.37%)	0.6
Non-Hodgkin Lymphoma	50 (3.85%)	119,080 (4.38%)	0.35

Table 3. Comparing primary malignancies in AS patients and controls using chi-square test.

compared to the controls. Male sex, white race, HLA B27 positivity, h/o IBD, NSAID use, and elevated markers of inflammation were associated with higher odds of cancer in AS patients.

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Abstract Number: 1327

Comorbidity Burden in Patients with Non-Radiographic Axial Spondyloarthritis at Least as High as in Ankylosing Spondylitis

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities

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Session Time: 9:00AM–11:00AM

Table 1. Patient characteristics

	Nr-axSpA n=86	AS n=168
Age, yrs	46 (11)	53 (13)
Male sex, n (%)	33 (38%)	105 (63%)
Symptom duration, yrs	20 (11)	29 (14)
HLA-B27 positive, n (%)	77 (90%)	143 (86%)
Sacroiliitis on plain X-ray, n (%)	0 (0%)	168 (100%)
SI-joint MRI available, n (%)	58 (67%)	79 (47%)
SI-joint bone marrow edema on MRI, n (%) [a]	26 (45%)	41 (52%)
Peripheral arthritis, n (%)	51 (59%)	83 (49%)
Dactylitis, n (%)	15 (17%)	13 (7.7%)
Heel enthesitis, n (%)	39 (45%)	65 (39%)
Level of education		
≤9 yrs, n (%)	6 (7.1%)	25 (15%)
10-12 yrs, n (%)	27 (32%)	39 (23%)
>12 yrs, n (%)	51 (61%)	103 (62%)
Smoking ever, n (%)	23 (27%)	72 (43%)
Current alcohol intake		
<1 standard unit per week	43 (50%)	69 (42%)
1-9 standard units per week	42 (49%)	89 (54%)
>10 standard units per week	1 (1.2%)	8 (4.8%)
Body mass index, kg/m^2	26 (5.0)	27 (4.6)
CRP, mg/L	2.6 (3.0)	4.3 (5.7)
ASDAS-CRP	1.8 (0.9)	1.9 (0.9)
BASDAI	3.0 (2.1)	2.9 (2.2)
BASFI	1.9 (2.1)	2.2 (2.3)
Ongoing NSAID use, n (%)	50 (59%)	101 (61%)
Ongoing csDMARDs, n (%)	18 (21%)	32 (19%)
Ongoing bDMARDs	33 (38%)	70 (42%)

Mean (SD) if not stated otherwise. a Previous or current SI-joint bone marrow edema according to the ASAS definition. Missing data, n (%): Symptom duration 2 (0.8%); HLA-B27 1 (0.4%); Level of education 3 (1.2%); Current alcohol intake 2 (0.8%); CRP 29 (11%); ASDAS-CRP 35 (14%); BASDAI 17 (6.7%); BASFI 19 (7.5%); NSAID use 3 (1.2%). ASAS, Asessment of SponyloArthritis international Society; ASDAS-CRP, ankylosing spondylitis disease activity score using CRP; BASDAI, Bath ankylosing spondylitis disease activity index; BASFI, Bath ankylosing spondylitis functional index; bDMARD, biologic disease-modifying anti-rheumatic drug; CRP, C-reactive protein; csDMARD, conventional synthetic disease-modifying anti-rheumatic drug; HLA, human leukocyte antigen; MRI, magnetic resonance imaging; yrs, years; NSAID, non-steroidal anti-inflammatory drug; SD, standard deviation; SI, sacroiliac.

Table 2. Comorbidity burden

	Nr-axSpA n=86	AS n=168
Myocardial infarction, n (%)	1 (1.2%)	5 (3.0%)
Congestive heart failure, n (%)	0 (0%)	0 (0%)
Peripheral vascular disease, n (%)	1 (1.2%)	0 (0%)
Cerebrovascular disease, n (%)	4 (4.7%)[b]	5 (3.0%)
Dementia, n (%)	0 (0%)	0 (0%)
Chronic pulmonary disease, n (%)	6 (7.0%)	5 (3.0%)
Connective tissue disease (apart from axSpA[a]), n (%)	0 (0%)	1 (0.6%)
Ulcer disease, n (%)	6 (7.0%)	13 (7.7%)
Liver disease, n (%)	1 (1.2%)[c]	1 (0.6%)[c]
Diabetes mellitus, n (%)	5 (5.8%)[d]	5 (3.0%)[d]
Moderate or severe renal disease, n (%)	1 (1.2%)	0 (0%)
Malignancy (solid tumor/leukemia/lymphoma), n (%)	2 (2.3%)	2 (1.2%)[e]
AIDS, n (%)	0 (0%)	0 (0%)
Charlson Comorbidity Index without age-points		
Mean (SD)	0.4 (0.8)	0.3 (0.7)
Median (range)	0 (0-4)	0 (0-6)
Comorbidity-count (n=0-13, according to the above)		
Mean (SD)	0.3 (0.7)	0.2 (0.5)
Median (range)	0 (0-3)	0 (0-3)
Any comorbidity (of the above), n (%)	19 (22%)	34 (20%)

No significant between-group difference in any of the individual comorbidities by Chi2-test / Fisher´s Exact Test, as appropriate. a Systemic lupus erythematous, polymyositis, mixed connective tissue disease, polymyalgia rheumatica or moderate to severe rheumatoid arthritis. b One nr-axSpA patient with hemiplegia. c None with moderate or severe liver disease. d Two AS and one nr-axSpA patient with end organ damage. e One AS patient with metastatic solid tumor. Nr-axSpA, non-radiographic axial spondyloarthritis; AS, ankylosing spondylitis; axSpA, axial spondyloarthritis; SD, standard deviation.

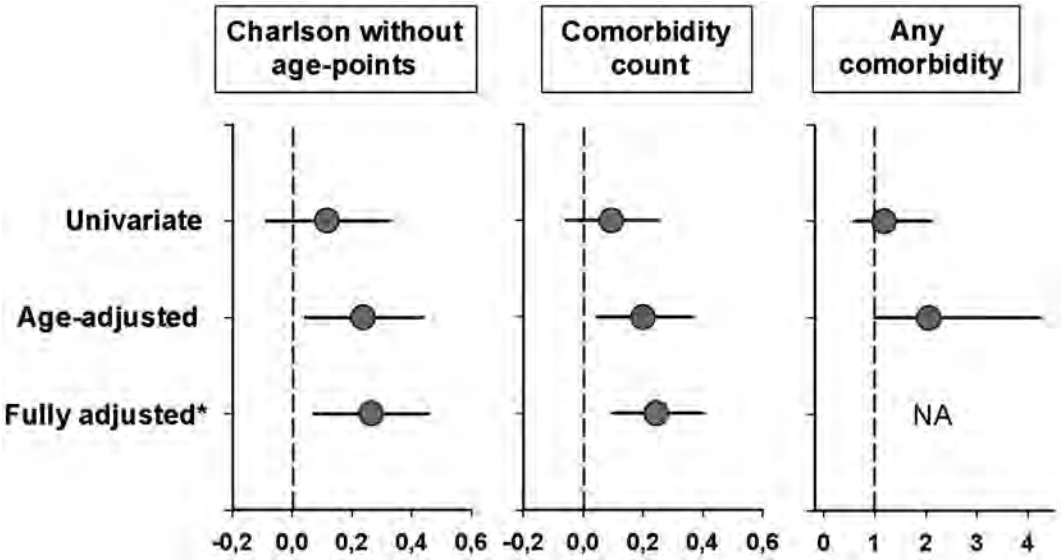

Figure. Differences between patients with nr-axSpA and AS (reference) regarding Charlson comorbidity index without age-points (left panel), comorbidity count (middle panel), and presence of any comorbidity (right panel). For the left and middle panels, data shown represent point estimate differences (dots) with 95% CI (whiskers) from unadjusted analyses, analyses adjusted only for age, and fully adjusted analyses (* adjustment for age, sex, education level, smoking, alcohol habits and body mass index). For the right panel, data shown represent odds ratios (dots) with 95% CI (whiskers) from unadjusted and age-adjusted analyses, respectively (further adjustment not possible due to too few events). NA, non-applicable.

Background/Purpose: Few studies have investigated the overall occurrence of comorbidities in patients with non-radiographic axial spondyloarthritis (nr-axSpA) in relation to ankylosing spondylitis (AS). Compared to nr-axSpA, AS patients are generally older and display higher inflammatory markers in blood, both known risk factors of comorbidity. The Charlson Comorbidity Index (CCI) is a commonly used instrument to assess comorbidity. Originally designed to predict mortality, the CCI assigns weighted points for both comorbidities and age, but can also be used without age-points.[1] The purpose of this study was to compare comorbidity burden between well-characterized patients with nr-axSpA and AS.

Methods: Patients with clinical axial spondyloarthritis diagnoses, consecutively enrolled in a population-based, cross-sectional cohort study, were thoroughly examined and classified as nr-axSpA (ASAS criteria; n=86) or AS (modified New York criteria; n=168). CCI scores without age-points were calculated from patient-reported data and compared between the nr-axSpA and AS groups. Age-points were omitted since we aimed to assess current comorbidity burden, rather than to predict mortality. A corresponding comparison was also conducted regarding the number of CCI associated comorbidities (comorbidity count; n=0-13, without weighted points) reported by each patient. Analyses were performed by linear regression, unadjusted as well as adjusted for age, sex, level of education (proxy for socioeconomic status), smoking, alcohol habits and body mass index. Due to the skewed distribution of CCI scores and comorbidity counts, confidence intervals were calculated by non-parametric bootstrapping with 10,000 iterations. Additionally, the proportion of patients in each group reporting ≥1 comorbidity (as defined by CCI) was compared by logistic regression, unadjusted and adjusted for age (further adjustment not possible due to few events).

Results: Patient characteristics for the nr-axSpA and AS groups are shown in Table 1. Compared to the AS group, nr-axSpA patients were younger and a greater proportion were women. Both groups showed a relatively small total number of comorbidities, and the occurrence of the individual comorbidities did not differ between the groups (Table 2). In unadjusted analyses, CCI without age-points, as well as comorbidity count, were not significantly different between the groups (Figure). However after adjustment for the younger age of the nr-axSpA patients, both CCI without age-points and comorbidity count were found to be significantly higher in the nr-axSpA group, and remained so also in the fully adjusted analyses (Figure). Finally, comparing the proportion of patients having ≥1 comorbidity produced analogous results (Figure).

Conclusion: Our results indicate that in a population-based, cross-sectional setting the burden of serious comorbidities, as assessed by CCI, is at least as high in patients with nr-axSpA as in AS. Despite the well-described lower systemic inflammation in patients with nr-axSpA, our results thus suggest that medical vigilance to target and prevent comorbidities in this group is equally important as in AS.

Reference

1. Charlson ME, et al. J Chron Dis. 1987;40:373-83.

Disclosure: J. Sagard, None; **E. Lindqvist**, None; **E. Mogard**, None; **A. Jöud**, None; **M. Geijer**, AbbVie, 5, Novartis, 5, Pfizer, 5; **T. Olofsson**, Merck Sharp & Dohme, 9, Eli Lilly, 9; **J. K. Wallman**, Abbvie, 5, Celgene, 5, Eli Lilly, 5, Novartis, 5, UCB Pharma, 5.

Abstract Number: 1328

Cardiac Biomarkers Are Associated with the Development of Cardiovascular Events in Patients with Psoriatic Arthritis and Psoriasis

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: N-terminal pro-brain-type natriuretic peptide (NT-proBNP) and troponin I (TnI) are established cardiac biomarkers that predict cardiovascular events (CVEs) and mortality in apparently healthy individuals and at-risk populations. While patients with psoriatic arthritis and psoriasis, collectively termed psoriatic disease (PsD), have an increased risk of developing CVEs, the use of these cardiac biomarkers to predict CV risk has not been investigated in this population. We aimed to evaluate the association between these cardiac biomarkers and incident CVEs, and assess their predictive value beyond the Framingham Risk Score (FRS).

Methods: A longitudinal cohort study was conducted in patients with PsD without prior history of CVEs. NT-proBNP and TnI concentrations were measured using automated clinical assays in the first available serum sample. The study outcome included any of the following CVEs occurring within the first 10 years of biomarker assessment: angina, myocardial infarction, congestive heart failure, transient ischemic attack, cerebrovascular accident, revascularization procedures and CV death. Associations with incident CVEs were analyzed separately for each biomarker using Cox proportional hazards regression models first adjusted for age and sex, and subsequently for the FRS. The added value of cardiac biomarkers to improve predictive performance beyond the FRS was assessed using the area under the receiver operator characteristic curve (AUC), net reclassification index (NRI) and integrated discrimination index (IDI).

Results: A total of 1000 patients with PsD were assessed between 2005 and 2019 (mean age 49 ± 12.8 years, 44.6% female) (**Table 1**). During a mean follow-up of 7.1 years, 72 (7.2%) patients developed incident CVEs. Both TnI (Hazard Ratio (HR) 3.63, 95% Confidence Interval (CI) 1.47, 8.95) and NT-proBNP (HR 1.78; 95% CI 1.16, 2.74) predicted CVEs independently of the FRS (**Figure 1**). The association was stronger in males than females. Including all cardiac biomarkers and the FRS in a single model, both TnI (HR 3.25, 95% CI 1.34, 7.88) and NT-proBNP (HR 1.68, 95% CI 1.12, 2.54) retained statistical significance. When comparing the predictive performance of the base model (FRS alone, AUC 74.3) to the expanded models, there was no significant improvement in any of the predictive indices with the addition of TnI (AUC 72.3, p = 0.26; NRI 0.10, p = 0.51; IDI 0.008, p = 0.29), NT-proBNP (AUC 74.2, p = 0.98; NRI 0.18, p = 0.13; IDI 0.011, p = 0.24), or both TnI and NT-proBNP (AUC 73.6, p = 0.78; NRI 0.23, p = 0.06; IDI 0.019, p =0.09) (**Figure 2**).

Table 1. Baseline characteristics of the study population

Variable	All Patients (n=1000)	Patients without CVE (n=928)	Patients with CVE (n=72)
	Mean ± SD / Frequency (%)		
PsA, no. (%)	648 (64.8)	590 (63.6)	58 (80.6)
PsC, no. (%)	352 (35.2)	338 (36.4)	14 (19.4)
Age (years)	49 ± 12.8	48.1 ± 12.6	60.4 ± 9.6
Male sex, no. (%)	554 (55.4)	510 (55)	44 (61.1)
Disease duration (years)	20.2 ± 14.1	19.8 ± 14	23.2 ± 15.4
Ethnicity, Caucasian (%)	834 (83.4)	768 (82.9)	66 (91.7)
Current smoker (%)	164 (16.4)	152 (16.4)	12 (16.7)
FRS (%)	8.2 ± 8.6	7.4 ± 7.9	17.8 ± 11.1
FRS category:			
• Low risk (<10%)	720 (72)	699 (75.3)	21 (29.2)
• Intermediate risk (10-19%)	176 (17.6)	156 (16.8)	20 (27.8)
• High risk (≥20%)	104 (10.4)	73 (7.9)	31 (43.1)
Diabetes	77 (7.7)	66 (7.1)	11 (15.3)
Hypertension	274 (27.4)	229 (24.7)	45 (62.5)
Use of anti-hypertensive medications (%)	207 (20.7)	171 (18.4)	36 (50)
Use of lipid-lowering medications (%)	100 (10)	81 (8.7)	19 (26.4)
Tender joint count[1]	3.8 ± 7.3	3.8 ± 7.4	3.5 ± 6
Swollen joint count[1]	1.5 ± 3.3	1.6 ± 3.3	1.2 ± 2.7
Damaged joint count[1]	6.2 ± 11.4	5.5 ± 10.6	13.2 ± 16.3
BMI (kg/m^2)	28.7 ± 5.9	28.5 ± 5.9	30.8 ± 6.5
PASI	4.1 ± 6.3	4.1 ± 6.3	4.2 ± 6
NT-proBNP (pg/ml)	63.3 ± 115.9	58.7 ± 104.1	122.6 ± 209
Troponin I (ng/L)	4.4 ± 5.1	4.2 ± 4.3	6.9 ± 10.8
Total Cholesterol (mmol/L)	4.2 ± 0.9	4.2 ± 0.9	4.4 ± 1
Triglycerides (mmol/L)	2 ± 5.4	2 ± 5.6	2 ± 1.2
LDL cholesterol (mmol/L)	1.6 ± 0.5	1.6 ± 0.5	1.7 ± 0.5
HDL cholesterol (mmol/L)	1.2 ± 0.3	1.2 ± 0.4	1.2 ± 0.3
Systolic blood pressure (mmHg)	122.2 ± 16.3	121.3 ± 15.9	133.8 ± 17.1
Diastolic blood pressure (mmHg)	76.8 ± 9.8	76.5 ± 9.8	80.7 ± 8.7
Current use of DMARDs	362 (36.2)	326 (35.1)	36 (50)
Current use of Biologics	214 (21.4)	200 (21.6)	14 (19.4)
Current use of NSAIDs (daily use)	265 (26.5)	240 (25.9)	25 (34.7)
Current use of steroids	23 (2.3)	21 (2.3)	2 (2.8)

[1] Applicable only to patients with psoriatic arthritis

CVE indicates cardiovascular events; DMARD, disease-modifying antirheumatic drug; FRS, Framingham Risk Score; HDL, high-density lipoprotein; LDL, low-density lipoprotein; NSAID, non-steroidal anti-inflammatory drug; NT-proBNP, N-terminal pro-brain-type natriuretic peptide; PASI, Psoriasis Area Severity Index; PsA, psoriatic arthritis; PsC, psoriasis without arthritis

Conclusion: In patients with PsD, elevated NT-proBNP and TnI predict incident CVEs independent of the FRS. We did not observe a significant improvement in the performance of the predictive model when combining these cardiac biomarkers with the FRS.

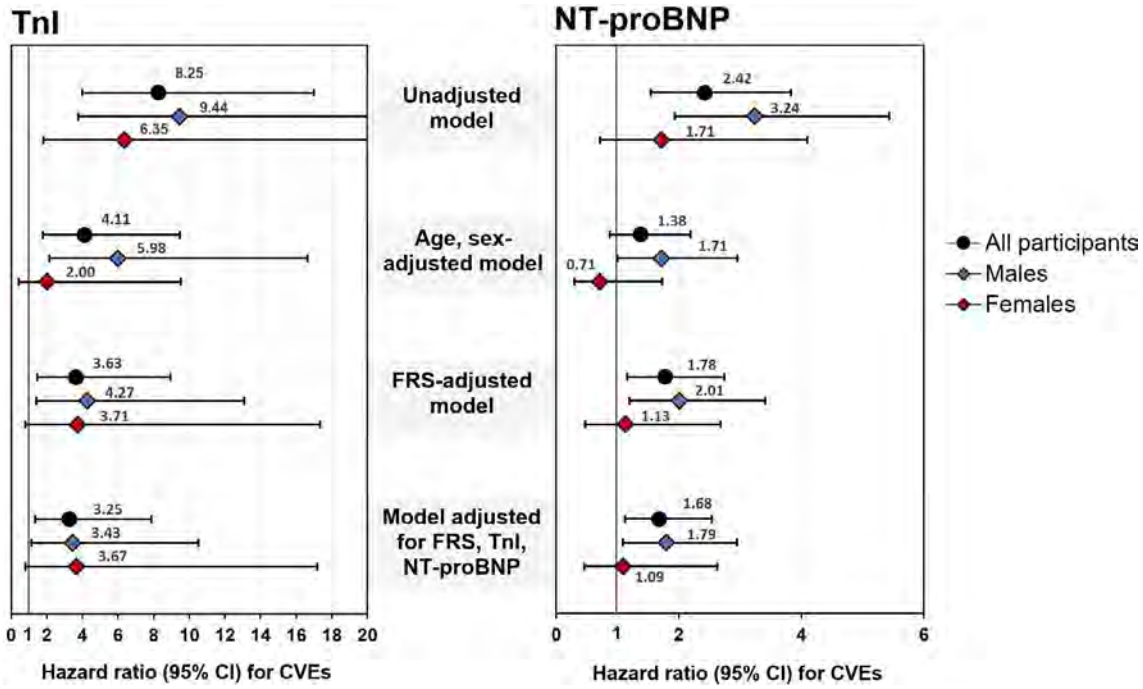

Figure 1. Hazard ratios of cardiac biomarker measures with incident cardiovascular events (n = 1000, 72 events). Error bars denote 95% confidence intervals. CI indicates confidence interval; CVEs, cardiovascular events; FRS, Framingham Risk Score; NT-proBNP, N-terminal pro-brain-type natriuretic peptide; TnI, troponin I.

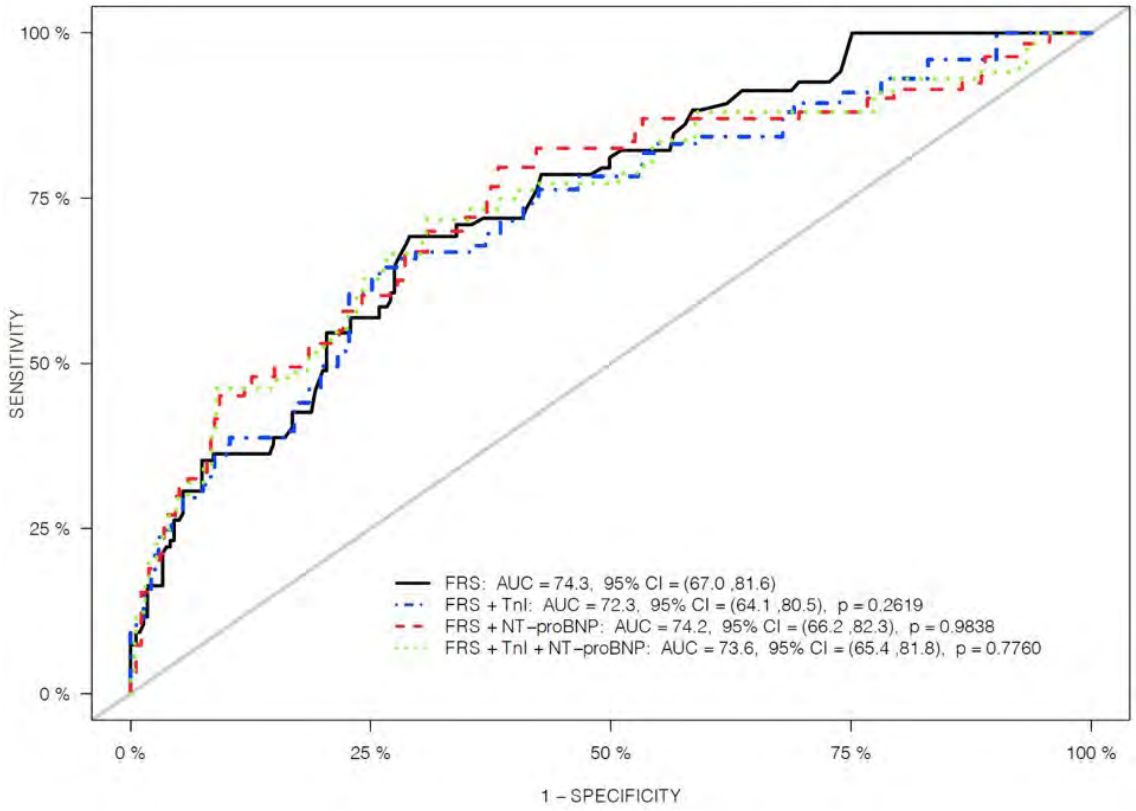

Figure 2. Comparison of the predictive performance of the base model (Framingham Risk Score alone) and expanded models for prediction of cardiovascular events in patients with psoriatic disease. AUC indicates area under the receiver operator characteristic curve; FRS, Framingham Risk Score; NT-proBNP, N-terminal pro-brain-type natriuretic peptide; TnI, troponin I.

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Abstract Number: 1329

Subclinical Atherosclerosis Risk in Psoriatic Arthritis: Could It Be Prevented?

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Table 1: Comparison between patients and controls regarding clinical characteristics and laboratory results

Item	Patient n= 81 Mean ± SD	Control n= 69 Mean ± SD	t	P	S
Age (years)	46.37 ± 7.29	46 ± 7.34	0.31	0.38	NS
BMI (kg/m)	27.39 ± 20.29	28.43 ± 4.17	-1.45	0.075	NS
IL1B (pg/ml)	21.3 ± 5.16	19.39 ± 4.15	2.12	0.02	S
HOMA-IR	2.44 ± 0.71	2.21 ± 0.47	2.28	0.01	S
Insulin (uIU/ml)	12.84 ± 1.54	12.31± 0.85	2.53	0.006	S
CIMT(mm)	0.61 ± 0.1	0.57 ± 0.1	2.84	0.002	S

Table 1. Comparison between patients and controls regarding clinical characteristics and laboratory results.
BMI, body mass index; n, number; SD, standard deviation; IL1-B,interlukin 1-B; HOMA-IR, homeostatic model assessment of insulin resistance; CIMT, carotd intima-media thichkness; kg, kilogram; m, meter; pg, picogram; ml, milliliter; ulU, micro-international unit; mm, millimeter.

Table 2: Correlation between CIMT and some parameters:

Parameter	CIMT		
	r	P	s
ESR(mm/hr)	-0.08	0.45	NS
CRP(mg/dl)	-0.15	0.18	NS
IL1B (pg/ml)	0.285	0.01	S
Insulin (uIU/ml)	0.275	0.013	S
HOMA-IR	0.25	0.023	S

Table 2. Correlation between CIMT and some parameters.
ESR, erythrocyte sedimentation rate; CRP, c-reactive protein; IL-1B, interlukin-1 beta; HOMA-IR, homeostatic model assessment of insulin resistance; CIMT, carotid intima-media thickenss; pg, picogram; ml, milliliter; ulU, micro-international unit; mm, millimeter; mg, milligram; hr, hour; dl, deciliter.

Background/Purpose: Psoriatic arthritis (PsA) is an immune-mediated inflammatory arthritis associated with psoriasis that can cause remarkable joint damage [(1)]. Subclinical cardiovascular disease (CVD) due to subclinical atherosclerosis is accelerated in PsA leading to overt cardiovascular events with increased mortality in those patients[(2)]. Chronic inflammation plays a crucial role in the pathogenesis of atherosclerosis in PsA, together with the conventional risk factors [(3)]. Intima-media thickness of the common carotid artery, evaluated by ultrasonography, is a good indicator of generalized atherosclerosis and coronary artery disease, giving early signs of subclinical atherosclerosis [(4)]. We aimed to investigate the role of interleukin-1 beta (IL-1β), homeostatic model assessment of insulin resistance (HOMA-IR), and insulin level as early predictors of subclinical atherosclerosis in patients with PsA.

Methods: The study included 81 patients with PsA and 69 matched healthy volunteers. Serum IL-1β, HOMA-IR, and insulin levels were assessed. Ultrasonographic measurement of carotid intima-media thickness (CIMT) was done for both common carotid arteries and the mean CIMT was calculated.

Results: Our patients and controls were matched regarding age, sex, and body mass index (BMI) ($P > 0.05$). Our study revealed a statistically significant difference between patients and controls regarding IL-1β, HOMA-IR, insulin level, and CIMT ($p < 0.05$) as illustrated in table (1). There was a statistically significant positive correlation between IL-1β, HOMA-IR, insulin level, and CIMT ($p< 0.05$), however, no significant correlation could be detected between ESR, CRP, and CIMT ($p >0.05$) as shown in table (2).

Conclusion: IL-1β, HOMA-IR, and insulin levels are correlated with CIMT in PsA. So, each of them can be used as a predictor of subclinical atherosclerosis in those patients. Consequently, IL-1β targeted therapy may have a pivotal role in the prevention of subclinical CVD in PsA.

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Disclosure: M. Farouk, None; **S. Moussa**, None; **R. Abdou**, None.

Abstract Number: 1330

Subclinical atherosclertoic disease in ankylosing spondylitis and non-radiographic axial spondyloarthritis. A multicenter study with 806 patients.

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster II: Extra-MSK & Comorbidities
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular (CV) mortality and morbidity is increased in ankylosing spondylitits (AS) as compared to the general population. Carotid plaque, considered as a surrogate marker for atherosclerosis associated with very high CV risk, is more prevalent in AS patients than in healthy controls. Nevertherless, we have no consistent data about subclinical atherosclerosis (SA) in non-radiographic axial spondyloarthritis (nr-axSpA). In this study we assessed the SA in nr-axspA compared with AS in the largest series studied so far, and established a predictive model to identify patients with high CV risk.

Methods: This is a transversal observational study from the AtheSpAin cohort, a Spanish multicenter cohort to study atherosclerosis in axSpA. We compared patients with AS vs those with nr-axSpA according to ASAS criteria. Carotid ultrasound (US) examination was done in all patients, included the measurement of carotid intima-media wall thickness (cIMT) in the common carotid artery and the detection of plaques in the extracranial carotid tree bilaterally, according to the Mannhein consensus. CV risk was calculated according to the systematic coronary risk evaluation (SCORE).

Results: A set of 639 patients with AS and 167 patients with nr-axSpA were recruited in this study. Patients with AS were mainly men, older and had a higher prevalence of cardiovascular risk factors compared to nr-axSpA patients. They also had higher levels of C reactive protein and estimated (CPR) and erythrocyte sedimentation rate (ESR). Comparison of baseline characteristics and clinical features between patients with AS and nr-axSpA is shown in **table 1**. After adjusting data for age, sex and cardiovascular morbidity, no difference in the prevalence of carotid plaques or in the carotid IMT was found between both groups.

We then analyzed the prevalence of carotid plaques in the groups of low and moderate CV risk according to the SCORE, finding no differences between AS and nr-axSpA (10.7 % Vs 10.1%, p=0.9 and 40.5 % Vs 45.5 %, p=0.94 respectively)

Considering the comparable atherosclerotic burden observed in nr-axSpA and AS, we designed a model to identify those patients diagnosed with any of these conditions with very high CV risk because of the presence of carotid plaques. A predictive model which included SCORE plus age, BASFI and ESR at time of disease diagnosis in patients with moderate SCORE showed a high specifity (88%) to detect very high risk patients, but with a limited sensitivity (41%) **table 2**. The AUC of this model was found to have higher discrimination than the SCORE AUC (0.652 Vs 0.592, p= 0,025).

Conclusion: SA disease in patients with nr-axSp is similar to those with AS, despite the higher inflammatory state of the latter. Many patients with axSpA with a moderate risk of CV events according to the SCORE are reclassified into very high risk after carotid US examination. Patients with higher age, ESR at the diagnosis of axSpA and BASFI are more likely to present carotid plaques in US examination.

Table 1. Demographics, cardiovascular risk factors, disease related data, and subclinical atherosclerosis assessment in patients with axial spondyloarthritis and non-radiographic axial spondyloartritis.

	AS	Non-Rx axSPA (total)	
	n=639	n=167	p value[1]
Men/Women, n	460/179	87/80	**0.000**
Age, years	50 ± 12	43 ± 11	**0.000**
History of classic CV risk factors, n (%)			
Current smokers	221 (35)	57 (34)	0.36
Have ever smoked	344 (54)	77 (46)	0.071
Obesity (BMI > 30 kg/m2)	153 (24)	28 (17)	**0.042**
Dyslipidemia	222 (35)	41 (25)	**0.011**
Hypertension	184 (29)	26 (16)	**0.000**
Diabetes Mellitus	49 (8)	6 (4)	0.061
Chronic kidney disease	14 (2)	2 (1)	0.55
Blood pressure, mm Hg			
Systolic	130 ± 17	125 ± 17	**0.001**
Diastolic	80 ± 11	78 ± 10	**0.031**
Total cholesterol, mg/dl	191 ± 39	192 ± 38	0.67
HDL cholesterol, mg/dl	53 ± 15	59 ± 20	**0.001**
LDL cholesterol, mg/dl	116 ± 34	114 ± 30	0.52
Triglycerides, mg/dl	119 ± 75	116 ± 78	0.55
Statins, n (%)			
Disease related data			
CRP, mg/l			
At time of study	2.7 (0.9-7.0)	1.0 (0.5-4.7)	**0.000**
At time of disease diagnosis	4.8 (1.4-12.0)	2.0 (0.6-8.0)	**0.008**
CRP >3 mg/L at time of diagnosis	359 (56)	70 (42)	**0.000**
ESR, mm/1st hour			
At time of study	7 (4-15)	6 (3-13)	0.46
At time of disease diagnosis	14 (6-29)	9 (3-20)	**0.000**
Mean disease duration, years			
Since first symptoms	17 (9-28)	7 (3-13)	**0.000**
Since diagnosis	11 (4-19)	2 (0-7)	**0.000**
HLA-B27 positive, n (%)	460 (72)	106 (63)	**0.002**
BASDAI	3.7 ± 2.3	4.1 ± 2.3	0.065
BASDAI > 4, n (%)	281 (44)	82 (49)	0.23
ASDAS	2.3 ± 1.0	2.3 ± 1.0	0.96
Inactive disease, n (%)	87 (14)	31 (19)	0.19
Low disease activity, n (%)	152 (24)	29 (17)	
High disease activity, n (%)	254 (40)	69 (41)	
Very high disease activity (>3.5), n (%	66 (10)	19 (11)	
BASFI	3.6 ± 2.6	3.4 ± 2.4	0.32
BASMI	2.9 ± 2.1	2.0 ± 1.4	**0.000**
Extraarticular maniphestations, n (%)			
Total	235 (37)	42 (25)	**0.005**
Uveitis	147 (23)	16 (10)	**0.000**
Psoriasis	70 (11)	16 (10)	0.60
Inflammatory bowel disease	43 (7)	11 (7)	0.94
Sinovitis, n (%)	214 (33)	66 (40)	0.14
Enthesitis, n(%)	191 (30)	65 (39)	**0.026**
Hip involvement n (%)	124 (19)	6 (4)	**0.000**
MASES	0 (0-2)	0 (0-3)	**0.011**
Syndesmophytes, n (%)	288 (45)	16 (10)	**0.000**
mSASSS	7 (2-21)	1 (0-4)	**0.000**
Therapy, n (%)			
NSAIDs	520 (81)	139 (83)	0.72
Corticosteroids	82 (13)	19 (11)	0.63
DMARDs	229 (36)	60 (36)	0.99
Anti-TNF	238 (37)	44 (26)	**0.008**
IL-17 inhibitors	14 (2)	2 (1)	0.75
Subclinical atherosclerosis			
Carotid IMT, mm	0.658 ± 0.149	0.588 ± 0.116	**0.000**
Carotid plaques, n (%)	222 (35)	37 (22)	**0.002**
Carotid IMT, mm*			0.13
Carotid plaques, n (%)*			0.54

Data represent means ± SD or median (IQR) when data were not normally distributed. BMI: body mass index; LDL: low-density lipoprotein; HDL: high-density lipoprotein; CRP: C reactive protein. ASDAS-CRP (Ankylosing Spondylitis Disease Activity Score) categories were defined as: disease activity < 1.3 inactivity; ≥ 1.3 to < 2.1 low disease activity; ≥ 2.1 to < 3.5 high disease activity; ≥ 3.5 very high. NSAID: Nonsteroidal anti-inflammatory drugs; DMARD: disease-modifying antirheumatic drug. TNF: tumor necrosis factor; Obesity: BMI >30 kg/m2. BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI Bath Ankylosing Spondylitis Metrology Index. BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; MASES: Maastricht Ankylosing Spondylitis Enthesitis Score. Significants 'p' are depicted in bold. *Adjusted for age, sex and CV comorbidity

Table 2. All the logistic regression model subsets for the prediction of reclassification in patients with axSpA included in the moderate-cardiovascular risk category according to the SCORE prior to carotid ultrasound assessment.

Variables	OR (95% CI)	p	Optimal Cutoff	Sensitivity, %	Specificity, %
Age, years	**1.10 (1.07-1.13)**	**0.000**	52	72	46
BASFI	1.08 (0.99-1.19)	0.081	3.6	67	56
ESR at time disease diagnosi	1.00 (0.99-1.02)	0.48	12	69	48
Pseudo R2	0.112				
AIC	209				
BIC	22				
AUC	0.668				
Sensitivity	41%				
Specificity	88%				
pfitHL	0.203				

Values in bold face are statistically significant. AIC: Akaike information criterion; BIC: Schwarz Bayesian criterion AUC: area under the curve; pfitHL: Hosmer-Lemeshow goodness-of-fit DMARD: disease-modifying antirheumatic drug; BASMI Bath Ankylosing Spondylitis Metrology Index.

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Abstract Number: 1331

Carotid Ultrasound Findings in Psoriatic Arthritis: A Case-control Study

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with psoriatic arthritis (PsA) have an increased risk of cardiovascular disease (CVD). The carotid ultrasound, which measures both carotid intima-media thickness (cIMT) and carotid plaque (CP), is a

Table 1. Clinical and demographic characteristics.			
Variable	PsA (n=69)	Controls (n=69)	*P*
Age(mean±SD)	53.58±10.946	53.86±7.313	NS
Women, n (%)	38(55.1)	59(85.5)	**<0.001**
Obese, n (%)	26(37.7)	28(40.6)	NS
Type 2 Diabetes, n (%)	14(20.3)	9(13)	NS
Hypertension, n (%)	27(39.1)	19(27.5)	NS
Dyslipidemia, n (%)	29(42)	24(34.8)	NS
Active smoker, n(%)	15(21.7)	12(17.4)	NS
Disease duration, median (q25-q75)	5(2.5-8)	-	-
Methotrexate, n (%)	46(66.7)	-	-
Biologics, n (%)	23(33.3)	-	-
DAS28-ESR, (mean±SD)	3.74±1.477	-	-
DAS28-CRP, (mean±SD)	2.43±1.088	-	-
DAPSA, median (q25-q75)	35(27.5-58.5)	-	-

Table 2. Carotid ultrasound findings.			
Variable	PsA (n=69)	Controls (n=69)	*P*
Any carotid plaque, n (%)	27(39.1)	17(24.6)	NS
Right carotid plaque, n (%)	18(26.1)	8(11.6)	**0.049**
Left carotid plaque, n (%)	19(27.5)	15(21.7)	NS
Increased cIMT, n (%)	9(13)	1(1.4)	**0.017**
Right cIMT, median (q25-q75)	0.58(0.46-0.76)	0.6(0.51-0.69)	NS
Left cIMT, median (q25-q75)	0.58(0.5-0.73)	0.61(0.54-0.78)	NS

non-invasive tool useful in the identification of subclinical atherosclerosis[1]. However, carotid ultrasound differences between PsA patients and general population have not yet been well described.

The aim of this study is to compare the carotid ultrasound characteristics in PsA patients with controls.

Methods: This cross-sectional study included 69 PsA patients that fulfilled the CASPAR (Classification Criteria for Psoriatic Arthritis) criteria and 69 controls matched by age and comorbidities. Patients with a history of previous atherosclerotic CVD (ischemic heart disease, cerebrovascular accident or peripheral arterial disease) and pregnancy were excluded. A clinical history and blood tests were performed. Carotid B-mode ultrasonography was used for measurements of cIMT and the presence of plaques. *Increased cIMT was defined as ≥0.9 mm to 1.1 mm. CP was defined* as a *focal narrowing ≥0.5 mm of the surrounding* lumen or a *cIMT ≥1.2 mm.* Descriptive analysis was done with frequencies (%), mean (±SD) and median (q25-q75), and comparisons with Chi square, Student´s t and Mann-Whitney U tests.

Results: A total of 138 subjects were included. Clinical and demographic characteristics are shown in Table 1. Increased cIMT and right carotid plaque were significantly more prevalent in PsA patients compared to controls

(p=0.017 and p=0.049, respectively). No significant differences were found in the prevalence of carotid plaque and in the intima-media thickness between groups.

Conclusion: Patients with psoriatic arthritis have a higher cardiovascular risk, as proven by the increased cIMT found on carotid ultrasound results. Therefore, it is opportune to perform a carotid ultrasound in patients with PsA to attain an optimal management of the disease.

The rheumatologist must acknowledge the importance of performing a complete cardiovascular evaluation to provide a correct treatment to diminish future cardiac events.

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Abstract Number: 1332

Identifying the as Patient at Risk: Is Aortic Root Diameter Associated with HLA-B27?

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

Background/Purpose: Ankylosing spondylitis (AS) is an inflammatory joint disease (IJD) associated with cardiac involvement particularly aortic valve regurgitation (AVR). AVR in AS is caused by inflammation of the aortic root and valves. Furthermore, HLA-B27 genotype is strongly associated with AS and with cardiac diseases in non-rheumatic patients. Therefore, the question arises whether HLA-B27 genotype results in an increased risk of developing AVR and aortic root dilatation in AS patients. In this study, we investigated the association between the aortic root diameter in HLA-B27 positive (+) versus HLA-B27 negative (-) patients in AS patients from the CARDAS cohort.

Methods: The CARDAS study is a cross-sectional study in AS patients between 50-75 years who were recruited from a large rheumatology outpatient clinic. Patients underwent cardiovascular screening including echocardiography, with 2D, spectral and colour flow Doppler. The aortic root was measured at sinuses of Valsalva during diastole. The aortic root diameter was corrected for body surface area (BSA) (aortic root index, cm/ m^2).

Results: 193 Consecutive AS patients were included of whom 158 (82%) HLA-B27 positive. HLA-B27+ and HLA-B27- AS subjects had a comparable disease duration, respectively 36 (±11) and 30 (±14) years, and a moderate disease activity assessed with the ASDAS-CRP, respectively 2.1 (±1.0) and (2.3 ±1.0). The aortic root index was higher in HLA-B27+ patients compared to HLA-B27- patients, respectively 1.76 ± 0.21 mm vs. 1.64 ± 0.14 mm, p< 0.001. Furthermore, HLA-B27+ AS patients compared to HLA B27- AS patients had more often aortic root dilatation (≥2.1 cm/

Table 1. Echocardiographic parameters

	HLA-B27 +	HLA-B27 -	p value
Echocardiography			
Aortic root, cm	3.35 ±0.43	3.25 ±0.28	0.12
Aortic root index, cm/m²	1.76 ±0.21	1.64 ±0.14	<0.001*
Aortic root dilatation (≥2,1 cm/m²)	11 (8)	1 (3)	0.3
Aortic regurgitation	34 (22)	8 (24)	0.8
Trace	13 (8)	3 (9)	
Mild	18 (12)	5 (15)	
Moderate	4 (3)	0	
Severe	1 (1)	0	
Prothesis	1 (1)	0	
Mitral regurgitation	52 (34)	17 (49)	0.25
Mild	49 (32)	16 (46)	
Moderate	3 (2)	1 (3)	
Severe	0 (0)	0 (0)	
Prothesis	0 (0)	0 (0)	

Values are displayed as mean ± standard deviation (SD) or frequencies with corresponding percentages (%). No cases of aortic valve stenosis and only one case of mitral valve stenosis were assessed. * Significance level of p ≤0.05.

m^2), respectively 11 (8%) and 1 (3%), p=0.3 (table 1). The presence of aortic root dilatation in HLA-B27+ AS patients was strongly associated with aortic valve regurgitation, p=0.003. Regression analysis showed a significant association between HLA-B27 and aortic root index corrected for age, sex and cardiovascular risk factors, B 0.091 (95%CI 0.015-0.168), p=0.02. Furthermore, male HLA-B27+ patients had a significant increased aortic root index compared to male HLA-B27- AS patients, respectively 1.76 (1.63-1.88) and 1.59 (1.53-1.68), p< 0.001.

Conclusion: In conclusion, our study demonstrates an increased aortic root index in elderly HLA-B27+ AS patients, specifically in male patients. Although, this did not result in an increased prevalence of aortic valve regurgitation in this subgroup, inflammation of the aortic root and valve in chronic inflammatory disease is progressive and may progress to severe complications. Therefore, to identify AS patients patient at risk for cardiac disease, we recommend echocardiographic monitoring in elderly male HLA-B27+ AS. Future studies should assess cost effectiveness of cardiologic screening in this subgroup.

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Abstract Number: 1333

Ankylosing Spondylitis Patients at Risk of Developing Aortic Valve Regurgitation, Need for Mandatory Echocardiography?

Milad Baniaamam[1], Sjoerd C. Heslinga[2], Laura Boekel[1], M. Louis Handoko[3], Thelma C. Konings[3], Otto Kamp[3], Vokko P. van Halm[4], J. Christiaan van Denderen[1], Irene van der Horst-Bruinsma[2] and **Mike Nurmohamed**[5], [1]Reade, Amsterdam, Netherlands, [2]Department of Rheumatology, Amsterdam UMC, location VU University Medical Centre, Amsterdam, Netherlands, [3]Department of Cardiology, Amsterdam UMC, location VU University Medical Centre, Amsterdam, Netherlands, [4]Department of Cardiology, Amsterdam UMC, location VU University Medical Centre, Amsterdam, [5]Amsterdam Rheumatology and immunology Center, location Reade and Amsterdam UMC, VU medical center, Amsterdam, Netherlands

SESSION INFORMATION

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Background/Purpose: The overall mortality rate in ankylosing spondylitis (AS) patients is increased by 60–90% compared with the general population. This higher mortality rate is predominately caused by cardiovascular disease (CVD) comprising an increased prevalence of cardiac diseases such as valvular heart disease, conduction disturbances and cardiomyopathies as well as atherosclerotic diseases such as myocardial infarctions. However, there is a lack of contemporary studies. Therefore, we investigated current prevalences of cardiac disorders in a well characterized cohort of Dutch patients with AS compared to osteoarthritis (OA) controls.

Methods: We performed a cross-sectional study in AS and OA patients between 50-75 years. Subjects were recruited from a large rheumatology outpatient clinic (Reade) in Amsterdam, the Netherlands. Patients underwent echocardiography with 2D, spectral and Color Doppler imaging. The echocardiogram was evaluated by an experienced and certified cardiologist. Diastolic dysfunction was assessed according to the ASE/EACVI 2016 guideline. Furthermore, blood sample, surveys and physical examination were done. Disease activity and function were measured with the BASFI, BASDAI and the ASDAS-CRP.

Results: A total of 193 consecutive AS patients were included with a median age of 60 (±7) years of which 72% men (138). The control group consisted of 70 OA patients (table 1). In the AS cohort the disease activity measures , BASDAI, ASDAS-CRP and BASFI, indicated moderate disease activity and were, respectively 3.1 (1.6-5.0), 2.1 (±1.0) and 3.5 (1.7-5.7). Anti-TNF was used by 43% of the AS patients. History of cardiovascular disease (CVD), i.e. angina pectoris, myocardial infarction, stroke and/or peripheral ischemia was comparable between the AS and OA cohort, respectively 9% (17) and 10% (7), p=0.81. Antihypertensives were significantly more often used in AS patients, 85

Table 1. Patient characteristics

	AS	OA	p
N	193	70	
Men (n, %)	138 (72)	40 (57)	0.028*
Age (years)	60 ±7	63 ±7	0.004*
Disease activity			
BASDAI	3.1 (1.6-5.0)	-	
ASDAS-CRP	2.1 ±1.0	-	
BASFI	3.5 (1.7-5.7)	-	
CVD			
History of CVD* (n, %)	17 (9)	7 (10)	0.81
Antihypertensives (n, %)	85 (44)	19 (27)	0.02
Aortic valve regurgitation (n, %)	41 (22)	7 (10)	0.04*
Trace (n, %)	16 (9)	6 (9)	
Mild (n, %)	23 (12)	6 (9)	
Moderate (n, %)	1 (1)	0	
Severe (n, %)	1 (1)	0	
Prosthesis (n, %)	1(1)	0	
Mitral valve regurgitation (n, %)	68 (36)	21 (33)	0.59
Diastolic dysfunction (n, %)	7 (3)	2 (3)	0.86

* Angina pectoris, myocardial infarction, stroke and/or peripheral ischemia

(44%) vs 19 (27%), p=0.02. Prevalences of systolic dysfunction and diastolic dysfunction did not differ significantly in AS and OA patients, respectively 6 (5%) vs 2 (5%), p=0.96 in systolic dysfunction and 7 (3%) vs 2 (3%), p=0.86 in diastolic dysfunction. Prevalence of aortic valve (AV) regurgitation was significantly higher in AS patients compared to OA patients, respectively 41 (22%) and 7 (10%), mostly with mild severity. The prevalence of mitral valve (MV) regurgitation did not differ between the AS and OA patients, respectively 68 (36%) vs 21 (33%), p=0.59. When corrected for age, gender and cardiovascular risk factors in a regression analysis, AS patients still had a substantially increased risk for AV regurgitation, odds ratio (OR) 2.8 95%CI 1.1-7.2, p=0.038.

Conclusion: This study demonstrates an almost tripled risk for developing AV regurgitation in Dutch AS patients. Although mostly mild in this age, due to the progressive nature of AV regurgitation in AS, echocardiographic screening should be considered in elderly AS patients.

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Abstract Number: 1334

Does Interstitial Lung Disease Represent a Real Comorbidity in Spondyloarthritis Patients? Results from an Ultrasound, Monocentric, Pilot Study

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Background/Purpose: Background: Interstitial lung disease (ILD) is a frequent complication in rheumatoid arthritis (RA) where it represents the most common extra-articular involvement (with a prevalence of about 10-60%) and the second cause of mortality (after cardiovascular diseases). Spondyloarthritides (SpA) are chronic arthritides that share with RA both a similar disease burden and similar therapeutical approaches. ILD evaluation is challenging, given the low sensitivity of X-ray and pulmonary function tests, and radiation linked to repetitive HRCT. Lung Ultrasound (LUS) has shown potential in the evaluation of ILD in autoimmune diseases. The aim of this study was to assess the prevalence of ILD in a cohort of SpA patients (pts) using LUS with respect to healthy controls (HC).

Methods: Consecutive SpA out-pts were examined by LUS, applying the definition for pleural line irregularity (PLI) recently provided by the OMERACT taskforce for LUS in systemic sclerosis (1). Seventy-one intercostal spaces were studied (14 in the anterior chest, 27 lateral and 30 posterior) in all the pts/HC using an Esaote MyLab25 Gold US

Tab I: average PLI score (N±DS)

	Total	Anterior	Posterior	Lateral
HC	10.3 ± 7.7	4 ± 3.2	5 ± 3.7	1.4 ± 2.2
PsA	20.1 ± 12.5	6.8 ± 3.9	10.2 ± 6.9	2.9 ± 4.1
AS	22.1 ± 10.7	7 ± 2.8	12 ± 9.5	3 ± 3.1

machine with a linear 7.5-10 MHz probe. The scoring system by Pinal-Fernandez et al (2) was applied and a total pleural score was calculated. Each patient answered to Italian-validated PROs on respiratory function (Leicester and Saint-George), global health (SF-36) and dyspnea (mMRC scale). Clinical data on disease-duration, disease-onset, disease-activity (at the moment of the examination) and MTX/biologics treatment were collected from the medical records.

Results: Fifty-six SpA pts (35 psoriatic arthritis -PsA- and 21 ankylosing spondylitis -AS-) and 56 HC were studied. No significant differences were demonstrated between groups (SpA vs HC and PsA vs AS) for age, sex, BMI and smoking habits. The total pleural score was significantly higher in SpA pts than in HC (20.9+-11.8 vs 10.3+-7.7; $p< 0.001$). A positive correlation was found between total PLI score and PLI score from anterior, posterior and lateral chest. The posterior part of the chest showed a higher PLI score than the anterior and lateral one (with the latter resulting to be significantly lower than the posterior PLI score). Higher differences in the PLI average value between SpA pts and HC were registered for posterior and anterior part of the chest. No differences were found between PsA and AS (with a not statistically significant difference in the posterior PLI score, which was slightly higher in AS pts) (Tab.I).

Conclusion: LUS examination shows a higher amount of PLI in SpA with respect to HC. References: 1- Delle Sedie A et al. Ann Rheum Dis 2019;78(Suppl 2):A834 2- Pinal-Fernandez I et al. Clin Exp Rheumatol 2015;33(4 Suppl 91):S136-41

Disclosure: A. Delle Sedie, None; **E. Calabresi**, None; **I. Romagnoli**, None; **L. Carli**, None; **M. Mosca**, None.

Abstract Number: 1335

Smoking, but Not Use of Complementary and Alternative Medicine Predicts Residual Functional Disability in Patients with Inflammatory Arthritis on Biologic Disease Modifying Anti-Rheumatic Drugs: Results from the Singapore National Biologics Register

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Background/Purpose: To describe the demographic and clinical characteristics of patients with inflammatory arthritis (IA) initiating biologic disease modifying anti-rheumatic drugs (bDMARD) who use complementary and alternative medicine (CAM), and determine the impact of CAM on predicting residual functional disability at six months, as measured by the modified Health Assessment Questionnaire (mHAQ).

Methods: A prospective inception cohort study of all patients ≥ 21 years old initiating a bDMARD for IA after July 2016 was conducted in three public-sector hospitals in Singapore. Baseline and follow-up data were obtained via face-to-face or telephonic questionnaires and abstraction from medical records. Baseline characteristics were compared using chi-square test for categorical variables; and t-test and Wilcoxon signed-rank test for continuous variables in gaussian and non-gaussian distributions respectively. CAM as a predictor of mHAQ ≥ 1 at six months after

Table 1: Baseline characteristics*				
Variable	**Total (N=299)**	**Ever-CAM users (N=93)**	**CAM non-users (N=204)**	**P-value+**
Age, years	49.0 ± 13.4	49.5 ± 13.5	48.8 ± 13.4	0.68
Male sex, no. (%)	107 (36.2)	39 (41.9)	68 (33.5)	0.16
Race, no. (%)				<0.001
Chinese	209 (70.4)	84 (90.3)	125 (61.3)	
Indian	40 (13.5)	3 (3.2)	37 (18.1)	
Malay	33 (11.1)	5 (5.4)	28 (13.7)	
Others	15 (5.1)	1 (1.1)	14 (6.9)	
Body mass index, kg/m^2	26.1 ± 5.9	24.5 ± 4.5	26.8 ± 6.3	0.002
Education level, no. (%)				0.08
Degree or Diploma	141 (47.6)	46 (50.0)	95 (46.6)	
Secondary or Vocational	107 (36.2)	26 (28.3)	81 (39.7)	
None or Primary	48 (16.2)	20 (21.7)	28 (13.7)	
English-speaking, no. (%)	236 (79.5)	61 (65.6)	175 (85.8)	<0.001
Married, no. (%)	191 (64.3)	60 (64.5)	131 (64.2)	0.96
Public Housing, no. (%)	242 (81.5)	73 (78.5)	169 (82.8)	0.37
In paid employment, no. (%)	203 (69.0)	66 (71.7)	137 (67.8)	0.50
Ever smoker, no. (%)	60 (20.2)	26 (28.0)	34 (16.7)	0.02
Alcohol use, no. (%)	71 (24.0)	31 (33.7)	40 (19.6)	0.009
Financial assistance, no. (%)				
Government	175 (58.5)	55 (59.1)	120 (58.8)	0.96
Self	128 (42.8)	35 (37.6)	92 (45.1)	0.23
Insurance	43 (14.4)	8 (8.6)	35 (17.2)	0.05
Voluntary welfare organisation	5 (1.7)	0 (0)	5 (2.5)	0.13
Others	29 (9.7)	8 (8.6)	21 (10.3)	0.65
Study site, no. (%)				0.001
Site A	141 (47.2)	47 (50.5)	94 (46.1)	
Site B	74 (24.8)	32 (34.4)	40 (19.6)	
Site C	84 (28.1)	14 (15.1)	70 (34.3)	
Clinical diagnosis, no. (%)				0.19
Rheumatoid arthritis	137 (45.8)	44 (47.3)	91 (44.6)	
Axial spondyloarthritis	69 (23.1)	27 (29.0)	42 (20.6)	
Psoriatic arthritis	68 (22.7)	17 (18.3)	51 (25.0)	
Other spondyloarthritis	25 (8.4)	5 (5.4)	20 (9.8)	
Disease duration, months, median [IQR]	12.7 [4.7, 38.5]	15.1 [5, 47.1]	12.7 [4.7, 38.5]	1.0
No previous biologic use, no. (%)	145 (71.4)	68 (73.9)	145 (71.4)	0.66
TNFi as index biologic, no. (%)	223 (75.3)	68 (73.9)	155 (76.0)	0.70
Baseline DAS-28	4.6 ± 1.2	4.7 ± 1.1	4.5 ± 1.2	0.42
Baseline BASDAI	4.7 ± 2.2	4.1 ± 1.9	5.0 ± 2.3	0.05
Baseline mHAQ, median [IQR]	0.4 [0.1, 0.9]	0.4 [0.1, 0.8]	0.5 [0.3, 0.9]	0.19
Co-morbidities, no. (%)				
Hyperlipidemia	119 (40.3)	34 (37.4)	85 (41.7)	0.49
Hypertension	93 (31.4)	29 (31.5)	64 (31.4)	0.98
Diabetes mellitus	42 (14.2)	12 (13.0)	30 (14.8)	0.69
Cardiovascular disease	20 (6.7)	2 (2.2)	18 (8.8)	0.04
Chronic kidney disease	8 (2.7)	5 (5.4)	3 (1.5)	0.05
CCI, no. (%)				0.47
CCI = 1	135 (48.2)	42 (49.4)	91 (47.2)	
CCI = 2	71 (25.4)	19 (22.4)	52 (26.9)	
CCI = 3	48 (17.1)	13 (15.3)	35 (18.1)	
CCI ≥ 4	26 (9.3)	11 (12.9)	15 (7.8)	

*Missing data have been omitted from % calculations. Plus-minus values are means ± standard deviation (SD). + P-values are for differences between CAM users and non-users and were calculated by chi-square test for categorical variables, and by t-test for normally distributed continuous variables and Wilcoxon signed-rank test for non-normally distributed continuous variables. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CAM, complementary and alternative medicine; CCI, Charlson's Co-morbidity Index; DAS-28, Disease Activity Score in 28 joints; IQR, interquartile range; mHAQ, modified Health Assessment Questionnaire; TNFi, tumour necrosis factor inhibitor.

Table 2: Predictors of modified Health Assessment Questionnaire score ≥1 at 6-months follow-up				
Predictor	**Univariate**		**Multivariate**	
	OR (95% CI)	**P-value**	**OR (95% CI)**	**P-value**
Age, years				
Bottom tertile, 22–44 years	1 (ref)	-	1 (ref)	-
Middle tertile, 45–56 years	2.16 (0.75 – 6.24)	0.15	0.20 (0.003 – 14.5)	0.47
Top tertile, 57–79 years	1.49 (0.49 – 4.56)	0.48	<0.001 (5.3E-10 – 0.34)	0.03
Females (vs males)	2.90 (0.95 – 8.81)	0.06	57.5 (0.06 – 53694.5)	0.25
Race				
Chinese	1 (ref)	-	1 (ref)	-
Malay	2.82 (0.90 – 8.84)	0.08	0.34 (0.003 – 38.7)	0.65
Indian	2.90 (0.99 – 8.47)	0.05	0.18 (0.004 – 8.08)	0.38
Others	1.13 (0.13 – 9.62)	0.91	<0.001 (4.8E-11 – 8.52)	0.10
Body mass index, kg/m^2				
Normal or underweight, < 25kg/m^2	1 (ref)	-	1 (ref)	-
Overweight, 25–29.9kg/m^2	0.72 (0.23 – 2.25)	0.57	7.07 (0.13 – 378.4)	0.34
Obese, ≥ 30kg/m^2	2.51 (0.96 – 6.55)	0.06	383.9 (0.66 – 224810.6)	0.07
Married (vs not married)	0.37 (0.16 – 0.87)	0.02	1.35 (0.09 – 20.5)	0.83
In paid employment (vs not)	0.22 (0.09 – 0.53)	0.001	0.05 (7.3E-4 – 3.21)	0.16
Ever-smokers (vs non-smokers)	1.87 (0.72 – 4.86)	0.20	938.9 (3.20 – 275884.1)	0.02
Ever-drinkers (vs non-drinkers)	0.66 (0.21 – 2.03)	0.47	-	-
Ever-CAM users (vs non-users)	0.40 (0.13 – 1.22)	0.11	0.05 (7.8E-4 – 3.06)	0.15
Self-funded (vs not)	0.35 (0.13 – 0.91)	0.03	0.20 (0.008 – 5.33)	0.34
Study site				
Site A	1 (ref)	-	1 (ref)	-
Site B	2.20 (0.75 – 6.46)	0.15	19.0 (0.48 – 750.5)	0.12
Site C	1.03 (0.39 – 2.77)	0.95	0.59 (0.02 – 14.5)	0.74
Clinical diagnosis				
Rheumatoid arthritis	1 (ref)	-	1 (ref)	-
Axial spondyloarthritis	0.10 (0.01 – 0.82)	0.03	<0.001 (2.1E-53 – 8.2E37)	0.75
Psoriatic arthritis	0.98 (0.38 – 2.50)	0.96	0.03 (0.003 – 2.07)	0.10
Other spondyloarthritis	0.39 (0.05 – 3.25)	0.39	0.22 (0.002 – 29.3)	0.54
Disease duration, months	1.00 (0.99 – 1.01)	0.74	-	-
TNFi as index biologic (vs non-TNF)	0.18 (0.07 – 0.43)	<0.001	0.04 (6.1E-4 – 2.88)	0.14
No previous biologic use (vs previous use)	0.35 (0.15 – 0.81)	0.01	0.32 (0.02 – 4.58)	0.40
Baseline DAS-28†	1.37 (0.89 – 2.10)	0.15	-	-
Baseline BASDAI†	2.01 (1.07 – 3.78)	0.03	-	-
Baseline mHAQ	8.21 (3.68 – 18.3)	<0.001	252.2 (5.34 – 11899.2)	0.005
CCI‡				
CCI = 1	1 (ref)	-	1 (ref)	-
CCI = 2	0.99 (0.28 – 3.47)	0.99	0.03 (1.8E-4 – 4.26)	0.16
CCI = 3	2.15 (0.69 – 6.71)	0.19	268.3 (0.76 – 94414.3)	0.06
CCI ≥ 4	2.18 (0.60 – 8.01)	0.24	237.4 (1.22 – 46184.4)	0.04

Variables were included in the multivariable model if they were significant at P ≤ 0.2 on univariate analysis. † Not included in the multivariable model due to collinearity with mHAQ. ‡ Hypertension and hyperlipidemia were statistically significant in the univariate analysis as well, but not included in the multivariate model due to collinearity with CCI. BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; CAM, complementary and alternative medicine; CCI, Charlson's Co-morbidity Index; DAS-28, Disease Activity Score in 28 joints; mHAQ, modified Health Assessment Questionnaire; TNFi, tumour necrosis factor inhibitor.

starting a bDMARD was analysed using multivariate logistic regression, adjusting for other baseline characteristics. Further, interaction of CAM use and smoking was tested.

Results: 299 patients (36.2% males, 70.4% Chinese) of mean (SD) age 49.0 (13.4) years were recruited. 45.8% had rheumatoid arthritis with a mean (SD) Disease Activity Score in 28-joints (DAS-28) of 4.6 (1.2). 54.2% had a spondyloarthropathy with a mean (SD) Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) of 4.7 (2.2). The

median (IQR) disease duration was 12.7 (4.7, 38.5) months, with a median (IQR) mHAQ of 0.4 (0.1, 0.9). 93 patients were current or prior CAM users, most commonly acupuncture (64.5%), powder (46.2%), tablets (36.6%), herbs (33.3%), suction (19.4%). Compared to non-users, CAM users had a lower mean body mass index (24.5 vs 26.8kg/m^2, p=0.002), were less likely to be English-speaking (65.5% vs 85.8%, p< 0.001), more likely to be smokers (28.0% vs 16.7%, p=0.02) and to drink alcohol (33.7% vs 19.6%, p=0.009), and less likely to have cardiovascular disease (2.2% vs 8.8%, p=0.04) (Table 1). Of the 223 patients with 6-month follow-up data, 27.4% were no longer on their index bDMARD. mHAQ was available for 206 patients, median (IQR) 0.1 (0, 0.5), 12.1% with mHAQ ≥ 1. There was no association of CAM use with high mHAQ and no interaction with smoking. Advanced age (odds ratio [OR] < 0.001 [95% CI 5.3E-10 – 0.34]), smoking (OR 938.9 [95% CI 3.20 – 275884.1]), baseline mHAQ (OR 252.2 [95% CI 5.34 – 11899.2]) and Charlson's Co-morbidity Index (CCI) score of ≥ 4 (OR 237.4 [95% CI 1.22 – 46184.4]) were independent predictors of high mHAQ (Table 2).

Conclusion: CAM use was not associated with high mHAQ at 6 months. Association with advanced age may be attributable to a tendency for elderly patients to under-report scores. Smoking was an independent predictor of residual functional disability at 6 months, even after adjusting for age, comorbidity and baseline mHAQ. More emphasis on smoking cessation may be useful to improve long-term functional outcomes in IA patients on bDMARDs.

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Abstract Number: 1336

Bone Mineral Density, Trabecular Bone Score and Proximal Femur 3D-DXA Analysis in Psoriatic Diseases

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Background/Purpose: current data regarding areal bone mineral density (aBMD) in patients with psoriasis (PsO) or psoriatic arthritis (PsA) are conflicting. Results on Trabecular Bone Score (TBS) in these patients are lacking. 3D-analysis of cortical and trabecular bone from hip DXA is a new method for non-invasive bone structure assessment, providing separate assessment of the cortical layer and trabecular macrostructure.

Methods: Case-control study (NCT02849795) in which 52 PsO and 52 PsA cases (CASPAR criteria) were each paired to a control subject matched for age, sex and body mass index (BMI). aB MD measurements at (L2-4) lumbar spine (LS), femoral neck (FN) and total hip (TH) were performed using DXA, Lunar GE. TBS was calculated from antero-posterior L2-L4 BMD image using TBS iNsight V1.8 (Med-Imaps, Pessac, France). 3D-SHAPER software (version 2.10, Galgo Medical S.L, Barcelona, Spain) was used to derive a 3D analysis from the hip DXA scans.

Results: LS and TH aBMD measurements did not differ between patients with PsO or PsA and their respective controls. Left FN BMD was higher in patients with PsO compared to controls (p = 0.028), a difference not observed on the

	PsA (N = 52)	PsA controls (N = 52)	PsO (N = 52)	PsO controls (N = 52)
Age (years)	52.5 ± 11.7	52.8 ±11.1	50.5 ± 12.8	50.7 ± 12.8
Sex (M/F)	25/27	25/27	38/14	36/15
Menopausal women	18 (67%)	16 (59%)	5 (36%)	8 (50%)
BMI (Kg/m²)	27.4 ± 5.9	27.7 ± 6.4	28.4 ± 5.8	28.2± 6.1
PASI	2.4 ± 4.1		8.4 ± 4.9	
CPDAI	7.4 ± 3.3			
ESR (mm/h)	19.8 ± 16.6 ***	6.9 ± 5.8	10.7 ± 8.8 ***	6.4 ± 6.4
CRP (mg/L)	10.5 ± 11.7 ***	3.9 ± 4.8	5.9 ± 9	4.7 ± 5.4
LS (L2-4) aBMD (g/cm²)	1.27 ± 0.49	1.2 ± 0.2	1.25 ± 0.2	1.2 ± 0.18
FN aBMD (g/cm²)				
right	0.96 ± 0.12	0.94 ± 0.14	0.98 ± 0.15	0.98 ± 0.15
left	0.96 ± 0.16	0.93 ± 0.12	1.0 ± 0.14 *	0.97 ± 0.13
TH aBMD (g/cm²)	1 ± 0.16	1 ± 015	1.11 ± 0.22	1.06 ± 0.2
L2-L4 TBS	1.32 ± 0.1	1.32 ± 0.15	1.23 ± 0.15 *	1.3 ± 0.16
Cortical sBMD (left FN) (mg/cm²)	169.7 ± 32.8	163.05 ± 29.7	182.0. ± 30.9 *	173.4 ± 30.3
Cth intertrochanteric (left FN) (mm)	1.91 ± 0.2	1.94 ± 0.2	2.03 ± 0.23 *	1.97 ± 0.2
Cth shaft (left FN) (mm)	2.98 ± 0.31	3.01 ± 0.3	3.19 ± 0.3 *	3.09 ± 0.3
cortical sBMD (left FN) (mg/cm²)				
neck	135.27 ± 26.9	129.67 ± 21.9	140.29 ± 24.2 *	134.6 ± 22.5
intertrochanteric	162.32 ± 31.1	155.3 ± 29.3	171.39 ± 29.1*	163.1 ± 28.9
shaft cort	269.2 ± 49	257.1 ± 47.3	286.2 ± 47.5 *	272.7 ± 45.2

Table 1:

patients' clinical characteristics, areal bone mineral density (lumbar spine, femoral neck, total hip), trabecular bone score and proximal femur DXA-derived 3D analysis in patients with psoriatic arthritis and their paired controls and in patients with psoriasis and their paired controls

PsA : psoriatic arthritis ; PsO : psoriasis ; M: male; F : female; BMI: body mass index; PASI : psoriasis area severity index ; CPDAI : composite psoriatic disease activity index ; ESR : erythrocyte sedimentation rate ; CRP : C-reactive protein ; aBMD : areal bone mineral density ; LS: lumbar spine; FN : femoral neck ; TH: total hip; TBS: trabecular bone score; sBMD : surface bone mineral density; Cth : cortical thickness.

Quantitative data are mean ± standard deviation.

* and *** : paired *t* test comparing patients with psoriatic arthritis or psoriasis alone to their respective controls.

* $p < 0.05$; *** $p < 0.001$.

right FN. TBS was similar in PsA patients and their controls while decreased values were observed in PsO patients ($p = 0.04$). In 3D analysis, none of the parameters differed between patients with PsA and their controls. For patients with PsO, no difference was found with the controls for 3D-DXA parameters from the right FN, while total hip cortical surface BMD (sBMD) of the left FN was higher in PsO compared to their controls ($p = 0.037$). Similarly, cortical thickness (Cth) of the intertrochanteric and shaft regions of the left FN was also higher in PsO ($p = 0.032$ and $p = 0.033$). Finally, analysis by region (neck, intertrochanteric and shaft) showed higher values for cortical sBMD from each region of the left FN in the patients with PsO (all $p < 0.05$).

Conclusion: Our results showed comparable aBMD, TBS and 3D proximal femur parameters in patients with PsA and controls. This supports that PsA population is not at increased risk of osteoporosis. In patients with PsO, while LS bone microarchitecture seems impaired, FN displayed better cortical parameters than the controls. Although these results seem marginal, they support the fact that patients with PsO are not at high risk for osteoporosis and hip fracture.

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Relationship of the Pro12Ala Polymorphism of the PPARg Gene with Inflammatory Activity, Osteoporosis and Obesity in Patients with Psoriatic Arthritis

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SESSION INFORMATION

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Background/Purpose: In the pathogenesis of psoriatic arthritis (PsA), increased inflammatory cytokines lead to increased RANGO-L activity and stimulation of osteoclasts, leading to osteoporosis. This comorbidity, closely related to other inflammatory joint diseases, has not been so documented in patients with PsA. Obesity is a frequent comorbidity in patients with PsA, in addition to being the basis of the metabolic syndrome, it affects the activity of the disease and

	C/C (Pro/Pro)	C/G (Pro/Ala)	P
Age	44,34(8,42)	44,88 (8,03)	0,82
Sex (Male/Female)	63/41	11/11	0,36
Tabaco(Active/Ex/No)	28/44/32	6/9/7	0,99
Physical activity	28,10(2,92)	28,12(2,41)	0,99
Dairy measures	2,43 (1,14)	3,40 (3,13)	0,14
BMI	27,27(4,02)	27,82(4,11)	0,77
25OHD(ng/mL)	24,13(13,24)	20,15(12,06)	0,49
PNP1 (ng/mL)	47,85(27,10)	41,19(17,90)	0,45
β-CrossLabs(ng/mL)	0,34(0,20)	0,32(0,16)	0,76
SJP	1,04 (1,03)	1,36(0,79)	0,16
ESR	16,62(14,32)	21,42(17,72)	0,27
CRP (mg/dL)	0,46(0,06)	0,73(0,96)	0,25

Table 1

the response to treatment. PPAR g is a nuclear receptor that behaves like a ligand-activated transcription factor, involved in processes such as inflammation, adipogenesis, or bone metabolism. **Objective:** Relate PPARg polymorphism (rs1801282) with osteoporosis, inflammatory activity, and obesity in a group of patients with psoriatic arthritis (PsA).

Methods: We analyzed the Pro12Ala polymorphism of the PPARg gene in 126 patients with PsA. To assess osteoporosis, bone mineral density in the spine and hip (BMD) and markers of bone formation and resorption (PNP1 and β-CrossLabs respectively) were measured. As variables that influence BMD, the units of dairy consumed daily, smoking (non-smokers, ex-smokers, and active smokers) and physical activity were measured. Inflammatory activity was measured by the number of swollen joints (SJP), the rate of globular sedimentation (ESR) and the C-reactive protein (CRP). For obesity, the body mass index (BMI) was measured. All patients with any disease or treatment that could alter phospho-calcium metabolism were excluded.

Results: 82.5% of the patients presented a homozygous C / C genotype (Pro / Pro), the rest a heterozygous C / G genotype (Pro / Ala). The baseline characteristics of the patients, the factors that influence BMD, BMI, markers of bone formation and resorption, and the inflammatory variables are shown in Table 1.

Patients carrying the alanine allele showed a lower BMD in the hip compared to those carrying the proline allele (0.84 + 0.07 vs. 0.89 + 0.12; $p < 0.01$). We did not find this significance for BMD in the lumbar spine (0.96 + 0.6 vs. 1.01 + 0.16; $p = 0.34$).

Conclusion: The alanine allele of the Pro12Ala polymorphism of the PPARg gene may represent, in patients with PsA, a genetic marker related to osteoporosis. Studies with a larger sample size can demonstrate whether this effect is due to a direct action on the bone or associated with an increase in inflammation.

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Abstract Number: 1338

Identification of Muscle Associated Key Genes to Support Axial Spondyloarthritis Diagnosis by Transcriptomic Approach, the MyoSpA Study

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Background/Purpose: Early diagnosis of axial Spondyloarthritis (axSpA) represents a major clinical challenge nowadays. Increasing evidence has determined that early diagnosis, prompt treatment initiation and early achievement of remission are the best predictors of long-term clinical, functional and radiographic outcomes. New tools to support the diagnosis and new therapeutic targets are needed.

This study aims to identify differentially expressed genes, overall and focusing in genes related with muscle function, that may improve the current clinical diagnosis approach for early axSpA and new therapeutic targets.

Methods: A cross-sectional study was conducted on 48 participants, 24 patients with axSpA (according to ASAS criteria) and 24 Healthy Controls, matched by gender, age and levels of physical activity. Peripheral blood samples were collected and RNA-Seq technology was performed. Normalization of raw data, and identification of differentially expressed genes was obtained using edgeR and limma-voom R packages. Gene Set Enrichment Analysis (GSEA) and Functional Enrichment analysis using Gene ontology (GO) and Kyoto Encyclopedia of Genes and Genomes (KEGG) annotations were also performed. A number of Differently Expressed Genes were highlighted.

Results: 76 genes were identified as being significantly differentially expressed between patients and controls. In detail, 59 downregulated (2 genes have Logfold change more than 1) and 17 upregulated genes (2 genes have Logfold change more than 1) are highlighted. These genes are mostly involved in Innate Immune Signalling and JAK/STAT pathways; some of them were already identified as conferring susceptibility for axSpa, as MICA, TLR5 and SOC3. In addition, several genes with functions of skeletal muscle development (gene1), muscle contraction (gene2) and formation of branched actin networks (gene3), were also identified.

Conclusion: The evidence disclosed that regulation of muscle development and contraction may be also engaged in physiopathology mechanisms of axSpA. Upon validation, these new findings could open new perspectives for diagnosis and therapeutic in axSpA.

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Abstract Number: 1339

COVID-19 in Patients with Inflammatory Arthritis: A Prospective Study on the Effects of Comorbidities and DMARDs on Clinical Outcomes

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Background/Purpose: The COVID-19 pandemic has quickly emerged as the most challenging global health crisis in a generation. Affecting initially China, New York City (NYC) quickly became the epicenter. Data has been scarce

for populations at the highest risk of infection, most notably immunosuppressed patients with underlying chronic inflammatory diseases or chronic use of anti-cytokine biologics and/or other immunomodulatory therapies. We aimed to characterize the hospitalization and death rates among patients with inflammatory arthritis (IA; rheumatoid arthritis and spondyloarthritis) affected by COVID-19 and to analyze the associations between comorbidities and immunomodulatory medications and infection outcomes.

Table. Comparison of baseline characteristics, medication use, and disease course in ambulatory and hospitalized IA patients with confirmed or highly suspected COVID-19 infection*

Characteristic	Total (n = 103)	Ambulatory (n = 76)	Hospitalized (n = 27)	p-value
Age- mean (range)	52.7 [28-88]	49.7 [28-82]	61.0 [34-88]	<0.001
Female- n (%)	74 (71.8)	56 (73.7)	18 (66.7)	0.65
Race- n (%)				0.88
White	65 (63.1)	48 (63.2)	17 (63.0)	
Black	15 (14.6)	10 (13.2)	5 (18.5)	
Asian	10 (9.7)	7 (9.2)	3 (11.1)	
Other	11 (10.7)	9 (11.8)	2 (7.4)	
Hispanic ethnicity- n (%)	17 (16.5)	12 (15.8)	5 (18.5)	0.98
COVID-19 positive- n (%)	80 (77.7)	53 (69.7)	27 (100.0)	0.003
COVID-19 suspect- n (%)	23 (22.3)	23 (30.3)	0 (0.0)	0.003
Primary Inflammatory Arthritis Diagnosis- n (%)				
Spondyloarthritis	56 (54)	47 (62)	9 (33)	0.02
Rheumatoid Arthritis	47 (46)	29 (38)	18 (67)	0.02
IA Disease Severity Prior to COVID-19 symptom onset				
In remission	24 (23)	18 (24)	6 (22)	1.00
Mild	39 (38)	28 (37)	11 (41)	0.90
Moderate	35 (34)	26 (34)	9 (33)	1.00
Severe	3 (3)	2 (3)	1 (4)	1.00
Body Mass Index- mean (SD)	28.7 (6.2)	28.1 (5.5)	30.5 (7.6)	0.08
Comorbidities- n (%)				
Congestive heart failure	4 (3.9)	2 (2.6)	2 (7.4)	0.60
Hypertension	24 (23.3)	11 (14.5)	13 (48.)	0.001
Diabetes	10 (9.7)	5 (6.6%)	5 (18.5)	0.16
Chronic obstructive pulmonary disease	5 (4.9)	1 (1.3)	4 (14.8)	0.02
Asthma	15 (14.6)	12 (15.8)	3 (11.1)	0.78
Severe kidney disease	1 (1.0)	0(0.0)	1 (3.7)	0.59
Chronic medications- n (%)				
ACE inhibitor /ARB	22 (21.4)	12 (15.8)	10 (37.0)	0.04
Any medication for primary IA diagnosis	97 (94.2)	70 (92.1)	27 (100.0)	0.31
Methotrexate	35 (34.0)	24 (31.6)	11 (40.7)	0.53
Hydroxychloroquine	13 (12.6)	7 (9.2)	6 (22.2)	0.16
Oral glucocorticoids	13 (12.6)	3 (3.9)	10 (37.0)	<0.001
Any biologic or JAK inhibitor	73 (70.9)	56 (73.7)	17 (63.0)	0.42
Tumor Necrosis Factor inhibitor	40 (38.8)	34 (44.7)	6 (22.2)	0.07
IL-17 blocker	18 (17.5)	16 (21.1)	2 (7.4)	0.19
IL-23 and IL12/23 blockers	5 (4.9)	5 (6.6)	0 (0.0)	0.40
JAK inhibitor	11 (10.7)	4 (5.3)	7 (25.9)	0.009
Relevant Medication Dose—mean (SD)				
Methotrexate	16.4 (5.5)	16.0 (5.9)	17.2 (4.8)	0.56
Oral glucocorticoids	10.0 (8.1)	17.5 (13.9)	7.7 (4.5)	0.06
COVID-19 Symptoms- n (%)				
Fever	86 (83.5)	64 (84.2)	22 (81.5)	0.98
Cough	81 (78.6)	60 (78.9)	21 (77.8)	1.00
Shortness of breath	65 (63.1)	42 (55.3)	23 (85.2)	0.01
Rhinorrhea	29 (28.2)	26 (34.2)	3 (11.1)	0.04
Sore throat	31 (30.1)	26 (34.2)	5 (18.5)	0.20
Diarrhea	147 (45.6)	38 (50.0)	9 (33.3)	0.21
Anosmia	44 (42.7)	38 (50.0)	6 (22.2)	0.02
Ageusia	50 (48.5)	43 (56.6)	7 (25.9)	0.01
Days from first symptom to hospital, mean (SD)			6.1 (3.9)	
Regular floor—n (%)			22 (81.5)	
Supplementary O2—n (%)			18 (66.7)	
Intensive care unit level care/mechanical ventilation—n (%)◊			4 (14.8)	
Death—n (%)◊			4 (14.8)	

* IA= inflammatory arthritis; ACE= angiotensin converting enzyme; ARB= angiotensin II receptor blockers; IL= interleukin; JAK= Janus Kinase; O2= oxygen.

◊ Of the four patients in the ICU, there were three death and one complete recovery. One other death occurred in unknown levels of care while hospitalized.

Methods: Recruitment stemmed from a larger NYU Langone Health study, namely Web-based Assessment of Autoimmune, Immune-Mediated, and Rheumatic Patients during the COVID-19 Pandemic (WARCOV). WARCOV is a prospective cohort of patients with established diagnosis of immune mediated inflammatory disease. Participants were referred from 46 NYU affiliated providers throughout NYC. Clinical, demographic, maintenance treatment, and disease course data and outcomes of individuals with IA with symptomatic COVID-19 were prospectively assessed via web-based questionnaire, individual phone calls, and electronic medical record review. Baseline characteristics and medication use were summarized for hospitalized and ambulatory patients, and outcomes were compared for each medication class using multivariable logistic regression.

Results: A total of 103 patients with IA were included in the study (n=80 confirmed and n=23 highly suspicious for COVID-19). 26% of participants required hospitalization, and 4% died. Patients who warranted hospitalization were significantly more likely to be older ($P< 0.001$) and have comorbid hypertension ($P=0.001$) and chronic obstructive pulmonary disease ($P=0.02$) (Table). IA patients taking oral glucocorticoids had a higher likelihood of being admitted for COVID-19 ($P< 0.001$) while those on maintenance anti-cytokine biologic therapies did not. After adjusting for age and sex, hypertension and oral glucocorticoid use remained significant risk factors for hospitalization (OR 3.33, 95% CI 1.16 to 9.60, $P=0.03$ and OR 21.12, 95% CI 4.09 to 109.03, $P<0.001$, respectively). Patients with rheumatoid arthritis were more likely to be hospitalized compared to those with spondyloarthritis, but were also older and more likely to be on oral glucocorticoids.

Conclusion: In patients with underlying IA, COVID-19 outcomes were worse in patients receiving glucocorticoids but, importantly, not in patients on maintenance anti-cytokine therapy. As with non-IA patients, age and hypertension were also associated with hospitalization. However, given our limitations of a relatively small number of hospitalizations and likely confounding by indication, caution should be taken in the interpretation of these results. Further work, currently underway, is needed to better understand whether immunomodulatory therapies affect COVID-19 incidence and its natural history.

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Abstract Number: 1340

Secukinumab Improves Pain, Morning Stiffness, Fatigue and Physical Function in Tumor Necrosis Factor Inhibitor-Naïve Patients with Non-Radiographic Axial Spondyloarthritis: Results from a Randomized Controlled Phase III Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with non-radiographic axial spondyloarthritis (nr-axSpA) suffer from comparable disease burden to patients with ankylosing spondylitis/radiographic axSpA (AS/r-axSpA), including inflammatory back pain, morning stiffness, fatigue, and reduced spinal mobility.[1] Secukinumab 150 mg has demonstrated sustained improvement in the signs and symptoms in patients with AS over 4 years.[2] Here, we report a post hoc analysis evaluating the effect of secukinumab treatment on back pain, morning stiffness, fatigue, and physical function in tumor necrosis factor inhibitor naïve (TNFi-naïve) patients with nr-axSpA from the PREVENT study (NCT02696031).

Methods: This study included patients with nr-axSpA receiving either subcutaneous secukinumab 150 mg with loading (LD), without loading (NL), or placebo (PBO).[3] Patients with inadequate response to treatment were permitted to switch to open-label secukinumab 150 mg or standard of care (TNFi) after Week 20 based on clinical judgement of disease activity by the investigator and the patient. This post-hoc analysis assessed nocturnal back pain scores (on visual analog scale [0–100]; ASAS outcome component), morning stiffness (overall level; on visual analog scale [0-10] ASAS outcome component), FACIT-Fatigue and SF-36 PCS scores in TNFi-naïve patients. Continuous values were imputed as mixed-effect model repeated measures (MMRM; valid under the missing at random assumption) for mean

Endpoints	Week	Secukinumab LD (N=164)	Secukinumab NL (N=166)	Placebo (N=171)
Nocturnal Back Pain[1]	BL[4]	70.81 (17.86)	70.86 (16.03)	70.29 (14.67)
	4[5]	-24.35 (2.00)§	-23.07 (1.99)‡	-16.67 (1.96)
	16[5]	-30.93 (2.23)†	-31.91 (2.22)†	-20.27 (2.19)
	52[6]	-40.9 (31.03)	-43.3 (29.93)	-
Overall Level of Morning Stiffness[1]	BL[4]	7.59 (1.66)	7.31 (1.95)	7.11 (1.60)
	4[5]	-2.62 (0.20)§	-2.49 (0.20)§	-1.73 (0.20)
	16[5]	-3.30 (0.22)†	-3.34 (0.22)†	-2.20 (0.22)
	52[6]	-4.55 (3.00)	-4.52 (2.74)	-
FACIT-Fatigue[2,3]	BL[4]	21.79 (9.28)	24.85 (10.60)	23.96 (9.87)
	16[5]	9.10 (0.74)†	8.61 (0.74)§	5.25 (0.73)
	52[6]	11.97 (11.70)	11.05 (10.95)	-
SF-36 PCS[2,3]	BL[4]	32.88 (7.72)	33.83 (7.06)	33.68 (6.69)
	16[5]	7.17 (0.61)†	6.66 (0.61)§	4.26 (0.60)
	52[6]	10.04 (10.78)	9.06 (9.60)	-

‡p<0.001, §p<0.01 and ‡p<0.05 vs. placebo.
[1]At Week 52 - number of evaluable patients were 139 for LD and 146 for NL groups; number of patients switched to open-label secukinumab 150 mg were 67 for LD and 68 for NL groups for both pain and morning stiffness.
[2]At Week 52 - number of evaluable patients were 146 for LD and 154 for NL groups; number of patients switched to open-label secukinumab 150 mg were 69 for LD and 71 for NL groups for fatigue and physical function.
[3]FACIT-Fatigue and SF-36 PCS was assessed at baseline and Weeks 16 and 52.
[4]Mean (SD) presented at BL (as observed).
[5]Mean change from BL (SE) using mixed model repeated measures at Weeks 4 and 16. For continuous variables, MMRM analysis was done only till Week 20.
[6]Mean change from BL (SD) as observed at Week 52.

BL, baseline; FACIT, Functional Assessment of Chronic Illness Therapy; LD, with loading dose; N, number of patients randomized; NA, not available; NL, without loading dose; SD, standard deviation; SE, standard error; SF-36 PCS, Short Form-36 Physical Component Summary; TNFi, Tumor Necrosis Factor inhibitor.

Table 1. Mean change from baseline up to Week 52 in TNFi-naïve population

Endpoints, % Responders	Week	Secukinumab LD (N=164)	Secukinumab NL (N=166)	Placebo (N=171)
Nocturnal Back Pain[1]	4	32.9	28.3	27.5
	16	47.6§	46.4§	30.4
	52[a]	65.5	69.9	-
Overall Level of Morning stiffness[1]	4	60.4§	59.6‡	46.8
	16	67.1‡	66.3‡	54.4
	52[a]	79.1	85.6	-
FACIT-Fatigue[2,3]	16	71.3†	62.0‡	49.7
	52[a]	74.0	77.9	-
SF-36 PCS[2,3]	16	65.9	64.5	58.5
	52[a]	75.3	75.3	-

†p<0.001, §p<0.01 and ‡p<0.05 vs. placebo.
Data presented using non-responder imputation at Weeks 4 and 16.
[a]Data presented as observed at Week 52.
[1]At Week 52 - number of evaluable patients were 139 for LD and 146 for NL groups; number of patients switched to open-label secukinumab 150 mg were 67 for LD and 68 for NL groups for both pain and morning stiffness.
[2]At Week 52 - number of evaluable patients were 146 for LD and 154 for NL groups; number of patients switched to open-label secukinumab 150 mg were 69 for LD and 71 for NL groups for fatigue and physical function.
[3]FACIT-Fatigue, SF-36 PCS was assessed at Weeks 16 and 52.

Table 2. Proportion of patients meeting MCID criteria up to Week 52 in TNFi-naïve population

change from baseline through Week 16 and as observed at Week 52. Minimal clinically important difference (MCID) data were assessed using non-responder imputation through Week 16 and as observed at Week 52.

Results: Overall, 501 TNFi-naïve patients were included in this analysis (LD, N=164; NL, N=166; PBO, N=171). Up to 64% of placebo and approximately 50% secukinumab treated patients switched to open label secukinumab 150 mg between Week 20 - 52. Secukinumab-treated patients vs PBO ($p< 0.05$) demonstrated a higher mean reduction from baseline in nocturnal back pain and morning stiffness, both at Weeks 4 and 16 which was sustained at Week 52 (**Table 1**). Also, improvements in secukinumab-treated patients vs PBO ($p< 0.05$) were reported in FACIT-Fatigue and SF-36 PCS scores from baseline at Weeks 16 and 52 (**Table 1**). At Week 16, a higher proportion of secukinumab-treated patients met the MCID criteria vs PBO ($p< 0.05$) across pre-specified efficacy assessments, which was sustained at Week 52 (**Table 2**).

Conclusion: Secukinumab provided clinically meaningful improvement in back pain, morning stiffness, fatigue, and physical function in TNFi-naïve patients with nr-axSpA over 52 weeks.

References

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3. Deodhar A et al. *Arthritis Rheumatol.* 2019;71 (suppl 10):L21.

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Abstract Number: 1341

Improvement in Patient-Reported Outcomes in Patients with Psoriatic Arthritis with Inadequate Response to Non-Biologic DMARDs Treated with Upadacitinib versus Placebo or Adalimumab: Results from a Phase 3 Study

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patient-reported outcomes (PROs) are important when evaluating treatment benefits in PsA. We present an analysis of PRO data from the SELECT-PsA 1 study.

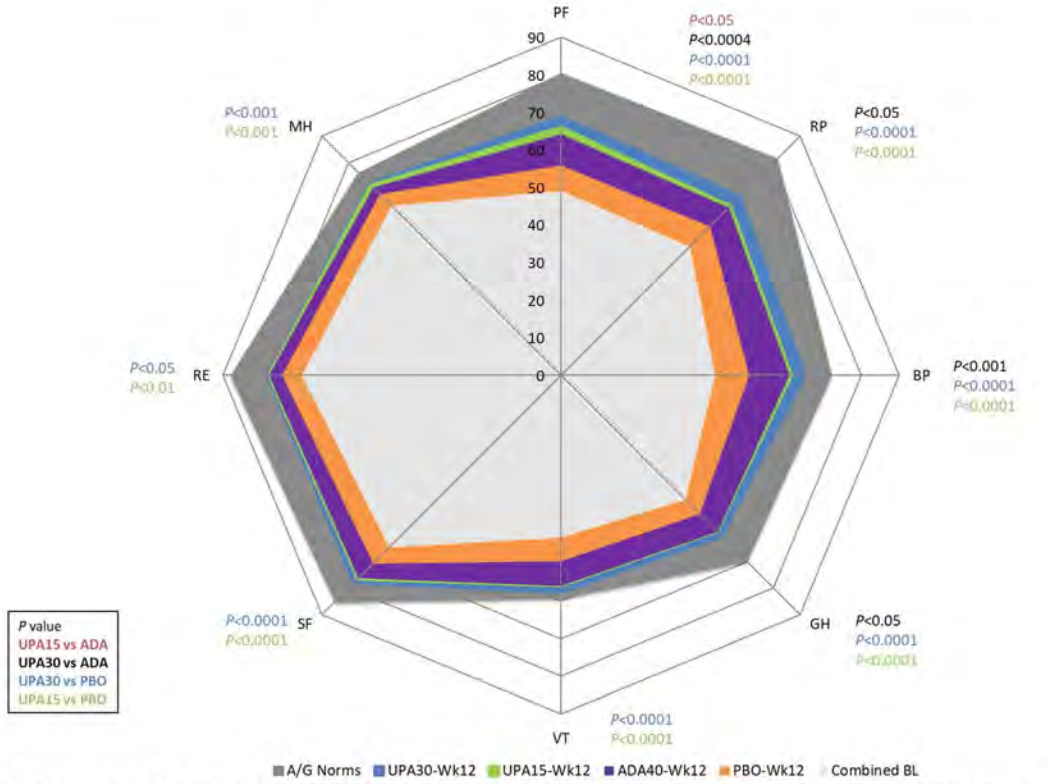
Methods: SELECT-PsA 1 (NCT03104400) is a Phase 3, randomized, placebo- (PBO) and active-controlled trial in patients with active PsA and inadequate responses to ≥1 non-biologic DMARD. Eligible patients were randomized to receive upadacitinib (UPA) 15 mg once daily (QD), UPA 30 mg QD, adalimumab (ADA) 40 mg every other week, or PBO for 24 weeks, with the primary endpoint assessment at Week 12. PROs included: Patient Global Assessment of Disease Activity (PtGA), Patient's Assessment of Pain, HAQ-Disability Index (HAQ-DI), Functional Assessment of Chronic Illness Therapy-Fatigue, 36-Item Short-Form Health Survey (SF-36), EuroQoL-5 Dimension, 5 level, Self-Assessment of Psoriasis Symptoms (SAPS), Work Productivity and Activity Impairment, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and morning stiffness (items 5 and 6 from the BASDAI). BASDAI was assessed in patients with presence of psoriatic spondylitis at baseline (BL). Least squares mean changes from BL to Week 12 (Week 16 for SAPS) were assessed. Percentages of patients reporting improvements ≥ minimal clinically important differences (MCID) from BL through Week 24 were compared between treatment groups. Number needed to treat (NNT) to achieve an additional MCID response was calculated at Weeks 12/24 for UPA vs PBO and ADA vs PBO.

Table. 1 Mean Change in PRO Scores From Baseline at Week 12

PRO	Placebo		UPA 15 mg QD		UPA 30 mg QD		ADA 40 mg EOW	
	Baseline score	Mean change	Baseline score	Mean change	Baseline score	Mean change	Baseline score	Mean change
PtGA, 0-10 NRS	6.3	−1.2	6.6	−2.7*	6.4	−3.1*†	6.3	−2.6
Pain, 0-10 NRS	6.1	−0.9	6.2	−2.3*	6.0	−2.7*†	5.9	−2.3
HAQ-DI	1.1	−0.14	1.2	−0.42*†	1.1	−0.47*†	1.1	−0.34
FACIT-F	30.3	2.8	29.0	6.3*	29.6	7.1*†	29.8	5.7
SF-36 PCS	35.2	3.2	34.7	7.9*†	35.6	8.9*†	35.9	6.8
SF-36 MCS	45.7	2.2	44.8	3.9*	45.7	3.4*	45.1	3.6
EQ-5D-5L	0.62	0.08	0.60	0.16*	0.61	0.18*	0.62	0.16
SAPS[a]	44.0	−8.2	44.0	−25.3*†	43.5	−28.1*†	43.0	−22.7
WPAI overall work impairment	49.9	−5.0	47.0	−20.1*	45.3	−19.5*	42.4	−17.1
WPAI activity impairment	49.5	−7.6	51.4	−19.2*	47.0	−21.2*†	48.5	−17.0
BASDAI[b]	5.8	−1.0	6.0	−2.2*	5.9	−2.6*	5.7	−2.4
Morning stiffness[c]	5.2	−1.0	5.6	−2.4*	5.4	−2.7*†	5.3	−2.1

*$P<0.05$ for UPA vs PBO. †$P<0.05$ for UPA vs ADA. Note: No formal statistical comparisons were conducted for ADA vs PBO.
[a]Results presented at Week 16 as SAPS was not assessed at Week 12. [b]In subjects with psoriatic spondylitis at baseline. [c]Mean of BASDAI Q5 and Q6.
ADA, adalimumab; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; EOW, every other week; EQ-5D-5L, EuroQoL-5 Dimension, 5 level index score; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCS, mental component summary; NRS, Numerical Rating Scale; PBO, placebo; PCS, physical component summary; PRO, patient-reported outcome; PtGA, Patient Global Assessment of Disease Activity; QD, once daily; SAPS, Self-Assessment of Psoriasis Symptoms; SF-36, 36-Item Short-Form Health Survey; UPA, upadacitinib; WPAI, Work Productivity and Activity Impairment.

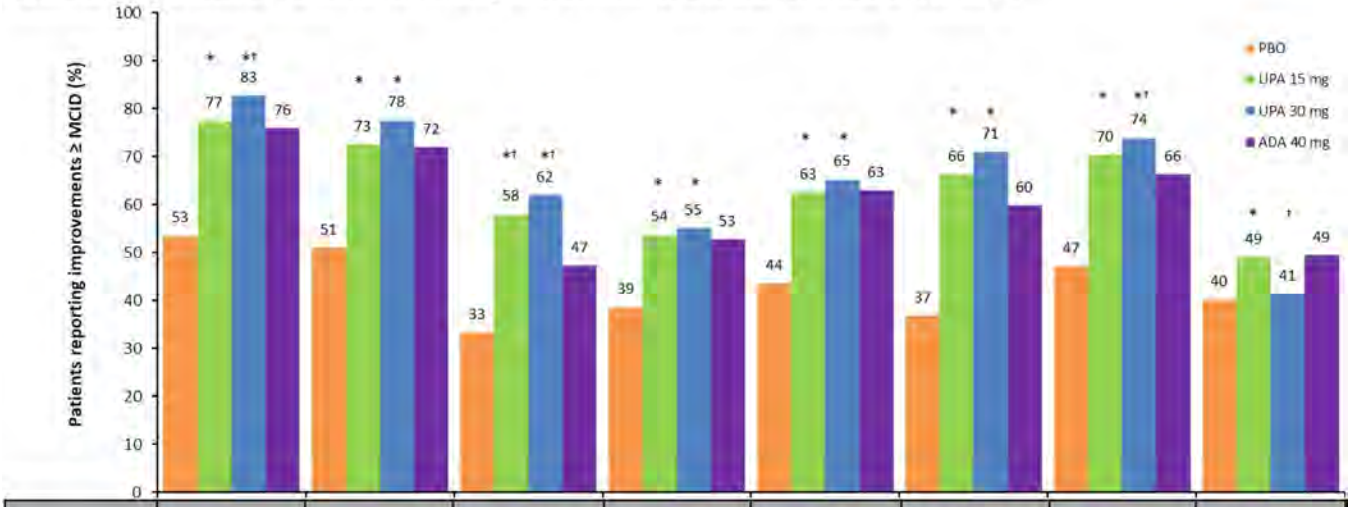
Figure 1. Spydergram of SF-36 Domain Changes From Baseline With UPA 15 mg, 30 mg vs PBO and ADA at Week 12



ADA, adalimumab; A/G Norms, age- and gender-matched normative values; BL, baseline; BP, bodily pain; GH, general health; MH, mental health; PBO, placebo; PF, physical functioning; RE, role-emotional; RP, role-physical; SF, social functioning; SF-36, 36-Item Short-Form Health Survey; UPA, upadacitinib; VT, vitality; Wk, week.

Results: Data from 1704 patients (UPA 15 mg: 429; UPA 30 mg: 423; PBO: 423; ADA: 429) were analyzed. At Week 12, both doses of UPA resulted in significant improvements from BL vs PBO across all PROs (**Table 1**). At Week 12, UPA 15 mg and 30 mg resulted in significant improvements from BL vs ADA in HAQ-DI, SAPS, and SF-36 physical component summary and UPA 30 mg vs ADA in 4 SF-36 domains (**Figure 1**). Compared with PBO, significantly more patients treated with UPA 15 mg and 30 mg reported improvements ≥ MCID in PtGA, pain, and HAQ-DI as early as

Figure 2. Proportion of Patients Reporting Improvements ≥ MCID[a] in PROs at Week 12



	PtGA NNT	Pain NNT	HAQ-DI NNT	FACIT-F NNT	EQ-5D-5L NNT	BASDAI NNT	SF-36 PCS NNT	SF-36 MCS NNT[b]
PBO	–	–	–	–	–	–	–	–
UPA 15 mg	4.2	4.6	4.1	6.6	5.3	3.4	4.3	11.4
UPA 30 mg	3.4	3.7	3.5	6.0	4.6	3.0	3.7	–
ADA 40 mg	4.5	4.7	7.3	7.1	5.2	4.4	5.2	10.8

*P<0.05 for UPA vs PBO. †P<0.05 for UPA vs ADA.

[a]MCID was defined as reduction of ≥1 point for PtGA, reduction of ≥1 point for pain, reduction of ≥0.35 units for HAQ-DI, increase of ≥4.0 points for FACIT-F, increase of ≥2.5 points for SF-36 PCS and MCS, increase of ≥0.05 for EQ-5D, and reduction of ≥1.1 points for BASDAI.

[b]NNTs vs PBO were not calculated for non-significant results.

ADA, adalimumab; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; EQ-5D-5L, EuroQoL-5 Dimension, 5 level index score; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCID, minimal clinically important difference; MCS, mental component summary; NNT, number needed to treat; PBO, placebo; PCS, physical component summary; PROs, patient-reported outcomes; PtGA, Patient Global Assessment of Disease Activity; SF-36, 36-Item Short-Form Health Survey; UPA, upadacitinib.

Week 2 (first post-BL visit) that were maintained through Week 24. At Week 12, the proportions of patients reporting improvements ≥ MCID were significantly greater with both doses of UPA vs PBO across all PROs except SF-36 mental component summary (UPA 30 mg) with NNTs ranging from 3.0–11.4 for all PROs (**Figure 2**). The proportions of UPA-treated (both doses) patients reporting improvements ≥ MCID at Week 12 were similar to ADA-treated patients across most PROs and significantly higher than ADA-treated patients in HAQ-DI; improvements were maintained through Week 24.

Conclusion: Treatment with UPA 15 mg or UPA 30 mg resulted in clinically meaningful improvements in PROs vs PBO at 12 weeks in biologic DMARD-naïve patients with active PsA, which were maintained or further improved at Week 24. Overall, improvements were similar between UPA 15 mg and UPA 30 mg and improvements with both doses of UPA were similar or greater than those reported with ADA.

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Abstract Number: 1342

Efficacy Outcomes Following Etanercept Withdrawal by Sustained Remission Status in Patients with Nr-axSpA: Results from RE-EMBARK

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
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Session Time: 9:00AM–11:00AM

Background/Purpose: Etanercept (ETN) is effective and well tolerated in patients with non-radiographic axial spondyloarthritis (nr-axSpA). However, there is limited information on the effects of withdrawing ETN treatment in patients who have achieved a significant clinical response. RE-EMBARK was a phase 4, multicenter, open-label, 3-period study that evaluated the effects of ETN withdrawal and retreatment on clinical efficacy in patients with nr-axSpA. The aim of this analysis was to evaluate differences in outcomes during treatment withdrawal (Period 2) based on sustained remission status during the active treatment phase (Period 1).

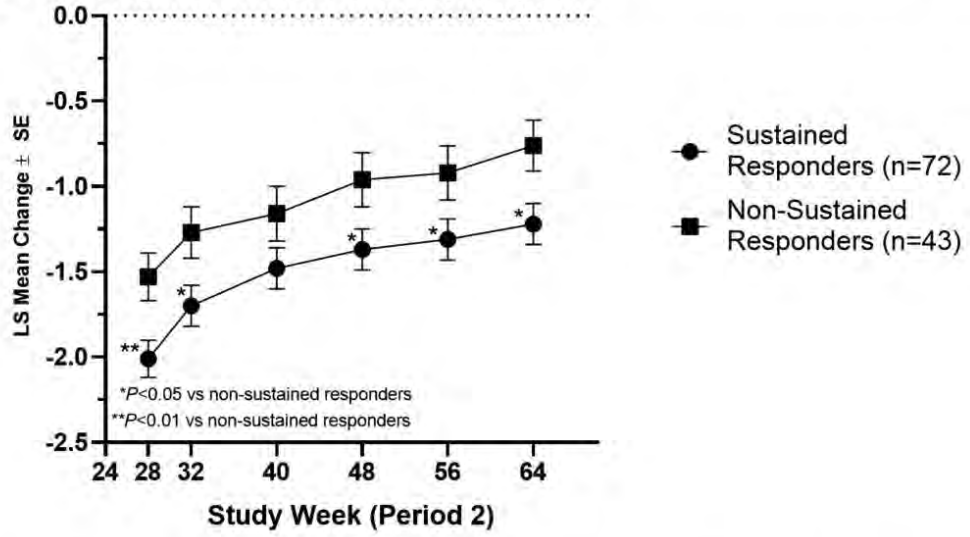
Methods: RE-EMBARK enrolled patients aged 18–49 years with active nr-axSpA who had an inadequate response to ≥2 nonsteroidal anti-inflammatory drugs (NSAIDs) and were taking a stable dose of an NSAID for at least 14 days before their first study dose of ETN. In Period 1, all patients received open-label ETN 50 mg once weekly and stable background NSAID for 24 weeks. Patients who achieved inactive disease (ASDAS-CRP < 1.3) at Week 24 were eligible to enter Period 2. In Period 2, ETN was withdrawn for up to 40 weeks. Patients with an nr-axSpA flare (ASDAS-ESR ≥2.1) during Period 2 were eligible to immediately enter Period 3. In Period 3, patients were retreated with open-label ETN 50 mg once weekly for 12 weeks. In this post-hoc analysis, sustained response (SR) during Period 1 was defined as ASDAS ESR inactive disease at week 24 and at either Week 12 or Week 16, and no flare at any of these time points.

Table 1. Baseline characteristics of patients with SR* versus non-SR patients during Period 1 of RE-EMBARK

Characteristics	SR patients (n = 72)	Non-SR patients (n = 43)
Age (years), mean ± SD	30.8 ± 7.7	36.3 ± 7.9
Men, n, (%)	56 (78)	18 (42)
White, n %	65 (90)	40 (93)
BMI, kg/m^2, mean ± SD	25.2 ± 3.9	26.4 ± 4.4
Duration (years) of disease symptoms, mean ± SD	1.4 ± 1.5	2.0 ± 1.4
Positive MRI sacroiliitis by ASAS criteria, n (%)	52 (72.2)	30 (69.8)
ASDAS-CRP score, mean ± SD	3.4 ± 1.0	3.4 ± 0.7
ASDAS-ESR score, mean ± SD	3.3 ± 1.0	3.7 ± 0.7
SPARCC MRI SIJ score, mean ± SD	12.9 ± 15.1	6.5 ± 11.0
SPARCC MRI 6 DVU spinal score, mean ± SD	2.6 ± 6.5	1.5 ± 3.0
HLA-B27-positive, n (%)	64 (88.9)	31 (72.1)
Concomitant DMARDs use, n (%)	2 (2.8)	0 (0.0)
Concomitant NSAID use, n (%)	72 (100.0)	43 (100.0)

*defined as ASDAS ESR < 1.3 at Week 24, plus ASDAS ESR <1.3 at Week 12 or Week 16 (where ASDAS ESR may not be >2.1 at either timepoint).
ASAS, Assessment in SpondyloArthritis international Society; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score with C-reactive protein; ASDAS-ESR, Ankylosing Spondylitis Disease Activity Score with erythrocyte sedimentation rate; BMI, body mass index; DVU, discovertebra; MRI, magnetic resonance imaging; SD, standard deviation; SIJ, sacroiliac joint; SPARCC, Spondyloarthritis Research Consortium of Canada; SR, sustained remission.

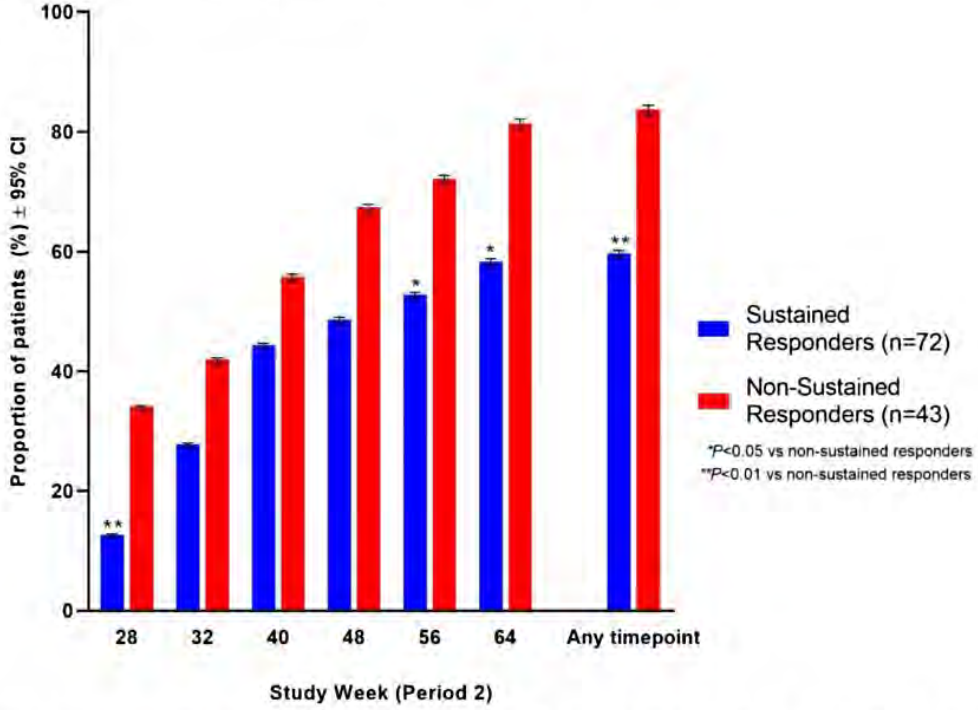
Figure 1. Least squares mean change over time in ASDAS-CRP from Period 1 baseline during Period 2 in sustained response and non-sustained response patients



Sustained response during Period 1 was defined as ASDAS ESR < 1.3 at Week 24, plus ASDAS ESR <1.3 at Week 12 or Week 16 (where ASDAS ESR may not be >2.1 at either timepoint).
ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score with C-reactive protein; LS, least squares; SE, standard error.

Baseline demographic and clinical characteristics of SR patients were compared with non-SR patients. Statistical analyses comparing SR versus non-SR patients were conducted using logistic models for binary endpoints and ANCOVA for continuous endpoints.

Figure 2. The proportion of sustained responders and non-sustained responders with flare (ASDAS-ESR ≥2.1) during Period 2



Sustained response during Period 1 was defined as ASDAS ESR < 1.3 at Week 24, plus ASDAS ESR <1.3 at Week 12 or Week 16 (where ASDAS ESR may not be >2.1 at either timepoint).
ASDAS-ESR, Ankylosing Spondylitis Disease Activity Score with Erythrocyte Sedimentation Rate; CI, confidence interval.

Results: A total of 209 patients were treated during Period 1, of which 119 (57%) achieved inactive disease and entered Period 2 (ETN treatment withdrawal). A total of 115 patients who had at least one efficacy evaluation during Period 2 were included in this post-hoc analysis, with 72 patients achieving SR versus 43 patients with non-SR. Period 1 SR patients were younger, had a higher SpondyloArthritis Research Consortium of Canada MRI sacroiliac joint score SIJ score, and were more likely to be HLA-B27 positive than non-SR patients (**Table 1**). In Period 2, Period 1 SR patients showed greater reductions in ASDAS-CRP than non-SR patients, which was statistically significant at Weeks 28, 32, 48, 56, and 64 (**Figure 1**). A significantly smaller proportion of Period 1 SR versus non-SR patients had a flare during Period 2 at Weeks 28, 56, 64, and all timepoints combined **(Figure 2**). When all timepoints were combined, 59.7% of Period 1 SR patients had a flare compared with 83.7% of non-SR patients.

Conclusion: Patients who demonstrated SR to ETN in Period 1 showed greater prolongation of efficacy and fewer flares when ETN treatment was withdrawn (Period 2) compared with non-SR patients. These results suggest on-treatment efficacy can affect how patients respond to withdrawal of ETN.

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Abstract Number: 1343

Early Real-World Experience of Tofacitinib for Psoriatic Arthritis: Data from a United States Healthcare Claims Database

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SESSION INFORMATION
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Background/Purpose: Tofacitinib is an oral Janus kinase inhibitor for the treatment of psoriatic arthritis (PsA). It was approved in the US in December 2017 for use in combination with non-biologic DMARDs. This analysis of real-world data assessed demographic and baseline clinical characteristics, as well as treatment persistence/adherence, in patients (pts) with PsA who had newly initiated tofacitinib treatment.

Methods: This retrospective cohort study included pts aged ≥ 18 years in the Truven MarketScan™ US Commercial and Medicare Supplemental Claims and Encounters database with ≥ 1 tofacitinib claim (first = index) between December 14, 2017–April 30, 2019, and PsA diagnoses (≥ 1 inpatient or ≥ 2 outpatient [30–365 days apart]) on or within 12 months pre-index. Pts were continuously enrolled for 12 months pre-index and 6 months post-index, with no

Table 1. Demographic and baseline clinical characteristics of pts with PsA initiating tofacitinib

	All pts (N=440)	Pts with no RA[a] (N=315)
Age, years[b]		
Mean (SD)	52.3 (10.6)	52.1 (10.8)
Median (IQR)	53.0 (46.8–59.0)	53.0 (46.5–59.0)
Female, n (%)	313 (71.1)	216 (68.6)
US region, n (%)[b]		
Midwest	62 (14.1)	49 (15.6)
Northeast	124 (28.2)	80 (25.4)
South	149 (33.9)	104 (33.0)
West	48 (10.9)	35 (11.1)
Unknown	57 (13.0)	47 (14.9)
Payor, n (%)[c]		
Commercial	395 (89.8)	280 (88.9)
Medicare	45 (10.2)	35 (11.1)
PsA duration, days[d]		
Mean (SD)	738.0 (326.0)	753.5 (319.2)
Median (IQR)	792.5 (458.0–1028.5)	818.0 (489.0–1031.5)
RA diagnosis on or within 12 months pre-index, n (%)	89 (20.2)	0

[a]Excludes pts with a diagnosis of RA on or within 12 months pre-index and within 6 months post-index; [b]Recorded on the index date; [c]First payor over the index date; [d]Days between PsA diagnosis and index date, excluding the end date
IQR, interquartile range; N, number of pts in each cohort; n, number of pts in each category; PsA, psoriatic arthritis; pts, patients; RA, rheumatoid arthritis; SD, standard deviation; US, United States

Table 2. History of advanced therapy and tofacitinib treatment regimen in pts with PsA

	All pts (N=440)	Pts with no RA[a] (N=315)
History of advanced therapy within 12 months pre-index		
Pts exposed to advanced therapy, n (%)[b]		
Any advanced therapy[c]	336 (76.4)	241 (76.5)
Secukinumab	113 (25.7)	91 (28.9)
Adalimumab	93 (21.1)	58 (18.4)
Apremilast	81 (18.4)	59 (18.7)
Etanercept	70 (15.9)	47 (14.9)
Unique advanced therapy prescriptions		
Mean (SD)	1.1 (0.8)	1.1 (0.8)
Median (IQR)	1 (1–2)	1 (1–2)
Range	0–4	0–4
Number of unique advanced therapies, n (%)		
0	104 (23.6)	74 (23.5)
1	214 (48.6)	153 (48.6)
2	100 (22.7)	73 (23.2)
≥3	22 (5.0)	15 (4.8)
Tofacitinib treatment regimen post-index		
Monotherapy, n (%)	267 (60.7)	197 (62.5)
Combination therapy, n (%)[d]	173 (39.3)	118 (37.5)
Methotrexate	107 (61.9)	79 (67.0)
Leflunomide	27 (15.6)	17 (14.4)
Hydroxychloroquine	18 (10.4)	5 (4.2)
Sulfasalazine	13 (7.5)	11 (9.3)
Apremilast	6 (3.5)	4 (3.4)
Other[e]	2 (1.2)	2 (1.7)

[a]Excludes pts with a diagnosis of RA on or within 12 months pre-index and within 6 months post-index; [b]Pts with ≥1 claim for bDMARDs or apremilast within 12 months pre-index; [c]Other advanced therapies reported in <10% of all pts were abatacept, certolizumab, golimumab, infliximab, ixekizumab, and ustekinumab; [d]Pts with ≥1 claim for a csDMARD or apremilast on or within 90 days post-index; [e]Other possible combination therapies included auranofin, aurothioglucose, azathioprine, chloroquine, cyclophosphamide, cyclosporine, gold sodium thiomalate, minocycline, penicillamine, tacrolimus, and thalidomide
bDMARD, biologic DMARD; csDMARD, conventional synthetic DMARD; DMARD, disease-modifying antirheumatic drug; IQR, interquartile range; N, number of pts in each cohort; n, number of pts in each category; PsA, psoriatic arthritis; pts, patients; RA, rheumatoid arthritis; SD, standard deviation

Table 3. Tofacitinib persistence and adherence in pts with PsA at 6 months post-index

	All pts		Pts with no RA[a]	
	Monotherapy (N=267)	Combination therapy[b] (N=173)	Monotherapy (N=197)	Combination therapy[b] (N=118)
Tofacitinib persistent, n (%)[c]	190 (71.2)	127 (73.4)	138 (70.1)	86 (72.9)
Tofacitinib PDC[d]				
Mean (SD)	0.7 (0.3)	0.8 (0.2)	0.7 (0.3)	0.8 (0.2)
Median (IQR)	0.8 (0.5–1.0)	0.9 (0.6–1.0)	0.8 (0.5–1.0)	0.9 (0.6–1.0)
Range	0.1–1.0	0.2–1.0	0.1–1.0	0.2–1.0
PDC ≥0.8, n (%)[e]	152 (56.9)	115 (66.5)	112 (56.9)	77 (65.3)

[a]Excludes pts with a diagnosis of RA on or within 12 months pre-index and within 6 months post-index; [b]Pts with ≥1 claim for a csDMARD or apremilast on or within 90 days post-index; [c]Pts with <60-day gap without tofacitinib treatment; [d]Number of days covered divided by number of days in the 6-month post-index period; [e]Pts achieving ≥80% of days covered
csDMARD, conventional synthetic DMARD; DMARD, disease-modifying antirheumatic drug; IQR, interquartile range; N, number of pts in each cohort; n, number of pts in each category; PDC, proportion of days covered; PsA, psoriatic arthritis; pts, patients; RA, rheumatoid arthritis; SD, standard deviation

pre-index claims for tofacitinib. Pt demographic and clinical characteristics on the day of index, history of treatment with advanced therapies (≥ 1 claim for biologic DMARDs or apremilast within 12 months pre-index), and tofacitinib treatment regimen (monotherapy or combination therapy [≥ 1 claim for conventional synthetic DMARDs or apremilast on or within 90 days post-index]) were recorded. Outcomes at 6 months post-index included tofacitinib persistence (< 60-day gap without tofacitinib treatment) and adherence (proportion of days covered ≥ 80% and medication possession ratio [data not shown]). A sensitivity check was performed by analyzing a sub-cohort which excluded pts with a diagnosis of rheumatoid arthritis (RA) on or within 12 months pre-index and within 6 months post-index.

Results: Of 17,321 pts receiving tofacitinib, 440 pts met the inclusion criteria for the overall cohort, with 315 pts included in the sub-cohort. In the overall cohort, pts were mostly female, with a mean age of 52.3 years and a mean PsA duration of 738 days (Table 1). Most pts were exposed to ≥ 1 advanced therapy (mean = 1.1; range = 0–4) within 12 months pre-index; most commonly secukinumab (Table 2). Overall, 39.3% of patients received tofacitinib combination therapy post-index; most commonly methotrexate (Table 2). Persistence was similar in pts receiving tofacitinib monotherapy (71.2%) vs combination therapy (73.4%; Table 3) at 6 months post-index. Adherence was slightly lower in pts receiving tofacitinib monotherapy (56.9%) vs combination therapy (66.5%; Table 3) at 6 months post-index. All results were similar in the sub-cohort (Tables 1–3).

Conclusion: This analysis of US-based claims data indicated that pts newly initiated tofacitinib treatment an average of 2 years after PsA diagnosis, with the majority (> 60%) of pts receiving tofacitinib as monotherapy. High levels of persistence and adherence to tofacitinib were observed 6 months after treatment initiation. Findings were similar when pts with PsA who also had a diagnosis of RA were excluded. Data are limited in that claims data cannot confirm that pts took the medication for which they filed a claim for.

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Abstract Number: 1344

Guselkumab, an IL-23 Inhibitor That Specifically Binds to the IL23p19-Subunit, for Active Psoriatic Arthritis: One Year Results of a Phase 3, Randomized, Double-Blind, Placebo-Controlled Study of Patients Who Were Biologic-Naïve or TNFα Inhibitor-Experienced

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Guselkumab (GUS), a monoclonal antibody that specifically binds to the p19-subunit of IL-23, is approved to treat psoriasis (PsO). At Week 24 of the Phase 3, double-blind, placebo (PBO)-controlled trial in patients (pts) with active PsA who were biologic-naïve or prior TNFα inhibitor (TNFi)-treated (DISCOVER-1), GUS 100 mg, given every 4/8 weeks (Q4W/Q8W), demonstrated efficacy for joint and skin symptoms, physical function,

Table 1. Observed Efficacy[1]	GUS Q4W		GUS Q8W		PBO (W0-24) X Q4W (W24-52)	
Data are % unless otherwise stated	W24	W52	W24	W52	W24	W52
Dactylitis at W0, n	37	37	49	44	47	43
Resolution	64.9	78.4	67.3	79.5	61.7	81.4
Enthesitis at W0, n	71	70	71	64	71	63
Resolution	49.3	62.9	40.8	56.3	31.0	69.8
≥3% BSA psoriasis, IGA ≥2 at W0, n	88	88	81	75	68	66
IGA 0/1 + ≥2-grade decrease	76.1	83.0	58.0	69.3	17.6	81.5[2]
PASI75	87.5	94.3	76.5	80.0	20.6	84.8
PASI90	63.6	76.1	50.6	66.7	13.2	72.7
PASI100	45.5	64.8	25.9	48.0	7.4	62.1
HAQ-DI, n	125	124	123	114	114	104
Mean change	-0.4	-0.5	-0.3	-0.4	-0.1	-0.4
SF-36 scores, n (mean change)	124	124	123	114	114	104
Physical Component – PCS	6.6	8.5	6.5	7.3	2.7	6.9
Mental Component - MCS	3.8	4.9	3.0	5.1	1.8	4.2
MDA, n	125	124	123	112	114	103
MDA response	31.2	40.3	23.6	33.9	12.3	31.1
VLDA, n	125	124	123	114	113	104
VLDA response	9.6	16.9	4.1	12.3	1.8	14.4

[1]Randomized pts still on study agent at W24; [2]n=65

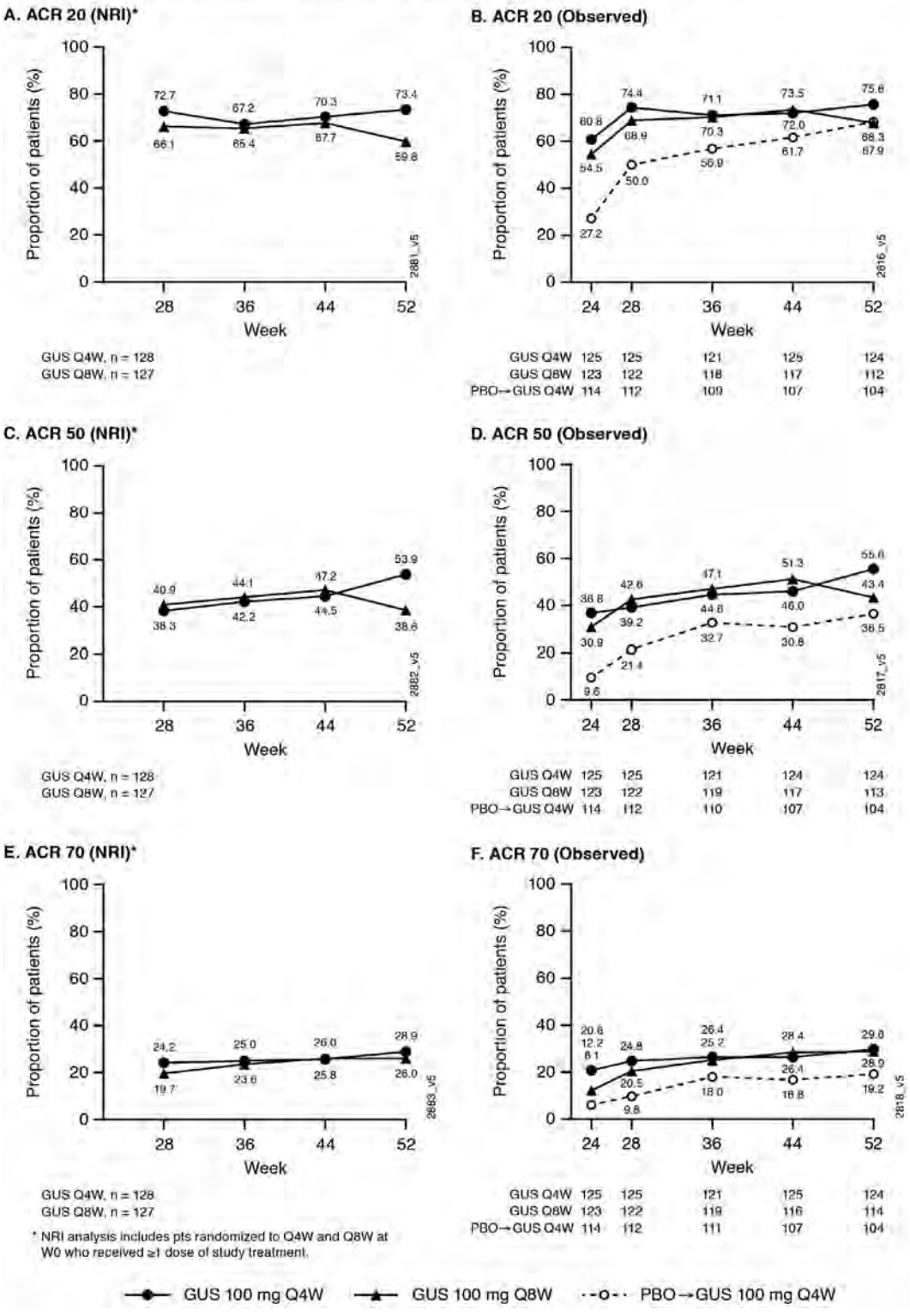
BSA, body surface area; GUS, guselkumab; HAQ-DI, Health Assessment Questionnaire-Disability Index; IGA, Investigator Global Assessment of Psoriasis; MCS, Mental Component Summary; MDA, minimal disease activity; PASI, Psoriasis Area and Severity Index; PBO, placebo; PCS, Physical Component Summary; Q4W, every 4 weeks; Q8W, every 8 weeks; SF-36, 36 item Short Form Health Survey; VLDA, very low disease activity; W, week.

and quality of life vs PBO. Adverse events (AEs) were consistent with GUS safety in PsO. This study assessed GUS efficacy and safety in pts with PsA through 1 year.

Methods: Adults with active PsA (≥3 swollen + ≥3 tender joints; CRP≥0.3 mg/dL) despite standard therapies were eligible. Approximately 30% of pts could have previously received ≤2 TNFi. Pts were randomized 1:1:1, stratified by Week 0 DMARD (Y/N) and prior TNFi use (Y/N), to GUS 100 mg Q4W; GUS 100 mg at Weeks 0 and 4, and Q8W; or PBO. At Week 24, PBO pts crossed over to GUS 100 mg Q4W (PBO X Q4W). Week 48 marked the last dose of study agent. ACR response rates at Week 52, based on non-responder imputation (NRI) for missing data and as observed in pts still on study agent at Week 24, are shown. Observed data for additional endpoints are shown. AEs were reported through Week 60.

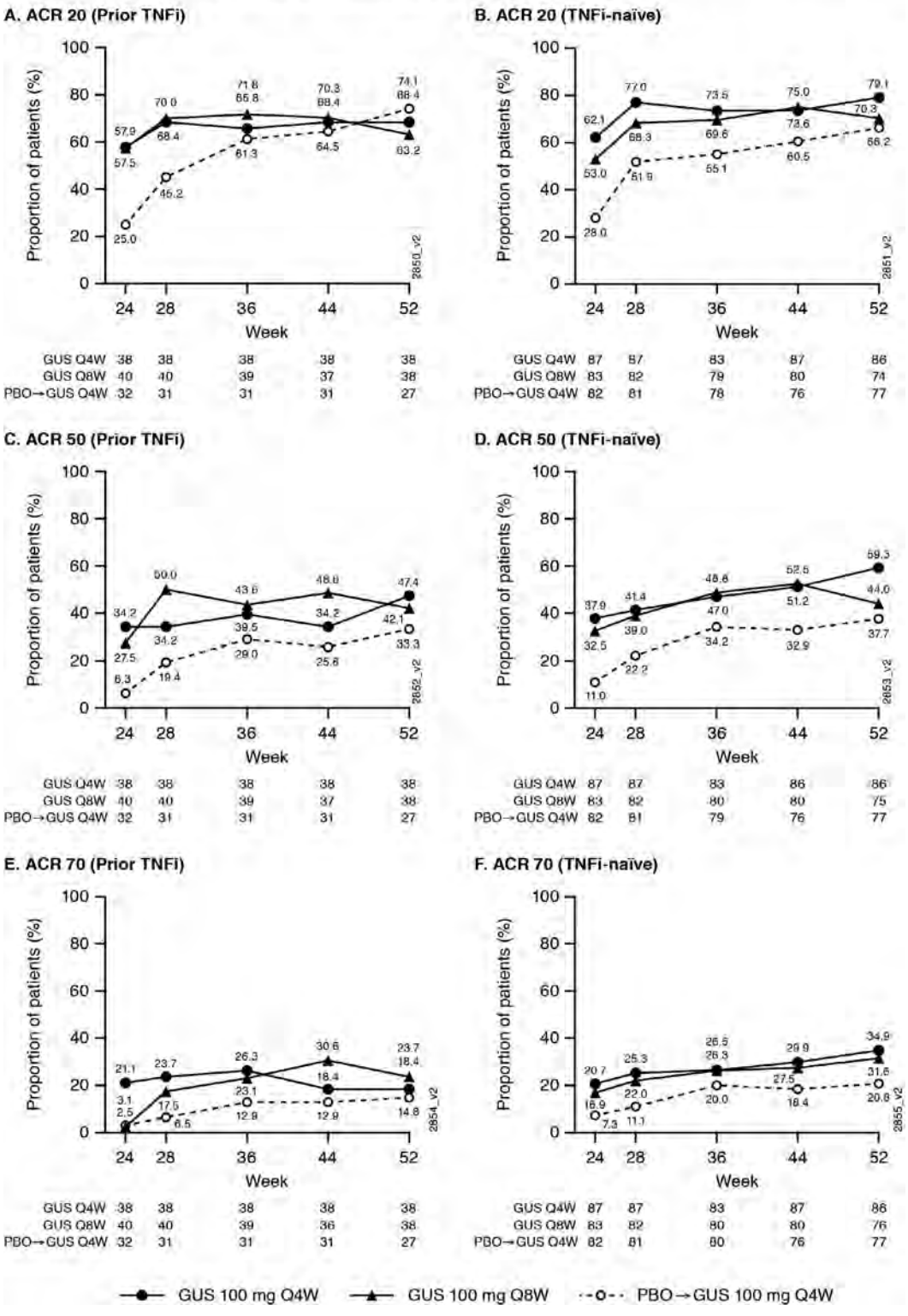
Results: 362/381 (95%) randomized pts continued study agent at Week 24 (125 Q4W, 123 Q8W, 114 PBO X Q4W), 347/381 (91%) pts completed treatment, and 343/381 (90%) completed the study. NRI ACR20 response rates were maintained at Week 52 (Q4W: 73%, Q8W: 60%; Fig. 1A). Similar response patterns were seen for the more stringent ACR50/70 criteria (Fig. 1C, E). Observed ACR responses, overall (Fig. 1B, D, F) and in pts with (Fig. 2A, C, E) and without (Fig. 2B, D, F) prior TNFi use, were also maintained at Week 52. Improvements in other clinical outcomes were also maintained at Week 52, and responses for pts crossing over from PBO X Q4W at Week 24 were generally consistent with other GUS-treated pts by Week 52 (Table 1). Through Week 24, 4 (2%) GUS- and 5 (4%) PBO-treated pts had serious AEs; no GUS-treated and 2 (2%) PBO-treated pts had a serious infection. Through Week 60, serious AEs and serious infections occurred in 4% and 1%, respectively, of all 369 GUS-treated pts. No GUS-treated pt died or had IBD, opportunistic infections or active tuberculosis, or anaphylactic or serum sickness-like reactions.

Fig 1. NRI and Observed ACR20 (**A & B**), ACR50 (**C & D**), and ACR70 (**E & F**) responses through W52
(Note: patients randomized to PBO crossed over to GUS Q4W at W24)



GUS, guselkumab; NRI, non-responder imputation; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; TNFi, tumor necrosis factor inhibitor.

Fig 2. Observed ACR20 (**A&B**), ACR50 (**C&D**), ACR70 (**E&F**) response rates from W24 through W52 by prior TNFi use (Note: patients randomized to PBO crossed over to GUS Q4W at W24)



GUS, guselkumab; PBO, placebo; Q4W, every 4 weeks; Q8W, every 8 weeks; TNFi, tumor necrosis factor inhibitor.

Conclusion: GUS Q4W and Q8W maintained improvements in joint symptoms through 1 year in pts with active PsA who were biologic-naïve or previously TNFi-treated. In pts continuing in the study, improvements in skin symptoms, dactylitis, enthesitis, physical function, and quality of life were also maintained through 1 year. GUS 100 mg Q4W and Q8W were safe and well-tolerated through study completion and consistent with GUS safety in PsO.[1]

Reference

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Disclosure: C. Ritchlin, None; **P. Helliwell**, AbbVie, 2, 8, Janssen, 2, Pfizer Inc, 8, Celgene, 8, Galapagos, 8, Amgen, 8, Novartis, 2, UCB, 8; **W. Boehncke**, Janssen Research & Development, LLC, 2, 5; **E. Hsia**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **A. Kollmeier**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **R. Subramanian**, Janssen Research & Development, LLC., 3; **X. Xu**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **S. Sheng**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **Y. Jiang**, None; **B. Zhou**, Janssen Reserach & Development, LLC, 3, Johnson & Johnson, 1; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2.

Abstract Number: 1345

Upadacitinib as Monotherapy and in Combination with Non-biologic DMARDs for the Treatment of Psoriatic Arthritis: Subgroup Analysis from Two Phase 3 Trials

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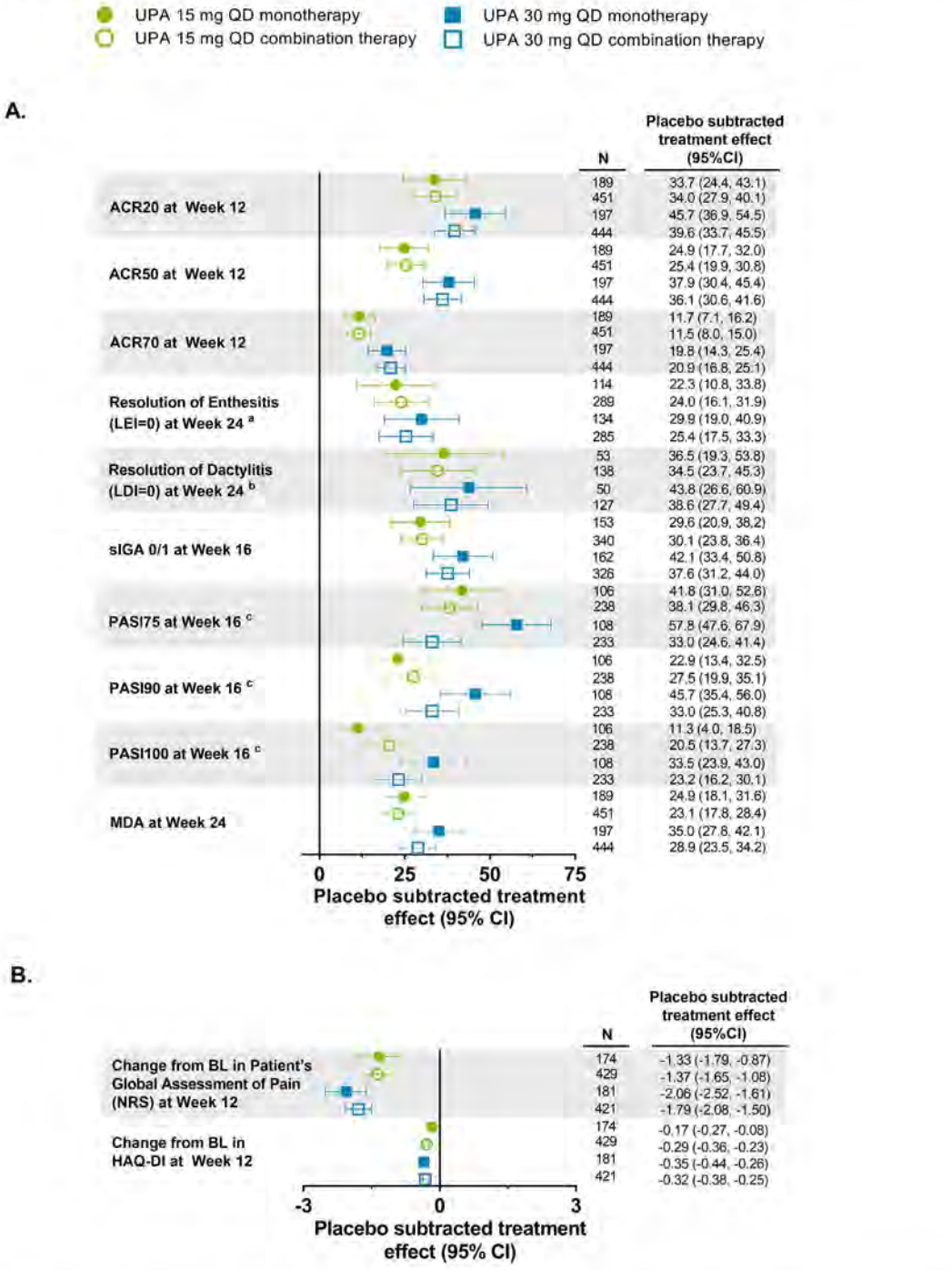
SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Approximately 40% of PsA patients (pts) on advanced therapy are on monotherapy.[1,2] Upadacitinib (UPA) has shown efficacy and safety in pts with active PsA in the Phase 3 SELECT-PsA 1 and SELECT-PsA 2 clinical trials.[3,4] This analysis assessed the efficacy and safety in the subgroups of pts who were treated with UPA as monotherapy or in combination with non-biologic disease-modifying antirheumatic drugs (non-bDMARDs).

Methods: The SELECT-PsA program enrolled pts with prior inadequate response (IR) or intolerance to ≥1 non-bDMARD (N=1705) and prior IR or intolerance to ≥1 bDMARD (N=642). Data from both trials was integrated for pts receiving placebo (PBO), UPA 15 mg once daily (QD) and UPA 30 mg QD; adalimumab data was excluded from this analysis as it was only evaluated in SELECT-PsA 1. Stable background treatment of ≤2 non-bDMARDs was permitted; background therapy was not required. This analysis includes comparison of UPA monotherapy and combination therapy for the endpoints: ACR20/50/70 responses and change from baseline in pain and HAQ-DI (Week 12); Static Investigator Global Assessment of Psoriasis of 0 or 1 and at least a 2-point improvement from baseline and PASI75/90/100 re-

Figure. Efficacy Outcomes in Patients Receiving Monotherapy and Combination Therapy: Placebo Subtracted Treatment Effect



[a] for patients with baseline LEI > 0; [b] for patients with baseline LDI > 0; [c] for patients with ≥ 3% body surface area psoriasis at baseline; ACR, American College of Rheumatology; BL, baseline; HAQ-DI, Health Assessment Questionnaire-Disability Index; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; PASI, Psoriasis Area Severity Index; QD, once daily; sIGA 0/1, Static Investigator Global Assessment of Psoriasis of 0 or 1 and at least a 2 point improvement from baseline.

sponses (Week 16); proportion of pts achieving resolution of enthesitis, dactylitis, and minimal disease activity (Week 24). Binary outcomes were analyzed using the Cochran-Mantel-Haenszel-method and continuous outcomes were analyzed using mixed-effects model for repeated measures in the subgroups of UPA monotherapy and

Table. Safety Summary Through Week 24 by Monotherapy and Combination Therapy						
Event, n (%)	Monotherapy			Combination		
	PBO (N=188)	UPA 15mg QD (N=189)	UPA 30mg QD (N=197)	PBO (N=447)	UPA 15mg QD (N=451)	UPA 30mg QD (N=444)
Any AE	127 (67.6)	124 (65.6)	145 (73.6)	264 (59.1)	298 (66.1)	331 (74.5)
Serious AE	8 (4.3)	9 (4.8)	9 (4.6)	9 (2.0)	17 (3.8)	35 (7.9)
AE leading to D/C of study drug	13 (6.9)	14 (7.4)	14 (7.1)	11 (2.5)	14 (3.1)	27 (6.1)
Deaths	1 (0.5)	0	0	1 (0.2)	0	0
Infection	65 (34.6)	67 (35.4)	88 (44.7)	148 (33.1)	173 (38.4)	203 (45.7)
Serious infection	2 (1.1)	1 (0.5)	2 (1.0)	3 (0.7)	5 (1.1)	15 (3.4)
Opportunistic infection excluding tuberculosis and herpes zoster	0	0	2 (1.0)	0	1 (0.2)	2 (0.5)
Herpes zoster	2 (1.1)	2 (1.1)	6 (3.0)	3 (0.7)	5 (1.1)	7 (1.6)
Active tuberculosis	0	0	0	0	0	0
Malignancy other than NMSC	0	3 (1.6)	1 (0.5)	0	0	2 (0.5)
NMSC	0	0	0	1 (0.2)	1 (0.2)	3 (0.7)
MACE (adjudicated)	0	0	0	1 (0.2)	1 (0.2)	0
VTE (adjudicated)	1 (0.5)	0	0	0	1 (0.2)	1 (0.2)
Hepatic disorder	5 (2.7)	8 (4.2)	14 (7.1)	14 (3.1)	35 (7.8)	56 (12.6)
Anemia	3 (1.6)	1 (0.5)	11 (5.6)	3 (0.7)	6 (1.3)	23 (5.2)
Neutropenia	1 (0.5)	2 (1.1)	6 (3.0)	1 (0.2)	4 (0.9)	21 (4.7)
Lymphopenia	0	2 (1.1)	2 (1.0)	5 (1.1)	6 (1.3)	15 (3.4)
CPK elevation	3 (1.6)	10 (5.3)	11 (5.6)	7 (1.6)	32 (7.1)	42 (9.5)

AE, adverse event; CPK, creatine phosphokinase; D/C, discontinuation; MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer; PBO, placebo; QD, once daily; UPA, upadacitinib; VTE, venous thromboembolic events.

combination therapy. Point estimates and 95% confidence intervals (CIs) of the PBO subtracted treatment effect were calculated. Treatment-emergent adverse events (TEAEs) were analyzed and summarized through Week 24.

Results: Of the 1916 pts included in the analysis, 574 (30%) received monotherapy and 1342 (70%) received combination therapy; 84% in the combination therapy group received MTX +/- another non-bDMARD. Both UPA monotherapy and combination therapy led to improvements in efficacy outcomes vs PBO (**Figure**). Across endpoints, for each UPA dose, generally consistent point estimates of the PBO subtracted treatment effect and associated overlapping CIs were observed between pts who were on UPA monotherapy and those who were on combination therapy. Generally, the frequency of AEs, including serious AEs, were comparable with UPA when administered as monotherapy and combination therapy (**Table**). The frequency of AEs of serious infections and hepatic disorder were lower with monotherapy while the frequency of AEs leading to discontinuation of study drug were lower with combination therapy. Most hepatic disorders were transient transaminase elevations.

Conclusion: In the SELECT PsA Phase 3 trials, the efficacy and safety of UPA was generally consistent when administered as monotherapy or when given in combination with non-bDMARDs. Results from this analysis support the use of UPA with or without concomitant non-bDMARDs.

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Disclosure: P. Nash, AbbVie, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8; **P. Richette**, AbbVie Inc., 1, Biogen, 1, Janssen, 1, BMS, 1, Roche, 1, Pfizer, 1, Amgen, 1, Sanofi-Aventis, 1, UCB, 1, Lilly, 1, Novartis, 1, Celgene, 1; **L. Gossec**, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis,

5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8; **A. Marchesoni**, AbbVie Inc., 1, BMS, 1, Celgene, 1, Eli Lilly, 1, Janssen, 1, MSD, 1, Novartis, 1, Pfizer, 1, UCB, 1; **K. Kato**, AbbVie Inc., 1, 3, 4; **E. Blondell**, AbbVie, 1, 3; **E. Lesser**, AbbVie Inc., 1, 2; **R. McCaskill**, AbbVie Inc., 1, 2; **D. Feng**, AbbVie Inc., 1, 2; **J. Anderson**, AbbVie Inc., 1, 3, 4; **E. Ruderman**, AbbVie Inc., 1, Amgen, 1, Gilead, 1, Janssen, 1, Lilly, 1, Novartis, 1, Pfizer, 1.

Abstract Number: 1346

Predicting Major Treatment Response to Tumor Necrosis Factor Inhibitorsin Patients with Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

	Eligible subjects (N = 1090)
TNFi	
• Adalimumab	40.90%
• Etanercept	59.10%
Age, year, mean (SD)	38.7 (11.7)
Male sex	75.30%
Body Mass Index, mean (SD)	25.6 (5.0)
Disease Duration, year, median (range)	5 (1 – 48)
Tender joint count (0-44), median (range)	2 (0 – 46)
Swollen joint count (0-44), median (range)	1 (0 – 33)
HLA-B27 positivity	85.50%
C Reactive Protein (mg/dl), median (range)	1.2 (0 – 17.1)
SpA features	
• Inflammatory Bowel Disease	1.60%
• psoriasis	3.70%
• Uveitis	10.50%
Medication use at baseline	
• Methotrexate	17.90%
• Sulfasalazine	24.70%
• Steroid	12.00%
BASDAI (0 – 10), mean (SD)	6.0 (2.6)
BASFI (0 – 10), mean (SD)	5.3 (2.2)
Night pain (0 – 10), mean (SD)	6.3 (2.2)
Total back pain (0 – 10), mean (SD)	6.5 (1.9)
Patient global assessment (0 – 10), mean (SD)	6.5 (1.9)
ASAS40	51.30%

Table 1. Baseline characteristics of eligible subjects. SD: standard deviation; SpA: spondyloarthritis; BASDAI: Bath ankylosing spondylitis disease activity index; BASFI: Bath ankylosing spondylitis functional index; ASAS40: Assessment of SpondyloArthritis International Society (ASAS) 40% response criteria.

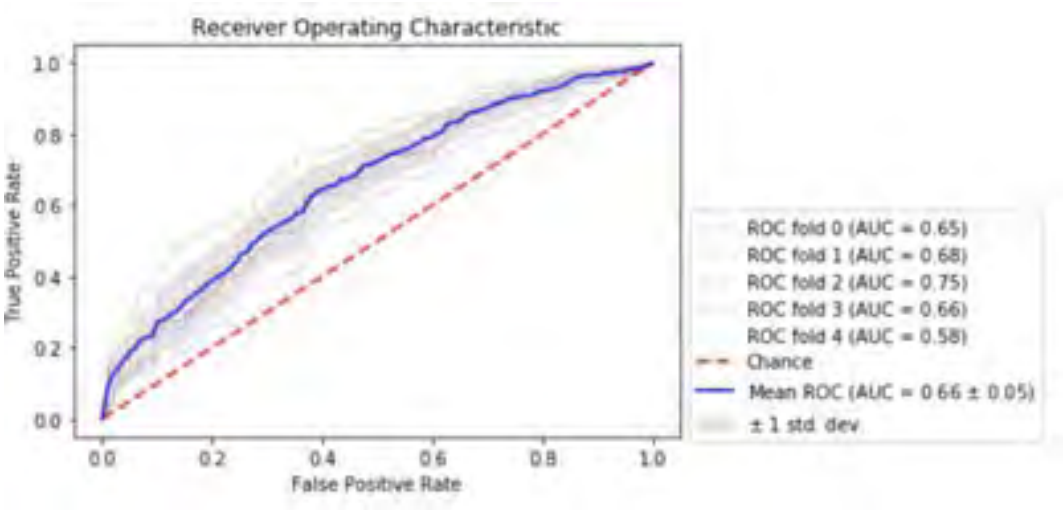

Figure 1. Performance of Random Forest Models in testing set using Receiver Operating Characteristic curves. ROC: receiver operating characteristic; AUC: area under the curve.

Background/Purpose: The treatment response to tumor necrosis factor inhibitors (TNFi) in patients with active ankylosing spondylitis (AS) is heterogeneous. In clinical practice, both patients and clinicians are interested to know how likely a patient will achieve a major response after initiating TNFi. The objective of this study is to develop a predictive model for a favorable response to TNFi based on baseline clinical features in patients with active AS.

Methods: We obtained individual patient data from randomized clinical trials of Adalimumab and Etanercept in active AS, and aggregated the participant data in the TNFi arms for a pooled analysis. The main outcome was major response at week 12, defined by achieving Ankylosing Spondylitis Assessment 40% (ASAS40) response. Baseline characteristics including age, sex, body mass index (BMI), disease duration, spondyloarthritis features, C-reactive protein (CRP), HLA-B27 positivity, and patient reported outcomes were included as predictors. The entire cohort was split by 5:1 for model development and validation. We used Random Forest algorithm to develop the predictive model with ranking of the importance of features, and the performance was examined using receiver operating characteristics area under the curve (ROC - AUC). The process was repeated independently for 5 times, and the final AUC was the average.

Results: A total of six RCTs of Adalimumab or Etanercept in patients with active AS were identified, and 1090 subjects who were in the TNFi arms were eligible and included in the analysis. Baseline characteristics are summarized in Table 1. Average age was 38.7 +/- 11.7 years, 75.3% were male patients, and 85.5% were HLA-B27 positive. Fifty-one percent of subjects achieved ASAS40 response at week 12. The Random Forest models had a small to medium effect with average AUC of 0.66 (Figure 1). At baseline, higher CRP level, worse night pain, younger age, worse patient global assessment, and lower BMI were the most important features that predicted a major response.

Conclusion: Using Random Forest algorithm, we developed a model to predict treatment response to TNFi in patients with active AS. Preliminary analysis showed a small to medium effect with AUC of 0.66. At baseline, higher CRP, worse night pain, younger age, worse patient global assessment, and lower BMI are the most important features in the prediction model.

Disclosure: R. Wang, Eli Lilly, 1, Novartis, 1; **A. Dasgupta**, None; **M. Ward**, None.

Abstract Number: 1347

Predictors of Response in Patients with Non-Radiographic Axial Spondyloarthritis Receiving Certolizumab Pegol in the C-axSpAnd Study

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Identification of predictive clinical factors of long-term treatment response in non-radiographic axial spondyloarthritis (nr-axSpA) may contribute to improved management of patients with this chronic disease. Certolizumab pegol (CZP) is currently the only FDA-approved tumor necrosis factor inhibitor (TNFi) for treatment of nr-axSpA.[1] We aim to identify whether any demographic or baseline characteristics of nr-axSpA patients from the C-axSpAnd study[2] are predictive of achieving a clinical response after 1 year of CZP treatment.

Methods: C-axSpAnd (NCT02552212) is a phase 3, interventional multicenter study including a completed 52-week double-blind, placebo-controlled period. Full study design is reported elsewhere.[2] Multivariate stepwise logistic regression analysis was used to identify predictors of response for the primary efficacy variable (ASDAS – major improvement [ASDAS-MI] at Week 52) and the main secondary efficacy variable (ASAS40 at Week 52) in patients randomized to CZP 200 mg every 2 weeks (Q2W). Predictive factors used in the model included demographic and baseline characteristics, and clinical outcomes at Week 12. A p value ≤0.05 was required for forward selection into the model and p=0.1 for backward elimination from the model. Non-responder imputation was used to account for missing data or values collected after switching to open-label treatment. A sensitivity analysis was conducted to ac-

Table 1: Predictive factors of Week 52 response in CZP-treated patients

Predictive factors for ASDAS-MI	Odds ratio	95% Wald confidence limits
MRI+/HLA-B27+ (n=90) vs MRI−/HLA-B27+ (n=38)	5.78	1.59–21.0
MRI+/HLA-B27− (n=29) vs MRI−/HLA-B27+ (n=38)	1.64	0.33–8.15
BASDAI at baseline (continuous)	1.91	1.30–2.80
Week 12 change from baseline in ASDAS (continuous)	0.14	0.07–0.29
Predictive factors for ASAS40	**Odds ratio**	**95% Wald confidence limits**
MRI+/HLA-B27+ (n=90) vs MRI−/HLA-B27+ (n=38)	4.75	1.58–14.28
MRI+/HLA-B27− (n=29) vs MRI−/HLA-B27+ (n=38)	1.60	0.41–6.23
BASMI at baseline (continuous)	0.71	0.50–0.999
Week 12 change from baseline in PtGADA (continuous)	0.74	0.61–0.90
Week 12 change from baseline in ASQoL (continuous)	0.02	0.002–0.21

An odds ratio >1 indicates a higher probability of the first subgroup (binary) or of larger values (continuous) having a predictive effect. ASAS40: Assessment of SpondyloArthritis international Society 40% response; ASDAS-MI: Ankylosing Spondylitis Disease Activity Score – major improvement; ASQoL: Ankylosing Spondylitis Quality of Life questionnaire; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; CZP: certolizumab pegol; HLA: human leukocyte antigen; MRI+/−: presence/absence of sacroiliitis on magnetic resonance imaging; PtGADA: Patient Global Assessment of Disease Activity.

count for patients who had changes in their non-biologic background medication during the 52-week placebo-controlled phase.

Results: 159/317 patients were randomized to CZP 200 mg Q2W and 158/317 to placebo. Predictive factors identified for Week 52 ASDAS-MI in the CZP-treated patients included those who were positive for both presence of sacroiliitis on MRI (MRI+) and human leukocyte antigen (HLA)-B27 (HLA+), those with a higher BASDAI at baseline, and those with a larger Week 12 improvement in ASDAS (**Table 1**). For ASAS40 response, MRI+/HLA-B27+ was also identified as a predictor of Week 52 response, along with a lower baseline BASMI and larger Week 12 improvements in PtGADA and ASQoL and (**Table 1**). Sensitivity analysis identified the same predictors for ASDAS-MI and ASAS40, with the exception of change from baseline in PtGADA as a predictor of ASAS40. Sensitivity analysis also identified achievement of Week 12 ASAS40 as a predictor of Week 52 ASAS40. In placebo-treated patients, no meaningful predictors of response at Week 52 were identified.

Conclusion: Presence of sacroiliitis on MRI and HLA-B27 positivity were identified as consistent predictors of Week 52 response (ASDAS-MI and ASAS40) in nr-axSpA patients treated with CZP. To our knowledge, this is the first report from an interventional 52-week placebo-controlled study in nr-axSpA to identify objective clinical features, particularly the presence of sacroiliac joint inflammation, as being predictive of response.

References

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Disclosure: W. Maksymowych, AbbVie, 2, 5, Janssen, 5, Lilly, 5, Pfizer, 2, 5, Novartis, 2, 5, Gilead, 5, UCB Pharma, 5, Boehringer Ingelheim, 5, Galapagos, 5; **T. Kumke**, UCB Pharma, 1, 3; **S. Auteri**, UCB Pharma, 1, 3; **B. Hoepken**, UCB Pharma, 1, 3; **L. Bauer**, UCB Pharma, 1, 3; **M. Rudwaleit**, Bristol-Myers Squibb, 5, 8, Chugai Pharmaceutical Co., Ltd., 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Novartis, 5, 8, UCB Pharma, 5, 8, AbbVie, 5, 8, Pfizer, 5, 8, Celgene, 8, Roche, 5, 8, Merck Sharp & Dohme, 5, 8.

Abstract Number: 1348

What Influence Do Clinical Domains Other Than Arthritis Have on Composite Clinical Outcomes in Psoriatic Arthritis?: Comparison of Treatment Effects in the SEAM-PsA Trial

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Table 1. Values at Baseline and Week 24 in the Overall Study Population

	Methotrexate Monotherapy N = 284	Etanercept Monotherapy N = 284	Combination Therapy N = 283
MDA			
MDA response at week 24, n/N (%)	65/284 (22.9)	102/284 (35.9) *P=0.005*	101/283 (35.7) *P=0.005*
PASDAS			
Baseline score, mean (SE) [n]	6.09 (0.07) [282]	6.05 (0.07) [279]	6.04 (0.07) [280]
Change from baseline at week 24, mean (SE) [n]	-1.98 (0.10) [246]	-2.64 (0.10) [250] *P<0.001*	-2.63 (0.11) [256] *P<0.001*
DAPSA			
Baseline score, mean (SE) [n]	46.5 (1.4) [283]	43.4 (1.4) [281]	43.8 (1.4) [281]
Change from baseline at week 24, mean (SE) [n]	-22.6 (1.4) [251]	-25.0 (1.3) [253] *P=0.24*	-24.9 (1.4) [256] *P=0.23*
LDI			
Baseline score, mean (SD) [n]	56.89 (174.56)	50.07 (137.2) [283]	44.11 (143.17) [282]
Baseline for patients with > 0 score, mean (SE) [n]	164.9 (26.9) [98]	147.6 (20.8) [96]	138.2 (23.9) [90]
Change from baseline at week 24 in patients with baseline LDI > 0, mean (SE) [n]	-128.8 (26.8) [89]	-119.1 (20.7) [89] *P=0.85*	-110.2 (22.7) [87] *P=0.68*
SPARCC			
Baseline score, mean (SD) [n]	3.9 (4.3)	3.7 (4.3) [283]	4.1 (4.5) [282]
Baseline for patients with > 0 score, mean (SE) [n]	5.7 (0.3) [191]	5.5 (0.3) [189]	5.9 (0.3) [196]
Change from baseline at week 24 in patients with baseline SPARCC >0, mean (SE) [n]	-3.1 (0.3) [167]	-3.0 (0.3) [173] *P=0.93*	-2.9 (0.3) [179] *P=0.70*
Psoriasis-affected BSA			
Baseline, mean (SD)	12.68 (18.78)	10.76 (14.66)	10.74 (15.58)
Baseline for patients with ≥ 10% BSA at baseline, mean (SE)	30.3 (2.3)	25.9 (1.7)	27.3 (2.0)
BSA % improvement from baseline in patients with baseline BSA ≥ 10%, mean (SE) [n]	65.7 (3.7) [92]	74.2 (3.3) [91] *P=0.12*	81.6 (2.8) [86] *P<0.001*
mNAPSI			
Baseline for patients with > 0 score, mean (SE) [n]	3.4 (0.2) [183]	3.5 (0.2) [205]	3.6 (0.2) [195]
Change from baseline at week 24 in patients with baseline mNAPSI >0, mean (SE) [n]	-1.1 (0.2) [121]	-1.5 (0.2) [115] *P=0.10*	-1.7 (0.2) [123] *P=0.020*

P-values are for comparisons with the methotrexate monotherapy arm. Only the P-values in bold for MDA at week 24 (key secondary endpoint) are statistically significant (calculated using a Bonferroni-based Gatekeeping Chain Procedure). All other P-values (italicized) are unadjusted and nominal. [n] is the number of patients analyzed for mean values (if different from the full analysis set). Data previously published in Mease et al. Arthritis Rheumatol. 2019;71:1112-1124.
BSA, (psoriasis-affected) body surface area; DAPSA, Disease Activity Index for Psoriatic Arthritis; LDI, Leeds Dactylitis Index; MDA, Minimal Disease Activity; mNAPSI, modified Nail Psoriasis Severity Index; PASDAS, Psoriatic Arthritis Disease Activity Score; SD, standard deviation; SE, standard error; SPARCC, Spondyloarthritis Research Consortium of Canada.

Table 2. Week 24 Treatment-Interaction Outcomes Adjusted by Presence/Severity of Disease Manifestations (Full Analysis Set; Using Observed Cases)

	Methotrexate Monotherapy N = 284			Etanercept Monotherapy* N = 284			Combination Therapy* N = 283		
Least Square Mean Estimate (SE)	MDA Achieved	PASDAS Change from Baseline	DAPSA Change from Baseline	MDA Achieved	PASDAS Change from Baseline	DAPSA Change from Baseline	MDA Achieved	PASDAS Change from	DAPSA Change from Baseline
SPARCC >0	0.16 (0.04)	-1.87 (0.14)	-23.54 (1.88)	0.28 (0.04) **P=0.008**	-2.56 (0.14) **P=0.0001**	-25.55 (1.88) P=0.39	0.29 (0.04) **P=0.005**	-2.50 (0.14) **P=0.0004**	-25.42 (1.81) P=0.42
SPARCC = 0	0.31 (0.05)	-1.93 (0.18)	-18.51 (2.42)	0.49 (0.06) P=0.22	-2.45 (0.19) **P=0.04**	-21.15 (2.52) P=0.42	0.47 (0.06) **P=0.041**	-2.56 (0.19) **P=0.014**	-21.18 (2.52) P=0.42
SPARCC >0 vs SPARCC = 0	-0.15 (0.06)	0.06 (0.22)	-5.03 (2.86)	-0.20 (0.07) P=0.56	-0.12 (0.22) P=0.56	-4.40 (2.87) P=0.88	-0.18 (0.07) P=0.78	0.06 (0.22) P=0.98	-4.24 (2.91) P=0.85
LDI >0	0.23 (0.05)	-2.21 (0.18)	-25.42 (2.41)	0.34 (0.05) P=0.11	-3.14 (0.18) **P<0.0001**	-29.20 (2.41) P=0.24	0.35 (0.05) P=0.072	-3.26 (0.18) **P<0.0001**	-32.15 (2.39) **P=0.04**
LDI = 0	0.22 (0.04)	-1.70 (0.14)	-19.48 (1.82	0.36 (0.04) **P=0.005**	-2.18 (0.14) **P=0.01**	-21.06 (1.90) P=0.50	0.35 (0.04) **P=0.009**	-2.12 (0.13) **P=0.02**	-19.65 (1.80) P=0.94
LDI >0 vs LDI = 0	0.01 (0.06)	-0.50 (0.21)	-5.94 (2.80)	-0.02 (0.06) P=0.69	-0.96 (0.21) P=0.12	-8.14 (2.82) P=0.58	0.01 (0.06) P=0.96	-1.15 (0.21) **P=0.03**	-12.50 (2.80) P=0.10
mNAPSI >1	0.21 (0.05)	-1.93 (0.17)	-22.55 (2.24)	0.34 (0.04 P=0.19	-2.72 (0.15) **P=0.0001**	-24.74 (2.13) P=0.42	0.39 (0.04) **P=0.0014**	-2.85 (0.15) **P<0.0001**	-26.13 (2.08) P=0.19
mNAPSI ≤1	0.14 (0.07)	-1.43 (0.31)	-16.82 (4.14)	0.29 (0.08) P=0.15	-2.02 (0.31) P=0.17	-20.58 (4.18) P=0.51	0.28 (0.08) P=0.16	-2.01 (0.29) P=0.16	-21.13 (3.87) P=0.43
mNAPSI >1 vs ≤1	0.07 (0.08)	-0.50 (0.34)	-5.73 (4.51)	0.05 (0.09) P=0.85	-0.70 (0.33) P=0.67	-4.15 (4.45) P=0.80	0.11 (0.09) P=0.73	-0.84 (0.31) P=0.46	-5.01 (4.17) P=0.91
BSA ≥ 10%	0.19 (0.05)	-2.01 (0.18)	-21.50 (2.37)	0.30 (0.05) P=0.10	-2.87 (0.18) **P=0.0004**	-25.51 (2.47) P=0.22	0.35 (0.05) **P=0.02**	-2.67 (0.18) **P=0.007**	-24.50 (2.43) P=0.36
BSA < 10%	0.23 (0.04)	-1.82 (0.14)	-21.78 (1.91)	0.37 (0.04) **P=0.006**	-2.32 (0.14) **P=0.006**	-23.09 (1.92) P=0.58	0.34 (0.04) **P=0.02**	-2.44 (0.14) **P=0.0006**	-23.74 (1.86) P=0.41
BSA ≥ 10% vs BSA <10%	-0.04 (0.06)	-0.19 (0.21)	0.27 (2.83)	-0.05 (0.06) P=0.74	-0.55 (0.21) P=0.23	-2.42 (2.85) P=0.50	0.01 (0.06) P=0.57	-0.23 (0.22) P=0.98	-0.76 (2.87) P=0.80

N = number of patients in the full analysis set. *P-values are nominal and are for comparison with methotrexate monotherapy.
BSA, (psoriasis-affected) body surface area; DAPSA, Disease Activity Index for Psoriatic Arthritis; LDI, Leeds Dactylitis Index; MDA, Minimal Disease Activity; mNAPSI, modified Nail Psoriasis Severity Index; PASDAS, Psoriatic Arthritis Disease Activity Score; SE, standard error; SPARCC, Spondyloarthritis Research Consortium of Canada.

Background/Purpose: Psoriatic arthritis is broadly characterized by clinical domains such as enthesitis, dactylitis, nail manifestations, and psoriasis. How these clinical domains influence the response to MTX and/or TNF inhibitor therapy remains unclear. Here we report the findings using data from the 48-week, SEAM-PsA trial.

Methods: In the SEAM-PsA trial, MTX and biologic-naïve adult patients with active PsA were randomized to three treatment arms; MTX (20 mg; N=284); ETN (50 mg; N=284); or Combo (ETN 50 mg + MTX 20 mg; N=283), given

weekly. Clinical outcomes (week 24) were measured as a percentage of patients achieving MDA, a change from baseline in PASDAS, and DAPSA scores. Patient subsets were based on clinical domains such as enthesitis (SPARCC), dactylitis (LDI), nail manifestations (mNAPSI) or psoriasis (BSA). Analyses comparing the ETN-containing arms with the MTX monotherapy arm used an ANCOVA model and was adjusted for baseline BMI status, prior non-biologic DMARD use, and a disease manifestation baseline status interaction term. P-values were unadjusted for multiplicity.

Results: The 3 treatment arms had similar baseline values (**Table 1**). Among patients with enthesitis, without dactylitis, and BSA< 10%, those patients receiving ETN monotherapy were more likely to achieve MDA compared with MTX monotherapy. The greater change in PASDAS scores observed in ETN monotherapy compared with MTX monotherapy were not influenced by the presence or absence of enthesitis, dactylitis or BSA≥10% (**Table 2**). Changes in DAPSA scores were similar across all clinical domains and treatment arms except for those patients with dactylitis in the Combo arm (**Table 2**).

Conclusion: For clinical domains that demonstrated differences between treatment arms, ETN arms presented better clinical outcomes when compared with MTX monotherapy. In addition, MDA and PASDAS reported consistent differences between treatment arms and are more sensitive at detecting therapy-mediated changes between clinical domains, whereas no differences were detected with DAPSA, except for dactylitis.

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Abstract Number: 1349

Guselkumab Provides Domain-Specific and Comprehensive Efficacy as Assessed Using Composite Endpoints in Patients with Active Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Guselkumab (GUS) is a human monoclonal antibody that specifically binds to the p19-subunit of IL-23. GUS has demonstrated efficacy across the various manifestations of PsA including skin, joint, soft tissue and structural damage at Week24 (W24) of DISCOVER-1[1] and DISCOVER-2[2], Phase 3 trials of patients (pts) with active PsA. Here we assess GUS efficacy through W24 in both studies utilizing composite indices.

Methods: Adult pts had active PsA despite standard therapies. DISCOVER-1 entry required ≥3 swollen & ≥3 tender joints and CRP ≥0.3 mg/dL; DISCOVER-2 required ≥5 swollen & ≥5 tender joints and CRP ≥0.6 mg/dL. 31% of DISCOVER-1 pts received 1-2 prior TNF inhibitors; DISCOVER-2 pts were biologic-naïve. Pts were randomized 1:1:1 to GUS 100 mg every 4 weeks (Q4W); GUS 100 mg at W0, W4, then every 8 weeks (Q8W); or placebo (PBO). Composite endpoints included: Psoriasis Disease Activity Score (PASDAS), Minimal Disease Activity (MDA), Very Low Disease Activity (VLDA), Modified Psoriatic Arthritis Responder Criteria (mPsARC; based on evaluation of 68 joints for tenderness and 66 for swelling),[3] Disease Activity Index for Psoriatic Arthritis (DAPSA), and clinical DAPSA (cDAPSA; determined by excluding CRP). Rates of achieving PASDAS Low/Very Low Disease Activity, MDA, VLDA, and DAPSA/cDAPSA Remission were pooled across studies (see **Fig1-2** for response criteria). GUS vs PBO comparisons employed a Cochran-Mantel-Haenszel test with baseline stratification factors or Fisher's exact test. Pts with missing data were imputed as nonresponders. P-values were not adjusted for multiplicity.

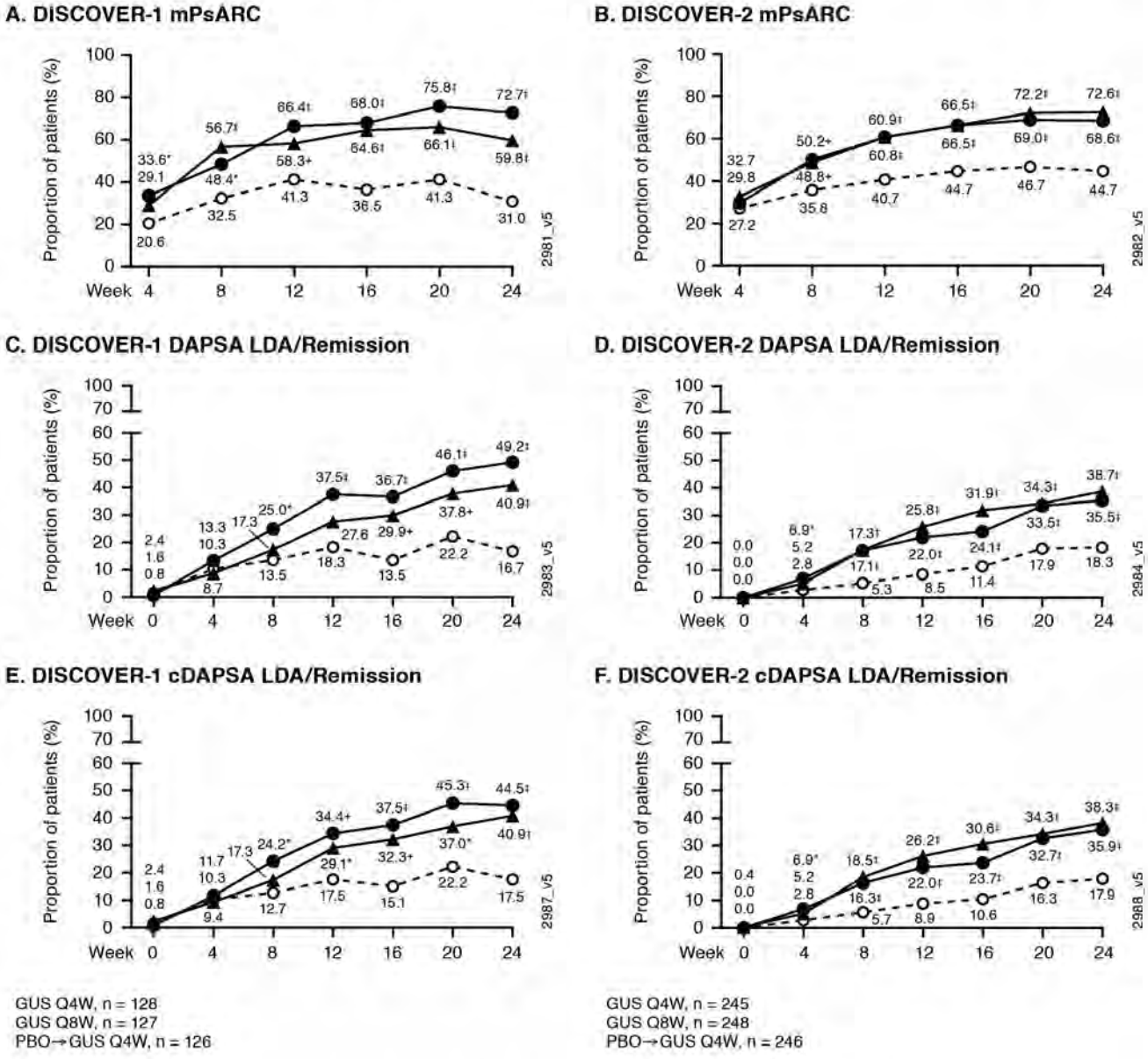
Table. Summary of baseline characteristics for DISCOVER-1 and DISCOVER-2 randomized and treated patients. Data are mean values unless stated otherwise.

	DISCOVER-1			DISCOVER-2		
	GUS Q4W	GUS Q8W	PBO	GUS Q4W	GUS Q8W	PBO
Randomized and treated patients	128	127	126	245	248	246
PsA duration (years)	6.6	6.4	7.2	5.5	5.1	5.8
Number of swollen joints (0-66)	8.6	10.9	10.1	12.9	11.7	12.3
Number of. tender joints (0-68)	17.7	20.2	19.8	22.4	19.8	21.6
Number of tender entheses (1-6)[a]	3.0	2.7	2.8	3.0	2.6	2.8
Patient pain score (0-10 VAS)	5.9	6.0	5.8	6.2	6.3	6.3
Patient global disease activity score (arthritis, 0-10 VAS)	6.1	6.5	6.1	6.4	6.5	6.5
Physician global disease activity score (0-10 VAS)	6.2	6.2	6.3	6.6	6.6	6.6
Median CRP (mg/dL)	0.6	0.7	0.8	1.2	1.3	1.2
Psoriasis Area and Severity Index (0-72)	9.5	8.4	7.7	10.8	9.7	9.3
Health Assessment Questionnaire Disability Index (0-3)	1.1	1.2	1.2	1.2	1.3	1.3
DAPSA score (remission ≤4; high disease activity >18]	39.4	45.2	43.3	49.7	46.3	48.8
PASDAS (low/very low ≤3.2; high >5.4)	6.1	6.3	6.2	6.6	6.6	6.6

[a] Among pts with Leeds enthesitis index (LEI) score >0 at baseline (DISCOVER-1 Q4W n=73; Q8W n=72; PBO n=77; DISCOVER-2 Q4W n=166; Q8W n=157; PBO n=175)

b Among pts with PASDAS score at baseline (DISCOVER-1 Q4W n=128; Q8W n=126; PBO n=126; DISCOVER-2 Q4W n=241; Q8W n=246; PBO n=241)

Figure 1. Proportions of DISCOVER-1 and DISCOVER-2 Patients Achieving mPsARC[a] Response (A, B), DAPSA LDA/Remission[b] (C, D), and cDAPSA LDA/Remission[b] (E, F) Through Week24.



Missing data imputed as nonresponse.

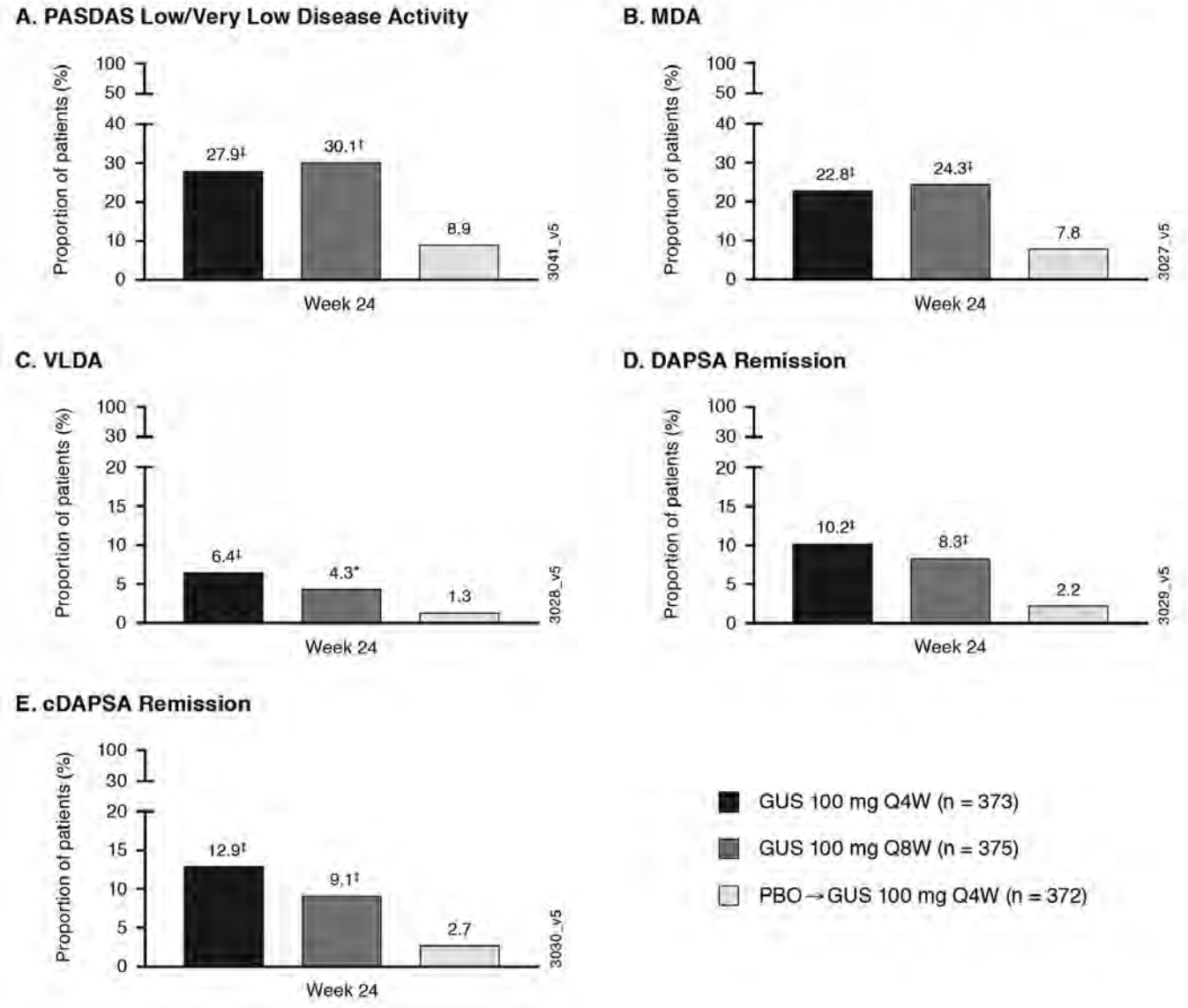
*, +, ‡ $p < 0.05$, 0.01, 0.001, respectively, vs placebo. Unadjusted (nominal) p values are not controlled for multiplicity and are descriptive/supportive only; no statistical significance should be implied.

a mPsARC response defined as ≥2 of 4 criteria (≥30% decrease in swollen joint count, ≥30% decrease in tender joint count, ≥20% improvement in patient's Global Assessment of Disease Activity (arthritis) on a visual analog scale [VAS]. 20% improvement in physician's Global Assessment of Disease Activity on a VAS), and ≥1 joint criteria with no deterioration in the other criteria.

b The DAPSA score sums tender joint count (0–68), swollen joint count (0–66), CRP (mg/dL), patient assessment of pain (0–10 VAS), and patient global assessment of disease activity (arthritis, 0–10 VAS). DAPSA LDA/Remission: ≤14. The cDAPSA score excludes CRP. cDAPSA LDA/Remission: ≤13.

Results: In randomized and treated pts in DISCOVER-1 (N=381) and DISCOVER-2 (N=739), baseline characteristics were generally well-balanced across groups and reflected moderate-to-severe disease activity (**Table**). Across studies, differences between GUS Q4W or Q8W and PBO were observed as early as Week 8 and continued to increase over time when response was assessed using the joint-focused mPsARC or DAPSA Low Disease Activity (LDA)/

Figure 2. Proportions of Pooled DISCOVER-1 and DISCOVER-2 Patients Achieving PASDAS Low/Very Low Disease Activity[a] (A), MDA[b] (B), VLDA[c] (C), DAPSA Remission[d] (D), and cDAPSA Remission[d] (E) at Week24.



Missing data imputed as nonresponse.

*, +, ‡ $p < 0.05$, 0.01, 0.001, respectively, vs placebo. Unadjusted (nominal) p values are not controlled for multiplicity and are descriptive/supportive only; no statistical significance should be implied.

a PASDAS calculated from the patient global assessment of arthritis and psoriasis (0-10 VAS), physician global assessment (0-10 VAS), swollen joint count (0-66), tender joint count (0-68), CRP, enthesitis score (measured by the Leeds Enthesitis Index), tender dactylitis count, and the 36-item Short-Form Health Survey Physical Component Summary Score. PASDAS Very low (≤1.9)/low (>1.9 to ≤3.2).

b MDA achieved if ≥5 of 7 criteria met (tender joint count ≤1, swollen joint count ≤1, psoriasis activity and severity index ≤1, patient's assessment of pain ≤15, patient's global assessment of disease activity ≤20, HAQ-DI score ≤0.5, tender entheseal points ≤1).

c VLDA achieved if 7/7 of the MDA criteria met

d The DAPSA score sums tender joint count (0–68), swollen joint count (0–66), CRP (mg/dL), patient assessment of pain (0–10 VAS), and patient global assessment of disease activity (arthritis, 0–10 VAS); DAPSA Remission: ≤4. The cDAPSA score sums tender joint count (0–68), swollen joint count (0–66), patient assessment of pain (0–10 VAS), and patient global assessment of disease activity (arthritis, 0–10 VAS); cDAPSA Remission: ≤4.

Remission composite endpoints. Also in both studies, response rates determined by omitting CRP in calculating cDAPSA were similar to DAPSA results (**Fig1**). Higher proportions of GUS Q4W- and Q8W-treated than PBO-treated pts also achieved PASDAS (28% and 30% vs 9%), MDA (23% and 24% vs 8%, respectively), VLDA (6% and 4% vs 1%), and remission determined using either DAPSA (10% and 8% vs 2%) or cDAPSA (13% and 9% vs 3%; **Fig2**).

Conclusion: Regardless of composite index employed or study population assessed, GUS 100 mg Q4W and Q8W provided robust benefits to patients with active PsA across multiple domains, indicating that GUS may offer a novel mechanism by which to treat the diverse manifestations of PsA. Excluding CRP from the DAPSA did not alter the instrument's ability to discern treatment effect.

References

[1]Deodhar A, et al. Lancet 2020;395:1115-25; [2]Mease P, et al. Lancet 2020;395:1126-36; [3]Mease PJ, et al. Arthritis Rheum 2005;52:3279–89.

Disclosure: L. Coates, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5; **C. Ritchlin**, None; **L. Gossec**, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8; **P. Helliwell**, AbbVie, 2, 8, Janssen, 2, Pfizer Inc, 8, Celgene, 8, Galapagos, 8, Amgen, 8, Novartis, 2, UCB, 8; **P. Rahman**, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5; **E. Hsia**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **A. Kollmeier**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **X. Xu**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **C. Karyekar**, Janssen Global Services, LLC, 3, Johnson & Johnson, 1, Janssen, 5; **M. Shawi**, Janssen Global Services, LLC, 3, Johnson & Johnson, 1; **W. Noël**, Janssen Medical Affairs, LLC, 1, 3; **Y. Jiang**, None; **S. Sheng**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **P. Agarwal**, Janssen Research & Development, LLC, 3, Johnson & Johnson, 1; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5.

Abstract Number: 1350

Safety Profile of Upadacitinib in Psoriatic Arthritis: Integrated Analysis from Two Phase 3 Trials

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Upadacitinib (UPA) has shown efficacy and safety in patients (pts) with active PsA in the Phase 3 SELECT-PsA 1 and SELECT-PsA 2 clinical trials. [1,2] Here we present the integrated safety data from the placebo (PBO)-controlled 24-week period of the clinical program.

Methods: The SELECT-PsA program enrolled pts with prior inadequate response (IR) or intolerance to ≥1 non-biologic DMARD (non-bDMARD) and prior IR or intolerance to ≥1 bDMARD. Both trials evaluated PBO, UPA 15 mg once

Table. Overview of Number and Percentage of Patients with TEAEs Through Week 24

Event, n (%)	PBO N=635	UPA 15 mg QD N=640	UPA 30 mg QD N=641	ADA 40 mg EOW N=429
AEs	391 (61.6)	422 (65.9)	476 (74.3)	278 (64.8)
Serious AEs	17 (2.7)	26 (4.1)	44 (6.9)	16 (3.7)
AEs leading to discontinuation	24 (3.8)	28 (4.4)	41 (6.4)	22 (5.1)
Deaths	2 (0.3)	0	0	0
AESIs				
Infection	213 (33.5)	240 (37.5)	291 (45.4)	146 (34.0)
Serious infection	5 (0.8)	6 (0.9)	17 (2.7)	3 (0.7)
Opportunistic infection	0	1 (0.2)	4 (0.6)	0
Herpes Zoster	5 (0.8)	7 (1.1)	13 (2.0)	0
Active tuberculosis	0	0	0	0
Non-melanoma skin cancer	1 (0.2)	1 (0.2)	3 (0.5)	0
Malignancy other than NMSC	0	3 (0.5)	3(0.5)	3 (0.7)
MACE (adjudicated)	1 (0.2)	1 (0.2)	0	2 (0.5)
VTE (adjudicated)	1 (0.2)	1 (0.2)	1 (0.2)	2 (0.5)
Gastrointestinal perforation (adjudicated)	0	0	0	0
Hepatic disorder	19 (3.0)	43 (6.7)	70 (10.9)	67 (15.6)
Anemia	6 (0.9)	7 (1.1)	34 (5.3)	1 (0.2)
Neutropenia	2 (0.8)	6 (0.9)	27 (4.2)	10 (2.3)
Lymphopenia	5 (0.8)	10 (3.5)	19 (6.8)	1 (0.5)
CPK elevation	10 (1.6)	42 (6.6)	53 (8.3)	24 (5.6)
Renal dysfunction	2 (0.3)	0	1 (0.2)	0

ADA, adalimumab; AE, adverse event; AESI, adverse event of special interest; CPK, creatine phosphokinase; EOW, every other week; MACE, major adverse cardiovascular events; NMSC, non-melanoma skin cancer; PBO, placebo; QD, once daily; TEAEs, treatment-emergent adverse events; VTE, venous thromboembolism; UPA, upadacitinib.

daily (QD; UPA15) and UPA 30 mg QD (UPA30); SELECT-PsA 1 also included the active comparator adalimumab (ADA).[1,2] Data was integrated for pts randomized to PBO, UPA15, or UPA30. Pts were permitted to be on monotherapy or on up to 2 non-biologic DMARDs concomitantly. Treatment-emergent adverse events (TEAEs) from the trials were analyzed and summarized. The number and percentage of pts with TEAEs through Week 24 are presented.

Results: The number of pts who received ≥ 1 dose of study drug and AEs are presented in the **Table**. The rates of TEAEs, serious AEs, and AEs leading to study drug discontinuation (D/C) were similar with PBO and UPA15 and higher with UPA30. Rates of serious infection (SIs) and herpes zoster (HZ) were similar with PBO and UPA15 and higher with UPA30. The most common SI was pneumonia. Most HZ events involved one dermatome; no central nervous system infection was reported. Opportunistic infections included 1 event of candida urethritis with UPA15, and 1 event each of pneumocystis jirovecii pneumonia, cytomegalovirus, candidiasis of the trachea, and oropharyngeal candidiasis with UPA30. Malignancies other than NMSC were reported at similar rates with UPA15 and UPA30; no events were reported with PBO. The rate of NMSC was similar with PBO, UPA15, and UPA30. The number of adjudicated major adverse cardiovascular events (MACE) and venous thromboembolic events (VTE) was < 0.5% for all arms, with similar rates reported with PBO, UPA15, and UPA30; all pts had at least one risk factor. VTEs included 1 deep vein thrombosis in PBO and 1 pulmonary embolism each in the two UPA arms. There were no adjudicated gastrointestinal perforations. Hepatic disorders were mostly transient transaminase increases. CPK elevations were reported more frequently in the UPA arms vs PBO and were mostly asymptomatic, and rarely led to study drug D/C; no rhabdomyolysis was reported. AEs of anemia, neutropenia, and lymphopenia were generally mild or moderate, non-serious, and uncommonly led to study drug D/C. The safety profile was generally consistent between UPA15 and ADA, except for lower rates of HZ, anemia, and lymphopenia and higher rates of hepatic disorders and neutropenia in the ADA arm. In contrast, the rates of most AEs were higher with UPA30 compared to ADA except for hepatic disorders.

Conclusion: The safety profiles of UPA15 and ADA were generally consistent; the rates of most AEs were higher with UPA30 compared to ADA. Through Week 24, the safety profile of UPA15 and UPA30 in PsA pts demonstrated consistent results compared to what has been observed with UPA in RA pts.[3]

References

1. McInnes IB, et al. Ann Rheum Dis, 2020; 79:12.
2. Genovese MC, et al. Ann Rheum Dis, 2020; 79:139.
3. Cohen SB, et al. Thu0167. Annals of the Rheumatic Diseases. 2019; 78:357

Disclosure: G. Burmester, AbbVie, 5, 8, Pfizer, 5, 8, Gilead Sciences, Inc., 5, 8, Eli Lilly, 5, 8, Novartis, 5, Celgene, 5; **K. Winthrop**, Pfizer, 2, 5, UCB, 2, 5, Abbvie, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Roche, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 5; **P. Nash**, AbbVie, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8; **P. Goupille**, AbbVie Inc., 1, 2, 3, Amgen, 1, 2, 3, Biogen, 1, 2, 3, BMS, 1, 2, 3, Celgene, 1, 2, 3, Chugai, 1, 2, 3, Janssen, 1, 2, 3, Lilly, 1, 2, 3, Medac, 1, 2, 3, MSD, 1, 2, 3, Nordic Pharma, 1, 2, 3, Novartis, 1, 2, 3, Pfizer, 1, 2, 3, Sanofi, 1, 2, 3, UCB, 1, 2, 3; **V. Azevedo**, AbbVie Inc., 1, 2, BMS, 1, 2, Pfizer, 1, 2, Janssen, 1, 2, Amgen, 1, 2, Novartis, 1, 2, Eli Lilly, 1, 2, UCB, 1, 2, Celltrion, 1, 2, GSK, 1, 2; **C. Salvarani**, AbbVie Inc., 1, 2, Roche, 1, 2, Sanofi-Genzyme, 1, 2, Pfizer, 1, 2, Lilly, 1, 2, Novartis, 1, 2, Amgen, 1, 2; **R. McCaskill**, AbbVie Inc., 1, 2; **J. Liu**, AbbVie Inc., 1, 2; **B. Pierre-Louis**, AbbVie Inc., 1, 2; **J. Anderson**, AbbVie Inc., 1, 3, 4; **E. Ruderman**, Eli Lilly and Company, 5, AbbVie Inc., 5, Amgen, 5, Gilead, 5, Janssen, 5, Novartis, 5, Pfizer, 2, 5.

Abstract Number: 1351

Efficacy of Ixekizumab versus Adalimumab in Psoriatic Arthritis (PsA) Patients with and Without Moderate-to-severe Psoriasis: 52-week Results from a Multicentre, Randomised Open-label Study

Lars Erik Kristensen[1], Masato Okada[2], William Tillett[3], Soyi Liu-Leage[4], Celine El Baou[5], Andrew Bradley[5], Gabriella Meszaros[4] and **Kurt de Vlam**[6], [1]The Parker Institute Copenhagen Denmark, Copenhagen, Denmark, Bispebjerg and Frederiksberg, Denmark, [2]St. Luke's International University, Tokyo, Japan, Chuo-ku, Tokyo, Japan, [3]Royal National Hospital for Rheumatic Diseases, Bath, UK; Department of Pharmacy and Pharmacology, University of Bath, Bath, UK, Bath, United Kingdom, [4]Eli Lilly and Company, Indianapolis, IN, [5]Eli Lilly and Company, Indianapolis, IN, USA, Indianapolis, IN, [6]Department of Rheumatology, University of Leuven, Belgium, Leuven, Belgium

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

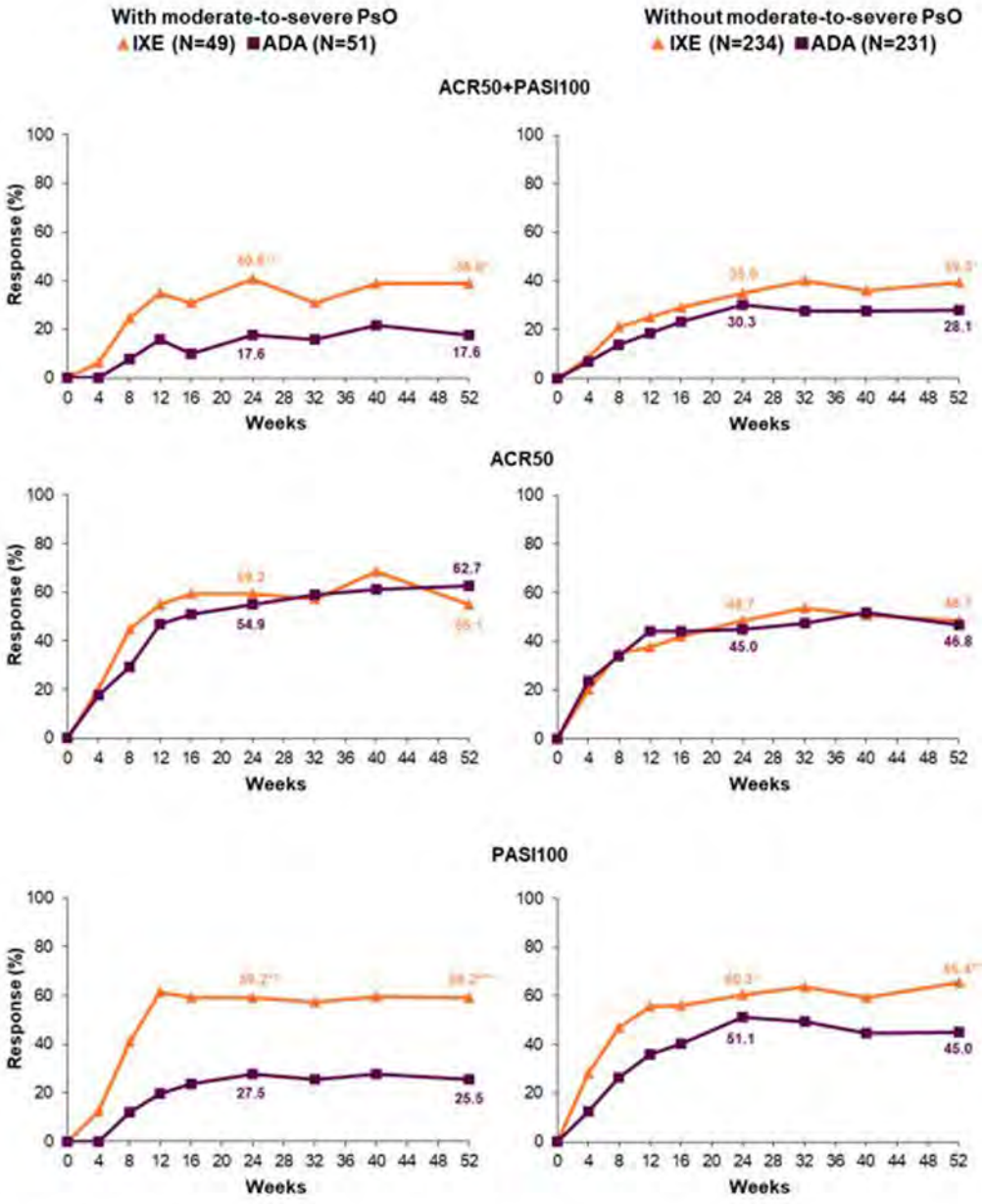
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Ixekizumab (IXE), a selective interleukin-17A antagonist, is approved for the treatment of active PsA, moderate-to-severe psoriasis (PsO), and radiographic/non-radiographic axial SpA in adults. The efficacy of IXE was compared to adalimumab (ADA) in patients (pts) with PsA and concomitant PsO in the SPIRIT-H2H (NCT03151551) study. Here we report results at weeks (wks) 24 and 52 from a subgroup analysis based on baseline PsO severity.

Methods: SPIRIT-H2H was a 52-wk, multicenter, randomized, open-label, rater-blinded, parallel-group study of biologic DMARD-naïve pts (N=566) with PsA and active PsO (≥3% body surface area involvement). Pts were randomized (stratified by concomitant use of conventional synthetic DMARDs and PsO severity) to IXE or ADA. Pts received on label dosing according to the severity of PsO. We report efficacy outcomes at wks 24 and 52 for the subgroup analysis of patients with/without moderate-to-severe PsO at baseline. The primary endpoint was the proportion of pts simultaneously achieving ≥50% improvement in ACR criteria (ACR50) and 100% improvement in PASI (PASI100) at

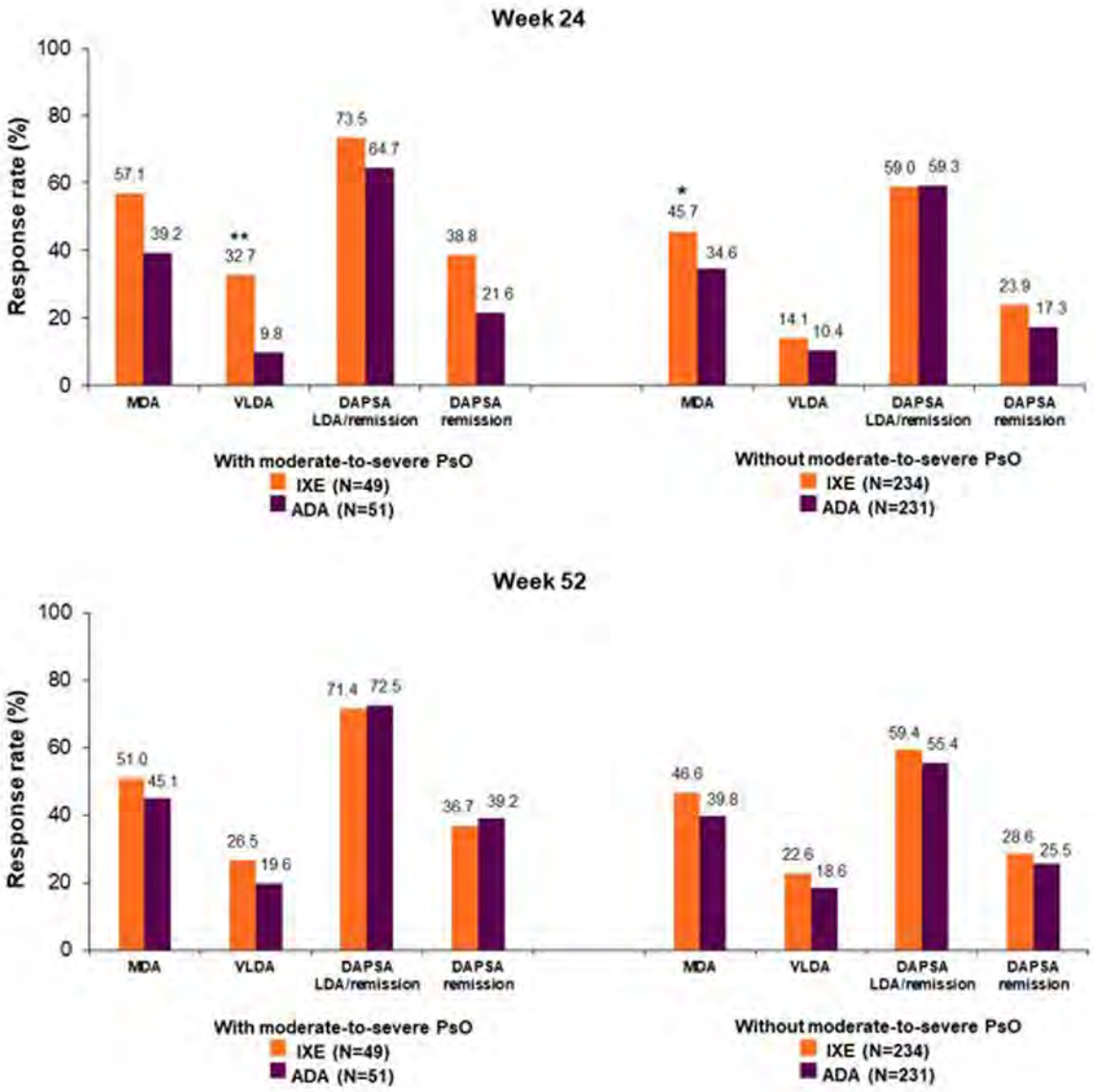
Figure 1. Key efficacy outcomes in pts with PsA based on PsO severity at baseline.



*p≤0.05, **p≤0.01, ***p≤0.001 vs. ADA. P-values from Fisher's exact test. †Interaction p≤0.10.
Patients with moderate-to-severe PsO (PASI ≥12, sPGA ≥3, BSA involvement ≥10%) received either IXE (160 mg at week 0, then 80 mg Q2W to week 12 and Q4W thereafter) or ADA (80 mg at week 0 then 40 mg Q2W). Patients without moderate-to-severe PsO received either IXE (160 mg at week 0, then 80 mg Q4W) or ADA (40 mg Q2W).
ACR50, ≥50% improvement in American College of Rheumatology criteria; ADA, adalimumab; BSA, body surface area; IXE, ixekizumab; PASI, Psoriasis Area and Severity Index; PASI100, 100% improvement in PASI; PsA, psoriatic arthritis; PsO, psoriasis; pts, patients; Q2W, every 2 weeks; Q4W, every 4 weeks; sPGA, static Physician's Global Assessment.

wk 24. Additional *post-hoc* analysis was performed for other endpoints. Logistic regression models were performed with treatment, baseline PsO severity and treatment-by-baseline PsO severity interaction as independent variables. Missing data were imputed using non-responder imputation. Differences in the proportion of responders between IXE and ADA in each subgroup were assessed using Fisher's exact test.

Figure 2. Composite outcomes and disease activity in pts with PsA based on PsO severity at baseline.



*p≤0.05, **p≤0.01 vs. ADA. P-values from Fisher's exact test. Data represent proportion of patients (%). Efficacy outcomes assessed in a *post-hoc* analysis. Interaction p-values at week 24 and 52, respectively: MDA, p=0.560 and p=0.931; VLDA, p=0.068 and p=0.784; DAPSA LDA/remission, p=0.371 and p=0.651; DAPSA remission, p=0.398 and p=0.571. Interaction p-values evaluated at the 0.10 significance level. Patients with moderate-to-severe PsO received either IXE (160 mg at week 0, then 80 mg Q2W to week 12 and Q4W thereafter) or ADA (80 mg at week 0 then 40 mg Q2W). Patients without moderate-to-severe PsO (PASI ≥12, sPGA ≥3, BSA involvement ≥10%) received either IXE (160 mg at week 0, then 80 mg Q4W) or ADA (40 mg Q2W).
ADA, adalimumab; BSA, body surface area; DAPSA, Disease Activity in PSoriatic Arthritis; IXE, ixekizumab; LDA, low disease activity; MDA, minimal disease activity (18 entheseal points); PASI, Psoriasis Area and Severity Index; PsA, psoriatic arthritis; PsO, psoriasis; pts, patients; Q2W, every 2 weeks; Q4W, every 4 weeks; sPGA, static Physician's Global Assessment; VLDA, very low disease activity (18 entheseal points).

Results: At baseline, 49/283 IXE-treated pts and 51/282 ADA-treated pts had moderate-to-severe PsO. A greater proportion of IXE-treated pts achieved the combined endpoint of ACR50+PASI100, and PASI100 compared to ADA at wks 24 and 52, regardless of baseline PsO severity (Figure 1). Similar efficacy was observed on the joints for IXE and ADA across both pt subgroups (Table). Faster improvement was observed for IXE than for ADA with respect to

Table. Other efficacy outcomes by subgroup based on PsO severity at baseline.

Proportion of pts, n/N (%)	Week 24				Week 52			
	With moderate-to-severe PsO		Without moderate-to-severe PsO		With moderate-to-severe PsO		Without moderate-to-severe PsO	
	IXE	ADA	IXE	ADA	IXE	ADA	IXE	ADA
ACR20	37/49 (75.5)	40/51 (78.4)	158/234 (67.5)	164/231 (71.0)	36/49 (73.5)	41/51 (80.4)	161/234 (68.8)	153/231 (66.2)
ACR70	21/49 (42.9)	17/51 (33.3)	69/234 (29.5)	56/231 (24.2)	21/49 (42.9)	20/51 (39.2)	79/234 (33.8)	76/231 (32.9)
PASI75	44/49 (89.8)	38/51 (74.5)	183/234 (78.2)*	157/231 (68.0)	42/49 (85.7)	41/51 (80.4)	180/234 (76.9)*	153/231 (66.2)
PASI90	41/49 (83.7)**	30/51 (58.8)	162/234 (69.2)**	128/231 (55.4)	40/49 (81.6)**	31/51 (60.8)	166/234 (70.9)***	122/231 (52.8)
SPARCC enthesitis	18/29 (62.1)†	25/36 (69.4)	89/160 (55.6)**	52/134 (38.8)	16/29 (55.2)	22/36 (61.1)	91/160 (56.9)*	60/134 (44.8)
LEI=0	15/25 (60.0)	18/28 (64.3)	80/134 (59.7)	63/118 (53.4)	14/25 (56.0)	18/28 (64.3)	84/134 (62.7)	65/118 (55.1)
LDI-B=0	9/9 (100.0)	19/19 (100.0)	28/33 (84.8)	35/39 (89.7)	8/9 (88.9)	18/19 (94.7)	27/33 (81.8)	29/39 (74.4)
NAPSI=0	28/37 (75.7)*†	21/41 (51.2)	83/154 (53.9)	67/136 (49.3)	29/37 (78.4)	28/41 (68.3)	100/154 (64.9)	76/136 (55.9)
DLQI (0,1)	29/49 (59.2)*†	17/51 (33.3)	145/234 (62.0)	129/231 (55.8)	27/49 (55.1)	19/51 (37.3)	140/234 (59.8)	118/231 (51.1)
HAQ-DI MCID ≥0.35	34/45 (75.6)	37/45 (82.2)	134/207 (64.7)	129/209 (61.7)	33/45 (73.3)	35/45 (77.8)	135/207 (65.2)	129/209 (61.7)

*p≤0.05, **p≤0.01, ***p≤0.001 vs. ADA. P-values from Fisher's exact test. †Interaction p≤0.10. Other efficacy outcome assessed in a *post-hoc* analysis.
Patients with moderate-to-severe PsO (PASI ≥12, sPGA ≥3, BSA involvement ≥10%) received either IXE (160 mg at week 0, then 80 mg Q2W to week 12 and Q4W thereafter) or ADA (80 mg at week 0 then 40 mg Q2W). Patients without moderate-to-severe PsO received either IXE (160 mg at week 0, then 80 mg Q4W) or ADA (40 mg Q2W).
ACR20/70, ≥20%/≥70% improvement in American College of Rheumatology criteria; ADA, adalimumab; BSA, body surface area; DLQI (0,1), Dermatology Life Quality Index 0 or 1; HAQ-DI MCID ≥0.35, Health Assessment Questionnaire–Disability Index minimal clinically important difference of ≥0.35 points; IXE, ixekizumab; LDI-B=0, complete resolution in Leeds Dactylitis Index–Basic; LEI=0, complete resolution in Leeds Enthesitis Index; n, number of patients in each subgroup; N, number of patients in the analysis population; NAPSI=0, complete resolution in Nail Psoriasis Severity Index; PASI, Psoriasis Area and Severity Index; PASI75/90/, ≥75%/≥90% improvement in PASI; PsA, psoriatic arthritis; PsO, psoriasis; pts, patients; Q2W, every 2 weeks; Q4W, every 4 weeks; SPARCC, Spondyloarthritis Research Consortium of Canada criteria; sPGA, static Physician's Global Assessment.

minimal disease activity (MDA) and Disease Activity in Psoriatic Arthritis (DAPSA) remission regardless of PsO severity, and for very low disease activity (VLDA) in pts with moderate-to-severe PsO (Figure 2).

Conclusion: In pts with active PsA, a significantly higher proportion of IXE-treated pts achieved the combined ACR50+PASI100 endpoint, and PASI100 at wk 52 compared to ADA, regardless of baseline PsO severity. ACR50 response at wks 24 and 52 was not influenced by different IXE dosing. Faster improvements in MDA and DAPSA remission were observed with IXE than with ADA.these subgroup analyses were consistent with data from the overall SPIRIT-H2H population.

Disclosure: L. Kristensen, AbbVie, 2, 8, Amgen Inc., 2, 8, Biogen, 2, 8, BMS, 2, 8, Eli Lilly, 2, 8, Janssen, 2, 8, Novartis, 2, 8, Pfizer, 2, 8, UCB Pharma, 2, 8, Sanofi, 2, 5, 8; **M. Okada**, Astellas, 8, Eli Lilly and Company, 8; **W. Tillett**, AbbVie, 5, 8, Amgen, 5, 8, Eli Lilly, 5, 8, Janssen, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB Pharma, 5, 8; **S. Liu-Leage**, Eli Lilly and Company, 3, 4; **C. El Baou**, Eli Lilly and Company, 9; **A. Bradley**, Eli Lilly and Company, 3; **G. Meszaros**, Eli Lilly and Company, 1, 3; **K. de Vlam**, Eli Lilly and Company, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5, 8, Celgene, 2, 5, 8, Pfizer, 2, 5, 8.

Abstract Number: 1352

Bimekizumab Maintenance of Response in Patients with Psoriatic Arthritis: 2-Year Results from a Phase 2b Dose-Ranging Study and Its Open-Label Extension

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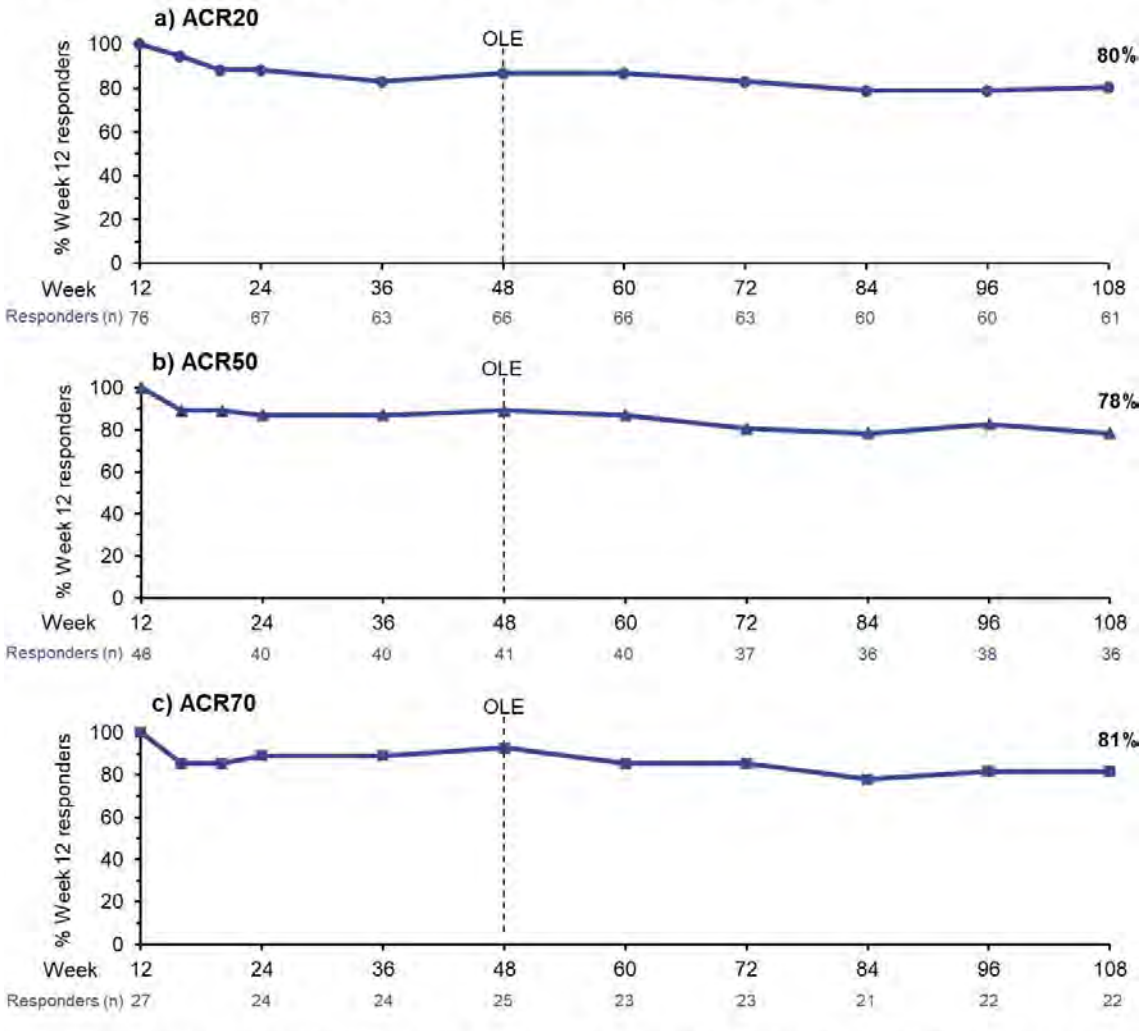
SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Bimekizumab (BKZ), a humanized monoclonal IgG1 antibody that selectively neutralizes interleukin (IL)-17A and IL-17F, has shown clinical improvements in joint and skin outcomes over 48 weeks (wks) in patients (pts) with active psoriatic arthritis.[1] The primary outcome of ACR50 response at Wk 12 of the dose-ranging BE ACTIVE study was achieved by 24–46% of pts across dosing arms.[1] Due to the chronic nature of PsA, maintaining a long-term treatment response at high levels of disease control is particularly important. We assess maintenance of response over approximately 2 years of BKZ treatment in pts who demonstrated a response to BKZ at Wk 12.

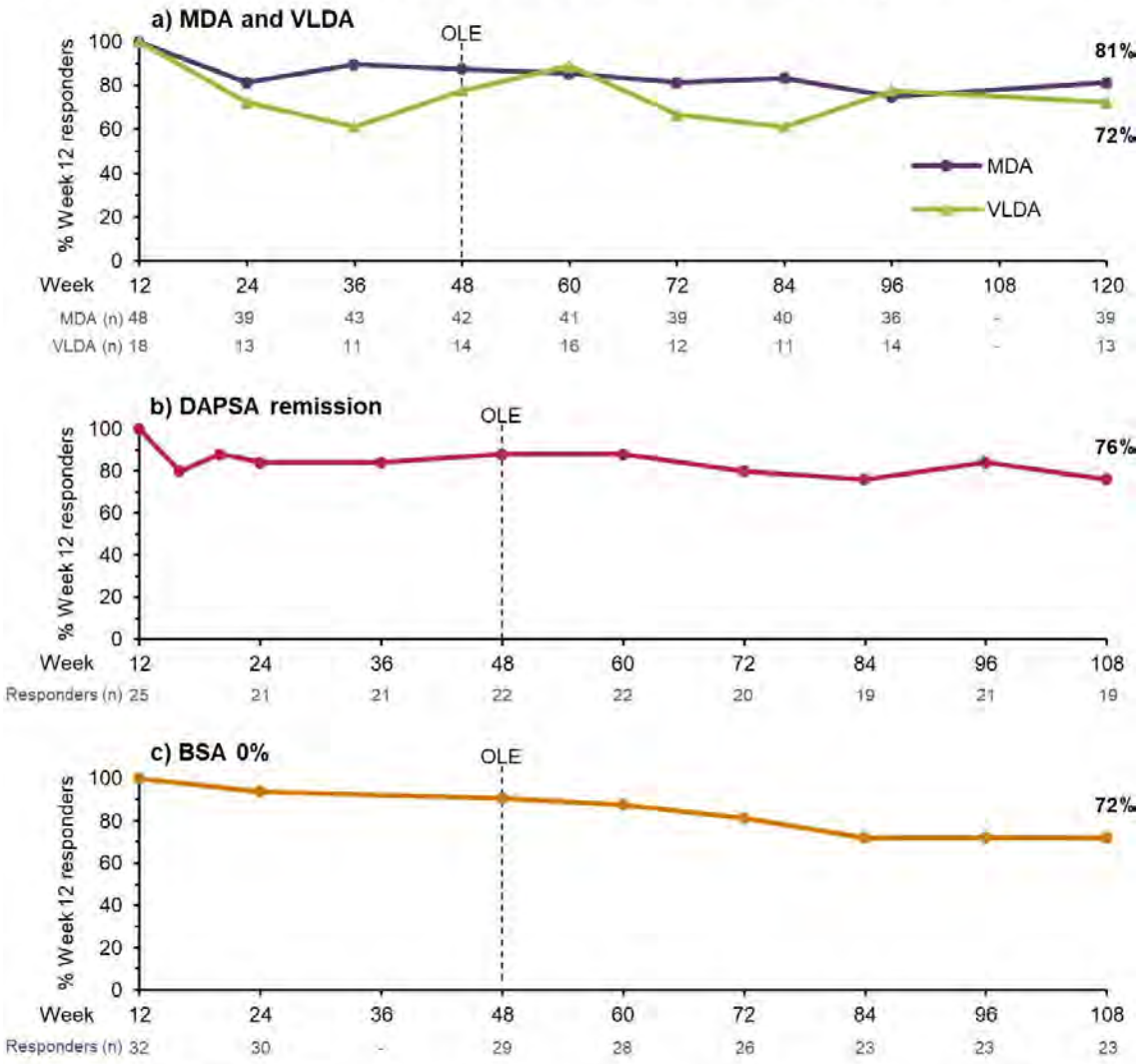
Methods: Pts who completed 48 wks of the BE ACTIVE study (NCT02969525; design described elsewhere)[1] without meeting withdrawal criteria, were eligible for BE ACTIVE 2 OLE entry (NCT03347110). BKZ was given at 160 mg every 4 wks (Q4W) regardless of previous dose. Analyses include pts randomized to the three highest BKZ doses at BE ACTIVE study baseline (BL): 160 mg, 160 mg with 320 mg loading dose (LD), and 320 mg. Maintenance of response

Figure 1: Maintenance of ACR20/50/70 response in Week 12 responders



123 patients were randomized to either BKZ 160 mg, BKZ 160 mg with a 320 mg loading dose, or BKZ 320 mg at baseline in the BE ACTIVE study. Non-responder imputation. BKZ: bimekizumab; OLE: open-label extension.

Figure 2: Maintenance of response to other outcomes in Week 12 responders, NRI



123 patients were randomized to either BKZ 160 mg, BKZ 160 mg with a 320 mg loading dose, or BKZ 320 mg at baseline in the BE ACTIVE study. 80 of 123 patients had BSA ≥3% at baseline. NRI was used for MDA, VLDA and BSA 0%. DAPSA remission is defined as DAPSA total score ≤4. For DAPSA remission data, if all components were missing, LOCF was used for DAPSA total score. BKZ: bimekizumab; BSA: body surface area; DAPSA: Disease Activity in PSoriatic Arthritis; LOCF: last observation carried forward; MDA: minimal disease activity; NRI: non-responder imputation; OLE: open-label extension; VLDA: very low disease activity.

is reported as the percentage (%) of BKZ-treated pts achieving a response at Wk 12, with maintained response over time. Outcomes include ACR20/50/70, minimal disease activity (MDA) and very low disease activity (VLDA), Disease Activity in PSoriatic Arthritis (DAPSA) remission, and body surface area (BSA) 0% (for those pts with BSA ≥3% at BL). Non-responder imputation (NRI) was used for missing data. Results are presented from Wk 12 (end of double-blind treatment) to Wk 108, or Wk 120 for outcomes not recorded at Wk 108. Rates of treatment-emergent adverse events (TEAEs) are reported for the Safety Set (pts who received ≥1 dose BKZ).

Results: At BL in the BE ACTIVE study, 123 pts were randomized to the three highest BKZ doses (160–320 mg). 109 pts entered the OLE, all receiving BKZ 160 mg Q4W. ACR20/50/70 were achieved by 76 (62%), 46 (37%), and 27 (22%) pts, respectively, at Wk 12 of the double-blind phase. MDA and VLDA criteria were met by 48 (39%) and 18 (15%) pts, respectively; likewise, the number of pts who achieved DAPSA remission and BSA 0% at Wk 12 were 25 (20%) and 32 (40% of the 80 pts with BSA ≥3% at BL), respectively. The majority of pts who achieved responses at Wk 12, across the different outcomes, maintained them to Wk 108 or Wk 120 (**Figures 1 and 2**). The % of pts

achieving ACR20/50/70 at Wk 12 who maintained the response to Wk 108 was 80/78/81%, respectively. MDA and VLDA responses were maintained at Wk 120 by 81% and 72% of Wk 12 responders, respectively; likewise, for DAPSA remission at Wk 108, the response from Wk 12 was maintained by 76%; for BSA 0%: 72%. TEAEs occurred in 87.7% of pts (exposure-adjusted event rate: 181.1/100 patient-years [PY]) and serious TEAEs in 9.3% (4.1/100 PY).

Conclusion: This BKZ-treated population, who achieved high levels of disease control as early as 12 weeks (including ACR50, MDA, VLDA, BSA 0% and DAPSA remission), demonstrated a consistent maintenance of response rate around 80% across both joint and skin outcomes. These results suggest that BKZ provides a robust maintenance of response over at least 2 years of treatment in pts with PsA.

Reference

1. Ritchlin C. Lancet 2020;395:427–440.

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Abstract Number: 1353

Achievement of Remission Is Associated with Improvement in Functionality in Certolizumab Pegol-Treated Patients with Psoriatic Arthritis, Irrespective of Pre-Existing Radiographic Structural Damage

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Pre-existing structural damage in patients with psoriatic arthritis (PsA) has been suggested to impact therapeutic improvements in disease activity and functional outcomes.[1,2] Here we evaluate whether pre-existing structural damage in patients with active PsA limits functional improvements from treatment with certolizumab

Table: Baseline mean HAQ-DI score and number of patients with HAQ-DI ≤0.5 by mTSS quartile and DAPSA disease state

mTSS Quartiles	Q1 <1.38	Q2 1.38 to <5.25	Q3 5.25 to <19.54	Q4 ≥19.54	Total
DAPSA disease state	Mean (SD) no. pts HAQ-DI ≤0.5 / Nobs [%]				
HDA	1.29 (0.60) 5/39 [12.8]	1.44 (0.61) 5/55 [9.1]	1.49 (0.65) 4/54 [7.4]	1.51 (0.55) 2/53 [3.8]	1.44 (0.61) 16/201 [8.0]
L/MoDA[a]	0.90 (0.51) 8/23 [34.8]	0.77 (0.52) 8/17 [47.1]	0.91 (0.58) 6/20 [30.0]	1.26 (0.47) 1/12 [8.3]	0.93 (0.54) 23/72 [31.9]
Total	1.15 (0.60) 13/62 [21.0]	1.28 (0.65) 13/72 [18.1]	1.33 (0.68) 10/74 [13.5]	1.47 (0.54) 3/65 [4.6]	1.31 (0.63) 39/273 [14.3]

No reported patients in DAPSA remission at baseline; data were pooled for all patients randomized to CZP 200 mg and 400 mg at baseline. [a] Includes total of 4 patients in LDA. CZP: certolizumab pegol; DAPSA: Disease Activity Index for Psoriatic Arthritis; HAQ-DI: Health Assessment Questionnaire Disability Index; HDA: high disease activity; LDA: low disease activity; L/MoDA: low/moderate disease activity; mTSS: van der Heijde modified total Sharp score; no.: number; Nobs: number observed; pts: patients; SD: standard deviation.

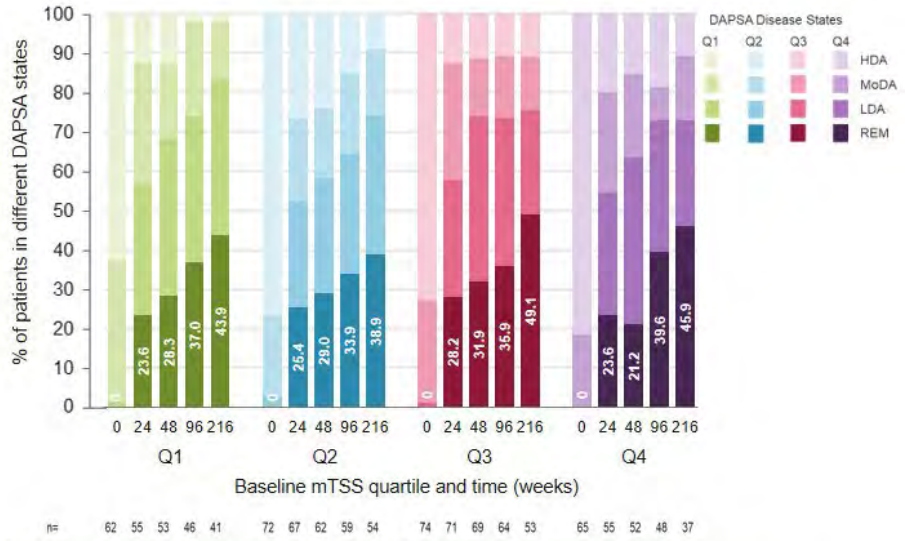
pegol (CZP) over 4 years. CZP is an Fc-free, PEGylated, tumor necrosis factor inhibitor that has shown long-term efficacy and safety in patients with PsA.[3]

Methods: Patients enrolled in RAPID-PsA (NCT01087788) with active PsA (≥3 tender joints; ≥3 swollen joints; ESR ≥28 mm/hour and/or CRP >upper limit of normal) who had failed treatment with ≥1 DMARD were randomized 1:1:1 to CZP 200 mg every 2 weeks (wks; Q2W), CZP 400 mg every 4 wks (Q4W) or placebo. Both CZP treatment arms received a loading dose of CZP 400 mg at Wks 0, 2, and 4, followed by the randomized dose regimen to Wk 216.[3] Current analyses are based on data pooled across active treatment arms. Radiographs taken at baseline and Wks 12, 24, 48, 96, 168 and 216/withdrawal were read using the van der Heijde modified Total Sharp Score (mTSS) for PsA (scores based on average of two readers). Patients were grouped according to baseline mTSS quartiles (Q1–Q4). Disease activity was assessed using Disease Activity Index for Psoriatic Arthritis (DAPSA; high disease activity [HDA]: >28; moderate [MoDA]: >14–≤28; low [LDA]: >4–≤14; remission: ≤4). Physical function was assessed using the Health Assessment Questionnaire Disability Index (HAQ-DI; ≤0.5 defined as no adverse impact on physical function).[4] The association of HAQ-DI, both change from baseline and achievement of ≤0.5, and concurrent DAPSA status was compared between the baseline mTSS groups using descriptive statistics.

Results: Of 409 patients randomized, 407 were assessed for mTSS. As expected, at baseline, HAQ-DI scores were numerically higher in patients in mTSS Q3 and Q4 than Q1 (**Table**). With CZP treatment, across all mTSS quartiles, the proportion of patients in DAPSA remission increased over time (**Figure 1**). Across all mTSS quartiles (Q1–Q4), at least 80% of patients who achieved DAPSA remission also achieved HAQ-DI ≤0.5 (no adverse impact on physical function) at Wk 24 of CZP treatment. Over 80% of patients in mTSS Q1 who achieved either DAPSA remission or LDA also achieved HAQ-DI ≤0.5 at Wk 24. However, for mTSS Q2–Q4, >90% of patients in DAPSA remission achieved HAQ-DI ≤0.5 as compared with only ~30–50% of patients with DAPSA LDA (**Figure 2**).

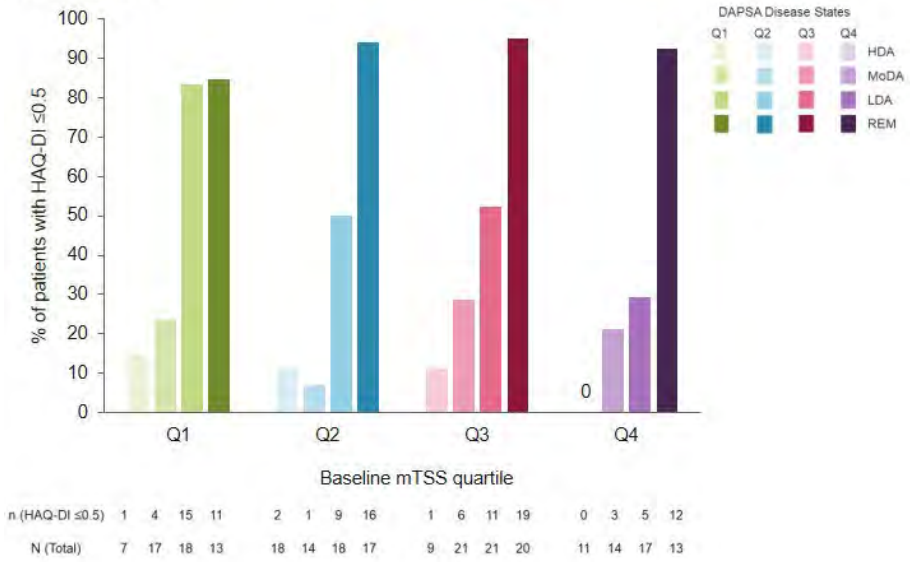
Conclusion: These data indicate that patients achieving a high level of disease control (DAPSA remission) over 4 years of treatment with CZP are likely to achieve a normative state in terms of physical function, regardless of pre-existing radiographic damage. However, a state of DAPSA LDA may not result in normalization of function in patients with pre-existing radiographic damage. This supports the rationale of aiming for remission in PsA.

Figure 1: Proportion of patients by DAPSA disease state over time and by baseline mTSS



Data were pooled for all patients randomized to CZP 200 mg and 400 mg at baseline; observed cases.
CZP: certolizumab pegol; DAPSA: Disease Activity Index for Psoriatic Arthritis; HDA: high disease activity; LDA: low disease activity; MoDA: moderate disease activity; mTSS: van der Heijde modified total Sharp score; REM: remission.

Figure 2: Achievement of HAQ-DI ≤0.5 at Week 24 by DAPSA disease state and by baseline mTSS



Data were pooled for all patients randomized to CZP 200 mg and 400 mg at baseline; observed cases.
CZP: certolizumab pegol; DAPSA: Disease Activity Index for Psoriatic Arthritis; HAQ-DI: Health Assessment Questionnaire Disability Index; HDA: high disease activity; LDA: low disease activity; MoDA: moderate disease activity; mTSS: van der Heijde modified total Sharp score; REM: remission.

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Disclosure: L. Coates, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5; **D. van der**

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Abstract Number: 1354

The Effect of 8 Years of TNF-α Blocking Therapy on Bone Mineral Density in Patients with Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) is a chronic inflammatory disease that mainly affects the axial skeleton. Bone loss reflected by low bone mineral density (BMD) is a common feature of AS and can already be observed at early stages of the disease. A recent cohort study of 135 AS patients reported 7.2% improvement in lumbar spine BMD and 2.2% improvement in hip BMD after 4 years of tumor necrosis factor-alpha (TNF-α) blocking therapy.[1] The objective of this study was to assess the effect of 8 years of TNF-α blocking therapy on BMD of the lumbar spine and hip in AS patients.

Methods: Included in this study were consecutive AS outpatients from the Groningen-Leeuwarden Axial SpA (GLAS) cohort who received TNF-α blocking therapy for at least 8 years. A maximum of one switch to another TNF-α inhibitor was allowed. Patients were excluded when they used bisphosphonates at baseline or during follow-up. BMD of the lumbar spine (anterior-posterior projection L1-L4) (LS-BMD) and hip (total proximal femur) (hip-BMD) was measured at baseline, 1 year, 2 years and then bi-annually using dual-energy X-ray absorptiometry (Hologic QDR Discovery (UMCG) or Hologic QDR Delphi (MCL), Waltman, MA, USA). Z-scores, the number of SD from the normal mean corrected for age and gender, were calculated using the NHANES reference database. Low BMD was defined as lumbar spine and/or hip BMD Z-score ≤1. Generalized estimating equations were used to analyze BMD over time within subjects. Pairwise contrast were used to compare baseline and follow-up visits. P values < 0.05 were considered statistically significant.

Results: In total, 131 AS patients were included; 73% were male, 83% HLA-B27+, mean age was 41.3 ± 10.8 years, median symptom duration 14 years (IQR 7-24), median CRP levels 13 mg/L (IQR 6-22), and 28% had poor vitamin 25(OH)D3 status (< 50) at baseline. 27% of patients switched to a second TNF-α inhibitor during follow-up and disease activity improved significantly during treatment: mean ASDASCRP 3.8 ± 0.8 at baseline and 2.1 ± 0.9 after 8 years (P< 0.001).

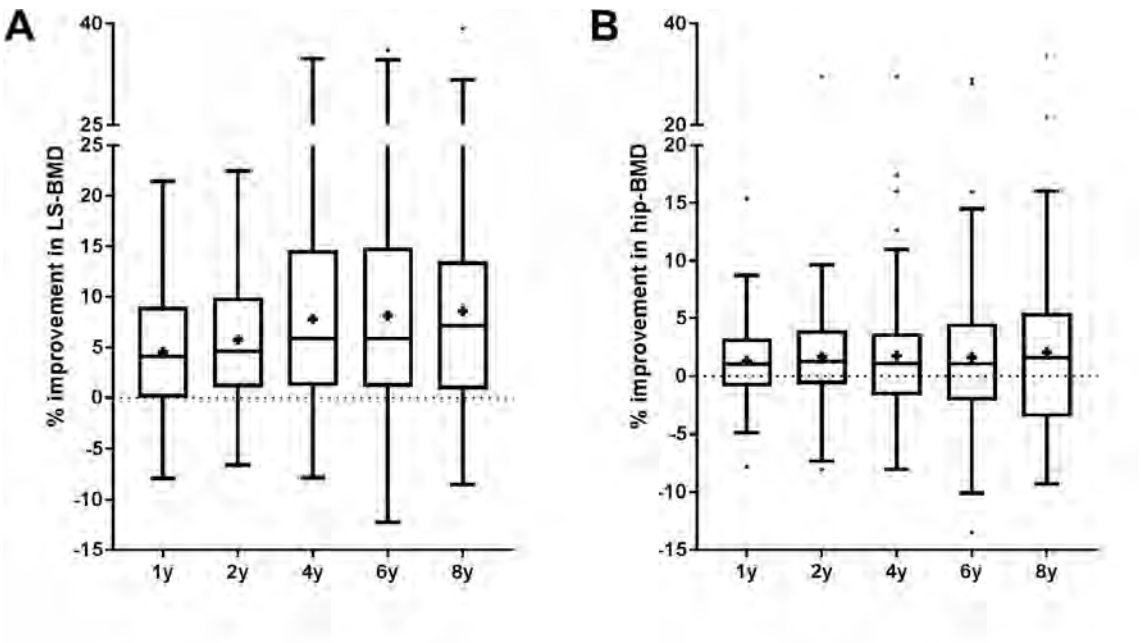

Figure 1. Percentage improvement during 8 years of TNF-α blocking therapy on LS-BMD (A) and hip-BMD (B) in patients with AS (n=131). Box-and-whisker plots (Tukey): boxes indicate medians with interquartile ranges, + indicates mean; whiskers indicate 1.5 times interquartile distances; • indicate outliers.

At baseline, low BMD at the lumbar spine and hip was present in 34% and 19% patients, respectively. Both LS-BMD and hip BMD Z-scores were significantly improved during TNF-α blocking therapy at all follow-up visits compared to baseline. Significant improvement compared to the previous time point was found up to and including 4 years for the lumbar spine and up to and including 2 years for the hip. Thereafter, flattening of improvement was observed. Median percentage of improvement in absolute BMD after 8 years of TNF-α blocking therapy compared to baseline was 7.1% (IQR 0.8-13.5) for the lumbar spine and 1.6% (IQR -3.5-5.5) for the hip (Figure 1).

Conclusion: In AS patients with established disease, both lumbar spine and hip BMD improved significantly at group level during 8 years of TNF-α blocking therapy. This effect was most pronounced in the lumbar spine, which corresponds to the disease process in AS. Main improvements in lumbar spine BMD were observed during the first 4 years of treatment.

References

1. Beek et al. J Bone Miner Res. 2019; jun;34(6):1041-8

Disclosure: M. Siderius, None; **F. Wink**, Abbvie, 5, Janssen, 5; **A. Spoorenberg**, Pfizer, 1, 2, Novartis, 1, 2, Abbvie pharmaceuticals, 1, 2, MSD, 1, UCB, 1; **S. Arends**, Pfizer, 2.

Abstract Number: 1355

Characterization of Remission in Patients with Psoriatic Arthritis Treated with Upadacitinib: Post-hoc Analysis from Two Phase 3 Trials

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Treat-to-target strategies in PsA recommend aiming for remission or low disease activity (LDA). Several disease activity measures are available including very low/minimal disease activity (VLDA/MDA), cut-

Table. Proportion of Patients Achieving Remission and LDA Measures

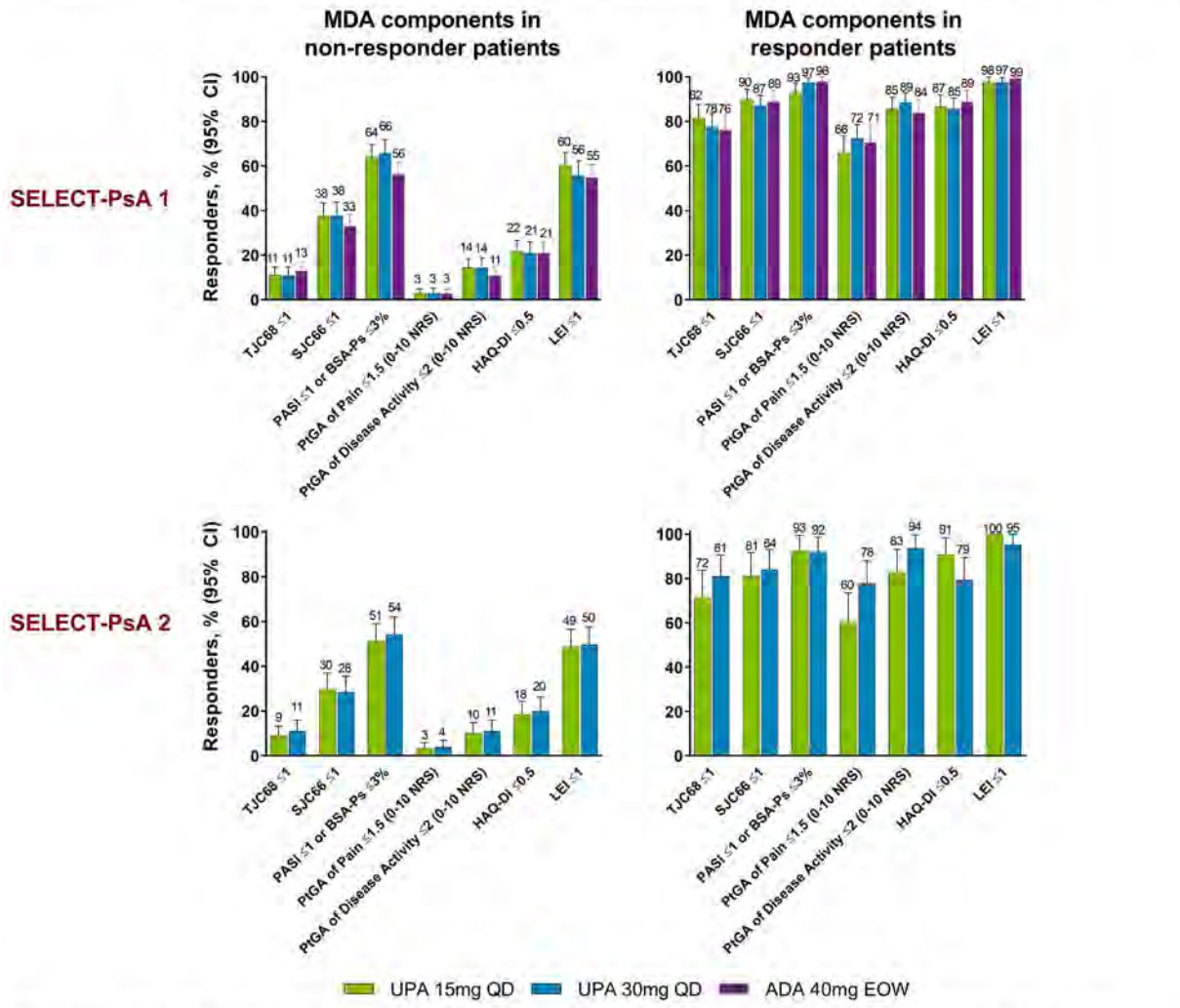
Endpoint, n (%)	SELECT-PsA 1 (non-biologic DMARD-IR)				SELECT-PsA 2 (biologic DMARD-IR)		
	PBO N=423	ADA 40mg QD N=429	UPA 15mg QD N=429	UPA 30mg QD N=423	PBO N=212	UPA 15mg QD N=211	UPA 30mg QD N=218
MDA, n (%)							
Week 12	27 (6.4)	107 (24.9)	106 (24.7) *	150 (35.5) *, †	9 (4.2)	35 (16.6) *	50 (22.9) *
Week 24	52 (12.3)	143 (33.3)	157 (36.6) *, ‡	192 (45.4) *, †, ‡	6 (2.8)	53 (25.1) *, ‡	63 (28.9) *, ‡
≥6 VLDA components							
Week 12	12 (2.8)	59 (13.8)	53 (12.4) *	82 (19.4) *, †	4 (1.9)	18 (8.5) *	31 (14.2) *
Week 24	25 (5.9)	90 (21.0)	105 (24.5) *	134 (31.7) *, †	3 (1.4)	26 (12.3) *	44 (20.2) *
VLDA							
Week 12	3 (0.7)	28 (6.5)	26 (6.1) *	44 (10.4) *, †	0	8 (3.8) *	14 (6.4) *
Week 24	11 (2.6)	62 (14.5)	55 (12.8) *	72 (17.0) *	3 (1.4)	16 (7.6) *	21 (9.6) *
DAPSA REM							
Week 12	0	16 (3.7)	27 (6.3) *	44 (10.4) *, †	0	7 (3.3) *	18 (8.3) *
Week 24	9 (2.1)	43 (10.0)	47 (11.0) *	79 (18.7) *, †	1 (0.5)	15 (7.1) *	28 (12.8) *
DAPSA LDA							
Week 12	47 (11.1)	140 (32.6)	148 (34.5) *	186 (44.0) *, †	16 (7.5)	53 (25.1) *	82 (37.6) *
Week 24	70 (16.5)	198 (46.2)	204 (47.6) *	235 (55.6) *, †	14 (6.6)	73 (34.6) *	91 (41.7) *
PASDAS REM							
Week 12	1 (0.2)	25 (5.8)	23 (5.4) *	57 (13.5) *, †	1 (0.5)	8 (3.8) *	20 (9.2) *
Week 24	12 (2.8)	51 (11.9)	60 (14.0) *	91 (21.5) *, †	4 (1.9)	20 (9.5) *	31 (14.2) *
PASDAS LDA							
Week 12	36 (8.5)	122 (28.4)	122 (28.4) *	158 (37.4) *, †	9 (4.2)	41 (19.4) *	68 (31.2) *
Week 24	63 (14.9)	168 (39.2)	195 (45.5) *	211 (49.9) *, †	9 (4.2)	69 (32.7) *	82 (37.6) *

*, P ≤ 0.05 for UPA15 and UPA30 vs PBO; †, P ≤ 0.05 for UPA30 vs ADA; ‡, Statistically significant in the multiplicity-controlled analysis.

MDA: 5/7 of TJC ≤ 1; SJC ≤ 1; PASI ≤ 1 or BSA-Ps ≤ 3%; Patient's Assessment of Pain NRS ≤ 1.5; PtGA-Disease Activity NRS ≤ 2.0; HAQ-DI score ≤ 0.5; and tender entheseal points ≤ 1.
VLDA: 7/7 of TJC ≤ 1; SJC ≤ 1; PASI ≤ 1 or BSA-Ps ≤ 3%; Patient's Assessment of Pain NRS ≤ 1.5; PtGA-Disease Activity NRS ≤ 2.0; HAQ-DI score ≤ 0.5; and tender entheseal points ≤ 1.
DAPSA = SJC66 + TJC68 + Pt pain (0-10 NRS) + PtGA (0-10 NRS) + hsCRP (in mg/dL); **DAPSA REM** ≤ 4; **DAPSA LDA** ≤ 14.
PASDAS = (((0.18 √(PGA)) + 0.159 √(PtGA) – 0.253 √(SF36-PCS) + 0.101 ln (SJC66 + 1) + 0.048 ln (TJC68 + 1) + 0.23 ln (Leeds Enthesitis Index + 1) + 0.37 ln (Tender Dactylitis Count + 1) + 0.102 ln (hsCRP + 1) + 2) * 1.5; **PASDAS REM** ≤ 1.9; **PASDAS LDA** ≤ 3.2.

ADA, adalimumab; BSA, body surface area; CI, confidence interval; DMARD, disease-modifying anti-rheumatic drug; HAQ-DI, Health Assessment Questionnaire – Disability Index; hsCRP, high-sensitivity C reactive protein; IR, inadequate response; LDA, low disease activity; MDA, minimal disease activity; NRS, numerical rating scale; PASI, Psoriasis Area Severity Index; Ps, psoriasis; PGA, Physician's Global Assessment; Pt, patient; PtGA, Patient's Global Assessment of Disease Activity; REM, remission; QD, once daily; SF-36, 36-Item Short Form Health Survey; SJC, Swollen Joint Count; TJC, Tender Joint Count; UPA, upadacitinib.

Figure. Proportion of Patients Achieving MDA Components at Week 24 in SELECT-PsA 1 and SELECT-PsA 2



ADA, adalimumab; BSA, body surface area; CI, confidence interval; EOW, every other week; HAQ-DI, Health Assessment Questionnaire – Disability Index; LEI, Leeds Enthesitis Indices; MDA, minimal disease activity; NRS, numerical rating scale; PASI, Psoriasis Area Severity Index; Ps, psoriasis; PtGA, Patient's Global Assessment of Disease Activity; QD, once daily; SJC, Swollen Joint Count; TJC, Tender Joint Count; UPA, upadacitinib.

offs based on the Disease Activity in PsA (DAPSA) score, and on the Psoriatic Arthritis Disease Activity Score (PASDAS) score.

We assessed the rates of patients (pts) achieving these criteria at Weeks 12 and 24 using data from the SELECT-PsA 1 and SELECT-PsA 2 Phase 3 studies.[1,2] Additionally, we assessed the distribution of individual MDA components among pts who did or did not achieve MDA criteria at Week 24.

Methods: This is a post-hoc analysis of 2 randomized controlled trials. In SELECT-PsA 1, pts with PsA and prior inadequate response (IR) or intolerance to ≥1 non-biologic DMARD (N=1705) were randomized to once daily upadacitinib (UPA) 15mg (UPA15), UPA 30mg (UPA30), adalimumab (ADA) 40mg every other week, or placebo (PBO). In SELECT-PsA 2, pts with prior IR or intolerance to ≥1 biologic DMARD (N=642) were randomized to UPA15, UPA30, or PBO. Remission and LDA were assessed using VLDA/MDA, DAPSA scores of ≤4/≤14, and PASDAS scores of ≤1.9/≤3.2, at Weeks 12 and 24 (**Table**).

For binary outcomes, non-responder imputation (NRI) was used for handling missing data. For MDA and related analyses, NRI was used for handling missing data; pts rescued at Week 16 were considered non-responders. Pairwise comparisons between UPA doses and PBO or ADA were conducted using the Cochran-Mantel-Haenszel test.

Results: Overall, 2345 pts were analyzed; mean age 51 years, 53% female. In both studies, higher rates of remission and LDA were observed with both UPA doses vs PBO at Weeks 12 and 24 (nominal P-values < 0.05 for both time points; **Table**). Generally, higher rates of remission and LDA were also observed with UPA30 vs ADA in non-biologic DMARD-IR pts (nominal P-values < 0.05). Greater rates of MDA/VLDA were observed at Weeks 12 and 24 with UPA15 and UPA30 vs PBO in both studies and with UPA30 vs ADA in non-biologic DMARD-IR pts (nominal P-values < 0.05 for all comparisons). The proportion of responder or non-responder pts receiving UPA15 or UPA30 was similar for each of the MDA components in both studies. At Week 24, more responder and non-responder pts in both studies achieved Swollen Joint Count (SJC) 66 ≤1, Psoriasis Area and Severity Index (PASI) ≤1 or Body Surface Area-Psoriasis (BSA-Ps) ≤3%, and Leeds Enthesitis Index (LEI) ≤1 (**Figure**). Conversely, the proportion of pts Achieving Tender Joint Count (TJC) 68 ≤1 and Pt's Global Assessment of Pain ≤1.5 tended to be lower.

Conclusion: Regardless of previous biologic DMARD failure, pts treated with UPA15 or UPA30 achieved a higher rate of remission or LDA measured by various disease activity measures vs PBO at Weeks 12 and 24; higher rates of response were observed in most of the remission and LDA measures with UPA30 vs ADA in non-biologic DMARD-IR pts. Among pts who did or did not achieve MDA criteria at Week 24, a greater proportion of UPA-treated pts achieved physician derived measures such as SJC ≤1, PASI ≤1 or BSA-Ps ≤3%, and LEI ≤1.

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Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **A. Kavanaugh**, AbbVie, 2, 9, Amgen, 2, 9, AstraZeneca, 2, 9, Bristol-Myers Squibb, 2, 9, Celgene, 2, 9, Janssen, 2, 9, Pfizer, 2, 9, Roche, 2, 9, UCB, 2, 9; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **O. FitzGerald**, AbbVie Inc., 2, 5, Amgen, 2, 5, Bristol Myers Squibb, 2, 5, Celgene, 2, 5, Janssen, 2, 5, Eli Llilly, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5; **E. Soriano**, AbbVie Inc., 2, 5, 8, Amgen, 2, 5, 8, Bristol Myers, 2, 5, 8, Celgene, 2, 5, 8, Janssen, 2, 5, 8, Lilly, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8; **P. Nash**, AbbVie, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8; **D. Feng**, AbbVie Inc., 1, 2; **A. Lertratanakul**, AbbVie Inc., 1, 3; **K. Douglas**, AbbVie Inc., 1, 2; **R. Lippe**, AbbVie Inc., 1, 3; **L. Gossec**, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8.

Abstract Number: 1356

Efficacy of Upadacitinib in Patients with Psoriatic Arthritis Stratified by Number of Prior Biologic Disease-modifying Anti-rheumatic Drugs

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SESSION INFORMATION

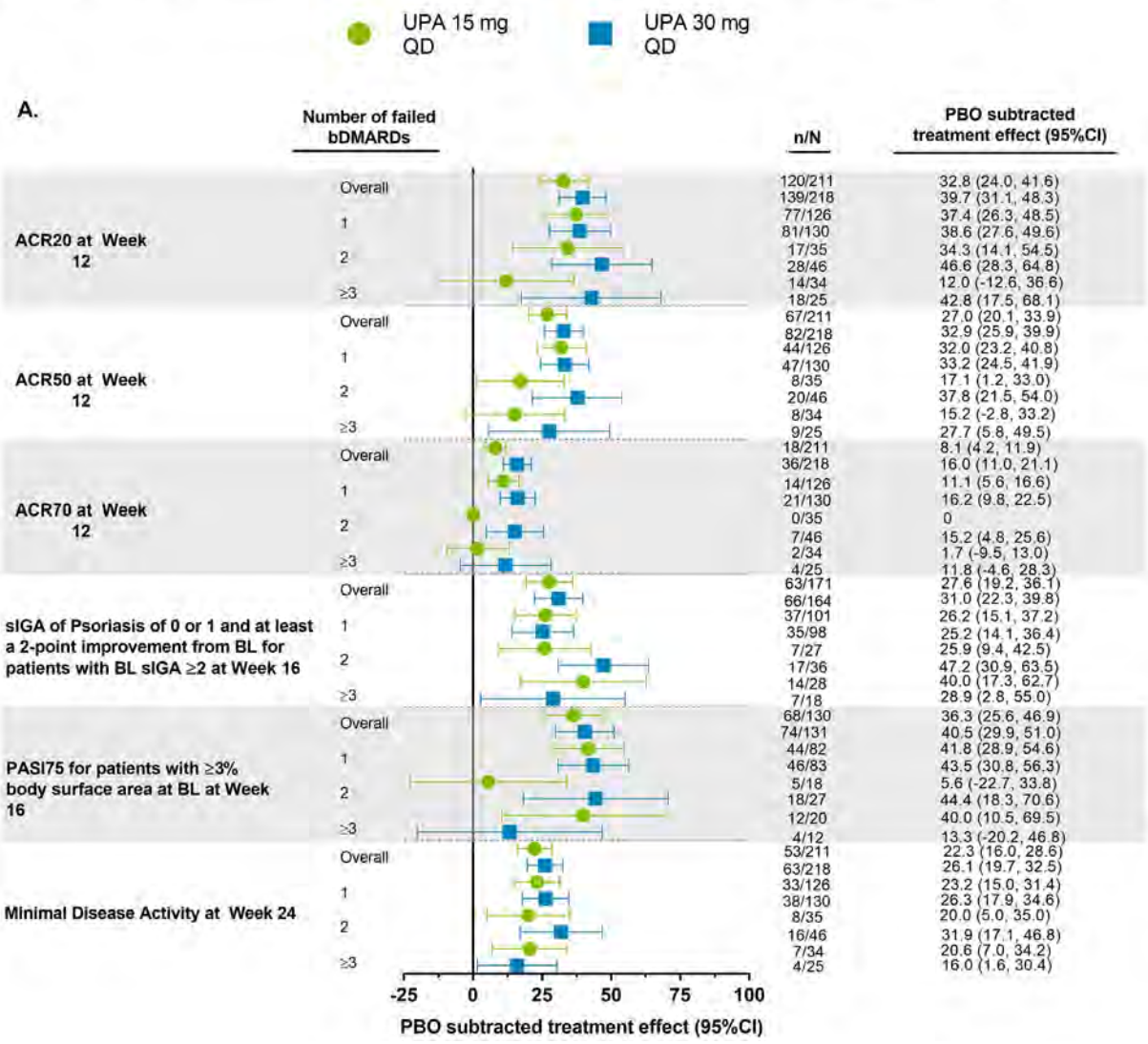
Session Date: Sunday, November 8, 2020

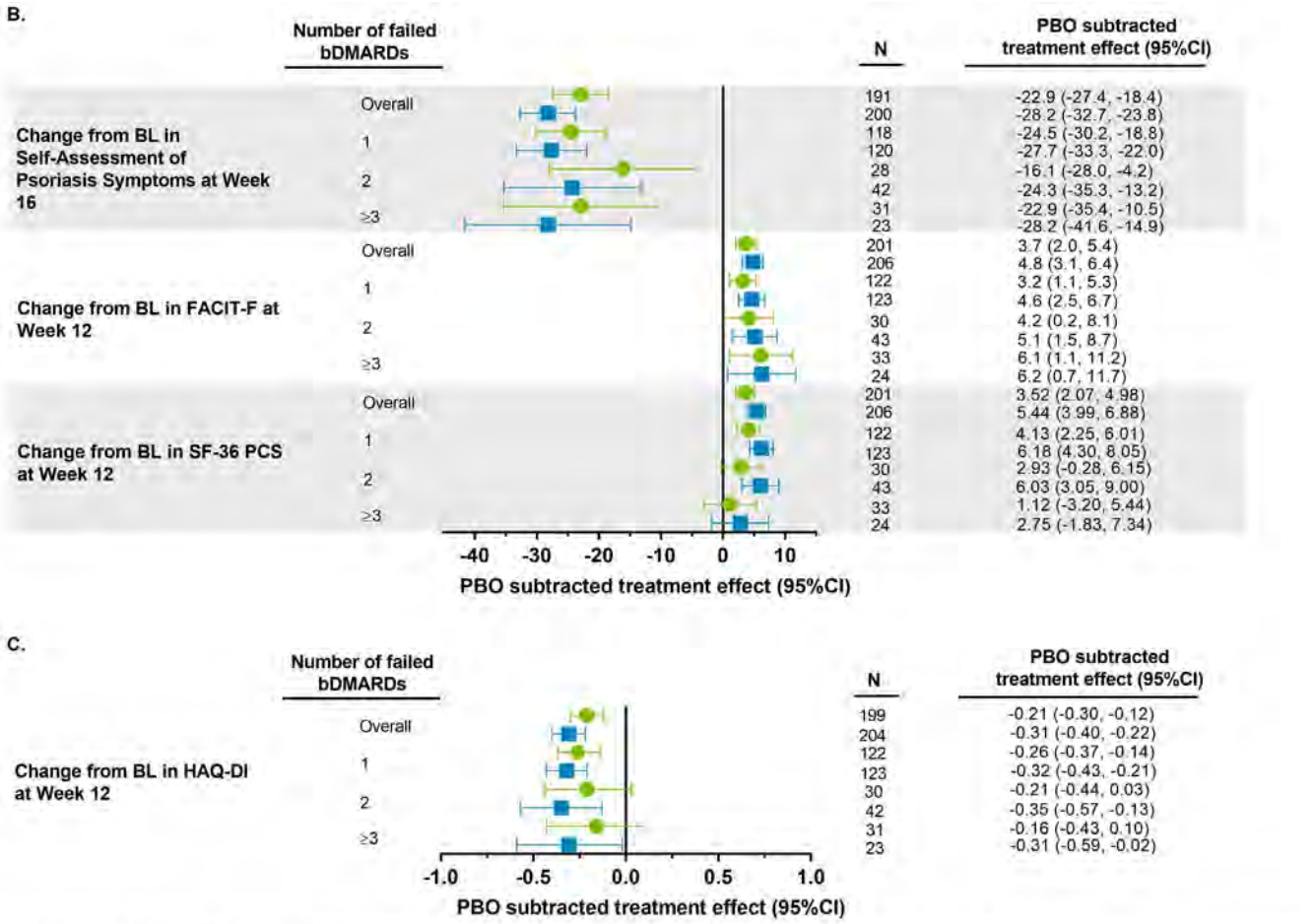
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Figure. Efficacy Outcomes by Prior bDMARD Exposure: Placebo Subtracted Treatment Effect





ACR20/50/70, American College of Rheumatology 20%/50%/70% improvement criteria;BL, baseline; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire - Disability Index; MDA, minimal disease activity; PASI, Psoriasis Area Severity Index; PBO, placebo; QD, once daily; SF-36 PCS, 36-Item Short Form Health Survey Physical Component Summary Score; sIGA, Static Investigator Global Assessment of Psoriasis.

Background/Purpose: Upadacitinib (UPA) has shown efficacy and safety in patients (pts) with active PsA in the Phase 3 SELECT-PsA 1 and SELECT-PsA 2 clinical trials.[1,2] Historically efficacy has been lower with second- and third-line therapy compared with first-line anti-TNF therapy in PsA;[3,4] however, clinical trial data that describe efficacy in pts who have had an inadequate response (IR) to multiple biologic DMARDs (bDMARDs) are limited. This analysis assessed the effects of prior bDMARD failure on UPA efficacy in the SELECT-PsA 2 trial.

Methods: The SELECT-PsA 2 study enrolled pts with prior IR or intolerance to ≥1 bDMARD (N=642). Pts were randomized to placebo (PBO), UPA 15 mg once daily (QD, UPA15), or UPA 30 mg QD (UPA30). Stable background treatment of ≤2 non-bDMARDs was permitted; background therapy was not required. Only the pts who had IR to ≥1 bDMARD were included in this analysis; pts were subgrouped based on the number of bDMARDs failed prior to enrollment (1, 2, or ≥3). This analysis includes assessment of proportion of pts achieving ACR20/50/70, and change in HAQ-DI, FACIT-Fatigue, and SF-36 Physical Component Summary at Wk 12; static Investigator Global Assessment of Psoriasis of 0 or 1 and at least a 2-point improvement from baseline, PASI75, and change in Self-Assessment of Psoriasis Symptoms at Wk 16; and proportion of pts achieving minimal disease activity (MDA) at Wk 24. Non-responder imputation was used for binary endpoints. Mixed-effects model for repeated measures was used for continuous endpoints. Point estimates and 95% confidence intervals (CIs) of the PBO subtracted treatment effect were calculated.

Results: 641 pts were randomized and received study drug; 92% were bDMARD-IR: 391 (61%) of pts failed 1 bDMARD, 116 (18%) failed 2 bDMARDs, and 83 (13%) failed ≥3 bDMARDs.

In the overall study population, UPA15 and UPA30 demonstrated superiority vs placebo for all endpoints evaluated. In this post hoc analysis, the PBO subtracted treatment effect demonstrates generally consistent efficacy as compared to the overall study population for UPA15 and UPA30 across efficacy endpoints in the subgroups of pts with IR to 1, 2, or ≥3 prior bDMARDs (**Figure**). Due to limited sample sizes for pts with IR to >1 bDMARD and the pt subsets analyzed for psoriasis-related endpoints, results should be interpreted with caution.

Conclusion: Upadacitinib demonstrated consistent efficacy in treating clinical manifestations of PsA including musculoskeletal symptoms, psoriasis, physical function, fatigue, and quality of life in pts with IR to 1 or multiple prior bDMARDs. In addition, comprehensive disease control as measured by MDA, was generally consistently achieved with upadacitinib regardless of number of prior bDMARDs tried.

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Abstract Number: 1357

Comparative Efficacy of Janus Kinase Inhibitors and TNF Inhibitors in Ankylosing Spondylitis: A Network Meta-Analysis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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Golimumab 2mg/kg														
1.28 (0.58,2.84)	Infliximab 5mg/kg													
1.29 (0.44,3.80)	1.01 (0.36,2.80)	Tofacitinib 5mg												
1.62 (0.59,4.44)	1.26 (0.49,3.26)	1.25 (0.38,4.14)	Filgotinib 200mg											
1.71 (0.85,3.46)	1.34 (0.73,2.46)	1.33 (0.51,3.43)	1.06 (0.44,2.52)	Adalimumab 40mg										
1.76 (0.81,3.80)	1.37 (0.69,2.73)	1.36 (0.50,3.71)	1.09 (0.43,2.74)	1.03 (0.58,1.82)	Etanercept 50mg									
1.81 (0.80,4.10)	1.41 (0.67,2.96)	1.40 (0.50,3.95)	1.12 (0.43,2.92)	1.05 (0.56,1.99)	1.03 (0.50,2.09)	Golimumab 100mg								
1.98 (0.97,4.03)	1.54 (0.83,2.87)	1.53 (0.59,3.99)	1.22 (0.51,2.93)	1.15 (0.71,1.89)	1.12 (0.72,1.75)	1.09 (0.57,2.09)	Etanercept 25mg							
2.03 (0.96,4.29)	1.58 (0.81,3.07)	1.57 (0.59,4.21)	1.25 (0.51,3.10)	1.18 (0.69,2.04)	1.15 (0.61,2.17)	1.12 (0.71,1.78)	1.02 (0.59,1.79)	Golimumab 50mg						
2.69 (1.00,7.25)	2.10 (0.83,5.31)	2.09 (0.64,6.76)	1.66 (0.55,5.07)	1.57 (0.67,3.66)	1.53 (0.62,3.78)	1.49 (0.58,3.84)	1.36 (0.58,3.20)	1.33 (0.55,3.23)	Infliximab 3mg/kg					
2.76 (1.20,6.32)	**2.15 (1.02,4.56)**	2.14 (0.75,6.08)	1.70 (0.64,4.51)	1.61 (0.84,3.08)	1.57 (0.76,3.23)	1.53 (0.71,3.31)	1.40 (0.72,2.70)	1.36 (0.68,2.74)	1.03 (0.39,2.66)	Certolizumab 400mg				
2.89 (1.23,6.79)	**2.26 (1.03,4.92)**	2.24 (0.77,6.50)	1.78 (0.66,4.82)	1.69 (0.85,3.33)	1.64 (0.77,3.49)	1.60 (0.72,3.56)	1.46 (0.73,2.92)	1.43 (0.69,2.96)	1.07 (0.40,2.85)	1.05 (0.47,2.36)	Upadacitinib 15mg			
3.53 (1.55,8.02)	**2.76 (1.31,5.79)**	2.74 (0.97,7.74)	2.18 (0.83,5.73)	**2.06 (1.09,3.90)**	2.01 (0.98,4.10)	1.96 (0.91,4.20)	1.79 (0.93,3.42)	1.74 (0.87,3.48)	1.31 (0.51,3.38)	1.28 (0.74,2.21)	1.22 (0.55,2.73)	Certolizumab 200mg		
4.30 (1.59,11.63)	**3.36 (1.32,8.52)**	**3.33 (1.38,8.03)**	2.66 (0.87,8.12)	**2.51 (1.07,5.87)**	2.45 (0.99,6.07)	2.38 (0.92,6.15)	2.17 (0.92,5.14)	2.12 (0.87,5.18)	1.60 (0.53,4.81)	1.56 (0.60,4.06)	1.49 (0.56,3.96)	1.22 (0.47,3.15)	Tofacitinib 10mg	
5.02 (1.86,13.55)	**3.92 (1.55,9.92)**	**3.89 (1.62,9.36)**	**3.10 (1.02,9.46)**	**2.93 (1.25,6.84)**	**2.86 (1.15,7.07)**	**2.78 (1.08,7.17)**	**2.54 (1.08,5.98)**	**2.48 (1.02,6.03)**	1.86 (0.62,5.60)	1.82 (0.70,4.73)	1.74 (0.65,4.62)	1.42 (0.55,3.67)	1.17 (0.54,2.53)	Tofacitinib 2mg
7.74 (4.18,14.34)	**6.04 (3.64,10.03)**	**6.00 (2.47,14.57)**	**4.78 (2.15,10.63)**	**4.52 (3.23,6.33)**	**4.41 (2.77,7.01)**	**4.29 (2.50,7.35)**	**3.92 (2.74,5.60)**	**3.82 (2.49,5.87)**	**2.88 (1.32,6.26)**	**2.81 (1.61,4.88)**	**2.68 (1.48,4.84)**	**2.19 (1.27,3.77)**	1.80 (0.82,3.93)	1.54 (0.71,3.36)	Placebo

Table 1. League table of pairwise comparisons for all treatments in the ASAS20 network meta-analysis.

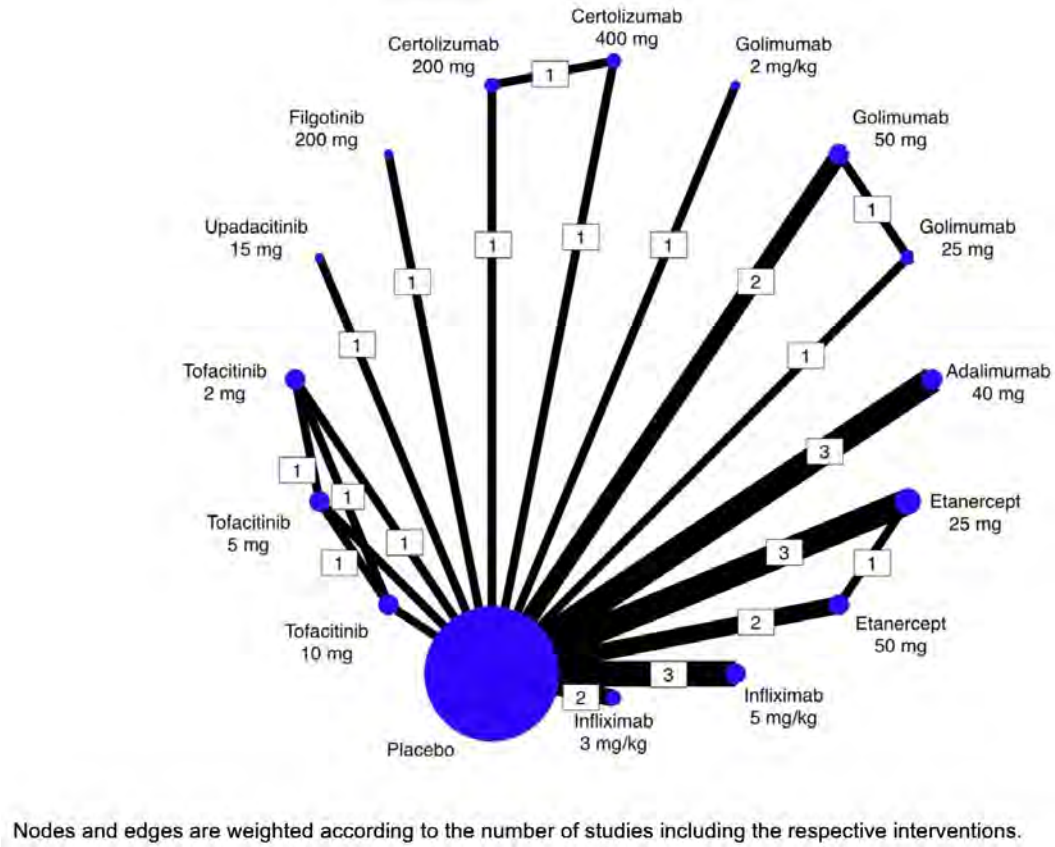

Figure 1. Network plot of the Active Ankylosing Spondylitis network (ASAS 20).

Background/Purpose: Active ankylosing spondylitis (AS) has been associated with poor quality of life and work disability in up to 50% of patients (1). There is an unmet medical need for treatment of patients with active axial disease who have an inadequate response to biologic DMARDs. Janus Kinase (JAK) inhibitors are not currently approved for use in active AS, but several clinical trials suggest their efficacy. Network meta-analyses (NMA) have been conducted to evaluate relative efficacy of JAK inhibitors and biologic therapies, however newer molecules like upadacitinib were

Probability of Best Outcome	Treatment	SUCRA
Optimal SUCRA (1-0.8)	Golimumab IV 2mg/kg	0.9
	Infliximab IV 5mg/kg	0.8
	Tofacitinib PO 5mg	0.8
Good SUCRA (0.7-0.5)	Filgotinib PO 200mg	0.7
	Adalimumab SC 40 mg	0.7
	Etanercept SC 50mg	0.7
	Golimumab SC 100mg	0.6
	Etanercept SC 25mg	0.6
	Golimumab SC 50mg	0.6
Effective SUCRA (0.4-0.2)	Infliximab IV 3mg/kg	0.4
	Certolizumab SC 400mg	0.4
	Upadacitinib PO 15mg	0.3
	Certolizumab SC 200mg	0.2

Abbreviations: IV: intravenous; PO: oral; SC: subcutaneous.

Table 2. The ranking probability of best outcome based on SUCRA.

not included (2). This study aims to compare the relative efficacy of JAK inhibitors and TNF inhibitors for the treatment of active AS.

Methods: We conducted a Bayesian NMA of randomized clinical trials (RCTs) examining the relative efficacy of TNF inhibitors and JAK inhibitors in patients with active AS who had inadequate response or intolerance to NSAIDs. Systematic review was performed in PubMed, EMBASE and Cochrane databases until February 2020. Studies of IL-17 inhibitors were excluded after analysis showed inconsistency likely due to high placebo responses. NMA was conducted by Stata 16.0 software using odds ratio (OR) with 95% credible interval (CrI) to assess the clinical effectiveness. Surface Under Cumulative Ranking curve (SUCRA) was used to analyze the relative efficacy ranking of different treatments in terms of achievement of ≥20% in the Assessment of Spondyloarthritis International Society Criteria (ASAS20) at 12-16 weeks.

Results: We identified 19 RCTs that enrolled 3,654 patients with active AS. There were 120 pairwise comparisons including 20 direct comparisons of 16 interventions (figure 1). Compared with placebo, all the interventions showed an improvement in ASAS20 response rate, except for tofacitinib 2mg twice a day (bid) and tofacitinib 10mg bid dose groups (Table 1). Golimumab IV 2mg/kg showed the highest response rate (OR 7.74, 95% CrI 4.18- 14.34). The ranking probability based on the SUCRA indicated that golimumab IV 2mg/kg (SUCRA = 0.9), infliximab IV 5mg/kg (SUCRA = 0.8) and tofacitinib 5mg bid (SUCRA = 0.8) had the highest probability of achieving the best (optimal) outcome. We subjectively ranked the best therapies, based on SUCRA cut-offs, as optimal (SUCRA ≥0.8), good (SUCRA 0.5-0.7), or effective (SUCRA ≤0.4) (table 2). There were no differences in effectiveness between TNF inhibitors and certolizumab was the lowest ranked (SUCRA=0.2). These analyses were not substantially different if we applied an ASAS40 outcome, although there were fewer studies reporting ASAS40 results. The comparisons involving certolizumab, tofacitinib 10mg and upadacitinib were limited in the number of participants and, thus, may have been underpowered to detect statistical significance.

Conclusion: In patients with active AS, golimumab 2mg IV, infliximab 5mg IV and tofacitinib 5mg bid were most efficacious in achieving ASAS 20. JAK inhibitors seem to be an efficacious alternative in management of AS for which larger clinical trials are warranted.

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Abstract Number: 1358

Certolizumab Pegol Efficacy in Patients with Non-Radiographic Axial Spondyloarthritis Stratified by Baseline MRI and C-Reactive Protein Status

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SESSION INFORMATION

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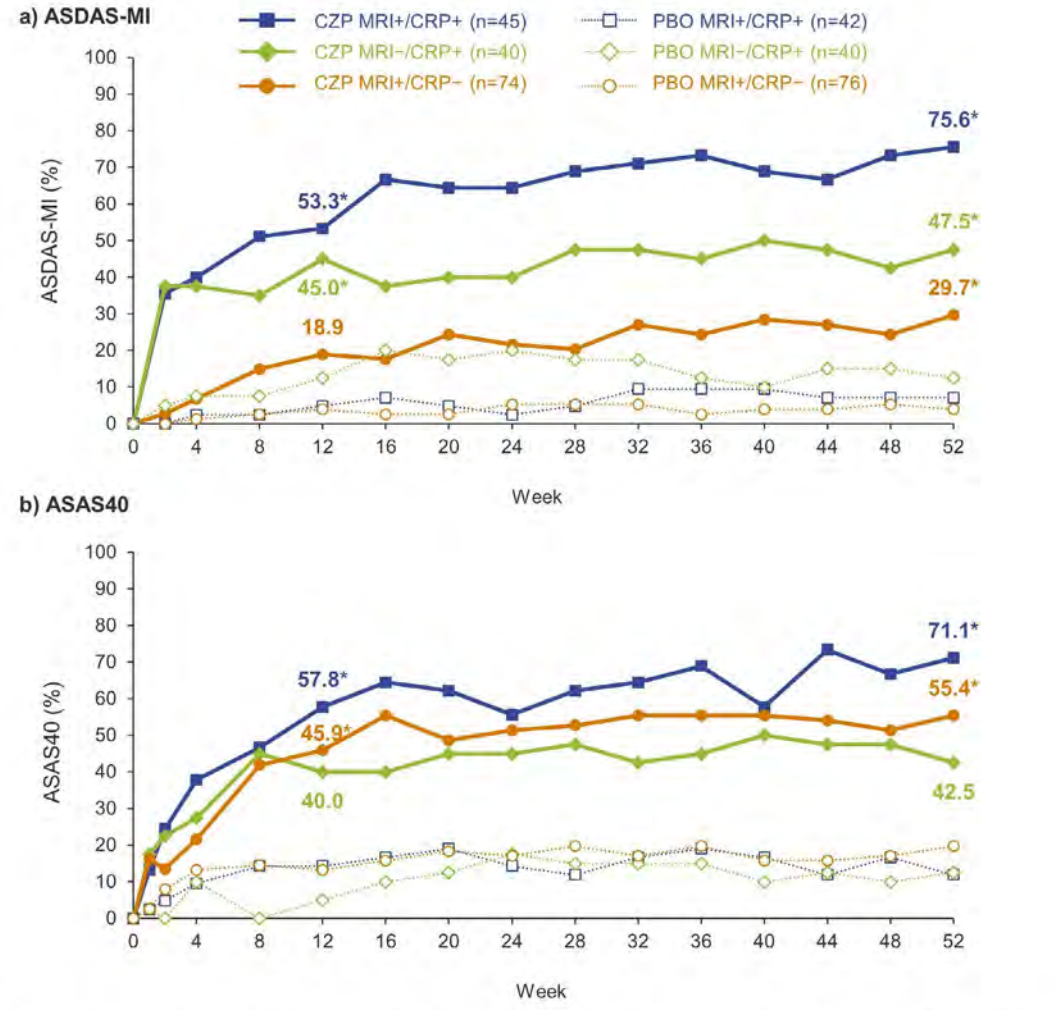
Background/Purpose: This post-hoc analysis from the phase 3 C-axSpAnd study aimed to evaluate whether the response to certolizumab pegol (CZP) in non-radiographic axial spondyloarthritis (nr-axSpA) is impacted by patients' baseline MRI and C-reactive protein (CRP) status.

Methods: C-axSpAnd (NCT02552212) is a 3-year, phase 3, multicenter study including a completed 52-week double-blind, placebo-controlled period.[1] Patients were adults with a diagnosis of axSpA, meeting Assessment of SpondyloArthritis international Society (ASAS), but not modified New York, classification criteria, active disease (Bath Ankylosing Spondylitis Disease Activity Index [BASDAI] >4, spinal pain >4), objective signs of inflammation (C-reactive protein [CRP] >10 mg/mL [CRP+] and/or evidence of sacroiliitis on MRI [MRI+]), who had failed ≥2 non-steroidal anti-inflammatory drugs (NSAIDs). Patients were randomized 1:1 to placebo or CZP (400 mg at Weeks 0, 2 and 4, then 200 mg every 2 weeks), which they received in addition to non-biologic background medication for 52 weeks. Adjustments to background medication or switching to open-label CZP (or other biologics) at any point was permitted. We report Ankylosing Spondylitis Disease Activity Score – major improvement (ASDAS-MI) and ASAS 40% response (ASAS40) for CZP-randomized patients according to prespecified subgroups based on MRI/CRP status (MRI+/CRP+, MRI–/CRP+, MRI+/CRP–). Comparisons between MRI/CRP subgroups are descriptive only; Week 12 (ASAS40) and Week 52 (ASDAS-MI) comparisons between CZP and placebo were pre-specified. Missing values, or values collected after switching to open-label treatment, were imputed using non-responder imputation.

Results: At baseline, a total of 317 patients were randomized, 159 to CZP (45 MRI+/CRP+, 40 MRI–/CRP+ and 74 MRI+/CRP–) and 158 to placebo (42 MRI+/CRP+, 40 MRI–/CRP+ and 76 MRI+/CRP–). At Week 52, ASDAS-MI was achieved in 47.2% and 7.0% of CZP and placebo-treated patients, respectively, and ASAS40 in 56.6% and 15.8%. When stratified by MRI/CRP status, response rates in all three subgroups for CZP-treated patients were also higher compared to placebo for both ASDAS-MI and ASAS40 at Week 12 and Week 52 (**Figure 1**). For ASDAS-MI, there was a greater difference in response rates between subgroups compared with ASAS40, with numerically higher response rates in the MRI+/CRP+ and MRI–/CRP+ subgroups vs the MRI+/CRP– subgroup (**Figure 1a**). Since the ASDAS value is largely dependent on the CRP value, this is to be expected. For ASAS40, the main secondary outcome, a

Figure 1. ASDAS-MI and ASAS40 response in patients stratified by baseline MRI/CRP status



Missing values, or values collected after switching to open-label treatment, were imputed using non-responder imputation. *p<0.001 for CZP vs PBO. ASAS40: Assessment of SpondyloArthritis international Society 40% response; ASDAS-MI: Ankylosing Spondylitis Disease Activity Score – major improvement; CRP: C-reactive protein; CZP: certolizumab pegol; PBO: placebo.

numerically higher response rate was also observed for the MRI+/CRP+ group, while response rates were comparable for the other groups (**Figure 1b**).

Conclusion: Clinically relevant responses were observed in nr-axSpA patients with either MRI and/or CRP positivity, with the highest response seen in the MRI+/CRP+ subgroup.

Reference

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Disclosure: A. Deodhar, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **L. Gensler**, AbbVie, 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB Pharma, 2, 5; **S. Hall**, AbbVie, 1, 2, Bristol-Myers Squibb, 1, 2, Lilly, 1, 2, Janssen, 1, 2, Pfizer, 1, 2, UCB Pharma, 1, 2, Novartis, 1, 2; **P. Robinson**,

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Abstract Number: 1359

Targeted Serum Proteomic Analysis Following Upadacitinib Treatment in Ankylosing Spondylitis Shows Robust Suppression of Innate and Adaptive Immune Pathways with Tissue Repair Modulation

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

Background/Purpose: Upadacitinib (UPA), an oral JAK inhibitor selective for JAK1, demonstrated efficacy in patients with active ankylosing spondylitis (AS) with an inadequate response (IR) to nonsteroidal anti-inflammatory drugs (NSAID) therapy in the SELECT-AXIS 1[1] trial.

To identify pathways modulated by UPA in AS patients with emphasis on those associated with response to treatment.

Methods: A subgroup of patients from the SELECT-AXIS 1 study, with available baseline and at least one follow up plasma sample during the placebo-controlled period, were selected for analysis (PBO, n= 65; UPA 15 mg QD, n=63). The levels of 92 inflammation related protein biomarkers (BioMs) were analyzed using the Olink® platform; change from baseline were expressed as Log_2 Fold Change; a repeated measure mixed linear model identified BioMs differentially modulated by UPA. Relationship between change in BioMs and change in clinical disease activity measures were derived using Pearson's correlation (ASDAS-CRP, BASDAI, and CRP) and Spearman's correlation (MRI Spine SPARCC). Pathway analysis was performed with Ingenuity® Pathway Analysis (Qiagen Inc.).

Results: Treatment with UPA 15 mg QD reduced the levels of BioMs associated with IFN, IL6, T Cells, M1 or "inflammatory" Macrophages, and Dendritic Cells (DC); and increased those of BioMs associated with tissue repair and hematopoiesis (**Table 1**). The type of pathways, inferred *in silico* based on BM data, suggests that UPA exerts broad inhibitory activity directly on multiple JAK1-dependent (IFNα/β, IFNγ, IL6, IL2, IL5, IL7, and OSM) and indirectly on JAK1-independent upstream pathways (IL1, IL23, IL17, IL18, and TNFα), resulting in the inhibition of key functional pathways such as leukocyte activation and mobility, inflammatory response, and damage to connective tissue. Improvement in ASDAS-CRP, BASDAI, and MRI spine SPARCC correlated with increase in BioMs associated with tissue repair (FGF5, DNER [Delta/Notch Like EGF Repeat Containing]) and hematopoiesis (FLT3LG,and SCF/KITLG), while improvement in ASDAS-CRP and CRP correlated with decrease in CCL23, CSF1, IL-6, and MMP1; and reduction in only CRP correlated with decrease in IFN- and of TNFα-related BioMs (**Table 2**).

Conclusion: Treatment of NSAID-IR AS patients with UPA 15 mg QD resulted in the coordinated decrease in multiple BioMs associated with the innate and adaptive immune responses, and in the increase in BioMs generally associated

Table 1: BioMs Significantly Modulated from Baseline by UPA

BIOMARKER	UNIPROT ID	GROUP	PBO WK4		PBO WK14		UPA 15 MG QD WK4		UPA 15 MG QD WK14	
			LSMEAN Log_2 FC	p Val	LSMEAN Log_2 FC	p Val	LSMEAN Log_2 FC	p Val	LSMEAN Log_2 FC	p Val
CXCL10	P02778	IFN / IL6	0.227	*	0.058	NS	-0.659	****	-0.407	***
CXCL11	O14625		0.044	NS	0.061	NS	-0.589	****	-0.362	**
CXCL9	Q07325		0.176	NS	-0.023	NS	-0.673	****	-0.478	***
IL6	P05231		0.028	NS	-0.016	NS	-0.683	****	-0.689	****
CCL19	Q99731	M1 MAC	0.073	NS	-0.005	NS	-0.638	****	-0.696	****
CSF-1	P09603		0.022	NS	-0.002	NS	-0.260	****	-0.208	****
IL-18	Q14116		-0.032	NS	-0.003	NS	-0.233	****	-0.092	*
MMP-1	P03956		-0.020	NS	-0.060	NS	-0.467	****	-0.294	**
TNF	P01375		0.049	NS	0.023	NS	-0.253	****	-0.147	**
TNFRSF9	Q07011		0.034	NS	0.001	NS	-0.317	****	-0.308	****
TNFSF14	O43557		-0.136	NS	-0.069	NS	-0.351	***	-0.213	*
CD8A	P01732	T CELL	-0.035	NS	-0.008	NS	-0.192	****	-0.235	****
IL-15RA	Q13261		-0.004	NS	-0.003	NS	-0.109	****	-0.074	**
IL-18R1	Q13478		-0.020	NS	-0.006	NS	-0.146	****	-0.078	*
SLAMF1	Q13291		0.051	NS	0.044	NS	-0.144	****	-0.197	****
TNFB	P01374		0.057	NS	0.019	NS	-0.187	****	-0.209	****
TRANCE	O14788		0.003	NS	0.023	NS	-0.181	**	-0.317	****
CCL23	P55773	DC	-0.020	NS	-0.059	NS	-0.230	****	-0.244	****
IL-12B	P29460		-0.005	NS	0.053	NS	-0.423	****	-0.339	****
MCP-4	Q99616		-0.158	NS	0.009	NS	-0.338	***	-0.231	*
CCL25	O15444	M2 MAC	0.071	NS	0.043	NS	0.114	**	0.202	****
CCL11	P51671	REPAIR / HEMAT	-0.042	NS	0.009	NS	0.152	***	0.259	****
CX3CL1	P78423		0.028	NS	0.024	NS	0.208	****	0.279	****
DNER	Q8NFT8		-0.014	NS	-0.013	NS	0.130	****	0.201	****
FGF-5	P12034		0.004	NS	0.018	NS	0.072	***	0.076	***
Flt3L	P49771		0.024	NS	0.059	NS	0.209	****	0.333	****
LIF-R	P42702		-0.014	NS	-0.012	NS	0.093	***	0.114	****
SCF	P21583		-0.038	NS	-0.040	NS	0.167	****	0.247	****
TWEAK	O43508		-0.090	*	-0.017	NS	0.125	**	0.157	***

Contrast to Baseline Significance: * p < 0.05 | ** p < 0.01 | *** p < 0.001 | **** p < 0.0001

with tissue repair and hematopoiesis. In silico pathway prediction indicates that treatment with UPA directly inhibits JAK1-dependent and indirectly JAK1-independent pathways, resulting in the down modulation of functional pathways related to inflammation and tissue damage which are known to be dysregulated in AS[2]. Based on this observation and on the correlation of change in BioMs with change in clinical measures, we hypothesize that both increase in BioMs associated with tissue repair and hematopoiesis, and decrease in BioMs associated with inflammation may contribute to the clinical activity of UPA in AS patients.

References

1. van der Heijde, D. et al. Lancet 394, 2108-2117 (2019).
2. Stoll, M.L. Clin Exp Rheumatol 29, 322-330 (2011).

Table 2: Correlation of UPA Induced Change in BM with Change in Clinical Measures

Biomarker	Change in ASADASCRP WEEK 14		Change in LOG_{10} hsCRP WEEK 14		Change in BASDAI WEEK 14		Change in MRI spine SPARCC WEEK 14	
	Pearson r	p Val	Pearson r	p Val	Pearson r	p Val	Spearman ρ	p Val
CCL11	-0.404	**	-0.234	NS	-0.402	**	-0.339	***
CX3CL1	-0.432	**	-0.251	NS	-0.422	**	-0.499	****
DNER	-0.463	***	-0.162	NS	-0.395	**	-0.310	***
FGF-5	-0.289	*	-0.043	NS	-0.381	**	-0.072	NS
Flt3L	-0.290	*	-0.045	NS	-0.351	**	-0.448	****
LIF-R	-0.377	**	-0.245	NS	-0.365	**	-0.211	*
SCF /KITLG	-0.418	**	-0.254	NS	-0.336	*	-0.446	****
TWEAK	-0.271	NS	-0.154	NS	-0.329	*	-0.249	**
CCL25	-0.140	NS	-0.068	NS	-0.256	NS	-0.207	*
IL-15RA	-0.055	NS	0.135	NS	-0.163	NS	-0.126	NS
IL18	-0.046	NS	0.076	NS	-0.132	NS	-0.039	NS
MCP-4/CCL13	-0.038	NS	-0.006	NS	-0.081	NS	0.000	NS
SLAMF1	-0.108	NS	0.139	NS	-0.170	NS	0.077	NS
TRANCE	0.055	NS	-0.133	NS	0.035	NS	-0.047	NS
CCL19	0.123	NS	0.382	**	0.029	NS	0.156	NS
CD8A	0.035	NS	0.288	*	-0.131	NS	0.110	NS
CXCL9	0.237	NS	0.341	*	0.071	NS	-0.064	NS
CXCL10	0.104	NS	0.374	**	-0.070	NS	-0.078	NS
CXCL11	0.244	NS	0.281	*	0.098	NS	0.113	NS
IL-12B	0.038	NS	0.312	*	-0.127	NS	0.033	NS
IL-18R1	0.151	NS	0.277	*	0.012	NS	0.136	NS
TNFA	0.121	NS	0.293	*	-0.090	NS	-0.031	NS
TNFRSF9	0.017	NS	0.318	*	-0.159	NS	-0.015	NS
TNFSF14	0.195	NS	0.320	*	0.016	NS	-0.030	NS
CCL23	0.324	*	0.410	**	0.114	NS	0.049	NS
CSF-1	0.130	NS	0.519	****	-0.162	NS	0.206	*
IL6	0.537	****	0.632	****	0.241	NS	0.220	*
MMP-1	0.342	*	0.209	NS	0.176	NS	0.151	NS
Correlation Significance: * $p < 0.05$ | ** $p < 0.01$ | *** $p < 0.001$ | **** $p < 0.0001$								

Disclosure: T. Sornasse, AbbVie Inc., 1, 3; **I. Song**, AbbVie, 1, 3; **T. Radstake**, AbbVie Inc., 1, 3; **D. McGonagle**, AbbVie Inc., 2, 8, Janssen Research & Development, LLC, 2.

Abstract Number: 1360

New-Onset Inflammatory Bowel Diseases Among IL-17 Inhibitors-Treated Patients: Results from the Case-Control MISSIL Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: A warning regarding safety of Interleukin 17 inhibitors (IL-17i) has been issued from data of randomized controlled trials (RCT) showing cases of new-onset inflammatory bowel diseases (NO-IBD). Real-world data are lacking. The objectives of the MISSIL (Maladies inflammatoires chroniques de l'Intestin SouS anti-IL 17) study are to describe NO-IBD associated with IL-17i, to identify risk factors, and to assess the incidence of NO-IBD in patients receiving treatment with IL-17i in France.

Methods: A French national registry was designed (MISSIL) to collect all cases of NO-IBD in patients treated with IL-17i from 2016 to 2019 in departments of rheumatology, dermatology and gastro-enterology, whatever the indication. A case–control study was performed with 3 controls per case randomly matched by gender, age (within 6 years), duration of disease (within 5 years) and underlying inflammatory disease from a database of previous studies of patients treated with IL-17i for spondyloarthritis and from centers participating in the MISSIL registry for psoriasis. NO-IBD events were analyzed using incidence rates (patient incidence rates per 100 patient-years – PY). We estimated the annual incidence rate of NO-IBD in patients treated with IL-17i. The numerator of the annual incidence rates consisted in the validated cases of NO-IBD from the MISSIL registry every year (from 2016 to 2019). The pharmaceutical firm provided its estimation of the annual number of patient-years (PY) treated with IL-17i for the denominator (from 2016 to 2019) in France.

Table 1 Characteristics of the 31 NO-IBD cases

	Cases of NO-IBD (n=31)
Age, years, SD	49.2 ± 14.6
Sex, female	14 (45%)
Underlying inflammatory disease	
-Spondyloarthritis	27 (87%)
-Psoriasis	4 (13%)
bDMARD-naïve	4 (13%)
previous bDMARD to Secukinumab	
-TNFi	20 (74%)
-Ustekinumab	7 (26%)
Symptoms	
-Diarrhoea	22 (71%)
-Loss of weight	21 (68%)
-Nausea and vomiting	4 (13%)
-Rectal bleeding	7 (26%)
-Mouth Ulcer	3 (10%)
-Anal fistula	2 (6%)
Median time to onset of NO-IBD symptoms, months, IQR	4.0 (1.5-7.5)
Median CRP at the onset of NO-IBD symptoms, mg/L	68.0 (34.0-177.5)
IL-17i discontinuation	31 (100%)
IBD treatment introduced after IL-17i	
-Corticosteroids	19 (61%)
-Mesalazine	8 (26%)
-Methotrexate	6 (38%)
-Thiopurine	4 (13%)
-TNFi	21 (68%)
-Ustekinumab	7 (26%)
-Guselkumab	1 (3%)
-Colectomy	2 (6%)
Outcomes	
-Complete resolution	17 (55%)
-Improvement	7 (23%)
-Stabilization	5 (16%)
-Death	2 (6%)

IL-17i= Interleukin 17 inhibitors. IQR= Interquartile. NO-IBD= new-onset inflammatory bowel diseases. SD= Standard Deviation. TNFi= Tumour Necrosis Factor inhibitor

Table 1 Characteristics of the 31 NO-IBD cases IL-17i= Interleukin 17 inhibitors. IQR= Interquartile. NO-IBD= new-onset inflammatory bowel diseases. SD= Standard Deviation. TNFi= Tumour Necrosis Factor inhibitor

Results: 31 cases of NO-IBD under secukinumab (SEK) were collected between January 2016 and December 2019: 27 patients treated for spondyloarthritis and 4 patients for psoriasis (**Table 1**). No case of NO-IBD was identified under ixekizumab. Mean age was 49.2 ± 14.6 years old and 14/31 were female; 14/24 were HLA-B27 positive, 10/25 had a radiographic sacroiliitis and 15/25 a MRI sacroiliitis. Only 4 were biological Disease-modifying antirheumatic drug (bDMARD)-naïve. The median time to onset of NO-IBD symptoms was 4.0 (1.5-7.5) months. The main symptoms were diarrhoea and loss of weight. Median CRP at the onset of symptoms was 68.0 mg/L (34.0-177.5). SEK was discontinued in all patients. Treatments received after SEK were: corticosteroids in 19 cases, infliximab in 14 cases, adalimumab in 7 cases, golimumab in 3 cases, ustekinumab in 7 cases and colectomy in 2 cases. The evolution was favourable with complete resolution (17/31), improvement (7/31) or stabilization (5/31). 2 patients died: one due to a massive myocardial infarction related to the severe undernutrition due to NO-IBD and one due to post-operative complications. The incidence of NO-IBD was 0.69/100 PY (7/1010) in 2016, 0.23/100 PY (11/4704) in 2017, 0.11/100

Table 2 Risk Factor of NO-IBD receiving secukinumab

			Univariate analysis		Multivariate analysis	
	Case (n=28)	Control (n=82)	OR (95% CI)	p Value	OR (95% CI)	p Value
≥ 2 prior bDMARDs	17/28 (61%)	69/82 (84%)	0.33 (0.13 to 0.85)	0.02	0.53 (0.10 to 2.75)	0.45
Combination with csDMARD	3/28 (11%)	20/82 (25%)	1.2 (0.40 to 3.90)	0.7		
Previously treated with infliximab	8/28 (29%)	29/76 (38%)	0.54(0.20 to 1.47)	0.2		
Previously treated with etanercept	13/28 (46%)	54/76 (71%)	0.38(0.16 to 0.92)	0.03	0.61(0.15 to 2.4)	0.48
Previously treated with adalimumab	19/28 (68%)	59/76 (78%)	0.5617 (0.18 to 1.74)	0.32		
Previously treated with golimumab	6/28 (21%)	28/76 (37%)	0.42(0.14 to 1.24)	0.12		
Previously treated with certolizumab	4/28 (14%)	16/76 (21%)	0.70 (0.21 to 2.35)	0.6		
Previously treated with ustekinumab	7/28 (25%)	17/82 (21%)	1.27 (0.42 to 3.84)	0.7		

bDMARD= biological Disease-modifying antirheumatic drug. csDMARD= conventional synthetic Disease-modifying antirheumatic drug. MTX= methotrexate

Table 2 Risk Factor of NO-IBD receiving secukinumab bDMARD= biological Disease-modifying antirheumatic drug. csDMARD= conventional synthetic Disease-modifying antirheumatic drug. MTX= methotrexate

PY(7/6550) in 2018 and 0.08/100PY (6/7951). There was no independent risk factor for NO-IBD in the case-control study (**Table 2**).

Conclusion: The outcome of NO-IBD was favorable after SEK discontinuation and introduction of IBD treatment in the vast majority of patients. No independent risk factor associated with NO-IBD in patients initiating SEK was identified.

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8; **P. Gaudin**, Lilly, 8, Novartis, 8; **C. Girard**, Novartis, 5, Leo Pharma, 5, Janssen, 5, Medac, 5, Abbvie, 5; **B. Gombert**, BMS, 8; **P. Goupille**, MSD France, 1, 2, Abbvie, 1, Amgen, 1, Biogaran, 1, 2, BMS, 1, Celgene, 1, Chugai, 1, Lilly, 1, Hospira, 1, Janssen, 1, Medac, 1, Nordic Pharma, 1, Novartis, 1, Sanofi-Genzyme, 1, Pfizer, 1, UCB Pharma, 1; **X. Guennoc**, None; **I. Henry-Desailly**, Abbvie, 8; **D. Jullien**, Abbvie, 5, Amgen, 5, Biogen, 5, Celgene, 5, Fresenius-Kabi, 5, Janssen, 5, Leo Pharma, 5, Lilly, 5, Medac, 5, Novartis, 5, Pfizer, 5, UCB, 5, Sanofi, 5, Abbvie, 8, Celgene, 8, Janssen, 8, Leo Pharma, 8, Medac, 8, Novartis, 8, Pfizer, 8; **E. Karimova**, None; **S. Lanot**, Abbvie, 8, Roche-Chugai, 8; **L. Le Dantec**, None; **T. Pascart**, novartis, 8, Horizon, 2; **L. Plastaras**, None; **N. Sultan-Bichat**, Janssen, 8, Abbvie, 8, Sanofi, 8, Novartis, 8, Leo Pharma, 8; **X. Truchet**, None; **S. Varin**, None; **D. Wendling**, None; **L. Gaboriau**, None; **D. Staumont-Sallé**, Lilly, 5, 8, Abbvie, 5, Leo Pharma, 5, Janssen, 5, 8, Novartis, 5, 8, Sanofi, 5, 8, Pfizer, 5, 8; **L. Peyrin-Biroulet**, Merck, 1, 2, Abbvie, 1, 2, Janssen, 1, 2, Genentech, 1, 2, Mitsubishi, 1, 2, Ferring, 1, 2, Norgine, 1, 2, Tillots, 1, 2, Vifor, 1, 2, Hospira/Pfizer, 1, 2, Celltrion, 1, 2, Takeda, 1, 2, Biogaran, 1, 2, Boehringer-Ingelheim, 1, 2, Lilly, 1, 2, HAC- Pharma, 1, 2, Index Pharmaceuticals, 1, 2, Amgen, 1, 2, Sandoz, 1, 2, Forward Pharma GmbH, 1, 2, Celgene, 1, 2, Biogen, 1, 2, Lycera, 1, 2, Samsung Bioepis, 1, 2, Theravance, 1, 2; **R. Flipo**, Abbvie, 1, 2, Biogen, 1, BMS, 1, Janssen, 1, 2, MSD, 1, Nordic, 1, Novartis, 1, 2, Pfizer, 1, 2, Roche-Chugai, 1, 2, Sanofi, 1.

Abstract Number: 1361

Secukinumab Significantly Decreased Joint Synovitis Measured by Power Doppler Ultrasonography in Biologic-naïve Patients with Active Psoriatic Arthritis: Primary (12-Week) Results from a Randomized, Placebo-Controlled Phase III Study

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Power Doppler (PD) ultrasonography (PDUS) is a sensitive non-invasive imaging technology used to assess joint synovitis and enthesitis of psoriatic arthritis (PsA) in clinical practice.[1,2] The European League Against Rheumatism and the Outcome Measures in Rheumatology (EULAR-OMERACT) developed a standardized and sensitive to change ultrasonography composite scoring system (the EULAR-OMERACT global synovitis score [GLOESS]) to detect and score joint synovitis.[3] Here we report primary (12-week) efficacy and safety results from the ULTIMATE study (NCT02662985), the first large, randomized, double-blind, placebo-controlled phase III study, primarily designed to assess the time course of response to subcutaneous secukinumab on joint synovitis with PDUS in patients with PsA.

Table: Efficacy of secukinumab at Week 12

Endpoints	Secukinumab (300 mg + 150 mg)[1] (N = 83)	Placebo (N = 83)	Difference/OR (95% CI)	*P*-values
Primary				
PDUS GLOESS, LS mean change (SE)[2,3]	–9.0 (0.9)	–5.8 (0.9)	Difference: –3.2[4] (–5.5; –0.8)	0.004
Secondary				
ACR20, % responders	68	34	OR: 4.1[5] (2.1; 8.0)	<0.0001
ACR50, % responders	46	9	OR: 8.9[5] (3.6; 22.0)	<0.0001
SPARCC enthesitis index, LS mean change (SE)[3]	–2.35 (0.28)	–1.65 (0.28)	Difference: –0.69[4] (–1.39; –0.002)	0.02

Data presented as non-responder imputation for binary variables and MMRM for continuous variables. Prespecified primary and secondary endpoints were analyzed according to a statistical hierarchy. Endpoints are shown in the order of testing. LS, least squares; MMRM, mixed-effect model repeated measures. N, total number of randomized patients.

1. Patients with psoriasis >10% of body surface area received 300 mg; remainder received 150 mg.
2. GLOESS using PDUS composite score of 24 paired joints; the range for the GLOESS is 0–144.
3. Adjusted means and mean change values are from MMRM including treatment, center, and analysis visit as factors, baseline score and weight as continuous covariates and treatment by analysis visit as an interaction term.
4. Difference in adjusted mean change.
5. Odds ratio.

Efficacy of secukinumab at Week 12

Methods: This is a 52-week study with a 12-week double-blind treatment period (TP 1) followed by 12-week open-label (TP 2) and 6-month open-label extension (TP 3). The study enrolled biologic-naïve patients with active PsA and inadequate response to conventional DMARD(s), with joint synovitis on PDUS (at least one joint [out of 48] with both total synovitis PDUS score and PD signal ≥2; or at least two joints with PDUS score ≥2 and PD signal ≥1) at screening and baseline and at least one clinical enthesitis site at baseline. Patients were randomized (1:1) to receive either secukinumab (300 or 150 mg according to severity of skin disease) or placebo weekly followed by 4-weekly dosing starting at Week 4. The primary endpoint was GLOESS, difference in mean change from baseline to Week 12 between secukinumab and placebo determined with mixed-effect model repeated measures analysis. Key secondary endpoints included proportion of patients with ACR20 and ACR50 responses at Week 12 and change in Spondyloarthritis Research Consortium of Canada (SPARCC) enthesitis index from baseline to Week 12. Safety analyses included all patients who received at least 1 dose of study treatment.

Results: Of 166 patients enrolled, 96% (160/166) completed 12-weeks treatment (secukinumab: 99% [82/83] and placebo: 94% [78/83]). Demographics and baseline clinical characteristics were comparable across groups; mean (SD) GLOESS was 24 (16) for secukinumab and 27 (17) for placebo. Mean baseline SPARCC enthesitis index was 4.2 (2.9) for secukinumab and 4.4 (3.3) for placebo. The primary endpoint was met; adjusted mean change in GLOESS was significantly higher with secukinumab vs placebo (–9.0 vs –5.8; $P = 0.004$) at Week 12 (Table), with statistical significance observed as early as Week 1. All key secondary endpoints were met (Table). No new or unexpected safety signals were reported.

Conclusion: Secukinumab demonstrated rapid and significant decrease in synovitis in a period of 12 weeks, as assessed by GLOESS in biologic-naïve patients with active PsA. Secukinumab also demonstrated superior efficacy on ACR20/50 responses and on SPARCC enthesitis vs placebo at Week 12. The safety profile of secukinumab was consistent with previous reports.

References

1. *D'Agostino MA and Coates LC. J Rheumatol 2019;46:337–39; 2. Uson J, et al. Rheumatol Clin 2018;14:27–35;* 3. *D'Agostino MA, et al. RMD Open 2017;3:e000428.*

Disclosure: M. D'Agostino, Sanofi, 5, 8, Novartis, 5, 8, BMS, 5, 8, Celgene, 5, 8, Roche, 5, 8, AbbVie, 5, 8, UCB, 5, 8, Eli Lilly, 5, 8; **G. Schett**, None; **A. López-Rdz**, Roche, 2, 5, 8, Eli Lilly, 2, 5, 8, Novartis, 2, 5, 8, BMS, 2, 5, 8, Neovacs, 2, 5, 8; **L. Šenolt**, AbbVie, 2, 5, 8, Amgen, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 8, Merck Sharp and Dohme, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8, Takeda, 8; **J. Maldonado-Cocco**, Pfizer, 2, 5, 8, Merck Sharp Dohme, 2, 5, 8, Novartis, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Roche, 2, 5, 8, Boehringer Ingelheim, 2, 5, 8, Schering-Plough, 2, 5, 8, Abbott, 2, 5, 8, UCB, 2, 5, 8, Eli Lilly and Company, 2, 5, 8, Gilead, 2, 5, 8; **R. Burgos-Vargas**, None; **E. Naredo**, AbbVie, 8, Roche, 8, BMS, 8, Pfizer, 8, UCB, 8, Eli Lilly, 2, 8, Novartis, 8, Janssen, 8, Celgene, 8; **P. Carron**, UCB, 2, 8, Merck Sharp Dohme, 2, 8, Pfizer, 2, 8, Novartis, 8, BMS, 8, AbbVie, 8, Eli Lilly, 8, Gilead, 8, Celgene, 8; **M. Boers**, BMS, 5, Novartis, 5, Pfizer, 5, GSK, 5, Mylan, 5; **A. Duggan**, Novartis, 3; **P. Goyanka**, Novartis, 3; **C. Gaillez**, Novartis, 1, 3.

Abstract Number: 1362

BASDAI Guided Treat-to-target Tapering of Tumor Necrosis Factor Inhibitors in Axial Spondyloarthritis: Results of the Retrospective TAPAS Study

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Tumor Necrosis Factor inhibitors (TNFi) have proven to be safe and effective in the treatment of axial spondyloarthritis (axSpA). However, they carry some disadvantages, such as adverse effects, patient burden, and costs, which could be reduced by treat-to-target (T2T) tapering. Although there is lack of high level evidence, guidelines suggest – based on experience in Rheumatoid Arthritis – that T2T tapering and discontinuation might be contemplated. However, there are no studies comparing T2T tapering and continuation in axSpA, with at least two studies ongoing (BIODOPT and DRESS-PS). As T2T treatment and tapering (BASDAI (Bath Ankylosing Spondylitis Disease Activity Index) guided) has been usual care in our axSpA population since 2012, this creates the opportunity to perform a retrospective controlled study.

Our objective was to assess the effect of T2T TNFi tapering on disease activity and TNFi dosage in axSpA patients with low disease activity (LDA).

Table 1. Baseline characteristics of axSpA patients

Characteristic	axSpA (N=169)	
Female, n (%)	66	(39%)
Age in years at inclusion, mean (SD)	46	(13)
Disease duration at inclusion, years, median (IQR)	12	(4-18)
HLA-B27 positivity, n (%)*	115	(86)
ASAS Criteria, n (%)**	137	(81)
Sacroiliitis on radiographic imaging , n (%)	87	(51)
Number of previous bDMARD, n (%)		
- 0	90	(53%)
- 1	50	(30%)
- 2 or 3	29	(17%)
Number of previous csDMARD, n (%)		
- 0	110	(65%)
- 1	35	(21%)
- ≥ 2	24	(14%)
Current bDMARD use, n (%)		
- Adalimumab	74	(44%)
- Etanercept	55	(33%)
- Golimumab	21	(12%)
- Infliximab	19	(11%)
Current csDMARD use, n (%)		
- None	150	(89%)
- Methotrexate	10	(6%)
- Leflunomide	1	(1%)
- Sulfasalazine	8	(5%)
Current NSAID use, n (%)	92	(54%)
Duration of current bDMARD use at inclusion, years, median (IQR)	4	(2-6)
Duration of follow-up, months, median (IQR)	41	(26-56)

*Available for 133 of 169 patients
**Rudwaleit M, Landewe R, van der Heijde D. SpondyloArthritis international Society (ASAS) classification criteria for axial spondyloarthritis (part II): validation and final selection. Ann Rheum Dis. 2009;68(6):777–83.

Methods: We performed a retrospective cohort study in all axSpA patients (clinical diagnosis) using TNFi who visited our outpatient clinic between April 2012 and October 2018. Patients with concomitant inflammatory disease preventing tapering were excluded and patients had to be eligible for tapering, defined as ≥ 6 months of TNFi treatment and ≥ 6 months of LDA (BASDAI < 4 or by judgement of physician and patient). Three different time periods were defined: i) continuation of TNFi; ii) TNFi tapering; iii) stable TNFi dosage after tapering. A mixed-model analysis was used to estimate mean BASDAI during these three time periods. This model included: age, gender, sacroiliitis, disease duration, and the following time-varying components: current dose reduction status (three time periods mentioned above), time since eligibility for tapering and use of concomitant conventional synthetic Disease-Modifying Antirheumatic Drugs (csDMARDs), and a random intercept and slope to account for inter-patient variability. Furthermore, a mean percentage of the Daily Defined Dose (%DDD) was calculated for each time period as secondary outcome.

Results: 169 patients were included, with a mean of 6.4 BASDAI measurements, of whom 118 attempted dose reduction at least once during follow-up. Median follow-up duration was 31 months (Inter Quartile Range (IQR) 20-47) for patients who never attempted dose reduction and 45 months (IQR 31-56) for those who did (table 1). The mixed

Table 2. Mixed Model results, estimation of mean BASDAI between three time periods corrected for potential confounders, with a random intercept and slope to account for inter-patient variability.

	Estimated effect	P-value	95 % CI Lower	Upper
Gender (reference is male)	1.05	<0.001	[0.57 - 1.54]	
Age (per year)	0.03	0.007	[0.01 - 0.05]	
Disease duration at baseline (per year)	0.03	0.047	[0.00 - 0.06]	
Time since baseline (per month)	0.03	0.394	[-0.04 - 0.11]	
csDMARD use (yes vs. no, time varying)	-0.12	0.649	[-0.64 - 0.40]	
Sacroiliitis at baseline (yes vs. no)	-0.18	0.462	[-0.67 - 0.31]	
Time period				
TNFi tapering vs. continuation	0.11	0.376	[-0.14 - 0.36]	
Stable TNFi dosage after tapering vs. continuation	0.21	0.172	[-0.09 - 0.51]	

model showed no significant difference in BASDAI between the three time periods. Higher age, female gender and longer disease duration were significantly associated with a higher BASDAI score (table 2). The mean percentage of the daily defined dose for the three time periods was 96% for the continuation period; 59% in the TNFi tapering period and 69% in the stable TNFi dosage period.

Conclusion: T2T tapering of TNFi appears to have no detrimental effect on disease activity in axSpA patients, compared with full dose continuation, and results in reduction in drug exposure. Trials are needed to investigate tapering in a prospective and randomized manner.

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Abstract Number: 1363

Efficacy of Secukinumab on Patient-Reported Outcomes in Patients with Active Psoriatic Arthritis Stratified by Prior Tumor Necrosis Factor Inhibitor Use: Post Hoc Analysis from a Phase 3 Trial

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

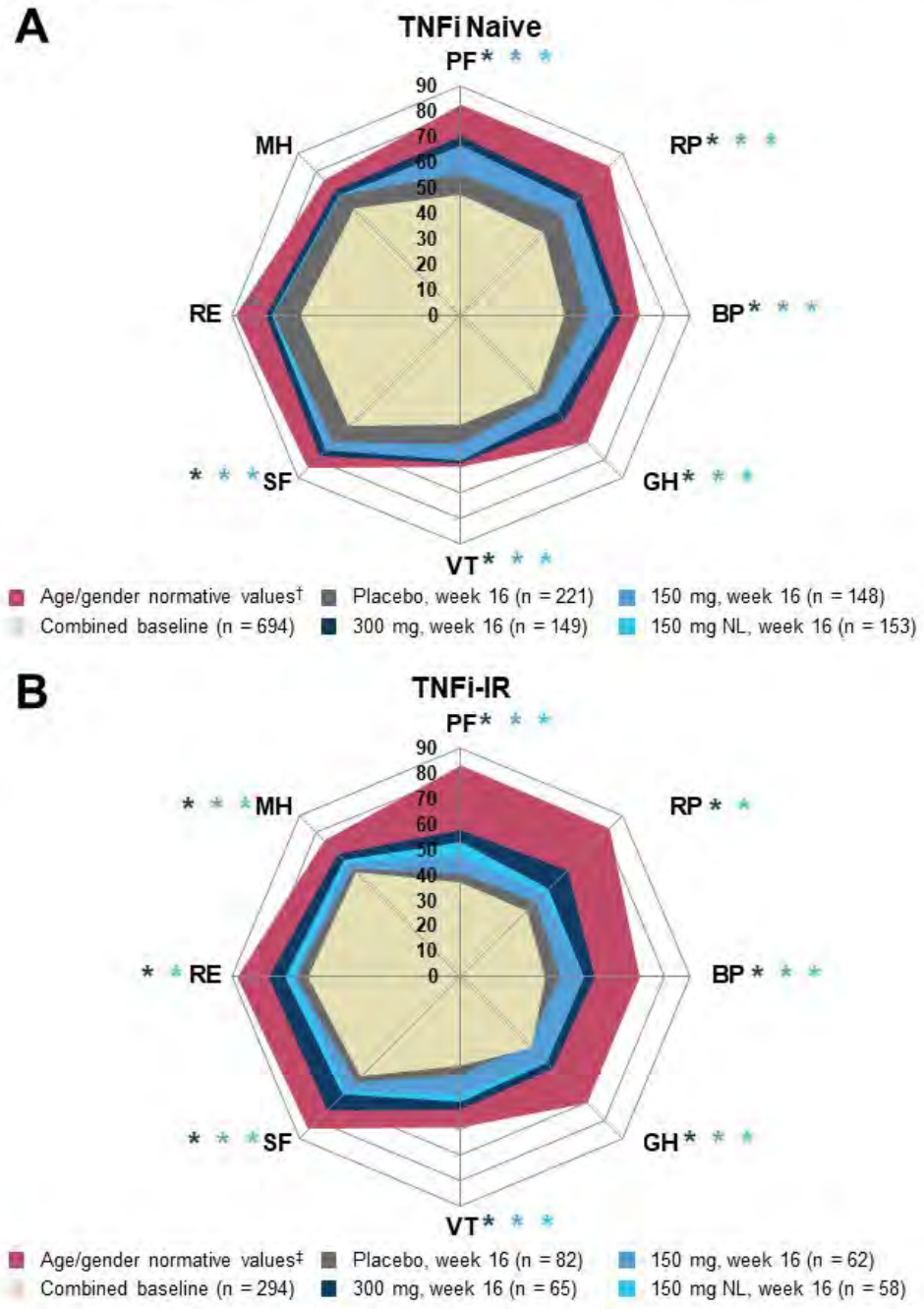
Background/Purpose: The phase 3 randomized controlled trial FUTURE 5 (NCT02404350) showed the efficacy of secukinumab (SEC) improving clinical signs, symptoms, and radiographic progression in patients with active psoriatic arthritis (PsA).[1] This post hoc analysis evaluated the efficacy of SEC improving patient-reported outcomes (PROs) in tumor necrosis factor inhibitor (TNFi)-naive and inadequate-responder (TNFi-IR) patients with PsA.

Methods: FUTURE 5 enrolled patients ≥ 18 years who met CASPAR with symptoms for ≥ 6 months at screening. Patients were randomized to receive SEC 300 mg, 150 mg, 150 mg no load (NL), or placebo (PBO) weekly from baseline to week 4 and every 4 weeks thereafter to week 16. Patients in the SEC 150 mg NL arm received PBO at weeks 1, 2, and 3. For this post hoc analysis, patients were stratified by prior TNFi use. PROs were assessed at baseline and selected visits through week 16. Mean changes from baseline in PROs and the proportions of patients reporting improvements ≥ minimum clinically important differences (MCIDs) and scores ≥ age/gender-matched normative values were assessed in each treatment group. PROs included patient global assessments of disease activity (PtGA) and psoriasis and arthritis (PtGA PsO/arthritis) visual analog scale (VAS), pain VAS, Health Assessment Questionnaire Disability Index (HAQ-DI), 36-item Short Form Health Survey (SF-36), Functional Assessment of Chronic Illness Therapy (FACIT)–Fatigue, and Dermatology Life Quality Index (DLQI; patients with psoriasis only).

Results: Baseline PRO scores were generally worse in the TNFi-IR vs TNFi-naive population. TNFi-naive and TNFi-IR patients in all SEC treatment groups reported significantly greater improvements in PtGA, PtGA PsO/arthritis, pain, HAQ-DI, SF-36 physical component summary (PCS), and DLQI at week 16 vs PBO. Treatment responses were higher in the SEC 300-mg arm vs SEC 150-mg and 150-mg NL arms at week 16 across most PROs, including all SF-36 domains (**Figure 1**). Significantly higher proportions of both TNFi-naive and TNFi-IR patients receiving SEC reported improvements ≥ MCID as early as week 1 in HAQ-DI and at week 16 across all PROs except SF-36 mental component summary score vs PBO. The proportions of patients reporting improvement ≥ MCID in pain and HAQ-DI (**Figure 2**), as well as PtGA PsO/arthritis, SF-36 PCS, and DLQI, were higher in TNFi-naive than TNFi-IR patients. More SEC-treated patients reported scores ≥ normative values in HAQ-DI, SF-36 PCS, and FACIT-Fatigue at week 16 vs PBO, with more patients in the TNFi-naive than the TNFi-IR sub-population reporting scores ≥ normative values (**Figure 3**).

Conclusion: Initiation of SEC as a first-line biologic in patients with PsA resulted in early, statistically significant, and clinically meaningful improvements in PROs across all doses, and significant and meaningful improvements in

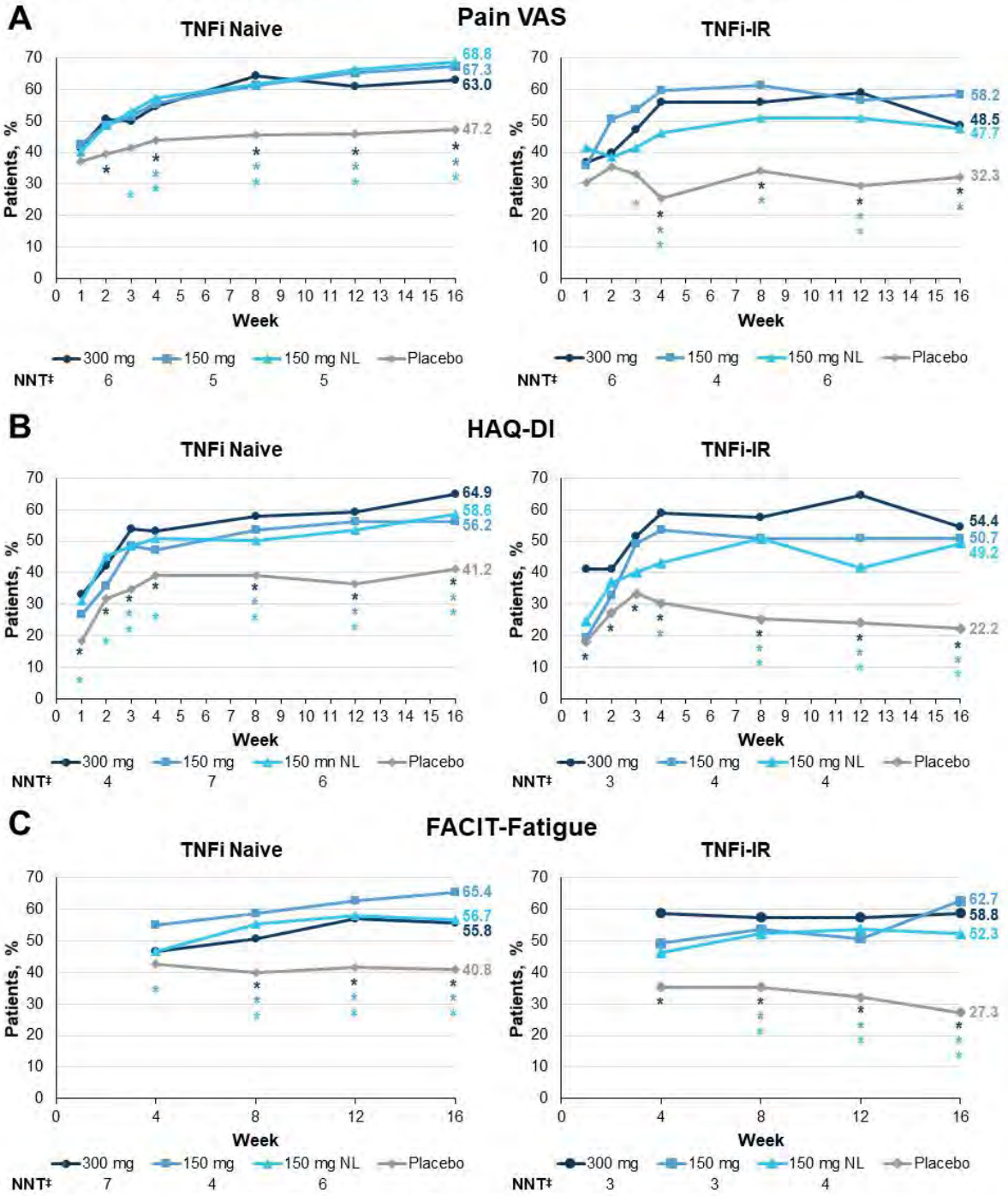
Figure 1. SF-36 Domain Scores at Baseline and Week 16 in **(A)** TNFi-Naive and **(B)** TNFi-IR Patients



BP, bodily pain; GH, general health; IR, inadequate response; MH, mental health; PF, physical functioning; RE, role-emotional; RP, role-physical; SF, social functioning; SF-36, 36-item Short Form Health Survey; TNFi, tumor necrosis factor inhibitor; VT, vitality.
* $P < 0.05$ compared with placebo.
† Age- and gender-matched normative values for SF-36 domains in TNFi-naive patients were defined as follows: PF, 82.5; RP, 83.2; BP, 73.0; GH, 70.45; VT, 59.0; SF, 85.2; RE, 88.5; MH, 75.9.
‡ Age- and gender-matched normative values for SF-36 domains in TNFi-IR patients were defined as follows: PF, 80.0; RP, 81.0; BP, 71.8; GH, 69.6; VT, 59.1; SF, 84.8; RE, 87.6; MH, 76.2.

TNFi-IR patients as later-line therapy. Treatment responses were higher in patients receiving SEC 300 mg vs 150 mg or 150 mg NL. TNFi-naive patients more frequently reported improvements ≥ MCID and scores ≥ normative values vs TNFi-IR patients, although TNFi-IR patients had lower baseline PRO scores and reported lower PBO responses.

Figure 2. Proportion of Patients Reporting Improvement from Baseline ≥ MCID† in **(A)** Pain, **(B)** HAQ-DI, and **(C)** FACIT-Fatigue Over 16 Weeks



FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire Disability Index; IR, inadequate response; MCID, minimum clinically important difference; NL, no load; NNT, number needed to treat; TNFi, tumor necrosis factor inhibitor, VAS, visual analog scale.

* $P < 0.05$ compared with placebo.

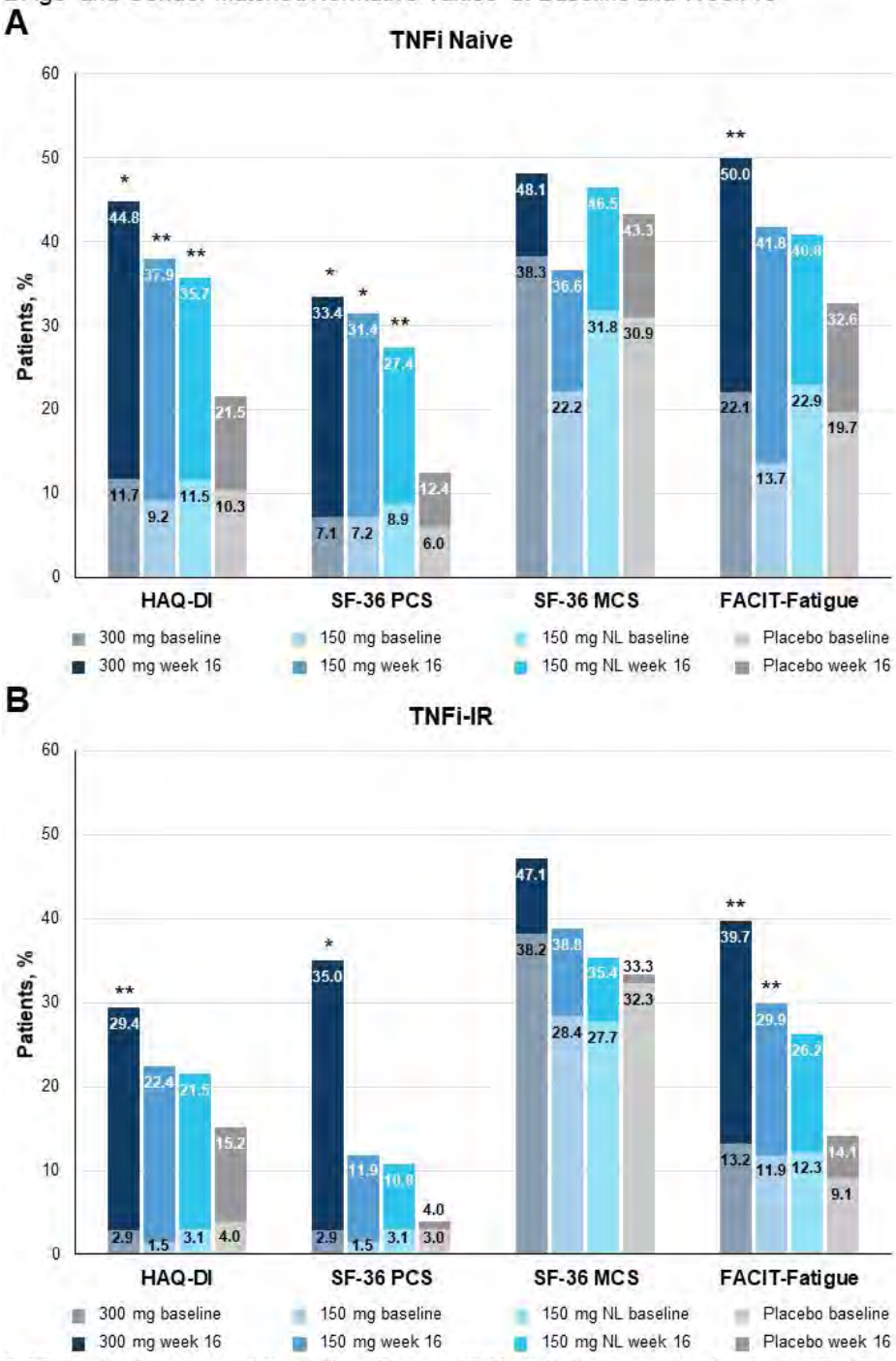
† MCIDs for PROs were defined as follows: pain VAS, ≥ 10; HAQ-DI, ≥ 0.35; FACIT-Fatigue, ≥ 4.

‡ NNT compared with placebo at week 16.

Reference

1. Mease P, et al. *Ann Rheum Dis.* 2018;77:890-7.

Figure 3. Proportion of **(A)** TNFi-Naive and **(B)** TNFi-IR Patients Reporting PRO Scores ≥ Age- and Gender-Matched Normative Values† at Baseline and Week 16



FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire Disability Index; IR, inadequate response; MCS, mental component summary; NL, no load; PCS, physical component summary; SF-36, 36-item Short Form Health Survey; TNFi, tumor necrosis factor inhibitor.

* $P < 0.05$ and ** $P < 0.01$ compared with placebo.

† Age- and gender-matched normative values for PROs were defined as follows: HAQ-DI, ≤ 0.25; SF-36 PCS ≥ 50; SF-36 MCS, ≥ 50; FACIT-fatigue, ≥ 40.1.

Disclosure: V. Strand, AbbVie, 5, Amgen, 5, Celltrion, 5, Janssen, 5, Merck, 5, Novartis, 5, Regeneron, 5, Sanofi, 5, UCB, 5, Genentech/Roche, 5, GSK, 5, Pfizer, 5, Bayer, 5, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, Galapagos, 5, Lilly, 5, Gilead, 5, Samsung, 5, Servier, 5, Setpoint, 5, Arena, 5, AstraZeneca, 5, Horizon, 5, Ichnos, 5, Inmedix, 5, Sandoz, 5; **G. Kaeley**, Novartis Pharmaceuticals Corporation, 5; **M. Bergman**, AbbVie, 5, 8, Amgen, 5,

8, Bristol-Myers Squibb, 5, 8, Genentech/Roche, 5, 8, Gilead, 5, 8, Janssen, 5, 8, Merck, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Regeneron, 5, 8, Sanofi, 5, 8, Sandoz, 5, 8, JNJ (parent of Janssen), 1; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **L. Coates**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5; **P. Hur**, Novartis Pharmaceuticals Corporation, 3; **N. Kim**, Novartis Pharmaceuticals Corporation, 9; **B. Parikh**, Novartis Pharmaceuticals Corporation, 3; **P. Pertel**, Novartis AG, 3; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5.

Abstract Number: 1364

Bimekizumab Long-Term Efficacy and Safety over 96 Weeks in Patients with Ankylosing Spondylitis: Interim Results from a Phase 2b Open-Label Extension Study

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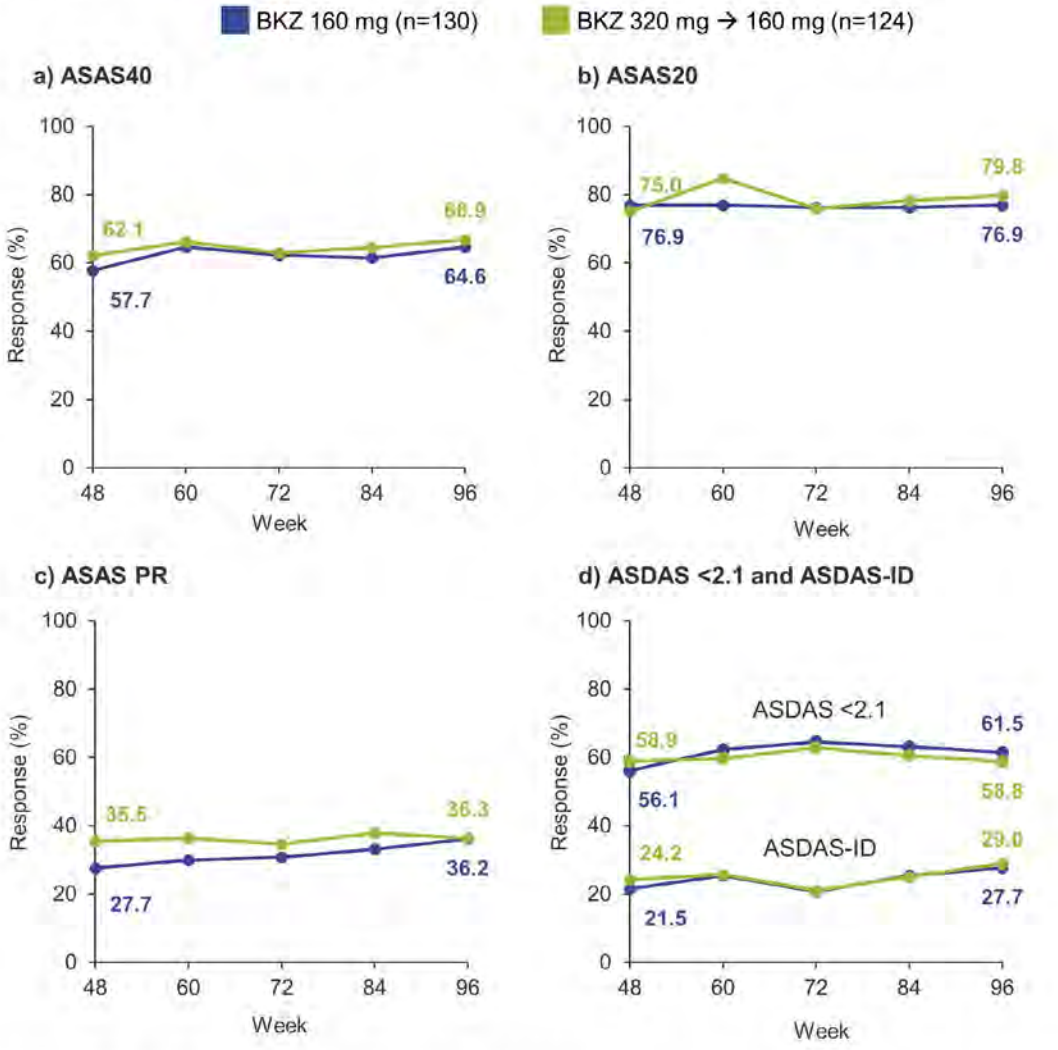
SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Bimekizumab (BKZ), a monoclonal antibody that selectively inhibits interleukin (IL)-17A and IL-17F, has demonstrated clinical efficacy in patients with ankylosing spondylitis (AS) treated over a period of 48 weeks.[1] We report 2-year interim efficacy and safety of BKZ in patients with active AS from a phase 2b dose-ranging study (BE AGILE; NCT02963506) and ongoing open-label extension (OLE; NCT03355573).

Methods: BE AGILE consisted of a 12-week dose-ranging period followed by a 36-week randomized period (BKZ 160 or 320 mg); full study design is described elsewhere.[1] Patients who completed 48 weeks' treatment in BE AGILE were eligible for entry into the OLE. All OLE patients received BKZ 160 mg every 4 weeks (Q4W) irrespective of previous dosing regimen. Efficacy and safety outcomes are presented from BE AGILE study baseline to Week 96. Efficacy outcomes are reported for the OLE Full Analysis Set (patients who had ≥1 dose of BKZ and ≥1 valid efficacy variable measurement since entry into the OLE), and include: Assessment of SpondyloArthritis international Society (ASAS) 40% and 20% response (ASAS40/20), ASAS partial remission (ASAS PR), Ankylosing Spondylitis Disease Activity Score (ASDAS) < 2.1, ASDAS inactive disease (ID: ASDAS < 1.3), ASDAS-CRP, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), Bath Ankylosing Spondylitis Metrology Index (BASMI) and Bath Ankylosing Spondylitis Functional Index (BASFI). Missing data were imputed using non-responder imputation (binary variables) or multiple imputation (continuous variables). Treatment-emergent adverse events (TEAEs) up to the 96-week treatment period cut-off and beyond are reported separately for the BE AGILE Safety Set and OLE Safety Set (patients who received ≥1 dose of BKZ on study entry).

Results: 262/303 (87%) patients randomized at BE AGILE study baseline completed Week 48, of whom 254/262 (97%) were included in the OLE Full Analysis Set, including 130 who continued on BKZ 160 mg Q4W and 124

Figure 1: Efficacy responses to Week 96 (OLE Week 48; non-responder imputation)



Full Analysis Set (N=254). ASAS: Assessment of SpondyloArthritis international Society; ASAS20/40: ASAS 20%/40% response; ASAS PR: ASAS partial remission; ASDAS: Ankylosing Spondylitis Disease Activity Score; BKZ: bimekizumab; ID: inactive disease (ASDAS<1.3); OLE: open-label extension.

dose-reduced from BKZ 320 mg Q4W to BKZ 160 mg Q4W. Of these, 238 (94%) had an efficacy assessment at Week 96. In BE AGILE, rapid improvements in efficacy outcomes were observed in BKZ-treated patients at Week 12; these further increased to Week 48 and were maintained during the OLE from Week 48–96 (**Figure 1, Table 1**). Responses were similar for patients on BKZ 160 mg and 320 mg at Week 48; and remained similar between patients continuing on BKZ 160 mg and those dose-reduced from BKZ 320 mg to 160 mg up to Week 96 (**Figure 1**). The exposure-adjusted incidence rate (EAIR) per 100 patient-years (PY) of TEAEs was 186.2 in BE AGILE (Weeks 0–48) and 111.7 in the OLE (Week 48 onwards); for serious TEAEs the EAIR/100 PY was 5.1 and 6.1, respectively (**Table 2**).

Conclusion: In patients with active AS who completed the first 48 weeks of BKZ treatment in BE AGILE, BKZ provides further sustained long-term improvements in key efficacy outcome measures over 96 weeks of treatment. Dose reduction from 320 mg to 160 mg Q4W was not followed by loss of response. There were no unexpected safety findings versus previous studies.

Table 1: Continuous efficacy outcomes to Week 96 (OLE Week 48; multiple imputation)

	BKZ 160 mg → 160 mg (N=130)			BKZ 320 mg → 160 mg (N=124)			All BKZ (N=254)		
Mean (SD)	**BL**	**Wk48**	**Wk96**	**BL**	**Wk48**	**Wk96**	**BL**	**Wk48**	**Wk96**
ASDAS-CRP	**3.9** (0.8)	**2.1** (0.9)	**1.9** (0.9)	**3.9** (0.8)	**2.0** (0.9)	**1.9** (0.9)	**3.9** (0.8)	**2.0** (0.9)	**1.9** (0.9)
BASDAI	**6.3** (1.3)	**2.8** (1.8)	**2.5** (1.8)	**6.5** (1.4)	**2.8** (2.1)	**2.7** (2.1)	**6.4** (1.4)	**2.8** (2.0)	**2.6** (2.0)
BASFI	**5.6** (1.9)	**3.0** (2.0)	**2.7** (2.1)	**5.8** (2.0)	**3.0** (2.4)	**2.8** (2.4)	**5.7** (1.9)	**3.0** (2.2)	**2.8** (2.2)
BASMI	**4.6** (1.7)	**4.0** (1.8)	**3.9** (1.7)	**4.8** (1.7)	**3.9** (1.8)	**3.9** (1.9)	**4.7** (1.7)	**4.0** (1.8)	**3.9** (1.8)

Full Analysis Set (N=254). BL corresponds to BE AGILE study BL. ASDAS: Ankylosing Spondylitis Disease Activity Score; BASDAI: Bath Ankylosing Spondylitis Disease Activity Index; BASFI: Bath Ankylosing Spondylitis Functional Index; BASMI: Bath Ankylosing Spondylitis Metrology Index; BKZ: bimekizumab; BL: baseline; CRP: C-reactive protein; OLE: open-label extension; SD: standard deviation; wk: week.

Table 2: Safety in BE AGILE (Weeks 0–48) and OLE (Week 48 onwards)

	BE AGILE Weeks 0–48			**OLE** Week 48 onwards
n (%) [EAIR/100 PY]	BKZ 160 mg (n=149; 114.2 PY)	BKZ 320 mg (n=150; 119.6 PY)	All BKZ (N=303; 261.3 PY)	All BKZ (N=255; 689.1 PY)
Any TEAE	103 (69.1) [168.7]	122 (81.3) [221.1]	235 (77.6) [186.2]	203 (79.6) [111.7]
Serious TEAEs	5 (3.4) [4.4]	6 (4.0) [5.1]	13 (4.3) [5.1]	27 (10.6) [6.1]
Study discontinuations due to TEAEs	7 (4.7)	10 (6.7)	20 (6.6)	12 (4.7)
Drug-related TEAEs	48 (32.2)	54 (36.0)	110 (36.3)	86 (33.7)
Deaths	1 (0.7)	0	1 (0.3)	1 (0.4)

TEAEs are reported for BE AGILE Safety Set (N=303) and OLE Safety Set (N=255); OLE safety data include TEAEs that occurred during Weeks 48–96 and beyond. There was one death in BE AGILE (cardiac arrest) and one in the OLE (road traffic accident), neither of which were considered treatment-related. BKZ: bimekizumab; EAIR: exposure-adjusted incidence rate; OLE: open-label extension; PY: patient-years; TEAE: treatment-emergent adverse event.

Reference

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Disclosure: X. Baraliakos, AbbVie, 2, 5, Celgene, 2, 5, Galapagos, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 2, 5, Chugai, 2, 5, MSD, 2, 5, Sandoz, 2, 5, Hexal, 2, 5; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **M. Dougados**, Pfizer, 5, 8, AbbVie, 5, 8, Roche, 5, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, 8, Novartis, 5, 8, Sanofi, 5, 8, Biogen, 5, 8, Merck Sharp &

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Abstract Number: 1365

Machine Learning-based Berlin Scoring of Magnetic Resonance Images of the Spine in Patients with Ankylosing Spondylitis: Analysis of Data from a Phase 3 Trial with Secukinumab

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SESSION INFORMATION
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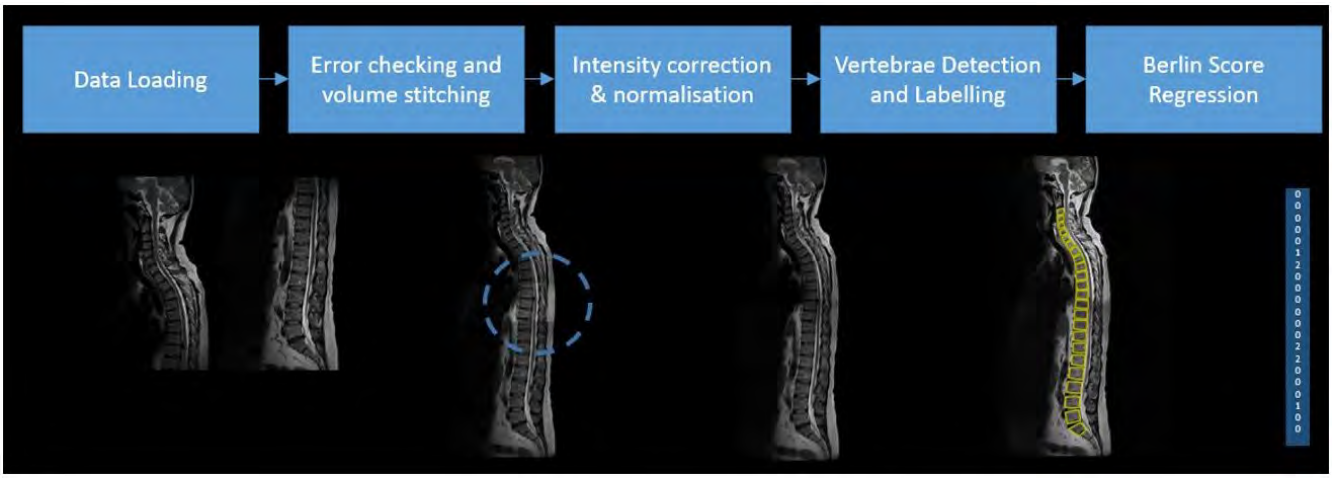
Background/Purpose: Magnetic resonance imaging (MRI) offers a non-invasive and objective method of early diagnosis and classification, monitoring disease burden and treatment response for patients (pts) with axial spondyloarthritis (axSpA).[1] Numerous scoring schemes such as the Ankylosing Spondylitis (AS) Spine MRI Activity (ASspiMRIa) score are available for the quantitative assessment of MRI, but are subject to intra- and inter-rater variability, are labor intensive and costly. Nevertheless, quantification of MRI changes has become an important tool to demonstrate treatment success of biologic drugs in axSpA. In this study, we evaluate the performance of machine learning (ML) based software for the automated Berlin grading of spinal MRI bone marrow edema in pts with AS and compare with expert scoring.

Methods: Fully automated ML software (Figure) was developed to detect and label 23 vertebrae, define vertebral units (VU) as per the Berlin modification of the ASspiMRIa score, and score each VU as either 0 (score of 0) or 1 (score of 1, 2 or 3). The ML algorithm was based on the previously developed SpineNet software.[2] Analysis included 108 pts from the secukinumab MEASURE 1 study[3], in which imaging was done using T1 and STIR sagittal MRI at baseline and Weeks 16, 52, 104, 156 and 208. Two expert readers (R1 and R2), blinded to treatment and visit, evaluated all images by Berlin-modified ASspiMRIa score. The scores from both readers were binned or categorized into two groups: 0 vs 1, 2, or 3. As a result of multiple pt time points and expert reading sessions, the complete dataset comprised of 10,988 VUs, (8,954 graded by R1, 9,010 graded by R2). Ten-way cross-validation at the VU level was used to train and validate the ML software. The dataset was split into 10 randomly selected subsets, ensuring that each pt appears in only one subset, after which 8 subsets were used for training the ML software, one was used to check for correct training, and one was used for validation. The process was repeated 10 times such that all 10 subsets were used for validation. Area-Under-the-Curve (AUC), accuracy weighted for the frequency of each category, sensitivity and specificity were calculated. Intra- and inter-reader accuracy were also calculated.



Processing pipeline of automated Berlin scoring software

	Software Score = 0	Software Score = 1, 2 or 3	Total VU scored
R1 Score = 0	6505 (75%)	2177 (25%)	8682
R1 Score = 1, 2 or 3	70 (26%)	202 (74%)	272
R2 Score = 0	5862 (70%)	2514 (30%)	8376
R2 Score = 1, 2 or 3	190 (30%)	444 (70%)	634
Percentages calculated as a fraction over the total in each row. Overall accuracy is the average of the highlighted percentages.			

Confusion matrix between the software, R1 and R2

Results: Average AUC and accuracy of the software in relation to expert readers' scores was 0.80 and 72% with a sensitivity of 0.72 and specificity of 0.72. The intra- and inter-reader agreement was 75% (R1), 83% (R2) and 73% respectively. Individual VU scoring of the software vs. readers are presented in the Table as a confusion matrix.

Conclusion: Automated scoring of MR images in AS pts was comparable to that of expert reader-based assessments. ML software has the potential to provide an automated guided-reading approach to scoring MR images, which may enable further clinical insights.

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Abstract Number: 1366

Secukinumab Improved Signs and Symptoms in Patients with Non-radiographic Axial Spondyloarthritis: Results from a Randomized Controlled Phase III Study Stratified by Baseline Objective Signs of Inflammation

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SESSION INFORMATION
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Background/Purpose: Active non-radiographic axial spondyloarthritis (nr-axSpA) is often determined on the basis of objective signs of inflammation (elevated C-reactive protein [CRP] and/or evidence of sacroiliitis on MRI).[1] Secukinumab (SEC) significantly improved signs and symptoms in patients (pts) with nr-axSpA in the PREVENT study (NCT02696031).[2] Here, we report a pre-planned exploratory analyses of the efficacy of SEC from PREVENT stratified by CRP and MRI status (positive and/or negative) at study entry.

Methods: Pts (555) fulfilling ASAS criteria for axSpA plus abnormal CRP and/or MRI, without evidence of radiographic changes in sacroiliac joints according to modified New York Criteria for AS were enrolled. All images were assessed centrally before inclusion. Pts were randomized (1:1:1) to subcutaneous SEC 150 mg with loading (LD), without loading (NL), or placebo (PBO) at baseline (BL), Weeks (Wks) 1, 2, 3, and 4, then every 4 wks (q4wk). NL pts received SEC 150 mg at BL and PBO at Wks 1, 2, 3, and 4, then 150 mg q4wk. Exploratory efficacy assessments by CRP and MRI status (positive and/or negative) at Wk 16 included ASAS40, BASDAI50, ASAS-partial remission (PR), and ASDAS-CRP inactive disease (ID) responses. Missing values were imputed as non-response.

Results: Response rates for ASAS40, BASDAI50, ASAS-PR, and ASDAS-CRP ID with SEC 150 mg LD or NL by CRP and MRI status are shown in the Table. Numerically higher response rates for SEC were observed vs PBO for all endpoints across subgroups with the most notable differences vs PBO observed for ASAS-PR and ASDAS-CRP ID.

Endpoints, % responders	Subgroups	SEC 150 mg LD	SEC 150 mg NL	PBO
ASAS40	CRP+MRI+	53.7	50.9	21.8
	CRP+MRI−	34.6	31.4	29.4
	CRP−MRI+	34.2	39.5	31.3
BASDAI50	CRP+MRI+	46.3	43.9	12.7
	CRP+ MRI−	32.7	33.3	25.5
	CRP−MRI+	34.2	35.5	23.8
ASAS-PR	CRP+MRI+	29.6	21.1	5.5
	CRP+MRI−	21.2	19.6	7.8
	CRP−MRI+	16.5	22.4	7.5
ASDAS-CRP ID	CRP+MRI+	27.8	22.8	1.8
	CRP+MRI−	13.5	13.7	5.9
	CRP−MRI+	20.3	26.3	13.8

NRI data is presented for all the variables.
Number of patients in CRP+MRI+ subgroup were 54 (LD), 57 (NL), and 55 (PBO); in CRP+MRI− subgroup were 52, 51 and 51; and in CRP−MRI+ subgroup were 79, 76 and 80.
CRP, C-reactive protein; ID, inactive disease; LD, with loading; MRI, magnetic resonance imaging; NRI, non-responder imputation; NL, without loading; PBO, placebo; PR, partial response; SEC, secukinumab.

Summary of efficacy results at Week 16

Conclusion: SEC provided numerically higher response rates vs PBO in pts with nr-axSpA across CRP and/or MRI positive subgroups.

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Disclosure: J. Braun, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, BMS, 2, 5, 8, Boehringer, 2, 5, 8, Celgene, 2, 5, 8, Celltrion, 2, 5, 8, Centocor, 2, 5, 8, Chugai, 2, 5, 8, EBEWE Pharma, 5, 8, Medac, 2, 5, 8, MSD, 2, 5, 8, Mundipharma, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, UCB, 2, 5, 8; **R. Blanco**, AbbVie, 2, 5, 8, MSD, 2, 5, 8, Roche, 2, 5, 8, Pfizer, 5, 8, Bristol-Myers Squibb, 5, 8, Janssen, 5, 8, Eli Lilly, 5, 8, UCB Pharma, 5, 8; **H. Marzo-Ortega**, Novartis, 2, 5, 8, Janssen, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, UCB, 5, 8, AbbVie Inc., 5, 8, Celgene, 5, 8, Takeda Pharmaceutical Company, 5, 8; **L. Gensler**, AbbVie, 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB Pharma, 2, 5; **F. Van den Bosch**, AbbVie, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Gilead, 5, Merck, 5, 8; **H. Kameda**, Abbvie, 1, 2, 3, Asahi-Kasei, 2, 5, 8, Chugai, 1, 2, Eisai, 2, Mitsubishi-Tanabe, 1, 2, Novartis, 1, 2, 3, Eli Lilly, 1, 2, Janssen, 1, 2, Sanofi, 5, 8, UCB, 1, Pfizer, 1, Astellas Pharma Inc., 2, 5, 8, Gilead Sciences, 5, 8, Bristol-Myers Squibb, 8; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8; **M. van de Sande**, Boehringer Ingelheim, 2, AbbVie, 5, Eli Lilly, 2, 5, MSD, 5, 8, Janssen, 2, Novartis, 2, 5, 8; **A. Wiksten**, Novartis, 1, 3; **B. Porter**, Novartis, 1, 3; **S. Moreno**, Novartis, 1, 3; **A. Shete**, Novartis, 1, 3; **H. Richards**, Novartis, 1, 3; **S. Haemmerle**, Novartis, 1, 2; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2.

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Impact of Ixekizumab on Work Productivity in Non-Radiographic Axial Spondyloarthritis Patients: Results from the COAST-X Trial at 52 Weeks

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SESSION INFORMATION

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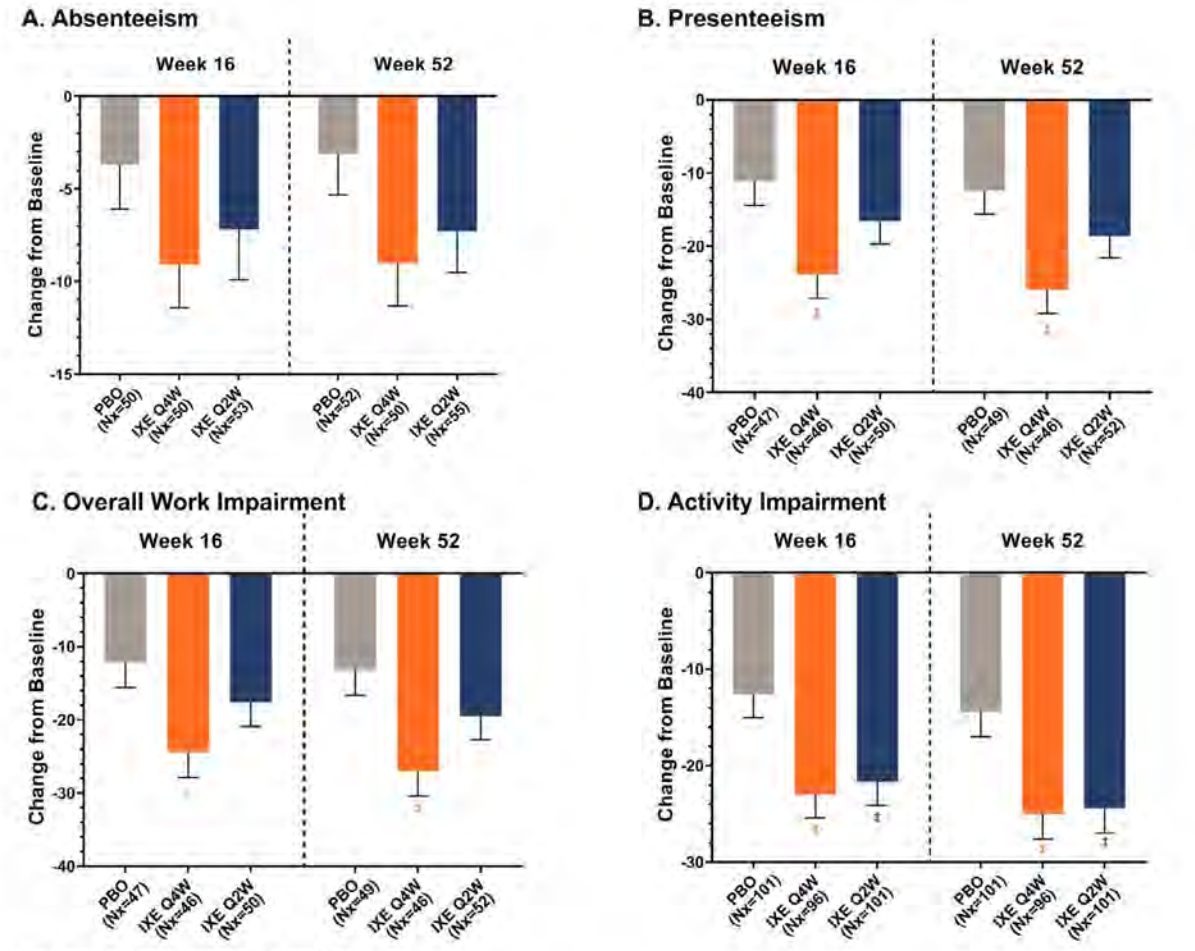
Background/Purpose: Patients with non-radiographic axial spondyloarthritis (nr-axSpA) experience impairments in health-related quality of life comparable to those seen in ankylosing spondylitis, including impacts on work productivity. Ixekizumab (IXE) is a high-affinity monoclonal antibody that selectively targets interleukin-17A and effectively treats axial spondyloarthritis.[1-3] This analysis evaluated the effect of IXE treatment for 52 weeks on work productivity and activity impairment as measured by absenteeism, presenteeism, overall work impairment, and activity impairment in patients with active nr-axSpA.

Methods: COAST-X (NCT02757352) was a phase 3, multicenter, randomized, double-blind, placebo-controlled, parallel-group outpatient study investigating the efficacy and safety of 80 mg IXE every 2 weeks (Q2W) and every 4 weeks (Q4W) compared to placebo (PBO) in 303 patients naïve to biologic disease-modifying anti-rheumatic drugs with active nr-axSpA during a 52-week treatment period. From Weeks 16 through 44, if patients' disease activity required escalation of treatment at investigator discretion, patients were switched to open-label IXE Q2W or subsequent tumor necrosis factor inhibitor treatment. Analysis was performed for the intent-to-treat population, which included data up to the time of biologic switching. Patients who switched to open-label IXE were considered non-responders. Changes from baseline in work productivity were measured for patients reporting full- or part-time work at Weeks 16 and 52 with the Work Productivity and Activity Impairment (WPAI) Questionnaire for Spondyloarthritis and analyzed with an analysis of covariance model including treatment, geographic region, screening magnetic resonance imaging and C-reactive protein level status, and baseline value as factors. Missing data was imputed using the modified baseline observation carried forward.

Results: A majority of patients (63.5–65.7%) reported part-time or full-time paid work at baseline, with baseline scores for presenteeism and overall work activity slightly higher for patients in the PBO arm ($p< 0.05$). Patients treated with IXE Q4W had significantly greater improvement than PBO in activity impairment at Weeks 16 ($p=0.003$) and 52 ($p=0.004$), presenteeism at Weeks 16 ($p=0.007$) and 52 ($p=0.003$), and overall work impairment at Weeks 16 ($p=0.014$) and 52 ($p=0.005$; Figure). Patients treated with IXE Q2W had significantly greater improvement than PBO in activity impairment at Weeks 16 ($p=0.007$) and 52 ($p=0.006$; Figure). Patients treated with either IXE regimen had numeric improvements in all WPAI measures compared to those receiving PBO at Weeks 16 and 52 (Figure).

Figure. Changes from Baseline in A) Absenteeism, B) Presenteeism, C) Overall Work Impairment, and D) Activity Impairment.



Values are LSM (SE) from mBOCF ANCOVA.

COAST-X treatment groups: PBO (N=105); IXE Q4W (N=96); IXE Q2W (N=102). Absenteeism, Presenteeism, and Overall Work Impairment were measured in patients reporting full- or part-time work.

P-values were from ANCOVA (treatment vs. placebo). *=p<0.05, ‡=p<0.01, †=p< 0.001.

ANCOVA=analysis of covariance; IXE Q2W=80 mg ixekizumab every 2 weeks; IXE Q4W=80 mg ixekizumab every 4 weeks; LSM=least squares mean; mBOCF=modified baseline observation carried forward; N=number of patients in the treatment group; Nx=number of patients with non-missing values; PBO=placebo; SE=standard error.

Conclusion: Patients with nr-axSpA treated with either IXE regimen had significant improvements in activity impairment compared to PBO. Patients receiving IXE Q4W also had significant improvements in presenteeism and overall work impairment.

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Vie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **L. Gensler**, AbbVie, 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB Pharma, 2, 5; **P. Rahman**, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5; **V. Navarro-Compán**, Novartis Pharma, 1, 5, 8, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, UCB, 5, 8; **H. Marzo-Ortega**, Novartis, 2, 5, 8, Janssen, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, UCB, 5, 8, AbbVie Inc., 5, 8, Celgene, 5, 8, Takeda Pharmaceutical Company, 5, 8; **T. Hunter**, Eli Lilly and Company, 1, 3; **D. Sandoval**, Eli Lilly and Company, 3; **A. Kronbergs**, Eli Lilly and Company, 1, 3; **B. Zhu**, Eli Lilly and Company, 1, 3; **A. Leung**, Syneos Health, 3; **V. Strand**, AbbVie, 5, Amgen, 5, Celltrion, 5, Janssen, 5, Merck, 5, Novartis, 5, Regeneron, 5, Sanofi, 5, UCB, 5, Genentech/Roche, 5, GSK, 5, Pfizer, 5, Bayer, 5, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, Galapagos, 5, Lilly, 5, Gilead, 5, Samsung, 5, Servier, 5, Setpoint, 5, Arena, 5, AstraZeneca, 5, Horizon, 5, Ichnos, 5, Inmedix, 5, Sandoz, 5.

Abstract Number: 1368

Proportions of Patients Achieving a Minimal Disease Activity State upon Treatment with Tildrakizumab in a Psoriatic Arthritis Phase 2b Study

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Tildrakizumab (TIL) is a high-affinity anti–interleukin-23p19 monoclonal antibody approved in the US, EU, and Australia to treat moderate to severe plaque psoriasis.[1] A randomized, double-blind, placebo-controlled, multiple-dose, phase 2b study evaluating the efficacy and safety of TIL in psoriatic arthritis (PsA) was recently completed (NCT02980692). The objective of this analysis was to characterize and evaluate the rate of minimal disease activity (MDA) up to week (W)52 from the phase 2b study.

Methods: Patients (pts) ≥18 years old with active PsA[2] and ≥3 tender and ≥3 swollen joints were randomized 1:1:1:1:1 to receive TIL 200 mg every 4 weeks (Q4W) to W52, TIL 200 mg every 12 weeks (Q12W) to W52, TIL 100 mg Q12W to W52, TIL 20 mg Q12W to W24→TIL 200 mg Q12W to W52, or placebo (PBO) Q4W to W24→TIL 200 mg Q12W to W52. MDA was assessed throughout the study; an MDA response was achieved when 5 of 7 criteria were met.[3] Safety was assessed throughout the study and included treatment-emergent adverse event (TEAE) monitoring.

Results: Of 500 pts screened, 391 were randomized and received ≥1 dose of study drug. At baseline, mean age was 48.8 years, 55% were female, 97% were White, mean body mass index was 29.7 kg/m^2, and pts had PsA for a median (range) of 4.4 (0–42.8) years since diagnosis. Baseline disease characteristics related to MDA varied little between study arms (**Table 1**).

	TIL 200 mg Q4W n = 78	TIL 200 mg Q12W n = 79	TIL 100 mg Q12W n = 77	TIL 20→200 mg Q12W n = 78	PBO→TIL 200 mg Q12W n = 79
Swollen joint count	10.4 ± 7.4	10.0 ± 8.0	11.0 ± 8.2	9.4 ± 6.4	11.8 ± 9.8
Tender joint count	16.6 ± 11.9	19.5 ± 13.9	21.3 ± 14.8	19.0 ± 13.0	19.7 ± 14.7
Patient GADA score	57.8 ± 18.3	61.1 ± 20.7	60.3 ± 20.2	61.9 ± 17.4	65.2 ± 18.1
Patient pain assessment	55.4 ± 19.1	59.6 ± 23.5	59.2 ± 22.1	60.9 ± 19.7	64.2 ± 20.4
Enthesitis (LEI) score*	3.1 ± 1.7	2.8 ± 1.7	3.2 ± 1.8	3.1 ± 1.7	2.8 ± 1.8
PASI†	7.6 ± 9.8	6.2 ± 7.4	8.8 ± 9.5	6.6 ± 7.0	5.0 ± 6.5
HAQ-DI score	1.0 ± 0.6	1.0 ± 0.6	1.0 ± 0.7	1.1 ± 0.6	1.2 ± 0.6

Data are reported as mean ± SD.
*For patients with baseline scores ≥1; N = 48, 43, 51, 55, and 43 for LEI.
†For analysis of baseline PASI, all patients were analyzed, regardless of % BSA involved; N = 75, 79, 76, 75, and 75 for TIL 200 mg Q4W, TIL 200 mg Q12W, TIL 100 mg, TIL 20 mg, and PBO.
BSA, body surface area; GADA, global assessment of disease activity; HAQ-DI, Health Assessment Questionnaire-Disability Index; LEI, Leeds Enthesitis Index; PASI, Psoriasis Area and Severity Index; PBO, placebo; Q4W, every 4 hours; Q12W, every 12 hours; SD, standard deviation; TIL, tildrakizumab.

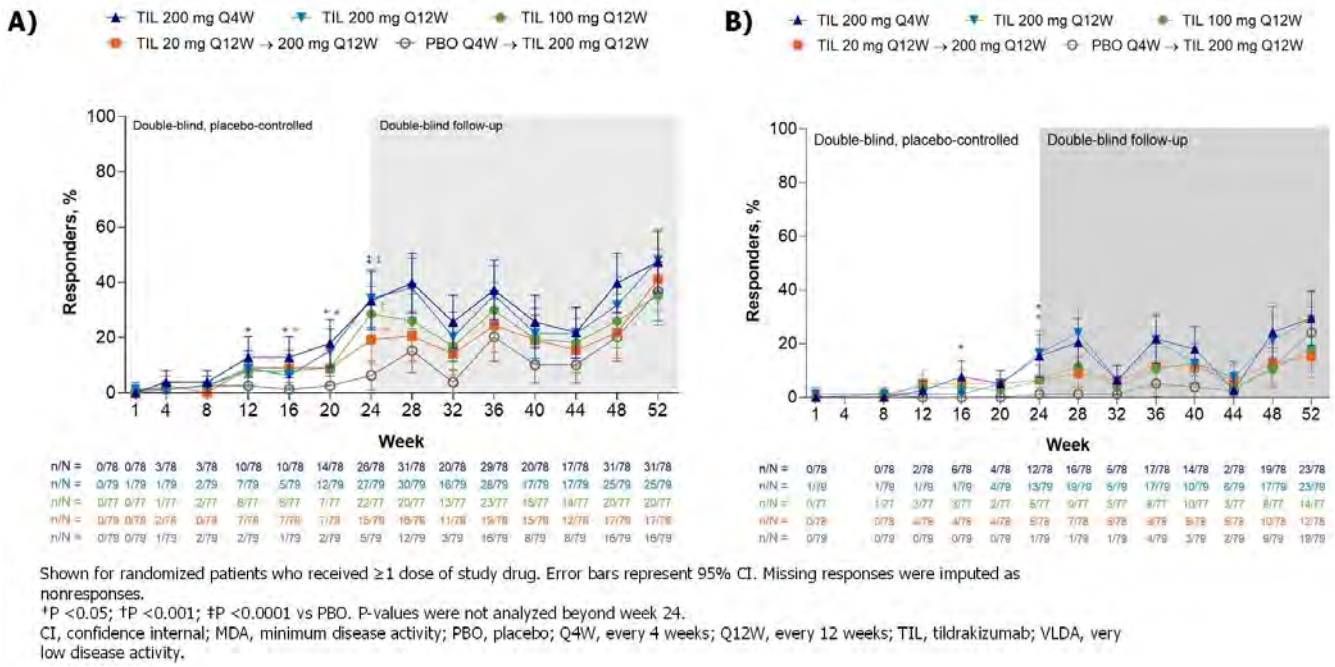
Table 1. Baseline disease characteristics related to minimal disease activity

	TIL 200 mg Q4W (n = 78)	TIL 200 mg Q12W (n = 79)	TIL 100 mg Q12W (n = 77)	TIL 20 mg Q12W (n = 78)	PBO Q4W (n = 79)
ACR20	79.5± 4.6 (0.0001)	77.2 ± 4.7 (0.0006)	71.4 ± 5.2 (0.0088)	73.1 ± 5.0 (0.0041)	50.6 ± 5.6
ACR50	52.6 ± 5.7 (0.0002)	50.6 ± 5.6 (0.0006)	45.5 ± 5.7 (0.0059)	39.7 ± 5.5 (0.0364)	24.1 ± 4.8
ACR70	28.2 ± 5.1 (0.0040)	29.1 ± 5.1 (0.0033)	22.1 ± 4.7 (0.0550)	16.7 ± 4.2 (0.2495)	10.1 ± 3.4
Tender joint counts ≤1	30.8 ± 5.2 (0.0107)	30.4 ± 5.2 (0.0152)	18.2 ± 4.4 (0.4556)	20.5 ± 4.6 (0.2939)	13.9 ± 3.9
Swollen joint counts ≤1	53.9 ± 5.6 (0.0006)	55.7 ± 5.6 (0.0002)	57.1 ± 5.6 (0.0002)	50.0 ± 5.7 (0.0030)	26.6 ± 5.0
HAQ-DI ≤0.5	39.7 ± 5.5 (0.0741)	54.4 ± 5.6 (0.0004)	48.1 ± 5.7 (0.0072)	37.2 ± 5.5 (0.1677)	26.6 ± 5.0
Tender entheseal points ≤1	80.3 ± 4.6 (0.4125)	79.8 ± 4.5 (0.4105)	75.0 ± 5.0 (0.9360)	71.8 ± 5.1 (0.6742)	74.4 ± 4.9
Patient VAS ≤15	43.6 ± 5.6 (0.0037)	41.8 ± 5.6 (0.0071)	32.5 ± 5.3 (0.1481)	24.4 ± 4.9 (0.6845)	21.5 ± 4.6
PtGA disease activity VAS ≤20	46.2 ± 5.6 (0.0043)	50.6 ± 5.6 (0.0006)	45.5 ± 5.7 (0.0076)	33.3 ± 5.3 (0.2044)	24.1 ± 4.8
PASI ≤1 or BSA ≤3	80.8 ± 4.5 (0.0369)	88.6 ± 3.6 (0.0008)	74.0 ± 5.0 (0.3082)	74.4 ± 4.9 (0.2321)	65.8 ± 5.3

Data are shown as response rate (%) ± SE unless otherwise noted; numbers in parentheses indicate P-values.
Missing responses were imputed as nonresponses.
BSA, body surface area; HAQ-DI, Health Assessment Questionnaire-Disability Index; PASI, Psoriasis Area and Severity Index; PBO, placebo; PtGA, Patients Global Assessment; Q4W, every 4 weeks; Q12W, every 12 weeks; SE, standard error; TIL, tildrakizumab; VAS, visual analog scale.

Table 2. Efficacy outcomes related to minimal disease activity at week 24

Significantly more patients receiving TIL vs PBO achieved MDA (19%–34% vs 6%; P ≤0.0172) by W24; the proportion further increased with continued TIL treatment to W52 (35%–48%), including pts who switched from PBO to TIL (37%) (**Figure**). At W24, there was a greater proportion of responders in TIL 200 mg Q12W and Q4W arms vs PBO across all MDA subcomponents except for tender entheseal points ≤1 and Health Assessment Questionnaire-Disability Index ≤0.05 (**Table 2**).



Shown for randomized patients who received ≥1 dose of study drug. Error bars represent 95% CI. Missing responses were imputed as nonresponses.
*P <0.05; †P <0.001; ‡P <0.0001 vs PBO. P-values were not analyzed beyond week 24.
CI, confidence internal; MDA, minimum disease activity; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab; VLDA, very low disease activity.

Figure. MDA responders (A) over time and (B) VLDA responders by treatment and time point

Among the overall pt population 64.5% and 3.3% experienced a TEAE and serious TEAE, respectively. Two (0.5%) pts had a fungal skin infection (candida, TIL 200 mg Q4W arm). One (0.3%) malignancy (intraductal proliferative breast lesion) occurred in the TIL 20→200 mg Q12W arm. One serious infection (chronic tonsillitis) was reported in the TIL 20 mg Q12W arm during the first 24 weeks. There were no reports of systemic candidiasis, uveitis, inflammatory bowel disease, major adverse cardiac events, or deaths over the 52 weeks of the study.

Conclusion: TIL produced clinically meaningful improvement in pts with PsA, resulting in a large proportion of pts achieving MDA by W52, and was well tolerated through W52. A 2-trial phase 3 program is underway.

References

1. Reich, et al. *Lancet* 2017;390:276–88.
2. Taylor, et al. *Arthritis Rheum* 2006;54:2665–73.
3. Coates, et al. *Ann Rheum Dis* 2010;69:48–53.

Disclosure: P. Nash, AbbVie, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8; **M. Luggen**, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Genentech, 2, 5, 8, Eli Lilly, 2, 5, 8, Nichi-Iko, 2, 5, 8, Novartis, 1, 5, 8, Pfizer, 2, 5, 8, Sun Pharmaceutical Industries, Inc., 2, 5, 8, R-Pharm, 2, 5, 8; **F. García Fructuoso**, AbbVie, 2, 5, 8, Eli Lilly, 2, 5, 8, Gedeon Richter, 2, 5, 8, Med-Immune, 2, 5, 8, Nichi-Iko, 2, 5, 8, Pfizer, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, Takeda, 2, 5, 8, UCB, 2, 5, 8; **R. Chou**, Sun Pharmaceutical Industries, Inc., 5; **A. Mendelsohn**, Sun Pharmaceutical Industries, Inc., 3, Johnson and Johnson, 1, 9; **S. Rozzo**, Sun Pharmaceutical Industries, Inc., 3; **I. McInnes**, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9.

Abstract Number: 1369

Efficacy of Tildrakizumab in PsA: DAPSA Remission and Low Disease Activity in PASDAS Through Week 52

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SESSION INFORMATION

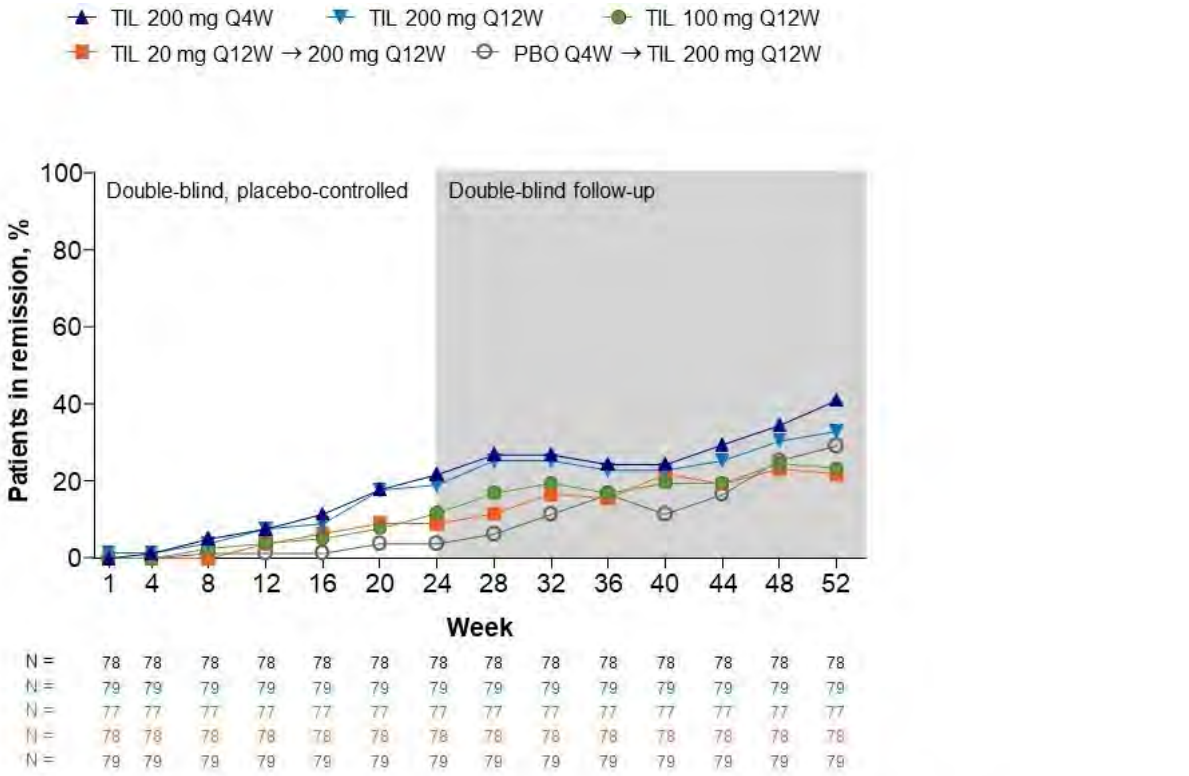
Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

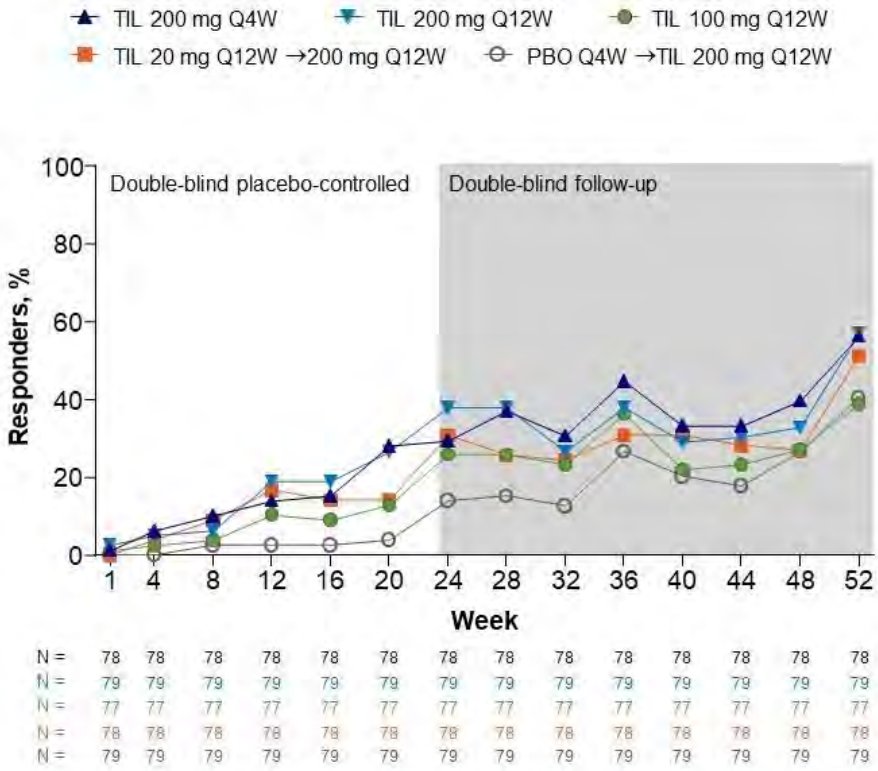
Session Time: 9:00AM–11:00AM

Background/Purpose: Tildrakizumab (TIL), an anti–interleukin-23p19 monoclonal antibody, is approved in the US, EU, and Australia for treatment of moderate to severe plaque psoriasis. A randomized, double-blind, placebo-controlled, multiple-dose, phase 2b study (NCT02980692) evaluating efficacy and safety of TIL for treatment of psoriatic arthritis (PsA) was recently completed. Treating to a target of remission or low disease activity has been recommended for patients with PsA.



Missing responses were imputed as nonresponses. DAPSA remission was defined as a score between 0–4.
N= Patients anlayzed.
P-values not analyzed.
DAPSA, Disease Activity in Psoriatic Arthritis; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

Figure 1. Proportion of patients in remission based on DAPSA



Missing responses were imputed as nonresponses. PASDAS low disease activity was defined as a score < 3.2.
N = Patients anlayzed.
P-values not analyzed.
PASDAS, Psoriatic Arthritis Disease Activity Score; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

	TIL 200 mg Q4W (n = 78)	TIL 200 mg Q12W (n = 79)	TIL 100 mg Q12W (n = 77)	TIL 20 mg→200 mg Q12W (n = 78)	PBO→TIL 200 mg Q12W (n = 79)
Any TEAE	51 (65.4)	50 (63.3)	53 (68.8)	51 (65.4)	47 (59.5)
Serious TEAEs	2 (2.6)	2 (2.5)	2 (2.6)	4 (5.1)	3 (3.8)
Discontinuations due to TEAEs	0	1 (1.3)	0	0	0
Deaths due to TEAEs	0	0	0	0	0
Any TEAE of special interest[a]	0	0	1 (1.3)	1 (1.3)	0
Any TEAE of clinical interest[b]	0	0	1 (1.3)	2 (2.6)	1 (1.3)
TEAEs of special or clinical interest (≥1)					
Pyelonephritis	0	0	1 (1.3)	0	0
Urinary tract infection	0	0	1 (1.3)	0	0
Depression	0	0	0	1 (1.3)	1 (1.3)
Aspartate aminotransferase increased	0	0	0	1 (1.3)	0
Blood bilirubin increased	0	0	0	1 (1.3)	0
Intraductal proliferative breast lesion	0	0	0	1 (1.3)	0

Data shown are n (%) for randomized patients who received ≥1 dose of study drug.
[a]AEs of special interest were major adverse cardiac events, malignancies, and severe infections.
[b]Any non-serious AEs of special interest.
PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TEAE, treatment emergent adverse event; TIL, tildrakizumab.

Table 1. Summary of safety findings to week 52

Methods: Patients (pts) ≥18 years old with PsA2 and ≥3 tender and ≥3 swollen joints were randomized 1:1:1:1:1 to receive TIL (200 mg once every 4 weeks [Q4W], 200 mg every 12 weeks [Q12W], 100 mg Q12W, or 20 mg Q12W) or placebo (PBO Q4W) to W24. Thereafter, PBO Q4W and TIL 20 mg Q12W arms crossed over to TIL 200 mg Q12W to W52. Post hoc analyses were performed to evaluate the proportion of pts with Psoriatic Arthritis Disease Activity Score (PASDAS) < 3.2 (low disease activity), and remission in Disease Activity in Psoriatic Arthritis (DAPSA) (defined as scores between 0–4). Adverse events (AEs), including treatment-emergent AEs (TEAEs) and serious AEs (SAEs), were monitored throughout the study. Because this was a post-hoc analysis, no statistical analyses were performed to compare tildrakizumab groups to placebo.

Results: Overall, 391/500 pts screened met the inclusion criteria; demographics and baseline disease characteristics were comparable between treatment groups.

At 24 weeks, a numerically greater proportion of patients in the TIL vs PBO arms achieved DAPSA remission, with the proportion of patients in remission increasing thereafter to week 52 (**Figure 1**). At week 24, there was a numerically greater proportion of patients in the TIL vs placebo arms with low disease activity in PASDAS < 3.2. The proportion of patients with PASDAS < 3.2 continued to increase up to week 52 (**Figure 2**).

From W0–W52, 64.5% and 3.3% of pts experienced a TEAE and SAE, respectively. The most common TEAEs were nasopharyngitis (8.4%) and upper respiratory tract infection (6.4%). Two (0.5%) patients had a fungal skin infection (candida, tildrakizumab 200 mg Q4W arm). Most TEAEs, including infections, were mild. No deaths were reported.

Conclusion: PsA pts treated with TIL achieved desirable low disease activity and remission targets of treatment. TIL was well tolerated among patients in all groups through 52 weeks of treatment.

References

1) Reich K, et al. *Lancet*. 2017;390(10091):276–88.
2) Taylor W, et al. *Arthritis Rheum*. 2006; 54(8):2665–73.

Disclosure: S. Chohan, Arizona Arthritis and Rheumatology Associates, 9; **A. Kavanaugh**, Eli Lilly and Company, 5; **V. Strand**, AbbVie, 5, Amgen, 5, Celltrion, 5, Janssen, 5, Merck, 5, Novartis, 5, Regeneron, 5, Sanofi, 5, UCB, 5, Genentech/Roche, 5, GSK, 5, Pfizer, 5, Bayer, 5, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, Galapagos, 5, Lilly, 5, Gilead, 5, Samsung, 5, Servier, 5, Setpoint, 5, Arena, 5, AstraZeneca, 5, Horizon, 5, Ichnos, 5, Inmedix, 5, Sandoz, 5; **R. Chou**, Sun Pharmaceutical Industries, Inc., 5; **A. Mendelsohn**, Sun Pharmaceutical Industries, Inc., 3, Johnson and Johnson, 1, 9; **S. Rozzo**, Sun Pharmaceutical Industries, Inc., 3; **P. Mease**, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5.

Abstract Number: 1370

A Delayed Effect of Tumor Necrosis Factor Inhibitors on Radiographic Spinal Progression in Patients with Axial Spondyloarthritis: Long-term Results from the German Spondyloarthritis Inception Cohort

Denis Poddubnyy[1], Valeria Rios Rodriguez[2], Murat Torgutalp[2], Ani Dilbaryan[2], Maryna Verba[2], Mikhail Protopopov[2], Fabian Proft[2], Judith Rademacher[2], Hildrun Haibel[2], Joachim Sieper[2] and Martin Rudwaleit[3], [1]Charité – Universitätsmedizin Berlin, Berlin, Germany, [2]Charité Universitätsmedizin Berlin, Berlin, Germany, [3]Department of Internal Medicine and Rheumatology, Klinikum Bielefeld, Germany

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: There are inconclusive data on the effect of tumor necrosis factor inhibitors (TNFi) on radiographic spinal progression in axial spondyloarthritis (axSpA). Although inflammation and new bone formation are linked in axSpA, TNFi failed to show inhibition of radiographic spinal progression over two years compared to historical cohorts in pivotal studies in radiographic axSpA. Subsequent observational studies suggested that a longer treatment duration, earlier treatment initiation and effective inflammation suppression might be required to achieve inhibition of radiographic progression.

The aim of the current study was to evaluate the effect of TNFi on radiographic spinal progression in patients with early axSpA in a long-term inception cohort.

Figure 1. Cumulative probability plots depicting mSASSS change scores over 2 years in patients with axial spondyloarthritis treated vs. not treated with TNFi in the current (A) or previous (B) 2-year interval.

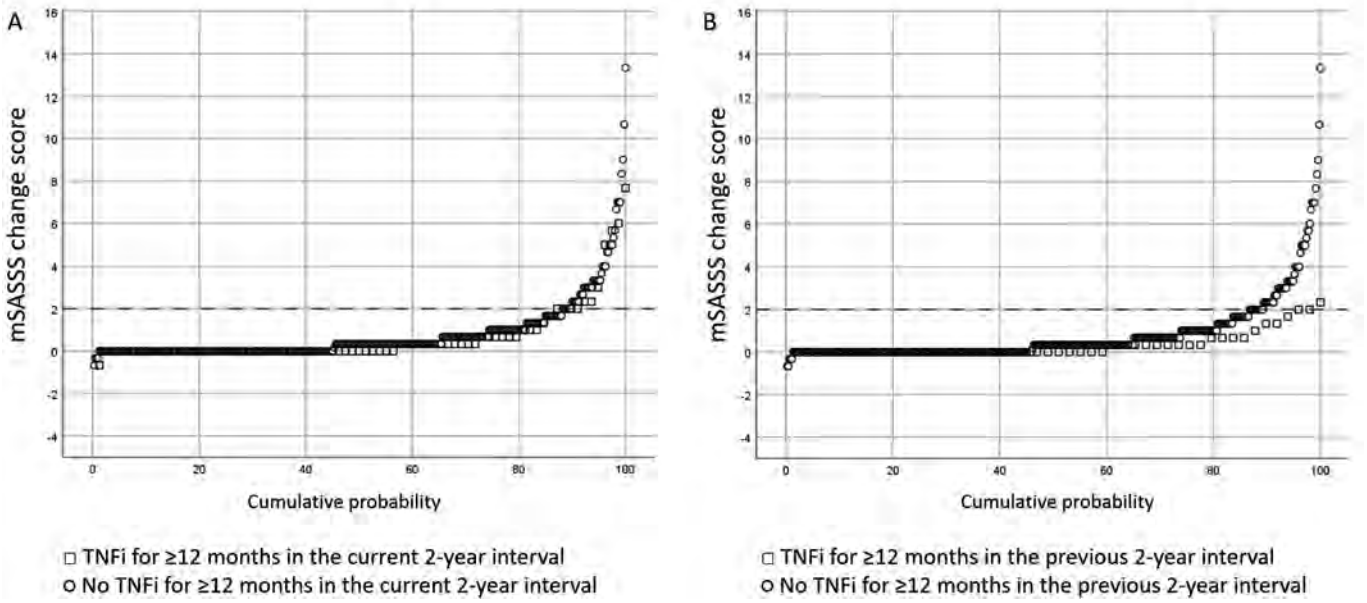
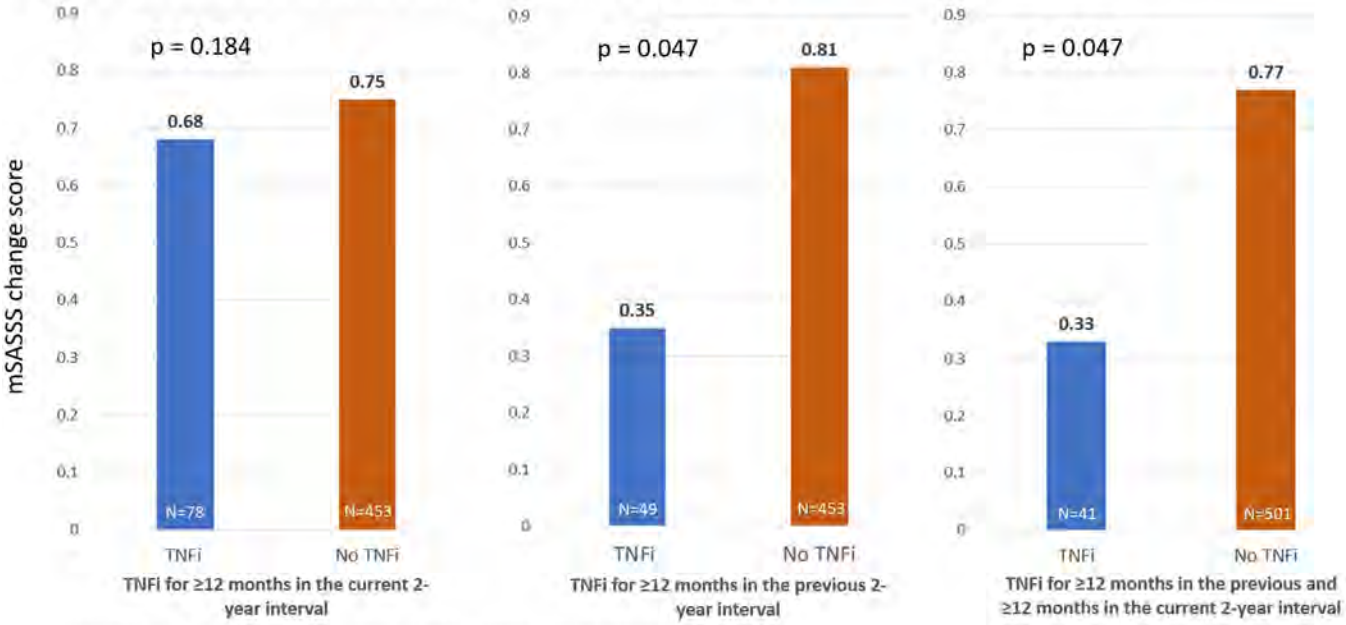


Figure 2. The mSASSS change scores over 2 years in patients with axial spondyloarthritis treated vs. not treated with TNFi in the current and/or previous 2-year interval.



N corresponds to the number of the 2-year radiographic intervals with the information on TNFi intake.
P values are derived from the Mann-Whitney U test.

Table. The association between the change of the mSASSS over two years and current and/or previous treatment with TNFi in the longitudinal generalized estimation equation analysis.

TNFi treatment definition		Reference	β* (95% CI)
TNFi for ≥12 months in the previous 2-year interval	**TNFi for ≥12 months in the current 2-year interval**		
	Yes	No TNFi for ≥12 months in the current 2-year interval	-0.25 (-0.69 to 0.19)
Yes		No TNFi for ≥12 months in the previous 2-year interval	**-0.51 (-0.83 to -0.20)**
Yes	**Yes**	No TNFi for ≥12 months in the current and previous 2-year intervals	**-0.56 (-1.02 to -0.10)**

*Parameter estimates from the multivariable models adjusted for sex, symptom duration at the beginning of the current 2-year interval, time-averaged ASDAS in the current 2-year interval, smoking in the current 2-year interval and performing exercises in the current 2-year interval.

Methods: A total of 266 patients with early axSpA (with r-axSpA with symptom duration ≤10 years and nr-axSpA with symptom duration ≤5 years) from the German Spondyloarthritis Inception Cohort (GESPIC) with at least two sets of spinal radiographs obtained at least 2 years apart during a 10-year follow-up were included. These patients contributed with a total of 542 2-year radiographic intervals. Spinal radiographs were evaluated by three trained and calibrated readers according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). The final mSASSS was calculated as a mean of three reader scores. The association between the current TNFi, previous TNFi and radiographic spinal progression defined as the absolute mSASSS change score over 2 years was analyzed using longitudinal generalized estimating equations (GEE) analysis.

Results: Only 9 patients were treated with a tumor necrosis factor inhibitor (TNFi) at baseline, and a total of 77 patients received TNFi during the entire follow-up period that gave 103 2-year intervals covered by TNFi of any duration, and 78 intervals covered by TNFi with treatment duration of at least 12 months. Radiographic spinal progression in axSpA patients receiving TNFi in the current 2-year interval was not different from progression in patients not treated with TNFi, while TNFi in the previous 2-year interval was associated with lower progression compared to patients without TNFi in this interval (Figures 1 and 2). The latter was also evident for patients who received TNFi in both previous and current 2-year intervals, i.e. patients treated with TNFi over 4 years. The longitudinal GEE analysis confirmed no significant association between current TNFi treatment and radiographic spinal progression but a significant association between TNFi in the previous 2-year interval (especially if this was continued also in the current interval giving 4 years in total) and the progression in the current one (Table).

Conclusion: TNFi treatment exhibits a delayed inhibitory effect on radiographic spinal progression in axSpA that becomes evident after 4 years of treatment.

Disclosure: D. Poddubnyy, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8; **V. Rios Rodriguez**, None; **M. Torgutalp**, None; **A. Dilbaryan**, None; **M. Verba**, None; **M. Protopopov**, None; **F. Proft**, Novartis, 2, 8, AbbVie, 8, AMGEN, 8, BMS, 8, Hexal, 8, Celgene, 8, Lilly, 8, MSD, 8, Pfizer, 8, Roche, 8, UCB, 8; **J. Rademacher**, None; **H. Haibel**, None; **J. Sieper**, AbbVie, 5, Novartis, 5, 8, Lilly, 8, Janssen, 5, Merck, 5, 8; **M. Rudwaleit**, Bristol-Myers Squibb, 5, 8, Chugai Pharmaceutical Co., Ltd., 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Novartis, 5, 8, UCB Pharma, 5, 8, AbbVie, 5, 8, Pfizer, 5, 8, Celgene, 8, Roche, 5, 8, Merck Sharp & Dohme, 5, 8.

Abstract Number: 1371

Improvement in Patient-Reported Outcomes for Upadacitinib versus Placebo Among Patients with Psoriatic Arthritis and an Inadequate Response to Biologic Disease-Modifying Anti-Rheumatic Drugs

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SESSION INFORMATION

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Table 1. Mean Change in PRO Scores From Baseline at Week 12

PRO	Placebo		UPA 15 mg QD		UPA 30 mg QD	
	Baseline score	Mean change	Baseline score	Mean change	Baseline score	Mean change
PtGA, 0–10 NRS	6.9	–0.6	6.8	–2.3*	6.6	–2.9*
Pain, 0–10 NRS	6.6	–0.5	6.3	–1.9*	6.2	–2.6*
HAQ-DI	1.2	–0.10	1.1	–0.30*	1.2	–0.41*
FACIT-F	26.4	1.3	27.9	5.0*	29.0	6.1*
SF-36 PCS	34.3	1.6	35.1	5.2*	34.7	7.1*
SF-36 MCS	43.7	–0.1	44.8	2.8*	46.4	3.1*
EQ-5D-5L	0.58	0.03	0.62	0.12*	0.61	0.15*
SAPS[a]	52.6	–1.5	49.5	–24.4*	47.6	–29.7*
WPAI overall work impairment	46.8	–0.5	46.0	–12.0*	44.9	–17.1*
WPAI activity impairment	55.3	-3.1	51.3	–14.1*	50.0	–18.8*
BASDAI[b]	6.6	–0.3	5.9	–1.4*	6.0	–2.0*
Morning stiffness[c]	5.8	–0.5	5.9	–1.9*	5.7	–2.3*

*$P<0.05$ for UPA vs PBO.
[a]Results presented at Week 16 as SAPS was not assessed at Week 12. [b]In subjects with psoriatic spondylitis at baseline. [c]Mean of BASDAI Q5 and Q6.
BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; EQ-5D-5L, EuroQoL-5 Dimension, 5 Level index score; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCS, mental component summary; NRS, numeric rating scale; PBO, placebo; PCS, physical component summary; PRO, patient-reported outcome; PtGA, Patient Global Assessment of Disease Activity; QD, once daily; SAPS, Self-Assessment of Psoriasis Symptoms; SF-36, 36-Item Short-Form Health Survey; UPA, upadacitinib; WPAI, Work Productivity and Activity Impairment.

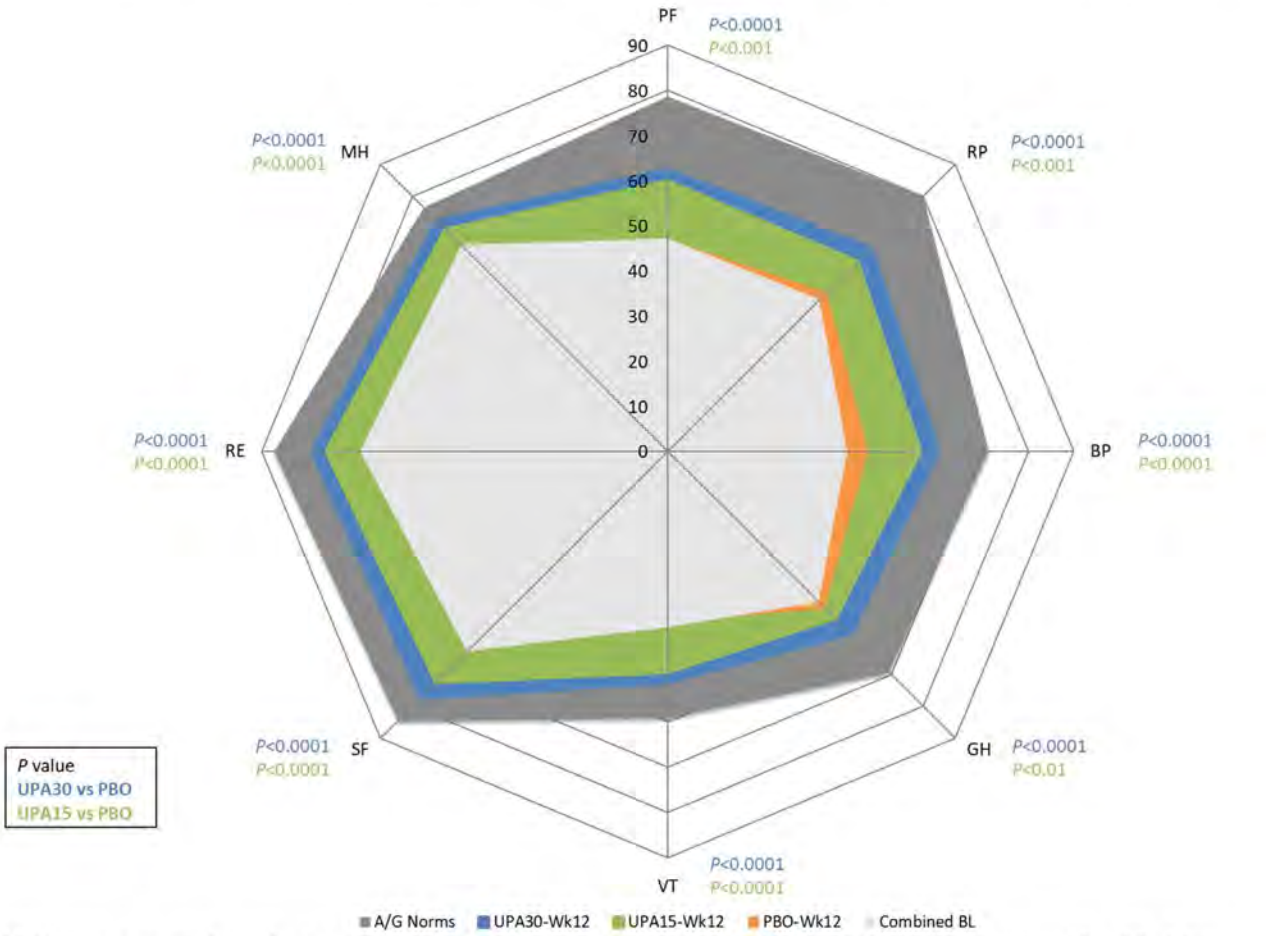
Background/Purpose: The efficacy and safety of upadacitinib (UPA), a selective Janus kinase inhibitor, in patients with PsA is under investigation in Phase 3 clinical trials. Patient-reported outcomes (PROs) are an important component in the evaluation of efficacy for a new therapy. This *post hoc* analysis evaluated the impact of UPA vs placebo (PBO) on PROs in patients with active PsA and an inadequate response to biologic DMARDs (bDMARD-IR).

Methods: Patients in SELECT-PsA 2 (NCT03104374), a Phase 3, randomized, PBO-controlled trial, received UPA 15 mg or UPA 30 mg once daily or PBO for 24 weeks, with the primary endpoint assessment at Week 12. The following PROs were assessed: Patient Global Assessment of Disease Activity (PtGA), Patient's Assessment of Pain, HAQ-Disability Index (HAQ-DI), Functional Assessment of Chronic Illness Therapy-Fatigue, 36-Item Short-Form Health Survey (SF-36), EQ-5D-5L, Self-Assessment of Psoriasis Symptoms (SAPS), Work Productivity and Activity Impairment, Bath Ankylosing Spondylitis Disease Activity Index (BASDAI), and morning stiffness (items 5 and 6 from the BASDAI). BASDAI was assessed in patients with evidence of psoriatic spondylitis at baseline (BL). Least squares mean changes from BL to Week 12 (Week 16 for SAPS) were assessed. The proportions of patients reporting improvements ≥ minimal clinically important differences (MCID) from BL through Week 24 were compared between both doses of UPA and PBO. The number needed to treat (NNT) to achieve 1 additional MCID response for each PRO of interest with UPA vs PBO were calculated at Weeks 12/24.

Results: Data from 641 patients (UPA 15 mg: 211; UPA 30 mg: 218; PBO: 212) were analyzed. Significant improvements from BL to Week 12 were reported with both doses of UPA vs PBO across all PROs, including all SF-36 domains (**Table, Figure 1**). Significantly greater proportions of patients receiving either dose of UPA vs PBO reported improvements ≥ MCID as early as Week 2 (the first post-BL visit) in PtGA, pain, and HAQ-DI. Compared with PBO at Week 12, a significantly greater proportion of patients receiving either dose of UPA reported improvements ≥ MCID across all PROs except SF-36 mental component summary (UPA 30 mg) (**Figure 2**). Improvements were maintained or further improved through Week 24. NNTs with UPA 15 mg and 30 mg ranged from 3–10 across PROs at Week 12.

Conclusion: Among bDMARD-IR patients with active PsA, treatment with UPA 15 mg or 30 mg once daily for 12 weeks resulted in clinically meaningful improvements in PROs, which were maintained or further improved through 24 weeks.

Figure 1. Spydergram of SF-36 Domain Changes From Baseline With UPA 15 mg, 30 mg vs PBO at Week 12



A/G Norms, age- and gender-matched normative values; BL, baseline; BP, bodily pain; GH, general health; MH, mental health; PBO, placebo; PF, physical functioning; RE, role-emotional; RP, role-physical; SF, social functioning; SF-36, 36-Item Short-Form Health Survey; UPA, upadacitinib; VT, vitality; Wk, week.

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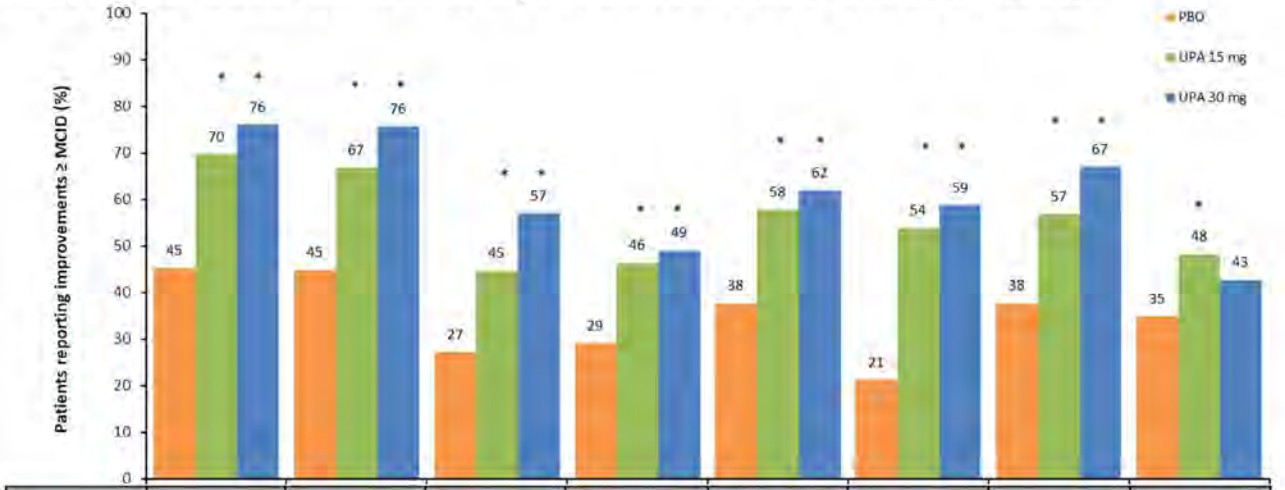
Figure 2. Proportion of Patients Reporting Improvements ≥ MCID[a] in PROs at Week 12



	PtGA NNT	Pain NNT	HAQ-DI NNT	FACIT-F NNT	EQ-5D-5L NNT	BASDAI NNT	SF-36 PCS NNT	SF-36 MCS NNT[b]
PBO	–	–	–	–	–	–	–	–
UPA 15 mg	4.1	4.5	5.7	5.8	5.0	3.2	5.2	7.4
UPA 30 mg	3.2	3.2	3.4	5.0	4.1	2.7	3.4	–

*$P<0.05$ for UPA vs PBO.

[a]MCID was defined as reduction of ≥1 point for PtGA, reduction of ≥1 point for pain, reduction of ≥0.35 units for HAQ-DI, increase of ≥4.0 points for FACIT-F, increase of ≥2.5 points for SF-36 PCS and MCS, increase of ≥0.05 for EQ-5D-5L, and reduction of ≥1.1 points for BASDAI.

[b]NNTs vs PBO were not calculated for non-significant results.

BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; EQ-5D-5L, EuroQoL-5 Dimension, 5 Level index score; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; HAQ-DI, Health Assessment Questionnaire-Disability Index; MCID, minimal clinically important difference; MCS, mental component summary; NNT, number needed to treat; PBO, placebo; PCS, physical component summary; PRO, patient-reported outcome; PtGA, Patient Global Assessment of Disease Activity; SF-36, 36-Item Short-Form Health Survey; UPA, upadacitinib.

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Abstract Number: 1372

Efficacy and Safety of Upadacitinib in Patients with Psoriatic Arthritis and Axial Involvement

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Background/Purpose: Upadacitinib (UPA) has demonstrated efficacy for the treatment of AS in patients (pts) who were NSAID inadequate responders (IR).[1] Pts with psoriatic arthritis (PsA) and axial involvment often exhibit greater disease activity and quality of life impairments compared with those without axial involvment. The aim of this analysis was to characterize PsA pts with and without axial involvement and compare efficacy of UPA vs placebo (PBO) in PsA pts with axial involvement.

Methods: In SELECT-PsA 1 (NCT03104400; N=1705, non-biologic DMARD IR) and SELECT-PsA 2 (NCT03104374; N=642, biologic DMARD IR), pts with active PsA (≥3 swollen and ≥3 tender joints), active or historical psoriasis, and

Table 1. Demographics and Baseline Characteristics

	SELECT-PsA 1 Study			SELECT-PsA 2 Study		
	With Psoriatic Spondylitis (n=534)	Without Psoriatic Spondylitis (n=1170)	*P* value*	With Psoriatic Spondylitis (n=219)	Without Psoriatic Spondylitis (n=421)	*P* value*
Female, n (%)	281 (52.6)	626 (53.5)	0.7348	116 (53.0)	231 (54.9)	0.6469
Age (years), mean (SD)	49.9 (13.0)	51.2 (11.9)	0.0611	52.5 (11.8)	53.8 (11.9)	0.1878
Weight (kg), mean (SD)	84.9 (19.6)	87.1 (20.6)	**0.0446**	89.7 (23.5)	88.4 (22.4)	0.5018
BMI (kg/m^2), mean (SD)	29.9 (6.5)	30.5 (6.9)	0.0810	31.6 (8.0)	31.3 (6.9)	0.6226
Duration of PsA symptoms (years), mean (SD)	10.0 (9.1) n=533	8.9 (8.3) n=1170	**0.0162**	13.0 (9.6) n=216	13.5 (11.0) n=420	0.5620
Tender Joint Count 68, mean (SD)	21.6 (15.1)	19.2 (13.5)	**0.0022**	27.5 ± 18.0	23.3 ± 16.2	**0.0027**
Swollen Joint Count 66, mean (SD)	11.7 (9.4)	11.0 (7.9)	0.1184	12.9 (9.2)	11.7 (8.7)	0.0804
Physician's Global Assessment (NRS 0–10), mean (SD)	6.7 (1.6)	6.5 (1.7)	**0.0437**	6.6 (1.8)	6.5 (1.7)	0.1897
HAQ-DI , mean (SD)	1.2 (0.6) n=531	1.1 (0.6) n=1164	**0.0170**	1.2 (0.6) n=218	1.2 (0.7) n=416	0.2049
CRP (mg/L), mean (SD)	12.8 (18.5)	10.5 (13.7)	**0.0127**	10.0 (16.4)	11.1 (18.9)	0.4227
BSA with psoriasis, n (%)						
<3%	250 (46.8)	608 (52.0)	**0.0486**	94 (42.9)	154 (36.6)	0.1181
≥3%	284 (53.2)	562 (48.0)		125 (57.1)	267 (63.4)	
Presence of Dactylitis†, n (%)	188 (35.2)	328 (28.0)	**0.0028**	69 (31.5)	100 (23.8)	**0.0348**
Presence of Enthesitis‡, n (%)	432 (80.9)	884 (75.6)	**0.0147**	189 (86.3)	337 (80.0)	**0.0125**
ASDAS–CRP, mean (SD)	3.4 (0.9) n=530	3.1 (1.0) n=1161	**<0.0001**	3.3 (1.0) n=217	3.2 (1.1) n=416	0.1032
BASDAI, mean (SD)	5.8 (2.0) n=530	5.3 (2.2) n=1161	**<0.0001**	6.2 (2.2) n=217	5.8 (2.2) n=416	0.0673
Morning Stiffness Duration (NRS 0–10; BASDAI Q6), mean (SD)	5.0 (3.0) n=530	4.7 (3.0) n=1161	**0.0368**	5.6 (3.2) n=217	5.1 (3.0) n=416	**0.0454**
Patient's Assessment of Inflammatory Neck, Back, or Hip Pain (NRS 0–10; BASDAI Q2), mean (SD)	5.8 (2.7) n=530	4.6 (3.2) n=1161	**<0.0001**	6.4 (2.8) n=217	5.4 (3.1) n=416	**0.0001**
Patient's Assessment of Overall Pain in Joints Other Than Neck, Back, or Hips (NRS 0–10; BASDAI Q3), mean (SD)	6.2 (2.4) n=530	5.9 (2.6) n=1161	**0.0286**	6.3 (2.3) n=217	6.2 (2.6) n=416	0.5308

ASDAS, ankylosing spondylitis disease activity score; BASDAI, Bath ankylosing spondylitis disease activity index; BMI, body mass index; CRP, C–reactive protein; HAQ–DI, health assessment questionnaire disability index; NRS, numeric rating scale; PsA, psoriatic arthritis. Treating rheumatologist assessed whether or not the patient has psoriatic spondylitis taking into consideration all that was known about the patient. *Calculated by t-test for continuous variables; calculated by chi-square test for categorical values (statistically significant *P* values [<0.05] are bolded). †Defined as Leeds Dactylitis Index >0. ‡Defined as Total Enthesitis Count >0.

Table 1

Table 2. Integrated Analysis of Efficacy in PsA Patients With Axial Involvement from SELECT-PsA 1 and PsA 2 Studies

Mean (SD), MMRM analysis	Placebo Wk 12/24: n=186/174	UPA 15 mg QD Wk 12/24: n=203/186	UPA 30 mg QD Wk 12/24: n=198/181
Δ BASDAI wk 12, mean (SD)	−0.56 (−0.84, −0.27)	−1.75 (−2.03, −1.48)*	−2.22 (−2.50, −1.94)*
Δ BASDAI wk 24, mean (SD)	−1.00 (−1.30, −0.69)	−2.61 (−2.91, −2.31)*	−2.71 (−3.01, −2.41)*
Δ BASDAI Q2 wk 12, mean (SD)	−0.6 (−1.0, −0.3)	−1.6 (−2.0, −1.3)*	−2.0 (−2.3, −1.6)*
Δ BASDAI Q2 wk 24, mean (SD)	−0.8 (−1.2, −0.5)	−2.5 (−2.9, −2.1)*	−2.4 (−2.8, −2.0)*
Δ BASDAI Q3 wk 12, mean (SD)	−0.68 (−1.02, −0.33)	−2.16 (−2.50, −1.83)*	−2.68 (−3.02, −2.34)*
Δ BASDAI Q3 wk 24, mean (SD)†	−1.20 (−1.57, −0.84)	−3.03 (−3.39, −2.67)*	−3.21 (−3.58, −2.85)*
Δ ASDAS wk 12, mean (SD)	−0.23 (−0.37, −0.09)	−1.22 (−1.35, −1.08)*	−1.46 (−1.60, −1.33)* n=197
Δ ASDAS wk 24, mean (SD)	−0.41 (−0.56, −0.27) n=172	−1.53 (−1.68, −1.39)*	−1.70 (−1.84, −1.55)*
% (95% CI), NRI analysis	**Placebo n=205**	**UPA 15 mg QD n=215**	**UPA 30 mg QD n=206**
BASDAI 50 wk 12, % (95% CI)	12.2 (7.7, 16.7)	31.2 (25.0, 37.4)*	43.7 (36.9, 50.5)*
BASDAI 50 wk 24, % (95% CI)	18.5 (13.2, 23.9)	49.3 (42.6, 56.0)*	47.1 (40.3, 53.9)*
ASDAS ID, wk 12, % (95% CI)	6.3 (3.0, 9.7)	20.9 (15.5, 26.4)*	33.5 (27.1, 39.9)*
ASDAS ID, wk 24, % (95% CI)	9.3 (5.3, 13.2)	37.2 (30.7, 43.7)*	43.2 (36.4, 50.0)*
ASDAS LDA, wk 12, % (95% CI)	18.0 (12.8, 23.3)	47.9 (41.2, 54.6)*	62.1 (55.5, 68.8)*
ASDAS LDA, wk 24, % (95% CI)	22.0 (16.3, 27.6)	57.7 (51.1, 64.3)*	65.0 (58.5, 71.6)*
ASDAS MI, wk 12, % (95% CI)	4.4 (1.6, 7.2)	24.7 (18.9, 30.4)*	30.1 (23.8, 36.4)*
ASDAS MI, wk 24, % (95% CI)	5.9 (2.6, 9.1)	34.9 (28.5, 41.3)*	38.3 (31.7, 45.0)*
ASDAS CII, wk 12, % (95% CI)	11.7 (7.3, 16.1)	49.8 (43.1, 60.7)*	60.7 (54.0, 67.3)*
ASDAS CII, wk 24, % (95% CI)	20.5 (15.0, 26.0)	56.3 (49.6, 62.9)*	59.2 (52.5, 65.9)*

ASDAS, ankylosing spondylitis disease activity score; Δ, change from baseline; CII, clinically important improvement; MMRM, Mixed–Effects Model Repeated Measurement; QD, daily; ID, inactive disease; LDA low disease activity; MI, major improvement; NRI, non-responder imputation; UPA, upadacitinib. *P<0.0001, UPA vs placebo; nominal P values are presented and were not adjusted for multiple testing. MMRM analysis with unstructured variance–covariance matrix, including treatment, visit, treatment–by–visit interaction, study, and the stratification factor of current DMARD use (yes/no) as fixed factors and the continuous fixed covariates of baseline measurement. NRI analysis with nominal P value constructed using the Mantel-Haenszel estimation adjusting for study and the main stratification factor of current DMARD use (yes/no); 95% CI for response rate calculated based on normal approximation to the binomial distribution.

on ≤2 non-biologic DMARDs were randomized to once daily UPA 15 mg, UPA 30 mg, adalimumab 40 mg every other week (SELECT-PsA 1 only), or PBO. At baseline (BL), the presence of psoriatic spondylitis was assessed by the investigator based on the totality of information available, and characteristics were compared for pts with and without axial involvement. Efficacy was assessed in pts with axial involvement using pooled data from the 2 studies for pts on PBO, UPA 15 mg, or UPA 30 mg. Assessments included change from BL in overall BASDAI, BASDAI question 2 (neck/back/hip pain) and question 3 (joint swelling/pain), and the AS Disease Activity Score (ASDAS) based on CRP, and the percentage of pts with BASDAI 50 response, ASDAS inactive disease (ID), ASDAS low disease activity (LDA), ASDAS major improvement (MI), and ASDAS clinically important improvement (CII) responses. Adverse events were reviewed to identify new onset or worsening uveitis and inflammatory bowel disease (IBD). Data are presented through the end of the 24-week PBO-controlled period.

Results: Prevalence of axial involvment was 31.3% in SELECT-PsA 1 and 34.2% in SELECT-PsA 2. Demographics and disease activity for pts with and without axial involvement are presented in **Table 1**. Treatment with UPA 15 mg and 30 mg resulted in significantly greater improvements from BL in the overall BASDAI, BASDAI Q2 (neck/back/hip pain) and Q3 (joint swelling/pain) and ASDAS-CRP endpoints at weeks 12 and 24 vs PBO (**Table 2**). Similarly, significantly higher percentages of pts on UPA 15 mg and 30 mg achieved BASDAI 50, ASDAS ID, LDA, MI, and CII at weeks 12 and 24 vs PBO (**Table 2**). Uveitis was reported in 2 pts on PBO (1 new onset; 1 flare) and 1 pt on UPA 30 mg (new onset). 1 event of Crohn's disease (flare) was reported on PBO; no IBD events were reported on UPA. Except for the uveitis flare on PBO, all uveitis and IBD events were reported in pts with psoriatic spondylitis.

Conclusion: Pts with PsA and axial involvement were more likely to have higher BL disease burden compared with those without axial involvement. Consistent with results observed in pts with AS, UPA was efficacious in treating axial symptoms in pts with psoriatic spondylits. Uveitis rates did not increase with UPA treatment, and UPA has shown efficacy in phase 2 IBD studies[2,3] with no IBD events reported in UPA-treated PsA pts.

1. van der Heijde D, et al. *Lancet*. 2019;394(10214):2108-2117.
2. Sandborn W, et al. *Gastroenterology* 2020;158:2123-2138.
3. Sandborn W, et al. *Gastroenterology* 2020;158:2139-2149.

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IL-23 Skin and Joint Profiling in Psoriatic Arthritis: Novel Perspectives in Understanding Clinical Responses to IL-23 Inhibitors

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Background/Purpose: PsA is a chronic heterogeneous inflammatory condition affecting up to 30% of patients with skin and/or nail psoriasis and the IL-23/IL-17 axis is believed to be key in psoriasis and PsA pathogenesis. Several drugs targeting the IL-23/IL-17 axis have been successfully tested in the context of psoriasis and PsA but, while 50-60% of patients achieve almost complete psoriasis clearance upon treatment, the joint disease improvement is modest. To date, the mechanism for the divergent skin-joint response remains largely unexplained. This study aims to determine the relationship between synovial versus skin transcriptional/histological profiles in patients with active PsA and to explore mechanistic links between diseased tissue pathology and clinical outcomes.

Methods: Twenty-seven patients fulfilling the ClASsification for Psoriatic ARthritis (CASPAR) criteria with active peripheral joint disease (>3 tender and >3 swollen joints) despite an adequate trial of at least two conventional synthetic DMARDs and either biologic-naïve or failing one or more TNF-α-inhibitor (anti-TNF) were enrolled in an observational/open-label study. Patients underwent biopsies of synovium and paired lesional/non-lesional skin before starting anti-TNF (if biologic-naïve; n=18) or ustekinumab (anti-IL-12/IL-23p40; if anti-TNF inadequate responders; n=9). Molecular analysis of 80-inflammation-related genes and protein levels for IL-23p40/IL-23p19/IL-23R were assessed by real-time-PCR and immunohistochemistry, respectively.

Results: At baseline, all patients had persistent active disease as per inclusion criteria. At 16-weeks-post-treatment, skin responses favoured ustekinumab, while joint responses favoured anti-TNF therapies. Principal-component-analysis revealed distinct clustering of synovial tissue gene expression away from the matched-skin. While *IL12B-IL23A*-

IL23R were homogeneously expressed in lesional skin, their expression was extremely heterogeneous in paired synovial tissues. Here, IL-23 transcriptomic/protein expression was strongly linked to patients with high-grade synovitis who, however, were not distinguishable by conventional clinimetric measures.

Conclusion: PsA synovial tissue shows a heterogeneous IL-23 axis profile when compared to matched skin. Synovial molecular-pathology may help to identify among clinically indistinguishable patients those with a greater probability of responding to IL-23 inhibitors.

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Abstract Number: 1374

Secukinumab in the Treatment of Dactylitis in Patients with Psoriatic Arthritis: Post Hoc Analysis Results from a Randomized Phase 3 Trial

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Dactylitis is a key and frequent clinical manifestation of psoriatic arthritis (PsA)[1] associated with significant disease burden and impaired function.[2–3] Randomized controlled trials designed to evaluate the impact of biologics on resolution of dactylitis are limited.[3] We report results of a post hoc analysis evaluating the effect of secukinumab (SEC) on PsA patients with dactylitis, from the FUTURE 5 trial (NCT02404350).[4]

Methods: FUTURE 5 is a randomized, double-blinded, placebo-controlled, 2-year phase 3 trial in patients with active PsA. Patients (aged ≥18 years) were randomized 2:2:2:3 to s.c. SEC 300 mg or 150 mg with loading dose (LD), 150 mg without loading dose (NL) or placebo. All groups received SEC or placebo at baseline, weeks (wks) 1, 2 and 3 and then every 4 wks from Wk 4. Exploratory efficacy analysis at Wks 16 and 52 included time to resolution of dactylitis by dactylitis severity, proportion of patients with resolution of dactylitis, ACR 20/50 response and Psoriasis Area and Severity Index (PASI) 90.

Results: Of the 996 patients in the trial, 389 (39%) had dactylitis (SEC 150 mg NL [N=103], 150 mg LD [N=80], 300 mg LD [N=82], and placebo [N=124]). The mean (SD) tender joint count, swollen joint count and dactylitis count at baseline was: 24.0 (17.0), 14.5 (11.4) and 4.1 (4.16) and 19.1 (14.8), 9.5 (8.5) and 0, respectively, in patients with (N=389) and without (N=607) dactylitis at baseline. Higher presence of enthesitis, hsCRP and skin disease were also observed in the dactylitis subset. Median time to resolution of dactylitis (days) [95% CI] in patients on SEC 150 mg NL, 150 mg LD, and 300 mg LD, was 85 [61.0, 113.0], 85 [57.0, 119.0] and 57 [30.0, 85.0], respectively. A higher proportion of SEC treated patients achieved resolution of dactylitis, ACR 20/50 and PASI90 responses vs. placebo at Wk16 with further improvements through Wk 52 (**Table 1**). Resolution of dactylitis based on the number of dactylitis count at baseline (≤2 and ≥3) are shown in **Table 2**. SEC 300 mg LD was associated with a faster time to resolution of dactylitis and higher ACR50 and PASI90 responses compared to SEC 150 mg.

	SEC 150 mg (No Load) N = 103	SEC 150 mg (Load) N = 80	SEC 300 mg (Load) N = 82	Placebo N = 124
Patients with dactylitis resolution, n/N (%)				
16 Wk	46/79 (58%)	58/100 (58%)	54/81 (67%)	40/116 (35%)
52Wk	58/70 (83%)	71/87 (82%)	58/72 (81%)	-
ACR20				
16 Wk	65	59	69.7	33
52 Wk	79.5	75.7	77	-
ACR50				
16 Wk	36	39.7	50	13
52 Wk	55.7	48.6	59.5	-
PASI90				
16 Wk	30.6	20	52.5	6.2
52 Wk	50	42.9	62.2	-
SEC, secukinumab; ACR, American College of Rheumatology; PASI, Psoriasis Area and Severity Index; Wk, week.				

Table 1. Efficacy outcomes in patients with baseline dactylitis (observed data)

	SEC 150 mg (No Load) N = 103		SEC 150 mg (Load) N = 80		SEC 300 mg (Load) N = 82		Placebo N = 124	
Dactylitis count at baseline	≤2	≥3	≤2	≥3	≤2	≥3	≤2	≥3
N	50	53	34	46	48	34	67	57
Patients with dactylitis resolution, n/N (%)								
16 wks	36/50 (72%)	20/53 (37.7%)	25/34 (73.5%)	21/46 (45.7)	37/48 (77.1%)	18/34 (53.3%)	35/67 (52.2%)	16/57 (28.1%)
52 wks	49/50 (97.8%)	47/53 (89.2%)	33/34 (96.7)	39/46 (85.8)	46/48 (95.8%)	29/34 (85.4%)	-	-
Time to resolution (days)								
Median (95% CI)	58 (30.0, 85.0	119 (85.0, 197.0)	44 (22.0, 85.0)	119 (78.0, 176.0)	44 (22.0, 57.0)	106 (57.0, 161.0)	89 (57.0, 169.0)	225 (167.0, 280.0)
SEC, secukinumab; ACR, American College of Rheumatology; PASI, Psoriasis Area and Severity Index; Wk, week.								

Table 2. Efficacy outcomes in patients with dactylitis at baseline ≤ 2 and ≥ 3 (observed data)

Conclusion: A higher level of disease burden was observed in patients with dactylitis compared to patients without dactylitis. SEC 300 mg was associated with a faster time to resolution of dactylitis, higher resolution of dactylitis irrespective of severity and higher responses on skin and joints.

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Abstract Number: 1375

Remission in Axial Spondyloarthritis: Is There a Difference Between NSAIDs and Biologics in the Real Life?

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Randomized-controlled trials (RCTs) done in axial spondyloarthritis (AxSpA) patients have shown that remission in Ankylosing Spondylitis and nonradiographic AxSpA patients treated without biologics (BIOL) occurs infrequently (Ref 1, 2). Few are known about remission rate (RR) in daily clinical practice. Our aim was to assess the remission rate (RR) in AxSpA patients in real life, and to compare the RR in AxSpA patients on NonSteroidal Anti-Inflammatory Drugs (NSAIDs) to RR for those on BIOL (anti-TNFα or IL-17A blockers).

Methods: This cross-sectional study reviewed clinical data from a single center (St-Luc university hospitals, UCLouvain, Brussels) from 01/2013 to 03/2019. Last visit available for clinical assessment was evaluated. Disease activity was measured using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and the Ankylosing Spondylitis Disease Activity Score using the C-reactive protein (ASDAS-CRP). Remission was defined as BASDAI < 4 and ASDAS-CRP < 1.3.

Results: Data from 551 AxSpA patients were reviewed. 353 were men (64.3%). In the entire cohort, 478 BASDAI and 316 ASDAS-CRP were recorded. The RR according to the BASDAI was 46.7% (n = 223), and 17.4% for the ASDAS-CRP (n = 55). To look for the treatment-related RR, we stratified by the treatment (NSAIDs vs BIOL). We had 285 patients on NSAIDs (177 men, 62.5%) and 266 on BIOL (176 men, 66%). 245 BASDAI were available for NSAIDs and

Table. Distribution of ASDAS-CRP values in both groups (n = 316).

	ASDAS-CRP < 1.3	ASDAS-CRP ≥ 1.3 < 2.1	ASDAS-CRP ≥ 2.1 ≤ 3.5	ASDAS-CRP > 3.5
NSAIDs (n = 172)	N = 27 (15.7%)	N = 41 (23.8%)	N = 70 (40.7%)	N = 34 (19.8%)
BIOL (n = 144)	N = 28 (19.4%)	N = 30 (20.8%)	N = 57 (39.6%)	N = 29 (20.1%)

233 for BIOL. 110 patients on NSAIDs (44.9%) and 113 on BIOL (48.5%) were in remission for BASDAI. Regarding ASDAS-CRP (see table below), data from 172 patients on NSAIDs and 144 on BIOL were available. Out of them, 27 (15.7%) and 28 (19.4%) were in remission for NSAIDs and BIOL respectively. Chi-square test: p = 0.853.

Conclusion: In the real life, RR in AxSpA is higher on BIOL even if compared to NSAIDs the difference is not statistically significant. However, many patients on NSAIDs achieve the remission.

References

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Abstract Number: 1376

Impact of Body Composition Measures on the Response to Biological Disease-modifying Anti-rheumatic Drugs in Patients with Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Data on the impact of body weight and body mass index (BMI) on the response to biological disease-modifying anti-rheumatic drugs (bDMARDs) in axial spondyloarthritis (axSpA) including ankylosing spondylitis (AS) are still contradictory. Data on the impact of different components of the body composition on the treatment response are lacking. The purpose of this study is to investigate the impact of body composition on the response to biological disease-modifying anti-rheumatic drugs (bDMARD) in patients with AS after 6 months of treatment.

Methods: Patients with AS (radiographic axSpA), fulfilling the modified New York criteria and starting a bDMARD therapy were recruited between 2015 and 2019 in an extension of the prospective German Spondyloarthritis Inception Cohort (GESPIC-AS). All patients were required to be candidates for bDMARD therapy at baseline with high disease activity (BASDAI >=4 and/or ASDAS >=2.1) despite previous treatment with nonsteroidal anti-inflammatory drugs. Disease activity measures (BASDAI, CRP, ASDAS), as well as body composition parameters were assessed

Variables	Univariable Analysis ß (95%CI)	Multivariable analysis*						
		Model 1 ß (95%CI)	Model 2 ß (95%CI)	Model 3 ß (95%CI)	Model 4 ß (95%CI)	Model 5 ß (95%CI)	Model 6 ß (95%CI)	Model 7 ß (95%CI)
BMI, kg/m^2	-0.016 (-0.063; 0.031)	**-0.043 (-0.079; -0.006)**	-	-	-	-	-	-
FMI, kg/m^2	-0.024 (-0.103; 0.054)	-	**-0.065 (-0.128; -0.003)**	-	-	-	-	-
FMMI,kg/m^2	-0.010 (-0.133; 0.112)	-	-	**-0.138 (-0.253; -0.022)**	-	-	-	-
SMM, kg	0.026 (-0.020; -0.071)	-	-	-	0.012 (-0.044; 0.069)	-	-	-
VAT, liters	0.069 (-0.099; 0.238)	-	-	-	-	-0.095 (-0.248; 0.057)	-	-
TBW, liters	0.020 (-0.016; 0.056)	-	-	-	-	-	0.007 (-0.036; 0.051)	-
ECW, liters	0.054 (-0.43; 0.150)	-	-	-	-	-	-	0.005 (-0.98; 0.107)

*Adjusted for age, sex, HLA-B27 status, symptom duration, and ASDAS at baseline.
BMI: Body Mass Index; FMI: Fat Mass Index; SMM: Skeletal Muscle mass; VAT: Visceral Adipose Tissue; AS: ankylosing spondylitis; bDMARD: biological disease-modifying anti-rheumatic drug; CI: 95% confidence interval.

Table. Univariable and multivariable linear regression analysis of the association between response to bDMARD treatment (change in the ASDAS score after 6 months) and body composition parameters in patients with AS (n=77)

at baseline and after 6 months of bDMARD treatment. Body composition was assessed by the bioelectrical impedance analysis (BIA). Weight, body mass index (BMI), fat mass index (FMI), fat free mass index (FFMI), skeletal muscle mass value (SMM), visceral adipose tissue (VAT), total body water (TBW), and extracellular water (ECW) values were collected. The primary measure of the treatment response was ASDAS change at month 6 as compared to baseline.

Results: A total of 129 patients with AS were included in this cohort. BIA was performed in 77 patients. There were 71.4% males, and 85.7% were HLA-B27 positive. At baseline, BASDAI was 5.4±1.4, CRP was 12.8±16.5 mg/l, and ASDAS - 3.0±1.0. The baseline BMI was 25.0±4.3 kg/m^2. A total of 75 patients were treated with TNFi, 2 patients received an IL-17 inhibitor.

A higher BMI at baseline was associated with a worse response to bDMARD therapy that was attributable to both, the fat mass as reflected by FMI and to the fat-free mass reflected by FFMI, but not to SMM or VAT or water components – Table. This effect was independent of age, sex, symptom duration, HLA-B27 status and ASDAS at baseline.

Conclusion: Both fat mass and fat free mass have an impact on the response to bDMARDs after 6 months of treatment in patients with AS. Interestingly, skeletal muscle mass, visceral fat as well as water components showed no association with treatment response.

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Abstract Number: 1377

Raynaud's Phenomenon and Systemic Sclerosis in Post-9/11 Deployed Veterans Receiving Care Veterans Health Administration Care

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The purpose of this project was to describe Raynaud's phenomenon (RP), very early diagnosis of systemic sclerosis (VEDOSS), and systemic sclerosis (SSc) in Veterans who were deployed in support of Post-9/11 operations. We sought to describe the military occupation specialty, clinical features, and medication use across the three diagnoses.

Methods: Individual Veterans medical records were assessed for RP (ICD-9 443.0), VEDOSS with swelling of hands (ICD-9 729.81) and RP (ICD-9 443.0), and SSc (ICD-9 710.1). The distribution of sociodemographic, military service branch, job classification, vasodilator use, and comorbidities were examined across the three classifications of disease. The chi-squared test and Fisher's exact were used to compare frequency of these categorical variables. Logistic regression was used to assess the likelihood of characteristics of the three classifications of disease.

Results: In this population of 607,665 individual Veteran medical records, 857 had RP, 45 met possible VEDOSS criteria, and 71 had a diagnosis of SSc. The majority of RP, VEDOSS and SSc cases were white males, but the likelihood of having RP, VEDOSS or SSc was higher in white females. The vast majority of RP, VEDOSS, and SSc cases were found in the Army service, with a rank of enlisted with the most common occupation specialties of electronic repair. However, those in craftworks, engineering or maintenance, and healthcare had a greater likelihood of RP. The use of vasodilators was low among RP, VEDOSS, and SSc. The most common comorbidities were pain and depression. Gastrointestinal tract symptoms typical for SSc patients were found in RP patients.

Conclusion: This is a unique Veteran population of predominately-male patients. Our data suggests that vasodilator medications are potentially being under-utilized in this RP, VEDOSS, and SSc Veteran population. Our data highlights mood and pain management is an important aspect of SSc care.

	No RP, VEDOSS, or SSc (n=606692)	Raynauds Phenomenon (n=857)	VEDOSS (n=49)	Systemic Sclerosis (n=71)
Age (years)				
< 29	345899 (57 %)	439 (51 %)	14 (31 %)	20 (28%)
30-39	137616 (23 %)	213 (25 %)	17 (38 %)	29 (41%)
40-49	98582 (16 %)	168 (20 %)	<25%	<25%
50+	24595 (4 %)	37 (4 %)	<5%	<15%
Married	271866 (45 %)	421 (51 %)	25 (56 %)	34 (48%)
Unmarried	335799 (55 %)	436 (49 %)	20 (45 %)	37 (52%)
Sex				
Male	528329 (87 %)	522 (61 %)	27 (60 %)	41 (58%)
Female	78363 (13 %)	335 (39 %)	18 (4 0%)	30 (42%)
Asian	15878 (3 %)	17 (2 %)	<5%	<5%
Black	107291 (18 %)	165 (19 %)	<20%	22 (31%)
Hispanic	71375 (12 %)	54 (6 %)	<5%	<15%
Native American	8690 (1 %)	<5%	0	<10%
White	395027 (65 %)	601 (70 %)	35 (78 %)	33 (47 %)
Unknown	8431 (1 %)	<5%	0	<5%
Education				
Less than high school	7813(1 %)	11 (1 %)	0	0
High School Graduate	46854 (77 %)	589 (69 %)	29 (64 %)	50 (70 %)
Some college	60347 (10 %)	105 (12 %)	<25%	<15%
College Graduate	46196 (8 %)	97 (11 %)	<15%	<15%
Post-College	15650 (3 %)	45 (5 %)	<10%	<5%
Unknown	8144 (1 %)	10 (1 %)	<10%	0
Air Force	66223 (11 %)	148 (17 %)	10 (22 %)	14 (20 %)
Coast Guard	77902 (13 %)	102 (12 %)	<10%	<15%
Marines	82524 (14 %)	71 (8 %)	<10%	<5%
Army	380043 (63 %)	536 (63 %)	29 (64 %)	42 (59 %)
National Guard/Reserves	245257 (40 %)	303 (35 %)	23 (51 %)	32 (45 %)
Active	361435 (60 %)	554 (65 %)	22 (49 %)	39 (55 %)
Rank				
Warrant/officer	42877 (7 %)	104 (12 %)	<10%	<10%
Enlisted	563815 (93 %)	753 (88 %)	41 (91 %)	65 (92 %)
Multiple Deployments				
Yes	319468 (53 %)	438 (51%)	24 (53 %)	34 (48 %)
No	287224 (4 %)	419 (49 %)	21 (47 %)	37 (52 %)
Job Category				
Administrative	79973 (14 %)	147(17 %)	<20%	14 (20 %)
Craftworkers	41036 (7 %)	74 (9 %)	<10%	<10%
Intelligence	44980 (7 %)	59 (7 %)	<10%	<10%
Health Care	27009 (1 %)	77 (9 %)	<15%	<10%
Tactical Operations	13490 (2 %)	14 (2 %)	<10%	0
Infantry	143653 (24 %)	133 (16 %)	<15%	<15%
Supply	102614 (17 %)	132 (15 %)	<20%	12 (17 %)
Allied Specialist	11470 (2 %)	21 (2 %)	0	<10%
Electronic Repairs	126193 (21 %)	164 (19 %)	<25%	19 (27 %)
Engineering/ Maintenance	6869 (1 %)	18(2 %)	<10%	<10%
Unknown	9425 (2 %)	18 (2 %)	<10%	<10%

Socio-demographics of the study population

	No RP, VEDOSS, or SSc (n=606692)	Raynauds Phenomenon (n=857)	VEDOSS (n=49)	Systemic Sclerosis (n=71)
Vasodilator use	92530 (15%)	410 (48 %)	21 (47 %)	45 (63 %)
Pain	228045 (38 %)	493(58 %)	37 (82 %)	46 (65 %)
Fecal incontinence	829 (0.1 %)	<1%	<5%	<5%
Esophageal Dyskinesia	564 (0.1 %)	<1%	0	<10%
Interstitial Lung Disease	11 (0 %)	0	0	<5%
Pulmonary Arterial Hypertension	542 (0.1 %)	<1%	0	15 (21 %)
Cancer	8736 (1 %)	27 (3 %)	0	<5%
High Blood Pressure	120368 (20 %)	222 (26 %)	13 (29 %)	33 (47 %)
Diabetes	29780 (5 %)	34 (4 %)	<5%	<10%
Anxiety	145477 (24 %)	269 (31 %)	11 (24 %)	21 (30 %)
Heart Disease	19297 (3 %)	50 (6 %)	6 (13 %)	<15%
Liver Disease	9740 (2 %)	14 (2%)	0	<10%
Kidney Disease	4545 (1 %)	18 (2 %)	0	<5%
Suicidal ideation/attempt	32050 (5 %)	59 (7 %)	<10%	<10%
Obesity	122838 (20 %)	134 (16 %)	<25%	12 (17 %)
Seizures	8821 (2 %)	21 (2 %)	<5%	<5%
Depression	219302 (36 %)	384 (45 %)	22 (49 %)	39 (55 %)
PTSD	257801(42 %)	394 (46 %)	22 (49 %)	26 (37 %)

Clinical features of the study population

	Raynauds Phenomenon (n=857)	VEDOSS (n=49)	Systemic Sclerosis (n=71)
Age (yrs)			
< 29	1.0		
30-39	1.3(1.1-1.5)*	3.4 (1.7-69)*	3.3 (1.9-6.1)*
40-49	1.40 (1.2- 1.7)*	3.4 (1.5-7.5)**	2.1 (1.1-4.3)*
50+	1.12(0.8-1.6)	3.7(1.1- 13.1)**	3.7 (1.58-9.3)*
Sex			
Male	1.0		
Female	4.5 (3.9-5.3)	5.6 (3.05-10.4)	4. 8 (2.8-8.0)
Race			
White vs. All others	1.5 (1.3-1.8)	2.5 (1.3-4.9)	0.6 (0.4-1.0)
Army vs. Other Armed Forces	1.0 (0.9-1.2)	-	0.8 (0.5-1.3)
Interstitial Lung Disease	0.001 (<0.001-999.99)	<0.001 (<0.001-999.99)	687 (76->999.999)
Pulmonary Arterial Hypertension	5.6 (2.3- 13.6)	<0.001 (<0.001-999.99)	234 (12.7-43.0)
Cancer	1.87 (1.3-2.8)	<0.001 (<0.001-999.99)	1.2 (04-4.2)
Job			
Craftworker	1.4 (1.0-1.8)	-	1.1 (0.4-3.2)
Electronic Equipment Worker	1.1 (0.8-1.3)	-	1.6 (0.8-3.3)
Engineering/Maintenance	1.8 (1.1-2.9)	-	2.2 (0.4-9.9)
Health Care	1.5 (1.1-2.0)	-	0.8 (0.3-2.5)
Infantry	0.9 (0.7-1.2)	-	1.0 (0.4-2.5)
Intelligence	1.0 (0.8-1.4)	-	1.3 (0.5-3.8)
Technical/Allied Specialist	1.3 (0.8-2.1)	-	0.8 (0.1-6.2)
Supply	0.9 (0.7-1.1)	-	1.0 (0.5-2.2)
Tactical Operations	0.8 (0.5-1.4)	-	<0.001 (<0.001-999.99)

Logistic Regression Estimates for Demographic, Clinical Features and Military Occupation Characteristics Associated with Raynaud's Phenomenon, Very Early Diagnosis of Systemic Sclerosis, and Systemic Sclerosis

Disclosure: T. Frech, None; **M. Murtaugh**, None; **M. Amuan**, None; **M. Pugh**, None.

Abstract Number: 1378

Understanding Diagnostic Pathways in Systemic Sclerosis and Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD)

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Interstitial lung disease (ILD) is a common manifestation of SSc. SSc-ILD is usually detected in a patient known to have SSc, but ILD may be the initial presentation of SSc. Optum is a health insurance database covering >60 million patients, which is representative of the commercially insured population in the US. We used data from the Optum database to investigate the documentation of ILD prior to a diagnosis of SSc.

Methods: The study period was between 1 January 2007 and 30 June 2019. The "ICD-9 cohort" comprised patients aged ≥18 years, with an SSc index date (date of first insurance claim related to SSc) between 1 January 2010 and 30 September 2015 based on ICD-9-CM codes, ≥2 medical claims associated with SSc on different dates within a 1-year period, and ≥3 years of continuous enrollment in the database prior to the SSc index date. The "ICD-10 cohort" comprised patients aged ≥18 years, with an SSc index date between 1 October 2017 and 30 June 2019 based on ICD-10-CM codes, ≥2 medical claims associated with SSc on different dates within a 1-year period, and ≥2 years of continuous enrollment in the database prior to the SSc index date. ILD was defined as ≥2 medical claims associated with ILD on different dates. We identified patients who had their second claim associated with ILD prior to their SSc index date in the two cohorts. Analyses were descriptive.

Results: The ICD-9 and ICD-10 cohorts consisted of 1779 and 1032 patients with SSc, respectively. In these two cohorts, 7.6% and 9.3% of patients respectively, had their second claim associated with ILD prior to their SSc index date (Table). The second ILD claim occurred >1 year prior to the SSc index date in 4.3% of patients in the ICD-9 cohort and 5.6% of patients in the ICD-10 cohort.

Table. Patients who had claims for ILD prior to a claim for SSc in the Optum database

	Patients with SSc based on ICD-9 codes (n=1779)	Patients with SSc based on ICD-10 codes (n=1032)
ILD at any time prior to SSc	136 (7.6)	96 (9.3)
ILD >90 days prior to SSc	100 (5.6)	76 (7.4)
ILD >180 days prior to SSc	92 (5.2)	68 (6.6)
ILD >1 year prior to SSc	76 (4.3)	58 (5.6)
ILD >2 years prior to SSc	48 (2.7)	36 (3.5)

Data are n (%) of patients who had their second ILD claim prior to their SSc index date.

Conclusion: Based on data from a large US health insurance database, 4–6% of patients with SSc had claims for ILD more than 1 year prior to a claim for SSc. These data are consistent with previous studies showing that SSc can have an impact on the lung early in the course of SSc and demonstrate the importance of screening patients with ILD for SSc.

Disclosure: S. Assassi, Momenta, 1, corbus, 1, Integrity Continuing Education, 1, Boehringer Ingelheim, 1, 2, 3; **N. Shao**, Boehringer Ingelheim Pharmaceuticals, 3; **Z. Yin**, Boehringer Ingelheim Pharmaceuticals, 3; **E. Volkmann**, Boehringer Ingelheim, 2, 5, Forbius, 2, 5, Corbus, 2; **D. Zoz**, Boehringer Ingelheim Pharmaceuticals, 3; **T. Leonard**, Boehringer Ingelheim Pharmaceuticals, 3.

Abstract Number: 1379

Clinical Outcomes Among Participants with Diffuse Systemic Sclerosis Contracting COVID-19 During Clinical Studies of Lenabasum: A Case Series

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with systemic sclerosis (SSc) may be at increased risk for severe outcomes with COVID-19, given the high rate of immunosuppressive medication use, underlying lung pathologies, and accompanying co-morbid conditions. Limited data are available on outcomes of COVID-19 infection in these patients.[1,2] The American College of Rheumatology (ACR) and the European League Against Rheumatism (EULAR) are collecting provider-entered COVID-19 cases in a registry of patients with rheumatic diseases.[3,4] We report number and outcomes of COVID-19 cases in regularly monitored diffuse cutaneous(dc) SSc patients followed in 2 open-label extension (OLE) studies of lenabasum, an orally-administered, non-immunosuppressive, selective cannabinoid receptor type 2 (CB2) agonist.

Methods: This cohort included participants satisfying ACR/EULAR criteria for SSc who were receiving lenabasum 20 mg BID in the OLE studies in a Phase 2 (NCT02465437) or Phase 3 trial (NCT03398837). Background therapy with immunosuppressive medications was allowed. COVID-19 infection rate was discerned by review of adverse events (AEs) and required a positive COVID-19 test. Outcome of COVID-19 was provided by treating physicians.

Results: Four/385 (0.11%) participants suffered a COVID-19 adverse event (AEs), including one serious AE (SAE). Mean age was 52 years (40-77), with 2 females, and all participants were white. Two had interstitial lung disease (ILD) and were being treated with mycophenolate mofetil (Table 1). One with ILD was asymptomatic and tested for Covid-19 because of contact with known COVID-19 positive individuals. This individual was treated with 5 days of hydroxychloroquine. During COVID-19 infection, 3 continued and 1 temporarily stopped lenabasum treatment due to hospitalization (SAE). This participant with ILD was hospitalized for 3 days and discharged home after 2 doses of experimental remdesivir, with full recovery 4 weeks after symptoms began. One received oxygen therapy in the emer-

Table 1. Summary of clinical characteristics of dcSSc study participants with COVID-19

Age/Sex/Race Serology	ILD (Yes/No) by CXR or HRCT, (Last ppFEV[1])	Concomitant Illness	Background Immuno-suppressive	Positive COVID-19 Test (Yes/No)	Status of Study Treatment	Patient Course	Anti-viral Treatment (Yes/No)	Serious AE (Yes/No)	Current Status of Patient
40/M/W ARA	No	Psoriasis	MMF*	Yes	Lenabasum 20mg BID* continued	Symptomatic with low grade fever, aches, nasal discharge, cough, and sweating. ER visit for chest tightness with a decreased aO^2 sat at 87% which increased to 94% on 1 L O^2 discharged home with O2 for 7 days	No	No	Recovered
77/F/W ARA	Yes by HRCT (81%)	Asthma	MMF, methyl-prednisolone	Yes	Lenabasum 20mg BID temporarily stopped for 22 days and then restarted after recovery	Symptomatic with fatigue, fever, chronic cough, myalgias, headache, vomiting; 3 days in hospital for hyponatremia, no ventilation.	Yes, on blinded trial with remdesivir	Yes	Recovered
45/F/W ARA	No	No	abatacept	Yes	Lenabasum 20 mg BID continued; abatacept held	Symptomatic with fatigue, myalgia, and cough; evaluated in ER without receiving oxygen and discharged to home with self quarantine	No	No	Recovered
47/M/W ATA	Yes by HRCT (77%)	No	MMF	Yes	Lenabasum 20mg BID continued; MMF held	Asymptomatic tested for positive contact; treated with home self-quarantine	Hydroxychloroquine	No	Asymptomatic

Abbreviations: dcSSc (diffuse cutaneous systemic sclerosis), ATA (anti-topoisomerase-1 antibody), ARA (anti-RNA polymerase III), ILD (interstitial lung disease), CXR (chest X-ray), HRCT (high resolution computed tomography), M (male), F (female), W (white), MMF (mycophenolate mofetil), BID (twice daily)

gency room (ER), then discharged home with oxygen for a week with subsequent full recovery. One symptomatic had an ER visit without requiring oxygen therapy and another asymptomatic did not have an ER visit; both did not require hospitalization and were self-quarantined.

Conclusion: The rate of confirmed COVID-19 infections (0.11%) in this cohort of dcSSc patients is about the same as the rate estimated from CDC data of June 5, 2020, adjusted for age (~0.1%). This suggests the diffuse cutaneous SSc subjects in this cohort are not more vulnerable to COVID-19 infection than the general population. All 4 trial participants despite 2 with confirmed ILD had acceptable outcomes, in the context of continued or resumed lenabasum treatments.

1. Ann Rheum Dis. 2020;79(5):668-669.
2. Avouac J, Airó P, Carlier N, et al. Ann Rheum Dis. 2020 Epub ahead of print.
3. ACR COVID-19 Global Rheumatology Alliance Registry https://rheum-covid.org/
4. EULAR COVID-19 Database https://www.eular.org/eular_covid19_database.cfm

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Disclosure: R. Domsic, Formation Biologics, 5, Eicos Sciences, Inc, 5, Corbus Pharmaceutical Holdings, 5; **L. Chung**, Eicos, 1, Reata, 1, Boehringer Ingelheim, 1, 2, Mitsubishi Tanabe, 1; **J. Molitor**, Corbus Pharmaceuticals Inc., 2, EICOS, 5, Pfizer, 2; **R. Spiera**, Roche-Genentech, 1, 2, GlaxoSmithKline, 1, 2, Bristol-Myers Squibb, 1, Boehringer Ingelheim, 1, ChemoCentryx, 1, Corbus Pharmaceuticals, 1, Sanofi, 1, InflaRx, 1, Janssen, 1, Forbius, 1, 2; **B. Bloom**, Corbus Pharmaceuticals Inc., 3; **B. White**, Corbus Pharmaceuticals, Inc., 1, 2, 3, 4; **Q. Dinh**, Corbus Pharmaceuticals Inc., 3.

Abstract Number: 1380

Digital Occlusive Arterial Disease on Laser Doppler Flowmetry Increases the Risk of Digital Ischemic Complications in Systemic Sclerosis: Results from a Single Center Referral Cohort (2001-2018)

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Vascular dysfunction is a key feature of systemic sclerosis (SSc), manifesting clinically as Raynaud's phenomenon (RP) with or without digital ischemia. Laser doppler flowmetry (LDF) with thermal challenge is a safe, noninvasive and reproducible technique to detect digital occlusive arterial disease (DOAD) with a high sensitivity and specificity of >90% (1). The presence and associations of DOAD in SSc are not well defined. We studied the prevalence and clinical correlates of DOAD on LDF in SSc patients referred for evaluation of RP at a tertiary referral center.

Methods: Medical records of all SSc patients meeting ACR/EULAR 2013 classification criteria that underwent upper extremity vascular study with LDF between Jan 2001-Dec 2018 at our institution were retrospectively reviewed to abstract the presence or absence of DOAD. The presence of DOAD on LDF was confirmed if pre- and post-warming skin blood flow was ≤206 arbitrary units. Severity of DOAD was assessed based on number of digits involved. Demographics, clinical characteristics, and outcomes were abstracted. Risk factors associated with presence of DOAD in SSc and correlation between presence and severity of DOAD with digital ischemic complications were studied.

Results: 304 SSc patients (mean age 57.1 ± 13.3 y, 81% female, 93% Caucasian) underwent LDF during the study period. Majority had limited cutaneous SSc (lcSSc) (79.6%) and 64.1% had a positive SSc specific antibody. Cohort characteristics are described in **Table 1**.

On LDF, presence of DOAD was noted in 243 (79.9%) SSc patients. Of these, 78.6% had lcSSc, 42.4% had a centromere antibody (Ab), 17.3% had a Scl-70 Ab, 53.5% had interstitial lung disease, 36.6% had pulmonary arterial hypertension, and 73.3% had gastrointestinal dysmotility (GID). Of 159 DOAD patients who had their digital nailfold examined, 70.4% had nailfold capillary abnormalities. After adjusting for age/sex, GID (OR: 2.73, $p < 0.001$) and telangiectasia (OR: 2.83, p 0.013) were significantly associated with DOAD on LDF.

Digital ischemic complications among SSc patients with DOAD were significantly higher than among those without DOAD (79.8% vs 41.0% had digital ulcers, 53.9% vs 26.2% had pitting/scars, 31.3% vs 8.2% had gangrene/amputation; $p < 0.001$). (**Figure 1**) Increasing severity of DOAD was associated with a statistically significant increase in incidence of digital ischemic complications as presented in **Table 2**.

Conclusion: To our knowledge, this is the first and largest study to describe the prevalence and predictors of DOAD on LDF in a well-defined cohort of SSc patients. The high prevalence of DOAD on LDF noted in SSc related RP makes it an important tool for evaluation of microangiopathy in SSc and distinguishing it from primary RP. The presence

	Overall (N=304)	No DOAD (N=61)	DOAD (N=243)	p-value
Demographics				
Age at procedure (years)- Median (Q1, Q3)	58.5 (48.8, 67.0)	57.0 (50.0, 66.0)	59.0 (48.0, 67.0)	0.859
Sex (Female)	247 (81.2%)	55 (90.2%)	192 (79.0%)	**0.046**
Race (White)	282 (92.8%)	58 (95.1%)	224 (92.2%)	0.795
BMI (kg/m^2) at LDF	25.2 (22.2, 29.7)	25.1 (22.6, 29.2)	25.3 (22.0, 30.1)	0.852
Smoking status				0.176
Never	172 (56.6%)	39 (63.9%)	133 (54.7%)	
Former	113 (37.2%)	21 (34.4%)	92 (37.9%)	
Current	19 (6.2%)	1 (1.6%)	18 (7.4%)	
Disease characteristics				
SSc subtype:				0.386
Limited	242 (79.6%)	51 (83.6%)	191 (78.6%)	
Diffuse	62 (20.4%)	10 (16.4%)	52 (21.4%)	
SSc specific antibodies:	195 (64.1%)	39 (63.9%)	156 (64.2%)	0.969
Centromere	132 (43.4%)	29 (47.5%)	103 (42.4%)	0.479
Scl-70	50 (16.4%)	8 (13.1%)	42 (17.3%)	**0.020**
RNA-Polymerase	20 (6.6%)	3 (4.9%)	17 (7.0%)	0.098
Time from SSc diagnosis to LDF (months)- Median (Q1, Q3)	12.9 (3.0, 73.2)	6.3 (1.6, 26.6)	16.9 (3.2, 85.9)	**0.006**
Raynaud's phenomenon	303 (99.7%)	61 (100.0%)	242 (99.6%)	
Abnormal nailfold capillaries**	146 (68.9%)	34 (64.2%)	112 (70.4%)	0.392
Upper extremity large vessel disease***	81 (26.6%)	10 (16.4%)	71 (29.2%)	**0.043**
Telangiectasias	265 (87.2%)	49 (80.3%)	216 (88.9%)	0.078
Calcinosis	114 (37.5%)	18 (29.5%)	96 (39.5%)	0.324
Interstitial lung disease	164 (53.9%)	34 (55.7%)	130 (53.5%)	0.754
Pulmonary hypertension	105 (34.5%)	16 (26.2%)	89 (36.6%)	0.127
Gastrointestinal dysmotility	209 (68.8%)	31 (50.8%)	178 (73.3%)	**< 0.001**
Renal crisis	18 (5.9%)	4 (6.6%)	14 (5.8%)	0.814
Medications				
Calcium channel blockers	234 (77.0%)	42 (68.9%)	192 (79.0%)	0.092
Endothelin receptor antagonists	45 (14.8%)	1 (1.6%)	44 (18.1%)	**0.001**
Phosphodiesterase inhibitors	98 (32.2%)	8 (13.1%)	90 (37.0%)	**< 0.001**
Prostacyclin/Prostaglandin-I_2	15 (4.9%)	0 (0.0%)	15 (6.2%)	**0.047**
Aspirin	208 (68.4%)	39 (63.9%)	169 (69.5%)	0.399
Alpha-blockers	99 (32.6%)	23 (37.7%)	76 (31.3%)	0.338
Statins	103 (33.9%)	18 (29.5%)	85 (35.0%)	0.420
Pentoxifylline (Trental)	25 (8.2%)	5 (8.2%)	20 (8.2%)	0.993
Angiotensin receptor blockers	45 (14.8%)	4 (6.6%)	41 (16.9%)	**0.043**
Topical nitroglycerine	33 (10.9%)	3 (4.9%)	30 (12.3%)	0.095
Botox injections	9 (3.0%)	0 (0.0%)	9 (3.7%)	0.127
Sympathectomy	22 (7.2%)	1 (1.6%)	21 (8.6%)	0.059
Comorbidities				
Hypertension	149 (49.0%)	29 (47.5%)	120 (49.4%)	0.797
Hypercholesterolemia	125 (41.1%)	25 (41.0%)	100 (41.2%)	0.981
Diabetes mellitus	22 (7.2%)	3 (4.9%)	19 (7.8%)	0.434
Coronary artery disease	54 (17.8%)	7 (11.5%)	47 (19.3%)	0.151
Digital ischemic complications	234 (77.0%)	27 (44.3%)	207 (85.2%)	**< 0.001**
Digital ulcer	219 (72.0%)	25 (41.0%)	194 (79.8%)	**< 0.001**
Digital tip pitting/scars	147 (48.4%)	16 (26.2%)	131 (53.9%)	**< 0.001**
Digital gangrene/amputation	81 (26.6%)	5 (8.2%)	76 (31.3%)	**< 0.001**

*Baseline characteristics were compared using Chi-square, Fisher exact or rank-sum tests.

**92 of 304 patients did not have a nailfold capillary examination documented.

***Diagnosis was based on vascular studies and physician diagnosis.

Table 1. Clinical Characteristics of 304 Systemic Sclerosis (SSc) Patients that Underwent Laser Doppler Flowmetry (LDF) with Thermal Challenge (2001-2018) Overall and by Presence or Absence of Digital Occlusive Arterial Disease (DOAD)*

and severity of DOAD also correlates with digital ischemic complications. Our study underscores the significance of LDF as a reliable non-invasive method for detecting DOAD and as a prognostic tool to identify patients at risk of

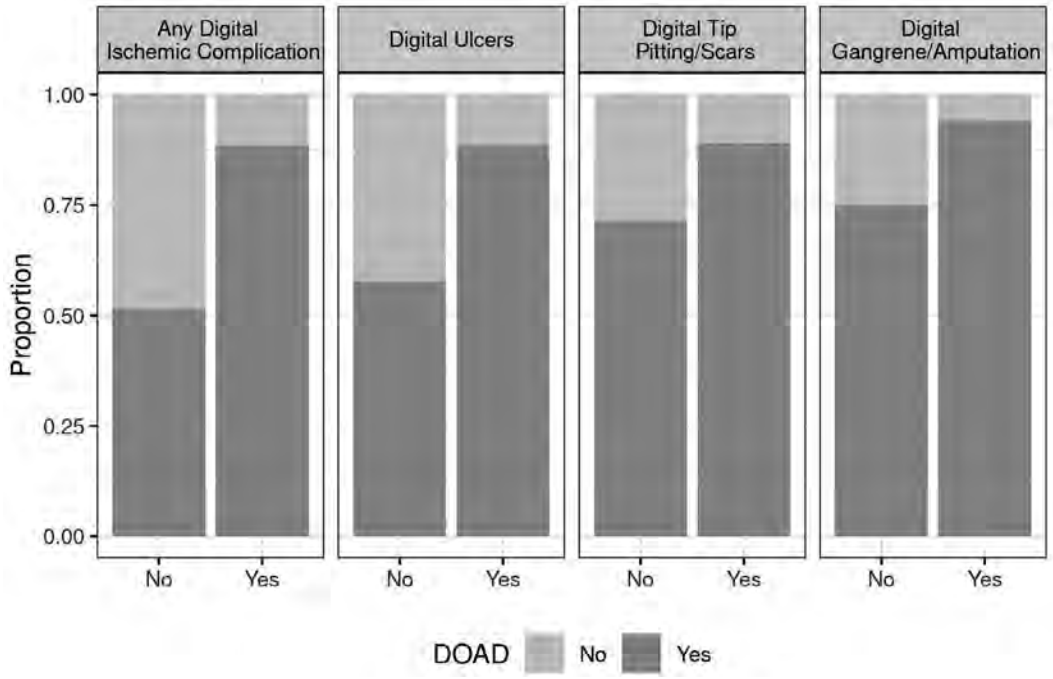

Figure 1. Correlation between Presence of Digital Occlusive Arterial Disease (DOAD) on Laser Doppler Flowmetry and Digital Ischemic Complications in Systemic Sclerosis

Digital Ischemic Complication	Severity (Digits) Modeled As:	Odds Ratio (OR) Reflects	OR	CI 95%	p-value
Digital Ulcer	Integer	Unit Increase	1.28	1.19-1.39	< 0.001
	Categorical	1-2 vs. 0	2.11	0.927-4.92	0.078
		3-7 vs. 0	5.57	2.84-11.2	< 0.001
		8-10 vs. 0	10.9	4.98-25.4	< 0.001
Digital Tip Pitting/Scars	Integer	Unit Increase	1.17	1.10-1.26	< 0.001
	Categorical	1-2 vs. 0	1.92	0.803-4.61	0.142
		3-7 vs. 0	2.62	1.35-5.28	0.006
		8-10 vs. 0	5.45	2.72-11.4	< 0.001
Digital Gangrene/Amputation	Integer	Unit Increase	1.26	1.16-1.37	< 0.001
	Categorical	1-2 vs. 0	1.36	0.317-5.48	0.665
		3-7 vs. 0	4.10	1.62-12.6	0.006
		8-10 vs. 0	9.05	3.60-27.7	< 0.001
Any Digital Ischemic Complication	Integer	Unit Increase	1.35	1.24-1.49	< 0.001
	Categorical	1-2 vs. 0	2.98	1.27-7.30	0.014
		3-7 vs. 0	6.16	3.08-12.7	< 0.001
		8-10 vs. 0	18.5	7.46-53.2	< 0.001

Table 2. Logistic Regression Models for the Association of Digital Ischemic Complications and Severity of Digital Occlusive Arterial Disease (DOAD) on Laser Doppler Flowmetry with Thermal Challenge

digital ulcers that need closer follow-up and more aggressive management of their vasculopathy to prevent ischemic complications.

(1) Mahe G et al. J Vasc Surg. 2014 Apr;59(4):1051-1057.e1

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Abstract Number: 1381

Real-World Mono-, Double and Triple Combination Treatment Patterns with Macitentan in Patients with Pulmonary Arterial Hypertension Associated with Connective Tissue Disease (PAH-CTD): Evidence from the Combined OPUS/OrPHeUS Dataset

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with PAH-CTD have a worse prognosis than patients with most other PAH etiologies. The OPsumit® USers (OPUS) Registry and OPsumit® Historical USers (OrPHeUS) study provide real-world evidence on the management of PAH-CTD patients newly treated with macitentan.

Methods: OPUS is a prospective, US, multicenter, drug registry ongoing since April 2014 (NCT02126943). OrPHeUS was a retrospective, US, multicenter chart review (NCT03197688); data collected October 2013–March 2017. Patient characteristics, safety and clinical outcomes are described by treatment pattern (mono-/double/triple therapy) at macitentan initiation (baseline) for PAH-CTD (WHO Clinical Classifications of PH Group 1) patients in the combined OPUS/OrPHeUS population. PAH etiology was investigator-assessed and not adjudicated.

Results: As of August 2019, the follow-up OPUS/OrPHeUS PAH population (N=4387) included 1130 PAH-CTD patients: 433 (38.3%) received macitentan monotherapy, 536 (47.4%) received double and 161 (14.2%) received triple combination therapy at baseline. Median (Q1, Q3) age was 63 (53, 70) years in mono-, 61 (50, 70) in double and 61 (51, 69) in triple therapy patients; most patients were female. In the monotherapy group, more patients were newly-diagnosed; median (Q1, Q3) time from diagnosis was 2.2 (0.6, 18.0) months in mono-, 8.7 (1.8, 37.1) in double and 34.8 (12.5, 80.4) in triple therapy patients. Of patients with WHO functional class (FC) recorded at baseline (49.2–57.3% of patients), 63.4% of mono-, 72.6% of double, and 68.2% of triple therapy patients were FC III/IV. Median (Q1, Q3) baseline 6-minute walk distance (reported in 32.1-40.7% of patients) was 274 (161, 366), 270 (194, 347), and 305 (226, 362) m in mono-, double and triple therapy patients. Treatment patterns at month 6 are shown in the Figure. Patients with ≥1 hepatic adverse event included 28 (6.5%), 36 (6.7%) and 21 (13.0%) on mono-, double and triple therapy. Macitentan was discontinued in 146/433 (33.7%) mono-, 188/536 (35.1%) double and 80/161 (49.7%) triple therapy patients: 59 (13.6%), 80 (14.9%) and 39 (24.2%) due to an adverse event. Kaplan-Meier (KM) estimates (95% CI) for mono-, double and triple therapy patients at macitentan initiation showed that 69% (64, 74), 62% (57, 66) and 61% (52, 69) of patients were free from hospitalization at 12 months; 12-month KM survival estimates (95% CI) were 94% (90, 96), 90% (87, 93) and 88% (81, 92).

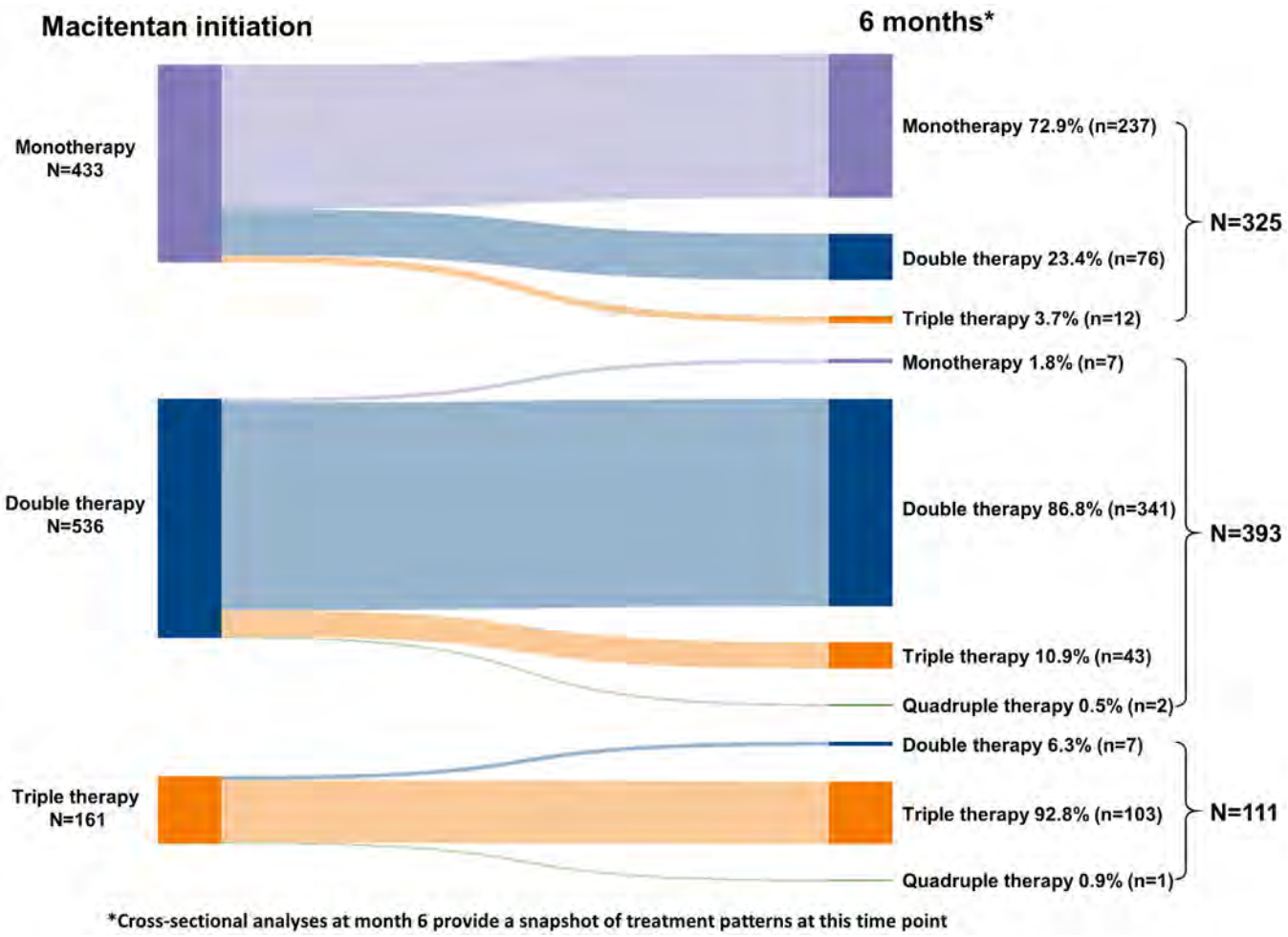

Figure. Treatment patterns at month 6

Conclusion: Despite the recommendation for combination therapy, a large proportion of patients received monotherapy at macitentan initiation and 6 months after initiation. For the vast majority of patients, combination treatment strategy did not change between baseline and 6 months.

Disclosure: M. Lammi, None; **K. Chin**, Actelion Pharmaceuticals Ltd, 2, 5, 8, United Therapeutics, 2, 5, 8, Ironwood Pharmaceuticals, 2, Bayer Healthcare (through UCSD), 5, Gossamer Bio, 8, American Heart Association, 6; **N. Kim**, Actelion Pharmaceuticals Ltd, 2, 5, 8, Bellerophen, 2, Eiger, 2, SoniVie, 2, Gilead, 2, Lung Biotechnology, 2, Gossamer, 2, Bayer Healthcare, 5, 8, Arena Pharmaceuticals, 5, 8, Merck, 5, United Therapeutics, 5; **V. McLaughlin**, Actelion Pharmaceuticals Ltd, 2, 5, 8, Acceleron, 2, 5, Bayer Healthcare, 2, 5, United Therapeutics, 2, 5, Reata Pharmaceutics, 2, SoniVie, 2, Arena Pharmaceuticals, 5, Caremark, 5, CiVi Biopharma, 5; **R. Zamanian**, Actelion Pharmaceuticals Ltd, 2, United Therapeutics, 2, Vivus, 5, Pfizer, 5, Selten, 5, Genentech, 1, 4, Morphogenic-IX, 8, FK-506 in PAH, 9; **M. Flynn**, Actelion Pharmaceuticals Ltd, 1, 3, 4; **S. Leroy**, Actelion Pharmaceuticals Ltd, 1, 3, 4; **R. Ong**, Actelion Pharmaceuticals Ltd, 3; **G. Wetherill**, Actelion Pharmaceuticals Ltd, 3; **R. Channick**, Actelion Pharmaceuticals Ltd,, 2, 5, 8, United Therapeutics, 2, Bayer Healthcare, 5, 8, Arena Pharmaceuticals, 5.

Abstract Number: 1382

Changes in Imaging Markers in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD) Treated with Nintedanib: Sub-Study of the SENSCIS Trial

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
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Background/Purpose: In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 44% compared with placebo. The effects of nintedanib on markers of lung damage on high-resolution computed tomography (HRCT) were assessed in a sub-study.

Methods: Patients enrolled in the SENSCIS trial had SSc with onset of first non-Raynaud symptom ≤7 years before screening and an extent of fibrotic ILD ≥10% on HRCT (based on assessment of the whole lung). Patients were randomized to receive nintedanib or placebo. In a sub-study, HRCT images were assessed at baseline and at week 52 or 60. The extent of regions with evidence of abnormalities (honeycombing and/or reticulation and/or ground-glass opacity) was assessed in both lungs and changes from baseline were categorized by two radiologists as “much better”, “better”, “same”, “worse”, “much worse” or “unknown”. Disagreement between the radiologists in the categories “much better” or “better” and “worse” or “much worse” were considered “intermediate better” or “intermediate worse”. An ordinal logistic regression analysis (proportional odds model) adjusted for anti-topoisomerase antibody I status was used to compare changes between the treatment groups. Changes from baseline in a quantitative fibrosis score, a measure of the extent (%) of reticular patterns with architectural distortion, were assessed using data-driven texture analysis. Analyses were conducted in patients who received trial medication up to at least week 24 and had an evaluable HRCT scan at week 52/60.

Results: Of 576 patients who participated in the SENSCIS trial, 150 participated in the HRCT sub-study (nintedanib 73, placebo 77). The rate of decline in FVC over 52 weeks was similar in the overall trial population and in patients who participated in the HRCT sub-study (Figure). Compared with the placebo group (n=59), a lower proportion of patients in the nintedanib group (n=52) had a worsening in qualitative parameters (i.e., “worse”, “intermediate worse”, or “much worse”) from baseline to week 52–60 (40.4% vs 45.8%) (Table). Ordinal logistic regression analysis demonstrated a numerically greater risk of worsening in qualitative parameters in the placebo group compared with the nintedanib group (OR 1.24 [95% CI: 0.63, 2.47]; p=0.53). Adjusted mean (SE) changes from baseline in quantitative fibrosis score were 2.50 (0.88) % in the nintedanib group (n=23) and 2.80 (0.73) % in the placebo group (n=31) (difference: –0.31% [95% CI: –2.36, 1.75]; p=0.77).

Figure. Rate of decline in FVC (mL/year) over 52 weeks in the overall SENSCIS trial population and in the HRCT sub-study

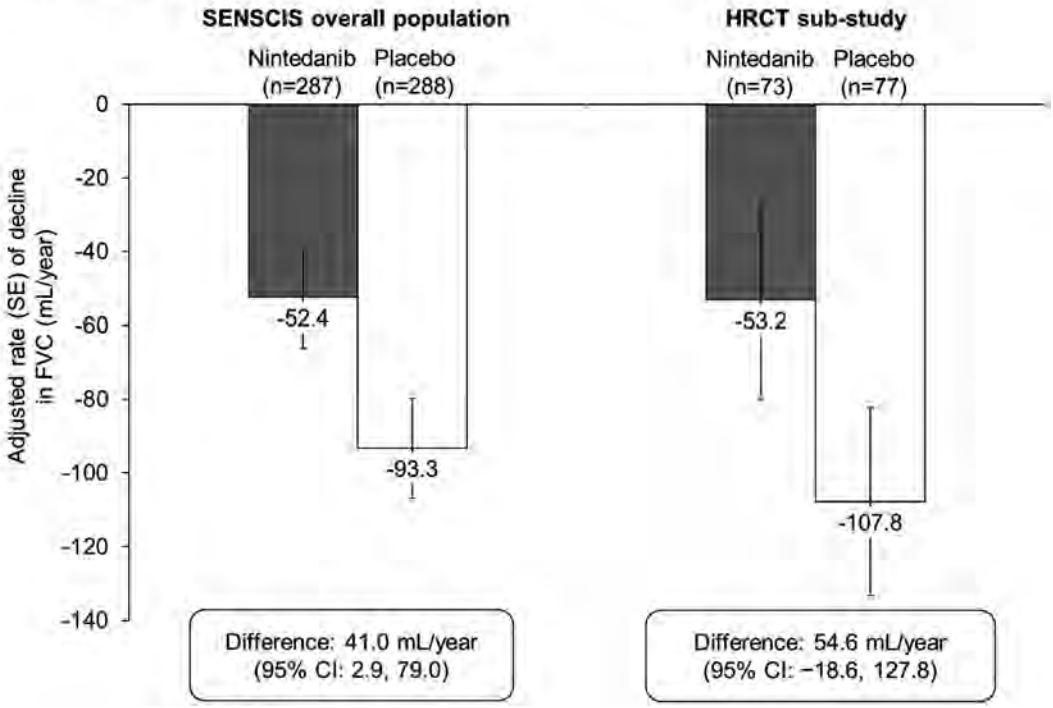

Table. Changes from baseline in the extent of regions with evidence of abnormalities (honeycombing and/or reticulation and/or ground-glass opacity) based on qualitative HRCT review

	Nintedanib (n=52)	**Placebo (n=59)**
Much better	0	0
Intermediate better	2 (3.8)	1 (1.7)
Better	7 (13.5)	8 (13.6)
Same	22 (42.3)	23 (39.0)
Worse	15 (28.8)	17 (28.8)
Intermediate worse	3 (5.8)	6 (10.2)
Much worse	3 (5.8)	4 (6.8)

Data are n (%) of patients with an evaluable HRCT scan. "Much better" = moderate decrease in honeycombing and/or reticulation and/or fibrotic ground glass opacity (GGO); decrease was >10%, as visually estimated. "Better" = definite but mild decrease in honeycombing and/or reticulation and/or fibrotic GGO; decrease was ≤10%, as visually estimated; decrease in extent of fibrosis, including change from fibrotic GGO to pure GGO, was considered improvement. "Same" = no change in honeycombing and/or reticulation and/or fibrotic GGO. "Worse" = definite but mild increase in honeycombing and/or reticulation and/or fibrotic GGO; increase was ≤10%, as visually estimated; increase in extent of fibrosis, including change from pure GGO to fibrotic GGO, was considered, worsening. "Much worse" = at least a moderate increase in honeycombing and/or reticulation and/or fibrotic GGO; increase was >10%, as visually estimated. Intermediate better" = the two radiologists disagreed between the categories "much better" and "better". "Intermediate worse" = the two radiologists disagreed between "worse" and "much worse".

Conclusion: In a sub-study of the SENSCIS trial, qualitative and quantitative changes on HRCT over 52–60 weeks were small. Numerical but non-significant trends towards less worsening were observed in patients treated with nintedanib versus placebo. These analyses were limited by the small number of patients who had an evaluable HRCT scan at the follow-up visit.

Disclosure: S. Humphries, Boehringer Ingelheim, 5, Veracyte, 2, Imidex LLC, 5; **E. Hachulla**, Boehringer Ingelheim, 5, Actelion Pharmaceuticals, 5, Roche, 5, Chugai, 5; **M. Hamblin**, Boehringer Ingelheim, 2, 8, Genentech, 2, 8, Biogen, 2, FibroGen, 2, Galapagos, 2, Galecto, 2, Promedior, 2, Mallinckrodt Pharmaceuticals, 2; **T. Ogura**, Boehringer Ingelheim, 6, 8, Eisai Co., Ltd, 8, Shionogi & Co., Ltd, 8; **D. Wormanns**, Boehringer Ingelheim, 5, Roche, 5, 8, GE Healthcare, 8; **C. Ittrich**, Boehringer Ingelheim, 3; **F. Risse**, Boehringer Ingelheim, 3; **M. Alves**, Boehringer Ingelheim, 3; **M. Gahlemann**, Boehringer Ingelheim, 1; **D. Lynch**, Boehringer Ingelheim, 5, Parexel, 5, Veracyte, 5, Daiichi Sankyo, 5.

Abstract Number: 1383

Tocilizumab Shows Potential in Preserving Lung Function in Systemic Sclerosis with Positive anti-topoisomerase-1 (Scl-70): A Single Centre Cohort Study

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Background/Purpose: Recent Phase II (faSScinate) and Phase III (focuSSced) clinical trials of tocilizumab versus placebo in early dcSSc highlighted the potential impact of tocilizumab on lung function with preservation of forced vital capacity (FVC) in those treated with tocilizumab, despite only a trend of benefit for skin fibrosis. Tocilizumab is approved for SSc patients with inflammatory arthritis overlap and has been used in this context at our centre. We report here our experience of tocilizumab in SSc and the impact on lung function.

Methods: In our retrospective study, all SSc patients attending our centre who had ever been on tocilizumab were identified. Most of these patients had overlap inflammatory arthritis. Patients who had participated in the faSScinate trial were excluded, whilst those receiving tocilizumab on a compassionate basis following the phase 3 focuSSced trial were included. Statistical analysis was carried out using the Mann-Whitney-U test.

Results: Of the 32 patients identified, 68.8% (n = 22) were classified as diffuse SSc and 75% (n = 24) patients were female. The most common autoantibodies were ATA (anti-topoisomerase antibody) (34.3%) and ARA (anti-RNA polymerase-III antibody) (18.8%). 46.9% (n = 17) patients had known interstitial lung disease. 6 patients received tocilizumab on a compassionate basis following completion of the open label phase of the focuSSced clinical trial, the remainder had overlap inflammatory arthritis. Mean age of disease onset was 38.6 years, and the median disease duration to tocilizumab initiation was 7.9 years. 11 patients discontinued tocilizumab: 6 due to cessation of the compassionate use access, 2 due to side effects, 3 due to lack of benefit.

75% (n = 24) patients had serial lung function data to compare FVC and DLCO before and after initiation of treatment. Baseline FVC prior to tocilizumab was 3.09L (sd = 0.98) or 91% predicted (sd = 19.7). Baseline DLCO prior to tocilizumab was 5.55ml/min/mmHg (sd = 2.21) or 61.1% predicted (sd = 17). Median duration on tocilizumab was 7 months (IQR =9.5). To standardise results, the yearly change rate in FVC and DLCO was calculated. Median change in % predicted FVC was -1.5% (IQR=10.7) and median change in % predicted DLCO was -0.5% (IQR=6.1). Subgroup analysis revealed a significant difference between autoantibody groups and change in FVC while on tocilizumab. It was notable that there was an increase in median change in FVC in patients with ATA antibody (3.27%, IQR=13.55) whereas there was a decrease in median change in FVC in all other autoantibody groups (-4.7%, IQR=11.1, p = 0.0019). There was a near significant difference in change in DLCO between these antibodies at 12 months (-2.6%, IQR = 4.7, p = 0.056) in favour of improvement in ATA subgroup.

Conclusion: Our findings support potential benefit for lung function in SSc patients on tocilizumab compared to placebo particularly in those with the ATA, and this is consistent with previous trial results. Presence of ATA confers a higher risk of extensive lung fibrosis in SSc, regardless of extent of skin involvement, and so early identification of these cases and use of tocilizumab may prevent development of clinically meaningful lung fibrosis and improve long-term outcome.

Disclosure: Y. Suleman, None; **K. Clark**, None; **S. Nihtyanova**, GlaxoSmithKline, 3; **V. Ong**, None; **C. Denton**, Janssen, 1, GlaxoSmithKline, 1, 2, Bayer, 1, Sanofi, 1, Inventiva, 1, 2, Boehringer Ingelheim, 1, Roche, 1, Bristol-Myers Squibb, 1, CSL Behring, 1, 2, UCB, 1, Leadiant Biosciences, 1, Corbus Pharmaceuticals, 1, Acceleron Pharma, 1, Horizon Therapeutics, 1, Forbius, 1, Servier, 1.

Abstract Number: 1384

Usage, Needs and Preferences Regarding Physical Therapy in Patients with Systemic Sclerosis

Sophie Liem[1], Nina van Leeuwen[2], Thea Vliet Vlieland[3], Lian de Pundert[4], Rita Schriemer[5], Julia Spierings[6], Madelon Vonk[7] and Jeska de Vries-Bouwstra[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]LUMC, Leiden, Netherlands, [3]Leiden University Medical Center, 2300 RC Leiden, Netherlands, [4]HAGA Hospital, The Hague, Netherlands, [5]NVLE, Utrecht, [6]University Medical Center Utrecht, Maastricht, Netherlands, [7]Department of Rheumatology, Radboud University Medical Center, Nijmegen, The Netherlands, Nijmegen, Netherlands

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Background/Purpose: The importance of non-pharmacologic interventions in systemic sclerosis (SSc) is increasingly recognized. Physical therapy is among the most frequently used interventions, but knowledge on its actual provision in daily practice and patients' perspectives on its delivery is absent. Therefore this study aimed to assess among patients with SSc the usage, contents, satisfaction, needs and preferences regarding the provision of physical therapy.

Methods: Four hundred and five SSc patients, fulfilling the ACR/EULAR 2013 criteria for SSc and participating in the multidisciplinary SSc care pathway of the Leiden University Medical Center were invited. They are seen by a physical therapist at the yearly assessment related to the care pathway, if treatment is needed they are referred to primary care. Between July-August 2019 they received a pen-and-paper questionnaire consisting of 39 questions regarding usage of physical therapy over the past two years (thirteen multiple-choice questions), contents (five multiple-choice

Table 1. Characteristics of the included systemic sclerosis patients (n=204)			
	Total (n=204)	**PT-group (n=127)**	**No-PT-group (n=77)**
Sociodemographic characteristics			
Age, years, median (IQR)	63 (55 – 71)	65 (57 – 71)	60 (51 – 70)
Female, n (%)	165 (81%)	106 (84%)	59 (77%)
Smoking: *Currently*, n (%)	21 (10%)	15 (12%)	6 (8%)
Former, n (%)	80 (39%)	53 (42%)	27 (35%)
Body Mass Index, kg/m^2, mean (SD)	25 (5)	25 (5)	25 (4)
Duration of non-Raynaud's phenomenon, years, median (IQR)	9 (5 – 15)	10 (5 – 16)	9 (5 – 12)
Clinical characteristics			
Type of SSc, limited, n (%)	136 (67%)	83 (66%)	53 (70%)
Modified Rodnan Skin Score, median (range)	3 (0 – 34)	2 (0 – 34)	3 (0 – 16)
Anti-Scl-70, n (%)	38 (21%)	19 (17%)	19 (27%)
Anti-centromere, n (%)	83 (46%)	58 (53%)	25 (35%)
DLCO, mean (SD)	63 (28)	62 (34)	66 (16)
FVC, median (IQR)	97 (86 – 110)	98 (86 – 110)	95 (85 – 110)
Interstitial lung disease according HRCT, n (%)	80 (39%)	44 (35%)	36 (47%)
Interstitial lung disease according to HRCT and FVC<70	13 (6%)	8 (6%)	5 (7%)
Pulmonary arterial hypertension, n (%)	13 (6%)	8 (6%)	5 (7%)
Six minute walk test: *Total distance meters*, median (IQR)	511 (432 – 600)	492 (417 – 588)	557 (457 – 612)
Decreased ejection fraction, n (%)^	14 (7%)	6 (5%)	8 (10%)
Renal crisis, n (%)	5 (3%)	5 (4%)	0
Proximal muscular weakness, n (%)	5 (3%)	5 (4%)	0
Immunotherapy current, n (%)^^	76 (37%)	47 (37%)	29 (38%)

IQR: interquartile range; n: number; SD: standard deviation

SSc: systemic sclerosis; DLCO: diffuse capacity for carbon monoxide, percentage of predicted; FVC: forced vital capacity, percentage of predicted.

PT-group: patients who have received PT in the past two years; No-PT-group: patients who did not receive PT in the past two years

^Decreased ejection fraction was defined as <54.

^^Immunotherapy included corticosteroids, methotrexate, cyclophosphamide, hydroxychloroquine, azathioprine and mycophenolic acid.

Table 1. Characteristics of the included systemic sclerosis patients (n=204)

questions), satisfaction (eight questions, 0-10 scale-based, multi-response, open field), and needs and preferences (thirteen questions, dichotomous, multi-response, open field).

Results: In total, 204 SSc patients (median age: 63 years, 80% female) were included (Table 1). Over the past two years, 62% (n=127) patients received physical therapy (PT-group; 94% in the primary care setting), whereas 38% (n=77) did not (No-PT-group). Regarding active treatment modalities, muscle strengthening (n=91, 71%), range of motion (n=88, 69%) and aerobic exercises (n=72, 56%) were most frequently mentioned (Table 2). Concerning passive modalities, 46% (n=59) of patients received massage and 16% (n=21) kinesiotaping. Twenty percent of patients reported SSc specific treatments including hand (n=20, 16%) and mouth (n=7, 6%) exercises. Thirty-one percent (n=40) of the patients were encouraged to spend time on physical activity at home. Seventy percent (n=142) of all

Table 2. Contents of physical therapy as reported by the systemic sclerosis patients (n=127)	
Active modalities	Number (percentages)
Aerobic exercises	72 (56%)
Muscle strengthening exercises	91 (71%)
Range of motion exercises	88 (69%)
Hand function exercises	20 (16%)
Mouth exercises	7 (6%)
Swallow exercises	1 (1%)
Balance exercises	55 (43%)
Passive modalities	
Relaxation exercises	10 (8%)
Massage	59 (46%)
Heat therapy	2 (2%)
Cold therapy	1 (1%)
Electrical therapy	7 (5%)
Dry needling	8 (6%)
Kinesiotaping	21 (16%)
Hydro therapy	7 (6%)
General	
Physical activity promotion	40 (31%)
Exercises to perform at home	100 (78%)
This table shows the contents of the received physical therapy as reported by the patients with systemic sclerosis who went to a physical therapist.	

Table 2. Contents of physical therapy as reported by the systemic sclerosis patients (n=127)

included patients indicated physical therapy as a valuable part of the standardized Care Pathway at the Leiden University Medical Center. Of the total group, 47% (n=96) patients preferred to receive more information regarding physical therapy and 63% (n=128) to continue/(re)start physical therapy in the near future, favoring individual continuous therapy (n=50/128, 39%) by physical therapist close to home (n=61/128, 48%). Eighty percent (n=163) stated that specific knowledge on systemic sclerosis and/or rheumatic diseases is necessary for physical therapists to treat systemic sclerosis patients.

Conclusion: Sixty-two percent of systemic sclerosis patients received physical therapy in a period of two years mostly consisting of active treatment.The use of passive treatment modalities and hand and mouth exercises was highly variable. Although all patients are seen once-yearly by a physical therapist in a multidisciplinary care pathway, more than half expressed an unmet need regarding physical therapy. These results could help improve content and patient education regarding physical therapy for SSc.

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Abstract Number: 1385

Physical Therapy in Patients with Systemic Sclerosis: The Perspective of Physical Therapists on Current Delivery and Educational Needs

Sophie Liem[1], Nina van Leeuwen[2], Thea Vliet Vlieland[3], Lian de Pundert[4], Rita Schriemer[5], Julia Spierings[6], Madelon Vonk[7] and Jeska de Vries-Bouwstra[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]LUMC, Leiden, Netherlands, [3]Leiden University Medical Center, 2300 RC Leiden, Netherlands, [4]HAGA Hospital, The Hague, Netherlands, [5]NVLE, Utrecht, [6]University Medical Center Utrecht, Maastricht, Netherlands, [7]Department of Rheumatology, Radboud University Medical Center, Nijmegen, The Netherlands, Nijmegen, Netherlands

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Background/Purpose: As there is currently no cure available for systemic sclerosis (SSc), nonpharmacologic care is an essential element in the management of the disease. Physical therapy is often used by SSc patients, but evidence on its optimal content is scarce and practice highly variable. To improve the delivery of care perspectives of the health care professional are crucial. Therefore, this study aimed to assess the perspectives of physical therapists treating patients with SSc on their current practice and educational needs regarding physical therapy.

Methods: SSc patients who participated in a cross-sectional study on the use of physical therapy were asked to invite their treating physical therapist, if applicable, to complete a questionnaire. The questionnaire consisted of 37 questions regarding sociodemographic information (thirteen questions), the content of treatment employed (eight questions), perceived knowledge and skills (four questions) and educational needs (twelve questions). The survey consisted of dichotomous- (yes/no) or multiple-choice questions, and multiple-answer options.

Results: In total, 127 patients reported the use of physical therapy over the past two years, and 48 physical therapists returned the questionnaire. Their median age was 44 years, 52% was female and 50% had more than 20 years of working experience. The median number of SSc patients currently treated was 1 (range: 1 – 4). Eighty-three percent (n=44) of physical therapists received a referral, of whom two-third (n=30/44) from a rheumatologist. Seventy percent (n=32/44) stated a perceived lack of medical information concerning the patient's disease manifestations in the referral letter. Range of motion (n=42, 88%), muscle strengthening (n=41, 85%) and aerobic (n=34, 71%) exercises were most often reported, followed by hand (n=20, 42%) and mouth (n=5, 10%) exercises. Concerning passive modalities, massage (n=24, 50%) and relaxation exercises (n=21, 44%) were performed most frequently. Thirty-five percent (n=11) indicated that a lack of knowledge on SSc was a problem during the treatment, meanwhile 98% (n=47) had tried to get more information on the disease; Google (n=32/47, 67%), asking the patient (n=25/47, 52%) or Pubmed (n=19/47, 40%) were the most frequently mentioned sources of information. Eighty-five percent (n=41) expressed the need for an interactive website with information on treatment of SSc patients specifically designed for physical therapists and 77% (n=37) for additional courses on SSc, with online delivery preferred by most of them (n=28/37, 76%).

Conclusion: The large majority of physical therapists treating patients with systemic sclerosis used active treatment modalities, but passive modalities were also relatively frequent. Additionally, more than 75% expressed an unmet need regarding information and education on systemic sclerosis. The development of such educational activities could be a starting point to optimize the content and quality of physical therapy and therefore could contribute to improvement of quality of multidisciplinary care in systemic sclerosis.

Table 1. Characteristics of included physical therapists (n=48)	
Sociodemographic characteristics	
Age, years, median (interquartile range)	44 (35 – 58)
Female, n (%)	25 (52%)
Health professional	
• Physical therapist, n (%)	43 (90%)
• Mensendieck therapist, n (%)	3 (6%)
• Cesar therapist, n (%)	2 (4%)
Work setting	
• Primary care, n (%)	46 (96%)
• Secondary care, n (%)	2 (4%)
Work experience	
• 0 – 10 years, n (%)	14 (29%)
• 11 – 20 years, n (%)	10 (21%)
• >20 years, n (%)	24 (50%)
Attended a course on rheumatic diseases, n (%)	23 (48%)
• National organization for health care professionals, n	18
• Local organization for health care professionals, n	7
• International organization for health care professionals, n	3
• Other, n	5
Member of a professional organization for health care professionals, n (%)	15 (31%)
• Dutch health care professionals organization for rheumatology (NPHR), n	5
• Dutch Patient Organization for Systemic Autoimmune Diseases (NVLE), n	0
• Dutch Society of Rheumatology (ReumaNederland) , n	10
• Local rheumatic network, n	7
Sub specialty*, n (%)	21 (49%)
• None, n	8
• Manual therapy, n	8
• Oncology/oedema therapy, n	7
• Company related, n	1
• Sport, n	2
• Psychosomatic, n	3
Caseload	
Total number of patients treating, median number (range):	
• SSc patients, currently	1 (1 - 4)
• SSc patients, in past two years	1 (1 - 3)
• Other rheumatic diseases, currently	4 (1 - 30)
*Only applicable for physical therapists.	
n: number; SSc: systemic sclerosis	

Table 1. Characteristics of included physical therapists (n=48)

Table 2. Contents of provided physical therapy as reported by physical therapists (n=48)	
Active modalities	Number (percentages)
Aerobic exercises	34 (71%)
Muscle strengthening exercises	41 (85%)
Range of motion exercises	42 (88%)
Hand function exercises	20 (42%)
Mouth exercises	5 (10%)
Swallow exercises	2 (4%)
Balance exercises	32 (67%)
Passive modalities	
Relaxation exercises	21 (44%)
Massage	24 (50%)
Heat therapy	2 (4%)
Cold therapy	0
Electrical therapy	3 (6%)
Dry needling	0
Kinesiotaping	8 (17%)
Hydro therapy	3 (6%)
General	
Physical activity promotion	25 (52%)
Exercises to perform at home	42 (88%)
Information provision	
Oral information	46 (96%)
Oral and paper information	18 (39%)
Paper information	2 (4%)
This table shows the reported content by physical therapists of the current delivered physical therapy to patients with systemic sclerosis.	

Table 2. Contents of provided physical therapy as reported by physical therapists (n=48)

Disclosure: S. Liem, None; **N. van Leeuwen**, None; **T. Vliet Vlieland**, None; **L. de Pundert**, None; **R. Schriemer**, None; **J. Spierings**, None; **M. Vonk**, Actelion Pharmaceuticals, 1, 2, 3, Boehringer Ingelheim, 1, 2, Roche, 1, 2, GlaxoSmithKline, 1, 2, Ferrer, 1; **J. de Vries-Bouwstra**, None.

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Clinical Correlates and Relevance of the UCLA GIT 2.0 Instrument for Indication for Esophagogastroduodenoscopy and Endoscopic Esophagitis in Real-life Patients with Systemic Sclerosis

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Table 1. Factors associated with referral to EGD

	Univariable random effects models			*Multivariable random effects models*			
Parameters	**OR**	**CI 95%**	**p**	**Models**	**OR**	**CI 95%**	**p**
Age	1.00	0.99 – 1.01	0.759	All models	0.99	0.97 – 1.01	0.269
Sex	0.64	0.38 – 1.05	0.078		0.66	0.33 – 1.33	0.242
Disease duration	1.01	0.99 – 1.02	0.454		1.00	0.98 – 1.02	0.926
SSc subset	1.00	0.66 – 1.51	1.000		1.27	0.67 – 2.40	0.471
mRSS	1.04	1.01 – 1.07	**0.005**		1.05	1.00 – 1.10	**0.030**
Hemoglobin	0.91	0.79 – 1.04	0.165		0.89	0.74 – 1.07	0.218
Proton pump inhibitor therapy	0.77	0.55 – 1.09	0.137		0.80	0.49 – 1.30	0.363
Body mass index	1.01	0.96 – 1.05	0.780		1.03	0.97 – 1.09	0.294
Forced vital capacity	1.00	0.99 – 1.01	0.630		1.00	0.99 – 1.01	0.948
Erythrocyte sedimentation rate	1.01	1.00 – 1.02	0.126		1.00	0.99 – 1.02	0.943
Heartburn	3.68	2.60 – 5.21	**<0.001**	Model 1	2.23	1.35 – 3.69	**0.002**
Regurgitation	2.51	1.64 – 3.84	**<0.001**		2.09	1.14 – 3.81	**0.017**
Dysphagia	3.38	2.34 – 4.89	**<0.001**		3.01	1.79 – 5.05	**<0.001**
Esophageal symptoms	3.24	2.19 – 4.78	**<0.001**	Model 2	1.91	1.14 – 3.18	**0.013**
Stomach symptoms	2.95	2.02 – 4.29	**<0.001**		2.12	1.24 – 3.61	**0.006**
UCLA GIT 2.0 reflux subscale	1.91	1.42 – 2.56	**<0.001**	Model 3	1.86	1.19 – 2.90	**0.006**
UCLA GIT 2.0 distention/bloating	1.51	1.23 – 1.87	**<0.001**	Model 4	1.50	1.12 – 2.01	**0.007**
UCLA GIT 2.0 social functioning	2.19	1.56 – 3.07	**<0.001**	Model 5	2.57	1.56 – 4.23	**<0.001**
UCLA GIT 2.0 emotional wellbeing	1.39	1.00 – 1.93	0.050	Model 6	1.32	0.80 – 2.19	0.274
UCLA GIT 2.0 total score	2.20	1.50 – 3.23	**<0.001**	Model 7	2.16	1.21 – 3.83	**0.009**

Table 1. Factors associated with referral to EGD

Background/Purpose: Gastrointestinal (GI) tract involvement is the most common of all internal organ involvement in systemic sclerosis (SSc). The University of California at Los Angeles, Scleroderma Clinical Trial Consortium, Gastrointestinal Tract Instrument 2.0 (UCLA GIT 2.0) is validated to capture GI morbidity in patients with SSc (1). However, the routine clinical investigation of GI involvement in these patients is not standardized and there is no consensus about when and how frequently an esophago-gastro-duodenoscopy (EGD) should be performed.

The aims of this study were to determine in an unselected, real-life cohort of patients with SSc, 1) if the UCLA GIT 2.0 could discriminate patients for whom a rheumatologist with experience in SSc would recommend an EGD, and 2) if the UCLA GIT 2.0 could identify patients with endoscopic esophagitis.

Methods: We selected patients fulfilling the ACR/EULAR 2013 criteria for SSc from the Zurich EUSTAR cohort, having completed at least once the UCLA GIT 2.0 questionnaire at an EUSTAR visit. We reviewed the medical charts of the selected patients from 2013 to 2019 and recorded data on EGD performed in an interval of ±3 months from a

Table 2. Factors associated with endoscopic esophagitis

	Univariable random effects models			*Multivariable random effects models*			
Parameters	**OR**	**CI 95%**	**p**	**Models**	**OR**	**CI 95%**	**p**
Age	0.98	0.95 – 1.00	0.076	All models	0.98	0.96 – 1.01	0.289
Sex	1.04	0.44 – 2.45	0.934		0.89	0.34 – 2.31	0.803
Disease duration	1.00	0.97 – 1.03	0.944		1.00	0.96 – 1.03	0.925
Proton pump inhibitor therapy	0.63	0.31 – 1.29	0.204		0.50	0.21 – 1.23	0.133
mRSS	1.09	1.03 – 1.15	0.001	Model 1	1.11	1.04 – 1.18	0.003
Hemoglobin	1.36	1.06 – 1.73	**0.015**	Model 2	1.33	1.00 – 1.77	0.051
Heartburn	1.78	0.87 – 3.62	0.113	Model 3	1.71	0.76 – 3.83	0.193
Regurgitation	1.38	0.63 – 3.03	0.418		1.43	0.59 – 3.46	0.433
Dysphagia	0.94	0.47 – 1.89	0.872		1.01	0.46 – 2.18	0.987
Esophageal symptoms	3.15	1.24 – 8.03	**0.016**	Model 4	3.25	1.00 – 10.54	**0.049**
Stomach symptoms	1.64	0.78 – 3.45	0.190		1.43	0.57 – 3.60	0.443
UCLA GIT 2.0 reflux subscale	1.07	0.59 – 1.94	0.816	Model 5	1.17	0.60 – 2.26	0.644
UCLA GIT 2.0 distention/bloating	0.63	0.39 – 1.01	0.054	Model 6	0.69	0.43 – 1.12	0.135
UCLA GIT 2.0 social functioning	0.65	0.31 – 1.35	0.245	Model 7	0.70	0.33 – 1.50	0.362
UCLA GIT 2.0 emotional wellbeing	0.77	0.36 – 1.62	0.484	Model 8	0.91	0.43 – 1.95	0.810
UCLA GIT 2.0 total score	0.67	0.28 – 1.60	0.367	Model 9	0.82	0.33 – 2.02	0.659

Table 2. Factors associated with endoscopic esophagitis

EUSTAR visit. We analyzed by general linear mixed effect models (GLMM) several parameters, including UCLA GIT 2.0 and its subscales, considered as potentially associated with 1) the referral to EGD and 2) endoscopic esophagitis.

Results: We identified 346 patients (82.7% female, median age 63 years, median disease duration 10 years, 23% with diffuse cutaneous SSc) satisfying the inclusion criteria, who filled in 940 UCLA GIT 2.0 questionnaires.

For the first objective, we excluded 31/940 visits because EGD was done shortly (< 3 months) before the EUSTAR visit. In the 909 remaining visits, EGD was recommended by the expert rheumatologists in 128 cases. The UCLA GIT 2.0 total score and some of its subscales (reflux, distention/bloating, social functioning score), but also the modified Rodnan skin score (mRSS) and esophageal and stomach symptoms by medical history were associated with the referral to EGD (Table 1).

For the second objective, we identified 177 EGD performed in 145 patients. In GLMM, esophageal symptoms and, to a lesser extent, mRSS, correlated with endoscopic esophagitis, while neither the total ULCA GIT 2.0 score nor any of its subscales showed any association with this finding (Table 2).

Conclusion: In a real-life setting, UCLA GIT 2.0 subscales (reflux, distention/bloating, social functioning) and total score strongly associated with expert interpretation of gastroesophageal symptoms and consecutive referral to EGD.

However, they showed no correlation with esophagitis on EGD. The main clinical association of esophagitis was the presence of esophageal symptoms.

Reference

(1) Khanna D, et al. Reliability and validity of the University of California, Los Angeles Scleroderma Clinical Trial Consortium Gastrointestinal Tract Instrument. Arthritis Rheum. 2009;61(9):1257-63.

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Abstract Number: 1387

Should Systemic Sclerosis Patients with Low Bicarbonate Have Replacement to Prevent Renal Dysfunction?

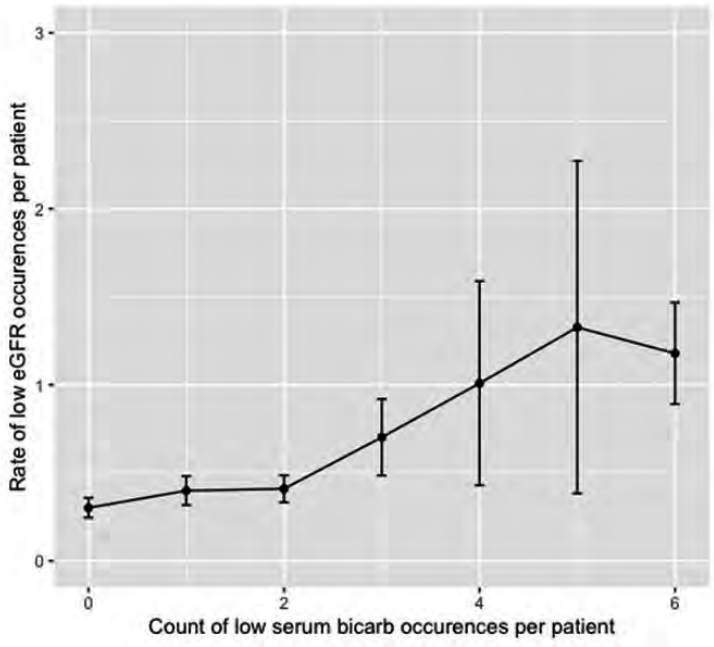
Megan Meier[1], Jacob Stever[2], Josephine Wright[1], Tracy Frech[3], Greg Stoddard[1] and Benjamin Tingey[1], [1]University of Utah, Salt Lake City, [2]University of Utah, SANDY, [3]University of Utah and Salt Lake Veterans Affair Medical Center, Salt Lake City, UT

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Scleroderma renal crisis (SRC) is a well-characterized condition in patients with systemic sclerosis, but systemic sclerosis patients frequently develop chronic kidney disease (CKD) without prior evidence of SRC. Retrospective analyses have shown that low serum bicarbonate predicts kidney failure and death in the general population. This study investigates the potential association of low serum bicarbonate levels (< 22 mmol/L) and the development of reduced kidney function in patients with SSc.

Methods: This was a retrospective cohort study comprised of patients with limited or systemic sclerosis (SSc) by 2013 ACR/EULAR criteria. Patients were recruited for participation from the University of Utah SSc Clinic from October, 2012 to March, 2017. Index and follow up bicarbonate levels and associated eGFR values were recorded. A serum bicarbonate level < 22 mmol/L and an eGFR < 60 ml/min/1.73m^2 were considered low values for the purposes of this study. Patients with normal versus low serum bicarbonate levels at index date were followed and compared longitudinally during the study period for the development of kidney dysfunction, manifested by low eGFR. A zero-inflated Poisson (ZIP) regressions model was applied to estimate the rate of predicted low eGFR labs associated with low serum bicarbonate occurrences per patient.

Figure 1. Rate of predicted low eGFR by low serum bicarbonate



The rate of predicted low eGFR occurrences, with error bars, plotted against the count of low serum-bicarbonate occurrences per patient .

Results: 143 patients met inclusion requirements for evaluation and had normal kidney function determined by eGFR at index date. In this SSc cohort, with each one count increase in low serum-bicarbonate labs, the rate of low eGFR labs increased (aIRR: 1.21; 95% CI: 1.05-1.40). This was a significant increase with P=0.01.

Conclusion: In a single center SSc cohort, low serial serum bicarbonate was associated with increased rates of reduced kidney function. Awareness of this association provides a means to screen for higher risk SSc patients and potentially intervene, given the reduction in morbidity and mortality seen with bicarbonate supplementation in patients with CKD in the general population.

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Abstract Number: 1388

A Systematic Assessment of Demographics, Clinical and Serological Features Associated with Colonic Hypomotility in Systemic Sclerosis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Colonic dysmotility affects up to 50% of patients with systemic sclerosis (SSc). While some patients have mild colonic disease, others experience severe complications, such as recurrent pseudo-obstruction and the requirement of total parenteral nutrition. Nevertheless, the clinical phenotype of patients with colonic hypomotility is not well-defined. We sought to identify the demographic, clinical, and serologic features that distinguish SSc patients with and without colonic hypomotility.

Methods: Patients with gastrointestinal (GI) symptoms from our Center who met SSc criteria were prospectively enrolled and underwent a scintigraphy-based whole gut transit (WGT) study. Eighty percent met 2013 ACR/EULAR criteria, 2% met ACR 1980 criteria, and 18% met CREST criteria. We performed a cross sectional analysis comparing

Table 1. Characteristics of the SSc patients with and without colonic hypomotility by WGT study in the Johns Hopkins Scleroderma Center cohort

Clinical and demographic features	Colonic Hypomotility (n=48)	No colonic hypomotility (n=52)	p-value
Age at first symptoms, mean (SD)	58.8 (10.8)	56.0 (12.5)	0.23
Disease duration from first SSc-associated symptom (Raynaud's or non-Raynaud's) to date of WGT study, median (IQR)	12.1 (8.0, 18.3)	11.6 (5.6, 23.7)	0.92
Female sex, % (n)	98 (47)	80 (43)	**<0.01†**
Race/Ethnicity			
White, % (n)	83 (39)	74 (39)	0.34
Ever smoker, % (n)	43 (20)	23 (11)	**0.04†**
SSc Type			
Limited cutaneous disease, % (n)	71 (32)	71 (36)	1.00
Severe GI disease, (≥3), %(n)	27 (12)	9 (4)	**0.03†**
Cardiac involvement (≥1), % (n)	6 (2)	11 (4)	0.67
Myopathy, % (n)	14 (6)	13 (6)	1.00
Sicca symptoms, % (n)	75 (33)	70 (33)	0.60
Raynaud's severity (≥2), % (n)	45 (20)	33 (15)	0.28
Lung involvement (≥1), % (n)	22 (8)	37 (13)	0.20
Cancer, % (n)	27 (12)	20 (9)	0.45
Telangiectasias, % (n)	89 (40)	67 (32)	**0.01†**
Dead, % (n)	2 (1)	4 (2)	0.62
Pulmonary function parameters			
FVC, % predicted, median (IQR)	81.5 (73.5, 89.5)	72.9 (64.3, 81.5)	0.14
DLCO, % predicted, median (IQR)	68.1 (61.3, 74.9)	58.1 (47.7, 68.6)	0.10
RVSP by echo (mmHg), median (IQR)	30 (25, 35)	34.5 (28, 36)	0.53
Antibodies, % (n)			
Scl-70 (i.e. Topoisomerase-1)	10.8 (4)	19.0 (7)	0.52
Centromere (CENP)	57.9 (22)	30.6 (11)	**0.02†**
RNA polymerase-3	0.0 (0)	7.1 (2)	0.21
U3RNP	2.9 (1)	2.9 (1)	1.00
Ku	2.6 (1)	5.6 (2)	0.61
PMScl	2.8 (1)	10 (3)	0.32

† statistically significant

GI = gastrointestinal; GI involvement = maximum Medsger GI severity score ≥3; Cardiac involvement = maximum Medsger cardiac severity score ≥ 1; Lung involvement = maximum Medsger cardiac severity score ≥ 1; FVC = forced vital capacity; DLCO = diffusing capacity of carbon monoxide; RSVP = estimated right ventricular systolic pressure by echocardiogram.

Table 1. Characteristics of the SSc patients with and without colonic hypomotility by WGT study in the Johns Hopkins Scleroderma Center cohort

demographic, clinical, and serologic features between SSc patients with and without colonic hypomotility by WGT. Clinical features were characterized using maximum severity scores recorded in the database. Univariate logistic regression was used to examine associations with colonic hypomotility. Multivariable models were then constructed using significant variables from the univariate analysis and potential confounders to determine whether the associations remained.

Results: One hundred patients with GI symptoms were enrolled and underwent WGT studies. Forty-eight percent had colonic hypomotility (i.e. < 67% colonic emptying by 72 hours of WGT study). Patients with colonic hypomotility were more likely to be female (98% vs. 80%; p< 0.01), have ever smoked (43% vs. 23%; p=0.04), have anti-centromere (CENP) autoantibodies (58% vs. 31%; p=0.02), have telangiectasias (89% vs. 67%; p = 0.01), and have a maximum Medsger GI Severity Score ≥3 (27% vs. 9%; p=0.03) compared to those without colonic hypomotility. Our univariate analyses found female sex [odd's ratio (OR)=12.02, 95% confidence interval (CI) 1.49-97.00; p=0.02], an-

Table 2. Cross-sectional univariate model evaluating the association between clinical, demographic, serologic features and colonic hypomotility in patients with SSc

Clinical and demographic features	Odds Ratio	95% Confidence Interval	p-value
Age at first symptom	1.02	0.99-1.05	0.23
Disease duration from first SSc-associated symptom (Raynaud's or non-Raynaud's) to date of WGT study	0.99	0.96-1.03	0.95
Female sex	12.02	1.49-97.00	**0.02†**
Race/Ethnicity			
White	1.75	0.66-4.64	0.26
Ever smoker	2.56	1.06-6.20	**0.04†**
SSc Type			
Limited cutaneous disease	1.02	0.42-2.47	0.96
Severe GI disease (≥3)	3.94	1.16-13.3	**0.03†**
Cardiac involvement (≥1)	0.47	0.08-2.74	0.40
Myopathy	1.08	0.32-3.66	0.90
Sicca symptoms	1.27	0.50-3.21	0.61
Raynaud's severity (≥2)	1.72	0.73-4.05	0.21
Lung involvement (≥1)	0.48	0.17-1.37	0.17
Pulmonary fibrosis	0.42	0.18-0.99	**0.05†**
Telangiectasias	4.00	1.32-12.00	**0.01†**
Calcinosis	0.87	0.34-2.00	0.77
Cancer	1.46	0.54-3.90	0.45
Dead	0.48	0.04-5.46	0.55
Pulmonary function parameters			
FVC‡	0.23	0.09-0.63	**<0.01†**
DLCO‡	0.42	0.16-1.00	0.07
RVSP by echo (mmHg)	0.97	0.88-1.07	0.55
Antibodies			
Scl70 (i.e. Topoisomerase-1)	0.52	0.14-1.95	0.33
Centromere (CENP)	3.13	1.20-8.14	**0.02†**
RNA polymerase-3	Omitted		
U3RNP	0.97	0.06-16.10	0.98
PmScl	0.26	0.03-2.61	0.25

† statistically significant

‡ Based on minimum value across all visits

GI = gastrointestinal; GI involvement = maximum Medsger GI severity score ≥3; Cardiac involvement = maximum Medsger cardiac severity score ≥ 1; Lung involvement = maximum Medsger cardiac severity score ≥ 1; FVC = forced vital capacity; DLCO = diffusing capacity of carbon monoxide; RSVP = estimated right ventricular systolic pressure by echocardiogram.

Table 2. Cross-sectional univariate model evaluating the association between clinical, demographic, serologic features and colonic hypomotility in patients with SSc

Table 3. Multivariable model evaluating the association between clinical, demographic, and serological features and colonic hypomotility after adjusting for significant covariates from the univariate analysis.			
Covariate	Odds Ratio	95% Confidence Interval	p-value
Age at first symptom	1.02	0.96-1.09	0.53
Disease duration from first SSc-associated symptom (Raynaud's or non-Raynaud's) to date of WGT study	0.98	0.92-1.04	0.52
Female	50.06	2.59-968.37	**0.01†**
Ever smoker	3.88	0.75-20.11	0.11
GI involvement (≥3)	7.64	0.72-80.94	0.09
Telangiectasias	5.72	0.88-37.33	0.07
FVC‡	0.17	0.03-0.87	**0.03†**
Anti-centromere (CENP) autoantibody	0.88	0.17-4.45	0.88

† statistically significant

‡ Based on minimum value across all visits

GI = gastrointestinal; GI involvement = maximum Medsger GI severity score ≥3; FVC = forced vital capacity.

Table 3. Multivariable model evaluating the association between clinical, demographic, and serological features and colonic hypomotility after adjusting for significant covariates from the univariate analysis.

ti-CENP autoantibodies (OR=3.13, 95%CI 1.20-8.14; p=0.02), telangiectasias (OR=4.00, 95%CI 1.32-12.00; p=0.01), and smoking (OR=2.56, 95%CI 1.06-6.20; p=0.04) to be significantly associated with colonic hypomotility. Patients with colonic hypomotility were less likely to have signs of pulmonary fibrosis, defined as crackles on exam or a chest X-ray/chest CT suggesting fibrosis (OR=0.42, 95%CI 0.18-0.99; p=0.05), and a low FVC (OR=0.23, 95%CI 0.09-0.63; p< 0.01). After adjusting for significant covariates from the univariate analysis and potential confounders, our multivariable model determined that female sex (OR=50.06, 95%CI 2.59-968.37; p=0.01) remained strongly associated with colonic hypomotility, and confirmed that patients with colonic hypomotility were less likely to have a low FVC (OR=0.17, 95% CI0.03-0.87; p=0.03).

Conclusion: Distinct clinical features such as female sex, anti-CENP autoantibodies, telangiectasias, and smoking associated with colonic hypomotility. Our study also suggested that patients with colonic hypomotility were less likely to have restrictive lung disease. The identification of these features can inform the diagnostic evaluation and study of disease mechanism in SSc patients with colonic hypomotility.

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Abstract Number: 1389

Clinical Characteristics and Treatment Outcome of a Cohort of Patients with Joint and Fascial Involvement in the Context of Chronic Graft versus Host Disease

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic graft-vs-host disease (cGVHD) is a major late complication of allogeneic hematopoietic stem cell transplantation (alloHSCT), typically occurring within three years post-transplant and affecting approx-

TABLE 1. BASELINE AND TRANSPLANT RELATED CHARACTERISTICS (N = 28)

VARIABLES	N (%)
Donor Type (related / unrelated)	13(46.4%)/15(53.6%)
Type of conditioning reduced intensity / myeloablative	18(64.25%)/10(35.7%)
Source of cells : peripheral blood / bone marrow	27(96.4%/1(3.6%)
cGVHD type quiescent / de novo / progressive	11(39.3%)/13(46.4%)/4(14.3%)
Other affected organs : -Mouth -Eyes -Lung -Liver -Gastrointestinal tract -Genital -Cutaneous	 6(21.4%) 10(35.7%) 2(7.1%) 3(10.7%) 0(0%) 2(7.1%) 16(57.14%)
Global Score at enrolment: NIH[1] (mild / moderate / severe)	5(17,8%)/9(32,1%)/14(50%)

[1] NIH: National Institute of Health

TABLE 2. CLINICAL MANIFESTATIONS AND THERAPIES (N = 28)

VARIABLES	N (%)/MEDIAN (RANGE)
Prodromic symptoms: yes / no	20(71%)/8(29%)
- Stiffness - Artromyalgia - Edema	2(7.1%) 17(60.7%) 3(10.7%)
Time until first visit	31.3 months (range 9-73)
Contracture Yes / No	18(64.3%)/10(35.7%)
Mobility limitation (mild / moderate)	13(46.4%)/9(32.1%)
ECOG[1] affected	11(39.2%)
Eosinophilia	17(60.7%)
Positive autoantibodies	8(28.5%)
First line therapies (corticosteroids)	28(100%)
Extracorporeal photoapheresis	19(67.9%)
Therapies of 2nd line/ 3rd or more	6(21.4%)/12 (42.8%)
Physiotherapy	14 (50%)
Response: complete / sequels	10(35.7%)/18(64.2%)

[1]ECOG: Eastern Cooperative Oncology Group scale to assess the quality of life

imately 30%-50% of allogeneic transplant survivors. Although cGVHD can involve many organ systems, joint and fascial involvement is relatively common, little known and can cause significant functional impairment.

Describe the clinical/transplant related characteristics, the therapeutic management and the clinical outcome of a cohort of patients with joint and fascial involvement in the context of cGVHD.

Methods: Observational and retrospective study to describe the clinical characteristics of 28 patients affected by joint and fascial cGVHD. The usual demographic variables, the transplant reason disease, the type of transplant,laboratory parameters, rescue therapies and their response were collected. The statistical analysis was done with Microsoft Excel 2007.

Results: Seventeen (60.7%) patients were male and 11 (39.35%) were women with a mean age of 48.75 years (range from 10 to 74). Acute myeloid leukemia was the most frequent cause of the transplant in 11 patients (39.3%)

Transplant related characteristics are reflected in Table 1 and the clinical manifestations, therapies received and their response in Table 2.. Eighteen (64,3%) presented irreversible contracture due to sclerosis that negatively impacts their quality of life and physical function (11/39%).

Four (14.2%) patients died during their follow-up, being the cause of death in 2 cases due to sepsis, in 1 case due to leukemia relapse and in 1 case attributable to cGVHD.

Conclusion: Nonspecific joint symptoms such as stiffness, edema or arthromyalgia may be factors that predict the development of joint/fascial involvement in cGVHD.

They should be closely monitored in order to be able to perform early stage diagnoses and implementation of proper treatment, including rehabilitation, in order to restore function and improve the quality of life of these patients.

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Abstract Number: 1390

Outcomes of Systemic Sclerosis Patients Who Were Primarily Admitted for Acute Myocardial Infarction from 2016 to 2017: Insights from the National Inpatient Sample

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Several systemic autoimmune rheumatic diseases have been shown to increase coronary artery disease (CAD) risk, notable rheumatoid arthritis and systemic lupus erythematosus. However, data on the risk of systemic sclerosis (SSc) and CAD is unclear. Although not a common finding, some studies have shown an increased prevalence of CAD in SSc patients. This has been attributed to the underlying vascular abnormalities. Other studies have failed to show a significant difference in the prevalence of CAD compared to the general population. The primary

Demographics and Outcomes of AMI hospitalizations in patients with and without Scleroderma in 2016-2017

Demographics/Outcomes	Scleroderma	No Scleroderma	P-value
Age (Mean) (Year)	66.7	66.9	0.786
Female (%)	82	37	<0.001
Caucasian (%)	71	73	0.540
Teaching Hospital (%)	74	66	0.013
Charlson Comorbidity Index ≥3 (%)	75	51	<0.001
Length of Stay (Mean) (Day)	5.3	4.4	0.038
Inpatient Mortality (%)	9.17	4.68	0.001

aim of this study was to assess the outcomes of SSc patients who were primarily hospitalized for acute myocardial infarction (AMI) from a nationally representative sample.

Methods: We used data from the National Inpatient Sample (NIS) for the period of 2016 to 2017 for adult AMI hospitalizations as a primary diagnosis and systemic sclerosis as a secondary diagnosis using ICD-10 codes. The proportion who met ACR classification criteria and disease activity status cannot be determined within the NIS database. We used STATA 15 for the data analysis and multivariate logistic regression to calculate the adjusted odds ratios for inpatient mortality in AMI hospitalizations.

Results: We identified a total of 1,305,889 AMI hospitalizations between 2016 and 2017 of which 1,145 (0.08%) had a diagnosis of SSc. Compared to the non-SSc group, patients with SSc were predominantly female (82.1% vs. 37.9%; p< 0.001). There was no statistically significant difference in the age between two groups of patients.

Compared to non-SSc hospitalizations with AMI, SSc hospitalizations had a higher unadjusted inpatient mortality rate (9.17% vs. 4.68%; p=0.001). After adjusting for gender, age, race, household income, hospital location, hospital teaching status, hospital bed size and Charlson Comorbidity Index, the odds ratio (OR) for hospital mortality due to AMI in SSC patients was higher and statistically significant (aOR=2.02; 95% CI= 1.28-3.19; p=0.002) compared to the non-SSc group. Length of stay was significantly longer in patients with SSc (5.3 vs 4.4 days; p=0.038).

Conclusion: In our study, unadjusted and adjusted inpatient mortality in SSc patients primarily hospitalized for AMI was higher than non-SSc patients with an adjusted odds ratio of 2.02. This finding indicates that patients with SSc may have worse outcomes for cardiovascular events when admitted for AMI. Further study in optimizing cardiovascular risk factors in SSc patients is paramount in order to minimize their cardiac morbidity and mortality.

Disclosure: A. Vafa, None; **O. Behnamfar**, None; **Y. Lin**, None.

Abstract Number: 1391

Associations Between Autoantibodies in Systemic Sclerosis and Cancer in a National Registry

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SESSION INFORMATION
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Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
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Background/Purpose: Autoantibodies are useful in systemic sclerosis (SSc) for predicting disease course. Some autoantibodies have been associated with a close temporal relationship with cancer. We investigated the association between SSc-specific and SSc-associated autoantibodies and cancer in a national registry.

Methods: Subjects recruited between 2004 and 2019 in a national SSc registry were studied (96% fulfill 2013 ACR/EULAR SSc classification criteria). The exposure was presence of SSc-specific/associated autoantibodies, namely anti-centromere (ACA), -topoisomerase I (ATA), -RNA polymerase 3 (ARNAP), -fibrillarin, -Th/To, -PM-Scl, -Ku,

Table 1. Baseline characteristics for all subjects and stratified by autoantibodies

	Total (n=1698)	Missing (%)	ACA (n=559/ 1431)	ATA (n=223/ 1431)	ARNAP (n=202/ 1431)	Anti-Ro52 (n=370/ 1431)	Anti-PmScl-75/100 (n=60/1431)	Anti-Nor90 (n=30/1431)	Anti-Th/To (n=17/1431)	Anti-Ku (n=14/1431)	Anti-Fibrillarin (n=8/1431)	Anti-U1RNP (n=75/1163)	Anti-BicD2 (n=121/490)	Anti-RNPC3 protein (n=17/297)
Age, years	55.3 (12.3)	<1%	57.6 (11.7)	51.1 (13.7)	55.7 (10.9)	56.9 (11.7)	54.9 (12.2)	54.0 (13.5)	58.1 (10.5)	54.2 (12.6)	50.3 (13.6)	50.0 (12.4)	56.1 (10.8)	55.5 (15.5)
Female	1469 (87%)	0%	515 (92%)	188 (84%)	164 (81%)	324 (88%)	51 (85%)	25 (83%)	15 (88%)	11 (79%)	6 (75%)	69 (92%)	105 (87%)	14 (82%)
White	1227 (79%)	8%	422 (81%)	139 (67%)	154 (79%)	271 (77%)	44 (81%)	22 (76%)	12 (75%)	4 (36%)	4 (50%)	56 (81%)	98 (88%)	11 (65%)
Smoking (ever)	919 (59%)	8%	305 (58%)	103 (49%)	126 (64%)	203 (57%)	29 (54)	17 (59%)	13 (76%)	4 (36%)	6 (75%)	44 (64%)	66 (60%)	7 (41%)
Disease duration, years	9.7 (9.2)	2%	10.8 (9.3)	7.9 (8.4)	7.4 (8.0)	10.5 (9.3)	11.1 (10.5)	11.3 (9.9)	8.7 (7.3)	9.6 (9.5)	2.9 (2.3)	12.3 (9.6)	10.6 (8.9)	14.8 (13.2)
Diffuse	608 (36%)	2%	89 (16%)	111 (50%)	158 (79%)	135 (37%)	19 (32%)	12 (40%)	5 (29%)	5 (36%)	5 (62%)	24 (32%)	30 (25%)	6 (35%)
mRSS	9.7 (9.5)	4%	6.6 (7.1)	12.1 (9.1)	17.7 (11.5)	9.6 (8.8)	8.3 (9.0)	10.8 (8.8)	7.1 (6.7)	9.5 (10.5)	19.0 (15.3)	8.0 (8.1)	6.9 (7.2)	8.7 (6.7)
Interstitial lung disease	502 (31%)	3%	94 (17%)	114 (52%)	69 (34%)	143 (39%)	18 (31%)	16 (53%)	8 (47%)	9 (69%)	0 (0%)	27 (37%)	28 (24%)	5 (29%)
Pulmonary hypertension	146 (10%)	16%	63 (13%)	12 (6%)	18 (10%)	50 (15%)	6 (12%)	3 (11%)	3 (20%)	2 (22%)	2 (29%)	7 (11%)	10 (9%)	3 (18%)
Myositis	168 (10%)	2%	26 (5%)	22 (10%)	21 (10%)	42 (11%)	12 (20%)	5 (17%)	2 (12%)	3 (21%)	1 (12%)	14 (19%)	13 (11%)	2 (12%)
Arthritis	501 (31%)	5%	142 (26%)	75 (35%)	56 (29%)	139 (38%)	22 (37%)	14 (50%)	5 (29%)	5 (38%)	2 (29%)	40 (56%)	37 (31%)	7 (44%)
Calcinosis	415 (25%)	2%	154 (28%)	56 (25%)	57 (28%)	96 (26%)	26 (44%)	11 (37%)	3 (18%)	3 (21%)	2 (25%)	17 (23%)	34 (28%)	5 (29%)
Telangiectasia	1204 (74%)	4%	430 (78%)	145 (68%)	140 (73%)	281 (80%)	44 (76%)	19 (63%)	11 (73%)	10 (77%)	6 (75%)	47 (66%)	93 (77%)	11 (65%)
Digital ulcers	829 (50%)	2%	278 (50%)	138 (62%)	105 (53%)	200 (54%)	36 (61%)	22 (73%)	10 (59%)	8 (57%)	3 (38%)	35 (47%)	60 (50%)	14 (82%)
GERD	1046 (70%)	13%	374 (74%)	138 (67%)	132 (69%)	224 (65%)	29 (54%)	19 (68%)	8 (53%)	7 (70%)	7 (88%)	56 (81%)	81 (73%)	12 (71%)
Dysphagia	791 (53%)	13%	290 (57%)	98 (47%)	95 (50%)	186 (55%)	26(49%)	15 (54%)	9 (60%)	5 (50%)	3 (38%)	43 (62%)	60 (54%)	6 (35%)
Antibiotics for SIBO	108 (7%)	3%	34 (6%)	10 (5%)	19 (10%)	28 (8%)	3 (5%)	0 (0%)	0 (0%)	1 (8%)	0 (0%)	3 (4%)	5 (4%)	1 (6%)
Scleroderma renal crisis	60 (4%)	3%	1 (1%)	6 (3%)	32 (16%)	12 (3%)	4 (7%)	3 (10%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (1%)	2 (12%)

For continuous variables: mean (standard deviation). For categorical variables: n (%). Autoantibodies include single-specificity and overlapping autoantibodies.
Abbreviations: ACA: anti-centromere antibodies; ARNAP: anti-RNA polymerase III antibodies; ATA: anti-topoisomerase I antibodies; GERD: gastroesophageal reflux disease; mRSS: modified Rodnan skin score; SIBO: small intestinal bacterial overgrowth

Table 1. Baseline characteristics for all subjects and stratified by autoantibodies

Table 2. Time interval between cancer diagnosis and systemic sclerosis onset in all subjects and stratified by autoantibodies

	Total	ACA	ATA	ARNAP	Anti-Ro52	Anti-PmScl-75/100	Anti-Nor90	Anti-Th/To	Anti-Ku	Anti-Fibrillarin	Anti-U1RNP	Anti-BicD2	Anti-RNPC3 protein
Cancer among all SSc subjects	231/1698 (13.6%)	84/559 (15.0%)	25/223 (11.2%)	30/202 (14.9%)	59/370 (16.0%)	13/60 (21.7%)	6/30 (20%)	2/17 (11.8%)	2/14 (14.3%)	1/8 (12.5%)	11/75 (14.7%)	21/121 (17.4%)	1/17 (5.9%)
Absolute interval between disease onset and first cancer diagnosis, years	10.0 (4.3-17.2)	10.2 (4.6-18.8)	13.5 (3.8-19.9)	7.8 (4.5-14.5)	9.0 (3.6-14.6)	14.0 (9.3-26.4)	7.0 (5.3-12.6)	11.1 (8.0-14.2)	14.7 (13.7-15.7)	2.3 (–)	10.2 (1.9-16.1)	10.9 (6.1-15.0)	29.8 (–)
Cancer diagnosis within 2 years among cancer subjects	27/207 (13.6%)	6/74 (8.1%)	5/20 (25%)	4/28 (14.3%)	5/54 (9.3%)	1/13 (7.7%)	0/5 (0%)	0/2 (0%)	0/2 (0%)	0/1 (0%)	3/10 (30%)	2/19 (10.5%)	0/1 (0%)
Cancer diagnosis within 2 years among all SSc subjects	1.8%	1.2%	2.8%	2.1%	1.5%	1.7%	0%	0%	0%	0%	4.4%	1.8%	0%
Cancer diagnosis within 3 years among cancer subjects	37/207 (17.9%)	11/74 (14.9%)	5/20 (25%)	6/28 (21.4%)	10/54 (18.5%)	1/13 (7.7%)	0/5 (0%)	0/2 (0%)	0/2 (0%)	1/1 (100%)	3/10 (30%)	4/19 (21.1%)	0/1 (0%)
Cancer diagnosis within 3 years among all SSc subjects	2.4%	2.2%	2.8%	3.2%	3.0%	1.7%	0%	0%	0%	12.5%	4.4%	3.7%	0%
Cancer diagnosis within 5 years among cancer subjects	58/207 (28.0%)	21/74 (28.4%)	6/20 (30%)	8/28 (28.6%)	18/54 (33.3%)	3/13 (23.1%)	1/5 (20%)	1/2 (50%)	0/2 (0%)	1/1 (100%)	4/10 (40%)	4/19 (21.1%)	0/1 (0%)
Cancer diagnosis within 5 years among all SSc subjects	3.8%	4.3%	3.4%	4.3%	5.3%	5.0%	4%	5.9%	0%	12.5%	5.9%	3.7%	0%

Abbreviations: ACA: anti-centromere antibodies; ARNAP: anti-RNA polymerase III antibodies; ATA: anti-topoisomerase I antibodies; SSc: systemic sclerosis.
For continuous variables: median (interquartile range). For categorical variables: n (%). Autoantibodies include single-specificity and overlapping autoantibodies.
Disease onset is defined as time of first non-Raynaud disease manifestation of systemic sclerosis.

Table 2. Time interval between cancer diagnosis and systemic sclerosis onset in all subjects and stratified by autoantibodies

-U1RNP, -NOR90, -Ro52, -RNPC3 and -BICD2. The primary outcome was cancer-associated SSc, defined as cancer occurring within 2, 3 and 5 years of first non-Raynaud SSc manifestation. Univariate logistic regression was used to compare the odds of cancer-associated SSc between the autoantibody subgroups, using anti-centromere as reference. Descriptive statistics were used to compare clinical characteristics of subjects with cancer to those without cancer.

Results: Out of 1698 SSc subjects, 1474 (86.8%) had at least partially available autoantibody data. Mean (SD) age was 55.3 (12.3) years, 87% were female and 59% had a smoking history. Table 1 shows baseline characteristics

Table 3. Univariate logistic regression analyses for the risk of cancer within 2, 3 and 5 years of systemic sclerosis onset according to autoantibody status

	OR (95% CI) for cancer diagnosis within 2 years of SSc onset	OR (95% CI) for cancer diagnosis within 3 years of SSc onset	OR (95% CI) for cancer diagnosis within 5 years of SSc onset
Anti-centromere	1.00 (reference)	1.00 (reference)	1.00 (reference)
Anti-topoisomerase I	2.18 (0.62-7.32)	1.18 (0.37-3.28)	0.73 (0.26-1.73)
Anti-RNA polymerase III	1.75 (0.36-7.20)	1.46 (0.45-4.17)	0.91 (0.32-2.20)
Anti-Ro52	1.57 (0.38-5.99)	1.64 (0.47-5.50)	1.43 (0.55-3.60)
Anti-PM-Scl 75/100	–	–	0.59 (0.03-2.95)
Anti-U1RNP	1.56 (0.08-9.96)	0.86 (0.05-4.72)	0.48 (0.03-2.41)

Abbreviations: CI: confidence interval; OR: odds ratio.
Disease onset is defined as the time of first non-Raynaud disease manifestation of systemic sclerosis.
Subjects who are positive for both anti-centromere and the studied autoantibody were excluded.
Risk estimates could not be calculated due to the small number of events for anti-Nor90, anti-Th/To, anti-Ku, anti-Fibrillarin, anti-BicD2 and anti-RNPC3 protein autoantibodies.

Table 3. Univariate logistic regression analyses for the risk of cancer within 2, 3 and 5 years of systemic sclerosis onset according to autoantibody status

stratified by autoantibodies. Cancer was diagnosed in 231 (13.6%) subjects. Median (IQR) time between cancer and disease onset was 7.0 (-0.7 to 16.4) years.

Table 2 shows the prevalence of cancer diagnosed within 2, 3 and 5 years of SSc onset, stratified by autoantibodies. Among 207 cancer subjects with available time data, 27 (13.6%), 37 (17.9%) and 58 (28.0%) were diagnosed with cancer within 2, 3 and 5 years of SSc onset. The most frequent types of cancers diagnosed within 5 years were breast (n=13), non-melanoma skin (NMSC, n=12), cervical/uterine (n=9) and hematological (n=8) cancers.

Overall, among all SSc subjects, no autoantibody was predictive of cancer-associated SSc (Table 3). However, ATA-positive subjects were more likely to have a solid cancer excluding NMSC (OR 6.6, 95% CI 1.4-46.4), especially breast cancer (OR 7.9, 95% CI 1.0-159.2), within 2 years of SSc onset. The risk of cancer-associated SSc was not significantly increased among ARNAP-positive subjects, although for solid cancers excluding NMSC, the OR was 5.8 (95% CI 0.56-125.8). Furthermore, subjects positive for at least 3 autoantibodies were more likely to develop cancer within 5 years of SSc onset compared to subjects with 1 or 2 autoantibodies (OR 3.0, 95% CI 1.3-6.1). Subjects who developed cancer within two years of SSc onset were generally younger (51.8 vs 57.9 years) and more frequently had a history of smoking (72% vs 59%) and scleroderma renal crisis (11% vs 3%).

Conclusion: In this study, ATA and overlapping autoantibodies were predictive of cancer-associated SSc for solid cancers excluding NMSC. Breast cancer was the most frequent type of cancer detected within 5 years of first non-Raynaud manifestation. Autoantibodies may help guide the approach to cancer screening. Larger studies are needed to define the risk of cancer-associated SSc within rarer autoantibody subgroups.

Disclosure: S. Lazizi, None; **M. Hudson**, None; **M. Baron**, None; **M. Fritzler**, Inova Diagnostics Inc, 5, 8, Werfen International, 5, 8; **S. Hoa**, None.

Abstract Number: 1392

Long-Term Tolerability of Aminaphtone in Raynaud's Phenomenon Secondary to Systemic Sclerosis

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Aminaphtone has been used for many years to treat microvascular disorders. *In vitro* Aminaphtone counteracts vasoconstriction downregulating endothelin-1 production and interferes with adhesion molecules and cadherin degradation thus defending vessels permeability (1-3). *In vivo* aminaphtone ameliorates clinical symptoms of several clinical conditions, including Raynaud's phenomenon (RP) (4).

The aim of the study was to evaluate long-term tolerability of standard dosage of Aminaphtone in a cohort of systemic sclerosis (SSc) patients with secondary RP.

Methods: Seventy-eight SSc patients (mean age 65±13 years; mean disease duration 9±7 years) treated with Aminaphtone due to active RP were enrolled (ACR/EULAR 2013 criteria). They were taking various concomitant treatments, including aspirin, calcium-channel blockers, cyclic intravenous iloprost, immunomodulators, endothelin receptor antagonists. SSc patients performed periodic clinical assessments and blood tests on average every four months per clinical practice. Duration of Aminaphtone administration, side effects, and self-assessment of Raynaud Condition Score (RCS) in a scale from 0 (absence of pain) to 10 (intolerable pain) were retrospectively taken into account.

Results: Duration of Aminaphtone administration (75 mg *bis in die* dosage, as standard initial posology) was between six and sixty-seven months (mean 31±20 months). During the follow-up, five patients (6.4%) referred headache as side effect: three of them had to reduce Aminaphtone posology to 75 mg per day, while maintaining clinical benefits. Periodic blood tests did not reveal any significant alteration attributable to Aminaphtone. No other side effects related to the drug appeared during the treatment period.

At baseline, mean RCS was 7.3±0.8. After 3 months of treatment sixty-four patients (82%) yet referred a subjective improvement of RCS (3.5±0.8, p=0.03), whereas 14 patients (18%) were clinically unsatisfied (RCS 6.1±0.4, p=0.12). In this last group, posology was increased to 75 mg *tris in die*, with a satisfactory amelioration in further nine patients (93.6%) (RCS 4.0±0.6 p=0.04), while five patients (6.4%) definitively discontinued therapy for subjective ineffectiveness within six months. Patients referred a sustained improvement of RCS along the observational period (31±20 months) (last RCS 3.7±0.7, p=0.03 vs baseline).

Conclusion: Aminaphtone shows an acceptable long-term tolerability along with sustained efficacy in the management of SSc-related RP, without disabling side effects. A randomized controlled trial for Aminaphtone use in the management of SSc-related RP is desirable.

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Abstract Number: 1393

Systemic Sclerosis: Subclinical Aterosclerosis and Morbimortality

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SESSION INFORMATION
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Background/Purpose: Rheumatic diseases are associated with accelerated atherosclerosis, and an increase in cardiovascular morbidity and mortality. This process is mediated by classic cardiovascular risk factors (CVRF), chronic inflammation and atherogenic treatments such as corticosteroids. In Systemic Sclerosis (SSc) cardiovascular complications have increased in recent decades, although the studies on subclinical atherosclerosis (sATS) in SSc show discordant results. Our objetive is to evaluate prospectively the relationship between subclinical atherosclerosis, cardiovascular morbidity and mortality in patients with SSc.

Methods: 120 consecutive patients with SSc who attended their medical regular review during November and December 2011 were included. We evaluated the presence of plaques and measured the right CCA IMT by B doppler US for the detection of sATS (IMT > 0.9mm and/or presence of plaque), review of classic CVRF and estimation of Medsger severity and EUSTAR activity index. Patients have been followed for 8 years, with at least annual consul-

	Absent n=78	Present n=42	
Diffuse cutaneous SSc	37.18%	26.12%	NS
mRSS	7.71 ± 6.32	6.38 ± 4.92	NS
High mRSS	9.69 ± 8.33	7.57 ± 4.74	NS
Arthritis	32.05%	28.57%	NS
Lung involvement	33.33%	30.95%	NS
PAH	10.26%	7.14%	NS
Cardiac involvement	15.38%	9.52%	NS
Digital ulcers	35.90%	35.83%	NS
AntiScl70	25.64%	21.43%	NS
ESR	20.12 ± 13.77	26.88 ±17.25	p =0.037*
CPR	0.65 ± 0.61	0.89 ± 0.7	p =0.041*
High activity index	11.54%	19.05%	NS
Damage index	6.67 ± 5.56	5.62 ± 4.9	NS
Σ Medsger index	5.37 ± 3.5	5.05 ± 3.45	NS

tation. In retrospect, the SCTC damage index, published in 2019, was obtained at the time of inclusion in the study. The clinical characteristics of the patients are collected since 1990 in a Prospective Longitudinal Observational Study (PLOS). Descriptive analysis was performed, using contigence tables for qualitative variables, and comparison of means for quantitative variables. The relationship between clinical characteristics, mortality, cardiovascular events (CVE), activity, severity and damage index, and sATS, was analyzed using binary logistic regression, adjusting for age and sex.

Results: 120 patients with SSc were included (93% female, age 60 ± 12 years). 42 of these patients (35%) had subclinical atherosclerosis. Age was statistically significant higher in patients with sATS compared to those without it (67.9±11.5 vs. 56.1±10.4 years, $p < 0.001$). We found no differences between groups in activity, damage and severity index (Table 1). Patients with sATS had higher levels of ESR and CRP, but the difference was not confirmed after adjusting for age (*). During the 8 years of follow- up, 9 CVE in 7 patients (5.8%): three myocardial infarction, one transient ischemic accident, one angor, one intermittent claudication and three refractory heart failure. The incidence of severe CVE was more than double in patients with SAtS (10.25% vs. 3.7%), but the difference was not significant. We found no relationship between the mortality of any cause, or the secondary to CVE, with sATS, in the 32 patients who died during the follow-up, 3 due to CVE (9.4%). The results are similar when we analyze only the presence of plaques.

Conclusion: In our study subclinical atherosclerosis is not related to higher mortality in patients with SSc, but it does seem to influence the occurrence of cardiovascular events. In addition, our results suggest that SSc does not influence the onset of accelerated atheromatosis.

Disclosure: M. Retuerto, None; **J. Rosales**, None; **M. Martin**, None; **B. Joven**, None; **P. Carreira**, None.

Abstract Number: 1394

Pathway to Systemic Sclerosis: Concerning Patients' Experiences During the Diagnostic Process

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

Background/Purpose: Receiving a diagnosis of systemic sclerosis (SSc) can be straightforward process for some, whereas others have a circuitous route. Given that complications can often arise early and lead to death, reducing the length of time until diagnosis is crucial (1). To the extent that understanding patients' experiences in the diagnostic process may help find ways to shorten it, we retrospectively examined the process patients with SSc experienced from the point of first symptoms through diagnosis.

Methods: Patients with SSc were approached to participate by their rheumatologist (specializing in scleroderma) during an office visit. Sixty-four patients (42% diffuse, 45% limited, 13% unknown) completed open-ended questions (e.g., what was your experience when you first felt unwell and when you were diagnosed with scleroderma).

Two researchers independently categorized responses; discrepancies were resolved by discussion. One researcher reviewed patients' records. All patients included met ACR-Eular criteria for diagnosis of systemic sclerosis.

Results: Regarding length of time from first symptoms to SSc diagnosis, 48% of patients reported being diagnosed within one year, 31% within 1-4 years, and 21% were diagnosed more than 4 years after the first symptoms appeared.

Overall, 75% of patients reported an initial symptom(s) involving their hands (53% Raynaud's). The 25% without symptoms involving hands commonly reported pain (50%), shortness of breath (31%), and gastrointestinal issues (19%).

Patients reported seeing up to seven health providers during the diagnostic process (*M* = 2.64). When patients first noticed symptoms, 33% saw their primary care physician (PCP) and/or a rheumatologist (27%), and 19% saw their PCP subsequently. Thirty-one percent of patients had a provider suspect SSc before it was diagnosed (13% of providers was a rheumatologist who referred them to a scleroderma specialist, 6% was their PCP). One-third of patients were diagnosed with another condition before receiving the scleroderma diagnosis. Some of these were a mis-diagnosis (e.g., carpal tunnel syndrome, lupus); others likely did have SSc as the underlying, but unrecognized, cause (e.g., arthritis, pulmonary arterial hypertension). Fifty percent of patients reported a SSc diagnosis from a scleroderma specialist, 38% from a different rheumatologist, and 3% from their PCP.

Conclusion: With 1 in 5 of patients being undiagnosed for more than four years, and only about 30% of patients having a health provider suspect a SSc diagnosis, educational efforts should make SSc a more salient diagnosis for providers. Three-quarters of patients reported initial symptoms involving their hands. About half of patients saw their PCP at some point in the diagnostic process, but only 9% reported their PCP suspected SSc.

Taken together, these data suggest educational efforts targeting PCPs and specialists to consider scleroderma more readily as a diagnostic possibility. SSc should be, but often is not, included in differential diagnosis of persistent hand complaints.

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Disclosure: F. Patricia, None; **L. Shapiro**, Actelion, 5; **N. Dorr**, None; **R. Lukasiewicz**, None; **F. Houser**, None; **M. Taylor**, None.

Abstract Number: 1395

Poor Maternal and Fetal Outcome in Indian Women with Systemic Sclerosis: Interview-based Study at a Tertiary Center in India

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Poor obstetric outcomes have been described in Systemic sclerosis (SSc) in the developed world. We assessed effect of the disease in Indian women and compared with world literature.

Methods: Women with SSc (>18 years, ACR/EULAR 2013 criteria)[1] registered at a tertiary care centre from 2010-2016 were contacted over the telephone. Apart from demographics, disease related features, obstetric history and social issues were recorded (Figure 1).

Results: Of 200 women, 94 (47%) could be contacted, 13 (of 94, 13.8%) deaths were recorded, and 75 (79.8%) agreed for an interview (baseline characteristics Table 1). Median age at diagnosis was 31 (22-38) years. Diffuse SSc was more common (56%).

127 conceptions before SSc were compared with 15 after the disease (Figure 2) to yield a higher odd of maternal [OR: 4.9] and foetal [OR: 9.9] complications, and low chances of a live births [OR: 0.23]. Pregnancies after SSc had higher spontaneous abortion, premature rupture of membrane (PROM), prolonged labor, oligohydramnios, maternal infection and intrauterine death (IUD), preterm delivery, low birth weight (LBW) (Table 1)]. Greater (66.7% vs 52%)[2] caesarean deliveries were recorded after disease onset. Social issues were reported by 12 (16%).

As compared to SSc in developed countries,[2,3,4] we found a similar caesarean (two-third) and preterm deliveries (one-fourth), whereas abortion rate was six times higher (26.6% vs 4%) and LBW was 20%, which was 1.5 times higher compared to IMPRESS cohort.[2]

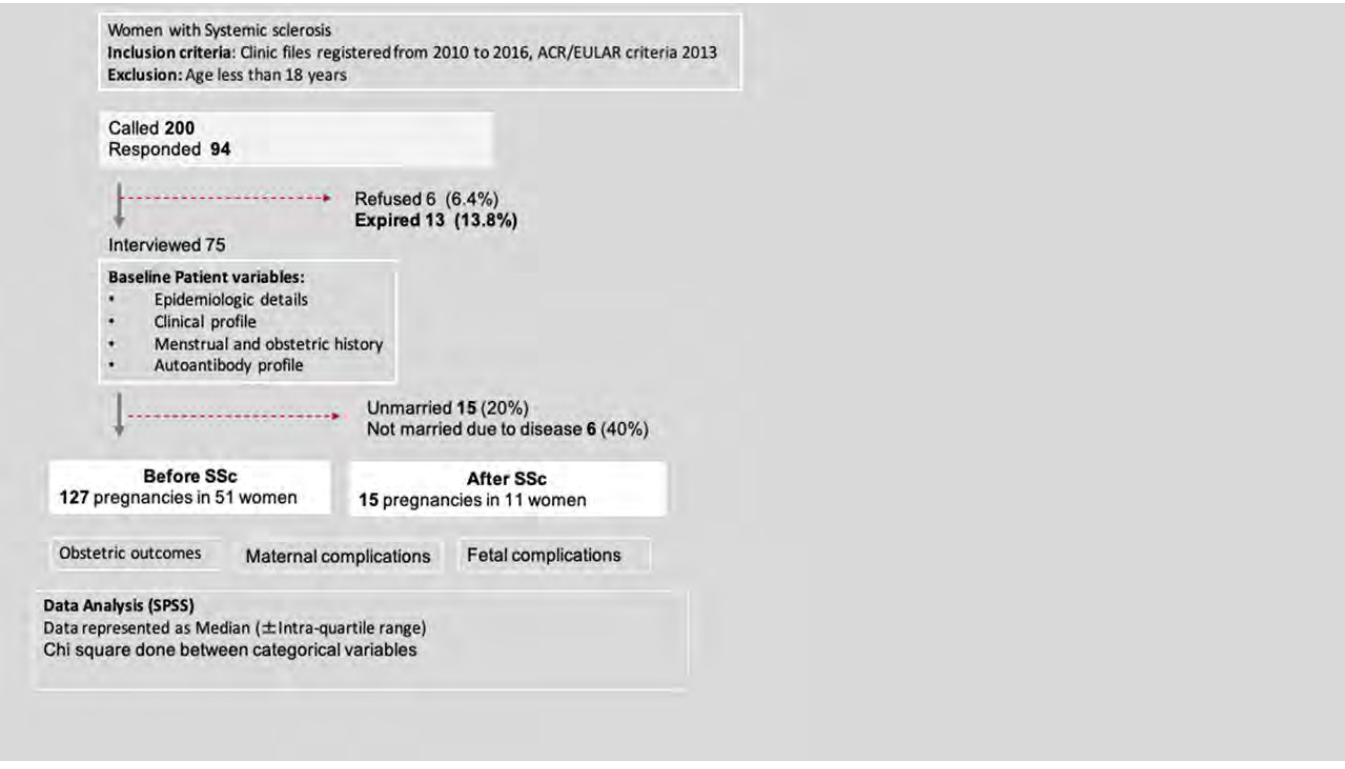

Figure 1. Detailed Methods

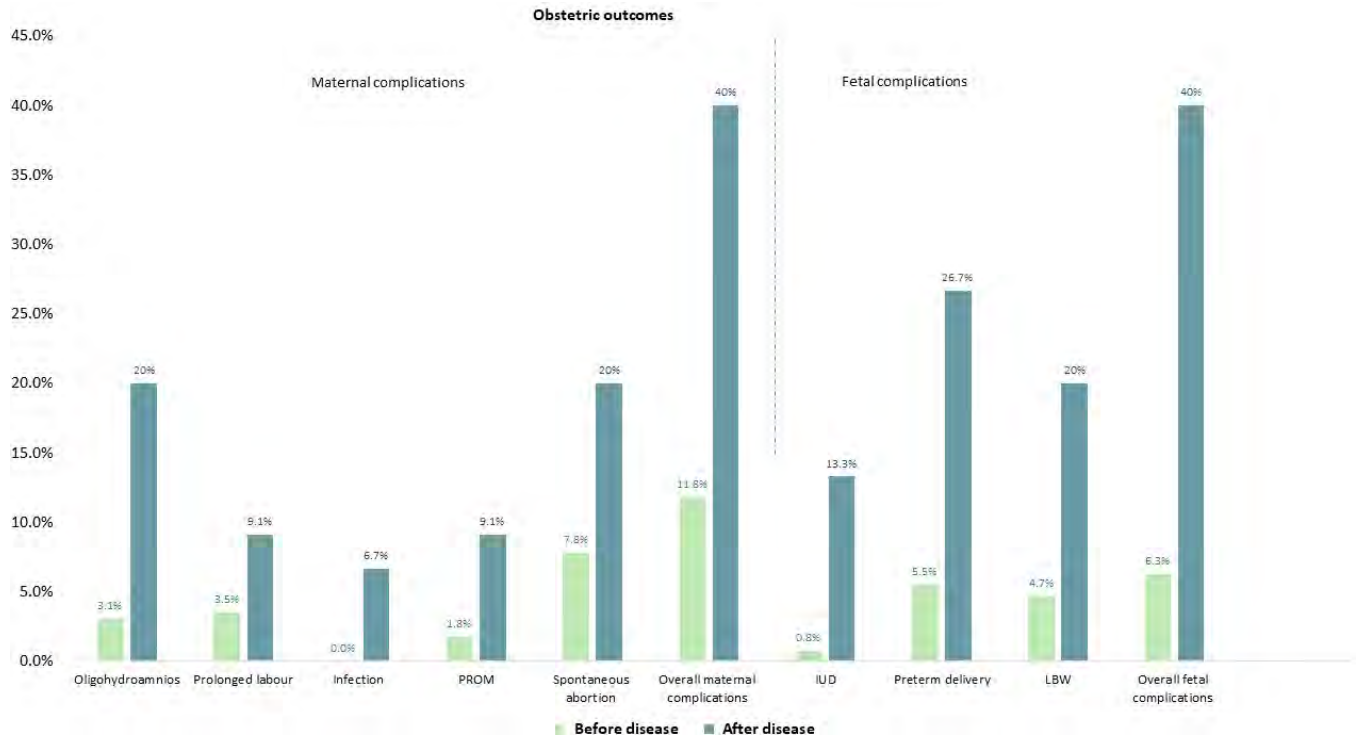

Figure 2. Maternal and fetal complications in Systemic sclerosis

Conclusion: SSc incurs high mortality, poor obstetric outcomes, greater maternal and foetal complications, and low birth weight in addition to social issues. The outcomes are worse in a low-middle income country than previously described from the developed world.

Pregnancies in SSc	Before Disease Onset n (%)	After Disease Onset n (%)	OR (CI)	p-value
Maternal complications				
APH	1 (0.9)	0 (0)		
PPH	3 (2.6)	0 (0)		
Abortions Spontaneous	10 (7.8)	3 (20)	2.54 (0.62-10.26)	0.19
PROM	4 (3.5)	1 (9.1)	2.59 (0.26-25.25)	0.41
Oligohydramnios	4 (3.1)	3 (20)	7.68 (1.5-38)	**0.004**
Prolonged labour	2 (1.8)	1 (9.1)	5.18 (0.43-61.81)	0.19
Infection	0 (0)	1 (6.7)	1.07 (1.5-38)	**0.004**
Overall maternal complications	15 (11.8)	6 (40)	4.9 (1.5-15.9)	**0.004**
Mode of delivery				
Induced	3 (2.4)	1 (6.7)	2.82 (0.27-28.88)	0.38
LSCS	14 (11)	10 (66.7)	16.14 (4.8-54)	**0.000**
Normal vaginal delivery	87 (76.3)	1 (9.1)	8.39 (1.06-66.26)	**0.04**
Fetal outcomes				
IUD	1 (0.8)	2 (13.3)	19.3 (1.6-228)	**0.001**
Preterm delivery	7 (5.5)	4 (26.7)	6.2 (1.5-24)	**0.004**
Low birth weight	6 (4.7)	3 (20)	5.04 (1.1-22.7)	**0.018**
Live births	110 (86.6)	9 (60)	0.23 (0.07-0.73)	**0.022**
Overall fetal complications	8 (6.3)	6 (40)	9.9 (2.8-34.8)	**0.000**

Abbreviations: APH-Antepartum hemorrhage, PPH- Postpartum hemorrhage, LSCS-Lower segment caesarian section, IUD- Intrauterine death

Table 1. Comparison of Obstetric outcomes before and after onset of Systemic sclerosis

Disclosure: R. Kharbanda, None; **N. R**, None; **D. Misra**, None; **L. Gupta**, None; **V. Agarwal**, None.

Abstract Number: 1396

Digital Artery Volume Index (Davix©) Predicts Onset of Future Digital Ulcers in Patients with Systemic Sclerosis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical Poster III

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Background/Purpose: Neointima proliferation is a key pathologic feature of Systemic Sclerosis (SSc), causing arterial vessel narrowing. It is a recognised culprit pathological lesion in Digital Ulcers (DUs), pulmonary artery hypertension and renal crisis. Nevertheless, there are no validated imaging techniques to assess the severity of vascular involvement in SSc. This study presents Digital Artery Volume index (DAVIX ©), a novel quantitative MRI based scoring for the assessment of the blood flow in the arteries and its validation in predicting the onset of DUs in SSc patients.

Methods: This study enrolled 91 (78 female) consecutive patients with Raynaud's phenomenon, with median disease duration of 4 years (IQR=1.91-9). Complete historical and prospective follow-up data were available for 68 patients. 63 patients fulfilled the 2013 ACR/EULAR classification criteria for SSc; 28 had score < 9. The data collected included: pulmonary function tests (PFTs), nailfold capillaroscopy, modified Rodnan Skin Score (mRSS), and Scleroderma Health Assessment Questionnaire Disability Index (sHAQ-DI). DAVIX of the dominant hand was calculated as % mean of the 4 fingers, employing proprietary algorithm by IAG. The distribution was analysed with D'Agostino-Pearson normality test. The median scores were compared by Mann-Whitney-Wilcoxon test; correlation with clinical parameters was performed using Spearman's or Pearson test, as appropriate (Prism 7).

Results: DAVIX correlated with mRSS (r=-0.258, p=0.017), DLCO% (r=0.338, p=0.008) and capillaroscopy pattern (r=-0.388, p=0.001). In patients with DUs, DAVIX showed a stronger correlation with DLCO% (r=0.786, p=0.048). DAVIX predicted the worsening of HAQ-DI (r=-0.295, p=0.029), sHAQ (r =-0.333, p=0.029) and VAS pain (r=-0.269, p=0.038) independently of the presence of DUs. In the context of DU, 7 patients had DUs at baseline (5 with a positive history for DUs). 12 patients developed DUs within 12 months, 3 of them had DUs at baseline. 38 patients did not have either previous or current DUs, neither did they develop new DUs within 12 months. DAVIX of patients with current DUs was lower than DAVIX of patients without DUs (0.18 vs 0.63 p=0.0093). DAVIX of patients with positive history of DUs was lower than in patient with a negative history (median 0.34 vs 0.64, p=0.0052). In patients without current DUs, DAVIX of patients who developed new DUs within 12 months of follow-up was 3-fold lower than in patients who did not develop DUs (0.21 vs 0.65, p=0.0156). ROC curve analysis indicated that DAVIX threshold < 0.49 conferred a 4 times higher risk of developing new DUs (67%) compared to overall risk of our population 17.6%.

Conclusion: The study demonstrates that DAVIX© is a feasible surrogate outcome measure of neointima proliferation in SSc and a useful imaging biomarker of vascular disease activity. Its predictive value of the future onset of DU could be used to stratify patients in clinical trials. The value of DAVIX in predicting the worsening of PROs and clinical parameters in overall patients, may offer insights on the role of vascular disease activity in the overall progression of SSc.

Disclosure: K. Gjeloshi, None; **G. Lettieri**, None; **F. Danzo**, None; **G. Abignano**, None; **M. Hinton**, IAG, Image Analysis Group, 3; **A. Dean**, None; **G. Cuomo**, None; **O. Kubassova**, IAG, Image Analysis Group, 3; **F. Del Galdo**, None.

Abstract Number: 1397

Clinical and Demographic Features of Morphea Patients with Mucocutaneous Involvement: A Cross Sectional Study from the Morphea of Adults and Children Cohort

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Table 1: Demographic and Clinical Features of Study Participants (**N=735**)

Characteristic	Linear (n=362)	Generalized (N=232)	Plaque (N=94)	Mixed (n=47)	P Value
Age at onset (y), median (IQR)					
	13 (7-25)	55 (40.5-63.5)	42.5 (27.3-54)	25 (13-43)	**<0.001[a]**
Sex, n (%)					
Female	281 (78%)	196 (84%)	84 (89%)	41 (87%)	**0.012[b]**
Male	81 (22%)	36 (16%)	10 (11%)	6 (13%)	
Race, n (%)					**0.004[b]**
Caucasian	253 (70%)	184 (79%)	73 (78%)	33 (72%)	
Black	10 (3%)	12 (5%)	8 (9%)	5 (11%)	
Hispanic	61 (17%)	28 (12%)	7 (7%)	5 (11%)	
Asian/Pacific Islander	19 (5%)	5 (2%)	2 (2%)	3 (6%)	
Other	19 (5%)	3 (1%)	4 (4%)	1 (2%)	
Mucocutaneous Involvement, n (%)					
Genital Involvement	2 (1%)	23 (10%)	2 (2%)	0 (0%)	**<0.001[b]**
Oral Involvement	17 (5%)	1 (0.4%)	0 (0%)	0 (0%)	**<0.001[b]**
LoSCAT component score, median (IQR)					
LoSAI	2 (0-6)	14 (5-29)	2 (0-6)	0 (0-2)	**<0.001[a]**
LoSDI	9 (5-16)	19 (13-31)	5 (4-9)	5 (4-11)	**<0.001[a]**
PGA-A	10 (0-30)	30 (15-60)	10 (0-30)	0 (0-20)	**<0.001[a]**
PGA-D	30 (20-50)	20 (10-40)	10 (5-17)	12 (10-20)	**<0.001[a]**
Clinical features and disease modifiers, n (%)					
Deep Involvement	241 (67%)	78 (34%)	44 (47%)	22 (47%)	**<0.001[b]**
Dermal Involvement	127 (35%)	82 (35%)	38 (40%)	22 (47%)	0.322[b]
Epidermal Involvement	23 (6%)	83 (36%)	8 (9%)	7 (15%)	**<0.001[b]**
Hair Loss in Lesion	93 (26%)	28 (12%)	3 (3%)	3 (6%)	**<0.001[b]**
Limited ROM	86 (24%)	50 (22%)	4 (4%)	5 (11%)	**<0.001[b]**
Contracture	5 (1%)	6 (3%)	0 (0%)	0 (0%)	0.257[b]
Joint Deformity	15 (4%)	0 (0%)	1 (1%)	0 (0%)	**0.004[b]**

IQR, Interquartile range; *LoSCAT,* Localized Scleroderma Cutaneous Assessment Tool; LoSAI, Localized Scleroderma Skin Activity Index, *LoSDI,* Localized Scleroderma Skin Damage Index; *PGA-A,* Physician Global Assessment of Disease Activity; *PGA-D,* Physician Global Assessment of Disease Damage; *ROM,* Range of Motion

* Pediatric onset was defined as onset of disease <18 years

[a] Values computed with Mann-Whitney U Test

[b] Values computed with chi-square test

Demographic and Clinical Features of Study Participants (N=735)

Table 2: Demographic and clinical characteristics by mucocutaneus involvement

Characteristic	Oral (n=18)	Genital (N=27)	P Value
Age at onset (y), median (IQR)	11.5 (8.3-15.8)	57 (27-63)	**<0.001[a]**
Sex, n (%)			**0.02[b]**
Female	14 (77.8%)	27 (100%)	
Male	4 (22.2%)	0 (0%)	
Race, n (%)			0.29[b]
Caucasian	12 (66.7%)	24 (88.9%)	
Black	1 (5.6%)	0 (0%)	
Hispanic	3 (16.7%)	1 (3.7%)	
Asian/Pacific Islander	0 (0%)	0 (0%)	
Other	2 (11.1%)	2 (7.4%)	
Morphea Type, n (%)			**<0.001[b]**
Linear	17 (94.4%)	2 (7.4%)	
ECDS	10 (55.6%)	0 (0%)	
PRS	11 (61.1%)	0 (0%)	
Generalized	1 (5.6%)	24 (85.2%)	
Isomorphic	0 (0%)	13 (48.2%)	
Symmetric	0 (0%)	5 (18.5%)	
Pansclerotic	0 (0%)	0 (0%)	
Plaque	0 (0%)	2 (7.4%)	
Mixed	0 (0%)	0 (0%)	
LoSCAT component score, median (IQR)			
LoSAI	0 (0-0)	6 (0-12)	**<0.001[a]**
LoSDI	9 (6.5-15.5)	15 (7-22)	0.2174[a]
PGA-A	0 (0-0)	13 (0-30)	**<0.001[a]**
PGA-D	32.5 (25.3-48.8)	15 (10-30)	**0.0006[a]**
DLQI, median (IQR)			
DLQI	3 (0-5.5)	6 (4-9)	0.065[a]
Clinical features and disease modifiers, n (%)			
Deep Involvement	18 (100%)	6 (22.2%)	**<0.001[b]**
Dermal Involvement	4 (22.2%)	12 (44.4%)	0.204[b]
Epidermal Involvement	1 (5.6%)	13 (48.2%)	**0.003[b]**
Hair Loss in Lesion	1 (5.6%)	2 (7.4%)	>0.999
Lichen Sclerosus Overlap	0 (0%)	22 (81.5%)	**<0.001[b]**
Limited ROM	5 (27.8%)	2 (7.4%)	0.098[b]

IQR, Interquartile range; *ECDS,* en Coup de Sabre; *PRS,* Parry-Romberg Syndrome; *LoSCAT,* Localized Scleroderma Cutaneous Assessment Tool; LoSAI, Localized Scleroderma Skin Activity

Demographic and clinical characteristics by mucocutaneus involvement

Background/Purpose: Morphea is an autoimmune skin condition that produces skin and soft tissue sclerosis. While clinical manifestations of morphea have been well-described, mucocutaneous findings such as oral and genital lesions have not been well-characterized. Thus, the aim of our study was to determine the demographic and clinical characteristics of morphea patients with mucocutaneous lesions.

Methods: The present study was a cross-sectional study of 735 patients in the Morphea of Adults and Children Cohort (MAC Cohort) from 2007 to 2018. We included participants with sufficient demographic and clinical data for analysis. Patient disease activity and damage were assessed by the Localized Scleroderma Cutaneous Assessment Tool (LoSCAT), including the Localized Scleroderma Activity Index (LoSAI) and Damage Index (LoSDI). Physician Global Assessment of Disease Activity (PGA-A) and Damage (PGA-D) were recorded. Presence of extragenital and genital lichen sclerosus atrophicus (LsA) and oral mucosa changes were determined by physical exam, histology, and/or referral to relevant specialties. Differences between demographic and clinical variables of groups of interest were analyzed by chi-squared tests for dichotomous variables while Kruskall-Wallis and Mann-Whitney U tests were used for continuous variables.

Results: Of 735 morphea patients, linear comprised 49% (n=362) and generalized comprised 32% (n=232) **(Table 1)**. The median age of morphea onset was older in generalized morphea than linear morphea (55 versus 13 years, $p< 0.001$). Oral lesions were present in 2.4% (n=18) of patients overall, of which the majority (94%) had linear morphea. Genital lesions were present in 27 (3.7%) of patients overall, the majority of which (85%) had generalized morphea **(Table 2).** Patients with oral morphea lesions had a younger age of onset than those with genital involvement (11.5 versus 57 years, respectively; $p< 0.001$). Patients with oral involvement were majority female (78%) while genital involvement were all female and majority Caucasian (89%). Genital morphea patients had LsA overlap in 82% (n=22) versus 0% with oral involvement ($p < 0.001$). Deep morphea was seen in 100% patients with oral involvement versus 22% of patients with genital involvement ($p < 0.001$). Median LoSAI and PGA-A scores for patients with oral involvement (0, IQR 0-0 and 0, IQR 0-0, respectively) was lower than patients with genital involvement (6, IQR 0-12 and 13, IQR 0-30, respectively) ($p < 0.001$ and $p< 0.001$, respectively). PGA-D scores were higher in oral morphea (32.5, IQR 25.3-48.8) than in genital morphea (15, IQR 10-30) ($p =0.001$).

Conclusion: Our study demonstrates mucocutaneous involvement in morphea is uncommon but occurs in a substantial number of those with specific morphea subsets. The presence of mucocutaneous lesions is associated with substantial morbidity. Oral morphea lesions predominate in younger patients with overlying facial linear morphea while genital lesions predominate in post-menopausal women with overlying extragenital LsA. Our results underscore the need to look for mucocutaneous findings in morphea, particularly those with the clinical subsets associated with these findings.

Disclosure: S. Prasad, None; **S. Black**, None; **S. Sharma**, None; **H. Jacobe**, None.

Abstract Number: 1398

The Isolated Nucleolar Pattern ANA Antibody in a Systemic Sclerosis Patient Cohort

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SESSION INFORMATION
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Background/Purpose: Systemic Sclerosis (SSc) patients with an isolated nucleolar patterned ANA (NUC ANA) make up about 15% of the SSc population, although the specific nucleolar antibody is not easily identified. We sought to characterize patients with an isolated nucleolar pattern ANA without other SSc specific antibodies and describe the clinical and laboratory features associated with this SSc subset.

Methods: A single-center, retrospective study of SSc patients as previously described (Moore, 2019) was used. African American (AA) and non-African American (non-AA) SSc patients were matched 1:1 based on sex, age, date, and disease duration at the first visit, and extent of cutaneous disease. Demographic and clinical features were compared by the presence of the antibody and race. Mortality risks were assessed by a Cox proportional hazards model with covariates of race and the presence of the NUC ANA.

Results: NUC ANA was seen in 81 of the 402 (20%) of the SSc patient, 49 (60%) were AA in the NUC ANA group compared to 48% in the non-NUC ANA group ($p< 0.05$) (Table 1). The NUC ANA patients presented with shorter disease duration at their first visit ($p= 0.000$) and developed more severe upper GI problems ($p=0.041$). They had more cardiac involvement, but not more severe pulmonary fibrosis(Table 2). Comparing AA patients in the NUC ANA group to the non-AA patients, the non-AA patients were more likely to have Raynaud's with digital pitting scars ($p=0.031$) while African Americans were more likely to have pericardial effusions ($p=0.043$). Although survival was not different from NUC ANA compared to non-NUC ANA, more patients with the NUC ANA died of pulmonary hypertension($p= 0.033$) and kidney disease ($p=0.046$)(Table 3).

Table 1. Baseline Characteristics by Race and Antibody*

Characteristic	Antibody Comparison		
	Non-NUC ANA (321)	NUC ANA (81)	P
Female, N (%)	278 (86.6)	71 (87.7)	0.803
African American, N (%)	153 (48)	49 (60)	**0.039†**
dcSSc, N (%)	3 (0.9)	2 (2.5)	0.265
Age at First Symptom	39.65±12.03 (298)	41.66±13.70 (78)	0.255
Disease Duration at First Visit	8.67±9.41 (296)	5.47±5.86 (78)	**0.000†**
Age at Diagnosis	43.17±13.92 (296)	44.37±14.15 (74)	0.508
Duration (dx to death)	9.95±8.62 (296)	7.68±5.40 (74)	**0.005†**

* All values are listed as mean +/- standard deviation, (N) unless otherwise noted. † denotes statistical significance. NUC= isolated nucleolar; dcSSc= diffuse cutaneous systemic sclerosis; dx= diagnosis.

Table 2. Clinical Features of the Isolated Nucleolar Antibody*						
	Antibody Comparison			Isolated Nucleolar by Race		
	non-NUC ANA	NUC ANA	P	AA	non-AA	P
Examination Features						
Inflammatory Arthritis	61 (19)	14 (17)	0.677	8 (16)	6 (19)	0.778
Contractures	115 (36)	24 (30)	0.295	14 (29)	10 (31)	0.796
Neuropathy	52 (16)	9 (11)	0.254	8 (16)	1 (3)	0.065
Calcinosis	37 (12)	6 (7)	0.284	3 (6)	3 (9)	0.585
Telangiectasia	107 (33)	33 (41)	0.211	18 (37)	15 (47)	0.364
Tendon Friction Rubs	52 (16)	13 (16)	0.974	8 (16)	5 (16)	0.933
Raynaud's Severity						
no Raynaud's	14 (4)	0 (0)	0.056	0 (0)	0 (0)	X
RP only	14846)	44 (54)	0.186	26 (53)	18 (56)	0.778
w/ digital pitting	15 (5)	8 (10)	0.072	2 (4)	6 (19)	**0.031**†
w/ digital ulcerations	122 (38)	25 (31)	0.233	19 (39)	6 (19)	0.056
w/ digital gangrene	22 (45)	4 (5)	0.531	2 (4)	2 (6)	0.66
GI Involvement						
No GI medication	52 (16)	16 (20)	0.271	9 (18)	7 (22)	0.455
GERD with medication	165 (74)	49 (61)	**0.041**†	29 (59)	20 (63)	0.475
Antibiotics for bacterial overgrowth	16 (5)	6 (7)	0.392	4 (8)	2 (6)	0.748
Pseudo-obstruction	6 (2)	3 (4)	0.319	1 (2)	2 (6)	0.327
Hospitalization for GI Disease	13 (4)	5 (6)	0.409	5 (10)	0 (0)	0.062
Requiring TPN	5 (2)	2 (3)	0.575	1 (2)	1 (3)	0.759
Pulmonary Features						
FVC, mean ± SD	74.94 ± 21.64	74.42 ± 17.68	0.831	75.09 ± 17.29	73.38 ± 18.23	0.688
DLCO, mean ± SD	55.16 ± 22.69	55.02 ± 20.5	0.717	51.73 ± 20.36	60.31 ± 19.98	0.082
Fibrosis per CT scans						
None	78 (24)	20 (25)	0.941	11 (22)	9 (28)	0.562
Mild/moderate	114 (34)	30 (37)	0.798	19 (39)	11 (34)	0.688
Severe	24 (7)	4 (5)	0.423	2 (4)	2 (6)	0.66
Not done	105 (33)	27 (33)	0.358	17 (35)	10 (31)	0.47
Home O_2 Use	52 (16)	14 (17)	0.801	9 (18)	5 (16)	0.75
PH by RHC	52 (16)	15 (19)	0.617	10 (20)	5 (16)	0.588
Cardiac Features						
LVEF, mean ± SD %	57.41 ± 8.67	60.213 ± 9.4	**0.028**†	58.99 ± 11.23	61.87± 5.97	0.24
PASP or RVSP, mean ±SD mmHg	35.34 ± 15.50	37.44 ± 17.69	0.389	40.75 ± 18.56	33.30± 15.96	0.125
Pericardial effusion	6 (2.46)	5 (7.69)	**0.043**†	5 (13.51)	0 (0)	**0.043**†
Severe cardiac disease**	30 (13)	6 (10)	0.106	5 (10)	1 (3)	0.234

*Values are reported as number (%) unless indicated otherwise. The actual cohort sizes are 81 isolated nucleolar ANA patients, 321 non-isolated nucleolar ANA antibody patients and within the isoNucANA cohort, there were 49 African Americans (AA) and 32 non-African Americans (non-AA). Not all tests were performed in all patients. Forced Vital Capacity (FVC):74 isolated nucleolar patients (isoNucANA) and 265 non-isoNucANA; diffusing capacity for carbon monoxide (DLco). 74 isoNucANA and 263 non-isoNucANA; Pulmonary Artery Systolic Pressure (PASP) or right ventricular systolic pressure (RVSP). 54 isoNucANA patients, 209 non-IsoNucANA, 30 AA w/ isoNucANA, 24 non-AA w/isoNucANA; Left ejection fraction (LVEF): 61 isoNucANA patients, 235 non-isoNucANA, 35AA isoNucANA, 26 non-AA isoNucANA. GERD= Gastroesophageal reflux disease; CT= computed tomography; RP; Raynaud's Phenomenon; GI= gastrointestinal; PH= pulmonary hypertension; RHC= right heart catheterization; non-IsoNucANA: non-isolated nucleolar ANA Antibody group.

X- statistic could not be calculated because the variable 'no Raynaud's' is a constant between African Americans and non-African Americans in this cohort

** Severe involvement characterized by pericardial effusion, arrhythmias requiring treatment or heart failure requiring treatment

† Statistically significant

Conclusion: Scleroderma specific nucleolar antibodies have not been easily characterized commercially except as an ANA with a nucleolar pattern. This study shows that 20% of our SSc patients had a NUC ANA and that AA had a higher frequency of NUC ANA. However, previous studies have shown more meaningful clinical associations with the specific nucleolar antibodies including anti-U3 RNP, (or fibrillarin), anti-Th/To, and PmScl. This study was not able to

Table 3. Death Causality by Race and Antibody*						
Characteristic	**Antibody Comparison**			**Isolated Nucleolar by Race**		
	Non-NUC ANA (321)	NUC ANA (81)	P	AA (49)	non-AA (32)	P
Death	51 (63)	14 (17)	0.760	9 (18)	5 (16)	0.750
SSc-Related Death	38 (75)	10 (71)	0.900	6 (67)	4 (80)	0.973
PF	7 (14)	2 (2.5)	0.875	0 (0)	2 (40)	0.076
pHT	4 (8)	4 (29)	**0.033†**	3 (33)	1 (20)	0.543
Cardiac	16 (31)	0 (0)	**0.040†**	0 (0)	0 (0)	X
Kidney	0 (0)	1 (7)	**0.046†**	1 (11)	0 (0)	0.416
Multisystem	11 (14)	3 (29)	0.903	2 (22)	1 (20)	0.824
Accident	1 (2)	0 (0)	0.615	0 (0)	0 (0)	X
Infection	1 (2)	0 (0)	0.615	0 (0)	0 (0)	X
Cancer	8 (16)	4 (29)	0.248	3 (33)	1 (20)	0.543

*All data presented as N (%). No data were missing for any category. X indicates an inability to calculate significance due to insufficient data. † indicates statistically significant values. Non-NUC ANA= non-isolated nucleolar ANA subjects, NUC ANA= isolated nucleolar ANA subjects, AA= African American, non-AA= non-African American, PF= pulmonary fibrosis, pHT= pulmonary hypertension. Pa

duplicate these studies using just the presence of a NUC ANA test. The newer commercially available multiplex line blot tests will likely be better able to more meaningfully classify SSc patients with a nucleolar antibody.

Disclosure: S. Elliott, None; **D. Moore**, None; **V. Steen**, Boehringer Ingelheim, 2, 5, corbus, 2, 5, eicos, 2, 5, genetech, 2, forbius, 5, galapagos, 5.

Abstract Number: 1399

Differential Impacts of TNFa Inhibitors on the Expression of Th Cytokines

Ching-Huang Ho[1], Andrea Silva[1] and **I-Cheng Ho**[2], [1]Brigham and Women's Hospital, Boston, MA, [2]Birgham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Inhibition of TNFα has emerged as an effective therapeutic approach for many autoimmune/inflammatory diseases.While the efficacy and safety profile of the five FDA-approved TNFis (etanercept, adalimumab,

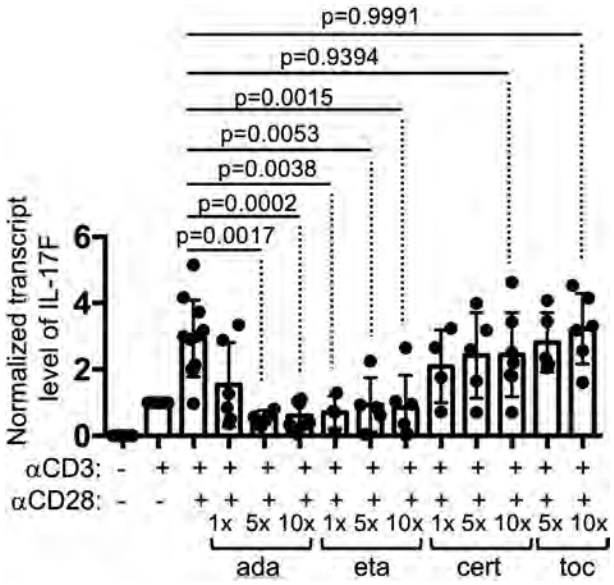

Figure 1. Drug-specific suppression of Th cytokine production by TNFis. PBMC of healthy donors were stimulated with anti-CD3 and/or anti-CD28 for 24 hours in the presence or absence of indicated TNFis at different concentrations (1X = 10 ug/ml for adalimumab, 25 ug/ml for etanercept, 10 ug/ml for certolizumab, and 20 ug/ml for tocilizumab). The transcript levels of IL-17F in the PBMC are shown. Statistical analysis was carried out with one-way ANOVA.

certolizumab, golimumab, and infliximab) are comparable in rheumatoid arthritis (RA), there exist some intriguing differences among them. For example, one RA patient may respond to one TNFi but not the others; etanercept is generally ineffective for inflammatory bowel diseases or uveitis. Post-hoc data have also uncovered several unexpected sided effects of TNFis, such as +ANA, lupus-like diseases, demyelinating diseases, and pustular psoriasis, which probably can be partly attributed to the induction of type 1 interferons. Interestingly, certolizumab may be less likely to induce lupus-like diseases. The mechanisms mediating such discrepancies among TNFis are still poorly understood. The goal of this project is to examine whether TNFis have differential impacts on the expression of Th cytokines.

Methods: PBMC from healthy donors were stimulated with anti-CD3/anti-CD28 for 24 hours in the presence or absence of adalimumab, etanercept, or certolizumab for 24 hours. The expression of Th cytokines in PBMC or subsequently purified Th cells was analyzed with qPCR as well as RNA-seq. Flow cytometry was used to examine the binding of TNFis to membrane TNFα.

Results: Adalimumab and etanercept, but not certolizumab, inhibited the expression of IL-17A/F and IL-2 in Th cells within anti-CD3-stimulated PBMC (Figure 1). This discordant effect between adalimumab and certolizumab was not due to neutralization of soluble TNFα or their differential binding to membrane TNFα. Instead, the unique effect of adalimumab required cell-cell contacts between Th cells and non-Th cells and was not recapitulated by cross-linking of the Fc of adalimumab. RNA-seq analyses further revealed that adalimumab also suppressed the expression of other effector Th cytokines, including IFNγ, IL-21, and IL-9, but reciprocally induced strong type 1 interferon signals and the expression of co-inhibitory molecules CD96 and PVRIG in Th cells.

Conclusion: Adalimumab, but not certolizumab, inhibits the expression of Th cytokines independently of neutralizing soluble TNFα. This phenomenon is very likely mediated by type 1 interferon signals and CD96/PVRIG co-inhibition. Elucidating the mechanism mediating the unique effect of adalimumab very likely will uncover novel mechanisms of action of TNFis and improve their efficacy and safety.

Disclosure: C. Ho, None; **A. Silva**, None; **I. Ho**, None.

Abstract Number: 1400

cAMP Response Element Modulator (CREM)α Promotes PD-1- effector CD4+ T Cells in Psoriasis and Psoriatic Arthritis

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SESSION INFORMATION

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Background/Purpose: Psoriasis is a systemic autoimmune/inflammatory condition that primarily affects the skin, but also other organ systems. Effector $CD4^+$ T lymphocytes have been identified as a key contributor to inflammation and tissue damage, but underlying molecular mechanisms remain poorly understood.

The transcription factor CREMα plays a role in effector CD4+ T cell differentiation and activation in autoimmune/inflammatory conditions through altering cytokine gene expression, favoring effector T cells. The inhibitory surface co-receptor programmed death (PD-)1 plays a key role in controlling effector T cell generation and activation. This study investigated the involvement of CREMα in the regulation of PD-1 and effector T cell generation in psoriasis and psoriatic arthritis.

Methods: CD4+ T cells were isolated from peripheral blood of controls (N=13), psoriasis (N=13) and psoriatic arthritis patients (N=9) to examine effector cytokine expression (LUMINEX mRNA probe and MSD protein assays), and monitor CD4+ T cell subset distribution (flow cytometry) and co-inhibitory PD-1 mRNA and surface protein expression (flow cytometry, mRNA probes, qPCR). Using chromatin immunoprecipitation assays and luciferase reported assays, we investigated recruitment and *trans*-regulatory effects of CREMα on the *PDCD1* promoter in wild-type and genetically modified CD4+ Jurkat T cells (CREMα overexpressing and CREMα-deficient cells).

Results: CD4+ T cells from psoriasis and psoriatic arthritis patients exhibit effector CD4+ T cell phenotypes with increased IL-17, and reduced IL-2 and inhibitory PD-1 co-receptor (mRNA and protein) expression. In effector CD4+ T cells, expression of the transcription factor CREMα is increased. Recruitment of CREMα to the *PDCD1* proximal promoter results in its *trans*-repression and subsequently reduced PD-1 mRNA and protein expression. Expression of PD-1 associates with IL-2 expression and inversely correlates with IL-17A expression in wild-type and CREMα overexpressing Jurkat CD4+ T cells.

Conclusion: CREMα promotes effector CD4+ T cells in psoriasis and psoriatic arthritis through inhibition of PD-1 co-receptor expression. This contributes to imbalanced IL-2 and IL-17 expression in psoriasis and psoriatic arthritis and potentially may extend to other effector T cell mediated autoimmune/inflammatory conditions. This suggests CREMα:PD-1 axis is a promising target in the search for disease biomarkers and treatment targets.

Disclosure: S. Hofmann, None; **F. Kapplusch**, None; **S. Abraham**, None; **S. Northey**, None; **S. Russ**, None; **F. Schulze**, None; **A. Surace**, None; **C. Hedrich**, None.

Abstract Number: 1401

Disease Mutation That Weakens ZAP70 Autoinhibition Enhances Responses to Weak and Self Ligands

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
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Background/Purpose: ZAP70, a cytoplasmic protein tyrosine kinase, is critical for TCR signaling and T cell development. Complete loss of function of ZAP70 in humans causes severe immunodeficiency. Autoimmune disease due to mutant *ZAP70* alleles in humans has not been reported until recently. Our previous study has shown that compound heterozygous mutations R192W/R360P in *ZAP70* are responsible for a new familial autoimmune syndrome manifested by bullous pemphigoid, colitis, proteinuria and autoantibody to factor VIII in early life. Cell line data showed that the R192W allele leads to reduced binding of mutant ZAP70 to the phosphorylated TCR zeta-chain, thus functions as a null-allele. In contrast, the R360P allele in the catalytic domain causes weak constitutive activation of the TCR pathway that is suppressed by the wild type (WT) but not the R192W allele. Therefore, the R360P allele is likely responsible for the disease, but the mechanism remains unclear. We hypothesize that the R360P allele interferes with ZAP70 autoinhibition, results in an increase in T cell antigen sensitivity, enhanced follicular helper T (Tfh) cell differentiation, and excessive auto-reactive T helper cell activity for B cells, thereby leading to a primarily autoantibody mediated disease.

Methods: Using *Zap70* R360P knock-in mice we generated and biochemical and functional assays, we assessed how the R360P mutation affects lymphocyte development, TCR signaling, and Tfh cell differentiation following LCMV infection.

Results: The structural location and biochemical signaling effects of the R360P mutation were consistent with weakening of the autoinhibitory conformation of ZAP70. Mice with a ZAP70 R360P mutation and polyclonal TCR repertoires exhibited relatively normal T cell development but showed evidence of increased signaling, as evidenced in the increase in ZAP70 Y319 phosphorylation and faster calcium mobilization following TCR stimulation. Additionally, the R360P mutation resulted in enhanced follicular helper T cell expansion following LCMV infection. When R360P or WT $CD8^+$-OTI T cells were stimulated by antigen presenting cells preloaded with peptides of different agonist potency, we observed marked augmentation of CD69 induction in R360P cells relative to that of WT cells in the responses to weak (Q4H7, G4) agonists, contrasting with only slight to no enhancement in the responses to strong (OVA, Q4R7) agonists. There was also enhanced proliferation of R360P $CD8^+$-OTI T cell than WT controls in response to weak and self peptides.

Conclusion: Our findings suggest that the R360P mutation is a weak hypermorphic allele of ZAP70, resulting in enhanced TCR signaling through disruption of ZAP70 autoinhibition, and enhanced Tfh cell expansion. The R360P

mutation may allow increased mature T cell sensitivity to weak and self-antigens that would normally be ignored by WT T cells, a mechanism that may contribute to the break of tolerance in human patients with R360P mutation.

Disclosure: L. Shen, None; **M. Matloubian**, None; **T. Kadlecek**, None; **A. Weiss**, Genentech, 5, Portola Pharmaceuticals, 5.

Abstract Number: 1402

Galectin-3 Decreases the Activity of 4-1BB by Facilitating Its Decoy Surface Binding in Rheumatoid Arthritis

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SESSION INFORMATION
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Background/Purpose: Orchestration of immune checkpoints is central for the outcome of immune activation, especially in patients with rheumatoid arthritis (RA). We have previously shown that galectin-9 (Gal-9) binding to 4-1BB is central for the increased cytokine production in RA[1]. Here we extend these studies, showing that Gal-3 has the opposite effect, leading to decreased 4-1BBL signaling in RA.

We hereby aim to investigate the modulatory potential of Gal-3 on 4-1BB in RA.

Methods: Gal-3 and 4-1BB were measured in plasma, synovial fluid and synovial tissue samples from RA patients (n=8). Fluorescence polarization and surface plasmon resonance (SPR) analyses were used to evaluate the binding between 4-1BB, 4-1BBL and Gal-3. Synovial fluid mononuclear cells (SFMCs) from patients with RA were cultured for 24 hours and co-incubated with either 4-1BB, 4-1BBL, Gal-3, or combinations thereof. Nanoparticle Tracking Analysis (NTA) was used to detect Gal-3 and 4-1BB complexes in healthy control (HC) plasma (n=10), RA plasma, and synovial fluid samples (n=10). Flow cytometry and Imagestream analyses were performed to detect complex-depletion to the cell membrane and evaluate the functional implications of complex-depletion. Glycan dependence was shown by addition of a Gal-3-specific inhibitor, lactose, or using PNGase F pretreatment of the cells.

Results: In RA, Gal-3 and 4-1BB levels in synovial fluid were increased by a factor 4 and 12 compared with paired plasma ($p< 0.05$), ($p< 0.01$) respectively. Cells expressing 4-1BB also co-expressed Gal-3 in the inflamed RA synovial tissue. Gal-3 was capable of binding to both soluble and membrane bound 4-1BB with a K_D=1.79 m M, without interfering with the binding of 4-1BBL. In plasma, Gal-3 was detected as part of complexes > 300 nm in size. Activated 4-1BB$^+$ T cells and 4-1BB transfected HEK293 cells were both capable of depleting these complexes from plasma ($p< 0.01$) . After cell mediated depletion, expression levels of Gal-3 and 4-1BB complexes were increased on the cell surface compared with untreated cells ($p< 0.05$). T he increase in 4-1BB expression was accompanied by a 4-fold decreased in TNFa production ($p< 0.01$). Gal-3^{high}4-1BB^{high} T cells, were now found to be less responsive to 4-1BBL stimulation. In RA patients, complexes containing Gal-3 were dramatically reduced in both plasma and synovial fluid ($p< 0.01$). The level of Gal-3 complexes in RA plasma correlated inversely with disease activity (DAS28crp). Pro-

duction of MCP-1 in SFMC cultures stimulated with Gal-3, followed by 4-1BBL, decreased by 50% compared with untreated cultures or cultures stimulated with either 4-1BBL or Gal-3 alone ($p < 0.05$).

Conclusion: Gal-3 is a carbohydrate-dependent 4-1BB binding protein, which does not block the co-binding of 4-1BBL. In plasma and synovial fluid, Gal-3 binds to s4-1BB and forms complexes which again can bind to T cells, followed by a decreased cytokine production. These observations provide evidence that galectins control the effects of 4-1BB signaling in RA by decoy binding, highlighting the interplay between galectins and an important checkpoint molecule in RA.

References

1. Nielsen MA et al. Rheumatology (Oxford). 2016

Disclosure: M. Nielsen, None; **K. Juul-Madsen**, None; **J. Stegmayr**, None; **C. Gao**, None; **T. Kragstrup**, Pfizer, 8, Eli Lilly, 8, Novartis, 8, UCB, 8, Gilead, 5, Bristol-Myers Squibb, 5, 8, iBiotech ApS, 4; **M. Hvid**, None; **T. Vorup-Jensen**, None; **R. Cummings**, None; **H. Leffler**, Galecto Biotech AB, 1, 2, 4, 5; **B. Deleuran**, None.

Abstract Number: 1403

Differential Effect of Abatacept vs TNF Blockers, on the Frequency of Circulating Follicular Helper (Tfh) and Periperal Helper (Tph) T Cells in Rheumatoid Arthritis

María-José Santos-Bornez[1], Paula Fortea-Gordo[1], Laura Nuño[1], Alejandro Villalba[1], Diana Peiteado[1], Irene Monjo[2], Alejandro Balsa[3] and Maria-Eugenia Miranda-Carus[1], [1]Hospital La Paz - IdiPAZ, Madrid, Spain, [2]Rheumatology, La Paz University Hospital- IdiPAZ, Madrid, Spain, [3]Rheumatology, La Paz University Hospital-IdiPAZ, Madrid, Spain

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

Background/Purpose: CXCR5+PD-1^{hi} follicular helper (Tfh) and CXCR5-PD-1^{hi} peripheral helper (Tph) T cells play an important role in the pathogenesis of Rheumatoid Arthritis (RA) by providing help to autoantibody secreting B cells. Whereas Tfh cells typically dwell in the germinal centers of lymphoid organs, Tph cells accumulate at inflamed tissues. An increased frequency of Tph cells and of circulating counterparts of Tfh cells have been described in the peripheral blood of patients with seropositive RA. Our objective was to examine the effect of treatment escalation using biological agents (TNF blockers or abatacept), on the frequency of circulating Tfh (cTfh) and Tph (cTph) cells in RA.

Methods: Peripheral blood was drawn from seropositive RA patients with an incomplete response to csDMARDS (n=29) who initiated biological therapy with TNF blockers (TNFb) (n= 17) or abatacept (n= 12), prescribed based on routine clinical practice. cTfh and cTph cell frequencies were determined by flow cytometry of freshly isolated PBMCs at the basal visit and 6 months after starting treatment escalation. For each patient, an age and gender-matched healthy control (HC) was also studied at both time points (n=29).

Results: As compared with HC, active RA patients receiving csDMARDs demonstrated a baseline increased frequency of both cTfh and cTph cells. A significant improvement of disease activity as determined by the DAS28 score

(ΔDAS28 >2.0) was apparent in all of the patients 6 months after initiating biologicals. At that time point, a significant reduction of the previously elevated cTph cell frequency was observed in both treatment groups. However, cTfh cells remained elevated in patients receiving TNFb notwithstanding a good therapeutic response, whereas subjects receiving abatacept experienced a significant abatement of their cTfh cell frequency. Experimental variation of the cTfh and cTph cell numbers in HC was minimal.

Conclusion: Abatacept but not TNFb, are able to bring down cTfh cell numbers in RA. This indicates that costimulation blockade can help attain an immunological remission, whereas TNF neutralization may allow a persistent pathogenic germinal center overactivity. At the same time, treatment with both abatacept and TNF blockers results in a downmodulation of the previouly elevated cTph cell numbers, in parallel with the remitting local joint inflammation.

Disclosure: M. Santos-Bornez, None; **P. Fortea-Gordo**, None; **L. Nuño**, None; **A. Villalba**, None; **D. Peiteado**, None; **I. Monjo**, None; **A. Balsa**, BMS, 9; **M. Miranda-Carus**, BMS, 9.

Abstract Number: 1404

Investigating the Dermatomyositis Skin Inflammatory Infiltrate Using Image Mass Cytometry

Jay Patel[1], Spandana Maddukuri[2], Yubin Li[3], Christina Bax[4] and Victoria Werth[3], [1]University of Pennsylvania and the Michael J. Crescenz VA Medical Center, Philadelphia, [2]University of Pennsylvania and the Michael J. Crescenz VA Medical Center, Montville, NJ, [3]University of Pennsylvania and the Michael J. Crescenz VA Medical Center, Philadelphia, PA, [4]University of Pennsylvania, Department of Dermatology, Philadelphia

SESSION INFORMATION
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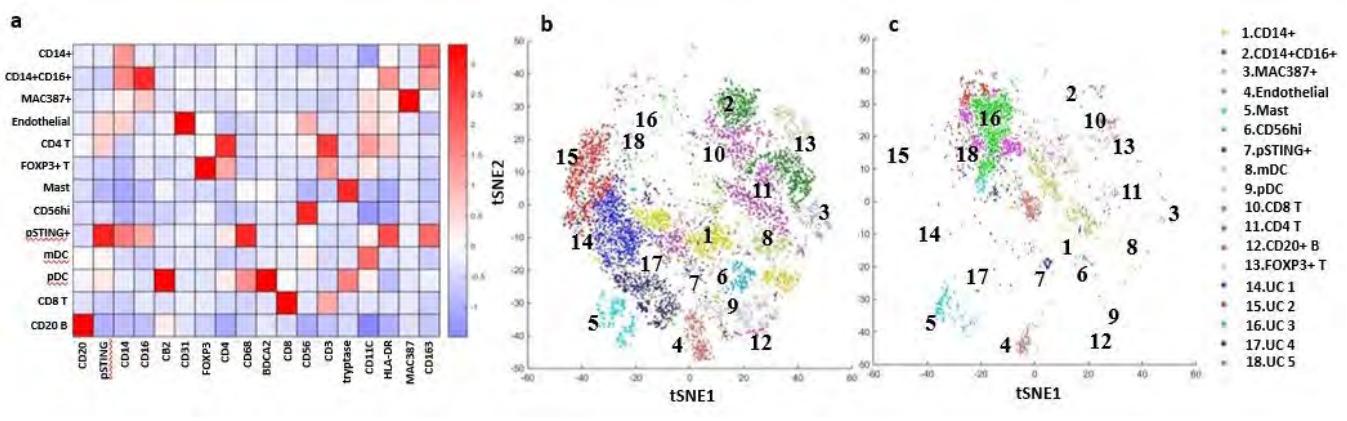
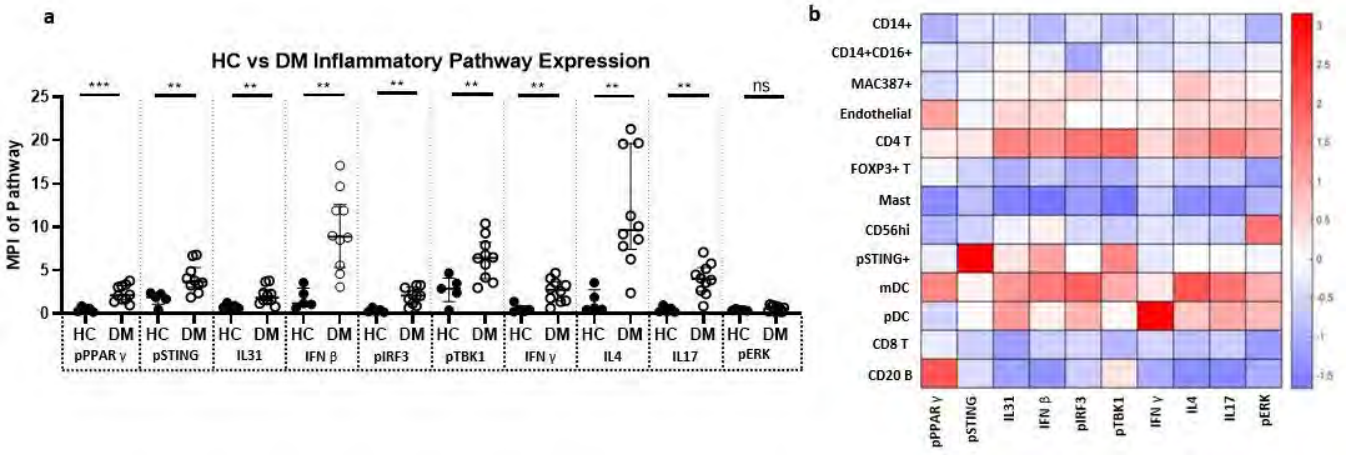
Background/Purpose: Dermatomyositis (DM) is a systemic autoimmune disease affecting the skin and muscles, among other organs. The inflammatory infiltrate in skin has not been fully characterized, but the type I interferon (IFN) system is thought to be a major contributor to disease and has the capacity to interact with multiple cell types. Previous studies have used single or double staining to characterize the complex inflammatory infiltrate, but we implemented image mass cytometry (IMC) and took an unbiased approach to identify possible cellular sources of the type I IFNs and other cytokines.

Methods: We evaluated skin biopsies from 10 patients with moderate-severe DM and 5 healthy controls (HC). IMC was implemented to identify the infiltrate at a single cell level using a diverse set of 37 metal conjugated antibodies. Biopsies were stained with a cocktail of the 37 markers and regions of 1mm x 2mm ablated using the Hyperion Imaging System. Cell were segmented using a nuclear app-based algorithm in Visiopharm. Per cell mean pixel intensity (MPI) analysis was performed using histoCAT. The Phenograph algorithm was used to cluster cells based on expression of cell type markers. Further gating for rare populations was performed using FlowJo and image based sliding scale gates. Statistical analysis included the Mann-Whitney and Spearman rank correlation tests.

Results: We identified CD14+, CD14+CD16+, MAC387+, Endothelial, CD4 T, FOXP3+ T, Mast cells, CD56+, myeloid dendritic (mDC), plasmacytoid dendritic (pDC), CD8+ T, pSTING+, and CD20+ B cells (Fig 1). Monocyte-macrophage diversity was observed with increased numbers of CD14+, CD14+CD16+, MAC387+, and pSTING+ macrophages in lesional DM skin ($p < 0.05$), with the CD14+ population correlating positively with the cutaneous dermatomyositis dis-

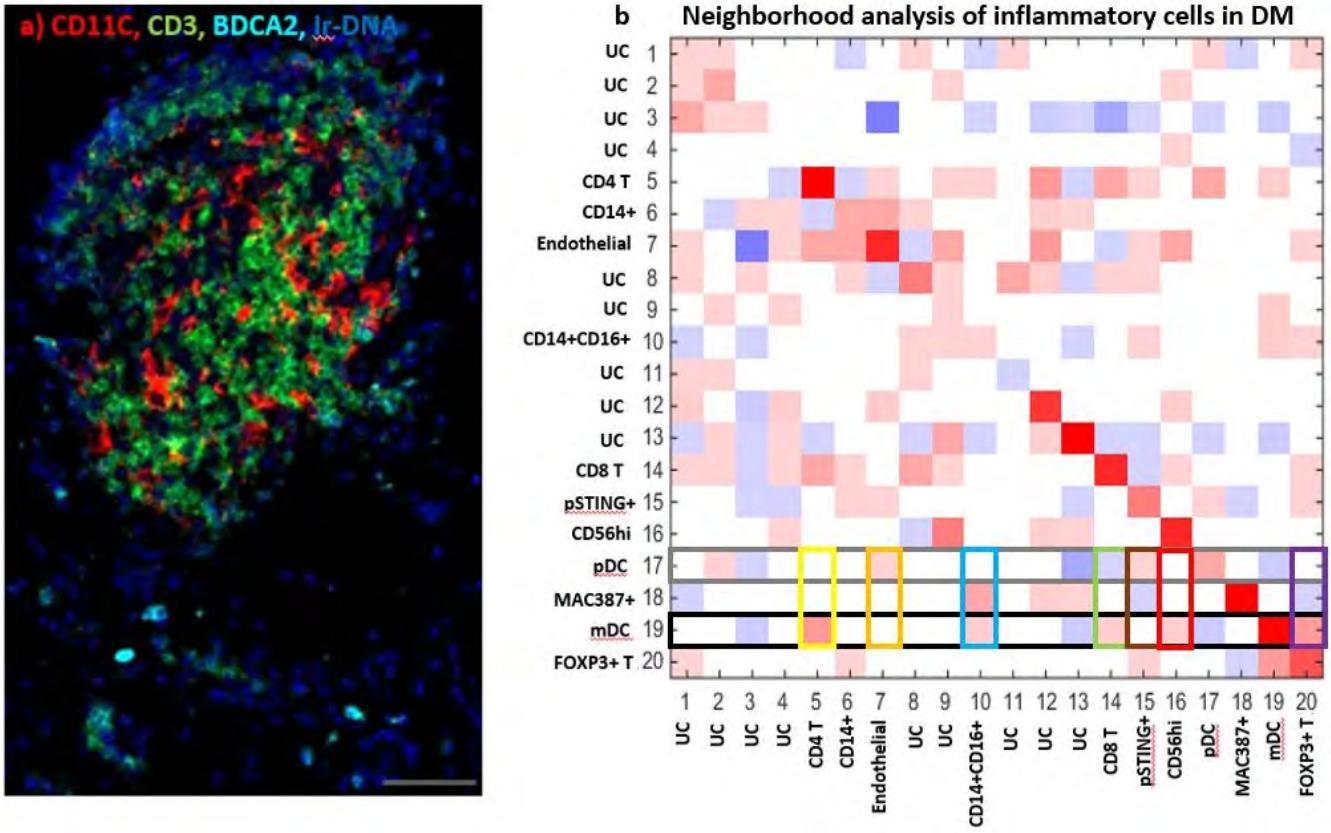


Immune Cells in Dermatomyositis Skin Lesions a) Heatmap of Different Cell Type Markers expressed the 13 cell populations identified: Monocytes (CD14+CD16-), mo-MAC (CD14+CD16+), Macrophages (MAC387+), Endothelial Cells (CD31+), CD4 T Cells (CD4+CD3+), Tregs (FOXP3+CD4+CD3+), Mast Cells (tryptase++), CD56+ Cells, pSTING+ mo-MAC (pSTING++,CD14+CD16+), mDC (CD11C+HLADR+), pDC (BDCA2+), CD8 T (CD8+CD3+), and CD20 B (CD20+). b) tSNE dimensional reduction plot of the different cell clusters identified in lesional DM skin c) tSNE dimensional reduction plot of the corresponding cell clusters in HC skin. Clusters 14-18 represent unidentified clusters (UC)



Inflammatory Pathway expression in Dermatomyositis Skin Lesions a) Expression of pPPARγ, pSTING, IL31, IFNβ, pIRF3, pTBK1, IFNγ, IL4, IL17 is increased in DM skin compared to HC skin. There is no significant difference between DM and HC skin pERK expression. b) Heatmap displaying the relative mean expression of each inflammatory pathway in each cell cluster * p<0.05, ** p<0.01, *** p<0.001

ease area and severity index (CDASI) (r=0.697, p=0.031). The T cell compartment revealed CD4, CD8, and FOXP3+ T cells with activated CD69+ circulating memory T cells correlating with CDASI scores (r=0.754, p=0.0151). Inflammatory pathways pPPARγ, pSTING, IL31, IFNβ, pIRF3, pTBK1, IFNγ, IL4, and IL17 were all upregulated compared to HC (p< 0.05, Fig 2); pERK did not differ. IFNβ protein is upregulated in T cell, macrophage, dendritic, and endothelial cell populations of DM skin (p< 0.05) with mDC IFNβ trending highest. IL4+ and IL31+ mDCs were found to correlate with a Skindex itch score (IL4+: r=0.6547, p=0.0448; IL31+: r=0.7310, p=0.0194). pDCs colocalize with IFNγ in addition to the known IFNβ. The endothelium, mDCs, and B cells in DM skin express pPPARγ. Neighborhood analysis reveals significant interactions between mDCs and CD4, CD8, FOXP3+ T cells while pDCs interact with pSTING+ macrophages (p< 0.05, Fig 3).



Neighborhood Analysis of Dermatomyositis skin infiltrate allowed for the visualization of different immune cells in DM skin and their spatial relationship to each other. CD11C+ mDCs (red, a) are seen to be intertwined with CD3+ T cells (green, a) whereas BDCA2+ pDCs are scattered throughout the tissue (cyan, a). Neighborhood analysis of n=7 DM lesional skin biopsies using histoCAT (b) reveals cell to cell interactions displayed as a heatmap with red representing a positive (neighbored) association ($p<0.05$), white as an insignificant association ($p>0.05$), and blue as a negative (avoided) association ($p<0.05$). Rows signify cells surrounding a cell type of interest. Columns signify the cell type of interest surrounding other cell types. The heatmap shows mDCs (black bar) may interact with CD4 T(yellow bar), CD14+CD16+ macrophages (cyan bar), CD8 T (green bar), CD56(NCAM) hi cells (red bar), and FOXP3+ T (purple bar) while pDCS (gray bar) may interact more with the endothelial cells (orange bar) and pSTING+ cells (brown bar). Scale bar (a) = 60 μm (gray).

Conclusion: The immune infiltrate in DM is complex and consists of a dominant monocyte-macrophage-myeloid cell axis that may contribute to IFNβ related pathogenesis and IL4, IL31 related pruritus. Findings of interest are CD14+ monocytes, pSTING+ macrophages, IFNγ+ pDCs, and pPPARγ+ endothelial cells and active mDCs, which requires further investigation. The use of IMC allows for single cell characterization of the immune cell population seen in DM skin and possible novel targeted therapeutics.

Disclosure: J. Patel, None; **S. Maddukuri**, None; **Y. Li**, None; **C. Bax**, None; **V. Werth**, Biogen, 2, 5.

Abstract Number: 1405

Evaluating the Cellular Composition of Anti-synthetase Syndrome and Dermatomyositis Skin Lesions Using Image Mass Cytometry

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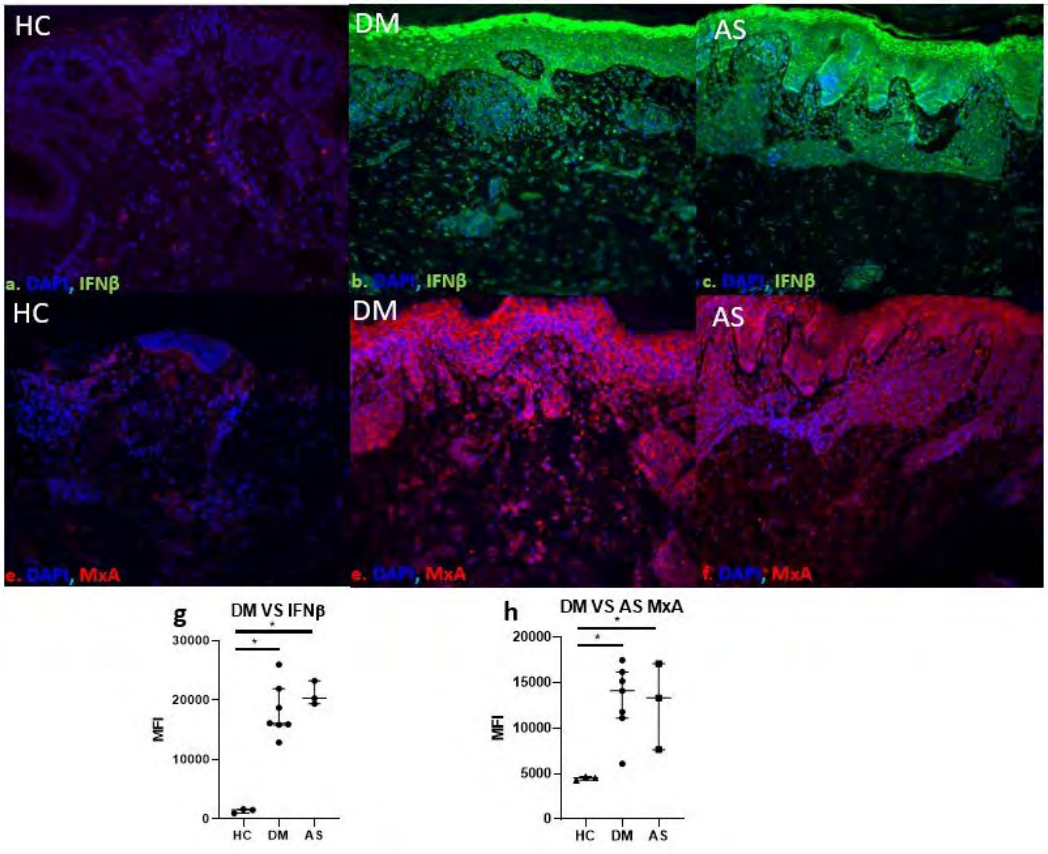
Session Time: 9:00AM–11:00AM

Background/Purpose: Antisynthetase syndrome (AS) is a systemic autoimmune disorder characterized by the presence of anti-aminoacyl-tRNA synthetase antibodies, myositis, interstitial lung disease (ILD), mechanics hands, and raynaud's phenomenon. Dermatomyositis (DM) is a similar autoimmune disorder with clinical features of muscle weakness, ILD, neoplasms, gottron's papules, and photosensitive cutaneous manifestations. Currently most clinicians see AS as a subclassification under DM due to the many similarities. Recently some studies have emerged identifying differences in the type I interferon system between AS and DM muscle and finger eruptions. Type I interferons are amplified in autoimmune diseases such as DM, as demonstrated by proteins such as MxA expression. To further characterize these differences, we investigated the cellular composition and inflammatory pathway profile using immunofluorescent staining (IF) and image mass cytometry (IMC).

Methods: We evaluated skin biopsies from back, arm, or leg of 7 DM patients, 3 AS patients, and 3 healthy control (HC). IF was performed on 3 biopsies from each group for IFNβ and MxA. Subsequently, IMC was implemented to further identify differences between DM and AS using metal conjugated antibodies. Biopsies were stained with a cocktail of markers and 1mm x 2mm regions were ablated using the Hyperion Imaging System. Cells were segmented using a nuclear app-based algorithm in Visiopharm. Per cell mean pixel intensity (MPI) analysis was performed using histoCAT. The Phenograph algorithm was used to cluster cells based on expression of cell type markers. The Kruskal Wallis test was used to identify immunofluorescence IFNβ and MxA differences between HC, DM, and AS groups corrected for multiple comparisons by controlling False Discovery Rate. The Mann Whitney test was used to identify differences in IMC cell populations and pathway expression between AS and DM skin lesions, including mDC IFNβ.

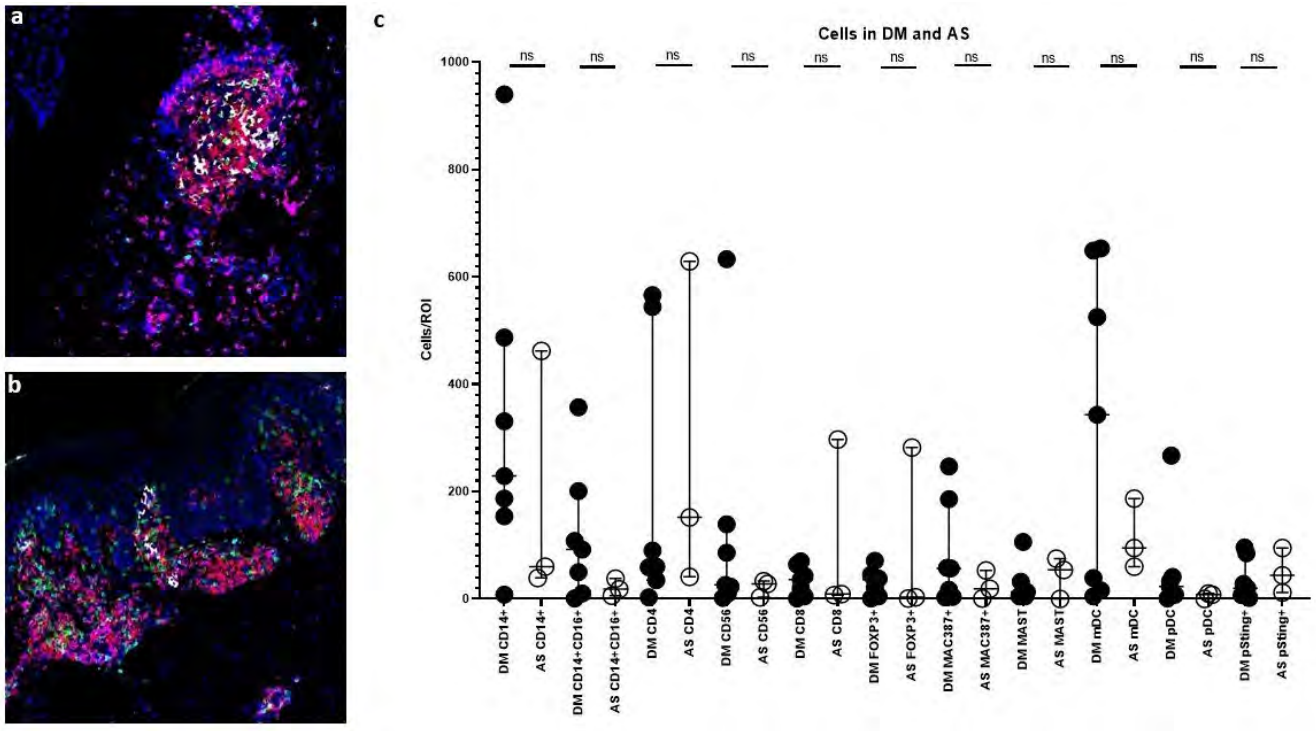
Results: IF of AS skin showed increased IFNβ and MxA compared to HC ($p < 0.05$, Fig 1) but there was no difference compared to DM IFNβ and MxA ($p > 0.05$, Fig 1). IMC cell clusters in AS and DM were similarly distributed and we identified no differences in the cell populations (macrophages, T cells, and dendritic cells) of AS and DM ($p > 0.05$, Fig 2). Despite no statistical differences in cells there is a trend for increased CD14+CD16+, mDCs, and pDCs in DM. Pathway expressions of pPPARγ, pSTING, IL31, IFNβ, MxA, pTBK1, IFNγ, and pERK also did not differ between AS and DM ($p > 0.05$, Fig 3). The pIRF3, IL4, and IL17 pathways were increased in DM compared to AS skin lesion ($p=0.04$, 0.01, and 0.01, Fig 3). Both AS and DM mDCs produced IFNβ (Fig3), but there was no difference in mDC IFNβ between AS and DM ($p > 0.05$, Fig 3).

Conclusion: A similar immune composition exists in AS and DM skin and there is a role for the type I interferon system in AS, however there may be differences in the extent of involvement due to decreased pIRF3,trends for decreased MxA, and dendritic cells. Additional differences in cytokines IL4 and IL17 exist with increased expression

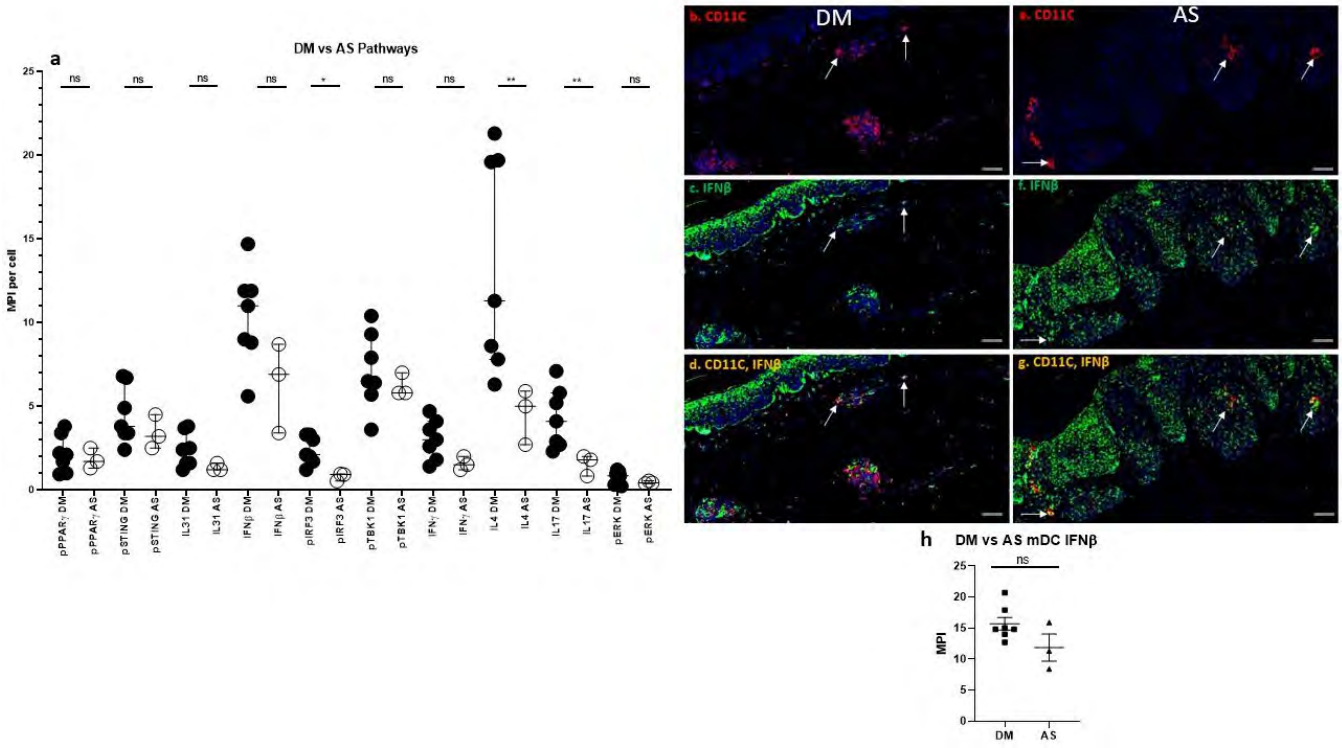


Immunofluorescence staining of IFNβ and MxA in HC, DM, and ASA skin a-c) HC skin has little IFNβ (green, a) compared to DM skin (b) and ASA skin (c). e-f) HC skin also has decreased MxA (red, d) compared to DM skin (e) and ASA skin (f) with DAPI in blue (a-f). Quantification of mean fluorescence intensity shows increased IFNβ in DM and ASA lesional skin compared to HC (g) and increased MxA expression in DM and ASA lesional skin compared to HC (h). Nuclei represented by DAPI (blue, a-f) * $p<0.05$

in DM. However, the two diseases overlap significantly supporting their current classification, but larger studies are still needed to clarify differences.



Immune Cell quantification between HC, DM, and AS patients using Image Mass Cytometry PhenoGraph populations. a-b) Multiplexed image of lesional DM(a) and AS(b) skin revealing similar cells CD4 (red), CD8(green), DNA (blue), CD11C+ (white), BDCA1+ (cyan), and CD14+ (magenta) cells. c) The cell counts of CD14+, CD14+CD16+, MAC387+, CD4+, FOXP3+, Mast, CD56+, pSTING+CD14+CD16+, mDC, pDC, and CD8 were compared between DM and AS skin lesions. No significant differences were found between DM and AS for all cell populations.



Mean Pathway Expression in skin lesions of DM and ASA patients a) The mean expression per cell of pathways pPPARγ, pSTING, IL31, IFNβ, pRF3, pTBK1, IFNγ, IL4, IL17, and pERK was compared between AS and DM skin lesions. No significant differences between DM and AS were observed for pPPARγ, pSTING, IL31, IFNβ, pTBK1, IFNγ, and pERK. DM skin had increased expression of pIRF3, IL4, and IL17. b-g) DM and AS mDCs express IFNβ. CD11C mDCs (red, b,e) overlap with IFNβ (green, c,f) as seen in yellow (d,g). Individual mDCs overlapping with IFNβ are highlighted with white arrows. Nuclei represented with Ir-Intercalator (blue, b-g). Scale bars (gray) = 50μm h) DM and AS mDCs do not differ in mean IFNβ expression at a single cell level. * p<0.05, ** p<0.01,

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Disclosure: J. Patel, None; **A. Ravishankar**, None; **S. Maddukuri**, None; **C. Bax**, None; **V. Werth**, Biogen, 2, 5.

Abstract Number: 1406

LAG-3$^+$ T Cells Are Diminished in Active Psoriatic Arthritis Patients and Their Restoration in Vitro Is Mediated by TNF Inhibitors

Smadar Gertel[1], Ari Polachek[2], Victoria Furer[3], David Levartovsky[3] and Ori Elkayam[4], [1]Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel, [2]Tel Aviv Sourasky Medical Center, Petah-Tikva, Israel, [3]Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, [4]Tel Aviv Sourasky Medical Center, Tel-Aviv, Israel

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is a chronic inflammatory arthritis associated with psoriasis. Aberrant T cell regulation has been implicated in the process of inflammation in PsA. One of the regulatory receptors expressed on T cells is lymphocyte-activation gene (LAG)-3. We aimed to assess the surface expression levels of LAG-3 on CD4$^+$ T cells derived from PsA patients with low and high disease activity in comparison with healthy controls and to determine the in vitro effect of biologics on the LAG-3$^+$ T cell population.

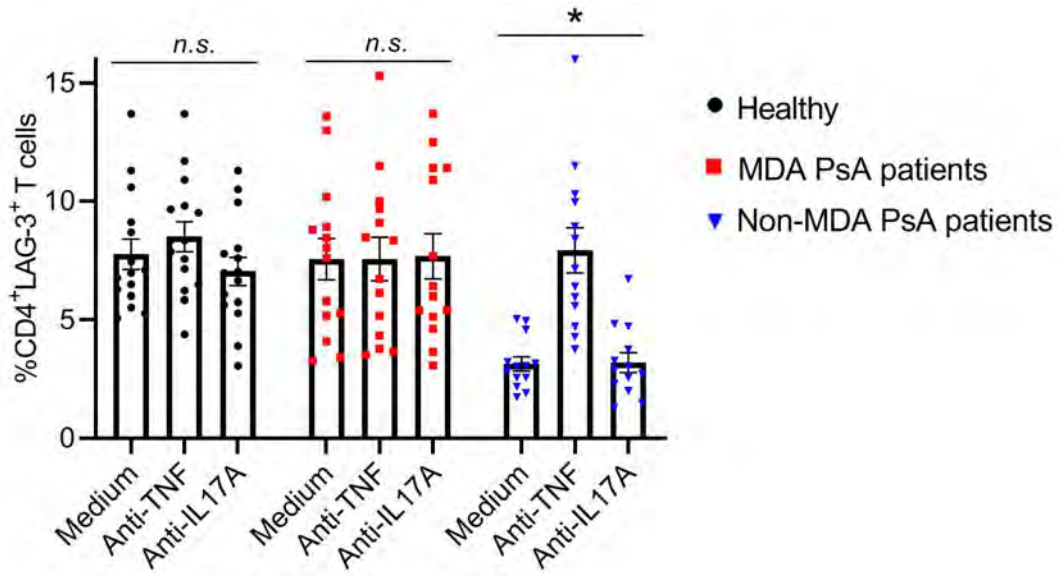


Figure 1. Levels of CD4+LAG-3+ T cells in PBMCs derived from healthy, MDA and non-MDA PsA patients and the ability of TNF and IL-17 inhibitors to modulate the CD4+LAG-3+ T cells in vitro. Freshly isolated PBMCs from healthy donors (n=15), MDA (n=14) and non-MDA (n=13) PsA patients were co-cultured for 5 days in RPMI medium alone or supplemented with TNF inhibitor (Adalimumab) or IL-17A inhibitor (Ixekizumab). Cells were subsequently stained with CD4 and LAG-3 Abs. Surface CD4 and LAG-3 expression was determined by flow cytometry. Graphs represent the mean percentages ±SEM of CD4+LAG-3+ T cells. Significance between groups was determined by Mann-Whitney U test, * $p < 0.0001$.

Methods: Consecutive patients with PsA were recruited to this study, clinically assessed and classified as having minimal disease activity (MDA) or non-MDA. healthy donors were included as controls. Peripheral blood mononuclear cells (PBMCs) were co-cultured with medium alone or with TNF or IL-17A inhibitors and their effect on $CD4^+LAG\text{-}3^+$ T cells proportion was determined.

Results: The basal levels of $CD4^+LAG\text{-}3^+$ T cells in fresh PBMCs was undetectable, we then used in vitro conditions to detect $CD4^+LAG\text{-}3^+$ T cells. In PBMCs derived from healthy controls (n=15) as well as from MDA PsA patients (n=14) the percentages of $CD4^+LAG\text{-}3^+$ T cells after 5 days of in vitro incubation with medium alone was (7.7±0.6 and 7.5±0.9, respectively). Supplementation of either TNF or IL-17A inhibitors to the culture had no effect on the percentages of $CD4^+LAG\text{-}3^+$ T cells (8.5±0.6, 7.0±0.6 and 7.6±0.9, 7.7±0.9, respectively) (Figure 1).

In contrast, significantly lower percentages of $CD4^+LAG\text{-}3^+$ T cells were found in non-MDA (n=13) (3.1±03, $p< 0.0001$) as compared to MDA PsA patients and healthy controls (7.7±0.6 and 7.5±0.9). In non-MDA PsA patients, incubation with TNF inhibitor restored the percentages of $CD4^+LAG\text{-}3^+$ T cells compared to medium control (7.9±0.9, $p< 0.0001$), to an equivalent levels as determined after incubation with medium alone in healthy and MDA PsA patients. On the other hand, after supplementation of IL-17A inhibitor the $CD4^+LAG\text{-}3^+$ T cells proportion remain low (3.2±0.4).

Moreover, there was a significant inverse correlation between percentages of $CD4^+LAG\text{-}3^+$ T cells after in vitro culture with medium alone and the clinical disease activity of the PsA patients in the cohort (CPDAI, r=-0.47, $p < 0.02$ and PASDAS, r=-0.51, $p < 0.008$).

Conclusion: Lower surface LAG-3 expression levels on $CD4^+$ T cells may reflect active PsA disease state. TNF inhibitors have potency to up-regulate this population. Larger studies are needed to verify this observation.

Disclosure: S. Gertel, None; **A. Polachek**, None; **V. Furer**, None; **D. Levartovsky**, None; **O. Elkayam**, None.

Abstract Number: 1407

Resolvin D5 Modulates Th17/Treg Cell Differentiation and Suppresses Osteoclastogenesis

Hirotaka Yamada[1], Jun Saegusa[2], Sho Sendo[3], Yo Ueda[4], Takaichi Okano[1], Yoshikazu Fujikawa[5], Yuzuru Yamamoto[6], Takumi Nagamoto[1], Yoshihide Ichise[1], Ikuko Naka[1], Kengo Akashi[7], Akira Onishi[7], Masakazu Shinohara[1] and Akio Morinobu[7], [1]Kobe University, Kobe, Japan, [2]Department of Clinical Laboratory, Kobe University Hospital, Kobe, Japan, [3]Kobe University, Kobe, [4]Kobe UniversityRheumatology and Clinical Immunology, Kobe University Hospital, Kobe, Japan, [5]Kobe University, Kobe city, Japan, [6]Kobe University, Kobe-city, Japan, [7]Rheumatology and Clinical Immunology, Kobe University Hospital, Kobe, Japan

SESSION INFORMATION

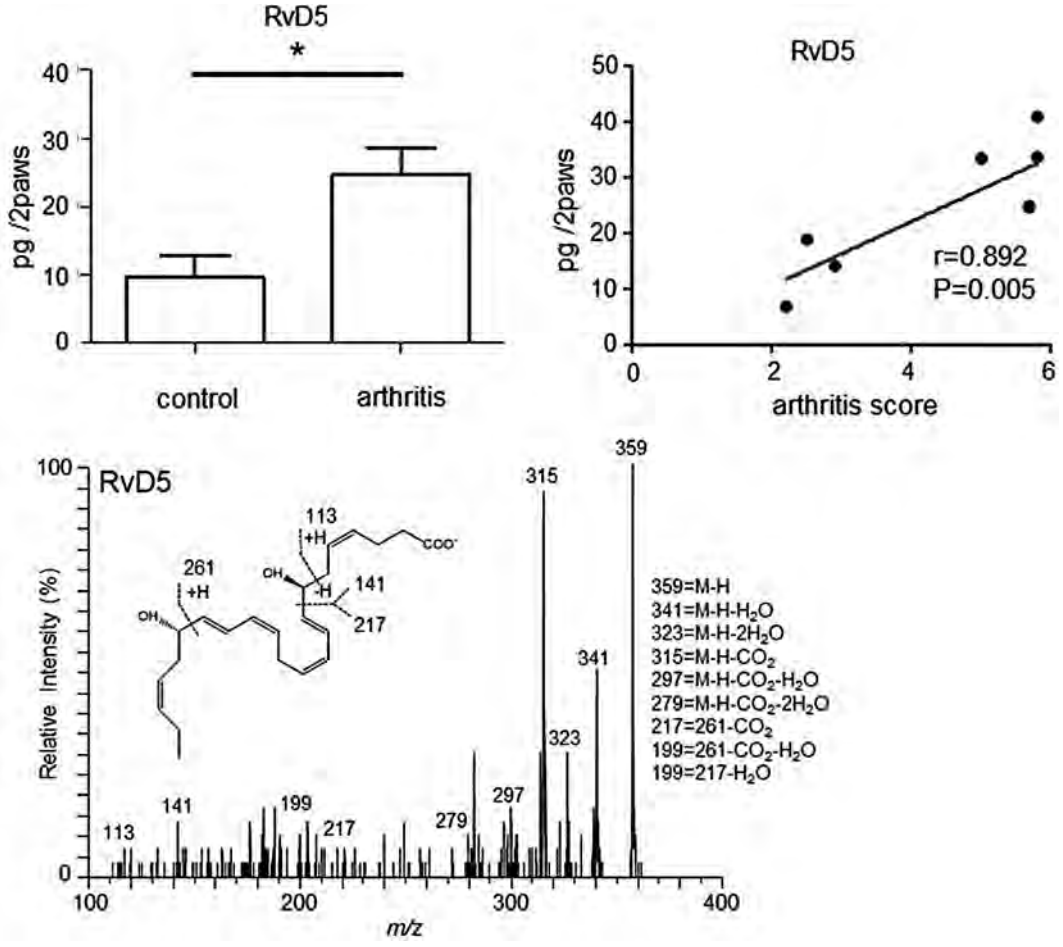
Session Date: Sunday, November 8, 2020

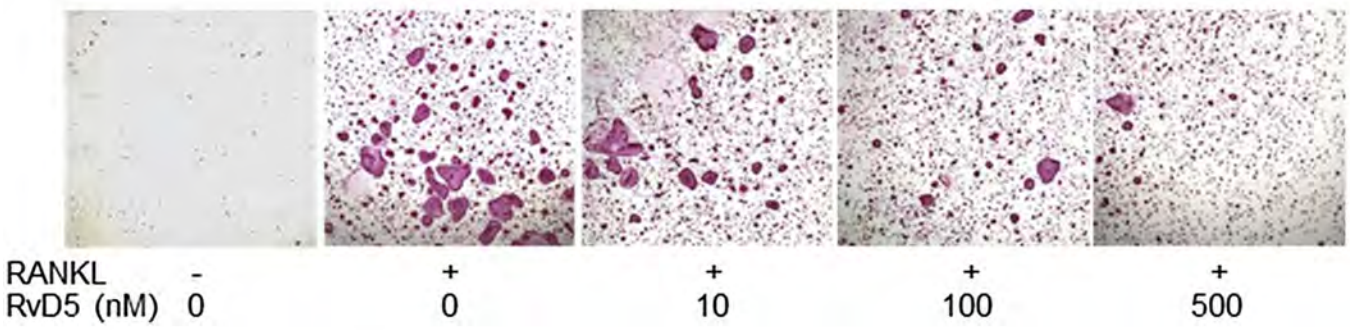
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster

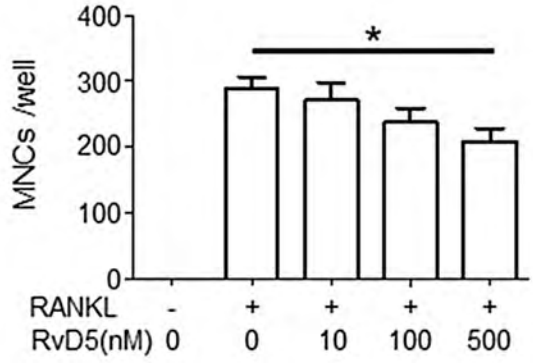
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Over the last two decades, it has become increasingly clear that resolution of acute inflammation is not a passive process, but requires active modulation. This is tightly regulated by families of novel potent bioactive lipid mediators (LM), which have been termed “specialized pro-resolving mediators” (SPMs), but little is known concerning their role in chronic inflammation, such as in rheumatoid arthritis (RA). This study was conducted to investigate whether LM are involved in the pathogenesis of RA.







Methods: We performed LM profiling on inflamed arthritic paws in a mouse model of RA by using lipid chromatography (LC) /mass spectrometry (MS) /MS-based LM metabololipidomics. $CD4^+$ T cells from splenocytes of SKG mice were cultured on anti-CD3/ CD28 mAbs precoated plate with IL-6/TGF-β, anti-IFNγ/IL-4 and SPMs were added daily from day 0. On day 3, cells were analyzed by flow cytometry. $CD4^+$ T cells were incubated with CFSE and RvD5 was added daily. On day 3, cell proliferation was analyzed by flow cytometry. Mouse bone marrow cells were cultured with M-CSF and RANKL and RvD5 was added daily. Tartrate-resistant acid phosphatase (TRAP)-positive multinucleated cells were defined as osteoclasts and counted under a microscope. Osteoclast differentiation markers were analyzed by quantitative RT-PCR.

Results: We found that RvE3, RvD1, RvD3, RvD5 and Maresin2 were significantly elevated in the arthritic paws. Of the elevated SPMs, levels of RvD5 correlated significantly with arthritis disease activity (Figure 1). We also found that RvD5 inhibited the differentiation of $Ror\gamma t^+$ Th17 cells and increased the population of $Foxp3^+$ regulatory T (Treg) cells. In addition, RvD5 inhibited $CD4^+$ T cell proliferation. Furthermore, RvD5 attenuated osteoclast differentiation and interfered osteoclastogenesis at the molecular level (Figure 2).

Conclusion: RvD5 is increased in the paws of arthritic mice, suppresses Th17 cell differentiation and $CD4^+$ T cell proliferation, facilitates Treg cell differentiation, and suppresses osteoclastogenesis.

Disclosure: H. Yamada, None; **J. Saegusa**, None; **S. Sendo**, None; **Y. Ueda**, None; **T. Okano**, None; **Y. Fujikawa**, None; **Y. Yamamoto**, None; **T. Nagamoto**, None; **Y. Ichise**, None; **I. Naka**, None; **K. Akashi**, None; **A. Onishi**, None; **M. Shinohara**, None; **A. Morinobu**, None.

Abstract Number: 1408

Metabolic Reprogramming in Memory CD4+ T Cells Is Associated with Immune Cell Dysfunction During Aging

Yuling Chen[1], Yuanchun Ye[2], Hao Wu[3], Pierre-Louis Krauß[1], Pelle Löwe[1], Moritz Pfeiffenberger[1], Lisa Ehlers[1], Thomas Buttgereit[4], Paula Hoff[5], Frank Buttgereit[6] and Timo Gaber[1], [1]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Rheumatology and Clinical Immunology, Berlin, Germany, [2]Charité – Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Hematology, Oncology and Tumor Immunology, Berlin, Germany, [3]Julius-Maximilians Universität Würzburg, Institut für Systemimmunologie, Würzburg, Germany, [4]Charité-Universitätsmedizin Berlin, corporate member of Freie Universität Berlin, Humboldt-Universität zu Berlin, and Berlin Institute of Health, Department of Dermatology, Venerology, and Allergology, Berlin, Germany, [5]Endokrinologikum Berlin, Rheumatologie, Berlin, Germany, [6]Charité University Medicine, Berlin, Germany

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Inflamm-aging is a chronic, sterile, low-grade inflammatory status, characterized by an increase of proinflammatory cytokines which participate in the development of most age-related diseases such as cancer, Alzheimer's disease, type 2 diabetes mellitus, stroke, cardiovascular diseases, and rheumatoid arthritis (RA). As cellular metabolism modulates T cell function, it can be assumed that metabolic changes accompany the differentiation of memory CD4+ T cells into senescent CD4+ T cell and contribute to memory CD4+ T cells dysfunction during aging. Therefore, we hypothesized that metabolic reprogramming in memory CD4+ T cells might represent an essential factor promoting immune cell dysfunction during aging, thereby fueling to the pathogenesis of age-related diseases including RA

Methods: To this end, we analyzed memory CD4+ T cells isolated from PBMCs of young donors (20-32 years) and old donors (52-67 years) by using MACS™ technology. *Ex vivo* memory CD4+ T cells were analyzed by Seahorse™ Technology to determine proton efflux rate (PER) as a measure of glycolysis (glycPER) and oxygen consumption rate (OCR) as a measure of mitochondrial respiration (mitoOCR). Cytokine expression and secretion was measured by flow cytometry and multiplex assay. Finally, TCR-stimulated memory CD4+ T cell proliferation was determined using CSFE and Ki-67 after 3 days and 4 days by flow cytometry.

Results: In a quiescent state, memory $CD4^+$ T cells from elderly individuals demonstrated a decrease in basal glycolysis and compensatory glycolysis, and an increase in the ratio of basal mitochondrial oxygen consumption rate (mitoOCR) to glycolytic proton efflux rate (glycoPER) while their mitochondrial profile was equivalent to that of young donors. In comparison to the younger reference group, memory $CD4^+$ T cells from aged donors presented a greater spare respiratory capacity after TCR-activation. Interestingly, we did not observe an impact of aging on memory $CD4^+$ T cell proliferation as determined by CFSE and Ki-67. Although the capacity of intracellular cytokine expression did not differ between the compared groups, the levels of secreted IFN-γ, IP-10, IL-6, IL-9, and MCAF were significantly higher in the supernatants of memory $CD4^+$ T cells taken from aged donors.

Conclusion: These findings suggest that metabolic reprogramming in human memory $CD4^+$ T cells during aging results in an increased expression of proinflammatory cytokines. This process may culminate in T cell dysfunction

and thus contribute to the pathogenesis of inflamm-aging and the development of age-related diseases such as rheumatoid arthritis (RA).

Disclosure: Y. Chen, None; **Y. Ye**, None; **H. Wu**, None; **P. Krauß**, None; **P. Löwe**, None; **M. Pfeiffenberger**, None; **L. Ehlers**, None; **T. Buttgereit**, None; **P. Hoff**, None; **F. Buttgereit**, AbbVie, 8, Eli Lilly, 8, Pfizer, 8, Roche, 8; **T. Gaber**, None.

Abstract Number: 1409

Lack of Conventional Acinar Cells in the Salivary Gland Following Anti PD-L1 and anti-PD-1 Immune Checkpoint Inhibitor Therapy

Sarah Pringle[1], Bert van der Vegt[1], Xiaoyan Wang[1], Nico van Bakelen[1], Arjan Vissink[1], Frans Kroese[2] and Hendrika Bootsma[2], [1]UMCG, Groningen, [2]University Medical Centre Groningen, Groningen, Netherlands

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Salivary glands (SGs) can be damaged by immune checkpoint inhibitor (ICI) therapy. In patients with ICI-induced SG dysfunction, 60% progress to fulfill the ACR-EULAR 2016 classification criteria for primary Sjögren's syndrome (pSS), owing to immune foci in SGs and/or anti-SSA autoantibody positivity. We report the SG tissue analysis of 2 patients with SG dysfunction after treatment with anti PD-L1 and PD-1 ICIs, compared to that of a dry mouth ("sicca") control and pSS patient.

Methods: Immunostaining for CD4, CD8, Keratin7 (K7), AQP5, Ki67, and PD-L1 was performed in two parotid SG biopsies from patients following ICI therapy, and in control and a pSS patient tissue. The first patient (male, 52 yrs) received fortnightly infusions of 10mg/kg durvalumab (anti-PD-L1 therapy), for non-small cell carcinoma (NSNLC). After 43 weeks (22 cycles) of treatment, the patient was not capable of producing stimulated or unstimulated whole saliva, and demonstrated SSA-positivity. The second patient (female, 74) received infusions of pembrolizumab (anti-PD-1) every 3 weeks for treatment of NSNLC, at a flat dose of 200mg. This patient was not capable of producing unstimulated whole saliva, and demonstrated reduced 0.12mL/min stimulated whole saliva production, after 15 weeks (5 cycles) of treatment. Both patients were SSA-positive following ICI treatment.

Results: In contrast to control and pSS tissue, following anti-PD-L1 and anti-PD-1 blockade, only few $AQP5^+$, classically shaped acinar cell clusters were observed in the parotid SG after treatment with anti-PD-L1 and anti-PD-1 biologicals (Fig. 1a-c). The parenchyma was dominated by hybrid epithelial structures containing a mixture of $AQP5^+$ (acinar cell marker) and $K7^+$ (intercalated duct marker) cells (Figure 1d-f). $AQP5^+K7^+$ cells were also detected. Cells with this unusual phenotype are not seen in control/pSS tissue. More $Ki67^+$ proliferating ID-like cells were detected following PD-L1 or PD-1 therapy, compared to control and pSS SGs. The SG post-PD-L1 and PD-1 therapy demonstrated focal and disperse lymphocytic sialadentitis. Infiltration was $CD4^+$ T cell-rich, although $CD8^+$ T cells were also present. $CD4^+$ and $CD8^+$ T cells were observed in-between and inside hybrid structures. $CD20^+$ B-cells were infrequent. No germinal centers, lymphoepithelial lesions or antibody class-switching following ICI therapy were observed. PD-L1 expression was detected in the SG parenchyma following anti-PD-L1 therapy.

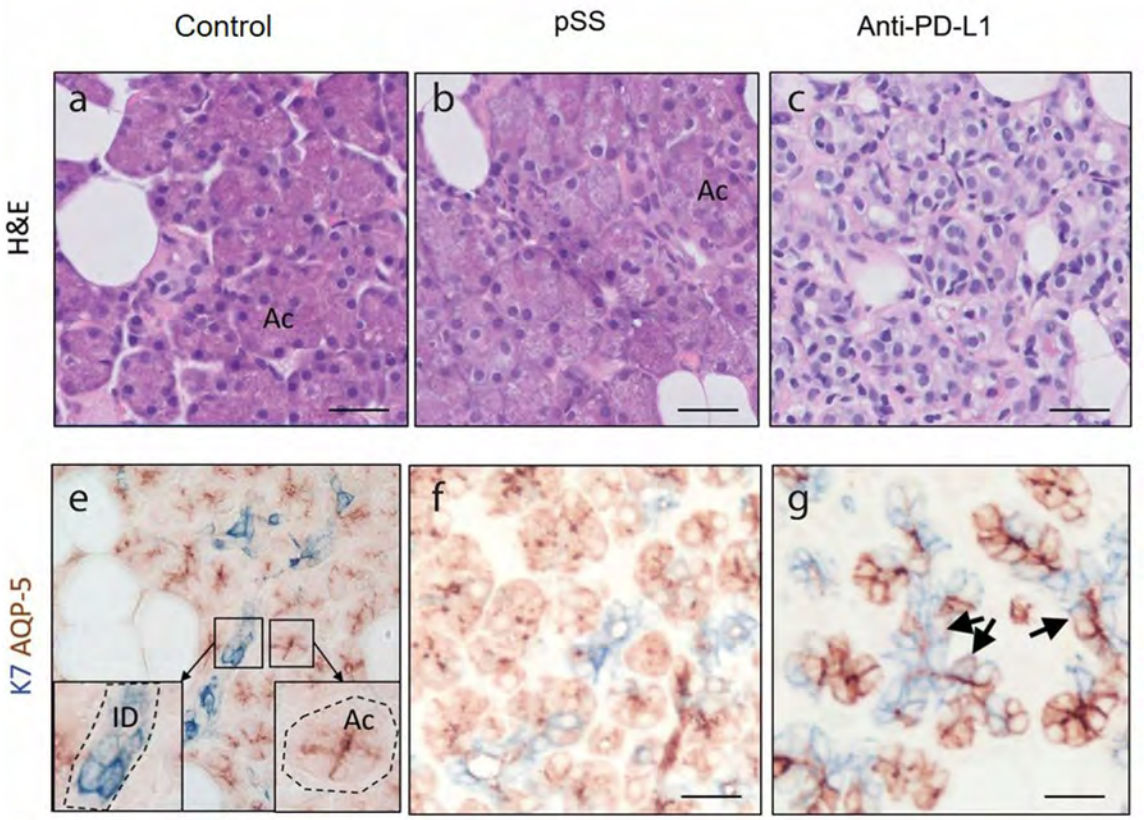


Figure 1. a-c) H&E staining of the parotid salivary gland in sicca control, pSS and post-PD-L1 ICI therapy, showing lack of conventional acinar cell morphology following ICI treatment. d-f) AQP5 and Keratin 7 (K7) double immunostaining, showing presence of unusual hybrid mixed AQP5+K7+ cells post-PD-L1 therapy.

Conclusion: Conventional SG acinar cells were lacking following both anti-PD-L1 and PD-1 ICI therapy. SGs demonstrated presence of hybrid intercalated duct-like structures. Understanding which mechanisms and dynamics underpin this aberrant parenchyma may be crucial to understand how SG dysfunction post-ICI therapy, and potentially other affected organs. Furthermore, although patients post-ICI therapy may fulfill the ACR-EULAR 2016 pSS criteria and demonstrate focal lymphocytic sialadentitis, the further histopathological characteristics do not resemble pSS.

Disclosure: S. Pringle, None; **B. van der Vegt**, Visiopharm, 5; **X. Wang**, None; **N. van Bakelen**, None; **A. Vissink**, None; **F. Kroese**, Bristol-Myers Squibb, 2, 5, 8, Roche, 8, Janssen-Cilag, 8; **H. Bootsma**, Bristol-Myers Squibb, 2, 5, 8, Roche, 2, 5, Novartis, 5, 8, Medimmune, 5, Union Chimique Belge, 5.

Abstract Number: 1410

Resident Memory T Cells Persist in Joints of Anakinra-Treated Mice in Spontaneous Arthritis Model

Anais Levescot[1], Margaret Chang[2], Alexandra Wactor[1], Rachel Blaustein[1], Nathan Nelson-Maney[1], Robert Fuhlbrigge[3] and Peter Nigrovic[4], [1]Brigham and Women's Hospital, Boston, MA, [2]Boston Children's Hospital, Boston, MA, [3]University of Colorado, Denver, CO, [4]Division of Rheumatology, Inflammation and Immunity, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; Division of Immunology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA, Boston

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammatory arthritis is characterized by chronic inflammation of joints which can be suppressed with immunomodulatory therapy. However, two-thirds of patients will have an arthritis flare when medication is stopped. We sought to understand how immune cells that persist in arthritic joints in remission may contribute to subsequent recurrence of disease.

Methods: Using IL-1 receptor antagonist (IL-1Ra)-deficient mice, a spontaneous model of T cell mediated arthritis, we identified animals early in arthritis who exhibit involvement of only one of paired major joints (ankle, wrist). We induced arthritis remission by administration of anakinra, an IL-1Ra analog, and then observed flare pattern when treatment was discontinued. Synovium was dissected from the mice and evaluated for the presence of T cell subsets by flow cytometry. Intraperitoneal injection of anti-Thy1.2 antibodies was utilized to deplete circulating T cells and assess tissue residency.

Results: In IL-1Ra deficient mice, unilateral joint inflammation is suppressed by treatment with anakinra. Intriguingly, subsequent discontinuation of therapy results in arthritis flare preferentially in the originally-inflamed joint, implying a mechanism of joint-specific memory. We identified a population of T cells with a cell surface protein signature consistent with resident memory T cells (CD44+CD62L-CD69+CD103+) is found in the synovium during remission. These cells are only present in joints that were previously inflamed, and persist in the synovium despite antibody-mediated depletion of circulating T lymphocytes, suggesting tissue residency.

Conclusion: Our data suggests that the persistence of T cells with a resident memory phenotype in the synovium of arthritic joints may contribute to arthritis flares when immunomodulatory medication is weaned.

Disclosure: A. Levescot, None; **M. Chang**, None; **A. Wactor**, None; **R. Blaustein**, None; **N. Nelson-Maney**, None; **R. Fuhlbrigge**, None; **P. Nigrovic**, Novartis, 2, 5, BMS, 2, 5, Pfizer, 2, 5, Sobi, 5, Miach Orthopedics, 5, Simcere, 5, XBiotech, 5, Quench Bio, 5, Siglion, 5, Cerecor, 5, UpToDate, 7, American Academy of Pediatrics, 7, CARRA, 9.

Abstract Number: 1411

CD8+ T Cell Subsets and Immune Checkpoint Profiles in Ankylosing Spondylitis Implicate Dysregulation of Cytotoxic T Lymphocytes (CTL)

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing Spondylitis (AS) is characterized by chronic inflammation which underlies the pain and precedes spinal ankylosis. The strongest genetic association with AS is the HLA-B27, implicating involvement of CD8+ cytotoxic T cells (CTL) in AS pathogenesis. To date, the CTL compartment that underlies AS inflammation

has yet to be fully defined. Our lab recently reported altered cytotoxicity profiles in CTL from AS patients, suggesting that dysregulated CTL with a cytotoxic phenotype are recruited to the joints. These findings suggest a central role of dysregulated CTLs in AS pathogenesis, warranting further investigation. Here we sought to characterize CTL subsets and immune checkpoint (IC) expression on CTL from patients with AS.

Methods: We performed immunophenotyping of peripheral blood mononuclear cells (PBMCs) and synovial fluid mononuclear cells (SFMCs) by flow cytometry. A 21- marker mass cytometry time-of-flight (CyTOF) panel is currently being developed to comprehensively assess the CTL compartment in AS patients.

Results: We identified a sub-cohort of AS patients with an enriched population of terminally differentiated memory CTL (up to 46.2% of all $CD8^+$ T cells, expressing $CD45RA^+CCR7^-$) in the periphery and elevated expression of the IC molecules PD-1 (18.3% vs 10.2% of total $CD8^+$ T cells) & TIGIT (17.3% vs. 4.4% of total $CD8^+$ T cells) on AS CTL compared to healthy controls. Effector memory CTL ($CD45RA^-CCR7^-$) were highly enriched in the SF. PD-1 expression is also highly upregulated in the synovial CTL (up to 75% of $CD8^+$ T cells), suggesting local immune activation. Despite PD-1 upregulation in these CTL subsets, evidence of immune exhaustion, as assessed by EOMES expression, was not found.

Conclusion: We demonstrate that CTL from AS patients are highly activated, and are characterized by a distinct immune phenotype which implicates an intrinsic CTL dysregulation in AS pathogenesis.

Disclosure: M. Tang, None; **Z. Qaiyum**, None; **M. Lim**, None; **R. Inman**, Abbvie, 5, Amgen, 5, Janssen, 5, Lilly, 5, Novartis, 5.

Abstract Number: 1412

A T Cell Intrinsic Role for Nod2 in Suppression of Th17-Mediated Experimental Arthritis and Uveitis: Implications for Blau Syndrome

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Mutations in nucleotide-binding oligomerization domain-containing protein 2 (*NOD2*) cause Blau syndrome, an inflammatory disorder characterized by uveitis, dermatitis, and polyarthritis. The antimicrobial functions of NOD2 are well established; yet the mechanism by which dysregulated NOD2 causes sterile inflammation remain unknown. Here we utilized experimental models of autoimmune arthritis and uveitis, and PBMCs from Blau syndrome patients to dissect a T cell-specific role for NOD2 in uveitis.

Methods: Arthritis was induced in SKG and $NOD2^{-/-}$SKG mice with a single intraperitoneal 1.5mg injection of zymosan and assessed by clinical scoring, near infrared imaging and histology. Uveitis was induced in $NOD2^{+/+}$ and $NOD2^{-/-}$ C57BL/6 mice by immunization with the retinal antigen interphotoreceptor retinoid-binding protein (IRBP) and assessed by clinical scoring and histology. Mice were treated with IL-17A/F mAb (R&D systems) beginning 24h

prior to disease induction. Lymphopenic Rag1$^{-/-}$ mice were reconstituted with NOD2$^{-/-}$ or NOD2$^{+/+}$ (WT) CD4+ T cells and arthritis or uveitis was induced. IL-17 production by T cells was evaluated by flow cytometry and ELISA. For T cell homeostasis studies, purified naive (CD62L^{hi}CD44^{-}) CD4+ T cells were differentiated under Th17 polarizing conditions (CellXVivo) or purified memory (CD62L^{-}CD44^{hi}) CD4+ T cells from naive mice were stimulated with anti-CD3 and anti-CD28, and activation state (CD69) and pro-inflammatory cytokine production was determined by flow cytometry ($n \geq 6$ mice/group and repeated 3X). Peripheral blood mononuclear cells from Blau Syndrome patients or healthy controls were cultured for 5 d, stimulated with PMA/ionomycin, and IL-17 was measured. Data were analyzed by Mann-Whitney, and $p < 0.05$ were considered significant.

Results: Lymphopenic recipients of NOD2-deficient T cells developed significantly worse arthritis and uveitis, implicating T cell-intrinsic NOD2 in suppression of disease. CD4+ T cells purified from arthritic and uveitic mice produced significantly more IL-17, and blockade of IL-17 mitigated the enhanced disease caused by NOD2-deficiency, indicating a direct role for T cell-intrinsic NOD2 in suppressing autoreactive Th17 responses. NOD2 was dispensable for Th17 differentiation of naïve CD4+ T cells. However, NOD2$^{-/-}$ memory (antigen-experienced) CD4+ T cells isolated from naïve mice when stimulated with anti-CD3 and anti-CD28 had enhanced expression of IL-17, the IL-17-associated transcription factor (RORγt) and the activation marker CD69. Importantly, stimulation of CD4+ T cells from Blau syndrome patients resulted in significantly more IL-17 production than those from healthy control T cells, suggesting a similar function for NOD2 in human disease.

Conclusion: We have uncovered a novel, T cell-intrinsic function for NOD2 as a negative regulator of T cell homeostasis and autoimmunity. Our work suggests that a "loss-of-function" in NOD2 (i.e. NOD2$^{-/-}$ mice) results in a "gain-of-function" in the ability of T cells to produce IL-17 and cause arthritis and uveitis. These findings could potentially change the way we view the immunopathology of Blau syndrome and open up new therapeutic options for patients.

Disclosure: R. Napier, None; **E. Lee**, None; **E. Vance**, None; **S. Lashley**, None; **L. Uebelhoer**, None; **C. Lancioni**, None; **R. Vehe**, None; **B. Binstadt**, None; **R. Caspi**, None; **H. Rosenzweig**, None.

Abstract Number: 1413

An Imbalance Between Regulatory and Inflammatory T Cell Subsets Distinguishes Systemic Autoimmune Rheumatic Disease Patients from Asymptomatic ANA^{+} Individuals

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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

Session Type: Poster Session C

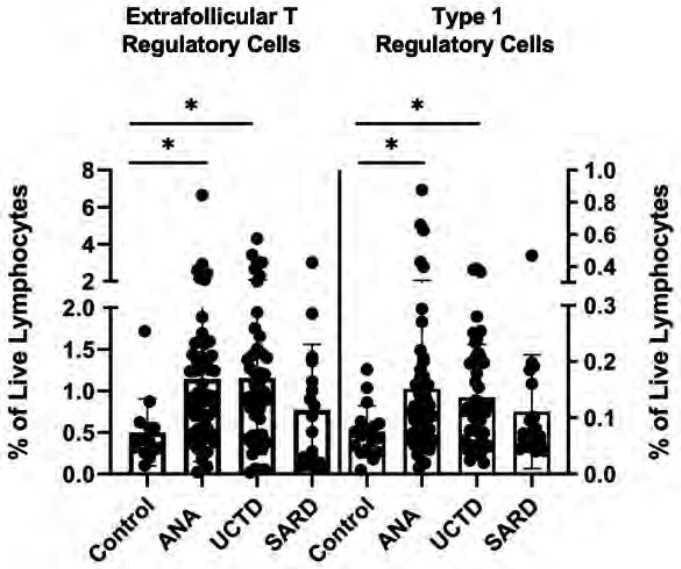
Session Time: 9:00AM–11:00AM

Background/Purpose: The anti-nuclear antibody (ANA)-associated systemic autoimmune rheumatic diseases (SARDs) are characterized by a prolonged preclinical phase in which ANAs are produced in the absence of symptoms. ANAs are also seen in healthy, non-symptomatic individuals (ANA^+NS), the majority of whom will not progress to SARD. Currently, the immunologic features that discriminate progressors from non-progressors are incompletely understood. Previous work has suggested that T regulatory (Treg) cell function may be disturbed in SARD. To determine whether alterations in these cell populations could contribute to SARD progression we investigated the balance between regulatory and inflammatory T cells in patient populations representative of the various stages in SARD development.

Methods: ANA^+ (IF ≥ 1:160) participants were recruited through the clinic and classified as ANA^+NS (n = 61), ANA^+ with ≥ 1 SARD classification criteria but lacking a SARD diagnosis (UCTD, n=54) or early SARD (SLE, n=10, SS, n=7, SSc, n=5, classified according to the 1997 ACR criteria, 2013 ACR-EULAR criteria, and the 2016 ACR-EULAR criteria, respectively). All SARD patients were within 2 years of diagnosis and not taking DMARDs (hydroxychloroquine allowed) or prednisone. ANA^- healthy controls (HC, n= 21) were recruited from clinical and laboratory staff. Peripheral blood mononuclear cells were isolated and stained with fluorochrome-labeled antibodies to identify immune cell populations via flow cytometry. Plasma aliquots retrieved from the same patients were used to measure TGF-ß1 levels (pg/ml) through ELISA. Statistical comparisons were made using the Kruskal-Wallis test.

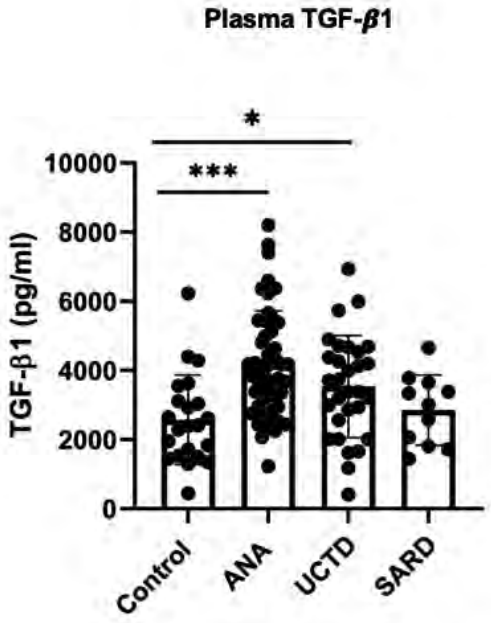
Results: ANA^+NS and UCTD patients had significant increases in the proportion of extrafollicular Tregs ($CD3^+CD4^+CXCR5^-PD1^{hi}FOXP3^+HELIOS^+$) and Type 1 ($CD3^+CD4^+CD45RA^-LAG3^+$) regulatory (Tr1) cells, relative to ANA^-HC, whereas the levels of these cells were similar to ANA^-HC in SARD patients (Figure 1). The same trends were observed for TGF-ß1 levels (Figure 2). In ANA^+NS individuals there was a moderate correlation between TGF-ß1 levels and the proportion of Tr1 cells (r=0.43, p=0.009), a population that has been previously shown to secrete this regulatory cytokine. To examine inflammatory T cell subsets, $CD3^+CD4^+CD45RA^-PD1^{hi}$ activated memory T peripheral ($CXCR5^-$, Tph) and

Figure 1 – Proportion of T Regulatory Subsets



* p ≤ 0.05, ** p ≤ 0.01, *** p ≤ 0.001

Figure 2 – Plasma TGF-β1 Measurements

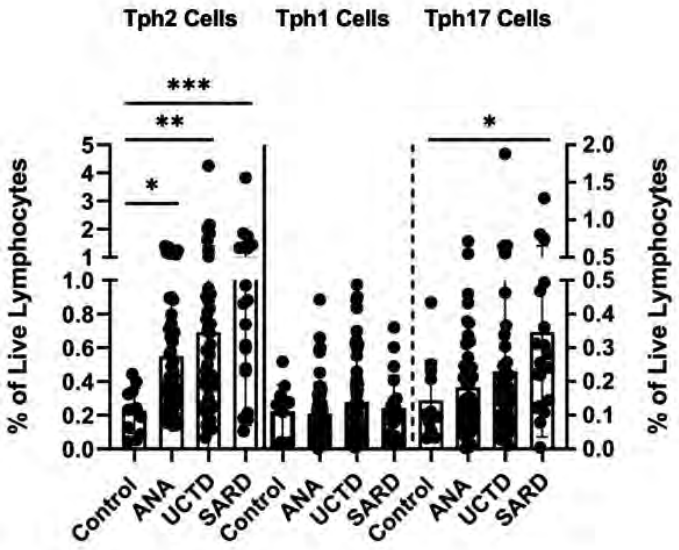


* p ≤ 0.05, ** p ≤ 0.01, *** p ≤ 0.001

follicular ($CXCR5^+$, Tfh) helper cells were gated and the proportion of Th1 ($CXCR3^+CCR6^-$), Th2 ($CXCR3^-CCR6^-$) and Th17 ($CXCR3^-CCR6^+$) cells in each subset were determined. As shown in Figure 3, increased proportions of Tph2 cells were seen in all ANA^+ patient subsets as compared to ANA^-HC but were most pronounced for SARD patients (Figure 3). Although similar trends were seen for Tph17 cells, the increase was only significant in SARD patients. The same but less significant trends were seen for Tfh cells (data not shown).

Conclusion: Our findings suggest that expanded proportions of extrafollicular Treg and Tr1 cells may act to regulate the autoimmune response in asymptomatic ANA^+ individuals and that in SARD patients this becomes attenuated resulting in an imbalance between regulatory and inflammatory T cell subsets which promotes disease development.

Figure 3 – Proportion of Inflammatory T Cell Subsets



* p ≤ 0.05, ** p ≤ 0.01, *** p ≤ 0.001

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Abstract Number: 1414

Highly Polyfunctional Metabolically Altered Pathogenic T Cells Accumulate in the Synovial Tissue of RA Patients and Arthralgia Subject but Not Healthy Control Synovial Tissue

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

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

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Effective treatment of Rheumatoid arthritis (RA) patients is achievable within a short window of opportunity following diagnosis. Identification of pathogenic immune mechanisms at a pre-RA stage would greatly benefit our understanding of the early events that govern disease progression and help identify early points of therapeutic intervention.

Characterization of pro-inflammatory T cell polyfunctionality in the periphery and synovial tissue of 'at-risk; subjects (Arthralgia) RA patients (RA) and healthy controls (HC).

Identification of pathogenic, synovial T cell subsets.

Characterization of metabolic status of pathogenic T cell populations.

Methods: Synovial biopsies from RA, AR and HC were obtained by arthroscopic surgery followed by RNAseq analysis (Guo et al., PLoS One, 2018). Single cell synovial tissue cell suspensions from RA, AR and HC and paired PBMC were stimulated *in vitro* and polyfunctional synovial T cell subsets examined by flow cytometric analysis, SPICE visualization and Flowsome unsupervised clustering. Flow-Imaging was utilised to confirm specific T cell cluster identification. Fluorescent Lifetime Imaging Microscopy (FLIM) was used to visualise metabolic status of specific T cell populations.

Results: T cell associated pro-inflammatory cytokines were increased in whole synovial tissue biopsy RNAseq analysis in RA patients and AR subjects compared to HCs. Flow cytometric analysis and SPICE revealed marked T cell polyfunctionality with similar pro-inflammatory cytokine profiles in RA and AR compared to HC, providing evidence of a dysregulated synovial T cell response that pre-dates clinical onset of disease. Cluster analysis led to the identification of highly polyfunctional T cell clusters and an accumulation of $CD4^{+}CD8^{+}$ double positive T cells in the synovial tissue of AR and RA but not in HC. Hybrid flow cytometry and imaging technique confirmed the cell membrane co-expression of CD4 and CD8 by a synovial T cell population. DP T cells do not share characteristics of NK T cells and their synovial accumulation correlates with DAS28(CRP). Initial studies utilising non-invasive FLIM technique and flow cytometric analysis revealed that DP T cells have an intermediate metabolic profile between CD4 and CD8 T cells and an activated mTOR pathway.

Conclusion: Highly polyfunctional pro-inflammatory T cell responses pre-date disease onset as demonstrated by the accumulation of polyfunctional T cells in the synovial tissue of pre-RA arthralgia subjects. These data highlight a key early pathogenic role for T cell plasticity and specific synovial T cell clusters including, DP T cells in RA.

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Abstract Number: 1415

Murine Roseolovirus Induces Autoimmune Disease and Development of Autoreactive T Cells and Autoantibodies

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Murine roseolovirus (MRV) is a recently sequenced beta-herpesvirus that is a natural murine pathogen and is genetically highly related to HHV6 and HHV7. The human roseoloviruses, HHV6 and HHV7, have been associated with autoimmune disease. Demonstrating causality has been difficult due to the ubiquitous and chronic nature of roseolovirus infections. Herein we have demonstrated that neonatal MRV infection induces autoimmune disease and development of autoantibodies in adult mice.

Methods: To evaluate the role of MRV in autoimmune disease, mice were infected within the first 48 hours of life. At 12 weeks post infection we performed autoantibody screening as well as histology to identify organ specific tissue inflammation. We utilized flow cytometry and immunofluorescence to characterize the immune response, both systemically and within tissues. Antiviral treatment with ganciclovir was utilized to inhibit viral replication.

Results: Our studies show that autoimmune gastritis occurs in the absence of detectable virus in the gastric mucosa. Neonatal MRV infection results in a transient reduction in thymic and peripheral $CD4^+Foxp3^+$ regulatory T cells (Treg). Ganciclovir (GCV), a potent inhibitor of replication of other beta-herpesviruses, inhibits MRV replication as well as MRV-mediated $CD4^+$ T cell and Treg depletion. Treatment with GCV early in life also reduces autoimmune gastritis, suggesting that MRV replication is necessary for altering immunologic tolerance early in life. The inflammatory infiltrate in the gastric mucosa is characterized by an increase in T cells, neutrophils and eosinophils. Furthermore, the $CD4^+$ T cells in the gastric mucosa express IL-17 and IL-4, demonstrating a Th2 and Th17 response. The development of autoimmune gastritis was found to be T cell dependent. Interestingly, neonatal MRV infection results in the production of a wide array of autoantibodies in adult mice, including those associated with rheumatologic disease such as dsDNA, Scl-70, SSA, SSB, Jo-1, Smith, GBM and MPO.

Conclusion: This study shows that neonatal infection with MRV results in the development of autoimmunity later in life, after acute infection has been cleared. Taken together, these findings strongly suggest that infection with a roseolovirus infection early in life results in disruption of immunologic tolerance and development of autoimmune disease.

Disclosure: T. Bigley, None; **J. Saenz**, None; **L. Yang**, None; **J. Mills**, None; **W. Yokoyama**, None.

Abstract Number: 1416

Effects of the COVID-19 Pandemic on Patients Living with Vasculitis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Vasculitis – ANCA-Associated Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: The COVID-19 pandemic has the potential to impact how patients with vasculitis interact with health care systems due to concerns about infections. This study aimed to analyze the concerns and health-related behaviors in patients with vasculitis during early phase of the COVID 19 pandemic in North America.

Methods: Patients with vasculitis were invited to complete an online survey through Vasculitis Patient-Powered Research Network in collaboration with the Vasculitis Foundation and the Relapsing Polychondritis Awareness and Support Foundation. Questions focused on concerns and behaviors related to doctors' visits, laboratory and other tests, medication use, and telehealth use. Differences based on age, diagnoses, immunosuppressive drugs, daily glucocorticoid (GC) doses, urban vs. rural location, education, income, and COVID-19 infection rates in patients' county were compared with Kruskal-Wallis (for concerns) or logistic regression, with telehealth analyses adjusted for date of survey completion. This report details findings from April 8, 2020 through May 29, 2020.

Results: Data from 662 patients were included: 90% Caucasians, 78% women (**Table 1**). Seven patients reported a diagnosis of COVID-19. Most patients (83%) expressed moderate or high levels of concern about COVID-19; 87% reported their vasculitis "moderately" or "extremely" affected their level of concern (**Figure 1**). Age >60 years ($p< 0.01$), female sex ($p=0.01$), and lung disease ($p< 0.01$) were associated with higher levels of concern. Immunosuppressive drug use and lung disease were associated with a higher likelihood that underlying vasculitis significantly affected level of concern ($p< 0.01$ each).

66% of patients reported avoiding doctors' visits, 46% avoided laboratory tests, and 40% avoided other tests. Age < 60 years, urban location, higher COVID-19 activity, higher income, higher concern levels, and prednisone dose >10 mg/day were each associated with greater likelihood of avoiding visits or tests. 10% of patients on immunosuppression stopped drugs, especially patients with respiratory illnesses (39% vs 8% without respiratory illness, $p< 0.01$). The most common reasons for drug stoppage were concern about infection (57%) and physician's advice (40%). Among 225 patients on rituximab, 43 (29%) reported avoiding an infusion.

44% of patients had telehealth visits; more visits were reported in younger patients, those on GC, and in Canada vs the USA (**Table 2**). Patients with telehealth visits were more likely to report getting information about COVID-19 from healthcare providers (65% vs 38%, $p< 0.01$).

Table 1: Demographic and Clinical Characteristics of Patients with Vasculitis in the Study Cohort

Sample size, N	662
Age (years)	55.4 +/- 14.0
Female	520 (78.5%)
Caucasian	598 (90.3%)
Hispanic	33 (5.0%)
United States	597 (90.2%)
Canada	65 (9.8%)
Rural*	51/573 (8.9%)
Urban	522/573 (91.1%)
County cases of COVID-19 per capita*	
Lowest tertile	84/571 (14.7%)
Middle tertile	264/571 (46.2%)
Highest tertile	223/571 (39.1%)
Vasculitis Types	
ANCA-associated vasculitis	
Granulomatosis with polyangiitis	286 (43.2%)
Microscopic polyangiitis	54 (8.2%)
Eosinophilic granulomatosis with polyangiitis	64 (9.7%)
ANCA unspecified	56 (8.5%)
Giant cell arteritis	30 (4.5%)
Takayasu's arteritis	16 (2.4%)
Relapsing polychondritis	56 (8.5%)
Other vasculitides	100 (15.1%)
Medications	
Rituximab	225 (34.0%)
Other biologics/JAKi	77 (11.6%)
Cyclophosphamide	11 (1.7%)
Methotrexate	109 (16.5%)
Azathioprine	96 (14.5%)
Mycophenolate	58 (8.8%)
Glucocorticoids	
None	364 (55.0%)
≤10mg/day	238 (36.0%)
>10mg/day	60 (9.1%)
NSAIDs	114 (17.2%)
Comorbidity	
Hypertension	278 (42.0%)
Heart disease	66 (10.0%)
Diabetes mellitus	76 (11.5%)
Asthma	179 (27.0%)
Chronic obstructive pulmonary disease	45 (6.8%)
Other chronic lung disease	73 (11.0%)
Kidney disease	162 (24.5%)
Malignancy	14 (2.1%)
Organ transplant	14 (2.1%)
Current smoking	25 (3.8%)

Number (%) and mean +/- standard deviation shown
* United States data based on patient zip code
DMARD: disease modifying anti-rheumatic drug; JAKi: Janus kinase inhibitor; NSAIDs: non-steroidal anti-inflammatory drugs

Table 2: Impact of COVID-19 Pandemic on Health-Related Behavior of Patients with Vasculitis

	N	Avoided going to doctor's office	Avoided getting laboratory tests	Avoided other tests (e.g. x-rays)	Avoided going to get an infusion (patients on rituximab)	Had a telehealth visit	Stopped medications**
All patients	662	439 (66.3%)	308 (46.5%)	265 (40.0%)	43/225 (19.1%)	306 (46.2%)	35/450 (7.8%)
AAV	460	302 (65.7%)	209 (45.4%)	171 (37.2%)	36/205 (17.6%)	194 (42.2%)	22/333 (6.6%)
GCA	30	19 (63.3%)	14 (46.7%)	14 (46.7%)	0/0 (0.0%)	14 (46.7%)	1/14 (7.1%)
Takayasu	16	12 (75.0%)	4 (25.0%)	4 (25.0%)	0/0 (0.0%)	8 (50.0%)	1/9 (11.1%)
Relapsing polychondritis	56	39 (69.6%)	29 (51.8%)	29 (51.8%)	1/6 (16.7%)	41 (73.2%)	6/42 (14.3%)
Other	100	67 (67.0%)	52 (52.0%)	47 (47.0%)	6/14 (42.9%)	49 (49.0%)	5/52 (9.6%)
Medications							
Rituximab	225	152 (67.6%)	95 (42.2%)	84 (37.3%)	43 (19.1%)	100 (44.4%)	21/208 (10.1%)
Other Biologic/JAKi/CYC	83	52 (62.7%)	36 (43.4%)	31 (37.3%)	N/A	52 (62.7%)	3/77 (3.9%)
AZA/MMF/MTX/TAC/CSP	166	107 (64.5%)	81 (48.8%)	74 (44.6%)	N/A	76 (45.8%)	8/147 (5.4%)
No DMARD	169	111 (65.7%)	84 (49.7%)	66 (39.1%)	N/A	68 (40.2%)	N/A
Glucocorticoids							
none	364	238 (65.4%)	167 (45.9%)	137 (37.6%)	26/116 (22.4%)	141 (38.7%)	19/221 (8.6%)
≤10mg	238	160 (67.2%)	111 (46.6%)	96 (40.3%)	13/87 (14.9%)	122 (51.3%)*	11/183 (6.0%)
>10mg	60	41 (68.3%)	30 (50.0%)	32 (53.3%)*	4/22 (18.2%)	43 (71.7%)*	5/46 (10.9%)
Urban county	524	353 (67.4%)	246 (46.9%)	219 (41.8%)	38/190 (20.0%)	230 (43.9%)	27/360 (7.5%)
Rural county	51	25 (49.0%)*	17 (33.3%)	13 (25.5%)*	4/17 (23.5%)	20 (39.2%)	3/36 (8.3%)
Median household income of zip code							
Lowest tertile	66	35 (53.0%)	24 (36.4%)	25 (37.9%)	7/25 (28.0%)	26 (39.4%)	4/47 (8.5%)
Middle tertile	111	72 (64.9%)	54 (48.6%)	43 (38.7%)	5/36 (13.9%)	51 (45.9%)	2/76 (2.6%)
Highest tertile	401	274 (68.3%)*	187 (46.6%)	166 (41.4%)	30/148 (20.3%)	175 (43.6%)	24/275 (8.7%)
Concerned about COVID-19							
Not at all, slightly, or somewhat concerned	113	54 (47.8%)	46 (40.7%)	28 (24.8%)	6/35 (17.1%)	57 (50.4%)	2/74 (2.7%)
Moderately or extremely concerned	549	385 (70.1%)*	262 (47.7%)	237 (43.2%)*	37/190 (19.5%)	249 (45.4%)	33/376 (8.8%)
United States	597	392 (65.7%)	274 (45.9%)	241 (40.4%)	43/215 (20.0%)	264 (44.2%)	33/412 (8.0%)
Canada	65	47 (72.3%)	34 (52.3%)	24 (36.9%)	0/10 (0.0%)	42 (64.6%)*	2/38 (5.3%)
Age <60	370	258 (69.7%)	190 (51.4%)	159 (43.0%)	27/135 (20.0%)	193 (52.2%)	26/264 (9.8%)
Age ≥60	292	181 (62.0%)*	118 (40.4%)*	106 (36.3%)*	16/90 (17.8%)	113 (38.7%)*	9/186 (4.8%)

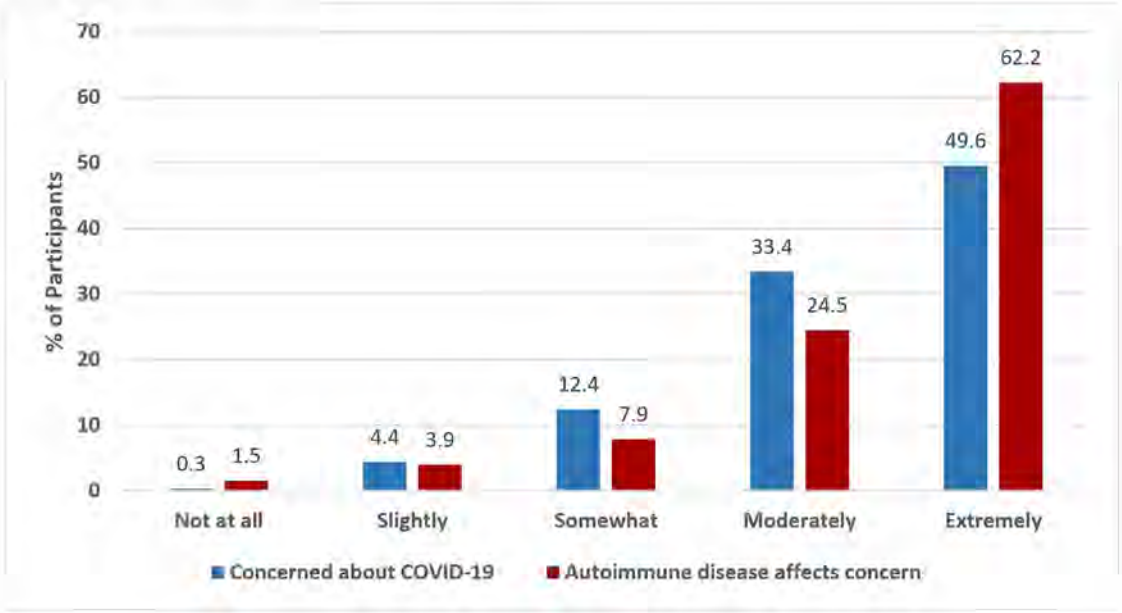
* $p < 0.05$ vs. the reference groups (granulomatosis with polyangiitis, rituximab, no glucocorticoid use, urban residence, lowest tertile of median household income, greater than high school education, or COVID-19 cases per capita, United States, age < 60) based on univariate logistic regression models except for telehealth visit analyses which were adjusted for date of entry into the study because of associations between calendar time and telehealth use; t tests were performed for continuous variables and chi square tests for categorical variables; p values are nominal in nature and should be interpreted in an exploratory manner

** Proportion stopping medications is among patients who were on immunosuppression/immunomodulatory therapy and did not report a respiratory illness or diagnosis of COVID-19

AAV: ANCA associated vasculitis, GPA: granulomatosis with polyangiitis, MPA: microscopic polyangiitis, EGPA: eosinophilic granulomatosis with polyangiitis, GCA: giant cell arteritis, JAKi: Janus kinase inhibitors, CYC: cyclophosphamide, AZA: azathioprine, MMF: mycophenolate, MTX: methotrexate, TAC: tacrolimus, CSP: cyclosporine; DMARD: Disease Modifying Anti-Rheumatic Drugs

Conclusion: In patients with vasculitis there were high levels of concern due to COVID-19 in the early months of the pandemic. Many patients avoided doctors' visits, laboratory and other tests, and stopped or delayed medications without consulting physicians. Healthcare utilization varied across demographics and geographies. Strategies to facilitate ongoing engagement with the health care system during the pandemic are warranted and should be tailored to specific subsets of patients with vasculitis.

Figure 1: Concern about COVID-19 and Effect of Having an Underlying Autoimmune Disease on Level of Concern Among Patients with Vasculitis



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Abstract Number: 1417

Risk of Relapse of ANCA-associated Vasculitis in Patients of 75 Years and Older: A Retrospective Study

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SESSION INFORMATION
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Background/Purpose: ANCA-associated vasculitis (AAV) frequently occurs among older patients, with different clinical presentations than the younger. Little is known on the outcome of older patients presenting with AAV. We aim to study the risk of relapse of patients with an AAV diagnosed after the age of 75 years.

Methods: Data from patients aged ≥65 years were extracted from the prospectively completed French Vasculitis Study Group (FVSG) database and from a call for observation of patients aged ≥75 years sent to the FVSG members on June 2019. Patients were included if they had a diagnosis of granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) or unclassified AAV (EMA classification criteria) made after the age of 65 and were either followed-up for 6 months or deceased. Patients aged ≥75 years were compared to those aged 65-75 years. Data on comorbidities, demography, disease phenotype, treatment, and outcome were collected. Primary end-point was risk of first relapse among those who achieved remission. To assess relapse risk, univariate and multivariate analysis was performed, using both Cox (using cause-specific hazard ratios, CSHR) and Fine- Gray models (using sub-distribution HR, SHR), taking death into account as a competing risk for relapse.

Results: We included 299 patients, 219 patients aged ≥75 years (median 79, IQR [77-83], 79 from the database and 140 from the call for observations) and 80 patients aged 65-75 years (median 70 years, IQR [68-72]) from the database. Diagnosis was GPA for 155 patients (52%), MPA for 136 patients (45%) and unclassified for 8 patients (3%). When compared with patients aged 65-75 years, those aged ≥75 years had lower relapse risks in multivariate analysis (CSHR 0.54, 95% IC 0.33 to 0.89, p=0.016), as well as when death was taken into account as a competing event (SHR 0.46, 95% IC 0.29 to 0.74, p=0.001). Patients aged ≥75 years also had lower relapse risks when adjusting on diagnosis of GPA (CHSR 0.56, 95% IC 0.35 to 0.90, p=0.017; SHR 0.56 95% IC 0.34 to 0.91, p=0.019), on variables composing Five Factor Score (FFS) 1996, as well as on variables composing FFS 2011. Patients aged ≥75 years had a lower risk of being treated with immunosuppressive therapy in addition to glucocorticoids (versus glucocorticoids alone), after adjusting for FFS 1996 (HR 0.29, 95% IC 0.12 to 0.70, p=0.023) and FFS 2011 (HR 0.29, 95% IC 0.12 to 0.71, p=0.007). Patients aged ≥75 years, for whom a combination of immunosuppressants and glucocorticoids is usually recommended and who followed that treatment regimen, had significantly lower relapse rates than those who were treated with glucocorticoids alone (CSHR 0.29, 95% IC 0.12 to 0.68, p=0.005; SHR 0.31, 95% IC 0.13 to 0.71, p=0.006).

Conclusion: Patients with a diagnosis of AAV after the age of 75 years had a lower risk of relapse than patients aged 65-75 years, after adjusting for confounders and using death as a competing risk of relapse. Patients aged ≥75 years had lower probabilities of being treated with a combination of immunosuppressants and glucocorticoids. However, patients aged ≥75 years still benefit from being treated with immunosuppressants and glucocorticoids when recommended, with a lower relapse risk.

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Abstract Number: 1418

Clinical Presentations and Follow-up Results of Granulomatosis with Polyangiitis: An Analysis of 8 Years Clinical Experience with 220 Patients from a National Referral Center

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Background/Purpose: Granulomatosis with polyangiitis (GPA) is a rare and life-threatening autoimmune disease. Due to the extremely low prevalence of GPA, monitoring of clinical characteristics and outcomes is critical. The objective of this study was to analyze the clinical presentations and follow-up results of patients diagnosed with the GPA at a national referral center in Iran.

Methods: Between 2012 and 2020, all consecutive GPA-diagnosed patients at Tehran University of Medical Sciences (Amir A'lam Hospital) were included. All patients fulfilled the 1990 ACR criteria and/or revised Chapel Hill nomenclature for GPA. Patients' demographic information, laboratory findings, and clinicopathological manifestations were retrospectively recorded in the GPA registry system.

Results: Overall, 220 GPA patients, including 112 (50.9%) men and 108 (49.1%) women, with the mean age of 44.4 ± 15.9 years, were diagnosed. The mean follow-up time was 24.6 months. The mean interval between disease onset and diagnosis was 23.6 months (ranged 6-300). Regarding clinical manifestation at diagnosis, ear nose throat (ENT) (99.5%), pulmonary (76.8%), and renal (46.8%) were the most commonly involved organs (Table 1). Sera positivity for anti-proteinase 3 (PR3)-ANCA and myeloperoxidase (MPO)-ANCA were found in 138 (63.3%) and 29 (13.3%) patients, respectively. Histologic data obtained from 140 patients, revealed the classical triad of vasculitis, necrosis, and granulomatous inflammation in 29 specimens (19%). Regarding inflammatory serological markers, high levels of CRP (>10 mg/L) was observed in 137 (62.8%) and high ESR levels (>30 mm/h) in 122 (55.9%) patients (Table 2). Regarding disease severity, the mean BVAS/WG and PGA scores at the time of diagnosis were calculated as 9.5 ± 4.3 and 5.9 ± 1.8, respectively. Accordingly, based on the BVAS/WG classification, 141 (64%) patients fell into severe and 79 (36%) in limited disease activity categories. Based on the last recorded follow-up, ENT, pulmonary, and renal were increased to 100%, 85.9%, and 56.8%, respectively. Among 103 patients with a minimum follow-up of 24 months, 161 relapses occurred (mean relapse count for each patient: 1.56). Sixty-nine (31.3 %) patients expired during the follow-up period, 46 (66.6 %) less than 1 year, 16 (23.1 %) between 1 to 5 years and 7 (10.1 %) after 5 years post-diagnosis. There was a significant change in the main causes of death in the study timeframe (p-value = 0.001). During the first year after diagnosis of GPA, the most common cause of death was active vasculitis (19 Of 46; 41.3%), whereas from years 1 to 5 after the diagnosis, the most frequent cause was cardiovascular (CVD) disease (8 Of 16; 50%), and from years 5 to 10, malignancy and CVD were the most common causes (3 Of 7; 42.8% each).

Conclusion: GPA has a progressive nature, which, despite the continuous treatment, it moves to a more severe form. GPA-related death might occur either as the results of disease directly (organs involvement) or long-term side-effects related to treatments (e.g., malignancy). Thereby, early diagnosis of disease, regular follow-up, and using non-car-

Clinical manifestations N=220	At diagnosis N (%)	During follow-up N (%)
General manifestations	73 (33.1)	87 (39.5)
Arthralgia/Arthritis	44 (20)	57 (25.9)
Fever ≥ 38°C	22 (10)	25 (11.3)
Night sweats/LAP/Weight loss/Myalgia	29 (13.1)	33 (15)
Cutaneous manifestations	30 (13.6)	33 (15)
Purpura	24 (10.9)	28 (12.7)
Gangrene	0 (0)	0 (0)
Skin ulcer	6 (2.7)	6 (2.7)
Mucous membranes/Eye manifestations	84 (38.1)	99 (45)
Mouth ulcer	27 (12.2)	30 (13.6)
Conjunctivitis/Episcleritis	25 (11.3)	30 (13.6)
Retro-orbital mass/Proptosis	32 (14.5)	38 (17.2)
Uveitis	3 (1.36)	4 (1.8)
Scleritis	2 (0.9)	4 (1.8)
Retinal exudates/Hemorrhage	2 (0.9)	2 (0.9)
Genital ulcer/Dacryocystitis/Keratitis	17 (7.7)	26 (11.8)
Erosion/Petosis/Cellulitis	15 (6.8)	15 (6.8)
Ear nose throat manifestations	219 (99.5)	220 (100)
Bloody nasal discharge/Nasal crusting/Ulcer	134 (60.9)	135 (61.3)
Sinus involvement	187 (85)	191 (86.8)
Swollen salivary glands	4 (1.8)	4 (1.8)
Subglottic inflammation	38 (17.2)	43 (19.5)
Conductive deafness	136 (61.8)	139 (63.1)
Sensorineural deafness	95 (43.1)	98 (44.5)
Mastoiditis/Rhinitis	172 (78.1)	174 (79)
Cardiovascular manifestations	10 (4.5)	12 (5.4)
Pericarditis	2 (0.9)	2 (0.9)
Thrombophlebitis	4 (1.8)	4 (1.8)
Heart failure/infarct	4 (1.8)	6 (2.7)
Gastrointestinal manifestations	18 (8.1)	21 (9.5)
Mesenteric ischemia	0 (0)	2 (0.9)
Effusion/Splenomegaly/Hepatomegaly	4 (1.8)	5 (2.2)
Pancreatitis/Hepatitis/Diarrhea	14 (6.3)	16 (7.2)
Pulmonary manifestations	169 (76.8)	189 (85.9)
Pleurisy	9 (4)	10 (4.5)
Nodules or cavities	97 (44)	102 (46.3)
Other infiltrate secondary to GPA	65 (29.5)	69 (31.3)
Endobronchial involvement	9 (4)	10 (4.5)
Alveolar hemorrhage	3 (1.3)	12 (5.4)
Respiratory failure	0 (0)	5 (2.2)
Sub-segmental atelectasis	67 (30.4)	68 (30.9)
Renal manifestations	103 (46.8)	125 (56.8)
Hematuria (no RBC cast)	81 (36.8)	94 (42.7)
RBC cast	14 (6.3)	15 (6.8)
Rise in Cr > 30% or fall in CCr > 25%	36 (16.3)	42 (19)
Proteinuria	62 (28.1)	77 (35)
Nervous system manifestations	76 (34.5)	84 (38.1)
Meningitis	2 (0.9)	3 (1.3)
Cord lesion	0 (0)	0 (0)
Stroke	13 (5.9)	15 (6.8)
Cranial nerve palsy	53 (24)	55 (25)
Sensory peripheral neuropathy	0 (0)	0 (0)
Motor mononeuritis multiplex	3 (1.3)	5 (2.2)
Headache	28 (12.7)	29 (13.1)
Encephalitis	2 (0.9)	2 (0.9)
Abbreviations LAP: Lymphadenopathy, Cr: Creatinine, CCr: clearance of creatinine		

Table 1. Clinical manifestations at diagnosis and during follow up obtained from a cohort of 220 GPA patients from 2012 to 2020 at a national referral center

Laboratory findings, n %	**n = 218**
PR3-ANCA positivity	138 (63.3)
MPO-ANCA positivity	29 (13.3)
PR3-ANCA (+) or MPO-ANCA (+)	164 (75.2)
ANCA negativity	54 (24.8)
CRP (> 10 mg/l)	137 (62.8)
ESR (> 30 mm/h)	122 (55.9)
Serum creatinine (> 1.3 mg/dl)	38 (17.4)
CBC – abnormalities:	
Leukocytosis (WBC> 11000/microL)	75 (34.4)
Lymphopenia (ALC <1000/microL)	38 (17.4)
Anemia (Hb<12.5 g/dl)	115 (52.7)
Thrombocytosis (PLT>400,000/microL)	52 (23.8)
Histologic data, n %	**n = 140**
Biopsy performed	152 (63.6)
Vasculitis	80 (52.6)
Granulomatous inflammation	81 (53.2)
Necrosis	59 (38.8)
Normal	4 (2.6)
Disease activity at diagnosis	**n = 220**
Total BVAS at diagnosis	13.5 ± 7.6
Total BVAS/WG at diagnosis	9.5 ± 4.3
PGA at diagnosis	5.9 ± 1.8
Severe disease at diagnosis, n %	141 (64)
Limited disease at diagnosis, n %	79 (36)

Table 2. Patients' laboratory and histological findings and disease activity at diagnosis

cinogenic therapies (e.g., rituximab instead of cyclophosphamide) could be useful to decrease disease severity and mortality rate.

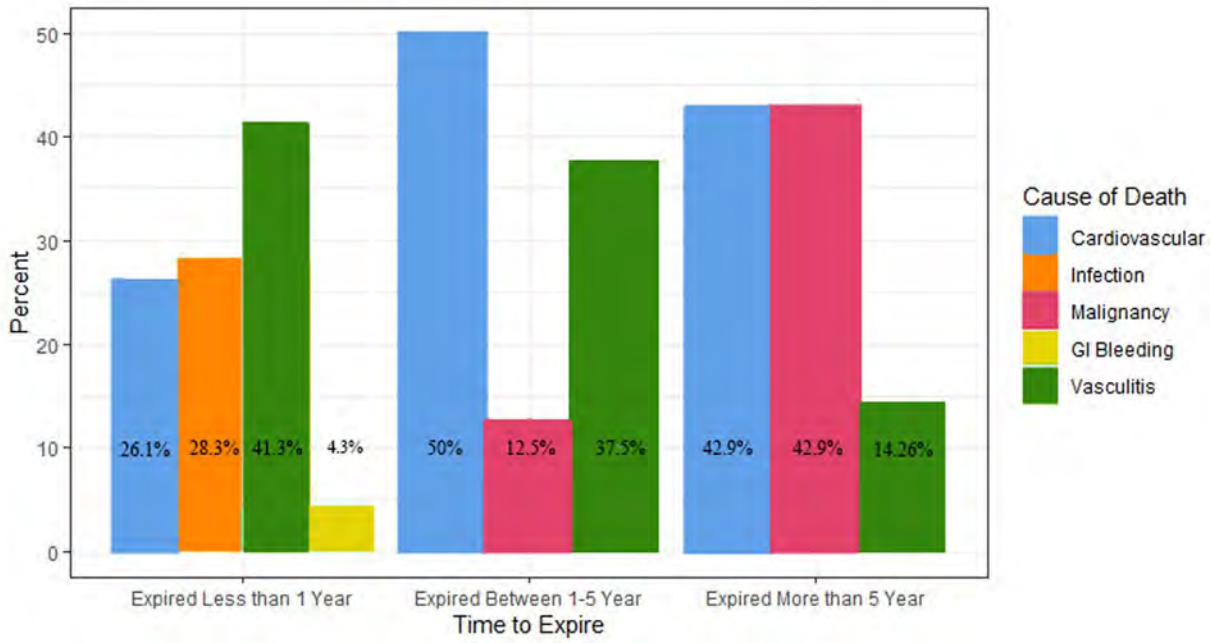

Figure 1. The causes of death during study timeframe.

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Abstract Number: 1419

Clinical Disease Might Be Divided into Two Phenotypes in ANCA Associated Vasculitis; Results of a Cluster Analysis

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SESSION INFORMATION

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Background/Purpose: One of the controversial matters in ANCA associated vasculitis is the definition of disease based on clinical characteristics since there is a remarkable overlap between disease groups. For instance, single organ disease like renal limited vasculitis (RLV) is not take place most of the definitions or classification criteria.

The aim of this study to determine clinical subgroups that may incorporate different clinical phenotypes, including RLV in AAV patients, followed up in two tertiary centres.

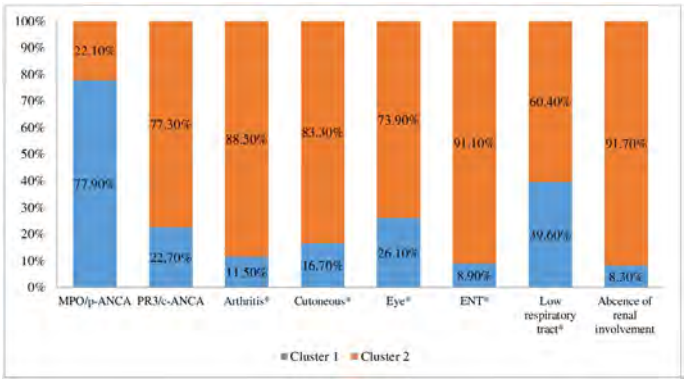

Table 1: Baseline characteristics of 165 patients with AAV

Age at diagnosis, mean years ± SD, (n)	51.6 ±15.2, 163
Male, n (%)	87 (52.7)
Labaratory results at diagnosis	
GFR =<60, n (%)	100/145 (69)
MPO-ANCA or p-ANCA	68 (41.2)
Pr3-ANCA or c-ANCA	97 (58.8)
Variants of AAV	
MPA	26 (15.8)
GPA	108 (65.5)
EGPA	11 (6.7)
RLV	20 (12.1)
Organ systems involved at diagnosis n (%)	
Cutaneous	24 (14.5)
Eye	23 (13.9)
Ear, nose and throat	90 (54.5)
Low respiratory tract	111 (67.3)
Cardiovascular system	5/163 (3.1)
Gastrointestinal system	10/164 (6.1)
Renal	129 (78.2)
Peripheral nervous system	16 (9.7)

GFR: glomeruler filtration rate; ANCA: antineutrophil cytoplasmic antibodies; Pr3: proteinase 3; MPO: myeloperoxidase; p-ANCA: perinuclear ANCA; c-ANCA: cytoplasmic ANCA; MPA: Microscopic Polyangiitis; GPA: Granulamatosis and Polyangiitis; EGPA: Eosinophilic Granulomatosis with Polyangiitis; RLV: Renal limited vasculitis

Methods: Baseline clinical features of AAV patients were studied. To analyse our data and identify sub-groups of AAV patients with similar clinical characteristics, a two-step cluster analysis using log-likelihood distance measures was performed. For clustering, we evaluated the following variables: gender, age at symptom onset, the presence of major organ involvement (renal, upper and lower respiratory tract, skin, joint, eye) and ANCA specificity

Results: In total 165 (87 [53%] male, age at diagnosis 51.6± 15.2 years) out of 238 (126 [53%] male, age at diagnosis 51.3± 15.6 years) AAV patients included in the analysis. Some of the demographic and clinical characteristics were summarized in table 1. There are two distinct clusters in AAV patients. Of 78% of those AAV patients with MPO/pANCA, 56% with renal involvement and 89% without ENT involvement were in Cluster 1. Of 77% those patients with PR3/cANCA, 89% with arthritis, 74% with eye involvement, 83% with skin, 91% with upper, and 60% with lower respiratory tract involvement and 92% of those without renal disease were in Cluster 2. Most of them (89%) classified as MPA and all as RLV were repositioned in Cluster 1, and 74% of GPA and 64% of EGPA patients were in Cluster 2.

Conclusion: Patients with AAV could be separated into two distinct categories. PR3 ANCA specificity and more organ/system involvement determine one and MPO ANCA specificity in renal disease define other subgroups.

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Abstract Number: 1420

Characterization of ANCA-Associated Vasculitis Among African American Patients

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Background/Purpose: ANCA-associated vasculitis (AAV) comprises a group of disorders characterized by inflammation of small and medium-sized arteries. Prevalence and phenotype of these diseases appear to vary across geographic and racial subgroups and information pertaining to the African American population is sparse. The objective of this study was to characterize clinical features in a cohort of African American patients with AAV compared to a matched cohort of Caucasian patients with AAV.

Methods: A retrospective electronic chart review was performed from 2007-2019 to identify patients with AAV within a single hospital network. African American and Caucasian patients were matched based on age and gender. Differences in clinical characteristics between the two groups were assessed by the Chi-square test for categorical variables and Mann-Whitney test for continuous variables, as appropriate.

Results: Thirty-five African American patients and 35 Caucasian patients with AAV were identified. Median age at diagnosis was 48 years (IQR 38-66) in the African American group, and 44 years (IQR 31-60) in Caucasian group; p=0.15. Twenty-four (69%) patients in each group were female; p=1.0. At time of presentation, African-American patients with AAV more frequently required admission to the Intensive Care Unit (58% versus 31%, p=0.02), received pulse dose steroids (83% versus 51%, p< 0.01), had lower hemoglobin values (median 10 g/dL versus 12.8 g/dL, p< 0.01), and higher creatinine levels (3.05 mg/dL versus 1.1 mg/dL, p=0.01) compared to Caucasian patients with AAV. African American patients with AAV also more frequently had renal involvement (80% versus 57%, p=0.02) and required hemodialysis at presentation (31% versus 11%, p=0.04), compared to Caucasian patients with AAV. There was a higher frequency of PR3-ANCA positivity in the Caucasian patient population (57% versus 29%, p=0.03) and a trend towards African American patients having a higher frequency of MPO-ANCA, although this did not reach statistical significance. There were no statistically significant differences in cutaneous manifestations, eye involvement, ENT involvement, subglottic stenosis, lung nodules or diffuse alveolar hemorrhage, or nervous system involvement between the two groups (TABLE).

Conclusion: African American patients with AAV had more severe disease at time of initial presentation, as demonstrated by more frequent Intensive Care Unit admissions, more frequent administration of pulse dose steroids, higher creatinine, and increased need for hemodialysis, when compared to the group of Caucasian patients with AAV. The observed differences in disease severity are likely multifactorial with potential causes including heterogeneity of vas-

Table:

Clinical Features of African American and Caucasian Patients with ANCA-associated Vasculitis			
	African American (n=35)	Caucasian (n=35)	p-value
Age at diagnosis (years, IQR)	48 (38-66)	44 (31-60)	0.15
Gender (Female, %)	24 (69%)	24 (69%)	1.0
ANCA type (n, %)			
Anti-PR3	10 (29%)	20 (57%)	**0.03**
Anti-MPO	18 (51%)	10 (29%)	0.09
ANCA-negative	5 (14%)	5 (14%)	1.0
Unknown status	2 (6%)	0 (0%)	0.49
ICU admission at presentation	18 (58%)	11 (31%)	**0.02**
Pulse dose steroids at presentation	29 (83%)	18 (51%)	**<0.01**
Hemoglobin (g/dL, median, IQR)	10 (9-11)	12.8 (12-13)	**<0.01**
Peak Creatinine (mg/dL, median, IQR)	3.05 (1.2-4.6)	1.1 0.8-1.9)	**0.01**
Hemodialysis at presentation	11 (31%)	4 (11%)	**0.04**
Organ Involvement			
Constitutional	33 (94%)	19 (54%)	**<0.01**
Cutaneous	7 (20%)	5 (14%)	0.52
Eye	5 (14%)	4 (11%)	0.72
ENT	15 (42%)	21 (60%)	0.15
Subglottic stenosis	2 (6%)	2 (6%)	1.00
Pulmonary			
Lung nodules	18 (51%)	16 (46%)	0.63
Diffuse alveolar hemorrhage	15 (42%)	9 (26%)	0.13
Renal	28 (80%)	20 (57%)	**0.02**
Nervous system	8 (23%)	8 (23%)	1.00

SD=standard deviation, ANCA=anti-neutrophil cytoplasmic antibody, PR3=proteinase 3, MPO=myeloperoxidase, ESRD=End stage renal disease, ICU=intensive care unit, IQR=interquartile range

Clinical Features of African American and Caucasian Patients with ANCA-associated Vasculitis

culitis presentation amongst different racial subgroups, comorbid conditions, access to care, treatment differences, environmental and socioeconomic factors. Additional studies to further delineate these factors are needed.

Disclosure: S. Khawaja, None; **S. Godbole**, None; **M. Kimoto**, None; **V. Steen**, Boehringer Ingelheim, 2, 5, corbus, 2, 5, eicos, 2, 5, genetech, 2, forbius, 5, galapagos, 5; **K. Quinn**, None.

Abstract Number: 1421

Clinical Features, Disease Activity and Prognosis of ANCA-Associated Vasculitis in US African Americans

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Vasculitis – ANCA-Associated Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV), including Granulomatosis with Polyangiitis (GPA), Eosinophilic Granulomatosis with Polyangiitis (EGPA) and Microscopic Polyangiitis (MPA), affect mostly Caucasians of European descent. Clinical presentation, clinical features, and prognosis of AAV in African Americans (AAs) have not been well described. The objective of this study was to compare the clinical features and outcomes at time of diagnosis of AA patients with AAV to Caucasian patients. Our hypothesis was that AA patients with AAV present with a higher frequency of MPA, greater disease severity, and experience higher mortality compared to Caucasian patients.

Table 1. Demographics, clinical and ANCA serologies in AA and Caucasian patients with AAV between 2003-2018

	African Americans (N= 32)	Caucasian (N= 64)	P-Value
Age, median (IQR)	47.5 (32.5)	61(19.5)	0.001
Male, n (%)	11 (34.4)	25 (39.1)	0.65
ANCA Type			
Negative	6 (18.8)	9 (14.1)	0.55
Positive			
P-ANCA	11 (42.3)	24 (43.6)	0.99
C-ANCA	13 (50)	27 (49.1)	
Double	2 (7.7)	4 (8)	
Anti-MPO	10 (35.7)	20 (33.3)	0.82
Anti-PR3	9 (33.3)	22 (36.7)	0.67
Phenotype			
GPA	16 (50)	41 (64.1)	0.32
MPA	15 (46.9)	20 (31.3)	
Renal Limited	6 (18.8)	3 (4.7)	0.06
EGPA	1 (3.1)	3 (4.7)	
Organ involvement			
Cutaneous	3 (9.4)	13 (20.3)	0.17
Ocular	3 (9.4)	9 (14.1)	0.51
ENT	9 (28.1)	28 (43.8)	0.14
Pulmonary	20 (62.5)	47 (73.4)	0.27
Cardiovascular	0	5 (7.81)	0.1
Renal	24 (75)	46 (71.9)	0.75
Nervous system	9(28.1)	18 (28.1)	1
MSK	13 (40.6)	35 (54.7)	0.19
Constitutional*	13 (40.6)	29 (46.3)	0.66

GPA= Granulomatosis with Polyangiitis EGPA = Eosinophilic Granulomatosis with Polyangiitis MPA = Microscopic with Polyangiitis, ENT= Ear, Nose & Throat, CNS= Central Nervous System MSK= Musculoskeletal, Cons*fevers, weight loss, myalgia, arthralgias

Table 1

Table 2. Demographics, laboratory and clinical characteristics at time of diagnosis of AA and Caucasians patients with GPA and MPA between 2003-2018

	GPA			MPA		
	AA (N= 16)	Caucasian (N=41)	P-value	AA (N=15)	Caucasian (N=20)	P value
Age, median (IQR)	35 (24)	55 (20)	0.0006	55 (20)	65 (13)	0.02
Male, n (%)	2 (12.5)	21 (51.2)	0.008	8 (53.3)	3 (15)	0.03
Duration of symptoms, days, median (IQR)	7 (23)	30 (114)	0.1	14 (18)	7 (27)	0.34
Time to diagnosis, months, median (IQR)	3.88 (11.5)	2 (3)	0.33	0 (1)	1 (2)	0.07
ANCA Type, n (%)						
Negative	3 (18.8)	6 (14.6)	0.7	2 (13.33)	2 (10)	1.0
Positive						
P-ANCA	1 (7.7)	6 (17.1)	0.35	10 (76.9)	16 (88.9)	0.6
C-ANCA	12 (92.3)	26 (74.3)		1 (7.7)	1 (5.6)	
Double	0	3 (8.6)		2 (15.4)	1 (5.6)	
Anti-MPO, n (%)	0	4 (10.5)	0.56	10 (76.9)	15 (79.0)	1.0
Anti-PR3, n (%)	8 (57.1)	22 (57.9)	0.96	1 (7.7)	0	0.4
Anti-PR3 and Anti-MPO negative, n (%)	6 (33.3)	12 (66.7)	0.15	2 (33.3)	4 (66.7)	0.4
Serum creatinine, Median (IQR)	0.8 (0.1)	1.2 (1.2)	0.04	2.9 (3.6)	2.2 (2.7)	0.19
CRP Median (IQR)	11.6 (11.3)	129.7 (140)	0.03	52.9 (148.5)	50.2 (113.3)	0.38
ESR, Median (IQR)	44.5 (39)	60 (45)	0.29	93.5 (113)	57.5 (34.5)	0.18
BVAS, median (IQR)	17.6 (24)	33 (16)	0.07	25 (8)	26.5 (15.5)	0.45
FFS, median (IQR)	1 (0)	1 (1)	0.36	2 (1)	2 (0.5)	0.36
Biopsy diagnostic, n (%)	9 (60)	27 (65.9)	0.69	14 (93.3)	16 (88.9)	1.0
Organ involvement, n (%)						
Cutaneous	1 (6.3)	9 (22)	0.25	1 (6.7)	3 (15)	0.62
Ocular	2 (12.5)	6 (14.6)	1.0	1 (6.7)	3 (15)	0.62
ENT	8 (50)	24 (58.5)	0.56	1 (6.7)	2 (10)	1.0
Pulmonary	13 (81.3)	30 (73.2)	0.73	6 (40)	15 (75)	0.08
Cardiovascular	0	2 (4.9)	1.0	0	2 (10)	0.5
Renal	9 (56.2)	28 (68.3)	0.39	14 (93.3)	17 (85)	0.62
CNS	4 (25)	9 (22)	1.0	4 (26.7)	6 (30)	1.0
MSK	8 (50)	24 (58.6)	0.56	5 (33.3)	9 (45)	0.73
Constitutional*	4 (25)	19 (46.3)	0.23	8 (53.3)	9 (45)	0.6
Deaths	0	2 (4.9)	1.0	3 (26.7)	0	0.07
Dialysis	3 (18.8)	7 (17.1)	1.0	3 (20.0)	2 (10)	0.6

GPA= Granulomatosis with Polyangiitis, EGPA = Eosinophilic Granulomatosis with Polyangiitis, MPA = Microscopic with polyangiitis, FFS= Five Factor score, BVAS = Birmingham Vasculitis Activity Score, CRP= C-Reactive Protein, ESR= Erythrocyte Sedimentation Rate , ENT= ear, nose & throat, CNS= Central Nervous System MSK= Musculoskeletal, *fevers, weight loss, myalgia, arthralgias

Table 2

Methods: We conducted a retrospective chart review of patients with ICD-9-CM and ICD-10 codes used for AAV (446.0, 446.4, 447.6 and M31.3, 31.7, M30.1, I77.6, M31.9, M31.8) between 1/2003 to 12/2018. Diagnosis was confirmed by two reviewers (one rheumatologist), and in case of discordance, a third reviewer was involved (rheumatologist). Race was verified through chart review. AA cases were randomly matched by year of diagnosis (± 4 years) in a 1:2 ratio with Caucasian controls. Demographics, clinical and laboratory features, disease activity and prognosis were abstracted by chart review using the Birmingham Vasculitis Activity Score (BVAS) 3 and Five-Factor Score (FFS). T-test, Chi-square and Fisher exact test were used for statistical analysis, when appropriate.

Results: 548 AA patients were identified using diagnostic codes. 56 AA patients were confirmed to have AAV via chart review but only 32 of these cases were confirmed using diagnostic criteria. We matched 64 similarly confirmed Caucasian controls. Compared to Caucasians, AA patients with AAV were younger (47.5 years [IQR 32.5] vs 61.0 years [IQR 19.5], p = 0.001). No other clinical or laboratory features were different compared to Caucasians (Table 1). In addition, we found no difference in frequency of GPA, MPA, or EGPA phenotypes between AA and Caucasians. Younger age at presentation was observed among AAs with GPA (35 [IQR 24] vs 55 [IQR 20), p = 0.006) and MPA (55.5 [IQR 20] vs 65.0 [IQR 13], p = 0.02) (Table 2). Compared with Caucasians, the proportion of women with GPA was higher among AAs (82.3% vs 47.8%, p = 0.008) but the proportion of AA men with MPA was higher (53.3% vs 15%, p = 0.03) (Table 2). There was no difference in disease activity, severity of manifestations or mortality.

Conclusion: In this single center retrospective study, AA patients with AAV presented at a younger age compared with Caucasians. No differences in mortality rates, clinical phenotypes, clinical and laboratory features, disease activity, prognostic scores, or mortality were observed.

Disclosure: L. Palomino, None; **A. Gaffo**, Amgen, 1; **S. Sattui**, None; **D. Sun**, None.

Abstract Number: 1422

Healthcare Utilization Among Patients Diagnosed with ANCA-Associated Vasculitis Between 2007 and 2014 in a Multi-Center Cohort Linked to Medicare Claims Data

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Vasculitis – ANCA-Associated Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: ANCA-associated vasculitis (AAV) leads to complications that contribute to poor quality of life and survival. Systemic vasculitis is associated with high healthcare utilization but little is known about healthcare utilization specifically in AAV, especially around the time of diagnosis when complications are common. Identifying utilization patterns is needed to define opportunities to improve care, to inform inputs for cost-effectiveness studies, and to support advocacy efforts to fund research in diseases that have a disproportionate impact on societal resources.

Methods: The Partners AAV Cohort is a consecutive inception cohort established at Partners HealthCare (PHS), a large healthcare system in New England. We included AAV cases diagnosed between 2007-2014 with available Medicare claims data who could be matched (by age, sex, and index date [AAV treatment initiation]) to a non-AAV control that received primary care at PHS and also had claims data available. Electronic health record data from cases and controls were linked deterministically to Medicare Parts A and B claims data, which contain details regarding ambulatory, inpatient, and emergency department visits and non-acute institutional visits (e.g., rehab). Healthcare utilization was compared using Chi Square tests and generalized estimating equations.

Results: We included 99 cases and controls. Age, sex, race, and baseline Charlson Comorbidity Index were similar between cases and controls (**Table 1**). There was an increase in emergency department (ED) and ambulatory visits (AV) and inpatient (IP) hospitalizations among AAV cases in the months preceding the index date (**Figure 1**). Compared to controls, cases were more likely to have at least one ED visit (67% vs 22%, P = < 0.001) and/or IP hospitalization (65% vs 15%, P= < 0.001) during the first six months following the index date (**Table 1**). AVs were more frequent among cases than controls throughout the study period (**Figure 1,** P< 0.001); in the first six months after the

	Cases	Controls
Age, treatment initiation (median, IQR)	75 [69, 80]	73 [67, 78]
Female (N, %)	68 (69)	68 (69)
MPO-ANCA+ (N, %)	78 (79)	
White (N, %)	95 (96)	86 (87)
CCI (median, IQR)	2 [1, 5]	2 [1, 3]

Table 1. Demographics Features of AAV Cases and Controls

	Cases				Controls				P-Value
	Median [IQR]	0 Visits N (%)	1 Visit N (%)	≥ 2 Visits N (%)	Median [IQR]	0 Visits N (%)	1 Visit N (%)	≥ 2 Visits N (%)	
Ambulatory Visits									
-6 months to Baseline	14 [7, 19]				5 [1, 13]				
Baseline to +6 months	22 [13, 33]				5 [1, 13]				
+6 to +12 months	14 [6, 25]				4 [0, 10]				
+12 to +18 months	9 [0, 20]				3 [0, 11]				
Inpatient Hospitalization									
-6 months to Baseline	0 [0, 0]	54 (56)	32 (32)	13 (13	0 [0, 0]	86 (87)	5 (5)	8 (8)	< 0.001
Baseline to +6 months	1 [0, 2]	35 (35)	31 (31)	33 (33)	0 [0, 0]	84 (85)	9 (9)	6 (6)	< 0.001
+6 to +12 months	0 [0, 0]	70 (71)	19 (19)	10 (10)	0 [0, 0]	87 (88)	9 (9)	3 (3)	0.010
+12 to +18 months	0 [0, 0]	82 (83)	8 (8)	9 (9)	0 [0, 0]	92 (93)	4 (4)	3 (3)	0.086
Emergency Department Visits									
-6 months to Baseline	1 [0, 2]	48 (48)	26 (26)	25 (26)	0 [0, 0]	80 (81)	9 (9)	10 (10)	< 0.001
Baseline to +6 months	1 [0, 2]	33 (33)	20 (20)	46 (47)	0 [0, 0]	77 (78)	11 (11)	11 (11)	< 0.001
+6 to +12 months	0 [0, 0]	65 (66)	18 (18)	16 (16)	0 [0, 0]	88 (89)	3 (3)	8 (8)	< 0.001
+12 to +18 months	0 [0, 0]	74 (75)	12 (12)	13 (13)	0 [0, 0]	85 (86)	7 (7)	7 (7)	0. 14
Non-Acute Institutional Stay									
-6 months to Baseline	0 [0, 0]	93 (94)	1 (1)	5 (5)	0 [0, 0]	92 (93)	1 (1)	6 (6)	0.95
Baseline to +6 months	0 [0, 0]	75 (76)	5 (5)	19 (19)	0 [0, 0]	89 (90)	1 (1)	9 (9)	0.024
+6 to +12 months	0 [0, 0]	90 (91)	1 (1)	8 (8)	0 [0, 0]	88 (89)	0 (0)	11 (11)	0.47
+12 to +18 months	0 [0, 0]	92 (93)	1 (1)	6 (6)	0 [0, 0]	93 (94)	1 (1)	5 (5)	0.95

Table 2. Healthcare Utilization Among AAV Cases and Controls Using Medicare Claims Data from 2007-2014

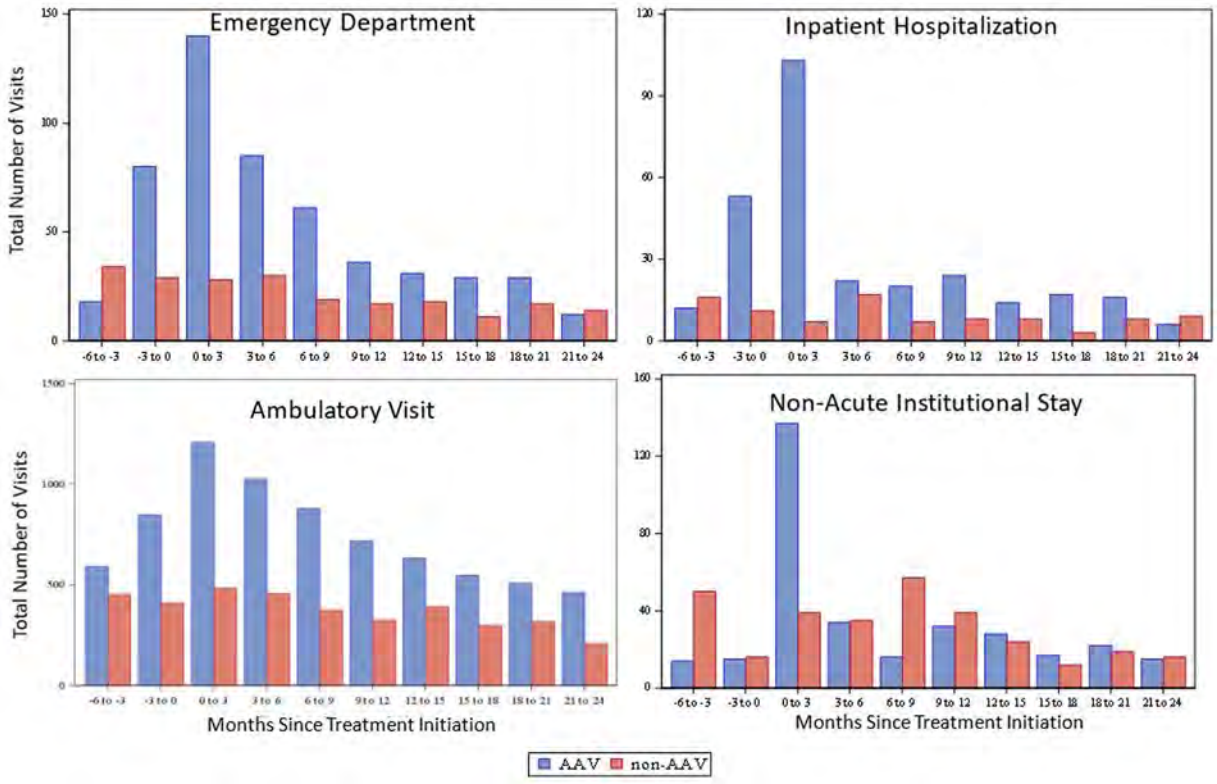

Figure 1. Healthcare Utilization in ANCA-Associated Vasculitis Before and After Treatment Initiation

index date, cases had a median of 22 [13, 33] AVs compared to 5 [1, 13] among controls (**Table 1**). Among cases, 33% had ≥ 2 IP hospitalizations in the six months after the index date while 35% had none. Following the index date, there was a gradual decrease in healthcare utilization among cases (**Figure 1**). More cases than controls had ≥ 1 non-acute institutional stay (24% vs 10%, P=0.02) in the first six months after the index date (**Table 1**).

Conclusion: Compared to controls, AAV patients have greater healthcare utilization in the period around diagnosis. These observations establish important benchmarks in AAV care and opportunities for improvement. First, increased utilization prior to diagnosis might reflect diagnostic delays that may be shortened with strategies that include better provider education and leveraging artificial intelligence in electronic health records. Second, high utilization appears to be concentrated in a subset of AAV patients (e.g., multiple hospitalizations) which may benefit from interventions to minimize readmission or unnecessary care. Studies are needed to identify modifiable risk factors associated with healthcare utilization in AAV.

Disclosure: Z. Wallace, Bristol-Myers Squibb, 2; **X. Fu**, None; **J. Stone**, None; **H. Choi**, AstraZeneca, 2, Takeda, 5, Selecta, 5, GlaxoSmithKline, 5, Horizon, 5; **R. Walensky**, None.

Abstract Number: 1423

Declining In-Hospital Mortality in Vasculitis: A 17-year U.S. National Study

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Vasculitis – ANCA-Associated Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: To our knowledge, only a few population-based studies for vasculitis mortality exist; and most are limited to vasculitis sub-types. Therefore, our study objective was to assess time-trends in in-hospital mortality in vasculitis and compare it to the general population, using the U.S. National Inpatient Sample (NIS).

Methods: We included the data from the Healthcare Cost and Utilization Project (HCUP) NIS from 1998 to 2014. The NIS is a de-identified national all-payer inpatient health care database that has a 20% stratified sample of hospital discharges. NIS is used frequently for creating U.S. national estimates.

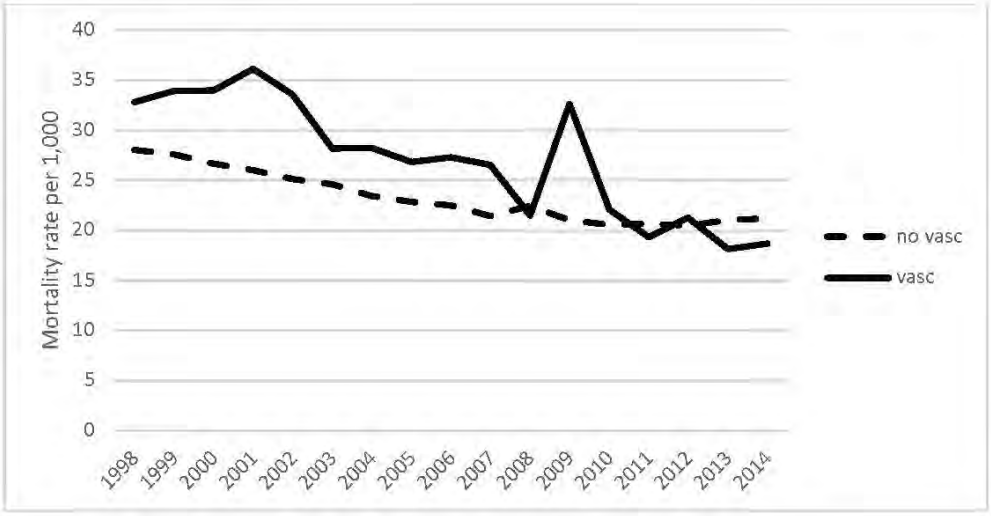
Cases of hospitalized vasculitis were defined based on the listing of 446.xx or 447.6 as the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) diagnostic codes in the primary diagnosis position. A previous study showed a sensitivity of 93% and specificity of 95% using this approach. We limited our study to 2014, the last year ICD-9-CM codes were used in the U.S. before switching to ICD-10-CM in 2015.

We calculated the unadjusted in-hospital mortality rates per 1,000 hospitalizations for people with versus without primary vasculitis hospitalizations, with the respective denominators. We calculated age-adjusted rates by grouping age in quintiles (< 20, 20-39, 40-59, 60-79, >79) and age- and sex-adjusted rates. We analyzed in-hospital mortality rate time-trends using the Cochran Armitage test, weighted by the number of hospitalizations each year.

Results: There were 266,461 primary vasculitis hospitalizations in 1998-2014 with 7,215 in-hospital deaths (2.7%). Mean age was 42.9 years, 57% were men, 50% were white, 30% had a Deyo-Charlson comorbidity score of ≥2 and 18% had a Medicaid payer (Table **1**).

Figure 1. Time-trends in unadjusted (A) and age- and sex-adjusted (B) in-hospital mortality rates per 1,000 population of hospitalizations in people with vasculitis compared to people without vasculitis.

A. Unadjusted



B. Age- and sex- adjusted

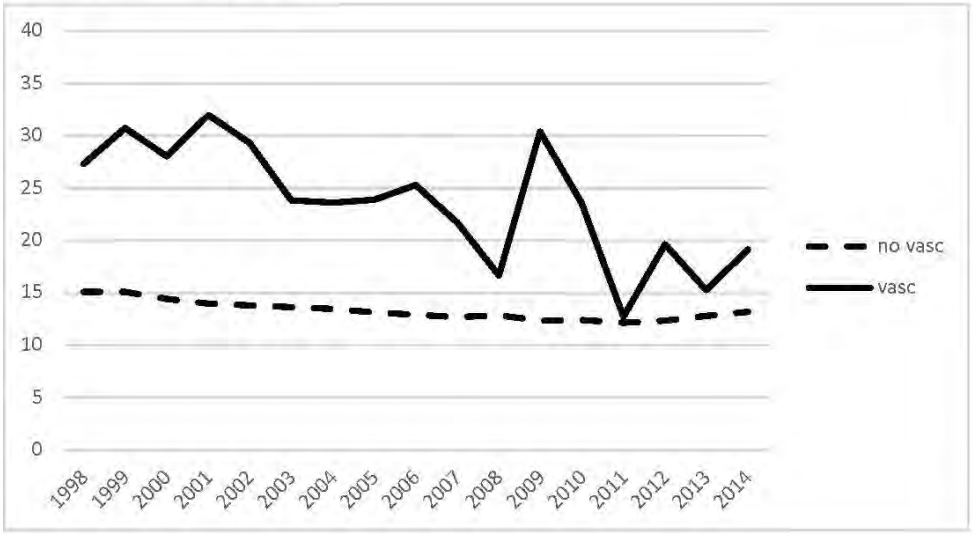


Figure 1 legend

The y-axis shows rate per 1,000 hospitalization claims with each respective denominator

Figure 1. Time-trends in unadjusted (A) and age- and sex-adjusted (B) in-hospital mortality rates per 1,000 population of hospitalizations in people with vasculitis compared to people without vasculitis. Figure 1 legend The y-axis shows rate per 1,000 hospitalization claims with each respective denominator

Unadjusted in-hospital mortality in primary vasculitis hospitalizations decreased by 43% from 32.8 per 1,000 in 1998 to 18.7 per 1,000 in 2014 ($p< 0.01$), compared to a 24.5% reduction in deaths for all NIS claims without vasculitis (28.1 to 21.2 per 1,000; $p< 0.01$; **Figure 1**).

Appendix 1. Demographic and clinical characteristics of people hospitalized with vasculitis in the U.S.

	Hospitalization with vasculitis; N (%), unless specified otherwise
Age, Mean (Std Error); median	42.98 (0.382); 48.4
Age category	
<50	134,837 (50.69%)
50-64	47,298 (17.78%)
65-79	55,283 (20.78%)
≥80	28,608 (10.75%)
Gender	
Female	114,360 (43.14%)
Male	150,715 (56.86%)
Race	
White	132,037 (49.55%)
Black	35,684 (13.39%)
Hispanic	26,693 (10.02%)
Other/Missing	72,037 (27.04%)
Deyo-Charlson Index Score	
0	132,956 (49.90%)
1	52,121 (19.56%)
≥2	81,384 (30.54%)
Income Category	
0-25th percentile	54,416 (20.86%)
25-50th percentile	65,186 (24.99%)
50-75th percentile	65,267 (25.02%)
75-100th percentile	75,968 (29.12%)
Insurance	
Medicare	90,812 (34.16%)
Medicaid	48,056 (18.08%)
Private	105,338 (39.62%)
Self	12,122 (4.56%)
Other	9,515 (3.58%)
Hospital Region	
Northeast	55,474 (20.82%)
Midwest	58,497 (21.95%)
South	101,008 (37.91%)
West	51,481 (19.32%)
Total Charge, Mean (Std Error); median	43,539 (570.3); 19,533
Discharge Status	
Inpatient	31,810 (12.36%)
Home	225,593 (87.64%)
Length of Stay, Mean (Std Error); median	6.81(0.048); 3.7
LOS cat	
≤3	136,575 (51.26%)
>3	129,886 (48.74%)
Died during hospitalization	7,214 (2.71%)

Table 1. Demographic and clinical characteristics of people hospitalized with vasculitis in the U.S.

Age- and sex-adjusted in-hospital mortality decreased both in primary vasculitis hospitalizations from 27.3 per 1,000 claims in 1998 to 19.1 in 2014 and non-vasculitis hospitalizations from 15.1 to 13.2 per 1,000 in 2014, respectively ($p< 0.01$; **Figure 1**; Table **2**). The age- and sex-adjusted mortality rate gap between those with versus without vasculitis narrowed (**Figure 1**); vasculitis to non-vasculitis in-hospital mortality ratio was 1.81 in 1998-2000 and 1.45 in 2013-2014 (Table **2**). Primary vasculitis hospitalizations per year remained fairly constant from 1998-2014 at 14-18,000 per year; rate was 43 per 100,000 NIS claims in 1998-2000 versus 43.2 in 2013-14; i.e., 0.05% of claims per year.

Appendix 2. Mortality rates per 1,000 population in people hospitalized without versus with Vasculitis: unadjusted based on the NIS sample; age- and age- and sex-adjusted rates based on the NIS sample and the census data

	No Vasculitis			Vasculitis		
Year	Unadjusted	Age-adjusted	Age- and sex-adjusted	Unadjusted	Age-adjusted	Age- and sex-adjusted
1998	28.1	14.4	15.1	32.8	27.1	27.3
1999	27.6	14.5	15.1	33.9	31.9	30.7
2000	26.7	13.8	14.4	34.0	27.2	28.0
2001	26.0	13.4	14.0	36.1	30.3	32.0
2002	25.1	13.2	13.8	33.6	29.4	29.3
2003	24.6	13.0	13.6	28.2	23.5	23.8
2004	23.5	12.8	13.5	28.3	23.1	23.6
2005	22.9	12.5	13.2	26.8	23.7	23.9
2006	22.5	12.3	12.9	27.3	25.4	25.3
2007	21.5	12.1	12.7	26.6	23.8	21.7
2008	22.4	12.3	12.9	21.5	17.0	16.7
2009	21.0	11.8	12.3	32.6	29.4	30.4
2010	20.6	11.9	12.4	22.1	23.5	23.5
2011	20.7	11.7	12.2	19.4	12.8	12.7
2012	20.5	11.9	12.4	21.3	19.6	19.6
2013	21.1	12.3	12.8	18.2	15.8	15.2
2014	21.2	12.7	13.2	18.7	18.1	19.1
% reduction - 1998 to 2014	**24.5%**	**11.8%**	**12.6%**	**43.0%**	**33.2%**	**30.0%**

Table 2. Mortality rates per 1,000 population in people hospitalized without versus with Vasculitis: unadjusted based on the NIS sample; age- and age- and sex-adjusted rates based on the NIS sample and the census data

Conclusion: Adjusted in-hospital mortality decreased significantly over time in both the general U.S. population and primary vasculitis hospitalization cohorts, and the absolute and relative reductions were larger for vasculitis hospitalizations. Age- and sex-adjusted in-hospital mortality was higher in vasculitis compared to the general population in both 1998 and 2014, but the gap narrowed over time.

Disclosure: J. Singh, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **J. Cleveland**, None.

Abstract Number: 1424

Outcomes of Hospitalizations for Acute Myocardial Infarction in Patients with ANCA Associated Vasculitis from the National Inpatient Sample

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Vasculitis – ANCA-Associated Poster

Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: Several studies in the past have shown significantly increased risks of cardiovascular disease in patients with ANCA associated vasculitis (AAV). This association is thought to be secondary to systemic inflammation as well as glucocorticoid use and their role in premature atherosclerosis. In this study, we aimed to evaluate the

Demographics and Outcomes of AMI hospitalizations in patients with and without AAV in 2016-2017

Demographics/Outcomes	AAV	No AAV	P-value
Female (%)	46	38	0.01
Caucasian (%)	67	71	0.31
Age (Year) (mean)	67.23	66.97	0.78
Insurance (%) Medicare Medicaid Private	 67 08 21	 59 09 26	0.14
Hospital Region (%) NE MW South West	 18 25 38 17	 17 22 40 19	0.68
Hospital Bed size (%) Small Medium Large	 14 35 50	 16 30 53	0.24
Urban Hospital (%)	90	92	0.45
Teaching Hospital (%)	67	66	0.81
Charlson Comorbidity Index ≥3 (%)	72	51	<0.01

outcomes of patients hospitalized for acute myocardial infarction (AMI) in those with and without a history of AAV in a nationally representative sample.

Methods: We used data from the National Inpatient Sample (NIS) for the period of 2016 to-2017 for adult AMI hospitalizations as a primary diagnosis and AAV as a secondary diagnosis using ICD-10 codes. The proportion who met ACR classification criteria cannot be determined with the NIS database. We used STATA.15 for the data analysis and logistic regression was applied to calculate adjusted odds ratios (aOR) for inpatient mortality and length of stay (LOS) in AMI hospitalizations in patients with and without a history of AAV.

Results: We identified a total of 1305889 AMI hospitalizations over a 2-year period of 2016 to 2017 of which 1040 patients had a history of AAV. There was no statistically significant difference in the age between two groups of patients. Compared to the patient without AAV, a higher proportion of patients were female in the AAV group (46% vs 38%; p= 0.01). There was a statistically significant difference in Charlson comorbidity index between two groups of AMI with AAV vs without AAV (72% vs 51%; P< 0.01)

In-hospital mortality after MI in patients with a history of AAV compared with those without AAV was not different (5.3% vs. 4.7%; P= 0.66). In Multivariate logistic regression model after adjusting for age, sex, hospital teaching status, hospital bed size, insurance status, and Charlson comorbidity index, there was no difference in the odds of in-hospital mortality in patients with history of AAV compared with no history of AAV (OR 1.06; 95% CI 0.57-1.97).

Unadjusted mean LOS in AMI patients with a history of AAV was not statistically different from those without AAV (5.02 vs. 4.44; P=0.09). In multivariate Regression model; after adjusting for age, sex, household income, Hospital location, Hospital teaching status, Hospital bed size, and Charlson comorbidity index, mean LOS following MI in patients with AAV vs. no AAV was not different (P=0.73).

Conclusion: Inpatient mortality after AMI as well as LOS were similar in patients with and without AAV in the 2-year period of 2016-2017 despite previously known greater risk of Cardiovascular disease in patients with AAV. These findings may be related to better disease control with Rituximab and reduction in the use of glucocorticoids in these patients.

Disclosure: A. Vafa, None; **M. Figueroa Sierra**, None; **O. Behnamfar**, None; **H. Babary**, None; **S. Afroz**, None; **Y. Lin**, None.

Abstract Number: 1425

Reduced Risk of Cardiovascular Diseases Events with Renal Transplantation in Granulomatosis with Polyangiitis in the United States: Data from the US Renal Data System

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SESSION INFORMATION
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Baseline Characteristic	All Waitlisted (n = 985)	Had Transplant (n = 640)
Age at ESRD onset, %		
<30 y	16	19
30–39 y	7	8
40–49 y	17	18
>50 y	59	54
Female, %	41	40
Mean BMI, kg/m2	27.2	27.0
Race/ethnicity, %	-	-
White	87	88
African American	8	8
Asian	1	1
Other	3	3
Hispanic, %	12	10
Organ Procurement and Transplantation Network region, %	-	-
1 (Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, eastern Vermont)	5	4
2 (Delaware; DC; Maryland; New Jersey; Pennsylvania; West Virginia; northern Virginia)	11	12
3 (Alabama, Arkansas, Florida, Georgia, Louisiana, Mississippi)	12	12
4 (Oklahoma, Texas)	8	8
5 (Arizona, California, Nevada, New Mexico, Utah)	13	12
6 (Alaska, Hawaii, Idaho, Montana, Oregon, Washington)	5	6
7 (Illinois, Minnesota, North Dakota, South Dakota, Wisconsin)	11	11
8 (Colorado, Iowa, Kansas, Missouri, Nebraska, Wyoming)	9	9
9 (New York, western Vermont)	6	5
10 (Indiana, Michigan, Ohio)	9	10
11 (Kentucky, North Carolina, South Carolina, Tennessee, Virginia)	11	11
Prior organ transplant, %	< 1	< 1
Comorbid conditions, %	-	-
Diabetes	9	8
Hypertension	66	64
CAD	5	4
CHF	7	5
CVA	3	3
Tobacco use	3	2
Cancer	3	2
Comorbidity score	0.6	0.5
First treatment method, %	-	-
Hemodialysis	88	87
Peritoneal dialysis	12	13

Table 1. Baseline Demographic and Disease-Specific Features

Background/Purpose: Granulomatosis with polyangiitis (GPA) is a common cause of glomerulonephritis and leads to end-stage renal disease (ESRD) in approximately 25% of patients. Both GPA and ESRD are associated with an increased risk of cardiovascular disease (CVD). In fact, CVD is the most common cause of death in GPA. Renal transplantation improves survival in GPA but its impact on risk of CVD events like myocardial infarction (MI) and cerebrovascular accident (CVA) is poorly understood in this unique population.

Methods: We identified all incident cases of ESRD due to GPA (ICD9=446.4) in the United States Renal Data System (USRDS) who were waitlisted for a renal transplant between 2000-2014. The USRDS captures nearly all patients with ESRD in the US and requires that nephrologists report the ESRD cause (ICD-9 code). The USRDS includes details regarding demographics, comorbidities, hospitalizations covered under Medicare Part A, and waitlist and transplant dates and statuses. All patients were followed to the earliest of: up to 3 years after transplant, end of Medicare coverage, death, or December 31, 2015. CVD outcomes of interested included non-fatal and fatal myocardial infarctions (MI) and ischemic cerebrovascular accident (CVA). We used a Cox regression model with transplantation as a time-varying exposure and accounted for the competing risk of non-CVD-related mortality to estimate the hazard ratio (HR) and 95% confidence intervals (CIs) of CVD events among those transplanted compared to those who remained on the waitlist. We adjusted for sociodemographics, comorbidities, and other covariates.

Results: During the study period, 985 patients with ESRD due to GPA were waitlisted for a renal transplant (**Table 1**); 640 (65%) received a renal transplant. The majority were male (59%) and white (87%). Mean age at waitlisting was 50.6 (±16.3) years. Among those who had a renal transplant, the mean age at transplant was 48.1 (±16.7) years.

Mean follow-up time was 2.8 years. During follow-up, 15 non-fatal MIs, 39 non-fatal CVAs, 13 fatal MIs, and 4 fatal CVAs occurred. In total, there were 68 CVD events. The incidence of a CVD event during follow-up was 13.8/1,000 person-years and 53.0/1,000 person-years in the group that did and did not receive a transplant, respectively. In fully-adjusted analyses, transplanted patients had a 70% lower risk of a CVD event compared to those who remained on the waitlist (HR 0.30, 95% CI 0.24-0.38). Our findings remained consistent when analyzing each CVD event individually in unadjusted analyses, accounting for the competing risk of death and other CVD events: non-fatal CVA (HR 0.34, 95% CI 0.27-0.43), non-fatal MI (HR 0.34, 95% CI 0.27-0.43), fatal CVA (HR 0.35, 95% CI 0.27-0.44), and fatal MI (HR 0.35, 95% CI 0.28-0.44).

Conclusion: In this nationwide study of ESRD due to GPA, renal transplantation was associated with a significantly reduced risk of non-fatal and fatal CVD events. Our findings highlight the importance of identifying barriers to transplantation in this patient population. Additionally, evaluating management strategies to reduce the risk of CVD events in patients on the waitlist will likely improve survival.

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Abstract Number: 1426

Prevalence of ANCA-associated Vasculitis and Spatial Association with Quarries in a French Northeast Region: A Capture-recapture and Geospatial Analysis

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SESSION INFORMATION

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Session Time: 9:00AM–11:00AM

Table 1: Characteristics of included patients at assessment.

	TOTAL (n = 185)	GPA (n = 120)	MPA (n = 35)	RLV (n = 30)
Age at diagnosis (years)	61 (12-91)	58 (13-91)	67 (12-89)	61 (30-82)
Male gender (n, %)	105 (57)	71 (59)	15 (43)	19 (63)
Disease duration (years)	5 (0-26)	5 (0-22)	4 (0-19)	5 (0-26)
Organ involvement (n, %)				
Renal	152 (82)	88 (73)	34 (97)	30 (100)
ENT	80 (43)	77 (64)	3 (9)	/
Pulmonary	103 (56)	83 (69)	20 (57)	/
Nervous system	41 (22)	35 (29)	6 (17)	/
Cutaneous	35 (19)	30 (25)	5 (14)	/
Eyes	22 (12)	21 (18)	1 (3)	/
Cardiovascular	15 (8)	9 (8)	6 (17)	/
Gastro-intestinal	11 (6)	9 (8)	2 (6)	/
ANCA positivity (n, %)	175 (95)	111 (93)	35 (100)	29 (97)
PR3	106 (57)	96 (80)	1 (3)	9 (30)
MPO	71 (38)	17 (14)	34 (97)	20 (67)
Histological proof (n, %)	139 (75)	89 (74)	20 (57)	30 (100)
FFS at diagnosis (n, %)	1 (0-3)	1 (0-3)	1 (0-3)	/
BVAS at diagnosis (n, %)	14 (1-39)	15 (1-39)	15.5 (5-21)	/

Values are expressed as number (percentage) or median (range). BVAS, Birmingham Vasculitis Activity Score; ENT, ear nose throat; FFS, Five Factor Score; MPO, myeloperoxidase; PR3, proteinase 3.

Background/Purpose: Studies addressing the epidemiology of ANCA-associated vasculitides (AAV) in different countries reported various prevalence rates and suggested that incidence may have increased over the past 30 years. Environmental factors may play an important role in the development of AAV. Exposure to silica, one of the strongest environmental substances causing overall autoimmunity, has particularly been associated with a higher risk of developing AAV. In the present work, we report the prevalence of granulomatosis with polyangiitis (GPA), microscopic polyangiitis (MPA) and renal limited vasculitis (RLV) in Alsace, a French Northeast region, and demonstrated a geospatial association between these diseases and quarries leading to crystalline silica exposure.

Methods: We performed a capture–recapture analysis using three separate sources : 1) hospital records from departments of medical specialties that were likely to diagnose AAV, 2) ANCA positivity in publicly-funded reference immunology laboratories, and 3) the database from the French National Health Insurance System. A case was included if the patient was alive and resided in Alsace on January 1, 2016, and fulfilled either the ACR classification criteria for GPA, either the Chapel Hill Consensus Conference CHCC 2012 revised definition of systemic vasculitides for both GPA and MPA. The European Medicines Agency (EMA) algorithm was used to distinguish GPA and MPA. RLV was defined as pauci-immune glomerulonephritis without evidence for extrarenal disease. Capture-recapture was used to estimate the number of cases missed by any of the sources and therefore the total number of cases. The spatial association between the number of cases and the number of quarries in each administrative entity (French “communes”) was assessed using geographical weighted regression.

Results: 910 potential eligible cases were identified. After exclusion of duplicates and non-matching demographic or medical criteria cases, 185 patients were included from the three sources (Figure 1). 120 were classified as GPA, 35

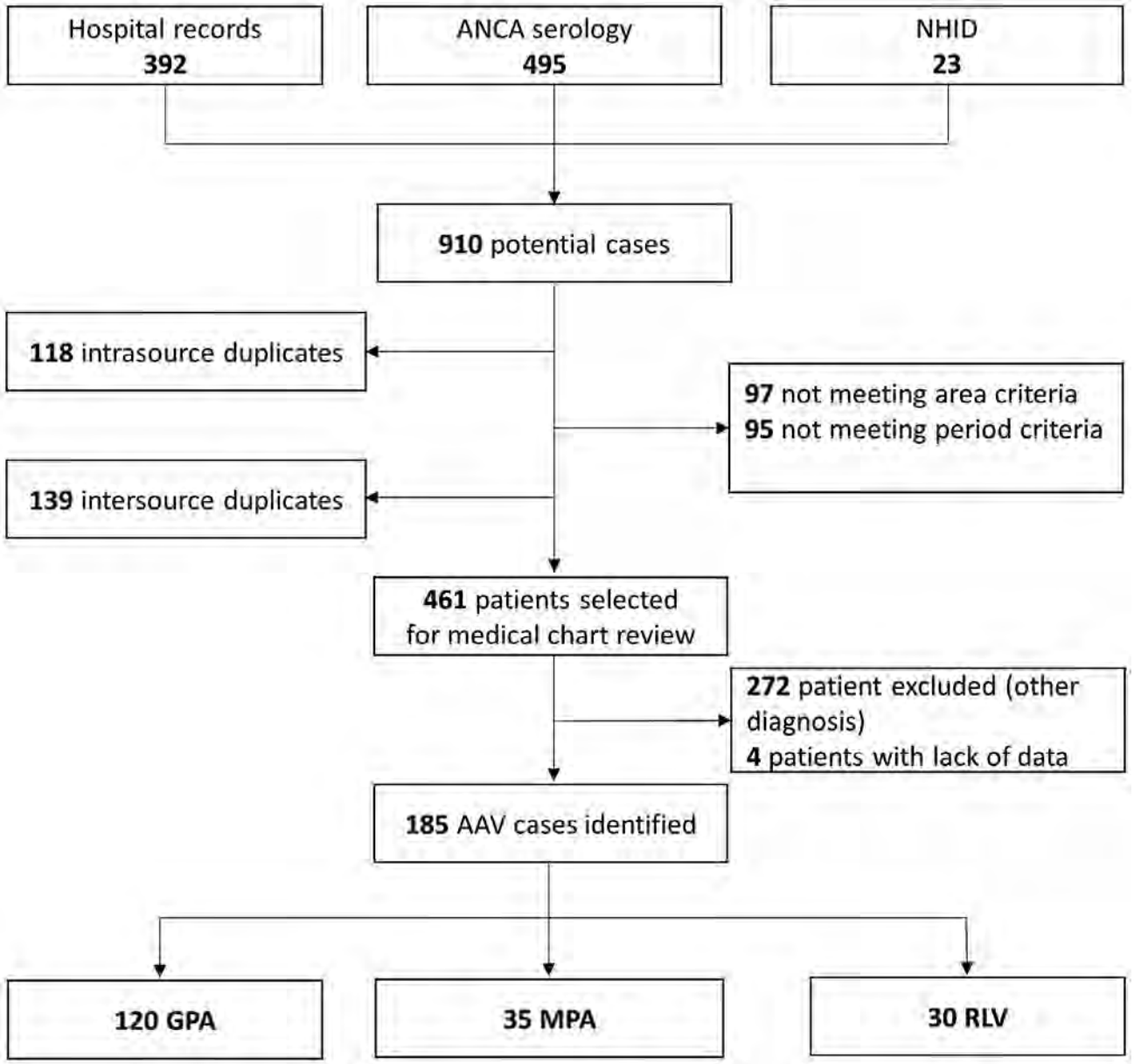

Figure 1. Flow chart of AAV cases identifications. AAV, ANCA-associated vasculitis; GPA, granulomatosis with polyangeitiis; MPA, micropolyangeitiis; NHID, National Health Insurance database; RLV, renal-limited vasculitis.

as MPA, 30 as RLV (Table 1). Capture-recapture estimated the number of cases missed by any source to 6.4 (95%CI 3.6-11.5), and the 2016 estimated prevalence in Alsace was 65.5 cases per million inhabitants (95%CI 47.3-93.0) for GPA, 19.1 (95%CI 11.3-34.3) for MPA, and 16.8 (95%CI 8.7-35.2) for RLV. This GPA prevalence was two times higher than that estimated in a North-eastern suburb of Paris in 2003. Geographical weighted regression models demonstrated a significant spatial association between presence of quarries and GPA cases ($p = 0.039$) but not MPA or RLV (Figure 2).

Conclusion: In a French region with a high density of extraction sites, the high prevalence of GPA and the spatial association between quarries and GPA supports the role of specific environmental etiologic factors. Further studies evaluating type and duration exposure should investigate the link between silica and AAV development.

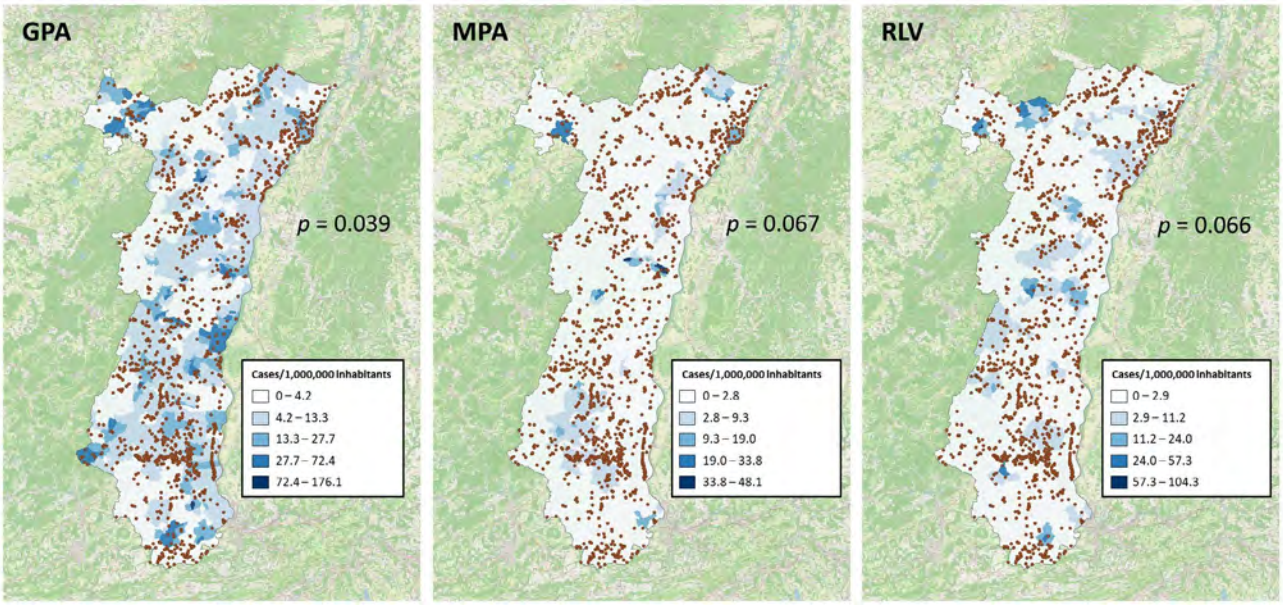

Figure 2. Spatial association between GPA cases and quarries in Alsace, France. Spatial association between the normalized prevalence of GPA, MPA and RLV (shown as the prevalence per 1,000,000 inhabitants with spatial Bayesian smoothing using Jenks natural breaks) and localization of quarries in Alsace, France.

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Abstract Number: 1427

Anti-IL5 Therapy for Eosinophilic Granulomatosis with Polyangiitis (EGPA) - An 18 Month Follow-up Study as a Steroid Sparing Therapeutic Approach

Allyson Egan[1], Pasupathy Sivasothy[2], Robin Gore[3], Caroline Owen[3], Marcos Del Martinez Pero[4], Rachel Jones[4], Lisa Willcocks[4], Rona Smith[4], Stella Burns[4] and David Jayne[5], [1]Vasculitis and Lupus Clinic, Department of Medicine, Addenbrooke's Hospital, Cambridge., London, United Kingdom, [2]Vasculitis and Lupus Clinic, Department of Medicine, Addenbrooke's Hospital, Cambridge., Cambridge, England, United Kingdom, [3]Department of Respiratory medicine, Addenbrooke's Hospital, Cambridge, Cambridge, United Kingdom, [4]Vasculitis and Lupus Clinic, Department of Medicine, Addenbrooke's Hospital, Cambridge., Cambridge, [5]Department of Medicine, Vasculitis and Lupus Research Group, University of Cambridge, Cambridge, UK, Cambridge, United Kingdom

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Table 1: EGPA patients receiving Mepolizumab therapy for ≥ [100mg s/c]

Demographics	All [n=13]
Gender ratio M/F	4M:9F
ANCA positive/ negative	ANCA: 3MPO, 1 PR3 positive/ 9 ANCA negative
Age of diagnosis of asthma	35 years [IQR 28.5-40]
Age of diagnosis of EGPA	47 years [IQR 43.5-53.5]
Median age	51 years [IQR 47.5- 60.5]
EGPA disease characteristics	N=13 [%]
Asthma	13 [100]
Serum eosinophilia or biopsy evidence [N= 12]	12 [100]
Pulmonary infiltrates, non-fixed	8[61.5]
Neuropathy, mono/poly	4[30.7]
Sino-nasal abnormality	12[92.3]
Glomerulonephritis	3[23]
Cardiovascular	4[30.7]
Prior Immunosuppressants	N=13 [%]
Steroids	13[100%]
Cyclophosphamide	6[46%]
Rituximab	6[46%]
Azathioprine	10[77%]
Mycophenolate mofetil	8[62%]
Methotrexate	4[31%]
Campath	1[7%]

EGPA patients receiving anti-IL5 therapy for greater than 18 months

Response to therapy		M0 [%]	Post M≥18 [%]
Prednisolone dose	N= 11		
Mean ±SD		20.9 mg ±11.7	10.27 mg ± 9.1
Eosinophil count	$X10^9/L$ N=7		
Mean ±SD		0.49 mg ±0.254	0.035±0.04
Creatinine	N=8		
Mean ±SD		60 ± 28.7	66.11±13.33
Continuation of anti-IL5 therapy	N=13		12/13 [92.3%]

	Long term plan > 18 months N=13 [%]		Current Months	Adjuvant therapy >18M
1	Continue		21	Azathioprine
2	Switched	Benralizumab	32	MMF started, IVIG [-]
3	Continue		26	
4	Switched	Reslizumab	24	
5	Discontinued	Rituximab	12	
6	Continue		23	
7	Continue		26	*MMF Stopped*
8	Continue		24	MTX Started
9	Switched	Benralizumab	23	*MMF Stopped*
10	Continue		21	
11	Continue		20	Rituximab
12	Continue		21	*Azathioprine stopped*
13	Continue		21	

Abbreviations: MMF = mycophenolate mofetil, IVIG = intravenous immunoglobulin, M = month

EGPA patients anti-IL5 therapy beyond eighteen months

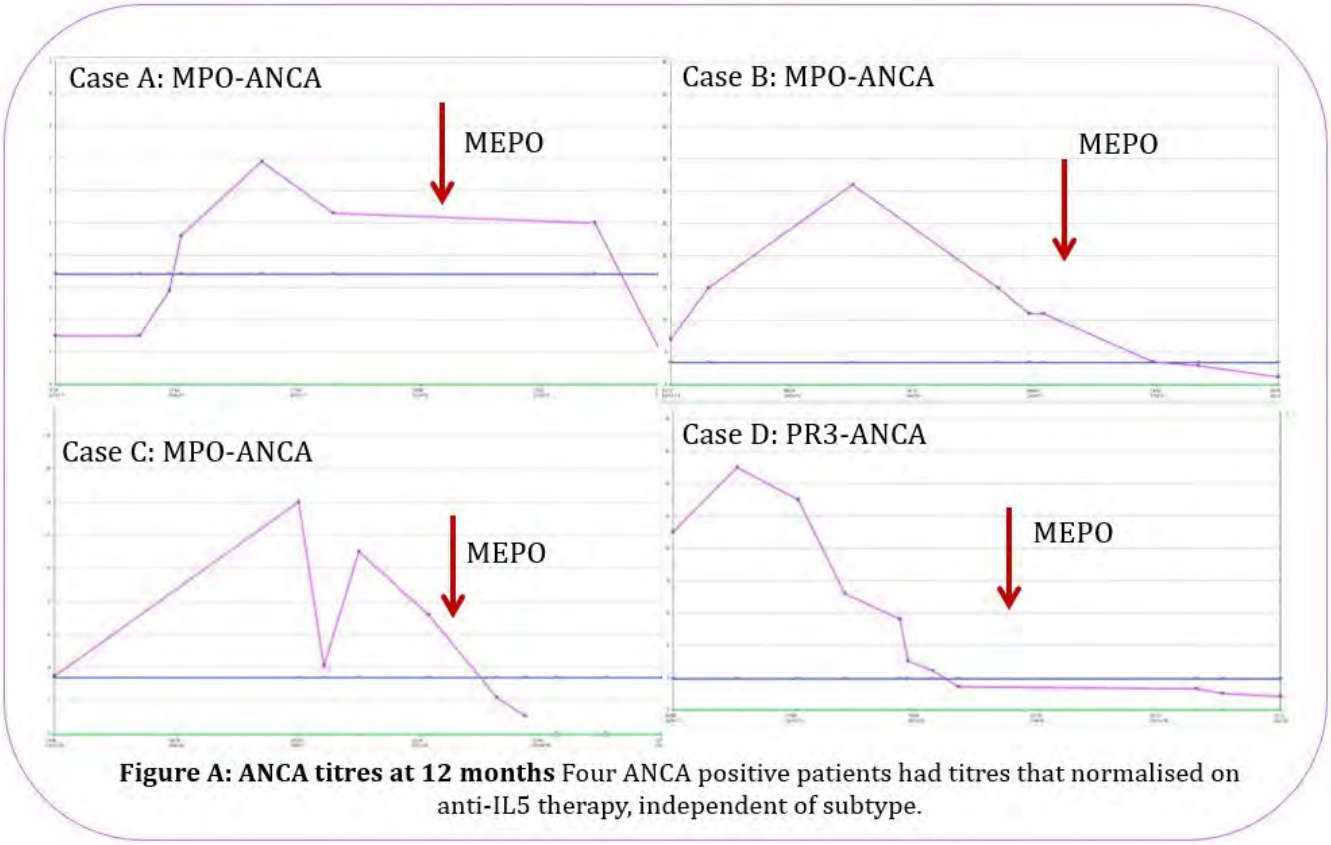

Figure A: ANCA titres at 12 months Four ANCA positive patients had titres that normalised on anti-IL5 therapy, independent of subtype.

ANCA titres at 12 months

Background/Purpose: EGPA is a small vessel vasculitis characterized by the presence of tissue eosinophilia, necrotizing vasculitis and granulomatous inflammation[1]. In the randomized, placebo-controlled MIRRA trial for relapsing and refractory EGPA, adjuvant therapy with 300mg anti-IL5 mAB Mepolizumab [MEPO], accrued longer times in remission, reduced steroid exposure and reduced relapse rates[2]. The aim of the study was to analyze the longer term outcome for EGPA patients who received MEPO monthly for 18 months [M] and beyond, at 100mg dosage.

Methods: This retrospective, descriptive study analyzed 13 patients with EGPA, who received 100mg s/c of MEPO therapy monthly. Time points of assessment included MEPO commencement [M0], month 12 [M12] and ≧ month 18 [M ≧ 18].

Results: This study demonstrates that anti-IL5 therapy serves as a favorable model for steroid minimization in EGPA, with an overall 50% reduction in steroid dosage. Adjuvant conventional immunosuppressants were stopped in 3 patients, and commenced in two. By 12 months, ANCA serology normalized in all four positive patients, BVAS reduced [n=13, mean±SD, 7.3±6.2 M0 to 2.23 ±1.69 M12], along with reduction in asthma Control questionnaire [n=5, mean ± SD, 2.92 ±1.27 M0 to 2.23±1.69 M12]. Well tolerated, at M≥18, anti-IL5 therapy demonstrated considerable clinical benefit, with 12 patients [92.3%] continuing anti-IL5 therapy beyond 18 months. Renal function was preserved. One patient had MEPO switched to Rituximab to treat both EGPA and new onset rheumatoid arthritis. Three patients were switched to alternative anti-IL5 therapies, benralizumab (x2) and Reslizumab (x1).

Conclusion: The relapsing nature of EGPA places a potential dependency of therapy on steroids, underscoring the importance of pathway specific biologics to minimize exposure, prevent tissue damage and ensure early response to therapy. There was a 50% reduction in steroid dosage in this study, with longer-term anti-IL5 therapy continued in 12/13 patients due to clinical benefits achieved. Adjuvant immunotherapy is well tolerated and reduced in some cases.

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Abstract Number: 1428

The Efficacy and Safety of Tocilizumab in Patients with Giant Cell Arteritis: A Systematic Review and Meta-Analysis

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SESSION INFORMATION

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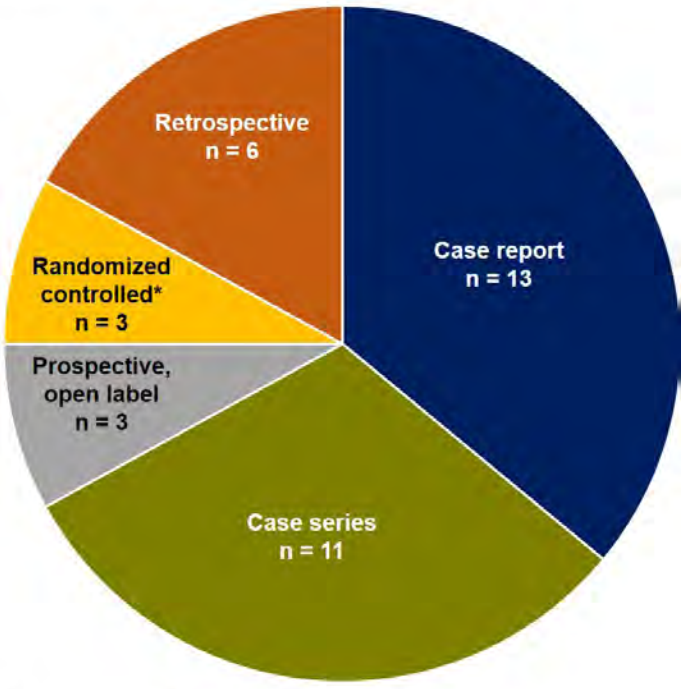
Figure 1. Study Types Included in Meta-Analysis



*The subcutaneous TCZ once-weekly and every-2-weeks treatment arms of the GiACTA trial were counted as separate studies.

Table 1. Summary of Patient Demographics, Clinical Characteristics and Study Therapies

	Across GCA Studies*; Unweighted† (n = 36 studies)	Weighted‡ Population Mean (n = 519 patients)
Patients newly diagnosed with GCA, %		
N	35	150
Mean (SE) [95% CI]	35.7 (7.3) [20.8 to 50.6]	29.9 (10.0) [9.5 to 50.2]
Median (IQR)	0.0 (0.0-95.0)	25.4 (0.0-46.6)
Patients with abnormal TAB, %§		
N	31	272
Mean (SE) [95% CI]	65.6 (6.1) [53.2 to 78.1]	58.8 (2.9) [52.9 to 64.6]
Median (IQR)	70.6 (37.5-100.0)	55.6 (51.9-67.2)
Age, years		
N	36	519
Mean (SE) [95% CI]	70.2 (0.8) [68.6 to 71.7]	70.8 (0.7) [69.4 to 72.2]
Female, %		
N	34	372
Mean (SE) [95% CI]	75.1 (4.9) [65.1 to 85.0]	72.2 (1.3) [72.6 to 77.7]
TCZ dose by route, n (%)		
IV	27 (75.0)	N/A
SC	3 (8.3)	N/A
IV or SC	2 (5.6)	N/A
TCZ duration, weeks		
IV, n	22	135
Mean (SE) [95% CI]	29.7 (2.8) [24.0 to 35.4]	31.7 (4.9) [21.4 to 42.0]
Median (IQR)	26.0 (20.0-37.3)	25.8 (20.8-41.9)
SC, n	3	150
Mean (SE) [95% CI]	43.3 (8.7) [6.0 to 80.6]	51.8 (0.3) [50.7 to 53.0]
Median (IQR)	52.0 (26.0-52.0)	38.9 (32.4-45.5)
Prednisone dose before TCZ initiated (excluding 1250 mg), mg/day‖		
N	26	481
Mean (SE) [95% CI]	27.3 (2.8) [21.6 to 33.1]	27.9 (2.8) [22.1 to 33.8]
Median (IQR)	26.3 (20.4-35.9)	25.3 (21.1-33.8)
Prednisone dose categories before TCZ initiated, n (%), mg/day		
0 to < 10	5 (13.9)	N/A
10 to < 30	15 (41.7)	N/A
30 to 60	9 (25.0)	N/A
1250	3 (8.3)	N/A
Prednisone dose at end of study, mg/day		
N	32	482
Mean (SE)	5.0 (1.2)	5.7 (0.9)
Median (IQR)	3.4 (0.5-5.0)	4.8 (3.9-6.9)
Prednisone duration, weeks		
N	20	277
Mean (SE) [95% CI]	25.6 (3.8) [17.6 to 33.5]	28.3 (3.1) [21.8 to 34.9]

GCA, giant cell arteritis; IQR, interquartile range; IV, intravenous; N/A, not applicable; qw, every week; q2w, every 2 weeks; SC, subcutaneous; TAB, temporal artery biopsy; TCZ, tocilizumab.
*The SC TCZ qw and q2w treatment arms of the GiACTA trial were counted as separate studies.
†The unweighted mean proportion was calculated by calculating the proportion for each study individually and then averaging studies. The unweighted mean was calculated by computing the mean of individual reported study means.
‡The weighted population mean proportion or weighted population mean was estimated by adjusting the mean in each case for the number of patients in each study.
§Not all patients undergo TAB, but the number of patients who did undergo TAB was not known for each study; therefore, the proportion of abnormal TAB was underestimated.
‖Methylprednisolone 1000 mg IV was converted to 1250-mg/day equivalent oral prednisone dose. Patients who reported taking 0 mg of prednisone are not included in the summary statistic calculations.

Background/Purpose: Tocilizumab (TCZ) has been proven to be safe and effective for the treatment of giant cell arteritis (GCA) in 2 randomized controlled trials; however, data from additional types of studies provide valuable information related to the treatment of GCA with TCZ. The objective of this study was to review and analyze efficacy and safety data for TCZ in GCA based on peer-reviewed publications to date.

Table 2. Summary of Remission, Relapse and Adverse Events

	Across GCA Studies*; Unweighted† (n = 36 studies)	Weighted‡ Population Mean (n = 519 patients)
Percentage of patients in investigator-defined remission at the end of the study§		
N	35	411
Mean (SE) [95% CI]	86.3 (4.3) [77.6 to 94.9]	79.3 (6.0) [67.2 to 91.4]
Percentage of patients who relapsed while receiving TCZ‖		
N	31	39
Mean (SE) [95% CI]	2.6 (1.3) [−0.18 to 5.31]	12.0 (4.5) [2.8 to 21.2]
Percentage of patients who relapsed after TCZ discontinuation¶		
N	20	41
Mean (SE) [95% CI]	26.4 (7.8) [10.1 to 42.7]	14.8 (5.8) [2.7 to 26.9]
Percentage of patients receiving no steroids at the end of follow-up		
N	31	170
Mean (SE) [95% CI]	41.8 (6.8) [27.8 to 55.8]	49.4 (8.1) [32.8 to 66.0)
Percentage of patients with SAEs after TCZ initiation		
N	35	72
Mean (SE) [95% CI]	14.0 (4.1) [5.5 to 22.4]	14.3 (1.3) [11.7 to 17.0]

CRP, C-reactive protein; ESP, erythrocyte sedimentation rate; GCA, giant cell arteritis; qw, every week; q2w, every 2 weeks; SAE, serious adverse event; TCZ, tocilizumab.
*The subcutaneous TCZ qw and q2w treatment arms of the GiACTA trial were counted as separate studies.
†The unweighted mean proportion is calculated by calculating the proportion for each study individually and then averaging studies. The unweighted mean was calculated by computing the mean of individual reported study means.
‡The weighted population mean proportion or weighted population mean was estimated by adjusting the mean in each case for the number of patients in each study.
§Investigator-defined remission included absence of signs and symptoms and normal acute-phase reactant levels (n = 13 [36%]); normal acute-phase reactant levels (n = 5 [14%]), absence of signs and symptoms (n = 4 [11%]); absence of signs and symptoms, normal acute-phase reactant levels and glucocorticoid taper (n = 4 [11%]); normal imaging and acute-phase reactant levels (n = 3 [8%]); absence of signs and symptoms and normal imaging (n = 2 [6%]); glucocorticoid taper and normal acute-phase reactant levels (n = 2 [6%]); absence of signs and symptoms and glucocorticoid taper (n = 1 [3%]); patient global assessment (n = 1 [3%]) and missing (n = 1 [3%]).
‖Investigator-defined relapse included recurrence of signs and symptoms and/or increase/re-increase in acute-phase reactant levels (n = 14 [38.9%]); recurrence of signs and symptoms (n = 6 [16.7%]); recurrence of signs and symptoms and inability to taper glucocorticoids (n = 3 [8.3%]); signs and symptoms, raised acute-phase reactant levels and active large-vessel vasculitis on positron emission tomography/computed tomography upon decrease in the prednisone dose (n = 1 [2.8%]); worsening or emergence of ≥ 2 of the following: signs and symptoms, increased erythrocyte sedimentation rate or C-reactive protein levels (CRP), polymyalgia rheumatica signs and symptoms, large-vessel vasculitis signs and symptoms (n = 1 [2.8%]); worsening or recurrence of clinical symptoms, increase in CRP levels attributable to vasculitis; need for glucocorticoid and/or immunosuppressant (n = 1 [2.8%]) and missing (n = 10 [27.8%]).
¶Data on follow-up of patients after TCZ discontinuation were not available. Thus, the estimate of the proportion of patients who relapsed after discontinuation of TCZ is potentially biased.

Methods: A systematic literature review was conducted according to the PRISMA guidelines. Publications were retrieved from the MEDLINE, Embase, Cochrane, Scopus and Web of Science databases. Publications of clinical trials and retrospective or prospective observational studies (April 11, 2005-October 8, 2019) including patients with GCA (classified based on ACR criteria and/or positive biopsy vs imaging) treated with TCZ and reporting a measure of efficacy were eligible for inclusion. Extracted data included year of publication, year(s) when the study was conducted, number of patients with GCA, method of GCA diagnosis, age and sex, TCZ treatment details (dose, route of administration, frequency, duration), clinical outcome (remission, relapse), serious adverse events (SAEs) following treatment

with TCZ, corticosteroid dose before and following TCZ initiation and imaging data following TCZ treatment. Results are presented for the studies (unweighted) and as the weighted population mean. Unweighted mean proportions were calculated as the average of the proportions reported from each study; unweighted means were calculated by computing the mean of individual reported study means. The weighted population proportion was estimated by calculating the total number of patients achieving an outcome and dividing by the total number of patients in all of the studies. The weighted population mean was equivalent to the sum of the individual patient's outcome values divided by the total number of patients in all of the studies.

Results: The search retrieved 664 references; 55 full-text articles were reviewed for eligibility, and 36 studies were included in the meta-analysis (**Figure 1**); the once-weekly and every-2-weeks subcutaneous (SC) TCZ arms of the GiACTA trial were counted as separate studies. A total of 519 patients were included. The median (IQR) duration of treatment with intravenous and SC TCZ was 26.0 (20.0-37.3) and 52.0 (26.0-52.0) weeks, respectively, across all studies in the unweighted analysis and 25.8 (20.8-41.9) and 38.9 (32.4-45.5) weeks in the weighted analysis (**Table 1**). The mean (SE) proportion of patients achieving investigator-defined remission at the end of the study was 86.3% (4.3%) and 79.3% (6.0%) in the unweighted and weighted analyses, respectively (**Table 2**). The mean (SE) proportion of patients who relapsed while receiving TCZ was 2.6% (1.3%) and 12.0% (4.5%) in the unweighted and weighted analyses, respectively. The median prednisone dose at the end of the study was < 5 mg/day, and the mean proportion of patients with SAEs after TCZ initiation was ≈ 14.0%.

Conclusion: A high proportion of patients with GCA treated with TCZ were in investigator-defined remission at the end of the study across all studies analyzed. These meta-analysis findings add to the evidence of the efficacy and safety of TCZ in GCA.

Disclosure: M. Koster, None; **K. Warrington**, Lilly, 2, Kiniksa, 2; **J. Han**, Genentech, Inc., 1, 2; **S. Mohan**, Genentech, Inc., 1, 2.

Abstract Number: 1429

An Evaluation of Real World Use of Biologics in Rare Systemic Vasculitides During Routine Clinical Care in the US

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Vasculitis – ANCA-Associated Poster
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Background/Purpose: The mainstay of treatment for vasculitis has been corticosteroids and other cytotoxic and immunosuppressive medications (e.g., cyclophosphamide, methotrexate) to promptly achieve and maintain remission. Novel treatment options for giant cell arteritis and some forms of polyangiitis have recently become available, however unmet need remains. The purpose of this study is to explore the real world use of biologic agents with different mechanisms of action in patients with Behçet's disease and other rare systemic vasculitides, despite a paucity of regulatory-approved options.

Methods: The OM1 Real World Data Cloud (OM1, Boston, MA), which collects, links and leverages structured and unstructured data from electronic medical records (EMR), claims and other sources in an ongoing and continuously

Table 1. Distribution of Select Treatments in Rare Vasculitides

	GPA	BD	PAN	MC	TA	MPA	EGPA
Overall patients with condition (N)	24,839	11,976	6,297	4,195	3,465	3,433	3,402
Age (years), n							
<18	421	681	320	10	305	122	27
≥ 18 to < 45	4,816	5,862	1,265	402	1,224	419	653
≥ 45 to < 65	10,102	4,242	2,540	2,035	1,282	1,167	1,544
≥ 65	9,500	1,191	2,172	1,748	654	1,725	1,178
Sex, n (%)							
Female	13,715 (55.2%)	8,992 (75.1%)	3,850 (61.1%)	2,469 (58.9%)	2,817 (81.3%)	2,251 (65.6%)	2,015 (59.2%)
Male	11,124 (44.8%)	2,984 (24.9%)	2,447 (38.9%)	1,726 (41.1%)	648 (18.7%)	1,182 (34.4%)	1,387 (40.8%)
Treatment, n (%)							
rituximab	*4,958 (20.0%)**	97 (0.8%)	775 (12.3%)	449 (10.7%)	38 (1.1%)	*1,072 (31.2%)**	308 (9.1%)
mepolizumab	25 (0.1%)	4 (<0.1%)	5 (<0.1%)	3 (<0.1%)	0	3 (<0.1%)	*365 (10.7%)**
TNF	47 (0.2%)	532 (4.4%)	29 (0.5%)	6 (0.01%)	140 (4.0%)	5 (0.1%)	3 (<0.1%)
IL-6	3 (<0.1%)	9 (<0.1%)	6 (<0.1%)	0	64 (1.8%)	3 (<0.1%)	0
IL-17	2 (<0.1%)	0	0	0	0	0	0
IL-12/23	4 (<0.1%)	8 (<0.1%)	0	1 (<0.1%)	0	0	0
abatacept	5 (<0.1%)	3 (<0.1%)	3 (<0.1%)	0	0	0	0

Abbreviations: Behcets disease (BD), Takayasu arteritis (TA), polyarteritis nodosa (PAN), mixed cryoglobulinemia (MC), granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA) and microscopic polyangiitis (MPA)

*At the time of this analysis, rituximab was indicated for adult patients with MPA and GPA forms of vasculitis only and mepolizumab was indicated for adult patients with EGPA

updating manner in the US, was used for the analysis. Use of anti-TNFs, anti-IL-6 agents and other select biologic disease-modifying anti-rheumatic drugs (DMARDs) and monoclonal antibodies between January 2013 and April 2020 were evaluated in patients diagnosed with Behcet's disease (BD), Takayasu's arteritis (TA), polyarteritis nodosa (PAN), mixed cryoglobulinemia (MC), granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA) and microscopic polyangiitis (MPA). For the DMARDs, patients with a documented diagnosis of one or more FDA-approved indications for each DMARD were excluded. By excluding patients with comorbidities (e.g., rheumatoid arthritis) included in the marketed indications for each agent, some patients for whom the agent was specifically used for vasculitis may have been omitted. Patients may have been treated with more than one biologic of interest.

Results: Overall, > 50,000 patients diagnosed with the vasculitides of interest were identified, with GPA and BD the most common (Table 1). Across the conditions of interest, the majority were female (62.7%). A small proportion of pediatric patients were identified. Amongst patients with BD, anti-TNFs were the most commonly used biologic (n=532, 4.4% of BD patients) followed by rituximab. While rituximab was frequently used in its indicated forms (GPA and MPA), it was also used across the other forms of vasculitis. Anti-TNF and anti-IL-6 use was noted in 140 (4.0%) and 64 (1.8%) of TA patients, respectively; rituximab was less commonly used. The other DMARDs evaluated were rarely observed.

Conclusion: If left untreated (or under-treated), systemic vasculitides can result in substantial multisystem morbidity. As the proinflammatory activity in the vasculitides involves many aspects of the immune system, it remains unclear

which mechanism of action is best suited in an individualized treatment setting. Harnessing real world experience may help inform clinical practice, including decisions to switch therapies, and clinical trial design.

Disclosure: K. Starzyk, None; **K. Milberg**, None; **A. Deshpande**, None; **G. Curhan**, OM1, 3, 4, 6, Brigham and Women's Hospital, 3, UpToDate, 7.

Abstract Number: 1430

The Role of Lung Biopsy in Pediatric ANCA-associated Vasculitis

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SESSION INFORMATION
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Background/Purpose: Anca-associated vasculitis (AAV) is characterized by vascular inflammation in multiple organs. The diagnosis can be made clinically using a number of different criteria. The lungs are commonly affected, with a broad range of manifestations described including cough, dyspnea, respiratory failure, and pulmonary hemorrhage. Multiple pulmonary histopathologic patterns have been described in AAV, which requires invasive tissue sampling through lung biopsy and is not without risk. Here, we have reviewed the histopathologic findings in a series of pediatric AAV, and discuss procedural outcomes and yield of lung biopsies in this population.

Methods: After IRB approval, we performed a retrospective chart review of all patients < 18 years of age presenting to our institution with a diagnosis of AAV who underwent lung biopsy. We reviewed histopathologic features, serologies, timing of biopsy, and complications.

Results: 14 patients met inclusion criteria, 9 patients with a diagnosis of microscopic polyangiitis (MPA), and 5 patients with granulomatosis with polyangiitis (GPA). 10/14 (71%) of the biopsies were performed between 2009 and 2013, and only 4 (29%) from 2015 to present. 13/14 patients required initial admission on presentation for respiratory symptoms. 11/14 required respiratory support. All patients had abnormal chest imaging at presentation. 11/14 had concerns for pulmonary hemorrhage. All 5 patients with GPA had an elevated serine protease-3 (PR3). Mean PR3 level was 703 AU/mL (range 49-1353 AU/mL). Myeloperoxidase (MPO) was elevated in all MPA patients. Mean MPO level was 109 AU/mL (range 24-186 AU/mL). The indication for biopsy was to confirm the diagnosis prior to initiating therapy in 11 patients (78%), as part of an infectious work-up in 2 (14%), and as part of an interstitial lung disease work-up in 1 (7%). 9/14 (64%) biopsies had findings consistent with a diagnosis of AAV, 4/9 (44%) of the MPA patients compared to 5/5 (100%) of the GPA patients. The most common findings on histopathology in GPA patients were vasculitis (100%), granulomatous changes (20%), and alveolar hemorrhage (60%). Only 44% of MPA patients had signs of vasculitis, but 100% showed signs of alveolar hemorrhage. The main post-procedure complication was pneumothorax, in 28% of patients.

Conclusion: We found that lung biopsy had a higher diagnostic yield in GPA compared to MPA. On histology, confirmation of vasculitis and pulmonary hemorrhage were the most common findings. In our cohort, the diagnosis of AAV was able to be made with clinical features and a positive serology in all cases. Therefore, considering the risks associated with obtaining a lung biopsy, they should not be routine and reserved for uncertain cases.

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Abstract Number: 1431

Interstitial Lung Disease in Patients with ANCA Associated Vasculitis – a Prospective Single Centre Study

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SESSION INFORMATION

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Background/Purpose: Recently, an association between anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV) and interstitial lung disease (ILD) has been uncovered. We aimed to determine the rate of ILD in our AAV patient cohort and to compare clinical characteristics of AAV patients with and without associated ILD.

Characteristic	ILD-AAV (13)	non-ILD- AAV (89)	p	Characteristic	ILD-AAV (13)	non-ILD-AAV (89)	p
Female	46.2	62.5	0.225	ENT	0	59.6	<0.001
Age*	76 (67;77)	66 (55;77)	0.163	Heart	0	6.7	1.0
Smoking	61.5	38.2	0.137	GI tract	15.4	7.9	0.322
Fever	61.5	52.8	0.767	Kidney	53.8	59.6	0.767
Weight loss	84.6	51.7	0.035	PNS	38.5	28.1	0.518
Arthritis	15.4	15.7	1.0	CNS	0	3.4	1.0
Myalgia	15.4	29.2	0.506	ANCA	100	92.1	0.591
Skin	7.7	20.2	0.453	a-MPO	92.3	46.1	0.002
Eye	0	27.0	0.035	a-PR3	7.7	46.1	0.013

Legend: * median (IQR)); ENT ear-nose-throat; GI gastrointestinal tract; PNS peripheral nervous system; CNS central nervous system;

Table 1. Clinical characteristics of ILD-AAV and non-ILD-AAV group

Methods: We analysed medical records of prospectively diagnosed and followed AAV patients at our secondary/tertiary rheumatology centre between January 2010 and May 2020. The diagnosis of ILD was based on lung HRCT findings.

Results: During the observation period, we identified 102 incipient AAV patients (50 had granulomatosis with polyangiitis, and 52 microscopic polyangiitis). Thirteen (12.7%) patients had ILD (ILD-AAV group). 12/13 had usual interstitial pneumonia (UIP) pattern and 1/13 non-specific fibrosis on HRCT. ILD was diagnosed in tandem with AAV in 9/13 patients, and 9 months to 5 years prior to AAV in 4/17 patients. Characteristics of ILD-AAV, and non-ILD-AAV groups are presented in Table 1. ILD-AAV patients more commonly reported of weight loss, less frequently had ENT involvement, and were predominantly a-MPO ANCA positive (92.3%). Follow up data were available for 90 AAV patients (88.2%; 13 ILD-AAV and 77 non-ILD-AAV). During the median (IQR) follow up of 30.6 (11.4; 62.8) months, 5/13 (38.5%) ILD-AAV patients died, compared to 7 (9.1%) deaths registered in non-ILD-AAV group. The crude mortality rate evaluated by Cox proportional hazards regression was significantly higher for AAV-ILD group (HR 5.5 (95%CI 1.7-17.3), p=0.004).

Conclusion: In our incipient AAV cohort 13% of patients presented with ILD. The AAV patients with ILD had a higher mortality rate than the rest of the cohort.

Disclosure: A. Hocevar, None; **K. Perdan Pirkmajer**, None; **M. Tomsic**, None; **Z. Rotar**, None.

Abstract Number: 1432

Thyroid Disease in Patients with ANCA-Associated Vasculitis

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Background/Purpose: Prior studies have found increased prevalence of thyroid disease in patients with ANCA-associated vasculitis (AAV), especially positive myeloperoxidase (MPO)-ANCA, but a majority of the patients in the studies had microscopic polyangiitis (MPA). The aim of this study was to evaluate the risk of thyroid disease between the different forms of AAV, and, to compare the clinical features of AAV in patients with and without thyroid disease.

Methods: Patients with the 3 forms of AAV (granulomatosis with polyangiitis (GPA), MPA and eosinophilic granulomatosis with polyangiitis (EGPA)) enrolled in a prospective, multicenter, longitudinal study were included. All patients were followed with standardized data collection. Information on thyroid disease was systematically collected. Logistic regression was used to evaluate the association of thyroid diseases with different clinical and laboratory variables.

Table 1: Characteristics of ANCA-associated vasculitis in patients with and without hypothyroidism.

Variable	With hypothyroidism, N= 145	Without hypothyroidism, N= 1170	OR* (95% CI)
Mean age±(SD), years	57.4 (14.03)	51.8 (15.9)	
Female sex, N (%)	113 (78%)	616 (53%)	
Clinical diagnosis			
GPA	93 (11)	773 (89)	1.10 (0.76, 1.61)
MPA	29 (17)	138 (83)	1.41 (0.89, 2.25)
EGPA	23 (8)	259 (92)	0.64 (0.40, 1.02)
ANCA status			
p-ANCA, N (%)	49 (33)	255 (22)	1.52 (1.03, 2.23)
c-ANCA, N (%)	54 (37)	525 (45)	0.87 (0.60, 1.25)
MPO, N (%)	61 (42)	282 (24)	1.89 (1.39, 2.76)
PR3, N (%)	59 (41)	598 (51)	0.79 (0.54, 1.14)
Negative, N (%)	21 (15)	223 (19)	0.69 (0.42, 1.14)

N=Number, OR=Odds ratio, CI=Confidence intervals, SD=standard deviation, GPA=granulomatosis with polyangiitis, MPA=microscopic polyangiitis, EGPA=eosinophilic granulomatosis with polyangiitis, p-ANCA=perinuclear ANCA, c-ANCA=cytoplasmic ANCA, MPO=myeloperoxidase, PR3=proteinase 3; *adjusted for age, sex

Results: The study included 1,315 patients with AAV, 55% female. Clinical diagnosis was GPA in 866 (66%), MPA in 167 (13%) and EGPA in 282 (21%). Mean age at entry into the cohort was 52.5 ±15.8 years. Thyroid disease was present in 163 patients (13%) including hypothyroidism in 145 (11%) and hyperthyroidism in 18 (1.4%). Women were more likely to have thyroid disease (OR 3.22, 95% CI 2.19, 4.75).

The age- and sex-adjusted risk of hypothyroidism by type of AAV and ANCA are in **Table 1.** Hypothyroidism was associated with positivity for p-ANCA or MPO, but not type of AAV (**Table 1**). Analyses in the subset of patients with GPA demonstrated that hypothyroidism was associated with MPO-ANCA positivity (OR 3.01, 95% CI 1.80, 5.02 compared to positive PR3) and p-ANCA (OR 2.32, 95% CI 1.27, 3.94 compared to c-ANCA).

The clinical features of AAV were compared between patients with and without hypothyroidism (**Table 2**). Patients with AAV and hypothyroidism had an increased risk of venous thrombosis.

Conclusion: This study confirms an association of hypothyroidism with p-ANCA/MPO in patients with AAV. Further strengthening this observation is the association of thyroid disease with MPO ANCA in the subset of patients with

Table 2: Comparison of organ involvement from ANCA-associated vasculitis in patients with and without hypothyroidism.

Variable	With hypothyroidism, N= 145	Without hypothyroidism, N= 1170	OR** (95% CI)
Constitutional, N (%)	111 (76)	911 (78)	0.74 (0.62, 1.42)
Ears, nose, throat, N (%)	106 (74)	930 (80)	0.83 (0.51, 1.39)
Cutaneous, N (%)	42 (29)	392 (34)	1.00 (0.67, 1.49)
Musculoskeletal, N (%)	82 (57)	671 (57)	1.02 (0.71, 1.48)
Ocular, N (%)	27 (19)	273 (23)	0.81 (0.51, 1.29)
Cardiac, N (%)	8 (6)	104 (9)	0.66 (0.29, 1.46)
Gastrointestinal, N (%)	2 (1)	70 (6)	0.84 (0.37, 1.89)
Pulmonary, N (%)	102 (71)	862 (74)	0.97 (0.65, 1.45)
Renal, N (%)	82 (57)	579 (50)	1.32 (0.87, 2.00)
Nervous system, N (%)	39 (27)	379 (32)	0.84 (0.54, 1.28)
Venous thromboembolism, N (%)	20 (14)	102 (9)	1.84 (1.07, 3.14)

N=Number, OR=Odds ratio, CI=Confidence intervals, SD=standard deviation, GPA=granulomatosis with polyangiitis, MPA=microscopic polyangiitis, EGPA=eosinophilic granulomatosis with polyangiitis, p-ANCA=perinuclear ANCA, c-ANCA=cytoplasmic ANCA, MPO=myeloperoxidase, PR3=proteinase 3
** adjusted for age, sex, type of ANCA vasculitis and any ANCA positivity

GPA. Previously hypothesized mechanisms for this finding include homology between thyroid peroxidase antibodies and MPO, or, general loss of tolerance to peroxidases. The increased risk of venous thromboembolism in patients with AAV and hypothyroidism warrants further investigation and may be due to additional effects of hypothyroidism on endothelial dysfunction or hypercoagulability.

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Abstract Number: 1433

Thyroid Disease in ANCA-associated Vasculitis. a Population-based Study

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Background/Purpose: A higher incidence of thyroid disease has been seen in patients with anti-neutrophil cytoplasmic antibody (ANCA)-associated vasculitis (AAV). We aim to assess the incidence rate, patients' characteristics and predictors of thyroid disease in patients with AAV.

Methods: Patients were included from two well characterized cohorts of AAV: (i) a population-based cohort from Southern Sweden and (ii) a cohort from a specialized centre; the Vasculitis and Lupus clinic, Addenbrookes Hospital, Cambridge, UK. Diagnosis of AAV was confirmed by review of medical records and patients were classified into AAV disease phenotypes according to the European Medicines Agency Algorithm 2007. The medical records were reviewed to identify patients with thyroid disease. The diagnosis of thyroid disease was supported by clinical characteristics, laboratory data and medication history and in some cases histopathology and radiological findings when available. Demographics, laboratory and clinical data from the date of AAV diagnosis were collected. Cases

Table 1. Characteristics of patients with and without thyroid disease

	No thyroid disease n=515	All Thyroid disease n=134	p
Sex, Female, n (%)	237 (46)	94 (70)	<0.001
Diagnosis GPA/MPA/EGPA	253/242/20	69/59/6	0.8
PR3-ANCA +, n (%)	249 (48.3)	54 (40.3)	0.2
MPO-ANCA +, n (%)	215 (41.7)	69 (51.5)	0.003
Age at diagnosis, years, mean ± SD,	62.3±16.6	61.1±16	0.5
Patients with ≥ 3 organs involved, n (%)	321 (62.3)	72 (53.7)	0.7
Laboratory data at diagnosis			
CRP, mg/l, median (IQR)	72(18-139)	55.5 (15-124)	0.1
ESR, mm/h, mean ± SD	64 ± 34	59 ± 32	0.3
Haemoglobin, g/l, mean ± SD	111 ± 20	107 ± 18	0.05
Platelet count, mean ± SD	373 ±144	382 ± 160	0.6
White blood cell count mean ± SD	13.8± 4.9	13.8 ± 12.3	0.98
S-creatinine, µmol/l, median (IQR)	136 (77-346)	135(80-270)	0.97
Organ system involved at diagnosis n (%)			
General	404 (78.4)	86 (64.2)	0.001
ENT	235 (45.6)	63 (47)	0.8
Chest	230 (44.7)	65 (48.5)	0.4
Nervous	82 (15.9)	21 (15.7)	0.9
Cutaneous	72 (14)	17(12.7)	0.7
Mucocutaneous and eyes	70 (13.6)	10 (7.5)	0.06
Cardiovascular	21 (4.1)	6 (4.5)	0.8
Abdominal	24 (4.7)	3 (2.2)	0.2
Renal	333 (65)	85 (63)	0.8
BVAS at diagnosis	14 (10-18.5)	15 (12-19)	0.2
VDI after 12 months	1 (0-2)	1 (0-3)	0.6
ESRD n (%)	79 (15)	13(10)	0.1
Deaths n (%)	175 (34)	24 (18)	<0.001

Table 2. Incidence rate of thyroid disease in 325 patients with ANCA associated vasculitis

	Number	Person years	Incidence/100 000 py	95% CI
All thyroid disease	29	4770	608	387- 829
LUND	16	2048	781	398-1164
CAMBRIDGE	13	2721	478	218-738
Hypothyroidism	17	4937	344	181-508
Hyperthyroidism	8	4755	143	44-242
Female	14	2249	623	296-949
Male	15	2520	595	294-897
PR3-ANCA +	17	2419	703	369-1039
MPO-ANCA +	10	1851	540.6	205-875

Table 3 Predictors of thyroid disease in patients with ANCA associated vasculitis using Cox-regression analysis

	Univariate analysis		*Multivariate analysis*	
Predictors	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**
Age at AAV diagnosis*	1.14 (0.88-1.46)	0.30	0.88 (0.62-1.24)	0.48
Sex, female	1.30 (0.60-2.80)	0.50	0.83 (0.32-2.16)	0.71
MPO-ANCA+	1.94 (0.84-4.49)	0.11	----------	------
PR3-ANCA+	0.42 (0.18-0.96)	0.04	0.32 (0.09-1.04)	0.05
S-creatinine**	1.03 (0.81-1.31)	0.78	1.12 (0.87-1.44)	0.36

*Age increments by 10 years; **S-creatinine increments by 100 μmol/l

of thyroid diagnosis after AAV onset were included in incidence and predictor analyses. Patient-years of follow up were calculated from AAV diagnosis to the earliest of thyroid diagnosis, death or end of study (Southern Sweden 01/ Jan/2019, Cambridge 01/Oct/2019. Vasculitis disease activity was assessed by the Birmingham Vasculitis Activity score. Irreversible organ damage was evaluated according to the Vasculitis Damage Index. Cox regression analysis was employed to study predictors of thyroid disease. The following variables from the time of AAV diagnosis were studied: Age, sex, ANCA specificity (proteinase-3 and myeloperoxidase) and serum creatinine.

Results: A total of 649 patients were included in this study (Lund = 325, Cambridge. = 324). 134 (21%) patients were diagnosed with thyroid disease, 29 (4.5%) were diagnosed after the onset of AAV. Table 1 summarizes clinical and outcome characteristics of all patients. Thyroid disease was more common in females and patients positive for MPO-ANCA. The incidence of all thyroid disease rate per 100 000 person-years of follow-up after AAV diagnosis was 608 for the whole study population, 781 in Lund-Sweden and 478 in Cambridge, UK, Table 2. The incidence rate for hypothyroidism was 344 /100 000 person-years and for hyperthyroidism 144/100 000 person-years. In Cox regression analysis a positive PR3-ANCA was associated with a lower risk of being diagnosed with thyroid disease even after adjustment for age and sex, Table 3.

Conclusion: After an AAV diagnosis the incidence of thyroid disease is higher than in the general population (incidence of hyperthyroidism in Sweden 25.8-43/100 000 person-years and incidence of hypothyroidism in UK, up to 297/100 000 person-years(1)). PR3-ANCA positivity is associated with less risk for thyroid disease after an AAV diagnosis, this is also true after adjustment for age and sex.

1. Taylor PN, Albrecht D, Scholz A, Gutierrez-Buey G, Lazarus JH, Dayan CM, et al. Global epidemiology of hyperthyroidism and hypothyroidism. Nature Reviews Endocrinology. 2018;14(5):301-16.

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Abstract Number: 1434

The Role of Sural Nerve Biopsy in the Diagnosis of Systemic Vasculitis – a Retrospective Study from Two Specialized Centres

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Background/Purpose: Vasculitis of the peripheral nervous system is seen mainly in systemic vasculitis involving small and medium sized vessels and in cases of single-organ vasculitis affecting the peripheral nerves. There are no pathognomonic tests to confirm a diagnosis of vasculitis other than histopathological findings of vasculitis affecting the vasa nervorum. However, the diagnostic yield of biopsies from affected peripheral nerves and the correlation of pathological confirmation with clinical features is largely unknown. The aims of this study were to (i) characterize patients undergoing sural nerve biopsy in the search of vasculitis, (ii) estimate the diagnostic yield, (iii) correlate biopsy findings with demographic, laboratory and clinical parameters, (iv) estimate the rate of surgical complications and (v) to study possible predictors of a positive biopsy.

Methods: A retrospective cohort study was conducted at Skåne University Hospital (Sweden) and Addenbrooke's Hospital (Cambridge, United Kingdom). Patients that underwent sural nerve biopsy between 2005 and 2019 in the region of Skåne were identified by search in the regional pathology database and by search on the surgical procedure code in the clinical register. Patients that underwent sural nerve biopsy between 2015-2019 at Addenbrooke's Hospital were identified by search in the local pathology database. A structured review of the medical case records and pathology reports was performed. Patients with a suspected vasculitis were included in the study. Histopathologic biopsy findings were recorded as definite, probable or non-vasculitis in accordance with validated guidelines. Definite and probable histopathologic biopsy findings were regarded as a positive biopsy. Surgical complications were recorded when available in the medical case record.

Results: Out of 94 identified patients, vasculitis was diagnosed in 40 (43%) patients based on findings in the sural nerve biopsy (definite =14, probable =26). (Table 1) A positive biopsy finding was associated with ANCA-positivity (p=0.029), a higher white blood cell count (p=0.007) and organ involvement other than from the nervous system at the time of the biopsy (p=0.039). A positive biopsy finding was associated with a longer median length of the biopsy sample (p=0.042). The biopsy sample length was 30 mm (IQR: 18-42.5) and 21 mm (IQR: 14-33) for positive and negative biopsies respectively. (Table 2) However, no parameter was shown to be an independent predictor of a positive biopsy after a multivariate adjustment of the regression model. Post-surgical follow-up was available in 60 patients with a reported sural nerve surgical complication rate of 17%. The most common presentations were wound infection (10%), wound dehiscence (7%), and delayed wound healing (5%). A concomitant muscle biopsy was performed in 11 patients. None of the muscle biopsies added to the diagnostic yield. (Table 1)

	All patients (n=94)
Demography	
Cambridge, Skåne	60 (64%), 34 (36%)
Age at biopsy, years	59 (SD: 15.05; range: 20-84)
Male sex	52 (55%)
Duration of symptoms prior to biopsy, months [1]	10 (IQR: 4.75-24)
Organ involvement	
BVAS [a], (median) [2]	8 (IQR: 6-11)
Laboratory	
White blood cell count, $x10^9/L$ [3]	8.75 (IQR: 7.4-12.9)
Erythrocyte sedimentation rate, mm/h [4]	28 (IQR: 9-43)
C-reactive protein, mg/L [5]	6 (IQR: 1.1-18)
ANCA-positivity, ELISA [6]	20 (28%)
Neurophysiology	
Pure sensory neuropathy [7]	14 (17%)
Pure motor neuropathy [7]	4 (5%)
Sensorimotor neuropathy [7]	62 (76%)
No neuropathy [7]	2 (2%)
Axonal neuropathy [8]	64 (74%)
Asymmetric pattern [b, 9]	42 (62%)
Multifocal mononeuropathy [c, 10]	30 (33%)
Surgical information	
Length of biopsy in mm [11]	22 (IQR: 15-40)
Concomitant muscle biopsy [d]	11 (12%)
Histopathology	
Definite vasculitis	14 (15%)
Probable vasculitis	26 (28%)
Insufficient sample	3 (3%)
Complications	
Any surgical complication [12]	10 (17%)
Wound infection [12]	6 (10%)
Wound dehiscence [12]	4 (7%)
Delayed wound healing [12]	3 (5%)

Data available for n=82 [1], n=89 [2], n=54 [3], n=45 [4], n=55 [5], n=72 [6], n=82 [7], n=87 [8], n=65 [9], n=90 [10], n=78 [11], n=60 [12].

ANCA=anti-neutrophil cytoplasmatic antibodies

[a] Birmingham vasculitis activity score at the time of the sural nerve biopsy..

[b] Pattern of neuropathy described as patchy and/or asymmetric in neurophysiology report.

[c] Multifocal mononeuropathy described in case record or neurophysiologic report.

[d] Muscle biopsy taken during the same session as the sural nerve biopsy.

Table 1. Cohort characteristics

Conclusion: Sural nerve biopsy is a useful and safe procedure to confirm a diagnosis of vasculitis especially in patients with a systemic involvement and positive ANCA. In this study, a combined nerve and muscle biopsy did not add to the diagnostic yield.

	Positive biopsy (n=40)	Negative biopsy (n=51)	*p*-value
Male sex	25 (63%)	25 (49%)	.200
Age at biopsy, years	58 (SD: 13.40)	59 (SD: 16.20)	.628
Duration of symptoms, months	6 (IQR: 3-21.75) [1]	12 (IQR: 6-28.5) [2]	.058
BVAS [a]	9 (IQR: 6-13) [3]	8 (IQR: 6-9) [4]	.122
Systemic organ involvement [b]	18 (46%) [5]	12 (25%) [6]	.039
WBC, $x10^9$/L	11 (IQR: 8.2-15.7) [7]	8 (6 IQR: 5-10.4) [8]	.007
ANCA-positivity, ELISA	14 (40%) [9]	6 (17%) [10]	.029
Multifocal mononeuropathy [c]	14 (38%) [11]	16 (32%) [12]	.571
Length of biopsy, mm	30 (IQR: 18-42.5) [13]	21 (IQR: 14-33) [14]	.042

Data available for n=36 [1], n=44 [2], n=38 [3], n=48 [4], n=39 [5], n=48 [6], n=25 [7], n=28 [8] n=35 [9], n=36 [10], n=37 [11], n=50 [12], n=33 [13], n=43 [14].
WBC=white blood cell count, ANCA=anti-neutrophil cytoplasmatic antibodies
[a] Birmingham vasculitis activity score at the time of the sural nerve biopsy.
[b] Any organ system involved other than general or nervous (according to BVAS) at the time of the sural nerve biopsy.
[c] Multifocal mononeuropathy described in case record or neurophysiologic report.

Table 2. Features in patients with positive vs. negative sural nerve biopsy (excluding patients with insufficient biopsy)

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Prognostic Factors for Mononeuritis Multiplex Associated with ANCA-associated Vasculitis

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Background/Purpose: ANCA-associated vasculitis (AAV) sometimes presents mononeuritis multiplex which worsens the prognosis and activity of daily living in patients. This study aimed to determine theprognostic factorsand clinical feature of mononeuritis multiplex associated with AAV.

Methods: Consecutive patients with AAV who visited Tokyo Medical Center between April 2006 and February 2020 were included in this study. We examined the following clinical features: prevalence of neuropathy, age of onset, sex, the worst blood test values before the initial therapy (WBC, Eo, MPO-ANCA, PR3-ANCA, and CRP levels), MMT score of 20 muscles (Max 100 points), and time (days) from the initial neuropathy to the initial induction therapies. Fisher's exact test, univariate analysis of variance, and logistic regression analysis were applied for evaluation of the risk.

Results: A total of 89 patients with AAV were identified. Among them, 19 patients had eosinophilic granulomatosis with polyangiitis (EGPA) (8 males and 11 females, mean age 59.3 ± 22.0), 9 patients had granulomatosis with polyangiitis (GPA) (0 males, 9 females, meanage 75.6 ± 3.9), and 61 patients had microscopic polyangiitis (MPA) (17 males, 44 females, mean age 78.2 ± 1.5). Of the 89 AAV patients, 26 had sensory neuropathy (15/19 EGPA (78.9%), 11/61 MPA (18.0%), and 0/9 GPA (0%)). Motor neuropathy was observed in 19 patients (EGPA 14/19 (73.7%), MPA 5/61 (8.2%), GPA 0/9 (0%)). 15 patients had both sensory and motor neuropathies (EGPA 12/19 (63.2%), MPA 3/61 (4.9%), GPA 0 (0%)).In patients with both sensory and motor neuropathy, sensory impairment preceded in all cases. AmongThe time from initial sensory neuropathy to initial induction therapy in patients with and without motor neuropathy was 34 ± 10.1 days and 30 ± 10.8 days (p = 0.77) respectively. Also, when comparing those who were treated within 3 days from the onset of motor neuropathy with those who were treated later, MMT score two weeks after the start of treatment were 92.15 ± 1.47 vs. 91.25 ± 2.65 (p = 0.77).

Between the patients with EGPA with and without sensory neuropathy, there were no significant differences in the following: highest WBC (19620.0 ± 2082.6 vs. 19350.0 ± 4033.5 cells/uL (p = 0.953)), highest Eo (10790.6 ± 1774.8 vs 12440.8 ± 3436.9 cells/uL (p = 0.6750)), and highest CRP levels (4.46 ± 0.96 vs 2.70 ± 1.85 mg/dL (p = 0.41)) before the initial therapy. On the other hand, comparing the EGPA patients with and without motor neuron disorder, CRP levels were significantly higher in those with motor impairment than those without (WBC 20978.6 ± 2049.8 vs. 15600.0 ± 3429.9 cells/uL (p = 0.20); Eo 12213.4 ± 1775.5 vs. 8127.0 ± 2971.0 cells/uL (p = 0.25); CRP 5.13 ± 0.89 vs. 1.20 ± 1.48 mg/dL (p = 0.04)). And in patients with motor neuropathy, the decrease in MMT score was significantly correlated with the worst levels of CRP (p = 0.001) while the decrease was not correlated with the other blood tests. In similar analyses of patients with MPA, there were no significant findings.

Conclusion: Worst CRP levels before the initial therapy are a poor prognosis factor for motor neuropathy in patients with EGPA. EGPA patients with high CRP levels need to be paid more attention to because of possible development of motor neuropathy.

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Incidence Rate, Predictors and Outcome of Stroke in Patients with ANCA Associated Vasculitis - A Population-based Study

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Background/Purpose: To study the incidence rate, predictors and outcome of stroke in patients with ANCA-associated vasculitis (AAV) within a defined population in southern Sweden.

Table 1 Standardized incidence ratio (SIR) of stroke in AAV-patients

	Observed	Expected	SIR	95% CI
All patients	20	14.2	1.41	(0.86-2.18)
<65 years	8	2.5	3.23	(1.39-6.36)
>65 years	12	11.7	1.03	(0.53-1.79)
Male	11	8.4	1.32	(0.66-2.36)
Female	9	5.8	1.55	(0.71-2.94)
GPA	11	7.9	1.40	(0.70-2.51)
MPA*	8	5.8	1.37	(0.59-2.70)
PR3-ANCA*positive	9	6.9	1.31	(0.60-2.49)
MPO-ANCA positive	10	6.5	1.54	(0.74-2.84)

SIR: Standardized incidence ratio, GPA: granulomatosis with polyangiitis, MPA: microscopic polyangiitis, PR3: proteinase-3, MPO: myeloperoxidase, ANCA: Antineutrophil cytoplasmic antibody. *1 patient had a diagnosis of Eosinophilic granulomatosis with polyangiitis and was ANCA-negative. This patient was therefore not included in the SIR-calculation of stroke in GPA/MPA and PR3/MPO-positive patients.

Table 2 Predictors of stroke in patients with ANCA associated vasculitis using Cox-regression analysis

	Univariate analysis		*Multivariate analysis*	
Predictors	**HR (95% CI)**	**P-value**	**HR (95% CI)**	**P-value**
Age at AAV diagnosis*	1.31 (0.94-1.81)	0.10	1.42 (0.97-2.08)	0.06
Sex, male	1.18 (0.49-2.86)	0.70	0.80 (0.31-2.06)	0.64
MPO-ANCA	1.35 (0.56-3.24)	0.50	0.52 (0.06-4.26)	0.54
PR3-ANCA	0.76 (0.31-1.89)	0.56	1.08 (0.12-9.26)	0.94
Platelet count**	1.05 (1.00-1.11)	0.04	1.06 (1.01-1.12)	0.01
MucMembeyes	2.84 (0.95-8.54)	0.06	3.14 (0.95-10.30)	0.06

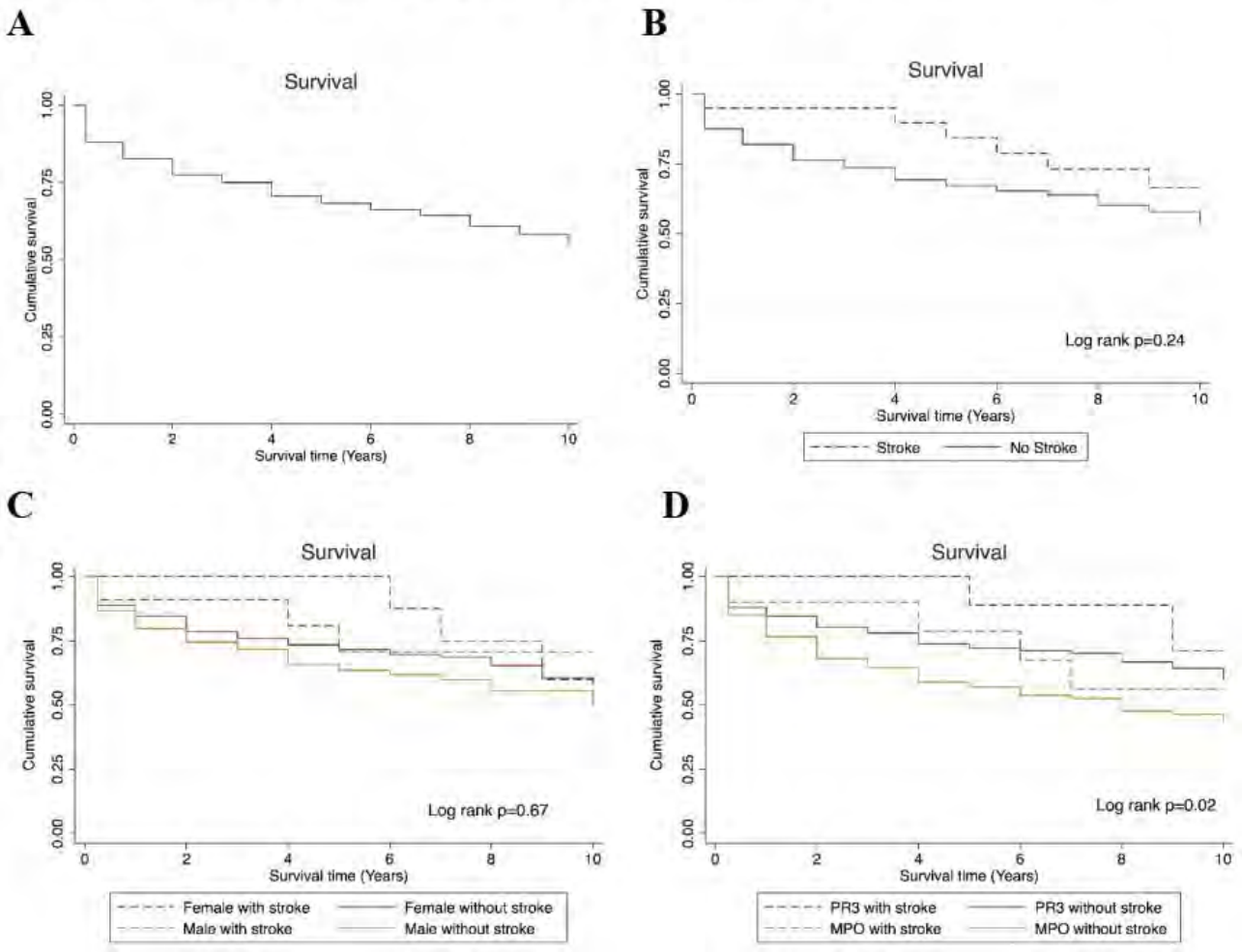
*: age increased by 10 years, **: platelets increased by 20, PR3: Proteinase-3, MPO: Myeloperoxidase, ANCA: Antineutrophil cytoplasmic antibody, HR: Hazard ratio, Mucmembeyes: Mucocutaneous/eyes involvement. Hazard-ratios were calculated by using Cox-regression analysis. P-value of <0.05 was regarded as statistically significant.

Methods: The study included a total of 325 patients diagnosed with AAV within a defined geographical area in Sweden (1997-2016). The diagnosis and classification of AAV was confirmed by case record review using the European Medicines Agency (EMA) algorithm. To identify AAV cases with stroke, two sources were used: (i) The Swedish Stroke Register (Riksstroke): a national stroke register operated since 1994 which includes all cases of stroke diagnosed at stroke-units in Sweden , (ii) The Skåne healthcare register (SHR), an administrative local register of all healthcare services provided to the population in Skåne, was used to identify patients diagnosed at departments not specialized in stroke-care. Diagnosis of stroke for cases identified by the SHR were verified by case record review. From the Riksstroke register we identified 10 controls for each AAV-patient, matched for age, sex and years of stroke diagnosis. Incidence rate of stroke in AAV-patients was calculated per 1000 person-years of follow-up. The person-year was calculated from date of AAV-diagnosis to either date of stroke, death or end of study, December 2018. Using data from the Swedish background population, standardized incidence ratio (SIR) of stroke was estimated. Cox-regression analysis was utilized to investigate predictors of stroke in AAV.

Results: Out of 325 AAV-patients, 20 (6%) suffered a stroke during the follow-up period. The incidence rate of stroke in AAV was 9.7 per 1000 person-years (95% CI 5.5-14.0) and was highest within the first year after AAV-diagnosis,

Figure 1

Survival curves in AAV according to Kaplan–Meier analysis. **(A)** Overall survival in 325 patients with AAV. **(B)** Survival in stroke vs non-stroke patients (P=0.24). **(C)** Survival according to gender (P=0.67). **(D)** Survival according to ANCA-serology (P=0.02) AAV: ANCA associated vasculitis, ANCA: ANCA: Antineutrophil cytoplasmic antibody, PR3: proteinase-3, MPO: myeloperoxidase. Log-rank test was used to calculated differences between groups. P-value of <0.05 was regarded as statistically significant.



20.5 per 1000 person-years of follow-up (95% CI 4.1-36.9). Patients diagnosed with AAV at age < 65 years had 3.2-fold increased risk of stroke compared with background population (Table 1). Platelet count at AAV diagnosis was identified as an independent predictor of stroke (Table 2). There were no differences in survival rates or other outcome measures of stroke between AAV patients and their controls. While comparing AAV patients with and without stroke, a higher survival rate in PR3-positive patients compared to MPO-positive patients was observed (Figure 1).

Conclusion: Incidence rate of stroke in AAV is highest during first year after AAV diagnosis and significantly higher than that of the background population among patients younger than 65 years at AAV diagnosis. An elevated platelet count at AAV-diagnosis was able to predict an increased risk of stroke. Prophylactic treatment with antithrombotic and anticoagulant drugs to prevent stroke-occurrence requires further exploration.

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Abstract Number: 1437

Measuring Disease Activity and Functional Status in Patients with Granulomatosis with Polyangiitis (Wegener's) (GPA)

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

Background/Purpose: Variable association between vasculitis activity and patient reported outcomes was reported in small groups of Granulomatosis with polyangiitis (GPA) patients in the literature so far. In this study we evaluated the utility of PROMIS (Patient-Reported Outcomes Measurement Information System) as potential indirect tool for predicting disease activity in patients with GPA.

Methods: A retrospective chart review study in GPA patients who were seen two or more times at the Cleveland Clinic vasculitis center was conducted between July 2016 and March 2019 to compare disease activity and damage measured by BVAS-WG and VDI scores with PROMIS data. BVAS-WG activity and vasculitis damage index (VDI) scores were calculated at each visit where PROMIS data was obtained. Further, glucocorticoids dose, and immuno-

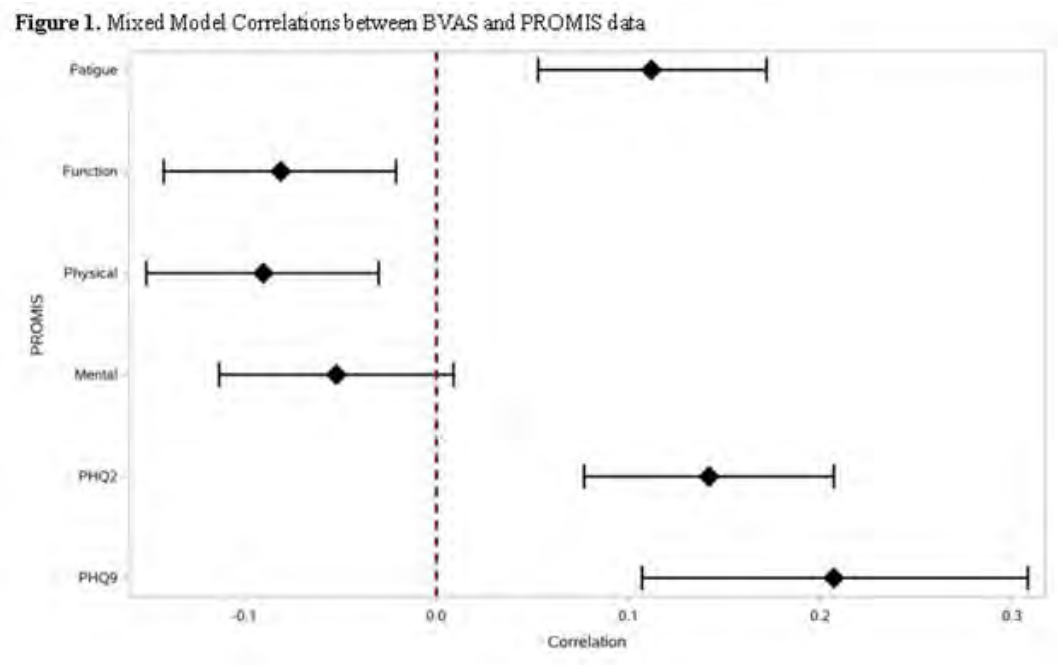


Figure 1. Mixed Model Correlation between BVAS and PROMIS data

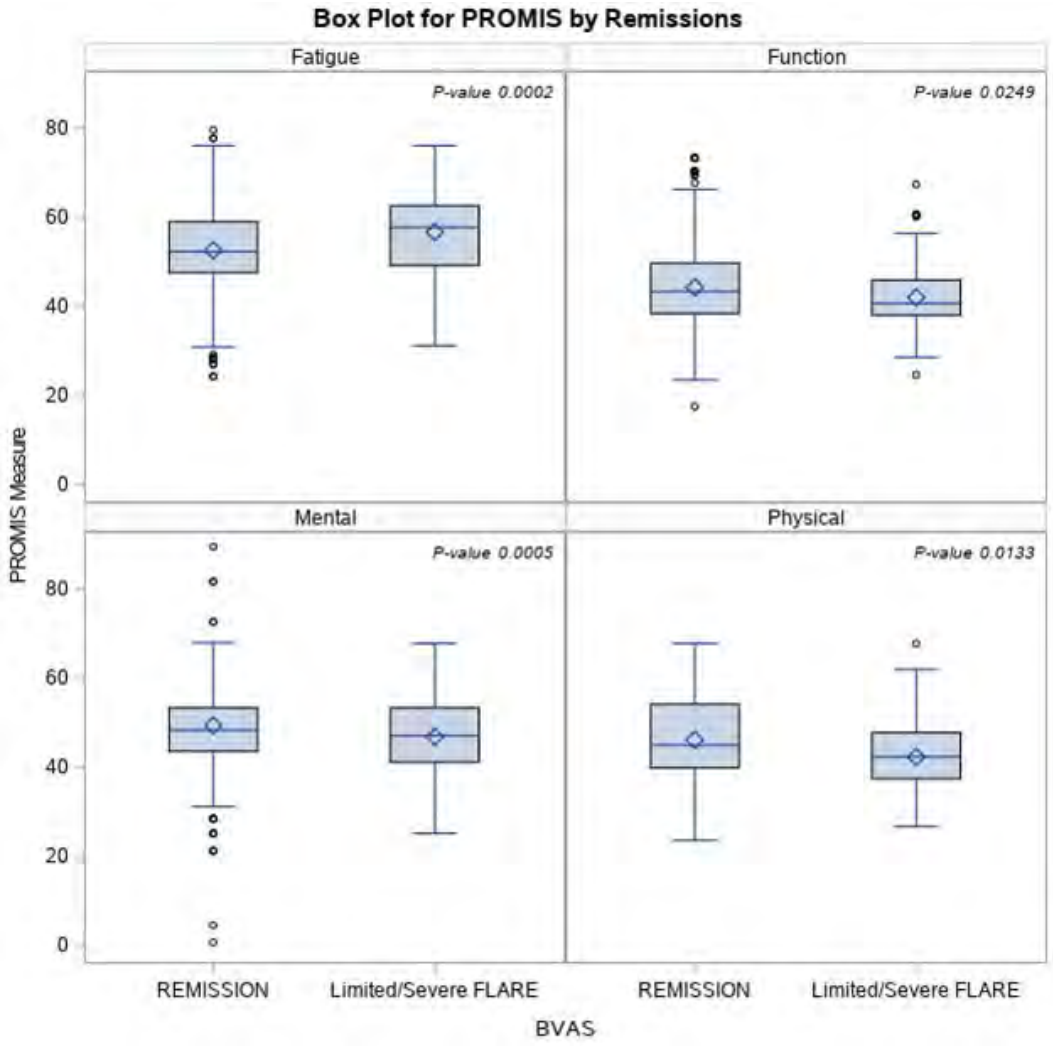


Figure 2. Box Plot for PROMIS by Remissions

suppressive medications were also recorded per each data set. Mixed effect models were used to calculate repeated measures correlations.

Results: 286 patients (median age at first visit 60 years, 53.8% females) with GPA were included in final analysis. Total 85 disease flares were reported (62 limited, 23 severe), median BVAS- WG score was 0 with a range (0-10).

BVAS-WG score was found to be positively correlating with fatigue ($r = 0.112$, $p < 0.001$), PHQ2($r = 0.142$, $p < 0.001$) and PHQ9 ($r = 0.207$, p-value< 0.001) respectively. However, BVAS -WG score seems to be negatively correlating with function ($r = -0.081$, $p = 0.009$) and physical score ($r = -0.090$, $p = 0.003$) (**Figure 1).** More interestingly, patients with flares had fatigue scores > by 4.1 units (p- value =0.001), PHQ2 scores > by 0.75 units (p- value = 0.001), Function scores < by 2.2 units (p- value= 0.025), physical scores < by 3.84 units (p-value= 0.001), and mental scores < by 2.54 units (p-value = 0.013) comparing to those were in remission (**Figure 2)**

Not surprisingly, as VDI score increases, fatigue ($r = 0.142$) and PHQ2 ($r = 0.145$) increase while function ($r = -0.295$) and physical scores decrease ($r = -0.213$).

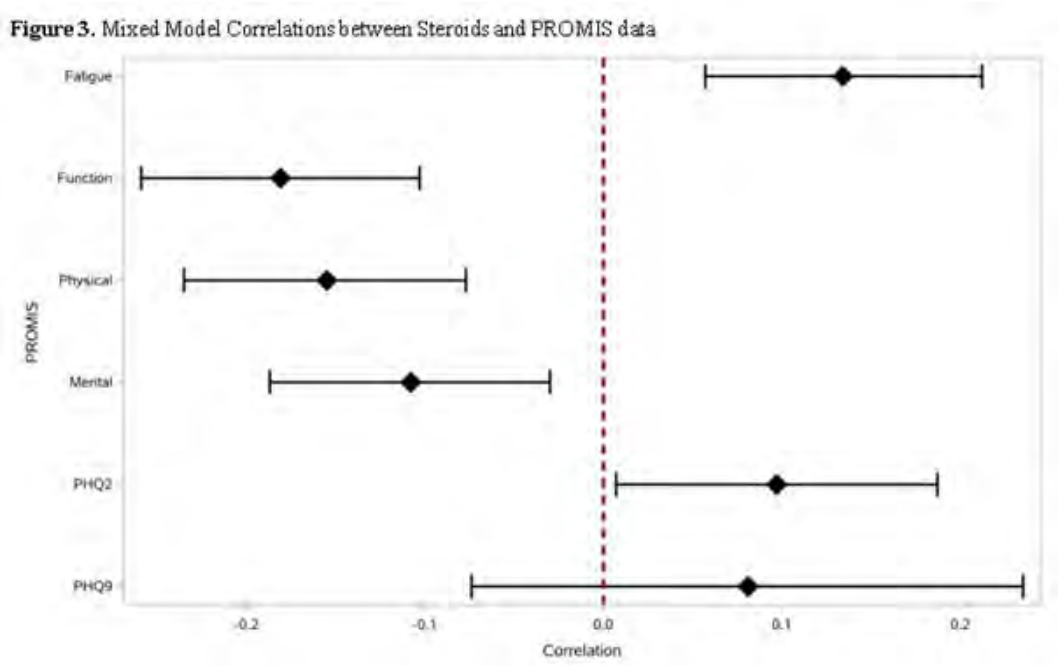


Figure 3. Mixed Model Correlation between Steriods and PROMIS data

In comparing for different glucocorticoids dose, and immunosuppressive medications, patients who received methotrexate and cyclophosphamide had higher PHQ2 scores on average by 1.03 and 0.76 units, respectively. Furthermore, methotrexate was found to be correlating negatively with function scores (b = -2.66, p-value=0.028).

Higher doses of glucocorticoid were positively associated with fatigue (r = 0.134, p-value = 0.001), and PHQ2 (r=0.097, p- value = 0.034) while higher doses were negatively associated with function (r = -0.181, p- value < 0.001), physical score (r = -155, p- value = < 0.001), and mental score (r = -0.108, p- value = 0.009). (**Figure 3)**

Conclusion: PROMIS weakly correlates with disease activity as measured by BVAS-WG and may successfully differentiate between different disease statutes.

Larger studies are needed to validate our study outcomes and the use of PROMIS as indirect tool in predicting disease activity in patients with GPA.

Disclosure: K. Yaseen, None; **I. Briskin**, None; **R. Hajj-ali**, ABBVIE, 1, Rockpoint, 1.

Abstract Number: 1438

Rituximab Immunogenicity in ANCA-associated Vasculitis (RITUXIMAV)

Jason Springer[1] and Ryan Funk[2], [1]University of Kansas Medical Center, Overland Park, KS, [2]UNIVERSITY OF KANSAS, Kansas City, KS

SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Vasculitis – ANCA-Associated Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

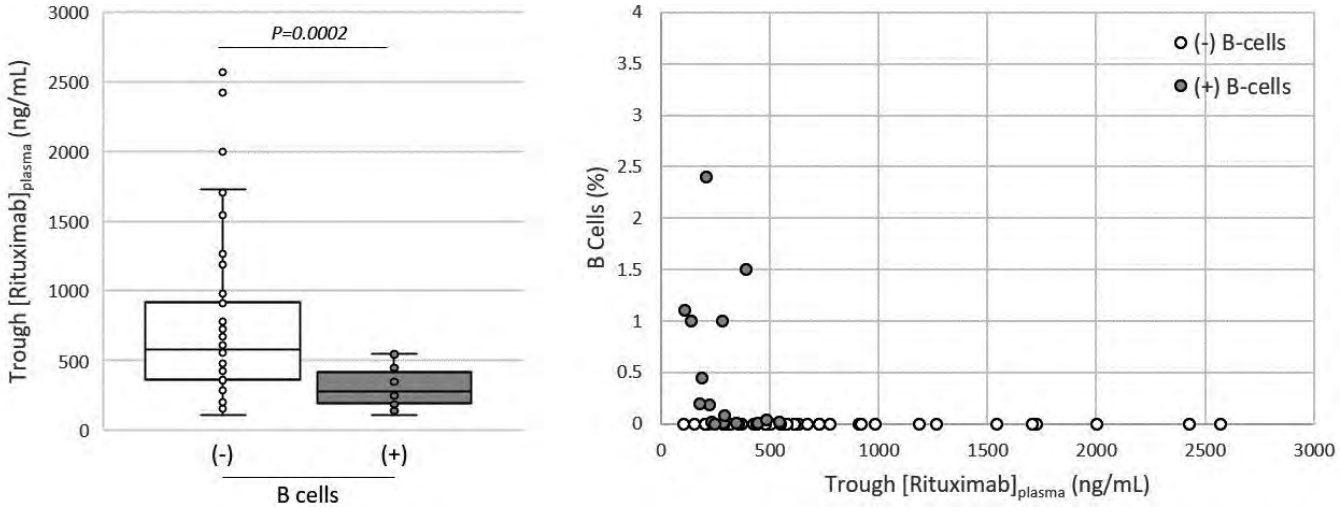


Figure 1. B-cell counts based on trough rituximab levels

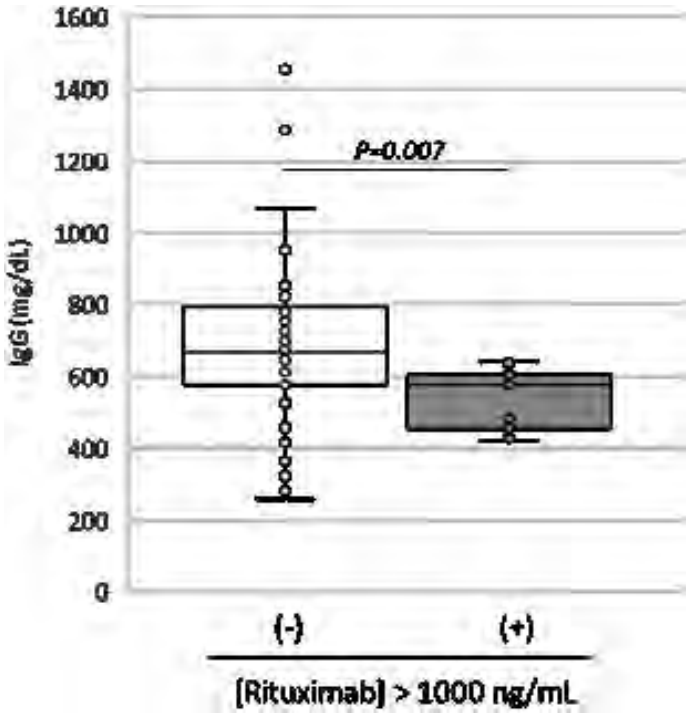


Figure 2. IgG based on trough rituximab levels.

Background/Purpose: Rituximab (RTX), an anti-CD20 chimeric monoclonal antibody, has been shown to be an effective maintenance therapy for granulomatosis with polyangitiis (GPA) and microscopic polyangiitis (MPA). There is very little data on the development of immunogenicity in patients with GPA/MPA receiving RTX for maintenance therapy. The purpose of this study is to determine a) the rate of anti-RTX antibody development, and b) if peripheral RTX and anti-RTX levels can be predictive of B-cell depletion, ANCA negativity and hypogammaglobulinemia in GPA/MPA patients receiving RTX for maintenance therapy.

Methods: Thirty patients with a diagnosis of GPA (n=25) or MPA (n=5) were recruited from a single center. Inclusion criteria included: a) previously received RTX within the last 8 months; b) in remission and c) receiving RTX maintenance therapy. Labs including trough peripheral RTX levels and anti-RTX antibodies were checked serially just before

infusions. The mean age at enrollment was 62.5 years (IQR 46.5-67.5), 70% were female, and 67% had undetectable B-cells at baseline. P-values were calculated using z-test and students t-test as appropriate.

Results: B-cell depletion was found to be more likely when the RTX trough level was greater than 500 ng/mL (93% versus 56% when trough < 500 ng/mL; p=0.002) (Figure 1). There was a non-significant trend toward a higher likelihood for both B-cell depletion and ANCA negativity by EIA when the RTX trough level was greater then 500 ng/mL (61% vs 41% when < 500 ng/mL, p=0.1354); however, the study was likely underpowered to find significance. Trough RTX levels > 1,000 ng/mL were associated with lower mean IgG levels (Figure 2).

Overall, 70% of samples had detectable anti-RTX levels. Anti-RTX levels did not correlate with B-cell depletion (p=1.0) or the combination of B-cell depletion and ANCA negativity (p=0.38). The presence of detectable anti-RTX levels were protective against the development of hypogammaglobulinemia (56% versus 83% without anti-RTX antibodies; p=0.041).

Conclusion: Some authors have supported dosing of RTX based on B-cell counts and ANCA testing, however a clear benefit of this approach has not been demonstrated. In addition, these approaches are reactionary to presumed under-dosing of RTX (i.e. either based on dose or frequency of dosing). Establishing target levels of RTX exposure offers the potential of an *a priori* precision dosing approach to RTX therapy in comparison to responsive monitoring of the effect of RTX. Establishing target RTX trough levels would allow for dosage determinations and adjustments based on population pharmacokinetic estimates to maximize the probability of clinical response and minimize the risk of toxicity. Based on the results of this study a RTX dosing algorithm personalized to the patient could be established. This would be a critical step towards personalized medicine in these forms of primary systemic vasculitis, and potentially other RTX treated diseases such as rheumatoid arthritis.

Disclosure: J. Springer, InflaRx, 2; **R. Funk**, None.

Abstract Number: 1439

Proteinase 3-Reactive B Cell Pool Restructuring After Rituximab and Risk of Relapse in Severe PR3-ANCA-Associated Vasculitis

Alvise Berti[1], Sophie Hillion[2], Marta Casal Moura[1], Amber Hummel[1], Eva Carmona[1], Tobias Peikert[1], Carol Langford[3], Peter A. Merkel[4], Paul Monach[5], Philip Seo[6], Robert Spiera[7], Eugene St Clair[8], Fernando C. Fervenza[1], Kristina Harris[9], John H. Stone[10], Jacques-Olivier Pers[11], Ulrich Specks[1] and Divi Cornec[12], [1]Mayo Clinic, Rochester, MN, [2]Brest University, Brest, Bretagne, France, [3]Cleveland Clinic, Moreland Hills, OH, [4]Division of Rheumatology University of Pennsylvania, Philadelphia, PA, [5]Brigham and Women's, Boston, [6]Johns Hopkins University, Baltimore, MD, [7]Division of Rheumatology, Hospital for Special Surgery, New York, New York, USA, New York, NY, [8]Duke University, Durham, NC, [9]Immune Tolerance Network, Bethesda, MD, [10]Massachusetts General Hospital Rheumatology Unit, Harvard Medical School, Boston, MA, [11]University of Brest, Brest, France, [12]Rheumatology Department, Brest University Hospital, Brest, France

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Vasculitis – ANCA-Associated Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In ANCA-associated vasculitis (AAV) B cells play a central pathogenic role and are instrumental for the production of ANCA, which are thought to mediate disease activity by triggering the activation and degranulation of neutrophils.

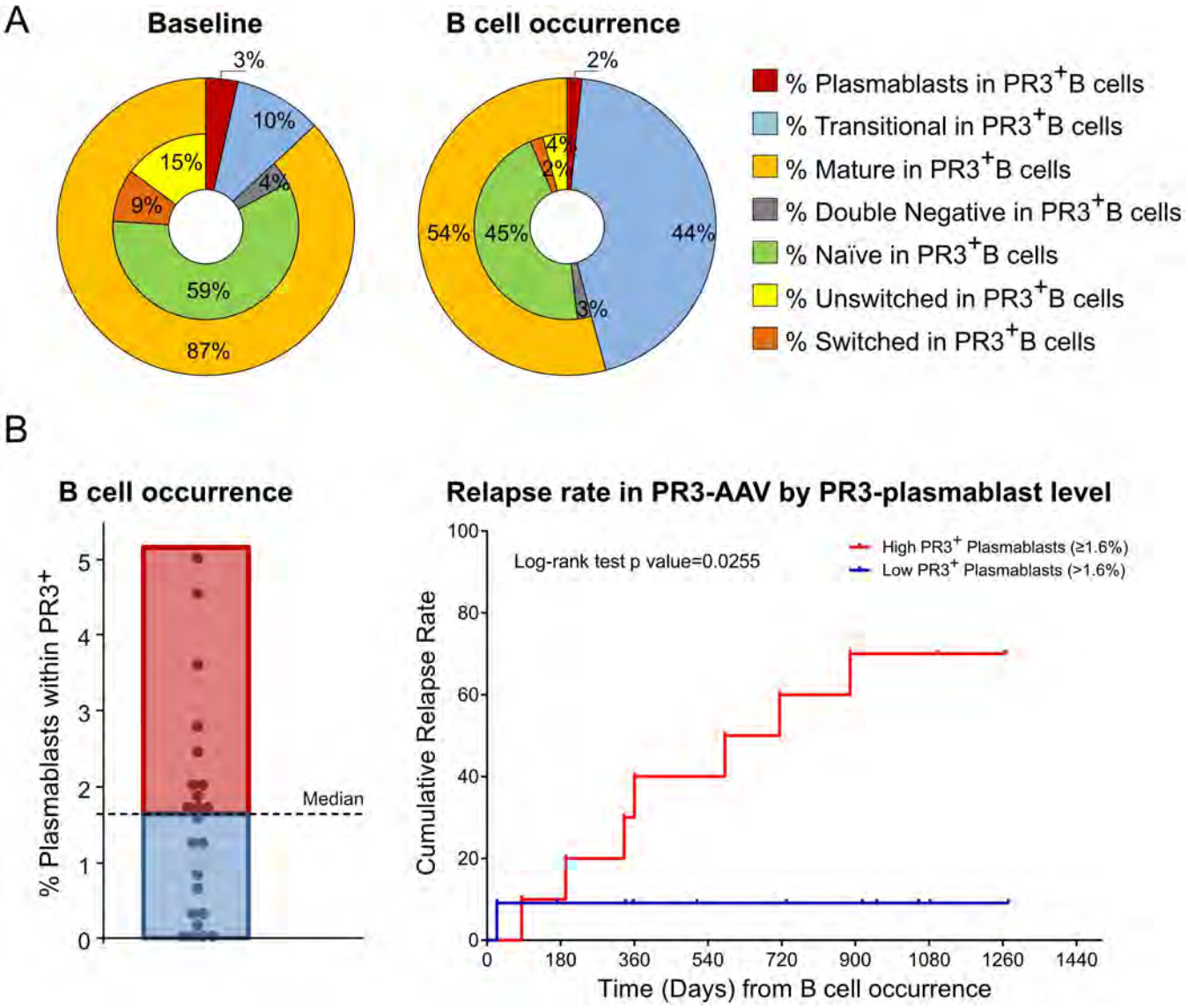


Figure 1. PR3+ B cells at baseline and B cell recurrence (A) and plasmablasts among the PR3+ B cell pool at B cell recurrence (B) among subjects with ANCA-associated vasculitis treated with rituximab.

We hypothesized that changes in the circulating proteinase 3 (PR3) reactive B cell ($PR3^+$ B cell) pool at the time of B cell recurrence after treatment with rituximab (RTX) and/or during the subsequent follow-up mirror disease course and relapses of PR3-AAV.

Methods: We performed sequential flow-cytometry on 148 samples of peripheral blood mononuclear cells (PBMC) from 23 well-characterized participants in the Rituximab for ANCA-Associated Vasculitis (RAVE) trial, treated with RTX for induction of remission and during long-term follow-up off therapy. Clinical data and outcomes were correlated with numbers of B cells and $PR3^+$ B cells; survival analyses and case-time-control analysis were performed by conditional logistic regression.

Results: Ten (43%) patients relapsed during the follow-up, 8 (35%) with severe disease. At baseline, clinical features, PR3-ANCA levels, $PR3^+$ B cells, and $PR3^+$ B cell subsets were similar between patients who relapsed (relapsers) and who did not relapse during the observation period (non-relapsers). All patients were studied for ≥18 months (observa-

tion period of the trial), for a mean of 44 months (25-75%IQR 31-54), without significant difference between relapsers and non-relapsers (p=0.98).

Two patients repopulated their B cells at 6 months; one relapsed and one did not during the follow-up. Total B cell counts and frequency were lower at B cell recurrence compared to baseline ($p< 0.01$). In contrast, the frequency of $PR3^+$ B cells was higher at B cell recurrence ($p< 0.01$), and pairwise comparisons showed that both B cell and $PR3^+$ B cell frequencies of transitional and naïve B cells were higher, while mature, unswitched and switched memory B cells were lower at the time of B cell recurrence compared to baseline ($p< 0.001$ in all comparisons) (**Figure 1A**).

At B cell recurrence, B cell subpopulations did not differ between relapsers and non-relapsers, while plasmablasts within the $PR3^+$ B cell pool were higher in relapsers, and associated with a shorter time to relapse (**Figure 1B**). Increased numbers of PR3+ plasmablasts were more likely to be found in patients that relapsed in the following 12 months ($p< 0.05$), and this increase was 50% more likely to occur in relapsers when compared to non-relapsers.

Conclusion: Our findings describe the restructuring of B cell and $PR3^+$ B cell compartments after B cell depletion with rituximab in PR3-AAV, and contribute to clarifying how early changes within the $PR3^+$ B cell pool associate with the future outcome of the patients with PR3-AAV. Our results highlight the importance of the expansion of peripheral blood $PR3^+$ B cells, which are linked to subsequent relapses. These findings contribute to a better understanding of the mechanisms governing the reconstitution of antigen-specific B cells after treatment with RTX in AAV.

Disclosure: A. Berti, None; **S. Hillion**, None; **M. Casal Moura**, None; **A. Hummel**, None; **E. Carmona**, None; **T. Peikert**, None; **C. Langford**, None; **P. Merkel**, AbbVie, 5, AstraZeneca, 2, 5, Biogen, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Insmed, 5, Jannsen, 5, Magenta, 5, Pfizer, 5, Sparrow, 5, Talaris, 5, UpToDate, 7; **P. Monach**, None; **P. Seo**, None; **R. Spiera**, Roche-Genentech, 1, 2, GlaxoSmithKline, 1, 2, Bristol-Myers Squibb, 1, Boehringer Ingelheim, 1, ChemoCentryx, 1, Corbus Pharmaceuticals, 1, Sanofi, 1, InflaRx, 1, Janssen, 1, Forbius, 1, 2; **E. St Clair**, None; **F. Fervenza**, None; **K. Harris**, None; **J. Stone**, Roche, 2, 5, Genentech, 2, 5; **J. Pers**, None; **U. Specks**, Genentech, 2; **D. Cornec**, Sanofi-Aventis, 9, Novartis, 9.

Abstract Number: 1440

The Myeloperoxidase (MPO) Anti-Neutrophilic Cytoplasmic Antibody (ANCA) Binding Epitope, $MPO_{447-459}$ Induces CD4 T-cell Proliferation in Patients with MPO-ANCA-associated Vasculitis

Matthew Terrill[1], Hendrik Nel[2], Yassmin Musthaffa[3], Wong Richard[4], Ross Francis[5], David Johnson[5], Greg Keir[6], David Gillis[7] and Ranjeny Thomas[8], [1]University of Queensland Diamantina Institute and Princess Alexandra Hospital, Rheumatology Department, Brisbane- Australia, Moffat beach, Queensland, Australia, [2]University of Queensland Diamantina Institute, Brisbane, Queensland, Australia, [3]University of Queensland Diamantina Institute, Brisbane, Australia, [4]Immunology Department, Princess Alexandra Hospital, Brisbane- Australia, Brisbane, Australia, [5]Renal Department, Princess Alexandra Hospital, Brisbane- Australia., Brisbane, Queensland, Australia, [6]Respiratory Department, Princess Alexandra Hospital, Brisbane- Australia., Brisbane, Queensland, Australia, [7]Immunopathology Department, Royal Women's and Children's Hospital, Brisbane- Australia., Brisbane, Queensland, Australia, [8]University of Queensland Diamantina Institute and Rheumatology Department, Princess Alexandra Hospital, Brisbane – Australia., Brisbane, Australia

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Vasculitis – ANCA-Associated Poster
Session Type: Poster Session C

Session Time: 9:00AM–11:00AM

Background/Purpose: In Myeloperoxidase (MPO) Anti Neutrophilic Cytoplasmic Antibody (ANCA)-Associated Vasculitis (MPO-AAV), murine and human studies suggest that the $MPO_{435-465}$ region, which includes ANCA-binding $MPO_{447-459}$, the CD4 $MPO_{435-454}$ epitope and CD8 $MPO_{457-465}$ epitope; is an immunogenic hotspot within the MPO heavy chain. To map the MPO peptide proliferative response in peripheral blood (PB) of MPO-AAV, we developed a T cell proliferation assay based on CFSE dilution, and assayed responses to MPO heavy chain peptides in participants with MPO-AAV, and age and sex-matched healthy controls.

Methods: MPO-AAV participants were included if they had a positive MPO-ANCA and Birmingham Vasculitis Activity Score (BVAS) ≥ 1 at diagnosis. We collected PB, isolated and froze mononuclear cells, thawed and stained them with CFSE, and cultured them for 7 days with no peptide, anti-CD3, tetanus toxoid, MPO peptides or pools of 10 overlapping 15mer MPO peptides derived from the $MPO_{279-745}$ heavy chain. The % proliferating CD3+CD4+ and CD8+ T cells in response to antigen or anti-CD3 was calculated by flow cytometry. The cell division index (CDI) was calculated as % divided in peptide-stimulated relative to % divided in unstimulated samples. All were genotyped for HLA-DR, DP and DQ.

Results: Nineteen participants with MPO-AAV were included, with mean age 65.32 (95% CI: 57.36- 73.27) and 14/19 were male (11 MPA, 3 GPA, 5 renal limited disease). Five had active disease. Of the healthy participants, mean age was 56.70 (95% CI: 43.32- 70.08), and 7/9 were male. MPO-AAV patients had a significantly greater CD4+ T cell CDI to MPO447-459 than healthy controls (p=0.015), with median CDI 3.20 (95% CI: 0.96- 5.80) in MPO-AAV and 0.67 (95% CI: 0.07- 0.89) in controls. CDI was greater in patients with remitted disease (median CDI 3.93, 95% CI: 0.52- 13.00), than in patients with active disease (median CDI 1.72, 95% CI: 0.96-3.89), but CDI did not correlate with ANCA titre. Within the MPO heavy chain, there was no significant increase in CDI among MPO-AAV patients towards any epitope other than $MPO_{447-461}$. CDI to $MPO_{435-365}$ among MPO-AAV patients with remitted disease was increased relative to patients with active disease. No peptide stimulated a significantly increased CD8+ proliferative response. HLA-DPB1*04:01 was enriched among patients with MPO-AAV (10/13; 76.92%) relative to controls (2/6; 33.33%), odds ratio 6.67 (95% CI: 0.79- 56.21). Carriage of this allele did not influence CDI to $MPO_{447-459}$.

Conclusion: CD4+ T cells from patients with MPO-AAV proliferate specifically to the $MPO_{447-459}$ epitope within the MPO heavy chain, and this response is greater after remission. An increased CDI to $MPO_{435-465}$ suggests that $MPO_{447-459}$ can be processed in culture from the longer peptide. T cell immunomodulation may be a suitable strategy for remitted MPO-AAV.

Disclosure: M. Terrill, None; **H. Nel**, None; **Y. Musthaffa**, None; **W. Richard**, None; **R. Francis**, None; **D. Johnson**, None; **G. Keir**, None; **D. Gillis**, None; **R. Thomas**, Abbvie, 8, BMS, 5, 8, Janssen-Cilag, 8.

Abstract Number: 1441

Effects of Belimumab on Renal Outcomes, Overall SLE Control and Biomarkers: Findings from a Phase 3, Randomized, Placebo-controlled 104-week Study in Patients with Active Lupus Nephritis

Richard Furie[1], Brad Rovin[2], Frédéric Houssiau[3], Gabriel Contreras[4], Ana Malvar[5], Amit Saxena[6], Xueqing Yu[7], Y K Onno Teng[8], Pieter van Paassen[9], Ellen M Ginzler[10], Diane Kamen[11], Mary Oldham[12], Damon Bass[13], Andre van Maurik[14], Mary Beth Welch[13], Yulia Green[15], Beulah Ji[15], Christi Kleoudis[16] and David Roth[17], [1]Northwell Health, Great Neck, NY, [2]The Ohio State University, Columbus, [3]Cliniques Universitaires Saint-Luc, Brussels, Belgium, [4]University of Miami Miller School of Medicine, Miami, [5]Organizacion Medica de Investigacion, Buenos Aires, Argentina, [6]NYU School of Medicine, New York, [7]Guangdong Provincial People's Hospital and Guangdong Academy of Medical Sciences, Guangzhou, China (People's Republic), [8]Leiden University Medical Center, Leiden, Netherlands, [9]Maastricht University, Academisch Ziekenhuis Maastricht, Maastricht, Netherlands, [10]SUNY Downstate Health Sciences University, Brooklyn, [11]Medical University of South Carolina, Charleston, SC, [12]GlaxoSmithKline, Stevenage, United Kingdom, [13]GlaxoSmithKline, Research Triangle Park, [14]GlaxoSmithKline, Stevenage, [15]GlaxoSmithKline, Uxbridge, [16]Parexel (*At the time of study), Durham, [17]GlaxoSmithKline, Collegeville

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Plenary Session III

Session Type: Plenary Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Belimumab (BEL) has demonstrated efficacy in systemic lupus erythematosus (SLE) in 4 positive pivotal trials. This study assessed the efficacy and safety of intravenous (IV) BEL plus standard therapy (ST) in patients (pts) with active lupus nephritis (LN).

Methods: This Phase 3, double-blind, placebo (PBO)-controlled study (GSK Study BEL114054; NCT01639339) randomized (1:1) adults with SLE and biopsy-proven LN (class III, IV, and/or V) to monthly BEL 10 mg/kg IV or PBO, plus ST. Randomization was stratified by race and treatment regimen (high-dose corticosteroids + either cyclophosphamide followed by azathioprine, or mycophenolate mofetil [MMF] followed by MMF). Primary endpoint: Primary Efficacy Renal Response (PERR; urine protein-creatinine ratio [uPCR] ≤0.7; estimated glomerular filtration rate [eGFR] no worse than 20% below pre-flare value or ≥60 ml/min/1.73m^2; no rescue therapy) at Week (Wk) 104. Key secondary endpoints: Complete Renal Response (CRR; uPCR < 0.5; eGFR no worse than 10% below pre-flare value or ≥90 ml/min/1.73m^2; no rescue therapy) at Wk 104; Ordinal Renal Response (ORR; CRR, PRR or no response) at Wk 104; PERR at Wk 52; time to renal-related event (defined in **Table 1**) or death. Wk 104 PERR/CRR were analyzed in subgroups: treatment regimens, LN class, race. Additional evaluations included: time to first severe SFI flare (defined in **Table 2**); proportions of pts with SLEDAI-S2K (defined in **Table 2**) score < 4 and with prednisone dose ≤7.5/5 mg/day, both at Wk 104; changes from baseline in biomarkers (anti-dsDNA, anti-C1q, C3, C4) at Wk 104; safety.

Results: Randomized pts: 448 (efficacy: 223/group; safety: 224/group). The study met its primary and key secondary endpoints (**Table 1**). Risk of a renal-related event or death was lower over the study with BEL vs PBO (HR [95% CI] 0.5 [0.3, 0.8]; p=0.001). **Table 2** displays additional endpoints. The odds of PERR/CRR responses at Wk 104 on BEL vs PBO were numerically greater for listed subgroups, except pure class V LN (**Figure**); however, in class V, a numerically greater proportion of BEL vs PBO pts achieved PERR/CRR response at Wk 52 (PERR: 44.4% vs 33.3%; CRR: 36.1% vs 27.8%, respectively).

At Wk 104, in pts with baseline autoantibodies, median (IQR) percent change from baseline (BEL vs PBO) in anti-dsDNA was –74.2 (–85.1, –49.5) vs –36.6 (–69.7, 28.6); and anti-C1q was –73.2 (–84.1, –59.0) vs –57.9 (–76.1, –33.2).

Table 1. Primary and key secondary endpoints

Endpoint, n (%)	PBO (n=223)	BEL 10 mg/kg IV (n=223)	Observed difference (%) vs placebo	OR/HR (95% CI) vs PBO	p-value
PERR at Wk 104*	72 (32.3)	96 (43.0)	10.8	OR 1.6 (1.0, 2.3)	0.031
CRR at Wk 104*	44 (19.7)	67 (30.0)	10.3	OR 1.7 (1.1, 2.7)	0.017
ORR at Wk 104*					
CRR	44 (19.7)	67 (30.0)	10.3	–	0.010
PRR†	38 (17.0)	39 (17.5)	0.5	–	
NR	141 (63.2)	117 (52.5)	−10.8	–	
PERR at Wk 52	79 (35.4)	104 (46.6)	11.2	OR 1.6 (1.1, 2.4)	0.025
Time to renal-related event or death‡	63 (28.3)¶	35 (15.7)¶	–	HR 0.5 (0.3, 0.8)	0.001

*p-value was from a rank ANCOVA model comparing belimumab and placebo with covariates for treatment group, induction regimen (CYC vs MMF), race (black vs non-black), baseline uPCR, and baseline eGFR. Study WD, TF, and IPD were imputed as non-responders; †defined as eGFR no worse than 10% below baseline value or within normal range, ≥50% decrease in uPCR (either uPCR <1.0 if baseline ratio ≤3.0, or uPCR <3.0 if baseline ratio >3.0), no rescue therapy, and not a CRR; ‡defined as the first event experienced among the following: end-stage renal disease/doubling of serum creatinine/renal worsening/renal disease–related treatment failure or death; ¶number/proportion of pts reporting the event ANCOVA, analysis of covariance; BEL, belimumab; CI, confidence interval; CRR, Complete Renal Response; CyC, cyclophosphamide; eGFR, estimated glomerular filtration rate; HR, hazard ratio; IPD, investigational product discontinuation; IV, intravenous; MMF, mycophenolate mofetil; NR, non-responder; OR, odds ratio; ORR, Ordinal Renal Response; PBO, placebo; PERR, Primary Efficacy Renal Response; PRR, Partial Renal Response; TF, treatment failure; uPCR, urine protein-creatinine ratio; WD, withdrawal; Wk, Week

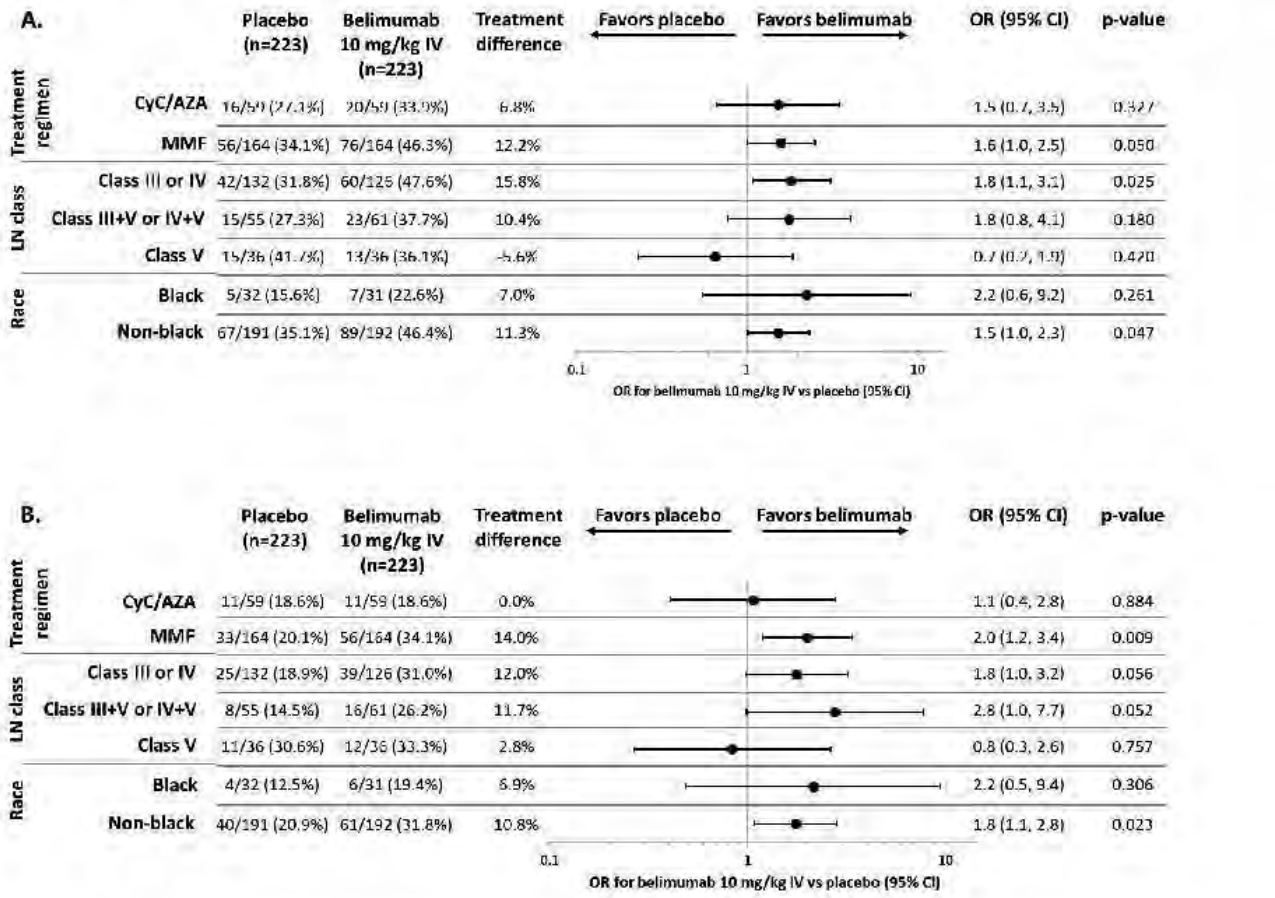
Table 2. Other efficacy endpoints

Endpoint, n (%)	PBO (n=223)	BEL 10 mg/kg IV (n=223)	OR/HR (95% CI) vs PBO	p-value
Time to first severe SFI flare*	70 (31.4)†	42 (18.8)†	HR 0.6 (0.4, 0.8)	0.004
SLEDAI-S2K‡ score <4 at Wk 104	41 (18.4)	62 (27.8)	OR 1.8 (1.1, 2.8)	0.016
Prednisone dose ≤7.5 mg/day at Wk 104§	66 (29.6)	91 (40.8)	OR 1.7 (1.1, 2.5)	0.014
Prednisone dose ≤5 mg/day at Wk 104§	62 (27.8)	82 (36.8)	OR 1.5 (1.0, 2.3)	0.044

*Defined as (event date − treatment start date) + 1; †number/proportion of pts reporting the event; ‡SLEDAI-S2K defined as SELENA-SLEDAI with proteinuria scoring as per SLEDAI-2000 rules; §pts required to taper steroids to ≤10 mg/day by Wk 24

BEL, belimumab; CI, confidence interval; HR, hazard ratio; IV, intravenous; OR, odds ratio; PBO, placebo; pts, patients; SELENA-SLEDAI, Safety of Estrogens in Lupus National Assessment-SLE Disease Activity Index; SFI, SELENA-SLEDAI Flare Index; SLE, Systemic Lupus Erythematosus

Figure. PERR at Wk 104 (A), and CRR at Wk 104 (B), both by treatment regimen, LN class, and race



AZA, azathioprine; CI, confidence interval; CRR, Complete Renal Response; CyC, cyclophosphamide; IV, intravenous; LN, lupus nephritis; MMF, mycophenolate mofetil; OR, odds ratio; PERR, Primary Efficacy Renal Response; Wk, week

In pts with low baseline complement levels, median (IQR) percent change from baseline (BEL vs PBO) in C3 was 43.8 (17.1, 88.9) vs 30.0 (13.5, 59.8) and in C4 was 115.5 (60.0, 177.8) vs 66.7 (22.2, 166.7).

Adverse events (AEs; ≥1) were reported for 95.5% of BEL and 94.2% of PBO pts; 12.9% of pts in each group had ≥1 AE resulting in study treatment discontinuation. Serious AEs (≥1) were reported for 25.9% of BEL and 29.9% of PBO pts, most commonly infections and infestations (13.8% of BEL vs 17.0% of PBO pts); 1.8% of BEL and 1.3% of PBO pts developed on-treatment fatal AEs (mainly due to infections).

Conclusion: In this large 2-year LN study, compared with ST alone, BEL plus ST improved renal outcomes, overall SLE disease activity, and biomarker levels, while reducing steroid use, with a favorable safety profile.

Disclosure: R. Furie, GSK, 1, 2; **B. Rovin**, GSK, 1, Aurinia, 5, AstraZeneca, 5, Novartis, 5, Alexion, 5, Bristol-Myers Squibb, 5; **F. Houssiau**, UCB, 1, GSK, 1; **G. Contreras**, Genentech, 1, 2, Merck, 1, 2; **A. Malvar**, None; **A. Saxena**, Glaxo Smith Kline, 1, Bristol Myers Squibb, 1; **X. Yu**, NSFC, 1, Baxter, 1, 2, 3, 4, Wanbang Biopharmaceuticals Co. Ltd, 1, 2, 3, Kyoowa Kirin Ltd, 1, 2, AstraZeneca, 1, 2, GSK, 1, 2, Fresenius Kabi, 1, 2, Elsevier, 1, CMA, 1, People's Medical Publishing House, 1; **Y. Teng**, GSK, 1, 2, Aurinia, 1, Novartis, 1; **P. van Paassen**, Alexion, 5; **E. Ginzler**,

Aurinia Pharmaceuticals, Inc., 2; **D. Kamen**, None; **M. Oldham**, GSK, 1, 2, 3; **D. Bass**, GSK, 1, 2, 3; **A. van Maurik**, GSK, 1, 2, 3; **M. Welch**, GSK, 1, 2, 3; **Y. Green**, GSK, 1, 2, 3; **B. Ji**, GSK, 1, 2, 3; **C. Kleoudis**, Parexel, 1, GSK, 1, 2; **D. Roth**, GSK, 1, 2, 3.

Abstract Number: 1442

Denosumab versus Oral Bisphosphonate for Osteoporosis in Long-term Glucocorticoid Users: A 12-month Randomized Controlled Trial

Chi Chiu Mok[1], Ling Yin Ho[1] and Kwok Man Ma[1], [1]Tuen Mun Hospital, Hong Kong, China (People's Republic)

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Plenary Session III
Session Type: Plenary Session
Session Time: 11:30AM–1:00PM

Background/Purpose: To compare the efficacy of denosumab (DEN) and oral alendronate (ALN) on spinal bone mineral density (BMD) in long-term glucocorticoid users.

Methods: Patients receiving long-term prednisolone treatment for medical illnesses were recruited. Inclusion criteria: (1) adult patients ^{3}18 years of age; (2) prednisolone ^{3}2.5mg/day for ^{3}1 year. Exclusion criteria: (1) previous use of DEN, teriparatide; (2) plan for pregnancy; (3) metabolic bone disease or unexplained hypocalcemia; (4) renal insufficiency. Participants were randomized to receive either: (1) DEN (60mg subcutaneously every 6 months); or (2) ALN (70mg/week). Calcium (Caltrate 3000mg/day) and vitamin D3 (cholecalciferol 1000IU/day) was given. BMD (femoral neck, total hip, lumbar spine) at month 0, 6 and 12 months were performed. Markers of bone turnover (serum P1NP and CTX) were also assayed at the same time points. The primary outcome was the difference of lumbar spine BMD change at month 12 between the two groups.

Results: 139 subjects were recruited (age 50.0±12.7 years): 69 assigned DEN and 70 assigned ALN. Underlying medical diseases: SLE (81%), RA (9.4%) and myositis (5%). Prednisolone dose at entry was 5.7±2.1mg/day. 56% of female patients were postmenopausal. 73(53%) of patients were osteoporotic (T score < -2.5) at the hip, femoral neck or lumbar spine. The mean body mass index (BMI) was 23.1±4.1kg/m^2 (11% patients had BMI< 18kg/m^2). 82(59%) patients were naive to bisphosphonates. Pre-existing fragility or vertebral fracture was present in 19 (14%) patients and 18 patients (13%) had a family history of fractures. Baseline demographic data, osteoporotic risk factors, and BMD at various sites were not significantly different between the two groups at entry. At month 12, a significant gain in BMD at the lumbar spine (+3.5±2.5%; p< 0.001) and the hip (+0.9±2.8%; p=0.01) was observed in DEN-treated patients, whereas the corresponding change was +2.5±2.9% (p< 0.001) and +1.6±2.7% (p< 0.001) in the ALN group. The spinal BMD at month 12 was significantly higher in the DEN than ALN group after adjustment for BMD values at baseline, age, sex and other osteoporosis risk factors that included smoking, drinking, cumulative steroid doses in one year, BMI, menopausal status and personal history of fracture (p=0.045). The differences in hip and femoral neck BMD were not significantly different between the two groups after adjustment for the same confounding factors. No new symptomatic fractures occurred in any participants at month 12. Adverse events were similar in frequency between the two treatment arms. Major infective episodes were uncommon (0.06/patient/year) and similar in the two groups. Minor upper gastrointestinal symptoms and non-specific dizziness were numerically more common in the ALN but arthralgia, minor infections (eg. upper respiratory tract) and new hypertension was more commonly reported in the DEN group. Three patients from ALN and 2 patients from DEN group were withdrawn from the study because of non-compliance but none withdrew because of adverse events.

Conclusion: In patients receiving long-term glucocorticoids, DEN is superior to ALN in raising the spinal BMD after 12 months' treatment. Both DEN and ALN were well tolerated.

Disclosure: C. Mok, None; **L. Ho**, None; **K. Ma**, None.

Abstract Number: 1443

High-dimensional Analyses of Checkpoint-inhibitor Related Arthritis Synovial Fluid Cells Reveal a Unique, Proliferating CD38^{hi} Cytotoxic CD8 T Cell Population Induced by Type I IFN

Runci Wang[1], Karmela Kim Chan[2], Amy Cunningham-Bussel[1], Gregory Vitone[3], Aidan Tirpack[2], Caroline Benson[2], Gregory Keras[4], Anna Helena Jonsson[5], Michael Brenner[5], Laura Donlin[6], Anne Bass[7] and Deepak Rao[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Hospital For Special Surgery, New York, NY, [3]Hospital for Special Surgery, New York, [4]Brigham and Women's Hospital, Division of Rheumatology, Inflammation, and Immunity, Boston, MA, [5]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [6]Hospital for Special Surgery, Weill Cornell Medicine, New York, [7]Hospital for Special Surgery/Weill Cornell Medicine, New York, NY

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Plenary Session III
Session Type: Plenary Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Checkpoint inhibitors (CI) used to treat cancer frequently trigger immune-related adverse events, including inflammatory arthritis. CI-related arthritis (CIrA) occurs in ~5% of treated patients, with clinical manifestations resembling rheumatoid arthritis (RA) and spondyloarthropathies (SpA). However, the cellular and molecular features of CIrA remain unknown, calling for a deeper understanding of its pathogenesis.

Methods: We conducted detailed immunophenotyping of synovial fluid (SF) mononuclear cells to compare CIrA, seropositive RA, and SpA using mass cytometry (CyTOF) (CIrA n=10, anti-PD-1-treated; 5 mono/oligoarthritis, 5 polyarthritis; RA n=11; SpA n=9). Significantly altered populations ($p< 0.05$) were identified using FlowSOM and validated by flow cytometry in additional SF and blood samples (CIrA n=15; RA n=15). SF CD8 T cell subpopulations were sorted for RNA-seq and intracellular staining. Transcriptomic features were recognized by identifying differentially expressed genes and by Gene Set Enrichment Analysis (GSEA) ($q< 0.25$). RA SF cells were cultured with cytokines (IFNα 1kU/mL or IFNγ 50ng/mL) and anti-CD3/CD28 for 72 hours and analyzed by flow cytometry.

Results: FlowSOM analysis of SF CyTOF revealed a CD38^{hi}CD127^{-} PD-1^{+} CD8 cell population uniquely expanded in CIrA (~25% of CD8 in CIrA, a 3.4-fold increase over RA/SpA), which was confirmed in additional SF samples by flow cytometry. In contrast, T cells with the converse CD38^{-}CD127^{+} phenotype were reduced in CIrA compared to RA/SpA. CD38^{hi}CD127^{-} CD8 cells were also expanded in blood of CIrA patients (5% of CD8 in CIrA, a 2.8-fold increase over RA) (Fig. 1).

RNA-seq analysis of the expanded CD38^{hi}CD127^{-} subset revealed significantly increased expression of inflammatory and cytotoxic molecules including granzyme A/B/H/K, perforin and IFNγ, with expression levels of these genes comparable to those in sorted KLRG1^{+} cytotoxic T cells. Flow cytometry of ex vivo stimulated T cells confirmed a higher frequency of granzyme B^{+} and perforin^{+} cells in the CD38^{hi}CD127- population (Fig. 2). GSEA revealed an increased proliferation signature in CD38^{hi}CD127^{-} cells compared to CD38^{-}CD127^{+} cells, with upregulation of genes involved in DNA replication, mitosis and cell division ($q< 0.1$, FC >1.5 over CD38^{-}CD127^{+} cells). This feature was not shared

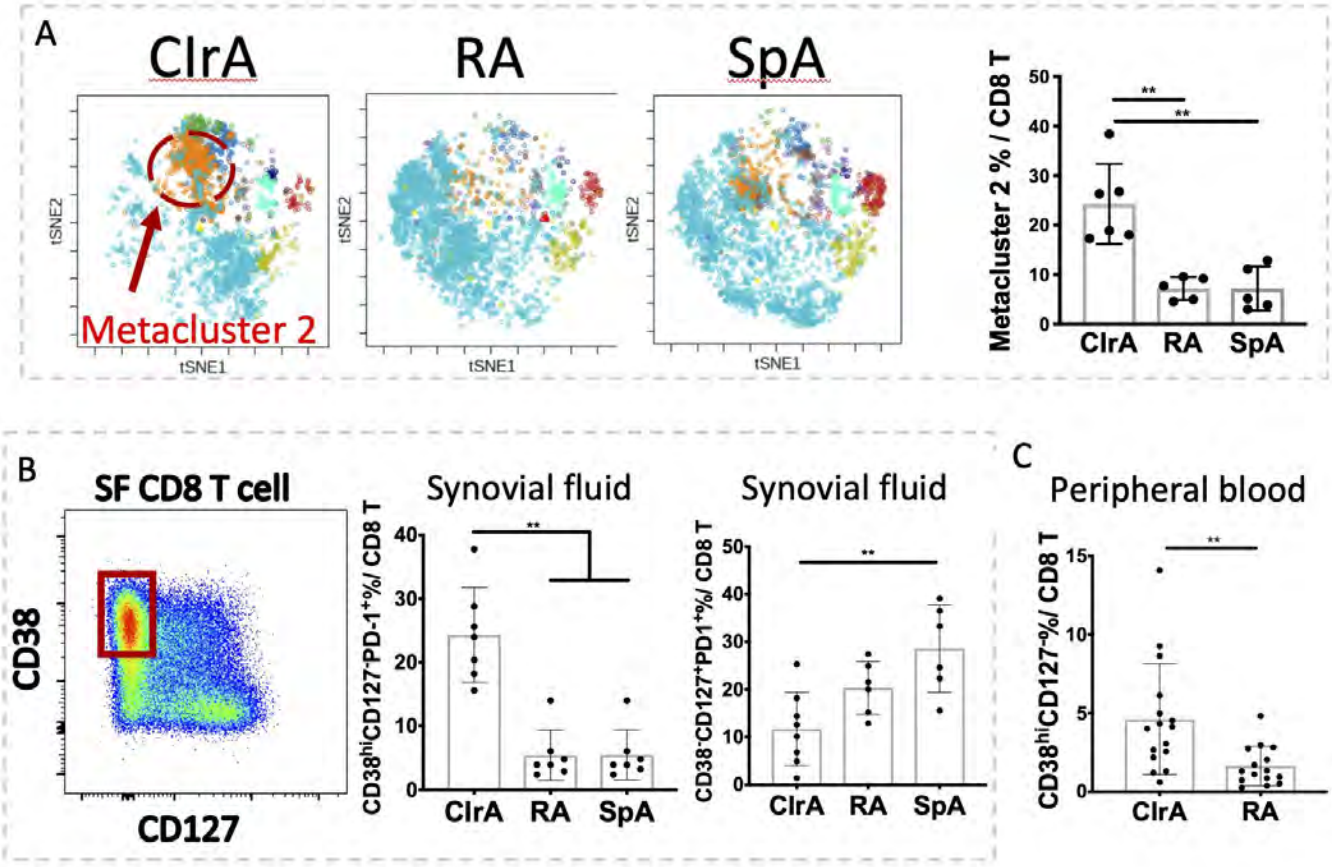


Figure 1. FlowSOM analysis of CD8 T cells revealed the expansion of a PD-1+CD38hiCD127- population in synovial fluid and peripheral blood of checkpoint inhibitor-related arthritis (ClrA). A) FlowSOM analysis of CyTOF CD8 T cells highlighted an expanded metacluster 2 in ClrA SF (Kruskal-Wallis test, ClrA n=6, RA/SpA n=5). B) Biaxial gating of flow cytometry data confirmed expanded CD38hiCD127-PD1+ cells and reduced CD38-CD127+ CD8 T cells in ClrA SF (Kruskal-Wallis test, n=7). C) CD38hiCD127- CD8 cells are expanded in blood of ClrA patients (t-test, n=15). Mean±SD shown, **p<0.01.

by PD1$^-$ cells or KLRG1$^+$ cells (Fig 3). CyTOF confirmed >40% of CD38^{hi} CD127$^-$ PD-1$^+$ CD8 T cells expressed Ki67. GSEA of SF T cells also revealed a marked enrichment of IFN-inducible genes in ClrA compared to SpA/RA. Treatment of RA SF T cells with IFNα, but not IFNγ, induced CD8 T cells to acquire a CD38^{hi}CD127$^-$ phenotype resembling that seen in ClrA (Fig. 3).

Conclusion: CyTOF analysis of SF mononuclear cells revealed a highly expanded PD-1$^+$CD38^{hi}CD127$^-$ CD8 T cell population in ClrA that is not shared by RA or SpA. This T cell subset shows cytotoxic and proliferative features at both the gene and protein expression level. CD38^{hi}CD127$^-$ CD8 T cells in ClrA samples showed an IFN signature, and treatment of T cells with IFNα induced this phenotype in vitro. This work reveals a unique T cell phenotype in ClrA and suggests type I IFN may be a pathologic driver in this condition.

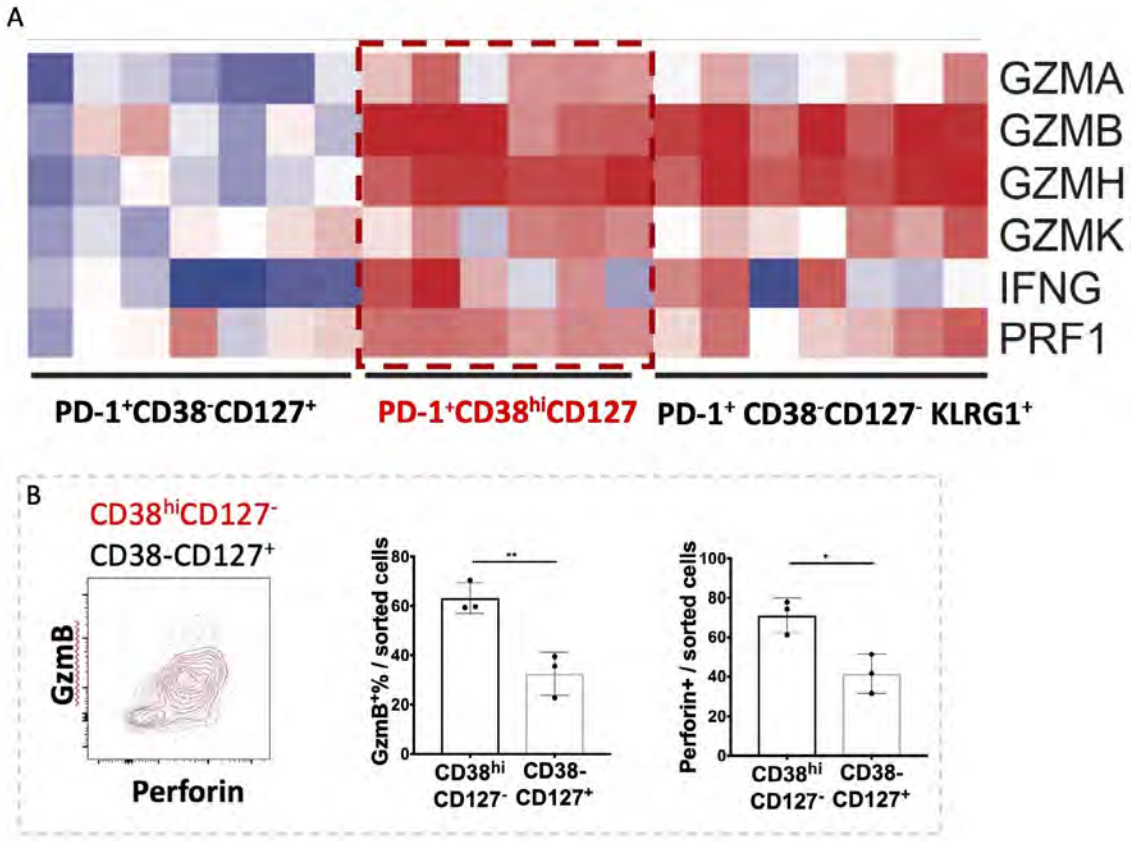


Figure 2. RNA-seq analysis and flow cytometry staining of CD38hiCD127- CD8 T cells in ClrA SF demonstrated cytotoxic and inflammatory features. A) Heatmap of cytotoxic molecules enriched in CD38hiCD127- cells. B) Enrichment of intracellular granzyme B and perforin in sorted CD38hiCD127- CD8 T cells. Mean±SD shown, *p<0.05, **p<0.01.

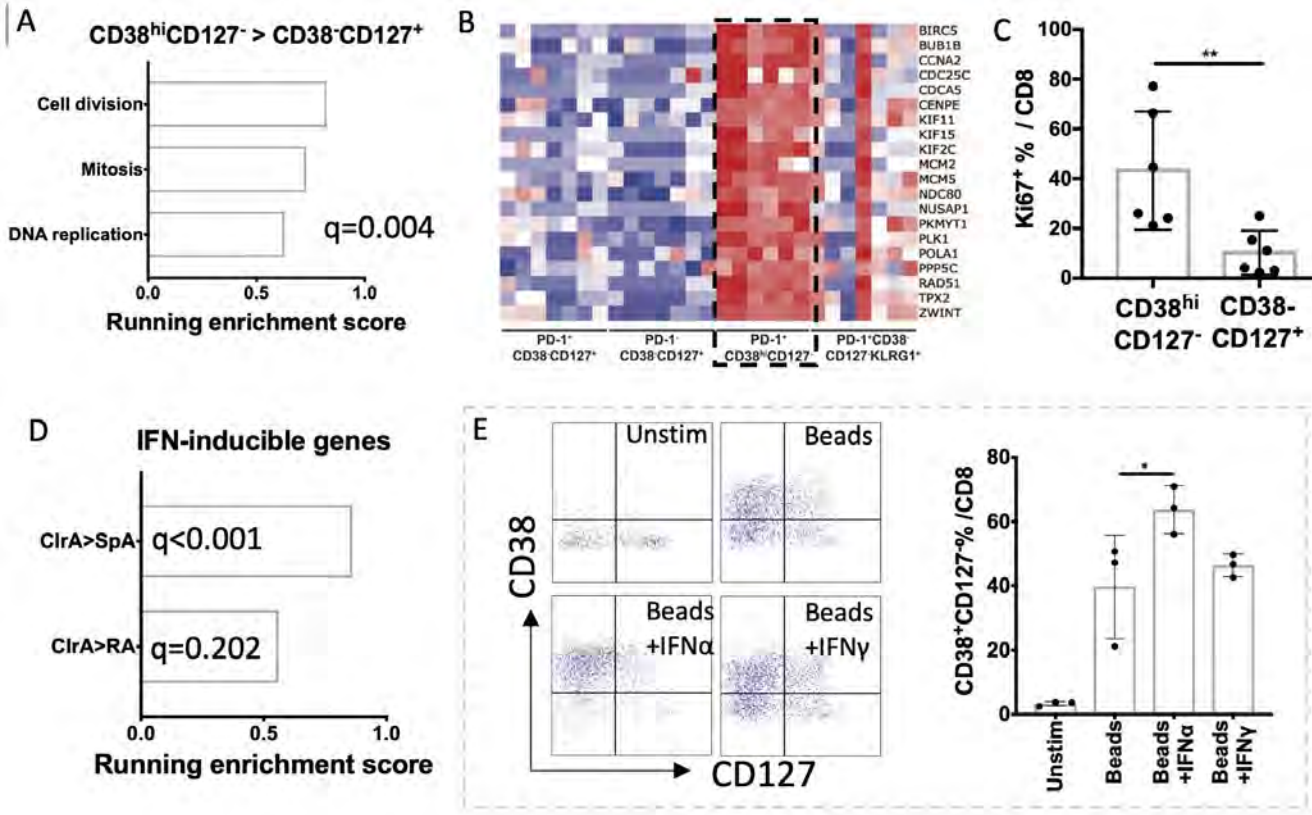


Figure 3. CD38hiCD127- CD8 T cells in ClrA SF showed a proliferation feature, and a phenotype induced by IFNα. A) GSEA identified enrichment of proliferation gene sets in CD38hiCD127- CD8 T cells; B) Heatmap of proliferation genes enriched in CD38hiCD127- CD8 T cells. C) CyTOF showed increased expression of Ki67 in CD38hiCD127- CD8 T cells. D) GSEA showed an IFN signature in ClrA cells. E) RA SF cells were cultured unstimulated or stimulated with anti-CD3/28 activation beads with or without IFNα or IFNγ as indicated for 72 hours. CD38hiCD127- phenotype resembling that seen in ClrA was induced by IFNα but not IFNγ. Mean±SD shown, *p<0.05, **p<0.01.

Disclosure: R. Wang, None; **K. Chan**, None; **A. Cunningham-Bussel**, None; **G. Vitone**, None; **A. Tirpack**, None; **C. Benson**, None; **G. Keras**, None; **A. Jonsson**, None; **M. Brenner**, None; **L. Donlin**, Stryker, 1, 2; **A. Bass**, None; **D. Rao**, None.

Abstract Number: 1444

Cluster-randomized Pragmatic Clinical Trial Evaluating the Potential Benefit of a Tight-control and Treat-to-target Strategy in Axial Spondyloarthritis: The Results of the TICOSPA Trial

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Plenary Session III
Session Type: Plenary Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Recommendations for axial spondyloarthritis (axSpA) management include tight control and treat-to-target (TC), but no study has evaluated its potential benefit. The objective of this trial was to evaluate the benefit of TC strategies in comparison to usual care (UC) in patients with axSpA.

Methods: *Study design:* Pragmatic, prospective, cluster-randomized controlled (2 arms), one-year trial (NCT03043846). *Centers*: 18 axSpA expert centers randomly allocated (1:1) to the treatment arm: TC vs. UC. *Patients*: axSpA diagnosis and ASAS criteria, non-optimally treated with NSAIDs, bDMARD-naïve, and ASDAS > 2.1 at inclusion. *Study treatment*: a) TC: the strategy was pre-specified by the scientific committee based on current axSpA recommendations and aiming at a target (ASDAS < 2.1); visits every 4w; b) UC arm: treatment decisions were at the rheumatologist's discretion with visits every 12w. *Outcomes:* the % of patients with a significant (>30%) improvement in the ASAS-HI score over one-year follow-up was the main outcome. Other outcomes (disease activity, quality of life, treatment, …) over follow-up were evaluated (Table 1). The number/type of adverse events were collected. *Statistical analysis*: this was an intention-to-treat analysis. To take into account the cluster-randomization design, for all outcomes, two models were performed: first a two-level mixed model with 2 random effects was used to estimate the % of responders/the change of the outcome over follow-up (i.e. mod1); in a second step, the imbalanced variables observed at baseline were included in the model (i.e.mod2). Cost-effectiveness was assessed by estimating the (baseline- and cluster-adjusted) incremental cost per quality-adjusted life-year (QALY) gained for TC vs. UC.

Results: 160 patients were included (80 in TC and 80 in UC). Mean age was 37.9(11.0) years with a disease duration of 3.7(6.2) years, 51.2% were males. A radiographic damage of the SI-joints, a (ever) positive MRI sacroiliitis and HLA-B27+ were seen in 46.9%, 81.9% and 75.0% patients respectively. Mean ASDAS at inclusion was 3.0 (0.7) and

	Estimated outcomes at week 48		Cluster-adjusted	Cluster and imbalance -adjusted
	TC	UC		
ASAS HI significant improvement (Main Outcome)	47.3%	36.1%	-	-
ASDAS LDA*	76.5%	59.5%	<0.01	0.03
ASDAS ID	25.9%	18.7%	-	-
ASDAS CII	61.2%	46.0%	<0.01	0.02
ASDAS MI	16.5%	14.9%	-	-
ASAS40	52.3%	34.7%	<0.01	0.01
ASAS20	94.9%	85.9%	<0.01	0.03
BASDAI 50	79.0%	43.8%	0.01	0.03
Physician Global (0-10)	2.0 (0.2)	1.8 (0.2)	-	-
CRP (mg/L)	3.9(1.4)	3.5 (1.5)	-	-
BASG (0-10)	2.6 (0.5)	3.4 (0.5)	0.09	-
BASFI (0-10)	1.7(0.5)	2.4 (0.5)	-	-
EQ5D	0.7(0.1)	0.8(0.1)	0.02	-
ASAS-NSAID score	1.5(2.2)	- 4.9 (2.9)	-	-

Legend: - : not statistically significant.

mean ASASHI was 8.6 (3.7). 72 patients per group attended the one-year visit. Although 47.3% vs. 36.1% patients in the TC and UC arms achieved a significant improvement in ASASHI at the one-year visit, the difference was not statistically significant, with either model. Across all other outcomes a trend was observed in favor of the TC arm (Table 1). The number of bDMARDs was significantly higher in TC arm (56.2% vs. 27.2%). The number of infections was comparable in both groups (15 vs. 16 in the TC and UC, respectively), with only 2 severe infections occurring in the UC arm. From a societal perspective, TC resulted in an additional 0.04 QALY and saved €265 when compared to UC and a 67% probability of being cost-effective at a cost-effectiveness threshold of €20,000 per QALY.

Conclusion: In this setting of SpA expert centers, UC resulted in a good outcome in a substantial number of patients but the TC was not superior for the primary outcome despite a greater number of bDMARDs prescription. Nevertheless, a general trend in favor of the tight control was observed, with a comparable safety profile and was found to be favorable from a societal health economic perspective.

Disclosure: A. Molto, ABBVIE, 5, BMS, 5, 8, LILLY, 5, NOVARTIS, 5, 8, UCB, 5, 8, GILEAD, 5; **C. Lopez-Medina**, None; **F. Van den Bosch**, AbbVie, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Gilead, 5, Merck, 5, 8; **A. Boonen**, AbbVie, 2, Galapagos, 5, Lilly, 5, Celgene, 2, UC, 5; **C. Webers**, None; **E. Dernis**, Abbvie, 5, BMS, 5, Celgene, 5, Roche-Chugai, 5, Janssen, 5, Lilly, 5, Medac, 5, MSD, 5, Nordic Pharma, 5, Novartis, 5, Sanofi, 5, UCB, 5; **F. van Gaalen**, Reuma Nederland, 1, Stichting vrienden van Sole Mio, 1, MSD, 1, Abbvie, 1, Novartis, 1; **M. Soubrier**, None; **P. Claudepierre**, Abbvie, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Merk, 5, 8, novartis, 5, 8, Lilly, 5, 8, Janssen, 5, 8, BMS, 5, 8; **A. Baillet**, None; **M. Starsman-Kool**, None; **A. Spoorenberg**, Pfizer, 1, 2, Novartis, 1, 2, Abbvie pharmaceuticals, 1, 2, MSD, 1, UCB, 1; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5; **M. Dougados**, Pfizer, 5, 8, AbbVie, 5, 8, Roche, 5, 8, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, 8, Novartis, 5, 8, Sanofi, 5, 8, Biogen, 5, 8, Merck Sharp & Dohme, 5, 8, UCB Pharma, 5, 8.

Abstract Number: 1445

Citrulline Reactive B Cells Are Present in the Lungs of Risk RA and Early Untreated RA

Vijay Joshua[1], Malena Loberg-Haarhaus[2], Akilan Krishnamurthy[1], Meng Sun[3], Christina Gerstner[4], Aase Hensvold[5], Khaled Amara[1], Lena Israelsson[1], Ragnhild Stålesen[6], Bence Rethi[7], Magnus Sköld[7], Johan Grunewald[1], Heidi Wähämaa[1], Caroline Grönwall[1], Vivianne Malmström[8] and Anca Catrina[5], [1]Karolinska Institutet, Stockholm, Sweden, [2]Rheumatology clinic, Karolinska University Hospital, Stockholm, Sweden, Stockholm, Stockholms Lan, Sweden, [3]Karolinska University Hospital and Karolinska Insitutet, Stockholm, Sweden, [4]Division of Rheumatology, Department of Medicine,Center for Molecular Medicine, Karolinska Institutet, Stockholm, Sweden, [5]Rheumatology Unit, Department of Medicine, Karolinska Institutet, Stockholm, Sweden, Stockholm, Stockholms Lan, Sweden, [6]Karolinska Institute, Stockholm, Sweden, [7]Karolinska Institutet, Stockholm, [8]Karolinska Institutet, Stockholm, Stockholms Lan, Sweden

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Plenary Session III
Session Type: Plenary Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Structural changes, increased tissue citrullination, signs of local inflammation and anti-citrullinated protein autoantibodies (ACPA) are present in the pulmonary compartment of early untreated seropositive

rheumatoid arthritis (RA). These findings provide evidence of a potential role for the lungs in generation and initiation of RA-associated autoimmunity. Here we aimed to investigate the presence of citrulline-reactive B cells in the lung compartment of early untreated RA patients by single-cell cloning of monoclonal antibodies (mAbs) from lung-derived B cells.

Methods: Bronchoalveolar lavage (BAL) fluid cells were obtained from ACPA positive individuals with arthralgia (n=4), early untreated ACPA positive RA (n=3) and ACPA negative RA (n=5) patients at the time of diagnosis. CD19+ B cells were single cell sorted by flow cytometry. Immunoglobulin heavy and light chain variable regions were PCR amplified, sequenced, and analyzed by V-Quest and IgBLAST towards the IMGT database to annotate variable gene usage. Sequences having high somatic hypermutations (SHM) and Fab N-glycosylation sites were selected to be cloned and expressed as human IgG1 recombinant mAbs. Citrulline reactivity was determined by CCP2 assay and in-house ELISA against citrullinated and native peptides from vimentin, a-enolase, fibrinogen and filaggrin. Polyreactivity was determined by reactivity against double stranded DNA, bacterial lipopolysaccharides (LPS) and insulin. The functional properties of mAbs were analyzed in osteoclastogenesis assay, fibroblast migration assay and neutrophil binding assay.

Results: Significant higher proportion of CD19+ B cells were found in ACPA positive compared to ACPA negative BAL (median 6.7% vs 0.79%). PCR amplification and subsequent BCR sequencing from 8 individuals yielded 581 paired heavy and light chain sequences. 49 monoclonal antibodies (from 5 individuals) were selected for expression based on high number of SHM and predicted Fab N-linked glycosylation. Notably, four of these selected mAbs (8%; 2 antibodies from each patient, one risk RA and one early untreated RA) were determined to be ACPAs by CCP2 ELISA. The 4 ACPAs had varying ACPA fine-specificity against citrullinated a-enolase, filaggrin, vimentin and fibrinogen peptides without any native peptide binding. All the 4 monoclonal ACPAs were negative in polyreactivity test. Clone L204:01A01 and L201:11C11 but not clone L201:10D07 and L204:05E10 bound to activated neutrophils (49.75% for clone A01 and 22.3% for clone C11). Clone L204:01A01 and L204:05E10 but not L201:10D07 and L201:11C11 induced osteoclastogenesis with a fold increase of 1.5 and 1.9 respectively. Clone L204:01A01 and L201:10D07 but not L201:11C11 and L204:05E10 promoted fibroblasts migration with a fold increase of 1.4 and 1.5 respectively.

Conclusion: We demonstrate for the first time that citrulline-reactive B cells producing pathogenic ACPAs are present in the lung compartment of seropositive individuals at risk for or having early untreated RA. This provides a strong link between the lung and the adaptive autoreactive response in RA, and support the hypothesis of the lung as one of the key sites of initiation and propagation of disease in RA.

Disclosure: V. Joshua, None; **M. Loberg-Haarhaus**, None; **A. Krishnamurthy**, None; **M. Sun**, None; **C. Gerstner**, None; **A. Hensvold**, None; **K. Amara**, None; **L. Israelsson**, None; **R. Stålesen**, None; **B. Rethi**, None; **M. Sköld**, None; **J. Grunewald**, None; **H. Wähämaa**, None; **C. Grönwall**, None; **V. Malmström**, Pfizer, 2; **A. Catrina**, None.

Abstract Number: 1446

Pregnancy Outcomes in Patients with Interstitial Lung Disease

Aardra Rajendran[1], Stephanie Giattino[2], Amanda Eudy[3], Aparna Swaminathan[4] and Megan Clowse[5], [1]Duke University, Lewisville, NC, [2]Duke University, Media, PA, [3]Duke University, Durham, NC, [4]Duke University, Durham, [5]Duke University, Chapel Hill, NC

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Plenary Session III
Session Type: Plenary Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Patients with interstitial lung disease (ILD) are often recommended to avoid conception or terminate pregnancy despite limited data on pregnancy outcomes and complications. Studies to date have only been conducted in small samples of 9-15 patients with mixed results. This study aims to retrospectively analyze pregnancy outcomes in the largest-to-date cohort of patients with ILD secondary to autoimmune disease to further inform providers and patients on the risks of pregnancy. We hypothesize that patients with more severe ILD as classified by physiologic measures will have worse pregnancy outcomes and increased complications.

Methods: Medical records in the Duke University Health System (1/1/1996 - 7/1/2019) were reviewed for pregnancies in patients with a diagnosis of ILD secondary to autoimmune disease. Pregnancies were classified according to severity of ILD based on percent predicted forced vital capacity (FVC % pred) or percent predicted diffusion capacity for carbon monoxide (DLCO % pred). Cutoff values included normal (DLCO % pred ≥ 80% and FVC % pred ≥ 80%), mild (DLCO % pred 61-79% or FVC % pred 60-79%), moderate (DLCO % pred 40-60% or FVC % pred 40-59%), and severe (DLCO % pred < 40% or FVC % pred < 40%). Adverse outcomes were defined using the composite PROMISSE-APO (preeclampsia, pre-term delivery < 36 weeks, small for gestational age (SGA) infant < 5th percentile, fetal death > 12 weeks, or neonatal death) and PROMISSE-APO SEVERE (preeclampsia and preterm delivery < 34

DELIVERY OUTCOMES	Total	No PFTs	Severe	Moderate	Mild	Normal	p-value[1]
	N=94	n=30	n=7	n=16	n=32	n=9	
PROMISSE APO[2]	25/73 (34%)	5/24 (21%)	5/5 (100%)	5/12 (42%)	7/24 (29%)	3/8 (38%)	0.03
PROMISSE APO-SEVERE[3]	11/73 (15%)	1/24 (4%)	3/5 (60%)	2/12 (17%)	4/24 (17%)	1/8 (13%)	0.2
Non-Live Births	28 (30%)	7 (23%)	4 (57%)	5 (31%)	11 (34%)	1 (11%)	0.3
Termination	9 (10%)	3 (10%)	1 (14%)	2 (13%)	3 (9%)	0 (0%)	0.7
Miscarriage	17 (23%)	4 (13%)	2 (29%)	3 (19%)	7 (22%)	1 (11%)	0.8
Stillbirth	2 (2%)	0 (0%)	1 (14%)	0 (05)	1 (3%)	0 (0%)	0.4
Live Births:	66 (70%)	23 (77%)	3 (43%)	11 (69%)	21 (66%)	8 (89%)	0.3
Gestational age at delivery (mean ± S.D.) (weeks)[4]	37.8 ± 2.6	38.2 ± 2.2	33.7 ± 4.2	37.9 ± 1.9	38.0 ± 2.8	37.5 ± 2.6	0.08
Preterm birth[4]	9/62 (15%)	2/21 (10%)	2/3 (67%)	1/11 (9%)	2/21 (10%)	2/6 (33%)	0.06
SGA < 10th percentile[4]	10/61 (16%)	3/21 (14%)	1/3 (33%)	0/11 (0%)	3/20 (15%)	3/6 (50%)	0.04
Preeclampsia	10/65 (15%)	1/22 (5%)	2/4 (50%)	4/11 (36%)	2/20 (10%)	1/8 (13%)	0.1

1. p-value comparisons are only made between pregnancies in the severe, moderate, mild, and normal groups. Pregnancies in patients without PFTs were not included in statistical analysis.
2. PROMISSE-APO: preeclampsia, pre-term delivery < 36 weeks, small for gestational age (SGA) infant < 5th percentile, fetal death > 12 weeks, or neonatal death. Pregnancy losses < 12 weeks were excluded as in the PROMISSE study (Kim et al., 2016).
3. PROMISSE-APO SEVERE: preeclampsia and preterm delivery < 34 weeks, preterm delivery < 30 weeks, fetal death > 12 weeks, or neonatal death. Pregnancy losses < 12 weeks were excluded as in the PROMISSE study (Kim et al., 2016).
4. Only singleton pregnancies included for analysis of gestational age at delivery, preterm birth and SGA < 10th percentile.

Figure 1. Delivery Outcomes

weeks, preterm delivery < 30 weeks, fetal death > 12 weeks, or neonatal death). Fisher's Exact Test and ANOVA was used to compare outcomes among patients in different severity groups.

Results: This study included 67 patients with 94 pregnancies (5 twin pergnancies). The average maternal age was 32.1 ± 6.0 years with 83% identifying as Black. Overall, 69% of pregnancies were diagnosed with sarcoidosis and the remaining 31% had a connective tissue disease associated ILD (CTD-ILD). Of the pregnancies with available measures to classify ILD severity (n=64), 11% were severe, 25% were moderate, 50% were mild, and 14% were normal. All the pregnancies in the severe group had CTD-ILD while 89% of pregnancies in the normal group had sarcoidosis (p=0.001 across groups).

Overall, 70% of pregnancies resulted in live births and 9 pregnancies (10%) were terminated (Fig. 1). There was a 15% rate of pre-eclampsia, 34% rate of PROMISSE-APO, and 15% rate of PROMISSE-APO SEVERE. Patients with severe disease had the highest rates of PROMISSE-APO (p=0.03 across groups).

There were no maternal deaths and only 2 pregnancies required intensive care unit care. Overall, 4 pregnancies experienced volume overload at the time of delivery, of which 1 patient developed postpartum heart failure. A total of 8 pregnancies required oxygen at the time of delivery, and 1 patient was intubated during pregnancy.

Conclusion: While adverse pregnancy outcomes are common in ILD pregnancies, especially in patients with more severe disease, overall maternal morbidity and mortality is low. Patients with ILD do not necessarily have to terminate pregnancies provided they have close monitoring before, during, and after pregnancy and appropriate subspecialist involvement.

Disclosure: A. Rajendran, Rheumatology Foundation Medical Student Preceptorship Award, 2; **S. Giattino**, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 2, Pfizer, 2; **A. Swaminathan**, None; **M. Clowse**, UCB, 5, GSK, 2, 5, Astra Zeneca, 5, Pfizer, 2.

Abstract Number: 1447

Vitamin D Deficiency Enhances Antiphospholipid Antibody-Mediated Thrombosis in a Passive Immunization Mouse Model

Rohan Willis[1], Karen Roye-Green[2], Zurina Romay-Penabad[1], Elizabeth Papalardo[1], Alvaro Schleh[3], Vijaya Murthy[4], Monica Smikle[2] and Emilio Gonzalez[1], [1]University of Texas Medical Branch, Galveston, TX, [2]University of the West Indies, Kingston, Jamaica, [3]Antiphospholipid Standardization Laboratory, GALVESTON, TX, [4]University of Texas Medical Branch, League City, TX

SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Antiphospholipid Syndrome
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Abnormal vitamin D levels occur frequently in antiphospholipid (APS) patients and are correlated with thrombosis. It remains unclear however if vitamin D deficiency observed in APS occurs as a part of disease pathogenesis, as a consequence of disease activity or as an incidental disease-modifying factor. This study aims to determine if induction of antiphospholipid antibody (aPL) induces changes in vitamin D levels (Phase I) and to evaluate the effect of vitamin D deficiency on aPL-mediated thrombosis in APS mouse models (Phase II).

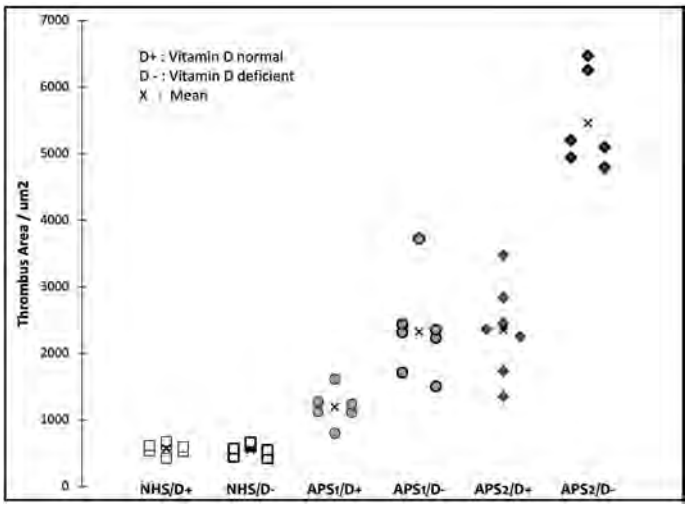

Figure 1. Cross-sectional area of induced thrombi in femoral vein of vitamin D deficient and normal mice treated with antiphospholipid and normal IgG

Methods: In Phase I, CD1 male mice (n= 5 to 7 per group) fed normal diets were immunized with either human β2GPI of varying doses (0.5ug, 1ug, 10ug or 150ug with adjuvant) once weekly for 3 doses to induce different levels of aPL activity or ovalbumin (OA) (10ug or 150ug). Serum was collected 4 weeks following initial immunization to measure 25 hydroxy vitamin D (25OHVD), aCL and anti-β2GPI levels by ELISA. In Phase II, CD1 male mice (n=5 to 7) were fed either a vitamin D normal (VDnorm) or deficient (VDdef) diet supplemented with calcium for 6 weeks until 25OHVD levels were stable. After stable 25OHVD levels, mice were then inoculated (2 doses over 48hrs) with either purified whole IgG from a primary APS (PAPS) patient (IgG APS 1), β2GPI-affinity purified IgG from a second PAPS patient (IgG APS 2) or whole IgG from normal human serum (IgG NHS) prior to thrombosis induction in the femoral vein. Blood was collected weekly after start of diet, immediately prior to IgG treatment and at time of thrombosis analysis.

Results: Phase I – IgG aCL and anti-β2PI levels were significantly higher in β2GPI immunized mice compared to control mice and increases were dependent on dose of antigen. However, there was no significant difference in 25OHVD levels among all the groups and all were normal (range 61.2±15.1 to 78.5±9.6 ng/ml, p=0.220). In phase II, VDdef mice developed vitamin D deficiency (< 20ng/ml) by W3, which continued until W6. Thrombus experiments were subsequently done at W4 and mean 25OHVD was significantly less in VDdef vs VDnorm mice (17.7±2.9 vs 36.1±7.8 ng/ml,p< 0.0001). Mean IgG anti-β2GPI levels were similar for VDdef vs VDnorm mice treated with IgG NHS (2.5±0.6 vs 2.8±0.4 G units), IgG APS 1 (75.9±0.2 vs 75.9±0.4) and IgG APS 2 (42.8±0.3 vs 42.3±0.3) at the time of surgery. Mean thrombus sizes in these 3 treatment groups were (555.9±89.5 vs 574.3±82.8 μm^2,p=0.902), (2327.8±709.8 vs 1195.6±265.5,p< 0.001) and (5461.8±715.8 vs 2353.7±694.7,p< 0.001) for VDdef vs VDnorm mice (Figure 1).

Conclusion: We provide the first mechanistic data indicating that vitamin D deficiency amplifies the thrombogenic effect of IgG aPL. This effect was demonstrated for aPL derived from 2 different primary APS patients. However, induction of aPL activity of varying strength in an active immunization model seemingly had no effect on vitamin D production and storage in the face of normal dietary intake. Future studies will focus on the immunomodulatory changes underlying the effect of vitamin D on the thrombogenic capacity of aPL and mechanisms that lead to abnormal vitamin D levels in APS patients.

Disclosure: R. Willis, Louisville APL Diagnostics Inc, 5, Pfizer, 2; **K. Roye-Green**, None; **Z. Romay-Penabad**, None; **E. Papalardo**, None; **A. Schleh**, Louisville APL Diagnostics Inc, 4; **V. Murthy**, None; **M. Smikle**, None; **E. Gonzalez**, None.

Abstract Number: 1448

Single-cell RNA Sequencing of Livedo Reticularis Skin Reveals Endothelial Pathology in Antiphospholipid Syndrome

Hui Shi[1], Allison Billi[1], Rachael Wasikowski[1], Kelsey Gockman[1], Alex Tsoi[1], Johann Gudjonsson[2] and Jason Knight[3], [1]University of Michigan, Ann Arbor, [2]University of Michigan, Ann ArborUniversity of Michigan, [3]Division of Rheumatology, University of Michigan, Ann Arbor, MI

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Antiphospholipid Syndrome
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Antiphospholipid syndrome (**APS**) is a thromboinflammatory disease that can present with a variety of clinical phenotypes. Livedo reticularis is the most common skin manifestation of APS, representing a netlike pattern of reddish-blue skin discoloration indicative of superficial vessels that have swollen in response to sluggish flow in the deeper vascular network. Interestingly, livedo reticularis is predictive of APS patients at higher risk of cerebrovascular events. Although the interaction between antiphospholipid antibodies (**aPL**) and endothelial cells are likely key mechanistic drivers of livedo reticularis, these cells have rarely been directly studied. Here, we used single-cell RNA sequencing to begin to characterize APS endothelial cells.

Methods: We applied single-cell RNA sequencing to skin biopsies of two APS patients with livedo reticularis and three matched controls with neither APS nor livedo; t-distributed stochastic neighbor embedding (**t-SNE**) was then

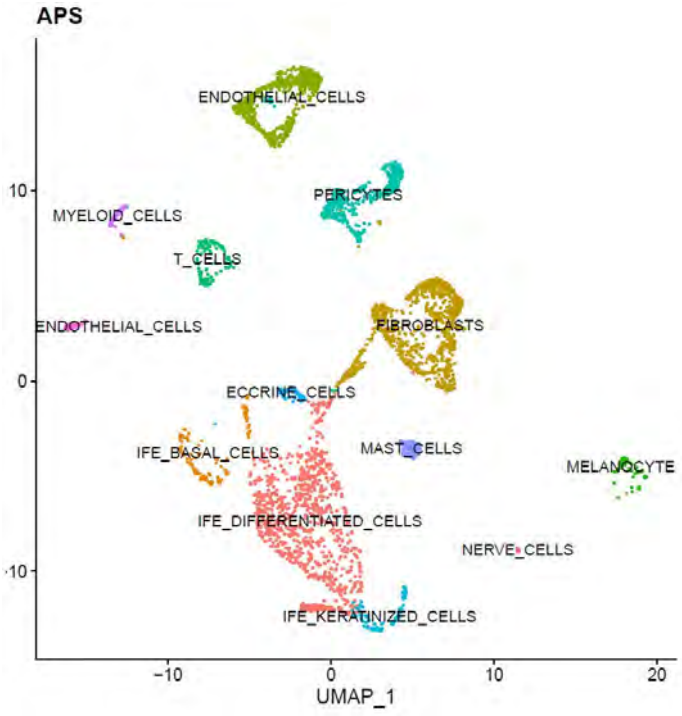

Figure 1. t-SNE analysis of the cells isolated from the antiphospholipid syndrome (APS) skin with livedo reticularis. Defined number of 13 clusters with every cluster represented by a different color.

used to identify the various cell types. We performed GO and pathway enrichment by using Database for Annotation, Visualization, and Integrated Discovery (**DAVID**) analysis.

Results: By combining the t-SNE analysis with the expression of known endothelial cell markers, we identified three subpopulations of endothelial cells among the sorted cells (**Figure 1**). Subsequently, we compared expression profiles between endothelial cells from healthy and APS skin and found significant upregulation of CD36 (a scavenger receptor) and TXNIP (a mediator of oxidative stress) in APS endothelial cells. Using DAVID analysis, we revealed that the APS endothelial cell expression profile is enriched for processes associated with cell adhesion, angiogenesis, and type I interferon signaling.

Conclusion: To our knowledge, this is the first direct analysis of gene expression in APS endothelial cells. These data suggest that APS endothelial cells from skin affected by livedo reticularis demonstrate a pattern of gene expression associated with endothelial activation and damage. We are actively recruiting additional patients into the study in pursuit of providing a foundation for future studies of vascular injury in APS.

Disclosure: H. Shi, None; **A. Billi**, None; **R. Wasikowski**, None; **K. Gockman**, None; **A. Tsoi**, None; **J. Gudjonsson**, Celgene, 2; **J. Knight**, None.

Abstract Number: 1449

Altered Splicing in Leukocytes from Patients with Antiphospholipid Syndrome, Systemic Lupus Erythematosus and Antiphospholipid Syndrome with Lupus: Clinical Involvement

Alejandra Maria Patiño-Trives[1], Alejandro Ibáñez-Costa[2], Carlos Pérez-Sánchez[1], Laura Pérez-Sanchez[3], Maria Luque-Tevar[1], Iván Arias de la Rosa[1], María-Carmen Abalos-Aguilera[1], Desirée Ruiz-Vilchez[4], Pedro Segui[5], Mario Espinosa[5], Nuria Barbarroja[1], Eduardo Collantes[4], Justo P. Castaño[5], Raul M Luque[5], María de los ángeles Aguirre-Zamorano[5] and **Chary Lopez-Pedrera**[1], [1]Rheumatology Department, Reina Sofia University Hospital/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba, Cordoba, Spain, Cordoba, Spain, [2]IMIBIC/University of Cordoba/Reina Sofia Hospital, Córdoba, [3]Hospital Universitario Reina Sofía, Córdoba, Spain, [4]Rheumatology Department, Reina Sofia University Hospital/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba, Cordoba, Spain, Córdoba, Spain, [5]IMIBIC/University of Cordoba/Reina Sofia Hospital, Cordoba

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Antiphospholipid Syndrome
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: To identify shared and differential changes in the splicing machinery of immune cells from antiphospholipid syndrome (APS), systemic lupus erythematosus (SLE) and antiphospholipid syndrome with lupus (APS plus SLE) patients, and their involvement in the activity and clinical profile of these autoimmune disorders.

Methods: Monocytes, lymphocytes and neutrophils from 70 patients (14 APS, 36 SLE and 20 APS plus SLE) and 23 healthy donors (HD) were purified by immunomagnetic selection. Then, 45 selected elements of the splicing machinery were evaluated using a microfluidic qPCR array (Fluidigm). In parallel, extensive clinical/serological evaluation was performed, comprising renal, obstetric and cardiovascular (CV) involvement, along with autoantibodies and inflammatory molecules. Correlation/association studies and logistic models among those clinical and analytical parameters were developed. Mechanistic *in vitro* studies were performed by incubation of HD-leukocytes with purified

aPL-IgG or anti-dsDNA-IgG. Overexpression of selected components was further performed to evaluate their role in the leukocytes' activity.

Results: Compared with HD, 35, 31 and 14 splicing machinery components were differentially expressed in monocytes, lymphocytes and neutrophils, respectively, from SLE patients; 25, 17 and 21 on APS patients, and 18, 29 and 23 in APS plus SLE patients.

Although a number of spliceosome components were found commonly deranged in the leukocyte subsets of the three disorders, each disease displayed an specific alteration, further associated with distinctive clinical features. Hence, in APS, altered expression of PRPF8 was linked to heightened CV-risk factors (HTA and dyslipidemia), thrombotic recurrences, and the CV events number. In APS plus SLE patients, RNU4 and SF3B1 were associated to CV-related parameters (HTA, microvascular endothelial dysfunction and apoB/A ratio). Besides, levels of these spliceosome components correlated with those of several plasma inflammatory mediators.

Lastly, in SLE patients, levels of key splicing machinery components (RNU6, PRPF8, RAVER1 and TCERG1) were associated to positivity for anti-dsDNA, activity of the disease (SLEDAI), the inflammatory plasma profile, and enhanced CV-risk factors (carotid-intimae media thickness, endothelial dysfunction and atherogenic index), along with obstetric complications and nephropathy.

Finally, *in vitro* treatment of HD lymphocytes with aPL-IgG or anti-dsDNA-IgG changed specific spliceosome components found altered *in vivo* in the three autoimmune diseases. The overexpression of selected spliceosome components in leukocytes further modulated the expression of inflammatory cytokines.

Conclusion: 1) The splicing machinery is profoundly altered in leukocytes from APS, APS plus SLE and SLE patients, and closely related to the activity of these diseases, their autoimmune and inflammatory profiles. 2) The analysis of the splicing machinery allows the segregation of APS, APS plus SLE and SLE, with specific components explaining the CV risk and organ involvement in these highly related autoimmune diseases.

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Disclosure: A. Patiño-Trives, None; **A. Ibáñez-Costa**, None; **C. Pérez-Sánchez**, None; **L. Pérez-Sanchez**, None; **M. Luque-Tevar**, None; **I. Arias de la Rosa**, None; **M. Abalos-Aguilera**, None; **D. Ruiz-Vilchez**, None; **P. Segui**, None; **M. Espinosa**, None; **N. Barbarroja**, None; **E. Collantes**, Abbvie Inc, 5, 8, Amgen, 5, 8, Eli Lilly and Company, 5, 8, Janssen Pharmaceutical, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer Inc, 5, 8, UCB, 5, 8; **J. Castaño**, None; **R. M Luque**, None; **M. Aguirre-Zamorano**, None; **C. Lopez-Pedrera**, None.

Abstract Number: 1450

Integrative Analysis of DNA Methylation and Gene Expression in Monocytes from Primary Antiphospholipid Syndrome Patients Identifies a Gene Expression Signature Associated with Their Atherothrombotic Phenotype

Carlos Pérez-Sánchez[1], M Angeles Aguirre[2], Alejandra Maria Patiño-Trives[1], Laura Pérez-Sanchez[3], Maria Luque-Tevar[1], Iván Arias de la Rosa[1], María-Carmen Abalos-Aguilera[1], Pedro Segui[4], Javier Rodriguez-Ubreva[5], Esteban Ballestar[5], Nuria Barbarroja[1], Eduardo Collantes-Estévez[2] and Chary Lopez-Pedrera[1], [1]Rheumatology Department, Reina Sofia University Hospital/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba, Cordoba, Spain, Cordoba, Spain, [2]Rheumatology Department, Reina Sofia University Hospital/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba, Cordoba, Spain, Córdoba, Spain, [3]Hospital Universitario Reina Sofía, Córdoba, Spain, [4]IMIBIC/University of Cordoba/Reina Sofia Hospital, Cordoba, [5]Josep Carreras Institute (IJC), Badalona, Spain

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Antiphospholipid Syndrome

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: 1. To develop integrated analyses of the genome-wide DNA methylation and gene expression profiles in monocytes from APS patients and assess their involvement in cardiovascular pathology. 2. To evaluate the role of antiphospholipid antibodies (aPL) in the regulation of these processes.

Methods: Thirty-three APS patients were included in the study. Monocytes were isolated from peripheral blood by positive immunomagnetic selection. The Illumina Infinium Methylation EPIC Beadchip was used to obtain DNA methylation profiles across approximately 850,000 CpGs. Total RNA was processed for sequencing library preparation using 75bp paired-end NextGen sequencing (Illumina NextSeq 500 instrument). To examine the impact of DNA methylation on the local regulation of gene expression, the Pearson correlation (r) was calculated between the beta values (β) of CpGs located in promoter regions and the normalized expression values of the corresponding genes. Functional classification of these genes was carried out by gene ontology analysis. Gene expression of selected genes was evaluated by RT-PCR. CV-risk parameters were further assessed, and correlation/association studies were developed with clinical/analytical variables. The effects of aPLs were also evaluated by *in vitro* studies.

Results: Integrative analysis of DNA methylation and gene expression identified 4727 mRNAs whose expression was linked to methylation levels. Functional classification of these genes revealed signatures associated with biological processes and pathways related to immune response, adhesion, oxidative stress and vascular signaling. Thus, correlation and association studies showed that altered mRNA expression of several genes whose altered expression was linked to aberrant methylation levels were further related to the CV-risk score, -aGAPSS- (TGFB1, SERPINB6, NFKB1, SLC25A24, IFNAR2, CXCL8, SOD2), the vascular involvement -type of thrombosis and thrombotic recurrences- (IFI52, IL18BP, IL6R, ITGA5, SLC25A26, STAT5A) and the microvascular endothelial dysfunction (HLA-DPA1, SLS25A26,SLC25A45, SERPINB9). Abnormal methylation and transcription levels of several genes were further associated with a pathological increase of the CIMT.

Lastly, expression levels of several genes related to cytokine-mediated signaling pathway, oxidative stress and mitochondrial dysfunction (PLXND1, CXCR4, PDE4A, TNFRSF1A, IL17RA, MMP17, CXXC1, IL10RA, TNFRSF1B, SER-

PINB6, NFKB2, SFPQ, ILF3, STAT5A, JAK2) correlated with aPL titers. In vitro studies further supported the role of aPLs as key players in the altered methylation and transcriptomic profiles of APS patients.

Conclusion: APS patients showed coordinately impaired methylation and gene expression profiles in monocytes of genes associated with clinical features of the disease such as autoantibody titers, CV risk score -aGAPSS-, thrombotic recurrences and early atherosclerosis. These results offered a map to the monocytes methylome and their influence on gene expression, and shed light on the pathophysiology of APS, paving the way for the development of effective biomarkers and therapeutics.

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Disclosure: C. Pérez-Sánchez, None; **M. Aguirre**, None; **A. Patiño-Trives**, None; **L. Pérez-Sanchez**, None; **M. Luque-Tevar**, None; **I. Arias de la Rosa**, None; **M. Abalos-Aguilera**, None; **P. Segui**, None; **J. Rodriguez-Ubreva**, None; **E. Ballestar**, None; **N. Barbarroja**, None; **E. Collantes-Estévez**, None; **C. Lopez-Pedrera**, None.

Abstract Number: 1451

Longitudinal Assessment of Anti-beta 2 Glycoprotein in SLE

Michelle Petri[1], Laurence Magder[2] and Daniel Goldman[1], [1]Johns Hopkins University School of Medicine, Timonium, MD, [2]University of Maryland, Baltimore, Baltimore, MD

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Antiphospholipid Syndrome
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Although anti-beta2 glycoprotein is one of the three antiphospholipid antibodies recognized in the Sydney APS classification criteria, it is one of the least studied. Lupus anticoagulant, the antiphospholipid antibody most associated with both thrombosis and adverse pregnancy outcomes, can be divided into two subsets: those that target beta2 glycoprotein I and those that target prothrombin (Blood 1995;86:617-23). In SLE, lupus anticoagulant can fluctuate over time, making it difficult to define which patient is “persistently positive”. Fluctuation could reflect change in SLE activity, change in SLE treatement, or both. We looked at two definitions of “positive”: 20 (medium) as in the classification criteria; or 40 as part of “triple positivity”. We sought to address some of these questions in our prospective SLE cohort.

Methods: The SLE patients met revised ACR and/or SLICC classification criteria. Anti-beta 2 glycoprotein IgG, IgM, and IgA were measured by ELISA (INOVA) at 2,393 visits in 1,417 patients. The patients were 92% female, 50% Caucasian, and 40% African-American. Forty-three percent of the patients had more than 1 assessment (57% had 1, 26% had 2, 10% had 3, and 7% had 4 or more assessments).

Results: Anti-beta 2 glycoprotein IgG > 20 (medium positive) or > 40 (high positive) was more common in Caucasians than in African-Americans (p=0.0012, 0.0089) but IgA > 20 or > 40 was more common in African-Americans (p=NS). Table 1 shows that about 40-76% of the time a patient who was positive at the first check became negative at the second check (but the converse was not true: most patients initially negative remained negative). Table 2 shows the effect of testing over multiple visits. IgA remained the most frequent isotype. There was minimal incremental value in serial testing overall. Table 3 shows a multiple variable model for the isotype (IgG) most associated with thrombosis. IgG anti-beta 2 glycoprotein was clearly less frequent in African-Americans and was also clearly reduced in those tak-

Isotype/cutoff	Of those positive on first visit, proportion negative on second visit	Of those negative on first visit, proportion positive on the second visit
IgA>20	39/97 (40%)	11/407 (3%)
IgA>40	26/53 (49%)	8/451 (2%)
IgG>20	12/23 (52%)	7/481 (1%)
IgG>40	8/14 (57%)	5/490 (1%)
IgM>20	47/62 (76%)	5/442 (1%)
IgM>40	13/20 (65%)	6/484 (1%)

Proportion who changed status from first to second visit.

Isotype	Number of visits	Ever >20	Ever>40
IgA	1 (n=810)	144 (18%)	71 (9%)
	2 (n=371)	79 (21%)	47 (13%)
	3 (n=142)	37 (26%)	18 (13%)
	4+ (n=92)	12 (25%)	8 (9%)
IgG	1 (n=810)	46 (6%)	33 (4%)
	2 (n=371)	23 (6%)	18 (5%)
	3 (n=142)	8 (6%)	3 (2%)
	4+ (n=92)	6 (7%)	3 (3%)
IgM	1 (n=810)	107 (13%)	34 (4%)
	2 (n=371)	41 (11%)	15 (4%)
	3 (n=142)	20 (14%)	9 (6%)
	4+ (n=92)	18 (20%)	7 (8%)

Number (%) ever positive, by number of assessments.

ing hydroxychloroquine. There was borderline evidence, in contrast, that it might be reduced by immunosuppression

Predictor and comparison	Odds Ratio (95% CI)	P-value
Black (vs. White)	0.42 (0.24, 0.75)	0.0032
Other (vs. White)	0.86 (0.39, 1.92)	0.72
Plaquenil	0.62 (0.41, 0.93)	0.022
Aspirin	1.97 (1.31, 2.98)	0.0013
Anticoagulant	2.97 (1.77, 5.00)	<0.0001
Immunosuppressant	0.65 (0.41, 1.02)	0.060

Multivariate model for association between predictors and Anti-beta 2 IgG

treatment (p=0.06). A similar multivariate model of IgA anti-beta 2 glycoprotein showed that hydroxychloroquine also reduced IgA (OR 0.72, 95% CI 0.58, 0.90; p=0.004).

Conclusion: Anti-beta 2 glycoprotein IgG is more common in Caucasian than African-American SLE, but the opposite is true for the IgA isotype. As with other antiphospholipid antibodies in SLE, there is considerable fluctuation over visits, with 40-76% becoming negative at a second check. Hydroxychloroquine use reduced both the IgG and IgA isotypes, again reinforcing the benefit of hydroxychloroquine in thrombosis reduction. The IgA anti-beta 2 glycoprotein finding is particularly important, in that hydroxychloroquine did not reduce IgA anticardiolipin (Lupus Sci Med 2016;3:e000107).

Disclosure: M. Petri, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmithKline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5; **L. Magder**, None; **D. Goldman**, None.

Abstract Number: 1452

Transcriptomic Meta-analysis Reveals a Core Transcriptional Program in Murine B Cell Anergy and Implicates Immunometabolic Regulation as a Central Pathway in Maintaining Non-responsiveness of Autoreactive B-cells in Both Mouse and Man

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SESSION INFORMATION
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Session Title: B Cell Biology & Targets in Autoimmune & Inflammatory Disease
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Background/Purpose: The mechanisms self-tolerance loss that lead to autoantibody-mediated autoimmune disease remain underdefined. The rapid reversibility of peripheral B-cell tolerance in murine models suggests that non-durable biochemical mechanisms predominate to enforce this state, termed anergy. However, transcriptomic differences between anergic B-cells and their naïve non-anergic counterparts have also been described in murine models. Current understanding holds that B-cell anergy is maintained through chronic antigen receptor stimulation. This suggests that a core transcriptional program might extend across B-cell anergy in autoantigen systems of differing specificity. Here, we sought to understand whether such a core transcriptional program exists and performed initial functional characterization of one implicated pathway.

Methods: Data used in this analysis was from a combination of publicly available microarray/RNA-Seq data and a previously unpublished RNA-Seq experiment. All experimental conditions compared anergic B-cells to their naïve non-anergic counterparts. Data were analyzed using the NetworkAnalyst platform. Following normalization and batch effect correction, meta-analysis comparing anergic to naïve non-anergic B cells was carried out using Fisher's method with a threshold of $P < 1E-8$. Pathway analysis was performed using Enrichr. For confirmatory studies, murine splenocytes or human PBMC were stained with CD36 along with B-cell subpopulation markers. For functional experiments, Ramos cells were pre-treated with palmitoyl-carnitine and calcium flux was determined kinetically following B-cell receptor crosslinking.

Results: Meta-analysis revealed 185 differentially expressed genes with this stringent significance threshold between anergic and naïve non-anergic B cells. Pathway analysis indicated expected enrichment of antigen receptor signaling pathway gene expression in anergic B cells. Surprisingly, genes involved in several metabolic pathways were differentially expressed. Of these, *Cd36* stood out as one of the genes with lowest relative expression in anergic B-cells. We focused on its role as a key regulator of several metabolic pathways. Indeed, flow cytometry confirmed decreased CD36 protein expression on anergic B cells in comparison to their naïve non-anergic counterparts within the wild type repertoire. Similar decreases were observed in BCR-transgenic mouse models of anergy and the peripheral

blood anergic human B-cell compartment. Ramos cells pre-treated with palmitoyl-carnitine, a metabolic intermediate downstream of CD36 exhibited dose-dependent suppression of calcium influx upon BCR-crosslinking.

Conclusion: Taken together, our results define a core transcriptional program of murine B-cell anergy and highlight metabolic pathways in the maintenance of tolerance in autoreactive B-cells. These findings are likely to inform our understanding of the long-term effects of therapies targeting metabolic pathways on the maintenance of tolerance in autoreactive B-cells. Further defining these mechanisms will nominate novel potential therapeutic approaches for autoimmune diseases.

Disclosure: I. Harley, None; **B. Crute**, None; **A. Getahun**, Helsinn Therapeutics, 3; **J. Cambier**, None.

Abstract Number: 1453

A First in Class Therapeutic Nanoparticle for Specific Targeting of Anti-citrullinated Protein Antibody Ameliorates Serum Transfer and Collagen Induced Arthritis

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Background/Purpose: Rheumatoid arthritis (RA) is an immune mediated inflammatory disease with autoimmune features, including antibodies to citrullinated proteins and peptides (ACPAs). Several in vitro studies have suggested a pathogenic role of ACPAs in RA. However, in vivo proof of this concept has been hampered by the lack of therapeutic strategies to reduce or deplete ACPA in serum and synovial fluid. Previously, we constructed a chitosan-hyaluronic acid nanoparticle formulation with the ability to use neutrophil recruitment as a delivery mechanism to inflamed joints.[1] We hypothesized that reducing ACPA levels would have a therapeutic effect by blocking cytokine production. In this study, we prepared and tested a series of therapeutic nanoparticles for specific targeting of ACPA in synovial fluid.

Methods: Nanoparticles were prepared by the microdroplet method and then decorated with synthetic cyclic citrullinated peptide aptamer PEP2, PEG/hexanoic acid and fluorophore (Cy5.5). Nanoparticles were characterized by dynamic light scattering (DLS), scanning electron microscopy (SEM) and high-performance liquid chromatography (HPLC). Nanoparticles were then used in a series of in vitro assays, including cell uptake with flow cytometry (FACS) detection, and in vivo studies including disease activity scores, cytokine measurements and near-infrared imaging.

Results: We screened a series of citrullinated peptide epitopes and identified a fibrinogen-derived 21-amino-acid-long citrullinated peptide showing high selectivity toward autoantibodies in RA samples. We incorporated this aptamer in the chitosan-hyaluronic acid nanoparticle formulation previously described. Average nanoparticle size was 230 nm ± 10 nm by DLS and SEM; z potential was -0.0012. Attachment efficiency of aptamer was 92% by HPLC. FACS study showed selective uptake of Cy5.5 labelled aptamer-nanoparticle conjugates by neutrophils in the concentration range 0.5 nM-4 nM. In vitro, the aptamer-nanoparticles dramatically decreased Ly6C expression in mouse

bone marrow cells analyzed by FACS. In vivo, over 50% reduction of disease activity was achieved in three weeks treatment using as little as 1 nM drug candidate (dosed every 48 hours) in the collagen-induced (CIA) mouse model of RA (N=30; $p< 0.001$ for treated vs placebo). The aptamer-nanoparticle conjugate, significantly reduced IL-6 and TNFα levels in the mouse sera ($p< 0.01$). Importantly, this effect was confirmed in the serum transfer arthritis model (N=10). The effects was not inferior compared with tocilizumab treated controls (N=30). To confirm mode of action, we applied Cy5.5-labelled aptamer-nanoparticles in the collagen induced mouse model (N=10), and analyzed the resulting uptake by near-infrared imaging. We confirmed over 6-fold higher accumulation of the signal in inflamed vs healthy joints ($p< 0.01$), which strongly supports the fact that the aptamer is highly specific to the inflammatory process.

Conclusion: Overall, we have designed a first in class therapeutic nanoparticle drug for specific targeting of anti-citrullinated protein antibodies. The marked effect of this nanoparticle observed in vivo holds promise for targeting ACPAs as a therapeutic option in RA.

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Abstract Number: 1454

B Cell-specific TLR7 Regulates Lupus in TLR9 Deficient Mice

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Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease that results in significant morbidity and mortality. In SLE, endosomal TLR7 and TLR9 are known to mediate the anti-self response. We found that TLR9 deletion in the MRL.Fas^{lpr} model of SLE exacerbates disease, despite the requirement of TLR9 for the formation of anti-DNA antibodies. This is dependent on TLR7, suggesting that TLR9 is protective while TLR7 drives pathology. Recently, we found that TLR9 mediates protection specifically in B cells; however, it is unknown whether TLR9 regulates TLR7 in the same cell (*cis*) or in different cells (*trans*). For example, while TLR9 regulates disease in B cells, TLR7 may exacerbate disease in DCs. Thus, a major goal of our lab is to understand the B cell-specific role of TLR7 to inform the development of targeted therapeutics for SLE.

Methods: The MRL.*Fas*^{lpr} model replicates many features of human SLE including ANA production, dermatitis, and renal disease starting from 9-11 weeks of age. MRL.*Fas*^{lpr} mice were generated with a B cell specific deletion of TLR7 (CD19-Cre TLR7$^{fl/fl}$) and compared to Cre- littermates. Deletion was assessed via cell sorting and qPCR of genomic DNA. Lupus pathology was analyzed in female and male mice at 19 and 22 weeks of age, respectively, with parameters including proteinuria, renal histology for interstitial and histologic disease, dermatitis, organ weight, and immune cell activation. CD19-Cre TLR7$^{fl/fl}$ mice were also crossed to TLR9$^{-/-}$MRL.*Fas*^{lpr} mice and analyzed at 16 and 19 weeks of age for females and males, respectively, to study B-cell intrinsic interactions between TLR7 and TLR9.

Results: Validation via qPCR showed specific but incomplete deletion of TLR7, with a 78.60% deletion efficiency in B cells, which was further reduced in plasmablasts. CD19-Cre TLR7$^{fl/fl}$ mice had reduced proteinuria but no analogous

decrease in kidney pathology or other disease parameters. Given the interaction between TLR9 and TLR7, and that TLR9 deficiency accelerates disease, we then studied the effects of B cell-specific TLR7 deficiency in TLR9$^{-/-}$ mice. The CD19-Cre TLR7$^{fl/fl}$ TLR9$^{-/-}$ mice exhibited reduced spleen weights (p=0.002) and an increased proportion of splenic naïve CD4+ T cells. More importantly, they exhibited a significant reduction in proteinuria (p=0.005), glomerulonephritis (p=0.0001), and interstitial nephritis (p=0.0002).

Conclusion: The inefficient deletion of TLR7 suggests that activated, "escapee" B cells could preferentially expand and explain the lack of disease regulation in the CD19-Cre TLR7$^{fl/fl}$ cohort. Conversely, a lack of regulation by TLR9 could allow B-cell specific TLR7 to exacerbate disease to an even greater degree than it could when TLR9 is present. This is suggested by the CD19-Cre TLR7$^{fl/fl}$ TLR9$^{-/-}$ cohort which shows a marked reduction in TLR9-driven lupus exacerbation when TLR7 is deleted in B cells. This supports the hypothesis that TLR9 regulation acts in *cis*, and that B cell specific TLR signaling is a major mediator of SLE. Ongoing studies will continue to address the cell specific roles of TLR7 via a mixed bone marrow chimera and DC specific deletion. Overall, these results indicate that targeting TLRs in B cells could be a viable therapeutic strategy in SLE.

Disclosure: H. Baxendell, None; **M. Kim**, None; **J. Tilstra**, None; **M. Shlomchik**, None.

Abstract Number: 1455

Functional Characterization of *PLCG2* Mutations Found in Subjects with Autoinflammation and *PLCG2*-Associated Antibody Deficiency and Immune Dysregulation (APLAID) Reveals Both Hypermorphic and Hypomorphic Mutants

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Background/Purpose: *PLCG2*-associated antibody deficiency and immune dysregulation (PLAID) and autoinflammatory PLAID (APLAID) are autosomal dominant diseases caused by mutations of *PLCG2.* APLAID is clinically characterized by episodic fever, severe interstitial lung disease (ILD), antibody deficiency and inflammation of the eyes, skin and gut. To date, 3 mutations have been reported to cause APLAID (S707Y, L848P, M1141K), each leading to increased PLCg2-dependent signaling following stimulation. Since our initial descriptions of PLAID/APLAID, we have received >100 referrals of patients with severe forms of immune dysregulation and mutations in *PLCG2*. Here, we leverage this cohort to expand our understanding of *PLCG2* variants that cause autoinflammatory phenotypes.

Methods: Subjects with immune dysregulation and mutations in *PLCG2* were referred to our group for evaluation; those with autoinflammatory features (episodic fever or ILD) were identified and their mutations were investigated. Characteristics of *PLCG2* variants, including allele frequencies, metrics of evolutionary conservation and predicted functional consequences, were assessed using Annovar. Mutant forms of *PLCG2* were generated for *in vitro* studies by site-directed mutagenesis of a GFP-tagged PLCg2 construct. Constructs were overexpressed in *Plcg2*-deficient DT40 B cells. Cells were assayed for BCR-induced calcium flux and ERK phosphorylation. Cells were stained with

the calcium-binding fluorophore, Indo-1, and intracellular calcium levels were observed by flow cytometry at baseline and following BCR cross-linking with anti-IgM antibody. Similarly, ERK phosphorylation was measured by flow cytometry before and after BCR-stimulation.

Results: We identified 16 subjects with autoinflammatory features bearing 16 ultra-rare/novel missense mutations of *PLCG2.* The most common autoinflammatory features were episodic fever (81%), cutaneous inflammation, including blistering, granulomatous or nodular skin lesions (63%) and ILD (38%). Arthritis and gastrointestinal inflammation were each present in 25% of patients, while half of patients had antibody deficiency. All mutations were located at evolutionarily conserved residues, each was predicted to alter protein function and 14 were previously unreported. Overexpression studies identified 3 groups of variants that produced distinct responses to BCR cross-linking: 1) 5 variants whose response was indistinguishable from wild type *PLCG2;* 2) 5 variants with hypermorphic responses consistent with S707Y; and 3) 6 variants with hypomorphic responses, 1 of which was amorphic. In all, we identified signaling alterations in 11/16 *PLCG2* mutations found in these patients.

Conclusion: This study describes 14 new mutations of *PLCG2* found in 16 APLAID patients with clinical features consistent with published cases. A third of the mutations produced a typical hypermorphic pattern in our *in vitro* system of B cell activation, but surprisingly, another third of variants reproducibly produced hypomorphic or amorphic responses. Future investigations should focus on the interrogation of primary patient cells and specific examination of differential effects in different *PLCG2*-expressing cells.

Disclosure: K. Baysac, None; **C. Fisher**, None; **H. Nakano**, None; **J. Milner**, None; **M. Ombrello**, None.

Abstract Number: 1456

Exploring the RA Bone Marrow Niche by Single-cell Technology to Identify Long Lived ACPA+ Plasma Cells

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Background/Purpose: Autoantibodies is a hallmark of rheumatoid arthritis, placing the adaptive immune system and B-cells centrally in the pathogenesis. The anti-citrullinated autoantibodies (ACPA) detected in the serum can be produced either by circulating plasma blasts, locally residing plasma cells the joint, or long-lived plasma cells in the bone marrow (BM). Here we use different single cell methods to investigate the bone marrow niche.

Methods: Bone marrow samples from proximal femur in RA patients undergoing hip joint replacement was processed to isolate mononuclear cells. In total four CCP2+ and one CCP2- RA patients were investigated. All patients were HLA shared epitope positive. Firstly, CD138+ plasma cells were single cell sorted by flow cytometry followed by BCR sequencing. For two of the RA patients, MACS enriched BM B cell and peripheral B cells were further investigated by 10X Genomics Chromium methodology for single-cell RNAseq profiling and immunoglobulin sequencing.

Selected paired heavy-light Ig-chains with N-glycosylation sites and high somatic hypermutation level were subsequently expressed as recombinant IgG and investigated for citrulline reactivity using an autoantigen array.

Results: For the single-cell sorted CD138+ cells, in total 509 complete IgG+ BCR sequences were generated and 44 monoclonal IgG were expressed (36 from CCP+ RA). Among the mAbs, two clones from two different patients were identified as CCP2+. One of these originated from an IgG4+ plasma cell and had strong reactivity and multi-specificity for different cit-peptides (e.g. cit-fibrinogen, cit-tenascin C, cit-hnRNP derived). 10X cell capture of 8391 BM B-cells from the same patient, generated 856 Ig with a RNAseq plasma cell profile (i.e. CD27+ XBP1+ MZB+ DERL3+ JCHAIN+ SSR4+) from 832 unique clones defined by paired HCDR3-LCDR3, occurring 1-6 times. Five 10X clones whereof two in plasma cell clusters were overlapping with the single cell sort (N=92). We observed a high frequency of both Fab glycosylation (31% of IgG+ plasma cells) and IgG4+ cells (6% of IgG+ plasma cells). Notably, also IgA+ plasma cells could be identified (37% IgA1+ 3% IgA2+). In comparison, by 10X, 24% BM IgG+ plasma cells from the CCP2- patient had Fab N-glyc sites and no IgG4+ were detected. We found no direct BCR overlap with the BM plasma cells in investigated paired peripheral B cells.

Conclusion: ACPA+ long lived plasma cells can be found in the bone marrow niche and BM-derived ACPA display multi-reactivity profiles as also seen in synovial ACPA+ plasma cells [1-2]. However, they may be relatively rare and no large clonal expansions were found. In the bone marrow, similar to blood, B-cell repertoire skewing with increased N-glycosylation and IgG4 frequencies can be observed.

References

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[2] Sahlström, P., et al. Different hierarchies of anti-modified protein autoantibody reactivities in rheumatoid arthritis. Arthritis Rheumatol. 2020

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Abstract Number: 1457

Two Minute Walking Distance and Other Timed Function Tests Are Superior to MMT-8 in Assessing Outcomes in Polymyositis and Dermatomyositis

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Background/Purpose: Inflammatory myositis are heterogenous group of diseases affecting skeletal muscles and multiple different organs. Assessing improvement in disease activity is done by Manual muscle testing (MMT) and Functional index 2(FI-2). These are time taking and need expertise to administer. Several Timed function tests (TFTs) like the 2- minute walk test (2MWT) or 30s raise from a chair test and 30s 1kg arm rise test may be better alternatives and less time taking. Moreover these tests can be self-administered by patients themselves. In the current world of accountability for treatment response and improvement in technology, these TFTs upon self-administration in particular time intervals have the potential to provide objective data on diseases status enabling the physician to make therapeutic decisions. We undertook a study with objective to evaluate the performance of TFT in assessing muscle diseases at baseline and to evaluate the performance of TFTs to detect change in muscle power and endurance with treatment.

Methods: This is an observational cohort study which included 29 patients with polymyositis and dermatomyositis satisfying ENMC classification criteria. Patients with inclusion body myositis, overlap myositis, chronic kidney disease, coexisting myocarditis, sepsis, malignancy, pregnancy were excluded. MMT8, FI-, EQ-5D and Timed function tests were done at baseline and after 3 months.

Results: The study had 29 patients of which 6 were polymyositis and 23 were dermatomyositis. Male to female ratio was 1:2.1. Anti-cell antibody was positive in 20 patients. Out of 29 patients, 11 had active disease and rest 18 had stable disease. Mean scores of MMT8, Fi-2 and TFTs are shown in table 1. The 3 TFTs had moderate to high correlation with MMT8 and FI-2 at baseline in inactive disease group but only with FI-2 in active disease as shown in Table 2. At 3 months, change in all 3 TFTs significantly correlated with change in Fi-2 in active disease, but in stable disease only 2MWD had moderate correlation with MMT8. (Table 3)

Conclusion: 2 Minute walk distance is a better alternative to the conventional muscle testing as it measures both power and endurance. This score can overcome the ceiling effect of MMT-8. Besides, owing to the ease of administration 2MWD may be used as a patient reported outcome measure in IIM.

Disclosure: S. Dunga, None; **C. Kavadichanda**, None; **V. Negi**, None.

Abstract Number: 1458

Slower Current Walking Speed Is Associated with Progression in Radiographic Knee Osteoarthritis: The Johnston County Osteoarthritis Project

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Background/Purpose: Poorer physical functioning as a single baseline measurement has been associated with increased risk of radiographic knee osteoarthritis (rKOA) progression, but it is unknown whether reduced physical functioning as well as its change over time is associated with rKOA progression. Slower walking speed, suggestive of

decreased physical functioning, or reductions in walking speed may be an early indicator of worsening osteoarthritis or contribute to underlying disease advancement.

Methods: We analyzed Johnston County Osteoarthritis Project data from baseline (1999-2004) and up to three follow up visits (2006-2010; 2013-2015; 2017-2018). Walking time was evaluated over an 8-foot walk distance in two trials; walking speed was calculated as the average of the trials and log-transformed. Progression of rKOA was defined as an increase of one Kellgren-Lawrence (K-L) grade or more in at least one knee between two visits. A joint statistical model (JM), incorporating a linear mixed effects model for repeated walking speed measures and a Cox proportional hazards model for time-to-event outcome of K-L grade increase, was used to evaluate the association between longitudinal walking speed measures and rKOA progression. Two separate JMs were run evaluating 1) change in walking speed (slope) over time (model 1) and 2) current walking speed adjusting for the slope (model 2) on risk of K-L grade increase. Both models were adjusted for sex, race, education, BMI and age at baseline.

Results: Our final sample consisted of 1,606 participants with at least one measurement of walking speed and a minimum of two visits with knee radiographs (average follow-up time was 8 ± 3 years). At baseline, mean age was 62 ± 9 years, over two-thirds of participants were women (67%), and mean walking speed was 3.5 ± 1.8 seconds per 8-foot walk distance. During follow-up, 1,077 (67%) participants had rKOA progression in at least one knee. Application of JM demonstrated model 2 incorporating both the current level and slope of walking speed had the best model fit (model 1 Bayesian Information Criterion [BIC] 6767 vs. model 2 BIC 5661). In model 2, slower current walking speed but not slope was associated with rKOA progression adjusted for sex, race, education, BMI and age at baseline. Specifically, a 50% slower walking speed was associated with 2-fold higher risk for progression (hazard ratio [HR] = 1.99; 95% CI, 1.08-3.67).

Conclusion: rKOA progression is associated with an individual's current level of walking speed and not on the reduction in walking speed over time. Treatment and interventions for individuals with knee OA aimed at improving physical function may help maintain or increase walking speed and slow rKOA progression regardless of the rate of decline.

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The Association of Frequent Knee Bending with Trajectories of Pain and Physical Function over 8 Years in Knee Osteoarthritis

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Background/Purpose: Frequent bending increases loading at the knee and is a risk factor for worsening knee pain associated with knee osteoarthritis (OA). Knee bending is also common during activities of daily living, such as climbing stairs, and beneficial for lower extremity strength. Presently, it is unclear if frequent knee bending is helpful or harmful for trajectories of pain and function, thus understanding this association is important to help weigh its costs

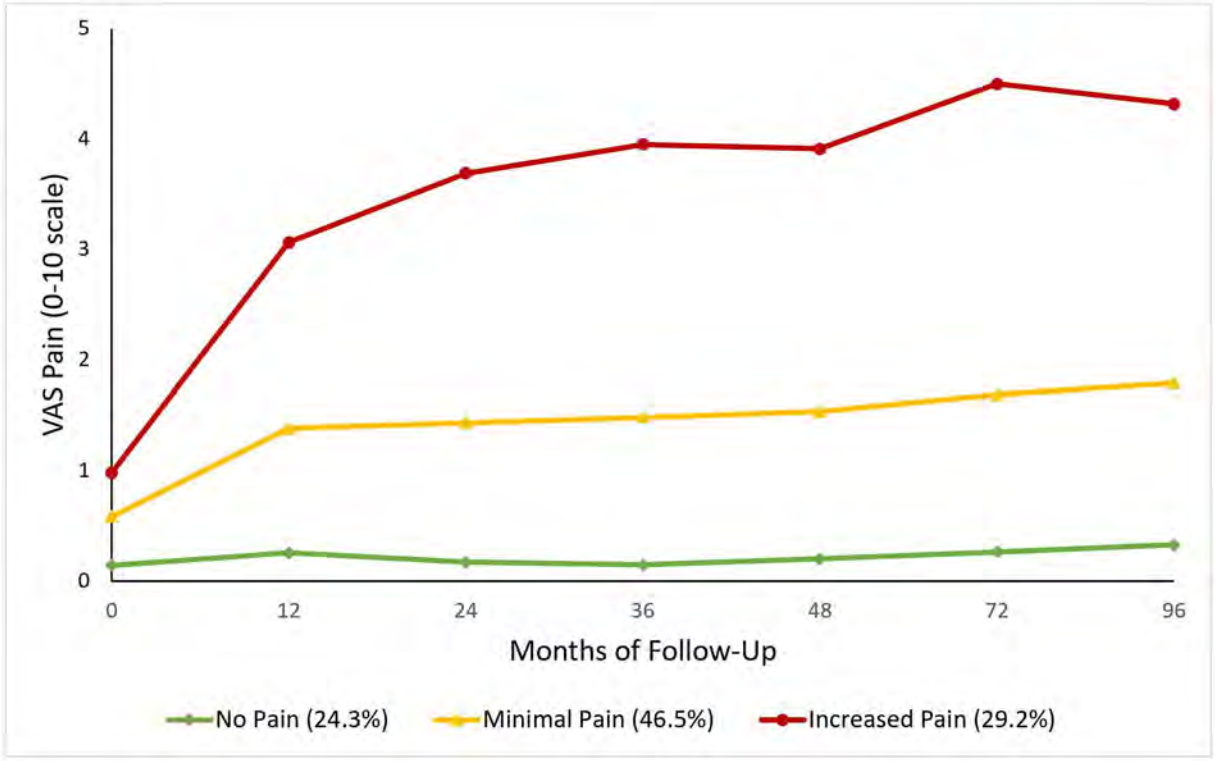

Figure 1. Trajectories of VAS pain over 96 months of follow-up

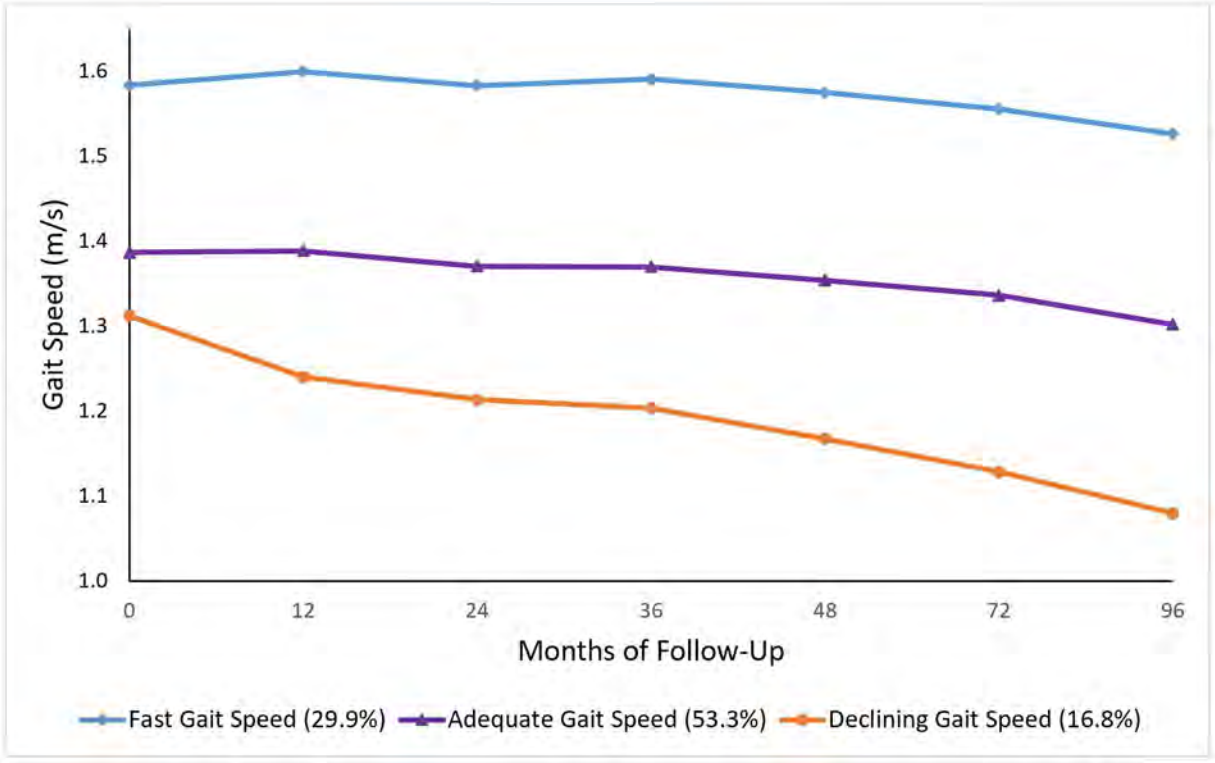

Figure 2. Trajectories of gait speed over 96 months of follow-up

		No Stair Use			No Lifting	
	% no stairs	*Unadjusted*	*Adjusted^*	*% no lifting*	*Unadjusted*	*Adjusted^*
Minimal Pain	141/387 (36.4%)	REF	REF	105/387 (27.1%)	REF	REF
Low Pain	269/737 (36.5%)	1.00 (0.78, 1.30)	0.96 (0.74, 1.25)	185/735 (25.2%)	0.90 (0.68, 1.19)	0.84 (0.62, 1.13)
Worsening Pain	170/450 (37.8%)	1.06 (0.80, 1.40)	0.97 (0.72, 1.29)	126/449 (28.1%)	1.05 (0.77, 1.42)	1.04 (0.75, 1.45)
		No Stair Use			**No Lifting**	
	% no stairs	*Unadjusted*	*Adjusted^*	*% no lifting*	*Unadjusted*	*Adjusted^*
No Decline	231/790 (29.2%)	REF	REF	132/789 (16.7%)	REF	REF
Minimal Decline	502/1437 (34.9%)	**1.30 (1.08, 1.57)**	1.14 (0.94, 1.40)	370/1436 (25.8%)	**1.73 (1.39, 2.16)**	**1.49 (1.18, 1.89)**
Fast Decline	181/440 (41.1%)	**1.69 (1.33, 2.16)**	**1.40 (1.06, 1.84)**	134/439 (30.5%)	**2.19 (1.66, 2.88)**	**1.61 (1.17, 2.21)**

^adjusted for BL age, sex, BMI, presence of comorbidity, and Physical Activity Scale for the Elderly (PASE) score

Table 1. Odds ratios and 95% confidence intervals for the association between frequent knee bending and pain and gait speed trajectory group membership

and benefits. Therefore, the purpose of this study was to investigate the association of knee bending and 8-year trajectories of pain and function in adults with or at risk for knee OA.

Methods: We used data from the Osteoarthritis Initiative, a prospective cohort study of adults with or at risk for knee OA. Knee bending activities over the previous 30 days were collected at baseline (BL) via two yes/no questions: (1) climbing up 10+ flights of stairs in 1 day (stair use) and (2) lifting/moving objects weighing 25+ lbs by hand in 1 day (lifting). Pain and function were assessed at BL and six follow-up (FU) visits (1, 2, 3, 4, 6, 8 years). Knee pain severity in the past 30 days was determined via a Visual Analogue Scale (VAS; 0-10). Function was assessed using self-selected gait speed over 20m. Samples were restricted to those with low pain (< 3/10) or good function (≥ 1.22m/s) at BL and trajectories were identified using group-based modeling. To determine the association between each knee bending activity and group membership for pain and function trajectories, we calculated odds ratios (OR) and 95% confidence intervals (95% CI) using multinomial logistic regression, adjusted for confounders.

Results: Of those with complete data at BL and at least 2 FU visits, two separate trajectory models were run for both pain (age: 61.9 ± 9.0 years, sex: 56.7% female, BMI: 27.7 ± 4.6 kg/m^2) and function (age: 60.1 ± 8.8 years, sex: 54.7% female, BMI: 27.8 ± 4.5 kg/m^2). We identified 3 pain trajectory groups: Minimal Pain, Low Pain, and Worsening Pain. The Worsening Pain trajectory group exceeded the Patient Acceptable Symptom State (> 3/10) by 24 months, while the other trajectories remained at 0 or 1 (Figure 1). However, no associations were found between knee bending activities and pain trajectory group membership. We identified 3 function trajectory groups: No Decline, Minimal Decline, and Fast Decline. The Fast Decline trajectory dropped below 1.22 m/s by 24 months, while the other trajectories remained above this cutoff with little decline over 8 years (Figure 2). Those who reported no stair use had 40% [1.40 (1.06, 1.84)] greater odds of being in the Fast Decline group relative to those who reported stair use. Those who reported no lifting had 49% [1.49 (1.18, 1.89)] and 61% [1.61 (1.17, 2.21)] greater odds of being in the No or Minimal Decline groups, respectively, relative to those who reported lifting.

Conclusion: Adults who did not engage in knee bending activities at BL had greater odds of membership in the slowest gait speed trajectory group, relative to those who did. Additionally, knee bending was not associated with any of the pain trajectories. This indicates that stair use and lifting may be unrelated to pain and favorably associated with gait speed trajectories in adults with or at risk for knee OA.

Disclosure: J. Jakiela, None; **D. Voinier**, None; **T. Bye**, None; **M. Tukis**, None; **K. Konyak**, None; **D. Orloff**, None; **D. White**, None.

Abstract Number: 1460

"Can I Help You with Your RA Today?": A Pilot Study on the User Experience with a Voice-Enabled Smartphone App to Virtually Monitor Disease Activity and Collect ePROs in Rheumatoid Arthritis

Meredith Murray[1], Stephen Penney[2], Adam Landman[3], Josephine Elias[2], Emma Richard[4], Bert Hartog[4] and Daniel H. Solomon[5], [1]Brigham and Women's Hospital, Medfield, MA, [2]Partners Healthcare, Boston, MA, [3]Brigham and Women's Hospital, Boston, MA, [4]Janssen Research & Development, LLC, Boston, MA, [5]Brigham & Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Clinical Practice II
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Rheumatoid Arthritis (RA) is a chronic disease that involves frequent patient-provider interaction and self-monitoring, both integral to successful disease management. We developed a novel mobile health smartphone app with a voice-enabled feature to help patients virtually track disease activity and ask general questions about RA. A user-centered design-based approach was used to develop and test the app. This abstract will present information from several phases of development and sources of information including: exit interviews from the previous (V1.0) trial, focus groups, adherence with a revised app (V2.0), outcome data (V2.0), and satisfaction surveys (V2.0).

Methods: We recruited patients with RA who participated in a prior trial of the same app (V1.0). They were asked to help design and test V2.0. We conducted exit interviews from the prior trial and used these results to develop a new prototype of V2.0 that included voice enablement and a question & answer (Q&A) function. The prototype was tested in two focus groups of patients (N=8) and one with providers (N=4). Based on focus group feedback, the V2.0 app was built and given to 26 patients to test for 60 days. The V2.0 app asks patients to fill in patient reported outcomes

Figure 1. Overall adherence during a 4-week period with daily PRO surveys on disease activity, mood, fatigue, sleep, function and pain.

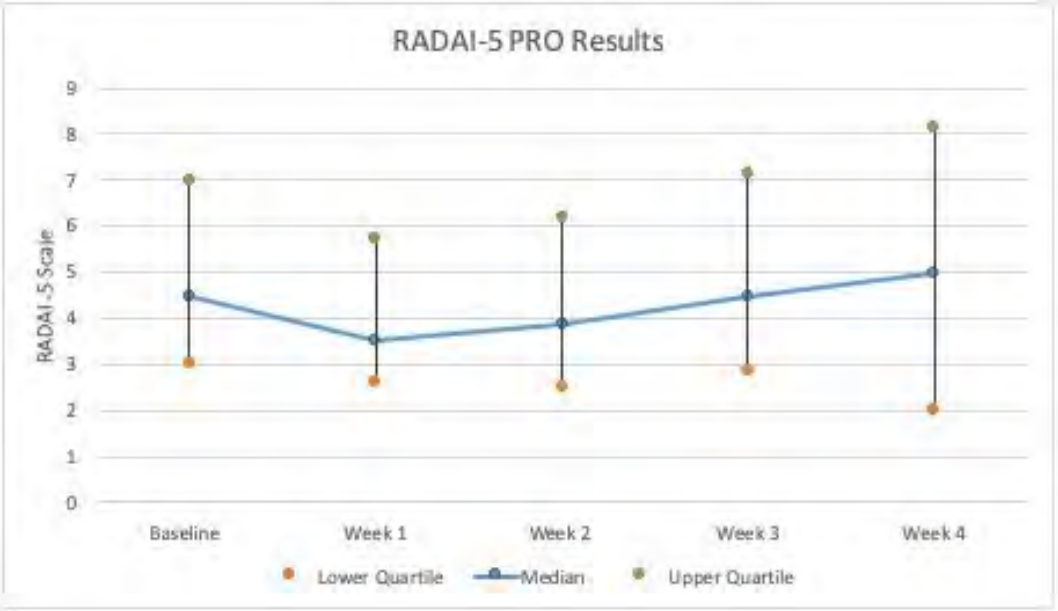

Figure 2. Results from the RADAI-5 PRO surveys, disseminated twice weekly, over a 4-week period with median values and interquartile ranges.

Patient Satisfaction	N, (%)
Overall Experience with App	
Very satisfied	7 (35)
Satisfied	10 (50)
Neither satisfied or dissatisfied	3 (15)
Dissatisfied	0 (0)
Experience Filling Out Surveys	
Very satisfied	10 (50)
Satisfied	9 (45)
Neither satisfied or dissatisfied	1 (5)
Dissatisfied	0 (0)
Experience Filling Out Surveys with Voice Assistant	
Very satisfied	3 (15)
Satisfied	3 (15)
Neither satisfied or dissatisfied	9 (45)
Dissatisfied	5 (25)
Patient Perception of Most Used Survey Method	
Voice more often	0 (0)
Touch more often	20 (100)
Not sure	0 (0)
Experience Using Voice Assistant For Q&A	
Very satisfied	3 (15)
Satisfied	3 (15)
Neither satisfied or dissatisfied	11 (55)
Dissatisfied	3 (15)

Table Patient satisfaction survey results after a 60-day trial testing the V2.0 app (N=20).

(PROs) daily; PROs rotate between disease activity, mood, fatigue, sleep, function and pain. After the trial, subjects completed satisfaction surveys to provide feedback on their experience. Adherence to PROs was defined as questions answered over total daily app questions.

Results: The exit interviews with V1.0 trial participants revealed several priorities for V2.0 including voice enablement and Q&A function. Focus groups showed the majority of participants found these functions helpful and also helped refine the Q&A library. These RA patients made suggestions regarding diction, speed and options embedded within the voice assistant. The 26 V2.0 trial patients were 77% female and 35% were aged 45-54 years. Interim analyses of adherence to daily PROs during the first 28-day period was 58% (95% CI ± 4.2) (Figure 1). Less than 1% of PROs were completed with the voice-enabled feature. Disease activity, measured twice weekly by the RADAI-5, was stable over four weeks, remaining within the moderate disease activity range (3.2 to 5.4) (Figure 2). Of the 20 patients who completed a satisfaction survey after a full 60-day trial, 85% of subjects were satisfied with their experience (Table). It appeared that only half of the patients had used the voice assistant; not all were satisfied with the voice assistant. The voice assistant had an overall 49% success rate at understanding and answering a user's request. Most questions focused on simple medication issues (dosage, interactions, time of day, etc).

Conclusion: We developed a novel mobile health PRO app (V2.0) with a voice assistant employing a user-centered design and conducted preliminary user testing. While adherence was moderate and disease activity was reported as stable, the voice assistant was not tried by all patients limiting feedback. While the Q&A library was widely used, not all patient questions could be answered and some participants were dissatisfied. Exit interviews will further examine patient experience to plan for the next iteration.

Disclosure: M. Murray, None; **S. Penney**, None; **A. Landman**, None; **J. Elias**, None; **E. Richard**, Johnson & Johnson, 3; **B. Hartog**, Janssen Pharmaceutica N.V., 1, 3; **D. Solomon**, Abbvie, 2, Amgen, 2, Genentech, 2, Janssen, 2, Corrona, 2, UpToDate, 7.

Abstract Number: 1461

Implementation, Feasibility and Acceptability of *Take Charge*, an Email Series to Increase Knowledge of Lupus Self-Management Skills

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Clinical Practice II
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: The Lupus Foundation of America developed and launched an educational email series, *Take Charge,* to provide people with lupus educational information, tools and resources on lupus self-management skills to increase knowledge of self-management skills, particularly in newly diagnosed individuals (diagnosis within past 12 months). Topics include: managing day-to-day challenges, explaining lupus to others, building social support, identifying and tracking lupus symptoms, preparing questions for medical appointments, and managing medications. Related skills are: increased self-awareness, communication and coping skills, and symptom and medication management. This abstract describes initial implementation and assessment of feasibility and acceptability of *Take Charge* measured through email campaign analytics and a post-series survey.

Self-Management Skill	Diagnosed within the past 12 months (n=107)	Diagnosed more than 1 year ago (n=347)
Developed my own coping strategy	40.2% (43)	38.0% (132)
Made an elevator speech to explain what lupus is to others	29.9% (32)*	17.6% (61)
Started building a social support network or logged into LupusConnect	28.0% (30)*	13.3% (46)
Identified and tracked my symptoms	59.8% (64)*	43.8% (152)
Got some questions ready for the next appointment with my doctor	62.6% (67)*	49.9% (173)
Started to track my medications or other treatments	32.7% (35)	23.3% (81)
None of the above	5.6% (6)	10.4% (36)

Table 1. Self-management skills reportedly tried, by diagnosis status; *indicates $p<0.05$

Methods: 8 total messages were distributed weekly to self-subscribed participants through an online communications platform, Luminate Online. 6 of the 8 messages focus on self-management topics and present additional resources, including worksheets and trackers, to further develop skills. The series ends with a 9-question post-series survey programmed in Qualtrics and summary of additional lupus resources. Participants reported time of lupus diagnosis and all self-management skills tried through multiple choice, and rated how interesting and helpful the series was on a scale of 1-10, with 10 being the most interesting and helpful. Open-text responses elicited feedback on likes/dislikes of the series and topics for future inclusion. Cross-tabulation analysis was conducted in Qualtrics.

Results: Nearly 6,500 individuals subscribed to *Take Charge*, with 45,792 emails sent at an average email open rate of 44.5% and click-through rate to provided resources of 11.8%. 494 participants completed the post-series survey, with 22% (n=107) reporting being newly diagnosed in the past 12 months, 70% (n=347) diagnosed more than 1 year ago, and the remaining were not yet diagnosed, indirectly connected or not connected to lupus at all. Top reported skills tried after series participation were preparing questions for medical appointments (55%, n=268), identifying and tracking symptoms (48%, n=238), and developing a coping strategy (39%, n=190). Newly diagnosed individuals were significantly more likely ($p< 0.05$) to report preparing questions for appointments, identifying and tracking symptoms, building a social support network, and making an elevator speech on lupus compared to those diagnosed more than 1 year ago (**Table 1**). Participants rated the series an average of 7.83 for interesting content and 7.96 for helpfulness. Lifestyle topics, such as diet and exercise, were highly recommended.

Conclusion: *Take Charge* is feasible to distribute through email communication platforms such as Luminate Online, with open and click-through rates higher than industry standards. *Take Charge* appears acceptable in interest, helpfulness, and delivering actionable self-management skills to newly diagnosed individuals with lupus. Future updates should include additional topics and updated evaluation tools to measure changes in knowledge, such as pre-post testing.

Disclosure: K. Tse, Lupus Foundation of America, 3; **M. Crimmings**, Lupus Foundation of America, 3; **M. Donnelly**, Lupus Foundation of America, 3; **R. Dossinger**, Lupus Foundation of America, 3; **L. Metelski**, Lupus Foundation of America, 3; **L. Boyce**, Lupus Foundation of America, 3.

Abstract Number: 1462

Intensity and Duration of Silica Exposure Increase Rheumatoid Arthritis Risk Among Coal Miners

Laura Trupin[1], Gabriela Schmajuk[2], Edward Yelin[1] and Paul Blanc[1], [1]UCSF, San Francisco, CA, [2]University of California, San Francisco, Atherton, CA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health I: RA
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Exposure to inhaled mineral dust, particularly silica, has been associated with increased risk of rheumatoid arthritis and other autoimmune diseases. Coal mining, which can involve substantial silica exposure, was strongly linked to risk of RA in our initial survey in the Appalachian region of the U.S.[1] Using additional survey data, we further analyzed the intensity and duration of coal mining-related exposure, in particular from silica, on the risk of RA.

Methods: We conducted a random digit dial telephone survey in 2019 within selected counties in the Appalachian region with the highest coal workers' pneumoconiosis mortality rates identified by NIOSH, based on our previously validated methods. Eligibility was limited to males age ≥50, with any work history. Structured telephone interviews included demographics, history and details of coal mining work, other occupational dust exposures, and self-reported physician diagnoses of arthritis, including RA. RA was defined 2 ways: based on a reported physician diagnosis and either glucocorticoids or DMARDS prescribed for joint symptoms. We used logistic regression analyses to estimate the risks of any type of arthritis and RA (by each definition), associated with coal mining and other occupational exposures to silica. Additional models estimated risks associated with extensive time worked in underground coal mining and coal mining jobs with high intensity silica exposure, based on data from occupational health analyses. All models controlled for age and smoking status (current/former/never). The models of RA risk excluded those reporting a diagnosis of arthritis but who did not meet the given study definition of RA.

Results: We interviewed a population sample of 2,008 men, average age 67±10 years, of whom 93% were white and 58% ever smokers. Coal mining work was reported by 409 (20%) and 557 (28%) reported work-related silica exposure outside of coal mining. Among coal miners, 258/409 had specific job tasks with likely high-intensity silica exposure and 263 worked underground. Arthritis was highly prevalent: 1171 (58%) reported a physician diagnosis of any type of arthritis, RA with glucocorticoids in 202 (10%), and RA with DMARDs in 88 (4%). Coal mining and other occupational silica exposure were associated with an increased odds of arthritis, with increased risk for RA using

Table 1. Arthritis and RA associated with coal and silica exposure from logistic regression models adjusted for smoking and age

	Model outcomes		
Coal and Silica exposure	Arthritis (any type) (n=2008)	RA (definition 1) (n=1039)	RA (definition 2) (n=925)
	Odds ratios (95% confidence intervals)		
No exposure to coal mining or other occupational silica	ref.	ref.	ref.
Model 1: Any exposure			
Coal mining exposure	2.3 (1.8, 2.9)	3.6 (2.4, 5.5)	3.4 (1.8, 6.5)
Silica exposure from non-coal occupations only	1.9 (1.5, 2.3)	3.2 (2.2, 4.6)	4.6 (2.7, 7.9)
Model 2: Intensity of exposure			
High silica coal mining exposure	2.5 (1.8, 3.4)	4.1 (2.6, 6.7)	3.9 (1.9, 8.0)
All other coal mining exposure	2.0 (1.4, 2.8)	2.9 (1.6, 5.2)	2.7 (1.1, 6.8)
Model 3: Underground mining exposure			
≥18 years	3.3 (2.1, 5.1)	5.9 (3.2, 11.0)	4.9 (1.9, 12.4)
1-18 years	1.9 (1.3, 2.9)	3.4 (1.9, 6.2)	3.8 (1.6, 9.0)
No underground work	1.9 (1.3, 2.8)	2.4 (1.3, 4.5)	2.4 (0.9, 6.1)

For all models, odds ratios shown are in reference to the unexposed group, and control for non-coal mining silica exposure, age, and smoking (never/former/current).
Models of RA exclude respondents who report arthritis not meeting the given definition.
Definition 1 based on report of doctor's diagnosis of RA, plus treatment with glucocorticoids.
Definition 2 based on report of doctor's diagnosis of RA, plus treatment with DMARDs, including methotrexate, sulfasalazine, hydroxycholoroqine, azathioprine, leflunomide, tofacitinib, etanercept, adalimumab, infliximab, golimumab, certulizumab, tocilizumab, abatacept, rituximab.
High silica coal mining jobs included roof bolter, slope or shaft construction work, and bulldozer, dragline, or scraper operator.

either definition (Table 1). Coal mining jobs with high intensity silica exposure and individuals with ≥18 years of underground mining manifested a further step-up in risk of RA.

Conclusion: This study provides further confirmatory evidence for coal mining as a significant risk factor for RA, most saliently by showing increasing risk with increasing exposure intensity and duration.

[1] Schmajuk, et al. *Arth Care Res* 2019; 71:1201-1215

Disclosure: L. Trupin, None; **G. Schmajuk**, None; **E. Yelin**, None; **P. Blanc**, None.

Abstract Number: 1463

Threshold Level for Long-term Healthy Diet Adherence to Reduce the Risk of Rheumatoid Arthritis Among Women in a Prospective Cohort Using a Marginal Structural Model Approach

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health I: RA
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Previous analyses in the Nurses' Health Study (NHS) cohorts have shown that eating a healthier diet, as measured by the Alternative Healthy Eating Index (AHEI), is associated with a reduced risk of rheumatoid arthritis (RA) particularly seropositive RA, among younger women. Here, we used a marginal structural model (MSM) approach to determine potential thresholds of dietary improvement on the risk of RA in women.

Methods: We followed 83,585 women in the NHS II (1995-2017) prospective study cohort, where information on lifestyle, diet, and health was obtained biennially through validated questionnaires. We fitted an MSM via weighted pooled logistic regression with inverse-probability-of-censoring and exposure weights to approximately calculate risk ratios (RR) and 95% confidence intervals (CI). The models were adjusted for baseline and time-varying covariates including age,body mass index, smoking, age at menarche, parity and breastfeeding status, menopausal status and hormone use, census tract median family income, prior diet, and total energy intake. Diet quality and risk of incident RA were investigated using dichotomous cut-points of AHEI score (cut-points: 60, 65, 70, 75; AHEI score ranged from 0, which represented the least healthy diet, to 110, which represented the healthiest diet) (**Table 2**).

Results: Over 1,475,223 person years, there were 337 confirmed incident cases of RA. At baseline, the mean age was 40.3 years (SD ±4.6) and the mean AHEI score was 57.1 points (SD ±13.8). During 22 years of follow-up there was a mean AHEI score improvement of 9.1 points (SD ±12.7). The risk of RA, comparing long-term adherence to an AHEI score of at least 75 points with maintaining dietary quality below this threshold, was reduced by more than 50% (RR 0.43; 95% CI 0.27, 0.67) (**Table 1**). Risk reduction was similar for seropositive RA (RR 0.41; 95% CI 0.22, 0.74) and seronegative RA (RR 0.47; 95% CI 0.25, 0.91) (**Table 1**). Maintaining AHEI scores below the threshold of 75 was not associated with a reduced risk of RA.

Conclusion: Our results suggest that adherence to higher diet quality at an AHEI threshold score of ≥75 points may lower the risk of RA by more than 50% in women. Such an improvement could be achieved by increasing fruit, vegetable, nut, legume, whole grain, omega-3, or polyunsaturated fat consumption, or by decreasing sodium, sugar-sweetened beverage, or red/processed meat consumption.

Table 1. Dietary changes required to improve Alternative Healthy Eating Index (AHEI) diet score.

AHEI Components	Change required to achieve 1-point improvement in AHEI diet score
Fruit	Adding 0.4 servings per day
Vegetables	Adding 0.5 servings per day
Nuts and legumes	Adding 0.1 servings per day
Whole grains	Adding 7.5 grams per day
Long-chain omega-3 fatty acids	Adding 25 mg per day
Polyunsaturated fat	Adding 0.8% of total energy
Trans fat	Eliminating 0.35% of total energy
Red and processed meat	Eliminating 0.15 servings per day
Sugar-sweetened beverages	Eliminating 0.1 servings per day
Sodium	Eliminating 222 milligrams per day
Alcohol	Eliminating 0.2 drinks per day

Table 2. Estimated risk of rheumatoid arthritis following long-term adherence to Alternative Healthy Eating Index (AHEI) diet score[1] in the Nurses' Health Study II (1995-2017).

Long-term AHEI diet score adherence models[1]	Percentage of women with long-term adherence to diet score at or above cut-point	All RA		Seropositive RA		Seronegative RA	
		RR	95% CI	RR	95% CI	RR	95% CI
Model 1: AHEI score ≥ 60 v. <60 *Least healthy diet*	40.3%	0.92	(0.59, 1.44)	1.04	(0.62, 1.75)	0.74	(0.32, 1.72)
Model 2: AHEI score ≥ 65 v. <65	28.6%	0.94	(0.62, 1.43)	1.13	(0.69, 1.84)	0.63	(0.29, 1.37)
Model 3: AHEI score ≥ 70 v. <70	18.6%	0.72	(0.48, 1.06)	0.75	(0.45, 1.26)	0.63	(0.35, 1.12)
Model 4: AHEI score ≥ 75 v. <75 *Most healthy diet*	11.1%	**0.43**	**(0.27, 0.67)**	**0.41**	**(0.22, 0.74)**	**0.47**	**(0.25, 0.91)**

1. Higher score indicates healthier diet (AHEI diet score range: 0-110) 2. Adjusted for baseline pervious AHEI score (continuous), age at menarche (12 months breastfeeding), menopausal status and hormone use (pre-menopausal, post-menopausal with never use, current use and past use), census tract median family income (quartiles), and total energy (quintiles).

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Abstract Number: 1464

Multi-Variate Approach Including Serology and Genetics for an Improved Identification of Patients at Risk of Developing Rheumatoid Arthritis

Céline Lamacchia[1], Maresa Grundhuber[2], Isabel Gehring[2], Pascale Roux Lombard[3], Michael John Nissen[1], Andrea Rubbert Roth[4], Ruediger Mueller[5], Ulrich Walker[6], Burkhard Moeller[7], Diego Kyburz[8], Adrian Ciurea[9], Sascha Swiniarski[10] and **Axel Finckh**[11], [1]Geneva University Hospital, Geneva - 14, Switzerland, [2]Thermo Fisher Scientific Phadia GmbH, Freiburg, Germany, [3]Geneva University Hospital, Geneva, Switzerland, [4]Klinik für Rheumatologie, Kantonsspital St Gallen, St Gallen, Sankt Gallen, Switzerland, [5]KSA: Aarau Hospital, Aarau, Switzerland, [6]Basel University Hospital, Basel, Switzerland, [7]Inselspital - University Hospital Bern, Bern, Switzerland, [8]University Hospital Basel, Basel, Switzerland, [9]University Hospital Zurich, Zurich, Switzerland, [10]Phadia GmbH / Thermo Fisher Scientific, Freiburg, Germany, [11]Division of Rheumatology, University Hospitals of Geneva, Geneva, Switzerland

SESSION INFORMATION
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Session Title: Epidemiology & Public Health I: RA
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: First-degree relatives of RA patients (FDR-RA) have an increased prevalence for rheumatoid arthritis (RA) [1] and joint symptoms [2]. Identification of individuals with imminent RA is key to achieve prevention in pre-clinical stages.

We developed a two-step approach combining established biomarkers including different isotypes, genetics and first symptoms (step 1) followed by multiple and high positivity for serologic marker (step 2) to identify FDR-RAs with a high risk to develop RA. Using this approach to identify patients before onset of disease could improve patient management in the future.

Methods: 1227 FDR-RAs from the Swiss multicenter cohort study SCREEN-RA were included in this study [3]. The established serologic biomarkers anti-CCP IgG/A, RF IgM/A (CE-IVD) and the prototype assay anti-RA33 IgM/A/G were measured. The NGS technology AmpliSeq™ on the Ion GeneStudio™ instruments (Thermo Fisher Scientific, USA) was used covering 320 variants specific for RA in a targeted sequencing run. Symptoms of the patients were

Figure 1

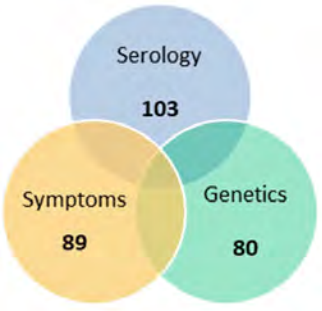

Figure 2

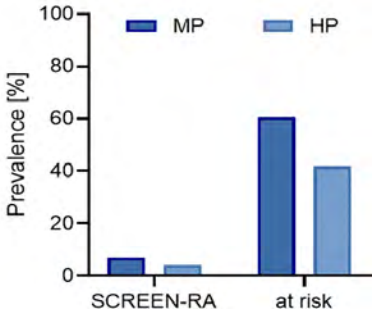

Figure 1. Venn diagram showing the identified individuals for each criterion and the individuals with ≥2 criteria positive. During step 1 of the approach, 51 individuals (4%) were highlighted as at risk. Fig 2: Additional 35 individuals (3%) were flagged during step 2 of the approach showing high or multiple positivity for the measured biomarkers

included using information from the Clinical Suspected Arthralgia (CSA) questionnaire. An algorithm based on Naïve Bayes was developed to combine serology, genetics and symptoms and in addition multiple and high positivity to define risk scores for each criterion for the included individuals. Individuals which had a high risk score for ≥2 criteria were flagged, as well as individuals with high or multiple positivity for the included biomarkers.

Results: For each individual the risk score for the three criteria (serology, genetics and symptoms) was calculated. 86 individuals (7%) were identified at high risk for developing RA including 51 individuals being positive for ≥ 2 criteria (step 1; Fig 1) and additional 35 individuals showed multiple positivity and/or high positivity for serologic markers (Fig 2). Individuals which were flagged during step 1 of the approach were not included in the numbers for step 2. Among 13 individuals diagnosed with incident clinical RA by rheumatologists, 9 of them (70%) were correctly identified by our approach.

Conclusion: The newly created algorithm including various risk factors could support the identification of individuals at risk to develop the disease in the near future and could allow a tight control. The highlighted individuals (n=86) will be followed up to identify imminent RA.

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Abstract Number: 1465

The Impact of the Combined Vaccination Scheme Against Streptococcus Pneumoniae on the Incidence of Related Infections in Patients with Rheumatoid Arthritis Treated with Biologic or Targeted Synthetic DMARD: Data from BIOBADASER 3.0

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health I: RA
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Respiratory infections are among the leading causes of hospitalization in rheumatoid arthritis (RA) and Streptococcus Pneumoniae (SP) is one of the most frequent pathogens involved. For these patients, the CDC recommends a combined vaccination scheme (CVS) using two types of vaccines but evidence on its effectiveness in this specific population remains insufficient.

Objectives: To assess the impact of the combined vaccination scheme on the incidence of SP infections in patients with RA treated with bDMARD and tsDMARD.

Methods: A cohort was nested in a register including patients with RA who were prescribed a bDMARD or tsDMARD (either naïve or switch) from October 1999 to November 2018. The stem register, BIOBADASER 3.0, is a national multicenter prospective register established in 1999 which recruits patients from 28 tertiary Spanish centers with an estimated national coverage of bDMARD and tsDMARD treatment in RA of 25%.

Vaccination Status assessment

Each center informed about the date when they implemented a systematic SP vaccination protocol and whether they were using the CVS. Those not adopting the latter were excluded from the analysis.

Outcomes

Invasive pneumococcal disease (IPD) and all-cause community-acquired pneumonia (CAP) were the main outcomes. However, since it is estimated that in a significant proportion of lower respiratory tract infections, SP presence is underdiagnosed, we also included all events reported using relevant MedDRA® codes related to this type of infection. Demographic and clinical features were also retrieved.

Statistical Analysis

Crude incidence rates (IR) were calculated for each outcome and its combination ("All SP-related infections"). Exposure was split into two periods, pre and post-vaccination, considering the date when the CVS was officially recommended in Spain (May 2015).

Variable	Study population n=1704
Age, years	60.57 (12.49)
Female Sex	1356 (79.58)
Current smoking	287 (16.84)
Disease duration, years	9.05 (7.93)
RF positive	875 (73.90)
ACPA positive	831 (71.20)
DAS28	4.63 (1.38)
BMI	27.47 (5.15)
Charlson index	2.37 (1.56)
Chronic pulmonary Disease	125 (9.25)
Diabetes mellitus	147 (9.01)

Table 1. Demographic and clinical characteristics of the study population. Categorical variables are expressed as number (%), quantitative variables as mean (standard deviation).

Period	Overall		≤65		>65	
	Pre-vac	Post-vac	Pre-vac	Post-vac	Pre-vac	Post-vac
All SP-related Infections						
Infections, n	70	97	56	70	14	27
PY	2192.6	5717.7	1895.4	4937.1	297.2	780.5
Crude IR (95% CI)	31.9 (25.3-40.4)	17.0 (13.9-20.7)	29.5 (22.7-38.4)	14.2 (11.2-17.9)	47.1 (27.9-79.5)	34.6 (23.7-50.4)
Invasive Pneumococcal Disease						
Infections, n	0	2	0	0	0	2
PY	-	6329.7		-	-	5438.1
Crude IR (95% CI)	-	0.3 (0.1-1.3)	-	-	-	0.4 (0.1-1.5)
Community-Acquired Pneumonia						
Infections, n	51	85	38	60	13	25
PY	2335.63	5830	2030.3	5040	305.3	790.4
Crude IR (95% CI)	21.8 (16.6-28.7)	14.6 (11.8-18.0)	18.7 (13.6-25.7)	11.9 (9.2-15.3)	42.6 (24.7-73.3)	31.6 (21.4-46.8)

Table 2. Incidence Ratios of infections related to Streptococcus Pneumoniae per 1000 PY according to age subgroup.

Adjusted Poisson regression Model		
Period		
Pre-Vaccination	ref	
Post-Vaccination	**0.25 (0.13-0.47)**	**0.001**
Sex		
Male	ref	
Female	1.22 (0.58-2.57)	0.603
Age		
≤65 years	ref	
>65 years	1.40 (0.57-3.435)	0.456
Charlson Index	1.29 (1.02-1.62)	0.03
Current smoking	0.91 (0.39-2.13)	0.827

Table 3. Adjusted Poisson regression model comparing pre-vaccination and post-vaccination periods adjusted for sex, age, Charlson Index and active smoking

Poisson regression modelling was carried out to estimate the incidence rate ratio (IRR) comparing both periods. Models were adjusted for potential confounders available such as sex, age, smoking and burden of comorbidity assessed with the Charlson Index which includes conditions such as diabetes mellitus, chronic respiratory diseases, chronic kidney disease, etc.

Results: Study population baseline features

A total of 1704 patients were included, their main features are shown in table 1. All participating centers reported using the CVS except for one that was, therefore, excluded from the analysis.

Incidence Rates

One-hundred and sixty-seven events were found; 2 for IPD, 136 for CAP and 29 for other lower respiratory tract infections. No IPD events were found in the pre-vac period. The IRs were higher in the pre-vac period for the remaining outcomes. Results are shown in Table 2

Crude and adjusted Incidence Rate Ratios

The IRR for all SP-related infections in the post- vac period was 0.25 (95% CI: 0.13 - 0.47) in the multivariable analysis. (table 3).

Conclusion: The incidence of infections due to SP experienced a decrease in RA patients taking bDMARD or tsDMARD after the introduction of the stepwise combined vaccination scheme that was independent of age, sex, smoking or comorbidities.

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Abstract Number: 1466

Multimorbidity in Rheumatoid Arthritis, Psoriatic Arthritis, Gout, and Osteoarthritis Within the Rheumatology Informatics System for Effectiveness (RISE) Registry

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health I: RA
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Rheumatic and musculoskeletal diseases (RMDs) often predispose the development of other chronic conditions, resulting in multimorbidity. While multimorbidity is increasingly being recognized and examined within individual RMDs, few studies have directly compared the burden and pattern of multimorbidity across RMDs.

Table 1. Patient Characteristics by Rheumatic and Musculoskeletal Disease from the RISE Registry				
	RA (n=152,214)	PsA (n=33,156)	Gout (n=19,781)	OA (n=151,669)
Demographics				
Age, years	63.8 (14.0)	57.6 (13.7)	66.3 (13.8)	69.0 (12.0)
Female sex, %	77.5	56.8	26.7	79.3
Race, %				
White	65.2	71.9	64.5	68.6
Black	8.1	1.7	10.2	6.6
Other	26.7	26.5	25.3	24.9
Insurance status				
Medicare	36.8	23.3	40.1	43.8
Medicaid	3.1	2.1	2.3	2.3
Private	34.2	45.7	34.0	28.4
Other	26.0	29.0	23.6	25.4
# of visits	3.1 (2.5)	2.9 (2.4)	1.9 (1.9)	2.3 (2.1)
Multimorbidity				
# RxRisk classes	8.6 (4.5)	7.7 (4.5)	8.7 (4.4)	8.1 (4.4)
≥5 RxRisk classes, %	78.9	71.5	79.3	77.0
Values mean (SD) unless otherwise indicated				

Table 1. Patient Characteristics by Rheumatic and Musculoskeletal Disease from the RISE Registry

Table 2. Multivariable Adjusted* Associations of Rheumatic and Musculoskeletal Diseases with Multimorbidity in the RISE Registry		
	Estimate	**P value**
Multimorbidity (≥5 RxRisk Categories)	Odds Ratio (95% CI)	
Rheumatoid arthritis	1 (referent)	-
Psoriatic arthritis	0.98 (0.95, 1.01)	0.15
Osteoarthritis	0.78 (0.76, 0.79)	<0.001
Gout	1.29 (1.23, 1.24)	<0.001
Multimorbidity burden (# RxRisk categories)	**Beta (95% CI)**	
Rheumatoid arthritis	0 (referent)	-
Psoriatic arthritis	-0.008 (-0.014, -0.002)	0.02
Osteoarthritis	-0.086 (-0.090, -0.082)	<0.001
Gout	0.054 (0.046, 0.062)	<0.001
*Models adjusted for age, sex, race, U.S. region, insurance status, number of visits, and size of rheumatology practice (# of providers).		

Table 2. Multivariable Adjusted Associations of Rheumatic and Musculoskeletal Diseases with Multimorbidity in the RISE Registry

Therefore, we aimed to compare multimorbidity between rheumatoid arthritis (RA), psoriatic arthritis (PsA), gout, and osteoarthritis (OA) within the Rheumatology Informatics System for Effectiveness (RISE) registry.

Methods: We conducted a cross-sectional study within the RISE registry, the largest EHR-enabled rheumatology registry in the U.S. We selected patients >18 years of age, with ≥2 RISE encounters over ≥30 days, and who fulfilled algorithms for RA, PsA, gout, or OA (≥2 consecutive visits with corresponding ICD-10 codes) in a hierarchical fashion to avoid patients contributing to multiple disease groups. Multimorbidity was assessed using the RxRisk, a medication-based index of chronic conditions, assessed using all available preceding data before the 2nd visit. We compared the frequency of multimorbidity (defined as receiving medications from ≥5 different RxRisk categories; Wallace E. et al. *BMJ Open*, 2016) across disease groups using multivariable logistic regression and the burden of multimorbidity (defined as the number of RxRisk categories) using multivariable negative binomial regression.

Results: We included 356,820 patients from the RISE registry (n=152,214 RA, n=33,156 PsA, n=19,781 gout, n=151,669 OA) with characteristics shown in **Table 1**. Patients with PsA were younger and more frequently Caucasian while male sex was more frequent in patients with gout or PsA. The odds of multimorbidity (35 RxRisk categories) were 1.29-fold higher in gout than RA (95% CI 1.23-1.34; **Table 2**). Compared to patients with RA, the prevalence of multimorbidity was similar in PsA (p=0.15) but less frequent in OA (OR 0.78, 95% CI 0.76-0.79). Similarly, a higher burden of multimorbidity (# of RxRisk categories) was observed in gout compared to RA (B=0.054, P< 0.001; **Table 2**). Both PsA (B=-0.008, P=0.02) and OA were associated with a lower burden of multimorbidity than RA (B=-0.086, P< 0.001). Distinct patterns of multimorbidity were noted across disease groups. Specifically, metabolic and cardiac RxRisk categories were most closely associated with gout, while thyroid and osteoporosis categories were most closely associated with RA and OA.

Conclusion: In this large, national, U.S. rheumatology EHR-based registry, multimorbidity was highly prevalent in RA, PsA, gout, and OA. Recognizing the tremendous burden and unique patterns of multimorbidity accompanying these conditions is an essential step for optimizing the management of RMDs in real-world populations.

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Abstract Number: 1467

Effectiveness of the Making It Work™ Program at Improving Presenteeism and Work Cessation in Workers with Inflammatory Arthritis – Results of a Randomized Controlled Trial

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Epidemiology & Public Health II: Risk Factors & Outcomes

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: Arthritis often leads to presenteeism (decreased at-work productivity) and permanent work disability, the worst occupational outcome of a disease, leading to reduced quality of life and cost to society. Yet, health services addressing employment needs of people with arthritis are lacking. We evaluated the effectiveness of the Making-it-Work™ (MIW), an online program developed to help people with inflammatory arthritis (IA) deal with employment issues.

Methods: A multi-center RCT evaluated the effectiveness of MIW at improving presenteeism and work cessation (WC) over two years. Participants were recruited from rheumatologist practices, consumer organizations and arthritis programs, in three provinces. Eligibility criteria: diagnosis of IA, employed, age 18-59, and concerned about ability to work. Participants were randomized 1:1 to MIW or usual care plus printed material on workplace tips. MIW consists

		CONTROL	INTERVENTION
	Number	282	282
	Retention at 2 years (%)	84%	85%
Sociodemographic	Age (mean(SD))	46.2 (9.8)	45.3 (10.0)
	Female (%)	217 (77)	222 (79)
	Caucasian (%)	223 (80)	231 (83)
	Completed Post-Secondary Education (%)	209 (74)	220 (78)
Health-related	Inflammatory Arthritis Type		
	RA	138 (24)	140 (25)
	PsA	48 (8)	47 (8)
	SpA	56 (10)	56 (10)
	SLE	40 (7)	39 (7)
	Disease duration Years (mean(SD))	10.6 (9.7)	9.3 (9.1)
	Joint Pain - NRS (mean(SD))	3.9 (2.4)	4.1 (2.7)
	Disease Activity (RADAI) (mean(SD))	3.66 (1.8)	3.70 (2)
	Physiscal Function - HAQ II (mean(SD))	0.7 (0.5)	0.7 (0.5)
	Fatigue NRS (mean(SD))	5.1 (2.5)	5.3 (2.7)
Work-related	Job type - NOC (%)		
	Management, science and education	210 (75)	222 (79)
	Sales, services, arts and sports	54 (19)	42 (15)
	Transportation, trades and production	17 (6)	18 (6)
	Self Employed (%)	52 (18)	47 (17)

Table 1. Sample characteristics

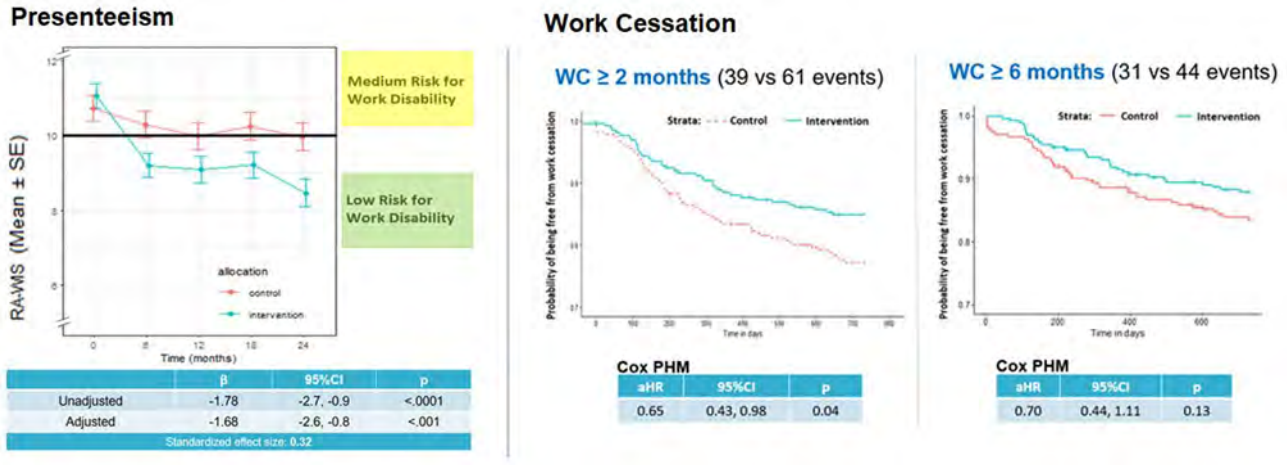

Figure 1. Effectiveness of the Making-it-Work(TM) program on Presenteeism and Work Cessation over 2 years

of five online self-learning modules and group meetings, and individual vocational counselling and ergonomic assessments. Questionnaires were administered every 6 months. Outcomes were presenteeism [Rheumatoid Arthritis Work Instability Scale (RA-WIS)], time to WC of ≥6 months duration, and time to WC ≥2 months (secondary outcome). Baseline characteristics (age, gender, ethnicity, occupation, education, disease duration and self-employment) were collected. Intention-to-treat longitudinal analysis of RA-WIS using linear mixed effect regression models with 2-year comparison as primary endpoint and survival analysis for time to WC using Kaplan-Meier and Cox Proportional Hazard models were performed. Sensitivity analyses were conducted with missing values imputed using last observation carried forward and worse possible outcomes; with square root transformation of RA-WIS outcome; and adjusting for baseline covariates. SAS version 9.4 was used.

Results: A total of 564 participants were recruited, with 85% completing 2-year follow-up. Baseline characteristics were similar between groups. Difference in means of RA-WIS scores was significantly lower in the intervention group from 6 months onwards, with the greatest difference observed at 2 years (-1.78, 95%CI: -2.7, -0.9, p< .0001), yielding a standardized effect size of 0.32. Sensitivity analysis revealed satisfactory robustness of results. Work cessation occurred less often in intervention than control groups, but only reached statistical significance for WC duration ≥2 months (WC ≥6 months: 31 vs 44 events, aHR 0.70, 95%CI: 0.44, 1.11, p-value: 0.13; WC ≥2 months: 39 vs 61 events, aHR: 0.65, 95%CI: 0.43, 0.98, p-value: 0.04).

Conclusion: Results of the RCT reveal the program was effective at improving presenteeism and preventing short-term WC. Effectiveness at preventing long-term work disability will be assessed at 5 years. This program fills one of the most important unmet needs for people with inflammatory arthritis.

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Abstract Number: 1468

The Association of Walking Speed from Short- and Standard-Distance Tests with Mortality Risk Among Adults with Radiographic Knee Osteoarthritis: Data from Johnston County Osteoarthritis Project, Osteoarthritis Initiative and Multicenter Osteoarthritis Study

Hiral Master[1], Tuhina Neogi[2], Leigh Callahan[3], Amanda Nelson[4], Michael LaValley[5], Rebecca Cleveland[6], Yvonne Golightly[7], Louise Thoma[8], Yuqing Zhang[9], Dana Voinier[10], Meredith Christiansen[11], Jason Jakiela[10], Michael Nevitt[12], Cora Lewis[13], Laura Frey Law[14] and Daniel White[10], [1]Vanderbilt University Medical Center, Nashville, TN, [2]Boston University School of Medicine, Boston, MA, [3]University of North Carolina Thurston Arthritis Research Center, Chapel Hill, NC, [4]University of North Carolina Chapel Hill, Chapel Hill, [5]Boston University School of Public Health, Boston, MA, [6]University of North Carolina, Chapel Hill, NC, [7]University of North Carolina at Chapel Hill Dept of Epidemiology, Chapel Hill, NC, [8]University of North Carolina at Chapel Hill, Chapel Hill, NC, [9]Massachusetts General Hospital, Harvard Medical School, Boston, [10]University of Delaware, Newark, DE, [11]University of Delaware, New York, NY, [12]University of California, San Francisco, San Francisco, CA, [13]University of Alabama Birmingham, Birmingham, AL, [14]University of Iowa, Iowa City, IA

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Epidemiology & Public Health II: Risk Factors & Outcomes

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Table: Maximal Likelihood Ratio (LR) Chi-Square (χ^2) Approach[d] to identify the optimal threshold of walking speed measured via a (A) 2.4-m walk test in the Johnston County Osteoarthritis Project (JoCoOA) and (B) 20-m walk test in the Osteoarthritis Initiative (OAI) and Multicenter Osteoarthritis Study (MOST), cohorts that predicted the risk of excess mortality and diagnostic evaluation of thresholds in adults with radiographic knee osteoarthritis (rKOA).

Thresholds	Number of deaths/Total people (%)		HR[95% CI]	[b]LR χ^2	Diagnostic Evaluation Value[95%CI]			
	Walk <threshold	Walk ≥threshold			Sensitivity	Specificity	Negative LR	Positive LR
(A) 2.4-m (short-distance) walk test administered in the JoCoOA								
0.4 m/s	54/132 (40.9)	236/1112 (21.2)	[a]1.69[1.23, 2.33]	24.8	18.6[14.3, 23.6]	91.8[89.9, 93.5]	0.89[0.84, 0.94]	2.3[1.7, 3.1]
[c]0.5 m/s	**94/243 (38.4)**	**196/1001 (19.6)**	**[a]1.60[1.22, 2.11]**	**[c]38.0**	**32.4[27.1, 38.1]**	**84.4[81.9, 86.6]**	**0.80[0.74, 0.87]**	**2.1[1.7, 2.6]**
0.6 m/s	141/430 (32.3)	149/814 (18.3)	[a]1.44[1.11, 1.88]	31.9	48.6[42.7, 54.5]	69.7[66.7, 72.6]	0.74[0.65, 0.83]	1.6[1.4, 1.9]
0.7 m/s	191/649 (29.4)	99/595 (16.6)	[a]1.50[1.14, 1.97]	30.0	65.9[60.1, 71.3]	52.0[48.8, 55.2]	0.66[0.55, 0.78]	1.4[1.2, 1.5]
(B) 20-m (standard-distance) walk test administered in the OAI and MOST								
1.0 m/s	53/537 (9.9)	196/3678 (5.3)	[a,c]1.42[1.00, 2.02]	20.7	21.3[16.4, 26.9]	87.8[86.7, 88.8]	0.90[0.84, 0.96]	1.7[1.4, 2.3]
1.1 m/s	101/1035 (9.8)	148/3180 (4.7)	[a,c]1.76[1.31, 2.36]	43.5	40.6[34.4, 46.9]	76.5[75.1, 77.8]	0.78[0.70, 0.86]	1.7[1.5, 2.0]
[c]1.2 m/s	**153/1738 (8.8)**	**96/2477 (3.9)**	**[a,c]1.96[1.47, 2.62]**	**[c]57.5**	**61.5[55.1, 67.5]**	**60.0[58.5, 61.6]**	**0.64[0.55, 0.75]**	**1.5[1.4, 1.7]**
1.3 m/s	186/2514 (7.4)	63/1701 (3.7)	[a,c]1.61[1.18, 2.21]	37.6	74.7[68.8, 80.0]	58.7[57.2, 60.2]	0.43[0.35, 0.53]	1.8[1.7, 2.0]

[a]Adjusted for baseline age, body mass index, sex, race, education, comorbidities, depression (≤ vs. >16), and symptomatic knee OA (yes or no);
[b]LR χ^2 values are obtained from unadjusted Cox models for (A) and from Cox model stratified by study orgin was used in (B);
[c]Cox model stratified by study oirigin (OAI or MOST) was used when the data from OAI and MOST cohorts were combined into one sample;
[d]Approach states that higher chi-square values represent greater concordance between the threshold and mortality;
[e]Model that yielded a maximum χ^2 value;
aHR=adjusted hazard ratio, CI=confidence interval

Background/Purpose: Patients with radiographic knee OA (rKOA) are at increased risk of mortality and walking difficulty may mediate this relation. Walking speed may be used to objectively assess walking difficulty. However, there is little consensus on the specification for testing distance, which may affect the values of walking speed. Subsequently, this difference may limit the ability to generalize results between different test distances. It is not known if speed measured from short (2.4-meter) and standard (20-meter) distance walk tests similarly predict mortality risk. Therefore, the purpose of the study was to investigate the association of walking speed measured via short and standard distances to mortality risk in adults with rKOA using three large longitudinal cohort studies in the United States.

Methods: We included participants with rKOA (presence of Kellgren Lawrence grade ≥2 in either knee) from the Johnston County Osteoarthritis Project (JoCoOA) which is longitudinal population-based cohort, Osteoarthritis Initiative (OAI) and Multicenter Osteoarthritis Study (MOST), latter two being cohorts of individuals with or at high risk of knee OA. Walking speed was measured via 2.4-meter walk test (short-distance) in JoCoOA and 20-meter walk test (standard-distance) in OAI and MOST. The data from OAI and MOST were combined because they measured walking speed in a similar fashion. To examine the association of baseline walking speed specific to each test with mortality risk over nine years, hazard ratios (HR) and 95% confidence intervals (CI) were calculated from Cox regression models adjusted for potential confounders. To identify an optimal threshold of walking speed specific to each test that best discriminiated mortality risk, Maximal Likelihood Ratio Chi-square Approach was utilized.

Results: Deaths after 9 years of follow-up occurred in 23.3% (290/1244) of JoCoOA (age [mean±sd] 65.2±10.8 years, BMI 31.9±7.7 kg/m^2, 67% female) and 5.9% (249/4215) of OAI and MOST (age 63.1±8.6 years, BMI 30.6±5.6 kg/m^2, 59% female). Walking 0.1 meters/second slower during short- and standard-distance walk tests was associated with 11% (HR[95%CI]; 1.11[1.05, 1.18]) and 12% (1.12[1.05, 1.20]) higher risk of mortality, respectively. Walking slower than 0.5 meters/second on short-distance walk test, and slower than 1.2 meters/second on standard-distance walk test, best discriminated those with and without excess mortality risk (Table).

Conclusion: Slower walking speed measured via short- and standard-distance walk tests was associated with increased mortality risk in adults with rKOA. The study findings on optimal thresholds should be viewed with caution because the short- and standard-distance walk tests were administered in different cohorts. However, a plausible explanation for the differences in the optimal thresholds between different walk tests may be due to the variability in test distances, which may affect the acceleration and deceleration walking phases to achieve a self-selected usual pace.

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Abstract Number: 1469

Characteristics of Adult Patients with Rheumatic Diseases During the COVID-19 Pandemic: Data from an International Patient Survey

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health II: Risk Factors & Outcomes
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Patients with rheumatic diseases are at increased risk of infection due to immune dysregulation and the use of immunosuppression. It is unknown whether they are also at increased risk of SARS-CoV-2 infection or of COVID-19-related complications. Using real-world data from the COVID-19 Global Rheumatology Alliance (C19-GRA) Patient Experience Survey, we describe the demographic and clinical characteristics of adult respondents and investigate risk factors related to COVID-19 infection.

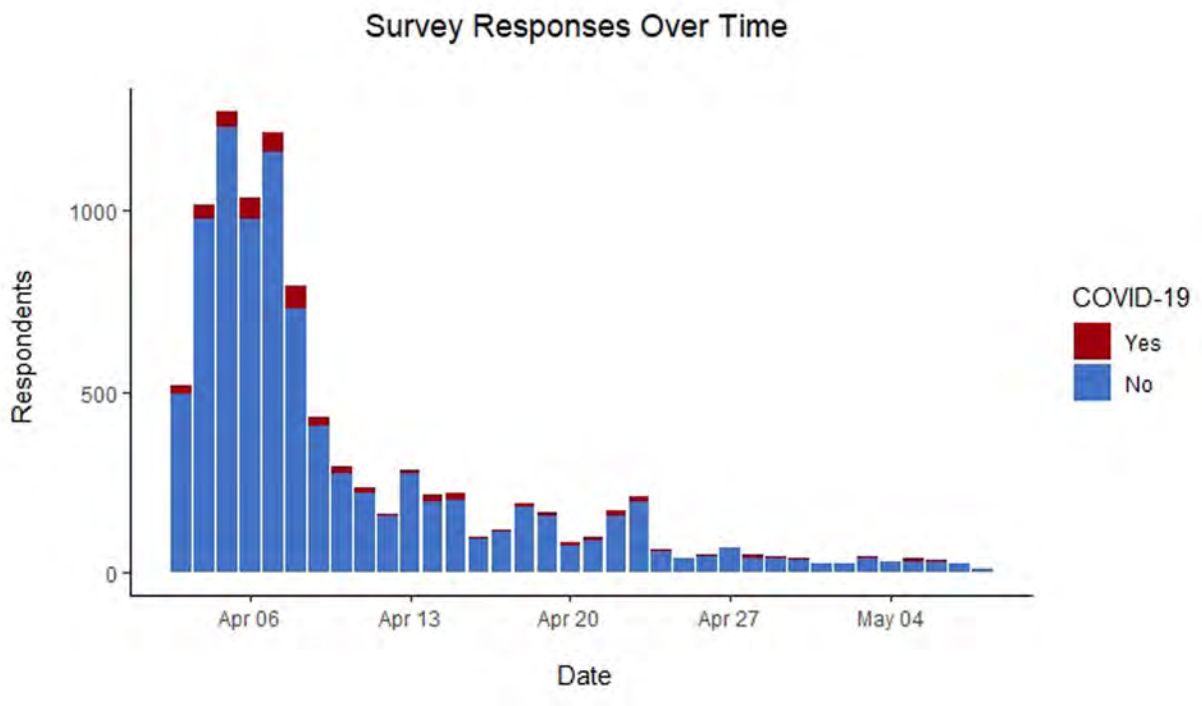

Figure 1. Survey respondents during the study period April 3 - May 8, 2020.

Table 1. Demographics and clinical characteristics of adults in the COVID-19 Global Rheumatology Alliance Patient Experience Survey (n=9,393)

	All Patients (n=9,393)	Patients with COVID-19 (n=519)	Patients without COVID-19 (n=8,874)
	N (%)	N (%)	N (%)
Gender			
Female	8453 (90)	477 (91.9)	7976 (89.9)
Male	908 (9.7)	36 (6.9)	872 (9.8)
Nonbinary	9 (0.1)	1 (0.2)	8 (0.1)
Prefer not to answer	23 (0.2)	5 (1)	18 (0.2)
Race / Ethnicity			
White	6334 (67.4)	412 (79.4)	5922 (66.7)
Latin American	1576 (16.8)	24 (4.6)	1552 (17.5)
Black	198 (2.1)	17 (3.3)	181 (2)
Asian	190 (2)	15 (2.9)	175 (2)
Native American / Aboriginal / First Nations	42 (0.4)	4 (0.8)	38 (0.4)
Other	1053 (11.2)	47 (9.1)	1006 (11.3)
Rheumatological Disease			
Rheumatoid arthritis	3626 (38.6)	172 (33.1)	3454 (38.9)
Systemic lupus erythematosus	2882 (30.7)	199 (38.3)	2683 (30.2)
Sjogren's syndrome	1290 (13.7)	96 (18.5)	1194 (13.5)
Ankylosing spondylitis	1006 (10.7)	40 (7.7)	966 (10.9)
Psoriatic arthritis	673 (7.2)	51 (9.8)	622 (7)
Anti-phospholipid antibody syndrome	497 (5.3)	42 (8.1)	455 (5.1)
Inflammatory myopathy	425 (4.5)	20 (3.9)	405 (4.6)
Mixed connective tissue disease	422 (4.5)	41 (7.9)	381 (4.3)
Other inflammatory arthritis	390 (4.2)	38 (7.3)	352 (4)
Inflammatory eye disease (scleritis, uveitis, etc.)	317 (3.4)	28 (5.4)	289 (3.3)
ANCA-associated vasculitis	305 (3.2)	14 (2.7)	291 (3.3)
Undifferentiated connective tissue disease	212 (2.3)	23 (4.4)	189 (2.1)
Systemic sclerosis	202 (2.2)	8 (1.5)	194 (2.2)
Other spondyloarthritis	183 (1.9)	16 (3.1)	167 (1.9)
Polymyalgia rheumatica	167 (1.8)	5 (1)	162 (1.8)
Autoinflammatory disease	159 (1.7)	12 (2.3)	147 (1.7)
Juvenile idiopathic arthritis	148 (1.6)	4 (0.8)	144 (1.6)
Behcet's syndrome	127 (1.4)	10 (1.9)	117 (1.3)
Still's Disease	103 (1.1)	7 (1.3)	96 (1.1)
Other Vasculitis	92 (1)	8 (1.5)	84 (0.9)
Crystalline arthritis	76 (0.8)	12 (2.3)	64 (0.7)
Giant cell arteritis	57 (0.6)	3 (0.6)	54 (0.6)
Sarcoidosis	57 (0.6)	7 (1.3)	50 (0.6)
IgG4-related disease	21 (0.2)	4 (0.8)	17 (0.2)
Chronic recurrent multifocal osteomyelitis	12 (0.1)	1 (0.2)	11 (0.1)
Medications			
csDMARDs	6657 (70.9)	371 (71.5)	6286 (70.8)
Steroids	3264 (34.7)	168 (32.4)	3096 (34.9)
Biologic DMARDs	2896 (30.8)	151 (29.1)	2745 (30.9)
tsDMARDs	299 (3.2)	11 (2.1)	288 (3.2)
Other	155 (1.7)	13 (2.5)	142 (1.6)
Comorbidities			
Pain Syndromes	2176 (23.2)	153 (29.5)	2023 (22.8)
Hypertension	2142 (22.8)	118 (22.7)	2024 (22.8)
Pulmonary	2010 (21.4)	187 (36)	1823 (20.5)
Metabolic	1103 (11.7)	82 (15.8)	1021 (11.5)
Immunologic	1005 (10.7)	88 (17)	917 (10.3)
Gastrointestinal	654 (7)	46 (8.9)	608 (6.9)
Renal	418 (4.5)	22 (4.2)	396 (4.5)
Psychiatric	425 (4.5)	29 (5.6)	396 (4.5)
Cardiovascular	347 (3.7)	15 (2.9)	332 (3.7)
Neurological/Neuromuscular	238 (2.5)	21 (4)	217 (2.4)
Dermatologic	199 (2.1)	17 (3.3)	182 (2.1)
Malignancy	114 (1.2)	4 (0.8)	110 (1.2)
WHO Region			
Region of the Americas	6164 (65.6)	338 (65.1)	5826 (65.7)
European Region	2725 (29)	159 (30.6)	2566 (28.9)
Western Pacific Region	258 (2.7)	14 (2.7)	244 (2.7)
South-East Asia Region	22 (0.2)	1 (0.2)	21 (0.2)
Eastern Mediterranean Region	140 (1.5)	6 (1.2)	134 (1.5)
African Region	84 (0.9)	1 (0.2)	83 (0.9)

Participants may have more than one condition and take more than one type of medication.
csDMARD medications included: antimalarials (hydroxychloroquine, chloroquine), azathioprine, cyclophosphamide, cyclosporine, leflunomide, methotrexate, mycophenolate mofetil/mycophenolic acid, sulfasalazine, tacrolimus.
bDMARD included: abatacept, belimumab, CD-20 inhibitors, IL-1 inhibitors, IL-6 inhibitors, IL-12/IL-23 inhibitors, IL-17 inhibitors, and anti-TNF.
tsDMARD included: Janus Kinase inhibitors
Other medications included: IVIG, apremilast, thalidomide

Table 2. Symptoms and hospitalization status of adults with COVID-19 (n=519).

	N (%)
Symptoms	
Malaise/fatigue	452 (87.1)
Cough	408 (78.6)
Headache	405 (78)
Dyspnea	344 (66.3)
Fever	343 (66.1)
Sore throat	342 (65.9)
Myalgias	321 (61.8)
Chest pain	271 (52.2)
Diarrhea	269 (51.8)
Arthralgias	253 (48.7)
Rhinorrhea	200 (38.5)
Dysgeusia	182 (35.1)
Anosmia	145 (27.9)
Abdominal pain	125 (24.1)
Irritability/confusion	122 (23.5)
Hospitalization Status	
Not hospitalized without difficulties performing ADLs	118 (22.74)
Not hospitalized but with some difficulties performing ADLs	329 (63.39)
Hospitalized but did not require a ventilatory support	59 (11.37)
Hospitalized and required ventilatory support	6 (1.16)
Missing	7 (1.35)

ADLs: activities of daily living such as bathing, eating, dressing, etc.

Table 2. Symptoms and hospitalization status of adults with COVID-19 (n=519).

Methods: We distributed a patient-reported outcomes survey for adults and parents of children with rheumatic diseases, regardless of COVID-19 status, to all six WHO regions and available in nine languages. The survey was disseminated through patient support organizations and on social media. Patients answered questions regarding their demographics, rheumatic disease diagnosis, medications, as well as COVID-19 diagnosis and its complications. We evaluate the demographics of adults within this study and describe the clinical characteristics of COVID-19 infection from April 3-May 8, 2020.

Results: A total of 9,393 adults completed the survey during the study period (Figure 1). Respondents represented all six WHO regions; most were female (90.0%) with a mean age of 46.1 (SD 12.8) (Table 1). Common diagnoses included rheumatoid arthritis (38.6%), systemic lupus erythematosus (SLE) (30.7%), and Sjogren's syndrome (13.7%). The majority of patients were taking conventional synthetic DMARDs (70.9%), while 34.7% and 30.8% were on steroids and biologic DMARDs, respectively. Comorbidities included pain syndromes (23.2%), hypertension (22.8%), and pulmonary diseases (21.4%).

Out of the patients surveyed, 519 (5.5%) endorsed having COVID-19 (Table 2). Frequently-reported COVID-19 symptoms included malaise/fatigue (87.1%), cough (78.6%), and headache (78.0%). Only 65 patients (12.5%) required hospitalization. When compared to the population without COVID-19, those with COVID-19 more often had diagnoses of SLE (38.3% vs. 30.2%, $p< 0.001$) and pulmonary comorbidities (36.0% vs. 20.5%, $p< 0.001$).

Conclusion: These results demonstrate the feasibility of conducting an international patient-reported outcomes survey to address the impact of the COVID-19 pandemic among patients with rheumatic diseases. Only 5.5% of patients with rheumatic diseases developed COVID-19 and the majority did not require hospitalization, even though most

were on immunosuppressive drugs. Patients with SLE and pulmonary comorbidities were overrepresented among those with COVID-19. Future subgroup analyses will explore the relationships between disease states and diagnosis of COVID-19.

Disclaimer: The views expressed here are those of the authors and participating members of the COVID-19 Global Rheumatology Alliance and do not necessarily represent the views of the American College of Rheumatology, the European League Against Rheumatism (EULAR), or any other organization.

Disclosure: J. Hausmann, Novartis, 5; **K. Kennedy**, Lyceum Health, 5; **S. Surangiwala**, None; **M. Larche**, AbbVie, 5, Amgen, 5, Boehringer-Ingelheim, 5, BMS, 5, Celgene, 5, Janssen, 5, Mallinckrodt, 5, Novartis, 5, Pfizer, 5, Roche, 5, Sandoz, 5, UCB, 5; **M. Levine**, None; **J. Liew**, None; **Z. Wallace**, Bristol-Myers Squibb, 2; **E. Sirotich**, Canadian Arthritis Patient Alliance, 9.

Abstract Number: 1470

Machine Learning-Based Prediction of Knee Replacement in Persons with and Without Radiographic Osteoarthritis Using Clinical and Imaging Features of Osteoarthritis: The Multicenter Osteoarthritis Study

S. Reza Jafarzadeh[1], David Felson[1], Michael Nevitt[2], James Torner[3], Cora Lewis[4], Frank Roemer[5], Ali Guermazi[1] and Tuhina Neogi[1], [1]Boston University School of Medicine, Boston, MA, [2]University of California, San Francisco, San Francisco, CA, [3]University of Iowa, Iowa City, IA, [4]University of Alabama Birmingham, Birmingham, AL, [5]Boston University School of Medicine, Boston, MA, and Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany, Erlangen, Germany

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Epidemiology & Public Health II: Risk Factors & Outcomes

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Stage of OA	# KR (Total)	Median AUC (2.5-, 97.5-th percentile) Across 100 Runs*	
		Only Clinical and Radiographic Features Included	Clinical, Radiographic, and MRI** Features Included
KL = 0 or 1	34 (1551)	0.78 (0.73, 0.89)	0.80 (0.75, 0.91)
KL = 2, 3 or 4	155 (806)	0.79 (0.76, 0.87)	0.80 (0.77, 0.88)
Any KL	189 (2357)	0.88 (0.87, 0.92)	0.88 (0.87, 0.92)

AUC: Area Under the Curve; KL: Kellgren and Lawrence Grading System; KR: Knee Replacement; MRI: Magnetic Resonance Imaging

* Algorithms included: Bayesian adaptive regression trees (BART), extreme gradient boosting, generalized linear models with convex penalties (that consisted least absolute shrinkage and selection operator [LASSO], ridge regression, and elastic net), logistic regression, random forest, and support vector machine.

** WORMS MRI features: cartilage morphology, osteophytes, bone marrow lesions, synovitis or effusion, meniscal tears and extrusion.

Table 1. Prediction accuracy of a stacked prediction model, expressed by the area under the curve across 100 runs, to predict knee replacement within 7 years.

Stage of OA	Top 10 Contributing Variables to KR Prediction Across 100 Runs (Frequency)	
	Only Clinical and Radiographic Features	**Clinical, Radiographic, and MRI** Features**
KL = 0 or 1	KL Grade (100) BMI (100) Malalignment (99) WOMAC Function: Difficulty in Light Chores (93) WOMAC Function: Difficulty in Sitting (76) History of Knee Injury (64) Race (63) PASE Score (61) WOMAC Pain: Walking (53) WOMAC Pain: Up Stairs (51)	Malalignment (97) [MRI] Osteophytes: Tibia Medial Central (95) BMI (94) [MRI] Cartilage Morphology: Femur Medial Anterior (88) KL Grade (86) WOMAC Function: Difficulty in Sitting (56) History of Knee Injury (48) [MRI] Bone Marrow Edema: Femur Lateral Anterior (47) [MRI] Cartilage Morphology: Femur Lateral Anterior (47) Race (46)
KL = 2, 3 or 4	Race (100) Malalignment (100) KL Grade (100) WOMAC Function: Difficulty in Heavy Chores (96) Sex (90) Osteophytes [OARSI Grades 0-3]: Femur Medial TF Compartment on PA View (90) JSN [OARSI Grades 0-3]: Lateral TF Compartment on PA View (81) Work for Pay (48) WOMAC Function: Difficulty in Putting on Socks (48) WOMAC Function: Difficulty in Difficulty, Getting In/Out of Bathtub (47)	Race (100) Malalignment (100) KL Grade (100) Sex (97) [MRI] Bone Marrow Edema: Tibia Medial Central (92) WOMAC Function: Difficulty in Heavy Chores (70) [MRI] Cartilage Morphology: Femur Lateral Posterior (69) [MRI] Osteophytes: Tibia Medial Posterior (68) [MRI] Osteophytes: Femur Medial Anterior (63) CES-D Score (34)
Any KL	Race (100) Malalignment (100) KL Grade (100) WOMAC Function: Difficulty in Putting on Socks (96) Osteophytes [OARSI Grades 0-3]: Femur Medial TF Compartment on PA View (90) JSN [OARSI Grades 0-3]: Lateral TF Compartment on PA View (78) Sex (63) WOMAC Function: Difficulty in Shopping (57) Osteophytes [OARSI Grades 0-3]: Femur Lateral TF Compartment on PA View (45) WOMAC Function: Difficulty in Lying Down (40)	Race (100) KL Grade (100) Malalignment (99) [MRI] Bone Marrow Edema: Tibia Medial Central (99) WOMAC Function: Difficulty in Putting on Socks (98) JSN [OARSI Grades 0-3]: Lateral TF Compartment on PA View (85) [MRI] Osteophytes: Tibia Medial Posterior (78) [MRI] Osteophytes: Tibia Lateral Central (74) Sex (47) WOMAC Function: Difficulty in Lying Down (41)

BMI: Body Mass Index; CES-D: Center for Epidemiologic Studies Depression Scale; JSN: Joint Space Narrowing; KL: Kellgren and Lawrence Grading System; KR: Knee Replacement; MRI: Magnetic Resonance Imaging; PA: Posteroanterior; PASE: Physical Activity Scale for the Elderly; TF: Tibiofemoral; WOMAC: Western Ontario and McMaster Universities Osteoarthritis Index

** WORMS MRI features: cartilage morphology, osteophytes, bone marrow lesions, synovitis or effusion, meniscal tears and extrusion.

Algorithms included: Bayesian adaptive regression trees (BART), extreme gradient boosting, generalized linear models with convex penalties (that consisted least absolute shrinkage and selection operator [LASSO], ridge regression, and elastic net), logistic regression, random forest, and support vector machine.

Table 2. Frequency of runs (out of 100) in which the listed variables were in the top 10 of contributors to the prediction of knee replacement within 7 years.

Background/Purpose: Prior studies of predictors of knee replacement (KR) have often included only a limited set of risk factors, been conducted primarily in knees with radiographic OA (ROA), and with short follow-up. Further, it is uncertain if addition of MRI data would improve prediction. We therefore evaluated clinical and imaging features of OA for their ability to predict KR over a 7-year period, including knees with and without ROA, and assessed the utility of adding MRI data.

Methods: We included data from the Multicenter Osteoarthritis (MOST) Study, a NIH-funded cohort of persons with or at risk of knee OA. We first limited the model to baseline demographics, clinical (e.g., WOMAC, other symptom questionnaires) and radiographic (KL, JSN, OST grades) data. In the full model, WORMS knee MRI features were added. KRs were confirmed by medical records and/or radiographs up to year 7. We used a random 80% of the sample for model development and training, and the remaining 20% for testing. We used an ensemble stacking approach, i.e., super learning, to combine multiple machine learning algorithms to develop a predictive model, which selects the optimal combination of algorithms to achieve a minimum mean square error in a multi-fold cross-validation to provide the highest predictive accuracy. See tables for algorithms included. We also developed stacked predictive models for knees with and without ROA at baseline. We repeated the random split of data into training and testing sets 100 times, and for each run, we repeated model development and training, and evaluated performance in the independent 20% test set. We then listed the top 10 variables that contributed most to the prediction of KR across 100 runs by calculating a variable importance measure

Results: Our study sample included 2357 participants (mean age 61.6 [SD: 7.8] years, 62% female). The median area under the receive operating characteristic curves (AUCs) across 100 runs with and without MRI data were similar (Table 1). MRI features improved prediction of KR in knees without ROA. Prediction performance was higher in the sample as a whole as opposed to knees with and without ROA due in part to sample size (Table 1). Several variables were important contributors to KR prediction, even in knees free of ROA, including malalignment, race, and certain functional limitations. MRI features contributed to KR prediction based on the variable importance measures across 100 runs (Table 2).

Conclusion: Clinical and radiographic structural features as well as MRI features predict KR within 7 years with substantial accuracy, including in knees that had no ROA at baseline. The super learning-based predictive model development performed well and models that included MRI features did not substantially improve AUC over the models that included only clinical and radiographic data. Malalignment appeared to be an important target. Certain functional limitations were important contributors to the prediction of KR, while WOMAC pain symptoms (pain with stairs) only featured prominently in the clinical and radiographic model for ROA-free knees, suggesting that function may be a more important driver than previously recognized.

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Abstract Number: 1471

Healthy Lifestyle and Risk of Rheumatoid Arthritis in Women: A Prospective Cohort Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Epidemiology & Public Health II: Risk Factors & Outcomes

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: Many potentially modifiable biobehavioral factors have been associated with the risk of developing rheumatoid arthritis (RA), but the benefit of adopting an overall healthy lifestyle has not yet been examined. We investigated whether a healthy lifestyle, defined by a healthy lifestyle index score (HLIS), was associated with the risk of developing RA, overall and for seropositive or seronegative subtypes. We hypothesized that an increasingly healthy lifestyle, as measured by the HLIS, would be associated with reduced risk of RA, and we aimed to estimate the population attributable risk of these behaviors for RA.

Methods: We analyzed female nurses in the Nurses' Health Study (NHS) (1986-2016) and NHSII (1991-2017). Behavioral, demographic, and medical information were assessed on biennial questionnaires. Incident RA was confirmed

Table. Hazard ratios (95% CIs)[a] for risk of incident RA according to continuous and categorical healthy lifestyle index score (HLIS) among women in Nurses' Health Study (1986-2016) and Nurses' Health Study II (1991-2017).

Model[b]	Continuous HLIS, per unit increase[c, d]	HLIS[d] Categorical					
		0	1	2	3	4	5
All RA							
No. of cases/person-years	1219/4,467,872	144/380,333	385/1,202,966	376/1,416,397	231/979,556	73/416,423	10/72,197
Age-adjusted model	**0.86 (0.82, 0.90)**	1 (Ref)	0.8 (0.72, 1.06)	**0.75 (0.62, 0.92)**	**0.68 (0.62, 0.92)**	**0.52 (0.39, 0.69)**	**0.40 (0.21, 0.76)**
Multivariable model	**0.87 (0.83-0.91)**	1 (Ref)	0.88 (0.73-1.07)	**0.77 (0.63-0.93)**	**0.70 (0.57-0.87)**	**0.54 (0.40-0.72)**	**0.42 (0.22-0.80)**
Seropositive RA							
No. of cases/person-years	776/4,462,124	90/379,675	248/1,201,232	238/1,414,631	146/978,456	50/416,005	4/72,126
Age-adjusted model	**0.86 (0.80, 0.91)**	1 (Ref)	0.89 (0.70, 1.14)	**0.75 (0.59, 0.96)**	**0.68 (0.52, 0.89)**	**0.55 (0.39, 0.78)**	**0.25 (0.09, 0.67)**
Multivariable model	**0.86 (0.81-0.92)**	1 (Ref)	0.90 (0.71-1.15)	**0.76 (0.60-0.97)**	**0.69 (0.53-0.90)**	**0.57 (0.40-0.81)**	**0.25 (0.09-0.69)**
Seronegative RA							
No. of cases/person-years	443/4,456,963	54/379,254	137/1,199,730	138/1,412,750	85/977,346	23/415,751	6/72,134
Age-adjusted model	**0.87 (0.80, 0.94)**	1 (Ref)	0.84 (0.61, 1.16)	0.76 (0.55, 1.04)	**0.68 (0.48, 0.96)**	**0.45 (0.28, 0.74)**	0.69 (0.30, 1.61)
Multivariable model	**0.88 (0.81-0.96)**	1 (Ref)	0.85 (0.62-1.17)	0.78 (0.57-1.07)	0.71 (0.51-1.01)	**0.49 (0.30-0.80)**	0.75 (0.32-1.76)

Abbreviations: CI, confidence interval; RA, rheumatoid arthritis.

[a]Hazard ratios were calculated by using time-varying Cox proportional hazards models.

[b]Age-adjusted model adjusted for age, questionnaire cycle, cohort.

Multivariable model adjusted for age, questionnaire cycle, cohort, census tract median family income (quartiles), parity and breastfeeding (nulliparous, parous/no breastfeeding, parous/1–12 mo breastfeeding, or parous/>12 mo breastfeeding), hormone use (premenopausal, postmenopausal with never use, current use, or past use).

[c]Healthy lifestyle index score (HLIS) as a continuous score from 0 (no low-risk factors) to 5 (all low risk factors), where a higher score reflects a healthier lifestyle.

[d]Low-risk factors were defined as: never smoking; moderate alcohol consumption (5-15g/day); healthy body weight (body mass index 18.5–24.9 kg/m^2); healthy diet (AHEA in top 40th percentile); and healthy level of physical activity (at least 19 Met-hours/week).

by medical record review. We created a healthy lifestyle index score (HLIS), following previous work and using 5 established biobehavioral RA risk factors: smoking, alcohol consumption, BMI, physical activity, and diet. For each factor, we created a binary variable with the "healthy" categories: never smoking; moderate alcohol use (5-15g, or about one drink/day), normal body weight (BMI 18.5–24.9 kg/m$^{2)}$); regular exercise (at least 19 MET-hours/week, equivalent to at least 30 minutes of brisk walking every day); and healthy diet (in the top 2/5ths of the Alternative Healthy Eating Index). These were summed to create a HLIS, ranging from 0-5. Cox proportional hazards models, adjusted for confounders, modeled associations between HLIS (as continuous or categorical variables) and incident RA, overall and by serostatus. We calculated the population attributable risk (PAR) to estimate the proportion of incident RA in this population that would be prevented if all participants had adopted 4 or 5 healthy lifestyle factors.

Results: Among 107,090 women (mean age 43.7 years), we identified 1,219 incident RA cases (776 seropositive and 443 seronegative) in 4,467,872 person-years of follow-up (mean 24.0 years/participant). Higher continuous HLIS score was associated with a lower risk of RA (HR 0.87, 95% CI 0.83-0.91 per unit increase) overall, as well as with a lower risk of both seropositive RA (HR 0.86, 95% CI 0.81-0.92) and seronegative RA (HR 0.88, 95% CI 0.81-0.96) (**Table**). Women with all 5 healthy lifestyle factors had the lowest risk of developing RA (HR 0.42, 95% CI 0.22-0.80) and seropositive RA (HR 0.25, 95% CI 0.09-0.69), compared to those with no healthy lifestyle factors. The PAR for adhering to 4 or 5 lifestyle factors was 35% for overall RA.

Conclusion: In this large prospective cohort with lengthy follow-up, women who had a larger number of healthy lifestyle biobehaviors had a corresponding lower risk of both seropositive and seronegative RA. A large proportion of RA risk reduction may be attributable to healthy lifestyle independent of other confounders.Table. Hazard ratios (95% CIs)a for risk of incident RA according to continuous and categorical healthy lifestyle index score (HLIS) among women in Nurses' Health Study (1986-2016) and Nurses' Health Study II (1991-2017).

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Abstract Number: 1472

Assessing Causal Associations of Urate Levels with Type 2 Diabetes and Related Glycemic Traits Using Bidirectional Mendelian Randomization

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health III: Risk Factors & Outcomes
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Type 2 diabetes (T2D) and gout/hyperuricemia frequently coexist, but the nature and direction of this relationship is unclear. Observational studies have reported positive associations between gout/SU levels and risk of T2D but are subject to residual confounding or reverse causality bias. We used bidirectional two-sample Mendelian randomization to obtain unconfounded evidence of these potential causal effects.

Outcome: Insulin resistance (HOMA-IR: log units)		
Analysis	**Effect size (95% CI)**	**p-value**
Inverse weighted variance (Primary)	0.0091 (-0.0136 to 0.0318)	0.43
MR-Egger	-0.0095 (-0.0411 to 0.0221)	0.56
Weighted Median	0.0100 (-0.0145 to 0.0345)	0.42
Weighted Mode	0.0101 (-0.0111 to 0.0313)	0.35
MR-PRESSO (outlier-corrected)	0.0159 (-0.0051 to 0.0369)	0.14
Wald ratio (single *SLC2A9* SNP: rs4447862)	0.0106 (-0.0173 to 0.0385)	0.46
Wald ratio (single *ABCG2* SNP: rs74904971)	0.0252 (-0.0288 to 0.0792)	0.36
Outcome: Fasting insulin levels (log pmol/L)		
Analysis	**Effect size (95% CI)**	**p-value**
Inverse weighted variance (Primary)	0.0136 (-0.0369 to 0.0642)	0.60
MR-Egger	-0.0597 (-0.1358 to 0.0164)	0.13
Weighted Median	-0.0009 (-0.0290 to 0.0271)	0.95
Weighted Mode	-0.0046 (-0.0299 to 0.0206)	0.72
MR-PRESSO (outlier-corrected)	0.0190 (-0.0088 to 0.0468)	0.19
Wald ratio (single *SLC2A9* SNP: rs4447862)	-0.0073 (-0.0251 to 0.0105)	0.42
Wald ratio (single *ABCG2* SNP: rs74904971)	0.0039 (-0.0269 to 0.0348)	0.80
Outcome: HbA1c levels (%)		
Analysis	**Effect size (95% CI)**	**p-value**
Inverse weighted variance (Primary)	0.0044 (-0.0170 to 0.0257)	0.69
MR-Egger	0.0104 (-0.0197 to 0.0406)	0.50
Weighted Median	0.0086 (-0.0120 to 0.0292)	0.41
Weighted Mode	0.0051 (-0.0138 to 0.0240)	0.60
MR-PRESSO (outlier-corrected)	0.0114 (-0.0066 to 0.0294)	0.22
Wald ratio (single *SLC2A9* SNP: rs4447862)	0.0079 (-0.0159 to 0.0316)	0.52
Wald ratio (single *ABCG2* SNP: rs74904971)	0.0165 (-0.0290 to 0.0621)	0.48
Outcome: Type 2 diabetes (odds ratio)		
Analysis	**Effect size (95% CI)**	**p-value**
Inverse weighted variance (Primary)	1.17 (0.94 to 1.46)	0.17
MR-Egger	1.60 (0.98 to 2.61)	0.07
Weighted Median	1.16 (0.87 to 1.55)	0.32
Weighted Mode	1.38 (0.97 to 1.96)	0.08
MR-PRESSO (outlier-corrected)	n/a	n/a
Wald ratio (single *SLC2A9* SNP: rs4447862)	0.94 (0.80 to 1.10)	0.42
Wald ratio (single *ABCG2* SNP: rs74904971)	0.97 (0.73 to 1.31)	0.86

Table 1. Causal effect estimates for genetically-determined serum urate levels (per 1 mg/dL) on type 2 diabetes risk and other glycemic trait levels

Methods: Aggregate data from three large genome-wide association studies were used to identify genetic variants (SNPs) associated with SU levels (CKDGEN Consortium (*Nat Genetics* 2019; n=288,649 European-ancestry individuals; 123 SNPs)), T2D (DIAbetes Genetics Replication And Meta-analysis consortium (DIAGRAM: >34,000 T2D cases and >114,000 controls)), and related glycemic traits (Meta-Analyses of Glucose and Insulin-related traits Consortium

All risk SNPs for fasting insulin, including pleiotropic SNP mapped to *GCKR*		
Analysis	**Effect size, mg/dL (95% CI)**	**p-value**
Inverse weighted variance (Primary)	0.37 (0.15 to 0.58)	< 0.001
MR-Egger	-0.14 (-0.75 to 0.47)	0.66
Weighted Median	0.58 (0.45 to 0.71)	< 0.0001
Weighted Mode	0.67 (0.48 to 0.86)	< 0.0001
MR-PRESSO (outlier-corrected)	0.55 (0.44 to 0.66)	< 0.0001
All risk SNPs for fasting insulin, excluding pleiotropic SNP mapped to *GCKR*		
Analysis	**Effect size, mg/dL (95% CI)**	**p-value**
Inverse weighted variance (Primary)	0.51 (0.35 to 0.66)	< 0.0001
MR-Egger	0.45 (0.00 to 0.90)	0.18
Weighted Median	0.58 (0.45 to 0.71)	< 0.0001
Weighted Mode	0.67 (0.47 to 0.86)	< 0.0001
MR-PRESSO (outlier-corrected)	0.57 (0.46 to 0.69)	< 0.0001

Table 2. Causal effect estimates for genetically-determined levels of fasting insulin (ascertained in non-diabetics) on levels of serum urate (mg/dL)

(MAGIC): >200,000 in people without diabetes). These SNPs served as instrumental variables for the genetically determined exposures at conception, thus free of confounding by all factors after birth (e.g., lifestyle factors).

We first assessed the association between genetically-determined SU levels and T2D and levels of 3 glycemic traits, insulin resistance (HOMA-IR), fasting insulin (FI), and HbA1c, using inverse variance weighted (IVW) meta-analysis methods. We also separately examined the effects of SNPs from genes which regulate SU levels, *SLC2A9* and *ABCG2,* estimating Wald ratios for these individual SNPs.

We then assessed the effects of genetically-determined T2D and glycemic traits on changes in SU levels, including and excluding a pleiotropic SNP (rs1260326) mapped to the *GCKR* gene.

In addition to the main IVW analyses, we generated MR-Egger, weighted median and mode, and MR-PRESSO estimates to account for potential heterogeneity and horizontal pleiotropy.

Analyses were performed with the TwoSampleMR and MR-PRESSO packages in R.

Results: Estimated effects of genetically-determined SU levels on each of the four outcomes (HOMA-IR, FI, HbA1c, and T2D) were small and non-significant (**Table 1**); this was consistent across MR estimates. The *SLC2A9* and *ABCG2* SNPs were strongly associated with SU levels (beta=0.33 mg/dL, R^2=2.4% and beta=0.25 mg/dL, R^2=0.7%, respectively; both p< 0.001), but neither were associated with T2D or any glycaemic traits (**Table 1**).

In the opposite direction, there was a strong association between genetically determined levels of FI and SU (beta=0.37 mg/dL, p=0.001) (**Table 2**), which strengthened after excluding the pleiotropic SNP in *GCKR* (beta=0.52 mg/dL (95% CI 0.35 to 0.66), p< 0.001).

Conclusion: Evidence from this Mendelian randomization analysis suggests that genetically raised fasting insulin, a measure of insulin resistance and precursor to T2D, is causally associated with hyperuricemia. Results are consistent with cross-sectional/observational studies and corroborate physiologic evidence for insulin's anti-uricosuric property. Conversely, our data do not support a causal association of SU with FI levels or T2D risk. Interventions targeting SU levels are unlikely to lower T2D risk, whereas lowering insulin resistance would lower risk of gout.

Disclosure: N. McCormick, None; **M. O'Connor**, None; **S. Marozoff**, None; **J. Choi**, None; **A. Leong**, None; **H. Choi**, AstraZeneca, 2, Takeda, 5, Selecta, 5, GlaxoSmithKline, 5, Horizon, 5.

Abstract Number: 1473

A Combination of Healthy Lifestyle Behaviors Reduce Risk of Incident Systemic Lupus Erythematosus in the Nurses' Health Studies

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health III: Risk Factors & Outcomes
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: While the association between lifestyle factors such as alcohol consumption, smoking, and body mass index (BMI) and risk of SLE have been previously investigated, it is unclear how these behaviors may combine to reduce SLE risk. We prospectively evaluated whether a healthy lifestyle was associated with the risk of incident SLE and its subtypes, dsDNA positive (+) versus dsDNA negative (-) SLE. We hypothesized that greater adherence to a healthier lifestyle would be inversely associated with SLE risk.

Methods: We included 217,623 female nurses in the Nurses' Health Study (NHS) (1976-2016) and NHSII (1989-2017). Lifestyle and environmental were collected at baseline and on subsequent biennial questionnaires. Incident SLE was confirmed by medical record review. Healthy Lifestyle Index Score (HLIS) was calculated at baseline and approximately every 4 years in follow-up, using three lifestyle behaviors: alcohol consumption, BMI and smoking. For

Table. Incident SLE risk among women in Nurses' Health Study (1976-2016) and Nurses' Health Study II (1989-2017) according to Healthy Lifestyle Index Score (HLIS[1]) behaviors defined as drinking alcohol in moderation (5g/day to 15g/day), maintaining a healthy body weight (body mass index in 18.5–24.9 kg/m^2), and never smokers and past smokers (quit more than 4 years ago).

	Overall SLE (n=283)				dsDNA-Positive SLE (n =120)				dsDNA-Negative SLE (n=163)			
	Cases/person-years	MV HR (95%CI)[2]	P	p-trend	Cases/person-years	MV HR (95%CI)[2]	P	p-trend	Cases/person-years	MV HR (95%CI)[2]	P	p-trend
0 behaviors	19/269502	1.00 (ref)	-	-	10/269391	1.00 (ref)	-	-	9/269379	1.00 (ref)	-	-
1 behavior	133/2337444	1.00 (0.61-1.62)	0.99	-	62/2336573	0.80 (0.41-1.58)	0.53	-	71/2336593	1.22 (0.60-2.45)	0.58	-
2 behaviors	110/2444354	0.73 (0.45-1.19)	0.21	-	38/2443370	**0.46 (0.23-0.93)**	**0.03**	-	72/2443709	1.05 (0.52-2.12)	0.88	-
3 behaviors	21/763933	**0.45 (0.24-0.85)**	**0.01**	-	10/763691	**0.39 (0.16-0.94)**	**0.04**	-	11/763706	0.53 (0.22-1.28)	0.16	-
Per unit increase in behavior	283/5815233	**0.75 (0.64-0.88)**	-	**0.0003**	120/5813025	**0.67 (0.53-0.85)**		**0.001**	163/5813388	**0.82 (0.67-1.00)**	-	**0.048**

Abbreviations: CI, confidence interval; HR, hazard ratio; MV, multivariable; PY, person-years.
[1]Healthy lifestyle index score (HLIS) as a summed score from 0 (no healthy behaviors) to 3 (all healthy behaviors) or continuous score (per 1 unit of behavior change)
[2]Multivariable (MV)-adjusted hazard ratios (HR) from time-varying Cox proportional hazards models, adjusted for age (months), questionnaire cycle, cohort, race, census-tract median household income, oral contraceptive use, age at menarche, menopausal status

each factor, we created a binary low risk or healthy variable, defined as drinking alcohol in moderation (5g-15g/day), normal body weight (BMI 18.5–24.9 kg/m^2), and never or past smokers (quit >4 years), each previously associated with reduced SLE risk. A time-varying Cox hazards regression model estimated hazard ratios (HRs [95% confidence intervals]) for SLE risk, overall and by dsDNA subtype. The HLIS was modeled both categorically and continuously for number of healthy behaviors. We also calculated the partial population attributable risk (PAR%), an estimate of the percentage of incident SLE cases in this population during follow-up that would not have occurred if all participants had been in the lowest risk HLIS group (3 healthy behaviors).

Results: There were 283 incident SLE cases (120 anti-dsDNA positive and 163 anti-dsDNA negative) during 5,815,233 person-years of follow-up. In multivariable-adjusted models, we found that a higher continuous HLIS score was associated with a lower SLE risk overall (HR 0.75 [95%CI 0.64-0.88]) and both dsDNA subtypes (positive HR 0.67 [95%CI 0.53-0.85] and negative HR 0.82 [95%CI 0.67-1.00]) (**Table**). Women with all 3 healthy SLE behaviors had the lowest risk (overall HR 0.45 [95%CI 0.24-0.85] and dsDNA-positive HR 0.39 [95%CI 0.16-0.94]) of developing SLE compared to women with no healthy behaviors. Women who consumed moderate amounts of alcohol had a lower risk of developing SLE overall compared to those who consumed less alcohol (HR 0.62 [95%CI 0.46-0.83]). In addition, women who were never and past smokers were less likely to develop anti-dsDNA positive SLE (HR 0.55 [95%CI 0.36-0.85]) compared to current smokers and those who quit within last 4 years. PAR% revealed that 43.7% of SLE risk in this cohort could be attributable to healthy behaviors not in the lowest risk HLIS group.

Conclusion: Adherence to a healthy lifestyle was associated with a lower risk of SLE development overall and by dsDNA subtype compared to less healthy lifestyle. A larger reduction in risk was seen with each additional healthy behavior. Over 43% of SLE risk could be reduced if everyone had adhered to all three healthy lifestyle behaviors.

Disclosure: M. Choi, None; **J. Hahn**, None; **S. Malspeis**, None; **E. Stevens**, None; **E. Karlson**, None; **J. Sparks**, Optum, 1, Janssen, 1, Inova, 1, Gilead, 1, Amgen, 1, Bristol-Myers Squibb, 1, 2; **K. Yoshida**, OM1, 1, Corrona, 1; **L. Kubzansky**, None; **K. Costenbader**, Glaxo Smith Kline, 5, UpToDate, 7, Lupus Foundation of America, 6, Neutrolis Inc, 5.

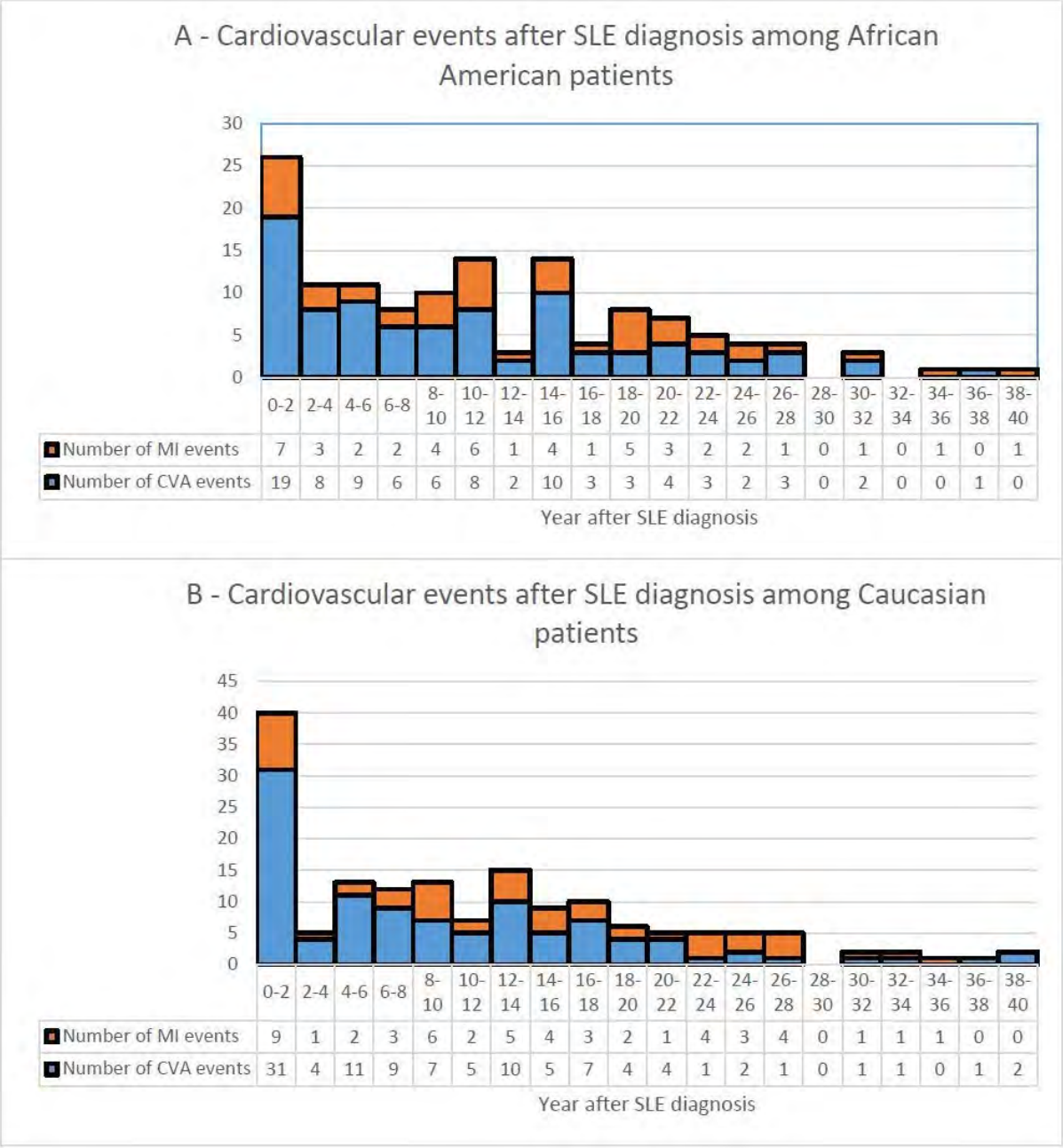
Abstract Number: 1474

Early Peak of Cardiovascular Events Occurs Equally in Caucasians and African-American SLE but Is Attributed to Different Risk Factors

Michelle Petri[1], Jessica Li[2] and Daniel Goldman[1], [1]Johns Hopkins University School of Medicine, Timonium, MD, [2]Johns Hopkins University, Baltimore, MD

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health III: Risk Factors & Outcomes
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

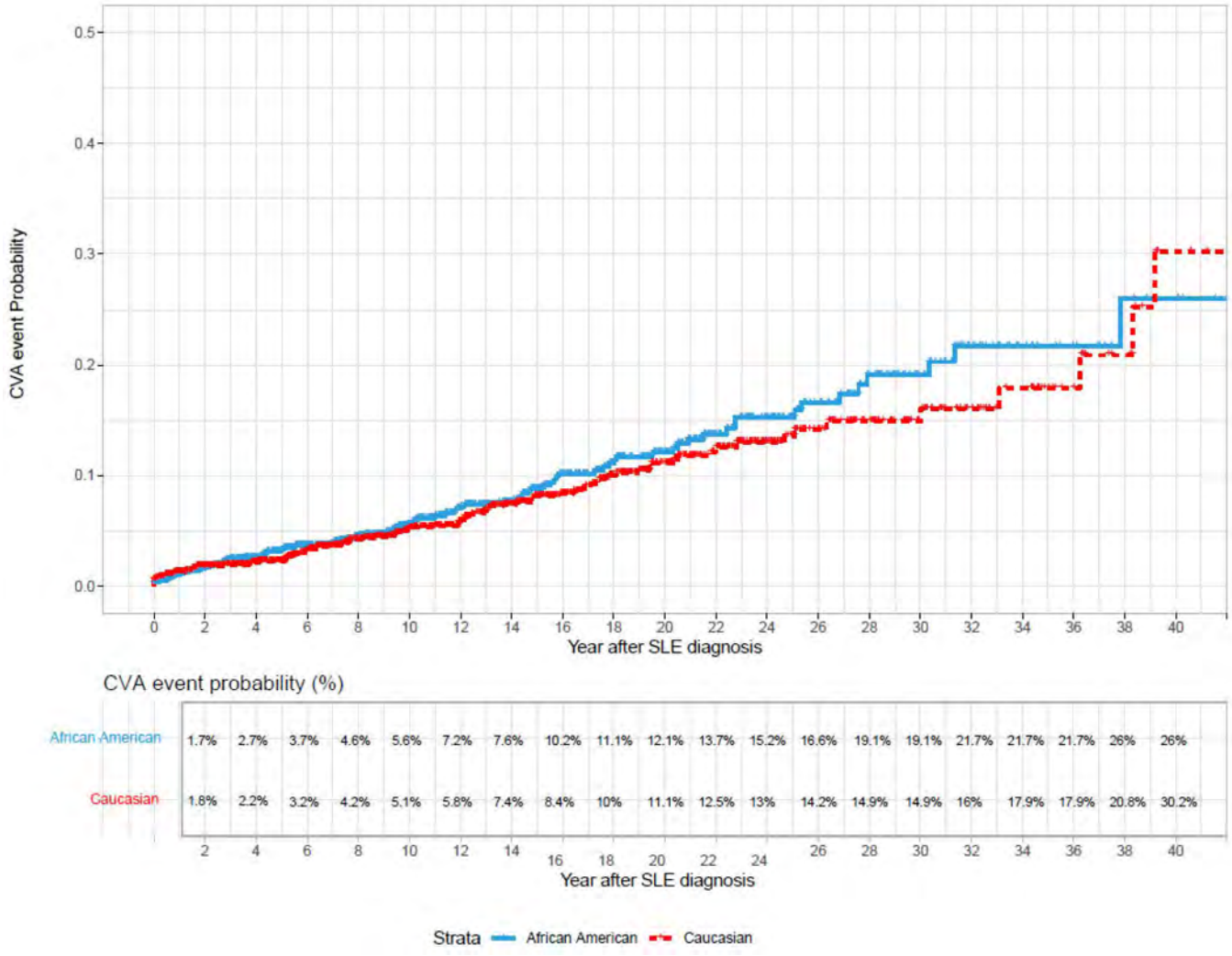
Background/Purpose: The classic bimodal pattern of morbidity/mortality in SLE highlighted that cardiovascular events occurred later in the natural history of SLE (Urowitz & Gladman. J Rheumatol 1980;7:412-16). This paradigm has now been challenged by the SLICC international inception cohort that found cardiovascular events early in the disease course (Urowitz et al. Lupus Sci Med 3:e000143, 2016). Furthermore, in the Georgia Lupus Registry, cardiovascular deaths peaked 1-2 years after diagnosis, with African-American ethnicity as the strongest predictor. We



Cardiovascular events (CVA and MI) by year after SLE diagnosis among African-American patients (A) and among Caucasian Patients (B)

examined the timing of cardiovascular events in a different U.S. cohort, balanced for Caucasian and African-American ethnicities.

Methods: SLE was defined by the revised ACR or SLICC classification criteria. Cardiovascular events were defined as myocardial infarction (MI) or stroke (ACC/AHA definition). In our cohort of 2,398 patients, 1,029 were African-American and 1,369 Caucasian. Nineteen were missing a SLE diagnosis date and 9 had missing data on events. There were 230 strokes and 116 myocardial infarctions.



Estimated Probability of Remaining Stroke Free for Caucasians and African Americans, by Year After SLE Diagnosis

Results: Figure 1A (African-American) and Figure 1B (Caucasian) show the number of cardiovascular events by ethnicity. The peak was years 0-2 after diagnosis for both ethnicities. Figure 2 is a Kaplan-Meier showing stroke probability by year after SLE diagnosis, with no difference found between African-American and Caucasian SLE. Similarly, there was no difference for MI. Table 1 shows that African-American and Caucasian SLE patients differed significantly in their risk factors for MI or for stroke. For example, hypertension was a significant risk factor in Caucasians for MI, while lupus anticoagulant was a significant risk factor in Caucasians for stroke.

Conclusion: In agreement with recent studies, we found an early peak of cardiovascular events (MI and stroke). Contrary to the Georgia Lupus Registry, we saw no difference for MI or storke in Caucasian vs. African-American patients by year after diagnosis. Instead, we found important differences in risk factors for stroke and MI in African-American vs Caucasian SLE patients.

	MI						CVA					
	All		African American		Caucasian		All		African American		Caucasian	
	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value	HR (95% CI)	p-value
Age at diagnosis	1.04 (1.02, 1.05)	**<0.0001**	1.02 (1, 1.05)	0.0916	1.05 (1.03, 1.07)	**<0.0001**	1.01 (0.99, 1.02)	0.2820	1.03 (1.01, 1.04)	**0.0045**	0.99 (0.98, 1.01)	0.3579
Sex: Male	2.82 (1.65, 4.83)	**0.0002**	2.77 (1.09, 7.07)	**0.0331**	2.98 (1.53, 5.81)	**0.0013**	0.96 (0.54, 1.68)	0.8780	0.93 (0.34, 2.56)	0.8956	0.99 (0.5, 1.96)	0.9669
African American	1.1 (0.74, 1.65)	0.6303	/	/	/	/	1.14 (0.85, 1.52)	0.3738	/	/	/	/
Low C3	1.01 (0.69, 1.58)	0.8363	1.09 (0.58, 2.01)	0.7967	0.99 (0.57, 1.74)	0.9828	1.74 (1.27, 2.38)	**0.0006**	1.87 (1.16, 3.01)	**0.0106**	1.62 (1.07, 2.47)	**0.0238**
Hypertension	1.73 (1.09, 2.74)	**0.0193**	1.08 (0.54, 2.16)	0.8297	2.36 (1.27, 4.36)	**0.0064**	2.05 (1.47, 2.87)	**<0.0001**	2.64 (1.43, 4.87)	**0.0020**	1.8 (1.19, 2.73)	**0.0057**
Lupus anticoagulant	1.48 (0.91, 2.41)	0.1108	1.88 (0.9, 3.92)	0.0942	1.27 (0.67, 2.43)	0.4667	1.78 (1.25, 2.51)	**0.0012**	1.32 (0.73, 2.37)	0.356	2.22 (1.43, 3.46)	**0.0004**
Anti-cardiolipin	0.93 (0.6, 1.46)	0.7642	1.04 (0.53, 2.04)	0.9117	0.85 (0.47, 1.55)	0.6036	1.5 (1.1, 2.05)	**0.0096**	1.5 (0.95, 2.37)	0.0828	1.53 (1, 2.32)	**0.048**
Cholesterol	2.48 (1.49, 4.11)	**0.0004**	3.35 (1.48, 7.54)	**0.0036**	1.98 (1.03, 3.79)	**0.0403**	2.14 (1.52, 3)	**<0.0001**	2.83 (1.66, 4.82)	**0.0001**	1.72 (1.1, 2.67)	**0.0164**
Diabetes	2.72 (1.48, 5.01)	**0.0013**	2.53 (1.11, 5.77)	**0.0267**	3.09 (1.22, 7.82)	**0.0174**	3.09 (1.95, 4.89)	**<0.0001**	2.98 (1.59, 5.56)	**0.0006**	3.22 (1.62, 6.42)	**0.0009**
Obesity	1.49 (0.98, 2.27)	0.0618	1.17 (0.62, 2.19)	0.6232	1.78 (1.01, 3.14)	**0.0454**	1.48 (1.1, 1.99)	**0.0105**	1.26 (0.8, 1.96)	0.3175	1.66 (1.11, 2.48)	**0.0143**
Ever smoking	2.04 (1.35, 3.08)	**0.0007**	1.76 (0.96, 3.23)	0.0660	2.32 (1.32, 4.07)	**0.0034**	1.18 (0.88, 1.58)	0.2755	1.36 (0.89, 2.08)	0.1592	1.03 (0.68, 1.55)	0.8979

HRs and p-values were calculated from cox proportional hazard models.

Associations Between Each Predictor and Event for All Patients and by Race

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Disclosure: M. Petri, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmithKline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5; **J. Li**, None; **D. Goldman**, None.

Abstract Number: 1475

Predictors of Thirty-Day Hospital Readmissions in Systemic Lupus Erythematosus in the US: A Nationwide Study

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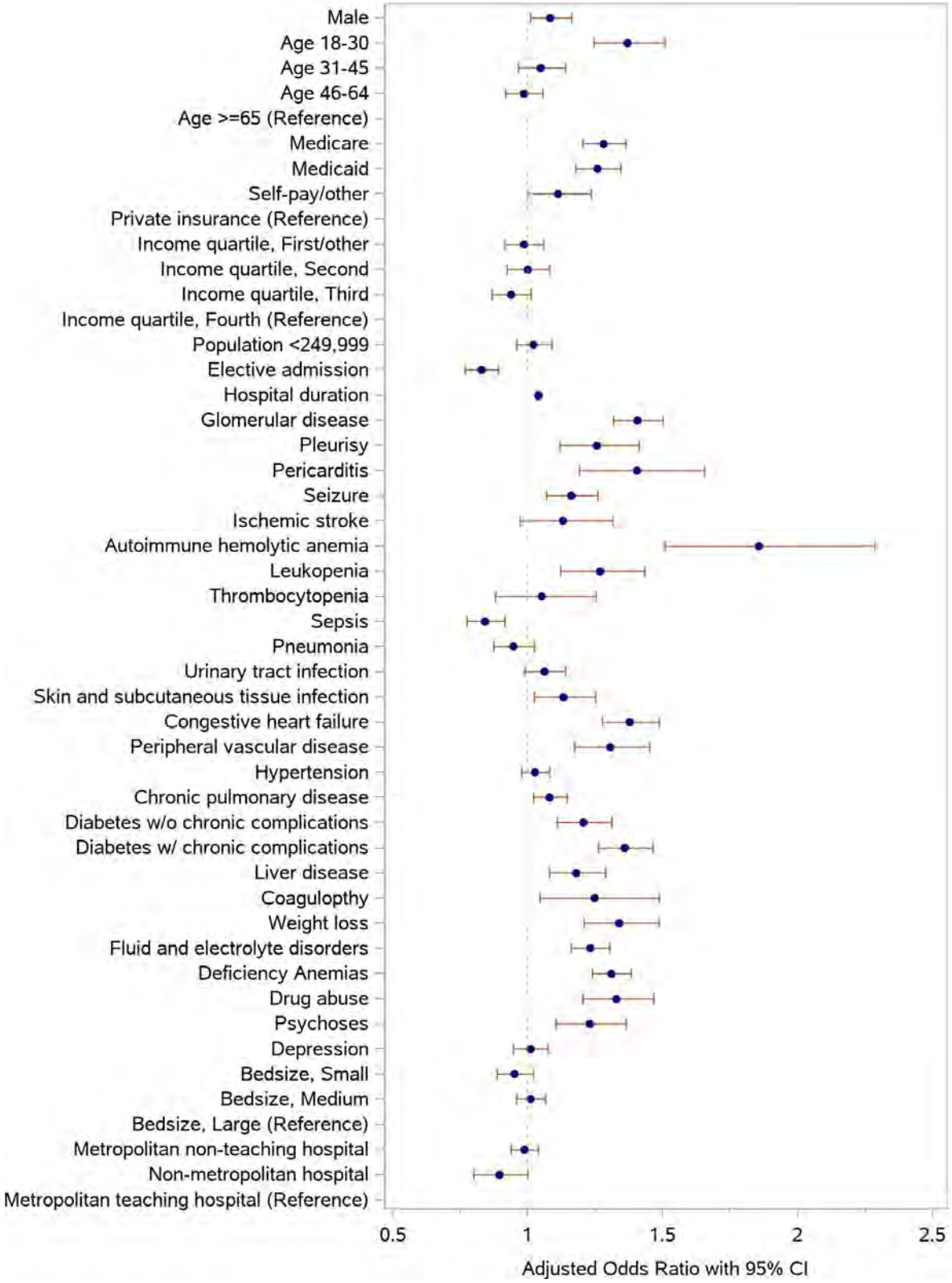

Multivariable Logistic Regression Model for Risk of 30-day Readmission in US Adults with Systemic Lupus Erythematosus, 2016-2017

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health III: Risk Factors & Outcomes
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Session Time: 5:00PM–5:50PM

Background/Purpose: For individuals with systemic lupus erythematosus (SLE), hospital readmission rate is associated with quality of care and prognosis. Our objective was to evaluate independent risk factors for readmission and determine the major reasons for readmission in a contemporary and nationally representative sample of SLE patients.

Methods: We used the Nationwide Readmissions Database (NRD) from the Healthcare Cost and Utilization Project (HCUP), which includes all-payer nation-wide data from US non-federal hospitalizations across 28 states, to identify adults with SLE who were discharged from hospital to home during January-November of 2016 and 2017. Subjects were identified using SLE ICD-10-CM primary and secondary diagnosis codes (M32.1-M32.9). 30-day all-cause readmissions were identified. Comorbidities were defined using the Elixhauser classification. Demographics (gender, age group, insurance, median income quartile by ZIP code, and population density), hospital-level variables (bedsize and teaching hospital), and SLE manifestation-related ICD-10-CM diagnosis codes (glomerular disease, pleurisy, pericarditis, seizure, ischemic stroke, autoimmune hemolytic anemia, leukopenia, and thrombocytopenia) were recorded. Survey-specific statistical methods were used to obtain weighted frequencies and percentages of study covariates. A multivariable survey-specific logistic regression model was used to identify factors associated with readmission adjusting for the covariates mentioned above. We identified the main cause of readmission using primary ICD-10-CM diagnosis codes for readmission and the HCUP Clinical Classifications Software, Refined.

Results: There were 132,400 hospitalized adults with SLE discharged home during the study period. 88.3% were female, with median age of 51.0 years (IQR 38.7-61.9). 18,973 (14.3%) people were readmitted within 30 days of discharge from their index hospitalization. Median hospital stay was 3.3 days (IQR 1.7-5.9) for readmitted patients and 2.5 (IQR 1.3-4.3) in patients without readmission. The predictors with largest magnitude of effect for readmission in an adjusted regression model were autoimmune hemolytic anemia [odds ratio (OR) 1.86, 95% CI 1.51-2.29], glomerular disease (OR 1.41, 95% CI 1.32-1.50), pericarditis (OR 1.40, 95% CI 1.19-1.66), heart failure (OR 1.38, 95% CI 1.28-1.49), and age 18-30 (OR 1.37, 95% CI 1.24-1.51, vs age ≥65) (Figure 1). The most common causes for readmission were sepsis (n=1,446, 7.6%), SLE (n=1,407, 7.4%), heart failure (n=668, 3.5%), pneumonia (n=605, 3.2%), and complication of surgical/medical care, injury (n=565, 3.0%) (Table 1).

Table 1. Frequencies and Percentages of Top 10 Reasons for Readmission in US Adults with Systemic Lupus Erythematosus, 2016-2017

Condition	Frequency	Percent
Sepsis	1,446	7.6
Systemic lupus erythematosus and connective tissue disorders	1,407	7.4
Heart failure	668	3.5
Pneumonia	605	3.2
Complication of other surgical or medical care, injury	565	3.0
Acute and unspecified renal failure	542	2.9
Chronic kidney disease	414	2.2
Skin and subcutaneous tissue infections	404	2.1
Fluid and electrolyte disorders	393	2.1
Complication of cardiovascular device, implant or graft	361	1.9

Conclusion: In this first nationally representative study of SLE readmissions, we identified independent risk factors for readmission in adult SLE patients discharged to home. The strongest identified risk factors were related to select SLE manifestations such as cytopenias and comorbidities such as diabetes and cardiopulmonary disease. Certain demographic features also contributed to risk, such as young age and public insurance.

Disclosure: R. Najjar, None; **S. Alexander**, None; **G. Hughes**, None; **J. Yazdany**, Eli Lilly, 5, Astra Zeneca, 5; **N. Singh**, Rheumatology Research Foundation, 2, American Heart Association, 2.

Abstract Number: 1476

Trends in Mortality and Cause-specific Mortality Among Patients with Psoriasis and Psoriatic Arthritis in Ontario, Canada

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Epidemiology & Public Health III: Risk Factors & Outcomes
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Several studies have consistently demonstrated that psoriasis is associated with an increased risk of mortality compared to the general population. However, the excess risk of mortality in psoriatic arthritis (PsA) is unclear, with observational studies yielding conflicting evidence. We aimed to compare overall and cause-specific mortality rates and their trends over time among patients with psoriasis, PsA and general population comparators without psoriatic disease living in Ontario, Canada.

Methods: We performed a population-based study using health administrative data among adult Ontario residents between 1996 and 2016. Patients diagnosed with psoriasis (from 1996 onward) and PsA (from 2008 onward) were identified using validated case definitions and compared with individuals without psoriatic disease. All-cause and cause-specific age- and sex-standardized mortality rates, standardized mortality ratios (SMRs) and excess mortality rates were computed for the years 1996 to 2016.

Results: A total of 176,858 psoriasis patients (2,524 deaths) and 15,430 PsA patients (221 deaths) were identified in 2016. All-cause mortality rates were greater among patients with psoriasis and PsA compared with the general population. The standardized mortality rate per 1000 (95% confidence interval [CI]) in 2016 was 8.26 (7.92, 8.62) among those with psoriasis and 9.25 (7.97, 10.69) among those with PsA compared to 6.82 (6.78, 6.86) in the general population. Patients with psoriasis and PsA had excess mortality rates of 5.70 (95% CI 5.20, 6.21) and 5.75 (95% CI 3.98, 7.71) per 1000 population, respectively. All-cause SMRs in 2016 were elevated for psoriasis: 1.18 (95% CI 1.13, 1.23); and PsA: 1.34 (95% CI 1.16, 1.52) (**Figure 1**). Standardized mortality rates decreased by approximately 30% over the study period in both disease groups, but remained elevated compared to the general population (**Figure 2**).

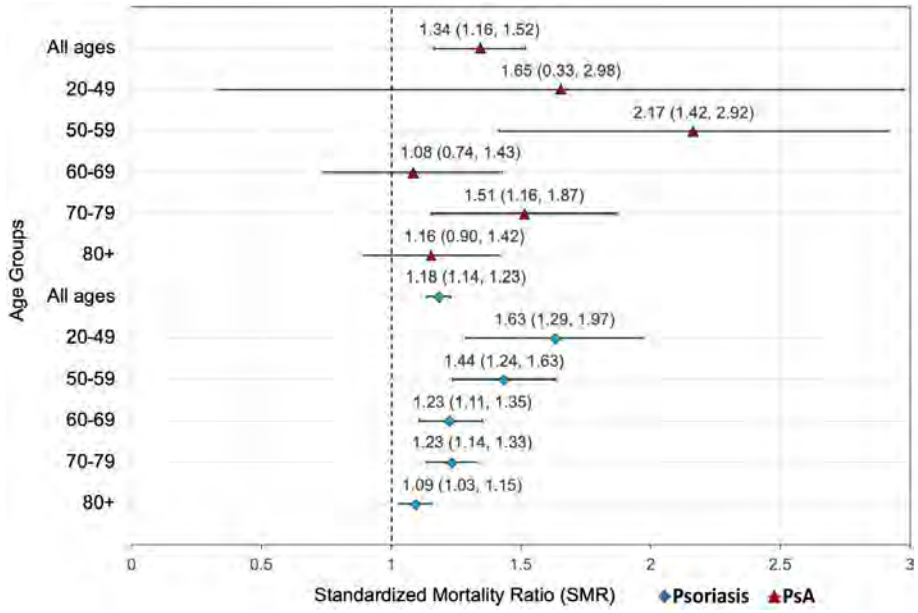

Figure 1. Age-specific Standardized Mortality Ratios (with 95% CI) in psoriatic arthritis (PsA) and psoriasis patients (2016).

The leading causes of death and corresponding SMRs in psoriasis patients were cancer (26.0%, SMR 1.11), circulatory diseases (25.6%, SMR 1.12), and respiratory conditions (11.7%, SMR 1.32) (**Figure 3**). In those with PsA, circulatory disease (26.2%, SMR 1.35) was the leading cause of death, followed by cancer (21.7%, SMR 0.96), and respiratory conditions (12.7%, SMR 1.69).

Conclusion: This study, the largest one to date that assessed trends in mortality rates and their underlying causes, showed that mortality rates in psoriasis and PsA have decreased over the past decade, but remain significantly elevated compared to the general population. Cardiovascular diseases, cancer and respiratory diseases remain the leading causes of mortality in psoriasis and PsA.

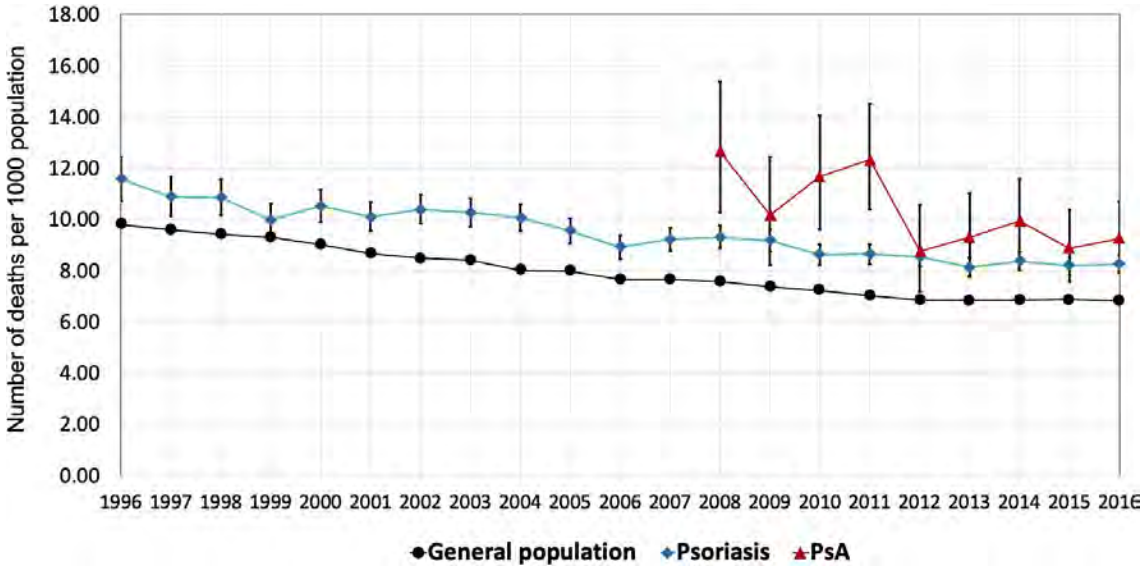

Figure 2. Annual age- and sex-standardized all-cause mortality rates among patients with psoriatic arthritis (PsA), psoriasis, and general population comparators (with 95% CI) from 1996 to 2016.

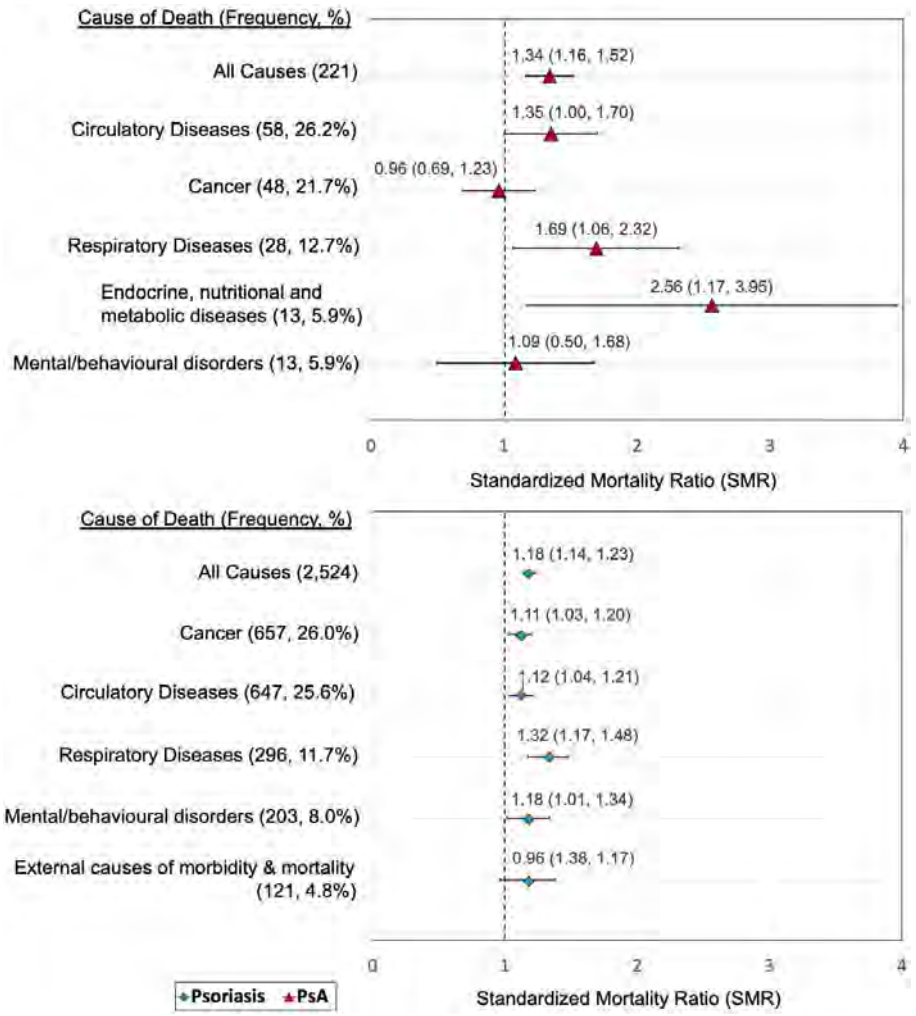

Figure 3. Standardized Mortality Ratios (with 95% CI) for the five leading causes of death in individuals with psoriatic arthritis (PsA) (top plot) and psoriasis (bottom plot) (2016). Causes of death are listed by chapter of the International Classification of Diseases, Tenth Revision.

Disclosure: K. Colaco, None; **J. Widdifield**, None; **J. Luo**, None; **C. Rosen**, Abbvie, 5, Novartis, 5, Eli Lilly, 5; **R. Alhusayen**, None; **J. Paterson**, None; **W. Campbell**, None; **K. Tu**, None; **S. Bernatsky**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **L. Eder**, AbbVie, 2, 5, 8, Eli Lilly, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5, 8, Celgene, 5, Novartis, 5.

Abstract Number: 1477

Adherence in Patients with Chronic Rheumatic Diseases Treated with Biological and Synthetic Targeted Therapies During COVID-19 Pandemic

Patricia Castro Pérez[1], Alberto Onteniente González[1], Angel Aragón Díez[1], Angel Gallegos Cid[1], Jesús Garcia-Arroba Muñoz[1] and Jose Manuel Rodriguez heredia[1], [1]Hospital de Getafe, Madrid, Spain

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases II: Evaluating Drug Therapies for COVID-19

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: Adherence to treatments for chronic rheumatic diseases is influenced by many factors, including the patient's belief in the development of adverse effects such as increased susceptibility to infection. It seems logical to think that immunosuppressive therapy increases the risk of severe affectation if SARS-CoV2 infection occurs and that many patients may tend to stop their biological treatment, especially in areas with a high incidence of COVID-19

The OBJECTIVE is to determinate the adherence in patients with rheumatic diseases treated with biological therapies during COVID-19 health crisis period in Madrid.

Methods: Prospective observational study. Telephone interviews were conducted between April 22 and May 15, 2020 (either by the rheumatologist or the hospital pharmacist) in patients with rheumatic diseases such us rheumatoid arthritis (RA), spondyloarthritis (SpA) and psoriatic arthritis (PsA) treated with any subcutaneus biological (bDMARD) or targeted synthetic disease-modifying antirheumatic drug (tsDMARD)

Patients were asked about continuation or discontinuation of any medication received for their chronic rheumatic disease, possible reasons that led to drug discontinuation (including fear of immunosuppresion and lack of resources/drug shortage), whether advise was received from a clinician or other sources. We also asked if they knew by the media channels that treatments for rheumatic diseases were being used in severe forms of COVID-19 infection. Patients were considered non-adherent if they had missed or delayed any of the prescribed doses. All patients received the medication through a home delivery system.

Results: We telephone-interviewed 400 patients followed-up in our centre (196 RA, 115 PsA and 89 SpA) during confinement period due to the coronavirus pandemic. 32 (8%) patients discontinued their treatment, 14 of them (43.75%) due to the fear of suffering the infection, 9 (28.12%) due to COVID-19 infection symptomatology , 4 (12.5%) for some reasons not related to COVID-19, 3 (9.38%) due to lack of resources/shortage of drug and 2 (6.25%) due to confirmed COVID-19 infection. 222 patients (58.57%) knew about the use of anti-rheumatic drugs for the treatment of COVID-19 infection.

Conclusion: Adherence to treatment for rheumatic diseases during the COVID-19 health crisis period was very high in Madrid, despite of being one of the cities hardest hit by the SARS-CoV-2.

A high Knowledge of the use of anti-rheumatic drugs for the treatment of COVID-19 on the media channels and the better access to treatments through a home delivery system has contributed to this adherence.

The main reasons that led to drug discontinuation was the fear of suffering the infection or for having COVID-19 infection symptomatology.

Although the presence of COVID-19 infection was not the reason for the survey, we only found 2 patients diagnosed of COVID-19 with positive PCR test for SARS-CoV-2, and 9 posible patients, due to the symptoms they reffered, among our 400 patients. However, these findings point in the direction that COVID-19 course and mortality in patients with chronic rheumatic diseases treated with b/tsDMARD do not differ from the general population. Doubtlessness, additional studies are still needed.

Disclosure: P. Castro Pérez, None; **A. Onteniente González**, None; **A. Aragón Díez**, None; **A. Gallegos Cid**, None; **J. Garcia-Arroba Muñoz**, None; **J. Rodriguez heredia**, None.

Abstract Number: 1478

A Multidisciplinary Registry of Patients with Autoinmune and Immune-Mediated Diseases with Symptomatic COVID-19 Infection from a Single Center

Juan C Sarmiento-Monroy[1], Gerard Espinosa[2], Fernanda Meira[1], Berta Caballol[3], Maria C Londoño[3], Sara Llufriu[3], Aina Moll[1], Luis Fernando Quintana Porras[1], Felipe Julio Ramirez Garcia[4], José Inciarte-Mundo[1], Elisabeth Solana[1], Yolanda Blanco[1], Eugenia Martinez[1], Victor Llorens[1], Sergio Prieto-González[5], Georgina Espigol[1], Jose C Milisenda[1], Maria C. Cid[5], Priscila Giavedoni[1], Jose M Mascaró[1], Isabel Blanco[1], Joan Albert Barbera[1], Oriol Sibila[1], Jordi Gratacos-Gines[1], Alfredo Adan[2], Alvaro Agustí[1], Raimon Sanmartí[6], Julián Panés[1], Ricard Cervera[1], Jordi Vila[1], Alex Soriano[1], Jose Gómez-Puerta[6] and On behalf INMUNOCOVID CLINIC[7], [1]Hospital Clinic de Barcelona, Barcelona, Catalonia, Spain, [2]Hospital Clinic, Barcelona, Catalonia, Spain, [3]Hospital Clinic de Barcelona, Barcelona, Spain, [4]Arthritis Unit, Rheumatology Dpt, Hospital Clinic, Barcelona, Spain, Barcelona, Catalonia, Spain, [5]Vasculitis Research Unit, Department of Systemic Autoimmune Diseases, Hospital Clínic de Barcelona, IDIBAPS, University of Barcelona, Barcelona, Spain., Barcelona, Catalonia, Spain, [6]Hospital Universitari Clínic de Barcelona, Barcelona, Catalonia, Spain, [7]Hospital Clinic de Barcelona, Barcelona

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases II: Evaluating Drug Therapies for COVID-19

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: National health authorities reported a prevalence of SARS-CoV-2 infection around 7% of the general population in Barcelona county (1). A recent report focused on autoimmune and immune-mediated inflammatory disease (AI/IMID) in Spain reported a slightly higher prevalence than in general population, especially in patients under targeted therapies and patients with systemic disease (2). Our aim was to analyze clinical characteristics and outcomes in a multidisciplinary cohort of patients with AI/IMID and symptomatic COVID-19 infection in a single tertiary center.

Methods: We included confirmed cases with RT-PCR SARS-CoV-2 test positive after nasopharyngeal swab according to Microbiology registry from Hospital Clinic of Barcelona from the 1st of March until May 29th, 2020. Data was matched with our registry of AI/IMID diseases. Additionally, patients under clinical follow-up for AI/IMID underwent a telephone survey to establish probable cases according CDC classification. We evaluated clinical characteristics and COVID-19 outcomes including clinical complications, need for ICU admission, and death as well as markers of systemic inflammatory response.

Results: From a total of 1,709 patients who gave positive for RT-PCR SARS-CoV-2, we identified 1,448 single patients. Around 5.000 patients with AI/IMID are under follow-up in our center. Thirty-one patients (23 female) with AI/IMID were identified, with a median age of 53 (IQR 25) years. Twenty-six cases were confirmed by PCR and 5 were diagnosed as probable cases. Main comorbidities included hypertension in 32% of cases and chronic pulmonary disease in 16%. Rheumatoid arthritis and inflammatory bowel disease were the most common diseases in 29% and 22%, respectively. Clinical characteristics of COVID-19 patients with AI/IMID are summarized in **Table 1**. Nine (29%) out of 31 patients were under glucocorticoid treatment (mean dose 7.0 ± 5.5 mg/d), 4 (12.9%) under hydroxychloroquine (HCQ), 9 under methotrexate (29%), and 8 (25.8%) under targeted synthetic/biologic DMARDs (mainly TNF inhibitors). A total of 16 (51%) patients had pneumonia and required admission. There were no differences between admission rates according to age, gender, underlying diagnosis, or baseline treatment. Most patients (87%) received the institutional standard treatment for COVID-19 with Lopinavir/ritonavir, HCQ and azithromycin. One patient had renal insufficiency and a pulmonary complication that resolved before discharge. Only 1 patient required ICU admission

	n/31 (%) Median (IQR)	n/Total population (%)
Female gender	23 (74.2)	
Age, years	53 (25)	
Comorbidities	22 (71)	
Hypertension	10 (32.3)	
Chronic pulmonary disease	5 (16.1)	
Hypothyroidism	5 (16.1)	
Type 2 Diabetes Mellitus	3 (9.7)	
AI/IMID		
Total	31 (100)	31/4.996 (0.62)
Disease duration, years	11 (20)	
Rheumatoid arthritis	9 (29.0)	9/600 (1.5)
Inflammatory bowel disease*	7 (22.6)	7/1.711 (0.4)
Behçet's disease	4 (12.9)	4/180 (2.2)
Spondyloarthritis	3 (9.7)	3/400 (0.7)
Systemic lupus erythematosus	3 (9.7)	3/ 500 (0.6)
Psoriatic arthritis	2 (6.5)	2/600 (0.3)
Systemic sclerosis	1 (3.2)	1/320 (0.3)
Autoimmune hepatitis	1(3.2)	1/255 (0.5)
Idiopathic uveitis	1 (3.2)	1/430 (0.23)
Total		
Baseline treatment		
Glucocorticoids	9 (29)	
csDMARDs	17 (54.8)	
Methotrexate	9 (29)	
HCQ	4 (12.9)	
Leflunomide	2 (6.5)	
Azathioprine	2 (6.5)	
ts/bDMARDs	8 (25.8)	
Anti-TNF	5 (16.1)	
Ustekinumab	1 (6.5)	
Vedolizumab	1 (6.5)	
Baricitinib	1 (6.5)	

*Crohn's disease and ulcerative colitis. AI/IMID: autoimmune and immune-mediated disease; csDMARDs: conventional synthetic Disease-modifying antirheumatic drugs; HCQ: hydroxychloroquine; IQR: interquartile range; ts/bDMARDs: targeted synthetic/biologic Disease-modifying antirheumatic drugs

Table 1. General characteristics of symptomatic COVID-19 patients with AI/IMID

and another patient died due to COVID-19 infection. Characteristics and clinical outcomes of patients admitted due to COVID-19 are summarized in **Table 2**. During admission, immunosuppressive therapies were stopped in 7 (43%) cases and ts/bDMARDs in 3 (18%) cases. Four patients presented a clinical flare.

Conclusion: In our center, less than 1% of patients with AI/IMID had symptomatic COVID-19 infection. Most patients had a satisfactory outcome; including patients under ts/bDMARDs and clinical fares during admission and follow-up were uncommon. We are running comparative analysis with other populations and evaluating the prevalence of asymptomatic COVID-19 infection in patients AI/IMID.

Disclosure: J. Sarmiento-Monroy, None; **G. Espinosa**, None; **F. Meira**, None; **B. Caballol**, None; **M. Londoño**, None; **S. Llufriu**, None; **A. Moll**, None; **L. Quintana Porras**, None; **F. Ramirez Garcia**, None; **J. Inciarte-Mundo**, None; **E. Solana**, None; **Y. Blanco**, None; **E. Martinez**, None; **V. Llorens**, None; **S. Prieto-González**, None; **G. Espigol**, None; **J. Milisenda**, None; **M. Cid**, Kiniksa, 2; **P. Giavedoni**, None; **J. Mascaró**, None; **I. Blanco**, None; **J. Barbera**, None; **O. Sibila**, None; **J. Gratacos-Gines**, None; **A. Adan**, None; **A. Agustí**, None; **R. Sanmartí**, None;

	n/16 (%) Median (IQR)
Female gender	11 (68.8)
Age, years	51 (35)
Symptom duration before admission, days	6 (6)
Main symptoms	
Cough	14 (87.5)
Dyspnea	4 (25)
Headache	4 (25)
Prognostic factors (*)	
C-reactive protein, > 1mg/dL	13 (81.3)
Ferritin, > 400 ng/mL	4 (25)
D-dimer, > 500 ng/mL	7 (43.8)
LDH, > 234 U/L	10 (62.5)
Lymphopenia, < 900 10^9/L	9 (56.3)
Anti-viral and anti-inflammatory treatment	
LPV/r + HCQ + AZT	14 (87.5)
Remdesivir	2 (12.5)
Glucocorticoids	4 (25)
Anti-IL-6	5 (31.3)
Anti-IL-1	2 (12.5)
Hospitalization duration, days	7 (9)
ICU admission	1 (6.3)
Complications	2 (12.5)
Respiratory	1 (6.3)
Acute kidney injury	1 (6.3)

AZT: azithromycin; HCQ: hydroxychloroquine; ICU: intensive care unit; IQR: interquartile range; LDH: lactate dehydrogenase; LPV/r: Lopinavir/ritonavir.
*Proportion of patients with abnormal values

Table 2. Characteristics and clinical outcomes of patients admitted due to COVID-19

J. Panés, None; **R. Cervera**, None; **J. Vila**, None; **A. Soriano**, None; **J. Gómez-Puerta**, Abbvie, 8, BMS, 8, GSK, 8, Lilly, 8, MSD, 8, Janssen, 8, Pfizer, 8, Roche, 5, 8; **O. INMUNOCOVID CLINIC**, None.

Abstract Number: 1479

Long-Term Effectiveness of Canakinumab in Autoinflammatory Diseases – Interim Analysis of the CAPS Subgroup from the RELIANCE Registry

Jasmin Kuemmerle-Deschner[1], Birgit Kortus-Goetze[2], Michael Borte[3], Ivan Foeldvari[4], Gerd Horneff[5], Ales Janda[6], Tilmann Kallinich[7], Prasad T. Oommen[8], Catharina Schuetz[9], Frank Weller-Heinemann[10], Julia Weber-Arden[11] and Norbert Blank[12], [1]University Hospital Tuebingen, Tuebingen, Germany, [2]Division of Nephrology, University of Marburg, Germany, Marburg, Germany, [3]ImmunoDeficiencyCenter Leipzig (IDCL), Hospital St. Georg gGmbH Leipzig, Germany, Leipzig, Germany, [4]Head of the Hamburg Centre for Pediatric and Adolescence Rheumatology, Budapest, Hungary, [5]Asklepios Clinic Sankt Augustin, Sankt Augustin, Germany, [6]Department of Pediatrics, University Hospital Ulm, Germany, Ulm, Germany, [7]Charite, Berlin, Germany, [8]Clinic of Pediatric Hematology, Oncology and Clinical Immunology, Heinrich-Heine-University Duesseldorf, Duesseldorf, Germany, [9]Department of Pediatric Immunology, University Hospital Dresden, Dresden, Germany, Dresden, Germany, [10]Klinikum Bremen-Mitte, Prof. Hess Kinderklinik, Bremen, Germany, Bremen, Germany, [11]Novartis Pharma GmbH, Nuremberg, Germany, [12]Department of Hematology, Oncology and Rheumatology, Internal Medicine V, University Hospital of Heidelberg, Eppelheim, Germany

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases II: Evaluating Drug Therapies for COVID-19

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: In the treatment of monogenic autoinflammatory diseases (AID), a heterogeneous group of diseases with excessive interleukin (IL)-1β release and severe systemic and organ inflammation, the anti-IL-1 inhibitor canakinumab (CAN) has been associated with rapid remission of symptoms in clinical trials as well as in real-life.[1,2]

The aim of the RELIANCE registry is to explore long-term effectiveness and safety of CAN under routine clinical practice conditions in patients with CAPS (cryopyrin-associated periodic syndromes, including Muckle-Wells syndrome [MWS], familial cold autoinflammatory syndrome [FCAS], neonatal onset multisystem inflammatory disease [NOMID]/chronic infantile neurological cutaneous and articular syndrome [CINCA]), FMF (familial Mediterranean fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/mevalonate kinase deficiency).

[1]Kuemmerle-Deschner et al. Rheumatology (Oxford). 2016;55(4):689-96

[2]De Benedetti et al. N Engl. J Med. 2018;378(20):1908-1919

Methods: This prospective, non-interventional, observational study based in Germany has a 3-year follow-up and enrolls pediatric ≥2 years and adult patients with clinically confirmed diagnoses of CAPS, FMF, TRAPS and HIDS/MKD routinely receiving CAN. In 6-monthly visits, clinical data and patient-reported outcomes are assessed. Study endpoints are long-term effectiveness and safety of CAN. Here, the CAPS cohort was analyzed.

Results: This 18-month interim-analysis includes 78 CAPS patients (49% females) enrolled by September 2019. Mean age at baseline was 25 years and mean duration of prior CAN treatment was 5.7 years. 64 patients (82%) had MWS, 2 FCAS, 7 NOMID/CINCA, 3 atypical CAPS and 2 lacked subtype diagnosis. Preferred CAN doses and inter-

Table 1: Patient and physician assessment of clinical CAPS disease activity and laboratory markers over time.

	Baseline	6 months	12 months	18 months
Number of patients, N	78	51	42	29
Mean age, years (SD)	25 (4; 79)	22 (4; 79)	20 (4; 58)	22 (4; 54)
Patient's assessment of disease activity 0-10, mean (min; max)	2.2 (0; 7)	1.8 (0; 7)	2.4 (0; 7)	2.8 (0; 8)
Patient's assessment of fatigue 0-10	2.9 (0; 9)	2.4 (0; 8)	2.8 (0; 8)	1.7 (0; 7)
Number (%) of patients without impairment of social life by disease	16 (49)	29 (76)	20 (61)	14 (67)
Number (%) of patients with days absent from school/work	25 (32.5)	11 (22)	14 (34)	15 (52)
Inflammatory markers, CRP/SAA, mean (mg/dL)	0.4 / 3.2	0.4 / 2.1	0.3 / 0.8	0.2 / 0.5
Number (%) of patients in disease remission (physician assessment)	55 (72)	38 (76)	29 (71)	22 (76)

Table 1. Patient and physician assessment of clinical CAPS disease activity and laboratory markers over time

Table 2: Patient-Reported Outcome: Median AIDAI Score Over 12 Months (no 18 months data available)

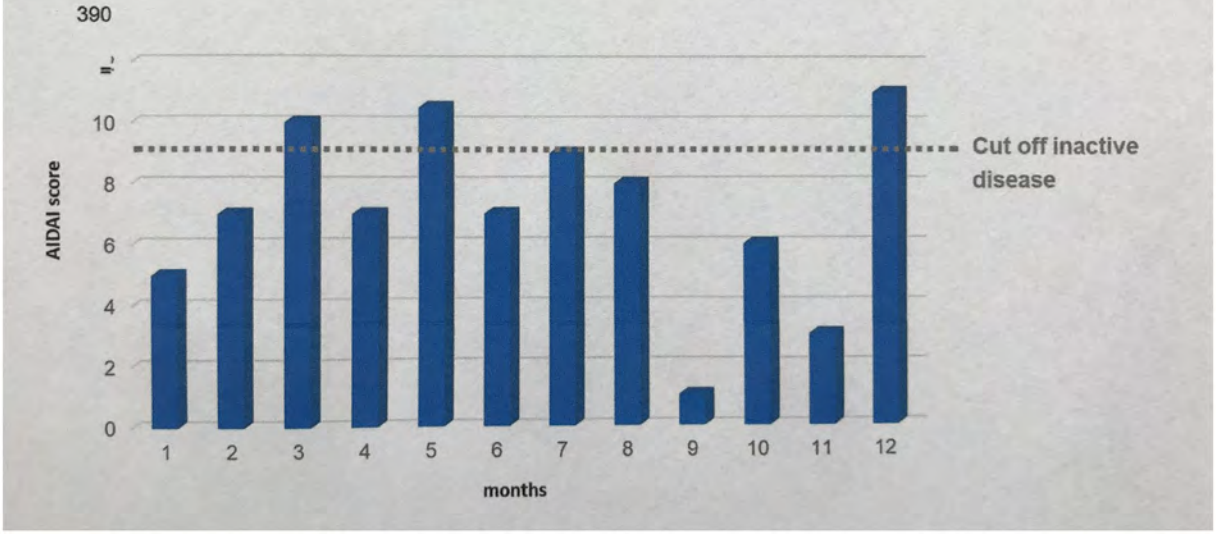

Table 2. Patient-Reported Outcome: Median AIDAI Score Over 12 Months (no 18 months data available)

Table 3: Adverse events – incident rates per 100 patient years

2nd Interim analysis main sample (MS1)

Event category	No. of events	Incidence rate per 100 patient years
Any adverse event	208	197.77
Any non-serious adverse event	181	172.09
Any not related non-serious adverse event	78	74.16
Any drug-related non-serious adverse event	103	97.93
Any serious adverse event	27	25.67
Any not related serious adverse event	11	10.46
Any drug-related serious adverse event	16	15.21

Table 3. Adverse events – incident rates per 100 patient years

vals (% of all injections) were 300 mg q4w (every 4 weeks; 10.4), 150 mg q4w (16.9), 150 mg q8w (13.7) and 150 mg more than q9w (9). Disease activity, fatigue and social impairment by patients' assessment, days absent from school/work, inflammatory markers, and remission by physician assessment were evaluated at 6-monthly intervals starting at baseline with last update at 18 months of follow-up (Table 1). The patient–reported AIDAI score of disease activity revealed inactive disease in 9 out of 12 months (Table 2). The results demonstrate sustained remission and disease control to remain stable over time. The incidence rate per 100 patient years was 25.67 for any serious adverse event (SAE) including 15.21 for serious drug-related adverse events (drSAE; Table 3). DrSAE were reported for 10/78 patients including cardiovascular disorder, pyrexia (3), chest pain, appendicitis, tonsillitis (2), haemophilus test positive,

circulatory collapse, febrile convulsion, skin disorders (3), tonsillectomy, and preterm delivery. No deaths were reported. 3/78 patients discontinued CAN, 2 due to inefficacy, 1 due to loss of efficacy.

Conclusion: The 18-month interim analysis of the RELIANCE study, the longest running real-life CAN registry, demonstrates that long-term CAN treatment is well tolerated and effective in CAPS patients.

Disclosure: J. Kuemmerle-Deschner, Novartis, 2, 5, AbbVie, 2, 5, SOBI, 2, 5; **B. Kortus-Goetze**, Novartis, 5; **M. Borte**, Pfizer, 2, Shire, 2; **I. Foeldvari**, Sanofi, 5, Chugai, 5, Amgen, 5, GSK, 5, Lilly, 5, BMS, 5, Abbvie, 5, Novartis, 5, gilead, 5; **G. Horneff**, Pfizer, 5, 8, AbbVie, 5, 8, Novartis, 5, 8, Sanofi, 5, 8; **A. Janda**, None; **T. Kallinich**, None; **P. Oommen**, Novartis, 5; **C. Schuetz**, None; **F. Weller-Heinemann**, None; **J. Weber-Arden**, Novartis, 3; **N. Blank**, None.

Abstract Number: 1480

Abatacept for the Treatment of IgG4-Related Disease

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases II: Evaluating Drug Therapies for COVID-19
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: To assess the efficacy and safety of abatacept (ABA) for the treatment of IgG4-related disease (IgG4-RD). To date, there are no FDA-approved treatments available for IgG4-RD. The efficacy of ABA in the context of IgG4-RD has been reported in a single case report but not yet studied further.

Methods: We conducted a prospective, open-label trial of ABA in 10 patients with active IgG4-RD. All subjects met the ACR/EULAR Classification Criteria for IgG4-RD and had active disease based on an IgG4-RD responder index (RI) of ≥2 with disease manifestations in at least one organ system at the time of screening. Patients received subcutaneous ABA 125 mg weekly for 24 weeks. Concurrent glucocorticoid treatment was permitted but was required to be discontinued by week 4. The primary endpoint, complete remission at 24 weeks, was defined as an IgG4-RD RI score of 0 and a secondary endpoint, disease response, was defined as improvement of ≥ 1 point in the IgG4-RD RI score from baseline. Achieving either outcome required no glucocorticoid use beyond week 4 and no disease flares. PBMCs were collected at baseline, 1-month and 3-month time points and B and T cell subsets were quantitated using a 25-parameter flow cytometry panel.

Results: Ten subjects were enrolled in the study between December 2018 and August 2019. Median age was 67.5 years, 70% were male and 90% Caucasian. Eight subjects had both orbital and salivary gland involvement, while five subjects had lung involvement. All patients had elevated serum IgG4 concentrations of at least 2-fold the upper limit of normal (range 170 to 1,359.5 mg/dL, median 480.5 mg/dL). Two subjects received prednisone with ABA. Three subjects (30%) achieved the primary endpoint of complete remission and two subjects (20%) had a disease response at week 24. ABA was stopped early in the remaining five subjects (50%) due to flare (N=1) or lack of response by week 12 (N=4). Although serum IgG4 concentrations declined in only two of the five subjects with any response, serum IgE concentrations declined in all five (baseline median 802 IU/mL, IQR 260-4981 IU/mL, 24 week median 470

IU/mL, IQR 138-2417 IU/mL). Response to treatment correlated most strongly with a reduction in circulating plasmablasts (p=0.016) with a trend towards significant reduction in HLA-DR$^+$ CD4$^+$ T cells (p=0.056). There was also a trend toward significant correlation between the change in plasmablast numbers and serum IgE but not with IgG4. Surface expression of CD86 on memory B cells was less detectable among responders as compared to non-responders (p=0.016). PD1$^+$CXCR5$^+$CD4$^+$ T cells did not correlate with clinical response, plasmablasts, serum IgE or serum IgG4. There was one adverse event (grade 2 thrombocytopenia) attributed to ABA.

Conclusion: Although subcutaneous ABA was associated with a high rate of treatment failure in patients with IgG4-RD, some patients had excellent clinical responses that correlated well with measures of immunologic response. Correlates of clinical response included reductions in serum IgE, circulating plasmablasts, activated CD4$^+$ T cells, and detectable surface expression of CD86. It is possible that the higher dose of ABA offered by intravenous administration may be more effective.

Disclosure: M. Matza, None; **C. Perugino**, Union Chimique Belge, 2, Bristol-Myers Squibb, 5; **L. Harvey**, None; **Z. Wallace**, Bristol-Myers Squibb, 2; **H. Liu**, None; **S. Pillai**, Abpro Inc., 6; **J. Stone**, Roche, 2, 5, Genentech, 2, 5.

Abstract Number: 1481

A Systematic Review to Quantify the Extent of Pharmaceutical Company Involvement in Rheumatology Consensus-Based Recommendations

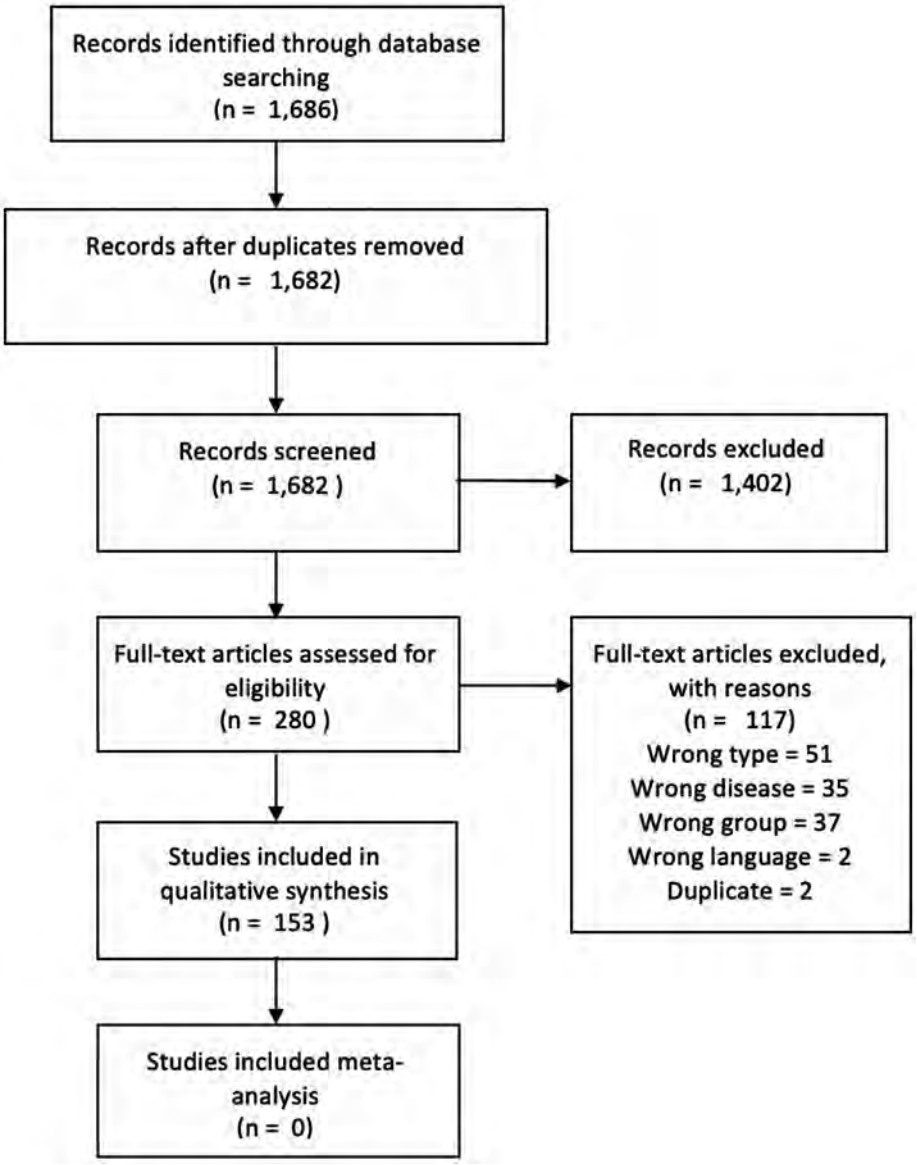
Dominique Feterman Jimenez[1], Garret Duron[2], Ali Duarte-Garcia[3], Paul Sufka[4], Samuel Whittle[5], Philip Robinson[6], Larry Prokop[3] and Michael Putman[7], [1]UConn Health Center, Farmington, CT, [2]HCA Memorial Health University Medical Center, Savannah, GA, [3]Mayo Clinic, Rochester, MN, [4]Healthpartners, St Paul, [5]Rheumatology Unit, The Queen Elizabeth Hospital, Springfield, South Australia, Australia, [6]University of Queensland, Herston, Queensland, Australia, [7]Northwestern University, Chicago, IL

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases II: Evaluating Drug Therapies for COVID-19
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Consensus-based recommendations guide standards of care for clinical practice. Pharmaceutical-industry involvement in producing such recommendations may undermine their objectivity. We performed a systematic review to quantify the extent of pharmaceutical company involvement in rheumatology consensus based recommendations in the field of rheumatology.

Methods: A comprehensive search of several databases from their inception to April 21st, 2020 was conducted. The search strategy was designed by an experienced librarian with input from the study's investigators. Eligibility criteria included (1) English language (2) consensus-based recommendations that assessed (3) pharmacotherapy of (4) rheumatic diseases after (5) January 1st, 2000. Pairs of reviewers screened articles and extracted data. Categorical variables were assessed using Fisher's exact test; yearly publications were analyzed using a linear regression.

Results: The search identified 1,686 articles, of which 153 were included. The most common subjects were rheumatoid arthritis 31/153 (20%), spondyloarthritis 18/153 (12%), osteoarthritis 10/153 (7%), crystal arthropathies 9/153 (6%), and vasculitis 9/153 (6%). The most common consensus-based methodologies were Delphi processes 77/187 (41%) and consensus conferences 69/187 (37%) (Figure 2A). Major societies (ACR, EULAR, BSR) endorsed 37/153 (24%), other organizations (professional societies or governments) endorsed 74/153 (48%), and 42/153 (28%) were



PRISMA Diagram

not endorsed (Figure 2B). Major society-endorsed guidelines were less likely to accept industry funding (5% vs. 31% other organizations vs. 67% not endorsed, $p < 0.001$), allow pharmaceutical involvement in the consensus process (3% vs. 9% other organizations vs. 21% not endorsed, $p = 0.03$), or allow an industry funded medical writer (0% vs. 3% other organizations vs. 19% not endorsed, $p = 0.006$). The percent of authors who declared any conflicts of interest increased over time across all consensus-based recommendations ($p < 0.001$) (Figure 2C). With regard to the projects that accepted funding from pharmaceutical companies, the industry sponsor was involved in the consensus based process in 16/53 (30%), provided a medical writer in 10/53 (19%), and was allowed to approve the final draft in 1/53 (2%) (Figure 2D).

Conclusion: The yearly production of consensus-based recommendations has significantly increased over time. Consensus-based recommendations that are not endorsed by major rheumatology societies frequently receive funding from pharmaceutical companies, which may be involved in the consensus-finding process or provide editorial support. Rheumatologists should be aware of this potential influence and policymakers should consider strategies to mitigate their impact.

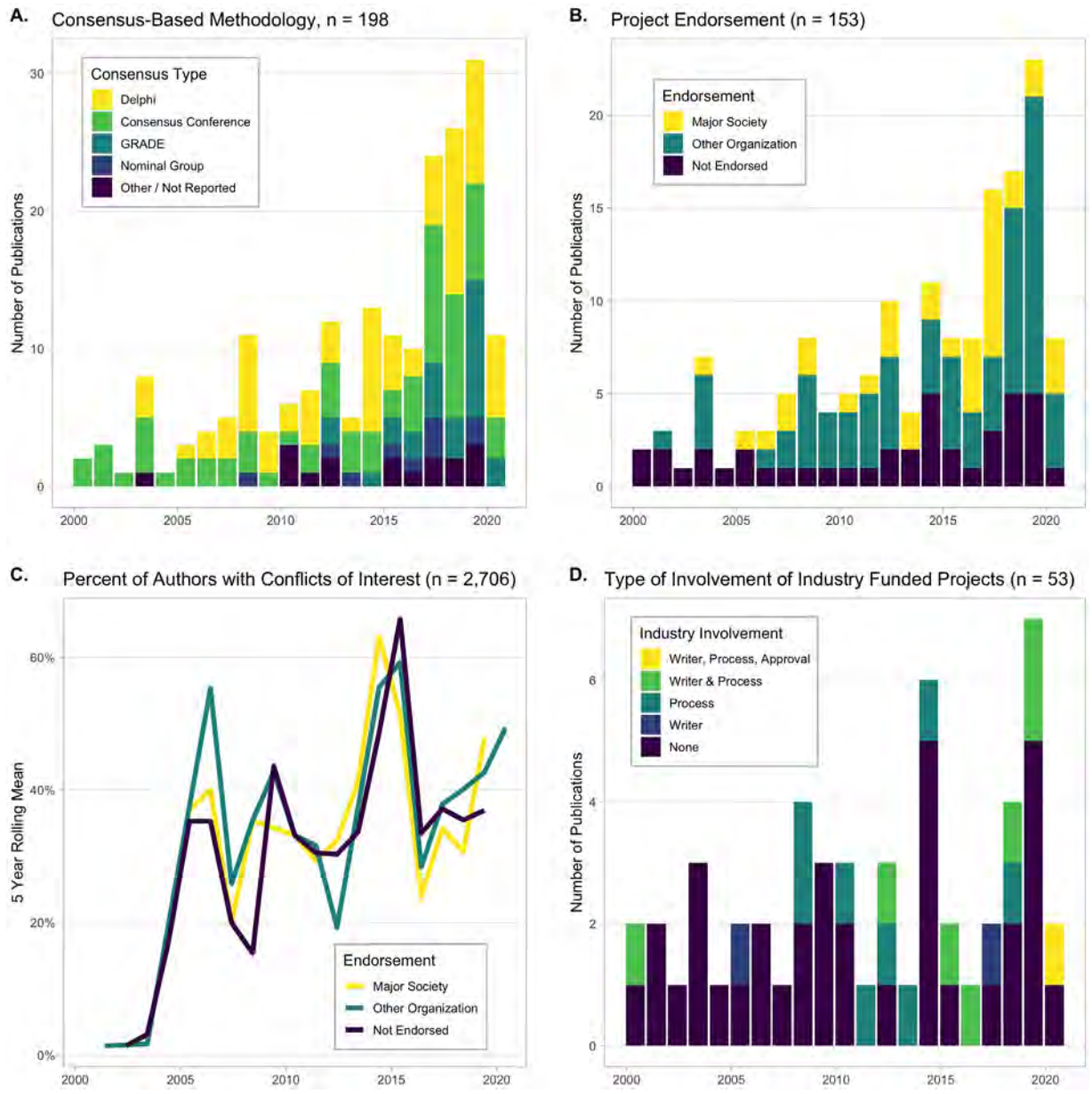


Figure 2. A. Number of publications utilizing major consensus-finding methodologies, n = 198. Number exceeds total number of publications because of studies that utilized mixed methods. B. Project endorsement by major society (ACR, EULAR, BSR), other organization (other professional societies, government groups), or not endorsed, n = 153. C. Percentage of authors per year who declared conflicts of interest, stratified by project endorsement. Data displayed as five year rolling mean for reporting clarity. D. Types of involvement by industry in industry funded projects over time, n = 53. Involvement categories were "Writer" (medical writer or editorial support), "Process" (involvement in the consensus-finding process), and "Approval" (pharmaceutical company having right to edit or approve the final manuscript).

Table 1: Characteristics of Consensus Based Recommendations, 2000-2020 (n = 153)

Characteristic	Overall	ACR / EULAR / BSR	Other Organization	Not Endorsed	
	Number (%)	*Number (%)*	*Number (%)*	*Number (%)*	p-value
Consensus Process*					
Delphi	76 (38%)	19 (51%)	41 (55%)	16 (38%	p = 0.19
Consensus Conference	69 (37%)	14 (38%)	27 (36%)	28 (67%)	p = 0.005
GRADE	26 (14%)	9 (24%)	13 (18%)	4 (10%)	p = 0.22
Nominal Group	10 (5%)	0 (0%)	8 (11%)	2 (5%)	p = 0.08
Other / Not Reported	6 (3%)	2 (5%)	10 (14%)	3 (7%)	p = 0.36
Industry Involvement					
Industry Funding	53 (35%)	2 (5%)	23 (31%)	28 (67%)	p < 0.001
Involvement in Process	17 (11%)	1 (3%)	7 (9%)	9 (21%)	p = 0.03
Provided Medical Writer	10 (7%)	0 (0%)	2 (3%)	8 (19%)	p = 0.006
Honoraria for Participation	6 (4%)	1 (3%)	2 (3%)	3 (7%)	p = 0.55
Approval Prior to Publication	1 (1%)	0 (0%)	0 (0%)	0 (0%)	p = 0.52
COI with Project Sponsor					
Overall	253 (9%)	0 (0%)	14 (19%)	18 (43%)	p < 0.001
1st Author	24 (16%)	0 (0%)	9 (12%)	15 (36%)	p < 0.001
Last Author	23 (15%)	0 (0%)	9 (12%)	14 (33%)	p < 0.001

*Number exceeds total number of studies due to some studies utilizing multiple processes
Abbreviations: Conflicts of interest (COI), The American College of Rheumatology (ACR), The European League Against Rheumatism (EULAR), Grading of Recommendations Assessment, Development and Evaluation (GRADE)

Disclosure: D. Feterman Jimenez, None; **G. Duron**, None; **A. Duarte-Garcia**, None; **P. Sufka**, Wiley Publishing, 5; **S. Whittle**, None; **P. Robinson**, Novartis, 2, 5, 8, UCB, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 5, Pfizer, 5, Abbvie, 5, 8, BMS, 9; **L. Prokop**, None; **M. Putman**, None.

Abstract Number: 1482

Joint Safety with Tanezumab: Integrated Analyses from Randomized Controlled Phase 3 Studies in Patients with Osteoarthritis

John Carrino[1], Timothy McAlindon[2], Eric Vignon[3], Mark Brown[4], Aimee Burr[4], Robert Fountaine[4], Glenn Pixton[5], Lars Viktrup[6], Christine West[7] and Kenneth Verburg[8], [1]Hospital for Special Surgery, Hackensack, NJ, [2]Tufts Medical Center, Boston, MA, [3]Université Claude Bernard Lyon 1, Pierre Benite, France, [4]Pfizer Inc., Groton, CT, [5]Pfizer Inc., Morrisville, NC, [6]Eli Lilly and Company, Indianapolis, IN, [7]Pfizer Inc, Groton, CT, [8]Pfizer Inc, Groton

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis I: Clinical Trials
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Tanezumab, a monoclonal antibody that inhibits nerve growth factor, has been shown effective in the management of osteoarthritis (OA) pain.[1,2] Due to the potential risk of rapidly progressive OA, recent phase 3 studies of subcutaneous tanezumab included a comprehensive prospective assessment of joint safety. The analy-

Table 1. Baseline disease characteristics, n (%)

Baseline characteristics	Placebo (n=514)	Tanezumab 2.5 mg (n=1530)	Tanezumab 2.5/5 mg (n=219)	Tanezumab 5 mg (n=1282)	NSAID (n=996)
Maximum KL Grade of Any Joint					
0	0	0	0	0	0
1	0	1 (0.1)	0	0	0
2	86 (16.7)	329 (21.5)	48 (21.9)	280 (21.8)	239 (24.0)
3	242 (47.1)	752 (49.2)	99 (45.2)	645 (50.3)	503 (50.5)
4	186 (36.2)	448 (29.3)	72 (32.9)	357 (27.8)	254 (25.5)
Number of Joints with KL Grade ≥ 2					
0	0	1 (0.1)	0	0	0
1	101 (19.6)	358 (23.4)	45 (20.5)	262 (20.4)	219 (22.0)
2	278 (54.1)	824 (53.9)	116 (53.0)	722 (56.3)	560 (56.2)
3	87 (16.9)	202 (13.2)	34 (15.5)	186 (14.5)	124 (12.4)
4	48 (9.3)	145 (9.5)	24 (11.0)	112 (8.7)	93 (9.3)

KL, Kellgren-Lawrence; OA, Osteoarthritis

Table 1. Baseline disease characteristics, n (%)

Table 2. Adjudicated joint safety outcomes, n (%)

	Placebo (n=514)	Tanezumab 2.5 mg (n=1530)	Tanezumab 2.5/5 mg (n=219)	Tanezumab 5 mg (n=1282)	NSAID (n=996)
Patients analyzed by the Adjudication Committee	24 (4.7)	157 (10.3)	17 (7.8)	204 (15.9)	49 (4.9)
Primary Composite Joint Safety Endpoint[1]	0	49 (3.2)	1 (0.5)	80 (6.2)	15 (1.5)
Rapidly Progressive OA type 1	0	35 (2.3)	1 (0.5)	54 (4.2)	10 (1.0)
Rapidly Progressive OA type 2	0	6 (0.4)	0	17 (1.3)	1 (0.1)
Primary Osteonecrosis	0	1 (0.1)	0	2 (0.2)	0
Pathological Fracture	0	0	0	0	0
Subchondral Insufficiency Fracture	0	7 (0.5)	0	7 (0.5)	4 (0.4)
Not Enough Information to Determine Rapid vs. Normal Progression of OA	0	2 (0.1)	0	0	0
Normal Progression of OA	22 (4.3)	96 (6.3)	16 (7.3)	98 (7.6)	27 (2.7)
Other Joint Outcome*	2 (0.4)	10 (0.7)	0	26 (2.0)	7 (0.7)

OA, osteoarthritis
Primary outcome for each subject is shown, according to the following hierarchy: primary osteonecrosis, rapidly progressive OA type 2, subchondral insufficiency fracture, pathological fracture, rapidly progressive OA type 1,not enough information to determine rapid vs. normal progression of OA, other, normal progression of osteoarthritis.
(1) The primary composite joint safety endpoint includes any subject with an adjudicated outcome of primary osteonecrosis, rapidly progressive OA type 1 or type 2, subchondral insufficiency fracture, or pathological fracture.
*Includes post-traumatic/post-procedure events and pre-existing conditions.

Table 2. Adjudicated joint safety outcomes, n (%)

ses summarized here include baseline population characteristics, adjudicated joint safety outcomes and sub-group analyses in the combined randomized, controlled, phase 3 OA tanezumab studies.

Methods: In study 1 (NCT02697773) patients received placebo, tanezumab 2.5 mg, or 2.5 mg then 5 mg (tanezumab 2.5/5 mg) over 16 weeks. In study 2 (NCT02709486) patients received placebo, tanezumab 2.5 mg, or tanezumab 5 mg over 24 weeks. In study 3 (NCT02528188) patients received tanezumab 2.5 mg, tanezumab 5 mg, or nonsteroidal anti-inflammatory drug (NSAID) over 56 weeks. Joint safety outcomes were adjudicated by a blinded external Adjudication Committee. The adjudicated composite joint safety endpoint (CJSE) included: primary osteonecrosis (ON), rapidly progressive OA type 1 (RPOA1) or type 2 (RPOA2), subchondral insufficiency fracture (SIF), or pathological

Table 3. Subgroups analyzed for potential association with adjudicated composite joint safety endpoint

Subgroups	Details	Association with CJSE
Demographic factors	Age: <65 versus ≥65, <75 versus ≥75), gender, BMI: <25, 25 to <30, 30 to <35, ≥35	No association
Baseline disease severity	Maximum KL Grade at baseline (2, 3, or 4), Number of joints with baseline KL Grade ≥2, Prior history of TJR, WOMAC Pain subscale score at baseline (<7, ≥7), WOMAC Physical Function subscale score at baseline (<7, ≥7), Patient's Global Assessment at baseline (Fair, Poor/Very Poor)	Possible association for maximum KL grade of 3 at baseline and WOMAC pain and physical function score ≥7 at baseline
Adverse events	Selected adverse events up to end of study: arthralgia, joint swelling, abnormal peripheral sensation, fracture, lower limb fracture, fall, and peripheral edema	Possible association for arthralgia and joint swelling
Efficacy Response: WOMAC Pain and Physical Function	≥50% change from baseline in WOMAC Pain response at Week 16, Patients with WOMAC Pain subscale scores ≤2 at two or more consecutive visits, Patients with ≥50% change from baseline in WOMAC Physical Function response at Week 16	No association
Sensory examinations in lower extremities	Standardized neurologic examinations carried out by investigators or designated physicians at each study site	No association
Concomitant medications (non-NSAID)	Use of intra-articular hyaluronic acid in the year prior to the study, use of intra-articular corticosteroid in the year prior to the study, concomitant cardiovascular prophylactic aspirin use, concomitant intra-articular corticosteroid use, concomitant bisphosphonate use, and concomitant acetaminophen use	No association
Concomitant NSAID use	Use of NSAID prior to occurrence of joint safety endpoint	No association
Baseline bone health	Including: history of osteopenia, history of osteoporosis	No association

BMI, Body mass index; KL, Kellgren-Lawrence; TJR, Total joint replacement; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

Table 3. Subgroups analyzed for potential association with adjudicated composite joint safety endpoint

fracture. Subgroups were cross-tabulated to investigate potential associations with outcomes descriptively with no formal statistical analysis.

Results: At baseline, maximum Kellgren-Lawrence (KL) grade of any joint and number of joints with KL grade ≥2 were similar across treatment groups (Table 1). A total of 451 patients were evaluated by the blinded adjudication committee; 145 were adjudicated to have a primary outcome which was a component of the CJSE: RPOA1 (69% 100/145), RPOA2 (17% 24/145), SIF (12% 18/145), and ON (2% 3/145) (Table 2). The proportion of patients with adjudicated

CJSE was higher in tanezumab-treated patients relative to placebo or NSAID and the incidence increased with increasing dose of tanezumab. RPOA1 typically occurred in the knee and in joints with KL grade 2 or 3 OA at baseline, although there were four events in joints that were KL grade 0 at baseline (two each in the tanezumab 2.5 mg and 5 mg treatment groups). For RPOA2, the affected joint was approximately evenly split between the hip and knee with two patients having shoulder as the affected joint (one each in the tanezumab 5 mg and NSAID groups). Most RPOA2 events occurred in joints with KL grade 3 or 4 OA at baseline. RPOA2 was more often associated with a total joint replacement than RPOA1. Multiple subgroups were investigated to assess potential associations with CJSE, with possible associations noted for baseline disease severity and adverse events of arthralgia and joint swelling (Table 3).

Conclusion: Patients enrolled in the combined phase 3 OA tanezumab studies had moderate to severe OA. The proportion of patients with adjudicated CJSE was higher in tanezumab-treated patients relative to placebo or NSAID and the incidence increased with increasing dose of tanezumab. Subgroup analyses did not reveal an association of CJSE with efficacy response.

Disclosure: J. Carrino, Covera Health, 5, Image Analysis Group, 5, Image Biopsy Lab, 5, Pfizer, 5, Simplify Medical, 5, Arthritis and Rheumatology journal, 9, Osteoarthritis Imaging journal, 9; **T. McAlindon**, Pfizer, 1, Sanofi Aventis US, 1, Kolon Tissuegene, 1, Samumed, 1, Seikagaku, 1, Kiniksa Pharmaceuticals, 1, Anika Therapeutics, 1; **E. Vignon**, Pfizer, 5; **M. Brown**, Pfizer, 1, 3; **A. Burr**, Pfizer Inc., 1, 2; **R. Fountaine**, Pfizer Inc., 1, 3, 4; **G. Pixton**, Pfizer Inc., 3, 4; **L. Viktrup**, Eli Lilly and Company, 1, 3; **C. West**, Pfizer Inc., 1, 3; **K. Verburg**, Pfizer Inc., 1, 2.

Abstract Number: 1483

A Randomised Controlled Trial Evaluating the Efficacy of Internet-based Exercises Aimed at Treating Knee Osteoarthritis (iBEAT-OA)

Sameer Gohir[1], Abhishek Abhishek[2], Anthony Kelly[2] and Ana M Valdes[3], [1]NIHR Nottingham Biomedical Research Centre, GRAYS ESSEX, England, United Kingdom, [2]University of Nottingham, Nottingham, United Kingdom, [3]NIHR Nottingham Biomedical Research Centre, School of Medicine, University of Nottingham, Nottingham, England, United Kingdom

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis I: Clinical Trials
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Osteoarthritis (OA) is the commonest cause of pain and disability in the general population and is usually managed by family doctors and physiotherapists. This study aimed to explore the benefits of digital delivery of exercises on pain, function, and other health-related outcomes in individuals with painful knee OA.

Methods: iBEAT-OA was a primary-care based randomised controlled trial in which participants with knee OA were 1:1 randomised to web-based exercises or usual care. The study was designed to ascertain whether, after 6 weeks, i-BEAT-OA was more effective to reduce the pain than continued usual care. The eligibility criteria are shown in Figure 1.

An app-based exercises platform known as Joint Academy (JA) was used as an intervention given to treatment arm. There were two face-to-face sessions with a physiotherapist for both arms, at enrolment and six weeks. Visual Analogue Score (VAS), Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC), The Arthritis Research UK Musculoskeletal Health Questionnaire (MSK-HQ), Pittsburgh Sleep Quality Index (PSQI), 30-second sit to stand

Figure 1: Inclusion and Exclusion Criteria for iBEAT-OA trial

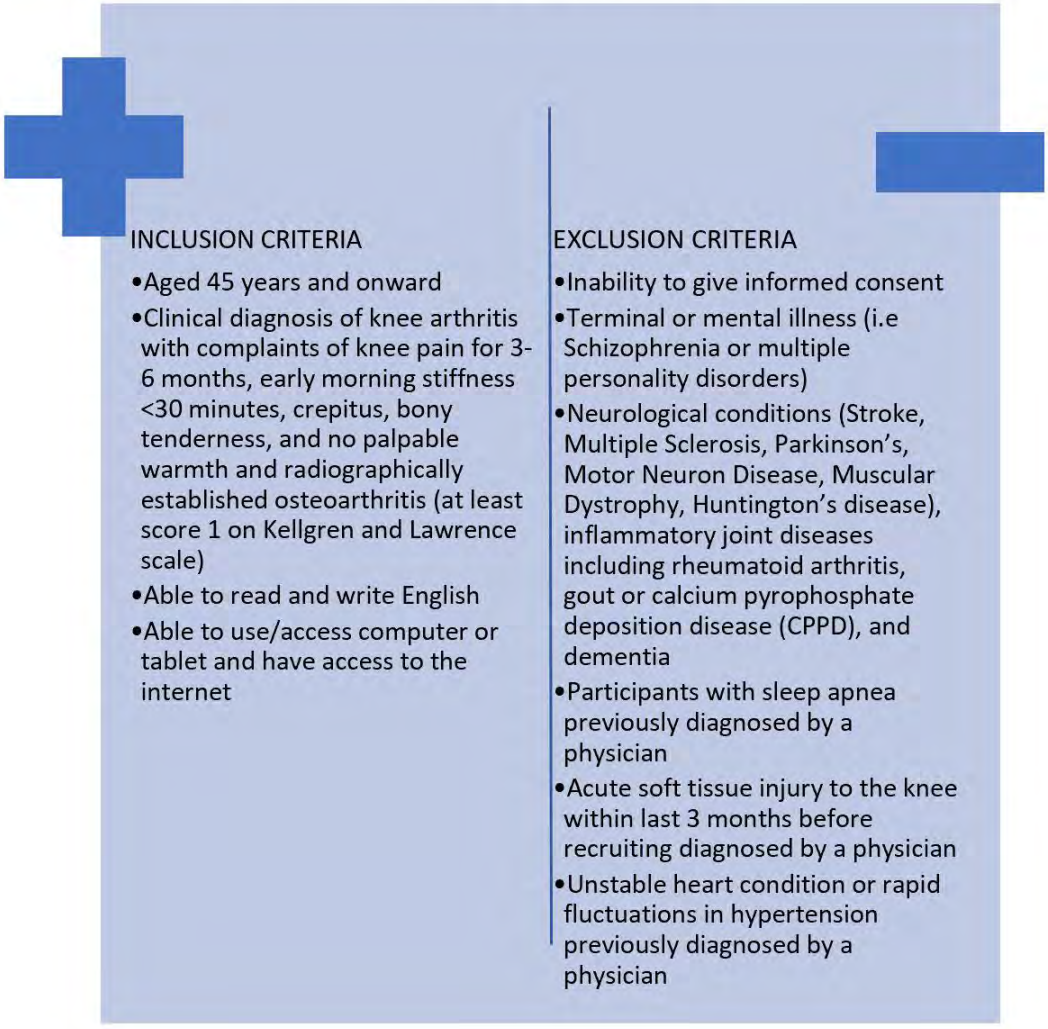


Figure 1. Inclusion and Exclusion Criteria for iBEAT-OA trial

test (30CST), Time up and go test (TUG), Quantitative Sensory Testing (QST), Maximum Voluntary Contraction (MVC)-isokinetic contraction of Quadriceps / Hamstring muscle, urine and blood samples were taken at baseline and at six weeks follow up. Participants were given an actigraphy device.

We compared groups at baseline and after 6 weeks by intention to treat.

The primary outcome was the change in pain (mean difference) assessed by visual analogue scores (VAS) between baseline and follow-up between the treatment and control arms. The difference within arms between baseline and follow-up was assessed using a paired t-test. A similar model was used for other variables. Regression analysis models were used to assess confounding factors. The threshold for statistical significance was set at level .05 with 2-sided testing.

Results: The recruitment was stopped in March 2020 due to COVID-19 lockdown instructions. In total, 105 participants (48 participants in the intervention arm and 57 participants in the control arm) had completed data for both baseline and follow-up assessments. No significant differences in baseline characteristics were seen (Table 1).

	Control Group	Intervention Group	P values
Age	67.96 (8.6)	65.23 (9.7)	P= 0.132
Women / Men	37 (64.91%) / 20 (35.09%)	34 (70.83%) / 14 (29.16%)	P= 0.518
BMI	31.9 (5.9)	30.4 (5.5)	P= 0.193
K/L Score	2.09	2.04	P= 0.643
1	18 (31.58%)	19 (39.58%)	
2	22 (38.6%)	13 (27.08%)	
3	11 (19.3%)	11 (22.9%)	
4	6 (10.5%)	5 (10.4%)	

Table 1: Baseline Characteristics

Table 1. Baseline Characteristics

The mean difference in pain as measured by a visual analogue scale (0-10) from baseline minus follow-up for the treatment arm was a drop of -1.79 [95%CI -1.16 to -2.41], for the control arm it was -0.39 [95%CI -0.97 to 0.18]. The mean difference between the treatment and control arms was 1.39 [95%CI 0.55-2.2] p< 0.0014 favouring the treatment arm.

Conclusion: Among participants with knee pain from OA, use of the Joint Academy app compared with control group resulted in an improvement in pain, function and muscle strength at 6 weeks follow-up that was statistically significant. Furthermore, there was improved muscle strength of hamstring and functional activities in intervention group. With COVID-19 pandemic, when social distancing is a vital prerequisite of staying safe, apps such as Joint Academy can be useful tools to manage knee OA at home.

Disclosure: S. Gohir, None; **A. Abhishek**, None; **A. Kelly**, None; **A. Valdes**, None.

Abstract Number: 1484

Efficacy of Tocilizumab in Patients with Hand Osteoarthritis: Double Blind, Randomized, Placebo Controlled, Multicenter Trial

Pascal Richette[1], Augustin Latourte[2], Jeremie Sellam[3], Daniel Wendling[4], Muriel Piperno[5], Philippe Goupille[6], Yves-Marie Pers[7], Florent Eymard[8], Sebastien Ottaviani[9], Paul Ornetti[10], Rene-Marc Flipo[11], Bruno Fautrel[12], Jean-Pierre Bertola[13], Eric Vicaut[14] and Xavier Chevalier[15], [1]Department of Rheumatology, Lariboisière Hospital, AP-HP Université de Paris, INSERM U1132, Paris, [2]Department of Rheumatology, Lariboisière Hospital, AP-HP Université de Paris, INSERM U1132, Paris, France, [3]AP-HP, Hôpital Saint-Antoine, Service de Rhumatologie, Centre de Recherche Saint-Antoine, INSERM UMR_S 938,Sorbonne Université, Paris, 75012, France, Paris, France, [4]CHU Besançon, department of rheumatology, Besancon, France, [5]Rheumatology Department, Lyon University Hospital, Lyon, France, [6]CHU Tours, department of rheumatology, Tours, France, [7]IRMB, University of Montpellier, Inserm U1183, University Hospital of Montpellier, Montpellier, France, [8]APHP Henri Mondor Hospital, Creteil, France, [9]Rheumatology Department, Bichat hospital, APHP, Paris, France, [10]CHU Dijon, INSERM CAPS 1093, plateforme d'investigation technologique CIC1432, Dijon, France, [11]Lille University Hospital, Lille, France, [12]Sorbonne University, INSERM, IPLES; Pitié-Salpêtrière Hospital, Paris, Ile-de-France, France, [13]CHUGAI PHARMA FRANCE, Paris, France, [14]Clinical Research Unit, Paris, [15]AP-HP, UPEC, Créteil

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Osteoarthritis I: Clinical Trials

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: To evaluate the efficacy of tocilizumab, an antibody against interleukin-6 receptor (IL-6R), in patients with hand osteoarthritis.

Methods: This was a multicenter, 12-week, randomized, double-blind, placebo-controlled study. Patients with symptomatic hand osteoarthritis (pain ≥ 40 on a 0–100-mm visual analogic scale [VAS] despite analgesics and non-steroidal anti-inflammatory drugs; at least 3 painful joints, Kellgren–Lawrence grade ≥ 2) were randomized to receive two infusions 4 weeks apart (week 0 and week 4) of tocilizumab (8 mg/kg IV) or a placebo. The primary endpoint was the change in VAS pain at week 6. Secondary outcomes included the number of painful and swollen joints, duration of morning stiffness, patients' and physicians' global assessment and function scores.

Results: Of 104 patients screened, 91 (82% women; mean age, 64.4 years) were randomly assigned and 79 completed the 12-week study visit. The mean change between baseline and week 6 on VAS pain (primary outcome) was -7.9 (SD 19.4) and -9.9 (SD 20.1) in the tocilizumab and placebo group (p=0.7). No significant treatment differences were observed at weeks 4, 6, 8 or 12 for any secondary outcomes. Overall, adverse events were slightly more frequent in the tocilizumab than placebo group.

Conclusion: Tocilizumab was no more effective than placebo for pain relief in patients with hand osteoarthritis.

Disclosure: P. Richette, None; **A. Latourte**, None; **J. Sellam**, None; **D. Wendling**, None; **M. Piperno**, Abbvie, 9, Janssen, 9, Biogen, 9, Pfizer, 9, Chugai, 9, Bristol-Myers Squibb, 9, Sandoz, 9; **P. Goupille**, MSD France, 1, 2, Abbvie, 1, Amgen, 1, Biogaran, 1, 2, BMS, 1, Celgene, 1, Chugai, 1, Lilly, 1, Hospira, 1, Janssen, 1, Medac, 1, Nordic Pharma, 1, Novartis, 1, Sanofi-Genzyme, 1, Pfizer, 1, UCB Pharma, 1; **Y. Pers**, None; **F. Eymard**, None; **S. Ottaviani**, None; **P. Ornetti**, None; **R. Flipo**, MSD France, 1, 2, Sanofi-Aventis, 1; **B. Fautrel**, MSD France, 1, 2, Abbvie, 1, 2, Pfizer, 1, 2, Biogen, 1, BMS, 1, Boehringer Ingelheim, 1, Celgene, 1, Janssen, 1, Lilly, 1, Medac, 1, Nordic Pharma, 1, Novartis, 1, Roche, 1, Sanofi-Aventis, 1, SOBI, 1, UCB Pharma, 1; **J. Bertola**, Roche-Chugai, 3; **E. Vicaut**, None; **X. Chevalier**, None.

Abstract Number: 1485

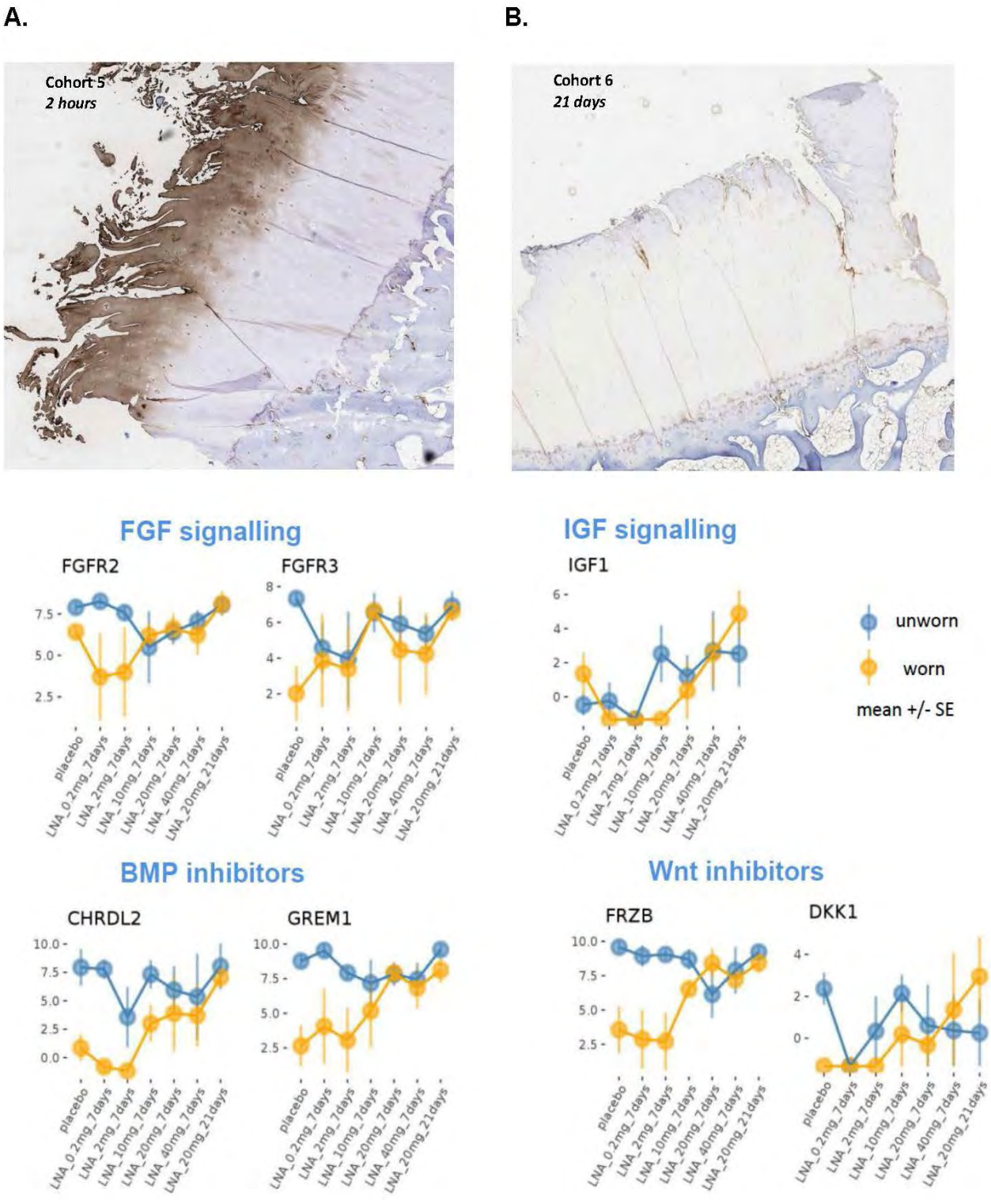
LNA043, a Novel Cartilage Regenerative Treatment for Osteoarthritis: Results from a First-In-Human Trial in Patients with Knee Osteoarthritis

Celeste Scotti[1], **Joseph Gimbel**[2], Didier Laurent[1], Aviv Madar[3], Thomas Peters[1], Yunyu Zhang[3], Florine Polus[1], Michael Beste[3], Igor Vostiar[1], Subhajit Choudhury[4], Nicole Gerwin[1], Jörg Goldhahn[5], Matthias Schieker[1] and Ronenn Roubenoff[1], [1]Novartis Institutes for BioMedical Research, Basel, Switzerland, [2]Arizona Research Center, Phoenix, [3]Novartis Institutes for BioMedical Research, Cambridge, [4]Biostatistics & Pharmacometrics, Novartis Healthcare Pvt. Ltd., Hyderabad, India, [5]Department of Health Sciences and Technology, ETH Zürich, Zurich, Switzerland

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis I: Clinical Trials
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: LNA043 is a modified human angiopoietin-like 3 (ANGPTL3) protein identified in a phenotypic screen for inducers of chondrogenesis and cartilage repair. The primary objective of this trial (NCT02491281) was to assess safety and tolerability of single intraarticular doses of LNA043 into the knee of patients with knee osteoarthritis (OA).

Figure 1.



Methods: A first-in-human, randomized, single-center, placebo-controlled, double-blind, single ascending dose trial was conducted in patients aged 50–75 years with knee OA scheduled for total knee replacement (TKR). Patients were randomized 3:1 (LNA043 to placebo) in each of 7 cohorts consisting of 4 patients each. The 5 increasing intraarticular dose levels ranging 0.2–40 mg (0.2 mg, 2 mg, 10 mg, 20 mg, 40 mg) administered 7 days before TKR. Two additional

20 mg dose levels were also administered 2 hours or 21 days before TKR. Key safety parameters included adverse events (AEs), injection-site reactions and detection of anti-drug antibodies against LNA043. Knee tissues were obtained during the TKR procedure to assess local exposure to LNA043 through immunohistochemical (IHC) staining, and cartilage biopsies were harvested from worn and unworn areas of the knee to perform RNA-Seq analysis.

Results: 30 patients were randomized to LNA043 (n=21) or placebo (n=7), 2 withdrew consent prior to treatment. Pertinent demographic information included: a mean age of 63 years, 68% female (n=19), and 96% Caucasian (n=27) participants. A total of 19 (14 on LNA043 and 5 on placebo) patients experienced at least one AE. The overall incidence of AEs for LNA043 was 66.7% (14/21). The overall incidence of AEs for placebo was 71.4% (5/7). One case of dry mouth/dysgeusia was reported in the 40 mg cohort, which resolved spontaneously and was considered mild. Ten non-study drug-related, serious AEs were reported in five patients (LNA043, n=3; placebo, n=2). Anti-LNA043 antibodies were not detected in the patients. After intraarticular injection, LNA043 was dose-dependently distributed from the joint to systemic circulation with C_{max} typically reached between 2 to 6 hours after the intraarticular injection. IHC demonstrated that LNA043 penetrated the articular cartilage shortly after injection (2 hours), with more pronounced penetration into the damaged areas (Figure 1A). LNA043 was not detectable in the articular cartilage or synovial-fluid 7 days post intraarticular injection. RNA-Seq analysis demonstrated modulation of several genes involved in cartilage homeostasis and repair, suggesting a broad effect by LNA043 up to 21 days post-injection (Figure 1B). These effects were both dose-dependent and mostly present in the worn cartilage tissue.

Conclusion: In this study, LNA043 displayed a favorable safety profile without any clinically significant drug-related safety signals or immunogenicity. In addition, LNA043 penetrated transiently into the articular cartilage; was quickly cleared locally and systemically; and elicited a chondroanabolic response as shown by modulating several pathways in chondrocytes involved in OA and cartilage repair at the RNA level. Further studies of LNA043 for treatment of knee OA are now in progress.

Disclosure: C. Scotti, Novartis, 1, 3; **J. Gimbel**, None; **D. Laurent**, Novartis, 1, 3; **A. Madar**, Novartis, 1, 3; **T. Peters**, Novartis, 1, 3; **Y. Zhang**, Novartis, 1, 3; **F. Polus**, Novartis, 1, 3; **M. Beste**, Novartis, 1, 3; **I. Vostiar**, Novartis, 1, 3; **S. Choudhury**, Novartis, 3; **N. Gerwin**, Novartis, 1, 3; **J. Goldhahn**, None; **M. Schieker**, Novartis, 1, 3; **R. Roubenoff**, Novartis, 1, 3.

Abstract Number: 1486

Long-term Efficacy and Safety of Intra-articular Sprifermin in Patients with Knee Osteoarthritis: Results from the 5-Year Forward Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Osteoarthritis I: Clinical Trials

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: The 5-year Phase II FORWARD study assessed the efficacy and safety of the potential disease-modifying osteoarthritis drug (DMOAD) sprifermin (recombinant human fibroblast growth factor 18) in patients with symptomatic, radiographic knee osteoarthritis (OA). Here, we report the long-term 5-year efficacy and safety results of FORWARD.

Methods: Patients were randomized 1:1:1:1:1 to intra-articular sprifermin 100 or 30 µg q6mo, 100 or 30 µg q12mo, or placebo (PBO), for 18 months. The treatment period-related analysis for the primary endpoint was at Year 2, with an extended 3-year observation period. The intent-to-treat (ITT) population included all randomized patients; the modified (m)ITT population all patients with a baseline and ≥1 qMRI reading up to Year 2. Post-hoc exploratory analysis was conducted in a 'subgroup at risk' (SAR, n=161), with minimum medial or lateral joint space width of 1.5–3.5 mm and WOMAC pain 40–90 at baseline. Treatment differences vs PBO were estimated using a repeated measures model controlling for baseline, treatment, time, pooled country and treatment by time interaction. Confidence intervals (CIs) were adjusted for multiplicity of treatments using Dunnett adjustment. Linear dose-effect trend tests were performed exploratively at each timepoint.

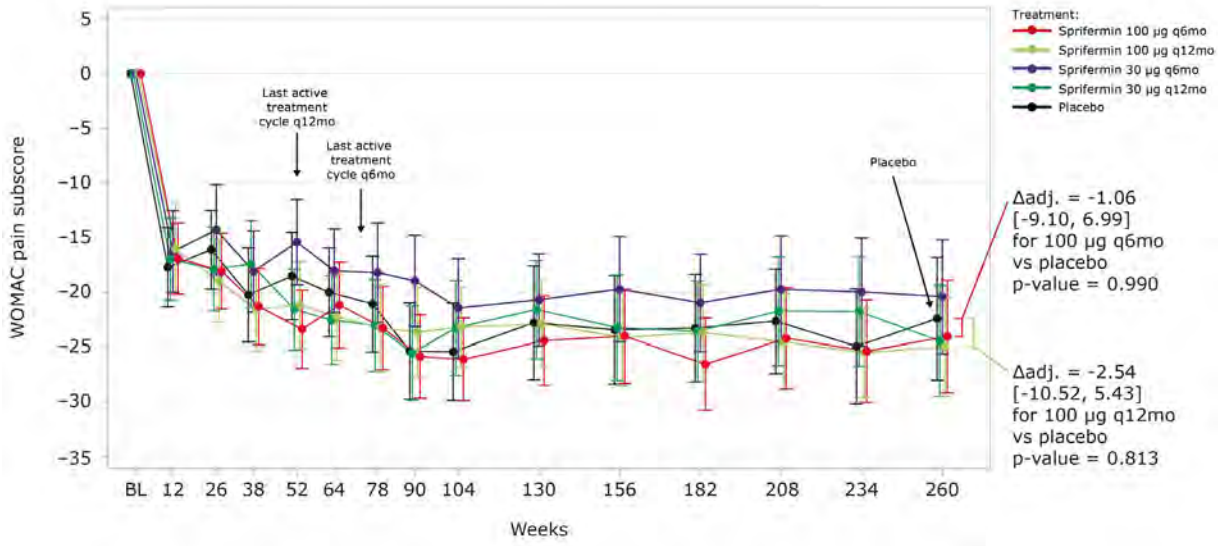
Results: 474 (86.3%) patients completed the primary 2-year observation period; 442 (80.5%) and 378 (69%) patients completed the 3- and 5-year extended follow-up periods, respectively. The significant dose-response effect of sprifermin on longitudinal change in total femorotibial joint (TFTJ) cartilage thickness (trend test, p< 0.001), and the 0.05 mm mean increase in TFTJ cartilage thickness with sprifermin 100 µg q6mo (highest dose) vs PBO (95% CI 0.004, 0.095; p=0.015; **Table 1**) observed at Year 2 were sustained to Year 5. WOMAC pain scores improved by ~50% from baseline to Year 5 in all cohorts, including PBO (**Figure 1**). Post-hoc analysis of the SAR identified a differentiation in WOMAC pain scores between the sprifermin 100 µg q6mo and PBO groups at Year 2 (–5.82; 95% CI –18.87, 7.23), Year 3 (–8.75; 95% CI –22.42, 4.92) and Year 5 (–10.08; 95% CI –25.68, 5.53; **Figure 2**). AEs were mostly moderate in severity. 181 patients (33%) reported serious AEs, none of which were deemed related to treatment. AE-related study withdrawals were < 10%, the majority of which were musculoskeletal and soft tissue disorders. At Year 5, there was no notable difference in the incidence of adverse events (AEs), serious AEs or study discontinuation due to AEs in any sprifermin group vs PBO.

Table 1. Cartilage thickness in the total femorotibial joint based on qMRI from Year 2 through to Year 5: mean change from baseline and adjusted difference vs placebo with sprifermin (mITT population; n = 494)

	Sprifermin 100 µg q12mo (N=99)		**Sprifermin 100 µg q6mo (N=101)**		**Trend test**
	Number of observations	Adjusted mean difference to placebo (95% CI; p)	Number of observations	Adjusted mean difference to placebo (95% CI; p)	
Year 2	90	**0.041** (0.014, 0.067; <0.001)	86	**0.050** (0.023, 0.077; <0.001)	***p<0.001***
Year 3	86	**0.021** (-0.013, 0.055; 0.332)	79	**0.054** (0.019, 0.089; <0.001)	***p<0.001***
Year 4	81	**0.033** (-0.009, 0.075; 0.127)	78	**0.055** (0.013, 0.098; 0.002)	***p<0.001***
Year 5	74	**0.024** (-0.021, 0.070; 0.406)	72	**0.049** (0.004, 0.095; 0.015)	***p<0.001***

p-values at time points other than Year 2 are nominal

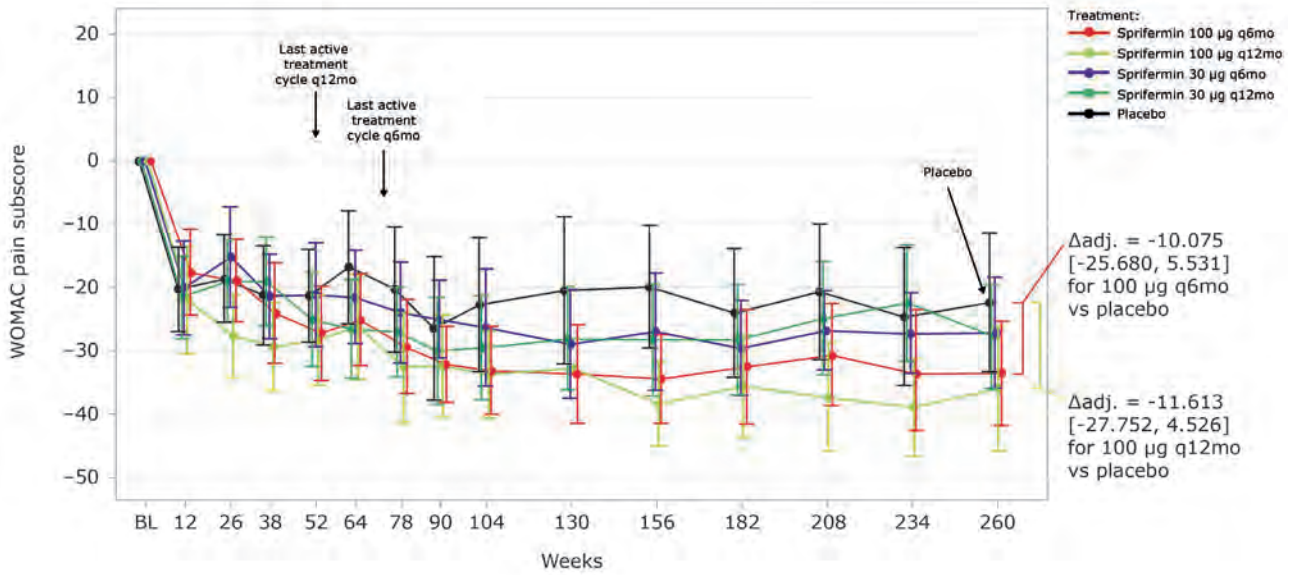
Figure 1. Change from baseline in WOMAC pain scores (ITT population; n=549)



Dose response p-value at Year 5 = 0.673

Abbreviations: **Δadj.**, adjusted mean difference [95% CI] to placebo at Year 5; **BL**, baseline; **CI**, confidence interval; **q6mo**, every 6 months; **q12mo**, every 12 months; **ITT**, intent-to-treat; **WOMAC**, Western Ontario and McMaster Universities Osteoarthritis Index.

Figure 2. Change from baseline in WOMAC pain scores in the "subgroup at risk" (n = 161) (post-hoc analysis)



Dose response p-value at year 5 = 0.046

Abbreviations: **Δadj.**, adjusted mean difference [95% CI] to placebo at Year 5; **BL**, baseline; **CI**, confidence interval; **q6mo**, every 6 months; **q12mo**, every 12 months; **WOMAC**, Western Ontario and McMaster Universities Osteoarthritis Index.

Conclusion: In FORWARD, the longest DMOAD study ever reported, sprifermin maintained long-term structural modification of articular cartilage vs PBO despite a 3.5-year treatment-free period, with no new safety signals. Pain improvement vs PBO was sustained in a subgroup at risk of structural and symptomatic progression. This suggests potential disease modification with sprifermin, with delayed knee OA structural progression and translation of structural modification to clinical benefit. It also identifies a potential target dose and patient population for future Phase III trials.

Disclosure: F. Eckstein, Chondromettrics GmbH, 1, 3, MerckKGaA, 2, 5, Kolon Tissuegene, 2, 5, Samumed, 2, 5, Abbvie, 5, Bioclinica, 2, 5, Servier, 2, 5, Galapagos, 2, 5, Novartis, 5, ICM, 2, 5, Healthlink, 5; **M. Hochberg**, Bone Therapeutics, 5, Bristol Myers Squibb, 5, Eli Lilly, 5, EMD Serono, 5, Gilead, 5, GlaxoSmithKline, 5, IBSA Institut Biochimique SA, 5, Novartis Pharma AG, 5, Noven Pharmaceuticals Inc., 5, Pfizer Inc., 5, Regenosine, 5, Samumed LLC, 5, Theralogix LLC, 5, Vizuri Health Sciences, 5, ACI Clinical, 5, Covance Inc., 5, Galapagos, 5, ICON plc, 5, IQVIA, 5, Elsevier, 7, Wolters Kluwer, 7, BriOri Biotech, 1, Theralogix LLC., 1, Rheumcon, Inc., 6; **H. Guehring**, Merck KGaA, 1, 3; **F. Moreau**, EMD Serono (a business of Merck KGaA, Darmstadt, Germany), 3; **V. Ona**, EMD Serono (a business of Merck KGaA, Darmstadt, Germany), 3; **A. Bihlet**, Nordic Bioscience A/S, 1, 3; **I. Byrjalsen**, Nordic Bioscience, 3; **J. Andersen**, Nordic Bioscience A/S, 1, 3; **B. Daelken**, Merck KGaA, 3; **O. Guenther**, Merck KGaA, 3; **C. Ladel**, Christoph Ladel, 3, Merck KGaA, 1, 3, Merck KGaA, 1, 3; **M. Michaelis**, Merck KGaA, 3; **P. Conaghan**, AbbVie, 1, 2, EMD Serono, 1, Flexion Therapeutics, 1, 2, Galapagos, 1, Gilead, 1, Novartis, 1, 2, Regeneron, 1, Samumed, 1, 2, GlaxoSmithKline, 5, Janssen, 5, Pfizer Inc, 5, Bristol-Myers Squibb, 2, Eli Lilly, 5.

Abstract Number: 1487

Biclustering Reveals Potential Knee Osteoarthritis Phenotypes in Exploratory Analyses: Data from the Osteoarthritis Initiative

Amanda Nelson[1], Thomas Keefe[2], Todd Schwartz[3], Richard Loeser[1], Yvonne Golightly[4], Liubov Arbeeva[1] and J Marron[2], [1]University of North Carolina at Chapel Hill Thurston Arthritis Research Center, Chapel Hill, NC, [2]University of North Carolina at Chapel Hill, Chapel Hill, NC, [3]University of North Carolina at Chapel Hill Dept of Biostatistics, Chapel Hill, NC, [4]University of North Carolina at Chapel Hill Dept of Epidemiology, Chapel Hill, NC

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis II: Clinical Aspects
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: To utilize novel methodologies to explore subgroups within the OAI clinical data.

Methods: From the OAI baseline dataset (n=4796 individuals with or at risk of knee OA/9592 knees; 116 clinical and demographic features; https://nda.nih.gov/oai/; *AllClinical00*), we excluded uninformative variables and features/knees with missing data leaving 86 features from 3322 people (6461 knees) for analyses. Continuous variables were transformed using a procedure to remove skewness and standardized (Feng 2016; https://doi.org/10.1002/sta4.104).

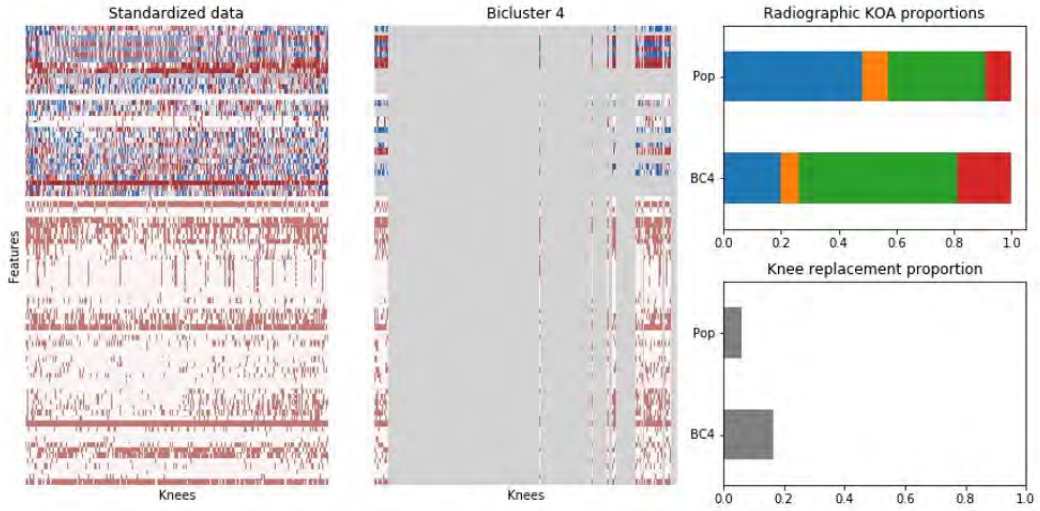
Biclustering (Cheng 2000; PMID 10977070) is particularly useful when different subsets of features are informative for some, but not all, knees. This method allows simultaneous clustering of the rows (knees) and columns (features) of the matrix, and automated discovery of similarities based on these attributes. A bicluster is then defined as a sub-matrix that is well-fit (i.e., larger R^2) by two-way ANOVA, in that the entries are close to a common value with adjustments for the rows and columns. We chose the parameters of the algorithm to balance competing desires for biclusters: strongly similar knees and sufficient sample size to provide potentially useful phenotypes.

Table 1. Summary of identified biclusters, number of knees and features included, and prognosis

Bicluster	n (knees)	N (people)	D (features)	R^2	Prognosis*
1	1425	960	80	0.37	Better for bicluster
2	2415	1649	69	0.30	Similar
3	1822	1294	63	0.31	Similar
4	188	147	70	0.64	Poorer for bicluster
5	238	191	64	0.53	Poorer for bicluster
6	258	194	63	0.31	Similar

*Summary prognosis for those knees in each bicluster compared to the full cohort of knees, based on outcomes shown in Figure 1, including knees without radiographic OA (rOA), knees developing incident rOA (baseline KLG=0-1 increasing to 2+), knees with prevalent rOA (baseline KLG=2+ without progression), knees with progressive rOA (baseline KLG=2+ with worsening KLG), and the proportion of knees undergoing TKR over 96 months.

Figure 1: Composite image showing **A**) heatmap of standardized OAI data (n=6461 knees; 86 features); **B**) heatmap of bicluster 4 (n=188 knees), **C and D**) outcomes for knees in the overall cohort compared with bicluster #4

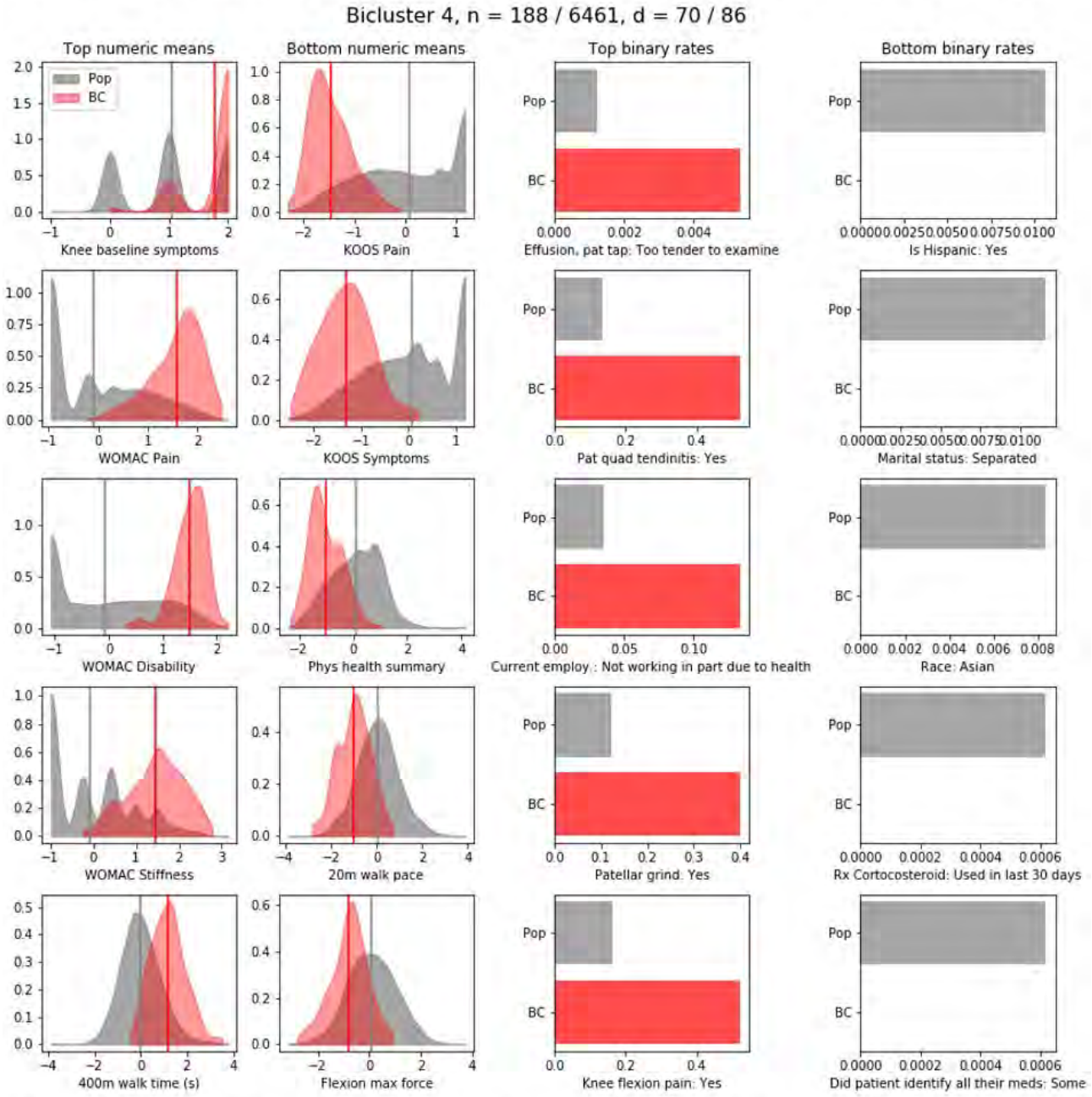


***A and B**: Red = positive standardized values, blue = negative standardized values, white = zero, gray = features not identified in bicluster 4. **C**: Blue: baseline KLG=0-1 without progression; Gold: baseline KLG=0-1 with progression; Green: baseline KLG=2+ without progression; Red: baseline KLG=2+ with progression. **D**: Proportion of TKR over 96 months in the cohort (top) and in the bicluster (bottom).*

After identifying potential biclusters, we characterized them by comparing the knees within the bicluster to the overall population of knees based on marginal distributions of features as well as outcomes (defined in **Table 1**) such as prevalent, incident, and progressive knee OA and provision of knee replacement (TKR) from baseline to 96 months.

Results: We found 6 biclusters (chosen until the clusters became too small to be useful, **Table 1**). As an example, bicluster #4 contained 188 knees (from 147 people) and 70 features (**Fig 1B**) and was characterized by greater frequency of both progressive OA (**Fig 1C**) and TKR (**Fig 1D**). We then compared the distribution of baseline features between the knees in bicluster #4 and the total population of knees (**Fig 2**). Features that were higher among the knees in bicluster #4 versus the overall population of knees included knee symptoms, WOMAC scores, 400-meter walk time, knee tenderness on exam, patellar quadriceps tendinitis, inability to work for health reasons, presence of

Figure 2: Distributions or proportions of main features differentiating knees in bicluster #4 from the total group of knees



Continuous or multi-level variables (post-standardization) are shown using density estimates (gray=distribution for whole population; red=distribution within the bicluster); binary variables are studied using bar graphs (note difference in scales). The top and bottom 5 of each type are explicitly shown.

patellar grind, and knee flexion pain. In contrast, knees included in the bicluster had lower values for KOOS (to be expected as the coding is opposite that of WOMAC), SF-12 physical summary scale, 20-meter walk speed, and maximal isometric flexion strength. These knees were less likely to be from Hispanic or Asian participants, individuals who were separated (versus any other marital status), and less frequently reported IA corticosteroids in the last 30 days.

Conclusion: We identified several biclusters (groups of features and knees) within the baseline OAI data with varying prognoses. Such biclusters may represent potential phenotypes (e.g., progressor phenotype(s)) within the larger cohort. Application of novel methodologies can provide new insights into OA phenotypes and development or progression of disease.

Disclosure: A. Nelson, None; **T. Keefe**, None; **T. Schwartz**, None; **R. Loeser**, Bioventus, 1, Unity Biotechnology, 1; **Y. Golightly**, None; **L. Arbeeva**, None; **J. Marron**, None.

Abstract Number: 1488

Application of the Knee Injury and Osteoarthritis Outcome Score Percentile Curves on Preoperative and up to 2 Years Postoperative Data of Patients Undergoing Total Knee Arthroplasty

Marieke Loef[1], Maaike G. Gademan[1], Daisy A. J. Latijnhouwers[1], Herman Kroon[1], Herman Kaptijn[2], Willem Marijnissen[3], Rob G. H. Nelissen[1], Thea Vliet Vlieland[4] and Margreet Kloppenburg[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]LangeLand Hospital, Zoetermeer, Netherlands, [3]Albert Schweitzer Hospital, Dordrecht, Netherlands, [4]Leiden University Medical Center, 2300 RC Leiden, Netherlands

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis II: Clinical Aspects
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Table 1. Pre- and postoperative KOOS scores

KOOS subscales	All Mean (SD)	N	Men Mean (SD)	Women Mean (SD)
Preoperative				
Pain	34 (17)	706	38 (18)	32 (16)
Symptoms	44 (17)	705	48 (18)	42 (17)
ADL function	42 (18)	706	45 (20)	40 (16)
Sport and recreation function	8 (12)	763	11 (14)	6 (11)
Quality of life	23 (15)	722	26 (16)	22 (14)
6 months postoperative				
Pain	77 (21)	588	79 (21)	76 (21)
Symptoms	69 (18)	590	66 (18)	69 (18)
ADL function	78 (20)	588	80 (19)	77 (20)
Sport and recreation function	36 (26)	628	41 (26)	33 (26)
Quality of life	59 (21)	591	58 (21)	59 (22)
12 months postoperative				
Pain	84 (20)	586	85 (19)	83 (21)
Symptoms	76 (18)	585	75 (19)	76 (18)
ADL function	82 (20)	588	84 (20)	82 (19)
Sport and recreation function	44 (29)	602	48 (30)	42 (29)
Quality of life	67 (23)	588	65 (23)	68 (23)
24 months postoperative				
Pain	83 (20)	415	85 (19)	82 (21)
Symptoms	77 (17)	399	76 (17)	78 (17)
ADL function	82 (20)	416	83 (19)	82 (20)
Sport and recreation function	43 (28)	416	50 (28)	39 (28)
Quality of life	66 (23)	414	64 (24)	66 (23)

Abbreviations: ADL = activities daily living, KOOS = Knee Injury and Osteoarthritis Outcome Score, SD = standard deviation

Background/Purpose: The interpretation of patient-reported outcomes, such as the Knee injury and Osteoarthritis Outcome Score (KOOS) questionnaire, can prove difficult if benchmarks are lacking. Therefore, we recently developed KOOS percentile curves with data from a Dutch population-based cohort (Loef et al. 2020. https://doi.org/10.1016/j.

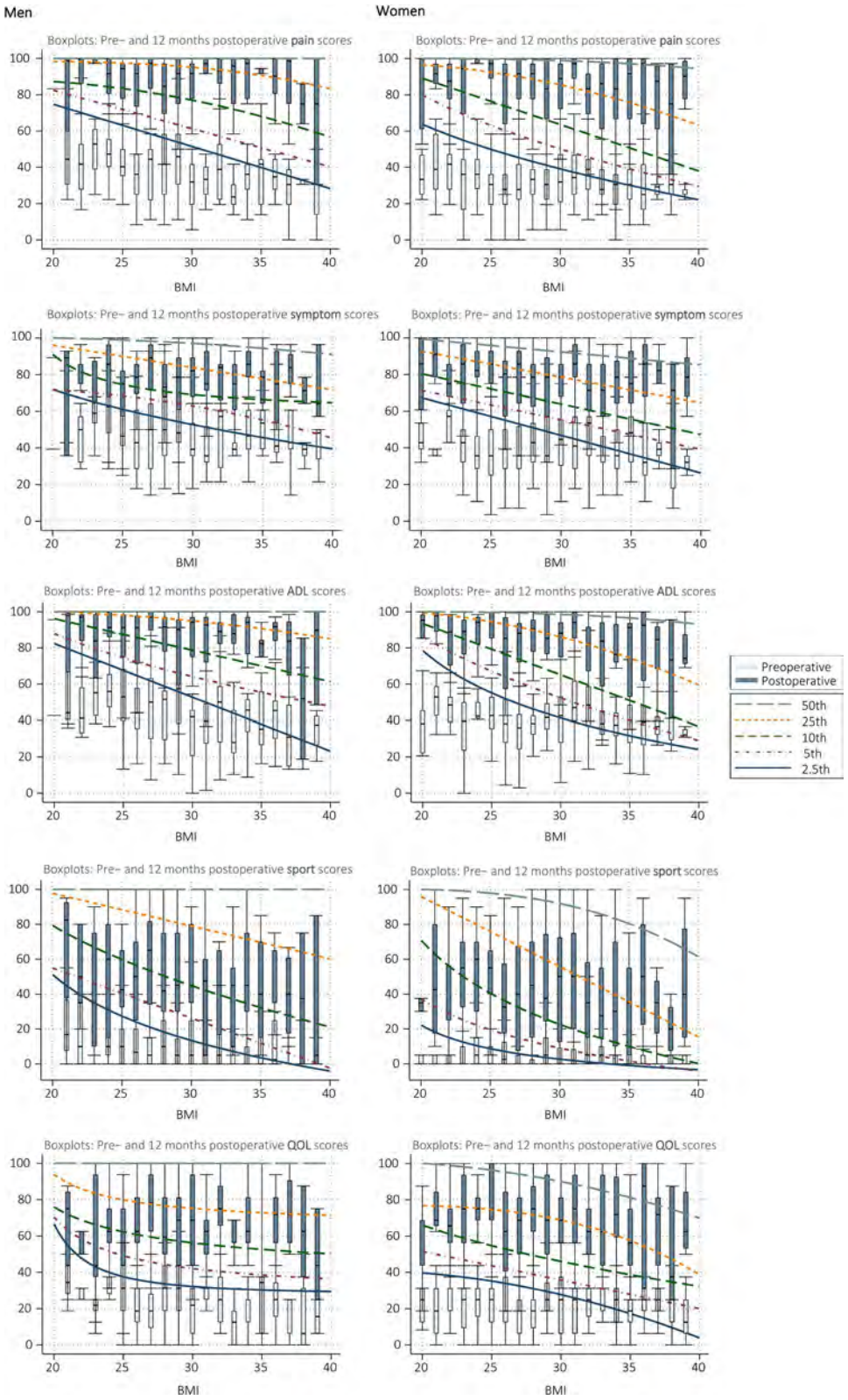


Figure 1. Preoperative and 12 months postoperative KOOS pain, symptoms, activities of daily living (ADL) function, sport and recreation function, and quality of life (QOL) subscale scores of men and women with knee OA undergoing TKA plotted on the KOOS percentile curves.

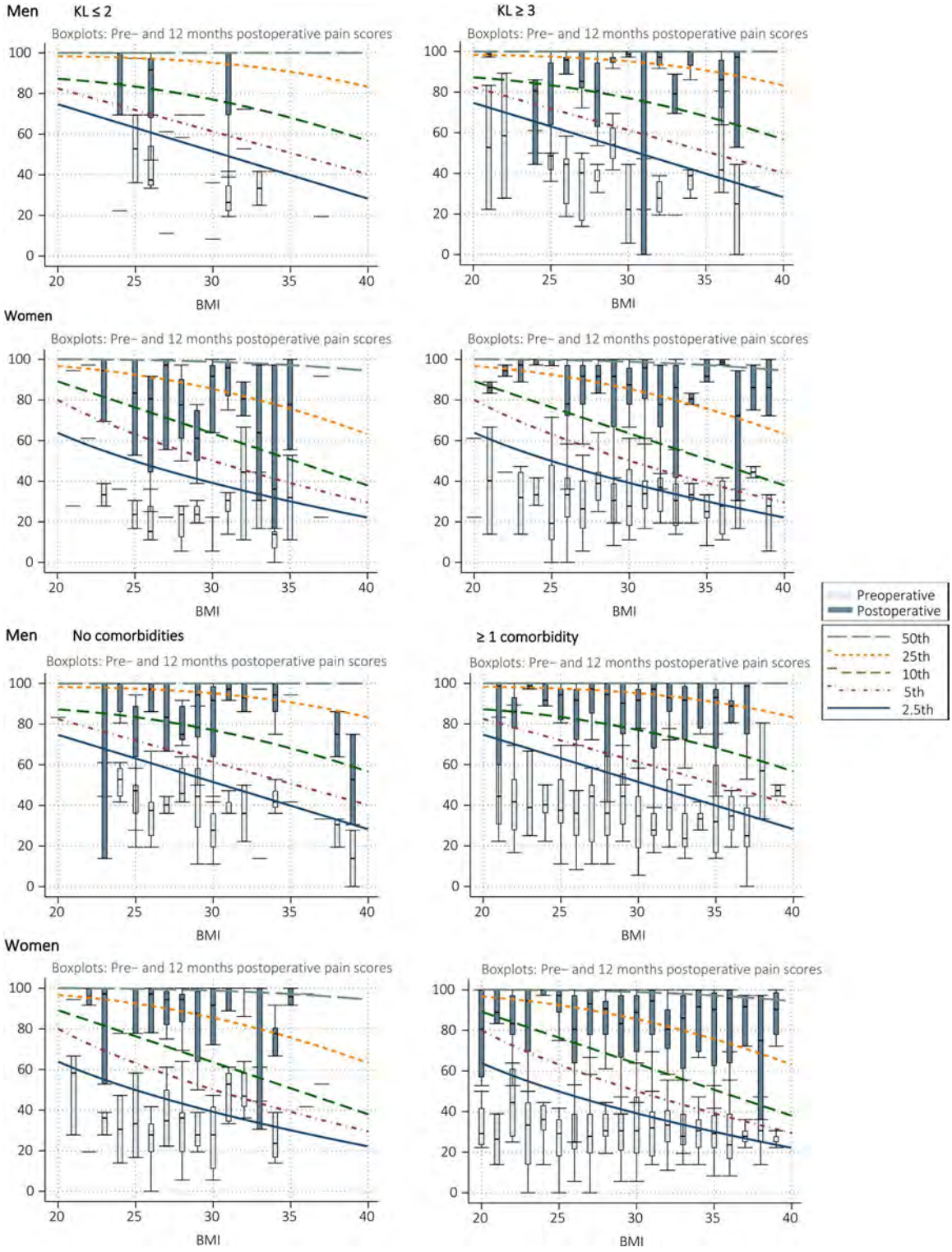


Figure 2. Preoperative and 12 months postoperative KOOS pain subscale scores of men and women with knee OA undergoing TKA, stratified by Kellgren-Lawrence score (upper quadrant), and by presence of comorbidities (lower quadrant).

joca.2020.03.014). With the present study, we aimed to investigate the application of the KOOS percentile curves using pre- and postoperative data of patients with knee osteoarthritis (OA) undergoing total knee arthroplasty (TKA).

Methods: We used data of the Longitudinal Leiden Orthopaedics Outcomes of Osteo-Arthritis study (LOAS) (van de Water et al. 2019. https://doi.org/10.2106/JBJS.18.00642). The current analyses are comprised of patients who have been included from June 2012 until June 2017, who were between 45 and 65 years of age, and undergoing primary TKA.KOOS subscale scores (0-100) were obtained preoperatively and 6, 12 and 24 months after TKA. Preoperative radiographs of the operated knee were assessed for radiographic OA severity according to the Kellgren-Lawrence (KL) grading system by an experienced musculoskeletal radiologist in a subset (37%) of patients. Comorbidities were self-reported using a standardized questionnaire. We stratified all analyses by sex. We plotted the median (interquartile range) population-level KOOS scores of all subscales on the previously developed population-based KOOS percentile curves(1). Additionally, we investigated differences in score trajectories between patients with preoperative KL scores ≤2 to ≥3, and presence (versus absence) of comorbidities.

Results: The study population consisted of 853 knee OA patients, of whom 62% were women. The mean (SD) age was 59 (5) years, mean BMI was 30 (5) kg/m2). Overall, 74% of the population had moderate to severe radiographic OA, a minority had no (4%), doubtful (6%) or minimal but definte (17%) radiographic OA. Comorbidities were present in 75% of patients. We observed poor KOOS scores across all subscales, which improved greatly postoperatively, with stabilization of scores after 12 months (table 1). Preoperatively, median KOOS scores of all subscales were at or below the 2.5th percentile. Scores increased to approximately the 25th percentile 12 months postoperatively. Greater improvements were observed in the subscale pain, and less improvements in the subscales sport and recreational function, and quality of life (figure 1). Patients with higher preoperative KL scores and without comorbidities showed greater improvements in KOOS scores (figure 2).

Conclusion: We applied KOOS data of knee OA patients undergoing TKA on the KOOS percentile curves, showcasing multiple ways these curves may be used in research and clinical care. In comparison to the general population, we observed poor preoperative KOOS scores, with large interpatient variation. Although major improvements were observed postoperatively, median population scores did not normalize to scores of the general population. The percentile curves may aid patient-clinician communication, improve management of treatment expectations and support shared-decision making.

Disclosure: M. Loef, None; **M. Gademan**, None; **D. Latijnhouwers**, None; **H. Kroon**, None; **H. Kaptijn**, None; **W. Marijnissen**, None; **R. Nelissen**, None; **T. Vliet Vlieland**, None; **M. Kloppenburg**, Dutch Arthritis society, 2.

Abstract Number: 1489

Relation of Pain Mechanisms to Development of Knee Pain in Osteoarthritis: The Multicenter Osteoarthritis Study

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis II: Clinical Aspects
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

QST measure	Adjusted Odds Ratio (95% CI)		
	Incident Frequent Knee Pain	Incident Frequent Intermittent or Constant Pain	WOMAC Pain Worsening
Temporal summation per SD unit increase	1.08 (0.96, 1.21)	**1.15 (1.02, 1.30)**	0.95 (0.87, 1.04)
PPT patella, per SD unit decrease	**1.16 (1.01, 1.32)**	**1.21 (1.04, 1.42)**	**1.14 (1.03, 1.25)**
PPT wrist, per SD unit decrease	1.02 (0.88, 1.19)	**1.21 (1.02, 1.43)**	**1.17 (1.04, 1.32)**
CPM≤1 (inefficient vs. efficient CPM)	1.23 (0.95, 1.59)	0.98 (0.75, 1.29)	1.04 (0.86, 1.26)

Relation of Quantitative Sensory Testing Measures of Ascending Facilitation and Descending Modulation to Risk of Developing Knee Pain or Knee Pain Worsening Over Two Years

Background/Purpose: Whether altered nociceptive signaling, such as pain sensitization and abnormal descending pain modulation, impact the risk of developing knee pain, more pain severity, and/or change in pain patterns from intermittent to more persistent pain over time is not clear. We used quantitative sensory testing (QST) to evaluate the relation of pain mechanisms to development and change in pain over 2 years.

Methods: We used data from the Multicenter Osteoarthritis (MOST) Study, a NIH-funded longitudinal cohort of people with or at risk of knee OA. The current analysis focusing on the 12th-year visit as the baseline for this analysis as this was the first visit at which descending pain modulation was assessed. All participants had pain questionnaires, knee radiographs, and QST at this baseline visit, and were assessed for pain outcomes every 8 months x3. QST comprised temporal summation (TS), pressure pain threshold (PPT), both of assess ascending pain facilitation, and conditioned pain modulation (CPM), a measure of descending pain modulation. TS was assessed with a set of weighted mechanical punctate probes. Degree of TS was defined as the difference in pain rating from the end of the train of 10 stimuli vs. the baseline. PPT at the wrist and patellae was assessed with an algometer as the point at which pressure first changed to slight pain. CPM was assessed using PPT at the wrist as the test stimulus pre- and post-conditioning stimulus (forearm ischemia); CPM was computed as the post-PPT: pre-PPT ratio. We evaluated the relation of each QST measure to the risk of development of: frequent knee pain (FKP) among those free of FKP at baseline, development of more frequent intermittent knee pain (indicated as at least “often”) or constant pain among those with no constant pain or only infrequent intermittent pain (occurring no more than “sometimes” based on the ICOAP) at baseline, and WOMAC worsening of ≥2/20 (MCID) over 2 years. We used logistic regression with GEE, adjusting for age, sex, BMI, race, catastrophizing, and depressive symptoms.

Results: 2794 participants were included (mean age 64, mean BMI 29.5, 57% female). More pain sensitization assessed by TS was associated with increased risk of developing more intermittent or constant pain over two years (**Table**). More pain sensitization by PPT at the patella and wrist were associated with higher risk of developing more intermittent or constant pain, and with WOMAC pain worsening. Lower PPT at the patella was additionally associated with higher risk of developing FKP. In contrast, inefficient CPM was not associated with development of any of these pain outcomes over two years.

Conclusion: Pain sensitization measures that reflect ascending pain facilitation were associated with increased risk of developing more frequent and/or more severe knee pain. In contrast, descending pain modulation did not appear to play a role in changing pain frequency or severity over time. These findings provide insights into the role of neurobiological pain mechanisms in the transition from acute to chronic pain in knee OA.

Disclosure: T. Neogi, Lilly, 1, EMD Merck Serono, 1, Novartis, 1, Regeneron, 1, Pfizer/Lilly, 1; **N. Wang**, None; **K. Aoyagi**, None; **L. Frey Law**, None; **C. Lewis**, None; **M. Nevitt**, None; **L. Carlesso**, None.

Abstract Number: 1490

Pain Rating Variability and Response to Treatment in Osteoarthritis Clinical Trials

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis II: Clinical Aspects
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Background/Purpose: Despite the known high inter- and intra-patient variability in analgesic responses in chronic pain, most interventional pain studies rely on single time point pain reports and do not take in consideration the dynamic effects of daily pain on the response to treatment. In this study we examined the between- and within-subject variability in pain ratings and their value as a predictor of treatment response.

Methods: Three hundred and eighty-nine osteoarthritis patients (OA) enrolled as part of a clinical trial (NCT00809783) were randomized in two groups: Naproxen 500 mg twice a day (NAP; n=113) and Placebo (PBO; n=276). All participants were to complete daily pain intensity diaries using a numeric rating scale (NRS; 0 to 10 points) for a period of 127 days (15 days before + 112 days during treatment). A logistic regression analysis of responders (30% pain improvement) and a linear longitudinal model were performed to determine whether the pre-treatment pain variation (standard deviation of pain, SD) was associated with treatment response and decreases in pain intensity.

Results: Longitudinal pain decrease was observed over time (NRS SD) with both treatments ($p< 0.001$); pain variability (PV) within subjects was stable over time (Pearson's R, pre/post treatment SD: PBO $r= 0.37$, $p< 0.00$; NAP=0.21 $p=0.03$). Pre-treatment pain variability significantly predicted response after 4, 8, 12 and 16 weeks (Table 1, $p< 0.05$). Next, we investigated the treatment effects subclassifying treatment groups based on their pain variability. The high

Predictor	Estimate	Std. Err.	Odds Ratio	P>|z|
at 4 weeks				
pain variability	0.710	0.214	2.034	0.001
at 8 weeks				
pain variability	0.833	0.228	2.301	0.000
at 12 weeks				
pain variability	0.548	0.235	1.730	0.019
at 16 weeks				
pain variability	0.492	0.249	1.635	0.049
* The following regression model: logit (responder -30 % pain decrease: 0,1) log(pain variability index [standard deviation before baseline]). OR odds ratio				

Table 1. Results of logistic regression analysis of clinical pain responders*

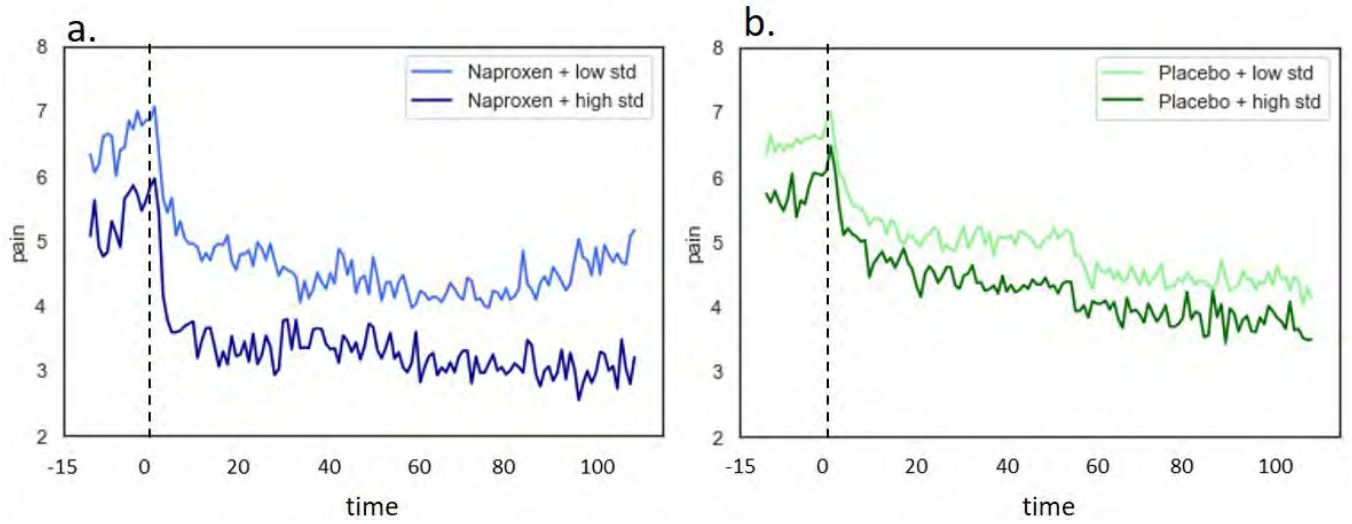

Figure 1. Longitudinal daily pain decreases over time. a. There is significant difference in pain decrease over time between high and low Naproxen groups (p<0.001). b. There is a significant decrease of pain over time, but not significant difference between high and low Placebo groups (p=0.09).

variability NAP subgroup presented significantly larger improvement in pain than the low variability subgroup (p< 0.001), and a similar trend was observed for the placebo group (p=0.09) (Figure 1).

Conclusion: Pain variability in patients with OA seems to be stable over time and independent of mean pain reduction. Pre-treatment higher pain variability associates both with categorical response to treatment (30% recovery), and linear pain reduction, thus constituting a marker of treatment response and a possible important effect to control for in OA clinical trials.Table 1. Results of logistic regression analysis of clinical pain responders*

Disclosure: C. Pinto, None; **J. Barroso**, None; **T. Schnitzer**, Pfizer, 1, 2, Lilly, 1, 2, Regeneron, 1, AstraZeneca, 1.

Abstract Number: 1491

Association of a Leaky Gut but Not Microbial Dysbiosis with Obesity-related OA: A Translational Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Osteoarthritis II: Clinical Aspects
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: To test the hypothesis that an altered gut microbiota (dysbiosis) plays a causal role in the obese OA phenotype (obesity with both hand and knee OA).

Methods: Stool and blood samples were collected from 92 participants with BMI ≥ 30 and age ≥ 55 yrs recruited from the Johnston County Osteoarthritis Project. OA cases (n=50) had clinical and/or radiographic hand OA, defined as

Table 1.

Participant Characteristic	Cases (N=50)	Controls (N=42)	p-value
Age, years	73.7 (6.9)	70.8 (6.4)	0.04
Female, N (%)	43 (86%)	26 (62%)	0.01
African American, N (%)	17 (34%)	18 (43%)	0.39
BMI, kg/m^2	36.3 (4.4)	33.4 (3.1)	0.001
WOMAC Pain Score, left knee	5.2 (5.1)	2.2 (3.7)	0.002
WOMAC Pain Score, right knee	5.3 (4.9)	1.8 (3.3)	0.0001
Maximum KL Grade			
0	0	1 (2.4%)	
1	0	32 (76.2%)	
2	2 (4.0%)	9 (21.4%)	
3	13 (26.0%)	0	
4	21 (42.0%)	0	
Total knee replacement	14 (28.0%)	0	

BMI, body mass index

WOMAC, Western Ontario and McMaster Universities Arthritis Index (range 0-20)

involvement of at least 3 joints across both hands, and had Kellgren-Lawrence (KL) grade 2-4 knee OA (or TKR) in at least one knee on preliminary reading. Controls (N=42) had no hand OA and KL grade 0-1 knees. Exclusions included consumption of antibiotics/probiotics or intestinal surgery within the past 6 weeks, known bowel disease or prior fecal microbiota transplantation. Compositional analysis of the gut microbiome was carried out by 16S rRNA bacterial amplicon sequencing. Data was analyzed using QIIME 1.9.0. Shannon index, Chao1, and Phylogenetic Diversity (PD) were estimated from sequencing data. Beta diversity estimates were calculated using weighted and unweighted Unifrac approaches. Permutation Multivariate Analysis of Variance (PERMANOVA) and Analysis of Similarities (ANOSIM) were used to test the null hypothesis that case and control microbial communities share the same distribution. The Wilcoxon tests adjusted for multiple comparisons were used to determine differences in relative genera abundances between case and control groupsl. Blood samples were used for a multiplex cytokine analysis (n=73) and measures of LPS and LPS binding protein (n=78). To test for causality, pooled fecal transplant from 5 cases and 5 controls were gavaged every 4 weeks to 31 germ-free mice (n=16 cases; n=15 controls). Mice were on a Western Diet (40% fat, high sucrose) for 40 weeks. Fecal samples were collected 2 weeks after each gavage. Knee OA was evaluated histologically (grading of cartilage damage, osteophytes and synovitis) at week 40.

Results: OA cases were slightly older with more females, higher BMI, greater WOMAC pain and KL grades (Table 1). Nine participants recruited as controls had KL grade 2 in one knee after final readings by the study radiologist. A sensitivity analysis was performed assigning these participants to the case group and this did not change any of the results. There were no significant differences in diversity between cases and controls. Likewise, there were no significant compositional differences between groups at the genus level. Cases had higher levels of osteopontin (a pro-inflammatory cytokine originally isolated from bone) and LPS (a sign of a leaky gut) (Fig 1).

Mice transplanted with case or control microbiota gained similar weight but exhibited a significant difference in microbial diversity (p=0.02, Fig.2). Both groups developed histologic findings of OA without any differences in OA severity between the groups.

Conclusion: The lack of differences in the gut microbiota yet increased serum LPS levels in obese humans with hand and knee OA suggest that a leaky gut allowing for greater absorption of LPS (and potentially other bacterial products), rather than a dysbiotic microbiota, may contribute to development of OA. This was supported by the failure to promote more severe OA in mice by microbial transplant from humans with OA.

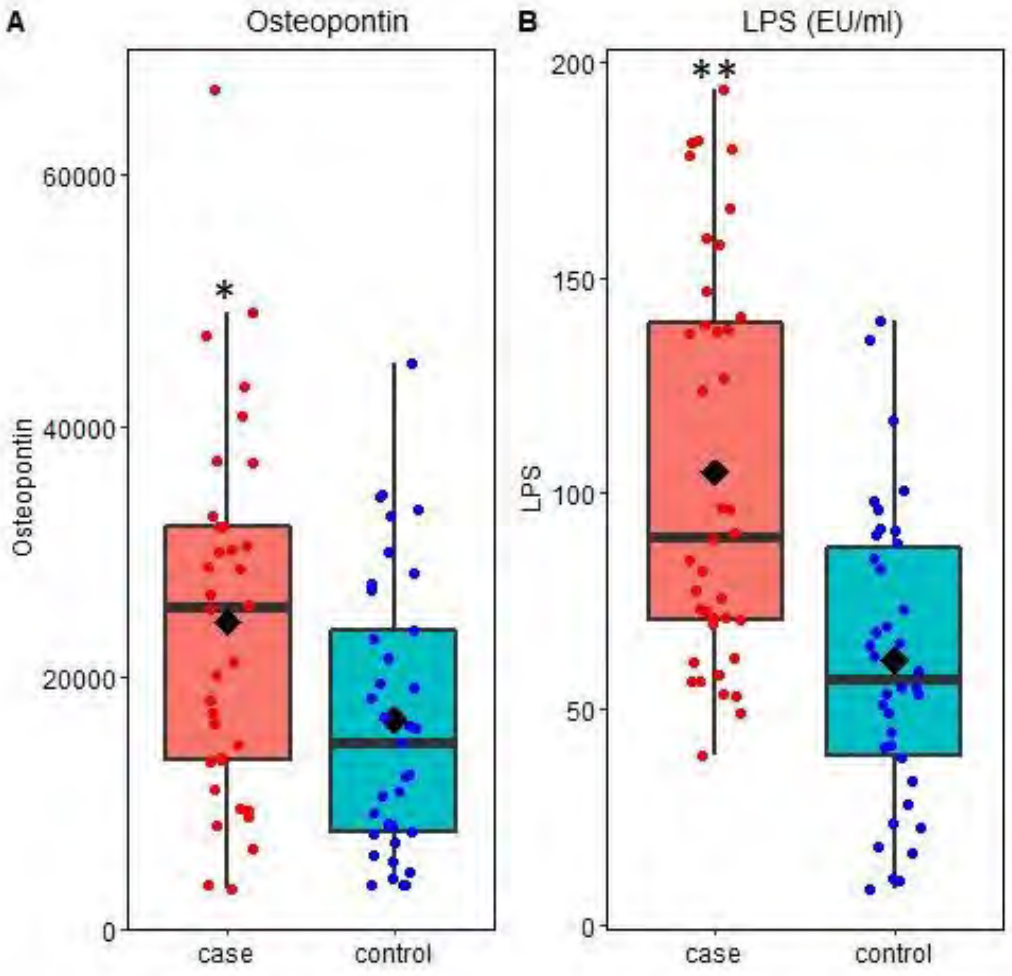

Fig.1 Osteopontin (A) and LPS (B) levels in OA cases and controls. Osteopontin measured in plasma shown as RFU values. LPS measured in serum shown as EU/ml. *p=0.01, **p<0.0001

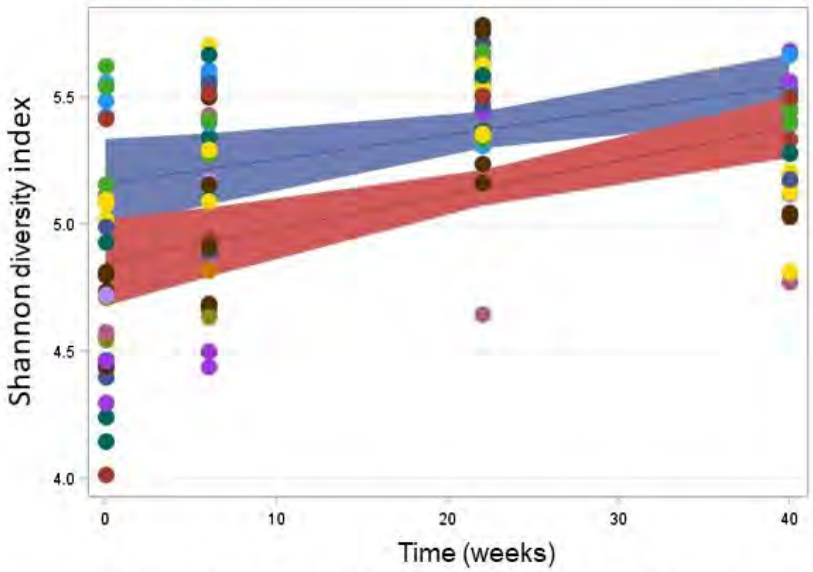

Fig.2 Longitudinal change in Shannon (alpha) diversity index over time in mouse fecal microbiota after pooled fecal transplants from human OA cases and controls. Colored dots indicate mice from the same cage. p=0.02 for difference between case and control over time.

Disclosure: R. Loeser, Bioventus, 1, Unity Biotechnology, 1; **L. Arbeeva**, None; **K. Kelley**, None; **A. Fodor**, None; **S. Sun**, None; **V. Ulici**, None; **L. Longobardi**, None; **Y. Cui**, None; **S. Sumner**, None; **A. Azcarate-Peril**, None; **B. Sartor**, None; **I. Carrol**, None; **A. Nelson**, None.

Abstract Number: 1492

The Childhood Arthritis and Rheumatology Research Alliance Start Time Optimization of Biologic Therapy in Polyarticular JIA Study: Report of Primary Study Outcomes

Yukiko Kimura[1], George Tomlinson[2], Laura Schanberg[3], Mary Ellen Riordan[4], Anne Dennos[5], Vincent Del Gaizo[6], atherine Murphy[7], Pamela F. Weiss[8], Brian Feldman[9] and Sarah Ringold[10], [1]Hackensack Meridian School of Medicine, Hackensack, NJ, [2]Department of Medicine, University Hospital Network, Toronto, Toronto, ON, Canada, [3]Duke University Medical Center, Durham, NC, [4]Hackensack University Medical Center, Westwood, NJ, [5]Duke University, Durham, NC, [6]Childhood Arthritis & Rheumatology Research Alliance (CARRA), Whitehouse Station, NJ, [7]Lousiana Department of Public Health, New Orleans, LA, [8]Children's Hospital of Philadelphia, Philadelphia, [9]The Hospital for Sick Children, Toronto, ON, Canada, [10]Seattle Children's, Seattle, WA

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Pediatric Rheumatology – Clinical I: Treatment of JIA

Session Type: Abstract Session

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Background/Purpose: There is uncertainty regarding when to start biologic medications for polyarticular juvenile idiopathic arthritis (P-JIA). The Childhood Arthritis and Rheumatology Research Alliance (CARRA) developed consensus treatment plans (CTPs) that reflect the most commonly used strategies for starting biologic treatment in untreated

P-JIA patients. The CARRA STOP-JIA study compared the effectiveness of the CARRA CTPs in achieving clinical inactive disease (CID) using a prospective, observational study design.

Methods: STOP-JIA compared 3 CARRA CTPs: 1) Step Up – starting non-biologic disease modifying anti-rheumatic drug (DMARD) monotherapy, adding biologic medication if needed after ≥ 3 months; 2) Early Combination - DMARD and biologic medication started together; and 3) Biologic First – starting biologic monotherapy, adding DMARD if needed after ≥ 3 months. There was no randomization. Data were collected approximately every 3 months using the CARRA Registry. The primary outcome was the proportion of children achieving CID off glucocorticoids (GC) at 12 months. The primary analysis was intention-to-treat. Propensity score (PS) weighting was used to balance baseline differences in potential confounders between CTPs. Multiple imputation was used to address missing data. Secondary outcomes included comparison of clinical Juvenile Arthritis Disease Activity Score based on 10 joints (cJADAS10) scores, patient-reported outcomes (PROs) and serious adverse events (SAEs).

Results: 400 participants were enrolled across 56 Registry sites. 64% chose Step Up, 25% Early Combination, and 11% Biologic First. There were significant baseline differences between CTP groups for several variables, including JIA categories, number of active joints, Physician Global Assessment of Disease Activity, and Juvenile Arthritis Dis-

Table 1. Baseline Patient Characteristics

	Overall	Step Up	Early Combination	Biologic First	p-value
n	400	257	100	43	
Age (mean (SD))	10.40 (4.94)	10.03 (5.03)	11.12 (4.54)	10.89 (5.17)	0.14
Male (%)	106 (26.5)	65 (25.3)	25 (25.0)	16 (37.2)	0.24
Race (%)					0.35
Black	30 (7.5)	17 (6.6)	7 (7.0)	6 (14.0)	
Other	79 (19.8)	47 (18.3)	24 (24.0)	8 (18.6)	
White	291 (72.8)	193 (75.1)	69 (69.0)	29 (67.4)	
Months Since Symptom onset (median [IQR])	6.10 [2.90, 16.11]	5.60 [2.76, 14.09]	7.31 [3.51, 17.16]	5.16 [2.10, 30.93]	0.42
Months Since Diagnosis (median [IQR])*	0.00 [0.00, 0.83]	0.00 [0.00, 0.80]	0.00 [0.00, 0.47]	0.47 [0.00, 2.12]	**0.03**
Disease Course (%)*					**0.001**
Enthesitis related	33 (8.2)	15 (5.8)	10 (10.0)	8 (18.6)	
Extended oligoarticular	14 (3.5)	12 (4.7)	0 (0.0)	2 (4.7)	
Poly (RF-)	242 (60.5)	171 (66.5)	54 (54.0)	17 (39.5)	
Poly (RF+)	78 (19.5)	42 (16.3)	28 (28.0)	8 (18.6)	
Psoriatic	23 (5.8)	12 (4.7)	5 (5.0)	6 (14.0)	
Undifferentiated	10 (2.5)	5 (1.9)	3 (3.0)	2 (4.7)	
Physician Global (mean (SD))*	5.52 (2.12)	5.07 (1.99)	6.41 (2.14)	6.14 (2.02)	**<0.001**
Parent Global (mean (SD))*	4.33 (2.68)	3.94 (2.70)	4.88 (2.51)	5.32 (2.51)	**0.001**
JADAS (mean (SD))*	18.08 (4.67)	17.08 (4.55)	20.18 (4.37)	19.05 (4.29)	**<0.001**
Active Joint Count (mean (SD))*	12.8 (8.6)	11.9 (8.1)	16 (9.42)	10.8 (7.9)	**<0.001**
Joints with limited range of motion (mean (SD))*	8.9 (8.4)	7.7 (7.2)	12 (9.9)	7.9 (8.6)	**<0.001**
Abnormal ESR (%)	129 (43.1)	74 (39.6)	40 (49.4)	15 (48.4)	0.27
Abnormal CRP (%)	99 (33.1)	57 (30.5)	31 (38.3)	11 (35.5)	0.44
CHAQ (mean (SD))*	0.90 (0.72)	0.80 (0.70)	1.05 (0.68)	1.14 (0.85)	**0.002**

RF: Rheumatoid factor; JADAS: Juvenile Arthritis Disease Activity Score. ESR: erythrocyte sedimentation rate; CRP: c-reactive protein; CHAQ: Childhood Health Assessment Questionnaire *$p<0.05$

Table 2. Clinical Inactive Disease (CID) Off Glucocorticoids (GC) and cJADAS10 Remission* Off GC at 12 Months after Propensity Score Weighting and Multiple Imputation (%, 95% CI)

Percentage with outcome in each CTP and 95% CI

	CID off GC	cJADAS Remission
Step Up	37.8 (29.4 ,46.2)	42.8 (35.7, 49.9)
Early Combination	47.3 (32.6, 62.0)	58.8 (46.4, 71.1)
Biologic First	33.6 (14.5, 52.6)	47.1 (25, 69.3)

Difference in percentages between CTPs with 95% CI

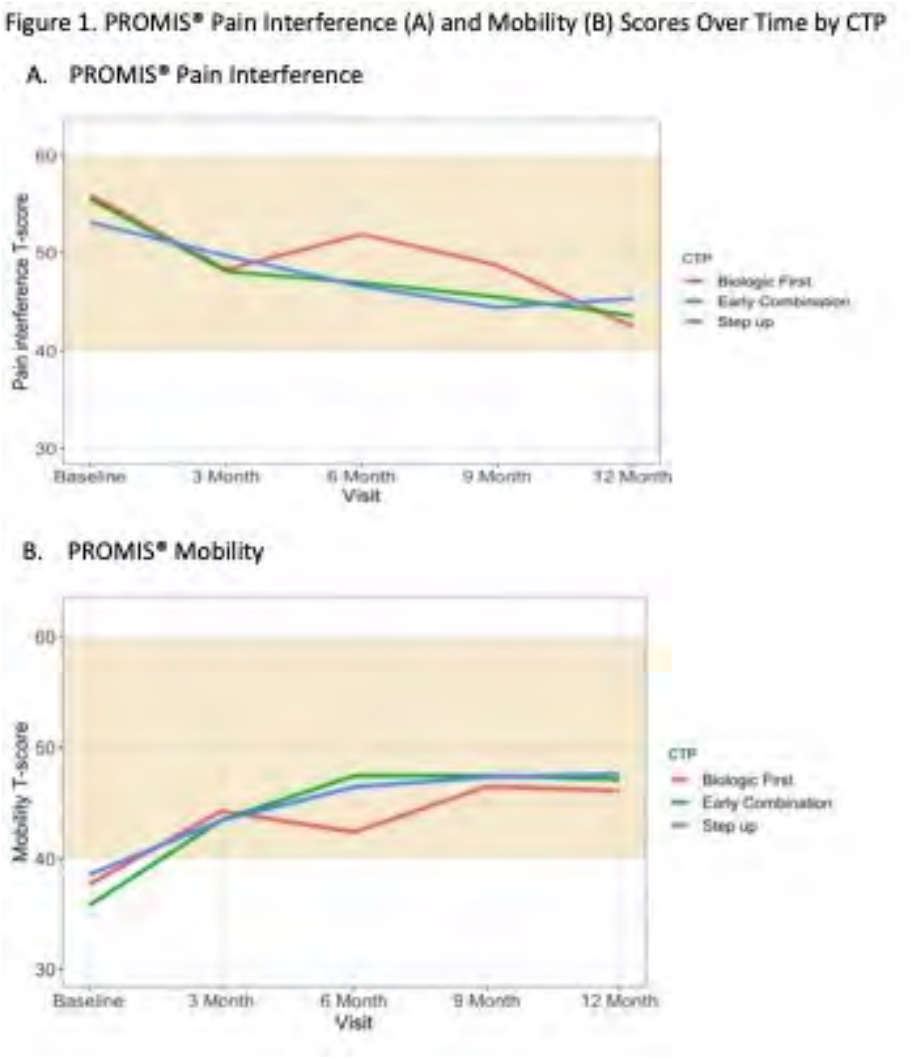
	CID off GC	cJADAS Remission
Biologic First vs Step Up	-4.2 (-23.3, 14.8) p=0.66	4.3 (-18.8, 27.5) p=0.7
Early Combination vs Step Up	9.5 (-4.1, 23.2) p=0.17	**16 (1.8, 30.2) p=0.02**
Biologic First vs Early Combination	-13.7 (-35.7, 8.2) p=0.22	-11.7 (-36.7, 13.3) p=0.43

*Clinical Juvenile Disease Activity Score based on 10 Joints (cJADAS10). Defined as score ≤ 2.5.

ease Activity Score (cJADAS10) scores (Table 1). Proportion of patients achieving CID at 12 months was 32% for Step Up, 37% Early Combination, and 24% Biologic First, with no statistically significant difference between groups. The differences remained not significant after PS weighting and multiple imputation (Table 2). Comparison of cJADAS10 levels of remission (≤ 2.5) at 12 months significantly favored Early Combination over Step Up after PS weighting and multiple imputation (66.6% versus 42.4%; p=0.02). There were no significant differences in either pain interference or mobility (PROMIS®) measures between CTPs over time, although both measures showed improvement over time (Figure 1). Seventeen SAEs were reported, most commonly infections.

Conclusion: Although there were no significant differences between CARRA P-JIA CTP groups in the primary endpoint of CID off GC, all CTP groups had improved disease activity during the study, and cJADAS10 scores showed significant differences. Planned secondary analyses, including subgroup analyses, timing of medication initiation/discontinuation, and reclassifying groups by CTP actually used, are underway and will generate additional information about the comparative effectiveness of the CTP approaches.

Figure 1. PROMIS® Pain Interference (A) and Mobility (B) Scores Over Time by CTP



Disclosure: Y. Kimura, CARRA, 9, Up to Date, 7, Genentech, 2; **G. Tomlinson**, None; **L. Schanberg**, UCB, 1, Sanofi, 1, BMS, 1, Sobi, 1, 2; **M. Riordan**, None; **A. Dennos**, None; **V. Del Gaizo**, CARRA, 1; **K. Murphy**, None; **P. Weiss**, Lilly, 1, Pfizer, 1; **B. Feldman**, Pfizer, 1, AB2-Bio, 1, Optum, 1, Novartis, 1; **S. Ringold**, CARRA, 1, Up to Date, 1.

Abstract Number: 1493

Distinct Patient-level Patterns of Response to Methotrexate in Juvenile Idiopathic Arthritis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Pediatric Rheumatology – Clinical I: Treatment of JIA
Session Type: Abstract Session
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Background/Purpose: Treatment response in JIA is often viewed as a binary outcome: response or non-response, usually assessed using composite, multidimensional measures, such as the juvenile arthritis disease activity score (JADAS). Within a composite outcome, there are likely different, identifiable patterns of response that cluster within subgroups of children and young people (CYP). Identifying these subgroups could assist the tailoring of stratified treatment approaches in JIA and offer further insights into understanding treatment response.

This study aimed to identify subgroups of CYP defined by different trajectories of individual JADAS components in the first year following initiation of methotrexate (MTX).

Methods: The discovery cohort for subgroup identification included MTX-naïve CYP with JIA at the point of MTX initiation, enrolled prior to January 2018 to either the BSPAR Etanercept Cohort Study (BSPAR-ETN) or the Biologics for Children with Rheumatic Diseases Study (BCRD), nationwide pharmacological registers. The Childhood Arthritis Prospective Study (CAPS), a multicentre JIA inception cohort, was used for verification. JADAS components (active joint count, physician's global assessment (PGA, 0-10cm), parental global evaluation (PGE, 0-10cm) and standardised ESR (0-10) were calculated based on data collected in the year following MTX initiation and log1p transformed for analysis.

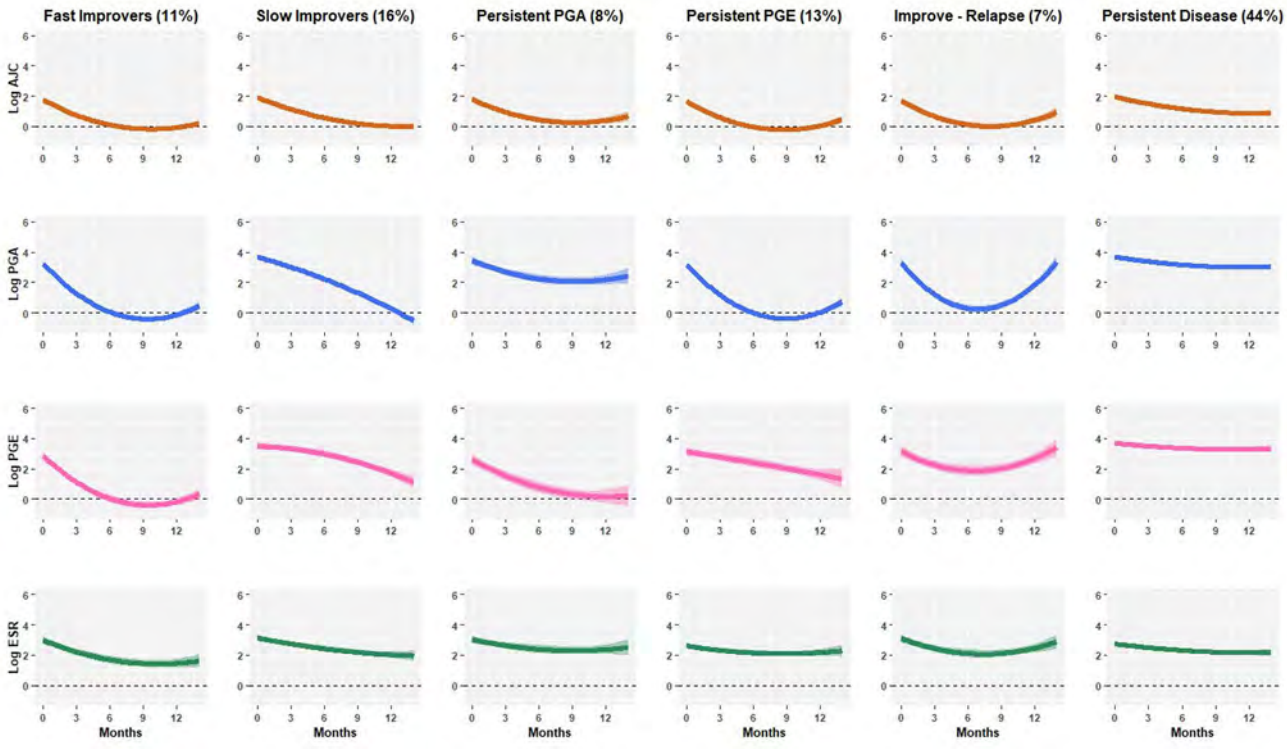

Figure 1. Clusters of MTX response identified in children and young people with JIA enrolled to the BSPAR-ETN or BCRD studies

Multivariate group-based trajectory models were used to explore MTX response clusters. Optimal models were selected based on a combination of model fit (BIC, relative entropy, average posterior probabilities), parsimony and clinical plausibility. Model development and selection were repeated independently in the verification cohort.

Results: The discovery cohort included 658 CYP, and in the verification cohort n=537. The majority were female (68%, 70%) and of white ethnicity (86%, 82%), with RF-negative JIA (35%, 33%), respectively.

Six disease trajectories following MTX were identified in the discovery cohort: Two groups improved across all JADAS components: Fast improvers (11%) and Slow Improvers (16%). A large group maintained persistent disease overall (44%). Two groups maintained one persistent disease feature despite otherwise improvement: Persistent PGA (8%) and Persistent PGE (13%). A final group experienced disease relapse (7%) (Figure 1). These results were verified in the CAPS cohort, with similar subgroups and group proportions identified, except for the relapse group, which was not evident in the CAPS cohort.

Conclusion: We identify six clusters of CYP following initiation of MTX, each with differing patterns of disease activity, suggesting a simple responder/non-responder analysis at a set point may be over-simplistic. Common patterns were identified across multiple, large, UK cohorts. Understanding both clinical factors associated with, and biological mechanisms underpinning, these subgroups would aid stratified treatment decisions in JIA.

Disclosure: S. Shoop-Worrall, None; **K. Hyrich**, Abbvie, 5, BMS, 2, UCB, 2, Pfizer, 2; **L. Wedderburn**, AbbVie, 2, Sobi, 2; **W. Thomson**, None; **N. Geifman**, None.

Abstract Number: 1494

Patient-Reported Adverse Events, Quality of Life and Treatment Adherence in Juvenile Idiopathic Arthritis: Analysis of Two Large International Cohorts

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SESSION INFORMATION
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Background/Purpose: Juvenile idiopathic arthritis (JIA) patients may experience significant medication-related adverse effects (AEs), which may adversely affect health-related quality of life (HRQOL), daily activities and treatment compliance. The study aims to investigate Patient-Reported Adverse Events (AEs) and their effects on HRQoL, school activity and therapeutic adherence, as captured by patient- and parent-reported outcome measures (PROMs).

Methods: Data on 13704 visits of 8402 patients were obtained from two large multi-center international studies, the pharmacovigilance registry Pharmachild and The EPidemiology, treatment and Outcome of Childhood Arthritis (EPOCA) cohort. Subjects who were on medications at the time of visit were included. PROMs were collected through the Juvenile Arthritis Multidimensional Assessment Report (JAMAR) and included checklists of AEs (18

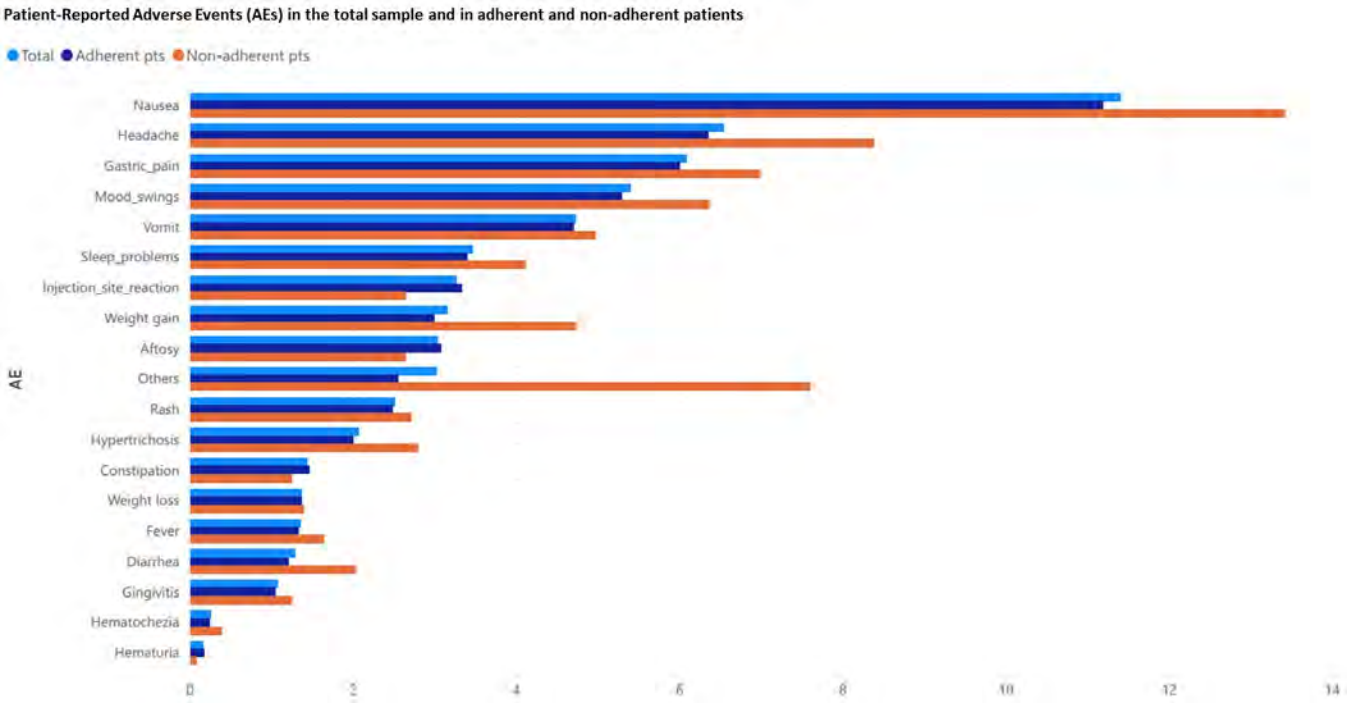

Figure 1. Frequencies (percentages) of Patient-Reported Adverse Events (AEs) in the total sample (light blue), adherent (dark blue) and non-adherent patients (orange).

items), disease-related school problems (5 items), self-reported treatment adherence (as a dichotomous variable) and reasons for non-compliance (5 items). Pain and overall well-being (PGA) were measured by 21-numbered circle visual analog scales. HRQoL was assessed through a ten-items Likert-type HRQoL scale encompassing a physical health (PhH) and psychosocial health (PsH) subscale, with higher scores indicating worse outcomes. The effects of

	Effects of Patient-Reported Adverse Events (AEs) on Patient Global Assessment of Overall Well Being (PGA)							Effects of Patient-Reported Adverse Events (AEs) on Psychosocial health subscale score (PsH)						
			95% Confidence Interval							95% Confidence Interval				
AEs	Estimate	SE	Lower	Upper	df	t	p	Estimate	SE	Lower	Upper	df	t	p
(Intercept)	2.7975	0.07365	2.65319	2.942	13706	37.986	< .001	2.7975	0.07365	2.65319	2.942	13706	37.986	< .001
Nausea	0.0599	0.05029	-0.03870	0.158	13846	1.190	0.234	0.0599	0.05029	-0.03870	0.158	13846	1.190	0.234
Headache	0.1534	0.06070	0.03439	0.272	13846	2.527	0.012	0.1534	0.06070	0.03439	0.272	13846	2.527	0.012
Gastric pain	0.1824	0.06176	0.06135	0.303	13845	2.953	0.003	0.1824	0.06176	0.06135	0.303	13845	2.953	0.003
Mood swings	0.5379	0.06756	0.40544	0.670	13823	7.961	< .001	0.5379	0.06756	0.40544	0.670	13823	7.961	< .001
Vomit	0.0617	0.06972	-0.07497	0.198	13848	0.885	0.376	0.0617	0.06972	-0.07497	0.198	13848	0.885	0.376
Sleep problems	0.2481	0.08268	0.08607	0.410	13826	3.001	0.003	0.2481	0.08268	0.08607	0.410	13826	3.001	0.003
Injection site reaction	0.1599	0.07752	0.00799	0.312	13708	2.063	0.039	0.1599	0.07752	0.00799	0.312	13708	2.063	0.039
Weight gain	0.1102	0.07998	-0.04655	0.267	13810	1.378	0.168	0.1102	0.07998	-0.04655	0.267	13810	1.378	0.168
Aftosy	0.1525	0.08256	-0.00930	0.314	13798	1.847	0.065	0.1525	0.08256	-0.00930	0.314	13798	1.847	0.065
Other	0.1469	0.07880	-0.00758	0.301	13712	1.864	0.062	0.1469	0.07880	-0.00758	0.301	13712	1.864	0.062

Figure 2. Results from linear mixed-effects regression models show the effects of the most commonly reported AEs (frequency > 3%) on Patient Global Assessment (PGA) and Psychosocial Health subscale score (PsH). The model for PGA is adjusted for pain levels and physician global assessment; the model for PsH is adjusted for physical health quality of life as measured by Physical Health subscale score (PhH).

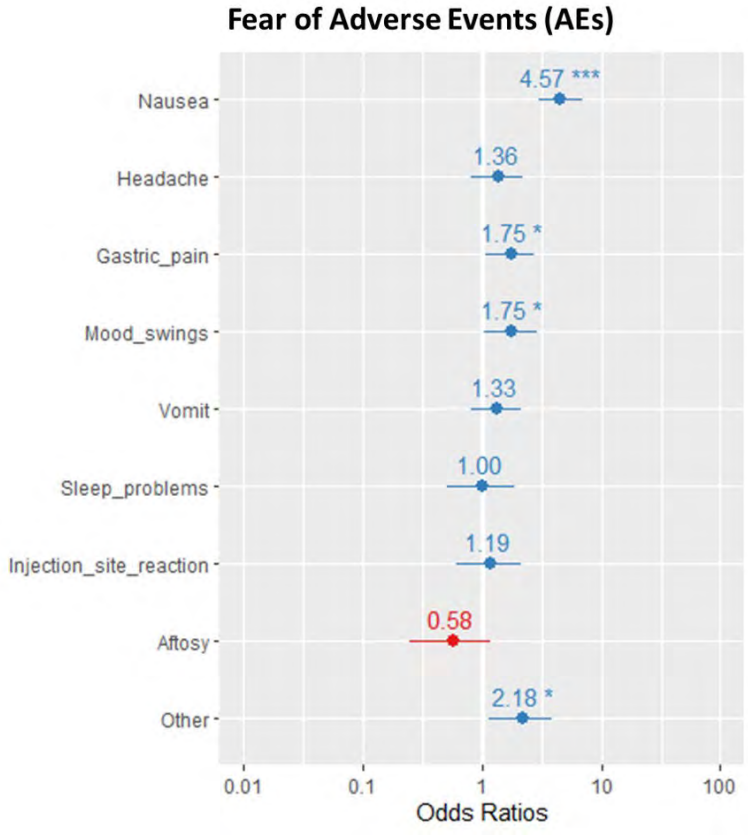

Figure 3. Risk (expressed as odds ratios) of self-reported non-adherence due to fear of Adverse Events (AEs) for individual AEs. * $p \leq 0.05$, *** $p \leq 0.001$

AEs on PGA, PsH scale, school problems, and self-reported non-adherence were analyzed using General Linear and Generalized Mixed Effects Models with random intercepts per individual.

Results: AEs were reported by 29,49% of patients. Frequencies of individual AEs are shown in Fig.1. Experiencing one or more AEs was associated to worse PGA (OR 1,46 95%CI 1.38-1.45, η^2 0.011, $p < .001$) and PsH score (OR 1.85, 95%CI 1.72-2.00, η^2 0.024, $p < .001$) and school problems (OR 1.82, 95%CI 1.64-2.01, $p < .001$) after adjustment for physician global assessment, PhH and pain levels. The effects of individual AEs on outcomes are reported in Fig. 2; mood swings, sleep problems and weight gain showed the highest impact on psychosocial health. Treatment non-adherence was reported by 9,27% of subjects; the most frequently cited reasons were drug refusal by the child (15,4%) and fear of adverse events (10,9%). Subjects reporting more than two AEs had a higher risk of non-adherence (OR 1.47, 95%CI 1.21 - 1.76, $p < .001$). Nausea was associated with non-compliance specifically due to fear of AEs, as shown in Fig. 3 (OR 4.57, 95%CI 2.98-6.92, $p < .001$).

Conclusion: AEs have a substantial impact on patients' quality of life, functioning and treatment adherence in JIA. The understanding treatment-related burden is vital to achieve good therapeutic compliance and improve outcomes in JIA.

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Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, R-Pharma, 5, 8, Sanofi, 5, 8, Servier, 5, 8, Sinergie, 5, 8, Sobi, 2, 5, 8, 9, AbbVie, 5, 8, Takeda, 5, 8.

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Tofacitinib for the Treatment of Patients with Juvenile Idiopathic Arthritis: An Interim Analysis of Data up to 5.5 Years from an Open-label, Long-term Extension Study

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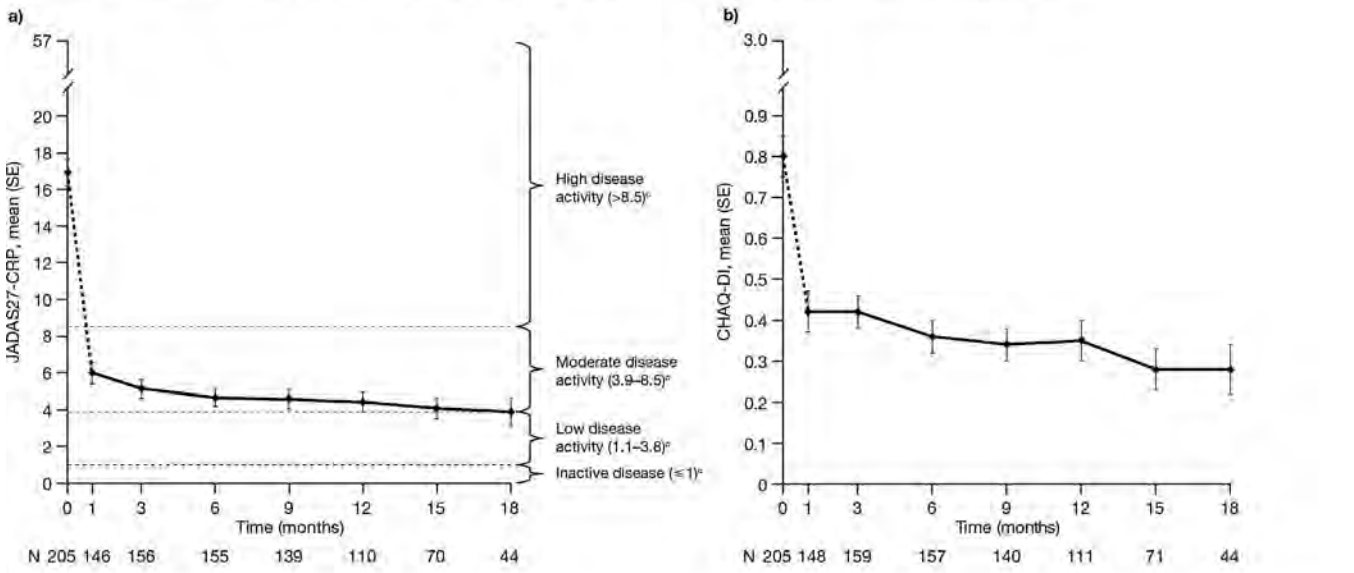
Figure 1. Observed efficacy of tofacitinib[a] in pts with JIA through M18: a) mean JADAS27-CRP[b] and b) mean CHAQ-DI[b]



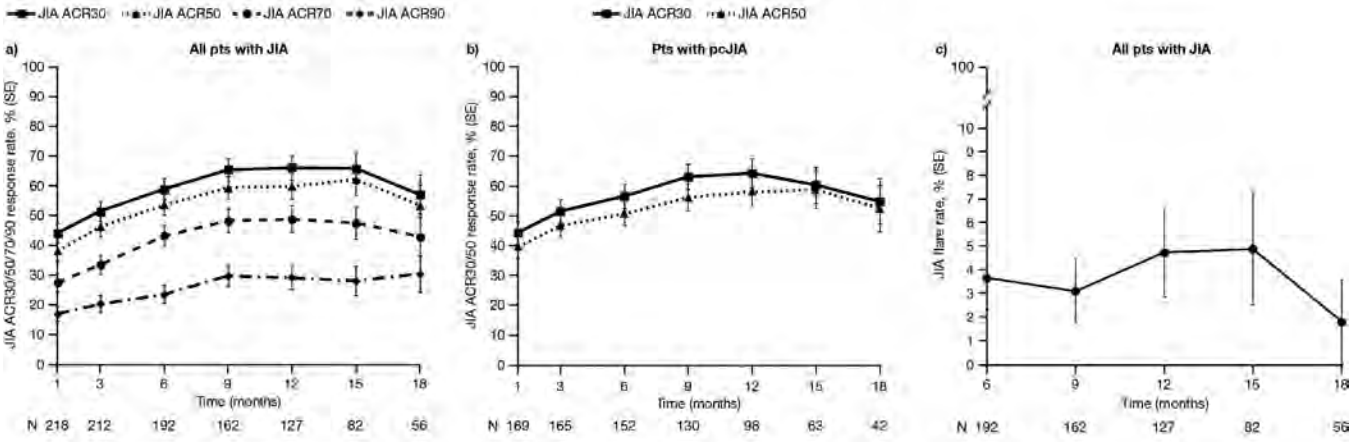
Missing values were not imputed

[a]Tofacitinib 5 mg BID or equivalent weight-based lower dose in pts <40 kg; [b]The dotted line represents the time between baseline (M0) and M1, as baseline values were those of the qualifying index study except for pts who enrolled more than 14 days after the end of study visit of the qualifying index study, whose baseline values were those of the LTE study; [c]Disease activity cut-offs shown in Figure 1a are for pts with >4 active joints ie all pts with pcJIA and some pts with PsA/ERA. In pts with PsA/ERA with ≤4 active joints, disease activity cut-offs are as follows: inactive disease ≤1; low disease activity, 1.1–2; moderate disease activity, 2.1–4.2; high disease activity >4.2 (Consolaro A et al. Pediatr Rheumatol Online J 2016; 14: 23)

BID, twice daily; CHAQ-DI, Childhood Health Assessment Questionnaire-Disability Index; ERA, enthesitis-related arthritis; JADAS27-CRP, Juvenile Arthritis Disease Activity Score in 27 joints, C-reactive protein; JIA, juvenile idiopathic arthritis; LTE, long-term extension; M, month; N, number of pts evaluated at each time point; pcJIA, polyarticular course JIA; PsA, psoriatic arthritis; pts, patients; SE, standard error

Figure 1

Figure 2. a) JIA ACR30/50/70/90 response rates[a] through M18 in all pts with JIA, b) JIA ACR30/50 response rates[a] in pts with pcJIA, and c) JIA flare rate[b] in all pts with JIA



Missing values were not imputed

[a]JIA ACR30/50/70/90 response criteria are defined as: 3 out of 6 JIA core set variables improving by ≥30/50/70/90%, respectively, with ≤1 variable worsening by ≥30%.[2] In pts with systemic JIA, the absence of fever due to systemic JIA in the preceding seven days is also required. Baseline values for determining JIA ACR30/50/70/90 response rates were those of the qualifying index study, except for pts who enrolled more than 14 days after the end of study visit of the qualifying index study, whose baseline values were those of the LTE study. As such, M1 was the first time point at which it was possible to calculate the JIA ACR30/50/70/90 response rates for all pts with available data; [b]Flare is defined as a worsening of ≥30% in ≥3 out of 6 JIA core set variables, with ≤1 variable improving by ≥30%.[3] Baseline values for determining JIA flare rate were those of the M3 visit of the LTE study. As such, M6 was the first time point at which it was possible to calculate the JIA flare rate

ACR, American College of Rheumatology; JIA, juvenile idiopathic arthritis; LTE, long-term extension; M, month; N, number of pts evaluated at each time point; pcJIA, polyarticular course JIA; pts, patients; SE, standard error

Figure 2

Background/Purpose: Tofacitinib is an oral JAK inhibitor that is being investigated for JIA. We report the safety, tolerability, and efficacy of tofacitinib in patients (pts) with JIA in an open-label, long-term extension study with up to 66 months of observation.

Methods: We performed an interim analysis of this ongoing study (NCT01500551; data cut-off: June 4, 2019; database not locked and subject to change). Eligible pts aged 2–≤ 18 years with polyarticular course (pc)JIA, juvenile (j)PsA, or ERA were enrolled after completing a Phase (P)1 (NCT01513902) or P3 (NCT02592434) tofacitinib index study, or after discontinuing from the index studies for reasons other than treatment-related serious adverse events (SAEs). Pts received open-label tofacitinib 5 mg BID or an equivalent weight-based lower dose. Safety endpoints, reported up to Month (M)66 for the overall cohort, were AEs (including AEs of special interest and laboratory test abnormalities) and active uveitis. Efficacy endpoints, reported through M18 for the overall cohort, included mean JADAS27-CRP, JADAS27-CRP minimal disease activity (scores ≤ 3.8 and ≤ 2 in pts with > 4 and ≤ 4 active joints, respectively[1]) rate, mean CHAQ-DI, JIA ACR30/50/70/90 response[2] rates, JIA ACR30/50 response rates for pts with pcJIA, JIA ACR clinical remission (ie inactive disease for 6 months continuously), and JIA flare[3] rate.

Results: 223 pts with pcJIA (n=172), jPsA (n=19), or ERA (n=21) were enrolled and received open-label tofacitinib (total follow-up 265.8 pt-years). Most pts were female (74.9%) and mean (range) age was 12.3 (3–18) years. Mean (median; range) tofacitinib exposure was 402.4 (347.0; 20.0–1,983.0) days. Over 66 months, 160 (71.7%) pts had AEs; 15 (6.7%) pts had SAEs; 13 (5.8%) pts discontinued due to AEs (Table). The most common AEs by MedDRA preferred term were upper respiratory tract infection (16.1% of pts), JIA exacerbation (8.5% of pts), and nasopharyngitis (8.5% of pts). Five (2.2%) pts had serious infections. Two (0.9%) pts had herpes zoster: one case was non-serious; the other case was serious and adjudicated as opportunistic. Laboratory test abnormality rates were ≤ 2.7% (Table).

Table. Summary of treatment-emergent AEs, AEs of special interest, and laboratory test abnormalities

	Tofacitinib[a] (N=223)
Pts with events, n (%)	
AEs	160 (71.7)
SAEs	15 (6.7)
Permanent discontinuations due to AEs	13 (5.8)
Dose reductions or temporary discontinuations due to AEs	43 (19.3)
Most common AEs (≥5% occurrence, by MedDRA preferred term)	
Upper respiratory tract infection	36 (16.1)
JIA exacerbation	19 (8.5)
Nasopharyngitis	19 (8.5)
Arthralgia	16 (7.2)
Viral infection	14 (6.3)
Headache	14 (6.3)
Sinusitis	12 (5.4)
Vomiting	12 (5.4)
AEs of special interest	
Death	0
Gastrointestinal perforation	0
Hepatic event	0
HZ (non-serious and serious)[b]	2 (0.9)
Interstitial lung disease	0
Major adverse cardiovascular event	0
Malignancy (including non-melanoma skin cancer)	0
Macrophage activation syndrome[c]	0
Opportunistic infections (excluding tuberculosis)[d]	1 (0.4)
Serious infection	5 (2.2)
Thrombotic event[e]	0
Tuberculosis	0
Pts with laboratory test abnormalities, n (%)[f]	
Hemoglobin	
<0.8× LLN	4 (1.8)
Lymphocytes	
<0.8× LLN	6 (2.7)
>1.2× ULN	1 (0.5)
Aspartate aminotransferase	
>3.0× ULN	0
Alanine aminotransferase	
>3.0× ULN	1 (0.5)
Cholesterol	
>1.3× ULN	0

Safety events were assessed from baseline through the data cut-off date
[a]Tofacitinib 5 mg BID or equivalent weight-based lower dose in pts <40 kg; [b]One serious case, one non-serious case; [c]Applicable to pts with systemic JIA without active systemic features only (N=11); [d]The serious HZ case was an opportunistic infection; [e]Includes deep vein thrombosis, pulmonary embolism, and arterial thromboembolism; [f]220 pts were evaluated for laboratory abnormalities, except cholesterol which was evaluated in 204 pts
AE, adverse event; BID, twice daily; HZ, herper zoster; JIA, juvenile idiopathic arthritis; LLN, lower limit of normal; MedDRA, Medical Dictionary for Regulatory Activities; N, number of pts evaluated; n, number of pts with event; pts, patients; SAE, serious AE; ULN, upper limit of normal

Table 1

One (0.4%) pt at M12 had active uveitis. Improvements in disease activity (JADAS27-CRP; Figure 1a) and physical functioning (CHAQ-DI; Figure 1b) were maintained through M18. In M1–18, JADAS27-CRP minimal disease activity rates were > 50%. JIA ACR30/50 response rates overall, and in pts with pcJIA, increased from M1 and were > 50%

from M6–18 (Figure 2a/b). JIA ACR70/90 response rates overall increased from M1 and were > 40% and > 20%, respectively, from M6–18 (Figure 2a). None of the 223 pts achieved JIA ACR clinical remission by M18. JIA flare rate was < 5% through M18 (Figure 2c).

Conclusion: In this open-label, long-term extension study of tofacitinib in pts with JIA, no new safety findings were observed over 66 months. Clinical efficacy was maintained over 18 months.

1. Consolaro A et al. Arthritis Rheum 2012; 64: 2366-2374.
2. Giannini EH et al. Arthritis Rheum 1997; 40: 1202-1209.
3. Brunner HI et al. J Rheumatol 2002; 29: 1058-1064.

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Abstract Number: 1496

Outcomes of an Evidence Based Guideline for the Treatment of Hemophagocytic Lymphohistiocytosis and Macrophage Activation Syndrome

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Background/Purpose: Rapid identification of HLH/MAS coupled with a multidisciplinary approach to management is essential to improve patient outcomes. We describe our experience with a newly instituted Evidence Based Guideline (EBG) for HLH/MAS at Boston Children's Hospital (BCH).

Methods: A diagnostic and therapeutic algorithm for HLH/MAS was developed at BCH based on literature review and expert opinion. This EBG was activated in 1/2018 with the goal to review quality metrics after implementation. An electronic medical record search algorithm (patients with an oncology and/or rheumatology note, fever ≥38.2°C, and ferritin ≥500 ng/mL) was developed to retrospectively identify all hospitalized patients in the EBG from 1/2018-4/2019. For comparison, patients with HLH/MAS treated at BCH before implementation of the EBG (3/2016-4/2018) were identified with the same search algorithm. The selected medical records were reviewed by an attending rheumatologist to confirm the HLH/MAS diagnosis and collect clinical data. Subjects with a previously known diagnosis of HLH/MAS before hospitalization were excluded.

Results: After initiation of the EBG, 12 girls and 15 boys with an average age of 8.8 years were identified by house staff as potential HLH/MAS patients and rheumatology was consulted for management. After rheumatology consult, 10 patients were diagnosed with HLH/MAS by the treating team. Of these, 6 met HLH 2004 criteria, and 9 met 2016 MAS classification criteria for systemic juvenile idiopathic arthritis (sJIA). In the comparison group, 20 patients were identified as having HLH/MAS prior to the start of the EBG (pre-EBG). Fifteen pre-EBG patients were diagnosed with HLH/MAS by the treating team during the hospital admission and 5 were identified during retrospective chart review by the study team. The 20 pre-EBG patients had an average age of 8.9 years (9 boys, 11 girls). Of these patients, 7 met HLH 2004 criteria and 18 met 2016 MAS classification criteria for sJIA.

The mean time to HLH/MAS diagnosis by the treating team was 8.4 days in the pre-EBG group at 2.8 days in the post-EBG group. The average hospital stay among pre-EBG patients was 34.0 days with a mean time to HLH/MAS directed treatment of 7.4 days. The same metrics in the post-EBG group were 29.9 days and 3.1 days, respectively. The most common first line treatments for both groups (pre-EBG, post-EBG) were IVIG (35.0%, 53.3%), Anakinra (30.0%, 20.0%), and glucocorticoids (15.0%, 20.0%). 30.0% of pre-EBG patients responded completely to first line treatment, compared to 40.0% post-EBG. The mortality rate during hospitalization was 25.0% in the pre-EBG group and 6.7% in the post-EBG group.

Conclusion: Implementation of an EBG for HLH/MAS was associated with superior outcomes in the post-EBG cohort compared to patients treated before the EBG was established. Notably, overall survival increased from 75.0% in the pre-EBG group to 93.3% in the post-EBG group. While improvements may be partially attributed to increased recognition and advances in treatment of HLH/MAS that have accumulated over time, this analysis also suggests that a multidisciplinary treatment pathway for HLH/MAS contributed to favorable outcomes.

Disclosure: K. Hoyt, None; **O. Halyabar**, None; **J. Han**, None; **S. Case**, None; **M. Chang**, None; **C. Platt**, None; **E. Cohen**, None; **M. Day-Lewis**, None; **F. Dedeoglu**, Novartis, 1; **J. Hausmann**, Novartis, 5; **E. Janssen**, None; **P. Lee**, None; **J. Lo**, None; **G. Priebe**, None; **M. Lo**, None; **E. Meidan**, None; **P. Nigrovic**, Novartis, 2, 5, BMS, 2, 5, Pfizer, 2, 5, Sobi, 5, Miach Orthopedics, 5, Simcere, 5, XBiotech, 5, Quench Bio, 5, Siglion, 5, Cerecor, 5, UpToDate, 7, American Academy of Pediatrics, 7, CARRA, 9; **J. Roberts**, None; **M. Son**, None; **R. Sundel**, None; **M. Gorman**, None; **B. Degar**, None; **M. Hazen**, None; **L. Henderson**, Adaptive Biotechnologies, 5, Sobi, 5, CARRA, 9.

Abstract Number: 1497

COVID-19 in Pregnant Patients with Rheumatic Disease: Data from the COVID-19 Global Rheumatology Alliance

Bonnie Bermas[1], Megan Clowse[2], Milena Gianfrancesco[3], Jonathan Hausmann[4], Pedro M Machado[5], Emily Sirotich[6], Helen Robinson[7], Anja Strangfeld[8], Jinoos Yazdany[9] and Philip Robinson[10], [1]UTSouthwestern.edu, Dallas, TX, [2]Duke University, Chapel Hill, NC, [3]University of California, San Francisco, San Francisco, CA, [4]Boston Children's Hospital / Beth Israel Deaconess Medical Center, Cambridge, MA, [5]University College London, London, United Kingdom, [6]McMaster University, Hamilton, ON, Canada, [7]University of Queensland School of Medicine, HERSTON, Queensland, Australia, [8]German Rheumatism Research Center, Berlin, Germany, [9]UCSF, San Francisco, CA, [10]University of Queensland, Herston, Queensland, Australia

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Reproductive Issues in Rheumatic Disorders

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Rheumatic Disease Diagnosis	
Systemic Lupus Erythematosus	6 (55%)
Rheumatoid arthritis	2 (18%)
Anti-phospholipid Antibody Syndrome	2 (18%)
Axial Spondyloarthritis	1 (9%)
Other Inflammatory Arthritis	1 (9%)
Inflammatory Myopathy	1 (9%)
COVID-19 Treatments	
No treatment except supportive care	6 (55%)
Anti-malarials (e.g. hydroxychloroquine)	4 (36%)
Oseltamivir	1 (9%)
Azithromycin	1(9%)
Glucocorticoids 10 mg/day	2 (18%)
Rheumatic Disease Medications	
No therapy	2 (18%)
Anti-TNF	2 (18%)
Anti-Malarials Alone	5 (45%)
Azathioprine	1 (9%)
Sulfasalazine & antimalarial	1 (9%)
Rheum Disease Medication Stopped	5 (45%)
Antimalarial alone	1
Anti-TNF	2
Azathioprine	1
Sulfasalazine & antimalarial	1

Table. Details of diagnoses and treatments

Background/Purpose: The impact of COVID-19 on pregnancy in patients with rheumatic disease is unknown. We describe COVID-19 outcomes in pregnant rheumatic disease patients reported to an international rheumatic diseases COVID-19 registry between March and June 2020.

Methods: Pregnant patients reported to the COVID-19 Global Rheumatology Alliance physician registries, which includes the COVID-19 EULAR registry, were included. The registry includes cases of COVID-19 in people with rheumatic diseases entered between 24 March 2020 to 22 May 2020.

Results: Eleven cases of pregnant women were reported: eight were white, one black, one Latin American, and one of other ethnicity. The mean age was 33 years (+ 6.5), range 20-45. Diagnoses included systemic lupus erythematosus (n=6), rheumatoid arthritis (n=2), inflammatory arthritis (n=1), inflammatory myositis (n=1), and axial spondyloarthritis (n=1). Two patients had coexisting antiphospholipid syndrome. None were smokers. Most patients' rheumatic disease was either low or in remission based on physician global assessment (n=9), although 2 had moderate disease activity. Background rheumatic disease treatment is shown in the table. Five of the 11 patients stopped their anti-rheumatic treatments at the time of their infection. Seven patients had COVID-19 diagnosed by polymerase chain reaction testing, two by symptoms alone, two unknown, and one each by computed tomography scan and chest x-ray (multiple responses allowed). Five cases were reported to have close contact with a confirmed or probable case of COVID-19 infection, and one had a history of travel to an area with documented cases of COVID-19 infection. The other cases had unknown or community-acquired COVID-19. Symptoms of COVID-19 infection included cough (n=8), fever (n=7), shortness of breath (n=4), diarrhea, anosmia, and arthralgia (each n=3). Most patients (n=6) received only supportive treatment (table). Forty-five percent of patients were hospitalized; the maximum care received by hospitalized patients was supplemental oxygen (n=1). There were two COVID-19 complications, one co-infection with *C. difficile* and one pneumonia. None of the patients died. The outcome of pregnancies is not yet known.

Conclusion: We report on 11 pregnant women with diverse rheumatic diseases and medications who developed COVID-19 infection. Five patients were hospitalized but only one required supplemental oxygen. There were two co-infections and no deaths. In this small series, outcomes of COVID-19 infected pregnant patients with rheumatic disease were favorable.

Disclosure: B. Bermas, None; **M. Clowse**, UCB, 5, GSK, 2, 5, Astra Zeneca, 5, Pfizer, 2; **M. Gianfrancesco**, None; **J. Hausmann**, Novartis, 5; **P. Machado**, Abbvie, 5, 8, Eli Lilly, 5, Novartis, 5, 8, UCB, 5, 8, Pfizer, 8; **E. Sirotich**, Canadian Arthritis Patient Alliance, 9; **H. Robinson**, None; **A. Strangfeld**, BMS, 8, MSD, 8, Pfizer, 8, Roche, 8, Sanofi Aventis, 8, Abbvie, 2, UCB, 8, Celltrion, 2, Eli Lilly, 2, Fresenius Kabi, 2, Mylan, 2, Hexal, 2, Samsung, 5; **J. Yazdany**, Eli Lilly, 5, Astra Zeneca, 5; **P. Robinson**, Novartis, 2, 5, 8, UCB, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 5, Pfizer, 5, Abbvie, 5, 8, BMS, 9.

Abstract Number: 1498

Pregnancy Outcomes in Patients with Axial Spondyloarthritis – a First Analysis of a European Collaboration of Pregnancy Registries

Yvette Meissner[1], Nathalie Costedoat-Chalumeau[2], Frauke Foerger[3], Doreen Goll[4], Anna Molto[5], Rebecca Özdemir[6], Marianne Wallenius[7], Anja Strangfeld[8] and Rebecca Fischer-Betz[9], [1]Deutsches Rheuma-Forschungszentrum, Berlin, Germany, [2]APHP, Université de Paris, Paris, France, [3]University Hospital and University of Bern, Bern, Switzerland, Bern, Switzerland, [4]Patient Research Partner, Berlin, Germany, [5]Rheumatology Department, Cochin Hospital, Paris, Paris, France, [6]Patient Research Partner, Duisburg, Germany, [7]University Hospital and Norwegian University of Science and Technology, Trondheim, Norway, [8]German Rheumatism Research Center, Berlin, Germany, [9]Department of Rheumatology and Hiller Research Unit Rheumatology, Heinrich Heine University, Duesseldorf, Germany, Duesseldorf, Germany

SESSION INFORMATION

Session Date: Sunday, November 8, 2020
Session Title: Reproductive Issues in Rheumatic Disorders
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Axial spondyloarthritis (axSpA) can affect women in their childbearing age. Data on pregnancy in axSpA patients are mainly retrospective and highly heterogeneous [1]. The aim of this analysis was to investigate pregnancy outcomes and health of live born children in women with axSpA in four prospective cohort studies.

Table 1: Maternal and disease characteristics

	EGR2 (FR)	RePreg (CH)	RevNatus (NO)	Rhekiss (DE)
No. of pregnancies	45	31	160	92
No. of patients	44	31	125	88
Age in years	32.0 ± 4.2	31.4 ± 4.0	30.5 ± 4.5	33.2 ± 4.4
Disease duration in years	6.0 ± 5.6	7.7 ± 4.6	3.2 ± 3.3	6.2 ± 5.3
HLA-B27 positive	26 (66.7)	23 (74.2)	79 (71.2)	54 (73.0)
Pre-gestational diabetes	0	0	1 (0.6)	1 (1.4)
Inflammatory bowel disease	0	0	4 (2.6)	5 (7.2)
Uveitis	0	0	3 (1.9)	3 (4.3)
BMI	26.5 ± 4.8	22.6 ± 2.5	24.4 ± 4.3	23.4 ± 4.3

Results are presented as mean ± SD or number (percentage)

Table 2: Pregnancy characteristics, obstetric and neonatal outcomes

	EGR2 (FR)	RePreg (CH)	RevNatus (NO)	Rhekiss (DE)
WGA at the first visit in pregnancy	11.9 ± 8.15	19.7 ± 9.4	12.9 ± 5.7	13.4 ± 5.4
Patients with 1 pregnancy	43 (95.5)	31 (100.0)	101 (80.8)	84 (95.5)
Primigravidae	18/45 (40.0)	15 (48.4)	47 (29.4)	37 (45.1)
Adverse events of interest				
Preeclampsia	1 (4.4)	0	4 (2.6)	0
Gestational diabetes	4 (8.9)	2 (6.5)	n.a.	5 (6.2)
Pregnancy outcomes			*(5 Outcomes missing)*	*(1 Outcome missing)*
Elective termination	1 (2.2)	0	2 (1.3)	0
Miscarriages (< WGA 20)	2 (4.4)	0	13 (8.4)	4 (4.4)
Pregnancy loss (>WGA 20)	2 (4.4)	0	0	0
Live birth	40 (88.9)	31 (100.0)	140 (90.3)	87 (95.6)
Outcomes of live births				
No. of neonates, singleton pregn.	40	30	139	78
No. of neonates, multiple pregn.	0	2	2	4
*Neonatal outcomes, only singleton pregnancies**				
WGA at delivery	39.1 ± 1.2	39.5 ± 1.5	38.9 ± 2.3	39.4 ± 2.0
Preterm birth	0	0	6 (4.3)	4 (5.4)
Birth weight in g	3253 ± 395[$]	3314 ± 519	3446 ± 526	3377 ± 522
Congenital malformation	0	0	n.a.[#]	4 (5.1)

*Results are presented as mean ± SD or number (percentage). WGA: gestational age in weeks. *Data for twins are not shown. [#]Malformations can be retrieved by national birth registry with a lag time of 2 years. [$]Missing information for 7 infants.*

[1] Giovannopoulou E et al. Curr Rheumatol Rev. 2017;13(3):162-9.

Methods: Data of four European pregnancy registries that collect data prospectively and collaborate in the European Network of Pregnancy registries in Rheumatology (EuNeP) were compiled and compared according to a pre-defined study protocol: EGR2 (France), RePreg (Switzerland), RevNatus (Norway) and Rhekiss (Germany). Women with a diagnosis of axSpA enrolled in one of the registries and with a known pregnancy outcome reported until June, August and September 2019, respectively, were eligible for the analysis. Each registry analysed their data descriptively and provided the results to the coordinating centre.

Results: A total of 328 pregnancies in 288 women were investigated. Mean age of patients was comparable between registries ranging from 31 to 33 years. However, disease duration (3-8 years) and proportion of patients with a positive HLA-B27 (64-74%) varied (Table 1). The axSpA diagnosis was either classified by ASAS criteria (fulfilment in EGR2: 93%, RePreg: 65%, RevNatus: 86%) or by ASAS criteria for axial/ peripheral SpA (Rhekiss: 81/ 34%). Preeclampsia occurred in 0-4% and gestational diabetes in 6-9% of patients. Rates for preterm birth were ≤5%, and congenital malformations were reported in 4 out of 287 neonates (Table 2).

Conclusion: Differences in study design and classification criteria result in slightliy different patient populations in each registry. The outcome of pregnancies was favourable. Preterm birth rates are within rates reported by the WHO for the EU general population. However, a selection bias of rather planned and well-controlled pregnancies cannot be ruled out. This is the first collaborative analysis of four European pregnancy registries in rheumatology. Descriptive data were combined, and will be – in a next step – pooled together.

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Disclosure: Y. Meissner, Pfizer, 8; **N. Costedoat-Chalumeau**, None; **F. Foerger**, UCB, 2, 5, 8, GSK, 5, 8, Roche, 5; **D. Goll**, None; **A. Molto**, ABBVIE, 5, BMS, 5, 8, LILLY, 5, NOVARTIS, 5, 8, UCB, 5, GILEAD, 5; **R. Özdemir**, None; **M. Wallenius**, None; **A. Strangfeld**, BMS, 8, MSD, 8, Pfizer, 8, Roche, 8, Sanofi Aventis, 8, Abbvie, 2, UCB, 8, Celltrion, 2, Eli Lilly, 2, Fresenius Kabi, 2, Mylan, 2, Hexal, 2, Samsung, 5; **R. Fischer-Betz**, UCB, 5, Abbvie, Amgen, Biogen, BMS, Celgene, Chugai, GSK, Janssen, Lilly, Medac, MSD, Novartis, Roche, UCB, Pfizer, 8.

Abstract Number: 1499

The Frequency of Contraception Documentation in Women with Lupus and Rheumatoid Arthritis Within the RISE Registry

Megan Clowse[1], Jing Li[2], Amanda Eudy[3], Mehret Birru Talabi[4] and Gabriela Schmajuk[5], [1]Duke University, Chapel Hill, NC, [2]University of California, San Francisco, San Francisco, CA, [3]Duke University, Durham, NC, [4]University of Pittsburgh, Pittsburgh, PA, [5]University of California, San Francisco, Atherton, CA

SESSION INFORMATION
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Session Title: Reproductive Issues in Rheumatic Disorders
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Several of the most commonly prescribed anti-rheumatic medications for women with rheumatic disease are known teratogens, posing a risk for pregnancy loss and birth defects if taken during pregnancy. Despite the importance of avoiding pregnancy while taking a teratogenic medication, within the U.S. an estimated 10-15% of pregnancies to women with rheumatic disease are conceived while the mother is using a teratogen. We

sought to understand the frequency of contraception documentation for women with systemic lupus erythematosus (SLE) and rheumatoid arthritis (RA) in a large U.S. electronic-health-record (EHR) based registry, and to identify disparities by teratogen prescription and patient race and ethnicity.

Methods: RISE (Rheumatology Informatics System for Effectiveness) is a national EHR-enabled rheumatology registry that passively collects data on all patients seen by participating practices. As of 2018, RISE held validated data from 1,113 clinicians in 226 practices, representing an estimated 32% of the U.S. clinical rheumatology workforce. Women of childbearing age (18-45 years) in 2018 and at least 2 visits with ICD-9 or -10 diagnosis codes for SLE or RA (at any time) were assessed for anti-rheumatic medication prescriptions and contraception documentation within a structured data field. The proportion of patients with documented contraception was compared by teratogen prescription and patient age and race/ethnicity.

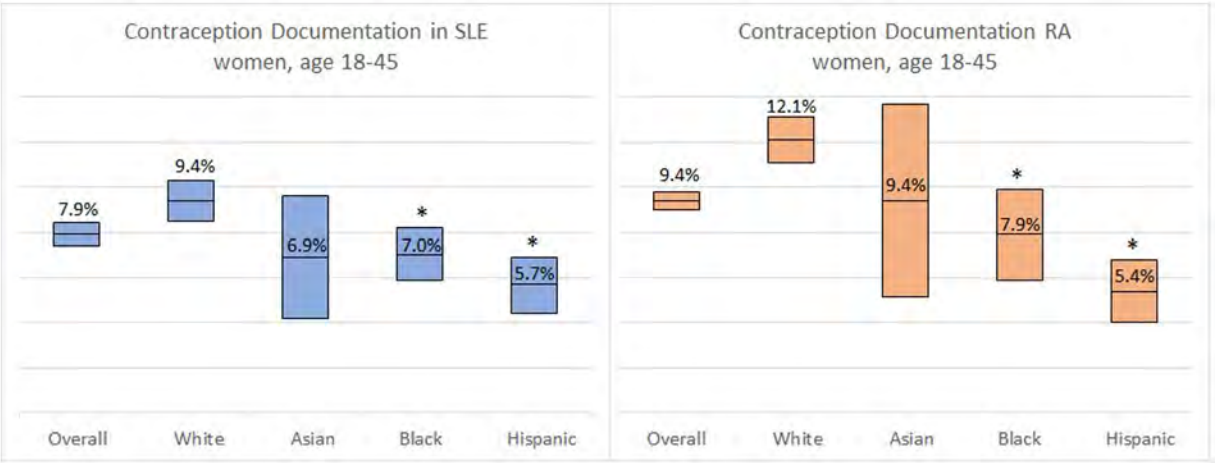
Results: In 2018, 110,359 women between the ages of 18-45 had at least 1 visit: 9,826 with SLE and 19,009 with RA. Overall, 8.9% had any contraception documented.

More women with RA than SLE had documentation of contraception (SLE 7.9%, RA 9.4%, p< 0.001). Among SLE patients, the rate of contraception documentation was similar whether or not the woman was prescribed a teratogenic anti-rheumatic medication. Among women with RA, however, contraception documentation was greater among women prescribed a teratogen than those prescribed only pregnancy-compatible medications (10.3% vs 9.1%, p=0.02).

The rate of contraception documentation was higher in white women (SLE 9.4%, RA 10.9% (see figure) compared to Hispanic women (SLE 5.7%, p=0< 0.001; RA 5.4%, p< 0.001) or black women (SLE 7.0, p< 0.001; RA 6.3, p< 0.001).

For women with SLE and RA, 1.5-1.7% of women used highly effective contraception (i.e., tubal ligation, intrauterine device, subdermal implant) and 5.0-5.6% had documentation of other forms of effective contraception (i.e., pill, patch, ring, or injection).

Conclusion: We found large gaps in contraception documentation within the RISE registry. While roughly 70% of women in the U.S. report using contraception, contraception was documented in < 10% of eligible women in RISE. While these data likely underestimate contraception use, they also highlight that many rheumatologists do not have a systematic approach to collecting and recording this information in the EHR. The racial disparities noted within this study require additional study, and may suggest that implicit bias plays a role in ascertaining and recording contraception use within the RISE Registry.



Contraception documentation among women with SLE and RA by race and ethnicity (mean noted, range is 95% CI; *p-value<0.001 compared to white women)

Disclosure: M. Clowse, UCB, 5, GSK, 2, 5, Astra Zeneca, 5, Pfizer, 2; **J. Li**, None; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 2, Pfizer, 2; **M. Birru Talabi**, None; **G. Schmajuk**, None.

Abstract Number: 1500

Electrocardiographic QT Intervals in Infants Exposed to Hydroxychloroquine Throughout Gestation

Deborah Friedman[1], Mimi Kim[2], Nathalie Costedoat-Chalumeau[3], Robert Clancy[4], Joshua Copel[5], Colin Phoon[6], Bettina Cuneo[7], Rebecca Cohen[6], Mala Masson[6], Benjamin Wainwright[6], Noel Zahr[8], Amit Saxena[4], Peter Izmirly[9] and Jill Buyon[10], [1]New York Medical College, Valhalla, [2]Albert Einstein College of Medicine, Bronx, [3]APHP, Université de Paris, Paris, France, [4]NYU School of Medicine, New York, [5]Yale School of Medicine, New Haven, [6]New York University School of Medicine, New York, [7]University of Colorado School of Medicine, Aurora, [8]Pitié-Salpêtrière University Hospital, Paris, France, [9]Department of Medicine, New York University School of Medicine, New York, NY, [10]Department of Medicine, NYU School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Reproductive Issues in Rheumatic Disorders

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

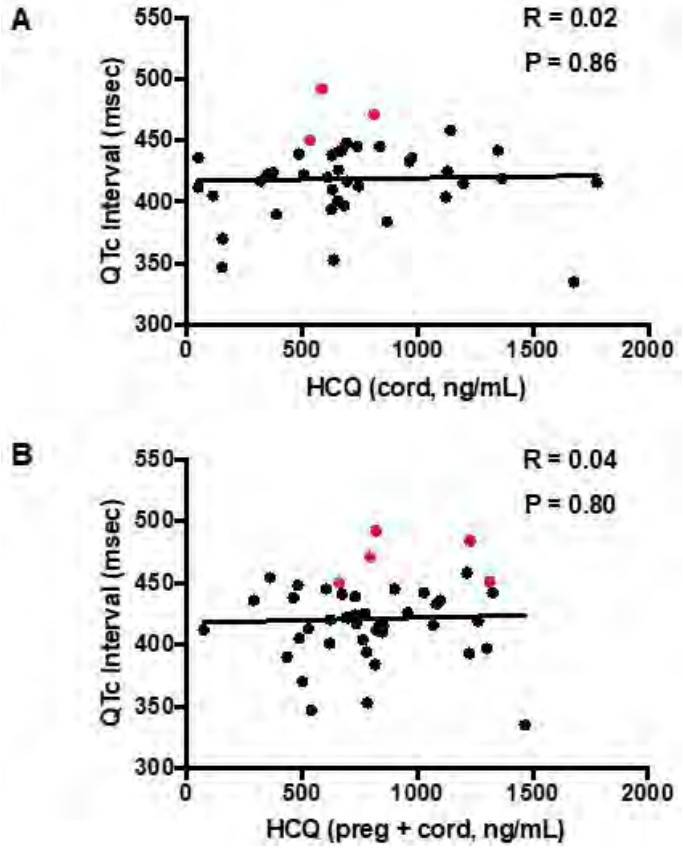


Figure 1. Correlation between blood HCQ levels and neonatal QTc. (Panel A) Cord HCQ is plotted against QTc. (Panel B) Overall mean HCQ levels (obtained by averaging all HCQ levels throughout an individual pregnancy and cord blood level) are plotted against QTc. Subjects with an abnormally prolonged QTc are designated with red bold circles. All QTc intervals were calculated using the Bazett formula (QTcB).

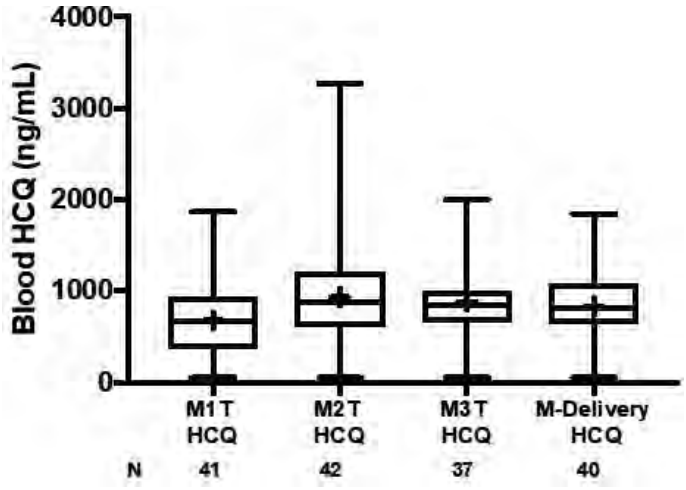


Figure 2. Box plots of maternal blood levels of HCQ during each trimester of pregnancy and delivery. M1T is baseline first trimester. M2T is second trimester. M3T is third trimester. M-Delivery is at the time of delivery. Median levels of HCQ (interquartile range) for M1T: 669 ng/mL (363-941); M2T: 877 ng/mL (604-1212); M3T: 849 ng/mL (652-1000); M-Delivery: 815 ng/mL (645-1080). Mean values denoted by + in box plot.

Background/Purpose: Based on inhibition of viral replication and limited reports on clinical efficacy, hydroxychloroquine (HCQ) was initially considered as a prophylaxis and treatment of COVID-19. Despite this optimism, more extensive reports have significantly dampened the promise of efficacy, however cardiac toxicity has surfaced raising attention to this complication. Although HCQ is generally considered safe during pregnancy based on studies in patients with systemic lupus erythematous and other rheumatic conditions, this initiative leveraged a unique opportunity to evaluate neonatal electrocardiograms (ECGs) in the context of HCQ levels to address any potential cardiotoxicity.

Methods: Neonatal ECGs and HCQ blood levels were available in a recently completed study evaluating the efficacy of HCQ 400mg daily to prevent the recurrence of congenital heart block associated with anti-SSA/Ro antibodies. The ECGs of affected newborns who met the primary outcome of advanced block were not included in this safety study so that the results only reflect those infants with no clinical cardiac disease. Using the Bazett formula to correct for heart rate, corrected QT (QTc) intervals were calculated and compared to age-matched normal values. For reference, the median (2^{nd} percentile – 98^{th} percentile) values for QTc were 413 (378-448) msec in males, and 420 (379-462) msec in females. QTc intervals were recorded in the absence of knowledge of the HCQ levels. Values exceeding 448 msec for males and 462 msec for females were considered abnormal. Levels of HCQ were assessed during each trimester of pregnancy and in the cord blood, providing unambiguous assurance of drug exposure.

Results: There were 45 ECGs available for interpretation within the first 4 months of life in unaffected infants. Overall, there was no correlation between cord blood levels of HCQ and the QTc (R = 0.02, P = 0.86) or the average value of HCQ levels obtained during each individual pregnancy and cord blood and the QTc (R = 0.04, P = 0.80), as shown in **Figure 1A and Figure 1B**. Likewise there was no correlation between the average of the maternal HCQ levels obtained at each trimester and delivery plus cord levels and the QTc on the ECGs of the 31 infants evaluated on day of life 1-4 (R = 0.08, P = 0.63) or those of the 14 children older than 4 days (R = 0.01, P = 0.95). Maternal values of HCQ were sustained throughout pregnancy and delivery (**Figure 2**). Mean QTc values were nearly identical between those in the highest and lowest quartiles of cord blood HCQ levels (P = 0.57) and between the highest and lowest quartiles of average HCQ levels during pregnancy (P = 0.54) (**Figure 3A and 3B**). Among these 45 infants, only 5 had prolongation of the QTc (11%; 95% CI: 4% - 24%), 2 marked and 3 marginal. No arrhythmias occurred in any neonate that was not known to have heart block.

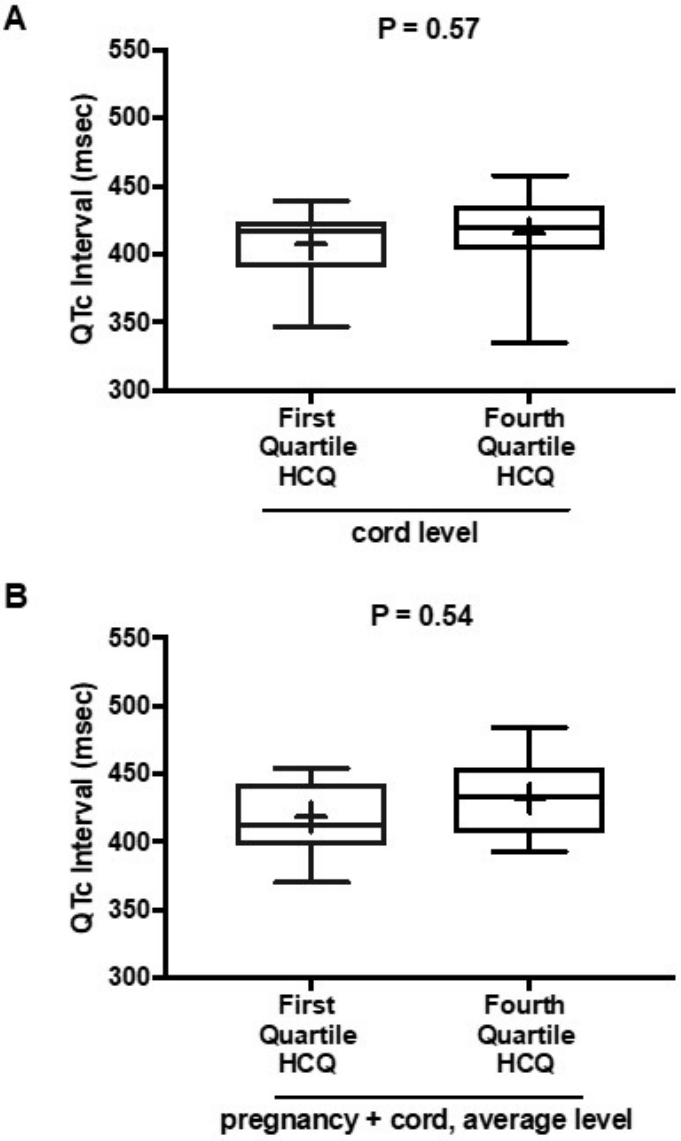


Figure 3. Box plots of QTc interval data for subjects in first and fourth quartiles of cord blood HCQ levels and average HCQ levels during pregnancy. (Panel A) Comparison of QTc between the first and fourth quartiles of HCQ cord blood levels. Median QTc (interquartile range) in first HCQ quartile: 417 msec (390- 424); in fourth HCQ quartile: 419 msec (404-436). (Panel B) Comparison of QTc between the first and fourth quartiles of HCQ levels averaged over pregnancy and cord blood. Median QTc (interquartile range) in first HCQ quartile: 413 msec (398, 443); in fourth HCQ quartile: 433 msec (407, 455). Mean values denoted by + in box plots. All QTc intervals were calculated using the Bazett formula (QTcB).

Conclusion: In aggregate, these data provide reassurances that the maternal use of HCQ is not associated with a high incidence of QTc prolongation in the neonate.

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Abstract Number: 1501

Obstetrical Outcome and Thromboses in a Multicentric Cohort of Antiphospholipid Syndrome (APS) Patients with Severe Preeclampsia: An Analysis of APS Classification Criteria

Maddalena Larosa[1], Nathalie Morel[2], Meriem Belhocine[3], Amelia Ruffatti[4], Nicolas Martin Silva[5], Romain Paule[6], Luc Mouthon[7], Michel Dreyfus[8], Jean-Charles Piette[9], Odile Souchaud-Debouverie[10], Catherine Deneux-Tharaux[11], Vassilis Tsatsaris[12], Emmanuelle Pannier Metzger[13], Gaëlle Guettrot-Imbert[14], Veronique Le Guern[15], Andrea Doria[16] and Nathalie Costedoat-Chalumeau[17], [1]Rheumatology Unit-Department of Medicine-University of Padova, Italy, Padova, Veneto, Italy, [2]AP-HP, université René-Descartes Paris V, hôpital Cochin, centre de référence maladies auto-immunes et systémiques rares, pôle médecine, service de médecine interne, Paris, France., Paris, Ile-de-France, France, [3]Hôpital Sacré-Coeur de Montréal , Montréal, Montreal, QC, Canada, [4]Department of Medicine, University of Padova, Padova, Veneto, Italy, [5]Centre Hospitalier et Universitaire de Caen, Caen, France, [6]Foch Hospital, Paris, France, [7]Hopital Cochin - Paris University, Paris, France, [8]CHU de Caen, Caen, France, [9]Department of Internal Medicine, Hôpital Pitié-Salpêtrière, Paris, France, Paris, France, [10]CENTRE HOSPITALIER UNIVERSITAIRE LA MILETRIE, poitiers, France, [11]INSERM U1153, Obstetrical, Perinatal and Pediatric Epidemiology Research Team, Center for Epidemiology and Statistics Sorbonne Paris Cité , Paris Descartes University , Paris , France, Paris, France, [12]Maternité Port-Royal,Hôpital Cochin, Paris, France, Paris, France, [13]Maternité Port-Royal,Hôpital Cochin, Paris, France, [14]Médecine Interne,Hôpital Cochin, paris, France, [15]Médecine Interne,Hôpital Cochin, Paris, France, Paris, France, [16]University of Padua, Padua, Italy, [17]APHP, Université de Paris, Paris, France

SESSION INFORMATION

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Background/Purpose: According to APS classification criteria[1], clinical manifestations of antiphospholipid syndrome (APS) consist in thrombotic and obstetric events, including severe preeclampsia (PE). Because little is known on this topic, our aim was to describe severe PE in a cohort of APS patients and to report the thrombotic and obstetrical outcomes in these patients.

Methods: Retrospective study of female patients referred to 5 French Internal Medicine departments and 1 Italian Rheumatology Unit with a severe PE according to standard definition[1], that occurred before 34 WG between 2000 and 2018 in patients with APS[2]. In case of more than one episode of severe PE in one given patient, we defined the index pregnancy as the first episode. We considered that women had been treated during pregnancy if they were prescribed low-dose aspirin (LDA) and/or low-molecular-weight heparin (LMWH) before the diagnosis of severe PE.

Results: The study included 40 women with APS, with a median follow-up after the index pregnancy with PE of 3 years. 12 (30%) had an associated SLE. 33 women (82.5%) had a positive LAC and 21 women (52.5%) had triple positivity anti-phospholipid (aPL) positivity.

- During the index pregnancy, PE occurred at a median term of 25.5 WG. 29 pregnancies (72.5%) led to a live birth but 5 severely premature neonates died (i.e. a total of 24 pregnancies resulted to a living child). Data on PE are described Table 1.
- Thrombotic criteria: 16 women (40%) had at least one thrombotic event. Their first thrombosis occurred before (n=14) or after the index pregnancy (n=2). Thromboses were venous (n=6), arterial (n=12), and/or micro-thrombotic (n=5). Four patients experienced a catastrophic APS (CAPS), 3 of them simultaneously with PE.

Table 1: Characteristics of the index pregnancies complicated with severe Preeclampsia in 40 patients with APS	
Patient's characteristics	**(N=40, %)**
Age of index pregnancy (first severe PE), (median, IQR)	30.5 (27-33)
Primiparous	21 (52.5)
Associated SLE	12 (30)
Abs profile	
Triple positivity for aPL antibodies	21 (52.5)
IgG/IgM anti-cardiolipin antibodies	34 (85.0)
IgG/IgM anti-β2GPI antibodies	25 (62.5)
LAC	33 (82.5)
Treatment (during index pregnancy, prior to PE)	
LDA	19 (47.5)
LMWH	19 (47.5)
Antimalarials	7 (17.5)
Corticosteroids	8 (20)
Immunosuppressants	3 (7.5)
None	17 (42.5)
Severe PE characteristics	
Live births	29 (72.5)
Neonatal deaths	5 (12.5)
PE term, WG (median, IQR)	25.5 (23-29)
Birth term, WG (median, IQR)	25.5 (23.7-30.3)
Preterm delivery (<37th WG)	22 (55)
Associated maternal complications	
HELLP	18 (45)
Eclampsia	6 (15)
Catastrophic APS	3 (7.5)
Placental abruptions	3 (7.5)
Associated fetal complications	
IUGR	18 (45)
IUFD	11 (27.5)

Legend to Table 1: APS: antiphospholipid syndrome; PE: preeclampsia; IQR: interquartile range; WG: weeks of gestation; SLE: systemic lupus erythematosus; Abs: antibodies; aPL: antiphospholipid; LAC: lupus anticoagulant; LDA: low dose aspirin; LMWH: Low Molecular Weight Heparin; HELLP: Hemolysis, elevated liver enzymes, low platelet; IUGR: intrauterine growth restriction; IUFD: intrauterine fetal death.

- Obstetrical criteria: when considering all their pregnancy (n=122), 17 patients (42.5%) had at least one intra-uterine fetal death (IUFD), and 19 women (47.5%) had at least one HELLP syndrome. None of the 40 patients presented 3 or more consecutive miscarriages.

Conclusion: During the 40 index pregnancies, severe PE occurred early in the pregnancy with a high rate of in utero (n=11) or neonatal (n=5) mortality of the offspring.

APS was characterized by a strong autoimmune anti-phospholipid serology and SLE was frequent (30%).

Among these 40 APS patients with severe PE, almost half also experienced at least one thrombosis, a HELLP syndrome and/or an IUFD. However, no overlap with the «three consecutive miscarriages" classification criterion was found in our cohort suggesting that the underlying physiopathology of these 2 obstetrical phenotypes are completely different.

References:

1. Diagnosis and Management of preeclampsia and eclampsia. International Journal of Gynecology &Obestetrics 2002;77:67-75.
2. Miyakis S, et al. International consensus statement on an update of the classification criteria for definite antiphospholipid syndrome (APS). J Thromb Haemost 2006;4:295e 306

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Abstract Number: 1502

Composite of Relevant Endpoints for Sjögren's Syndrome (CRESS)

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Several recent randomized controlled trials that used the validated ESSDAI as primary endpoint failed, partly explained by relatively large response rates in the placebo group. Since primary Sjögren's Syndrome (pSS) is a very heterogeneous disease, a composite endpoint including multiple disease aspects may be more appropriate to demonstrate clinical efficacy. Therefore, our objective was to develop a composite endpoint for pSS based on expert opinion and analysis of trial data.

Methods: According to expert opinion, 5 items were found to be most relevant to assess the effect of treatment in pSS: systemic disease activity, patient-reported symptoms, tear gland, salivary gland and serological items. These items were tested using data from the randomized, double-blind, placebo-controlled ASAPIII trial at week 24.[1] Cut-off points were based on ROC analysis to assess discrimination of effect between patients on abatacept (n=40) and placebo (n=39) and on expert opinion.

Table 1: Overview of the Composite of Relevant Endpoints for Sjögren's Syndrome (CRESS): definition of response of the 5 complementary items		
Item	**Measurement**	**Definition of response**
Systemic disease activity	ClinESSDAI	Score <5 (low disease activity)
Patient-reported symptoms	ESSPRI	Decrease of ≥1 point or ≥15% from baseline
Tear gland*	Schirmer/OSS**	If abnormal score at baseline: • Or increase of ≥5 mm in Schirmer • Decrease of ≥2 points in OSS Or if both normal at baseline: • No change to abnormal in Schirmer and OSS
Salivary gland*	UWS/SGUS	• Increase of ≥25% or if score is 0 at baseline any increase in UWS • Or decrease of ≥25% in total Hocevar score
Serological	RF/IgG	• Decrease of ≥25% in RF • Or decrease of ≥10% in IgG
Total CRESS responder		Response on ≥3 items of 5
*CRESS can also be used without OSS and SGUS if these tests are not available **Mean of both eyes Abbreviations: ClinESSDAI: Clinical EULAR Sjögren's syndrome disease activity index; ESSPRI: EULAR Sjögren's syndrome patient reported index; OSS: Ocular Staining Score; UWS: unstimulated whole saliva; SGUS: salivary gland ultrasonography; RF: rheumatoid factor; IgG: Immunoglobulin G		

Table 1. Overview of the Composite of Relevant Endpoints for Sjögren's Syndrome (CRESS): definition of response of the 5 complementary items

Table 2: CRESS response rates at week 24 of abatacept and placebo groups			
Item	**Measurement**	**Responders abatacept**	**Responders placebo**
Systemic disease activity	ClinESSDAI	45%	27%
Patient-reported symptoms	ESSPRI	58%	22%
Tear gland	Schirmer/OSS	58%	36%
Salivary gland	UWS/SGUS	58%	41%
Serological	RF/IgG	64%	19%
Total CRESS responder	**Response on ≥3 items of 5**	**65%**	**18%**
Abbreviations: see Table 1			

Table 2 CRESS response rates at week 24 of abatacept and placebo groups

Results: The 'Composite of Relevant Endpoints in Sjögren's Syndrome' (CRESS) consists of 5 complementary items. The definition of response for each item is presented in Table 1. For measuring systemic disease activity, ClinESSDAI[2] is used as it showed higher discrimination compared to ESSDAI and because the biological domain is separately in-

Table 3: Response and non-response on individual items in CRESS responders		
Measurement	Abatacept n=26 CRESS responders	Placebo n=7 CRESS responders
ClinESSDAI	16 vs. 10	5 vs. 2
ESSPRI	18 vs. 8	4 vs. 3
Schirmer/OSS	19 vs. 7	5 vs. 2
UWS/SGUS	19 vs. 7	4 vs. 3
RF/IgG	18 vs. 8	4 vs. 3
Abbreviations: see Table 1		

Table 3. Response and non-response on individual items in CRESS responders

cluded in the CRESS. ROC analysis for absolute or relative change in ClinESSDAI showed no discrimination between treatment groups (AUC 0.534 and 0.565), therefore low disease activity (< 5) in ClinESSDAI was used. Patient-reported symptoms are measured with ESSPRI. As ROC analysis showed optimal cut-off points of -0.83 and -13.8% (AUC 0.621 and 0.629), the previously validated definition of ESSPRI response (≥15% or 1 point)[3] was used. Tear and salivary gland items include both glandular function and imaging. Cut-off points were based on expert opinion, taking measurement variation into account. The CRESS can also be used without OSS and SGUS if these tests are not available, leaving Schirmer's and UWS for assessing the tear and salivary gland item with similar response rates in both treatment groups. The serological item includes serum levels of RF-IgM and IgG. ROC analysis showed optimal cut-off points of -23% and -2.2% (AUC 0.861 and 0.615), respectively, which were set to ≥25% and ≥10% decrease to minimize placebo response due to natural variation. Total CRESS response was defined as response on ≥3 of the 5 items. The CRESS response per item for abatacept and placebo treatment groups is presented in Table 2. The total CRESS response rate was 65% vs. 18% (p< 0.001). As shown in Table 3, response to the 5 CRESS items is well-balanced.

Conclusion: The newly developed 'Composite of Relevant Endpoints for Sjögren's Syndrome' (CRESS) enables discrimination between active treatment (abatacept) and placebo treatment in pSS patients. All items contribute equally to CRESS response. Validation analyses in independent, global, multi-center, placebo-controlled trials in pSS patients will be performed.

References

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[2]Seror et al. Ann Rheum Dis. 2016;75(11):1945-50.
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Abstract Number: 1503

Ultra High-resolution Ultrasound (UHFUS) of Labial Salivary Glands Might Help to Avoid Unnecessary Lip Biopsy in Patients with Sicca Syndrome

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SESSION INFORMATION
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Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Major salivary gland ultrasonography (SGUS) has an established role as a first-line imaging tool in the diagnosis of primary Sjögren's syndrome (pSS). Nowadays, however, interest is also arisen in last-generation ultra high-resolution ultrasound (UHFUS) transducers, which can produce frequencies up to 70 MHz and achieve tissue resolution up to 30 μm, opening up new possibilities for the study of labial salivary glands (LSG).Purpose: to compare the diagnostic accuracy of LSG-UHFUS with SGUS and to investigate the usefulness of UHFUS in LSG biopsy preoperative planning.

Methods: Consecutive patients undergoing a LSG for clinically suspected pSS were included in this study from January 2018 to March 2020. UHFUS of LSG was performed by using VEVO MD, equipped with a 70 MHz probe, scanning first the central compartment of the inferior lip, and then both peripheral compartments. The following parameters were evaluated: distribution of the glands, parenchymal inhomogeneity (score 0-3, from normal to evident), and fibrosis. UHFUS imaging was used to help locate the LSG for the US-guided biopsy. SGUS findings were defined according to previous studies exploring both parotid and submandibular glands.

Results: We included a total of 138 patients with suspected pSS: out of them, 61 (44.2%) received a diagnosis of pSS (ACR 2016 criteria) and 77 (55.8%) were diagnosed as no-SS sicca controls. The two groups did not differ in their demographic features, USFR and ESSPRI. With respect to no-SS sicca controls, pSS patients presented both a higher SGUS scores and a higher UHFUS scores in both central and peripheral labial compartments ($p< 0.001$). UHFUS scores significantly correlated with parotid SGUS scores ($r=0.385$, $p=0.001$), submandibular SGUS scores ($r=0.463$, $p=0.001$), and with the minor salivary gland focus score ($r=0.407$, $p=0.001$); moreover, UHFUS scores were significantly associated with anti-Ro/SSA, anti-La/SSB, RF and hyper-IgG ($p< 0.05$). By using a cut-off score$\geq$2, UHFUS sensitivity was slightly higher than SGUS (63.9% vs 60.7%) whereas UHFUS specificity was lower (71.4% vs 79.2%). However, by using a cut-off score$<$ 1, UHFUS sensitivity raised up to 98.4% with a negative predictive value of 93.8%. In our cohort, the sequential combination of the two US techniques (UHFUS followed by SGUS) and the use of different UHFUS cut-off scores would have avoided unnecessary lip biopsy in 46/77 (59.7%) patients with sicca syndrome and no-pSS.

Conclusion: UHFUS of LSG appeared feasible and sensitive in pSS, potentially offering unique advantages in LSG biopsy preoperative planning to avoid unnecessary lip biopsy in patients with sicca symptoms.

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Abstract Number: 1504

Four Distinct Symptom-Based Clusters Identified from the Sjögren's Foundation Survey

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SESSION INFORMATION
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Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Relief of symptoms is a *sine qua non* for successful drug development in Sjögren's syndrome (SS). However, symptom-based patient experience is understudied, particularly how these symptoms cluster in patients, potentially impacting immunosuppressive agent selection or outcome definitions. Recently, 4 distinct symptom-based groups with unique ESSDAI and lab profiles were identified by analyzing the UK Primary SS Registry cohort of 608 patients (Tarn et al. 2019). Our objective was to determine the generalizability of these findings in a larger US population and report medication use, quality of life, symptoms, and systemic manifestations unique to these clusters.

Methods: A survey, conducted by the Sjögren's Foundation, was completed by 2,961 adults with self-reported SS. Unsupervised hierarchical clustering was applied using Ward's method to identify the optimal phenotypically similar clusters based on self-reported severity of: 1) anxiety (never-daily), 2) depression (never-daily), 3) pain (visual analogue scale [VAS] 0-10), 4) fatigue (VAS), and 5) dryness (VAS). We tabulated demographic features, medications, quality of life, and SS-specific symptom frequency and systemic manifestations within each cluster. We used ANOVA or Chi-square to identify cluster differences, controlling for age, sex, race, and social security disability (SSD).

Results: The analysis yielded 4 clusters among 2,806 participants with complete data on the 5 key symptoms (Figure 1), as previously described. Clusters were characterized by low symptom burden (LSB; 14% prevalence) and high symptom burden (HSB; 30%) in all categories; high dryness and fatigue but low anxiety and depression (HDF; 34%) and high anxiety and depression but low dryness and fatigue (HAD; 22%). Diagnosis age and sex were similar but SSD significantly differed between clusters (1% in LSB and 15% in HSB) (Table). Analgesic use was significantly different between groups and highest in the HSB group (35% used opioids). HSB and HDF groups used more prescription eye drops (54% and 51%) and secretagogues (39% both), than other groups. Significant differences in systemic medication use included highest corticosteroid use in the HSB group (22%) and HCQ use in the HAD group (47%). The HSB group had more emotional burden (94%) than the LSB group (43%). The groups differed in all SS-specific symptoms (Figure 2A). Systemic manifestations differed significantly by clusters for inflammatory arthritis, interstitial lung disease, and neuropathy, but other systemic manifestations, like leukopenia and lymphoma, demonstrated no difference (Figure 2B).

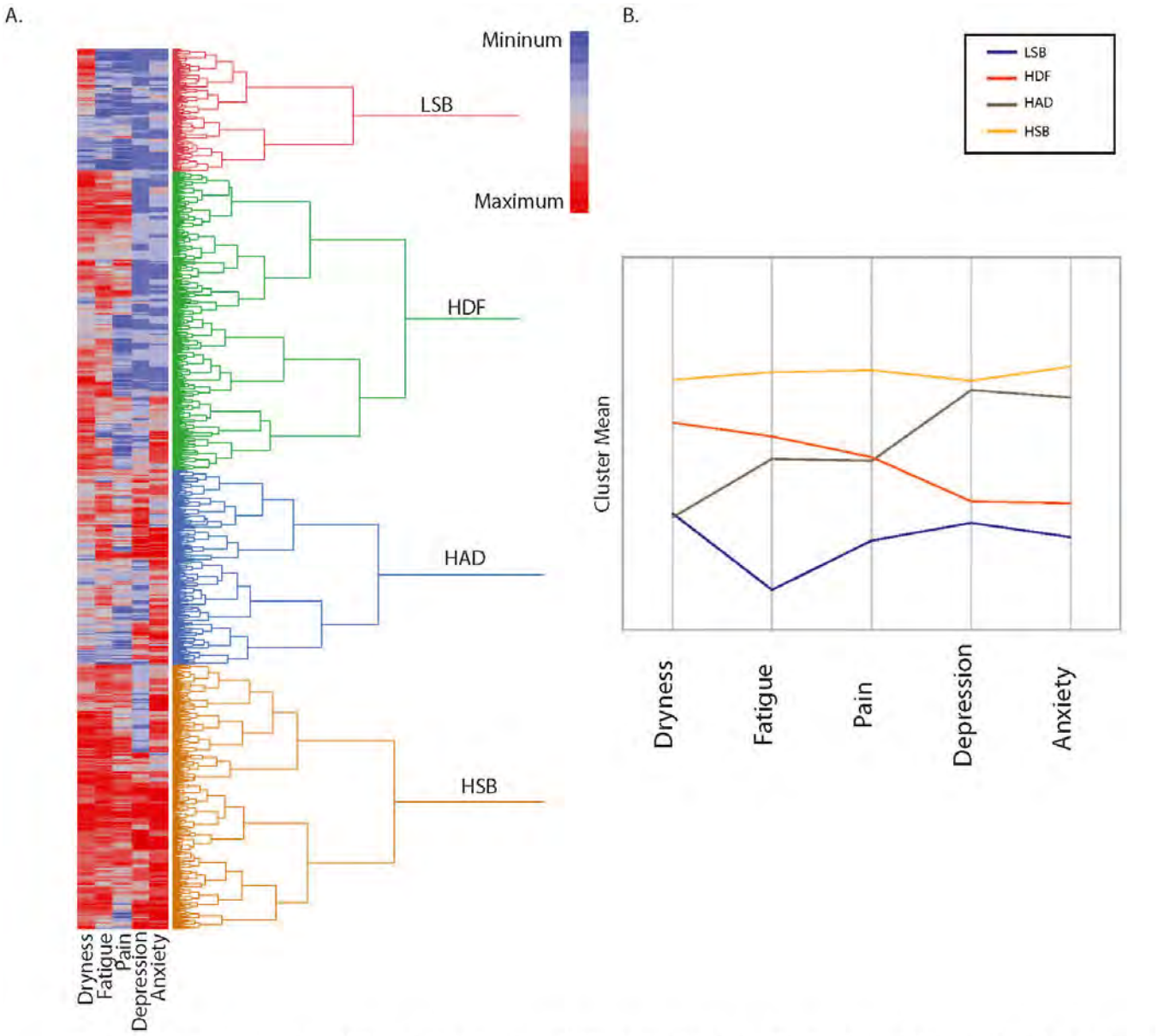

Figure 1. Four symptom based SS hierarchical clusters. A) Heat map demonstrating hierarchical clusters based on dryness, fatigue, pain, depression and anxiety. B) Cluster means of dryness, fatigue, pain, depression and anxiety. LSB= Low Symptom Burden; HDF=High Dryness and Fatigue; HAD=High Anxiety and Depression; HSB=High Symptom Burden

Conclusion: We verified the observation by Tarn et al. that 5 key symptoms can define 4 distinct clusters in SS patients. The HSB group is associated with more disability, symptomatic medication use, SS-specific symptoms and lower quality of life, but not as consistently with systemic manifestations. Findings highlight unique SS disease cluster profiles independent of age, sex, and some classical disease manifestations. We propose future phenotypic cluster research to better define subsets of this heterogeneous disease, and ultimately inform targeted therapies.

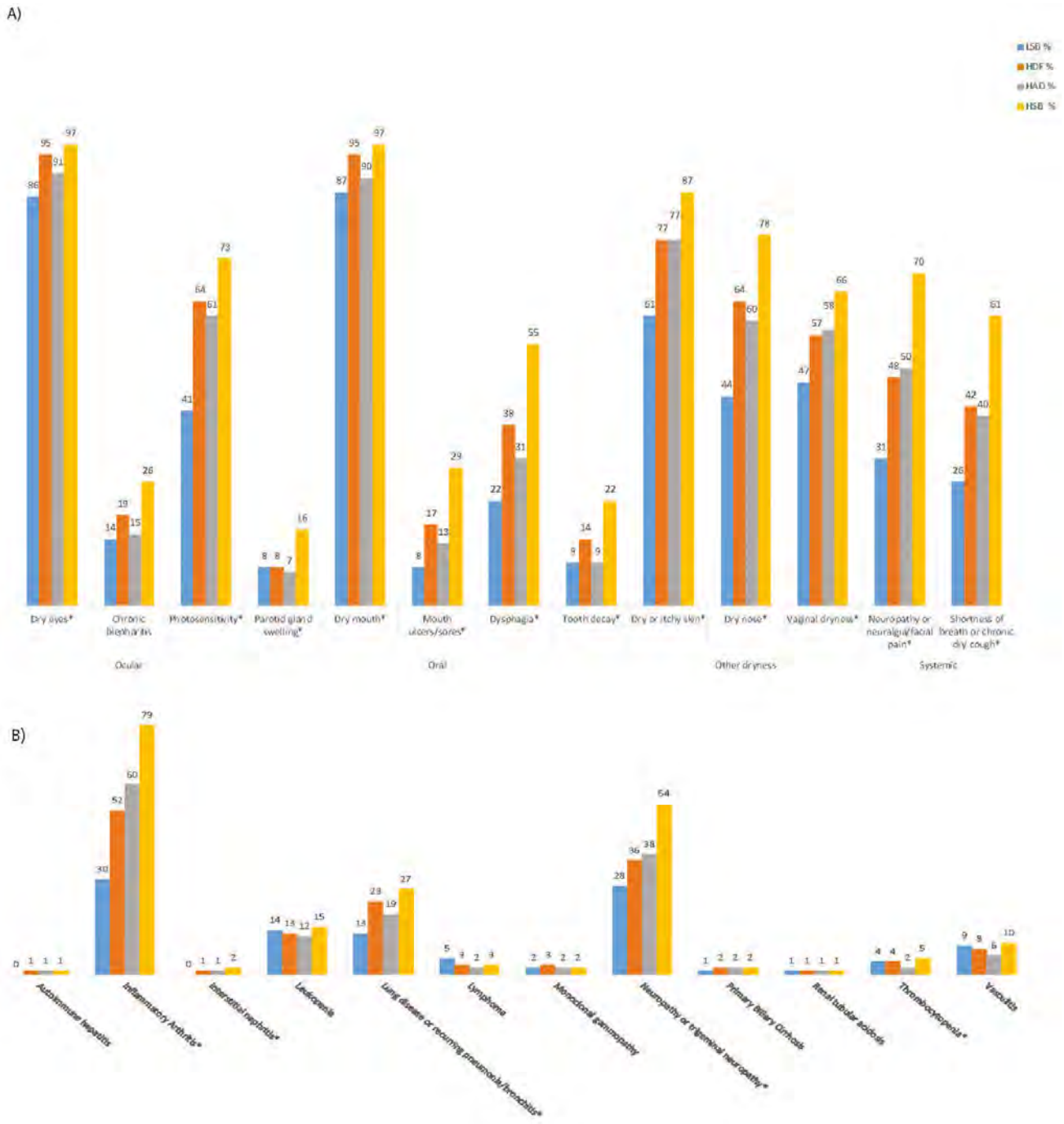

Figure 2. Frequency of reported symptoms and signs among symptom-based hierarchical clusters. A) Percent prevalence is reported for each symptom (present if experienced weekly or daily) within LSB, HDF, HAD, and LSB groups. B) Percent prevalence is reported for each sign within LSB, HDF, HAD, and LSB groups. LSB=low symptom burden; HDF=high dryness & fatigue; HAD=high anxiety and depression; LSB=low symptom burden. *p<0.05. Model is adjusted for age, sex, race,and social security disability.

Table. Symptom-Based Cluster Baseline Demographics (n=2806)

	LSB (n=390)	HDF (n=951)	HAD (n=622)	HSB (n=843)	p
Age mean (SD)					
Age at diagnosis	51.9 (13)	52.8 (13)	51.8 (12)	52.1 (12)	.35
Age at time of survey	64.4 (12)	66.6 (11)	62.8 (12)	64.0 (12)	<.001
Female n (%)	363 (93)	913 (96)	596 (96)	843 (97)	.06
Employment					.16
Full time	89 (23)	170 (19)	140 (23)	155 (20)	
Part time	28 (7)	55 (6)	45 (8)	43 (6)	
Retired	197 (52)	506 (56)	269 (45)	334 (43)	
Other	65 (17)	180 (20)	143 (24)	243 (31)	
Social Security Disability	5 (1)	61 (6)	37 (6)	124 (15)	<.0001
Medication Use n (%)*					
Ocular					
Autologous eye serum	21 (5)	47 (5)	22 (3)	71 (8)	<.001
Non-prescription eye drops or ointments	331 (85)	877 (92)	561 (90)	779 (92)	<.001
Prescription eye drops	157 (40)	489 (51)	275 (44)	457 (54)	<.0001
Oral					
Saliva substitutes	93 (24)	343 (36)	169 (27)	368 (44)	<.0001
Secretagogues	116 (30)	367 (39)	200 (32)	326 (39)	<.01
Systemic					
Biologics	23 (6)	49 (5)	35 (6)	58 (7)	.63
Corticosteroids	48 (12)	172 (18)	88 (14)	183 (22)	<.01
DMARDs	156 (40)	407 (43)	288 (46)	417 (50)	.06
Hydroxychloroquine	150 (39)	383 (40)	291 (47)	390 (46)	.03
Other					
Ibuprofen or other anti-inflammatory	154 (39)	451 (47)	316 (51)	459 (54)	<.0001
Prescription opioid analgesic	27 (7)	187 (20)	130 (21)	292 (35)	<.0001
Anti-depressants	36 (9)	152 (16)	262 (42)	368 (44)	<.0001
Quality of Life*					
SS adds significant emotional burden to life'	164 (43)	634 (68)	508 (83)	774 (94)	<.0001
SS affects ability to be independent'	6 (2)	147 (17)	118 (20)	341 (43)	<.0001

High symptom burden (HSB); High dryness and fatigue (HDF); High anxiety and depression (HAD); Low symptom burden (LSB); Standard deviation (SD); DMARDs=Hydroxychloroquine, methotrexate, azathioprine, mycophenolate, leflunomide, sulfasalazine, etc.). *Adjusted for age, sex, ethnicity and social security disability.

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Abstract Number: 1505

Antibodies Binding Ro/SSA and Muscarinic 3 Receptor in Sjogren's Syndrome

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Sjögren's Syndrome
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Sjögren's syndrome is characterized by exocrine gland dysfunction and autoantibody production. Some data suggest autoantibodies binding the muscarinic 3 receptor (M3R) mediate poor function of the salvary gland. We have previously produced recombinant human monoclonal antibodies (rhMab) from antibody-se-

creting B cells (ASC) infiltrating the salivary glands of Sjögren's syndrome subjects. We undertook this study to determine anti-M3R properties of these rhMab.

Methods: Minor salivary gland biopsies were obtained in a comprehensive sicca evaluation clinic. ABCs were single cell purified with heavy and light genes amplified by PCR. These genes were then expressed in 239 cells with production of monoclonal IgG or IgM. The rhMab were assayed for anti-Ro, Ro peptide and M3R extracellular loop (ECL) peptides by ELISA. Ability to act as an agonist or antagonist of M3R was assessed via GeneBlazer™ M3-NFAT-bla CHO-K1 (M3R) cell line (K1716).

Results: We studied 47 rhMabs from SS subjects and 18 from non-SS sicca subjects. There were 10/47 and 0/18 hrMab from the SS and non-SS sicca subjects, respectively, that were positive for binding to M3R ECL2 (p=0.05) and 5/47 SS vs. 0/18 non-SS sicca subjects that were positive for M3R ECL3 (p=0.311). Four of the rhMabs (1-G04k, 1-E06k, 2-D06k and 5-E04k) from one SS patient (pSS-3) bound both M3R ECL2 and ECL3. When we considered positivity to either M3R ECL2 or ECL3, 11 of 47 rhMabs from SS subjects bound, while 0 of 18 rhMabs from non-SS sicca subjects bound (p=0.03 by 2-tailed Fisher's Exact Test). Several rhMab that bound M3R ECL2 showed high affinity binding (Kd values ranging from 10-7 to 10-9). Among the Ro60-binding rhMab derived from SS subjects, 8/23 (34.8%) also bound M3R ECL2. and 4/23 (17%) bound the M3R ECL3 by ELISA. None of the anti-Ro60 rhMab from the non-SS sicca subjects bound either M3R ECL2 or ECL3. Of 65 rhMab, 4 from the SS group (all from pSS-3) and 2 from the non-SS sicca group (1 from NSS-1 and 1 from NSS-4) showed M3R antagonist activity.

Conclusion: Recombinant monoclonal antibodies derived from salivary gland infiltrating antibody secreting cells bind M3R extracellular loop. Some of these antibodies show M3R inhibitory activity; and, thus, may be directly involved in salivary gland dysfunction.

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Abstract Number: 1506

Correction of Sjögren's Syndrome Fluid Secretion Deficits in Salivary Gland Acinar Cells by Aquaporin-1 Gene Transfer

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Background/Purpose: The hallmark clinical complaints in Sjögren's syndrome (SS) are dry mouth and dry eyes related to salivary and lacrimal glands dysfunction. Reduced salivation reflects underlying fluid secretion deficits in the membrane permeability of acinar cells. In several animal models, including SS, increasing the membrane permeability using gene transfer of human aquaporin 1 (hAQP1) effectively restores fluid secretion. Indeed, hAQP1 gene transfer improved salivation and dry mouth in patients with radiation-induced xerostomia. Presently, there are no long-term effective therapies for most patients with dry mouth. To address this unmet clinical need we tested the ability of ex vivo adeno-associated virus serotype-2 (AAV2)-hAQP1 gene transfer to restore fluid secretion in human labial salivary

glands (LSG) from SS patients and identify predictive molecular signatures of responsiveness. We hypothesize that by restoring water permeability in acinar cells of salivary glands it is possible to correct salivary hypofunction in SS.

Methods: Sixteen (N=16) subjects provided informed consent and were evaluated in the NIDCR Sjögren's Syndrome Clinic. Subjects received comprehensive rheumatologic, ophthalmologic, and oral/salivary evaluations including LSG biopsies; nine subjects met the 2016 American College of Rheumatology SS criteria. LSG biopsies were divided into RNA*later* for storage or immediately micro-dissected into lobule preparations for ex vivo culture. Lobules were transferred to 24-well transwell plates and cultured at the air-media interface. Two hours after equilibration, LSG lobules were transduced with 6.25E+11 particles of AAV2-hAQP1 and 1.35E+11 AAV2-mCherry or 1.35E+11 AAV2-mCherry alone as a control. After 24 hours of transduction, the volume change response to 2uM carbachol was measured. Remaining lobules were fixed in 4% paraformaldehyde for immunofluorescence (IF) or preserved in RNA*later* for RNA sequencing.

Results: AAV2-hAQP1 transduction corrected both SS ($p = 0.02$) and non-SS ($p < 0.01$) LSG fluid secretion deficits up to 80% of normal. AAV2-hAQP1 transduction was confirmed using IF for hAQP1 expression and mCherry fluorescence in the acinar tissues. The RNA-sequencing analysis showed that responders to AQP1 transduction have a lower molecular signature for mesenchymal markers.

Conclusion: Our data suggest that, in the context of SS pathophysiology with sufficient secretory parenchyma in the glands of patients, SS salivary hypofunction can be recovered using AAV2-hAQP1.

Disclosure: P. Perez, None; **B. Warner**, None; **S. Wainer**, None; **Y. Ji**, None; **T. Pranzatelli**, None; **J. Chiorini**, None.

Abstract Number: 1507

Longitudinal Analysis of ANA Assay Performance in SLE from the SLICC Inception Cohort

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes II: Bench to Bedside

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Anti-nuclear antibodies (ANA) are important biomarkers for the diagnosis and classification of systemic lupus erythematosus (SLE). However, emerging data from cross-sectional studies suggest variation in the performance between ANA assays. The purpose of this project was to compare the performance of three different ANA assays in a longitudinal analysis of samples from the Systemic Lupus International Collaborating Clinics (SLICC) Inception Cohort.

Methods: We used demographic, clinical, and serological data of SLICC patients who fulfilled the 1997 Updated ACR SLE Classification Criteria and were enrolled within 15 months of diagnosis. Samples from enrolment and follow-up visits at years 3 and 5, were assayed using three FDA-approved ANA tests, including two HEp-2 indirect immuno-fluorescence assays, IFA1 (BioRad, Hercules, USA) and IFA2 (NovaLite, Inova Diagnostics, San Diego, USA), and an

enzyme-linked immunosorbent assay (ELISA) (Inova Diagnostics, San Diego, USA), at one central laboratory (Calgary, AB). A positive test was defined as a titer of ≥1:80 for IFA1 and IFA2 and ≥20 chemiluminescent units (CU) for the ELISA. The frequency of positivity, titer and patterns among different ANA assays were compared using weighted kappa statistics (κ) and McNemar tests. Longitudinal analysis of ANA titers was assessed for IFA1 and IFA2 using a mixed-effects restricted maximum likelihood regression model fitting a quadratic trend with unstructured co-variance. ANA patterns were categorized into three groups: 1) pure nuclear (e.g. homogeneous, speckled), 2) cytoplasmic and mitotic patterns (e.g. dense fine speckled and centrosome), and 3) mixed nuclear, cytoplasmic and mitotic patterns.

Results: 806 patients were included; 88.7% were female and mean age at diagnosis was 35.2 (SD 13.6) years. At enrolment, the frequency of ANA positivity by IFA1, IFA2, and ELISA was high (99.6%, 98.3%, and 96.7% respectively) (**Table**) and there was strong agreement between IFA1 and IFA2 (99.6% agreement) and IFA1 and ELISA (98.4%), but significant differences were detected for IFA2 and ELISA (95.7% agreement, $p< 0.05$ on McNemar's test). Over five years of follow-up, the prevalence and agreement in ANA positivity remained high for IFA1 and IFA2, decreasing slightly only for ELISA (91.5% positivity and 91.4% agreement with IFA2 at year 5). There was fair to moderate agreement between IFA1 and IFA2 titres at enrolment (84.7% agreement, κ=0.52), year 3 (77.0%, κ=0.32), and year 5 (80.1%, κ=0.37). A quadratic trend model revealed that IFA1 titers decreased more rapidly compared to IFA2 ($p< 0.001$) (**Figure 1**). There was fair to moderate agreement between IFA1 and IFA2 ANA patterns at enrolment (75.4% agreement, κ=0.45), year 3 (66.7%, κ=0.28), and year 5 (69.4%, κ=0.37) (**Figure 2**). Pure nuclear patterns were the most common, followed by mixed patterns.

Table. ANA positivity and inter-test percentage agreement among indirect immunofluorescence assays (IFA) 1 and 2 and enzyme-linked immunosorbent assay (ELISA) at enrolment, year 3 and year 5

	Enrolment (%)			Year 3 (%)			Year 5 (%)		
	IFA1	IFA2	ELISA	IFA1	IFA2	ELISA	IFA1	IFA2	ELISA
Positivity	99.6	98.3	96.7	96.8	98.6	92.6	98.4	98.8	91.5
Agreement									
IFA1	-	-	-	-	-	-	-	-	-
IFA2	99.6	-	-	97.2	-	-	98.4	-	-
ELISA	98.4	95.7*	-	94.8	92.4**	-	97.6	91.4**	-

**p<0.001, *p<0.05 using McNemar's Test

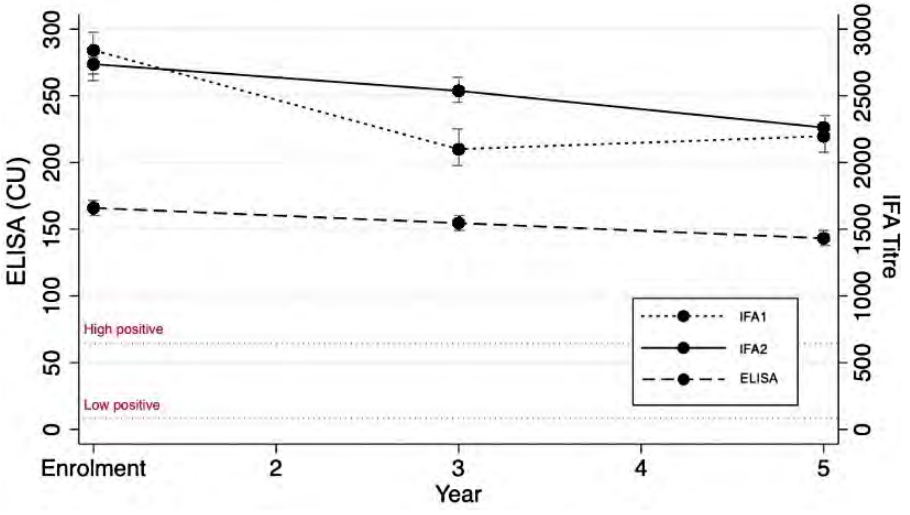
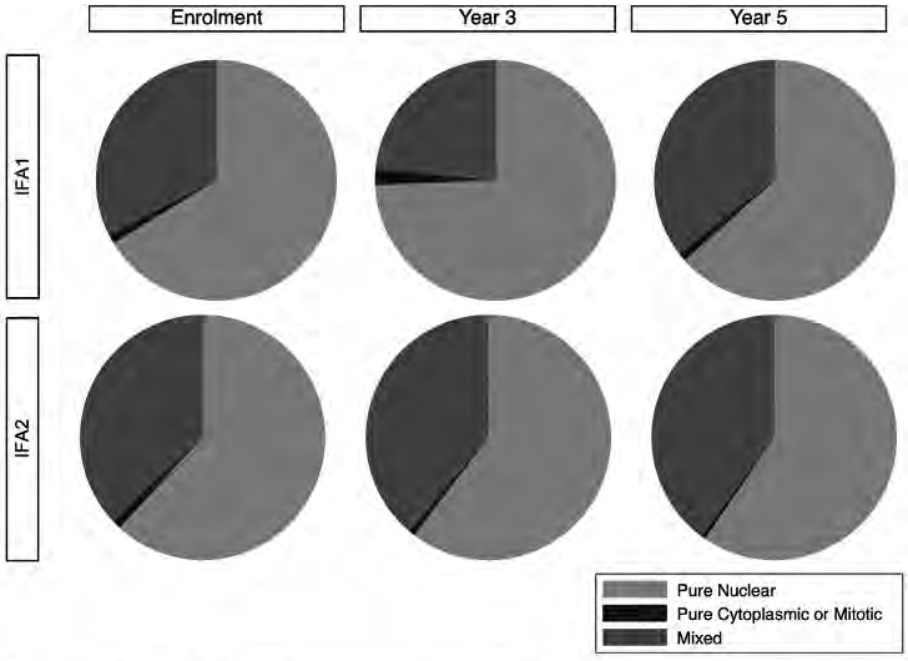


Figure 1. ANA titres decrease over time with indirect immunofluorescence assay (IFA) 1, IFA2, and enzyme-linked immunosorbent assay (ELISA) in chemiluminescent units (CU).



Time	Enrolment	Year 3	Year 5
%Agree (kappa)	75.4 (0.45)**	66.7 (0.28)**	69.4 (0.37)**

Figure 2. ANA patterns over time with indirect immunofluorescence assays (IFA) 1 and 2. **p<0.0001 using weighted kappa statistics.

Conclusion: In recent-onset SLE, early ANA positivity is 96.7-99.6% depending on the test. Agreement between the two IFA's was high at diagnosis and sustained over five years but was lower between one of the IFA's and ELISA. While titers did decrease slightly over time, ANA patterns remained largely unchanged. A future study with a longer follow-up period and clinical correlation is underway.

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Abstract Number: 1508

Blood-Brain Barrier Leakage in Systemic Lupus Erythematosus Is Associated with Gray Matter Loss and Cognitive Impairment

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes II: Bench to Bedside
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Cognitive impairment is the most frequent manifestation of neuropsychiatric systemic lupus erythematosus (NPSLE), yet the mechanisms underlying it remain poorly understood. The purpose of our study was to examine the association between blood-brain barrier (BBB) integrity, brain volume and cognitive dysfunction in adult patients with systemic lupus erythematosus (SLE).

Methods: A total of 65 ambulatory SLE patients and 9 healthy controls underwent dynamic contrast-enhanced magnetic resonance imaging (DCE-MRI) scanning, for quantitative assessment of blood-brain barrier (BBB) permeability. Volumetric data was extracted using the VolBrain pipeline. Global cognitive function and performance in five individual cognitive domains was compared between patients with normal versus extensive BBB leakage.

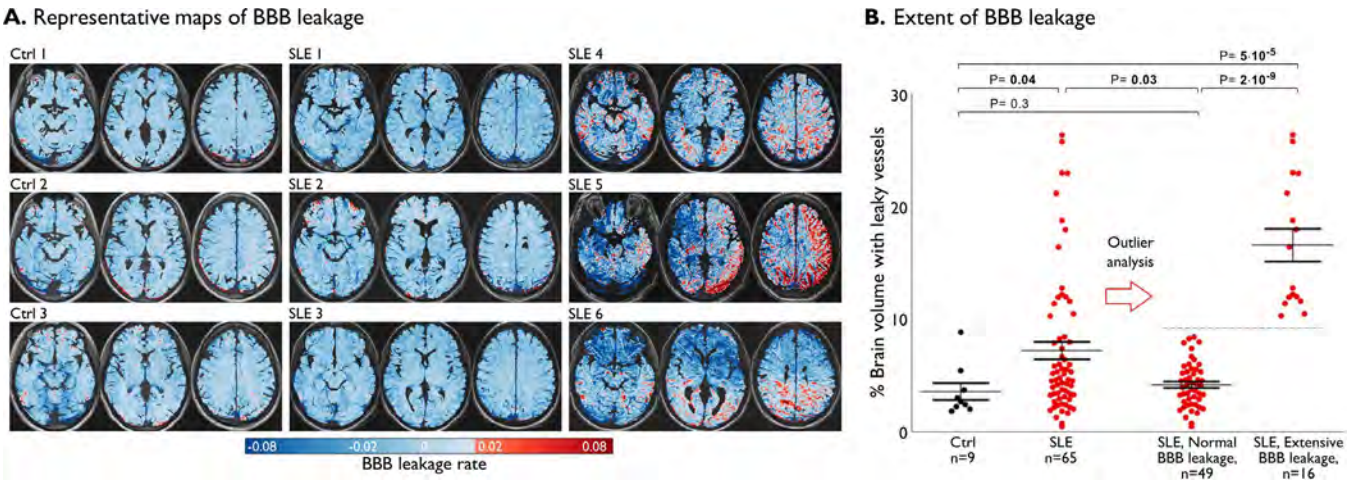

Figure 1. A sub-group of SLE patients have extensive BBB leakage. A. The rate of BBB leakage was quantified for every brain voxel. Shades of blue represent tissue with non-permeable BBB and shades of red represent contrast agent accumulation due to BBB leakage. A qualitative review of leakage maps in these selected cases illustrates that some SLE patients are visually comparable to controls, while others exhibit visibly higher number of voxels with BBB leakage. B. The percent of brain volume with BBB leakage was quantified for each subject, revealing a significant difference between SLE patients and controls (p=0.04). Outlier analysis of all 74 participants identified a group with "extensive BBB leakage", consisting of 16 SLE patients; and a group termed "normal BBB leakage", consisting of 9 controls and 49 SLE patients.

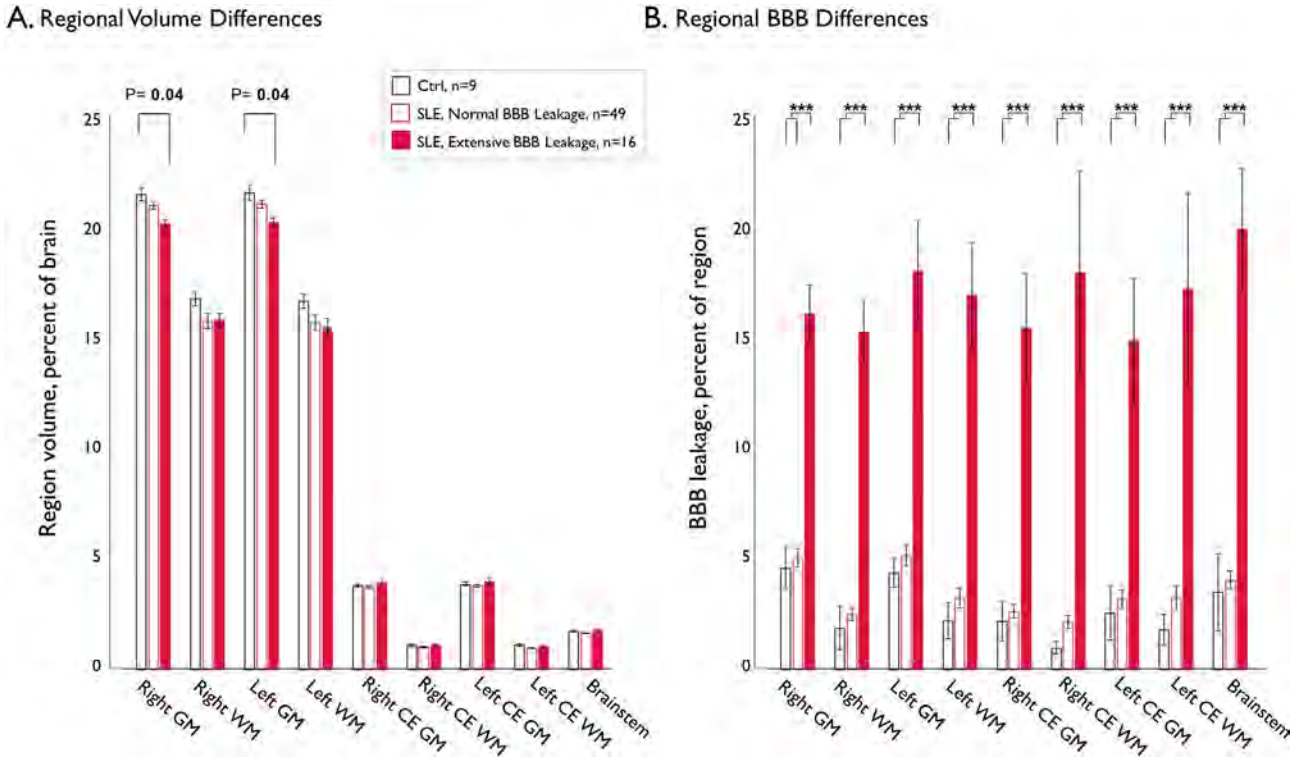

Figure 2. Extensive BBB leakage in SLE patients is associated with smaller gray matter volume. A. Depiction of the nine largest brain structures (of the 23 regions compared between the groups) illustrates the reduced right- and left- gray matter volumes in patients with extensive BBB leakage compared to controls (p=0.04, corrected for multiple comparisons). There were no volumetric differences in any other regions. B. Comparison of BBB leakage in the same 23 brain structures revealed that the 'extensive BBB leakage group' had higher levels of leakage in all regions (the same nine regions are depicted in B and A), compared to patients with normal BBB leakage and controls (p≤0.001, corrected for multiple comparisons). The Wilcoxon rank sum test was used to compare between the groups, and the false discovery rate algorithm was used to correct for multiple comparisons. Error bars denote standard error of the mean. Asterisks denote level of significance, with ***p≤0.001. GM, gray matter; WM, white matter; CE, cerebellum.

Results: Patients were predominantly female (87.7%) and Caucasian (89%) with a mean±SD age of 48.9 ± 13.3 years and disease duration of 15.1 ± 10.5 years. All patients had quiescent SLE and prior NP events attributable to SLE were present in 23% of patients. Impairment in at least one of five cognitive domains was found in 47.7% of patients. SLE patients had significantly higher levels of BBB leakage compared to controls (p=0.04). Extensive BBB leakage (affecting over >9% of brain volume) was identified only in SLE patients (16/65; 24.6%), who also had smaller right and left cerebral gray matter volumes compared to controls (p=0.04). Extensive BBB leakage was associated with lower global cognitive scores (p=0.02), and with the presence of impairment in one or more cognitive domains (p=0.01).

Conclusion: Our findings provide evidence for an association between extensive BBB leakage and changes in both brain structure and cognitive function in SLE patients. Future studies should investigate the mechanisms underlying BBB-mediated cognitive impairment, the diagnostic utility of BBB imaging, and the potential of targeting the BBB as a therapeutic strategy in SLE patients.

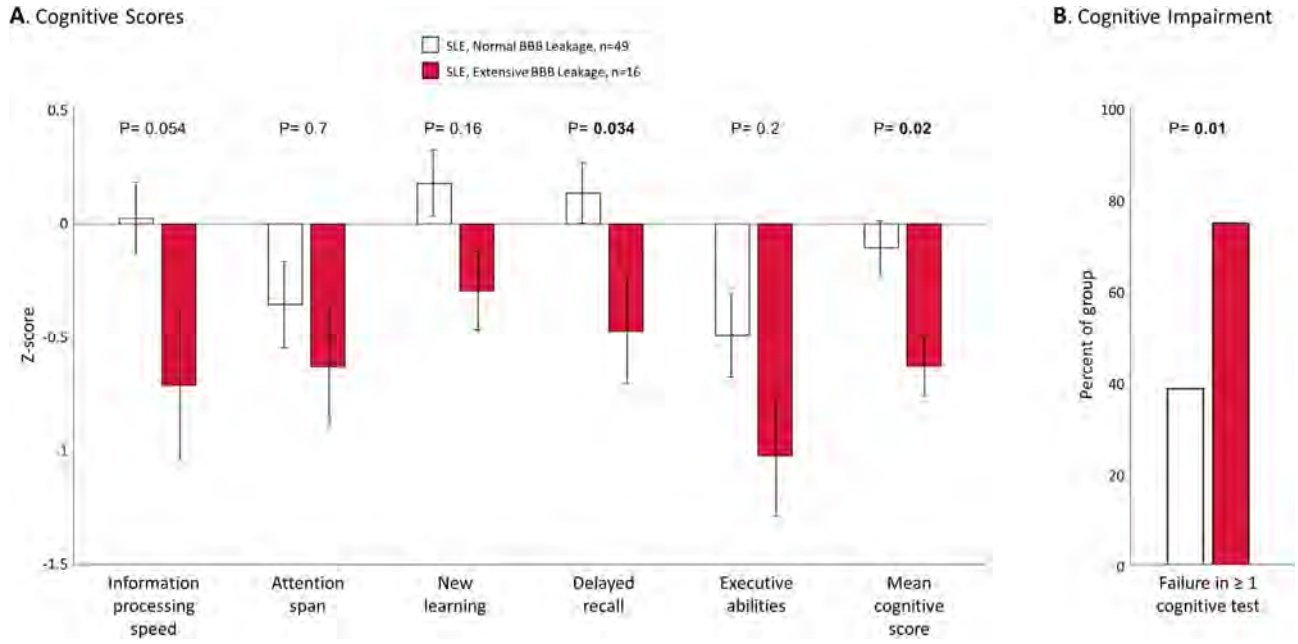

Figure 3. Extensive BBB leakage in SLE patients is associated with cognitive impairment. A. SLE patients with extensive BBB leakage had worse delayed recall and lower mean cognitive scores (averaged Z-scores of the five examined cognitive domains) compared to patients with normal BBB leakage (p=0.02, Wilcoxon rank sum test). B. The extensive BBB leakage group also had a significantly higher percent of subjects failing at least one cognitive test (p=0.01, chi-square test). Error bars denote standard error of the mean.

Disclosure: L. Kamintsky, None; **S. Beyea**, None; **J. Fisk**, None; **J. Hashmi**, None; **A. Omisade**, None; **C. Calkin**, None; **T. Bardouille**, None; **C. Bowen**, None; **M. Quraan**, None; **A. Mitnitski**, None; **K. Matheson**, None; **A. Friedman**, None; **J. Hanly**, None.

Abstract Number: 1509

Leukocyte Telomere Length and Childhood Onset of Systemic Lupus Erythematosus in the Black Women's Experiences Living with Lupus (BeWELL) Study

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes II: Bench to Bedside

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Childhood-onset SLE is generally more aggressive than adult-onset SLE. Leukocyte telomere length (LTL) has been posited to reflect immune system aging. Short LTL in particular has been associated with chronic health conditions mediated by inflammatory pathways as well as all-cause mortality. Prior studies have found evidence for shorter LTL among patients with SLE compared to healthy controls. However, no studies to date have compared LTL among SLE patients diagnosed in childhood vs. adulthood.

Table 1: Descriptive Characteristics of Black Women with SLE in the Black Women's Experience Living with Lupus (BeWELL) Study

Characteristic	Childhood-Onset SLE (n=40)	Adult-Onset SLE (n=375)	Total Sample* (n=415)
Age in Years, M (SD)	38.28 (12.48)	47.29 (11.35)	46.42 (11.75)
Years Since Diagnosis, M (SD)	23.88 (13.30)	14.80 (9.26)	15.68 (10.07)
Disease Damage†, M (SD)	2.98 (2.59)	2.70 (2.48)	2.73 (2.49)
Body Mass Index, M (SD)	29.68 (7.96)	31.01 (8.09)	30.88 (8.08)
LTL (T/S), M (SD)	1.46 (0.37)	1.39 (0.28)	1.40 (0.29)
Relationship Status, N (%)			
Married or marriage-like	12 (30.00)	178 (47.47)	190 (45.78)
Romantic relationship	3 (7.50)	23 (6.13)	26 (6.27)
Divorced/separated or widowed	5 (12.50)	85 (22.67)	90 (21.69)
Single, never married	20 (50.00)	89 (23.73)	109 (26.27)
Education, N (%)			
Less than high school	2 (5.00)	32 (8.53)	34 (8.19)
High school	8 (20.00)	67 (17.87)	75 (18.07)
Some college	22 (55.00)	165 (44.00)	187 (45.06)
Bachelor's degree or higher	8 (20.00)	111 (29.60)	119 (28.67)
Income-Poverty Ratio, N (%)			
< 1.00	20 (50.00)	111 (29.60)	131 (31.57)
1.00 – 1.99	11 (27.50)	127 (33.87)	138 (33.25)
2.00 – 4.00	6 (15.00)	92 (24.53)	98 (23.61)
> 4.00	3 (7.50)	45 (12.00)	48 (11.57)
Insurance Status, N (%)			
Public	14 (35.00)	138 (36.80)	152 (36.63)
Private	20 (50.00)	195 (52.00)	215 (51.81)
None	6 (15.00)	42 (11.20)	48 (11.57)
Current Smoker, N (%)	3 (7.50)	57 (15.20)	60 (14.46)

*Total sample was age-restricted to participants < 70 years

† Disease damage assessed with the Brief Index of Lupus Damage

N = number; M = mean; LTL (T/S) = leukocyte telomere length (telomere to single copy gene ratio)

Table 1

Methods: Data are from the Black Women's Experiences Living with Lupus (BeWELL) Study. A total of 438 Black women living in the Atlanta, Georgia metropolitan area with a validated diagnosis of SLE (≥ 4 American College of Rheumatology SLE criteria or 3 criteria with a diagnosis of SLE by a board-certified rheumatologist) were recruited between April 2015-May 2017. Multivariable linear regression analyses were conducted examining childhood diag-

Table 2: Regression Results Examining Associations Between Childhood-Onset SLE and Leukocyte Telomere Length in the Black Women's Experiences Living with Lupus (BeWELL) Study (n=415)

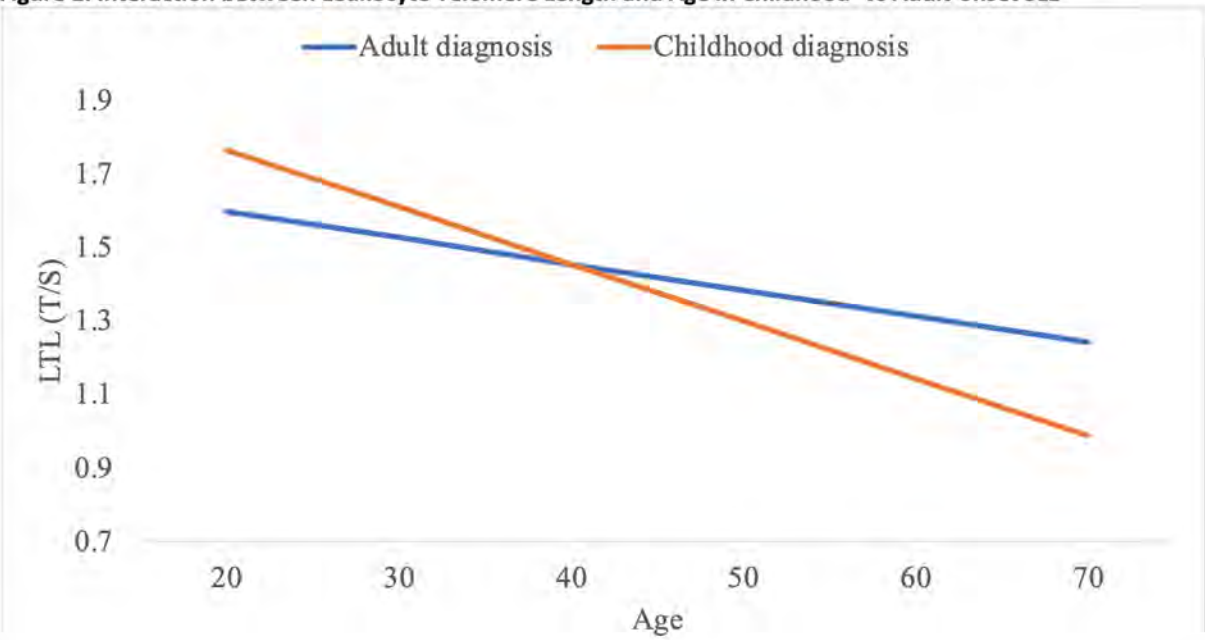
Variable	Model 1		Model 2		Model 3		Model 4	
	b	95% CI	b	95% CI	b	95% CI	b	95% CI
Age	-0.008	(-0.011, -0.005)	-0.007	(-0.010, 0.004)	-0.006	(-0.009, -0.003)	-0.006	(-0.009, 0.003)
Childhood diagnosis	0.007	(-0.089, 0.103)	0.339	(0.027, 0.652)	0.373	(-0.060, -0.687)	0.314	(-0.002, -0.629)
Age*childhood diagnosis			0.008	(0.016, 0.001)	-0.009	(-0.016, -0.001)	0.007	(-0.015, 0.001)
≥ 10-year disease duration					0.063	(-0.002, 0.127)	--	--
Disease duration (continuous)					--	--	-0.002	(-0.006, 0.002)

Note: Total sample was age-restricted to participants < 70 years.

All models adjust for the following covariates: relationship status, education, income-poverty ratio category, insurance status, disease damage (BILD), body mass index, and smoking status.

Table 2

Figure 1: Interaction between Leukocyte Telomere Length and Age in Childhood- vs Adult-onset SLE



LTL (T/S) = leukocyte telomere length (telomere to single copy gene ratio)

Figure 1

nosis of SLE (< 18 years of age derived from self-reported age and disease duration) in relation to LTL assayed from dried blood spots, measured as the relative telomere to single copy gene (T/S) ratio.

Results: Seven participants without a valid measure of LTL were excluded from analyses. Among those diagnosed in childhood, the oldest participant was 69 years of age. Analyses were restricted to those < 70 years of age resulting in a total analytic sample size of 415. A total of 40 participants (9.6%) were diagnosed in childhood. Multivariable linear regression analyses were conducted adjusting for a range of demographic, socioeconomic and health-related

covariates, including smoking status, body mass index, and disease damage measured using the Brief Index of Lupus Damage (Table 2). Results indicated no main effect of childhood diagnosis on LTL (Model 1: b=0.007, 95% CI: -0.089, 0.103). However, the interaction between age and childhood diagnosis was significant (Model 2: b—0.008, -0.016, -0.001), indicating a steeper inverse association between age and LTL among those diagnosed in childhood compared to those diagnosed in adulthood (Figure 2). This interaction continued to be significant at p=0.024 (Model 3) after controlling for disease duration measured dichotomously (< 10 years vs. >= 10 years); and was marginally significant at p=0.083 (Model 4) when examined continuously.

Conclusion: This cross-sectional analysis suggests that Black women with childhood-onset SLE may undergo accelerated LTL shortening compared to their adult-onset counterparts. We found that this relationship persisted even after controlling for differences in SLE damage and disease duration. Future longitudinal research modeling within-person change in LTL over time that includes larger samples of those diagnosed in childhood may help to uncover if this finding is an artifact of cohort effects, or if there are other mechanisms involved in more rapid LTL shortening in this population. Despite limitations, these findings inform research on immunosenescence mechanisms of SLE.

Disclosure: J. Bridges, None; **K. Chung**, None; **C. Martz**, None; **E. Smitherman**, None; **C. Drenkard**, None; **S. Lim**, None; **D. Chae**, None.

Abstract Number: 1510

Platelet-bound C4d Is Associated with Platelet Activation and Arterial Thrombotic Events

Yevgeniya Gartshteyn[1], Adam Mor[2], Daichi Shimbo[2], Leila Khalili[3], Teja Kapoor[4], Laura Geraldino-Pardilla[5], Roberta Vezza Alexander[6], Thierry Dervieux[7] and Anca Askanase[2], [1]Columbia University College of Physicians and Surgeons, Glen Rock, NJ, [2]Columbia University College of Physicians and Surgeons, New York, NY, [3]Columbia University Medical Center, New Haven, CT, [4]Columbia University College of Physicians and Surgeons, Leonia, NJ, [5]Division of Rheumatology, Columbia University Vagelos College of Physicians and Surgeons, New York, [6]Exagen Inc, Vista, CA, [7]Prometheus Biosciences Inc, Irvine, CA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes II: Bench to Bedside
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Platelets have a well-defined role in arterial thrombosis, and platelet-bound complement activation products (PC4d) correlate with vascular thromboses in patients with Systemic Lupus Erythematosus (SLE). The mechanistic link between PC4d and thrombosis has not been studied to date.

Methods: Using a cross-sectional design, we evaluated the associations between PC4d and arterial thrombosis, as well as between PC4d and platelet volumetric measures (count and volume). Platelet reactivity was assessed using the gold-standard technique of light-transmittance aggregometry (LTA). Decreasing doses of adenosine diphosphate (ADP) were used to induce platelet aggregation; a dose-response curve for ADP vs maximal aggregation was constructed for each patient. The ADP concentration at which 50% of maximal aggregation defined the EC_{50}. Patients on anti-platelet agents were excluded.

Results: 150 SLE patients were included; their average age was 40±13 years, 38% were antiphospholipid antibody (aPL) positive, 18% were taking prednisone ≥7.5mg/day, 29% had hypertension, 19% were smokers, 5% had di-

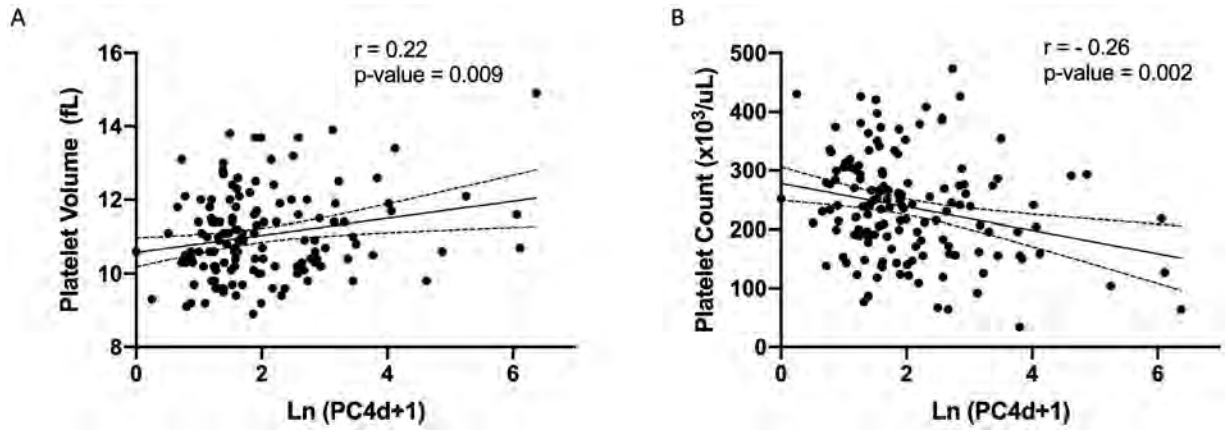


Figure 1. PC4d levels correlate with mean platelet volume and count. Correlation between PC4d levels, natural log transformed (Ln), and A, mean platelet volume and B, platelet count. r is the Pearson's correlation coefficient.

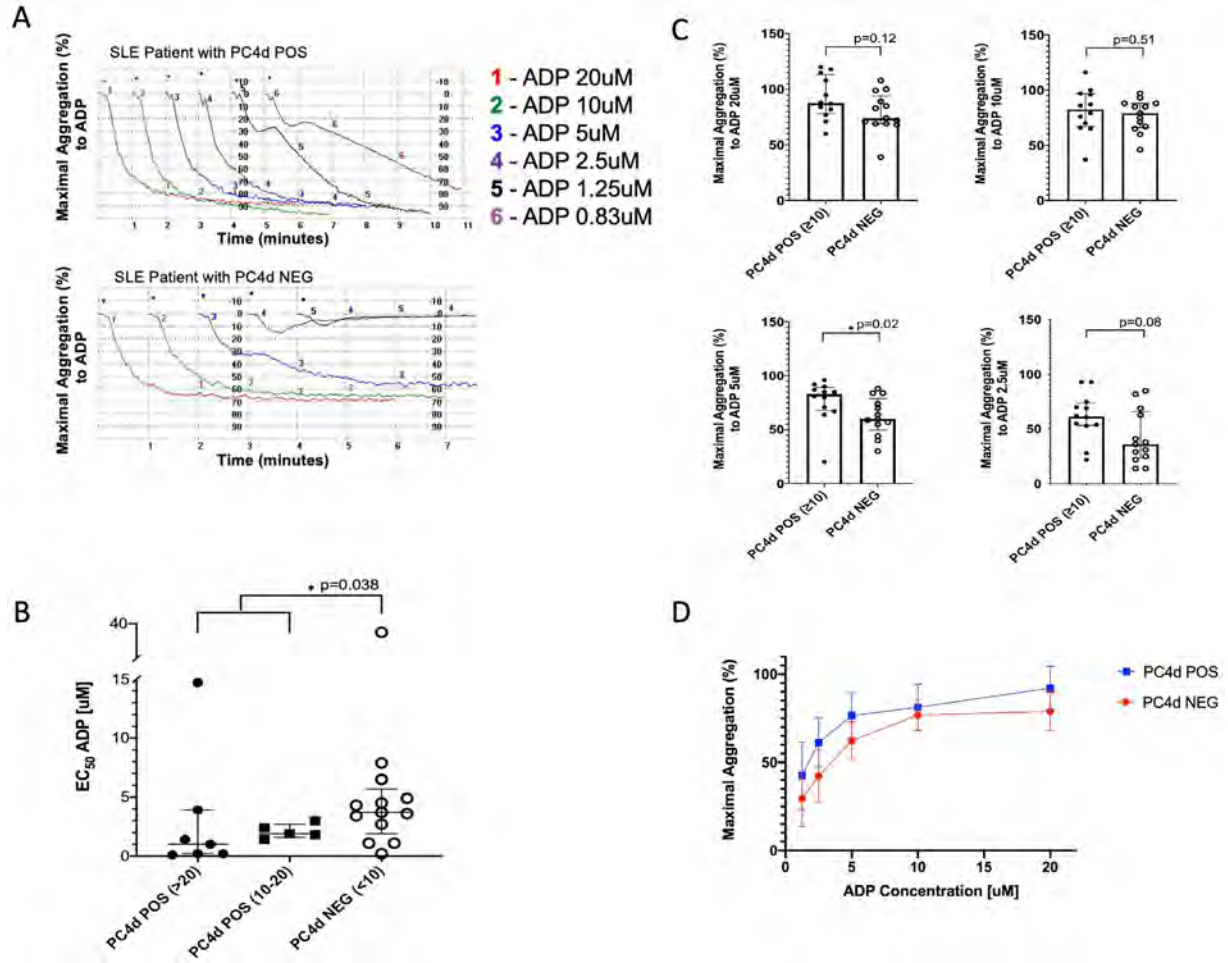


Figure 2. PC4d POS (PC4d≥10) platelets, as compared with PC4d NEG (PC4d≤10) platelets, aggregate more in response to addition of ADP agonist. A, Representative platelet aggregation curves from a PC4d POS patient (top) and a PC4d NEG patient (bottom). Decreasing concentrations of ADP agonist were added to platelet rich plasma and the aggregation response was recorded for six minutes. B, Platelet aggregation was analyzed as EC50, expressed as the ADP concentration [uM] that achieves 50% of the maximal aggregation. A lower EC50 indicates greater platelet sensitivity to the addition of the platelet aggregation agonist. C and D, Maximal platelet aggregation response after the addition of 20, 10, 5 and 2.5uM ADP agonist. Bars show the median ± IQR; Patients on aspirin were excluded. *p-value≤0.05.

abetes, mean total cholesterol and LDL 173±52 and 93±41 respectively. Thirteen arterial events (5 myocardial infarctions, 8 strokes) occurred within 5 years of enrollment. Arterial events were associated with PC4d levels (log transformed given positive skewness): for every one unit increase in log PC4d the odds of an arterial even increased by 70% (OR 1.7, p< 0.05) when adjusting for the significant covariates identified on the univariable analysis (aPL, smoking, and prednisone ≥7.5mg/day use). A PC4d cutoff of 10MFI had the greatest area under the curve of 0.71±0.08 for detecting arterial events.

PC4d levels correlated with lower platelet counts (r=-0.26, p=0.002) and larger platelet volumes (r=0.22, p=0.009). Platelet aggregation was tested in 12 patients with PC4d net MFI and 13 patients with PC4d< 10; aPL were present in 5/12 and 7/13 patients in each group. EC_{50} values were significantly lower in patients with PC4d10 net MFI compared with PC4d< 10 (1.6 vs. 3.7, p=0.038). The maximal aggregation response in PC4d positive patients, as compared to PC4d negative patients, trended towards greater aggregation at all concentrations of ADP agonist, and was statistically significant at 5 µmol.

Conclusion: PC4d is associated with arterial events in SLE. PC4d platelets were fewer in number, larger, and hyper-aggregable, suggesting that PC4d may be a mechanistic marker for vascular disease in SLE.

Disclosure: Y. Gartshteyn, None; **A. Mor**, None; **D. Shimbo**, None; **L. Khalili**, None; **T. Kapoor**, None; **L. Geraldino-Pardilla**, Pfizer, 1, BMS, 1; **R. Alexander**, Exagen Inc, 1; **T. Dervieux**, Exagen, 6; **A. Askanase**, GlaxoSmithKline, 2, 5, AstraZeneca, 2, 5, AbbVie, 5, Bristol Myers Squibb, 5, Janssen, 2, Eli Lilly, 2, Pfizer, 2, LuCIN, 2, Mallinckrodt Pharmaceuticals, 2.

Abstract Number: 1511

Clinical Features and Select Dysregulated Immune Parameters Distinguish Blood Relatives Who Remain Clinically Stable or Progress to Incomplete Lupus or Classified SLE in the Lupus Autoimmunity in Relatives (LAUREL) Follow-up Cohort

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
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Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Identifying populations at risk of SLE is essential to curtail inflammatory damage and identify individuals for prevention trials. Unaffected blood relatives (BRs) of lupus patients have increased risk of SLE. Some BRs have autoantibodies (AutoAbs) or SLE clinical features, but do not progress, some progress, but do not meet the

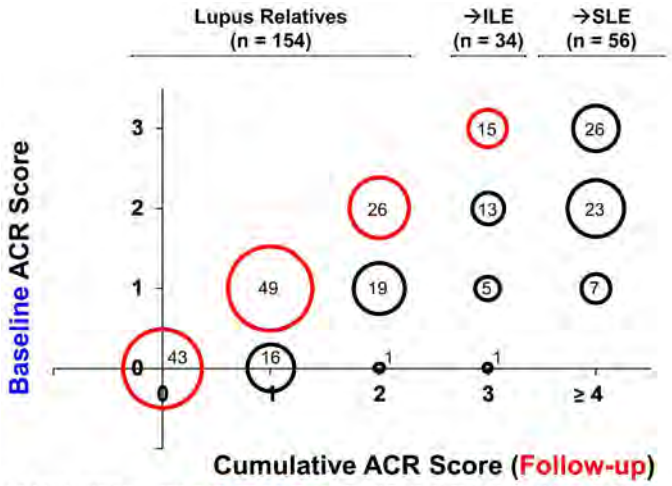
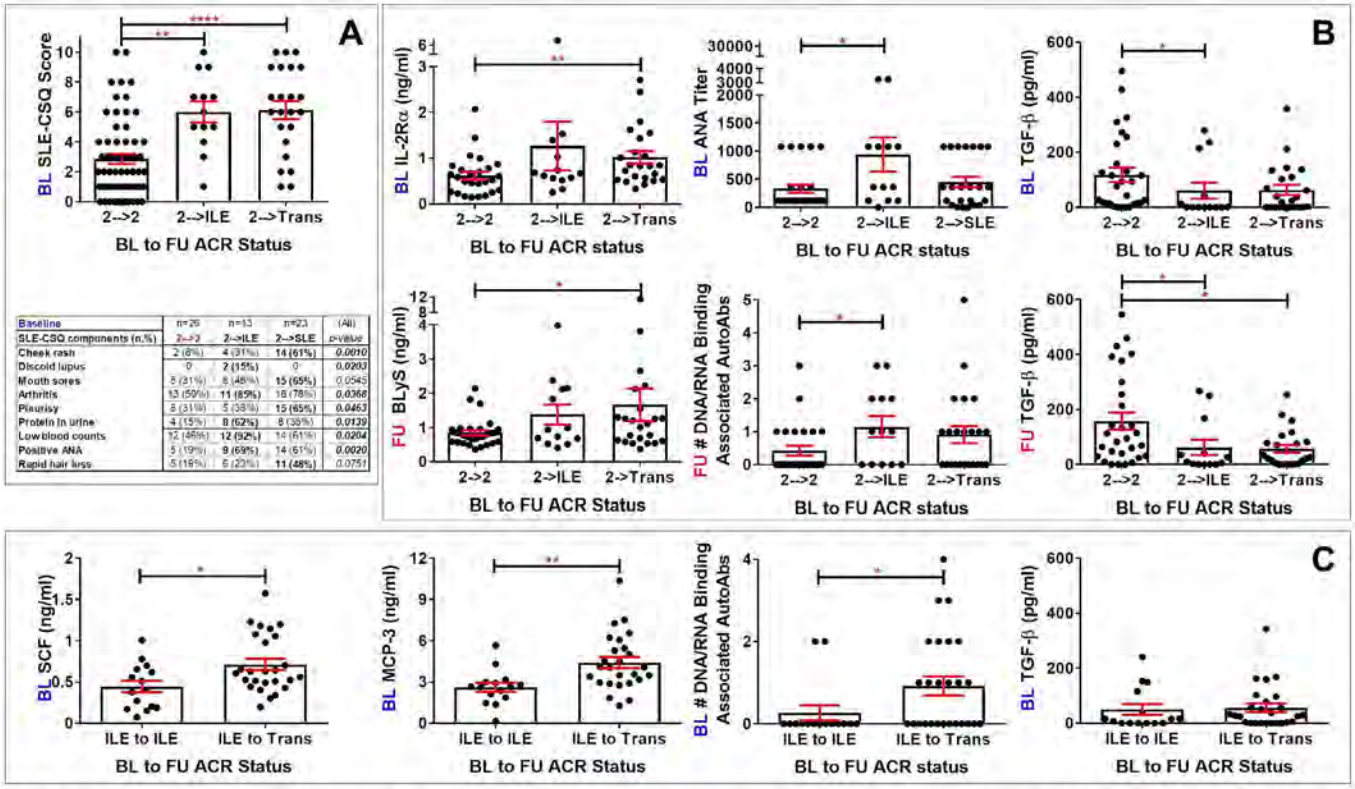


Fig. 1 ACR Criteria **Progressors** vs. **Non-progressors** Comparing Baseline (BL) and Follow-up (FU) Visits in LAUREL Cohort. Bubble plot of number of ACR criteria (ACR Score) at BL (y-axis, 0-3) vs. FU (x-axis, 0- ≥4). Lupus relatives with no change in number of ACR Score between BL and FU are **Non-progressors** (**red** circles), while all other lupus relatives met additional ACR classification criteria (**Progressors, black** circles). Incomplete Lupus (ILE) = 3 ACR criteria; SLE = ≥ 4 ACR criteria (1997 Update of the 1982 American College of Rheumatology Revised Criteria). Bubble size based on number of lupus relatives (within or adjacent to bubble) representing intersection of ACR Scores between BL and FU.



Baseline	n=26	n=13	n=23	(All)
SLE-CSQ components (n,%)	2-->2	2-->ILE	2-->SLE	p-value
Cheek rash	2 (8%)	4 (31%)	14 (61%)	*0.0010*
Discoid lupus	0	2 (15%)	0	*0.0203*
Mouth sores	8 (31%)	6 (46%)	15 (65%)	*0.0545*
Arthritis	13 (50%)	11 (85%)	18 (78%)	*0.0368*
Pleurisy	8 (31%)	5 (38%)	15 (65%)	*0.0463*
Protein in urine	4 (15%)	8 (62%)	8 (35%)	*0.0139*
Low blood counts	12 (46%)	12 (92%)	14 (61%)	*0.0204*
Positive ANA	5 (19%)	9 (69%)	14 (61%)	*0.0020*
Rapid hair loss	5 (19%)	6 (23%)	11 (48%)	*0.0751*

Fig. 2 SLE-CSQ and Immune Features in **Progressors** vs. **Non-progressors** at Baseline (BL) or Follow-up (FU) Visits in LAUREL Cohort. **A**. SLE-CSQ Score and components in lupus relatives with ACR Score = 2 at **BL** who do not progress or progress to ILE or SLE at **FU**. **B**. Systemic levels of IL-2Rα, ANA titer, and Native TGF-β at **BL**, as well as levels of BLyS, # SLE-associated autoantibody (AutoAb) specificities, and Native TGF-β at **FU** in lupus relatives with ACR Score = 2 at **BL** who do not progress or progress to ILE or SLE at **FU**. **C**. Systemic levels of SCF, MCP-3, # SLE-associated AutoAb specificities, and Native TGF-β at **BL** in lupus relatives with ILE at **BL** who do not progress or progress to SLE at **FU**. Categorical significance determined by Chi-square. Continuous variable significance determined by Mann-Whitney or Kruskal-Wallis with Dunn's multiple comparison. *$p<0.05$, **$p<0.01$, ****$p<0.0001$

required ≥ 4 ACR classification criteria (incomplete lupus, ILE), while others progress to classified SLE. The goal of this study is to determine factors that distinguish previously healthy BRs who remain stable or subsequently progress to ILE or SLE.

Methods: This is a nested study of re-enrolled BRs of SLE patients (n=436) who previously enrolled in a genetics study (mean time to follow-up = 6.3 yrs) and did not meet SLE classification at baseline (BL). Of the 177 (41%) and 259 (59%) who did/did not meet additional ACR criteria at follow-up (FU) in this cohort, we compared the 56 BRs who transitioned to SLE (≥4 ACR criteria) to 34 BRs who met 3 ACR criteria (ILE) at FU and 154 race/sex/age (± 5 years) matched BRs with < 3 ACR criteria at FU. BRs provided clinical and demographic information, and completed the SLE-specific portion of the CTD Screening Questionnaire (CSQ) at BL and FU. Medical records were reviewed for ACR classification criteria. BL and FU plasma samples were assessed for autoantibody production (ANA, anti-dsDNA, aCL, Ro, La, Sm, nRNP, and ribosomal p antibodies) and for 52 soluble inflammatory and regulatory mediators by xMAP and ELISA assay.

Results: 133/244 (55%) of BRs evaluated in this nested cohort did not have any change in ACR criteria between BL and FU (**Fig. 1**, red circles, Nonprogressors [NP]), while the remaining 111 BRs accrued ≥1 classification criteria (**Fig. 1**, black circles, Progressors). There was no difference in time to FU between NP and Progressor BRs. No significant differences were seen in ACR criteria, either at BL or FU, between BRs with ILE at BL who were NP vs. those who progressed to SLE at FU. Yet, a number of differences were seen at BL in BRs meeting 2 ACR criteria at BL who were NP vs. those who progressed to ILE or SLE at FU. NP BRs with BL ACR Score = 2 were more likely to meet immunologic criteria ($p< 0.0001$), while those BRs with ACR score ≤ 2 who progressed to ILE or SLE were more likely to meet clinical criteria at BL, particularly malar rash ($p=0.0126$) or arthritis ($p=0.0054$). In addition, these same NP had significantly lower SLE-CSQ scores and features at BL (**Fig. 2A**), with lower plasma levels of IL-2Rα and lower ANA titers. At FU, ACR Score = 2 NP had lower levels of BLyS and accumulated fewer AutoAbs (**Fig. 2B**). At both BL and FU, levels of the regulatory mediator Native TGF-β were significantly higher in ACR Score = 2 NP (**Fig. 2B**). For those BRs with ILE at BL, those who progressed to SLE at FU had higher BL levels of SCF, MCP-3, and more AutoAb specificities than BL ILE NP BRs, with no difference in levels of Native TGF-β (**Fig. 2C**).

Conclusion: BRs of known SLE patients who progress to ILE or SLE compared to BRs who remain stable are more likely to have elevated inflammatory mediators, reduced regulatory mediators, and meet as few as one clinical ACR classification criterion. This suggests that ANA or serologic positivity alone is not predictive of progression to ILE or SLE in lupus relatives.

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Abstract Number: 1512

Trajectory Analysis of Repeat Renal Biopsies Identified Previous Endocapillary Proliferation as Predictor of Damage and End Stage Renal Disease in Pure Membranous Lupus Nephritis

Andrea Fava[1], Avi Rosenberg[2], Serena Bagnasco[2], Paride Fenaroli[2], Jessica Li[1], Jose Monroy-Trujillo[2], Derek Fine[2] and Michelle Petri[3], [1]Johns Hopkins University, Baltimore, MD, [2]Johns Hopkins University, Baltimore, [3]Johns Hopkins University School of Medicine, Baltimore

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes III: Lupus Nephritis

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: Pure membranous (class V) lupus nephritis is considered a less aggressive phenotype, but renal fibrosis and chronic kidney disease may develop. Whether this chronic damage is related to previous inflammatory changes before the biopsy date has not been adequately studied.

Methods: All patients met the revised ACR and/or SLICC SLE classification criteria. We analyzed data from 220 patients with lupus nephritis (543 biopsies) with at least two renal biopsies obtained for clinical purposes. The median time between biopsies was 4 years [IQR 2-9 years]. Patients with pure membranous lupus nephritis on the second biopsy were observed for a median of 7.5 years [IQR 4-12 years]. New onset of end stage renal disease (ESRD) was defined estimated glomerular filtration rate (eGFR) < 15 ml/min/1.73m^2, initiation of dialysis, or renal transplantation. Histological chronic changes in pure class V lupus nephritis biopsies were scored by 2 nephropathologists using the NIH chronicity index and averaged when discordant.

Results: Lupus nephritis transitioned to a different class in 136/220 (62%) on repeat biopsy. Pure class V transitioned to proliferative lupus nephritis in 41.5% (**Figure 1A**). In patients with pure class V on the second biopsy, proliferative lupus nephritis was detected in 52% of the first biopsies (**Figure 1B)**. Surprisingly, the NIH chronicity index did not differ between class V vs. class III and IV (p=0.5) and it was numerically higher **(Figure 2A**). The chronicity index in repeat biopsies was higher than in first biopsies. In particular, patients with proliferative lupus nephritis in the first biopsy who transitioned to class V had numerically worse chronicity index than those with class V in the first biopsy

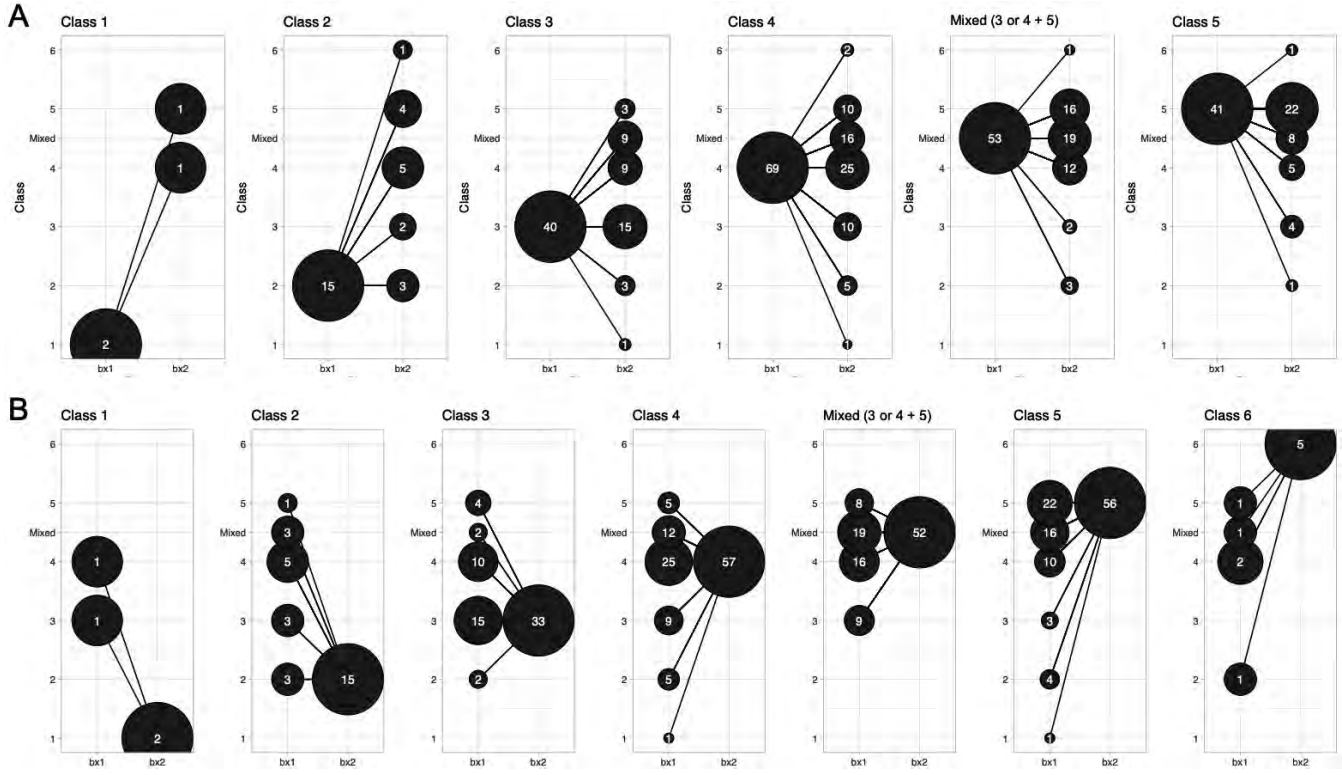

Figure 1. Transition across lupus nephritis classes in repeat renal biopsies. Change of ISN class from first (bx1) to second (bx2) biopsy according the class of the first (A) or the second biopsy (B). Numbers in the circles indicate the number of biopsies. The size of the circle indicates the proportion of biopsies within each ISN class for each plot.

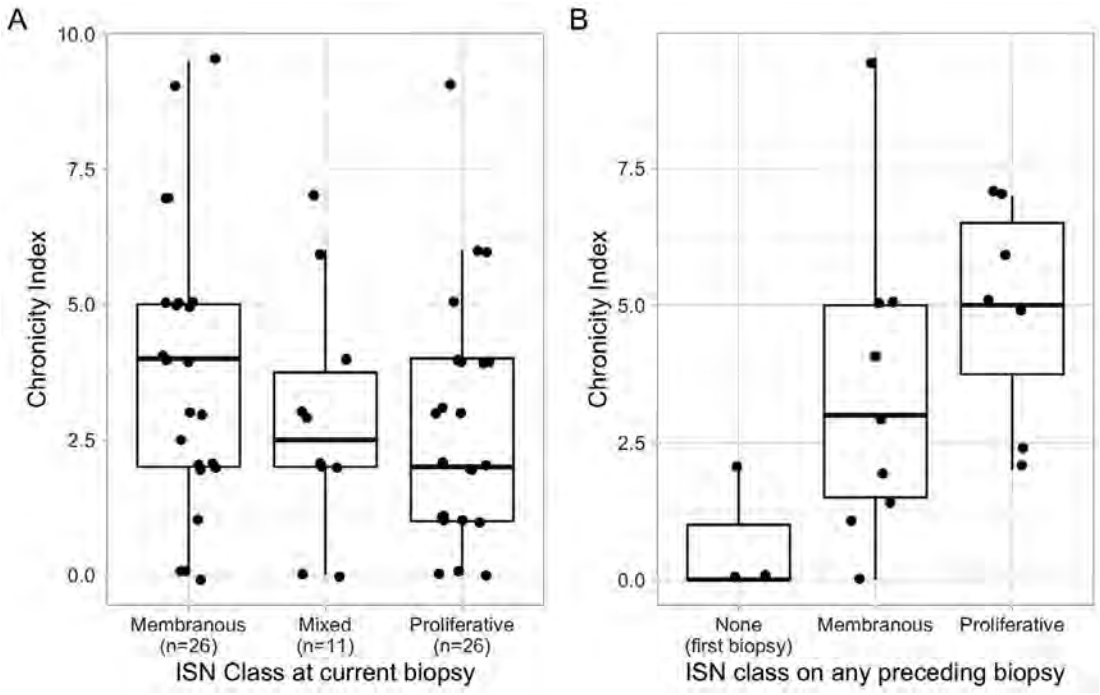

Figure 2. Chronic renal damage is observed in pure class V lupus nephritis and is associated with previous episodes of proliferative disease. (A) NIH chronicity index in the nephritis cohort. There was no statistically significant difference across groups. (B) NIH chronicity index in pure class V renal biopsies according to the class of the preceding renal biopsies.

(5 [3.75-6.5] vs. 3 [1.5-5], p=0.13) (**Figure 2B**). New onset ESRD was observed in 5/52 (9.6%) patients with pure class V. All 5 patients (100%) had proliferative lupus nephritis in the first biopsy (p=0.04) (**Figure 3**).

Conclusion: Lupus nephritis is a dynamic disease, with the separation of membranous and proliferative an artificial division based on a kidney biopsy. Non-proliferative lupus nephritis may be preceded by proliferative disease which is associated with risk of ESRD. Chronic damage, a known negative prognostic factor, is commonly observed in pure membranous nephritis and it is associated with previous proliferative disease. The management of membranous lupus nephritis should involve immunosuppression to address the high frequency of proliferative nephritis on repeat (or preceding) biopsies to proliferative disease and quantification of chronic damage should be pursued in all classes.

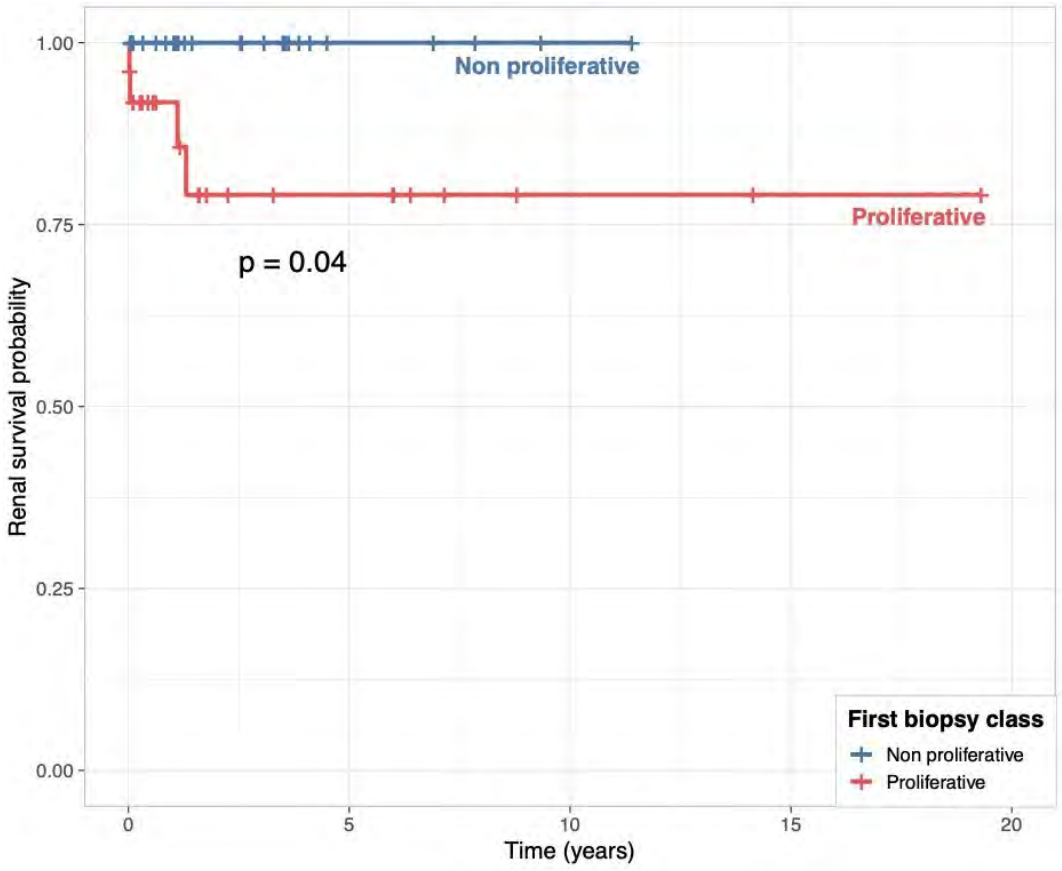

Figure 3. Renal survival of patients with pure class V lupus nephritis in a repeat renal biopsy according the histological class of the initial biopsy. P value was calculated using the log rank test.

Disclosure: A. Fava, None; **A. Rosenberg**, None; **S. Bagnasco**, None; **P. Fenaroli**, None; **J. Li**, None; **J. Monroy-Trujillo**, None; **D. Fine**, GSK, 5; **M. Petri**, AbbVie, 5, Amgen, 5, AstraZeneca, 2, 5, BMS, 5, Decision Resources, 5, GSK, 2, 5, INOVA, 5, IQVIA, 5, Janssen, 5, Eli Lilly, 2, 5, Merck EMD Serono, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5, Exagen, 2.

Abstract Number: 1513

Role of Platelet C4d in Thrombosis and Lupus Nephritis

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes III: Lupus Nephritis

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Disease activity	Estimated difference in each disease activity item (relative to a person's average) as a function of differences in a person's Platelet C4d levels (relative to that person's average Platelet C4d levels)	
	Mean difference (95% CI)	**P-value**
PGA	0.01 (-0.005, 0.03)	0.1661
Total SLEDAI	0.05 (-0.01, 0.10)	0.1197
Specific items		
C3 level	-0.12 (-0.65, 0.41)	0.6642
C4 level	-0.03 (-0.15, 0.09)	0.6469
Log anti-dsDNA	0.001 (-0.03, 0.03)	0.9413
Urine protein/cr ratio	0.022 (0.01, 0.03)	0.0005

Estimated difference in disease activity variables at each visit per 10 unit difference in between the patient's Platelet C4d at that visit and the person's average Platelet C4d.

Pc4d level categories	% of visits with pr/cr>=0.5
<5	12/201 (6.0%)
5-<10	8/77 (10.4%)
10-<20	8/56 (14.3%)
20-<30	15/79 (19.0%)

Pr/cr ratio were missing in 10 visits

Percentage of patient visits with urine protein/cr ≥ 0.5 g at each platelet C4d level.

Background/Purpose: The SLE thrombosis risk equation contains three components: lupus anticoagulant (dRVVT), low C3 and C4d bound to platelets (platelet C4d). We examined the role of platelet C4d in association with thrombosis and proteinuria.

Methods: A total of 150 patients, consented to the study, were enrolled with a maximum of 3 visits per patient (424 visits): baseline, 6 month follow up, and 12 month follow up. Platelet C4d was measured by flow cytometry and expressed as net mean Fluorescence intensity (MFI). An abnormal platelet C4d was defined as a net MFI >20. GEE models were used to assess the relationship between disease activity measures and platelet C4d, accounting for within patient correlations. Linear mixed effects model was used to evaluate the within-patient associations.

Results: This analysis included 150 patients: 86% were female; 34.7% were African-American; and 55.3% were Caucasian. The mean age at diagnosis was 30.7 years (SD=14.1 years). 206 visits had a platelet C4d net MFI< 5, 77 visits had a net MFI between 5 and 10, 59 visits were 10-< 20, 27 were 20-< 30, and 54 were 30 or above. Adjusting for age at visit, race, and sex, platelet C4d was associated with low complement (OR 3.65 (2.11, 6.32), p< 0.0001) and increased anti-dsDNA (OR 1.77 (1.16, 2.72), p=0.0083). In a comparison of intermittent or persistently positive vs normal platelet C4d, positive platelet C4d was associated with deep vein thrombosis (OR 6.14 (1.43, 26.31), p=0.0144), any venous thrombosis (OR 12.3 (2.48,61.53), p=0.0022), and any venous or arterial thrombosis (OR 5.54 (1.84, 16.66), p=0.0023). A "within patient" analysis was also done (Table 1), showing a significant increase in urine protein/cr (p=0.0005). The percentage of patient visits with urine protein/cr ≥ 0.5 g at each platelet C4d level is shown in Table 2.

Conclusion: Platelet C4d represents the importance of immunothrombosis in SLE: that thrombosis reflects cross-talk between coagulation, complement and platelets. In our between patient analyses, platelet C4d was associated with serologies (low complement and anti-dsDNA) and both arterial and venous thrombosis. In our within patient analyses, it was associated with proteinuria. The association with proteinuria is novel and may be one of the ways that serologies – which are more common in lupus nephritis – act to effect thrombosis risk and organ damage.

Disclosure: M. Petri, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmithKline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5; **J. Li**, None; **J. Conklin**, Exagen, 1, 2; **T. O'Malley**, Exagen, 1, 2; **J. Ligayon**, Exagen Diagnositics, 1, 2; **L. Wolover**, Exagen Diagnositics, 1, 2; **T. Dervieux**, Exagen, 1.

Abstract Number: 1514

The Impact of Renal Transplantation on Cardiovascular Events Among Patients with End-State Kidney Disease Due to Lupus Nephritis: A Nationwide Cohort Study

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SESSION INFORMATION
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Session Title: SLE – Diagnosis, Manifestations, & Outcomes III: Lupus Nephritis
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: A major complication of systemic lupus erythematosus (SLE) is the progression of lupus nephritis (LN) to end-stage kidney disease (ESKD). Both SLE and ESKD are associated with increased risks of cardiovascular disease (CVD). Renal transplantation improves survival among patients with LN-ESKD. We sought to assess the potential impact of renal transplantation on CVD events in LN-ESKD.

Methods: We identified all incident cases of ESKD due to SLE (ICD9 710.0) in the United States Renal Data System (USRDS) between 2000 and 2014. The USRDS captures nearly all patients with ESKD in the US and includes the cause of ESKD by ICD9 code as well as demographics, comorbidities, and dates of waitlist entry, transplantation and death including the cause of death. Hospitalizations are additionally captured under Medicare Part A. We restricted our study population to patients who were waitlisted for transplant to limit the potential bias of confounding by indication and required Medicare enrollment. To account for time-varying variables, we performed sequential cohort matching on the basis of age, sex, and time since initiation of dialysis.We sequentially matched patients on their transplant date (index date) 1:1 with comparators who remained active on the waitlist on that date. Follow-up began at the date of transplant or matching and ended at the time of death, end of Medicare coverage, three years following the index date, transplantation (control group only, at which point a participant would be matched and begin follow-up time in the transplant group), or January 1, 2015, whichever came first. The outcomes of interest were CVD events, including non-fatal and fatal myocardial infarctions (MI) and non-fatal and fatal cerebrovascular accidents (CVA). We determined CVD event rates in the groups that did and did not have transplants, accounting for competing risk of death, and calculated hazard ratios (HRs) using a stratified Cox proportional hazards model, additionally adjusting for race/ethnicity, time on waitlist, first ESKD treatment modality, ESKD-specific comorbidity score, Organ Procurement and Transplant Network region, and history of any organ transplant.

Results: We identified 1,250 patients who had a transplant and 1,250 matched comparators. These groups were well-balanced by age, sex, time since initiation of dialysis, and time since entry onto the waitlist (**Table 1**). Over mean 2.26 years of follow up, 24 patients who had a transplant and 68 who did not have a transplant had a CVD event,

Baseline Characteristics	Transplanted	Not Transplanted
N	1250	1250
Age* (years, mean)	38	38
Female (%)	88	88
BMI (mean, kg/m^2)	26	27
Race (%)		
White	46	35
African American	44	55
Asian	5	5
Other	5	4
Hispanic (%)	23	22
OPTN Region (%)		
1 (CT, ME, MA, NH, RI, Eastern VT)	3	3
2 (DE, DC, MD, NJ, PA, WV, Northern VA)	11	9
3 (AL, AR, FL, GA, LA, MS)	17	19
4 (OK, TX)	13	10
5 (AZ, CA, NV, NM, UT)	14	16
6 (AK, HI, ID, MT, OR, WA)	3	3
7 (IL, MN, ND, SD, WI)	7	8
8 (CO, IA, KA, MO, NE, WY	5	5
9 (NY, Western VT)	8	9
10 (IN, MI, OH)	7	8
11 (KY, NC, SC, TN, VA)	13	12
Prior Organ Transplant (%)	< 1	< 1
Comorbidity Score*	7.0 (4.7)	7.5 (5.1)
Time on dialysis (years, mean [SD])*	2.9 (2.1)	2.9 (2.1)
Time on waitlist (years, mean [SD])*	2.1 (1.8)	1.8 (1.7)
First Modality (%)		
Hemodialysis	83	85
Peritoneal Dialysis	17	15

Table 1. Characteristics of Patients with End-Stage Kidney Disease Due to Lupus Nephritis, Transplanted and Matched Comparators

yielding CVD event rates of 7.2 per 1000 person-years and 29.6 per 1000 person-years, respectively (HR, 0.56 [95% CI, 0.51-0.61]) (**Table 2**). After adjustment for covariates, the HR was 0.55 (95% CI, 0.50- 0.60). The findings were similar within subgroups by age, sex, and African American race. The adjusted HRs were 0.54 (95% CI, 0.50-0.59) for MI and 0.54 (95% CI, 0.50-0.59) for CVA.

	Total Follow-up, person-years	Events, n	Incident rate* (95% CI)	Unadjusted HR (95% CI)	Fully-Adjusted HR† (95% CI)
Overall CV Events	5654	92	16.3 (12.9-19.6)	-	-
Transplanted	3355	24	7.2 (4.3-10.0)	0.56 (0.51-0.61)	0.55 (0.50-0.60)
Not Transplanted	2300	68	29.6 (22.5-36.6)	1.0	1.0
Age at ESKD Onset					
< 40 Years	3192	41	12.8 (8.9-16.8)	-	-
Transplanted	1904	12	6.3 (2.7-9.9)	0.54 (0.49-0.61)	0.53 (0.48-0.60)
Not Transplanted	1288	29	22.5 (14.3-30.7)	1.0	1.0
≥ 40 Years	2407	50	20.8 (15.0-26.5)	-	-
Transplanted	1417	12	8.5 (3.7-13.3)	0.57 (0.50-0.65)	0.56 (0.49-0.63)
Not Transplanted	990	38	38.4 (26.2-50.6)	1.0	1.0
Sex					
Female	4973	82	16.5 (12.9-20.1)	-	-
Transplanted	2936	21	7.2 (4.1-10.2)	0.57 (0.52-0.62)	0.56 (0.52-0.62)
Not Transplanted	2038	61	29.9 (22.4-37.4)	1.0	1.0
Race‡					
African American	1459	31	21.2 (13.8-28.7)	-	-
Transplanted	856	11	12.9 (5.3-20.4)	0.59 (0.50-0.70)	0.58 (0.49-0.69)
Not Transplanted	603	20	33.2 (18.6-47.7)	1.0	1.0
Stroke	5660	65	11.5 (8.7-14.3)	-	-
Transplanted	3358	21	6.3 (3.6-8.9)	0.55 (0.51-0.60)	0.54 (0.50-0.59)
Not Transplanted	2303	44	19.1 (13.5-24.8)	1.0	1.0
Myocardial Infarction	5682	30	5.3 (3.4-7.2)	-	-
Transplanted	3365	<10	-	0.55 (0.51-0.60)	0.54 (0.50-0.59)
Not Transplanted	2317	27	11.7 (7.3-16.0)	1.0	1.0

HR, hazard ratio; ESKD, end-stage kidney disease
*Per 1,000 Person Years; †Additionally adjusted for race/ethnicity, mean time on waitlist, first ESKD treatment method, comorbidity score, Organ Procurement and Transplant Network region, and history of organ transplant; ‡Numbers of events are too few to display among non-African American and Hispanic patient subgroups (not shown) and for myocardial infarction.

Table 2. Cardiovascular Events According to Transplant Status Among Matched Patients with End-Stage Kidney Disease Due to Lupus Nephritis

Conclusion: In this nationwide study of ESKD due to LN, renal transplantation was associated with a reduced risk of CVD events, including MI and CVA. Our findings highlight the importance of identifying barriers to transplantation in this population, as improved access could reduce CVD morbidity and mortality.

Disclosure: A. Jorge, None; **X. Fu**, None; **Y. Zhang**, None; **H. Choi**, AstraZeneca, 2, Takeda, 5, Selecta, 5, GlaxoSmithKline, 5, Horizon, 5; **Z. Wallace**, None.

Abstract Number: 1515

Renal Responder Status and Associated Clinical Variables in the Lupus Accelerating Medicines Partnership Cohort

Philip Carlucci[1], Andrea Fava[2], Kristina Deonaraine[1], Jessica Li[3], David Wofsy[4], Judith James[5], Chaim Putterman[6], Betty Diamond[7], Derek Fine[8], Jose Monroy-Trujillo[8], Kristin Haag[8], William Apruzzese[9], H. Michael Belmont[10], Peter Izmirly[11], Sean Connery[12], Fernanda Payan-Schober[12], Richard Furie[13], Celine Berthier[14], Maria Dall'Era[15], Kerry Cho[16], Diane Kamen[17], Kenneth Kalunian[18], The Accelerating Medicines Partnership in SLE Network[19], Michelle Petri[20] and Jill Buyon[21], [1]New York University School of Medicine, New York, [2]Johns Hopkins, Baltimore, [3]Johns Hopkins University, Baltimore, MD, [4]University of California San Francisco, San Francisco, CA, [5]Oklahoma Medical Research Foundation, Oklahoma City, [6]Albert Einstein College of Medicine, Bronx, NY, [7]Northwell Health, Hartford, [8]Johns Hopkins University, Baltimore, [9]., Boston, [10]NYU School of Medicine, New York, NY, [11]Department of Medicine, New York University School of Medicine, New York, NY, [12]Texas Tech University Health Sciences Center, Lubbock, [13]Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, [14]University of Michigan, Ann Arbor, [15]Division of Rheumatology, University of California, San Francisco, CA, [16]University of California San Francisco, San Francisco, [17]Medical University of South Carolina, Charleston, SC, [18]School of Health Sciences, University of California, La Jolla, [19]Multiple Institutions, Multiple Cities, [20]Johns Hopkins University School of Medicine, Baltimore, [21]Department of Medicine, NYU School of Medicine, New York, NY

SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes III: Lupus Nephritis

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: Poor therapeutic response rates contribute to the increased morbidity and mortality associated with lupus nephritis. Early identification of patients likely to respond is crucial as delays in treatment associate with worse outcomes. This study evaluated response using prospectively collected data obtained from the multi-ethnic/racial, multi-center Accelerating Medicines Partnership (AMP) lupus nephritis cohort. This cohort represents a real-world clinical setting using provider chosen standard of care and uniform collection of data.

Medications	Nonresponder at 26 weeks N=64	Partial Responder at 26 weeks N=33	Complete Responder at 26 weeks N=34	3-way p-value	2-way p-value
Hydroxychloroquine, N (%)	54 (85.7)	27 (81.8)	26 (76.5)	0.521	0.388
Azathioprine, N (%)	7 (11.1)	0 (0.0)	1 (2.9)	0.065	0.313
Tacrolimus, N (%)	1 (1.6)	1 (3.0)	1 (2.9)	0.868	1.000
Mycophenolate Mofetil, N (%)	31 (49.2)	22 (66.7)	26 (76.5)	**0.023**	**0.017**
Tacrolimus + Mycophenolate mofetil, N (%)	7 (10.9)	2 (6.1)	2 (5.9)	0.591	0.647
Rituxan, N (%)	1 (1.6)	1 (3.0)	1 (2.9)	0.868	1.000
Cyclophosphamide, N (%)	7 (11.1)	3 (9.1)	3 (8.8)	0.919	0.997
Rituxan + Cyclophosphamide, N (%)	1 (1.6)	0 (0.0)	0 (0.0)	0.59	1.000
Pulse steroids, N (%)	0 (0%)	0 (0%)	0 (0%)	.	.
Prednisone, N (%)	34 (54.0)	24 (72.7)	27 (79.4)	**0.025**	**0.024**

Table 1. Medications received at 12 weeks by responder status. 2-way p-values compare nonresponders to complete responders

Baseline Characteristics	Nonresponder N=67	Partial Responder N=33	Complete Responder N=36	3-way p-value	2-way p-value
SLEDAI, median [IQR]	10.00 [8.00, 13.00]	12.00 [10.00, 18.00]	12.00 [8.00, 16.00]	**0.021**	0.112
Extrarenal SLEDAI*, mean (SD)	1.76 (2.42)	2.06 (2.38)	3.33 (6.98)	0.18	0.098
SLICC, mean (SD)	8.32 (2.35) N=63	8.42 (1.88) N=31	8.83 (2.29)	0.533	0.291
Anti-dsDNA positive, N (%)	41 (62.1) N=66	26 (81.2) N=32	30 (85.7) N=35	**0.019**	**0.025**
C3 mg/dL, median [IQR]	72.40 [48.75, 107.75] N=66	66.00 [43.00, 90.00]	60.50 [46.75, 79.50]	0.442	0.238
Low C3, N (%)	40 (60.6)	22 (66.7)	26 (72.2)	0.49	0.339
C4 mg/dL, median [IQR]	12.41 [8.00, 22.80] N=66	11.00 [8.00, 19.00]	11.50 [6.00, 15.97]	0.338	0.15
Low C4, N (%)	33 (50.0)	19 (57.6)	25 (69.4)	0.165	0.092
Creatinine mg/dL, median [IQR]	0.99 [0.80, 1.40] N=65	0.90 [0.66, 1.48] N=31	0.83 [0.70, 1.10]	0.118	**0.033**
Creatinine, N (%)					
High	25 (38.5)	11 (35.5)	6 (16.7)	0.087	0.075
Low	3 (4.6)	4 (12.9)	2 (5.6)		
UPCR, mean (SD)	3.24 (2.68)	5.05 (2.93)	2.30 (1.31)	**<0.001**	**0.051**
Hemoglobin g/dL, median [IQR]	10.60 [8.85, 11.85]	9.90 [9.00, 11.10]	10.20 [9.25, 12.20]	0.396	0.945
Low Hemoglobin, N (%)	48 (71.6)	27 (81.8)	25 (69.4)	0.45	0.995
WBC $10^3/mm^3$, median [IQR]	4.72 [3.73, 6.80]	6.40 [4.10, 8.88]	6.11 [4.38, 7.72]	0.06	0.106
WBC, N (%)				0.087	0.087
High	2 (3.0)	4 (12.1)	2 (5.6)		
Low	25 (37.3)	8 (24.2)	6 (16.7)		
Lymphocyte count $10^3/mm^3$, median [IQR]	1.10 [0.60, 1.60] N=66	0.90 [0.70, 1.40] N=31	1.06 [0.60, 1.56] N=34	0.517	0.692
Low Lymphocyte, N (%)	32 (48.5)	19 (61.3)	18 (52.9)	0.499	0.833
Platelet count $10^3/mm^3$, mean (SD)	234.79 (75.74)	279.24 (104.63)	245.33 (94.42)	0.063	0.539
Low Platelet, N (%)	9 (13.4)	3 (9.1)	5 (13.9)	0.792	1.000
Albumin g/dL, mean (SD)	3.07 (0.77) N=64	2.88 (0.72) N=28	3.24 (0.64) N=35	0.155	0.291
Low Albumin, N (%)	39 (60.9)	24 (82.8)	21 (60.0)	0.087	1.000

Table 2. Baseline characteristics by response status at 26 weeks. 2-way p-values compare nonresponders to complete responders. *Excludes points for low complement, anti-dsDNA positivity, hematuria, pyuria, proteinuria, and casts

Methods: This study included SLE patients based on ACR or SLICC classification enrolled in AMP who met the following criteria: urine protein-creatine ratio (UPCR) > 1 at entry, and histologic biopsy Class III, IV, V, or mixed. Patients were followed at 3, 12, 26 and 52 wks with demographics, history, laboratory results, disease activity, and medica-

Laboratory measure	Nonresponder N=67	Partial Responder N=33	Complete Responder N=36	3-way p-value	2-way p-value
C3*	16.00 [1.00, 27.60] N=37	29.00 [9.75, 56.25] N=22	31.50 [5.68, 39.75] N=24	**0.03**	**0.042**
C4*	3.00 [-0.90, 6.00] N=33	8.00 [5.48, 12.00] N=19	5.50 [3.38, 10.00] N=24	**0.014**	**0.028**
Creatinine	0.01 [-0.10, 0.14] N=60	-0.10 [-0.27, 0.04] N=31	-0.03 [-0.19, 0.08] N=34	0.142	0.171
UPCR	-0.15 [-0.91, 1.01] N=62	-1.97 [-3.41, -0.83] N=28	-1.56 [-1.94, -0.92] N=33	**<0.001**	**<0.001**
Hemoglobin	0.15 [-0.60, 1.15] N=62	0.60 [-0.30, 2.00]	1.60 [-0.10, 2.10] N=33	**0.03**	**0.01**
WBC	-0.04 [-1.30, 1.62] N=62	1.10 [-1.30, 2.50]	1.36 [-0.99, 3.61] N=33	0.286	0.13
Lymphocyte	-0.13 [-0.42, 0.20] N=55	0.34 [-0.08, 0.62] N=30	0.16 [-0.17, 0.60] N=31	**0.002**	**0.015**
Platelet	24.50 [-22.25, 60.50] N=62	14.00 [-20.00, 48.00]	25.00 [-11.00, 67.00] N=33	0.801	0.555
Albumin	0.20 [-0.10, 0.45] N=59	0.50 [0.27, 0.80] N=28	0.45 [0.20, 0.90] N=30	**0.001**	**0.006**

Table 3. Change in laboratory values at 12 weeks compared to baseline by response status. Data are presented as median [IQR], 2-way p-values compare nonresponders to complete responders. *Includes only patients who had low complement at baseline.

tions recorded at each visit. Follow up data were available for 136 patients at 26 wks and 118 at 52 wks. Complete response was defined as a reduction in UPCR to < .5, a normal serum creatinine or no greater than 125% of baseline, and < 10 mg prednisone at time of response assessment. Patients were partial responders if UPCR decreased > 50% but remained >.5 and nonresponders if < 50% reduction in UPCR and/or did not meet the other response criteria.

Results: Medications were reported at 12 wks (Table 1). The complete response rate was 26% at both 26 and 52 wks. For patients undergoing a first biopsy, the rates were 37% and 40% and for those with repeat biopsies, the rates were lower at 21% and 19% respectively (p=0.042 at 26 wks; p=0.015 at 52 wks). The complete response at 26 wks was generally sustained with only 4 of 27 patients experiencing a relapse at 52 wks. At 26 wks, patients with membranous histology were less likely to be complete responders than patients with proliferative histology.

This trend was observed regardless of biopsy number and persisted for response status at 52 wks. Although baseline activity score did not predict responder status, complete responders had a significantly lower chronicity index than nonresponders (mean + SD, 2.26 + 2.22 vs 3.83 + 2.57, p=0.016) at 26 wks with similar results at 52 wks. Responder status at 26 and 52 wks whether first or repeat biopsy was independent of extrarenal disease at entry (Table 2). Complete responder status was associated with positive anti-dsDNA serology at baseline for repeat biopsy patients. Complete responders had a greater change in C3, hemoglobin, lymphocyte count, albumin, and UPCR at 12 wks compared to baseline values than nonresponders (Table 3). Similar trends were observed when considering response status at 52 wks.

Conclusion: The low complete response rates reported in the AMP cohort are consistent with findings in blinded controlled trials of standard-of-care therapies and support the critical need for new therapeutics particularly in patients undergoing repeat biopsies and those with increased chronicity.

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Abstract Number: 1516

The Value of Renal Biopsy at Lower Levels of Proteinuria in Patients Enrolled in the Lupus Accelerating Medicines Partnership

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes III: Lupus Nephritis

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: Lupus nephritis continues to be the complication with the highest standardized mortality ratio in Systemic Lupus Erythematosus (SLE), and a late diagnosis associates with worse outcomes. Clinicians traditionally rely on proteinuria to drive decisions regarding renal biopsy and subsequent management. Since threshold levels for such determinations are variable but critically important, this study leveraged the well-phenotyped multi-center multi- racial Accelerating Medicines Partnership (AMP) lupus nephritis cohort, to address whether urine protein to creatinine ratios (UPCR) between .5 and 1 differ from higher ratios with regard to clinical, serologic and histologic variables.

Methods: 239 patients fulfilling ACR or SLICC criteria for SLE with a random or 24 hr uPCR > or = .5 and histologic biopsy Class III, IV, V, or mixed were consecutively enrolled in AMP at the time of renal biopsy and demographics, clinical history, medications, disease activity as assessed by the hybrid SELENA-SLEDAI were recorded. Patients with biopsy Classes I, II and VI were ineligible. Patients were followed at 3, 12, 26 and 52 weeks.

Results: At baseline, 38 patients had a UPCR < 1 (A), 113 had a UPCR 1-3 (B) , and 88 had a UPCR > 3 (C). There were 14 additional patients with UPCR < 1, and 11 patients with UPCR > 1 who had biopsy class I or II. In group A, there were significantly more male patients (44% A; 23% B; 26% C, p=0.012) with no differences in age, race or ethnicity. Neither the SLEDAI nor serologic parameters (anti-dsDNA, C3, or C4) distinguished among the groups. Those in group C had a significantly increased creatinine and decreased hemoglobin and albumin compared to the other two groups (Table 1). Patients in group A trended toward having an increased frequency of proliferative histology (Table 2). This trend was not observed when considering patients for whom this was their first biopsy, but was significant for repeat biopsy patients (56% A; 41% B; 24% C, p=0.03). The activity index was independent of UPCR regardless of biopsy number. However, those in group C had a significantly higher chronicity index than those with lower UPCR. This correlation was shown for patients with a repeat biopsy (r=0.2299, p=0.003) but not first biopsy patients (r=0.0891, p=0.45). Although medications did not differ at baseline among the groups, at 12 weeks, for each group significantly more patients were taking Mycophenolate Mofetil than at the time of biopsy (Table 3).

Baseline Characteristics	Group A UPCR < 1 N=38	Group B UPCR 1-3 N=113	Group C UPCR > 3 N=88	3-way p-value	A vs B p-value	A vs C p-value
SLEDAI, median [IQR]	9.00 [6.00, 12.75]	10.00 [8.00, 16.00]	12.00 [6.75, 14.50]	0.247	0.132	0.116
SLICC, mean (SD)	7.75 (2.64) N=36	8.33 (2.27) N=109	8.04 (2.19) N=81	0.383	0.205	0.541
Anti-DNA positive, N (%)	28 (77.8) N=36	86 (78.2) N=110	52 (64.2) N=81	0.078	1.00	0.214
Low C3, N (%)	24 (64.9%) N=37	69 (62.7) N=110	54 (62.1) N=86	0.792	0.971	0.927
Low C4, N (%)	16 (43.2) N=37	60 (54.5) N=110	48 (55.2) N=87	0.604	0.317	0.308
Anti-Sm positive, N (%)	22 (73.3) N=30	47 (50.0) N=94	43 (56.6) N=76	0.080	**0.042**	0.169
Creatinine mg/dL, median [IQR]	0.83 [0.76, 1.00]	0.88 [0.70, 1.14] N=110	1.12 [0.74, 1.80] N=85	**0.005**	0.963	**0.022**
Albumin g/dL, mean (SD)	3.67 (0.52) N=36	3.43 (0.55) N=105	2.75 (0.69) N=83	**<0.001**	**0.022**	**<0.001**
Hemoglobin g/dL, median [IQR]	11.30 [9.93, 12.75]	10.75 [9.57, 12.22] N=112	10.00 [8.80, 11.60] N=87	**0.012**	0.358	**0.011**
Pyuria, N (%)	9 (23.7)	36 (31.9)	33 (37.5)	0.307	0.454	0.192
Hematuria, N (%)	10 (26.3)	39 (34.5)	34 (38.6)	0.410	0.463	0.259
Arthritis, N (%)	5 (13.2)	12 (10.6)	16 (18.2)	0.302	0.895	0.664
Rash, N (%)	5 (13.2)	16 (14.2)	17 (19.3)	0.538	1.000	0.562
Alopecia, N (%)	5 (13.2)	22 (19.5)	12 (13.6)	0.458	0.526	1.000
Pleurisy, N (%)	1 (2.6)	6 (5.3)	5 (5.7)	0.758	0.816	0.778
Leukopenia, N (%)	7 (18.4)	19 (16.8)	11 (12.5)	0.606	1.000	0.552
Mucosal Ulcer, N (%)	1 (2.6)	5 (4.4)	6 (6.8)	0.567	0.992	0.605
Casts, N (%)	0 (0.0)	2 (1.8)	8 (9.1)	**0.014**	0.996	0.128

Table 1. Baseline lupus activity by UPCR group.

Biopsy Characteristics	Group A UPCR < 1 N=38	Group B UPCR 1-3 N=113	Group C UPCR > 3 N=88	3-way p-value	A vs B p-value	A vs C p-value
First Biopsy, N (%)	20 (52.6)	47 (41.6)	33 (37.5)	0.286	0.319	0.167
Activity, mean (SD)	6.29 (3.12)	5.49 (4.26)	6.72 (5.49)	0.292	0.428	0.733
Chronicity, mean (SD)	2.57 (1.86)	2.66 (2.33)	3.91 (2.75)	**0.007**	0.869	**0.042**
Biopsy Class, N (%)				0.337	0.709	0.232
Membranous	9 (23.7)	34 (30.1)	25 (28.4)	0.751	0.449	0.583
Mixed	10 (26.3)	30 (26.5)	33 (37.5)	0.204	0.978	0.224
Proliferative	19 (50.0)	49 (43.4)	30 (34.1)	0.195	0.477	0.093

Table 2. Biopsy characteristics by UPCR group.

Conclusion: A significant proportion of both first and recurrent biopsies in patients with a UPCR < 1 have proliferative histology and accompanying activity scores similar to that of patients with nephrotic range proteinuria. These results support renal biopsy at thresholds lower than a UPCR of 1 since histologic findings can inform therapeutic decisions.

Medications	A UPCR < 1 at baseline			B UPCR 1-3 at baseline			C UPCR > 3 at baseline		
	Baseline	12 weeks	p-value	Baseline	12 weeks	p-value	Baseline	12 weeks	p-value
	N=36			N=94			N=69		
Hydroxychloroquine, N (%)	31 (86%)	32 (89%)	0.56	83 (88%)	81 (86%)	0.75	56 (81%)	56 (81%)	1.0
Azathioprine, N (%)	4 (11%)	3 (8%)	0.32	14 (15%)	5 (5%)	**0.01**	5 (7%)	3 (4%)	0.69
Cyclophosphamide, N (%)	0 (0%)	0 (0%)	*	1 (1%)	10 (11%)	**0.004**	0 (0%)	5 (7%)	0.063
Tacrolimus, N (%)	1 (3%)	1 (3%)	1.0	5 (5%)	10 (11%)	0.18	7 (10%)	8 (12%)	1.0
Mycophenolate Mofetil, N (%)	17 (47%)	28 (78%)	**0.003**	49 (52%)	64 (68%)	**0.017**	35 (51%)	51 (74%)	**0.003**
Rituximab, N (%)	0 (0%)	1 (3%)	1.0	0 (0%)	3 (3%)	0.25	1 (1%)	2 (3%)	1.0
Prednisone, N (%)	22 (61%)	25 (69%)	0.38	54 (57%)	62 (66%)	0.077	39 (57%)	42 (61%)	0.61
Pulse steroids, N (%)	1 (3%)	0 (0%)	1.0	3 (3%)	0 (0%)	0.25	5 (7%)	0 (0%)	0.063

Table 3: Comparison of medications at baseline and 12 weeks for each UPCR group

Disclosure: P. Carlucci, None; **K. Deonaraine**, None; **A. Fava**, None; **J. Li**, None; **D. Wofsy**, GlaxoSmithKline, 9, Novartis, 9, Principia, 5; **J. James**, None; **C. Putterman**, Equillium, 1, 2; **B. Diamond**, None; **D. Fine**, GSK, 5; **J. Monroy-Trujillo**, None; **K. Haag**, None; **W. Apruzzese**, None; **H. Belmont**, Exagen, 5; **P. Izmirly**, GSK, 5; **S. Connery**, None; **F. Payan-Schober**, None; **R. Furie**, AstraZeneca/MedImmune, 2, 5; **C. Berthier**, None; **M. Dall'Era**, Janssen, 5, AstraZeneca, 5; **K. Cho**, None; **D. Kamen**, None; **K. Kalunian**, AstraZeneca, 2, 5, AbbVie, 2, 5, Amgen, 2, 5, Biogen, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, Equillium, 2, 5, Gilead Sciences, Inc., 2, 5, Genentech, 2, 5, ILTOO, 2, 5, Janssen, 2, 5, Lupus Research Alliance, 2, 5, Nektar, 2, 5, Pfizer, 2, 5, Roche, 2, 5, Sanford Consortium, 2, 5, Vielabio, 2, 5; **T. Accelerating Medicines Partnership in SLE Network**, None; **M. Petri**, AbbVie, 5, Amgen, 5, AstraZeneca, 2, 5, BMS, 5, Decision Resources, 5, GSK, 2, 5, INOVA, 5, IQVIA, 5, Janssen, 5, Eli Lilly, 2, 5, Merck EMD Serono, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5, Exagen, 2; **J. Buyon**, None.

Abstract Number: 1517

Metabolic Regulation of Type 3 Innate Lymphoid Cells by Intestinal Bacteria-Derived Indoles in Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Intestinal microbial dysbiosis, intestinal inflammation, and Th17 immunity are all linked to the pathophysiology of ankylosing spondylitis (AS); however, the mechanisms linking them remain unknown. Using three

unbiased approaches, we hypothesized that microbial dysbiosis in AS results in altered bacterial metabolites that expand IL-17-producing immune cells.

Methods: Healthy controls (HC, N=23) and patients with AS (N=24) were recruited while undergoing standard-of-care colonoscopy. Thirty distal colon biopsies and rectal swabs were obtained from each subject. Four biopsies were submitted for metabolomics screening via LC-MS while the remaining were homogenized and analyzed by single cell RNA sequencing (scRNA-seq, 2 subjects per group) and flow cytometry (remaining) to validate findings. Bacterial DNA was extracted from the rectal swabs, underwent shotgun sequencing, and analyzed using the HumanN2 software suite.

Results: ScRNA-seq identified a unique population in AS versus HC that transcriptionally segregated with T cells but lacked traditional T cell markers. Flow cytometry validated a significant expansion of type 3 innate lymphoid cells (ILC3s) in the intestinal tissue from patients with AS. By LC-MS, multiple metabolites within the tryptophan pathway were found to be significantly increased in AS vs HC, including indole-3-acetate (relative tissue concentration 153,583±156,338 vs 36,124±29,764, $p< 0.0003$) and indole-3-acetaldehyde (relative tissue concentration 2,615,095±1,890,967 vs 1,068,847±1,158,350, $p< 0.0005$), which are bacteria-specific products of tryptophan metabolism. Metagenomic analysis of the bacterial populations in AS identified altered metabolic pathways involving amino acid synthesis/degradation. In particular, there was a predilection towards tryptophan synthesis in HC while other tryptophan metabolism pathways were altered in AS.

Conclusion: In this study we identified altered tryptophan metabolism with a corresponding increase in ILC3s in intestinal tissue from patients with AS, which may link intestinal pathology to Th17 immunity in AS. Future studies will focus on the mechanistic pathways between tryptophan metabolism and ILC3 development.

Disclosure: A. Berlinberg, None; **A. Lefferts**, None; **E. Regner**, None; **A. Stahly**, None; **K. Kuhn**, None.

Abstract Number: 1518

The Role for Neutrophils in the Early Phases of Enthesitis in Spondyloarthritis

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science

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Session Time: 5:00PM–5:50PM

Background/Purpose: Neutrophils are present in the early phases of spondyloarthritis (SpA)-associated uveitis, skin and intestinal disease, but their role in enthesitis remains unknown. We investigated the role of neutrophils in the experimental SKG mouse model and in human axial enthesis tissue.

Methods: SKG mice have been shown to manifest multiple features of SpA. Arthritis in 9-week old female SKG mice was synchronized via intraperitoneal injections of curdlan and peripheral arthritis was scored weekly. Histology of ankles and spine were performed at serial time points. Formalin-fixed, paraffin-embedded (FFPE) tissue samples from entheseal sites around ankles and proximal tail vertebrae were obtained 2-3 weeks after curdlan injection (representing early inflammation) and subjected to laser capture microscopy. Whole transcriptome analysis was carried out using Affymetrix gene array MTA 1.0 and data was analyzed via IPA. Immunohistochemical staining for S100A8, a neutrophil product, and for MPO, a neutrophil marker, were performed at both sites. In conjunction with murine experimental work, normal human spinous process entheses were obtained from patients undergoing spinal decompression or thoracic or lumbar scoliosis surgery. IHC for MPO was performed on human FFPE enthesis to confirm the presence of neutrophils. Isolated neutrophils from peri-entheseal bone were stimulated with the fungal adjuvant zymosan and IFNγ and supernatants were probed for IL-23 secretion by ELISA.

Results: SKG mice developed early inflammation at enthesial sites around ankles and proximal tail vertebrae that included many neutrophils. The highest expression of transcripts arising from neutrophils included the alarmins S100A8 and S100A9 (calprotectin) and IL-23-associated genes, identified in both peripheral and axial enthesitis. In normal human axial enthesis, occasional neutrophils were evident. Upon fungal stimulation in vitro, these produced IL-23 protein, while isolated human entheseal fibroblasts stimulated with the fungal adjuvant mannan produced chemokines including IL-8, an important in the recruitment of neutrophils.

Conclusion: Neutrophil genes and pathways (including S100A8/9, cathepsin S, clec4d, clec7a) are upregulated early in the inflammatory infiltrate at entheseal sites. Neutrophils obtained from human entheses can be induced to produce IL-23 and may be an important early source of this cytokine that is critical for early SpA pathogenesis.

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Abstract Number: 1519

Interleukin-17D, a Cytokine Derived from Stromal Cells, Attenuates Joint Inflammation

Sijia Chen[1], Catherine Manning[2], Melissa van Tok[3], Yukiko Maeda[4], Daniel Montoro[5], Jung-Min Kim[6], Jeroen den Dunnen[3], Nataliya Yeremenko[3], Jae-Hyuck Shim[4], Dominique Baeten[7] and Ellen Gravallese[8], [1]Brigham and Women's Hospital, Boston, [2]Brigham and Women's Hospital, Boston, [3]Amsterdam University Medical Centers, Amsterdam, Netherlands, [4]University of Massachusetts Medical School, worcester, MA, [5]Broad Institute of Massachusetts Institute of Technology and Harvard, Boston, [6]University of Massachusetts Medical School, Worcester, [7]UCB Pharma / Amsterdam University Medical Centers, Amsterdam, Netherlands, [8]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
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Background/Purpose: Interleukin(IL)-17D is a little recognized member of the IL-17 family of cytokines. While the activities of IL-17A and IL-17F in the pathogenesis of spondyloarthritis (SpA) are established, a role for IL-17D in SpA and tissue inflammation has not yet been demonstrated.

Methods: In order to identify the cell types that express IL-17D in SpA synovial tissue and in primary human cells, we performed RNA sequencing, qPCR and IF analyses. We isolated fibroblast-like synoviocytes (FLS) from inflamed SpA synovial tissues, and stimulated cultured FLS with cytokines or subjected FLS to osteogenic differentiation. To determine a potential role for IL-17D in bone, femurs from *il17d*$^{-/-}$ mice were assessed by micro-computed tomography analysis. Serum transfer arthritis (STA) was also induced in *il17d*$^{-/-}$ mice and we performed subsequent Luminex assays to assess circulating cytokine expression at peak inflammation.

Results: In SpA inflamed synovial tissues, we demonstrate that *IL-17D* mRNA is more highly expressed than any other IL-17 family member, and that IL-17D is expressed by FLS that stain positive for markers of multipotent mesenchymal stromal cells (MSCs). *In vitro,* FLS express *IL-17D* at baseline. Osteogenic differentiation upregulates *IL-17D* mRNA in FLS when differentiated to osteoblast-like cells. *In vivo*, cells with the morphologic appearance of osteoblasts in bone sections also express IL-17D. However, *Il17d*$^{-/-}$ mice fail to demonstrate a bone phenotype, suggesting that IL-17D deletion does not impact bone homeostasis. Importantly, there is an inverse correlation between IL-17D expression and inflammation *in vitro and in vivo.* Anti-IL-17A treatment in SpA patients decreases synovial inflammation, and correlates with an increase in synovial *IL-17D* mRNA expression. Additionally, *Il17d*$^{-/-}$ mice demonstrate a more severe arthritis than littermate controls, and show elevated levels of pro-inflammatory cytokines at peak inflammation in STA, including TNFα, MCP-1 and MIP-1α.

Conclusion: These data demonstrate that IL-17D is the most highly-expressed IL-17 family member in inflamed SpA synovium. We localized IL-17D expression to stromal cells, including FLS. Furthermore, *IL-17D* expression is downregulated during human and experimental SpA inflammation, and evidence from STA indicates that this cytokine may exert an anti-inflammatory effect on joint inflammation.

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Abstract Number: 1520

Characterisation of Rheumatoid and Psoriatic Arthritis Synovial Fibroblasts

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SESSION INFORMATION
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Session Type: Abstract Session
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Background/Purpose: The synovial inflammation observed in Rheumatoid Arthritis (RA) and Psoriatic Arthritis (PsA) is characterised by synovial fibroblast hyperplasia, leukocyte infiltration, neoangiogenesis and hypoxia. These features cause the inflamed synovium to adopt a tumour-like phenotype which facilitates the invasion of adjacent cartilage. Pathogenic differences between RA and PsA are observed in the vascular morphology pattern, synovial tissue (ST) cellular infiltrates and lining-layer thickness. While synovial fibroblasts (FLS) have generally been considered as

a heterogeneous population of cells with specific functions, recent studies have identified distinct FLS subsets which differentially contribute to disease pathogenesis. $CD34^{-}THY1^{+}$ FLS are increased in RA synovial sublining compared to that of OA, and are reported to sustain synovitis. In contrast, $CD34^{-}THY1^{-}$ FLS were elevated in the OA synovial lining layer and are thought to contribute to cartilage and bone degradation. The aim of this study was to compare the phenotypic, metabolic and functional profiles of PsA-FLS compared to RA-FLS.

Methods: Single cell analysis of PsA and RA ST cell suspensions were analysed for specific synovial fibroblast subsets and metabolic markers by 14-colour flow cytometry. Fibroblasts were defined as CD45-CD146-CD31-podoplanin+. Subsets were further defined according to CD34 and THY1 expression and analysed for pmTOR, pS6, GLUT1 and pSTAT3 expression. The metabolic profiles of primary RA- and PsA-FLS were analysed using the XFe96-Extracellular Flux Analyzer. Gene expression for metabolic and inflammatory mediators was determined by quantitative-PCR. Cell migration and invasion were determined by wound repair scratch assays and Transwell Matrigel™ invasion chambers. All patients satisfy ACR classification criteria for RA and CASPAR criteria for PsA.

Results: A significant increase in the $podoplanin^{+}CD34^{-}THY1^{+}$ FLS subset was demonstrated in RA synovial tissue single cell suspensions compared to that of PsA ($p=0.0003$). In contrast, a significant increase in $podoplanin^{+}CD34^{-}THY1^{-}$ FLS subset was observed in PsA ($p< 0.0001$). In both RA and PsA, GLUT1 and pSTAT3 were slightly elevated in the $THY1^{+}$ subset, while pmTOR and pS6 were slightly elevated in the $THY1^{-}$ subset. Expression of glycolytic genes HK2, GAPDH, PKM2 and LDHA and the glucose receptors GLUT-1 and GLUT-3 were significantly increased in cultured RA-FLS compared to PsA-FLS. This was paralleled by an overall increase in the ECAR:OCR ratio in RA-FLS compared to PsA-FLS, demonstrating a shift to a more glycolytic phenotype in RA, an effect associated with an increase in disease activity score, DAS28. Finally, a significant increase ICAM-1 and MMP-1 expression was demonstrated in RA-FLS compared to PsA-FLS, in addition to an increase in their migratory and invasive capacity.

Conclusion: This study demonstrates, for the first time, distinct differences in FLS subsets in RA synovial biopsies compared to PsA, with an increase in the more invasive, $podoplanin^{+}CD34^{-}THY1^{+}$ FLS observed in RA. This was consistent with an increase in their metabolic profile and functional capacity and reflects the clinical observations of disease activity.

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Abstract Number: 1521

A Novel Gut-joint Migratory TCRab+ Cell Subset Relies on sphingosine-1-phosphate for Tissue Localization

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SESSION INFORMATION
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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science
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Background/Purpose: Despite findings of similar immune cellular phenotypes in the gut and joint of patients with spondyloarthritis, the mechanistic linkage between intestinal immunology and the subsequent pathogenic targeting of the enthesis by gut-originating cells have not been defined. Prior work in our lab demonstrated a correlation between the numbers of colon intraepithelial lymphocytes (IELs) and circulating lymphocytes, leading us to hypothesize that IELs migrate from the colon to the enthesis as one mechanistic link between the colon and joint.

Methods: We used the KikGR transgenic mouse in which colonoscopy guided violet light allows labeling of cells in the distal colon, termed photo-conversion. Following photo-conversion, we evaluated the Achilles enthesis for the presence and characteristics of labeled cells by flow cytometry in two models: the TNF^{DARE} model of spontaneous inflammatory bowel disease and arthritis and hock injection of complete Fruend's adjuvant (CFA). IEL recruitment to the colon epithelium was evaluated using microarray and confirmed by qPCR, the pan spingosine-1-phosphate receptor (S1PR) antagonist FTY720 to interrupt cellular trafficking, and LysM-Cre x $MyD88^{fl/fl}$ mice.

Results: Following photo-conversion of the distal colon, we identified colon-labeled CD3+TCRab+ cells in the Achilles enthesis within 72 hours. The numbers of trafficked T cells significantly increased in the entheses during inflammation caused by either CFA or in TNF^{DARE} mice compared to non-arthritic controls; however, the percentage of gut-derived cells remained at ~10% regardless of the presence of arthritis. Following this discovery, we hypothesized that the function of IELs may be affected by their interactions in the gut. Therefore, we investigated how IELs localize and interact with the colon epithelium. By microarray and qPCR, we identified that the trafficking receptor S1PR1 was significantly expressed on IELs compared to lamina propria T cells. The S1PR inhibitor FTY720 blocked IEL localization to the colon epithelium, and gut-joint trafficking was ablated. Finally, we identified that MyD88 expression by myeloid cells was critical for IEL localization via S1P, and treatment of bone marrow derived dendritic cells (BMDCs) with cecal contents induces *sphk1* expression in a MyD88 dependent fashion, which was sufficient to induce T cell migration in an S1P-dependent fashion.

Conclusion: Altogether, our data demonstrate a model of gut-joint trafficking. Bacterial signals through MyD88 in myeloid cells stimulate the S1P pathway to recruit IELs to the colon epithelium. Although the specific interaction with the epithelium and impact on T cells is yet to be elucidated, we hypothesize that this interaction functionally alters IELs. The colon IELs then traffic to the joint, where their role in inflammation likely depends upon the functional programming they receive in the intestine. These findings may shed light into pathogenic mechanisms connecting the gut and joint in spondyloarthritis.

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Abstract Number: 1522

Biomarkers of Hemodynamic Severity of Systemic-Sclerosis Associated Pulmonary Arterial Hypertension by Serum Proteome Analysis

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SESSION INFORMATION
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Background/Purpose: To investigate alterations in the serum proteome of patients with systemic sclerosis (SSc)-associated pulmonary hypertension (PAH), to identify proteins that correlated with hemodynamic severity and to determine their possible role in the pathogenesis of the disease.

Methods: Eligible patients were recruited from Boston, Lille, Kremlin-Bicêtre and Grenoble SSc and PH referral centers. Patients were included if they fulfilled the following criteria: diagnosis of SSc according to 2013 ACR/EULAR criteria, limited cutaneous subtype, no extensive interstitial lung disease (ILD) according to Goh criteria, and no treatment with PAH-specific therapy. Patients were classified as cases if they had a definitive diagnosis of PAH confirmed by right heart catheterization (RHC) and a serum sample collected on the same day as RHC. They were classified as controls if they had no sign suggestive of PAH on echocardiography.

Results: In a first exploratory step, serum expression of 1129 proteins was assessed in 15 cases and 16 controls by a high-throughput proteomic assay (SOMAscan). We identified 53 proteins differentially expressed between the 2 groups. Among these 53 candidates, only 2 correlated significantly with pulmonary vascular resistance (PVR): chemerin (p=0.01, ρ=0.62) and SET nuclear proto-oncogen (SET) (p=0.01, ρ=0.62).

To validate these results, serum levels of chemerin and SET were measured by ELISA assay in 25 additional cases and 19 additional controls. Chemerin levels were confirmed to be significantly higher in cases (p=0.01) and correlated with PVR (p=0.01, ρ=0.46) in this independent cohort.

In a second step, to study the potential pathophysiological role of chemerin, we performed confocal immunofluorescence analyses on explanted lungs of healthy controls, SSc-ILD without PAH and SSc-PAH patients. Chemerin receptor, CMKLR1, was significantly increased on SSc-ILD and SSc-PAH pulmonary artery smooth muscle cells (PA-SMC).

We then tested the effect of chemerin on PA-SMC proliferation by stimulating PA-SMCs from idiopathic pulmonary arterial hypertension (iPAH) patients with serum from SSc patients with and without PH, in the presence or absence of a CMKLR1 inhibitor. PA-SMCs from iPAH were confirmed to have higher mRNA expression of CMKLR1 than controls (p=0.03). Serum from SSc-PH patients induced a significantly higher PA-SMC proliferation (p=0.005) than serum from controls. This difference was no longer significant (p=0.69) when adding the CMKLR1 inhibitor aNETA.

Conclusion: Chemerin is a surrogate biomarker for PVR in SSc-PAH. Increased chemerin and its receptor, CMKLR1, contribute to the SSc-PAH pathogenesis by inducing PA-SMC proliferation.

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Abstract Number: 1523

Pulmonary Cytokine, Chemokine and Growth Factor Profiles of Distinct Radiographic Patterns of Interstitial Lung Disease in Systemic Sclerosis

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SESSION INFORMATION
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Session Title: Systemic Sclerosis & Related Disorders – Basic Science
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: The radiological hallmarks of systemic sclerosis-related interstitial lung disease (SSc-ILD) include interstitial inflammation (ground glass opacity) with reticular changes (fibrosis). The precise pathobiology of these radiographic manifestations is unknown. We hypothesized that certain cytokines, chemokines and growth factors may uniquely associate with distinct radiographic patterns of ILD in SSc.

Methods: We measured the concentrations of 68 chemokines, cytokines and growth factors from bronchoalveolar lavage (BAL) fluid of 103 patients with SSc-ILD who participated in Scleroderma Lung Study I (1). SLS I randomized SSc-ILD participants to 1 year of oral cyclophosphamide versus placebo, followed by 1 year off all treatment. Bronchoscopy was performed at baseline in SLS I. Quantitative imaging analysis (QIA) was used to calculate the extent of radiographic fibrosis (QLF) and ground glass opacity (GGO) on the baseline HRCT of the chest. Kendall tau's correlations were calculated to examine the relationship between BAL proteins and QLF and GGO scores, separately, for the whole lung. Multivariable linear regression models were created to determine the key BAL proteins associated with QLF and GGO scores using a backward selection process in combination with evaluation of the Akaike information criterion (AIC). The bootstrap procedure was employed for internal validation.

Table 1. BAL proteins associated with quantitative extent of radiographic fibrosis in the whole lung based on a multivariable linear regression model.*

BAL Protein	Estimate	Standard Error	P-value
IL-4	-4.86	2.04	0.0198
MCP-3	4.23	1.56	0.0082
RANK	1.71	0.68	0.0140
TNF-α	-2.40	0.84	0.0057
HGF	1.87	1.13	0.1029
Endoglin	-0.01	0.01	0.0748
VEGF	-1.28	0.90	0.1594
TGF-α	2.67	2.25	0.2396

*Adjusted R-square for the model = 0.38; AIC = 472.39.

Table 2. BAL proteins associated with quantitative radiographic extent of ground glass opacity in the whole lung based on a multivariable linear regression model.*

BAL Protein	Estimate	Standard Error	P-value
IL-15	-1.88	0.84	0.0271
IL-5	-5.26	2.41	0.0318
IFN-γ	4.10	2.04	0.0484

*Adjusted R-square for the model = 0.10; AIC = 484.73.

Results: QLF scores correlated significantly with 25 different proteins from several biologic pathways including pro-fibrotic factors (transforming growth factor beta [TGF-β], platelet-derived growth factor [PDGF]), proteins involved in tissue remodeling (Matrix metallopeptidase [MMP]-1,7,8,9; Hepatocyte growth factor [HGF]), and those involved in monocyte/macrophage migration and activation (Monocyte chemoattractant protein [MCP]-1,3; macrophage colony-stimulating factor [MCSF]). GGO scores correlated with 7 different proteins that are mediators of immune response and inflammation (interleukin [IL]-5, IL-15, IL-1 receptor antagonist and interferon gamma [IFN-γ]) with limited overlap to proteins that related to fibrosis. Vascular endothelial growth factor (VEGF) levels were lower in patients with more extensive GGO and QLF, suggesting that vascular changes are an important feature of SSc-ILD. In the multivariate models, IL-4, MCP-3, receptor activator of NF-κB (RANK), tumor necrosis factor alpha (TNF-α) were independently associated with QLF (Table 1); whereas, IL-15, IL-5 and IFN-γ were independently associated with GGO (Table 2).

Conclusion: In a diverse and comprehensive analysis of BAL proteins from a well-characterized SSc-ILD cohort, the findings suggest that specific biological signatures underlie distinct radiographic features of ILD in SSc. These proteins may represent important therapeutic targets and serve to help define specific phenotypes of SSc-ILD (inflammation predominant versus fibrosis predominant), which may ultimately lead to the development of personalized treatment approaches in this patient population.

Disclosure: E. Volkmann, Boehringer Ingelheim, 2, 5, Forbius, 2, 5, Corbus, 2; **D. Tashkin**, None; **N. Li**, None; **M. Leng**, None; **G. Kim**, None; **J. Goldin**, None; **A. Harui**, None; **M. Roth**, Genentech/Roche, 1.

Abstract Number: 1524

Interstitial Lung Disease, Kidney Inflammation and Myositis Are Induced by Transfer of PBMC Derived from Systemic Sclerosis Patients into Rag2$^{-/-}$/ IL2rg$^{-/-}$ mice

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Systemic Sclerosis & Related Disorders – Basic Science

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: To explore the pathogenic potential of lymphocytes in systemic sclerosis (SSc) and granulomatosis with polyangiitis (GPA), a humanized mouse model was generated by transferring human peripheral blood mononuclear cells (PBMC) into immunocompromised mice.

Methods: PBMC derived from patients with SSc and GPA were isolated, characerized by flow cytometry and infused into RAG2/IL2rg double- deficient mice. PBMC from healthy donors (HD) and from rituximab-treated SSc patients served as controls. Twelve weeks later, peripheral blood and tissues from recipient mice were collected and the latter examined by histology and immunohistology. Autoantibodies were analyzed in peripheral blood using ELISA or immunofluorescence assay on HEp-2 cells.

Results: Following transfer of PBMC derived from patients with SSc, total IgG and, in particular, SSc-related autoantibodies such as anti-AT1R, anti-ETAR antibodies and ANA were detected in recipient mice. In addition, infiltration of human lymphocytes was observed in multiple organs of recipient mice. In addition, infiltrations of human lymphocytes were observed in multiple organs of recipient mice, particularly lung, kindey and muscles. By contrast, although PBMC derived from HD or GPA patients also survived in recipient mice, no production of human autoantibodies and only marginal infiltration of human immune cells in lung, kidney, or muscles was found. Furthermore, transfer of PBMC derived from SSc patients predominantly featured an infiltration of human B cells in lung, kidneys and muscles, while no such cells were detected following transfer of PBMC derived from rituximab-treated SSc patients.

Conclusion: The humanized mouse model using adoptive transfer is indicative for intrinsic immune cell defects and argues for a pivotal role of B cells in the pathogenesis of SSc. It provides a powerful tool to study interstitial lung disease as so far under-recognized disease manifestations such as myositis and interstitial nephritis.

Disclosure: X. Yue, None; **F. Petersen**, None; **X. Yu**, None; **G. Riemekasten**, None; **P. Lamprecht**, None; **A. Müller**, None; **J. Yin**, None.

Abstract Number: 1525

Intergenic *HLA* Variants in African American Patients with Systemic Sclerosis Regulate Expression of HLA-DRB1

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SESSION INFORMATION

Session Date: Sunday, November 8, 2020

Session Title: Systemic Sclerosis & Related Disorders – Basic Science

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Genome-wide association study (GWAS) from the Genome Research in African American Scleroderma Patients (GRASP) cohort has identified the human leukocyte antigen (*HLA*) region as the strongest genetic risk factor in SSc. The functional roles of *HLA* variants in SSc susceptibility are largely unknown. We hypothesize that SSc-associated HLA variants overlap with one of the classes of *cis*-regulatory modules (CRMs) such as enhancer to regulate gene expression. CRMs can be mapped using DNase I hypersensitive site sequencing (DNase-Seq) or assay for transposase-accessible chromatin with high throughput sequencing (ATAC-Seq) giving information regarding chromatin accessibility. Thus, chromatin accessibility in the SSc-relevant cell types would be crucial in interpreting the function of these variants.

Methods: Genotyping data using the Illumina Multi-Ethnic Global array (MEGA) from the GRASP cohort were analyzed to identify the top *HLA* variant. Expression quantitative trait loci (eQTL) analysis was performed for the risk variants using RNA sequencing data from the Genotype-Tissue Expression (GTEx) project. Epstein-Barr virus-transformed B (EBV-B) cells with wild type, heterozygous and homozygous alleles for the most highly associated *HLA* variant were used to confirm the expression of *HLA-II* genes using RNA-sequencing. Protein expression was confirmed by flow

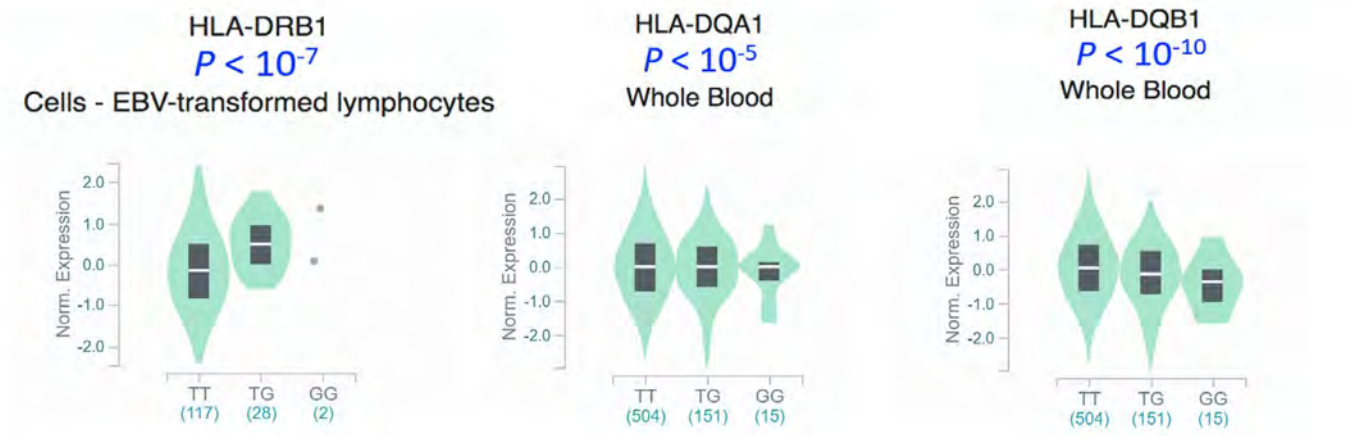

Figure 1. GTEx HLA-DRB1, HLA-DQA1 and HLA-DQB1 expression by rs9469201 variant

cytometry and confocal microscopy. Chromatin accessibility at the variant position in EBV-B cells is being identified using ATAC-seq.

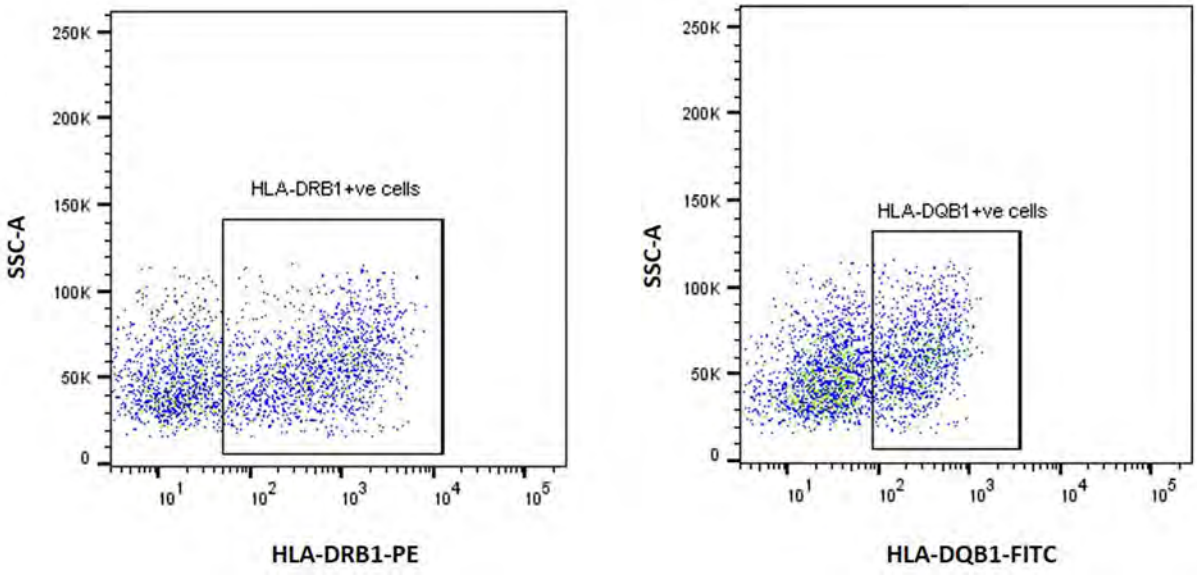

Figure 2. Flow cytometry plots for EBV-B cells with wild type allele stained for HLA-DRB1 and HLA-DQB1 protein using fluorochrome conjugated antibodies.

Results: The top variant in the African American GWAS was rs9469201, near the *HLA-DQA1* gene with an odds ratio of 2.13 (P=4.5x10^{-20}). eQTL analysis suggested decreased expression of *HLA-DQA1/-DQB1* (in whole blood) and increased expression of *HLA-DRB1* (in EBV-B cells) for the risk allele (Figure 1). This is particularly intriguing because we have previously reported two HLA-DRB1 alleles (*HLA-DRB1*08:04* and *-DRB1*11:02*) as independent risk factors in African American SSc. The rs9469201 variant was found not to be in linkage disequilibrium with the *HLA-DRB1*08:04* allele. Flow cytometry (Figure 2) and confocal microscopy (Figure 3) confirmed the expression of HLA-DRB1 and HLA-DQB1. ATAC-Seq analysis of the EBV-B cells is currently ongoing.

Conclusion: Our preliminary findings suggest that peptide presentation by HLA molecules as well as the relative expression of the specific HLA molecule presenting the peptide are both important in SSc pathogenesis. Future direc-

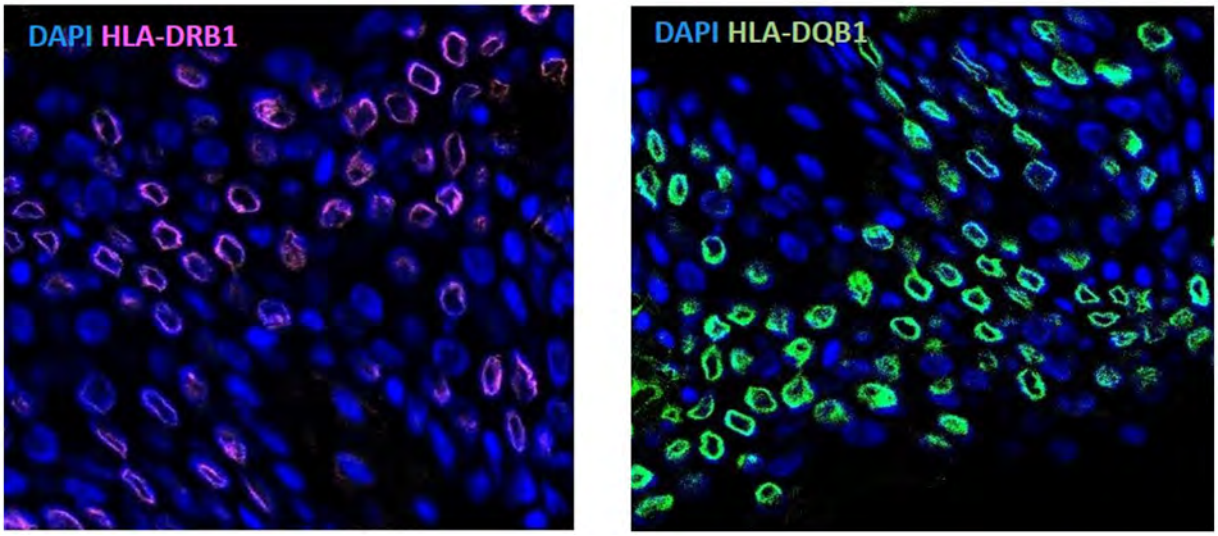

Figure 3. Confocal microscopy image for HLA-DRB1 and HLA-DQB1 stained cells for the wild type allele.

tions will involve CRISPR/Cas9 based deletion of CRMs-with overlapping *HLA* variants, and subsequent evaluation of the changes in *HLA-II* gene expression. Transcription factor binding at the *HLA* variant site will be accessed using chromatin immunoprecipitation with sequencing (ChIP-seq) in EBV-B cells. This study will elucidate the functional role of the *HLA* variants in allele-specific *HLA-II* gene expression in SSc.

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Abstract Number: 1526

Single Cell Analysis of Skin and Blood of Scleroderma Patients Towards Identification of New Disease Mechanisms, Prognostic Biomarkers and Potential Therapeutic Targets

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SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Systemic Sclerosis & Related Disorders – Basic Science
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Systemic sclerosis (SSc) is characterized by fibrosis, microangiopathy and immune dysregulation. Despite many years of research, the pathogenesis of SSc is poorly understood; there is no approved therapy and biomarkers for early diagnosis, assessment of disease activity, prediction of complications and prognosis. Current technologies that investigate bulk populations of cells lack the depth and resolution needed to define the small skin stromal and immune subsets that drive SSc progression. Advances in the field of single-cell RNA has opened the way for unbiased dissection of complex niches into single cells, and identification of unique cell subtypes, pathways, markers and target genes. Our aims are to understand SSc pathogenesis by comprehensive characterization of stromal and immune cells in the skin and blood of SSc patients and detection of specific intra-skin cell states, pathways, and cell-cell interactions in SSc patients compared to healthy controls.

Methods: We applied the massively parallel single cell RNA-seq (MARS-seq) technique developed in our lab to conduct a comprehensive single-cell analysis of skin stromal and immune cells obtained from punch biopsy together with blood immune cells from 79 SSc patients (44 dSSc, 35 lSSc) at different stages of disease progression, and 35 healthy controls. The perturbed signaling pathways, pathogenic stromal or immune cell subsets are characterized using CyTOF, Immunohistochemistry, **P**hysical **I**nteracting **C**ell sequencing (**PIC**-seq), and *in vitro* functional assays.

Results: We collected data from a total of 49,831 high-quality skin stromal cells, and 61,365 high-quality blood and skin immune cells. Our MetaCell analytical method resulting in a detailed map of 389 meta cells in the immune cell compartment organized into 14 broad lineages (e.g skin T, B and NK cells, Dendritic cells, Monocyte). In the stromal cell compartment, we found 294 meta cells organized into 17 broad lineages including: Fibroblasts, Pericytes, Vascular cells, and other cells. To our surprise, analysis of the immune cell compartment revealed only minor changes in the cell composition and gene expression in patients compared with controls. In the dermal fibroblast lineage we found a small cluster of cells that were significantly diminished in the SSc patients compared with control. This subset expressed genes associated with fibrosis, vascular remodeling, and most importantly, display stem cell-like phenotypic markers that are different from other known skin stem cells located in the hair follicle and subcutaneous fat. We further found significant increased number of subsets of pericytes and vascular cells in SSc patients compared with controls. Finally, we found known and novel pathways that play crucial roles in SSc pathogenesis.

Conclusion: Our study provides the most comprehensive dataset in single cell resolution in SSc, and suggests a paradigm shift in the understanding of SSc. The MARS-seq can serve as a vehicle for discovering immune-stromal

cell crosstalk, for finding new biomarkers for early SSc diagnosis and for tailoring and identification of new therapeutic targets.

Disclosure: C. Gur, None; **P. 158626**, None; **H. Peleg**, None; **S. Aamar**, None; **F. Kharouf**, None; **A. Elazary**, None; **Y. Braun-Moscovici**, None; **S. Wang**, None; **I. Amit**, None.

Abstract Number: 1527

Tofacitinib Inhibits Angiogenesis Through Its Opposite Effects on Pro- and Anti-angiogenic Factors

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Angiogenesis plays a key role in the progression of rheumatoid arthritis (RA), but the mechanisms regulating this process are not fully elucidated. EMMPRIN is a multi-functional protein that can induce the expression of matrix metalloproteinases (MMPs) and vascular endothelial growth factor (VEGF), which are pro-angiogenic. Tofacitinib, a small molecule inhibitor of Janus Kinase (JAK) 1 and JAK3, in use for treatment of RA, has been shown to inhibit production of cytokines. However, its effects on angiogenesis, and specifically on EMMPRIN expression and activity, are not yet clear.

Methods: To determine the effects of Tofacitinib on the expression of EMMPRIN, MMP-9 and VEGF, as well as on the expression of the anti-angiogenic proteins endostatin and thrombospondin-1 (Tsp-1).

Results: The co-culture increased the secretion of MMP-9 and VEGF compared to the single culture of HT1080 cells (by 1.5-fold and 1.4-fold respectively, $p< 0.05$) and decreased the secretion of endostatin and Tsp-1 (by ~45%, $p< 0.05$); however, EMMPRIN secretion was unaffected. Tofacitinib significantly inhibited the secretion of EMMPRIN, VEGF and MMP-9 (by 16%, 39%, 29% respectively, $p< 0.01$), whereas secretion of endostatin, but not of Tsp-1, was increased (1.7-fold, $p=0.0074$). The ratio between VEGF and endostatin, a measure of the overall angiogenic potential, was reduced by 54% by the addition of Tofacitinib ($p=0.0005$). Likewise, CM from the co-cultured cells after incubation with Tofacitinib demonstrated reduction (12.7%, $p=0.0441$) in the ability of endothelial cells to migrate and to form closed lumens (17%, $p=0.0002$).

Conclusion: We suggest that the interactions between monocytes and fibroblasts lead to an angiogenic switch, as they enhance pro-angiogenic factors and decrease anti-angiogenic mediators. Tofacitinib reversed these effects by enhancing endostatin secretion and reducing the accumulation of EMMPRIN, VEGF and MMP-9. Thus, the inhibitory effect of tofacitinib on angiogenesis may contribute to its efficacy in treating inflammatory arthritis.

Disclosure: D. Zisman, Pfizer, 2; **M. Rahat**, None; **E. Simanovich**, None; **E. Mellins**, None; **A. Haddad**, None; **T. Gazitt**, None; **J. Feld**, None; **M. Rahat**, None.

Abstract Number: 1528

Filgotinib Inhibits Monocyte Differentiation and Pro Inflammatoly Cytokine Production in Osteoblasts

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is a systemic autoimmune disease characterized by inflammation and joint destruction. Filgotinib is a selective small molecule inhibitor of JAK 1 enzymes, and is currently in clinical development for the treatment of rheumatoid arthritis (RA). However, a direct role of filgotinib for osteogenesis has not been demonstrated. Here, we examined filgotinib inhibited monocyte differentiation and proinflammatoly cytokine production in osteoblasts.

Methods: To determine if the JAK-STAT enzyme was expressed in RA osteoblasts and MG63 (human osteosarcoma cell line), we performed immunohistochemistry. In order to confirm that filgotinib inhibited STAT signaling phosphorylation, interleukin (IL)-6 and IL-6 receptor (IL-6R) stimulated MG63 was used for western blotting. To determine whether filgotinib was involved in proinflammatoly cytokine production, monocyte chemotactic protein-1(MCP-1)/CCL2, IL-8/CXCL8, receptor activator for nuclear factor -κB ligand (RANKL) and CXCL16 in filgotinib treated MG63 conditioned medium was measured using enzyme-linked immunosorbent assay (ELISA). Finally, to confirm if monocyte was differentiated with filgotinib, THP-1 (human acute monocytic leukemia cell line) was cultured with filgotinib treated MG63 conditioned medium.

Results: JAK1, 2 and 3 was expressed in osteoblast and MG63. We found that phosphorylated STAT1 and STAT3 signaling in IL-6 and IL-6R stimulated filgotinib treated MG63 was significantly decreased at 10 minutes compared to nontreated MG63. MCP-1/CCL2 in filgotinib treated MG63 conditioned medium was significantly decreased compared with in nontreated MG63 conditioned medium (12.8 ± 0.6 pg/ml and 41.6 ± 0.0 pg/ml, $p < 0.05$, respectively). CXCL16 in in filgotinib treated MG63 conditioned medium was also significantly decreased compared with in nontreated MG63 conditioned medium (12.8 ± 0.6 pg/ml and 41.6 ± 0.0 pg/ml, $p < 0.05$, respectively). Additionally, THP-1 with IL-6 and IL-6R treated MG63 conditioned medium differentiated into multinuclear cells. On the other hand, THP-1 with filgotinib treated MG63 conditioned medium did not differentiate into multinuclear cells.

Conclusion: Filgotinib inhibited proinflammatory cytokine production and monocyte differentiation. These data indicate that filgotinib acts on bone metabolism, suggesting that filgotinib may prevent bone destruction.

Disclosure: T. Isozaki, None; **Y. Ikari**, None; **T. Kasama**, None.

Abstract Number: 1529

Differentially Expressed Chemokines and Cytokines in Peripheral Blood Mononuclear Cells (PBMCs) of Rheumatoid Arthritis (RA) Patients

Noha Elemam[1], Mahmood Hachim[2], Suad Hannawi[3] and Azzam Maghazachi[4], [1]University of Sharjah, Sharjah, United Arab Emirates, [2]Mohammed Bin Rashid University Of Medicine and Health Sciences, Dubai, [3]Ministry of Health and Prevention, Dubai, United Arab Emirates, [4]University of Sharjah, Sharjah

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Cytokines & Cell Trafficking Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is the most prevalent autoimmune disease, where various immune cells are associated such as monocytes, natural killer (NK) cells, B cells, and T cells. Additionally, soluble mediators aid in the interaction between immune and non-immune cells. Cytokines are soluble mediators that play a crucial role in the inflammatory processes that could lead to joint destruction associated with RA, while chemokines play a major role in the migration of various cell types into inflammatory sites in RA (Brennan and McInnes 2008, Szekanecz, Vegvari, et al. 2010, Elemam, Hannawi, et al. 2020). In this study, we aimed at exploring chemokines and cytokines that could possibly be used to aid in evaluating the differences between healthy controls and RA patients.

Methods: Publicly available transcriptome dataset (GSE64708) of peripheral blood mononuclear cells (PBMCs) of RA patients and healthy controls were analyzed using the GEO2R tool. Then, the cytokines and chemokines were selected from the top 250 significant genes. Whole blood samples were collected from the recruited 17 RA patients (satisfying the 2010 ACR/EULAR classification criteria for RA) and 16 healthy controls (with no diagnosis of autoimmune diseases). Then, blood was separated to obtain PBMCs using the Ficoll density gradient method. RNA was extracted and gene expression was assessed using qRT-PCR. Statistical analysis was done using the unpaired t-test or Mann-Whitney test, after the assessment of data distribution. P-value < 0.05 was considered statistically significant.

Results: In silico analysis showed that several chemokines, cytokines, and innate receptors such as toll-like receptors were differentially expressed between RA patients and healthy controls. Hence, some of these cytokine and chemokine ligands and receptors were validated and assessed in PBMCs of RA patients and healthy controls. Regarding the chemokines, CCR4, CCL2, CKLF, and CXCL10 were found to be upregulated in RA patients (Figure 1). Similarly, the proinflammatory chemokine IL-1β, IL-1 receptor antagonist (IL1RN) as well as the cytokine receptor

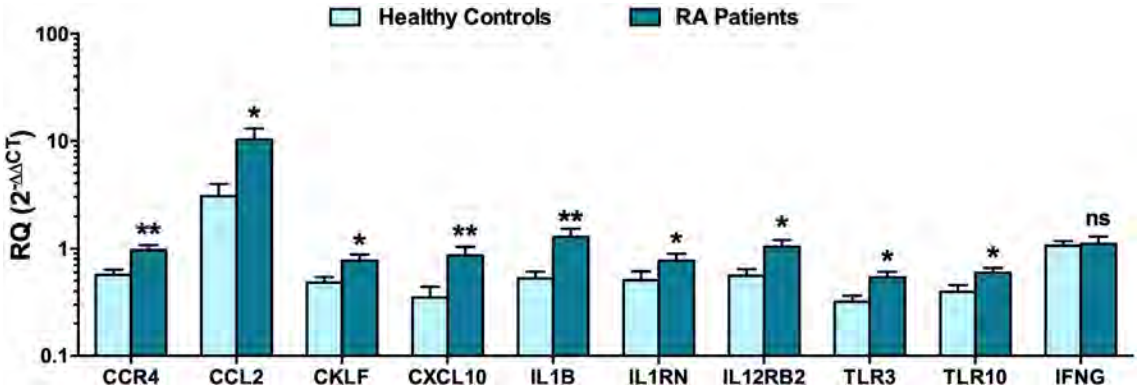

Figure 1. Assessment of gene expression of chemokines, cytokines, and toll-like receptors in the PBMCs of RA patients and healthy controls.

component IL12RB2 exhibited an upregulation in the PBMCs of RA patients while the T helper 1 cytokine IFN-γ did not display any differential expression in PBMCs of RA patients. Furthermore, the innate toll-like receptors TLR3 and TLR10 were upregulated in PBMCs of RA patients.

Conclusion: In conclusion, certain chemokines and cytokines seem to play a major role in the pathogenesis of RA disease. Gene expression of these molecules; CCR4, CCL2, CKLF, CXCL10, IL-1β, IL-1RN, IL12RB2, TLR3, and TLR10 in PBMCs could be used as promising biomarkers for RA disease.

Disclosure: N. Elemam, None; **M. Hachim**, None; **S. Hannawi**, None; **A. Maghazachi**, None.

Abstract Number: 1530

Activin a and Follistatin Alter Endothelial Cell and Rheumatoid Arthritis Synovial Fibroblast Adhesion and Interaction

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SESSION INFORMATION
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Background/Purpose: Activin A and follistatin belong to an anti-inflammatory auto-regulatory cycle. Patients with rheumatoid arthritis (RA) have increased activin A levels in the synovial fluid and tissue. During inflammation, activin A is released systemically, then inducing its antagonist follistatin. This negative feedback is active in different cell types but not RA synovial fibroblasts (SF). Fibroblasts are known to interact with endothelial cells in inflamed tissues. Objective: Evaluation of the role of activin A and follistatin on RASF and endothelial cell interactions.

Methods: RA synovium was used for RASF isolation, HUVEC were commercially obtained. RASF and HUVEC were stimulated in mono- and coculture. Direct: RASF together with HUVEC; indirect: inserts with HUVEC separated by a membrane from RASF in the lower chamber. Stimuli: 15ng/ml activin A, 500ng/ml follistatin, 1ng/ml IL-1. Proteins were measured by ELISA. Proliferation was analyzed by BrdU assay. RASF were Calcein-AM stained for short-term cell adhesion assays in direct coculture. Cells were transferred to 24-well plates after 18h stimulation. After adhesion for 1h, non-adherent cells were removed by shaking 3x 5 min. Afterwards, cells were quantified. For the flow-adhesion assay, HUVEC were cultured on rat tail collagen coated capillary slides. HUVEC and RASF were stimulated for 4h with TNF, TNF+activin A or TNF+follistatin. After stimulation, 1x10^6 RASF were resuspended in 20ml medium. Two 1min videos were recorded at 18.4ml/h and 30.5ml/h using TNF-stimulated HUVEC or TNF-stimulated RASF on activin A or follistatin stimulated HUVEC.

Results: IL-1 induced activin A in RASF and HUVEC monoculture (8-fold, $p< 0.01$, 4-fold, $p< 0.05$) and direct and indirect coculture (5-fold, $p< 0.05$; 4-fold, $p< 0.05$). IL-1-induced activin A release was reduced by follistatin in HUVEC monoculture (12-fold, $p< 0.01$, n=5), direct and indirect coculture (10-fold, $p< 0.01$; 5-fold, $p< 0.01$) compared to IL-1 alone but not in RASF monoculture. IL-1-induced IL-6 release was reduced by activin A in HUVEC (42.6%, $p< 0.05$)

and indirect coculture (31.8%, p< 0.05) but not in RASF monoculture and direct coculture. Follistatin did not alter IL-6 responses. IL-1 induced VEGF in RASF but not in HUVEC and was not altered by activin A. Proliferation of RASF, HUVEC or both was not altered by activin A or follistatin. Short-term adhesion showed no significant influence of activin A or follistatin (n=3). Flow adhesion assay showed reduced adherence / rolling of RASF on HUVEC stimulated with TNFα and activin A.

Conclusion: In direct and indirect coculture of HUVEC with RASF the effect on HUVEC is dominant leading to reduced IL-1-induced activin A release. However, the IL-1-induced IL-6 release in RASF or HUVECs was decreased by activin A in HUVEC monoculture and indirect coculture but not during cell-contact of both cell types. The direct interaction of RASF with HUVEC seems to prevent the reducing activin A effect on IL-6 release in HUVECs. Activin A seems to not to have an impact on short-term cell adhesion but first observations show that activin A has an influence on selectin-mediated adhesion under flow conditions.

Disclosure: H. Scholz, None; **I. Aykara**, None; **K. Frommer**, None; **S. Rehart**, None; **U. Müller-Ladner**, Biogen, 8; **E. Neumann**, None.

Abstract Number: 1531

Characterization of Cytokine/chemokine Profile in Patient-derived M1/ M2 Macrophages to Identify Biomarkers for Genetically-defined Systemic Autoinflammatory Diseases

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Background/Purpose: Genetic mutations in key regulatory molecules of the innate immune system cause autoinflammatory diseases through propagation of hyperinflammatory responses. Monocytes/ macrophages regulate inflammatory processes during infection and homeostasis by secreting a wide range of cytokines and chemokines that control recruitment and migration of immune cells to inflamed tissue, and their biological functions through immune cell differentiation and polarization. We characterized the cytokine/chemokine profile of peripheral blood monocyte-derived M1-, and M2-macrophages (M1-, M2-MDMs) from patients (pts) with genetically defined systemic autoinflammatory diseases (SAIDs) and controls.

Methods: Whole blood from pts enrolled in the IRB approved study (NCT 02974595) with IL-1 mediated SAIDs NOMID (n=3), DIRA (n=4), Majeed Syndrome (n=1); interferon-mediated diseases CANDLE (n=3) SAVI (n=3); IL-18 mediated diseases NLRC4-MAS (n=2), IL-18PAP-MAS(n=1), Blau syndrome (n=4), NEMO-NDAS (n=3); and healthy controls (HC) (n=6) were assessed. M1-, M2-MDMs) from culture with GM-CSF or M-CSF for 6 days were assessed with and without LPS+ATP stimulation. Human Cytokine Array and ELISA were used for cytokine/chemokine profiling. SAVI monocytes died upon in vitro M1-M2 MDM differentiation. Differentiation into rounded and flat shaped M1-MDMs and elongated or spindle shaped M2-MDMs was 80-90% and 70-80% respectively for all samples.

Results: IL-1β secretion from M1-MDMs was higher in NOMID, DIRA and Majeed syndrome pts upon stimulation with LPS and ATP compared to HC and other SAID pts. In NOMID pts, IL-1b was equally elevated in M1-and M2 MDMs, whereas IL-18 was produced in M1- and M2-MDMs in NLRC4-MAS and in M2-MDMs in IL-18PAP-MAS. TNF and IL-6 were highest in stimulated M1-MDMs in NOD2 and NLRC4 MAS pts. compared to HC ($p< 0.05$) and in stimulated M2-MDMs in Majeed, CANDLE, NOD2 and NLRC4 pts. Among chemokines, CCL2/MCP-1 which recruit monocyte into inflamed tissues was constitutively expressed in M1/M2-MDMs of CANDLE and NOD2 and M1-MDM of NLRC4-MAS pts. M2-MDMs derived from Majeed and DIRA pts. produced significantly higher levels of CCL5/RANTES and CXCL10/IP-10 ($p< 0.05$). IP-10 secretion was not seen in CANDLE or NEMO-NDAS. IL-8 and CXCL1, two neutrophil-attracting chemokines were high in most autoinflammatory disease groups, moreover, M2-MDMs of CANDLE and Majeed pts constitutively released IL-8. As expected, IL-1ra was absent in unstimulated and stimulated DIRA M1-, and M2-MDSs. Moreover, CANLDE MDMs did not show an upregulation of IL-1ra distinct from IL-1 mediated diseases.

Conclusion: Taken together, differentiation of monocytes into M1 and M2 MDMs leads to variable but disease-specific regulation of pro-inflammatory cytokine and chemokine production. The value of this system in assessing monocyte and macrophage polarization defects and in assessing the proinflammatory dysregulation in various SAIDs need to be further explored. Particularly, whether such systems proof useful in conditions where more than one cytokine/chemokine are dysregulated and in suggesting treatment targets needs to be evaluated in the future.

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The Non-psychotropic Phytocannabinoids Cannabigerol and Tetrahydrocannabinolic Acid Inhibit Rheumatoid Arthritis Synovial Fibroblast Function by Targeting the Wasabi Receptor TRPA1

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Background/Purpose: While medical cannabis is available for german patients since 2017, its use to alleviate symptoms of rheumatic diseases is not recommended due to a lack of clinical studies. While cannabis might be beneficial to treat neuropathic pain, the impact on inflammation has not been assessed adequately. In this study, we investigated the effects of the two non-psychotropic plant cannabinoids, cannabigerol (CBG) and tetrahydrocannabinolic acid (THCA) on the function of rheumatoid arthritis synovial fibroblasts (RASF).

Methods: RASF were treated with THCA and CBG together with TNF or vehicle. After three days, proliferation and cytokine production (IL-6, IL-8 and MMP-3) were assessed. Furthermore, intracellular calcium mobilization and cell death were investigated.

Results: CBG and THCA decreased the proliferation of RASF *in vitro* ($p < 0.001$), which was dependent on concentration of cannabinoids and fetal calf serum content of the culture medium. This was accompanied by reduced production of IL-6, IL-8 and MMP-3 ($p < 0.001$). CBG and THCA increased intracellular calcium ($p < 0.001$) levels and the uptake of the viability dye PoPo3 ($p < 0.001$), which was inhibited by antagonizing the wasabi receptor TRPA1 (transient receptor potential type ankyrin). In addition, we observed significant cell death in response to THCA and CBG, which was inhibited by the mitochondrial transition pore inhibitor cyclosporin A. In contrast to TNF pre-stimulated RASF, the effects of CBG and THCA on cytokine production, proliferation, cell death and calcium mobilization were absent or less pronounced in unstimulated RASF.

Conclusion: CBG and THCA showed robust anti-inflammatory effects preferentially in TNF-activated RASF by targeting the wasabi receptor TRPA1. This ion channel might be a novel therapeutic target since it exerts a crucial influence on the function of RASF, which, *in vivo* contribute to the pro-inflammatory environment in the rheumatoid joint.

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Abstract Number: 1533

Ultrasound Joint Inflammation but Not Disease Activity Score at 28 Joints Is Reflective of the Severity of Joint Damage in Patients with Rheumatoid Arthritis

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Background/Purpose: With increased use of musculoskeletal ultrasound (US) among rheumatologists, it will be necessary to understand what additional clinical information may be derived from US joint assessment versus routine clinical assessment in patients with rheumatoid arthritis (RA). Our study aims to gain further insight into this by studying the severity of joint damage in RA patients classified based on their US joint inflammation findings and their disease activity score at 28 joints (DAS28). By comparing with DAS28, this cross-sectional study mimics what happens in routine clinical practice, whereby clinicians often rely on routine clinical measures (like DAS28) for RA disease activity assessment.

Methods: US power Doppler (PD) and grey scale (GS) joint inflammation were graded semi-quantitatively (0-3), while bone erosion was scored dichotomously (Yes=1 or No=0) at each joint recess. Patients were categorized into 4 US patient groups: group 1 (PD positive and GS ≥median score of 35.5); group 2 (PD negative and GS ≥ median score);

Ultrasound erosion score Mean (95% CI)		Differences (95% CI) between		P-value Group 4 vs.	
Group 1: PD positive and GS ⩾ median score	9.75 (6.69, 12.81)	**Groups 1 and 4**	**6.35 (0.78, 11.83)**	**Group 1**	**0.026***
Group 2: PD negative and GS ⩾ median score	7.33 (-4.11, 18.78)	Group 2 and 4	3.93 (-19.95, 27.81)	Group 2	0.572
Group 3: PD positive and GS < median score	3.3 (2.17, 4.43)	Group 3 and 4	-0.10 (-2.58, 2.38)	Group 3	0.932
Group 4: PD negative and GS < median score	3.4 (1.11, 5.69)				

Statistically significant: *P<0.05.

Table 1. Comparison of ultrasound erosion scores between the ultrasound patient groups.

Ultrasound erosion score Mean (95% CI)		Differences (95% CI) between		P-value Remission vs.	
HDA: DAS28 > 5.1	5.25 (2.32, 8.18)	HDA and remission	-0.08 (-6.74, 6.58)	HDA	0.978
MDA: 3.2 ≤ DAS28 ≤ 5.1	7.93 (4.63, 11.24)	MDA and remission	2.60 (-3.67, 8.87)	MDA	0.396
LDA: 2.6 ≤ DAS28 < 3.2	3.4 (1.81, 4.99)	LDA and remission	-1.93 (-7.46, 3.59)	LDA	0.449
Remission: DAS28 < 2.6	5.33 (1.2, 9.47)				

HDA, high disease activity; MDA, moderate disease activity; LDA, low disease activity; DAS28, disease activity score at 28 joints.

Table 2. Comparison of ultrasound erosion scores between the DAS28 disease severity categories.

group 3 (PD positive and GS < median score); group 4 (PD negative and GS < median score). US erosion scores were compared (a) between patients in groups 1 vs. 4, groups 2 vs. 4 and groups 3 vs. 4 and (b) between patients with high (> 5.1), moderate (≥ 3.2 and ≤ 5.1) and low (≥ 2.6 and < 3.2) DAS28 scores versus those in DAS28 remission (< 2.6). All comparative analyses were performed using the unpaired student's T-test.

Results: 1080 joints and 1800 joint recesses from bilateral elbows, wrists, ankles and small joints of the hands and feet were scanned in 30 adult RA patients with the following baseline characteristics: 76.7 % Chinese; 93.3% female; mean (SD) DAS28 of 3.58 (1.20); mean (SD) disease duration of 70.3 (61.2) months; 90% on conventional DMARD (methotrexate, sulfasalazine, hydroxychloroquine and/or leflunomide). Table 1 summarizes the comparison of US erosion scores between the 4 ultrasound patient groups. The mean (95% CI) US erosion scores were significantly higher (p=0.026) for groups 1 vs. 4 (9.75 (6.69, 12.81) vs. 3.4 (1.11, 5.69), respectively) with a difference (95% CI) of 6.35 (0.78, 11.83). US erosion scores were, however, not significantly different (P-values all >0.05) for patients in groups 2 vs. 4 and 3 vs. 4. Table 2 summarizes the comparison of US erosion scores between the DAS28 disease severity categories. The US erosion scores of patients with high, moderate and low DAS28 disease severity categories were not significantly different (P-values all >0.05) from that of patients in DAS28 remission.

Conclusion: US joint inflammation assessment – and not DAS28 – is reflective of the severity of joint damage in RA patients. Specifically, the severity of US-detected bone erosions was significantly greater when both positive PD and a greater degree of GS joint inflammation were present. This association was not observed when either component was absent. Given this advantage of US joint inflammation assessment over DAS28 assessment, the former may po-

tentially help identify RA patients with a more aggressive disease course requiring more intensive treatment, although this will need to be further evaluated in future studies.

Disclosure: Y. Tan, None; **H. Li**, None; **J. Allen Jr**, None; **J. Thumboo**, None.

Abstract Number: 1534

Combined Thermal and Ultrasound Imaging in Rheumatoid Arthritis Is Superior to Either Imaging Alone in Terms of Correlation with the 28-joint Disease Activity Score

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Background/Purpose: Combined thermal and ultrasound (US) imaging modalities in detecting joint inflammation in rheumatoid arthritis (RA) has not been evaluated relative to thermal or US imaging alone. Therefore, we aim to compare outcomes of the combined imaging modalities versus single imaging modality using the routinely performed 28-joint disease activity score (DAS28).

Methods: Thermography and ultrasonography were performed on 22 joint sites (bilateral hands and wrists) at the same study visit. Maximum (Tmax), minimum (Tmin) and average (Tavg) temperatures at each joint were recorded. For each patient, the lowest Tmin temperature among all joints testing negative for joint inflammation by both US power Doppler (PD) and grey-scale (GS) was defined as the patient's control temperature and subtracted from Tmax, Tmin and Tavg temperatures at all 22 joints for that patient. Differences with the control temperature for the respective parameters (Tmax, Tmin and Tavg) were then summed across all joints to obtain MAX, MIN and AVG values for each patient. US PD and GS joint inflammation scores (graded semi-quantitatively 0-3 at each joint recess), respectively, were summed for the 22 joints to obtain Total PD and Total GS scores per patient. MAX (PD), MIN (PD) and AVG (PD) represent the results of combined thermal and US PD imaging. As a greater PD vascularity indicates more inflammation at the joints, when a patient's Total PD score was greater than the median value, to increase its weightage to the combined imaging scores, the patient's MAX (PD), MIN (PD) and AVG (PD) were derived by multiplying MAX, MIN and AVG by a factor of 2. Otherwise, the patient's MAX (PD), MIN (PD) and AVG (PD) remained the same as the MAX, MIN and AVG (without multiplying by 2).

Results: In this cross-sectional study, 814 joints were studied in 37 RA patients with the following patients' baseline characteristics: mean (SD) age, 56.5 (13.8) years; majority female, 28/37 (75.7%); majority Chinese, 28/37 (75.7%); mean (SD) disease duration of 30.9 (45.3) months; mean (SD) DAS28 of 4.43 (1.12); 31/37 (83.8%) patients were on one or more DMARDs (methotrexate, sulfasalazine, hydroxychloroquine and/or tofacitinib). Table 1 summarizes results of the correlation analysis between the imaging parameters and DAS28. Specifically, only MAX (PD) and AVG (PD) exhibited statistically significant correlation with DAS28 scores (MAX (PD): correlation coefficient (95% CI) 0.393 (0.079, 0.636), P=0.016; AVG (PD): 0.376 (0.060, 0.624), P=0.022). Figure 1 shows the scatter plots for the combined thermal and US imaging parameters versus DAS28. Table 2 summarizes the results of the simple linear regressions

Parameter	Correlation coefficient (95% CI)	P- value	Parameter	Correlation coefficient (95% CI)	P- value
MAX	0.258 (-0.072, 0.537)	0.123	Total GS	0.186 (-0.147, 0.481)	0.270
MIN	0.141 (-0.192, 0.445)	0.406	**MAX (PD)**	**0.393 (0.079, 0.636)**	**0.016***
AVG	0.235 (-0.096, 0.52)	0.161	**AVG (PD)**	**0.376 (0.060, 0.624)**	**0.022***
Total PD	0.247 (-0.084, 0.528)	0.141	MIN (PD)	0.298 (-0.029, 0.567)	0.074

*Statistically significant at P<0.05

Table 1. Correlation between imaging parameters and DAS28.

	Prediction of DAS28	
Parameter	Coefficient (95% CI)	P-value
Total PD	0.0978 (-0.0295, 0.2252)	0.1411
Total GS	0.0304 (-0.0228, 0.0836)	0.2704
MAX	0.0133 (-0.0032, 0.0298)	0.1231
AVG	0.0150 (-0.0056, 0.0356)	0.1613
MIN	0.0113 (-0.0150, 0.0375)	0.4060
MAX (PD)	0.0086 (0.0019, 0.0153)	**0.0161**
AVG (PD)	0.0112 (0.0021, 0.0203)	**0.0217**
MIN (PD)	0.0122 (-0.0008, 0.0251)	0.0736

Statistically significant: * p<0.05

Table 2. Results of linear regression between the imaging parameters and DAS28.

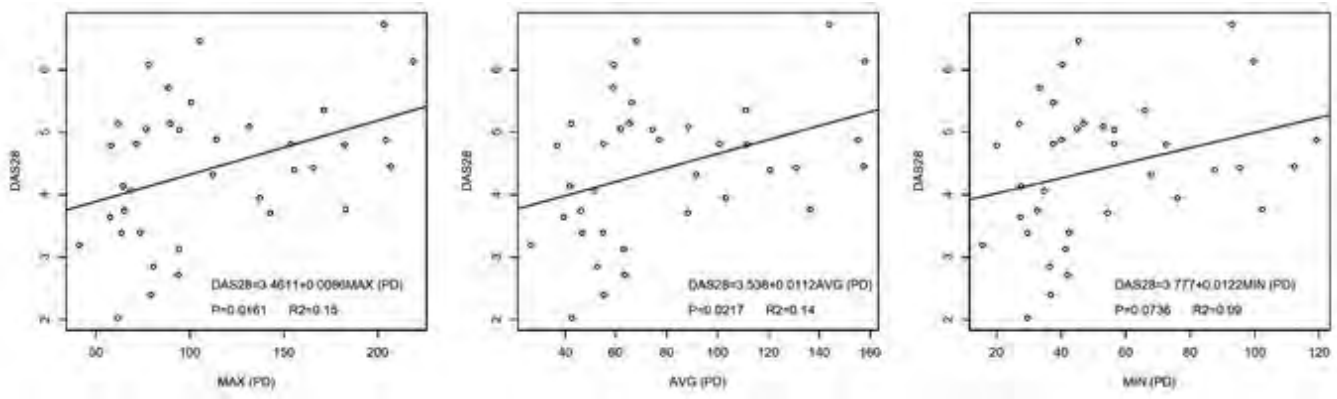

Figure1. Scatter plots for the combined thermal and ultrasound imaging parameters versus DAS28.

between the imaging parameters and DAS28. Specifically, only MAX (PD) and AVG (PD) were shown to be significantly correlated with DAS28 (MAX (PD): coefficient (95% CI), 0.0086 (0.0019, 0.0153); P=0.0161); AVG (PD): coefficient (95% CI), 0.0112 (0.0021, 0.0203); P=0.0217).

Conclusion: For the first time ever, combined thermal and US imaging in RA have been shown to be superior to either imaging modality alone in terms of correlation with DAS28. Longitudinal studies testing the use of combined thermal and US imaging in RA will be required.

Disclosure: Y. Tan, None; **C. Hong**, None; **H. Li**, None; **J. Allen Jr**, None; **J. Thumboo**, None.

Abstract Number: 1535

Frequency and Anatomic Distribution of Magnetic Resonance Imaging Lesions in the Sacro-iliac Joints of Healthy Subjects and Patients with Spondyloarthritis

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Background/Purpose: Lesions detected by magnetic resonance imaging (MRI) of the sacroiliac joints are critical to the diagnosis of non-radiographic axial spondyloarthritis. However, some lesions, such as bone marrow edema (BME), usually observed in patients with spondyloarthritis may be encountered in other conditions. BME have been described in patients with nonspecific back pain, healthy subjects, women with postpartum and in athletes. Moreover, it has recently been shown that structural lesions of the sacroiliac joint, such as erosions and fat metaplasia, may be present in healthy subjects.

To evaluate and compare the frequency and location of lesions (BME, subchondral condensation, fat metaplasia, erosions and ankylosis) on MRIs of the sacroiliac joint of healthy individuals and patients with spondyloarthritis.

Methods: This is a retrospective study conducted at the University Hospital of Besançon including 200 patients, each having received an MRI of the sacroiliac joints in coronal section and in T1 and Semicoronal short tau inversion recovery sequences. Two experienced readers evaluated the whole set of images to detect erosions, subchondral condensation, fat metaplasia, BME and ankylosis according to the definitions established by the Assessment of SpondyloArthritis MRI working group. We subdivided a sacroiliac joint into three segments, upper, medium and lower along the cranio-caudal axis. Within the middle segment, we retained 3 portions: anterior, intermediate, posterior along the ventro-dorsal axis. Overall, one sacroiliac joint contained five quadrants on the iliac side and five quadrants on the sacral side. Thus, there were 20 quadrants defined for the two sacroiliac joints of each patient.

Results: Collected MRI of 200 patients (62% female), 96 patients had spondyloarthritis (mean age 37.4±11.8 years, 48% HLA-B27+), 104 subjects were unaffected by the disease (mean age 39.9±11.6 years, 11% HLA-B27+). Of the 96 spondyloarthritis patients, 62 (65%) had inflammatory buttock pain compared to 26 (25%) in the group without spondyloarthritis. BME was seen in 62 (65%) patients with spondyloarthritis mainly in the iliac quadrant of the intermediate middle segment and in 21 (20%) patients without spondyloarthritis predominantly in the antero-middle quadrant. There were equal BME in women and men with spondyloarthritis. Subchondral condensation occurred in 45% of patients without spondyloarthritis, mostly in the antero-middle quadrant and in 36% of patients with spondyloarthritis. Fat metaplasia was present in 35% of spondyloarthritis patients and in 23% of control patients. Erosions were seen in 31% of healthy patients and in 61% of patients with spondyloarthritis.

Conclusion: In this large retrospective cohort, we observed a significant frequency of inflammatory but also structural lesions on MRIs of sacroiliacs joints from healthy patients, which could lead to the misdiagnosis of spondyloarthritis. Fine identification of the location of these lesions is crucial to avoid erroneous diagnosis.

Disclosure: S. Hecquet, None; **J. Lustig**, None; **F. Verhoeven**, None; **M. Chouk**, None; **S. Aubry**, None; **D. Wendling**, None; **C. Prati**, None.

Abstract Number: 1536

Ultrasound as an Imaging Biomarker of Early Response to Tocilizumab and Methotrexate in Early Rheumatoid Arthritis, TOVERA – a Longitudinal Study

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Background/Purpose: The combination of methotrexate (MTX) and tocilizumab (TCZ) has been proven to be superior to MTX alone in early rheumatoid arthritis (RA)[1] and was able to prevent radiographic progression. Ultrasound (US) has become a valid imaging modality in managing RA. Together with clinical examination, US may allow a comprehensive monitoring of response to therapy. So far, few data are available concerning the early response to TCZ plus MTX in very early RA (VERA).

In this study we aimed to assess the early US response to TCZ plus MTX in VERA, DMARD-naïve patients.

Methods: In this open-label, single-arm study, VERA patients received TCZ (162 mg/week, subcutaneously) and MTX (15-20 mg/week, *per os*) for 24 weeks as induction therapy, followed by MTX as maintenance therapy. RA was diagnosed according to the 2010 ACR/European league against rheumatism (EULAR) criteria. All patients who fulfilled the inclusion criteria (ClinicalTrials.gov: NCT02837146) underwent blood tests, clinical and ultrasound examinations at the predefined time-points: 0,2,4,8,12,24,32,48,54 weeks (w). Ultrasound examination of 34 joints (elbows, wrists, MCP [1-5, bilateral], PIP ([2-5, bilateral], knees, ankles and MTP [2-5, bilateral]) was performed blindly to clinical data. Gray-scale (GS), power-Doppler (PD) scores, and the global *OMERACT*-EULAR synovitis score (*GLOESS*) were assessed in each joint. The sum of individual scores was calculated for 17-joint score (JS) (whole joint set), 10-JS (wrists, MCP, ankles and MTP joints), 12-JS[2], and 7-JS[3].

Results: Forty-four patients (77% women), aged 46.7 ± 12.4 years, completed the 24-week period. Two-thirds (72.7%) were positive for anti-citrullinated protein antibody (ACPA) and 18.2% had bone erosions. At baseline, the mean 28 swollen joints count (28-SJC) was 7.55± 4.5, mean disease activity score (DAS28)-CRP score was 5.2 ± 0.15, mean simplified clinical activity score (SDAI) was 31.4 ± 1.9, mean clinical activity score (CDAI) was 29.1 ± 1.8 and mean health assessments questionnaire (HAQ) score was 1.3 ± 0.1. The C-reactive protein (CRP) decreased significantly at 2w ($p< 0.05$) and, accordingly DAS28-CRP score decreased significantly at 4w ($p< 0.05$). The 28-SJC and CDAI scores decreased significantly at 8w ($p< 0.05$). The HAQ and visual analogue scale (VAS) disease activity reported by patients decreased significantly at 8w ($p< 0.05$) and VAS fatigue at 12w ($p< 0.05$).

The GLOESS and GS scores allowed us detecting the earliest significant treatment response at 2w and PD scores at 4w ($p< 0.05$). Among US joint subsets, 17-JS ($p< 0.01$), 12-JS ($p< 0.05$) and 10-JS ($p< 0.05$) were able to detect the earliest treatment response at 2w. The 7-joint score detected the earliest response at 4w, both in GS and PD ($p< 0.05$).

Conclusion: US scores were able to detect therapeutic response to TCZ plus MTX earlier than clinical scores and may therefore be a promising imaging biomarker.

References

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3. Backhaus M *et al.* Arthritis Rheum 2009; 61: 1194-1201.

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Abstract Number: 1537

Usefulness of Ultrasound Assessment of Sarcopenia in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcopenia, the age-related loss of muscle mass and function, is associated with numerous risk factors, including rheumatoid arthritis (RA). Although standard diagnostic tool for sarcopenia include dual-energy X-ray absorptiometry and bioelectrical impedance analysis (BIA), ultrasound (US) has a unique advantage to measure muscle quantity as well as muscle quality. Muscle echogenicity reflect intramuscular lipids and fibrosis, and it can be used as a marker of muscle quality. We sought to determine usefulness of US in discriminating patients with RA with sarcopenia from those without. We also assessed correlation between US echogenicity and various clinical measures of physical function and muscle volume.

Methods: 50 female patients with RA, aged 50 years or older, who fulfilled 2010 ACR/EULAR RA Classification Criteria were recruited and cross-sectionally studied. Clinical parameters such as age, BMI, CDAI, pharmacological treatments including corticosteroid and biologics, as well as comorbidities such as diabetes mellitus were assessed. Diagnosis of sarcopenia was based on 2019 updated Asian Working Group for Sarcopenia definition. Because handgrip test is often difficult for RA patients, chair-stand test was selected as primary assessment tool of physical function. BIA was used for the measurement of muscle volume. For US analysis, we used LOGIQ S8 (GE, USA; linear-array transducer) equipment. Cross sectional images of biceps brachii (BB), vastus lateralis (VL), and rectus femoris (RF) were obtained at predetermined position bilaterally. Mean US echogenicity was then calculated. On measuring US

	Sarcopenia	Non-sarcopenia	P value
Number	14 (28%)	36 (72%)	
Age (years)	77.5 ± 6.42	65.89 ± 8.87	**0.00005**
BMI	23.48 ± 2.76	23.77 ± 4.4	0.824
Duration (months)	196.08 ± 217.98	80.12 ± 84.25	**0.0117**
ACPA (%)	34 (68%)	16 (32%)	0.309
RF (%)	10 (71.43%)	31 (75.61%)	0.202
CDAI	6.2 ± 5.91	2.84 ± 2.34	**0.006**
Current CS use (%)	4 (28.57%)	5 (14.28%)	0.254
Current Biologics use (%)	13 (92.86%)	16 (45.71%)	**0.0031**
Joint surgery (%)	6 (42.86 %)	7 (20%)	0.152
SARC-F	4.14 ± 2.07	1.4 ± 1.48	**0.000004**
BB echogenicity	80.89 ± 17.89	73.67 ± 17.74	0.218
VL echogenicity	78.37 ± 18.14	62.67 ± 16.05	**0.0061**
RF echogenicity	89.18 ± 17.82	73.63 ± 16.45	**0.0071**

Table 1. Clinical and imaging features of RA patients with or without sarcopenia. Abbreviation. ACPA: anti-citrullinated peptide antibodies. BMI: body-mass index. CS: corticosteroid. RF: rheumatoid factor.

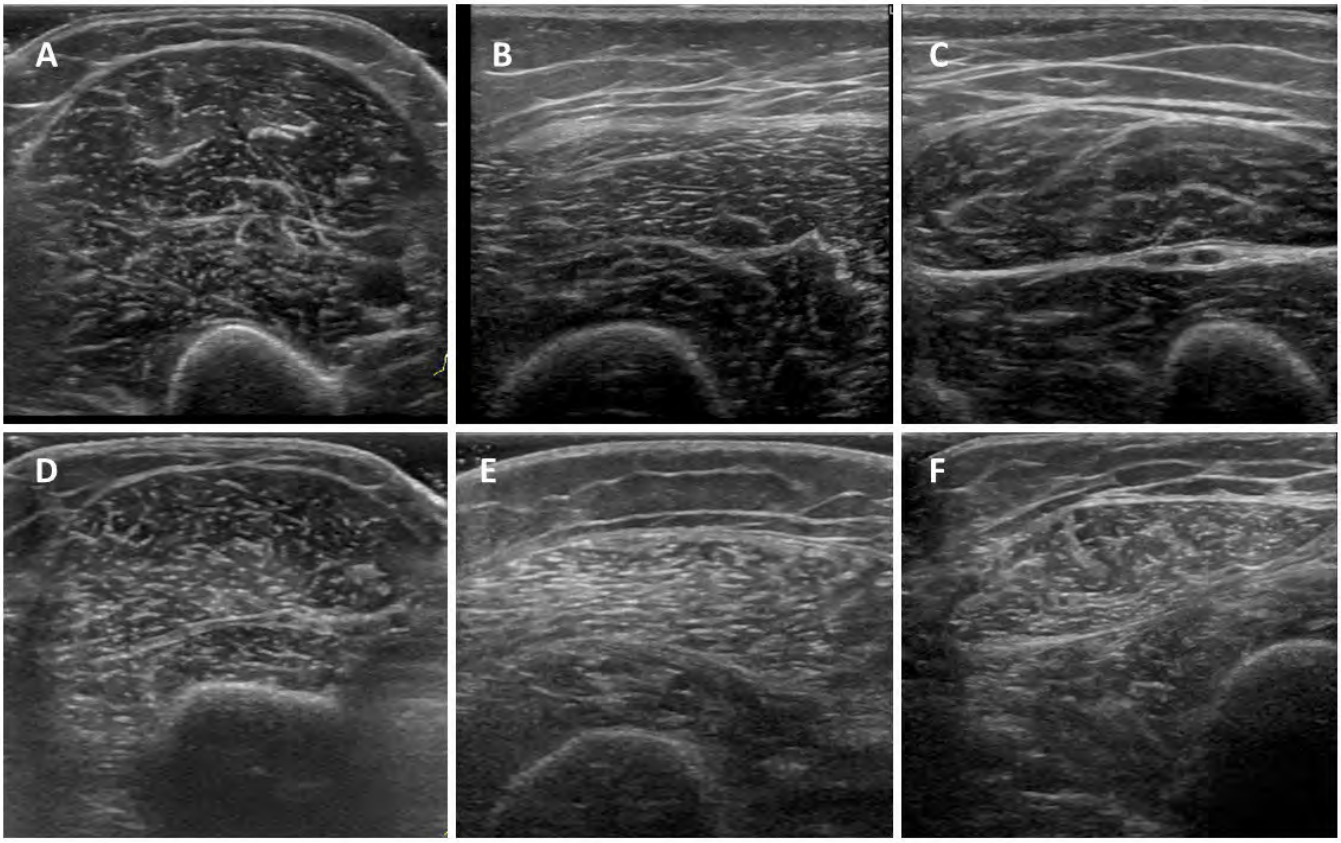

Figure 1. US image of biceps brachii (A, D), vastus lateralis (B, E), and rectus femoris (C, F). A-C. A 60 year old patient with normal physical function and muscle volume. D-F. A 84 year old patient with sarcopenia. The latter patient showed higher intramuscular echogenicity of vastus lateralis and rectus femoris.

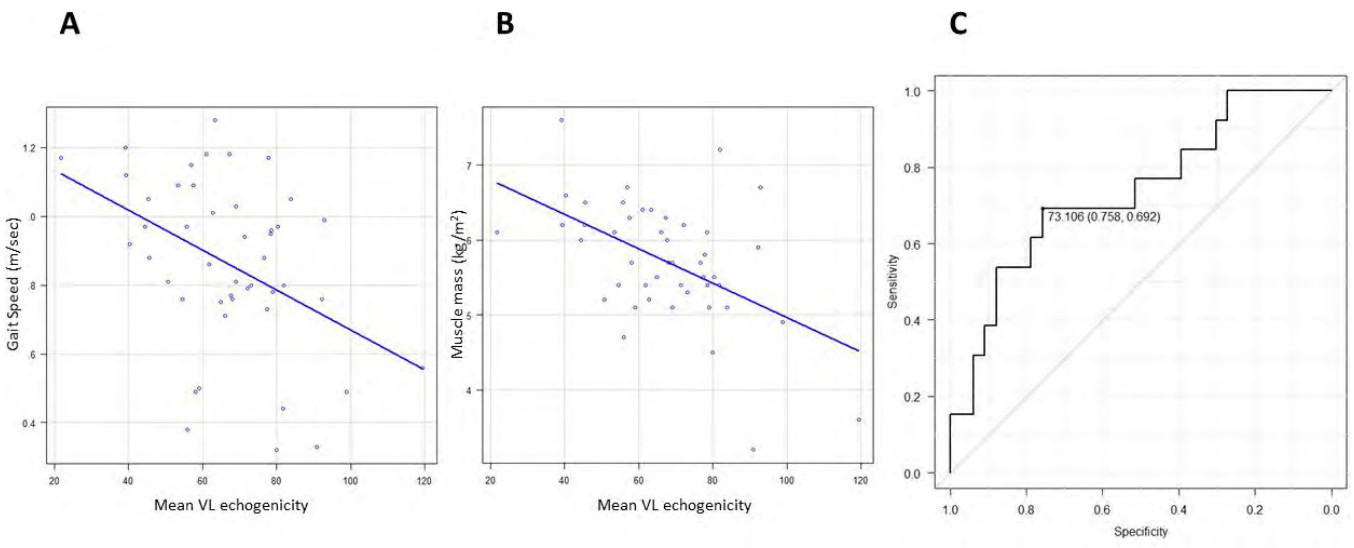

Figure 2. Significant correlation between US echogenicity of VL and gait speed (A), and muscle volume (B). US echogenicity of VL showed moderate discriminative capacity with the area under the ROC curve of 0.737 (95% CI, 0.569 – 0.904).

echogenicity, regions of interest were manually drawn by using ImageJ. All statistical analyses were performed using EZR, a graphical user interface for R. The p value of < 0.05 was determined as the cutoff for statistical significance.

Results: Mean age was 69.7 ± 7.23. 14 patients (28 %) were diagnosed as sarcopenia. 34 patients (68%) were positive for anti-CCP antibody. Age, disease duration, SARC-F, CDAI, current biologics use were significantly associated with presence of sarcopenia. Patients with sarcopenia had significantly increased US echogenicity of VL compared to those without (78.4 ± 18.15 vs 62.7 ± 16.05, p = 0.006). US echogenicity of VL showed the area under the ROC curve of 0.737 (95% CI, 0.569 – 0.904). In addition, US echogenicity showed significant negative correlation between gait speed (r = -0.507, p = 0.0003) and muscle volume (r = -0.423, p = 0.003).

Conclusion: US echogenicity of VL was useful in discriminating the RA patients with sarcopenia from those without. In addition, it showed significant correlation with both muscle volume and physical function. We suggest muscle US can be used as an assessment tool of sarcopenia in patients with RA and further studies incorporating more patients and longitudinal follow up would be needed.

Disclosure: T. Yoshida, None; **Y. Kumon**, None.

Abstract Number: 1538

Doppler Ultrasound Predicts Successful Discontinuation of Biological DMARDs in Rheumatoid Arthritis Patients in Sustained Clinical Remission

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Imaging of Rheumatic Diseases Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: There is an increasing interest in tapering or even discontinuing biological disease-modifying anti-rheumatic drugs (bDMARDs) in rheumatoid arthritis (RA) patients in sustained remission. The aim was to assess the potential role of ultrasound (US) for predicting successful tapering and successful discontinuation.

Methods: Patients with RA on bDMARDs in sustained disease activity score remission (DAS28-CRP < 2.6) and no radiographic progression the previous year were included(1). At baseline, clinical assessment, MRI and x-ray were performed as part of a standardized tapering regimen. Further, synovitis in 24 joints was scored 0-3 by US using the OMERACT scoring system for synovitis. At patient level, greyscale (GS), Doppler and the Global OMERACT/EULAR US Synovitis Score GLOESS synovitis sum scores were calculated. The bDMARD was reduced to 2/3 of standard dose at baseline, ½ dose after 16 weeks, and discontinued after 32 weeks. If flare occurred (defined as either DAS28-CRP≥2.6 and ΔDAS28-CRP≥1.2 from baseline, or erosive progression on X-ray and/or MRI) tapering was stopped and the dose escalated to the previous level. Final state of treatment was assessed after 2-years.

Logistic regression analyses were used to identify factors associated with successful tapering and successful discontinuation at 2 years follow-up. For all models, variables shown in Table 1 except MRI were included (separate models for ultrasound “24-joint-score” and “hands-only score”). Additional analyses including MRI variables (combined inflammation and combined damage) were performed. Missing data in independent variables were imputed with multiple imputation by chained equations (50 imputed datasets). Variables with p< 0.25 in univariate analyses were included in the initial multivariate model. Backward selection was performed to derive the final multivariate models using a significance level of 0.05.

Table 1 Baseline characteristics

	All patients n=125	Successful tapering n=76	Full dose n=47	p-value	Discontinued n=19	Not discontinued n=104	p-value
Demographic characteristics							
Women, %	67%	59%	81%	**0.022**	68%	67%	1
Age, median (IQR), years	60 (48-67)	60 (47-67)	60 (48-68)	0.471	56 (49-64)	60 (47-67)	0.595
Disease duration, median (IQR), years	11 (7-18)	11 (7-16)	12 (7-20)	0.250	10 (6-13)	11 (7-19)	0.280
Current smoker, %	18%	19%	18%	1	29%	16%	0.305
Time in remission before tapering, median (IQR), years	2 (1-3)	2 (1-3)	2 (1-3)	0.402	2 (2-3)	2 (1-3)	0.665
Concomitant DMARD, %	88%	86%	91%	0.404	95%	87%	0.463
Number of previous bDMARDs, %				**0.032**			0.273
0	64%	71%	51%		84%	60%	
1	25%	24%	28%		16%	27%	
2	6%	3%	13%		0%	8%	
≥3	5%	3%	9%		0%	6%	
RF positive, %	69%	66%	72%	0.576	37%	74%	**0.003**
Anti-CCP positive, %	79%	76%	85%	0.344	74%	81%	0.537
Clinical measures							
HAQ (0-3), median (IQR)	0.2 (0.0-0.8)	0.1 (0.0-0.6)	0.4 (0.0-1.0)	0.070	0.0 (0.0-0.4)	0.2 (0.0-0.8)	0.211
DAS28-CRP, median (IQR)	1.8 (1.6-2.1)	1.8 (1.6-2.1)	1.8 (1.6-2.1)	0.747	1.8 (1.6-1.9)	1.8 (1.7-2.1)	0.338
ACR/EULAR remission, %	38%	42%	30%	0.238	42%	37%	0.839
Radiographic measures							
TSS (0-448), median (IQR)	14 (4-46)	10 (4-28)	20 (3-52)	0.176	9 (1-38)	15 (5-45)	0.246
Presence of X-ray erosion, %	78%	76%	83%	0.514	58%	83%	**0.033**
MRI measures							
Combined inflammation score (0-129), median (IQR)	7 (3-12)	6 (2-12)	10 (5-16)	**0.018**	6 (2-10)	7 (3-13)	0.400
Combined damage score (0-314), median (IQR)	4 (1-18)	2 (1-11)	11 (3-39)	**0.003**	4 (1-14)	5 (1-20)	0.709
Ultrasound inflammatory measures							
Grey scale sum score - hands-only (0-30), median (IQR)	2 (0-5)	2 (0-5)	3 (1-5)	0.302	1 (0-2)	3 (1-5)	**0.023**
Grey scale sum score – 24-joints (0-72), median (IQR)	5 (2-9)	5 (2-9)	5 (3-9)	0.692	3 (2-6)	5 (2-9)	0.090
Doppler sum score hands-only (0-30), median (IQR)	0 (0-1)	0 (0-1)	0 (0-2)	0.228	0 (0-0)	0 (0-1)	**0.035**
Doppler sum score - 24-joints (0-72), median (IQR)	0 (0-1)	0 (0-1)	1 (0-2)	0.121	0 (0-0)	0 (0-2)	**0.007**
GLOESS hands-only (0-30), median (IQR)	2 (0-5)	2 (0-5)	3 (1-5)	0.257	1 (0-2)	3 (1-5)	**0.017**
GLOESS - 24-joints (0-72), median (IQR)	5 (2-9)	5 (2-9)	5 (3-9)	0.632	3 (2-6)	5 (3-9)	0.074

Successful tapering: patients on less than full dose of bDMARD at 2-year follow-up. Full dose: patients on full dose of bDMARD at 2-year follow-up. Discontinued: patients that discontinued of bDMARDs at 2-year follow-up. Not discontinued: patients that were not discontinued of bDMARDs at 2-year follow-up. p-values for differences between treatment groups by Kruskal-Wallis test for numeric measures and chi-squared test or Fisher's exact test, as appropriate, for binary and categorical measures; bold indicates p-values<0.05. Anti-CCP: Anti-Cyclic Citrullinated Protein antibodies; ACR: American College of Rheumatology; bDMARD: biological Disease-Modifying Antirheumatic Drug; CRP: C-Reactive Protein; DAS28-CRP: 28-joint Disease Activity Score with CRP; DMARD: Disease-Modifying Antirheumatic Drug; EULAR: European League Against Rheumatism; GLOESS: Global OMERACT/EULAR Ultrasound Synovitis Score; HAQ: Health Assessment Questionnaire; IQR: Interquartile Range; RF: IgM- Rheumatoid Factor; MRI combined inflammation score (the sum of synovitis(0-3), tenosynovitis(0-3), bone marrow oedema (0-3)); MRI combined damage score (the sum of bone erosions (0-10) and joint space narrowing (0-4)); TSS: Total Sharp van der Heijde score. 24 joints: bilateral wrist, metacarpophalangeal joint 2-5, elbow, knee, ankle and metatarsophalenageal joint 2-5.

Results: One-hundred-and-twenty-five patients completed 2-year follow-up. At 2 years, 47 patients (38%) were back on full dose, 59 (46%) tapered to 2/3 or ½ dose and, 19 (15%) had discontinued the bDMARD. A lower number of previous bDMARDs was an independent predictor for successful tapering (OR=0.54; p=0.006) (table 2). Negative

Table 2 Multivariate logistic regression analyses for successful tapering and successful discontinuation in imputed data after applying backward selection (MRI not included). 123 patients were available for analyses.

	Successful tapering					
	Ultrasound			Ultrasound (hands only)		
	OR	95% CI	p-value	OR	95% CI	p-value
Number of previous bDMARDs	0.54	(0.33 - 0.84)	0.006	0.54	(0.33 - 0.84)	0.006
	Successful discontinuation					
	Ultrasound			Ultrasound (hands only)		
	OR	95% CI	p-value	OR	95% CI	p-value
RF positive	0.26	(0.09 - 0.74)	0.012	0.20	(0.07 - 0.56)	0.002
Doppler sum score	0.44	(0.15 - 0.87)	0.013			

p-values by likelihood ratio tests. bDMARD: biological Disease-Modifying Antirheumatic Drug; CI: confidence interval; OR: odds ratio; RF: IgM-Rheumatoid Factor.

IgM-RF (OR=0.26; p=0.012) and low Doppler sum score for 24 joints (OR=0.44; p=0.013) but not for hands alone, predicted successful discontinuation. Including MRI variables in the model did not affect the predictive value of Doppler sum score. GLOESS sum score was unable to predict successful tapering or discontinuation.

Conclusion: A low Doppler 24-joint sum score and negative IgM-RF at baseline were independent predictors for successful discontinuation of bDMARDs at 2-years' follow-up. Low number of previous bDMARD, but not baseline US, predicted successful tapering.

Ref: 1. Brahe CH et al. Rheumatology (Oxford).2019;58:110-119.

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Abstract Number: 1539

Diagnostic Value of Ultrasound Halo Count and Halo Score in Giant Cell Arteritis: A Retrospective Study from Routine Care

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Ultrasound (US) of temporal (TA) and axillary arteries is recommended as the first imaging modality in patients with suspected predominantly cranial giant cell arteritis (GCA) and recently, two US scoring systems, the halo count and Halo Score, have been proposed to quantify the extent of vascular inflammation. We aim to assess the diagnostic value of both scoring systems and its association with systemic inflammation in patients with GCA seen in routine clinical practice.

Methods: This is a retrospective observational study including patients suspected of having GCA over a 9-month period. Baseline clinical and laboratory parameters were retrieved from the electronic health records. All patients underwent bilateral US examination of the three TA segments and extracranial (carotid, subclavian and axillary) arteries as part of a diagnostic fast track pathway (FTP). The FTP is offered to all patients with suspected GCA who will receive an appointment for the US examination within 24 hours. The extent of vascular inflammation was quantified according to the halo count (number of TA segments and axillary arteries with a halo) and the Halo Score (a composite index that incorporates the thickness of each halo). TA biopsy (TAB) was performed according to the treating clinician criteria. The gold standard for GCA was the clinical diagnosis after 6 months of follow-up by the treating clinician. Differences between groups were determined by Chi-squared and Student-t tests, validity was analyzed by receiver operating characteristic (ROC) curves and correlations were determined by Spearman's rank correlation coefficient (rho).

	Total n=58	Patients with GCA n=15	Patients without GCA n=43	p
Age, mean (SD)	74.7 (10.9)	76.5 (10.2)	74 (11.3)	0.431
Sex, no. of female	38 (65.5%)	8 (53.3%)	30 (69.8%)	0.249
Baseline use of steroids, no. of patients	28 (49.1%)	6 (40%)	22 (52.4%)	0.410
Temporal artery biopsy positive n=11, no. of patients	3 (27.3%)	3 (37.5%)	0 (0%)	0.491
TAB lenght (mm) n=11, mean (SD)	5.5 (3.1)	5.9 (3.6)	4.7 (1.5)	0.6
Fullfilling 1990 GCA criteria, no. of patients	13 (22.4%)	5 (33.3%)	8 (18.6%)	0.239
Headache, no. of patients	30 (51.7%)	11 (73.3%)	19 (44.2%)	0.052
Scalp tenderness, no. of patients	4 (6.9%)	2 (13.3%)	2 (4.7%)	0.273
Jaw claudication, no. of patients	10 (17.2%)	7 (46.7%)	3 (7%)	**0.002**
Visual symptoms, no. of patients	10 (17.2%)	5 (33.3%)	5 (11.6%)	0.055
Fever, no. of patients	7 (12.1%)	2 (13.3%)	5 (11.6%)	1
Polymyalgia, no. of patients	27 (46.6%)	10 (66.7%)	17 (39.5%)	0.07
Ocular ischaemia, no. of patients	3 (5.2%)	1 (6.7%)	2 (4.7%)	1
Abnormal TA clinical examination, no. of patients	4 (6.9%)	2 (13.3%)	2 (4.7%)	0.273
CRP (mg/dL), mean (SD)	4.5(6.7)	9.3 (8.8)	2.7 (4.6)	**0.001**
ESR (mm/h), mean (SD)	51.2 (33.7)	65.7 (33.2)	46.1 (33.1)	0.075
Haemoglobin (g/dL), mean (SD)	12.6 (1.7)	11.9 (1.6)	12.9 (1.6)	0.05
Platelets 10^9/L, mean (SD)	266.8 (96)	307.5 (104.1)	252.2 (89.7)	0.081
Positive US findings, no. of patients	15 (25.9%)	13 (86.7%)	2 (4.7%)	**<0.001**
Temporal artery positive US findings, no. of patients	11 (19%)	10 (66.7%)	1 (2.3%)	**<0.001**
Axillary positive US findings, no. of patients	8 (13.8%)	7 (46.7%)	1 (2.3%)	**<0.001**
Temporal artery + Axillary positive US findings, no. of patients	4 (7%)	4 (26.7%)	0 (0%)	**0.003**
Halo sign positive, no. of patients	15 (25.9%)	13 (86.7%)	2 (4.7%)	**<0.001**
Compression sign positive, no. of patients	8 (13.8%)	7 (46.7%)	1 (2.3%)	**<0.001**
Halo Count, mean (SD)	0.7 (1.4)	2.5 (1.9)	0.04 (0.2)	**<0.001**
Halo Score, mean (SD)	4.5 (8.7)	15.8 (9.9)	0.5 (2.7)	**<0.001**

Table 1. Clinical, laboratory and ultrasound findings of patients included in the fast track pathway

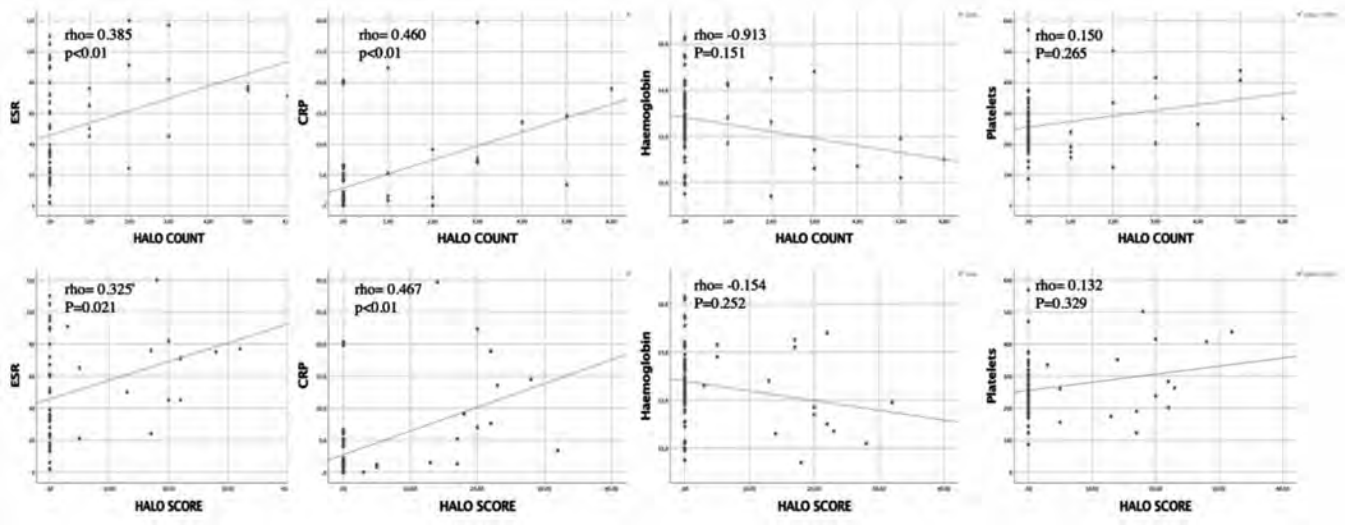

Figure 1. Correlations between halo count and Halo Score with markers of systemic inflammation (ESR CRP, haemoglobin and platelets)

Results: A total of 58 patients were evaluated in the FTP. Mean age was 74.7 years and 65.5% females. Clinical characteristics and US variables of patients with and without GCA are shown in Table 1. A clinical diagnosis of GCA was established in 15 (25.9%) patients. Only 4.7% patients without GCA versus 86.7% with GCA had positive US findings according to the ultrasonographer criteria (sensitivity (Sens) 86.7%, specificity (Spec) 95.3%, positive likelihood ratio (LR+) 18.4 and negative likelihood ratio (LR-) 0.14). Halo count and Halo Score showed similar diagnostic accuracy for a clinical diagnosis of GCA (area under the ROC curve of 0.892 and 0.921 respectively). The optimal cut-off point for halo count was ≥1 (Sens 80%, Spec 95.3, LR+ 17.02, LR- 0.21) and for Halo Score ≥2 (Sens 86.7%, Spec 95.3%, LR+ 18.4, LR- 0.14). Statistically moderate positive correlations were found between halo count and Halo Score and ESR (rho 0.385 and 0.325, p< 0.05) and CRP (rho 0.460 and 0.467, p< 0.01), but not with haemoglobin and platelet count (p >0.05) (Figure 1).

Conclusion: The extent of vascular inflammation by US halo count and Halo Score can help to support the diagnosis of GCA in routine care as they correlate with laboratory markers of systemic inflammation, mainly CRP. Although both scoring systems need further validation, they can be easily implemented in FTP of patients with GCA.

Disclosure: J. Molina Collada, None; **J. Martínez-Barrio**, None; **B. Serrano-Benavente**, None; **I. Castrejon Fernandez**, None; **L. Caballero Motta**, None; **L. Trives Folguera**, None; **J. Alvaro-Gracia**, Abbvie, 2, 5, 8, lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, UCB, 5, 8, Sanofi, 5, 8.

Abstract Number: 1540

Association Between Disease Activity and Left Ventricular Systolic Function in Patients with Rheumatoid Arthritis: A Case-Control Study

Elías Abraham Rodríguez[1], Dionicio Ángel Galarza-Delgado[2], José Ramón Azpiri López[3], Iris Jazmín Colunga Pedraza[4], **Salvador Lugo Pérez**[3], Itzel Corina Zárate Salinas[3], Paola Fernanda Frausto Lerma[4], Alejandra Pérez Villar[4], Mayra Alejandra Reyes Soto[4] and Raymundo Vera[5], [1]Hospital Universitario "José Eleuterio González", Monterrey, Mexico, [2]Rheumatology Service, Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma Nuevo León, Monterrey, Nuevo Leon, Mexico, [3]Cardiology Service, Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma Nuevo León, Monterrey, Mexico, [4]Rheumatology service, Hospital Universitario "Dr. José Eleuterio González", Universidad Autónoma Nuevo León, Monterrey, Mexico, [5]Cardiology Service Hospital Universitario "José Eleuterio González", Monterrey, Mexico

SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with Rheumatoid Arthritis(RA) have a higher prevalence of Cardiovascular Disease (CVD), which is the most common cause of death in this group. Disease activity seems to be an independent risk factor for CVD, but there is controversy at the impact on left ventricular systolic function (LVSF). LVSF may be assessed by conventional methods like left ventricular ejection fraction (LVEF) and myocardial shortening or by novel techniques evaluating myocardial strain such as speckle tracking echocardiography (STE).

Methods: Observational, cross-sectional study. RA patients aged 40-75 years that fulfilled the 2010 ACR/EULAR classification criteria and matched controls were included. Patients with a poor US window, history of previous CVD (ischemic heart disease, cerebrovascular accident or peripheral arterial disease), and pregnancy were excluded. Individuals were evaluated using two-dimensional speckle tracking echocardiography performed and reviewed by 2 certified echocardiographers. LVEF and myocardial strains (circumferential, longitudinal, and radial) were measured; differences were solved by consensus. Descriptive analysis was done with measures of central tendency and dispersion. Student-t and Mann-Whitney U tests were used for comparisons.

Table 1. Demographic and clinical characteristics.

	RA (n= 70)	Control (n= 70)	*P*
Female, n (%)	67 (95.7)	69 (98.6)	NS
Age, mean ± SD	52,4±6,7	52,0±6,1	NS
Type 2 Diabetes Mellitus, n (%)	9 (12.9)	7 (10)	NS
Hypertension, n (%)	14 (20)	16 (22.9)	NS
Dyslipidemia, n (%)	16 (22.9)	17 (24.3)	NS
Active smoking, n (%)	11 (10.9)	8 (16.3)	NS
Disease duration, years, median (q25 –q75)	8.0(3.0-15.0)	-	-
DAS-28-PCR, median (q25 –q75)	3.2(2.1-3.9)	-	-

Table 2. Echocardiographic findings

	LVEF	***P***	**CS**	***P***
RA, mean ± SD	63.0±4.3	**0.022**	-16.4±4.5	NS
Controls, mean ± SD	64.7±3.8		-16.2±4.1	
	LVEF	***P***	**CS**	***P***
Remission or low disease activity, median (q25 –q75)	64.0(60.0-66.0)	NS	-15.1(-17.2- -12.2)	**0.006**
Moderate and high diseases activity, median (q25 –q75)	63.0(60.0-66.0)		-18.1(-22.0- -13.9)	

***LVEF**= Left ventricular ejection fraction*
***CS**= Circumferential strain*

Results: A total of 140 subjects were included. Demographic and clinical characteristics are shown in Table 1. RA patients were divided into 2 groups, according to disease activity by DAS 28-CRP (remission or low activity and moderate or high activity). Echocardiographic parameters were compared between the RA group and controls also between the 2 groups in which RA patients were divided by disease activity Table 2. The LVEF was lower in RA subjects compared with controls (p= 0.022), however, LVEF was normal (> 52% in men and >54% in women) in both groups. There was a significant difference in the circumferential strain (CS) between RA patients based on the disease activity by DAS 28-CRP (p= 0.006).

Conclusion: The decrease in circumferential strain depends on disease activity. Myocardial strain by speckle tracking echocardiography may detect early myocardial dysfunction in RA. The rheumatologist needs to establish an appropriate treatment to achieve the disease remission or low disease activity, as there is an impact of the disease activity on the myocardial function.

Disclosure: E. Rodríguez, None; **D. Galarza-Delgado**, None; **J. Azpiri López**, None; **I. Colunga Pedraza**, None; **S. Lugo Pérez**, None; **I. Zárate Salinas**, None; **P. Frausto Lerma**, None; **A. Pérez Villar**, None; **M. Reyes Soto**, None; **R. Vera**, None.

Abstract Number: 1541

Ultrasound in Knee Osteoarthritis: Reader Performance, Sonographic Features, and Correlation with Radiographic Findings

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Radiography is the most widespread imaging technique used in the evaluation of knee osteoarthritis (KOA), and MRI is known to be specific in characterization of cartilage disease. However, both modalities have their limitations, and there remains need for a reproducible and widely available imaging technique for characterization of KOA disease severity. The utility of ultrasound (US) in inflammatory arthritis is well documented. In KOA, however, the typical sonographic findings are less clear, and can be operator dependent. This study aims to describe sonographic features of KOA, assess reader reliability, and correlate to radiographic findings.

Methods: 161 patients with end stage KOA were prospectively enrolled two weeks prior to knee replacement to undergo knee ultrasound. 31 sonographic features pertinent to KOA were assessed, including osteophyte size, meniscal extrusion (Figure 1), synovial thickness and cartilage erosion. Bangdiwala's B statistic and intraclass correlation coefficient (ICC) were used to assess rater agreement and interrater reliability, respectively, for 2 raters in 75 knees. Spearman's rank correlation (ρ) was used to assess for association between US and radiographic findings.

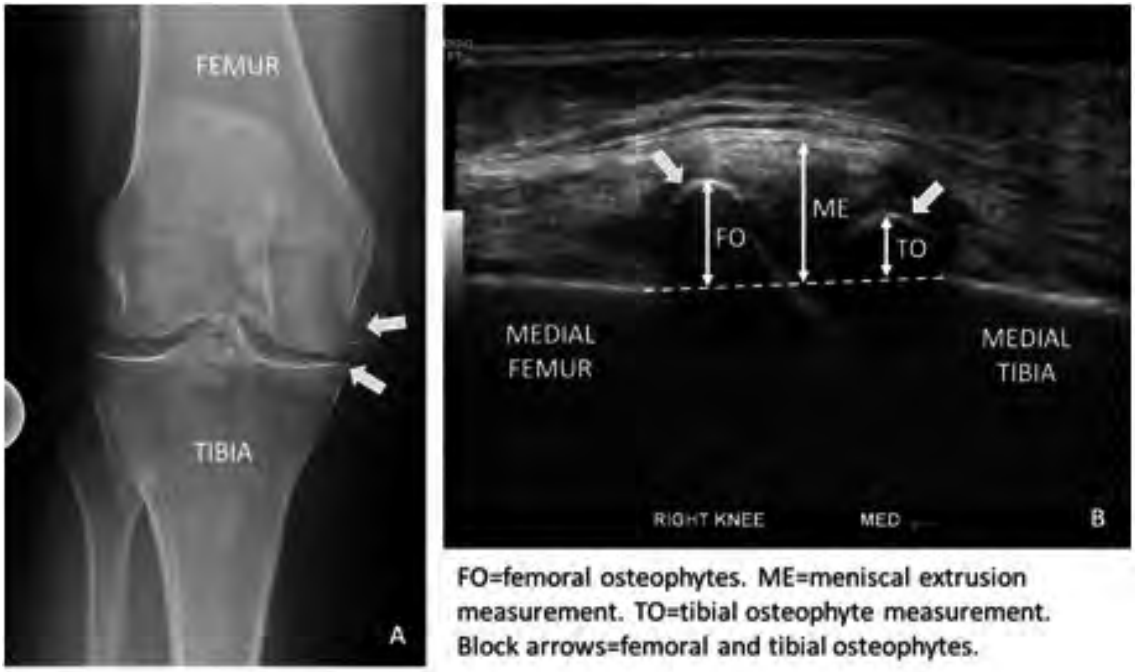

Figure 1. Radiograph of the right knee (A) with corresponding sonographic image of the medial knee (B) in end stage knee osteoarthritis. Measurement technique for femoral and tibial osteophyte and meniscal extrusion depicted.

Ultrasound Metric	X-Ray Metric	N	Spearman's ρ	95% CI	p-value
Medial Joint Line Meniscal Extrusion	KL Grade of Knee OA	144	0.31	(0.15, 0.45)	<.001
Medial Joint Line Meniscal Extrusion	Degrees of Varus	81	0.24	(0.03, 0.44)	0.028
Medial Joint Line Meniscal Extrusion	Degrees of Valgus	62	-0.48	(-0.65, -0.26)	<.001
Lateral Joint Line Meniscal Extrusion	KL Grade of Knee OA	143	0.17	(0.01, 0.33)	0.037
Lateral Joint Line Meniscal Extrusion	Degrees of Valgus	65	0.44	(0.22, 0.62)	<.001
Medial Joint Line Osteophytes on Tibial Joint Line	KL Grade of Knee OA	137	0.31	(0.15, 0.45)	<.001
Medial Joint Line Osteophytes on Tibial Joint Line	Degrees of Varus	80	0.21	(-0.01, 0.41)	0.06
Medial Joint Line Osteophytes on Femoral Joint Line	KL Grade of Knee OA	141	0.38	(0.23, 0.51)	<.001
Lateral Joint Line Osteophytes on Femoral Joint Line	KL Grade of Knee OA	139	0.3	(0.13, 0.44)	<.001
Lateral Joint Line Osteophytes on Femoral Joint Line	Degrees of Valgus	63	0.42	(0.19, 0.60)	<.001

Table 1: Significant correlations between ultrasound and radiographic metrics in patients with end stage knee osteoarthritis.

Results: In this cohort of 161 knees, 94 (58%) revealed no to mild suprapatellar synovial thickness. Joint line osteophytes tended to be larger medially, and on the femoral side. The degree of meniscal extrusion was worse at the medial side. There was almost perfect to perfect (0.81-1) rater agreement for 14 of 24 features assessed, includ-

ing presence of effusion, synovial hyperemia, degree of synovial thickening, patella tendinopathy. Substantial rater agreement (0.70-0.80) was found for medial/lateral joint line synovial thickening, degree of cartilage erosion, presence of Baker's cyst, and quadriceps tendinosis. Measures of synovial thickness, osteophyte size, degree of meniscal extrusion showed excellent interrater reliability (0.73-0.99), while interrater reliability of Baker's cyst wall thickness measurement was fair (0.53). Degree of medial and lateral meniscal extrusion correlated with the degree of knee varus and valgus, respectively. Degree of medial and lateral meniscal extrusion, medial tibial and femoral osteophyte size, and lateral femoral osteophyte size correlated with the Kellgren-Lawrence (KL) grade of KOA. However, significant correlations between US and x-ray findings were fair at most (Table 1). Presence or degree of synovial thickening did not correlate with KL grade of KOA, or with the degree of knee varus/valgus.

Conclusion: Patients with KOA had larger medial side osteophytes, and worse degrees of medial meniscal extrusion, compared to the lateral side. The majority of patients presented with no to mild suprapatellar synovial thickening. The majority of sonographic measurements performed in the knee demonstrates high agreement and reliability across raters. Sonographic features of meniscal extrusion and osteophyte size correlated with radiographic measures of knee alignment, and with radiographic K-L grade of KOA. Ongoing studies will correlate these sonographic features of KOA with clinical and histologic findings.

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Abstract Number: 1542

The Role of Dual Energy Computed Tomography (DECT) in the Differentiation of Gout and Calcium Pyrophosphate Deposition Disease

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Imaging of Rheumatic Diseases Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Differentiation of gout and calcium pyrophosphate deposition disease (CPPD) is sometimes difficult as patients often present with a similar clinical picture. Arthrocentesis and subsequent polarization microscopy (PM) remains the gold standard but novel diagnostic approaches such as non-invasive dual energy computed

	DECT	US	Conventional radiographs	Suspected clinical Diagnosis
Gout	n=30	n=30	n=26	n=30
Sensitivity	59.1% (0.36-0.79)	90.9% (0.71-0.99)	55.6% (0.31 - 0.79)	81.8% (0.60-0.95)
Specificity	100% (0.63-1.00)	75% (0.35-0.97)	100% (0.63 - 1.00)	87.5% (0.47-1.00)
CPPD	n=30	n=30	n=26	n=30
Sensitivity	37.5% (0.09-0.76)	87.5% (0.47-1.00)	25% (0.01 - 0.81)	75.0% (0.35-0.97)
Specificity	81.8% (0.60-0.95)	90.1% (0.71-0.99)	72.3% (0.50 - 0.89)	100% (0.85-1.00)

Table 1. Sensitivities and specificities of examinations in gout and calcium pyrophosphate deposition disease (95% CI in brackets).

tomography (DECT) have recently been validated for gout. Currently, limited data is available on DECT in patients with CPPD. Our objective was to analyse the diagnostic impact of DECT in gout and CPPD when compared to the gold standard of PM. We further compared the results of PM to ultrasound (US), conventional radiographs (CR), and suspected clinical diagnosis (SCD). Additionally, 12 laboratory parameters were analysed.

Methods: Thirty patients with suspected gout (n = 22) or CPPD (n = 8) were included. Two independent readers assessed colour coded, as well as 80 and 120 kV DECT images for signs of monosodium urate (MSU) crystals or CPP deposition. US, CR, and the SCD were also compared to PM results. US examinations were performed by certified musculoskeletal ultrasound specialists. The association of up to 12 laboratory parameters such as uric acid, thyroid stimulating hormone, and C-reactive protein (CRP) with the PM results was analysed.

Results: Sensitivity of DECT for gout was 59.1% (95% CI 0.36-0.79) with a specificity of 100% (95% CI 0.63-1.00). Concerning CPPD, the sensitivity and specificity of DECT was 37.5% (95% CI 0.09-0.76) and 81.8% (95% CI 0.60-0.95) respectively. US had the highest sensitivity of 90.9% (95% CI 0.71-0.99) with a specificity of 75% (95% CI 0.35-0.97) for gout, while the sensitivity and specificity for CPPD were 87.5% (95% CI 0.47-1.0) and 90.1% (95% CI 0.71-0.99) respectively. The SCD had the second highest sensitivity for gout at 81.8% (95% CI 0.60-0.95) with a comparable sensitivity of 75% (95% CI 0.35-0.97) for CPPD. Uric acid levels were elevated in 26% of gout patients and 25% of CPPD patients. While elevated CRP levels were observed in 60% of gout patients and in 88% of CPPD patients. None of the 12 laboratory parameters were found to be significantly linked to either disease.

Conclusion: DECT is a non-invasive imaging tool for gout but might have a lower sensitivity than published by previous studies (59.1% vs 90%[1]). DECT sensitivity for CPPD was 37.5% (95% CI 0.09-0.76) in a sample group of eight patients. Both US and the SCD had higher sensitivities than DECT for gout and CPPD. Further studies with larger patient cohorts are needed in order to determine the diagnostic utility of DECT in CPPD.

Disclosure: D. Kravchenko, None; **P. Karakostas**, None; **P. Brossart**, None; **C. Behning**, None; **C. Meyer**, None; **V. Schaefer**, None.

Abstract Number: 1543

Prevalence of Ultrasound Findings Suggestive of Inflammatory Arthritis in Children with Skin Psoriasis (ChildEchoPso)

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Imaging of Rheumatic Diseases Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The prevalence of psoriasis in children is estimated between 0.5-1% (1), and can be associated with musculoskeletal involvement, althought the prevalence and typology of such involvement is unknown. (2)

Over the last years ultrasound associated with Doppler (PDUS) has become an important tool for evaluating joint involvement in children. Several studies have shown the high sensitivity of this technique for detecting joint involvement, as well as high acceptability, due to the lack of radiation or of sedation (3).

To the best to our knowledge this is the first study aiming to evaluate the prevalence of ultrasound involvement of joints and entheses in children with PsO.

Methods: Observational cross-sectional study aiming at evaluating 150 consecutive children (≤16 years) with skin PsO. For each child a standardized clinical and ultrasound evaluation of joint and entheses was performed at the following bilateral sites: a) Entheses: quadriceps tendon, proximal and distal patellar ligament, Achilles tendon, plantar fascia and extensor elbow tendon), b) joints: metacarpophalangeal, proximal and distal interphalangeal, wrist, elbow,

Table 1	Total (n=49)	Asymptomatic (n=36)	Symptomatic (n=13)	p
Females	22 (44.9%)	15 (42%)	7 (53.8%)	NS
Age	**9 ± 4**	**9 ± 4**	**11 ± 4**	**<0.05**
Pso duration (years)	**3.4 ± 3.3**	**2.6 ± 2.6**	**5.6 ± 4.1**	**<0.01**
PASI	5.2 ± 4.0	5.2 ± 4.4	5.2 ± 3.2	NS
BSA	4.5 ± 3.7	4.6 ± 4.1	4.1 ± 2.2	NS
Nail involvement	28 (57%)	20 (56%)	8 (61%)	NS
Plaques psoriasis	27 (55%)	19 (53%)	8 (61%)	NS
TJC ≥1, n/tot (%)	**10 (20%)**	**0 (0)**	**10 (77%)**	**<0.001**
SJC ≥1, n/tot (%)	**2 (4%)**	**0 (0)**	**2 (15%)**	**<0.05**
Entheseal pain, n/tot (%)	**9 (18%)**	**0 (0)**	**9 (69%)**	**<0.001**
Dactylitis	0	0	0	NA

* Mean ± SD. ** n (%). PASI: Psoriasis area severity index. BSA: Body surface area. TJC: Tender Joint Count. SJC: Swollen Joint Count.

Table 1. Demographic and clinical characteristics.

Table 2	Total (n=49)	Asymptomatic (n=36)	Symptomatic (n=13)	p
≥1 ultrasound abnormality, n/tot (%)	**24 (49%)**	**14 (38.9%)**	**10 (76.9%)**	**<0.05**
≥1 joint effusion, n/tot (%)	16 (32.7%)	10 (27.8%)	6 (46.2%)	NS
≥1 synovitis, n/tot (%)	**5 (10.2%)**	**1 (2.8%)**	**4 (30.8%)**	**<0.01**
≥1enthesitis, n/tot (%)	8 (16.3%)	4 (11.1%)	4 (30.8%)	NS
≥1 tenosynovitis, n/tot (%)	2 (4.1%)	1 (2.8%)	1 (7.7%)	NS
≥1 nail with modified structure, n/tot (%)	26 (53.1%)	21 (58.3%)	5 (38.5%)	NS

Table 2. PDUS Findings.

knee, ankle, and metatarsophalangeal. The presence of spontaneous pain was also recorded. Ultrasound was performed by an independent assessor, blinded to clinical assessment and symptoms.

Results: 49 patients were included until now. Thirteen patients (26%) presented some painful joint or enthesis, 27 patients (55%) had family history of PsO and none of them had family history of psoriatic arthritis. Demographic and clinical characteristics are shown in Table1, whilst PDUS findings in Table 2.

Conclusion: Presence of ultrasound abnormalities was higher in the symptomatic group and the most prevalent inflammatory ultrasound findings were synovitis and enthesitis. Ultrasound may be useful to detect subclinical involvement in children with PsO and musculoskeletal symptoms.

Disclosure: L. Coronel, None; **T. Gudu**, None; **S. Ruel-Gagné**, None; **H. Gouze**, None; **F. Vidal**, None; **I. Padovano**, None; **F. Constantino**, None; **M. Breban**, None; **E. Mahe**, None; **M. D'Agostino**, AbbVie, 5, 8, Bristol Myers Squibb, 5, 8, Novartis, 5, 8, Roche, 5, 8.

Abstract Number: 1544

Tc99m Tilmanocept Imaging Is an Early Predictor of Clinical Response in Rheumatoid Arthritis Patients Beginning New Anti-TNFα Therapy

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis **(**RA) is a serious and potentially debilitating disease, but low disease activity and even clinical remission can be obtained if an effective therapy can be identified early in the course of the disease. Imaging with Tc99m tilmanocept, a high affinity ligand to CD206 expressed on activated macrophages, offers the potential to meet this need by providing an objective, quantifiable readout of changes in macrophage density in the joints of patients undergoing initiation or change of bDMARD therapy. These macrophage density changes may be observable weeks before disease modification can be detected with standard clinical assessments. This earlier

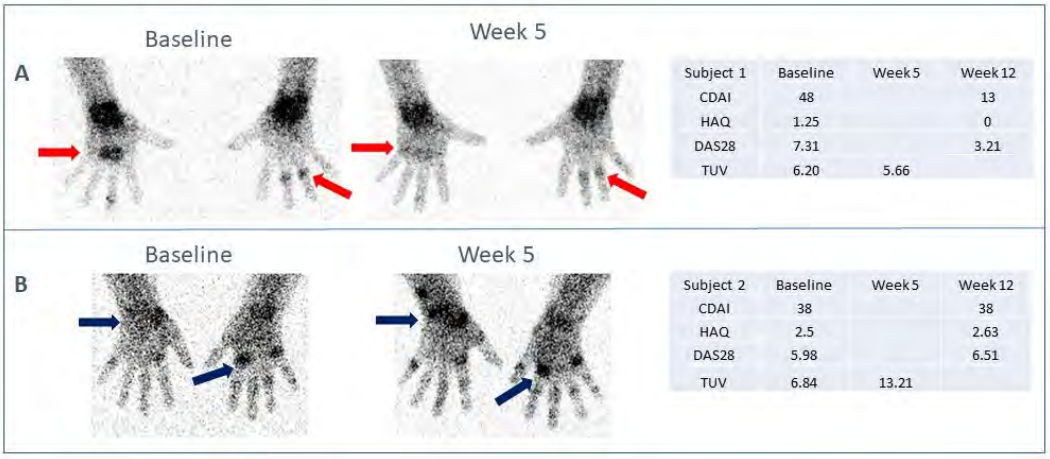

Figure 1. Quantification of Tc99m tilmanocept at Baseline and Week 5 is predictive of clinical efficacy at Week 12. Representative Baseline and Week 5 images and Tc99m tilmanocept quantification (Tilmanocept Uptake Value; TUV) demonstrate changes in localization that are sensitive to and predictive of clinical response at Week 12. Images show decrease in signal localization predictive of clinical response (Panel A) and increase in signal localization predictive of clinical non-response (Panel B) at Week 12.

readout would allow for more timely modifications of the treatment strategy and earlier identification of an effective therapy, thus reducing the likelihood of permanent joint damage associated with ineffective therapy and the potential for side effects from exposure to these ineffective therapies.

Methods: An interim analysis of our Phase 2b trial (NCT03938636) was performed using data from 15 subjects with active RA (DAS28 ≥ 3.2; ACR/EULAR 2010 Classification Criteria ≥ 6) set to begin a new or first-time treatment regimen with an anti-TNFα therapy. Hand/wrist planar gamma camera images were obtained at baseline prior to initiation of new treatment, 5 weeks post-therapy initiation, and 12 weeks post-therapy initiation for 11 of the 15 subjects at the time of the analysis. The remaining subjects had completed baseline and 5-week imaging only at the time of this analysis. Images were quantitatively assessed to detect localization within synovial spaces of bilateral hands and wrists by determining average pixel intensity in each region of interest relative to average pixel intensity in an adjacent reference region. Additionally, a panel of established clinical assessments (CDAI, DAS28, HAQ-DI) was performed at each time point in order to compare imaging results with clinical evaluations over the 12-week time course.

Results: In 9 out of 11 subjects with 12-week clinical data available at the time of analysis, Tc99m tilmanocept imaging from baseline to week 5 was predictive of clinical outcome at 12 weeks (Figure 1). Global Tc99m tilmanocept signals declined by an average of 46% from baseline to week 5 in those subjects correctly predicted as responding significantly to anti-TNFα treatment by week 12. In subjects correctly predicted by imaging not to have a significant clinical response by week 12, Tc99m tilmanocept signals increased by an average of 44% from baseline to week 5. Combined data from all 15 subjects demonstrated that baseline global Tc99m tilmanocept uptake values in joints with RA-involved inflammation spanned a range of values of over an order of magnitude. These preliminary results indicate that marked changes in Tc99m tilmanocept global uptake values by week 5 presage clinical efficacy evaluations at week 12 of treatment.

Conclusion: These interim data are supportive of the hypotheses that Tc99m tilmanocept imaging can provide quantifiable imaging assessment of RA-involved joints that enables early prediction of clinical response as well as longitudinal monitoring of clinical status.

Disclosure: M. Leach, Navidea Biopharmaceuticals, 3; **D. Ralph**, Navidea Biopharmaceuticals, 1, 3; **B. Potter**, Navidea Biopharmaceuticals, 4; **B. Abbruzzese**, Navidea Biopharmaceuticals, 1, 3; **R. Hershey**, Navidea Biopharmaceuticals, 1, 3; **J. Fitzpatrick**, None; **K. Repp**, Navidea Biopharmaceuticals, 3; **H. Shakhtra**, Navidea Biopharma-

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Abstract Number: 1545

An Artificial Intelligence (AI) Assistant Identifying Spinal Diffuse Idiopathic Skeletal Hyperostosis on Plain X-rays: A Pilot Deep Learning Study

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Diffuse idiopathic skeletal hyperostosis (DISH) is a non-inflammatory condition most classically seen in the spine, and is characterized by ossification of the spinal ligaments and entheses. DISH may be asymptomatic, but in some cases is associated with back pain and stiffness. Risk factors include male sex, increasing age, obesity and metabolic syndrome. Important radiographic mimics of DISH include osteoarthritis and ankylosing spondylitis There are multiple classification criteria for DISH, though the 1976 Resnick and Niwayama classification criteria are best known (1).

While xrays are used to identify DISH, it can still be challenging for trainees and primary care health professionals to distinguish it from its mimics. We conducted a pilot study to develop an Artificial Intelligence (AI) assistant, trained to identify DISH from 'non-DISH' on xrays by using convolution neural network (CNN). CNN is the most popular model for imaging classification in deep learning.

Methods: DISH patients were identified from our university's radiology database, using word search 'DISH' or 'Diffuse idiopathic skeletal hyperostosis' in all cervical, thoracic or lumbosacral radiographs in the year 2015. Diagnosis of DISH was confirmed by 2 board certified radiologists, and either completely fulfilled Resnick criteria or incompletely fulfilled Resnick criteria but were still felt to have DISH based on radiologists' expert opinion. We also compiled a list of age and sex-matched patients with spinal x-rays from 2015 who lacked DISH based on the radiologists' read.

All image data were imported into R statistical language/Rstudio. We used a CNN to train a classification rule for spinal xrays of DISH vs. non-DISH using the keras and tensorflow R packages. 90% of each group was used as training data and the rest were used as test data to evaluate the accuracy of the classification rule.

Results: 116 patients with DISH and 262 matched controls were included. The image size was cropped from 601x524 pixels to 461 x 345 pixels to remove unnecessary solid background and add-on information before the CNN training. The trained CNN was a sequential model with 2 convolution layers (64 or 32 rectified linear units), 2 dense layers (one layer with 16 rectified linear units and the other with 1 sigmoid unit), and others. The network was trained by the RMSprop optimizer and validation split = 0.2 with 100 epochs. The overall training accuracy of the classification rule

by CNN was 92% (sensitivity 75% and specificity 100%). The overall test accuracy was 89% (sensitivity 70% and specificity 98%).

Conclusion: The trained AI-assistant has reasonable sensitivity and very high specificity. In this pilot study, we demonstrated that a CNN-based AI-assist for identifying DISH xrays could be trained from scratch with a moderate size of images that seemed to perform reasonably well. The future research will be focusing on improving the accuracy of the AI-assistant with more images.

Disclosure: S. Ringsted, None; **N. Sathe**, None; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **D. Choi**, None.

Abstract Number: 1546

Ultrasound, Magnetic Resonance Imaging and Radiography of the Fingers' Joints of Psoriatic Arthritis Patients

Ari Polachek[1], Victoria Furer[2], Mirna Zureik[3], Sharon Nevo[3], Liran Mendel[4], David Levartovsky[2], Jonathan Wollman[4], Valerie Aloush[2], Reut Tzemach[4], Ofir Elalouf[5], Marina Anouk[6], Mark Berman[2], Ilana Kaufman[7], Yael Lahat goldstein[2], Hagit Sarbagil-Maman[8], Sara Borok Lev-Ran[2], Adi Broide[3], Lihi Eder[9], Daphna Paran[2], Moshe Iluz[10], Iris Eshed[11] and Ori Elkayam[3], [1]Tel Aviv Sourasky Medical Center, Petah-Tikva, Israel, [2]Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, [3]Tel Aviv Sourasky Medical Center, Tel-Aviv, Israel, [4]Souraaky Medical Center, Tel-Aviv, Israel, [5]Souraaky Medical Center, Herzliya, Israel, [6]Souraaky Medical Center, Tel Aviv, Israel, [7]Tel Aviv Sourasky Medical Center, Petah-Tiqwa, Israel, [8]Tel-Aviv Sourasky Medical Center, Kiryat Ono, Israel, [9]University of Toronto, Toronto, ON, Canada, [10]Souraaky Medical Center, Tel-Aviv, [11]Sheba Medical Center, Tel-Aviv, Israel

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Ultrasound (US), magnetic resonance imaging (MRI) and conventional radiography are the leading imaging modalities for musculoskeletal (MSK) assessment in PsA. However, little is reported about the discrepancies between these tools in PsA patients. The aim of this study is to examine the agreement between these modalities and to evaluate the sensitivity and specificity of US and X-ray with MRI as gold standard in PsA patients.

Methods: The study population included consecutive PsA patients (CASPAR criteria) that were prospectively recruited. All patients underwent clinical assessment including complete history taking, physical examination, questionnaires for disease activity and quality of life assessment and blood test for acute phase reactants. US (gray scale and Doppler), contrast enhanced MRI and AP and oblique radiographs of MCP, PIP and DIP joints of one most clinically involved matched hand. US and MRI evaluated synovitis, flexor tenosynovitis and extensor paratenonitis. US, MRI and radiography evaluated erosions and bone proliferations. The time interval between the US and MRI was maximum 3 days and the US, MRI and X-ray readers were blinded to clinical data. NSAIDs were hold for 3 days before US and MRI assessment. The US images were scored according to the EULAR-OMERACT, the MRI images according to the PsAMRIS scoring system and the X-ray according to the Psoriatic Arthritis Ratingen Score (PARS) method. Positive values for comparison were ≥1. Agreement between MRI and US was calculated based on kappa and prevalence-adjusted bias-adjusted kappa (PABAK) values. Sensitivity and specificity of US and X-ray with MRI as gold standard was calculated as well.

Table 1: Prevalence of lesions for each group of joints

		US Value ≥1	MRI Value ≥1	X-Ray Value ≥1	P-Value
Synovitis*					
MCP, n (%)		101 (20.2)	79 (15.8)		0.07
PIP, n (%)		43 (8.6)	38 (7.6)		0.6
DIP, n (%)		16 (4)	14 (3.5)		0.7
Extensor paratenonitis					
MCP, n (%)	Gray scale	20 (4)	19 (3.8)		0.9
	Doppler	5 (1)			
PIP, n (%)	Gray scale	37 (7.4)	23 (4.6)		0.06
	Doppler	3 (0.6)			
DIP, n (%)	Gray scale	6 (1.5)	8 (2)		0.6
	Doppler	2 (0.5)			
Flexor tenosynovitis					
MCP, n (%)	Gray scale	32 (6.4)	33 (6.6)		0.9
	Doppler	7 (1.4)			
PIP, n (%)	Gray scale	24 (4.8)	16 (3.2)		0.2
	Doppler	5 (1)			
DIP, n (%)	Gray scale	7 (1.8)	5 (1.2)		0.6
	Doppler	0			
Erosions					
MCP, n (%)		20 (4)	24 (4.8)	3 (0.9)	*0.005*
PIP, n (%)		11 (2.2)	9 (1.8)	7 (2.5)	*0.71*
DIP, n (%)		4 (1)	4 (1)	8 (2.9)	*0.13*
Bone proliferations					
MCP, n (%)		41 (8.2)	8 (1.6)	25 (7.1)	<0.001
PIP, n (%)		81 (16.2)	12 (2.4)	57 (16.3)	<0.001
DIP, n (%)		117 (29.2)	3 (0.8)	74 (26.4)	<0.001

*According to the EULAR-OMERACT definition

Table 1. Prevalence of lesions for each group of joints

Results: One hundred PsA patients were included (mean age: 51.2 years with 59% females) and 29 patients were in minimal disease activity. The prevalence of synovitis, flexor tenosynovitis, extensor paratenonitis were similar between the US and MRI assessments. Erosions were significantly increased in US and MRI compared to X-RAY in MCPs level (p=0.005), while bone proliferations were significantly increased in US and X-ray compared to MRI (p< 0.001) (Table 1). The absolute agreement between US and MRI was good-very good for synovitis (85%-96%, PABAK=0.7-0.92), flexor tenosynovitis (93%-98% PABAK=0.87-0.96) and for extensor paratenonitis (95%-98%, PABAK=0.9-0.97) (Table 2). Agreement between US, MRI and X-Ray for erosions was very good (96%-98%, PABAK=0.92-0.97) and for bone proliferations good-very good (71%-93%, PABAK= 0.47-0.87). Sensitivity of US with MRI as gold standard was higher for synovitis 0.5-0.86, extensor paratenonitis (0.63-0.85) than for flexor tenosynovitis (0.1-0.75), while the specificity was high in each evaluated domain (0.89-0.98) (Table 3).

Conclusion: There is very good agreement between US and MRI for the detection of finger inflammatory changes. US, X-ray and MRI have good to very good agreement for structural changes.

Table 2: Agreement between the different imaging modalities with both Kappa and prevalence adjusted biased adjusted Kappa (PABAK)

	US vs MRI			X-Ray vs US			X-Ray vs MRI		
	Agreement	Kappa	Prevalence adjusted Kappa	Agreement	Kappa	Prevalence adjusted Kappa	Agreement	Kappa	Prevalence adjusted Kappa
Synovitis									
MCP	85%	0.5	0.7						
PIP	95%	0.64	0.89						
DIP	96%	0.45	0.92						
Extensor Paratenonitis									
MCP	97%	0.6	0.94						
PIP	95%	0.58	0.9						
DIP	98%	0.56	0.97						
Flexor Tenosynovitis									
MCP	93%	0.46	0.87						
PIP	95%	0.32	0.89						
DIP	98%	0.32	0.96						
Erosions									
MCP	96%	0.56	0.92	97%	0.12	0.94	97%	0.14	0.93
PIP	98%	0.66	0.97	98%	0.49	0.97	98%	0.54	0.97
DIP	98%	0.21	0.96	98%	0.4	0.96	97%	0.17	0.94
Bone Proliferations									
MCP	93%	0.22	0.85	93%	0.52	0.87	93%	<0.1	0.86
PIP	86%	0.23	0.72	90%	0.65	0.81	85%	0.14	0.69
DIP	71%	0.04	0.43	87%	0.68	0.75	74%	<0.1	0.47

Table 2. Agreement between the different imaging modalities with both Kappa and prevalence adjusted biased adjusted Kappa (PABAK)

Table 3: Sensitivity and specificity of US and X-Ray with MRI as gold standard

	US		X-RAY	
	Sensitivity	Specificity	Sensitivity	Specificity
Synovitis				
MCP	0.67	0.89		
PIP	0.86	0.96		
DIP	0.5	0.98		
Extensor Paratenonitis				
MCP	0.63	0.98		
PIP	0.85	0.96		
DIP	0.75	0.99		
Flexor Tenosynovitis				
MCP	0.48	0.96		
PIP	0.75	0.96		
DIP	<0.1	0.99		
Erosions				
MCP	0.52	0.98	0.1	0.99
PIP	0.67	0.99	0.5	0.99
DIP	<0.1	0.99	0.33	0.97
Bone Proliferations				
MCP	*0.75*	*0.92*	*NA*	*NA*
PIP	*1*	*0.85*	*0.66*	*0.85*
DIP	*NA*	*NA*	*NA*	*NA*

Table 3. Sensitivity and specificity of US and X-Ray with MRI as gold standard

Disclosure: A. Polachek, None; **V. Furer**, None; **M. Zureik**, None; **S. Nevo**, None; **L. Mendel**, None; **D. Levartovsky**, None; **J. Wollman**, None; **V. Aloush**, None; **R. Tzemach**, None; **O. Elalouf**, None; **M. Anouk**, None; **M. Berman**, None; **I. Kaufman**, None; **Y. Lahat goldstein**, None; **H. Sarbagil-Maman**, None; **S. Borok Lev-Ran**, None; **A. Broide**, None; **L. Eder**, None; **D. Paran**, None; **M. Iluz**, None; **I. Eshed**, None; **O. Elkayam**, None.

Abstract Number: 1547

Role of Artificial Intelligence in Assessment of Peripheral Joint MRI in Inflammatory Arthritis: A Systematic Review and Meta-analysis

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SESSION INFORMATION

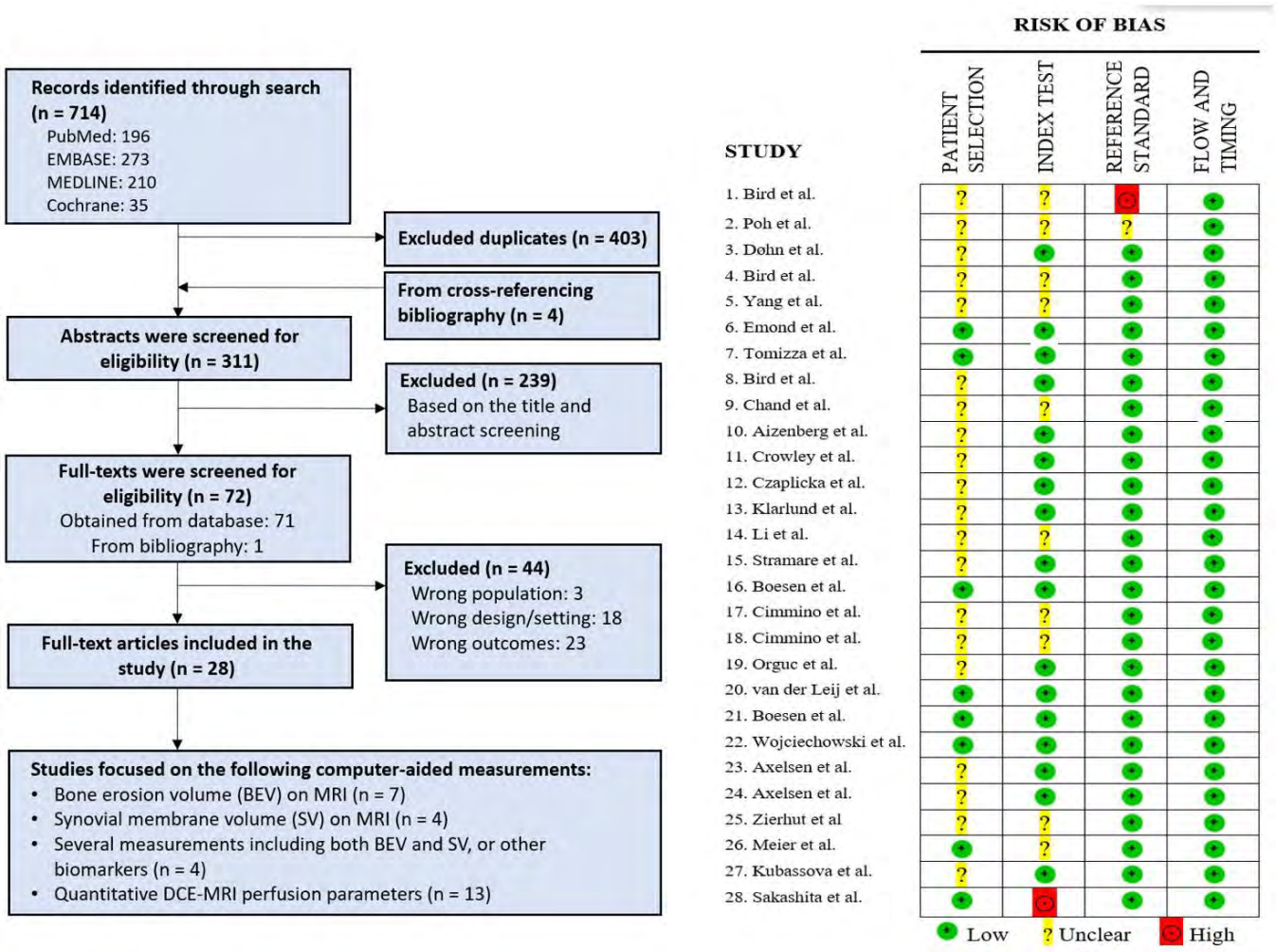
Session Date: Monday, November 9, 2020

Session Title: Imaging of Rheumatic Diseases Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: To summarize the feasibility, reliability, and validity of computer-aided quantification of joint destruction and synovitis on MRI using artificial intelligence (AI) based methods in patients with inflammatory arthritis.



PRISMA flowchart diagram for study selection and risk of bias assessment using the QUADAS-2 tool. No concern was detected regarding the applicability of patient selection, index test, and reference standard.

Methods: A systematic literature search was performed on PubMed, EMBASE, SCOPUS, and Cochrane databases for original articles published from January 01, 1985 to June 02, 2020. We selected studies in which patients with inflammatory arthritis were enrolled, and arthritis-related structural damage/synovitis in peripheral joints were assessed on non-CE, CE, or DCE-MRI using (semi)automated methods. Data were pooled using random-effects model. Publication bias was addressed using the Begg and Mazumdar test and the trim and fill method. Subgroup analysis and meta-regression were performed.

Results: 28 studies consisting of 1342 MRIs were included (age=54.8; 66.7%female; duration of arthritis=3.6years). Pooled analysis showed an overall excellent intra- and inter-reader reliability for computer-aided quantification of bone erosion volume (BEV) (*r*=0.97(95%CI:0.92–0.99) and 0.93(0.87–0.97)), synovial membrane volume (SV) (*r*=0.98(0.90–0.99) and 0.86(0.78–0.91)), and DCE-MRI perfusion parameters (*r*=0.99(0.82–1) for maximum enhancement, *r*=0.99(0.94–1) for initial rate enhancement, *r*=0.96(0.85–0.99) for and total number of enhancing voxels (N-total)). Meta-regression analysis showed that computer-aided and manual methods provide comparable reliability for quantification of bone erosion, synovitis, and perfusion parameters (*P*>0.05). Computer-aided measurement of BEV (*r*=0.92), SV (*r*=0.82), and DCE-MRI biomarkers (*r*=0.72 N-total; *r*=0.74 N-plateau; *r*=0.64 N-washout) were significantly correlated with the OMERACT RAMRIS scores (*P*< 0.01). Among clinical and laboratory factors, SV was mod-

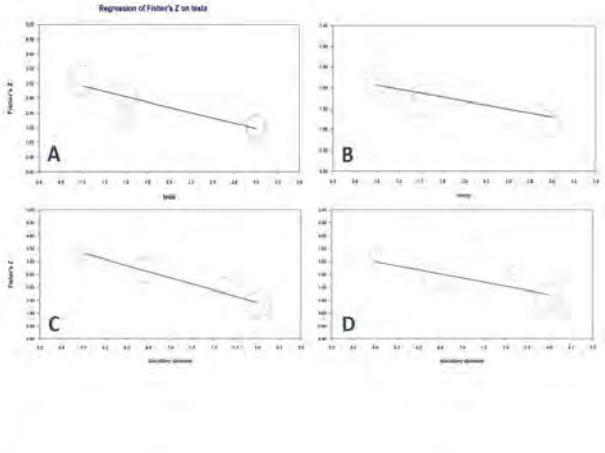
Study	Publication Year	Joint region(s)	Main outcome (semi)automated measures	No. of Subjects	Female (%)	Age (Mean)	Duration of disease (Mean)	Imaging (T and slice thickness)	Manual measurement(s)	(Semi)automated measurement(s)
1. Bird et al.	2002	MCP	[illegible]	7	N/A	N/A	N/A	MRI (1.5T;) and 8mm)	OMERACT MRI scoring	OSIRIS software, semi-automated
2. Poh et al.	2019	MCP	[illegible]	32	78.1%	50.5	4.0	MRI (1.5T;) mm)	OMERACT MRI scoring	OSIRIS software, semi-automated
3. Dohn et al.	2005	MCP	[illegible]	17	76.5%	52.0	N/A	MRI (0.6T; N/A)	OMERACT MRI scoring	OSIRIS software, semi-automated
4. Bird et al.	2003	Hand and Wrist	[illegible]	12	80%	46.0	6.0	MRI (1.5T; 3-4 mm)	OMERACT MRI scoring	OSIRIS software, semi-automated
5. Yang et al.	2015	Hand and Wrist	[illegible]	10	81%	52.0	7.6	MRI and DCE-MRI (3T; 1 mm)	OMERACT MRI scoring and manual volume	Semi-automated
6. Emond et al.	2012	MCP	[illegible]	40	72%	42 to 61	N/A	MRI (1T; 1 mm)	Manual volume	Semi-automated
7. Tomizza et al.	2015	MCP	[illegible]	100	70.6%	57.4	3.0	MRI (1T; 1 mm)	No	Semi-automated
8. Bird et al.	2005	Wrist and MCP	[illegible]	10	N/A	N/A	N/A	MRI (1.5T; 3 mm)	OMERACT MRI scoring	OSIRIS software, semi-automated
9. Chand et al.	2011	Wrist	[illegible]	30	63.2%	57.1	6.7	MRI (3T; 2 mm)	OMERACT MRI scoring	OSIRIX software, semi-automated
10. Aizenberg et al.	2017	Wrist	[illegible]	103	61.2%	54.7	-2-	MRI (1.5T; 3 mm)	OMERACT MRI scoring	Automated
11. Crowley et al.	2011	Wrist	[illegible]	22	68.2%	52	-2-	MRI (3T; 1.5 – 2.1 mm)	OMERACT MRI scoring	OSIRIX software, semi-automated
12. Czapliicka et al.	2015	Wrist	[illegible]	32	87.5%	47	10	CE-MRI and DCE-MRI (0.2T; 0.7 mm)	OMERACT MRI scoring	Automated
13. Klarlund et al.	1999	MCP	[illegible]	42	N/A	55	8	CE-MRI (1T; 3 mm)	Manual semi-quantitative score	XPrime software, Automated
14. Li et al.	2012	Wrist	[illegible]	14	78.6%	53.7	N/A	MRI and DCE-MRI (3T; 2 mm)	No	Automated
15. Stramare et al.	2014	Hand and Wrist	[illegible]	10	87.5%	50	17	CE-MRI (1.5T; 0.7 – 3 mm)	OMERACT RAMRIS and SAMRIS scoring	Automated
16. Boesen et al.	2011	Wrist	[illegible]	46	76.1%	56	5.5	DCE-MRI (0.2T; 5 mm)	Manual measurement (REE and RE)	Dynamika RA, Automated
17. Cimmino et al.	2012	Wrist	[illegible]	17	76.5%	53.6	N/A	DCE-MRI (0.2T; 5 mm)	No	Dynamika software, semi-automated
18. Cimmino et al.	2014	Wrist	[illegible]	10	60%	52.9	6.3	DCE-MRI (0.2T; 5 mm)	OMERACT RAMRIS scoring, Manual measurement	Dynamika software, semi-automated
19. Orgue et al.	2013	Wrist and MCP	[illegible]	80	87.5%	51.1	3.8	Non-CE and DCE-MRI (1.5T; 2.5 mm)	OMERACT RAMRIS scoring	Automated
20. van der Leij et al.	2010	Knee	[illegible]	10	50%	39	N/A	DCE-MRI (1.5T; 4 mm)	Manual measurement	Semi-automated
21. Boesen et al.	2012	Wrist	[illegible]	54	N/A	52	11	DCE-MRI (0.2T; 5 mm)	OMERACT RAMRIS scoring	Dynamika software, (semi-automated
22. Wojciechowski et al.	2013	Wrist	[illegible]	59	N/A	47	N/A	DCE-MRI (0.2T; 3.5 mm)	OMERACT RAMRIS scoring	Dynamika software, (semi-automated
23. Axelsen et al.	2013	Knee	[illegible]	12	N/A	59	5	DCE-MRI (1.5T; 5 mm)	No	Dynamika software, (semi-automated
24. Axelsen et al.	2012	Knee	[illegible]	17	82.4%	64	8	DCE-MRI (1.5T; 5 mm)	No	Dynamika software, (semi-automated
25. Zierhut et al.	2007	Wrist	[illegible]	12	58%	43	N/A	DCE-MRI (1.5T; 3 mm)	Manual measurement (REE and RE)	Kinetic parameter, automated
26. Meier et al.	2014	Wrist and Hand.	[illegible]	58	53.6%	55	1	DCE-MRI (3T; N/A)	No	Automated
27. Kubassova et al.	2010	Wrist and Hand	[illegible]	140	N/A	62.7	5	DCE-MRI (0.2T; 5 mm)	No	Dynamika software, (semi-automated
28. Sakashita et al.	2013	Wrist and Hand	[illegible]	8	87.5%	55	11	DCE-MRI (3T; 2 mm)	OMERACT RAMRIS scoring	Semi-automated

Study	Intra-reader reliability	Inter-reader reliability	Correlation with clinical variables	Correlation with established manual MRI-based scores	Time of measures
1. Bird et al. (1)	Yes	Yes	No	Yes (RAMRIS)	Yes
2. Poh et al. (2)	Yes	Yes	Yes	Yes (RAMRIS)	Yes
3. Dohn et al. (3)	Yes	No	No	Yes (RAMRIS)	No
4. Bird et al. (4)	Yes	Yes	Yes	Yes (RAMRIS)	Yes
5. Yang et al. (5)	Yes	Yes	No	Yes (RAMRIS/manual)	Yes
6. Emond et al. (6)	Yes	Yes	No	Yes (manual)	Yes
7. Tomizza et al. (7)	Yes	Yes	No	No	No
8. Bird et al. (8)	No	Yes	No	No	No
9. Chand et al. (9)	Yes	Yes	Yes	Yes (RAMRIS)	Yes
10. Aizenberg et al. (10)	No	No	No	Yes (RAMRIS)	No
11. Crowley et al. (11)	Yes	Yes	No	Yes (RAMRIS)	No
12. Czapliicka et al. (12)	No	No	No	Yes (RAMRIS/manual)	No
13. Klarlund et al. (13)	Yes	Yes	Yes	Yes (manual)	No
14. Li et al. (14)	Yes	Yes	Yes	No	No
15. Stramare et al. (15)	No	No	Yes	Yes	No
16. Boesen et al. (16)	Yes	No	No	Yes	No
17. Cimmino et al. (17)	No.	No	Yes	No	No
18. Cimmino et al. (18)	Yes	Yes	No	No	No
19. Orgue et al. (19)	No	No	No	Yes	No
20. van der Leij et al. (20)	Yes	No	No	No	No
21. Boesen et al. (21)	No	No	Yes (no data)	Yes	Yes
22. Wojciechowski et al. (22)	No	No	No	Yes	No
23. Axelsen et al. (23)	Yes	Yes	No	No	No
24. Axelsen et al. (24)	Yes	Yes	Yes	No	No
25. Zierhut et al. (25)	No	No	No	Yes (manual)	No
26. Meier et al. (26)	No	No	Yes	No	No
27. Kubassova et al. (27)	No	No	No	No	Yes
28. Sakashita et al. (28)	No	No	No	No	Yes

Search String	Category	No.
#1 ("artificial intelligence"[MeSH Terms] OR "artificial intelligence"[Text Word] OR "automatic sensing"[Text Word] OR "deep learning"[Text Word] OR "AI"[Text Word] OR "machine learning"[MeSH Terms] OR "machine learning"[Text Word] OR "automated"[Text Word] OR "automated"[Text Word] OR "semiautomated"[Text Word] OR "semi-automated"[Text Word] OR "semi automated"[Text Word] OR "automatic"[Text Word] OR "semiautomatic"[Text Word] OR "semi-automatic"[Text Word] OR "semi automatic"[Text Word] OR "neural network classifying"[Text Word] OR "convolutional neural network"[Text Word] OR "neural network"[Text Word] OR "Computer-Assisted"[Text Word] OR "Computer-Aided"[Text Word])	AI	628570
#2 ("arthritis"[Title/Abstract] AND ("arthritis"[MeSH Terms] OR "rheumatoid arthritis"[MeSH Terms] OR "psoriasis"[TW] OR "psoriatic arthritis"[MeSH Terms] OR "arthritis"[Text Word] OR "rheumatoid arthritis"[Text Word] OR "psoriasis"[Text Word] OR "psoriatic arthritis"[Text Word]))	Arthritis	1741
#3 ("Magnetic Resonance Imaging"[MeSH Terms] OR "Magnetic Resonance Imaging"[Text Word] OR "MRI"[Text Word] OR "Magnetic Resonance"[Text Word] OR "Rheumatoid Arthritis MRI Quantification"[Text Word])	Imaging	242
#4 ("MCP"[Text Word] OR "metacarpophalangeal"[Text Word] OR "PIP"[Text Word] OR "proximal interphalangeal"[Text Word] OR "DIP"[Text Word] OR "distal interphalangeal"[Text Word] OR "wrist"[MeSH Terms] OR "hand"[MeSH Terms] OR "knee"[MeSH Terms] OR "wrist"[Text Word] OR "hand"[Text Word] OR "knee"[Text Word]OR "tibiofemoral"[Text Word] OR "patellofemoral"[Text Word] OR "hindfoot"[Text Word] OR "hind foot"[Text Word] OR "MTP"[Text Word] OR "metatarsophalangeal"[Text Word] OR "foot"[MeSH Terms] OR "ankle"[MeSH Terms] OR "joints"[MeSH Terms] OR "joint"[Text Word] OR "foot"[Text Word] OR "ankle"[Text Word] OR "joints"[Text Word])	Joint	206
#5 (NOT ("animals"[MeSH Terms]) NOT "humans"[MeSH Terms])	Human	200
#6 Time: Between 1/1/1999 and 6/2/2020	Time	196
#7 #1 AND #2 AND #3 AND #4 NOT #5, AND #6	Overall	196

General characteristics of included studies in the meta-analysis and details of the search strategy, using the keywords and the number of retrieved entries from PubMed.

(Semi)automated measurements	Bone erosion volume (BEV)	Synovial membrane volume (SV)	DCE-MRI perfusion parameters				
			ME	IRE	N-total	N-plateau	N-washout
Intra-reader reliability							
Pooled ICC (95% CI), I² value	0.97 (0.92–0.99), 91%	0.98 (0.90–1.0), 93%	0.99 (0.82–1.0), 97%	0.99 (0.94–1.0), 97%	0.96 (0.85–0.99), 80%	N/A	N/A
Adjusted pooled ICC (95% CI)	0.97 (0.92–0.99)	0.92 (0.57–0.99)	0.89 (-0.30–0.99)	0.98 (0.73–0.99)	0.90 (0.70–0.97)	N/A	N/A
No. of studies (MRIs)	8 (244)	4 (108)	3 (68)	4 (85)	3 (65)	N/A	N/A
Inter-reader reliability							
Pooled ICC (95% CI), I² value	0.93 (0.87–0.97), 79%	0.86 (0.78–0.91), 28%	N/A	N/A	N/A	N/A	N/A
Adjusted pooled ICC (95% CI)	0.93 (0.87–0.97)	0.83 (0.74–0.89)	N/A	N/A	N/A	N/A	N/A
No. of studies (MRIs)	8 (237)	4 (108)	N/A	N/A	N/A	N/A	N/A
Correlation with the RAMRIS or manual measurements							
Pooled ICC (95% CI), I² value	0.92 (0.80–0.97), 84.1%	0.82 (0.74–0.87), 0%	Range= 0.05–0.80	Range= 0.18–0.34	Range= 0.42–0.75	Range= 0.41–0.77	Range= 0.44–0.62
Adjusted pooled ICC (95% CI)	0.92 (0.80–0.97)	0.82 (0.74–0.87)	N/A	N/A	N/A	N/A	N/A
No. of studies (MRIs)	7 (144)	5 (140)	2 (70)	2 (70)	2 (113)	2 (113)	2 (113)
Correlation with clinical variables							
Pooled ICC (95% CI), I² value	N/A	ESR= 0.53 (0.28–0.72), 22.4%	N/A	DAS-28 P-value= 0.003–0.01	DAS-28 P-value= 0.003–0.01	N/A	N/A
Adjusted pooled ICC (95% CI)	N/A	ESR= 0.53 (0.28–0.72), 22.4%	N/A	N/A	N/A	N/A	N/A
No. of studies (MRIs)	N/A	ESR= 3 (70)	N/A	2 (27)	2 (27)	N/A	N/A
Time needed to perform measurements							
Pooled mean (range), minutes	13.97 (2.6 – 23.5)	15.14 (8.2 – 20)			4.0 (3.0 – 8.0)		
No. of studies (MRIs)	5 (105)	3 (66)			2 (194)		



Results of pooled analysis and meta-regression: Pooled ICC values for intra- and inter-reader realibility of each computer-aided measurement, correlation values between computer-aided measurements and manual scores/ clinical findings, and time needed to perform each image analysis method (Table). Meta-regression analysis for the association between the field-strength of MR scanner (tesla of MRI) and intra-reader (Fig A) and inter-reader (Fig B) reliability of computer-aided measurement of bone erosion volume (BEV) on MRI. Meta-regression analysis for the association between the duration of disease, form the onset of inflammatory arthritis (years), and intra-reader (Fig C) and inter-reader (Fig D) reliability of computer-aided measurement of synovial membrane volume (SV) on MRI.

erately correlated with ESR level (r=0.52, P< 0.01). On average, (semi)automated analysis of BEV/SV and DCE-MRI takes 17mins (vs. 9mins for OMERACT RAMRIS method) and 4mins (vs. 33mins for manual reading), respectively.

Conclusion: AI-based methods demonstrate feasibility, reliability and validity when utilized to quantify MRI pathologies of peripheral joints in patients with inflammatory arthritis; this provides a sound basis for future research. Computer-aided evaluation of inflammatory arthritis on non-CE and CE-MRI, and DCE-MRI could be considered as an alternative to conventional observer-based methods.

Disclosure: A. Haj-Mirzaian, None; **O. Kubassova**, IAG, Image Analysis Group, 3; **M. Boesen**, IAG, 5, Abbvie, 5, Eli Lilly, 5, Esaote, 5, Siemens, 5, Celgene, 5, UCB, 5, Roche Pfizer, 5, Astra Zeneca, 5, Takeda, 5, Rottapharm, 5; **P. Bird**, Abbvie, 5, Pfizer, 5, 8, Novartis, 5, 8, Gilead, 5, UCB, 5, Eli Lilly and Company, 5, 8; **J. Carrino**, Covera Health, 5, Image Analysis Group, 5, Image Biopsy Lab, 5, Pfizer, 5, Simplify Medical, 5, Arthritis and Rheumatology journal, 9, Osteoarthritis Imaging journal, 9.

Abstract Number: 1548

Blood Pressure, BMI and Sex Affect Optical Spectral Transmission Imaging Measurements of the Hands

Annelies Blanken[1], Conny van der Laken[2] and Mike Nurmohamed[3], [1]Amsterdam Rheumatology and immunology Center location Reade, Amsterdam, Netherlands, [2]Amsterdam Rheumatology and immunology Center, location Amsterdam UMC, VU medical center, Amsterdam, Netherlands, [3]Amsterdam Rheumatology and immunology Center, location Reade and Amsterdam UMC, VU medical center, Amsterdam, Netherlands

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Optical spectral transmission imaging (OST) is a new imaging method designed to measure inflammation in the hands of rheumatoid arthritis (RA) patients. The device uses a pressure cuff to occlude venous blood flow, resulting in an increased blood pool in the hands of the patient. In inflamed joints transmission of light through this blood pool is altered due to higher blood content, lower oxygenation and stronger hemodynamics at the location of inflammation. However, altered hemodynamics not related to inflammatory arthritis might also influence OST measurements. In this study we investigated whether hemodynamic and other cardiovascular parameters affect OST in healthy participants.

Methods: OST measurement was done in 37 healthy participants using the HandScan device (Hemics, the Netherlands). Carotid intima media thickness (IMT), pulse wave velocity (PWV) and augmentation index (AIx) were measured with ultrasound and SphygmoCor tonometry. Age, sex, diastolic and systolic blood pressure, pulse, hypertension (defined as systolic blood pressure >140 mmHg or diastolic blood pressure > 90 mmHg or antihypertensive treatment), total cholesterol, HDL, LDL, total/HDL cholesterol ratio, body mass index (BMI), European SCORE risk assessment, smoking status, cardiovascular history and medication use were collected during the same visit. Associations were investigated using univariate linear regression and multivariate regression adjusting for age and sex.

Results: Participants were 53 ± 8 years old and 65% was female. Systolic and diastolic blood pressure was 129 ± 19 mmHg and 80 ± 9 mmHg respectively and 22% used antihypertensive treatment, 8% an anticoagulant and 11% a statin. In total 38% had hypertension and 8% had a history of cardiovascular disease.

Table 1. Cardiovascular and hemodynamic parameters associated with higher OST measurement

	Univariate			Adjusted for age and sex		
	B	95%CI	p	B	95%CI	p
Hypertension (y/n)	2.39	0.12 - 4.67	0.04	2.41	0.37 - 4.45	0.02
Systolic blood pressure	0.08	0.03 - 0.14	0.005	0.07	0.02 - 0.12	0.01
Diastolic blood pressure	0.20	0.08 - 0.32	0.001	0.19	0.09 - 0.29	0.001
BMI	0.24	-0.01 - 0.48	0.06	0.26	0.05 - 0.47	0.02
Sex (male/female)*	3.67	1.56 - 5.78	0.001	3.54	1.29 - 5.79	0.003
European SCORE**	1.24	0.09 - 2.39	0.04	n/a		

*Adjusted for age only, **Not adjusted because age and sex are included in the European SCORE

Mean OST value was 12.69 ± 3.47 and all values were between 5.00 and 20.78. Cardiovascular and hemodynamic parameters that were associated with higher OST measurement were: hypertension (14.18 ± 1.12 versus 11.79 ± 0.69), systolic and diastole blood pressure, BMI and European SCORE (table 1). Also, male sex was associated with a higher OST with and without adjustment for age (15.05 ± 1.04 versus 11.41 ± 0.62 for females). Other parameters (age, cholesterol, pulse, IMT, having carotid plaque, PWV, AI, cardiovascular history, smoking status and statin, anti-hypertensive drug and/or anticoagulant use) were not associated with the OST measurement (p >0.13).

Excluding the 5 (14%) participants with hand osteoarthritis showed comparable results, except for BMI and hypertension. BMI was also significantly associated with OST in the univariate analysis (B 0.24, 95%CI 0.01-0.47, p=0.039), while hypertension lost its statistical significance (uni B 1.74, 95%CI -0.69-4.17, p=0.15; multi B 1.44, 95%CI -0.61-3.48, p=0.16).

Conclusion: High blood pressure, BMI, male sex and European SCORE are associated with increased OST values in healthy participants. This indicates that differences in OST measurements of RA patients might not only reflect inflammatory burden but is also dependent on sex, blood pressure and body composition. This should be taken into account when using optical spectral transmission imaging for the assessment of inflammation in RA patients.

Disclosure: A. Blanken, None; **C. van der Laken**, None; **M. Nurmohamed**, None.

Abstract Number: 1549

Joint Damage and Malalignment Determine Articular Tenderness More Than Inflammation in Rheumatoid Arthritis, Psoriatic Arthritis or Osteoarthritis in Established Disease

Mihaela Popescu[1], Victoria Schimpl[2], Gabriela Supp[3], Martina Durechova[3], Paul Studenic[3], Michael Zauner[3], Josef Smolen[3], Daniel Aletaha[4], Peter Mandl[3] and **Irina Gessl**[3], [1]Hôpital Maisonneuve-Rosemont, Montreal, Canada, [2]Medical University of Vienna, Vienna, Austria, [3]Division of Rheumatology, Department of Medicine III, Medical University of Vienna, Vienna, Austria, [4]Division of Rheumatology, Department of Medicine III, Medical University of Vienna,, Vienna, Austria

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

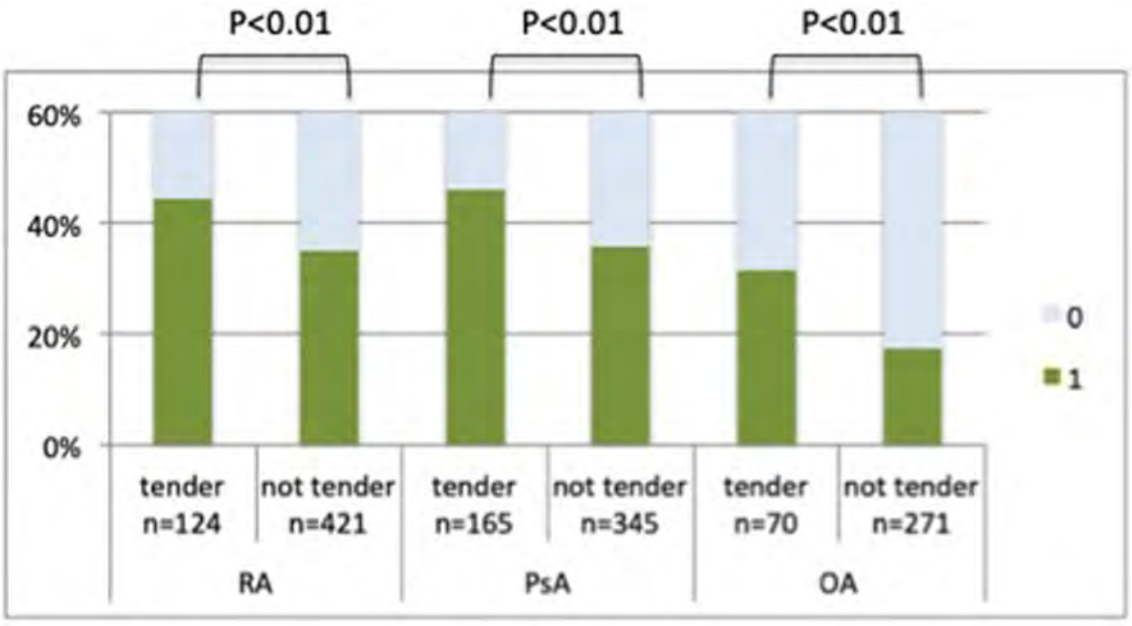


Figure 1. Difference of damage score (0 vs. ≥1) in patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA) and osteoarthritis (OA).

Background/Purpose: To determine whether clinical tenderness can be considered a sign of inflammatory joint activity in patients with rheumatoid arthritis (RA), osteoarthritis (OA) or psoriatic arthritis (PsA).

Methods: Patients diagnosed with RA, PsA and OA underwent clinical and ultrasound examination of wrists and finger joints. Gray scale signs of synovitis (GS) and Power Doppler signal (PD) were evaluated using a semiquantitative grading system. Radiographs of the hands were scored for erosions, joint space narrowing, osteophytes and malalignment and a binary damage score was calculated. Differences in PD and GS between tender non-swollen (TNS) vs. non-tender non-swollen joints (NTNS) were calculated by Chi-Square test and prediction of tenderness was assessed by sex- and age-adjusted binary logistic regression analysis.

Results: There was no difference in the frequency of PD positivity between TNS and NTNS joints in RA (p=0.18), PsA (p=0.59) or OA (p=0.96) (Fig. 1). However, PD had a significant impact on tenderness in non-swollen joints in patients with a disease duration of less than 2 years, both in RA (OR 2.22, 95%CI 1.12-4.43, p=0.02) and in PsA (OR 3.26, 95%CI 1.21-8.81, p=0.02). The radiographic damage score had a significant impact on tenderness in non-swollen joints in RA (OR 1.8, 95%CI 1.17-2.86, p< 0.01), PsA (OR 1.84, 95%CI 1.18-2.86; p< 0.01) and OA (OR 1.89, 95%CI 1.03-3.46; p=0.04) (Fig. 2).

Conclusion: Tenderness might not always be a sign of active inflammation in RA, PsA and OA. While inflammation may play a role in early disease, tenderness in established disease may be better explained by joint damage and malalignment.

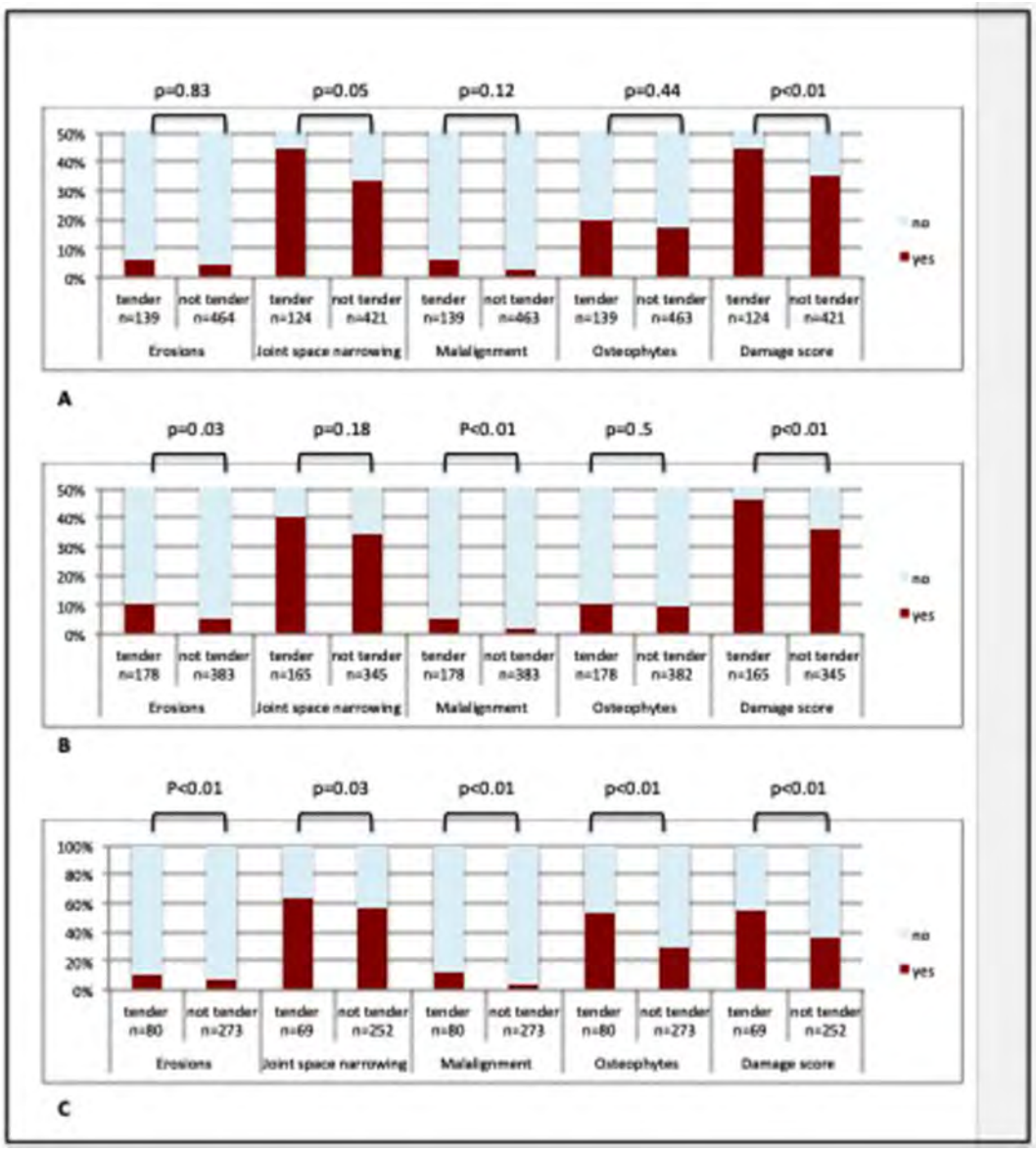


Figure 2. Difference of detected erosions (0 vs. ≥1), joint space narrowing (0 vs. ≥1), malalignment (presence/ absence), osteophytes (presence/ absence) and damage score (0 vs. ≥1) in patients with rheumatoid arthritis (A), psoriatic arthritis (B) and osteoarthritis (C). Impact of erosions (semiquantitatively), joint space narrowing (semiquantitatively), malalignment, osteophytes and damage score on tenderness in non-swollen joints was calculated by age- and sex-adjusted binary logistic regression.

Disclosure: M. Popescu, None; **V. Schimpl**, None; **G. Supp**, None; **M. Durechova**, None; **P. Studenic**, None; **M. Zauner**, None; **J. Smolen**, AbbVie, 2, 5, 8, AstraZeneca, 2, 5, 8, Eli Lilly, 2, 5, 8, Celgene, 5, 8, Celltrion, 5, 8, Chugai, 5, 8, Gilead, 5, 8, ILTOO, 5, 8, Janssen, 5, 8, Kabi, 5, 8, Novartis-Sandoz, 5, 8, Pfizer Inc, 5, 8, Samsung, 5, 8, Sanofi, 5, 8; **D. Aletaha**, UCB, 5, 8, Eli Lilly, 5, 8, Gilead Sciences, Inc., 2, 5, Janssen, 5, Sanofi/Genzyme, 5, 8, AbbVie, 2, 5, 8, Amgen, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, Roche, 2, 5, 8, Merck Sharp & Dohme, 2, 5, 8, Bristol-Myers Squibb, 8, Celgene, 5, 8, Medac, 5, 8, Sandoz, 5, 8; **P. Mandl**, AbbVie, 9, BMS, 9, Chugai, 9, MSD, 9, Janssen, 9, Lilly, 9, Novartis, 9, Pfizer, 9, Roche, 9; **I. Gessl**, Sobi, 9.

Abstract Number: 1550

Change in Tophus Size Measured with Dual-energy CT and Ultrasound: A 1-year Multicenter Follow-up Study

Tristan Pascart[1], Pascal Richette[2], Sebastien Ottaviani[3], Laurène Norberciak[1], Hang Korng EA[4], Frédéric Lioté[5], Jérémy Ora[6], Julie Legrand[1], Valérie Bousson[6], Elyas Mahdjoub[7] and Jean--Francois Budzik[8], [1]GHICL, Lomme, France, [2]Department of Rheumatology, Lariboisière Hospital, Paris, France, [3]Rheumatology Department, Bichat hospital, APHP, Paris, France, [4]Universite de Paris, AP-HP, INSERM, paris, France, [5]AP-HP, Paris, France, [6]Lariboisière Hospital, Paris, France, [7]Bichat Hospital, Paris, France, [8]University of Lille, Lille, France

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Imaging of Rheumatic Diseases Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Dual-Energy computed tomography (DECT) and ultrasound are the two techniques able to identify and measure monosodium urate (MSU) crystal deposition, and both are considered for monitoring crystal depletion during urate lowering therapy (ULT). Particularly, both techniques are able to measure tophi, but it is unknown if their assessment of tophus size are correlated throughout follow-up. The objective of this study was to determine if the evolution of tophus volume measured with DECT and ultrasound were correlated during the first year of ULT.

Methods: Gout patients naïve of ULT and presenting with at least 1 ultrasound tophus of the knees or ankles/feet were recruited in three French referral centers to undergo DECT scans, and were followed-up with ultrasound and

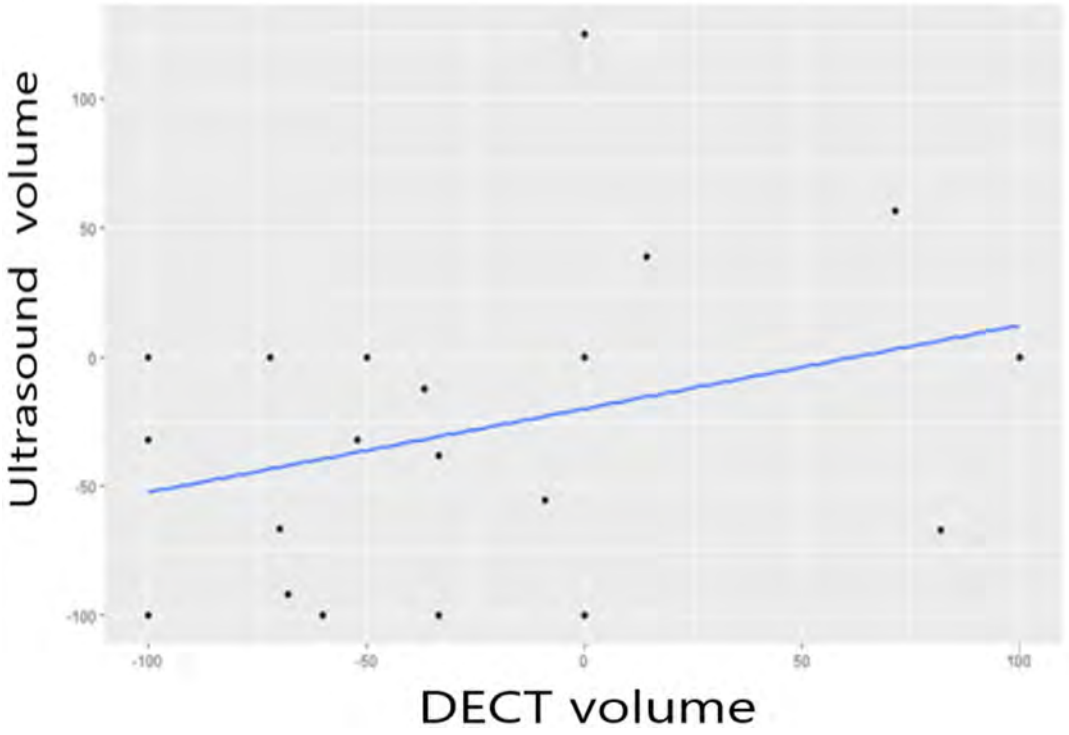


Figure 1. Evolution (in % from baseline) at month 6 of the index tophus measured with dual-energy computed tomography (DECT) and ultrasound.

DECT scans at months 6 and 12. The largest tophus in ultrasound was considered as the index tophus and measured with both techniques. The primary endpoint was the correlation between the evolution of the volumes of the index tophus measured with DECT and ultrasound assessed by the Spearman coefficient correlation (ρ) and its 95% confidence interval at months 6 and 12.

Results: A total of 41 patients were included; they were mostly males (83.3%) and aged in average 63.7 years (±12.3). Baseline serum urate levels were 515.2 µmol/L (±85) (=8.6mg/dL) and 58.3% had subcutaneous tophi. Most index tophi were localized at the 1st MTP joint (53.9%) and had a volume of 0.87 cm^3 (±1.39). 17 patients were lost to follow-up and 4 patients had index tophi that were not detected by DECT at baseline. The relative decrease of the volume of the index tophi at months 6 and 12 measured with ultrasound was -50% [-79.2%;0%] and -75.6% [-94.2%;-25%], respectively, while the decrease measured with DECT was -32.1% [-85.8%;0%] and -37.1% [-88.5%;0%], respectively.

The correlation between the volumes of the index tophi measured with ultrasound and DECT was poor with ρ=0.29 [-0.22;0.65] at month 6 and ρ=-0.03 [-0.66;0.65] at month 12. The correlation between the decrease of the DECT tophus index volume and the global volume of MSU crystal deposition measured with DECT was very good at both months 6 and 12 with ρ=0.82 [0.55;0.93] and 0.83 [0.5;0.96]. The correlation between the decrease of the volume of the index tophus measured with ultrasound and the decrease of the volume of overall MSU crystal deposition measured with DECT was at best moderate with ρ=0.35 [-0.16;0.75] at month 6 and 0.42 [-0.44 ; 0.82] at month 12.

Conclusion: Ultrasound and DECT do not provide the same assessment of MSU crystal depletion during the first year of ULT. The two techniques are not inter-changeable when considering monitoring gout treatment with imaging, especially when considering the follow-up of a target tophus.

Disclosure: T. Pascart, Horizon Therapeutics, 2, Novartis, 8; **P. Richette**, AbbVie Inc., 1, Biogen, 1, Janssen, 1, BMS, 1, Roche, 1, Pfizer, 1, Amgen, 1, Sanofi-Aventis, 1, UCB, 1, Lilly, 1, Novartis, 1, Celgene, 1; **S. Ottaviani**, None; **L. Norberciak**, None; **H. EA**, None; **F. Lioté**, LILLY FRANCE, 5, 8, SANOFI GENZYME, 8, SANDOZ, 5, NORDIC PHARMA, 8, LILLY FRANCE, 3; **J. Ora**, None; **J. Legrand**, None; **V. Bousson**, None; **E. Mahdjoub**, None; **J. Budzik**, None.

Abstract Number: 1551

Rapid Effect of Tofacitinib in Reducing US Joint and Tendon Inflammatory Lesions of RA Patients: Data from a 24 Weeks Longitudinal Study

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SESSION INFORMATION

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Session Title: Imaging of Rheumatic Diseases Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: To explore the effects of tofacitinib (Tofa) on US lesions in a consecutive series of patients with active RA MTX and/or bioDMARDs -IR.

Methods: In this observational, open label, longitudinal, m*ulticenter* study, patients received Tofa 5 mg twice daily ± MTX ± corticosteroids for 24 weeks. All patients underwent clinical, laboratory and US examinations in a standardized manner according to the EULAR guidelines for musculoskeletal US in rheumatology. Inclusion criteria required an OMERACT-EULAR composite US score for grading synovitis of ≥2 in at least two MCPs. US examinations were performed at baseline (T0), 2w (T1), 4w (T2), 12w (T3) and 24w (T4) for bilateral 20 joint sites and bilateral 20 tendon sites. For each patients we obtained two US joint scores (GS score and PD score) summing up the value of a 0-3 semiquantitative scale for each joint and a cumulative joint score summing up the values of the OMERACT combined joint score. Moreover we calculated two tenosynovitis scores (GS and PD) by summing the 0-3 score for each tendon. US examination were done in each centre, by the same sonographer, with the same US equipment (Esaote My Lab 70 Class, 12–18 MHz transducers) after a reliability test between the sonographers. Sonographers were blinded to clinical evaluations. Clinical and US data obtained at T0, T1, T2, T3 and T4 examinations were compared (T-test for paired samples) and correlated (Spearman's Rho).

Results: In total, 37 patients were enrolled and completed the 6 month period study (F 30 (81%), mean age : 58.5±12.6y), mean disease duration : 8.4+6.4y, ACPA + : 24 (66%) , baseline DAS28 : 4.8±1.2, HAQ : 1.3±0.7, CRP : 2.25±3.1 mg/dl). Joint (GS, PD and combined-PDUS) and tendon US scores (GS and PD) were significantly reduced as early as T1 examination as well as at T2, T3 and T4 visits as compared to baseline values ($p < 0.001$ for all comparisons). There was a statistical significant correlation between reduction of PD and GS teno-score at T1 examination and HAQ improvement at T4 visit (rho 0.607, $p < 0.001$ and rho 0.408, $p = 0.017$ respectively). Improvement of joint US scores (GS, PD and PDUS-combined) correlated at T4 examination with the reduction of serum CRP levels (rho 0.418, $p = 0.036$, rho 0.495, $p=0.004$ and rho 0.454, $p=0.009$ respectively). We did not found any correlation between the variations of DAS28 and any US scores at any visits.

Conclusion: These preliminary results provide evidence that Tofa treatment leads to early (two weeks) and persistent reduction of US signs of inflammation both at tendon and joint level.

Disclosure: G. Germanò, None; **P. Macchioni**, None; **G. Ciancio**, None; **F. Crescentini**, None; **A. Caruso**, None; **B. Maranini**, None; **S. Bonazza**, None; **G. Sandri**, None; **M. Mascia**, None; **G. Marcello**, None; **C. Salvarani**, None.

Abstract Number: 1552

Ultrasound Doppler Enthesitis Shows Sensitivity to Change After Biological Therapy in Spondyloarthritis and Psoriatic Arthritis Patients

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Parameter	Baseline n=25	After 3 months n=25	After 6 months n=22	Baseline vs 3 months[a]	Baseline vs 6 months[a]	3 months vs 6 months[a]
Clinical parameters						
DAS28	3.6 (2.3-4.2)	3.0 (1.4-3.7)	2.0 (2.0-3.0)	0.180	**0.005***	0.317
BASDAI	6.7 (6.1-7.4)	3.0 (1.0-5.0)	6.0 (3.0-6.0)	0.093	**0.013***	0.141
BASFI	6.1 (4.2-7.6)	4.0 (2.0-6.0)	6.0 (5.0-7.0)	0.271	**0.047***	0.257
VAS (0-100) pain	65.0 (50-80)	55.0 (32-70)	50.0 (20-70)	**0.047***	**0.003***	0.173
Patient Global Assessment (0-100)	70 (57-72)	55 (42-70)	60.0 (30-62)	0.053	**0.003***	0.178
Physician Global Assessment GA (0-100)	50.0 (40-50)	30.0 (15-40)	22.5 (10-40)	**0.001**	**0.002***	0.722
MASES	0.0 (0.0-2.0)	0.0 (0.0-0.0)	0.0 (0.0-0.5)	**0.040**	0.369	0.461
Laboratory parameters						
CRP (mg/L)	8.2 (1.6-20)	5.0 (1.0-9.5)	2 (1.0-8.0)	0.227	**0.024***	0.193
ESR (mm/h)	11 (7.5-21)	7.0 (4.0-11)	6.0 (4.0-11)	0.183	0.061	0.754
Ultrasound parameters						
MASEI score	31 (21-38)	21.0 (18-26)	25.5 (20-30)	**0.002***	**0.012***	0.089
PD US MASEI enthesis count	2.0 (2.0-3.0)	1.0 (0.0-2.0)	1.0 (0.0-2.0)	**0.041***	**0.004***	0.773
PD US OMERACT enthesis count	1.0 (1.5-3.0)	1.0 (0.0-1.0)	1.0 (0.0-1.0)	**0.046***	**0.009***	0.429

Table 2. Clinical, laboratory and MASEI evaluation at baseline, 3- and 6-month follow-up visits aWilcoxon test between time visits

Background/Purpose: The assessment of activity in spondyloarthritis (SpA) and psoriatic arthritis (PsA) involves several domains, including enthesitis. Clinical enthesitis has shown low sensitivity, specificity and reliability. The MAdrid Sonographic Enthesitis Index (MASEI) is a feasible and reliable ultrasound score, but its responsiveness to treatment has not yet been evaluated. Our aim was to explore the sensitivity to change of power Doppler (PD) enthesitis in active spondyloarthritis (SpA) and psoriatic arthritis (PsA) patients.

Methods: Longitudinal study in patients with SpA and PsA with active disease (defined as patients who were going to start or switch biologic disease modifying antirheumatic drugs (bDMARD) therapy). The MAdrid Sonographic Enthesitis Index (MASEI) was performed at baseline, 3- and 6-months visits. MASEI and Outcome Measures in Rheumatology (OMERACT) PD enthesitis definitions were checked. A reliability analysis among three readers was performed with ultrasound (US) recorded videos.

Results: US examinations of 25 patients were included, of whom 13(52%) were ankylosing spondylitis (AS) patients, 9(36%) PsA and 3(12%) non radiographic axial spondyloarthritis (nr-axSpA). Median age was 49 (41-61) years and 13(52%) patients were females. Median DAS28 3.6 (2.3-4.2), median BASDAI 6.7 (6.1-7.4), and CRP values 8.2 (1.6-20), reflect moderate-high disease activity at baseline. Both MASEI and OMERACT PD enthesitis improved significantly at 3- and 6-month follow-up visits ($p< 0.05$) (Table 1) and showed sensitivity to change with a standard error of measurement (SEM) of 0.47 and 0.61 respectively. Improvement in clinical activity outcomes was significantly associated with a decreased of the MASEI and OMERACT PD enthesitis count ($p< 0.05$). Reliability of MASEI and OMERACT PD definitions among the three readers was excellent (kappa 0.918 and 0.865 respectively).

Conclusion: PD enthesitis significantly improves at 3- and 6- months of follow up in patients under bDMARD treatment. Both MASEI and OMERACT PD definitions of US active enthesitis reflect treatment response.

Disclosure: J. Molina Collada, None; **C. Macía-Villa**, None; **C. Plasencia**, None; **J. Alvaro-Gracia**, Abbvie, 2, 5, 8, lilly, 2, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 5, 8, UCB, 5, 8, Sanofi, 5, 8; **E. De Miguel**, AbbVie, 2, 5, 8, BMS, 8, MSD, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 8, UCB, 8.

Abstract Number: 1553

Optical Tomography Can Accurately Diagnose Lupus Arthritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Incapacitating inflammatory arthritis occurs in up to 88% of patients with systemic lupus erythematosus (SLE). Arthritis is present in 70-80% of lupus patients in clinical trials. There is continued debate as to whether tenderness in the absence of swelling constitutes active lupus arthritis and should be scored on activity instruments. The confusion over arthritis scoring impacts clinical care and trials. There is an unmet need for a simple tool that can objectively assess lupus arthritis; near-infrared optical imaging has the potential to address this need. Over the last decade the technology has been optimized for use in brain imaging, breast cancer, and peripheral ischemia. Studies have also shown its utility in rheumatoid arthritis. Near-infrared light illuminates the tissues and transmitted and reflected light intensities are measured. Maps computed from these measurements show the spatial distribution of physiological parameters. Changes in optical properties caused by physiologic changes form the basis for its diagnostic capabilities. Using a so-called frequency-domain optical imaging (FDOI) system[1] we evaluated the proximal interphalangeal (PIP) joints of 16 SLE patients and 10 healthy volunteers.

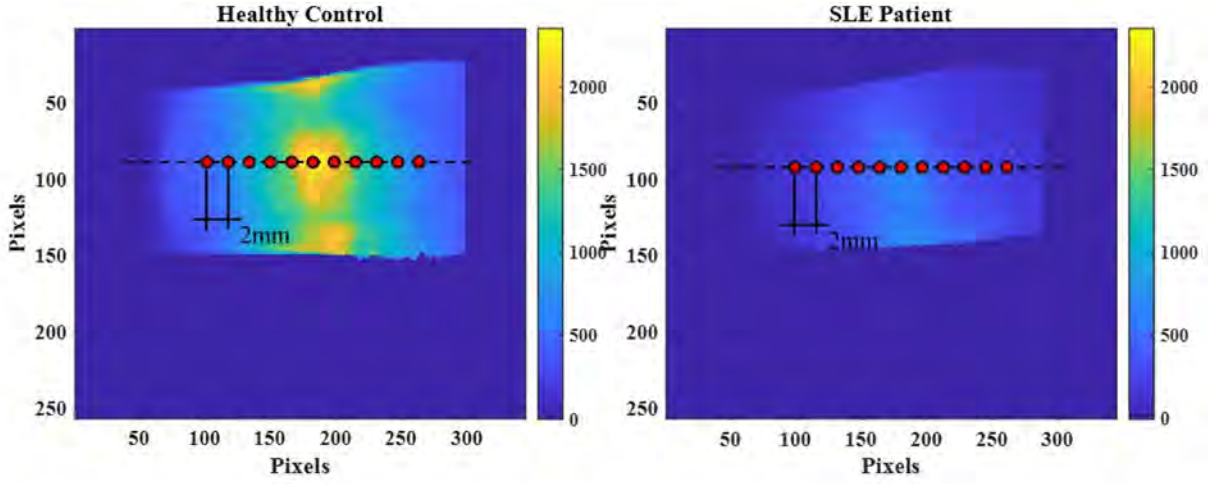

Fig. 1. Examples of amplitude images obtained from the index finger of a healthy volunteer (PIP2) (left) and the index finger of a SLE patient (PIP2) with lupus arthritis joint (right). The images were generated by a frequency-domain optical imaging (FDOI) system. The red dots indicate the positions of the 11 sources used in this study. The images shown above are the mean value from 11 amplitude images, one per source position. The bright yellow area on the left panel corresponds to the PIP joint, a similar region in light blue is also visible in the right panel. Note that the amplitude of the transmitted light intensity is much lower in the SLE patients compared to the healthy volunteer.

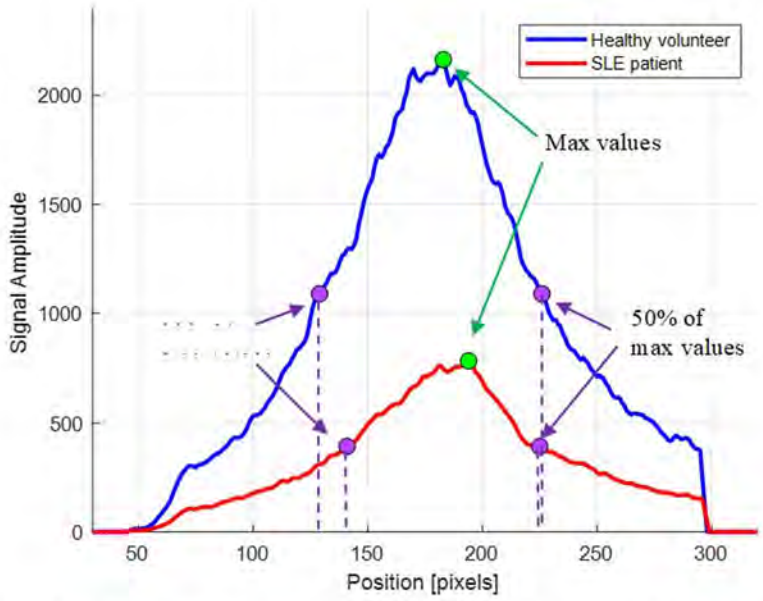

Fig. 2. Example of mean amplitude obtained along the length of the finger shown in Fig.1 from the same control subject (blue) and SLE patient (red). The maximum value is highlighted in green. The points at 50% of the max value are highlighted in purple; the number of pixels between them was selected as the third parameter for the linear discriminant analysis.

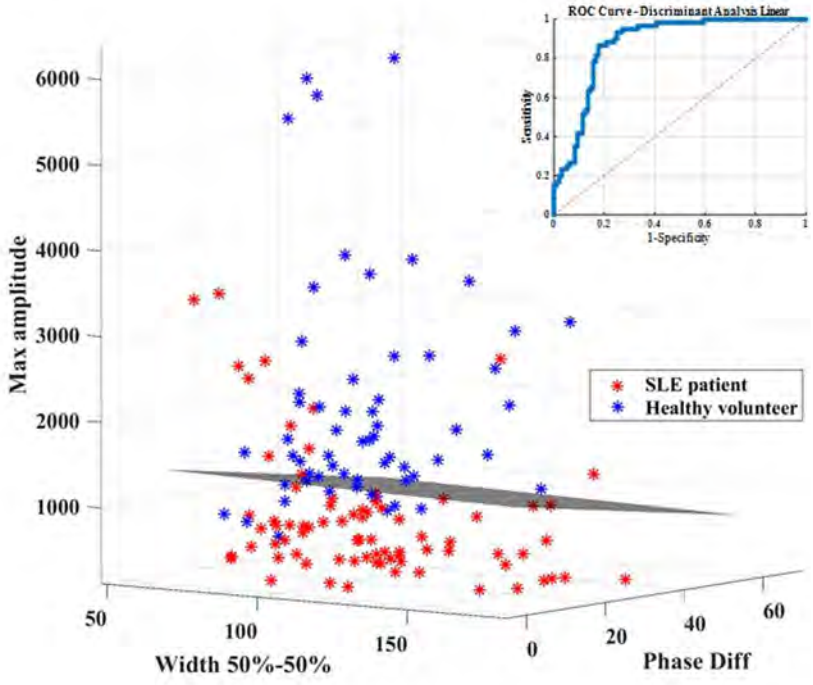

Fig. 3. Linear discriminant analysis of the three parameters for the 2nd, 3rd, and 4th PIP joints. The healthy volunteers are represented by blue dots, SLE patients with swollen and/or tender fingers by red dots. The black plane is the cut-off for evaluating sensitivity and specificity, which maximizes J-value. The upper right corner shows the corresponding ROC curve.

Methods: The FDOI system consists of a laser diode projecting a 1-mm - 670nm optical beam at 11 different positions along the PIP joints, 2mm apart, lengthwise. Fig.1 shows with the positions of the source. At each point, 16 images are acquired at different phases by a camera. The FDOI system is operated at a frequency of 300 MHz. PIPs 2-4 bilaterally were evaluated. A total of 60 healthy joints from 10 healthy volunteers and 96 joints from 16 patients with SLE arthritis were analyzed. Amplitudes and phases signals were generated using a demodulation algorithm.[1] The fingers' sizes (width and thickness) were measured using a caliper.

Results: The 16 patients with SLE arthritis (94% women, mean age 43±10 years, disease duration 14±8 years) had 74 swollen and/or tender PIP joints. Considering the mean signals from the 11 illumination positions (see Figs. 1 and 2), a discriminant analysis was done considering three variables: the maximum amplitude at the peak of the curve obtained, the maximum difference of the phase signals, and the number of pixels between 50% of the maximum value on the left and on the right of the peak. A receiver-operating curve (ROC) analysis showed an area under the curve (AUC) of 0.88 with correspondent sensitivity of 87% and specificity of 80% (Fig. 3).

Conclusion: These pilot data show that FDOI measurements of the PIP joints provide a clear difference between SLE patients and healthy subjects. If confirmed in a larger clinical study, FDOI could bring objectivity to the quantification of SLE arthritis. Compared to joint counts, US, and MR imaging, the advantages of FDOI are non-invasiveness, objectivity (eliminates inter-rater variability and operator dependency), low cost, and high speed of performance (~5 min).

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Abstract Number: 1554

Response to Tocilizumab in Large Vessel Vasculitis According to the Extent of Baseline ^{18}F-FDG Vascular Uptake

Lara Sanchez-Bilbao[1], Diana Prieto-Peña[2], Inigo Gonzalez-Mazon[3], David Martinez-Lopez[4], Monica Calderon-Goercke[5], Isabel Martínez-Rodríguez[5], Ignacio Banzo[5], Miguel Ángel González-Gay[6] and Ricardo Blanco[1], [1]Hospital Universitario Marques de Valdecilla, Santander, Spain, [2]Research group on genetic epidemiology and atherosclerosis in systemic diseases and in metabolic bone diseases of the musculoskeletal system, IDIVAL; and Department of Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [3]Hospital Universitario Marques de Valdecilla, Bezana, Spain, [4]Hospital Universitario Marques de Valdecilla, Santander (SPAIN), Spain, [5]Hospital Universitario Marqués de Valdecilla, Santander, Cantabria, Spain, [6]Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: ^{18}F-fluodeoxyglucose positron emission tomography (^{18}F-FDG PET/CT) is useful to establish the presence and extent of large vessel vasculitis (LVV). Tocilizumab (TCZ) has shown efficacy in the management of LVV. However, it is unknown if the extent of FDG vascular uptake may influence the clinical response to TCZ.

Our aim was to assess whether the extent of baseline FDG vascular uptake in PET/CT scans correlates to clinical and serological evolution in patients with LVV under TCZ therapy.

TABLE 1

	1-2 vascular affected areas (n=13)	≥3 vascular affected areas (n=17)	P
Demographic data			
Age, *mean ± SD*	66.0 ± 10.8	64.8 ± 10.7	0.77
Sex (women), *n (%)*	11 (84.6)	13 (76.5)	0.67
Evolution time before TCZ therapy (months), *median [IQR]*	26.0 [3.5-34.0]	5.0 [1.5-10.0]	0.02
Laboratory markers			
ESR (mm/1st hour), *mean ± SD*	30.0 ± 27.3	34.8 ± 27.6	0.64
CRP (mg/dL), *mean ± SD*	1.3 ± 1.2	1.8 ± 1.7	0.28
Previous treatment			
Prednisone dose (mg/day), *mean ± SD*	9.4 ± 6.2	7.9 ± 6.9	0.53
TCZ therapy			
Intravenous infusions, n *(%)*	10 (76.9)	11 (64.7)	0.47
Combined with MTX, n *(%)*	6 (46.2)	8 (47.1)	0.96

TABLE 2

	1-2 vascular affected areas (n=13)	≥ 3 vascular affected areas (n=17)	P
Complete clinical improvement, *n/N (%)*			
- 6 months	11/13 (84.6)	12/17 (70.6)	0.43
- 12 months	12/13 (92.3)	13/17 (76.5)	0.36
- 18 months	10/11 (90.9)	11/12 (91.7)	0.99
- 24 months	8/8 (100)	9/10 (90.0)	0.99
Normalization of ESR and/or CRP, *n/N (%)*			
- 6 months	13/13 (100)	16/17 (94.1)	0.99
- 12 months	13/13 (100)	16/17 (94.1)	0.99
- 18 months	11/11 (100)	11/12 (91.7)	0.99
- 24 months	8/8 (100)	10/10 (100)	0.99
Dose of Prednisone (mg/day), *median [IQR]*			
- 6 months	5.0 [1.3-5.0]	5.0 [0.0-5.0]	0.98
- 12 months	2.5 [0.0-3.8]	0.0 [0.0-5.0]	0.97
- 18 months	0.0 [0.0-2.5]	0.0 [0.0-1.9]	0.72
- 24 months	0.0 [0.0- 2.2]	0.0 [0.0-2.5]	0.77

Methods: Comparative single-center study of 30 patients with LVV treated with TCZ who were divided into two groups depending on the extent of FDG vascular uptake in the baseline PET/CT scan: **a)** 1-2 affected areas, **b)** ≥affected 3 areas. Vascular FDG uptake was qualitatively assessed by two experienced nuclear medicine physicians in five areas (supra aortic trunks, thoracic aorta, abdominal aorta, iliac arteries, femorotibial arteries). We assessed clinical improvement (no improvement/partial/complete), normalization of acute phase reactants (CRP ≤0.5mg/dL and/or ESR ≤ 20 mm/1st hour) and reduction of prednisone dose (mg/day).

Results: We included 30 (24 women/6 men); mean age 65.3±10.6 years. 13 patients exhibited FDG vascular uptake in < 3 areas whereas 17 patients had ≥3 affected areas. There was a trend to higher ESR/CRP and shorter evolution of clinical symptoms before TCZ onset in patients with ≥3 affected areas (**TABLE 1**). Most of the patients received TCZ as intravenous infusions and almost half of them received combined therapy with MTX in both groups. Clinical and serological evolution and reduction of prednisone dose is shown in the **TABLE 2**. No statistical differences were found between both groups. However, patients with ≥ 3 affected areas tended to experience a slower clinical response.

Conclusion: TCZ therapy was effective in patients with LVV regardless the extent of FDG vascular uptake in the baseline PET/CT scan. However, a trend to a slower clinical response was observed in patients with ≥3 affected areas.

Disclosure: L. Sanchez-Bilbao, None; **D. Prieto-Peña**, None; **I. Gonzalez-Mazon**, None; **D. Martinez-Lopez**, Lilly, 2; **M. Calderon-Goercke**, None; **I. Martínez-Rodríguez**, None; **I. Banzo**, None; **M. González-Gay**, None; **R. Blanco**, None.

Abstract Number: 1555

^{18}F-NaF PET/CT Identifies Active Calcium Uptake in Calcinosis Due to Dermatomyositis and Scleroderma

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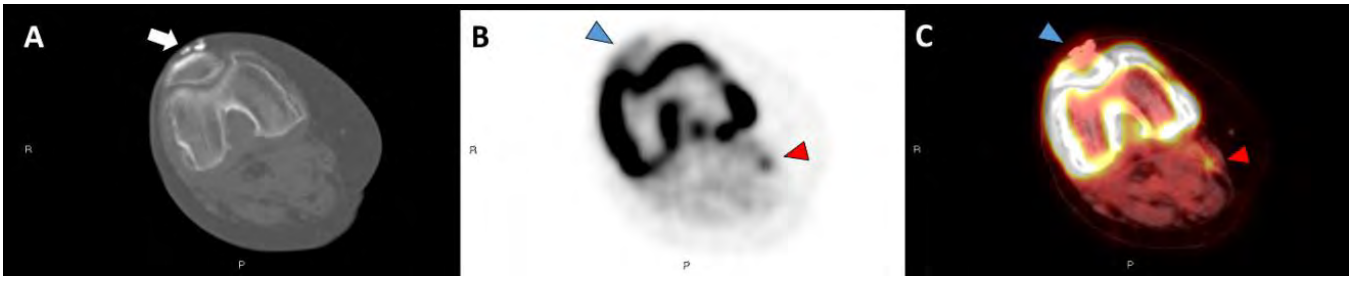
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Ectopic soft tissue deposition of hydroxyapatite (calcinosis) is a frequent and morbid complication of dermatomyositis and scleroderma with no known effective pharmacologic treatment. ^{18}F-NaF PET/CT detects active hydroxyapatite deposition in benign and malignant bone disorders and may identify subclinical and actively calcifying lesions in scleroderma- and dermatomyositis-related calcinosis.

Methods: In this pilot study, we enrolled three adults with dermatomyositis and three adults with scleroderma, all with new calcinosis deposits within the past six months. Each participant underwent ^{18}F-NaF PET/CT as well as a clinical examination for assessment of calcinosis. We recorded the number, locations, and standardized uptake values (SUVs) of deposits for each ^{18}F-NaF PET/CT.



Axial CT image in bone windows (A) demonstrates calcinosis involving the quadriceps and patellar tendon complex overlying the left patella. Axial 18F-NaF PET/CT images (B and C) demonstrate mild activity along this calcified complex (blue arrowheads). However, there is focal PET signal activity located along the semimebranosus muscle without associated calcification on CT (red arrowheads). These findings may suggest increased sensitivity of 18F-NaF PET imaging in detecting pre-calcified disease involvement.

Full-body coronal 18F-NaF PET image of Patient 6 demonstrating the distribution and intensity of 18F-NaF uptake. Note the intense activity in the upper arms and around the knees as well as widespread uptake in the thighs and pelvic girdle. There is also increased uptake in the axial skeleton, indicating increased systemic bone turnover

Results: ^{18}F-NaF PET/CT detected heterogeneous uptake in calcinosis deposits appearing homogeneous on CT. ^{18}F-NaF PET/CT also detected calcium uptake where there was no visible calcification on CT. We noted increased uptake of ^{18}F-NaF in the axial skeleton of one patient with multiple actively calcifying deposits, consistent with increased systemic bone turnover. Some joints also demonstrated increased ^{18}F-NaF uptake, consistent with arthritic remodeling.

Conclusion: ^{18}F-NaF uptake on PET/CT is heterogeneous, even in radiographically homogeneous deposits, and identifies actively calcifying and subclinical deposits not apparent on CT. ^{18}F-NaF uptake on PET/CT may be an early and sensitive marker of disease activity in calcinosis due to scleroderma and dermatomyositis.

Disclosure: C. Richardson, None; **M. Javadi**, None; **A. Shah**, None; **L. Solnes**, None; **F. Wigley**, None; **L. Hummers**, Corbus Pharmaceuticals, 1, 2, Boehringer Ingelheim, 1, 2, CSL Behring, 1, 2, Cumberland Pharmaceuticals, 1, Medpace, 1, Glaxo Smith Kline, 1, Kadmon Corporation, 1; **L. Christopher-Stine**, None.

Abstract Number: 1556

Assessing Calcinosis in Dermatomyositis with Computed Tomography and Calcium Scoring

Prateek Gowda[1], Briana Cervantes[2], Lisa G. Rider[3], Frederick W. Miller[4], Marcus Chen[4] and Adam Schiffenbauer[4], [1]NIBIB, Baltimore, MD, [2]NIEHS, Silver Spring, MD, [3]Environmental Autoimmunity Group, Clinical Research Branch, NIEHS, NIH, Garrett Park, MD, [4]National Institutes of Health, Bethesda, MD

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Calcinosis is a condition in which calcium salts are deposited in and around soft tissue and is observed in up to 30% of adult dermatomyositis (DM) patients and up to 70% of juvenile dermatomyositis (JDM) patients. Clinical assessment of calcinosis is usually conducted with a physical assessment or through radiographic imaging consisting of plain X-rays. However, due to the two-dimensional nature of these X-ray images, much is still not known about the spatial properties of calcification and the relative densities of the lesions. The objective of the study was to utilize whole-body computed tomography (CT) imaging and calcium scoring techniques as tools for calcinosis assessment in a prospective cohort of patients with DM and JDM.

Methods: Thirty-one patients (14 DM and 17 JDM) who fulfilled Bohan and Peter Classification criteria as probable or definite DM, the EULAR-ACR for definite DM, and with calcinosis identified by physical examination or prior imaging studies were included. Non-contrast whole-body CT scans were obtained using generic and ultra-low dose radiation procedures. Scans were read qualitatively and quantitated using imaging software. We calculated the sensitivity and specificity of calcinosis detection against a physician physical exam. We quantified calcinosis burden using the Agatston scoring technique.

Results: We identified five distinct calcinosis patterns: Clustered, Disjoint, Interfascial, Confluent, and Fluid-filled. Patients often exhibited multiple types of calcification. The most common patterns were the Clustered and Interfascial type seen in 19 and 7 patients, respectively. Novel locations of calcinosis were observed, including the cardiac tissue, pelvic and shoulder bursa, and the spermatic cord. The regions of highest and lowest calcinosis occurrence were the proximal legs (86.7%) and head & neck (40%), respectively. There was moderate agreement for calcinosis detection between the physical exam and CT ($\kappa = 0.45$, 95% confidence interval [95% CI] 0.38, 0.52). Physician physical exams had a sensitivity of 59% and a specificity of 90% compared to CT detection. Quantitative measures using Agatston scoring for calcinosis were used in regional distributions across the body. Total average Agatston score, normalized by patient height, was 3128.52 ± 5868.52 (adult DM: 1741.93 ± 2347.21, JDM: 4630.67 ± 8024.76), with no difference by clinical subgroup. A higher calcium score correlated with higher Physician Global Damage, Calcinosis Severity scores, and disease duration.

Conclusion: Whole-body CT scans and the Agatston scoring metric define distinct calcinosis patterns and provide novel insights relating to calcinosis in DM and JDM patients. Physician physical examinations underrepresented the presence of calcium. Calcium scoring of CT scans correlated with clinical measures, which suggests that this method may be used to assess calcinosis and follow its progression.

Disclosure: P. Gowda, None; **B. Cervantes**, None; **L. Rider**, NIEHS, NIH, 2, Cure JM Foundation, 2, Bristol Myers Squibb, 2, Hope Pharmaceuticals, 2, Eli Lilly and Company, 9, MedImmune/AstraZeneca, 9; **F. Miller**, None; **M. Chen**, None; **A. Schiffenbauer**, None.

Abstract Number: 1557

Lymphatics as a Biomarker of Joint Physiology: Near-Infrared Imaging of Indocyanine Green Identifies Novel Routes of Lymphatic Drainage from Metacarpophalangeal Joints in Healthy Human Hands

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Imaging of Rheumatic Diseases Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: In our previous work, we discovered that patients with active hand RA have reduced lymphatic drainage of indocyanine green (ICG) from the web spaces adjacent to metacarpophalangeal (MCP) joints visualized by near-infrared (NIR) imaging.[1] We also noted an associated decrease in draining lymphatic vessels (LVs) on the basilic surface of the hand as one of many potential mechanisms mediating the impaired lymphatic function.[1] While these changes represent important biomarker potential in identifying RA patients with active disease, we wanted to more directly assess MCP joint-specific lymphatic drainage in a pilot study of healthy subjects utilizing NIR-ICG imaging. In addition, we aimed to validate the lymphatic tributaries identified via NIR-ICG imaging using a novel

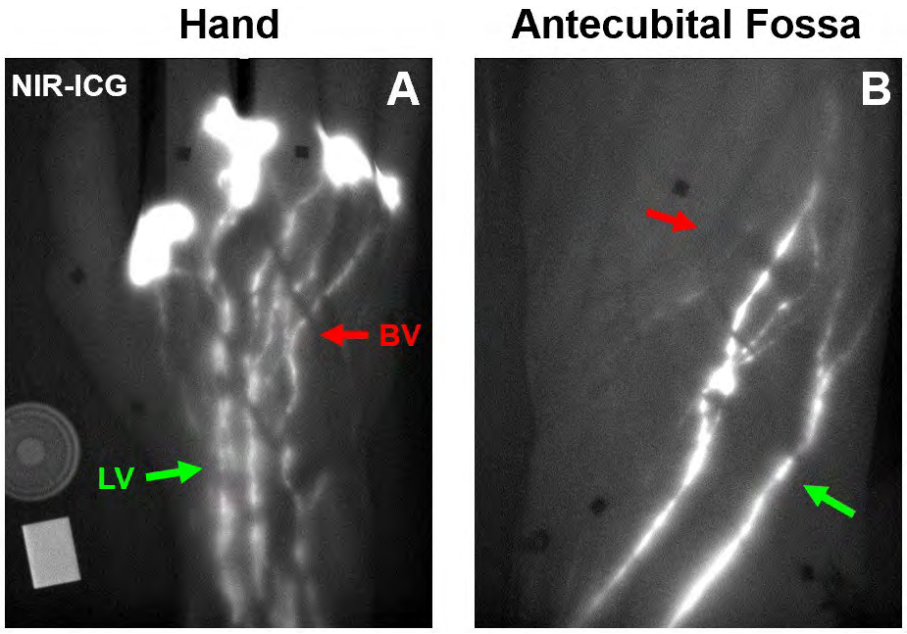

Figure 1. Lymphatic vessels identified by dynamic NIR imaging following ICG web space injections in healthy human hands. Representative images of web space draining lymphatic vessels (white, green arrows) adjacent to blood vessels (dark, red arrows) in the hand (A) and antecubital fossa (B).

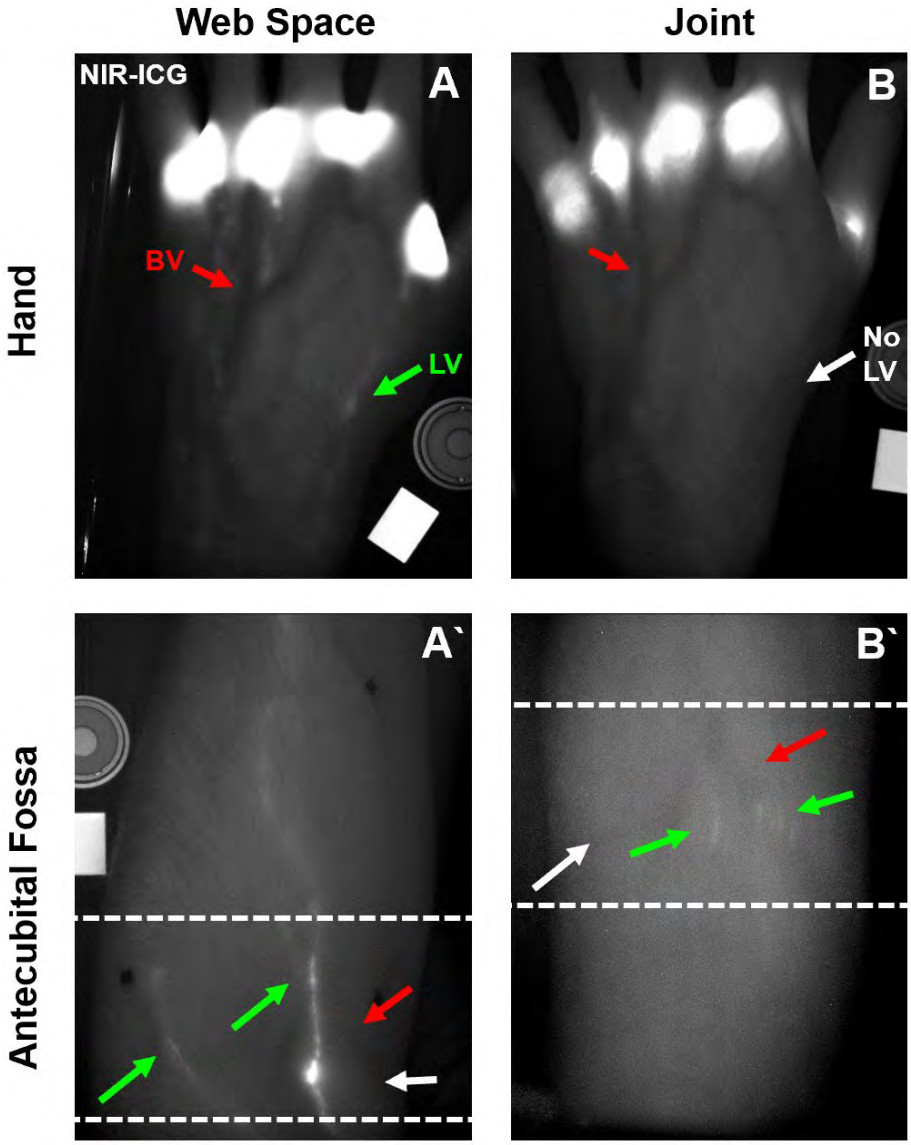

Figure 2. Dynamic NIR-ICG imaging reveals distinct lymphatic vessels draining the MCP joint versus the adjacent web space. NIR-ICG imaging showing verified LVs (white vessels, green arrows) and adjacent superficial BVs (dark vessels, red arrows) in the hand (A) and antecubital fossa (A`, dashed lines) following ID ICG web space injections. In contrast, IA MCP joint injections of ICG show no identifiable LVs (white arrows) in the hand (B) and different draining LVs in the antecubital fossa (B`, dashed lines) of the same subject.

dual-agent relaxation contrast magnetic resonance lymphography (DARC-MRL) technique successful in identifying lymphatic vessels in patients with lymphedema.[2]

1. Bell et al. 2020 *Arthritis & Rheumatology*. https://doi.org/10.1002/art.41311.
2. Ripley et al. 2017 *Radiology*. 286(2):705-714.

Methods: All of the experiments were approved by the University of Rochester IRB and the FDA (NCT02680067). A total of ten healthy subjects will be recruited for this pilot study. We conducted lymphatic imaging of the hands and forearms at four visits using different methods of imaging and routes of contrast administration: 1) NIR-ICG web spaces, 2) NIR-ICG MCP joints, 3) DARC-MRL web spaces, and 4) DARC-MRL MCP joints. For NIR-ICG imaging, 0.1 mL of 100 μM ICG was injected intradermally (ID) into the web spaces or intra-articularly (IA) into the MCP joints. To capture the DARC-MRL imaging, subjects received intravenous ferumoxytol diluted in normal saline to 60 mL total

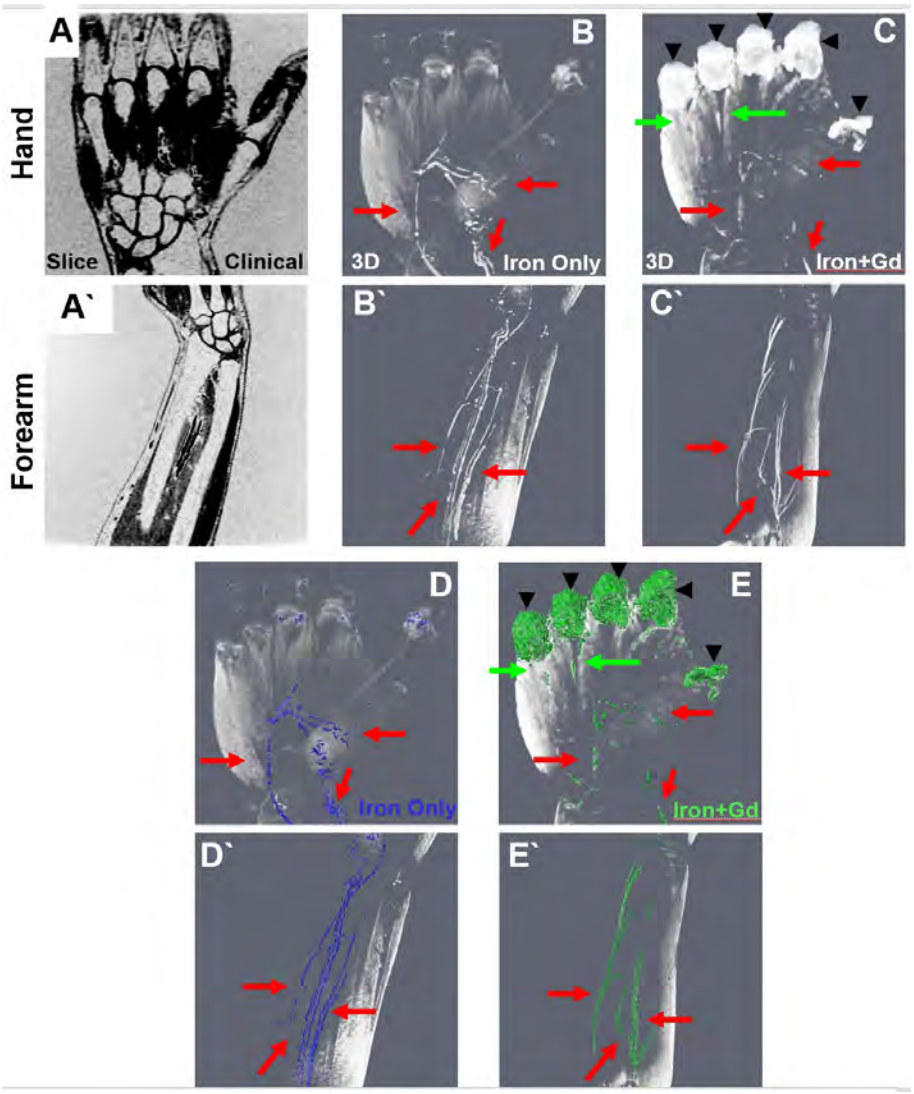

Figure 3. MCP joint draining lymphatic vessels using DARC-MRL. To assess the distinct lymphatic drainage of the MCP joints throughout the hand and forearm, DARC-MRL following IV iron infusion and gadolinium joint injections was performed on the same healthy subject. Prior to the joint injections, intravenous iron was administered and utilized as contrast enhancement to generate a scout image of the blood vasculature. Following the gadolinium joint injections, image sequences were captured at TR 11.2 and TE 8.5; under these conditions, the iron infused blood should quench, while the lymphatic vessels are enhanced by the gadolinium based on previous DARC-MRL methods. Inverted representative images of the hand (A) and of the forearm (A`) in a healthy subject are shown for orientation. Note that the background is white, demonstrating that the sequence was inverted. 3D renderings of the iron scout sequence showing the hand (B) and forearm (B`) demonstrate contrast enhanced blood vessels (red arrows). The images following the gadolinium joint injections indicate successful administration of the gadolinium into the MCP joint space (arrow heads) with contrast enhanced lymphatic vessels draining directly from the joint (green arrows) that are not visualized thereafter in the hand (C) or forearm (C`). The blood vessels remain partially enhanced in this sequence (red arrows) demonstrating incomplete quenching using this method (C, C`). Automated segmentation using thresholding of the contrast enhanced vasculature before (D, D`) and after (E, E`) gadolinium administration to the MCP joint shows the similar blood vessels (red arrows) and the unique lymphatic vessels (green arrows).

volume at 5 mg iron/kg body weight at a rate of 0.1 mL/sec. Subjects were then administered 0.5 mL of gadolinium-diethylenetriamine pentaacetic acid (Gd-DTPA) either ID in the web spaces or IA in the MCP joints.

Results: The results from two healthy subjects thus far indicate that MCP joint-draining LVs travel deep to the superficial LVs associated with the web space **(Figures 1 & 2)** and may follow novel routes shuttling lymph unexpectedly retrograde from the MCP to the proximal interphalangeal (PIP) joint. In addition, our current methods of DARC-MRL

do not have the appropriate resolution or suppression of the blood vessels (BVs) to accurately identify small healthy LVs **(Figure 3)**.

Conclusion: This is the first study to date that has directly visualized MCP joint-draining LVs and performed DARC-MRL in healthy subjects. Our analysis thus far suggests that LVs draining MCP joints represent an entirely distinct lymphatic vascular network than those draining the adjacent web spaces. In addition, improvement in the DARC-MRL technique will provide a valuable understanding of the lymphatic architecture draining MCP joints and alterations in this lymphatic anatomy in patients with RA. As future studies continue to evaluate the joint-draining LVs, and their function during RA progression, we will be able to better define the lymphatic system as a biomarker of active arthritis towards beneficial clinical application.

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Abstract Number: 1558

Cinematic Rendering Enables Depiction of Bone Anabolic Effects in Patients Treated with Baricitinib

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Preclinical studies show that tsDMARDs such as baricitinib may be a therapeutic agent for bone anabolic effects by increasing osteoblast function in inflammatory conditions.[1] High-resolution CT imaging (HR-pQCT) allows the determination of volumetric, peripheral bone mineral density of trabecular and cortical bone

Table 1
Patient characteristics and volumetric bone density of the radial bone

demographics	patient 1	patient 2	patient 3
age (y)	63	59	80
sex	w	m	w
CCP status	+	+	+
Baricitinib treatment 12 months	4 mg	4 mg	2 mg
DAS28-CRP after 12 months	- 1,03	- 1,34	- 1,26
bone density*			
Dtotal (% after 1 year)	+ 41,8 %	+ 3,8 %	+ 16,4 %
D trab (% after 1 year)	+ 49,9%	+ 5,9 %	+ 18,1 %
Dcort (% after 1 year)	+ 0,0 %	+ 0,5 %	+ 0,5 %

*volumetric bone mineral density of the radius (vBMD) in mg hydroxylapatite / mm³; Dtotal (total vBMD); Dtrab (trabecular vBMD); Dcort (cortical vBMD)

Figure 1

a) 2018 b) 2019

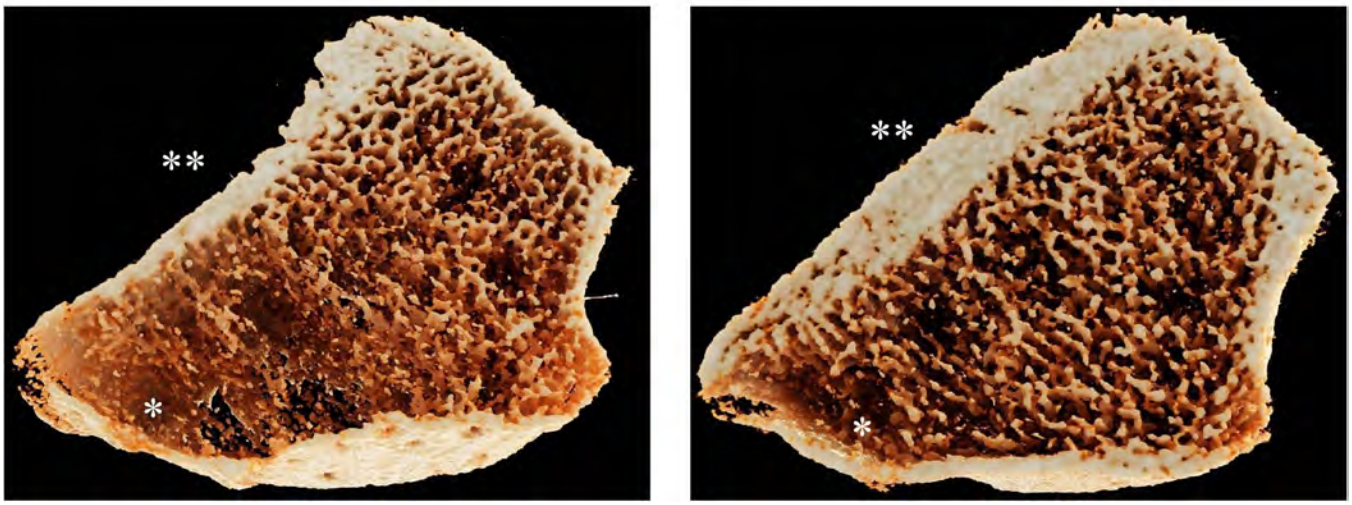

Figure 1. High resolution CT images of the radius from patient 1 are visualized with Cinematic Rendering at two time points (figure 1a and figure 1b). * illustrates changes in trabecular bone.

in patients with rheumatic diseases in vivo with a resolution of 82 micrometers voxel size. [2] Recently introduced rendering techniques such as cinematic rendering, developed by Siemens Healthineers allow a fotorealistic- insight into the bone on microstructural level in vivo.(3)

To test whether HR-pQCT images, segmented by cinematic rendering depict changes in bone mineral density in patients treated with baricitinib.

Methods: Bone density measurements of two time points of the radial bone from patients with active rheumatoid arthritis who are part of an ongoing, prospective cohort (ethics 19_18B;324_16) receiving baricitinb were analyzed. Volumetric bone density (vBMD) of the entire radius (Dtotal) in mg/hydroxyapatite / cm^3 was determined as well as the cortical (Dcort) and trabecular (Dtrab) part of the bone. The measurements were registered using the software supplied by the manufacturer Scanco to determine the percentage change of vBMD. Images were post-processed using cinematic rendering technique to visualize pathologies in detail.

Results: Clinical characteristics are shown in table 1. We included three patients as a proof of concept analysis. All patients showed an improvement in clinical scores. We were able to display bone microstructure using cinematic rendering technique in great detail (figure 1) proving the feasibility to visualize bone microstructure with cinematic rendering at two time points. Furthermore, our preliminary data regarding vBMD shows that anabolic effects were observed for trabecular bone in particular. One patient displayed an increase of 49%.

Conclusion: The preliminary data reported here underline the potential impact of tsDMARDs therapy on secondary peripheral osteoporosis in patients with rheumatoid arthritis. These observations led to a prospective clinical trial, investigating effects of tsDMARDS (baricitinib) on bone metabolism(EUDRA-CT 2018-001164-32).

1. Adam, S., N. Simon, U. Steffen, F.T. Andes, C. Scholtysek, D.I.H. Muller, D. Weidner, D. Andreev, A. Kleyer, S. Culemann, M. Hahn, G. Schett, G. Kronke, S. Frey, and A.J. Hueber, JAK inhibition increases bone mass in steady-state conditions and ameliorates pathological bone loss by stimulating osteoblast function. Sci Transl Med, 2020. **12**(530).

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3. https://www.siemens-healthineers.com/de/medical-imaging-it/advanced-visualization-solutions/syngovia-cinematic

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Disclosure: S. Bayat, Novartis, 8; **D. Simon**, Novartis, 8, Lilly, 5, 8, Janssen, 8, AbbVie, 5; **L. Schuster**, None; **G. Schett**, None; **A. Kleyer**, Lilly, 8, Novartis, 8, BMS, 8, Sanofi, 8, Gilead, 8.

Abstract Number: 1559

Fully Automatic Assessment of Nail Fold Capillaroscopy Software - Early Results

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Changes in capillaroscopy nailfold image are a valuable element in the diagnostic procedure and monitoring of systemic sclerosis as well as other systemic diseases. However, manual image assessment is time consuming and the classification of observed changes is subjective. This makes it difficult to compare the results of tests evaluated by different physician, as well as to thoroughly analyse the progression that occurs between repeated tests. The aim of the study is to validate an automated software for classification of nailfold capillary image as normal or disturbed

Methods: From among the available resources, 100 normal capillaroscopy images and 100 with varying severity of pathological changes were selected. manual image analysis was performed twice. In the teaching program prepared for this purpose (Figure 1), region of interest (ROI) was determined and individual capillaries were marked, images were classified as correct and changed. The neural network was trained using the fast.ai library (based on PyTorch).

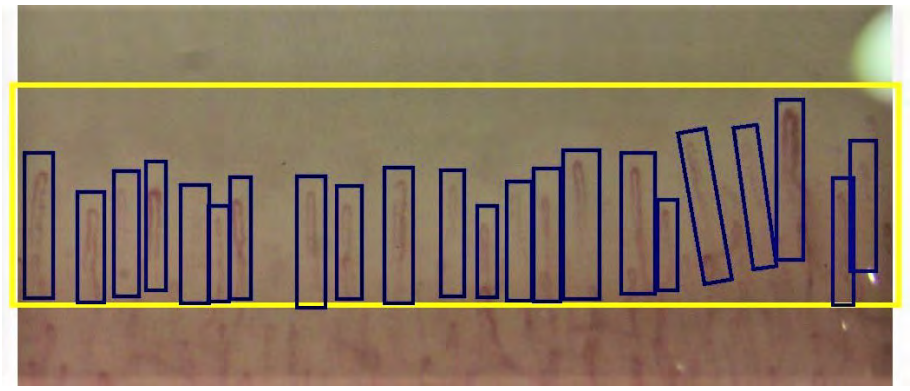

Figure. 1 Screen from training capillaroscopy software with manually marked region of interest (ROI) and individual capillaries

The ResNet-34 deep residual neural network was chosen, as it is widely known to perform image recognition and classification. The dataset was split on training, validation and test sets, using a proportion 70/20/10. Due to a small number of images, 10-fold cross-validation with validation and test set was performed.

Results: The manual annotations (normal/disturbed) of images were treated as ground truth. Sensitivity and the specificity of validation set (the 20% subset of images used for validation during the neural network training process) were, respectively, 89.0% and 89.4%, while for test set, these metrics were reported as 89.0% and 86.9%, respectively

Conclusion: Pilot software for the fully automatic assessment of capillaroscopic image can be a useful tool for quick classification of correct and changed capillaroscopy pattern. In the course of further work on the software, additional functionalities allowing for capillary counting, shape and clinical pattern classification will be developed

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Disclosure: O. Brzezińska, None; **K. Rychlicki-Kicior**, None; **J. Makowska**, None.

Abstract Number: 1560

Measuring Asymmetry in Facial Morphea via 3D Stereophotogrammetry

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Morphea is an autoimmune disorder causing sclerosis and inflammation of the skin and subcutaneous tissue. Facial morphea can cause substantial disfigurement and negative impact on quality of life. Existing clinical measures such as the LoSCAT likely fail to capture the severity of facial morphea due to their body site driven approach and difficulty in quantifying tissue loss making it difficult to assess severity and response to treatment. 3D stereophotogrammetry is a non-invasive, readily available modality that has been used measure facial asymmetry in disorders such as cleft palate. The aim of this pilot study was to investigate the feasibility of use of this

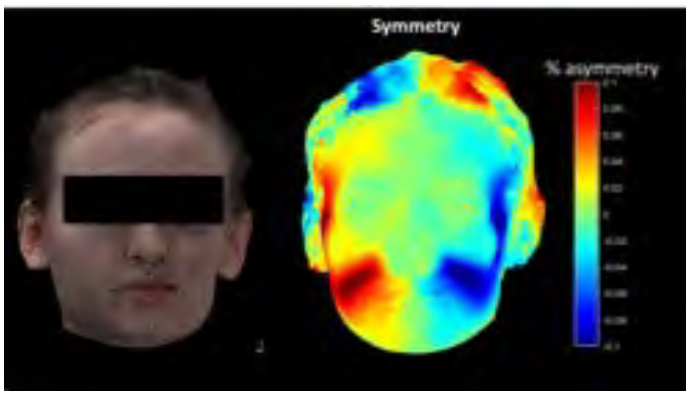

Figure 1 shows a 3D image and heat map created by the 3D stereophotogrammetry technique, which demonstrates pathologic asymmetry in a morphea patient.

Total Patients	23	
Age, median (IQR)	26	16.5-29
Pediatric, No. (%)	16	70%
Adult, No. (%)	7	30%
Sex, No. (%)		
Female	17	74%
Male	6	26%
Race, No. (%)		
Caucasian	14	61%
African American	2	9%
Hispanic	5	22%
Other	2	9%
Subtype, No. (%)		
En Coup De Sabre	12	52%
Parry Romberg	3	13%
Both	1	4%
Neither	7	30%
Extra-facial involvement, No. (%)		
Yes	8	35%
No	15	65%
Clinical Scores, median (IQR)		
mLoSSI	0	0-0
LoSDI	7	4.5-12.5
Face and Neck LoSDI	5	3.5-6
PGA-A	0	0-0
PGA-D	32	22-52
Treatment at time of imaging, No. (%)		
Methotrexate	5	22%
Mycophenolate mofetil	1	4%
Topical immunomodulators	4	17%
Topical steroids	1	4%
None	15	65%
Quality of life data, median (IQR)		
DLQI	2	1-6
Skindex-29, Emotions	53.75	25-66.25
Skindex-29, Symptoms	8.93	0-22.3
Skindex-29, Function	12.5	4.69-23.5

Table 1 provides demographic and clinical information of participants.

	Forehead	Cheek				Nose	Mouth
		All	Preauricular	Zygomatic	Lower		
Mean Difference (mm)							
Mean	1.7	1.5	1.6	1.3	1.5	1.3	1.0
Median	1.5	1.3	1.4	1.0	1.4	0.6	0.9
IQR	1.2-2.1	1-2	0.8-2.2	0.7-1.6	0.8-2.2	0.6-1.1	0.6-1.3
Std Dev	0.79	0.66	0.84	0.90	0.83	1.99	0.50
5% Maximum Difference (mm)							
Mean	1.6	3.7	3.8	2.8	3.4	3.6	2.9
Median	1.5	3.0	2.1	2.4	3.1	2.6	2.7
IQR	3-6.2	2.3-4.3	2.5-3.7	1.5-2.6	2-4.1	2.2-3.8	2.3-3.5
Std Dev	1.89	2.37	2.57	2.48	2.09	3.62	1.60

Table 2 provides asymmetry values in millimeters of study patients as determined through 3D stereophotogrammetry.

modality in identifying asymmetry in facial morphea, and to compare 3D stereophotogrammetry to clinical assessment.

Methods: 23 participants with facial morphea were recruited from the Morphea in Adults and Children Cohort at UT Southwestern Medical Center. They were evaluated by a single dermatologist (HJ), at which time they were assigned

a LoSCAT score, a clinical morphea subtype, and completed validated quality of life questionnaires. Participants then underwent 3D stereophotogrammetry. Facial asymmetry (mm) was determined by calculating the distance between layers of stereolithography images using an in-house written mathematical model in MATLAB, thus quantifying the amount of atrophy (Figure 1 gives an example of a 3D image and heat map generated from this technique). In order to analyze asymmetry in specific anatomical regions of interest, established anatomical landmarks were used to segment facial subunits of interest, and both mean and maximum 5% values were calculated in order to account for dilution.

Results: The majority of patients were children (70%), female (74%), Caucasian (61%), and had linear morphea (en coup de sabre) (52%). Table 1 provides demographic and clinical information of participants. Based on a previously published standard of 1.2mm to define pathologic asymmetry, 22 of 23 patients showed pathologic asymmetry in every facial subunit (Table 2 provides asymmetry values). In order of greatest to least asymmetry, the facial subunits were ranked as follows: forehead, cheek, nose, then mouth. While LoSDI scores did not correlate with asymmetry values, PGA-D values correlated significantly to mean mouth (p=0.0021) and cheek asymmetry (p=0.04). Quality of life measures also showed correlation with asymmetry in the lower face (p=0.013).

Conclusion: Results of this pilot study indicate that the majority of facial morphea lesions produce asymmetry that can be quantified using 3D stereophotogrammetry. Interestingly, we found that both physicians and patients attributed greater severity to lesions affecting the lower part of the face while actual percent asymmetry was greatest in the forehead, indicating that percent asymmetry alone does not drive impact on patients. Taken together, these results confirm that the LoSCAT alone is an inadequate measure of facial morphea and the use of 3D facial imaging maybe a valuable addition to evaluation. Further studies using this modality are needed to determine clinically important difference in facial asymmetry and sensitivity to change.

Disclosure: L. Abbas, None; **J. Day**, None; **H. Jacobe**, None.

Abstract Number: 1561

Findings Compatible with Axial Spondyloarthritis in Radiologist Reports

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Imaging of Rheumatic Diseases Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The sacroiliac joint (SIJ) has a distinct anatomical shape that can pose challenges to standard planar imaging techniques making the detection of subtle changes difficult[1]. SIJ radiographs are a very important tool for the evaluation of disease in patients with suspected axial spondyloarthritis (axSpA). With lack of a reliable biomarker and limitations in physical examination, clinicians are reliant on the interpretation of plain films by radiologists, who may or may not be trained in musculoskeletal radiology[2]. This study characterizes the details reported by radiologists in their reports of SIJ radiographs and compares their scoring with formal interpretations by trained readers.

Methods: SIJ 3-view (Ferguson and obliques) radiographs of US Veterans enrolled in the Program to Understand Long-term Outcomes of Spondylarthritis (PULSAR) registry were evaluated by three trained readers using the scoring from the modified New York (mNY) criteria. Corresponding radiology reports were then evaluated for the presence of terms used to apply mNY scores (erosions, sclerosis, joint narrowing or widening, ankylosis, and blurring), descriptions regarding the severity of any abnormality (no abnormality, mild/possible abnormality, clear abnormality), and the presence of sacroiliitis or axSpA. Classification of sacroiliitis based on consensus mNY grade by trained readers was compared with corresponding radiologist interpretation. Radiograph interpretations were evaluated for association with HLAB27 status.

Results: Reports from 90 radiographs (180 joints) revealed that among patients described as having sacroiliitis or axSpA by the radiologist report, no particular finding was described more frequently than 20% when considering laterality separately and no finding was present more than 31% of the time when assessing either side for abnormalities. Similarly, among patients classified as axSpA by consensus of the three readers, no particular finding was described more frequently than 32% of the time when assessing either side. The most frequent described findings were ankylosis (31.2%) and erosions (29.0%). Compared with the gold-standard consensus interpretation by three trained readers, the radiologist report demonstrated a sensitivity of 57.6% (95% CI 44.1-70.4) and specificity of 93.3% (95% CI 68.1-99.8) for identifying sacroiliitis/axSpA. The strength of the association between HLAB27 status and classification of AS was also greater for the consensus of three readers (ß=0.465, R^2=0.288) than the radiologist report (ß=0.319, R^2=0.090).

Conclusion: In patients likely to have axSpA, radiology reports only describe specific findings suggestive of axSpA in a minority of cases. Classification of axSpA by radiology reports is less well associated with HLAB27 status than a consensus of trained readers. Rheumatologists should consider training to read SIJ radiographs themselves, rather than relying exclusively upon radiology reports.

Disclosure: R. Sen, None; **E. Kim**, None; **E. Manning**, None; **E. Anderson**, None; **K. Maier**, None; **E. Cheng**, None; **L. Caplan**, None.

Abstract Number: 1562

Subclinical Joint Inflammation of Hands by Magnetic Resonance Imaging in Patients with Psoriatic Arthritis in Clinical Remission Compared to Active Disease

Victoria Furer[1], Ari Polachek[2], David Levartovsky[1], Jonathan Wollman[3], Mirna Zureik[3], Daphna Paran[1], Hagit Sarbagil-Maman[4], Sara Borok Lev-Ran[1], Mark Berman[1], Ilana Kaufman[5], Adi Broide[3], Valerie Aloush[1], Yael Lahat goldstein[1], Sharon Nevo[3], Iris Eshed[6] and Ori Elkayam[3], [1]Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, [2]Tel Aviv Sourasky Medical Center, Petah-Tikva, Israel, [3]Tel Aviv Sourasky Medical Center, Tel-Aviv, Israel, [4]Tel-Aviv Sourasky Medical Center, Kiryat Ono, Israel, [5]Tel Aviv Sourasky Medical Center, Petah-Tiqwa, Israel, [6]Sheba Medical Center, Tel-Aviv, Israel

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Imaging of Rheumatic Diseases Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Assessment of disease activity in psoriatic arthritis (PsA) is based on tender and swollen joint counts (TJC and SJC, respectively). Yet, the prevalence of subclinical synovitis in patients in clinical remission

Demographic characteristics	
Gender: male/female, n [%]	49 (57%)/59 (59%)
Age, mean [SD]	51.2 [12.6]
BMI, mean [SD]	27.6 [5.0]
Disease characteristics	
Psoriasis duration, years, mean [SD]	19.0 [15.3]
Psoriasis severity scores:	
BSA, mean [SD]	1.1 [2.2]
PASI, mean [SD]	1.4 [2.8]
PsA duration, years, mean [SD]	10.3 [11.2]
Tender joint count (TJC68), mean [SD]	9.0 [10.0]
MRI-examined hand TJC (TJC14), mean [SD]	2.0 [2.9]
Swollen joint count (SJC66), mean [SD]	1.0 [2.5]
MRI-examined hand SJC (SJC14), mean [SD]	0.4 [0.8]
C-reactive protein (CRP, mg/L), mean [SD]	8.0 [6.1]
ESR, mean [SD]	22.0 [14.2]
Patient pain, VAS, mean [SD]	5.0 [3.1]
Patient global assessment, VAS, mean [SD]	5.3 [3.0]
HAQ, mean [SD]	0.9 [0.8]
Physician global assessment, VAS, mean [SD]	2.1 [2.1]
Minimal disease activity (MDA), n [%]	29 (29%)
DAPSA remission (score 0-4), n [%]	13 [13%]
Treatment modalities	
Current sDMARD, n [%]/methotrexate, n [%]	42 (42.0%)/34 (34.0%)
Current biologic treatment, n [%]	54 [54.0%]
TNF inhibitors, n [%]	39 (39.0%)
IL17 inhibitors, n [%]	13 [13.0%]
IL12/IL23 inhibitor, n [%]	2 [2.0%]
Hand MRI findings	
PsAMRIS, units, mean [SD]	6.8 [14.6]
Inflammatory lesions prevalence	
Total synovitis (MCP, PIP, DIP joints), n [%]	47 [47%]
Flexor tenosynovitis, n [%]	20 [20%]
Periarticular inflammation, n [%]	17 [17%]
Bone marrow edema, n [%]	24 [24%]
Structural lesions prevalence	
Erosions, n [%]	19 [19%]
Bone proliferation, n [%]	8 [8%]

Legend:

PsA – psoriatic arthritis, MRI-magnetic resonance imaging, BMI – body mass index, BSA – body surface area; PASI - psoriasis area severity index; DAPSA - Disease Activity Index for Psoriatic Arthritis (DAPSA); HAQ, health assessment questionnaire; IL – interleukin; MCP – metacarpophalangeal, PIP – proximal interphalangeal, DIP – distal interphalangeal, PsA – psoriatic arthritis; sDMARD – synthetic disease modifying anti-rheumatic drug; TNF – anti-tumor necrosis factor; VAS – visual analogue scale

Table 1. Clinical characteristics and hand MRI findings in the PsA cohort.

is unknown. The purpose of this study is to estimate the MRI-detected prevalence and distribution of subclinical inflammatory changes of hands joints in patients with PsA in remission based on physical examination in comparison to active disease and to determine the sensitivity and specificity of physical examination findings using MRI-verified pathology as the standard of reference.

Methods: One-hundred consecutive, prospectively recruited patients with peripheral PsA (CASPAR criteria) underwent clinical evaluation and MRI of a predominantly involved hand performed within 72 hours from the clinical examination. Metacarpophalangeal (MCP), proximal (PIP) and distal interphalangeal (DIP) joints were scored according to the OMERACT PsAMRIS performed by an expert musculoskeletal radiologist, blinded for clinical data.

Results: Clinical characteristics and prevalence of MRI findings of the whole study cohort (n=100) and subgroups stratified by normal (TJC and/or SJC=0) (n=43) and abnormal clinical examination (n=57) are presented in Tables 1 and 2, respectively. Patients with active disease were older, had higher BMI, and longer duration of PsA compared to patients in clinical remission, 53.6±11.8 vs 48±13.0 years, p=0.025; 28.6±4.9 vs 26.3±4.9, p=0.021; 11.6 ±12.9 vs 8.1 ± 8.1 years, p=0.085, respectively. Otherwise, both subgroups were comparable in severity of psoriasis and treatment modalities. Total PsAMRIS and PsAMRIS of PIP joints were significantly higher in patients with active disease compared to patients in clinical remission, 9.8±18.4 vs 2.74±4.7, p=0.016 and 3.1±7.2 vs 0.6±1.4, p=0.026, respectively, with the same, though non-significant, trend for PsAMRIS of MCP and DIP joints. The overall prevalence of MRI inflammatory lesions in patients in clinical remission was low. Yet, subclinical synovitis was detected in 37.2% of patients, predominantly distributed in the MCP joints (37.2%), followed by equally affected PIP and DIP joints (11.6%). Flexor tenosynovitis and bone marrow edema were equally present in 11.6%, and periarticular inflammation in 2.3 %. The prevalence of MCP synovitis and flexor tenosynovitis was higher in patients with active disease but did not reach a statistical significance, whereas the difference was significant for other inflammatory MRI parameters (Table 2).

	Normal 0 tender and/or swollen joint/hand n=43	Abnormal ≥1 tender and/or swollen joints/hand n=57	p-value
Demographic characteristics			
Gender, Female, n, [%]	28 [65.1%]	31 [54.4%]	0.382
Age, mean [SD]	48.0 [13.0]	53.6 [11.8]	0.025
BMI, mean [SD]	26.3 [4.9]	28.6 [4.9]	0.021
Clinical Characteristics			
Psoriasis duration, years, mean [SD]	15.8[13.5]	21.2 [16.3]	0.082
Psoriasis severity scores: BSA, mean [SD] PASI, mean [SD]	 0.9 [1.4] 1.1 [1.9]	 1.2 [2.6] 1.7 [3.3]	 0.425 0.321
PsA duration, years, mean [SD]	8.1 [8.1]	11.6 [12.9]	0.085
C-reactive protein (CRP; mg/dL), mean [SD]	0.9 [1.2]	0.7 [0.6]	0.232
Minimal disease activity (MDA), n [%]	24 [55.8%]	5 [8.8%]	<0.001
DAPSA, mean [SD] DAPSA remission (score 0-4), n [%]	11.45 [10.0] 11 [25.6%]	27.9 [14.1] 1 [1.8%]	< 0.001 < 0.001
Treatment modalities			
Current sDMARD, n, [%] /methotrexate, n [%]	17 [39.5%]/ 15 [34.9%]/	25 [43.9%]/ 19 [33.3%]	0.819 1.000
Current biologic treatment, n, [%] TNF inhibitors, n, [%] IL17 inhibitors, n, [%] IL12/IL23 inhibitor, n, [%]	25 [58.1%] 21 [48.8%] 4 [9.3%] 0 [0.0%]	29 [50.9%] 18 [31.6%] 9 [15.8%] 2 [3.5%]	0.604 0.122 0.513 0.603
Hand MRI findings			
PsAMRIS, units, mean [SD]	2.74 [4.7]	9.8 [18.4]	0.016
Inflammatory lesions prevalence			
Total synovitis (MCP, PIP, DIP joints), n [%]	16 [37.2%]	31 [54.4%]	0.133
Flexor tenosynovitis, n [%]	5 [11.6%]	15 [26.3%]	0.117
Periarticular inflammation, n [%]	1 [2.3%]	16 [28.1%]	0.002
Bone marrow edema, n [%]	5 [11.6%]	19 [33.3%]	0.023
Structural lesions prevalence			
Erosions, n [%]	5 [11.6%]	14 [24.6%]	0.169
Bone proliferation, n [%]	3 [7.0%]	5 [8.8%]	1.000

Table 2. Clinical characteristics in PsA patients and hand MRI findings stratified by normal versus abnormal clinical examination of hand joints.

The sensitivity and specificity of physical examination of hand (TJC and/or SJC ≥1) for the corresponding MRI-detected synovitis were 66% and 51%, respectively, and for a combined MRI global inflammation score, including a summation of all the PsAMRIS components, were 69% and 63%, respectively.

Conclusion: MRI-detected subclinical synovitis, represented mainly as synovitis of MCP joints and flexor tenosynovitis was detected in up to third of PsA patients with a normal clinical hand examination. Further research is required to assess the pathogenetic role of subclinical hand inflammation for structural progression.

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Abstract Number: 1563

High Impact Sports Leads to Inflammatory Responses at Entheseal Sites Results of the BEAT Study (Badminton Enthesitis Arthrosonography Study)

David Simon[1], **Arnd Kleyer**[1], Koray Tascilar[1], Sara Bayat[2], Johannes Knitza[3], Larissa Valor-Mendez[4], Marina Schweiger[5], Georg Schett[6] and Axel Hueber[7], [1]Department of Internal Medicine 3, Friedrich-Alexander University (FAU) Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Bayern, Germany, [2]Department of Internal Medicine 3, Friedrich-Alexander University (FAU) Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Germany, [3]Department of Internal Medicine 3 – Rheumatology and Immunology, Friedrich-Alexander University Erlangen-Nürnberg, University Hospital Erlangen, Erlangen, Germany, Erlangen, Germany, [4]Department of Internal Medicine 3, Rheumatology and Immunology, University Hospital Erlangen, Erlangen, Bayern, Germany, [5]Department of Internal Medicine 3, Rheumatology and Immunology, Erlangen, Germany, [6]Friedrich-Alexander-Universität Erlangen-Nuremberg, Erlangen, Germany, [7]Sektion Rheumatologie, Sozialstiftung Bamberg, Bamberg, Germany

SESSION INFORMATION
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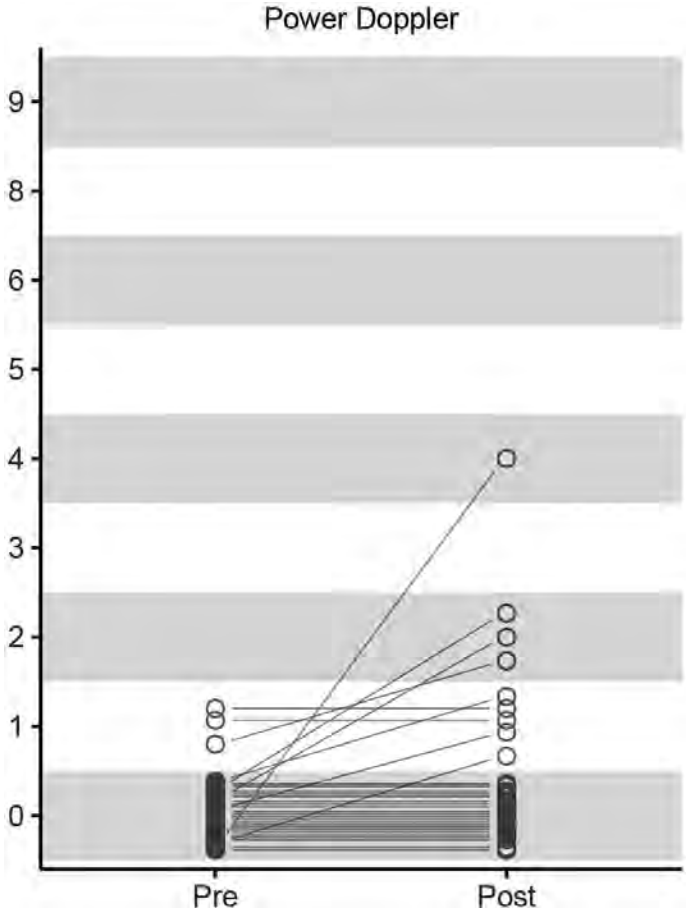
Background/Purpose: Biomechanical stress triggers entheseal inflammation in psoriatic disease [1,2]. However, there is only limited data on the impact of mechanical stress on entheseal sites in healthy subjects. Musculoskeletal ultrasound can detect acute inflammatory changes at entheseal sites using power doppler (PD) technology. Competitive badminton is a demanding stop-and-go sport that puts strain especially on entheseal sites and is therefore an ideal sport to assess the impact of physical activity on the synovial-entheseal complex. Thus, we aimed to test whether intensive pyhsical stimulation of the musculoskeletal system by badminton training leads to an immediate inflammatory response at entheseal sites measured by PD ultrasound.

Methods: In this interventional study (BEAT, **B**adminton **E**nthesitis **A**rthrosonography **S**tudy), competitive players from two different badminton clubs were recruited. Only subjects without chronic inflammatory diseases were included. A physical examination comprising an examination of 29 entheses (SPARCC, LEI, MASES) of all players was performed just before and after 60 minutes of intensive training. Ultrasound of entheseal sites (achilles tendon, patella tendon at the tibial insertion, epicondylus humeri lateralis; all both sides) was also performed immediately before and after the training by an independent assessors using a Samsung HS50 machine with a linear probe (16 MHZ). The presence of inflammatory entheseal components was assessed using a validated scoring system. [3] Scores at each site were summed to derive an empirical total score for each participant for visual comparison. Pre- and post-match scores were compared using linear mixed effects models. We used interaction terms to assess possible differential effects on patella, elbow or achilles entheses. The study was approved by the ethics committee and all subjects provided informed consent.

Results: 32 players (22 men, 10 women) with an average age of 31.1±13.0 years were included. On average they had been playing badminton for 16.2±10.1 years. 192 entheseal sites were examined twice. The respective empirical total scores for PD examination were 0.1 (0.3) before and 0.5 (0.9) after training. Overall 7 participants (22%) showed an increased empirical total PD score as shown in the figure. A mixed effects model shows that there was an increase in PD scores after the game, with a mean increase per region of 0.06 (95%CI 0.01 to 0.12, p=0.017).

Conclusion: Ultrasonographic assessment of entheses after an hour of high-impact exercise in healthy individuals show a significant increase in PD activity at entheseal sites. The magnitude of these changes however seems rather



small and only in a subset of individuals. However, these results underline the concept of mechano-inflammation and needs to be further assessed in a population with known risk factors for developing spondyloarthritis or psoriatic disease. Linearity assumption for the bounded discrete ultrasound scores is a shortcoming of this analysis.

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Abstract Number: 1564

Feasibility of Ultra-low-dose, Short-duration, Total-body Evaluation of Inflammatory Arthritis Using uEXPLORER 18F-FDG PET/CT

Soumajyoti Sarkar[1], Siba Raychaudhuri[2], Lorenzo Nardo[3], Heather Hunt[3], Denise Caudle[4], Mike Nguyen[4], Simon Cherry[4], Ramsey Badawi[4], Abhijit Chaudhari[5] and **Yasser Abdelhafez**[3], [1]University of California, Davis, Davis, [2]Division of Rheumatology, Allergy & Clinical Immunology, University of California School of Medicine, Davis, and VA Medical Center Sacramento, Sacramento, CA, [3]University of California Davis, Sacramento, CA, [4]University of California Davis, Sacramento, [5]University of California, Davis, Sacramento, CA

SESSION INFORMATION
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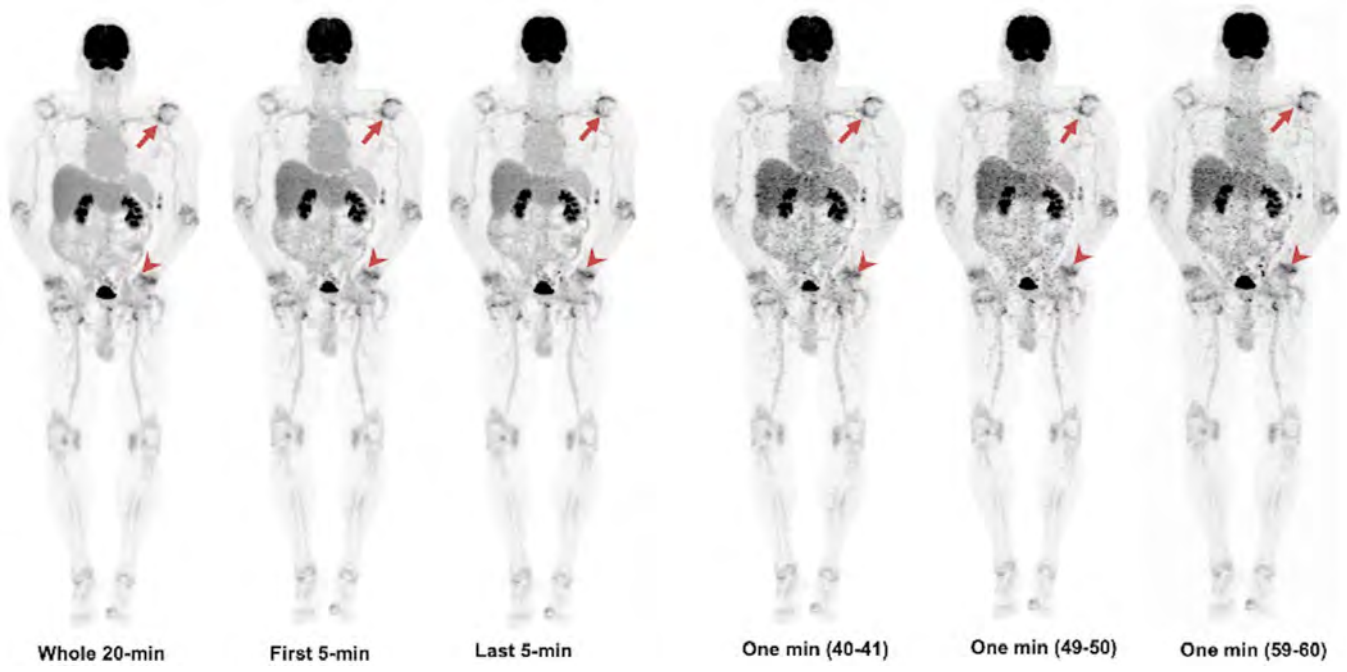
Background/Purpose: The uEXPLORER system enables the unique, simultaneous acquisition of PET data over the entire adult human body with a high-sensitivity, alongside concurrent CT data. We hypothesized that these unique characteristics of the uEXPLORER system will yield shorter scan time and reduction in radiation dose, both crucial to an arthritic population. We aimed to prospectively (1) document the glucose uptake patterns – using the radiotracer ^{18}F-FDG – in arthritic lesions across the entire body of participants with established rheumatoid arthritis (RA), psoriatic arthritis (PsA) and osteoarthritis (OA); and (2) evaluate the influence of shortening the scan time or dose reduction on image quality.

Methods: An ultra-low-dose 18F-FDG scanning protocol was employed in 14 patients (all males, 59±13 yrs) with RA (n=3), PsA (n=8) or OA (n=3) (injected radiotracer dose 75.5±4.4 MBq (1/5th of standard clinical dose)). PET/CT scans were acquired for 20-min starting at 40-min after the injection of 18F-FDG; data were then reconstructed as a single frame (20-min long), four 5-min frames, and twenty 1-min frames, using the same standard protocol. A single volume of interest (VOI) >3cm3 was drawn on the ascending aorta as a background blood pool [BP], and on arthritic lesions to calculate target-to-background ratio (TBR). Coefficient of variation (COV%) was used to estimate image noise and was calculated from the VOIs in the BP.

Results: uEXPLORER scans were successfully conducted for the 14 participants. The entire body was in the field-of-view in all participants. The effective dose from the PET radiotracer and ultra-low-dose CT was approximately 2.7



Maximum intensity projection total body images of a 72-year-old male (172 cm, 85 kg) with established diagnosis of psoriatic arthritis. Images were acquired for 20-min duration starting at 40-min after IV injection of 77.6 MBq of 18F-FDG. Images were further subsampled in software into 5-min and 1-min frames. Note that changes in tracer intensity in the left shoulder (arrow) and wrist (arrowhead) are preserved over the different frames.

mSv compared to typically ~14-15 mSv for clinical PET/CT scans on standard scanners. When evaluating the most active lesion, the average TBR was 1.3±0.4. The COV for the 20-min, 5-min, and 1-min scans were (median [range]): 8 [6,13], 15 [8,25], 31 [16, 57]. Qualitatively, all lesions detected on 20-min images could also be seen on 5-min images. Although lesions were still visualized on 1-min frames (TBR=1.4±0.5), the surrounding tissue background was elevated, and the image quality was sub-optimal.

Conclusion: All joints of the body could be visualized simultaneously and assessed in the same phase of radiotracer uptake on uEXPLORER PET/CT scans. Scan times as short as 5-min, with 1/5th of the standard 18F-FDG dose, appeared to be feasible and provide image quality not inferior to the full 20-min PET/CT scan. Further work is warranted to evaluate the methods on more participants, and further develop software-based methods to enhance the image quality of shorter duration scans.

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Abstract Number: 1565

Joint Cartilage Damage Evaluated by Ultrasound in Patients with Systemic Lupus Erythematosus

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Background/Purpose: Arthritis in systemic lupus erythematosus (SLE) is typically non-erosive, although some patients with SLE show erosive destruction or Jaccoud's arthropathy. Previously we have confirmed the usefulness of the direct imaging of finger joint cartilage by ultrasound (US) in patients with rheumatoid arthritis. In this study, we aimed to examine cartilage lesions in patients with SLE by US.

Methods: We enrolled 44 SLE patients with an episode of joint symptoms and 42 healthy subjects. The cartilage thickness of bilateral metacarpophalangeal (MCP) and proximal interphalangeal (PIP) joints of the 2nd to 5th fingers were visualized from a dorsal view with joints in approximately 90 degrees flexion and measured at the middle portion. Furthermore, one US examiner performed the semiquantitative scoring of the recorded cartilage images in a blinded manner on a scale of 0–2. Continuous variables from the two groups were analyzed using the Mann–Whitney U test. The relationships among the continuous variables were assessed using the Spearman's rank correlation coefficient.

Results: Female predominance, height and weight were similar between the two groups, although patients with SLE were younger than healthy subjects. The total cartilage thickness of 16 joints tended to be decreased in SLE patients as compared with healthy control (the median 7.0 versus 7.5, p=0.057; and 4.1 versus 4.4 in MCP joints and 2.9 versus 3.0 in PIP joints, respectively). The cartilage thickness of MCP joints was significantly correlated with that of PIP joints (rho=0.40, p=0.007), and the cartilage thickness of MCP/PIP was independent of patients' age, height

and disease duration. The total semi-quantitative score of 16 joints was comparable between patients with SLE and healthy subjects (the median 4.0 versus 4.0, p=0.395; and 2.0 versus 2.0 in MCP joints and 2.0 versus 2.0 in PIP joints, respectively).

Conclusion: The evaluation of finger joint cartilage damage by US is valid and the cartilage damage is limited in most of the patients with SLE.

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Abstract Number: 1566

Onset and Disease Course of Inflammatory Arthritis in Patients Receiving Immune Checkpoint Inhibitor Therapy at a Single Institution

Christina Boutsicaris[1], Angelo Ciliberti[2], Elizabeth Lockerman[1], Faizah Siddique[3] and Rochella Ostrowski[1], [1]Loyola University Medical Center, Maywood, IL, [2]Loyola University Medical Center, Oak Park, IL, [3]Loyola University Medical Center, Lombard, IL

SESSION INFORMATION
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Background/Purpose: Immune checkpoint inhibitors (ICI) have improved outcomes for many types of cancer, but the therapy is known to cause immune-related adverse events (IRAE). ICI can cause early or late onset inflammatory arthritis, which can continue after stopping ICI[1,2]. Many cases are negative for RF and ACPA. Timely recognition and treatment may improve symptoms and facilitate continuation of cancer therapy.

Methods: We reviewed the Loyola University Medical Center database to identify patients who had new-onset arthritis in the setting of ICI cancer therapy. We collected data on clinical and diagnostic features and outcome measures. Patients received at least one dose of ICI (atezolizumab, durvalumab, ipilimumab, nivolumab, pembrolizumab) between January 1, 2011 and October 31, 2019 and were identified on manual review by two rheumatologists. Definite inflammatory arthritis was based on the presence of documented diagnosis by a physician, exam, or imaging findings. Probable diagnosis was based on clinical description. Arthritis course was described as resolved or sustained, with sustained defined as at least 3 months of arthritis symptoms or treatment. Tumor response was categorized according to the Response Evaluation Criteria for Solid Tumors on oncology follow up. We used descriptive statistics, with frequency and percentage for categorical variables.

Results: A total of 801 patients received ICI. Among these, 28 patients were identified as having ICI-induced arthritis (Table 1, Fig. 1). Median age was 57.5 years. Most common tumor types were melanoma, renal, non-small cell lung, and bladder. Mean follow up time from ICI start was 24.3 months (range 4-62).

RF and ACPA were negative in all 5 patients for whom they were measured. One patient had a positive RF that pre-dated cancer therapy. 32% of patients had severe IRAE (hepatitis, hypophysitis, adrenal insufficiency, ITP, pancytopenia, severe colitis). Patients with a resolved course of arthritis were more likely to have a favorable cancer outcome than those with a sustained course (100% of 8 vs. 67% of 15), but this did not reach statistical significance. Of

Demographics of patients in case series (n = 28)		
Gender		
	Female	12 (43%)
	Male	16 (57%)
Age at ICI start		
	18-29	2 (7%)
	30-39	3 (11%)
	40-49	5 (18%)
	50-59	6 (21%)
	60-69	6 (21%)
	>70	6 (21%)
Race/Ethnicity		
	African-American	2 (7%)
	Caucasian	23 (82%)
	Hispanic	3 (11%)
Smoking status		
	Never	10 (36%)
	Past/Current	18 (64%)
Menopausal status (n = 12)		
	Pre	2 (17%)
	Post	10 (83%)
Clinical characteristics, diagnostic findings, and management		
Specific ICI		
	Nivolumab	19 (68%)
	Ipilimumab	10 (36%)
	Pembrolizumab	10 (36%)
	Combination therapy	8 (29%)
Rheumatology referral		10 (36%)
Arthritis therapy		
	Corticosteroids	24 (86%)
	csDMARD	6 (21%)
	Biologic	1 (4%)
Other significant IRAE at any time		
	Yes, severe IRAE	16 (57%), 9 (32%)
	No	12 (43%)
Cancer outcome at most recent follow-up		
	Complete response/ No evidence of disease	9 (32%)
	Partial response	3 (11%)
	Stable disease	7 (25%)
	Progressive disease	9 (32%)

Table 1

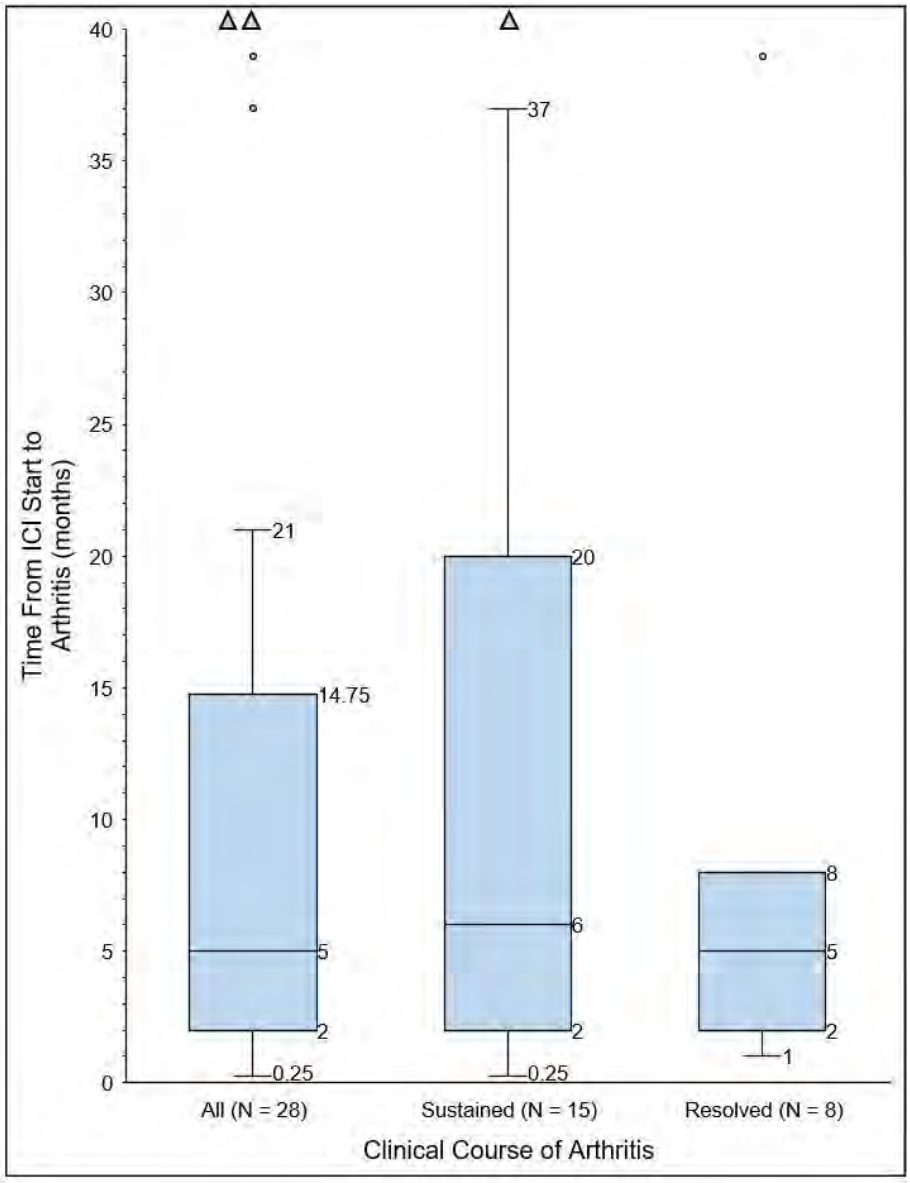

Figure 1. Delay from Immune Checkpoint Inhibitor Start to Arthritis

7 patients who were treated with DMARD or biologic, cancer outcomes included 6 who had no evidence of disease or have stable disease. Of the 8 patients who received combination ICI, 5 had a sustained course. Five patients did not have enough follow up data to define their arthritis course.

Conclusion: Our case series shows that patients can develop IRAE arthritis beyond six months of ICI therapy and that later onset IRAE arthritis trends towards a sustained arthritis course. Patients with a resolved IRAE arthritis course were more likely to have a favorable cancer outcome. IRAE interrupting cancer treatment may contribute to our observations and warrants further study into identifying predictors of IRAE development. Additionally, a concern about treating IRAE with immunosuppression is that treatment could diminish the effects of cancer therapy. However, many patients treated for IRAE arthritis in this series had favorable cancer outcomes.

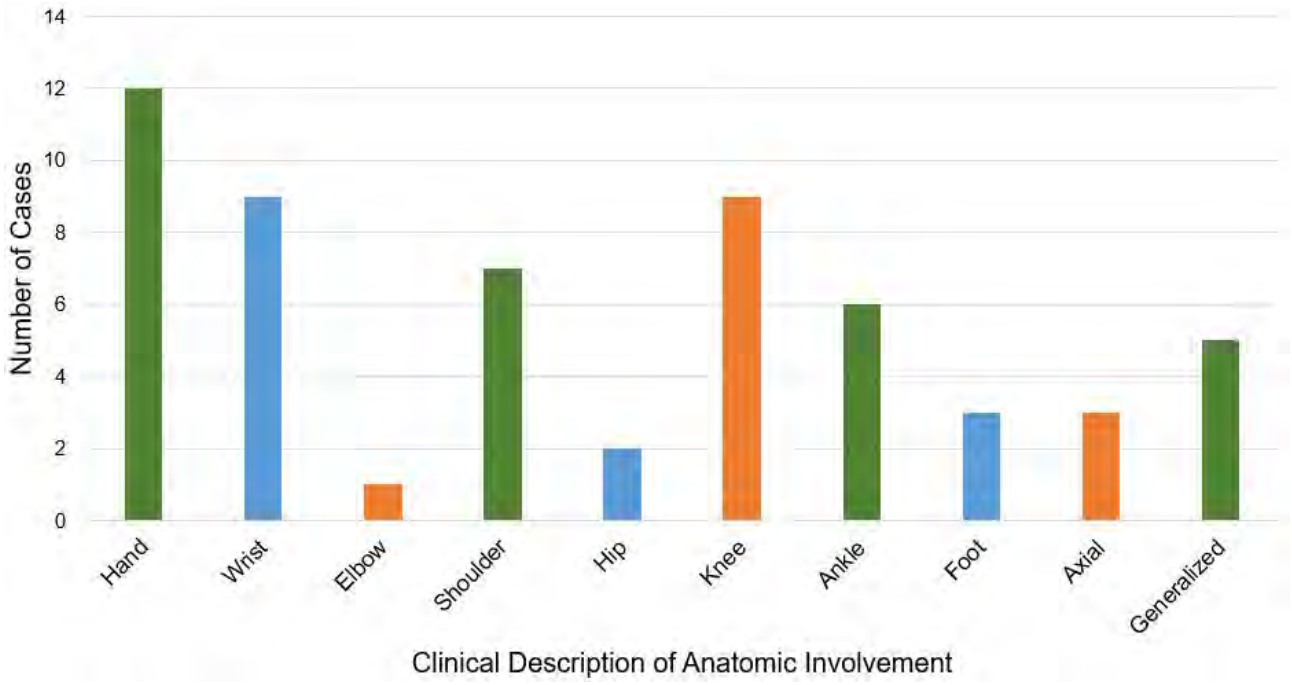

Figure 2. Frequency of Anatomic Sites of IRAE Arthritis Symptoms

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2. Jamal S et al. *J Rheumatol*. 2020;47(2):166–175.

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Abstract Number: 1567

Association of Blood Count Biomarkers and Clinical Features with Immune Related Adverse Events (irAEs) in Patients with Cancer Treated with Checkpoint Inhibitors (CPI)

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
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Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with cancer treated with CPI can develop irAEs. Since immune changes may impact blood counts and ratios, we hypothesized that those would be associated with irAEs. We also investigated the asso-

ciation between irAEs and personal or family history of autoimmune disease (AD), combination of CPI and/or history of chronic infection.

Methods: We performed a retrospective cohort study and identified patients with solid and hematologic malignancies who started CPI (anti-PD1/PDL1 and anti-CTLA-4) in 2018. We defined irAEs as both rheumatologic and non-rheumatologic. The association between irAEs, baseline absolute neutrophil (ANC), lymphocyte (ALC), monocyte count (AMC), neutrophil to lymphocyte (NLR), monocyte to lymphocyte (MLR), platelet to lymphocyte ratio (PLR), was assessed by logistic regression (LR) with robust standard errors adjusting for age, sex, smoking history, cancer type, ECOG performance status (PS), concomitant systemic therapy, personal or family history of AD and chronic infection. LR with robust standard errors was also used to examine the relationship between irAEs and personal or family history of AD, combination of CPI and chronic infection adjusting for age, sex, smoking history, cancer type, ECOG PS, and concomitant systemic therapy. After Bonferroni correction, alpha level was set to 0.005 for all statistical testing.

Results: A total of 193 patients were identified with median age 64 (range 23-92), 47% women; 49% with smoking history; 23% had lung cancer, 21% skin cancer, 56% other cancers; 19% received concomitant CPI and 32% other systemic therapy plus CPI. Rheumatologic irAEs were reported in 10%, and non-rheumatologic irAEs in 23% of patients. Association between irAEs, blood biomarkers and clinical features are described in **Table.** Development of irAEs was significantly associated with higher baseline ALC (OR: 2.43, 95%CI: 1.39-4.22, p=0.002) and lower baseline MLR (OR: 0.09, 95%CI: 0.02-0.42, p=0.002). Patients with pre-existing AD (OR: 5.14, 95%CI: 2.18-12.15, p< 0.001) were also more likely to experience irAEs during treatment with CPI.

Table. Association of lab biomarkers as continuous variables and clinical features with irAEs

	OR	95% CI	p-value
Absolute neutrophil count (ANC)	1.06	0.96 – 1.18	0.25
Absolute lymphocyte count (ALC)	2.43	1.39 – 4.22	0.002
Absolute monocyte count (AMC)	1.93	0.40 – 9.34	0.42
Neutrophil:Lymphocyte ratio (NLR)	0.90	0.82 – 0.99	0.03
Monocyte:Lymphocyte ratio (MLR)	0.09	0.02 – 0.42	0.002
Platelet:Lymphocyte ratio (PLR)*	0.96	0.94 – 0.99	0.01
Personal history of autoimmune disease	5.14	2.18– 12.15	<0.001
Family history of autoimmune disease	4.02	1.45 – 11.13	0.008
Combination of CPIs vs single agent	2.92	1.19 – 7.16	0.02
Chronic infection	0.51	0.18 – 1.44	0.20

*PLR was calculated at (platelet count/10)/absolute lymphocyte count

Conclusion: In patients with cancer treated with CPI, irAE development was associated with higher baseline ALC, lower MLR and pre-existing history of AD. Further validation is required to test our generated hypothesis that blood count subsets could be used as inexpensive and easily obtained biomarkers to predict the development of irAEs in clinical practice.

Disclosure: D. Michailidou, None; **A. Khaki**, Merck & Co, Inc., 1, Sanofi S. A., 1; **G. Wang**, None; **L. Diamantopoulos**, None; **P. Grivas**, AstraZeneca, 1, Bayer, 1, EMDSerono, 1, Exelixis, 1, Genzyme, 1, GlaxoSmithKline, 1, Janssen, 1, Merck, 1, 2, Mirati Therapeutics, 1, Pfizer, 1, 2, Roche, 1, Seattle Genetics, 1, Bavarian Nordic, 1, Bristol Myers Squibb, 1, Clovis Oncology, 1, Debiopharm, 1, Immunomedics, 1, QED Therapeutics, 1, 2.

Abstract Number: 1568

Impact of the SARS-CoV-2 Pandemic on a Cohort of Patients with Rheumatic Complications of Immune Checkpoint Inhibitors: A Registry Survey Study

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Background/Purpose: It is not known whether cancer patients being treated with immune checkpoint inhibitors (ICI) and/or immunosuppression are more vulnerable to SARS-CoV-2 or more apt to have severe manifestations of the disease. We aimed to describe oncology and rheumatology treatment practices in ICI-treated patients with a history of rheumatic immune-related adverse events (irAE) during the March-April 2020 “surge” in SARS-CoV-2 infections in the New York Tri-State area, and to determine the frequency of SARS-CoV-2 infection in these patients.

Methods: A 23-question email survey was administered via RedCap on April, 16 2020 to all living patients enrolled in our institutional ICI rheumatic irAE registry, who had consented to future studies. Participants who did not fill out the form electronically were contacted via telephone and if they agreed, completed the survey verbally. The survey included questions about current cancer status, ICI and immunosuppressant medication use, irAE status, history of SARS-CoV-2 symptoms or diagnosed infection, as well as a free text question asking, “Is there anything else you would like to tell us about how coronavirus has affected you personally?”

Results: The survey was sent to 92 registry patients. Thirty-nine completed the survey electronically and 26 by telephone (response rate 71%). After excluding 2 patients who never received ICI, 63 patients were analyzed (**Table 1**). Patients who had been on ICI within the last 6 months (n=25) and those who discontinued ICI because of the pandemic (n=7) were identified as patient subsets. There were no significant differences between the groups, although there was a trend toward ICI therapy more often being held in female patients, those on ICI monotherapy and those with a good cancer response. None of the patients who had their ICI held had active arthritis or other irAE requiring immunosuppression. In patients on immunosuppression for irAE, none had changes made in these medications pre-emptively as a result of the pandemic. **Table 2** highlights characteristics of patients with proven or presumed SARS-CoV-2 infection. Four of 5 were men, and 3 had renal cell carcinoma (RCC), proportionally higher than the

Table 1. Patient Characteristics

Characteristics	Entire cohort (n=63)	Patients on ICI at outset of SARS-CoV-2 pandemic (n=25)	
		Continued their ICI (n=18)	Held their ICI (n=7)
Female, n (%)	37 (59)	8 (44)	5 (71)
Age, mean (SD)	63.4 (11.5)	64.4 (12.2)	66.6 (11.3)
Caucasian, n (%)	56 (89)	15 (83)	6 (86)
Cancer type, n (%)			
- Melanoma	17 (27)	3 (17)	2 (29)
- Renal	14 (22)	4 (22)	0
- Urothelial	10 (16)	3 (17)	3 (43)
- NSCLC	8 (13)	2 (11)	1 (14)
- Other	14 (22)	6 (33)	1 (14)
ICI, n (%)			
- Monotherapy	44 (70)	12 (67)	7 (100)
- Combination	19 (30)	6 (33)	0 (0)
Cancer response, n (%)			
- CR/PR/Stable	49 (78)	15 (83)	7 (100)
- Progression	10 (22)	3 (17)	0
Rheumatologic irAE, n (%)			
- Small joint arthritis	22 (35)	4 (22)	4 (57)
- Activated OA	9 (14)	3 (17)	2 (29)
- PMR	7 (11)	2 (11)	0
- Large joint arthritis	6 (10)	2 (11)	1 (14)
- Arthralgia	6 (10)	2 (11)	0
- Sicca syndrome	3 (5)	2 (11)	0
- Myositis	2 (3)	0 (0)	0
- Other	8 (13)	3 (17)	0
Arthritis medications*, n (%)			
- No medications	19 (30)	4 (22)	2 (29)
- NSAIDs	9 (14)	2(11)	1 (14)
- Steroids	26 (41)	9 (50)	4 (57)
- HCQ	6 (10)	2 (11)	1 (14)
- MTX	4 (6)	2 (11)	0
- Anti-TNF	5 (6)	2 (11)	0
- Tocilizumab	3 (5)	1 (6)	0
Any arthritis medication changes due to SARS-CoV-2?	No	No	No

Key: ICI = immune checkpoint inhibitor; NSCLC = non-small cell lung cancer; CR = complete response; PR = partial response; irAE = immune-related adverse effect; OA = osteoarthritis; PMR = polymyalgia rheumatica; NSAIDs = nonsteroidal anti-inflammatory drugs; HCQ = hydroxychloroquine; MTX = methotrexate; Anti-TNF = Anti-tumor necrosis factor.
*Totals do not add up to 100% given that patients can be on multiple medications at a given time

Table 1. Patient Characteristics

overall cohort both for gender and cancer type. The 2 patients still on active ICI were on combination therapy and prednisone at the time of infection. The other 3 were no longer on either ICI or immunosuppression. 37/63 (59%) responded to the free-text question and, of those, 30 (81%) expressed depression, anxiety/fear, frustration and economic hardship while 7 (19 %) remained optimistic and positive **(Table 3)**.

Conclusion: Oncologists held ICI in a quarter of registry cancer patients in the context of the SARS-CoV-2 pandemic, particularly women on ICI monotherapy who had had a good cancer response. Five patients (8%) developed SARS-CoV-2 infection during the NY Tri-state "surge" of March-April 2020, but all were able to recover uneventfully despite their advanced age. Four of 5 with SARS-CoV-2 infection were male, 3 had RCC and 2 were on combination ICI. Larger studies are needed to determine whether RCC and/or combination ICI are risk factors for SARS-CoV-2 infection.

Table 2. Case series of SARS-CoV-2 patients (positive and presumed positive)

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age, Gender	79M	69F	53M	41M	72M
Race	Caucasian	Caucasian	African-American	Caucasian	Caucasian
Cancer	Renal cell Carcinoma	Pleomorphic sarcoma	Renal cell Carcinoma	Renal cell Carcinoma	NSCLC
ICI	Monotherapy	Combination	Monotherapy	Combination	Combination
Last ICI dose	6/4/18	6/1/17	4/1/19	3/6/20	3/18/20
Cancer status	Stable	CR	Stable	PR	Stable
Arthritis status	Ongoing, stable	Ongoing, stable	Resolved	Ongoing, stable	Ongoing, improving
Anti-rheumatic medications	None	NSAIDs	None	Prednisone 20mg daily (for ICI-colitis)	Prednisone 7.5mg daily
SARS-CoV-2 Symptoms	Cough, fever, headache, dizziness, weakness, diarrhea, change in taste	Cough, loss of smell and taste	Mental fatigue	Cough, shortness of breath	Loss of smell for five days
Hospitalized	No	No	No	Yes, for ICI-colitis; never intubated	No
Calendar month of illness	April 2020	March 2020	April 2020	March 2020	March 2020
State of residence	New York	New York	New York	New York	New Jersey
SARS-CoV-2 testing	No	No	Yes	Yes	Yes

Key: NSCLC = non-small cell lung cancer; ICI = immune checkpoint inhibitor; CR = complete response, PR = partial response, NSAID = nonsteroidal anti-inflammatory drugs

Table 2. Case series of SARS-CoV-2 patients

Table 3. Sample answers to the survey free text question, grouped by theme

Anxiety/fear
- "It made me terrified to leave home"
- "I have concerns being on an immunosuppressive drug during this time"
- "Anxiety that I can't go outside and have no control of anything"
- "This situation creates a lot of stress. I'm afraid to leave my house"
- "Can't leave the house…it is frightening"
- "I have fear and anxiety…getting food is not easy"
Depression
- "Death of my friends due to the virus"
- "I am lonely"
- "Sad and depressing…can't visit family"
- "I go day by day. Some days are bad"
Frustration being homebound
- "Can't stand being in the house"
- "I have developed muscle atrophy from not being able to go to gyms. This sucks!"
- "Bored staying at home"
- "Staying home, very isolated"
Economic concerns
- "I lost employment"
- "Preoccupied and worried financially. No work, zero income. Future is unknown"
Optimism
- "I am doing great"
- "Doing great, going on hikes and yard work in Vermont…no one in sight"
- "Happy that I'm doing well"
- "Doing well, staying indoors"

Sample answers to free text question regarding SARS-CoV-2 pandemic, grouped by theme

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Disclosure: N. Ghosh, None; **A. Tirpack**, None; **C. Benson**, None; **G. Vitone**, None; **K. Chan**, None; **A. Bass**, None.

Abstract Number: 1569

Immune Related Adverse Events Related to Check Point Inhibitors Among Outpatients in an Academic Center

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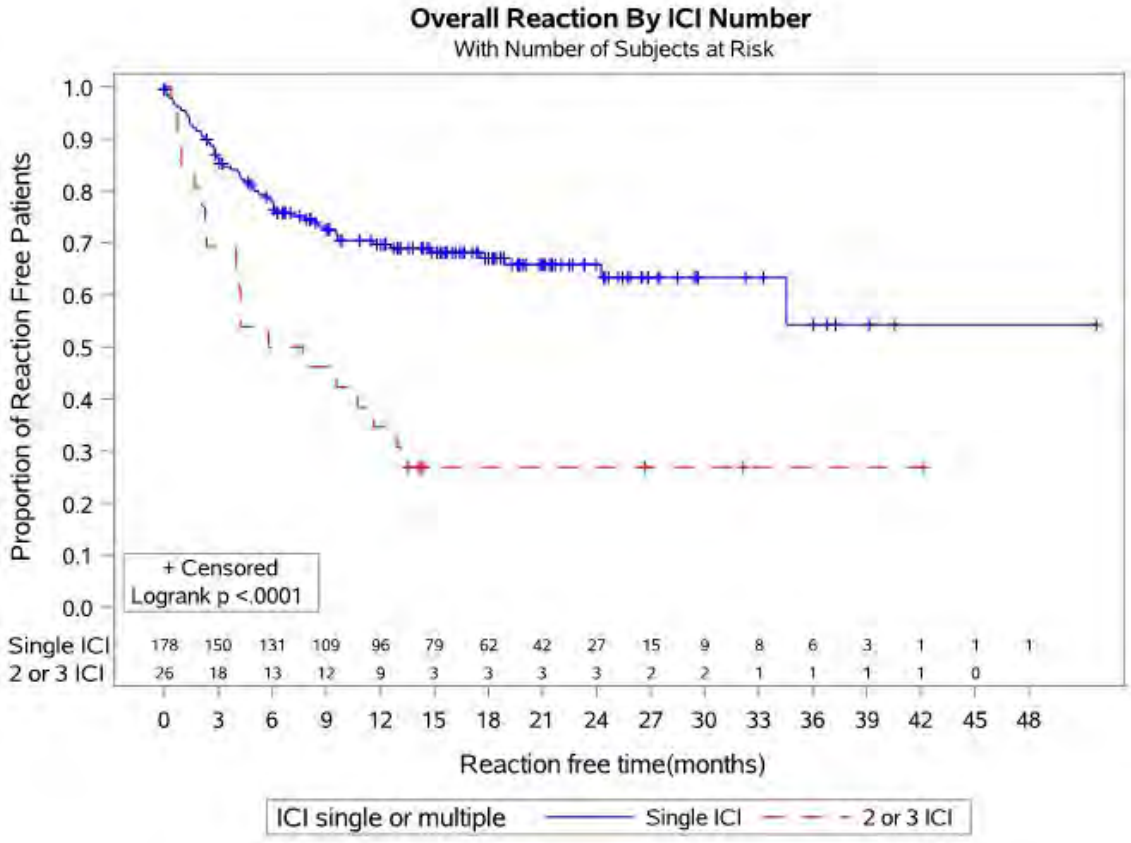
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Immunological Complications of Therapy Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Immune check point inhibitors (ICIs) allow the body to recognize tumor cells as non-self, resulting in immune-cell mediated tumor cell destruction. These therapies have the potential for adverse reactions secondary to excessive immune activation. Retrospective studies have identified several immune related adverse effects (irAE) and less commonly rheumatic immune related adverse effects (RhirAE). Little is known about factors that predispose patients to irAE, their treatments and correlation of irAE with response. Our study aimed to classify irAEs,

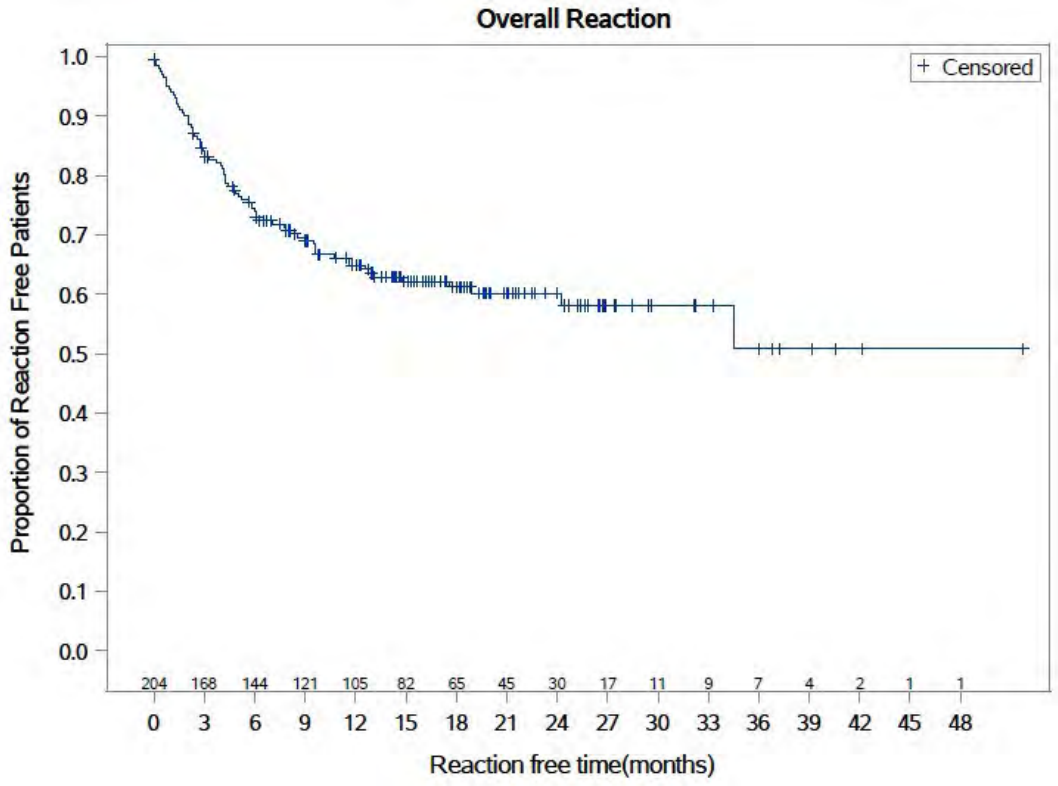
especially those related with rheumatic diseases, including their timing and risk factors. Additionally, we aim to collect data regarding current referral and management practices in a single academic center to improve knowledge gaps.

Methods: Retrospective chart review was performed evaluating patients at Stephenson Cancer Center exposed to at least 3 months of ICI therapy between 1/1/19 and 6/30/19. Patients under the age of 18, those with Type I DM or pregnancy were excluded. Demographic data, data regarding irAE and treatment, and disease outcomes were obtained through manual chart review.

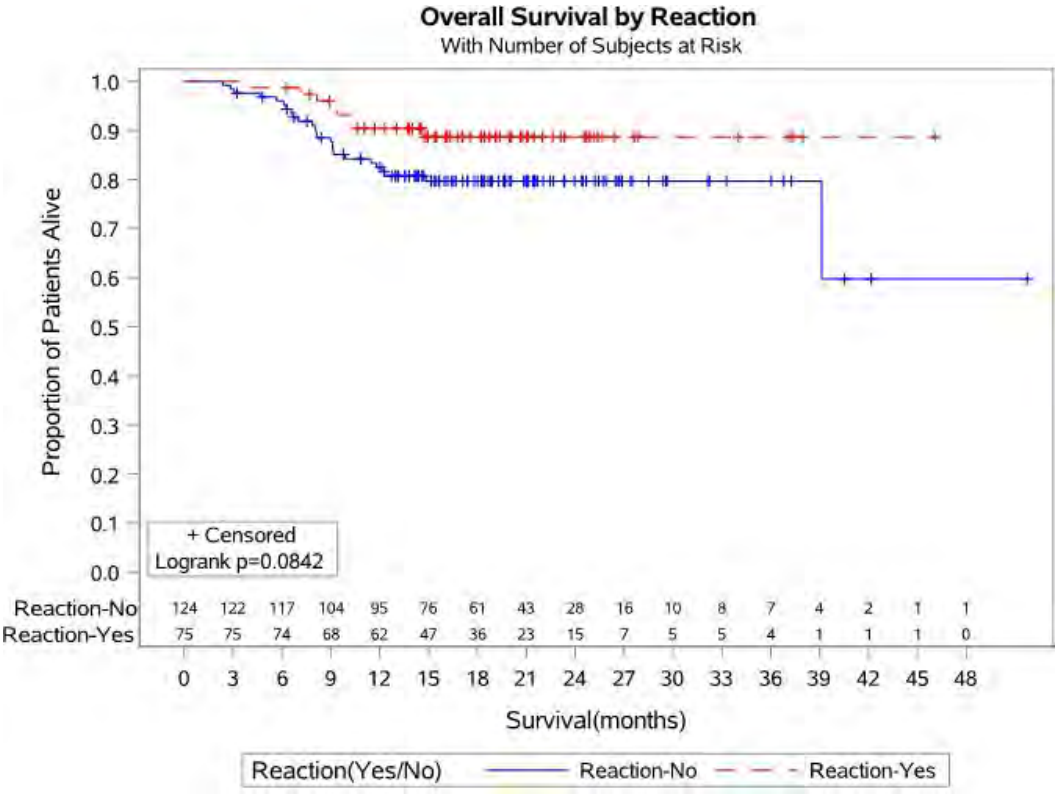
Results: 206 patients met study inclusion criteria, of which 78 had an irAE related to ICI with 7 patients having more than one reaction. The average time to onset of irAE after initiation of ICI was 164.2 days (3-1036 days). Non-small cell lung cancer (26.9%) was the most common cancer followed by melanoma (21.8%) and renal cell carcinoma (17.9%) that were equally distributed in the two groups. Pembrolizumab was the most used agent followed by nivolumab and atezolizumab. There were no significant differences between gender, age, underlying cancer type, cancer stage, and different ICI among patients who developed irAE (37.9%) and those who did not (62.1%). However, combination therapy was more likely to cause an irAE (Reaction rate: 71.42% $p < 0.0001$). Thyroiditis (30.6%) and rash (25.9%) were most common adverse reactions. RhirAE were rare with one patient with myositis, two with uveitis and one patient with arthritis. 93.6% of patients developed irAE requiring treatment, with 63% requiring steroids and 5.4% requiring disease-modifying antirheumatic drugs (DMARDS). Treatment with ICI was interrupted/stopped in 127 patients (61.6%) of which 19 patients stopped treatment due to irAE (14.9%) with 1 patient referred to rheumatology for evaluation.



IrAE in single vs multiple ICIs.



Average Lag period between ICI therapy and iRAE



IrAE and over all survival

Conclusion: Our study shows that irAE are common among patients treated with ICI. Treatment is continued in majority of patients and only 14.9% requiring change in therapy due to reactions. Our study did not have enough patients with prior rheumatic conditions to determine if these agents worsen underlying disease. Majority of reactions required treatment, often with steroids. There was no significant difference in age or gender between two groups, suggesting that these are not unique risk factors. Most irAE occurred around 5.3 months after starting ICI. Sustained ICI therapy and combination therapy is more likely to result in an irAE,suggesting that clinicians should monitor patients for reactions at all times.

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Abstract Number: 1570

Immune Checkpoint Inhibitor Treatment in Cancer: Immunomodulator Use and Evaluation by Rheumatology

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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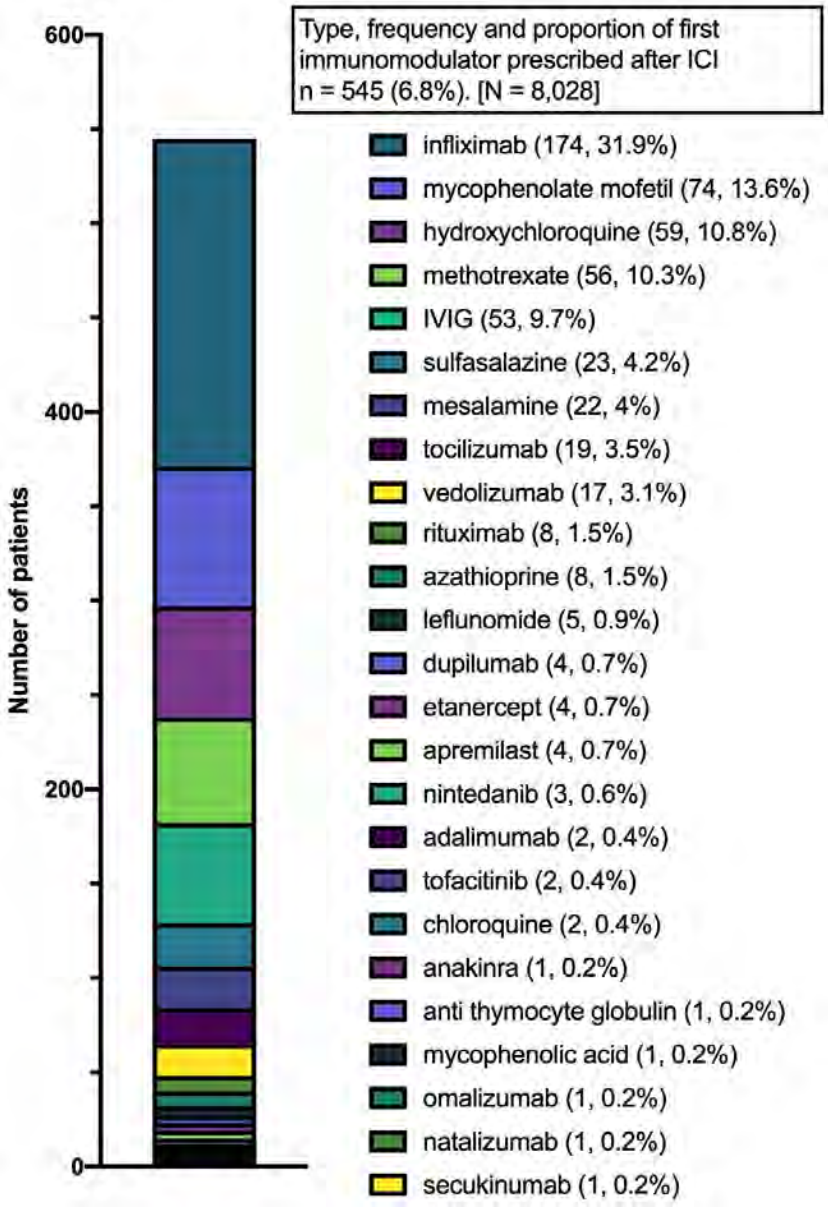
Background/Purpose: Immune checkpoint inhibitors (ICI) are used to treat an expanding number of cancers. Many cancer patients treated with ICI develop immune-related adverse events (irAE) or flares of pre-existing autoimmune disease. These can be severe and/or refractory and may require treatment with immunomodulators (IM), commonly prescribed by rheumatologists. The aim of this study was to determine the frequency of IM use, specific initial IM drugs used, and involvement of rheumatology in the care of cancer patients treated with ICI.

Methods: We performed a descriptive study of all cancer patients initiating an ICI in a large tertiary academic health care system and cancer center. Patients receiving prescriptions of IM drugs after ICI were identified through an electronic query of prescriptions and clinical encounters. IM drugs were considered a proxy for the occurrence of an irAE or flare of a pre-existing autoimmune disease. We did not study NSAIDs or glucocorticoids since these medications are commonly prescribed for many indications and are non-specific for irAEs or pre-existing autoimmune disease flares. All prescriptions for IM that could also be used for cancer, organ rejection or stem cell transplant indications (methotrexate, rituximab, and mycophenolate mofetil) were manually reviewed to include only patients who received these drugs for treatment of an irAE or autoimmune disease flare. If multiple IMs were prescribed after ICI, we only included the initial IM, to avoid counting a single patient more than once. We also identified all clinical encounters with a rheumatologist in our healthcare system occurring after ICI initiation and reported the proportion and frequency of ICI- and IM-treated cancer patients who were evaluated by rheumatology.

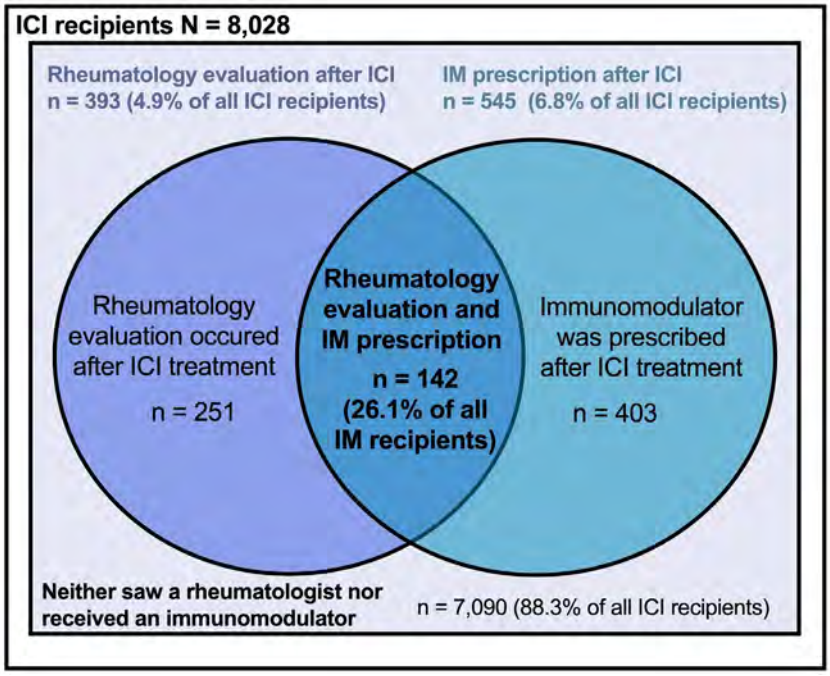
Results: We identified 8,028 cancer patients who initiated an ICI (mean age 64.4 years, female 43%). The most common ICIs were: pembrolizumab (47%), nivolumab (28%), ipilimumab (8.0%) and combination ipilimumab/nivolumab (8.0%), (**Figure 1**). Among ICI recipients, 6.8% subsequently received a prescription for an IM. Among all patients who received an IM following ICI treatment, the most common initial IMs were: infliximab (32.0%), mycophenolate mofetil (13.6%) hydroxychloroquine (10.8%), and methotrexate (10.3%). Among all ICI recipients, 4.9% (n = 393)



Frequency and proportion of initial immunomodulator (IM) prescribed (n=545).

were evaluated by rheumatology of which 1.8% (n = 142) received an IM after ICI start. Of all ICI-treated patients who received an IM, 26.1% were evaluated by a rheumatologist (**Figure 2**).

Conclusion: In this large single-center study, 6.8% of ICI-treated cancer patients had severe/refractory irAEs or underlying autoimmune disease flares that required treatment with IM. While determination of the indication for IM use in these patients is underway, these results provide a summary of which IM are initially considered after glucocorticoids, in cancer patients receiving ICI. While not all types of irAEs require rheumatology involvement, notably, only one-fourth of ICI-treated patients who received an IM were also evaluated by a rheumatologist suggesting that oncologists and other specialists prescribe most IM in these patients.



Frequency and proportion of patients with rheumatology evaluation and immunomodulator (IM) use among immune checkpoint inhibitor (ICI)-treated cancer patients (N=8,028).

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Abstract Number: 1571

Distinct T Cell Responses in Inflammatory Arthritis Associated with Combined CTLA-4 and PD-1 Inhibitor Therapy

Sang Kim[1], Jean Tayar[2], Maria Suarez-Almazor[3], Huifang Lu[4], Yang-Zhi Zhao[5], Margarita Divenko[5], William Padron[5], Emma Rodriguez[5], Sattva Neelapu[5], Jennifer Wang[5], Amish Shah[5], Nizar Tannir[5], Don Gibbons[5], Guillermo Garcia-Manero[5], Hussein Tawbi[5], Patrick Hwu[5], Andrew Futreal[5], Adi Diab[5] and Roza Nurieva[5], [1]The Univesrity of Texas MD Andesron Cancer Center, Pearland, TX, [2]The University of Texas, MD Anderson Cancer Center, Houston, TX, [3]University of Texas MD Anderson Cancer Center, Houston, TX, [4]MD Anderson, Houston, TX, [5]MD Anderson, Houston

SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Immunological Complications of Therapy Poster
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Background/Purpose: Despite of unprecedented clinical success in cancer therapeutics, immune checkpoint inhibitors (ICIs) are associated with immune-related adverse events (irAEs), including arthritis (arthritis-irAE). Arthritis-irAE can not only cause bone erosions but also warrant early termination of ICI treatment. Further, treatment for the arthri-

tis-irAE can mitigate anti-tumor immunity revived by the ICI treatment. To overcome such clinical challenges, understanding the pathophysiology of arthritis-irAE is critical; however, these mechanisms remain unknown.

Methods: We collected and performed immunoprofiling of synovial fluid from seven patients with active arthritis-irAE and three control patients with osteoarthritis. In parallel, we examined the impact of ICIs on collagen induced arthritis (CIA).

Results: Four patients developed arthritis after PD-1 inhibitor monotherapy and three after combination therapy with CTLA-4 and PD-1 inhibitors. Two patients in the combination therapy group required interleukin (IL)-6 receptor inhibitor therapy in addition to steroids, compared with one patient in the monotherapy group (sulfasalazine). IL-17-producing $CD4^+$ T cells (Th17) were enriched in the combination therapy group compared to monotherapy group (1.01±0.73% in live $CD4^+$ T cells in the monotherapy group compared with 3.19±0.31% in the combination therapy group; P=0.005). Synovial fluid levels of IL-6 and IL-17A, key cytokines for Th17 cell differentiation and function, were higher in the combination ICI therapy group than in the monotherapy group, suggesting the role of Th17-related cytokines in disease pathogenesis. Like humans, ICIs, especially in combinations, facilitate the development and progression of CIA. Importantly, although not reached statistical significance, like humans, collagen-specific Th17 cells were enriched in CIA mice receiving combined ICI treatment.

Conclusion: Our data suggests that Th17 cells, especially in post combination ICI therapy, play a critical role in the disease pathogenesis. Comprehensive studies with more patients/controls along with recapitulating mouse models will unmask underlying mechanisms of arthritis-irAE. Further, understanding of altered immunity in the arthritis-irAE will provide insights of inflammatory arthritis secondary to the classical autoimmune diseases.

Disclosure: S. Kim, None; **J. Tayar**, None; **M. Suarez-Almazor**, None; **H. Lu**, None; **Y. Zhao**, None; **M. Divenko**, None; **W. Padron**, None; **E. Rodriguez**, None; **S. Neelapu**, None; **J. Wang**, None; **A. Shah**, None; **N. Tannir**, None; **D. Gibbons**, None; **G. Garcia-Manero**, None; **H. Tawbi**, None; **P. Hwu**, None; **A. Futreal**, None; **A. Diab**, None; **R. Nurieva**, None.

Abstract Number: 1572

Clinical Characteristics of Methotrexate Associated Lymphoproliferative Disorders and RA Treatment After Lymphoproliferative Onset in 92 Cases

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

Background/Purpose: Lymphoproliferative disorders (LPD) that develop in rheumatoid arthritis (RA) patients treated with MTX (MTX-LPD) is one of the important complications for RA patients. MTX-LPD has varied pathologies includ-

		SR (n=63)	CTx (n=29)	p
Age	(yr.)	66.2 ± 11.5	65.9 ± 9.52	0.9150
Gender	M : F	18 : 44	9 : 20	0.8455
RA duration	(yr.)	11.9 ± 7.60	15.8 ± 11.4	0.0646
Laboratory data				
sIL-2R	(U/ml)	1585.7 ± 1595.1	5097.2 ± 4664.5	< 0.0001
LDH	(U/l)	256.6 ± 86.1	330.7 ± 164.6	0.0565
Extranodal involvement	(%)	56.5	41.4	0.1800
Histology		DLBCL 15 HL 5 FL 1 PTCL 1 AILT 1 MALT 3 THRLBCL 1 Polymorphic 1 Reactive 4 Unknown 12 No biopsy 19	DLBCL 20 HL 4 IVL1 TCL 1 TCRLBCL1 MCL 1 Unknown 1	

Patients profile of MTX-LPD cases.

ing various clinical manifestation and histological finding. Therefore, we need more information about MTX-LPD. In addition, it has not been established for RA treatment after the onset of MTX-LPD. We investigate the clinical characteristics of MTX-LPD and RA treatment after the onset of MTX-LPD.

Methods: We enrolled 92 MTX-LPD patients from Kagawa Prefecture, Japan between June 2005 and March 2020. Patients were diagnosed RA according to American College of Rheumatology (ACR) 1987 classification criteria or ACR/European League Against Rheumatism (EULAR) 2010 classification criteria, and treated with disease modifying antirheumatic drugs (DMARDs) including MTX. We collected as follow information; age, gender, duration of RA, laboratory data (LDH and sIL-2R) and treatment of MTX-LPD. We divided 92 MTX-LPD cases into spontaneous regression cases (SR group) and cases that treated with chemotherapy after MTX discontinuation (CTx group), and compared the difference between two groups. In addition, we investigated RA treatment after the onset of MTX-LPD.

Results: Characteristics of 92 MTX-LPD patients are as follow; mean age 66.2±10.9 years, 64 female, duration of RA 13.1±9.1 years. 62 patients (67.4%) were spontaneously improved by discontinuing MTX. The level of sIL-2R was significantly lower in SR group ($p< 0.0001$). Furthermore, the rate of extranodal lesion was more in SR group compared with CTx group (56.5% vs 41.4%). 73 patients (76.1%) were proven MTX-LPD histologically. In these patients, diffuse large B-cell lymphoma (DLBCL) was the most frequent histological diagnosis of MTX-LPD (38.0%). As regards RA treatment after MTX-LPD onset, conventional synthetic DMARDs alone, biologics or JAK inhibitors and NSAIDs or PSL alone treatment were 34, 20 and 10 cases respectively. The remaining cases were untreated, or unknown due to transferred to another hospital.

Conclusion: We indicated clinical characteristics of MTX-LPD with RA patients. In this study, we suggested that the serum sIL-2R level may predict SR of MTX-LPD. Additionally, biologics and JAK inhibitor have been used in many cases to control of RA activity after the onset of MTX-LPD. However, the association of JAK inhibitor and LPD onset is not clarify, and we need to accumulate the cases in the future.

Disclosure: T. Kameda, None; **S. Nakashima**, None; **M. Inoo**, None; **I. Onishi**, None; **N. Kurata**, None; **R. Wakiya**, None; **M. Fahmy Mansour**, None; **K. Sugihara**, None; **Y. Ushio**, None; **M. Kato**, None; **H. Shimada**, None; **H. Dobashi**, None.

Abstract Number: 1573

Gout as an Immune-Related Adverse Event from Immune Checkpoint Inhibitors

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SESSION INFORMATION
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Background/Purpose: Immune checkpoint inhibitors (ICI) are novel treatments approved for various tumours including melanoma, lung and kidney. By interacting with immunoregulatory molecules (programmed death-1 (PD-1), PD-1 ligand (PD-L1), or cytotoxic T-lymphocyte associated protein (CTLA-4)), ICI prevent inhibition of T-cells and thereby increase immune activity. However, this T-cell activation also dysregulates immune self-tolerance and causes immune-related adverse events (irAE) such as inflammatory arthritis, myositis, and polymyalgia rheumatica. Despite increases in ICI use, reports of crystal arthropathies as a potential irAE remain rare with only 2 cases of pseudogout and 2 cases of unspecified crystalline arthritis. Furthermore, despite reports of tumor lysis syndrome and hyperuricemia from ICI, gout was not specifically reported. We report our center's experience with ICI-associated gout and explore the potential pathophysiology behind this entity.

Methods: We reviewed all patients referred to the university adult rheumatology clinic between 2017 and 2020 for acute gout flares after receiving mono- or combination-ICI. After receiving individual informed consent, their electronic medical chart was reviewed for history relevant to their cancer and gout. Gout was confirmed by combination of imaging, classic podagra history, and joint aspirations.

Results: We identified 6 patients. They were all diagnosed at a mean age of 63 years with solid tumours (squamous cell carcinoma of the larynx or skin, lung adenocarcinoma, renal cell carcinoma, melanoma) and received a PD-1 inhibitor. Three patient also received an additional ICI as a combination therapy: 1 received CTLA-4 inhibitor (ipilimumab) while 2 received ipilimumab or placebo as part of clinical trials.

All patients previously had gout. Their last flare was at least 1 year prior to first ICI dose. While patients had risk factors for gout exacerbation including alcohol, hypertension, thiazide diuretic use, obesity, dyslipidemia, and elevated baseline creatinine and urate levels, these factors were non-contributory to post-ICI gout flares.

Four patients experienced gout flares after their first ICI infusion while 2 patients flared after multiple ICI infusions. Patterns of gout flares were not typical of classical gout with only 1 patient presenting with acute monoarticular involvement and 5 patients presenting with acute, acute-on-chronic, or chronic oligoarticular involvements. Affected joints included first metatarsophalangeal joint, knees, elbows, and smaller joints (wrist, hands, feet). All patients responded well to usual gout therapies and tolerated continuation of ICI with positive cancer response.

Conclusion: Although many irAE have previously been described, this is the first to report gout as a potential irAE. Potential mechanisms include loss of T-cell inhibition by ICI leading to unchecked inflammation from uric acid crystals; increased white blood cell turnover rates; and consequence of tumour lysis syndrome. With increased survival of stage four cancer patients with ICI, early identification and management of gout is an important aspect of improving patient quality of life.

Disclosure: K. Lee, None; **C. Ye**, None; **S. Elahi**, None.

Abstract Number: 1574

Over Half of Patients with Immune Checkpoint Inhibitor-related Myositis, Myasthenia Gravis and/or Myocarditis Have Autoantibodies: Results from a Systematic Literature Review

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Although immune checkpoint inhibitor (ICI) cancer treatments are known to activate cytotoxic T-cells, autoantibodies may also contribute to the development of immune-related adverse events (irAE). Patients with ICI-associated myositis are said to rarely have autoantibodies. We performed a systematic literature review of irAE cases and case series to determine the prevalence of autoantibodies in patients with ICI-induced myositis, myasthenia gravis (MG) and/or myocarditis, and to identify characteristics of seropositive and seronegative patients.

Methods: PubMed, Embase and Cochrane databases were searched for reports of ICI-induced irAE. Publications were included if they provided results of autoantibody testing at the individual patient level. Here we report on the subset of publications describing ICI-induced myositis, MG and/or myocarditis. Descriptive statistics were used to summarize results.

Results: We screened 12,207 articles and subsequently, 1249 full texts. We included 69 publications that described autoantibody testing in 150 patients with myositis, MG and/or myocarditis. Eighty-nine patients (59%) had at least one autoantibody, including 4 of 5 tested patients with myocarditis alone, and 5 of 6 with the combination of myositis, MG and myocarditis (**Table 1**). The prevalence of autoantibodies was the same across ICI and cancer types. Seropositive patients had a higher median creatinine phosphate kinase (CPK) (4300 u/L vs. 1959 u/L), a slightly earlier time of irAE onset (3.6 weeks vs. 4.1 weeks) and were less likely to resolve their irAE (27% vs 45%). Sixty percent of tested patients had a muscle-specific antibody (MSA) (25%) and/or MG-specific (56%) antibody (**Table 2**). Only 1/15 tested

Table 1. Characteristics of patients with and without any antibody measured (total n=150)

Patient characteristics [n=denominator]	Any antibody present*	No antibody present
Number (%)	**89 (59)**	61 (41)
Mean age (SD), years [n=122]	68.8 (12.3)	68.9 (12.3)
Sex, male n/n % [n=124]	53/80 (66)	31/44 (70)
Myositis (any), n % [n=123][1]	**73 (59)**	50 (41)
- Myalgias	23 (32)	16 (32)
- Proximal muscle weakness	35 (48)	23 (46)
- Bulbar distribution	13 (18)	15 (30)
- Ocular distribution	27 (37)	19 (38)
• Diagnostic muscle biopsy for myositis, n/n tested (%)	18/21 (86)	16/17 (94)
• Diagnostic EMG for myositis, n/n tested (%)	15/20 (75)	14/15 (93)
• Median peak CPK (IQR), units/L [n=106]	4300 (1587, 7540)	1959 (944, 3615)
Myasthenia (any), n % [n=55]	**34 (62)**	21 (38)
• Positive diagnostic testing[2], n (%)	18 (53)	13 (62)
Myocarditis (any), n % [n=34]	**22 (65)**	12 (35)
Combinations of presentations [n=150]		
- Myositis alone, n (%) [n=66]	35 (53)	31 (47)
- Myasthenia alone, n (%) [n=19]	9 (47)	10 (53)
- Myocarditis alone, n (%) [n=5]	**4 (80)**	1 (20)
- Myositis + Myasthenia, n (%) [n=30]	**20 (67)**	10 (33)
- Myositis + Myocarditis, n (%) [n=23]	13 (57)	10 (43)
- Myasthenia + Myocarditis, n (%) [n=1]	1 (100)	0
- Myositis + Myasthenia + Myocarditis, n (%) [n=6]	**5 (83)**	1 (17)
Cancer type, n/n % [n=119]		
- Melanoma	31/76 (41)	17/43 (39)
- NSCLC	16/76 (21)	11/43 (26)
- RCC/urothelial	12/76 (15)	4/43 (9)
- Thymoma	8/76 (11)	0
- Other	9/76 (12)	11/43 (26)
ICI therapy, n/n % [n=147]		
- PD-1/PD-L1 monotherapy	69/88 (78)	50/59 (83)
- CTLA-4 monotherapy	5/88 (6)	3/59 (5)
- Combination therapy	14/88 (16)	7/59 (12)
Median time to irAE (IQR), weeks [n=116]	**3.6 (2, 5.1)**	4.1 (3.5, 6.5)
- Range time to irAE, weeks	[0.6, 11.1]	[1.3, 51]
Median doses to irAE (IQR), [n=107]	2 (1, 2)	2 (2,4)
IrAE outcome, n/n % [n=135]		
- Resolved	**22 (27)**	23 (45)
- Improved/ongoing	38/76 (46)	18 (35)
- Death from irAE	**23 (28)**	10 (20)
Cancer status at time of publication, n/n % [n=86]		
- No progression	25/55 (45)	12/28 (43)
- Progression	11/55 (20)	5/28 (18)
- Death from myositis	19/55 (35)	11/28 (39)
ICI usage, n/n % [n=102]		
- Continued throughout	1/54 (2)	3/48 (6)
- Interrupted	18/54 (33)	16/48 (33)
- Permanently discontinued	35/54 (65)	29/48 (60)

Key: EMG = electromyography; CPK = creatinine phosphate kinase; NSCLC = non-small cell lung cancer; RCC = renal cell carcinoma; ICI = immune checkpoint inhibitor; PD-1/PD-L1 = programmed cell death protein 1/programmed death ligand-1; irAE = immune-related adverse event.

*Any antibody includes anti-nuclear antibody, ANCA, RF, anti-CCP, dsDNA, smooth muscle antibody, anti-thyroglobulin, anti-thyroid receptor, anti-thyroid peroxidase

[1]Myositis presentations could include any combination of manifestations listed below (numbers do not equal 100%)

[2]Positive diagnostic testing included diagnostic findings on EMG, sfEMG, ice test, tensilon test, edrophonium test

Characteristics of seropositive and seronegative patients

Table 2. Prevalence of autoantibodies

	Patients positive, n	Patients tested, n	% positive
MSA, any	15	60	**25**
- MSA, only	13	--	--
- MSA + ACh Ab	1	--	--
- MSA + Striated Ab	1	--	--
ACh Ab, any	36	109	**33**
- ACh Ab, only	22	--	--
- ACh Ab + Striated Ab	14	--	--
Striated Ab, any	38	67	**57**
- Striated Ab, only	24	--	--
MuSK Ab	0	12	0
Any MG-specific* Ab	61	109	**56**
Any MSA or MG-specific Ab	73	121	**60**
Paraneoplastic Ab panel	1	15	6.7
Anti-nuclear Ab, any	20	54	37
- Anti-nuclear Ab, only	4	--	--
Other[1], any	7	17	41

Key: Ab= antibody, MSA = Muscle-specific antibody (specific antibodies: Jo-1, PL-7, PL-12, KS, Mi-2, p155/p140, EJ, Ku, OJ, PM/Scl, SRP, Smith/RNP (ENA), Ro50/Ro60, SAE, NXP2, MDA5, TIF1-y, 3-hydroxy-3methylglutaryl-coenzyme A reductase)
ACh Ab = Acetylcholine-related antibodies (Acetylcholine receptor binding, blocking, modulating antibodies, acetylcholinesterase antibody); Striated Ab (specific antibodies: titin, striated muscle, Kv1.4 (voltage-gated Potassium channel), ryanodine receptor, myosin, alpha-actin); MuSK = Muscle specific kinase antibody; MG = myasthenia gravis; MG-specific Ab include: Anti-ACh, anti-striated, anti-MuSK
[1]Other antibodies include: anti-nuclear antibody, ANCA, RF, anti-CCP, dsDNA, smooth muscle antibody, anti-thyroglobulin, anti-thyroid receptor, anti-thyroid peroxidase

Prevalence of autoantibodies

patients had a paraneoplastic autoantibody, while 20/54 (37%) tested were ANA positive. Over 90% of patients with MSA or striated antibodies presented with myositis, whereas 17/22 (77%) with only Acetylcholine-related antibodies (ACh) presented with MG (**Table 3**). A subset of patients (n=14) with both anti-striated and anti-ACh presented with variable myositis and MG symptoms. Patients with anti-ACh had worse irAE outcomes - only 10% with symptom resolution and 48% died.

Conclusion: Almost two-thirds of patients with ICI-induced myositis, MG and/or myocarditis have autoantibodies. Patients with myositis typically have MSA or striated antibodies. The presence of anti-ACh in isolation is found almost exclusively in patients presenting with MG and these patients tend to have a worse prognosis. Prospective studies are needed to determine whether autoantibodies are present prior to ICI and could serve as biomarkers of future serious irAE.

Table 3. Comparison of patients with specific autoantibody profiles

Patient characteristics	Any MSA Ab (n=15)	Anti-ACh only (n=22)	Anti-striated only (n=24)	Anti-striated AND Anti-ACh (n=14)
Mean age (SD), years	73 (6.5)	69 (14)	68 (13)	73 (12)
Male, n/n (%)	8/10 (80)	14/22 (64)	18/24 (75)	8/14 (57)
Myositis[1] (any), n (%)	**14 (93)**	13 (59)	**22 (92)**	14 (100)
- Myalgias, %	4 (29)	5 (23)	6 (25)	3 (21)
- Proximal muscle weakness, n (%)	7 (50)	7 (54)	8 (33)	7 (50)
- Bulbar distribution, n (%)	7 (50)	6 (27)	7 (29)	8 (57)
- Ocular distribution, n (%)	7 (50)	10 (45)	15 (63)	7 (50)
- Positive testing for myositis[2], n/n %	10/10 (100)	3/6 (50)	6/6 (100)	6/7 (86)
- Median peak CPK (IQR), units/L	4210 (2258,5772)	2682 (1926,8840)	5350 (1343,8602)	1904 (1247,6200)
Myasthenia (any), n (%)	3 (20)	**17 (77)**	9 (38)	5 (36)
Myocarditis (any), n (%)	5 (33)	8 (36)	4 (17)	2 (14)
Combinations of presentations				
Myositis alone, n (%)	8 (53)	1 (5)	11 (46)	8 (57)
Myasthenia alone, n (%)	1 (7)	**7 (32)**	1 (4)	0
Myocarditis alone, n (%)	0	2 (9)	1 (4)	0
Myositis + Myasthenia, n (%)	1 (7)	6 (27)	8 (33)	4 (29)
Myositis + Myocarditis, n (%)	4 (26)	2 (9)	3 (13)	1 (7)
Myasthenia + Myocarditis, n (%)	0	0	0	0
Myositis + Myasthenia + Myocarditis, n (%)	1 (7)	4 (18)	0	1 (7)
Cancer type, n/n (%)				
- Melanoma	7/11 (64)	10/21 (48)	3/21 (14)	4/11 (36)
- NSCLC	0	2/21 (10)	9/21 (43)	1/11 (9)
- RCC/urothelial	1/11 (9)	4/21 (19)	5/21 (24)	2/11 (18)
- Thymoma	0	4/21 (19)	0	3/11 (27)
- Other	3/11 (27)	1/21 (5)	4/21 (19)	1/11 (9)
ICI therapy, n (%)				
- PD-1/PD-L1 monotherapy	13 (86)	18 (82)	18 (75)	12 (83)
- CTLA-4 monotherapy	0	2 (9)	0	0
- Combination therapy	2 (14)	2 (9)	6 (25)	2 (17)
Median time to irAE (IQR), weeks	3.3 (3, 5)	4 (2, 6)	4 (3, 4.3)	3 (2.2, 4.5)
Median doses to irAE (IQR)	2 (2, 2)	1 (1, 2)	2 (2, 2)	1 (1, 2)
IrAE outcome, n/n (%)				
- Resolved	5/12 (42)	**2/21 (10)**	9/23 (39)	4/14 (29)
- Improved/ongoing	3/12 (25)	9/21 (42)	9/23 (39)	8/14 (57)
- Death from irAE	4/12 (33)	**10/21 (48)**	5/23 (22)	2/14 (14)
Cancer status at time of publication, n/n (%)				
- No progression	2/8 (25)	4/13 (31)	12/20 (60)	3/10 (30)
- Progression	0	1/13 (15)	4/20 (20)	4/10 (40)
- Death	6/8 (75)	8/13 (54)	4/20 (20)	3/10 (30)

Key: Ab= antibody, MSA = Muscle-specific antibody (specific antibodies: Jo-1, PL-7, PL-12, KS, Mi-2, p155/p140, EJ, Ku, OJ, PM/Scl, SRP, Smith/RNP (ENA), Ro50/Ro60, SAE, NXP2, MDA5, TIF1-γ, 3-hydroxy-3methylglutaryl-coenzyme A reductase)
ACh Ab = Acetylcholine-related antibodies (Acetylcholine receptor binding, blocking, modulating antibodies, acetylcholinesterase antibody); Striated Ab (specific antibodies: titin, striated muscle, Kv1.4 (voltage-gated Potassium channel), ryanodine receptor, myosin, alpha-actin); CPK = creatinine phosphate kinase; NSCLC = non-small cell lung cancer; RCC = renal cell carcinoma; ICI = immune checkpoint inhibitor; PD-1/PD-L1 = programmed cell death protein 1/programmed death ligand-1; irAE = immune-related adverse event.
[1]Myositis presentations could include any combination of manifestations listed below (numbers do not equal 100%)
[2]Positive testing included diagnostic findings on EMG, MRI and/or muscle biopsy

Characteristics of patients with specific autoantibody profiles

Disclosure: N. Ghosh, None; **K. Chan**, None; **B. Jivanelli**, None; **A. Bass**, None.

Abstract Number: 1575

CD6 Is a Target for Cancer Immunotherapy

Jeffrey Ruth[1], **Mikel Gurrea Rubio**[2], Kalana Athukorala[3], Stephanie Rasmussen[1], Weber Daniel[1], Peggy Randon[1], M Asif Amin[1], Phillip Campbell[1], Pei-suen Tsou[1], Yang Mao-Draayer[1], Qi Wu[4], Matthew Lind[1], Rosemary Gedert[1], Thomas Lanigan[1], Venkateshwar Keshamouni[1], Nora Singer[5], Feng Lin[6] and David Fox[7], [1]University of Michigan, Ann Arbor, MI, [2]Division of Rheumatology, University of Michigan, Canton, MI, [3]University of Michigan, Ann Arbor, MN, [4]University of Michigan, Ann Arbor, [5]The MetroHealth System, Case Western Reserve University School of Medicine, Cleveland, OH, [6]Cleveland Clinic Foundation, Cleveland, OH, [7]Division of Rheumatology, University of Michigan, Ann Arbor, MI

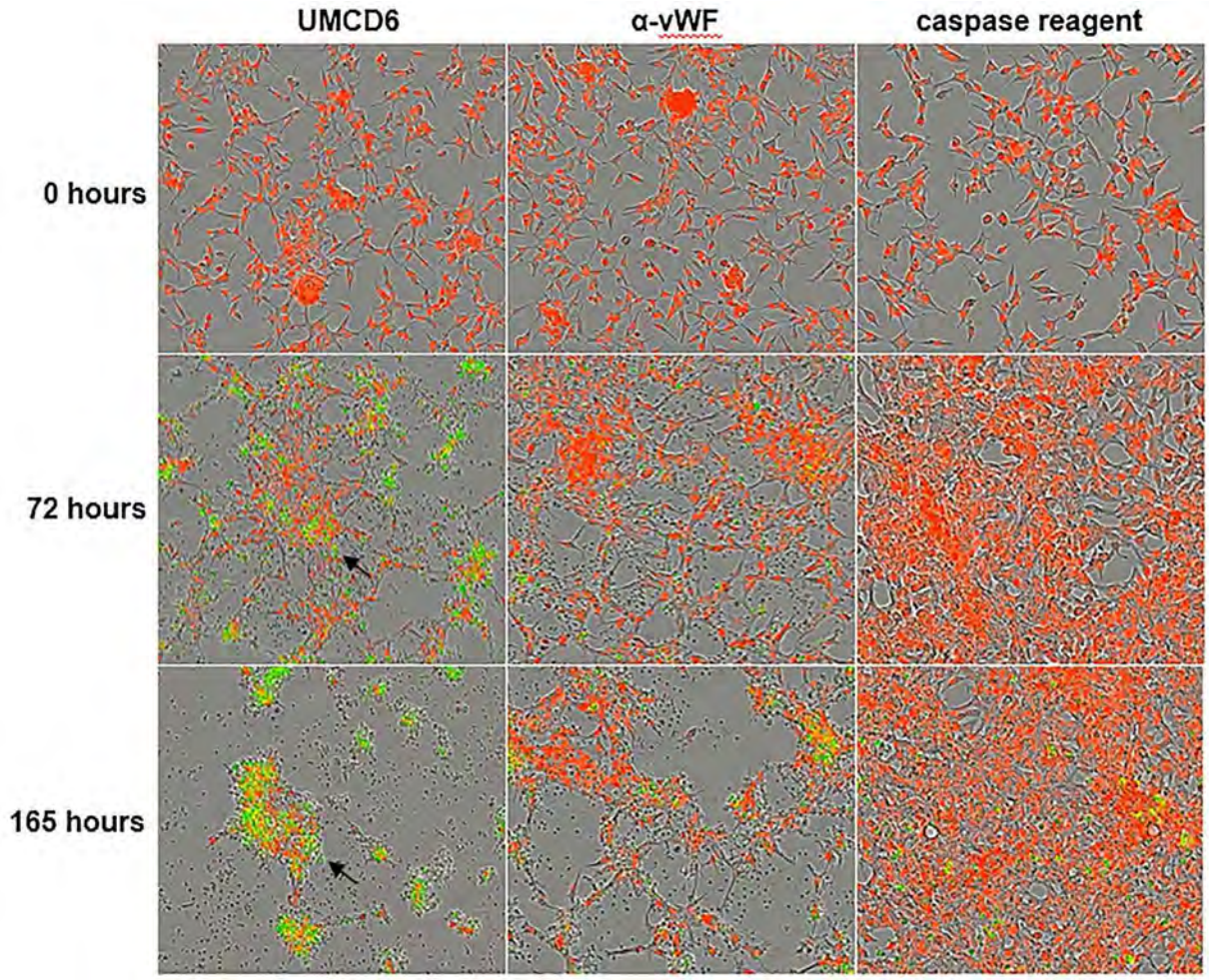
SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Immunological Complications of Therapy Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM



Supplemental Figure S2. ***UMCD6 enhances LNCaP prostate cancer cell killing in vitro by human PBMCs.*** In the absence of mAbs and/or PBMCs (right column – untreated wells), LNCAP proliferation was unimpeded (fluorescent red cells). LNCAP prostate cancer cells co-cultured with UMCD6-treated PBMCs displayed profound clumping and caspase expression (fluorescent green dye) at 72 hours and were almost completely eliminated by 165 hours (see arrows). In the presence of control antibody and PBMCs modest killing of LNCaP cells was observed, but viable cancer cells persisted. The experiment was performed using the IncuCyte imaging device and the pictures were taken directly from a movie of this assay that is included in the supplementary material.

The anti-CD6 monoclonal antibody UMCD6 induces lymphocytes to kill cancer cells.

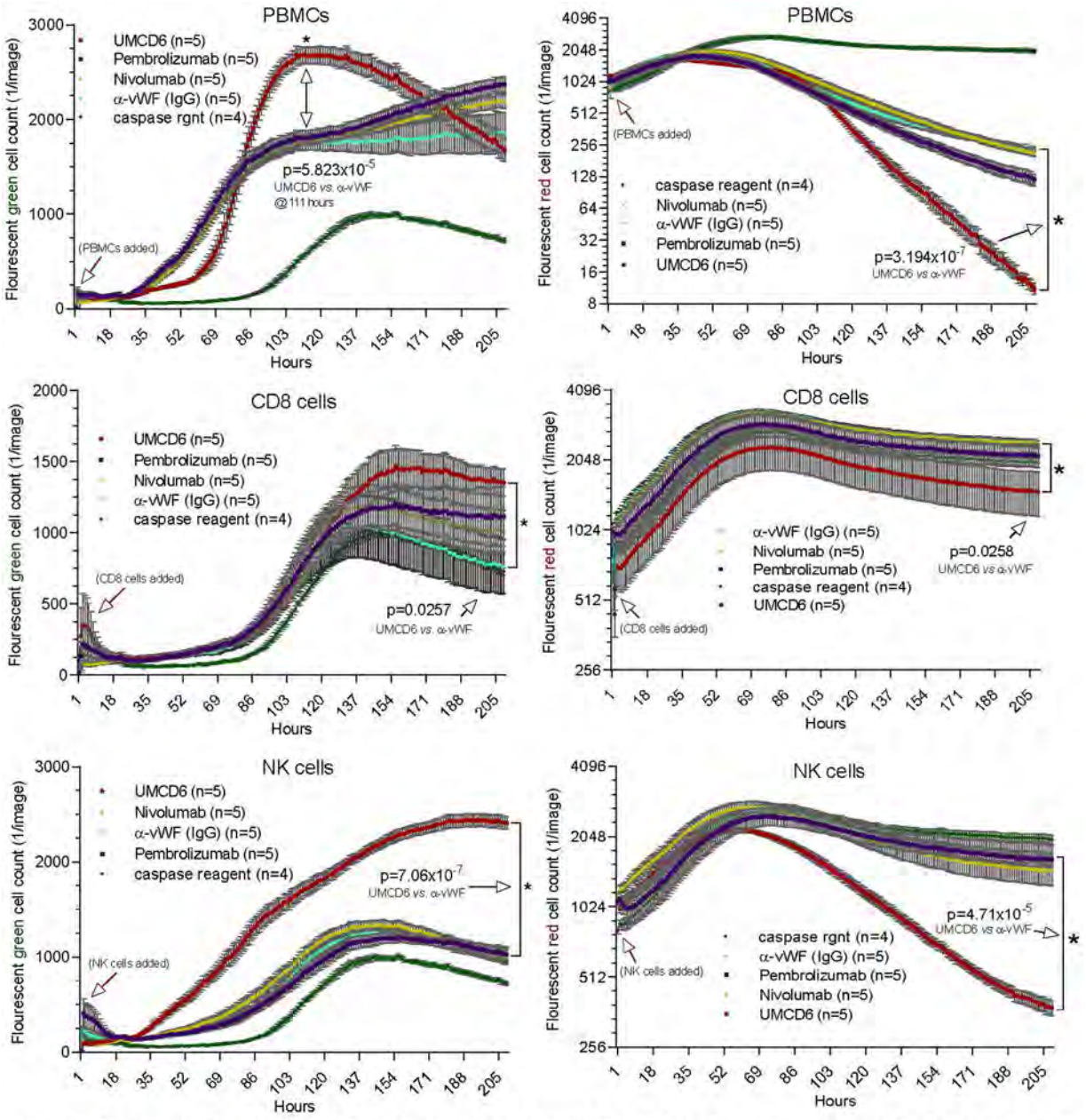


Figure 5. ***CD6+ NK cells treated with UMCD6 are highly effective at killing MDA-MB-231 tumor cells.*** **Upper panel:** Tumor cell killing assays were set up using 50,000 immune cells and 20,000 MDA-MB-231 HBCCs and antibodies at 10ug/mL. PBMCs pre-incubated with UMCD6 killed tumor cells much more effectively than PBMCs pre-incubated with IgG control antibody, pembrolizumab or nivolumab (right panels, red fluorescence tumor cell survival with *y-axis* $\log_2$) and cell death (left panels, green fluorescence, caspase sensitive with *y-axis* linear). **Middle panel:** Isolated CD8+ cells showed enhanced killing and lower tumor cell survival in co-cultures with UMCD6, compared to the other antibodies. **Lower panel:** Only UMCD6 induced tumor cell killing by purified NK cells.

UMCD6 directly activates cytotoxic lymphocytes and is more potent than conventional checkpoint inhibitors.

Background/Purpose: Limitations of checkpoint inhibitor immunotherapy include induction of autoimmune syndromes and resistance of many cancers. Definition of additional molecular targets is required. CD6, expressed by most human T lymphocytes and a subset of natural killer (NK) cells, engages the ligands CD166/ALCAM and CD318. Interrupting CD6 interaction with its ligands prevents or reverses mouse models of rheumatoid arthritis, multiple sclerosis and uveitis, due to suppression by UMCD6 of differentiation of effector Th1 and Th17 cells. As CD6 ligands are broadly expressed on cancer cells and high expression of CD318 is associated with aggressive and metastatic

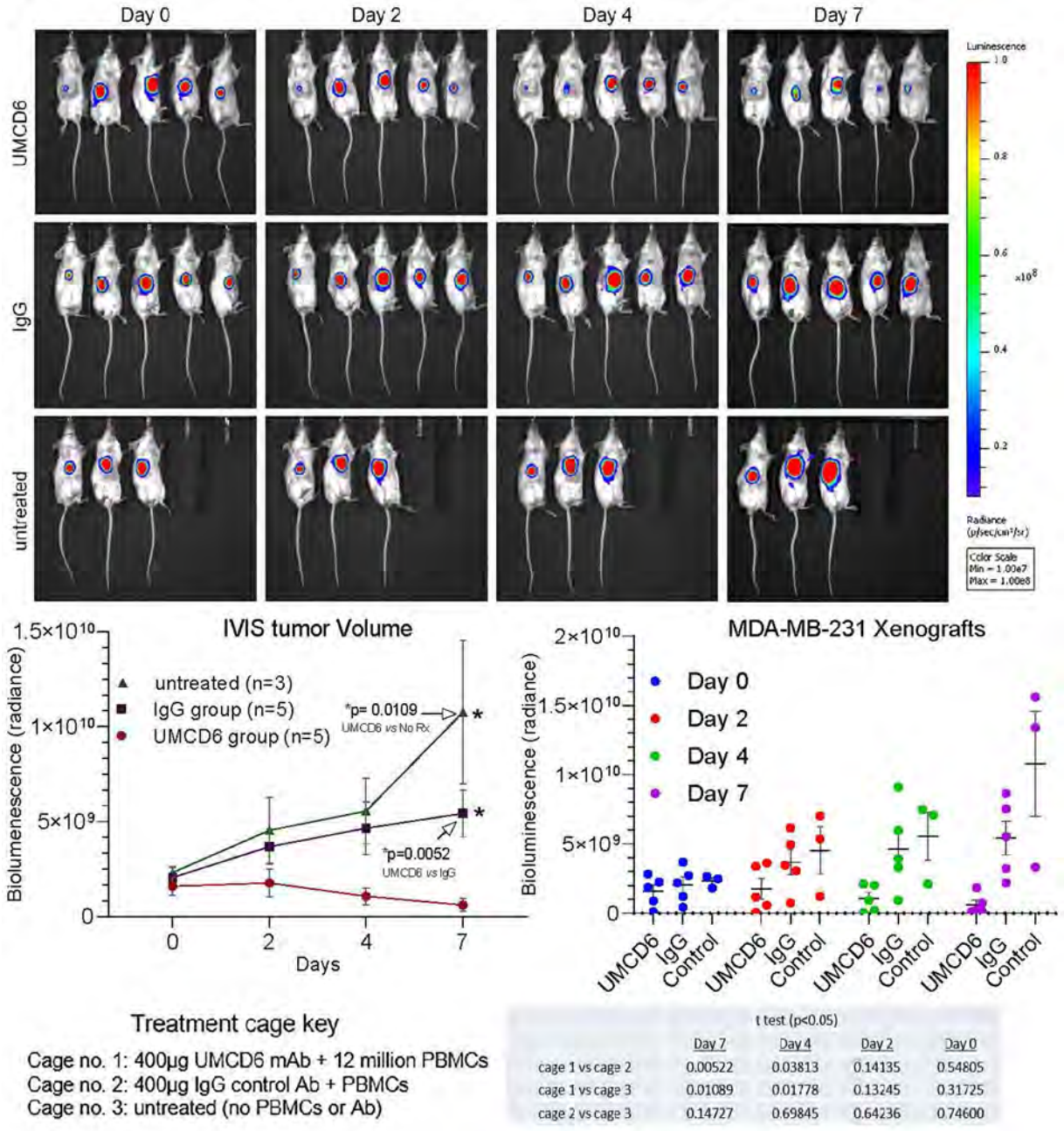


Figure 6. ***UMCD6 reduces tumor size in SCID beige mice.*** Human breast cancer cells (MDA $5x10^6$ cells) were inoculated s.c. in the ventral aspect of the abdomen of female SCID beige mice. Once tumors reached a size of about $100mm^3$ some mice were administered $12x10^6$ human PBMCs by tail vein (considered day 0). The next day mice that had received PBMCs were injected i.p. with either 0.4 mg control IgG or UMCD6. Mice not administered PBMCs received no antibodies (untreated). Tumors were measured by IVIS (*in vivo* imaging) thereafter. The effect of UMCD6 on tumor volume can be seen at day 4 and 7 after UMCD6 administration (*p<0.05) compared to both the IgG and no-treatment groups. Data represents mean of 3-5 animals ± sem.

UMCD6 induces lymphocyte-mediated cancer regression in vivo.

cancer, we hypothesized that interruption of CD6/CD6 ligand interactions would enhance lymphocyte killing of cancer cells.

Methods: Flow cytometry was used to define expression of CD6 ligands on human breast, lung and prostate cancer cell lines. Soluble CD318 was measured by ELISA. To develop cell lines with nuclear red fluorescence for live imaging,

cancer cells were transfected with an mKate2 2X nuclear localization fusion construct. Co-cultures of cancer cells with peripheral blood mononuclear cells (PBMC) or purified CD4+, CD8+ and NK cells were imaged in an IncuCyte® S3 Live Cell Analysis System every 30-60 minutes for 5 to 7 days. A caspase-sensitive green fluorescent dye detected dying cancer cells. To monitor tumor growth by bioluminescent imaging i*n vivo*, MDA-MB-231 breast cancer cells were transduced with a luciferase lentivirus reporter. SCID/beige mice were injected sc with 5×10^6 luciferase-transfected breast cancer cells. Tumors were imaged by bioluminescence and at day 26 mice received 1.2×10^7 PBMCs iv. The next day mice received a single dose of UMCD6 or an IgG control antibody (400µg/mouse ip). Tumor growth was measured by bioluminescence, using a Xenogen IVIS 200 instrument. Tumors were removed at day 36 and examined by fluorescent immunohistology.

Results: Most human cancer cell lines were strongly positive for both CD318 and CD166. CD318+ lines shed soluble CD318 at concentrations that were chemotactic for CD6+ lymphocytes. UMCD6 strikingly augmented killing of breast, lung or prostate cancer cells in co-cultures with human lymphocytes, through direct effects on both CD8+ T cells and NK cells, increasing cancer cell death and lowering cancer cell survival more robustly than checkpoint inhibitors that interrupt PD-1/PD-L1. UMCD6 also augmented *in vivo* killing by PBMC of a human breast cancer line xeno-transplanted into immunodeficient mice. A single injection of 0.4 mg per mouse one day after infusion of PBMC led to near disappearance of tumors in mice that received UMCD6 but not control IgG. Histology showed extensive infiltration and activation of T lymphocytes and NK cells, with the NK cells over-represented in the tumor-infiltrating lymphocytes

Conclusion: The combined capabilities of UMCD6 to control autoimmunity through effects on CD4+ lymphocyte differentiation, while enhancing killing of cancer cells through distinct effects on CD8+ and NK cells, open a potential new approach to cancer immunotherapy that would suppress rather than instigate autoimmunity.

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Abstract Number: 1576

Acute Respiratory Viral Adverse Events During Use of Antirheumatic Disease Therapies: A Scoping Review

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Immunological Complications of Therapy Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: COVID-19 threatens the health of people worldwide, although it remains unclear to what extent antirheumatic disease therapies increase susceptibility to complications of viral respiratory infections. We conducted a scoping review of available evidence regarding the frequency and severity of acute respiratory viral adverse events (AEs) related to antirheumatic disease therapies.

Methods: Studies reporting primary data on acute respiratory viral AEs in patients using antirheumatic medications were identified via systematic search of MEDLINE, Scopus, Embase, Proquest Dissertations and Theses, Cochrane Database of Systematic Reviews, and OpenGrey databases and supplemental hand search of PubMed for additional

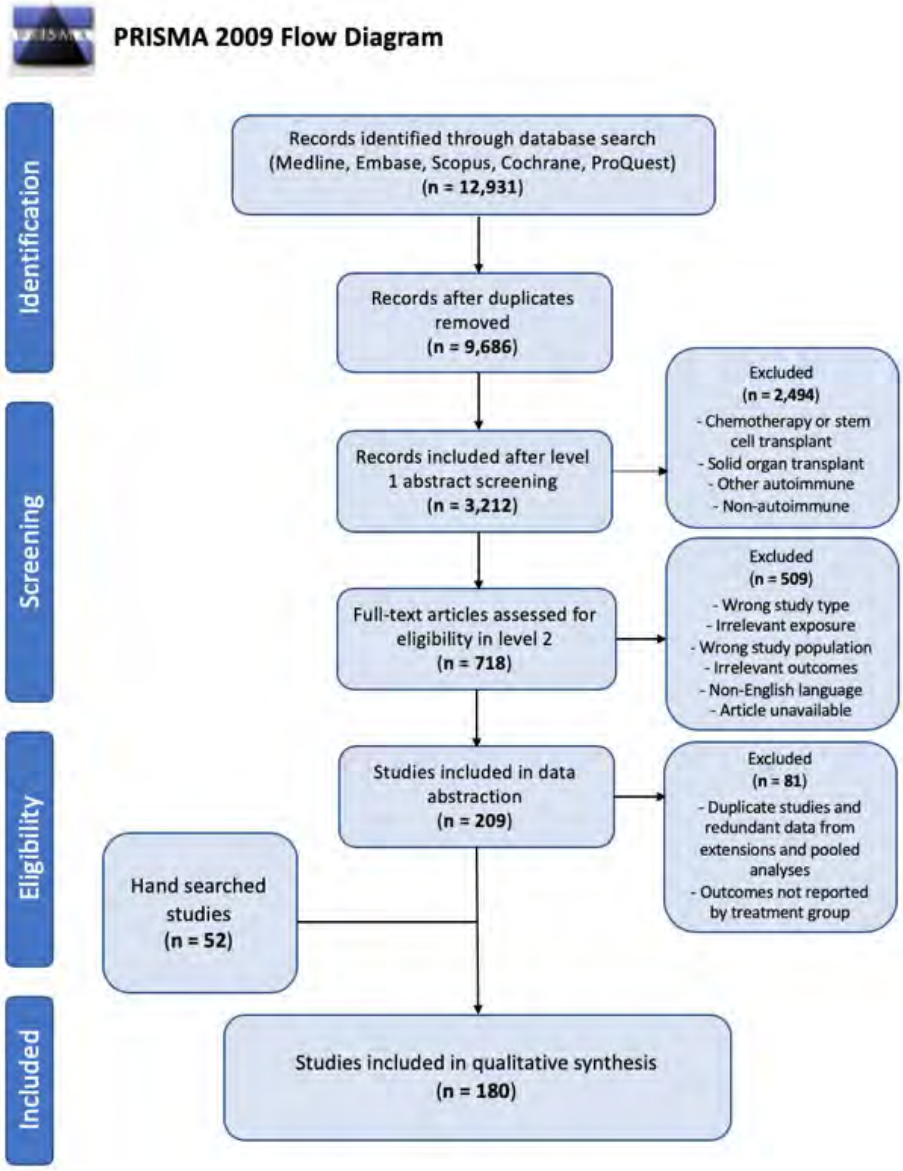

Figure 1. PRISMA flow diagram for the scoping review process.

Characteristics	Number of studies (Total 180)	Number of patients (Total 480,344)	%Studies	%Patients
Publication Year				
1991-2000	3	498	1.67%	0.10%
2001-2010	37	111403	20.56%	23.19%
2011-2020	140	368443	77.78%	76.70%
Publication Type				
Case series	32	4485	17.78%	0.93%
Other observational studies	44	395486	24.44%	82.33%
Randomized controlled trial	89	39041	49.44%	8.13%
Pooled safety analysis/postmarketing surveillance	15	41332	8.33%	8.60%
Continent				
Multiple	68	55621	37.78%	11.58%
North America	41	379488	22.78%	79.00%
Europe	30	19078	16.67%	3.97%
Asia	28	17105	15.56%	3.56%
Oceania	3	999	1.67%	0.21%
South America	1	60	0.56%	0.01%
Not specified	9	7993	5.00%	1.66%
Condition Studied				
Antiphospholipid Syndrome	1	19	0.56%	0.00%
Autoinflammatory	2	115	1.11%	0.02%
Axial spondyloarthritis	10	4081	5.56%	0.85%
Gout	1	312	0.56%	0.06%
Inflammatory bowel disease	5	1322	2.78%	0.28%
Juvenile idiopathic arthritis	8	891	4.44%	0.19%
Myositis	1	18	0.56%	0.00%
Neuromyelitis optica	2	181	1.11%	0.04%
Osteoarthritis	3	2636	1.67%	0.55%
Psoriasis	6	2587	3.33%	0.54%
Psoriatic arthritis	18	9678	10.00%	2.01%
Rheumatoid arthritis	72	391014	40.00%	81.40%
Systemic lupus erythematosus	27	51149	15.00%	10.65%
Systemic sclerosis	3	235	1.67%	0.05%
Vasculitis	9	1348	5.00%	0.28%
Multiple/Unspecified	12	14758	6.67%	3.07%
Drug Studied				
Acute Anti-inflammatory Drugs	13	112124	7.22%	23.34%
Conventional DMARDs (Non-Immunosuppressive)	5	26494	2.78%	5.52%
Conventional DMARDs (Immunosuppressive)	48	89328	26.67%	18.60%
Targeted Synthetic DMARDs	20	59597	11.11%	12.41%
T-cell Directed Biological DMARDs	10	94969	5.56%	19.77%
B-cell Directed Biological DMARDs	29	34832	16.11%	7.25%
Cytokine Directed Biological DMARDs	94	425104	52.22%	88.50%
Other	3	813	1.67%	0.17%
Outcomes				
Upper respiratory tract infection only	54		30.00%	
Lower respiratory tract infection only	67		37.22%	
Both upper and lower respiratory tract infection	56		31.11%	
Other viral infection	3		1.67%	
Hospitalization	11		6.11%	
Mortality	4		2.22%	

Table 1. Summary of general characteristics of included studies

relevant clinical trials. Data from eligible studies were charted by pairs of independent reviewers using a data abstraction tool.

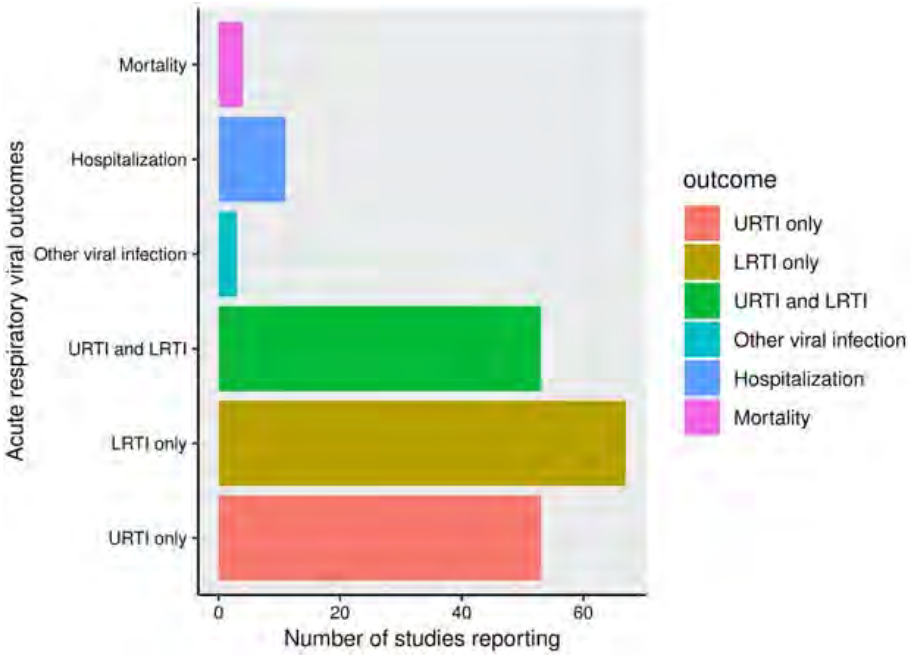

Figure 2. Acute respiratory viral outcomes reported in included studies. Mortality represents mortality secondary to an acute respiratory infection (including viral); Hospitalization represents hospitalization secondary to an acute respiratory infection (including viral); URTI, upper respiratory tract infection, includes sinusitis, nasopharyngitis, pharyngitis; LRTI, lower respiratory tract infection, includes bronchitis, pneumonia.

Results: 9,686 unique references were screened (Figure 1). After title and abstract screening, full-text screening, and the supplemental hand search, 180 studies (Table 1) were identified for data charting. The majority of studies were recently published (since 2011), of observational design, and from North America. 52% of studies focused on use of cytokine-directed bDMARDs; diseases of interest were most commonly RA (40%) and SLE (15%).

Domains of reported acute respiratory viral events and associated outcomes are shown (Figure 2). While the data are limited with regard to specific viral outcomes, they suggest that use of glucocorticoids, JAK inhibitors (especially high-dose), TNF inhibitors, and IL-17 inhibitors may be associated with a higher frequency of respiratory viral AEs compared to placebo. Available data suggest no increased frequency or risk of respiratory viral AEs with NSAIDs, hydroxychloroquine, sulfasalazine, methotrexate, azathioprine, mycophenolate mofetil, cyclophosphamide, or apremilast. One large cohort study demonstrated an association with leflunomide use and increased risk of acute viral respiratory AEs compared to non-use.

Conclusion: This scoping review identified that some classes of antirheumatic medications may be associated with increased risk of acute respiratory viral AEs in patients with rheumatic diseases. However, definitive data are lacking and future studies should address this knowledge gap. More granular reporting of viral respiratory AEs in future study designs would be helpful for rheumatology patients and practitioners to better interpret the risks of individual medications. In the context of the COVID-19 pandemic, increased widespread respiratory viral PCR testing offers immediate research opportunities to clarify the safety of antirheumatic therapies in terms of viral respiratory complications.

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Abstract Number: 1577

Immune Checkpoint Inhibitor-Induced Inflammatory Arthritis Impact on Function and Patient-Reported Quality of Life Measures Varies Depending on Pattern of Arthritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Background/Purpose: Immune checkpoint inhibitors (ICIs) have emerged as a paradigm shift in the treatment of malignancies, but can have significant side effects, termed immune related adverse events (IRAEs), that resemble autoimmune diseases. Inflammatory arthritis (ICI-IA) has significant impact on function, but little is understood about these patterns of arthritis and the specific quality of life impairment.

Methods: We performed a retrospective review of patients at one academic center who experienced ICI-IA and required referral to a rheumatologist in the collaborative Oncology-Rheumatology clinic. All patients were evaluated and completed a Health Assessment Questionnaire Disability Index (HAQ-DI). The pattern of ICI-IA was classified by a single rheumatologist based on the arthritis pattern as: inflammatory symmetrical polyarthritis (RA-like, IA), polymyalgia rheumatica-like (PMR), seronegative spondyloarthritis-like (SpA) and exacerbation of osteoarthritis-like (OA). Demographics (gender, age, and race) and malignancy (type, IRAE, type of ICI) data was collected. HAQ-DI, pain and patient global activity (PGA) visual analogue scores were compared based of the type of inflammatory arthritis using average and mean scores.

Results: Our review included 30 patients with ICI-IA: 12 with IA, 4 with PMR, 3 with SpA and 11 with OA. As expected for this age group, a majority, specifically 23, had pre-existent degenerative joint disease (DJD) and 5 had inflammatory arthritis (1 with rheumatoid arthritis (RA), 2 with psoriatic arthritis (PsA), and 2 with gout). Most patients were male (23, 76.6%), and all were Caucasian. The malignancy data and type of ICI are in Table 2. In terms of the patient reported outcomes, the overall HAQ-DI score was 0.57 ± 0.47, indicating that there was little effect of these arthropathies on overall functionality. The pain visual analogue scale had an average score of 41.8 ± 31.4 mm and the Patient Global Assessment had an overall score of 25.6 ± 26.7 mm.

Conclusion: The overall results suggest that the PMR-like pattern of ICI-IA is the most impactful based on the total HAQ scores. In contrast, the pain scores are higher in the SpA group, followed by the IA group. The overall PGA is highest in the IA group, followed by the SpA group. Interestingly, the HAQ scores were lower than the reported average scores of degenerative (0.8) or inflammatory arthritis (1.2). Our sample sizes for the subgroups are currently too small to allow for further statistical analyses of association or subgroup comparisons. Continued patient recruitment and further follow up will allow for understanding of the ICI-IA phenotypes will help understand and improve functionality and quality of life.

	PD-1/PD-L1 (N=16)	CTLA-4 (N=3)	PD-1/PD-L1 and CTLA-4 (N=11)
Average Age (y)	73	68	61
Gender	-Males: 10 -Females: 6	-Males: 3 -Females: 0	-Males: 10 -Females: 1
Type of Malignancies	-Malignant Melanoma (12) -Hodgkin's Lymphoma (1) -Metastatic Basal Cell Carcinoma (1) -Metastatic Urothelial Carcinoma (2)	-Metastatic Melanoma (3)	-Metastatic Melanoma (9) -Metastatic Merkel Cell Carcinoma (1) -Metastatic Squamous Cell Carcinoma (1)
Pre-existing Rheumatic Conditions	-None (1) -DJD (13) -RA (1) -PsA (1)	-PsA (1) -DJD (2)	-None (1) -Gout (2) -DJD (8)
Type of ICI-IA	-OA (7) -IA (6) -PMR (2) -SpA (1)	-OA (1) -IA (1) -SpA(1)	-OA (3) -IA (5) -PMR (2) -SpA (1)
Other IRAEs	-Iritis (1) -Pancreatitis (1) -Hepatitis/elevated liver enzymes (1) -Mucositis (1) -Dermatitis/Rash (2) -Colitis (1) -Nephritis (1) -Seizure (1)	-Colitis (1) -Sinusitis (1) -Proctitis (1) -Epididymitis (1)	-Colitis (6) -Rash/Dermatitis (1) -Hepatitis/elevated liver enzymes (2) -Pancreatitis (2) -Sinusitis (1)
Discontinuation of ICI due to IA	1 patient	0 patients	3 patients

Table 1. Characteristics of ICI-IA patients broken down by ICI subtype.

	IA (N=12)	PMR (N=4)	SpA (N=3)	OA (N=11)
HAQ Domain: Dressing	0.36	0.75	0	0.36
HAQ Domain: Arising	0.73	1.25	0	0.73
HAQ Domain: Eating	0	0	0	0
HAQ Domain: Walking	0.82	1.5	0	0.82
HAQ Domain: Hygiene	0.82	1.5	0	0.82
HAQ Domain: Reach	0.73	1.5	0.33	0.73
HAQ Domain: Grip	0	0.5	0	0
HAQ Domain: Activities	0.82	1.5	0	0.82
Overall HAQ Score	0.58	1.03	0.04	0.52
Pain VAS (mm), Mean ± SD	43.3 ± 32.5	30.4 ± 31.6	71.3 ± 23.4	36.5 ± 32.5
PGA (mm), Mean ± SD	30.4 ± 31.6	24.8 ± 15.3	26.2 ± 21.9	20.5 ± 24.4

Table 2. The averages of each HAQ-DI domain for each subset of inflammatory arthritis, in addition to the means for pain VAS and PGA

Disclosure: J. Sarazin, None; **A. Impens**, None; **N. Abdulaziz**, None; **S. Anderson**, None; **L. Fecher**, None; **C. Lao**, None; **E. Schiopu**, Octapharma, 2.

Abstract Number: 1578

Rituximab Hypersensitivity in Rheumatic and Inflammatory Diseases: Role of Skin Testing

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SESSION INFORMATION

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Background/Purpose: Infusion-related reactions have been reported with rituximab, a monoclonal antibody targeting the CD20 antigen on B cells, and may result in discontinuation of the medication and/or changing to a potentially less effective alternative agent. A positive skin testing with a non- irritating dose of a medication is thought to predict an IgE mediated reaction which includes life-threatening anaphylaxis. Furthermore, rituximab skin testing in lymphoma patients may correlate with the severity of IgE hypersensitivity[1].

To our knowledge, there is no data establishing the value of rituximab skin testing in patients with rheumatological conditions who have a presumed IgE mediated hypersensitivity reaction. We present our observational analysis on

#	Diagnosis	Immunosuppresant Medications use at the time of skin testing	Severity of reaction and manifestations	Medications used to treat reaction	Skin testing Results: Positive/Negative
1	Granulomatous polyangitis	Prednisone 3mg daily	Mild: Hives and Skin rash	IV Decadron 10mg and Benadryl 25mg IV	Negative
2	Rheumatoid arthritis	None	Mild: Shortness of breath, tightness in throat and chest, and dizziness	IV Solumedrol and Benadryl 25mg IV	Negative
3	Rheumatoid arthritis	Leflunomide 20mg daily	Mild: Tightness in chest and shortness of breath	IV Decadron 10mg and Benadryl 25mg	Negative
4	Neuromyelitis optica	Methotrexate	Mild: Diffuse Skin rash	IV Solumedrol and Benadryl 25mg IV	Negative
5	Pemphigus Vulgaris	Prednisone 20mg daily	Mild: Shortness of breath	IV Solumedrol and Benadryl 25mg IV	Negative
6	Rheumatoid arthritis	Certolizumab pegol	Mild: Rash on scalp, shortness of breath	IV Solumedrol and Benadryl 25mg IV	Could not complete testing due to poor histamine response (control)
7	Rheumatoid arthritis	Certolizumab pegol	Severe: Shortness of breath and rash	IV Solumedrol and Benadryl 25mg IV and Intramuscular Epinephrine	Negative
8	Systemic Lupus Erythematosus	Prednisone 20mg daily	Severe: Shortness of breath, skin rash, throat tightness and abdominal pain	IV Solumedrol and Benadryl 25mg IV and Intramuscular Epinephrine	Positive

Table 1

skin testing results in rheumatology patients who previously developed presumed IgE hypersensitivity reactions to rituximab, and whether the skin testing results correlated to the severity of the clinical reaction.

Methods: We present the skin testing results from a retrospective review of 8 patients followed from January 2000 through September 2019 with systemic rheumatologic conditions who developed presumed IgE mediated hypersensitivity reactions while receiving rituximab. Patients previously underwent epi-cutaneous prick testing using rituximab at a concentration of 10 mg/mL. If negative testing resulted at 10mg/ml concentration (defined as a wheal diameter measured less than 3mm), testing proceeded to intradermal injections of 1:1000, 1:100, and 1:10 dilutions of the full strength. Testing was discontinued and defined as a positive with a wheal 3mm or greater than the histamine control. We defined a “mild” IgE mediated reaction as that involving one organ system which did not require epinephrine. A “severe” IgE reaction has two or more organ system involvement which required epinephrine administration.

Results: Regardless of background immunosuppressive agents, all patients except one mounted an appropriate histamine response. Patients 1-5 and 7 developed “mild” IgE reactions and had negative skin testing. Patient 8 had severe IgE reactions requiring epinephrine IM and on testing mounted a positive intradermal test. A summary of patient characteristics and skin testing results are provided in Table 1.

Conclusion: Rituximab skin testing has not been studied in patients with underlying rheumatic and inflammatory diseases. Our preliminary analysis demonstrates mild presumed IgE reactions can possibly predict negative skin testing. A negative test may then allow clinicians to have discussions with patients on the possibility of re-challenging the medication if no alternative medications are suitable. Additionally, our analysis demonstrates that patients are able to mount an adequate histamine response despite immunosuppression by their disease and current medications.

Further studies will be needed to evaluate the utility in the evaluation of skin testing in rheumatic and inflammatory conditions.

Disclosure: S. Penumarty, None; **J. Quintero Betancourt**, None; **E. Capitle**, None; **R. Khianey**, None.

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Assessing the Effect of Calcineurin Inhibitors for Immune-related Adverse Event Management on Tumor Response

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Background/Purpose: High grade immune-related adverse events (irAEs) to cancer immune checkpoint inhibitors (ICI) require considerable immunosuppression (IS) with high-dose steroids and steroid-sparing IS (SSIS) for steroid-dependent cases. T lymphocyte-specific IS has generally been avoided or used with significant caution due to the fear that these agents may negatively impact ICI efficacy. We sought to determine whether T cell-specific IS agents, such as calcineurin inhibitors (CNIs), have an adverse effect on tumor control when compared to primarily immunomodulatory drugs (IMDs) such as hydroxychloroquine and sulfasalazine..

Methods: We retrospectively analyzed clinical annotations of adult patients treated with ICIs for malignancy from 1/1/2000-12/31/2019, highlighting patients who were managed with SSIS, specifically those most commonly used for autoimmune disease therapy. Topical IS use was excluded. Patients were categorized as tumor responders or non-responders, and irAEs were graded according to National Cancer Institute's Common Terminology Criteria for Adverse Events (CTCAE). Progression-free survival (PFS) was assessed via Kaplan-Meier curve.

Results: 1331 unique individuals were prescribed > = 1 ICIs, with 526 prescribed systemic steroids (39.5%) and 90 (6.8%) patients prescribed SSIS agents (25 patients with > 1 SSIS): mycophenolate (39), methotrexate (26), leflunomide (5), azathioprine (3), rituximab (24), tocilizumab (3), infliximab (8), etanercept (1), adalimumab (1), golimumab (1) and CNIs (18): cyclosporine, tacrolimus. IMDs hydroxychloroquine (6) and sulfasalazine (5) were also prescribed. The objective response rate was 50.0% in the CNI group compared to 45.5% in the IMD cohort and 45.4% in the irAE group (CTCAE grade matched) with steroids alone without any SSIS. Median PFS was compared between CNI cohort (5.4 months, range 1.3-34 months) to IMD (1.1 months, range 0.4-6.4, p = 0.02) and steroid alone (2.4 months, range 0.69-17.7, p = 0.48). Multiple regression analysis identified irAE presence as an independent correlate to tumor response (p = 0.02).

Conclusion: T cell-specific IS should not be excluded from irAE treatment algorithm as we observed that PFS was comparable to immunomodulators and similar efficacy was observed compared to steroids alone. Rapid identification and management of irAEs can help mitigate morbidity but there are virtually no reliable clinical trials to guide irAE management with SSIS. These findings support the need for larger, prospective evaluation of immunosuppression use for high grade irAE therapy.

Factors associated with Tumor Response		
	Odds Ratio (95% confidence intervals)	p-value
Age at cancer diagnosis	0.06 (-0.08- 0.21)	0.41
Gender	2.89 (-2.16- 7.940185)	0.26
Race	-4.73 (-11.51- 2.04)	0.17
Tumor type	-0.09 (-0.65- 0.47)	0.74
ICI agent(s)	6.10 (-0.32- 12.52)	0.06
irAE development	-4.91 (-9.47- -0.34)	0.02*
IS agent	-3.02 (-7.33- 1.29)	0.17
Number of IS agents	0.23 (-3.54- 4.01)	0.90

Model Likelihood ratio 18.10 with p-value 0.0115
*Statistically significant at p<0.05
ICI: Immune checkpoint inhibitor
irAE: Immune-related adverse events
IS: Immunosuppressive

Disclosure: P. Reid, n/a, 9; **D. Olson**, None; **T. Gajewski**, None.

Abstract Number: 1580

Generalized Immune Activation in Structures Related to PMR or GCA on PET/CT Assessment Does Not Occur in Immune Checkpoint Inhibitor-Treated Patients Who Do Not Go on to Develop Rheumatic Immune-Related Adverse Events

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SESSION INFORMATION
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Background/Purpose: The pathogenesis of rheumatic immune-related adverse events (irAEs) from checkpoint inhibitor cancer immunotherapy directed against programmed cell death protein 1 (PD-1) and programmed death ligand 1 (PD-L1) remains unknown, even though they are a consequence of pharmacologic inhibition of a specific immune mechanism. Given that some irAEs resemble polymyalgia rheumatica (PMR) or giant cell arteritis (GCA), a disease whose pathogenesis is poorly understood, observations regarding the pathogenesis of PMR-like or GCA-like irAEs are of significant interest. One proposed pathogenic mechanism involves generalized immune activation leading to a spectrum of subclinical disease. Interrogation of this hypothesis may be aided by PET/CT, which is frequently utilized for oncological staging purposes but is also useful in classical PMR or GCA diagnosis. If PMR or GCA irAEs merely represent a spectrum of generalized immune activation, low-grade subclinical PMR or GCA-related changes on PET/CT might be expected to be seen in patients who receive immunotherapy, irrespective of whether they develop clinically evident rheumatic irAEs. This study investigated whether such changes occurred in patients receiving immunotherapy who did not develop clinically evident rheumatic irAEs.

Methods: Consecutive patients exposed to PD-1 or PD-L1 inhibitor immunotherapy at a single center had scintigraphic uptake calculated by a nuclear medicine physician experienced in assessment of vasculitis. Patients were included if they had had ^{18}F-fluorodeoxyglucose (^{18}F-FDG) PET/CT imaging both within the two weeks prior to immunotherapy initiation and after at least eleven weeks of immunotherapy. Patients who went on to develop a rheumatic irAE were excluded, as were patients with scintigraphic evidence of liver metastases owing to their potential influence on scoring of uptake. Quantification of ^{18}F-FDG uptake by maximum standardized uptake values (maximum standard unit value, SUV_{max}) was performed at sites relevant to PMR or GCA (17 sites relevant to PMR, 17 sites relevant to GCA) in paired scans, and the difference calculated.

Results: Twenty-four patients receiving nivolumab, pembrolizumab or avelumab met the inclusion criteria, primarily for melanoma, non-small cell lung cancer, or lymphoma. The mean age at the time of the first scan was 67, 71% were male, and 66% had a complete or partial oncological response at best response. No statistically or clinically significant difference in SUV_{max} was noted at any PMR or GCA-relevant anatomical site interrogated. Latent class analysis did not reveal clusters identifiable by cancer type, best response, or presence of combination therapy.

Conclusion: Patients treated with PD-1/PD-L1 inhibitors without clinically evident rheumatic irAEs do not develop subclinical PMR or GCA-like changes on PET/CT. This supports the proposition that PMR-like and GCA-like irAEs are a distinct entity with stochastic onset, and do not simply represent generalized immune activation induced by immunotherapy.

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Abstract Number: 1581

Neutrophil to Lymphocyte Ratio as a Predictor of Immune-Related Adverse Events in CTLA-4 Treated Patients: A Retrospective Review

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Background/Purpose: Immune checkpoint inhibitors (ICIs) target checkpoint proteins PD-1/PD-L1 and CTLA-4 to activate and enhance the cytotoxic effects of T lymphocytes against tumor cells [1-2]. This systemic effect disrupts immune homeostasis and can result in immune-related adverse events (irAEs) affecting a wide variety of organs, including rheumatic presentations. Interestingly, irAEs are also reflective of anti-tumor efficacy [3].

There are currently no biomarkers that predict impending irAEs. Several studies demonstrated an association between low neutrophil-to-lymphocyte ratio (NLR) and the risk of irAEs in patients treated with PD-1/PD-L1 blockade (Table 1). To date, the literature is limited on whether NLR may serve as a marker for irAEs in patients undergoing CTLA-4 blockade. As CTLA4 blockade affects a separate and distinct checkpoint pathway, we sought to understand the utility of NLR in this treatment group.

NLR cut off	OR	p value	Cancer Type	Immunotherapy	Reference
<3	2.2 (1.1-4.1)	0.018	NSCLC	Nivo > Pembro	[4]
>3	0.37 (0.17-0.81)	0.012	Lung CA, Melanoma, Lymphoma mainly	Pembro	[5]
<5	0.97 (0.39-2.39)	0.939	NSCLC	Nivo	[6]
<5	0.051(0.02–0.14)	<0.001	NSCLC	PD-1 (nivo, pembro, Toripalimab, Sintilimab)	[7]

Table 1. Previously published data on NLR and odds ratio for irAE. NLR cut off values to determine "low" vs. "high" were variable across the papers, as was cancer subtype.

Methods: Under IRB approval, we conducted a retrospective electronic medical record review of oncology patients treated with ipilimumab (anti-CTLA4) at UNC Chapel Hill from 1/2004 to 7/2017. NLR was calculated from CBCs prior to initiation of ICI and compared against irAE type and incidence using logistic regression models to obtain odds ratios adjusted for age, sex, and ICI therapy type.

	N=112	
Characteristics	n*	%*
Age, mean ± SD years (range = 17 to 81)	57.2	±13.0
Female	49	43.8
IPI only	40	35.7
IPI with NIVO	57	50.9
IPI with PEMBRO	15	13.4
ICI therapy varied		
N/L ratio, mean ± SD (range = 0.20 to 45.3)	4.61	±4.93
N/L ratio < 4 (lit)	60	53.6
N/L ratio < 5 (lit)	79	70.5
ln(N/L) ratio, mean ± SD (range = -1.63 to 3.81)	1.28	±0.67
irAE		
GI/HEP	49	43.8
DERM	43	38.4
ENDO	32	28.6
RHEUM/MSK	10	8.9
PULM	4	3.6
OPTHL	4	3.6
NEURO	5	4.5
RENAL	3	2.7
Count of organ systems presenting with irAEs		
0	31	27.7
1	34	30.4
2	26	23.2
3	20	17.9
4	1	0.9
At least 1 type of irAE	81	72.3
At least 2 types of irAEs	47	42.0
At least 3 types of irAEs	21	18.8

Table 2. Characteristics of study population. Stratified by ICI therapy, NLR ratio, organ system of irAE, count of organ systems presenting with irAEs, and number of irAE types

Risk Factor: NLR Cut Off	Unit of Comparison	Outcome: irAE	Adjusted OR (95% CI)	
NLR<4	NLR<4 vs NLR≥4	**Any irAE**	2.41 (1.02, 5.69)	
NLR<5	NLR<5 vs NLR≥5	**Any irAE**	4.42 (1.76, 11.1)	
		GI/HEP		
NLR<4	NLR<4 vs NLR≥4		1.00 (0.47, 2.13)	
NLR<5	NLR<5 vs NLR≥5		1.96 (0.83, 4.65)	
		DERM	Men	Women
NLR<4	NLR<4 vs NLR≥4		0.85 (0.31, 2.34)	4.40 (1.17, 16.6)
NLR<5	NLR<5 vs NLR≥5		0.99 (0.33, 2.98)	12.2 (1.40, 106)
		ENDO		
NLR<4	NLR<4 vs NLR≥4		1.25 (0.53, 2.92)	
NLR<5	NLR<5 vs NLR≥5		0.78 (0.32, 1.93)	
		RHEUM/MSK		
NLR<4	NLR<4 vs NLR≥4		1.33 (0.35, 5.07)	
NLR<5	NLR<5 vs NLR≥5		4.34 (0.52, 36.4)	

Table 3: Odds ratio for irAE based on NLR cut off (4 and 5) first with relation to the entire patient population and then stratified by organ system. Effect modification for the association between NLR and irAE incidence was assessed and reported if two-way interactions between NLR and age, sex, or ICI therapy were p<0.10. A statistically significant association between a low pre-ICI treatment NLR value and risk of irAE was found. This statistically significant effect is lost when stratifying by organ system. A strong estimate of association was observed between NLR<5 and rheum irAE, this estimate is notably imprecise.

Results: 112 patients received ipilimumab (35.7% monotherapy with 64.3% in combination with other ICIs) and irAEs occurred in 72.3% of patients (Table 2). Lower NLR was shown to be associated with an increased risk of irAEs of any severity in patients treated with ipilimumab (Table 3). When stratifying irAEs by organ system, there was no statistically significant effect found. Despite this, the data suggest an association of NLR< 5 with rheumatologic irAEs. In addition, we noted an association of low NLR with dermatologic irAEs among women. While an exploratory endpoint, this difference between women and men is an intriguing finding not previously reported.

Conclusion: Our data investigating low NLR as a predictor for irAEs in CTLA-4 treated patients shows a similar association to that reported with PD-1 blockade. Furthermore, the effect size in our population is similar to previously published data with PD-1 blockade [4-7], suggesting this effect is not unique to cancer type or ICI type. The statistical significance was lost when stratified by organ system, suggesting a lack of power. Also of note is the difference in effect size based on NLR cut off value. To date, there is no standard value. While the data suggests NLR may be a predictor for irAE, it also encourages further investigation into organ specific irAEs, sex differences, and setting a standard for NLR cut off.

Disclosure: M. Cunningham, None; **C. Alvarez**, None; **S. Saxena Beem**, None; **T. Schwartz**, None; **R. Ishizawar**, None.

Abstract Number: 1582

Average Follow-up Time After Telemedicine Visit Is Longer Than Conventional Face-to-Face Visit in Outpatient Rheumatology Practice During COVID-19 Pandemic

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Session Time: 9:00AM–11:00AM

Background/Purpose: In the era of recent COVID-19 crisis, outpatient rheumatology practices resorted to telemedicine to deliver longitudinal care, a fundamental component of chronic disease management. However, little is known regarding time to follow up after telemedicine visits as compared to conventional face-to-face encounters as a marker of longitudinal care.

Methods: We used electronic medical records (EMR) data from 1/1/2020 to 5/20/2020 to capture all encounters in the outpatient rheumatology practice. On March 12, when Rhode Island approved telemedicine visits as payable by insurers, telemedicine visits were captured in EMR like face-to-face visits. For both telemedicine and face-to-face visits, we captured data for patient demographics, date of visit, key diagnoses addressed at the visit identified by ICD-10 billing codes, complexity of visit based on CPT codes and scheduled follow-up in rheumatology clinic. The CPT codes for complexity of visit were 99201 to 99215 for initial and subsequent visits by either modality of care. CPT codes unique to telemedicine were transformed into their equivalent CPT codes from 99201 to 99215 based on their time factor.

Time to follow-up was calculated as the difference between scheduled follow-up and date of the current visit and expressed in days. We assessed the variation in time to follow-up by reporting mean with standard deviation across key rheumatic diagnoses and complexity of visits. Due to non-normality of the distribution of follow-up time, the Mann-Whitney U test was used to compare differences of follow-up time between face-to-face and telemedicine encounters across rheumatic diagnoses and complexity of visits.

Results: A total of 2,356 visits were completed by the rheumatology division between 1/1/2020 and 5/20/2020, of which 621 (26.4%) were via telemedicine. There was higher uptake of telemedicine amongst women and older patients. Telemedicine encounters were billed lower CPT codes as compared to face-to-face encounters (Table 1). The follow-rate between the 2 groups was similar (30.8% v. 32.4%). The time to follow-up was longer with telemedicine visits as compared to face-to-face visit (86.6 ± 52.1 v. 73.2 ± 45.6 days, $p < 0.01$). This was also noted for encounters with higher complexity billing codes (Table 2).

Conclusion: In the face of COVID-19 pandemic, the follow-rate after telemedicine was similar to that of face-to-face encounter with longer follow-up time with telemedicine across all complexities of visits. While the fear of COVID-19 pandemic may be reason for this observation, it also suggests that telemedicine could be a useful adjunct to face-to-face visits for longitudinal care of patients with rheumatic illnesses.

Table 1. Telemedicine uptake characteristics in outpatient Rheumatology clinic between January 1, 2020 and May 20, 2020 (N = 2,356 encounters).

Characteristic	Telemedicine Encounters		Face to Face Encounters	
	N	%	N	%
Overall	621		1,735	
*Age**				
<40	69	11.11	257	14.81
40-59	188	30.27	530	30.55
60-79	304	48.95	795	45.82
>=80	60	9.82	153	8.82
*Gender**				
Male	162	26.09	544	31.35
Female	459	73.91	1191	68.65
*Complexity of the visit**				
CPT99201	-	-	-	-
CPT99202	-	-	2	0.12
CPT99203	1	0.16	4	0.23
CPT99204	17	2.74	288	16.60
CPT99205	5	0.81	119	6.86
CPT99211	-		-	
CPT99212	86	13.85	10	0.58
CPT99213	326	52.50	482	27.78
CPT99214	154	24.80	734	42.31
CPT99215	34	5.48	87	5.01
Rheumatology-related diagnoses				
Inflammatory Polyarthritis	233	37.52	529	30.49
Crystal Arthritis	48	7.73	131	7.55
Osteoarthritis	149	23.99	471	27.15
Connective Tissue Diseases	101	16.26	259	14.93
Osteoporosis	47	7.57	102	5.88
Soft tissue rheumatism	14	2.25	63	3.63
Fibromyalgia and Chronic pain	72	11.59	240	13.83
Vasculitis	63	10.14	149	8.59
Follow-up scheduled or completed	191	30.8	562	32.4

* $p < 0.05$

Table 1. Telemedicine uptake characteristics in outpatient Rheumatology clinic between January 1, 2020 and May 20, 2020 (N = 2,356 encounters).

Table 2. Comparison of length of time to follow-up (in days) among face-to-face and telemedicine encounters in outpatient rheumatology clinic between January 1, 2020 and May 20, 2020

Diagnosis	Modality	CPT codes			
	Complexity of the follow-up encounter (Mean ± SD)				
		99213	99214	99215	Across All Complexities
Inflammatory Polyarthritis	F2F	79.3 (50.7)	78.8 (34.9)	50.3 (31.7)	73.7 (39.0)
	TM	89.5 (53.3)	64.3 (34.0)	51.2 (42.1)	77.3 (46.5)
Crystal Arthritis	F2F	109.7 (37.5)	69.5 (27.9)	69.5 (10.6)	69.0 (36.7)
	TM	112.4 (56.8)	93.3 (45.2)	NA	111.9 (53.3)
Osteoarthritis	F2F	81.8 (49.7)	74.0 (33.7)	46.2 (29.2)	68.5 (40.6)
	TM	98.8 (57.0)	87.4 (24.8)	63.8 (25.0)	89.1 (46.7)
Connective Tissue Diseases	F2F	84.6 (48.9)	79.7 (43.5)	49.2 (27.4)	71.0 (42.5)
	TM	88.8 (25.1)	74.8 (47.1)	45.3 (48.3)	75.2 (42.4)
Soft tissue rheumatism	F2F	100.2 (99.1)	88 (29.0)	NA	84.3 (60.0)
	TM	141 (60.8)	29 (38.2)	49 (NA)	77.8 (68.4)
Fibromyalgia and Chronic pain	F2F	93.1 (61.5)	87 (60.0)	92 (NA)	81.1 (55.2)
	TM	114.8 (41.1)	85.6 (37.5)	63 (NA)	95.8 (40.0)
Vasculitides	F2F	97.3 (26.7)	69.7 (32.4)	56.3 (31.0)	74.3 (33.7)
	TM	94.2 (26)	101 (31.9)	86.3 (29.1)	93.7 (33.6)
All Rheumatology Visits	F2F	86.9 (55.6)	79.2 (38.7)	49.0 (28.1)	73.2 (45.6)
	TM	96.1 (52.3)	82.5 (53.3)	61.5 (39.0)	86.6 (52.1)

Table 2. Comparison of length of time to follow-up (in days) among face-to-face and telemedicine encounters in outpatient rheumatology clinic between January 1, 2020 and May 20, 2020

Disclosure: D. Dalal, None; **T. Chu**, None; **B. Crough**, None; **J. Molino**, None; **D. Hemendinger**, None; **B. Ramratnam**, None.

Abstract Number: 1583

Impact of Telehealth Implementation on Practice Patterns and Electronic Health Record Utilization During COVID19

Mithu Maheswaranathan[1], Philip Chu[1], Andrew Johannemann[1], Megan Clowse[2], Lisa Criscione-Schreiber[3] and David Leverenz[1], [1]Duke University, Durham, NC, [2]Duke University, Chapel Hill, NC, [3]Duke University School of Medicine, Durham, NC

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Measures & Measurement of Healthcare Quality Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The COVID19 pandemic necessitated practice changes throughout health systems worldwide. Our academic rheumatology practice rapidly adopted telehealth (telephone or video visits), with unknown consequences regarding providers' time spent in the electronic health record (EHR) and ability to maintain patient care. We therefore analyzed changes in EHR utilization with telehealth implementation within our practice during COVID19.

Figure 1: Number of Rheumatology Visits as In-Person vs Telemedicine over Time, Pre/Post Telehealth Implementation

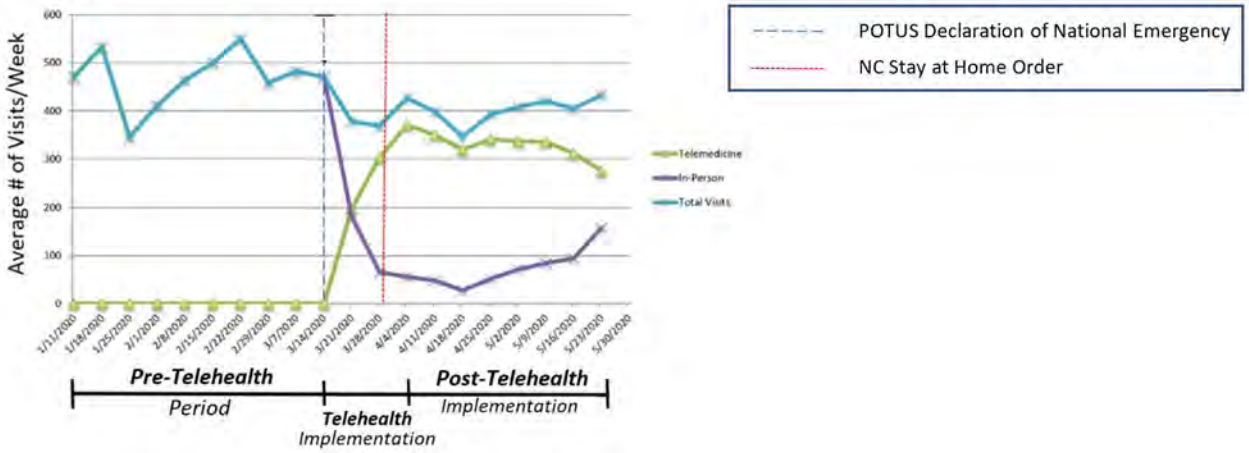
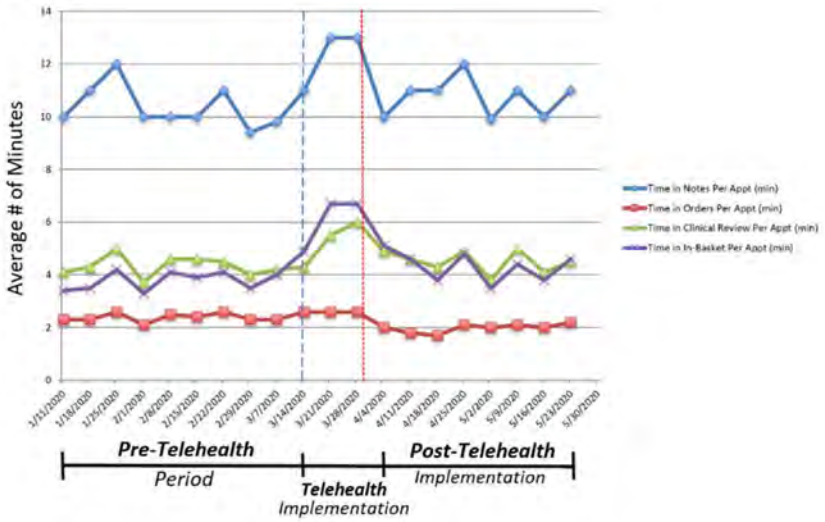


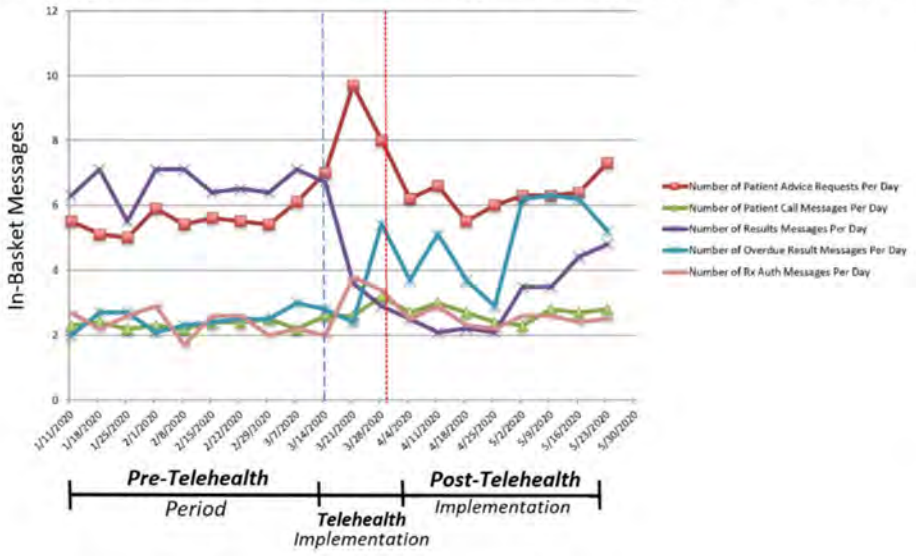
Figure 2: Average Time in the Electronic Health Record (EHR) per Appointment, Pre/Post Telehealth Implementation



Methods: Data were obtained using Slicer Dicer and Signal, analytic data tools in our EHR to evaluate practice patterns. We evaluated changes in the proportion of in-person versus telehealth visits, physician time spent per scheduled appointment in EHR activities (notes, orders, clinical review, and in-basket), and number of in-basket messages per day. Data were analyzed using descriptive statistics.

Results: In response to the COVID-19 pandemic and national emergency declared on March 13, 2020, our practice (28 providers) began transitioning to telehealth on March 15. During the Pre-Telehealth Period (Jan 5 - Mar 14), there was an average of 468 in-person visits/week and 0 telehealth visits. During the Telehealth Implementation Period (Mar 15 - Apr 4), the proportion of total visits completed via Telehealth expanded rapidly: 52% in Week 1, 82% in Week 2, and 87% in Week 3 (**Figure 1**). Post-Telehealth Implementation (Apr 4 - May 23), telehealth visits peaked at 92% (Apr 18) followed by a gradual decline to 63% (May 23). The average number of total visits per week in the Post-Telehealth Implementation Period was 400, a 15% decline compared with the Pre-Telehealth Period.

Figure 3: Average Number of In-Basket Messages Per Day, Pre/Post Telehealth Implementation



During the Telehealth Implementation Period, we observed increased average EHR time per appointment in notes, in-basket and clinical review while time in orders remained stable (**Figure 2**). The average number of in-basket messages/day for patient advice requests, prescription authorization requests, and overdue lab result messages all increased (**Figure 3**). During the Post-Telehealth Implementation Period, patient advice and prescription authorization requests approached Pre-Telehealth levels, with a delayed increase in overdue lab result messages/day (**Figure 3**).

Conclusion: During the COVID-19 pandemic, our practice's clinical volume only declined by 15% by rapidly shifting from all in-person visits to 87% of visits (>300/week) by Telehealth over 3 weeks. This transition required more time spent in multiple EHR activities and more in-basket requests (especially patient advice and prescription requests) during telehealth implementation. We hypothesize that this reflects increased time spent coordinating care, answering patient questions about COVID19, and refilling hydroxychloroquine and other DMARDs in advance of potential shortages. Subsequently, our overall EHR utilization returned near baseline, suggesting sustainability of this practice pattern. During telehealth implementation, we observed a decrease in result messages per day, highlighting the difficulty of obtaining medication toxicity monitoring and other laboratory testing during telehealth. We plan to continue monitoring this data with future shifts in practice.

Disclosure: M. Maheswaranathan, None; **P. Chu**, None; **A. Johannemann**, None; **M. Clowse**, UCB, 5, GSK, 2, 5, Astra Zeneca, 5, Pfizer, 2; **L. Criscione-Schreiber**, None; **D. Leverenz**, None.

Abstract Number: 1584

Telemedicine Visits During COVID-19 Improved Clinic Show Rates

Reem Alkilany[1] and Raymond Hong[2], [1]MetroHealth medical center, lakewood, OH, [2]Metrohealth Medical center, Richfield, OH

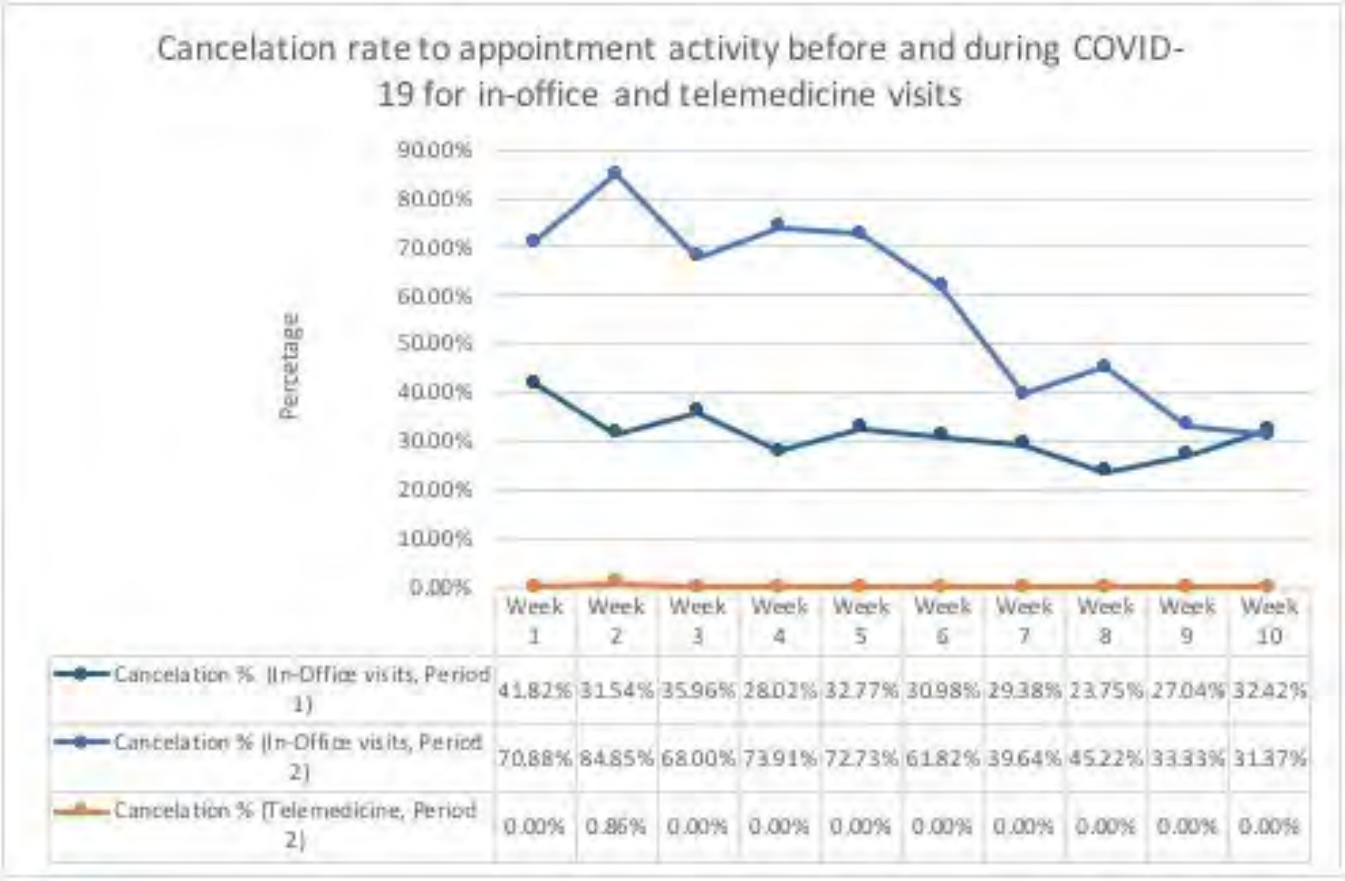
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The COVID-19 pandemic has tremendously affected the healthcare sector. State of Ohio officials recommended to hold in-person outpatient visits and elective procedures to limit virus spread. Many patients with chronic illnesses had reduced access to healthcare, this prompted the necessity to take active steps to continue delivering healthcare while ensuring safety for both patients and healthcare providers.

The MetroHealth System is an academic, public health care institution that services the population of Cuyahoga County in Cleveland, OH. Within 1 week of the State of Ohio issuing a statewide order limiting gatherings in March 2020, the Rheumatology outpatient clinics implemented telemedicine by video or telephone limiting in person visit sonly when deemed medically necessary. Anecdotally, Rheumatology providers reported improved clinic show rates with telemedicine visits, prompting this quality improvement project.

Our aim is to investigate and compare completed visit, no show, and cancellation rates between in-person and telemedicine appointments to see if telemedicine has a beneficial impact on access to Rheumatology ambulatory clinics

Methods: Using Reporting Workbench in our Epic electronic health record, we collected data retrospectively pertaining to rheumatology outpatient appointments at the MetroHealth System between Jan 3-May 31, 2020 - a 20-week period. Appointments were allocated into 3 categories: canceled; no-show; and completed. Data was segmented into in-person versus telemedicine, weekly stratified. figures 1-3.



	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10
Cancelation % (In-Office visits, Period 1)	41.82%	31.54%	35.96%	28.02%	32.77%	30.98%	29.38%	23.75%	27.04%	32.42%
Cancelation % (In-Office visits, Period 2)	70.88%	84.85%	68.00%	73.91%	72.73%	61.82%	39.64%	45.22%	33.33%	31.37%
Cancelation % (Telemedicine, Period 2)	0.00%	0.86%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%	0.00%

This graph illustrates overall cancelation rates: # canceled/ appointment activity (cancels + no shows + completed) - Period 1 is between Jan 3rd to Mar 15th, before the initial State of Ohio executive order responding to the COVID-19 pandemic - Period 2 is between Mar 16th - May 31st, immediately following the initial State of Ohio executive order responding to the COVID-19 pandemic

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10
Complete % per Clinic Activity (In-Office visits, Period 1)	73.96%	79.78%	80.70%	83.21%	80.67%	81.89%	82.30%	82.79%	86.21%	75.61%
Complete % per Clinic Activity (In-Office visits, Period 2)	50.79%	60.00%	68.75%	66.67%	66.67%	66.67%	82.09%	71.43%	75.71%	72.86%
Complete % per Clinic Activity (Telemedicine, Period 2)	91.67%	91.30%	85.98%	94.79%	99.01%	91.57%	90.00%	83.33%	94.12%	87.88%

This graph illustrates completed visit rate per on-schedule appointments: # completed visits/ on-schedule appointments (completed visits+ no show). - Period one is between Jan 3rd to Mar 15th, before the initial State of Ohio executive order responding to the COVID-19 pandemic - Period two is between Mar 16th - May 31st, immediately following the initial State of Ohio executive order responding to the COVID-19 pandemic

For analysis, the data was divided into two 10-week periods: period 1, the pre-COVID19 interval (Jan 3-Mar 15, 2020) and period 2, during COVID19 pandemic (Mar16-May 31, 2020). During period 1, the only modality was in-person visits, while during period 2 telemedicine started taking place in addition to in-person visits. Appointment Activity denoted the sum of cancellations, no shows, and completed visits. On-Schedule appointment totals summed no show and completed visits. Rates of cancelations, no shows, and completed visits were compared to Appointment Activity totals as well as On-Schedule totals.

Results: Telemedicine appointment cancellations were nearly zero (1 out of 825 telemedicine appointments offered) in the 10-week During COVID-19 period as compared to the pre-COVID-19 period where 527 appointments were cancelled, all in-person appointments. No shows also trended down in period 2 when there were 191 no shows (121 in-person and 70 telemedicine) versus 220 no shows in period 1 where only in-person visits were offered. This led to a slight increase in completed visits During COVID-19 when 1038 had a completed appointment (754 telemedicine and 284 in-person); whereas, pre-COVID-19 resulted in 930 completed in-person.

Conclusion: Barriers to accessing in-person healthcare because of transportation or other issues has been a challenge that might be conquered by telemedicine. The offering of telemedicine had seemingly favorable impacts on access to Rheumatology ambulatory clinics at our academic, public health system. We encourage examining the incorporation of telemedicine in our routine clinic visits to improve patient's appointment adherence.

	Week 1	Week 2	Week 3	Week 4	Week 5	Week 6	Week 7	Week 8	Week 9	Week 10
No Show% per Clinic Activity (In-Office visits, Period 1)	26.04%	20.22%	19.30%	16.79%	19.33%	18.11%	17.70%	17.21%	13.79%	24.39%
No Show% per Clinic Activity (In-Office visits, Period 2)	49.21%	40.00%	31.25%	33.33%	33.33%	33.33%	17.91%	28.57%	24.29%	27.14%
No Show% per Clinic Activity (Telemedicine, Period 2)	8.33%	8.70%	14.02%	5.21%	0.99%	8.43%	10.00%	16.67%	5.88%	12.12%

This graph illustrates no-show rate per on-schedule appointments: # no show/on-schedule appointments (completed+ no show) - Period 1 is between Jan 3rd to Mar 15th, before the initial State of Ohio executive order responding to the COVID-19 pandemic - Period two is between Mar 16th - May 31st, immediately following the initial State of Ohio executive order responding to the COVID-19 pandemic

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Disclosure: R. Alkilany, None; **R. Hong**, None.

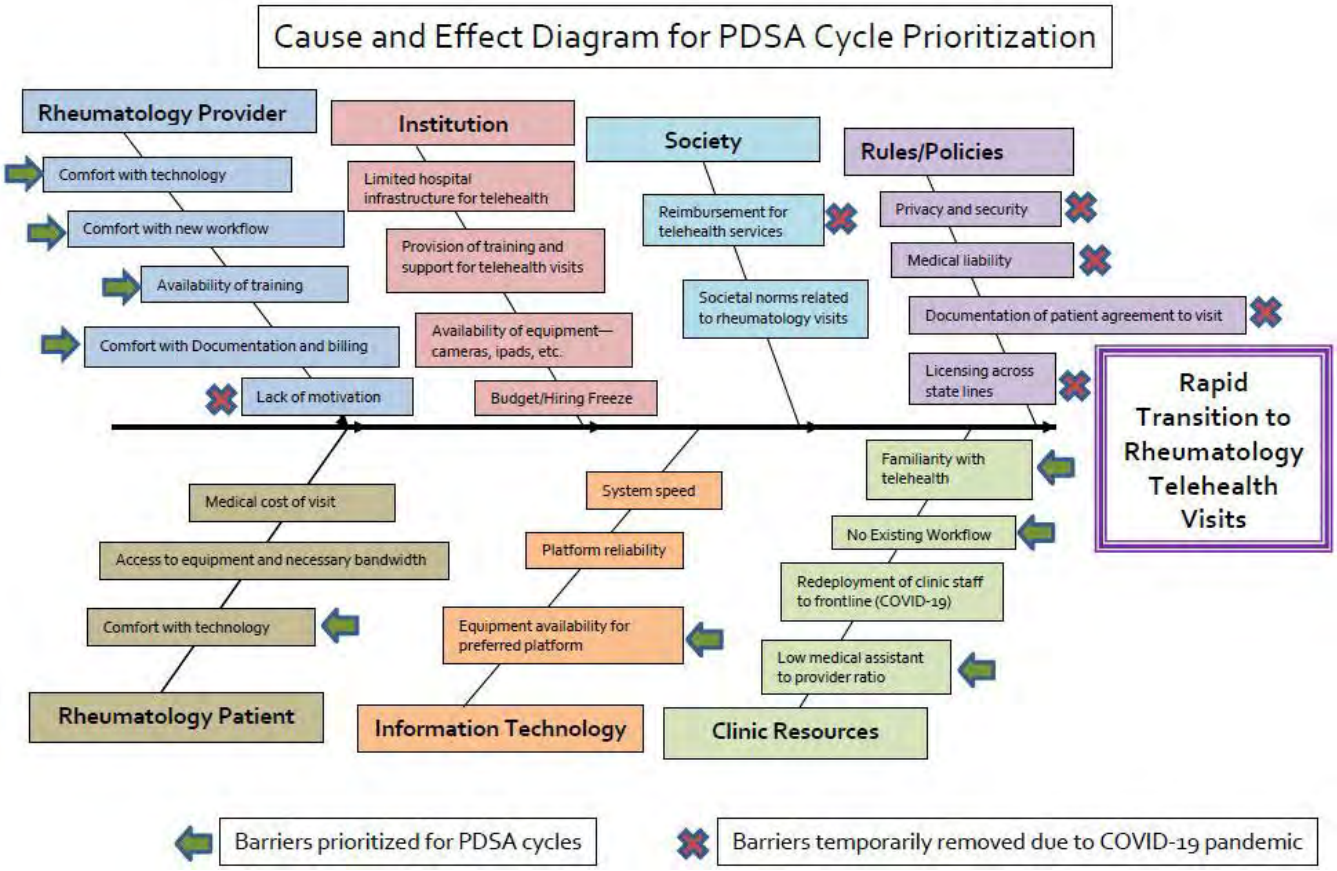
Abstract Number: 1585

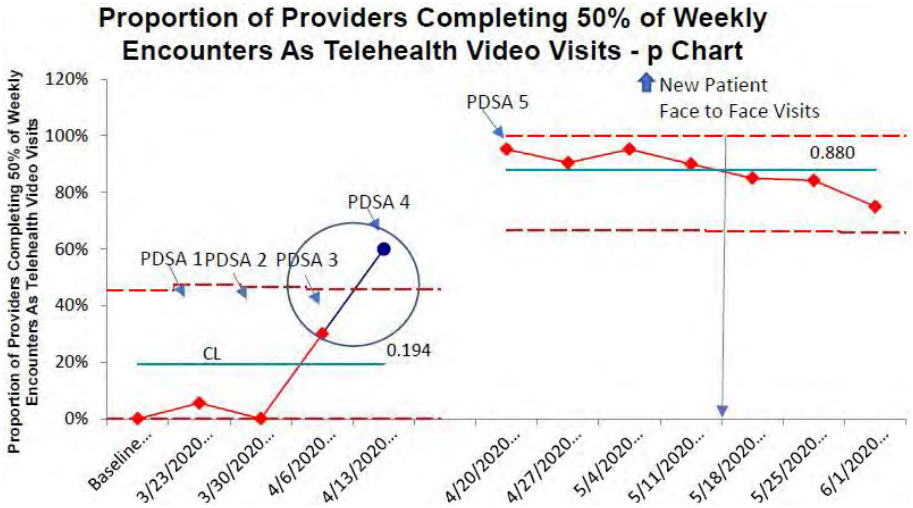
Lessons Learned Through Rapid Quality Improvement for Telehealth Implementation in an Academic Rheumatology Practice During the COVID-19 Pandemic

Julie Thomas[1], Dorota Lebiedz-Odrobina[1], Kyle Register[1], Francesca Ferrara[1], Danielle Barlow[1], Alicia Riddle[1] and Karla Miller[2], [1]University of Utah, Salt Lake City, UT, [2]Veterans Affairs Salt Lake City Health Care System, Salt Lake City, UT

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

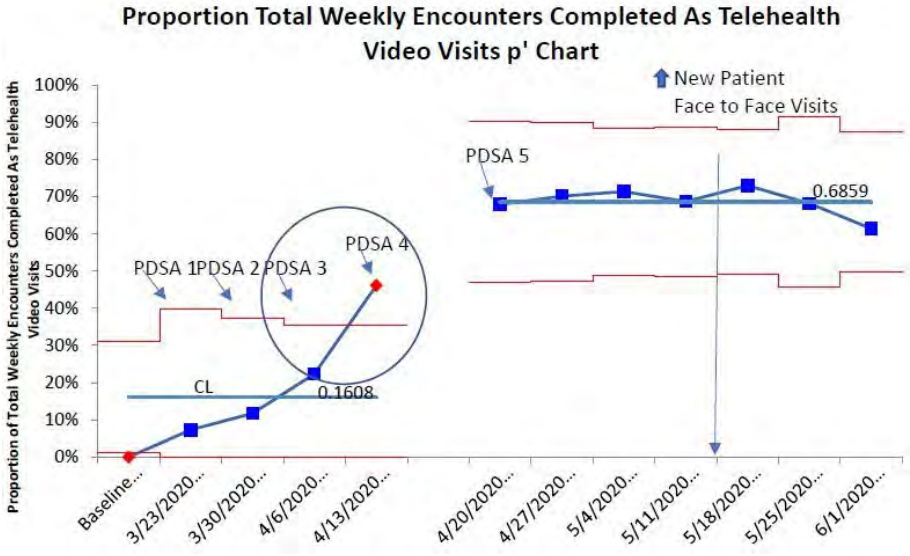
Background/Purpose: The COVID-19 pandemic created an urgent need for access to care while preserving patient safety through social distancing. Prior to the pandemic, patients were seen solely face to face for all visits in our aca-





demic practice, consisting of 17 rheumatologists and 5 advanced practice providers. We utilized quality improvement (QI) methods in rapid cycles to accelerate telehealth implementation and report our outcomes and lessons learned in this process to guide future telehealth efforts.

Methods: An inter-professional rheumatology telehealth team was established. We utilized the Define-Measure-Analyze-Improve-Control framework, Lean Six Sigma tools, and project charter to design this project. The primary impact measures were to increase the percentage of rheumatology providers utilizing [3]50% video for patient visits from 0 to 90% and to increase the percentage of video visits from 0 to 70% between 3/23/20 and 4/20/20. We aimed to



maintain the measures while social distancing policies remained in effect (6/1/2020). Balancing measures included provider patient satisfaction scores and visit volume. Baseline data were obtained between 1/7/20 and 3/13/20. We used a cause and effect diagram and voice of the customer (point-of care observations and provider survey) to prioritize Plan-Do-Study-Act (PDSA) cycles and statistical process control p-charts for primary impact measure analysis using QI macros for Microsoft Excel.

Results: Cause and effect analysis indicated provider, staff, and patient education and restructuring of clinic resources as high priority areas for PDSA cycles, while policy barriers were temporarily removed (Figure 1). Weekly PDSA cycles included telehealth education, live demonstration, pre-visit workflow development, simplification, and standardization, respectively. In the baseline period, no telehealth visits occurred, weekly visit average was 473, and patient satisfaction score was 95 of 99. We achieved 95% of providers conducting ≥ 50% of visits as video and 70% of total weekly visits conducted by video by week 5, with the greatest increase attributed to PDSA cycles 3 and 4 (Figures 2 and 3). Measures were maintained for three additional weeks before a slight decline after new patient face-to-face visits were added 5/15/20. Provider patient satisfaction scores remained stable and total rheumatology visit volume decreased by 60% in the first week followed by a steady increase to baseline with video visits as the primary visit type. Provider survey identified three major barriers to telehealth implementation: patient access/ability to use telehealth, interstate licensing, and clinic staff support.

Conclusion: The temporary removal of policy barriers and use of QI methods facilitated rapid and robust telehealth implementation in our academic practice in the face of a pandemic. This process identified the development, simplification, and standardization of pre-visit telehealth workflow as crucial factors for rapid and sustained success and allowed recovery of visit volume, while maintaining patient satisfaction and safety. Future efforts will focus on hybrid clinic workflows that can be rapidly scaled while addressing patient and provider barriers to telehealth.

Disclosure: J. Thomas, None; **D. Lebiedz-Odrobina**, None; **K. Register**, None; **F. Ferrara**, None; **D. Barlow**, None; **A. Riddle**, None; **K. Miller**, None.

Abstract Number: 1586

Rheum Service: Comprehensive Virtual Care During COVID-19

Stephanie Gottheil[1] and Joseph Carson[1], [1]London Rheumatology, London, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: During COVID-19, patients require timely access to rheumatologists while adhering to physical distancing guidelines. In this quality improvement project, we developed a comprehensive virtual pathway for rheumatology consults in a new community practice. We aimed to deliver a virtual experience, called "Rheum Service", which rivaled or exceeded traditional in-person care.

Methods: We used quality improvement methods to implement a virtual process with three phases: pre-visit, visit, and post-visit. In the pre-visit phase, we emailed appointment details and digital questionnaires to patients, and offered training for video-calls. In the visit phase, we enlisted multiple secure video platforms in case of technical difficulties. In the post-visit phase, we offered patients a digital consultation report and access to secure physician messaging.

Our outcome measures were the percentage of 1) consults using video-calling; 2) patients interested in future video appointments; and 3) video-visit diagnoses that changed after in-person visits. We collected data for all new consults between April 8 - June 11, 2020, and we emailed anonymized patient experience surveys one week after all video consults.

Results: Pre-visit, we scheduled 135 new patients in the 10 week study period; 119 (88%) by video, 15 (11%) by phone, and 1 (1%) by office visit. Twenty-one patients (16%) did not have a video-enabled device, 6 of whom borrowed a device. Prior to their appointment dates, 88% (119/135) of all patients completed questionnaires, and 10% (12/119) of the video cohort participated in video training.

We completed 98% (116/119) of scheduled video consults. During these visits, 6% (7/116) suffered technical difficulties, requiring a switch to phone or another video platform.

Post-visit, all patients with email (125/135, 93%) received a secure message containing a summary report. Of these patients, 38% (48/125) sent their rheumatologist at least one question through the secure messaging system. Our post-visit survey was completed by 38% (48/125) of patients, most of whom were satisfied with their virtual experience (Figure 1). When asked if they would like to have another appointment by video, 68% (32/48) said 'yes', 28% (13/48) were 'not sure', and 4% (2/48) declined. Within the study period, 38 patients had an in-person follow-up visit; 84% (32/38) maintained the same diagnosis from their video consult, while 16% (6/38) had a revised diagnosis.

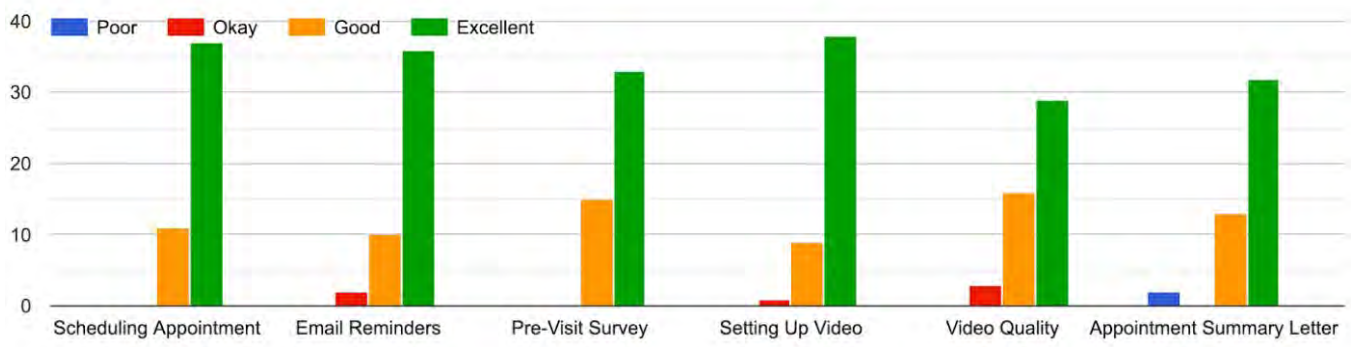


Figure 1. Patient Experience Survey Results (n = 48).

Conclusion: We delivered high quality virtual care to new rheumatology patients during the COVID-19 pandemic. Our interventions reduced barriers to video consults and increased communication through digital channels. We believe that more patients could benefit from virtual care by improving access to video-enabled devices and providing pre-visit training.

Disclosure: S. Gottheil, None; **J. Carson**, None.

Abstract Number: 1587

Improving Cardiovascular Risk Assessment in Patients with Rheumatoid Arthritis and Systemic Lupus Erythematosus in an Internal Medicine Resident Clinic: A Quality Improvement Initiative

Anna Falls[1], Peta-Gay Ricketts[1], Kelli Fox[1], Teresa George[1] and Chelsey Petz[1], [1]OhioHealth Riverside Methodist Hospital, Columbus, OH

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Cardiovascular disease is one of the leading causes of death in rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE) patients. Its risk in RA and SLE is comparable to that of diabetes. Observational studies show that RA patients frequently have unidentified and untreated risk factors due to gaps in screening. There are currently no guidelines in the United States on cardiovascular risk reduction for patients with autoimmune diseases. EULAR guidelines have suggested multiplying 10-year ACC/AHA atherosclerotic cardiovascular disease (ASCVD) risk scores by 1.5. A 2015 study by Ozen et al. found that screening for 10-year ASCVD risk scores of >5% led to increased detection of subclinical atherosclerosis. Our aim is to increase the rate of annual lipid screening in RA and SLE patients at our resident clinic. We also aim to increase the use of statin therapy in patients with 10-year ASCVD risk scores ≥5%.

Methods: Baseline data was established by reviewing electronic medical records (EMRs) of patients with SLE and RA in the internal medicine resident clinic. Two plan-do-study-act (PDSA) cycles were performed over a four-month period. First, we developed a custom EMR note template for the resident rheumatology clinic that prompted residents to review lipid screening, calculate 10-year ASCVD risk score, determine if patients were on appropriate statin therapy, and notify the patient's primary care provider as needed. We also provided resident education on ASCVD risk assessment and utilization of note template. Second, we adjusted the note template to prompt residents to notify clinic staff to schedule an office visit for cardiovascular risk assessment if indicated and provided additional resident education.

Results: We reviewed 79 patients in the pre-intervention period (73.4% RA, 20.3% SLE, 6.3% SLE and RA). Ninety-two percent of patients were ≥ 40 years old, 82% were female, and 41% had comorbid conditions of diabetes mellitus, coronary artery disease, or cerebrovascular accident. After PDSA cycle 2, 88 patients with similar baseline characteristics were reviewed. Rates of documented lipid screening (92.4% vs 93.2%, p = 0.846) and annual lipid screening (62.0% vs 60.2%, p = 0.812) did not show improvement. The proportion of patients with 10-year ASCVD risk scores ≥ 5% on statin therapy in the current population (33.3% vs 57.9%, p = 0.038) showed improvement; a subgroup analysis of the original 79 patients (33.3% vs 58.3%, p = 0.038) also showed improvement.

Conclusion: In our clinic, there was a statistically significant increase in the proportion of patients on statin therapy with 10-year ASCVD risk scores ≥5% in the current and baseline populations. The rate of yearly lipid screening remained unchanged despite the use of a custom EMR template. Future PDSA cycles will focus on improving the rate of annual lipid screening.

Disclosure: A. Falls, None; **P. Ricketts**, None; **K. Fox**, None; **T. George**, None; **C. Petz**, None.

Abstract Number: 1588

A Quality Improvement Project to Improve Bone Densitometry Ordering in Adult Patients on Chronic Glucocorticoids

Katherine Kaufman[1], Philip Chu[1], Mithu Maheswaranathan[1], Andrew Johannemann[1], D Ryan Anderson[1], Isaac Smith[1], Akrithi Udupa[1], Mary Buckley[1], Laura Cannon[1], Rachel Randell[1] and David Leverenz[1], [1]Duke University, DURHAM, NC

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The 2017 ACR guideline for glucocorticoid-induced osteoporosis (GIOP) recommends DXA testing in patients aged ≥40 years on chronic glucocorticoids. We performed a quality improvement project to measure and improve provider adherence to this guideline in an academic adult rheumatology practice.

Methods: This project was led by adult and pediatric rheumatology fellows at our institution as part of our annual quality improvement curriculum. Our primary aim was to increase the percentage of patients aged ≥40 on prednisone with a DXA scan in the last 2 years from 15% to 30%. A secondary measure was the percentage of visits containing prednisone orders in which a DXA scan was ordered. Additional analyses were performed by patient age, sex, and ordering provider. Data were obtained with Slicer Dicer, an analytic data tool within our electronic health record (EHR), and validated by manual review of charts over a two-week period in 10/2019. Data were analyzed using descriptive statistics. We conducted these cycles using Plan-Do-Study-Act (PDSA) methodology: (1) combined pediatric and

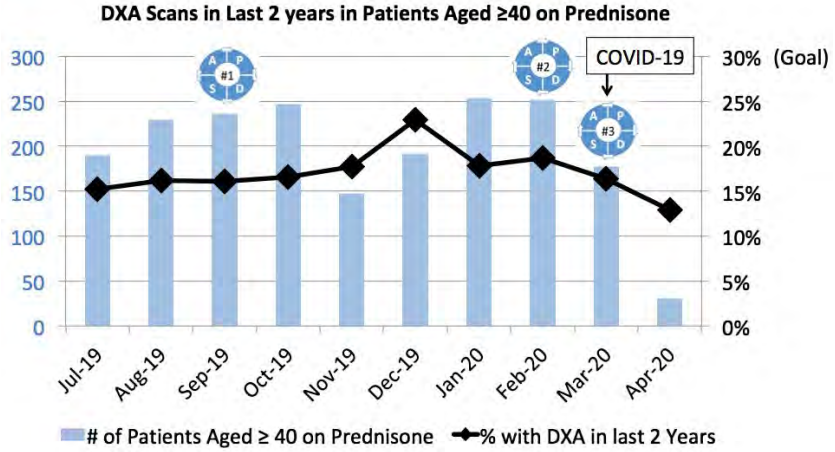


Figure 1. Percentage of patients with a DXA scan in the last 2 years (line) among patients aged ≥40 on prednisone seen in rheumatology clinic each month (bars).

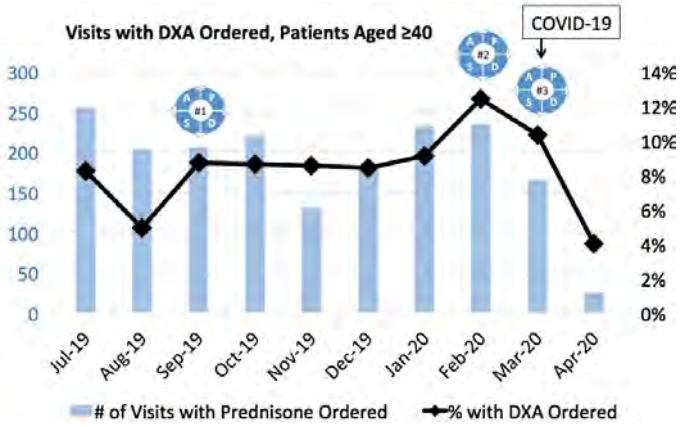


Figure 2. Percentage of visits with DXA scan ordered (line) among rheumatology visits with a prednisone order and patient aged ≥40 each month (bars).

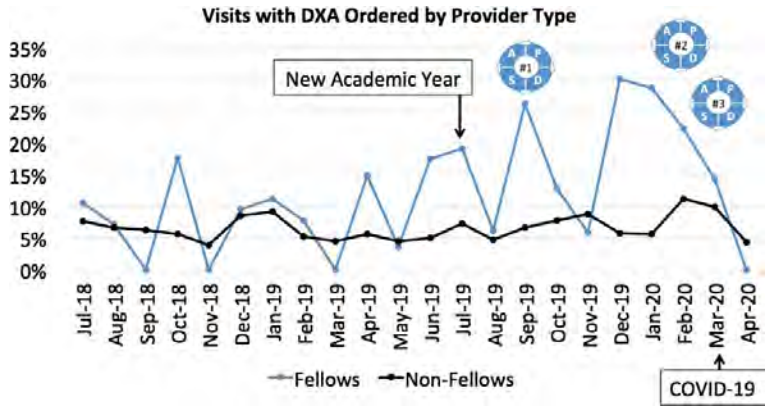


Figure 3. Percentage of visits with DXA scan ordered by provider type

adult rheumatology grand rounds describing the project, (2) presentation on GIOP by an endocrinology expert, and (3) data feedback on DXA scan ordering rates and distribution of EHR tools for easily identifying the last DXA scan.

Results: The percentage of patients aged ≥40 on prednisone with a DXA scan in the last 2 years increased from 15.2% among patients seen in 7/2019 to a maximum of 22.9% by 12/2019 after PDSA 1, was 18.7% after PDSA 2 in 2/2020, then declined despite PDSA 3 with onset of COVID19 (Figure 1). Among all patients seen from 7/1/19 – 4/30/20 (n = 1629), the highest percentage was in women aged ≥ 65 (31.6%, n = 443), followed by women aged 40 – 65 (18.2%, n = 752), men aged ≥ 65 (16.1%, n = 211), and men aged 40 – 65 (15.7%, n = 223).

The percentage of visits containing prednisone orders in which a DXA scan was ordered increased from 8.2% in 7/2019 to a maximum of 12.4% after PDSA 2 in 2/2020, then declined with onset of COVID19 (Figure 2). Among all visits with prednisone orders from 7/1/19 – 4/30/20, DXA scan ordering rates varied among 30 providers from 0.0% - 29.2% (IQR 4.3% - 18.4%). Compared with the 2018 – 2019 academic year, DXA scan ordering rates increased among fellows throughout the project (Figure 3).

The manual chart review included 93 patients and 82 visits. Chronic prednisone use (≥ 2.5mg daily for ≥ 3 months) occurred in 65.6% of patients and 59.6% of visits. The rest were on less prednisone or only took short courses. The manual chart review also demonstrated that our search for patients with a DXA scan in the last 2 years only identified scans done at our institution; 29% of all DXA scans occurred outside our institution.

Conclusion: We have not yet met our primary aim of increasing the percentage of patients aged ≥ 40 on prednisone with a DXA scan in the last 2 years from 15% to 30%; initial improvements were negated with onset of COVID19. However, we succeeded in validating a method for tracking this data over time, enabling ongoing efforts to improve adherence to the 2017 ACR GIOP guidelines. Furthermore, the large variability in DXA scan ordering rates and substantial improvement among fellows leading this project suggest that change is possible.

Disclosure: K. Kaufman, None; **P. Chu**, None; **M. Maheswaranathan**, None; **A. Johannemann**, None; **D. Anderson**, None; **I. Smith**, None; **A. Udupa**, None; **M. Buckley**, None; **L. Cannon**, None; **R. Randell**, Merck, 1, 2, Biogen Inc, 1; **D. Leverenz**, None.

Abstract Number: 1589

An Initiative to Improve Timely Glucocorticoid Tapering in Vasculitis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Vasculitis guidelines recommend scheduled glucocorticoid (GC) tapering to avoid toxicity. In an audit of 130 consecutive new patients on GC assessed in our tertiary Vasculitis Clinic (July 2017-October 2018), 33 (25%) were taking prednisone >10mg above target dose, based on GC initiation date. We aimed to increase the proportion of new patients taking appropriate GC doses to >90% by August 2019.

Methods: Interventions were (1) triaging patients on prednisone >20 mg to be seen in < 2 months (2) "fax- back" tapering suggestions based on current ANCA-associated vasculitis (AAV) and large vessel vasculitis (LVV) recommendations, sent to all physicians referring patients on GC. For the first several months, referring physicians' offices were contacted 1-2 weeks following the "fax-back" to determine if physicians had seen the suggestions. The primary outcome was the proportion of patients taking "appropriate" GC (< or =10 mg above target prednisone dose) at first visit, measured through interrupted time series. Other measures included clinic wait times, the proportion of patients starting to taper GC, and disease flares during tapering.

Results: Following physician triaging (December 2018), mean wait times for new patients on GC decreased from 81 days (95% CI 70-92) in the preceding 6 months to 64 days (95%CI 57-70). After introduction of "fax-back" in February 2019, only 29% of referring physicians were personally seeing the GC tapering suggestions. Following iterative modifications to the "fax-back" format, this increased to 73% by May 2019. Among patients referred for AAV/LVV, comparing pre-intervention (July 2017-January 2019) to post-intervention (February-October 2019) periods, the proportion of patients who had started to taper GC by their first visit increased from 71% (95%CI 62-78; n=83/117) to 94% (95%CI 84-98; n=49/52), and mean prednisone dose at first visit decreased from 30 mg (95%CI 27-33) to 22 mg (95%CI 18-26). Among non-AAV/LVV referrals, GC tapering trajectories did not change during the same periods. The proportion of patients ultimately taking "appropriate" GC doses at their first visit, overall and among the AAV/

Table: GC tapering trajectories among patients referred to the Vasculitis Clinic, before and after a "fax-back" intervention with tapering suggestions for AAV and LVV

Referral population	AAV and LVV		All other vasculitis	
Time period	Pre-intervention (Jul/17-Jan/19) n=117	Post-intervention (Feb/19-Oct/19) n=52	Pre-intervention (Jul/17-Jan/19) n=55	Post-intervention (Feb/19-Oct/19) n=22
Prednisone start dose, mg/day (95% CI)	52.1 (49-55)	52.7 (48-57)	50.2 (45-55)	45.5 (36-55)
Proportion who started tapering GC n(%) (95% CI)	**83 (71%) (62-78)[a]**	**49 (94%) (84-98)[a]**	44 (80%) (68-88)	17 (77%) (57-90)
Prednisone dose at first visit, mean mg/day (95% CI)	**29.9 (27-33)[b]**	**21.7 (18-26)[b]**	24.4 (20-29)	23.6 (17-31)
Proportion of patients taking target GC dose n(%) (95% CI)	84 (72%) (63-79)	40 (77%) (64-86)	48 (87%) (76-94)	20 (91%) (72-97)
Potential/definite vasculitis flares n(%) (95% CI)	11 (9%) (5-16)	7 (13%) (7-25)	7 (13%) (6-24)	5 (23%) (10-43)

a,b pairs designate significant difference ($p<0.05$)
GC, glucocorticoid; CI, Confidence Interval; AAV, ANCA-associated vasculitis; LVV, Large Vessel Vasculitis

LVV subset, did not significantly increase after the interventions. Potential/definite disease flares during tapering were similar before and after the "fax-back" intervention.

Conclusion: In this novel "GC stewardship" initiative to limit avoidable harm in vasculitis, we decreased wait times among GC-users. After introducing "fax-back" tapering suggestions, we observed increased tapering and lower GC doses at first visit among patients referred for AAV/LVV. Alternative knowledge dissemination strategies are needed to further improve timely GC tapering in vasculitis.

Disclosure: A. Mendel, None; **D. Ennis**, None; **S. Lake**, None; **S. Carette**, None; **C. Pagnoux**, Chemocentryx, 1, GlaxoSmithKline, 1, 2, 3, Sanofi, 1, Hoffman-LaRoche, 1, 2, 3.

Abstract Number: 1590

Bone Health in ANCA - Associated Vasculitis Patients

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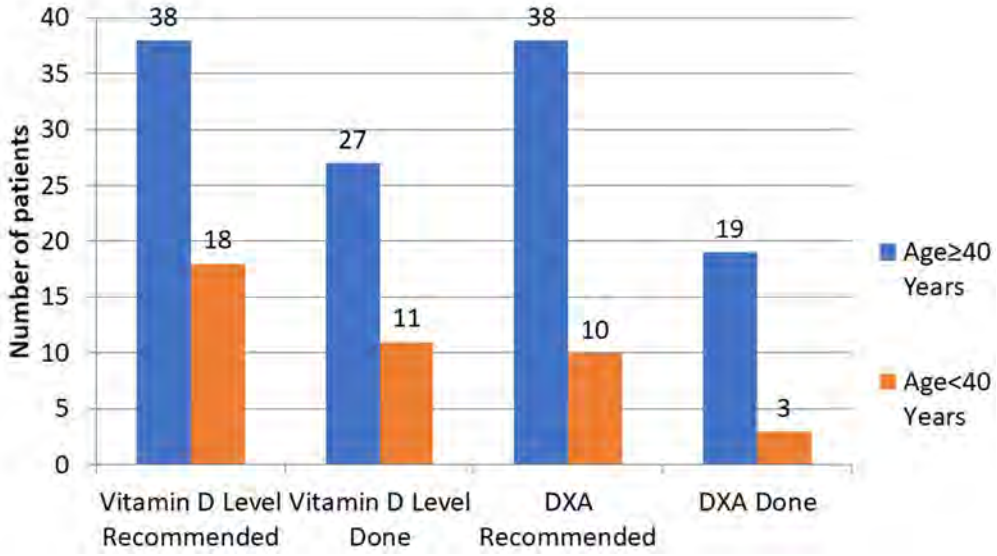
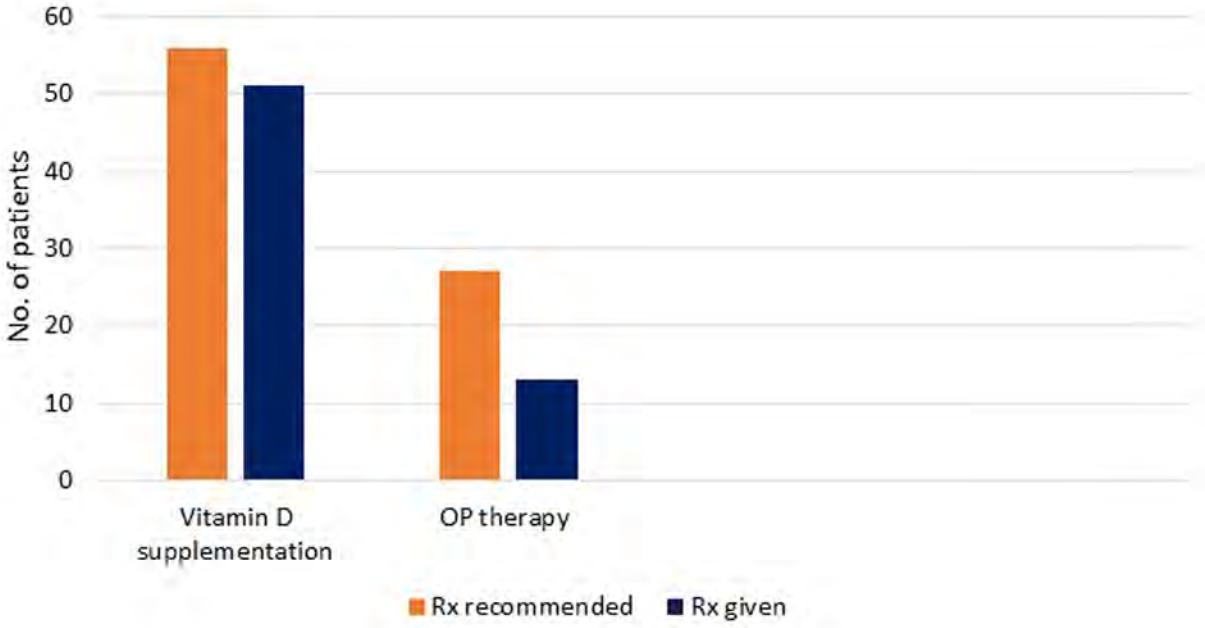
SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Graph 1



Graph 2



Background/Purpose: Glucocorticoids (GC) are an important mode of therapy in ANCA associated vasculitis (AAV), and osteoporosis (OP) and fractures are potential adverse effects seen. The revised 2017 Glucocorticoid-induced osteoporosis guidelines by the American College of Rheumatology (ACR) categorizes patients into low, moderate and high fracture risk groups and provides recommendations. Our aim was to analyze the implementation of the guideline in AAV patients. This was a quality improvement (QI) initiative to identify potential targets for improving practice.

Comparison of tests done in patient groups (Table 1)

	Age≥40 Years n=38	Age<40 Years n=18	Fisher's Exact Test p-value
Vit D Level ordered	71% (27)	61% (11)	0.545
DXA ordered	50% (19)	30% (3)	0.307

Methods: Patients with vasculitis (AAV) were identified in 2 academic centers by generating an electronic medical record query during the period of 2012-2019. Patients with inadequate information at baseline and follow up, steroid use of < 3 months and steroid naive patients were excluded. 56 patients were included in the study. Demographics, OP risk factors, duration and dose of GC, bone mineral density (BMD) results were collected. Guideline adherence was assessed by analyzing the following: obtaining baseline DXA, testing of vitamin D levels, calcium and vitamin D supplementation and initiation of OP therapy. Fisher's exact test was used to determine if proportional differences existed in tests ordered between patients ≥ and < 40 yrs

Results: The mean age of the patients was 52.16 yrs (range 16 - 84 yrs) with 67.8 % (n=38) being females. Majority (n= 31, 59.6%) were on steroids for > 1 yr; with minimum duration of 3 months and minimum initial dose of 5 mg. Six (11.5%) had prior OP fracture. Though DXA is recommended in all patients ≥ 40 yrs, only 50% (n=19) had BMD tested (graph 1). 50 % (n=10) had OP and 64.7% were treated with bisphosphonates, 20% by denosumab and 10% by teriparatide. No prior OP fracture was seen in patients < 40 yrs. 56% (n= 10) met criteria based on OP risk factors for BMD testing at baseline and only 30% (n=3) were tested (graph 1). 43.7% also met BMD screening criteria based on cumulative steroid dose, however none of them underwent testing. There was no significant difference in ordering of DXA tests between the 2 age groups (p=0.307, table 1). 92.3% were advised calcium and vitamin D supplementation, however only 67.8 % had the levels checked (see graph 1) and there was no statistically significant difference in ordering of Vitamin D levels between the age groups (Table1). 69.2% of patients were in high and moderate fracture risk group that met criteria for OP therapy and only 33.3% received pharmacologic therapy (see graph 2). Patients < 40 yrs on continued GC dose of ≥ 7.5mg/day for > 6 months have moderate fracture risk based on BMD (z score < 3, rapid bone loss >10%). Due to inadequate BMD testing in patients < 40 yrs, risk stratification for pharmacologic therapy could not be done.

Conclusion: GIOP is a potentially reversible condition. In the study however, adherence to the guideline was inadequate in regards to ordering baseline DXA, checking vitamin D levels and starting OP therapy in high and moderate risk patients, especially in patients < 40 yrs. Hence this project identifies a potential QI initiative that can be implemented to improve the above practice methods in patients treated with long term steroids for many rheumatological conditions not just limited to vasculitis.

Disclosure: D. Ragesh Panikkath, None; **S. Lee**, None; **C. Downey**, None.

Abstract Number: 1591

A Quality Improvement Project to Increase Vitamin D Prescribing for Pediatric Patients on Glucocorticoids

Katherine Kaufman[1], Mary Buckley[1], Laura Cannon[1], Rachel Randell[1], Philip Chu[1], Mithu Maheswaranathan[1], Andrew Johannemann[1], D Ryan Anderson[1], Isaac Smith[1], Akrithi Udupa[1] and David Leverenz[1], [1]Duke University, DURHAM, NC

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Chronic glucocorticoid treatment in children increases the risk of bone loss, fractures, and reduced adult skeletal mass. The 2017 ACR Glucocorticoid-Induced Osteoporosis (GIOP) guidelines recommend optimizing vitamin D intake to mitigate these risks. We performed a quality improvement project to measure and improve provider adherence to this guideline in an academic pediatric rheumatology clinic.

Methods: This project was led by pediatric and adult rheumatology fellows at our institution as part of our annual quality improvement curriculum. Our primary aim was to increase the percentage of pediatric patients treated with glucocorticoids prescribed a vitamin D supplement from less than 30% to 50%. A secondary measure was the percentage of patients on glucocorticoids with a vitamin D level checked in the preceding year. Using Plan-Do-Study-Act (PDSA) methodology, we conducted these cycles: (1) a combined pediatric and adult rheumatology divisional grand rounds describing the project, (2) a pediatric rheumatology conference focused on discussion of the project, and (3) a presentation on bone health by a pediatric endocrinologist. Data were obtained using Slicer Dicer, an analytic data tool available within our electronic health record (EPIC). Data were validated at baseline by manual chart review of all patients taking glucocorticoids

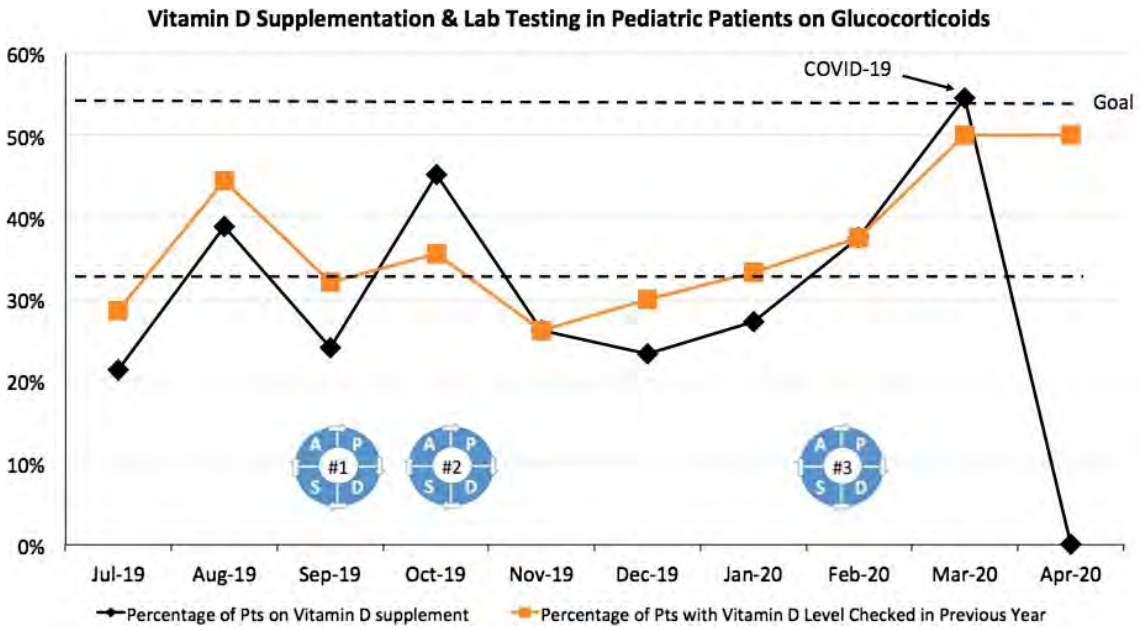


Figure 1. Run chart for vitamin D supplementation (black) and vitamin D levels checked (orange) by month in pediatric patients on glucocorticoids. The PDSA cycles are as follows: 9/17/2019- Combined Adult and Pediatric Rheumatology QI Introductory Grand Rounds; 10/3/2019- Pediatric Divisional QI Introduction; 2/6/2020- Pediatric Endocrinology Bone Health Educational Lecture. Our academic center started seeing an impact from the COVID-19 infection in mid-March 2020.

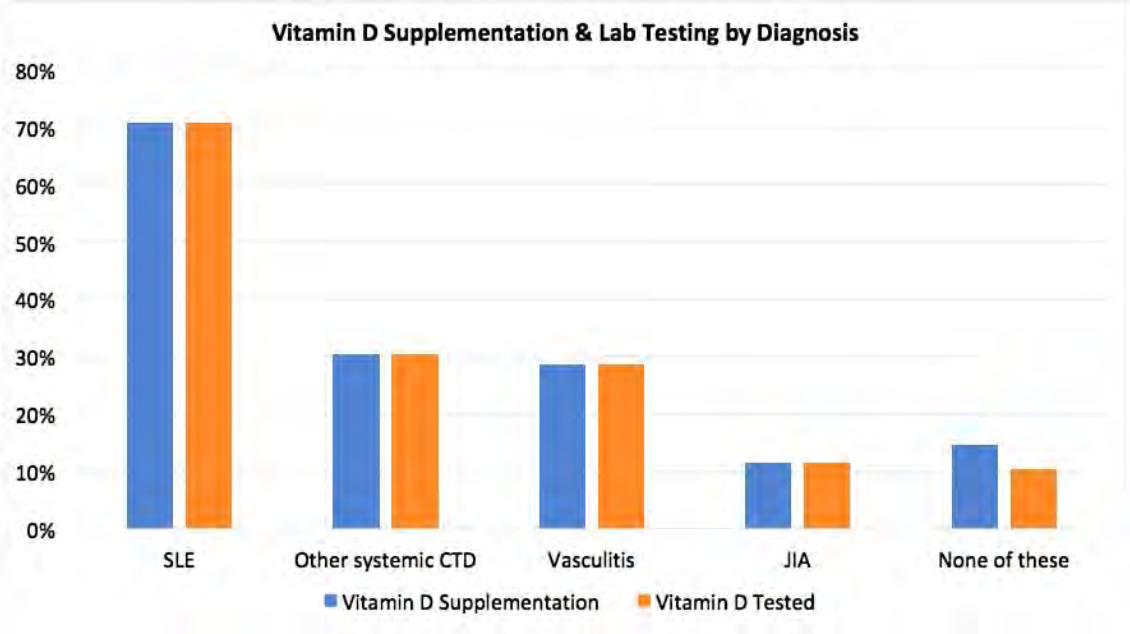


Figure 2. The percentage of patients on glucocorticoids who have an active prescription for a vitamin D supplement (blue) and who have had a vitamin D level checked in the preceding year (orange) by diagnosis. Other CTDs = JDM, localized scleroderma, SS, SSc, UCTD.

in pediatric rheumatology clinic in October 2019. Additional analyses were performed based on rheumatologic diagnosis (defined by ICD-10 codes) and age. Data were analyzed using descriptive statistics.

Results: The Slicer Dicer search at baseline in July 2019 revealed that 21.4% of patients on glucocorticoids were prescribed a vitamin D supplement, and 28.6% had a vitamin D level checked in the preceding year. By March 2020, vitamin D supplementation increased to 54.5% (Figure 1), and the percentage of patients with a vitamin D level checked increased to 50%. The largest rise in vitamin D prescriptions occurred following PDSA cycle 3.

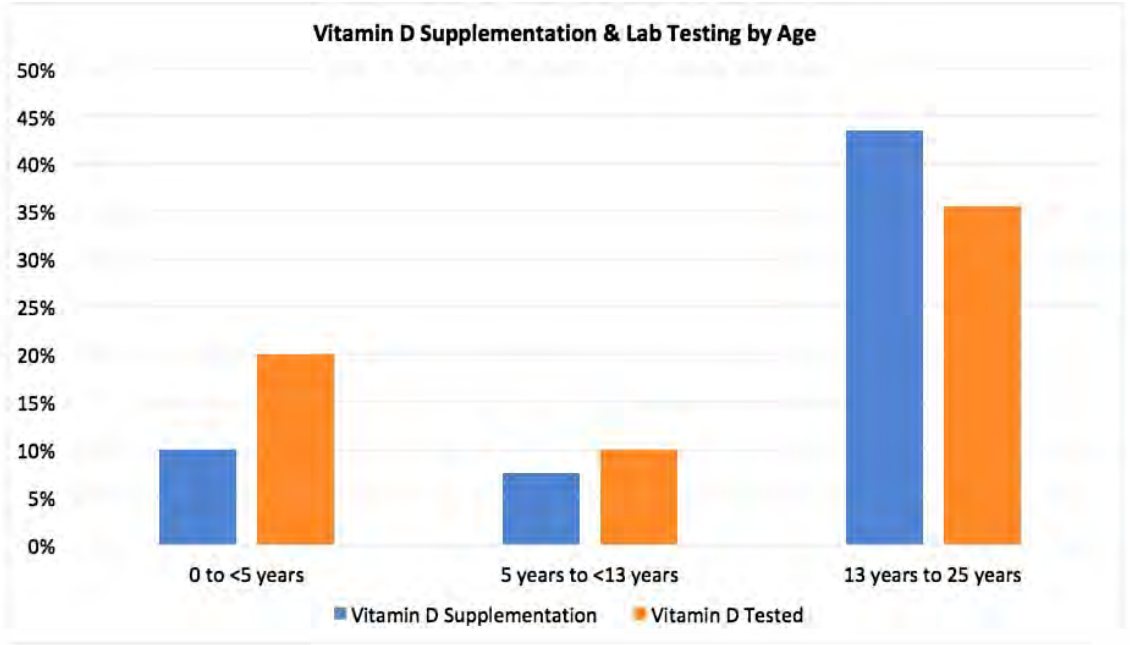


Figure 3. The percentage of patients on glucocorticoids who have an active prescription for a vitamin D supplement (blue) and who have had a vitamin D level checked in the preceding year (orange) by age. Other CTDs = JDM, localized scleroderma, SS, SSc, UCTD.

Throughout the project, vitamin D supplementation in patients with SLE was 70.6% (n=34), other connective tissue diseases 30.4% (n=23), vasculitis 28.6% (n=7), and JIA 11.5% (n=26) (Figure 2). When stratifying by age, vitamin D supplementation was 10% in patients < 5 (n=10), 7.5% in patients 5 to 13 (n=40), and 43.4% in patients ≥13 (n=83) (Figure 3). Rates of vitamin D levels checked were similar to vitamin D supplementation rates in each group.

Manual review of 31 patient charts in October 2019 revealed that 69% were prescribed glucocorticoids for >3 months. Of the patients prescribed chronic glucocorticoids, 45% had an active vitamin D prescription, and 37.5% had a preceding vitamin D level. Analysis by Slicer Dicer found that 45% were prescribed vitamin D and 35.5% had a preceding vitamin D level in October 2019.

Conclusion: We met our aim of increasing the percentage pediatric rheumatology patients on glucocorticoids taking vitamin D supplementation from 30% to 50%. The largest rise occurred after education from pediatric endocrinology. The highest levels of vitamin D supplementation were seen in patients with SLE and patients aged 13 to 25. Future interventions could focus on other diagnoses and age groups.

Disclosure: K. Kaufman, None; **M. Buckley**, None; **L. Cannon**, None; **R. Randell**, Merck, 1, 2, Biogen Inc, 1; **P. Chu**, None; **M. Maheswaranathan**, None; **A. Johannemann**, None; **D. Anderson**, None; **I. Smith**, None; **A. Udupa**, None; **D. Leverenz**, None.

Abstract Number: 1592

Improving Documentation of Smoking Cessation Counseling Among Spondyloarthropathy Smokers

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SESSION INFORMATION
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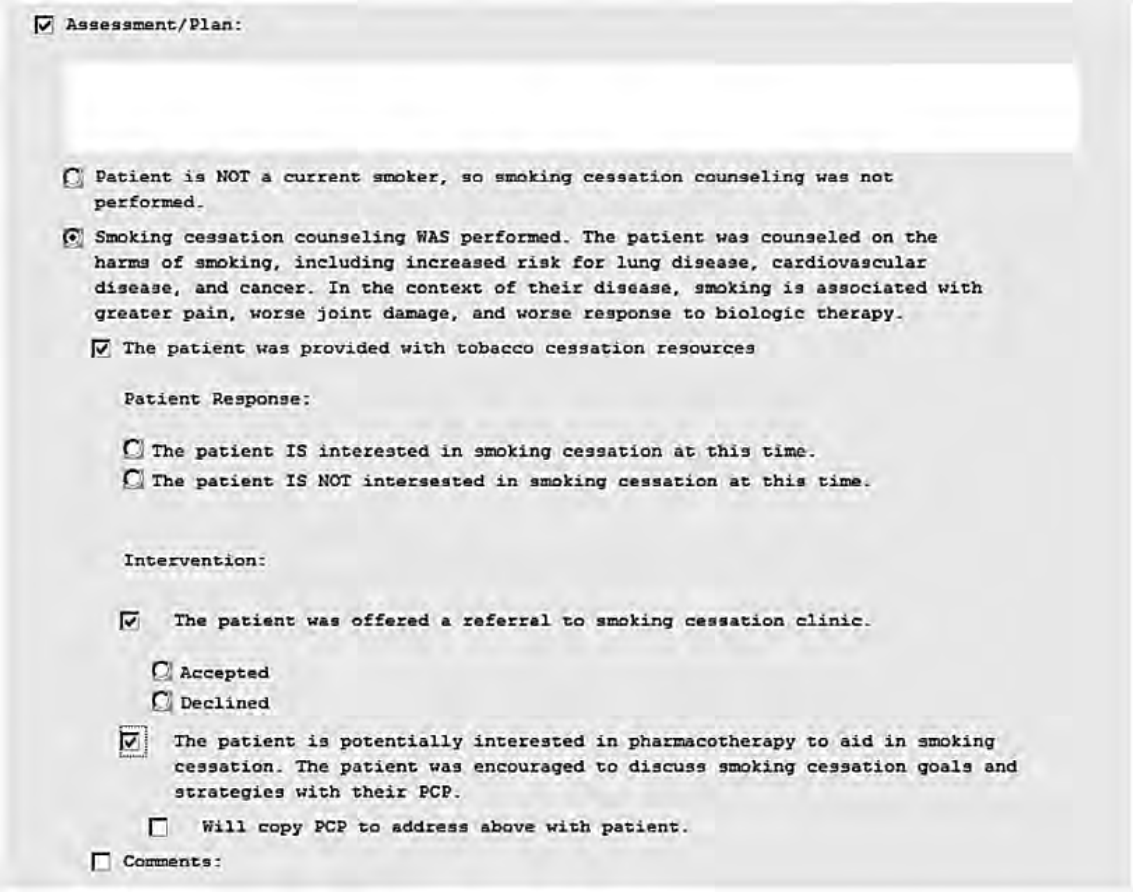
Background/Purpose: Smoking is prevalent among patients with spondyloarthropathies (SpA) and is associated with higher disease activity, poorer quality of life, and dampened response to biologic therapy. Despite the strong recommendation for smoking cessation in the 2018 American College of Rheumatology guidelines for management of psoriatic arthritis, providers do not routinely counsel smokers in the context of their disease (SpA). The goal of this quality improvement project was to improve documentation of smoking cessation counseling for SpA smokers at a busy Veteran Affairs (VA) Medical Center rheumatology clinic. The VA is an ideal setting to conduct this project since robust, evidence-based tobacco cessation modalities can be integrated into primary and specialty clinic care settings.

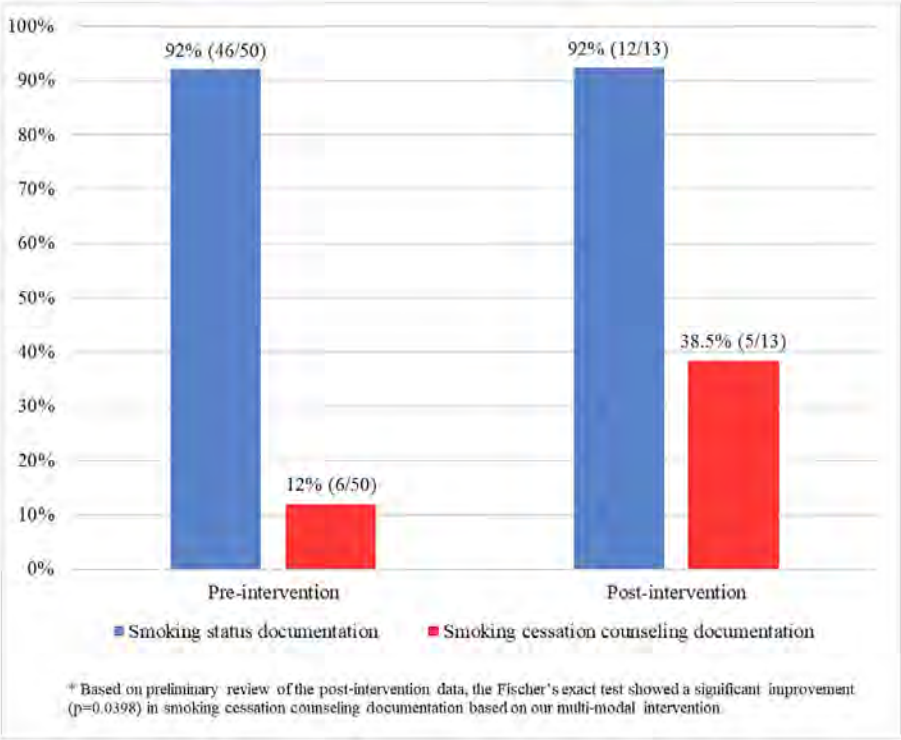
Methods: Baseline documentation rates of smoking status and smoking cessation counseling were obtained via chart review of patients diagnosed with ankylosing spondylitis, inflammatory bowel disease (IBD)-associated arthritis, and psoriatic arthritis who were current smokers seen for follow-up (8/2017-6/2018). We implemented a four step multi-modal intervention that included: a) a modified clinic note template (effective 1/2020) with specific prompts to address tobacco use (Figure 1), b) educating providers and nurses regarding the importance of counseling and template adherence, c) introducing a paper slip on top of intake documents to remind providers to inquire about smoking,



and d) equipping the clinic with brochures on cessation resources. Preliminary post-intervention data from follow-up visits were collected until the novel coronavirus disease 2019 (COVID-19) outbreak altered clinic workflow (1/2020-3/2020). Differences in documentation rates pre- and post-intervention were analyzed using Fischer's exact test.

Results: In the pre-intervention phase, 50 smokers were identified among 498 SpA patients, indicating a 10% baseline smoking rate. Rheumatologists documented smoking status for 92% of smokers and smoking cessation counseling for 12% of smokers. In the early post-intervention phase, we identified 13 smokers (15%) among 87 SpA patients. Utilization of the modified clinic note template was 30% (26/87). With our multi-modal intervention, the smoking status documentation rate remained at 92%, while the counseling documentation rate increased to 38.5% (Figure 2).

Conclusion: The baseline documentation rate of smoking cessation counseling for SpA smokers is low among rheumatology providers. Because of the COVID-19 outbreak, reduced outpatient volumes and unanticipated changes in clinic workflow have imposed limitations on post-intervention data collection. Nevertheless, our preliminary data suggest that a multi-modal intervention can improve documentation of smoking cessation counseling; this improvement may be sustainable with continued staff education on counseling and consistent template use. Our next steps will involve evaluation of receipt of smoking counseling and further reduction in smoking rates.



Disclosure: Y. Chao, None; **J. Hutto**, None; **E. Joerns**, None; **R. Arora**, None; **U. Makris**, None; **S. Reddy**, None.

Abstract Number: 1593

Adherence to Weight-Based Dosing Guidelines in Patients Receiving Hydroxychloroquine for Rheumatoid Arthritis and Systemic Lupus Erythematosus: Results of a Quality Improvement Initiative

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
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Background/Purpose: Hydroxychloroquine (HCQ) is a commonly prescribed medication for systemic lupus erythematosus (SLE), rheumatoid arthritis (RA), and other rheumatic diseases. HCQ may rarely cause retinopathy. This risk correlates with both daily dose and duration of use[1]. In addition to screening ophthalmologic examinations, the most recent guidelines by the American Academy of Ophthalmology recommend limiting the dose of HCQ to 5mg/kg/day of actual body weight[1]. After reviewing our practice's dosing of HCQ and adherence to these guidelines in 2018, we assessed the impact of sharing prescribing data with individual providers and implementing nurse-aided decision support for HCQ refill requests.

Methods: We previously performed a single-center retrospective analysis of 801 adult patients receiving HCQ for SLE or RA in our rheumatology practice at Beth Israel Deaconess Medical Center between January 1, 2018 and De-

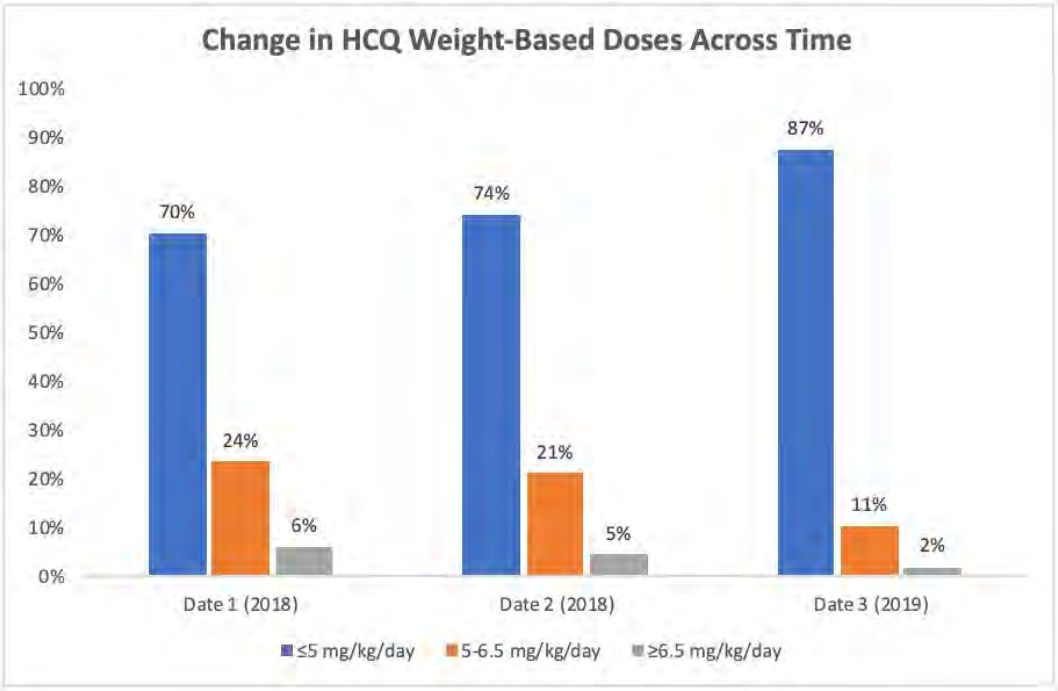

Figure 1. Change in HCQ Weight Based Doses Across Time. Date 1 and Date 2 represent the "pre-intervention" time points in 2018. Date 3 represents the "post-intervention" time point in 2019.

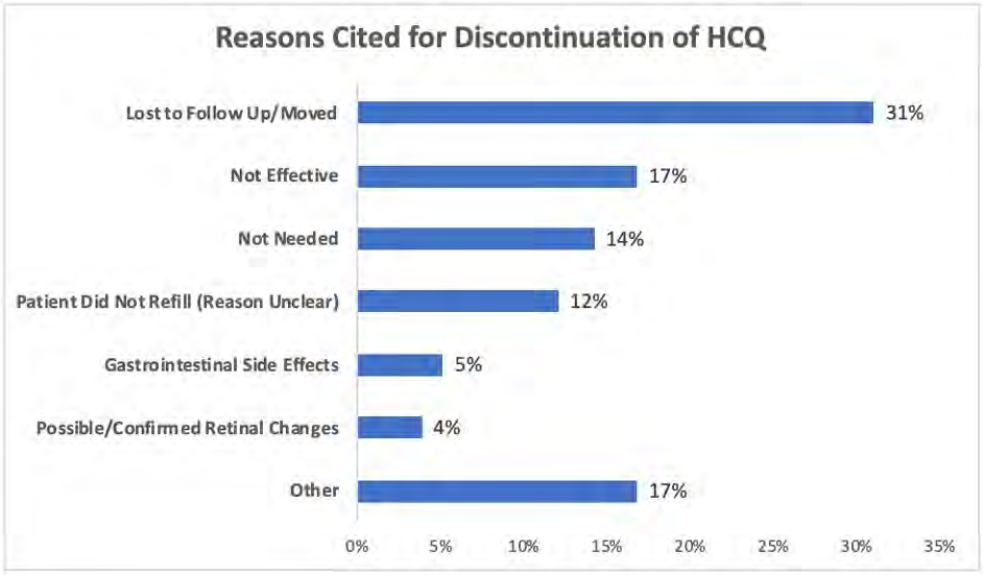

Figure 2. Reasons Cited for Discontinuation of HCQ. "Other" less common reasons for discontinuation included: non-ophthalmologic neurologic side effect, medication interaction, rash, rethinking diagnosis, death of patient, pregnancy, macular degeneration (concern for inability to safely monitor for retinal toxicity), hair loss, hyponatremia, G6PD deficiency, pill size, polypharmacy, tongue swelling, and mood.

cember 31, 2018. We calculated the weight-based dose of HCQ at two separate time points, separated by at least 6 months to allow for "loading dose" adjustments. In mid-2019, we implemented a two-pronged quality improvement intervention:

1. We shared aggregate dosing averages with all providers in the practice, then privately shared individual prescribing data with each provider, including a list of patients dosed >5mg/kg/day at both recorded time points in 2018.

2. We introduced nurse-aided decision support for HCQ refill requests. For each request, nurses calculated the weight-based dose before sending the request to the prescribing physician along with an alert if the dose was >5mg/kg/day.

One year after the initial analysis, we reviewed the same 801 patients included in the initial analysis, and recorded the current weight and HCQ dose. We used this data to calculate aggregate dosing averages for the practice, and dosing changes for individual patients. We used McNemar's test to assess for statistical significance of the changes.

Results: Of 801 patients included in the 2018 analysis, 674 continued to receive their care within our practice and remained on HCQ through the end of 2019. 154 patients were dosed >5mg/kg/day at both measured time points during 2018, and of those patients, 93 (60%) were dose-reduced to £5mg/kg/day by date 3. Between Date 2 in 2018 ("pre-intervention") and Date 3 in 2019 ("post-intervention"), there was a statistically significant increase in the proportion of patients dosed < 5mg/kg/day, from 74% to 87% (p< 0.0001) (*Figure 1*). HCQ was discontinued in 232 patients between 2018 and 2019. Of those patients, the most commonly cited reasons were "loss to follow up/moved away" (31%), "not effective" (17%), and "no longer needed" (14%) (*Figure 2*). In 9 patients (4%), HCQ was discontinued due to possible or confirmed retinopathy identified by ophthalmologic screening exam.

Conclusion: Our quality improvement intervention led to a statistically significant increase in the proportion of patients taking HCQ dosed according to the current recommended guidelines. These findings highlight provider feedback and nurse-aided decision support as two potentially effective strategies for improving adherence with the guidelines.

Disclosure: T. Skorupa, None; **R. Shmerling**, None.

Abstract Number: 1594

Hydroxychloroquine Prescribing Habits and Provider Opinion on Dosing Guidelines in the Rheumatology and Dermatology Practices of an Academic Institution

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: One rare but devastating adverse event related to the use of hydroxychloroquine (HCQ) is retinal toxicity. Retinal toxicity rates from HCQ can be as high as 7.5% and is dose-related. In 2016, the American Academy of Ophthalmology (AAO) issued weight-based guidelines recommending that daily dosing not exceed 5 mg/kg/day. However, there are concerns from those prescribing this medication that dose reduction might decrease the benefit of this medication. We wanted to analyze HCQ prescribing habits and opinions on these guidelines in our academic institution. We also conducted a prospective, non-controlled, quality improvement study to examine if a tool in the electronic medical record (EMR) affected compliance with these guidelines or affected provider's perspectives on these guidelines.

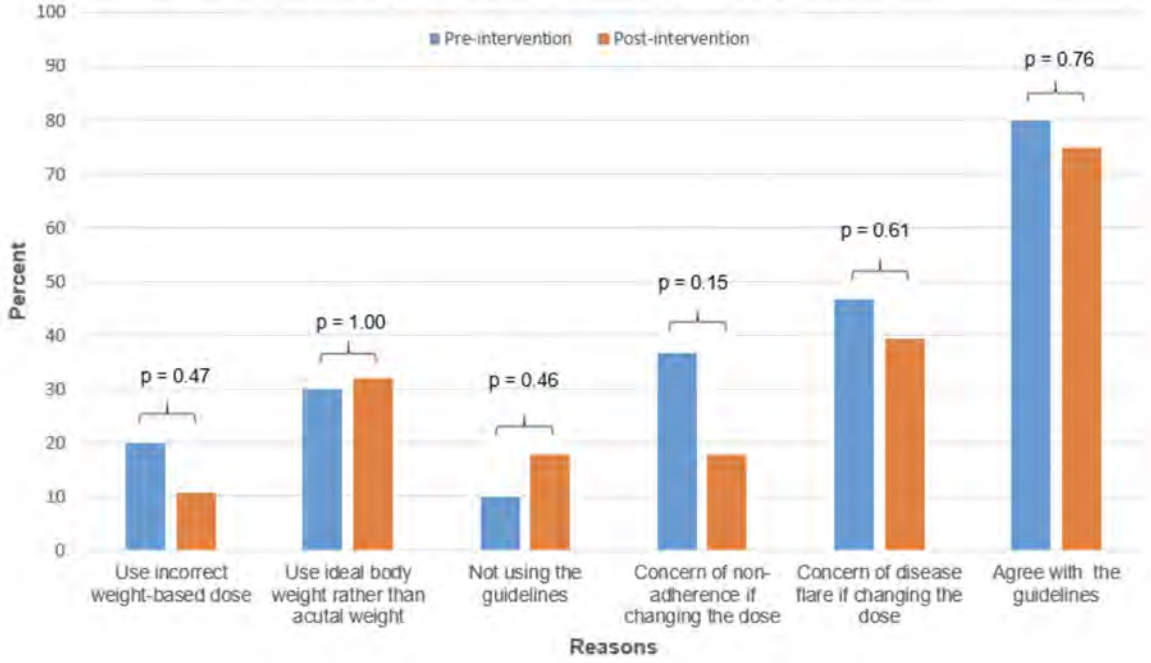
Table 1. Hydroxychloroquine Dosing Before Intervention

HCQ Dose (mg/kg/day)	Rheumatology [n (%)]			Dermatology [n (%)]		
	Female	Male	Total	Female	Male	Total
≤5	626 (80.5)	152 (19.5)	778 (69.0)	122 (71.8)	48 (28.2)	170 (60.3)
5.1 - 6.5	256 (92.4)	21 (7.6)	277 (24.6)	65 (83.3)	13 (16.7)	78 (27.7)
≥6.6	70 (95.9)	3 (4.1)	73 (6.5)	32 (94.1)	2 (5.9)	34 (12.1)
Total	952 (84.4)	176 (15.6)	1128 (100.0)	219 (77.7)	63 (22.3)	282 (100.0)

Table2 Hydroxychloroquine Dosing After Intervention

HCQ Dose (mg/kg/day)	Rheumatology [n (%)]			Dermatology [n (%)]		
	Female	Male	Total	Female	Male	Total
≤5	705 (79.1)	186 (20.9)	891 (76.9)	53 (67.9)	25 (32.1)	78 (73.6)
5.1 - 6.5	197 (88.7)	25 (11.3)	222 (19.2)	19 (86.4)	3 (13.6)	22 (20.8)
>6.6	42 (93.3)	3 (6.7)	45 (3.9)	4 (66.7)	2 (33.3)	6 (5.7)
Total	944 (81.5)	214 (18.5)	1158 (100.0)	76 (71.7)	30 (28.3)	106 (100.0)

Figure 1. Reasons for Incorrect Hydroxychloroquine Dosage and Opinions on The Guidelines Before and After the Intervention



Methods: Survey data was collected from prescribers. Chart review on patients prescribed HCQ, was collected. Survey data included: awareness of guidelines, self-reported compliance with guidelines, and opinion of guidelines. All data were collected pre-intervention (June 2017 - January 2019) and post-intervention (March 2019 - April 2020). In January 2019 we released an EMR tool which prompted guideline-based weight-based dosing whenever HCQ was prescribed. Results were analyzed using descriptive statistics for demographic data and Fisher's exact tests for comparisons of proportions between groups.

Results: Pre-intervention: We reviewed 1,128 rheumatology charts. 350 (31.0%) rheumatology patients were prescribed HCQ >5.0 mg/kg/day. We reviewed 282 dermatology charts. 112 (39.7%) dermatology patients were prescribed HCQ >5.0 mg/kg/day. Combining rheumatology and dermatology patients, 462 (32.8%) were prescribed HCQ >5.0 mg/kg/day (Table 1). Post-intervention: We analyzed 1,158 rheumatology charts. 267 (23.1%) rheumatology patients were prescribed HCQ >5.0 mg/kg/day. We reviewed 106 dermatology charts. 28 (26.4%) dermatology patients were prescribed HCQ >5.0 mg/kg/day. Combining rheumatology and dermatology patients, 295 (23.3%) were prescribed HCQ >5.0 mg/kg/day (Table 2). Post-intervention, there was a 9.5% increase in patients prescribed HCQ ≤5 mg/kg/day (p-value < 0.0001). Pre-intervention, we compiled 18 surveys from rheumatology and 12 surveys from dermatology; post-intervention, we compiled 16 surveys from rheumatology and 12 surveys from dermatology (Fig 1). Post-intervention, there were reductions in the number of rheumatologists who incorrectly identified the guideline-based weight-based dosing recommendation of HCQ; there was no change in dermatologists. Combined, there was an overall reduction but not of statistical significance (p=0.47).

Conclusion: Our research finds ongoing hesitation towards compliance with the 2016 AAO recommendations for HCQ weight-based dosing. There is ongoing unfamiliarity with the details of the recommendations therein. Prescribed HCQ doses in practice often exceeded the recommended daily dose. Finally, our research shows that appropriate EMR intervention, prompting appropriate and safe weight-based dosing of HCQ, can improve compliance with these guidelines. We believe that this will lead to improved patient safety over the lifetime.

Disclosure: R. Overbury, None; **J. Pupaibool**, None; **C. Hansen**, None; **D. Lebiedz-Odrobina**, None.

Abstract Number: 1595

Using Rheumatoid Arthritis Communication Tool Developed by the RISE Learning Collaborative to Promote Shared Decision-Making

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Patient care is moving from physician directed treatment to a co-design framework that focuses on creating a partnership between patients and physicians. This new framework is centered on patients' values, with the aim of enhancing care by improving mutual understanding, goal alignment and patient-physician shared decision making (SDM). Our objective was to implement and evaluate the impact of a Rheumatoid Arthritis (RA) SDM tool, with the goal of improving SDM between RA patients and their providers.

Methods: A vital component to effectively improve outcomes in RA patients is by establishing personalized treatment plans and targets through SDM. An SDM tool (Figure 1) developed by the RISE Learning Collaborative (RISE-LC), a learning network established in March 2019 to coordinate quality improvement (QI) efforts in adult rheumatology practices across multiple centers, was introduced into our academic rheumatology clinic workflow (Figure 2) in January 2020.

We conducted a retrospective chart review of 99 patients: 50 of them with visits in September – December, prior to implementation of the SDM tool and 49 of them with a visit between January-March 2020, following tool implementation. The patients in each group categorized based on their CDAI scores: Remission: 0-2.8, Low disease activity (LDA): 2.9–10, Low-moderate disease activity (LMDA): 10.1–16, high-moderate disease activity (HMDA): 16.1–22 and high disease activity (HDA): >22. We used Minitab (Version 19.2020.1) for statistical analysis, and used two-sample t-test and two-proportion test to compare the 2 cohorts' demographics, goals for the visit, CDAI scores, number of medications patients were on, number of associated co-morbidities and whether patients had a change in therapy.

Results: 89.9% (89/99) of the included patients were females (see Table 1). Among the patients who used the SDM tool, 65.3% used less than 2 lines to answer the question 'what's on my mind for today's visit?'. Having less pain was the most common goal (65.3%) overall and this did not vary with the level of disease activity. The second most common goal was to avoid medication side effects (40.8%), which was listed more frequently for patients in LDA (47.3% or 9/19) and LMDA (50% or 6/12) groups. The patients who had a change in therapy in the non-SDM cohort were younger and had higher CDAI scores. Comparing other parameters did not reach statistical significance. See Table 1

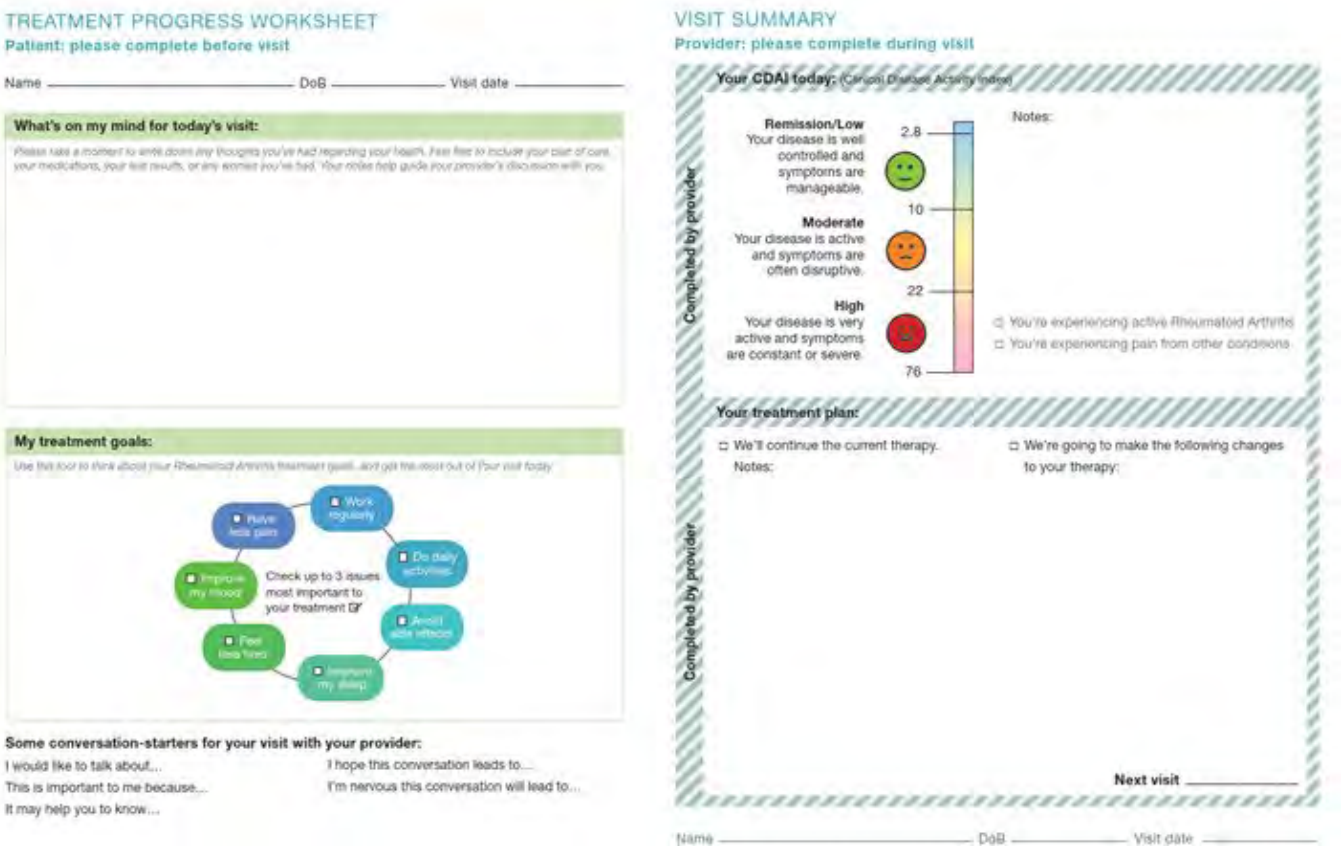

Figure 1 SDM Tool

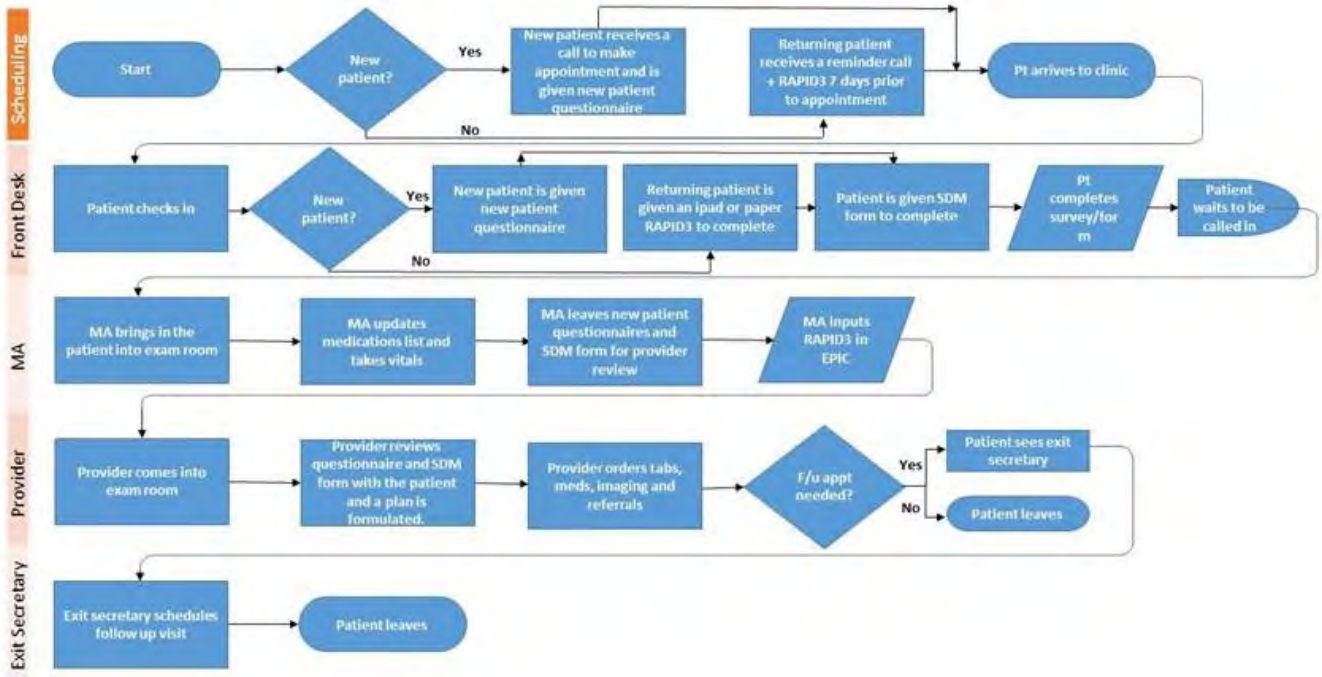

Figure 2. UT Southwestern Rheumatology Clinic Workflow

	SDM Tool Cohort N=49			Non-SDM Tool Cohort N=50			
Average age	61			62.2			p-value: 0.733
Sex	Female: 45 Male: 4			Female: 44 Male: 6			
Race	African American: 19 White: 19 Asian: 2 Other: 1 Unknown: 7			African American: 18 White: 23 Asian: 1 Other: 2 Unknown: 6			
Patients Making Change to Therapy	38.8%			40%			p-value: 0.901
Therapy changed?	Yes	No	p-value	Yes	No	p-value	
Average clinical disease activity (CDAI) scores	10.4	9	0.514	12.8	8.15	0.039	
Average number of medications	10.2	9.6	0.656	9.5	9.4	0.982	
Average Age (years)	60.68	61.2	0.905	56	60	0.030	
Average number of comorbid conditions	4.15	4.33	0.826	4.45	4.6	0.823	

Table 1. Comparing SDM Tool Cohort With Non-SDM Tool Cohort

Conclusion: Implementation of a SDM tool was feasible in our practice. Analysis of SDM tool content revealed that most patients had focused goals; less pain was the most common goal followed by having fewer medication side effects. As the disease activity increased, patients were willing to make changes to therapy. No early differences in treatment escalation were seen among those using the SDM tool, but larger studies are ongoing to assess the impact of tool implementation. Next steps also include incorporating SDM tool components into a rheumatology dashboard in our electronic health record.

Disclosure: J. Eseddi, None; **P. Bajaj**, None; **G. Schmajuk**, None; **J. Yazdany**, Eli Lilly, 1, Astra Zeneca, 1; **S. Kazi**, ABIM, 1, Regeneron, 1, Sanofi, 1.

Abstract Number: 1596

Coproduction of Care for Veterans with RA: Improving Elicitation and Documentation of Patient Goals

Swathi Reddy[1], Kyawt Shwin[1], Rashmi Arora[1], Sarah Homann[2], Lisa Johnson[3], Yusuf Chao[4], Aricca Van Citters[3], Brant Oliver[5], Guy Eakin[6], Eugene Nelson[3], Andreas Reimold[1] and Salahuddin Kazi[1], [1]Veterans Affairs North Texas Healthcare System / UT Southwestern Medical Center, Dallas, TX, [2]Veterans Affairs Tennessee Valley Healthcare System / Vanderbilt University Medical Center, Nashville, TN, [3]The Dartmouth Institute for Health Policy & Clinical Practice, Lebanon, NH, [4]UT Southwestern Medical Center, Dallas, TX, [5]The Dartmouth Institute for Health Policy & Clinical Practice / Veterans Affairs National Quality Scholars Fellowship in Healthcare Quality & Safety, Lebanon, NH, [6]Arthritis Foundation, Atlanta, GA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Coproduction of healthcare services offers a pathway to increase patient engagement in care. Patients and clinicians coproduce care by working together to: (1) co-assess health status; (2) co-decide next steps in the care plan based on the patient's goals; (3) co-design the care plan to fit the patient's goals, context, and capabilities; and, (4) co-deliver self-care and professional services to achieve goals of care. This initiative aimed to increase patient engagement by eliciting their goals and concerns, incorporating them into the clinic discussion, and documenting coproduced goals as part of the care plan in the electronic health record (EHR) for at least 50% of veterans with RA by December 2019.

Methods: Our multi-phase intervention included: (1) creation of a new intake form to elicit patient's main goals and concerns; (2) adaptation of the clinical work flow to incorporate patient goals and concerns as part of the clinic visit discussion, supported by a motivational interviewing course to educate clinicians in patient-centered counseling; and, (3) modification of the after visit summary (AVS) template in the EHR to document coproduced goals and next steps to support patient self-management. We used the Plan-Do-Study-Act methodology to test, evaluate, and modify the patient prompt through four cycles of revisions. Input was obtained from patients and clinical care team members (5 attending physicians, 1 fellow physician, 1 nurse practitioner, and 4 nurses). The final patient prompt asked of all RA outpatients contains three questions (**Figure 1**). Modifications to the AVS include a text box entitled "Your Goal is" followed by "Next Steps to Achieve Goal." Process and outcome data were collected from a random sample of 30% of the RA population seen at the Rheumatology clinic in the baseline (November-December 2017, n=70) and post-intervention (November-December 2019, n=65) periods.

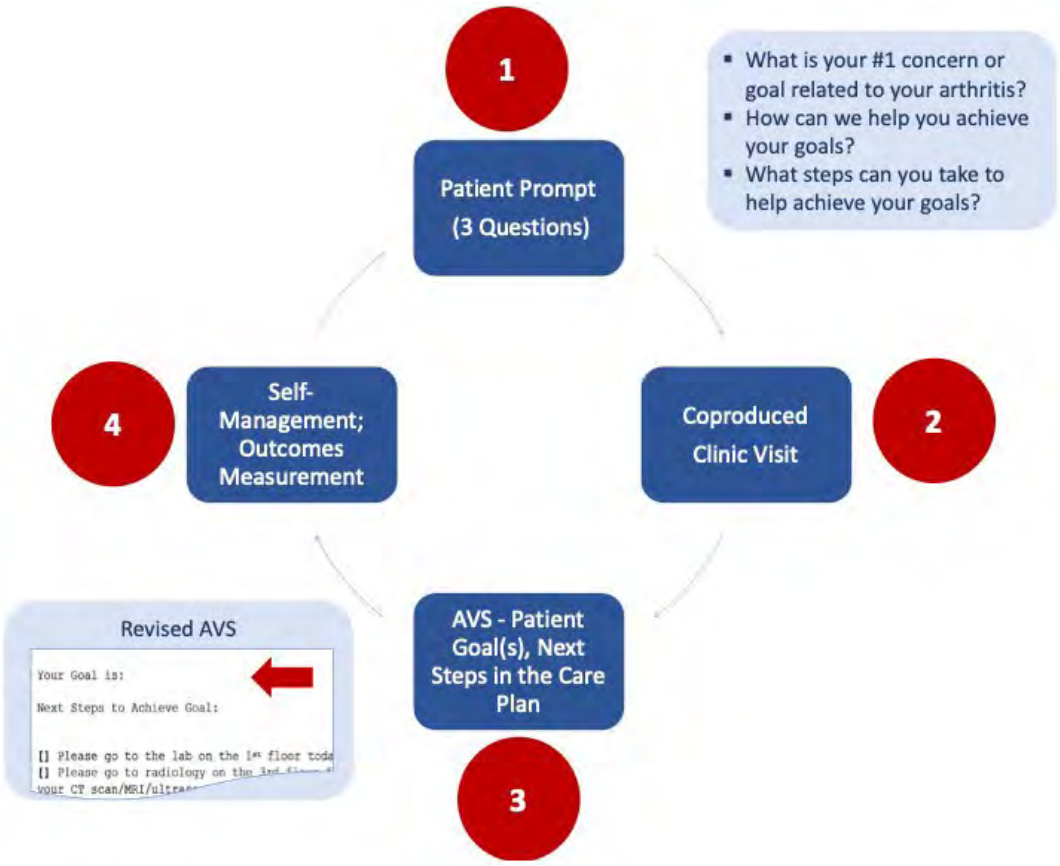

Figure 1. Coproduction of Care Initiative for Veterans with RA

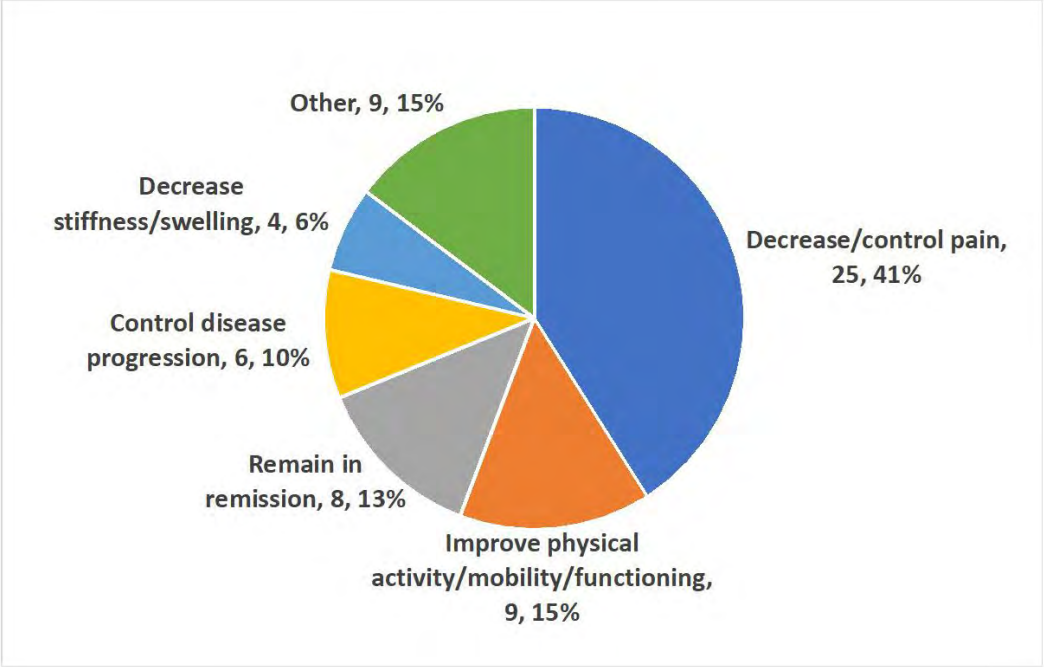

Figure 2. Coproduced Goals of Care Documented in the AVS (Post-Intervention: November-December 2019; n=61 goals, identified by 48 patients)

	Baseline: Nov/Dec 2017 n=70	Post-Intervention: Nov/Dec 2019 n=65
Age, years (mean, SD)	62.4 (11.1)	69.3 (10.8)
% Male	93% (65/70)	77% (50/65)
Disease Activity (% low or in remission)		
Clinical Disease Activity Index (CDAI)	66% (46/70)	71% (46/65)
Disease Activity Score-28 (DAS-28)	54% (38/70)	64% (35/55)
Functional Status (mean, SD)		
Health Assessment Questionnaire (HAQ) 0-3	1.2 (0.7) (n=60)	1.1 (0.7) (n=48)
Joint Exam (mean, SD)		
Total tender joint count 0-28	4.0 (6.9) (n=59)	2.9 (4.8) (n=56)
Total swollen joint count 0-28	0.7 (2.4) (n=59)	1.5 (3.9) (n=58)
Clinical Lab Markers (mean, SD)		
CRP mg/dL	1.2 (1.6) (n=69)	1.3 (2.1) (n=55)
ESR mm/hr	24.2 (18.4) (n=70)	24.1 (20.3) (n=55)
Patient Global Score 0-100mm (mean, SD)	46.6 (25.8) (n=61)	41.5 (28.2) (n=48)
Physician Global Score 0-100mm (mean, SD)	27.6 (21.0) (n=44)	23.7 (18.1) (n=50)
Documentation of Goals of Care	n/a	87% (48/55)

Table 1. Patient Data Comparison – Baseline and Post-Intervention Periods

Results: Coproduced goals of care were documented in 87% of the available AVS (n=55) in the post-intervention period, exceeding our aim. The most frequent coproduced goal was to decrease/control pain (41%, n=25), followed by improve physical activity/mobility/functioning (15%, n=9), and remain in remission (13%, n=8) (**Figure 2**). Data collection included patient characteristics, measures of disease activity, functional status, tender and swollen joint counts, patient and physician global scores, and clinical lab markers (**Table 1)**. A trend towards increased percentage of patients in disease remission, decreased tender joint count, and improved patient and physician global scores was noted.

Conclusion: Clinicians in a high-volume clinic can successfully partner with their RA patients to coproduce care by eliciting their goals, engaging in shared decision making about next steps, and documenting coproduced goals and care plans in the EHR. Areas of further exploration include: (1) monthly collection and tracking of health outcomes and patient satisfaction data over time, (2) measurement of patient self-reported effort towards meeting their goal(s) and identification of ways to bolster goal achievement, and (3) application of the coproduction process to telemedicine visits.

Disclosure: S. Reddy, None; **K. Shwin**, None; **R. Arora**, None; **S. Homann**, Pfizer, 2; **L. Johnson**, None; **Y. Chao**, None; **A. Van Citters**, None; **B. Oliver**, None; **G. Eakin**, None; **E. Nelson**, None; **A. Reimold**, Lilly, 5, Abbvie, 2, Pfizer, 2; **S. Kazi**, ABIM, 1, Regeneron, 1, Sanofi, 1.

Abstract Number: 1597

Use of a Clinical Dashboard Improves the Documentation of Disease Severity Scores and May Facilitate the Implementation of Treat to Target Therapy

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
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Background/Purpose: Rheumatoid Arthritis (RA) management guidelines recommend the collection of Disease Activity Measures (DAMs) to direct therapy as a component of a "treat-to-target" (T2T) strategy. A goal of the Veterans Affairs Rheumatoid Arthritis (VARA) registry is to systematically collect 6 clinical DAMs and two laboratory DAMs at each visit using note templates (Table 1). The real-time calculation of disease severity scores such as DAS28 is not part of the standard VARA protocol. We developed an on-line clinical dashboard that collects real-time DAMs and displays them longitudinally to calculate disease activity scores including DAS28 in real-time. In this study, we evaluated the association of clinical dashboard utilization with 1) DAS28 capture in the medical record and 2) the frequency of major changes in RA therapy.

Methods: Clinical notes from initial clinic visits for each US Veteran enrolled in VARA from a single site (between 10/2012 and 6/2018 - when the dashboard became available) were evaluated for documentation of 8 possible DAMs and whether major therapeutic changes (MTCs) were undertaken. We compared clinic notes for visits where the clinical dashboard was deployed for data collection with visits where the clinical dashboard was not used. MTC was defined as: initiation of synthetic or biologic disease-modifying antirheumatic drug (DMARD); DMARD dose escalation ≥25%; prednisone use (new agent or after 90-day gap); prednisone dose increased 25%; and/or corticosteroid injection in ≥2 joints. We also recorded changes and/or escalation in therapy even if it did not meet MTC criteria. Each MTC or lack of MTC was classified as being consistent or not consistent with ACR guidelines and our previously published potential optimal DAS28 threshold for MTC (See Table 2 Footnote).

Results: The 146 RA patients with a visit using the dashboard were similar to the 201 patients in whom the dashboard was not used referent to age, disease duration, clinical RA features, DAMs and overall DAS28 (Table 1). Clinic notes for patient visits using the dashboard were significantly more likely to record a DAS28 (75.3%) than visits not using the dashboard (2.0%) ($p < 0.001$) (Table 2). There was no significant difference in likelihood of an MTC, (20.5% vs 16.4%) or any therapeutic escalation (33.6% vs 27.4%) (Table 2). Management decisions to escalate therapy as recommended in ACR guidelines were more common at DAS28 >3.2 threshold for change (70.5% vs 60.2%, $p=0.046$) and DAS28 >3.8 threshold for change (77.4% vs. 66.7%, $p=0.029$).

Conclusion: Utilization of a clinical dashboard can improve documentation of disease activity scores such as DAS28 in real time. Further study is needed to determine if the use of a clinical dashboard will improve the implementation of care that is concordant with best practices and whether this leads to improvements in long-term patient outcomes.

Table 1

Demographic Category	Dash User (n=146)**	Dash Non-User (n=201)*	*p*-value***
Average Age at implementation (years)	68.6±10.2	67.8±10.4	NS
Average Disease Duration (years)	15.1±11.5	14.6±10.8	NS
Male Gender	126 (86%)	178 (89%)	NS
Rheumatoid Factor Positive	103 (71%)	145 (72%)	NS
aCCP Positive[‡]	109 (75%)	159 (79%)	NS
Race			
Caucasian	135 (92%)	187 (93%)	NS
African American	2 (1%)	3 (1%)	NS
Hispanic	6 (4%)	8 (4%)	NS
Other	3 (2%)	3 (1%)	NS
Smoking Status			
Current	32 (22%)	45 (22%)	NS
Former	74 (51%)	101 (50%)	NS
Non-Smoker	38 (26%)	52 (26%)	NS
Unknown smoker status	2 (1%)	3 (1%)	NS
Years of Education (years)	14.2±2.5	13.9±2.5	NS
Clinical Parameters			
Joint Tenderness count	4.8±6.1	4.9±5.9	NS
Joint Swelling count	2.7±3.8	2.8±4.3	NS
Patient Global Disease Assessment	37.4±23.7	32.6±22.5	NS
Provider Global Disease Assessment	23.0±20.9	21.4±18.5	NS
Global Pain Score	4.4±2.6	4.0±2.4	NS
HAQ[‡‡]	0.8±0.5	0.8±0.6	NS
ESR[‡‡‡]	13.3±14.7	15.4±17.6	NS
CRP[†]	0.9±1.5	0.9±1.2	NS
DAS28[††]	3.2±1.6	3.2±1.5	NS
> 5.1 (High)	25 (17%)	26 (13%)	NS
3.2 - 5.1 (Moderate)	36 (25%)	71 (35%)	0.03
2.6 - 3.2 (Low Activity)	25 (17%)	24 (12%)	NS
<2.6 (Remission)	60 (41%)	80 (40%)	NS

*Patients with first clinic visits for VARA patients after dashboard availability that did not utilize the clinical dashboard
**Patients with first clinic visits for VARA patients after dashboard availability that utilized the clinical dashboard
***NS = Not significant
‡aCCP = Anti-cyclic citrullinated peptide antibody
‡‡MHAQ = Modified health assessment questionnaire
‡‡‡ESR = Erythrocyte sedimentation rate
†CRP = C-reactive protein
††DAS28 = Disease activity score for 28 joint count

Table 2

	Dash User (n=146)	Dash Non-User (n=201)	p-value
DAS28 reported in the note	110 (75.3%)	4 (2.0%)	<0.00001
Major Therapeutic Change (MTC)*	30/146 (20.5%)	33/201 (16.4%)	NS
DAS28 >5.1 (n=74)	14/25 (56.0%)	10/26 (38.5%)	NS
DAS28 3.2-5.1 (n=146)	10/36 (27.8%)	15/71 (21.1%)	NS
DAS28 2.6-3.1 (n=70)	4/25 (16.0%)	3/24 (12.5%)	NS
DAS28 <2.6 (n=196)	2/60 (3.3%)	5/80 (6.3%)	NS
MTC plus any modification or escalation in therapy**	49/146 (33.6%)	55/201 (27.4%)	NS
DAS28 >5.1 (n=74)	16/25 (64.0%)	13/26 (50.0%)	NS
DAS28 3.2-5.1 (n=146)	13/36 (36.1%)	21/71 (29.6%)	NS
DAS28 2.6-3.1 (n=70)	8/25 (32.0%)	8/24 (33.3%)	NS
DAS28 <2.6 (n=196)	12/60 (20.0%)	13/80 (16.3%)	NS
Change made consistent with guidelines with varying T2T thresholds			
DAS28 treatment threshold of 3.2	103 (70.5%)	121 (60.2%)	0.046
DAS28 treatment threshold of 3.8‡	113 (77.4%)	134 (66.7%)	0.029

*Major therapeutic Change (MTC) defined as: initiation of synthetic or biologic disease-modifying antirheumatic drug (sDMARD, bDMARD); DMARD dose escalation ≥25%; prednisone use (new agent or after 90-day gap); prednisone dose increased 25%; and/or corticosteroid injection in ≥2 joints.

**These data include any MTC that was implemented as well as any other interventions including addition of NSAIDs, switching sDMARD agent, decrease in dose of sDMARD, single joint injection.

‡3.8 cutoff decided upon based on previous observations that an empirical treatment threshold for implementing MTC exists at a higher point than the 3.2 calculated threshold for MTC implementation as recommended per ACR guidelines. Sauer et al, ACR Abstract #2870 Atlanta, 2019. Thresholds for Disease Activity Measures DAS28, CDAI, and RAPID3 Do Not Align with Clinical Practice Patterns of Rheumatoid Arthritis (RA) Disease Management Decisions.

Disclosure: T. Nelson, None; **G. Kunkel**, None; **G. Cannon**, Amgen, Inc., 2, Merck, 2.

Abstract Number: 1598

Efficacy of Universal Depression Screening in a Rheumatology Clinic

Osman Bhatty[1] and Michael Lucke[1], [1]Allegheny Health Network, Pittsburgh, PA

SESSION INFORMATION
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Session Type: Poster Session D
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Background/Purpose: Depression has long been viewed as a comorbid condition in rheumatic diseases. Population studies have confirmed an increased incidence in patients with rheumatoid arthritis, systemic lupus erythematosus and systemic sclerosis. Additionally, studies have shown worse disease outcomes including increased mortality in patients with rheumatoid arthritis underscoring the need to identify and address depression in these populations.

Results of PHQ-9 Screening (table 1)		
Total Patients (n =530)		
Positive	Addressed	7
	Unaddressed	19
Negative	Total	423
Not Done	Total	81

Patients with Established Rheumatic Disease in Positive or Incomplete Screens (table 2)	
Total Patients (n=61)	
PHQ9 Status:	
Positive, Addressed	4
Positive, Unaddressed	14
Not Completed	43
Disease:	
SLE	14
Sjogrens	2
Rheumatoid Arthritis	20
PMR	6
Gout	6
Myosiits	3
SpA	4
UCTD	2
AAV	2
HLH	1
SCLE	1

Provider Perspectives on Co-morbid Depression (table 3)			
Question Asked	**Agree**	**Disagree**	**Neither**
Does it change management?	75% (9/12)	8% (1/12)	8% (1/12)
Does we play a role?	83% (10/12)	8% (1/12)	8% (1/12)
If not notified of screen, assume negative?	17% (2/12)	25% (3/12)	58% (7/12)
	Most or sometimes	**Seldom or Never**	
I have enough time during the visit to address screens	42% (5/12)	58% (7/12)	

This study assesses rates of screening and identifying depression after implementation of universal PHQ9 depression screening in an outpatient rheumatology clinic. We further evaluate any impact of rheumatologic diagnosis on rates of screening and explore provider beliefs on the role of the rheumatologist in addressing comorbid depression.

Methods: Universal PHQ9 screening was implemented in an outpatient rheumatology clinic consisting of physicians, physician assistants, and rheumatology fellows. Medical assistants would perform PHQ2 screens on all patients prior to their encounters and if positive would then perform full PHQ9 screens. If these were positive then the provider responsible for the encounter was notified and further triaging was left to their discretion.

A retrospective chart review of 16 random clinic dates between January 2020 and March 2020 was conducted. Race, age, gender and reason for clinic visit were collected. Each patient's PHQ9 score was identified as well as their "established rheumatic disease" defined as what was entered into their reason for follow up by the provider or documented as such in the note. The chart was then reviewed to see if the provider responded to the screen by referring to a behavioral health liaison, adding this to the problem list, or discussing it in their assessment and plan. If none of these actions were done then the screen was considered to be "Not Addressed".

Also, an anonymous survey was performed to assess rheumatology provider beliefs pertaining to co-morbid depression screening.

Results: Out of 530 patient visits, 432 had PHQ9 completed. 26/432 PHQ9 screens were positive (6%). Among positive screens, only 27% (7/26) were addressed (table 1). Out of the 18 patients with rheumatic disease that screened positive only 4 were addressed. There were also a large number of patients with rheumatic disease (43) who did not have screening performed at all despite clinic protocol (table 2). Out of the 12 providers that completed the survey the majority felt that co-morbid depression changed management (75%) and that they played a role (83%). 58% of providers felt they seldom or never had time to address the screens (table 3).

Conclusion: In spite of universal screening and the in office presence of a behavioral health liaison, the majority of positive PHQ9 results were not addressed. This trend remained true in patients with established rheumatic diseases suggesting that although providers recognize the importance of co-morbid depression there remains a care delivery gap in this subset of patients even with the addition of extra protocols and resources.

Disclosure: O. Bhatty, None; **M. Lucke**, Abbvie, 5.

Abstract Number: 1599

Workflows for Collecting and Using Patient-reported Outcomes Across Rheumatology Practices

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SESSION INFORMATION

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Table 1: Patient Reported Outcome Workflow Survey Results from 12 RISE PRO LC Centers

Center Characteristics	Counts (n=12)
Institution Type	
Public (County or public university affiliate)	9 (75%)
Private	1 (8%)
Veterans Administration Hospital (VA)	2 (17%)
Electronic Medical Record Type	
EPIC	6 (50%)
Other[1]	4 (33%)
No response	2 (17%)
PRO Collection	
What types of PROs are collected?	
CDAI	2 (17%)
RAPID3	5 (42%)
Both	3 (25%)
No response	2 (16%)
How are they collected?	
Paper only	10 (83.3%)
Tablet only	1 (8.3%)
Paper, tablet, online patient portal	1 (8.3%)
When/Where are PROs collected?	
Exam Room	5 (42%)
Waiting Room	5 (42%)
Pre-visit	1 (8%)
Multiple locations	1 (8%)
Who collects PROs?	
Support staff[2]	6 (50%)
Clinician[3]	3 (25%)
Both	3 (25%)
PRO Entry into EMR	
How are PROs stored in the EMR?	
In structured fields	6 (50%)
In the narrative of clinical notes	6 (50%)
Who enters PROs in EMRs?	
Support staff[2]	2 (16.7%)
Clinician[3]	3 (25%)
Both	2 (16.7%)
No response	5 (42%)
PRO Access and Sharing	
Do clinicians access PROs and if so, how?	
Yes, using a structured field[4]	4 (33%)
Yes, using notes (including automated text phrases)	3 (25%)
Yes, in multiple ways	3 (25%)
No response	2 (17%)
Can patients access PROs and if so, how?	
Yes, shared by MD at visit	7 (58)
Yes, accessed via online portal	1 (8%)
No	2 (17%)
No response	2 (17%)

[1]NextGen®, CPRS, or eClinical Works
[2]MA, administrative staff
[3]MD, NP, or PA
[4]Flowsheet, tabular view or other structured data field

Table 1. Patient Reported Outcome Workflow Survey Results from 12 RISE PRO LC Centers

Background/Purpose: The use of patient reported outcomes (PROs) during rheumatology visits may facilitate shared decision making and encourage patients to share their health goals. However, few studies have analyzed how PROs are collected, stored, and discussed with patients in clinical practice. The Rheumatology Informatics System for Effectiveness Patient Reported Outcome Learning Collaborative (RISE PRO LC) launched in March 2019 as a national coalition of 15 medical centers from 10 states to exchange quality improvement ideas, such as how to leverage the electronic health record (EHR) to utilize PROs for patient care. We surveyed participating sites about PRO workflows and potential barriers to using PROs to engage patients in decisions about their RA treatment during office visits.

Methods: During the first quarter of 2020, 12 RISE PRO LC site physician champions completed a survey about PRO workflows. The survey collected information on the PROs used routinely in practice, the EHR systems employed, and also qualitative information about when and how PROs were collected, how the data were stored and retrieved, and how PROs were shared with patients. Descriptive statistics and thematic analysis using an inductive approach were used to analyze the survey data. Responses were coded, grouped into themes, and summarized.

Results: Of the 12 centers with responses, 2 were Veterans Affairs sites, and 10 were clinics associated with an academic medical center or county health system. EPIC systems was the most commonly reported EHR, followed by NextGen® and CPRS. For PRO collection, 10 of 12 sites used paper forms solely to collect PROs from patients in waiting rooms or exam rooms, while 1 used tablets alone. One site used paper forms, tablets, and an online patient portal for collection. Frequently cited challenges for PRO collection included inconsistent staffing, busy workflows for medical assistants, and language barriers. For PRO documentation in the EHR, 6 sites relied on structured data fields, while the remaining sites required providers to type PROs in the free-text of clinical notes. The sites that captured PROs in structured fields reported EHR capacity to review prior PRO scores longitudinally. Nine centers reported that clinicians regularly shared PROs with each patient during clinical visits. Only 1 site had capacity for patients to view PRO results between clinical encounters. Four of 6 sites that recorded PROs in structured EHR fields reported regularly sharing PROs with patients either during or after a clinical encounter (Table 1).

Conclusion: Although RA PROs were routinely collected in the participating rheumatology clinics surveyed, processes to gather, access and share PROs with patients highly varied. A vast majority of practices still employ paper surveys to collect PROs, and only half reported having structured data fields in their EHRs to store and longitudinally track PROs over time. PRO results were inconsistently shared with patients. These findings suggest significant opportunities to optimize workflows to collect, longitudinally store, and share PROs with patients to promote shared decision-making during rheumatology encounters.

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Relationship Between Electronic Health Record Vendor and Performance on Patient-reported Outcome Quality Measures in the ACR's Rheumatology Informatics System for Effectiveness (RISE) Registry

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SESSION INFORMATION

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Practice characteristics	N = 220
Number of providers in practice, N (%)	
1-4	162 (73.6)
5-9	44 (20.0)
10-20	14 (6.4)
Practice type, N (%)	
Single-Specialty Group Practice	117 (53.2)
Solo Practitioner	61 (27.7)
Multi-Specialty Group Practice	27 (12.3)
Other clinical setting	11 (5.0)
Health System	4 (1.8)
EHR software, N (%)	
NextGen	75 (34.1)
eClinicalWorks	32 (14.5)
Amazing Charts	21 (9.5)
eMDs	11 (5.0)
GE Centricity	10 (4.5)
Allscripts	8 (3.6)
Aprima	8 (3.6)
Other*	55 (25.0)
U.S. regions	
South	98 (44.5)
West	48 (21.8)
Northeast	42 (19.1)
Midwest	32 (14.5)
Practice-level patient characteristics (mean (SD))	
Proportion of patients ≥ 65 years old	0.46 (0.09)
Proportion of female patients	0.77 (0.05)
Proportion of non-white patients	0.25 (0.22)
Proportion of non-commercial insurance	0.54 (0.16)
*Other included any EHR used in < 2% of practices, including Lytec MD, Medent, Medisoft, Raintree System IC, MD office, Integrity, Carecloud, MedTrio, Greenway/Primesuite, iPatientCare, Prime Clinical System, MacPractice MD, IMS, SRS EHR, PrognoCIS, Cerner, Practice Fusion, DrChrono, Chart Maker Clinical, STI, American Medical Software, Athena Clinicals, Praxis EMR, RheumDocs, Greenway Intergy, Athena UniCharts, ChartLogic, SD: standard deviation.	

Table 1. Characteristics of practices in the RISE registry.

	Disease activity Performance % (95% CIs)	Functional status Performance % (95% CIs)
EHR type		
NextGen	55.4 (45.9, 64.9)	52.1 (42.9, 61.4)
eClinicalWorks	38.9 (26.1, 51.6)	42.3 (29.9, 54.8)
Amazing Charts	47.2 (31.4, 62.9)	51.9 (35.9, 67.8)
eMDs	**27.6 (6.2, 48.9)**	29.7 (8.3, 51.1)
GE Centricity	60.0 (37.9, 82.1)	55.9 (34.1, 77.8)
Allscripts	**29.5 (0, 27.6)**	**2.7 (0, 27.8)**
Aprima	47. 2 (22.1, 71.8)	43.9 (19.0, 68.9)
Other*	**14.8 (5.2, 24.3)**	**8.3 (0, 21.9)**

*Other included any EHR used in < 2% of practices, including Lytec MD, Medent, Medisoft, Raintree System IC, MD office, Integrity, Carecloud, MedTrio, Greenway/Primesuite, iPatientCare, Prime Clinical System, MacPractice MD, IMS, SRS EHR, PrognoCIS, Cerner, Practice Fusion, DrChrono, Chart Maker Clinical, STI, American Medical Software, Athena Clinicals, Praxis EMR, RheumDocs, Greenway Intergy, Athena UniCharts, ChartLogic,
Marginal means estimated using multivariate regression models.
Confidence intervals <0 were truncated.
Bold performance and CI results indicate the EHR vendor in this row is statistically significant different from NextGen ($p<0.05$).

Table 2. Association of EHR type with PRO documentation.

Background/Purpose: Routine collection of disease activity and patient reported outcomes (PROs) such as functional status assessment in rheumatoid arthritis (RA) are nationally endorsed quality measures and an important component of tracking outcomes and improving care. However, little is known about the health information technology barriers and facilitators to the routine collection of disease activity and PROs in rheumatology practice: there may be features of specific electronic health record (EHR) systems used by rheumatologists that facilitate collection of RA outcomes. Using the American College of Rheumatology's RISE registry of practices across the U.S., we analyzed the relationship between EHR type and performance on RA disease activity and functional status quality measures.

Methods: We analyzed 2018 data from practices enrolled in RISE. Our primary outcome was practice-level performance on 2 quality measures: (1) Disease activity assessment for patients with RA (the percentage of patients in a practice whose disease activity was assessed using a standardized tool at ≥ 50% encounters during 2018); (2) Functional status assessment for patients with RA (the percentage of patients in a practice whose functional status was assessed using a standardized tool at least once during 2018). Multivariable linear regression models were used to examine the independent effect of EHR type on practice-level performance after adjusting for practice characteristics (practice type, size, and geographic region). To account for differences in case mix, we also adjusted for aggregate characteristics of patients seen in the practice (proportion of patients≥65 years, proportion female, proportion non-White, and proportion with non-commercial insurance).

Results: We included 220 practices who cared for 314,793 patients; the median (IQR) number of patients per practice was 982 (397, 1993). Most were single-specialty group practices (53.2%). NextGen was the most commonly used EHR vendor (48.1%), followed by eClinicalWorks (15.8%; Table 1). Overall, mean (SD) practice-level performance was 39% (37) for disease activity and 34% (38) for functional status. Even after adjusting for practice characteristics and patient case mix, performance on disease activity and functional status assessments was dramatically lower in some practices with less commonly used EHRs (Table 2).

Conclusion: Among practices participating in RISE in 2018, we found significant variation in performance on RA disease activity and functional status PRO measures across EHRs, even after adjusting for practice characteristics and case-mix. Although a causal relationship cannot be determined here, future research should investigate whether

features of EHRs that facilitate rheumatology practice, such as the ability to enter PRO data into structured fields, may facilitate higher quality of care. Sharing features and developing rheumatology-specific standards for EHRs could help promote the routine collection of RA measures, which in turn could improve RA outcomes.

Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

Keywords:

EHRs, quality measures

Disclosure: N. Hammam, None; **G. Schmajuk**, None; **J. Li**, None; **M. Evans**, None; **J. Kay**, None; **J. Yazdany**, Eli Lilly, 1, Astra Zeneca, 1.

Abstract Number: 1601

Pilot Testing Supports Utility of a Point-of-Care Dashboard to Enhance Patient and Clinician Partnerships in the Management of RA

Stephanie Mathew[1], John Mecchella[1], Lisa Johnson[2], Aricca Van Citters[2], Stacy Courtnay[3], Jennifer Marden[4], Jabeen Ahmad[2], Guy Eakin[5], Eugene Nelson[2], Salahuddin Kazi[6] and Scott Pompa[1], [1]Dartmouth-Hitchcock Medical Center, Lebanon, NH, [2]The Dartmouth Institute for Health Policy & Clinical Practice, Lebanon, NH, [3]Patient Partner, Atlanta, GA, [4]Dartmouth-Hitchcock Medical Center; Patient Partner, Lebanon, NH, [5]Arthritis Foundation, Atlanta, GA, [6]Veterans Affairs North Texas Healthcare System / UT Southwestern Medical Center, Dallas, TX

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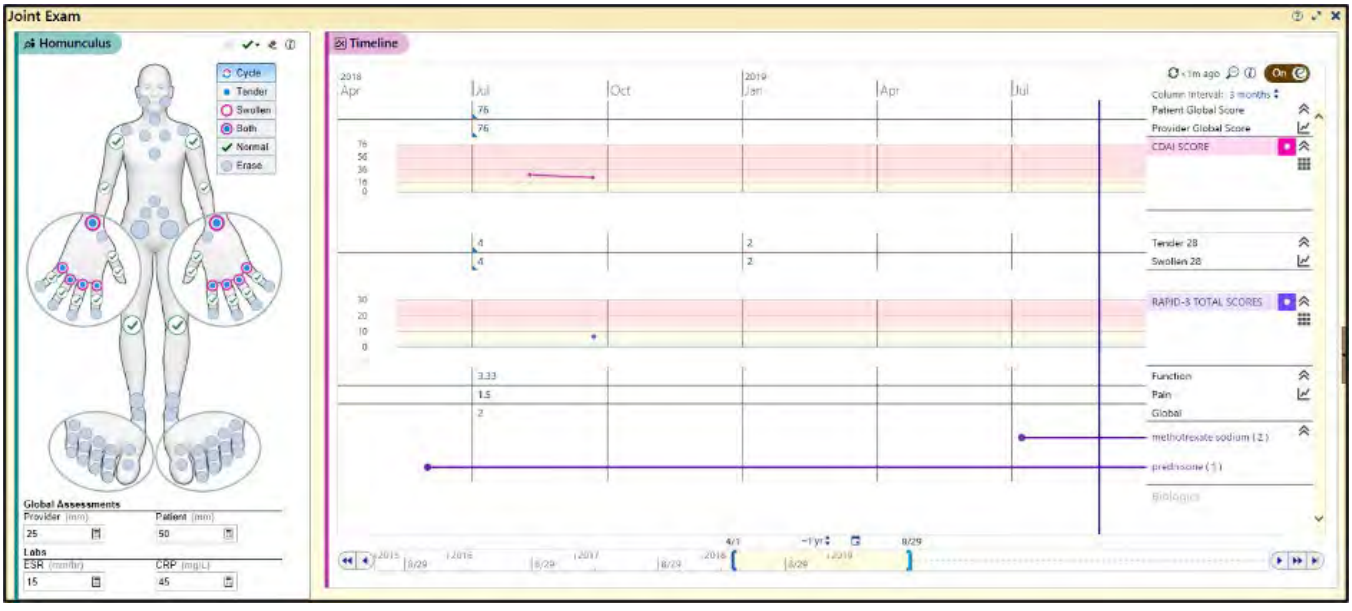

Figure 1. Rheumatology Dashboard (Epic Electronic Health Record) © 2020 Epic Systems Corporation. Used with Permission.

Background/Purpose: Increasing evidence exists that health outcomes are improved when people living with a chronic condition partner with their clinicians to coproduce their care based on their values, preferences, goals, and the best scientific evidence. This partnership may be aided by a data display tool, or dashboard, that presents longitudinal patient-reported outcomes (PROs), clinical data, and medications and is reviewed together to co-assess health status and co-decide next steps in the plan of care. This study assesses the utility of a dashboard to support coproduction of care for adults with RA.

Methods: We pilot tested the rheumatology dashboard with two rheumatologists and their adult RA patients at a rural academic health system. The dashboard resides within the Epic electronic health record and aggregates PROs and clinical data in real-time for review by the patient and clinician together (**Figure 1**). PRO data include the Routine Assessment of Patient Index Data (RAPID3); and, clinical data include the Clinical Disease Activity Index. RA-specific medications (Biologics, DMARDs, steroids, NSAIDs) map to the dashboard. Consecutive RA patients completed a a 19-item survey following their clinic visit to assess the impact of the dashboard on communication and shared decision making with their clinicians. Data were collected between January and March 2020. Feedback from clinicians was collected during biweekly meetings with the research team.

Results: Nineteen consecutive adult RA patients completed the post-visit survey. Mean (SD) age was 57 (12), 79% were female, 56% had a greater than high school education, and 39% had actively flaring RA (self-assessed). Three-quarters of patients (14 of 19) submitted pre-visit questionnaires (RAPID3) prior to their visit. Of those patients, 74% discussed the RAPID3 results with their clinician, and the clinician shared the dashboard in almost every visit that they discussed the RAPID3 (13 of 14). Two-thirds of patients (9 of 14) felt that the data and information in the dashboard was useful in discussions with their clinicians, helped them talk about what matters most, and helped them work with their clinician to make healthcare decisions. Half (7 of 14) felt that the dashboard helped them create a care plan that they could act on at home. Less than a third (4 of 14) thought that the data and information changed the content or focus of the discussion. Two thirds of patients (9 of 14) would recommend the dashboard to a friend or colleague with RA. Clinicians valued the ability to review and discuss with patients their disease activity over time and the impact of medications on their health status. Limitations included the small sample size as a result of decreased in-clinic visits during the study timeframe due to Covid-19.

Conclusion: Our study demonstrates that the rheumatology dashboard supports in-person review and discussion of PROs and clinical data and facilitates a meaningful dialogue and shared decision making between RA patients and their clinicians. Additional efforts are ongoing to spread the dashboard use to other clinicians in the department and to determine optimal use of the dashboard during telehealth visits.

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Abstract Number: 1602

Assessing the Psychometric Properties of a Measure of Patient Empowerment with Patients with Arthritis

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Background/Purpose: The Health Care Empowerment Questionnaire (HCEQ) was developed for use in a general sample of patients to measure individual empowerment in health care and services (Gagnon et al., 2006), which can be considered an aspect of experience of care. The aim of this study was to validate the HCEQ, a patient-reported experience measure (PREM), for use with patients with arthritis and other rheumatic diseases by assessing its psychometric properties.

Methods: Data were collected from a convenience sample of adults with arthritis through online surveys administered between March 2019 to March 2020 through the Arthritis Foundation's LiveYes! INSIGHTS program. Experiences and importance of patient empowerment were measured using two domains of the HCEQ: Involvement in Decisions (6 items), which we call Patient Information Seeking, and Involvement in Interactions (8 items), which we call Result of Self-Advocacy. A larger sample was used to assess HCEQ internal consistency through Cronbach's alphas for each of the two subscales, as well as its measure structure through a confirmatory factor analysis (CFA; n=9229). A sub-sample of participants meeting inclusion criteria, including having completed the survey twice within 7 to 14 days, was used to assess test-retest reliability through Pearson correlation coefficients (n=186). Information on face validity was gathered from another sample of patients through qualitative data collection methods (n=5-59).

Results: After appropriate modifications, the CFA indicated good fit to the data for the two-factor structure of the HCEQ with this population, according to model fit indices (RMSEA = .047; CFI = .997; TLI = .993; SRMR = .012). The exception was the chi square, which was significant ($X^2 = 214.150$, $p < .001$), though this is susceptible to error when there are large sample sizes, as is the case here. Internal consistency was strong, with a Cronbach's alpha of .94 for both Patient Information Seeking and Result of Self-Advocacy. Test-retest reliability was moderate for Patient Information Seeking (r=.67) and good for Result of Self-Advocacy (r=.77). Qualitative data analysis indicated adequate face validity of the HCEQ for patients with arthritis.

Items by Subdomain	Lead-in and Response Options*	
	During the last 6 months, did you feel that...	*During the last 6 months, how important is it that...*
Patient Information-Seeking	Not at all (1)	Not important at all (1)
You asked for explanations	Somewhat (2)	Slightly important (2)
You asked questions	Quite a bit (3)	Very important (3)
You asked for advice	Very much (4)	Extremely important (4)
Result of Self-Advocacy		
You were able to talk to a professional to answer your questions		
Your choices were respected		
You obtained all the information you wanted		
You got the help you needed		

Note: Respondents rated feeling and importance of each item. Scores are calculated by summing the cross-product of feeling and importance ratings for items within the subdomain. There are three items in the Involvement in Decision subdomains and four items in the Involvement in Interactions, so the possible ranges are 3-48 points and 4-64 points, respectively.

Subdomains of the HCEQ, including items on each subdomain, lead-in to the items, and response options.

Conclusion: The HCEQ demonstrates promising psychometric properties when used with a sample of patients with arthritis and other rheumatic diseases. This lays the foundation for future work assessing additional psychometric properties of the HCEQ and examining patients' experiences with and desire for empowerment both for individuals with arthritis and in comparison to individuals with other conditions.

Disclosure: E. Knight-Zhang, None; **K. Carluzzo**, None; **K. Schifferdecker**, None; **E. Creek**, None; **R. Butcher**, None; **G. Eakin**, None.

Abstract Number: 1603

P4 Index Correlates with RAPID3 and Disease-Specific Indices in Rheumatoid Arthritis (RA) and Axial Spondyloarthritis (axSpA)

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Session Time: 9:00AM–11:00AM

Background/Purpose: RAPID3 scores correlate well with disease-specific indices, including the Clinical Disease Activity Index (CDAI) in RA and Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) in axSpA, and are being widely used in clinical practice[1,2]. However, being a patient-reported outcome, RAPID3 can be affected by additional sources of pain, including fibromyalgia, prior joint damage, and psychosocial reasons such as anxiety or depression. Adding a physician global estimate (MD Glob) to RAPID3 (we termed it P4 index: pain, physical function, patient global, and physician (MD) global) may add an objective component and help filter out extraneous factors affecting disease activity measurements. In this observational study, we assessed performance of P4 index by comparing it against RAPID3 and CDAI in RA and RAPID3 and BASDAI in axSpA patients.

Methods: Consecutive patients with RA and axSpA under the care of three clinicians at one academic Rheumatology center completed the Multidimensional Health Assessment Questionnaire (MDHAQ) during their clinic visits with RAPID3 scores subsequently calculated. CDAI and BASDAI scores, respectively, were also recorded at the same visit and the clinician would separately report a physician global estimate (MD Glob) in the Electronic Medical Record. P4 score was calculated by adding MD Glob to the RAPID3 score (score range 0 to 40). Statistical significance between all scores was analyzed using Spearman correlation coefficients. Subgroup analysis was performed including only RA and axSpA patients with concomitant osteoarthritis, fibromyalgia, or anxiety/depression.

Results: We enrolled 40 patients with RA and 17 patients with axSpA; additional enrollment was limited by the coronavirus pandemic. Among RA patients, the mean (SD) CDAI was 8.8 (10.1), mean (SD) RAPID3 was 8.48 (7.9), and mean (SD) P4 was 11.2 (9.7). CDAI and RAPID3 correlated significantly (rho=0.91, $p< 0.001$). CDAI and P4 also correlated significantly and at somewhat higher levels than RAPID3 (rho=0.95, $p< 0.001$). Similar results were noted in subgroup analysis for RA patients (Table 1). Among axSpA patients, the mean (SD) BASDAI was 4.6 (2.5), mean (SD) RAPID3 was 12.7 (8.1), and mean P4 was 16.7 (9.9). BASDAI and RAPID3 correlated significantly (rho=0.81, $p< 0.001$). BASDAI and P4 also correlated significantly at a similar level (rho=0.82, $p< 0.001$). Subgroup analysis of axSpA patients showed similar results (rho=0.87 vs 0.88, see Table 2).

Table 1a. Spearman correlation coefficients for CDAI, RAPID3, and P4 indices in patients with RA (n=40)		
p<0.001 for all comparisons	CDAI	RAPID3
P4	0.9460	0.9838
RAPID3	0.9087	
Table 1b. Spearman correlation coefficients for CDAI, RAPID3, and P4 indices in RA patients with concomitant osteoarthritis, fibromyalgia, or anxiety/depression (n=30)		
p<0.001 for all comparisons	CDAI	RAPID3
P4	0.9459	0.9773
RAPID3	0.9040	

Table 2a. Spearman correlation coefficients for BASDAI, RAPID3, and P4 indices in patients with axSpA (n=17)		
p<0.001 for all comparisons	BASDAI	RAPID3
P4	0.8196	0.9933
RAPID3	0.8134	
Table 2b. Spearman correlation coefficients for BASDAI, RAPID3, and P4 indices in axSpA patients with concomitant osteoarthritis, fibromyalgia, or anxiety/depression (n=14)		
p<0.001 for all comparisons	BASDAI	RAPID3
P4	0.8845	0.9923
RAPID3	0.8711	

Tables 1 and 2

Conclusion: Our study demonstrates a high degree of correlation between P4 index and RAPID3 as well as validated disease-specific activity indices in both RA and axSpA patients. P4 index has an objective component in the form of MD Glob that may help to adjust for extraneous factors affecting disease activity measurement and management decisions. It would be important to confirm our findings in subsequent larger studies. Overall, using the P4 index may be a quick and practical way to more reliably trend disease activity in RA and axSpA.

1. Pincus T, et al. (2010) Arthritis Care & Research, 62(2):181-189.

2. Danve A, et al. (2015) J Clinical Rheumatology, 34:117-124.

Disclosure: A. Danve, Novartis, 1, 2, Abbvie, 5, Medscape, 5, Peerview, 8; **B. Hsiao**, None; **P. Zhang**, None.

Abstract Number: 1604

The Impact of the COVID-19 Pandemic on Rheumatology Practice: A Study in 15 Arab Countries

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Measures & Measurement of Healthcare Quality Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: To date, information about the impact of the Coronavirus Disease (COVID-19) pandemic on rheumatology practice and on rheumatologists is limited.

The primary objective of the study was to evaluate the impact of the COVID-19 pandemic on rheumatology practice in the Arab countries. Secondary objectives were to evaluate the impact of COVID-19 on the rheumatologists and to develop recommendations to improve the rheumatology practice.

	Levant	Gulf	North Africa	All	p
Number (%)	255 (30%)	173 (20%)	424 (50%)	**858**	
Participation rate (% of all rheumatologists)	68.0	43.6	17.7	**27.0**	
Age Groups, N (%)					
25-34	21 (12%)	92 (36%)	93 (22%)	**207 (24%)**	<0.001
35-44	76 (44%)	70 (28%)	172 (41%)	**312 (37%)**	
45-54	50 (29%)	42 (17%)	84 (20%)	**179 (21%)**	
55-64	22 (13%)	40 (16%)	62 (15%)	**124 (15%)**	
65-74	3 (2%)	10 (4%)	12 (3%)	**25 (3%)**	
Male Gender, N (%)	137 (54%)	96 (56%)	106 (25%)	**341 (40%)**	<0.001
Rheumatology practice, Mean years (SD)	11.8 (10.6)	11.9 (8.1)	15.0 (9.5)	**13.4 (9.7)**	0.001
Sector, n (%)					
- **Private sector**	150 (59%)	50 (29%)	208 (49%)	**412 (48%)**	<0.001
- **Public sector**	112 (44%)	114 (66%)	91 (22%)	**319 (37%)**	
- **University hospital**	117 (46%)	43 (25%)	223 (53%)	**386 (45%)**	
Institution implicated in COVID-19 frontline, N (%)	81 (33%)	100 (59%)	121 (34%)	**304 (39%)**	<0.001
Physician involved in COVID-19 frontline, N (%)	45 (18%)	50 (29%)	90 (21%)	**187 (22%)**	<0.001

Table 1. Characteristics of the 858 rheumatologists

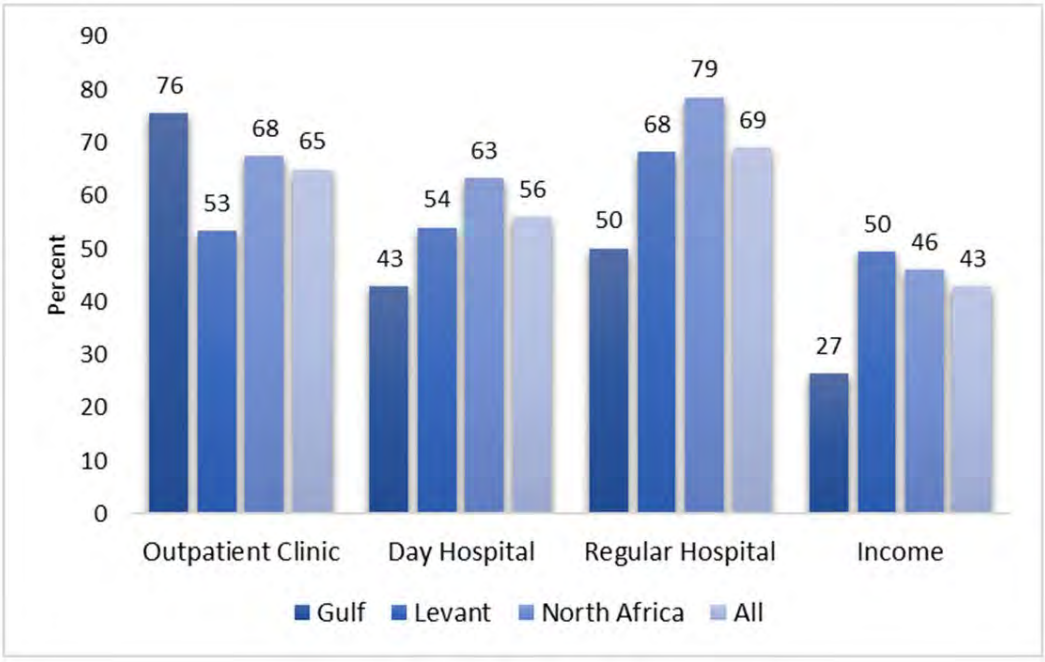


Figure 1. Impact of the COVID-19 on the rheumatology practice (outpatient clinic, day hospital, hospital and income).

Variable	OR*	95% CI		p-value
Region				
North Africa	1			<0.001
Levant	0.268	0.166	0.434	<0.001
Gulf	0.598	0.383	0.935	0.024
Using telemedicine	1.712	1.199	2.443	0.003
Impact on income	1.011	1.005	1.018	<0.001
Private sector	0.477	0.292	0.779	0.003

*After adjusting on: age, agreeing using telemedicine, institution with COVID-19, frontline management of COVID-19, patient with COVID-19, HCQ shortage, personal infection with SARS-CoV-2, sectors' number

Table 2. Factors associated with a higher impact on the outpatient clinic activity

Methods: A cross-sectional 21-items web survey was designed by members of the Arab League of Associations for Rheumatology (ArLAR) and validated by its scientific committee in English and in French. The survey was disseminated by e-mail and on social media to all rheumatologists in the 15 ArLAR countries. It comprised 19 close-ended questions about demographic characteristics, impact of the pandemic on the activities (in percentage, where 100% corresponds to complete suspension), attitude towards telemedicine, and two open-ended questions about the unmet needs and the ways to improve the practice. Recommendations were developed to improve practice during the pandemic.

Results: Between May 9 and May 24, 2020, 858 rheumatologists were included in the analysis (27.3% of registered rheumatologists in the ArLAR countries), 37% were in the 35-44 years age category, 60% were females and 48% worked in the private sector (Table 1). The impact of COVID-19 on the rheumatology practice was significant (Figure 1), with a decrease of 69% on hospitalization, 65% on outpatient clinic, 56% on infusion centers and 43% on income. A higher impact on the outpatient clinic activity was associated with the region (highest impact in North Africa, lowest

in the Levant), using telemedicine, and impact on income, The higher impact was negatively associated with working in the private sector (compared to the public sector and university teaching hospitals) (Tabl2 2). Telemedicine was used in 70% of cases, but mostly based on traditional telephone contacts and e-mails, and was reimbursed in only 12%. The mental impact related to the stress caused by COVID-19 was reported in 77% of the respondents (minor in 60.4%, major in 16.7% of cases). Fifteen rheumatologists (1.8%) were personally infected. The participants reported 156 cases of COVID-19 among their patients, of whom 22% died. The top-cited unmet needs were: access to drugs and a telemedicine platform.

Conclusion: The COVID-19 pandemic had a significant negative impact on the rheumatology practice in the Arab countries. Accordingly, better access to drugs and providing telemedicine platforms are recommended to improve rheumatology practice in the region.

Disclosure: N. Ziade, None; **I. Hmamouchi**, None; **L. El Kibbi**, None; **N. Abdulateef**, None; **H. Halabi**, None; **F. Abutiban**, None; **W. Hamdi**, None; **M. el Rakawi**, None; **M. Eissa**, None; **B. Masri**, None.

Abstract Number: 1605

Knowledge of Biosimilars and Perceptions of Biosimilar Naming Conventions in Clinical Practice

Criswell Lavery[1], Marianna Olave[2], Charles Leonard[1], Vincent Lo Re[1], Jonathan Kay[3] and Joshua Baker[1], [1]University of Pennsylvania, Philadelphia, PA, [2]Corporal Michael J. Crescenz VA Medical Center, Philadelphia, PA, [3]University of Massachusetts Medical School, Worcester, MA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The market introduction of biosimilars has generated the need for novel biologic naming conventions, in part to support pharmacovigilance. We evaluated the familiarity of health care practitioners and other clinical professionals with biosimilars and their perceptions regarding the Food and Drug Administration's (FDA's) nomenclature for biologics in clinical practice. We hypothesized that health care providers would be unfamiliar with key concepts surrounding biosimilars and the FDA four-character suffix and would vary in their perceived value of the naming guidance in clinical practice.

Methods: A survey was emailed every two weeks over a two-month period to health care professionals within two large health care systems in the Philadelphia area: University of Pennsylvania Health System and the Corporal Michael J. Crescenz VA Medical Center. The survey was sent to prescribers and other health care administrators such as pharmacists, nurses, and medical coders. Prescribers received a survey if they had previously prescribed at least one biosimilar therapy from a query of prescription data from the electronic medical record. The survey assessed knowledge of key aspects of biosimilar therapies and the perceived utility of the FDA naming convention in practice. Differences in responses across prespecified sub-groups were tested using c^2 and Fisher's exact tests.

Results: The survey was sent to 506 prescribers and other clinical staff; 50 were returned from inactive email addresses. Of the remaining 456, 83 (~18%) responded. Most were from the University of Pennsylvania, with the highest number of responses coming from the Divisions of Hematology/Oncology and Rheumatology, and the Department of Pharmacy. Of respondents that identified being 'out of training', 14 (45%) had >10 years of clinical experience. Of

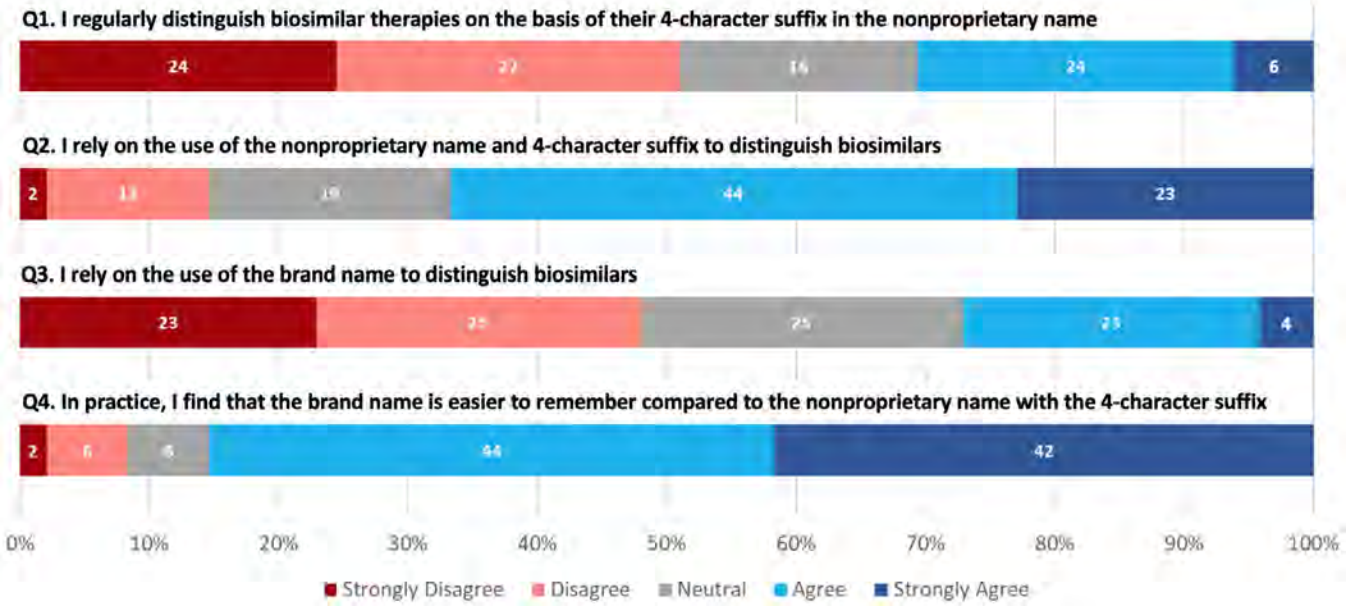
Table 1. Biosimilar

	Answered Correctly	Answered Incorrectly	p-value
K1. A biosimilar that has been approved by a regulatory body through a highly regulated pathway has a similar efficacy and comparable safety and immunogenicity compared to the originator product. (True)			
Overall	67 (81%)	16	
Prescribers	51 (77%)	15	0.17
Administrators	16 (94%)	1	
Those who use biosimilars	48 (96%)	2	<0.001
Those who don't use biosimilars	19 (58%)	14	
K2. Biosimilars are generics of originator biologic drugs. (False)			
Overall	43 (52%)	40	
Prescribers	28 (42%)	38	<0.001
Administrators	15 (88%)	2	
Those who use biosimilars	31 (52%)	29	0.04
Those who don't use biosimilars	12 (36%)	21	
K3. A biologic must have the exact amino acid sequence as the originator product. (True)			
Overall	26 (31%)	57	
Prescribers	21 (32%)	45	1
Administrators	5 (29%)	12	
Those who use biosimilars	22 (44%)	28	0.003
Those who don't use biosimilars	4 (12%)	29	
K4. Biosimilars are "interchangeable" with the originator product. (False)			
Overall	29 (35%)	54	
Prescribers	20 (30%)	46	0.14
Administrators	9 (53%)	8	
Those who use biosimilars	19 (38%)	31	0.63
Those who don't use biosimilars	10 (30%)	23	
K5. There is similar variability between originator product lots as there is a variability between biosimilars and originator products. (True)			
Overall	43 (52%)	40	
Prescribers	34 (52%)	32	1
Administrators	9 (53%)	8	
Those who use biosimilars	33 (66%)	17	0.003
Those who don't use biosimilars	10 (30%)	23	

This table includes the results of True and False questions designed to test knowledge of basic concepts of biosimilar therapies. All respondents are stratified by Prescribers vs. Administrators, and Those who use biosimilars vs. Those who don't use biosimilars in practice. For the purposes of these questions, "Those who use biosimilar drugs" includes both Prescribers as well as Administrators who encounter biologics. The correct answer is included at the end of the question. Total correct answers shown alongside in percentages. Incorrect totals include any marked 'Unsure' responses.

those still 'in training', 27 (93%) were residents or fellows. Although respondents had a general understanding of the regulatory criteria for approval, knowledge about biosimilars was generally poor (**Table 1**). For example, only 52% of all respondents correctly identified that a biosimilar differed from a generic drug. When asked about biosimilar

Figure 1. Biosimilar Use

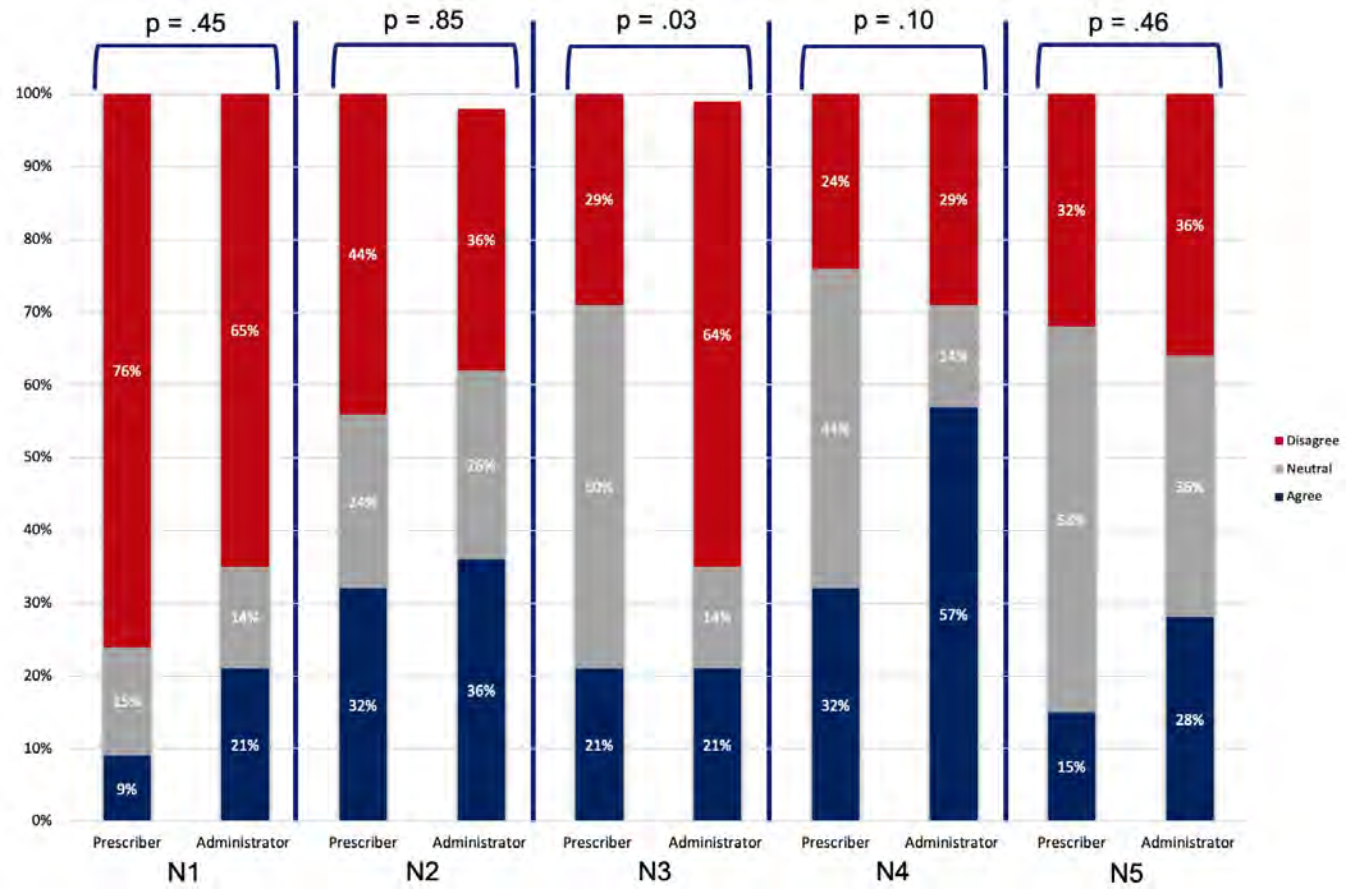


Questions related to general use of biosimilar identifiers in clinical practice. All questions included: To what degree do you agree with the following?

naming conventions, 67% reported using the brand name in clinical practice to distinguish between biosimilars and reference products. In contrast, as shown in Figure 1 (**Q1**), only a minority of respondents reported regular use of the four-character suffix to identify biologic therapies. Overall, there was little agreement on the utility of the four-character suffix in many aspects of care. For example, a majority of respondents (68% overall) indicated a neutral response when asked if the four-character suffix promoted medical errors (**Figure 2, N5**). Most prescribers (76%) disagreed that the 4-character suffix affected their decision to use biosimilars.

Conclusion: These survey findings suggest a knowledge gap with regard to biosimilars and lack of consensus about the usefulness of employing the four-character suffix in clinical practice. The lack of overall familiarity with biosimilars may also have contributed to a lack of comfort with the naming convention.

Figure 2. Naming Preference



Questions regarding naming preferences. All questions included: To what degree do you agree with the following? The questions are detailed below: N1. I am less likely to use biosimilars compared to the originator product because the nonproprietary names of biosimilars are different from the originator product. N2. I have experienced that the use of brand names to distinguish biosimilars introduces commercial bias in clinical practice. N3. The 4-character suffix in the non-proprietary name influences patients to think there are important differences between biosimilars and the originator products. N4. The 4-character suffix in the nonproprietary name causes inefficiencies due to inconsistencies with other naming systems in practice. N5. The use of the 4-character suffix in the nonproprietary name to distinguish biosimilar therapies in practice promotes medication errors in the ordering of biologics.

Disclosure: C. Lavery, None; **M. Olave**, None; **C. Leonard**, None; **V. Lo Re**, None; **J. Kay**, Pfizer Inc., 9, Alvotech Suisse AG, 1, Arena Pharmaceuticals, Inc., 1, Boehringer Ingelheim GmbH, 1, Celltrion Healthcare Co. Ltd., 1, Mylan Inc., 5, Novartis AG, 5, Samsung Bioepis, 5, Sandoz Inc., 5, Gilead Sciences, Inc., 9; **J. Baker**, None.

Abstract Number: 1606

Mortality with Idiopathic Inflammatory Myositis in an Academic Hospital Setting: A Five-year Retrospective Study

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Idiopathic inflammatory myositis is a diverse group of muscle diseases characterized by muscle inflammation and dysfunction. Approximately 3-7/100,000 cases are diagnosed per year in the United States. Eight major subgroups were defined in the 2017 EULAR/ACR classification criteria including polymyositis and dermatomyositis. Recent availability of specific antibodies has helped to further phenotype myositis. Historically, these diseases have been associated with poor prognosis as many patients suffer interstitial lung disease, malignancies,

Table 1. Characteristics of Myositis Patients Admitted (n=20)	
Mean Age	53
Females	13/20 (65%)
Average CK (Min, Max)	5621 (23, 18128)
Myositis-Specific-Antibodies (MSA) Tested	17/20 (85%) • 0 MSA tested: 3 (15%) • 1-3 MSA tested: 9 (45%) • 8 MSA tested: 5 (25%) • 11 MSA tested: 3 (15%)
Positive MSA	9/17 (52%) PL7/SRP, JO1, SRP, Mi2, CN1a, PL7, CN1a, SRP, MDA5
Malignancy	2/20 (10%)
ILD	8/20 (40%)
Swallow Study Completed	9/20 (45%)
Mortality	5/20 (25%)

Table 1. Characteristics of Myositis Patients Admitted

Table 2. Characteristics of Deceased Myositis Patients (n=5)	
Mean Age	60.8
Females	2/5 (40%)
Average CK (Min, Max)	1536 (49, 3156)
Myositis-Specific-Antibodies (MSA) Tested	3/5 (60%) • 0 MSA tested: 2/5 (40%) • 1-3 MSA tested: 1/5 (20%) • 8 MSA tested: 1/5 (20%) • 11 MSA tested: 1/5 (20%)
Positive MSA	2/3 (66%) patients tested MSA+ Mi2, MDA5
Malignancy associated	1/5 (20%)
ILD associated	4/5 (80%)
Swallow Study Completed	1/5 (20%)
Spirometry Completed	4/5 (80%)

Table 2. Characteristics of Deceased Myositis Patients

and infections. In fact, 10-year survival rates for myositis varies from 57-71% depending on the cohort analyzed. A low threshold for diagnosis, treatment and medication escalation is important due to the significant morbidly and mortality.

The aim of our study was to assess prevalence and mortality rate of patients with inflammatory myositis admitted to University of Florida Health-Jacksonville in the past 5 years. The goal was to determine factors associated with mortality in this patient population that could be modified in future. Ultimately, this study is to aid in the development of institutional protocols to improve survival of patients with inflammatory myositis.

Methods: Retrospective evaluation of patients admitted with inflammatory myositis and mortality during the hospitalization was completed by electronic medical record review from 1/1/2014-12/31/2018. Patients were generated by providing the Information Technology department with a list of International Classification of Disease (ICD) 9 and 10 diagnosis codes related to myositis.

Results: The search generated yielded 1489 charts, of which 46 patients were identified as idiopathic inflammatory myositis. Of these patients, 20 were specifically admitted for worsening myositis features with a mortality of 5 patients, yielding a 25% mortality rate. Characteristics of myositis patients admitted and deceased are given in Tables 1 and 2. The major causes of death were respiratory failure and dysphagia. We noted 3/5 patients had mortality related to dysphagia and 2/5 patients had mortality related to respiratory failure. We also noted 4/5 deceased patients suffered from interstitial lung disease and only 1/5 had a swallow study, 4/5 had spirometry completed, and 3/5 patients had myositis-specific-antibodies tested.

Conclusion: Although dysphagia and interstitial lung disease are known features of myositis clinical syndromes, they portended a worse prognosis for our myositis population. This study highlighted the importance of aspiration and respiratory monitoring in patients suffering from inflammatory myositis as related to mortality. Process improvement should include routine evaluation of swallowing, precautions for aspiration as well as monitoring negative inspiratory function in patients admitted with myositis. In addition, obtaining myositis-specific-antibodies may be beneficial to risk stratify patients that may be resistant to treatment, leading to mortality.

Disclosure: J. Kaler, None; **Z. Vaghaiwalla**, None; **G. Kaeley**, Novartis Pharmaceuticals Corporation, 5; **M. Thway**, None.

Abstract Number: 1607

Effectiveness of Dietary Counseling on Gout Management and Risk Factors for Metabolic Syndrome in Gout Patients

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Gout is the most prevalent inflammatory arthritis globally. Despite treatment advances, the prevalence of gout has continued to increase over the last several decades. There has also been increasing evidence

that gout has a strong association with the metabolic syndrome. This suggests that gout is likely both an inflammatory and a metabolic disease that has a significant effect on quality of life and healthcare costs. While current recommendations support aggressive medical therapy for gout treatment, dietary counseling is less emphasized. We hypothesize that emphasis on nonpharmacological therapy will likely improve management and the metabolic syndrome in gout patients.

Methods: A retrospective cohort study was created from 2009-2016 involving Long Beach Veterans Affairs Hospital gout patients (n= 130) based on International Classification of Disease version 9 or 10. Patients were then stratified into two cohorts: received diet counseling (n=100) and no diet counseling (n=30). Data was reviewed for 24 months following initial gout diagnosis or intervention. Management was evaluated based on frequency of flares and related ED visits, change in creatinine clearance, serum uric acid levels (sUA), and changes to risk factors for metabolic syndrome including blood pressure, body mass index (BMI), cholesterol panel and hemoglobin A1c levels (HA1c) at six-month intervals.

Results: Although patients in both cohorts had a trend of fewer gout attacks with time, those who received diet counseling had a significant decrease in number of attacks by 12 months ($p = 0.002$), and more so in 18 months ($p = 0.001$). After diet counseling, more patients reached their target sUA (sUA< 6 for nontophaceous gout and sUA< 5 for tophaceous gout) ($p = 0.002$) in 6 months and remained at goal at 24 months ($p < 0.001$), with improved creatinine clearance ($p = 0.06$) and HDL ($p = 0.08$). Patients with improved LDL and HDL values were more likely to have improved sUA levels (R^2=0.4, slope 0.03 and R^2=0.4, slope 0.16, respectively) by 6 months. Patients with improved HA1c and LDL values had fewer ED visits within the first 6 months (R^2=0.4, slope 0.14 and R^2=0.4, slope 0.05, respectively). Patients with improved HA1c were associated with decreased sUA at18 months (R^2=0.5, slope 0.2).

Conclusion: Gout patients who receive diet counseling had better control of sUA and a lower rate of future attacks and ED visits. Risk factors associated with metabolic syndrome improved in these patients, with better control of their HA1c, LDL and HDL, and they achieved lower sUA levels. This implies that controlling diabetes and hyperlipidemia in patients may help improve gout management. Given the serious complications and increased cardiovascular risks that can be associated with metabolic syndrome, optimization of gout through a nonpharmacologic intervention such as diet counseling can enhance clinical outcomes and optimize healthcare resources.

Disclosure: J. Chang, Gilead, 1; **J. Tsui**, None; **M. Wong**, None.

Abstract Number: 1608

Survey of Minimally-Invasive Ultrasound-Guided Synovial Biopsy Performed at Rheumatology Centres

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

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Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Ultrasound-guided synovial biopsy (USGSBx) is a well-established minimally-invasive alternative to arthroscopy for sampling synovial tissue. Adverse event rates in published studies are favourable by comparison with arthroscopy, but a large-scale evaluation of the safety of these procedures is required.

Methods: A survey of USGSBx safety and practice was devised within the European Synovitis Study Group (ESSG). Respondents were asked to complete either an online web-form, or a spreadsheet data-collection tool encompassing centre-level information regarding facilities and training for USGSBx, anonymised information about USGSBx practitioners, and a comprehensive list of USGSBx procedures with any resultant complications. A systematic literature search was performed and email survey invitations sent to individuals featuring on publications reporting the use of USGSBx. ESSG members, and those known to be involved in USGSBx as part of a network or collaboration were also invited, and respondents asked to identify any other centres in their country believed to be performing USGSBx. One response was requested per centre.

Results: The first 15 responses from centres in 11 countries and encompassing 35 practitioners are presented. 10 centres reported performing USGSBx needle biopsies, and 7 using the portal & forceps technique. 8 centres arranged for routine patient follow-up face-to-face, with 5 centres following patients by telephone. 8 centres routinely issued patients with an alert card after their procedure.

1874 biopsies were reported, 1252 (67%) performed primarily for research, and 622 (33%) for a clinical indication. Intra-articular steroid was administered after 162 (8.6%) of the procedures. Procedures performed on 15 anatomical structures were reported, with the most commonly sampled being the knee (54%), wrist (29%), metacarpophalangeal (6%), ankle (5%), elbow (1%), shoulder (1%), metatarsophalangeal (1%), hip (1%) and proximal interphalangeal (1%)

	Frequency of complications	
	n	%
No reported complication	**1671**	**89.2%**
Total of reported complications	**210**	**11.2%**
Resolving arthralgia or local pain requiring analgesia	132	7.0%
Reaccumulation of fluid requiring review	24	1.3%
Presyncopal episode	13	0.7%
Prolonged superficial bleeding	9	0.5%
Post-procedure flare of arthritis	6	0.3%
Mild superficial haematoma	5	0.3%
Nerve damage - transient	4	0.2%
Wound infection	3	0.2%
Haemarthrosis	3	0.2%
Transient erythema	3	0.2%
Wound leakage	2	0.1%
*Tendon limitation without rupture	2	0.1%
Anxiety	1	0.1%
*Instrument failure	1	0.1%
Mild muscular haematoma	1	0.1%
*Nerve damage - persistent	1	0.1%

Table 1. Complications arising from minimally-invasive ultrasound-guided synovial biopsy procedures (1881 reports from 1874 procedures); major complications marked with asterisk (*)

joints. Other structures sampled included tendon sheaths, subacromial and subdeltoid bursae, acromioclavicular, sternoclavicular, and naviculocuneiform joints (all < 1%).

210 complications were reported from 1874 USGSBx procedures (see Table 1). For 5 procedures, 2 complications were reported, and for one 1 further procedure, 3 complications were reported. 4 major complications (marked with asterisk) were reported (0.21%), with no report of joint infection, thrombophlebitis, or deep venous thrombosis. 8 complications (none major) were reported in 162 procedures (4.9%) during which intra-articular steroid was used, and 202 complications reported in 1517 procedures (11.8%) in which intra-articular steroid was not used. Structures in which complications rates exceeded the average of 11.2% included the naviculocuneiform joint (1/1, 100%), elbow (8/27, 30%), MTP (4/16, 25%), and knee (123/1010, 12%) joints, although the sample size for some procedures is low.

Conclusion: Preliminary results of this survey of over 1,800 procedures, support the safety and tolerability of the minimally-invasive ultrasound-guided approach as an alternative to arthroscopy for synovial biopsy procedures.

Disclosure: B. Dyke, None; **M. Maybury**, None; **S. Alivernini**, None; **J. Cañete**, None; **O. De Lucia**, None; **J. Fonseca**, None; **N. Gullick**, None; **S. Just**, None; **D. Kane**, None; **J. Koski**, Roche Holding AG-Genusschein, 1; **A. Manzo**, Pfizer, 5, 8, Bristol-Myers Squibb, 5, 8, Sanofi, 8, Abbvie, 5, 8, Eli Lilly, 8, Novartis, 8, Gilead, 5; **L. Meric de Bellefon**, None; **R. Mullan**, None; **A. Najm**, None; **A. Pratt**, None; **F. Ramirez Garcia**, None; **C. Rawlings**, None; **F. Rayner**, None; **V. Romão**, None; **I. Sahbudin**, None; **D. Tabechian**, None; **A. Filer**, roche, 2, abbvie, 8.

Abstract Number: 1609

The Accuracy of Administrative Health Data for Identifying Patients with Rheumatoid Arthritis: A Validation Study Using Medical Records in Western Australia

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The use of large administrative health datasets is increasingly important in Rheumatology for disease trends and outcome research. We established the West Australian Rheumatic Disease Epidemiological Registry containing longitudinal health data for over 10000 patients with Rheumatoid Arthritis (RA) in Western Australia (WA). Accuracy of coding for RA is essential to validity of the datasets. We investigated the diagnostic accuracy of International Classification of Diseases (ICD) based discharge codes for RA at WA's largest tertiary hospital.

Methods: Medical records for RA patients randomly selected from the hospital discharge database with ICD 10 codes (M05.00–M06.99) from 2008–2020 were retrospectively reviewed. Rheumatologist-reported diagnosis and ACR/EULAR classification were used as gold standards to determine positive predictive value (PPV) with 95% Confidence Interval (CI) for RA primary diagnostic codes.

Results: Medical chart review was completed for 87 patients (mean age 64.7 years, 67% female). Total of 80 (92%) patients had specialist confirmed RA diagnoses, while seven patients (8%) had alternate clinical diagnoses providing a PPV of 93.5% (95%CI: 89.9 to 95.86). Overall, 69 out 87 patients (79.3%) fulfilled ACR/EULAR classification criteria

Table 1: Accuracy measures of different algorithms for random sample of RA patients with one or more RA codes.

	Rheumatologist-reported diagnosis				ACR/EULAR classification criteria			
Administrative data	SN	SP	PPV	NPV	SN	SP	PPV	NPV
One or more RA primary codes	90%	28.5%	93.5%	7.6%	89.8%	16.6%	80.5%	30%
One or more RA biological infusion codes	25%	71.4%	90.9%	7.7%	20.3%	55.5%	63.6%	15.3%
Two or more RA codes including biological codes	60%	85.7%	97.9%	15.8%	56.5%	44.4%	79.6%	21%

SN=Sensitivity, SP=Specificity, PPV= positive predictive value, NPV= Negative predictive value.

Table 1. Accuracy measures of different algorithms for random sample of RA patients with one or more RA codes.

based on RA primary diagnostic codes with a PPV of 80.5% (95%CI: 76.81 to 83.7). A combination of a diagnostic RA code with biologic infusion codes in two or more codes increased the PPV to 97.9%.

Conclusion: Hospital discharge diagnostic codes in WA identify RA patients with a high degree of accuracy. Combining a primary diagnostic code for RA with biological infusion codes can further increase the PPV.

Disclosure: K. Almutairi, None; **J. Nossent**, None; **D. Preen**, None; **H. Keen**, Pfizer Australia, 8, Abbvie Australia, 8; **K. Rogers**, None; **C. Inderjeeth**, Novartis Australia, 8, Amgen, 5, 8, Kiniksa, 2, Paradigm, 2, BMS, 2.

Abstract Number: 1610

Cutaneous Side Effects of Hydroxychloroquine in Rheumatic Diseases –Combination of "Traditional" Multivariate Analysis for Risk Factors AndClassification Model Development Using Supervised Machine Learning –Single Centre Retrospective Cohort Study in India

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is associated with varied cutaneous side effects but only few studies in literature characterizing the risk factors for this. Recently machine learning tools have emerged as a promising option for predicting various outcomes. The aim of our study was to use "traditional" multivariate analysis along with novel machine learning (ML) methodology to analyze and predict for the occurrence of cutaneous side effects with HCQ usage.

Methods: Demographic, clinical details, laboratory parameters, treatment details of HCQ (dose/mg/kg, cumulative dose, duration of therapy) and coexistent DMARD prescription were collected for patients who were treated with HCQ for autoimmune rheumatic diseases from 2015 to 2019. Development of cutaneous side effects was the primary outcome of the study and the subtypes of cutaneous side effect were also noted (hyperpigmentation, photosensitivity and pruritus) retrospectively. Univariate and multivariate logistic regression for the primary outcome was done using SPSS 20.0. To develop the ML classification models for prediction of the primary outcome, we used Random Forest, Logistic Regression and K-nearest neighbour (KNN) algorithms from Python-3.0's scikit library. Hyperparameter tuning and five-fold cross validation were done for all three ML classifiers. After the three classifer models were trained, they were compared using accuracy scores on the test dataset. Precision and area under 'receiver operating curve' (AUC) of the highest accuracy model were also analyzed.

Results: Baseline characteristics of the 430 participants recruited are shown in Figure 1(A). 198 patients (46.04%) developed cutaneous side effects of which the most common was hyperpigmentation (n =182, 42.3%).15 patients stopped HCQ due to the cutaneous side effects. Figure 1(A) also shows the results of the univariate and multivariate regression analysis for development of cutaneous side effects. The risk factors identified were the cumulative dose of HCQ > 216,000 mg (OR 1.82, 1.22-2.73), combination treatment with MMF(OR 2.13, 1.10-4.09), or AZA(OR 2.05,

Figure 1A : Characteristics of HCQ cohort stratified for cutaneous side effects along with univariate analysis

	Cutaneous side effects developed	No cutaneous side effects developed	Odds ratio and confidence intervals of univariate analysis
Demographic Parameters			
Age group			
• <30 year	50	45	p= 0.233 (OR 1.00)
• 30 -60 year	117	140	p= 0.237 (OR 1.33, 0.83-2.13)
• >60 year	31	47	p= 0.092 (OR 1.68, 0.91-3.09)
Gender			
• Male	24	28	p= 0.987 (OR 1.00, 0.562-1.79)
• Female	174	204	
Co-morbidities			
• Type 2 Diabetes Mellitus	27 of 198	40 of 232	p= 0.305 (OR 1.39, 0.77-2.24)
• Hypertension	32 of 198	51 of 232	p= 0.129 (OR 1.46, 0.89-2.38)
• Dyslipidemia	14 of 198	20 of 232	p= 0.553 (OR 1.24, 0.60-2.52)
• Chronic Liver Disease	3 of 198	4 of 232	p= 0.865 (OR 1.14, 0.25-5.15)
• Hypothyroidism	28 of 198	39 of 232	p= 0.447 (OR 1.22, 0.72-2.07)
• CVA	1 of 198	5 of 232	p= 0.182 (OR 4.33, 0.50-37.45)
• CAD	5 of 198	5 of 232	p= 0.104 (OR 5.98, 0.69- 51.66)
HCQ Prescription Pattern			
Initial Dose			
• 400 mg/day	139	175	p= 0.270 (OR 1.27, 0.83-1.95)
• < 400 mg/day	58	57	
Current Dose			
• 400 mg/day	94	153	**p = 0.000** (OR 2.14, 1.45- 3.16)
• < 400 mg/day	104	79	
Dosing Pattern			
• Once-daily	107	84	**p = 0.000** (OR 2.07, 1.40- 3.05)
• Divided Dosing	91	148	
Duration of treatment			
• <30 months	127	167	p= 0.082 (OR 1.43, 0.95-2.16)
• = 30 months	71	65	
Cumulative dose			
• < 216000 mg	84	137	
• = 216000 mg	114	95	**p = 0.001** (OR 1.96, 1.33-2.87)
Dosing as per body weight			
• <5.35 mg/kg	111	106	
• =5.35 mg/kg	87	126	**p = 0.032** (OR 1.51, 1.03-2.22)
Primary disease			
• RA	88	120	p= 0.958 (OR 1.01, 0.64-1.61)
• SLE	61	46	**p = 0.033** (OR 0.56, 0.33- 0.95)
• Others	49	66	
Combination treatment with other immunosuppressive agents			
Steroids	85 of 198	101 of 232	p= 0.900 (OR 1.02, 0.69-1.50)
Methotrexate	81 of 198	103 of 232	p= 0.466 (OR 1.15, 0.78-1.69)
Sulfasalazine	29 of 198	27 of 198	p= 0.356 (OR 0.76, 0.43-1.34)
Leflunomide	30 of 198	37 of 232	p= 0.820 (OR 1.06, 0.62-1.79)
MMF	31 or 198	20 of 232	**p= 0.026** (OR 1.96, 1.08- 3.57)
AZA	27 of 198	20 of 232	p= 0.099 (OR 1.67, 0.90-3.08)
Other relavant details			
Baseline Ocular Screening	98 of 198	106 of 232	p= 0.431 (OR 1.16, 0.79-1.70)
Regular Follow up	184 of 198	204 of 232	p= 0.085 (OR 1.80, 0.92-3.53)
Previous Skin Disease	11 of 198	8 of 232	p= 0.124 (OR2.21, 0.80-6.10)
RF positivity	85 of 198	80 of 232	p= 0.073 (OR 1.43, 0.967-2.11)
ANA positivity	59 of 198	47 of 232	**p= 0.023** (OR 1.67, 1.07-2.59)

Figure 1B : Multivariate analysis of the risk factors for development of cutaneous side effects

Identified risk factor	p-value (odds ratio and confidence intervals of multivariate analysis)
Cumulative dose (216000 mg or more)	**p= 0.004** (OR 1.82, 1.22-2.73)
ANA positivity	**p= 0.027** (OR 1.72, 1.06-2.8)
RF positivity	**p= 0.000** (OR 2.38, 1.51-3.76)
MMF combination	**p= 0.024** (OR 2.13, 1.10-4.09)
AZA combination	**p= 0.036** (OR 2.05, 1.04-4.01)

Abbreviations: OR Odds ratio, CAD coronary artery disease, CVA cerebro vascular accident

Figure 1

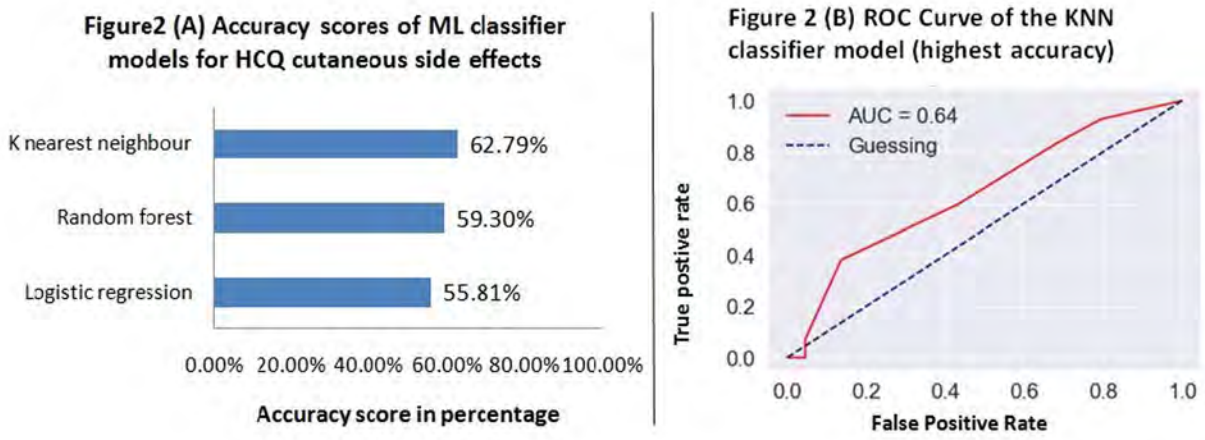

Figure 2

1.04-4.01) ANA positive (OR 1.72, 1.06-2.8), and RF positive(OR 2.38, 1.51-3.76) . Accuracy scores of three ML models are shown in figure 2A, with the KNN classifier model having the best performance. It achieved a 62.79% accuracy with precision of 0.6 and AUC of 0.64 (figure 2B).

Conclusion: Cutaneous side effects are common with HCQ treatment. While traditional statistical methods can help identify the risk factors, usage of supervised ML methods could help predict development of cutaneous side effects in an individual patient. Larger dataset analysis could allow for development of tailored therapeutic regimens avoiding adverse events.

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Abstract Number: 1611

Documentation of Pregnancy Counseling in SSA-Positive Patients of Childbearing Potential: A Cross-Sectional Study

Heinrich-Karl Greenblatt[1] and Elena Weinstein[1], [1]University of Colorado School of Medicine, Aurora, CO

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) and primary Sjogren's Syndrome (SS) are highly associated with anti-SSA (anti-Ro) seropositivity. Anti-SSA autoantibodies may cross the placenta, causing a range of cutaneous and cardiac manifestations in the neonate. Approximately 2% of SSA-positive pregnancies result in complete congenital heart block, which is often fatal. Echocardiographic monitoring and early treatment with hydroxychloroquine may improve outcomes in SSA-positive pregnancies. Published data suggest that the majority of rheumatology clinic patients with the potential for high-risk pregnancies do not receive pre-pregnancy counseling, possibly due to provider anxiety or uncertainty in this area. We examined the rate of documentation of pre-pregnancy counseling in the specific case of SSA seropositivity.

Methods: We performed a cross-sectional study of 213 SSA-seropositive female patients age < 45 at a large, academic Rheumatology clinic. The majority of patients had a diagnosis of SLE or SS. We excluded 40 patients with a history of surgical birth control (e.g., tubal ligation or hysterectomy). For the remaining 173 patients, we manually reviewed electronic medical records to determine whether a discussion about the risks of SSA-seropositive pregnancy had ever been documented. We further ascertained several co-variates, including: lifetime history of normal, healthy pregnancy; lifetime history of spontaneous abortion and gender of the primary rheumatologist

Results: 67 out of 173 patients (39 percent) had documented counseling by a Rheumatologist regarding the risks of SSA-positive pregnancy. 84 patients (49 percent) had a history of at least one pregnancy; 35 of these had a history of at least one spontaneous abortion. . The rate of documented counseling was similar among patients with a primarily female Rheumatologist (39 percent) as compared to a primarily male Rheumatologist (34 percent).

Conclusion: Less than half of SSA-seropositive patients of childbearing potential have documented evidence of relevant pre-pregnancy counseling. Provider gender was not associated with a difference in the rate of counseling. These results corroborate previous data suggesting that high-risk Rheumatology clinic patients may not receive adequate pre-pregnancy counseling. Notably, these findings suggest that pre-pregnancy counseling is also underutilized in the specific instance of SSA seropositivity. Dedicated quality improvement initiatives are needed to increase the rates of SSA-specific pre-pregnancy counseling, as well as to ensure that such counseling is documented appropriately.

Disclosure: H. Greenblatt, None; **E. Weinstein**, None.

Abstract Number: 1612

Assessing Patient Self-Reported Transition Readiness in a Large Pediatric Rheumatology Center

Alexander Alexander[1], Mary Robichaux[2], Priyanka Moolchandani[1], Cristina Saez[1], Ariel Coleman[3], JaLeen Rogers[3], Danielle Guffey[1], Anne Dykes[3], Miriah Gillispie-Taylor[1] and Tiphanie Vogel[4], [1]Baylor College of Medicine, Houston, [2]Baylor College of Medicine, Houston, TX, [3]Texas Children's Hospital, Houston, [4]Baylor College of Medicine/Texas Children's Hospital, Houston, TX

SESSION INFORMATION
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Background/Purpose: Pediatric rheumatology patients need effective transition from pediatric to adult providers. Texas Children's Hospital (TCH) rheumatology clinic providers have developed a transition pathway, the BRIDGE (Baylor Rheumatology Initiative: Developing and Guiding Engagement), based on defined elements of transition and utilizing an electronic medical record-based transition planning tool (TPT) to help with transition preparation.

Methods: The validated, self-administered Adolescent Assessment of Preparation for Transition (ADAPT) survey generates 3 composite scores (out of 100) for counseling on transition self-management and prescription medications, and on transfer planning. Return adolescent patients aged 14-19 years were surveyed regardless of diagnosis. Surveys were emailed via a REDCap database on the morning of clinic appointments between August-December 2018 and November 2019-May 2020. Surveys were scored and analyzed against demographics.

Results: 302 patients completed at least 1 survey. Serial surveys were collected on 59 respondents. Most respondents were female (71%) and white (75%); 42% were Hispanic. Most patients were privately insured (57%) or covered by Medicaid/Children's Health Insurance Program (38%). The most common diagnosis was juvenile arthritis (30%). Average initial ADAPT scores for all respondents were 37/100 for transition self-management, 66/100 for medication management, and 17/100 for transfer planning. Scores in all three domains increased with increasing patient age at first ADAPT survey ($p< 0.001$). Survey scores in self-management increased by 17 for each year since the first survey ($p< 0.001$), medications increased by 16 for each year since the first survey ($p< 0.001$), and transfer planning by 23 for each year since the first survey ($p< 0.001$). For transfer planning, higher patient age at first ADAPT survey was associated with larger increases in score over time. We noted that, on average, privately insured patients had 11-point lower initial scores in self-management than publicly insured patients ($p=0.029$). Further, we noted that, on average, English speaking patients scored 22 points lower on self-management and 20 points lower on medications than non-English speakers ($p=0.001$).

Conclusion: Our clinic has developed a method to assess patient self-reported transition readiness. Our data indicates that participating patients improved over time in all domains measured by the ADAPT survey. Going forward, we plan to analyze outcomes of transitioned patients to assess the efficacy of our pathway. Our ultimate goal is to create a sustainable and successful BRIDGE between pediatric and adult rheumatology care.

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Abstract Number: 1613

Improving Transition Policy Dissemination and Care Team Communication in Pediatric Rheumatology Clinic Through Standardization of Workflow and Electronic Health Record Documentation

Rosemary Peterson[1], Emily Liebling[1], Beth Rutstein[2], Julie Chase[1], Atiye Bilgic Dagci[3], Melissa Argraves[3], Jon Burnham[1], Lisa Wiater[3], Deborah Bieniakowski[3], Danielle Dodson[3], Jane Kennedy[3], Cora Sears[3] and Joyce Chang[1], [1]Children's Hospital of Philadelphia, Philadelphia, PA, [2]The Children's Hospital of Philadelphia, Philadelphia, PA, [3]Children's Hospital of Philadelphia, Philadelphia

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: Morbidity and mortality increase when young adults with chronic disease transfer from pediatric to adult care. Structured healthcare transition processes improve outcomes, yet are rarely successfully implemented by pediatric rheumatology practices. Our goal was to standardize transition preparation and communication within a pediatric rheumatology care team to facilitate safe and timely transfer of patients to adult care.

Methods: This study was completed by a multi-disciplinary team of physicians, nurses and social worders within the Division of Rheumatology at a tertiary care pediatric hospital. Two of 4 key drivers were selected: 1) communication within the care team and 2) transition preparation (Figure 1). Standardizing review of the practice's transition policy with patients and families, a core component of the Got Transition Six Core Elements of Health Care Transition™

national guidelines, was selected as the initial secondary driver to improve. We included youth age 14 and older, with a clinical diagnosis of juvenile idiopathic arthritis, systemic lupus erythematosus, Sjogren's syndrome, mixed connective tissue disease, vasculitis, or juvenile dermatomyositis, and ^{3}2 Rheumatology follow-up visits. Consensus on revisions to a pre-existing transition policy was obtained through regular QI and staff meetings. Baseline patient surveys to assess awareness of the transition policy and transfer timing were collected 1 week per month from November 2019 to January 2020. In December 2019, nurses began to review printed transition policies with eligible patients during clinic visits and document review in the electronic health record (EHR) utilizing a standardized template

Table 1. Baseline Characteristics and Pre-implementation Survey Results (n = 57)

Age group	n (%)
14 to 15 years-old	19 (33%)
16 to 17 years-old	13 (23%)
≥ 18 years-old	25 (44%)
Disease*	
SLE/Sjogrens/MCTD	12 (21%)
JIA	41 (72%)
Vasculitis	3 (5%)
JDM	1 (2%)
Gender	
Male	19 (33%)
Female	38 (67%)
Survey results	
Transition policy receipt	9 (16%)
Transition discussion	24 (42%)

*SLE (systemic lupus erythematosus), MCTD (mixed connective tissue disease), JIA (juvenile idiopathic arthritis, JDM (juvenile dermatomyositis)

Figure 1.

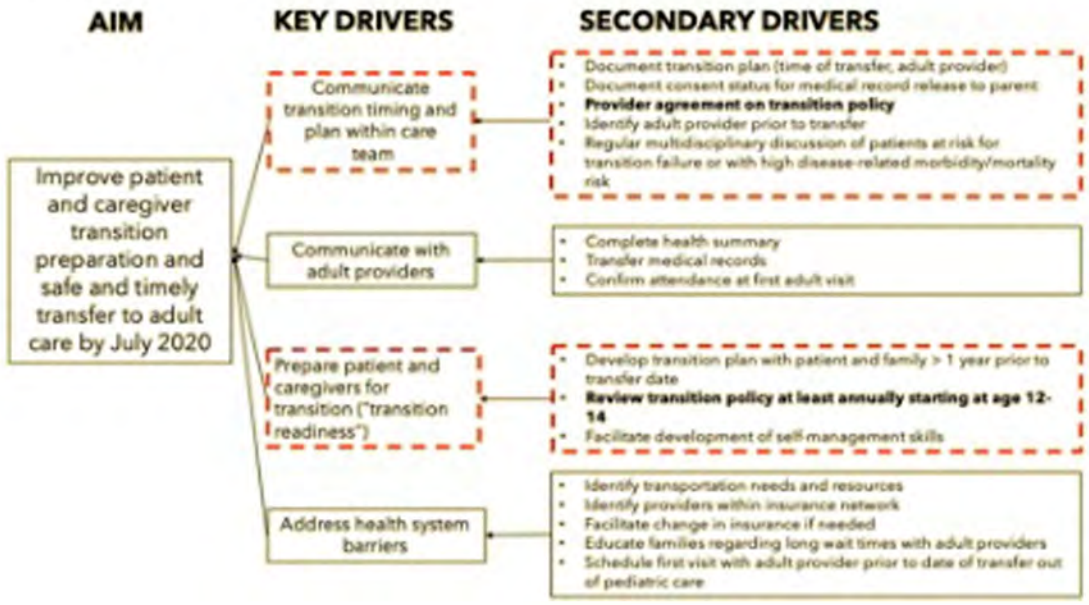
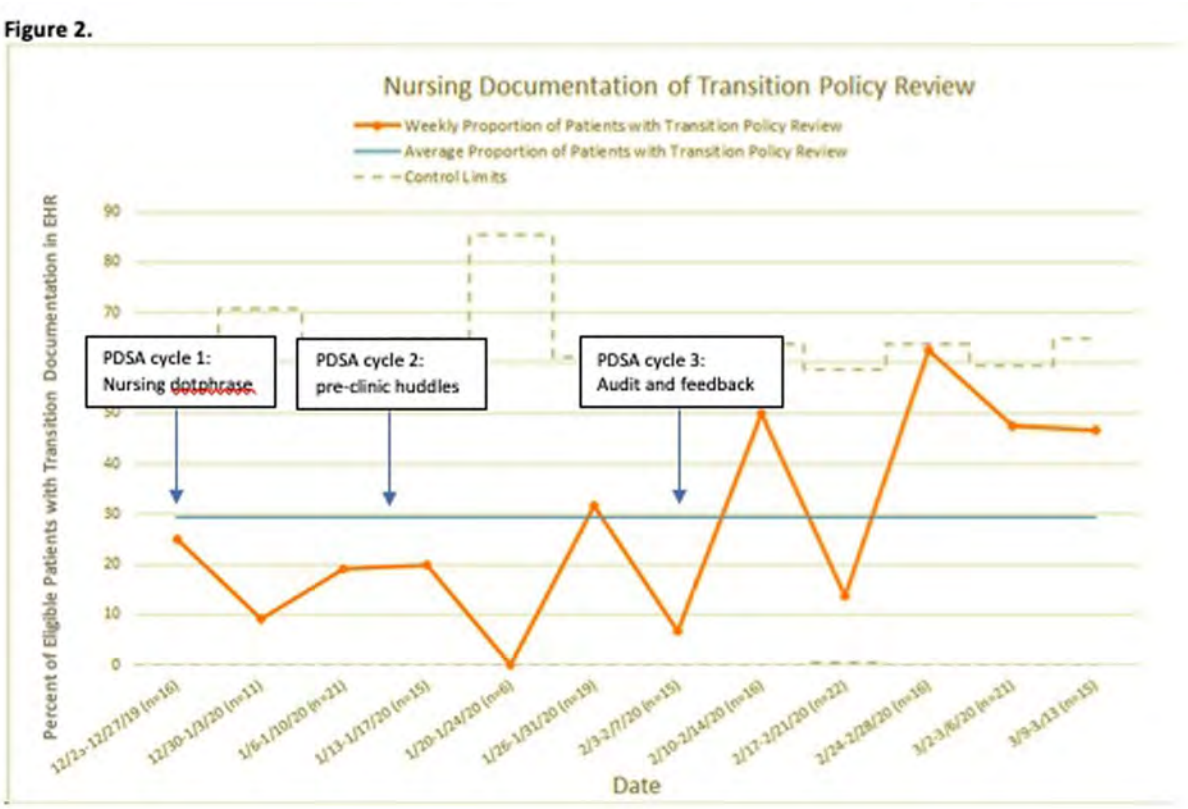


Figure 2.



(Plan-Do-Study-Act (PDSA) cycle 1). In January 2020, pre-clinic team huddles were initiated to more consistently identify eligible patients (PDSA cycle 2). In February 2020, audit and feedback with review of monthly performance with the nursing team was added to monthly QI meetings (PDSA cycle 3).

Results: Table 1 summarizes baseline characteristics and survey data for all 57 respondents. Prior to implementation, 16% of patients reported prior transition policy receipt. Of patients age 18 and older (n = 25), only 32% had received the transition policy and 68% had discussed transfer timing with their care team. The proportion of eligible patients with EHR documentation of transition policy review was trending toward improvement at the time of project interruption in March 2020 due to COVID-19 (18% pre-implementation versus 42% post-implementation; Figure 2). Only 1 week of patient surveys reflecting the impact of interventions on awareness and understanding of the transition policy were able to be obtained prior to temporary cessation of routine in-person visits.

Conclusion: A minority of youth report receiving a transition policy or discussing timing of transfer to adult care with their care team. Workflow and EHR standardization, enhanced care team communication, and performance audit and feedback, may be effective strategies to implement transition processes. Future work is needed to determine the effect of regular transition policy review on patient preparation and safe and timely transfer to adult care.

Disclosure: R. Peterson, None; **E. Liebling**, None; **B. Rutstein**, None; **J. Chase**, None; **A. Bilgic Dagci**, None; **M. Argraves**, None; **J. Burnham**, None; **L. Wiater**, None; **D. Bieniakowski**, None; **D. Dodson**, None; **J. Kennedy**, None; **C. Sears**, None; **J. Chang**, None.

Abstract Number: 1614

Use of a Best Practice Alert to Encourage Transition Planning and Readiness

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Measures & Measurement of Healthcare Quality Poster

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Background/Purpose: Transitioning children with chronic diseases from pediatric to adult care can be challenging. Patients are faced with the emotional shock of entering a new healthcare environment, along with the many technical burdens of learning how to navigate a complex new system. It is no wonder that both morbidity and mortality are higher in the time surrounding transition to adult care.

Fortunately, there is a movement to create standardized processes which empower patients to take ownership of their care. At our institution, rheumatology is a leader in this space. We have utilized the 6 core elements from "Got-Transition" to develop a transition pathway. This included the creation of a transition policy (element 1), as well as a data registry to track patients (element 2). The utilization of a transition planning tool, or TPT, allows for progress on readiness and planning (elements 3 and 4). The TPT is an electronic medical record (EMR) based flowsheet which helps guide providers in preparing patients for transition across multiple domains including medications, appointments, refills and insurance.

The aim of this project was to increase transition readiness and planning by increasing TPT use. We did this by tracking and encouraging TPT use or acknowledgement by providers in our rheumatology clinic.

Methods: In January 2019, a best practice alert (BPA) was created and embedded into the EMR to serve as a reminder for rheumatology providers to use the TPT with their transition aged patients (1567 patient encounters). Providers could also acknowledge why they didn't use the TPT. Use of the tool was refined through a series of PDSA cycles. The first PDSA cycle was used to gather baseline data to determine how the BPA influenced TPT use. The second cycle involved encouraging providers to utilize the tool at regular section meetings. In the third cycle, we worked to optimize integration of the BPA into the EMR. In the fourth cycle, transition coordinators were present at a majority of clinic sessions, serving as a reminder to use the TPT.

Results: There was a statistically significant increase in TPT use over time from the beginning to the end of the year ($p < 0.001$). TPT use plateaued around July 2019, with usage at 45% of eligible patient visits, up from only 16% of visits in January. If both use *and* acknowledgement are considered, the TPT was addressed in 95% of patient visits in July, up from only 24% in January. The two most common acknowledgements from providers who did not use the TPT were an active disease flare, in which the provider focused on acute issues (15% of acknowledgements), and clinic being too busy to utilize the TPT (32% of acknowledgements).

Conclusion: Our data suggests that a BPA incorporated into provider workflow is an effective means to promote transition planning using a TPT. As providers frequently cited time constraints as a key limitation in utilization of the TPT, we are working on securing dedicated transition support to achieve standardized transition readiness and planning. Going forward, we plan to finalize our transition pathway (transfer and completion, elements 5 and 6), and monitor outcomes, such as whether increased TPT use correlates with more successful transition into adult care.

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Abstract Number: 1615

Assessing Preparation for Care Transition Among Adolescents with Rheumatologic Disease: A Quality Assessment with Patient Survey

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SESSION INFORMATION
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Background/Purpose: Despite the risk for poor outcomes and gaps in care in the transition from pediatric to adult care, most pediatric rheumatology centers lack formal pathways for transition. We evaluated preparation for transition with a validated quality measure in a single pediatric rheumatology center.

Methods: Patients 16 and older were sent the ADolescent Assessment of Preparation for Transition (ADAPT) survey via email. This quality measure assesses preparation for transition in three domains: (1) self-management, (2) prescription medications, and (3) transfer planning using specific questions about transition counseling received (Table 2). Responses were converted to composite scores and analyzed using descriptive statistics. The association of patient illness and demographic factors with composite transition scores were assessed using t-tests, ANOVA and linear regression. Logistic regression was used to evaluate for independent predictors of transition readiness.

Results: 78 of 337 patients completed the survey (response rate of 23%), of whom 77 had a visit within 1 year and were eligible to complete the assessment tool. Demographics and disease types are reported in Table 1.

Patients most frequently endorsed receiving counseling on taking charge of their health and remembering to take medications, but less than half reported receiving specific counseling about transitioning to an adult provider (Table 2).

Patients ages 16-18 had significantly lower scores in all domains as compared to those 19 years and older (Table 3). Patients with lower education attainment compared with those who had attended some college or higher had lower scores in self- management (1.51 vs 2.52, p=0.0002), prescription medication counseling (1.96 vs 2.41, p= 0.029), and transfer planning (0.27 vs 1.62, p< 0.001). Patients with a diagnosis of MCTD, Sjogrens or SLE had higher

Table 1. Patient Characteristics

	n (%) or Mean (SD)
Race*	
White	66 (86)
Black or African American	8 (10)
Asian	1 (1)
Ethnicity*	
Not Hispanic, Latino, or Spanish Origin	72 (94)
Puerto Rican	3 (4)
Other Hispanic, Latino, or Spanish Origin	2 (3)
Female	64 (83)
Age (years)	18.9 (2.0)
Education	
9th grade	2 (3)
10th grade	9 (12)
11th grade	13 (17)
12th grade, high school graduate, or GED	13 (17)
Some college	33 (43)
College graduate	7 (9)
Primary Rheumatologic Diagnosis**	
JIA	52 (68)
Uveitis (idiopathic)	2 (3)
CRMO	3 (4)
SLE	8 (10)
MCTD	4 (5)
Sjogrens	3 (4)
JDM/inflammatory myositis	3 (4)
Other vasculitis	4 (5)
Length of time seeing doctor	
At least 6 months but less than 1 year	2 (3)
At least 1 year but less than 3 years	20 (26)
At least 3 years but less than 5 years	19 (25)
5 years or more	36 (47)
Frequency of visits in past year	
1 time	17 (22)
2 times	24 (31)
3 times	17 (22)
4 times	13 (17)
5 to 9 times	4 (5)
10 or more times	2 (3)
Health status	
Excellent	10 (13)
Very good	18 (23)
Good	32 (42)
Fair	15 (19)
Poor	2 (3)

* Some patients selected multiple or no race/ethnicity categories; numbers do not sum to 100%

** Some patients have more than 1 primary rheumatologic diagnosis

Table 1. Patient Characteristics

Table 2. Selected Transition Preparation Measures

Survey Question	Yes n (%)	No n (%)
In the last 12 months, did you talk with this provider without your parent or guardian in the room?	46 (59.7%)	31 (40.3%)
In the last 12 months, did you and this provider talk about you being more in charge of your health?	53 (68.8%)	24 (31.2%)
In the last 12 months, did you and this provider talk about whether you may need to change to a new provider who treats mostly adults?	31 (40.8%)	45 (59.2%)
In the last 12 months, did this provider ask if you had any questions or concerns about changing to a new provider who treats mostly adults?	22 (71.0%)	9 (29.0%)
In the last 12 months, did you and this provider talk about a specific plan for changing to a new provider who treats mostly adults?	14 (45.2%)	17 (54.8%)
In the last 12 months, did you and this provider talk about remembering to take your medicines?	37 (75.5%)	12 (24.5%)
Composite scores	Mean (SD)	
Self-management (n=77; score out of 4)	2.0 (1.2)	
Medication counseling (n=49; score out of 3)	2.2 (0.7)	
Transfer planning (n=76; score out of 4)	1.0 (1.4)	
Total transition composite score (n=77; % of items answered yes)	0.45 (0.25)	

Table 2. Selected Transition Preparation Measures

self-management scores than those with other diagnoses (2.6 vs 1.9; p=0.048). Non-white patients indicated they had received more thorough medication counseling than white patients (2.71 vs 2.07, p=0.027).

When controlling for age, educational attainment remained an independent predictor of transfer planning (Beta=1.00, 95% CI [0.06, 1.95], p=0.037), but not of other measures. Patients with longer duration of seeing their physician had higher transition preparation scores (r=0.26, p=0.021).

Conclusion: Few adolescents in our cohort endorsed receiving comprehensive transition counseling, including discussion of transfer planning. Patients who were younger and with lower levels of education had lower preparation scores. A long-term relationship with providers was associated with higher transition preparation scores. Further research including longitudinal assessment of transition preparation is needed to evaluate effective processes to assist vulnerable populations.

Table 3. Transition Preparation Scores by Demographic Characteristics

Composite Area	Demographic	Mean Score †	Std. Dev.	Freq.	F	Prob > F
Self-management	Age 18 and under vs. 19 and over	1.5; 2.56	1.18; 1.04	38; 39	17.56	0.0001
	High school or less vs. some college or more	1.51; 2.52	1.17; 1.09	37; 40	15.49	0.0002
	White vs. non-white	2.36; 1.98	1.12; 1.24	11; 66	0.89	0.3475
	Hispanic/Latino vs. non-Hispanic	2.0; 2.04	1.87; 1.19	5; 72	0.01	0.9422
	Male vs. female	1.92; 2.06	1.50; 1.18	13; 64	0.14	0.7120
	Fair or poor vs. good or better health status	2.05; 2.03	1.34; 1.21	17; 60	0.01	0.9404
	SLE, Sjogrens, MCTD vs. other diagnosis	2.6; 1.90	1.18; 1.21	15; 62	4.03	0.0482
Medication counseling	Age 18 and under vs. 19 and over	1.93; 2.48	0.66; 0.68	28; 21	8.02	0.0068
	High school or less vs. some college or more	1.96; 2.41	0.65; 0.73	27; 22	5.09	0.0288
	White vs. non-white	2.71; 2.07	0.49; 0.71	42; 7	5.25	0.0265
	Hispanic/Latino vs. Non-Hispanic	2.33; 2.15	0.58; 0.73	3; 46	0.18	0.6762
	Male vs. female	1.66; 2.23	0.82; 0.68	6; 43	3.44	0.0697
	Fair or poor vs. good or better health status	2; 2.22	0.82; 0.68	13; 36	0.92	0.3436
	SLE, Sjogrens, MCTD vs. other diagnosis	2.4; 2.10	0.52; 0.75	10; 39	1.38	0.2461
Transfer planning	Age 18 and under vs. 19 and over	0.34; 1.58	0.81; 1.52	38; 38	19.59	<0.0001
	High school or less vs. some college or more	0.27; 1.62	0.69; 1.52	37; 39	24.32	<0.0001
	White vs. non-white	0.92; 1.18	1.30; 1.72	65; 11	0.34	0.5633
	Hispanic/Latino vs. Non-Hispanic	1.75; 0.92	2.06; 1.32	4; 72	1.43	0.2357
	Male vs. female	0.42; 1.06	0.90; 1.41	12; 64	2.32	0.1323
	Fair or poor vs. good or better health status	0.71; 1.03	1.36; 1.36	17; 59	0.76	0.3848
	SLE, Sjogrens, MCTD vs. other diagnosis	1; 0.95	1.65; 1.30	15; 61	0.02	0.9012

† Scores calculated as number of positive answers (higher score indicates patients reported more transition counseling).

Table 3. Transition Preparation Scores by Demographic Characteristics

Disclosure: J. Roberts, None; **O. Halyabar**, None; **C. Petty**, None; **M. Son**, None.

Abstract Number: 1616

Systematic Review of Effectiveness Outcomes Reported in Rheumatology Transition Literature

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Background/Purpose: In young patients with rheumatologic disease, transition from pediatric to adult care is a complex process. Poor transitional care leads to health deterioration, loss to follow-up and increased morbidity. The "best" transition care model remains elusive and is complicated by how effectiveness and/or success of transition programs are defined and measured. In this review, we aimed to identify: 1) outcomes used in rheumatology transition literature to measure a "successful transition", and 2) tools used to determine these outcomes.

Methods: A systematic review was conducted by adapting a previously published search strategy using OVID Medline and Embase. The search was conducted in duplicate and discrepancies were reconciled. English articles meeting the following criteria were selected: 1) primary study; 2) pediatric-to-adult rheumatology transition program; 3) quantifiable outcomes reported. Of 506 abstracts reviewed, 69 were selected for full text review and 28 met the final inclusion criteria.

Results: Outcomes reported in rheumatology transition literature were divided into categories. The following categories of outcomes were used to measure a "successful transition" among the 28 studies that met the inclusion criteria: transfer completion (13 studies, 46.4%), transition readiness (5 studies, 17.9%), patient satisfaction (9 studies, 32.1%), disease activity/ functional ability (22 studies, 78.6%), and quality of life (10 studies, 35.7%).

Transfer completion was measured by various definitions of attendance at an adult appointment. Transition readiness was measured using 2 tools: SLE Transition Readiness Questionnaire (SLE-TRQ), and Transition Readiness Assessment Questionnaire (TRAQ). Patient satisfaction was measured using 3 tools, with the most frequently used being the "Mind the Gap" instrument. Disease activity/ functional ability was measured using 9 tools, with the most frequently used being the Child Health Assessment Questionnaire (CHAQ). Quality of life was measured using 6 tools, with the most frequently used being the 36-Item Short Form Health Survey (SF-36). Of the tools identified among the 28 studies, 11 were rheumatology-specific and the remaining were not specific to one disease or clinical area.

Conclusion: This rheumatology transition literature review identified several outcomes and tools used to report transition success and experiences. Variability in outcome measures makes comparisons between studies and between transition programs challenging. There is need for consensus on which outcomes are most meaningful for patients to allow for effectiveness of models to be determined.

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Abstract Number: 1617

New Juvenile Idiopathic Arthritis Quality Measure Set for the Pediatric Rheumatology Care and Outcomes Improvement Network

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SESSION INFORMATION

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Background/Purpose: The Pediatric Rheumatology Care and Outcomes Improvement Network (PR-COIN) is a learning network to support pediatric rheumatology centers in improving care delivery and patient outcomes. This growing network, now 21 centers, was established in 2011 and has tracked outcome and process measures over time. PR-COIN recently modified its quality measure (QM) set that coincided with a registry migration of 5,905 patients to a new platform to support optimal data reporting. This report highlights the network's new QMs and provides some performance on these measures from a large JIA cohort enrolled in the network registry.

Methods: The network's initial process measures were based on a published set of QMs for JIA that was developed utilizing an evidence-based approach and consensus methodology. Outcome measures were created using published, validated JIA outcome assessments. Taking into consideration 3 main measure attributes – clinical health importance, scientific validity, and feasibility – in addition to new best practices, PR-COIN modified the QM set in 2019 with parent input and developed operational definitions. QMs were tested using patient data for validation. Network teams enter and/or auto-upload patient data into the PR-COIN registry to populate the measures, and statistical process control charts are utilized to display monthly performance.

Results: PR-COIN's QM set consists of 20 measures, including 16 clinical and 4 data quality measures (**Table 1**). Outcome measures for disease control include evaluation of the clinical Juvenile Arthritis Disease Activity Score (cJADAS10), clinically inactive disease, the active joint count, and the time to inactive disease. Patient-reported outcomes are comprised of optimal physical function, low or no pain, low patient global assessment of overall well-being, and low pain interference. Treat to Target interventions, including setting a treatment target and use of clinical decision support, will be tracked as process measures in addition to the use of self-management support and appropriate medication safety monitoring. A new balancing measure regarding infection-related hospitalizations rounds out the QM set. **Figure 1** is an example run chart of a disease control outcome measure – mean disease activity score by cJADAS10 (scale 0-30) of all JIA patients – demonstrating the aggregate performance of 8 PR-COIN sites. This cu-

Measure Group	Measure Classification	Measure Subgroup	Measure Title
Clinical Measures	Outcome Measures	Disease Control	Percent of JIA patients with oligoarthritis or polyarthritis with inactive disease or low disease activity by cJADAS10
			Mean cJADAS10 score
			Percent of all JIA patients with clinical inactive disease
			Mean active joint count for all JIA patients
			Percent of JIA patients with oligoarthritis or polyarthritis who achieve inactive or low disease activity by 6 months
		Quality of Life	Percent of patients with optimal physical function
			Percent of patients with pain score ≤3
			Percent of patients with patient global assessment ≤2
			Mean patient global assessment of well-being
			Percent of patients with pain interference T score <60
	Process Measures	Model Treatment	Percent of polyarticular course patients with treatment target set
			Percent of visits with provider attestation of disease activity status for Treat to Target
			Percent of visits where treatment was provided using clinical decision support
			Percent of patients who received self-management support
			Percent of patients who received appropriate medication safety monitoring
	Balancing Measure		Time between hospitalization for infections for all patients
Data Quality Measures			Percent of visits with all critical data recorded
			Percent of patients with a visit recorded in last 13 months
			Percent of JIA population that is enrolled in PR-COIN
			Percent of patients enrolled within 120 days of diagnosis

cJADAS10, clinical juvenile arthritis disease activity score

Table 1. PR-COIN Quality Measures for Juvenile Idiopathic Arthritis.

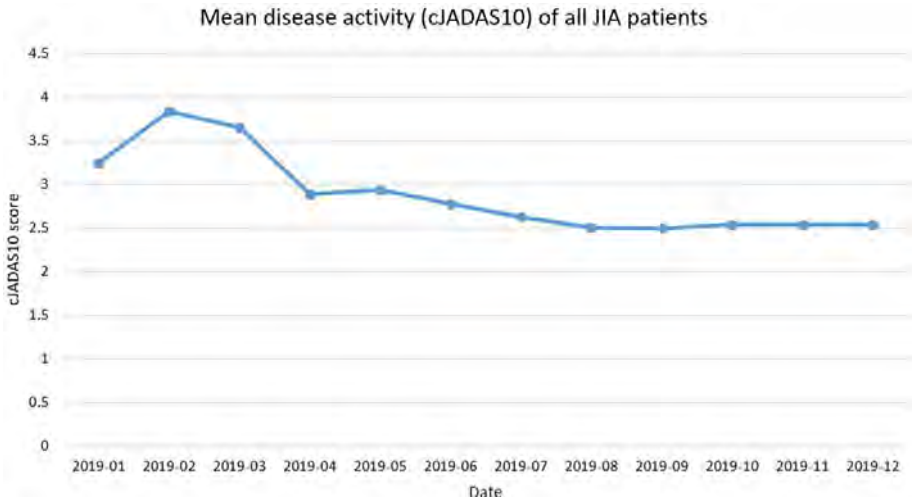

Figure 1. Mean disease activity score by cJADAS10 of JIA patients in PR-COIN.

mulative measure has been stable at 2.5 over the last 5 months. **Figure 2** is an example run chart using collaborative data of a patient-reported quality of life outcome measure, the mean patient global assessment of well-being (scale 0-10). This score has been around 1.26 for the last several months.

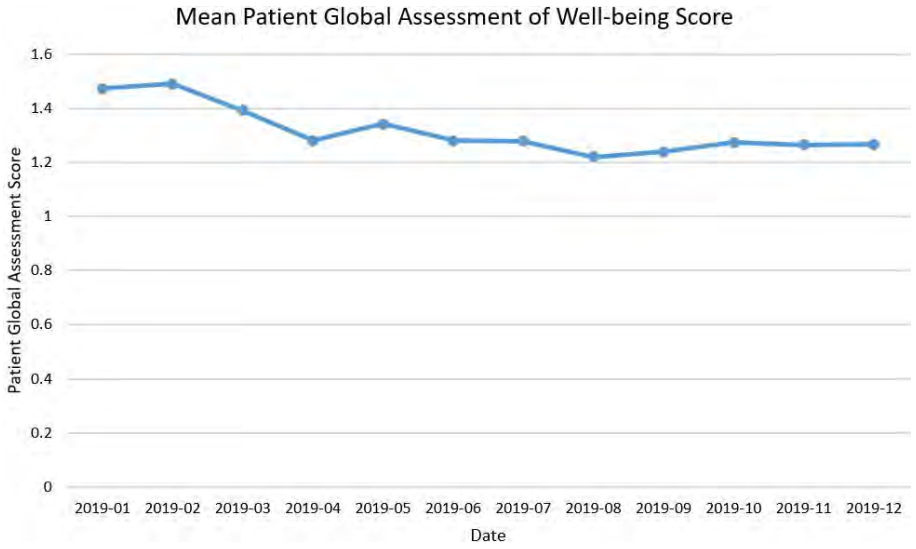

Figure 2. Mean patient global assessment of well-being score for JIA patients in PR-COIN.

Conclusion: PR-COIN has enhanced its comprehensive and varied QM set for the care of patients with JIA. Having clinically important measures that are tested for feasibility on a large cohort of patients with JIA can maximize quality improvement efforts to optimize care delivery.

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Abstract Number: 1618

Frequency and Cost of Repeat HLA-B27 Testing Within the National Capital Consortium over a Calendar Year

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SESSION INFORMATION

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Background/Purpose: Human leukocyte antigens (HLAs) are proteins encoded for by the major histocompatibility complex located on the short arm of chromosome six. One such allele, HLA-B27 is known to have a strong association with ankylosing spondylitis (AS) and is present in over 90% of Caucasian AS patients. The National Capital Consortium's (NCC) HLA-B27 testing is conducted as a polymerase chain reaction (PCR), sequence-specific oligonucleotide probe analysis. As this is a genetic test, repeating the assay multiple times for the same individual patient is

of limited diagnostic utility. The intent of this project was to determine the number of repeat HLA-B27 tests that occur within the NCC during a calendar year and the approximate cost associated with this repeat testing.

Methods: A record of all HLA-B27 tests ordered in the NCC between January 1 2019 and December 31 2019 was obtained. Chart reviews were performed to identify whether these patients had prior HLA-B27 testing conducted over the lifetime of the patient in the electronic medical record (EMR) and the number of prior tests. Ordering location of the testing (primary care, ophthalmology/optometry, rheumatology, other specialty clinic, inpatient, and outside provider) was also recorded. The cost of repeat testing was then estimated per the facility's contract with LabCorp.

Results: Between January 1 2019 and December 31 2019, 460 HLA-B27 tests were conducted for patients within the NCC. Of these, 33 (7%) represented repeat tests associated with a cost of approximately 5,610 dollars. Five of the thirty-two HLA-B27 tests ordered by outside providers (16%) represented repeat studies associated with a cost of approximately 850 dollars. The specialty with the second highest percentage of repeat tests was ophthalmology and optometry (8 repeat tests, 13% of all tests ordered by the specialty, $1,360 spent in repeat tests), followed by pediatric rheumatology (5, 11%, $850), other specialty clinics (6, 5%, $1,020), primary care (7, 5%, $1,190), and adult rheumatology (2, 5%, $340).

Conclusion: In this review of ordering practices, repeat HLA-B27 testing accounted for 7% of tests ordered in the NCC over one calendar year. While the majority of HLA-B27 tests were ordered in the primary care setting, the highest rates of repeat testing were conducted by outside providers, ophthalmology/optometry, and pediatric rheumatology. This repeat testing is not insignificant; when extrapolated it represents an estimated ten year cost of over $56,000 to our facility. We hypothesize that lack of access to our facility's EMR, use of order sets, and insufficient time to review the EMR represent major factors contributing to repeat HLA-B27 testing. Our findings suggest that efforts to reduce HLA-B27's inclusion in order sets and introduction of EMR "flags" to prevent repeat ordering may reflect reasonable interventions to lower repeat testing within our system.

Disclosure: A. Stein, None; **C. Anderson**, None; **A. Collamer**, None.

Abstract Number: 1619

Immunoglobulin G Subclass Ordering Patterns for IgG4-Related Disease at an Academic Medical Center

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Background/Purpose: We have noticed an increasing number of serum IgG4 levels ordered over the last several years at our institution. This study was performed to better understand the clinical indications for IgG4 testing among inpatient general medicine providers and how those trends have changed from 2015 to 2019. We also sought to determine if there was any comparative change in rheumatology providers' behavior regarding IgG4 testing.

Methods: We used SlicerDicer, an analytic tool in our EHR, to identify patients with IgG subclasses ordered by inpatient general medicine or rheumatology providers in 2015 and 2019. Charts were manually reviewed to determine

Table 1. Statistical analysis of proportion of patients tested for IgG4-RD.

	Inpatient General Medicine IgG4 Testing				
	2015		2019		
	n	%	n	%	*p* value
Total patients with IgG4 level sent	60	-	133	-	
IgG4 level sent for suspected IgG4-RD	31	52%	79	59%	
IgG4 level sent for other reason	29	48%	54	41%	
Known IgG4-RD at time of testing	0	0%	2	2%	
No known IgG4-RD at time of testing	31	52%	77	58%	
Total patients with any lab test sent	26076	-	29100	-	
Patients tested for IgG4-RD among all patients with any lab test sent	31/26076	0.12%	77/29100	0.26%	< 0.001
	Outpatient Rheumatology IgG4 Testing				
	2015		2019		
	n	%	n	%	*p* value
Total patients with IgG4 level sent	24	-	67	-	
IgG4 level sent for suspected IgG4-RD	18	75%	50	75%	
IgG4 level sent for other reason	6	25%	17	25%	
Known IgG4-RD at time of testing	1	4%	11	16%	
No known IgG4-RD at time of testing	17	71%	39	58%	
Total patients with any lab test sent	5216	-	9246	-	
Patients tested for IgG4-RD among all patients with any lab test sent	17/5216	0.33%	39/9246	0.42%	0.4059

Table 2. Proportion of patients with elevated IgG4 levels, biopsies performed, and ultimate diagnosis of IgG4-RD.

Inpatient General Medicine IgG4 Testing					
	2015		2019		
	n	%	n	%	*p* value
Among patients tested for IgG4-RD	31		77		
IgG4 levels elevated	5	16%	6	8%	0.2891
Biopsy performed	9	29%	32	42%	0.2762
Diagnosed with IgG4-RD	1	3%	1	1%	0.4936
Outpatient Rheumatology IgG4 Testing					
	2015		2019		
	n	%	n	%	*p* value
Among patients tested for IgG4-RD	17		39		
IgG4 levels elevated	3	18%	5	13%	0.6876
Biopsy performed	9	53%	24	62%	0.5691
Diagnosed with IgG4-RD	2	12%	7	18%	0.7072

clinical indications for IgG subclass testing as determined by provider documentation at the time of ordering. Using a pre-specified adjudication algorithm, patients were excluded if IgG subsets were sent for an indication other than IgG4-Related Disease (IgG-RD) or if they already had a known diagnosis of IgG4-RD. For included patients, we also evaluated IgG4 levels, imaging, biopsies, and final diagnoses. Fisher's exact test (Social Science Statistics open software) was used to compare 2015 and 2019 data. Other data were analyzed using descriptive statistics.

Results: Among general medicine providers, there was a significant increase in patients tested for suspected IgG4-RD with serum IgG subclasses from 2015 (n = 31, 0.12% of all patients with any lab order) to 2019 (n = 77, 0.26%), p< 0.001 (table 1). There were no changes in the proportion of patients with elevated IgG4 levels, biopsies obtained, or a diagnosis of IgG4-RD from 2015 to 2019 (table 2). Notably, only 1 general medicine patient was diagnosed with IgG4-RD in 2015 and 1 in 2019. There was a significant decrease in the proportion of general medicine patients tested

	INPATIENT GENERAL MEDICINE IgG4 TESTING				
	2015 (n = 31)		2019 (n = 77)		
Clinical indications for IgG4 testing	**n**	**%**	**n**	**%**	***p* value**
Pancreatic disease	21	68%	39	51%	0.1352
Hepatobiliary disease	4	13%	23	30%	0.0861
Aortitis/other large vessel disease	0	0%	2	3%	1.0
Retroperitoneal fibrosis	3	10%	0	0%	0.022
Salivary/lacrimal gland enlargement	1	3%	0	0%	0.287
Orbital inflammatory disease	0	0%	9	12%	0.0571
Lymphadenopathy	0	0%	0	0%	-
Pulmonary disease	0	0%	1	1%	1.0
Kidney disease	0	0%	0	0%	-
Pericardial disease	1	3%	0	0%	0.287
Mediastinal disease	0	0%	1	1%	1.0
Other indications	1	3%	3	4%	1.0
	OUTPATIENT RHEUMATOLOGY IgG4 TESTING				
	2015 (n = 17)		2019 (n = 39)		
Clinical indications for IgG4 testing	**n**	**%**	**n**	**%**	***p* value**
Pancreatic disease	1	6%	2	5%	1.0
Hepatobiliary disease	1	6%	0	0%	0.3036
Aortitis /other large vessel disease	3	18%	5	13%	0.6876
Retroperitoneal fibrosis	2	12%	7	18%	0.7072
Salivary/lacrimal gland enlargement	3	18%	8	21%	1.0
Orbital inflammatory disease	2	12%	4	10%	1.0
Lymphadenopathy	1	6%	4	10%	1.0
Pulmonary disease	0	0%	2	5%	1.0
Kidney disease	0	0%	3	8%	0.5456
Pericardial disease	2	12%	1	3%	0.287
Mediastinal disease	0	0%	0	0%	-
Other indications	3	18%	9	23%	0.7378

Table 3. A review of clinical characteristics and indications of patients tested for IgG4-RD.

with IgG subclasses for IgG4-RD due to retroperitoneal fibrosis (10% in 2015 vs 0% in 2019, p=0.022) and a trend towards more patients tested due to hepatobiliary disease (13% vs 30%, p=0.0861) and orbital inflammatory disease (0% vs 9%, p=0.0571), table 3. There were no significant changes in IgG subclass testing patterns by rheumatology providersfrom 2015 to 2019.

Conclusion: Despite a more than two-fold increase in IgG subclass testing for IgG4-RD by inpatient general medicine providers from 2015 to 2019, the number of patients ultimately diagnosed with IgG4-RD did not change. The trend towards increased IgG subclass testing for hepatobiliary disease and orbital inflammatory disease suggests increased provider awareness of some of this condition's protean manifestations beyond the pancreas; however, the decrease in IgG subclass testing for retroperitoneal fibrosis and the minimal testing for other major clinical manifestations of IgG4-RD in either 2015 or 2019 suggests that this condition remains under-recognized. In contrast, there were no major changes in IgG subclass testing by rheumatologists from 2015 to 2019. Overall, this study reveals potential knowledge gaps regarding the workup of IgG4-RD among inpatient internal medicine providers and highlights the need for an educational intervention to address appropriate indications for IgG subclass testing in different clinical scenarios.

Disclosure: L. Eder, None; **D. Leverenz**, None.

Abstract Number: 1620

Hepatitis B Screening Practices When Prescribing Tocilizumab or Tofacitinib in Real World Practice

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Hepatitis B virus (HBV) reactivation can complicate treatment with immunosuppressive medications. Reactivation risk varies by the status of HBV infection but has been reported in up to one third of patients receiving immunosuppression. While HBV screening is indicated prior to initiation of tumor necrosis factor inhibitors, recommendations are inconsistent regarding HBV screening when prescribing tocilizumab (TCZ) or tofacitinib (TOF),

Table 1: Baseline characteristics of subjects initiating tocilizumab or tofacitinib

Variable	Tocilizumab (N=764)	Tofacitinib (N=495)
Age (years), median (IQR)	64 (51-73)	60 (51-70)
Female sex, n (%)	596 (78)	435 (88)
Race/Ethnicity, n (%)*		
White, non-Hispanic	643 (84)	416 (84)
Black, non-Hispanic	33 (4)	21 (4)
Asian, non-Hispanic	27 (4)	11 (2)
Hispanic	28 (4)	20 (4)
Other or not reported	21 (3)	27 (5)
Diagnosis, n (%)		
Rheumatoid arthritis	393 (51)	381 (77)
Vasculitis	189 (25)	3 (1)
Psoriatic arthritis	9 (1)	30 (6)
Other inflammatory arthritis	73 (10)	26 (5)
Juvenile Idiopathic Arthritis or Adult-Onset Still's Disease	36 (5)	6 (1)
Other diagnosis	64 (8)	49 (10)
Medication History		
Prior DMARD	531 (70)	424 (86)
Prior biologic	485 (63)	383 (77)
Prior DMARD and biologic	426 (56)	348 (70)
No prior DMARD or biologic	174 (23)	36 (7)

IQR: interquartile range; DMARD: disease-modifying anti-rheumatic drug
*Numbers in tocilizumab group do not add up to 100% due to rounding

Table 1. Baseline characteristics of subjects initiating tocilizumab or tofacitinib

and scant data exist regarding real-world practice. Our objective was to determine providers' HBV screening practices when prescribing TCZ and TOF.

Methods: We identified patients initiating TCZ or TOF in the Mass General Brigham (MGB) Healthcare System from retrospective review of electronic health records. Adult patients were included if they had ≥ 1 prescription for either TCZ or TOF and an outpatient rheumatology encounter in MGB. We characterized all available HBV screening data

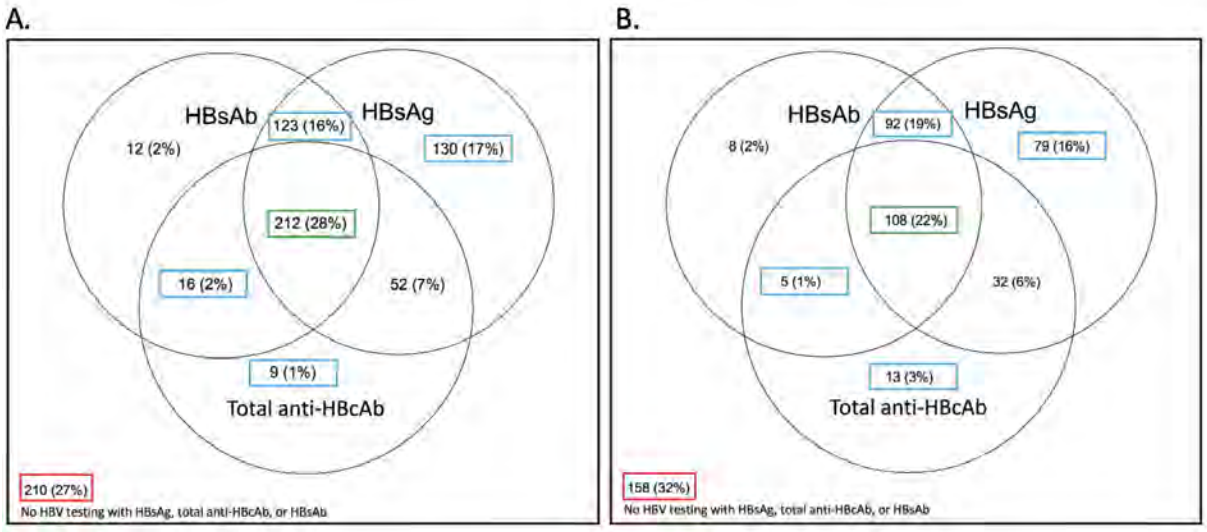
Table 2: Complete, partial, and inappropriate hepatitis B virus (HBV) screening among patients initiating tocilizumab and tofacitinib

Variable	Tocilizumab (N=764), n (%)	Tofacitinib (N=495), n (%)
Complete	212 (28)	108 (22)
Partial	278 (36)	189 (38)
Absent	210 (27)	158 (32)
Inappropriate*	163 (22)	177 (36)

*Inappropriate screening refers to anyone with testing for HBV e-antigen, HBcAb IgM, or HBV deoxyribonucleic acid (DNA) without a positive HBsAg or total anti-HBcAb, regardless of whether they had complete, partial, or absent HBV testing. Thus, percentages do not add up to 100%.

Table 2. Complete, partial, and inappropriate hepatitis B virus (HBV) screening among patients initiating tocilizumab and tofacitinib

Figure 1: Complete, partial, and absent hepatitis B virus screening among patients initiating (A) tocilizumab (n=764) and (B) tofacitinib (n=495)



Green boxes indicate complete HBV screening.
Blue boxes indicate partial HBV screening.
Red boxes indicate absent HBV screening.
Inappropriate HBV screening includes additional laboratory testing and therefore is not represented in the figure above.

Figure 1. Complete, partial, and absent hepatitis B virus screening among patients initiating (A) tocilizumab (n=764) and (B) tofacitinib (n=495)

(1995-2018) prior to or within 30 days of the first TCZ or TOF prescription as: complete (HBV surface antigen [HBsAg], HBV total core antibody [total anti-HBcAb], and HBV surface antibody [HBsAb]), partial (HBsAg or total anti-HBcAb but not both), and inappropriate (HBV e-antigen, HBcAb IgM, or HBV deoxyribonucleic acid [DNA] without a positive HBsAg or total anti-HBcAb).

Results: Among 913 patients prescribed TCZ and 630 prescribed TOF, we identified 764 patients prescribed TCZ and 495 prescribed TOF who had an outpatient rheumatology encounter in MGB. Median age was 64 years and 60 years in the TCZ and TOF groups, respectively; most were white and female. Rheumatoid arthritis was the most common indication (TCZ [51%] and TOF [77%]) (**Table 1**). Complete HBV screening was performed in 212 (28%) TCZ patients and 108 (22%) TOF patients (**Table 2** and **Figure 1**). Partial HBV screening was performed in 278 (36%) TCZ patients and 189 (38%) TOF patients. Inappropriate HBV testing was performed in 163 (22%) TCZ patients and 177 (36%) TOF patients. No appropriate HBV screening was performed in 210 (27%) TCZ patients and 158 (32%) TOF patients.

Conclusion: Fewer than 30% of patients prescribed TCZ or TOF for rheumatologic indications had complete HBV screening, which underscores the lack of consistent guidelines regarding HBV screening for this population. More than a quarter had inappropriate HBV screening, which contributes to medical errors and healthcare resource waste. The frequency of partial, inappropriate, or absent HBV screening among patients prescribed TCZ or TOF suggests that provider education and electronic health record system alerts could improve HBV screening practices.

Disclosure: N. Serling-Boyd, None; **A. Mohareb**, None; **A. Kim**, Biomarin, Inc, 7; **E. Hyle**, None; **Z. Wallace**, Bristol-Myers Squibb, 2.

Abstract Number: 1621

Cervical Cancer Screening Among Women with Systemic Lupus Erythematosus or Prescribed Tumor Necrosis Alpha-inhibitors Who Receive Outpatient Rheumatology Care

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Cervical cancer screening is important for women with systemic lupus erythematosus (SLE) and women prescribed TNF-alpha inhibitors (TNFi), as they have an increased risk of cervical dysplasia and cancer due to immune dysfunction and/or suppression. We describe receipt of guidelines-concordant cervical cancer screening among women receiving rheumatology care in a large Pennsylvania healthcare system. We explored whether women with SLE or prescribed TNFi would be more likely to receive guideline-concordant screening than women with average risk of cervical cancer.

Methods: Cervical cancer screening was compared between women ages 18-50 who had ≥ 2 rheumatology visits between 2007 and 2014, ≥ 1 documented screening test, and diagnosis of SLE or usage of TNFi's (cases) vs. fibro-

Table 1. Cervical cancer screening guidelines

Cervical Cancer Screening Guidelines	Change in Guidelines	Definition of Guideline-Concordant Screening
1. American College of Obstetricians and Gynecologists (ACOG)	Prior to 2009: Cervical cancer screening required annually After 2009: Every two years if younger than 30 years old, and every 3 years if 30 years of age or older	Women were required to meet at least one set of screening criteria (ACOG or USPTF) contemporaneous with the screening service
2. United States Preventive Task Force (USPTF)	In 2012: Cervical cancer screening every 3 years among women younger than 30 years old if negative cytology and screen every 5 years among women 30 years and older with negative human papillomavirus (HPV) co-testing.	

myalgia only (control). Outcomes and predictors were identified in the electronic health record by medication lists, ICD-9 and procedure codes. Guideline-concordant screening was defined as adherence with contemporaneous U.S. guidelines (Table 1), with six-month buffers added to each testing interval to account for potential scheduling constraints. Descriptive statistics were calculated and compared between groups using Chi-square or two-sample t-tests. Logistic regression was used to evaluate associations between each key predictor and the outcome variable; adjusted models included age, race/ethnicity, health insurance, and documented cervical dysplasia. Women without screening data (SLE: n=108; TNFi: n= 270) were excluded as they may have received screening outside of the health-care system; however, as some may not have had any screening tests completed, we also performed a separate sensitivity analysis categorizing these women as non-adherent with guidelines.

Results: Table 2 describes characteristics of controls (n=867), SLE cases (n=160), and TNFi cases (n=415). Guideline-concordant screening was conducted for 84% for controls, and 81% for SLE and 77% for TNFi cases. SLE cases were as likely as controls to receive guideline-concordant screening (OR 1.04, 95% CI: 0.49, 2.2) (Table 3), whereas TNFi cases were significantly less likely (aOR 0.56, 95% CI: 0.33, 0.95). As compared to whites, guideline-concordant screening was also less likely among non-white TNFi cases (aOR 0.55, 95% CI: 0.31, 0.99) and marginally less likely among non-white SLE cases (aOR 0.61, 95% CI: 0.32, 1.2). Having health insurance was associated with guideline-concordant screening among cases. Primary care or gynecology visits did not explain differences in screening. In sensitivity analyses, the relationship between SLE and guideline-concordant screening was unchanged but was attenuated for TNFi cases.

Conclusion: Women at increased risk of cervical dysplasia/cancer were not more likely to receive guideline-concordant cervical cancer screening than women with average risk, and women who used TNFi were significantly less likely. Rheumatologists should help to ensure that patients with elevated cervical cancer risk are informed about their risks and referred for appropriate screening; additional strategies to ensure screening equity for marginalized populations must also be identified.

Table 2. Patient Characteristics

VARIABLE	Mean± S.D. or N (%)	Control (N=867)	SLE (N=160)	p-value‡	TNFi Usage (N=415)	p-value‡
		(a)	(b)	(a vs. b)	(c)	(a vs. c)
BASELINE AGE		38.0±7.5	35.8±8.4	**0.001****	38.5±7.1	0.215
RACE/ETHNICITY	White	727 (84%)	106 (66%)	**<.001****	357 (86%)	**0.015***
	Black	94 (11%)	39 (24%)		30 (7%)	
	Asian	5 (1%)	4 (3%)		9 (2%)	
	Hispanic/other	41 (5%)	11 (7%)		19 (5%)	
MARITAL STATUS	Single	320 (37%)	80 (50%)	**0.006****	140 (34%)	**0.001****
	Married	407 (47%)	67 (42%)		236 (57%)	
	Divorced	101 (12%)	9 (6%)		23 (6%)	
	Other	39 (5%)	4 (3%)		16 (4%)	
RHEUMATOLOGY VISITS		5.4±5.0	10.2±7.3	**<.001****	11.0±7.1	**<.001****
PRIMARY CARE VISIT (≥ 1 VISIT)		414 (48%)	76 (48%)	0.95	178 (43%)	0.10
GYNECOLOGY VISIT (≥ 1 VISIT)		329 (38%)	73 (46%)	0.08	144 (35%)	0.26
INSURANCE	None or <95% insured during follow-up	221 (25%)	54 (34%)	**0.030***	134 (32%)	**0.011***
	Insured	646 (75%)	106 (66%)		281 (68%)	
YEARS OF FOLLOW-UP		4.1±2.1	4.9±2.4	**<.001****	4.8±2.1	**<.001****
HPV TESTING	Yes	304 (35%)	72 (45%)	**0.017***	163 (39%)	0.142
CERVICAL DYSPLASIA	Yes	44 (5%)	9 (6%)	0.773	21 (5%)	0.991
GUIDELINE-CONCORDANT CERVICAL CANCER SCREENING (with 6-month buffer)	Yes	232/277 (84%)	50/62 (81%)	0.554	111/145 (77%)	0.072

‡ t-test or Pearson's χ^2 test
Control- Fibromyalgia
TNFi – Tumor necrosis factor alpha inhibitor
SLE- Systemic lupus erythematosus

Table 3. Logistic Regression Models of the Separate Associations of SLE Diagnosis and TNFi usage on Guideline-Concordant Cervical Cancer Screening

	Frequencies		Odds Ratio	
1. Systemic Lupus Erythematosus (SLE)	Guideline-Concordant Screening	Not Guideline-Concordant Screening	Univariate Model	Full Model
SLE use	50 (18%)	12 (21%)	0.81 (0.40, 1.6)	1.04 (0.49)
Age	36.7 ± 7.6	36.5 ± 7.5	1.00 (0.97, 1.0)	1.0 (0.96, 1.0)
Insurance (vs no insurance)	188 (67%)	21 (37%)	3.43 (1.90, 6.2)	3.12 (1.7, 5.7)
History of cervical dysplasia	44 (16%)	7 (12%)	1.32 (0.56, 3.1)	1.28 (0.53, 3.1)
Nonwhite (vs White)	65 (23%)	22 (39%)	0.48 (0.26, 0.87)	0.61 (0.32, 1.15)
	Frequencies		**Odds Ratios**	
2. TNF-alpha inhibitor use (TNFi)	Guideline-Concordant Screening	Not Guideline-Concordant Screening	Univariate Model	Full Model
TNFi use	111 (32%)	34 (43%)	0.63 (0.38, 1.0)	0.56 (0.33, 0.9)
Age	37.7 ± 7.1	36.8 ± 7.4	1.02 (0.98, 1.05)	1.02 (0.99, 1.06)
Insurance (vs no insurance)	243 (71%)	28 (35%)	4.43 (2.64, 7.42)	4.07 (2.39, 6.94)
History of cervical dysplasia	54 (16%)	9 (11%)	1.45 (0.68, 3.08)	1.44 (0.65, 3.18)
Nonwhite (vs White)	58 (17%)	26 (33%)	0.41 (0.24, 0.72)	0.5 (0.31, 0.99)

Disclosure: M. Birru Talabi, None; **K. Jeong**, None; **K. Abebe**, None; **M. Clowse**, UCB, 5, GSK, 2, 5, Astra Zeneca, 5, Pfizer, 2; **R. Domsic**, Formation Biologics, 5, Eicos Sciences, Inc, 5, Corbus Pharmaceutical Holdings, 5; **S. Borrero**, None.

Abstract Number: 1622

Determining the Zoster Vaccination Rate Among Veterans on Chronic Immunosuppressive Therapy at the Southeast Louisiana Veterans Healthcare System – a Quality Indicator

Hannah Kenninger[1], Rachel Dayno[1], Nkechinyere Emejuaiwe[2], Ileannette Robledo-Vega[3], Whitney Bembry[1], Myriam Guevara[4] and Soham Mahato[5], [1]Tulane University School of Medicine, New Orleans, LA, [2]Southeast Louisiana Veterans Healthcare System, New Orlenas, LA, [3]Louisiana State University Health Sciences Center, New Orlenas, LA, [4]Lousiana State University Health Sciences Center, New Orleans, LA, [5]LSUHSC School of Public Health, New Orleans, LA

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Measures & Measurement of Healthcare Quality Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Herpes Zoster (HZ) causes an infection commonly known as shingles. Patients with HZ are at increased risk for post-herpetic neuralgia, which is painful for patients and costly for the United States (US) healthcare system. Certain medications and diseases such as RA, SLE, and IBD weaken the immune system making the body more susceptible to HZ. Two vaccines are available in the US. Zostavax, a live-attenuated vaccine (ZVL), was approved by the FDA in 2006 and Shingrix, an adjuvanted recombinant zoster vaccine (RZV), was approved in 2017. ZVL reduces the risk of HZ by 65% in patients aged 50-59, and by 50% in patients aged 60-69. Despite the relative

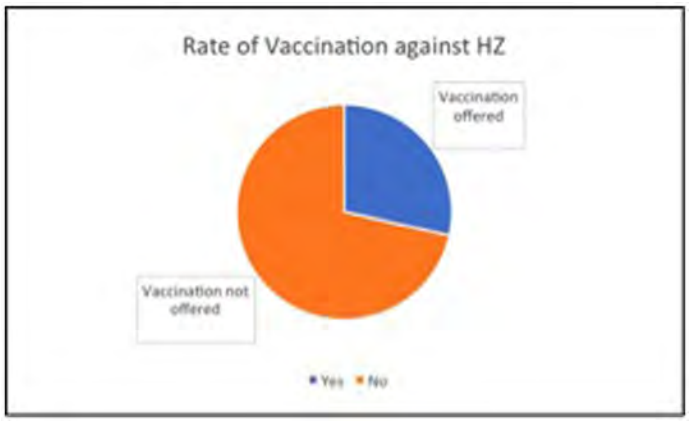

Figure 1. Rate of Vaccination against HZ

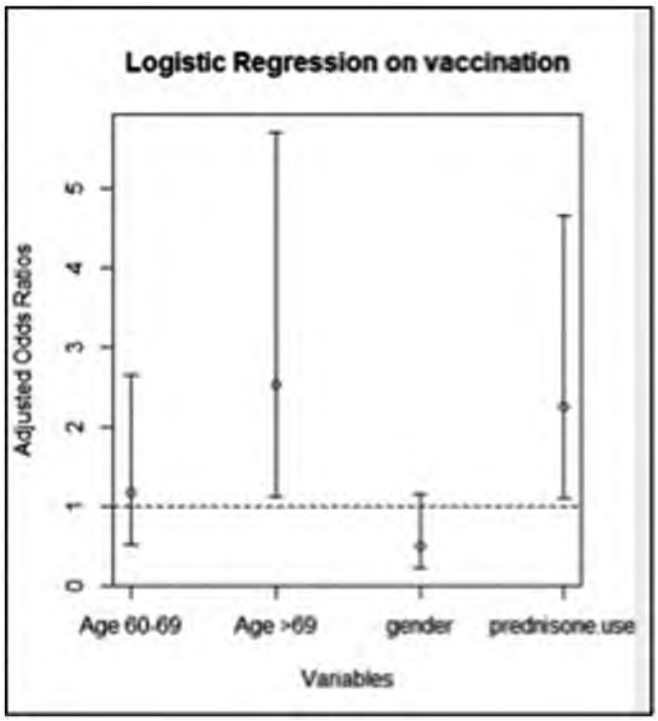

Figure 2. Vaccination Offered: Odds Ratios with 95% Confidence Interval

reduction of HZ with vaccination, rates in the general population remain low. Vaccination rates in 2016 were estimated at 33.4% among adults 60 years and older and 37.4% among adults 65 years and older.

The objective was to determine zoster vaccination rates of ZVL or RZV in patients on chronic immunosuppressive therapy at the Southeast Louisiana Veterans Healthcare System. We describe the correlation between vaccination rate and age, race, immunosuppressive medication and diagnosis.

Methods: This was a descriptive study with a retrospective review of records in the Computerized Patient Record System (CPRS). We included veterans 50 years and older treated with the following immunosuppressive medications: AZA, MMF, cyclosporine, MTX, LEF, tofacitinib, infliximab, adalimumab, etanercept, abatacept, rituximab or certolizumab from January 1, 2016 through December 31, 2018 (n= 601). Veterans with a history of malignancy, diabetes

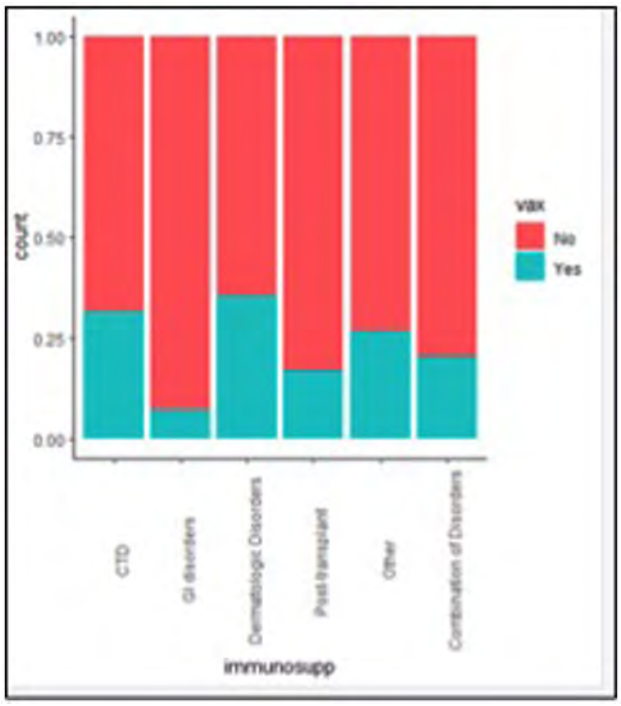

Figure 3. Rate vaccination was offered with respect to the diagnosis requiring immunosuppression

mellitus, HIV infection or death during the study period were excluded (n= 369). Charts were reviewed to determine receipt of ZVL or RZV and identify concurrent glucocorticoid therapy.

Results: 31 (13.4%) patients in our study population were vaccinated against HZ (Figure 1). Of the 232 patients included in the study, 66 (28.4%) were offered vaccination and 166 (71.6%) were not. Of the patients offered vaccination, 35 (53%) refused or had no documentation of receipt of vaccination. Of those vaccinated, 24 (77.4%) received RZV and 7 (22.6%) received ZVL.

Age and glucocorticoid therapy had a significant effect on whether vaccination was offered (Figure 2). Patients 70 years and older were 2.52 times more likely to be offered vaccination than patients less than 60 years of age (reference group). Patients on prednisone therapy were 2.26 times more likely to be offered vaccination than those not on prednisone therapy.

Patients on immunosuppressive therapy for gastrointestinal disorders were less likely to receive vaccination against HZ (Figure 3).

Race, gender and immunosuppressive medication did not influence the offer of vaccination against HZ in our study cohort.

Conclusion: The rate of vaccination against HZ in patients on immunosuppressive therapy in our study population was low despite the accessibility of vaccines. This is concerning given the risk of infection in this population and the proven efficacy of zoster vaccination. An extension of this study will explore factors that influencevaccination ratesand investigate interventions to improve vaccination rates. Interventions should include both provider and patient education.

Disclosure: H. Kenninger, None; **R. Dayno**, None; **N. Emejuaiwe**, None; **I. Robledo-Vega**, None; **W. Bembry**, None; **M. Guevara**, None; **S. Mahato**, None.

Abstract Number: 1623

Improving Pneumococcal Vaccination Rates Among Immunosuppressed Adults in an Academic Rheumatology Clinic Utilizing a Nurse Driven Protocol

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatology patients are particularly vulnerable to pneumococcal infection due to both their underlying disease and immunosuppressive therapy. Thus, quality improvement metrics include increasing pneumococcal vaccination rate in rheumatology patients. Our goal was to implement a nurse driven protocol to increase by 10% the pneumococcal conjugate and polysaccharide vaccination rate during a three month period among immunosuppressed patients aged 19-64 years old followed at an academic adult rheumatology clinic.

Table 1 Pneumococcal vaccination for significantly immunosuppressed patients aged 19 years and older

For all adult patients

1) **On immunosuppressive therapy or with intent to start immunosuppressive therapy or**
2) **Significant immunocompromising conditions:** CSF leaks, cochlear implants Congenital or acquired asplenia, Sickle cell disease, Chronic renal failure, congenital or acquired immunodeficiency, generalized malignancy, HIV infection, Hodgkin's disease, Iatrogenic immunosuppression, leukemia, lymphoma, multiple myeloma, nephrotic syndrome, solid organ transplant

-Absolute contraindication: Allergy to PCV13/PPSV23 or Tdap vaccination
-Consider deferring pneumococcal vaccination for patients on Rituximab or receipt of Rituximab in the last 6 months (see below for further guidance*)

Prior Pneumonia vaccination status	Recommendation
No pneumococcal vaccinations or Unknown vaccination history	- Give PCV13 then PPSV23 at least 8 weeks later - 5 years later, repeat PPSV23 unless previous PPSV23 given at age ³ 65
1 dose PPSV23	- Give PCV13 at least 1 year after PPSV23 - Repeat PPSV23** at least 5 years after previous PPSV23 and at least 8 weeks after PCV13 if the previous PPSV23 was administered at age <65
2 doses PPSV23	- Give PCV13 at least 1 year after last PPSV23
PCV13 only	- Give PPSV23 at least 8 weeks after PCV13 - Repeat PPSV23 at least 5 years later
PCV13 and 1 dose PPSV23	- Repeat PPSV23 at least 5 years after previous PPSV 23** and at least 8 weeks after PCV13 if the previous PPSV23 was at age <65 - Nothing to do if the previous PPSV23 was at age ³ 65
PCV13 and 2 doses PPSV23	- Nothing to do if patient is under 65 years old at time of completion of vaccination. If over age 65 see recommendations below ***

*For patients undergoing consideration for Rituximab therapy it is optimal to give pneumococcal vaccines at least two weeks prior to therapy. For patients currently receiving Rituximab therapy, wait at least 6 months after the last dose of Rituximab before administering pneumococcal vaccination

**Revaccination of PPSV 23 before the age of 65 is not required in patients with CSF leaks or cochlear implants and in immunocompetent patients (includes those with alcoholism, chronic heart, liver, lung disease, cigarette smoking and diabetes mellitus).

Table1. Pneumococcal Vaccination For Significantly Immunosuppressed Patients Aged 19 Years And Older

ACR 2020 Abstract

Figure 1:

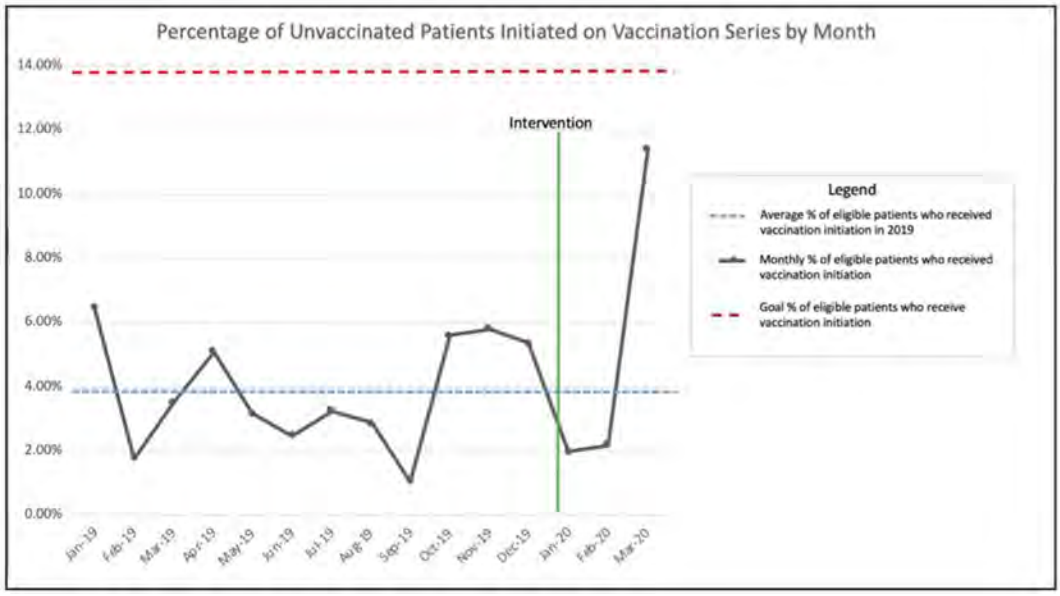


Figure 1. Percentage Of Unvaccinated Patients Initiated On Vaccination Series By Month

Methods: Eligible adults aged 19-64 years old were identified in the Electronic Medical Record (EMR) using a search protocol based on pre-set immunosuppressive medication group. We calculated baseline vaccination rate by assessing whether patients had received either the Pneumovax23 (PPSV23) or Prevnar13 (PCV13) or both vaccines from January 1, 2019 - December 31, 2019. We developed a nurse-driven workflow for vaccination implementation in the clinic. Using Center for Disease Control (CDC) guidelines, we created a pneumococcal vaccination protocol (Table 1) and converted it into a university approved Standing Medical Order (SMO) to be used by the nursing staff. We held educational sessions for the nursing staff to review the protocols and workflow. Staff re-training was implemented mid-way through the cycle. Post-intervention pneumococcal vaccination rates were calculated on a monthly basis.

Results: Baseline rate of both PCV13 and PPSV23 immunization (full immunization) for immunosuppressed rheumatology patients aged 19-64 years in 2019 was 6.6%. Baseline rate of unique patients within the target population who had received any type of immunization in our clinic (either PCV13, PPSV23, or both) was 25.3%.

Average monthly percentage of unvaccinated patients within target population seen in our clinic in 2019 was 73.2%. Percent of eligible patients who had pneumococcal vaccination series initiated, on average per month, in our clinic was 3.9% for 2019.

Start date for the intervention phase of project was January 1, 2020. We obtained post-intervention vaccination data for Jan-March 21, 2020 [a truncated three month time period due to COVID-19 pandemic clinic changes]. While the percentage of initiation of vaccination series continued to be low in Jan and Feb 2020, we achieved 11.4% vaccination rate of previously unvaccinated patients in March 2020 (Figure 1), which represents a nearly three fold increase over baseline vaccination rate.

Conclusion: During a three month cycle of nurse-driven SMO protocol to implement pneumococcal vaccination, we were able to increase our pneumococcal vaccination initiation rate of eligible immunocompromised patients from

baseline of 3.9% to 11.4%. Overall vaccination rates of eligible patients remain low, but we anticipate that continued use of a nurse driven protocol will improve this rate. Our study suggests that using a nurse-driven SMO protocol is a useful tool in improving vaccination rate amongst immunocompromised rheumatology patients. The post-intervention data is currently scarce; however, we hope to obtain four months more worth of data after the clinics are anticipated to re-open in June 2020.

Disclosure: E. Joerns, Pfizer, 2; **B. Bermas**, None; **P. Bajaj**, None; **N. Pokala**, None; **R. Arasaratnam**, None; **J. Reisch**, None; **D. Wang**, None.

Abstract Number: 1624

Improving Pneumococcal Vaccination in Veterans with Rheumatic Diseases

Sarah Homann[1], Michelle Ormseth[2], Christianne Roumie[2] and Robert Dittus[2], [1]Veterans Affairs Tennessee Valley Healthcare System / Vanderbilt University Medical Center, Nashville, TN, [2]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

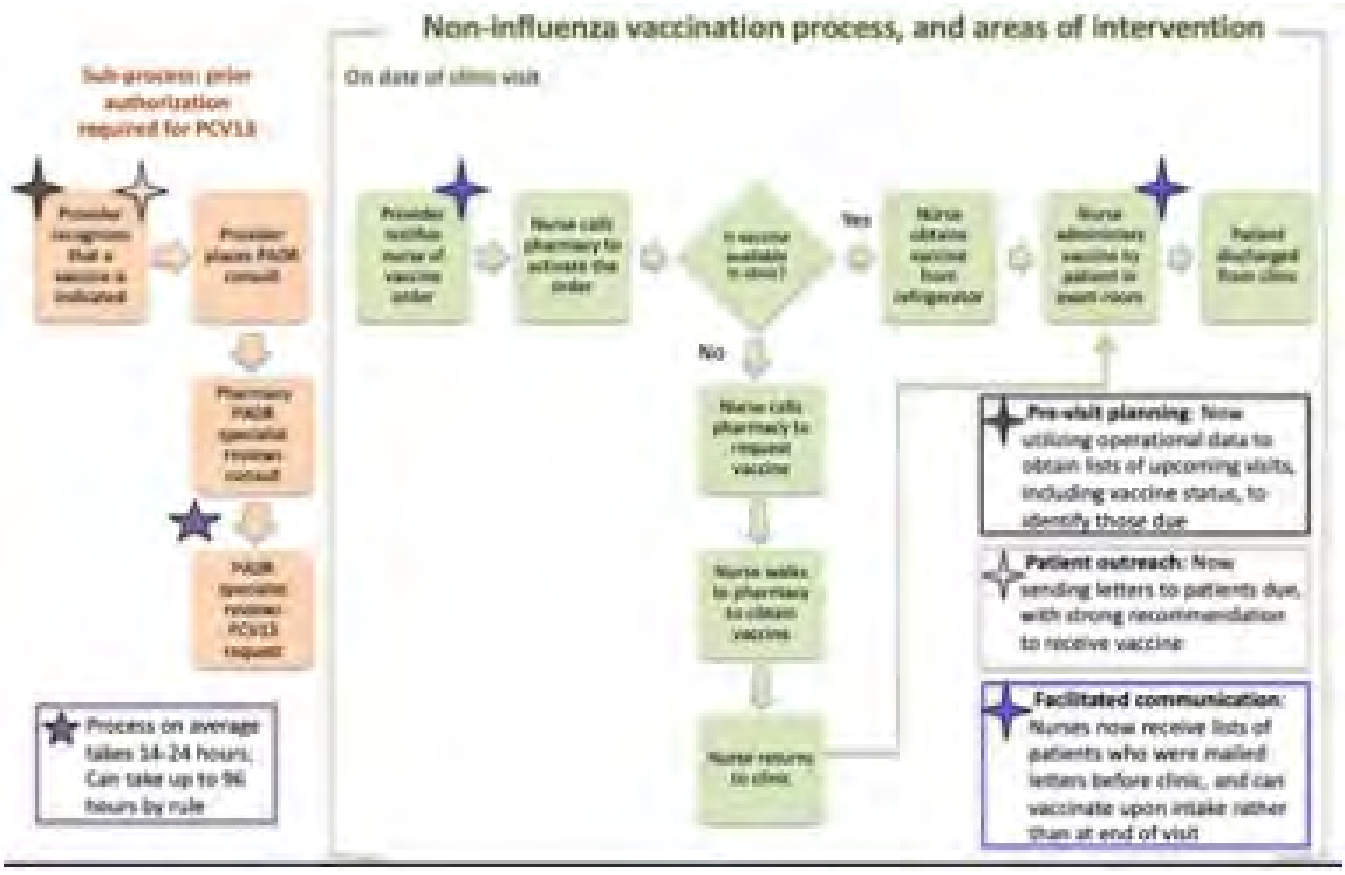
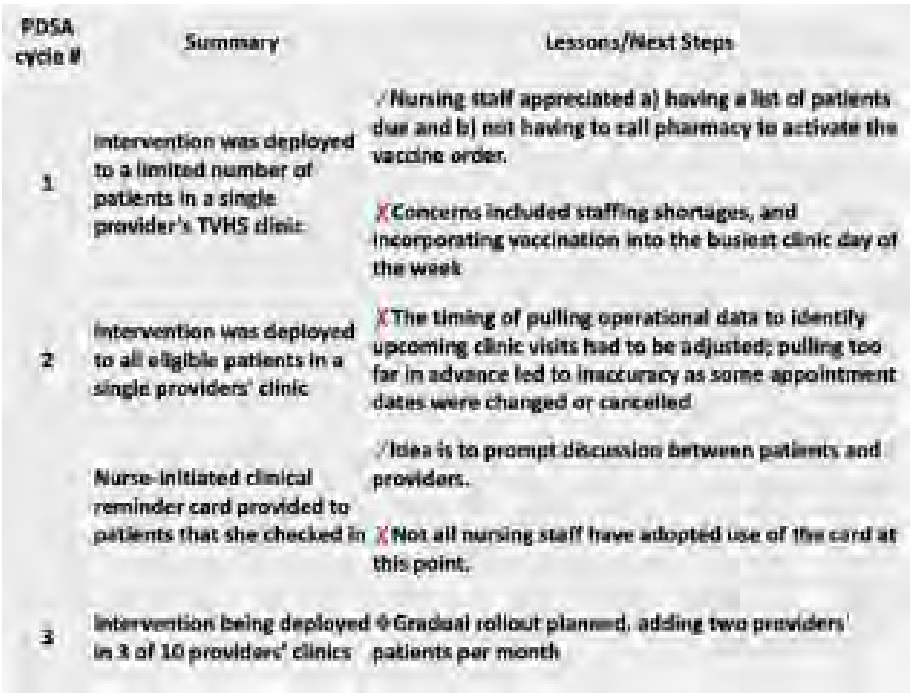


Figure 1. Process Map and Intervention



PDSA cycle #	Summary	Lessons/Next Steps
1	Intervention was deployed to a limited number of patients in a single provider's TVHS clinic	✓Nursing staff appreciated a) having a list of patients due and b) not having to call pharmacy to activate the vaccine order. ✗Concerns included staffing shortages, and incorporating vaccination into the busiest clinic day of the week
2	Intervention was deployed to all eligible patients in a single providers' clinic	✗The timing of pulling operational data to identify upcoming clinic visits had to be adjusted; pulling too far in advance led to inaccuracy as some appointment dates were changed or cancelled
	Nurse-initiated clinical reminder card provided to patients that she checked in	✓Idea is to prompt discussion between patients and providers. ✗Not all nursing staff have adopted use of the card at this point.
3	Intervention being deployed in 3 of 10 providers' clinics	✧Gradual rollout planned, adding two providers' patients per month

Figure 2. PDSA Summary

Background/Purpose: Patients with rheumatic diseases are at increased risk of invasive pneumococcal disease. Both pneumococcal conjugate vaccine (PCV13) and pneumococcal polysaccharide vaccine (PPSV23) are recommended for patients on immunosuppressant medications. However, under-vaccination of this population is common. The aim of this quality improvement project was to decrease the percent of patients in Tennessee Valley Healthcare System (TVHS) Rheumatology clinic due for vaccination in a given month from the baseline of 36% to a goal of 28% within 6 months.

Methods: Barriers to vaccination were identified and an intervention was designed incorporating patient outreach, provider outreach, and health system components (Figure 1). The primary outcome measure was the percent of randomly sampled patients due for a pneumococcal vaccination, assessed monthly. Process measures include the number of vaccinations administered in rheumatology clinic each month. Balancing measures included qualitative feedback from staff. The Plan Do Study Act (PDSA) cycle methodology was used to test and analyze process changes (Figure 2).

Results: Statistical process control (SPC) charts were used to visualize results (Figure 3). Post-implementation, the overall percent of patients due for a pneumococcal vaccination is statistically unchanged thus far, though trending downwards. The number of pneumococcal vaccines administered in clinic was steadily rising with a special cause signal seen in January 2020, however this change was not sustained. In the 9 month pre-intervention period, 38 vaccinations in total were administered in Rheumatology clinic, whereas in the post-intervention implementation period 54 vaccines were given in just 5 months.

Conclusion: A combination of operational data use, pre-visit planning, and patient outreach can lead to increased pneumococcal vaccination rates in a rheumatology clinic setting. The lack of statistically significant change in our primary outcome measure is likely explained by our sampling strategy, which samples from all providers' clinics, though the intervention had only been rolled out in about half of the providers' clinics before the COVID-19 pandemic. A more upstream process measure is the number of pneumococcal vaccinations administered in clinic each month, where

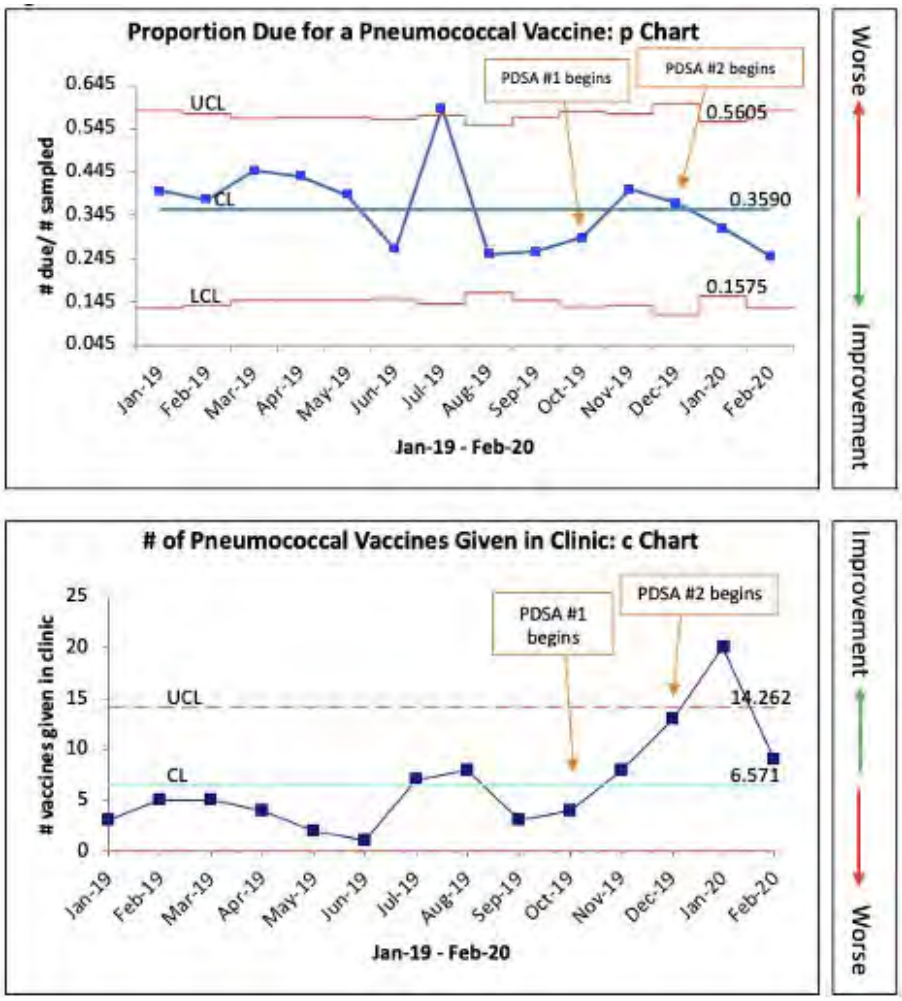


Figure 3. SPC Charts

we have seen signs of improvement. Next steps include 1) ongoing rollout to the clinics of all rheumatology providers, 2) development of an educational intervention for providers regarding the complex pneumococcal vaccination schedule, and 3) adaptations to the clinic templated note to include reminders and facilitate ordering.

Disclosure: S. Homann, Pfizer, 2; **M. Ormseth**, None; **C. Roumie**, None; **R. Dittus**, None.

Abstract Number: 1625

Pneumocystis Jiroveci Pneumonia in Immunocompromised Patients with Rheumatologic Disease in a Single, Tertiary Medical Center

Zahra Rehman[1], Megan Krause[1], Jessica Newman[2] and Pooja Bhadbhade[1], [1]The University of Kansas Medical Center, Kansas City, KS, [2]The University of Kansas Medical Center, Kansas City

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Measures & Measurement of Healthcare Quality Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Pneumocystis jiroveci pneumonia (PJP) is rare, but can be fatal among immunocompromised. There is no consensus on indications for PJP prophylaxis in rheumatologic patients. The challenge involves the benefit of prophylaxis with antimicrobials versus the risk of adverse events caused by the prophylactic medication.

Methods: A retrospective chart review was conducted to identify patients with PJP and a rheumatologic disease including rheumatoid arthritis (RA), Sjogren's syndrome, systemic lupus erythematosus (SLE), granulomatosis with polyangiitis (GPA), eosinophilic granulomatosis with polyangiitis (EGPA), microscopic polyangiitis (MPA), giant cell arteritis, polyarteritis nodosa, Takayasu's arteritis, dermatomyositis (DM), polymyositis, and systemic sclerosis (SSc) at a single, tertiary academic medical center between 1/1/2007 and 1/1/2019. Electronic medical records were reviewed to confirm diagnoses. PJP was based on clinical symptoms, laboratory studies (bronchoalveolar lavage PCR, Fungitell, beta 1,3 glucan, lactate dehydrogenase), radiographic findings, and infectious disease assessment. Data regarding immunosuppressants, prednisone use, lymphocyte count, interstitial lung disease (ILD), and use of prophylaxis was abstracted. PJP prophylaxis recommendations commonly used in rheumatologic patients were reviewed and indications for prophylaxis were determined.

Results: Fifteen patients were confirmed with a diagnosis of a rheumatologic disease and PJP. Diseases noted were RA in 5 patients, GPA in 3 patients, MPA in 2 patients, SLE in 1 patient, DM in 1 patient, psoriatic arthritis in 1 patient, antiphospholipid syndrome and autoimmune hemolytic anemia in 1 patient, and limited cutaneous SSc and necrotizing myopathy in 1 patient. Of these patients, 1 with SLE developed PJP despite prophylaxis with atovaquone. The other 14 patients did not receive prophylaxis. Fourteen of the 15 patients were on prednisone and 13 of these patients were on at least one additional immunosuppressant. Twelve of the 15 patients had lymphopenia at the time of PJP diagnosis, and 5 had ILD.

Four of the 15 patients who developed PJP were on low dose prednisone with at least one immunosuppressant. One of the 15 patients was on 3 immunosuppressants and no steroids. Three of these 5 patients had RA without ILD, 1 had PsA, and 1 had SSc with ILD and necrotizing myopathy. These 5 patients are considered low risk and prophylaxis would not be indicated due to current recommendations.

The remaining 10 patients would have been candidates for prophylaxis due to their dose and duration of prednisone, concurrent immunosuppression, or underlying disease.

Conclusion: Based on recommendations commonly used for PJP prophylaxis in patients with rheumatologic diseases, 10 of the 15 patients would have been candidates for prophylaxis and PJP may have been prevented, but 5 patients were considered low risk with no prophylactic indication. Although rheumatologists need to improve on utilizing PJP prophylaxis for high risk patients, this study indicates that further research is needed to determine individualized risk for initiating prophylaxis in rheumatologic patients who are not considered high risk for developing PJP.

Disclosure: Z. Rehman, None; **M. Krause**, None; **J. Newman**, None; **P. Bhadbhade**, None.

Abstract Number: 1626

Long-Term Follow-Up of Renal Transplantation Due to Lupus Nephritis. Single Universitary Center Experience

Lara Sanchez-Bilbao[1], Marina De Cos-Gomez[2], Inigo Gonzalez-Mazon[3], David Martinez-Lopez[4], Juan Carlos Ruiz-San Millan[2], Miguel Ángel González-Gay[5] and Ricardo Blanco[1], [1]Hospital Universitario Marques de Valdecilla, Santander, Spain, [2]Hospital Universitario Marqués de Valdecilla, Santander, Cantabria, Spain, [3]Hospital Universitario Marques de Valdecilla, Bezana, Spain, [4]Hospital Universitario Marques de Valdecilla, Santander (SPAIN), Spain, [5]Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster III: Therapies

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is a severe complication of systemic lupus erythematosus (SLE). Approximately 10-20% of LN develop end stage renal disease (ESRD) and need replacement therapy. Renal transplantation may be a good option. However, concerns about LN recurrence after renal transplantation have been reported.

In a series of 23 patients with first renal transplantation due to LN our aim was to assess **a)** clinical features, **b)** renal transplantation as replacement therapy, **c)** SLE flares after transplantation.

Methods: Observational study of unselected all consecutive patients studied in a single reference University Hospital with**: a)** diagnosis of SLE by ACR/SLICC 2012 criteria. **b)** diagnosis of NL by performing biopsy (according to the World Health Organization and International Society of Nephrology/Renal Pathology Society classification), **c)** first renal transplant. Cumulative survival rates after transplantation were estimated by the Kaplan-Meier method.

Results: We studied 23 (16 women/7 men) patients with first renal transplantation due to LN; mean age at SLE diagnosis of 26.37±12.70 years and mean age at kidney transplantation of 39.80±11.27 years. Mean follow-up of 12.18±9.02 years. Demographic baseline characteristics and clinical manifestations of these patients are shown in **TABLE 1.**

The main clinical manifestations at diagnosis were articular (n= 12; 52.17%) and cutaneous (n=13; 56.52%). On the other hand, 16 patients (69.6%) presented impaired renal function at diagnosis. In the other 7 patients (30.4%), this manifestation appeared with a delay of diagnosis from the onset of symptoms of 13.17±7.73 years.

Renal biopsy had been performed in 21 patients with LN: type II LN (n=2; 9.1%), type III (n=8; 36.4%), type IV (n=9; 40.9%) and type V (n=2; 9.1%).

Graft and patients survival function after transplantation is represented in **Figure 1 and 2.**

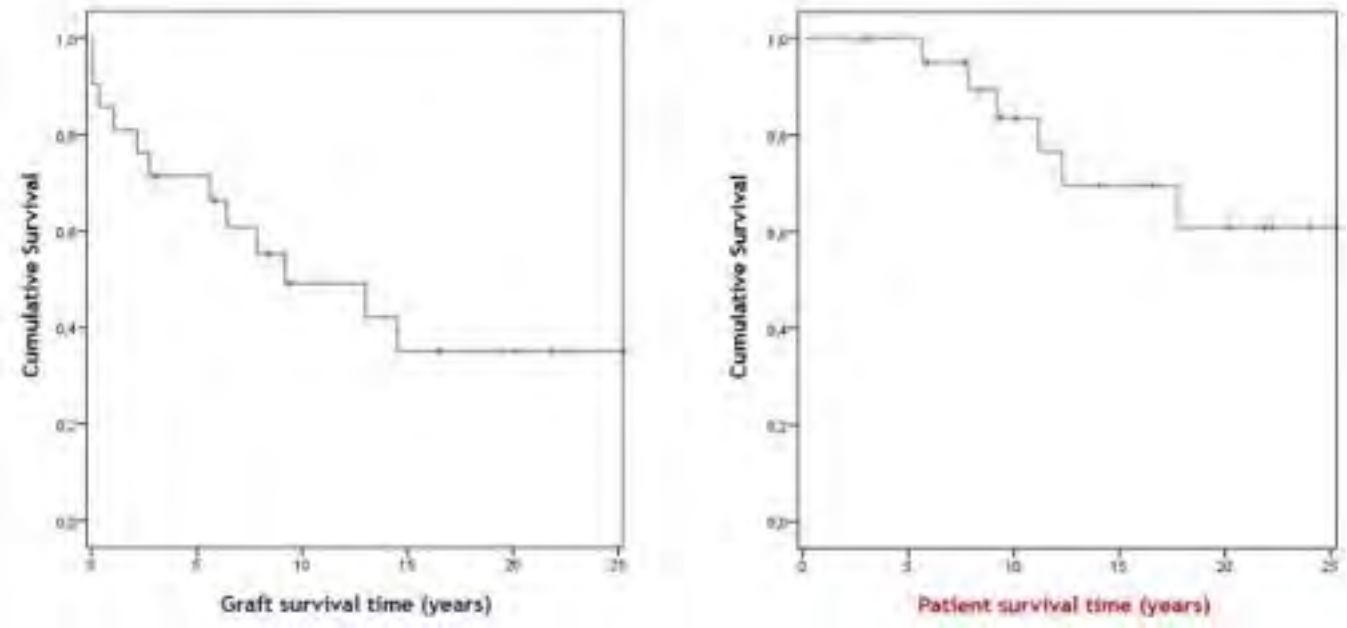
Regarding lupus flares after transplantation, 3 patients (13.04 %) developed a lupus flare: 2 cases presented as extrarenal disease (one of them was a pneumonitis and the other one was a cutaneous and articular flare) and only 1 case with histological recurrence in the graft (Mean follow-up 15 ±9.84 years).

Conclusion: Renal transplantation is a safe alternative therapy for ESRD in this population and can provide a long-term survival. However, it is very important to consider the occurrence of flares even in the long-term post-transplant.

TABLE 1. Demographic baseline characteristics and clinical manifestations of patients with renal transplantation due to LN.

DEMOGRAPHIC PARAMETERS	
Sex, n (%)	7 ♂ / 16 ♀ (30.4%/69.06%)
Age at SLE diagnosis (years), mean ± SD	26.37±12.70
Age at renal transplantation, mean ± SD	39.80±11.27
SLE RELATED DATA	
Systemic symptoms	**12.0 (52.17)**
- Fever, n (%)	8.0 (34.78)
- Weight loss, n (%)	3.0 (30.0)
- Asthenia, n (%)	3.0 (30.0)
Articular affection	**12.0 (52.17)**
- Joint swelling, n (%)	9.0 (39.13)
- Arthralgia, n (%)	3.0 (13.04)
Skin affection	**13.0 (56.52)**
- Malar erythema, n (%)	2.0 (8.6)
- Discoid lupus, n (%)	0.0 (0.0)
- Photosensitivity, n (%)	3.0 (13.04)
- Ulcers, n (%)	5.0 (21.73)
- Alopecia, n (%)	3.0 (13.04)
- Raynaud, n (%)	1.0 (4.34)
SLE RELATED DATA	
Renal involvement	**16.0 (69.56)**
Hematological involvement	**13.0 (56.52)**
- Anemia, n (%)	6.0 (26.10)
- Leukopenia, n (%)	5.0 (21.73)
- Plaquetopenia, n (%)	2.0 (8.70)
Pericarditis	**2.0 (8.70)**
Nervous system	**6.0 (26.10)**
- Peripheral, n (%)	1.0 (4.34)
- Central	4.0 (17.40)

Figures 1 and 2.



Disclosure: L. Sanchez-Bilbao, None; **M. De Cos-Gomez**, None; **I. Gonzalez-Mazon**, None; **D. Martinez-Lopez**, Lilly, 2; **J. Ruiz-San Millan**, None; **M. González-Gay**, None; **R. Blanco**, None.

Abstract Number: 1627

Phase I Trial of High-dose Hydroxychloroquine for the Treatment of Ambulatory Patients with Mild COVID-19: A Study in the Effects of Shifting Public Opinion on Patient Enrollment

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster III: Therapies
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Coronavirus disease 2019 (COVID-19) was first recognized in December 2019 and quickly became a global pandemic within months. Amidst a myriad of uncertainties, early data from in-vitro analysis and a small-population retrospective study demonstrated promise for hydroxychloroquine (HCQ), a small molecule oral drug prevalently used for rheumatic diseases and previously in malarial therapy. The news of HCQ and its use in COVID-19 disseminated through social media channels and rose to international attention before proper conduct of large population, prospective clinical studies. It is within this capricious global environment that we discuss the unique pharmacokinetic (PK) reasoning for use of high dose HCQ in mild COVID-19 and subsequent proceedings of our phase I clinical trial and associated challenges.

Methods: We conducted a single-center, single-arm tolerability study for ambulatory patients with mild COVID-19 and risk factors for progression to moderate or severe disease. Physiologically based PK modeling suggests HCQ loading doses between 400 mg BID and 600 mg BID are effective in achieving desired lung tissue concentration, potentially enabling a faster clinical effect. Enrollment and consent were obtained remotely through a telephonic interaction between a physician and participant while the participant utilized the REDCap electronic consent platform. Participants took HCQ 600 mg twice daily for 5 days. Changes in symptoms and side effects were assessed via daily telephone questionnaire, with tolerability of HCQ at day 14 as the primary endpoint. Tolerability of the regimen was deemed acceptable if 80% of patients completed the protocol. Figure 1 shows the timeline of media releases with HCQ study recruitment.

Results: Ultimately, only 7 patients were enrolled in the study and 6 completed the 5 day course. Five patients (71%) tolerated the course without any side effects. One patient developed headaches, while another had nausea, vomiting, and diarrhea, was lost to follow up, and later hospitalized. After numerous reports in the media of potential severe side effects and ineffectiveness of HCQ for COVID-19 treatment, public opinion of HCQ shifted and potential participants became unwilling to be enrolled in the study, leading to its termination on 5/29/2020.

Conclusion: While a limited number of participants enrolled, no serious side effects were noted with use of high dose HCQ in mild COVID-19. We demonstrate that a large cohort prospective trial properly assessing HCQ in mild COVID-19 has many challenges in the current atmosphere, but given the tolerability of high doses HCQ, future research should give consideration of studying the potential benefit of this dose in rheumatic disease. (clinicaltrials.gov, *NCT04351620*)

Disclosure: P. Onkka, None; **P. Reid**, n/a, 9; **I. Bauer Ventura**, None; **B. Labadie**, None; **R. Jan**, None.

Abstract Number: 1628

Management of Gout After Pegloticase; Observations of US Clinical Practice from Trio Health and the American Rheumatology Network (ARN)

Nehad Soloman[1], Mona Amin[2], Simon Helfgott[3], Alexander Hu[4], Kent Kwas Huston[5], Jordan Leonard[6], Kelsey Milligan[7], Scott Milligan[7], Jasvinder Singh[8], John Tesser[9] and Colin Edgerton[10], [1]Arizona Arthritis & Rheumatology Associates, P.C., Peoria, AZ, [2]Arizona Arthritis & Rheumatology Associates, P.C., Scottsdale, AZ, [3]BWH- HMS, Boston, MA, [4]Arizona Arthritis & Rheumatology Associates, P.C., New Orleans, LA, [5]Kansas City Physician Partners, Kansas City, MO, [6]Arizona Arthritis & Rheumatology Associates, P.C., Phoenix, AZ, [7]Trio Health, Louisville, CO, [8]University of Alabama at Birmingham, Birmingham, AL, [9]Arizona Arthritis & Rheumatology Associates, Phoenix, AZ, [10]Articularis Healthcare, Summerville, SC

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster III: Therapies

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Pegloticase is approved for severe gout in patients that are intolerant to, or whose disease is ineffectively controlled by, other uric acid lowering therapies (ULTs). The positioning of pegloticase as the last therapeutic option begs the question, how is gout managed once pegloticase is discontinued? Here we examine treatment following pegloticase for patients in US clinical care.

Methods: The ARN-TRIO Rheumatology registry contains EMR (fielded and open text), lab, procedure, infusion, medical claims, and specialty pharmacy data generated in care of >75,000 patients by ARN, a network of independent practices with >200 rheumatologists across the US. This study included data for gout-diagnosed patients who initiated their last pegloticase course between Jan 2015 and Dec 2019 with >90 days follow-up from pegloticase discontinuation (index). Comparisons were made using t-test for continuous variables and chi-square or Fischer's exact tests for categorical variables. Time to event analyses were by Kaplan-Meier and log-rank test. To assess consistency of control of sUA < 6 mg/dL, evaluations were limited to patients with 2+ sUA measures within the period of interest.

Results: 70 of 213 pegloticase-treated patients met study criteria; by time of assessment which was ≥90 days past pegloticase discontinuation, 49/70 (70%) initiated a ULT. [FIGURE 1] Median time from index to ULT initiation was 13 days; 76% (37/49) of initiations occurred within 30 days, 90% (44/49) 90 days, and 96% (47/49) 180 days. Median follow up for patients who did not initiate a subsequent ULT was 404 days, greater than but not significantly different from patients that did initiate ULT post-pegloticase (322 days, p=0.270). The absence of kidney disease was significantly associated with ULT initiation (39/47, 83% v. 14/23, 61% non-initiators, p=0.043). Variables NOT associated with ULT initiation within 180 days post-pegloticase included age, gender, race, ethnicity, payer, CVD, diabetes, non-gout rheumatic diseases, duration of prior pegloticase, and serum uric acid (sUA) ≥6 mg/dL during pegloticase or at pegloticase discontinuation. Of the 47 patients that initiated subsequent ULT within 180 days, 22 of 47 had 2+ sUA measures during treatment, and 9/22 (41%) had 2+ sUA ≥6 mg/dL. Two or more sUA results post-pegloticase were provided for 6/23 patients that did not initiate ULT within 180 days; 5/6 (83%) had 2+ sUA ≥6 mg/dL. [FIGURES 2 & 3]

Conclusion: After pegloticase discontinuation, most patients quickly initiated allopurinol. Consistent sUA < 6 ml/dL was not maintained post-pegloticase for half (14/28) of the evaluable patients. As the new 2020 ACR Guidelines for

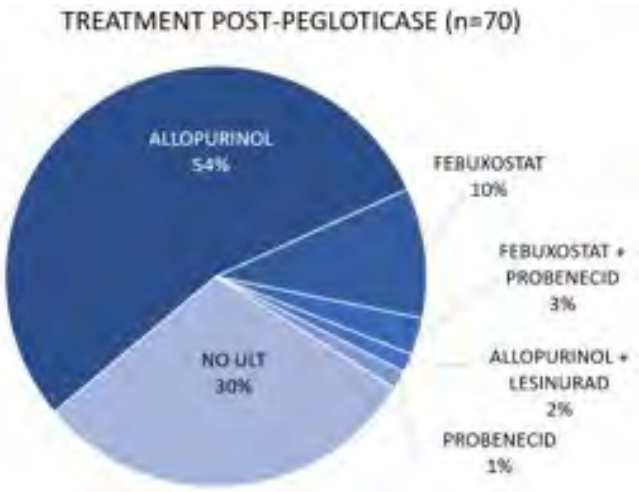

Figure 1. Treatment after pegloticase discontinuation (n=70)

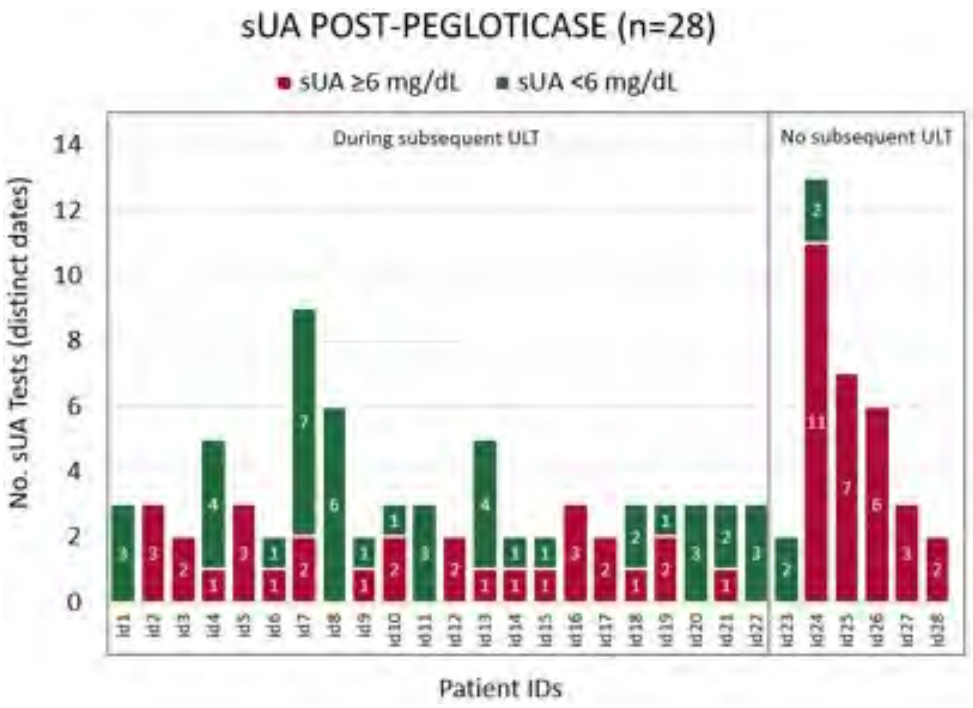

Figure 2. sUA test counts and results during ULT following pegloticase discontinuation (n=28)

the Management of Gout advises the treat to target approach to maintain sUA < 6 ml/dL, our results highlight the need for new ULTs and/or better strategies to maximize benefit with available therapies.

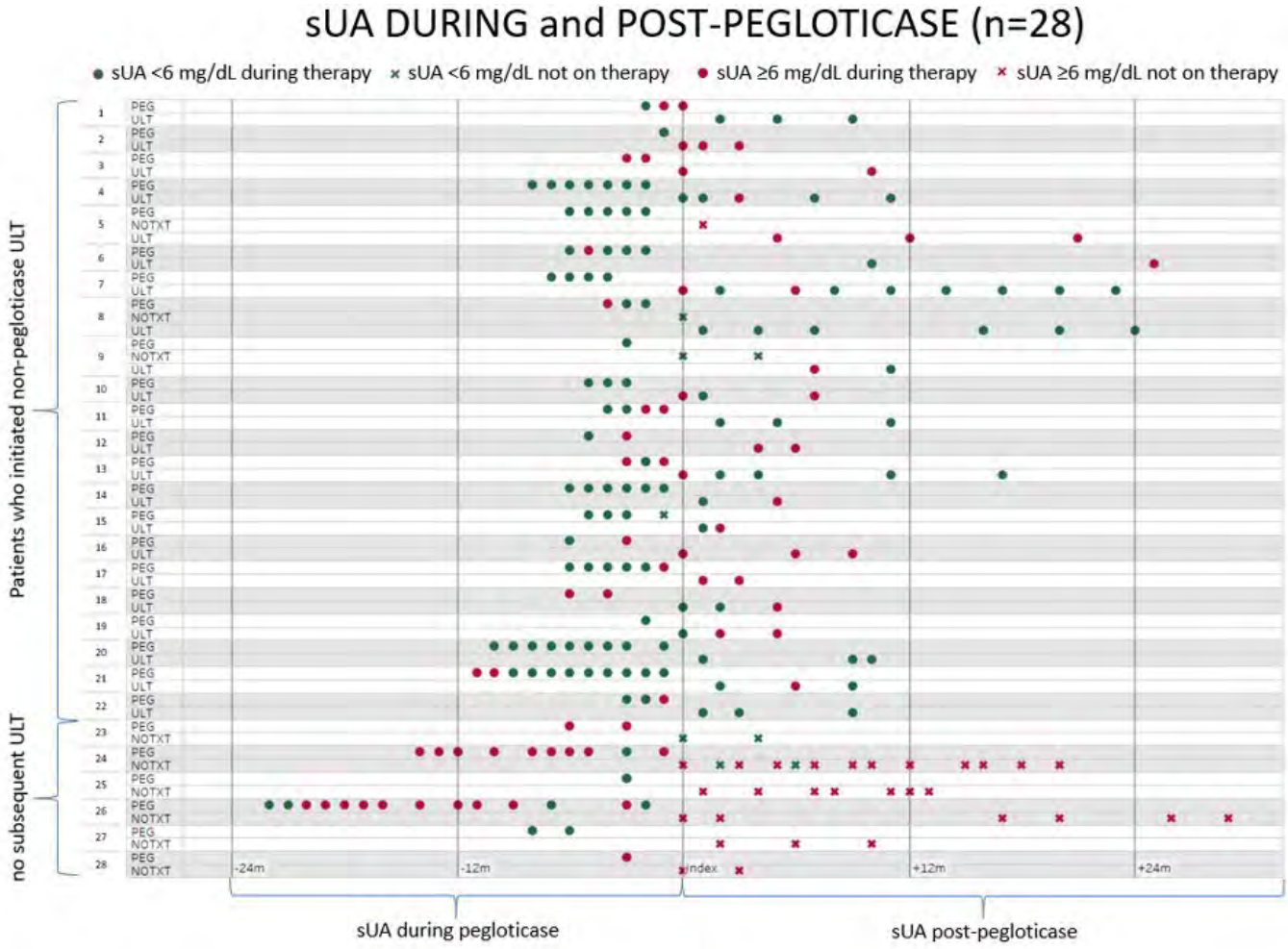

Figure 3. Alternative view of the patients in Figure 2, including sUA results during and after pegloticase treatment (n=28)

Disclosure: N. Soloman, Horizon, 5, 8, Amgen, 2, 8, Abbvie, 2, 5, 8, UCB, 2, 5, 8, Novartis, 5, 8, Jannsen, 2, 8, Pfizer, 8, Lilly, 2, GSK, 2, 5, 8; **M. Amin**, Horizon, 5, Lilly, 5; **S. Helfgott**, Abbvie, 5; **A. Hu**, Horizon, 8; **K. Huston**, None; **J. Leonard**, None; **K. Milligan**, Gilead, 2; **S. Milligan**, Gilead, 2; **J. Singh**, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **J. Tesser**, Janssen, 1, 2, 3, Abbvie, 1, 2, 3, Sun Pharma, 1, 2, 3, Novartis, 1, 2, Lilly, 1, 2, 3, BMS, 1, 2, 3, Pfizer, 1, 2, 3, Amgen, 1; **C. Edgerton**, Sandoz, 5.

Abstract Number: 1629

Management of Gout with Pegloticase; Real-World Utilization and Outcomes from Trio Health and the American Rheumatology Network (ARN)

Nehad Soloman[1], Mona Amin[2], Kimmi Cox[3], Simon Helfgott[4], Alexander Hu[5], Kent Kwas Huston[6], Jordan Leonard[7], Scott Milligan[3], Jasvinder Singh[8], John Tesser[9] and Colin Edgerton[10], [1]Arizona Arthritis & Rheumatology Associates, P.C., Peoria, AZ, [2]Arizona Arthritis & Rheumatology Associates, P.C., Scottsdale, AZ, [3]Trio Health, Louisville, CO, [4]BWH- HMS, Boston, MA, [5]Arizona Arthritis & Rheumatology Associates, P.C., New Orleans, LA, [6]Kansas City Physician Partners, Kansas City, MO, [7]Arizona Arthritis & Rheumatology Associates, P.C., Phoenix, AZ, [8]University of Alabama at Birmingham, Birmingham, AL, [9]Arizona Arthritis & Rheumatology Associates, Phoenix, AZ, [10]Articularis Healthcare, Summerville, SC

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster III: Therapies

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Infusion reactions and other adverse events associated with pegloticase may lead to discontinuation of treatment in patient populations that have already failed or are intolerant to other uric acid lowering therapies (ULTs). Maximizing the benefit of pegloticase is critical in the absence of other suitable ULTs. Here, we examine use of pegloticase for patients in US clinical care and identify variables associated with longer time on therapy.

Methods: The ARN-TRIO Rheumatology registry contains EMR (fielded and open text), lab, procedure, infusion, medical claims, and specialty pharmacy data generated in care of >75,000 patients by ARN, a network of independent practices with >200 rheumatologists across the US. This study included data for gout-diagnosed patients who

Patient Demographics – no (%) unless indicated	
Follow up (days) from index- mean (range)	516 (181-1700)
Male	88 (80%)
Age - mean (range)	59.5 (31-85)
<50	26 (24%)
50-64	38 (35%)
65-74	33 (30%)
75+	13 (12%)
Race	
black	15 (14%)
white	54 (49%)
other	1 (1%)
unknown	40 (36%)
Payer	
Commercial	60 (55%)
Medicaid	8 (7%)
Medicare	38 (35%)
other	4 (4%)
Disease	
Kidney disease	36 (33%)
baseline sUA ≥6 mg/dL	36/101 (36%)
Osteoarthritis / osteopenia	19 (17%)
Concurrent immune-modulating therapies	
methotrexate (25), tocilizumab (1), rituximab (1) , apremilast (1)	28 (25%)

Table 1. Study population characteristics

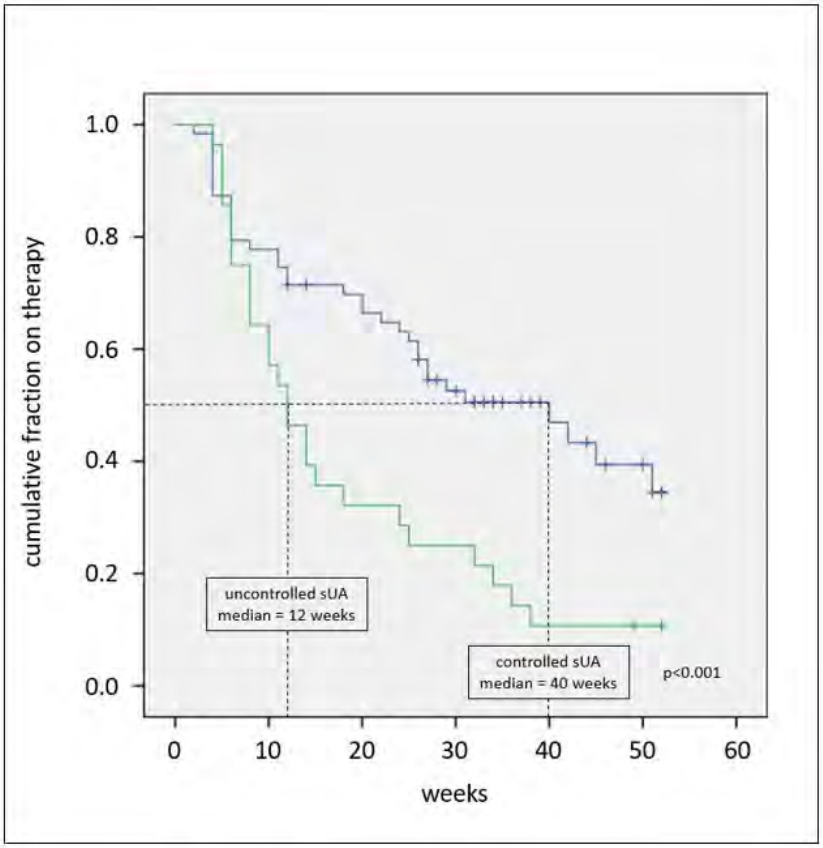

Figure 1. Time to unplanned pegloticase discontinuation stratified by uncontrolled (2+ sUA ≥ 6 mg/dL , green, n=28) or controlled (<2 sUA ≥ 6 mg/dL, blue, n=63) sUA

initiated their last pegloticase course between Jul 2015 and Oct 2019 with >180 days follow-up from pegloticase initiation (index). A course was defined as pegloticase infusions spaced < 90 days apart. Chart reviews were conducted for all study patients to determine treatment status (ongoing vs. discontinued) and reasons for discontinuation. To assess consistency of control of sUA < 6 mg/dL, evaluations were limited to patients with 2+ sUA measures during treatment. Time to event analyses were by Kaplan-Meier and log-rank or Wilcoxon test.

Results: 110 of 213 pegloticase-treated patients met study criteria. [TABLE 1] At time of assessment, 84% (95) had discontinued treatment; 19% (18/95) discontinued as intended upon meeting treatment goals, 39% (37/95) lack or loss of efficacy, 16% (15/95) adverse events, 8% (8/95) lost to follow up, 2% (2/95) each for cost or payer denial and unrelated health issues, and 17% (16/95) unknown. Of the 15 patients who discontinued therapy due to adverse events, 80% (12) cited infusion and/or allergic reactions. Median times to discontinuation were 20 weeks overall and 22 weeks for non-planned discontinuation. Controlled sUA (< 2 sUA ≥6 mg/dL) and concurrent use of immune-modulating therapies (predominantly methotrexate) were associated with a significantly longer pegloticase duration. [FIGURES 1 & 2] Variables NOT associated with unplanned discontinuation were race, gender, age, payer type, kidney disease, osteoarthritis or osteoporosis, baseline sUA, and pegloticase infusion schedule. None of the 12 patients who discontinued due to infusion or allergic reactions received concurrent immune-modulating therapies.

Conclusion: These observations suggest that treatment with pegloticase may be lengthened with concomitant use of immune-modulating therapies; however, a larger scale prospective study should be done to further elucidate the benefits of immunomodulation beyond durability of treatment, including safety benefits such as minimal to no infusion reactions.

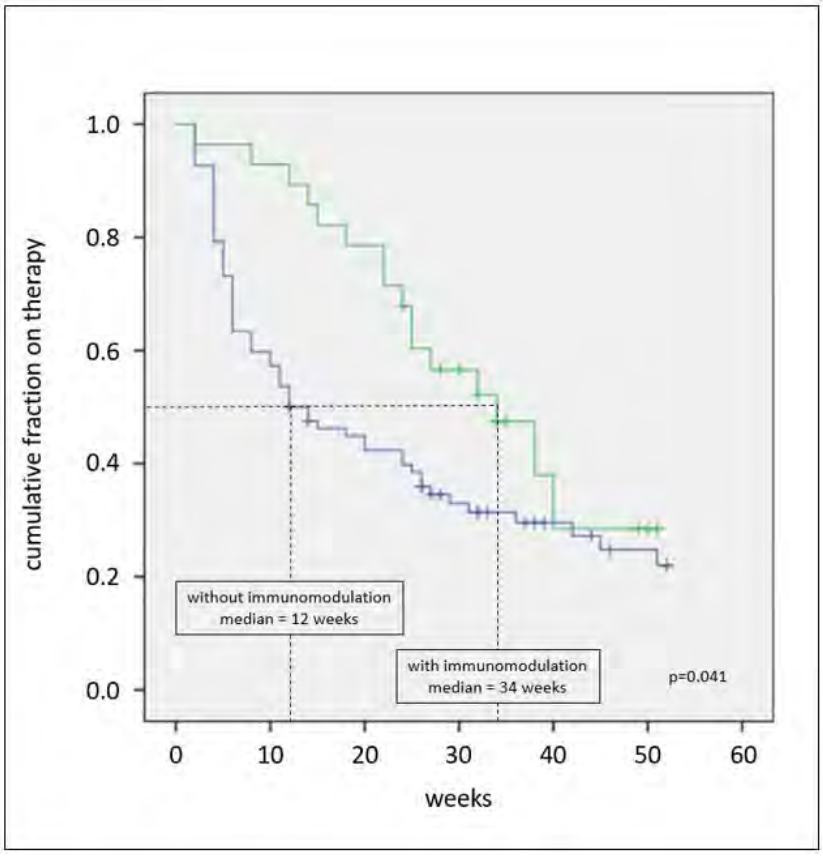

Figure 2. Time to unplanned pegloticase discontinuation stratified by presence (green, n=28) or absence (blue, n=82) of concurrent immune-modulating therapies

Disclosure: N. Soloman, Horizon, 5, 8, Amgen, 2, 8, Abbvie, 2, 5, 8, UCB, 2, 5, 8, Novartis, 5, 8, Jannsen, 2, 8, Pfizer, 8, Lilly, 2, GSK, 2, 5, 8; **M. Amin**, Horizon, 5, Lilly, 5; **K. Cox**, Gilead, 2; **S. Helfgott**, Abbvie, 5; **A. Hu**, Horizon, 8; **K. Huston**, None; **J. Leonard**, None; **S. Milligan**, Gilead, 2; **J. Singh**, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **J. Tesser**, Janssen, 1, 2, 3, Abbvie, 1, 2, 3, Sun Pharma, 1, 2, 3, Novartis, 1, 2, Lilly, 1, 2, 3, BMS, 1, 2, 3, Pfizer, 1, 2, 3, Amgen, 1; **C. Edgerton**, Sandoz, 5.

Abstract Number: 1630

Long-term Safety of Tildrakizumab in Patients with Moderate to Severe Plaque Psoriasis: Incidence of Confirmed Major Adverse Cardiovascular Events Through 3 Years (148 Weeks) from Two Phase 3 Trials

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster III: Therapies
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Tildrakizumab (TIL) is a high-affinity anti–interleukin-23p19 monoclonal antibody that is approved for the treatment of moderate to severe plaque psoriasis. The objective of this study was to evaluate major adverse cardiovascular events (MACE) in two phase 3 trials: reSURFACE 1 (NCT01722331) and reSURFACE 2 (NCT01729754).

Methods: This is a post hoc pooled analysis of adult patients with moderate to severe plaque psoriasis from two 3-part, parallel-group, double-blinded, randomized controlled trials: reSURFACE 1 (64 week) and reSURFACE 2 (52 week). Detailed methodology has previously been published. Safety data over 148 weeks, pooled across trials and treatment groups, were included. Groups were defined as placebo, etanercept (until week 28), TIL 100 mg (100 mg only in ≥1 part of the study), TIL 200 mg (200 mg only in ≥1 part of the study), continuous TIL 100 mg (100 mg throughout the three double-blinded parts plus open-label extension), continuous TIL 200 mg (200 mg throughout all parts), TIL 100/200 mg (any TIL dose in ≥1 part), and continuous TIL 100/200 mg (consistently exposed to TIL, but dose change possible throughout all parts). Exposure-adjusted incidence rates (EAIR) for confirmed MACE (including non-fatal myocardial infarction, non-fatal stroke, unstable angina, coronary revascularization, resuscitated cardiac arrest, and cardiovascular deaths that were confirmed as “cardiovascular” or “sudden”) were reported.

Results: Overall, 928 patients on TIL 200 mg, 872 on TIL 100 mg, 316 on continuous TIL 200 mg, 352 on continuous TIL 100 mg, 543 on placebo, 1646 on TIL 100/200 mg, 808 on continuous TIL 100/200 mg, and 313 on etanercept were included. EAIR for MACE were 0.54 (TIL 200 mg), 0.40 (TIL 100 mg), 0.29 (continuous TIL 200 mg), 0.36 (continuous TIL 100 mg), 0.49 (placebo), 0.47 (TIL 100/200 mg), 0.35 (continuous TIL 100/200 mg), and 0.65 (etanercept) per 100 patient-years of exposure.

Conclusion: Tildrakizumab had a favorable long-term safety profile as demonstrated by a low rate of MACE (comparable to etanercept and placebo) in patients with moderate to severe plaque psoriasis.

Disclosure: L. Iversen, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 2, 5, 8, Bristol Meyers Squibb, 2, 5, 8, Boehringer Ingelheim, 2, 5, 8, Celgene, 2, 5, 8, Centocor, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen-Cilag, 2, 5, 8, Kyowa Kirin, 2, 5, 8, LEO Pharma, 2, 5, 8, Merck Sharp & Dohme, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8, Almirall, 2, 5, 8; **C. Griffiths**, AbbVie, 2, 8, Almirall, 2, 8, Bristol Meyers Squibb, 2, 8, Celgene, 2, 8, Eli Lilly, 2, 8, Galderma, 2, 8, Janssen, 2, 8, LEO Pharma, 2, 8, Novartis, 2, 8, Sandoz, 2, 8, UCB Pharma, 2, 8; **A. Peserico**, None; **I. Pau-Charles**, Almirall, 3; **A. Blauvelt**, AbbVie, 2, 5, 8, Aclaris, 2, 5, Almirall, 2, 5, Arena, 2, 5, Athenex, 2, 5, Boehringer Ingelheim, 2, 5, Bristol Meyers Squibb, 2, 5, Dermavant, 2, 5, Dermira, 2, 5, Eli Lilly, 2, 5, Forte, 2, 5, Galderma, 2, 5, Janssen, 2, 5, LEO Pharma, 2, 5, Novartis, 2, 5, Ortho, 2, 5, Pfizer, 2, 5, Rapt, 2, 5, Regeneron, 2, 5, Sandoz, 2, 5, Sanofi Genzyme, 2, 5, Sun Pharma, 2, 5, UCB Pharma, 2, 5; **D. Thaçi**, Janssen Research & Development, LLC, 2, AbbVie, 5, 8, Almirall, 5, 8, Bioskin, 5, 8, Boehringer Ingelheim, 5, 8, Celgene, 2, 5, 8, Dignity, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, GlaxoSmithKline, 5, 8, LEO Pharma, 5, 8, Medac, 5, 8, Merck Sharp & Dohme, 5, 8, Morphosys, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, Regeneron, 5, 8, Samsung Sandoz-Hexal, 5, 8, Sanofi, 5, 8, Sun Pharmaceutical Industries, Inc., 5, 8, UCB, 5, 8; **K. Reich**, Janssen Research & Development, LLC, 2, AbbVie, 2, 5, 8, Affibody, 2, 5, 8, Almirall, 2, 5, 8, Amgen, 2, 5, 8, Biogen, 2, 5, 8, Boehringer Ingelheim, 2, 5, 8, Celgene, 2, 5, 8, Centocor, 2, 5, 8, Covagen, 2, 5, 8, Eli Lilly, 2, 5, 8, Forward Pharma, 2, 5, 8, Fresenius Medical Care, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Janssen-Cilag, 2, 5, 8, Kyowa Kirin, 2, 5, 8, LEO Pharma, 2, 5, 8, Medac, 2, 5, 8, Merck Sharp & Dohme, 2, 5, 8, Novartis, 2, 5, 8, Miltenyi Biotec, 2, 5, 8, Ocean Pharma, 2, 5, 8, Pfizer, 2, 5, 8, Regeneron, 2, 5, 8, Samsung Bioepis, 2, 5, 8, Sanofi, 2, 5, 8, Takeda, 2, 5, 8, UCB, 2, 5, 8, Valeant, 2, 5, 8, Xenoport, 2, 5, 8.

Abstract Number: 1631

No Increased Risk of Liver Dysfunction from Tildrakizumab Treatment: Post Hoc Analyses of the Tildrakizumab Psoriasis Clinical Program

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster III: Therapies

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Tildrakizumab (TIL) is a high-affinity, humanized, immunoglobulin G1κ, anti–interleukin-23p19 monoclonal antibody approved for the treatment of moderate to severe plaque psoriasis. We evaluated adverse events related to liver function in the clinical development program for TIL.

Methods: This post hoc analysis included patients with moderate to severe chronic plaque psoriasis in 1 phase 2b (P05495, NCT01225731) and 2 phase 3 trials (reSURFACE 1 and 2, NCT01722331 and NCT01729754). In P05495, patients received placebo (PBO) or TIL 5, 25, 100, or 200 mg. In reSURFACE 1 and 2, patients received PBO or TIL 100 or 200 mg; reSURFACE 2 had an additional etanercept (ETN) 50 mg arm up to week (W)28. Patients were treated at W0 and W4 and then every 12 weeks, and were followed for up to W52 (P05495/reSURFACE 2) or 64 (reSURFACE 1). The primary safety population was all subjects as treated (≥1 dose of study treatment). We evaluated liver function test (LFT) findings in patients receiving TIL 100 or 200 mg using pooled safety data from the base studies (P05495, n = 355; reSURFACE 1, n = 771; reSURFACE 2, n = 1090). LFT events of clinical interest were defined as elevated aspartate or alanine transaminase (AST or ALT) levels ≥3 times the upper limit of normal (ULN) and elevated total bilirubin (BILI) levels ≥2 times the ULN combined with alkaline phosphatase levels (ALP) < 2 times the ULN. Extension study data are also provided.

Results: In the PBO-controlled periods, 2 patients (0.6%) in the PBO and 1 (0.1%) in the TIL 200 mg group discontinued due to elevated LFT. In the base study periods, the numbers of patients (patients with events/100 patient-years) with elevated LFT leading to treatment discontinuation were similar between PBO (2 [0.91]) and TIL (4 [0.21]) groups. No patients discontinued in the ETN group due to elevated LFT. Two patients had elevated LFT events of clinical interest not related to study treatment. During the extension, no patients met the criteria for elevated LFT events of clinical interest. In the base study safety pool, there were no patterns of worsening in AST, ALP, and BILI levels over the study course for patients with continuous TIL 100/200 mg exposure. Of patients with normal ALT levels at baseline, 26% had a high ALT result at some point during the study. Similar patterns were seen in the extension.

Conclusion: Patients receiving TIL had low rates of increased liver function or drug-induced liver injury, similar to patients receiving PBO or ETN. There were no consistent signals for LFT worsening over the study course.

Disclosure: M. Lebwohl, AbbVie, 2, Amgen, 2, Arcutis, 2, 5, Boehringer Ingelheim, 2, 5, Dermavant, 2, 5, Eli Lilly, 2, Incyte, 2, Janssen Research & Development, LLC, 2, LEO Pharmaceuticals, 2, 5, Ortho Dermatologics, 2, Pfizer, 2, 5, UCB, Inc., 2, Aditum Bio, 5, Allergan, 5, Almirall, 5, Avotres Therapeutics, 5, BirchBioMed Inc., 5, BMD skincare, 5, Bristol-Myers Squibb, 5, Castle Biosciences, 5, Corrona, 5, Evelo, 5, Facilitate International Dermatologic Education, 5, Foundation for Research and Education in Dermatology, 5, Inozyme Pharma, 5, Kyowa Kirin, 5, Meiji Seika Pharma,

5, Menlo, 5, Mitsubishi, 5, Neuroderm, 5, Promius/Dr. Reddy's Laboratories, 5, Serono, 5, Theravance, 5, Verrica, 5, Mount Sinai, 3, Cara Therapeutics, 5; **D. West**, Pfizer, 5, Galderma, 5, Dermtech, 5, DEF Conference, 5; **A. Mendelsohn**, Sun Pharmaceutical Industries, Inc., 3, Johnson and Johnson, 1, 9; **S. Rozzo**, Sun Pharmaceutical Industries, Inc., 3; **G. Girolomoni**, Eli Lilly, 2, 5, MSD, 2, AbbVie, 5, Biogen, 5, Celgene, 5, LEO Pharma, 5, Pfizer, 5, Regeneron, 5, Sanofi, 5, 8, Abiogen, 8, Sandoz, 8.

Abstract Number: 1632

Long-Term Efficacy and Safety of Canakinumab in Patients with Autoinflammatory Periodic Fever Syndromes – First Interim Analysis of the FMF-TRAPS-HIDS/MKD Subgroup of the RELIANCE Registry

Joerg Henes[1], Norbert Blank[2], Michael Borte[3], Ivan Foeldvari[4], Gerd Horneff[5], Markus Hufnagel[6], Tilmann Kallinich[7], Birgit Kortus-Goetze[8], Catharina Schuetz[9], Frank Weller-Heinemann[10], Julia Weber-Arden[11] and Jasmin Kuemmerle-Deschner[12], [1]Department of Internal Medicine II, Rheumatology, University Hospital Tuebingen, Germany, Tuebingen, Germany, [2]Department of Hematology, Oncology and Rheumatology, Internal Medicine V, University Hospital of Heidelberg, Eppelheim, Germany, [3]ImmunoDeficiencyCenter Leipzig (IDCL), Hospital St. Georg gGmbH Leipzig, Germany, Leipzig, Germany, [4]Head of the Hamburg Centre for Pediatric and Adolescence Rheumatology, Budapest, Hungary, [5]Asklepios Clinic Sankt Augustin, Sankt Augustin, Germany, [6]Division of Pediatric Infectious Diseases and Rheumatology, Department of Pediatrics and Adolescent Medicine, University Hospital Medical Center, Medical Faculty, University of Freiburg, Germany, Freiburg, Germany, [7]Charite, Berlin, Germany, [8]Division of Nephrology, University of Marburg, Germany, Marburg, Germany, [9]Department of Pediatric Immunology, University Hospital Dresden, Dresden, Germany, Dresden, Germany, [10]Klinikum Bremen-Mitte, Prof. Hess Kinderklinik, Bremen, Germany, Bremen, Germany, [11]Novartis Pharma GmbH, Nuremberg, Germany, [12]University Hospital Tuebingen, Tuebingen, Germany

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster III: Therapies

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Autoinflammatory periodic fever syndromes characterized by excessive interleukin(IL)-1ß release and severe systemic and organ inflammation have been successfully treated with the anti-IL-1ß inhibitor canakinumab. In clinical trial situations and real life, rapid remission of symptoms and normalization of laboratory parameters were observed in most patients.[1-3]

The present study explores long-term effectiveness and safety of canakinumab under routine clinical practice conditions in pediatric and adult patients with CAPS (cryopyrin-associated periodic syndromes), FMF (familial Mediterranean fever), TRAPS (tumor necrosis factor receptor-associated periodic syndrome) and HIDS/MKD (hyperimmunoglobulinemia D syndrome/mevalonate kinase deficiency).

[1]Lachmann et al. N Engl J Med. 2009;360(23):2416-25

[2]Kuemmerle-Deschner et al. Rheumatology (Oxford). 2016;55(4):689-96

[3]De Benedetti et al. N Engl J Med. 2018;378(20):1908-1919

Methods: RELIANCE is a prospective, non-interventional, multi-center, observational study based in Germany with a 3-year follow-up period. Pediatric (age ≥2 years) and adult patients with clinically confirmed diagnoses of CAPS, FMF, TRAPS and HIDS/MKD that routinely receive canakinumab are enrolled in order to evaluate effectiveness and safety

	FMF				TRAPS	HIDS
	Baseline	Baseline*	6 months	12 months	Baseline	Baseline
Number of patients, N	29	16	16	15	10	2
Mean age, years (SD)	26 (5; 56)	16 (5; 47)	16 (5; 47)	16 (5; 47)	22 (4; 43)	11 (5; 18)
Female (%)	15 (52)	7 (44)	7 (44)	7 (44)	5 (56)	1 (50)
Mean duration of prior CAN treatment, years (min; max)	2.2 (0; 6)	2.2 (0; 6)	2.2 (0; 6)	2.2 (0; 6)	1 (0; 2)	3 (2; 4)
Patient's assessment of disease activity 0-10, mean (min; max)	3 (0; 10)	2.8 (0; 8)	2.2 (0; 7)	2.1 (0; 5)	2.1 (0; 5)	0 (0; 0)
Patient's assessment of fatigue 0-10, mean (min; max)	4.4 (0; 9)	4.6 (0; 9)	3.9 (0; 8)	3.9 (0; 10)	3.4 (0; 8)	0 (0; 0)
Number (%) of patients without impairment of social life by disease	9 (42.9)	6 (50.0)	6 (46.2)	6 (50.0)	1 (20.0)	0 (0.0)
Number (%) of patients with days absent from school/work	5 (17)	2 (13)	5 (31)	7 (47)	4 (44)	2 (100)
CRP, mean (mg/dL)	0.9	0.5	0.6	0.3	2.0	0.1
SAA, mean (mg/dL)	5.3	2.4	2.4	8.8	7.9	0.6
ESR, mean (mm/h)	15.4	12.2	10.2	6.9	35.8	5.0
Number (%) of patients in disease remission (physician assessment)	12 (41.4)	8 (50.0)	10 (62.5)	9 (60.0)	3 (33)	2 (100)
SAE, N (%)	0 (0)	0 (0)	2 (12.5)	2 (12.5)	0 (0)	0 (0)

Table 1. Baseline characteristics of the FMF/TRAPS/HIDS-subgroup and preliminary 6-month interim data of 16 FMF patients *Baseline of FMF patient subset (N=16) with preliminary 6 and 12-month data

of canakinumab under standard clinical practice conditions. Evaluation of disease activity and fatigue by patients' assessment, days absent from school/work due to study indication, inflammatory markers and physician assessment of disease remission was performed at baseline and will be further assessed at 6-monthly intervals within the 3-year observation period of the study.

Results: This first interim analysis of 41 patients enrolled by September 2019, diagnosed with FMF (n=29), TRAPS (n=10) and HIDS/MKD (n=2), includes baseline data as well as preliminary 12-month data of a FMF subset (N=16). Mean age at baseline for FMF-TRAPS-HIDS/MKD patients was 26-22-11 years and mean duration of prior canakinumab treatment was 2.2-1-3 years.

Preliminary results of the FMF subset of N=16 patients diagnosed with FMF indicate stable remission and disease control during observation period. Within the first study interval, no major changes were observed regarding physician ratings, patient reported outcomes and inflammatory markers (Table 1). The AIDAI score of disease activity revealed inactive disease in 9 out of 12 months (Table 2). Preferred canakinumab doses and intervals (% of all injections) were 150 mg every 4 weeks (24), 150 mg every 6 weeks (11), and 150 mg every 8 weeks (21). Any serious adverse events were reported for 2 patients including tonsillectomy (drug-related) and arthritis. No study discontinuations were observed.

Conclusion: Baseline characteristics of the FMF-TRAPS-HIDS/MKD-subgroup are reported. In addition, first interim data of FMF patients available from the RELIANCE registry show that long-term CAN treatment is well tolerated and effective in FMF patients.

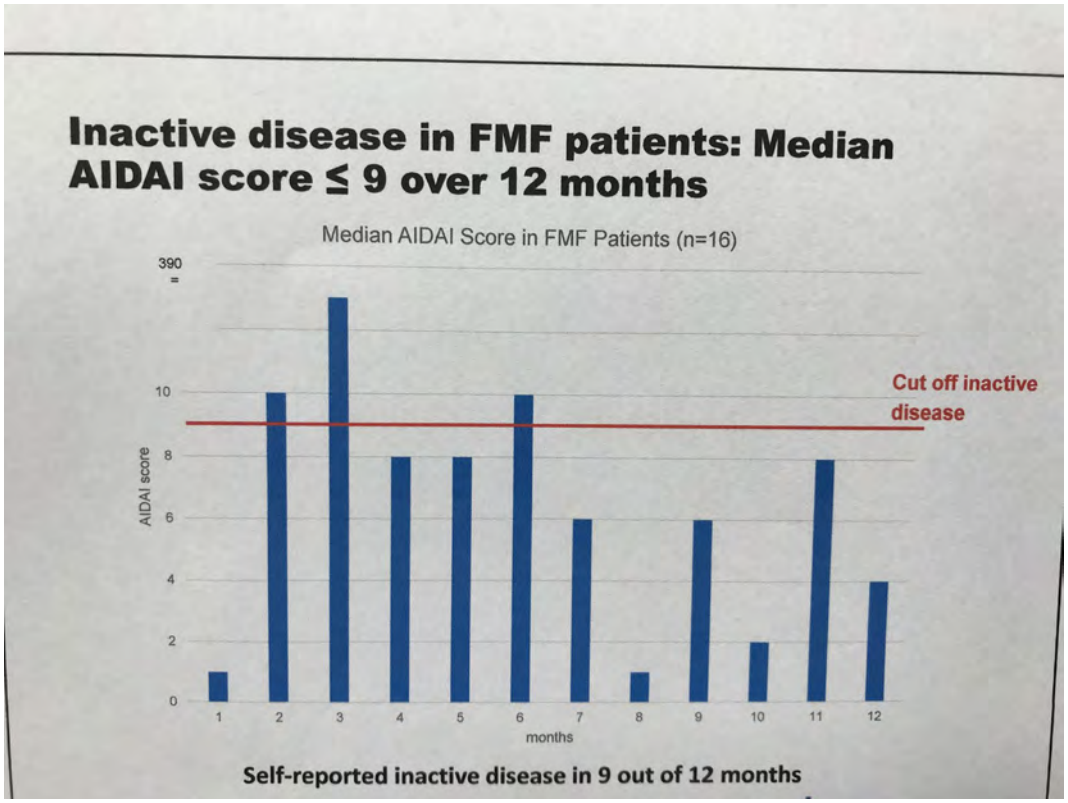


Table 2. Median AIDAI Score of the FMF subgroup (n=16) Over 12 Months

Disclosure: J. Henes, Novartis, 2, 5, Roche-Chugai, 2, 5; **N. Blank**, None; **M. Borte**, Pfizer, 2, Shire, 2; **I. Foeldvari**, Sanofi, 5, Chugai, 5, Amgen, 5, GSK, 5, Lilly, 5, BMS, 5, Abbvie, 5, Novartis, 5, gilead, 5; **G. Horneff**, Pfizer, 5, 8, AbbVie, 5, 8, Novartis, 5, 8, Sanofi, 5, 8; **M. Hufnagel**, None; **T. Kallinich**, None; **B. Kortus-Goetze**, Novartis, 5; **C. Schuetz**, None; **F. Weller-Heinemann**, None; **J. Weber-Arden**, Novartis, 3; **J. Kuemmerle-Deschner**, Novartis, 2, 5, AbbVie, 2, 5, SOBI, 2, 5.

Abstract Number: 1633

A Randomized, Double-Blind, Placebo-Controlled Study of Anakinra in Pediatric and Adult Patients with Still's Disease

Laura Schanberg[1], Peter Nigrovic[2], Ashley Cooper[3], Winn Chatham[4], Shoghik Akoghlanian[5], Namrata Singh[6], C. Egla Rabinovich[7], Akaluck Thatayatikom[8], Alysha Taxter[9], Jonathan Hausmann[10], Milan Zdravkovic[11], Sven Ohlman[11], Henrik Andersson[11], Susanna Cederholm[11], Gunilla Huledal[11], Rayfel Schneider[12] and Fabrizio De Benedetti[13], [1]Duke University Medical Center, Durham, NC, [2]Division of Rheumatology, Inflammation and Immunity, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; Division of Immunology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA, Boston, [3]Children's Mercy Kansas City, Kansas City, MO, [4]University of Alabama at Birmingham, Birmingham, AL, [5]Nationwide Children's Hospital, Columbus, [6]University of Washington, Bellevue, WA, [7]Duke University Hospital, Durham, NC, [8]Department of Pediatrics, University of Florida, Gainesville, FL, [9]Wake Forest Baptist Medical Center, Winston-Salem, [10]Boston Children's Hospital / Beth Israel Deaconess Medical Center, Cambridge, MA, [11]Sobi, Stockholm, Sweden, [12]University of Toronto, The Hospital for Sick Children, Toronto, Canada, [13]Division of Rheumatology, Laboratory of Immuno-Rheumatology, IRCCS Ospedale Pediatrico Bambino Gesù, Rome, Italy, Rome, Italy

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster III: Therapies
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Still's disease, including both systemic juvenile idiopathic arthritis (SJIA) and adult-onset Still's disease (AOSD), is a rare systemic auto-inflammatory disorder associated with an activated IL-1 pathway. The purpose of the anaSTILLs study (anakinra in Still's disease) was to build on earlier evidence and evaluate, in a controlled setting, the efficacy and safety of anakinra (IL-1 receptor antagonist), in patients with active, newly diagnosed Still's disease across all age groups.

Methods: The anaSTILLs study (NCT03265132) was a randomized, double-blind, placebo-controlled, 12-week study including patients with active and newly diagnosed Still's disease (adapted ILAR criteria if < 16 years of age, Yama-

Figure 1: anaSTILLs clinical study design

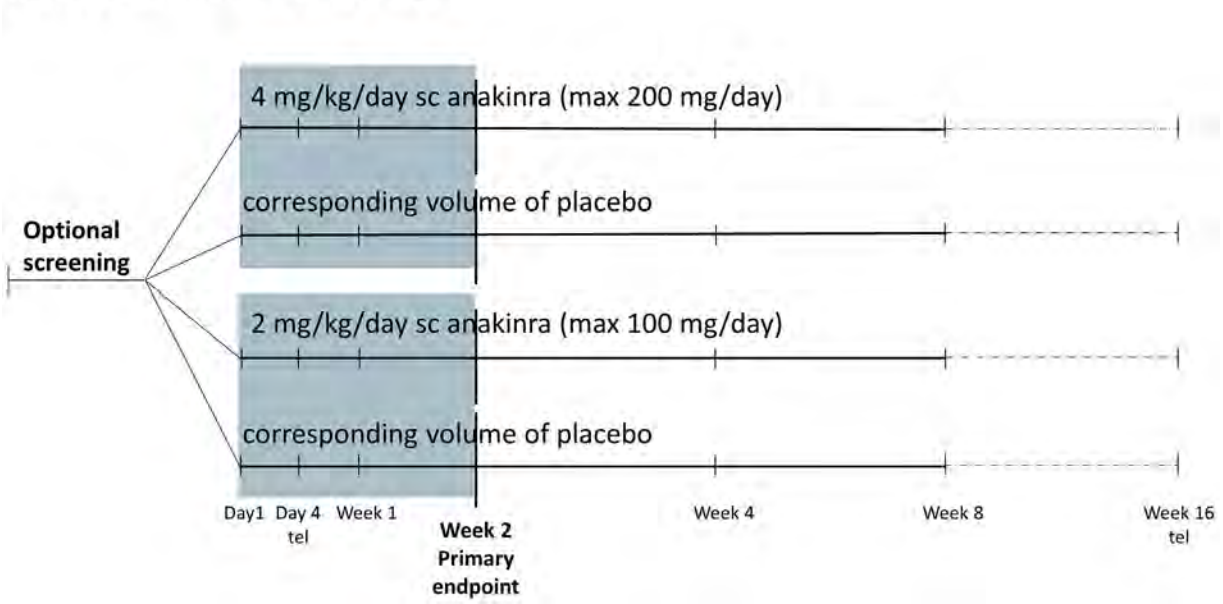
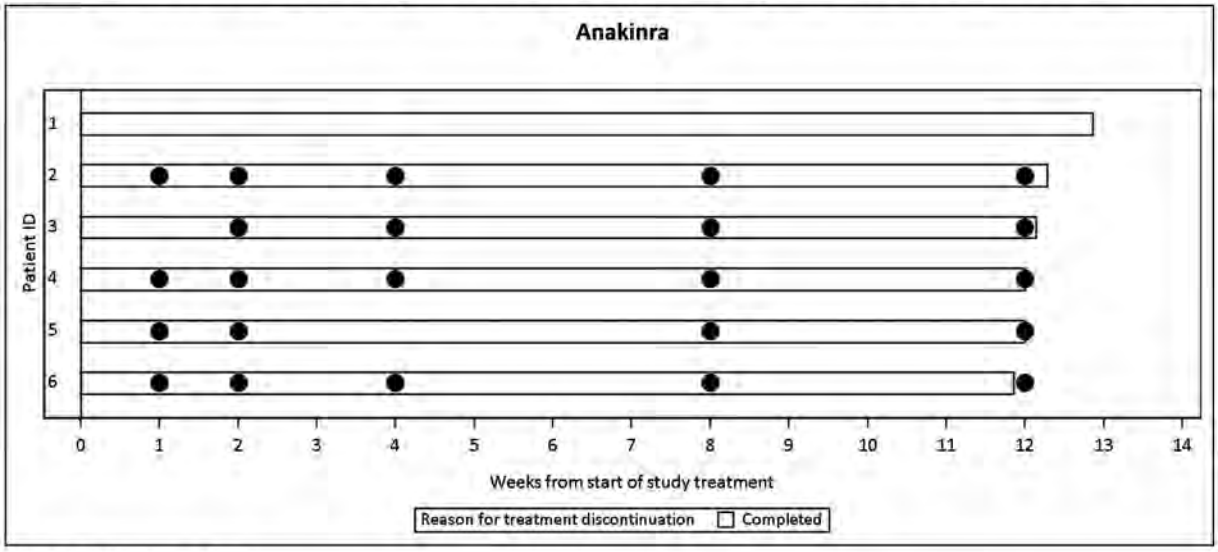


Table 1. ACR response with absence of fever at Week 2

Primary & secondary endpoints	Response (Anakinra) n (%) N=6	Response (Placebo) n (%) N=5	Difference (Anakinra-Placebo)	95% exact CI for difference	Fisher's exact test p-value
ACR30*	6 (100.0)	0 (0.0)	1.00	0.42, 1.00	0.0022
ACR50*	6 (100.0)	0 (0.0)	1.00	0.42, 1.00	0.0022
ACR70*	6 (100.0)	0 (0.0)	1.00	0.42, 1.00	0.0022
ACR90*	5 (83.3)	0 (0.0)	0.83	0.24, 1.00	0.0152

*With absence of fever at Week 2

Figure 2: Individual ACR90 response with absence of fever, and treatment duration over time



Bars indicate time on study drug.
● Bullets indicate ACR90 response at the particular week.
Patient 1 had sustained ACR70 response but not ACR90.

guchi criteria if ≥16 years of age at disease onset). Patients were randomized to anakinra 2 mg/kg (max 100 mg/day), 4 mg/kg (max 200 mg/day) or placebo. The primary objective was to demonstrate the efficacy of anakinra versus placebo as assessed by ACR30 response with absence of fever at Week 2. Secondary objectives included: early onset of efficacy, sustained efficacy, time to study drug discontinuation, safety, pharmacokinetics (PK), clinical signs and biomarkers.

Results: Twelve patients were randomized and received study treatment: 6 to anakinra (2 mg/kg n=2, 4 mg/kg n=4) and 6 to placebo. Due to slow recruitment the study was terminated early. One patient was excluded from the efficacy analyses since he/she was later diagnosed with lymphoma, not Still's disease. 11 patients were analyzed for efficacy (anakinra n=6, placebo n=5), 8 children (median [range] age=4.0 [1-11] years) and 3 adults (median [range] age=32.0 [25-51] years). 55% were male and the mean (range) symptom duration was 74.2 (12-222) days. All patients on anakinra but none on placebo achieved ACR30 response with absence of fever at Week 2 (p-value=0.0022). The efficacy of anakinra was supported by superiority to placebo in ACR50/70/90 responses with absence of fever at Week 2. All placebo patients discontinued the study within 6 weeks, 2 due to progressive disease, 2 due to lack of efficacy and 1 due to withdrawal by the patient. A numerically greater proportion of patients in the anakinra group had early onset of efficacy (Week 1) compared to placebo, as assessed by ACR30. ACR30/50/70/90 responses in anakinra-treated patients were sustained throughout the study period. No unexpected safety findings were observed. Based on serum anakinra concentrations Week 12, Cmax was 2920 ng/mL at 4.0 hours (dose: 4.1 mg/kg) in a 1-year-old patient, and Cmax was 1060 ng/mL at 2.1 hours (dose: 1.5 mg/kg) in a 6-year-old patient.

Conclusion: Anakinra is superior to placebo in the treatment of Still's disease. The safety and PK results are consistent with previous anakinra experience. These results confirm the benefits of anakinra treatment in patients with active, newly diagnosed Still's disease across ages.

Disclosure: L. Schanberg, UCB, 1, Sanofi, 1, BMS, 1, Sobi, 1, 2; **P. Nigrovic**, Novartis, 2, 5, BMS, 2, 5, Pfizer, 2, 5, Sobi, 5, Miach Orthopedics, 5, Simcere, 5, XBiotech, 5, Quench Bio, 5, Siglion, 5, Cerecor, 5, UpToDate, 7, American Academy of Pediatrics, 7, CARRA, 9; **A. Cooper**, None; **W. Chatham**, Sobi, 2, 5; **S. Akoghlanian**, None; **N. Singh**,

Rheumatology Research Foundation, 2, American Heart Association, 2; **C. Rabinovich**, AbbVie, 2, CARRA, 2, UCB Pharma, 2, Janssen Research & Development, 2; **A. Thatayatikom**, None; **A. Taxter**, None; **J. Hausmann**, Novartis, 5; **M. Zdravkovic**, Sobi, 1, 3, 6; **S. Ohlman**, Sobi, 1; **H. Andersson**, Sobi, 3; **S. Cederholm**, Sobi, 1; **G. Huledal**, Sobi, 3; **R. Schneider**, Novartis, 5, Sobi, 5, Novimmune, 5, Roche, 5; **F. De Benedetti**, Novartis, 2, 8, Novimmune, 2, 9, Sobi, 2, 8, 9, Roche, 2, 8, Pfizer, 2, Sanofi, 2, AbbVie, 8.

Abstract Number: 1634

Etiologies and Management of Hemophagocytic Lymphohistiocytosis: Is It Time for an Updated Protocol and Targeted Treatments?

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster III: Therapies
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Hemophagocytic lymphohistiocytosis (HLH) is a rare life-threatening disease characterized by immune-overstimulation and a hyperinflammatory response resulting in cytokine storm and multi-organ failure.[1]

	Age	Gender	Predisposing Condition	Immunosuppressive Treatment prior to Onset	Precipitating Factor	Treatment	Outcome
P1	53	F	Marginal cell lymphoma	Rituximab and bendamustine	Pyelonephritis and Pneumonia	HLH-94 Protocol, antibiotics	Deceased
P2	37	F	Juvenile idiopathic arthritis	Abatacept and azathioprine	EBV	Methylprednisolone 1000mg x 3 days	Resolution
P3	22	F	-	-	Streptococcal toxic shock syndrome	HLH-94 Protocol, IVIg, antibiotics	Deceased
P4	21	M	Crohn's disease	6-mercaptopurine	CMV	Methylprednisolone 1000mg x 3 days, antivirals, tocilizumab 4mg/kg	Resolution
P5	47	M	B-cell lymphoma, psoriasis and CVID	R-EPOCH, topical steroids, phototherapy	MRSA cellulitis	HLH-94 Protocol, antibiotics, antifungals	Deceased
P6	19	M	Adult onset Still's disease	Anakinra	EBV	Anakinra, methylprednisolone 1000mg x 3 days	Resolution
P7	30	F	Dermatomyositis	Prednisone	Pharyngitis with negative serology	Methylprednisolone 1000mg x 5 days IVIg 2g/kg over 5 days, cyclosporine 125mg, then rituximab	Resolution
P8	36	F	T cell lymphoproliferative disorder	Cyclophosphamide, vincristine, prednisone	T cell lymphoproliferative disorder	HLH-94 protocol then alemtuzumab	Recurrent HLH, then deceased
P9	43	M	NK cell leukemia	HLH-2004 Protocol	NK cell leukemia	HLH-94 Protocol	Deceased
P10	46	F	SLE, Kikuchi disease	Hydroxychloroquine	SLE flare	Methylprednisolone 1000mg x 3 days, IVIG 2g/kg over 5 days, then rituximab 375mg weekly x 4 weeks	Resolution
P11	18	F	-	-	Pyelonephritis	Antibiotics	Resolution
P12	25	M	-	-	Mycoplasma pneumonia	HLH-94 Protocol, antibiotics	Deceased
P13	33	F	NK cell lymphoma	Gemcitabine, cisplatin, dexamethasone	MAC pneumonia	HLH-94 protocol, antibiotics	Deceased
P14	60	M	S/P Liver transplant for alcoholic cirrhosis and HCV	Mycophenolate and tacrolimus	Invasive aspergillosis, pneumonia	HLH-94 protocol, antibiotics, antifungals	Deceased
P15	50	F	SLE	-	Possible autoimmune hepatitis	HLH-94 protocol, cyclophosphamide, IVIg	Deceased

Table 1. Therapeutic Approaches and Outcomes (1/2)

	Age	Gender	Predisposing Condition	Immunosuppressive Treatment Prior to Onset	Precipitating Factor	Treatment	Outcome
P16	70	F	T cell lymphoma, sarcoidosis	R-CHOP	EBV	Methylprednisolone 1000mg x 3 days then R-CHOP	Resolution
P17	35	M	-	-	Group G streptococcus Lemierre's disease	Antibiotics, surgery	Resolution
P18	62	M	Peripheral T-cell lymphoma of the thorax	EPOCH	-	HLH-94 protocol	Resolution
P19	29	M	-	-	EBV	HLH-94 protocol, ganciclovir	Resolution
P20	21	F	Systemic juvenile idiopathic arthritis	Methotrexate and tocilizumab	EBV	Methylprednisolone 1000mg x 3 days	Resolution
P21	65	F	Rheumatoid arthritis	Methotrexate, prednisone, etanercept	Large B cell lymphoma	HLH-94 protocol	Deceased
P22	38	F	SLE	Hydroxychloroquine	Influenza	Supportive therapy	Resolution
P23	56	M	Ulcerative colitis	Azathioprine and mesalamine	CMV	Ganciclovir	Resolution
P24	29	F	S/P Kidney transplant for membranoproliferative glomerulonephritis	Mycophenolate, tacrolimus, and prednisone	-	HLH-94 protocol	Deceased
P25	27	F	Adult onset Still's disease	Prednisone	-	HLH-94 protocol	Recurrence of HLH, invasive fungal infection
P26	24	F	Pituitary tumor s/p resection	-	CMV	Antiviral, antibiotics	Deceased
P27	55	M	-	-	HSV encephalitis, MSSA pneumonia	Acyclovir, antibiotics	Resolution
P28	33	M	SLE	Hydroxychloroquine, cyclophosphamide 1 year prior	MSSA bursitis	Antibiotics, methylprednisolone 1000mg x 3 days	Resolution
P29	51	M	Angioimmunoblastic T-cell lymphoma	-	Angioimmunoblastic T-cell lymphoma	HLH-94 protocol	Resolution

* R-CHOP = rituximab, cyclophosphamide, doxorubicin, vincristine, and prednisone; EPOCH = etoposide, vincristine, doxorubicin, and prednisone; EBV = Epstein Barr Virus; CMV = cytomegalovirus; SLE = systemic lupus erythematosus; HLH-94 protocol = dexamethasone daily (10 mg/m^2 for 2 weeks, 5 mg/m^2 for 2 weeks, 2.5 mg/m^2 for 2 weeks, 1.25 mg/m^2 for 1 week, and taper and discontinue during one week; then pulses every second week with 10 mg/m^2 for 3 days), etoposide 150 mg/m^2 IV, cyclosporine A aiming at trough levels of 200 µg/L, intrathecal methotrexate 12mg per dose if with progressive neurological symptoms [16]

Table 1. Therapeutic Approaches and Outcomes (2/2)

Secondary HLH usually occurs in adults in the setting of malignancy, infection, or a rheumatic condition. It is often triggered by an infection such as Epstein-Barr virus (EBV).[1] Secondary HLH occurring in patients with autoimmune diseases is referred to as macrophage activation syndrome (MAS). The approach to the management of secondary HLH can be confusing and problematic due to the rarity of the condition and the heterogeneity of treatment approaches for HLH. The aim of this study was to study the patients diagnosed with hemophagocytic lymphohistiocytosis at our center, and to compare their predisposing conditions, treatments, and outcomes.

Methods: We conducted a retrospective chart review of all patients over 18 years of age diagnosed with hemophagocytic lymphohistiocytosis at our center between 2013 and 2019. Patients who met HLH-2004 or H-score criteria were included in this study. The patients' presentations, management, and outcomes were analyzed.

Results: Twenty-nine patients with hemophagocytic lymphohistiocytosis met inclusion criteria. 7 patients had a malignancy, 11 had a rheumatic disease, 6 had an infection alone, 2 were transplant patients, and 3 had a combination of malignancy, rheumatic disease, and/or infection. Of all the patients treated with the HLH-94 protocol 73% (11/15) died, 13% (2/15) had recurrence of HLH, and 6% (1/15) developed an invasive fungal infection. The patients with underlying rheumatologic conditions received targeted personalized therapy with pulse steroids, tocilizumab, anakinra, IVIg, cyclosporin, rituximab and/or cyclophosphamide in addition to antiviral/antibiotic therapy. All of the patients treated with targeted therapy had resolution of HLH.

Conclusion: Our findings suggest that the rheumatologic patient population responds well to a targeted and more personalized therapeutic approach, and poorly to the standard HLH-94 protocol. It is unclear whether the poor outcomes found with the use of the HLH protocol are secondary to the protocol itself, or the aggressive nature of

malignancy-associated HLH. HLH is a rare life-threatening disease, and further studies are needed to develop more tailored therapeutic regimens.

Disclosure: T. Posas-Mendoza, None; **C. McLeod**, None; **W. Davis**, None; **R. Quinet**, None.

Abstract Number: 1635

Profile of Topical Diclofenac Sodium Gel 1% (Voltaren®) Users in a United States Longitudinal Electronic Health Records Database

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SESSION INFORMATION
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Background/Purpose: Diclofenac sodium gel 1% (DSG), a topical non-steroidal anti-inflammatory drug (NSAID), is effective for the relief of osteoarthritis (OA) pain in the elbows, wrists, hands, feet, ankles, and knees. Over-the-counter (OTC) NSAIDs, including DSG, carry label warnings for systemic side effects, such as gastrointestinal (GI), cardiovascular (CV), and hepatic events. However, in controlled clinical trials, DSG had similar rates of these adverse events as placebo, with only application-site reactions reported more frequently. This study was conducted to support the switch of DSG from a prescription to an OTC product in the USA (OTC approved February 2020) and to further evaluate DSG for NSAID-associated events of interest (EOIs) in a real-world setting.

Methods: This retrospective, longitudinal cohort study sourced data from the United States Department of Defense Military Health System (MHS) electronic health records database. The study period was 01Jan2007 to 31Dec2016. Individuals with ≥1 prescription for DSG dispensed between 01Jan2008 and 30June2016 (screening period) and ≥1 year of continuous enrollment/eligibility in the MHS prior to their first DSG prescription fill in the screening period (index date) were included. ICD-9-CM/ICD-10-CM diagnosis, ICD-9-CM/ICD-10-PCS procedure codes, and medications (as proxy) were used to identify specific EOIs (ie, GI, hepatic, or renal injury/disease, CV event/disease, incident or exacerbated hypertension, skin reactions, misuse/abuse, and death). These were assessed from the index date until earliest occurrence of last DSG treatment episode end date, disenrollment from MHS, death, or end of study (follow-up period).

Results: For 521,593 individuals with ≥1 DSG prescription fill who met study criteria, mean age was 57 years and 60% were female; the median duration of follow-up was 60 days. Overall, 79% of the study population had baseline diagnoses of musculoskeletal and/or connective tissue diseases, and 32% had a baseline diagnosis of OA (**Table 1**). Comorbidities included obesity, diabetes, smoking, alcohol use, and lupus (**Table 1**). At baseline, >50% of patients also had filled prescriptions for NSAIDs or opioids. Overall, 93% of the population had risk factors at baseline associated with ≥1 of the 7 study EOIs (excluding death; **Table 1**); baseline risk factors for GI, CV, hypertension, and hepatic events were 79%, 63%, 52%, and 49%, respectively. In presence of baseline risk factors, 26% of the population experienced ≥1 EOI during the study period; mean (SD) time from index date to first event was 244 (369) days. An average of 2.5 DSG prescription fills per patient was dispensed during the study period (**Table 2**).

Table 1. Baseline Medical History and Comorbid Conditions of Individuals With DSG Prescriptions in the MHS Database From January 1, 2008 – December 31, 2016

	N	%
All individuals	521,593	*100*
Charleson-Deyo score, mean (SD)	0.9	*1.4*
DSG indicated conditions		
Osteoarthritis	169,460	*32.5*
Osteoarthritis of hand/wrist/elbow	25,193	*4.8*
Osteoarthritis of knee/ankle/foot	89,440	*17.1*
Other arthritis conditions		
Rheumatoid arthritis	21,084	*4.0*
Ankylosing spondylitis	14,384	*2.8*
No indicated condition at baseline	337,357	*64.7*
Days from closest indicated condition / other arthritis condition to index date	95.9	*100.8*
At least 1 risk factor at baseline	484,458	*92.9*
Hepatic	257,204	*49.3*
Cardiovascular	330,599	*63.4*
Hypertension	272,385	*52.2*
Gastrointestinal	409,774	*78.6*
Renal	145,311	*27.9*
Skin	145,028	*27.8*
Misuse/Abuse	114,697	*22.0*
Baseline comorbid conditions of interest		
All Individuals	521,593	*100*
Lupus	4,223	*0.8*
Diabetes	106,608	*20.4*
Smoking	60,152	*11.5*
Alcohol use	4,956	*1.0*
History of obesity	115,692	*22.2*
BMI calculated from vital statistics[a]		
Age 20+ years	513,052	*100*
<19	2,016	*0.4*
19 to <25	41,121	*8.0*
25 to <30	73,967	*14.4*
30 to <40	59,952	*11.7*
40+	7,498	*1.5*
Missing	328,498	*64.0*

[a]Calculation based on individual's last vital statistics measurements reported prior to their index date.
BMI, body mass index; DSG, diclofenac sodium gel 1%; MHS, Military Health System.

Table 2. Treatment Patterns Associated With DSG Use During the Study Period: Data From the MHS Database From January 1, 2008 – December 31, 2016

	N	%
All individuals	**521,593**	***100***
Number of DSG prescriptions dispensed		
Mean, SD	2.5	*3.6*
1 prescription	301,441	*57.8*
2 prescriptions	91,065	*17.5*
3+ prescriptions	129,087	*24.7*
Number of therapy periods		
Mean, SD	1.9	*1.8*
Median	1	
Maximum	31	
1 therapy period	329,238	*63.1*
2 therapy periods	95,738	*18.4*
3+ therapy periods	96,617	*18.5*

DSG, diclofenac sodium gel 1%; GI, gastrointestinal; MHS, Military Health System.

Conclusion: The >500,000 DSG users in this retrospective study were generally older, more likely to be female, and had baseline comorbidities and risk factors of interest. Over half had a history of NSAID or opioid use at baseline. This study found that few DSG users (< 15%) had any single EOI despite baseline comorbidities and risk for these events, and that the EOIs on average occurred after the last prescription fill when DSG was no longer being used.

Disclosure: A. Kenneally, GSK Consumer Healthcare, 3; **F. Bariguian**, GSK Consumer Healthcare, 3; **R. Petruschke**, GSK Consumer Healthcare, 3; **A. Tave**, GSK Consumer Healthcare, 2; **J. Edison**, Department of Defense, 9; **N. Sicignano**, None; **F. Barbone**, GSK Consumer Healthcare, 3.

Abstract Number: 1636

8 Years Follow-Up of a Novel Autoinflammatory Disease: CD59 Malfunction Causes Hemolytic Anemia, Recurrent Guillain-Barre Syndrome, and Strokes in Pediatric Populations and Respond Well to Eculizumab and Pozelimab

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SESSION INFORMATION
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Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster III: Therapies
Session Type: Poster Session D
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Background/Purpose: In 2013 we have described the first patients with a novel autoinflammatory disease manifested in 4 children with recurrent Guillain-Barre syndrome and hemolytic anemia in infancy due to loss of function of CD59 (Nevo et al., Blood). Since then, additional 3 mutations were recognized and clinical course of 14 patients was

documented. Eculizumab was started in all patients and polezimab in one patient and clinical course was evaluated using clinical scores questionnaires and follow-up and laboratory evaluation.

Methods: The 4 mutations, p.Cys64Tyr, p.Asp24Val, p.Asp24Valfs*, and p.Ala16Alafs*, were identified in 14 individuals with CD59 malfunction. All 14 presented with recurrent Guillain-Barré syndrome or chronic inflammatory demyelinating polyneuropathy, recurrent strokes, and chronic hemolysis. The molecular consequences of the 4 mutations and their effects on CD59 expression, localization, glycosylation, degradation, secretion, and function was evaluated and treatment with eculizumab or pozelimab was established with a follow-up up to 7 years. All patients responded well to eculizumab. One patient developed hypersensitivity to eculizumab that was successfully switched to pozelimab with similar clinical and in vitro complement inhibition effect.

In this study we aimed to determine whether chronic hemolysis and cumulative doses of steroid and IV IgG were reduced, and neurological deficits compared to those observed before treatment, were ameliorated. Treatment response was evaluated every 4 weeks over 6-8 years and included examination with gross motor scoring ASIA and INCAT, laboratory examination, and SF-12 fulfillment. Neurological relapses and the cumulative dose of IVIG and/or corticosteroids before and after initiation of treatment were documented. RBCs and neutrophils were stained to evaluate C5b-9 deposition. ClinicalTrials.gov, NCT01579838.

Results: All patients responded well to eculizumab. One patient developed hypersensitivity to eculizumab that was successfully switched to pozelimab with similar clinical and in vitro complement inhibition effect.

A 7-8 years follow-up in 4 patients showed a dramatic and significant neurological amelioration in the upper limbs and trunk with a more modest amelioration in the lower limbs was observed and maintained in all patients. Corticosteroids and immunoglobulin treatment, which had been used extensively prior to eculizumab initiation, was completely stopped. No patient suffered a relapse during the treatment period despite infections, and there were no hospital admissions apart fro 2 admissions due to reduced drug administration and allergic reaction. Decreased deposition of C3bi and C5b-9 on RBCs and neutrophils was documented ($p < 0.0001$). The SF-12 health questionnaires indicated significant improvement ($p < 0.003$).

Conclusion: The autoinflammatory disease seen with CD59 congenital malfunction was well controlled by eculizumab and pozelimab

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Disclosure: D. Mevorach, None; **N. Karbian**, None.

Abstract Number: 1637

Comparison of Nation-wide Epidemical Study on 2009 and That on 2019 Revealed That Improvement of Disease Severity and Mortality Rate May Come from Progress of Proficient Management in Patients with Relapsing Polychondritis in Japan

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Type: Poster Session D
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Background/Purpose: We conducted a retrospective survey study in 2009 and collected clinical data of 239 patients with relapsing polychondritis (RP). Using the survey data, we found a strong inverse relationship between ear and airway involvement, suggesting that the two major clinical symptoms of RP occurred in a mutually exclusive manner (Arthritis Rheumatol. 2018). When we divided the patients into three subgroups, namely patients with airway involvement (A subgroup, 20% of 239 patients), patients with ear involvement (E subgroup, 49%), and patients with both ear and airway involvement (B subgroup, 29%), patients in B subgroup had more progressive and longer disease course (Medicine. 2018). Actually, 59% patients presented with ear involvement at disease onset and a third of the patients were allocated into B subgroup (patients with both ear and airway involvement) with a high mortality rate (BMC Rheumatol. 2020). To confirm the issue, we conducted 2nd nationwide survey in 2019.

Methods: The survey questionnaire was sent to Japanese major medical facilities and outpatient clinics in 2019. In this study, we analyzed clinical data of 128 patients with RP of the 2nd survey and made comparison with those of 239 patients with RP of the 1st survey.

Results: In 2019 survey, patient age, disease duration, and male to female ratio were 60.7 ± 1.36 years (57.4 ± 1.07 years in the 1st survey conducted 2009), 8.26 ± 0.74 years (4.76 ± 0.33 years), and 1.13:1 (1.13:1), respectively. The disease duration in 2019 survey was significantly longer than those in 2009 survey ($p < 0.001$). Numbers of the involved organs per-patient basis of 2019 survey were 1.30 ± 0.06 organs at disease onset and 3.09 ± 0.13 organs at the last follow-up (8.26 years). In 2009 survey, numbers of the involved organs at onset were 1.13 ± 0.02 organs and increased to 3.13 ± 0.09 organs at the last (4.76 years). The comparison suggests that the disease progressed modestly taking more time in 2019 survey. The prognostic stages tended to improve (from 2.45 ± 0.07 to 2.21 ± 0.07, $p = 0.06$) and the mortality rate declined significantly (from 9.2% to 2.3%, $p = 0.01$) in the 2019 survey compared with 2009 survey. At the last follow-up, incidence of ear (79% versus 89%, $p = 0.02$) and joint involvement (39% vs. 57%, $p = 0.001$) was significantly higher in 2019 survey than that in 2009 survey. Incidence of airway (49% vs. 28%, $p = 0.001$) and CNS (12% vs. 4.7%, $p = 0.03$) involvement was significantly lower in 2019 survey than that in 2009 survey. Use of immunosuppressants (except steroids) was significantly frequent in 2019 survey (59.4 ± 4.36%) than that in 2009 survey (37.2 ± 3.13%, $p < 0.001$).

Conclusion: In patients with RP, incidence of airway involvement and their mortality rate declined significantly during the decade in Japan. We are hard to exclude a possibility that RP spontaneously became mild in the decade. Nonetheless, our second survey suggests important implications of current treatment and/or management of RP, including advances of medications.

Disclosure: J. Shimizu, None; **Y. Yamano**, None; **K. Kawahata**, Pfizer Inc, 2, 5, 8; **N. Suzuki**, None.

Abstract Number: 1638

Systemic Treatment in Behçet's Disease According to Clinical Phenotypes. Study of 111 Patients

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SESSION INFORMATION

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Background/Purpose: Behçet's disease (BD) is a multisystemic vasculitis. Different clinical phenotypes can be distinguished. Systemic corticosteroids are the most used drugs in BD. Conventional and biological immunosuppressants (IS) may also be used. **Objectives**: To evaluate the systemic treatment of BD according to clinical domains

Methods: Study of all consecutive 111 patients diagnosed with definitive or possible BD by expert rheumatologists in a well-defined population of Northern Spain, between 1980 and 2019. Most of them met the International Criteria for BD (ICBD) Study of all consecutive 111 patients diagnosed with definitive or possible BD by expert rheumatologists in a well-defined population of Northern Spain, between 1980 and 2019. Most of them met the International Criteria for BD (ICBD).

TABLE 1

CLINICAL PHENOTYPES	Cases N (%)	COLCH	COS	Dosis total IS	AZA	MTX	CYA	MMF	TLD	APR	DAP
Oral ulcers	110 (99.1)	85 (77.9)	81 (73.6)	51 (46.4)	30 (27.3)	25 (22.7)	14 (12.7)	2 (1.8)	6 (5.5)	6 (5.5)	3 (2.7)
Genital ulcers	69 (62.2)	56 (81.2)	51 (74)	32 (46.4)	17 (24.6)	16 (23.2)	10 (14.5)	1 (1.5)	5 (7.2)	2 (3.4)	3 (4.3)
Cutaneous lesions	76 (68.5)	58 (76.3)	61 (80.3)	52 (68.4)	32 (42.1)	22 (29)	9 (11.8)	0	5 (6.6)	6 (7.9)	3 (4)
Ocular manifestations	39 (35.1)	27 (69.2)	36 (92.3)	19 (48.7)	17 (43.6)	12 (30.8)	11 (28.2)	2 (5.1)	4 (10.3)	2 (5.1)	2 (5.1)
Neurological involvement	20 (18)	12 (60)	15 (75)	15 (75)	3 (15)	4 (20)	3 (15)	1 (5)	0	0	1 (5)
Vascular manifestations	11 (10)	8 (72.7)	9 (81.8)	5 (45.5)	3 (27.3)	3 (27.3)	1 (9.1)	0	0	0	0
Gastrointestinal involvement	4 (3.6)	2 (50)	1 (25)	1 (25)	1 (25)	0	0	0	0	0	0
TOTAL	111	85 (76.6)	85 (76.6)	51 (46)	30 (27)	25 (22.5)	14 (12.6)	2 (1.8)	6 (5.4)	6 (5.4)	3 (2.7)

Abbreviations: COLCH: Colchicine; OCS: Oral Corticosteroids; IS: Immunosuppressants; AZA: Azathioprine; MTX: Methotrexate; CYA: Cyclosporine A; MMF: Mycophenolate Mofetil; TLD: Thalidomide; APR: Apremilast; DAP: Dapsone.

TABLE 2

CLINICAL PHENOTYPES	BT	ADA	IFX	ETN	TCZ	No improvement	Partial improvement	Complete response
Oral ulcers	28 (35.5)	22 (20)	12 (11)	3 (2.7)	2 (1.8)	22 (20)	22 (20)	66 (60)
Genital ulcers	17 (24.7)	13 (18.8)	8 (11.6)	2 (2.9)	1 (1.4)	16 (23.2)	12 (17.4)	41 (59.4)
Cutaneous lesions	21 (27.6)	18 (23.7)	8 (10.5)	3 (4)	2 (2.6)	8 (10.5)	19 (25)	49 (64.5)
Ocular manifestations	19 (50)	16 (42.1)	9 (23.7)	1 (2.6)	2 (5.3)	0	8(21)	30 (79)
Neurological involvement	7 (35)	2 (10)	4 (20)	1 (5)	0	3 (15)	5 (25)	12 (60)
Vascular manifestations	4 (36.4)	3 (27.3)	2 (18.2)	1 (9.1)	1 (9.1)	2 (18.2)	4(36.4)	5 (45.5)
Gastrointestinal involvement	0	0	0	0	0	1 (25)	1 (25)	2 (50)
TOTAL	28 (25.2)	22 (19.8)	12 (10.8)	3 (2.7)	2 (1.8)	22 (19.8)	22 (19.8)	67 (60.4)

Abbreviations: BT: Biologic Therapy; ADA: Adalimumab; IFX: Infliximab; ETN: Etanercept; TCZ: Tocilizumab

Results: We studied 111 patients (62 women/49 men), mean age at diagnosis 36.8±13.2 years. After a mean follow-up of 81.4±85 months, all patients required systemic treatment (TABLE 1-2). Biological therapy (n=28) was indicated by ocular manifestations (n=13; 46.4%) persistent, severe and refractory oral ulcers (n=10, 35.7%), neurological (n=2; 7.1%), musculoskeletal (n=2; 7.1%) or cutaneous involvement (1; 3.6%). Adalimumab and Infliximab were the biological therapy more frequently used.

Conclusion: Most patients with BD required oral corticosteroids and colchicine. Almost half required conventional IS. Up to a third required biologic therapy, especially by ocular involvement. Most patients had clinical improvement.

Disclosure: D. Martinez-Lopez, Lilly, 2; **L. Sanchez-Bilbao**, None; **C. Alvarez-Reguera**, None; **A. Herrero Morant**, None; **I. Gonzalez-Mazon**, None; **J. Martín-Varillas**, None; **G. Suarez-Amorin**, None; **P. Setien-Preciados**, None; **C. Mata-Arnaiz**, None; **M. González-Gay**, None; **R. Blanco**, None.

Abstract Number: 1639

Preliminary Baseline Subject Demographics and Disease Characteristics in a Phase 3 Clinical Trial of the Safety and Efficacy of Lenabasum in Dermatomyositis (DETERMINE)

Victoria Werth[1], Chester Oddis[2], David Fiorentino[3], Nancy Dgetluck[4], Quinn Dinh[5], Michael Tillinger[6], Barbara White[5] and Ingrid Lundberg[7], [1]University of Pennsylvania and the Michael J. Crescenz VA Medical Center, Philadelphia, PA, [2]Department of Medicine, Division of Rheumatology, University of Pittsburgh, Pittsburgh, PA, [3]Department of Dermatology, Stanford University, Redwood City, CA, [4]Corbus Pharmaceuticals, Inc., Norwood, MA, [5]Corbus Pharmaceuticals, Norwood, MA, [6]Corbus Pharmaceuticals Inc., Norwood, MA, [7]Division of Rheumatology, Department of Medicine, Karolinska Institutet,, Stockholm, Sweden

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Miscellaneous Rheumatic & Inflammatory Diseases Poster III: Therapies

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: There is significant unmet need for new treatments to achieve disease control in dermatomyositis (DM), because of limited efficacy or toxicity of immunosuppressive agents or refractory disease.[1] Lenabasum is an oral, selective cannabinoid receptor type 2 (CB_2) agonist that resolves inflammation and attenuates fibrotic processes. In a Phase 2 DM trial (NCT02466243), lenabasum vs. placebo treatment was well tolerated and associated

Table 1. Preliminary Overall Baseline Subject Demographics, Disease Characteristics, and Background Immunomodulating Treatments in Phase 3 JBT101-DM-002 Trial[a]

	Overall n/129 (%) or mean ± SD
Demographics	
Female	102 (79%)
Age, years	51.8 ± 12.3
Body mass index, kg/m^2	27.6 ± 6.9
Race	
White	90 (70%)
Asian	22 (17%)
Non-white Hispanic or Latino	10 (7.8%)
Black	1 (0.5%)
Other/unknown	6 (4.7%)
Disease Characteristics	
Classic DM[b]	109 (85%)
Clinically Amyopathic DM[b]	20 (15%)
Disease duration (months)	81 ± 84.9
CDASI activity (0 – 100)	26 ± 12.2
CDASI >14	111 (86%)
MMT-8 (0 – 150)	135 ± 14
Subjects with MMT-8 < 150	112 (87%)
MMT-8 in subjects with MMT-8 < 143	128 ± 13
Subjects with MMT-8 < 143	87 (67%)
≥ 1 elevated muscle enzyme[c]	48 (37%)
HAQ-DI (0 – 3)	0.83 ± 0.71
HAQ pain VAS (0 – 100)	34 ± 27
EMGA VAS (0-10 cm)	5.4 ± 1.8
PtGA VAS (0-10 cm)	5.1 ± 2.3
MDGA VAS (0-10 cm)	5.5 ± 1.8
Interstitial lung disease[d]	42 (33%)
Background Immunomodulating Treatments	
Prednisone/prednisolone daily dose in those receiving corticosteroids, mg (min-max)[e]	9.5 (2.5-20)
> 10 mg corticosteroid daily	18 (14%)
≥ 1 immunomodulator	108 (84%)
≥ 2 immunomodulators	72 (56%)
Corticosteroids	67 (52%)
Methotrexate	30 (23%)
Hydroxychloroquine	23 (18%)
Intravenous immunoglobulin	22 (17%)
Mycophenolate mofetil	19 (15%)
Azathioprine	14 (11%)
Other[f]	26 (24%)

[a] Data blinded to treatment assignment and immunomodulating treatments include immunosuppressive therapies, hydroxychloroquine, and IVIG
[b] Diagnosed by Bohan and Peter criteria and/or ACR/EULAR criteria
[c] % of enzyme elevations > upper limit of normal [LDH (22.5%); CK (15.5%); AST (12.4%); aldolase (10.4%); ALT (8.5%)].
[d] Interstitial lung disease is defined as history of fibrosis on CXR, history of interstitial lung disease on CT scan of the lungs, or forced vital capacity (FVC), % predicted < 80% at baseline.
[e] Maximum daily dose of prednisone allowed is 20 mg or equivalent dose
[f] Other immunomodulators (e.g. rituximab, tacrolimus, cyclosporine)

with improvement in Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) activity score and other efficacy outcomes.[2] Efficacy and safety of lenabasum in DM is being tested in a global, randomized, double-blind, placebo-controlled Phase 3 trial (NCT03813160). Preliminary baseline demographics, disease characteristics, and immunomodulating treatments in the first 129 enrolled subjects are presented as blinded data. This is the largest interventional, placebo-controlled trial to date in DM.

Methods: 150 subjects will be enrolled in an ongoing trial with sites in North America, Europe, and Asia. Subjects are ≥ 18 years of age, with a diagnosis of DM by Bohan and Peter or ACR/EULAR criteria.[3,4] Stable doses of immunomodulating medications are allowed. Disease must be active by physician assessment with ≥ 1 of 3 criteria: 1. Physician global activity (MDGA) ≥ 3 cm [10 cm visual analogue scale (VAS)] and Manual Muscle Testing (MMT)-8 score ≤ 142 points (max 150); 2. Sum of MDGA, patient global activity (PtGA), and extramuscular global assessment (EMGA) VAS scores ≥ 10 cm (each 10 cm VAS scales); or 3. MDGA ≥ 3 cm and CDASI activity score > 14 (≥ moderate/severe skin activity).

Results: As of May 31, 2020, 129 subjects were dosed (**Table 1)**. Most subjects are female (79%), white (70%), and middle-aged. More have classic (85%) than clinically amyopathic DM (15%). Most (86%) have significant moderate/severe skin activity (CDASI > 14). Most (87%) have muscle weakness with mean MMT-8 ± SD, 135 ± 14, and 37% have ≥ 1 elevated muscle enzyme test. Physician-reported outcomes include EMGA VAS score = 5.4 ± 1.76 and MDGA VAS score = 5.5 ± 1.75. Patient-reported outcomes include Health Assessment Questionnaire-Disability Index (HAQ-DI) score = 0.83 ± 0.713, pain score on HAQ-DI = 34 ± 27, and PtGA VAS score = 5.1 ± 2.32. Glucocorticoids were used in 52% of subjects. Eighty-four percent were on ≥ 1 immunomodulating drug and 56% were on ≥2.

Conclusion: Baseline demographics of enrolled subjects are as expected (majority white, female, and middle-aged) and reflects the estimated proportion of classic to clinically amyopathic patients in the overall DM population (~5:1). Most subjects are concurrently receiving immunomodulatory drugs and have active, refractory disease with glucocorticoid use in half of subjects.

1. J Am Acad Dermatol. 2020;82:267-81.

2. Arthritis Rheumatol. 2019;71 (suppl 10).

3. Arthritis Rheumatol. 2017;69:2271-82.

4. N Engl J Med. 1975;292:344-7 and N Engl J Med. 1975;292:403-7.

Disclosure: V. Werth, Biogen, 2, 5; **C. Oddis**, Genentech, 2; **D. Fiorentino**, None; **N. Dgetluck**, Corbus Pharmaceuticals Inc., 3; **Q. Dinh**, Corbus Pharmaceuticals Inc., 3; **M. Tillinger**, Corbus Pharmaceuticals Inc., 3; **B. White**, Corbus Pharmaceuticals, Inc., 1, 2, 3, 4; **I. Lundberg**, Bristol Myers Squibb, 2, Astra Zeneca, 2.

Abstract Number: 1640

Clinically Important Improvement in Osteoarthritis Pain at Week 16 After Subcutaneous Administration of Tanezumab: Pooled Analysis from International Studies

Thomas Schnitzer[1], Francis Berenbaum[2], Philip G Conaghan[3], Robert Dworkin[4], Takaharu Yamabe[5], Isabelle Davignon[5], Stefan Wilhelm[6], Erika Dragon[7] and Lars Viktrup[6], [1]Northwestern University Feinberg School of Medicine, Chicago, IL, [2]AP-HP, Hôpital Saint-Antoine, Service de Rhumatologie, Centre de Recherche Saint-Antoine, INSERM UMR_S 938,Sorbonne Université, Paris, 75012, France, Paris, France, [3]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, and National Institute for Health Research Leeds Biomedical Research Centre, Leeds, United Kingdom, [4]University of Rochester School of Medicine and Dentistry, Rochester, NY, [5]Pfizer Inc, Groton, CT, [6]Eli Lilly and Company, Indianapolis, IN, [7]Pfizer Ltd, Budapest, Hungary

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Osteoarthritis – Clinical Poster II

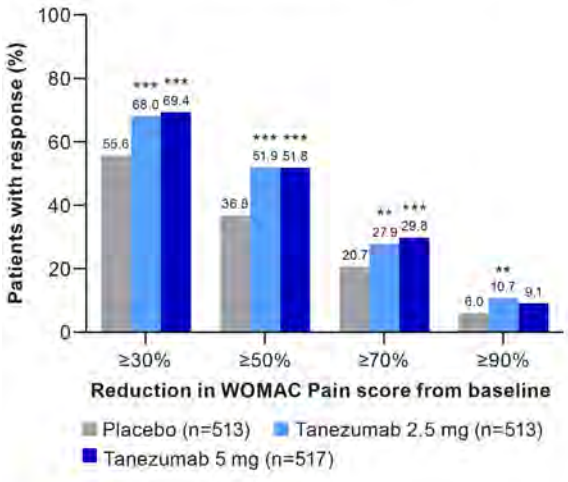
Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Tanezumab is under investigation for the treatment of moderate to severe OA pain. As part of the phase 3 OA program, two randomized, placebo-controlled studies were completed and the data reported separately. Both studies showed early and sustained pain relief, following subcutaneous administration of tanezumab, at the time of the respective primary endpoints. The objective of this pooled analysis of 2 studies was to evaluate the treatment response of tanezumab versus placebo as assessed by reductions in the WOMAC Pain subscale of ≥30%, ≥50%, ≥70% or ≥90% at Week 16. Reductions from baseline of ≥30% (moderate) or ≥50% (substantial) are often reported to be clinically important improvements.

Methods: Both phase 3 studies were randomized, double-blind, and placebo-controlled. Study 1, with primary endpoint at Week 24, enrolled patients from Europe or Japan (NCT02709486) who then received 3 doses of placebo, tanezumab 2.5 mg or tanezumab 5 mg (at baseline, Week 8 and Week 16). Study 2, with primary endpoint at Week 16, was a dose-titration study conducted in North America (NCT02697773) with three arms: placebo at baseline

Figure 1. Proportion of patients with ≥30%, ≥50%, ≥70% or ≥90% reduction from baseline in WOMAC Pain at Week 16



* $P \leq 0.05$; ** $P \leq 0.01$; *** $P \leq 0.001$ versus placebo
WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

and Week 8, tanezumab 2.5 mg at baseline and Week 8, or tanezumab 2.5 mg at baseline and tanezumab 5 mg at Week 8. Data from this study's dose-titration group (tanezumab 2.5 mg to 5 mg at Week 8) were pooled with the study 1 tanezumab 5 mg group for analyses at Week 16. Eligibility criteria included OA diagnosis (hip or knee, ACR criteria, Kellgren-Lawrence grade ≥2); WOMAC Pain and Physical Function scores ≥5; Patient's Global Assessment of Osteoarthritis 'fair', 'poor' or 'very poor'; and a history of acetaminophen, nonsteroidal anti-inflammatory drugs, and tramadol/opioids being inadequate or unsuitable. The proportions of patients with ≥30%, ≥50%, ≥70% or ≥90% reduction from baseline at Week 16 in WOMAC Pain were estimated by logistic regression.

Results: A total of 1545 patients were evaluated. The index joint was the knee for 84.1% (1299/1545) of patients. Radiographic severity of the index joint was Kellgren-Lawrence grade 3 or 4 for 77.1% (1191/1545) of patients. Baseline WOMAC Pain scores were 6.9 ± 1.1 (mean ± standard deviation) in all three pooled groups. The proportion of patients achieving improvement from baseline in WOMAC Pain at Week 16 of ≥30% (55.6%, 68.0% and 69.4% in the placebo, tanezumab 2.5 mg and tanezumab 5 mg groups, respectively), ≥50% (36.8%, 51.9% and 51.8%, respectively), or ≥70% (20.7%, 27.9% and 29.8%, respectively) was significantly greater in both tanezumab treatment groups compared with the placebo group (all $P< 0.05$ versus placebo; Figure 1). The proportion of patients with ≥90% improvement was significantly greater in the tanezumab 2.5 mg group (10.7%; $P< 0.05$), but not in the tanezumab 5 mg group (9.1%), compared with the placebo group (6.0%).

Conclusion: The pooled analysis of these studies showed that at Week 16, a significantly higher proportion of patients achieved a clinically important improvement in pain when treated with tanezumab (both treatment groups) than placebo, with little difference between the tanezumab treatment groups. Funded by Pfizer and Lilly.

Disclosure: T. Schnitzer, Pfizer, 1, 2, Lilly, 1, 2, Regeneron, 1, AstraZeneca, 1; **F. Berenbaum**, Pfizer, 1, Eli Lilly, 1; **P. Conaghan**, AbbVie, 1, 2, EMD Serono, 1, Flexion Therapeutics, 1, 2, Galapagos, 1, Gilead, 1, Novartis, 1, 2, Regeneron, 1, Samumed, 1, 2, GlaxoSmithKline, 5, Janssen, 5, Pfizer Inc, 5, Bristol-Myers Squibb, 2, Eli Lilly, 5; **R. Dworkin**, abide, 1, acadia, 1, Analgesic Solutions, 1, Asahi_kasei, 1, Biogen, 1, Centrexion, 1, Clexio, 1, Decibel, 1, Eli Lilly, 1, Glenmark, 1, Hope, 1, Lotus, 1, Mainstay, 1, Merck, 1, Neurana, 1, NeuroBo, 1, Novaremed, 1, Novartis, 1, Pfizer, 1, Regenacy, 1, Sanifit, 1, Scilex, 1, Semnur, 1, Sollis, 1, Vertex, 1, Vizuri, 1; **T. Yamabe**, Pfizer, 1, 2; **I. Davignon**, Pfizer, 1, 2; **S. Wilhelm**, Eli Lilly and Company, 1, 2; **E. Dragon**, Pfizer, 1, 2; **L. Viktrup**, Eli Lilly and Company, 1, 3.

Abstract Number: 1641

Clinically Important Improvements in Patients with Osteoarthritis Treated with Subcutaneous Tanezumab: Results from a 56-Week Randomized NSAID-Controlled Study

David Hunter[1], Tuhina Neogi[2], Melvin Churchill[3], Ivan Shirinsky[4], Masanari Omata[5], Alexander White[6], Ali Guermazi[2], Robert Fountaine[7], Glenn Pixton[8], Lars Viktrup[9], Mark Brown[7], Christine West[10] and Kenneth Verburg[11], [1]Institute of Bone and Joint Research, University of Sydney, St Leonards, New South Wales, Australia, [2]Boston University School of Medicine, Boston, MA, [3]Arthritis Center of Nebraska, Lincoln, NE, [4]Federal State Budgetary Scientific Institution Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russia, [5]Ohimachi Orthopaedic Clinic, Tokyo, Japan, [6]Progessive Medical Research, Port Orange, FL, [7]Pfizer Inc., Groton, CT, [8]Pfizer Inc., Morrisville, NC, [9]Eli Lilly and Company, Indianapolis, IN, [10]Pfizer Inc, Groton, CT, [11]Pfizer Inc, Groton

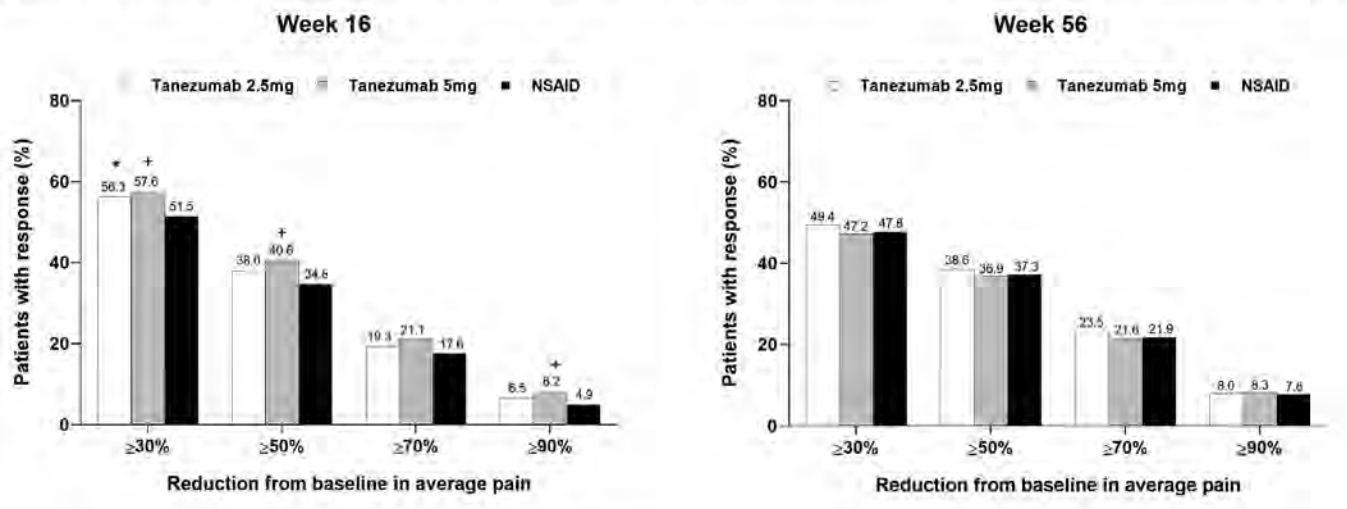
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Subcutaneous (SC) tanezumab, a monoclonal antibody that inhibits nerve growth factor, was investigated for the relief of signs and symptoms of moderate-severe OA in patients (pts) for whom use of other analgesics was ineffective or not appropriate in a randomized NSAID-controlled global long-term safety study (NCT02528188). The current analysis examines the effect of tanezumab versus NSAID on clinically important improvements in pts with OA.

Methods: Eligible pts had hip or knee OA based on ACR criteria with x-ray confirmation; baseline (BL) WOMAC Pain and Physical Function subscale scores of ≥5; BL Pt Global Assessment of OA (PGA-OA) of "fair", "poor", or "very poor"; history of inadequate pain relief with acetaminophen; inadequate pain relief with/intolerance to tramadol or opioids, or unwilling to take opioids. Pts were on a qualifying, stable dose of NSAID before study entry. Pts received SC tanezumab (2.5 mg or 5 mg every 8 Wks) or oral NSAID (BID) over the 56-Wk treatment period. At Wk 16, pts who did not have the required efficacy response (≥15% reduction from BL in WOMAC Pain subscale score at Wk 2, 4, or 8, and ≥30% reduction from BL at Wk 16) were discontinued from study treatment and entered the safety follow-up period. The proportion of pts who had a reduction from BL of ≥30%, ≥50%, ≥70% or ≥90% in average weekly pain (electronic pain diary) was evaluated at Wks 16 and 56. Pt Acceptable Symptom State (PASS; the value beyond which pts consider themselves well) and Minimum Clinically Important Improvement (MCII; smallest change in measurement that signifies an important improvement in a pt's symptoms) were evaluated at Wks 16 and 56 using Tubach and colleagues' composite endpoints of improvement based on average pain, WOMAC Physical Function and PGA-OA (definitions provided in Figure 2).[1,2] Responders in average pain, PASS, and MCII are post-hoc analyses. Unadjusted p-values are presented.

Results: In total, 3,021 pts were randomized and 2,996 received at least 1 dose of blinded SC study drug and are included in the efficacy analyses. A total of 1,312 pts completed the treatment period (42–45% across treatment groups). BL pt characteristics were similar across treatment groups: mean age 60.3–61.2 years; female 63.6–66.5%; duration of index joint OA 7.9–8.1 years; index joint was knee 84.9–85.5%, and hip in 14.5–15.1%. The proportion of pts with reductions from BL in average pain was significantly greater for tanezumab (2.5 mg, ≥30% responders; 5 mg, ≥30%, ≥50%, and ≥90% responders) versus NSAID at Wk 16 and largely similar across treatment groups at Wk 56 for all categories of response (Figure 1). There were no significant differences in the proportion of pts achieving MCII and PASS between treatment groups at Wks 16 and 56 (Figure 2).

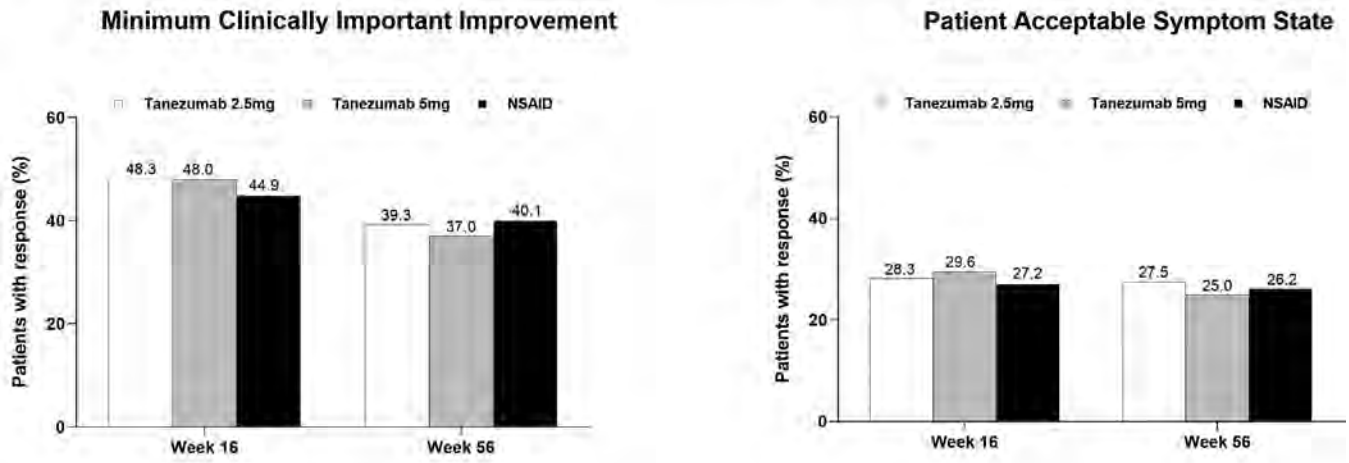
Figure 1 Treatment response: Proportion of patients with percent reduction from baseline in average pain (ITT, mixed BOCF/LOCF)



* Unadjusted $P \leq 0.05$ for tanezumab 2.5mg versus NSAID. + Unadjusted $P \leq 0.05$ for tanezumab 5mg versus NSAID.

BOCF, baseline observation carried forward; ITT, intent to treat; LOCF, last observation carried forward

Figure 2 Proportion of patients with clinically important improvement (ITT, mixed BOCF/LOCF)



BOCF, baseline observation carried forward; ITT, intent to treat; LOCF, last observation carried forward

Minimum Clinically Important Improvement = improvement from baseline in OA pain in index joint (knee ≥1.99, hip ≥1.53) and WOMAC Physical function (knee ≥0.91, hip ≥0.79) and PGA-OA in ≥1 category.

Patient Acceptable Symptom State: OA pain score for index joint (knee ≤3.23, hip ≤3.50) and WOMAC Physical Function (knee ≤3.10, hip ≤3.44) and PGA-OA of "good" or "very good".

Conclusion: The majority of tanezumab treated pts had a clinically important pain improvement (≥30%) at Wk 16, significantly more than with NSAID. The composite pain and function improvement and acceptable severity level after treatment was similar for tanezumab and NSAID.

Disclosures: Sponsored by Pfizer and Eli Lilly & Company.

References:

1. Tubach F, et al. Ann Rheum Dis. 2005; 64(1): 34–7.
2. Tubach F, et al. Ann Rheum Dis. 2005; 64(1): 29–33.

Disclosure: D. Hunter, Pfizer, Lilly, 1, Merck Serono, 1; **T. Neogi**, Lilly, 1, EMD Merck Serono, 1, Novartis, 1, Regeneron, 1, Pfizer/Lilly, 1; **M. Churchill**, None; **I. Shirinsky**, None; **M. Omata**, None; **A. White**, None; **A. Guermazi**, AstraZeneca, 1, Pfizer, 1, MerckSerono, 1, Galapagos, 1, Roche, 1, TissueGene, 1, Boston Imaging Core Lab, 1; **R. Fountaine**, Pfizer Inc., 1, 3, 4; **G. Pixton**, Pfizer Inc., 3, 4; **L. Viktrup**, Eli Lilly and Company, 1, 3; **M. Brown**, Pfizer, 1, 3; **C. West**, Pfizer Inc., 1, 3; **K. Verburg**, Pfizer Inc., 1, 2.

Abstract Number: 1642

Observed Efficacy with Subcutaneous Tanezumab Is Early and Maintained in Patients with Osteoarthritis: Results from a 56-Week Randomized NSAID-Controlled Study

Tuhina Neogi[1], David Hunter[2], Melvin Churchill[3], Ivan Shirinsky[4], Masanari Omata[5], Alexander White[6], Ali Guermazi[1], Robert Fountaine[7], Glenn Pixton[8], Lars Viktrup[9], Mark Brown[7], Christine West[10] and Kenneth Verburg[11], [1]Boston University School of Medicine, Boston, MA, [2]Institute of Bone and Joint Research, University of Sydney, St Leonards, New South Wales, Australia, [3]Arthritis Center of Nebraska, Lincoln, NE, [4]Federal State Budgetary Scientific Institution Research Institute of Fundamental and Clinical Immunology, Novosibirsk, Russia, [5]Ohimachi Orthopaedic Clinic, Tokyo, Japan, [6]Progessive Medical Research, Port Orange, FL, [7]Pfizer Inc., Groton, CT, [8]Pfizer Inc., Morrisville, NC, [9]Eli Lilly and Company, Indianapolis, IN, [10]Pfizer Inc, Groton, CT, [11]Pfizer Inc, Groton

SESSION INFORMATION

Session Date: Monday, November 9, 2020

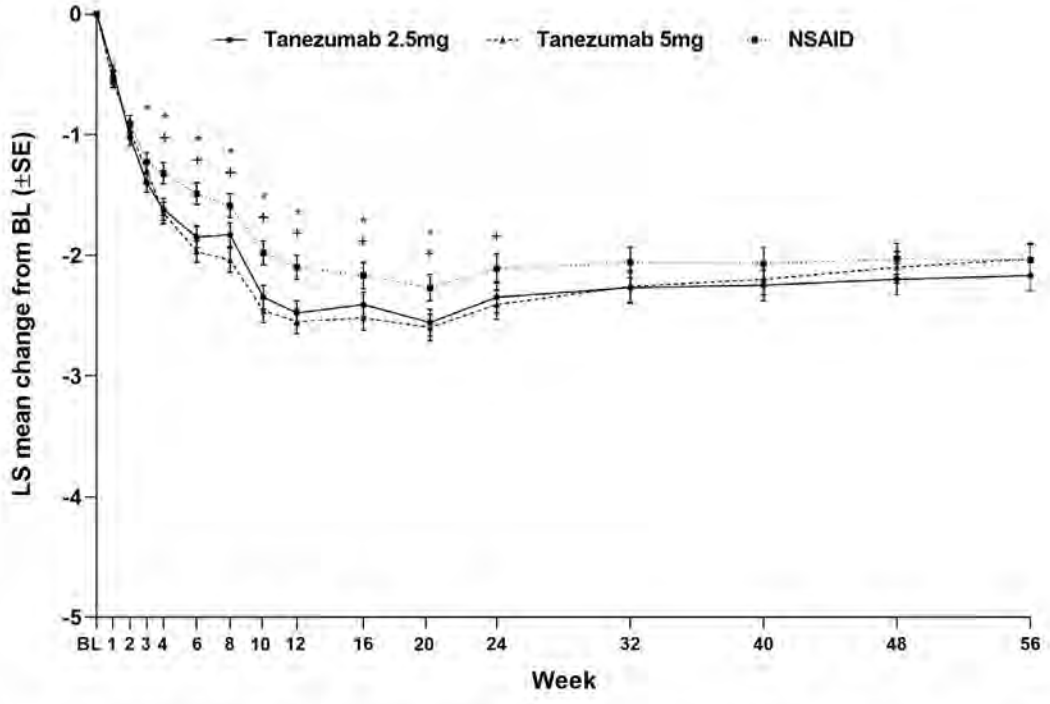
Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Subcutaneous (SC) tanezumab, a monoclonal antibody that inhibits nerve growth factor, was investigated for the relief of signs and symptoms of moderate-severe OA in patients (pts) for whom use of oth-

Figure 1 Change from baseline in average pain in index joint through Week 56 (ITT population, Multiple imputation)

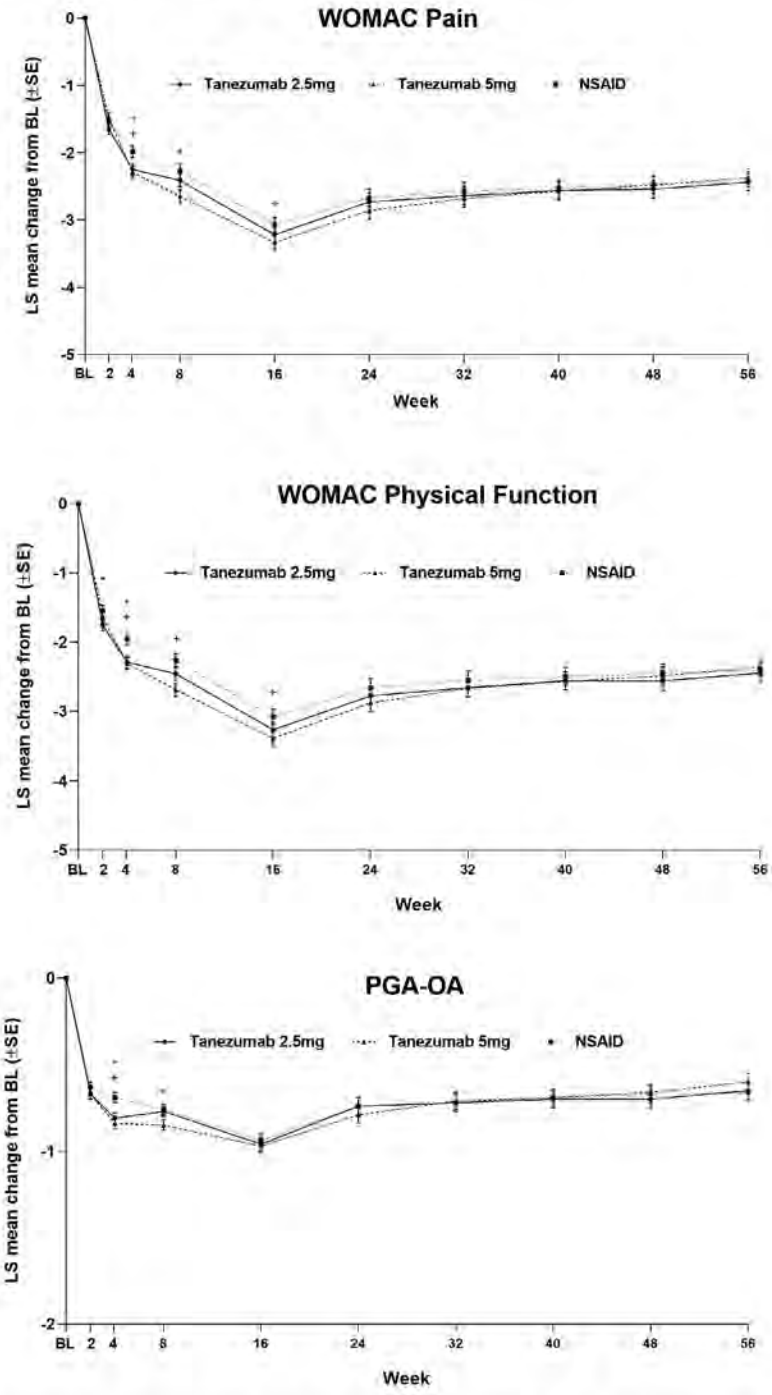


* Unadjusted $P \leq 0.05$ for tanezumab 2.5mg versus NSAID. + Unadjusted $P \leq 0.05$ for tanezumab 5mg versus NSAID.

Weeks 20 to 56 represent averages of the values reported during the 4-week interval up to and including the given week.

BL, baseline; ITT, intent to treat; LS, least squares; SE, standard error

Figure 2 Change from baseline up to Week 56 in WOMAC Pain, Physical Function and PGA-OA scores (ITT population, Multiple imputation)



* Unadjusted $P \leq 0.05$ for tanezumab 2.5mg versus NSAID. + Unadjusted $P \leq 0.05$ for tanezumab 5mg versus NSAID.

BL, baseline; ITT, intent to treat; LS, least squares; PGA-OA, Patient Global Assessment of OA; SE, standard error

er analgesics was ineffective or not appropriate in a randomized NSAID-controlled long-term global safety study (NCT02528188). The primary safety (joint safety over 80 weeks [Wk]) and coprimary efficacy endpoints (pain, function, and Pt Global Assessment of OA [PGA-OA] at Wk 16) were recently disclosed.[1,2] The current analysis examines

the time-course and longer term maintenance of treatment effect of tanezumab versus NSAID on pain and physical function through Wk 56.

Methods: Eligible pts had hip or knee OA based on ACR criteria with x-ray confirmation; baseline (BL) WOMAC Pain and Physical Function subscale scores of ≥5; BL PGA-OA of "fair", "poor", or "very poor"; history of inadequate pain relief with acetaminophen; inadequate pain relief with/intolerance tramadol or opioids, or unwilling to take opioids. Pts were on a qualifying, stable dose of NSAID before study entry. Pts received SC tanezumab (2.5 mg or 5 mg every 8 Wks) or oral NSAID (BID) over the 56-Wk treatment period. At Wk 16, pts who did not have the required efficacy response (≥15% reduction from BL at Wk 2, 4, or 8, and ≥30% reduction from BL in WOMAC Pain at Wk 16) were discontinued from study treatment and entered the safety follow-up period. Pts were permitted to use rescue medication (≤3000 mg/day acetaminophen) up to 3 days/Wk up to Wk 16 and daily thereafter. Treatment effect through Wk 56 versus NSAID was evaluated by measuring change from BL in average index joint pain (electronic pain diary: daily from Day 1 to Wk 16, then weekly to end of study) and WOMAC Pain and Physical Function, and PGA-OA scores (Wk 2 through Wk 56 at clinic visits). Unadjusted p-values are presented.

Results: In total, 3,021 pts were randomized and 2,996 included in the efficacy analyses. A total of 1,312 pts completed the treatment period (42–45% across treatment groups). BL pt characteristics were similar across treatment groups: mean age 60.3–61.2 years; duration of index joint OA 7.9–8.1 years; index joint was the knee 84.9–85.5%; female 63.6–66.5%. Reductions from BL in average index joint pain scores were largely similar across treatment groups from BL to Wk 4 (Figure 1). From Wk 4 to Wk 20 reductions were significantly greater ($P \leq 0.05$) in both tanezumab groups versus NSAID. Changes from BL in WOMAC Pain, Physical Function and PGA-OA scores were largely similar across treatment groups but there were scattered significant improvements for pts receiving tanezumab versus NSAID at Wks 4, 8 and 16 (Figure 2). Changes in WOMAC Pain, Physical Function and PGA-OA scores across treatment groups were generally maintained up to Wk 56.

Conclusion: Pts with moderate-severe hip or knee OA treated with tanezumab or NSAID experienced an early improvement in pain and function that was maintained long-term.

Disclosures: Sponsored by Pfizer and Eli Lilly & Company.

References:

1. Hochberg M, et al. ACR/ARHP 2019 Annual Scientific Meeting. 2019;71(S10):4888.
2. Hochberg M, et al. ACR/ARHP 2019 Annual Scientific Meeting. 2019;71(S10):2243.

Disclosure: T. Neogi, Lilly, 1, EMD Merck Serono, 1, Novartis, 1, Regeneron, 1, Pfizer/Lilly, 1; **D. Hunter**, Pfizer, Lilly, 1, Merck Serono, 1; **M. Churchill**, None; **I. Shirinsky**, None; **M. Omata**, None; **A. White**, None; **A. Guermazi**, AstraZeneca, 1, Pfizer, 1, MerckSerono, 1, Galapagos, 1, Roche, 1, TissueGene, 1, Boston Imaging Core Lab, 1; **R. Fountaine**, Pfizer Inc., 1, 3, 4; **G. Pixton**, Pfizer Inc., 3, 4; **L. Viktrup**, Eli Lilly and Company, 1, 3; **M. Brown**, Pfizer, 1, 3; **C. West**, Pfizer Inc., 1, 3; **K. Verburg**, Pfizer Inc., 1, 2.

Abstract Number: 1643

Evaluating Analgesic Response to Subcutaneous Tanezumab in Patients with Inadequate Treatment Response to Other Analgesics Based on Daily E-pain Diaries: A Pooled Analysis of 2 Randomized, Placebo-controlled Studies

Thomas Schnitzer[1], Francis Berenbaum[2], Isabelle Davignon[3], Ruoyong Yang[4], Lars Viktrup[5], Christine West[3] and Kenneth Verburg[6], [1]Northwestern University Feinberg School of Medicine, Chicago, IL, [2]AP-HP, Hôpital Saint-Antoine, Service de Rhumatologie, Centre de Recherche Saint-Antoine, INSERM UMR_S 938,Sorbonne Université, Paris, 75012, France, Paris, France, [3]Pfizer Inc, Groton, CT, [4]Pfizer Inc.,, New York, [5]Eli Lilly and Company, Indianapolis, IN, [6]Pfizer Inc, Groton

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Tanezumab is a monoclonal antibody against nerve growth factor being investigated for treatment of the signs and symptoms of osteoarthritis (OA). Subcutaneous tanezumab was efficacious, based on Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain, WOMAC Function, and Patient's Global Assessment of Osteoarthritis scores, in 2 recent Phase 3 studies, one in North America, and one in Europe and Japan in patients with moderate-to-severe OA of the knee or hip for whom standard of care treatment was not adequate. The current pooled analysis assessed the onset and maintenance of analgesic response to tanezumab in these patients, based on daily pain scores recorded in an electronic diary (e-diary).

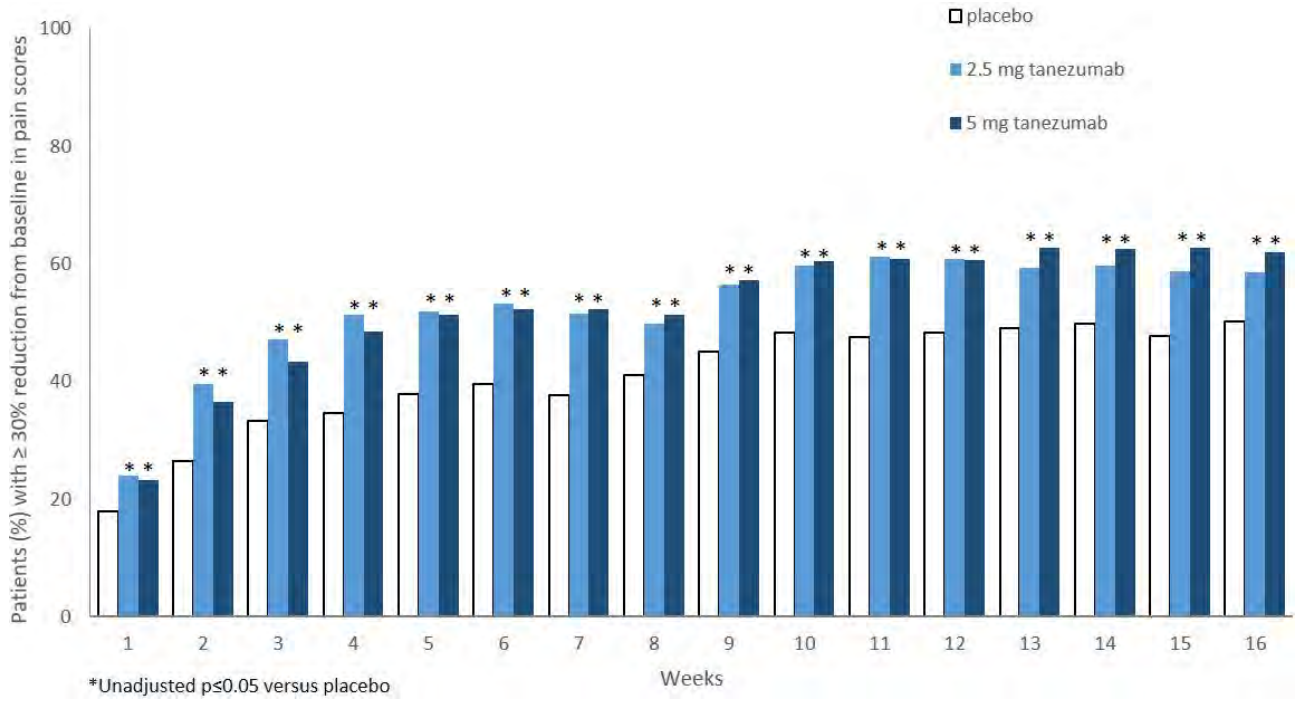


Figure 1. Proportion of patients with a ≥ 30% improvement in pain score

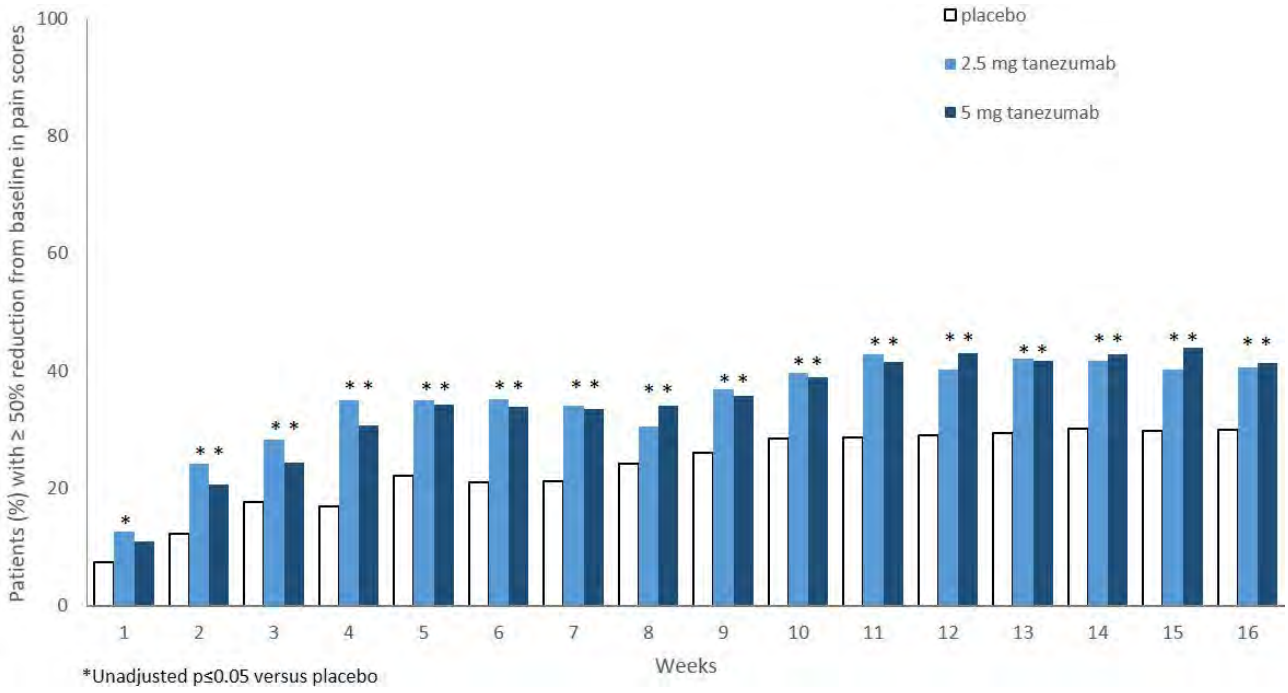


Figure 2. Proportion of patients with a ≥ 50% improvement in pain score

Methods: In study A4091056 (clinicaltrials.gov: NCT02697773), patients received 16-week treatment with placebo, tanezumab 2.5 mg (baseline and week 8), or tanezumab 2.5/5 mg (2.5 mg at baseline and 5 mg at week 8; included in the 5 mg group for the current pooled 16-week analysis). In study A4091057 (clinicaltrials.gov: NCT02709486), patients received placebo or tanezumab (2.5 mg or 5 mg) every 8 weeks for 24 weeks. Average pain over the past 24 hours was collected daily in the e-diary during the treatment period using an 11-point numeric rating scale (NRS; from 0 = no pain to 10 = worst possible pain). In the current analysis, the proportion of patients who achieved ≥30% or ≥50% decrease from baseline in NRS pain scores, based on weekly average of daily scores, were compared between placebo and tanezumab groups at each study week through week 16 using a logistic regression model. The median time to achieve ≥30% or ≥50% improvements in pain were compared between groups using a Kaplan-Meier analysis.

Results: Overall, 1545 patients were included in the analysis: placebo (n = 514), tanezumab 2.5 mg (n = 514), or tanezumab 5 mg (n = 517). Significant improvement over placebo was observed by Week 1 in both tanezumab groups for the ≥30% level. For the ≥50% level, significant improvement over placebo was observed by Week 1 for tanezumab 2.5 mg and by Week 2 for tanezumab 5 mg. These significant differences from placebo were maintained at all weeks up to Week 16 for both tanezumab groups at both response levels ($p < 0.05$ Figures 1 and 2). The time to achieve 30% and 50% response was significantly faster in the tanezumab groups than in the placebo group. The median (95% CI) time to onset of a ≥30% decrease in pain score from baseline was approximately 3 weeks for the tanezumab 2.5 mg group (range 3-4 weeks; $p < 0.0001$) and 4 weeks for 5 mg (range 3-5 weeks; $p=0.0002$) compared to 8 weeks for placebo (range 6-10 weeks; Table 1). The median time to onset of a ≥50% decrease in pain score from baseline was approximately 11 weeks in the tanezumab 2.5 mg and 5 mg groups (ranges 9-15 and 9-13 weeks, respectively; $p < 0.0001$). Not enough patients achieved a 50% response in the placebo group to calculate median time to onset (Table 1).

Conclusion: Tanezumab treatment resulted in significantly more patients reaching moderate (30%) or substantial (50%) improvements in pain compared with placebo as early as Week 1 and through Week 16. The median time to reach ≥30% and ≥50% improvement were 3-4 weeks and 11 weeks, respectively for tanezumab treated patients.

Group	Number (%) of patients achieving threshold[a]	Quartile 1[b] Time in weeks (95% CI)	Median[c] Time in weeks (95% CI)	p-value[e]
Placebo				
≥30%	328 (63.8%)	2 (2,3)	8 (6,10)	
≥50%	223 (43.4%)	5 (4,7)	Unable to calculate[d]	
Tanezumab 2.5 mg				
≥30%	377 (73.3%)	2 (1,2)	3 (3,4)	<0.0001
≥50%	281 (54.7%)	2 (2,3)	11 (9,15)	<0.0001
Tanezumab 5 mg				
≥30%	380 (73.5%)	2 (1,2)	4 (3,5)	0.0002
≥50%	291 (56.3%)	3 (2,4)	11 (9,13)	<0.0001

Table based on Kaplan Meier Analysis

[a] Total N was 514, 514, 517 for the placebo, tanezumab 2.5 mg and tanezumab 5 mg treatment groups, respectively. Percentages are based on overall proportion of responders through week 16.

[b] Quartile 1 reflects the time (in weeks) for 25% of patients to reach the response threshold

[c] Median reflects the time (in weeks) for 50% of patients to reach the response threshold.

[d] An insufficient number of patients achieved the ≥50% response threshold to perform median calculation.

[e] Versus placebo
Note: Q3 data is not presented as less than 75% of patients across treatment groups achieved the response thresholds of interest.

CI = Confidence interval.

Table 1. Time to ≥30% and ≥50% Improvement from Baseline in Pain Numeric Scale score

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Disclosure: T. Schnitzer, Pfizer, 1, 2, Lilly, 1, 2, Regeneron, 1, AstraZeneca, 1; **F. Berenbaum**, Pfizer, 1, Eli Lilly, 1; **I. Davignon**, Pfizer, 1, 2; **R. Yang**, Pfizer Inc., 1, 2; **L. Viktrup**, Eli Lilly and Company, 1, 3; **C. West**, Pfizer Inc., 1, 3; **K. Verburg**, Pfizer Inc., 1, 2.

Abstract Number: 1644

Radiographic Exclusionary Findings During Screening for Three Phase III Trials of Subcutaneous Tanezumab in Patients with Moderate to Severe Hip or Knee Osteoarthritis

Ali Guermazi[1], Frank Roemer[2], Andrew Kompel[1], Luis Diaz[3], Michel Crema[4], Mark Brown[5], Anne Hickman[5], Glenn Pixton[6], Lars Viktrup[7], Robert Fountaine[5], Aimee Burr[5], Sarah Sherlock[5] and Christine West[8], [1]Boston University School of Medicine, Boston, MA, [2]Boston University School of Medicine, Boston, MA, and Friedrich-Alexander University Erlangen-Nuremberg, Erlangen, Germany, Erlangen, Germany, [3]Boston Veteran Affairs Healthcare System, Boston, MA, [4]Boston University School of Medicine, Paris, France, [5]Pfizer Inc., Groton, CT, [6]Pfizer Inc., Morrisville, NC, [7]Eli Lilly and Company, Indianapolis, IN, [8]Pfizer Inc, Groton, CT

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Tanezumab is a nerve growth factor monoclonal antibody in development for osteoarthritis (OA). Following a clinical hold due to concerns around adverse joint events, the tanezumab clinical trial program implemented comprehensive radiographic eligibility criteria. We describe the frequencies of exclusionary radiographic findings during screening in three Phase III randomized studies of subcutaneous tanezumab.

Methods: NCT02697773[1] was a 40-week placebo-controlled study (16-week treatment). NCT02709486[2] was a 48-week placebo-controlled study (24-week treatment). NCT02528188[3,4] was an 80-week active-controlled (oral NSAID) study (56-week treatment). Bilateral shoulder, hip and knee screening radiographs were taken by trained imaging technologists and read by one of five central musculoskeletal radiology experts (central readers). Central readers were trained using a program-specific imaging atlas and underwent periodic re-calibration sessions.[5] Eligibility criteria for all studies included an OA diagnosis in the index hip or knee based on ACR criteria and a Kellgren Lawrence (KL) grade of ≥2 on radiograph as diagnosed by the central reader. Radiographic exclusion criteria included a KL grade of 0 or 1 in a non-index knee or hip with patient reported pain of ≥7 on a 0-10 numerical rating scale, without other exclusionary radiographic findings (discordant pain to X-ray), confounding joint or systemic conditions (severe malalignment of the knee, inflammatory joint disease etc.), presence of rapidly progressive OA type 2 (RPOA2), or potential risk factors for RPOA (such as osteonecrosis, subchondral insufficiency fracture, or atrophic OA; Figure 1) in any joint.

Results: In the three studies, conducted at >480 international sites, 23,079 patients were screened and 13,797 proceeded to radiography (producing 81,055 knee, hip or shoulder screening radiographs read by the central reader). Overall, 8024 patients (58.2%) were declared radiographically eligible. Among the 5773 (41.8%) patients declared

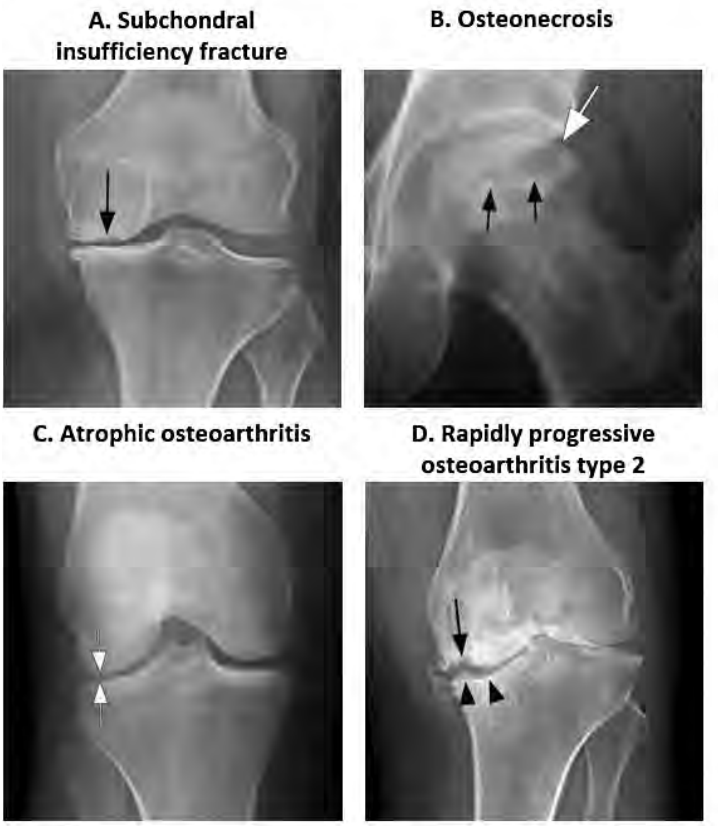
Table 1: Most common exclusionary radiographic findings from three Phase III trials of subcutaneous tanezumab.

	Knee radiographs (n = 26,597)		Hip radiographs (n = 26,938)		Shoulder radiographs (n = 27,520)	
Exclusionary radiologic finding	n radiographs (%)	Observed frequency during screening	n radiographs (%)	Observed frequency during screening	n radiographs (%)	Observed frequency during screening
Discordant pain to X-ray[a]	2508 (9.43 %)	~1 in 10 X-rays	2612 (9.70%)	~1 in 10 X-rays	N/A	N/A
Severe malalignment of the knee[b]	751 (2.82%)	~1 in 35 X-rays	N/A	N/A	N/A	N/A
Subchondral insufficiency fracture[c]	586 (2.20%)	~1 in 50 X-rays	61 (0.23%)	~1 in 500 X-rays	10 (0.04%)	~1 in 2500 X-rays
Atrophic/hypotrophic OA[d]	486 (1.83%)	~1 in 50 X-rays	105 (0.39%)	~1 in 250 X-rays	3 (0.01%)	~1 in 10,000 X-rays
Osteonecrosis[e]	119 (0.45%)	~1 in 250 X-rays	323 (1.20%)	~1 in 100 X-rays	82 (0.30%)	~1 in 325 X-rays
RPOA type 2[f]	18 (0.07%)	~1 in 1500 X-rays	110 (0.41%)	~1 in 250 X-rays	14 (0.05%)	~1 in 2000 X-rays

One or more exclusionary radiological finding may have been reported for each patient or from each radiograph. Exclusionary findings as defined in Roemer F., et al. Osteoarthritis Cartilage. 2015. 23(S1):S22–42. [a]Patient reported pain of ≥7 on a 0-10 numerical rating scale with a Kellgren Lawrence grade of 0 or 1 in a non-index hip or knee, without other exclusionary radiographic findings. [b]Cut-off of ≥10° varus or valgus on the anterior–posterior view. [c]Focal bone defect, or loss of sphericity of the articular surface and/or focal radiolucency in the subchondral trabecular bone, with or without adjacent cortical defect. [d]Joint space narrowing without relevant osteophyte formation and absence of erosions or other radiographic signs of inflammatory arthritis. [e]Focal circumscribed or extended region of infarcted bone. [f]Abnormal bone loss or destruction, including limited or total collapse of at least one subchondral surface that is not a feature of conventional advanced osteoarthritis. N/A, not applicable

Table 1. Most common exclusionary radiographic findings from three Phase III trials of subcutaneous tanezumab

Figure 1: Examples of exclusionary radiographic findings



A. Anteriorposterior radiograph of a left knee with definite medial joint space narrowing (i.e. Kellgren-Lawrence grade 3) at screening shows medial femoral subchondral collapse as the result of **subchondral insufficiency fracture (SIF)** with mild depression of the medial femoral surface. In addition, there is surrounding sclerosis.
B. Anteroposterior radiograph of a left hip shows femoral head **osteonecrosis** as geographic lucency of the femoral head demarcated by curve linear sclerosis (black arrows). In addition there is loss of femoral head sphericity with focal cortical collapse (white arrow).
C. Anteroposterior radiograph of a right knee shows definite joint space narrowing at the lateral tibio-femoral compartment (arrows) without osteophyte formation classifying this knee as **atrophic osteoarthritis**.
D. Deformity of the medial femoral (arrow) and tibial articular surface (arrowheads) is noted in this anteroposterior left knee radiograph representing **rapidly progressive osteoarthritis (RPOA) Type 2**. In addition there is articular surface collapse especially of the tibial plateau. Consequent varus deformity is observed.

Figure 1. Examples of exclusionary radiographic findings

ineligible, exclusionary radiographic findings were noted in 1 (4116 [29.8%]), 2 (1268 [9.2%]), 3 (279 [2.0%]), 4 (108 [0.8%]), or 6 joints (2 [0.01%]). The most common exclusionary radiographic finding in both knees and hips was discordant pain to X-ray (Table 1; ~1 in 10 screening X-rays), with other findings being much rarer (≤~1 in 35), particularly

in the hip (≤~1 in 100). Exclusionary radiographic findings were rare in the shoulder — the most common was osteonecrosis (~1 in 325, vs ~1 in 250 and 100 in the knee and hip, respectively).

Conclusion: Conclusion: The Phase III tanezumab trial program included comprehensive radiographic screening. The most common exclusionary finding in knees and hips was pain discordant to X-ray (~1 in 10 screening X-rays).

Disclosures: Studies sponsored by Pfizer and Eli Lilly and Company.

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2. Berenbaum F., et al. Ann Rheum Dis. 2020. 79:800-10.
3. Hochberg M., et al. ACR/ARHP Annual Scientific Meeting. 2019. 71(s10):2243.
4. Hochberg M., et al. ACR/ARHP Annual Scientific Meeting. 2019. 71(S10):4888.
5. Roemer F., et al. Semin Arthritis Rheum. 2017. 47(3):323-30.

Disclosure: A. Guermazi, AstraZeneca, 1, Pfizer, 1, MerckSerono, 1, Galapagos, 1, Roche, 1, TissueGene, 1, Boston Imaging Core Lab, 1; **F. Roemer**, Boston Imaging Core Lab (BICL), LLC, 1, Calibr - California Institute for Biomedical Research, 1; **A. Kompel**, Boston Imaging Core Lab (BICL), LLC, 1; **L. Diaz**, None; **M. Crema**, Boston Imaging Core Lab, 1; **M. Brown**, Pfizer, 1, 3; **A. Hickman**, Pfizer Inc., 1, 3; **G. Pixton**, Pfizer Inc., 3, 4; **L. Viktrup**, Eli Lilly and Company, 1, 3; **R. Fountaine**, Pfizer Inc., 1, 3, 4; **A. Burr**, Pfizer Inc., 1, 2; **S. Sherlock**, Pfizer Inc., 1, 2; **C. West**, Pfizer Inc., 1, 3.

Abstract Number: 1645

Placebo Group Responses in Clinical Trials of Patients with Osteoarthritis: Data from the Tanezumab Development Program

Luana Colloca[1], Robert Dworkin[2], John Farrar[3], Leslie Tive[4], Ed Whalen[5], Jerry Yang[4], Lars Viktrup[6], Mark Brown[7], Christine West[7] and Kenneth Verburg[8], [1]University of Maryland, Baltimore, [2]University of Rochester School of Medicine and Dentistry, Rochester, NY, [3]University of Pennsylvania, Philadelphia, PA, [4]Pfizer Inc, New York, NY, [5]Pfizer Inc, New York, [6]Eli Lilly and Company, Indianapolis, IN, [7]Pfizer Inc, Groton, CT, [8]Pfizer Inc, Groton

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The level of placebo group response in clinical trials for chronic pain conditions is a concern for the development of novel analgesics[1]. Here, we investigate the placebo group responses over time in data from the clinical studies of tanezumab, a monoclonal antibody against nerve growth factor which is intended for the relief of signs and symptoms of moderate to severe osteoarthritis (OA) in adult patients for whom use of other analgesics is ineffective or not appropriate.

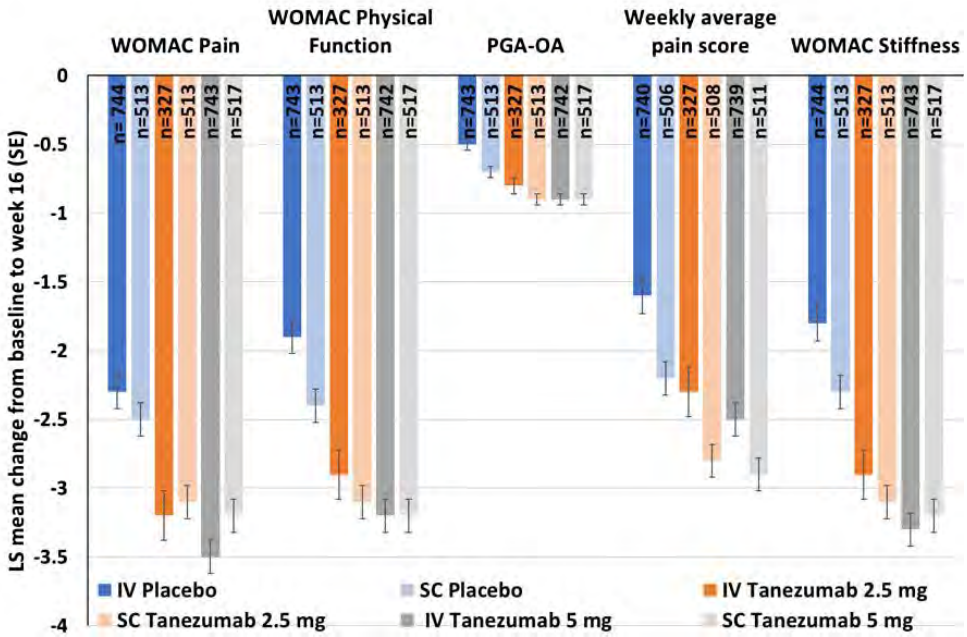
Methods: Tanezumab studies from 2008 to 2018 were included in these analyses. Those completed prior to 2015 utilized intravenous (IV) administration, while those conducted after 2015 used subcutaneous (SC) administration. We used data from IV and SC studies to create two cohorts to examine the change in placebo group responses over time. Data from 4 studies (NCT00733902, NCT00744471, NCT00830063 and NCT00863304), conducted between

Table 1. Treatment discontinuations: IV versus SC pooled data.

Patients n (%)	IV cohort (n=1814)			SC cohort (n=1545)		
	Placebo (n=744)	Tanezumab 2.5 mg (n=327)	Tanezumab 5 mg (n=743)	Placebo (n=514)	Tanezumab 2.5 mg (n=514)	Tanezumab 5 mg (n=517)
All reasons	329 (44.2)	87 (26.6)	180 (24.2)	84 (16.3)	49 (9.5)	53 (10.3)
Adverse event	25 (3.4)	9 (2.8)	25 (3.4)	12 (2.3)	8 (1.6)	7 (1.4)
Death	1 (0.1)	0	0	0	0	2 (0.4)
Lost to follow-up	1 (0.1)	0	7 (0.9)	3 (0.6)	3 (0.6)	3 (0.6)
Study terminated by sponsor	2 (0.3)	0	3(0.4)	0	0	0
Withdrawal by subject	45 (6.0)	10 (3.1)	32 (4.3)	22 (4.3)	19 (3.7)	20 (3.9)
Insufficient clinical response	241 (32.4)	58 (17.7)	98(13.2)	31 (6.0)	8 (1.6)	7 (1.4)
Protocol violation	8 (1.1)	9 (2.8)	9 (1.2)	4 (0.8)	4 (0.8)	1 (0.2)
Other	6 (0.8)	1 (0.3)	6 (0.8)	12 (2.3)	7 (1.4)	13 (2.5)

The incidences of withdrawal by reason were determined through completion of the treatment period of each study. IV, intravenous; SC, subcutaneous

Figure 1. Change from baseline to week 16 in efficacy endpoints: IV versus SC pooled data.



A change from baseline <0 represents an improvement in all outcomes. IV, intravenous; LS, least squares; PGA-OA, patient global assessment of osteoarthritis; SC, subcutaneous; SE, standard error; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index

2008–2010, were pooled to create the IV cohort (n=1814). The SC cohort (n=1545) comprised data from 2 studies, conducted between 2016–2018 (NCT02697773 and NCT02709486). Although there were some differences in the patient populations in the IV and SC cohorts, all studies enrolled patients with a diagnosis of OA in the hip or knee, baseline Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC) Pain subscale scores of ≥5 in the index joint and Patient Global Assessment of OA (PGA-OA) of "fair", "poor" or "very poor". A WOMAC Physical Function score ≥5 at baseline was also required, with the exception of IV studies NCT00830063 and NCT00863304, which

required a score ≥4. Treatments were administered every 8 weeks for 16 ([IV: NCT00830063 and NCT00863304] [SC: NCT02697773]) or 24 weeks [IV: NCT00733902 and NCT00744471] [SC: NCT02709486]).

Results: The percentage of patients who discontinued from the SC cohort for any reason and particularly for insufficient clinical response was lower, compared with the IV cohort (**Table 1**). The change from baseline to week 16 in the efficacy endpoints of WOMAC Pain, WOMAC Physical Function, PGA-OA, weekly average pain score and WOMAC Stiffness revealed consistently greater placebo group improvements in the SC cohort, compared with the IV cohort (**Figure 1**).

Conclusion: These data showed an increased placebo group response in patients receiving SC administration in a later time period (2016-2018), compared with IV administration in an earlier time period (2008-2010) across the tanezumab development program. Further analyses will be presented to examine the factors that account for these differences, for example, changes in the route of administration, temporal trends in the patients enrolling in the trials or in the study sites and differences in clinical trial design. These analyses may help advance drug development by identifying critical factors that may increase placebo group responses and thereby limit the assay sensitivity of clinical trials to identify truly efficacious pain treatments.

These studies were sponsored by Pfizer and Lilly. Medical writing support was provided by Steven Moore, PhD, of Engage Scientific Solutions and was funded by Pfizer and Lilly.

References

1. Tuttle et al., *Pain*; 2015; 156:2616-26.

Disclosure: L. Colloca, None; **R. Dworkin**, abide, 1, acadia, 1, Analgesic Solutions, 1, Asahi_kasei, 1, Biogen, 1, Centrexion, 1, Clexio, 1, Decibel, 1, Eli Lilly, 1, Glenmark, 1, Hope, 1, Lotus, 1, Mainstay, 1, Merck, 1, Neurana, 1, NeuroBo, 1, Novaremed, 1, Novartis, 1, Pfizer, 1, Regenacy, 1, Sanifit, 1, Scilex, 1, Semnur, 1, Sollis, 1, Vertex, 1, Vizuri, 1; **J. Farrar**, None; **L. Tive**, Pfizer Inc, 1, 3; **E. Whalen**, Pfizer Inc, 1, 3; **J. Yang**, Pfizer Inc, 1, 3; **L. Viktrup**, Eli Lilly and Company, 1, 3; **M. Brown**, Pfizer Inc, 1, 3; **C. West**, Pfizer Inc., 1, 3; **K. Verburg**, Pfizer Inc., 1, 2.

Abstract Number: 1646

Use of Prescription Nonsteroidal Anti-inflammatory Drugs (NSAIDs) in Adults with Hip/Knee Osteoarthritis (OA) at Increased Risk for NSAID-related Adverse Events

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: NSAIDs are commonly used for OA pain, but the benefits of pain relief must be carefully weighed against the potential risk for gastrointestinal (GI), cardiovascular (CV), and renal adverse events (AEs). In-

Table 1. Risk factors for NSAID-related AEs*			
Risk	**GI**	**CV**	**Renal**
High	History of complicated ulcer (perforation, obstruction, or GI bleeding), or ≥2 moderate risk factors	Stroke, heart failure, or ischemic heart disease (myocardial infarction, angina)	Chronic kidney disease, stage 4 or higher
Moderate	History of uncomplicated ulcer, dyspepsia/ gastroesophageal reflux disease; age ≥65 years; or concurrent use of anticoagulants, corticosteroids (oral/nasal), aspirin, selective serotonin reuptake inhibitors, or antiplatelet therapy	≥3 of the following: peripheral arterial disease, hypertension, hyperlipidemia, diabetes, or age ≥65 years	–
Low	No risk factors	No risk factors	–
*References: Bhatt DL, et al. *Circulation*. 2008;118:1894–1909; Lanza FL, et al. *Am J Gastroenterol*. 2009;104:728–738; NICE Clinical Knowledge Summaries. NSAIDs – prescribing issues (August 2019): https://www.evidence.nhs.uk/; Fogleman CD. *Am Fam Physician*. 2013;87:354–356; Chan FKL, et al. *Am J Gastroenterol*. 2008;103:2908–2918; US Food and Drug Administration. Medication Guide for Nonsteroidal Anti-inflammatory drugs (NSAIDs): https://www.fda.gov/media/72932/download; Laine L. *Gastroenterology*. 2014;147:730–733; Lanas A. *Rheumatology (Oxford)*. 2010;49(suppl 2):ii3–ii10; Koffeman AR et al. *Br J Gen Pract*. 2014;64:e191–e198; Kolasinski SL, et al. *Arthritis Care Res (Hoboken)*. 2020;72:149–162.			

Table 1. Risk factors for NSAID-related AEs*

Table 2. Clinical guideline recommendations on NSAID use by risk for NSAID-related AEs	
Baseline risk for NSAID-related AE (n; %*)	**Guideline recommendations†**
High GI risk and low CV risk (15,171; 6.9%)	Non-selective NSAIDs not recommended
High GI risk and moderate CV risk (10,455; 4.8%)	Non-selective NSAIDs not recommended
High GI risk and high CV risk, or high renal risk (7,640; 3.5%)	Any NSAID not recommended
Low-to-moderate GI risk and high CV risk (12,886; 5.9%)	COX-2 or non-selective NSAIDs (except naproxen [≤1,000 mg/day] or ibuprofen [≤1,200 mg/day]) not recommended
Low-to-moderate GI risk and moderate CV risk (28,364; 13.0%)	COX-2 or non-selective NSAIDs (except naproxen [≤1,000 mg/day] or ibuprofen [≤1,200 mg/day]) not recommended
Low-to-moderate GI risk and low CV risk (143,833; 65.9%)	No recommendation against NSAID use
*Based on the study population (N=218,349). †References: Bhatt DL, et al. *Circulation*. 2008;118:1894–1909; Lanza FL, et al. *Am J Gastroenterol*. 2009;104:728–738; NICE Clinical Knowledge Summaries. NSAIDs – prescribing issues (August 2019): https://www.evidence.nhs.uk/; Chan FKL, et al. *Am J Gastroenterol*. 2008;103:2908–2918.	

Table 2. Clinical guideline recommendations on NSAID use by risk for NSAID-related AEs

creased risk for these AEs changes the risk-benefit profile of certain NSAIDs such that they are not recommended by clinical treatment guidelines. However, information for real-world NSAID use despite these recommendations is lacking. This study aimed to evaluate the use of prescription NSAIDs among patients with hip/knee OA for whom specific NSAID treatment is not recommended per clinical treatment guidelines.

Methods: This retrospective cohort study used the IBM MarketScan® claim database (July 2016–June 2019). Adult patients with a diagnosis of hip/knee OA between July 2017 and June 2018 (index date) were identified. If more than one diagnosis was available, one was randomly selected as the index date. Patients were required to have 1 year of continuous enrollment before the index date (baseline period) to establish their baseline risks (high, moderate, or

Table 3. 1-year rate* of NSAID use that was inconsistent with clinical guideline recommendations	
Baseline risk profile	**NSAID use inconsistent with clinical guideline recommendations, % (95% CI)**
Overall†	49.1 (48.7–49.4)
High GI risk and low CV risk	63.8 (63.0–64.5)
High GI risk and moderate CV risk	58.8 (57.7–59.7)
High GI risk and high CV risk, or high renal risk	61.0 (59.9–62.1)
Low-to-moderate GI risk and high CV risk	51.8 (51.0–52.7)
Low-to-moderate GI risk and moderate CV risk	33.2 (32.7–33.8)
*Based on 1-year cumulative incidence from the Kaplan–Meier survival analysis. †Patients with low-to-moderate GI risk and low CV risk were excluded from this analysis because the guidelines did not recommend against use of NSAIDs in this population (table 2). CI, confidence interval.	

Table 3. 1-year rate* of NSAID use that was inconsistent with clinical guideline recommendations

low) for NSAID-related GI, CV, and renal AEs, respectively (table 1), and were categorized into 6 risk profiles based on clinical guidelines (table 2). Patients were followed post-index to assess specific prescription NSAID use that was not recommended per the patient's risk profile, and Kaplan–Meier survival analyses were used to estimate 1-year cumulative incidence rates.

Results: Among 218,349 adults with hip/knee OA (mean age ± standard deviation, 60.8 ± 11.1 years; 61.9% female; 74.4%/25.6% commercial/Medicare), 65.9% (n=143,833) had no evidence of increased risk. Therefore, for these patients, there was no guideline recommendation against NSAID use (table 2). Among the remaining patients (n=74,516; 34.1%), the 1-year rate of NSAID use that was not consistent with guideline recommendations was 49.1% overall and ranged from 33.2%–63.8% for the different risk profiles (table 3). The subgroup of patients at high risk of NSAID-related GI AEs and at low risk of NSAID-related CV AEs (6.9% of the study population) had the highest 1-year rate of NSAID use that was not consistent with guideline recommendation (63.8%; table 3).

Conclusion: This study showed that in the real-world setting, over one-third of patients with hip/knee OA were found to have risk factors that could increase their risk for NSAID-related AEs. Approximately half of these patients had evidence of prescription NSAID use that was inconsistent with guideline recommendations, suggesting the lack of reliable pain medications for OA patients. These results emphasize the need to consider the risks associated with NSAIDs and to individualize OA management strategies to mitigate the risk of NSAID-related AEs. This study was limited by the lack of information on the use of over-the-counter NSAIDs and drugs that would decrease the risk of NSAID-related AEs, as well as by the inability to distinguish between short-term and long-term prescription NSAID use.

Disclosure: J. Patel, Regeneron Pharmaceuticals, 2; **W. Wei**, Regeneron Pharmaceuticals, 1, 3; **R. Bannuru**, Regeneron Pharmaceuticals, 5; **R. Iyer**, Teva Pharmaceutical Industries, 1, 3; **N. Shaikh**, Regeneron Pharmaceuticals, 2; **T. LeMasters**, Regeneron Pharmaceuticals, 2; **C. Iloabuchi**, Regeneron Pharmaceuticals, 2; **D. Wang**, Regeneron Pharmaceuticals, 1, 3; **U. Sambamoorthi**, Regeneron Pharmaceuticals, 2.

Abstract Number: 1647

An Oleuropein-based Dietary Supplement Improves Joint Function in Older People with High Knee Joint Pain

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study was to investigate the effects of a 6-month intervention with an Olive Leaf Extract (OLE) standardized for oleuropein content on knee functionality and biomarkers of bone/cartilage metabolism and inflammation.

Methods: The study was a randomized, double-blind, placebo-controlled, multi-centric trial of 124 subjects with mild knee pain or mobility issues. Subjects were randomized equally to receive twice a day one capsule of either maltodextrin (control treatment, CT) or 125-mg OLE (Bonolive™, an Olive Leaf Extract containing 50 mg of Oleuropein) for 6 months. The co-primary endpoints were Knee injury and Osteoarthritis Outcome Score (KOOS) using a self-administered questionnaire and serum Coll2-1NO2 specific biomarker of cartilage degradation. The secondary endpoints were each of the five sub-scales of the KOOS questionnaire, Knee pain VAS score at rest and at walking, OARSI core set of performance-based tests and serum biomarkers (Coll2-1, MPO, CTX1, osteocalcin, PGE_2 and Vplex cytokines assay in serum) and concentration of Oleuropein's metabolites in urine.

Results: Primary (global KOOS score, biomarker Coll2-1 NO2) and secondary endpoints (the five subscales of the KOOS score) improved time dependently in both groups. OLE treatment showed significantly elevated urinary oleuropein metabolites (oleuropein aglycone, hydroxytyrosol, homovanillyl alcohol and isomer of homovanillyl alcohol), and was well tolerated without significant differences in number of subjects with adverse events. At 6 months, OLE group showed a higher global KOOS score compared to placebo (treatment difference = 3.73; 95% CI = [-4.08;11.54]; p = 0.34), without significant changes of inflammatory and cartilage remodeling biomarkers. Subgroup analyses demonstrated a large and significant treatment effect of OLE in subjects with high walking pain at baseline (14.4; 95% CI = [1.19;27.63], p=0.03). This was observed at 6 months for the global KOOS score and each different subscale and for pain at walking (-23.07;95% CI = [-41.8;-4.2];p=0.02). These treatment effects at 6 months were significant for KOOS score as well as for the subscales Pain and QoL and the pain at walking.

Conclusion: OLE was not effective on joint discomfort in people with low to moderate pain at baseline but significantly benefited subjects with high pain at treatment initiation. As oleuropein is well-tolerated, OLE can be used to relieve knee joint pain and enhance mobility in subjects with articular pain the most painful subjects.

Disclosure: M. Horcajada, Nestlé, 3; **M. Beaumont**, Nestlé, 3; **N. Sauvageot**, Nestlé, 3; **M. Saboundjian**, Nestlé, 3; **L. Poquet**, Nestle, 3; **A. Hick**, Artialis SA, 3; **B. Costes**, Artialis SA, 3; **Y. Henrotin**, Artialis SA, 1.

Abstract Number: 1648

Comparison of Methotrexate and Glucosamine in Primary Knee Osteoarthritis with Inflammation

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
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Background/Purpose: Many patients suffering from knee OA show swelling, warmth along with pain which are features of inflammation. There are no accepted pharmacological therapy for osteoarthritis that target inflammation though inflammation plays a crucial role in pain generation and progressive joint damage.

There are some evidence that Methotrexate may be useful in knee osteoarthritis. The latest ACR recommendation for OA is not in favour of MTX, but it seems they have more weight to the evidence in case of hand OA than knee OA. ACR recommendation found no evidence of usefulness of glucosamine also, another very commonly used drug for knee OA.

We decided to evaluate the effect of methotrexate in primary knee OA with inflammation in comparison with glucosamine as placebo.

Methods: Primary knee OA of both sex, aged 40-65 years, having swelling and pain of both knee joints for at least six months with radiographic OA and consent to study were recruited. Exclusion criteria consisted of KL grade 4, secondary OA, arthroscopy or intra articular injections in last three months, uncontrolled Diabetes, renal, hepatic diseases or gout.

Patients with signs of local inflammation i.e. pain swelling of whole knee and warmth were checked for ESR and CRP.

If there was increase in both in one occasion or either of them in two occasions 1 month apart (ESR >30mm/1st Hr and CRP >1.5 times of reference), they were placed in systemic Inflammatory group.

Others were placed in non-inflammatory group.

Blood was collected from all patients and healthy controls for testing of selected biomarkers.

Patients in the inflammatory group were stringently screened for Inflammatory arthritis by clinical examination, blood tests, Musculoskeletal ultrasound, X-ray..

MRI of knee was done in all patients of Inflammatory group.

Then, patients of inflammatory group were randomly allocated to receive Methotrexate (15-20 mg/week) or Glucosamine (placebo) and followed monthly for three months.

All patients were allowed to take paracetamol and tramadol on as needed basis. NSAIDs were given in the beginning for 7-10 days to improve compliance.

WOMAC (CRD Pune version) was measured at beginning and end of three months.

Results: Total 344 primary knee OA patients who fulfilled the inclusion and exclusion criteria, were examined from July 2016 to June 2019 in Department of Rheumatology, IPGME&R and SSKM Hospital, Kolkata.

249 patients had local inflammation (swelling of both knees). 172 patients of them had elevated ESR/CRP, both in one occasion or either of them in two occasions 1 month apart.

Table 1: Demography

	Non inflammatory group (N=77)	Inflammatory group (N=172)
Age	51.85±7.027	51.56±7.030
Sex	32:56	11:104
CRP	Normal	Raised
ESR	17.43±6.142	44.46±16.398
WOMAC	45.20±15.472	49.356±15.037

Demography

Parameter	Patient number	Pre-MTX	Post-MTX	P value
ESR	78	44±19	35±16	0.0007
CRP	78	Reactive	non-reactive	
WOMAC	78	52±14	38±17	P<0.0001

Patients suffering from primary knee OA with inflammation receiving MTX

Parameter	Patient number	Pre glucosamine	Post-glucosamine	P value
ESR	59	39±13	43±19	0.2947
CRP	59	Reactive	reactive	
WOMAC	59	47±16	43±19	0.1877

Patients suffering from primary knee OA with inflammation receiving Glucosamine

Table 2: Patients suffering from primary knee OA with inflammation receiving MTX

Table 3: Patients suffering from primary knee OA with inflammation receiving Glucosamine

Conclusion: We found significant improvement in WOMAC, ESR and CRP in patients suffering from primary knee OA with inflammation after three months of taking methotrexate while there was insignificant effect with glucosamine, used as placebo. Our study provides proof that oral Methotrexate may be an important intervention in primary knee osteoarthritis with inflammation.

Disclosure: B. Ghosh, None; **S. Haldar**, None; **M. Saha**, None.

Abstract Number: 1649

Effect of Knee Aspiration and Intra-articular Corticosteroid Injection on Gait Biomechanics and Strength Impairment in Patients with Signs of Inflammation Due to Knee Osteoarthritis

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SESSION INFORMATION
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Session Title: Osteoarthritis – Clinical Poster II
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Background/Purpose: Synovial inflammation in knees with OA can be measured with musculoskeletal ultrasound (MSK US), is associated with increased pain and disease progression, and may adversely affect joint biomechanics. Knee effusion has been associated with quadriceps avoidance gait (decreased external knee flexion moment (KFM) during walking, altered quadriceps and hamstring activation) in patients with knee OA, however, the effect of treating knee inflammation on gait biomechanics and strength is unknown. The purposes of this study were to: 1) investigate the effects of treating knee inflammation on gait biomechanics, strength and patient-reported outcomes in patients with knee OA and inflammation, and 2) explore the associations between these measures.

Methods: 72 knees from 51 patients with knee OA and signs of moderate synovitis and effusion on MSK US underwent bilateral gait biomechanics, strength and US assessments, and completed knee-specific numeric rating scales (NRS) for pain and Knee Injury and Osteoarthritis Outcome Scores (KOOS) before and 3 weeks after receiving an US-guided knee aspiration and injection of 40 mg triamcinolone acetonide. Three-dimensional quantitative gait analysis was completed using a 12-camera motion capture system and floor-mounted force plate to calculate knee angles and moments, with the peak external KFM as the primary outcome. Knee extension and flexion strength (peak torque in Nm) was tested using an isokinetic dynamometer (90°/s). US assessments were performed using a linear 3-12 MHz probe. The suprapatellar recess was scanned in the long axis view (medial, lateral, midline) with the knee flexed to 20°. All US exams were graded using the OMERACT system for inflammatory features of knee OA. Paired T-tests were used to determine mean changes and 95% confidence intervals from pre to 3 weeks post injection for all measures. Mixed effects regression with robust sandwich estimators was then used to evaluate the associations between potential predictors and peak KFM during walking. Random intercepts and slopes were specified by patient ID, time and limb. Potential predictors included US regional score (0-9), effusion depth (mm), gait speed (m/s), NRS (0-10), and quadriceps strength (Nm). Only knees undergoing aspiration and injection were evaluated.

Results: Baseline demographic and clinical characteristics are presented in Table 1. US regional score, effusion depth and NRS pain decreased post injection (Table 2). The peak KFM during walking, quadriceps and hamstring

Characteristic	
Sex (M / F)	17 / 34
Age (± SD)	63.3 (10.16)
BMI, kg/m^2 (± SD)	28.78 (6.52)
Knee KL Grade	
0	9
1	20
2	19
3	20
4	4
Knee US Regional Score	
0-3	38
4-6	33
7-9	1
Maximum Effusion Depth, mm (± SD)	5.71 (2.50)

Table 1. Demographic and clinical characteristics (n=51 patients, 72 knees)

Variable	Post-Injection (±SD)	Pre-Injection (±SD)	Mean Difference (95% CI)	p-value
Ultrasound Regional Score	**4.63 (2.72)**	**5.56 (2.12)**	**-0.93 (-1.41-0.45)**	**<0.01**
Effusion Depth (mm)	**4.68 (3.13)**	**5.71 (2.50)**	**-1.03 (-1.69, -0.37)**	**<0.01**
Speed (m/s)	**1.07 (0.22)**	**0.97 (0.24)**	**0.10 (0.03, 0.18)**	**<0.01**
Peak Knee Angle (degrees) During Walking				
Varus	-2.64 (5.26)	-0.69 (12.30)	-1.95 (-4.41, 0.52)	0.12
Flexion	15.61 (6.63)	15.21 (5.81)	0.40 (-0.97, 1.77)	0.56
Extension	3.73 (6.19)	4.64 (6.03)	-0.91 (-2.34, 0.52)	0.21
Internal Rotation	-4.74 (12.24)	-4.41 (14.70)	-0.33 (-3.15, 2.49)	0.82
External Rotation	-13.54 (11.49)	-12.86 (13.03)	-0.68 (-3.55, 2.20)	0.64
Peak Knee Moment (%BW*ht) During Walking				
First Peak Adduction	2.43 (1.09)	2.44 (0.98)	-0.01 (-0.13, 0.13)	0.92
Second Peak Adduction	2.28 (1.09)	2.27 (1.04)	0.01 (-0.16, 0.18)	0.91
Flexion	**1.40 (1.05)**	**1.10 (1.13)**	**0.30 (0.13, 0.49)**	**<0.01**
Extension	-2.44 (1.16)	-2.30 (1.06)	-0.14 (-0.36, 0.08)	0.20
Internal Rotation	-0.91 (0.38)	-0.91 (0.34)	0.00 (-0.05, 0.05)	0.10
External Rotation	0.03 (0.06)	0.02 (0.05)	0.01 (-0.00, 0.02)	0.15
Strength (Peak Torque Nm)				
Quadriceps	**84.43 (33.70)**	**80.08 (32.99)**	**4.35 (0.30, 8.41)**	**0.04**
Hamstring	**41.01 (18.85)**	**37.13 (17.80)**	**3.88 (1.37, 6.39)**	**<0.01**
KOOS Scores (/100)				
KOOS Symptoms	**64.17 (19.95)**	**58.86 (21.80)**	**4.90 (1.40, 8.40)**	**<0.01**
KOOS Pain	**64.79 (21.10)**	**58.92 (21.89)**	**5.87 (1.91, 9.83)**	**<0.01**
KOOS Daily Living	**35.12 (38.02)**	**30.15 (36.12)**	**4.97 (1.51, 8.45)**	**<0.01**
KOOS Quality of Life	50.58 (21.99)	46.99 (23.84)	3.33 (-0.79, 7.47)	0.11
KOOS Sport	43.31 (31.18)	41.37 (26.82)	1.94 (-5.80, 9.69)	0.62
NRS Pain	**2.26 (2.39)**	**3.35 (2.88)**	**-1.09 (-1.72, -0.44)**	**<0.01**

Table 2. Descriptive statistics for outcome measures pre and 3 weeks post injection.

Variable	Unstandardized β coefficient	Robust Standard Errors	95% Confidence Intervals	p-value	Variance	Robust Standard Errors of Variance
US Regional	0.04	0.05	-0.05, 0.14	0.40	-	-
Effusion	-0.03	0.03	-0.09, 0.03	0.36	-	-
Gait speed (m/s)	**1.40**	**0.40**	**0.62, 2.18**	**<0.01**	-	-
Quads strength (Nm)	0.00	0.00	-0.01, 0.01	0.92	-	-
NRS Pain	**-0.06**	**0.02**	**-0.11, -0.02**	**<0.01**	-	-
Time	0.07	0.13	-0.19, 0.34	0.59	-	-
Intercept	0.03	0.47	-0.90, 0.95	0.95	0.54	0.21

Table 3. Linear mixed effects model estimates

strength and KOOS subscales (symptoms, pain, daily living) increased post injection (Table 2). While controlling for time and limb, increases in gait speed and reductions in NRS pain were associated with greater peak KFM (Table 3).

Conclusion: Aspiration and corticosteroid injection improves signs of inflammation on MSK US, gait biomechanics associated with quadriceps avoidance gait, strength, and patient-reported measures of pain and function in patients

with knee OA. Greater gait speed and lesser knee pain were associated with less quadriceps avoidance gait. This suggests that local knee inflammation may contribute to abnormal gait biomechanics, however, further research is needed to understand the mechanism.

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Abstract Number: 1650

A Double-Blind Randomized Trial to Evaluate the Efficacy of Corticosteroid Injections for Osteoarthritis of the Knee Using Mobile Devices

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The value of intra-articular (IA) corticosteroid injections for osteoarthritis of the knee (KOA) has recently been called into question. Variability in clinical trial design has resulted in inconsistent results from clinical studies evaluating efficacy of this commonly performed procedure. We designed a pilot and feasibility double-blind trial to evaluate the benefit of IA corticosteroid injections with monitoring of response using mobile devices at 2-week intervals.

Methods: Participants with KOA, ages 40-80, who were either receiving or found to be a candidate for ia corticosteroid injection by their physician were eligible for enrollment. Participants received a Fitbit™ activity monitor and were signed up to an online platform (*Way To Health*). Participants were randomized after a 2-4 week run-in period to assess baseline physical activity. Participant could receive 40 mg methylprednisolone acetate plus 2 mL 1% lidocaine or 2 mL 1% lidocaine only in each affected knee. Participants were also randomized in a factorial design to receive social incentives to promote exercise (not shown here). Participants and study staff were blinded to treatment allocation and the research pharmacist prepared an opacified syringe to the physician at the time of the injection. Text messages were sent at 2-week intervals to remind participants to complete the Knee Injury and Osteoarthritis Outcome Score (KOOS). The Minimal Clinically Important Difference (MCID) for KOOS subscales ranges between 16 and 18. The primary outcome was the change in total KOOS from baseline. We compared change in KOOS across treatment groups incorporating all outcome measures over 12 weeks (2, 4, 6, 8, 10, and 12 weeks) using linear regression with generalized estimating equations. Sensitivity analyses were performed utilizing a last-observation-carried-forward (LOCF) approach.

Results: At the time of this interim analysis, 27 out of 32 planned participants (24 male) were randomized (Figure 1). Baseline characteristics are shown in Table 1. A total of 18 had completed all 12 weeks of follow-up. Participants that

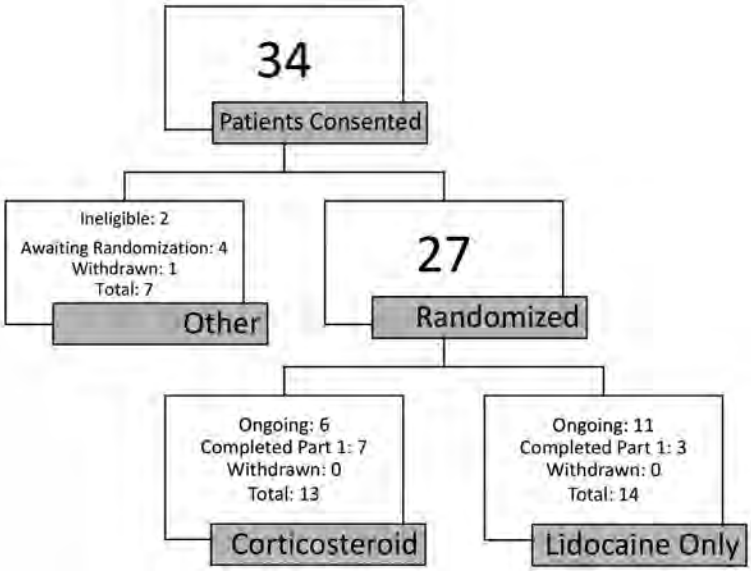

Figure 1. Consort Diagram. Corticosteroid Lidocaine Only N 13 14 Age 58.4 (2.0) 63.1 (2.1) Female, N (%) 2 (15%) 1 (7%) Black 9 (69%) 11 (79%) BMI 35.5 (1.8) 31.8 (1.5) Current Smoker 2 (15%) 2 (14%) K-L grade 3 (2, 4) 4 (3, 4) Baseline KOOS 38.8 (17.2) 44.0 (14.4) Prior Injections 13 (100%) 14 (100%)

received corticosteroids had significantly greater improvement in overall KOOS score [B: 10.2 (2.7, 17.7) p=0.007]. This pattern was observed for all KOOS sub-scales (Figure 2), and was most prominent between weeks 4 and 10 weeks of follow-up. Three adverse events were reported during the trial; none were considered related to the intervention. The effect was robust with imputation of missing values in sensitivity analyses using LOCF [B: 10.2 (2.8, 17.6) p=0.007]. In addition, among the 18 participants that had completed follow-up, the difference was significant at 12-weeks [B: 14.4 (0.58, 28.1) p=0.007]. The number needed to treat to achieve an improvement in pain at least as much as the MCID was 3.

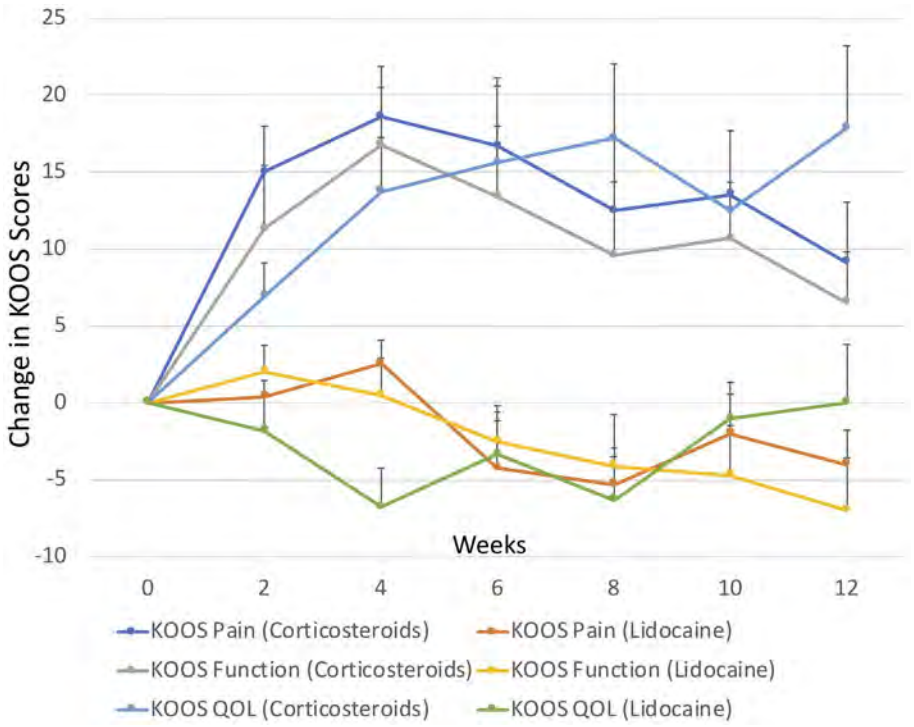

Figure 2. Mean change from baseline (SE) in KOOS scores (pain, function, and quality of life) over 12 weeks of follow-up by treatment arm.

	Corticosteroid	Lidocaine Only
N	13	14
Age	58.4 (2.0)	63.1 (2.1)
Female, N (%)	2 (15%)	1 (7%)
Black	9 (69%)	11 (79%)
BMI	35.5 (1.8)	31.8 (1.5)
Current Smoker	2 (15%)	2 (14%)
K-L grade	3 (2, 4)	4 (3, 4)
Baseline KOOS	38.8 (17.2)	44.0 (14.4)
Prior Injections	13 (100%)	14 (100%)
Exercise Incentive	6 (46%)	7 (50%)

Table 1. Patient characteristics at enrollment among participants receiving corticosteroids + lidocaine v. lidocaine only.

Conclusion: In this pilot double-blinded randomized trial, there was a significant benefit of ia corticosteroid injections compared to lidocaine. The intervention was beneficial in terms of pain, function, and quality of life and was clinically-important in magnitude, though the effects start to diminish by week 12. This study suggests that trials evaluating benefits of IA corticosteroid should consider the importance of short-term benefits.

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Abstract Number: 1651

Efficacy and Safety of Multiple Intra-articular Corticosteroid Injections for Osteoarthritis – a Systematic Review and Meta-analysis of Randomised Controlled Trials and Observational Studies

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Osteoarthritis (OA) is the most common form of arthritis worldwide and is becoming more prevalent with the increasing age of the population. As Intra-articular Corticosteroids (IACS) in clinical practice are often given serially to improve patient symptoms, we undertook this systemic review to summarise literature for the two key clinically relevant questions- are multiple IACS injections effective for OA and are they safe?

Table 1 Characteristics of studies with efficacy data of multiple IACS

Author Year	Joint	Intervention					Comparator					Time points measured (weeks)
		Number patients	Name	Dose	Number of injections	Interval	Number patients	Name	Dose	Number injections	Interval	
Hyaluronic acid as comparator												
Bisicchia 2016	Knee	75	6-methyl-prednisolone acetate	40mg	2	Day 0 and week 1	75	Hyaluronic acid	Not stated	2	Day 0 and week 1	0, 6, 12, 26, 52
Bjornland 2007	TMJ	20	Betametasone sodium phosphate	Not stated	2	Day 0 and week 1	20	Hylan G-F20	0.7-1ml	2	Day 0 and week 1	0, 2, 4, 26
Davalillo 2015	Knee	91	Betametasonedipropionate 5mg+ Betametasone sodium phosphate 2mg	5mg +2mg	2	Day 0 and week 4	89	Hyaluronic acid 1%	Not stated	5	Day 0 and weekly thereafter	0, 13, 26, 39, 52
Monfort 2014	1st CMC	40	Betametasone disodium phosphate + Betametasone acetate	1.5mg + 1.5mg	3	Day 0, week 1, and week 2	48	Hyaluronic acid	5mg	3	Day 0, week 1 and week 2	0, 1, 2, 4, 12, 24
Normal saline as comparator												
McAlindon 2017	Knee	70	Triamcinolone	40mg	8	Day 0 and then every 12 weeks	70	0.9 % Normal saline	1ml	8	Day 0 and then every 12 weeks	0, 13, 26, 39, 52, 65, 78, 91, 104
Raynauld 2002	Knee	34	Triamcinolone acetonide	40mg	8	Day 0 and then every 12 weeks	34	0.9% Normal saline	1ml	8	Day 0 and then every 12 weeks	0, 13, 26, 39, 52, 65, 78, 91, 104

TMJ temporomandibular joint; CMC carpometacarpal joint

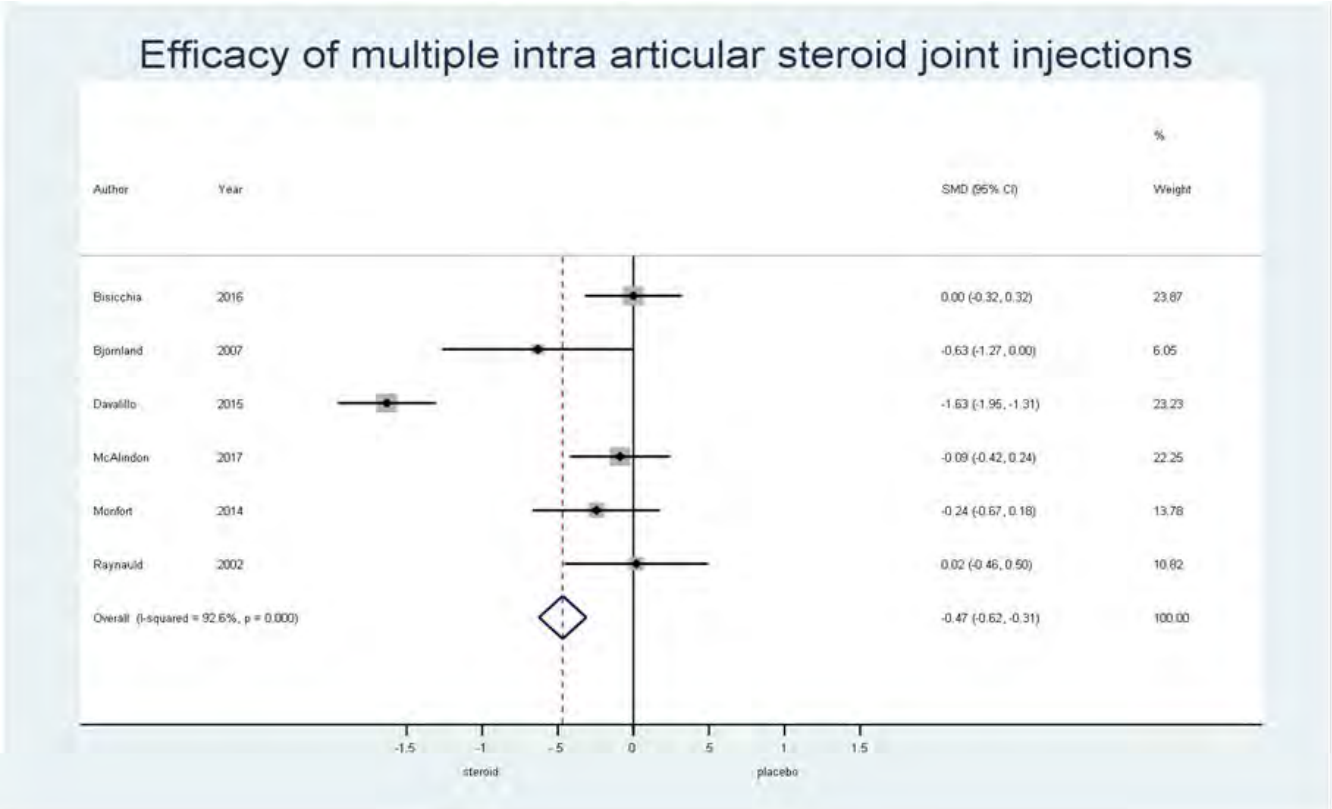


Figure 1. Forest plot of effects size for pain relief

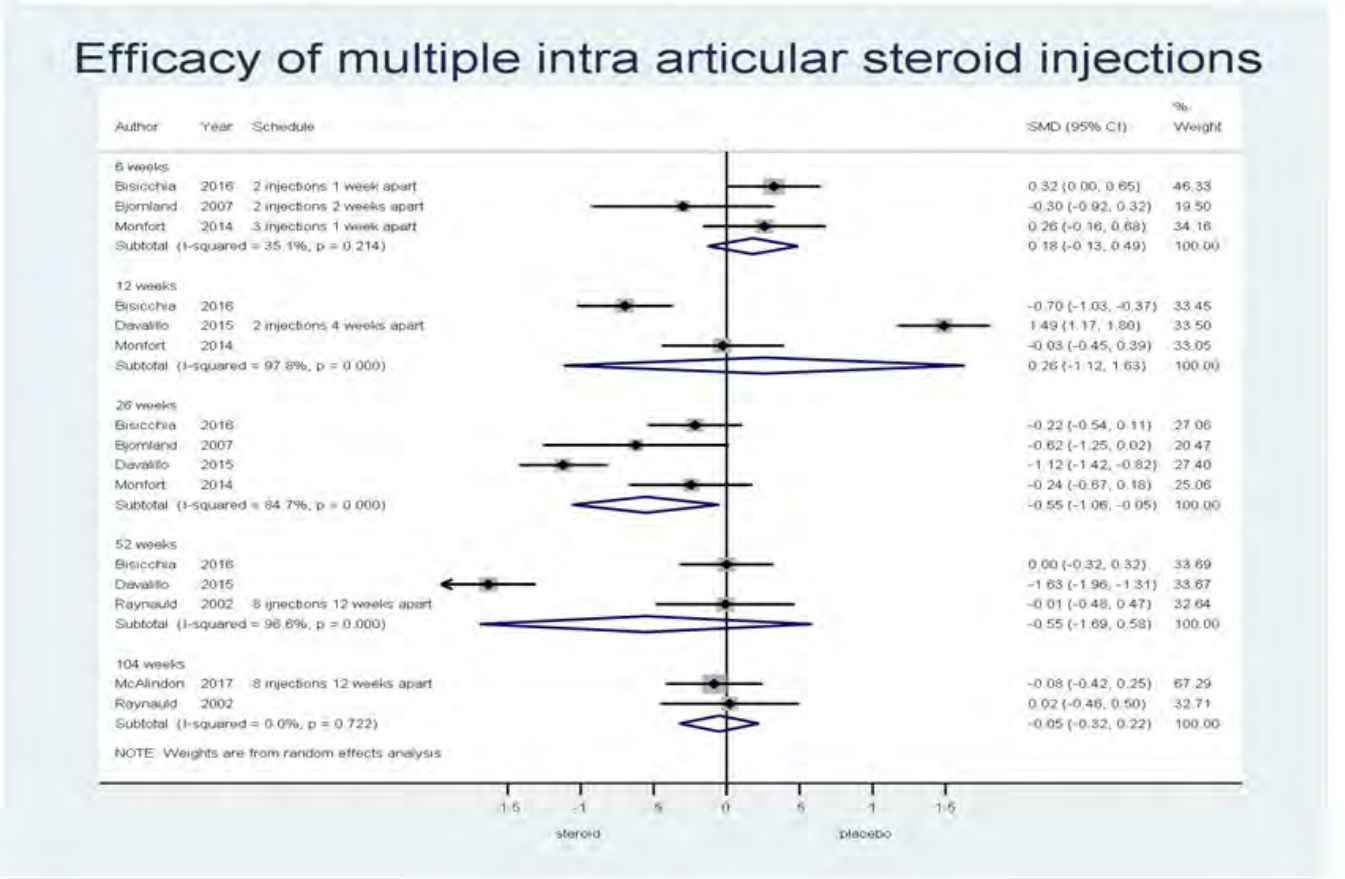


Figure 2. Forest plot of subgroup analysis of pain scores according to varying time points

Methods: Systematic literature searches was performed in January 2019 using the databases MEDLINE, EMBASE, AMED, Web of Science, PubMed, Cochrane Library, and Google Scholar. Relevant references were also explored. A structured search strategy was used for both efficacy and safety. Data extracted included study design characteristics, participant details, characteristics of IACS (including dosage, frequency and duration of treatment), comparator used and outcomes examined. Any discrepancies were resolved through discussion of papers by the reviewers.

Results: Six RCTs were included for efficacy assessment (Table 1). The use of multiple IACS appeared to be better than comparator (SMD for pain -0.47, 95% CI -0.62, -0.31). An I^2 statistic of 92.6% indicates a great deal of heterogeneity (figure 1). However one study stood out strongly in favour of IACS (SMD -1.63, 95% CI -1.95, -1.31). With a weighting of 23% this was further excluded as an outlier of results. This resulted in the overall change in VAS between IACS and comparator being not statistically different (SMD -0.12, 95% CI -0.29, 0.06), with improved heterogeneity (I^2 0.00%, p value 0.444).

Subgroup analysis by comparator showed no separation of regular IACS from placebo, though timing of pain assessments was questionable. Figure 2 shows the subgroup analysis according to varying time points at 6, 12, 26, 52 and 106 weeks. Apart from pain reduction on 26 months (SMD -0.55, 95%CI -1.06 to -0.05), no difference was observed between IACS and comparator.

Fourteen RCTs and two observational studies were assessed for the safety of multiple IACS. Minor local adverse events were similar in both groups. One RCT found that regular IACS every 3 months for 2 years caused greater cartilage loss compared to saline injection (-0.21mm vs 0.10mm). One cohort study found that multiple IACS injections

associated with worsening of joint space narrowing (HR 3.02, 95% CI 2.25-4.05) and increased risk of total joint replacement (HR 2.54, 95% CI 1.81- 3.57).

Conclusion: This systematic review included RCTs of regularly repeated IACS injections, using different steroid regimes and different joint sites, and with infrequent pain assessment predominantly undertaken just prior to each injection. This makes it difficult to come to any firm conclusion about the efficacy of multiple IACS injection however it would appear that multiple IACS injections overall are no better than placebo for OA pain. The preliminary finding of a detrimental effect on structural OA progression warrants further investigation. Efficacy and safety of multiple IACS reflecting recommended best practice has yet to be assessed.

Disclosure: S. Ayub, None; **J. Kaur**, None; **M. Hui**, None; **M. Hall**, None; **M. Doherty**, None; **W. Zhang**, None.

Abstract Number: 1652

Progression of Knee OA with Use of Intra-articular Corticosteroids (CS) vs Hyaluronic Acid (HA)

Justin Bucci[1], Xiaoyang Chen[1], James Torner[2], Michael Nevitt[3], Cora Lewis[4] and David Felson[5], [1]Boston University, Boston, MA, [2]University of Iowa, Iowa City, IA, [3]University of California, San Francisco, Orinda, CA, [4]University of Alabama Birmingham, Birmingham, AL, [5]Boston University School of Medicine, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent studies have questioned whether CS injections (CSI), a popular treatment recommended by guidelines, hasten progression of knee OA. A recent cohort study suggested a three-fold higher risk for knee OA progression with CSI.

Table 1. Pre-injection Clinical and Radiographic Status

Variable	Single Reported CSI (n=523)	Single Reported HAI (n=126)	>1 Reported CSI (n=124)	>1 Reported HAI (n=19)
Age in years (mean)	66.8	65.7	66.5	65.7
% Women	69.4%	49.2%	66.1%	63.2%
BMI in kg/m2 (mean)	30.3	30.7	29.8	31.8
XJRS (mean) (0-3)	1.00	1.36	1.04	1.42
KL (mean) (0-4)	1.85	2.07	1.91	2.32

Table 1

Table 2. Annualized Difference in Rate of Radiographic Progression Between CSI and HAI*

Comparison	JSN (Δ grade/year)	KL (Δ grade/year)	JSW250 (OAI) (Δ mm/year)
Single Reported HAI vs CSI	0.023 (95% CI:-0.056-0.10, p=0.57)	0.047 (95% CI:-0.041-0.13, p=0.30)	-0.018 (95% CI:-0.16-0.12, p=0.80)
>1 Reported HAI vs CSI	-0.060 (95% CI: -0.20-0.071, p=0.35)	-0.061 (95% CI: -0.23-0.11, p=0.48)	0.033 (95% CI: -0.26-0.33, p=0.82)

*Reported in comparison to CSI, positive values reflect lower rates of progression for CSI and negative values higher rates for CSI. Analyses adjusted for age, sex, BMI, study of origin and baseline KL grade.

Table 2

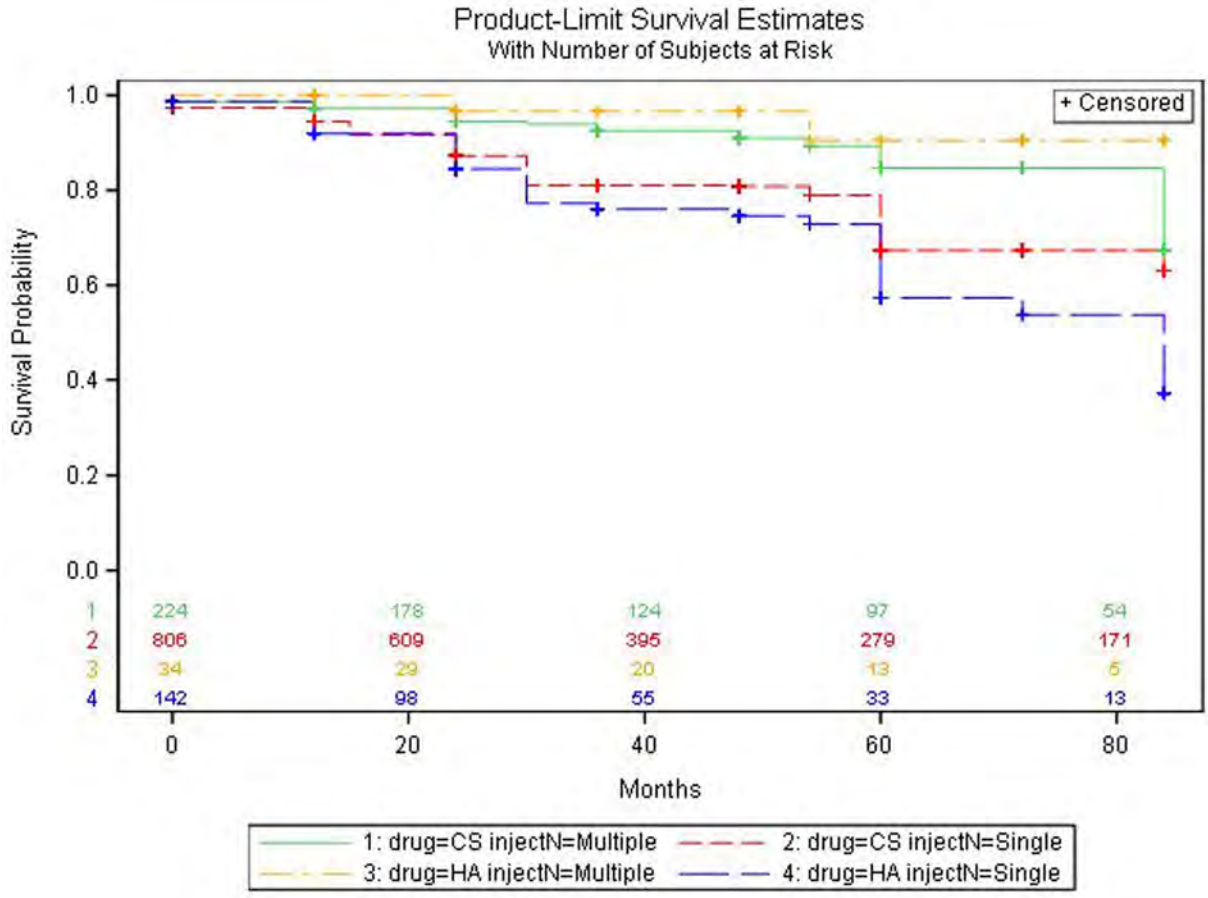


Figure 1

A limitation of such studies is CSI recipients have more advanced knee OA, which is itself a risk factor for OA progression, making it impossible, despite statistical adjustments, to compare those undergoing CSI to those who do not report injections. Patients receiving HA injections (HAI) are a natural comparator to those receiving CSI, as HAI has not been associated with cartilage loss. The purpose of this study was to assess whether CSI was associated with increased rates on knee OA progression in comparison to HAI.

Methods: We used 2 cohort studies of knee OA, MOST and OAI, to look at rates of x-ray progression and total knee replacement (TKR) among CSI or HAI recipients. OAI and MOST visits were performed every 12 and 30 months, respectively, and included knee x-rays and questions about HAI or CSI in the preceding 6 months. The studies use similar acquisition and reading protocols. Kellgren and Lawrence grades (KL) (0-4), joint space narrowing (JSN) (0-3) were scored for both studies and in OAI, medial joint space (JWS250) was measured.

For analysis of x-ray progression, we excluded knees with baseline KL 4, CSI or HAI reported at first visit, and recipients of HAI and CSI. We compared x-rays from the visit before first reported injection to x-rays at the visit after the last injection. TKR without post-injection x-ray was assigned KL grade 4 and JSN 3 at visit at which TKR was first present. Annualized deterioration rates were calculated for KL, JSN and JWS250. Using multivariable linear regression, we examined deterioration rates for reports of injections at single and multiple exams adjusting for age, sex, BMI, study, and baseline KL grade. For TKR survival analysis, we added subjects who reported injections at baseline visits. TKR events were censored after 7 years from first reported injection.

Results: 792 knees were analyzed, of which 647 reported CSI use and 145 reported HAI use. 124 reported CSI and 19 reported HAI at >1 visit. For additional characteristics, see table 1.

Unadjusted analysis for time to TKR is shown in figure 1. The rate of TKR was greater among those with single exam reports of HAI than of CSI (p=.04) but not different for those reporting at multiple exams, although numbers were small. Multivariable analysis showed similar rates of radiographic progression between CSI and HAI among subjects reporting injections at single or multiple exams (table 2).

Conclusion: CSI for knee OA was not associated with higher rate of radiographic progression or progression to TKR than HAI. The risk of disease progression attributed to CSI in earlier studies may reflect the presence of more severe OA in those undergoing injections.

Disclosure: J. Bucci, None; **X. Chen**, None; **J. Torner**, None; **M. Nevitt**, None; **C. Lewis**, None; **D. Felson**, None.

Abstract Number: 1653

Bilateral vs Unilateral Total Knee Arthroplasty: Racial Variation in Utilization and In-Hospital Major Complication Rates

Bella Mehta[1], Kaylee Ho[2], Jennifer Bido[3], Stavros Memtsoudis[3], Michael Parks[4], Susan Goodman[1], Linda Russell[5] and Said Ibrahim[6], [1]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [2]Weill Cornell Medicine, New York, [3]Hospital for Special Surgery, New York, [4]Hospital for Special Surgery, Weill Cornell Medicine, New York, [5]Hospital for Special Surgery/Weill Cornell Medicine, New York, NY, [6]Weill Cornell Medicine, Cleveland, OH

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Compared to White Patients, African Americans (AAs) are reported to have lower utilization and higher complication rates outcomes in Unilateral Total knee arthroplasty (UTKA). It is unclear whether racial variations exist for Bilateral TKA (BTKA)

Variable	Unilateral TKA N = 5,528,429 (Unweighted N = 1,131,329)	Bilateral TKA N = 276,194 (Unweighted N = 56,675)	P[a]
Patient Characteristics			
Age, mean (SE)	67.4 (0.02)	65.0 (0.06)	<.0001
Sex: Female, n(%)	3,429,484 (62.1)	154,442 (55.9)	<.0001
Race, n(%):			
White	4,051,648 (50.9)	212,468 (76.9)	<.0001
African American	352,933 (6.4)	14,441 (5.2)	
Other	464,407 (8.4)	16,443 (6.0)	
Missing	659,439 (11.9)	32,842 (11.9)	
Insurance, n(%):			<.0001
Medicaid/Medicare	3,334,412 (60.3)	132,400 (47.9)	
Private	1,987,693 (36.0)	135,046 (48.9)	
Other	196,313 (3.6)	7935 (2.9)	
Missing	10,011 (0.2)	814 (0.3)	
Median Household Income, n(%):			<.0001
0-25th percentile	1,195,291 (22.0)	54,786 (20.2)	
26th to 50th percentile (median)	1,457,458 (26.8)	70,589 (26.0)	
51st to 75th percentile	1,453,058 (26.7)	72,734 (26.8)	
76th to 100th percentile	1,329,802 (24.5)	73,386 (27.0)	
Morbid Obesity, n(%)	401,892 (7.3)	20,411 (7.4)	0.47
Elixhauser Index[d], n(%):			<.0001
0	716,559 (13.0)	41,550 (15.0)	
1-4	4,484,941 (81.1)	220,638 (80.0)	
≥ 5	326,928 (5.9)	14,007 (5.1)	
Hospital Characteristics			
Hospital Region, n(%):			<.0001
Northeast	917,803 (16.6)	66,665 (24.1)	
Midwest	1,506,373 (27.2)	76,960 (27.9)	
South	2,014,531 (36.4)	93,533 (33.9)	
West	1,089,721 (19.7)	39,037 (14.1)	
Hospital Bedsize, n(%):			0.13
Small	1,194,134 (21.7)	54,440 (19.8)	
Medium	1,483,188 (26.9)	75,706 (27.5)	
Large	2,834,371 (51.4)	144,900 (53.0)	
Hospital Volume (cases per year), n(%):			<.0001
<100	2,045,350 (37.0)	86,630 (31.4)	
100-200	1,267,000 (22.9)	60,708 (22.0)	
>200	2,216,078 (40.1)	128,856 (46.7)	
Hospital Location/Teaching status, n(%):			<.0001
Rural	626,057 (11.4)	38,329 (13.9)	
Urban nonteaching	2,312,373 (42.0)	101,667 (37.0)	
Urban teaching	2,573,263 (46.7)	135,051 (49.1)	

Note:

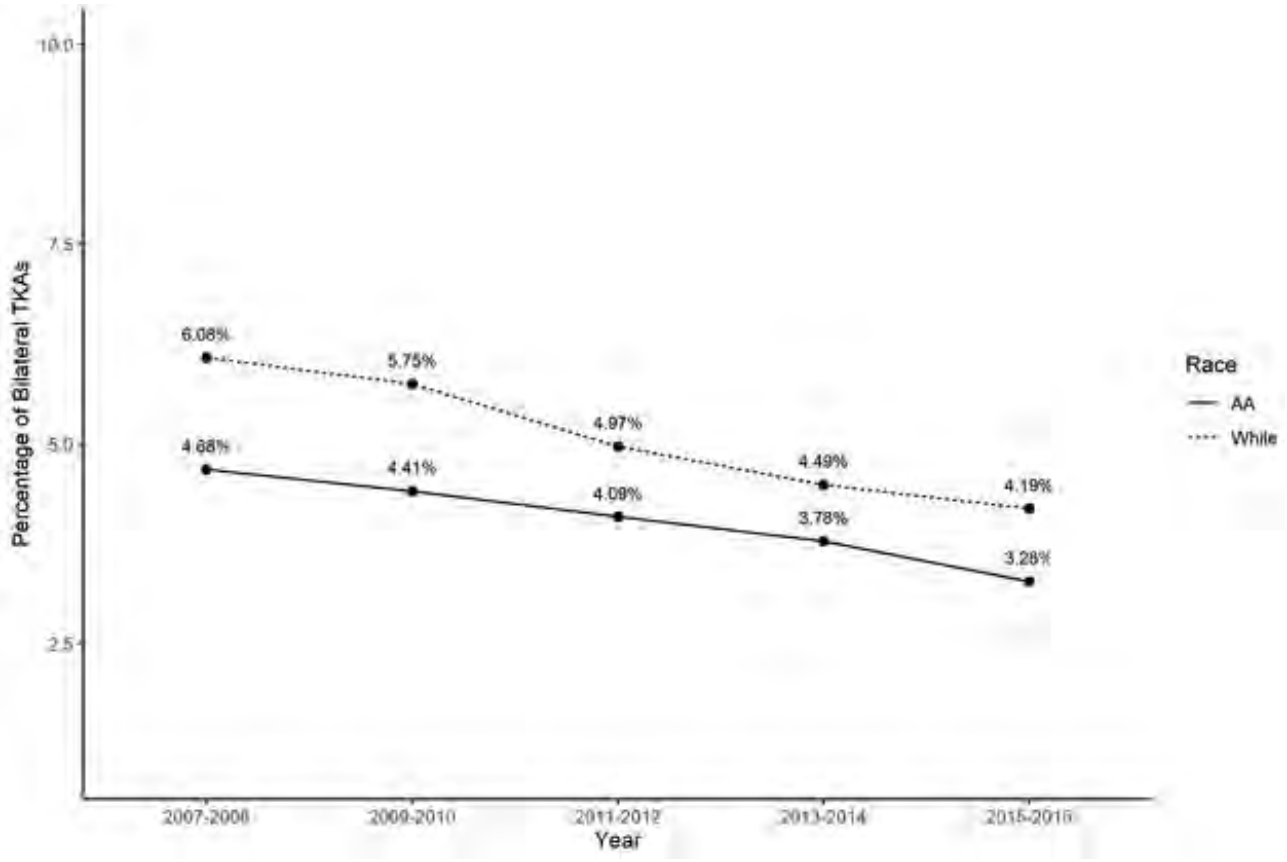
All values were estimated using sampling weights and hospital clusters.

[a]P-values are calculated based on the Rao-Scott chi-square test for all categorical variables and 2-sample independent t-test for continuous variables. Significance levels: * = p<0.05, ** = p<0.01, *** = p<0.001.

[b]Clinical comorbidities were identified based on coding algorithms developed by Quan and colleagues (enhanced Elixhauser version), using either ICD-9-CM or ICD-10 codes, as appropriate. The Elixhauser co-morbidity index score is calculated based on the cumulative number of comorbidity conditions.

Weighted frequencies and percentages of demographic characteristics among unilateral TKA vs. bilateral TKA.

Methods: In this retrospective analysis, we sought to examine BTKA vs UTKA utilization and in-hospital complications comparing AAs and Whites. Using the National Inpatient Sample (NIS)- Healthcare Cost and Utilization Project (HCUP) database (2007-2016), we computed differences in temporal trends in utilization and major in-hospital com-

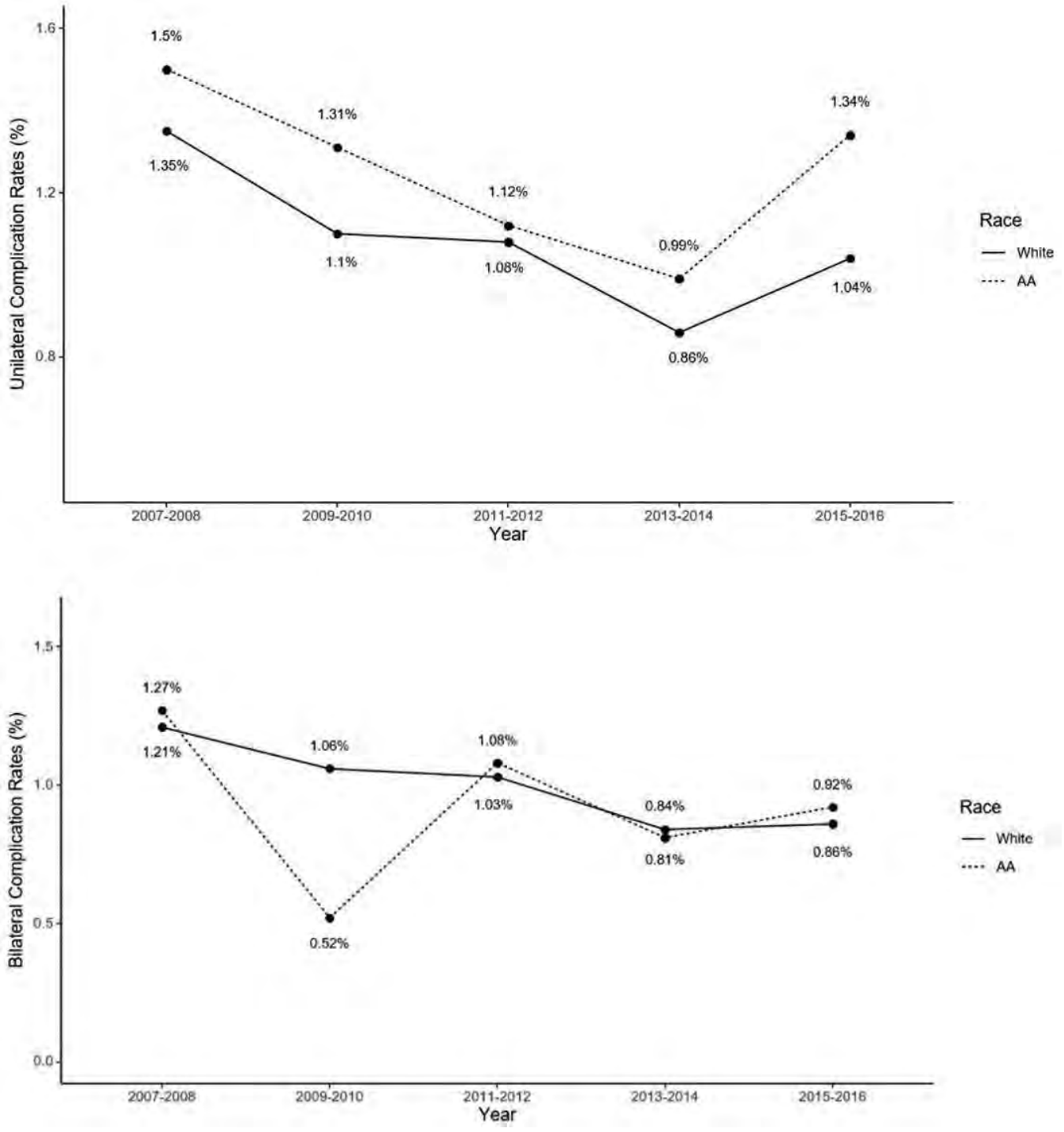


Utilization of Bilateral Total Knee Arthroplasty (TKA) amongst all TKAs stratified between Whites and African Americans.

plication rates of BTKA vs UTKA comparing AAs and Whites. All patients ≥ 50 years who underwent elective primary TKA were included. We performed multivariable logistic regression models to assess racial differences in trends adjusting for individual (age, sex, Elixhauser comorbidity index, and morbid obesity), hospital level (hospital volume, bed size, region and teaching status) and community level (median household income) variables. Discharge weights were used to enable nationwide estimates. We used multiple imputation procedures to impute values for 12% missing race information.

Results: An estimated 276,194 BTKA and 5,528,429 UTKA were performed in US. The proportion of BTKA amongst all TKAs declined from 5.53% in 2007-08 to 4.03% in 2015-16. AAs were significantly less likely to undergo BTKA compared to Whites throughout the study period (4.68% in AAs vs 6.08% in Whites in 2007-08, whereas 3.28% AAs vs 4.19% Whites in 2015-16, trend $P < 0.001$). In-hospital complication rates for UTKA were higher in AAs compared to Whites throughout the study period (1.35% Whites vs 1.50% AAs, 2007-08, 1.00% Whites vs 1.35% AAs in 2015-16, trend $P < .0001$). However, for BTKA, the in-hospital complication rates varied between Whites and AA throughout the study period (1.21% Whites vs 1.27% AAs, 2007-08; 1.03% Whites vs. 1.08% AAs, 2011-12; 0.86% Whites and 0.92% AAs, 2015-16, trend $P = 0.09$).

Conclusion: In this nationwide sample of patients from 2007-2016 who underwent total knee arthroplasty, the utilization rate of BKTA was higher in Whites compared to AAs. On the other hand, while AAs have consistently higher in-hospital complication rates in UTKA over the time period, this pattern was not consistent for BTKA.



Unilateral and Bilateral Total knee Arthroplasty in-hospital Complications in Whites and African Americans

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Disclosure: B. Mehta, Novartis, 1; **K. Ho**, None; **J. Bido**, None; **S. Memtsoudis**, Teikoku, 1, Sandoz Inco, 1, HATH, 1; **M. Parks**, ZimmerBiomet, 1; **S. Goodman**, Pfizer, 1, Novartis, 1, UCB, 1, regenosine, 1, 2, Horizon, 1; **L. Russell**, None; **S. Ibrahim**, None.

Abstract Number: 1654

The Relationship Between Patient-Reported Readiness for Total Knee Arthroplasty and the Likelihood of a Good Outcome at One Year

Gillian Hawker[1], Barbara Conner-Spady[2], Eric Bohm[3], Michael Dunbar[4], Allyson Jones[5], Bheeshma Ravi[1], Tom Noseworthy[2], Linda Woodhouse[6], Peter Faris[7], Donald Dick[8], James Powell[2], Paulose Paul[5] and Deborah Marshall[2], [1]University of Toronto, Toronto, ON, Canada, [2]University of Calgary, Calgary, AB, Canada, [3]Concordia Hip & Knee Institute, University of Manitoba, Winnipeg, MB, Canada, [4]Dalhousie University, Halifax, NS, Canada, [5]University of Alberta, Edmonton, AB, Canada, [6]Curtin University, Perth, Western Australia, Australia, [7]Alberta Health Services, Calgary, ON, Canada, [8]Alberta Bone and Joint Health Institute, Edmonton, AB, Canada

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: In prior qualitative research, we found that patients with knee osteoarthritis (OA) equated appropriateness for total knee arthroplasty (TKA) with candidacy for the procedure. Pain intensity, the ability to cope with the pain and how the pain affected quality of life were seen as important factors determining surgical candidacy. The importance of psychological readiness and a positive attitude, were additionally perceived as critical to achievement of a good TKA outcome. The current study examined the relationship between patients' pre-operative psychological readiness for TKA and surgical outcome at one year.

Methods: This prospective cohort study recruited knee OA patients aged 30+ years referred for TKA at two hip/knee surgery centers in Alberta, Canada. All participants met ACR criteria for knee OA. Those who received primary, unilateral TKA completed questionnaires pre-TKA to assess TKA readiness (Patient Acceptable Symptom State – knee symptoms acceptable/unacceptable; Perceived Arthritis Coping Efficacy; General Self-Efficacy; definite willingness to undergo TKA - yes/no) and covariates (age, sex, WOMAC pain, Knee injury and Osteoarthritis Outcome Score Physical Function [KOOS-PS], Patient Health Questionnaire depression scale, BMI, comorbidities), and one year post-TKA to assess TKA outcome. A good TKA outcome was defined as improved knee symptoms (OARSI-OMERACT responder criteria) AND overall satisfaction with TKA results (yes/no). Using multivariable logistic regression, we examined the relationship of our exposures to a good TKA outcome, before and after controlling for covariates.

Results: Of 1,272 TKA recipients assessed at one year, 1,030 without complications and with data for the primary outcome were included (mean age 66.9 years [SD 8.8]; 58.5% female). 79.3% achieved a good TKA outcome. In multivariable analysis, controlling for covariates, unacceptable knee symptoms and definite willingness to undergo TKA were associated with higher odds of a good TKA outcome (adjusted ORs 1.55, 95% CI, 1.06 - 2.71, and 1.70, 95% CI 1.09 - 2.66, respectively).

Conclusion: Among OA TKA recipients, greater psychological readiness for TKA was associated with higher odds of a good TKA outcome. Incorporation of patient readiness in TKA decision-making may enhance patient outcomes and appropriate use of TKA.

Disclosure: G. Hawker, University of Toronto, 2; **B. Conner-Spady**, None; **E. Bohm**, None; **M. Dunbar**, None; **A. Jones**, None; **B. Ravi**, None; **T. Noseworthy**, None; **L. Woodhouse**, None; **P. Faris**, None; **D. Dick**, None; **J. Powell**, None; **P. Paul**, None; **D. Marshall**, University of Calgary, 2.

Abstract Number: 1655

Pain Reduction Post Total Knee Replacement in Opioid Users and Non-users

Lindsey MacFarlane[1], Yinzhu Jin[1], Yvonne Lee[2], Joyce Lii[3], Jeffrey Katz[4], Patricia Franklin[5] and Seoyoung Kim[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Northwestern University Feinberg School of Medicine, Chicago, IL, [3]Brigham and Women's Hospital, Boston, [4]Harvard Medical School / The Orthopaedic and Arthritis Center for Outcomes Research (OrACORe) at Brigham and Women's Hospital, Boston, MA, [5]Northwestern University, Chicago

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: End-stage knee osteoarthritis (OA) is often managed with opioids and total knee replacement (TKR). Studies ascertaining opioid use via record review are conflicting as to whether opioid users experience similar pain reduction post TKR compared to non-users. We used claims data to identify opioid prescriptions and analyzed pain response after TKR among naïve, intermittent and continuous opioid users.

Methods: We used Medicare claims data (Parts A/B/D 2010-2014) linked to data from the FORCE-TJR, a research cohort of U.S. patients receiving total joint replacement who completed the Knee Injury and Osteoarthritis Outcome Score (KOOS) at baseline and follow-up. Included patients were ≥ 65 years old, received TKR, and had continuous enrollment in Medicare for the 360 days prior to TKR. We assessed for opioid dispensation in each of the 12 months leading up to TKR. We categorized pre-baseline opioid use as follows, naïve: patients with no opioid prescription, intermittent: those with opioid prescription ≥1 and < 12 months, continuous: patients with a prescription in all 12 months. KOOS Pain (0-100, 100 best) was measured at baseline and at 6 and 12-months post-TKR. We compared post-TKR KOOS Pain at 6 and 12 months among the opioid use groups. We then developed linear regression models to ascertain the association between opioid use and KOOS Pain at 12-months follow up and change in KOOS Pain from baseline to 12-months. For patients not providing 12-month KOOS scores, 6-month data were used. We considered the following covariates baseline KOOS Pain, age, sex, race, body mass index, mental component summary (MCS), comorbidity index, medication use (NSAIDs, COX-2 inhibitors, gabapentin and pregabalin), and indicators of widespread pain- back pain, non-operative knee pain, and neuropathic pain.

Results: We included 799 patients; 372 were opioid naïve, 385 intermittent users and 42 continuous users. Mean age was 72-73 years and 69-76% were female. Continuous (44±20 p=0.04) and intermittent (47±17 p=0.03) users reported worse KOOS Pain at baseline compared to opioid naïve (50±16) patients. Continuous and intermittent users had more comorbidities and reported greater pain in the back and other knee (Table 1). There were no statistically significant differences in KOOS Pain between opioid users and non-users at 6 and 12-month follow-up (Figure 1). Unadjusted KOOS Pain at 12mo follow up and change in KOOS Pain was similar across the opioid use categories with 85 (Δ=35) for naïve patients, 86 (Δ=38) for intermittent users and 82 (Δ=38) for continuous users. Adjusting for baseline KOOS Pain, and further for demographics, MCS, comorbidity index, medication use and indicators of widespread pain attenuated the difference in both KOOS Pain and change in KOOS Pain across the opioid use categories (Table 2). The differences among the opioid use groups in both the unadjusted and adjusted models are small (effect size < 0.26) and unlikely to be clinically meaningful.

Table 1: Baseline characteristics by opioid use category			
	Opioid Use		
	Naïve (n=372)	Intermittent (n=385)	Continuous (n=42)
Age, years, mean (SD)	74 (6)	73 (6)*	72 (7)*
BMI, kg/m^2, mean (SD)	30 (5)	30 (6)	31 (6)
SF-36 Mental component summary, mean (SD)	55 (11)	52 (12)*	51 (14)*
Combined co-morbidity index, mean (SD)	0.8 (2)	1 (2)*	2 (3)*
KOOS Pain index knee, mean (SD)	50 (16)	47 (17)*	44 (20)*
Gender			
Female, n (%)	255 (69)	270 (70)	32 (76)
Race			
% White, n (%)	350 (94)	354 (92)	31 (74)*
% Black or Other, n (%)	22 (6)	31 (8)	11 (26)*
Neuropathic pain, n (%)	75 (20)	120 (31)*	14 (33)
Backpain, n, (%)			
None/mild	292 (79)	245 (64)*	24 (57)*
Moderate/severe	75 (20)	136 (35)*	17 (41)*
Non-operative knee pain, n (%)			
None/mild	306 (82)	297 (77)	26 (62)*
Moderate/severe	36 (10)	62 (16)*	13 (31)*
Medication usage, n (%)			
Antidepressants/ benzodiazepines	85 (23)	164 (43)*	23 (55)*
NSAID/coxib	148 (40)	206 (54)*	22 (52)
Gabapentin/pregabalin	20 (5)	64 (17)*	18 (43)*
BMI; body mass index MME; morphine milligram equivalent KOOS; Knee injury and osteoarthritis score NSAID; non-steroidal anti-inflammatory drugs COXIB- COX-2 inhibitor * $p<0.05$ for opioid user group compared to opioid naïve			

Table 1

Conclusion: Opioid users, whether intermittent or continuous, achieved similar improvement in knee pain post TKR as opioid naïve patients. This suggests that baseline opioid use alone does not predict which patients will have symptomatic benefit from TKR.

Table 2: Least Squared Means (95% CI) for KOOS Pain post-total knee replacement			
KOOS Pain at 12-months follow up			
	Unadjusted	Model 1[a]	Model 2[b]
Baseline opioid use			
Naïve	85 (83, 87)	85 (83, 86)	80 (69, 92)
Intermittent	86 (84, 87)	86 (85, 88)	83 (72, 94)
Continuous	82 (77, 87)	83 (78, 88)	82 (70, 93)
Change in KOOS Pain from baseline to 12-months			
	Unadjusted	Model 1[a]	Model 2b
Baseline opioid use			
Naïve	35 (33, 37)	36 (35, 38)	32 (20, 43)
Intermittent	38 (36, 40)	38 (36, 39)	35 (24, 46)
Continuous	38 (32, 44)	35 (30, 39)	33 (21, 45)

KOOS: Knee Injury and Osteoarthritis Outcome Score

a. Model 1- adjusted for baseline KOOS Pain

b. Model 2- Model 1 + adjusted for age, sex, race, mental component summary score, comorbidity index, medications (non-steroidal anti-inflammatory drugs, coxibs, gabapentin, pregabalin), baseline contralateral knee pain, back pain, neuropathic pain

Table 1

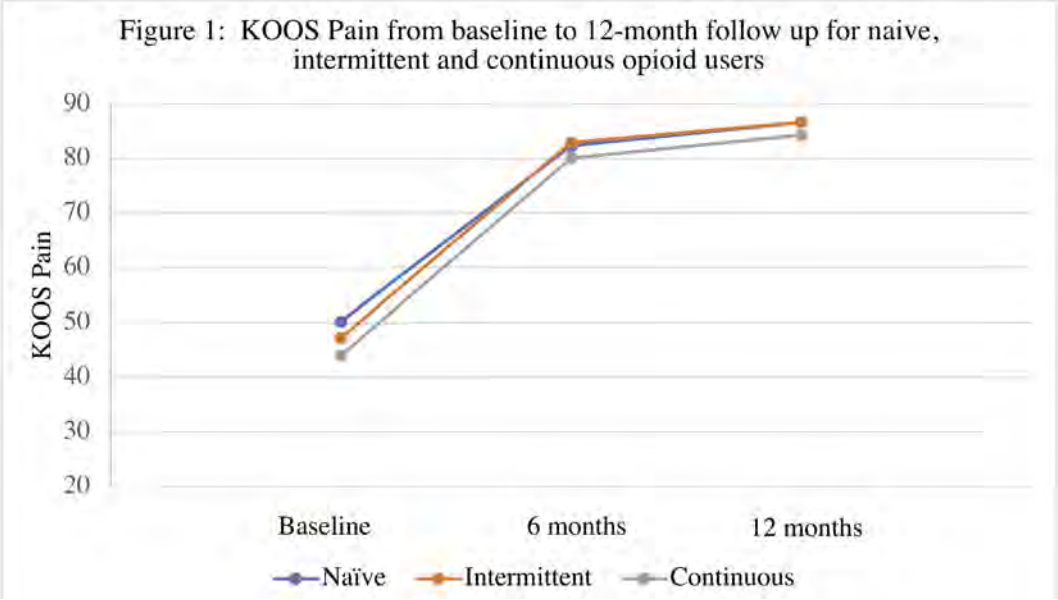

Figure 1

Disclosure: L. MacFarlane, Amgen, 2, Samumed, 2, Flexion, 2; **Y. Jin**, None; **Y. Lee**, Highland Instruments, Inc., 1, 2, Pfizer, 1, 2, Cigna-Express Scripts, 1; **J. Lii**, None; **J. Katz**, Samumed, 2, Flexion, 2; **P. Franklin**, None; **S. Kim**, Pfizer, 1, Roche, 1, AbbVie, 1, Bristol-Myers Squibb, 1.

Abstract Number: 1656

Knee OA Outcomes in Patients with Severe Obesity Following Bariatric Surgery or Total Knee Arthroplasty

Jonathan Samuels[1], Stephen Zak[2], Ran Schwarzkopf[2], Christine Ren-Fielding[3], Manish Parikh[4], Alex McLawhorn[5], James Browne[6], Peter Hallowell[7], Brian Irving[8], Craig Wood[9], Christopher Still[9] and Peter Benotti[9], [1]NYU Langone, Rye Brook, NY, [2]NYU Langone Health, New York, NY, [3]NYU Langone Health, New YOrk, [4]Bellevue Hospital, New York, NY, [5]Hospital for Special Surgeyr, New York, [6]University of Virginia, Charlottesville, VA, [7]University of Virginia, Charlottesville, [8]Louisiana State University, Baton Rouge,, LA, [9]Obesity institute at Geisinger, Danville

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: High body mass index (BMI, kg/m^2) is a modifiable risk factor that has been associated with the development and progression of osteoarthritis (OA) and knee pain. While total knee arthroplasty (TKA) is the gold standard for the treatment of end stage OA, morbidly obese patients (BMI≥40kg/m^2) are often required to lose weight prior to TKA due to increased surgical risk and a higher rate of complications. While conservative weight-loss often fails to help these patients, bariatric surgery can be an alternative option. Here we present interim data from the trial

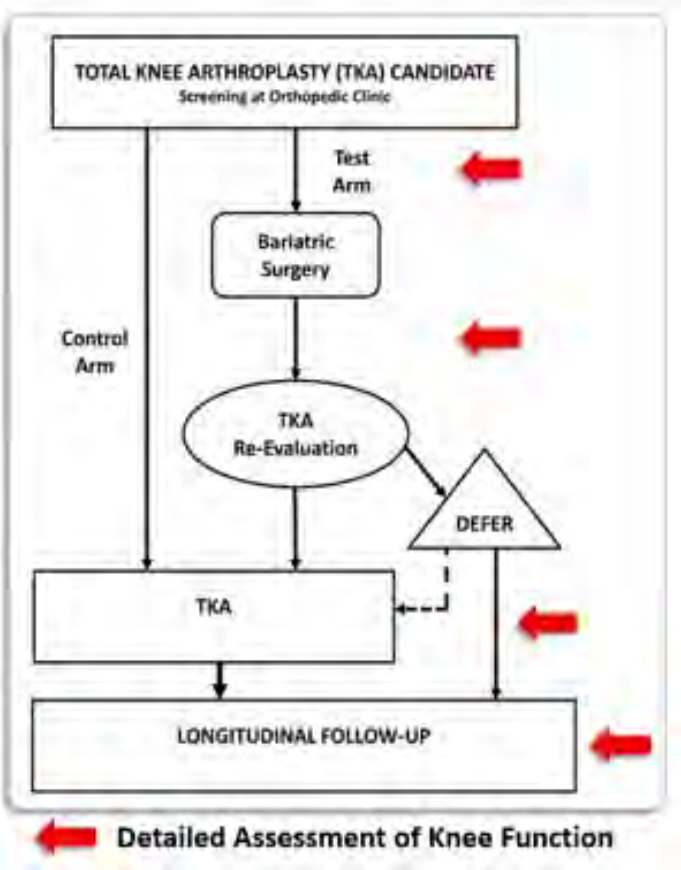

Figure 1. Study flowchart

entitled "Surgical Weight-loss to Improve Functional Status Trajectories following arthroplasty for painful knee osteoarthritis**".** This current multi-center, prospective study compares pain and functional outcomes in patients receiving bariatric surgery prior to TKA versus obese patients who go straight to TKA.

Methods: Patients with BMI ≥40 kg/m^2 and painful knee osteoarthritis who met the indications for TKA were recruited at four hospital centers. Patients with a BMI >35 kg/m^2 were also recruited if they had a qualifying comorbid condition including obstructive sleep apnea, diabetes, hypertension or hyperlipidemia. Patients were assigned to either the bariatric (BAR) or TKA arm based on surgical choice (goal n=150 for each arm), with all bariatric patients having anatomy-altering sleeve gastrectomy or gastric bypass. At baseline and several time points after surgery **(Figure 1)**, we documented height, weight, the Knee injury and Osteoarthritis Outcome Score (KOOS), visual analog pain (VAS) scales, and the Western Ontario and McMaster Universities Arthritis Index (WOMAC), and had patients perform functional assessments (Timed-Up and Go, 30-second Chair Stand and 40-meter fast paced walk test). We targeted minimum detectable change (MDC) in outcomes for the VAS for knee pain (33% reduction), Timed Up and Go (decrease by 2 seconds), 30-second Chair Stand (increase by 2 reps), 40-meter fast paced walk (increase by 0.16 m/s), WOMAC score (16% reduction), and the KOOS pain score (10-point improvement). Using a logistic regression to adjust for age and baseline BMI, we compared the percentage of patients in the two arms who achieved an MDC for the various outcomes.

Results: To date, 25 BAR and 28 TKA patients have completed their follow-up visits through at least 6 months. Although there was a similar sex distribution, the bariatric group was younger (52 vs 60 years old, p=0.0023) with a higher baseline BMI (47.0 vs 41.6 p=0.0006). Most bariatric patients achieved comparable improvement to the TKA cohort with regards to the benchmarks of the 30-second Chair Stand (TKA 54% vs BAR 33%, p=0.156), KOOS pain score (TKA 91% vs BAR 67%, p=0.130), the Visual Analog Pain Scale (TKA 50% vs BAR 39%, p=0.466), Timed Up and Go test (TKA 43% vs BAR 22%, p=0.141) and the 40-meter fast paced walk (TKA 61% vs BAR 35%, p=0.073). The TKA cohort had a greater percent with a MDC for the WOMAC (TKA 88% vs BAR 54%, p=0.030).

Conclusion: In morbidly obese patients who are eligible for TKA, bariatric surgery may result in modest improvements in knee outcomes and may eventually delay the need for a TKA.

Disclosure: J. Samuels, None; **S. Zak**, None; **R. Schwarzkopf**, Smith & Nephew, 1, 2, 3, Intelijoint, 1, 2, Gauss Surgical, 1, PSI, 1; **C. Ren-Fielding**, Covidien LP, 1, Ethicon Inc., 1, Intuitive Surgical, Inc., 1, Levita Magnetics International Corp, 1, W. L. Gore & Associates, Inc., 1, Allergan Inc., 1, Nalpropion Pharmaceuticals LLC, 1; **M. Parikh**, None; **A. McLawhorn**, None; **J. Browne**, DJO Surgical, 1, 2, OsteoRemedies, 1, Huron Therapeutics, 1; **P. Hallowell**, None; **B. Irving**, None; **C. Wood**, None; **C. Still**, Ethicon Endosurgery, 2, Novo Nordisk, 2, 5, 8; **P. Benotti**, None.

Abstract Number: 1657

Do Comorbidities Limit Improvement in Pain and Physical Function After Total Knee Arthroplasty in Patients with Knee Osteoarthritis?

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Osteoarthritis – Clinical Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Individuals with knee osteoarthritis (OA) are increasingly living with multiple comorbid conditions. The presence of comorbidities has been associated with having worse OA symptoms but few studies have assessed their impact on response to OA treatment. We assessed the impact if any of comorbidities on improvement in pain and physical function (patient-reported and performance-based) in recipients of total knee arthroplasty (TKA) for knee OA.

Methods: In the BEST Knee prospective cohort study, patients with knee OA underwent assessment one month prior and 12 months after TKA at two tertiary referral centres in Alberta Canada. Standardized questionnaires assessed sociodemographics social support smoking status self-reported comorbidities and patient-reported outcomes (WOMAC pain, KOOS physical function short-form). Using multivariable generalized-estimating-equation extension of linear regression accounting for potential clustering by surgeon and adjusting for potential confounders we assessed the impact of specific comorbid conditions a priori hypothesized to impact pain and function and total number of conditions reflective of total comorbidity burden separately on change in patient-reported knee pain and physical function at 12 months after TKA. In an exploratory analysis in a subset of patients for whom six-minute walk test (6MWT) a performance-based measure of functional exercise capacity was performed one month prior and 12 months after TKA we assessed the impact of specific and total number of comorbid conditions on change in walking distance.

Results: 1027 participants were included (Table 1) 278 for the 6MWT subset. Mean age was 67 years (SD 8.87) 60% were female 59.3% had a BMI ≥ 30 kg/m2 and 85% reported at least one comorbidity. Individuals with higher number of comorbidities had worse pre-TKA scores for pain physical function and walking distance. At follow-up

Table 1. Characteristics of participants and outcomes, overall and by comorbidity count.

Characteristic	Overall (n=1027)	Number of comorbidities*				
		0 (n=154)	1 (n=278)	2 (n=284)	≥3 (n=311)	p-value**
Demographics						
Mean age (years) (SD)	67.10 (8.87)/1027	65.16 (9.48)/154	66.53 (8.95)/278	67.38 (8.62)/284	68.17 (8.57)/311	0.004
Female – no. (%)	618 (60.18)/1027	94 (61.04)/154	165 (59.35)/278	171 (60.21)/284	188 (60.45)/311	0.99
Post-secondary education – no. (%)	562 (55.86)/1006	91 (61.49) 148	159 (57.61)/276	146 (51.96)/281	166 (55.15)/301	0.26
Current smoking – no. (%)	76 (7.49)/1015	8 (5.37)/149	21 (7.55)/278	16 (5.73)/279	31 (10.03)/309	0.17
Social support						
Mean Lubben Social Network Score (0-30) (SD)	17.71 (5.53)/988	18.19 (5.74)/141	17.92 (5.37)/270	17.67 (5.24)/278	17.32 (5.83)/299	0.40
Comorbidities						
Obesity (BMI >= 30 kg/m²)	609 (59.30)/1027	-	-	-	-	-
Heart disease – no (%)	148 (15.16)/976	-	-	-	-	-
Hypertension – no (%)	529 (52.95)/999	-	-	-	-	-
Diabetes mellitus – no (%)	160 (16.31)/981	-	-	-	-	-
Lung disease – no (%)	98 (10.04)/976	-	-	-	-	-
Cancer – no (%)	63 (6.48)/972	-	-	-	-	-
Other painful disorder*** – no (%)	42 (4.09)/1027	-	-	-	-	-
Back pain – no (%)	488 (49.69)/982	-	-	-	-	-
Depressed mood (PHQ-8 ≥10) – no (%)	275 (26.91)/1022	-	-	-	-	-
Liver Disease – no (%)	12 (1.25)/958	-	-	-	-	-
Kidney Disease – no (%)	28 (2.87)/974	-	-	-	-	-
Gastrointestinal disease – no (%)	114 (11.68)/976	-	-	-	-	-
Anemia/hematological disease – no (%)	29 (3.01)/935	-	-	-	-	-
Median total number troublesome joints (including index joint) (IQR)	2 (1, 3)/1006	-	-	-	-	-
Baseline clinical characteristics						
Mean WOMAC pain (0-100) (SD)****	57.59 (17.03)/1027	51.65 (16.44)/154	57.92 (16.47)/278	58.31 (17.04)/284	59.56 (17.24)/311	<0.001
Mean KOOS physical function short form (0-100) (SD)****	53.23 (17.29)/1027	48.67 (18.05)/154	51.92 (15.40)/278	53.09 (17.61)/284	56.80 (17.58)/311	<0.001
Change from baseline at 12 months after TKA						
Mean WOMAC pain change (SD)	-42.66 (23.52)/1027	-40.58 (20.34)/154	-43.19 (23.57)/278	-42.33 (24.37)/284	-43.53 (24.18)/311	0.61
Mean KOOS physical function short form change (SD)	-30.10 (23.72)/1027	-28.71 (22.59)/154	-28.94 (22.35)/278	-28.39 (25.09)/284	-33.39 (23.93)/311	0.03
6MWT subsample****						
	Overall (n=278)	Number of comorbidities*				
		0 (n=40)	1 (n=80)	2 (n=75)	≥3 (n=83)	p-value
Mean baseline 6MWT (m) (SD)	323.09 (104.66)	404.79 (83.13)	315.53 (105.76)	310.53 (98.50)	302.36 (101.45)	<0.001
Mean change in 6MWT (m) (SD)	72.86 (90.98)	68.07 (80.20)	81.30 (96.96)	69.52 (89.36)	70.06 (92.42)	0.81

QIC, quasi-information criteria; WOMAC, Western Ontario and McMaster Universities Arthritis Index; KOOS, knee osteoarthritis outcome score physical function short-form; 6MWT, six-minute walk test

* Sum of 12 conditions (did not include obesity or total number of troublesome joints)
** 2-tailed p-value for ANOVA or X^2 tests, as appropriate
*** Other painful disorder defined as: fibromyalgia, migraines and/or neurological disease
**** WOMAC/KOOS – higher scores indicate worse pain/function
***** EQ5D – higher score indicates better quality of life
****** Subsample of individuals who underwent 6MWT were similar in demographic characteristics to full sample

Table 2. Association between specific and total number of comorbidities with change in pain, physical function, and walking ability 12 months after total knee arthroplasty.

Independent variable	Dependent variable		
	WOMAC pain Adjusted beta coefficient (95% CI) *	**KOOS physical function** Adjusted beta coefficient (95% CI)*	**6MWT walking ability** Adjusted beta coefficient (95% CI) * (subsample)
Primary model: Specific comorbid conditions			
Obesity	1.45 (-1.04, 3.94)	0.91 (-1.52, 3.34)	9.87 (-9.95, 29.69)
Heart disease	1.80 (-2.61, 6.22)	-0.46 (-4.00, 3.05)	8.33 (-22.22, 38.89)
Lung disease	-1.41 (-7.28, 3.29)	-3.42 (-8.62, 1.79)	7.53 (-28.28, 43.35)
Diabetes	-1.41 (-5.49, 2.67)	0.37 (-3.51, 4.24)	-18.05 (-50.41, 14.31)
Cancer	4.93 (-2.21, 12.07)	**8.35 (1.75, 14.96)**	-0.29 (-66.23, 65.65)
Back pain	2.18 (-0.51, 4.68)	**3.32 (0.58, 6.07)**	-19.29 (-48.83, 10.25)
Gastrointestinal disease	-2.57 (-7.23, 2.10)	-0.80 (-5.92, 4.33)	29.69 (0.49, 58.88)
Anemia/ hematological disease	2.55 (-4.60, 9.70)	-3.29 (-11.09, 4.52)	-12.19 (-75.77, 51.39)
Other painful/disabling disorders**	1.35 (-8.08, 10.78)	-3.06 (-10.22, 4.10)	-10.07 (-73.02, 52.87)
Total number troublesome joints, per joint	**-1.26 (-2.36, -0.15)**	-0.46 (-1.38, 0.46)	5.57 (-3.57, 14.71)
Depressed mood***	**-9.93 (-13.80, -6.05)**	**-13.39 (-17.27, -9.50)**	8.97 (-16.38, 34.33)
	n=880 QIC 897.12 QiCu 897.00	n=880 QIC 892.81 QICu 897.00	n=245 QIC 257.03 QICu 262.00
Secondary model: Number of comorbid conditions (ref = 0)**			
1	**-4.58 (-8.72, -0.45)**	-0.66 (-4.60, 3.28)	17.16 (-6.17, 40.49)
2	-3.80 (-9.00, 1.39)	-0.32 (-6.47, 5.83)	5.07 (-12.32, 22.46)
≥ 3	**-5.83 (-10.43, -1.24)**	**-5.41 (-10.34, -0.48)**	2.57 (-20.81, 25.94)
	n=971 QIC 979.19	n=971 QIC 978.77	n=264 QIC 267.32

QIC, quasi-information criteria; WOMAC, Western Ontario and McMaster Universities Arthritis Index; KOOS, knee osteoarthritis outcome score physical function short-form; 6MWT, six-minute walk test

*Models adjusted for age, sex, education, smoking status, and social support, as well as clustering by surgeon

** Other painful disorder defined as: fibromyalgia, migraines and/or neurological disease

*** Depressed mood defined as PHQ-8 score ≥10

**** Total number of conditions include 12 conditions assessed (did not include obesity or total number of troublesome joints, but included kidney disease, liver disease and hypertension that were not included as specific conditions)

mean changes in pain function and walking distance were similar for those with and without comorbidities (Table 1). In regression analysis back pain (ß=3.3, 95% CI: 0.6 to 6.1) and cancer (ß=8.4, 95% CI 1.8 to 15.0) were associated with less improvement in patient-reported physical function while depressed mood and a higher total number of conditions were associated with greater improvement in both pain and function. No specific conditions were associated with less improvement in pain. Improvement in walking distance after TKA as measured by the 6MWT was unrelated to specific and total number of conditions (Table 2).

Conclusion: For individuals with knee OA most comorbid conditions do not limit improvement in pain physical function and walking distance (6MWT) after TKA. Understanding response to OA treatment in individuals with comorbidities is important for individualized patient counselling. For patients living with comorbidities these findings are important as improvement in long-term OA outcomes may facilitate better engagement in self-management such as physical activity for their other conditions.

Disclosure: L. King, None; **E. Waugh**, None; **A. Jones**, None; **D. Marshall**, University of Calgary, 2; **G. Hawker**, University of Toronto, 2.

Abstract Number: 1658

Mediation of the Association Between Obesity and Osteoarthritis by Blood Pressure, Arterial Stiffness, and Subclinical Atherosclerosis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Obesity-related metabolic dysregulation may lead to atherosclerotic vascular changes. It has been hypothesized that a compromised blood flow may cause detrimental changes to the subchondral bone and decrease nutrient supply to the cartilage. To which extent atherosclerosis may explain the association between obesity and osteoarthritis has not been investigated. Therefore, we aimed to investigate the role of blood pressure, arterial stiffness (pulse wave velocity (PWV)) and subclinical atherosclerosis (carotid intima-media thickness (IMT), popliteal vessel wall thickness (VWT)) as mediators of the association of obesity with hand and knee osteoarthritis.

Methods: We used cross-sectional data from the population-based NEO study, excluding participants with concomitant rheumatic diseases (n = 323) and missing physical examination (n = 14), resulting in 6,334 participants. Clinical hand and knee osteoarthritis were defined by the ACR classification criteria. Eight percent of the participants satisfied the ACR classification criteria for hand osteoarthritis, and 10% of participants was classified with clinical knee osteoarthritis. Structural knee osteoarthritis was assessed on MRI in a subpopulation (n = 1,285). Popliteal VWT was assessed on MRI (n = 1,095), using VesselMASS for semi-automated detection of the vessel wall boundaries. Aortic PWV was estimated on abdominal velocity-encoded MRI (n = 2,580). Carotid IMT was assessed by ultrasonography in all participants. Blood pressure was corrected for the use of antihypertensive medication (systolic +15 mmHg, diastolic +10 mmHg). Continuous variables were standardized (mean 0, standard deviation 1). Associations between BMI and osteoarthritis were assessed with logistic regression analyses, adjusted for age, sex and education. Subsequently, possible mediators were added to the model. The assumptions for mediation according to the Baron and Kenny framework were assessed, and if fulfilled the percentage mediation was calculated.

Results: The population consisted of 55% women, with a mean age of 56 years and BMI of 26 kg/m2. Clinical hand osteoarthritis was present in 8%, clinical knee osteoarthritis in 10% and structural knee osteoarthritis in 12% of participants. Mean blood pressure was 134/85 mmHg. Mean carotid IMT was 0.62 mm, popliteal VWT was 0.53 mm, and PWV was 6.56 m/s (table 1). BMI was positively associated with all osteoarthritis outcomes. Carotid IMT partially mediated the association of BMI with clinical hand osteoarthritis (10.6 (6.2; 30.5)%) and structural knee osteoarthri-

Table 1. Characteristics of the weighted NEO study population

	Overall n = 6,334
General patient characteristics	
Age (year)	56 (6)
Sex (% women)	55
Education (% high)	46
Body mass index (kg/m²)	26 (4)
History of cardiovascular disease (%)	6
Lipid lowering medication (% users)	11
Antihypertensive medication (% users)	23
Exposure variables	
Systolic blood pressure (mmHg)*	134 (19)
Diastolic blood pressure (mmHg)*	85 (12)
Hypertension† (%)	62
Carotid intima-media thickness (mm)	0.62 (0.09)
Popliteal artery vessel wall thickness (mm)^	0.53 (0.05)
Pulse wave velocity (m/s)^	6.56 (1.30)
Osteoarthritis phenotypes	
Clinical hand OA (%)	8
Clinical knee OA (%)	10
Structural knee OA (%)~	12

Results are based on analyses weighted towards the BMI distribution of the general population (n=6,334). ^Popliteal VWT (n=1,095) and PWV (n=2,382) measurements are performed in MRI subpopulations. ~Percentage of participants who underwent knee MRI (n=1,285). Numbers represent mean (SD) unless otherwise specified. Blood pressure was adjusted for antihypertensive medication use when applicable (systolic +15 mmHg, diastolic +10 mmHg). †Defined as a systolic pressure ≥130 mmHg or diastolic pressure ≥85 mmHg or antihypertensive mediation use.

tis (3.1 (1.9; 7.3)%). Diastolic blood pressure (2.1 (1.6; 3.0)%) limitedly mediated the association between BMI and clinical knee osteoarthritis. PWV and popliteal VWT did not mediate the association between BMI and osteoarthritis.

Conclusion: Blood pressure and carotid IMT limitedly mediated the association of BMI with hand and knee osteoarthritis, suggesting that such mediation is questionable in the middle-aged population.

Table 2. Mediation of the association of BMI with OA by blood pressure, arterial stiffness and atherosclerosis

	Total effect C	Indirect effect A	Direct effect C' Indirect effect B	Mediation % (95% CI)
	Clinical hand OA OR (95% CI)	Mediator β (95% CI)	Clinical hand OA OR (95% CI)	
BMI	1.22 (1.08; 1.37)	0.21 (0.18; 0.25)	1.22 (1.08; 1.38)	NA
Systolic BP			0.98 (0.84; 1.14)	
BMI	1.22 (1.08; 1.37)	0.28 (0.25; 0.32)	1.22 (1.08; 1.38)	NA
Diastolic BP			0.98 (0.84; 1.15)	
BMI	1.21 (1.08; 1.36)	0.23 (0.19; 0.27)	1.19 (1.05; 1.34)	10.6 (6.2; 30.5)
Carotid IMT			1.09 (0.94; 1.25)	
BMI	1.56 (1.17; 2.08)	0.01 (-0.06; 0.09)	1.55 (1.16; 2.07)	NA
Popliteal VWT			1.14 (0.84; 1.55)	
BMI	1.41 (1.15; 1.73)	0.05 (-0.01; 0.11)	1.41 (1.15; 1.73)	NA
Aorta PWV			1.04 (0.81; 1.33)	
	Clinical knee OA OR (95% CI)	Mediator β (95% CI)	Clinical knee OA OR (95% CI)	
BMI	1.46 (1.32; 1.62)	0.21 (0.17; 0.24)	1.46 (1.31; 1.62)	NA
Systolic BP			1.02 (0.90; 1.15)	
BMI	1.46 (1.32; 1.62)	0.27 (0.24; 0.31)	1.45 (1.31; 1.62)	2.1 (1.6; 3.0)
Diastolic BP			1.03 (0.91; 1.15)	
BMI	1.46 (1.32; 1.62)	0.24 (0.20; 0.27)	1.47 (1.33; 1.62)	NA
Carotid IMT			0.97 (0.86; 1.09)	
BMI	1.20 (0.88; 1.64)	0.03 (-0.04; 0.11)	1.21 (0.89; 1.64)	NA
Popliteal VWT			0.95 (0.74; 1.24)	
BMI	1.37 (1.12; 1.67)	0.05 (-0.00; 0.11)	1.37 (1.12; 1.67)	NA
Aorta PWV			0.96 (0.76; 1.21)	
	Structural knee OA OR (95% CI)	Mediator β (95% CI)	Structural knee OA OR (95% CI)	
BMI	1.58 (1.24; 2.03)	0.29 (0.21; 0.38)	1.67 (1.33; 2.12)	NA
Systolic BP			0.81 (0.64; 1.02)	
BMI	1.58 (1.24; 2.03)	0.35 (0.27; 0.43)	1.65 (1.30; 2.09)	NA
Diastolic BP			0.87 (0.70; 1.09)	
BMI	1.58 (1.23; 2.03)	0.33 (0.25; 0.40)	1.56 (1.19; 2.06)	3.1 (1.9; 7.3)
Carotid IMT			1.03 (0.80; 1.34)	
BMI	1.50 (1.13; 1.99)	0.00 (-0.07; 0.08)	1.50 (1.13; 1.99)	NA
Popliteal VWT			1.09 (0.85; 1.38)	

Results are based on analyses weighted towards the BMI distribution of the general population (n = 6,334). Analysis regarding popliteal VWT (n = 1,095) and aorta PWV (n = 2,580) were assessed in a subpopulation. Continuous variables were standardized (mean 0, SD 1). SD BMI = 4.41, SD carotid IMT = 0.09, SD popliteal VWT = 0.05, SD aorta PWV = 1.30. Abbreviations: BMI = body mass index, BP = blood pressure, CI = confidence interval, IMT = intima-media thickness, OA = osteoarthritis, OR = odds ratio, PWV = pulse wave velocity, VWT = vessel wall thickness

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Abstract Number: 1659

Synergistic Effect of Quadriceps Weakness and Obesity in Women at Risk of Knee Osteoarthritis

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SESSION INFORMATION

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Background/Purpose: Quadriceps weakness is associated with an increased risk of incident symptomatic and radiographic knee osteoarthritis (OA), particularly in women. Stronger quadriceps muscles may confer a protective effect by acting as shock absorbers and joint stabilizers, especially if excess load across the joint is conferred by obesity, one of the strongest known risk factors for knee OA. Compared to men, women are more likely to have weaker quadriceps muscles leading to joint instability and articular damage. Thus, we investigated whether increased loading with obesity works synergistically with quadriceps weakness to increase the risk of developing knee OA, and whether this effect differs in men versus women.

Methods: We included participants from the Multicenter Osteoarthritis (MOST) Study, a NIH-funded longitudinal cohort of adults with or at risk for knee OA. Isokinetic quadriceps strength from baseline was categorized into sex-specific tertiles, with quadriceps weakness defined as being in the lowest tertile (yes/no). Obesity (yes/no) was defined as body mass index ≥30kg/m^2 at baseline. Our outcomes at 60-month follow-up were incident **radiographic OA** (ROA) (KL-grade ≥2) and **symptomatic OA (SOA)** (radiographic OA with frequent knee pain in the same knee), among those without ROA and SOA, respectively at baseline. To determine the synergistic effect of quadriceps weakness and obesity on the risk of knee OA, we performed knee based, sex-stratified log-binomial regression models, calculating beta coefficients to estimate the risk differences, adjusting for pertinent confounders.

Results: At baseline, mean age was 61yrs, 58% women, mean BMI 29.4 kg/m2. By 60 month follow up, 305 out of 1870 knees (16.31%) developed incident ROA and 492 of 2816 knees (17.47%) SOA. Obese women had 22% more risk of incident ROA than nonobese women. Although quadriceps weakness did not affect the risk difference for incident ROA, there was a trend towards obese women's risk being 34% more for developing ROA with concomitant quadriceps weakness than those without obesity and quadriceps weakness (*p = 0.10 interaction of weakness and obesity*). Obese women had a 24% higher incidence of SOA than nonobese women. Quadriceps weakness itself did not affect SOA risk (< 1% risk difference) in women but obese women's risk with quadriceps weakness had a 43% higher risk of SOA incidence than nonobese and non-weak women (p= 0.0004 *interaction of weakness and obesity*). In men, neither obesity, quadriceps weakness nor their combination had significant effect on risk of either ROA or SOA. See Table.

Conclusion: We found the presence of obesity with quadriceps weakness to have a synergistic effect on higher risk of radiographic and symptomatic knee OA in women, but did not find any significant effect of obesity, quadriceps weakness, or the combination of the two on the risk of these outcomes in men.

Table: Cumulative incident risk difference in radiographic and symptomatic OA risk by quadriceps weakness, obesity, and interaction of both, stratified by sex

	ROA*	P value	SOA**	P value
# Knees (%)	305/1870 (16.31%)		492/2816 (17.47%)	
	Risk difference***		Risk difference***	
Quadriceps weakness				
Men (%)	-1.2 %	0.75	-1.9%	0.56
Women (%)	-0.3%	0.93	0.1%	0.97
Obesity				
Men (%)	1.8%	0.70	8.3%	0.08
Women (%)	22.4%	**0.001**	24.5%	**<0.0001**
Interaction effect Of obesity and quadriceps weakness				
Men (%)	-10.5%	0.06	-0.1%	0.98
Women (%)	+11.7%	0.10	+18.6%	**0.0004**
Quadriceps weakness AND Obesity vs. no quadriceps weakness and noobesity				
Men (%)	-10.5+1.8-1.2= 9.9%		-0.1+8.3-1.9 =6.3%	
Women (%)	22.4+11.7-0.3=33.8%		18.6+24.5+0.1=43.2%	

ROA: radiographic osteoarthritis; SOA: symptomatic osteoarthritis;
*Adjusted for Age, Trauma
**Adjusted additionally for depression
***Positive signs indicate higher and negative signs indicate lower risk for ROS/SOA.

Disclosure: J. Rubio, None; **D. Felson**, None; **X. Chen**, None; **K. Bacon**, None; **N. Segal**, None; **M. Nevitt**, None; **C. Lewis**, None; **T. Neogi**, Lilly, 1, EMD Merck Serono, 1, Novartis, 1, Regeneron, 1, Pfizer/Lilly, 1; **D. Misra**, None.

Abstract Number: 1660

Sleep Disturbance and Pain Severity and Multi-site Pain: A Prospective 10.7-year Follow-up Study

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Sleep disturbance is often comorbid with chronic pain disorders, with emerging evidence suggesting a stronger effect of sleep disturbance on pain than vice versa; however, few studies have evaluated the long-term effect of sleep disturbance on pain. This study sought to examine the association of sleep disturbance with knee pain severity and number of painful sites (NPS) and investigate whether persistent sleep disturbance increases the risk of persistent pain.

Methods: 1,099 community-dwelling older adults (age: mean±SD, 63±7.5 years; 51% female) were recruited and followed-up at 2.6, 5.1 and 10.7-year later. Data on demographics, body mass index, physical activity, comorbidities were collected. At each time-point, sleep disturbance, knee pain severity and NPS were assessed by using questionnaires. Radiographic knee osteoarthritis (ROA) was measured using x-ray. Multi-site pain (MSP) was defined as NPS ≥2. Persistent pain was defined as having knee pain or MSP at all time-points. Multivariable mixed-effects models and log-binomial regression were applied for the analyses.

Results: Sleep disturbance was associated with greater knee pain severity (β 0.91, 95%CI 0.70-1.11) and higher risk of having more NPS [(Relative risk (RR) 1.10, 95%CI 1.07-1.14] in a dose-response manner in multivariable analyse with adjustment for age, sex, body mass index, physical activity, comorbidities, pain medications, ever smoking, emotional problems, employment, and education level. Persistent sleep disturbance was associated with a greater risk of persistent knee pain (RR 1.90, 1.26-2.87) and MSP (RR 1.29, 1.07-1.56). In participants with ROA, results were similar apart from the link between sleep disturbance and persistent pain.

pain.

Conclusion: Sleep disturbance was independently associated with greater pain severity and significantly increases risk for MSP with a long-term effect of sleep on pain in general and ROA population, suggesting beneficial effects of treating sleep problems on long-term pain control.

Disclosure: F. Pan, None; **J. Tian**, None; **F. Cicuttini**, None; **G. Jones**, None.

Abstract Number: 1661

Systematic Review and Meta-Analysis of the Prevalence of Neuropathic-Like Pain and Pain Sensitisation in People with Knee and Hip Osteoarthritis

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SESSION INFORMATION
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Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Pain in osteoarthritis (OA) may be nociceptive or neuropathic-like in nature. In knee OA, pain severity is known to be poorly correlated with joint damage. Identifying a patient's pain profile may guide the provision of specific therapy. We sought to determine the prevalence of neuropathic-like pain (NP) and pain sensitisation (PS) as defined by self-report questionnaires in people with knee and hip OA.

Methods: MEDLINE, EMBASE, CINAHL were systematically searched in duplicate (1990-April 2020) for full text articles presenting the prevalence of NP and PS in knee and hip OA using self-report questionnaires, with ≥30 participants, age ≥18 years. Data were extracted into a prespecified form in duplicate. Risk of bias was assessed using the National Institute of Health Quality Assessment Tool for Observational Cohort and Cross Sectional Studies. Meta-analysis was performed using RevMan, using a random effects model. Heterogeneity between studies and subgroups was assessed using Cochran's Q and I^2 statistics.

Results: From 2706 non-duplicated references, 39 studies were included (2011-2020), from Europe (n=17), Asia (n=14), North America (n=4), Oceania (n=3) and Africa (n=1). Thirty-six studies reported on knee pain and 6 on hip pain. Study populations were recruited from hospital outpatients (n= 21), presurgical candidates (n=10), trials (n=5) and community (n=3). NP was defined using the following self-report questionnaire tools: PainDETECT (PDQ, n=30 studies), Douleur Neuropathique 4 (DN4, n=5), Self-Report Leeds Assessment of Neuropathic Symptoms and Signs (S-LANSS, n=2). PS was defined by Central Sensitisation Index (CSI, n=6) and Fibromyalgia Survey Questionnaire (FSQ n=1).

For knee OA, the prevalence of possible NP, defined by PDQ score ≥13 was 40% (95% CI 32-48%, p< 0.00001, I^2=97%). The prevalence of probable NP, defined by PDQ score ≥19 was 20% (95% CI 15-24%, p< 0.00001, I^2=94%). Using PDQ, there were no significant differences in prevalence between study population subgroups, for possible or probable NP (I^2 = 0%). The prevalence of NP using S-LANSS was 32% (95% CI 26-38%, I^2=0%, p=0.43), and using DN4 was 41% (95% CI 24-59%, p< 0.001, I^2=97%). The prevalence of PS using CSI was 36% (95% CI 12-59%, p< 0.001, I^2=95%).

For hip OA, the prevalence of possible NP (PDQ score ≥13) was 28% (95% CI 10-45%, p< 0.001, I^2=92%). The prevalence of probable NP (PDQ score ≥19) was 9% (95% CI 6-13%, I^2=0%, p< 0.00001). Using PDQ, the overall prevalence of possible NP was similar across multiple study population sources (I^2 = 0%).The prevalence of NP using DN4 was 22% in 1 study. One study used FSQ to assess PS but did not report prevalence.

Conclusion: Using self-report questionnaire tools, NP was determined to be more prevalent in knee than hip OA. Further study is required into the prevalence of PS in knee and hip OA and differences between tools. The prevalence of NP in knee and hip OA were similar for each joint across study population sources. This suggests that NP pain is unrelated to OA severity. NP may be used to phenotype patients, enabling targeted analgesic and non-pharmacological therapy in OA and potential improvement to quality of life.

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Abstract Number: 1662

Do Weight-bearing versus Non-weight-bearing Pain Reflect Different Pain Mechanisms in Knee Osteoarthritis?: The Multicenter Osteoarthritis Study

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Osteoarthritis – Clinical Poster II

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Background/Purpose: Pain with weightbearing in knee OA is thought to be related to the activation of nociceptors; however, this is not considered the sole mechanism by which pain is experienced in OA as it would not explain the

Table 1. Results for the multivariable analyses of the association between QST measures and individual or grouped WOMAC pain questions (n=5479 knees)

At least moderate pain with:	QST Measures of Pain Processing							
	PPT tertiles (patella)			PPT tertiles (wrist)			TS (per unit increase)	Efficient CPM (present/absent)
	Lowest (Ref)	Middle	Highest [least pain sensitized]	Lowest (Ref)	Middle	Highest [least pain sensitized]		
Walking n=465 (8.5%)	1.0	0.65 (0.51, 0.83)	0.45 (0.33, 0.60)	1.0	0.81 (0.62, 1.06)	0.51 (0.38, 0.69)	1.09 (0.98, 1.21)	0.88 (0.69, 1.11)
Standing n=443 (8.1%)	1.0	0.60 (0.46, 0.78)	0.51 (0.37, 0.70)	1.0	0.69 (0.51, 0.92)	0.54 (0.39, 0.76)	1.06 (0.95, 1.19)	1.06 (0.83, 1.37)
Stair Climbing n=1280 (23.5%)	1.0	0.72 (0.61, 0.84)	0.56 (0.46, 0.67)	1.0	0.88 (0.73, 1.07)	0.64 (0.52, 0.78)	1.11 (1.02, 1.19)	1.01 (0.86, 1.18)
Sitting n=309 (5.6%)	1.0	0.69 (0.52, 0.93)	0.53 (0.37, 0.76)	1.0	0.77 (0.56, 1.07)	0.72 (0.50, 1.03)	1.00 (0.88, 1.14)	1.02 (0.77, 1.35)
Lying in bed n=359 (6.6%)	1.0	0.87 (0.66, 1.13)	0.63 (0.46, 0.87)	1.0	0.92 (0.69, 1.25)	0.83 (0.59, 1.16)	1.04 (0.93, 1.16)	0.91 (0.70, 1.18)
Any Weight-bearing activity* n=989 (18.1%)	1.0	0.71 (0.60, 0.83)	0.55 (0.46, 0.66)	1.0	0.86 (0.71, 1.03)	0.64 (0.53, 0.78)	1.10 (1.02, 1.19)	0.99 (0.84, 1.16)
Any Non-weight-bearing Activities* n=77 (1.4%)	1.0	0.78 (0.61, 0.99)	0.64 (0.48, 0.85)	1.0	0.86 (0.66, 1.13)	0.76 (0.56, 1.03)	1.08 (0.97, 1.20)	0.96 (0.76, 1.22)

OR, 95% CI presented for all models. All models adjusted for age, sex, BMI, catastrophizing, depressive symptoms, and widespread pain.
*Weightbearing includes walking up- and downstairs, walking on a flat surface, and standing. Non-weight-bearing includes pain while sitting and while in bed.
Abbreviations: QST, quantitative sensory testing; PPT, pain pressure thresholds; TS, temporal summation; CPM, conditioned pain modulation. TS is presented as a continous measure.

Table 1. Results for the multivariable analyses of the association between QST measures and individual or grouped WOMAC pain questions (n=5479 knees)

pain with non-weight-bearing that often occurs. Pain sensitization, reflecting altered pain processing, may contribute to pain at rest or while sleeping. The aim of this study was to determine the extent to which pain with different degrees of weight-bearing were associated with objective measures of pain sensitization.

Methods: Participants from the Multicenter Osteoarthritis (MOST) study, a longitudinal prospective cohort of older adults with or at risk of knee OA, were included in this cross-sectional analysis. Mechanical pressure pain threshold (PPT) at the wrist and patellae were assessed with a handheld algometer, and categorized into sex-specific tertiles. Lower PPTs indicate greater sensitization. Weighted mechanical punctate probes were used to assess temporal summation (TS) at the wrist, an indicator of central sensitization, with a train of 10 stimuli at 1 Hz; increase in pain by the end of the train indicates TS. Adequacy of conditioned pain modulation (CPM) was determined by assessing PPT at the wrist (test stimulus, PPT1) with forearm ischemia as the conditioning stimulus, followed by PPT reassessment (PPT2). Adequate CPM (pain inhibition) was operationalized as PPT2:PPT1 >1. Individual WOMAC pain questions were dichotomized as having at least moderate pain on each question, and categorized into weight-bearing pain (stairs, standing, walking) vs. non-weight-bearing pain (sitting, nocturnal), based on having moderate or greater pain on at least one question. We evaluated the relation of each QST measure to WOMAC pain questions or categories using logistic regression, adjusting for age, sex, body mass index (BMI), catastrophizing, depressive symptoms, and widespread pain.

Results: 2749 subjects were included (mean age 64±11, 57% female, mean BMI 29.5±5.7 kg/m^2). Higher patellar PPT was significantly associated with lower odds of reporting at least moderate pain for each WOMAC pain question (**Table 1**), with similar magnitudes of association for weight-bearing and non-weight-bearing pain. Higher wrist PPT was significantly associated with weight-bearing activities, while TS was only significantly associated with stair climbing; neither were significant associated with non-weightbearing pain. Adequate CPM was not significantly associated with either weight-bearing or non-weight-bearing.

Conclusion: Greater peripheral sensitization, as assessed by patellar PPT, was associated with having moderate pain with both weight-bearing and non-weight-bearing activities. Wrist PPT and TS, reflecting central sensitization, were significantly associated with weight-bearing but not non-weight-bearing pain. CPM, a marker of descending pain modulation, was not significantly associated with either category of pain. Our findings may challenge the hypothesis that non-weight-bearing pain may reflect greater pain sensitization than pain while weight-bearing. The contribution of other pain mechanisms, including inflammation, should be further explored.

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Abstract Number: 1663

Walking for Exercise May Be Symptom and Structure Modifying for Those with Established OA and with Varus Alignment - Data from the Osteoarthritis Initiative

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
Session Type: Poster Session D
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Background/Purpose: Walking for exercise is recommended for knee osteoarthritis (OA) management though benefits have not been demonstrated in epidemiologic studies. We aimed to assess the relationship between walking for exercise and symptom or structure progression in those with knee OA.

Methods: This was a nested cohort study within the Osteoarthritis Initiative (OAI) of those ≥ 50 years old with radiographic OA (ROA) at baseline. A modified version of the Historical Physical Activity Survey Instrument was used to assess walking for exercise during ages ≥ 50 years old, dichotomously and with 4 levels of walking, including the referent group, those who did not walk for exercise. At baseline and 48-month visits, participants were assessed for frequent knee pain and Kellgren-Lawrence (KL) grade and medial joint space narrowing (JSN) on posterior-anterior semi-flexed knee radiographs. ROA was defined as KL ≥ 2. Outcomes were: 1) *New knee pain* - frequent knee pain absent at baseline but present at 48 months (only including those without frequent knee pain at baseline), 2) *KL worsening* - increase in KL grade, 3) *Medial JSN worsening* - increase in medial JSN score, and 4) *Improved knee pain* - frequent knee pain present at baseline but absent at 48 months (only including those with frequent knee pain at baseline). Participants with knee arthroplasty between baseline and 48 months were classified as having new knee pain and KL and Medial JSN worsening. Assessed on long limb films, the Hip-Knee-Ankle angles defined static alignment: 1) varus: ≤ -2°, 2) valgus: ≥ +2°, 3) neutral: between -2° and +2°. Including only ROA knees, we performed logistic regression using generalized estimating equations to account for correlation between knees, adjusting for age, sex, and baseline KL grade. Analyses were stratified by static alignment.

Results: Of 1203 participants, 73% walked for exercise. New knee pain was less common in those who walked (OR 0.6; 95%CI 0.4 – 0.8) (see Table). In varus knees, results were similar but also less KL (OR 0.7; 95%CI 0.5 - 1.0) and medial JSN progression (OR 0.7; 95%CI 0.5 – 0.9) was observed (See Table). Neutral and valgus analyses had insufficient numbers to calculate ORs; however in neutral knees, those who walked had more improved knee pain (47% v 39%) but no structural benefits. In valgus knees, those who walked for exercise had modestly more new knee pain (33% v. 29%), KL progression (20% v. 15%) and medial JSN worsening (9% v. 5%).

Conclusion: Walking may be disease modifying for knee OA. In individuals ≥ 50 years old with knee OA, walking for exercise was associated with less development of frequent knee pain. There may be differential effects of walking based on static alignment. In varus knees, walking was also associated with less structural progression. These findings support that walking for exercise should be encouraged for most people with knee OA. A clinical trial to confirm these findings is warranted.

Table. Odds Ratios of outcomes based on walking status; unadjusted and *adjusted for age, sex, and baseline KL grade.

	Prevalence of Outcome	Unadjusted Odds Ratios	Adjusted Odds Ratios*
ALL PARTICIPANTS			
Outcome: New knee pain			
Non-Walkers	103/280 (37%)	Referent	Referent
Walkers (Y/N)	223/852 (26%)	***0.6 (0.4 – 0.8)***	***0.6 (0.4 – 0.8)***
Low Level Walkers	74/285 (26%)	***0.6 (0.4 – 0.9)***	***0.6 (0.4 – 0.9)***
Mid Level Walkers	75/249 (30%)	0.7 (0.5 – 1.1)	0.7 (0.5 – 1.1)
High Level Walkers	74/318 (23%)	***0.5 (0.4 – 0.8)***	***0.5 (0.3 – 0.8)***
Outcome: KL worsening			
Non-Walkers	105/503 (21%)	Referent	Referent
Walkers (Y/N)	234/1305 (18%)	0.8 (0.6 – 1.1)	0.8 (0.6 – 1.1)
Low Level Walkers	75/461 (20%)	0.9 (0.7 – 1.3)	0.9 (0.7 – 1.3)
Mid Level Walkers	48/372 (16%)	0.7 (0.5 – 1.1)	0.7 (0.5 – 1.1)
High Level Walkers	61/472 (18%)	0.8 (0.6 – 1.2)	0.8 (0.6 – 1.2)
Outcome: Medial JSN worsening			
Non-Walkers	137/503 (27%)	Referent	Referent
Walkers (Y/N)	281/1305 (22%)	0.7 (0.6 – 1.0)	0.8 (0.6 – 1.0)
Low Level Walkers	102/461 (22%)	0.8 (0.6 – 1.1)	0.9 (0.6 – 1.2)
Mid Level Walkers	75/372 (20%)	0.7 (0.5 – 1.0)	0.7 (0.5 – 1.1)
High Level Walkers	104/472 (22%)	0.8 (0.6 – 1.0)	0.8 (0.6 – 1.1)
Outcome: Improved knee pain			
Non-Walkers	93/223 (42%)	Referent	Referent
Walkers (Y/N)	180/453 (40%)	0.9 (0.7 – 1.3)	0.8 (0.6 – 1.2)
Low Level Walkers	66/176 (38%)	0.8 (0.5 – 1.3)	0.8 (0.5 – 1.3)
Mid Level Walkers	49/123 (40%)	0.9 (0.6 – 1.5)	0.8 (0.5 – 1.4)
High Level Walkers	65/154 (42%)	1.0 (0.7 – 1.6)	0.9 (0.6 – 1.4)
VARUS ONLY participants			
Outcome: New Knee Pain			
Non-Walkers	66/172 (38%)	Referent	Referent
Walkers (Y/N)	123/464 (26%)	***0.6 (0.4 – 0.9)***	***0.6 (0.4 – 0.9)***
Low Level Walkers	45/147 (31%)	0.7 (0.4 – 1.2)	0.7 (0.4 – 1.3)
Mid Level Walkers	38/136 (28%)	0.6 (0.4 – 1.1)	0.6 (0.4 – 1.1)
High Level Walkers	40/181 (22%)	***0.5 (0.3 – 0.8)***	***0.4 (0.3 – 0.8)***
Outcome: KL Worsening			
Non-Walkers	83/312 (27%)	Referent	Referent
Walkers (Y/N)	141/719 (20%)	***0.7 (0.5 – 0.9)***	***0.7 (0.5 – 1.0)***
Low Level Walkers	59/252 (23%)	0.8 (0.6 – 1.3)	0.9 (0.6 – 1.3)
Mid Level Walkers	32/201 (16%)	***0.5 (0.3 – 0.8)***	***0.5 (0.3 – 0.9)***
High Level Walkers	50/266 (19%)	***0.6 (0.4 – 1.0)***	***0.7 (0.4 – 1.0)***
Outcome: Medial JSN Worsening			
Non-Walkers	120/312 (38%)	Referent	Referent
Walkers (Y/N)	196/719 (27%)	***0.6 (0.5 – 0.8)***	***0.7 (0.5 – 0.9)***
Low Level Walkers	67/252 (27%)	***0.6 (0.4 – 0.9)***	***0.7 (0.4 – 1.0)***
Mid Level Walkers	53/201 (27%)	***0.6 (0.4 – 0.9)***	***0.6 (0.4 – 1.0)***
High Level Walkers	76/266 (29%)	***0.6 (0.4 – 0.9)***	***0.7 (0.5 – 1.0)***
Outcome: Improved Knee Pain			
Non-Walkers	58/140 (41%)	Referent	Referent
Walkers (Y/N)	94/255 (37%)	0.8 (0.5 – 1.3)	0.8 (0.4 – 1.1)
Low Level Walkers	38/105 (36%)	0.8 (0.5 – 1.4)	0.7 (0.4 – 1.3)
Mid Level Walkers	26/65 (40%)	0.9 (0.5 – 1.8)	0.8 (0.4 – 1.6)
High Level Walkers	30/85 (35%)	0.8 (0.4 – 1.4)	0.6 (0.3 – 1.1)

Table 1. Odds Ratios of outcomes based on walking status; unadjusted and *adjusted for age, sex, and baseline KL grade.

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Abstract Number: 1664

Walking Energetics, Fatigue, and Physical Activity in People with Knee Osteoarthritis

Kharma Foucher[1], Burcu Aydemir[1] and Chun-Hao Huang[1], [1]University of Illinois at Chicago, Chicago, IL

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis – Clinical Poster II
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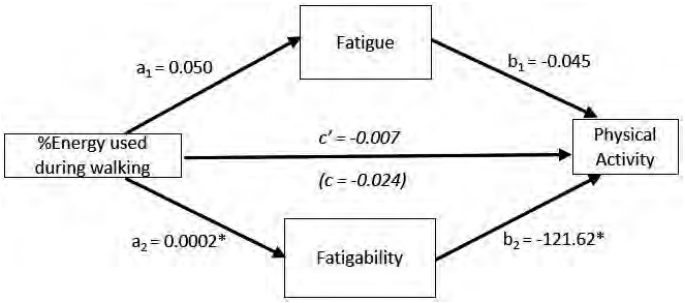
Background/Purpose: Osteoarthritis (OA) is associated with limitations in physical activity (PA) for many reasons which are not fully understood. While pain can be associated with reduced PA, other biomechanical and psychological factors can also be limiting. Walking energetics, specifically the amount of energy used for walking relative to total energy capacity, has been proposed as a mechanism by which PA is reduced in older adults. Fatigue is a common symptom of OA and has been linked to reduced PA in this group. Fatigability is a separate but related construct that may also be associated with PA in people with OA. These factors have not been previously investigated together. The purpose of this study was to evaluate the association of walking energetics, fatigue, and fatigability on PA in people

Table 1. Associations between UCLA activity scores and predictor variables.

	% Energy used for walking	VO_2cost	Fatigue Score	Fatigability Score	KOOS pain score
Spearman's Rho	-0.379	-0.517	-0.585	-0.573	0.569
p value	0.042	0.004	< 0.001	0.001	0.001



Fatigability mediates the association between percent energy used for walking and physical activity.

with knee OA. We hypothesized that people who use an increased amount of energy for walking, experience more fatigue, or are more fatigable are less active.

Methods: We tested our hypothesis in 29 people with knee OA (age 58 ± 9 years, 10 M/19 F, BMI 33.5 ± 5.8 kg/m^2). We assessed PA by self-report using the UCLA activity score. We used a six-minute walk test to measure VO_2max, then used a portable oxygen exchange system to measure percent energy used during walking (100 * VO_2rate/VO_2max) and VO_2cost at preferred speeds. We used the KOOS pain subscale to characterize pain. We used the PROMIS Fatigue survey and a treadmill-based fatigability test to assess overall fatigue and performance-related fatigability. We used Spearman correlations and regression analysis to test our hypotheses.

Results: UCLA scores ranged from 2, indicating "mostly inactive", to 10, indicating "regularly participate in impact sports" (mean 5 ± 2). Percent energy used during walking, VO_2cost, fatigue, and fatigability were all associated with lower PA (Table 1). These associations persisted when controlling for pain. Together, pain, percent energy used for walking or VO_2cost, fatigue and fatigability predicted 57.7 to 58.4% of the variance in UCLA scores ($p < 0.001$). Fatigability mediated the association between percent energy used for walking and PA (Figure 1). There was no evidence that fatigue or fatigability mediated the association between VO_2cost and PA.

Conclusion: Walking energetic factors are important predictors of PA in knee OA even after controlling for pain. The effect of walking energetics on PA may work through its impact on fatigability. Walking energetics may be a useful target to promote PA in people with OA and may have beneficial effects on fatigue as well. The effect of biomechanical interventions for knee OA on walking energetics should be considered to avoid potential adverse effects on PA.

Disclosure: K. Foucher, None; **B. Aydemir**, None; **C. Huang**, None.

Abstract Number: 1665

Sociodemographic and Clinical Predictors of Childhood-Onset SLE Disease Activity in the Childhood Arthritis and Rheumatology Research Alliance Registry

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with childhood-onset systemic lupus erythematosus (cSLE) are at high risk for early morbidity and mortality, but predictors of moderate/high cSLE disease activity have not been well-studied. Our objective was to determine sociodemographic and clinical predictors for moderate/high disease activity scores in a cohort of North American cSLE patients. Our hypothesis was minority race/ethnicity, lower household income, lower parental education, and non-private insurance status would be associated with moderate/high disease activity at follow-up.

Table 1. Sociodemographic and Clinical Predictors of Disease Activity at Most Recent Follow-up Visit				
	Total Cohort (n=423)	SLEDAI-2K ≤ 4 (n=310)	SLEDAI-2K > 4 (n=113)	p-value
Sociodemographic Characteristics				
Female, n (%)	359 (85)	259 (84)	100 (89)	0.2090
Minority race / ethnicity, n (%)	317 (75)	234 (75)	83 (73)	0.6695
Household income, n (%)				0.4342
<$25,000	55 (13)	36 (12)	19 (17)	
$25-74,999	98 (23)	70 (23)	28 (25)	
>$75,000	189 (45)	144 (46)	45 (40)	
Unknown/Prefer not to answer	81 (19)	60 (19)	21 (19)	
Parent education level, n (%)				0.9438
≤High school	131 (31)	97 (31)	34 (30)	
At least some college	205 (48)	150 (48)	55 (49)	
Unknown/Prefer not to answer	87 (21)	63 (20)	24 (21)	
Non-private insurance status, n (%)	211 (50)	148 (48)	63 (56)	0.1449
Clinical Characteristics				
Age at diagnosis, mean (SD)	13.8 (2.9)	13.7 (2.9)	14.0 (2.9)	0.1477
Number of ACR classification criteria, mean (SD)	5.2 (1.6)	5.0 (1.6)	5.7 (1.6)	0.0004
Number of SLICC classification criteria, mean (SD)	8.2 (2.6)	7.9 (2.5)	8.9 (2.5)	0.0004
Presence of lupus nephritis, n (%)	175 (41)	129 (42)	46 (41)	0.8672
Presence of neuropsychiatric lupus, n (%)	117 (28)	78 (25)	39 (35)	0.0571
Symptom onset to diagnosis, mean (SD) months	6.5 (12.0)	6.8 (13.0)	5.6 (8.4)	0.9939
Diagnosis to CARRA Registry enrollment, mean (SD) months	13.8 (20.0)	14.4 (20.1)	12.0 (19.7)	0.0129
Diagnosis to most recent follow-up visit, mean (SD) months	27.1 (22.2)	27.9 (22.3)	24.7 (21.7)	0.0609
SLEDAI-2K at enrollment, median (IQR)	4 (1-10)	2 (0-8)	7 (2-13)	0.0129
Physician global assessment of disease activity (0-10) at enrollment, median (IQR)	2 (0.5-4)	2 (0-3)	3 (2-5)	0.0332

Table 1. Sociodemographic and Clinical Predictors of Disease Activity at Most Recent Follow-up Visit

Methods: The Childhood Arthritis and Rheumatic Disease Research Alliance (CARRA) Registry enrolls patients with cSLE from >65 North American pediatric rheumatology centers. We performed a cross-sectional analysis of CARRA Registry data collected prospectively from March 2017 to December 2019. Patients with cSLE or probable cSLE with at least two study visits at least 6 months apart were included. Disease activity at most recent follow-up visit was measured using **Systemic Lupus Erythematosus Disease Activity Index 2000 (**SLEDAI-2K, range 0-105) and dichotomized as low disease activity, SLEDAI-2K ≤ 4, or moderate/high disease activity, SLEDAI-2K > 4. Chi-square and two-sample Student *t* tests were performed to compare sociodemographic and clinical characteristics between patients with low vs. moderate/high disease activity at most recent follow-up. Multivariable logistic regression was conducted to determine predictors for SLEDAI-2K > 4 at most recent follow-up.

Results: There were 423 eligible patients with cSLE (Table 1). The mean ± SD time from diagnosis to most recent follow-up was 27.1 ± 22.2 months. The cohort was 85% female, 27% Black, 25% White, 24% Hispanic, and 17% Asian with a mean ± SD age at diagnosis of 13.8 ± 2.9 years. Lupus nephritis was present in 41% and neuropsychiatric

Table 2. Multivariable-Adjusted Odds Ratios for SLEDAI > 4		
Variable	Odds Ratio (95% CI)	*p* value
Female	1.328 (0.635-2.780)	0.4512
Non-white race/ethnicity	0.748 (0.408-1.371)	0.3470
Household income		
$25-74,999	referent	
<$25,000	1.164 (0.479-2.829)	0.7373
>$75,000	0.806 (0.411-1.582)	0.5305
Parent education level		
≤High school	0.655 (0.300-1.430)	0.2886
At least some college	0.896 (0.434-1.850)	0.7669
Non-private insurance status	1.395 (0.792-2.457)	0.2495
Age at diagnosis	1.054 (0.957-1.162)	0.2828
Presence of lupus nephritis	1.242 (0.727-2.121)	0.4283
Presence of neuropsychiatric lupus	0.894 (0.503-1.589)	0.7022
Symptom onset to diagnosis	0.992 (0.970-1.014)	0.4603
Diagnosis to enrollment	1.009 (0.968-1.051)	0.6779
Diagnosis to follow-up visit	0.997 (0.961-1.033)	0.8558
SLEDAI-2K at enrollment	1.044 (1.003-1.086)	0.0333
PGA at enrollment	1.161 (1.029-1.310)	0.0153

Table 2. Multivariable-Adjusted Odds Ratios for SLEDAI > 4

lupus in 28%. At the most recent visit, the range of SLEDAI-2K scores was 0-25, and 27% of patients had SLEDAI-2K > 4. Results of univariate analyses showed there were not statistically significant differences in sociodemographic variables between patients with low vs. moderate/high disease activity (Table 1). However, patients with moderate/high disease activity at most recent follow-up had statistically higher number of ACR and SLICC criteria, SLEDAI-2K at enrollment, and physician global assessment (PGA) at enrollment and shorter time from diagnosis to enrollment (Table 1). Using multivariable logistic regression adjusted for disease duration, SLEDAI-2K at enrollment (OR=1.04, 95% CI=1.003–1.086) and PGA at enrollment (OR=1.16, 95% CI=1.029–1.310) remained independently associated with moderate/high disease activity.

Conclusion: This analysis demonstrates a substantial proportion of patients with cSLE in the CARRA Registry have moderate/high disease activity at most recent follow-up. Disease activity at registry enrollment, measured by SLEDAI-2K and PGA, was the only predictor of moderate/high disease activity. Interestingly, sociodemographic charac-

teristics did not predict moderate/high disease activity. Improved understanding of modifiers of cSLE disease activity is needed for the development of targeted interventions to improve outcomes.

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Abstract Number: 1666

Elucidating Research Priorities in Childhood-Onset Systemic Lupus Erythematosus: A Qualitative Study

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: An estimated 15 to 20% of patients with systemic lupus erythematosus (SLE) have childhood-onset SLE (cSLE). Given the early onset of cSLE, patients often experience significant burden due to cSLE disease, comorbidities and immunosuppressive treatment. There is a pressing need for high quality, comprehensive research efforts to define the natural history, best treatments, access to care and disparities in care for cSLE patients. Building on a previously published survey study of clinicians caring for cSLE patients to describe research priorities in cSLE, the primary objective of this study was to conduct expert interviews to define a cSLE research agenda.

Methods: Individuals with identified expertise in cSLE were recruited worldwide using a purposive sampling technique including providers from several disciplines: pediatric rheumatology, pediatric nephrology, dermatology, psychiatry, medicine/pediatrics, and adolescent medicine. Experts participated in open-ended, semi-structured qualitative interviews. Interviews were designed to elicit expert perspectives on research priorities, optimal research approaches, and factors that facilitate and hinder advancing cSLE research. Interviews were digitally recorded, transcribed, and de-identified for qualitative analysis. 30 interviews were conducted between January and May 2020. Analysis for underlying themes of cSLE expert perspectives was performed using a constant comparative approach in which summaries and themes of each expert's interview transcript informed the presence or absence of themes in subsequent cases (iteration). Two researchers conducted the analysis. To establish a consistent identification of themes, the first third of transcripts were analyzed by both researchers. The remaining transcripts were summarized by one researcher followed by a review from the second researcher to look for any missed additional elements.

Results: Several notable themes emerged from analysis of the interview data, supported by illustrative quotes (Table). A salient priority identified among interviewees was the importance of better (and more targeted) treatment for cSLE. Two major barriers to the development of new therapies were lack of pediatric clinical drug trials and need for biomarker research. Interviewees also identified individual investigator barriers to performing cSLE research, including obtaining funding to conduct projects, and having adequate time to conduct research. Last, collaboration was

cSLE Research Priority and/or Barrier	Quote
Need for new medications and targeted therapies	"And I think right now we're finding drugs that might work in a small subset of people and then throwing them at the whole group of lupus at large and often not seeing results which is really not surprising. So really molecularly genetically immunophenotyping our patients and then finding subsets, identifying potential targets for discovery or potential targets for tailoring appropriate therapy. That's what I see is the biggest gap." "…we know that we have certain drugs for treatment for lupus, but we don't know some of the differences in different populations. So is the Hispanic population that's in Texas and California, do they react the same way to medications as maybe our African-American group that is here in [State 1] or in [State 2]? And then…Caucasian males tend to have really severe lupus nephritis when they actually get lupus, which is rare, but why is that?"
Need for more pediatric clinical trials	"So better alignment of the pharmaceutical companies' motivations and needs with the FDA's perspective as to physicians and with the clinicians' desires and patients' desires in terms of the drugs, is important" "So, I would say that inclusion of children in clinical trials of emerging therapies for lupus is of the utmost importance, so that they can have access to newly developed therapies very early on in their life cycle."
Need for biomarker research and better understanding of disease biomarkers	"[I] think that making sure that tissue was included in [a registry] as well – so not just blood and urine, but also kidney tissue from kidney biopsies and skin tissue from – some punch biopsies and if we can get joint tissue from – or joint fluid or anything like that – I think that those sorts of things are big, huge investments." "But if you asked me to prioritize, I would say biomarkers, looking at precision-based treatments based on pathophysiology's, and then sorting through clinical phenotypes so that when we think through therapy, we're comparing the right groups and we're thinking about the right outcomes… It's not a single cell disease that we can study and think about in clean way. I think that's why, in some ways, any biomarker analysis has to start with a cohesive homogenous clinical phenotype of patients. And so, trying to stratify out what the buckets we should be looking at to do that work becomes really complicated when this is 5, or 10, or 15 diseases and not one."
Need for more funding resources for investigators and dedicated protected time to conduct research	"And I feel like, as physicians, our time gets sort of fractionated into these teeny little pieces like three days a week we're in clinic all day. And then, those days you're basically like a shift worker. You have absolutely no time. And then the other days you get pulled into meetings, things appear on your calendar. There's almost no space to think and write and be creative. And, without that, I don't think we can move this work forward." "And then another barrier is that…we have a very worrisome shortage of people doing basic and translational investigation in pediatric rheumatology. And we don't have the manpower within our workforce to do this – because there are so few pediatric rheumatologists, most of them with the exception of a few big centers are required to do a large burden of clinical care. And it's really tough then to, A, find the people to do it who have the time to do it and, B, have the mentors who can teach the next generation to do it and I think that's a huge problem that we need to address."
Need for collaboration between centers	"I think we need to come up with better ways to fund and to reward involvement in collaborative research…for example – if people are calling in once a month to be on a workgroup to design a research study, no one's getting reimbursed for that time. And so…if we want to have the CARRA registry succeed, we need to be able to reimburse the PIs and the sites for what they're doing to enroll those patients and to get all those patients' data shared." "And as much as we can, we try to work together with other sites. You know, one site chosen as the where the principle investigator is, and then multiple other sites contributing patients, or samples, or whatever it is depending on the study. I think that's really the key in this disease, in a rare disease. In any rare disease collaboration is the key for research."

Table: Illustrative quotes from cSLE providers discussing research priorities and barriers to advancement of research for cSLE.

identified as a necessity within the cSLE research community, recognizing The Childhood Arthritis and Rheumatology Research Alliance (CARRA) as a powerful tool for multi-center collaboration in cSLE research.

Conclusion: cSLE expert interviewees identified the need for improved targeted therapies through pediatric clinical drug trials and biomarker research as well as collaboration between researchers and centers as research priorities. Funding and protected time for research are major individual barriers to involvement in cSLE research.

Disclosure: L. Cannon, None; **A. Skelley-Caliendo**, None; **A. Hersh**, None; **A. Knight**, None.

Abstract Number: 1667

Development of Autoimmune Diseases and HLA Associations in Children with Neonatal Lupus and Their Unaffected Siblings

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SESSION INFORMATION
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Background/Purpose: Neonatal Lupus (NL) is a model of passively acquired autoimmunity conferred by exposure to maternal anti-Ro antibodies with major manifestations being congenital heart block (CHB) and/or cutaneous disease. This study was initiated to address the development of de novo autoimmunity in these children and identify associated clinical and genetic risk factors.

Methods: In a retrospective cohort study of enrollees in the Research Registry for Neonatal Lupus (RRNL), 511 children exposed to anti-Ro in utero responded to a follow up questionnaire focused on symptoms of autoimmunity. Self-reported diseases were confirmed via medical record review. Bivariate analyses were performed with potential risk factors for the development of autoimmune disease (AD) and included the NL status per se, a disease severity score based on mortality risk factors, and maternal AD (inclusive of lupus, Sjogren's syndrome, psoriasis, rheumatoid arthritis, or thyroid disease). A subset of 99 CHB, 9 cutaneous, and 55 unaffected anti-Ro exposed RRNL individuals were genotyped at Class II HLA DRB1 and DQB1 four-digit alleles, which were assigned by imputation (HIBAG) or sequencing. Generalized estimating equations (logit link, exchangeable correlation) were used to test for associations between HLA alleles and the development of AD.

Results: Of the respondents, 182 offspring had CHB, 95 had cutaneous only NL and 234 were siblings without NL. Females comprised 53% and 80% were Caucasian. The mean age was 14.2±9.7; 4% age 0-2 years, 48% 2-13 years, and 47% > 13 years. An AD developed in 38 offspring (20 CHB, 7 cutaneous NL, 11 non-NL siblings; Table 1). The most prevalent AD was thyroid disease. The development of an AD was significantly associated with presence of CHB vs. cutaneous only or non-NL siblings (11% vs. 5%, p=0.033). The maternal health status did not influence the development of an AD in the child (7% mothers with AD vs. 6% asymptomatic mothers, p=0.67). Mean NL severity score was higher in offspring with AD (3.8±4.8 vs. 2.2±4.0, p= 0.031). Other markers of fetal CHB disease severity were associated with subsequent AD development, including in-utero exposure to fluorinated steroids (15% vs. 6%, p=0.088) and beta agonists such as terbutaline (23% vs. 9%, p=0.043). In the study of 163 RRNL cases with HLA data (20 with AD, 143 without), HLA DRB1*03:01 (OR 3.4, CI 1.46-7.90, p=0.0045), DQA1*05:01 (OR 3.39, CI 1.16-9.92, p=0.0262), and DQB1*02:01 (OR 4.28, CI 1.73-10.62, p=0.0017) were associated with increased risk of AD (of

Subject	Gender	Race	NL Manifestation	Autoimmune Diagnosis	Age of diagnosis (years)	Maternal Rheumatic Disease	NL Severity Score
1	M	C	CHB	Hypothyroid	0	SLE/SS	5
2	F	C	CHB	Hypothyroid	0.1	SS	NA
3	F	C	CHB	Psoriasis/T1D	3/10	SS	14
4	M	C	CHB	ITP	3.5	SLE	8
5	F	C	CHB	Celiac/Hypothyroid	4/6	SLE	5
6	M	C	CHB	T1D	5	Asymptomatic	NA
7	M	C	CHB	T1D/Hypothyroid	6.5/8	Asymptomatic	5
8	F	C	CHB	JIA	7	SS	8
9	F	C	CHB	Psoriasis/Iritis	8/12	Asymptomatic	5
10	M	O	CHB	T1D	10	Asymptomatic	8
11	F	C	CHB	T1D/Hypothyroid	12/23	Asymptomatic	5
12	M	C	CHB	IBD	12	SLE	NA
13	M	C	CHB	Hypothyroid	15	SS	5
14	M	C	CHB	IBD	17	Asymptomatic	5
15	F	C	CHB	Scleroderma	20	Asymptomatic	5
16	F	C	CHB	Hypothyroid	31	SS	NA
17	F	C	CHB	SS	33	SS	14
18	F	C	CHB	UAS (ANA, arthralgias, ESR, Raynaud's)	43	SLE	14
19	M	A	CHB	Alopecia Aresta, Atopic Dermatitis	NA	Asymptomatic	14
20	F	O	CHB	JIA	NA	SS	8
21	F	C	Cutaneous	Autoimmune thyroiditis with hyperthyroid	5	Asymptomatic	0
22	F	C	Cutaneous	Grave's Disease	8	SLE/SS	0
23	F	O	Cutaneous	Hypothyroid	10	Asymptomatic	0
24	M	C	Cutaneous	Psoriasis	13	SLE	0
25	F	C	Cutaneous	UAS (ANA, centromere, joint pains, sicca symptoms)	17	SS	0
26	M	C	Cutaneous	IBD	19	SLE/SS	0
27	F	C	Cutaneous	Hypothyroid	26	SLE/SS	0
28	F	O	Asymptomatic	T1D	4	Asymptomatic	0
29	M	C	Asymptomatic	T1D	5	SLE/SS	0
30	F	C	Asymptomatic	Autoimmune Aplastic Anemia	7	SS	0
31	M	C	Asymptomatic	T1D/Hypothyroid	8/8	Asymptomatic	0
32	M	O	Asymptomatic	Psoriasis	9	SS	0
33	F	C	Asymptomatic	Hypothyroid	9	SLE/SS	0
34	M	C	Asymptomatic	Hypothyroid	17	Asymptomatic	0
35	M	C	Asymptomatic	IBD	18	SLE	0
36	F	C	Asymptomatic	Celiac Disease	18	SS	0
37	F	C	Asymptomatic	SLE/SS	21/21	SLE/SS	0
38	M	C	Asymptomatic	Sarcoidosis	22	SLE/SS	0

M = Male; F = Female; C = Caucasian; O = Other Race; A = Asian; CHB = Congenital Heart Block; T1D = Type 1 Diabetes; ITP = Immune Thrombocytopenic Purpura; JIA = Juvenile Idiopathic Arthritis; IBD = Inflammatory Bowel Disease; UAS = Undifferentiated Autoimmune Syndrome; SLE = Systemic Lupus Erythematosus; SS = Sjogren's Syndrome; NA = Not Available

Table 1

note, these loci are in high linkage disequilibrium). In contrast, these alleles were not significantly associated with development of CHB (99 CHB vs. 64 without).

Conclusion: The development of an autoimmune disease was more common in anti-Ro exposed children with CHB, greater NL severity, and MHC Class II haplotypes. These factors may relate to an inherent susceptibility to inflammation and fibrosis, occuring in utero and later in life.

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Abstract Number: 1668

Long-Term Outcomes in Children Born to Anti-Ro and/or Anti-La Positive Mothers

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

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Background/Purpose: Neonatal Lupus Erythematosus (NLE) is an acquired autoimmune disorder associated with the transplacental passage of maternal anti-Ro and/or anti-La antibodies. Previous studies have suggested that children born to anti-Ro/La antibody positive mothers with a rheumatic disease, might be at greater risk of developing autoimmune and non-autoimmune diseases, as children or young adults. The aim of this study was to determine the prevalence of autoimmune and non-autoimmune diseases in children born to anti-Ro/La positive mothers.

Methods: We conducted a cohort study of infants seen in the NLE clinic at SickKids Hospital between 1987-2019. Infants born to anti-Ro/La antibody positive mothers in the Greater Toronto Area were referred to the NLE clinic. Surveys were sent to those children discharged from the NLE clinic and consented to this study. We invited parents of patients ≥ 1y and < 18 years of age, and patients >18 y of age to complete a follow-up questionnaire via RED-Cap survey link. The survey included questions about autoimmune diseases such as rheumatic diseases (arthritis, connective tissue disease, vasculitis) and non-rheumatic diseases (psoriasis, thyroid disease, inflammatory bowel disease, type I diabetes), and non-autoimmune diseases such as allergic (seasonal allergies, anaphylaxis, asthma, eczema, urticaria), neurodevelopmental (autism, attention deficit hyperactivity disorder, global developmental delay), and neuropsychiatric diagnoses (anxiety, depression, tics, seizures, obsessive-compulsive disorder). NLE manifestations and maternal disease status during pregnancy were obtained from a dedicated database prospectively collected. Descriptive statistics were used for demographic characteristics and clinical features of NLE. Prevalence of autoimmune and non-autoimmune diseases were compared using Fisher's exact test.

Results: We sent 354 surveys with a completion rate of 61% (n=217). Eight patients were excluded due to unconfirmed antibody status during pregnancy. We included 209 children born to 166 unique mothers. Median age at questionnaire completion was 6 years (IQR: 3,11), 50% female (**Table 1)**. Forty-seven percent (n=96) of the children had NLE, and 67% (n=141) of the children were born to a woman with a rheumatic disease diagnosis during pregnancy. In our cohort, allergic diseases were the most frequent reported at 28% (n=59) and only 6 patients (3%) had developed

Table 1: Characteristics of children born to women with positive anti-Ro and/or anti-La antibodies (n=209)

Characteristics	n (%)
Female	105 (50)
Age (median, IQR years)	6 (3, 11)
Ethnic Group	
European	65 (31)
Non-European	69 (33)
Mixed	39 (19)
Missing ethnicity	36 (17)
Children with NLE manifestations*	96 (47)
Hepatic	56 (58)
Hematologic	37 (39)
Cutaneous	18 (19)
Cardiac	12 (13)
Neurologic	6 (6)
Maternal health status during pregnancy	
Rheumatic disease	141 (67)
SLE	101 (72)
SS	23 (16)
RA	11 (8)
Other**	6 (4)
No rheumatic disease	68 (33)

*NLE disease status missing in 4 patients.
**Other rheumatic diseases: Antiphospholipid syndrome, Fibromyalgia, Overlap syndrome, Rheumatoid Arthritis, Undifferentiated connective tissue disease, Mixed connective tissue disease.

Table 1. Characteristics of children born to women with positive anti-Ro and/or anti-La antibodies (n=209)

Table 2: Reported Disease Diagnosis of Children Born to Women with and without a Rheumatic Disease Status during Pregnancy (n=209)

Disease	Children born to women with rheumatic disease (n=141) n (%)	Children born to women with no rheumatic disease (n=68) n (%)	p-value
Autoimmune			
Rheumatic	1 (1)	1 (1)	0.54
Non-Rheumatic	2 (1)	2 (3)	0.59
Allergic	43 (30)	16 (24)	0.32
Neurodevelopmental	16 (11)	6 (9)	0.63
Neuropsychiatric	8 (6)	2 (3)	0.50

Table 2. Reported Disease Diagnosis of Children Born to Women with and without a Rheumatic Disease Status during Pregnancy (n=209)

autoimmune diseases. There was no difference in the prevalence of reported diseases/conditions between children born to a mother with or without rheumatic disease (**Table 2)**.

Conclusion: In our multiethnic population of children born to women with positive anti-Ro and/or anti-La antibodies, there was no significant difference in the prevalence of autoimmune and non-autoimmune diseases between children with and without NLE manifestations, or born to women with and without a rheumatic disease during pregnancy. This is one of the largest cohort studies investigating long-term outcomes in this population. Continued recruitment of older participants will improve our ability to detect diseases with onset in young adulthood.

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Abstract Number: 1669

Genetics of Age at Diagnosis in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Genome wide association studies (GWAS) have identified >90 SNPs associated with systemic lupus erythematosus (SLE) risk. However, there may be additional loci impacting the age of diagnosis. The purpose of this study is to identify genetic variants for age of SLE diagnosis.

Methods: Our cohort included patients with childhood-onset SLE (cSLE) diagnosed < 18 years of age, and adult-onset SLE (aSLE), who met ACR and/or SLICC classification criteria for SLE. All patients were followed at tertiary care centers: Toronto Western Hospital, Hospital for Sick Children (Toronto), University of Manitoba (Winnipeg), Lurie Children's Hospital of Chicago, St. Joseph's Health Centre (London, ON), and Hospital for Special Surgery (New York). We censored patients with age at diagnosis ≥ 70 years. Patients were genotyped on the Illumina Multiethnic Array (MEGA), and ungenotyped SNPs were imputed using the Haplotype Reference Consortium (HRC) reference. We restricted to SNPs with a minor allele frequency (MAF) ≥ 0.01 and imputation quality ≥ 0.8. Ancestry was genetically inferred from principal components (PCs) and ADMIXTURE calculated in reference to 1000 Genome Project (1KGP). Non-HLA, additive SLE weighted genetic risk scores (GRSs) were computed using published SLE GWAS log-odds ratio weights. Single-variant genome-wide linear regression of age of SLE diagnosis was performed with GENESIS. Multivariate models were adjusted for sex, aSLE/cSLE status, indicator for center, 5 PCs and SLE non-HLA GRS. We

Age SLE diagnosis, years (Median [IQR])		Total (n=1093)	cSLE (n=589)	aSLE (n=504)
		17.1 [13.6, 30.8]	13.9 [11.5, 15.8]	32.2 [25.4, 42.6]
Sex	**Sample size (%)**			
Female	957 (88)	17.6 [13.8, 31.8]	14.1 [11.5, 15.8]	32.1 [25.5, 42.5]
Male	136 (12)	15.1 [12.5, 22.1]	13.3 [11.7, 15.6]	32.2 [24.4, 44.1]
Ancestry				
European	390 (36)	21.0 [14.5, 36.6]	14.3 [11.9, 16.0]	34.3 [26.8, 45.5]
East Asian	248 (23)	16.6 [13.3, 25.8]	14.2 [11.9, 16.0]	30.8 [23.9, 40.3]
African	130 (12)	19.5 [14.5, 33.1]	14.4 [11.6, 16.3]	32.9 [25.8, 41.0]
South Asian	74 (7)	17.2 [13.5, 30.4]	13.6 [10.4, 15.5]	30.6 [26.3, 45.5]
Amerindian	52 (5)	15.4 [13.0, 30.0]	13.4 [12.1, 15.3]	33.2 [25.2, 39.1]
Admixed	199 (18)	15.9 [12.4, 24.7]	13.2 [10.1, 15.7]	29.6 [23.1, 38.8]

Table 1. Age at systemic lupus erythematosus diagnosis, overall and stratified by sex and ancestry

also completed a genome-wide test of cSLE risk (vs. aSLE) using a logistic regression model adjusted for the same covariates.

Results: Our cohort included 1093 patients, 88% female. 36% were of European ancestry, 23% East Asian and 18% Admixed. The median age at diagnosis was 17.1y (IQR 13.6, 30.8) (Table 1). We included 8.9M SNPs in GWAS. The most significant SNP associated with age at SLE diagnosis in the linear model was on chr11, rs138239231 (Beta 10.0y, SE 1.85y, $P=5.73x10^{-8}$, MAF 0.01) upstream of *DHCR7* and *NADSYN1*. *DHCR7* encodes an enzyme involved in cholesterol metabolism, and *NADSYN1* encodes a coenzyme involved in metabolic redox reactions and cell signalling. The second locus on chr14 (rs144180822: Beta 5.7y, SE 1.15y, $P=7.15x10^{-7}$, MAF 0.03) is intronic to *NUBPL*, a gene encoding an iron/sulfur protein involved in the assembly of a mitochondrial inner membrane enzyme. In the logistic model, the most significant SNPs were on chr1, rs12024309 upstream to anti-sense RNA *SMG7-AS1* (OR 0.5, [95% CI: 0.4, 0.7], $P=1.16x10^{-6}$, MAF 0.39); chr4, rs10001705 upstream to *HS3ST1,* involved in the biosynthesis of anticoagulant heparin sulfate (OR 3, [95% CI:1.9, 4.6], $P=1.31x10^{-6}$, MAF 0.11); on chr17, rs116981214, intronic to *MRPL45P2*, a mitochondrial ribosomal protein (OR 4.7, [95% CI: 2.5, 8.7], $P=1.46x10^{-6}$, MAF 0.05). None of these loci reached genome-wide significance ($P< 5x10^{-8}$).

Conclusion: In our multiethnic cSLE and aSLE cohort, GWAS did not identify a genome-wide significant SNP association with the age at diagnosis or cSLE risk. We identified 2 loci near genome-wide significance for age at SLE diagnosis, and 3 near genome-wide significance for cSLE risk. We plan to expand our analyses including more patients.

Disclosure: R. Carlomagno, None; **F. Liao**, None; **J. Cao**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **M. Klein-Gitelman**, None; **A. Knight**, None; **D. Levy**, None; **K. Onel**, None; **A. Paterson**, None; **C. Peschken**, GSK, 5, Eli-Lilly, 5, Astra Zeneca, 5; **J. Pope**, AbbVie, 2, 5, Amgen, 5, 8, Lilly, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 5, 8, Sandoz, 5, 8, Roche, 2, 5, 8, Pfizer, 5, 8, Novartis, 5, 8, Merck, 2, 5, 8, Janssen, 5, 8, Gilead Sciences, Inc., 2, 5, BMS, 2, 5, 8, Abbott, 5, Actelion, 5, AstraZeneca, 5, Bayer, 5, Boehringer Ingelheim, 5, EICOS, 5, Emerald, 5, GlaxoSmithKline, 5, Medexus, 5, Seattle Genetics, 2; **Z. Touma**, None; **M. Urowitz**, None; **D. Webber**, None; **J. Wither**, None; **E. Silverman**, None; **L. Hiraki**, None.

Abstract Number: 1670

Low Copy Number of Long C4 Genes Is a Genetic Risk Factor for Childhood Onset SLE (cSLE) but Is Associated with Higher Age of Disease Onset

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Hypocomplementemia is a marked feature of systemic lupus erythematosus (SLE), which may be a result of consumption initiated by immune complexes between self-nuclear antigens and autoantibodies. Lower copy number of C4 genes is cited as a risk factor for SLE. Located in the MHC class III region on chromosome 6, there are two versions of C4 genes: the long gene and the short gene. This variation is triggered by the integration of an endogenous retrovirus HERV-K(C4) into intron 9 of the long genes. The role that long and short C4 genes plays in SLE pathogenesis remains unclear. This is especially important for childhood onset SLE (cSLE), as childhood-onset SLE conveys worse disease outcomes when compared to adult onset SLE. To help further understand the role of C4 genetic variants in the immune pathogenesis of cSLE, we performed a cross-sectional case-control study of 37 patients with cSLE (mean age: 19.08±3.22 yo; 81.1% female) and 40 healthy children (mean age: 19.30±3.75 yo; 75% female).

Methods: EDTA-Blood samples were obtained after informed consent and assent. Blood differentials for all samples were measured using a Sysmex automated hematology analyzer. Plasma protein concentrations of complement C4 and C3 were assayed by radial immunodiffusions (Binding Sites, UK); polymorphisms of C4 proteins for C4A and C4B allotypes were determined by immunofixation; gene copy numbers of total C4, C4A, C4B, long C4 genes and short C4 genes were elucidated by multiple genomic Southern blot analyses. Binary analyses of categorical data were performed by Chi^2 analyses. Continuous data between groups were compared by Student's t-test or analyzed by linear regression. Because of small sample size, our pilot analysis is focused on Caucasian patients (N=21) and Caucasian healthy controls (N=31).

Results: We observed significantly lower lymphocyte counts (1.81±0.87 $x10^3$ /ml vs 2.51±0.75x $x10^3$ /ml, p=0.0004) and complement C4 plasma protein concentrations (19.8±7.7 mg/dL vs 25.4±7.4 mg/dL; p=0.002), plus lower C4 protein yield per copy of C4 genes (5.63±1.84 mg/dL vs 6.59±1.79 mg/dL; p=0.025) in cSLE patients than in controls. The mean protein levels for complement C3 were similar between patients and controls (126.4 vs 133.0, p=0.25). Genetically, the copy number of long C4 genes was significantly lower among cSLE patients (2.30±1.081) than controls (2.903±0.944; p=0.04). Subjects with only one or two copies of long C4 genes had an odds ratio of 6.36 (95% CI: 1.83-22.1) on genetic risk of cSLE (p=0.0023). The age of onset or diagnosis among patients with cSLE was inversely correlated with copy number of long C4 genes (R^2=0.38, p=0.0036), a phenomenon that remains true when patients with other racial groups were included in the analyses (R^2=0.23, p=0.0032).

Conclusion: Diversities of complement C4 genes and variation in levels of plasma C4 proteins are both a cause and an effect of cSLE. Intriguingly, the inverse relation of copy number long C4 genes with age of onset was an unex-

pected finding and its clinical implications, though, is yet to be explored. A larger study sample will help us better understand the potential role that long C4 gene plays in SLE pathogenesis and its implications on lupus disease activity or clinical outcomes.

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Abstract Number: 1671

Identifying Rare Genetic Variants in Childhood-onset Monogenic Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Among children diagnosed with systemic lupus erythematosus (SLE), there exists monogenic forms of SLE, where rare variants in a single gene lead to disease. The aim of this study was to calculate the burden of rare variants in monogenic SLE genes, in children suspected of monogenic SLE or lupus-like disease.

Methods: From the Hospital for Sick Children (SickKids) Lupus clinic, we identified patients suspected of monogenic SLE due to young-onset disease (< 11y), one or more affected first-degree relatives, and/or history of consanguinity. We completed paired end whole genome sequencing (WGS) using an Illumina HiSeq X platform (n=69) or paired end whole exome sequencing (WES) with an Illumina HiSeq 2500 platform (n=3). Variant calling was performed with GATK and HAS, and functional annotation with ANNOVAR. We prioritized rare exonic variants (MAF< 1%) based on predicted functional impact (frameshift, nonsynonymous and stop-gain) and 36 monogenic lupus genes. Chi-squared tests identified a subset of variants with an increased burden in monogenic SLE cases compared to relevant ethnic controls (Bonferroni correction p< 8.9E-4). Polyphen, SIFT and CADD scores (≥30) predicted damaging and/or deleterious variants.

Participants also underwent genotyping on the Illumina multiethnic MEGA or GSA array. Ancestry was genetically inferred using principal component and ADMIXTURE, or by self-report (Canada census ethnicity categories). Additive non-HLA and HLA SLE genetic risk scores (GRSs) were calculated using common risk single nucleotide polymorphisms. We tested the relationship between GRSs and the number of rare monogenic SLE variants with functional impact using Spearman correlation (r_s) coefficients.

Chr	Position	Gene	Referent Allele	Alternative Allele	cSLE MAF	Referent MAF (1)	p value (2)
1	22965784	*C1QA*	C	T	0.014	0	6.53E-12
1	22974076	*C1QC*	G	A	0.007	1.20E-4	3.01E-4
3	58191226 (3)	*DNASE1L3*	ATG	A	0.028	0	4.23E-35
3	58183689	*DNASE1L3*	G	C	0.014	3.18E-5	3.97E-37
6	31996484 (3)	*C4B*	T	C	0.014	4.20E-4	6.61E-9
12	7187985	*C1R*	C	T	0.007	8.43E-5	1.53E-5
19	12774178	*MAN2B1*	T	C	0.007	0	5.11E-9

Table. Frequency of predicted deleterious monogenic SLE variants in monogenic SLE cases compared to referent populations. (1) MAF reported for relevant referent population in gnomAD v2.1.1. (2) Chi-squared tests used to compare cSLE and referent variant frequencies. (3) Variant found in more than one monogenic cSLE patient.

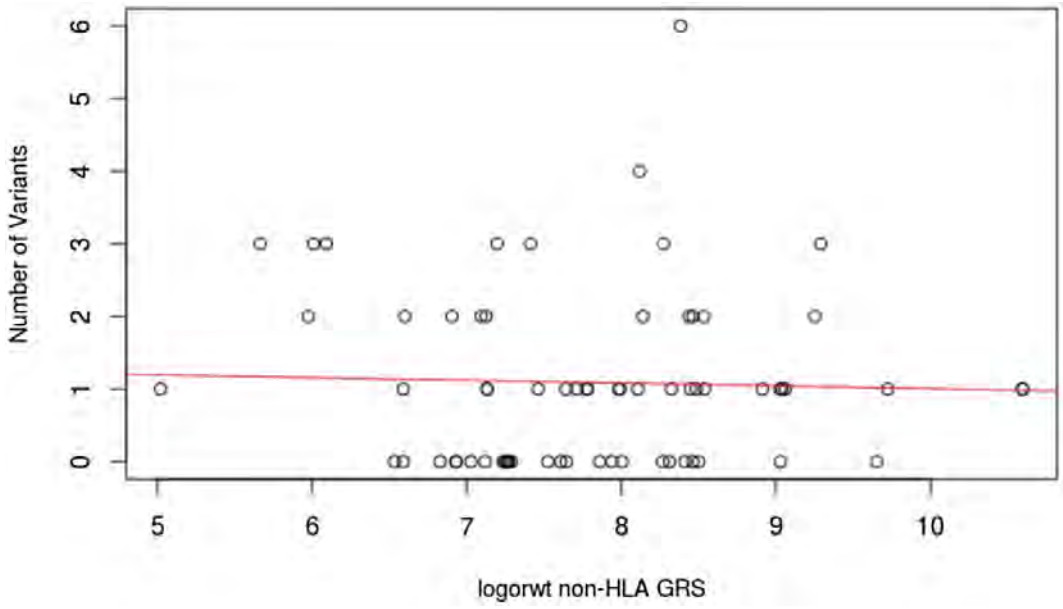

Figure. Correlation between non-HLA GRS and rare monogenic SLE variants with functional impact*. *Data of 68 patients with non-HLA GRS and WGS data.

Results: The cohort included 72 suspected monogenic SLE patients, 65 with SLE and 7 with lupus-like disease (79% females), with a median age of diagnosis of 8 years (IQR=7,10). The majority of patients were admixed (33%) or European (29%). WGS analysis showed 1032 rare variants in monogenic SLE genes, with a median of 17 variants/gene (IQR= 10,32) and 14 variants/person (IQR=11,17). We identified 56 exonic variants with predicted functional impact, of which 18 variants in 24 patients had a significantly higher frequency in monogenic SLE cases compared to referent populations. We found 7 variants predicted to be disease-causing in 9 SLE patients, in genes: *C1QA, C1QC, C1R, C4B, DNASE1L3* and *MAN2B1* (Table).

In 68 individuals with calculated GRSs, we did not observe a correlation between the burden of rare monogenic SLE variants with functional impact and SLE HLA GRS (r_s= 0.11, p=0.65) or non-HLA GRS (r_s= 0.04, p=0.78) (Figure).

Conclusion: In our cohort of suspected monogenic SLE patients, WES/WGS identified a likely causal genetic variant in 13% of patients. We did not detect a significant correlation between the number of rare monogenic SLE variants with functional impact and non-HLA or HLA GRS. Studies with larger cohort sizes are needed to validate our findings.

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Abstract Number: 1672

Renal Activity Index for Lupus Nephritis Distinguishes Active Renal Disease Among Childhood Systemic Lupus Erythematosus Patients

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Renal involvement in childhood-onset systemic lupus erythematosus (cSLE) is a major cause of morbidity and mortality. Current tools to identify lupus nephritis (LN) fall short compared to renal biopsy. The renal activity index in lupus (RAIL) was developed using 6 urinary biomarkers to reflect disease activity(1).

Purpose: To test the usefulness of the RAIL in the clinical setting to identify children with active LN.

Methods: Urine samples were collected cross-sectionally from cSLE patients at the time of active LN or routine clinic visit. Patients were classified into active LN, inactive LN or non-LN SLE based on results of a renal biopsy and/or absence of LN determined by routine urinalysis. The following urine biomarkers are included in the RAIL score (neutrophil gelatinase-associated lipocalin, ceruloplasmin, monocyte chemoattractant protein-1, adiponectin, hemopexin, kidney injury molecule-1, urinary protein and creatinine). Analysis was done by Enzyme-linked immunosorbent assay (ELISA) and nephelometry. RAIL scores were calculated per the defined algorithm. The accuracy of the RAIL score was compared between groups.

Results: Among 117 cSLE patients, 37 had active LN, 30 had inactive LN and 50 had no LN. Clinical characteristics and distribution of RAIL scores are outlined in Table 1. RAIL scores of inactive LN and no-LN group largely overlapped so they were combined in one group (Group 2) and compared to active LN (Group 1). The RAIL score was significantly higher in Group 1 vs Group 2 (median 0.7 vs -1.1 respectively, $p< 0.0001$). The RAIL score diagnostic accuracy was assessed in a multivariable regression model. Adjusting for patient's age and extra-renal SLE activity index (SLEDAI) score, the RAIL score was associated with odds ratio of 2.16 (95%CI 1.4-3.3, $p=0.001$) for active LN vs. inactive LN and non-LN SLE. A receiver operating curve for a RAIL cut-off score of 0.35 produced an area under the curve of 0.9

Table 1. Clinical characteristics and distribution of RAIL scores among Group 1 (active LN) and Group 2 (inactive LN + non-LN SLE) patients.

	Group 1 N = 37	Group 2 N = 80	*p*-value
Age (y)	15 (13-17)	18 (16-21)	<0.0001
NIH-AI[¥]	9 (4-13)	0 (0-0)	<0.0001
NIH-CI[¥]	1 (0-2.75)	0 (0-0)	0.12
Extra-renal SLEDAI	9 (6-13)	2 (0-4)	<.0001
GFR	91 (60-129)	108 (98-126)	0.05
Urinary creatinine	92 (61-191)	134 (73-183)	0.32
Urinary protein	254 (98-404)	21 (11-50)	<.0001
Urinary microalbumin	254 (189-316)	15 (9-43)	<.0001
RAIL Score	0.7 (-0.1-1.6)	-1.1 (-2.5-0.3)	<.0001

Values represent median (interquantile range).

[¥] Includes only active (N=24) and inactive LN (N=4) patients with renal biopsies within 30 days of urine collection.

Table 1. Clinical characteristics and distribution of RAIL scores among Group 1 (active LN) and Group 2 (inactive LN + non-LN SLE) patients.

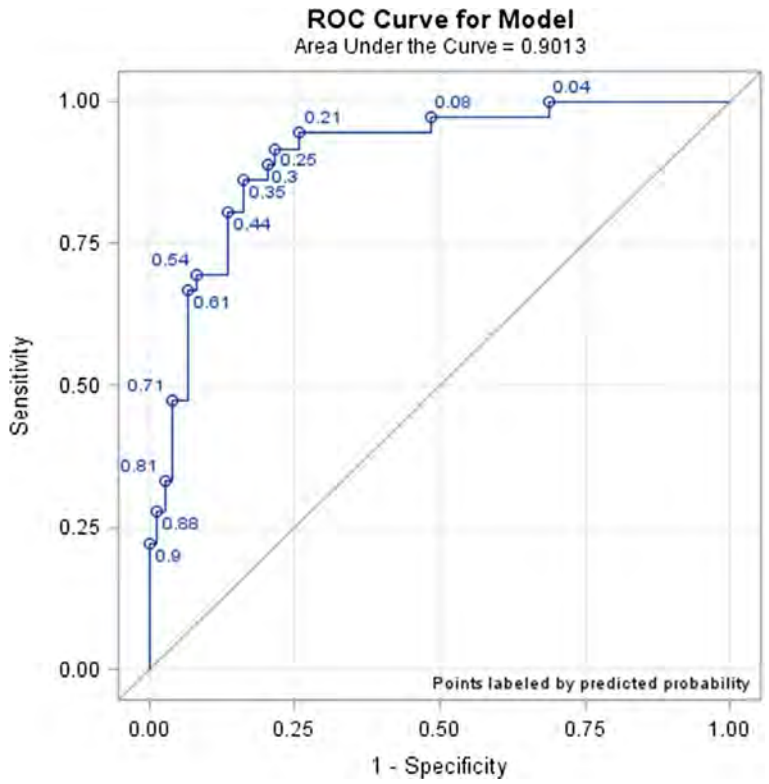

Figure 1. Receiver Operating Curve (ROC) for the RAIL score in differentiating active LN (Group 1) from Inactive LN & non-LN SLE (Group 2).

(sensitivity 86%, specificity 84%) for active LN. A RAIL score < 0.35 had a negative likelihood ratio of 0.17. Further adjustment for urinary protein and creatinine did not significantly influence the results.

Conclusion: The RAIL score is highly accurate in distinguishing active LN identified by renal biopsy, from inactive LN and non-LN SLE. A score of 0.35 identifies cSLE patients who very likely have active LN.

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Abstract Number: 1673

Principles of Pediatric Lupus Nephritis in a Contemporary Multi-Center Cohort

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Lupus nephritis (LN) is a well-established and life-threatening manifestation of systemic lupus erythematosus (SLE) that is more common in children than adults. The demographics of childhood-onset SLE (cSLE) and management of disease have changed over time, prompting the need to update outcomes. The purpose of this study is to use the Childhood Arthritis and Rheumatology Research Alliance (CARRA) prospective registry to validate historical principles about LN in a contemporary, real-world cohort.

Methods: Through literature review of LN studies in cSLE patients from 1992 to 2012, the following principles were identified:

- 20%-75% of cSLE patients will develop LN
- LN develops within 1 year of diagnosis in 82% of cSLE patients; 92% develop LN within 2 years of diagnosis
- Membranous (ISN/RPS class V) LN more often presents with nephrotic-range proteinuria than does proliferative LN (class III or IV)
- Short-term renal outcomes are worse in Black vs non-Black patients
- Short-term renal outcomes are worse in patients who present with eGFR < 60mL/min/1.73 m2 and/or moderate proteinuria (urine protein: creatinine ratio (UPC) > 1 mg/mg)
- Rituximab is used as a steroid-sparing agent for induction in proliferative LN

The CARRA registry was queried to determine the rates of LN in cSLE, time from diagnosis to LN, presentation at LN onset, short-term renal outcomes, and instances of rituximab as induction therapy. The eGFR (calculated by the modified Schwartz equation) was separated into 3 stages of chronic kidney disease (CKD) for analysis: 1: >60ml/min/1.73 m^2, 2: 30-60ml/min/1.73 m^2, and 3: < 30ml/min1.73 m^2. Occurrences of end-stage renal disease (ESRD),

Table 1. Class of LN at LN diagnosis

LN Class	*N*	*Percentage*
III/IV	138	73.0%
III/IV + V	22	11.6%
V only	29	15.3%

Table 2. GFR State at diagnosis and follow-up

Initial GFR (mL/1.73m²/min)	*N(%)*	*CKD 1/2 at follow up, N(%)*	*CKD 3 at follow up, N(%)*	*CKD 4/5 at follow up, N(%)*
>60	167 (71%)	121 (96.0%)	3 (2.4%)	2 (1.6%)
30-60	11 (5%)	7 (87.5%)	1 (12.5%)	0 (0.0%)
<30	2 (1%)	0 (0.0%)	1 (100%)	0 (0.0%)
Unknown	54 (23%)			

transplant, and dialysis were recorded. We compared eGFR change over time in Black vs non-Black subjects. This study was exempt from Institutional Board Review.

Results: Of the 675 cSLE patients in the CARRA registry, 235 (35%) had documented LN. Of those, 74% were diagnosed with LN within 1 year and 87% within 2 years of cSLE diagnosis. Table 1 describes the LN classes. eGFR decline was more common in Black cSLE patients than non-Black patients (p=0.04). Changes in eGFR over time are described in Table 2. Three patients were documented as being on dialysis. Nine were reported to have ESRD. No renal transplants were reported. Of those with LN, 24.3% were treated with rituximab with no statistically significant difference by LN class, sex, or age.

Conclusion: In the CARRA registry, 35% have LN, in range of prior literature estimates. Of those that have LN, 74% developed it within the first year of their lupus diagnosis, slightly lower than prior reports of 82%. Black race remains associated with worse short-term renal outcomes. In short-term follow up, most eGFR remained unchanged or improved and ESRD was rare. A study limitation is the inception cohort is 2 years old and some data were unavailable. Efforts are underway to study long-term outcomes in the CARRA registry to better inform on contemporary rates and outcomes of LN in cSLE.

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Abstract Number: 1674

Pediatric and Adolescent One Year Protocol Kidney Biopsies Should Be Performed, Even in Patients with Complete Remission of Their Lupus Nephritis

Peter Yorgin[1], Suhas Radhakrishna[1], Caitlin Carter[1], Johanna Chang[1], Katayoon Shayan[1], Lieuko Nguyen[1], Peter Chiraseveenuprapund[1] and Robert Sheets[2], [1]UCSD/Rady Children's Hospital, San Diego, CA, [2]University of California San Diego, San Diego, CA

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The value of one-year protocol kidney biopsies in children who have proliferative lupus nephritis (LN) is unclear, particularly in patients who meet CARRA criteria for a complete renal response.

Methods: Subjects < 18 yrs of age, who met ACR systemic lupus erythematosus (SLE) classification criteria with initial kidney biopsy (KBx) proven proliferative LN at Rady Children's Hospital San Diego (RCHSD) between 1/1/2010 – 12/31/2019 and a pre-planned one year protocol KBx (0.75-1.25 years), were selected for this study. Kidney biopsies were read by RCHSD Pathologists. CARRA criteria for complete response (CR), partial remission (PR) and flare (F) were assessed at the time of protocol KBx. Patients were allocated into either CR or non-complete response (PR and F) groups (NCR) for analysis. UCSD/RCHSD IRB 200870X

Results: Of the 19 patients who had a one year protocol KBx, there were 11 CR (58%) and 8 NCR study subjects. There were no statistically significant differences between CR and NCR patients at initial KBx. Induction therapy was different between the two groups, with CR subjects more likely to receive intravenous cyclophosphamide (CTX). Patients with CR had significantly improved ISN/RPS class and lower NIH activity and chronicity scores on follow up biopsy compared to the NCR group. There was no statistically significant worsening in CR NIH chronicity scores. All SLEDAI scores in CR group at the time of protocol KBx were 4 or less, but 2 NCR patients also had SLEDAI scores of 4. All but one patient in the NCR group had a change (n=4) or increase in maintenance immunosuppression (n=3) after their KBx. Five CR subjects had no change in immunosuppression; while 6 (55%) had a decrease in immunosuppression. CR patients with immunosuppression reduction were more likely to have a decrease of ≥5 in NIH activity scores. There was one perinephric hemorrhage out of 38 KBx (2.6%) that necessitated an overnight hospital stay.

Conclusion: One year protocol KBx were beneficial in most patients with proliferative LN because the KBx provided histopathologic data to support a change in immunosuppression. Subjects meeting the CARRA criteria for complete renal response (CR) at had significantly better one year protocol KBx outcomes with greater ISN/RPS class improvement, and lower NIH activity and chronicity scores. Unexpectedly, two CR patients had KBx that no longer met the criteria for ISN/RPS class 1. CTX induction therapy of proliferative LN may have been a factor leading to better outcomes. While it is not unexpected that immunosuppression was changed or increased in nearly all NCR patients, the improved KBx results in CR subjects created a decision tree, where physicians either: 1) continued the effective

	Baseline		p-value	At protocol biopsy		p-value
	CR (n = 11)	NCR (n=8)		CR (n = 11)	NCR (n=8)	
Age (years)	13.9 ± 2.3	13.7 ± 2.0	0.43	15.0 ± 2.4	14.8 ± 2.0	0.86
Gender	Male: 1 Females: 11	Male: 1 Females: 7	0.23			
Ethnicity	Hispanic: 7 Other: 4	Hispanic: 7 Other: 1	0.07			
ISN/RPS class	Class 4: 9 Class 4+5: 1 Class 3: 1	Class 4: 7 Class 3: 1	0.34	Class 4: 1 Class 4+5: 1 Class 3+5: 1 Class 3: 2 Class 2: 4 Class 0/1: 2	Class 4: 5 Class 4+5: 1 Class 3+5: 1 Class 3: 1	<0.001*
Induction therapy	10 cyclophosphamide 1 other	4 cyclophosphamide 4 other	<0.001			
Activity	8.1 ± 4.1	7.8 ± 4.8	0.44	2.4 ± 1.4	6.0 ± 3.1	0.006
Chronicity	1.8 ± 1.5	1.0 ± 0.9	0.08	1.9 ± 1.4	3.3 ± 2.6	0.02
SLEDAI	17.3 ± 4.8	21.0 ± 5.9	0.17	1.5 ± 1.8	8.5 ± 4.4	0.002
eGFR	150.7 ± 59.9	135.8 ± 59.7	0.60	157.1 ± 32.7	134.1 ± 40.5	0.21
Uprot/Ucreat (mg/mg)	2.7 ± 3.3	5.2 ± 6.0	0.32	0.1 ± 0.0	3.8 ± 6.9	0.03

*Chi-square analysis performed comparing improved vs same/worse ISN/RPS class

*Chi-square analysis performed comparing improved vs same/worse ISN/RPS class

immunosuppression, or 2) decreased immunosuppression. One year protocol KBx were associated with a low risk of serious adverse events. Study limitations include: a single center, non-randomized cohort, physician-directed protocol KBx selection and grouping of partial remission and flare groups into the NCR group. A prospective randomized trial would be able to determine if decreasing immunosuppression at one year for CR subjects would yield acceptable outcomes, as assessed by a two year protocol KBx.

Disclosure: P. Yorgin, None; **S. Radhakrishna**, None; **C. Carter**, Reata Pharmaceuticals, 1; **J. Chang**, None; **K. Shayan**, None; **L. Nguyen**, None; **P. Chiraseveenuprapund**, Childhood arthritis and rheumatology research alliance, 1; **R. Sheets**, None.

Abstract Number: 1675

Microstructural Damage Is Associated with Age at Disease-onset and Cognitive Impairment in Systemic Lupus Erythematosus

Paulo Julio[1], Renan Frittoli[1], Aline Lapa[1], Thais Caldeira[1], Leticia Rittner[1], Fernando Cendes[1], Roberto Marini[1], Paula Fernandes[1], Lilian Costallat[1] and **Simone Appenzeller**[1], [1]UNICAMP, Campinas, Brazil

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: To compare corpus callosum (CC) volume and diffusion tensor imaging in systemic lupus erythematosus according to age of disease-onset.

Methods: We selected 75 patients with childhood-onset (c)SLE [mean age of 24.6 years (SD 4.6) and disease duration of 11.6 years (SD 4.8)] and two control groups: 1. Matched by disease duration, consisting of 51 patients with adult-onset (a)SLE [mean age of 32.4 (SD 3.2)] and disease duration of 11.5 years (SD 4.2)] and 2. Matched by age consisting of 77 healthy controls (HC) [mean age of 28 years (DP 3.6)]. A complete clinical, laboratory and neurological evaluation was performed in all subjects. Cognitive impairment were screened with Montreal Cognitive Assessment (MoCA), mood and anxiety disorders were determined through Beck Inventory. SLE patients were further assessed for disease activity [SLE Disease Activity Index (SLEDAI)], damage [Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI)] and current and cumulative drug exposures. All subjects underwent MRI examination with a Philips 3T scanner. Sagittal T1-weighted images were used for CC segmentation using FreeSurfer. Diffusion Weighted Images (DWI) were analyzed in FSL tool and scalar maps of the Fractional Anisotropy (FA), Mean Diffusivity (MD), Axial Diffusivity (AD) and Radial Diffusivity (RD) were calculated. The CC was parcellated based on DTI. Using the scalar maps we obtained the average and standard deviation of FA, MD, AD and RD for the segmented CC and each parcel. P values < 0.05 were considered statistically significant.

Results: We observed similar CC volume in cSLE [mean volume = 6410.19mm^3 (SD 2026.85)] when compared to aSLE [mean volume = 6658.61mm3 (SD = 2121.50)]; p=0.465] and HC [mean volume=7216.40mm3 (DP 1991.61)]; p=0.175]. When CC was divided into different portions, we observed significant smaller volumes in the mid-anterior region, the central portion, the mid-posterior portion ($p^<0.001$) in cSLE and HC. No significant difference was observed between CC parcels in cSLE and aSLE and between aSLE and HC. We observed that FA values were significantly lower cSLE (0.63603; SD±0.0665) when compared with the aSLE (0.677624 SD ± 0.08920; p=0.002) and HC (0.699624;SD±0.07920; p=0.001). Increased MD (0.00096,SD±0.00014), RD (0.00057, SD±0.00015) and AD (0.0017, SD± 0.00014) were observed in cSLE when compared to aSLE [(MD:0.00096, SD ± 0.00014; p = 0.002); (RD:0.00048, SD ± 0.00019; p = 0.002); (AD:0.0016, SD±0.00011; p=0.024)] and HC [(MD:0.00116, SD±0.00024; p< 0.001); (RD:0.00052, SD± 0.00023; p< 0.001); (AD:0.0020, SD±0.00018; p=0.014)]. MoCA scores were significantly lower in cSLE [20.82(SD±4.6)] when compared to aSLE [23.27(SD±4.4); p=0.005] and HC [26.52(SD±2.6); p< 0.001]. No significant differences between BDI and BAI scores were observed (p >0.05). When comparing MoCA scores with diffusion parameters we observed a correlation with FA (r=0.65; p=0.03), MD (r=0.7; p=0.03) and RD (r=0.647; p=0.04).

Conclusion: We observed more frequently microstructural changes in the corpus callosum in adults with cSLE when compared to aSLE with similar disease duration and HC. Microstructural changes can explain worse neurocognitive outcome in cSLE.

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Abstract Number: 1676

Neuropsychiatric Involvement in Juvenile-onset Systemic Lupus Erythematosus (JSLE): Data from the UK JSLE Cohort Study

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Juvenile-onset systemic lupus erythematosus (JSLE) is a rare autoimmune/inflammatory disease, accounting for up to 20% of SLE cases. Though clinically similar to adult-onset disease, it frequently follows a more severe course. Neuropsychiatric (NP) involvement in JSLE can be aggressive and significantly affect patients' quality of life as well as disease outcomes.

The aim of this study was to describe the demographic characteristics, clinical and laboratory features of NP involvement in JSLE.

Methods: We analyzed data from JSLE patients enrolled in the UK JSLE Cohort Study between August 2006 and June 2019. Demographic (age, gender, ethnicity, family history), clinical (1997 ACR classification criteria, disease activity BILAG, SLICC, and damage index SLICC-SDI) and laboratory (ESR, CRP, CBC with diff, ANA, anti-ENA, anti-dsDNA, aCL, lipid profile, renal function, C3, C4, Ig levels, thyroid function, UA) data collected at disease onset and at last visit were analyzed.

Results: A total of 428 JSLE patients were included, with a female:male ratio of 5.4:1. The median age at diagnosis was 12.2 years (range: 0-17). A majority of JSLE patients were Caucasian (51.4%), followed by patients of South Asian (23.3%), Black African/Caribbean (16.7%), and East Asian (6.5%) descent. Patients with headaches as the only NP symptom were excluded here, because of the low specificity of this feature.

Overall, one quarter of JSLE patients (107/428, 25%) showed NP features; in 48.5% of these cases, NP symptoms were the presenting manifestation. The median age at disease onset and ethnic composition did not differ between sub-cohorts with vs without NP involvement. Most frequently recorded NP manifestations included cognitive impairment (n=45, 42%), seizures (n=21, 20%), psychotic features (n=11, 10%), peripheral nerve involvement (n=9, 8%), cerebral vasculitis (n=10, 9%), and ischaemic stroke (n=7, 6%). Headache was an accompanying manifestation in 74% of all NP-JSLE patients.

While no differences were recorded in autoantibody patterns and immune cell counts, lower platelet counts (< 100.000/mmc) were found in patients with NP involvement (p=0.02). Children with NP involvement showed both a higher number of ACR criteria (mean 4.9 *vs* 4.6, p=0.07) and higher SLICC scores (0.3 *vs* 0.2, p=0.029) at disease onset.

As compared to JSLE patients without neurological involvement, at diagnosis, patients with NP-JSLE exhibited higher disease activity (pBILAG) in the constitutional (p< 0.01) and ophthalmologic (p< 0.05) domains. At last visit, NP-JSLE patients had an increased number of ACR criteria (mean 6 vs 5.5; p< 0.001) and more damage (SLICC) (mean 1.2 vs 0.4; p< 0.001). Comparing JSLE patients with primary NP involvement to individuals who developed NP symptoms later, patients with early NP involvement exhibited more damage (SLICC) at diagnosis (mean 0.63 vs 0.05; p< 0.01) and last visit (mean 1.7 vs 0.7; p< 0.01).

Conclusion: Approximately 25% of JSLE patients enrolled in the UK JSLE Cohort Study have NP involvement. Patients with NP involvement exhibit higher disease activity and more disease-associated damage when compared to patients without NP involvement.

Disclosure: T. Giani, None; **E. Smith**, None; **R. Cimaz**, None; **M. Beresford**, None; **C. Hedrich**, None.

Abstract Number: 1677

Schizophrenia Genetics and Neuropsychiatric Features in Childhood-Onset Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

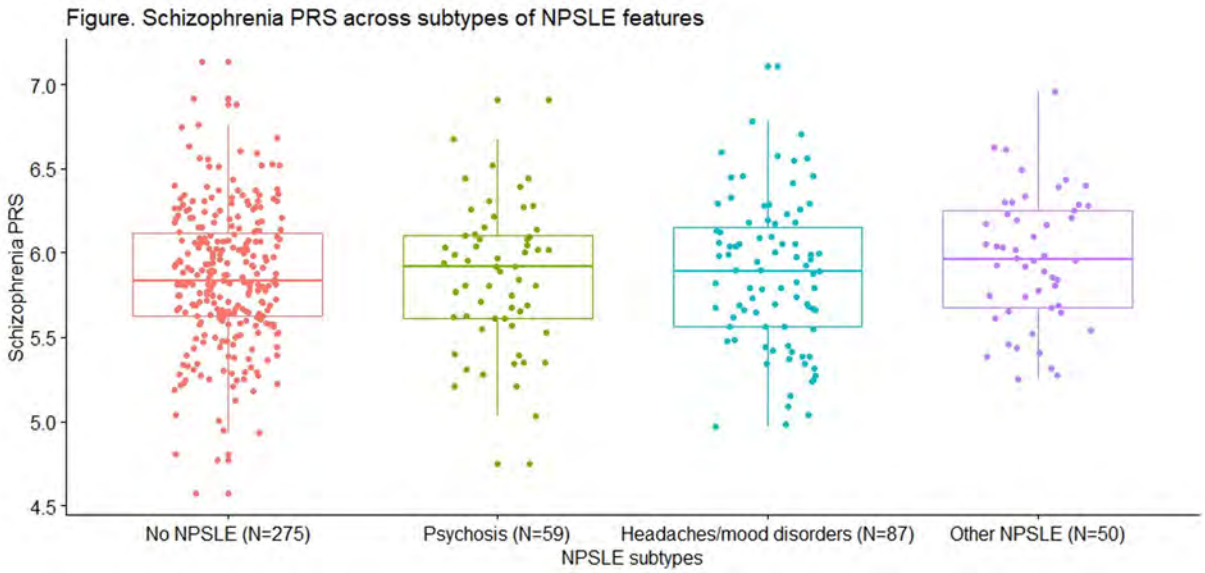
Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Prior studies indicate that schizophrenia and systemic lupus erythematosus (SLE) share genetic risk loci. Despite overlapping phenotypic features such as psychosis, little is known of the link between genetic susceptibility for schizophrenia and neuropsychiatric SLE (NPSLE). We aimed to examine the association between a polygenic risk score (PRS) for schizophrenia and NPSLE as well as NPSLE feature subtypes in childhood-onset SLE (cSLE) patients.

Methods: Study participants from the cSLE Lupus Clinic at the Hospital for Sick Children, met ≥ 4 of the ACR and/or SLICC SLE classification criteria. Patients were genotyped on the multiethnic Illumina MEGA array. Un-genotyped single nucleotide polymorphisms (SNPs) were imputed. Principal components (PCs) were calculated using the 1000 Genomes Project (1KGP) and the Haplotype Reference Consortium as referents and ancestry was genetically inferred. We calculated an additive schizophrenia risk-weighted PRS using genome-wide significant SNPs ($P< 5x10^{-8}$) from the largest published schizophrenia GWAS to date. The following SNPs were excluded: insertion/deletions, sex chromosomes, MHC region, minor allele frequency < 5%, imputation quality < 0.8 and SNPs within 500kb of and in $r^2 \geq 0.1$ with more significant markers. Demographic and clinical data were extracted from the Lupus database. NPSLE events were defined using ACR case definitions. We defined two outcomes compared to absence of NPSLE features: 1) any NPSLE features and 2) subtypes of NPSLE features: psychosis, headaches and/or mood disorders, other NPSLE. NPSLE features were independently validated by two pediatric rheumatologists. We tested the association of the schizophrenia PRS and NPSLE using logistic and multinomial regressions, adjusted for sex, age at SLE diagnosis, follow-up duration, the first five PCs, the presence of antiphospholipid antibodies, and non-HLA SLE PRS.

Results: Our cohort included 471 participants with cSLE. Median age at SLE diagnosis was 13.8 years (IQR,11.3-15.6), 82% were female and 31% were European. In total, 42% of all participants had ≥1 NPSLE feature: 59 (13%) had psychosis, 87 (18%) had headaches and/or mood disorders and 50 (11%) had other NPSLE features. Median follow-up was 5.0 years (IQR,3.2-7.8). The GWAS PRS included 83 SNPs. A higher schizophrenia PRS was not significantly associated with having any NPSLE features versus having no NPSLE features (OR=1.18, 95%CI 0.73-



NPSLE, neuropsychiatric systemic lupus erythematosus; PRS, polygenic risk scores.

1.94, p=0.49). A higher schizophrenia PRS was not significantly associated with having psychosis (OR=0.92, 95%CI 0.44-1.94, p=0.84), headaches and/or mood disorders (OR=1.05, 95%CI 0.56-1.98, p=0.88) or other NPSLE features (OR=1.96, 95%CI 0.86-4.46, p=0.11) compared to having no NPSLE features (Figure).

Conclusion: We did not observe a statistically significant association between PRS for schizophrenia and NPSLE features in cSLE. We found a trend toward significance with higher schizophrenia PRS being associated with a higher odds of non-psychosis NPSLE features, which warrants further validation. Next steps include creating a PRS adding SNPs moderately associated with schizophrenia and testing the association with NPSLE.

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Abstract Number: 1678

Hydroxychloroquine Blood Levels Predicts 6-Months Disease Activity in Juvenile Lupus Nephritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Renal involvement is reported in up to 80% of juvenile systemic lupus erithematosus (JSLE) and its among the most severe manifestations in these population. Antimalarials are one of the cornerstones of lupus treatment with beneficial effects in maintenance of disease remission. In fact, low hydroxychloroquine (HCQ) blood levels are predictors of flare in adult lupus patients. The aim of this study is to determine the HCQ cut-off levels which

Table 1 – Baseline characteristics of 60 stable juvenile lupus nephritis (LN) patients with and without disease flares during six months of follow-up

	Flare (baseline data) (n= 19)	Without flare (baseline data) (n= 41)	p
Demographics			
Current age, years	16.3 ± 3.1	16.8 ± 3.2	0.557
Female gender	14 (74)	33 (80)	1.000
Non-Caucasian	11 (58)	14 (34)	0.098
BMI, Kg/m2	24.2 ± 4.3	24.5 ± 4.9	0.820
Number of school years	10 (5-13)	12 (6-17)	0.146
High sociodemographic status	8 (42)	20 (49)	0.782
Hydroxychloroquine (HCQ)			
HCQ dose, mg/Kg/day	4.8 ± 0.5	4.6 ± 0.5	0.170
HCQ cumulative dose, Kg	609.3 ± 443.1	551.2 ± 338.7	0.583
HCQ blood concentration, ng/mL	557.5 (53.4 – 2137.8)	1061.9 (53.4 – 2137.8)	**0.012**
Duration of HCQ use, years	5 (0.7 – 11.6)	5 (0.7 – 12.1)	0.843
Adherence < 80%*	8 (42)	18 (44)	1.000
Disease parameters			
Disease duration, years	5.1 ± 3.9	5.6 ± 3.6	0.620
SLEDAI-2K score	2 (0-10)	2 (0-16)	0.622
Hypocomplementemia	7 (37)	10 (24)	0.365
Positive Anti-dsDNA antibodies	10 (53)	12 (29)	0.094
Creatinine, mg/dL	0.61 (0.47–0.85)	0.66 (0.27 – 1.22)	0.236
GFR, mL/min per 1.73m2	144,49 (106,60-187,23)	132,31 (74.39-268.89)	0.273
Protein/creatinin, g/g	0.1 (0.05 – 1.0)	0.16 (0.05 – 1.56)	0.164
Hemoglobin, g/dl	12.5 ± 1.2	12.8 ± 1.4	0.570
Leucocytes, x 103	5.07 (1.59 – 9.54)	5.75 (2.8 – 14.67)	0.078
Lymphocytes, x 103	1.36 (0.4 – 3.53)	1.52 (0.42 -8.22)	0.679
Platelets, x 103	247 ± 74	247 ± 80	1.000
Concomitant treatment			
Prednisone	12 (63)	24 (59)	0.784
Current dose, mg/day	7.5 (2.5 – 20)	10 (2.5 -30)	0.268
Azathioprine	5 (26)	9 (22)	0.750
Mycophenolate mofetil	11 (58)	28 (68)	0.562
IVCYC	0 (0)	1 (2)	1.000
Cyclosporine	1 (5)	0 (0)	0.317
Methotrexate	0 (0)	2 (5)	1.000
Rituximab	1 (5)	2 (5)	1.000

Results are expressed in median (minimum-maximum values) and n (%), BMI - body mass index, SLEDAI-2K - Systemic Lupus Erythematosus Disease Activity Index 2000, SLICC/ACR-DI Systemic Lupus International Collaborating Clinics/American College of Rheumatology-Damage Index, IVCYC – intravenous cyclophosphamide.

* Ratio of the number of medication doses taken and the number of doses prescribed during the time between first study visit and the refill date of the medication.

predicts flare and to assess the adherence pattern by overall blood HCQ concentration in juvenile lupus nephritis (LN) patients.

Methods: Juvenile LN patients under the prescribed HCQ 2016-American Academy Ophtalmology (AAO) recommended dose for at least six months were prospectively followed. Participants were evaluated at baseline (BL) and 6-months for clinical, laboratorial data and HCQ blood levels (high-performance liquid chromatography-tandem mass spectrometry). Disease flare was defined as increase ≥3 in SLEDAI-2K and/or increase in immunosuppressive/ glucocorticoid.

Results: Sixty JSLE patients, 80% female, mean age of 16.6 ± 3.13 years and mean disease duration of 5.5 ± 3.65 years were included. Nineteen patients (32%) evolved with disease activity after 5.8 (1.6 – 9.8) months. Participants with flare presented a lower BL median HCQ blood level compared to stable patients [557.5 (53.5 – 2137.8) ng/ml vs. 1061.9 (53.5 – 2137.8) ng/ml, p=0.009]. There were no differences in demographic data, disease parameters and concomitant treatment in both groups. A ROC curve analysis demonstrated a BL blood HCQ cut-off level of 573.45 ng/ml as predictor of disease reactivation, with an OR=3.75 (95%CI 1.19-11.76, p=0.023) for flare (Table 1). Flare frequencies were lower in patients with adequate BL HCQ blood levels (> 573 ng/ml) compared to those with inadequate levels (≤ 573 ng/ml) (21% vs. 50%, p=0.042). A prospective 6-months blood HCQ monitoring was performed in 54 patients, demonstrating an overall stable pattern from baseline to the final evaluation in McNemar's analysis (p=0.359) with most patients (57%) presenting fluctuating/ persistently low levels (≤573 ng/ml). Among those with persistently inadequate HCQ pattern (n=12) half activated disease during this period. The higher frequency of flares in patients with persistently low HCQ levels vs. persistently adequate (50% vs. 26%, p=0.260) or vs. fluctuating levels (50% vs. 26%, p=0.255) did not reach statistical significance.

Conclusion: In conclusion, we demonstrated for the first time that HCQ blood cut-off level of 573 ng/ml predicts 6-months flare in juvenile lupus nephritis patients under prescribed HCQ 2016-AAO dose. We further observed that most of these patients have compliance issues reinforcing the need for a close surveillance particularly in those with levels below the defined cut-off. (Clinicaltrials.gov number #NCT03122431).

Disclosure: V. Balbi, None; **C. Silva**, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4), 2, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #303422/2015-7), 2; **T. Pedrosa**, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP #2017/14352-7), 2; **R. Pereira**, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #301805/2013-0), 2; **L. Campos**, None; **E. Leon**, None; **N. Duarte**, None; **V. Carvalho**, None; **S. Pasoto**, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4), 2; **D. Rosario**, None; **L. Brandao**, None; **E. Bonfa**, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4), 2, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #305068/2014-8), 2; **N. Aikawa**, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4), 2.

Abstract Number: 1679

Developing a Standardized Corticosteroid Dosing Regimen in Pediatric Proliferative Lupus Nephritis

Nathalie Chalhoub[1], Kelly Rouster-Stevens[2], Marisa Klein-Gitelman[3], Karen Onel[4], Beatrice Goilav[5], Sonia Savani[6], Natasha Ruth[6], Tingting Qiu[7], Najla Aljaberi[8], Jianghong Deng[9], Angela Merritt[8], Benjamin Laskin[10], Anna Carmela Sagcal-Gironella[11], Stacy Ardoin[12], Deborah Levy[13], Scott Wenderfer[14], Bin Huang[7], Hermine I Brunner[15] and LaUNCH Project Investigators[16], [1]The University of Cincinnati College of Medicine, Cincinnati, OH, [2]Emory University/Children's Healthcare of Atlanta, Atlanta, GA, [3]Division of Rheumatology, Department of Pediatrics, Ann & Robert H. Lurie Children's Hospital of Chicago, Chicago, IL, [4]Pediatric Rheumatology, Hospital for Special Surgery, New York, NY, [5]The Children's Hospital at Montefiore, Albert Einstein College of Medicine, Bronx, NY, [6]Medical University of South Carolina, Charleston, SC, [7]Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [8]Division of Rheumatology, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [9]Beijing Children's Hospital, Beijing, China (People's Republic), [10]Children's Hospital of Philadelphia, Philadelphia, [11]Hackensack Meridian School of Medicine at Seton Hall University, Hackensack, NJ, [12]Nationwide Children's Hospital, Columbus, OH, [13]Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, [14]Renal Section, Baylor College of Medicine and Texas Children's Hospital, Houston, TX, [15]PRCSG, Cincinnati Children's Hospital Medical Center, Cincinnati, OH, [16]LUpus Nephritis and Cellcept precision dosing in cHildren (LaUNCH), Cincinnati, OH

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Corticosteroids (CS) remain the mainstay of therapy for childhood-onset systemic lupus erythematosus (cSLE). However, widely accepted strategies for oral (PO) or intravenous (IV) CS dosing are lacking. We aimed to 1) develop a standardized CS dosing regimen (SSR) and 2) achieve consensus for this SSR among pediatric rheumatology and nephrology physicians treating cSLE, including lupus nephritis (LN).

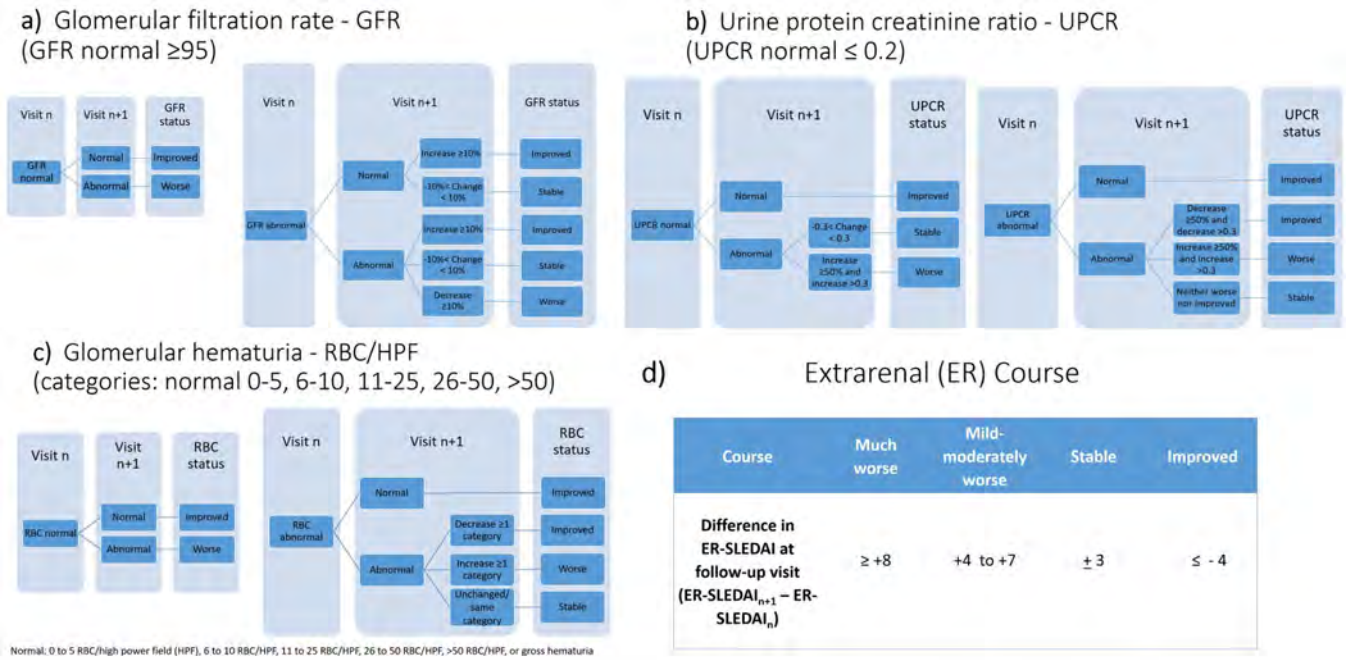

Figure 1. Consensus definitions for assessing changes in lupus nephritis response variables (LN-RVs) and extrarenal (ER) disease activity between clinical encounters

INITIAL 4 WEEKS OF INDUCTION THERAPY		
PO CS		**IV CS**
Patients≥50 kg	Prednisone* 60 mg/day divided in up to 4 doses	Up to 3 doses (30 mg/kg; max 1 gram of methylprednisolone)
Patients<50 kg	Prednisone 1.5 mg/kg/day	
Median–lowest PO CS dose at week 4**	40 mg/day - 30 mg/day	
WEEKS 5 – 26 OF INDUCTION THERAPY (based on LN and extrarenal trends since last visit)		
LN course *(assumption stable extrarenal)*	*Much worse*	Increase PO CS to 50-60 mg/day; Re-assess in 1-3 weeks; if response is (a) *Satisfactory→ No IV CS; (b) Non-satisfactory→ IV pulses + PO CS* Possible change of immunosuppressive drug
	Mild-moderately worse	Increase PO CS by about 30% (if dose < 40 mg; max 60 mg)
	Active stable	Stable PO CS dose (if dose < 40 mg; else: slow decrease)
	Improved active or PRR[1]	Slow decrease of PO CS dose
	CRR[2]	More pronounced decrease of PO CS dose
Extrarenal course *(assumption stable LN)*	*Much worse*	Increase PO CS dose; Re-assess in 1-3 weeks; if response is (a) *Satisfactory→ No IV CS; (b) Non-satisfactory → IV pulses + PO CS* Possible change of immunosuppressive drug
	Mild-moderately worse	Increase PO CS by 20% for doses < 40 mg; otherwise stable PO CS dose
	Active stable or improved active	Stable PO CS dose
	Inactive[3]	Decrease PO CS dose
Median–lowest PO CS dose at week 26	12.5 - 10 mg/day	
BEYOND 26 WEEKS POST KIDNEY BIOPSY - MAINTENANCE THERAPY		
LN course *(assumption stable extrarenal)*	*Flare[4] after PRR/CRR*	Prednisone ≥ 40 mg, irrespective of extrarenal course Re-assess in 1-3 weeks; if response is (a) *Satisfactory→ No IV CS; (b) Non-satisfactory→ IV pulses + PO CS*
	Worse after PRR/CRR	Increase PO CS dose FIRST
	PRR stable	Slow decrease of the CS dose
	Inactive/CRR or PRR improved	More pronounced decrease of the CS dose
Extrarenal course *(assumption at least sustained PRR)*	*Much worse*	Increase PO CS dose by 30-50% (max 60 mg); Re-assess in 1-3 weeks; if response is (a) *Satisfactory → No IV CS; (b) Non-satisfactory → IV pulses + PO CS* Possible change of immunosuppressive drug
	Mild-moderately worse	Increase PO CS dose by 25% for doses < 40 mg; otherwise stable PO CS dose
	Stable/Improved/Inactive	Decrease PO CS dose

*Or CS equivalent dose; **For patients ≥ 50 kg
[1]PRR (Partial renal remission): >50% improvement of ≥2 lupus nephritis response variables (LN-RVs) PLUS remaining LN-RV is NOT worse.
[2]CRR (Complete renal remission): All LN-RVs are NORMAL.
[3]Inactive extrarenal (ER) disease activity: ER-SLEDAI$_{n+1}$ (at follow up visit) ≤ +2
[4]LN flare defined by at least 1 of the LN-RV changes being persistently present on ≥2 subsequent time points ≥1week apart. LN-RV changes are defined as a) newly abnormal GFR, b) abnormal GFR that decreased by >10%, c) persistent increase of UPCR to ≥0.5, after CRR, d) persistent doubling of UPCR with values ≥1.0, after PRR, or e) newly active or worsening glomerular hematuria.

Table 1. Corticosteroid (CS) use provided by the standardized CS dosing regimen (SSR)

Methods: Consensus formation techniques were used. A Delphi questionnaire was completed to select relevant covariates influencing CS dosing in LN (Step 1). Retrospective data from 147 children with proliferative LN at 8 major cSLE treatment sites in North America were used to generate Patient Profiles (PP) describing cSLE course at 2 subsequent visits (Step 2). PP were sent to 142 physicians experienced in cSLE to rate the course of LN and extrarenal

disease and propose PO and IV CS dose adjustments (Step 3). Using PP data for which consensus was achieved, an SSR was developed (Step 4) and refined based on responses from another questionnaire and a focus group of experienced physicians (Step 5). Then, the SSR was validated (Step 6) using a second subset of PP describing disease course for up to 6 months since the time of initial kidney biopsy. Consensus was defined as agreement by majority (>50%) of PP ratings (Step 3, Step 6).

Results: In Steps 1 and 3, 103 physicians answered Delphi questions and rated 353 PP (response rate: 73%). In Step 6, 18 physicians (mean 13.4 years of experience) were asked to review 33 PP each resulting in 564 PP ratings, of which 437 (77.5%) and 460 (81.6%) yielded consensus on PO and IV CS dosing respectively. PO and IV CS dosing depends on the patient's weight, the course of extrarenal activity, measured by the extrarenal SLEDAI score (Figure 1d), and the course of LN, described by changes/status of 3 LN response variables (LN-RVs, Figure 1a-c). The SSR reflects dosing customs agreed upon by physicians. Table 1 summarizes the SSR with focus on 2 disease courses (1:stable extrarenal/various LN; 2:stable LN/various extrarenal), with permutations of extrarenal disease course (much worse, mild-moderately worse, active stable/improved, inactive) and LN course (flare, mild-moderately worse, active stable/improved/partial or complete renal remission). Doses of PO CS ≥ 40 mg are guided by LN course except in major extrarenal flares with potential organ damage. IV CS are used for worsening disease courses that fail to respond to PO CS of ≥ 40 mg up to 4 weeks (Table 1). Small decreases of PO CS occur even with stable LN or extrarenal activity. Complete renal remission allows more pronounced reduction of PO CS. Beyond 6 months post kidney biopsy (maintenance therapy), CS dosing is informed by the renal response during induction therapy, the course of LN, and extrarenal activity (Table 1).

Conclusion: The proposed standardized CS dosing regimen for LN in cSLE may be useful for clinical care and regulation of background CS use during clinical trials of new medications for cSLE.

Disclosure: N. Chalhoub, None; **K. Rouster-Stevens**, None; **M. Klein-Gitelman**, None; **K. Onel**, None; **B. Goilav**, None; **S. Savani**, None; **N. Ruth**, None; **T. Qiu**, None; **N. Aljaberi**, None; **J. Deng**, None; **A. Merritt**, None; **B. Laskin**, None; **A. Sagcal-Gironella**, None; **S. Ardoin**, None; **D. Levy**, None; **S. Wenderfer**, Bristol-Myers Squibb, 1; **B. Huang**, None; **H. Brunner**, Bristol-Myers Squibb, 2, 5, MedImmune, 2, Novartis, 2, 8, Pfizer Inc, 2, 5, AbbVie, 5, AstraZeneca-MedImmune, 5, Bayer, 5, Biocon, 5, Boehringer Ingelheim, 5, Janssen, 5, Eli Lilly, 5, R-Pharm, 5, Roche, 5, 8, Cincinnati Children's Hospital Medical Center, 3, GlaxoSmithKline, 8; **L. Project Investigators**, None.

Abstract Number: 1680

Lupus Anticoagulant as a Predictor of Adverse Outcomes in Children with Venous Thromboembolism

Elizabeth Sloan[1] and Ayesha Zia[1], [1]UT Southwestern Medical Center, Dallas, TX

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The presence of antiphospholipid antibodies, including lupus anticoagulant (LA), is a risk factor for development of venous thromboembolism (VTE) in children. The impact of transient LA positivity on clinical outcomes of VTE are unknown. We investigated (1) the association of clinical outcomes with LA positivity at VTE di-

Characteristics	Lupus anticoagulant positive (N=28)	Lupus anticoagulant negative (N=50)	p-value
Age (years)	11±5.9	10.4±6.7	0.6838
Male	17 (60.7%)	26 (52%)	0.4579
Race			
White	22 (78.6%)	31 (62%)	0.1325
Non-white	6 (21.4%)	19 (38%)	
BMI z-scores (WHO)	1.66±1.44	0.71±1.51	0.0081
Inherited thrombophilia	4 (14.3%)	10 (20.4%)	0.5028
Primary VTE type			0.5433
Extremity	12 (42.9%)	25 (50%)	
Non-extremity	6 (21.4%)	13 (26%)	
Pulmonary Embolus	10 (35.7%)	12 (24%)	
Diagnosis labs			
D-dimer (ng/mL)	4988±5065	3666±5095	0.2873
Factor VIII (%)	232±66	207±74	0.1615
CRP (mg/L)	101±76	64±73	0.1642

Table 1. Demographic Characteristics

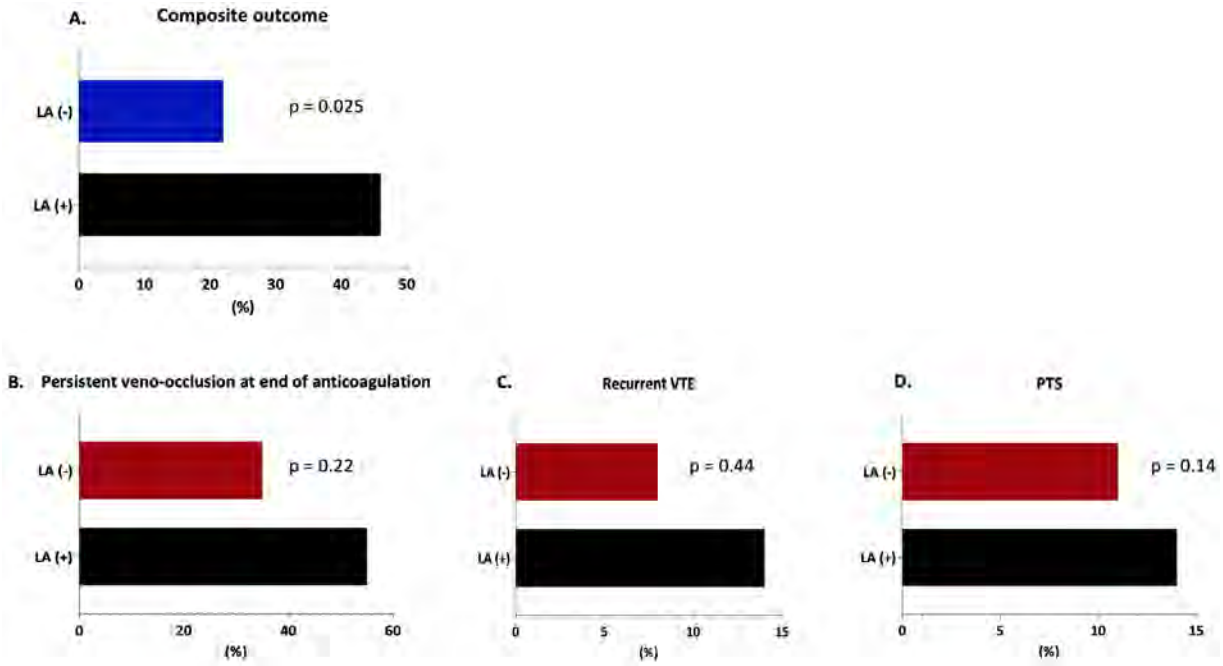

Figure 1. Impact of LA positivity on the development of clinical outcomes

agnosis in the acute and chronic VTE phases and (2) the impact of LA at VTE diagnosis with fibrinolysis in the acute and chronic VTE phases.

Methods: We utilized a nested case-control study design to identify pediatric cases (VTE patients with positive LA at VTE diagnosis) and controls (VTE patients without LA at VTE diagnosis) nested within an ongoing prospective cohort

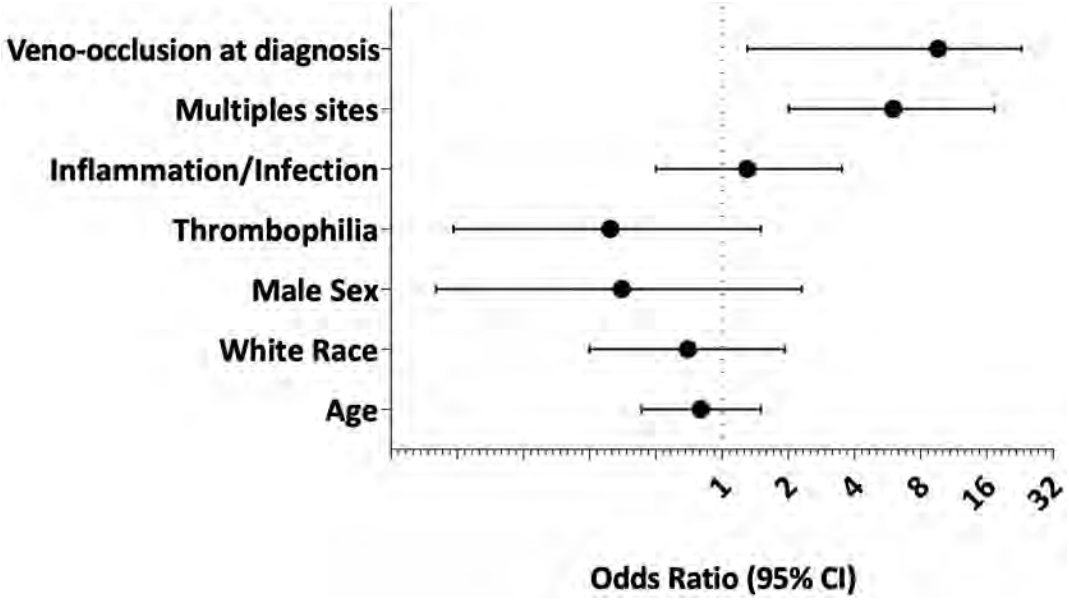

Figure 2. Predictors of composite clinical outcomes in LA positive patients

study. Patients without a known lupus anticoagulant status within 4 weeks of VTE were excluded. We assessed participants for a composite clinical outcome of persistent veno-occlusion, recurrent VTE, or post-thrombotic syndrome (PTS) at 12 months post-diagnosis and a translational outcome of fibrinolysis capacity using a modified thromboelastography at 3- and 12-months post-diagnosis. We examined demographic and clinical characteristics between the cases and controls by univariate analysis and constructed a multivariable logistic regression model to identify predictors of our outcomes in LA positive patients.

Results: We identified 50 controls and 28 cases in our cohort. Baseline characteristics between both groups were similar with the exception of a higher BMI in the LA positive group (*Table 1*). Children with LA positivity at VTE diagnosis were more likely to present with thrombosis at multiple sites (46% vs. 18%, p=0.0074) and more likely to develop the composite clinical outcome (46% vs. 22% p=0.025) despite LA resolution at follow-up (*Figure 1*). In children with transient LA positivity, complete veno-occlusion and multi-site involvement at VTE diagnosis predicted the composite clinical outcomes at 12 months post-diagnosis. (*Figure 2)*. No difference in fibrinolysis was observed at 3 months, but LA positive children were hypofibrinolytic at 12 months; this was not associated with BMI.

Conclusion: We present the first evidence that hypercoagulability induced by transient LA is prognostic in pediatric VTE. Children with LA positivity, even if transient, represent a unique subset of patients with adverse VTE outcomes in the acute and chronic VTE phases independent of inherited thrombophilia, inflammatory and infectious states. Larger studies are needed to validate our findings and to investigate if LA positive children require higher intensity of anticoagulation or upfront thrombolysis in the acute VTE phase to prevent adverse outcomes in the chronic phase.

Disclosure: E. Sloan, None; **A. Zia**, None.

Abstract Number: 1681

Hemophagocytic Lymphohistiocytosis (HLH) Gene Variants in Childhood-onset SLE (cSLE) with Macrophage Activation Syndrome (MAS)

Piya Lahiry[1], Sergey Naumenko[2], Fangming Liao[3], Daniela Dominguez[4], Andrea Knight[5], Deborah Levy[6], Melissa Misztal[7], Lawrence Ng[8], Earl D. Silverman[9] and Linda Hiraki[10], [1]Hospital for Sick Children, Toronto, ON, Canada, [2]The Centre for Computational Medicine, Research Institute, The Hospital for Sick Children, Toronto, ON, Canada, [3]Genetics & Genome Biology, Research Institute, The Hospital for Sick Children, Toronto, Canada, [4]Division of Rheumatology, The Hospital for Sick Children, Toronto, Canada, [5]Division of Rheumatology, The Hospital for Sick Children and Department of Paediatrics, University of Toronto, Toronto, ON, Canada, [6]Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, [7]Genetics & Genome Biology, Research Institute, The Hospital for Sick Children, Oakville, ON, Canada, [8]Division of Rheumatology, Hospital for Sick Children, Toronto, Canada, [9]Division of Rheumatology, The Hospital for Sick Children, Translational Medicine, Research Institute, The Hospital for Sick Children, and Department of Paediatrics, University of Toronto., Toronto, ON, Canada, [10]Division of Rheumatology, The Hospital for Sick Children, Child Health Evaluative Sciences, Research Institute, The Hospital for Sick Children, and Department of Paediatrics, University of Toronto., Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Familial Hemophagocytic lymphohistiocytosis (fHLH) is an autosomal recessive, hyper-inflammatory, life-threatening disease. Macrophage activation syndrome (MAS) is also known as secondary HLH due to the clinical and biological similarities. MAS is increasingly recognized as a complication of systemic lupus erythematosus (SLE). This study compares the frequency of HLH genetic variants in childhood-onset SLE (cSLE) patients with and without MAS.

Methods: Our retrospective cohort was drawn from the Lupus Clinic at SickKids Hospital (Toronto) from 1987-2018. All participants met ACR, and/or SLICC SLE classification criteria. MAS diagnosis was based on expert physician diagnosis. The non-MAS cSLE comparator group was comprised of patients suspected monogenic SLE with whole genome sequencing (WGS). The non-MAS patients had young age of diagnosis (< 11y), consanguineous parents or multiple SLE affected first-degree relatives. Patients with MAS had paired-end whole exome sequencing (WES) by Illumina HiSeq 2500 platform (read depth 70-118X). Patients without MAS had paired-end WGS by Illumina HiSeq X platform (read depth 37-40X). Variant calling was completed with GATK and HAS and functionally annotated with ANNOVAR at The Centre for Applied Genomics (TCAG) in SickKids (annotation pipeline, v26.2, v.26.5). We restricted analyses to exonic regions in the following 16 HLH-genes (*AP3B1, BLOC1S6, CD27, GATA2, ITK, LYST, MAGT1, NLRC4, PRF1, RAB27A, SH2D1A, SLC7A7, STX11, STXBP2, UNC13D, XIAP*). Missense variants with MAF < 0.05 were prioritized. Ancestry was genetically inferred from multiethnic genotyping arrays (Illumina MEGA or GSA) using the ADMIXTURE software and the 1000 Genomes Project as reference. Otherwise, we used self-reported ethnicity according to Canada census categories. Demographic and baseline characteristics were extracted from the Lupus dataset, and analyzed using summary statistics. Medians and interquartile ranges (IQR) were calculated for non-normally distributed data and P-values were derived using two-tailed Fischer exact test.

Results: Our cohort consisted of 19 patients with MAS and 64 without MAS. The age of cSLE diagnosis was younger in the non-MAS cohort but the ethnicity distributions were no different between the two cohorts (Table). Eleven (58%) MAS and 39 (61%) non-MAS patients had exonic HLH variants; 6 (32%) MAS and 30 (47%) non-MAS had missense

		cSLE_MAS (n= 19)	cSLE_no MAS (n= 62)	P*
Sex: Female [n (%)]		16 (84)	53 (83)	1.00
Ancestry: [n (%)]^				
	European	2 (11)	19 (31)	0.13
	East Asian	6 (32)	7 (11)	0.07
	South Asian	4 (21)	5 (8.1)	0.20
	African	2 (11)	7 (11)	1.00
	Amerindian	0	5 (8.1)	0.59
	Mixed	5 (26)	19 (31)	0.78
Median age of SLE diagnosis, yrs (IQR)		12 (8.6, 14.7)	8.6 (7, 10)	
Patients with HLH variants [n (%)]				
	Exonic	11 (58)	39 (61)	0.79
	Missense	6 (32)	30 (47)	0.29

^ Inferred Ancestry – used the 2M MEGA array genotyped-data to identify ethnicity; for those who did not have MEGA array, self-reported Ethnicity was used.

* Fischer exact test was used -- https://www.graphpad.com/quickcalcs/contingency1/; P<0.05 is statistically significant

Table. Demographic and HLH variant comparison of cSLE patients with and without MAS

HLH variants. All these HLH variants were heterozygotes. There was no statistically significant difference in the number of HLH variants (exonic or missense) between MAS and non-MAS cohorts.

Conclusion: We did not observe a difference in the number of HLH exonic or missense variants in cSLE patients with MAS compared to those without MAS. Although this is the largest study of HLH variants in cSLE to date, our sample size had limited power to detect significant differences in rare variants which may have included variants associated with HLH. The non-MAS comparator cohort was likely enriched with rare pathogenic variants based on selection criteria for WGS. Future sequencing studies in larger cohorts of MAS and non-MAS cSLE patients are required to validate our findings.

Disclosure: P. Lahiry, None; **S. Naumenko**, None; **F. Liao**, None; **D. Dominguez**, None; **A. Knight**, None; **D. Levy**, None; **M. Misztal**, None; **L. Ng**, None; **E. Silverman**, None; **L. Hiraki**, None.

Abstract Number: 1682

Goal-Setting Improves Transition Readiness in Adolescents with Juvenile Idiopathic Arthritis and Systemic Lupus Erythematosus

Teresa Semalulu[1], Karen Beattie[1], Jeanine McColl[1], Arzoo Alam[2], Steffy Thomas[2], Julie Herrington[3], Jan Willem Gorter[2], Tania Cellucci[2], Stephanie Garner[1], Liane Heale[2], Mark Matsos[1] and Michelle Batthish[4], [1]McMaster University, Hamilton, ON, Canada, [2]McMaster University, Hamilton, Canada, [3]ACPAC - University of Toronto, Hamilton, ON, Canada, [4]McMaster Children's Hospital, Hamilton, ON, Canada

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The transition from pediatric to adult rheumatology care is associated with increased morbidity, mortality and loss to follow-up. This is largely due to a dramatic change in expectations as patients move from a family-centred, multidisciplinary pediatric care model to adult care models, which require independence and active engagement by the patient. Thus, adolescents must acquire sufficient self-management skills in order to successfully navigate the adult health care system independently. Comprehensive transition programs must recognize the variability in transition preparedness among similarly-aged individuals and allow for individualized intervention accordingly. The objective of our study was to assess the impact of goal-setting on changes in transition-readiness among adolescents with JIA and jSLE.

Methods: Patients (age 14-19) with JIA and jSLE were recruited from pediatric and young adult rheumatology transition clinics at a single academic institution. To assess transition readiness, each participant completed the TRANSITION-Q questionnaire. This self-administered, validated, 14-item questionnaire (max score = 100) is used to assess healthcare self-management skills as a proxy for preparedness for transition from pediatric to adult care. Participants completed the TRANSITION-Q at the time of consent and at all subsequent follow-up visits thereafter. Time between visits was at the physicians' discretion. Upon completion of the TRANSITION-Q at each appointment, goals were established with multidisciplinary care members in areas identified as needing improvement based on the participants' responses. Descriptive statistics were summarized for patient characteristics at baseline and for TRANSITION-Q scores at each time point.

Baseline Characteristics

	Mean (SD) or n (%)	Range
Age (years)	16.7 (1.0)	14-19
Female	27 (19)	-
JIA **cSLE**	30 (81) 7 (16)	-
Age at diagnosis (years)	12.6 (3.9)	2-18
Disease duration (years)	4.1 (3.9)	0-14

Baseline Characteristics

TRANSITION-Q Scores

TRANSITION-Q Scores

Results: Among 37 respondents, 10 were male and 23 were female (mean (SD) age 16.7 (1.0) years); n=30 JIA (81%), n=7 jSLE (19%). Thirty-two participants were seen twice (mean (SD) follow-up time 6.4 (2.5) months),14 were seen 3 times (mean (SD) time from first to second follow-up 3.4 (1.7) months) and 2 were seen 4 times (mean(SD) time from second to third follow-up 2.8 (2.0) months). Mean (SD) TRANSITION-Q scores at baseline and 3 follow-ups were 60.8 (14.8), 67.5 (11.5), 73.0 (9.4), and 76.0 (8.5), respectively.

Conclusion: We observed increases in TRANSITION-Q scores over time in this cohort. Goal setting and using a validated tool to track self-management skills may be particularly beneficial as self-management skills appeared to improve over time among our patient population.

Disclosure: T. Semalulu, None; **K. Beattie**, None; **J. McColl**, None; **A. Alam**, None; **S. Thomas**, None; **J. Herrington**, None; **J. Gorter**, None; **T. Cellucci**, None; **S. Garner**, None; **L. Heale**, None; **M. Matsos**, None; **M. Batthish**, Abbvie, 2.

Abstract Number: 1683

Ready or Not? Measuring Readiness for Transition to Adult Care in Adolescents with JIA & jSLE

Jeanine McColl[1], Teresa Semalulu[1], Arzoo Alam[2], Steffy Thomas[2], Julie Herrington[3], Jan Willem Gorter[2], Tania Cellucci[2], Stephanie Garner[2], Liane Heale[2], Mark Matsos[2], Karen Beattie[1] and Michelle Batthish[4], [1]McMaster University, Hamilton, ON, Canada, [2]McMaster University, Hamilton, Canada, [3]The Canadian Arthritis Society, Hamilton, Canada, [4]McMaster Children's Hospital, Hamilton, ON, Canada

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Transitioning from pediatric to adult care represents a particularly vulnerable period among patients with JIA and jSLE. The shift to adult care is often unsuccessful, with patients being lost to follow-up or non-adherent to medications. Transition programs must support adolescents in acquiring and improving skills necessary to manage their own disease. Measuring patients' current level of transition readiness is the first step in identifying areas for improvement in self-management skills and the transition process itself. Our objectives were to 1) examine variability in transition readiness using the Transition-Q in adolescents with JIA and jSLE; 2) determine the association between age and Transition-Q scores; and 3) identify areas that may be the biggest challenges to these adolescents.

Methods: Over a one-year period, patients 14-20 years of age with JIA or jSLE were recruited from transition and young adult clinics at a single academic institution. Participants completed the Transition-Q, a validated 14-item

	Mean (SD) or n (%)	Range
Age (years)	16.4 (1.3)	14-20
Female	48 (45)	-
Diagnosis JIA jSLE	 61 (87.1) 9 (12.9)	-
Age at diagnosis (years)	11.7 (4.6)	1-17
Disease duration (years)	4.6 (4.5)	0-16
Transition-Q score[2]	59.7 (14.9)	31-100

Table 1 Baseline Characteristics (n=70)

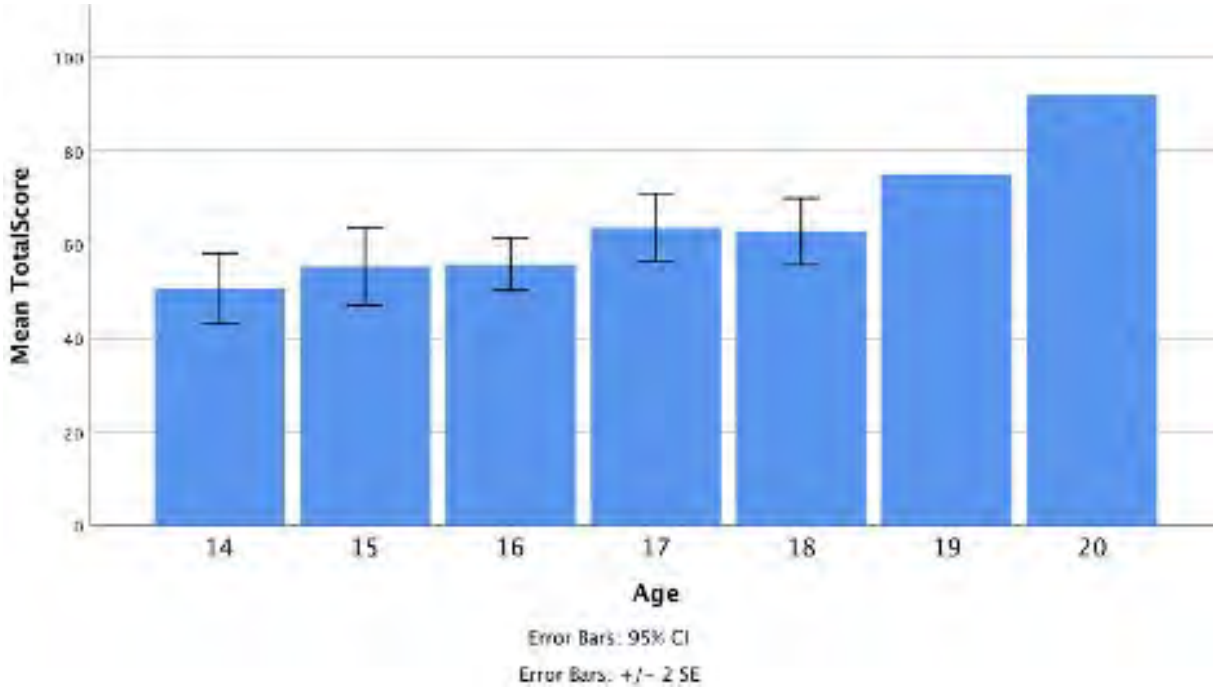

Figure 1 Mean Total Transition-Q Scores by Age

questionnaire which assesses healthcare self-management skills as a proxy for readiness to transition to adult care. Adolescents respond "never," "sometimes," or "always" to each question. Total scores range from 0-100; higher scores indicate greater transition readiness. Descriptive statistics summarized patient characteristics and Transition-Q scores. Differences in Transition-Q scores between sexes and diseases were explored using independent t-tests. Regression analyses determined the association between Transition-Q scores and age, controlling for sex and disease duration. Frequencies of responses to each question were determined.

Results: Of 70 participants (mean (SD) age 16.4 (1.3) years, 68.6% female), 61 had JIA and 9 had jSLE (Table 1). The mean (SD) Transition-Q score was 59.8 (14.9). Females had significantly higher mean total Transition-Q scores (62.3 (14.5)) compared to males (54.5 (14.9), p=0.043). The mean (SD) total Transition-Q score was 58.7 (15.2) amongst those with JIA and 67.9 (11.1) amongst those with jSLE (p= 0.105). Transition-Q scores significantly increased with age after accounting for sex and disease duration (standardized β=0.380, p=0.001) (Table 1). Most patients responded "never" to "I travel on my own to a doctor's appointment" (82.9%), "I see the doctor or nurse on my own during an appointment" (60.0%), "I drop off or pick up prescriptions when I need medicine" (58.6%) and "I book my own doctor's appointments" (58.6%).

Conclusion: This is the first study to use the Transition-Q to measure transition readiness in adolescent rheumatology patients. Transition readiness varied between and within age groups yet increased with age. Compared to males, females had higher total Transition-Q scores reflecting higher self-management skills. There was no difference in total Transition-Q scores between individuals with JIA compared to jSLE. Future work will examine the trajectory of changes in Transition-Q scores within patients over time, including after they transition to adult care. We will explore strategies to improve self-management skills and, subsequently, Transition-Q scores.

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Abstract Number: 1684

Increase in Emergency Department Visits and Hospitalizations, Decrease in Outpatient Visits Following Transition to Adult Rheumatologic Care

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Many children with rheumatic disease have active disease as adults, and health care gaps often occur in the transition from pediatric to adult care. We evaluated health care utilization during the adult to pediatric transition.

Methods: This IRB-approved, retrospective study evaluated individuals with rheumatic disease transferring from a pediatric to an adult health system (1/1/2006 -12/31/2016). Subjects age ≥ 8 yrs by 1/1/2010 with ≥ 1 visit before age 20 y, ≥ 2 visits with same rheumatology-related ICD-9 and 10 diagnostic codes (RDC), initial visit with RDC in the children's health system , ≥1 visit with RDC in adult system, and ≥ 1 rheumatology specialty provider visit were included. Pre-transition period was defined as time between first and last rheumatology visits in the children's health system. Transition period was time from last pediatric rheumatology visit to second adult rheumatology visit, and post-transition period was time between second and last adult rheumatology visits. Gender, self-reported race/ethnicity, medication (disease modifying anti-rheumatic drugs or biologic) use, diagnosis and household income [estimated by post-transition zip code using US Census Bureau American Community Survey (2014-2018)] were analyzed. Mixed effects binomial modeling of the dichotomous variable of ≥ 1 emergency department (ED) visit or hospitalization was performed examining variables denoted in Table 1. Poisson modeling of the continuous outcomes of number of rheumatology and non-rheumatology office visits was performed including predictors in Table 1 except period duration.

Variable	Pre-transition (122)	Transition (122)	Post-transition (93)
Male (n, %)	26 (21.3)	26 (21.3)	19 (20.4)
Non-white race (n, %)	32 (26.2)	32 (26.2)	26 (28.0)
Inflammatory arthritis* (n, %)	81 (66.4)	83 (68.0)	60 (64.5)
Lupus* (n, %)	36 (29.5)	37 (30.3)	31 (33.3)
Other autoimmune* (n, %)	20 (16.4)	22 (18.0)	18 (19.4)
Vasculitis* (n, %)	7 (5.7)	7 (5.7)	6 (6.50)
DMARD use (n, %)	73 (59.8)	91 (74.6)	72 (77.4)
Biologic/small molecule (n, %)	56 (45.9)	63 (51.6)	45 (48.4)
≥ 1 ED visit or hospitalization (n, %)	46 (37.7)	103 (84.4)	82 (88.2)
No. of rheumatology office visits (median, interquartile range)	22 (11-37)	1 (1-1)	3 (1-8)
No. of non-rheumatology office visits (median, interquartile range)	14.5 (3-36)	1 (0-2)	3 (1-7)
Duration of period (days, interquartile range)	1339.5 (805-1855)	190 (90.5-366.5)	567 (204-1044)

Table 2: Variables Associated with Emergency Department Visits and Hospitalizations During Transition to Adult Rheumatologic Care

Variable	Odds Ratio (95% CI)	P-value
Transition period	17.53 (7.85-39.19)	< 0.001
Post-transition period	19.62 (8.83-43.58)	< 0.001
Duration of period	1.00 (1.00-1.00)	0.136
Median household income*	0.99 (0.98-0.99)	0.026
Inflammatory arthritis diagnosis	1.44 (0.48-4.36)	0.514
Vasculitis diagnosis	7.22 (1.29-40.53)	0.025
Lupus diagnosis	2.80 (0.96-8.17)	0.060
Other autoimmune diagnosis	0.83 (0.35-1.99)	0.676

Table 3: Variables Associated with Outpatient Office Visits During Transition to Adult Rheumatologic Care

Variable	Coefficient (95% CI)	P-value
Rheumatology office visits		
Transition period	-0.78 (-0.99, -0.56)	< 0.001
Post-transition period	-1.20 (-1.56, -0.84)	< 0.001
Non-white race	0.37 (0.12, 0.62)	0.003
Non-rheumatology office visits		
Transition period	-0.71 (-1.11, -0.30)	0.001
Post-transition period	-0.65 (-0.99, -0.31)	< 0.001
Non-white race	0.64 (0.20, 1.08)	0.005

Results: 122 subjects met inclusion criteria for analysis. Of these, 93 (76%) reached post-transition period; 96 (79%) were female and were 32 (26%) non-white. Median household income was $67,872 (IQR $46,013 - $81,813). Patient characteristics during the transition periods are summarized in Table 1. Median transition time was 190 days (IQR 90.5 - 366.5). As noted in Table 2, risk of ≥ 1 ED visit or hospitalization significantly increased during transition period (OR 17.5; 95% CI 7.8 - 39.2), post-transition period (OR 19.6; 95% CI 8.8 - 43.6) and with diagnosis of vasculitis (OR 7.2; 95% CI 1.3 - 40.5). As shown in Table 3, the number of rheumatology and non-rheumatology office visits, corrected for period duration and other co-variates, decreased during transition and post-transition periods and was lower in non-white subjects.

Conclusion: In this retrospective analysis of health care transition over a 10 yr period between large pediatric and adult medical facilities, the rate of transition to adult care was 76%, higher than in most reported studies, and the median time between last pediatric and second adult rheumatology visits was ≥ 6 months. ED use and hospitalization significantly increased in the transition and post-transition periods and in individuals with vasculitis. Both rheumatology and non-rheumatology office visits decreased in the transition and post-transition periods. Non-white individuals had fewer office visits. These results suggest that efforts to increase post-transition outpatient care have the potential to reduce ED visits and hospitalizations.

Disclosure: P. Jensen, None; **J. Greco**, None; **K. Jackson**, None; **S. Ardoin**, None.

Abstract Number: 1685

Impact of the COVID-19 Pandemic Among Children with Rheumatic Diseases from Around the Globe

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Children with rheumatic diseases face unknown risks in the setting of the COVID-19 pandemic. These children are often immunosuppressed due to their underlying disease or the medications used to treat them. It is unknown whether children with rheumatic diseases are at increased risk of SARS CoV-2 infection or of developing serious disease complications should they become infected. We report on the pediatric data from the COVID-19 Global Rheumatology Alliance (C19-GRA) Patient Experience Survey.

Methods: The C19-GRA launched an international Patient Experience Survey for adults and parents of children with rheumatic disease, with or without COVID-19 infection. The survey was distributed online through patient support organizations and on social media. Parents completed the data on behalf of their children, including their child's rheumatic disease diagnosis, medications, disease activity (as measured by a visual analog scale from 0-10, where 0=very good and 10=very poor), whether or not they developed COVID-19, and COVID-19 disease outcomes. Parents also completed the PROMIS Parent Proxy Scale v1.0 – Global Health 7. We report on data for children less than 18 years of age from April 3-May 8, 2020.

Results: A total of 427 children are included in the analyses. Their demographics and clinical characteristics are shown in Table 1. Most respondents resided in the Americas (64.9%) and were white (73.3%), female (63.0%), and between the ages of 5-14 (64.9%). The majority of patients had juvenile idiopathic arthritis, and most were taking conventional synthetic DMARDs (csDMARDs) and/or biologic DMARDs (bDMARDs). The median disease activity score was 3 (IQR 1-6). The median T-score of the PROMIS Global Health measure was 43.9. Within this group, only 5 children (1.2%) were diagnosed with COVID-19, and none required hospitalization. Their COVID-19 disease experience is shown in Table 2.

Conclusion: In this international survey of children with rheumatic diseases, only a handful of children developed COVID-19, all of whom had benign outcomes. Similar to otherwise healthy children, those with rheumatic disease do not seem to be at greater risk of developing COVID-19 or of COVID-19-related complications, even while taking immunosuppressive medications. Limitations of this study include a convenience sample of parents engaged in social media, which may not be representative of the pediatric rheumatology population. Data were self-reported and could not be verified. Future studies should assess the long-term effect of COVID-19 infection in patients with rheumatic disease, as well as assess the rates of complications such as Multisystem Inflammatory Syndrome in Children (MIS-C).

Table 1. Demographic and clinical characteristics of children in the C19-GRA Patient Experience Survey (n=427).

	N	%
Gender		
Female	269	63
Male	154	36.1
Nonbinary	2	0.5
Prefer not to answer	2	0.5
Race/Ethnicity		
White	313	73.3
Other	51	11.9
Latin American	47	11
Black	8	1.9
Asian	7	1.6
Native American / Aboriginal / First Nations	1	0.2
Age		
0 to 4	56	13.1
5 to 9	134	31.4
10 to 14	143	33.5
15 to 17	94	22
WHO Region		
Region of the Americas	277	64.9
European Region	125	29.3
African Region	14	3.3
Western Pacific Region	7	1.6
South-East Asia Region	3	0.7
Eastern Mediterranean Region	1	0.2
Rheumatic disease diagnosis		
Juvenile idiopathic arthritis	174	40.7
Systemic JIA	115	26.9
Autoinflammatory disease	74	17.3
Systemic lupus erythematosus	50	11.7
Inflammatory myopathy	16	3.7
Inflammatory eye disease	16	3.7
CRMO	13	3
Vasculitis	10	2.3
Behcet's syndrome	8	1.9
Antiphospholipid syndrome	7	1.6
MCTD	7	1.6
UCTD	5	1.2
Systemic sclerosis	4	0.9
Sjogren's Syndrome	1	0.2
Comorbidities		
Asthma	56	13.1
Immunodeficiency	46	10.8
Other lung disease	24	5.6
Pain Syndromes	18	4.2
IBD	16	3.7
Other	55	12.9
Medications		
csDMARDs	233	54.6
Biologic DMARDs	221	51.8
NSAIDs	198	46.4
Steroids	113	26.5
tsDMARDs	8	1.9
Other	16	3.7

Participants may have more than one condition and take more than one type of medication.
csDMARD medications included: antimalarials (hydroxychloroquine, chloroquine), azathioprine, cyclophosphamide, cyclosporine, leflunomide, methotrexate, mycophenolate mofetil/mycophenolic acid, sulfasalazine, tacrolimus.
bDMARD included: abatacept, belimumab, CD-20 inhibitors, IL-1 inhibitors, IL-6 inhibitors, IL-12/IL-23 inhibitors, IL-17 inhibitors, and anti-TNF.
tsDMARD included: Janus Kinase inhibitors.
Other included: IVIG, apremilast, thalidomide.
bDMARD, biologic DMARD; csDMARD, conventional synthetic DMARD; tsDMARD targeted synthetic DMARD, DMARD, disease-modifying antirheumatic drug; NSAID, non-steroidal anti-inflammatory drug; TNF, tumor necrosis factor.

Table 1. Demographic and clinical characteristics of children in the C19-GRA Patient Experience Survey (n=427).

Table 2. COVID-19 disease characteristics among children with rheumatic diseases (n=5).

	N	%
Rheumatic disease diagnosis		
Juvenile idiopathic arthritis	2	40
Autoinflammatory disease	2	40
Systemic JIA	1	20
COVID-19 symptoms		
Malaise	4	80
Fever	3	60
Headache	3	60
Sore throat	3	60
Arthralgias	3	60
Chest pain	2	40
Abdominal pain	2	40
Cough	2	40
Myalgias	1	20
Vomiting	1	20
Anosmia	1	20
Rhinorrhea	1	20
Irritability/confusion	1	20
How COVID-19 diagnosis was made		
Self-diagnosis	3	60
Physician diagnosis based on symptoms	2	40
Length of illness		
5 days or less	2	40
20+ days	2	40
Unresolved at time of survey (13+ days)	1	20
COVID-19 Severity		
Not hospitalized, some limitations in ADLs	3	60
Not hospitalized, no limitation in ADLs	2	40
Potential COVID-19 exposures		
Close contact with COVID-19	1	20
Healthcare facility contact	1	20
None/don't know	3	60
Rheumatic disease control at time of COVID-19 diagnosis		
Mean disease activity score*	2.4 (range 0-7)	
Rheumatic disease medications at time of COVID-19 diagnosis		
NSAIDs	3	60
Methotrexate	1	20
None	1	20

*Disease activity score is a visual analog scale from 0=very well to 10=very poor. ADLs: activities of daily living. NSAID: non-steroidal anti-inflammatory drug.

Table 2. COVID-19 disease characteristics among children with rheumatic diseases (n=5).

Disclaimer: The views expressed here are those of the authors and participating members of the COVID-19 Global Rheumatology Alliance and do not necessarily represent the views of the American College of Rheumatology, the European League Against Rheumatism (EULAR), or any other organization.

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The COV-ASAKI Survey from the Pediatric Tuscany Network During COVID-19 Era

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: At the end of April 2020, national and international Pediatrics scientific societies diffused an alert about a rise in the number of pediatric severe, inflammatory syndrome, coronavirus 2 (SARS-CoV-2) related, resembling Kawasaki disease (KD).

Methods: The Pediatric Rheumatology Tuscany Network worked out the COV-ASAKI survey to track children who received a KD diagnosis in during COVID-19 pandemic in a region hosting 593.606 people aged less than 18 years. We retrospectively collected demographics, clinical and imaging findings, treatment and outcome of KD children between February 1st to April 30th, 2020 and compared the number of cases in the 2020 index trimester with the same trimesters of the previous 5 years and overall with the total number in the last 5 years.

	Age Weight Comorbidities	Clinical presentation	Pharmacological treatment	Imaging results	Laboratory results	SARS COV-2 tests	Hospital length of stay	Outcome
Patient 1 (Female, Caucasian)	3 years, 15 Kg No comorbidities	5 days fever (T> 38°C), rash, palm-plantar edema, conjunctivitis, cheilitis, lymphadenopathy, irritability, arthralgia	IVIG, aspirin and iv. antibiotics	Normal abdominal US and echocardiography	WBC 14,380 cells/mm^3, ESR 53 mm/h, CRP 12.5 mg/dL, ALT 238 UI/l	Nasopharyngeal swab: negative Serological test: negative	8 days	Complete recovery
Patient 2 (Male, Caucasian)	4 years, 15 Kg, No comorbidities	6 days fever (T> 38°C), rash, conjunctivitis, cheilitis, lymphadenopathy, irritability, vomiting	IVIG, aspirin and iv. antibiotics	Normal abdominal US and echocardiography	WBC 25,570 cells/mm3, PLT 528,000 cells/mm3, ESR 120 mm/h, CRP 16.4 mg/dL, fibrinogen 937 mg/dL	Not performed	7 days	Complete recovery
Patient 3 (Male, Caucasian)	4 years, 17 Kg, No comorbidities	9 days fever (T> 38°C), rash, palm-plantar edema cheilitis, lymphadenopathy, irritability, myalgia	IVIG, aspirin and iv. antibiotics	Normal echocardiography	WBC 11,550 cells/mm^3, ESR 63 mm/h, CRP 10 mg/dL, ferritin 116 ng/mL	Nasopharyngeal swab: negative Serological test: negative	8 days	Complete recovery
Patient 4 (Female, Caucasian)	2 years, 11 Kg, Congenital hypothyroidism	5 days fever (T> 38°C), rash, conjunctivitis, cheilitis, dyspnea, irritability	IVIG, aspirin and iv. antibiotics	Normal echocardiography, reactive lymphadenopathy at neck US, pneumonitis at chest US	WBC 3,470 cells/mm^3, L 711 cells/mm^3, ESR 4 mm/h, CRP 2.1 mg/dL	Not performed	16 days	Complete recovery
Patient 5 (Female, Caucasian)	2 years, 11 Kg, No comorbidities	5 days fever (T> 38°C), rash, conjunctivitis, cheilitis, lymphadenopathy, irritability	Methylprednisolone, IVIG, aspirin and iv. antibiotics	Normal abdominal US and echocardiography, pneumonitis at chest XR	WBC 9,360 cells/mm^3, PLT 277,000 cells/mm3, Hb 8,3 g/dL, ESR 76 mm/h, CRP 4.61 mg/dL, ferritin 866 ng/dL, triglycerides 419 mg/dL, albumin 1.98 g/dL	Nasopharyngeal swab: negative Serological test: negative	15 days	Complete recovery
Patient 6 (Female, Asiatic)	2 years, 12 Kg, No comorbidities	5 days fever (T> 38°C), febrile seizures, rash, conjunctivitis, cheilitis, palm-plantar edema lymphadenopathy, arthritis	IVIG, aspirin and iv. antibiotics	Normal echocardiography, pneumonitis at chest XR, hydrops of the gallbladder at abdominal US	WBC 12,600 cells/mm^3, ESR 59 mm/h, CRP 26.02 mg/dL, ALT 485 UI/L, AST 536 UI/L, fibrinogen 924 mg/dL, ferritin 227 ng/mL	Nasopharyngeal swab: negative Serological test: negative	11 days	Complete recovery
Patient 7 (Male, Caucasian)	1.5 years, 10.4 kg, No comorbidities	5 days fever (T> 38°C), rash, conjunctivitis, cheilitis	IVIG, aspirin and iv. antibiotics	Normal echocardiography	WBC 17,280 cells/mm^3, ESR 31 mm/h, Hb 9.8 g/dL CRP 5.96 mg/dL	Not performed	10 days	Complete recovery
Patient 8 (Female, Caucasian)	4 years, 15.5 Kg, No comorbidities	5 days fever (T> 38°C), rash, conjunctivitis, cheilitis lymphadenopathy	IVIG and aspirin	Normal echocardiography, hydrops of the gallbladder at abdominal US	WBC 19,900 cells/mm^3, ESR 120 mm/h, CRP 25.72 mg/dL, fibrinogen 620 mg/dL, ferritin 183 ng/mL	Nasopharyngeal swab: negative Serological test: not performed	9 days	Complete recovery

Abbreviations: IVIG =Intravenous immunoglobulins, iv.=intravenous, US=ultrasonography, XR=radiography, MRI: magnetic resonance, WBC=white blood cells count, PLT=platelets, L= lymphocytes, Hb= hemoglobin, ESR=erythrocyte sedimentation rate, CRP=C-reactive protein, ALT= alanine aminotransferase, AST= aspartate aminotransferase, PT=prothrombin time

Table1. Demographics, clinical findings, imaging findings, treatment, and outcome of Kawasaki syndrome patients

Results: 8 children were diagnosed as KD, with an incidence rate of 2.6/ month. 1 child presented an incomplete KD. 7 were Caucasian and 1 Asiatic, without any underlying disease. 6 recovered after one course of intravenous immunoglobulins (IVIG), no specific intensive support was required. 1 patient needed two IVIG courses, a young girl developed an incipient macrophage activation syndrome (MAS) responsive to a single steroid pulse. The SARS-CoV-2 on nasopharyngeal swab, available in 6/8 children, was negative. 4 KD children, sampled for antibodies after recovery, resulted negative. No coronary involvement was reported. From February 1st and April 30th, 1992 nasopharyngeal swabs have been performed to the Tuscan children admitted to the hospitals: 85/1992 (4.3%) resulted positive for SARS CoV-2. 50 serological tests have been performed with 7 positive results. Considering the previous 5 years, 165 children were diagnosed with KD (incidence 2.7 per month). 59 were incomplete forms; 3 developed MAS and 1 experienced Kawasaki disease shock syndrome (KDSS). 38 showed coronary involvement , 11 received steroid pulses and additional 3 biologic therapy. No statistically significant difference in the incidence/month was found (RR 1.09, 95% CI 0.52-2.04, p=0.76), neither limiting the analysis to the 45 KD children diagnosed during the same corresponding 3-months of the last 5 years: 3 vs 2.6 (RR 1, 95% CI 0.46-1.98, p=0.96). Chi square analysis with Fisher's exact test correction failed to detect significant differences among the principal outcomes of KD children observed during the COVID-19 time and in the last 5 years: incomplete KD 59 *vs* 1, c^2=1.82; KDSS 1 *vs* 0, c^2=0.04; MAS: 3 *vs* 1, c^2=3.85; coronary involvement 38 *vs* 0, c^2=2.36. The same results have been detected adjusting the analysis for the 45 cases during the corresponding trimesters of the last 5 years (p=n.s, Fisher's exact test).

Conclusion: In Tuscany, during the COVID-19 pandemic, almost all KD patients, showed a mild disease course and completely recovered without complications. The long-lasting collaboration and the well-structured communication of our pediatric network provided a prompt intervention in new KD cases during COVID-19 pandemic and allowed a comparison between 2020 KD cluster and the previous ones, A comparison between our data and the results seen worldwide will be helpful to define the multifaceted nature of the pediatric COVID-19 and its potential relationship with the KD.

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Abstract Number: 1687

Kawasaki Disease Shock Syndrome in the Intensive Care Unit: A Single Center Cohort

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Time: 9:00AM–11:00AM

Background/Purpose: Kawasaki disease (KD), a well described vasculitis of childhood, is the leading cause of acquired heart disease in developed countries. Kawasaki disease shock syndrome (KDSS) has been described in a limited number of small single center cohorts and case reports but its incidence and prognosis are poorly understood. Here we aim to add to the existing body of knowledge by describing patients with the diagnoses of KD and shock at our institution.

Methods: With IRB approval, the electronic medical record was used to retrospectively identify a total of 9286 PICU admissions between March 2012 and February 2016, 269 of whom had rheumatology consult. Of those 269, 30 patients (11 %) had KD and 27 (90%) had the specific diagnosis of KDSS. Five patients were excluded whose hypotension was documented after IVIG initiation and seven patients were excluded who did not have documented evidence of shock. The diagnosis of shock was confirmed by the combination of clinical concern requiring PICU admission and objective evidence, defined by hypotension for age or laboratory evidence of impaired perfusion (lactate > 2.0 mmol/L or mixed venous sat < 70%). The 18 remaining patients' charts were reviewed for the features presented in tables and results.

Results: The patients described in our cohort were predominantly African American (39%) and Hispanic (44%) and mostly male (61%) (table 1). The median age was 3.9 years and the median duration of fever was 8 days (table 2). Laboratory values are provided in table 3. Eight (44%) patients required inotropic support for their shock with one requiring extracorporal membrane oxygenation (ECMO). The shock was mostly distributive in nature with only one patient presenting with isolated cardiogenic shock with pulmonary edema. Fifteen patients (83%) received pulse dose steroids, 11 (61%) received daily steroids and 3 (17%) received no steroids. Steroids were given an average of 2 days after the first IVIG. Five patients (28%) received a second IVIG. Two patients received infliximab after fever resolution. On initial echocardiograms, six patients (33%) had systolic dysfunction and two (11%) had coronary dilation with z-score > 2.5. On the 6-8 week echocardiogram, three (17%) had coronary dilation with z-score > 2.5 but this had resolved by recent follow-up in all but one patient (6%). The prevalence of shock in KD was 1 in 27 patients, while prevalence of KDSS in the PICU was 1 in 550 admissions.

Conclusion: All of our KDSS patients had good coronary outcomes except one patient who required ECMO. Our coronary outcomes at last echo were better than previously published data and the majority of our patients received steroids. However, there were 3 patients who received no steroids and also had good coronary outcomes. The steroids were not typically given immediately as distinguishing KDSS from sepsis without blood cultures can be

Feature	Proportion (Positive/Total)
Diagnostic Criteria	12/18 Complete, 5/18 Incomplete, 1/18 Echo
Sex	11/18 Male
Ethnicity	8/18 Hispanic, 7/18 African American, 4/18 Asian
Systolic dysfunction	6/18 patients with evidence of systolic dysfunction
Hemodynamic Shock Features	9/18 Hypotension, 1/18 Pulmonary edema
Biochemical Shock Features (Lactate > 2 mmol/L or Mixed venous sat < 70%)	14/15 Low mixed venous sat, 5/14 elevated lactate
Inotropic support	8/18
Received pulse steroids	15/18
Received daily steroids	11/18
Fevered through first IVIG	5/18
Fevered through second IVIG	1/5
Received infliximab	2/18
First echo coronary changes	2/18 with coronary dilation with Z score > 2.5 on first echo
Aneurysm at 6-8 week echo	3/18 with aneurysm
Aneurysm at last echo	1/18 with persistent aneurysm

Table 1. Patient Characteristics, Shock Features, Coronary Outcome

Feature	Mean	Median	Range
Age (years)	4.3	3.9	0.4 - 14.2
Day of Illness of First IVIG	7.3	6	4 - 20
Fever Duration (days)	9.6	8	4 - 33
Admission Duration (days)	10.8	7.5	3 - 45
Day of First IVMP after IVIG	1	2	0 - 9
Number of IVMP pulses	2.9	3	0 - 8
Duration of oral steroids (days)	30	38	0 - 72
Duration of follow–up (years)	2.4	2.2	0.1 - 6.2

Table 2. Patient Age and Therapy

challenging. The true utility of steroids is limited by the small cohort size and variety of dosing regimens. KDSS is an uncommon diagnosis in the PICU and it is important for the intensivist to consider this diagnosis in patients presenting with shock.

Lab (normal values)	Total Patients Measured	Mean	Median	Range
Initial CRP (< 1.0 mg/dL)	18	22	23.9	4.6 - 41.8
Maximum CRP (< 1.0 mg/dL)	18	23.2	24.3	4.6 - 41.8
Initial ESR (<= 20 mm/hr)	16	57.7	58	13 - 99
Initial Platelets (150 – 450 x 10^3/µL)	18	280	310	67 - 485
Minimum Platelets (150 – 450 x 10^3/µL)	18	186	154	37 - 416
Maximum Platelets (150 – 450 x 10^3/µL)	18	738	761	318 - 1342
Maximum Ferritin (10 – 70 ng/mL)	16	335	250	93 - 997
Maximum INR (0.8 – 1.2)	17	1.5	1.2	1 - 3.9
Maximum PTT (24.8 – 34.4 sec)	17	38.3	36	23.7 - 81.8
Max BNP (< 100 pg/mL)	10	1938	1183	117 - 1596
Maximum Lactate (0.2 -1.7 mmol/L)	14	2.7	1.75	0.8 - 13.5
Minimum Mixed Venous Saturation (85 – 100 %)	15	59	60	40 - 93

Table 3. Laboratory Values

Disclosure: M. Bray, None; **J. Rammel**, None; **A. Ramirez**, None; **K. Sexson**, None; **F. Lam**, None; **E. Muscal**, None; **M. DeGuzman**, None.

Abstract Number: 1688

Long-term Hearing Loss, Anxiety and Neurodevelopmental Outcomes Following Kawasaki Disease: A Population-based Cohort Study

Cal Robinson[1], Francis Lao[2], Rahul Chanchlani[1], Anastasia Gayowsky[3], Sandeep Brar[4], Elizabeth Darling[5], Catherine Demers[5], Tapas Mondal[1], Rulan Parekh[6], Hsien Seow[5] and Michelle Batthish[1], [1]McMaster Children's Hospital, Hamilton, ON, Canada, [2]Michael G. DeGroote School of Medicine, McMaster University, Hamilton, ON, Canada, [3]ICES McMaster, Hamilton, ON, Canada, [4]University of California, San Fransisco, [5]McMaster University, Hamilton, ON, Canada, [6]University of Toronto, Toronto, Canada

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The incidence of Kawasaki disease (KD) is increasing in Ontario. Cardiovascular sequelae following KD are well-described. However, there are limited and conflicting non-cardiovascular outcome data among KD survivors. Our objectives were to determine the incidence and risk of hearing loss, anxiety, developmental disorders, intellectual disabilities and attention-deficit/hyperactivity disorder (ADHD) among KD survivors *vs.* non-exposed children.

Methods: We included all Ontario children (≤18yr) surviving hospitalization with a KD diagnosis between 1995-2018, through validated algorithms using population-based health administrative databases. We excluded children with a prior KD diagnosis, non-residents, and those with incomplete records. KD cases were matched with 100 non-exposed children by age, sex and index admission year. Follow-up continued until death or March 2019. We calculated the prevalence, incidence (per 1000 person-years (py)) and unadjusted hazard ratios (HR) for each outcome between 0-1yr, 1-5yr, 5-10yr and >10yr.

Results: Among 4,597 KD survivors and 459,700 non-exposed children (median 11.1yr follow-up), KD survivors had more hearing loss: 364 cases (7.9%) *vs.* 31,442 (6.8%); anxiety disorders: 1,213 (26.4%) *vs.* 99,965 (21.8%); developmental disorders: 398 (8.7%) *vs.* 28,211 (6.1%); intellectual disabilities: 52 (1.1%) *vs.* 2,931 (0.6%); and ADHD: 21 (0.5%) *vs.* 1,214 (0.3%). Compared to non-exposed children, KD survivors were at increased risk of hearing loss between 0-1yr (HR 1.25 [95%CI 1.00-1.54]); anxiety disorders between 0-1yr (HR 1.75 [1.46-2.10]), 1-5yr (HR 1.12 [1.00-1.27]) and 5-10yr (HR 1.12 [1.00-1.25]); developmental disorders between 0-1yr (HR 1.66 [1.42-1.93]) and 1-5yr

Outcome	KD survivors (N=4597)		Non-exposed (N=459,700)		0-1 years		1-5 years		5-10 years		> 10 years	
	n (%)	Incidence (/1000py)	n (%)	Incidence (/1000py)	HR	95% CI	HR	95% CI	HR	95% CI	HR	95% CI
Hearing loss †	364 (7.9)	7.45	31,442 (6.8)	6.92	1.25	1.00 - 1.54	1.00	0.86 - 1.16	1.17	0.93 - 1.48	1.22	0.89 - 1.68
Anxiety disorder ‡	1,213 (26.4)	27.67	99,965 (21.8)	23.92	1.75	1.46 - 2.10	1.12	1.00 - 1.27	1.12	1.00 - 1.25	1.08	0.99 - 1.18
Intellectual disability	51 (1.1)	0.98	2,931 (0.6)	0.61	1.08	0.51 - 2.28	1.64	1.07 - 2.53	1.50	0.80 - 2.81	2.55	1.47 - 4.43
Developmental disorder §	398 (8.7)	8.15	28,211 (6.1)	6.11	1.66	1.42 – 1.93	1.24	1.06 - 1.46	1.23	0.95 - 1.58	1.13	0.73 - 1.73
ADHD	17 (0.4)	0.33	1,214 (0.3)	0.25	NR*	NR	NR	NR	NR	NR	1.97	1.11 - 3.48

* NR: not reported as ≤ 5 individuals
Abbreviations: py – person-years, ADHD – Attention-deficit/hyperactivity disorder
† Hearing loss includes sensorineural hearing loss, conductive hearing loss, hearing aid insertion or adjustment
‡ Anxiety disorders includes generalized anxiety, phobias, panic disorder, obsessive-compulsive disorder, adjustment disorders, conversion disorders and somatoform disorders
§ Developmental disorders includes speech and language disorders, specific learning disorders, developmental coordination disorder, autism spectrum disorder and disintegrative disorders

Table 1. Incidence and risk of hearing loss, anxiety and neurodevelopmental disorders, comparing KD vs. non-exposed children at 0-1yr, 1-5yr, 5-10yr and >10yr follow-up

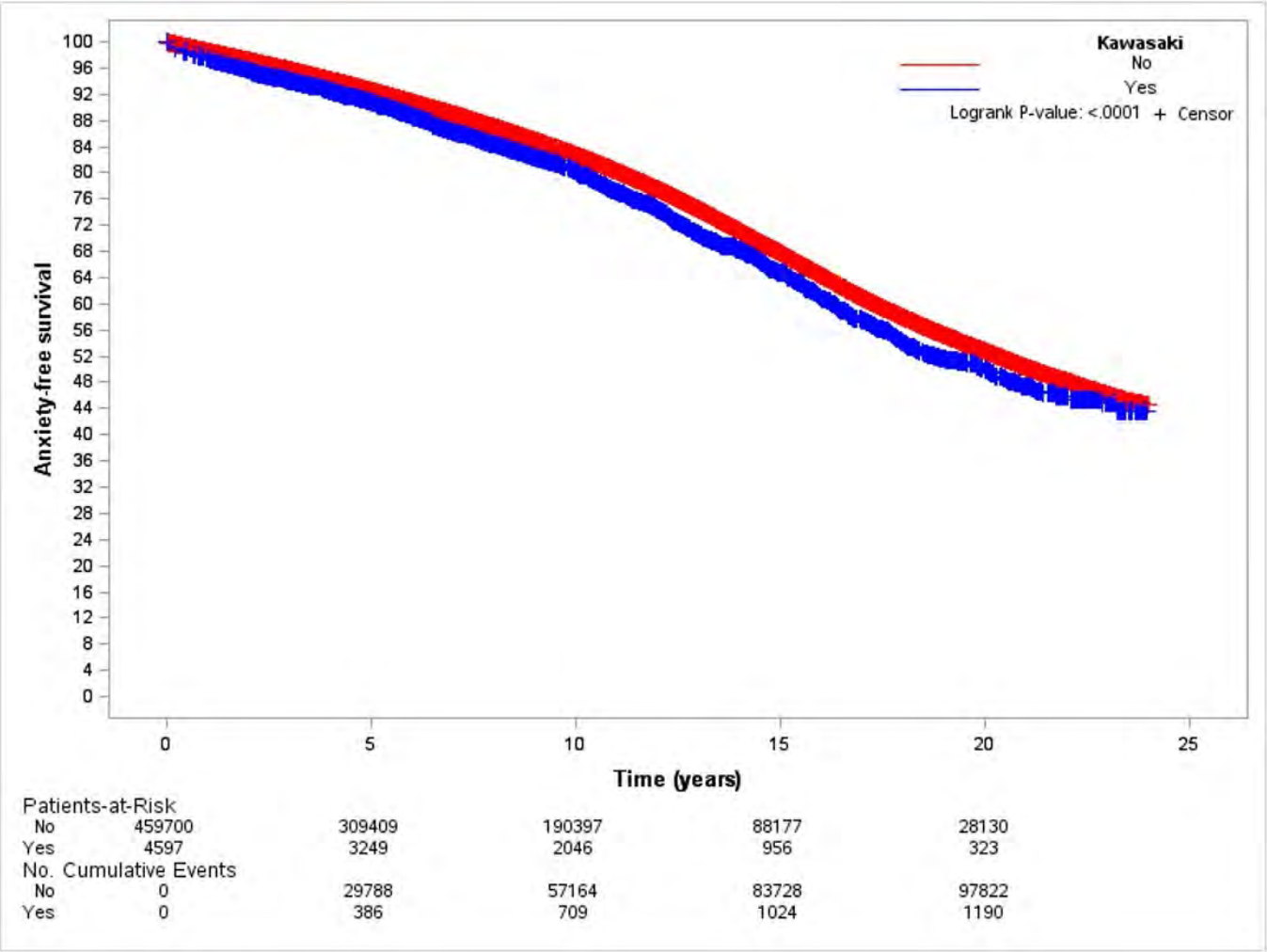

Figure 1. Anxiety disorder-free survival among KD survivors vs. non-exposed children

(HR 1.24 [1.06-1.46]); intellectual disabilities between 1-5yr (HR 1.64 [1.07-2.53]) and >10yr (HR 2.55 [1.47-4.43]); and ADHD >10yr after index hospitalization (HR 1.97 [1.11-3.48]).

Conclusion: KD survivors are at increased risks of adverse neurodevelopmental outcomes, which may impair their academic and social functioning. This justifies enhanced developmental and audiological surveillance of KD survivors.

Disclosure: C. Robinson, None; **F. Lao**, None; **R. Chanchlani**, None; **A. Gayowsky**, None; **S. Brar**, None; **E. Darling**, None; **C. Demers**, None; **T. Mondal**, None; **R. Parekh**, None; **H. Seow**, None; **M. Batthish**, Abbvie, 2.

Abstract Number: 1689

Unexpectedly High Incidence of Kawasaki Disease in a Well-Characterized Population in Atlantic Canada

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Kawasaki Disease (KD), a systemic vasculitis of unknown etiology, is now the leading cause of acquired heart disease in children in North America. Its reported incidence varies widely around the world. A recent pan-Canadian study utilizing hospital discharge data reported an unexpectedly high incidence of KD in Atlantic Canada. The primary goal of this study was to validate the finding of a high incidence of KD in an Atlantic Canadian province and review factors contributing to the frequency in our population.

Methods: Our study was a retrospective review of all patients less than 16 years of age from the province of Nova Scotia (NS) diagnosed with KD between July 2007 and June 2018. All children with KD in NS undergo echocardiography evaluated in one central location. We used the cardiology and discharge databases of the pediatric tertiary care center, and the provincial Medical Examiner database to identify patients with KD. Clinical information was collected by health record review using a standardized form following local ethics approval. The 2011 Canadian census population data were used to calculate incidence rates and determine the proportion of the population of Asian descent.

Results: Out of the 309 possible KD cases that we identified, 220 residents of the province were diagnosed with KD during the study period. Exclusions are shown in Figure 1. Patients were included if they were treated for KD with IVIG (87%) or, if untreated, the physician diagnosed KD and obtained echo follow-up (13%). Cases where the physician subsequently doubted the diagnosis of KD were recorded. The annual incidence was 29.6, 13.9 and 1.6 per 100,000 children < 5 years, 5 to less than 10 years and 10 to less than 15 years, respectively (recurrence rate 1.8%). The male to female ratio was 1.3:1; the median age was 3.6 years (range 18 days-14.6 years). 61.4% and 23.2% met American Heart Association criteria for complete and incomplete KD, respectively. All patients diagnosed in the acute phase received IVIG; 12% of patients were refractory to the initial IVIG dose; 8% of treated patients received steroid and or biologic therapy. 14 (6%) developed a coronary artery aneurysm (CAA) during the disease course. One death from cardiac arrest occurred in a child with a large CAA with thrombosis. The proportion of our population of Asian descent was 1.25%.

Conclusion: We have confirmed a high incidence of KD in the specified Atlantic province. Other features of KD (age, sex, recurrence rate, IVIG resistance and CAA) are similar to previous studies. The incidence is higher than that reported in Europe and the United States (4.5-15 and 19 per 100,000 children < 5 years, respectively), similar to Canadian provinces with significantly higher proportions of the population of Asian descent (20-26 per 100,000 children < 5 years), and among the highest reported outside of Asia. Local population ethnicity does not explain our findings. Our comprehensive method to capture KD patients may have contributed to the detection of the higher than expect-

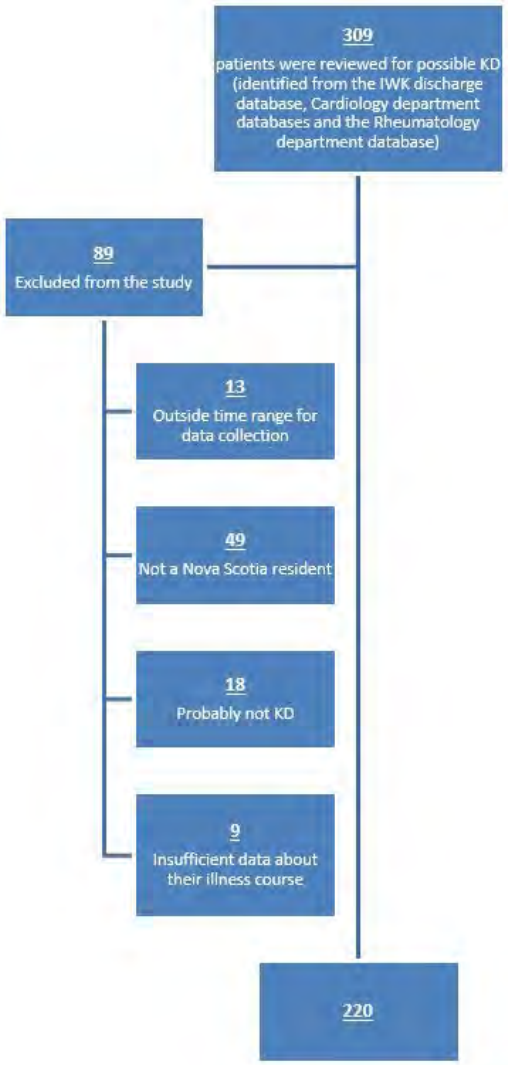

Figure 1: Reasons for exclusion of cases of possible of KD identified through the review of the cardiology and discharge databases.

ed incidence, raising the possibility that the incidence of KD has been underestimated in other populations. The role of environmental and genetic factors also deserves further study.

Disclosure: A. Alkanhal, None; **J. Saunders**, None; **F. Altammar**, None; **A. Huber**, None; **A. Lynk**, None; **A. MacLeod**, None; **O. Ortiz-Alvarez**, None; **M. Adams**, None; **S. Ramsey**, None; **E. Stringer**, None; **A. Warren**, None; **B. Lang**, None.

Abstract Number: 1690

Henoch-Schönlein Purpura Nephritis: Different Histological Classifications, but Which One Is Most Strongly Associated to the Outcome of the Disease? Pilot Study of the Paediatric Rheumatology European Society Vasculitis Working Party

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Henoch-Schönlein purpura nephritis (HSPN) is the main and almost the only cause of morbidity and mortality among children suffering from this most common vasculitis in childhood. Several classifications are used in the analysis of renal biopsies in HSPN, but it is unknown which one has the strongest association with the severity and outcome. The aim of the study was to compare the four most commonly used histological classifications for HSPN to determinate which one is the best predictor of disease outcome and to establish which variables of each histological classification have the strongest association with unfavorable outcomes.

Methods: The cross-sectional study included 69 patients with HSPN (diagnosed by EULAR/PRES/PRINTO criteria) and available renal biopsy specimens for analysis using 4 histological classifications for HSPN (the International Study of Kidney Disease in Children (ISKDC) classification, the Oxford classification, the Haas histologic classification of IgA nephropathy and the modified semi-quantitative classification (SQC), developed by Koskela *et al.*). The clinical outcome was defined through 4 categories, graded according to the modified classification of Counahan (physical examination, hematuria, proteinuria, urine albumin-to-creatinine ratio, hypertension and eGFR). The linear relationships between outcome and histological classifications were analysed using ordinal regressions using the first-order of polynomial orthogonal contrasts.

Results: The SQC classification proved to be the best, reducing the deviation (of the model-predicted outcome value from the observed value) by 9.5% (X^2_1=13,89, p < 0,001), followed by the Oxford classification with a deviation reduction of 8.0% (X^2_1=11,76, p = 0,001), then the ISKDC classification with a decrease in deviation of 3.3% (X^2_1=4,89, p = 0,027), and the worst was the Haas classification with a decrease in deviation of 2.1% (X^2_1=3,06, p = 0,080). Analysis of individual variables of Oxford and SQC classifications showed that with increasing values in the variables of interstitial fibrosis (t_{66} = 3,23, p = 0,002), tubular atrophy (t_{66} = 2,94, p = 0,005) and tubular dilatation (t_{66} = 2,40, p = 0,019) in the SQC classification, and endocapillary hypercellularity (t_{66} = 3,14, p = 0,003) and crescents (t_{66} = 2,07, p = 0,043) in the Oxford classification the outcome worsens.

Conclusion: The pilot study showed that the SQC classification, developed by Koskela *et al.*, has the strongest association with the severity and outcome of HSPN, followed by the Oxford classification, while other classifications are less related to the outcome of the disease. Although crescents on renal biopsy were considered the most important outcome indicators, this pilot study suggests that tubulointerstitial changes could be even more important as predictors of poor outcome. Histological changes in the interstitium and renal tubules of HSPN patients should be further explored in order to have an even better predictive value in terms of disease outcomes and to be incorporated into existing or new classifications, on the basis of which guidelines for the treatment of patients would be developed.

SUPPORT: Croatian Science Foundation project IP-2019-04-8822.

Disclosure: M. Held, None; **M. Sestan**, None; **M. Coric**, None; **S. Bulimbasic**, None; **T. Giani**, None; **N. Martin**, None; **N. Cekada**, None; **S. Srsen**, None; **A. Gudelj Gracanin**, None; **D. Kifer**, None; **M. Heshin**, None; **A. Ravelli**, AbbVie, BMS, Pfizer, Hoffman LaRoche, Novartis, Centocor, "Francesco Angelini" and Reckitt Benckiser., 1, 2; **R. Cimaz**, None; **S. Ozen**, SOBI, 1, Novartis, 1; **A. Gagro**, None; **M. Frkovic**, None; **M. Jelusic**, None.

Abstract Number: 1691

Applied Geostatistics in Pediatric Rheumatology – Spatial Clustering of IgA Vasculitis

Matej Sapina[1], Marijan Frkovic[2], Mario Sestan[2], Sasa Srsen[3], Aleksandar Ovuka[4], Mateja Batnozic Varga[5], Nastasia Cekada[2], Karolina Kramaric[6], Dario Brdaric[7], Kresimir Milas[5], Alenka Gagro[8] and Marija Jelusic[2], [1]University Hospital Centre Osijek, Josip Juraj Strossmayer University of Osijek, Medical Faculty Osijek, Faculty of Dental Medicine and Health, Osijek, Croatia, Osijek, Osjecko-Baranjska, Croatia, [2]University of Zagreb School of Medicine, University Hospital Centre Zagreb, Zagreb, Croatia, Zagreb, Grad Zagreb, Croatia, [3]University Hospital Centre Split, University of Split School of Medicine, Split, Croatia, Split, Splitsko-Dalmatinska, Croatia, [4]University Hospital Centre Rijeka, University of Rijeka School of Medicine, Rijeka, Croatia, Rijeka, Primorsko-Goranska, Croatia, [5]University Hospital Centre Osijek, Josip Juraj Strossmayer University of Osijek, Medical Faculty Osijek, Croatia, Osijek, Osjecko-Baranjska, Croatia, [6]University Hospital Centre Osijek, Josip Juraj Strossmayer University of Osijek, Faculty of Dental Medicine and Health Osijek, Croatia, Osijek, Osjecko-Baranjska, Croatia, [7]Josip Juraj Strossmayer University of Osijek, Faculty of Dental Medicine and Health, Institute of Public Health for the Osijek-Baranja County, Osijek, Croatia, Osijek, Osjecko-Baranjska, Croatia, [8]Children's Hospital Zagreb, Josip Juraj Strossmayer University of Osijek, Medical Faculty Osijek, Zagreb, Croatia, Zagreb, Grad Zagreb, Croatia

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: IgA vasculitis (IgAV) is the most common childhood vasculitis, which etiology seems to be related to the combination of genetic as well as environmental factors. The application of geostatistical analyses in medicine was mostly focused on the analysis of infectious diseases spreading showing the significance of spatiotemporal trends in diseases spreading. Unfortunately, there is only a small amount of research on the application of geostatistical analyses on rheumatic diseases. The aim of this research was to investigate whether geospatial analytical tools can be applied in characterizing the spatial distribution of rheumatic diseases, especially IgAV.

Methods: A retrospective database was created containing the data from patients diagnosed with IgAV in five tertiary hospitals in Croatia, over a ten years period between 2009 and 2019. The average annual incidence of IgAV based on the population census data from 2011. Descriptive choropleth maps were created to observe the spatial distributions of raw and Bayesian adjusted incidence data. Three geospatial methods: spatial-empirical Bayesian smoothing, local

spatial autocorrelations assessed with Moran's I, and local identifiers of spatial autocorrelations (LISA) were applied to make inferences about the spatial incidence distribution of IgaV.

Results: 596 patients, of which 52.52% male, and 47.48% females, were included in the study with a median age of 6.42 (4.42 – 8.84). The estimated average annual incidence was 7.47 with a 95% confidence interval between 6.88 and 8.98 per 100 000 children. The raw data showed the highest number of cases in the cities with a higher population count. However, spatial empirical Bayes smoothed average annual incidenes were clustered similarly around these areas. Three statistically significant clusters were found: two in the Mediterranean, and one in the continental part of Croatia. The obtained Morran's I autocorrelation coefficient was 0.493, which showed significant positive spatial autocorrelation of IgAV. LISA analysis further identified those areas as statistically significant higher incidence clusters with an estimated average annual incidence above 13 per 100 000 children.

Conclusion: This study shows that IgAV exhibits spatial clustering features. While applying modern analytical methods on pediatric IgAV, this research shows the potential application of geostatistical analysis in identifying clusters in noncommunicable diseases that were previously not known. Further research is needed to investigate the importance and relationship of temporal trends in spatial clustering.

SUPPORT: Croatian Science Foundation project IP-2019-04-8822.

Disclosure: M. Sapina, None; **M. Frkovic**, None; **M. Sestan**, None; **S. Srsen**, None; **A. Ovuka**, None; **M. Batnozic Varga**, None; **N. Cekada**, None; **K. Kramaric**, None; **D. Brdaric**, None; **K. Milas**, None; **A. Gagro**, None; **M. Jelusic**, None.

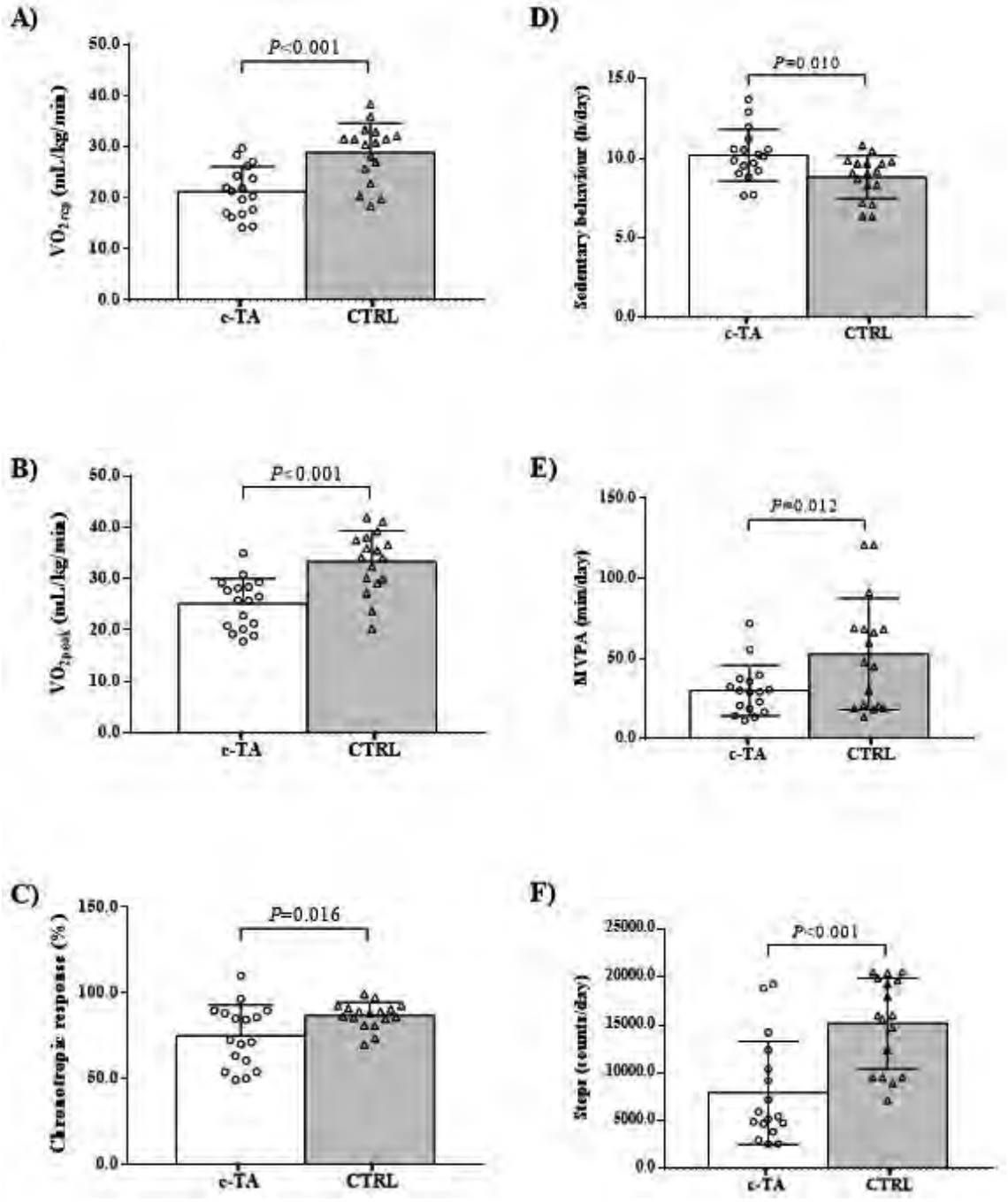
Abstract Number: 1692

Poor Physical Activity Levels and Cardiorespiratory Fitness Among Patients with Childhood-Onset Takayasu Arteritis in Remission

Camilla Astley[1], Saulo Gil[2], Gleice Clemente[3], Maria Teresa Terreri[4], Lucia Campos[5], Nadia Aikawa[5], Ana Lucia de-Sá Pinto[2], Rosa Pereira[5], Hamilton Roschel[2] and Bruno Gualano[2], [1]University of Sao Paulo, Sao Paulo, Sao Paulo, Brazil, [2]University of Sao Paulo, Sao paulo, Brazil, [3]Federal University of Sao Paulo, Sao Paulo, Brazil, [4]Federal University of São Paulo, São Paulo, Brazil, [5]Hospital das Clínicas, Faculdade de Medicina da Universidade de Sao Paulo (HCFMUSP), Sao Paulo, Sao Paulo, Brazil

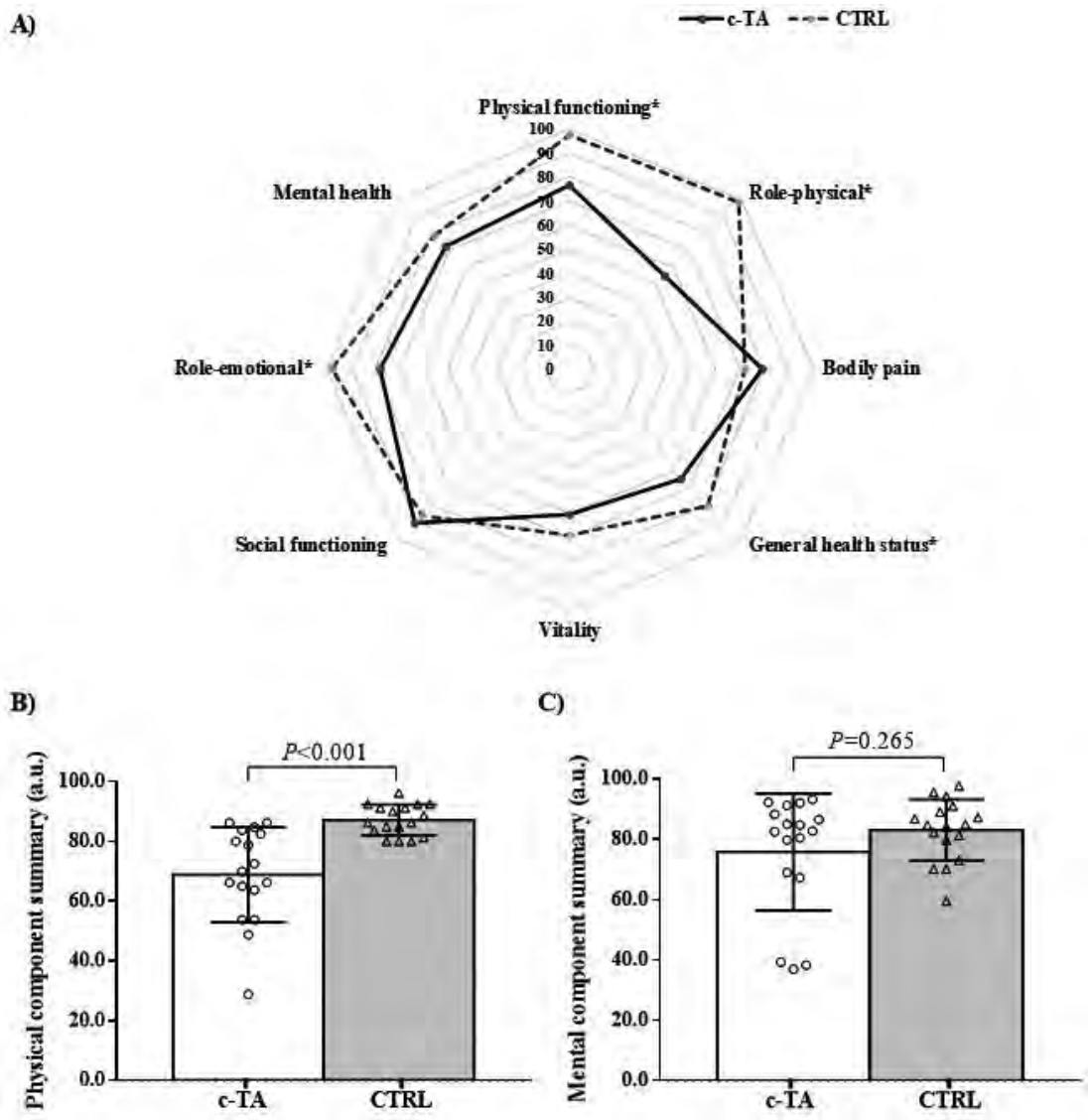
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Childhood-onset Takayasu Arteritis (c-TA) is a rare, granulomatous, chronic large-vessel vasculitis that involves mostly the aorta and its major branches with a high mortality rate (~35%) related to cardiovascular diseases, such as arterial occlusions and stenosis, ischemia or aneurysm formations. Due to the putative limitations imposed by the disease, the cardiovascular involvement, and other indirect factors (e.g., superprotection by parents and health practitioners, low self-efficacy and, social isolation), one could speculate that c-TA patients could also experience low physical activity levels and decreased aerobic conditioning. Therefore, assessing physical activity and cardiorespiratory fitness levels along with health-related quality of life (HRQL) and various traditional and non-traditional risk factors related to physical activity and physical capacity among c-TA patients *vs.* healthy controls remains clinically relevant for clinical practitioners.



Cardiorespiratory fitness and objectively-measured physical activity in patients with childhood-onset Takayasu Arteritis (c-TA) and healthy controls (CTRL). Panel A) Respiratory compensation point (VO2rcp); Panel B) Peak oxygen uptake (VO2peak); Panel C) chronotropic response; Panel D) Sedentary behavior; Panel E) Moderate-to-vigorous physical activity (MVPA); Panel F) Steps per day.

Methods: We recruited c-TA patients with non-active disease (n=17) from three rheumatological centers in Sao Paulo. An age- and sex-matched healthy controls (n=17) were also enrolled in the study. We assessed physical activity levels (Actigraph GT3X accelerometers), aerobic capacity (a maximum graded exercise test on a treadmill), systemic inflammation (IFN-γ, IL-10, IL-12p70, IL-1ra, IL-1β, IL-6, TNF-α, VEGF and PDGF), cardiometabolic markers, dis-



Healthy-related quality of life in patients with childhood-onset Takayasu Arteritis (c-TA) and healthy controls (CTRL). Panel A) Short Form-36 health survey domains between-group; B) Physical health domain; Panel C) Mental health domain.

ease-related parameters (Indian Takayasu Arteritis Clinical Activity Score; ITAS2010 and Pediatric Vasculitis Activity Score; PVAS), and HRQL (short-form health survey with 36 questions).

Results: The summary results from this study can be found in Figure 1. c-TA patients showed greater time spent in sedentary behavior (P=0.010), and lower moderate-to-vigorous physical activity (P>0.001) and lower step counts per day (P>0.001). VO_{2rpc} (P< 0.001), VO_{2peak} (P< 0.001) and chronotropic response (P=0.016) were significantly lower in c-TA patients. c-TA patients had worse HRQL in physical domain (P< 0.001). In the SF-36 subscales, functional capacity, physical appearance, and general health status were reduced in patients in comparison with CTRL (all P< 0.05). Inflammatory and angiogenesis markers did not differ between groups. However, c-TA patients displayed worse insulin sensitivity, based on insulin fasting (P=0.050), HOMA-IR (P=0.033) and lower HDL cholesterol levels (P=0.017) *vs.* CTRL (data not shown).

Conclusion: c-TA patients exhibited reduced physical activity levels and aerobic capacity, worse cardiometabolic risk factors and HRQL parameter compared with healthy peers. Physical inactivity and aerobic deconditioning emerge as potentially novel risk factors for c-TA. The role of physical activity interventions in preventing poor outcomes and improving HRQL in c-TA remains to be explored.

Disclosure: C. Astley, None; **S. Gil**, None; **G. Clemente**, None; **M. Terreri**, None; **L. Campos**, None; **N. Aikawa**, Fundação de Amparo à Pesquisa do Estado de São Paulo (FAPESP #2015/03756-4), 2; **A. de-Sá Pinto**, None; **R. Pereira**, Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq #301805/2013-0), 2; **H. Roschel**, None; **B. Gualano**, None.

Abstract Number: 1693

Evaluation of B-cell Depletion with Rituximab and IVIG Concurrent Treatment in Pediatric Autoimmune Brain Disease

Alexis Wilsey[1], Laura Cannon[2], Stephanie Johannes[2] and Heather Van Mater[2], [1]Duke University School of Medicine, Durham, [2]Duke University, Durham, NC

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Rituximab is standard therapy for autoimmune brain disease (ABD) including autoimmune encephalitis (AE) and Neuromyelitis Optica Spectrum Disease (NMOSD). Recommendations for continuing concurrent intravenous immunoglobulin (IVIG) during rituximab treatment in patients with ABD vary. Mechanisms of rituximab B cell depletion include antibody-dependent cell-mediated and complement mediated cytotoxicity. In contrast,

Table 1. Comparing Rituximab and IVIG to Rituximab Alone and Early Lymphocyte Repopulation

	Concurrent IVIG	Rituximab alone
Number of Instances	125	36
Number of Instances in Patients with AE	103	15
Number of Instances in Patients with NMO or NMOSD	22	21
Number Repopulated	80*	22*
% Repopulated	64.2%	61.1%
Average Number of Days to Repopulation from last Rituximab dose, mean (SD)	221.7 (226.7)**	215.6 (102.3)**
% Repopulated Escalated to Next Line	20%***	13.6%***
% Non-Repopulated Escalated to Next Line Therapy	6.7	0

*No statistical significance on chi-square analysis, p=.7. **No statistical significance on t-test, p=.9. ***No statistical significance on chi-square analysis, p=.5.

Table 2. Hypogammaglobulinemia in Pediatric Patients with ABD Treated with Rituximab

Number of Patients with Hypogammaglobulinemia (percent)	8 (16.3%)
Average Number of Doses of Rituximab prior to Hypogammaglobulinemia, mean (range)	7.3 (3-12)
Average Months, mean (range) Since first Rituximab Dose Since last Rituximab Dose Since last IVIG Dose	 35.1 (8-51) 12.2 (.3-40) 18.5 (2-72)
Number of Instances: Supplemented with IVIG Serious Infection Requiring Hospitalization	9 (7/8 patients) 4 (2 sinusitis, 2 pneumonia) 3

Table 3. Duration of Rituximab Therapy and Reason for Discontinuation

Number of Patients on Continuous Maintenance Therapy < 12 Months 13-24 Months > 24 Months	 16 14 19
Patients Continuing Rituximab	17 (34%)
Patients Escalated to Next Line Therapy	8 (16%)
Patients Discontinuing Rituximab Remission/Lack of Active Disease Lack of Response Other Reasons	24 (49%) 14 (29%) 6 (12%) 4 (8%)

IVIG's immunomodulation includes attenuation of many of these same mechanisms. Despite the frequent use of IVIG as adjunct therapy, there is little data on how concomitant use may affect B-cell depletion and efficacy.

The objective of this study was to determine if concurrent treatment of rituximab with IVIG altered B-cell depletion and time to repopulation in pediatric patients with ABD. We also assessed rates of hypogammaglobinemia (hypogam), duration of continuous maintenance therapy, and reasons for discontinuation of therapy.

Methods: We conducted a retrospective chart review of 58 patients who received rituximab for ABD. All patients met criteria for probable autoimmune encephalitis defined by a multidisciplinary team including a pediatric neurologist, rheumatologist and psychiatrist or NMOSD per established criteria. 49 patients met our inclusion criteria: follow-up for $\geq$1 year, standard rituximab induction, and CD19/CD20 counts recorded post-treatment.

We calculated time from most recent rituximab dosing to CD19/CD20 repopulation (defined as CD19 or CD20 $\geq$0.2%) and noted if IVIG was given within 4 weeks. We evaluated duration of rituximab therapy, concurrent IVIG, B cell repopulation, frequency of hypogam and serious infections. We noted the longest consecutive period of maintenance therapy for each patient. Dosing intervals for maintenance therapy varied from every 3 to 12 months, reflecting evolving recommendations for optimal dosing and early repopulation. Rationale for discontinuation was determined through chart review.

Results: 161 doses of rituximab were given in 49 patients, with 125 given concurrently with IVIG and 36 without. There was no statistical difference in B-cell repopulation in concomitant treatment compared to rituximab alone, in mean time to repopulation, or percent requiring escalation to next line therapy, as noted in Table 1.

We observed hypogam in only 8 of our patients (16% of study population). All patients with serious infection had prompt recovery with replacement dose IVIG and antibiotics. Hypogam was noted on average 12.2 months after last rituximab and 18.5 months after last IVIG.

33 patients (67%) received prolonged treatment (>1 year), of which 14 were on maintenance therapy 13-24 months and 19 on therapy for over 24 months. Of note, NMO patients in our practice continue rituximab chronically given high rates of relapse, even in clinical remission. 35% of patients continued rituximab at the completion of this study, 29% ended therapy for remission, 16% escalated to a different DMARD and 12% failed to respond with no escalation.

Conclusion: There was no difference in rates or time to B cell repletion in patients treated with rituximab alone vs concurrent IVIG treatment. Rates of hypogammaglobinemia were low in our cohort.

Disclosure: A. Wilsey, None; **L. Cannon**, None; **S. Johannes**, None; **H. Van Mater**, None.

Abstract Number: 1694

Risk Factors Associated with *Pneumocystis Jirovecii* Pneumonia in Juvenile Myositis in North America

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: *Pneumocystis jirovecii* pneumonia (PJP) is associated with significant morbidity and mortality in adult myositis patients; however, few studies have examined PJP in juvenile myositis (JIIM). The purpose of this study was to determine risk factors and clinical phenotypes associated with PJP in JIIM.

Methods: An electronic REDCap questionnaire regarding myositis features, disease course, medications, and PJP infection characteristics was completed by treating physicians for 13 JIIM patients who developed PJP (PJP[+]) from the United States and Canada. Myositis features and medications were compared to 147 JIIM patients without PJP (PJP[-]) from similar geographic regions who enrolled in National Institutes of Health natural history studies.

Results: The median age at PJP diagnosis was 6.1 years (IQR 2.6-10.5). PJP occurred shortly after myositis diagnosis in the majority of patients, with a median time from JIIM diagnosis to PJP diagnosis of 2.3 months (IQR 1.7-7). At PJP diagnosis, overall JIIM disease severity was rated as moderate or severe in 10/13 patients. PJP[+] patients were more often of Asian ancestry than PJP[-] patients (OR 8.7; 95% CI 1.3-57.9). Anti-MDA5 autoantibodies (OR 12.5; 95% CI 3.0-52.4), digital infarcts (OR 43.8; 95% CI 4.2-460.2), skin ulcerations (OR 12.0; 95% CI 3.5-41.2), and interstitial lung disease (ILD) (OR 10.6; 95% CI 2.1-53.9) were more frequent in PJP[+] than PJP[-] patients. Before PJP diagnosis, patients more frequently received pulse steroids (OR 3.8; 95% CI 1.2-12.4), rituximab (OR 52; 95% CI 5.2-515.4), and a greater number of immunosuppressive therapies, including corticosteroids, immunosuppressive drugs, and/or rituximab (OR 2.4; 95% CI 1.3-4.5) compared to PJP[-] patients; daily corticosteroid dose, however, did not differ between PJP[+] and PJP[-] patients. Seven PJP[+] patients were admitted to the intensive care unit, and four patients died due to PJP or its complications.

Conclusion: We identified that PJP more often affects JIIM patients early in their disease course, when patients have more severe manifestations requiring more intensive therapy. Importantly, we also identified anti-MDA5 autoantibodies, digital infarcts, skin ulcerations, and ILD as risk factors for developing PJP infection in JIIM. Thus, prophylaxis should be strongly considered in JIIM patients, especially those early in the disease course with these clinical features, and those who have received IVMP and multiple immunosuppressive therapies, particularly rituximab.

Disclosure: S. Sabbagh, None; **J. Neely**, None; **A. Chow**, None; **M. DeGuzman**, None; **J. Lai**, None; **S. Lvovich**, None; **T. McGrath**, None; **M. Pereira**, None; **I. Pinal-Fernandez**, None; **J. Roberts**, None; **K. Rouster-Stevens**, None; **H. Schmeling**, None; **A. Sura**, None; **G. Tarshish**, None; **L. Tucker**, None; **L. Rider**, NIEHS, NIH, 2, Cure JM Foundation, 2, Bristol Myers Squibb, 2, Hope Pharmaceuticals, 2, Eli Lilly and Company, 9, MedImmune/AstraZeneca, 9; **S. Kim**, None.

Abstract Number: 1695

Anti-Melanoma Differentiation Associated Protein 5 (MDA5) Positive Juvenile Dermatomyositis: Focus on the Lung

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Pediatric Rheumatology – Clinical Poster III: SLE, Vasculitis, & JDM
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: A subset of juvenile dermatomyositis (JDM), clinically amyopathic dermatomyositis (CADM), is uncommon and mainly described in adults. CADM is classically characterized by skin ulcerations, minimal muscle involvement, and interstitial lung disease (ILD). Anti-MDA5 antibodies are associated with CADM and ILD. A subset of anti-MDA5 patients have rapidly progressive ILD (RP-ILD), that is typically fatal. Limited data exists on pulmonary manifestations of these presentations in pediatric patients. We aimed to describe pulmonary manifestations, as well as outcomes, in a cohort of patients with pediatric anti-MDA5-associated lung disease.

Methods: A retrospective chart review was completed on patients < 18 years of age at presentation with the diagnosis of JDM, ILD and positive anti-MDA5 antibodies.

Results: 10 patients were identified: 60% male, 70% White, 30% Black, 40% Hispanic. The mean age at symptom onset was 9.6±6.8 years, at diagnosis it was 10±6.8 years. The systems affected at initial presentation were integumentary (100%), musculoskeletal (90%) and respiratory (60%). 40% presented without respiratory symptoms, but were subsequently found to have lung disease. Skin manifestations included nonspecific erythema (70%), Gottron's papules (60%), ulcerations (50%) and heliotrope rash (40%). Musculoskeletal symptoms included arthritis (80%), mild weakness (60%), and muscular tenderness (50%). Mean creatine kinase was 92.7±69.3 units/L.

Respiratory symptoms at presentation included shortness of breath (67%), cough (67%), chest pain (33%), and wheezing (17%). Four patients required respiratory support; 1 nasal cannula, 1 high frequency oscillatory ventilation and 2 extracorporeal membrane oxygenation (ECMO). All patients had abnormal chest CT; findings included consolidation(s) (60%), pneumomediastinum (50%), ground glass opacities (50%), and nodules (30%). 8 patients had pulmonary function testing showing a diffusion defect in 75% and a restrictive pattern in 25%. At last follow-up (range 6 months-5 years), diffusion defects (60%) and dyspnea on exertion (30%) were still noted. All 3 patients with RP-ILD were toddlers at presentation (16, 21, and 25 months). 2 of the 3, both those requiring ECMO, died due to respiratory failure and diffuse alveolar damage refractory to extensive immunomodulatory therapy. The surviving patient with RP-ILD required mechanical ventilation for 14 months, but is now well off all therapies for 4 years. Treatment ranged: more than 1 patient was treated with corticosteroids (100%), hydroxychloroquine (70%), IVIG (50%), methotrexate (50%), rituximab (40%), azathioprine (40%), plasma exchange (30%), NSAIDs (10%), mycophenolate mofetil (10%), and cyclophosphamide (10%).

Conclusion: The pediatric presentation of anti-MDA5-associated CADM is similar to the adult disease, patients had skin ulcerations and lung disease, but minimal muscle involvement. Pneumomediastinum was common. RP-ILD was fatal in 2 of 3 cases. There is a need for further studies on this variant of JDM, specifically treatment options and investigations of younger patients who seem to be at higher risk of severe disease.

Disclosure: D. Moreno McNeill, None; **M. Gillispie-Taylor**, None; **K. Baszis**, Novartis, 8; **E. Sayad**, None; **M. Silva Carmona**, None; **T. Vogel**, None.

Abstract Number: 1696

Measuring Quality Improvement from CME Participants: Results from the RAPID® CME Initiative

Stephen Bender[1], Michael Weinblatt[2] and Daniel Duch[1], [1]FACTORx, Cherry Hill, NJ, [2]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Professional Education Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Medical claims data have been used since 2008 to measure the implementation of the diagnostic and referral strategies resulting from participation in RAPID® CME activities. Since its inception, over 69,782 clinicians have completed at least one RAPID® CME activity. We have reported statistically significant improvements in the participants' diagnostic and referral performance (Bender S, et al. *CE Measure*, 2016;10:10-15). While measuring diagnostic and referral patterns is critical to the success of the initiative, the claims database is limited in its ability to provide objective measures in other areas that the RAPID® curriculum addresses. Therefore, an electronic

medical record analysis was used to determine the curriculum's effectiveness in improving clinician's performance of quality measures associated with rheumatoid arthritis (RA): smoking cessation counseling, cardiovascular (CV) risk, tuberculosis (TB) testing, influenza and other vaccination strategies.

Methods: A retrospective medical record review of recruited providers' patients was conducted for 23 primary care providers (PCP) meeting the study's inclusion criteria. To be included in the study, CME participants needed to be a primary care provider currently managing RA patients interested in improving the quality of the care of their RA patients. In order to assess effectiveness of CME on the use of quality measures and patient care, a two-part chart review (pre/post) was conducted with same data compared from random samples of providers' patients. The target population was defined as all patients, who received a diagnosis of RA, that were being treated by participants of the CME activities. Baseline reviews of 202 random charts from 23 PCPs were examined and compared on follow up with 198 charts from 21 of the same providers who also had participated in baseline chart examination. Patient inclusion criteria included: RA patients >18 years of age; RA ICD–10 codes present; and patients should be seen at least once/year. The quality measures were: Care plan; preventive care and screening; Pneumonia Vaccination Status for Older Adults; Pain Assessment and Follow-Up; falls plan of care; TB screening; tobacco use screening; screening for high blood pressure and follow-up documented; TB Prevention for pso, PsA and RA Patients on a Biological Immune Response Modifier.

Results: Statistically significant improvements were observed for five of the nine quality measures. Measures reaching statistical significance included: Care plan (9.39% Pre/24.29% Post/P-value < 0.0001); preventive care and screening (24.83% Pre/30.14% Post/P-value 0.0422); Pain Assessment and Follow-Up (3.66% Pre/6.59% Post/P-value 0.0096); high blood pressure screening and follow-up (86.1% Pre/94.9% Post/P-value < 0.0001); TB Prevention for pso, PsA and RA Patients on a Biological Immune Response Modifier (1.41% Pre/5.33% Post/P-value 0.0126).

Conclusion: A CME initiative improved clinical performance of learners that will lead to improved care and outcomes for RA patients. While limited in its ability to reach a large number of clinicians, use of electronic medical record data is a useful tool for assessing performance change.

Disclosure: S. Bender, None; **M. Weinblatt**, Crescendo Bioscience, 1, Bristol Myers Squibb, 1, Sanofi, 2, Lilly, 1, Amgen, 1, AbbVie, 5, Amgen, 2, 5, Arena, 5, Bristol Myers Squibb, 2, 5, Canfite, 1, 5, Corrona, 5, Crescendo, 2, 5, GlaxoSmithKline, 5, Gilead, 9, Horizon, 9, Johnson and Johnson, 9, Lilly, 2, 9, Pfizer, 9, Scipher, 1, 9, Set Point, 9, Roche, 9, Canfite, 1, Inmedix, 1, Lycera, 1, Vorso, 1, Scipher, 1; **D. Duch**, None.

Abstract Number: 1697

Immune Related Adverse Events from Checkpoint Inhibitor Therapy: Survey of Hospitalists' Awareness and Experiences

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Professional Education Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

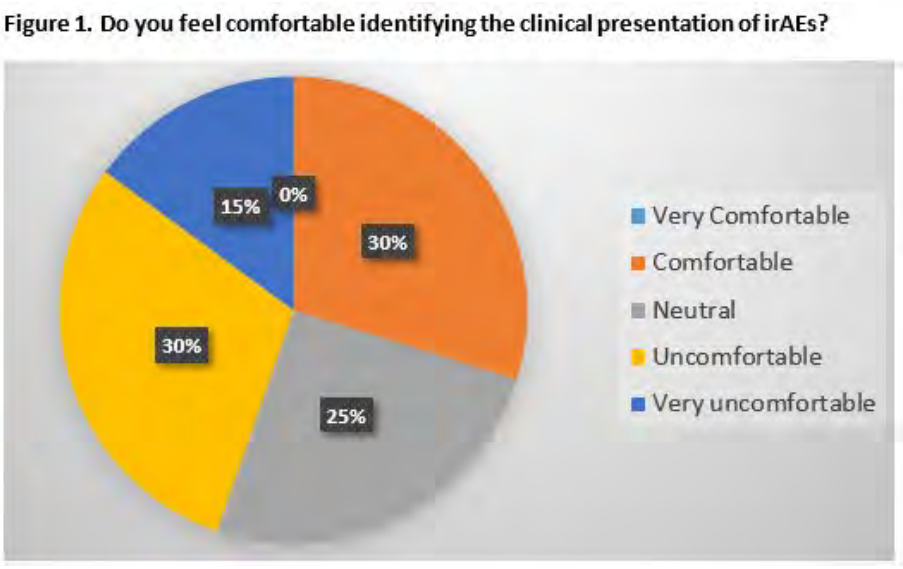

Figure 1. Do you feel comfortable identifying the clinical presentation of irAEs?

Background/Purpose: The introduction of immunologic checkpoint inhibitor therapy (ICI) has caused a paradigm shift in the world of cancer treatment. Their use, however, is attended by a slew of untoward, off-target effects that appear to be autoimmune and/or autoinflammatory in origin called immune related adverse events (irAEs), which pose diagnostic and management challenges. With the increasing use ICI for a growing number of indications, more health care providers are encountering patients with irAEs in outpatient clinic, the emergency room and the hospital wards. While education on irAEs amongst non-oncologists has improved on some fronts[1], we believe there still remain large knowledge gaps. We developed a survey to assess awareness and experience with ICI and irAEs amongst hospitalists

Methods: An online survey was generated using SurveyPlanet and distributed via e-mail to the population of hospitalists at the Cleveland Clinic Main Campus and The Ohio State Wexner School of Medicine. The survey questions aimed to assess hospitalists' awareness surrounding ICI and irAEs including whether they had encountered these

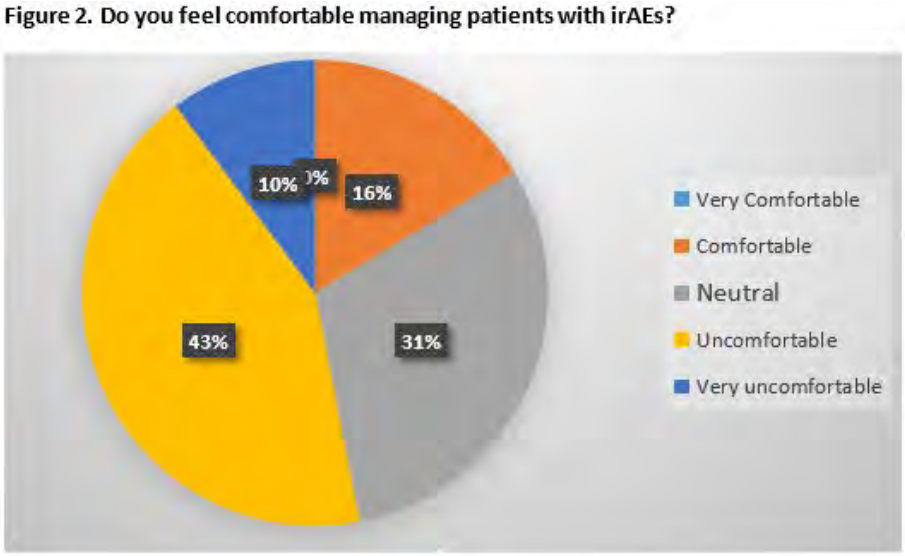

Figure 2. Do you feel comfortable managing patients with irAEs?

patients in the hospital, what types of irAEs were encountered, and comfort level with identifying and managing irAEs. A data use agreement between Cleveland Clinic and The Ohio State Wexner Medical Center was completed.

Results: The survey was sent to 90 hospitalists at the Cleveland Clinic and 92 hospitalists at The Ohio State Wexner School of Medicine with a response rate of 49/182 (27%). The majority of responders (61.2%) were between the ages of 30-40, and 28.6% were aged 40-50. Most were aware of ICIs and irAEs. 24/49 (49%) had encountered an irAE in the hospital, most often involving the gastrointestinal tract, lung or skin. Only about a third felt comfortable identifying the clinical presentation of irAEs (29.8%) and even fewer felt comfortable managing (16.3%) irAEs (Figures 1 and 2). Most expressed desire for more resources to learn about diagnosis and treatment of irAEs, with preferred tools being online learning modules (23/44), grand rounds (16/44), webcast (4/44) and other (3/44).

Conclusion: irAEs represent a new area of medicine that requires multidisciplinary collaboration for optimal management. New educational resources will be required for all medical professionals encountering these patients, including hospitalists.

References:

1. Kostine M, Cappelli LC, Calabrese C, et al. Addressing immune-related adverse events of cancer immunotherapy: how prepared are rheumatologists? *Annals of Rheumatic Disiease* 2018. In press.

Disclosure: C. Calabrese, Abbvie, 1, Regeneron, 1; **A. Meara**, None; **V. Janamanchi**, None.

Abstract Number: 1698

Polyarthritis Workup in Primary Care Setting : How Are We Doing?

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Professional Education Poster
Session Type: Poster Session D
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Background/Purpose: Joint pain is a common presenting complaint in Primary Care with around 54.4 million adults diagnosed with some form of arthritis per 2013 CDC survey. Polyarthritis is defined as joint symptoms involving >/= 5 joints. It includes inflammatory and non-inflammatory arthritis. Rheumatoid arthritis (RA) is a primary consideration of inflammatory polyarthritis. Per the current American College of Rheumatology (ACR) classification criteria, the work up of inflammatory polyarthritis should include CBC, ESR, Rheumatoid Factor (RF), anti-cyclic citrullinated peptide antibody (anti-CCP), if RA is suspected. The specificity of anti-CCP underlies the rationale for checking RF and anti-CCP concurrently. We aim to understand the current practices of Polyarthritis work up in primary care physicians. (PCPs)

Methods: A cross-sectional survey was created via Redcap and administered to PCPs - Staff and Resident, across the Cleveland Clinic Enterprise in November 2019. It enquired about physician demographics, practice characteristics, knowledge and physician-reported ordering practices related to patients presenting with polyarthritis. We reviewed data from our electronic medical record (Epic) through the use of slicer-dicer, in order to identify patients with

Table 1: Physician Survey Respondent Demographics

Staff Physicians (N = 43, 47%)		
Site of Practice	Main Campus Community Hospital STJ*	23% 74% 2%
Years in Practice	0-2 years 3-5 years 6-10 years >10 years	9% 7% 14% 70%
Number of Patients with polyarthritis seen in the last 6 months	Zero 1 to 5 6 to 10 11 to 20 >20	2% 54% 19% 14% 12%
Resident Physicians (N = 49, 53%)		
Level of Training	PGY-1 PGY-2 PGY-3	33% 27% 20 41%
Number of patients with polyarthritis seen in last 6 months	Zero 1 to 5 6 to 10 11 to 20 >20	31% 53% 8% 4% 4%

*STJ = Stephanie Tubbs Jones (largest community site in East Cleveland)

Table 1. Physician Survey Respondent Demographics . @STJ = Stephanie Tubbs Jones

ICD-10 codes for Polyarthritis seen in the primary care setting between 9-2018 and 9-2019 and associated orders placed by providers. Statistical analysis was completed using descriptive statistics and Fisher's exact test of independence to find relationships between.

Results: The survey was sent to 325 physicians with a 28% response rate; the demographics of the 92 survey respondents are described in Table 1. Slicer-dicer data from EPIC showed RF was ordered 30% more than anti-CCP. Self-reported survey reveals similar discordance with 32% of respondents reported they would order both an RF and anti-CCP, and 33% would order only an RF. Both staff and residents report being unfamiliar with the guideline-based workup of polyarthritis (Table 2). Most respondents reported ordering an ESR and CRP (83% and 79%, respective-

Table 2: Physician-reported experience, attitudes and knowledge related to polyarthritis management in the ambulatory setting.

Survey Question	All respondents (N=92, % yes responses)	Staff Physicians (N=43, % yes responses)	Resident Physicians (N=49, % yes responses)
Do you evaluate patients with polyarthritis in your practice?	79%	95%	65%
Are you comfortable evaluating patients with polyarthritis?	62%	91%	37%
Are you familiar with guidelines for workup of polyarthritis?	18%	4%	35%
Do you have any difficulty finding orders for work up of polyarthritis?	37%	19%	53%

Table 2. Physician-reported experience, attitudes and knowledge related to polyarthritis management in the ambulatory setting.

Table 3: Physician-reported ordering practices for the workup of polyarthritis at the initial visit.

	All respondents (N=92)	Staff Physicians (N=43)	Resident Physicians (N=49)
CBC	25%	28%	22%
CBC with Diff	59%	58%	59%
Renal Functional Panel	11%	5%	16%
Complete Metabolic Panel	71%	88%	55%
ESR	83%	91%	76%
CRP	79%	84%	76%
RF	64%	74%	55%
Anti-CCP	39%	51%	29%
No lab Test	6%	0%	8%
RF and CCP ordering practices			
RF and Anti-CCP	31%	42%	22%
Only RF	33%	33%	33%
Only Anti-CCP	8%	9%	6%
No RF or CCP	28%	16%	39%

Table 3. Physician-reported ordering practices for the workup of polyarthritis at the initial visit.

ly), with 64% of respondents selected RF and 39% selected anti-CCP in the initial work-up of polyarthritis (Table 3). There was a statistically significant association between physician-reported evidence-based ordering of both an RF and anti-CCP with respondents being staff physicians ($P \leq 0.001$) and self-reported knowledge of guidelines ($P \leq 0.001$).

Conclusion: Physician-reported and observational EMR data suggest that the workup of polyarthritis in the primary care setting, as it relates to the ordering of RF and anti-CCP antibodies, is frequently incongruent with ACR recommendations. Guideline-discordant ordering practices are more common with residents and in those who report lacking knowledge of the guidelines. This suggests that physician experience and knowledge are the most likely underlying drivers of guideline-based workups of polyarthritis in the primary care clinic. We plan to address this issue by building an order set into our EMR that will provide decision support to promote workups of polyarthritis congruent with the ACR recommendations, thereby improving knowledge and practice.

Disclosure: R. Desai, None; **C. Calabrese**, Abbvie, 1, Regeneron, 1; **N. Patel**, None; **J. Donato**, None.

Abstract Number: 1699

Training Residents to 'Choose Wisely' When Testing for Antinuclear Antibodies

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Professional Education Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

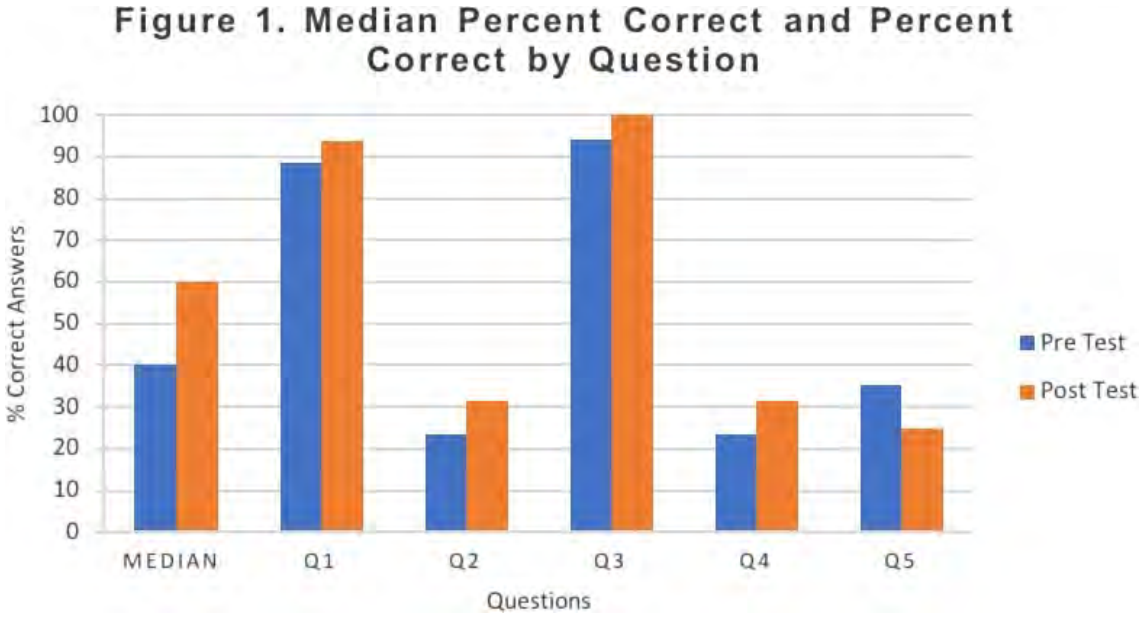

Figure 1. Median Percent Correct and Percent Correct by Questions

Background/Purpose: In many hospitals residents are the first providers to evaluate new patients. Consequently, residents often initiate the work-up of newly admitted patients. Multiple studies have shown that anti-nuclear antibody (ANA) testing is overutilized in both inpatient and outpatient settings [1,2]. Inappropriate ordering and misinterpretation of this test can lead to a subsequent cascade of unnecessary investigation which may lead to iatrogenic harm and waste resources. ABIM/ACR "*Choosing Wisely"* recommendations include: **Don't test ANA sub-serologies without a positive ANA and clinical suspicion of immune-mediated disease.**

Thus, it is vital that residents receive training about appropriate ANA testing. The aim of this study was to assess the effectiveness of an educational intervention on the appropriateness of ordering ANA testing in a community-based internal medicine program.

Methods: A 30-minute evidence-based presentation on ANA testing was developed and delivered to residents, medical students and faculty attending the weekly Internal Medicine (IM) resident didactics. Topics covered included:

1. ACR's "Choosing Wisely" recommendations for ANA testing
2. Clinical scenarios with discussions of appropriateness of ordering ANA in different patient cases
3. Methods used for ANA testing
4. Operating characteristics of ANA including: sensitivity, specificity and positive predictive value.
5. Interpretation of titers, patterns and specific ANA antibodies.

Five patient case scenarios evaluating each of the covered knowledge domains were created for use as a pre/post-test measure. These were administered as a pre and post-intervention test to all attendees. To assure the content validity of the presentation, the presentation and questionnaire were reviewed, edited and approved by the IM Residency Education Director (a hospitalist), an IM residency core faculty (a primary care physician), a Scholarly Activity support person and a board-certified rheumatologist. To assess the quality of test questions we conducted item analysis [3].

Results: Thirteen residents, three medical students and one faculty member participated. The median percentage of correct answers for the pre and post-tests were 40% and 60%, respectively (Figure 1). The number of correct

answers increased in 4 of 5 questions and decreased in the 5th question. The mean item difficulty index was 0.529 (range 0.235 – 0.941) and mean discrimination index was 0.305 (range 0.235-.353). All were above the 0.20 threshold which is considered satisfactory.

Conclusion: Residents should be educated regarding the ACR Choosing Wisely recommendations. The intervention overall showed improved knowledge scores on post-tests. Revision of test questions may provide better discrimination of knowledge gains.

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Disclosure: I. Qaiser, None; **T. Koehler**, None; **R. Martin**, Abbvie, 9, Amgen, 9, Eli Lilly, 9.

Abstract Number: 1700

Curricular Implementation of the Rheumatic Disease Patient Expert Program: The Students' Perspective

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Professional Education Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Medical education can be enriched by embracing patient involvement so that students can learn about rheumatic diseases (RMD) from patient experts. Patient experts have developed an expertise in their chronic disease by living with it, acquiring knowledge from courses and being empowered with the skills, needed to play an active role in teaching other patients and healthcare providers. In order to enhance students' knowledge about rheumatic diseases , improve their listening and communication skills, the Cyprus League Against Rheumatism in collaboration with University of Cyprus Medical School initiated a pilot, novel interactive educational activity. The objective of this study is to obtain feedback from the students about the program in order to assess the impact on the students' education and evaluate its integration in the school's curriculum

Methods: During the internal medicine rotation in year 4, the medical students had the opportunity to participate in a 2-hour session with a trained rheumatic disease patient expert. Each group comprised of 5 students, one attending rheumatologist and one patient expert. Through the session, the students had the opportunity to listen to the patient's journey, learn about symptoms and emotions, and were able to share thoughts and ask questions. The patient expert also demonstrated the hand musculoskeletal exam and students had the opportunity to practice with the patient and receive feedback. At the end of the academic year, an online survey was sent to 88 students by email and they

Question:	Strongly agree/agree response, number (%)
Were you satisfied with the introduction provided by the expert patient?	52 (91,2%)
Did you have enough contact/communication with the expert patient?	54 (93,1%)
Was the patient expert active in your teaching?	55 (93,2%)
Did the patient expert engage all students in relevant, meaningful learning?	53 (89,8%)
Was the expert patient committed to the program?	54 (91,5%)
Were you satisfied with the presentation of the hand and wrist anatomy by the expert patient?	39 (66,1%)
Were you satisfied with the demonstration of hand and wrist examination by the expert patient?	49 (83,1%)
Did you learn about assistive devices and aids for patients with rheumatic diseases?	45 (76,2%)
Did you learn about Rheumatic disorders from the patients' perspective?	54 (91,6%)
Did you learn about any possible stigma or stereotypes that may exist about rheumatic disorders?	49 (83,1%)
Do you feel that you improved your communication skills?	41 (69,5%)
Did you learn about the effect that patient autonomy has on the illness progression and management?	55 (93,2%)
Did the patient expert program help you grow as a professional?	45 (76,3%)
Was the learning environment safe and supportive?	56 (94,9%)
Did you have the opportunity to ask questions about the expert patient?	57 (96,6%)
Would you recommend the patient expert program to other students?	53 (89,8%)
Do you feel the patient expert program should be part of the medical school curriculum?	53 (89,8%)

Table. Patient expert program questionnaire results

were asked to fill out a 19-item question evaluation using a Likert-scale response and a free text comments section to assess the program.

Results: The voluntary response rate was 59 (67%) and 38(64,4%) were females. Overall, most of the participants had a favorable experience with the program (strongly agree/agree response on the Likert scale response), as shown in the Table. Fifty-four (93.1%) were satisfied with the communication they had with the patient, 55 (93.2%) felt the patient was active in their teaching, and engage them in meaningful learning, 53(89.8%).

Lower satisfaction was reported in the improvement of communication skills (n=41, 69%) and the hand and wrist anatomy presentation (n=39, 66%), however, 49(83%) of students were satisfied with the hand and wrist examination. Forty-five (76.3%) believe that the program helped them grow as professionals. The vast majority, 53(89%) of the students would recommend the program to their fellow students and they strongly believe that it should be a part of the medical school's curriculum (n=53, 89%).

Conclusion: The patient expert program is a novel educational activity that has a positive impact on medical students' education including enhanced communication skills, and professional growth. The students would recom-

mend it to their peers and they also believe it should be integrated into the school's curriculum. The program's implementation will raise awareness for RMD, might attract more students in the field of rheumatology, and promote the patient-centered care approach.

Disclosure: E. Sophocleous, None; **A. Phoka**, None; **K. Parperis**, None.

Abstract Number: 1701

Development and Validity Evidence for a Tool to Assess the Performance of Shoulder Injections

Andrea Ramirez-Gomez[1], Amber Deptola[1], Colin Diffie[2], John Metzler[1], Peter McDonnell[1], Nathan Olafsen[1] and Lisa Zickuhr[3], [1]Washington University School of Medicine, St. Louis, MO, [2]Washington University, Saint Louis, MO, [3]Washington University/B-JH/SLCH Consortium, St. Louis, MO

SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Background/Purpose: Shoulder pain is common. Subacromial bursa and intra-articular glucocorticoid injections can provide pain relief while avoiding the risks associated with systemic therapies. The American Board of Internal Medicine recommends internists achieve competence in arthrocenteses, but medicine residents at our institution report little practice doing them. Furthermore, validated assessment methods for these procedures are not published, making it difficult to decide when trainees achieve competence. We aim to develop and gather validity evidence for a tool that assesses the performance of shoulder injections.

Methods: A multi-disciplinary team of internists, physiatrists, and rheumatologists created a checklist and global rating score to assess the performance of shoulder injections. We used a modified Delphi to reach consensus on what to include as checklist items and assigned points to each one, weighing key maneuvers more heavily. We taught medicine interns the procedure on simulation models and observed them performing subacromial bursa injections for impingement syndrome during objective structured clinical examinations (OSCE). We graded their performances against our checklist, our global rating score, and a modified version of the Global Rating Scale for the Evaluation of Technical Skills in the Operating Room (GRSETSOR) that excluded items unique to surgery. Two graders evaluated 30% of the OSCEs. We totaled our checklist and global rating scale scores to compare with total GRSETSOR scores with Pearson's correlation coefficient in Excel. We calculated the intraclass correlation coefficient (ICC) to measure inter-rater reliability with SPSS (2019, Chicago, IL); 13 dual-graded OSCEs were needed to measure an ICC of 0.7 with 95% confidence.

Results: A global rating score and ten items related to pre-procedural, procedural, and post-procedural shoulder injection tasks met consensus for inclusion in our checklist. Checklist items totaled 28 possible points, and the global rating score ranged from one to nine points, set with behavioral anchors. 45 interns participated in our study, consenting to let us use their OSCE scores to calculate psychometrics. Out of the 45 participants, 19 had two raters evaluate their OSCE performances simultaneously. Our checklist and global rating score totals correlated well with the modified GRSETSOR scores ($r=0.71$, r^2 0.50, $p < 0.0001$, figure 1). ICC measured 0.835 (95% confidence interval 0.58-0.94) on evaluations with two raters.

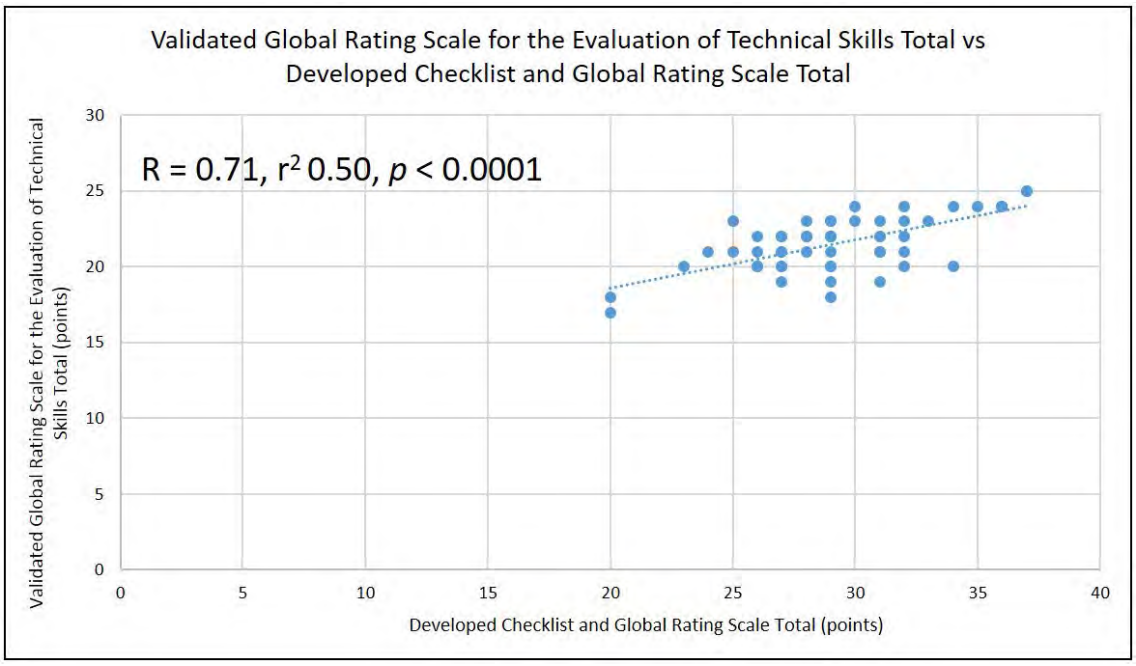

Figure 1. Correlation of validated Global Rating Scale for the Evaluation of Technical Skills in the Operating Room scores with total scores from our developed Checklist and Global Rating Score for Shoulder Injections. Pearson's correlation coefficient (r), R-squared (r2), and p value were calculated and demonstrate positive correlation between the two measures.

Conclusion: We developed a tool that assesses the performance of shoulder injections with strong supporting validity evidence. Our use of a multi-disciplinary team and modified Delphi method enhances content validity, while strong correlation of total scores with the modified GRSETSOR and high inter-rater reliability indicate relational and internal structure validity, respectively. This tool can be used to assess simulated performance of shoulder injections; further study is needed to measure its utility in clinical settings.

Reference:

Doyle JD, Webber EM, Sidhu RS. A universal global rating scale for the evaluation of technical skills in the operating room. *Am J Surg*. 2007;193(5):551-555. https://doi.org/10.1016/j.amjsurg.2007.02.003

Disclosure: A. Ramirez-Gomez, None; **A. Deptola**, None; **C. Diffie**, None; **J. Metzler**, None; **P. McDonnell**, None; **N. Olafsen**, None; **L. Zickuhr**, None.

Abstract Number: 1702

RA-Related Knowledge and Skills of Rheumatology Fellows Among 20 US Academic Institutions

Sandeep Agarwal[1], Rebecca Manno[2], Kristina Fajardo[3], Laura Simone[3], Jeff Carter[3] and Tamar Sapir[3], [1]Baylor College of Medicine, Houston, TX, [2]Johns Hopkins University School of Medicine, St. Thomas, Virgin Islands, U.S., U.S. Virgin Islands, [3]PRIME Education, LLC, Fort Lauderdale, FL

SESSION INFORMATION

Session Date: Monday, November 9, 2020
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Session Time: 9:00AM–11:00AM

Figure 1. Participants' Top Challenges in Managing Moderate to Severe RA

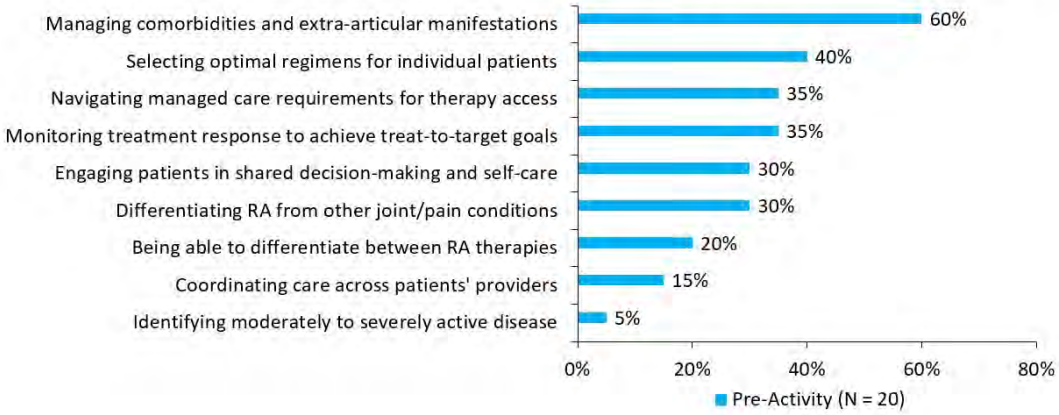


Figure 2. Participants' Confidence in Various Aspects of RA Management

Proportion of Rheumatology Residents/Fellows Who Rated High or Very High Confidence on a 5-point Likert Scale

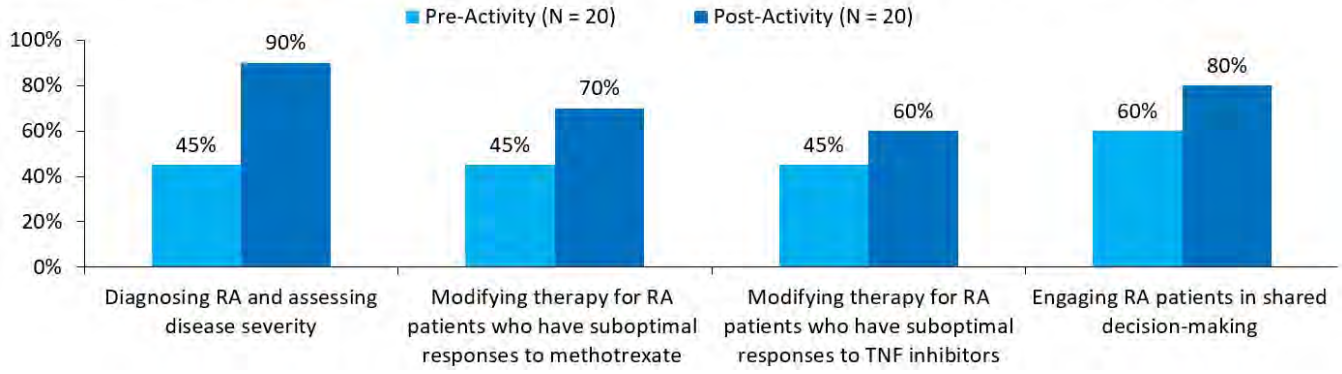
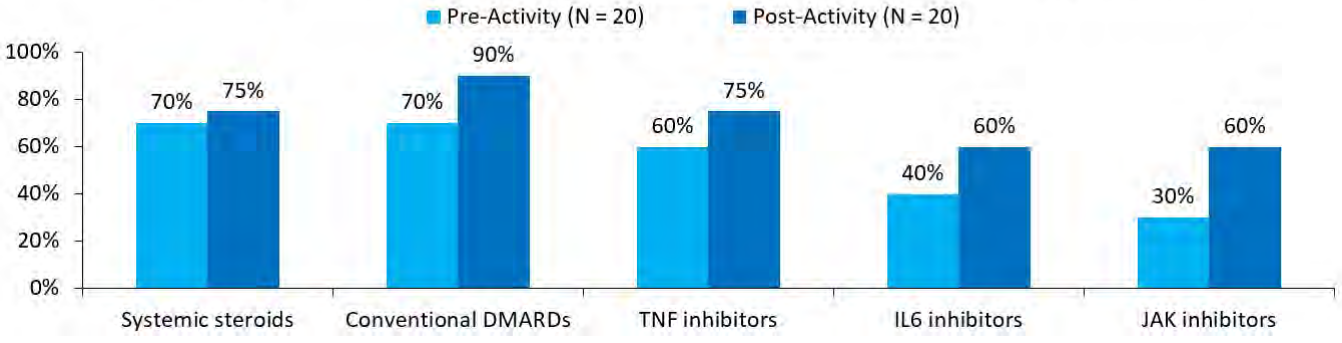


Figure 3. Participants' Confidence in Prescribing or Managing RA Therapies

Proportion of Rheumatology Residents/Fellows Who Rated High or Very High Confidence on a 5-point Likert Scale



Background/Purpose: As the rheumatology workforce experiences an alarming shortage, it is critical that rheumatology fellows receive advanced training experiences to reinforce their commitment to rheumatology patient care and to strengthen their knowledge, competency, and skills in evidence-based management for common conditions like rheumatoid arthritis (RA). As part of a continuing medical education (CME) program in RA, we conducted a survey study in which rheumatology fellows rated their training in RA care.

Methods: On October 5, 2019, rheumatology residents and fellows from 20 US-based academic institutions were selected by their program directors to attend a 1-day educational workshop in RA. Three RA experts designed and led the interactive presentations, case-based discussions, and Q&A sessions. Pre-program surveys included items for trainees to assess and rate their challenges, confidence, and experience in various aspects of RA care. Post-program surveys included items assessing the impact of the education in these domains.

Results: Surveys were completed by 20 rheumatology residents and fellows (10% PGY2, 15% PGY3, and 75% fellows); 70% were female and had a median age of 31 years old. Participants indicated their main challenges in RA care are managing comorbidities and extra-articular manifestations (60%); selecting optimal regimens for individual patients (40%); navigating managed care requirements (35%); and monitoring treatment response to achieve treat-to-target goals (35%; Figure 1). Methods used by the participants to assess RA disease activity included joint examination (95%), clinical judgement (90%), laboratory tests (80%), validated disease severity scores (75%), and patient-reported outcomes (40%).

Before the education, low proportions of participants reported high confidence in performing various aspects of RA care, including diagnosing RA and assessing disease severity (45% with high or very high confidence), modifying therapy for patients with inadequate response to methotrexate (45%) or TNF inhibitors (45%), and engaging patients in shared decision-making (60%; Figure 2). After the education, participants reported increased confidence in these domains. In a separate question, 70% of participants reported high or very high confidence in prescribing or managing patients who are on systemic steroids and conventional synthetic DMARDs (Figure 3); lower proportions of participants reported high or very high confidence in prescribing or managing patients on TNF, IL-6, and JAK inhibitors (60%, 40%, and 30% respectively). These proportions also increased in post-program survey.

Lastly, the survey assessed participants' perspectives on strategies for addressing the shortage of rheumatologists in the US. Most participants (55%) indicated that creating collaborative models with primary care would have the largest impact on addressing patient needs in the immediate future.

Conclusion: Educational gaps exist among rheumatology residents and fellows in their confidence, perspectives, and experience in RA patient care. These findings can help develop additional education opportunities for fellows that help close these gaps.

Disclosure: S. Agarwal, None; **R. Manno**, None; **K. Fajardo**, None; **L. Simone**, None; **J. Carter**, None; **T. Sapir**, None.

Abstract Number: 1703

Gender Equity in Academic Rheumatology – Is There a Gender Gap at European Rheumatology Congresses?

Neelam Hassan[1], Leonieke van Mens[2], Uta Kiltz[3], Concha Delgado[4], Pavel Ovseiko[5], Laure Gossec[6] and **Laura Coates**[7], [1]Musculoskeletal Research Unit, University of Bristol, UK., Bristol, United Kingdom, [2]Clinical Immunology & Rheumatology, Amsterdam Rheumatology and immunology Center, Academic Medical Center/University of Amsterdam, amsterdam, Netherlands, [3]Rheumazentrum Ruhrgebiet, Ruhr-University Bochum, Herne, Germany, [4]Hospital Clínico Universitario Lozano Blesa. Zaragoza., Zaragoza, Spain, [5]Radcliffe Department of Medicine, University of Oxford, Oxford, United Kingdom, [6]Sorbonne Université and Hôpital Universitaire Pitié Salpêtrière, Paris, France, [7]University of Oxford, Oxford, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Professional Education Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: While increasing numbers of women are choosing rheumatology, they remain underrepresented in academic medicine, particularly in senior leadership roles. The reasons for this are multifactorial but increased visibility of women leaders as role models has been proposed as one of the solutions. National and international academic congresses could promote gender equity among speakers.

In recent American College of Rheumatology (ACR) Annual Meeting, 42.8% of speakers and moderators were women in 2017, versus 47.0% in 2018 (1) and 49.1% in 2019 (personal communication). Such data were not available in Europe. The purpose of this study, within the remit of the EULAR Gender Equity Taskforce (2), was to describe the proportion of women invited as moderators or speakers to the European League Against Rheumatism (EULAR) Annual Congresses and National Congresses in Europe.

Methods: Using published congress materials, we determined the proportions of women included in the congresses as either moderators or invited speakers, for EULAR (2015-2019) and 2019 national congresses in France, Germany, Italy, Spain and UK. Individual speakers could be counted multiple times, if they had multiple roles within each congress. For EULAR congresses, we further categorized by Clinical/Science, Health Professionals in Rheumatology (HPR) and People with Arthritis and Rheumatism (PARE) sessions.

Results: The proportion of combined women speakers and moderators at EULAR between 2015 and 2019 varied from 39.7 to 43.2% with no obvious trend over time (Fig 1). Proportions of women moderators and invited speakers were similar. There were much greater proportions of female speakers in the HPR and PARE sessions (over 50% consistently) but these sessions represent < 30% of the EULAR congress invitations (Fig 1). Representation of women at national meetings in France and Germany appeared lower than that in Spain, the UK and at EULAR (Fig 2).

Conclusion: Women account for approximately 40% or less of invited moderators and speakers at the European congresses reviewed, whilst many national congresses are lower. A comparison with the available historical data on women moderators at EULAR in 2003 (16%) and in 2004 (19%) indicates formidable change over the last 15 years (3). Yet, our data does not show an improvement in gender equity in recent years at EULAR congresses, as was seen for the ACR meetings. The establishment of the EULAR Task Force on Gender Equity in Academic Rheumatology signals the commitment of EULAR to accelerate the pace of change in Europe.

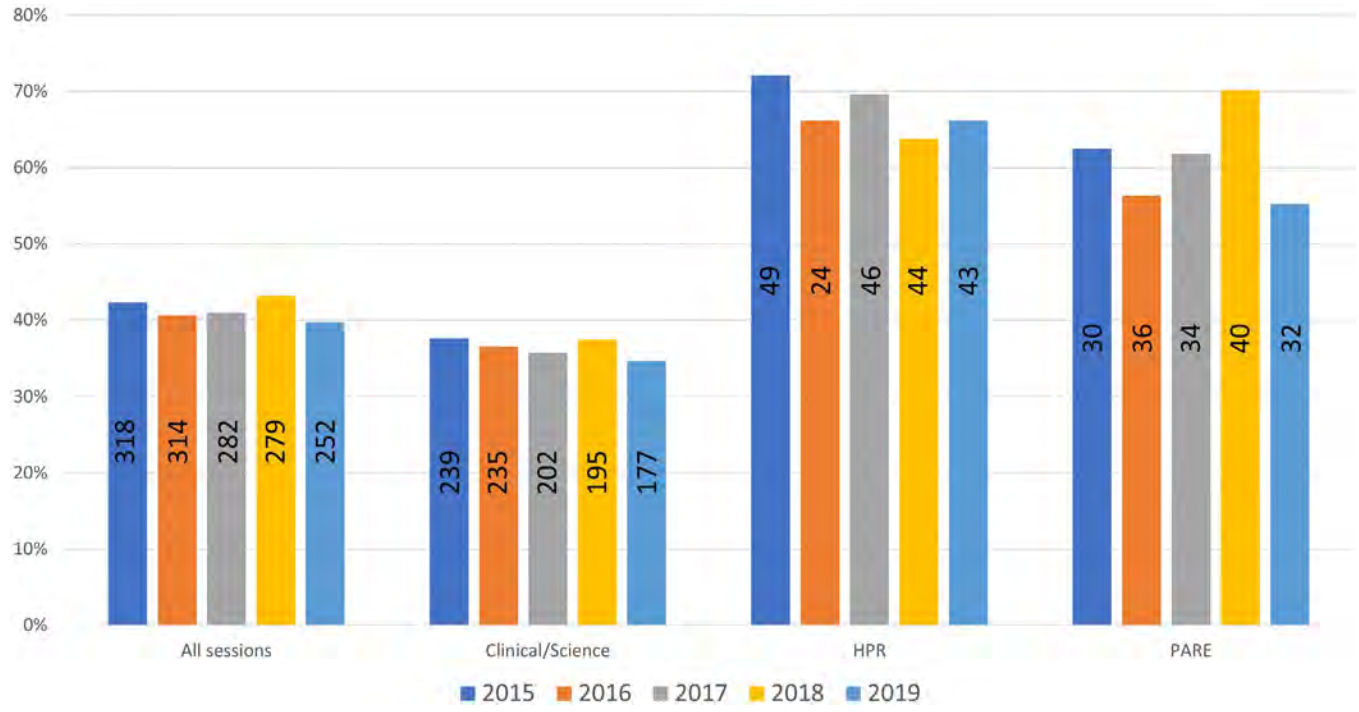


Figure 1. Proportion of women invited to participate in EULAR sessions, by type of session

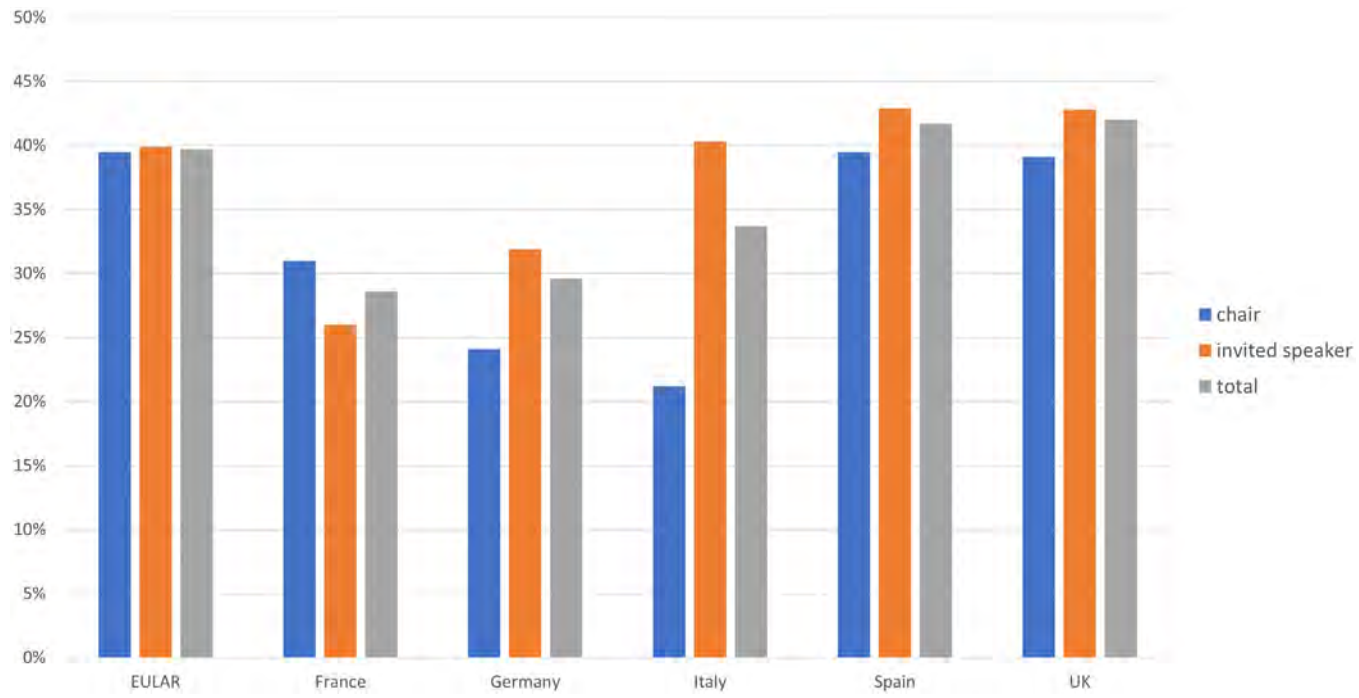


Figure 2. Proportion of women invited as chairs and Invited Speakers at EULAR and National Congresses in Europe in 2019

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Disclosure: N. Hassan, None; **L. van Mens**, None; **U. Kiltz**, Abbvie, 2, 5, Biocad, 2, 5, Biogen, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Grünenthal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5; **C. Delgado**, None; **P. Ovseiko**, None; **L. Gossec**, Sandoz, 1, AbbVie, 5, 8, Amgen Inc., 5, 8, Biogen, 5, 8, Janssen, 5, 8, Celgene, 5, 8, Eli Lilly, 1, 5, 8, Novartis, 5, 8, Pfizer, 1, 5, 8, UCB Pharma, 5, 8, Sanofi, 5, 8; **L. Coates**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Amgen Inc., 5, 8, Gilead, 5, 8, Janssen, 5, 8, UCB Pharma, 5, 8, Eli Lilly, 2, 5, 8, Biogen, 8, Medac, 8, Boehringer Ingelheim, 5, MSD, 5.

Abstract Number: 1704

Identifying Primary Care Clinician Knowledge Gaps and Needs in Rheumatologic Care for Rural Veterans

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Professional Education Poster
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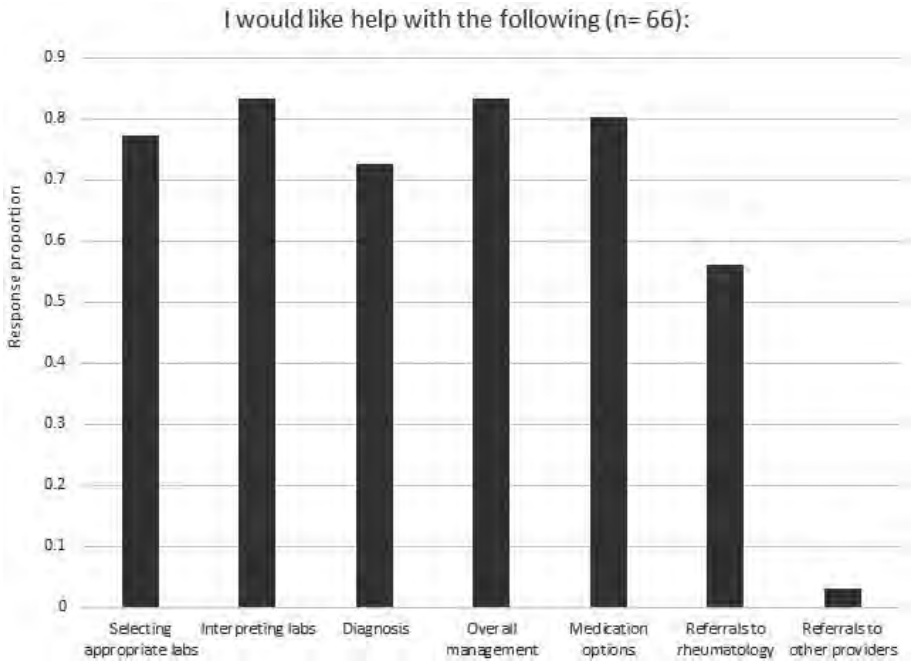
Session Time: 9:00AM–11:00AM

Background/Purpose: One in 3 U.S. Veterans live with arthritis, the number one cause of disability. Despite this high prevalence, much needed care may be limited or delayed due to far distance to the nearest specialist, or even lack of specialists. There is an anticipated shortage of rheumatologists in the next 5 years in the Veterans Administration (VA). To overcome these barriers, VA adapted the Extension for Community Health Care Outcomes (ECHO) model for specialists to share expertise with primary care clinicians. Rheumatology VA-ECHO aims to improve care quality and access to care for Veterans who may not have access to a rheumatologist. Our objective was to identify gaps in knowledge and support for primary care clinicians serving rural Veterans in order to effectively expand the newly established Rheumatology VA-ECHO.

Methods: Two VA rheumatologists and a clinical psychologist developed a survey to assess primary care clinician confidence in diagnosing and caring for patients with select rheumatologic conditions. Additionally, the survey asked about clinician knowledge of, experiences with, and barriers to attending rheumatology-specific VA-ECHO sessions. Primary care clinicians in the Pacific Northwest who care for at least 50 rural Veterans were eligible to participate. A total of 313 clinicians were sent a REDCap survey invitation. Responses were collected for a period of 2 weeks. Data were analyzed using descriptive statistics.

Results: A total of 69 survey responses were collected (22% response rate). Respondents had a mean age of 52 (SD= 10.5), predominantly identified as female (60%), were physicians (43%) or nurse practitioners (43%), and had been serving rural Veterans for more than 5 years (65%). Most clinicians reported feeling somewhat comfortable taking a history (58%), performing a physical exam (60%), ordering labs (53%), interpreting labs (39%), and managing follow-up care (37%) for patients with rheumatologic conditions. Clinician confidence level in diagnosing and managing rheumatologic diseases varied based on disease (Table 1). Clinicians reported being very confident in diagnosing (77%) and managing (72%) osteoarthritis which contrasted with most clinicians reported no confidence in diagnosing (54%) and managing (56%) systemic sclerosis. While more than half of the sample had heard of VA-ECHO (64%), n (88%) had never attended a VA-ECHO session and 97% reported not knowing where to find past sessions. Despite this, 72% of respondents felt that they would benefit from additional rheumatology educational resources (Figure 1).



Proportion of respondents (y-axis) who reported they would like help with the following tasks (x-axis): selecting appropriate labs, interpreting labs, diagnosis, overall management, medication options, referrals to rheumatology or other providers.

Conclusion: Primary care clinicians caring for rural or highly rural Veterans agree that they would benefit from additional rheumatology specialty support and education around diagnosing and managing rheumatologic diseases. Despite this, few clinicians surveyed reported ever attending a Rheumatology VA-ECHO session, and even fewer knew how to locate an archived session. In order to continue to provide high quality rheumatologic care to rural Veteran populations, health systems should consider implementing organizational supports that draw awareness to and encourage use of resources such as Rheumatology VA-ECHO.

Disclosure: R. Matsumoto, None; **J. Kahler**, None; **J. Dougherty**, None; **M. Bach**, None; **J. Barton**, None.

Abstract Number: 1705

In-Person Musculoskeletal Exam Demonstration by Rheumatologist More Effective Than Virtual PowerPoint Presentation in Teaching Internal Medicine Residents

Deepa Shah[1] and Shuwei Wang[2], [1]Morristown Medical Center, Morristown, [2]Morristown Medical Center, Morristown, NJ

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Professional Education Poster
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Session Time: 9:00AM–11:00AM

Background/Purpose: The musculoskeletal exam is critical to rheumatologists for evaluating and diagnosing patients with joint pain. The goal of our study was to compare differences in comfort and satisfaction level among

Table 1. Pretest and Posttest Comparison of In-Person Demonstration versus Virtual PowerPoint Lecture of Rheumatological Physical Examination

	In-Person Demonstration (n = 10)			Virtual PowerPoint Lecture			Compare In Person vs Virtual PPT Lecture **	
	Pre Test	Post Test	P value*	Pre Test	Post Test	P value*	Pre Tests, p	Post Test, p
Comfort in Detecting ROM and Palpation								
Cervical Spine	3 (2, 4)	4 (4, 5)	0.016	3 (2, 3)	4 (3, 4)	0.005	0.5	0.04
Shoulders	4 (4, 4)	5 (4, 5)	0.046	3 (3, 4)	4 (3, 4)	0.015	0.009	0.025
Elbows	4 (3, 4)	4.5 (4, 5)	0.01	3 (3, 4)	4 (3, 4)	0.009	0.22	0.007
Wrists	4 (3, 4)	5 (4, 5)	0.016	3 (3, 4)	4 (3, 4)	0.008	0.11	0.003
Hands	4 (2, 4)	4.5 (4, 5)	0.01	3 (3, 4)	4 (3, 4)	0.059	0.76	0.056
Back	3 (3, 4)	4.5 (4, 5)	0.004	3 (3, 4)	4 (3, 4)	0.046	0.9	0.01
Hips	3 (2, 4)	5 (4, 5)	0.004	3 (2, 3)	4 (3, 4)	0.003	0.76	0.004
Knees	4 (4, 5)	5 (4, 5)	0.046	3 (3, 4)	4 (3, 4)	0.025	0.002	0.001
Ankles	3 (2, 4)	4.5 (4, 5)	0.005	3 (2, 3)	4 (3, 4)	0.002	0.4	0.02
Feet	3 (2, 4)	4 (4, 5)	0.01	3 (3, 3)	4 (3, 4)	0.003	0.9	0.09
Comfort in Detecting Synovitis								
MCPs***	2 (2, 3)	4 (3, 5)	0.007	3 (2, 4)	3 (3, 4)	0.015	0.45	0.28
PIPs/DIPs***	2 (2, 3)	4 (3, 5)	0.007	3 (2, 3)	3 (3, 4)	0.046	0.39	0.28
Knees***	3 (2, 4)	4 (4, 5)	0.016	3 (2, 3)	4 (3, 4)	0.009	0.41	0.1
Comfort in Maneuvers								
Hawkins-Kennedy Test	1 (1, 2)	3.5 (3, 4)	0.007	3 (1, 4)	4 (3, 4)	0.009	0.09	0.85
Empty Can test	3.5 (1, 5)	5 (4, 5)	0.01	4 (3, 5)	4 (3, 4)	0.42	0.67	0.052
Cross Arm Test	2 (1, 4)	5 (5, 5)	0.01	3 (2, 4)	4 (3, 4)	0.07	0.4	0.002
Phalen's Test & Tinel's sign	4 (4, 5)	5 (5, 5)	0.03	4 (3, 5)	4 (3, 5)	0.88	0.42	0.005
Modified Schober's Test	1 (1, 2)	5 (4, 5)	0.004	2 (1, 2)	4 (3, 4)	0.002	0.24	0.005
Occiput Wall Test	1 (1, 2)	5 (5, 5)	0.004	2 (1, 3)	4 (3, 4)	0.003	0.2	0.002
Patrick Test/FABER	1.5 (1, 4)	4.5 (4, 5)	0.005	2 (1, 3)	3 (3, 5)	0.004	0.85	0.049
Rheumatology Interest	1.5 (1, 3)	2 (1, 3)	0.32	1 (1, 1)	1 (1, 1)	>0.99	0.04	0.016

Note: Median reported (25% quartile, 75% quartile)

- *Wilcoxon Matched-Paired Signed Rank Test
- **Wilcoxon rank sum (Mann Whitney) test
- *** MCP: Metacarpophalangeal joint, PIP: Proximal interphalangeal joint, DIP: Distal interphalangeal joint

internal medicine residents after receiving a single in-person demonstration by a rheumatologist versus a virtual PowerPoint presentation for learning the musculoskeletal exam.

Methods: We compared two cohorts with one group receiving an in-person demonstration of a complete musculoskeletal exam by a board certified rheumatologist, while the second group received a virtual PowerPoint presentation with diagrams and explanations by the same rheumatologist. Each group received a pretest and posttest evaluating comfort level with assessing range of motion/palpation of joints, detecting synovitis, maneuvers used by rheumatologists as well as interest in rheumatology and satisfaction level. Residents used a ranking system on a scale of 1 through 5, with 1 being the least and 5 being the most comfortable or satisfied. Within each cohort, the pretest and posttest were compared using the Wilcoxon Matched Paired Signed Rank Test and the Wilcoxon rank sum (Mann Whitney) test was used for comparison between cohorts.

Results: Twenty four internal medicine residents ranging from postgraduate year (PGY) 1 to 3 completed the study. When comparing the pretest and posttest within each group, there was improvement in comfort level in most joint exams and maneuvers. Notably, while the in-person group showed an increase in comfort level with the Empty-can test, Phalen/Tinel's test and hand range of motion/palpation on their posttests, the PowerPoint group did not have statistical improvement.

The pretests between groups did not have many significant differences indicating comparable baseline comfort levels with musculoskeletal exam. When comparing posttests, the in-person group had a greater increase in comfort level

with most range of motion/palpation joint examinations and maneuvers (Table 1). It was particularly helpful to have in-person demonstration for the Modified Schober's, Occiput Wall, and Patrick/FABER tests. Between groups, we did not detect statistical difference in posttest comfort levels for hands and feet range of motion/palpation, detecting synovitis in hands and knees, Hawkins-Kennedy test, and Empty Can test. The learners did not report increase in rheumatology interest after both sessions. The in-person group had increased pretest interest which could potentially introduce selection bias into the study.

Limitations included the small sample size, low interest in rheumatology, and PowerPoint presentation given virtually due to COVID-19 pandemic. Strengths include the comparable groups and both teaching sessions were given by the same rheumatologist.

Conclusion: We found the in-person demonstration of musculoskeletal exam by a rheumatologist was more effective than a virtual PowerPoint presentation for learning most joint exams and musculoskeletal maneuvers among internal medicine residents. More studies are needed to further investigate the most effective teaching modalities for musculoskeletal learning and interest in rheumatology.

Disclosure: D. Shah, None; **S. Wang**, None.

Abstract Number: 1706

Advanced Integrated Science Courses: A Novel Approach to Medical Student Science Education

Eli Miloslavsky[1], Henrike Besche[2] and John Flanagan[2], [1]Massachusetts General Hospital, Harvard Medical School,, Boston, MA, [2]Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Professional Education Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Scientific research is at the core of evidence-based medicine, and is transforming medical care at an increasingly rapid pace. The ability of students to engage with science as life-long learners is an important goal of undergraduate medical education and critical for practicing rheumatologists. However, there has been a trend towards shortening pre-clinical science curricula and less than 25% of medical schools incorporate science education in the clerkship years and beyond. We developed and evaluated the Advanced Integrated Science Courses (AISCs), a novel approach to teaching science in the post core-clerkship phase of the new *Pathways* curriculum at Harvard Medical School.

Methods: Following a 14 month pre-clinical curriculum that teaches foundational science concepts, the AISCs in contrast focus on frontier research and how it influences medical care. Students choose from a menu of basic, translational and population science courses in order to personalize the experience and align it with their anticipated career path (Table 1). Courses such as Immunology, Medications and Evidence as well as Health Systems Science are particularly relevant to rheumatology.

The AISCs aim to develop students' ability to engage with science by focusing on teaching four generalizable skills: 1) find and critically evaluate research information, 2) communicate science to peers or patients, 3) evaluate how

Table 1 – AISCs by year first offered

2018	Added 2019	Planned additions in 2020 and 2021
Cancer biology	Translational biomedical engineering	Health systems science
Computationally enabled medicine	Global and community medicine	Sex- and gender-informed medicine
Human genetics	Metabolism, nutrition & lifestyle medicine	
Immunology		
Microbiology & infectious disease		
Neurobiology		
Medications and evidence		
Regenerative biomedicine		

AISCs by year first offered

Table 2 – Student course ratings

	2018 Mean (SD)	2019 Mean (SD)
Overall satisfaction	1.80 (0.97)	1.49 (0.82)
Improved ability to find and critically evaluate research information	1.73 (0.94)	1.53 (0.77)
Improved my ability to communicate scientific information	1.75 (0.94)	1.45 (0.67)
Improved ability to evaluate influence of new research on patient care	1.64 (0.82)	1.47 (0.77)
Improved my ability to formulate questions suitable for investigation	1.78 (0.95)	1.51 (0.68)
Engaged me to apply critical thinking to solve problems	1.68 (1.11)	1.51 (0.91)
Clinical experiences contributed to my learning	1.75 (1.06)	1.68 (1.03)

* 1-5 scale with 1 being the highest rating and 5 the lowest

Student course ratings

research influences patient care, and 4) formulate questions and ideas for research and innovation. In addition to common learning objectives, the AISCs have common elements such as an experiential component to explore the bi-directional relationship between science and medicine, allocated time for self-directed learning, reliance on active learning techniques, required projects to facilitate student inquiry and a shared student evaluation method. The focus of the curriculum is on gaining skills rather than memorizing content.

Results: Over the first two years of the *Pathways* curriculum, of the 351 students enrolled in an AISC, 301 completed the course evaluation (86% response rate). Overall students rated the AISCs highly, 1.80 in 2018 and 1.49 in 2019 on a 1-5 scale with 1 being the highest score (Table 2). Most students felt that the AISCs improved their ability to accomplish each of the four course objectives. Free-text responses demonstrated that students valued the generalizable skills gained in the AISCs, exposure to cutting edge research, integration of clinical experiences, and the opportunity to interact with experts in the field as particular strengths of the curriculum.

Conclusion: We describe a novel spiral science curriculum with AISCs designed to engage students in the dialogue between medicine and frontier research, at a developmentally appropriate stage following the core clerkships. The focus of the curriculum on a common skill set to engage productively with frontier science, rather than content delivery, was a key factor in facilitating the development of a unified curriculum across multiple disciplines. Personalization and experiential learning components enabled the curriculum to be well received by the students and successfully engaged science faculty in undergraduate medical education.

Disclosure: E. Miloslavsky, None; **H. Besche**, None; **J. Flanagan**, None.

Abstract Number: 1707

Development and Delivery of Continuing Education Interventions Promoting Shared Decision Making in Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: A core CMS policy goal is to improve patient experience by encouraging patient-centered care and shared decision making (SDM). However, SDM techniques are underutilized in rheumatology practice[1]. We created two continuing medical education (CME) activities that present ACR guidelines, treat-to-target (T2T) concepts, and SDM as vehicles to increase the equity of the provision of healthcare[2] for rheumatoid arthritis (RA).

Methods: A live workshop (LW) and an online course (OC) were designed to explain ACR RA guidelines, treat-to-target concepts as well as to demonstrate and practice using SDM with the goal of aligning treatment with patient goals. In interviews with four rheumatologists, we identified three 'swimming lanes' in the RA patient experience of choosing DMARDs. This led to the development of Option Table Patient Decision Aids (PtDAs) presenting three common choice sets for a patient considering starting their 1st, 2nd or 3rd DMARD. PtDAs provide specific probabilities about outcomes to structure clinical discussion with patients and their deliberation after the visit. See figure 1.

Nearly half of the 90-minute workshop for rheumatology providers was focused on teaching SDM. Learners listened to a skill-oriented explanation of SDM as a multi-step interviewing procedure based on observable domains[3]. They then viewed a demonstration of SDM by a faculty and a patient-actor. A PtDA was used to support the clinical encounter by providing facts about options and structuring comparison of attributes of the DMARDs in the choice set being considered. Finally, learners practiced a new SDM encounter supported by a PtDA in pairs followed by debriefing.

A 75-minute online activity was developed based on the recorded workshop and disseminated on myCME.com to a broad audience of rheumatology providers and other clinicians.

Results: There were 54 participants in the LW and 1337 in the OC. After the interventions, 92% and 93% believed they could effectively engage in T2T-SDM, 78% and 93% believed the PtDA enhanced their learning of SDM. Comparing pre-post knowledge assessment, both groups (LW 56 to 82% and OC 57 to 99%) increased their ability to recognize patient statements consistent with being engaged in SDM. 59% of LW and 43% of OC intended to make changes in their practice as a result of participation

Conclusion: Both LW and OC reinforced positive attitudes towards learning about T2T and SDM. Modeling and active practice of SDM using a PtDA influenced beliefs, knowledge, and intentions to change practice related to SDM.

Option Table Decision Aid: For a Patient With Rheumatoid Arthritis Considering Starting Their Third DMARD

	RECOMMENDED OPTIONS				
Medication options	**Infused anti-TNF (ie, infliximab)**	**T-cell modulator (ie, abatacept)**	**B-cell depletion (ie, rituximab)**	**Anti-IL-6 (ie, tocilizumab)**	**JAK inhibitor (ie, tofacitinib or baricitinib*)**
Year of FDA approval	1999-2009	2005	2006	2008	2012, 2018*
How taken	Infusion	Injection or infusion	Infusion	Injection or infusion	Pill
Frequency	Every 4-8 weeks	Injection weekly or infusion monthly	At weeks 0 and 2, then every 6 months	Injection every 1-2 weeks or infusion monthly	Once daily
Benefits					
Power to suppress arthritis (ACR 20)	60 of 100 will improve	68 of 100 will improve	52 of 100 will improve	59 of 100 will improve	56 of 100 will improve
Power to slow joint damage (0-4+)	4+	4+	4+	4+	4+
Harms					
Risk of serious infection (event/100 patient years of use)	6 in 100	3 in 100	5 in 100	6 in 100	3 in 100
Other risks and side effects	Infusion reaction, immune reaction, skin cancer	Worsening COPD	Infusion reaction, immune reaction, rare infection (PML)	↑ liver test, ↑ lipids, ↓ blood counts, immune reaction	↑ liver test, ↑ lipids, ↓ blood counts, diverticulitis, blood clots*
Special population considerations	Caution with pregnancy; TB reactivation, fungus, or virus infection; worsening heart failure	Avoid pregnancy; avoid in hepatitis B; TB reactivation, fungus, or virus infection	Avoid pregnancy; avoid in hepatitis B; TB reactivation, fungus, or virus infection	Avoid pregnancy; TB reactivation, fungus, or virus infection; diverticulitis; BCP less effective	Avoid pregnancy; TB reactivation, fungus, or virus infection; caution in kidney disease
Practical Issues					
Safety monitoring plan (ACR guidelines)	Pretreatment: CXR, hepatitis B and C, TB test; labs every 6 months; yearly TB test	Pretreatment: CXR, hepatitis B and C, TB test; labs every 6 months; yearly TB test	Pretreatment: CXR, hepatitis B and C, TB test; labs every 6 months; yearly TB test	Pretreatment: CXR, hepatitis B and C, TB test; labs every 1-3 months; yearly TB test	Pretreatment: CXR, hepatitis B and C, TB test; labs every 3 months; yearly TB test
What is my monthly cost? (dependent on health plan)					

DMARD=disease modifying anti-rheumatic drug. ACR=American College of Rheumatology. COPD=chronic obstructive pulmonary disease. PML=progressive multifocal leukoencephalopathy. BCP=birth control pills. TB=tuberculosis. CXR=chest x-ray.

Option Table Decision Aid: For a Patient With Rheumatoid Arthritis Considering Starting Their Third DMARD

References:

1. Martin RW et al. Patient Beliefs and Preference to Initiate a Proposed Medication in Rheumatoid Arthritis. Arthritis Rheumatol 2017;69 (suppl 10).
2. Wennberg JE Tracking Medicine: A Researcher's Quest to Understand Health Care. Oxford University Press, USA. 2010 1st edition. pp209-264.
3. Elwyn G, et al. Shared decision making: developing the OPTION scale for measuring patient involvement. BMJ Quality & Safety 2003;12:93-99.

Disclosure: R. Martin, Abbvie, 9, Amgen, 9, Eli Lilly, 9; **M. Shershneva**, Eli Lilly, 2; **L. Zurkovsky**, Teva, 1.

Abstract Number: 1708

Itching to Learn: Infusion Reactions Curriculum for Medicine Trainees

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Professional Education Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Comfort level with managing acute infusion reactions	Pre-curriculum	Post-curriculum
Extremely comfortable	0.00%	60.71%
Somewhat comfortable	38.89%	35.71%
Somewhat uncomfortable	61.1%	3.57%
Extremely uncomfortable	0.00%	0.00%

Table 1. Comfort level with managing acute infusion reactions before and after exposure to the infusion reactions curriculum

Confidence in managing acute infusion reactions	Pre-curriculum	Post-curriculum
Extremely confident	0.00%	67.86%
Somewhat confident	50.00%	32.14%
Somewhat not confident	34.38%	0.00%
Not at all confident	15.63%	0.00%

Table 2. Confidence in managing acute infusion reactions before and after exposure to the infusion reactions curriculum

Background/Purpose: Despite frequent use of infusion therapies, previous studies have demonstrated that trainees are poorly knowledgeable in managing infusion reactions, resulting in patient safety concerns. There are no easily implementable curricula addressing this barrier. The goal of this project was to refine, implement, and evaluate a concise and exportable curriculum on infusion reactions management for rheumatology fellows.

Methods: Fellows from 6 training programs completed an online pre-curriculum survey. Participants were emailed a link to a 9-minute educational video describing the pathophysiology and management of infusion reactions with a focus on anaphylaxis. The following week, fellows managed a simulated infusion reaction in a telephone conversation with "an infusion nurse." Two examiners scored simulation performance on a standardized form, then provided immediate feedback. A post-curriculum survey assessed changes in self-reported confidence and comfort managing acute infusion reactions.

Results: *Pre-curriculum*. Learning about infusion reactions was deemed "extremely" or "somewhat useful" by 92% (30/32). While 72% of respondents indicated no prior formal training on identification or management of infusion reactions, 54% had been directly involved in managing an acute infusion reaction; 87% of those were involved in more than one. Of fellows who had managed infusion reactions, 61.1% reported feeling "somewhat uncomfortable" doing it (Table 1). Exactly one half of the participants were "somewhat not confident" or "not at all confident" in doing so (Table 2).

Simulation. Fellows generally performed well, especially on the topics directly addressed in the video. However, learners across institutions missed similar expected tasks of infusion reaction management, such as activating EMS, ordering oxygen, notifying family, and adding the medication to the allergy list.

Post-curriculum. After completing the curriculum, 96% (27/28) of respondents reported feeling "extremely comfortable" or "somewhat comfortable" managing infusion reactions. All participants reported feeling either "extremely confident" or "somewhat confident" in their ability to manage these reactions. Fellows provided overwhelming positive feedback after the simulation.

Conclusion: This short curriculum successfully addressed a knowledge gap in management of acute infusion reactions in rheumatology fellows. Fellows agreed that the curriculum was needed. Respondents across institutions missed performing similar tasks on the infusion reaction simulation. Completing the curriculum increased participants' comfort and confidence in their ability to manage infusion reactions. Ongoing improvements are focused on creating a fully online interactive curriculum including an updated simulation script, a high-fidelity simulation exercise with real-time feedback, and expanding the curriculum to medicine residents and other subspecialty fellows.

Disclosure: A. Bagrova, None; **L. Eder**, None; **L. Criscione-Schreiber**, None.

Abstract Number: 1709

Teaching Clinical Application of Bayesian Reasoning in Rheumatology to Internal Medicine Residents and Medical Students

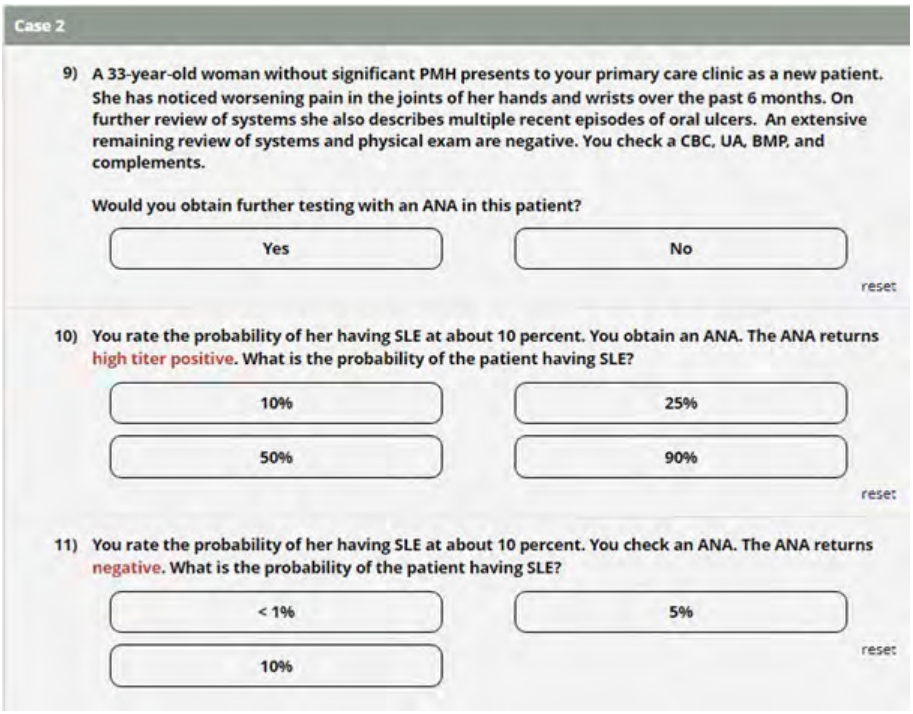
Joshua Gavin[1], Kristen Fadel[1], Yashswee KC[2], Evan Dombrosky[3], Sandra Johnson[4], Huzaefah Syed[5], Beth Rubinstein[6], Stamatina Danielides[6] and Abhishek Nandan[7], [1]Virginia Commonwealth University School of Medicine, Richmond, [2]Virginia Commonwealth University School of Medicine, Henrico, VA, [3]Virginia Commonwealth University School of Medicine, Glen Allen, VA, [4]Virginia Commonwealth University Health Systems, Richmond, [5]VCU Health, Richmond, VA, [6]Virginia Commonwealth University School of Medicine, Richmond, VA, [7]VCUHS and VA Medical Center- Richmond, VA, Richmond, VA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Professional Education Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Evidence-based medicine (EBM) is becoming an increasingly important skill in the clinical application of diagnostic reasoning. Didactic lectures focusing on EBM concepts are a common tool to teach trainees the skills to accurately assess and apply scientific information into clinical practice. However, this instruction format has not been demonstrated to be optimal for retention and application of knowledge. Other methods for learning statistics and critical appraisal certainly exist and include modules, self-directed programs, and problem-based learning.

We sought to create a brief module with the inclusion of adult learning theories to optimize delivery of knowledge of EBM concepts to residents and medical students and to assess the yield of the learners. Our purpose was to assess whether the use of this module would: 1) Increase learner comfort in the clinical application of likelihood ratios and 2) Improve appropriate application of rheumatologic testing at our center with this intervention.

Methods: The study was conducted at Virginia Commonwealth University School of Medicine (VCU SOM). We developed a short PowerPoint-slide based module with pre and post-test focused on application of Bayesian reasoning. Internal medicine residents and medical students on their rheumatology rotations were asked to complete our module. The pre-test was done immediately prior to the module and the post-test immediately following completion of the module. The test included 14 case-based questions evaluating application of Bayesian reasoning. An example



Example of the Survey Questions

of a typical case-based application question is included in Figure 1. Data was collected and stored on a secure cloud-based program, then analyzed using the student's t-test.

Results: A total of 12 trainees completed the pilot module with the pre-test and post-test. Five of the trainees were internal medicine residents and seven trainees were medical students. Baseline mean pre-test scores were 66.6% correct and the mean post-test score was 79.8%. Pre-test scores (P-Value = 0.0701) and post-test scores (P-Value = 0.0809) were not significantly different when comparing internal medicine residents to medical student. Completion of the EBM module led to significant improvement from pre- to post-test scores with a mean improvement of 13.20% (P-Value = 0.0147) as well as an improvement in comfort level of 21 points overall on a 1-100 scale (P-Value = 0.0082.

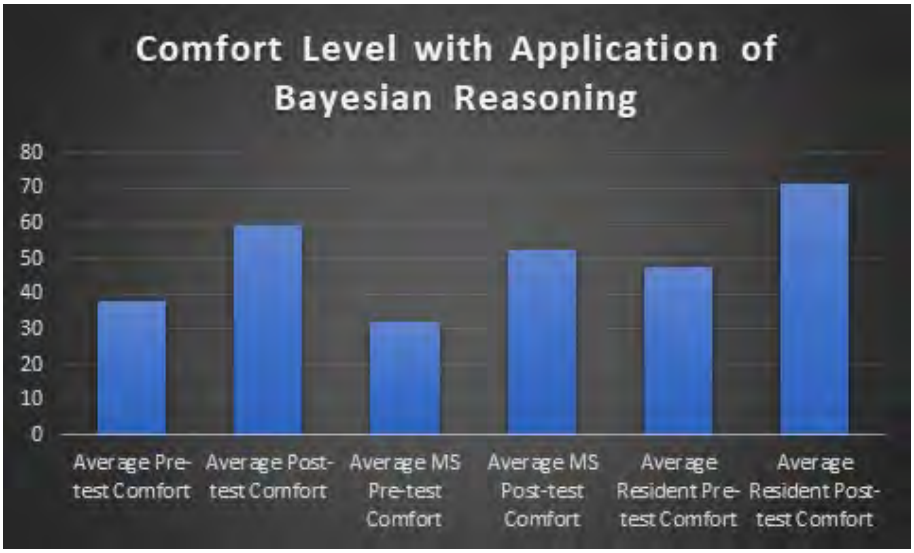


Figure 2. Comfort Levels from 0-100

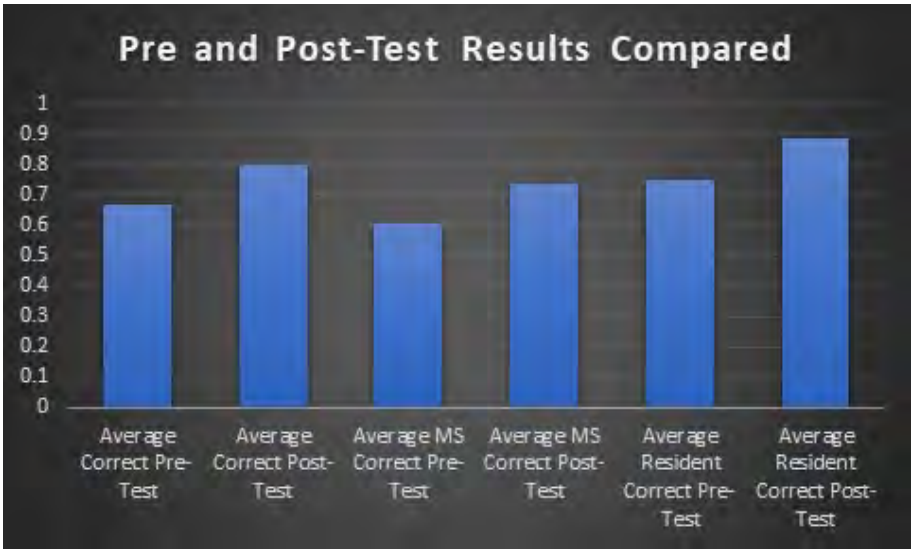


Figure 3

Conclusion: Our pilot study suggests that integrating rheumatology-oriented EBM didactics within internal medicine residency curriculum and internal medicine rotation of medical students results in immediate improvement and comfort with application of EBM concepts. The growing complexity of diagnostic testing in medicine and especially rheumatology highlights the importance of applying approachable and pragmatic methodology to appropriately utilize these tools. Re-testing after 12 months to evaluate durability of knowledge is a logical next step. We plan to continue to encourage trainee participation in our module. The module serves as a portion of the larger virtual curriculum that we are building at the VCU SOM for didactics in rheumatology.

Disclosure: J. Gavin, None; **K. Fadel**, None; **Y. KC**, None; **E. Dombrosky**, None; **S. Johnson**, None; **H. Syed**, None; **B. Rubinstein**, None; **S. Danielides**, None; **A. Nandan**, None.

Abstract Number: 1710

Remote Rheumapalooza: Reboot of a Foundational Rheumatology Curriculum for Pre-Clinical Medical Students in the Era of Virtual Learning

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SESSION INFORMATION
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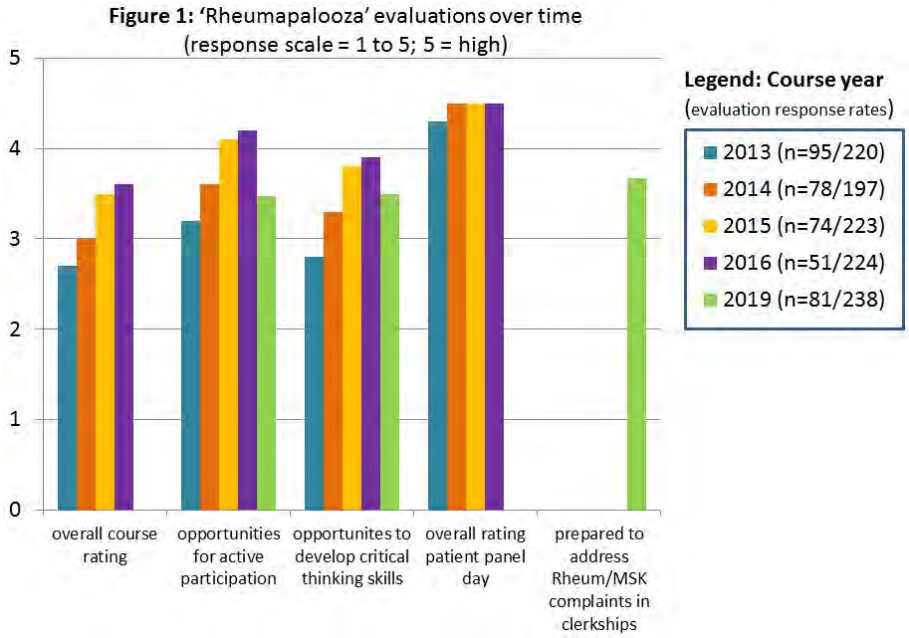
Background/Purpose: The original Rheumapalooza course was a required, independent 12 hour curriculum for pre-clinical medical students in the UWSOM from 2010 - 2016[1,2]. In 2015, the UWSOM implemented a new organ-based, flipped-classroom curriculum for entering students. Pre-clinical coursework was condensed from 24 to 18 months. In the new 'Foundations' curriculum students are divided between 6 regional campuses across five states (WA, WY, AK, MT, ID) for instruction. Site autonomy in delivery methods is encouraged, however course objectives,



Rheumapalooza Course Evaluations Over Time

learning opportunities and assessments must be uniform. These changes presented new educational challenges for the delivery of rheumatology content.

Methods: Rheumatology components are now taught throughout disparate courses including immunology and musculoskeletal blocks. After Foundations, preclinical students enter a 3 month distance learning course to prepare for the USMLE Step exam and to transition to required clerkships. A 5 session day of basic rheumatology content was developed as part of the final week and implemented in 2018. 'Remote Rheumapalooza' was adapted from previous course content: Introduction to Medical Decision Making, Developing Approach to Musculoskeletal Complaints, MSK radiology, Case Based Rheumatology and Rheumatology Patient Panel. Sessions were offered in a webinar format via ZOOM to allow synchronous student participation across the region. Attendance was on a 'selective' basis; students were required to attend a minimum number of hours during the week. Session evaluations were required to claim credit for participation and allowed tracking of virtual attendance. Based on positive feedback, 'Remote Rheumapalooza' was offered again in winter 2019. In March 2020, the COVID-19 pandemic led to closure of all UW campuses and recorded sessions from 2019 were re-utilized for distance learning.

Results: Student attendance at one or more Rheumatology sessions in 2019 was relatively high (range: 67-146/238). Individual sessions were rated 'useful and practical' (mean rating: 4.3-4.6; 1-5 Likert Scale). Comparison to parallel evaluation questions from the historical course indicated comparable ratings, with perhaps a loss in 'opportunities for active participation' (Figure1). Qualitative feedback highlighted the importance of hearing the patients' stories and observing how physicians interacted with patients. Some students requested more general musculoskeletal review and less detailed rheumatology content.

Conclusion: Implementation of a 5 hour webinar format 'Remote Rheumapalooza' was associated with high student attendance and comparable student ratings to the prior in-person course. Replication of the 'tour' of patient panel physical findings was most challenging from an educational design standpoint, however, students still found value in hearing patients' stories via webinar. This work has important ramifications given increasing reliance on distance

learning. Additional work is needed to enhance active participation in virtual sessions and to evaluate retention of concepts during clerkships.

1. Emery H, Gardner G. [abstract]. Arthritis Rheum 2010;62 Suppl 10.

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Disclosure: K. Hayward, None; **M. Kiefer**, None; **H. Emery**, None.

Abstract Number: 1711

Musculoskeletal Sarcoidosis Learning Module for Internal Medicine Trainees: Developing a Rheumatology Curriculum

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Session Time: 9:00AM–11:00AM

Background/Purpose: Sarcoidosis is a systemic, multi-organ disease frequently overlooked in the development of a differential diagnosis. Although typically considered a pulmonary disease, management decisions often fall to the Rheumatologist especially in the context of sarcoid-related arthritis or the initiation of immunosuppressive therapy. We sought to create an interactive module to train internal medicine residents and medical students in the diagnosis and management ofmusculoskeletal sarcoidosis. This module is a part of a larger module-based Rheumatology curriculum undergoing development at Virginia Commonwealth University School of Medicine (VCU SOM). Our goal is to assess whether this module improves internal medicine trainee's understanding of musculoskeletal sarcoidosis.

Methods: This study was internally conducted at VCUSOM. We developed a module with a pre- and post-test focused on the varying presentations of musculoskeletal sarcoidosis. The module was based on a clinical case presentation to allow trainees to demonstrate their ability to obtain a thorough history and physical exam, order appropriate labs and imaging, create an appropriate differential diagnosis for musculoskeletal sarcoidosis, and reach an accurate final diagnosis. The module progresses to cover treatment options and reviews the different subtypes of musculoskeletal sarcoidosis, ultimately covering joint, muscular, and osseous sarcoid presentations. Internal medicine residents and medical students were asked to complete our module. The pre-test was done immediately prior to the module and the post-test immediately following completion of the module. The test included eight questions evaluating knowledge of the varying clinical presentations, features, and treatment of musculoskeletal sarcoidosis. The questions are included in Figure 1. Data was collected and stored on a secure cloud-based program, REDCap, and then analyzed using the students' t-test.

Figure 1. Pre- and post-test questionnaire.

#	Question	Answer Choices
1	What is the most common musculoskeletal manifestation of sarcoidosis?	- Chronic sarcoid arthritis - Heerfordt's syndrome - Lofgren's syndrome - Jaccoud's arthropathy - Sarcoid monoarthritis
2	Which manifestation of sarcoidosis does not require a biopsy?	- Lofgren's syndrome - Jaccoud's arthropathy - Sarcoid monoarthritis
3	What is typically seen histopathologically in sarcoidosis?	- Caseating granulomas - Non-caseating granulomas
4	What is the triad of Lofgren's syndrome? (Select 3)	- Arthritis - Hypercalcemia - Hilar lymphadenopathy - Erythema nodosum - Elevated 1,25(OH)2 Vitamin D - Elevated ESR
5	Which muscle groups are typically involved in sarcoid myopathy?	- Proximal - Distal
6	Which bones are most commonly affected in osseous sarcoid?	- Axial - Peripheral (hands) - Peripheral (knees)
7	What other diagnosis is considered in the differential for osseous sarcoid?	- Free text
8	Which immunosuppressant can be used in the treatment of sarcoidosis?	- Calcineurin inhibitors - DMARDs - Interleukin inhibitors

DMARDs = Disease modifying anti-rheumatic drugs

Figure 1. Pre- and post-test questionnaire.

Results: The module was tested by nine medical students and one fellow at VCU SOM. We observed a significant difference between the percentage correct for the pre- and post-tests (Figure 2), from an average of 46.25% to 90% (P-Value = < 0.001). Feedback was consistently positive and the comments are summarized in Figure 3.

Figure 2. Results of pre- and post-tests.

ID	Pre-test Percent Correct (%)	Post-test Percent Correct (%)
1	62.5	100
2	25	100
3	25	87.5
4	37.5	87.5
5	25	87.5
6	25	75
7	50	87.5
8	87.5	100
9	62.5	87.5
10	62.5	87.5
Average	46.25	90

Figure 2. Results of pre- and post-tests.

Figure 3. Summary of student feedback.

Summary of Student Feedback
"Great module. I liked the slides saying what you would rule out and the reasons for ruling them out. I would love some prognostic information… it would be nice to get some insight on mortality and morbidity so we know how to frame the disease when talking to patients."
"I thought the module was really great overall. I love the "ruling out" step. So many modules I do have the "what differential to consider?", but not so much the "how do you rule these things out?" logic."
"I think the presentation is great! The information is certainly all there, might be good to include a few more relevant pictures of imaging findings."
"All information was very concise and straight forward. Would consider including any associated conditions or specific pearls to pay attention to in the clinic about how to manage these patients (like what struggles they encounter or challenges to caring for them). Overall, very clear and great!"

Figure 3. Summary of student feedback.

Conclusion: Our pilot study suggests that integrating a sarcoidosis module within the internal medicine residency curriculum and the pre-clinical medical student curriculum may result in improved knowledge and recognition of musculoskeletal sarcoidosis. We plan to continue to recruit medical trainees to participate in our module, which serves as a portion of the larger virtual curriculum that we are building at the VCU SOM for didactics in rheumatology. We hope in future studies to evaluate a larger sample size and evaluate trainees for long term retention of knowledge gained through this module.

Disclosure: K. Fadel, None; **E. Dombrosky**, None; **H. Syed**, None; **J. Gavin**, None; **A. Nandan**, None; **S. Danielides**, None; **B. Rubinstein**, None; **Y. KC**, None; **S. Johnson**, None.

Abstract Number: 1712

Implementation of a Musculoskeletal Ultrasound (MSUS) Curriculum in an Academic Rheumatology Fellowship Within an Integrated Health System: A Four-Year Experience

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Professional Education Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Musculoskeletal Ultrasound has become a significant training tool in rheumatology fellowships. A recent survey showed 94% of rheumatology fellowships have implemented a teaching program for US with 41% having implemented a curriculum. The ACR developed a teaching curriculum as a model for programs in 2019, updating the core curriculum from 2015. Our institution started MSUS training in 2012 as part of our training programs career tracks, which include medical education, quality improvement and osteoporosis management. This was revamped in 2016. We report the implementation of our MSUS curriculum.

Methods: MSUS training involves a two-year curriculum. The first year introduces the basics of ultrasound (US) and the second year is tailored to those pursuing MSUS as part of their career path. The curriculum was designed from the blueprint for RhMSUS certification and milestones were created for skills necessary to master MSUS (Table 1).

The first year focuses on developing basic US skills concentrating on understanding how to use and maintain equipment, learning basic anatomy based on 2017 EULAR guidelines and USSONAR US protocols for US scanning and acquiring studies. Fellows participate in monthly US clinics and didactic sessions with teaching based on a scanned area of interest. There are 8 hours of clinic and 6 hours of didactics monthly.

Table 1. Milestone requirements for 1st year MSUS ultrasound curriculum

MSUS COMPETENCY/ GOALS	Medical Knowledge	Patient Care	Practice-Based Learning	Systems Based Practice	Interpersonal & Communication Skills	Professionalism
First Year – PGY4	1. Learning the basic anatomy to recognize normal structures on ultrasound examinations 2. Recognize the abnormalities consistent with specific pathology and the definition of those pathologies as dictated by the literature. 3. Select the most appropriate transducer, based on patient and examination factors, in order to obtain optimal images. 4. Hands-on training sessions and didactics to improve technical skills	1. Educate the patient by explaining the role of and alternatives to the ultrasound examination in order to establish consent. 2. Understand specific reason for ordering laboratory tests and cost of laboratory tests used in pediatric rheumatology cases. 3. Demonstrate competency and sterile technique in joint aspiration in children.	1. Recognize when ultrasound would assist in establishing a diagnosis by analyzing clinical information and diagnostic testing in order to identify appropriate patients. 2 State the indication for the ultrasound study in order to document the reason for the examination. 3. Maintain a clinical portfolio of Ultrasound studies performed	1. Modify the environment by adjusting ambient lighting and temperature in order to optimize the ultrasound examination. 2. Position the patient and the ultrasound machine appropriately in order to allow safe and comfortable performance of the examination and to obtain high quality diagnostic images.	1. Label all images and clips using appropriate sonographic terminology in order to identify the examined structures. 2. Save images and clips using a system that is reliable and that permits retrieval in order to provide for documentation and report generation 3. Clearly discuss risks, benefits and procedures in children and parents of children with rheumatic diseases.	1. Recognize clinical scenarios where ultrasound use is inappropriate, not indicated, or outside the scope of the practitioner's expertise in order to optimize patient management and maintain the credibility and integrity of ultrasound in the field of rheumatology 2. Maintain equipment in good working order by conducting regular inspections and making necessary repairs in order to ensure acquisition of reliable images. 3. Clean the transducer with a disinfectant after each examination in order to prevent the transmission of infection. 4. Demonstrate integrity in reporting clinical findings of your ultrasounds

Table 2. Milestone requirements for second year MSUS ultrasound curriculum

MSUS COMPETENCY/ GOALS	Medical Knowledge	Patient Care	Practice-Based Learning	Systems Based Practice	Interpersonal & Communication Skills	Professionalism
Second Year – PGY5	1. Exhibit mastery of the ultrasound anatomy to recognize normal structures 2. Continue to improve skills at recognizing pathology in musculoskeletal ultrasound 3. Adjust B-mode settings by applying knowledge of sonographic principles for individual probes and body regions in order to obtain optimal images 4. Adjust Doppler settings by applying knowledge of sonographic principles for individual probes and body regions in order to obtain optimal images. 5. Lead didactic and hands on training session with the ultrasound machine	1. Determine if ultrasound guidance is likely to improve the outcome of a planned procedure by reviewing findings of the examination in order to maximize the probability of effective treatment. 2. Develop a differential diagnosis of findings on imaging studies.	1. Determine the appropriateness of ultrasound guidance of an intervention by incorporating best available evidence in order to optimize patient management. 2. Use aseptic technique as it applies to ultrasound-guided procedures in order to minimize the risk of infection. 3. Identify patient conditions where ultrasound can evaluate treatment response and disease progression, based on the best available evidence, in order to optimize patient management and education	1. Correlate ultrasound findings with the physical examination, available laboratory tests, and other imaging modalities in order to integrate diagnostic testing into a comprehensive management plan. 2. Refer patients for further evaluation when the practitioner is unable to answer the clinical question using the ultrasound examination in order to optimize care.	1. Report the technical components and quality of the examination when appropriate in order to clarify the context of examination. 2. Report ultrasound findings and conclusions using sonographic terminology in order to document findings clearly and guide further care. 3. Be able to maintain a sound relationship with patients over the course of the fellow's fellowship.	1. Store the ultrasound report and images in a secure, retrievable, and reliable manner in order to ensure ongoing coordination and quality of care. 2. Demonstrate respect for all patients regardless of race, gender and socioeconomic background.

The second year is a MSUS track year tailored to advanced US training. Fellows have three months of US through the academic year with focus on enhancing US skills while improving recognition of pathology. There is an increased focus in procedural US training with opportunities to perform US guided arthrocentesis and injection. Fellows apply to participate in the USSONAR course in the second year. Those who are unable to participate in USSONAR will

attend an US course that meets requirement for certification. There are 8 hours of clinic and 6 hours of didactics in addition to rotations and assignments for the 2nd years.

The goal of our curriculum and training course is to progress rheumatology fellows into certified ultrasonographers. Fellows are expected to sit for RhMSUS certification prior to completion of their fellowship. This curriculum allows fellows to meet required ACR pathways for RhMSUS certification.

Results: Over 4 years, 8 rheumatology fellows have participated in the MSUS program within our fellowship. Of those fellows, 6/8 have participated in the USSONAR training program in addition to their fellowship training, 5/6 fellows completed USSONAR certification. Seven fellows have completed RhMSUS certification with the eighth soon to take the exam, 7/7 fellows passed their certification exam. Of the fellows who have graduated, 4/6 have consistently utilized MSUS in clinical practice.

Conclusion: Our institution has successfully implemented a robust MSUS curriculum utilizing EULAR guidelines and USSONAR US protocols. We have been able to train rheumatology fellows to be competent musculoskeletal ultrasonographers and become RhMSUS certified prior to graduation. New opportunities include providing fellows with handheld US devices to enhance training. This will be a pilot program starting in the 2020-21 academic year.

Disclosure: D. Bulbin, Novartis, 5, 8, Alexion, 8; **B. Oppermann**, UCB, 8, Abbvie, 8; **J. Cote**, None; **D. Pugliese**, None; **A. Denio**, None.

Abstract Number: 1713

Exploring Novel Tenosynovitis and Combined Inflammation Imaging Outcomes: Results from a Randomized Controlled Trial in Early Rheumatoid Arthritis

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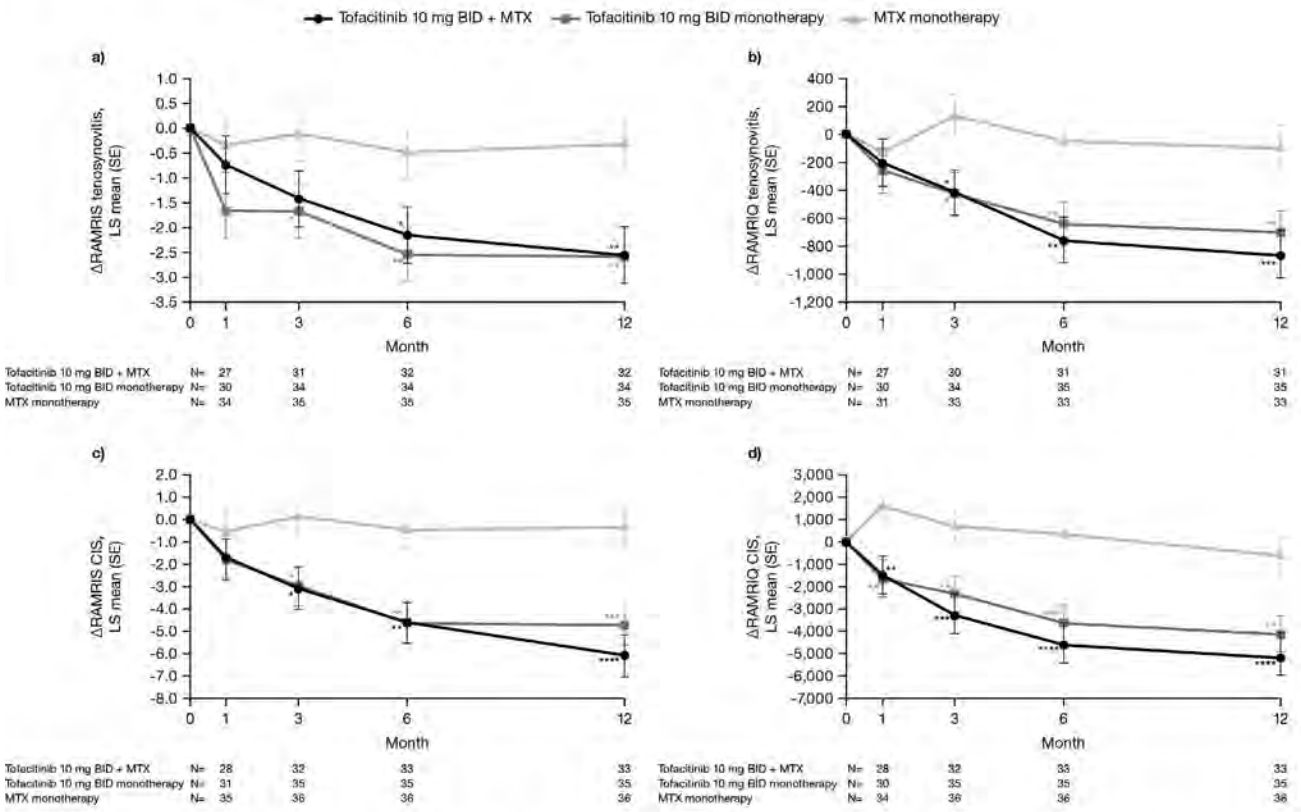
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: MRI trial outcomes have largely focused on synovitis, bone marrow edema (BME), and erosions. Tenosynovitis is a common manifestation of RA, but is relatively understudied; a combined inflammation score (CIS) that sums the 3 inflammatory markers (synovitis, BME, and tenosynovitis) may be a highly responsive outcome measure. We have previously demonstrated the responsiveness of the OMERACT RA MRI scoring system (RAMRIS) and a machine-learning derived automated tool (RAMRIQ) in a randomized trial of tofacitinib and MTX in MTX-naïve patients (pts) with early RA.[1] This post hoc analysis evaluated the effects of tofacitinib ± MTX on MRI tenosynovitis and CIS in pts with early RA using semiquantitative and quantitative MRI outcomes.

Figure. a) ΔRAMRIS tenosynovitis, b) ΔRAMRIQ tenosynovitis, c) ΔRAMRIS CIS, and d) ΔRAMRIQ CIS at Months 1, 3, 6, and 12 (FAS)



*p<0.05, **p<0.01, ***p<0.001, ****p<0.0001 for comparisons of tofacitinib ± MTX vs MTX monotherapy, assessed using a mixed-effect model for repeated measures; missing values were imputed by LOCF; tenosynovitis and CIS were assessed using combined data from MCP and wrist joints; CIS was calculated by the sum of synovitis, BME, and tenosynovitis values
Δ, change from baseline; BID, twice daily; BME, bone marrow edema; CIS, combined inflammation score; FAS, full analysis set; LOCF, last observation carried forward; LS, least squares; MCP, metacarpophalangeal; MRI, magnetic resonance imaging; MTX, methotrexate; N, number of patients with values at baseline and the timepoint of interest; RA, rheumatoid arthritis; RAMRIQ, automated quantitative RA MRI assessment system, automated RAMRIS; RAMRIS, RA MRI scoring system; SE, standard error

Table. Correlations between a) BL RAMRIS and BL RAMRIQ tenosynovitis and CIS vs BL DAS28-4(CRP) (N=109) and b) ΔRAMRIS and ΔRAMRIQ tenosynovitis and CIS at Month 12 vs ΔDAS28-4(CRP) at Month 12 (N=73), using pooled data across all three treatment arms[a]

a)

All treatment arms[a]	BL RAMRIS tenosynovitis		BL RAMRIS CIS		BL RAMRIQ tenosynovitis		BL RAMRIQ CIS	
	Correlation	p value	Correlation	p value	Correlation	p value	Correlation	p value
BL DAS28-4(CRP)	0.366	0.0001	0.399	<0.0001	0.205	0.037	0.180	0.062

b)

All treatment arms[a]	ΔRAMRIS tenosynovitis		ΔRAMRIS CIS		ΔRAMRIQ tenosynovitis		ΔRAMRIQ CIS	
	Correlation	p value	Correlation	p value	Correlation	p value	Correlation	p value
ΔDAS28-4(CRP)	0.531	<0.0001	0.554	<0.0001	0.543	<0.0001	0.564	<0.0001

[a]For this analysis, data were pooled across all three treatment arms (tofacitinib 10 mg BID + MTX, tofacitinib 10 mg BID monotherapy, MTX monotherapy)
Spearman's rank correlation coefficients and p values were calculated for the correlation of BL RAMRIS and BL RAMRIQ tenosynovitis and CIS vs BL DAS28-4(CRP) and ΔRAMRIS and ΔRAMRIQ tenosynovitis and CIS at Month 12 vs ΔDAS28-4(CRP) at Month 12; tenosynovitis and CIS were assessed using combined data from MCP and wrist joints; CIS was calculated by the sum of synovitis, BME, and tenosynovitis values
Δ, change from baseline; BID, twice daily; BL, baseline; BME, bone marrow edema; CIS, combined inflammation score; DAS28-4(CRP), Disease Activity Score in 28 joints, C-reactive protein; MCP, metacarpophalangeal; MRI, magnetic resonance imaging; MTX, methotrexate; N, number of patients with values at baseline and timepoint of interest; RA, rheumatoid arthritis; RAMRIQ, automated quantitative RA MRI assessment system, automated RAMRIS; RAMRIS, RA MRI scoring system

Methods: Study A3921068 (NCT01164579) was a 1-year, exploratory, Phase 2, randomized controlled trial comparing tofacitinib 10 mg twice daily (BID) ± MTX, and MTX monotherapy, in MTX-naïve pts with early, active RA.[1] MRI of unilateral wrist and MCP joints was performed at screening/baseline (BL) and Months (M)1, 3, 6, and 12. MRI tenosynovitis and CIS were assessed using RAMRIS and RAMRIQ. Changes from BL (Δ) in RAMRIS and RAMRIQ tenosynovitis and CIS were evaluated at M1, 3, 6, and 12. Data were assessed using a mixed-effect model for repeated measures, with treatment arms as factors and BL values as covariates. Using data pooled across all treatment arms, Spearman's rank correlation coefficients were calculated for associations between BL RAMRIS and BL RAMRIQ tenosynovitis and CIS vs BL DAS28-4(C-reactive protein [CRP]) and between ΔRAMRIS and ΔRAMRIQ tenosynovitis and CIS at M12 vs ΔDAS28-4(CRP) at M12.

Results: In total, 109 pts were randomized and treated (mean RA duration 0.7 years). ΔRAMRIS and ΔRAMRIQ tenosynovitis (Figure a,b) and ΔRAMRIS and ΔRAMRIQ CIS (Figure c,d) were generally significantly greater at M3, 6, and 12 in pts receiving tofacitinib ± MTX vs MTX alone, with significant improvements also seen at M1 for ΔRAMRIQ CIS. Compared with RAMRIS, RAMRIQ outcomes were generally more responsive to treatment with tofacitinib ± MTX. Significant correlations were seen between BL RAMRIS and BL RAMRIQ tenosynovitis and BL RAMRIS CIS vs BL DAS28-4(CRP), while significant correlations were also observed between ΔRAMRIS and ΔRAMRIQ tenosynovitis and CIS at M12 vs ΔDAS28-4(CRP) at M12 (Table). In general, stronger correlations were seen between BL DAS28-4(CRP) and BL RAMRIS parameters vs BL RAMRIQ parameters, whereas correlations were similar between ΔDAS28-4(CRP) at M12 and ΔRAMRIS and ΔRAMRIQ parameters at M12.

Conclusion: Responsiveness of RAMRIS and RAMRIQ tenosynovitis and CIS was demonstrated with significant improvements through M12 in pts receiving tofacitinib 10 mg BID ± MTX vs MTX alone. Construct validity for RAMRIS and RAMRIQ tenosynovitis and CIS was evident from correlations with DAS28-4(CRP). Further work is required to validate these novel imaging biomarkers in terms of relative responsiveness and prediction for later structural progression.

1. Conaghan PG et al. Ann Rheum Dis 2016; 75: 1024-1033.

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Disclosure: P. Conaghan, AbbVie, 1, 2, EMD Serono, 1, Flexion Therapeutics, 1, 2, Galapagos, 1, Gilead, 1, Novartis, 1, 2, Regeneron, 1, Samumed, 1, 2, GlaxoSmithKline, 5, Janssen, 5, Pfizer Inc, 5, Bristol-Myers Squibb, 2, Eli Lilly, 5; **M. Østergaard**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Hospira, 5, 8, Janssen, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Novo Nordisk, 5, Orion, 5, 8, Regeneron, 5, Roche, 5, 8, UCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, Boehringer Ingelheim, 5, 8, Sandoz, 5, 8, Sanofi, 5, 8; **O. Troum**, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celgene, 8, Centocor, 2, Corrona, 2, Eli Lilly, 5, Horizon, 5, 8, Novartis, 2, 8, Pfizer Inc, 2, 5, 8, Sanofi-Genzyme, 8; **Z. Xie**, Pfizer Inc, 1, 3; **A. Brett**, Imporphics Ltd, a wholly owned subsidiary of Stryker Corp, 1, 3; **M. Snyder**, Pfizer Inc, 1, 3; **A. Ebrahim**, Pfizer Inc, 1, 3; **D. Chapman**, Pfizer Inc, 1, 3; **G. Sawyerr**, Syneos Health, 3; **J. Andrews**, Pfizer Inc, 1, 3.

Abstract Number: 1714

Disease Activity Trajectories for Early and Established Rheumatoid Arthritis: Real World Results from a Rheumatoid Arthritis Cohort

Mohammad Movahedi[1], Angela Cesta[2], Xiuying Li[3] and **Claire Bombardier**[4], [1]Toronto General Hospital Research Institute, University Health Network, Toronto, ON, Canada, [2]Toronto General Hospital Research Institute, Toronto, ON, Canada, [3]Toronto General Hospital Research Institute, Toronto, Canada, [4]Institute for Work and Health, Toronto, ON, Canada

SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Description of disease activity status in patients with rheumatoid arthritis (RA) at fixed points in time modelled as continuous (e.g. number of swollen joints counts), dichotomous variable (e.g. remission or low disease status using composite measures) do not reflect the patient's disease course in chronic and relapsing RA. We proposed to describe the longitudinal disease activity trajectories for patients with early and established RA over two years' follow-up in routine clinical care.

Methods: RA patients enrolled in the Ontario Best Practices Research Initiative (OBRI) with available DAS28-ESR over two years of follow-up were included. Using a latent growth curve modelling (LCGM), subgroups of patients following distinct pattern of DAS28-ESR change over time were identified. Model selection was based on Bayesian information criterion (BIC).

Results: A total of 1273 patients were included, 454 (36%) with early RA and 819 (64%) with established RA. At baseline, patients with early RA were significantly younger (57.3 vs. 59.1 years) and with higher DAS28-ESR (4.6 vs. 4.3), and were less likely to have an erosion (25.0% vs. 59.7%), to be RF-positive (70.3% vs. 76.8%), and to use biologic DMARDs (7.0% vs. 29.2%).

In patients with early RA (Figure 1A), three subgroups of patients were identified by LCGM with a better fit (BIC: -3070.84). Almost 88% patients with moderate disease activity reached remission (group 1: 48.4%) or low disease status (group 2: 39.3%) at year 2, while 12% of patients with high disease profile remained in a moderate state (group 3).

In patients with established RA (Figure 1B), seven subgroup of patients were identified by LCGM with a better fit (BIC: -5378.13). After 2 years' follow-up, 37.5% of patients in remission or low disease state at baseline remained

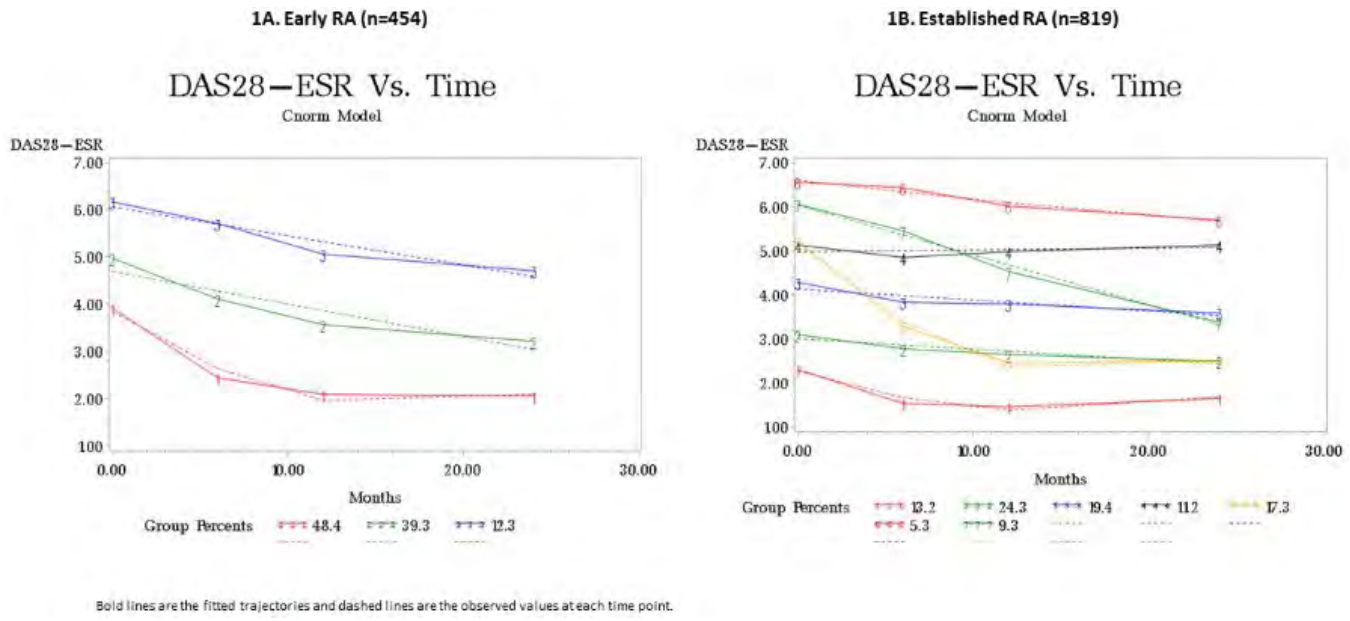

Figure 1. Observed and fitted trajectories from latent growth curve analysis in patients with early and established RA.

or reached to remission (group 1 and 2, respectively). Only 17.3% of patients with high disease activity at baseline reached remission (group 5). 16.5% patients with high disease activity at baseline remained in high disease status at year 2 (group 4 and 6). Two other group of patients (group 3 and 7) with moderate or high disease activity at baseline remained in a moderate state after two years.

Conclusion: Disease course is different between early and established RA. While 70% of early RA patients with moderate or high disease profiles reached remission, only 17% of established patients with high disease activity achieved remission after 2 years of follow-up. These findings suggest the potential effects of receiving early treatment and health care. The impact of sociodemographic, clinical and medication profile on disease course will be examined as future work for this study.

Disclosure: M. Movahedi, None; **A. Cesta**, None; **X. Li**, None; **C. Bombardier**, CIHR, 2, MOHLTC, 2, Abbvie, 2, Amgen, 2, Janssen, 2, Medexus, 2, Merck, 2, 5, Novartis, 2, Pfizer, 2.

Abstract Number: 1715

Longitudinal Patterns of Remission in Real-World Early Rheumatoid Arthritis Patients: Results from the Canadian Early Arthritis Cohort (CATCH)

Orit Schieir[1], Glen Hazlewood[2], Susan Bartlett[3], Marie-France Valois[3], Louis Bessette[4], Gilles Boire[5], Carol Hitchon[6], Edward Keystone[7], Janet Pope[8], Carter Thorne[9], Diane Tin[9], Vivian Bykerk[10] and Canadian Early Arthritis Cohort (CATCH) Investigators[11], [1]Canadian Early Arthritis Cohort Study, Montreal, Canada, [2]University of Calgary, Calgary, AB, Canada, [3]McGill University, Montreal, Canada, [4]Laval University, Quebec, Canada, [5]Universite de Sherbrooke, Sherbrooke, Canada, [6]University of Manitoba, Winnipeg, MB, Canada, [7]The Rebecca MacDonald Centre for Arthritis, Mt. Sinai Hospital, Toronto, Canada, [8]Department of Medicine, University of Western Ontario, St. Joseph's Health Centre, London, ON, Canada, [9]Southlake Regional Health Centre, Newmarket, ON, Canada, [10]Hospital for Special Surgery, New York, NY, [11]Canadian Early Arthritis Cohort (CATCH) Study, Toronto, Canada

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Early diagnosis and rapid initiation of DMARDs following a treat-to-target approach have made remission a realizable goal for many persons living with RA. Despite contemporary improvements in early RA remission outcomes, less is known about: How often, and how long remission is sustained for, and what factors may contribute to loss of remission/ disease control over time. The objective of the present study was to describe longitudinal patterns of remission in real-world early RA patients over a 12-24 months follow up period.

Methods: Data were from participants enrolled in the Canadian Early Arthritis Cohort (CATCH), a prospective study of "real-world" early RA patients (symptoms < 1 year) treated in rheumatology clinics across Canada from 2007-2019. The study sample was limited to patients with active disease at enrolment who later reached remission (SDAI<=3.3) and were followed for 12-24 months post-remission. SDAI remission status over the 12-24m follow up period was classified into 3 patterns: Pattern 1 - Sustained remission (REM → REM); Pattern 2 - Transient remission (REM → LDA), and Pattern 3 - Transient remission (REM → MDA/HDA). Multi-adjusted multinomial regression was used to identify predictors of transient remission patterns (Pattern 2 and Pattern 3) vs. sustained remission (Pattern 1), respectively.

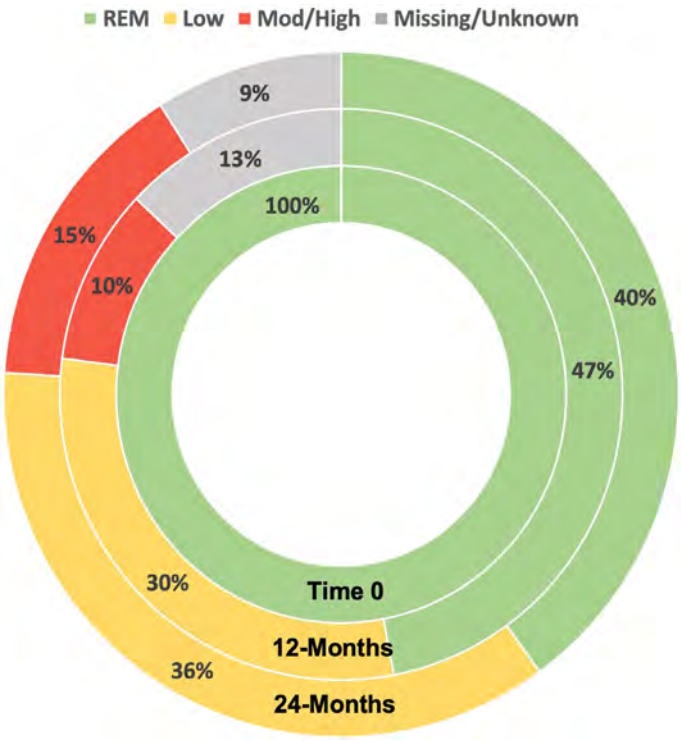

Figure. Distribution of Disease Activity Status 12-24 after RA Patients First Reach SDAI REM

	Pattern 2 (REM → LDA) vs. Pattern 1 (REM → REM) OR (95% CI)	Pattern 3 (REM →HDA/MDA) vs. Pattern 1 (REM → REM) OR (95% CI)
Age, years	1.01 (1.00, 1.02)	1.01 (0.99, 1.02)
Sex, Female vs. Male	**1.78 (1.33, 2.39)**	**1.63 (1.09, 2.44)**
Current smoker vs. past or never smoker	**1.57 (1.09, 2.28)**	**1.53 (0.95, 2.47)**
Comorbidities, RDCI ^ (range 0-9)	**1.11 (0.99, 1.25)**	**1.30 (1.13, 1.50)**
RF+ or ACPA +	**1.38 (1.03, 1.85)**	**1.21 (0.81, 1.80)**
Early MTX treatment (≦ 3-months)	1.18 (0.85, 1.63)	0.76 (0.51, 1.12)
Time to first SDAI remission, (months)	1.01 (1.00, 1.01)	1.01 (1.00, 1.02)
Treatment reduction after REM vs. No Change	1.33 (0.96, 1.86)	1.01 (0.62, 1.64)

Table. Multi-Adjusted Multinomial Regression Results of Predictors of Transient Remission Patterns over 24-Month Follow Up

Results: Among all early RA patients enrolled in CATCH, 1691/ 3054 (55%) had ever reached SDAI remission. Among those that reached remission, 1,419 completed at least 12-24 months of study follow-up post remission and were included in the present study. At study enrolment, most were female (70%), mean(sd) SDAI disease activity was high (27(15)) and most patients (92%) were being treated with csDMARDs. Over the follow up period, 47% of patients sustained remission by 12-months and, only 40% by 24 months (Figure). Transitions from REM→LDA (36%) were more common than REM→MDA/HDA (15%) by 24 months (Figure).Female sex, smoking, higher comorbidity index and positive serology, were significantly associated with transient remission patterns (Table). Results also suggest possible associations between transient remission patterns and older age, longer time to first remission, lack of early MTX treatment and reducing treatment after remission, but confidence intervals were inconclusive (Table).

Conclusion: Results of this large longitudinal study suggests that < 50% of real-world early RA patients that reached remission, sustained remission for 12-24m. Closer monitoring of RA patients with prognostic indicators for transient

remission, and additional research aimed at improving the understanding of why remission is lost may help more patients sustain remission for longer periods.

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Abstract Number: 1716

Predictors of Unacceptable Pain and Unacceptable Pain with Low Inflammation in Early Rheumatoid Arthritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Pain is a common and debilitating symptom in patients with rheumatoid arthritis (RA). In early RA it is usually due to ongoing inflammation and synovitis, but over time a substantial proportion of patients experience pain without laboratory or clinical signs of inflammation.

The objective of this study was to investigate predictors of unacceptable pain and unacceptable pain with low inflammation one year after diagnosis in patients with RA.

Methods: Consecutive patients with early RA (symptom duration < 12 months, fulfilling the 1987 ACR criteria and/or the 2010 ACR/EULAR criteria) were recruited between January 2012 and March 2016 from a defined geographical area. Patients were managed according to usual care, and were followed for one year after diagnosis. Pain was assessed using a visual analogue scale (VAS; 0-100 mm). Unacceptable pain was defined as VAS pain > 40 based on

Table 1. Baseline predictors of unacceptable pain one year after diagnosis in patients with early RA.

Variable	Odds ratio	95 % Confidence interval
Female sex	2.59	1.09 – 6.13
RF seropositivity	1.31	0.60 – 2.87
Anti-CCP seropositivity	0.59	0.29 – 1.22
Age	1.07	0.72 – 1.60
Symptom duration	1.04	0.73 – 1.50
VAS pain	1.35	0.91 – 2.02
DAS28	1.06	0.69 – 1.63
SJC28	0.96	0.67 – 1.40
TJC28	1.07	0.76 – 1.49
HAQ	1.58	1.08 – 2.30
CRP	0.99	0.72 – 1.35
ESR	1.01	0.94 – 1.46
VAS PGA	1.26	0.83 – 1.92

Univariate logistic regression analysis. Odds ratios are calculated per standard deviation for continuous variables. Unacceptable pain: VAS pain > 40. RF = rheumatoid factor; anti-CCP = anti-cyclic citrullinated peptide; VAS = Visual Analogue Scale; DAS28 = Disease Activity Score in 28 joints; SJC28 = Swollen Joint Count in 28 joints; TJC28 = Tender Joint Count in 28 joints; HAQ = Health Assessment Questionnaire; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; PGA = patient global assessment.

Table 2. Baseline predictors of unacceptable pain with low inflammation one year after diagnosis in patients with early RA.

Variable	Odds ratio	95 % Confidence interval
Female sex	3.72	1.22 – 11.34
RF seropositivity	0.82	0.36 – 1.87
Anti-CCP seropositivity	0.67	0.30 – 1.50
Age	1.26	0.79 – 2.01
Symptom duration	1.07	0.72 – 1.60
VAS pain	1.40	0.90 – 2.17
DAS28	1.09	0.68 – 1.74
SJC28	0.90	0.60 – 1.35
TJC28	0.96	0.66 – 1.41
HAQ	1.50	1.00 – 2.25
CRP	0.72	0.43 – 1.19
ESR	0.83	0.53 – 1.30
VAS PGA	1.38	0.87 – 2.20

Univariate logistic regression analysis. Odds ratios are calculated per standard deviation for continuous variables. Unacceptable pain: VAS pain > 40. Low inflammation: CRP < 10 mg/l. RF = rheumatoid factor; anti-CCP = anti-cyclic citrullinated peptide; VAS = Visual Analogue Scale; DAS28 = Disease Activity Score in 28 joints; SJC28 = Swollen Joint Count in 28 joints; TJC28 = Tender Joint Count in 28 joints; HAQ = Health Assessment Questionnaire; CRP = C-reactive protein; ESR = erythrocyte sedimentation rate; PGA = patient global assessment.

the patient acceptable symptom state (PASS) (1), and low inflammation as CRP < 10 mg/l (2). Baseline predictors of unacceptable pain, and unacceptable pain with low inflammation, were evaluated using logistic regression analysis.

Results: A total of 263 patients with early RA (mean age 59 years, 73 % female, 67 % anti-CCP positive, median symptom duration 5 months) were included, and 183 attended the 1-year follow-up. After one year 32 % had unac-

ceptable pain and 22 % had unacceptable pain with low inflammation, the latter thus accounting for 69 % of all unacceptable pain. High scores for the Health Assessment Questionnaire (HAQ) disability index at baseline, and female sex were associated with unacceptable pain (Table 1) and also with unacceptable pain with low inflammation (Table 2) at 1 year in univariate analysis, whereas there were no such associations for swollen joint count or laboratory markers of inflammation (Table 1, Table 2). In multivariate logistic regression analysis, there was an independent association between higher HAQ and unacceptable pain after 1 year [adjusted odds ratio (OR); 1.56 per SD (95 % CI 1.06-2.28) (SD 0.65)] with a similar trend for patients with unacceptable pain and low inflammation (OR 1.47 per SD; 95 % CI 0.98 – 2.21).

Conclusion: Almost 1/3 of early RA patients reported unacceptable pain one year after diagnosis, implying the need for improvement in pain treatment. Patients with high self-reported disability at baseline were at increased risk of unacceptable pain at 1 year. This could be due to ineffective coping strategies and inactivity. The association between female sex and persistent unacceptable pain could indicate sex differences in disease severity, or in propensity for chronic pain. Unacceptable pain 1 year after RA diagnosis was not associated with any objective baseline measures of disease activity, indicating the need to find other predictors for long time severity of pain.

References

1. Tubach et al. *Arthrits Care Res* 2012; 64: 1699-707.
2. Olofsson et al. *Arthritis Care Res.* Online First 20 May 2020. doi:100.1002/acr.242664.

Disclosure: A. Eberhard, None; **T. Olofsson**, Merck Sharp & Dohme, 9, Eli Lilly, 9; **S. Bergman**, None; **T. Mandl**, Novartis, 3; **C. Turesson**, Roche, 1, 2, Abbvie, 1, Pfizer, 1, Bristol-Myers Squibb, 1, 2.

Abstract Number: 1717

Impact of Treatments on Favorable Outcome over the First 10 Years of Disease in Early Rheumatoid Arthritis: Results from a WCE Model in the ESPOIR Cohort

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Long-term observational studies on the prediction of favorable outcome (FO) in rheumatoid arthritis (RA) have mostly considered patients baseline characteristics and have rarely evaluated the specific impact of treatments in real world settings.

The objective of this study was to assess the impact of treatments exposure on the 10-year FO in early rheumatoid arthritis (RA).

Exposure tested	Reference	OR (95%CI)
Treatments intakes during the last 120 months		
csDMARD & bDMARD for last 10 years	No treatment for last 10 years	1.10 (0.88-1.38)
Testing the interest of an early initiation of csDMARDs (not combined with bDMARD)		
csDMARD started at inclusion (month 0)	csDMARD after 3 months of follow-up	1.05 (1.03-1.07)
csDMARD started at inclusion (month 0)	csDMARD after 6 months of follow-up	1.19 (1.11-1.27)
csDMARD started at inclusion (month 0)	csDMARD after 12 months of follow-up	1.53 (1.29-1.83)
Testing the interest of an early initiation of bDMARDs (in association with csDMARD)		
bDMARD after 3 months of follow-up	csDMARD started at inclusion (month 0)	0.99 (0.82-1.20)
bDMARD after 6 months of follow-up	csDMARD started at inclusion (month 0)	0.99 (0.82-1.19)
bDMARD after 12 months of follow-up	csDMARD started at inclusion (month 0)	1.03 (0.86-1.23)
bDMARD after 24 months of follow-up	csDMARD started at inclusion (month 0)	1.16 (0.99-1.38)

Table 1. odd ratios for the association of patterns of drug regimen with 10-year favorable outcome

Methods: The 349 patients of the Etude et Suivi des Polyarthrites Indifférenciées Récentes (ESPOIR) cohort fulfilling ACR/EULAR 2010 criteria at baseline and having complete DAS28 and HAQ data at 10 years were considered in the present study. FO was defined at 10 years as DAS28 $\leq$ 2.6 and HAQ $\leq$ 0.5. Three RA treatments were considered: glucocorticoids (GC), conventional synthetic and biologic Disease-Modifying Anti-Rheumatic Drugs (csDMARDs and bDMARDs), which posologies were standardized by the mean of dose quotients (DoseQ). Drug exposure was modelled with Weighted Cumulative Exposure (WCE) variables [1], considering the intensity of drug exposure defined as a weighted function of past doses, and was incorporated into a logistic regression model that also included baseline clinical, biological and radiological characteristics. The predictive performance of this WCE model was compared to models considering on the one hand only baseline characteristics (BSL model) and on the other, baseline characteristics and binary treatments exposure - in other terms, “ever exposed, yes or no” (BIT model).

Results: Overall, FO at 10 years occurred in 158 (45.3%) patients. GC exposure was significantly associated with favorable outcome in univariate analysis only, and therefore was not included in the final WCE combined model.

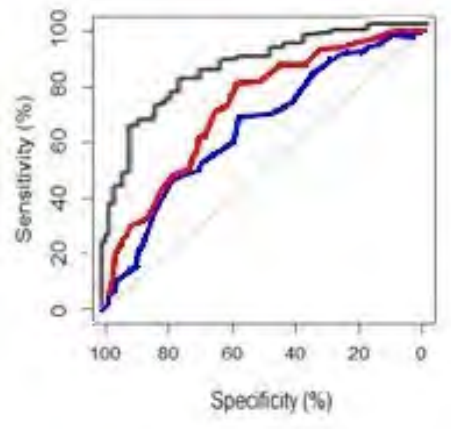

Figure 1. Receiver Operating Characteristic curves of BSL model (blue), BIT model (red) and WCE combined model (black) for 10-year favorable outcome

In the final WCE model, the joint exposure to 1 DoseQ of csDMARD and 1 DoseQ of bDMARD during the 10-year follow-up was not significantly associated with FO compared to patients receiving no treatment: OR=1.10 (95% CI: 0.88-1.38).

Early csDMARD initiation, i.e., as soon as the cohort inclusion, was significantly associated with the occurrence of FO at 10 years (Table 1).

Initiation of a bDMARD between the 3rd month and 2nd year of follow-up in combination with a csDMARD was not significantly better compared to early csDMARD initiation (Table 1).

The final WCE model was better at predicting FO at 10 years compared to the BSL and BIT models: AUC=0.85 (95% CI: 0.81-0.89), AUC=0.65 (95% CI: 0.60-0.71) and AUC=0.72 (95% CI: 0.66-0.79) respectively (Figure 1).

Conclusion: The early initiation of csDMARDs is associated with the occurrence of favorable outcome at 10 years in RA patients. This study confirms that initiating a csDMARD as 1st line treatment and keeping targeted DMARD as 2nd (or more) line is associated with favorable outcome at 10 years, with no loss of chance for the early RA patient.

[1] Dixon WG et al. Immediate and delayed impact of oral glucocorticoid therapy on risk of serious infection in older patients with rheumatoid arthritis: a nested case-control analysis. Ann Rheum Dis 2012;71(7):1128-33.

Disclosure: J. Kedra, None; **D. Hajage**, None; **A. Lafourcade**, None; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **M. Dougados**, Pfizer, 1, 2, Abbvie, 1, 2, UCB, 1, 2, Merck, 1, 2, Lilly, 1, 2, BMS, 1, 2, Roche, 1, 2, Novartis, 1, 2; **B. Fautrel**, MSD France, 1, 2, Abbvie, 1, 2, Pfizer, 1, 2, Biogen, 1, BMS, 1, Boehringer Ingelheim, 1, Celgene, 1, Janssen, 1, Lilly, 1, Medac, 1, Nordic Pharma, 1, Novartis, 1, Roche, 1, Sanofi-Aventis, 1, SOBI, 1, UCB Pharma, 1.

Abstract Number: 1718

Impact of Treatments on Radiographic Progression over the First 10 Years of Disease in Early Rheumatoid Arthritis: Results from the ESPOIR Cohort

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Exposure tested	Reference	OR (95%CI)
Treatments intakes during the last 120 months		
csDMARD & bDMARD for last 10 years	No treatment for last 10 years	0.04 (0.002-0.72)
Testing the interest of an early initiation of csDMARDs (not combined with bDMARD)		
csDMARD started at inclusion (month 0)	csDMARD after 3 months of follow-up	0.79 (0.65-0.96)
csDMARD started at inclusion (month 0)	csDMARD after 6 months of follow-up	0.41 (0.19-0.86)
csDMARD started at inclusion (month 0)	csDMARD after 12 months of follow-up	0.13 (0.02-0.80)
Testing the interest of an early initiation of bDMARDs (in association with csDMARD)		
bDMARD after 3 months of follow-up	csDMARD started at inclusion (month 0)	0.23 (0.05-1.16)
bDMARD after 6 months of follow-up	csDMARD started at inclusion (month 0)	0.23 (0.05-1.16)
bDMARD after 12 months of follow-up	csDMARD started at inclusion (month 0)	0.26 (0.06-1.10)
bDMARD after 24 months of follow-up	csDMARD started at inclusion (month 0)	0.24 (0.05-1.14)
bDMARD after 36 months of follow-up	csDMARD started at inclusion (month 0)	0.32 (0.09-1.16)

Table 1. Odd ratios for the association of patterns of drug regimen with 10-year radiographic progression

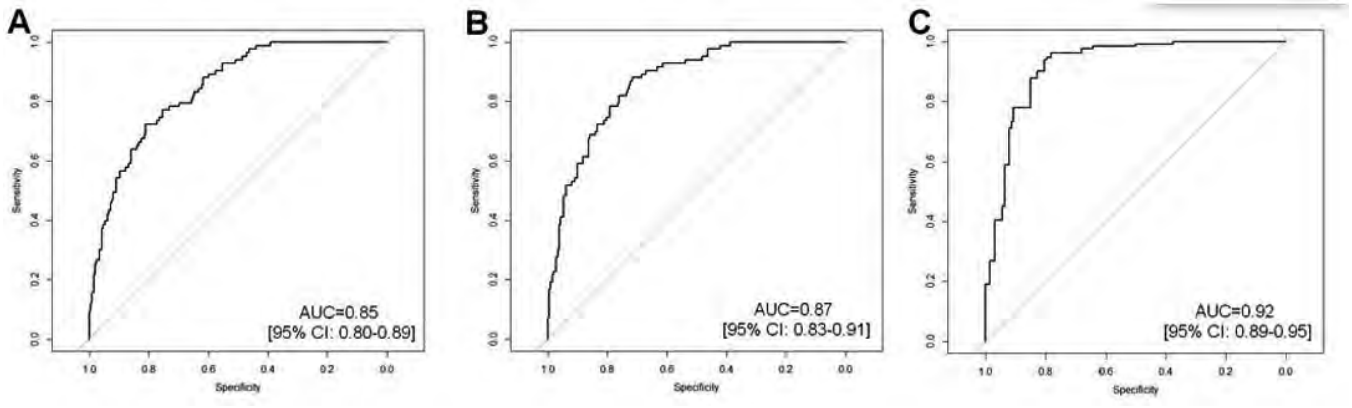

Figure 1. Receiver Operating Characteristic curves of BSL model (A), BIT model (B) and WCE combined model (C) for 10-year radiographic progression

Background/Purpose: Long-term observational studies on the prediction of structural damage progression (SDP) in rheumatoid arthritis (RA) have mostly considered patients baseline characteristics and have rarely evaluated the specific impact of treatments in real world settings.

The objective of this study was to assess the impact of treatment exposure on the 10-year radiographic progression in early rheumatoid arthritis (RA).

Methods: The 310 patients of the Etude et Suivi des Polyarthrites Indifférenciées Récentes (ESPOIR) cohort fulfilling ACR/EULAR 2010 criteria at baseline and having complete radiographic data at baseline and 10 years were considered in the present study. SDP was defined at 10 years as a significant increase of the Sharp/van der Heijde score, i.e., superior to the Smallest Detectable Change (SDC) of 11.5 at 10 years. Three RA treatments were considered: glucocorticoids (GC), conventional synthetic and biologic Disease-Modifying Anti-Rheumatic Drugs (csDMARDs and bDMARDs), which posologies were standardized by the mean of dose quotients (DoseQ). Drug exposure was modelled with Weighted Cumulative Exposure (WCE) variables [1], considering the intensity of drug exposure defined as a weighted function of past doses, and was incorporated into a logistic regression model that also included baseline clinical, biological and radiological characteristics. The predictive performance of this WCE model was compared to models considering on the one hand only baseline characteristics (BSL model) and on the other, baseline characteristics and binary treatments exposure - in other terms, “ever exposed, yes or no” (BIT model).

Results: Overall, SDP at 10 years occurred in 85 (27.4%) patients. In the final WCE model, the combined exposure to 1 DoseQ of csDMARD and 1 DoseQ of bDMARD during the 10-year follow-up was associated with a significant protective effect on SDP compared to patients receiving no treatment: OR=0.04 (95% CI: 0.002-0.72). Early csDMARD initiation, i.e., as soon as the cohort inclusion was associated with a significantly lower risk of SDP compared to later initiation (after month 3 or more) (Table 1).

Initiation of a bDMARD between the 3rd month and 3rd year of follow-up in combination with a csDMARD was not significantly superior to early csDMARD initiation (Table 1).

The final WCE model was better at predicting SDP at 10 years compared to the BSL and BIT models: AUC=0.92 (95% CI: 0.89-0.95), AUC=0.85 (95% CI: 0.80-0.89) and AUC=0.87 (95% CI: 0.83-0.91) respectively (Figure 1).

Of note, GC exposure was significantly associated with SDP only in the univariate analysis and did not remain significant when baseline characteristics are considered.

Conclusion: CsDMARDs and bDMARDs have a protective effect on radiographic progression at 10 years in RA patients. This effect is better captured by the WCE model compared to models with binary treatments exposure and should be more frequently used in further studies.

[1] Dixon WG, Abrahamowicz M, Beauchamp ME et al. Immediate and delayed impact of oral glucocorticoid therapy on risk of serious infectious in older patients with rheumatoid arthritis: a nested case-control analysis. Ann Rheum Dis 2012;71(7):1128-33.

Disclosure: J. Kedra, None; **D. Hajage**, None; **A. Lafourcade**, None; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **M. Dougados**, Pfizer, 1, 2, Abbvie, 1, 2, UCB, 1, 2, Merck, 1, 2, Lilly, 1, 2, BMS, 1, 2, Roche, 1, 2, Novartis, 1, 2; **B. Fautrel**, MSD France, 1, 2, Abbvie, 1, 2, Pfizer, 1, 2, Biogen, 1, BMS, 1, Boehringer Ingelheim, 1, Celgene, 1, Janssen, 1, Lilly, 1, Medac, 1, Nordic Pharma, 1, Novartis, 1, Roche, 1, Sanofi-Aventis, 1, SOBI, 1, UCB Pharma, 1.

Abstract Number: 1719

Prevalence and Trajectory of Erosions, Synovitis, and Bone Marrow Edema in Feet of Patients with Early Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Imaging studies have shown that erosions emerge early in RA and is associated with worsening pain and function. Despite erosions being just as prevalent in feet as in hands in patients with RA, their development in relation to synovitis and bone marrow edema (BME) have mainly been studied in the hands. This study examines the prevalence and longitudinal trajectory of erosions, BME, and synovitis in metatarsophalangeal joints (MTPJs) in patients with early RA over 2 years of treatment. We also describe correlations between changes in erosions, synovitis, and BME at the joint level.

Methods: Treatment naïve patients with early RA (symptom duration < 2 years) were recruited from an academic rheumatology clinic. MRI of the most symptomatic forefoot was acquired at baseline, year 1 and ≥2 years using a 1.0T peripheral scanner (GE Medical). Metatarsophalangeal joints 2-5 were semi-quantitatively graded by a MSK radiologist for erosions (0-10), synovitis (0-3) and BME (0-3) according to OMERACT guidelines. Synovitis was graded per joint, while erosions and BME were graded for the metatarsal head and phalangeal base individually so the maximum scores per MTPJ were 20 for erosions and 6 for BME. The MSK radiologist was blinded to clinical assessments and previous imaging. Patients were treated per standard of care. Descriptive statistics characterized the study population. Paired t-tests were performed for changes in erosions, synovitis, and BME over time. Correlations between changes in erosions, synovitis, and BME were conducted per joint using Pearson's correlation coefficient.

Results: 32 patients with early RA were included. 87.5% of patients were female and the average age was 51.7 (SD=10.4). At baseline, 29 patients (90.6%) had at least one grade ≥1 erosion, 21 (65.6%) had at least one MTPJ with grade ≥1 synovitis, and 19 (61.3%) had at least one joint with grade ≥1 BME. The proportion of MTPJs with ero-

Table 1. Proportion of joints with erosions, synovitis, and BME over time

	MTPJs visualized for erosions	Joints with erosions (%)	MTPJs visualized for synovitis	Joints with synovitis (%)	Joints visualized for BME	Joints with BME (%)
MTPJ2						
BL	30	23 (76.7%)	32	17 (53.1%)	31	14 (45.2%)
1Y	29	25 (86.2%)	31	18 (58.1%)	31	3 (9.7%)
2y	29	23 (79.3%)	32	14 (43.8%)	28	3 (10.7%)
MTPJ3						
BL	30	21 (70%)	32	15 (46.9%)	31	13 (41.9%)
1Y	31	25 (80.6%)	32	17 (53.1%)	32	4 (12.5%)
2Y	29	23 (79.3%)	32	14 (43.8%)	28	5 (17.9%)
MTPJ4						
BL	30	18 (60.0%)	32	11 (34.4%)	31	10 (32.3%)
1Y	30	13 (43.3%)	31	12 (38.7%)	32	3 (9.4%)
2Y	29	13 (44.8%)	31	8 (25.8%)	28	4 (14.3%)
MTPJ5						
BL	27	9 (33.3%)	32	4 (12.5%)	29	3 (10.3%)
1Y	29	6 (20.7%)	32	9 (28.1%)	31	4 (12.9%)
2Y	22	6 (27.3%)	28	6 (21.4%)	22	3 (13.6%)

BL: baseline; 1Y: 1-year; 2Y: 2+-years; BME: bone marrow edema; MTPJ: metatarsophalangeal joint

Table 1. Proportion of joints with erosions, synovitis, and BME over time

sions, synovitis, and BME are shown in Table 1. Overall changes in erosions, synovitis, and BME are shown in Figure 1. Erosions overall did not significantly change over time. Significant reductions in overall synovitis scores, MTPJ2, and MTPJ3 synovitis scores were seen between year 1 and ≥2 years. Overall BME scores improved in year 1 and were sustained at ≥2 years. BME improved in MTPJ2, MTPJ3, and MTPJ4. Positive correlations were seen between changes in synovitis and BME in MTPJ2 and MTPJ5.

Conclusion: In patients with early RA, standard of care saw overall reductions in synovitis by year 2, BME by year 1, and no progression in overall erosion scores on MRI. MTPJ2 and MTPJ3 appeared to be the most active joints. Overall improvements in synovitis is attributed to MTPJ2 and MTPJ3, while other MTPJs did not progress. Over all reductions in BME is attributed to MTPJ2, MTPJ3, and MTPJ4, while other MTPJs did not progress.

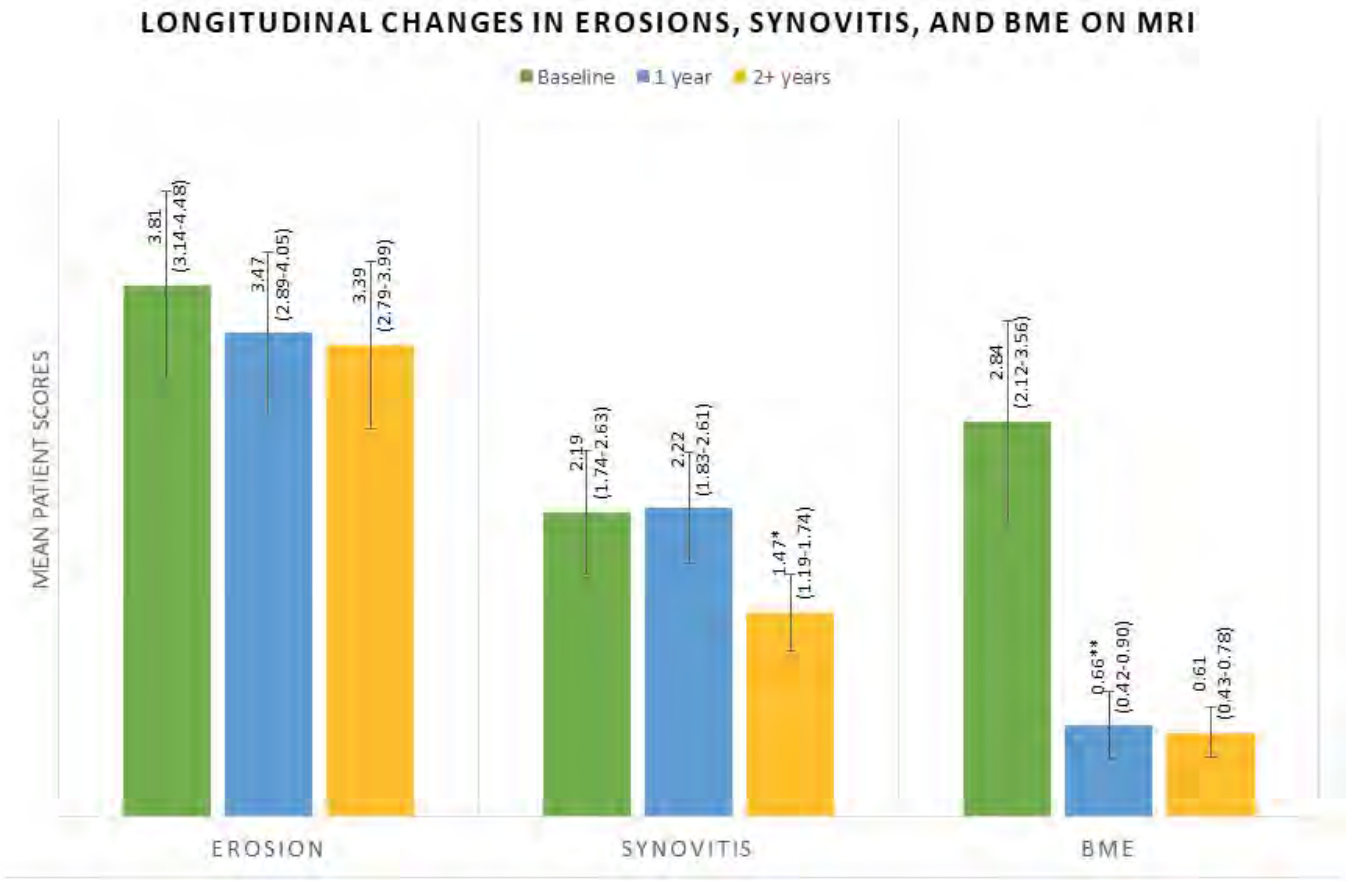

Figure 1. Longitudinal changes in overall erosions, synovitis, and BME

Disclosure: Z. Ma, None; **H. Zou**, None; **M. Yelovich**, None; **S. Totterman**, None; **K. Beattie**, None; **M. Larche**, AbbVie, 5, Amgen, 5, Boehringer-Ingelheim, 5, BMS, 5, Celgene, 5, Janssen, 5, Mallinckrodt, 5, Novartis, 5, Pfizer, 5, Roche, 5, Sandoz, 5, UCB, 5.

Abstract Number: 1720

Factors Associated with an Increased Risk of Imminent Rheumatoid Arthritis in ACPA+ Individuals

Hyoun-Ah Kim[1], Ryan Peterson[2], Gary Firestein[3], David Boyle[4], Jane Buckner[5], Sylvia Posso[6], Eddie James[5], William Robinson[7], Jaron Arbet[2], LauraKay Moss[8], Roger Gilmore[8], Lindsay Hartje[8], Saman Barzideh[8], Jennifer Seifert[9], Navin Rao[10], Frédéric Baribaud[11], Sunil Nagpal[12], Alyssa Johnson[13], V Michael Holers[14] and Kevin D. Deane[15], [1]University of Colorado Anschutz Medical Campus and Ajou University School of Medicine, Aurora, CO, [2]Department of Biostatistics and Informatics, Colorado School of Public Health, Aurora, CO, [3]University of California, San Diego, La Jolla, CA, [4]UC San Diego, San Diego, CA, [5]Center for Translational Immunology, Benaroya Research Institute at Virginia Mason, Seattle, WA, [6]Benaroya Research Institute at Virginia Mason, Seattle, WA, [7]Stanford University, Palo Alto, CA, [8]University of Colorado Anschutz Medical Campus, Aurora, CO, [9]Division of Rheumatology, University of Colorado School of Medicine, Anschutz Medical Campus, Aurora, CO, USA, Littleton, CO, [10]Janssen R&D, Spring House, PA, [11]Janssen Research & Development, LLC, Spring House, PA, [12]Janssen Reserach and Development, Spring House, PA, [13]Janssen Research and Development, Spring House, PA, [14]Division of Rheumatology, University of Colorado School of Medicine, Anschutz Medical Campus, Aurora, CO, USA, Colorado, [15]2 Division of Rheumatology, University of Colorado School of Medicine, Anschutz Medical Campus, Aurora, CO, USA, Colorado

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Individuals at high-risk for future rheumatoid arthritis (RA) may be identified by screening for circulating RA-related autoantibodies including antibodies to citrullinated protein antigens (ACPA). The purpose of this study was to evaluate a new cohort of ACPA+ individuals to identify factors associated with progression to and timing of inflammatory arthritis (IA) onset in order to develop prediction models and to identify factors that may be target candidates for prevention.

Table 1. Baseline characteristics of enrolled population			
	Anti-CCP3 negative	Anti-CCP3 positive	p-value
n	156	86	
Age	57.8 ± 12.2	57.6 ± 12.4	0.914
Female	105 (67.3)	59 (68.6)	1.000
Non-Hispanic white	124 (79.5)	69 (80.2)	1.000
BMI	26.8 ± 5.7	27.7 ± 5.2	0.208
Ever smoker	50 (32.1)	28 (32.9)	0.886
Current smoker	3 (1.9)	5 (5.9)	0.134
Ever alcohol history	142 (91.0)	76 (89.4)	0.655
Any alcohol intake past a year	112 (71.8)	59 (69.4)	0.767
Total serving alcohol amount	20.24 ± 28.95	23.96 ± 58.99	0.516
>=1 allele with SE	74 (47.4)	44 (51.2)	0.594
Positivity of anti-CCP3	0 (0)	86 (100)	<0.001
Positivity of RFIgA	4 (2.6)	12 (14.0)	0.002
Positivity of RFIgG	13 (8.3)	19 (22.1)	0.005
Positivity of RFIgM	19 (12.2)	22 (25.6)	0.012
Positivity of RFIgA, G and M	0 (0)	8 (9.3)	<0.001
CRP level	2.76 ± 3.27	2.68 ± 2.83	0.847
These data are presented with n (%) or mean ± SD and are analyzed with independent t-test or Chi-square test. Abbreviations: BMI=body mass index; CCP3=cyclic citrullinated peptide-3; RF=rheumatoid factor; Ig=immunoglobulin; CRP=C-reactive protein			

Table 1. Baseline characteristics of enrolled population

Table 2. Unadjusted hazard ratios (HR) for each risk factor treating time-to-RA as the outcome*			
Risk factors	HR	95% CI	p-value
Age (decade)	1.05	0.71, 1.57	0.80
Gender (male)	0.87	0.31, 2.5	0.80
BMI	1.12	1.02, 1.2	0.020
Current smoker	1.35	0.18, 10.31	0.77
Any alcohol intake in past year	0.22	0.08, 0.60	0.005
Total servings of alcohol per month	0.94	0.88, 1.00	0.040
One or more alleles containing the shared epitope	3.14	1.01, 9.75	0.048
CRP level (z-score)	1.03	0.62, 1.72	0.90
Anti-CCP3 level (z-score)	1.50	1.00, 2.24	0.050
Number of RF isotypes positive (IgA, IgG, or IgM)	1.91	1.30, 2.82	<0.001
RFIgA, IgG and IgM positive	7.82	2.80, 21.85	<0.001
*These data were analyzed with univariate Cox regression models. Abbreviations: BMI, body mass index; CCP3, cyclic citrullinated protein 3; RF, rheumatoid factor; IgA, immunoglobulin A; CRP, C-reactive protein.			

Table 2. Unadjusted hazard ratios (HR) for each risk factor treating time-to-RA as the outcome

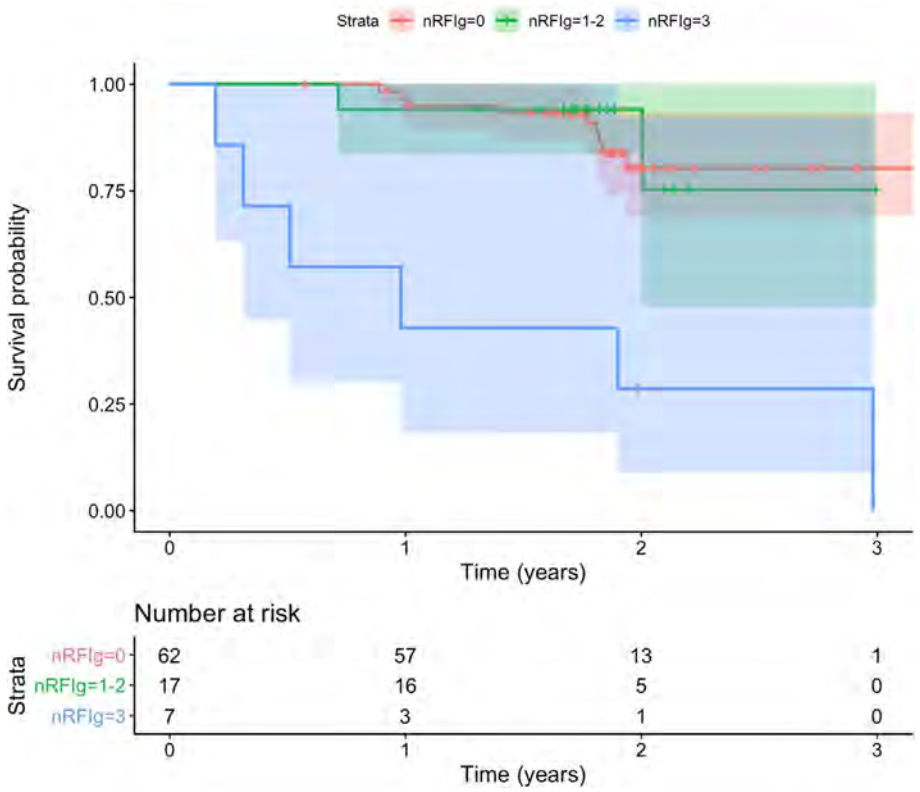

Figure 1. RA-free survival stratified by baseline RF Ig status. Note, nRFIg=0 (red line) if neither IgM, IgA, nor IgG were positive, RFIg=1-2 (green line) if any 1 or two of RF isotypes were positive, and RFIg = 3 (blue line) if all three RF isotypes were positive.

Methods: ACPA- healthy controls (n=156) and ACPA+ subjects without IA at baseline (n=86) were enrolled in the Targeting Immune Responses for Prevention of Rheumatoid Arthritis (TIP-RA) study. Subjects were identified through clinics, and screening of relatives of patients with RA, and health-fairs. Clinical characteristics and laboratory results were obtained every year for up to 3 years' follow-up. ACPA was evaluated by anti-CCP3 (IgG, Inova) and rheumatoid factor (RF) by ELISA for IgA, IgG and IgM isotypes (Inova). Other biomarkers included assessment of C-reactive protein and the shared epitope (SE). Baseline clinical and biomarker characteristics were compared between ACPA-positive individuals who developed RA and those who did not. In addition, univariate Cox regression analyses were used to estimate hazard ratios (HRs) for each risk factor of RA development.

Results: Characteristics of the ACPA- and ACPA+ subjects are presented in Table 1. Among the 86 ACPA+ subjects, 18 (20.9%) developed RA after a mean of 470 days from baseline, with 15/18 (83.3%) meeting ACR/EULAR classification criteria at the time of presentation of IA. Within the ACPA+ subjects, a higher BMI was associated with an increased risk for developing IA/RA (Table 2); in contrast, any alcohol intake in the past year was associated with decreased risk of IA/RA. Past or current smoking was not associated with increased risk for IA/RA, although rates of smoking were low. The presence of one or more alleles containing the SE was also associated with increased risk of incident IA/RA. Furthermore, within the ACPA+ subjects, for every additional RF isotype that was positive, the risk for incident IA/RA increased by 91%. In particular, baseline positivity of RFIgA, IgG and IgM was associated with the highest risk of development of IA/RA (Table 2 and Figure 1).

Conclusion: The findings of an increased risk of incident IA/RA in ACPA+ subjects associated with higher BMI and lower risk associated with alcohol intake replicate findings from other studies (de Hair 2012; Scott 2013). Moreover, these findings suggest that BMI and alcohol are mechanistically related to biologic pathways in propagation from autoimmunity to clinically-apparent IA/RA; these findings also support that modification of these factors may be con-

sidered in RA prevention (Zacchardeli 2019). In addition, the increased risk of incident IA/RA with SE and RF isotype positivity, respectively, suggests these markers can be used to improve prediction of the imminent onset of RA; these latter findings also highlight the importance of the SE and RFs in the pathophysiology of RA development and especially in the transition from Pre-RA to clinically-apparent disease.

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Abstract Number: 1721

Increasing Autoantibody Positivity During Pre-RA Is Associated with the Imminent Development of Classifiable RA

Heinrich-Karl Greenblatt[1], Ted Mikuls[2], Jess Edison[3], Marie Feser[4], Mark Parish[5], LauraKay Moss[5], Elizabeth Mewshaw[6] and Kevin D. Deane[7], [1]University of Colorado School of Medicine, Aurora, CO, [2]University of Nebraska Medical Center, Omaha, NE, [3]Walter Reed National Military Medical Center, Bethesda, [4]Division of Rheumatology, University of Colorado School of Medicine, Anschutz Medical Campus, Aurora, CO, USA, Colorado, [5]University of Colorado Anschutz Medical Campus, Aurora, CO, [6]Walter Reed National Military Medical Center, Bethesda, MD, [7]2 Division of Rheumatology, University of Colorado School of Medicine, Anschutz Medical Campus, Aurora, CO, USA, Colorado

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Autoantibodies including rheumatoid factor (RF) and antibodies to citrullinated protein antigens (ACPA) may be elevated during a period that can be termed 'Pre-RA'. In addition, there are findings supporting that there is an expansion of autoimmunity in Pre-RA; however, this has typically been demonstrated using research grade assays and therefore the increasing positivity of commercially available ACPA and RF is less well known. As such, the purpose of this study was to evaluate how an increasing number of commercially-available autoantibodies testing during Pre-RA relates to the development of imminent RA.

Methods: Two-hundred and fifteen RA cases, each with approximately 3 pre- and 1 post-RA serum samples, were identified from the Department of Defense Serum Repository. All case samples were tested by ELISA for anti-CCP2 (IgG, Axis-Shield), CCP3 (IgG, Inova), RF-IgM, A and G (Inova). Manufacturer suggested cut-offs were used for the CCP assays, and a level present in < 2% of 156 controls was used for the RF's. Comparison of autoantibody prevalence within a time point was performed using chi-squared and Fisher's exact testing. Analyses of autoantibody positivity over time within cases as individual biomarkers or as an overall count were performed using analyses that account for repeated measures within subjects (e.g. ANOVA).

Results: Characteristics of the 215 cases are reported in **Table 1**, and the positive rates of all autoantibodies as individual tests and counts are presented in **Table 2**. The prevalence of all antibodies increased from the earlier pre-RA time point (a mean of 11.6 years prior to RA diagnosis) to immediately pre-RA diagnosis (a mean of 0.9 years prior to RA diagnosis) although there was no significant increase in positive rates of any of these autoantibodies when comparing the immediate pre- and post-RA diagnosis samples. There were no significant differences in rates of positivity

Table 1. Characteristics of the 215 subjects who developed rheumatoid arthritis	
n	215
Female (%)	48.0
Age at diagnosis of RA (or sample testing), mean (SD)*	37.0 (7.9)
Non-Hispanic White (%)	58
Ever smoker (%)	32

Table 1. Characteristics of the 215 subjects who developed rheumatoid arthritis

Table 2. Autoantibody prevalence and counts over time pre- and post-RA diagnosis in 215 RA cases					
	Earliest Pre-RA Sample	Intermediate Pre-RA Sample	Immediate Pre-RA Sample	Post-RA Sample	p-value*
Mean time (years) pre- or post-RA diagnosis	-11.5 (5.2)	-2.7 (1.5)	-0.9 (0.8)	1.3 (0.9)	n/a
CCP2	18.6	53.3	71.4	71.5	<0.001
CCP3	22.3	59.3	73.7	75.2	<0.001
RFIgM	8.8	35.0	52.6	52.3	<0.001
RFIgG	4.2	13.1	18.8	16.4	<0.001
RFIgA	7.4	28.0	40.4	40.2	<0.001
Overall count of number of positive autoantibodies, mean (SD)	0.61 (1.15)	1.89 (1.71)	2.57 (1.70)	2.56 (1.61)	<0.001
*This p-value is for the comparison of the rates of positivity of each autoantibody or autoantibody counts over time and uses models that account for repeated samples. **at all time points, the prevalence of positivity of CCP2 and CCP3 was significantly higher ($p<0.05$) when compared to any RF.					

Table 2. Autoantibody prevalence and counts over time pre- and post-RA diagnosis in 215 RA cases

at any time period between CCP2 and CCP3 although CCP3 had a slightly higher prevalence of positivity at earlier time points. At all times points, both CCP2 and CCP3 were positive in a greater number of subjects than any of the RF isotypes. The number of positive autoantibodies also increased over time, with the highest mean count of autoantibodies of 2.57 at the immediate pre-RA diagnosis period.

Conclusion: In these subjects CCP2 and CCP3 perform in a similar manner, although both are present in a higher number of subjects in the earlier time periods than RF. In addition, higher mean counts of antibodies are present in the immediate pre-RA period. These findings suggest that there is an expansion of autoantibody positivity across ACPA and RF assays. Furthermore, testing for these widely-available assays and identifying a high number of positives may be useful to identify subjects in Pre-RA who may imminently transition to clinically-apparent and classifiable RA

Disclosure: H. Greenblatt, None; **T. Mikuls**, Horizon Therapeutics, 2; **J. Edison**, Department of Defense, 9; **M. Fesser**, None; **M. Parish**, None; **L. Moss**, None; **E. Mewshaw**, None; **K. D. Deane**, None.

Abstract Number: 1722

Predicting Rheumatoid Arthritis Using the Symptoms in Persons at Risk of Rheumatoid Arthritis (SPARRA) Questionnaire

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Accurate prediction of rheumatoid arthritis (RA) development in persons at risk can help to select individuals for early intervention trials. At-risk individuals exhibit a high prevalence of diverse symptoms [1,2] and information on the predictive ability of symptoms or symptom complexes is still largely lacking. We investigated if symptoms could predict RA development in persons at risk, using the validated 'Symptoms in Persons At Risk of Rheumatoid Arthritis' (SPARRA) questionnaire.

Methods: Individuals at-risk of RA from four different cohorts from the Netherlands (n=122), United Kingdom (n=77), Sweden (n=13) and Switzerland (n=20), were asked to complete the SPARRA questionnaire, consisting of 69 questions (previously described [3]). Individuals were persons with anticitrullinated protein antibodies (ACPA) and/or rheumatoid factor (RF; n=135), having relevant symptoms (arthralgia suspicious for progression to RA) with or without RA-specific antibodies, (n=77) or first degree relatives (FDR, n=20) of RA patients. Follow up was ≥ 24 months or until clinical arthritis development. Univariable analyses preselecting possible predictors (Cox regression, $p < 0.2$) was followed by stepwise forward selection ($p < 0.1$) to create a multivariable prediction model. To test the added value of the SPARRA items over the clinical prediction model by van de Stadt et al [4], the likelihood ratio (LR) test was used to compare the van de Stadt model with and without SPARRA items

Results: The mean age of all participants was 51 years, 69% was female. In total, 58 persons (25%) developed clinical arthritis (n=23, 26, 7, 2 respectively in the 4 groups) after a median of 7 months (IQR 5.3 – 17.8). In total, 22 SPARRA questions were preselected and entered in the stepwise forward selection procedure. The symptoms that predicted time to development of arthritis are shown in table 1. The symptom 'pain that moves from one side to the other' showed added value to the van de Stadt model in predicting arthritis (LR test $p = 0.012$, AUC 0.73 (extended model) versus AUC 0.71 (van de Stadt model)).

Conclusion: Specific symptom details such as pattern of pain or degree of joint swelling can provide useful additional information to estimate a person's RA risk. Our next steps are 1) to develop a new prediction model using both SPARRA data and clinical data and distinguishing between seropositive and seronegative individuals and 2) to create a shortened version of the SPARRA questionnaire to be used in prospective at-risk cohorts to enable homogenous symptom data collection. This will further improve our understanding of the prevalence and predictive ability of greatly diverse symptoms in different at-risk populations.

	B	HR (95% CI)	p
Does your joint pain move from joint to joint?			
Nonmoving, from arms to legs, from legs to arms (ref)	1	1	
From one side to the other	0,98	2,66 (1.47-4.84)	0.001
Over the past month how many days of the month have you had fatigue?			
0 (ref)	1	1	
1 to 5 days	-0.79	0.46 (0.19-1.08)	0.073
6 to 15 days	-0.98	0,38 (0.16-0.91)	0.029
16 to 30 days	-0.98	0.38 (0.19-0.80)	0.010
Over the past month how much joint swelling have you had?			
None or mild (ref)	1	1	
Moderate or severe	1,07	2,92 (1,52-5.62)	0.001

Table 1 Multivariable prediction model of SPARRA questions to predict clinical arthritis

1. Smolik I et al. J Rheumatol. 2013;40(6):818-24.

2. Stack RJ et al. Arthritis Care Res (Hoboken). 2013;65(12):1916-26.

3. van Beers-Tas MH et al. RMD Open. 2018;4(1):e000641.

4. van de Stadt LA et al. Ann Rheum Dis. 2013;72(12):1920-6.

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Abstract Number: 1723

RA Flare Prediction via Machine Learning and Algorithm Based on SSDM Big Data

Yan Zhao[1], Rong Mu[2], Xiaomei Li[3], Hongsheng Sun[4], Cundong Mi[5], Guosheng Wang[3], Shengqian Xu[6], Minghua Xu[7], Haiying Chen[8], Qingchun Huang[9], Ling Lei[10], HaiLi Shen[11], Hui Xiao[12], Yuhua Jia[13], Bing Wu[13], Xin Chen[12], Shengsong Jia[12] and Fei Xiao[13], [1]Peking Union Medical College hospital, Beijing, Beijing, China (People's Republic), [2]People's Hospital, Beijing University Medical School, Beijing, Beijing, China (People's Republic), [3]the First Affiliated Hospital of University of Science and Technology of China, Hefei, Anhui, China (People's Republic), [4]Shandong Provincial Hospital Affiliated to Shandong University, Jinan, Shandong, China (People's Republic), [5]The Second Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi, China (People's Republic), [6]the First Affiliated Hospital of Anhui Medical University, Hefei, Anhui, China (People's Republic), [7]Affiliated Hospital of Hebei University, Baoding, Hebei, China (People's Republic), [8]The Third Affiliated Hospital of Hebei Medical University, Shijiazhuang, Hebei, China (People's Republic), [9]Guangdong Provincial Hospital of Chinese Medicine, Guangzhou, Guangdong, China (People's Republic), [10]The First Affiliated Hospital of Guangxi Medical University, Nanning, Guangxi, China (People's Republic), [11]Second Hospital of Lanzhou University, Lanzhou, Gansu, China (People's Republic), [12]Shanghai Gothic Internet Technology Co., Ltd., Shanghai, Shanghai, China (People's Republic), [13]Shanghai Gothic Internet Technology Co., Ltd., Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

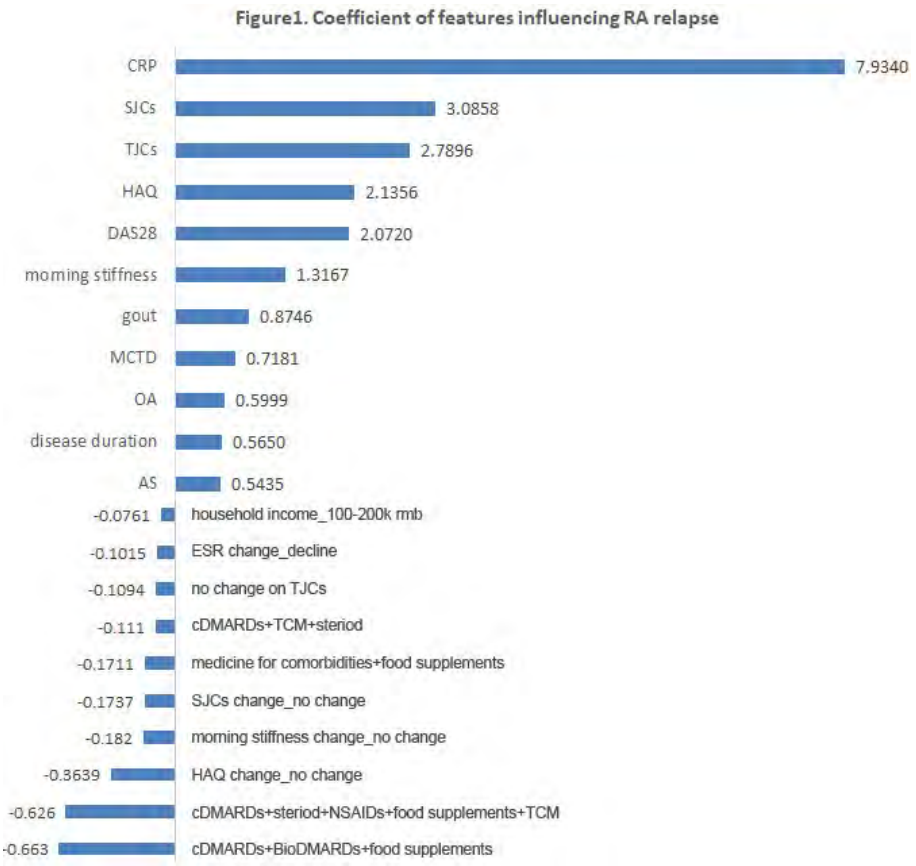

Figure 1. Coefficient of features influencing RA relapse.

Background/Purpose: Flare, relapse from status of treat-to-target (T2T, DAS28< =3.2), is hard predicted. We try to make it predictable by applying machine learning to a database from smart system of disease management (SSDM). SSDM is an interactive mobile disease management APPs. The aim of this study is to develop and validate machine learning algorithms for flare prediction in RA.

Methods: Patients were trained using SSDM and input their data, including demographic, comorbidities (COMBs), lab test, medications and monthly self-assessments, including DAS28, HAQ, SF-36, Hospital Anxiety and Depression Scale (HADS). The data was uploaded to cloud and synchronized to the mobile of authorized rheumatologists. The COMBs were by ICD-9, and medications were listed as cDMARDs, Bio (BioDMARDs), NSAIDs, Steroid, FS (food supplements), MC (medicine for COMBs), TCM (Traditional Chinese Medicine), and combinations.

Results: From Jan of 2015 to Jan of 2020, 8811 RA patients, 85% female and 15% male, used to reach T2T. 4556 were flare-free and 4255 suffering at least one flare. The average 160 attributes were extracted from each flare-free patient at time of reaching T2T, and each flare patients at time of 3 months before the flare. Patients were randomly assigned as model setup (training) group (70%) and validation (testing) group30%.

For training, data were processed using Python with statistical analyses in R. In R, random forests were implemented. Logistic regression via glm in base R. The random forest comprises a set of decision trees. “Splits” in the decision trees reflect binary (i.e., yes/no) respect to attributors. Bootstrapping was used to assess, quantify, and adjust for model optimism. Model performance was evaluated using AUC, precision and recall metrics. Brier scores for accuracy of probabilistic predictions ranged from 0 to 1 (0 is perfect discrimination).

The testing showed model performance for prediction windows are 0.78 for AUC (95% CI), 0.71 for Recall (sensitivity), 0.195 for Brier score, and 0.68 for precision (true positive 893, false positive 417, false negative 367, true negative 966).

Based on weighing in the random forest, the top 10 pro-flare attributes were CRP, swollen joint count (SJC), tender joint count (TJC), HAQ, DAS28, morning stiffness, gout, MCTD, OA, duration; while top 10 anti-flare attributes were cDMARDs+Bio, cDMARDs+steroid+NSAIDs, stable on HAQ, on morning stiffness, on SJC, medicine on COMBs, cDMARDs+TCM, stable on TJC, on ESR, income at 100-200k (Fig.1). The top weighing COMBs for pro-flaring were gout (0.81), MRD (0.75), OA (0.56), AS (0.48). The monotherapies with either Bio or NSAIDs, or steroid, or TCM was pro-flare; while with cDMARDs was anti-flare (-0.21).

Conclusion: The attempt to develop a machine learning algorithm for RA flare prediction is successful. The discrimination was acceptable. The attributes of both pro-flare and anti-flare are identified, which may inspire the proactive intervention.

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Abstract Number: 1724

A Feasible and Efficient Approach to Implementing Rheumatoid Arthritis Disease Activity Measure in a Busy Rheumatology Clinic: A Quality Improvement Project

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The treatment of Rheumatoid Arthritis (RA) has witnessed a substantial change over last the 20 years, with disease remission becoming an achievable goal. Treat-to-target philosophy, which shows improvement in outcome, is the recommended approach to managing RA. This includes regular evaluation of the disease activity and adjusting patient's therapy as necessary to achieve the target of remission or low disease activity. The American College of Rheumatology recommends five tools for the measurement of disease activity in RA. Patient Activity Score II (PAS II) is one of these validated tools that quantify disease activity using patient-reported outcomes (PROs). Using these tools consistently can help guide therapy plans to achieve treat-to-target approach. We aim to enhance the use of PAS II in a busy rheumatology clinic using animation video and infographics.

Methods: The project was conducted over a 10-month period and was divided into two months pre-intervention period and eight months intervention period. Pre-intervention data about the use of any disease activity measure scale for all RA patients who were seen in the rheumatology clinic were collected. The intervention included distributing infographics (figure 1) and an animation video (see the link below) that explains the project to our rheumatology clinic

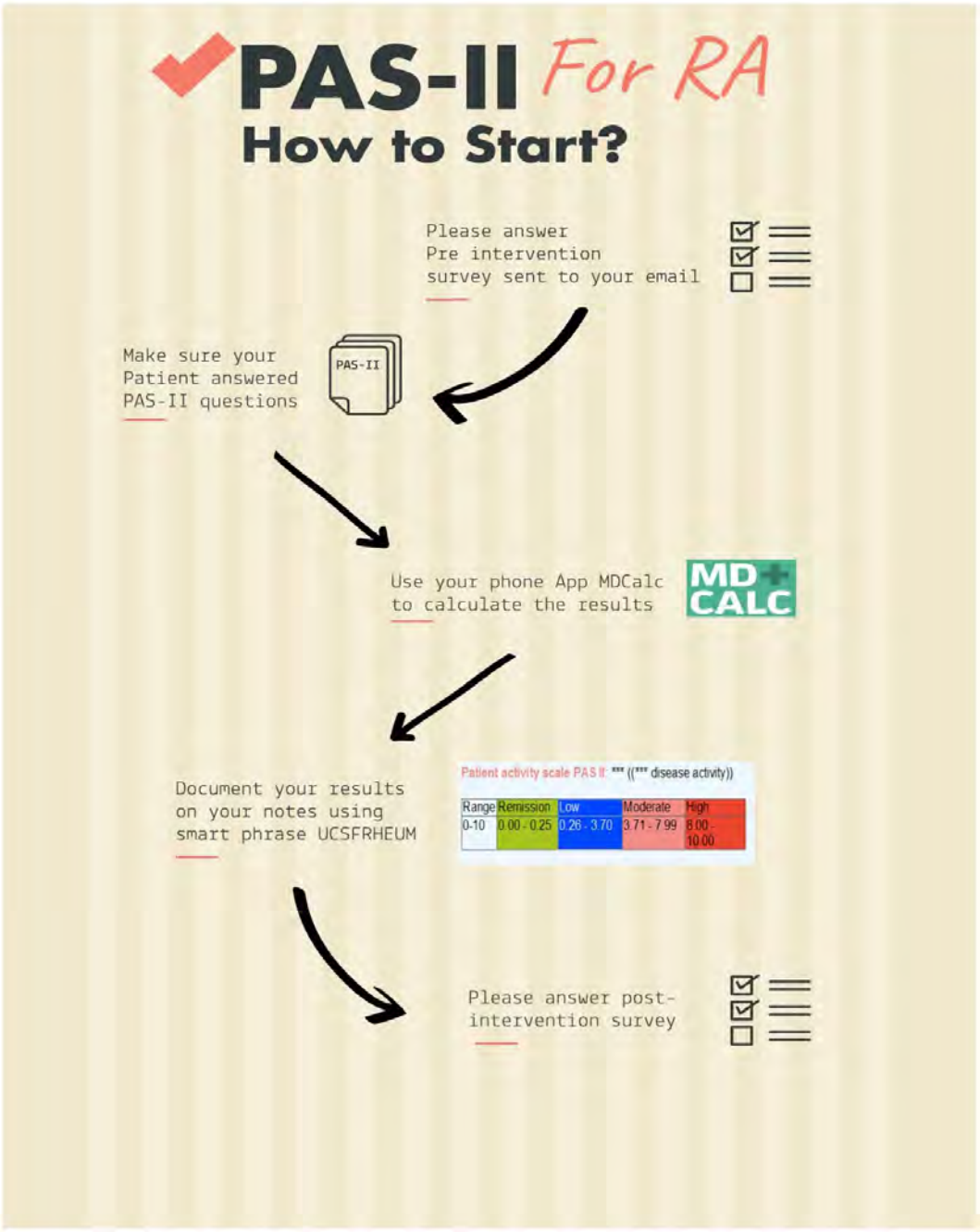
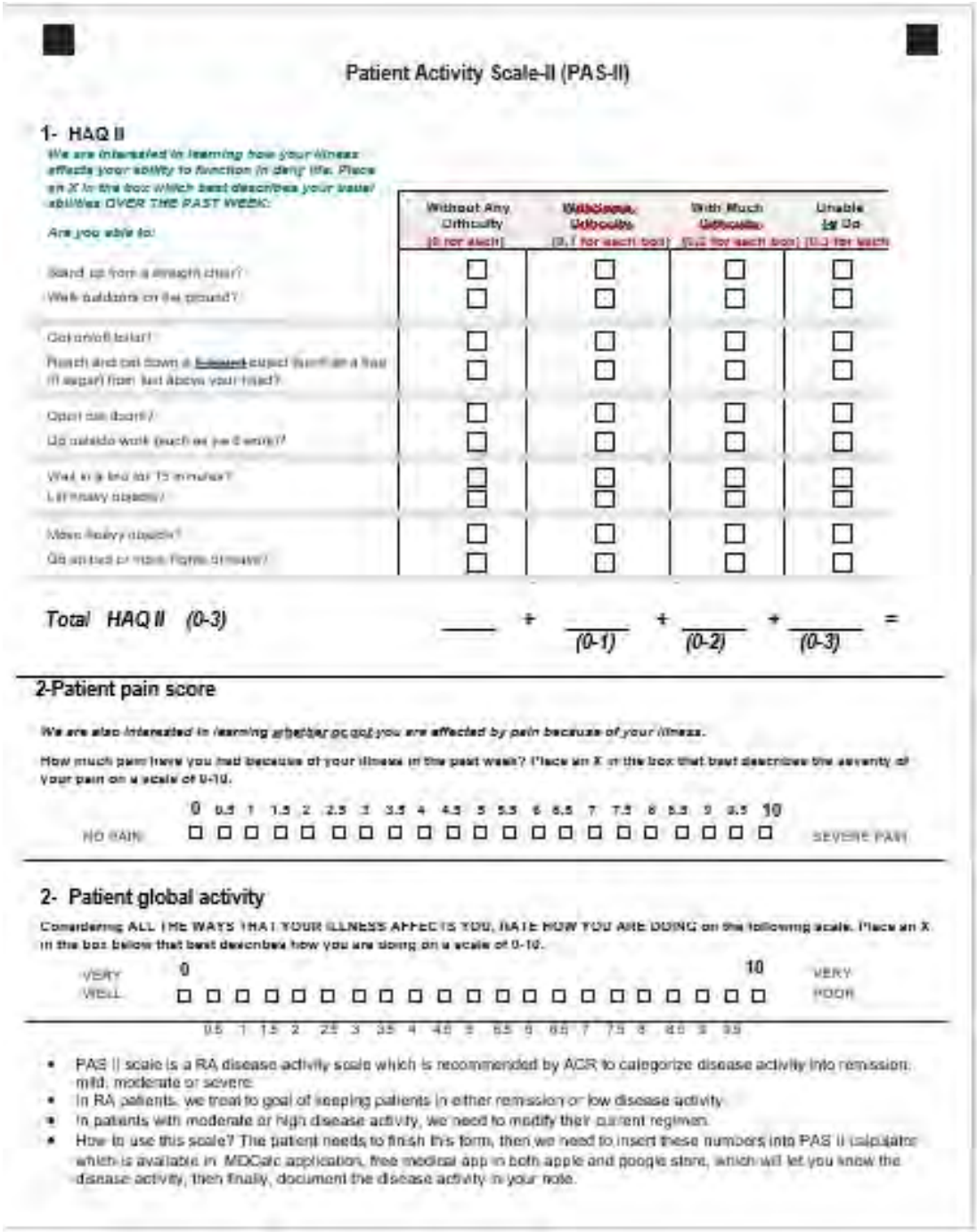


Figure 1. Workflow infographic

providers. These were sent through emails and provided on-site our rheumatology clinic providers. The clinic staff received a brief session about the workflow process. PAS II questionnaire (figure 2) was distributed to all RA patients who have confirmed RA diagnosis to complete at the time of check-in. MDCalc (A free medical mobile application) was used by providers to calculate the PAS II score and insert the results in the visit note. The intervention period data about the use of PAS II was collected and compared with the pre-intervention data.

Results: Pre-intervention data showed that 4% (1/24) of RA patients had a documented disease activity measure in their charts. Intervention period data showed that 106 RA patients were seen in our clinic and 76% (81/106) had a documented PAS II scale in their charts. Most of them were seropositive 88%. In terms of disease activity, 56% had



Patient Activity Scale-II (PAS-II)

1- HAQ II

We are interested in learning how your illness affects your ability to function in daily life. Place an X in the box which best describes your usual abilities OVER THE PAST WEEK:

Are you able to:

	Without Any Difficulty (0 for each)	With Some Difficulty (0.7 for each box)	With Much Difficulty (1.3 for each box)	Unable to Do (1.3 for each)
Stand up from a straight chair?	☐	☐	☐	☐
Walk outdoors on flat ground?	☐	☐	☐	☐
Get on/off toilet?	☐	☐	☐	☐
Reach and get down a 5-pound object (such as a bag of sugar) from just above your head?	☐	☐	☐	☐
Open car doors?	☐	☐	☐	☐
Do outside work (such as yard work)?	☐	☐	☐	☐
Walk in a line for 15 minutes?	☐	☐	☐	☐
Lift heavy objects?	☐	☐	☐	☐
Move heavy objects?	☐	☐	☐	☐
Do sports or more rigorous activities?	☐	☐	☐	☐

Total HAQ II (0-3) ____ + ____ (0-1) + ____ (0-2) + ____ (0-3) =

2-Patient pain score

We are also interested in learning whether or not you are affected by pain because of your illness.

How much pain have you had because of your illness in the past week? Place an X on the box that best describes the severity of your pain on a scale of 0-10.

0 0.5 1 1.5 2 2.5 3 3.5 4 4.5 5 5.5 6 6.5 7 7.5 8 8.5 9 9.5 10

NO PAIN ☐ SEVERE PAIN

2- Patient global activity

Considering ALL THE WAYS THAT YOUR ILLNESS AFFECTS YOU, RATE HOW YOU ARE DOING on the following scale. Place an X in the box below that best describes how you are doing on a scale of 0-10.

VERY WELL 0 ☐ 10 VERY POOR

0.5 1 1.5 2 2.5 3 3.5 4 4.5 5 5.5 6 6.5 7 7.5 8 8.5 9 9.5

- PAS II scale is a RA disease activity scale which is recommended by ACR to categorize disease activity into remission, mild, moderate or severe.
- In RA patients, we treat to goal of keeping patients in either remission or low disease activity.
- In patients with moderate or high disease activity, we need to modify their current regimen.
- How to use this scale? The patient needs to finish this form, then we need to insert these numbers into PAS II calculator which is available in MDCalc application, free medical app in both apple and google store, which will let you know the disease activity, then finally, document the disease activity in your note.

Figure 2. PAS II questionnaire

moderate disease activity, 23% had high disease activity and 21% were in remission or had low disease activity. We noticed that 45% of our RA patients are on biologics and 92% of these patients have PAS II scale in their charts.

Conclusion: We achieved our goal of implementing and maintaining the use of PAS II in a busy rheumatology clinic efficiently through the usage of infographics, simple animation video, PAS II questionnaire paper form, free mobile application, and single educational sessions for rheumatology clinic staff. We believe that our project may be applicable to other busy clinics as it is efficient, cost-effective, and feasible. PROs measures such as PASII, when consistently and judiciously used, may also help facilitate the acquisition of highly expensive biologic treatments that would have

Video link: https://vimeo.com/329981657

Video link and Bar code

encountered extreme health insurance coverage hurdles. Furthermore, regular documentation of disease activity can help researchers who target RA treatments to collect and analyze data more efficiently and more uniformly.

Disclosure: A. H.Ali, None; **A. Elghafri**, None; **M. Mohameden**, None; **M. Sidhu**, None; **C. Reyes Yuvienco**, None.

Abstract Number: 1725

An Investigation of the Relationship Between Patient Reported Outcomes and Biomarkers in a Community Rheumatology Practice

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Disease presentation and progression in rheumatoid arthritis (RA) is highly heterogeneous and requires careful consideration of outcome measurements to be used for individual patients. Here we explore the relationship between disease activity as measured by a standard patient report outcome measure (RAPID3) and multi-biomarker disease activity score (MBDA) across patient phenotypes and therapy regimens within a single community rheumatology practice.

Methods: Unstructured and structured de-identified data from 2019 of patients who satisfied ACR classification criteria for rheumatoid arthritis, were extracted from the electronic health record, including patient demographics, medication history, comorbidities, laboratory values, patient-reported outcomes, swollen joint counts (SJC), and ultrasound evaluation findings (US). The last available disease activity measures were recorded for each patient in

Table 1: Patient Demographics, Comorbidities, and Outcome Measurements Based on Medication Regimens					
Characteristic	**MTX Monotherapy (n = 46)**	**HCQ Monotherapy (n = 38)**	**Any bDMARD (n = 319)**	**Any bDMARD + MTX (n = 78)**	**All Patients (n= 516)**
Age, mean (SD), years	66.6 (15.0)	58.1 (14.0)	60.7 (14.4)	62.5 (11.6)	61.8 (14.7)
Female (%)	33 (72)	35 (92)	255 (80)	61 (78)	411 (80)
White (%)	41 (89)	28 (74)	280 (88)	68 (87)	445 (86)
BMI, mean (SD)	27.7 (5.4)	27.3 (6.2)	28.0 (6.4)	29.11 (7.0)	28.1 (6.5)
Smoking Status (% Former or Current)	15 (33)	6 (16)	79 (25)	24 (31)	127 (25)
Seropositive %	32	42	46	42	44
Seronegative %	68	58	54	58	56
Diabetes (%)	8 (17)	2 (5)	25 (8)	6 (8)	49 (10)
Cardiovascular Disease (%)	8 (17)	9 (24)	84 (26)	25 (32)	136 (2)
Mean SJC (SD)	1.5 (2.7)	1.1 (2.2)	2.0 (2.8)	1.8 (2.6)	1.9 (2.8)
Percentage of Patient Power Doppler Positive	23	16	25	20	26
Mean MBDA (SD)	26.3 (10.3)	24.8 (5.9)	29.5 (12.1)	31.4 (12.2)	29.4 (12.0)
% Low (<30)	70	78	56	51	56
% Medium (30 to 44)	24	22	34	36	34
% High (>44)	5	0	10	13	10
Mean RAPID3 (SD)	8.3 (6.0)	7.4 (6.1)	10.1 (6.6)	9.2 (6.3)	9.5 (6.5)
% Low / Remission (≤6)	49	61	35	37	40
% Medium (>6 to ≤12)	23	28	25	26	26
% High (≥13)	28	11	40	37	34
Correlation between RAPID3 and Vectra (Pearson's correlation coefficient [p-value])	-0.07 (0.68)	-0.27 (0.18)	0.15 (0.01)	0.26 (0.03)	0.14 (0.006)

Table 1. Patient Demographics, Comorbidities, and Outcome Measurements Based on Medication Regimens

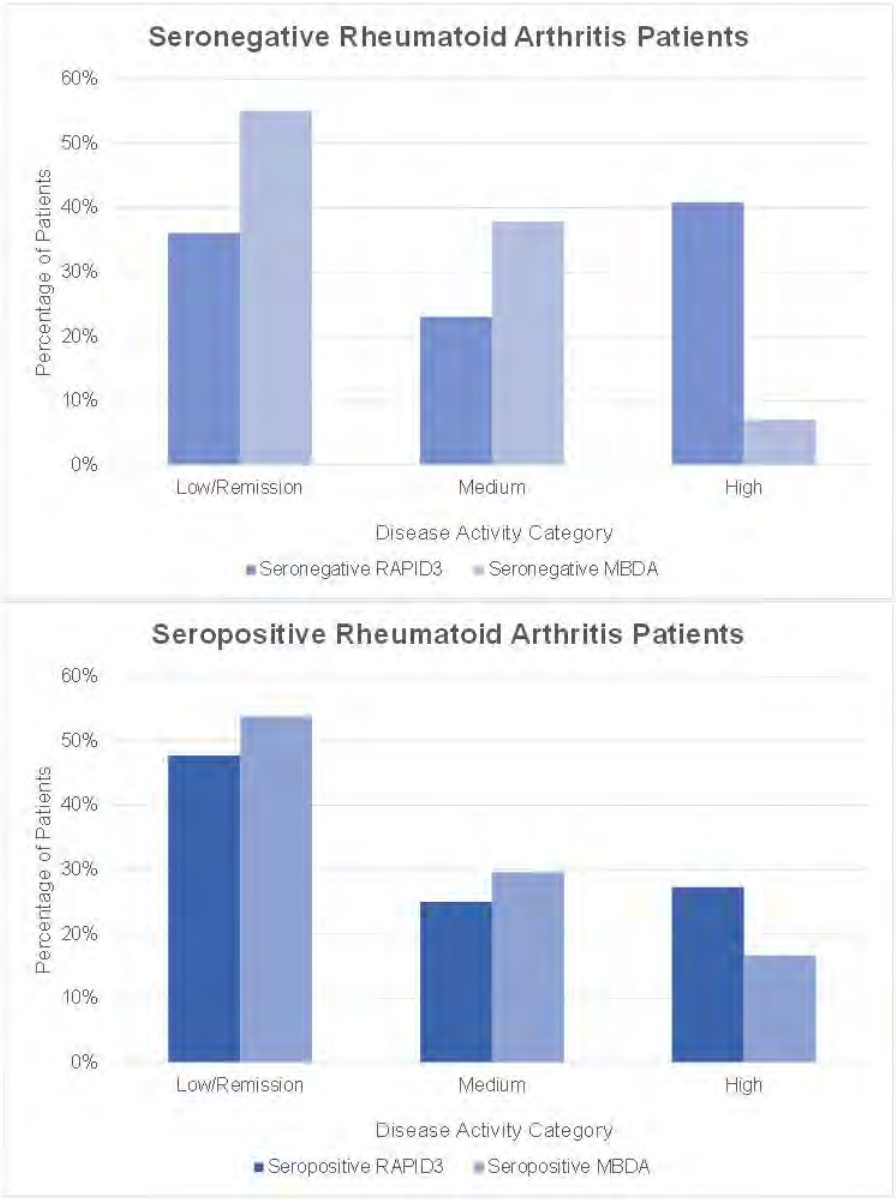
2019, and stable RA patients were defined as those with no change of DMARD therapy for at least 6 months prior to their last visit in 2019. Differences in patient outcomes and laboratory values were determined based on standard correlation analysis.

Results: Out of 757 RA patients with at least one medication script in 2019, 516 (68%) patients with stable RA were identified. Baseline demographics (Table 1) include mean [SD] age, 61.8 [14.7] years; 80% female; and mean [SD] BMI 28.1 [6.5]. Patient demographics, comorbidities, and outcome measurements based on medication regimens are summarized in Table 1. As shown in Figure 1, patients routinely displayed higher disease activity when measured using RAPID3 as compared to MBDA, and this effect was more pronounced in seronegative patients. While highly significant (p=0.006), the Pearson's correlation coefficient between RAPID3 and MBDA was 0.14 among all patients, and 0.30 among seropositive patients (p=0.0004). There was no significant correlation between RAPID3 and MBDA (p=0.18) among seronegative patients. In the subset of patients maintained on methotrexate or hydroxychloroquine monotherapy, there was also no significant correlation between RAPID3 and MBDA in either MTX or HCQ monotherapy groups (MTX: r = -0.07, p = 0.68; HCQ: r = -0.27, p = 0.18). For patients maintained on bDMARD therapy, there was a significant but weak correlation between RAPID3 and MBDA (r = 0.15; p=0.01). These findings are summarized in Table 2.

Conclusion: Here we characterize the rheumatoid arthritis patient panel in a community rheumatology practice and demonstrate a significant difference between patient reported outcomes (as measured by RAPID3) and serum inflammatory markers (MBDA). Patients frequently had a higher RAPID3 disease activity level compared to their MBDA disease activity level, suggesting the need for a multi-faceted approach to measuring RA disease activity in individual patients. Further studies exploring optimal outcome metrics for different patient phenotypes within rheumatoid arthritis are indicated.

Table 2: Characteristics and Disease Activity Measurement Relationships by Serology Finding		
Characteristic	**Seropositive Patients (n = 137)**	**Seronegative Patients (n = 179)**
Age, mean (SD), years	61.2 (15.0)	62.9 (14.6)
Female (%)	112 (82)	134 (75)
White (%)	108 (79)	154 (86)
BMI, mean (SD)	27.8 (5.8)	26.9 (6.9)
Smoking Status (% Former or Current)	32 (23)	51 (29)
Diabetes (%)	13 (9)	16 (9)
Cardiovascular Disease (%)	44 (32)	48 (27)
Medications		
Biological DMARD / JAK (%)	82 (60)	95 (53)
Conventional DMARD (%)	81 (59)	121 (68)
Mean SJC (SD)	2.0 (2.9)	2.0 (2.7)
Percentage of Patient Power Doppler Positive	26	30
Mean MBDA (SD)	31.3 (13.2)	28.1 (10.0)
% Low (<30)	53	57
% Medium (30-44)	31	37
% High (>44)	16	6
Mean RAPID3 (SD)	7.7 (6.1)	10.1 (6.6)
% Low / Remission (≤6)	52	36
% Medium (>6 to ≤12)	25	24
% High (≥13)	23	40
Correlation between RAPID3 and Vectra (Pearson's correlation coefficient [p-value])	0.26 (0.005)	0.11 (0.184)

Table 2. Characteristics and Disease Activity Measurement Relationships by Serology Finding



Percentages of Seropositive and Seronegative Rheumatoid Arthritis Patients Grouped by Disease Activity Category in RAPID3 and MBDA

Disclosure: E. He, Roivant Sciences, 5, Synovium, 4; **P. Yalamanchi**, Roivant Sciences, 5, Synovium, 4; **W. Arnold**, None; **E. Arnold**, None.

Abstract Number: 1726

Assessment of the Components of RAPID3 Patient Reported Outcomes in an Community Rheumatology Practice

Elston He[1], Pratyusha Yalamanchi[2], William Arnold[3] and **Erin Arnold**[4], [1]Synovium, Inc., Philadelphia, PA, [2]Michigan Medicine, Ann Arbor, MI, [3]Retired, Wilmette, IL, [4]Private Practice, Orthopaedics and Rheumatology of the North Shore, Wilmette, IL

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Patient reported outcomes are integral to measuring patient response to treatment for rheumatoid arthritis (RA). RAPID3 is a patient reported outcome metric that consists of three categories: pain, global assessment of health, and physical functional assessment. Here we investigate the relationship between the components of RAPID3 and serum biomarkers as measures of disease activity among RA patients within a private rheumatology practice.

Methods: Unstructured and structured de-identified data from 2019 of patients who satisfied ACR classification criteria for rheumatoid arthritis were extracted from the electronic medical record, including medication history, laboratory values, and patient reported outcomes. The last available RAPID3 composite score, RAPID3 component variable scores, and multi-biomarker disease activity (MBDA) values were recorded for each patient in 2019. Stable RA patients were defined as those with no change of DMARD therapy for at least 6 months prior to their last visit in 2019. Relationships between variable and aggregate scores were determined based on standard t-test and correlation analysis.

Results: Among a total of 516 patients with stable RA, 477 patients had available RAPID3 composite and component variable scores, and 407 patients had MBDA values. There was a weak, though significant correlation between RAPID3 composite score and MBDA score (Pearson's correlation coefficient 0.16; p=0.0012). Considering the component RAPID3 variables, pain scale and patient global score were most highly correlated (r=0.83; p< 0.0001), while physical functional was the least correlated, with r=0.61 (p< 0.0001) and r = 0.59 (p< 0.0001) between patient global and pain, respectively. Interestingly, patient global and pain scores were not significantly different (p=0.36), but physical function assessment scores were significantly different from both patient global and pain assessments (p< 0.0001; p< 0.0001, respectively). The distribution of component variable scores is shown in Figure 1. Comparing the components of RAPID3 with the composite RAPID3 score, physical function was the least correlated of the three (r=0.77; p< 0.0001). All three component variables of RAPID3 had significant correlations with MBDA, with physical function assessment score as the most significantly correlated (r=0.18; p< 0.0001).

Table 1: Correlation Matrix Between Each RAPID3 Component, RAPID3, and MBDA (Pearson's correlation coefficient [p-value])

Characteristic	Patient Global	Pain Score	Physical Function	RAPID3	MBDA
Patient Global		0.83 (<0.0001)	0.61 (<0.0001)	0.94 (<0.0001)	0.14 (0.005)
Pain Score			0.59 (<0.0001)	0.93 (<0.0001)	0.13 (0.005)
Physical Function				0.77 (<0.0001)	0.18 (<0.0001)

Table 1. Correlation Matrix Between Each RAPID3 Component, RAPID3, and MBDA (Pearson's correlation coefficient [p-value])

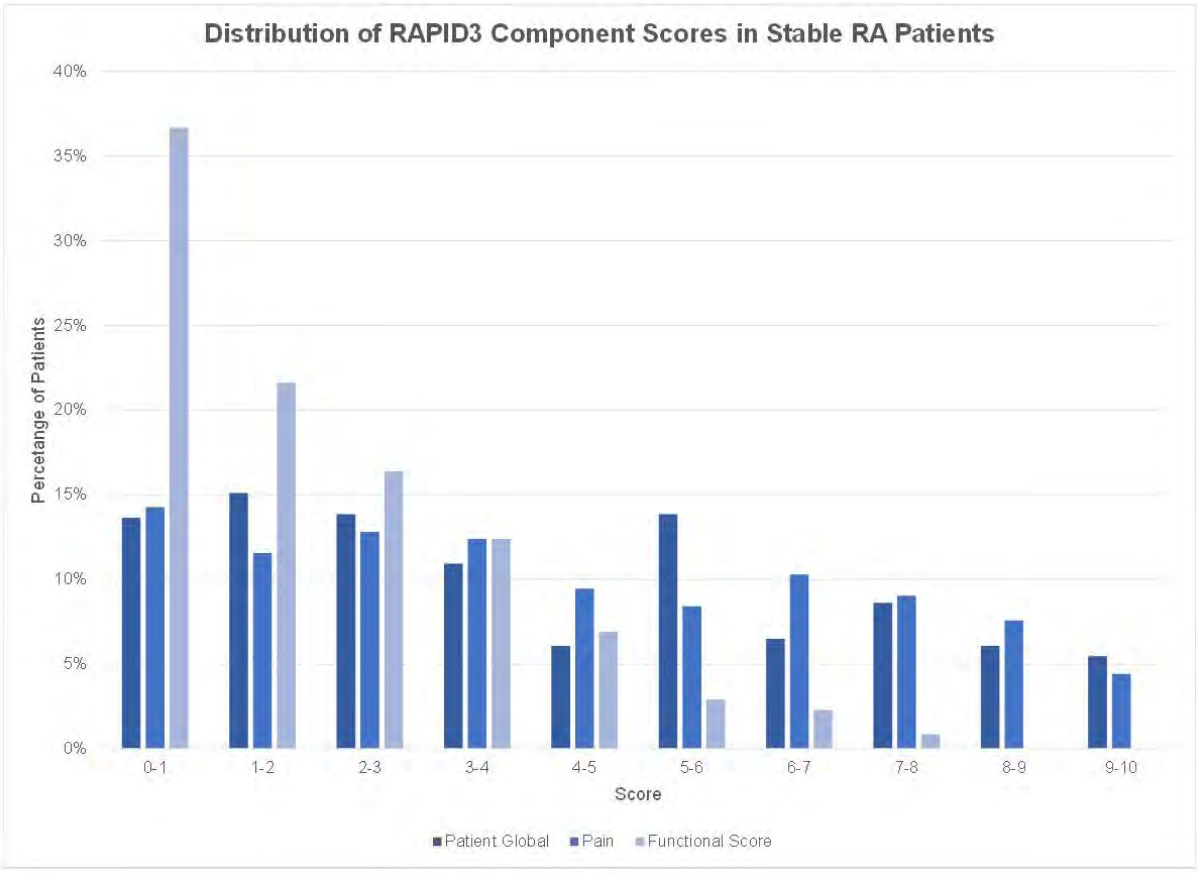


Figure 1. Distribution of RAPID3 Component Scores in a Stable RA Population

Conclusion: Here we identify a strong positive correlation between patient reported outcomes for the categories of pain and global assessment in the RAPID3 assessment among a large rheumatoid arthritis patient panel within a community rheumatology practice. While pain and patient global assessment appear to be the primary drivers of overall RAPID3 scores, the functional component of RAPID3 more closely correlates with serum biomarkers reflecting inflammation such as the MBDA. While RAPID3 reflects patient pain and response to pain, it fails to correlate with markers of inflammation like the MBDA score, which drive changes in medication regimen in our own practice. Further research is needed to understand the relationship between RAPID3 and serum inflammatory markers in various patient phenotypes within the rheumatoid arthritis patient population.

Disclosure: E. He, Roivant Sciences, 5, Synovium, 4; **P. Yalamanchi**, Roivant Sciences, 5, Synovium, 4; **W. Arnold**, None; **E. Arnold**, None.

Abstract Number: 1727

Patterns of Fatigue in Early RA over 10 Years: Results from the ESPOIR Cohort

Samantha Rodriguez-Muguruza[1], Bernard Combe[2], Oliver Valero[3], Francis Guillemin[4], Alejandro Olivé-Marqués[5], Bruno Fautrel[6], Ramon Fontova[1] and Cédric Lukas[7], [1]Joan XXIII Hospital, Tarragona, Spain, [2]University of Montpellier, Montpellier, France, [3]Department of Statistics, Autonoma de Barcelona University, Barcelona, Spain, [4]Universite de Lorraine CIC INSERM, Nancy, France, [5]Hospital Germans Trias i Pujol, Barcelona, Spain, [6]Sorbonne University, INSERM, IPLES; Pitié-Salpêtrière Hospital, Paris, Ile-de-France, France, [7]CHU Montpellier and University of Montpellier, Montpellier, France

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: to determine and characterize fatigue trajectories over 10 years of follow-up in a cohort of early RA patients.

Methods: We selected patients fulfilling the 2010 ACR/EULAR criteria for RA included in the ESPOIR cohort. Cluster analysis with Ward's method was used to obtain fatigue trajectories over the course of 10 years from enrolment. To evaluate differences between baseline variables and fatigue trajectories, Chi-square analyses and ANOVA were used. A multivariate linear regression model with repeated measures was developed to determine the relationship between score of fatigue and other variables over 10 years of follow-up.

Results: We analysed 598 patients. Cluster analysis revealed 3 trajectories: high (18%), moderate (52%) and low fatigue (30%). At baseline, patients with high fatigue trajectory reported significantly higher duration and intensity of morning stiffness, higher HAQ score, higher number of tender joints, higher levels of pain, higher number of awakenings due to arthritis, higher DAS28 levels, increased psychological distress and higher levels of physician and patient global assessment than patients with moderate or low fatigue trajectory (Table 1).

The multivariate linear regression mixed model confirmed that young age, increased psychological distress, high pain level, high morning stiffness intensity, high levels of patient and physician global assessment were related to high levels of fatigue over time (Table 2).

Conclusion: Baseline clinical measures and baseline patient-reported measures of functional status better distinguished the three fatigue trajectories. We did not find differences between trajectories in baseline laboratory measures. Patients with higher levels of pain, psychological distress, morning stiffness intensity also experienced more severe fatigue over time.

Table 1. Baseline chactereristics by fatigue trajectory groups

	Trayectory groups						
	High fatigue	n	Moderate fatigue	n	Low fatigue	n	*p*
Female	94 (87.9)	107	245 (78.3)	313	120 (67.4)	178	0.003
Age at disease onset, years	47.0 (12.1)	107	49.3(11.7)	313	48.7 (12.7)	178	0.230
Hemoglobin (mg/dL)	13.0 (1.3)	107	12.9 (1.3)	313	12.9 (1.2)	177	0.473
CRP (mg/L)	21.1 (32.6)	105	22.4 (36.7)	310	26.9 (35.6)	173	0.312
ESR (mm/hour)	28.5 (22.9)	106	30.1 (25.5)	309	31.7 (25.5)	175	0.568
Morning stiffness, duration, minutes	144.4 (303.0)	107	102.2 (193.7)	313	71.4 (78.1)	178	0.009
Morning stiffness intensity (VAS 0-100)	57.7 (26.8)	107	54.5 (26.8)	313	45.6 (28.0)	178	<0.001
DAS 28	5.6 (1.16)	106	5.4 (1.2)	308	5.1 (1.3)	173	0.004
HAQ score (0-3 scale)	1.3 (0.75)	107	1.1 (0.67)	308	0.85 (0.63	178	<0.001
Swollen joint count/28	8.5 (5.2)	57	8.4 (5.9)	150	8.4 (5.8)	83	0.9874
Tender joint count/28	11.9 (8.0)	57	9.6 (7.2)	150	8.3 (6.9)	83	0.0164
Physician global assessment (VAS 0-100)	59.9 (20.3)	107	54.7 (20.6)	312	47.2 (22.2)	177	<0.001
Patient global assessment (VAS 0-100)	71.7 (21.1)	107	62.9 (22.6)	312	52.7 (26.8)	177	<0.001
SF-36 bodily pain scale	64.7 (18.9)	107	55.9 (18.3)	313	55.9 (18.3)	178	<0.001
Awakenings due to pain	2.4 (2.9)	107	1.9 (2.6)	313	1.5 (1.9)	178	0.0176
MHI-5 score (psychological distress)	41.9 (19.5)	107	51.8 (19.1)	313	60.5 (17.9)	178	<0.001
History of thyroid problems*	10 (9.4)	107	36 (11.5)	313	22 (12.4)	178	0.73
Sjogren's syndrome*	51 (47.6)	107	96 (30.7)	313	32 (17.9)	178	<0.001

Table 2: Results for final multivariate linear mixed model of fatigue cluster

Variable	p	Estimate	Standard Error
Age at disease onset	<0.001	-0.	0.041
MHI-5	<0.001	-0.331	0.017
Morning stiffness intensity	<0.001	0.174	0.016
Patient global assessment	<0.001	0.097	0.018
Physician global assessment	0.0395	0.041	0.020
SF-36 bodily pain scale	<0.001	0.067	0.018

Disclosure: S. Rodriguez-Muguruza, None; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **O. Valero**, None; **F. Guillemin**, Expanscience, 2; **A. Olivé-Marqués**, None; **B. Fautrel**, MSD France, 1, 2, Abbvie, 1, 2, Pfizer, 1, 2, Biogen, 1, BMS, 1, Boehringer Ingelheim, 1, Celgene, 1, Janssen, 1, Lilly, 1, Medac, 1, Nordic Pharma, 1, Novartis, 1, Roche, 1, Sanofi-Aventis, 1, SOBI, 1, UCB Pharma, 1; **R. Fontova**, None; **C. Lukas**, None.

Abstract Number: 1728

Patient-Reported Outcomes of Upadacitinib versus Abatacept in Patients with Rheumatoid Arthritis and an Inadequate Response to Biologic Disease-Modifying Antirheumatic Drugs: 12-Week Results of a Phase 3 Study

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: In patients with active rheumatoid arthritis (RA), treatment with upadacitinib (UPA) has resulted in clinically meaningful improvements in patient-reported outcomes (PROs). This *post hoc* analysis of SELECT-CHOICE (NCT03086343), a phase 3, double-blind randomized clinical trial, evaluated the benefits of UPA vs intravenous (IV) abatacept (ABA) with background conventional synthetic DMARDs (csDMARDs) on PROs in patients with active RA and inadequate response or intolerance to biologic DMARDs (bDMARD-IR).

Methods: Patients in SELECT-CHOICE received UPA (oral 15 mg once daily) or ABA (IV) while on stable csDMARD therapy. PROs included: Patient Global Assessment of Disease Activity (PtGA) by visual analog scale (VAS), patient's assessment of pain by VAS, Health Assessment Questionnaire Disability Index (HAQ-DI), duration and severity of morning (AM) stiffness, 36-Item Short Form Health Survey (SF-36), Functional Assessment of Chronic Illness Therapy-Fatigue, Work Productivity and Activity Impairment (WPAI), and EuroQol 5-dimension 5-level (EQ-5D-5L) index score. Least squares mean (LSM) changes from baseline (BL) to Week 12 were based on an analysis of covariance model. The proportions of patients reporting improvements from BL to Week 12 that were ≥ minimal clinically important differences (MCID) or scores ≥ normative values were calculated for UPA and ABA treatment; comparisons used chi-square tests. Time to response, defined as improvement ≥ MCID, was assessed by Kaplan-Meier analysis and compared using the log-rank test.

Results: Data from 612 patients were analyzed (303 received UPA and 309 received ABA). The mean age was 56 years and mean duration of RA was 12 years. Thirty-two percent received >1 prior bDMARD and 72% received concomitant MTX at BL. At Week 12, UPA treatment resulted in statistically significant LSM changes from BL vs ABA in PtGA, pain, HAQ-DI, severity of AM stiffness, EQ-5D-5L, WPAI activity impairment domain, and in 3/8 SF-36 domains and physical component summary (PCS) score (**Table**). Compared with ABA at Week 12, significantly more UPA-treated patients reported improvements ≥ MCID in HAQ-DI and in 4/8 SF-36 domain scores and PCS score. The proportion of UPA- vs ABA-treated patients reporting scores ≥ normative values were significantly greater in PtGA (37% vs 23%), HAQ-DI (18% vs 10%), EQ-5D-5L (22% vs 13%), and SF-36 PCS (17% vs 8%), including physical

Table. LSM Changes from Baseline and Percentage of Responders at Week 12 After UPA Initiation

PRO	LSM Changes From Baseline		Patients Reporting Improvements ≥ MCID[a], n (%)	
	UPA 15 mg QD (n=303)	ABA (n=309)	UPA 15 mg QD (n=303)	ABA (n=308)
PtGA	−33.85*	−28.35	222 (73)	225 (73)
Pain VAS	−35.27*	−29.98	226 (75)	231 (75)
HAQ-DI	−0.65*	−0.48	225 (74)*	198 (64)
FACIT-F	9.61	8.35	205 (68)	192 (62)
AM stiffness severity[b]	−3.31*	−2.81	238 (79)	223 (72)
AM stiffness duration[c]	−74.36	−70.83	60 (20)	62 (20)
EQ-5D-5L	0.26*	0.21	221 (73)	209 (68)
WPAI overall work impairment	−25.67	−22.14	65 (59)	46 (53)
WPAI activity impairment	−26.77*	−20.96	221 (73)	210 (68)
SF-36 PCS	9.62*	7.03	239 (79)*	204 (66)
SF-36 MCS	5.63	5.80	168 (55)	173 (56)
SF-36 PF	8.64*	5.93	238 (79)*	202 (66)
SF-36 RP	7.93	6.89	236 (78)*	212 (69)
SF-36 BP	12.24*	9.81	251 (83)*	233 (76)
SF-36 GH	6.70*	4.96	216 (71)*	193 (63)
SF-36 VT	8.64	7.65	220 (73)	207 (67)
SF-36 SF	7.76	6.61	196 (65)	185 (60)
SF-36 RE	5.54	5.49	172 (57)	173 (56)
SF-36 MH	6.89	6.29	207 (68)	191 (62)

*P<0.05 for UPA vs ABA. P values represent statistical significance between groups. [a]MCID was defined as reduction of ≥10 mm for PtGA and pain, ≥1 for severity of morning stiffness, reduction of ≥0.22 units for HAQ-DI, increase of ≥4 points for FACIT-F, proxied at 1/2 standard deviation for duration of morning stiffness, increase of ≥0.05 points for EQ-5D-5L, reduction of 7% in score for WPAI, increase of ≥2.5 points for SF-36 PCS and MCS, and an increase ≥5.0 for all SF-36 domains. [b]Assessed on a numeric scale of 1–10, with 10 being the worst level. [c]Duration in minutes.

ABA, abatacept; AM, morning; BP, bodily pain; EQ-5D-5L, EuroQol 5-dimension 5-level index score; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; GH, general health; HAQ-DI, Health Assessment Questionnaire Disability Index; LSM, least squares mean; MCID, minimal clinically important difference; MCS, mental component summary; MH, mental health; PCS, physical component summary; PF, physical functioning; PRO, patient-reported outcome; PtGA, Patient Global Assessment of Disease Activity; QD, once daily; RE, role emotional; RP, role physical; SF, social functioning; SF-36, 36-Item Short Form Health Survey; UPA, upadacitinib; VAS, visual analog scale; VT, vitality; WPAI, Work Productivity and Activity Impairment.

functioning (21% vs 11%), bodily pain (33% vs 23%), and general health (24% vs 17%) domains. The median time to response was significantly shorter (P< 0.01) for UPA- vs ABA-treated patients in HAQ-DI (2 weeks vs 4 weeks).

Conclusion: Among bDMARD-IR patients with moderate to severely active RA, treatment with UPA or ABA resulted in clinically meaningful improvements in PROs at Week 12. Overall, greater improvements in PROs especially in the key domains of physical functioning, pain, and general health, were observed with treatment with UPA compared with ABA; improvements in HAQ-DI were observed earlier in UPA- vs ABA-treated patients.

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Abstract Number: 1729

Associations Between Patient Reported Outcomes and Impairments of Work and Activity in Patients with Rheumatoid Arthritis Who Achieved Clinical Remission; Retrospective Analysis Using the IORRA Database

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Disease burden and subjective symptoms of rheumatoid arthritis (RA) remain even after achieving clinical remission or low disease activity. Impairments to work and societal/daily activity are relevant burdens for patients with RA. However, detailed analyses are rarely performed. For exploring a better strategy aiming at less burden beyond Treat-to-Target strategy, it is essential to evaluate details of subjective symptoms collected as patient-reported-outcomes (PROs) and their relationship to work productivity and activity impairment (WPAI). The purpose of this study was to explore patient-reported outcomes (PROs) related to WPAI in patients with RA who achieved clinical remission.

Methods: The Institute of Rheumatology Rheumatoid Arthritis (IORRA) database is an established cohort database with RA in Tokyo Women's Medical University since 2000. RA patients ≥18 years who met the 1987 American College of Rheumatology classification criteria for RA and SDAI remission criteria (SDAI≤3.3) within the IORRA dataset col-

	Pain VAS	Pt-GA	J-HAQ-DI	Duration of MJS
Absenteeism (n=955)	0.11 [0.04, 0.17]	0.11 [0.04, 0.17]	0.15 [0.09, 0.21]	0.14 [0.08, 0.20]
Presenteeism (n=1,092)	0.52 [0.47, 0.56]	0.46 [0.41, 0.51]	0.44 [0.39, 0.48]	0.24 [0.18, 0.29]
Work productivity loss (n=942)	0.50 [0.45, 0.55]	0.44 [0.39, 0.49]	0.44 [0.39, 0.49]	0.26 [0.20, 0.32]
Daily activity impairment (n=1,945)	0.60 [0.57, 0.63]	0.58 [0.55, 0.61]	0.55 [0.52, 0.58]	0.23 [0.19, 0.27]

Correlation coefficient between WPAI and each PRO. Values are Spearman's rank correlation coefficient [95% confidence interval]. WPAI, Work Productivity and Activity Impairment; PRO, patient-reported outcomes; VAS, visual analogue scale; J-HAQ-DI, Japanese version of Healthcare Assessment Questionnaire-Disability Index; MJS, morning joint stiffness

	Absenteeism (n=955)	Presenteeism (n=1,092)	Work productivity loss (n=942)	Daily activity impairment (n=1,945)
Age	0.50%	0.20%	0.00%	0.90%
Sex	0.90%	0.10%	0.00%	1.10%
RA disease duration	0.00%	5.60%	6.00%	4.80%
BMI	0.50%	0.10%	0.00%	0.10%
TJC	16.80%	2.70%	1.80%	1.60%
SJC	2.00%	0.50%	1.00%	0.00%
CRP	0.80%	0.10%	0.20%	0.00%
ESR (1 hour)	14.00%	0.80%	1.30%	0.70%
Ph-GA	0.30%	0.30%	0.10%	0.00%
CCI	7.00%	2.80%	3.00%	2.40%
PRO				
Pain VAS	1.80%	57.40%	51.10%	53.70%
Pt-GA	5.00%	6.40%	7.30%	7.30%
J-HAQ-DI	6.00%	17.40%	16.30%	26.00%
Duration of MJS	18.00%	3.70%	6.80%	0.10%
Number of hospitalization in last 6 months	12.10%	0.70%	3.20%	0.00%
History of joint surgery	2.10%	0.40%	1.10%	1.10%
History of surgery other than joint surgery	1.10%	0.30%	0.40%	0.00%
History of fracture	8.50%	0.20%	0.00%	0.10%
Residual	2.60%	0.30%	0.40%	0.10%

Contribution to variance in WPAI score. WPAI, Work Productivity and Activity Impairment; RA, Rheumatoid arthritis; BMI, Body Mass Index; TJC, Tender joint count; SJC, Swollen joint count; CRP,C-reactive protein; ESR, Erythrocyte sedimentation rate; Ph-GA, Physician's global assessment; CCI, Charlson Comorbidity Index; PRO, patient-reported outcomes; VAS, visual analogue scale; Pt-GA, Patient's global assessment; J-HAQ-DI, Japanese version of Health-care Assessment Questionnaire-Disability Index; MJS, morning joint stiffness

lected in October 2017 were used for this analysis. Pain-VAS [0–100 mm], patients' global assessment VAS (Pt-GA) [0–100 mm], Healthcare Assessment Questionnaire-Disability Index (Japanese version; J-HAQ-DI), and duration of morning joint stiffness (MJS) were evaluated. To measure impact on work productivity during the past 7 days, the WPAI-RA instrument (absenteeism, presenteeism, work productivity loss, and daily activity impairment) was used. Spearman's rank correlation coefficient with 95% confidence interval (95% CI) was calculated to evaluate correlation between each WPAI item and each PRO. To evaluate the degree of contribution of each PRO to WPAI, an ANOVA model was constructed. The contribution of each PRO was calculated based on the sum squares of each PRO divided by total sum squares.

Results: Mean age of the 2,614 patients was 62.4 years; 85.1% were female; and mean DAS28-ESR and SDAI was 2.0 and 1.3, respectively. Mean scores of WPAI were 1.1% for absenteeism (percent work time missed due to RA), 6.5% for presenteeism (percent impairment while working due to RA), 7.4% for work impairment, and 10.2% for activity impairment. Mean pain VAS and Pt-GA were 7.1 and 7.5, respectively, and mean J-HAQ-DI score was 0.3. MJS was reported in 17.6% of patients with a mean duration of 45.3 minutes. Pain VAS showed the strongest pos-

itive correlation with each score of WPAI except for absenteeism (Spearman's rank correlation coefficient [95% CI] 0.52 [0.47, 0.56] for presenteeism, 0.50 [0.45, 0.55] for work impairment, and 0.60 [0.57, 0.63] for activity impairment) (Table 1). MJS contributed the most to absenteeism (18.0%) while pain-VAS contributed the most to presenteeism (57.4%), work productivity loss (51.1%), and daily activity impairment (53.7%) (Table 2). J-HAQ-DI was the second most contributing factor to all scores of WPAI (6.0% for absenteeism, 17.4% for presenteeism, 16.3% for work productivity loss, and 26.0% for daily activity impairment).

Conclusion: Pain-VAS and J-HAQ-DI highly contributed to WPAI. This study indicates that improvement in these PROs may lead to less burden of RA patients in clinical remission.

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Abstract Number: 1730

Comparison of MBDA Score, Patient Global Assessment and Evaluator Global Assessment for Predicting Risk of Radiographic Progression

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: To compare the abilities of MBDA score, patient global assessment (PGA) and evaluator global assessment (EGA) to assess risk for radiographic progression (RP), and to assess the ability of MBDA score to predict RP among patients with concordant or discordant PGA and EGA.

Methods: Patients were pooled from two RCTs of patients with recent onset RA treated with conventional and biologic DMARDs (OPERA and SWEFOT, N=386) and from a registry of patients with predominantly established RA and diverse treatments (BRASS, N=380). Pearson correlations were determined between MBDA scores (adjusted for the effects of age, sex and adiposity) (scale 1-100), PGA and EGA (each on a scale of 1-10) at baseline. PGA and EGA were considered discordant when they differed by >2.5. Univariate logistic regression assessed ability to predict RP (ΔTSS >5 over 1 year) for MBDA score, PGA and EGA as continuous variables; and for discordance of PGA and EGA as 2-level (concordant vs. discordant) or 3-level (PGA >EGA, concordant, EGA >PGA) categorical variables. Multivariable regression considered the main effect and interaction terms of the MBDA score, as a continuous variable, paired with each other variable, to test the ability of each pair to assess risk of RP. All models included a random effect on cohort. Odds ratios were reported for every 10-unit increase in MBDA score. Frequency of RP was determined in subgroups with MBDA score low (< 30), moderate (30-44) or high (>44) for patient groups based on PGA/EGA concordance or discordance.

Results: The 766 patients studied were 76% female, 76% positive for RF and/or anti-CCP Ab, with mean age 55 years, DAS28-CRP 4.7, CRP 22 mg/L, CDAI 26, SJC 9.1, PGA 4.4, EGA 3.4, MBDA score 53. No interaction was

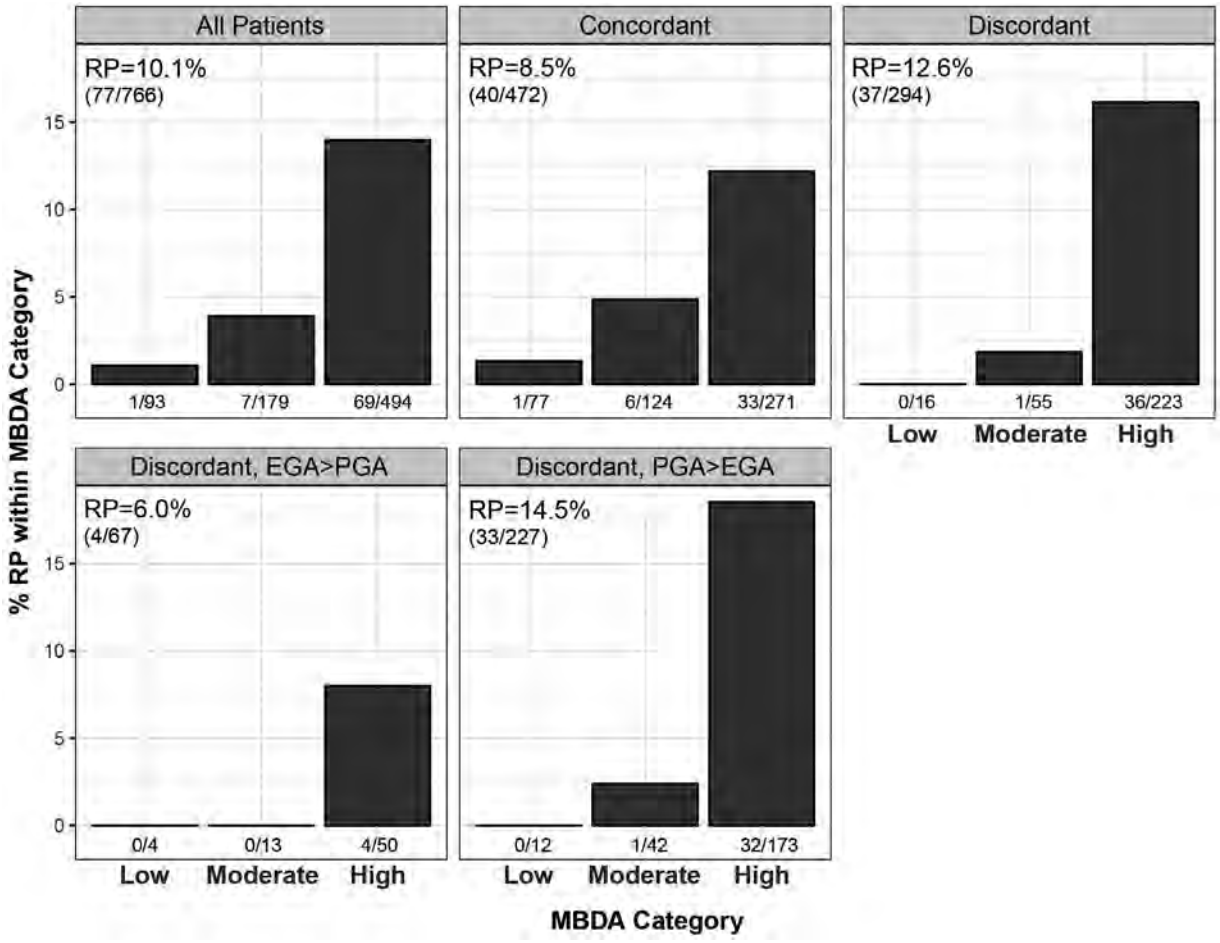

Figure 1. Rate of radiographic progression (RP) by MBDA category for patient groups based on concordance or discordance of Patient Global Assessment (PGA) and Evaluator Global Assessment (EGA).

seen between MBDA score and type of cohort (early vs established RA). PGA and EGA were discordant in 294 of 766 (38%) patients and were weakly to moderately correlated (r=0.38). Among discordant patients, PGA was >EGA in 227 cases and EGA was >PGA in 67 cases. Correlations between MBDA score and PGA or EGA were r=0.41 and r=0.34, respectively. In univariate analyses, MBDA score was a statistically significant predictor of radiographic progression (OR=1.53, $p=6.3x10^{-8}$) whereas PGA, EGA, 2-level discordance and 3-level discordance were not (p=0.38, 0.47, 0.74, 0.83, respectively). In multivariable analyses, significant interactions were observed between MBDA score and discordance (2-level, p=0.0029; 3-level, p=0.0087). The interaction analysis demonstrated, in PGA/EGA-concordant patients, low risk of radiographic progression when MBDA score was low and elevated risk when it was high (OR=1.33 [1.1, 1.59]). A relationship between MBDA score and RP risk was also demonstrated, with heightened trend, among discordant patients with PGA >EGA (OR=2.04 [1.53, 2.81]) and EGA >PGA (OR=3.43 [1.37, 13.8]) (Figure 1).

Conclusion: MBDA score was a significant predictor of radiographic progression, whereas PGA and EGA were not. MBDA score predicted progression whether PGA and EGA were concordant or discordant. These results suggest that MBDA score detects joint-damaging disease activity more accurately than PGA and EGA and it does so whether or not PGA and EGA are in agreement.

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Abstract Number: 1731

Development of a Disease Activity Index for Rheumatoid Arthritis Patients Using the HandScan

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Disease activity in rheumatoid arthritis (RA) patients is usually measured by an index like DAS28,[1] a composite measure consisting of 28 swollen and/or tender joint counts (SJC28/TJC28), an acute phase reactant (APR, e.g. ESR/CRP) and patient's general health, typically using a visual analogue scale (VAS). Particularly assessment of joint counts is time consuming, requires a trained health professional and its inter-observer variety is high. The HandScan is developed to measure inflammation in hand joints using optical spectral transmission (OST, score 0-66) within 5 minutes, without taking time of a health professional.[2] The correlation between DAS28 and a sin-

Table 1 Patient demographics and clinical data

Patient demographics (N=1505)	
Females	976 (65%)
Age in years	65.5 (12.1)
Disease duration in years	11.5 (8.3)
RF positive patients	1068 (71%)
Clinical data	
Number of observations	3358
DAS28	2.5 (1.3)
ESR in mm 1st hr	9.0 (5.0–21.0)
SJC	0 (0 – 2)
TJC	0 (0 – 2)
VAS	30.0 (10.0–50.0)
OST	12.6 (5.0)

Data are n (%), or mean (SD), or median (IQR).

Table 2 Diagnostic values of DAS-OST

DAS28 disease activity state	AU ROC	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	Accuracy (%)
Remission	0.93	84	86	89	79	85
LDA	0.92	88	75	91	69	85
HDA	0.97	49	99	75	98	98

AU ROC= area under the receiver operating characteristic curve, Remission= DAS28<2.6, LDA= low disease activity (DAS28<3.2), HDA= High disease activity (DAS28≥5.1), PPV= positive predictive value, NPV= negative predictive value.

References

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2. Besselink N., et al. Trials. 2019;20:226
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gle measurement of OST is moderate.[3] We hypothesised that a composite measure consisting of OST (representing joint inflammation), VAS and APR would lead to an appropriate disease activity index.

Objective:

To develop and validate a composite disease activity index for assessing RA patients using OST values obtained by the HandScan.

Methods: At a single Rheumatology centre routinely using the Handscan, RA patients with at least one concurrent OST-score and DAS28 measurement were included. Data was extracted from medical records. A random sample of 2/3 of the patients was used as development cohort, the remaining 1/3 was used as validation cohort. In the development cohort, linear regression analyses with DAS28 as outcome were performed to create a disease activity index (DAS-OST). In these analyses, OST-score, ESR and VAS, as well as gender, age, disease duration and RF-status, were evaluated as predictor variables. A final model was derived, based on statistical significance and model fit. Patients were classified as being in DAS28 based remission, low and high disease activity by DAS-OST using the established DAS28 cut-offs. In the validation cohort, agreement of DAS28 and DAS-OST was estimated with a two-way mixed effect intra-class correlation coefficient (ICC) and the measurement error was estimated using the Bland and Altman method. Diagnostic accuracy were determined for DAS-OST using the cut-offs as defined above for all disease activity states.

Results: Data of 3358 observations within 1505 unique RA patients were extracted. Patients' demographic and clinical data are shown in Table 1.

The formula for DAS-OST derived in the development cohort was: -0.44 + OST*0.03 + male*-0.11 + LN(ESR)*0.77 + VAS*0.03.

In the validation cohort, the explained variance of DAS-OST was 78%. For agreement, the ICC was 0.88 (95%CI 0.87-0.90) and the measurement error was 0.58. Diagnostic accuracy of DAS-OST for DAS28 based remission, LDA and HDA remission is shown in Table 2.

Conclusion: Using the HandScan, disease activity can be accurately estimated in RA patients, when its score is combined with ESR, VAS and gender into an objective disease activity index (DAS-OST).

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Abstract Number: 1732

Machine Learning Coupled with Patient Reported Outcome Data to Classify & Predict RA Disease Activity

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Patient reported outcome (PRO) data have assumed increasing importance in the care of rheumatoid arthritis (RA) patients. However, physician-derived disease activity measures such as CDAI remain the most-accepted metrics to assess RA. The possibility that newer, longitudinal PRO might proxy for the CDAI has not been evaluated.

Methods: Using data from the Comparative and Pragmatic Study of Golimumab IV vs. Infliximab (AWARE), we evaluated RA patients initiating one of these two therapies who started in moderate or high disease activity and remained under observation through 6 months or stopped due to lack of efficacy. The prediction target was CDAI and CDAI disease activity category at Month 6. Candidate predictors included baseline CDAI, baseline PROs including those from the NIH PROMIS system (e.g. Pain Interference, Fatigue, Physical Function, Sleep Disturbance), and followup PROs at month 1 and 6 (+-30 days). Data were randomly partitioned into training (2/3) and test (1/3) datasets. Multiple machine learning (ML) methods (e.g. Gradient Boosting: XGBoost, Random Forests: RF, elasticnet regularization: ER, support vector machine: SVM) were used to both predict CDAI, and classify CDAI disease activity category (remission/low vs. moderate/high). Feature selection was conducted using R package mlr3 and hyper-parameter tuning was conducted using a random search method. Model performance evaluated cross-validated error comparing different ML approaches using both train and test data.

Results: A total of 391 AWARE patients were analyzed. Of these, the distribution of disease activity by CDAI at month 6 was remission (4.9%), low (26.6%), moderate (31.4%), and high (37.1%). In univariate analysis examining outcomes at 6 months (Table 1), and depending on which modeling method was used, the most important features included

Feature	Attained Remission/LDA by CDAI (n=123)	Remained in moderate/high disease activity by CDAI (n=268)	P value	SMD
Age	60.2 (13.1)	59.3 (13.0)	0.5255	0.0691
Female Sex	30 (24.4)	38.0 (14.2)	0.0198	0.2610
Baseline CDAI	26.4 (12.0)	35.8 (13.3)	<0.0001	0.7365
Baseline PROMIS				
Ability to Participate in Social Roles	47.3 (7.9)	42.5 (7.5)	<0.0001	0.6226
Anxiety	49.9 (9.4)	55.1 (9.7)	<0.0001	0.5432
Depression	48.5 (9.1)	53.1 (9.3)	<0.0001	0.4895
Fatigue (4 Item)	55.2 (9.9)	60.5 (8.7)	<0.0001	0.5743
Pain Intensity (0-10 Scale)	5.1 (2.0)	6.4 (1.9)	<0.0001	0.6376
Pain Interference (4 Item)	59.9 (6.8)	64.5 (6.5)	<0.0001	0.6878
Physical Function	40.9 (6.8)	36.9 (5.5)	<0.0001	0.6510
PROMIS Fatigue (7 Item)	56.5 (8.3)	60.6 (7.0)	<0.0001	0.5355
Pain Interference (6 Item)	58.9 (6.9)	63.5 (6.1)	<0.0001	0.7047
Sleep Disturbance	51.4 (8.7)	56.9 (8.3)	<0.0001	0.6418
Change in PROMIS				
Ability to Participate in Social Roles	3.3 (7.2)	1. 6 (7.0)	**0.0270**	0.2405
Anxiety	-1.8 (7.5)	-2.3 (7.8)	0.5267	0.0696
Depression	-1.1 (6.8)	-1.9 (7.8)	0.3480	0.1049
Fatigue	-3.2 (8.1)	-1.9 (7.9)	0.1474	0.1572
Pain Intensity (0-10 Scale)	-1.7 (2.3)	-0.9 (2.0)	**0.0002**	0.4015
Pain Interference (4 Item)	-5.1 (7.7)	-2.8 (6.2)	**0.0017**	0.3300
Physical Function	3.0 (6.5)	1. 2 (4.6)	**0.0017**	0.3223
Fatigue (7 Item)	-3.9 (6.7)	-2.5 (6.0)	**0.0357**	0.2244
Pain Interference (6 Item)	-5.2 (7.4)	-3.0 (6.0)	**0.0019**	0.3263
Sleep Disturbance	-1.5 (7.9)	-1.8 (7.3)	0.6974	0.0417
Data shown as n(%) or mean (SD)				

Table 1. Factors associated with attaining remission or low disease activity (CDAI ≤10) at visit 3 (month 6)

	Classification after regression				Direct classification			
	SN	SP	PPV	ACC	SN	SP	PPV	ACC
Linear regression	0.38	0.93	0.65	0.79	0.38	0.90	0.57	0.76
Random forest	0.26	0.99	0.90	0.80	0.53	0.91	0.67	0.81
Elastic net regularization	0.38	0.95	0.72	0.80	0.53	0.86	0.56	0.77
XGBoost	0.65	0.71	0.44	0.69	0.35	0.90	0.55	0.76
Support vector machine	0.32	0.94	0.65	0.78	0.18	0.97	0.67	0.76

Table 2. Model performance in Test data

pain intensity, PROMIS measures (social participation, pain interference, pain intensity, and physical function), baseline CDAI, and age. Among all ML methods , random forest performed best. To classify LDA/remission vs. moderate/high based on regression, accuracy ranged from 0.69 (XGBoost) to 0.80 (RF) (Table 2, left). VM, ER, and RF had high specificity, ranging from 0.93 for SVM to 0.99 for RF; but low sensitivity, ranging from 0.26 for RF to 0.38 for ER. XGBoost had adequate sensitivity (0.65) and specificity (0.71). Predicted vs. observed CDAI (Figure) showed some patients had higher observed than predicted CDAI at month 6. Direct classification generated somewhat similar or lower model performance (Table 2, right).

Conclusion: Machine learning methods coupled with longitudinal PRO data appear useful and can achieve 80-90% accuracy to classify RA disease activity among patients starting a new biologic. This approach has promise for

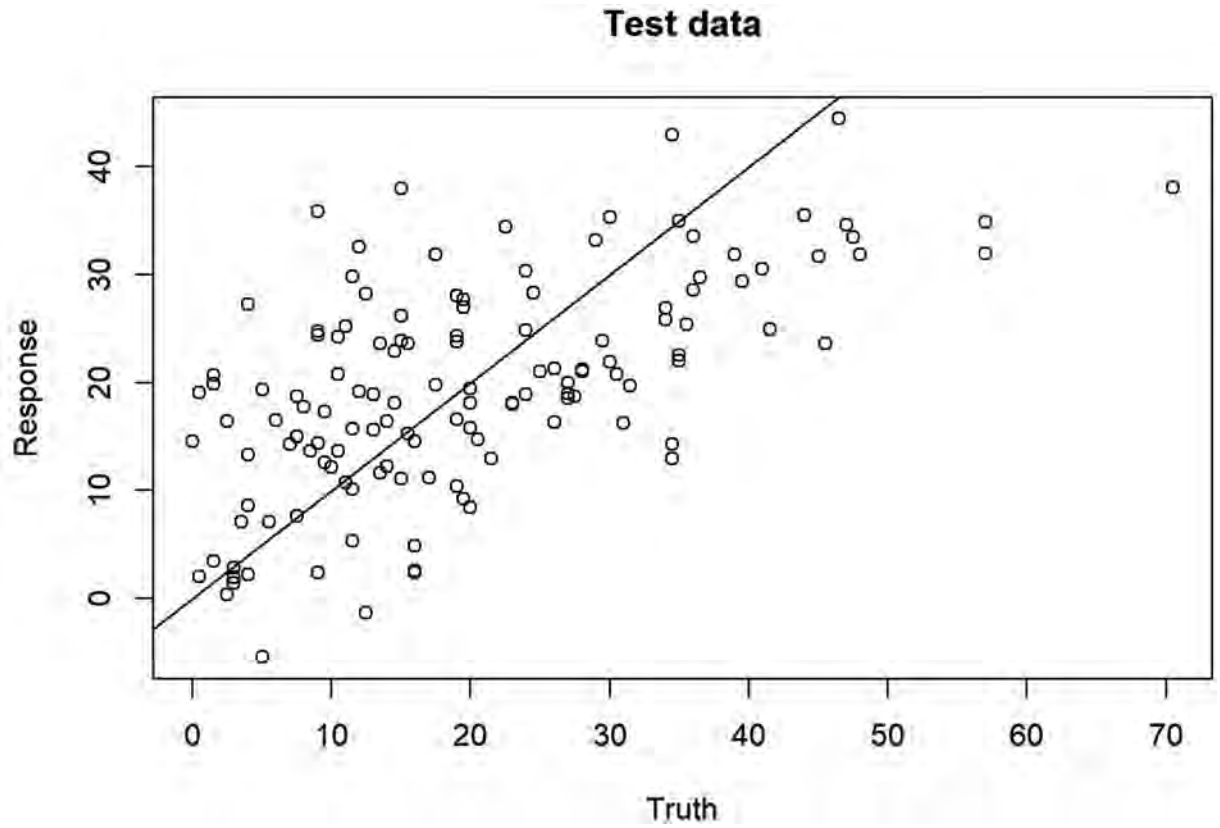


Figure. Predicted vs. Observed CDAI at visit 3 (month 6) by RandomForest

real-world evidence generation in the common circumstance where physician-derived disease activity data is not available yet PRO measures are.

Disclosure: J. Curtis, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **F. Xie**, None; **S. Kafka**, Janssen Scientific Affairs, LLC, 1, 3; **S. Black**, Janssen Scientific Affairs, LLC, 1, 3.

Abstract Number: 1733

Patients with Rheumatoid Arthritis and Comorbid Depression Have High Levels of RAPID3 (Routine Assessment of Patient Index Data) and FAST3 (Fibromyalgia Assessment Screening Index) on a Multidimensional Health Assessment Questionnaire (MDHAQ)

Rosa Morlà[1], Tengfei Li[2], Jose Inciarte-Mundo[3], Isabel Castrejon Fernandez[4], Jose Gómez-Puerta[5], Raimon Sanmartí[5] and Theodore Pincus[6], [1]Hospital Universitari Clínic de Barcelona, Barcelona, Spain, [2]Georgetown University, Washigton, [3]Hospital Universitari Clínic de Barcelona, Barcelona, [4]Hospital General Universitario Gregorio Marañón, Chicago, IL, [5]Hospital Universitari Clínic de Barcelona, Barcelona, Catalonia, Spain, [6]Rush University Medical Center, Chicago, IL

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with rheumatoid arthritis (RA) have higher comorbid depression and/or fibromyalgia (FM) than the general population. A multidimensional health-assessment questionnaire (MDHAQ) includes two queries concerning depression that provide a depression index (MDHAQ-DEP) which gives similar results to 2 widely used depression scales, Patient Health Questionnaire-9 (PHQ-9) and Hospital Anxiety and Depression Scale (HADS-D)[1]. The MDHAQ also provides 2 other indices: 1. RAPID3 (routine assessment of patient index data) to assess clinical status with similar results to DAS28 and CDAI, 2. FAST3 (fibromyalgia assessment screening tool), with similar results

	Range	All patients	Negative MDHAQ-DEP Screen	Positive MDHAQ-DEP screen	p
Demographic data					
# patients		N=102	N=68	N=33	
Age (years), mean (SD)		58.8 (12.2)	60 (12.2)	57 (12.3)	0.360
Sex – female, # (%)		84 (82%)	53 (78%)	30 (91%)	0.110
Education (years), mean (SD)		11.8 (4.3)	12 (4.4)	11 (4.2)	0.527
MDHAQ measures, mean (SD)					
FN	0-10	2.4 (1.8)	1.8 (1.4)	3.8 (1.7)	<0.0001
Pain	0-10	4.5 (2.8)	3.5 (2.5)	6.5 (2.3)	<0.0001
PATGL	0-10	4.6 (2.8)	3.6 (2.4)	6.8 (2.4)	<0.0001
RADAI	0-48	12.4 (11.0)	9.1 (9.1)	19.2 (11.9)	<0.0001
60-sx checklist	0-60	12.6 (10.0)	8.8 (7.1)	20.7 (10.5)	<0.0001
Fatigue	0-10	4.2 (2.9)	3.1 (2.6)	6.5 (2.2)	<0.0001
MDHAQ RAPID 3 Index					
RAPID3 scores, mean (SD)	0-30	11.6 (6.8)	8.9 (5.7)	17.2 (5.6)	<0.0001
RAPID3-remission # (%)	0-3	14 (13.7%)	13 (19.1%)	1 (3.0%)	<0.0001
RAPID3-low severity # (%)	3.1-6	12 (11.8%)	12 (17.6%)	0	
RAPID3-mod severity # (%)	6.1-12	28 (27.5%)	21 (30.9%)	6 (18.2%)	
RAPID3-high severity # (%)	12.1-30	48 (47.1%)	22 (32.4%)	26 (78.8%)	
MDHAQ FAST FM Indices					
FAST3P, mean (SD)	0-3	1.1 (1.2)	0.6 (1.0)	1.9 (1.1)	<0.0001
FAST3F, mean (SD)	0-3	1.0 (1.1)	0.6 (1.0)	1.9 (1.0)	<0.0001
FAST4, mean (SD)	0-4	1.4 (1.5)	0.8 (1.3)	2.6 (1.3)	<0.0001
FAST3P, # (%) ≥2	Y/N	32 (31.4%)	12 (17.6%)	20 (60.6%)	<0.0001
FAST3F, # (%) ≥2	Y/N	34 (33.3%)	13 (19.1%)	21 (63.6%)	<0.0001
FAST4, # (%) ≥3	Y/N	27 (26.5%)	10 (14.7%)	17 (51.5%)	<0.0001
Depression scales					
PHQ-9 mean score	0-10	6.8 (6.6)	3.6 (3.4)	13.2 (6.8)	<0.0001
PHQ-9 # (%) depressed	Y/N	28 (27%)	5 (7.4%)	22 (66.7%)	<0.0001
HADS-D mean score	0-21	5.5 (4.9)	3.3 (3.7)	9.9 (3.9)	<0.0001
HADS-D # (%) depressed	Y/N	33 (32%)	8 (11.8%)	25 (75.8%)	<0.0001

Table. Mean scores and # of RA patients according to MDHAQ depression (MDHAQ-DEP) negative or positive status

to formal FM criteria. We analyzed routine care RA patients for scores for RAPID3, FAST3, MDHAQ-DEP and 2 depression scales, PHQ-9 and HADS-D.

Methods: RA patients in routine care in Barcelona, Spain completed an MDHAQ, which includes 0-10 scores for physical function (FN), pain (PN), patient global assessment (PATGL), fatigue (FT), 0-48 -report RA disease activity index (RADAI) painful joint count, 0-60 symptom checklist (SX), one of which is depression, and a query concerning depression in the patient friendly HAQ format, scored 0–3.3 to give a 0–9.9 psychological MDHAQ index. MDHAQ indices include 0–30 RAPID3=FN+PN+PATGL, 3 cumulative indices to screen for FM: 0-3 FAST3-P - 1 each for PN ≥6, RADAI≥16, and SX≥16 (2/3=FM), 0-3 FAST3-F - 1 each for FT≥6, RADAI≥16, and SX≥16 (2/3=FM), and 0-4 FAST4 - 1 each for PN≥6, FT≥6, RADAI≥16, and SX≥16 (3/4=FM) and MDHAQ-DEP, based on a positive response on the depression SX query (Yes/No) or a score of ≥2.2 on the HAQ-like depression scale. Patients also completed the 0-27 PHQ-9 (≥10=depression), and 0-21 HADS-D (≥8=depression) scales. We compared RA patients who were MDHAQ-DEP positive and negative according to demographic data, scores for MDHAQ measures, RAPID3 and FAST3 indices, and PHQ-9 and HADS-D depression scales, using Student t tests, Wilcoxon rank-sum tests, chi-square tests or Fisher's exact tests as appropriate.

Results: Among 102 patients, mean age was 58.8 years, mean education level 11.8 years, and 82% were female (Table). Mean RAPID3 was 11.6 (moderate severity), including 8.9 in 68 DEP-negative versus 17.2 in 33 DEP-positive patients ($p< 0.0001$), with similar patterns for all component scores (Table). High or moderate severity was seen in 97% of DEP-positive versus 63% of DEP-negative patients. FM FAST3-P, FAST3-F, and FAST4 screening were positive in 52-64% of DEP-positive vs 15-19% of DEP-negative patients. Scores on PHQ-9 and HADS-D also differed significantly in the 2 groups (Table, $p< 0.0001$).

Conclusion: RA patients positive for depression showed higher mean RAPID3 and FAST indices for FM. These associations must be considered in interpreting RAPID3 scores in clinical care in relation to treat-to-target recommendations.

Reference: 1. Morlà R et al. *Arthritis Rheumatol.* 2019; 71 (suppl 10).

Disclosure: R. Morlà, None; **T. Li**, None; **J. Inciarte-Mundo**, None; **I. Castrejon Fernandez**, None; **J. Gómez-Puerta**, Abbvie, 8, BMS, 8, GSK, 8, Lilly, 8, MSD, 8, Janssen, 8, Pfizer, 8, Roche, 5, 8; **R. Sanmartí**, None; **T. Pincus**, Medical History Services LLC, 9.

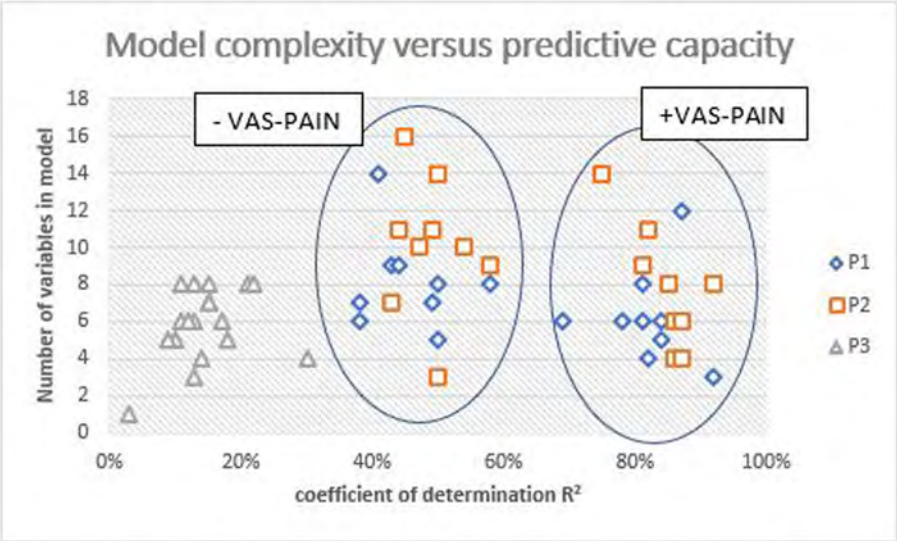
Abstract Number: 1734

The Challenge of Assessing Wellbeing from the Patients` Perspective in Early Rheumatoid Arthritis

Diederik De Cock[1], Tianna Poffe[2], Geert Verbeke[2], Sofia Pazmino[1], Veerle Stouten[1], Delphine Bertrand[1], Rene Westhovens[3] and Patrick Verschueren[4], [1]KU Leuven, Leuven, Belgium, [2]KU Leuven, Leuven, [3]University Hospitals Leuven, Belgium, Leuven, Belgium, [4]University Hospital Leuven, Leuven, Belgium

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Figure 1: R^2 and number of variables per model of wellbeing



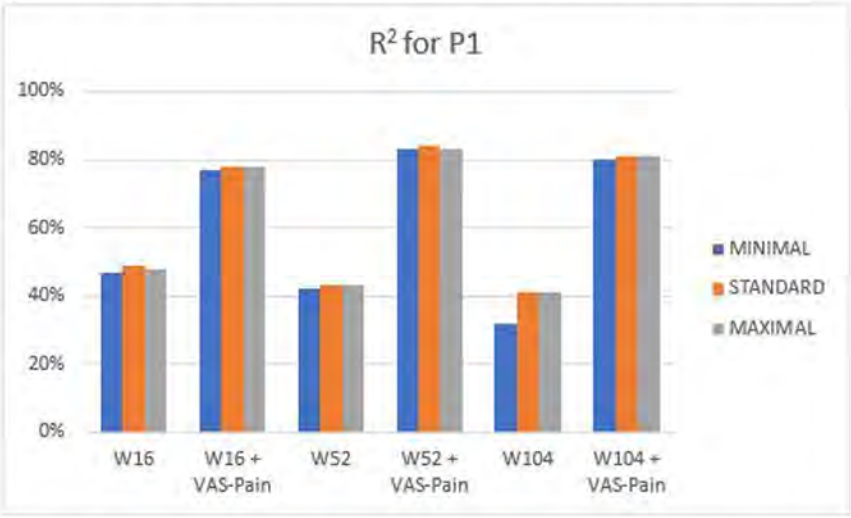
Each symbol represents one of the 54 model. Vas-PAIN is present in models with high R^2

Table 1: Root mean square error of test dataset per model

	RMSE - All patients			RMSE - Patients in remission			RMSE - Patients not in remission		
	P1	P2	P3	P1	P2	P3	P1	P2	P3
W16	15.3	11.2	15.6	16.5	17.6	15.6	16.9	18.2	17.9
W16 + VAS-Pain	9.6	7.0	9.9	10.6	10.1	8.5	16.2	18.2	17.9
W52	18.5	17.5	17.3	17.3	17.1	12.9	17.0	12.3	19.3
W52 + VAS-Pain	10.2	8.9	6.9	8.5	8.5	9.7	16.6	11.8	19.5
W104	14.9	21.2	14.0	17.4	16.9	12.1	17.4	15.5	20.3
W104 + VAS-Pain	7.0	10.6	9.4	9.4	9.5	8.9	17.9	16.2	21.8

RMSE (0-100) = root mean square error. Lower values indicate better fit. Thresholds lower than 10 in green, between 10 and 20 in orange, and over 20 in red.

Figure 2: Comparison of standard model with minimal and maximal input sensitivity analyses



Sensitivity analyses were regression models (1 - MINIMAL) only including the common predictors from previous models or (2 - MAXIMAL) selecting all predictors present in ≥1 model. Proxy P1 was chosen as example. Results for P2/P3 were similar.

Background/Purpose: Although more effective therapeutics and treatment strategies for Rheumatoid Arthritis (RA) have improved many patient-reported outcomes (PROs), still a sizeable number of patients in clinical remission report reduced wellbeing.Therefore, we explored PROs contributing to wellbeing of patients with early RA.

Methods: Patients from the 2-year pragmatic treat-to-target Care in Early Rheumatoid Arthritis (CareRA) trial were included. Patients were treated intensively, with combinations of csDMARDs and glucocorticoids, except 1 group starting MTX only in a tight-step-up approach.

Eight different validated questionnaires were taken, including the Arthritis Self-Efficacy Scale (ASES), the multidimensional Fatigue Inventory (MFI), the Pittsburgh Sleep Quality Index (PSQI) the Revised Illness Perception Questionnaire (IPQ-R), the Utrecht Coping List (UCL), the Short Form 36 (SF-36), RA Quality of Life questionnaire (RA-QOL) and the Social Support List (SSL). Questionnaires were obtained at baseline, week (W)16, 52 and 104 except for the IPQ and UCL, which were only taken at baseline and W16.

Regression models were constructed to define wellbeing at W16, 52 and 104. Three proxies for patient wellbeing were chosen, on a scale of 0-100: (P1) Patient Global Assessment (PGA) on a Visual Analogue Scale (VAS); (P2) a patient factor derived from a previous principal component analysis combining PGA, pain and fatigue on VAS and the Health Assessment Questionnaire (HAQ)[1]; and (P3) based on the time-weighted average of reconstructed EuroQoL-5 Dimension (EQ-5D) scores based on HAQ, age, pain on VAS and gender[2]. Three patients` groups per time point were created including all patients, patients in remission (DAS28crp< 2.6) and not in remission. As predictors, all subscales of the 8 validated questionnaires, summing to 83 variables, with and without VAS-Pain were used per time point in 54 models in total. Data reduction used forward, backward and stepwise selection based on the Aikake information criteria. Missing data was handled by multiple imputation (n= 15).

Models were validated by randomly splitting the data in a training (75%) and test (25%) set. The root mean square error (RMSE) compared these 2 datasets to test model robustness. We performed sensitivity analyses with regression models (1 - MINIMAL) only including the common predictors from previous models or (2 - MAXIMAL) selecting all predictors present in ≥1 model.

[1]Pazmino et al. Ann Rheum Dis. 2020;79 (S1):578

[2]Pazmino et al. Ann Rheum Dis. 2020;79(5):556-565

Results: In total, 379 patients were included. Overall, 63 of the 83 predictors were used in the regression analyses. Figure 1 shows the complexity versus the predictive capacity per model. Table 2 gives the RMSE per model. R^2 for the original models was between 3-92%, for minimal models 6%-86%, and for maximal models 1%-87%. Figure 2 compares the standard to the sensitivity analyses for PGA.

Conclusion: VAS-pain remains essential in determining patient wellbeing, even in patients in remission where pain levels should be theoretically lower. Determining uniformly patient wellbeing is challenging as different definitions lead to ambiguous results.

Disclosure: D. De Cock, None; **T. Poffe**, None; **G. Verbeke**, None; **S. Pazmino**, None; **V. Stouten**, None; **D. Bertrand**, None; **R. Westhovens**, Celltrion, Inc., 2, 5, Galapagos NV, 2, 5, Gilead Sciences, Inc., 2, 5; **P. Verschueren**, Pfizer, 9.

Abstract Number: 1735

Effect of Aerobic Land-based Exercise Intervention on Fatigue in Rheumatoid Arthritis: A Systematic Review and Meta-analysis

Samar Aboulenain[1], Arezo Farhangi[2], Elie Donath[1] and Ozlem Pala[3], [1]University of Miami Miller School, West Palm Beach, FL, [2]University of Miami Miller School, Palm Beach Gardens, FL, [3]University of Miami Miller School, Fort Lauderdale, FL

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Persistent fatigue can be debilitating for patients with rheumatoid arthritis (RA). Although fatigue partially improves after the initiation of DMARDs, suggesting an inflammatory process, it does not fully resolve with control of the disease activity. There is a glaring need for effective treatment options for the management of fatigue in patients with RA. This study is aimed to evaluate the efficacy of aerobic exercise intervention programs on lowering fatigue levels in patients with RA.

Methods: A systematic review of the literature was conducted through Pubmed, Embase and Cochrane Library from April 2014 to March 2020. This research was partially drawn from a prior meta-analysis/systematic review of the literature in which five studies were identified from 1985 to April 2014. Rongen-van Dartel, S. A., Repping-Wuts, H., Flendrie, M., Bleijenberg, G., Metsios, G. S., van den Hout, W. B., van den Ende, C. H., Neuberger, G., Reid, A., van Riel, P. L., & Fransen, J. (2015). Effect of Aerobic Exercise Training on Fatigue in Rheumatoid Arthritis: A Meta-Analysis. Arthritis care & research, 67(8), 1054–1062. https://doi.org/10.1002/acr.22561 Randomized controlled trials (RCTs) evaluating the effect of supervised land-based aerobic moderate-to-high physical activity on clinical outcomes of adult patients who meet the ACR/EULAR classification criteria of RA were considered for inclusion. Those studies implementing exercise interventions for less than 15 minutes duration in each session, less than two sessions per week, or less than four weeks follow up duration were excluded. Meta-analyses were conducted using fixed-effects modeling to estimate the pooled effect sizes. Standardized mean difference (SDM) and 95%Confidence intervals (CI)

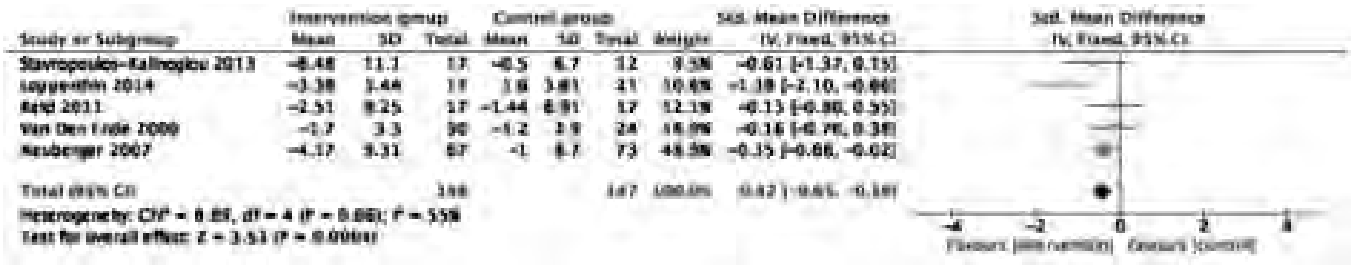


Figure 1. Forest plot of the short-term analysis for the effect of physical activity intervention on fatigue level on patients with rheumatoid arthritis. SD: standard deviation. IV: inverse variance. CI: confidence interval.

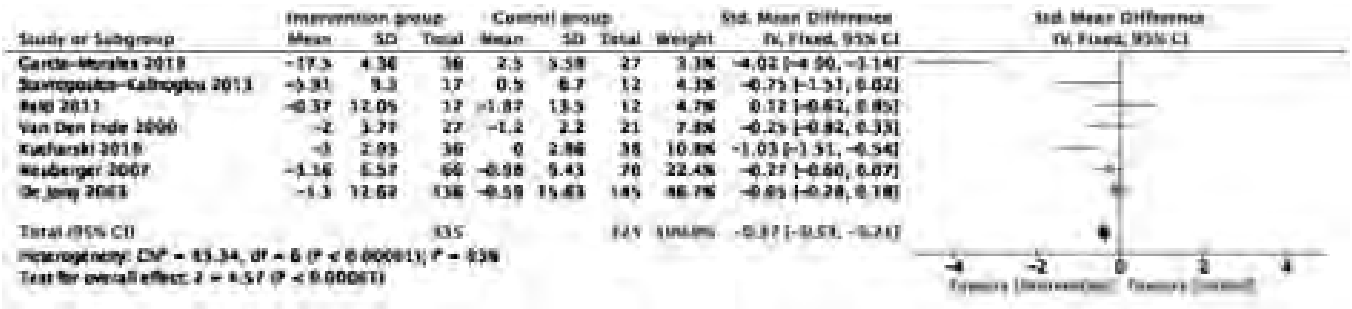


Figure 2. Forest plot of the long-term analysis for the effect of physical activity intervention on fatigue level on patients with rheumatoid arthritis. SD: standard deviation. IV: inverse variance. CI: confidence interval.

are reported at short-term follow up (4-12 weeks) and long-term follow-up (20-24 weeks) after enrollment. Heterogeneity was further explored with I-squared testing and sub-group analyses.

Results: Eight RCTs were selected with a total of 713 participants. There were five and seven studies, respectively, conducting short-term and long-term analyses. Aerobic land-based physical activity interventions were found to improve fatigue score at short-term follow-up (-0.42, 95%CI [-0.65, -0.19], $p < 0.001$) (Figure 1) and long-term follow-up (-0.37, 95%CI [-0.53, -0.21], $p < 0.001$) (Figure 2). Heterogeneity was moderately elevated in the short-term analysis and significantly elevated in the long-term analysis. The high heterogeneity in the long-term analysis was markedly reduced when excluding studies that selected special populations (n=2), including only women in one study or only elderly in the other study.

Conclusion: Moderate-to-high land-based aerobic exercise for at least 4 weeks is an effective intervention to improve fatigue in adult patients with rheumatoid arthritis. Physical activity may have a more potent effect on fatigue in women and elderly patients with rheumatoid arthritis. More RCTs are needed to evaluate the effect of exercise in these special populations.

Disclosure: S. Aboulenain, None; **A. Farhangi**, None; **E. Donath**, None; **O. Pala**, None.

Abstract Number: 1736

Health Assessment Questionnaire Predicts All-Cause Mortality at One Year in Patients with Early Rheumatoid Arthritis

Safoora Fatima[1], Orit Schieir[2], Marie-France Valois[3], Susan Bartlett[3], Louis Bessette[4], Gilles Boire[5], Glen Hazlewood[6], Carol Hitchon[7], Edward C Keystone[8], Diane Tin[9], Carter Thorne[9], Vivian Bykerk[10], Janet Pope[11] and Canadian Early Arthritis Cohort (CATCH) Investigators[12], [1]University of Western Ontario, London, ON, Canada, [2]Canadian Early Arthritis Cohort Study, Montreal, Canada, [3]McGill University, Montreal, Canada, [4]Laval University, Quebec, Canada, [5]Universite de Sherbrooke, Sherbrooke, Canada, [6]University of Calgary, Calgary, AB, Canada, [7]University of Manitoba, Winnipeg, MB, Canada, [8]Mount Sinai Hospital, Toronto, ON, Canada, [9]Southlake Regional Health Centre, Newmarket, ON, Canada, [10]Hospital for Special Surgery, New York, NY, [11]Department of Medicine, University of Western Ontario, St. Joseph's Health Centre, London, ON, Canada, [12]Canadian Early Arthritis Cohort (CATCH) Study, Toronto, Canada

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with RA are at greater risk of mortality than the general population. Higher HAQ disability has been associated with hospitalizations and mortality in established RA; whether HAQ disability predicts mortality in early RA (ERA) is unknown.

Methods: Data were from adult early RA patients (symptoms < 1 year) enrolled in the Canadian Early Arthritis Cohort (CATCH) between 2007 and 2017; who initiated treatment with 1 or more DMARDs and had completed HAQ data at baseline and 1 year. Descriptive statistics, t-tests and chi-square tests were used to summarize and compare baseline patient characteristics including sociodemographic variables, RA characteristics and comorbidities amongst deceased and non-deceased patients. Discrete-time proportional hazards models were used to estimate crude and multi-adjusted associations between HAQ at baseline and 1 year, respectively, with all-cause mortality in each year of follow up.

Results: 1724 patients with early RA; mean age 55 years and 72% female were included. Over 10 years, 62 deaths (2.4%) occurred. Deceased patients had higher HAQ scores and DAS28(disease activity) scores at baseline and 1 year versus the non-deceased group. Age, male sex, lower education, smoking, more comorbidities, higher baseline disease activity and steroid use were associated with mortality in unadjusted survival models. Contrary to HAQ at baseline, the association between all-cause mortality and HAQ at 1 year remained significant even after adjusting for age, gender, comorbidities, disease activity, smoking, education, seropositivity, symptom duration and steroid use in adjusted survival models. HAQ baseline unadjusted hazard OR was 1.46 (CI 1.02-2.09) and adjusted 1.25 (CI 0.81-1.94) vs. HAQ at 1 year unadjusted hazard OR was 2.58 (CI 1.78-3.72) and adjusted 1.75 (CI 1.10-2.77).

Conclusion: Higher self-reported disability (high HAQ) at 1 year was significantly associated with all-cause mortality in a large early RA cohort suggesting that poorer disease control and function in the first year of RA contributes to higher mortality.

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Celltrion, 2, 5, 8, Eli Lilly, 2, 5, 8, Pfizer Inc, 2, 5, 8, Merck, 2, 5, 8, Sandoz, 2, 5, 8, Samsung Bioepsis, 2, 5, 8, Myriad Autoimmune, 2, 5, 8, Purapharm, 2, 5, 8, Janssen, 2, 5, 8, Sanofi-Genzyme, 2, 5, 8, Amgen, 2, 5, 8, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, F. Hoffman-La Roche Ltd., 2, 5, 8, Genentech, 2, 5, 8, Gilead, 2, 5, 8, UCB, 2, 5, 8; **D. Tin**, None; **C. Thorne**, Abbvie, 1, 2, Amgen, 1, 2, Celgene, 1, 2, CaREBiodam, 1, Centocor, 1, Janssen, 1, Lilly, 1, Medexus/Medac, 1, 2, Merck, 1, Novartis, 1, 2, Pfizer, 1, 2, Sanofi, 1; **V. Bykerk**, Amgen, 1, BMS, 1, Gilead, 1, Sanofi-Genzyme/Regeneron, 1, Scipher, 1, Pfizer, 1, UCB, 1, NIH, 1; **J. Pope**, AbbVie, 2, 5, Amgen, 5, 8, Lilly, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 5, 8, Sandoz, 5, 8, Roche, 2, 5, 8, Pfizer, 5, 8, Novartis, 5, 8, Merck, 2, 5, 8, Janssen, 5, 8, Gilead Sciences, Inc., 2, 5, BMS, 2, 5, 8, Abbott, 5, Actelion, 5, AstraZeneca, 5, Bayer, 5, Boehringer Ingelheim, 5, EICOS, 5, Emerald, 5, GlaxoSmithKline, 5, Medexus, 5, Seattle Genetics, 2; **C. (CATCH) Investigators**, Amgen, 2, Pfizer Canada, 2, Medexus Inc., 2, Eli Lilly Canada, 2, Merck Canada, 2, Sandoz Canada, Biopharmaceuticals, 2, Gilead Sciences Canada, 2, Hoffmann-LaRoche, 2, Janssen Biotech, 2, UCB Canada, 2, Bristol-Myers Squibb Canada, 2, Sanofi Genzyme, 2, AbbVie Corporation, 2.

Abstract Number: 1737

What Influences Fatigue Improvement in Rheumatoid Arthritis? A Prospective Cohort Study

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Fatigue is a common and debilitating complication in patients with rheumatoid arthritis (RA). Its mechanism is not fully elucidated, and when persistent is often challenging to manage. It often does not fully resolve despite treatment with DMARDs thus raising the necessity to uncover other factors that might influence its improvement. This study aimed to explore the characteristics that might have an influence on fatigue improvement in adult patients with RA.

Methods: A single-centered prospective cohort study of patients ≥18 years old who were enrolled in the Corrona RA Registry from 2011 to 2020. Fatigue level was measured using the fatigue Visual Analog Scale (VAS-F) 0-100 at the time of enrollment and 6, 12 and 24 months follow-up appointments. The minimal clinically important difference (MCID) for the fatigue VAS (6.7% change from baseline) was used to assess the change in fatigue level compared to baseline. Univariate and multivariate (adjusting for age, gender and BMI) logistic regression analyses were performed to examine the association between fatigue improvement at 12 months and a wide variety of baseline demographics and disease characteristics.

Results: One hundred and eleven patients with RA were identified, of which 52 reported fatigue scores at 12 months. The median (interquartile range [IQR]) for age was 55 (44-61) years and the majority were Caucasian (67%), females (88%), and with an above-average BMI (71%). The median (interquartile range [IQR]) of the fatigue scores at enrollment and 12 months were 40 (8-70) and 38 (5-58), respectively. At 12 months, fatigue level improved in half of the population (Table 1).

	6 months	12 months	24 months
VAS-F [Median (IQR)]*	35 (5-60)	38 (5-58)	13 (5-52.5)
Improved %	53%	50%	69%
Worsened %	31%	31%	21%
Unchanged %	16%	19%	10%

VAS-F; fatigue Visual Analog Scale. IQR; interquartile range. *Scores reported on a scale of 0-100 mm on which higher numbers indicate greater fatigue.

Table 1. Fatigue score and progression in the study participants at 6, 12 and 24 months compared to baseline.

In a univariate analysis, several predictors were noted to be associated with improved fatigue scores. These included female gender ($p< 0.001$), non-smokers ($p< 0.01$) and increased baseline fatigue levels ($p=0.04$). Several other variables, including depression, showed a trend towards significance. These variables were further investigated by multivariate analyses (adjusting for age, gender and BMI). As may be expected, each additional unit in baseline fatigue was associated with a 2.7% increased likelihood of improvement in fatigue at one year (OR 1.027, 95% CI 1.006-1.048, $p=0.01$). Additionally, non-smokers were found to be highly likely to improve fatigue levels at year-end (OR 7.63, 95% CI 1.11-52.63, $p=0.04$) and those with baseline depression were found to be highly unlikely to improve fatigue levels (OR 0.17, 95% CI 0.03-0.82, $p=0.03$).

Many other variables were examined, and none found to be significantly associated with the outcome of interest including BMI, employment status, physical activity level, pain control, number of comorbidities, duration of RA, change in CDAI score, starting biological DMARDs, or RF and CCP seropositivity.

Conclusion: We observed in this cohort study an improvement in fatigue level in half of the population. Fatigue improvement was associated with female gender, non-smokers, lack of depression and higher levels of fatigue at baseline.

Disclosure: S. Aboulenain, None; **E. Donath**, None; **O. Pala**, None.

Abstract Number: 1738

Promote Treat-to-Target for RA via Empowering Patients: A Cohort Study from China by Smart System of Disease Management (SSDM)

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Treat-to-Target (T2T) strategy are critical for the treatment of RA, but Chinese rheumatologists can hardly provide patients with a complete assessment in the clinic due to limited time. According to DAS28 scores, disease activity of the cohort was divided into four groups: remission (Rem), low (LDA), moderate (MDA) and high (HDA) disease activity. T2T, achieving a DAS28 score lower than 2.6 (Rem) or below 3.2 (LDA), is the main management strategy recommended by ACR and EULAR. To evaluate the patterns of T2T and related influential factors among RA patients after applying SSDM with repeated self-assessment in the real world.

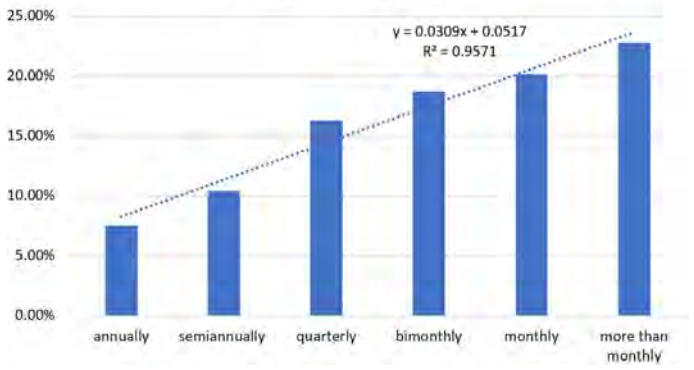
Methods: SSDM is a mobile application for disease management. Patients were trained to do DAS28 assessment with SSDM and required for repeating self-assessment after leaving the hospital. After entry by patients, data can be synchronized to the SSDM terminal of authorized rheumatologists. Based on the patients' data, rheumatologists will provide medical advices to them.

Results: From Jan 2015 to Jan 2020, 68,103 RA patients enrolled in SSDM. The mean age of 51.58±12.86 years old and median disease duration is 3.83 years. 52,355 patients performed self-assessment of DAS28, HAQ and morning stiffness duration totally for 114,792 times. Proportion of patients in Rem, LDA, MDA and HDA was 26%, 17%, 44% and 13% respectively at baseline. Among them, 5,488 RA patients from 219 hospitals across China were followed up for more than 12 months through SSDM.

The rate of T2T achievers were 50.20% (2,755/5,488) at baseline, and improved significantly to 65.14% (3,575/5,488) after 12 months follow up, $p< 0.05$. Among T2T achievers at baseline, 77.20% (2,127/2,755) maintained T2T, 22.80% (628/2,755) relapsed. Of patients who didn't achieve T2T at baseline, only 56.75% (1,551/2,733) achieved T2T after 12 months follow up.

The frequency of self-assessment for DAS28 on T2T has been analyzed. Results indicated that the more frequent of the self-assessments being performed by patients, the higher improvement of T2T rate will be. The improvement rates of T2T in the subgroups which self-assessed with SSDM by annually, semiannually, quarterly, bimonthly, monthly and more frequent than monthly were 7.49%, 10.40%, 16.29%, 18.73%, 20.13% and 22.77% respectively.

Figure 1. The improvement rate of T2T in the subgroups with assessment frequency



The improvement rate (y) of T2T was positively correlated with the frequency of self-assessment for DAS28(x) independently. The regression equation as "y = 0.0309x + 0.0517", r = 0.9785, p< 0.01 (Figure 1).

Conclusion: Significant improvement was observed under applying SSDM through empowering RA patients. After proactive disease management via SSDM for more than 12 months, patients with DAS28< =3.2 score at baseline had a significantly higher retention rate of Rem disease activity. The patients who performed more frequent self-assessments had lower probability of relapse and higher rate of T2T. SSDM is a valuable tool for long term follow-up through empowering patients.

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Abstract Number: 1739

Patients with Early Rheumatoid Arthritis Considered to Have a Favourable Risk Profile and Treated According to a Step-up Strategy Have an Increased Risk of Chronic Analgesic Consumption

Sofia Pazmino[1], Annelies Boonen[2], Diederik De Cock[1], Veerle Stouten[1], Delphine Bertrand[1], Johan Joly[3], Rene Westhovens[4] and Patrick Verschueren[5], [1]KU Leuven, Leuven, Belgium, [2]Maastricht University Medical Center, Maastricht, Netherlands, [3]University Hospitals Leuven, Leuven, Vlaams-Brabant, Belgium, [4]University Hospitals Leuven, Belgium, Leuven, Belgium, [5]University Hospital Leuven, Leuven, Belgium

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Pain remains the highest priority for improvement to patients with Rheumatoid Arthritis (RA). Analgesic prescription in RA was historically a stand-alone approach and afterwards in conjunction with different strategies incorporating early introduction of DMARDs.

We aim to explore the analgesics prescribed in patients with early RA with a favourable risk profile during the first 2 years in the Care in early RA (CareRA) trial.

Methods: Patients with early RA (≤1 year) and a low-risk profile recruited in the 2-year pragmatic investigator-initiated treat-to-target CareRA trial were studied. Low-risk patients (fulfilling 2/3: absence of erosions, negativity to rheumatoid factor and anti-citrullinated protein antibodies, low disease activity score) were randomized to either methotrexate (MTX) 15mg/week with a step-down glucocorticoid (GC) scheme (prednisone 30mg)-COBRA Slim-, or to MTX 15mg/week and no oral GC -Tight-Step-Up-(TSU). All concomitant prescriptions for analgesics for each patient were recorded, including name, dosage, frequency, start/end date and indication as free text. Chronic intake (≥90 days during the trial) of NSAIDs, acetaminophen, or opioids including tramadol, and antidepressants prescribed for musculoskeletal (MSK) pain were considered.

Comparisons were performed with chi-square when appropriate and corrected for multiple testing with Holm's method.

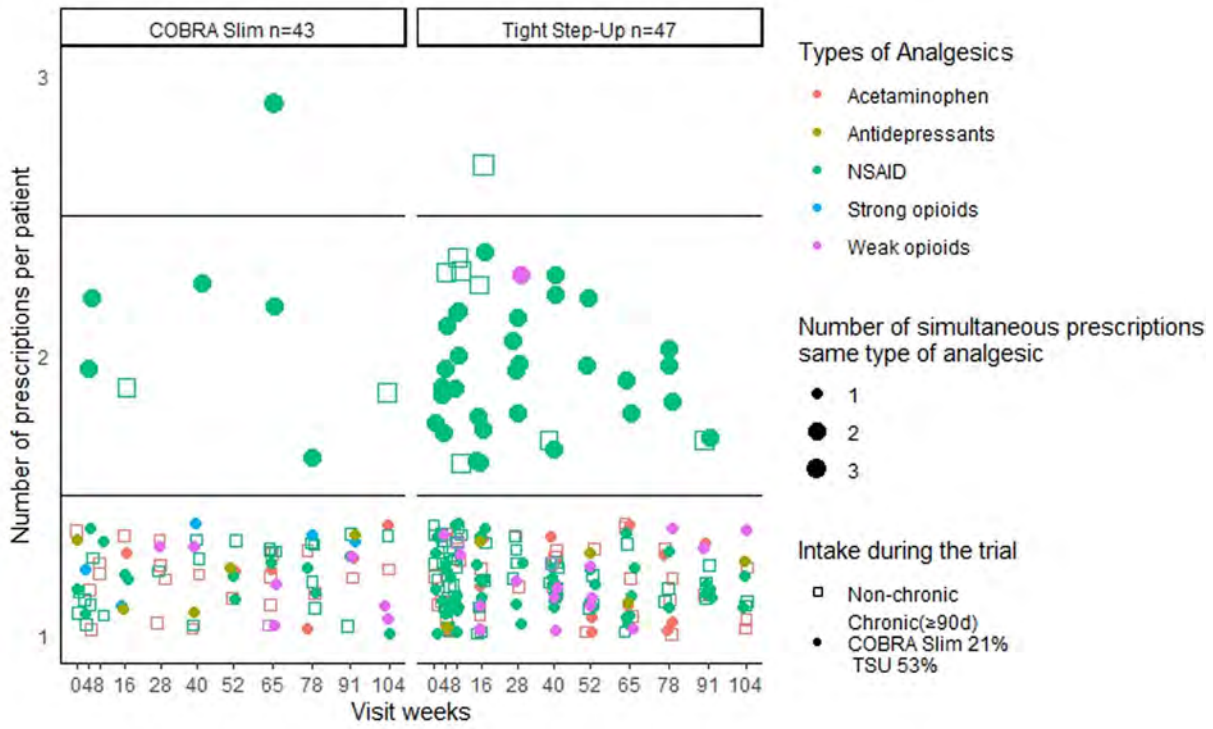

Figure 1. Graphical representation of drug intake at every visit-week during the trial

Results: Of the 90 patients recruited in the *low-risk* group, 43 were randomized to COBRA Slim and 47 to TSU. COBRA Slim, had a total of 67 analgesic prescriptions for MSK pain during the trial for 26/43 (60%) patients of which 9/43(21%) daily chronically (DC). TSU had a total of 107 analgesic prescriptions for 43/47 (92%) patients of which 25/47(53%) DC. At baseline, 18/43 (42%) patients starting COBRA Slim and 28/47 (60%) starting TSU used analgesics (p=0.14). Before the start of the study 33/43 (77%) of patients in the COBRA Slim and 32/47 (68%) in the TSU arm had been using analgesics (p=0.5). The total number of patients on analgesics at any time during the study (p< 0.001) and chronically (p< 0.01) was significantly different between treatment arms. Number of patients DC on NSAIDs was also significantly different (p< 0.05) between COBRA Slim 6/43 (14%) and TSU 19/47 (40%). Figure 1 is a graphical representation of the drug intake at every visit week during the trial. Each mark is a prescribed analgesic per patient, per time point; a bigger mark means more than one prescription of the same analgesic type per patient per timepoint.

Conclusion: Almost every patient in TSU was prescribed an analgesic for MSK pain compared to 60% in the group treated with MTX and a step-down GC scheme (COBRA Slim). Chronic analgesic intake was more than double in TSU. It is notable that even in patients considered to have a favourable risk profile, when the initial treatment did not include oral GC bridging, there was a significant consumption of analgesics becoming chronic for a significant proportion of them. To benefit maximally from the window of opportunity for treating early RA, intensive remission induction strategies (with GCs) should be applied even in patients without traditional factors of poor prognosis.

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Abstract Number: 1740

Determinants of Influenza Vaccine Hesitancy in Rheumatoid Arthritis According to the WHO-SAGE Matrix

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: In rheumatoid arthritis (RA), influenza infection and its complications are important causes of hospitalization and death. Although routine annual inactivated influenza vaccine (IIV) is recommended in RA, a significant proportion of patients delay the acceptance or refuse vaccines despite the availability of vaccine services (i.e. vaccine hesitancy). Understanding the causes of vaccine hesitancy in RA is key to improve vaccination coverage and thus reduce the burden of influenza.

Methods: Between November and March 2020, we conducted a cross-sectional study of consecutive RA patients presenting to a rheumatology clinic at a large Canadian tertiary hospital. Patients completed a survey on determinants of influenza vaccine hesitancy developed by the WHO-Strategic Advisory Group of Experts (SAGE) on immunization. Questions addressed individual, group, and contextual influences, as well as vaccine-specific issues involved in vaccine acceptance. Patients were classified into 3 groups based on how likely it was for them to get the IIV: 'unlikely' (refused IIV), 'likely' (accepted IIV) or 'uncertain'. Multivariate logistic regression was performed to evaluate factors associated with vaccine refusal.

Results: We studied 101 patients with a mean age (±SD) of 54±19 years, and RA duration 10±8.8 years; 74% were females. Over a third (38%) of the patients did not receive IIV the previous year, and 47% reported not having received the IIV on a yearly basis since RA onset. In total, 58% accepted IIV, 28% refused IIV, and 14% were uncertain. Among the contextual influences of vaccine acceptance: (a) 73% of RA patients trust that the government was making decisions in their best interest with respect to IIV, (b) 29% considered that the IIV should be compulsory, and (c) 42% trust pharmaceutical companies to provide safe and effective flu vaccines. Individual and group experiences identified to influence vaccine acceptance in RA included: (a) previous bad reactions (27%), (b) not enough information about IIV and its safety (37%), (c) concerns about IIV safety (46%), and (d) uncertainty about IIV benefits (39%). Almost half (42%) were willing to pay for IIV, and the same percent (42%) were willing to take time off from work to get the IIV. In multivariate analysis, RA patients who refused IIV were less likely to trust pharmaceutical companies to provide safe and effective vaccines (odds ratio-OR, 95% confidence interval-CI) 43.46 (1.41, >999); and were less likely to consider that IIV should be compulsory 50.89 (1.51, >999).

Conclusion: Over 40% of RA patients living in a universal, publicly funded health-care system have some degree of IIV hesitancy. Contextual and individual influences contribute to this complex and context-specific phenomenon. Actionable hesitancy determinants include those that relate to education on the benefits and safety of the IIV.

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Abstract Number: 1741

Does Preventive Care Matter? (in RA)

Morgan Greenwald[1], JoAnn Ball[1], Shannon Lopez[1], Monica Berg[1] and Maria Greenwald[1], [1]Desert Medical Advances, Palm Desert, CA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Preventive medical care improves morbidity and mortality. The assessment included 28,105 RA patients from prospective randomized trials.

Methods: Nested data from a single site was compared to global data in 34 pivotal studies using immune therapies for RA. Another 5 studies in long term follow up in older RA patients were also analyzed. Data was extracted from NDAs submitted for FDA approval for 5 TNFi therapies, 5 JAKi therapies, rituximab, abatacept, IL-1, and IL-6 therapy. The nested site participated in each study, so entry criteria, age, concomitant medication, and intervention were identical. All subjects fulfilled the ACR criteria for RA and trials had IRB approval. Safety results for the global sites in the NDA are available to the public from accessdata.fda.gov. Safety data of special interest were incidence of death from any cause, MACE, pneumonia, and zoster. The nested site instituted 10 specific preventive care measures. These included:

1) vaccination for influenza, pneumonia, and zoster; 2) hypertensive treatment for blood pressure >140/90; 3) diabetes treatment if HbA1C >9; 4) treatment for uric acid >7; 5) statin therapy if LDL >120; 6) treatment if BMI >30 including staff dietician every 3 months; 7) chewable aspirin 81 mg/d; 8) prenatal vitamin for 1 mg folate; 9) daily sinus wash to decrease URI (NeilMed); 10) no use of corticosteroids or narcotics. All preventive measures were conducted at the nested site.

Results: (tables 1, 2, 3)

Zoster: There were 18,696 subjects in JAKi trials in the global population and 562 at the nested site. Zoster incidence in trials using JAKi decreased between 2005-2020. Key to this decline was Zostavax approval in 2006 and Shringrix approval in 2017. At the nested site, zoster vaccines for all started in 2006.

Pneumonia and Death due to Infection: There were 28,105 subjects in the global population and 924 subjects at the nested site. Pneumonia events were lower in the nested site than the global population, both in the long term trials (ages 63-70) and in the shorter trials (ages 51-53). All nested site subjects had pneumonia vaccination. Deaths due to infection were lower at the nested site (about one third of deaths in RA were due to pneumonia).

Mortality: There were 4469 global subjects and 154 at the nested site in the older population of the long term trials. Mortality was less at the nested site in these older subjects. In the shorter trials with younger subjects, of the 28,105 global subjects and 924 in the nested site, overall mortality was not different.

Mace: MACE events were not better at the nested site for the older population (followed 3-7 years) nor the younger population (followed 6 months to 2 years).

ZOSTER Events Time Line (RA patients on JAKi)

2006 Zostavax approved — 2017 Shringrix approved

	2005	2006	2012*	2020*
Global events	5.8% (CI 4.5-6.7)	4.4% (CI 3.7-9.2)	2.6% (CI 1.6-3.8)	3.4% (CI 0.8-4.9)
Nested site events	12% (CI 1.1-16)	2%* (CI 1-3.3)	1%* (CI 0.2-1.4)	0.7%* (CI .07-1.3)
p	ns	ns	<0.02*	<0.02*
* All patients in the nested site were vaccinated for zoster				

Table 1

Long term JAKi studies f/u for 3-7 years (Avg age 63 at BL to 70 at f/u)

Rate % (95%CI)

Global	Mortality*	Pneumonia*	InfectionDeath*	URI	Zoster*	MACE	Thrombosis*
N= 4969	2.8%(1.1-3.8)	5.6%(4.4-9.3)	1%(0.5-1.4)	47%(41-54)	3.3%(2.9-3.6)	0.9%(0.3-2.0)	1.3%(0.5-1.5)
Nested site							
N = 154	0.3%(0.1-0.8)	0.5%(0.4-0.9)	0	40%(35-47)	0.5%(0.4-0.7)	0.5%(.4-.7)	0.6%(.4-.9)
p value	<0.007	<0.002	<0.002	ns	<0.001	ns	<0.03

*Nested site events were significantly lower for infectious endpoints of pneumonia, infectious deaths, and zoster.
Nested site had lower mortality and thrombotic events over 3-7 years.
JAKi included are tofacitinib, baricitinib, upadacitinib, and filgotinib.
TB was very rare in all studies (<0.2%)
81% female subjects, 22% from USA.

Table 2

Thrombotic events

The nested site had fewer thrombotic events in the JAKi trials and subjects took chewable aspirin 81 mg/d.

Conclusion: This is a causal inference study using prospective data from 39 trials. Vaccination is a likely explanation for less zoster, pneumonia, infectious deaths, and mortality at the nested site. The lack of any data over 10 years limits efforts to measure reduction of uncommon MACE events (control of blood pressure, diabetes, cholesterol and diet). Vaccines are clearly necessary in medical care for RA. Vetted data from NDAs can yield insight for healthcare.

Studies of RA with Immune Rx and f/u 6 mo—24 mo (Avg age 51 at BL to 53 at f/u)

Rate % (95%CI)

Global	Mortality	Pneumonia*	Inf Death*	URI	Zoster*	MACE	Thrombosis
N= 28,105	0.65%(0.4-.8)	3.6%(1.1-4.5	1%(0.8-1.7)	48%(21-70)	1.7%(0.5-2.5)	0.5%(0.4-.9)	NA
Nested site							
N= 924	0.8%(0.3-1.1)	0.2%(0.1-.25)	0	35%(20-44)	0.6%(0.4-1)	0.6%(0.4-.9)	0
p value	ns	<0.004	<0.001	ns	<0.05	ns	NA

*Nested site events were significantly lower in infectious endpoints of pneumonia, infectious deaths, and zoster.
Average age 51, 79% female, 82% Caucasian, 50% USA
TB was very rare in all studies 0.2%
Data was not consistently collected for thrombotic events in the majority of short term trials.
Biologic studies included in the NDA submission data: tofacitinib, baricitinib, upadacitinib, filgotinib, peficitinib, adalimumab, etanercept, certolizumab, Infliximab, rituximab, abatacept, tocilizumab, anakinra, canakinumab

Table 3

Disclosure: M. Greenwald, None; **J. Ball**, None; **S. Lopez**, None; **M. Berg**, None; **M. Greenwald**, None.

Abstract Number: 1742

Patients' and Rheumatologists' Perceptions on Preventive Intervention in Rheumatoid Arthritis and Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Persons at risk of developing rheumatoid arthritis (RA) may benefit from lifestyle[1] or pharmacological[2] interventions aimed at primary prevention. Although less studied, the same may apply to persons at risk of axial spondyloarthritis (axSpA)[3]. Our aim was to investigate and compare the willingness of individuals at risk of RA or axSpA and rheumatologists to initiate preventive intervention.

Methods: Individuals at risk of RA (arthralgia and anti-citrullinated protein antibodies (ACPA) and / or rheumatoid factor (RF) positivity without arthritis (RA risk cohort; n=100)), healthy first degree relatives of HLA-B27 positive axSpA patients (SpA risk cohort; n=38) and Dutch rheumatologists (n=49) completed a survey on preventive intervention in the at risk phase of RA (RA risk cohort and rheumatologists) or axSpA (SpA risk cohort) which included questions on

Disease risk	At risk of RA (%)	At risk of axSpA (%)	Rheumatologists (%)	At risk of RA versus axSpA	at risk of RA versus rheumatologists
	100% effective medication, no side effects				
30%	53	55	74	p = 0.812	**p = 0.017**
70%	69	92	92	**p = 0.005**	**p = 0.002**
	100% effective medication, minor side effects or immune suppression				
30%	26	29	31	p = 0.727	p = 0.554
70%	40	66	76	**p = 0.007**	**p < 0.001**
	100% effective medication, minor general side effects				
30%	40	47	88	p = 0.433	**p <0.001**
	Medication postpones disease development for 10 years, no side effects				
70%	61	66	57	p = 0.604	p = 0.652

axSpA: axial spondyloarthritis, RA: rheumatoid arthritis

Table 1. Willingness to start preventive medication

disease perception, lifestyle intervention (i.e. smoking, alcohol consumption, exercise and various dietary changes) and preventive medication[4].

Results: Participants considered RA and axSpA to be a serious disease (median VAS (0-10) 6.5 (RA) and 6 (SpA)). Despite some concern about their increased risk, most did not expect to develop the disease (median VAS 3 for both). Participants were willing to change a median of 7 out of 13 lifestyle components in multiple areas, whereas only 35% of rheumatologists gave lifestyle advice to >50% of at risk patients. The willingness to use 100% effective preventive medication without side effects was 53% (RA), 55% (SpA) and 74% (rheumatologists) at a 30% disease risk. This increased to 69% (RA) and 92% (SpA and rheumatologists) at a 70% disease risk. With minor side effects, willingness was 26%, 29% and 31% (30% risk) versus 40%, 66% and 76% (70% risk), respectively. Differences are shown in table 1.

Conclusion: Disease risk perception and willingness to start preventive intervention are similar between patients at risk of RA or axSpA. They seem highly willing to make several lifestyle changes to decrease disease risk and are generally willing to use medication in case of a clearly increased risk. Rheumatologists are overall more likely than at-risk patients to start preventive medication. Lifestyle advice was not given by the majority of rheumatologists contrasting with patients' high willingness to adjust lifestyle.

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[3] Brown MA et al. Ann Rheum Dis. 2000;59(11):883-6

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Disclosure: L. van Boheemen, None; **J. Bolt**, None; **M. ter Wee**, None; **H. de Jong**, None; **M. van de Sande**, Boehringer Ingelheim, 2, AbbVie, 5, Eli Lilly, 2, 5, MSD, 5, 8, Janssen, 2, Novartis, 2, 5, 8; **D. van Schaardenburg**, None.

Abstract Number: 1743

Perioperative Steroids in Rheumatoid Arthritis Patients Having Total Joint Replacements: Help or Harm?

Tariq Chukir[1], **Susan Goodman**[2], Haley Tornberg[3], Huong Do[4], Charlene Thomas[5], Alana Sigmund[3], Peter Sculco[6], Bella Mehta[6], Linda Russell[6], Mark Figgie[2] and Emily Stein[7], [1]Weill Cornell Medicine and New York Presbyterian Hospital, New York, [2]Hospital for Special Surgery, Weill Cornell Medicine, New York, NY, [3]Hospital for Special Surgery, New York, [4]Hospital for Special Surgery, New York, NY, [5]Weill Cornell Medicine, New York, [6]Hospital for Special Surgery/ Weill Cornell Medicine, New York, NY, [7]Endocrine Service, Hospital for special surgery, Department of Medicine, Weill Cornell Medical College, New York, NY

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

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Session Time: 9:00AM–11:00AM

Background/Purpose: Optimal perioperative glucocorticoids (GC) dosing for rheumatoid arthritis (RA) patients on chronic GCs undergoing total joint replacement is unknown. Ideal GC dosing prevents perioperative hypotension while also avoiding the complications associated with higher GC exposure. The purpose of this study was to determine whether preoperative GC exposure or perioperative GC dosing was associated with risk of complications in a large cohort of RA patients undergoing TJA.

Methods: A retrospective chart review was performed to identify patients with RA undergoing TJA at a single, high-volume institution. Glucocorticoid usage was recorded for all patients as well as cumulative perioperative GC dose during hospitalization. GC exposure was assessed by the number of doses, single or multiple, and cumulative amount of GC administered over the hospitalization period (in milligrams). Outcomes of interest included incidence of perioperative hypotension and inpatient complications (hyperglycemia, defined as blood glucose level > 180mg/dL, local or systemic infection, and cardiovascular events). Multivariable logistic regression was performed to evaluate the impact of GC dosing on these adverse events.

Results: Four hundred and thirty two RA patients undergoing TJA were included with 233 (54%) undergoing TKA. Mean age was 64±12 years and 78% were women. One hundred and thirty (30%) RA TJA patients were on chronic GC treatment (mean daily dose 7±4mg) and median cumulative perioperative GC dose was 37mg [IQR 27, 57]. Cumulative inpatient dose of GC was not associated with risk for perioperative hypotension during the hospitalization [unadjusted OR 1.00 (0.99-1.01) p=0.66]. Patients who received multiple doses had more post-operative adverse events compared to those who received single GC doses. Multivariable logistic regression adjusting for age, BMI and Charlson Comorbidity Index, showed patients with higher cumulative GC dose had higher risk for short-term complications with every 10 mg increase in GC dosing increasing inpatient complication risk by 8.4%, (p=0.02).

Conclusion: This study of 432 RA patients undergoing TJA found a 32% incidence of chronic preoperative GC usage. GC dosing during the intra- and early post-operative period was not associated with risk of hypotension. However, patients with higher GC exposure were more likely to have hyperglycemia and catheter-associated urinary tract infection (CAUTI). These findings suggest lower GC dosing does not increase risk of hypotensive perioperative events and avoids the increased risk of inpatient complications associated with high GC dosing regiments. Further research is needed to determine the optimal perioperative regimen for patients with RA undergoing arthroplasty.

	Single Dose	*Multiple Doses*	*P-Value*
	N=238	*N=149*	
Age (years)	65.0 [58.0;71.0]	64.0 [55.0;72.0]	0.24
Female Sex:	189 (79%)	116 (78%)	0.81
Race			0.18
Black	18 (8%)	18 (12%)	
Other	23 (10%)	18 (12%)	
White	195 (83%)	109 (75%)	
Ethnicity Group			0.01
Hispanic or Latino	12 (5%)	19 (13%)	
Not Hispanic or Latino	224 (95%)	126 (87%)	
Body mass index (kg/m^2)	28.1 [24.4;32.4]	28.8 [24.5;33.3]	0.39
Surgery Type:			0.99
Hip Replacement	110 (46 %)	69 (46%)	
Knee Replacement	128 (54%)	80 (54%)	
Anesthesia Type			0.26
Regional	216 (91%)	129 (87%)	
Other (Peripheral, Neuroaxial, and General)	22 (9%)	20 (13%)	
Congestive Heart Failure	0 (0%)	3 (2%)	0.06
Valvular Disease	14 (6%)	8 (5%)	0.99
Pulmonary Hypertension	0 (0%)	1 (1%)	0.39
Peripheral Vascular Disease	1 (0%)	2 (1%)	0.56
Neurological Disorders	6 (3%)	5 (3%)	0.76
Chronic Pulmonary Disease	38 (16%)	22 (15%)	0.86
Diabetes	18 (8%)	16 (11%)	0.37
Diabetes Medication at Home:	25 (11%)	17 (11%)	0.91
Home Insulin Use:	1 (0%)	5 (3%)	0.03
Insulin Administered during admission:	15 (6%)	15 (10%)	0.25
Renal Failure	6 (3%)	5 (3%)	0.76
Liver Disease	2 (1%)	3 (2%)	0.38
Active cancer	0 (0%)	1 (1%)	0.39
Hypercoagulable disease	15 (6%)	9 (6%)	0.99
Hypertension	108 (45%)	77 (52%)	0.27
Anti-Hypertensive Medication at Home:	79 (33%)	61 (41%)	0.15
Systolic Blood Pressure Prior to Surgery	132 [121;143]	132 [120;147]	0.59
Anti-rheumatic medications			
TNF inhibitors	65 (27%)	34 (23%)	0.39
non-TNF Biologic	26 (11%)	21 (14%)	0.44
Conventional Synthetic DMARDs	167 (70%)	102 (69%)	0.81
Number of GC Doses Over Entire Admission	1.00 [1.00;1.00]	5.00 [3.00;8.00]	<0.001
Cumulative GC Dose (Prednisone Equivalent) over Entire Admission (mg)	26.7 [26.7;40.0]	71.4 [45.5;97.5]	<0.001

Baseline characteristics of patients according to perioperative GC exposure.

Predictor	Adjusted Odds Ratio	95 % CI	P-Value
Charlson Comorbidity Index	1.84	(1.39, 2.50)	<0.001
Age at Admission	1.03	(0.997, 1.06)	0.09
BMI	1.07	(1.02, 1.13)	0.003
Cumulative GC dose	1.01	(0.99, 1.01)	0.02

Multivariable regression: association of cumulative GC dose and patient characteristics with complications following arthroplasty

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Abstract Number: 1744

The STAtins to Prevent Rheumatoid Arthritis (STAPRA) Trial: Clinical Results and Subsequent Qualitative Study, a Mixed Method Evaluation

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SESSION INFORMATION

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Session Type: Poster Session D

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Background/Purpose: Persons at high risk of developing rheumatoid arthritis (RA) may benefit from a low-risk pharmacological intervention aimed at primary prevention. Previous studies demonstrated disease-modifying effects of statins in RA patients[1] as well as an association between statin use and a decreased risk of RA development[2]. We designed a multi-center, randomized, double-blind, placebo-controlled trial to investigate if atorvastatin use for 3 years could prevent arthritis. Subsequently, we conducted qualitative research to determine barriers and facilitators for prevention trial participation.

Methods: Individuals at high risk of RA, i.e. arthralgia without arthritis and anti-citrullinated protein antibody (ACPA) >3xULN or both ACPA and rheumatoid factor (RF), were randomized to atorvastatin 40 mg daily or placebo for 3 years. The primary endpoint was clinical arthritis development. The pre-calculated sample size was 220 participants. After trial inclusions were stopped, we conducted focus group interviews with individuals who participated or declined participation in the STAPRA trial or the Arthritis Prevention In the Pre-clinical Phase of RA with abatacept (APIPPRA) trial[3].

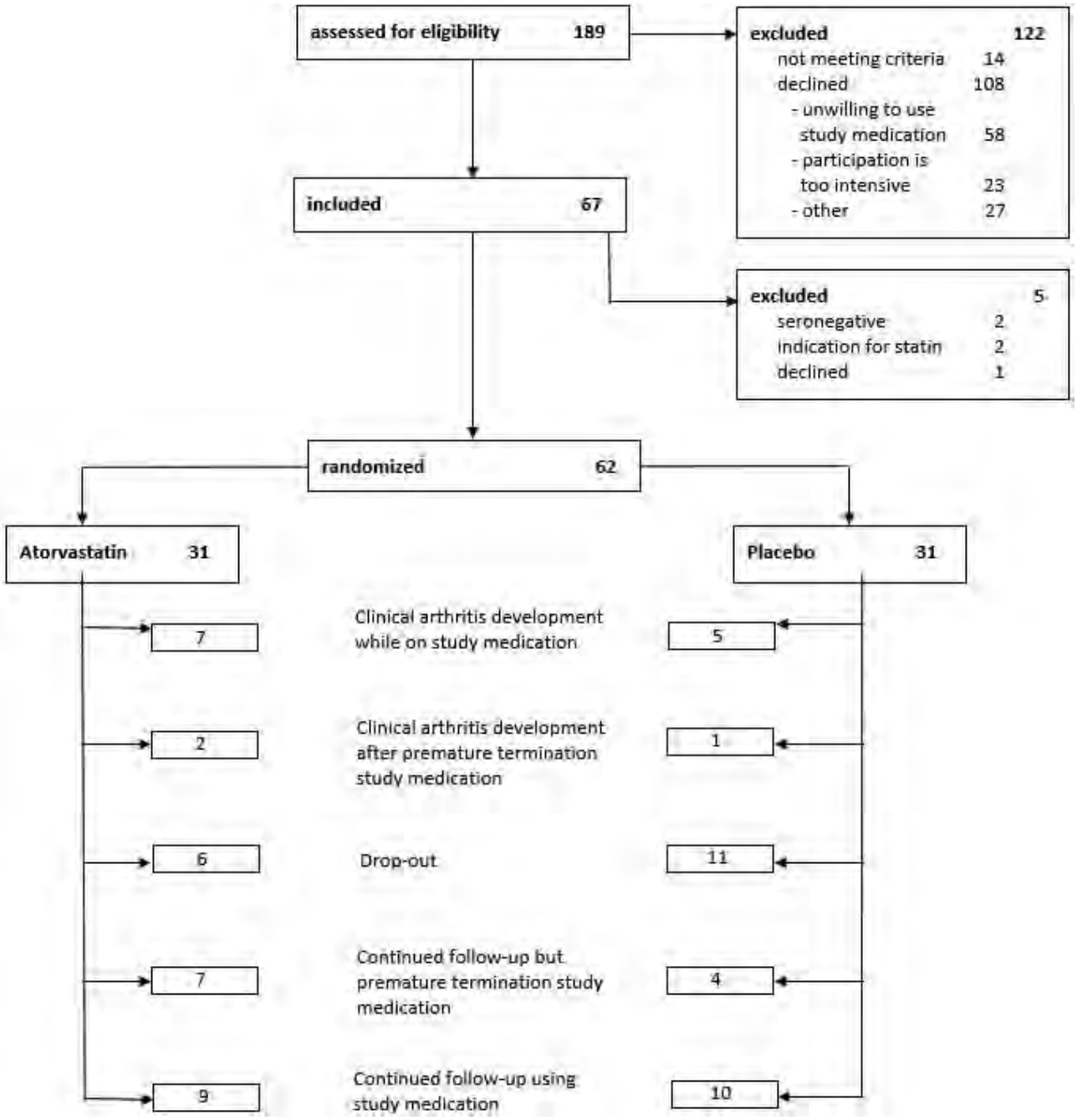

Figure 1. Flowchart STAPRA study

Results: Sixty-seven individuals were included in the STAPRA trial (figure 1). Inclusion was stopped after 38 months due to the low inclusion rate, and analyses were performed 1 year later. Mean age was 48 years, 74% was female, mean follow up was 18 (0-36) months. Fifteen individuals (24%) developed clinical arthritis: 9/31 (29%) in the atorvastatin group and 6/31 (19%) in the placebo group after a median period of 9 (IQR 5.5-26.5) months (atorvastatin) and 4 (0-14.8) months (placebo): HR 0.71, 95% CI 0.3-2.0. In our center, 4 out of 14 eligible individuals participated in the APIPPRA trial. Eighteen individuals participated in the focus group discussions, 3 were asked for APIPPRA of which 1 participated, 15 were asked for STAPRA of which 8 participated. Seven barriers or facilitators for prevention trial participation emerged: (1) trial medication, (2) symptom severity, (3) treatment options, (4) study burden, (5) feeling of acknowledgement (6) own risk assessment and (7) altruism.

Conclusion: The results of the STAPRA trial are inconclusive due to severe difficulties with patient inclusion and low treatment adherence. The focus group study revealed several themes that play an important role in at-risk individuals' decision whether or not to participate in a prevention trial. These should be taken into account when designing preventive trials and will be important in optimizing acceptance and adherence to preventive treatment.

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[2] Chodick G et al. PLoS Med. 2010;7(9):e1000336

[3] Al-Laith M et al. Trials. 2019;20(1):429.

Disclosure: L. van Boheemen, None; **M. ter Wee**, None; **S. Turk**, None; **M. van Beers**, None; **W. Bos**, None; **D. Marsman**, None; **E. Griep**, None; **M. Starmans**, None; **C. Popa**, None; **A. van Sijl**, None; **B. Seppen**, None; **M. Boers**, None; **M. Nurmohamed**, None; **D. van Schaardenburg**, None.

Abstract Number: 1745

A Novel Method for Predicting 1-Year Retention of Abatacept Using Machine Learning Techniques

Rieke Alten[1], Claire Behar[2], Christine Boileau[2], Pierre Merckaert[2], Ebenezer Afari[2], Virginie Vannier-Moreau[3], Sean Connolly[3], Yedid Elbez[2], Pierre-Antoine Juge[4] and Karissa Lozenski[3], [1]Schlosspark-Klinik, Universitätsmedizin, Berlin, Germany, [2]Excelya, Boulogne-Billancourt, France, [3]Bristol-Myers Squibb Company, Princeton, NJ, [4]Université de Paris, Service de Rhumatologie Hôpital Bichat-Claude Bernard, AP-HP, Paris, France

SESSION INFORMATION
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Background/Purpose: In the ACTION (NCT02109666) study, using multivariable Cox proportional hazards regression models, patient (pt) global assessment of pain, country, reason for stopping last biologic, number of prior biologic treatments (txs), abatacept (ABA) monotherapy, RF/anti-CCP status, previous neoplasms, psychiatric disorders and

Table 1. Performance metrics comparison after optimization

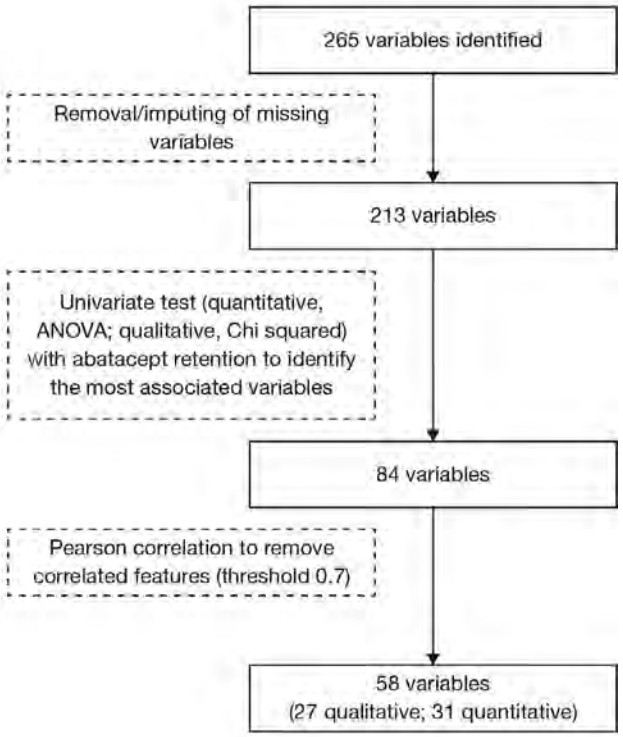
Model/metrics[a]	Training mean accuracy	Validation mean accuracy	Testing accuracy	ROC AUC	Precision	Recall	F1-score
Gradient boosting classifier	0.869	0.599	**0.667**	0.610	0.652	0.667	0.652
Multi-layer perceptron classifier	0.637	0.603	0.667	0.611	0.653	0.667	0.655
Logistic regression	0.610	0.606	0.636	0.553	0.605	0.636	0.600
Random forest	0.615	0.605	0.629	0.521	0.597	0.629	0.535
Decision tree	0.596	0.595	0.626	0.495	0.505	0.626	0.504
Linear SVC	0.628	0.613	0.612	0.551	0.591	0.612	0.596

Bold indicates the model that had the best prediction testing accuracy and the most interpretable model for feature importance.

[a]Precision, recall and F1-score are weighted average based on retention (1) and no retention (0).

AUC=area under the curve; ROC=receiver operating characteristic; SVC=support vector classification.

Figure 1. Variables used in the modeling



ANOVA=analysis of variance.

cardiac disorders were identified as predictors of 1-year retention to ABA tx.[1] The objective of our study was to use machine learning as an innovative and complementary approach in order to identify pts with 1-year ABA retention.

Methods: Supervised learning was used for classification. A binary variable was used where retention=1 and no retention=0. Retention was defined as tx for >365 days or ≤365 days in pts who achieved remission or major clinical response. The number of variables identified and used in the models is shown in **Figure 1**. A subset of features was selected to prevent under-fitting or over-fitting. Label and OneHot encoding were applied for categorical variables and MinMax scaling was applied to convert all continuous variables to the same scale. The models tested for predictive performance were: logistic regression, support vector machine, naïve Bayes, decision tree, random forest, gradient boosting and multi-layer perceptron. For each model, a recursive feature elimination with cross validation was applied. For the best performing model (gradient boosting), the database was divided into two sets: a training/validation set (n=2021) and a test set (n=329). Accuracy was defined as the number of correct predictions divided by the total number of predictions. Precision, recall and F1-score were estimated for predictions on both retention and no retention and were then weight-averaged to obtain overall performance scores. The importance score of each variable was estimated.

Results: In total, 2350 pts included from May 2008 to December 2013 had a mean retention rate of 59.3% at 1 year. The gradient boosting classifier model had the best prediction testing accuracy (67%) and was the most interpretable

model for feature importance (**Table 1**). The importance score for each predictor did not describe a linear correlation with retention or directionality; rather, the higher the score, the more important the variable for retention prediction. Predictive information was shared between all 51 variables; 8 of which overlapped with those identified in the Cox regression model.[1] The five most influencing variables were the duration of previous biologic DMARDs, pt global pain assessment, RA duration, physician global disease activity assessment and HAQ-DI.

Conclusion: The gradient-boosting model identified predictors of retention in addition to those identified by multivariable Cox regression models in ACTION.[1] The models and predictors identified could be further improved by including other RA datasets. Machine learning offers a complementary approach to biostatistics and may lead to better identification of pts with RA, and their tx retention, hence supporting personalized, clinical decision making in a real-world setting.

Reference

1. Alten R, et al. *RMD Open* 2017;3:e000538.

Medical writing: Claire Line (Caudex)

Disclosure: R. Alten, Pfizer, 2, 8, Gilead Sciences, Inc., 2, Novartis, 2, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 5, Lilly, 2, 5, UCB, 2, 5; **C. Behar**, Bristol-Myers Squibb Company, 9; **C. Boileau**, Bristol-Myers Squibb Company, 9; **P. Merckaert**, Bristol-Myers Squibb Company, 9; **E. Afari**, Bristol-Myers Squibb Company, 9; **V. Vannier-Moreau**, Bristol-Myers Squibb Company, 3; **S. Connolly**, Bristol-Myers Squibb Company, 1, 3, 4; **Y. Elbez**, Bristol-Myers Squibb Company, 9; **P. Juge**, Bristol-Myers Squibb Company, 5; **K. Lozenski**, Bristol-Myers Squibb Company, 3.

Abstract Number: 1746

Association of Obesity with Treatment Response to Methotrexate or Tumor Necrosis Factor Inhibitors in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Background/Purpose: Obesity affects 30-40% of RA patients and is associated with higher clinical disease activity measures and progressive disability. Studies suggest that obesity may be associated with poor response to TNF inhibitors (TNFi), but the degree to which these prior results were impacted by unmeasured confounding factors is unclear. We aimed to evaluate differences in response to MTX and TNFi across BMI categories among RA patients in a real-world setting, accounting for multiple confounding factors.

Methods: We conducted a retrospective cohort study within the Veterans Affairs RA registry. Adult patients initiating a course of MTX or TNFi (with no use in prior 90 days) who had at least moderate disease activity (DAS28 >3.2) at baseline and one or more clinical visit with DAS28 30 days to 6 months later were included. BMI (kg/m^2) was categorized as underweight (< 20), normal (20-25), overweight (25-30), class 1 obesity (30-35) and class 2-3 obesity (>35). Response was defined as achieving at least low disease activity (LDA; DAS28 < 3.2) *or* the minimally clinically

BMI category, kg/m²	<20	20-25	25-30	30-35	>35	p-value
Methotrexate Starters (n=471)						
Number of drug courses (N=738), n (%)	45 (6.1)	152 (20.6)	233 (31.6)	165 (22.4)	143 (19.4)	
Demographics						
Age in yrs, mean (SD)	73 (10.2)	75 (10.8)	71 (10)	68 (10.8)	66 (9.3)	<0.001
Male, n (%)	39 (86.6)	144 (95.3)	214 (92.2)	145 (87.8)	121 (84.6)	0.016
White, n (%)	35 (77.7)	129 (84.8)	180 (77.2)	124 (75.1)	114 (79.7)	0.276
Disease and Treatment Characteristics						
Pain score, mean (SD)	5.8 (2.1)	5.7 (2.3)	5.5 (2.5)	5.7 (2.3)	5.6 (2.6)	0.925
Disease Duration, median (IQR)	11.1 (7.8, 16.1)	11.3 (5.2, 22.8).3)	10.7 (3.5, 22.1)	7.3 (2.5, 17.8)	6.5 (3.7, 14.0)	0.002
DAS-28, median (IQR)	4.5 (3.6, 5.3)	4.6 (3.9, 5.2)	4.4 (3.8, 5.1)	4.8 (3.8, 5.2)	4.9 (4.2, 5.6)	0.002
MHAQ, median (IQR)	1.2 (0.8, 1.5)	1.3 (0.8, 1.6)	1.1 (0.6, 1.4)	1.3 (0.6, 1.4)	1.3 (0.9, 1.8)	0.002
RF positivity, n (%)	38 (84.4)	120 (78.9)	186 (79.8)	129 (78.1)	119 (83.2)	0.750
CCP positivity, n (%)	38 (84.4)	120 (78.9)	186 (79.8)	129 (78.1)	119 (83.2)	0.750
csDMARD count, median (IQR)	6.5 (3, 10.5)	5 (2, 8)	4 (2, 7)	4 (2, 7)	5 (3, 9)	<0.001
Other concurrent csDMARD use, n (%)	5 (8.9%)	22 (10.2%)	29 (9.4%)	30 (13.7%)	15 (7.5%)	0.306
Number of prior biologics, median (IQR)	1 (0,1)	1 (0, 1)	1 (0, 2)	1 (0,1)	1 (0, 3)	0.002
Concomitant biologic start, n (%)	8 (17.7)	18 (11.8)	26 (11.1)	19 (11.5)	10 (6.9)	0.328
Comorbidities						
DM, n (%)	7 (15.5)	44 (28.9)	62 (26.6)	54 (32.7)	69 (48.2)	<0.001
Hypertension, n (%)	6 (13.3)	35 (23)	53 (22.7)	53 (32.1)	45 (31.4)	0.025
OA, n (%)	24 (53.3)	67 (44)	93 (39.9)	81 (49)	88 (61.5)	0.001
Opiate use, n (%)	10 (22.2)	51 (33.5)	65 (27.9)	46 (27.8)	57 (39.8)	0.058
TNFi starters (n=509)						
Number of drug courses N=1165, n (%)	74 (6.4)	281 (24.2)	411 (35.3)	248 (21.3)	151 (13)	
Demographics						
Age in yrs, mean (SD)	74.1 (8.4)	73.7 (10.8)	69.2 (9.9)	67.6 (9.3)	66 (8)	<0.001
Male, n (%)	69 (93.2)	264 (93.9)	379 (92.2)	220 (88.7)	136 (90)	0.225
White, n (%)	66 (89.1)	226 (80.4)	341 (82.9)	175 (70.5)	120 (79.4)	0.001
Disease and Treatment Characteristics						
Pain score, mean (SD)	5.3 (2.7)	5.7 (2.7)	5.8 (2.5)	6 (2.7)	5.8 (2.5)	0.313
Disease Duration, median (IQR)	12.4 (6.9, 21.6)	14.8 (5.7, 23.4)	12.3 (4.8, 21.9)	8.1 (3.2, 14.7)	6.6 (3.5, 14.2)	<0.001
DAS-28, median (IQR)	4.6 (4.1, 5.7)	4.7 (4.1, 5.6)	4.5 (3.9, 5.5)	4.6 (4, 5.5)	4.7 (4, 5.4)	0.460
MHAQ, median (IQR)	1.2 (0.6, 1.6)	1.1 (0.7, 1.5)	1.3 (0.9, 1.6)	1.2 (0.7, 1.6)	1.3 (0.8, 1.7)	0.033
RF positivity, n (%)	72 (97.3)	236 (83.9)	343 (83.4)	209 (84.2)	118 (78.1)	0.011
CCP positivity, n (%)	73 (98.6)	228 (81.1)	325 (79)	198 (79.8)	110 (72.8)	<0.001
csDMARD count, median (IQR)	5 (2, 6)	5 (2.5, 7)	4 (2, 6)	4 (2, 6)	4 (3, 6)	0.011
Any concurrent csDMARD use, n (%)	38 (51.3)	104 (37)	149 (36.2)	75 (30.2)	38 (25.1)	0.001
Number of prior biologics, median IQR)	1 (1,2)	1 (1, 2)	1 (1, 2)	1 (1, 2)	1 (1,2)	0.115
Comorbidities						
DM, n (%)	16 (21.6)	79 (28.1)	94 (22.8)	93 (37.5)	83 (54.9)	<0.001
Hypertension, n (%)	4 (5.4)	84 (29.8)	78 (18.9)	58 (23.3)	34 (22.5)	<0.001
OA, n (%)	42 (56.7)	123 (43.7)	196 (47.6)	114 (45.9)	95 (62.9)	0.001
Opiate use, n (%)	45 (60.8)	130 (46.2)	127 (30.9)	74 (29.8)	52 (34.4)	<0.001

Table 1. Baseline characteristics of MTX and TNFi initiators stratified by BMI category

important difference (MCID) in DAS28 (>=1.2) within 6 months. We also extracted disease duration, Multi-Dimensional HAQ score, smoking status, and extra-articular features of disease from the database. Comorbidities were obtained from medical record databases within 1-year prior to initiation. Anti–CCP antibody and RF were measured in banked serum obtained at the time of enrolment. Concurrent RA medications, including prior courses of conventional DMARDs and biologic therapies were determined from VA pharmacy data. The association between BMI and response to treatment within 6 months was estimated in logistic regression models adjusted for demographics, calendar year, RA severity factors, prior/concomitant therapies, and comorbidities at baseline.

Results: We identified 738 eligible MTX courses (471 unique patients) and 1165 TNFi courses (509 unique patients). In both cohorts, the population was primarily male (90% in MTX, 92% in TNFi), and two-thirds were either overweight or obese (73% in MTX, 70% in TNFi). Median baseline DAS28 score was higher among severely obese MTX initiators.

	MTX initiators			
	Univariate analysis (odds of response within 6 months)		Multivariate analysis* (odds of response within 6 months)	
BMI Category	LDA OR (95% CI)	MCID OR (95% CI)	LDA OR (95% CI)	MCID OR (95% CI)
BMI <20 kg/m²	0.86 (0.4 - 1.81)	0.78 (0.39 - 1.57)	1.06 (0.44-2.51)	0.86 (0.38-1.93)
BMI 20-25 kg/m²	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
BMI 25-30 kg/m²	1.1 (0.71 – 1.72)	0.78 (0.51 - 1.2)	1.22 (0.72-2.06)	0.84 (0.51-1.37)
BMI 30-35 kg/m²	1.08 (0.67 - 1.74)	0.74 (0.46 - 1.17)	1.26 (0.71-2.24)	0.81 (0.47-1.4)
BMI ≥35 kg/m²	0.75 (0.45 - 1.25)	1.16 (0.73 - 1.85)	0.96 (0.50-1.86)	1.09 (0.60-1.97)
	TNFi initiators			
BMI <20 kg/m²	0.73 (0.41 - 1.31)	0.77 (0.45 - 1.31)	0.71 (0.35-1.42)	0.91 (0.49-1.68)
BMI 20-25 kg/m²	1.00 (reference)	1.00 (reference)	1.00 (reference)	1.00 (reference)
BMI 25-30 kg/m²	1.14 (0.82 - 1.57)	0.91 (0.67 - 1.24)	1.07 (0.73-1.57)	0.94 (0.65-1.37)
BMI 30-35 kg/m²	1.43 (1 - 2.05)	1.14 (0.81 - 1.61)	1.45 (0.95-2.23)	1.13 (0.74-1.71)
BMI ≥35 kg/m²	1.3 (0.86 - 1.97)	1.16 (0.78 - 1.73)	1.24 (0.74-2.09)	1.18 (0.71-1.95)

*Adjusted for CCP and RF positivity, use of leflunomide/sulfasalazine/hydroxychloroquine/MTX/biologic at baseline, other concurrent csDMARD initiation, prednisone use, baseline MD-HAQ, baseline pain scale, prior MTX use, number of prior biologics used, number of prior csDMARDs used, smoking category, comorbidities such as lung disease, psychiatric disorders, neoplasms, osteoarthritis, diabetes, hypertension, osteoporosis, fractures, spine disease, vascular disorders, NSAID/opiate use, anemia, and physician documented presence of nodules/radiographic changes.

Table 2. Univariate and multivariate analyses reporting response percent and fully adjusted odds ratio, respectively, among methotrexate and tumor necrosis factor inhibitor initiators

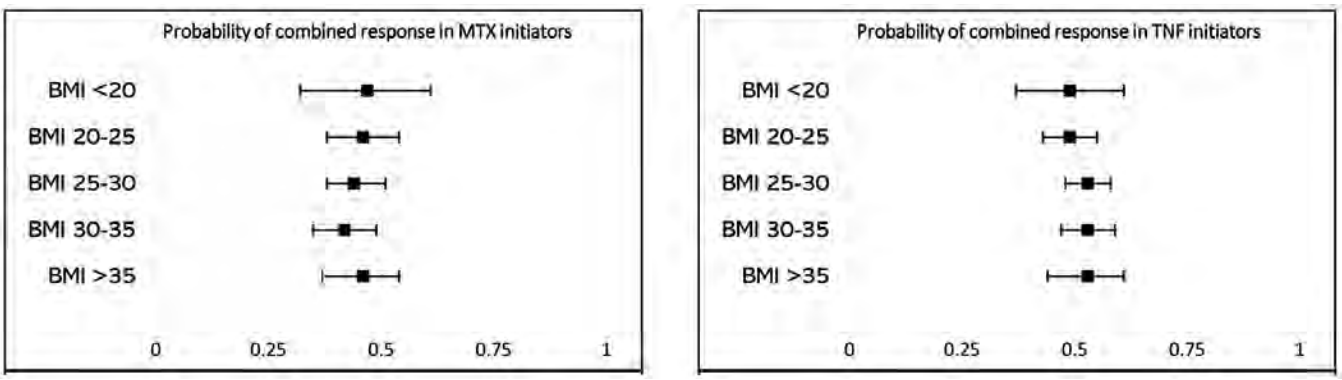

Figure 1. Predicted probabilities of combined (primary) response in methotrexate and tumor necrosis factor inhibitor initiators based on logistic regression models

Other characteristics are depicted in **Table 1**. The overall unadjusted response was achieved in 45% of MTX courses and 52% of TNFi courses. While the response rates were numerically lowest among underweight patients in TNFi cohorts before and after adjustment, responses were not associated with BMI categories in either cohort with or without adjustment (all p >0.10). In adjusted models, the odds of clinical response for all outcomes were similar across BMI categories in both cohorts (**Table 2**; **Fig 1**).

Conclusion: In this predominantly male veteran population, clinical response following the initiation of MTX or TNFi for RA in a real-world registry data did not meaningfully differ by BMI categories after controlling for a robust set of covariates. These findings argue against a biological basis for differences in treatment response in RA patients with higher BMI. Future head to head comparison studies among obese patients may be necessary to determine whether a particular treatment strategy is more efficacious in this group.

Disclosure: D. Poudel, None; **T. Mikuls**, Horizon Therapeutics, 2; **M. George**, Bristol-Myers Squibb, 2; **B. England**, None; **G. Cannon**, Amgen, Inc., 2, Merck, 2; **B. Sauer**, None; **J. Baker**, None.

Abstract Number: 1747

Brain fMRI Predicts Responses to Certolizumab Pegol in RA. an International, Multi-center, Randomized, Double-blind, Placebo-controlled Trial (PreCePRA)

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Personalization of RA treatment is not optimal due to lack of predictors. We previously demonstrated in RA patients that central nervous system (CNS) pain response to tender joint compression, measured by using functional MRI (fMRI) of the brain rapidly wanes after 24 hours of anti-TNF administration and that a higher pre-treatment BOLD signal volume seems to predict clinical response to treatment with certolizumab-pegol (CZP)1,2. We therefore hypothesized that the CNS pain response upon compression of a painful joint could predict subsequent anti-TNF treatment response.

Methods: Adult RA patients fulfilling the 2010 ACR/EULAR classification criteria with a DAS28 >3.2 under stable DMARD treatment for at least 3 months were eligible. Patients underwent fMRI scanning of the brain at screening for stratification by CNS pain response. Whole brain BOLD-signal-voxel-count of 700 units classifying between low and high, and were randomized to CZP or placebo (2:1) The primary outcome was low disease activity (LDA, DAS28 ≤3.2) after 12 weeks of treatment.

Results: 156 RA patients, inadequate responders to csDMARD, signed the informed consent. 139 patients (46/47, 46/49 and 42/43) (99 females, 71%) with moderate-high disease activity (mean (SD) DAS-28: 4.83 (1.03)) could be included respectively and completed the 12-week study treatment. Geometric mean (SD) numbers of baseline BOLD

e-1 Baseline characteristics of the study population overall and by study groups.

		Overall	Study group		
			Certolizumab-High	Certolizumab-Low	Placebo
		139	43	49	47
rs, mean (SD)		54.3 (11.8)	54.3 (10.8)	56.5 (12.2)	52.1 (12.0)
%)	Female	99 (71.2)	34 (79.1)	35 (71.4)	30 (63.8)
	Male	40 (28.8)	9 (20.9)	14 (28.6)	17 (36.2)
tion, years	Mean(SD)	6.2 (8.1)	6.0 (8.3)	6.4 (8.6)	6.2 (7.6)
	Median(IQR)	2.0 (1.0-8.0)	2.0 (1.0-9.0)	3.0 (1.0-8.0)	3.0 (1.0-8.0)
(%)	Negative	34 (24.5)	15 (34.9)	9 (18.4)	10 (21.3)
	Positive	105 (75.5)	28 (65.1)	40 (81.6)	37 (78.7)
)	Negative	39 (28.1)	12 (27.9)	13 (26.5)	14 (29.8)
	Positive	100 (71.9)	31 (72.1)	36 (73.5)	33 (70.2)
ioints (28), mean (SD)		10.2 (6.5)	9.3 (6.4)	11.3 (6.7)	9.9 (6.2)
joints (28), mean (SD)		7.9 (5.3)	7.0 (4.4)	8.7 (6.3)	8.0 (4.8)
global VAS, mm, mean (SD)		58.0 (20.0)	57.2 (19.9)	59.1 (17.8)	57.6 (22.5)
n global VAS, mm, mean (SD)		49.6 (18.7)	46.0 (20.2)	49.5 (19.2)	53.1 (16.2)
S, mm, mean (SD)		55.2 (19.3)	53.5 (18.0)	57.1 (17.0)	54.9 (22.7)
s/h, mean (SD)		25.8 (19.9)	23.7 (19.0)	25.2 (17.1)	28.2 (23.2)
/L, mean (SD)		8.7 (13.0)	6.8 (12.7)	7.9 (8.7)	11.2

signal positive voxels were 559 (10), 81 (12) and 2498 (3) in the 3 arms respectively. The mean DAS28 (SD) scores after 12 weeks of study treatment were Placebo: 3.89 (1.29), CZP-L: 3.42 (1.06) and CZP-H: 3.06 (1.04). LDA was achieved in 12/47 patients (25.5 %) in placebo, 22/49 (44.9%) in the CZP-L, and 25/43, (58.1%) in the CZP-H arm. The linear effect term for the ordinal study group variable supported a linear trend of increasing CZP treatment effect with increasing baseline CNS pain response. RR (95% CI) for achieving LDA with each unit increase in treatment category over placebo was 1.79 (1.24 to 2.74, p=0.003).

Conclusion: A higher pre-treatment brain activity in response to pain measured with fMRI predicts the chance of achieving low disease activity with CZP treatment.

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8, Sanofi, 8, Gilead, 8; **D. Simon**, Novartis, 8, Lilly, 5, 8, Janssen, 8, AbbVie, 5; **L. Valor Mendez**, None; **V. Schoenau**, None; **J. Prade**, None; **M. Sergeeva**, None; **M. Sulvakumar**, None; **S. Strobelt**, None; **L. Konerth**, None; **F. Behrens**, AbbVie, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Chugai, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, UCB, 5, 8, BMS, 5, 8, Celgene, 5, 8, MSD, 5, 8, Biotest, 5, 8, Sanofi, 5, 8, Genzyme, 5, 8, Lilly, 5, 8, Boehringer, 5, 8, Galapagos, 5, 8; **C. Baerwald**, None; **S. Finzel**, None; **R. Voll**, None; **A. Hueber**, None; **J. Roesch**, None; **E. Feist**, AbbVie, 5, 8, BMS, 5, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8, Sobi, 5, 8; **J. da Silva**, MyFibromyalgia®, a webcompany delivering services to patients with Fibromyalgia, 9; **A. Doerfler**, None; **N. Damjanov**, AbbVie, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Richter Gedeon, 5, 8, MSD, 5, 8, Novartis, 5, 8; **A. Hess**, None; **G. Schett**, None.

Abstract Number: 1748

Effects of Abatacept and Tumor Necrosis Factor Inhibitor on the Normal Glycosylated Hemoglobin Level in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) and diabetes mellitus (DM) are associated with inflammation. Abatacept has been reported to be effective for type 1 diabetes. We aimed to investigate the influence of tumor necrosis factor inhibitors (TNFi) and abatacept (ABT) on the glucose metabolism of patients with RA.

Methods: Patients with RA treated with TNFi or ABT from 2008 to 2018 were studied based on the All Showa University of RA (ASHURA) database. The association between glycosylated hemoglobin (HbA1c) level reduction and treatment was evaluated. Of 629 patients treated with these biologic agents, 159 with available HbA1c medical records were included (TNFi, n = 111; ABT, n = 48). The following background factors were investigated: age; sex; type of biological disease-modifying antirheumatic drugs (bDMARDs); dosage of methotrexate (MTX) and prednisolone (PSL); usage of conventional synthetic DMARD and nonsteroidal anti-inflammatory drugs; body mass index (BMI); smoking history; HbA1c; presence or absence of hypertension and dyslipidemia; and serum creatinine, C-reactive protein, and matrix metalloproteinase-3 levels. We also used the simplified disease activity index (SDAI) to evaluate RA disease activity. Propensity was calculated based on age; sex; BMI; smoking history; PSL dosage; MTX dosage; SDAI; creatinine; estimated glomerular filtration rate; presence or absence of diabetes, hypertension, and dyslipidemia; and HbA1c, and 44 patients in each group were extracted by propensity score matching. The primary endpoint was HbA1c levels before, and after 6 months and 1 year, which was determined using the repeated-measures analysis of variance (ANOVA).

Results: The HbA1c level decreased from 5.9 ± 0.79 to 5.7 ± 0.29 and 6.0 ± 2.20 in the TNFi group and from 5.9 ± 0.66 to 5.8 ± 0.00 and 5.8 ± 0.64 in the ABT group before treatment and after 6 months and 1 year, respectively. No interaction was observed among the groups. A significant difference was not observed among the groups ($p = 0.76$) and even during the treatment period ($p = 0.85$) by repeated-measures ANOVA.

Conclusion: Our study suggests that neither ABT nor TNF treatment may affect normal HbA1c levels in patients with RA.

Disclosure: Y. Miwa, None; **Y. Mitamura**, None.

Abstract Number: 1749

Efficacy of Filgotinib in Patients with Rheumatoid Arthritis with Poor Prognostic Factors: Post Hoc Analysis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients (pts) with rheumatoid arthritis (RA) with poor prognostic factors (PPF) are at risk for RA progression if disease activity is not rapidly controlled. In FINCH 3 (NCT02886728), filgotinib (FIL) — an oral, potent, selective JAK1 inhibitor — was effective relative to methotrexate monotherapy (MTX mono) in MTX-naïve patients with ≥1 PPF—erosions, seropositivity for rheumatoid factor (RF) or anti-cyclic citrullinated peptide (CCP), or hsCRP ≥4 mg/L.[1] This post hoc analysis examined FIL efficacy in FINCH 3 pts with multiple PPF.

Methods: The global, phase 3, double-blind, active-controlled FINCH 3 study randomized MTX-naïve pts with moderately to severely active RA 2:1:1:2 to oral FIL 200 mg once daily + MTX ≤20 mg weekly, FIL 100 mg + MTX, FIL 200 mg mono, or PBO + MTX up to week (W)52. This subgroup analysis included pts with all 4 of the following PPF at baseline (PPF pts): erosions, seropositivity for RF or anti-CCP, hsCRP ≥4 mg/L, and DAS(28)CRP >5.1. Comparisons were not adjusted for multiplicity.

Results: Of 1249 pts randomized and treated in FINCH 3, 510 had all 4 PPF. At baseline, relative to the overall FINCH 3 population, PPF pts had longer mean disease duration (2.4 vs

2.2 years); higher mean hsCRP (27.9 vs 17.5 mg/L), mTSS (17.9 vs 13.3), DAS28(CRP) (6.3 vs 5.7), HAQ-DI (1.76 vs 1.56), CDAI (44.3 vs 39.8), and SDAI (47.1 vs 41.5); and greater frequency of seropositivity for RF (90.6% vs 67.9%), anti-CCP (92.4% vs 68.5%), or both

(82.9% vs 59.6%). Efficacy in PPF pts was comparable to data from all FINCH 3 pts (**Table, Figures 1–2**). PPF pts receiving FIL 200 mg with or without MTX vs MTX mono had higher frequencies of ACR20/50/70 response and greater improvement in HAQ-DI at W24; responses were numerically greater for FIL 200 mg + MTX vs FIL 100 mg + MTX or FIL 200 mg mono (**Table**) and were evident by W12 (data not shown). Radiographic progression at W24 was lower in PPF pts receiving FIL 200 mg + MTX or FIL 200 mg mono vs MTX mono (**Figure 1**).

Table. Efficacy outcomes in patients with 4 PPF and all FINCH 3 patients at W24

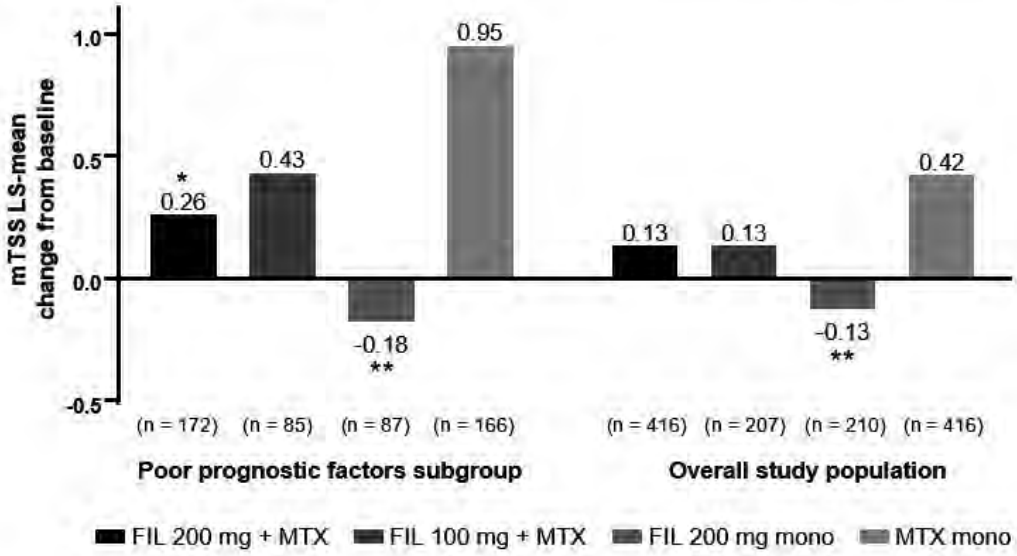
	FIL 200 mg + MTX		FIL 100 mg + MTX		FIL 200 mg mono		MTX mono	
	PPF	All	PPF	All	PPF	All	PPF	All
n	172	416	85	207	87	210	166	416
ACR20, %	85.5*	81.0***	83.5	80.2*	81.6	78.1	74.7	71.4
ACR50, %	70.3***	61.5***	58.8	57.0**	59.8	58.1**	48.2	45.7
ACR70, %	54.1***	43.8***	37.6	40.1***	43.7*	40.0***	28.3	26.0
HAQ-DI[a]	−1.2***	−0.94***	−1.0*	−0.90**	−1.0*	−0.89*	−0.9	−0.79

[a]Mean change from baseline.

*, p <0.05; **, p <0.01; ***, p <0.001 vs MTX mono, not adjusted for multiplicity.

FIL, filgotinib; mono, monotherapy; MTX, methotrexate; PPF, poor prognostic factors.

Figure 1. Change in mTSS from baseline at W24 in FINCH 3 patients with 4 poor prognostic factors and all FINCH 3 patients

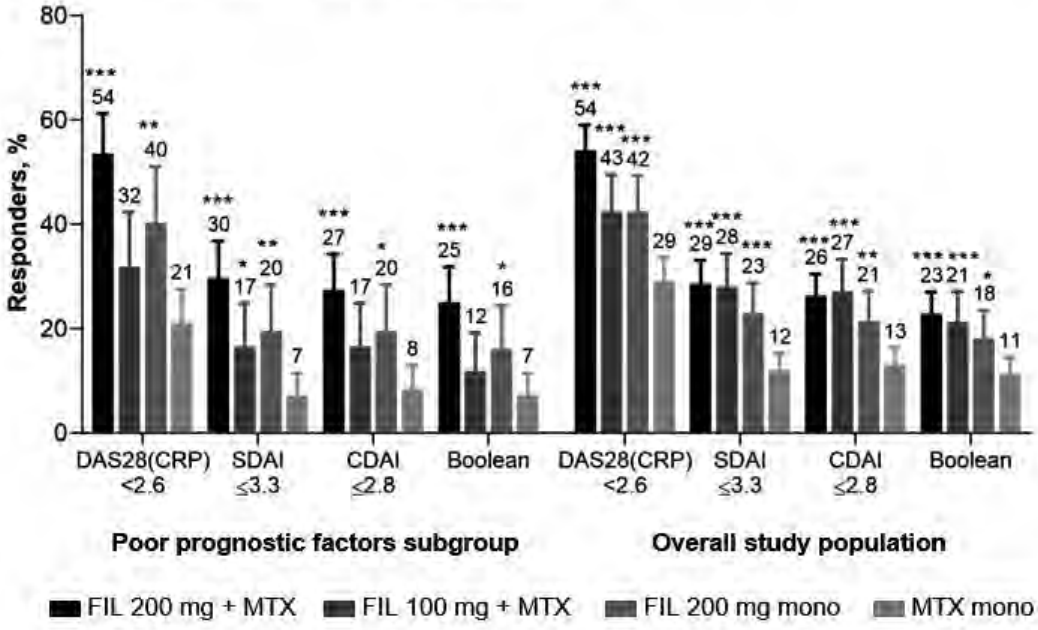


*, p <0.05; **, p <0.01 vs MTX mono; not adjusted for multiplicity.

FIL, filgotinib; LS, least-squares; mono, monotherapy; mTSS, van der Heijde modified total Sharp score; MTX, methotrexate; W, week.

Proportions of PPF pts receiving FIL 200 mg with or without MTX who achieved DAS28(CRP) < 2.6, CDAI ≤2.8, SDAI ≤3.3, and Boolean remission at W24 (**Figure 2**) were larger vs pts receiving MTX mono and numerically greater vs pts receiving FIL 100 mg + MTX.

Figure 2. Rates of DAS28(CRP) <2.6, CDAI ≤2.8, SDAI ≤3.3, and Boolean remission at W24 in FINCH 3 patients with 4 PPF and all FINCH 3 patients



*, p <0.05; **, p <0.01; ***, p <0.001 vs MTX alone; not adjusted for multiplicity.

FIL, filgotinib; mono, monotherapy; MTX, methotrexate; PPF, poor prognostic factors; W, week.

Conclusion: FIL treatment provided rapid and deep disease control including higher rates of remission and other clinical outcomes, improved physical function, and less radiographic progression compared with MTX alone in MTX-naïve pts with RA with 4 PPF, a population at risk for severe progressive disease. In pts with 4 PPF, W24 remission rates following FIL 200 mg with or without MTX were higher vs MTX mono and numerically higher vs FIL 100 mg + MTX.

1. Westhovens et al. Ann Rheum Dis 2019;78(Suppl2):259–60.

Disclosure: D. Aletaha, UCB, 5, 8, Eli Lilly, 5, 8, Gilead Sciences, Inc., 2, 5, Janssen, 5, Sanofi/Genzyme, 5, 8, AbbVie, 2, 5, 8, Amgen, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, Roche, 2, 5, 8, Merck Sharp & Dohme, 2, 5, 8, Bristol-Myers Squibb, 8, Celgene, 5, 8, Medac, 5, 8, Sandoz, 5, 8; **R. Westhovens**, Celltrion, Inc., 2, 5, Galapagos NV, 2, 5, Gilead Sciences, Inc., 2, 5; **C. Gaujoux-Viala**, AbbVie, 5, Amgen, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Eli Lilly, 5, Gilead Sciences, Inc., 5, Janssen, 5, 8, Medac, 5, Merck-Serono, 5, Mylan, 5, 8, Nordic Pharma, 5, Novartis, 5, 8, Pfizer, 5, Roche, 5, Sandoz, 5, 8, Sanofi, 5, UCB, 5; **G. Adami**, None; **A. Matsumoto**, AbbVie, 2, 5, Bristol-Myers Squibb, 2, Eli Lilly, 2, Galapagos NV, 2, Gilead Sciences, Inc., 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, Pfizer, 2, Sanofi, 2, UCB, 2, Regeneron, 2, Novartis, 5, 8; **P. Bird**, AbbVie, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 5, 8, Novartis, 5, 8, Pfizer, 5, 8; **O. Messina**, Amgen, 8, Americas Health Foundation, 8, Pfizer, 8; **M. Buch**, Pfizer, 2, Roche, 2, UCB, 2, AbbVie, 5, Eli Lilly and Company, 5, Gilead Sciences, Inc., 5, Merck-Serono, 5, Sandoz, 5, Sanofi, 5; **B. Bartok**, Gilead Sciences, Inc., 1, 3; **Z. Yin**, Gilead Sciences, Inc., 1, 3; **Y. Guo**, Gilead Sciences, Inc., 1, 3; **T. Hendrikx**, Galapagos, 1, 3; **G. Burmester**, AbbVie, 5, 8, Pfizer, 5, 8, Gilead Sciences, Inc., 5, 8, Eli Lilly, 5, 8, Novartis, 5, Celgene, 5.

Abstract Number: 1750

Longitudinal Change in the Central Nervous System Pain Response After Treatment with Certolizumab or Placebo. a Post-hoc Analysis from the Pre-CEPRA Trial

Juergen Rech[1], Hannah Schenker[2], Koray Tascilar[1], Melanie Hagen[2], Larissa Valor Mendez[2], Verena Schoenau[3], Marina Sergeeva[4], Jutta Prade[4], Mageshvar Sulvakumar[5], Laura Konert[6], Arnd Kleyer[1], David Simon[1], Sandra Strobelt[4], Frank Behrens[7], Christoph Baerwald[8], Stephanie Finzel[9], Reinhard Voll[10], Axel Hueber[11], Eugen Feist[12], Julie Roesch[13], José A. P. da Silva[14], Arnd Doerfler[13], Nemanja Damjanov[15], Andreas Hess[16] and Georg Schett[17], [1]Department of Internal Medicine 3, Friedrich-Alexander University (FAU) Erlangen-Nuremberg and Universitätsklinikum Erlangen, Erlangen, Bayern, Germany, [2]Department of Internal Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, 91054, Erlangen, Germany, Erlangen, Germany, [3]Department of Internal Medicine 3 - Rheumatology and Immunology, Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, 91054, Erlangen, Germany, Erlangen, [4]Institute for Experimental Pharmacology, Erlangen, Germany, [5]Insitute for Experimental Pharmacology, FAU Erlangen-Nuremberg, Erlangen, Germany, [6]Institute for Experimental Pharmacology, FAU Erlangen-Nürnberg, Erlangen, [7]CIRI/Rheumatology & Fraunhofer TMP, Goethe University, Frankfurt, Germany, [8]Uniklinik Leipzig, Medizinische Klinik III - Bereich Rheumatologie, Leipzig, Germany, [9]Universitätsklinikum Freiburg, Klinik für Rheumatologie und Klinische Immunologie, Freiburg, Germany, [10]Universitätsklinikum Freiburg, Klinik für Rheumatologie und Klinische Immunologie, Freibrug, [11]Section Rheumatology, Sozialstiftung Bamberg, Bamberg, Germany, [12]Department of Rheumatology, Helios Vogelsang-Gommern, Vogelsang-Gommern, Germany, [13]Abteilung für Neuroradiologie, Friedrich-Alexander University (FAU) Erlangen-Nürnberg and Universitätsklinikum Erlangen, 91054, Erlangen, Germany, Erlangen, Germany, [14]9.Centro Hospitalar e Universitário Coimbra (Rheumatology Department), Coimbra, Portugal, Coimbra, Portugal, [15]Belgrade University School of Medicine, Belgrade, Serbia, [16]Institute for Experimental Pharmacology, Erlangen, [17]Friedrich-Alexander-Universität Erlangen- Nuremberg, Erlangen, Germany

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Biologicals - bring a hope of recovery or amelioration to people suffering from RA, but only half of the patients respond to such treatment. Therefore, finding reliable biomarkers predicting response is very valuable. Previously we demonstrated that central nervous system (CNS) response to nociceptive stimuli, measured by fMRI of the brain, decreases already after 24 hours and that a higher pre-treatment BOLD signal volume seems to predict clinical response to treatment with certolizumab-pegol (CZP). 1,2 Therefore we hypothesized that the CNS response upon compression of a painful joint could predict subsequent anti-TNF treatment response.

To follow the longitudinal effect of CZP treatment on brain activity in RA patients stratified byhigh and low brain activation volumes measured by BOLD fMRI at baseline and to compare their brain activity during 24 weeks of treatment to that of placebo in DMARD-refractory RA patients.

Methods: Adult RA patients fulfilling the 2010 ACR/EULAR classification criteria with a DAS28 >3.2 under stable DMARD treatment for at least 3 months were eligible. Patients underwent the first fMRI at screening for stratification. Whole brain BOLD-signal-voxel-count of 700 classifying between low and high and patients were randomized to CZP or placebo (2:1 ratio) resulting in 3 study arms (CZP low voxel count (CZP-L), CZP high voxel count (CZP-H), and placebo). The second fMRI was performed after 12 and the third fMRI – after 24 weeks. In parallel control stimulation we measured brain activation during non-painful finger tapping.

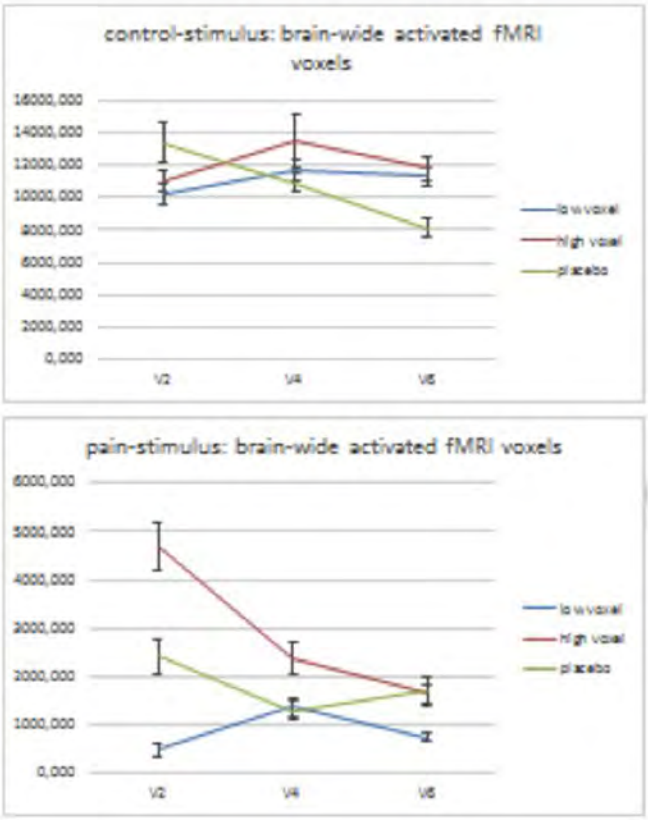


Fig-1: BOLD fMRI responses to painful stimulation (A: compression of a painful joint) and control stimulation (B: finger tapping) over the 3 consecutive MRI measurements. Plotted are mean values + SEM with respective n.

Results: 156 patients, inadequate responders to csDMARD signed the informed consent. In the finger tapping control paradigm, fMRI showed no significant changes in the number of brain-wide activated voxels in CZP-L and CZP-H arms, but, surprisingly, there was a significant decrease (p=0.043) in the placebo arm in fMRI-3 compared to the pre-treatment fMRI-1 value. By painful stimulation in CZP-L fMRI showed significant increase in the number of brain-wide activated voxels (p=0.043) in fMRI-2 as compared to fMRI-1 with no further significant changes. Most importantly, in CZP-H the number of activated voxels was significantly reduced (p=0.037) in fMRI-2 and continued to decrease further in fMRI-3 (p=0.007).

Conclusion: As revealed by our study high pre-treatment fMRI BOLD brain activity in response to pain seems to serve as a (long-term) positive predictor of patient's response to CZP treatment.

Disclosure: J. Rech, Abbie, Biogen, BMS, Chugai, Celgene, EliLilly, Gilead, GSK, Janssen, MSD, Novartis, Roche, Sanofi, Sobi, UCB, 5, 8; **H. Schenker**, None; **K. Tascilar**, None; **M. Hagen**, None; **L. Valor Mendez**, None; **V. Schoenau**, None; **M. Sergeeva**, None; **J. Prade**, None; **M. Sulvakumar**, None; **L. Konert**, None; **A. Kleyer**, Lilly, 8, Novartis, 8, BMS, 8, Sanofi, 8, Gilead, 8; **D. Simon**, Novartis, 8, Lilly, 5, 8, Janssen, 8, AbbVie, 5; **S. Strobelt**, None; **F. Behrens**, AbbVie, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Chugai, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, UCB, 5, 8, BMS, 5, 8, Celgene, 5, 8, MSD, 5, 8, Biotest, 5, 8, Sanofi, 5, 8, Genzyme, 5, 8, Lilly, 5, 8, Boehringer, 5, 8, Galapagos, 5, 8; **C. Baerwald**, None; **S. Finzel**, None; **R. Voll**, None; **A. Hueber**, None; **E. Feist**, AbbVie, 5, 8, BMS, 5, 8, Lilly, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi, 5, 8, Sobi, 5, 8; **J. Roesch**, None; **J. da Silva**, MyFibromyalgia®, a webcompany delivering services to patients with Fibromyalgia, 9; **A. Doerfler**, None; **N. Damjanov**, None; **A. Hess**, None; **G. Schett**, None.

Abstract Number: 1751

Forecasting Healthcare Utilization in Rheumatoid Arthritis: A Machine Learning Predictive Model of Emergency Department Visits and Prednisone Initiation in a Single Tertiary Academic Center

Elston He[1], Eli Cornblath[2], Pratyusha Yalamanchi[3], Alexis Ogdie[2], Joshua Baker[2] and **Michael George**[2], [1]Synovium, Inc., Philadelphia, PA, [2]University of Pennsylvania, Philadelphia, PA, [3]Michigan Medicine, Ann Arbor, MI

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite recent advances in therapy, 42% of patients with rheumatoid arthritis (RA) nationwide had moderate or high disease activity at their most recent visit. Given that uncontrolled disease often results in increased healthcare utilization through emergency department (ED) visits and initiation of prednisone use, early identification and intervention offers the opportunity to identify high risk populations and optimize allocation of healthcare resources. Therefore, our objective was to develop and validate a longitudinal machine learning model to predict ED visits and prednisone initiation for patients with RA.

Methods: Patients with RA at a tertiary care center 2010-2018 were identified based on ≥2 diagnoses of RA from a rheumatology outpatient encounter and DMARD use. Structured electronic health record data was used to identify demographics, lab values, medication history, comorbidities, and healthcare visits. Follow-up was divided into 6 month intervals, and a longitudinal machine learning model using gradient boosting machines (GBMs) was used to predict (1) ED visits within 6 months (limited to visits within the health system) and (2) prednisone initiation within 6 months (excluding patients with use in the preceding 6 months). Nested, patient-stratified cross-validation was used to ensure GBMs could accurately predict outcomes of interest in unseen data. Model performance was quantified using the area under the receiver operating characteristic curve with Youden's J used to choose a cut-point optimizing sensitivity and specificity.

Results: A total of 1831 patients with RA were identified from 2010-18. Baseline demographics included mean [SD] age, 55.05 [14.47] years; 1499 [81.87%] female; and 991 [54.12%] white. 714 patients with ED visits were identified,

Table 1: Gradient Boosting Machines Model Performance Predicting Utilization Within RA Population

	Frequency of Outcome Per Six Month Outcome Window	
	ED Visit	Prednisone Initiation
Area Under the Receiver Operating Characteristic Curve (AUC [95% CI])	0.86 [0.84-0.87]	0.71 [0.70-0.73]
Sensitivity	0.7715	0.7052
Specificity	0.7933	0.6354
Number of Qualifying Six Month Outcome Windows	32958	27114
Number of Outcomes	2006	1604
Incidence Rate (Frequency of Outcome Per Six Month Outcome Window)	0.0609	0.0592
Positive Predictive Value	0.1900	0.1077
Negative Predictive Value	0.9818	0.9715

Table 1. Gradient Boosting Machines Model Performance Predicting Utilization Within RA Population

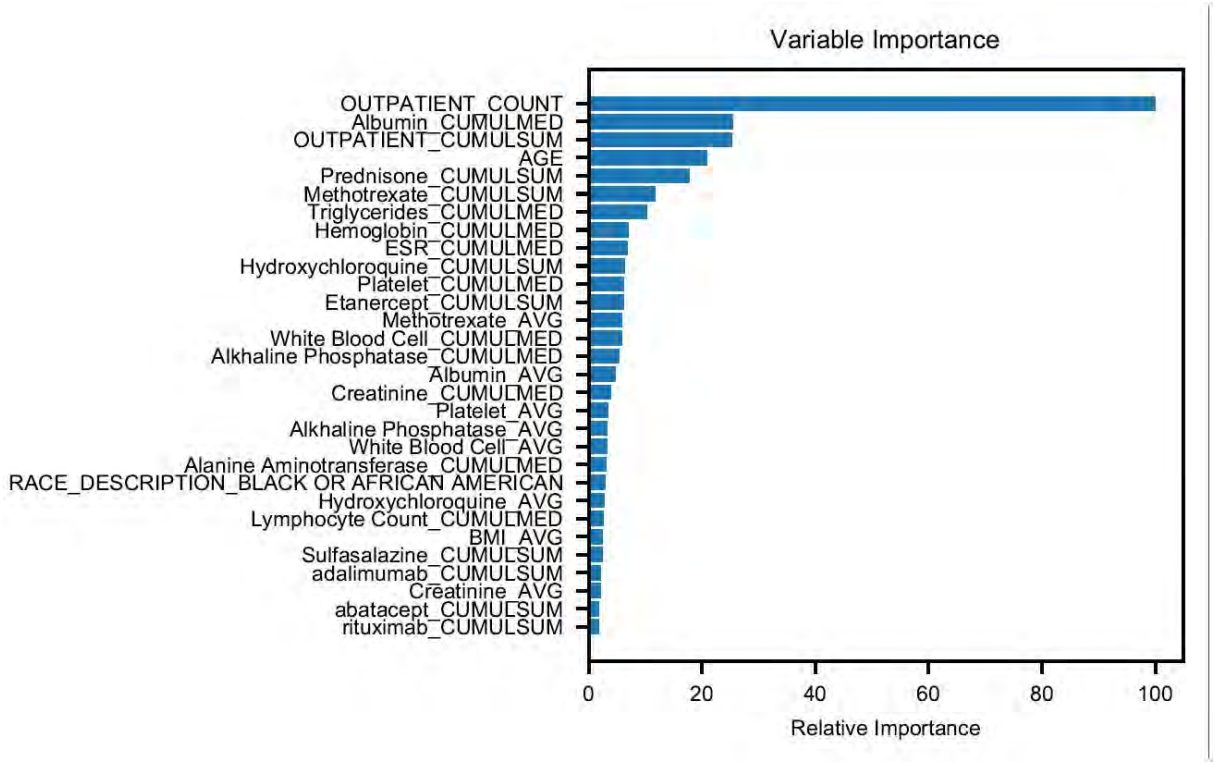


Figure 1. Importance of each predictor variable for ED visits, measured by the decrement in accuracy created by randomly permuting each variable. Key: _AVG: non-weighted average value of measurements within previous 6 month window; _COUNT: the number of visits in previous 6 month time window; _CUMULSUM: cumulative total of measurement for entire history up to the current time point; _CUMULMED: median value of measurement for entire

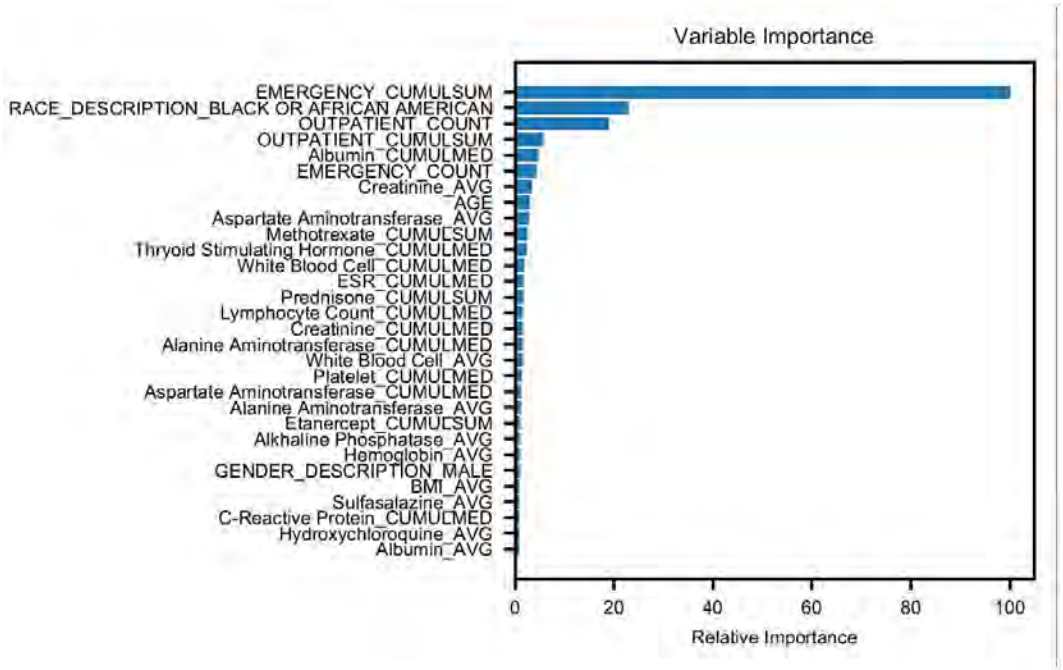


Figure 2. Importance of each predictor variable for prednisone initiation, measured by the decrement in accuracy created by randomly permuting each variable. Key: _AVG: non-weighted average value of measurements within previous 6 month window; _COUNT: the number of visits in previous 6 month time window; _CUMULSUM: cumulative total of measurement for entire history up to the current time point; _CUMULMED: median value of measurement for entire history up to the current time point.

and 1318 patients were identified as having a prednisone prescription at any time during follow-up. The AUCs for prediction of prednisone initiation and ED visits were of 0.71 (95% CI: 0.70-0.73) and 0.86 (95% CI: 0.84-0.87) respectively, with a sensitivity of 0.77 and a specificity of 0.79 for ED visits. Importantly, GBM performance exceeded that of ridge regression (prednisone initiation: AUC of 0.65, 95% CI: 0.61-0.68; emergency visits, AUC of 0.75, 95% CI: 0.72-0.77), suggesting capture of important non-linearities. Significant predictors of ED visits within 6 months include total number of prior ED and outpatient visits, black race, age, elevated white blood cell count, prednisone use, elevated BMI, kidney function (as measured by creatinine), prior conventional DMARD use (methotrexate or hydroxychloroquine), elevated liver enzymes, and elevated TSH. Predictors of ED visits and initiation of prednisone use are shown in Figures 1 and 2, respectively.

Conclusion: Here we demonstrate an internally validated, predictive model for ED visits and initiation of prednisone usage in patients with rheumatoid arthritis using machine learning methodology. This demonstrates that models built on electronic health record data can accurately predict complex disease outcomes within a health system and have the potential to optimize care delivery for diverse patient populations.

Disclosure: E. He, Roivant Sciences, 5, Synovium, 4; **E. Cornblath**, Synovium, 5; **P. Yalamanchi**, Roivant Sciences, 5, Synovium, 4; **A. Ogdie**, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1; **J. Baker**, None; **M. George**, Bristol-Myers Squibb, 2.

Abstract Number: 1752

Prediction of Responder and Non-responder to JAK Inhibitors in Patients with Rheumatoid Arthritis: A Pilot Study with Integrative Cluster Analysis

Masanari Sugawara[1], Yuichiro Fujieda[2], Atsushi Noguchi[3], Shun Tanimura[4], Yuka Shimizu[5], Ikuma Nakagawa[6], Hiroki Takahashi[7], Michihito Kono[8], Masaru Kato[2], Kenji Oku[2], Olga Amengual[2] and Tatsuya Atsumi[9], [1]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo city, Hokkaido, Japan, [2]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Hokkaido, Japan, [3]Department of Internal Medicine and General Medicine, Japanese Red Cross Kitami Hospital, Sapporo, Japan, [4]Department of Internal Medicine, Tomakomai City Hospital, Tomakomai, Hokkaido, Japan, [5]3rd Department of Internal medicine, Hokkaido P.W.F.A.C Obihiro-Kosei General Hospital, Sapporo, Japan, [6]Department of Internal Medicine, Takikawa Municipal Hospital, Sapporo, Japan, [7]Department of Rheumatology and Clinical Immunology, Sapporo Medical University School of Medicine, Sapporo, Japan, [8]Department of Rheumatology, Endocrinology and Nephrology, Graduate School of Medicine and Faculty of Medicine, Hokkaido University, Sapporo, Japan, [9]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine, Hokkaido University, Sapparo, Hokkaido, Japan

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: [Background]

Oral Janus kinase inhibitors (JAKi) show dramatical efficacy to reduce the disease activity in patients with rheumatoid arthritis (RA). However, there remain some patients who respond to inadequately JAKi treatment (JAKi-IR)[1,2] and the clinical characteristics of JAKi-IR in RA have not been fully demonstrated.

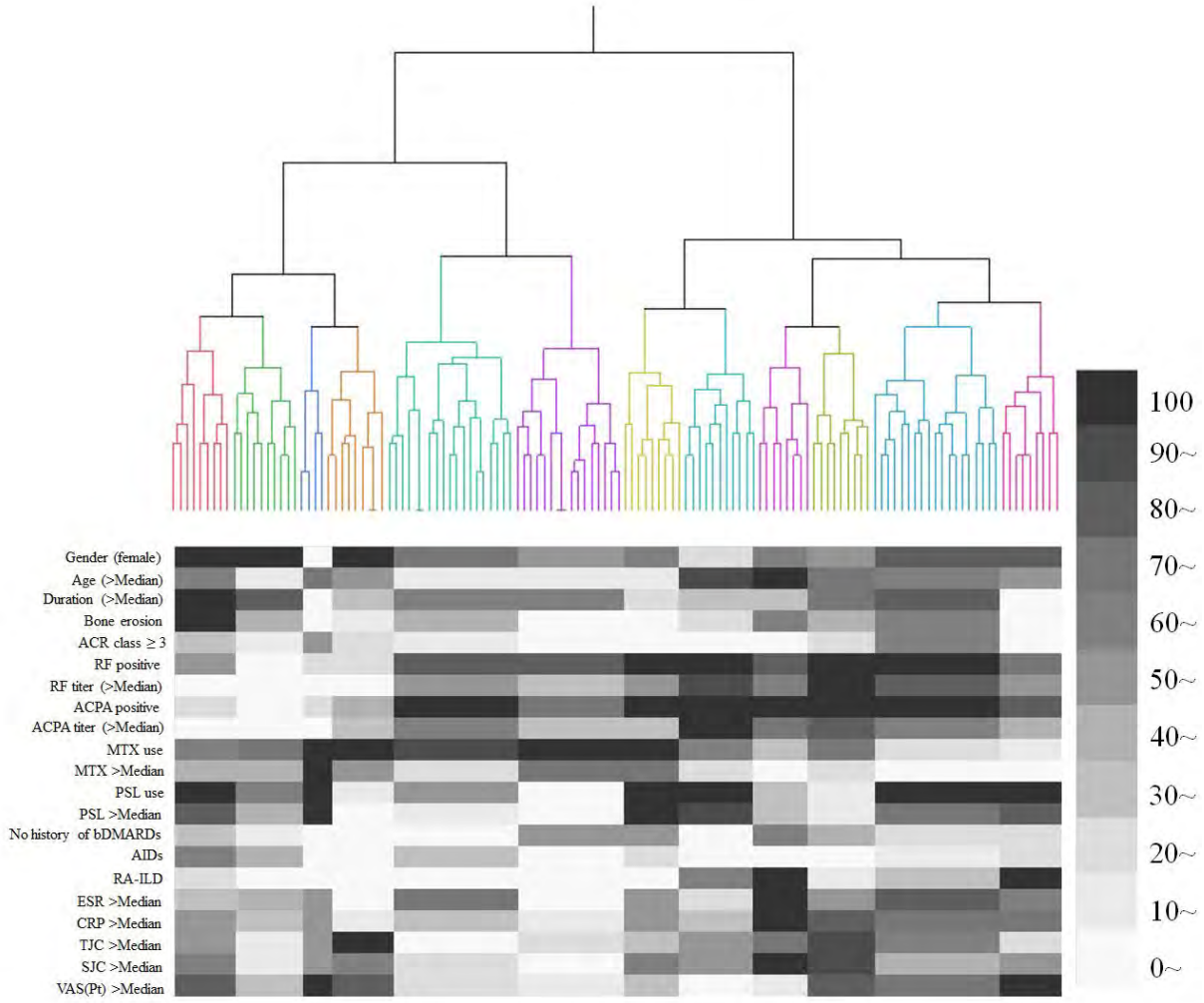


Figure 1

[Objective]

To clarify the characteristics of JAKi-IR in patients with RA based on cluster analysis.

Methods: This retrospective study comprised 132 RA patients who were treated with JAKi (Tofacitinib or Baricitinib) between July 2013 and September 2019 in five facilities. We assessed the disease activity at the baseline, at 12 weeks after JAKi treatment or at the time point of withdrawing JAKi using the Disease Activity Score (DAS28) and the American College of Rheumatology (ACR) response criteria. JAKi-IR was defined as patients with non-response to JAKi depending on ACR20 non-response or non-improvement in DAS28-CRP (△DAS28-CRP< 1.2 from baseline) in 12 weeks. Discontinuation of JAKi due to remission achievement was excluded from the latter. Hierarchical cluster analysis was performed with the following variables at baseline: gender, age, disease duration, bone erosion, ACR functional classification (Class ≥3), rheumatoid arthritis related interstitial lung disease (RA-ILD) or other autoimmune disease (AID), anti-citrullinated protein antibody (ACPA), rheumatoid factor (RF), use/dose of methotrexate (MTX) and prednisolone (PSL), serum ESR/CRP, tender/swollen joint counts (TJC/SJC), visual analog scale by patients (VAS-Pt), and history of biologic disease-modifying antirheumatic drugs (DMARDs).

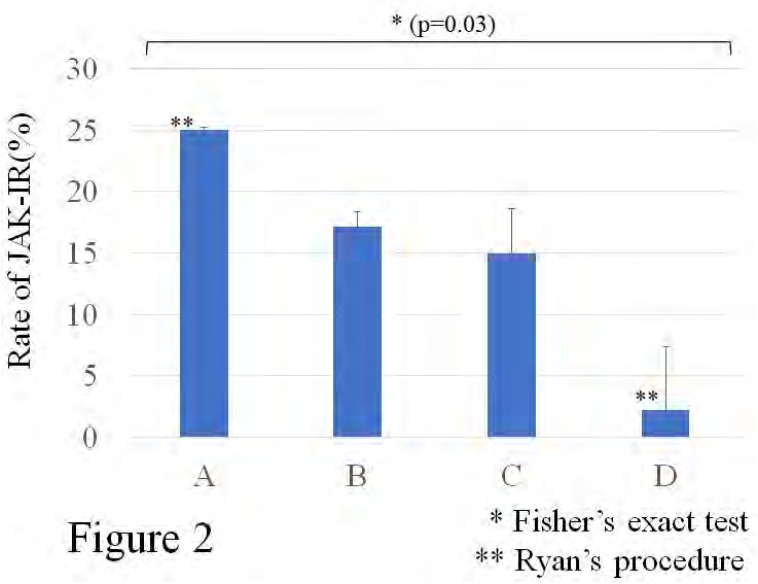


Figure 2

Results: The 132 enrolled patients were classified into four groups (Group A, B, C and D) by cluster analysis (Figure1). The characteristics of each group are as follows, Group A(n=32): seronegative, presence of bone erosion, absence of RA-ILD. Group B(n=35): younger age, seropositive, absence of bone erosion and RA-ILD. Group C(n=20): male, seropositive, presence of RA-ILD. Group D (n=45): older age, seropositive, without MTX treatment, presence of bone erosion and RA-ILD. The rate of JAKi-IR was found in Group A:25%, Group B:17%, Group C:15%, and Group D:2.2%, respectively (Figure2). Notably, Group A showed higher rate of JAKi-IR compared with Group D (Fisher's exact test (p=0.03) and Ryan's procedure).

Conclusion: We identified the characteristics of JAKi-IR. Seronegative but destructive phenotype without lung disease may less benefit from JAKi treatment.

Disclosure: M. Sugawara, None; **Y. Fujieda**, None; **A. Noguchi**, None; **S. Tanimura**, None; **Y. Shimizu**, None; **I. Nakagawa**, None; **H. Takahashi**, None; **M. Kono**, None; **M. Kato**, None; **K. Oku**, None; **O. Amengual**, None; **T. Atsumi**, AbbVie Inc., 5, 8, 9, UCB Japan Co.,Ltd., 5, 8, Eisai Co., Ltd., 8, Gilead Sciences, Inc., 5, 8, Bristol Myers Squibb Co., 2, 8, Chugai Pharmaceutical Co., Ltd., 2, 8, 9, Mitsubishi Tanabe Pharma Corporation, 8, 9, Eli Lilly Japan K.K., 2, 5, 8, Astellas Pharma Inc., 8, 9, Pfizer Inc., 2, 8, 9, Daiichi Sankyo Company, Limited, 5, 8, 9.

Abstract Number: 1753

Substantial Work Limitations in Patients with Rheumatoid Arthritis Despite Optimal Treat-to-Target (T2T) Drug Therapy Intervention

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is associated with restrictions on occupational participation caused by periods of sick leave (absenteeism), reduced productivity at work due to disease (presenteeism) and occupational disability, which account for a significant proportion of indirect costs. We investigate the prevalence and development of occupational participation with a sole focus on absenteeism and employment after drug therapy intervention.

Methods: Data from the multi-center German study "Effectivity of nurse-led care" which examined patients with rheumatoid factor and/or APCA-positive RA after T2T regimen prospectively over 12 months from 01/2018 to 12/2019 were analyzed. A total of 178 patients of working age (18 to 67 years) were included in this evaluation. Disease activity presented through DAS28(CRP) and ability to work measured by the Work Productivity and Activity Impairment Questionnaire (WPAI) were examined at baseline and month 12.

Results: The mean age of the patients was 54 years (median 55; standard deviation (SD) 9.01) and 133 (74.3%) of the patients were female. During the course of the study, there was a significant decrease in DAS28 from 4.27 (SD 1.13) at baseline to 2.52 (SD 1.09; $p< 0.001$) after 12 months. At the end of the study 63% of the patients were in remission (DAS28< 2.6) and 11.2% had low disease activity (DAS28 2.6-3.2). At baseline, 38.8% (n=69) and at the end of the study 41.9% (n=67) of patients were not working. Of the working population, 34.7% were in part-time employment (< 32 hours per week) at baseline and 35.6% at 12 months. The weekly working time also remained almost unchanged during the course of the study, with 29.5 hours (median 32) at baseline and 30.8 hours (median 33) at 12 months. Of those working full-time (n=89), 31.5% (n=14) were absent at the beginning of the study, which tended to decline to 19.1% (n=17) at month 12 (p=0.089). In patients with absenteeism, sickness-related absence from work accounted for 47.6% (SD: 36.8) of total working hours at baseline and 73.5% (SD: 30.03) at the end of the study. Patients with no restrictions on occupational participation showed a significantly greater drop in DAS28 from 3.99 (SD 0.99) at baseline to 2.14 (SD 0.90) at baseline than patients with restrictions (DAS28 4.42 (SD 1.14) at baseline to 2.69 (SD 1.12) at baseline; $p< 0.001$).

Conclusion: Despite T2T and good therapeutic effect according to DAS28, there are clear and persistent limitations in occupational participation. Patients with restricted occupational participation show a significantly increased disease activity. To reduce indirect costs in RA, further optimization of disease management is necessary.

The research leading to these results has received funding from the German Innovationsfunds, Agreement No 01NVF16029.

Disclosure: S. Meyer, None; **J. Hoeper**, None; **K. Hoeper**, None; **T. Witte**, None; **D. Meyer-Olson**, None.

Abstract Number: 1754

The Point of No Return? Functional Disability in Patients with Rheumatoid Arthritis versus the General Population: Results from a Population-based Cohort Study

Elena Myasoedova[1], John Davis[1], Vanessa Kronzer[1], Rachel Giblon[1], Elizabeth Atkinson[1] and Cynthia Crowson[2], [1]Mayo Clinic, Rochester, MN, [2]Mayo Clinic, Rochester, Minnesota, USA, Rochester, MN

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Despite the advances in treatment of rheumatoid arthritis (RA), many patients do not achieve remission or full physical functioning. We have previously shown that patients with RA have a significantly higher prevalence of functional disability (FD) than non-RA subjects across RA disease duration, age and calendar time. However, the pattern of improvement or worsening of functional status in RA vs non-RA patients over time has not been studied. We aimed to assess time spent in FD and transition probability between different levels of FD in patients with RA vs the non-RA subjects after RA incidence/ index date.

Methods: This retrospective population-based cohort study included residents of a geographical area who met 1987 ACR criteria for RA in 1999-2013 and a cohort of non-RA subjects from the same area matched by age and sex. Index date was RA incidence date for RA subjects and incidence date of the matching RA patient for non-RA subjects. Activities of Daily Living (ADL) were recorded annually since 1999 based on patient provided information about performing 6 ADLs without assistance: feeding oneself, dressing, using the toilet, bathing, walking and housekeeping. FD was defined as having difficulty with ≥1 of the 6 ADLs. Changes in the number of disabilities were considered to be state transitions. Multi-state modeling was used to estimate the probability of transitioning between FD states, with

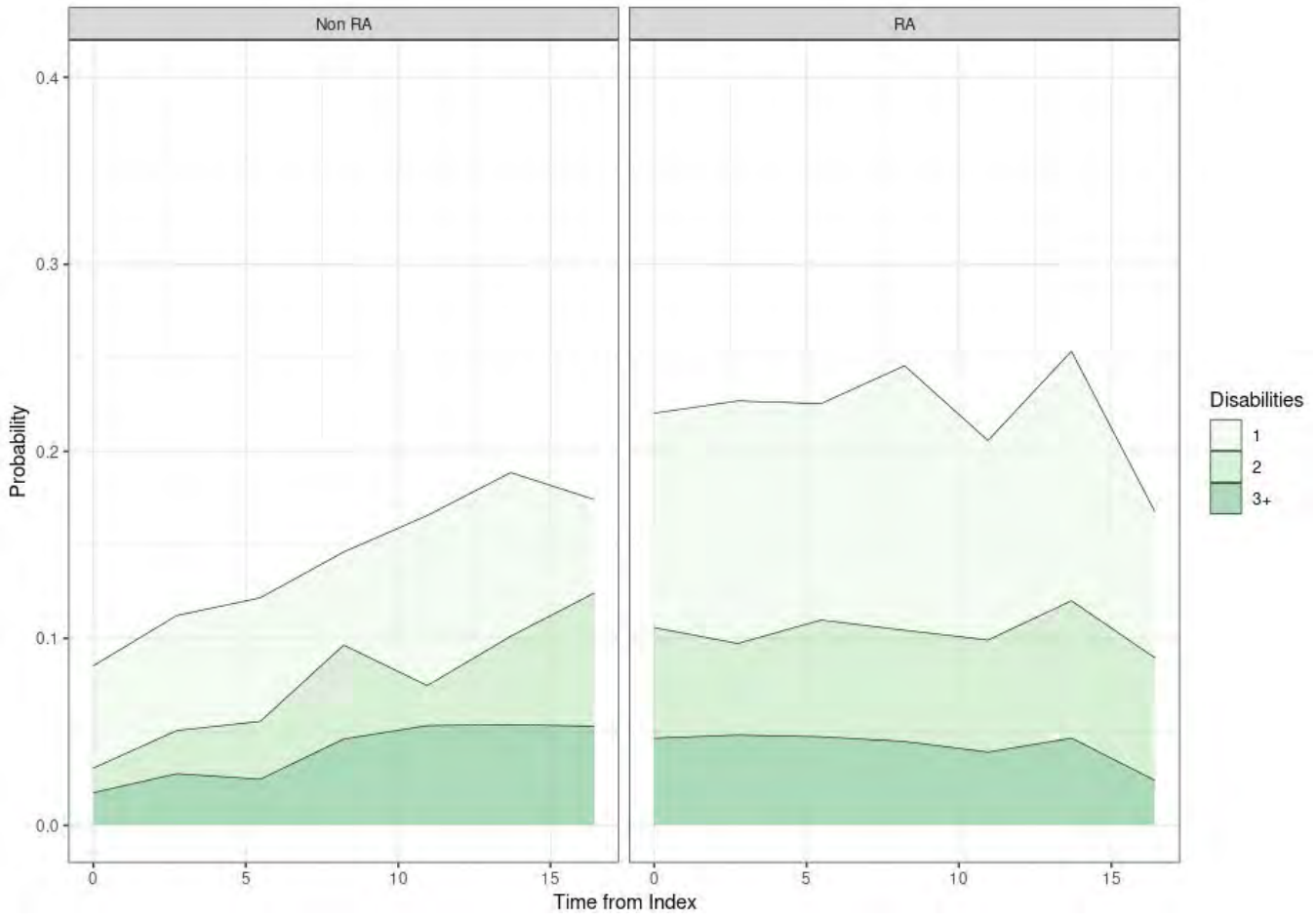

Figure 1. Probability of functional disability in 558 rheumatoid arthritis (RA) versus 457 non-RA patients after RA incidence/ index date

death as a final state. Cox models of multistate data were used to assess the risk of transition with 95 percent confidence intervals (CI) between the levels of FD, adjusting for age, sex, calendar year of index, smoking, and obesity.

Results: A total of 558 patients with RA (mean age 55.4 years, 71% females, 64% RF/CCP positive) and 457 non-RA subjects (mean age 56.5, 70% females) completed 6,594 questionnaires (3,875 RA and 2,719 non-RA) from 1/5/1999 to 1/5/2018 on or after index date. Figure 1 shows probability of FD in RA vs non-RA patients after the index date. In the first 15 years of disease, patients with RA expect to spend 10.1 years without FD and 1.7 years with 1 FD vs 11.6 years ($p< 0.001$) and 0.9 years ($p< 0.001$) in non-RA subjects, respectively. Probability of no FD at index is 78% in RA and 92% in non-RA. By 10 years after index date, probability of no FD in RA is 65%; probability of 1 disability 11%; 2 disabilities 6%, and ≥3 disabilities 1%, compared to 73%; 7%; 5% and 1% in the non-RA subjects, respectively. Risk of transitioning from no FD to FD is significantly higher in RA vs non-RA subjects: Hazard Ratio (HR) 2.4; 95%CI 1.9-3.0. Patients with RA and non-RA subjects have similar risk of returning from FD to no FD (HR 1.2; 95%CI 0.93-1.6). Results did not differ by RF/CCP status.

Conclusion: Patients with RA have a significantly higher probability of any level of FD over RA disease duration, less time spent with no FD, and a 2-fold increased risk of transitioning from no FD to FD, but a similar risk of transitioning back to normal functional status during RA disease course compared to their non-RA counterparts. Our findings suggest that in the era of advanced therapeutics for RA disease management, FD remains an area of ongoing concern, leaving an ample room for improvement of functional outcomes in RA.

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Abstract Number: 1755

Body Mass Index Trajectory and Variability in Rheumatoid Arthritis

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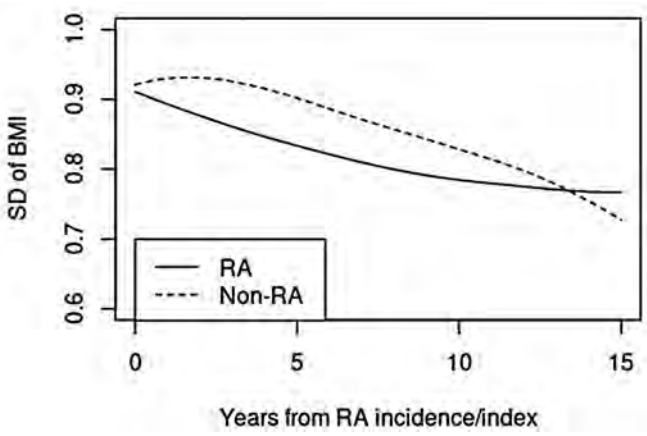
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Past studies have examined associations between BMI and disease activity [1, 2, 3], but few studies have characterized BMI trajectory over the disease course of RA, and there are no known prior studies assessing BMI variability over time in RA patients. We compared BMI trends and variability over time between RA and matched non-RA subjects.

Methods: The study population comprised residents of a geographically defined area with incident RA (age ≥18 years, 1987 ACR criteria met in 1995-2009) and non-RA subjects from the same underlying population with similar age, sex and calendar year of index. All subjects were followed until death, migration, or 01/July/2019. Follow-up was truncated for comparability. Visit-to-visit BMI variability was defined as the within-subject standard deviation (SD) for BMI. Generalized additive models with smoothing splines and random effects to account for multiple measurements per subject were used to illustrate trends in BMI measurements over time.



Results: The study included 558 patients with RA (mean age 55.6 years; 69% female) and 556 patients without RA (mean age 55.7 years, 69% female). Mean (±SD) BMI of patients with incident RA (28.8 ±6.4 kg/m^2) was not significantly different from that of non-RA subjects (28.9 ±6.8 kg/m^2, p=0.94). Models of time trends in BMI demonstrated no significant change in BMI over time for the non-RA subjects (-0.01 kg/m^2 per year, 95% CI:-0.05, 0.5, p=0.58) and a non-significant decline over time for the RA (-0.05 kg/m^2 per year, 95% CI: -0.10, 0.0, p=0.058). Among patients with RA, no differences were found for BMI trend according to sex (p=0.93) or RF/CCP-positivity (p=0.32). There was no evidence of higher variability of BMI measurements over time in patients with RA compared to subjects without RA (SD of random effects: 6.5 RA vs 6.7 non-RA). The figure shows the trends in within-subject SD for RA and non-RA based on consecutive sets of 6 BMI measures.

Conclusion: Our findings demonstrate a minimal decline in BMI over time in the RA population, perhaps reflecting the phenomenon of rheumatoid cachexia. While we were surprised that the RA population did not demonstrate higher BMI variability over time compared to the non-RA population due to weight variation secondary to corticosteroid use, further studies are needed to understand the reasons and implications of these trends.

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Disclosure: G. Challener, None; **E. Myasoedova**, None; **C. Crowson**, Myriad Genetics, 1, Pfizer, 1; **R. Giblon**, None; **J. Davis**, Pfizer, 2, AbbVie, 5, 8, Sanofi-Genzyme, 5, 8.

Abstract Number: 1756

Comparable Long-Term Outcomes Among DAS28-ESR-based Remission Criteria and ACR/EULAR Definitions in Patients with Established Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: To compare long-term clinical and radiographic outcomes among five sets of remission criteria [four clinical and one Ultrasound (US)-based] in a cohort of RA patients in a clinical care setting.

Methods: RA patients in remission (DAS28-ESR < 2.6) were selected. Hand US assessments were performed, and serum levels of inflammation/angiogenesis biomarkers were determined at baseline. Changes in baseline treatment and radiographic progression, defined as the variation in the modified Sharp van der Heijde score (mSHS) at 5 years, were analyzed.

To define remission, five different concepts were used, as follows: DAS28-ESR< 2.6, SDAI< 3.3, CDAI< 2.8, Boolean criteria and score Power Doppler (PD)=0.

Results: Eighty-seven patients with DAS28-ESR< 2.6 were included (table 1). One third fulfilled SDAI (33.3%), CDAI (31%) and Boolean (35.6%) remission criteria and 25.3% had no PD signal in the US evaluation.

26 patients (29.9%) changed the therapy, ranging from 13.6% (PD remission) to 33.3% (CDAI remission) (p=0.11) (Table 2).

Serum levels of ANG (p=0.015) and TNFa (p=0.025) were significantly lower in patients with Boolean remission, whereas IL-18 levels were significantly lower in those with PD remission (p=0.049). Patients without PD in the US assessment had significantly lower mSHS erosion progression (p=0.014) at 5 years (Figure).

Conclusion: Patients with established RA in DAS28-ESR remission had comparable clinical and radiographic outcomes than SDAI, CDAI and Boolean definitions in a clinical care setting. US remission remained as the closest to structural damage abrogation.

	Total patients
	n=87
Age (years), mean (SD)*	57.06 (12.26)
Male, n (%)	13 (14.9)
BMI, mean (SD)	25.44 (5.20)
Disease duration (months), mean (SD)	145.62 (113.03)
TJC, mean (SD)	0.13 (0.39)
SJC, mean (SD)	0.26 (0.67)
Patient GA, mean (SD)	21.84 (11.96)
Physician GA, mean (SD)	17.59 (9.99)
mHAQ, mean (SD)	0.224 (0.333)
ESR (mm/h), mean (SD)	12.22 (7.18)
CRP (mg/dL), mean (SD)	0.26 (0.39)
DAS28-ESR, mean (SD)	2.07 (0.45)
SDAI, mean (SD)	4.62 (2.19)
CDAI, mean (SD)	4.37 (2.22)
RF, n (%),	65 (74.7)
RF (IU), mean (SD)	191.75 (314.71)
ACPA, n (%)	71 (81.6)
ACPA titres (IU/ml), mean (SD)	609.67 (641.32)
PDN, n (%)	27 (31)
csDMARD, n (%)	73 (83.9)
bDMARD, n (%)	54 (62.1)
PDUS (%)	65 (74.7)

Table 1. Baseline characteristics. *Data are expressed as mean (standard deviation) or as percentage; ACPA: anti-cyclic citrullinated peptide/protein antibody; bDMARD: biological Disease-Modifying antirheumatic drug; BMI: Body Mass Index; CDAI: Clinical Disease Activity Index; CRP: C-Reactive Protein; csDMARD: conventional synthetic Disease-Modifying antirheumatic drug; DAS: Disease Activity Score; ESR: erythrocyte sedimentation rate; GA: Global Assessment; mHAQ: Modified Health Assessment Questionnaire; PDN: prednisone; PDUS: Power Doppler Ultrasound; RF: Rheumatoid Factor; TJC: tender joint count; SDAI: Simplified Disease Activity Index; SJC: swollen joint count; SH: synovial hypertrophy.

	Baseline		Clinical Follow-up at 5 years			
			Remission at 5 years		Change Treatment	
	n	%	n	%	n	%
DAS28-ESR Rem	87	100	59	67,8	26	29,9
SDAI Rem	29	33,3	16	18,4	9	31
CDAI Rem	27	31	15	17,2	9	33,3
Boolean Rem	31	35,6	15	17,2	10	32,3
PD Rem	22	25,2	No data		3	13,6

Table 2. Rates of remission and baseline and clinical Follow-up at five years. CDAI: Clinical Disease Activity Index; DAS: Disease Activity Score; ESR: erythrocyte sedimentation rate; PD: Power Doppler; Rem: Remission; SDAI: Simplified Disease Activity Index.

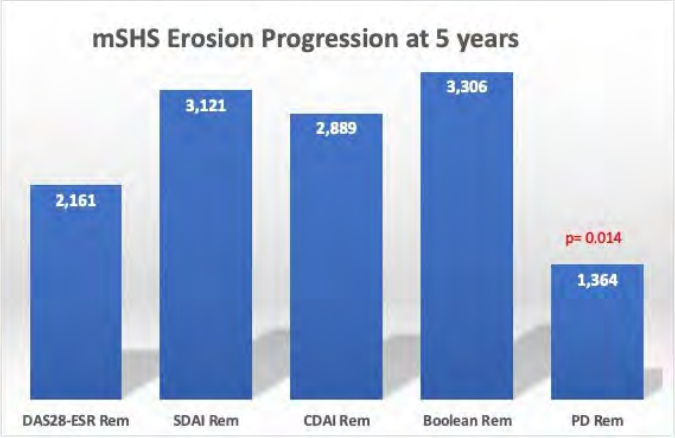

Figure. mSHS Erosion Progression at five years. Data are expressed as mean of mSHS erosion subscore. CDAI: Clinical Disease Activity Index; DAS: Disease Activity Score; ESR: erythrocyte sedimentation rate; mdc: minimum detectable change; mSHS: modified Sharp van der Heijde Score; PD: Power Doppler; Rem: Remission; SDAI: Simplified Disease Activity Index;

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Abstract Number: 1757

High-Intensity Interval Training Increases Rheumatoid Arthritis Cardiorespiratory Fitness in Association with Improvements in CD4+ T Cell and Skeletal Muscle Mitochondrial Metabolism

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

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Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Persons with rheumatoid arthritis (RA) have poor cardiorespiratory fitness and are at increased risk for cardiometabolic co-morbidities. Endurance exercise training improves cardiorespiratory fitness in RA and lessens risk for cardiovascular disease and mortality in the general population; however, the pathways that contribute to the beneficial effects of exercise are largely unknown. In this study of RA participants completing a high-intensity interval training (HIIT) program, our goal was to identify relationships between improvements in cardiorespiratory fitness with changes in peripheral T cell and skeletal muscle mitochondrial metabolism.

Methods: Previously sedentary RA participants (n=12), who all satisfied 1987 ACR criteria, underwent phlebotomy and skeletal muscle biopsies before and after 10 weeks of HIIT. Available paired samples of peripheral blood mononuclear cells (n=6) and skeletal muscle (n=9) were used for primary analyses. Isolated peripheral CD4+ T cell mitochondrial respiration and glycolytic metabolism were assessed via Seahorse XF extracellular flux analyzer. Peripheral lymphocyte and CD4+ T cell subpopulations were measured by flow cytometry. Skeletal muscle mitochondrial metabolism was assessed via citrate synthase (CS) and carnitine acetyltransferase (CrAT) enzyme activity assays, and electron transport chain Western blot protein quantification. To inform mitochondrial metabolism analyses, targeted skeletal muscle and plasma metabolomic profiling (n=12) were performed. Relationships were assessed using Spearman's correlations.

Results: Increases in RA cardiorespiratory fitness following HIIT were significantly associated with increases in RA peripheral CD4+ T cell basal and maximal respiration (rho=0.89, p=0.019 for both) and skeletal muscle CrAT activity (rho=0.70, p=0.036). Increases in CD4+ T cell mitochondrial respiration were significantly associated with increases in circulating naïve CD4+CCR7+CD45RA+ T cells (rho=0.89, p=0.019) and multiple skeletal muscle acylcarnitines. There was large interindividual variability in RA immune cell and skeletal muscle mitochondrial metabolism responses; however, skeletal muscle CrAT activity (mean increase=23.19%, SD=8.24%; p=0.035) significantly improved following HIIT.

Conclusion: In RA, exercise training-related increases in cardiorespiratory fitness associate with improvements in peripheral helper T cell and skeletal muscle oxidative metabolism, which are themselves related. Monitoring of cardiorespiratory fitness with individualized exercise prescription may be valuable in the management of chronic inflammation and cardiometabolic risk in RA.

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Abstract Number: 1758

Prevalence and Incidence of Infection and Venous Thromboembolism in Rheumatoid Arthritis Patients Newly Initiating Various DMARD Classes: Real-World Analysis of 2012–2016 US Medicare Data

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Table 1. Patient and study characteristics by index treatment

Index treatment	Overall		csDMARD(s)		TNFi		anti-IL6		anti-CD20		anti-CD80/86		JAKi	
	N	%	N	%	N	%	N	%	N	%	N	%	N	%
N of patients	13041	100.0	8378	100	2518	100	565	100	142	100	845	100	593	100
Treatment history prior to index treatment														
DMARD-naive (no prior DMARD)	8730	66.9	8378	100	223	8.86	21	3.72	45	31.69	40	4.73	23	3.88
csDMARD-IR (prior csDMARD use only)	2653	20.3			2011	79.86	108	19.12	40	28.17	341	40.36	153	25.8
bDMARD-IR (prior bDMARD use)	1658	12.7			283	11.24	436	77.17	57	40.14	463	54.79	417	70.32
Any csDMARD use prior to index treatment	4662	31.2			2254	89.52	466	82.48	87	61.27	744	88.05	511	86.17
Age (years)														
Mean, SD	68.9	10.8	70.0	10.6	66.7	10.6	67.9	10.1	68.2	12.4	69.0	10.5	63.6	11.9
Median (25th; 75th)	69.9	(65.1; 75.7)	70.8	(66.4; 76.6)	68.1	(60.9; 73.2)	69.0	(65.2; 73.8)	69.8	(66.0; 76.6)	70.1	(65.3; 75.7)	65.9	(54.9; 72.5)
Gender (n, %)														
Male	2859	21.9	2003	23.91	516	20.49	94	16.64	32	22.54	127	15.03	87	14.67
Female	10182	78.1	6375	76.09	2002	79.51	471	83.36	110	77.46	718	84.97	506	85.33
Race (n, %)														
White	10582	81.1	6833	81.56	2029	80.58	466	82.48	124	87.32	695	82.25	435	73.36
Black	1434	11.0	933	11.14	266	10.56	57	10.09	*	*	73	8.64	97	16.36
Others	1025	7.9	612	7.3	223	8.86	42	7.43	*	*	77	9.11	61	10.29
Payer Type (n, %)														
Medicare only	9863	76.6	6036	72.05	2,275	90.35	490	86.73	124	87.32	750	88.76	308	51.94
Medicare/Medicaid dual	3058	23.5	2342	27.95	243	9.65	75	13.27	18	12.68	95	11.24	285	48.06
Follow-up time (days)														
Mean, SD	882.6	309.8	889	307	882	320	885	294	884	309	856	322	835	298
Median (25th; 75th)	870.0	(611; 1138)	873	(622; 1144)	873	(597; 1140)	906	(615; 1110)	879	(629; 1082)	825	(576; 1144)	809	(584; 1070)
Duration on therapy (days)														
Mean, SD	411.1	362.2	399	367	440	353	448	351	317	343	469	355	358	339
Median (25th; 75th)	301.0	(102; 620)	270	(90; 616)	355	(145; 626)	355	(151; 666)	200	(34; 437)	399	(170; 663)	229	(88; 565)
Duration on therapy (days) in patients with Medicare/Medicaid dual														
Mean, SD	348.9	336.1	340	340	393	311	322	268	328	314	396	325	381	343
Median (25th; 75th)	219.5	(89; 519)	204	(82; 506)	336	(125; 553)	204	(109; 485)	364	(56; 393)	315	(119; 579)	262	(101; 600)

* value suppressed if patient count < 11 as required by Medicare report policy
bDMARD, biologic DMARD; cs DMARD, conventional synthetic DMARD; JAKi Janus kinase inhibitor; TNFi, TNF-α inhibitor

Table 2. Prevalence (%) of VTE and infection during the 12-month baseline

Index DMARD	Overall N = 13,041	csDMARD n = 8,378	TNFi n = 2,518	anti-IL6 n = 565	anti-CD20 n = 142	anti-CD80/86 n = 845	JAKi n = 593	*P* value§
Prevalence, %								
VTE (DVT or PE)†	4.4	4.4	3.9	6.9	*	4.6	4.1	.0520
Deep vein thrombosis (DVT)	3.6	3.6	3.3	6.0	*	3.4	3.5	.0653
Pulmonary embolism (PE)	1.5	1.6	1.2	*	*	1.8	*	.4761
Infection, any‡	81.9	78.9	85.4	89.0	95.8	88.9	89.0	< .0001
Serious infection	16.6	16.1	16.0	15.9	24.6	20.8	18.5	.0007
Opportunistic infection	9.7	8.5	11.0	10.6	15.5	13.6	11.6	< .0001
Herpes zoster	3.4	3.2	3.8	3.0	*	4.1	3.9	.2865

* value suppressed if number of events < 11 as required by Medicare report policy;
† VTE, venous thromboembolism, identified based on diagnosis code for DVT or PE;
‡ Infection identified by diagnosis code for infection or use of antibiotics or antivirals;
§ *P* values estimated using Chi-square test comparing among the different DMARD classes;
csDMARD, conventional synthetic DMARD; Jake, Janus kinase inhibitor; TNFi, TNF-α inhibitor

Table 2

Background/Purpose: RA patients have an increased risk of infection[1] and venous thromboembolism (VTE)[2]. Although rates of serious infection and VTE have been reported for Medicare recipients with RA, the scope of previous publications has been limited to a select number of targeted immunomodulators[3,4]. This study examined the prevalence and incidence of infection and VTE in US Medicare RA patients initiating any of the available DMARDs.

Methods: Within the 20% sample of Medicare fee-for-service beneficiaries, the study population comprised of RA patients (without malignancy or non-RA autoimmune disease) with first initiation (index date; 01/2013–12/2015) of various classes of DMARDs: csDMARD, TNF-a inhibitor (TNFi), anti-IL6, anti-CD20, anti-CD80/86, and/or Janus kinase inhibitor (JAKi). The observation period involved baseline (one-year prior to index date) and follow-up (from index date until discontinuation, Medicare disenrollment, death, or 12/31/2016). Conditions of interest included VTE

Table 3. Incidence (P100PY) of VTE or infection while on index DMARD regimen

Index DMARD	Overall	csDMARD	TNFi	anti-IL6	anti-CD20	anti-CD80/86	JAKi	*P* value§
Incidence, P100PY								
VTE (DVT or PE)†	2.4	2.4	2.1	2.7	*	3.0	2.2	.1192
Deep vein thrombosis (DVT)	1.9	2.0	1.6	2.7	*	2.3	*	.1055
Pulmonary embolism (PE)	0.9	0.9	0.8	*	*	*	*	.1126
Infection, any‡	249.6	321.5	147.8	167.3	340.9	164.7	159.9	< .0001
Serious infection	17.6	17.0	18.3	19.3	30.2	15.4	21.9	.0036
Opportunistic infection	10.2	9.6	10.3	10.9	18.3	10.2	15.8	.0003
Herpes zoster	4.1	3.7	4.1	5.2	*	3.3	8.6	< .0001

* value suppressed if number of events < 11 as required by Medicare report policy;
† VTE, venous thromboembolism, identified based on diagnosis code for DVT or PE; patients with VTE during baseline were excluded from incidence estimate;
‡ Infection identified by diagnosis code for infection or use of antibiotics or antivirals; patients with infection within 60 days prior to initiation of index therapy were excluded from the incidence estimate;
§ *P* values estimated from univariate Cox regressions comparing among the different DMARD classes;
csDMARD, conventional synthetic DMARD; JAKi, Janus kinase inhibitor; P100PY, per 100 patient-years; TNFi, TNF-α inhibitor

Table 3

(deep-vein thrombosis and pulmonary embolism, defined based on diagnosis codes), overall infection (based on diagnostic codes or use of antibiotics/antivirals), serious infection (based on inpatient or emergency department diagnostic codes in any position, or outpatient use of intravenous antibiotics), opportunistic infection (based on diagnostic codes), and herpes zoster (HZ, based on diagnostic codes). We calculated baseline prevalence (%) and on-treatment incidence (number of new events per 100 patient-years [P100PY] during index DMARD treatment) of these conditions. Incident infection analyses excluded patients with infection within 60 days before index date. Incident VTE analyses excluded patients with any pre-index VTE.

Results: The 13,041 RA patients (78.1% female; mean age 68.9 years at index date) initiated the following index therapies: csDMARD (64.3%), TNFi (19.3%), anti-IL6 (4.3%), anti-CD20 (1.1%), anti-CD80/86 (6.5%), and JAKi (4.5%). The median follow-up time ranged 2.2–2.5 years, and median time on index therapy ranged 0.5–1.1 years (Table 1).

In the 12 months prior to initiating index therapy, patients experienced VTE (prevalence 4.4%) and infections (81.9%), serious infections (16.6%), opportunistic infections (9.7%), and HZ (3.4%). (Table 2). The on-therapy incidence P100PY was 2.4 for VTE (range 2.1–3.0), 249.6 for infection (range 147.8–340.9), 17.6 for serious infection (range 15.4–30.2), and 10.2 for opportunistic infection overall (range 9.6–18.3), including 4.1 for HZ (range 3.3–8.6) (Table 3).

Conclusion: VTE and infection affected Medicare beneficiaries with RA before initiating a new DMARD therapy. While on the new treatment regimen, patients developed recurrent or novel infections or novel VTE cases. Understanding the prevalence and incidence of these conditions can help clinicians and population-health decision makers optimize treatment choices.

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Abstract Number: 1759

Rheumatoid Arthritis Affects the Ossicular Joints: A Human Otopathologic Study

Melissa Castillo-Bustamante[1], Marc Polanik[1], Dhrumi Gandhi[1], Elliott Kozin[1] and Aaron Remenschneider[1], [1]Massachusetts Eye and Ear Infirmary/Harvard University, Boston, MA

SESSION INFORMATION
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Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Inflammation of synovial joints in small and large extremities is commonly seen in Rheumatoid arthritis (RA). To date little is known about how this disease affects the synovial, diarthroidal incudomallear (IMJ) located in the middle ear. Previous clinical reports of hearing impairment and altered middle ear impedance in patients with RA have not been substantiated with defined changes along the ossicular chain. Herein, we performed an otopathologic analysis in human specimens with a history of RA during life.

Methods: The National Temporal Bone Registry was queried for cases with history of RA during life. Otopathologic analysis was performed in individuals with RA and compared to age matched controls. Outcomes included descriptive middle ear pathology, volumetric measurements of the IMJ synovial space and immunohistochemical analysis of the IMJ using CD3 and CD20.

Results: Twenty-one ears (specimens) with RA and 18 controls were identified. Mean age was not significantly different between RA and control groups: 65.3 vs 69.3, (p=0.441). In RA and control group females were mainly affected, 75% and 80%, respectively. Middle ear findings in specimens with RA included: IMJ disarticulation, bone erosion of incus and malleus and demineralization of IMJ. These findings were not present in any control specimen. In specimens with RA, diminished spaces between the osseous surfaces in the lateral sides of the ossicles were seen. A loss of total, calcified and hyaline cartilage in lateral and medial sides of the incus was found in RA specimens compared to controls. Diminished synovial space volume of the IMJ was found in RA specimens but not in controls [(2.62 mL (SD 0.49mL) vs 38.4 mL(SD 81.1 mL), (p=0.004)]. CD3 and CD20 staining was intensely positive within the IMJ space of RA specimens, while controls showed weak IMJ space staining with CD3 and no staining with CD20.

Conclusion: The incudomalleolar joint in patients with RA demonstrate pathologic differences when compared to controls. Cartilage areas and synovial spaces of the RA group were smaller than controls. CD3/CD20 positivity in RA suggests distinct inflammatory involvement of the IMJ. Further study of the functional affects of observed changes on sound transmission is needed.

Disclosure: M. Castillo-Bustamante, None; **M. Polanik**, None; **D. Gandhi**, None; **E. Kozin**, None; **A. Remenschneider**, None.

Abstract Number: 1760

The Association Between the Risk of Venous Thromboembolism and Disease Activity in Patients with Rheumatoid Arthritis: A Retrospective Observational Study

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid arthritis (RA) is an immune-mediated synovial disease with chronic inflammation. Systemic inflammation is considered one of risk factors for venous thromboembolism (VTE), which includes both deep venous thrombosis (DVT) and pulmonary embolus (PE). RA patients are thought to be at risk of developing thromboembolic events due to multiple factors. However, less is known about association of systemic inflammation and VTE in patients with RA. We aimed to clarify the clinical features and risk factors of VTE in RA patients.

Methods: We retrospectively reviewed the prevalence of VTE in RA patients who visited Hokkaido University Hospital with more than 2 years follow-up from 2010 to 2019. In this study, 28 cases diagnosed with VTE were identified during that period. All patients fulfilled 2010 American College of Rheumatology (ACR)/ European League Against Rheumatism (EULAR) classification criteria. VTE was confirmed by the venous ultrasound and/or enhanced CT regardless of symptoms. The patients who had been diagnosed with DVT or PE prior to 2010, or had used anticoagulant and/or antiplatelet drugs were excluded. To evaluate the risk factors for the development of VTE, we randomly selected 144 patients without VTE (non-VTE) and registered demographic, clinical, and treatment profile. Disease Activity Score-28 for Rheumatoid Arthritis (DAS28) were calculated in VTE cases and in non-VTE cases at the last regular follow-up visits before onset of the VTE and within the study period, respectively. The risk factors were identified by multivariate logistic regression analysis. The study was approved by the Institutional Review Board of Hokkaido university Hospital.

Results: This study comprised a total of 1379 cases (1076 women/303 men; median age at diagnosis 54 years [Interquartile range (IQR) 42-64]) and median follow up duration was 7 years (IQR 5-9). The prevalence of VTE was 0.20 % (28 of 1379 cases) and the median age at the time of diagnosis of VTE was 74 years (IQR 65.5-79). The rate of female patients was 72.9 %. In the VTE cases, five (17.9%) and three (10.7%) patients had history of orthopedic surgery and malignant disease, respectively. Univariate analysis showed no difference between VTE and non-VTE in the presence of smoking history, hypertension, dyslipidemia, diabetes mellitus, chronic kidney disease, and treatment with JAK inhibitor or NSAIDs. Body mass index (BMI), the presence of interstitial lung diseases and glucocorticoid usage were identified as risk factors of VTE (p=0.001). Furthermore, the rates of moderate and high disease activity in RA (DAS-28CRP > 2.7) were higher in VTE cases compared to non-VTE cases (p=0.01). In multivariate logistic regression analysis, high disease activity in RA was significantly associated with the development of VTE (p= 0.02, Odds Ratio 5.88, 95% Confidence Interval 1.32-26.17).

Conclusion: High disease activity in RA was identified as a risk factor of VTE, suggesting that clinical remission would be beneficial for preventing VTE.

Disclosure: M. Yoshimura, None; **Y. Fujieda**, None; **M. Kono**, GlaxoSmithKline K.K., 2; **M. Kato**, None; **K. Oku**, None; **O. Amengual**, None; **T. Atsumi**, AbbVie Inc., 5, 8, 9, UCB Japan Co.,Ltd., 5, 8, Eisai Co., Ltd., 8, Gilead Sciences, Inc., 5, 8, Bristol Myers Squibb Co., 2, 8, Chugai Pharmaceutical Co., Ltd., 2, 8, 9, Mitsubishi Tanabe Pharma Corporation, 8, 9, Eli Lilly Japan K.K., 2, 5, 8, Astellas Pharma Inc., 8, 9, Pfizer Inc., 2, 8, 9, Daiichi Sankyo Company, Limited, 5, 8, 9.

Abstract Number: 1761

Rheumatoid Arthritis Inpatient Mortality: An Analysis of the National Inpatient Sample

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatoid Arthritis (RA) is a chronic autoimmune disease with increased mortality. Little national-level data is available on inpatient mortality in RA patients. In this report, we use a large Unites States (U.S) population-based database to analyze the principal discharge diagnosis for RA patients experiencing inpatient mortality.

Methods: Data were abstracted from the National Inpatient Sample (NIS) Database. This is the largest inpatient hospitalization database in the U.S. It is a nationally representative sample of 20% of hospitalizations from approximately 1000 hospitals. The numbers in the databases are weighted to optimize national estimates. The NIS was searched for hospitalizations in 2017 with an ICD-10 RA codes M05 and M06 as the principal or secondary diagnosis. The total number of RA discharges, number of in-hospital deaths, percentage of in-hospital deaths, length of stay (LOS), total hospital charges were recorded. The "principal discharge diagnosis" in RA patients experiencing in-hospital death was divided into 19 ICD 10 code categories.

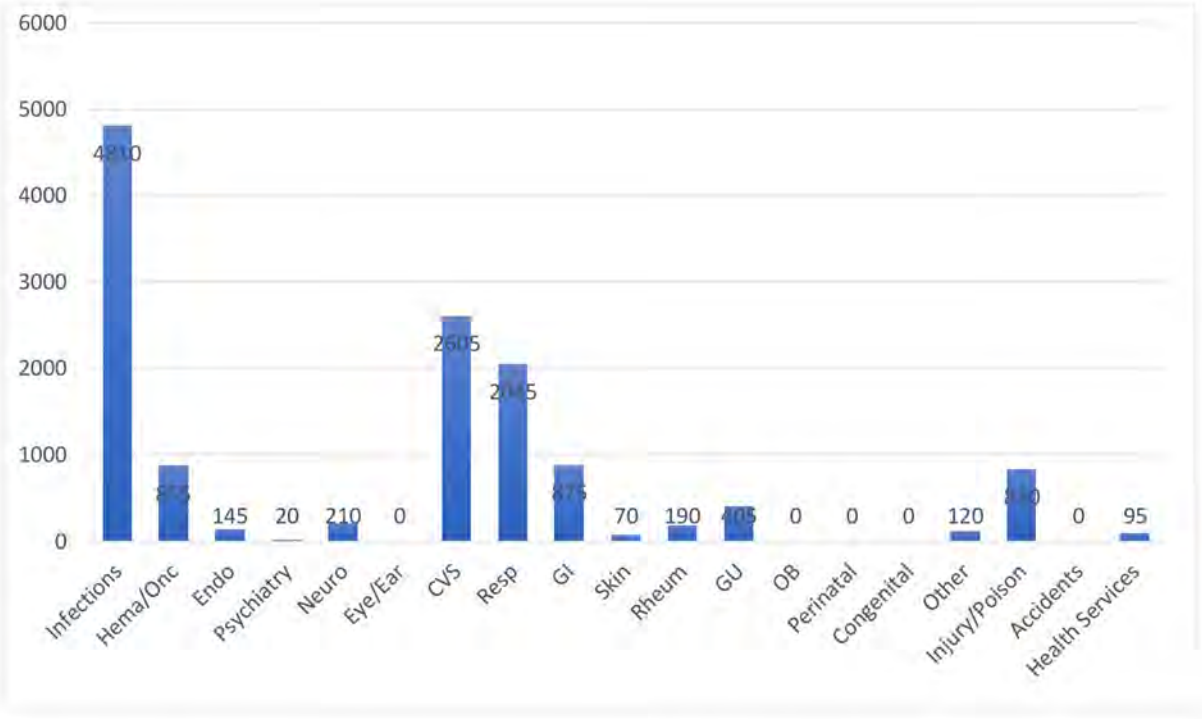
Results: There were over 30 million discharges included in the 2017 NIS database. Of those, 565,440 hospitalizations were for patients aged 18 years or above, who had either a principal or secondary ICD 10 code for RA. 13,285 of these patients (2.35%) experienced in-hospital mortality. These patients were mainly female 70.19%, whites 64.85%, average age of 74.31 years, average LOS of 7.04 days and mean total hospital charges of $101,210. The top 5 principal discharge ICD 10 code categories in RA patients experiencing inpatient mortality in descending order of frequency were as follows (see table 1 and figure 1): infections 4810 (36.20%), cardiovascular 2605 (19.60%), respiratory 2045 (15.39%), digestive system 875 (6.59%), hematology/oncology 865 (6.51%). The most common principal diagnoses in RA patients with in-hospital mortality were sepsis, followed by acute and chronic hypoxic respiratory failure, aspiration pneumonitis, non-ST segment myocardial infarction, and acute kidney injury in descending order of frequency.

Conclusion: For adult RA patients experiencing in-hospital mortality, infections were the most common ICD 10 code category, and sepsis was the most common specific ICD 10 code principal diagnosis of hospitalization. Preventive

Admission Category	Number of Deaths
Certain infections and parasitic diseases	4810
Neoplasms & diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	865
Endocrine, nutritional and metabolic diseases	145
Mental, behavioral and neurodevelopmental disorders	20
Diseases of the nervous system	210
Diseases of the eye and adnexa and Ear	0
Diseases of the circulatory system	2605
Diseases of the respiratory system	2045
Diseases of the digestive system	875
Diseases of the skin and subcutaneous tissue	70
Diseases of the musculoskeletal system and connective tissue	190
Diseases of the genitourinary system	405
Pregnancy, childbirth, and puerperium	0
Certain conditions originating in the perinatal period	0
Congenital malformations, deformations, and chromosomal abnormalities	0
Symptoms, signs, and abnormal clinical laboratory findings, not elsewhere classified	120
Injury, poisoning, and certain other consequences of external causes	830
External causes of morbidity (accidents & violence)	0
Factors influencing health status and contact with health services	95

Table 1. ICD-10 code admission category for Rheumatoid arthritis hospitalizations with inpatient mortality

measures, prompt diagnosis, and management of sepsis are needed to reduce the rate of inpatient mortality for RA patients.



N/B: Numbers represent number of deaths for each ICD 10 category

Abbreviations: RA: Rheumatoid Arthritis, OB: Obstetrics & gynecology, GU: Genito-urinary, Rheum: Rheumatological, GI: Gastrointestinal, Resp: Respiratory, Hema/onc: Hematologic/Oncology, Endo: Endocrine, Neuro: Neurological, CVS: Cardiovascular

Figure 1. Clustered column chart of ICD 10 admission category for RA hospitalizations with inpatient mortality

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Disclosure: E. Edigin, None; **P. Eseaton**, None; **A. Manadan**, None.

Abstract Number: 1762

Benefit and Risk Profiles of Janus Kinase Inhibitors Approved in the US for the Treatment of RA

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: In clinical practice, drug treatment decisions must account for the expected benefit from a drug along with its potential risks. Evaluating the number needed to treat (NNT) and the number needed to harm

Trial	RA-BEACON[1]		ORAL STEP[3]		SELECT BEYOND[2]	
NNT or NNH and Response (percentage of patients) at Week 12	BARI (N=174)	PBO (N=176)	TOFA (N=133)	PBO (N=132)	UPA (N=164)	PBO (N=169)
NNT						
ACR20						
NNT (95% CI)	5 (4, 9)		6 (4, 17)		3 (3, 4)	
Response	48.9	27.3	41.7	24.4	64.6	28.4
ACR50						
NNT (95% CI)	9 (6, 20)		6 (4, 11)		5 (4, 8)	
Response	20.1	8.0	26.5	8.4	34.1	11.8
ACR70						
NNT (95% CI)	10 (7, 20)		9 (6, 17)		20 (10, ∞*)	
Response	12.6	2.3	13.6	1.5	11.6	6.5
NNH						
AEs leading to discontinuation						
NNH (95% CI)	56 (17, ∞*)		143 (not reported)		NA**	
Event	4.0	2.3	6.0	5.3	2.4	5.3
SAEs						
NNH (95% CI)	NA**		NA**		21 (not reported)	
Event	1.7	4	1.5	4.5	4.9	0.0

* ∞ : when the difference between treatment and PBO is positive, but the CI includes 0, the upper bound for the CI is set to ∞

**NA: the AE was more frequent with PBO than active treatment; the difference between treatment and PBO is ≤0

Abbreviations: ACR20/50/70: proportion of patients achieving ≥20%, 50%, or 70% improvement from baseline, respectively, with American College of Rheumatology response; AE: adverse event; BARI: baricitinib 2 mg/day; PBO: placebo; SAE: serious adverse events; TOFA: tofacitinib 5 mg twice daily; UPA: upadacitinib 15 mg/day

Number needed to treat and number needed to harm at Week 12 for baricitinib, tofacitinib, and upadacitinib

(NNH), together, is one approach to inform about the benefit-risk profile of a drug. The objective of this analysis is to report the NNT and NNH of Janus kinase (JAK) inhibitors approved in the US, baricitinib 2 mg/day (BARI), tofacitinib 5 mg twice daily (TOFA), and upadacitinib 15 mg/day (UPA), in RA patients who have an inadequate response to TNF inhibitors (TNFi-IR).

Methods: Data were from published Phase 3 randomized, double-blind clinical trials (RCTs) in TNFi-IR RA patients. In the BARI and UPA RCTs, patients were required to have an RA diagnosis defined by the 2010 ACR classification criteria,[1,2] whereas patients in the TOFA RCT were required to have an RA diagnosis based on the 1987 ACR criteria.[3] The respective treatment and placebo (PBO) sample sizes included 174 and 176 BARI and PBO patients,[1] 133 and 132 TOFA and PBO patients,[2] and 164 and 169 UPA and PBO patients.[3] Endpoints were evaluated at 12 weeks and included the reported proportion of patients who achieved American College of Rheumatology 20%, 50%, or 70% response (ACR20, ACR50, ACR70, respectively) for NNT and percentage of patients who experienced adverse events (AEs) leading to study discontinuation or serious AEs (SAEs) for NNH. NNT and NNH were calculated as 100 / difference (95% CI) of response or event rate between treatment and PBO.

Results: Across trials, patient age ranged from an average of 54 to 58 years (yrs) and 99-100% of patients had prior use of at least one biologic DMARD or TNFi, specifically. The duration of disease ranged from 11-15 yrs. The percentage of patients experiencing the given endpoints with treatment vs. PBO and the associated NNT or NNH are presented in the Table by study. The NNTs were < 10 for BARI, TOFA, and UPA with ACR20 and ACR50. The NNH values varied by JAK inhibitor and by event type.

Conclusion: There is no methodology that can be considered a gold-standard to evaluate the benefit and risk profile of a drug in a specific population. Across different studies of patients with refractory RA, JAK inhibitors have a favorable benefit and risk profile. Each drug delivers benefits with an associated level of risk, and these are not the same from drug to drug. NNT and NNH is one strategy for clinicians to standardize the benefit-risk assessment across different clinical programs that can be useful to support better informed decision making in clinical practice.

References: [1]Genovese, et al. NEJM 2016; 374:1243-1252; [2]Genovese, et al. Lancet 2018; 391: 2513-24; [3]Burmester, Lancet 2013; 381:451-60

Disclosure: A. Wells, Abbvie, 1, 2, Eli Lilly & Co., 1, 2; **K. Griffing**, Eli Lilly and Company, 1, 3; **A. Quebe**, Eli Lilly & Co., 1, 2; **L. Sun**, Eli Lilly & Co., 1, 2; **H. Zhang**, Eli Lilly & Co., 1; **P. Reis**, Eli Lilly and Company, 3, 4, AbbVie Inc., 4.

Abstract Number: 1763

Blending Hierarchical Cluster Analysis and Cluster-Specific Regressions to Predict Clinical Outcome to Tofacitinib Treatment in Patients with Rheumatoid Arthritis

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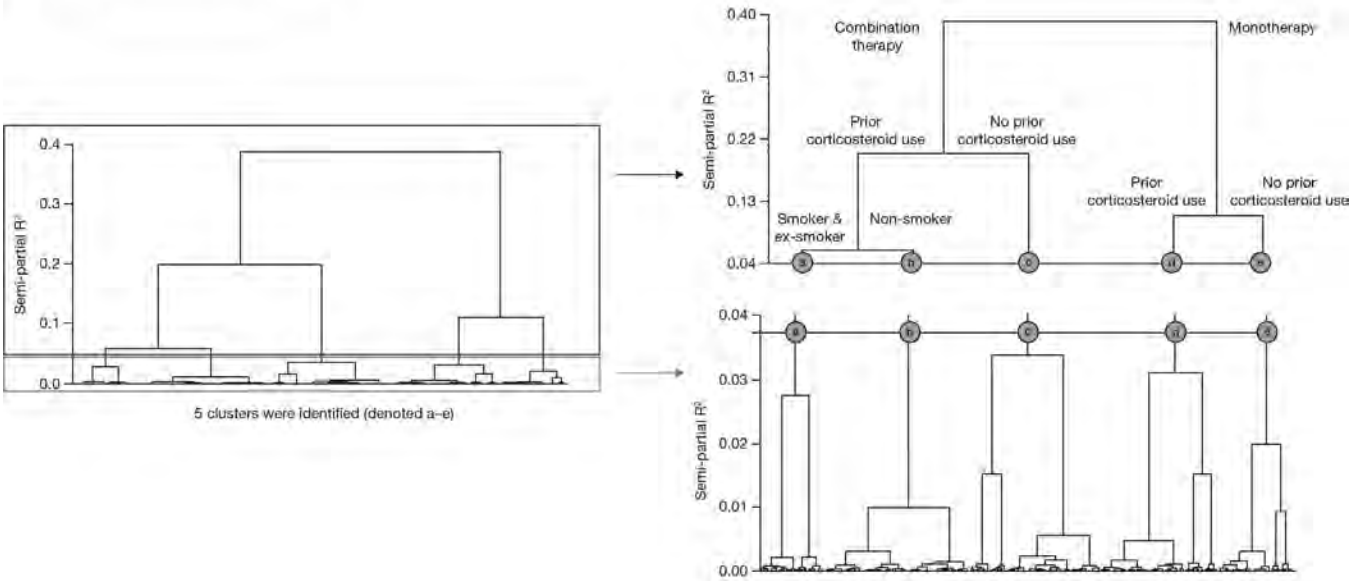
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Diagnosis, Manifestations, & Outcomes Poster IV: Lifespan of a Disease
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Patients with RA exhibit wide variations in response to therapy. Early treatment response profiles may help us to better predict subsequent treatment response, thus expediting treatment optimization, improving outcomes, and reducing exposure to ineffective therapies. This exploratory study aimed to predict treatment outcomes to tofacitinib in patients with RA using hierarchical cluster analysis of baseline (BL) data, and cluster-specific regressions using BL data only vs BL data + early treatment response profiles.

Methods: This analysis included data from Phase 3 (NCT00814307; NCT00847613; NCT00856544; NCT00853385) and Phase 3b/4 (NCT02187055) randomized controlled trials (RCTs) of tofacitinib in patients with RA. Data were included from patients randomized to receive tofacitinib 5 mg twice daily (BID; monotherapy or + MTX/other csDMARDs) with ≥ 4 Clinical Disease Activity Index (CDAI) data points during 6 months of treatment and moderate/high BL CDAI severity; patients who discontinued the RCTs were assessed case-by-case for inclusion. A bottom-up hierarchical cluster analysis (using BL data) was conducted to improve prediction of tofacitinib response by identifying patient subgroups for cluster-specific regression models (using BL data ± early response profiles). The primary outcome was prediction of CDAI responder status at Month (M)6, using BL, M1, and M3 data, defined as achievement of minimum clinically important difference (MCID; CDAI change of 11/6/2 for patients with high/moderate/low BL CDAI severity); achievement of low disease activity (2.8< CDAI ≤ 10) or remission (CDAI ≤ 2.8) (ie treat-to-target approach for response) was also assessed. For cluster-specific regressions, patients of each cluster were randomized to a training (model development) or testing (model evaluation) dataset. The algorithm for outcome prediction consisted of all fixed BL demographics (eg age) ± time-lagged (M1 and M3) covariates (eg CDAI).

Figure 1. Hierarchical cluster analysis dendrogram



The semi-partial R^2 measures the homogeneity of merged clusters. This value reflects decreasing homogeneity of members in a cluster as clusters are combined to make new clusters.
Semi-partial R^2 values ranging from 0.034 to 0.058 were deemed to reflect an appropriate tradeoff of low semi-partial R^2 and not too many fragmented clusters.
Cluster 'a' (n=192) = smoker/ex-smoker>prior corticosteroid use>combination therapy; cluster 'b' (n=446) = non-smoker>prior corticosteroid use>combination therapy;
cluster 'c' (n=401) = no prior corticosteroid use>combination therapy; cluster 'd' (n=354) = prior corticosteroid use>monotherapy; and cluster 'e' (n=224) = no prior corticosteroid use>monotherapy

Figure 2. Prediction of CDAI responder status at Month 6 in the testing dataset, as defined by MCID or T2T responder criteria,[a] in optimized, cluster-specific regressions using data for a) BL variables only or b) baseline + time-lagged covariates. Prediction of responder status was compared with the true responder status to determine whether the prediction was correct or incorrect. The total proportion of patients for whom prediction of outcome (response or non-response) was correct may differ slightly from the sum of correct response and correct non-response, due to number rounding

a)

MCID

Total patients with correct predictions: 353/435 (81.1%)		True MCID responder status at Month 6	
		No response	Response
Predicted MCID responder status at Month 6	No response	5/435 (1.2%)	15/435 (3.4%)
	Response	67/435 (15.4%)	348/435 (80.0%)

T2T

Total patients with correct predictions: 272/435 (62.5%)		True T2T responder status at Month 6	
		No response	Response
Predicted MCID responder status at Month 6	No response	233/435 (53.6%)	148/435 (34.0%)
	Response	15/435 (3.4%)	39/435 (9.0%)

b)

MCID

Total patients with correct predictions: 367/435 (84.4%)		True MCID responder status at Month 6	
		No response	Response
Predicted MCID responder status at Month 6	No response	13/435 (3.0%)	9/435 (2.1%)
	Response	59/435 (13.6%)	354/435 (81.4%)

T2T

Total patients with correct predictions: 352/435 (80.9%)		True T2T responder status at Month 6	
		No response	Response
Predicted MCID responder status at Month 6	No response	209/435 (48.0%)	44/435 (10.1%)
	Response	39/435 (9.0%)	143/435 (32.9%)

[a]CDAI response was defined as achievement of MCID (CDAI change of 11/6/2 for patients with high/moderate/low BL CDAI severity) or achievement of low disease activity (2.8< CDAI ≤10) or remission (CDAI ≤2.8) (ie T2T approach for clinical response)
BL, baseline; CDAI, Clinical Disease Activity Index; MCID, minimum clinically important difference; T2T, treat-to-target

Results: Data from 1,617 patients with RA using tofacitinib 5 mg BID were included. Hierarchical cluster analysis using BL data had 6 clustering variables (tofacitinib monotherapy/combination therapy, prior corticosteroid use, smoking status, BL CDAI, BL HAQ-DI, BL pain discordance) and 5 unique clusters (ie subgroups; Figure 1). The train-

ing dataset (1,182 patients; 73.1%) was used to develop cluster-specific regressions which were then assessed in a testing dataset (435 patients; 26.9%). When regression models were used to predict outcome in the testing dataset using only BL data, prediction of MCID-defined CDAI responder status at M6 was correct for 81.1% of patients (Figure 2). Using BL + time-lagged covariates, prediction of MCID-defined CDAI responder status was correct for 84.4% of patients (Figure 2).

Conclusion: This hybrid of clustering and cluster-specific regressions, taking into account early treatment response profiles, is an interesting approach worthy of further exploration for predicting and improving long-term tofacitinib treatment outcomes in patients with RA.

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Abstract Number: 1764

Disease Modifying Anti-rheumatic Drug and Biologic Therapy in Pregnancy: A Single-center Mixed Methods Study

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Rheumatic diseases including rheumatoid arthritis, seronegative inflammatory arthritis and systemic lupus erythematosus can be associated with significant morbidity in women of child-bearing age. Both these diseases themselves and their treatments have been shown to impact fetal and maternal outcomes. Although there is growing evidence outlining safety of many anti-rheumatic drugs (ARDs) in pregnancy, many patients discontinue treatments in the peripartum period due to concern of fetal harm. This study sought to identify perinatal medication use patterns at a single tertiary care center and to understand patient perspectives surrounding their use.

Methods: Electronic medical records were reviewed for women attending the rheumatic diseases in pregnancy clinic, a rheumatology clinic with subspecialty input, at St. Michael's Hospital in Toronto, Canada, from January 2013 until November 2019. A 12-item questionnaire was administered to women attending this clinic to explore patient perspectives. Data was analyzed using descriptive statistics.

Results: Thirty-eight women and forty-five pregnancies were identified, with rheumatoid arthritis (N=12, 32%), systemic lupus erythematosus (N=18, 27%) and seronegative arthritis (n=8, 16%) representing the majority. Twenty-nine patients (60%) were exposed to disease modifying anti-rheumatic drugs (DMARDs) and eight patients (16%) were exposed to biologics during pregnancy. Of those who experienced medication changes in the perinatal period, the highest proportion (57%) occurred pre-partum, with fewer changes in each trimester, as pregnancy progressed. Patients who received pre-pregnancy counselling were more likely to have pre-pregnancy medication adjustments and were more likely to utilize a DMARD or biologic during pregnancy. The survey was completed by 19 respondents. Fourteen women (74%) reported that they would consider ARD use in pregnancy with the highest degree of comfort reported for DMARDs (N=16, 84%), compared to steroids (N=3, 16%), non-steroidal anti-inflammatory drugs (N=6, 32%) and biologics (N=2, 11%). Fifteen participants (79%) felt that their questions were adequately answered by health care providers with the majority (79%) describing their rheumatologist as their primary information source. Most patients believed that information received from healthcare providers was helpful (N=15, 79%) and felt that they were provided adequate resources to inform decisions about medication use in pregnancy (N=11, 58%).

Conclusion: While the majority of women with rheumatic diseases in our cohort continued on ARD therapy during pregnancy, most survey respondents reported discomfort with use of steroids, NSAIDs, biologics and DMARDs, despite evidence of their safety in recent literature. This discrepancy between patient perspectives and available evidence is important to consider when counseling patients on ARD use in pregnancy. Survey respondents relied on their rheumatologist as their primary information source, highlighting the important role specialists can play in informing patient perspectives surrounding ARD use in pregnancy.

Disclosure: L. Glick, None; **J. Shamis**, Janssen, 1; **T. McGhie**, None; **D. Mahendira**, None.

Abstract Number: 1765

Obstetric Outcomes in Younger Women Less Than 21 Years of Age Compared to Women Between Age 21 and 25 Years with Rheumatic Disease

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Very young maternal age has been described as a risk factor for several adverse obstetric outcomes. This study aimed to investigate whether younger women with rheumatic diseases had differential risk for adverse obstetric outcomes compared to older age groups.

Methods: We queried a retrospective California birth cohort of 3 million singleton live births between 2011-2017 created from linked birth certificates and hospital discharge summaries. ICD-9/10 codes were used to classify women with rheumatoid arthritis (RA), juvenile idiopathic arthritis (JIA), ankylosing spondylitis (AS), psoriatic arthritis (PsA), and systemic lupus erythematosus (SLE). Outcomes of interest were preterm birth, very preterm birth, small for gestational age offspring, offspring requiring NICU admission, gestational diabetes, preeclampsia, and caesarean

delivery. In multivariable log-linear regression, risk of each outcome was assessed in women less than 21 years of age compared to women between 21 and 25 years of age. Models were adjusted for maternal race/ethnicity, body mass index, payer source, anxiety, depression, bipolar disorder, smoking, drug abuse, alcohol abuse, and history of hypertension or diabetes. Risk ratios were first estimated for women with any rheumatic disease, and then repeated for women with RA/JIA or SLE.

Results: A total of 1,769 women 25 years or younger with any rheumatic disease were identified, with 394 under the age of 21. Women with any rheumatic condition under age 21 overall had a lower risk for caesarean delivery (aRR 0.67, 95% CI 0.55-0.81) and gestational diabetes (aRR 0.55, 95% CI 0.36-0.84) than women age 21-25. When analyzed by specific rheumatic disease, women with RA or JIA under age 21 had a higher risk for preterm birth (aRR 1.45, 95% CI 1.01-2.08) as compared to women age 21-25. This increased risk was not observed in very young women with SLE.

Conclusion: The majority of obstetric outcomes did not differ between very young women and women age 21-25 with rheumatic diseases. Risk of caesarean delivery and gestational diabetes may be decreased in younger women compared to older women with rheumatic diseases. Our study did suggest that for RA or JIA, younger age may be associated with a higher risk of preterm delivery.

Disclosure: C. Smith, None; **C. Chambers**, Amgen, Inc, 1, AstraZeneca, 1, Celgene, 1, GlaxoSmithKline, 1, Janssen Pharmaceuticals, 1, Pfizer, Inc, 1, Regeneron, 1, Hoffman La-Roche-Genentech, 1, Genzyme Sanofi-Aventis, 1, Takeda Pharmaceutical Company Limited, 1, Sanofi, 1, UCB Pharma, USA, 1, Sun Pharma Global FZE, 1, Gerber Foundation, 1; **R. Baer**, None; **L. Jelliffe-Pawlowski**, None; **G. Bandoli**, None.

Abstract Number: 1766

Trends of Pregnancy Outcomes in a Large Electronic Health Record Cohort of Systemic Lupus Erythematosus Patients

April Barnado[1], Alex Camai[1] and Lee Wheless[1], [1]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Studying pregnancy in systemic lupus erythematosus (SLE) is difficult given its relative rarity. Electronic health record (EHR) contain longitudinal data to serve as a powerful tool. Using a previously validated algorithm, we identified SLE pregnancies in a large EHR. We then examined demographics, medications, and outcomes in SLE pregnancies from 1991 to 2017.

Methods: We used a de-identified EHR with over 3 million subjects. We selected individuals using a validated algorithm of ≥ 4 counts of the SLE ICD-9 (710.0) or ICD-10 codes (M32.1*, M32.8, M32.9) and ≥ 1 ICD-9 or ICD-10 code for pregnancy-related diagnoses yielding 234 potential subjects. We extracted demographic, disease characteristics, medications, and pregnancy outcomes from chart review. SLE cases were diagnosed by a rheumatologist. We primarily analyzed only pregnancies that occurred after SLE diagnosis but then compared pregnancy outcomes before and after SLE diagnosis. SLE medication use was defined as ever use during pregnancy. In addition to a cross-sectional analysis of pregnancy outcomes, we assessed outcomes and medication use over time in 5 year increments.

Table 1. Characteristics of Systemic Lupus Erythematosus Pregnancies.

Characteristics	SLE pregnancies that occurred after SLE diagnosis (n = 168)
Race (%)	
White	58%
African American	33%
Unknown	4%
Asian	3%
Other	2%
Ethnicity (%)	
Hispanic	6%
Mean age at delivery ± standard deviation (range)	28 ± 6 (16-41)
SLE nephritis	45%
Antiphospholipid antibody syndrome	29%
Ever SLE medication use during pregnancy	
Hydroxychloroquine	42%
Corticosteroids	63%
Azathioprine	14%
Aspirin	28%
Anticoagulants	21%
Pregnancy Outcomes	
Live Birth	85%
Caesarean section	49%
Mean gestational age (weeks) ± standard deviation	35 ± 4
Mean birthweight (kg) ± standard deviation	2.37 ± 0.97
Pre-term birth	42%
Preeclampsia	24%
Preterm preeclampsia	82%

Results: Of the 234 potential SLE subjects with pregnancies, there were 208 total pregnancies to definite SLE cases with 168 pregnancies occurring after SLE diagnosis and 40 pregnancies occurring before SLE diagnosis. Of 168 pregnancies that occurred after SLE diagnosis, 58% were to White women and 33% to African American women with 45% complicated by SLE nephritis and 29% antiphospholipid antibody syndrome (Table 1). Overall, SLE medication use was low with 42% of pregnancies with antimalarial use and 28% with aspirin use. Aspirin use was low over time. Antimalarial use increased over time with a peak of 62% in 2015 (Figure 1). Overall, live birth rate was 85% with 49% delivering surgically. The preterm birth rate was 42%. Preeclampsia complicated 24% of pregnancies with most occurring preterm at 82%. Mean gestational age was 35 weeks. Over time, live birth rates were similar with an increase in Caesarean section and preterm deliveries in 2005 with a subsequent decline (Figure 2). Rates for pregnancy outcome were not significantly different in pregnancies occurring before vs. after SLE diagnosis.

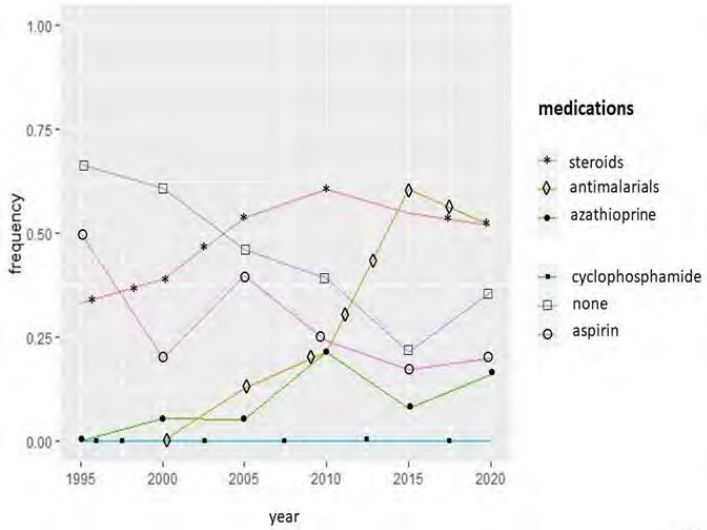

Figure 1. Trends of medication use in Systemic Lupus Erythematosus pregnancies from 1991 to 2017. The x axis shows year in the electronic health record ranging from 1991 to 2017. The y axis shows frequency of ever use of medications during pregnancy. Medications are listed to the right of the figure.

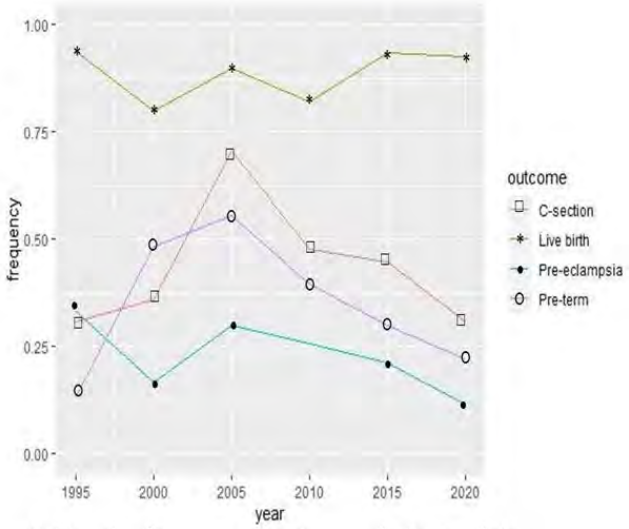

Figure 2. Trends of pregnancy outcomes in Systemic Lupus Erythematosus pregnancies from 1991 to 2017. The x axis shows year in the electronic health record ranging from 1991 to 2017. The y axis shows frequency of the pregnancy outcome. Pregnancy outcomes are listed to the right of the figure.

Conclusion: Using a large EHR, we demonstrate higher than expected rates of preterm birth and preeclampsia in SLE. These rates have not improved over time. Recommended medications in SLE pregnancy, particularly aspirin, are not dramatically increasing over time despite recommendations for use in all SLE pregnancies. These trends demonstrate the need for guideline implementation to improve SLE pregnancy outcomes.

Disclosure: A. Barnado, Nashville Biosciences, 1; **A. Camai**, None; **L. Wheless**, None.

Abstract Number: 1767

Maternal Peripartum Outcomes Are Similar to the General Population in Rheumatoid Arthritis Pregnancies

Sarah Tarplin[1], Alex Camai[1] and April Barnado[1], [1]Vanderbilt University Medical Center, Nashville, TN

SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Background/Purpose: Data on birth outcomes to women with rheumatoid arthritis (RA) are limited and conflicting. Some studies indicate that women with well controlled RA have birth outcomes similar to the general population, while others show higher rates of preterm birth and cesarean section. There are few studies assessing how RA impacts maternal peripartum outcomes such as maternal infection rates and blood transfusions. Using a real-world, electronic health record (EHR) cohort, we assessed RA medication use, fetal, and maternal peripartum outcomes.

Methods: In a large, de-identified EHR with over 3 million subjects and data from 1990 to 2019, we identified possible RA births. We used at least 1 delivery-related ICD-9 or ICD-10-CM code and a validated RA algorithm requiring

Table 1. Maternal and disease characteristics of pregnant women with rheumatoid arthritis.

Maternal characteristics	Pregnancies in Rheumatoid Arthritis Patients (n = 82)[a]
Mean Age at Delivery ± Standard Deviation (Range)	31 ± 5 (18-42)
Race (%)	
Caucasian	77%
African American	10%
Multirace	4%
Asian/Pacific Islander	2%
Missing	2%
Ethnicity	
Hispanic/Latino	5%
Disease characteristics	
Seropositive (RF or CCP positive)	54%
Erosive disease[b]	15%
Mean age at RA diagnosis[c]	26 ± 5
Mean disease duration at delivery[d] (years)	5 ± 4
Medication use during pregnancy (%)	
Corticosteroid use	
Ever during pregnancy	40%
At time of delivery	39%
Antimalarial use	
Ever during pregnancy	7%
At time of delivery	6%
DMARD use	
Ever during pregnancy	9%
At time of delivery	6%
TNF Inhibitor use	
Ever during pregnancy	6%
At time of delivery	2%

[a]All pregnancies occurred after Rheumatoid arthritis diagnosis.
[b]Based on keyword search of clinical notes and radiology reports.
[c]Rheumatoid arthritis diagnosis based on chart review.
[d]Time in years from Rheumatoid arthritis diagnosis based on chart review to delivery date.

at least 1 ICD-9 (714*) or ICD-10-CM RA codes (M05*, M06.0, M06.2, M06.3, M06.8, M06.9), ever mention of a RA medication, and a RA keyword with a positive predictive value of 90%. RA cases were diagnosed by a rheumatologist, and we included pregnancies that occurred after RA diagnosis. We assessed seropositivity, age at RA diagnosis, and presence of erosive RA based on keyword search of notes and radiology reports. Medication use was defined as ever use during the pregnancy and at time of delivery. We assessed maternal and fetal outcomes with preeclampsia diagnosed by an obstetrician. Maternal peripartum outcomes included rates of blood transfusion, rates of infection at up to 6 weeks postpartum as defined by a clinician, and length of hospital stay in days.

Results: We identified 82 pregnancies that occurred after RA diagnosis. Our RA cohort was predominantly White (77%) with 54% being seropositive and 15% having erosive disease (Table 1). Prednisone use ever during pregnancy and at the time of delivery was common (40% and 39%, respectively). Disease modifying anti-rheumatic drugs

Table 2: Maternal peripartum and fetal outcomes in pregnancies to women with rheumatoid arthritis.

Maternal peripartum outcomes	Pregnancies in Rheumatoid Arthritis Patients (n = 82)[a]
Transfusion (%)	
Platelets	0%
Red Blood Cells	1%
Infection (%)	
Any	6%
Endometritis	5%
Surgical site infection	0%
Pneumonia	0%
Cellulitis	1%
Length of Stay (days)	
Mean ± standard deviation	6 ± 10
(Range)	(1-53)
Median	4
Fetal outcomes	
Cesarean section	37%
Term (= 37 weeks)	50%
Preterm	20%
Miscarriage	17%
Stillbirth	5%
Termination	1%
Mean gestational age (weeks) ± standard deviation	37 ± 3
Mean birthweight (grams) ± standard deviation (Range)	2,872 ± 657 (1915-4423)
Preeclampsia	6%
Preeclampsia occurring preterm	19%
Apgar scores[b] at 1 minute	
Mean ± standard deviation	8 ± 1
Median	8
Apgar scores[b] at 5 minutes	
Mean ± standard deviation	9 ± 1
Median	9

[a]All pregnancies occurred after Rheumatoid arthritis diagnosis.
[b]Apgar scores range from 1 to 9.

(DMARDs) and tumor necrosis factor inhibitor (TNFi) use during pregnancy were low (9% and 6%) with only 16% of pregnancies occurring before the first TNFi approval. For most cases, TNFis were discontinued prior to delivery. Rates of preterm delivery were higher than the general population (20% vs. 10%) but similar to rates in other RA studies (15-20%). Rates of preeclampsia (6%) and caesarean section (39%) for our cohort were no different than the general population and were similar to other RA studies (Table 2). Overall, infection rates were low with only 5 pregnancies (6%) having any infection. Of these 5 pregnancies with infection, 4 had endometritis and 1 cellulitis with no surgical site infections. In our cohort, the rate of peripartum red blood cell transfusions was 1%, which was similar to the general population. Median length of stay of 4 days was similar to the general population.

Conclusion: We identified pregnancies to RA mothers in a real-world, large EHR cohort. Corticosteroid use was common during pregnancy and at the time of delivery while DMARD and TNFi use was rare. Women with RA were at in-

creased risk for preterm birth but had rates of preeclampsia and caesarean section similar to the general population. Compared to the general population, women with RA also had similar rates of peripartum infection and transfusions.

Disclosure: S. Tarplin, None; **A. Camai**, None; **A. Barnado**, Nashville Biosciences, 1.

Abstract Number: 1768

The Importance of Pregnancy Planning in Lupus Pregnancies

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SESSION INFORMATION
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Background/Purpose: Given the clinical importance of the pre-conception period in lupus pregnancy management and because pregnancy planning can be potentially improved, this study explores the role of planning on lupus pregnancy outcomes. We hypothesize that women with lupus with planned pregnancies will have fewer pregnancy complications.

Methods: The Maternal Autoimmune Disease Research Alliance (MADRA) was reviewed for lupus pregnancies (1/1/2018 to 4/1/2020) and SLE diagnosis was confirmed by Systemic Lupus Collaborating Clinics (SLICC) criteria. The London Measure of Unplanned Pregnancy (LMUP) classified lupus pregnancies as Planned or Not Planned (Am-

DELIVERY OUTCOMES[1]	Overall	LMUP Not Planned	LMUP Planned	p-value
	N=35	n=15	n=20	
PROMISSE-APO[2]	20/33 (61%)	11/14 (79%)	9/19 (47%)	0.09
PROMISSE APO-SEVERE[3]	6/33 (18%)	6/14 (43%)	0/19 (0%)	0.003
Severe Neonatal Outcome[4]	13/29 (45%)	7/10 (70%)	6/19 (32%)	0.06
Non-live Births:	6 (17%)	5 (33%)	1 (5%)	0.06
Termination	1 (3%)	1 (7%)	0 (0%)	0.4
Miscarriage	4 (11%)	3 (20%)	1 (5%)	0.3
Stillbirth	1 (3%)	1 (7%)	0 (0%)	0.4
Live Births:	29 (83%)	10 (67%)	19 (95%)	0.06
Gestational age at delivery, weeks (mean ± S.D.) (range)	36.2 ± 3.4 (24-39)	35.3 ± 5.1 (24-39)	36.7 ± 2.2 (30 – 39)	0.4
Preterm Birth	10/29 (34%)	4/10 (40%)	6/19 (32%)	0.7
SGA < 10th percentile	7/29 (24%)	4/10 (40%)	3/19 (16%)	0.2
Preeclampsia	8/30 (27%)	5/11 (45%)	3/19 (16%)	0.1

1. Delivery outcomes were missing for 8 pregnancies as patients had either not delivered as of 4/1/2020 (n=7) or data was unavailable through chart review (n=1).
2. PROMISSE-APO: neonatal death, fetal death > 12 weeks, preeclampsia, pre-term delivery < 36 weeks, or small for gestational age (SGA) < 5th percentile. Pregnancy losses < 12 weeks were excluded as in the PROMISSE study (Kim et al., 2016).
3. PROMISSE-APO SEVERE: neonatal death, fetal death > 12 weeks, preeclampsia and pre-term delivery < 34 weeks, or pre-term delivery < 30 weeks. Pregnancy losses < 12 weeks were excluded as in the PROMISSE study (Kim et al., 2016).
4. Severe neonatal outcomes: neonatal death, NICU stay > 1 week, APGAR < 7 at 5 minutes, or SGA < 5th percentile

Figure 1. Demographics and Comorbidities

DEMOGRAPHICS	Overall N=43	LMUP Not Planned n=17	LMUP Planned n=26	p-value
Maternal Age, years (mean ± S.D.)	29.4 ± 5.4	26.5 ± 5.3	31.3 ± 4.6	0.005
Race:				0.5
Black	18 (42%)	9 (53%)	9 (35%)	
White	16 (37%)	5 (29%)	11 (42%)	
Other	9 (21%)	3 (18%)	6 (23%)	
Ethnicity: Hispanic	4 (9%)	2 (12%)	2 (8%)	1.0
Marital Status: Single	9 (21%)	7 (41%)	2 (8%)	0.02
Living Situation: Living alone or with children	4 (9%)	2 (12%)	2 (8%)	1.0
Education Level: Less than college	16 (37%)	12 (71%)	4 (15%)	0.0004
Health Insurance: Medicaid	15 (35%)	11 (65%)	4 (15%)	0.003
Income:				
Annual Income < $50,000	14/40 (35%)	11/17 (65%)	3/23 (13%)	0.002
Annual Income > $150,000	6/40 (15%)	2/17 (12%)	4/23 (17%)	1.0
COMORBIDITIES	**Overall N=43**	**LMUP Not Planned n=17**	**LMUP Planned n=26**	**p-value**
Chronic Hypertension	10 (23%)	4 (24%)	6 (23%)	1.0
Diabetes Mellitus	0 (0%)	0 (0%)	0 (0%)	--
Antiphospholipid Syndrome	3 (7%)	1 (6%)	2 (8%)	1.0
Pre-conception SLE Activity (PGA) (mean ± S.D.)	0.6 ± 0.6	1.0 ± 0.6	0.3 ± 0.5	0.001

Figure 2. Delivery Outcomes

bivalent or Unplanned), and the Physician's Global Assessment (PGA) quantified disease activity. Adverse outcomes were defined using the composite PROMISSE-APO SEVERE (neonatal death, fetal death > 12 weeks, preeclampsia and pre-term delivery < 34 weeks, or pre-term delivery < 30 weeks) and a composite severe neonatal outcomes variable (neonatal death, NICU stay > 1 week, APGAR < 7 at 5 minutes, or SGA < 5th percentile).

Results: This study included 43 lupus patients with 43 pregnancies (no twins). Average maternal age was 29.4 years with 42% identifying as Black or African American. Overall, 60% of pregnancies were Planned and 40% were Not Planned (37% Ambivalent, 2% Unplanned). Women with Not Planned pregnancies were more likely to be younger, have less than a college education, have an income less than $50,000 per year, and require Medicaid. Additionally, women with Not Planned pregnancies had higher pre-pregnancy SLE activity (Fig. 1). Of the 35 pregnancies with delivery outcomes, women with Not Planned pregnancies had increased PROMISSE-APO SEVERE and severe neonatal outcomes as compared to those with Planned pregnancies (Fig. 2). Pre-conception SLE activity, race, and socio-economic disadvantage were not independently associated with adverse maternal-fetal outcomes. Women with Not Planned pregnancies were more likely to discontinue all pregnancy-compatible SLE medications in the peri-conception period (23% vs 0%; p=0.03) and require addition of at least one SLE medication during pregnancy (100% vs 30%; p < 0.0001). They were also less likely to receive pre-conception counseling with a rheumatologist (19% vs 58%; p=0.02) and take prenatal vitamins (6% vs 77%; p< 0.0001). Overall, 76% of women with Not Planned pregnancies did not use contraception prior to pregnancy, while 24% reported using contraception sometimes.

Conclusion: Whether a woman with lupus had a planned pregnancy or not was the primary predictor of adverse outcomes in this cohort. Women with planned pregnancies had higher rates of pre-conception counseling, increased adherence to pregnancy compatible SLE medications, and were more likely to conceive when disease activity was quiescent or low, all of which can help improve outcomes. Avoiding conception when a woman with lupus is not

medically prepared for pregnancy is a modifiable intervention that can decrease morbidity and mortality for mother and baby.

Disclosure: A. Rajendran, Rheumatology Foundation Medical Student Preceptorship Award, 2; **A. Eudy**, NIH NCATS Award Number 1KL2TR002554, 2, Pfizer, 2; **S. Balevic**, None; **M. Clowse**, UCB, 5, GSK, 2, 5, Astra Zeneca, 5, Pfizer, 2.

Abstract Number: 1769

Patient-reported COVID-19 Infection in Pregnant Women with Rheumatic Disease: Data from the COVID-19 Global Rheumatology Alliance Patient Experience Survey

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Reproductive Issues in Rheumatic Disorders Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The impact of COVID-19 on pregnancy in patients with rheumatic disease is unknown. We describe COVID-19 outcomes in pregnant women with rheumatic disease who self-reported to the COVID-19 Global Rheumatology Alliance (C19-GRA) Patient Experience Survey.

Methods: The C19-GRA launched the Patient Experience Survey for adults and parents of children with rheumatic disease, with or without COVID-19 infection. This patient-reported survey was distributed online through patient support organizations and on social media. The survey was available to an international audience and collected data on rheumatic disease diagnosis, medications, COVID-19 outcomes, and pregnancy status. The survey launched on April 3, and we report data until May 26, 2020. The study was approved by the IRB at Boston Children's Hospital.

Results: Out of more than 10,000 patients who answered the survey, six patients self-reported with COVID-19 infection and pregnancy. Four were white, one pacific islander, and one pacific islander/south Asian. The mean age was 36 years, range 26-45 years. Four were pregnant at the time of COVID-19 infection, one was within six weeks of delivery, and one became pregnant within six weeks of infection. Two were current smokers, four were non-smokers. Their rheumatic diagnoses were rheumatoid arthritis & Sjögren syndrome (n=1), undifferentiated connective tissue disease (n=1), SLE & Sjögren syndrome (n=1), anti-phospholipid antibody syndrome (n=1), Bechet's disease (n=1) and psoriatic arthritis, Sjögren syndrome, and scleritis/uveitis (n=1). The patients reported taking the following medications: TNF inhibitor (n=1), glucocorticoid monotherapy (prednisone 10mg, n=1), antimalarial monotherapy (n=1), antimalarial & glucocorticoid (prednisone 40mg, n=1) and cyclosporine (n=1) and none (n=1). Symptoms of COVID-19 included cough (n=6), malaise/fatigue (n=5), muscle aches (n=5), sore throat (n=5), myalgia (n=5), fever (n=4), shortness of breath (n=4) and loss of taste (n=2). The diagnosis was made by a doctor based on a positive test (n=1), by a doctor based on symptoms (n=3), and self-diagnosis by the patient (n=2). The one patient who had a positive test re-

ceived colchicine and azithromycin for treatment of COVID-19 and another patient reported receiving steroids. Three cases had work-related exposures: two healthcare employees and a patient that was exposed to an ill co-worker in her office; three others reported potential exposures in healthcare facilities. No patient was hospitalized, two patients reported no difficulties performing activities of daily living (ADLs), and four did report difficulties performing ADLs.

Conclusion: In this small series of patients with rheumatic disease and COVID-19, patient-reported outcomes were favorable. Although patient-reported outcomes have limitations especially with regard to the accuracy of self-diagnosis, they may add to the knowledge on the course of COVID-19 in pregnant patients. Future studies should follow the long-term effects of COVID-19 on the pregnancy, mother, and child.

Disclosure: J. Hausmann, Novartis, 5; **E. Sirotich**, Canadian Arthritis Patient Alliance, 9; **B. Bermas**, None; **M. Clowse**, UCB, 5, GSK, 2, 5, Astra Zeneca, 5, Pfizer, 2; **M. Gianfrancesco**, None; **P. Machado**, Abbvie, 5, 8, Eli Lilly, 5, Novartis, 5, 8, UCB, 5, 8, Pfizer, 8; **H. Robinson**, None; **A. Strangfeld**, BMS, 8, MSD, 8, Pfizer, 8, Roche, 8, Sanofi Aventis, 8, Abbvie, 2, UCB, 8, Celltrion, 2, Eli Lilly, 2, Fresenius Kabi, 2, Mylan, 2, Hexal, 2, Samsung, 5; **J. Yazdany**, Eli Lilly, 5, Astra Zeneca, 5; **P. Robinson**, Novartis, 2, 5, 8, UCB, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 5, Pfizer, 5, Abbvie, 5, 8, BMS, 9.

Abstract Number: 1770

Lupus Low Disease Activity State Protects Against Pre-Term Birth

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Background/Purpose: Lupus low disease activity state (LLDAS) (Ann Rheum Dis. 2016;75:1615–21.) combine both low disease activity (SLEDAI score of ≤4, PGA >=1 no flare, no severe organ involvement) and prednisone reduction (>= 7.5 mg). Being in LLDAS for 50% or more of follow-up visits results in a 50% reduction in organ damage (Arthritis Rheumatol 2018;70:1790-5). LLDAS has been a useful secondary outcome measure in randomized clinical trials. We asked whether being in LLDAS at the start of pregnancy predicted the pregnancy outcome.

Methods: All patients met revised ACR or SLICC classification criteria. At each visit, LLDAS was calculated. The start date of each pregnancy was determined. At each visit, we created a variable to indicate the trimester of the pregnancy. To evaluate whether LLDAS at the first pregnancy visit associated with pregnancy outcomes, a GEE model was used to account for the same patient contributing more than one pregnancy.

Results: There were 636 pregnancies (from 435 patients: 36% African American, 54.5% Caucasian) that had LLDAS status determined at the first pregnant visit. Of these 636 pregnancies, there were 537 births, 77 miscarriages, and 22 terminations. 291 patients had 1 pregnancy, 100 had 2, and 44 had 3 recorded. There was no association between reaching LLDAS at the first pregnancy visit and miscarriage (OR 0.71, 95% CI 0.44, 1.15, p=0.16, adjusted for age and race). Table 1 shows the association between LLDAS at the first pregnancy visit and preterm birth, with 537 pregnancies eligible for analysis. There was strong evidence of an association between LLDAS at first pregnant visit and preterm birth. Next, we looked at pregnancies that had the first visit in the first trimester. There were 462 pregnancies included. Once again, there was no association with miscarriage (OR 0.76, 95% CI 0.45, 1.29 p=0.312 adjusted for

	Reaching LLDAS at first pregnancy visit	n (%)	Adjusted OR (95% CI)	Adjusted p-value
Prematurity (GA<37 weeks)	No	100/225 (44.4%)	1.00 (ref)	
	Yes	69/213 (22.1%)	0.41 (0.29, 0.59)	<0.0001
Extreme prematurity (GA<28 weeks)	No	16/225 (7.1%)	1.00 (ref)	
	Yes	4/312 (1.3%)	0.20 (0.06, 0.59)	0.0036
n represents the number of pregnancies OR and p-value were adjusted for the contribution of multiple pregnancies from the same patient, age at the visit, and race				

Table 1. Association between LLDAS at first pregnancy visit and preterm birth

	Reaching LLDAS at first trimester visit	n (%)	Adjusted OR (95% CI)	Adjusted p-value
Prematurity (GA<37 weeks)	No	71/164 (43.3%)	1.00 (ref)	
	Yes	51/232 (22.0%)	0.43 (0.28, 0.67)	0.0001
Extreme prematurity (GA<28 weeks)	No	13/164 (7.9%)	1.00 (ref)	
	Yes	4/232 (1.7%)	0.25 (0.08, 0.80)	0.0197
n represents the number of pregnancies OR and p-value were adjusted for the contribution of multiple pregnancies from the same patient, age at the visit, and race				

Table 2. Association between LLDAS at first trimester visit and preterm birth

age and race). Table 2 shows the analysis of being in LLDAS at the first trimester and preterm birth (396 pregnancies were eligible for analysis). The same strong protective effect of being in LLDAS against preterm birth was found.

Conclusion: Currently, women with SLE are told that their SLE should be "in remission" for 6 months prior to conception. Our data suggest that being in LLDAS may be sufficient to protect against preterm birth, which numerically remains the most frequent adverse pregnancy outcome in SLE. LLDAS does not protect against miscarriage (likely because antiphospholipid antibodies contribute to miscarriage risk). LLDAS is a more realistic pre-pregnancy clinical goal, as durable remission is difficult to achieve in SLE.

Disclosure: M. Petri, AbbVie, 5, Amgen, 5, AstraZeneca, 2, 5, BMS, 5, Decision Resources, 5, GSK, 2, 5, INOVA, 5, IQVIA, 5, Janssen, 5, Eli Lilly, 2, 5, Merck EMD Serono, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5, Exagen, 2; **J. Li**, None; **D. Goldman**, None.

Abstract Number: 1771

Fertility and Pregnancy Outcomes in Women with Spondyloarthritis: A Systematic Review and Meta-analysis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Women with spondyloarthritis (SpA) are often affected by the disease during their reproductive years[1]. However, little is known about the impact of the disease and its treatments on fertility and pregnancy outcomes, as well as the effect of pregnancy itself on disease activity[2].

The aim of the study was to determine the effects of spondyloarthritis on fertility and pregnancy outcomes in women with SpA.

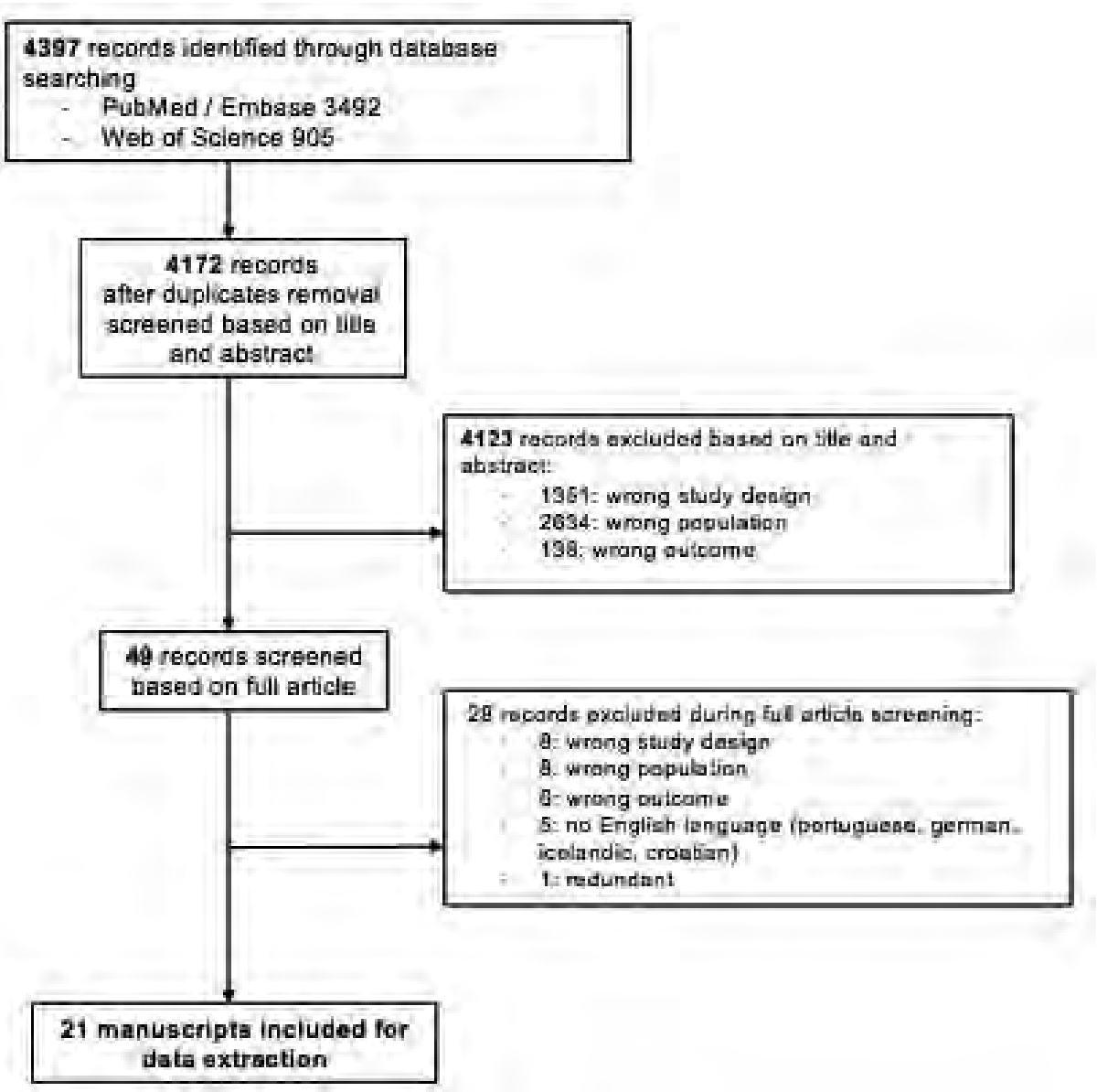

Figure 1. Flow Chart

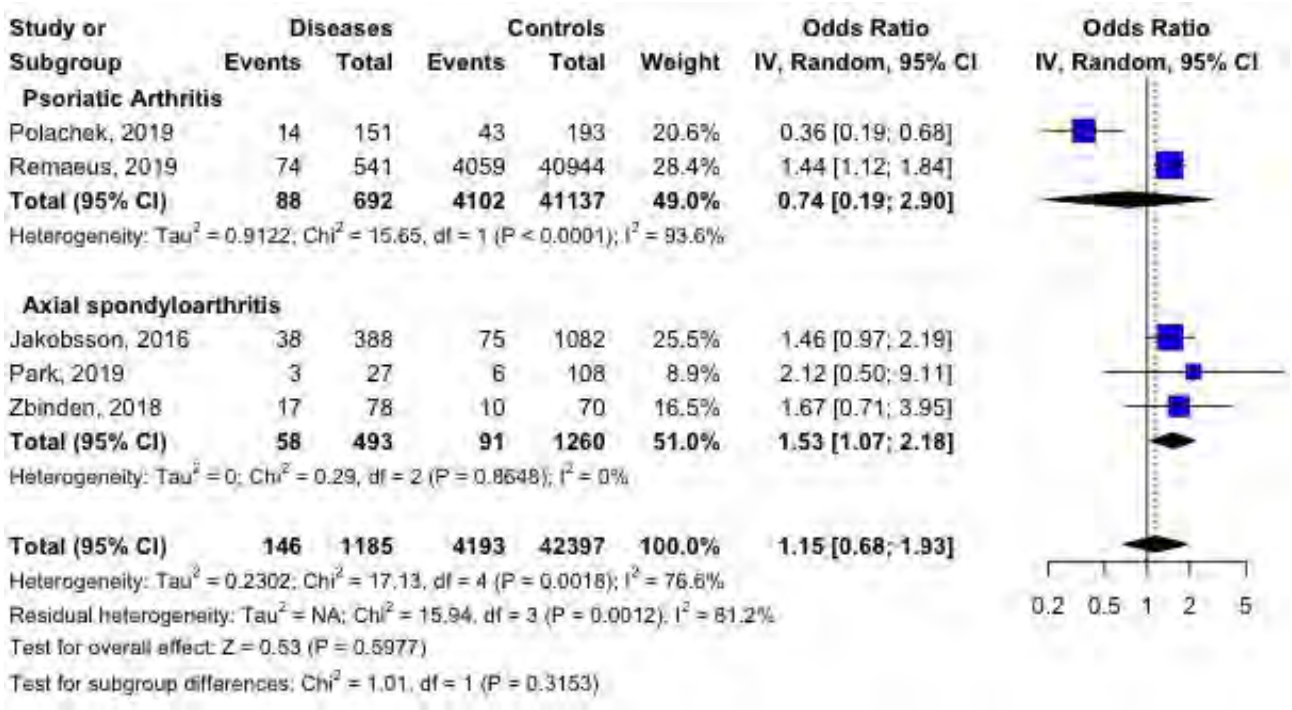

Figure 2 Risk of emergency caesarean section in psoriatic arthritis and axial spondyloarthritis patients

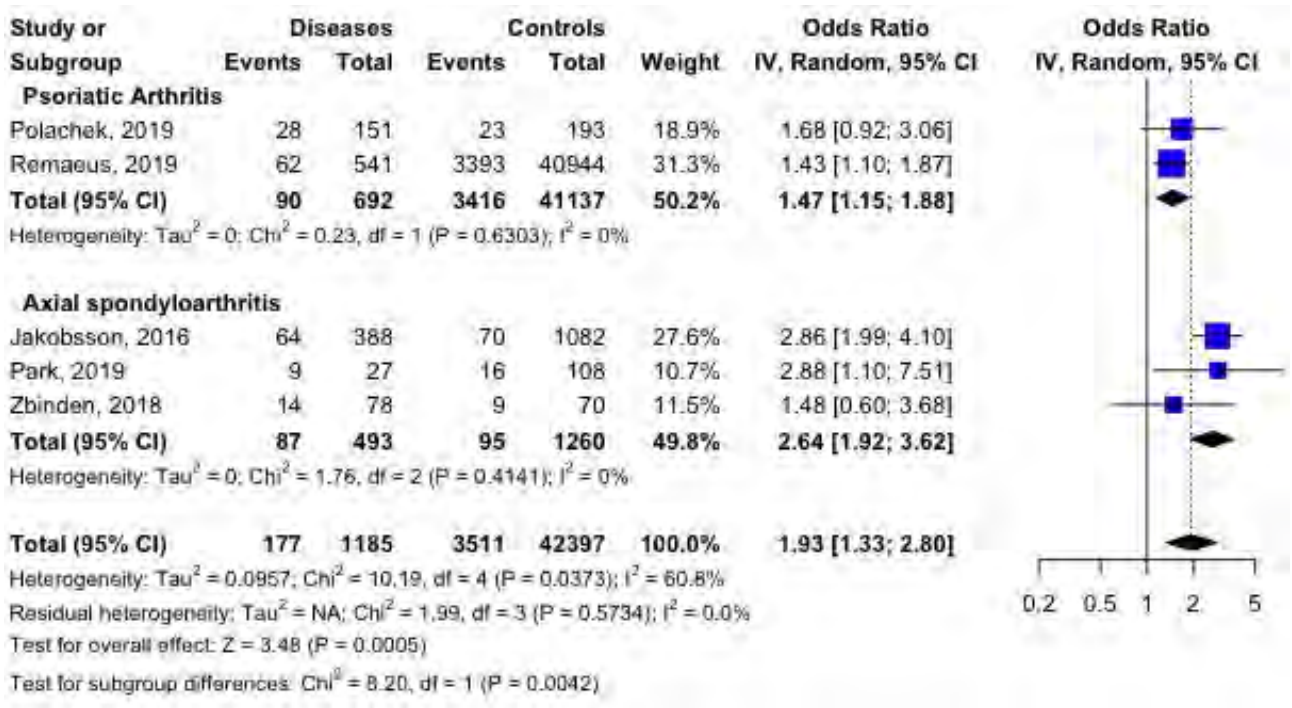

Figure 3 Risk of elective caesarean section in psoriatic arthritis and axial spondyloarthritis patients

Methods: We searched Pubmed, Embase, and Web of Science until 1 November 2019, without any language restriction. All studies assessing fertility, pregnancy outcomes and disease activity during pregnancy in women with spondyloarthritis (axial SpA (axSpA) but also peripheral SpA, including psoriatic arthritis (PsA)) were eligible. The heterogeneity between studies was quantified (I^2), and multiple meta-regressions were carried out to identify potential

sources of heterogeneity. In case I^2 was < 50%, a random-effects model was used to pool the available data. Prevalence of events was described as percentages. The odds ratio (OR) and corresponding 95% confidence interval (CI) were used to assess the associations between the disease and the pregnancy outcomes.

Results: Within 4397 eligible studies, 21 articles fulfilling the selection criteria were included in the review, assessing overall 3306 patients (2578 with axSpA and 728 with PsA) and 4104 pregnancies compared to 42248 healthy controls (in 11 studies with a control group). Among the included studies, the risk of bias was evaluated as high, moderate and low in respectively 12, 1 and 8 studies.

Regarding pregnancy outcomes, several studies report an increased risk of preterm birth (pooled OR 1,64 [1,15-2,33], I^2=24% in axSpA and pooled OR 1,62 [1,23-2,15], I^2=0,0% in PsA), small for gestational age (pooled OR 2,05, [1,09-3,89], I^2=5,8% in axSpA), preeclampsia (pooled OR 1,59, [1,11-2,27], I^2=0% in axSpA) and caesarean section (pooled OR 1,70 [1,44-2,00], I^2=19,9% in axSpA and pooled OR 1,71 [1,14-2,55], I^2=74,3% in PsA), without any other unfavourable pregnancy outcome (miscarriage, stillbirth or gestational diabetes). Further analysis found a significant higher risk for elective caesarean (pooled OR 2,64, [1,92-3,62], I^2=0,0% in axSpA and pooled OR 1,47, [1,15-1,88], I^2=0,0% in PsA), without increased risk for emergency caesarean in PsA. There was no substantial heterogeneity in the majority of meta-analyses.

Conclusion: Although based on observational data, this work is to our knowledge, the first systematic review and meta-analysis concerned with this subject. SpA seems to be associated with an increased risk of preterm birth, small for gestational age, preeclampsia and caesarean section. The analysis of the impact of pregnancy on disease activity in this setting is currently ongoing.

Disclosure: S. Hamroun, None; **A. Hamroun**, None; **J. Bigna**, None; **F. Foerger**, UCB, 2, 5, 8, GSK, 5, 8, Roche, 5; **E. Allado**, None; **A. Molto**, ABBVIE, 5, BMS, 5, 8, LILLY, 5, NOVARTIS, 5, 8, UCB, 5, GILEAD, 5.

Abstract Number: 1772

Vaccinations of Infants Born to Mothers on TNF Inhibitors: Safe Administration of Live-vaccines Given Per the National Immunization Program

Eman Satti[1], Nawal Hadwan[1] and Samar Al Emadi[1], [1]Hamad medical corporation, DOHA, Qatar

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Reproductive Issues in Rheumatic Disorders Poster
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Background/Purpose: Biologic Disease-Modifying agents (bDMARDs) including TNF inhibitors are increasingly used during pregnancy over the last few decades for a variety of autoimmune conditions. Nevertheless, limited data is available regarding their safety through pregnancy, particularly in the third trimester. Previous reports of discriminated BCG and severe neonatal neutropenia has made many practitioners defer live-attenuated vaccines from the routine schedule. The international guidelines still recommend holding most TNF inhibitors for several half-lives before delivery, due to the significant levels found in the neonates. Many mothers are advised to adjust the immunization schedule of their infants accordingly.

Recent accumulating data from IBD in pregnancy started to support the safety of infliximab use throughout pregnancy. Due to the paucity of data in this regard, we have planned this study.

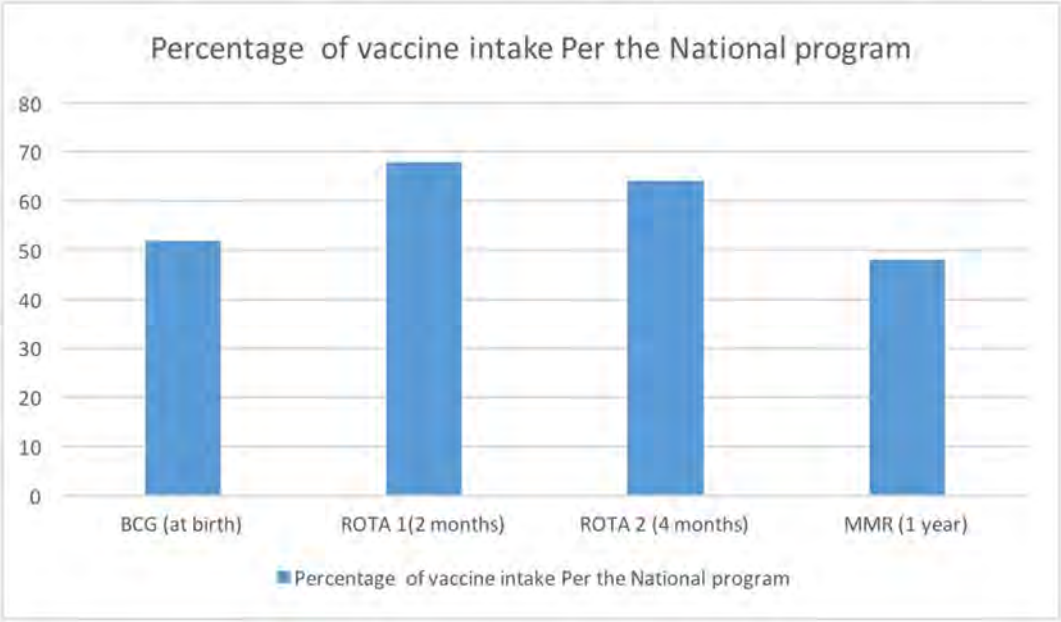
Methods: We surveyed the electronic records of two registries from the IBD and Rheumatology clinics at the largest tertiary hospital in Qatar. We included all women who completed their pregnancies on biologics (minimum of 3 months of biologic use during pregnancy). Cases of abortion, IUFD, and neonatal death were excluded. We have analyzed the clinical data of infants who were 6 months of age or older. Data were recorded in a pre-specified datasheet. Then we ran a descriptive analysis using SPSS software.

Results: Since 2017, we identified 30 completed pregnancies on TNF blockers. Out of these, twenty-five infants were more than 6 months of age.

Mean maternal age at pregnancy was 29.5 years (22-42)
Underlying autoimmune diseases: IBD (13), RA (7), PSA(2), SPA (3).
TNF inhibitors used: Infliximab(7), Adalimumab(5), Etanercept(2), and Certolizumab (10).
The mean duration of TNF inhibitor use during pregnancy was 6.8 months (5-9 months).
TNF inhibitors were taken throughout pregnancy in 15 cases: certolizumab (6), Infliximab (4), and adalimumab (2).
In 2 pregnancies, Etanercept was taken for 7 months followed by Certolizumab until birth.

Mean gestational age at birth was 36.8 weeks (34-41).
Prematurity was recorded in 7 cases (34-37 weeks) and LBW in 1 case.
Two neonates required NICU admission for ARDS.
Five cases of neonatal jaundice were identified. No congenital anomalies reported.

Immunization Data:
Live attenuated vaccines: Thirteen infants (52%) received BCG vaccine at birth, 17(68%) received ROTA vaccine at 2 months, 16 (64%) received ROTA booster at 4 months and 12 (46%) infants received MMR at 1 year.
No complications related to the vaccines were recorded.



Infections during Infancy:
Mean number of infection encounters during infancy was 2 encounters (0-5).
Infections reported were: URTI, bronchiolitis and otitis media. One infant got COVID19 mild infection.
Mean number of encounters that required antibiotics was 10 in 9 infants.

Conclusion: We have identified high rate of infants who received live-attenuated vaccines per the national immunization program without complications. This observation was also associated with high rate of maternal TNF inhibitor use throughout pregnancy. No alarming concern about repeated infections reported in this study.

Disclosure: E. Satti, None; **N. Hadwan**, None; **S. Al Emadi**, None.

Abstract Number: 1773

Worse Maternal and Fetal Outcomes Among Hospitalized U.S. Pregnant Women with Systemic Lupus Erythematosus (SLE) and Rheumatoid Arthritis (RA)

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SESSION INFORMATION
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Background/Purpose: Prior studies suggest women with SLE and RA may have higher age-adjusted risk of adverse pregnancy outcomes. We evaluated maternal and fetal complications and racial/ethnic disparities among pregnant women with SLE and RA using a national sample of hospital admissions.

Methods: We used the National Inpatient Sample (NIS), which after weighting provides annual estimates for more than 35 million community hospitalizations in the US. Analysis was limited to pregnant women without missing relevant variables hospitalized in 2016 and 2017. Admissions with SLE and RA were captured in ICD-10-CM codes (M32.1x, M32.8, M32.9 and M05, M06.0, M06.2, M06.8, M06.9, M08.0 respectively). We compared the proportion of discharge outcomes with maternal death, intrauterine fetal demise (IUFD), preeclampsia/eclampsia, premature rupture of membranes (PROM), and placental complications (placental disorders, placenta previa, or abruptio placentae) among patients with SLE, RA, and neither condition using chi-squared tests. We used Poisson regression to model outcomes as a function of disease, including age, race/ethnicity, insurance, and income level in the ZIP Code of residence as covariates. To evaluate racial/ethnic disparities across disease groups, we included an interaction term for race/ethnicity and disease (SLE, RA, neither) if the interaction was significant in the model. Weighted population estimates are presented, except if otherwise specified. All analyses accounted for the complex sampling design of the NIS.

Results: An estimated 11,100 (0.15%) community hospital admissions for pregnant women with SLE, 10,065 (0.13%) with RA, and 7,612,897 for women with neither condition occurred in the U.S. in 2016 and 2017. Maternal death

Table 1. Maternal and Fetal Outcomes among U.S. Hospitalized Pregnant Women with SLE, RA, and Neither Condition

	IUFD		Preeclampsia/Eclampsia		PROM		Placental complications	
	% of discharges	RR	% of discharges	RR	% of discharges	RR	% of discharges	RR
No RA/SLE (n=7,612,897)	1.02%	Ref	5.70%	Ref	7.47%	Ref	2.58%	Ref
SLE (n=11,100)	2.11%	2.06 (1.57, 2.71)*	11.57%	2.03 (1.80, 2.28)*	6.59%	0.88 (0.75, 1.03)	3.71%	1.44 (1.17, 1.77)*
RA (n=10,065)	1.11%	1.09 (0.71, 1.66)	7.45%	1.31 (1.11, 1.53)*	9.59%	1.28 (1.12, 1.47)*	3.39%	1.31 (1.06, 1.62)*

IUFD = intrauterine fetal demise; PROM = premature rupture of membranes; placental complications include ICD-10-CM codes for placental disorders, placenta previa, or abruptio placentae. Percent of discharges based on marginal predictions from adjusted Poisson model. RR= adjusted relative risk obtained from Poisson model including age, race, income quartile in ZIP Code of residence, insurance as covariates. Models for IUFD and preeclampsia/eclampsia also include an interaction term for race/ethnicity and disease. Ref = reference group. *Signifies statistical significance, p <0.05. n weighted based on NIS guidelines to generate national estimates.

Table 2. Risk of Outcome for Pregnant U.S. Hospitalized Blacks Compared to Whites

	IUFD	Preeclampsia/Eclampsia
	RR Black vs. white	RR Black vs. white
No RA/SLE	1.98 (1.90, 2.07)*	1.58 (1.54, 1.62)*
SLE	3.31 (1.78, 6.15)*	1.32 (1.01, 1.74)*
RA	2.41 (0.90, 6.46)	1.39 (0.91, 2.13)

IUFD = intrauterine fetal demise; PROM = premature rupture of membranes; placental complications include ICD-10-CM codes for placental disorders, placenta previa, or abruptio placentae. RR= adjusted relative risk obtained from Poisson model including age, race, income quartile in ZIP Code of residence, insurance as covariates, and an interaction term for race/ethnicity and disease. *Signifies statistical significance, p <0.05.

was a rare event, accounting for less than 10 observations for admissions with either SLE or RA, and approximately 0.01% of general pregnancy related admissions. Admissions with a diagnosis of IUFD, preeclampsia/eclampsia, and placental complications were more likely among patients with SLE than the general pregnant population ($p< 0.05$) (Table 1). Similarly, admissions for patients with RA were more likely to have a diagnosis of preeclampsia/eclampsia, PROM, and placental complications compared to the general pregnant population ($p< 0.05$). The risk of IUFD and preeclampsia/eclampsia was higher among Blacks compared to whites ($p< 0.05$) both among the general pregnant population and those with SLE, but not among those with RA (Table 2).

Conclusion: Pregnant patients with SLE and RA have worse maternal and fetal outcomes including increased risk of intrauterine fetal demise, preeclampsia/eclampsia, PROM, or placental complications compared to other hospitalized pregnant women. Admitted pregnant Black patients with SLE, like those in the general population, continue to be at higher risk of poor maternal and fetal outcomes compared to whites. In contrast, there was no significant difference in the risk of analyzed maternal and fetal complications for Black compared to white RA patients. Women with SLE and RA continue to be at increased risk of pregnancy complications suggesting that additional obstetric research and interventions are indicated to improve outcomes in these patients.

Disclosure: C. Anastasiou, None; **L. Trupin**, None; **P. Katz**, None; **Z. Izadi**, None; **M. Gianfrancesco**, None; **G. Schmajuk**, None; **J. Yazdany**, Eli Lilly, 5, Astra Zeneca, 5.

Abstract Number: 1774

Making Decisions About Medication Use, Pregnancy, and Having Children Among Women with Rheumatoid Arthritis: A Constructivist Grounded Theory Study

Nevena Rebic[1], Ria Garg[2], Sarah Munro[2], Glen Hazlewood[3], Neda Amiri[2], Nick Bansback[2], Stephanie Ensworth[2], Corisande Baldwin[4], Laurie Proulx[5] and Mary De Vera[1], [1]Arthritis Research Canada, University of British Columbia, Vancouver, BC, Canada, [2]University of British Columbia, Vancouver, BC, Canada, [3]University of Calgary, Calgary, AB, Canada, [4]University of British Columbia, Calgary, AB, Canada, [5]Canadian Arthritis Patient Alliance, Ottawa, Canada

SESSION INFORMATION
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Background/Purpose: Despite guidelines for managing rheumatoid arthritis (RA) in pregnancy, high rates of discontinuation of disease-modifying anti-rheumatic drugs (DMARDs) considered safe for women with RA during pregnancy may suggest a translation gap of emerging clinical knowledge to patients. We examined the process of making treatment and pregnancy decisions among women with RA.

Methods: *Study design.* We conducted a mixed-methods qualitative research study. *Participants.* Through collaborations with rheumatologists and patient partners, we used poster and social media advertisements to recruit a purposive sample of female participants who were 18 years or older, had an RA diagnosis confirmed by a rheumatologist, lived in Canada, and were able to communicate in English or French. *Data collection.* We collected data through semi-structured focus group and individual interviews using telephone and video conferencing technology. Focus groups were composed of participants with similar pregnancy and medication use experiences. *Data analysis.* We analysed data using a Constructivist Grounded Theory approach within a feminist theoretical framework, which involved steps of line-by-line coding, focused coding and categorizing, and theoretical coding. Data collection and analysis were iterative and continued until saturation of themes was achieved.

Results: We recruited 22 participants across Canada who had a mean age of 34 years, median 7 years since RA diagnosis, and most (86%) were married or co-habited with a partner. Overall, 36% had never been pregnant, 55% had previously been pregnant, and 9% were pregnant at the time of interview. Of those who had experienced pregnancy, 58% had at least one pregnancy while diagnosed with RA and of those, a further 67% used DMARD(s) during a pregnancy. Over half (55%) reported intending to have future children through childbearing or other means. We constructed a framework (see **Figure 1**) depicting the dynamic relationships between 4 identified decision-making processes: 1) using medications, 2) having children, 3) planning pregnancy, and 4) parenting. Moreover, we elicited the complex influence of contextual factors on these processes, particularly attitudes towards health and medications, disease onset and severity, familial support system, and healthcare provider relationship.

Conclusion: Our framework provides insight into how women have made reproductive health decisions in the context of managing RA. By understanding the practical and emotional aspects of this process, healthcare providers can identify opportunities for intervention or care adaptation leading to improved health outcomes for women and babies. Our findings demonstrate that a patient-centred approach to care supports women with RA in making better reproductive choices that align with their individual values.

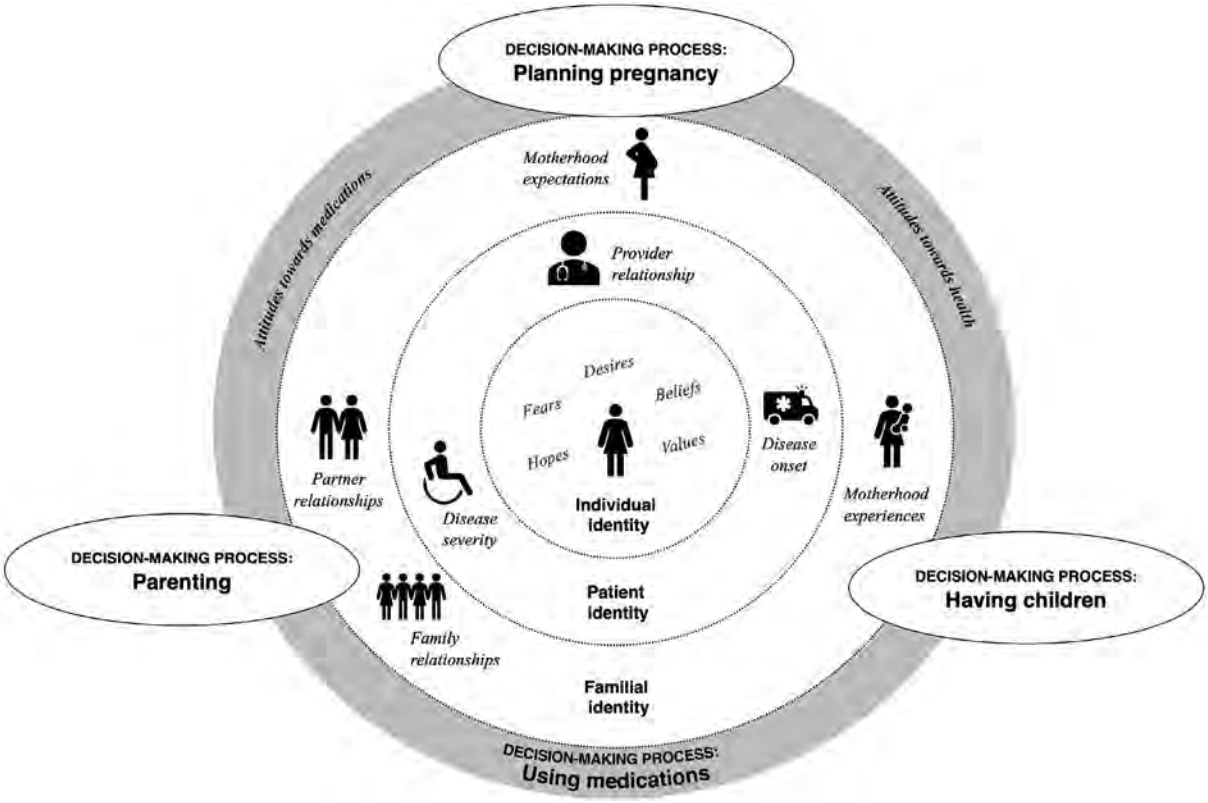

Figure 1. A constructivist, woman-centred, grounded theory framework for making pregnancy and family decisions in relation to living with rheumatoid arthritis. INDIVIDUAL IDENTITY: encompasses a woman's personal hopes, desires, beliefs, values, and fears about her life. PATIENT IDENTITY: encompasses a woman's experiences of being a patient, including the timing of disease onset, disease experience and severity, and relationships with healthcare providers. FAMILIAL IDENTITY: encompasses a woman's experience of being a member of a family, including expectations of motherhood, motherhood experiences, and relationships with family and/or romantic partner(s). Dotted lines: demonstrate that a woman's identities are fluid, overlapping, and influence one another. Gray shading: demonstrates that medication decisions occur in a dynamic context between a woman's identities and other decision-making processes.

Disclosure: N. Rebic, None; **R. Garg**, None; **S. Munro**, None; **G. Hazlewood**, None; **N. Amiri**, None; **N. Bansback**, None; **S. Ensworth**, None; **C. Baldwin**, None; **L. Proulx**, None; **M. De Vera**, None.

Abstract Number: 1775

Risk Factors for Adverse Pregnancy Outcomes of Women with Positive for Antiphospholipid Antibodies Treated with Conventional Therapies

Hiromi Shimada[1], Risa Wakiya[2], Mai Mahmound Fahmy Mansour[1], Shusaku Nakashima[1], Mikiya Kato[1], Koichi Sugihara[1], Yusuke Ushio[1], Tomohiro Kameda[1] and Hiroaki Dobashi[3], [1]Department of Internal Medicine, Division of Haematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa University., Kita-gun, Kagawa, Japan, [2]Department of Internal Medicine, Division of Haematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa University., Kagawa, Kagawa, Japan, [3]Department of Internal Medicine, Division of Haematology, Rheumatology and Respiratory Medicine, Faculty of Medicine, Kagawa University, Kagawa, Japan

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Reproductive Issues in Rheumatic Disorders Poster

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Session Time: 9:00AM–11:00AM

Background/Purpose: Antiphospholipid antibodies induce several obstetric complications including recurrent spontaneous abortion, preterm birth, intrauterine fetal death. EULAR recommendations for antiphospholipid syndrome (APS) indicates low dose aspirin (LDA) and/or low weight molecule heparin (LWMH) as a conventional therapy for APS[1]. However, Pregnant women with antiphospholipid antibodies sometimes had adverse pregnancy outcomes (APOs) under the appropriate conventional treatment. We hereby investigated the risk factors for APOs in the patients with antiphospholipid antibodies under the conventional therapies.

Methods: We retrospectively examined 28 patients who were positive for antiphospholipid antibodies and treated with conventional therapies (LDA and/or LWMH). They were managed from planning for pregnancy to delivery in our institution. We analyzed whether history of obstetric complications, types or numbers of positive auto-antibodies,

	n=38
Mean age at delivery (years old)	31.1 ± 5.0
Disease duration (years)	5.5 ± 4.7
Complicated autoimmune disease	
Systemic lupus erythematosus (n (%))	9 (32.1)
Rheumatoid arthritis (n (%))	6 (21.4)
Mixed connective tissue disease (n (%))	3 (10.7)
Sjogren syndrome (n (%))	3 (10.7)
Histories of obstetric and thrombotic complications	16 (57.1)
Spontaneous abortion (n (%))	4 (14.3)
Stillbirth (n (%))	2 (7.1)
Thrombosis (n (%))	
Type of antiphospholipid antibodies	
Lupus anticoagulant (n (%))	15 (57.7)
Anti-cardiolipin antibody (n (%))	15 (57.7)
Anti-CLβ2GPI antibody (n (%))	7 (26.9)
Numbers of positive antibodies	
Single/Double/Triple (n (%))	19 (73.0)/1 (3.8)/6 (23.1)
Treatment agents during pregnancy	
Glucocorticoid use (n (%))	16 (57.1)
Mean dose of glucocorticoid (mg/day)	4.9 ± 6.0
Hydroxychloroquine use (n (%))	4 (14.3)
LDA and LWMH/LDA or LWMH (n (%))	11 (39.2)/17 (60.7)

Table 1. Patients characteristics.Values are presented as mean ± standard deviation or number (percentage). LDA; low dose aspirin, LWMH; low weight molecule heparin.

	APOs (+) (n=11)	APOs (-) (n=15)	P value
Histories of Obstetric and thrombotic complications			
Spontaneous abortion (n (%))##	4 (36.4)	11 (73.3)	0.11
Stillbirth (n (%))##	2 (18.2)	1 (6.7)	0.56
Thrombosis (n (%))##	0 (0)	2 (13.3)	0.49
Type of antiphospholipid antibodies			
Lupus anticoagulant (n (%))##	9 (81.8)	5 (38.5)	<0.05*
Anti-cardiolipin antibody (n (%))##	5 (45.5)	9 (69.2)	0.41
Anti-CLβ2GPI antibody (n (%))##	2 (18.2)	5 (38.5)	0.39
Numbers of positive antibodies			
Single/Double/Triple##	8/1/2	9/0/4	0.46
Treatment agents during pregnancy			
Glucocorticoid use (n (%))##	10 (90.9)	4 (26.7)	<0.01*
Mean dose of glucocorticoid (mg/day)#	9.1 ± 6.4	1.5 ± 3.7	<0.01*
Hydroxychloroquine use (n (%))##	1 (9.1)	3 (20.0)	0.61
LDA and LWMH (n (%))##	3 (27.3)	8 (53.3)	0.25

Table 2. The analysis of risk factors for adverse pregnancy outcomes. Values are presented as mean ± standard deviation or number (percentage). #; Wilcoxon rank sum test, NULL; Fisher exact test, *; P<0.05. APOs; adverse pregnancy outcomes, LDA; low dose aspirin, LWMH; low weight molecule heparin.

and treatment agents except for APS during pregnancy influenced on APOs (including spontaneous abortion, stillbirth, preterm birth, low birth weight, and preeclampsia).

Results: Fifty-three cases (28.5%) of all 186 pregnancies cases complicated with connective tissue disease was positive for antiphospholipid. Patients characteristics in this study was shown in *Table 1*. Twenty-eight cases (52.8%) were treated with conventional therapies (LDA and/or LWMH). As for the type of CTD complicated, nine cases (32.1%) were systemic lupus erythematosus. The type of antiphospholipid antibodies was as followed; presence of triple antiphospholipid antibodies was 6 cases, double was 1 case, single was 21 cases. Eleven cases (39.3%) were treated with both LDA and LWMH, and the others were treated with either of them. APOs occurred in 11 cases (45.8%), which excluded 2 cases of induced abortion. In the group which had occurred APOs, the rate of positive for lupus anticoagulant (LAC) was significantly higher than the other group (P< 0.05, Table 2). In addition, the frequency of glucocorticoid use and mean glucocorticoid dose was also significant higher (Both of them was P< 0.01) in patients with APOs. However, there was no significance focusd on history of obstetric and thrombotic complications, the number of positive auto-antibodies, treatment regimen for APS such as LDA and/or LWMH.

Conclusion: In our study, LAC positivity, glucocorticoid use and mean glucocorticoid administration during pregnancy amount is associated with the development of APO in antiphospholipid antibody-positive pregnant patients under conventional treatment. It was shown that there was no significant difference in the development of APOs between LDA + LWMH, LDA alone and LWMH alone. Treatment with at least one or more anticoagulant drugs reduced APO

development in women with positive antiphospholipid antibodies. Additionally, in other treatments, it is needed to note the risk of glucocorticoid use for APOs in CTD patients with APS.

Disclosure: H. Shimada, None; **R. Wakiya**, None; **M. Fahmy Mansour**, None; **S. Nakashima**, None; **M. Kato**, None; **K. Sugihara**, None; **Y. Ushio**, None; **T. Kameda**, None; **H. Dobashi**, None.

Abstract Number: 1776

Safety and Beneficial Effects of Hydroxychloroquine on Pregnancy Outcomes in Women with Systemic Lupus Erythematosus

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SESSION INFORMATION
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Background/Purpose: The use of hydroxychloroquine (HCQ) has long been established in Systemic Lupus Erythematosus

(SLE) and especially as applicable drug during pregnancy. Recently, beneficial effects and safety of HCQ have been re-discussed in the light of a change in the summary of product characteristics in some countries. More current studies are required to provide patients with evidence-based advice regarding this essential drug when counselling for pregnancy.

We therefore sought to examine the impact of HCQ on pregnancy outcomes of SLE women in a real-world cohort.

Methods: Pregnancies of women with SLE from an outpatient pregnancy clinic were prospectively evaluated before and throughout gestation. Maternal and fetal outcomes in women without HCQ therapy (group A) were compared to pregnancies under HCQ treatment from 1st trimester on (group B). A multiple logistic regression was performed with adjustment for confounding factors.

Results: We enrolled 184 live births from singleton pregnancies in 145 women (n=77 with HCQ and n=107 w/o HCQ). One neonatal death (group B) occurred after severe preeclampsia at 24 weeks of gestation (w/g) linked to noncompliance in a woman with high-risk aPL profile. One child (group B) was born with mycophenolate mofetil embryopathy.

Women in the HCQ group had a significantly lower rate of preterm births [aOR 0.31 (95%-CI: 0.15-

0.64), p = 0.026]. Regarding preeclampsia, we found a tendency towards less incidence with the use of HCQ [aOR 0.49 (95%-CI: 0.23-1.03), p = 0.24]. These improved outcomes are opposed by a higher frequency of risk factors in group B (lupus nephritis, high-risk aPL profile, slightly more hypertension) and a tendency towards more severe SLE (expressed in terms of increased use of Azathioprine) (Table 1). Nevertheless, women with HCQ therapy experienced significantly less flares during pregnancy [aOR 0.18 (95%-CI: 0.09-0.38), p = 0.013].

Conclusion: Compared to pregnancies without HCQ, those with HCQ showed significantly lower rates of flares and preterm births and tended to have fewer pre-eclampsia. Like other studies on HCQ in lupus pregnancy, this one is

		All pregnancies (n=184)	No HCQ in pregnancy (n=107)	HCQ during pregnancy (n=77)
	Age (years), median (IQR)	31.0 (28.0-34.0)	31.0 (29.0-34.0)	30.0 (27.0-33.0)
	Hypertension, n (%)	29 (15.8%)	16 (15.0%)	13 (16.9%)
	Preconception counselling, n (%)	122 (66.3%)	69 (64.5%)	53 (68.8%)
SLE disease & therapy characteristics	Disease duration (years), median (IQR)	6.7 (2.9-10.3)	7.0 (3.0-10.0)	6.7 (2.1-11.0)
	Lupus nephritis*1, n (%)	51 (27.7%)	25 (23.4%)	26 (33.8%)
	High-risk aPL profile*2, n (%)	39 (21.3%)	21 (19.8%)	18 (23.4%)
	SLEDAI*1, median (IQR)	2.0 (0-4.0)	2.0 (0.0-4.0)	2.0 (2.0-4.0)
	Anti-dsDNA, n (%)	102 (55.7%)	47 (44.3%)	55 (71.4%)
	Anti-SSA/Ro and/or Anti-SSB/La, n (%)	91 (49.7%)	55 (51.9%)	36 (46.8%)
	Azathioprine*1, n (%)	38 (20.7%)	18 (16.8%)	20 (26.0%)
	Low dose Aspirin*3, n (%)	74 (41.1%)	34 (32.7%)	40 (52.6%)
Obstetrical history	Nulliparous, n (%)	113 (61.4%)	63 (58.9%)	50 (64.9%)
	Previous fetal loss, n (%)	39 (21.2%)	22 (20.6%)	17 (22.1%)
	Previous (pre-)eclampsia or HELLP, n (%)	14 (7.6%)	8 (7.5%)	6 (7.8%)
	Previous congenital heart block, n (%)	1 (0.54%)	-	1 (1.3%)

*1last visit before pregnancy, *2according to the 2019 EULAR recommendations, *3until 16 w/g

Table 1. Patient characteristics

		All pregnancies (n=184)	No HCQ in pregnancy (n=107)	HCQ during pregnancy (n=77)
Pregnancy outcome	(mild-moderate) flare*4, n (%)	44 (29.5%)	30 (34.9%)	14 (22.2%)
	Preterm birth*5, n (%)	46 (25%)	30 (28.0%)	16 (20.8%)
	Preeclampsia, n (%)	24 (13%)	15 (14.0%)	9 (11.7%)
	Intrauterine growth restriction, n (%)	3 (1.7%)	1 (1.0%)	2 (2.6%)
	Congenital heart block, n (%)	1 (0.54%)	-	1 (1.3%)

*4increase in SLEPDAI ≥ 4 or increase in prednisolone ≥ 5mg/d, *5< 37 w/g

Table 2. Pregnancy outcomes

influenced by the indication and adherence. However, since the safety of HCQ is confirmed, it is in line with current recommendations to continue HCQ throughout pregnancy.

Disclosure: I. Haase, None; **M. Schneider**, GSK, UCB, Abbvie, 2, Abbvie, Alexion, Astra Zeneca, BMS, Boehringer Ingelheim, Gilead, Lilly, Sanofi, UCB, 5, Abbvie, Astra Zeneca, BMS, Chugai, GSK, Lilly, Pfizer, Sanofi, 8; **R. Brinks**, None; **R. Fischer-Betz**, UCB, 5, Abbvie, Amgen, Biogen, BMS, Celgene, Chugai, GSK, Janssen, Lilly, Medac, MSD, Novartis, Roche, UCB, Pfizer, 8.

Abstract Number: 1777

Low Dose Aspirin to Prevent Pre-eclampsia in SLE Pregnancies – Counselling Helps to Realize Our Full Potential

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Women with Systemic Lupus Erythematosus (SLE) face a higher risk of pre-eclampsia, especially those with additional risk factors. Low dose aspirin (LDA) is known to protect against pre-eclampsia in non-autoimmune patients. Consequently, the EULAR recommends starting LDA in those women at risk preconceptionally or latest until gestational week 16. We sought to examine the use of LDA in a real-world cohort in relation to different risk factors and the provision of preconception counselling.

Methods: Pregnancies of women with SLE from an outpatient pregnancy clinic were evaluated before and throughout pregnancy. Clinical characteristics including pre-eclampsia risk factors, disease activity (SLEDAI) and medication use were analysed. Association of Aspirin use (latest from week 16 on) with different risk factors or preconception counselling was analysed using χ^2 tests.

Results: We enrolled 201 pregnancies in 136 women. 57.8% of pregnancies showed a high-risk profile for pre-eclampsia (history of pre-eclampsia, multifetal gestation, chronic hypertension, lupus nephritis or aPL), another 26.6% had at least one moderate risk factor (nulliparous, body mass index >30 or age >35).

LDA was administered in 43.3% of pregnancies. LDA use was significantly higher in those with a high-risk profile (63.5% vs. 16.7%) [OR 8.59 (95%-CI: 4.19-18.62), p< 0.001], but not in those with a moderate-risk profile. Still, 36.5% of those at high risk and 83% of those at moderate risk did not receive Aspirin. In a descending order, aPL, multifetal gestation, lupus nephritis and nulliparity were associated with a higher LDA use, whereas the other risk factors were not.

Preconception counselling significantly increased Aspirin administration [OR 2.36 (95%-CI: 1.23-4.63), p< 0.01], especially in those at high risk [OR 4.12 (95%-CI 1.72-10.16), p< 0.001]. Overall, LDA use increased from 1995 to 2019 (χ^2 test for trend in proportions, p< 0.001).

Conclusion: We found a high prevalence of pre-eclampsia risk factors in our real-world cohort of pregnant SLE patients, which was contrasted by an overall infrequent use of LDA during pregnancy. Preconception counselling prior to conception allows more women, especially those with an additional risk profile, to receive LDA at an early stage, which may contribute to a better pregnancy outcome.

	All pregnancies (n=201)	No LDA therapy (n=114)	LDA therapy (n=87)
Age (years), median (IQR)	31 (28-34)	30.5 (27-34)	31 (29-33)
Age > 35, n (%)	42 (20.9%)	27 (23.7%)	15 (17.2%)
BMI, median (IQR)	23 (22-24)	23 (22-25)	23 (22-24)
BMI > 30, n (%)	12 (6.1%)	6 (5.4%)	6 (7.0%)
Chronic Hypertension, n (%)	34 (16.9%)	17 (14.9%)	17 (19.5%)
CKD III[*1] or higher, n (%)	4 (2.2%)	2 (1.9%)	2 (2.5%)
Preconception counselling, n (%)	131 (65.2%)	65 (57.0%)	66 (75.9%)
Year of preconceptional visit			
1995-1999, n (%)	23	19 (82.6%)	4 (17.4%)
2000-2004, n (%)	49	34 (69.4%)	15 (30.6%)
2005-2009, n (%)	49	31 (63.3%)	18 (36.7%)
2010-2014, n (%)	58	25 (43.1%)	33 (56.9%)
2015-2019, n (%)	22	5 (22.7%)	17 (77.3%)
Obstetrical history and characteristics			
Nulliparous, n (%)	123 (61.2%)	60 (52.6%)	63 (72.4%)
Previous fetal loss, n (%)	40 (19.9%)	14 (12.3%)	26 (29.9%)
Previous pre-eclampsia, n (%)	16 (8%)	7 (6.1%)	9 (10.3%)
Multifetal gestation, n (%)	8 (4.2%)	1 (0.9%)	7 (8.5%)
SLE characteristics			
Disease duration (years), median (IQR)	6.4 (2.7-10.8)	6.0 (2.2-10.13)	7.0 (3.0-11.0)
SLEDAI, median (IQR)	2.0 (0-4.0)	2.0 (0-4.0)	2.0 (2.0-4.0)
Lupus nephritis, n (%)	58 (28.9%)	24 (21.1%)	34 (29.1%)
Anti-dsDNA antibodies, n (%)	111 (55.5%)	57 (50.4%)	54 (62.1%)
Prednisolone therapy, n (%)	100 (49.8%)	57 (50.0%)	43 (49.4%)
Prednisolone (mg/d), median (IQR)	5.0 (5.0-7.25)	5.0 (5.0-8.0)	5.0 (5.0-5.0)
Antiphospholipid status			
APS, n (%)	31 (15.4%)	3 (2.6%)	28 (32.2%)
Any positive aPL, n (%)	48 (24%)	7 (6.2%)	41 (47.1%)
LAC, n (%)	31 (15.5%)	3 (2.7%)	28 (32.2%)
ACL, n (%)	33 (16.5%)	5 (4.4%)	28 (32.2%)
β2-GP1, n (%)	28 (14%)	4 (3.5%)	24 (27.6%)

BMI = body mass index, APS = Antiphospholipid syndrome, aPL = Antiphospholipid antibody, LAC = Lupus anticoagulant, ACL = Anticardiolipin antibody, β2-GP1 = β2-Glycoprotein I antibody, CKD = chronic kidney disease, IUGR = intrauterine growth restriction; *1 eGFR (MDRD) < 60 ml/min/1.73m²

Table 1. Patient characteristics and pre-conceptional risk profile

Disclosure: I. Haase, None; **M. Schneider**, GSK, UCB, Abbvie, 2, Abbvie, Alexion, Astra Zeneca, BMS, Boehringer Ingelheim, Gilead, Lilly, Sanofi, UCB, 5, Abbvie, Astra Zeneca, BMS, Chugai, GSK, Lilly, Pfizer, Sanofi, 8; **R. Brinks**, None; **R. Fischer-Betz**, UCB, 5, Abbvie, Amgen, Biogen, BMS, Celgene, Chugai, GSK, Janssen, Lilly, Medac, MSD, Novartis, Roche, UCB, Pfizer, 8.

Abstract Number: 1778

Improving Teratogenic Medication Consent and Sexual Activity Screening in Adolescent and Young Females: A Pediatric Rheumatology Reproductive Health Initiative

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SESSION INFORMATION

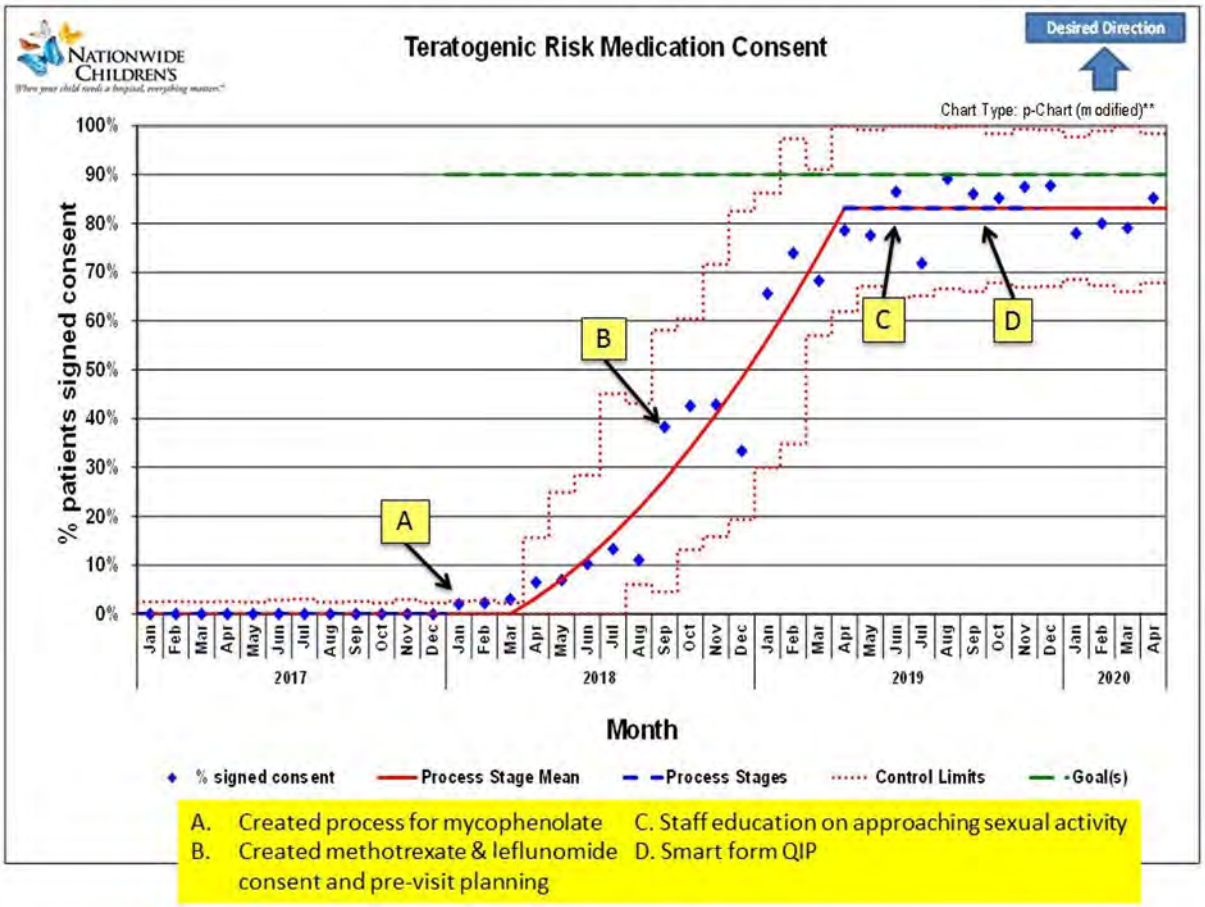
Session Date: Monday, November 9, 2020

Session Title: Reproductive Issues in Rheumatic Disorders Poster

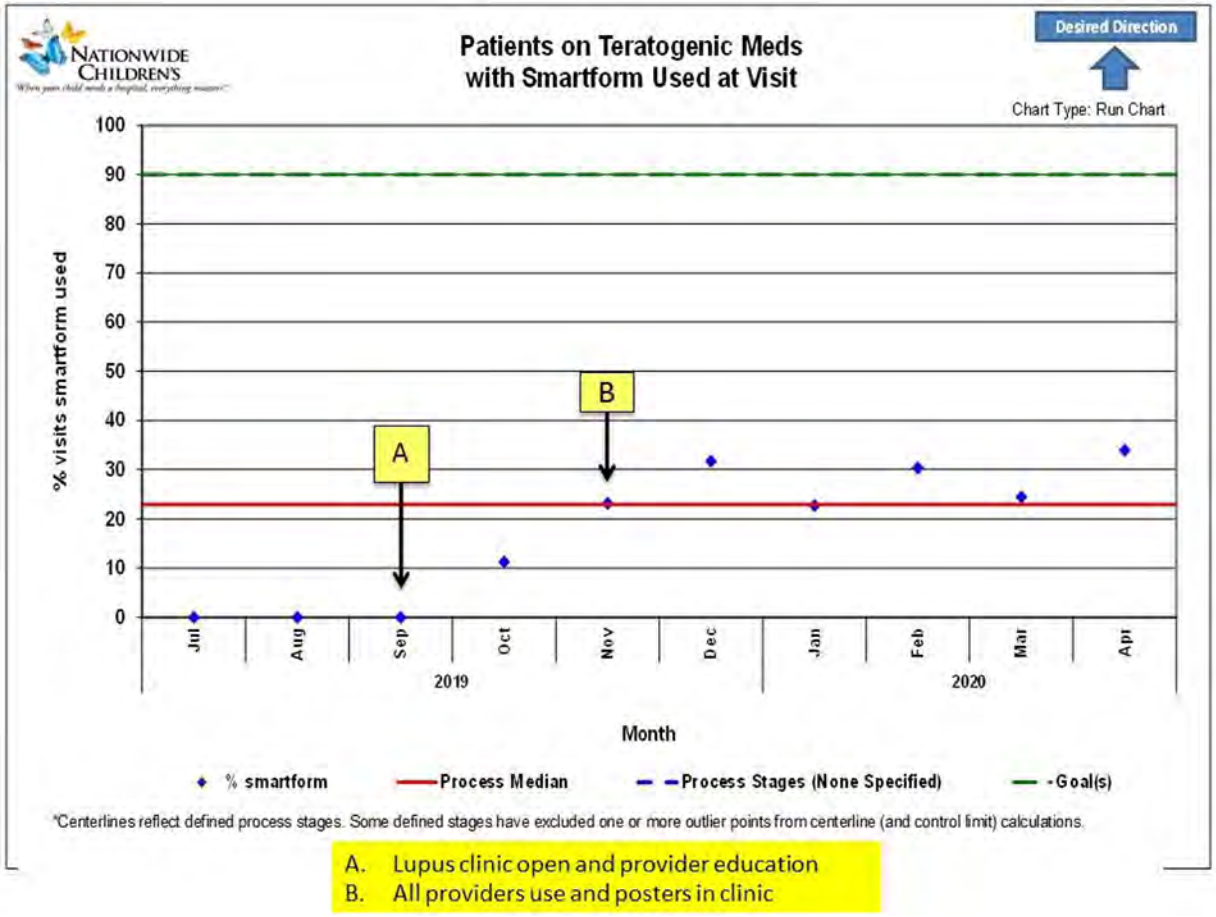
Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Adolescent and young women with rheumatic diseases are often prescribed teratogenic medications to manage their disease. Published reports indicate that the frequency of reproductive health counseling



Run chart for sexual history documentation within electronic health record smartform at each visit for all patients on teratogenic medications age 12 years and older with annotated QI PDSA interventions.

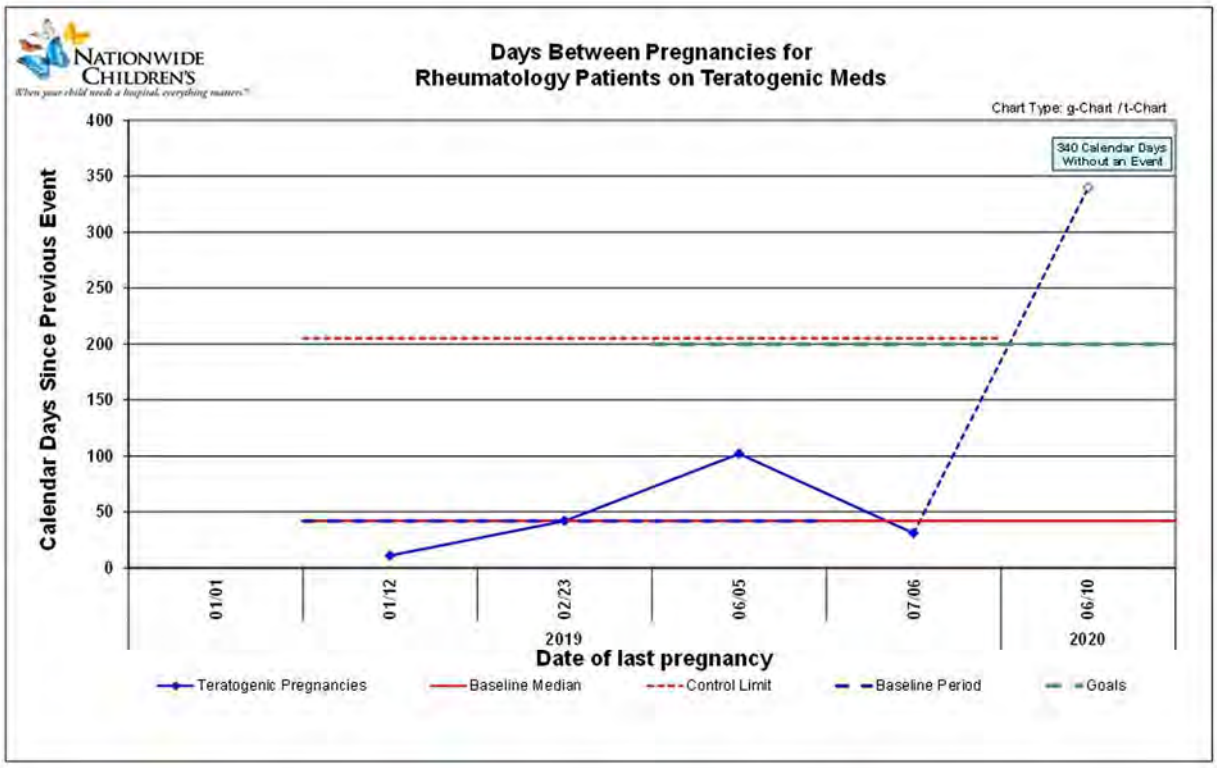


P-chart for teratogenic risk medication consent for all females patients 12 years and older on teratogenic medications with annotated QI PDSA cycle interventions.

is low in this population, allowing a significant risk of fetal exposure to teratogenic medications. This three-year project aimed to prevent pregnancies in adolescent and young women on teratogenic medications and consisted of two phased initiatives: annual teratogenic medication consents and sexual history documentation at every visit.

Methods: The Institute for Healthcare Improvement model for quality improvement (QI) was used for this project. Each phase included a baseline assessment review and several PDSA cycles. In 2018, annual teratogenic medication consents were created and implemented to facilitate education about teratogenic and fetotoxic risks associated with certain medications. At baseline, there was no consistent documentation of teratogenic medication and/or counseling received by females who were prescribed teratogenic medications. In 2019, we developed sexual history form that was incorporated into the electronic health record to help guide provider discussions with patients and families at every visit and to develop pregnancy prevention plans. Baseline data revealed that none of our female patients who were prescribed teratogenic medications had appropriate sexual history documentation during their clinic visits. To assess the success of reaching our aim of among adolescent and young women using teratogenic medications, we measured days between pregnancies for females on teratogenic medications. In January 2019, days between pregnancies for females on teratogenic medications was determined to be 42 days.

Results: The percentage of females that received annual teratogenic consents increased from 0% to 85% after 18 months. After 8 months, the proportion of female patients that had appropriate sexual history documentation at every visit increased from 0% to 35%. For females on teratogenic medications, the days between reported pregnancies increased from 42 days between pregnancies in January 2019 to >340 days in June 2020.



G-chart indicating days between pregnancies for patients on teratogenic medications followed in rheumatology clinic.

Conclusion: The implementation of a phased QI project to prevent pregnancies among adolescent and young women using teratogenic medications has been successful within our institution. Coming initiatives, such as routine pregnancy screening and ongoing pregnancy-prevention plans, will help to prevent exposure of teratogenic medications to pregnant females and enhance safe use of these medications. We hope expand aspects of this project to other divisions within our institution and potentially across institutions, as well.

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Abstract Number: 1779

Gap in Contraceptive Education to Females with Rheumatic Disease on Teratogenic Medications

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Reproductive Issues in Rheumatic Disorders Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Table 1. Relationship of patient education on drug teratogenicity with use of birth control in patients treated with DMARDs.

		Birth Control Use		P values
Drug	**Education**	**Yes**	**No**	
MTX/RA	Yes	39	28	0.0346
	No	29	43	
MTX/SLE	Yes	38	27	0.7309
	No	31	25	
MTX/PsA	Yes	10	8	0.1498
	No	8	16	
MTX/JIA	Yes	2	2	>0.9999
	No	5	5	
MTX/AS	Yes	5	0	0.1667
	No	2	2	
MTX/VAS	Yes	0	0	n/a
	No	1	2	
MMF/RA	Yes	2	1	n/a
	No	0	0	
MMF/SLE	Yes	25	28	0.4131
	No	20	31	
MMF/VAS	Yes	1	1	n/a
	No	0	0	
LFN/RA	Yes	9	4	0.7721
	No	7	4	
LFN/SLE	Yes	6	6	0.3615
	No	5	2	
LFN/PsA	Yes	0	1	0.3865
	No	1	1	
CP/VAS	Yes	0	0	n/a
	No	0	1	

SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; PsA, psoriatic arthritis; JIA, juvenile inflammatory arthritis; AS, ankylosing spondylitis; VAS, vasculitis. MTX, methotrexate, MMF, mycophenolate mofetic or mycophenolic acid; LFN, leflunomide; CP, cyclophosphamide; edu, educated; BC, birth control.

Background/Purpose: Teratogenic disease-modifying anti-rheumatic disease modifying drugs (DMARDs) are often prescribed to women of childbearing age. Contraception represents an important area of reproductive health for female patients with rheumatic diseases. Counseling prior to starting DMARDs can help prevent the potential pregnancy risks associated with such medications. Methotrexate (MTX), cyclophosphamide (CP), leflunomide (LFN) and mycophenolate (MMF) are commonly used DMARDs, which can be highly teratogenic.

Methods: The use of high-risk medications was retrospectively evaluated in 484 female rheumatic disease patients of childbearing age (13 to 45 years old) as documented in the electronic medical records of Upstate University Hospital between 2013-2019. Charts were reviewed for medication use, documentation of education and use birth control (medication, sterilization, or postmenopausal) (Table 1 &2). Statistical analysis was performed with chi-square or Fisher's exact test using GraphPad version 8.0 software. Two-tailed $p < 0.05$ was considered significant.

Table 2: Percent of patients educated on teratogenic medications.

Rheumatic disease	Total Dx	% educated on MTX	% educated on LFN	% educated on MMF	% educated CP
SLE	244	(65/121) 54%	(12/19) 63%	(53/104) 51%	n/a
RA	166	(67/139) 48%	(13/24) 54%	(3/3) 100%	n/a
PsA	45	(18/42) 43%	(1/3) 33%	n/a	n/a
JIA	14	(4/10) 29%	n/a	n/a	n/a
AS	9	(7/9) 78%	n/a	n/a	n/a
Vasculitis	6	(1/0) 100%	n/a	(0/3) 0%	(0/1) 0%

SLE, systemic lupus erythematosus; RA, rheumatoid arthritis; PsA, psoriatic arthritis; JIA, juvenile inflammatory arthritis; AS, ankylosing spondylitis. MTX, methotrexate, MMF, mycophenolate mofetic or mycophenolic acid; LFN, leflunomide; CP, cyclophosphamide; edu, educated; BC, birth control.

Results: 484 DMARD-treated patients were evaluated for documentation of education on drug teratogenicity and compliance with use of birth controls. 76% of patients were Caucasian, 18% were African American or Hispanic and 6% were Indian, Asian or Native American. 50% (243/484) of patients were educated regarding potential teratogenic complications that only resulted in greater use of contraceptives in methotrexate-treated patients with rheumatoid arthritis (Table 1).

Conclusion: In the USA, it is estimated that about 5.8% of all pregnancies are exposed to category D or X medications [1]. More than 50% of all pregnancies in the USA are unplanned [2]. This is concerning, especially for our rheumatic disease patients who are already at risk. Potential teratogenic medications should be thoroughly reviewed with patients so that preventive measures could be employed. Despite the common consensus for contraceptive education, there still remains a gap in implementing this standard clinical practice, especially among patients with SLE [3,4]. In our facility, teratogenicity of potential drugs and family counseling was provided only 50% of the time, indicating major gaps in family planning counseling among childbearing aged women with rheumatic diseases. To ensure that our patients receive proper family planning and counseling, a collaboration among rheumatologist, primary care physicians and obstetrician-gynecologists is critical. Our study demonstrates critical gaps in counseling and compliance with use of teratogenic medications. Future intervention should address barriers in counseling, compliance and documentation of teratogenic medication use.

Disclosure: A. Perl, None; **S. Mian**, None; **J. Ben Gabr**, None.

Abstract Number: 1780

Maternal and Fetal Outcomes in Pregnant Women with Psoriatic Arthritis: A Systematic Literature Review

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Reproductive Issues in Rheumatic Disorders Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Study	Type of study	Population Pregnancies/Women	Pregnancy outcomes in PsA patients vs controls	
Remaeus, 2019	Prospective, nationwide cohort study	PsA: 483/NR Controls: 40499/25594	**Preterm births**: 36 (7.4%) vs 1961 (4.9%); aOR 1.59 (1.09-2.32), p<0.05 **Small for gestational age**: 13 (2.7%) vs 1054 (2.6%); aOR 1.01 (0.55-1.85), p=NS **Stillbirth**: 2 (0.4%) vs 130 (0.3%) **Neonatal death**: 1 (0.2%) vs 55 (0.1%)	**Cesarian section**: 118 (24.4%) vs 7325 (18.1%); aOR 1.41 (1.08-1.84), p<0.05 **Pre-eclampsia**: 22 (4.5%) vs 1376 (3.4%); aOR 1.18 (0.71-1.96), p=NS **Gestational diabetes**: 6 (1.2%) vs 353 (0.9%); aOR 1.49 (0.66-3.37), p=NS
Smith, 2019	Prospective cohort study	PsA: 117/117 Controls: 717/717	**Preterm births**: 16 (13.7%) vs 61 (8.5%); aRR 1.69 (0.94-3.03), p=NS **Moderate preterm birth** (≥32 and <37 weeks): 16 (13.7%) vs 55 (7.7%); aRR 1.81 (1.01-3.26), p<0.05 **Low birth weight**: 11 (9.4%) vs 48 (6.7%), aRR: 1.52 (0.76-3.04), p=NS	**Cesarian section**: 57 (48.7%) vs 188 (26.2%); aRR 1.63 (1.26-2.12), p<0.05 **Pre-eclampsia**: 10 (8.5%) vs 27 (3.8%); aRR 2.22 (0.98-5.04), p=NS **Gestational diabetes**: 11 (9.4%) vs 43 (6.1%); aRR 1.41 (0.70-2.87), p=NS **Pregnancy-induced hypertension**: 11 (9.4%) vs 31 (4.3%); aRR 1.11 (0.53-2.32), p=NS
Strouse, 2019	Retrospective cohort study	PsA: 161/161 Controls: 10244/10244	**Preterm births**: 25 (15.5%) vs 962 (9.4%), OR 1.77 (1.15-2.73), p<0.01 **Small for gestational age**: 17 (10.6%) vs 892 (8.7%), OR 1.24 (0.75-2.06), p=NS	
Bröms, 2018	Prospective cohort study	PsA: 870/NR Controls: 860520/NR	**Preterm births**: 54 (6.2%) vs 41443 (4.8%), OR 1.25 (0.94–1.65) **Small for gestational age**: 14 (1.6%) vs 18560 (2.2%), OR 0.72 (0.42–1.22) **Low birth weight**: 32 (3.7%) vs 28515 (3.3%), OR 1.07 (0.75–1.52)	**Elective cesarian section**: 123 (14.1%) vs 73855 (8.6%), OR 1.47 (1.18–1.81) **Preeclampsia**: 44 (5.1%) vs 28355 (3.3%), OR 1.49 (1.08–2.05) **Gestational hypertension**: 36 (4.1%) vs 20203 (2.3%), OR 1.60 (1.13–2.29) **Gestational diabetes**: 23 (2.6%) vs 15705 (1.8%), OR 1.21 (0.79–1.87)
Polachek, 2018	Retrospective questionnaire-based study	PsA: 151/74 Controls: 193/74	**Stillbirth**: 1 (1%) vs 1 (1%) **Spontaneous miscarriage**: 32 (21%) vs 32 (17%) **Perinatal/neonatal death**: 0 (0%) vs 0/ (0%) **Planned cesarian section**: 28 (48%) vs 23 51%)	**Emergency cesarian section**: 14 (12%) vs 23 (15.5%) **Pre-eclampsia**: 1 (1%) vs 13 (7%) **Pregnancy-induced hypertension**: 5 (3%) vs 0 (0%) **Gestational diabetes**: 6 (4%) vs 0 (0%)

aOR: adjusted odds ratio; aRR: adjusted risk ratio; NR: not reported; NS: non-significant; OR: odds ratio.

Maternal and fetal outcomes in PsA patients.

Background/Purpose: The onset of psoriatic arthritis (PsA) often occurs between the ages of 30 and 50 years. Accordingly, many female patients are diagnosed during childbearing age, potentially impacting their pregnancy outcomes. However, there is a paucity of data concerning the fetal and maternal outcomes in this population and most of the information is extrapolated from studies on rheumatoid arthritis (RA). We aim to review the available evidence on the relationship between PsA and adverse pregnancy outcomes.

Methods: We systematically searched two databases, PubMed and Embase, for original studies from inception of the databases until May 31, 2020, addressing fetal and maternal outcomes in pregnant women with PsA. A variety of terms adjusted to the specificities of the two databases and related to key subject areas of the review question were used. The search was filtered to only include human participants and publications in English. The eligible studies had to present a comparator group (healthy individuals or patients without known auto-immune rheumatic diseases – ARD's), as well as at least one clinical outcome of interest. Studies including patients with other ARD's were eligible only if results from patients with PsA were presented separately. Two authors independently selected studies and extracted data.

Results: Of a total of 708 references, 5 observational studies fulfilled the inclusion criteria: 3 prospective and 2 retrospective studies (table 1).

Concerning maternal outcomes, the odds of delivery by caesarian section was higher among PsA women compared with the control groups, in 3 out of 4 studies. However, the majority of studies did not find an increased risk of pre-eclampsia or gestational hypertension among PsA patients. Likewise, no study has found an increased risk of gestational diabetes in pregnant women with PsA.

Regarding fetal outcomes, 3 studies revealed an increased risk of preterm birth in PsA patients, out of 4 studies reporting this outcome. Spontaneous miscarriages, stillbirths, neonatal deaths and small for gestational age newborns occurred at similar rates in women with PsA and the comparator groups, across the different studies.

Only one of the included studies, has assessed the influence of disease activity in the outcomes. Smith et al observed that active disease (defined as RAPID3 score ≥ 7 and HAQ >0.5) at 32 weeks of gestation increased the risk for preterm birth in PsA.

Conclusion: Despite the limited available data, these studies suggest an increased risk for delivery by caesarian section and preterm births among pregnant women with PsA. Increased disease activity seems to contribute to a higher risk of preterm birth as in RA. Nonetheless, this effect should be further examined.

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Abstract Number: 1781

Pregnancy After Bariatric Surgery in Women with Rheumatic Diseases and Association with Adverse Birth Outcomes

Namrata Singh[1], Rebecca Baer[2], Maya Swaminathan[3], Shireesh Saurabh[4], Jeffrey Sparks[5], Gretchen Bandoli[6], Elena Flowers[7], Laura Jelliffe-Pawlowski[2] and Kelli Ryckman[8], [1]University of Washington, Bellevue, WA, [2]University of California San Francisco, San Francisco, [3]University of Washington, Seattle, WA, [4]Kaiser Permanente WA, Bellevue, WA, [5]Brigham and Women's Hospital, Boston, MA, [6]University of California San Diego, La Jolla, CA, [7]UCSF, San Francisco, CA, [8]University of Iowa, Iowa City

SESSION INFORMATION
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Background/Purpose: Autoimmune rheumatic diseases (ARD) and bariatric surgery are each risk factors for adverse birth outcomes. To date, no study has investigated their combined impact on birth outcomes. The objective of this study was to evaluate the impact of bariatric surgery on pregnancy in patients with ARD with and without bariatric surgery.

Methods: This retrospective cohort study included infants born between 20–44 weeks of gestation in California between 2011–2018. Birth certificates were linked to maternal and infant hospital and emergency department discharge records. History of maternal bariatric surgery and ARD was identified from discharge records. We compared combinations of ARD and bariatric surgery to women with an ARD and no bariatric surgery for adverse maternal and infant outcomes.

Results: The study included 3,574,165 pregnancies, of whom 10,823 (0.3%) had an ARD and 8,172 (0.22%) of the total women had a history of bariatric surgery. There were 86 women (0.0022%) with both an ARD and a history of bariatric surgery. Among women with bariatric surgery and no ARD, the incidence of preterm birth was 13.9%. Among women with ARD and no bariatric surgery it was 18%. Among women with both an ARD and a history of bariatric surgery the incidence was 19.8%. Women with a history of bariatric surgery and an ARD had similar risk of having a preterm birth, small for gestational age or large for gestational age infant, or a cesarean delivery compared

Table 1. Relative risk of adverse outcomes among women with a history of bariatric surgery stratified by ARD

	Any ARD		No ARD	
	With bariatric surgery	Without bariatric surgery	With bariatric surgery	Without bariatric surgery
Pregnancies	86	10,737	8,086	3,555,256
Perinatal mortality, n (%)	*	65 (0.6)	51 (0.6)	10,260 (0.3)
RR (95%CI)	-	-	**2.2 (1.7, 2.9)**	1.0 (Ref)
aRR (95%CI)	-	-	**1.9 (1.4, 2.5)**	1.0 (Ref)
Congenital anomalies, n (%)	*	418 (3.9)	309 (3.8)	95,352 (2.7)
RR (95%CI)	-	-	**1.4 (1.3, 1.6)**	1.0 (Ref)
aRR (95%CI)	-	-	**1.3 (1.1, 1.4)**	1.0 (Ref)
Preterm birth, n (%)	17 (19.8)	1,933 (18.0)	1,127 (13.9)	290,080 (8.2)
RR (95%CI)	1.1 (0.7, 1.8)	1.0 (Ref)	**1.7 (1.6, 1.8)**	1.0 (Ref)
aRR (95%CI)	1.1 (0.7, 1.8)	1.0 (Ref)	**1.3 (1.2, 1.4)**	1.0 (Ref)
SGA, n (%)	11 (12.8)	1,580 (14.7)	1,147 (14.2)	327,435 (9.2)
RR (95%CI)	0.9 (0.5, 1.6)	1.0 (Ref)	**1.5 (1.5, 1.6)**	1.0 (Ref)
aRR (95%CI)	1.1 (0.6, 2.1)	1.0 (Ref)	**1.9 (1.8, 2.0)**	1.0 (Ref)
LGA, n (%)	8 (9.3)	767 (7.1)	568 (7.0)	330,698 (9.3)
RR (95%CI)	1.3 (0.6, 2.6)	1.0 (Ref)	**0.8 (0.7, 0.8)**	1.0 (Ref)

to women with an ARD and no history of bariatric surgery (Table 1). Over 20% of infants born to women with a history of ARD and bariatric surgery were admitted to the NICU compared to 13.0% of infants born to those with an ARD and no history of bariatric surgery (adjusted relative risk, aRR, 1.7, 95% CI 1.1 to 2.8).

Conclusion: Our study shows that women with ARD already have a high occurrence of several adverse birth outcomes, and this was not further increased by a history of bariatric surgery. The infants born to women with a history of ARD and bariatric surgery were admitted to the NICU significantly more than the infants born to women with an ARD and no history of bariatric surgery.

aRR (95%CI)	0.9 (0.4, 1.7)	1.0 (Ref)	**0.5 (0.5, 0.6)**	1.0 (Ref)
NICU admission, n (%)	18 (20.9)	1,391 (13.0)	777 (9.6)	228,658 (6.4)
RR (95%CI)	**1.6 (1.0, 2.6)**	1.0 (Ref)	**1.5 (1.4, 1.6)**	1.0 (Ref)
aRR (95%CI)	**1.7 (1.1, 2.8)**	1.0 (Ref)	**1.1 (1.1, 1.2)**	1.0 (Ref)
Cesarean section, n (%)	47 (54.7)	4,822 (44.9)	3,920 (48.5)	1,199,290 (33.7)
RR (95%CI)	1.2 (0.9, 1.6)	1.0 (Ref)	**1.4 (1.4, 1.5)**	1.0 (Ref)
aRR (95%CI)	1.1 (0.8, 1.4)	1.0 (Ref)	**1.1 (1.1, 1.2)**	1.0 (Ref)
Assisted birth, n (%)	*	572 (5.3)	346 (4.3)	227,366 (6.4)
RR (95%CI)	-	-	**0.7 (0.6, 0.7)**	1.0 (Ref)
aRR (95%CI)	-	-	**0.9 (0.8, 1.0)**	1.0 (Ref)

ARD: autoimmune rheumatic disease; aRR: adjusted relative risk; SGA: small for gestational age; LGA: large for gestational age; NICU: neonatal intensive care unit

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Abstract Number: 1782

Use of a Patient-reported Survey to Document Contraceptive Use and Interest in Pregnancy to Identify Patients with Unmet Pregnancy Prevention and Planning Needs

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SESSION INFORMATION
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Background/Purpose: Pregnancies in women with lupus who conceive when their disease is active or they are taking a teratogen are at increased risk for pregnancy loss, as well as preterm delivery and birth defects, with long-term consequences for their children. To avoid potentially catastrophic outcomes, pregnancy should coincide with periods when disease quiescence can be maintained with pregnancy-compatible medications. To achieve this, rheumatolo-

gists need to identify the women in need of pregnancy planning or contraceptive guidance. Our goal is to assess the pregnancy planning and prevention needs within a university lupus clinic.

Methods: All study participants were enrolled in a prospective registry, met SLICC criteria for SLE, were female, and age 18 to 45. On an intake form for each lupus clinic visit, women answered 1) "Would you like to get pregnant in the next 12 months," and 2) contraceptive use and type. Demographics, medications, and disease activity parameters were collected within the lupus registry. Women who did not complete the survey were excluded from analysis. Fisher's and t-tests compared women with and without contraceptive use and pregnancy intention.

Results: The survey was completed by 95% of the 134 women of reproductive age. Of these, 61% were black, 8% Hispanic, 46% were married and 64% had a college degree.

Contraception: 60% of women with lupus reported contraceptive use. Of these, 44% were using highly effective contraception, including an IUD (n=20), implant (n=7), or surgical sterilization (n=7). There were similar rates of contraceptive use by race, education, income, and marital status. Contraceptive use did not differ by severity of lupus symptoms, with similar rates in women with and without proteinuria, and with or without active Type 1 or Type 2 SLE symptoms.

The rate of contraception use was higher among women taking a teratogen (76%) compared to those not taking a teratogen (49%, p=0.004). While there was no difference in contraception use with or without HCQ, fewer women used contraception when taking AZA (30%, p< 0.001) and more women used contraception when taking MMF (77%, p=0.04).

Pregnancy Intention: 21 (17%) of women were interested in getting pregnant in the following year. These women were just as likely to report using contraception (62%) as women not interested in pregnancy (58%). There was no difference in demographic characteristics or lupus activity between women who did and did not want to conceive, though only one woman of 14 with active nephritis was interested in pregnancy. Both married (22%) and unmarried women (9%, p=0.06) were interested in pregnancy. Significantly more women on pregnancy-compatible medications than teratogens were interested in pregnancy (25% vs 8%, p=0.01).

Conclusion: This study demonstrates that systematic, patient-reported measures of pregnancy interest and contraceptive use are effective tools to identify women with unmet reproductive health needs. There were no demographic or lupus activity characteristics that would have otherwise identified these women for specific attention, highlighting the importance of routine screening to target pre-conception counseling and contraception guidance to the appropriate women at the appropriate time

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Abstract Number: 1783

Experience of Pregnant Rheumatology Outpatients from a Tertiary Hospital in New York City During the COVID-19 Pandemic

Bessie Stamm[1], Gregory Vitone[2], Marianna Frey[3], JoAnn Vega[1], Jane Salmon[3], Mary Crow[3], Vivian Bykerk[3], Michael Lockshin[1], Lisa Sammaritano[1], Lisa Mandl[3] and Medha Barbhaiya[1], [1]Hospital for Special Surgery, Barbara Volcker Center for Women and Rheumatic Diseases, New York, NY, [2]Hospital for Special Surgery, New York, [3]Hospital for Special Surgery, New York, NY

SESSION INFORMATION

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Background/Purpose: We aimed to evaluate the experience of pregnant rheumatology patients during the peak of the COVID-19 pandemic in New York City.

Methods: We emailed a secure web-based survey to 26,045 patients aged ≥18 years who were evaluated at least once by a rheumatologist from April 1, 2018-April 1, 2020 at a tertiary academic center in New York City. Patients received three secure e-mail invitations to complete the survey; a subset of patients with missing or incorrect e-mails were contacted by telephone. We collected detailed information including COVID-19 exposure and symptoms, rheumatic disease history and medications, sociodemographic factors, and 5 domains from the PROMIS-29 to assess psychosocial factors. We requested pregnancy data from any women aged 18 to 50. Women were asked to indicate

Table 1. Baseline Characteristics of Pregnant versus Non-Pregnant Rheumatology Patients from a Tertiary Hospital in New York City

	Pregnant n=61	Non-Pregnant n=1,469	p-values
Age (years; Mean, SD)	36.1 (4.9)	38.3(8.1)	**0.036**
Race (N, %)			0.595
White	45 (74%)	1,100 (75%)	
Asian or Indian Subcontinent	8 (13%)	128 (9%)	
Black or African American	3 (5%)	112 (8%)	
Unknown/Not Reported **	5(8%)	131 (9%)	
Ethnicity (N, %)			**<0.001**
Hispanic or Latino	3 (5%)	185 (13%)	
Not Hispanic or Latino	52 (85%)	1,197(81%)	
Unknown/Prefer Not to Answer	6 (10%)	34 (6%)	
Married or partnered (N, %)	54 (88%)	759(52%)	**<0.001**
Household Income (N, %)			
$150,000+	40 (65%)	558 (38%)	**<0.001**
<$150,000	19 (31%)	678 (46%)	
Unknown	2 (4%)	233 (16%)	
Systemic Rheumatic Diseases (N, %)		**(n=1,369)**	
Patients with SRD	41 (67%)	1,040 (76%)	0.119
• RA	9, (15%)	207 (20%)	
• SLE	13,(21%)	135 (13%)	
• Spondyloarthritis	7, (11%)	114 (11%)	
• Scleroderma/Vasculitis/Myositis	3,(5%)	68 (6%)	
• Overlap	6 (10%)	286 (28)	
• Antiphospholipid Syndrome	3 (5%)	231 (22%)	
Patients without SRD	20	329	
Medications taken in the last 6 months (N, %)			
Anti-Malarials (Chloroquine or Hydroxychloroquine)	21 (34%)	469 (32%)	0.422
Biologics§	8 (13%)	311 (21%)	
Conventional DMARDs‡	8 (13%)	309 (21%)	
Corticosteroids	9 (15%)	286 (19%)	

**Unknown includes American Indian or Alaskan Native, Native Hawaiian or other Pacific Islander
§Abatacept, Belimumab, TNF inhibitors, IL-6 inhibitors, IL-1 inhibitors, IL-12/23 inhibitors, IL-17 inhibitors, Cyclophosphamide
‡Leflunomide, Methotrexate, Mycophenolate, Azathioprine, Sulfasalazine
P-value threshold of <0.05 considered to be significant and indicated in bold

Table 2. Experiences of Pregnant versus Non-Pregnant Rheumatology Patients from a Tertiary Hospital in New York City During the COVID-19 Pandemic

	Pregnant n=61	Non-Pregnant n=1,469	p-values
Employment Status as of January 1, 2020 (N, %)			
Employed	52 (85%)	1,112 (76%)	0.087
Unemployed/Retired/Other	9 (15%)	357 (5%)	
Change in Employment Status during Pandemic (N, %)	**(n=55)**	**(n=1,255)**	0.466
Salary Reduction	8 (14%)	116 (9%)	
Employer Terminated Employment/Started New Job	3 (6%)	99 (8%)	
No Change	39 (71%)	879 (70%)	
Other*	5 (9%)	161 (13%)	
Working from home during the pandemic (N, %)	45 (74%)	961(65%)	0.178
Average Number of Cohabitants during pandemic (Mean, SD)	2.3(1.3)	2.3(1.5)	1.0
Confirmed or Suspected COVID-19€ (N, %)	5 (8%)	166(11%)	0.451
Time Spent at Home During Pandemic (N, %)		**(n=1,453)**	
>95% of Time	50 (82%)	1101 (76%)	0.059
50-95% of Time	11(18%)	301(21%)	
<50% of Time		51 (3%)	
COVID-19 symptoms lasting for ≥4 days (N, %)	28 (46%)	707 (48%)	0.733
Exposure to individuals with COVID-19 (N, %)	17 (28%)	441(30%)	0.719
High Risk of COVID-19 Exposure at Work	**N=52**	**N=1,112**	
	24 (46%)	371(33%)	**<0.001**
PROMIS-29 SCORES¥ (Mean, SD)	**(n=58)**	**(n=1,375)**	
Depression	48.7 (7.6)	53.5(8.8)	**<0.001**
Anxiety	58.9 (8.1)	60.4 (8.4)	0.182
Fatigue	53.3(9.4)	55.0 (10.8)	0.238
Sleep Disturbance	53.5(5.9)	53.4 (6.7)	0.911
Pain Interference	49.3 (8.4)	53.1(9.8)	**0.004**

*Employer no longer able to employ; cannot work due to suspected/confirmed COVID-19; cannot work due to lack of childcare, eldercare, sick family member; personal concerns about COVID-19
€Confirmed by nasopharyngeal PCR testing; Suspected if told by a healthcare provider of likely diagnosis.
¥ Compared to standard reference of general population
P-value threshold of <0.05 considered to be significant and indicated in bold

pregnancy status on January 1, 2020 or at the time of survey completion. T-tests and Chi-square tests were used when appropriate to compare pregnant and non-pregnant patients.

Results: 6,908 patients responded to our survey overall, of whom 1,510 were women aged 18 to 50 (22%). 61/1,510 (4%) were either pregnant on January 1, 2020 or pregnant at the time of completing the survey. Mean age of the 61 pregnant women was 36.1±4.9 years, 74% were white, 85% not Hispanic or Latino, and 88% were married/partnered ($p < 0.001$). Pregnant survey respondents were significantly younger, more likely to be married, have higher household income, and less likely to be Hispanic than non-pregnant patients **(Table 1)**. Although fewer pregnant women took biologics, DMARDs, or corticosteroids the differences were not significant. Nearly one-third of patients in both groups reported taking antimalarials in the previous 6 months. Both groups lived with an average of 2.3 other people, and a similar percent had confirmed or suspected COVID-19 (by positive nasopharyngeal PCR test or physician indicated) (8% and 11%). Among patients who were employed, significantly more pregnant patients indicated a high risk of COVDI-19 exposure at work. Depression and pain interference were significantly worse in non-pregnant patients based on PROMIS-29 scores, but not clinically significant**(Table 2)**. In the pregnancy group, 57% noted changes to prenatal OB/GYN care during the COVID-19 pandemic; in-person OB/GYN visits were rescheduled to telemedicine visits (28%) and some in-person OB/GYN visits were cancelled and not rescheduled (16%). By the time of survey completion, 22/61 pregnancies were complete, with a mean gestational age of 38.1±1weeks. Pregnancy outcomes included: 10 (45%) vaginal deliveries, 5 (23%) C-Sections, and 3 (14%) miscarriage/termination. 23% of women who

Table 3. Pregnancy Outcomes and Changes to Pre-Natal Care in 61Rheumatology Patients who Reported Pregnancy During the COVID-19 Pandemic	

Pregnancy Outcomes
• Total Pregnancies
• Pregnant at the time of survey completion
• No longer pregnant at the time of survey completion
  • Vaginal Delivery
  • C-Section
  • Miscarriage/termination
  • Reason pregnancy ended not specified
	
	61
	39
	22
	10 (45%)
	5 (23%)
	3 (14%)
	4 (18%)

Changes to Prenatal OB/GYN Care during the COVID-19 Pandemic (N, %) • Prenatal care unchanged • Regular in-person OB/GYN visits are rescheduled to telemedicine • In-person OB/GYN visits cancelled not rescheduled; • OB/GYN in-person visits only for urgent issues and procedures) • Other *	 20 (33%) 17 (28%) 18(29%) 12(20%)
COVID-19 Affected Delivery (N, %) Yes	**n=22** 5 (23%)
Effect of COVID-19 Pandemic on delivery (N, %) • Not permitted to have anyone (e.g. partner, family member, doula, midwife with me when I delivered) • Other **	**n=5** 1(5%) 4 (18%)
* Other changes to prenatal care: Changed OB/GYN due to visitor policy at hospital post-delivery; regular OB visits curbside and high-risk visits in-person with extra precautions; some appointments in-person while some were via telemedicine. ** Other reasons cited: No visitors; partner had to leave soon after delivery, pediatrician stopped taking new patients and had to switch to new practice.	

delivered stated the pandemic affected their deliveries, with the most frequent reason being no visitors permitted in the hospital or spouses needing to depart shortly after delivery **(Table 3)**.

Conclusion: During the peak of the COVID-19 pandemic in New York City, pregnant rheumatology patients had unique experiences that influenced their prenatal OB/GYN care and pregnancy experience. Future longitudinal studies will investigate the underlying risk factors and impact of the COVID-19 pandemic on pregnancy outcomes in rheumatic disease patients.

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Abstract Number: 1784

Roles and Perspectives of Partners of Women with Rheumatoid Arthritis on Reproductive Decision Making: A Constructivist Grounded Theory Study

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Background/Purpose: Partners of women with rheumatoid arthritis (RA) often take on caregiving roles given the debilitating nature of RA. No research to date has explored partners' roles with respect to reproductive decision-making. Our objective was to explore the perspectives, attitudes, and experiences of partners of women with RA regarding reproductive decisions around family building.

Methods: Study Design: We conducted a qualitative research study involving semi-structured interviews. **Participants:** Individuals were eligible if they were 18 years or older, had a partner with RA who participated in our related study on how women with RA make family-building decisions, and were able to communicate in English. We define 'partners' as individuals within an intimate relationship. **Data gathering:** We conducted semi-structured telephone and video conference interviews lasting 30 to 60 minutes. Each interview followed an intensive approach characterized by use of open-ended questions. **Analysis:** We applied a constructivist grounded theory approach, which involved initial line-by-line coding, a strategy which promotes conceptualization of emerging themes. Afterwards we conducted focused coding which led to development of themes as indicated by theoretical saturation.

Results: We interviewed 9 partners of women with RA. All participants identified as male with a median age of 34 years. Overall, 44% had at least one child with a woman with RA while the rest had not had children with a women with RA. Additionally, 77% were considering conceiving children with their significant other with RA. Emerging themes from our analysis indicate that couples discuss reproductive options early and throughout their relationship and share the decisions for building a family. In an effort to aid their significant other, partners also discussed methods of providing support. Partners described impacts on their mental health and well-being related to additional stressors of supporting their significant other and making reproductive decisions, as well as expressing a desire for childcare support from extended family. After having children with women with RA, partners indicated a change in perspective towards pregnancy and RA management, often resulting in the decision to have fewer children. **Table 1** shows themes and representative quotes.

Conclusion: Our findings demonstrate the far-reaching impacts of RA and reproductive decision-making on the partners of women with RA. Participants expressed taking part in shared decision-making with their partner, concern for their significant others' physical health during pregnancy, and described impacts on their own mental health. Overall, our findings highlight the need for comprehensive supports for *both* women with RA and their partners throughout family building and pregnancy. Healthcare providers can identify opportunities for intervention or care adaptation that involves women with RA and their partners minimizing stress and the negative impacts on the family.

Theme 1: Discussing reproductive decisions early and throughout the relationship
'When we first started our relationship, she was very clear and up front about it at the beginning. It was almost just like a, it was just a hurdle.' (Partner 5)
'It's been like an ongoing sort of conversation over the last few years, […] it's been like a few discussions for short periods of time over a long period of time.' (Partner 4)
Theme 2: Sharing family building decisions
'I think it's been very much a mutual effort. I think it's a shared load, so we have explored IVF, we've explored egg donation, we've gone to the clinic together, I've done all the testing.' (Partner 3)
'When we were thinking about having another child and we actually kind of decided not to because of the requirements again to go off medication for family planning.' (Partner 7)
Theme 3: Providing support to partner with RA
'I've never had to go through that so I, the only thing I can do is just be supportive and try to be you know like just as pleasant as I can about the subject and support her whatever way she needs.' (Partner 5)
'At the end of the day it's not my decision a lot of the times, right, and it's more so just being supportive. Like I can give my opinion and say where what I believe is right but at the end of the day it's really her decision.' (Partner 4)
Theme 4: impacting mental health and well-being
'It's definitely had an impact for sure, just a lot of, definitely a lot of added stress […] how she's feeling today physically and mentally. Is she gonna have a flare?' (Partner 9)
'It's pretty difficult to see your partner go through that kind of level of kind of pain and angst […] that's obviously hard. And then again, when you kind of paint a picture in your head of like I said how things you think are gonna go and then they don't really go that way, it's also very difficult.' (Partner 7)
Theme 5: Seeking childcare support from extended family
'Which side of the family we'd get more support from because we need to be realistic and say that look, if she's going through pain or I'm going through pain, you know somebody needs to look after that child.' (Partner 2)
'Basically help taking care of the kids sort of thing because I guess with two kids and if I'm basically a caretaker to two children and potentially a caretaker to my wife, that's a bit of a workload.' (Partner 6)
Theme 6: Changing perspective towards pregnancy and RA management
'So definitely both wanted more kids but just looking at kind of reality and the risk factors, it wasn't worth the risk to either of us to keep having children.' (Partner 6)
'"I see you more mortal than myself after the pregnancy," because she nearly died three times […]I said, "for the first time ever, the reality has hit to me where your life is more fragile than mine."' (Partner 8)

Themes and representative quotes

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Abstract Number: 1785

Use of Contraceptive Methods in Mexican Women with Rheumatic Diseases

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Reproductive Issues in Rheumatic Disorders Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The importance of safe and effective contraception for women with rheumatic diseases has been increasing. Several studies have demonstrated that carefully planned pregnancies are related with better outcomes making the use of contraceptive methods (CM) more significant. The objective is to describe the use of methods of contraception among Rheumatoid Arthritis (RA) and Systemic Lupus Erythematosus (SLE).

Methods: A Cross-sectional study, where women aged 18-45 followed in our outpatient clinic of reproductive health, pregnancy and rheumatic diseases (CEER), at Monterrey, Mexico, were questioned about the use of CM. Sociodemographic data was collected from the medical record. CM were classified as Ineffective (10-25% pregnant each year), effective (6-9% pregnant each year) and highly effective (< 1% pregnant each year). Methotrexate, Mycophenolate, Cyclophosphamide, Thalidomide and Leflunomide were considered as teratogenic drugs. The statistical analysis was performed using SPSS 24.0. A $p < 0.05$ was taken to indicate statistical significance.

Results: A total of 91 patients were included, 35 (38.5%) SLE patients with a median age of 30 years (22-39) and 56 (61.5%) RA patients with a median age of 34.5 years (27.25-40). From the total population, 58 (63.7%) reported the use of teratogenic drugs, with a higher use in RA patients ($p < .001$). Socio-demographic characteristics are listed in Table 1.

	RA (N=56)	SLE (N=35)	P
AGE, YEARS, MEDIAN (IQR)	34.5 (27.25 - 40)	30 (22-39)	
DISEASE DURATION, YEARS, MEDIAN (IQR)	3.5 (1.2 - 7.7)	4 (1-7)	
ONSET OF SEXUAL ACTIVITY,N (%)	46 (82.1)	24 (68.6)	.135
ONSET OF SEXUAL ACTIVITY AGE, MEDIAN (IQR)	18 (17-20)	14 (17-20)	
SEXUALLY ACTIVE, N (%)*	34 (60.7)	18 (51.4)	.384
USE OF TERATOGENIC DRUGS, N (%)	44 (78.6%)	14 (40%)	<.001

Table 1. Socio-demographic characteristics. RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus. *Sexual activity in the last month.

		GRADE OF EFFECTIVENESS		
	Contraceptive counseling n (%)	Ineffective n (%)	Effective n (%)	Highly effective n (%)
RA (n= 46)	30 (65.2)	12 (40)	1 (3.3)	17 (56.6)
SLE (n= 24)	19 (79.1)	9 (47.3)	1 (5.2)	9 (47.3)
Total n= 70*	49 (70)	21 (42)	2 (4)	26 (53)

Table 2. Methods according to effectiveness in patients who received contraception counseling. RA: Rheumatoid Arthritis; SLE: Systemic Lupus Erythematosus. * Total of patients that have started sexual activity.

Graphs 1. Use of contraceptive methods among patients who had started sexual activity. This graphic shows the percentage (%) of contraceptive methods used by Rheumatoid Arthritis (RA) n= 46 and Systemic Lupus Erythematosus (SLE) n=24 patients, which are categorized by the grade of effectiveness. IUD: Intrauterine Device. Only were included patients that had started sexual activity.

Among the patients that had started sexual activity (SLE n=24, RA n=46), highly effective methods were the most frequent, used by a total of 39 (55.7%) women. The most common CM in RA was tubal ligation reported by 20 (43.5%) patients, nevertheless 9 (37.5%) SLE patients mentioned that they did not used any method. Graphs 1.

From the group who started sexual activity, 49 (70%) patients received contraceptive counseling, however, 21 (42%) patients were using ineffective CM. Table 2.

Conclusion: Only 70% of the women with rheumatic diseases received a contraceptive counseling and despite this 42% continued using an ineffective method. It is necessary to promote the counseling and use of contraception and provide a multidisciplinary support among this high-risk population.

Disclosure: J. Diaz-Angulo, None; **C. Skinner-Taylor**, None; **L. Perez-Barbosa**, None; **E. Barriga-Maldonado**, None; **M. Valdovinos**, None; **R. Pineda-Sic**, None; **J. Cardenas-de la Garza**, None; **G. Figueroa-Parra**, None; **J. Riega-Torres**, None; **D. Galarza-Delgado**, None.

Abstract Number: 1786

Reproductive Health Outcomes in Women with RA and PsA

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Reproductive Issues in Rheumatic Disorders Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: RA improves in pregnancy and flares postpartum. Active disease causes adverse fetal outcomes. In PsA, the data is less clear as many of these studies are retrospective, lack validated disease activity scores and predate biologic use. We sought to compare disease activity plus maternal and fetal outcomes between RA and PsA.

	RA(n=23)	PsA (n=11)
Age		
Median (range)	36 (27-43)	36 (27-39)
Medications		
Prednisolone	5 (22%)	1(9%)
csDMARD	7 (30%)	2(18%)
NSAIDs	1 (4%)	1 (9%)
TNFi*	4 (17%)	8 (73%)
Non-TNFi biologic	3 (13%)	2 (18%)
Aspirin	6 (26%)	2 (18%)

*p=0.001, Mann Whitney U test

Table 1. Patient characteristics

	Pregnancy planning		Pregnant		Postpartum	
	RA	PsA	RA	PsA	RA	PsA
VAS, mm	40 (20-50)	35 (20-50)	30 (0-90)	30 (0-100)	30 (20-70)	50 (0-100)
28 TJC	0 (0-12)	6.5 (1-12)	0 (0-10)	0 (0-2)	2 (0-8)	1 (0-2)
28 SJC	0 (0-12)	1.5 (1-12)	0 (0-10)	0 (0-2)	1 (0-8)	1 (0-2)
CRP	7.75 (3-13)	1.85 (2-2)	4.35 (1-14)	4.75 (3-14)	14 (3-299)	1.5 (1-2)
DAS28CRP-3	3.52 (1.65-5.40)	3.31 (2.48-4.14)	1.89 (1.31-5.13)	1.86 (1.65-3.17)	3.21 (1.69-5.01)	2.16 (1.59-2.73)

Data presented as median (range)

Table 2. Disease activity

	RA (n=15)	PsA (n=5)
Method of delivery		
Spontaneous vaginal delivery	6 (40%)	4 (80%)
Assisted vaginal delivery	3 (20%)	0
Emergency Caesarean section	4 (27%)	1 (20%)
Elective Caesarean section	2 (13%)	0
Birth outcome		
Female child	8 (57%)	4 (80%)
Birthweight, kg[1]	3.49 (2.94-3.91)	3.18 (1.02-4.02)
Gestational age, weeks	40.5 (37.4-41.6)	39.0 (25.6-40.4)
Preterm birth	0	1 (20%)
5 Minute APGAR score	9 (9-9)	8.5 (7-9)
Maternal adverse outcome	5 (33%)	1 (20%)
Caesarean section wound infection	2 (14%)	1 (20%)
3rd or 4th degree tear[2]	3 (21%)	0
Fetal adverse outcomes		
Neonatal ICU admission	0	1 (20%)
Foetal ventilator requirement	0	1 (20%)
Foetal jaundice	1 (7%)	1 (20%)
Foetal anemia	0	1 (20%)
Foetal hypoglycemia	1 (7%)	0

1). Nationally=3.49kg 2). General population rate 3%

Table 3. Maternal and fetal outcomes

Methods: This is a prospective study of women attending our multidisciplinary combined rheumatology obstetrics service. Patients were seen pre-pregnancy, once per trimester and at 3 months postpartum. DAS28CRP-3 was used to assess disease activity as this is validated in pregnancy. Between group differences were analyzed using Pearson Chi square, Fischer's exact test or Mann-Whitney U test as appropriate.

Results: 34 patients were included in the study (Table 1). Overall, disease activity scores decreased during pregnancy and increased postpartum (Table 2). Maternal and fetal outcomes are shown in Table 3.

Conclusion: In this small study, disease activity generally improved in pregnancy and flared postpartum. There were adverse maternal outcomes in 33% of RA and 20% of PsA patients. Adverse fetal outcomes were seen in the offspring of 7% of RA and 20% of PsA patients. Compared to the general Irish population, birthweights were similar, maternal age was older and rates of Caesarean section were higher.

Disclosure: K. Murray, None; **L. Moore**, None; **P. Gallagher**, None; **Y. Alammari**, None; **C. O'Brien**, None; **C. Brophy**, None; **F. McAuliffe**, None; **D. Veale**, AbbVie, 2, Health Beacon, 1, Janssen, 2, 8, Pfizer, 2, 5, 8, Novartis, 2, 5, 8, UCB, 2, 5.

Abstract Number: 1787

Differences in Chromatin Architecture Between Treatment Naïve Pediatric and Adult Lupus Patients

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is possibly triggered by gene-environment interactions. We showed most of the SLE haplotypes encompass genomic regions enriched for epigenetic marks associated with enhancer function in immune cells, suggesting altered gene regulation. Data remain scarce on how epigenetic variance contributes to disease risk in pediatric SLE (pSLE). Our objectives were to identify differences in chromatin architecture in treatment-naïve pSLE compared to healthy children (HC) and to compare these differences to epigenetic data from treatment-naïve adult SLE patients.

Methods: We used the assay for transposase-accessible chromatin-sequencing (ATACseq) in 8 treatment-naïve pSLE patients and 5 HC to investigate whether regions of open chromatin unique to pSLE patients demonstrate enrichment for transcriptional regulators, using standard computational approaches and a false discovery rate of < 0.05. We used similar methodology to interrogate adult SLE data from a public GEO set to compare our pSLE findings.

Results: The mean age of onset was 13.75 (range 7-17) years in pSLE, and mean SLEDAI was 12.8 (range 6-24). We identified 245 differentially accessible regions (DAR) around peaks unique to pSLE, of which over 50% appear to be more accessible in pSLE than HC. Of the unique peaks, 46-60% are located more than 100kb from the nearest transcription start site (nTSS), implying many transcription factors may be acting on distal enhancers to regulate transcription. Variant calling within DAR found 3864 genes belonging to 129 different biologic processes (BP), most

notably cellular activation in immune response, regulation of proliferation, and responses to external stimuli. Similar results were seen in adult SLE data: over 50% of peaks in adult SLE are located distal to nTSS, and 3263 genes within DAR belong to 135 different BP, including cellular activation in immune response and complement activation.

Conclusion: We demonstrate an epigenetically-distinct profile in pSLE B cells when compared to HC, indicating pSLE B cells are predisposed for disease development. Pathways of significance analyses identified immunologic pathways important in the pro-inflammatory response in pSLE and adult SLE patients. Thus, increased chromatin accessibility in genomic regions controlling activation of the inflammatory and immune responses suggest transcriptional dysregulation of key players in immune cell activation plays an important role in pathogenesis of SLE.

Disclosure: J. Hui-Yuen, None; **F. Jenkins**, None; **K. Jiang**, None; **S. Malkiel**, None; **B. Diamond**, None; **J. Jarvis**, None.

Abstract Number: 1788

Assessment of the Impact of Interferon Levels on Cognitive Dysfunction in Patients with SLE

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Cognitive impairment (CI) is among the earliest and the most prevalent manifestations of SLE. Previous studies have demonstrated that the increased levels of interferon (IFN)-induced gene expression in SLE are positively correlated with SLE disease activity and severity. The aim of this study is to examine the relationship between IFN levels and cognition as measured by the American College of Rheumatology neuropsychological battery (ACR-NB).

Methods: 301 consecutive consenting SLE patients (18 – 65 years old) attending a single center between Aug 2017 and Jan 2019 were enrolled in the study. IFN-induced gene expression was quantified by nanoString on RNA isolated from whole peripheral blood archive in TEMPUS tubes. The $\log_2$ transformed normalized levels of five IFN-induced genes were summed to produce the IFN5 score. Cognition was measured using the ACR-NB (19 tests) representing manual dexterity, processing speed, language, simple attention, memory and executive function domains. Using age and gender stratified normative data, patients were classified on the ACR NB as having CI if a z-score of ≤-1.5 was observed in ≥ 2 domains or z ≤-2.0 in ≥1 domain. Principal Component Analysis (PCA) was used to explore the relationships among cognitive tests, interferon levels and SLE disease duration.

Figure 1. Distribution of individual participants in the cohort classified by (A) presence or absence of cognitive impairment, (B) interferon levels

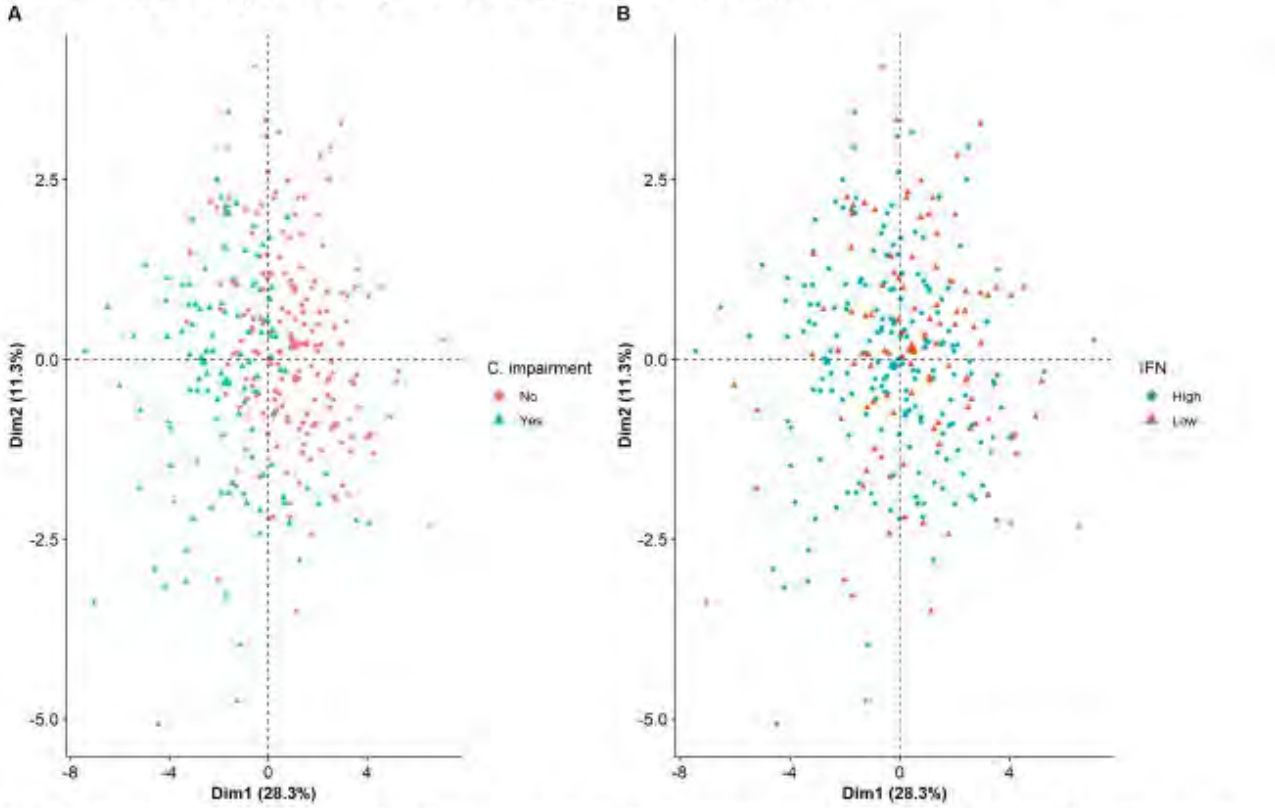

Figure 1. Axis x represents the first cognitive dimension (explaining 28.3% of the variance) and axis y represents the second dimension. Distribution of individual participants in the cohort classified by presence or absence of cognitive impairment (A), and interferon level (B). CI was operationalized as a z-score of ≤-1.5 on ≥2 domains or z ≤-2.0 on ≥1 domain.

In PCA, the variance-covariance matrix of the cognitive tests was decomposed into a series of eigenvectors with corresponding eigenvalues. Each eigenvalue constitutes the variance of the linear combination of all test scores weighted by values contained in the corresponding eigenvector. This method reduces the dimensionality of the experimental data and to summarize the association between the variables in the data. To preserve the largest portion of the total variance explained by PCA, we only retained the first two components.

Moreover, we included IFN levels and SLE disease duration as supplementary variables.

Results: Of 301 patients, 89.0% were women, mean age 40.9 ± 12.1 and mean disease duration 14 ± 10.1 years at study entry. PCA cognitive tests loaded onto 2 dimensions explained 39.6% of the variance in neuropsychological performance. The 1st dimension (explained 28.3% of the total variance) was correlated mainly with more complex cognitive tests and primarily explained CI status of participants. The second dimension (11.3%) was mainly explained by measures of simple information processing or motor speed.

Fig 1a shows the patients' component scores coloured by ACR-NB binary definition for CI and non-CI. This 1st dimension splits CI and non-CI patients at baseline. No clustering was observed when participants were categorized based on interferon level (Fig. 1b). No relationship was found between the cognitive tests and IFN levels or disease duration (Fig. 2). A weak negative correlation was also observed between interferon levels and RCFT and hand tapping, though this was not significant (Fig. 2).

Figure 2: Relationship between Interferon levels and neuropsychological tests

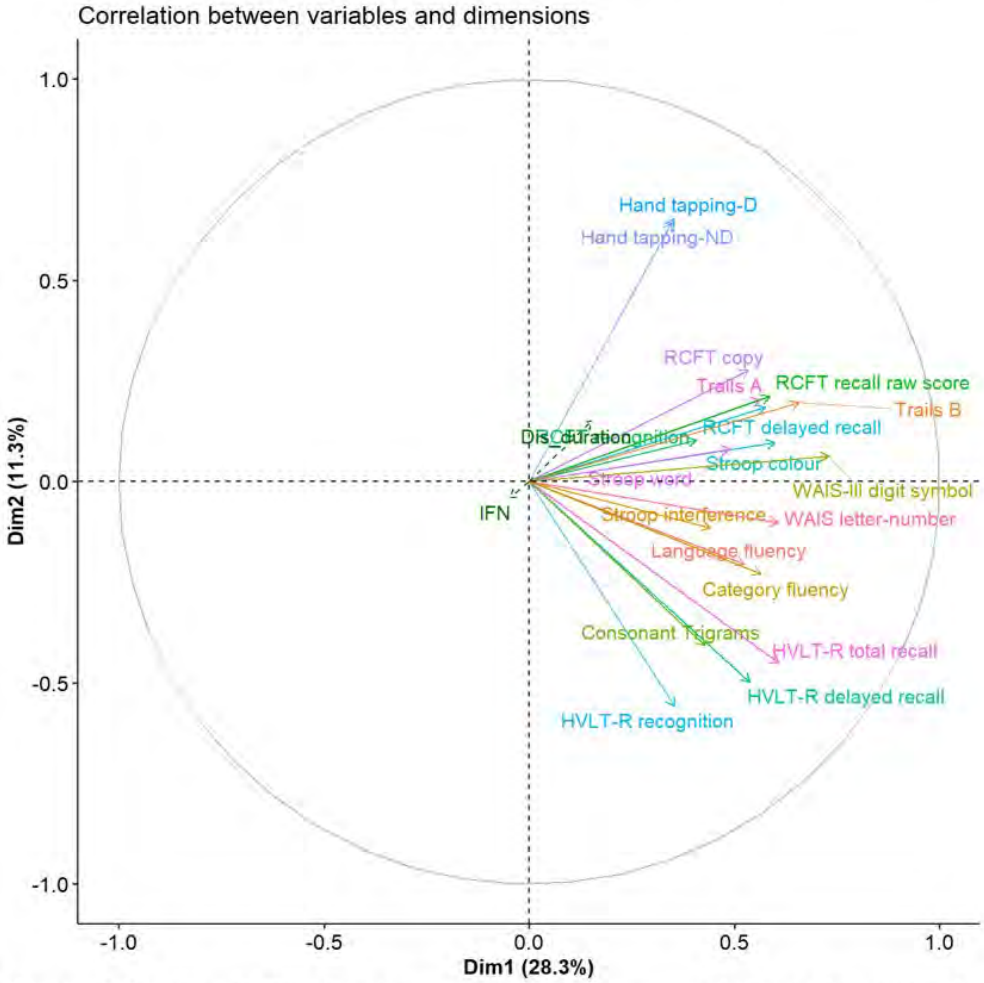

Figure 2. Results of PCA showing representative neuropsychological tests in relation to the two cognitive dimensions. Axis x represents the first dimension explaining 28.5% of the variance in cognition and axis y represents the second dimension. The length of each arrow represents the strength of the relationship between the variable it represents, and the cognitive dimensions found in our PCA. Variables whose representative arrows are close in proximity are more strongly related. Moreover, we observe that IFN was not related neither with the 1st dimension nor the second one.

Conclusion: This study assessed the relationship between IFN levels and cognitive function in patients with SLE. Using PCA analysis, we found no association between IFN levels and any cognitive tests, even after considering factors such as SLE disease duration.

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Abstract Number: 1789

Time to Renal Insufficiency Based on 25(OH)-Vitamin D Levels

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Vitamin D is correctly classified as a sterol-hormone rather than a vitamin (Semin Nephrol 1986;6:4-20). It has multiple immunomodulatory effects, as well as cardiovascular and hematologic benefits (such as reduction in thrombosis). In SLE patients who are vitamin D insufficient/deficient, vitamin D supplementation clearly improves proteinuria (Arthritis Rheum 65:1865-71, 2013) with a plateau at a 25(OH)-vitamin D level of 40 ng/mL. In fact, vitamin D helps proteinuria in diverse renal diseases (Int J Environ Res Public Health 2018;15:1773).

Methods: The SLE patients met revised ACR or SLICC classification criteria. This analysis included 73,221 person months (6,102 person years) from 1,220 patients (93% female, 38% African-American, 52% Caucasian). 48.5% were

Subgroup	Renal Insuff. events	Person-years of follow up	Rate of events per 1000 person years	Rate Ratio (95% CI)	p-value
All	147	6102	24.1		
Sex					
Female	130	5671	22.9	1.00 (Ref)	
Male	17	431	39.5	1.72 (1.04, 2.86)	0.0351
Ethnicity					
Caucasian	63	3228	19.5	1.00 (Ref)	
African American	68	2324	29.3	1.5 (1.06, 2.11)	0.0204
Other	16	550	29.1	1.49 (0.86, 2.58)	0.1534
Age at person month					
<30	16	699	22.9	1.00 (Ref)	
30-<40	28	1513	18.5	0.81 (0.44, 1.49)	0.497
>=40	103	3890	26.5	1.16 (0.68, 1.96)	0.5881
Smoking					
Never	99	4170	23.7	1.00 (Ref)	
Ever	47	1900	24.7	1.04 (0.74, 1.48)	0.8145
BMI					
<20	9	471	19.1	1.31 (0.62, 2.76)	0.4759
20-<25	30	2058	14.6	1.00 (Ref)	
25-<30	45	1656	27.2	1.87 (1.18, 2.96)	0.0082
30-<35	34	991	34.3	2.36 (1.44, 3.85)	0.0006
>=35	29	924	31.4	2.16 (1.29, 3.59)	0.0032
Education					
<=12	45	1672	26.9	1.00 (Ref)	
>12	100	4397	22.7	0.84 (0.59, 1.2)	0.348
Income					
<$30,000	37	1397	26.5	1.00 (Ref)	
$30,000-$65,000	55	1911	28.8	1.09 (0.72, 1.65)	0.6963
>=$65,000	51	2713	18.8	0.71 (0.46, 1.08)	0.1119

Table 1. Rates of renal insufficiency events by demographics and patients characteristics

Subgroup	events	Person-years of follow up	Rate of events per 1000 person years	rate ratio (95% CI)	p-value	Adjusted rate ratio[1] (95% CI)	Adjusted p-value[1]
First vitamin D level							
<10	13	349	37.3	1.71 (0.9, 3.26)	0.1008	1.7 (0.88, 3.3)	0.1157
10-<20	36	1222	29.5	1.35 (0.84, 2.17)	0.2106	1.34 (0.83, 2.18)	0.235
20-<30	36	1496	24.1	1.1 (0.69, 1.77)	0.6807	1.13 (0.7, 1.82)	0.6216
30-<40	33	1514	21.8	1.00 (ref)		1.00 (ref)	
40-<50	15	976	15.4	0.71 (0.38, 1.3)	0.2623	0.7 (0.38, 1.3)	0.2575
50-<60	6	308	19.5	0.89 (0.37, 2.13)	0.7997	1.14 (0.47, 2.76)	0.7635
>=60	8	237	33.7	1.55 (0.71, 3.36)	0.2676	1.65 (0.76, 3.57)	0.2074
Most recent vitamin D level							
<10	4	72	55.9	2.78 (0.98, 7.85)	0.0544	2.97 (1.04, 8.48)	0.0415
10-<20	17	441	38.5	1.91 (1.06, 3.43)	0.0307	2.02 (1.11, 3.65)	0.0204
20-<30	27	1120	24.1	1.19 (0.72, 1.99)	0.4967	1.27 (0.76, 2.12)	0.352
30-<40	33	1632	20.2	1.00 (ref)		1.00 (ref)	
40-<50	35	1396	25.1	1.24 (0.77, 2)	0.3751	1.2 (0.74, 1.93)	0.4568
50-<60	19	826	23.0	1.14 (0.65, 2)	0.6549	1.07 (0.61, 1.9)	0.8028
>=60	12	615	19.5	0.97 (0.5, 1.87)	0.9175	0.92 (0.47, 1.79)	0.8084
Mean vitamin D level							
<10	18	414	43.4	1.71 (0.53, 5.51)	0.3684	1.75 (0.54, 5.69)	0.3508
10-<20	24	1162	20.6	1.72 (1, 2.97)	0.0515	1.81 (1.04, 3.16)	0.0367
20-<30	46	1818	25.3	0.82 (0.5, 1.34)	0.4188	0.86 (0.52, 1.41)	0.5407
30-<40	35	1636	21.4	1.00 (ref)		1.00 (ref)	
40-<50	13	771	16.9	0.84 (0.54, 1.31)	0.4532	0.81 (0.52, 1.26)	0.3526
50-<60	8	231	34.7	0.67 (0.36, 1.23)	0.1955	0.62 (0.33, 1.14)	0.1251
>=60	18	414	43.4	1.37 (0.65, 2.91)	0.4113	1.4 (0.66, 2.98)	0.3811
Rate ratios and p-values were adjusted for age, sex, race, BMI							

Table 2. Rates of renal insufficiency events by 25(OH)-vitamin D levels

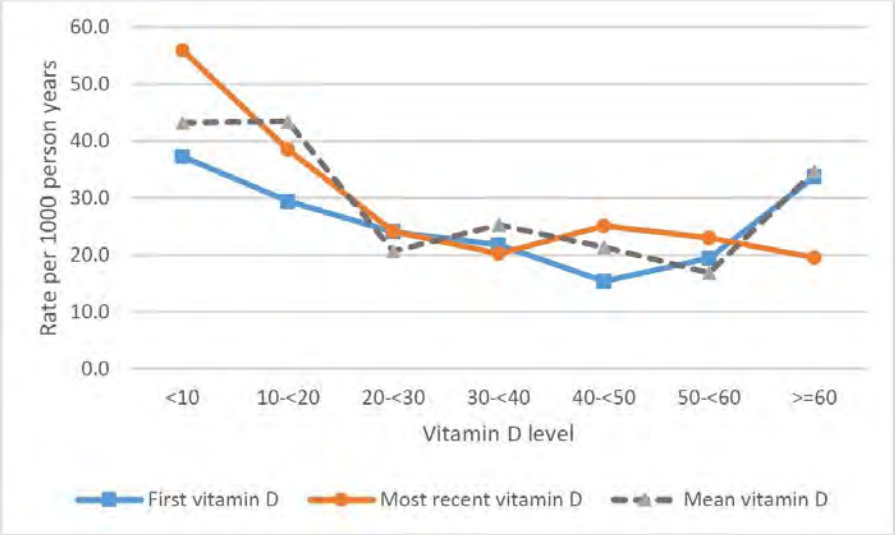

Figure 1. Rates of renal insufficiency by 25(OH)-vitamin D levels

diagnosed at age < 30 years. Vitamin D levels were measured regularly starting mid-2009. Renal insufficiency was defined as creatinine (CR) ≥1.5 mg/dl or < 50% function. For this analysis, a dataset with one record for each month of follow up for each person was constructed. Mean prior vitamin D levels were calculated over all previous months. Patients were followed from the first measure of 25(OH)-vitamin D level to first incident of renal insufficiency or their

last recorded visit. To calculate the rate of renal insufficiency in each demographic or clinical subgroup, the number of renal insufficiency events was divided by the number of person months at risk and then converted to rates per 1,000 person years. Pooled logistic regression was used to assess the relationship between vitamin D blood levels and rates of renal insufficiency.

Results: Table 1 shows the association between patient characteristics and the rate of renal insufficiency. Renal insufficiency was more common in males, African-Americans and obese patients. Table 2 shows the association between Vitamin D level tertiles and the rate of renal insufficiency. There was a significantly elevated risk of renal insufficiency among those in the extremely low levels of 25(OH)-vitamin D (< 20 ng/mL). Figure 1 shows the trend of rates of renal insufficiency by vitamin D levels. The effect of 25(OH)-vitamin D < 20 ng/mL was clearly shown regardless if we used first, most recent or mean level of 25(OH)-vitamin D. Results were adjusted for race, age, sex and BMI.

Conclusion: The benefit of vitamin D supplementation to reduce proteinuria in SLE brought the benefit of this sterol-hormone as an immunomodulatory to the forefront. Now our data show that very low 25(OH)-vitamin D levels < 20 ng/mL are associated with renal insufficiency (adjusted for ethnicity, as African-Americans have lower levels).

Disclosure: M. Petri, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmithKline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5; **J. Li**, None; **D. Goldman**, None.

Abstract Number: 1790

Association of Telomere Length and the Systemic Lupus International Collaborating Clinics Frailty Index (SLICC-FI) in Long Standing Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Frailty, an emerging concept in SLE, represents an individual's ability to respond to physiologic stress. The first lupus-specific frailty index, the SLICC-FI, was recently shown to predict mortality and damage accrual in the SLICC disease inception cohort. Multiple studies confirm that telomere length is significantly shorter in patients with SLE, however there is conflicting evidence regarding the role of telomeres in mediating frailty in the geriatric population. The objectives of this study were 1) to assess if frail patients with SLE have shorter telomere length compared to non-frail patients and 2) to examine the relationship between telomere length and changes in frailty over time.

Table 1: Patient Characteristics of patients in SOLVABLE cohort

Patient Characteristics (N=131) *	Mean (SD) or n (%)
Age (yrs), mean (SD)	46.28 (10.16)
Race, n (%)	
White	80 (61.07%)
African American	34 (25.95%)
Hispanic	9 (6.87%)
Asian	8 (6.11%)
Education, n (%)	
Less than high school diploma	5 (3.82%)
High school diploma	35 (17.71%)
College graduate	56 (42.75%)
Advanced degree	36 (26.72%)
Body Mass Index (kg/m^2), mean (SD)	28.20 (7.74)
SLE Characteristics	
Age at diagnosis (yrs), mean (SD)	30.78 (10.90)
Disease duration (yrs), mean (SD)	15.51 (8.84)
SLEDAI-2K score, mean (SD)	3.87 (4.12)
SLICC Damage Index score, mean (SD)	2.24 (2.13)
Medication Use	
Corticosteroids, n (%)	49 (37.40%)
Plaquenil, n (%)	106 (80.92%)
Immunosuppressants, n (%)	54 (41.22%)

* At SOLVABLE 3-year follow up visit

Methods: Data was analyzed from 131 of 185 adult women who met the following criteria: 1) 1997 revised ACR criteria for definite lupus, 2) enrolled in the Study of Lupus Vascular and Bone Long-Term Endpoints (SOLVABLE) cohort consisting of adult women from the Chicago Lupus Database and 3) telomere length measured from whole blood by PCR at 3-year follow up visit, which is the baseline time point for this study. Adapted SLICC-FI scores consisting of 46 health deficits were calculated at baseline (3-year follow-up visit) and 2 years after baseline (5-year follow-up visit). Using baseline SLICC-FI scores, patients were categorized as frail (SLICC-FI >0.21), least fit (0.10< SLICC-FI≤0.21) or relatively fit (SLICC-FI ≤0.10). We used median quantile regression models to calculate unadjusted and age-adjusted median telomere length (95% confidence limit [CI]) among all participants and by the three frailty categories. Median quantile regression was used to examine the association of baseline telomere length with subsequent change in frailty.

Results: At baseline, 131 patients had mean (SD) age of 46.28 (10.16) years, mean disease duration of 15.51 (8.84) years, and mean (SD) SLICC-Damage Index score of 2.24 (2.13). Mean (SD) SLICC-FI score was 0.17 (0.09), with 29.77%, 44.27%, and 25.95% of patients categorized as frail, least fit, and relatively fit respectively. Frail patients had the shortest median telomere length of 3.25 (95% CI 2.43, 4.27) kb, while least fit and relatively fit patients had telomere length of 3.51 (95% CI 2.83, 4.23) kb and 3.35 (95% CI 2.77, 4.97) kb respectively; these differences were

Table 2: Median and 95% Confidence Limits of Telomere Length Stratified by Frailty Status in SOLVABLE cohort

Telomere Length (kb)	Overall	Frailty Status			P value*
		Relatively Fit (SLICC-FI ≤ 0.10)	Least Fit (0.10<SLICC-FI ≤ 0.21)	Frail (SLICC-FI > 0.21)	
	Median (95% Confidence Limits) N=131	Median (95% Confidence Limits) N=34	Median (95% Confidence Limits) N=58	Median (95% Confidence Limits) N=39	
Unadjusted	3.35 (2.76, 3.95)	3.35 (2.77, 4.97)	3.51 (2.83, 4.23)	3.25 (2.43, 4.27)	0.94
Age-adjusted (centered at mean, 46.28 years)	3.32 (3.07, 3.75)	3.21 (2.79, 4.87)	3.52 (2.70, 4.30)	3.19 (2.40, 4.26)	0.88

* P-value from Wald test comparing median telomere length by frailty status.

not statistically significant (p=0.94). The results were similar after adjusting for baseline age. Baseline telomere length was not associated with median of subsequent change in frailty score (coefficient = 0.0002, 95% CI -0.004, 0.003).

Conclusion: Cross-sectionally, there was not a statistically significant association between telomere length and frailty status. Telomere length was not associated with subsequent change in frailty score in our study, though this may be limited by short follow up time and the small sample size. Further studies are needed to determine the predictive value of telomere length as a biomarker of frailty in lupus patients.

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Abstract Number: 1791

Renal Tubular Complement C9 Deposition Is Associated with Renal Tubular Damage and Fibrosis in Lupus Nephritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside

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Session Time: 9:00AM–11:00AM

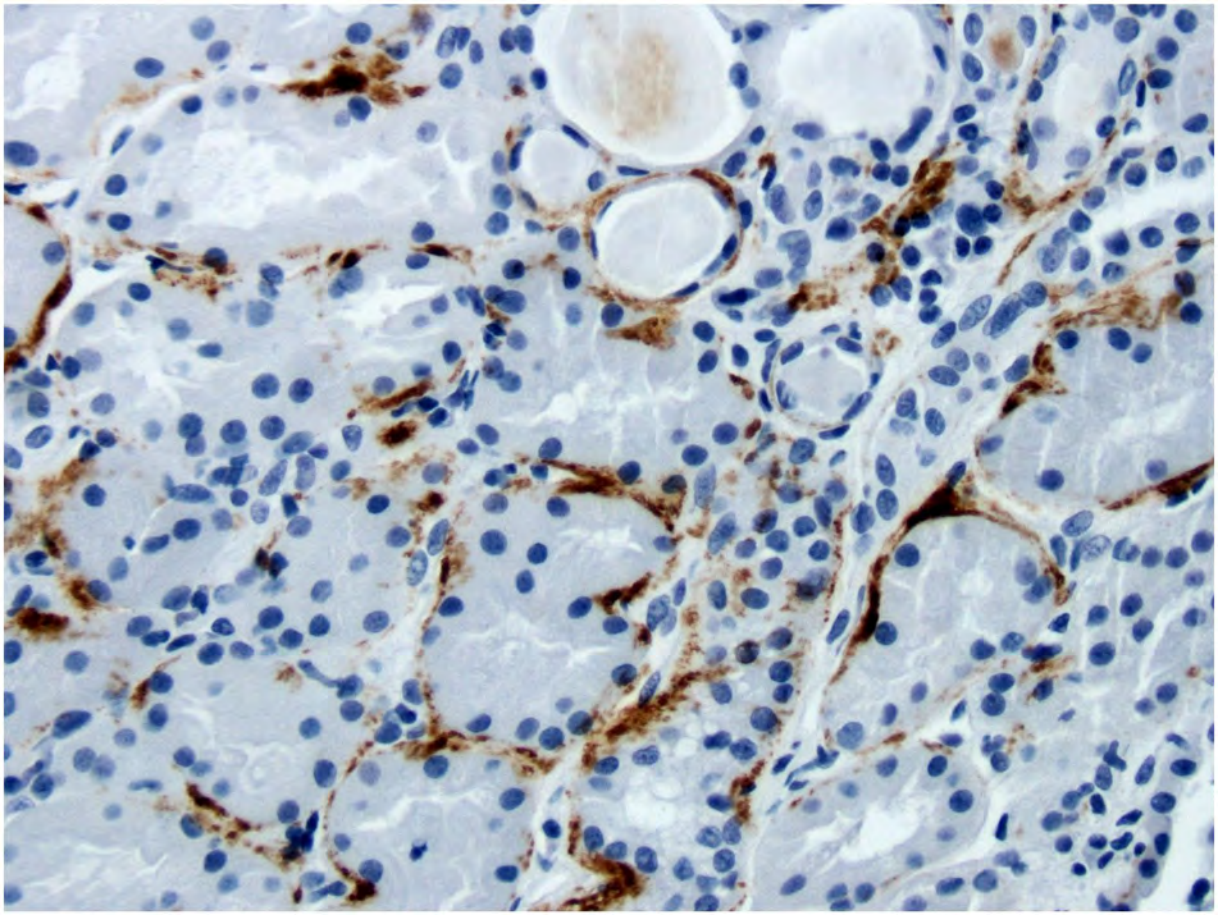
TABLE: Comparisons of Tubular C9+ and C9- Biopsies

	Positive for Tubular C9 (n = 7)	Negative for Tubular C9 (n = 23)	P- Value
Clinical Parameters			
Age, median (IQR), years	36 (31, 56)	27 (21, 39)	0.20
Male sex, n (%)	2 (28.6%)	4 (17.4%)	0.60
Hispanic, n (%)	4 (57.1%)	7 (30.4%)	0.37
eGFR, median (IQR), mL/min/1.73 m^2	57.9 (16.1-139.6)	118.2 (95.2-13.0)	0.17
Creatinine, median (IQR), mg/dL	1.6 (0.5-3)	0.7 (0.6-0.8)	0.23
Urine protein, median (IQR), g/24hr at biopsy	6.2 (3.3- 13.1)	2.4 (1.3-4.6)	<0.01
Urine protein, median (IQR), g/24hr at 6 months	1.08 (1.03-8.25)	0.68 (0.21-2.12)	0.06
Albumin, mean ± SD, g/dL	2.5 ± 0.6	3.1 ± 0.7	0.05
Renal Biopsy Light Microscopy			
Proliferative or mixed ISN/RPS class (3, 4, 3+5, 4+5), n (%)	6 (85.7%)	17 (73.9%)	>0.99
Moderate NIH Chronicity Index (score 4-7), n (%)	3 (42.9%)	2 (8.7%)	0.07
Moderate NIH Activity Index (score 6-14), n (%)	2 (28.6%)	10 (43.5%)	0.67
> 20% Interstitial fibrosis, n (%),	3 (42.9%)	0 (0%)	0.01
> 10% Global glomerulosclerosis, n (%)	5 (71.3%)	5 (21.7%)	0.03
Number of crescents	1 (0-2)	0 (0-2)	0.82
C9 deposition, non-tubular			
Glomerular (score >0), n (%)	3 (42.9%)	10 (43.5%)	>0.99
Arterioles/arteries (score >0), n (%)	6 (85.7%)	12 (52.2%)	0.19

Background/Purpose: Tubulointerstitial damage in lupus nephritis (LN) is a strong predictor of progression to chronic kidney disease (CKD) and end stage renal disease (ESRD). While prior studies showed complement activation mediates glomerular injury, the role of complement in renal tubular damage has not been evaluated. The objective of this study is to investigate the association between complement activation as measured by tubular complement 9 (C9) deposition with interstitial fibrosis and tubular atrophy (IFTA) in LN.

Methods: LN biopsies from July 2014 to July 2016 were evaluated. Chromogenic immunohistochemistry was performed on formalin-fixed, paraffin-embedded, 4-µm human renal biopsy sections using unconjugated, murine anti-human Complement C9 (Hycult Biotech, clone X197) as a marker of the membrane attack complex (MAC) activation. C3 glomerulopathy was used as a positive control and normal kidney served as a negative control. Tubular basement membrane C9 staining intensity was analyzed as absent (0) versus present (1 to 3) scored on a semi-quantitative scale by a renal pathologist. IFTA was categorized as 0–10%, 11–20%, and >20%. Clinical parameters were assessed at the time of biopsy and 6 months post biopsy.

Results: Renal biopsies from 30 LN patients were studied, of which 23 (77%) were proliferative LN. There were 24 (80%) women, mean age 33 (standard deviation) (12) years. Positive tubular C9 staining (C9+) was observed in 7 (23%) biopsies. At the time of renal biopsy, C9+ patients had significantly higher proteinuria, compared to C9- patients: median (interquartile range) 6.2g (3.3-13.1) vs. 2.4g (1.3-4.6), p< 0.01. The differences persisted at 6 months after induction therapy: 1.08g (1.0-8.3) in C9+ vs. 0.68g (0.2-2.1) in C9- patients, p=0.06. Tubular C9 deposition was associated with the finding of interstitial fibrosis on biopsy: 3 out of 7 (42.9%) had >20% interstitial fibrosis as com-



Patient with LN Class V, 2+ tubular C9 deposition and 30 to 40% IFTA.

pared to none in the C9- group, p=< 0.01. Higher proportion of C9+ patients had moderate NIH Chronicity index: 3 out of 7 (42.9%) vs 2 out of 23 (8.7%) in the C9- group, p=0.07. There was no significant difference in eGFR at renal biopsy between the two groups.

Conclusion: Tubular C9 deposition is associated with proteinuria, interstitial fibrosis and increased chronicity which are predictors of progression to ESRD. Complement activation may play an important role in tubulointerstitial damage in LN.

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Abstract Number: 1792

Platelet-bound C4d Is Associated with an Increased Risk of Arterial and Venous Thromboses in SLE

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside

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Background/Purpose: Platelet-bound complement activation products (PC4d), defined as PC4d20 net mean fluorescent intensity [MFI], or a thrombotic risk score that includes PC4d, C3 and anti-phosphatidylserine/prothrombin antibodies (anti-PS/PT IgG) (1) correlate with venous thromboses in SLE. The current study was initiated to further evaluate the association between PC4d and arterial and venous thrombotic events.

Methods: Using a cross-sectional design, we examined the association of PC4d, measured by flow cytometry, with thrombosis. PC4d was dichotomized and we evaluated the ability of different cutoff values, ranging from 5 to 20 net MFI, to discriminate for the history of vascular events. The thrombotic risk was calculated as previously described (1).

Results: 150 SLE patients (40 ±13 years old, 91% female, 33% Hispanic, 26% African American) were included; 38% had antiphospholipid antibodies (aPL). Thirty-one vascular events (18 venous, 13 arterial) occurred within five years of study enrollment. Arterial and venous events, as compared to no events, were associated with higher PC4d levels (median [IQR] 13.6 [4.4-24.0] and 13.2 [3.2-22.3] vs. 4.0 [2.5-8.3] net MFI, respectively, $p< 0.05$). In a multivariable model adjusting for all significant co-variates identified in the univariable analysis (aPL, smoking, antimalarial use and prednisone ≥7.5mg/day), the association between all vascular events and PC4d (natural log transformed) remained significant (OR 1.7 95%CI 1.2-2.5, p=0.005).

	Sensitivity	Specificity	Youden J Statistic		Sensitivity	Specificity	Youden J Statistic
Venous Events:				Arterial Events:			
PC4d ≥ 20	44%	89%	0.34	PC4d ≥ 20	39%	89%	0.28
PC4d ≥ 15	44%	84%	0.29	PC4d ≥ 15	39%	84%	0.23
PC4d ≥ 10	56%	78%	0.33	PC4d ≥ 10	62%	78%	0.39
PC4d ≥ 5	67%	57%	0.23	PC4d ≥ 5	69%	57%	0.26
PC4d levels are expressed as net MFI.							

Table 1. Sensitivity and specificity of different PC4d cutoff levels for history of venous and arterial vascular events.

Event	Sensitivity (%) [95% CI]	Specificity [95% CI]	OR [95% CI]
Any thrombosis	35 [17, 56]	86 [78, 91]	3.15 [1.21, 8.19]
Arterial thrombosis	45 [17, 77]	84 [77, 90]	4.44 [1.24, 15.91]
Venous thrombosis	33 [13, 59]	84 [77, 90]	2.65 [0.89, 7.88]
CVA	25 [3, 65]	82 [75, 88]	1.56 [0.30, 8.18]
DVT	25 [5, 57]	83 [75, 89]	1.58 [0.40, 6.29]
MI	100 [29, 100]	84 [77, 89]	∞ [NaN, ∞]

Table 2. Sensitivity, specificity, and odds ratio (OR) with 95% confidence intervals [95% CI] are reported for thrombotic score ≥ 2. The thrombotic score was calculated using cutoff for PC4d of 10 MFI. CVA: cardiovascular accidents, DVT: deep vein thrombosis, MI: myocardial infarction, NaN: not a number.

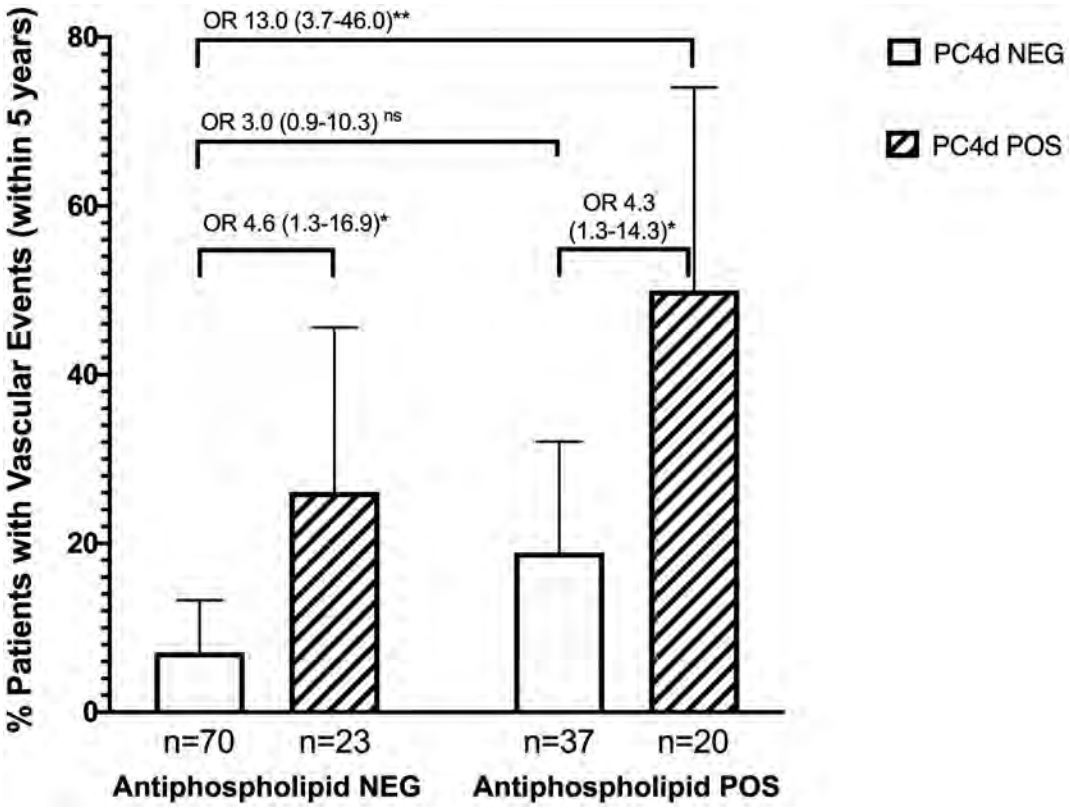

Figure 1. Vascular Events in SLE Stratified by Antiphospholipid Antibody (aPL) status and PC4d. Percent patients with a history of a vascular event within five years of study enrollment, stratified by aPL presence (NEG=negative; POS=positive) and PC4d status (NEG=PC4d 0.05.

The optimal PC4d cut-off point for vascular thromboses was identified to be 10 net MFI, with a sensitivity and specificity for venous events of 56% and 78%, and for arterial 62% and 78% (Table 1); PC4d≥10 net MFI, as compared to PC4d≥20 net MFI, resulted in a greater detection of individuals with vascular events (16/28 vs 11/28 respectively). Stratifying by aPL status, PC4d10 was associated with a history of any vascular event, with a stronger association seen in patients positive for both aPL and PC4d - OR 4.6 95% CI 1.3-16.9 for PC4d+/aPL- and OR 13.0 95% CI 3.7-46.0 for PC4d+/aPL+ as compared with PC4d-/aPL- patients (Figure 1). A thrombotic score ≥ 2 (calculated using PC4d≥10) was associated with all events (arterial and venous) – OR 3.15 [95% CI 1.21, 8.19] and with arterial thrombosis - OR 4.44 [95% CI 1.24, 15.91] (Table 2).

Conclusion: PC4d and the thrombotic score associate with thrombotic events in SLE. The 10 net MFI PC4d cutoff was optimal for identifying patients with thromboses, and more specifically arterial events. PC4d10 could function more effectively as a biomarker of cardiovascular events, providing a novel risk indicator independent of aPL antibodies.

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Abstract Number: 1793

Safety of Obtaining Research Tissue During Clinically Indicated Kidney Biopsies: Data from the Lupus Accelerating Medicines Partnership

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SESSION INFORMATION

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Background/Purpose: Lupus nephritis (LN) is a major complication of systemic lupus erythematous (SLE) and affects ~60% of patients during the course of their disease, leading to significant morbidity and mortality. Previous studies examining the safety of percutaneous kidney biopsy to diagnose LN have found variable complication rates depending on disease type studied, ranging from 4-11% in autoimmune/SLE patients to 15-17% in safety studies of any kidney disease. The purpose of our study was to define the safety of obtaining additional tissue for research during clinically indicated renal biopsies in a SLE cohort.

Methods: Patients were enrolled across 15 clinical US sites in the SLE Accelerating Medicines Partnership (AMP). Kidney biopsies were clinically indicated to evaluate proteinuria (urine protein creatinine ratio [uPCR] > 0.5). Patients with a history of renal transplant, use of rituximab within 6 months of biopsy, and current pregnancy were excluded. Ultrasound/CT-guided kidney biopsies were performed by interventional radiologists/nephrologists generally using an 18-gauge needle although technique, number of routine passes and core lengths varied. An additional core taken solely for research purposes, or a piece of core with sufficient glomeruli remaining from the routine passes and not required for clinical diagnosis, was collected. All adverse events (AEs) occurring within 30 days of biopsy were reported, including duration, severity, type, and resolution.

Results: 482 patients underwent a renal biopsy between 2014 and 2020. All patients met criteria for SLE (ACR or SLICC) and the majority were female (85%). Pathologic assessment of clinical biopsies revealed ISN/RPS Class I-VI for most biopsies, although 45 biopsies (9%) yielded a non-LN diagnosis (Table 1). Overall, 37 patients (8%) experienced an AE with several more than one, with a total of 41 AEs reported. Of these AEs, 8 (20%) were considered by the site investigator to be unrelated or unlikely to be related (included pain, shortness of breath, cardiac arrest, fall, and hemoglobin decrease due to sepsis) and 33 (80%) were deemed possibly, probably, or definitely related to the study procedure. Of these events, 9/33 (28%) were mild, 10 (30%) were moderate, and 12 (36%) were deemed severe. In 18 patients (4%) the AEs were considered serious as defined by inpatient or prolonged hospitalization, significant incapacity, or requiring intervention to prevent permanent impairment. The most common related AEs

	All, N=482	without AE, N=445	with AE, N=37
Age, mean ± SD	36.2 ± 12.3 (N=434)	36.1 ± 12.3 (N=397)	37.5 ± 12.5 (N=37)
Gender, N (%)			
Female	394 (81.7%)	361 (81.1%)	33 (89.2%)
Male	70 (14.5%)	67 (15.1%)	3 (8.1%)
Unknown	18 (3.7%)	17 (3.8%)	1 (2.7%)
Race, N (%)			
Asian	70 (14.5%)	60 (13.5%)	10 (27.0%)
Black	199 (41.3%)	187 (42.0%)	12 (32.4%)
White	153 (31.7%)	12 (31.9%)	11 (29.7%)
Unknown/Other	60 (12.4%)	56 (12.6%)	4 (10.8%)
Ethnicity, N (%)			
Hispanic/Latino	124 (25.7%)	116 (26.1%)	8 (21.6%)
Not Hispanic/Latino	338 (70.1%)	310 (69.7%)	28 (75.7%)
Unknown	20 (4.1%)	19 (4.3%)	1 (2.7%)
Diagnosis, N (%)			
Class I	9 (1.9%)	8 (1.8%)	1 (2.7%)
Class II	32 (6.6%)	30 (6.7%)	2 (5.4%)
Class III	80 (16.6%)	78 (17.5%)	2 (5.4%)
Class IV	62 (12.9%)	57 (12.8%)	5 (13.5%)
Class V	110 (22.8%)	97 (21.8%)	13 (35.1%)
Class III/V	66 (13.7%)	60 (13.5%)	6 (16.2%)
Class IV/V	49 (10.2%)	44 (9.9%)	5 (13.5%)
Class III/IV	6 (1.2%)	6 (1.3%)	0 (0.0%)
Class VI	18 (3.7%)	18 (4.0%)	0 (0.0%)
Other	45 (9.3%)	43 (9.7%)	2 (5.4%)
Insufficient tissue for diagnosis	5 (1.0%)	4 (0.9%)	1 (2.7%)
Medication, N (%)			
Hydroxychloroquine	344 (84.9%)	310 (83.6%)	34 (100.0%)
Prednisone	245 (60.5%)	224 (60.4%)	21 (61.8%)
Azathioprine	31 (7.7%)	25 (6.7%)	6 (17.6%)
Mycophenolate mofetil	149 (36.8%)	140 (37.7%)	9 (26.5%)
Pulse steroids	16 (4.0%)	10 (2.7%)	6 (17.6%)
Cyclophosphamide	4 (1.0%)	2 (0.5%)	2 (5.9%)
Tacrolimus	19 (4.7%)	17 (4.6%)	2 (5.9%)
Clinical Laboratory Values			
Random uPCR, mean	3.00	2.92	3.89
Serum creatinine, mean	1.4	1.4	1.18
Research biopsy length (mm), mean	8.4	8.5	6

Table 1. Patient characteristics at time of kidney biopsy.

were bleed-related complications, including hematoma, hemorrhage, and hemoglobin decrease (N= 29). Of these, 18 required hospitalization, with 4 of these patients receiving a blood transfusion. All 29 bleed-related complications resolved. The length of the research biopsy did not associate with an AE.

Conclusion: Procurement of an additional kidney biopsy core for research purposes in SLE patients undergoing a clinically-indicated kidney biopsy did not result in an increase in adverse events compared to the adverse event rate

in prior studies of the safety of percutaneous kidney biopsy. Accordingly, inclusion of a research core should be considered feasible for future studies to advance discovery of new therapeutic targets and prognostic indicators in LN.

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Abstract Number: 1794

Systemic Lupus Erythematosus and Geomagnetic Disturbances: A Time Series Analysis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
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Session Time: 9:00AM–11:00AM

Background/Purpose: To examine the influence of solar cycle and geomagnetic effects on SLE disease activity.

Methods: The data used for the analysis consisted of 327 observations of 27-day Physician Global Assessment (PGA) averages of patients with SLE seen in the Hopkins Lupus Center from 1996-2020. The considered geomagnetic indices were the AP index (geomagnetic activity), sunspot number index R (area of solar surface covered by spots), the F10.7 index (noise level generated by the sun at a wavelength of 10.7 cm at the earth's orbit), the AU index (upper auroral electrojet index), and high energy (> 60 Mev) proton flux events. Geomagnetic data were obtained from the Goddard Space Flight Center Space Physics Data Facility. A time series decomposition of the PGA averages was performed as the first step. The linear relationships between the PGA and the geomagnetic indices were examined using parametric statistical methods such as Pearson's correlation and linear regression, while the nonlinear relationships were examined using nonparametric statistical methods such as Spearman's rho and Kernel regression.

Results: After time series deconstruction of PGA averages, the seasonality explained a significant fraction of the variance of the time series (R^2 =38.7%) with one cycle completed every 16 years. Increases in the number of high energy proton fluxes were associated with decreases in the PGA ($p< 0.05$). Increases in sunspot number index R anticipated decreases in the PGA ($p< 0.05$). Increases in the Ap index were associated with decreases in the PGA ($p< 0.1$).

Conclusion: The seasonality of the PGA averages (one cycle every 16 years) explains a significant fraction of the variance of the time series. Geomagnetic disturbances, including the level of geomagnetic activity, sunspot numbers, and high proton flux events may explain part of the described seasonality seen in SLE.

Disclosure: G. Stojan, None; **F. Giammarino**, None; **M. Petri**, AbbVie, 5, Amgen, 5, AstraZeneca, 2, 5, BMS, 5, Decision Resources, 5, GSK, 2, 5, INOVA, 5, IQVIA, 5, Janssen, 5, Eli Lilly, 2, 5, Merck EMD Serono, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5, Exagen, 2.

Abstract Number: 1795

Intracellular Homocysteine and Homocysteine Metabolites in Systemic Lupus Erythematosus (SLE)

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: In SLE, homocysteine has been shown to be a potentially modifiable, independent risk factor for stroke and thrombotic events. All previous epidemiological studies used total plasma homocysteine as a disease marker, but it remains unclear whether plasma or intracellular homocysteine is causing detrimental effects. Folic acid (0.5 mg/day) supplementation does lower homocysteine in plasma as expected, but homocysteine and all its metabolites in white bloods cells remain unaffected (1). We hypothesized that intracellular homocysteine and homocysteine metabolite levels in patients with SLE are disproportionately elevated compared to the levels seen in healthy subjects and that intracellular homocysteine and homocysteine metabolite levels are independently associated with coronary plaque in SLE.

Methods: A liquid chromatography coupled to tandem mass spectrometry absolute quantification assay was used for the determination of 6 analytes in both plasma and PBMCs: homocysteine (Hcy), S-adenosylmethionine (SAM), S-adenosylhomocysteine (SAH), methionine (Met), cystathionine (Cysta), and 5-methyltetrahydrofolate (5m-THF). We then compared intracellular (PBMC) and extracellular (plasma) homocysteine and homocysteine metabolite (SAM, SAH, Met, Cysta, 5m-THF) concentrations in 10 patients who met ACR or SLICC classification criteria for SLE and in 10 age, sex, and ethnicity matched controls. Subjects with a history of diabetes mellitus, cardiovascular disease, hypertension, alcohol consumption in excess of 3 units per day, anemia, renal insufficiency (serum creatinine >1.5mg/dl), and pregnancy were excluded. All SLE patients had two coronary CT angiography (CCTA) studies (follow up mean=3.77 years, SD=0.94 years) as screening for occult coronary atherosclerotic disease in asymptomatic individuals. Fisher's t-test was used to analyze the differences between homocysteine and homocysteine metabolite levels in SLE and controls. The correlation between metabolite levels and coronary plaque volumes was analyzed using Pearson correlation.

Results: Plasma from SLE patients had higher levels of homocysteine ($P < 0.0001$), SAH ($P < 0.05$), SAM ($P < 0.001$), and lower levels of Met ($P < 0.05$) and Cysta ($P < 0.001$) compared to controls. PBMC intracellular concentrations from SLE patients had higher levels of Cysta ($p < 0.05$), SAH ($p < 0.05$), SAM ($p < 0.001$) and lower levels of 5m-THF ($p < 0.001$). Plasma SAH showed a positive correlation to the total coronary plaque, calcified plaque, and noncalcified plaque measured by CCTA ($p < 0.05$).

Conclusion: Intracellular concentrations of homocysteine metabolites were significantly different between SLE patients and controls, despite similar intracellular homocysteine levels. Plasma S-adenosylhomocysteine was positively

correlated to total coronary plaque, calcified plaque, and noncalcified plaque. Further studies are needed to clarify the importance of intracellular homocysteine metabolites as cardiovascular risk factors in SLE.

Disclosure: G. Stojan, None; **J. Li**, None; **A. Raj**, None; **M. Kane**, None; **M. Petri**, AbbVie, 5, Amgen, 5, AstraZeneca, 2, 5, BMS, 5, Decision Resources, 5, GSK, 2, 5, INOVA, 5, IQVIA, 5, Janssen, 5, Eli Lilly, 2, 5, Merck EMD Serono, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5, Exagen, 2.

Abstract Number: 1796

A Panel of Urinary Proteins Predicts Active Lupus Nephritis and Response to Rituximab Treatment

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Approximately 30% of patients with adult-onset systemic lupus erythematosus (SLE) develop lupus nephritis (LN). Presence and/or severity of LN are currently assessed by renal biopsy, but biomarkers in serum or urine samples may provide an avenue for non-invasive routine testing.

Methods: 197 SLE patients and 48 healthy controls were recruited, and urine samples collected. 75 of the SLE patients had active LN and 104 had no or inactive renal disease. Concentrations of lipocalin-like prostaglandin D synthase (LPGDS), transferrin, alpha-1-acid glycoprotein (AGP-1), ceruloplasmin, monocyte chemoattractant protein 1 (MCP-1) and soluble vascular cell adhesion molecule-1 (sVCAM-1) were quantified by MILLIPLEX® Multiplex Assays using the MAGPIX Luminex xMAP platform. Binary logistic regression was conducted to examine whether proteins levels associate with active renal involvement and/or response to rituximab treatment.

Results: Urine levels of transferrin ($p< 0.005$), AGP-1 ($p< 0.0001$), MCP-1 ($p< 0.001$) and sVCAM-1 ($p< 0.005$) were significantly higher in SLE patients when compared to healthy controls. Furthermore, levels of transferrin, AGP-1, ceruloplasmin, MCP-1 and sVCAM-1 (all $p< 0.0001$) were significantly higher in SLE patients with active LN when compared to patients without active LN. A combination of five urine proteins, namely LPGDS, transferrin, ceruloplasmin, MCP-1 and sVCAM-1 was a good predictor of active LN (AUC 0.898). A combined model of LPGDS, transferrin, AGP-1, ceruloplasmin, MCP-1 and sVCAM-1 predicted response to rituximab treatment at 12 months (AUC 0.818).

Conclusion: Findings support the use of a urinary protein panel to identify active LN and potentially predict response to treatment with rituximab in adult SLE patients. Prospective studies are required to confirm findings.

Disclosure: J. Davies, None; **E. Carlsson**, None; **A. Midgley**, None; **E. Smith**, None; **I. Bruce**, Genzyme/Sanofi, 2, GlaxoSmithKline, 2, 5, 8, Roche, 2, UCB, 2, 5, 8, Eli Lilly, 5, Merck Serono, 5, ILTOO, 5, AstraZeneca, 8; **M. Beresford**, None; **C. Hedrich**, None.

Abstract Number: 1797

A Multianalyte Assay Panel (MAP) with Algorithm Containing Cell-Bound Complement Activation Products (CB-CAPs) Is Superior to Anti-dsDNA and Low Serum Complement Levels in Predicting Transition of Probable Lupus to ACR Classified Lupus Within 2 Years

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: We reported previously (R*amsey-Goldman et al., Arthritis Rheumatol 2020)* that score > 0.8 of a multianalyte assay panel (MAP) with algorithm predicts fulfillment of a 4th ACR criterion 9-18 months (median 12) after enrollment in patients with probable systemic lupus erythematosus (pSLE). We continued to follow pSLE to better evaluate transition to classifiable SLE.

Methods: pSLE, defined as fulfilling 3 ACR criteria, were followed at academic lupus centers. At enrollment, 35 (38%) of the 92 pSLE fulfilled SLICC criteria. CB-CAPs - C4d bound to erythrocytes (EC4d) and B-cells (BC4d) - were measured by quantitative flow cytometry, serum C3 and C4 by turbidimetry, and autoantibodies by ELISA. Anti-dsDNA positivity was confirmed by immunofluorescence (IFA). MAP index consists of an algorithm with CB-CAPs and autoantibodies (Dervieux et al., *J Immunol Methods* 2017). Initial decision analysis with Youden index showed that MAP > 0.8 and EC4d > 20 mean fluorescence intensity units (MFI) reflected the optimal cutoffs for transition to ACR classifiable SLE; the same cutoffs were used for analysis of all follow-up visits. Time to fulfillment of ACR criteria was evaluated by Kaplan-Meier analysis; associations were analyzed by log-rank test and Cox proportional hazards model and are expressed as hazards ratio (HR).

Results: Of the 92 pSLE, 74 had 1 or 2 follow-up visits 9-35 months after enrollment for a total of 128 visits. Overall, 28 pSLE (30.4%) transitioned to ACR classifiable SLE: 16 (57%) in the 1st year and 12 (43%) in the 2nd. The clinical or laboratory features that defined fulfillment of ACR criteria are in Table 1. Use of hydroxychloroquine and immunosuppressants was similar in those who did and did not transition to SLE. Of the 17 subjects who accrued hematological criteria during the study (11 as the sole criterion and 6 as one of the new criteria), a minority were on immunosuppressants: 6 at enrollment, 5 at the 1st visit, and 3 at the 2nd. Neither SLICC criteria nor individual biomarkers were significantly associated with transition to SLE (Table 2). Only MAP > 0.8 had significantly high HR for transition to SLE; EC4d > 20 MFI, low complement, and anti-dsDNA were not significant (Table 2).

Conclusion: The majority of pSLE transitioned within a year. MAP > 0.8 predicted disease evolution into classifiable SLE better than other biomarkers or fulfillment of SLICC criteria.

	New ACR criteria from baseline to 12 months	New ACR criteria from 13 to 26 months
Hematological	10	7
Ulcers	4	2
Pleuritis or pericarditis	2	0
Immunological	2	4
Arthritis	2	1
Discoid rash	1	0
Photosensitivity	1	2
Renal	0	1

Table 1. Clinical and laboratory features leading to the transition of pSLE to SLE. The 16 individuals who fulfilled ACR criteria within 1 year (≤365 days) accrued a total of 22 new ACR criteria, with hematological being the most common. The 12 subjects who fulfilled ACR criteria after the 1st year of follow up (>365 days) accrued a total of 15 criteria, with hematological being again the most common. Of note, 2 subjects who fulfilled ACR criteria within 12 months accrued additional criteria after this time point (an immunological criterion and ulcers); these criteria are included in the table.

Variables at enrollment	HR	95% CI	p-value
SLICC criteria	1.82	0.86 – 3.84	0.116
Low C3 and/or C4	1.02	0.24 – 4.29	0.984
Anti-dsDNA (IFA)	2.04	0.71 – 5.91	0.188
Positive CB-CAPs (EC4d and/or BC4d)	1.36	0.61 – 3.01	0.454
EC4d>20 MFI	2.07	0.86 – 4.94	0.103
MAP>0.8	2.72	1.25 – 5.93	0.012

Table 2. Hazard ratio (HR) of variables measured at enrollment in predicting fulfillment of ACR classification criteria in the pSLE population. Data of 128 follow-up visits (n=127 for MAP) that occurred 9 to 35 months after enrollment were analyzed. CB-CAPs: cell-bound complement activation products; MAP: multianalyte assay panel with algorithm; HR: hazard ratio; CI: confidence intervals.

Disclosure: R. Ramsey-Goldman, None; **R. Alexander**, Exagen Inc, 1; **C. Arriens**, BMS, 1, 2, GSK, 1; **S. Narain**, None; **E. Massarotti**, Exagen, 1, EMD Serono, 1; **D. Wallace**, Exagen, 1, 2, Exagen, 1, 2; **A. Saxena**, Glaxo Smith Kline, 1, Bristol Myers Squibb, 1; **C. Collins**, GSK, 1, Abbvie, 1, 2, Novartis, 1, Exagen, 1, 2; **C. Putterman**, Equillium, 1, 2; **K. Kalunian**, Roche, 5, Biogen, 5, Janssen, 5, AstraZeneca, 5, Lupus Research Alliance, 2, Pfizer, 2, Sanford Consortium, 2, Eli Lilly, 5, Genetech, 5, Gilead, 5, ILTOO, 5, Nektar, 5, Viela, 5, Equillium, 5, Bristol-Meyers Squibb, 5; **A. Sace**, None; **R. LaFon**, None; **J. Ligayon**, Exagen Inc, 1; **J. Conklin**, Exagen, 1, 2; **A. Weinstein**, Exagen, 1, 2.

Abstract Number: 1798

IgE Anti-dsDNA Antibodies in Systemic Lupus Erythematosus Are Associated with Higher Disease Activity at the Baseline and in Longterm Follow-up

Omer Pamuk[1], Zerai Manna[2], Rutha Adhanom[2], Xiaobai Li[3], Mariana Kaplan[4] and Sarfaraz Hasni[2], [1]Rheumatology Fellowship and Training Branch, NIAMS/NIH, Bethesda, MD, [2]Lupus Clinical Trials Unit, NIAMS/NIH, Bethesda, MD, [3]Biostatistics and Clinical Epidemiology Service, Clinical Center, NIH, Bethesda, MD, [4]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD

SESSION INFORMATION

Session Date: Monday, November 9, 2020

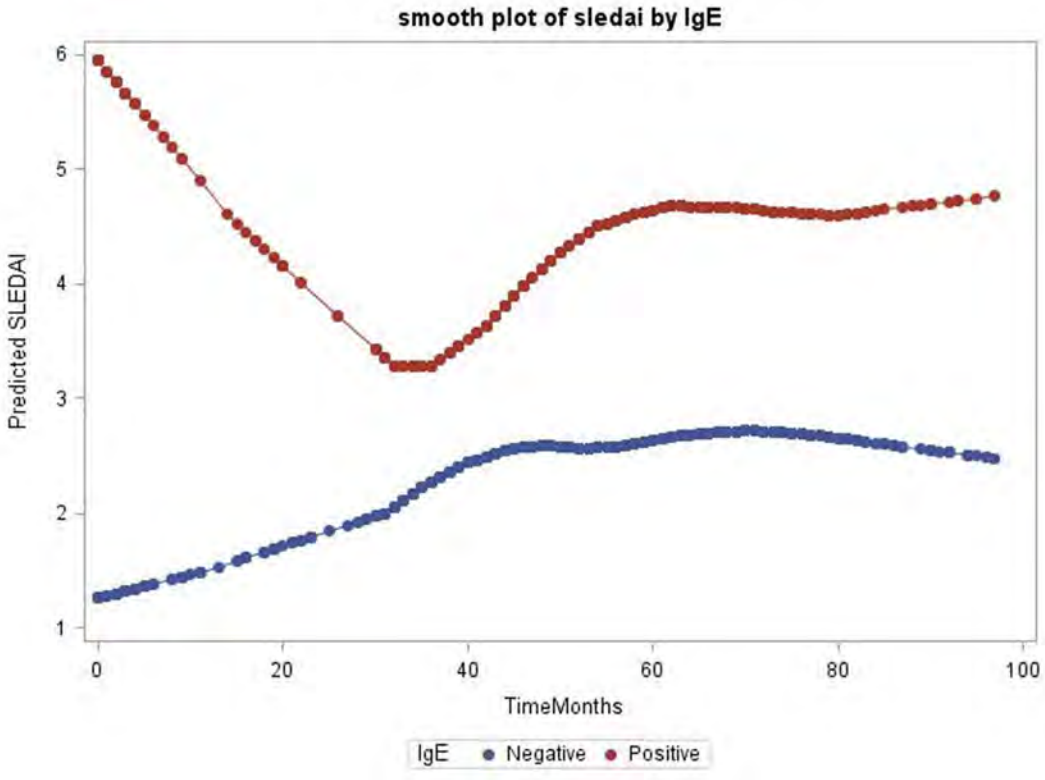
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside

Session Type: Poster Session D

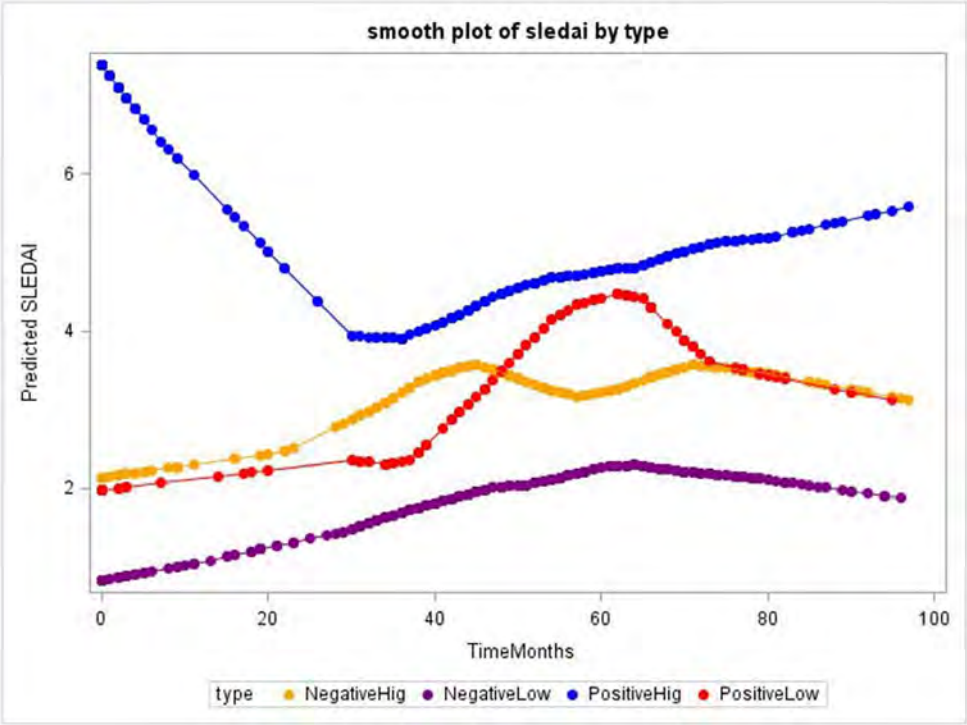
Session Time: 9:00AM–11:00AM

	dsDNA IgE-positive	dsDNA IgE-negative
n (F/M)	28 (24/4)	67 (57/10)
Age (mean±SD)	40±13.7	43.5±15.5
African-American, n (%)	6 (21.4)	23 (34.3)
Hispanic, n (%)	8 (28.6)	10 (14.9)
Asian, n (%)	7 (25)	9 (13.5)
White, n (%)	7 (25)	25 (37.3)
Nephritis, n (%)	18 (64.3)	36 (53.7)
High IFN score, n (%)	17 (60.7)	22 (32.8)*

Demographic and clinical features of the SLE patients.



SELENA-SLEDAI scores of patients during the study by dsDNA-IgE autoantibody.



SELENA-SLEDAI scores of patients by dsDNA-IgE autoantibody and IFN score.

Background/Purpose: Recent reports indicate that autoreactive anti-dsDNA IgE autoantibodies and IgE immune complexes and can activate innate and adaptive immunity leading to amplification of lupus immune dyeregulation including induction of type I Interferon (IFN) responses. The aim of this study is to understand the differences in long-term outcomes of SLE patients with or without IgE autoantibodies with high vs. low IFN gene score at baseline.

Methods: The study included 95 adult SLE subjects who fulfilled the 1997 ACR SLE criteria and were enrolled in an IRB approved long-term natural history study. In addition to clinical evaluation, Safety of Estrogen in Lupus National Assessment - SLE Disease Activity Index (SELENA-SLEDAI) scores were recorded at baseline, 36, 60, and 84 month follow-up periods. Anti-dsDNA-IgE autoantibodies were measured by ELISA and a 21-Type I IFN inducible gene composite score was derived from whole blood RNA sequencing at baseline. A high IFN score was defined as an IFN score of >4. The patients were divided into four groups: IgE-positive/high IFN score, IgE-positive/low IFN score, IgE-negative/high IFN score, and IgE-negative/low IFN score. SLE flare was defined as an increase of ≥4 points in the SELENA-SLEDAI score. The locally weighted scatter plot smoother (LOESS) curves were generated for each group to identify longitudinal trends in SELENA-SLEDAI scores. Wilcoxon ranked sum test was used to compare the IgE-positive subjects with the IgE-negative subjects, and to compare the IgE-positive/high IFN score with IgE-negative/low IFN score subjects.

Results: The clinical and demographic features of the SLE subjects are shown in Table 1. Patients with IgE anti-dsDNA antibodies (n=28) were found to have high IFN scores (p=0.012). The IgE-positive group had higher SELENA-SLEDAI scores at baseline and during follow-up (p values, < 0.001, 0.008 and 0.04, at baseline, 60 and 84 months, respectively) (Fig 1). The subset of patients with anti-dsDNA-IgE-positive/high IFN score(n=17) were found to have significantly higher baseline SELENA-SLEDAI scores that remained elevated during the study period (p values, < 0.001, 0.03, 0.07 and 0.009 at baseline, 36, 60 and 84 month, respectively) (Fig 2). The IgE-negative/Low IFN score group (n=45) had the lowest SLE disease activity compared to the other groups (47.7% vs. 64.7%, p=0.09) and the longest flare-free interval (74 months) when compared to the other groups.

Conclusion: SLE patients that are positive for anti-dsDNA-IgE autoantibodies display higher lupus disease activity and IFN scores compared to the anti-dsDNA-IgE negative group. A combination of IgE positive antibodies and high IFN score is associated with significantly enhanced lupus disease activity during longterm follow-up. Our study suggests that presence of IgE autoantibodies and elevated IFN gene score represents a subset of patients with persistently active disease despite standard of care. As omalizumab, a monoclonal antibody against IgE, can modulate type I IFN responses, this study further supports that strategies that target IgE autoantibodies may benefit specific subgroups of SLE subjects.

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Abstract Number: 1799

High Fat-Diet as a Catalyst to Lupus Development and Autoimmunity in MRL/lpr Mice

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is an autoimmune disease with features of autoantibodies, skin rash, kidney and other multiple organ involvement. Evidence shows that obesity is a major factor contributing to the onset and progression of autoimmune diseases including SLE and is highly linked to their cumulative organ damage. Our previous study and others have shown that circulating T follicular helper (Tfh) cells are implicated in promoting B cells production of autoantibodies and shape the composition of the gut microbiota thus modulating obesity. In this study, we evaluated the impact of high fat diet (HFD) on the development of SLE and obesity, and the pathophysiologic link of obesity, SLE, and Tfh cells in MRL/lpr lupus prone mice.

Methods: Thirty MRL/lpr mice were fed a regular diet (RD, 10% calories from fat) or high fat diet (HFD, 60% calories from fat) beginning at 2 months of age, half male and half female. Their body weights and skin lesions were recorded weekly. Urine protein was assessed weekly by Bradford assay. Blood was collected monthly for serum IgG, anti-dsDNA antibody, and anti-nuclear antibody (ANA) detection. At week 14, mice were euthanized, their spleen were measured and weighed. Kidney and skin biopsy were embedded in paraffin and tissue sections for H&E, PAS, and Masson's staining to detect lupus histopathological lesions and quantified as kidney index and histological skin score based on glomerular cellularity, glomerular deposits, interstitial inflammation, and inflammatory dermatitis. Tfh cells ($CD4^+CXCR5^+$) were examined in blood and splenic sections by flow cytometry and immunofluorescent staining.

Results: The HFD group induced a significant increase in mouse body weight by week 3 and continued until week 14 compared to RD group ($p< 0.05$ to $p< 0.01$). Skin lesions on the dorsum of neck, forehead, and ears in HFD group, resembling human discoid lupus, manifested as earliest as week 6 and occurred in 55.6% of the HFD group vs 11.1%

of the RD group ($p< 0.05$). Splenomegaly was observed in the HFD mice ($p< 0.05$). Proteinuria was increased from week 11 to week 14 in HFD group. There was an increase trend of anti-dsDNA antibody and serum IgG titer in HFD group, but no difference of ANA was observed between HFD and RD groups. HFD mice also had a higher histological score of skin ($p< 0.05$) and higher acute and chronic index of kidney than RD mice. Significant increase of $CD4^+CXCR5^+$ Tfh cells was observed in both blood and spleen in HFD group mice.

Conclusion: Our results show that a high fat diet induced an accelerated and more severe form of lupus development and autoimmunity in MRL/lpr mice. This indicates that HFD exacerbates the development of SLE. The elevated disease course in HFD mice was accompanied by increased of Tfh cells. Interventions of healthy diet or targeting Tfh cells may improve both lupus symptoms and outcomes in genetically predisposed SLE patients.

Disclosure: H. Ali, None; **J. Meng**, None; **X. Shi**, None; **L. Hellmers**, None; **S. Dhulipala**, None; **P. Kachur**, None; **T. Posas-Mendoza**, None; **R. Quinet**, None; **W. Davis**, None; **J. Zakem**, None; **Z. You**, None; **X. Zhang**, None.

Abstract Number: 1800

Association of Air Pollution with Systemic Lupus Erythematosus Disease Activity in the Central Valley of California

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex multisystem autoimmune disease that affects at least 300,000 people in the United States creating a substantial socioeconomic burden. The exact etiology of SLE remains largely unknown. Both genetic factors and environmental exposures have been implicated in the etiology and progression of SLE. Air pollution is one of the major environmental factors that have been proposed in the study of SLE exacerbation. Fine and ultrafine particles measuring 2.5μm (PM2.5) are major contributors to air pollution. Wildfires can increase PM2.5 significantly and affect individuals' health negatively. Due to topographical and meteorological conditions in the central valley of California, the area is prone to air pollution and this can be well pronounced during active wildfires in the surrounding areas. In this study, we aim to study the correlation between the frequency of SLE flares and air quality measures.

Methods: This is a retrospective study. Data for SLE patients with the following criteria were collected: age 18 or above, confirmed diagnosis of SLE (by ACR 2019 criteria, tissue diagnosis, or rheumatologist-confirmed), who had an ED visit or were admitted during the year 2018 for SLE flare. The following data for Fresno county covering the year 2018 were collected using the environmental protection agency website: PM2.5, Ozone, and average daily temperature. The data were averaged for each week of the year and the counts of SLE flares were examined during each week. Pearson correlation tests were used to analyze the correlation of air quality measures with the frequency of SLE flares (Pearson correlation coefficients and 2- tailed p values were reported).

Results: A total of 432 SLE ED and inpatient encounters were reviewed, of those 257 met the study criteria for SLE with 94 SLE flares. The mean age was 40 with 93% of patients being females. Pearson correlation coefficient for the Ozone

air quality index and SLE flares was found to be -0.244 (p value= 0.08). Correlation coefficient results for PM2.5 levels air quality index and average temperature were -0.103 (p value= 0.465) and -0.198 (p value= 0.155) respectively.

Conclusion: In our study, there was no statistically significant correlation between SLE flares and levels of different pollutants including PM2.5 and Ozone. There was also no statistically significant correlation between the average daily temperature and the frequency of SLE flares. We suggest there might be a signal that it is in our unique population's genetics or cultural differences that might be paving way for their flares or their healthcare access. Our study is an important pilot to support the need for assessing the possibly unique genetic makeup in our population, considering that weather might not be the major flare trigger. Larger studies are needed to assess the association and causation between SLE flares and air pollution.

Disclosure: M. Mohameden, None; **A. H.Ali**, None; **Z. Li**, None; **Y. Abejie**, None; **R. Jain**, None; **C. Reyes Yuvienco**, None.

Abstract Number: 1801

An Engineered Extracellular Matrix-rich Decellularized Substrate Based Podocytes Culture System to Study Intracellular Complement Production and Activation

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SESSION INFORMATION
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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
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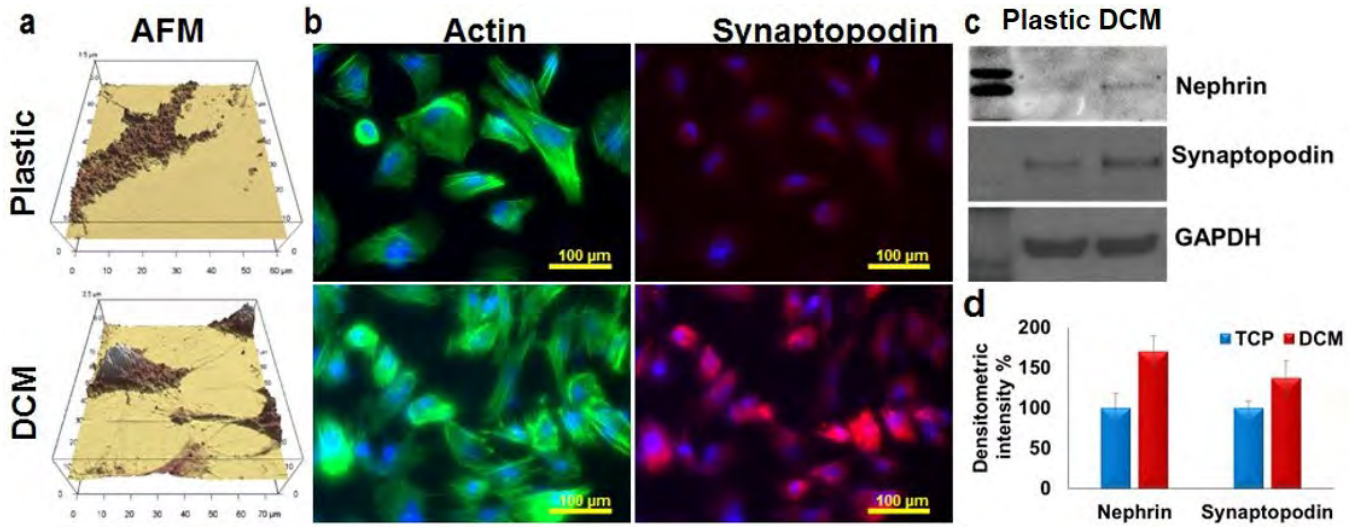
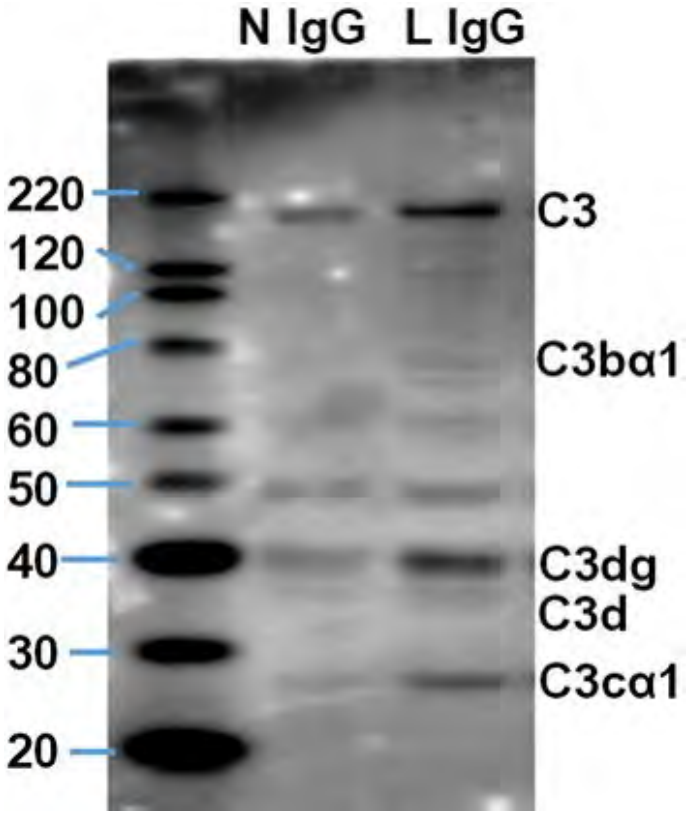
Background/Purpose: Current technologies do not support long-term cell viability, differentiation and maintenance of podocytes. We developed a biophysical approach, termed macromolecular crowding (MMC), to create extracellular matrix (ECM)-rich tissue equivalents and decellularization. This approach generates decellularized grafts that scaffold podocytes to grow in an environment similar to native conditions. To show a potential application of this newly designed culture system we studied complement (C) activation in podocytes exposed to IgG from individuals with lupus nephritis (LN) and hypoxia.

Methods: Human skin fibroblasts were cultured under MMC and then decellularized. Human immortalized podocytes were cultured on the decellularized matrix (DCM) at 33°C for 7 days and at 37°C for 14 days (https://doi.org/10.1002/adfm.201908752). ECM deposition in the DCM-coated dishes was analyzed by SDS-PAGE, immunofluorescence (IF) and atomic force microscopy and expression of podocyte markers by western blotting (WB) and IF. Podocytes were then exposed to IgG from patients with LN or Dimethyloxalylglycine (DMOG) and C activation was studied (WB and IF).

Results: We found that DCM-coated dishes contained all major ECM molecules (laminin, fibronectin, collagen I and IV) and podocytes survived and differentiated on DCM-coated plates significantly better than on non-coated plates, as shown by the development of interdigitating foot process and increased expression of nephrin and synaptopodin (fig. 1). Podocytes exposed to LN IgG (fig. 2) or DMOG (fig. 3) displayed increased levels of complement molecules (C3, C4, C5, C5b9) and C3 activation products.

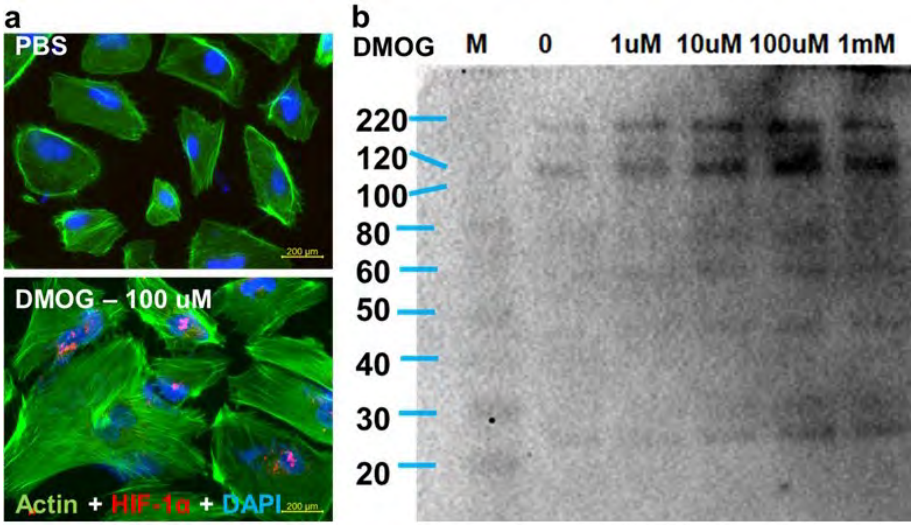


(a) Atomic Force Microscopy (AFM) shows better podocyte morphology with interdigitating foot processes on DCM-coated dishes. (b) Immunofluorescence shows enhanced expression and co-localization of actin and synaptopodin on DCM-coated dishes. Western blotting (c) (densitometric readings d,) confirmed higher expression of nephrin and synaptopodin on decellularized ECM rich substrate.



Lupus IgG enhances production of activated C3 molecules. Lupus IgG (L IgG), Normal IgG (N IgG).

Conclusion: Engineering in vitro microenvironment with decellularized matrix enhances podocyte viability, native physiology and morphology. This novel system enabled us to demonstrate increased complement factor production by podocytes exposed to LN IgG or hypoxia and intracellular complement activation.



(b) DMOG enhances production of activated C3 molecules.Exposure of podocytes to DMOG (a) upregulates expression of HIF-1α and (b) enhances production of C3 split products. Western blotting analysis of activated C3 using a pan-C3 antibody that detects activated C3 split molecules.

Disclosure: A. Satyam, None; **M. Tsokos**, None; **G. Tsokos**, None.

Abstract Number: 1802

Vitamin D Level: Predictor of SLE Disease Activity in AA Cohort with CLE?

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: There are few predominant African American (AA) epidemiological studies in Cutaneous Lupus Erythematosus (CLE). The Gilliam classification divides CLE into lupus specific, acute cutaneous LE (ACLE), subacute cutaneous lupus (SCLE) and chronic variants (CDLE). Evidence shows SLE can lead to lower vitamin D levels since patients are usually photosensitive and advised to practice sun protection measurements. Also, it is important to consider the probability that vitamin D (Vit. D) deficiency could have a role in the prediction of disease activity given its role on the immune system. The aim of our study was to evaluate the correlation between vitamin D level and disease activity based on laboratory markers, in an AA CLE cohort.

Methods: From Rheumatology and Dermatology clinic at University Medical Center, New Orleans, a total of 182 patients' charts were retrospectively reviewed from 2015 to 2019. Using ICD-10 codes we cross reference the diagnosis of SLE, DLE, other local LE and SCLE. A total of 67 patients' data extracted including: age, ethnicity, smoking, ANA,

Table 1: Demographics

Skin manifestation	Numbers (%)	Ethnicity (%) AA	Gender (%) F	Smoking	ANA +	SSA +	dsDNA +	C3(<80) low	Pr/Cr (<450) normal	Vit. D Def (<12)
SCLE	14 (21)	14 (100)	14 (100)	6 (43)	8 (57)	9 (64)	7 (50)	3 (21)	3 (21)	3 (21)
CCLE	53 (79)	48 (91)	42 (79)	31 (58)	28 (53)	13 (25)	11 (21)	10 (19)	12 (23)	16 (30)

SCLE: Subacute Cutaneous Lupus Erythematosus; CCLE: Chronic Cutaneous Lupus Erythematosus; AA: African American; F: Female; Pr/Cr: Protein/Creatinine ratio; Vit. D Def: Vitamin D Deficiency.

Table 1. Demographics

Table 2: Basic Descriptive Statistics for the Independent Variables:

	N (%)	Estimate change in Vitamin D (ng/ml)	p-value
ANA			
No=0	26 (47)		
Yes=1	29 (53)	3.8	0.14
SSA positive			
No=0	33 (60)		
Yes=1	22 (40)	-5.13	0.05*
C3			
Below 80=1	13 (24)		
Above 80=2	42 (76)	8.24	<0.05**
Protein-Creatinine been considered			
SSA			
No=0	33 (60)		
Yes=1	22 (40)	-6.28	<0.05**
protein-creatinine ratio			
High	14 (25)		
Normal	41 (75)	10.26	<0.05**

** significant based on 0.05 level of significance, * significant based on 0.1 level of significance. C3 measured in mg/dl.

Table 2. Basic Descriptive Statistics for the Independent Variables

SSA and anti-ds DNA positivity, complement 3 (C3) and complement 4 (C4) levels, Protein/Creatinine ratio (Pr/cr) (< 450 mg/g normal), and Vit. D levels (< 12 ng/ml deficiency). 5 of those patients were excluded since not AA and 4 additional for missing data. In analysis including variable "Pr/cr ratio", 4 patients had missing data with a total of 54 patients included. Vit. D value was the dependent variable and the remaining were independent variables. For all variables, we calculated frequency and percentage (Table 1). Fisher's exact test found there was correlation in ANA, SSA, C3, pr/cr ratio in predicting patient's vitamin D. Only these variables were considered for a stepwise linear regression.

Results: Demographic description in Table 1(mean age: 45 yrs.; female: n=56, male = 11). First, we considered the non-stratified group and excluded pr/cr variable. Assuming equal power for all variables a stepwise linear regression predicted the following variables associated with low Vit D: CD3 value < 80 had a decrease in Vit. D level by 8.3 ng/ml compared with CD3 value > 80 ($p < 0.05$); SSA positive, associated with decrease of Vit. D by 5.13 ng/ml compared to SSA negative patients ($p = 0.05$) (Table 2). When data was stratified based SCLE and CCLE (Table 1), only CCLE patients C3 values < 80 had significant association with lower Vit. D by 7.90 ng/ml ($p< 0.05$) (Table 3). There was not significant predictor for SCLE possibly due to small sample size. Finally, adding pr/cr ratio as independent variable to the whole group, SSA positivity, C3 by association and increase pr/cr ratio are significantly associated with low Vit D. When all variables are considered as equal then we can expect patients with increased pr/cr ratio had a decrease in Vitamin D level of 10.26 ng/ml compared with patients whose values are normal ($p < 0.05$).

Table 3: Basic Descriptive Statistics for CCLE Patients

	Estimate change in Vitamin D (ng/ml)	p-value
Gender		
Female		
Male	6.22	0.13
ANA		
No=0		
Yes=1	5.61	0.09*
SSA positive		
No=0		
Yes=1	-6.80	0.06*
C3		
Below 80=1		
Above 80=2	7.90	<0.05**
Protein-Creatinine is considered		
SSA		
No=0		
Yes=1	-6.28	<0.05**
protein-creatinine ratio		
High		
Normal	10.26	<0.05**

** significant based on 0.05 level of significance, * significant based on 0.1 level of significance

Table 3. Basic Descriptive Statistics for CCLE Patients

Conclusion: To the best of our knowledge this is the first AA CLE cohort. Our findings showed decreased C3 levels, SSA positivity and increased pr/cr ratio correlate with Vitamin D deficiency. This association was statistically significant and carries a clinically importance given Vitamin D could be used as a surrogate marker for systemic disease activity in AA with CLE.

Disclosure: I. Robledo-Vega, None; **J. Scheinuk**, None; **E. Pardo**, None; **A. Pratt**, None; **S. Mahato**, None; **A. Chapple**, None; **M. Guevara**, None.

Abstract Number: 1803

Ability of Innate, Adaptive, and TNF-Superfamily Immune Pathways to Characterize Disease Activity and Inform a Refined Lupus Disease Activity Immune in a Confirmatory Cohort of SLE Patients

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic autoimmune disease driven by complex immune dysregulation, involving altered immune mediators and accumulation of autoantibody (AutoAb) specificities. We have previously identified patterns of disordered immunity associated with development of SLE (Munroe et al. Ann Rheum Dis. 2016; Lu et al. J. Autoimmun. 2016). This study seeks to determine an optimal panel of markers that can distinguish those SLE patients with active disease and help to refine a Lupus Disease Activity Immune Index (LDAII).

Methods: We procured 200 samples from 150 patients classified with SLE on dates of low disease scores measured by the hybrid SLEDAI (hSLEDAI) (< 4, range 0-3, n=100) or active disease (≥ 4, range 4-30, n=100). Race/sex/age-matched healthy control (Ctl) samples (n=50) were also evaluated. SLE-linked plasma immune mediators (n = 35) were evaluated by Ella™ microfluidic immunoassay and serum SLE-associated AutoAb specificities, including dsDNA, chromatin, Ro/SSA, La/SSB, Sm, SmRNP, RNP, and ribosomal P, were assessed by Bioplex® 2200 xMAP assay. A subset of 24 log-transformed immune mediators were further evaluated using random forest applied machine learning modeling to determine an optimal subset of mediators to inform the LDAII. The LDAII is the sum of log-transformed, standardized immune mediators, weighted by the Spearman r correlation coefficient of immune mediator levels vs. either hSLEDAI scores or number of SLE-associated AutoAb specificities, which correlates with clinical disease activity (Spearman r = 0.289, $p< 0.0001$).

Results: No difference in age, ethnicity, or sex was noted between low or active clinical disease. After adjusting for multiple comparisons (Bonferroni corrected $p< 0.0021$), IFN-α, IL-2Rα, TNF-α, TNFRII, IP-10, MIG, and IL-10 remained significantly correlated with hSLEDAI scores (Spearman r=0.221-0.388), and 22/35 soluble mediators significantly correlated with accrued SLE-associated autoantibodies, including the top 12 LDAII informative mediators listed in the **Table**. Forward selection of the 24 mediators ranked by variable importance (**Figure [A]**) drew 12 mediators that best distinguished between controls, low disease and active disease (**Table**). These top 12 immune mediators best informed and maximized the performance of a newly refined LDAII (**Figure [B]**). The LDAII, weighted either by hSLEDAI score ($p< 0.0001$) or number of AutoAb specificities ($p=0.0060$), significantly correlated with disease activity in SLE patients and identified patients with renal involvement ($p< 0.01$), where SCF and TNFRII ($p< 0.0001$) were significantly altered. In addition, the LDAII distinguished patients with dsDNA binding and low complement as well as clinically and serologically active vs. quiescent disease states ($p< 0.0001$), differentiated by TNF-α, IL-2Rα, IP-10, and IL-10 levels ($p\leq 0.001$)

Most Informative Soluble Mediators Associated With SLE Clinical Disease Activity

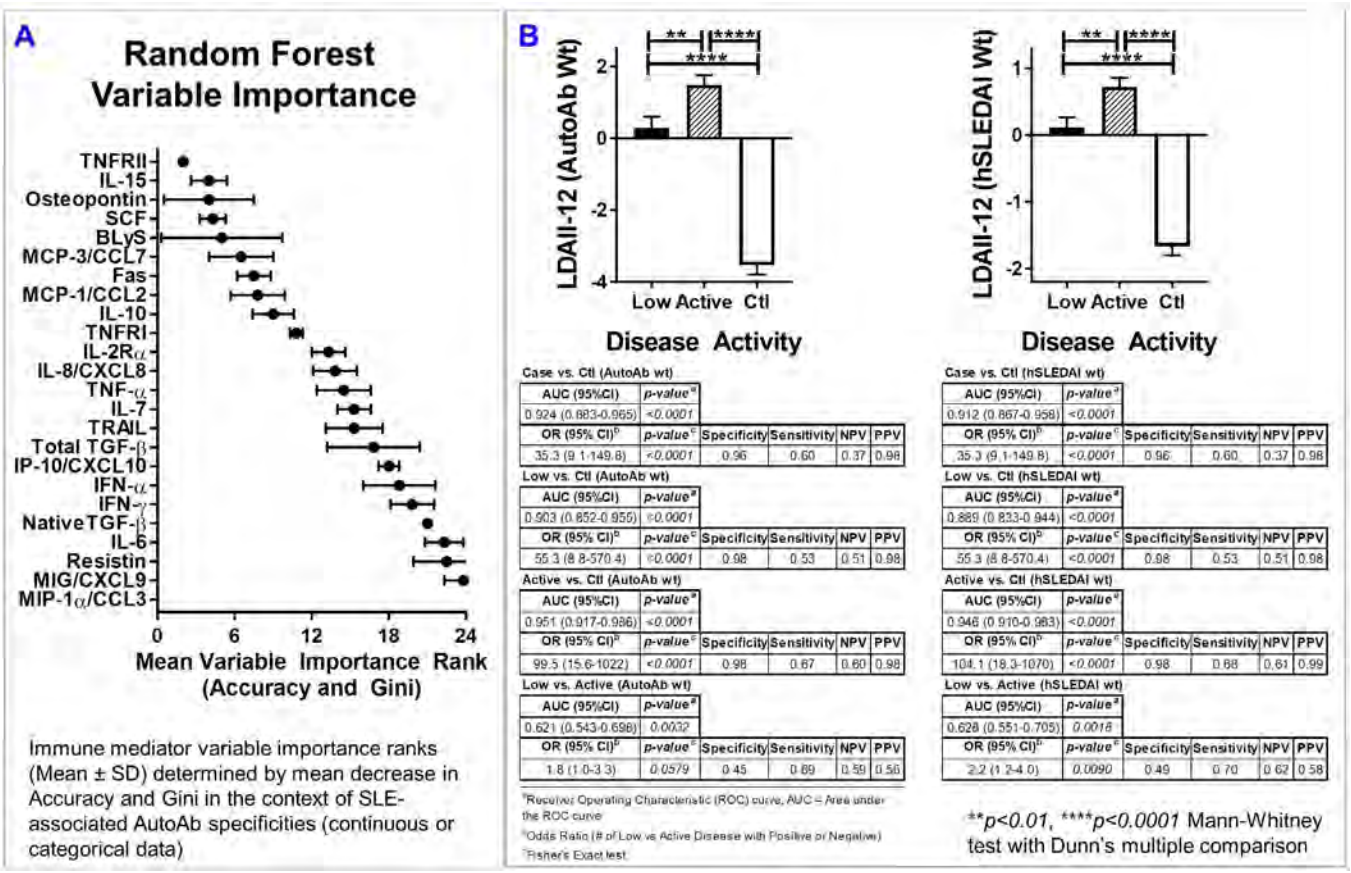
		SLE Patients						Active vs Ctl	Low vs Ctl	Active vs Low	Soluble Mediators vs. # AutoAb Specificities (Cases and Ctls)			Soluble Mediators vs. hSLEDAI Score (Cases)		
Rank	Analyte[a]	Active[b] Mean	SEM	Low[b] Mean	SEM	Ctl Mean	SEM	p-value[c]	p-value[c]	p-value[c]	Spearman r	95% CI	p value[d]	Spearman r	95% CI	p value[d]
1	TNFRII (p75)	4916	328	4592	720	2071	84	***<0.0001***	***<0.0001***	***0.0007***	0.477	0.371 to 0.571	***<0.0001***	0.283	0.149 to 0.409	***<0.0001***
2	IL-15	9.4	2.2	5.3	0.7	2.1	0.2	***<0.0001***	***<0.0001***	*0.1681*	0.477	0.371 to 0.571	***<0.0001***	0.167	0.025 to 0.303	*0.0181*
3	Osteopontin	169844	50532	114957	12278	45203	3485	***<0.0001***	***<0.0001***	*0.0929*	0.346	0.228 to 0.455	***<0.0001***	0.154	0.011 to 0.290	*0.0285*
4	SCF	1565	83	1462	88	875	31	***<0.0001***	***<0.0001***	*0.1515*	0.293	0.171 to 0.407	***<0.0001***	0.096	-0.047 to 0.236	*0.1742*
5	BLyS	1383	94	1208	80	623	21	***<0.0001***	***<0.0001***	*0.0425*	0.487	0.382 to 0.579	***<0.0001***	0.182	0.041 to 0.317	*0.0098*
6	MCP-3/CCL7	19.4	10.9	10.7	4.9	2.9	0.8	***<0.0001***	***<0.0001***	*0.0178*	0.225	0.099 to 0.343	***0.0004***	0.107	-0.036 to 0.246	*0.1303*
7	Fas	15080	517	13676	511	9583	380	***<0.0001***	***<0.0001***	*0.0185*	0.345	0.226 to 0.454	***<0.0001***	0.185	0.043 to 0.319	*0.0088*
8	MCP-1/CCL2	513	65	388	28	195	11	***<0.0001***	***<0.0001***	*0.0350*	0.430	0.318 to 0.418	***<0.0001***	0.155	0.012 to 0.291	*0.0285*
9	IL-10	6.0	0.5	4.5	0.4	1.9	0.1	***<0.0001***	***<0.0001***	***0.0007***	0.494	0.390 to 0.586	***<0.0001***	0.265	0.127 to 0.393	***0.0001***
10	TNFRI (p55)	2124	187	1946	276	961	41	***<0.0001***	***<0.0001***	*0.0067*	0.299	0.177 to 0.412	***<0.0001***	0.197	0.056 to 0.330	*0.0052*
11	IL-2Rα	2127	110	1775	84	1062	54	***<0.0001***	***<0.0001***	***0.0013***	0.441	0.331 to 0.539	***<0.0001***	0.238	0.098 to 0.368	***0.0007***
12	IL-8/CXCL8	22.4	5.5	16.8	5.7	31.6	8.6	*0.0010*	*0.0102*	*0.0344*	0.199	0.072 to 0.319	***0.0017***	0.185	0.043 to 0.319	*0.0087*

[a]Soluble mediator concentration in pg/ml (Mean and SEM) in 200 SLE Cases vs. 50 race/sex/age-matched Healthy Controls (Ctl)

[b]Low = hSLEDAI < 4 (n=100); Active = hSLEDAI ≥ 4 (n=100)

[c]Significance determined by Mann-Whitney test; Bonferroni corrected significance ***p=0.0042***

[d]Spearman correlation, Bonferroni corrected significance ***p=0.0042***



Conclusion: We have refined the LDAII in order to characterize SLE patients with active clinical disease. Treatment to target using a sensitive and objective biologic surrogate for clinical disease activity could help improve disease management and prevent organ damage in SLE.

Disclosure: M. Munroe, Progentec Diagnostics, Inc., 2, 9; **W. DeJager**, None; **S. Macwana**, None; **L. Tran**, None; **J. Guthridge**, None; **E. Jupe**, Progentec Diagnostics, Inc., 3; **D. DeFreese**, Progentec Diagnostics, Inc., 3; **R. Newhardt**, Progentec Diagnostics, Inc., 3; **M. Purushothaman**, Progentec Diagnostics, Inc., 3; **S. Sharma**, Progentec Diagnostics, Inc., 3; **N. Redinger**, None; **T. Aberle**, None; **S. Kamp**, None; **C. Arriens**, BMS, 1, 2, GSK, 1; **E. Chakravarty**, None; **J. Merrill**, Bristol Myers Squibb, 2, 5, GlaxoSmithKline, 2, 5, AstraZeneca, 5, AbbVie, 5, Amgen, 5, Aurinia, 5, EMD Serono, 5, Remegen, 5, Janssen, 5, Provention, 5, UCB, 5; **J. James**, Progentec Diagnostics, Inc., 9.

Abstract Number: 1804

Impact of the Kynurenine/Tryptophan Pathway on Cognitive Dysfunction and Depression in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Tryptophan (TRP) is metabolized to kynurenine (KYN), quinolonic acid [QA, a N-methyl D-aspartate receptor (NMDAR) agonist] and kynurenic acid (KA, an NMDAR antagonist). KYN/TRP pathway stimulation by IFNa may create a potential neurotoxic QA/KA imbalance in SLE. We investigated QA/KA ratios in SLE subjects vs. healthy controls (HC) and their associations with cognition and depression.

Methods: We recruited 74 SLE subjects who met ACR criteria and had no focal neurologic or primary neuropsychiatric (NP) disorders and 74 HC. We assessed cognition and mood with the Automated Neuropsychological Assessment Metrics (ANAM), depression with the Beck Depression Index, and serum levels of KYN, TRP, QA, and KA with HPLC. Exclusion criteria included alcohol or illicit drug abuse, infection, and current narcotic/psychiatric medication use.

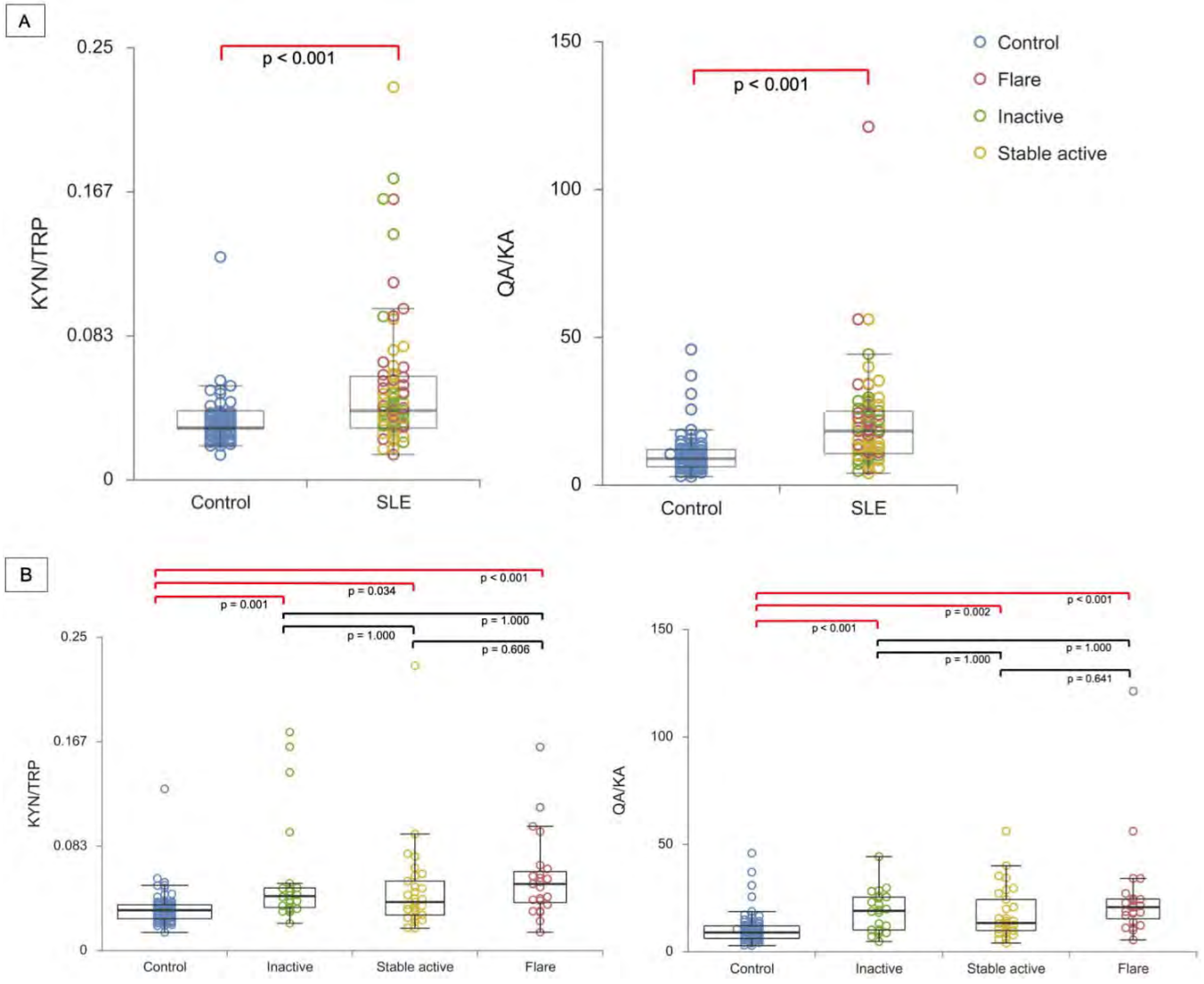

Figure 1. Serum KYN/TRP pathway metabolite ratios in SLE subjects and healthy controls (HC). The serum KYN/TRP and QA/KA ratios measured by HPLC are displayed both in all SLE subjects compared to HC (A) and in SLE subjects grouped by disease activity and HC (B). Circles represent a particular subject, and the color represents the disease activity group of that subject.

Subject Characteristics and NP Performance		SLE (N = 74)	HC (N = 74)	p	Flare (N=23)	Stable Active (N=29)	Inactive (N=22)	p
Age (mean # years +/- SD, range)		37.6 +/- 9.6 (22 – 57)	36.2 +/- 9.4 (18 – 55)	p=0.38	37.3 +/- 10.9 (23 – 57)	38.8 +/- 8.4 (23 – 53)	36.5 +/- 9.8 (22 – 55)	p=0.71
Ethnicity (Hispanic/Latino)		13 (17.6%)	14 (18.9%)	p=0.83	6 (26.1%)	3 (10.3%)	4 (18.2%)	p=0.33
Race	Black	45 (60.8%)	41 (55.4%)	p=0.79	16 (69.6%)	17 (58.6%)	12 (54.5%)	p=0.17
	White	16 (21.6%)	19 (25.7%)		4 (17.4%)	4 (13.8%)	8 (36.4%)	
	Other	13 (17.6%)	14 (18.9%)		3 (13.0%)	8 (27.6%)	2 (9.1%)	
Education Level (mean # years +/- SD, range)		15.7 +/- 2.4 (10 – 22)	16.2 +/- 2.5 (7.5 – 21)	p=0.20	15.6 +/- 2.5 (11 – 20)	15.9 +/- 2.3 (12 – 19)	15.6 +/- 2.6 (10 – 22)	p=0.89
Computer Experience	**Extensive**	**20 (27.0%)**	**34 (45.9%)**	**p=0.02[a]**	7 (30.4%)	7 (24.1%)	6 (27.3%)	p=0.64
	Moderate	41 (55.4%)	35 (47.3%)		11 (47.8%)	19 (65.5%)	11 (50%)	
	Some	**13 (17.6%)**	**5 (6.8%)**		5 (21.7%)	3 (10.3%)	5 (22.7%)	
Employment Status	**Unemployed**	**23 (31.1%)**	**7 (9.5%)**	**p<0.01**	8 (34.8%)	9 (31.0%)	6 (27.3%)	p=0.86
Self-reported cognitive dysfunction		**33 (44.6%)**	**2 (2.7%)**	**p<0.01**	13 (56.5%)	13 (44.8%)	7 (31.8%)	p=0.25
Disease duration Mean +/- SD (range)		12.3 +/- 8.4 (1 – 38)	n/a	n/a	11.2 +/- 8.4 (1 – 35)	12.6 +/- 8.4 (2 – 37)	13.1 +/- 8.7 (2 – 38)	p=0.75
Total SELENA SLEDAI score Mean +/- SD (range)		5.4 +/- 5.0 (0 – 29)	n/a	n/a	**9.7 +/- 6.0 (2 – 29)**	**4.8 +/- 3.1 (0 – 14)**	**1.6 +/- 1.6 (0 – 4)**	**p<0.01[b]**
Prednisone dose (mg/day; median +/- IQR; range)		2.8 +/- 10.0 (0 – 75)	n/a	n/a	**10.0 +/- 30.0 (0 – 75)**	5.0 +/- 10.0 (0 – 60)	**1.0 +/- 5.0 (0 – 10)**	**p=0.01[c]**
Current hydroxychloroquine use		55 (74.3%)	n/a	n/a	18 (78.3%)	23 (79.3%)	14 (63.6%)	p=0.39
Current immunosuppressant use		36 (48.6%)	n/a	n/a	8 (34.8%)	14 (48.3%)	14 (63.6%)	p=0.15
Anti-dsDNA positive (≥ 30 IU/mL)		52 (70.3%)	n/a	n/a	18 (78.3%)	22 (75.9%)	12 (54.5%)	p=0.15
C3 low (< 81 mg/dL)		29 (39.2%)	n/a	n/a	14 (60.9%)	9 (31.0%)	6 (27.3%)	p=0.04[d]
C4 low (< 13 mg/dL)		25 (33.8%)	n/a	n/a	**12 (52.2%)**	10 (34.5%)	**3 (13.6%)**	**p=0.02[e]**
aCL (IgG, IgM, or IgA) positive (≥ 40 MPL)		5 (6.8%)	n/a	n/a	2 (8.7%)	0 (0%)	3 (13.6%)	p=0.14
Platelet count (K/uL), normal range: 150 – 400 Mean +/- SD (range)		286.2 +/- 105.7 (139 – 709)	270.6 +/- 64.2 (172 – 458)	p=0.75	327.7 +/- 203.0 (139 – 709)	271.4 +/- 155.0 (142 – 442)	262.4 +/- 59.4 (161 – 366)	p=0.15
Automated Neuropsychological Assessment Metric								
Simple Reaction Time (SRT) *visuomotor processing speed, simple motor speed, attention*		**363.8 +/- 88.0**	**321.1 +/- 65.4**	**p<0.01**	366.6 +/- 94.4	347.7 +/- 76.8	382.0 +/- 95.0	p=0.41
Matching Grids (MG) *visuospatial processing*		**29.6 +/- 9.9**	**34.0 +/- 11.8**	**p=0.02**	31.1 +/- 11.0	30.0 +/- 10.5	27.5 +/- 7.7	p=0.48
Match to Sample (MTS) *working memory, visuospatial processing*		**25.5 +/- 8.6**	**31.8 +/- 12.0**	**p<0.01**	26.4 +/- 9.6	26.4 +/- 8.5	23.4 +/- 7.5	p=0.46
Running Memory Continuous Performance Task (RMCPT) *vigilance, sustained attention, working memory*		**73.4 +/- 14.7**	**84.0 +/- 15.6**	**p<0.01**	75.7 +/- 14.9	71.6 +/- 16.1	73.3 +/- 12.9	p=0.62
Spatial Processing Simultaneous (SP) *mental rotation, visuospatial skills*		24.0 +/- 7.0	26.3 +/- 8.8	p=0.26	23.7 +/- 5.9	25.3 +/- 7.1	22.6 +/- 7.8	p=0.38
2x2 array **Non-Spatial Memory Test (NSM)** *working memory*		**1.8 +/- 0.6**	**2.1 +/- 0.7**	**p<0.01**	1.7 +/- 0.5	1.9 +/- 0.6	1.8 +/- 0.5	p=0.44
Spatial Memory Test (SM) *spatial memory*		**3.6 +/- 1.1**	**4.3 +/- 1.6**	**p=0.01**	3.6 +/- 1.2	3.7 +/- 1.0	3.7 +/- 1.2	p=0.82
Beck Depression Index (BDI) score, range: 0 – 63; median +/- IQR (range)		**9.0 +/- 12.3 (0 – 44)**	**1.5 +/- 3.0 (0 – 34)**	**p<0.01**	**10.0 +/- 12.0 (0 – 28)**	**10.0 +/- 13.5 (0 – 30)**	**2.5 +/- 8.0 (0 – 44)**	**p<0.01[f]**
# BDI scores > 13 (%)		**19 (25.7%)**	**1 (1.4%)**	**p<0.01**	9 (39.1%)	8 (27.6%)	2 (9.1%)	p=0.07

Table 1 SLE subject and healthy control (HC) characteristics and neuropsychological (NP) test performance. All data is reported either as a mean (or median where indicated) +/- standard deviation (or interquartile range), or as a frequency (%). All data refers to that which was collected at the time of evaluation. Data comparing SLE and HC, as well as comparisons among SLE disease activity groups, are displayed. a. Extensive and Some (p=0.009) b. Flare and Inactive (p=0.000), Flare and Stable Active (p=0.000), Stable Active and Inactive (p=0.019) c. Flare and Inactive (p=0.004) d. No significant differences among groups after correction for multiple comparisons e. Flare and Inactive (p=0.006) f. Flare and Inactive (p=0.002), Stable Active and Inactive (p=0.029)

Variables with a Significant, Negative Impact on Test Performance	Individual Cognitive Tests#						
SLE and HC combined	**SRT**	**MG**	**MTS**	**RMCPT**	**SP**	**NSM**	**SM**
Age	X**	X**	X**	X**	X*	X**	X**
Black race (versus White or Other)	X*	X**				X**	X**
Anger score			X**	X**		X**	X**
History of psychiatric illness requiring medication			X**	X**		X*	
SLE (versus HC)	X*			X*			
Decreased computer experience (versus extensive)						X**	X**
SLE only							
Age		X**	X**	X**			X*
History of psychiatric illness requiring medication	X**		X*	X**		X**	
Increased platelet count	X*	X**			X*		
History of peripheral thrombosis		X*	X*				
Anxiety score				X**	X**		
Decreased computer experience (versus extensive)						X**	X**
QA/KA ratio			X*				

Table 2 Results of multivariable analysis to determine predictors of neuropsychological test performance. Results of multivariable models that included all subjects ("SLE and HC combined," top section) and those that included only SLE subjects ("SLE Only," bottom section) are displayed. Variables with a significant, negative impact on a particular ANAM test (see Table 1) are indicated with an "X." The Spatial Processing (SP) test column is grayed-out since SLE subjects did not perform significantly worse than HC on this test. # All of the test scores were significantly lower in SLE compared to HC except for the Spatial Processing test (SP) *p<0.05 **p<0.01

SLE disease activity (DA) was defined as Inactive [clinical SLEDAI=0 and PGA≤0.5 and prednisone≤10 mg, and lack of flare on the SELENA-SLEDAI Flare Index]; Stable Active (clinical SLEDAI >0 or PGA >0.5 or prednisone >10 mg and lack of flare) or Flare (mild/moderate or severe flare on the Flare Index). We assessed differences in demographic and clinical characteristics, NP test scores, and KYN/TRP pathway metabolites between SLE and HC and among the SLE DA groups, and the association of variables with NP performance (Spearman's correlation/t-test/Mann-Whitney/ANOVA/Kruskal-Wallis/chi square/Fisher's exact test). Multivariable modeling was used to assess the impact of variables on NP task performance in SLE and HC combined, and SLE only; variables on univariate screen ($p< 0.1$) were included.

Results: There were no demographic or educational differences in SLE vs. HC. SLE subjects performed worse than HC on all behavioral tasks and most cognitive tests (Table 1). Among SLE, there was a significant positive correlation between SLEDAI and MTS scores ($r = 0.236$, $p=0.04$), SLE with active disease had higher depression scores vs. Inactive ($p< 0.01$) and Inactive trended towards worse scores on most cognitive tests vs. Flare. Prednisone dose did not associate with cognitive or depression scores. Serum KYN/TRP and QA/KA ratios were elevated in SLE vs. HC ($p< 0.01$) (Fig. 1A), and there were no differences in either ratio among SLE DA groups (Fig. 1B). In SLE and HC combined, elevated QA/KA significantly correlated with increased SRT ($r = 0.217$, $p< 0.01$), poor performance on MTS ($r = -0.307$, $p< 0.01$) and RMCPT ($r = -0.311$, $p< 0.01$), and with higher depression scores ($r = 0.335$, $p< 0.01$) (Table 1). In SLE alone, an elevated QA/KA correlated with poor performance on MTS ($r = -0.237$, $p=0.04$), and trended towards slightly higher odds of depression (OR = 1.03, 95% CI=0.99-1.06, $p=0.09$). Multivariable modeling revealed that the QA/KA ratio negatively impacted MTS scores (Table 2), while increased SLEDAI had a positive impact.

Conclusion: Elevated serum KYN/TRP and QA/KA ratios indicate KYN/TRP pathway activation in SLE. Surprisingly, DA associated with improved cognitive performance. An increased QA/KA ratio, after controlling for other factors, associated with poor cognitive performance on a working memory task, supporting its further study as a potential biomarker for SLE-related cognitive dysfunction.

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Abstract Number: 1805

Longitudinal Analysis of IFN Status and Disease Characteristics in SLE

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
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Session Time: 9:00AM–11:00AM

Background/Purpose: The type 1 interferon (IFN) cytokine family is key to the pathogenesis of SLE, evidenced by the expression of IFN stimulated genes (ISGs) in most patients. Phenotypic differences between SLE patients who express ISGs (IFN high) and those who do not (IFN low) are not well understood. With the emergence of IFN blocking drugs, it is important to examine the clinical utility of IFN status testing. We report the results of longitudinal analysis of IFN and clinical status in SLE.

Methods: 205 patients meeting ACR criteria for SLE were recruited at a tertiary centre where extensive clinical data are collected prospectively on consenting subjects. Whole blood RNA samples were collected in PAXgene tubes. IFN status was determined using the IFN module from Modular Immune Profile Test (DxTerity Diagnostics).

Results: 729 results (205 patients, 142 with longitudinal samples) were analysed. At baseline, 62.9% of patients were IFN high, 30.2% IFN low and 6.8% borderline. Compared to IFN low patients, IFN high were more likely to be of Eastern Asian ethnicity (45.0 vs 25.8%, p = 0.01), were younger at SLE onset (median [IQR] 27[18-35] vs 33 [25-47] years, p = 0.0001), and were more likely to be positive for anti-Ro (65.3 vs 34.7% p = < 0.0001), anti-La (29.2 vs 11.3% p = 0.01) and anti-RNP (36.1% vs 15.1% p = 0.007) antibodies. In patients with multiple samples, 87.3% had stable ISG status. In longitudinal follow up (median 630 [459-707] days), IFN high patients had higher disease activity (median [IQR] time adjusted mean SLEDAI2K (4.2 [2.8-5.7] vs 2.0 [1.3-4.2], p=< 0.0001), more flares (mild/moderate 53.5 vs 25.8%, p = 0.0003; severe 26.4 vs 6.5%, p = 0.0009) and spent less observed time in lupus low disease activity state (LLDAS) (median 55.5% [26.3-85.5] vs 84.0 [53.0-100]%, p = 0.0003). IFN high patients were more likely to have active arthritis (21.7 vs 6.5%, p = 0.007), skin disease (38.8 vs 14.5%, p = 0.007), leukopenia (26.4 vs 6.5%, p = 0.0009) and haematuria (20.2 vs 8.1%, p = 0.03). More IFN high patients required DMARD therapy (74.6 vs 55.9%, p = 0.02) and IFN high patients had higher prednisolone exposure (median time-adjusted mean dose 1.7 [0-5.7] vs 0.0[0-2.9] mg, p = 0.004). There was no difference in overall SLICC damage index, however there were differences in damage domains. IFN low patients had more malignancy (11.6 vs 2.4%, p = 0.01) and diabetes (13.3 vs 1.6%, p = 0.002). IFN high patients trended towards more mucocutaneous damage (19.2 vs 8.3%, p=0.08). However, in individual patients, there was no association between ISG level and any disease activity marker over time.

Of 18 patients with varying IFN status over time, 12 had ISG fluctuations that were < 2SD from the mean fluctuation seen in stable ISG patients. Of the remaining 6 patients with larger ISG fluctuations, 5 had high dose (≥25mg) prednisolone or cyclophosphamide therapy temporally associated with ISG reduction.

Conclusion: IFN high SLE patients had significantly more disease activity than IFN low patients. They were more likely to be of Asian than Caucasian ethnicity, had younger onset of disease and displayed more auto-antibodies.

The majority of patients had stable IFN status, and major changes in ISG expression related to high dose immunosuppression.

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Abstract Number: 1806

The Association of Interferon-α with Kynurenine/Tryptophan Pathway Activation in Systemic Lupus Erythematosus

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Background/Purpose: Type I IFN contributes to SLE pathogenesis and stimulates the kynurenine/tryptophan (KYN/TRP) pathway, producing elevated quinolinic acid (QA) levels relative to kynurenic acid (KA) and thus creating a potential neurotoxic imbalance. We found that SLE subjects have elevated KYN/TRP and QA/KA ratios vs. healthy controls (HC), and that the QA/KA ratio correlated with poor working memory performance after controlling for other factors (submitted abstract). We hypothesized that peripheral blood interferon stimulated gene (ISG) expression would associate with QA/KA ratios in these same subjects.

Figure 1. Principal component analysis (PCA) of gene expression in SLE compared to healthy controls (HC). PCA conducted on DESeq2 normalized and variance stabilized gene expression values using the function prcomp in R version 3.5 is displayed[1]. The default top 500 most highly variant genes were selected. 1. Kolde, R., 2012 Package 'pheatmap'. Bioconductor 1–6. Available at: https://CRAN.R-project.org/package=pheatmap

Table 1 Subject Characteristics		SLE (N = 72)	HC (N = 73)	*p*
Age (mean # years +/- SD, range)		37.9 +/- 9.6 (22 – 57)	36.2 +/- 9.5 (18 – 55)	0.28
Ethnicity (Hispanic/Latino)		13 (18.1%)	13 (17.8%)	0.97
Race	Black	43 (59.7%)	41 (56.2%)	0.91
	White	16 (22.2%)	18 (24.7%)	
	Other	13 (18.1%)	14 (19.2%)	
Self-reported cognitive dysfunction (memory loss, forgetfulness, and/or difficulty concentrating)		**32 (44.4%)**	**2 (2.7%)**	**<0.01**
QA/KA ratio Median +/- IQR (range)		**18.4 +/- 14.7** **(4.0 - 121.2)**	**8.9 +/- 5.8** **(2.9 - 45.9)**	**<0.01**
KYN/TRP ratio Median +/- IQR (range)		**0.04 +/- 0.03** **(0.01 - 0.23)**	**0.03 +/- 0.01** **(0.01 - 0.13)**	**<0.01**
Disease duration Mean +/- SD (range)		12.3 +/- 8.5 (1 – 38)	n/a	n/a
SELENA SLEDAI score Mean +/- SD (range)		5.4 +/- 5.1 (0 – 29)	n/a	n/a
Prednisone dose (mg/day; median +/- IQR, range)		2.5 +/- 10.0 (0 – 75)	n/a	n/a
Current hydroxychloroquine use		54 (75.0%)	n/a	n/a
Current immunosuppressant use		34 (47.2%)	n/a	n/a
Anti-dsDNA positive (> 29 IU/mL)		50 (69.4%)	n/a	n/a
C3 low (< 81 mg/dL)		28 (38.9%)	n/a	n/a
C4 low (< 13 mg/dL)		24 (33.3%)	n/a	n/a

Table 1. SLE subject and healthy control (HC) characteristics and KYN/TRP pathway metabolite ratios. All data is reported either as a mean (or median where indicated) +/- standard deviation (or interquartile range), or as a frequency (%). All data refers to that which was collected at the time of evaluation.

Methods: We measured ISG expression (whole blood RNA sequencing) and serum levels of KYN, TRP, QA, and KA (HPLC) in 72 SLE subjects and 73 HC. ISG were identified based on published gene sets, and the Interferome database.[1, 2] IFN scores were derived for each subject to quantify individual ISG expression and analyze associations with metabolite ratios. Since it is unknown which ISG contribute most to an "IFN signature," we used 4 approaches to define IFN scores (Table 2). Expression was measured by fold change (FC) relative to HC, a point system for FC, or z-scores. Differences in characteristics and metabolite ratios in SLE vs. HC were assessed (t-test, Mann-Whitney, or chi square), and Spearman's correlations were determined between metabolite ratios and IFN scores among SLE subjects; significance was set at $p < 0.05$.

Results: There were no demographic differences between SLE and HC, and SLE subjects had higher median metabolite ratios (Table 1). There were 933 genes that had ≥2-fold differential expression in SLE vs. HC ($p < 0.05$). Of 110 ISG reported by Arazi et al, 108 had ≥2-fold higher expression in SLE vs. HC. Unsupervised principal component analysis (PCA) distinguished SLE from HC (Figure 1); of the top 100 most variant genes, 70 were ISG. IFN scores, based on the first 3 objective approaches, correlated with KYN/TRP but not with QA/KA ratios (Table 2). However, 82 of the 933 differentially expressed genes correlated with QA/KA ratios ($p < 0.05$), and 38 (46%) were ISG; 31/38 (82%) of these were type I responsive ISG. A Targeted IFN score (approach 4a) using these 38 ISG correlated with QA/KA and

Approach		IFN score method	KYN/TRP	p	QA/KA	p
1		FC	r = 0.269	0.022	r = 0.080	0.504
		Adjusted FC	r = 0.271	0.021	r = 0.080	0.502
		Z-score	r = 0.271	0.021	r = 0.062	0.607
2		FC	r = 0.252	0.033	r = 0.085	0.479
		Adjusted FC	r = 0.248	0.035	r = 0.084	0.482
		Z-score	r = 0.226	0.056	r = 0.060	0.617
3		FC	r = 0.272	0.021	r = 0.106	0.375
		Adjusted FC	r = 0.266	0.024	r = 0.102	0.394
		Z-score	r = 0.294	0.012	r = 0.120	0.314
4	a. Targeted IFN score (38 genes*)	FC	r = 0.278	0.018	r = 0.453	<0.001
		Adjusted FC	r = 0.294	0.012	r = 0.460	<0.001
		Z-score	r = 0.296	0.012	r = 0.447	<0.001
	b. Targeted-Modular IFN score (CCL8, CXCL10, LAP3)	FC	r = 0.253	0.032	r = 0.433	<0.001
		Adjusted FC	r = 0.245	0.038	r = 0.410	<0.001
		Z-score	r = 0.234	0.048	r = 0.418	<0.001

Table 2. Correlations Between IFN Scores, Defined by 4 Approaches, and KYN/TRP Pathway Metabolite Ratios in SLE subjects. Approach 1 derived an IFN score from the 70 ISG that were in the top 100 most variably expressed genes between SLE and HC determined by PCA, Approach 2 included all of the 110 ISG reported by Arazi et al in their single cell RNA sequencing analysis of IFN response in infiltrating cells in lupus nephritis, and Approach 3 included 19 ISG from the 110 ISG included in Approach 2 that are more responsive to type I IFN than type II IFN, according to the Chiche et al modules of co-expressed ISG. Approach 4a included ISG that had significant, positive correlations with the QA/KA ratio, and 4b included 3 ISG from 4a that were also included in the 110 Arazi ISG set and in the Chiche modules and are associated with neuroinflammation.[1, 2] Scores were computed using fold change (FC) relative to HC, adjusted FC (point system) and z-scores. Spearman's correlation coefficients (r) are shown between each IFN score (grouped by approach, and the method used to compute the score) and the metabolite ratios. Significant correlations are highlighted in red. *Refers to the 38 ISG that had a significant, positive correlation with the QA/KA ratio in SLE subjects 1. van Weering, H.R., et al., CXCL10/CXCR3 signaling in glia cells differentially affects NMDA-induced cell death in CA and DG neurons of the mouse hippocampus. Hippocampus, 2011. 21(2): p. 220-32. 2. Banisor, I., et al., Involvement of beta-chemokines in the development of inflammatory demyelination. J Neuroinflammation, 2005. 2(1): p. 7.

KYN/TRP ratios (Table 2). A separate Targeted-Modular IFN score comprised of 3 type I ISG (CCL8, CXCL10, LAP3) included in published ISG sets and associated with neuroinflammation, also correlated with both ratios (Table 2, 4b).

Conclusion: This is the first study in SLE subjects to demonstrate an association between ISG expression, KYN/TRP pathway activation, and an elevated QA/KA ratio. The targeted IFN scores need validation in a separate cohort to justify their utility as a biomarker for IFN-mediated KYN/TRP pathway activation, and their potential use in measuring success of anti-IFN therapies in SLE to ameliorate a potential neurotoxic QA/KA imbalance.

References

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Abstract Number: 1807

The Extent of Tubulointerstitial Inflammation in Lupus Nephritis Identifies Two Distinctive Subgroups: Impact on Inflammation Characteristics and Prognosis in Patients with Lupus Nephritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
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Background/Purpose: Lupus nephritis is common clinical manifestation and contributes significantly to mortality in systemic lupus erythematosus (SLE).

Recently several studies has been reported that severity of tubulointerstitial inflammation (TII) is associated with subsequent renal failure. However, it has not yet been reported histologic characteristics and prognosis by extent of TII in patients with lupus nephritis who had conventional treatment.

Methods: Ninety-four patients with lupus nephritis, who had conventional treatment and renal biopsy, were enrolled in this study. The extent of tubulointerstitial lymphocytic infiltrates was semi-quantitated (grade 1-4) using standard histochemical staining. Quantified apoptotic regulator protein, the B cell lymphoma 2 protein (Bcl-2), expressions in selected lymphocyte subsets were measured using novel computational approaches when applied to multicolor confocal images. Histologic characteristics and prognosis as well as clinical and laboratory characteristics were compared between mild (grade 1-2) and severe (graded 3-4) TII. Follow-up datas were obtained and survival analysis was carried out to determine.

Results: TII was a common pathologic finding, 61.7% percent of biopsy samples were graded as 1, 13.8% as 2, 14.9% as 3, and 9% as 4. When TII was divided into mild (grade 1-2) and severe (grade 3-4), patients with severe TII were significantly higher in serum creatinine, but not with double-stranded DNA (ds DNA) antibodies, serum complement 3/4, SLE disease activity (SLEDAI) and degree of proteinuria at the time of biopsies. Expression of bcl-2 and bcl-2 in CD4 positive cells were significantly higher in severe TII compared to in mild TII in lupus nephritis (p=0.040 and p=0.003, respectively) while those were not significant in IgA vasculitis. The mean follow-up time was 150.3 ± 7.0 months and overall, 9 patients died as a result of disease progression (n=6) and infection (n=3). Patients with severe TII were at greater risk for renal failure compared to those with mild TII (p=0.001). However, both glomerular proliferation and laboratory markers including baseline ds DNA, complement, SLEDAI and degree of proteinuria did not affect on long term renal failure. After multivariate logistic analysis including age and sex, severe TII provided poor prognostic information for renal failure (hazard ratio 4.5, 95% confidence interval 1.4–14.5; p = 0.011).

Conclusion: A significantly higher elevated bcl-2, especially in CD4 positve cells, was found in severe TII compared to mild TII in lupus nephritis whereas there was comparable bcl-2 expression in IgA vasculitis irrespective of inflammation extent. TII severity was independent predictor for a worse outcome in lupus nephritis patients with conventional treatment.

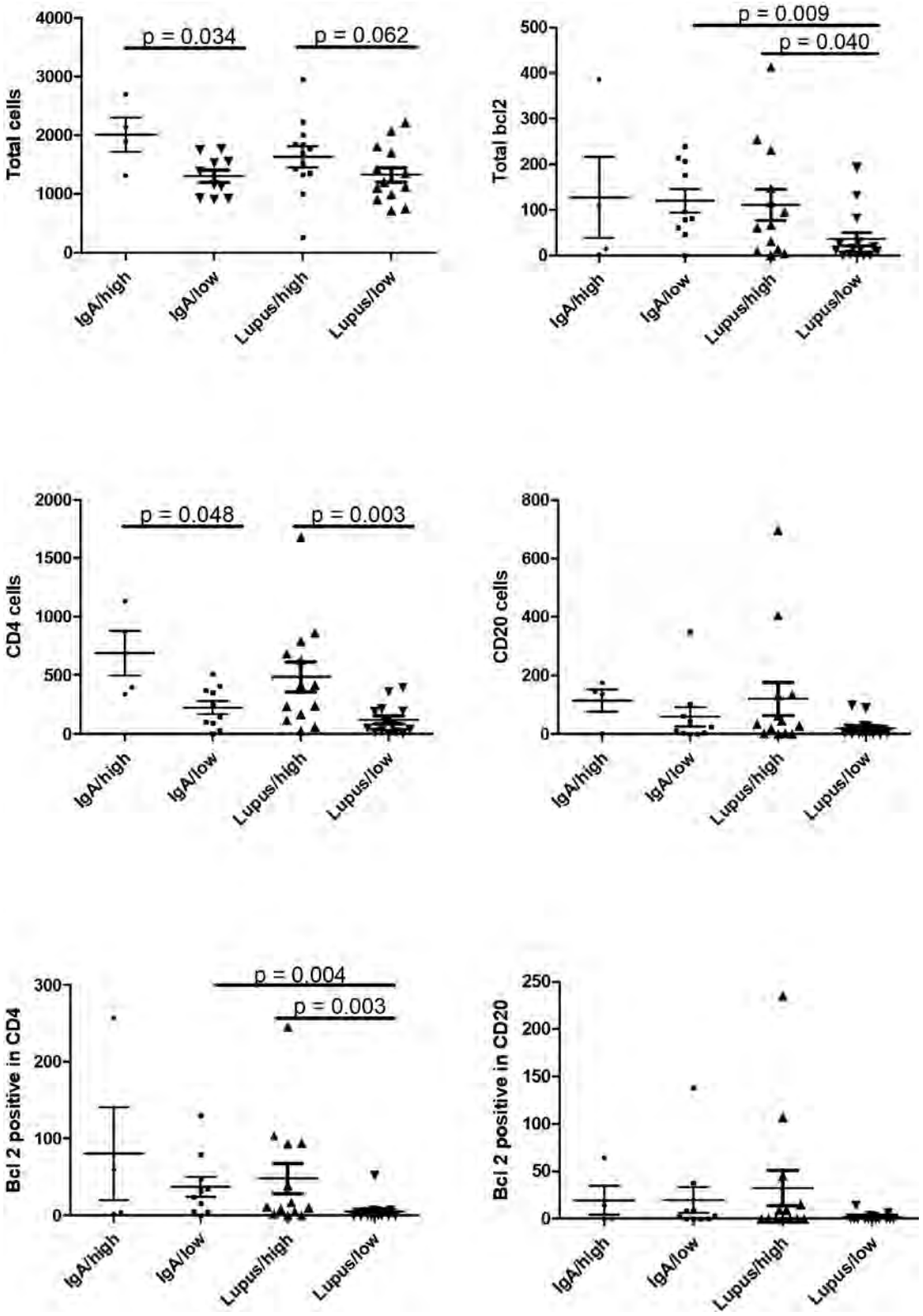

Figure 1

Disclosure: S. Lee, None; **E. Nam**, None; **M. Han**, None; **Y. Kim**, None.

Abstract Number: 1808

Erythrocyte Complement Receptor 1 (ECR1) and Erythrocyte Bound C4d (EC4d) Associate with Adverse Pregnancy Outcomes and Preeclampsia in Pregnant Women with Systemic Lupus Erythematosus (SLE)

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Background/Purpose: Despite improvement in management and outcomes of pregnancies complicated by SLE, the risk of adverse events and preeclampsia (PE) continues to exceed that of healthy women. Activation of the complement system has been associated with adverse pregnancy outcomes (APO). This study extends prior observations and addresses whether detection of erythrocyte complement receptor 1 (ECR1) and C4d bound to erythrocytes (EC4d) predict APO

Methods: Pregnant women fulfilled ACR or SLICC criteria for SLE. Serum complement proteins C3 and C4 were measured by immunoturbidimetry and anti-dsDNA by ELISA. ECR1 and EC4d were measured by quantitative flow cytometry and are expressed as net mean fluorescence intensity (MFI). Disease activity was evaluated by the SLE Pregnancy Disease Activity Index (SLEPDAI) and the physician global assessment (PGA on a 0 to 3 scale) without knowledge of study analytes. Statistical analysis consisted of t-test and determination of diagnostic odds ratio (DOR) to evaluate association of inflammatory biomarkers (including ECR1 and EC4d) with APO (defined as neonatal death, pre-term delivery [< 36 weeks due to placental insufficiency], < 5th percentile for gestational age [SGA]) and PE at any time.

Results: A total of 51 women (33% white, 27% black, 18% Asians, 18% Hispanics, 4% of other races) had a total of 56 pregnancies (mean age 32 years, range 17 to 42) and 168 visits (median=3) during their pregnancy (n=34, 59, and 49 in first, second, and third trimesters, respectively) or postpartum period (n=26). The average SLEPDAI was 2.8, 3.5, and 2.9 in first, second, and third trimesters, respectively and PGA was 0.39, 0.54, and 0.40. APO and PE data are reported in the **Figure**. Overall 22% of pregnancies resulted in an APO. Specifically, 12 pregnancies resulted in a total of 19 APO (3 neonatal deaths; 8 births < 36 weeks [range 25 – 35.9 weeks] and 8 SGA). Eleven pregnancies in 10 women resulted in PE. ECR1, EC4d, and C4 were significantly associated with APO when all visits that occurred during pregnancy (n=142) were analyzed. ECR1 and EC4d also associated with PE. Anti-dsDNA and C3 were not associated with any of these outcomes (**Table; top**). Analysis of the individual APO showed that ECR1 was associated with preterm delivery (**Table; top**). For preterm delivery, area under the receiver operating characteristic curve of ECR1 was 0.697 (95% CI: 0.585-0.808). At ECR1 < 5.5 net MFI (optimum cutoff), sensitivity and specificity were 72% and 79%, respectively (Youden index = 0.51). Low ECR1 (< 5.5 net MFI) remained significant for preterm delivery when only baseline visits that occurred in the first trimester (n=32 visits with 7 pregnancies experiencing 9 APO) were analyzed (DOR = 30.67) (**Table; bottom**).

Conclusion: This prospective study demonstrates that low ECR1 and elevated EC4d are associated with APO and late PE in SLE pregnancies. Of the traditional biomarkers in SLE (C3, C4, dsDNA) only low C4 associated with APO.

TOP

All visits that occurred at any time during pregnancy (n=142)						
	APO		Preeclampsia (PE)		Preterm delivery (<36 weeks)	
Marker	T-Test (p)	DOR [95% CI]	T-Test (p)	DOR [95% CI]	T-Test (p)	DOR [95% CI]
ECR1 (net MFI; < 5.5 net MFI)	**<0.01**	5.27 [2.27, 12.26]	**0.01**	4.91 [2.17, 11.13]	**<0.01**	9.54 [3.57, 25.47]
EC4d (net MFI; > 14 net MFI)	**0.04**	1.89 [0.80, 4.46]	**<0.01**	2.72 [1.13, 6.56]	0.11	0.96 [0.39, 2.32]
C3 (mg/dL; < 81.1 mg/dL)	0.99	1.29 [0.32, 5.17]	0.43	1.17 [0.29, 4.71]	0.19	1.84 [0.45, 7.51]
C4 (mg/dL; < 12.9 mg/dL)	**0.03**	1.30 [0.51, 3.29]	0.91	0.72 [0.27, 1.96]	0.48	2.02 [0.77, 5.33]
Anti-dsDNA (units; > 301 Units)	0.79	1.16 [0.52, 2.60]	0.92	1.03 [0.46, 2.27]	0.85	0.96 [0.39, 2.37]

BOTTOM

Pregnancies for whom the first study visit occurred in the first trimester (n=32)						
	APO		Preeclampsia (PE)		Preterm delivery (<36 weeks)	
Marker	T-Test (p)	DOR [95% CI]	T-Test (p)	DOR [95% CI]	T-Test (p)	DOR [95% CI]
ECR1 (net MFI; < 5.5 net MFI)	0.09	9.33 [1.36, 63.96]	0.58	3.75 [0.59, 23.66]	**<0.01**	30.67 [2.52, 373.55]
EC4d (net MFI; > 14 net MFI)	0.32	1.79 [0.29, 11.13]	0.15	5.08 [0.53, 48.86]	0.41	0.94 [0.13, 6.63]
C3 (mg/dL; < 81.1 mg/dL)	0.85	0.50 [0.05, 5.04]	0.88	0.50 [0.05, 5.04]	0.80	0.83 [0.08, 8.95]
C4 (mg/dL; < 12.9 mg/dL)	0.14	0.80 [0.13, 5.07]	0.32	0.28 [0.03, 2.70]	0.17	0.47 [0.05, 4.88]
Anti-dsDNA (units; > 301 Units)	0.78	0.56 [0.09, 3.49]	0.67	0.56 [0.09, 3.49]	0.75	0.34 [0.03, 3.49]

Table. T-test and diagnostic odds ratio (DOR) of complement markers (EC4d, ECR1, serum C3, and serum C4) and anti-dsDNA to evaluate association and prediction of APO, preeclampsia (PE) and preterm delivery. Data of all visits during pregnancy (post-partum visits excluded, n=142; TOP) and of baseline visits that occurred in the first trimester (n=32; BOTTOM) were analyzed. Two women had 2 visits each in the first trimester; thus, there was a total of 34 visits in the first trimester, of which 32 were baseline. Note that some patients had baseline visits after the first trimester. For t-test, continuous variables were analyzed, while variables were considered positive or negative (based on the cutoffs indicated in the table) for DOR calculation. DOR is reported with 95% confidence intervals [95% CI]. Significant p values (<0.05) are bolded.

Importantly, low ECR1 early in pregnancy predicted preterm delivery and, to a lesser extent, other APO. In conclusion, complement activation as measured by EC4d and ECR1 may be a predictor of pregnancy complications.

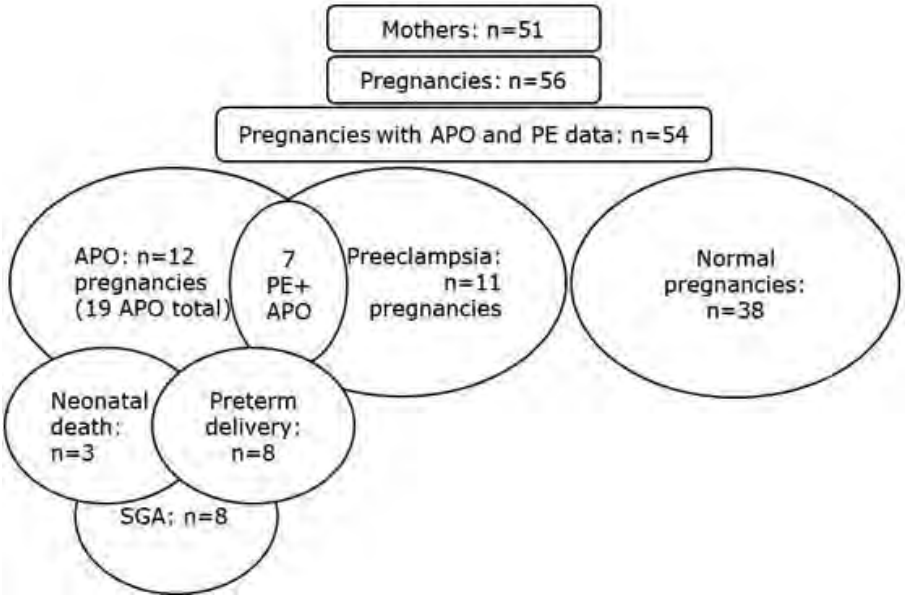

Figure. Flowchart of the patient population

Disclosure: J. Buyon, Exagen Diagnostics, 1; **J. Conklin**, Exagen, 1, 2; **M. Golpanian**, None; **J. Ligayon**, Exagen Inc, 1; **T. Dervieux**, Exagen, 1, Exagen, 1; **P. Izmirly**, None; **H. Belmont**, Exagen Inc, 8; **J. Salmon**, UCB, 1, 2, BMS, 1, 2, Abbott, 1, Pfizer, 1, Johnson & Johnson, 1, Lilly, 1, Merck, 1, Regeneron, 1; **R. Alexander**, Exagen Inc, 1.

Abstract Number: 1809

Serum Cytokine Profiling in Systemic Lupus Erythematosus, Analysed Using Unsupervised Machine Learning, Reveals Clinically Relevant Clusters

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is a heterogeneous disease, where a better understanding of molecular differences between patients is needed in order to direct therapy. Existing approaches generally examine mRNA expression, whereas therapeutic targets are mostly soluble or cellular proteins. We aimed to evaluate whether a serum cytokine proteomic profile of SLE patients analysed using an unbiased approach would yield clinically meaningful results.

Methods: Demographic and clinical data of SLE patients (ACR criteria) including disease activity (SLEDAI2K) and organ damage (SLICC Damage Index (SDI)), and matching serum samples, were collected prospectively. A wide-angled serum cytokine proteomics analysis was conducted using Quantibody, Luminex, and ELISA platforms. To reduce heterogeneous data complexity and remove redundant variables, unsupervised feature selection methods were

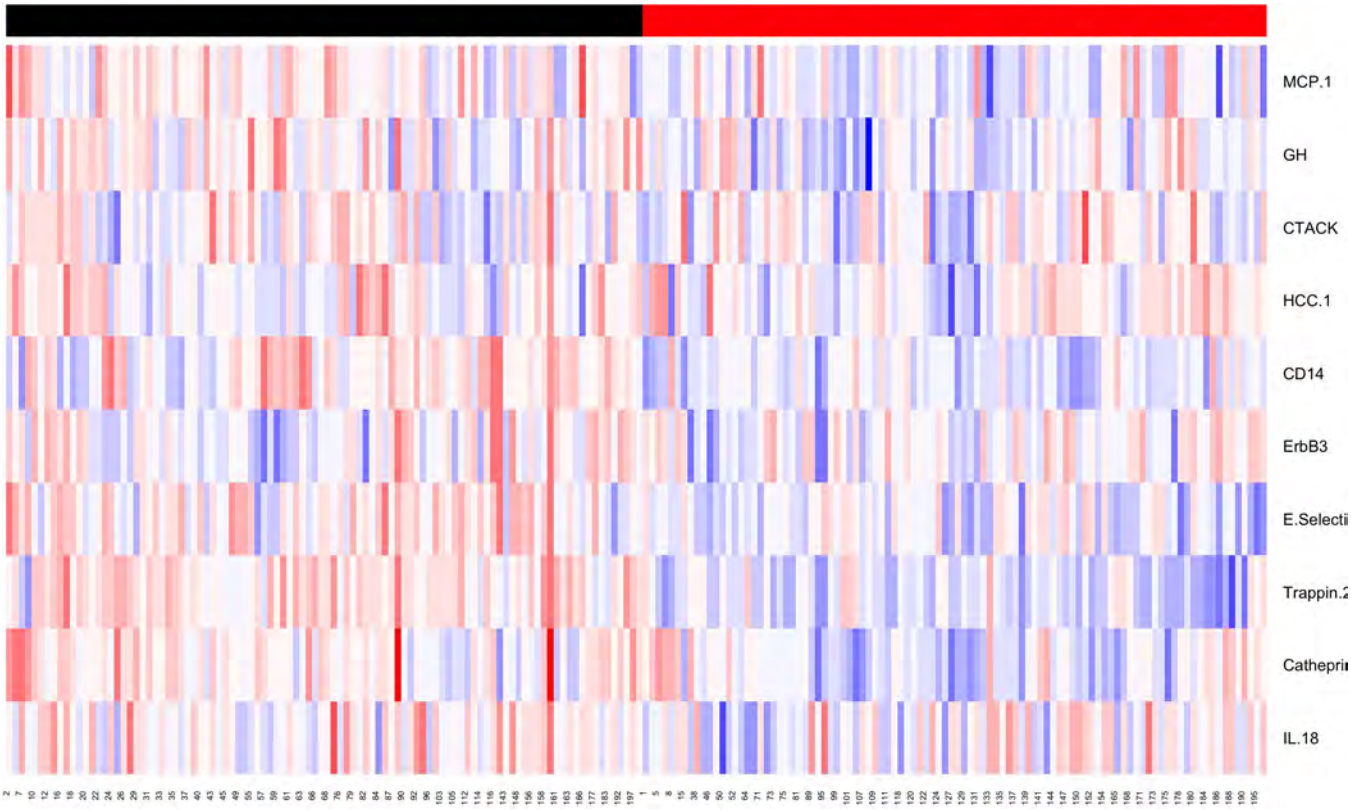

Figure 1. Heat map of 10 analytes, selected using unsupervised feature selection on 211 analytes measured in healthy subjects and SLE patients and clustered using k-means techniques, in SLE patients (n=198). Two clusters (indicated by red or black on top row) were identified in SLE.

applied. For clustering, machine learning approaches were used, and optimal cluster number confirmed by consensus clustering.

Results: 198 SLE patients (median [IQR] age 46.7 [36.7, 56.3] years, 88.4% female, median SLEDAI2K 4 [2, 6], 52.5% with organ damage) and 37 sex/ethnicity-matched healthy subjects were recruited. 211 serum analytes were measured. Using unsupervised feature selection methods, we identified a reduced set of 10/211 analytes (MCP-1, GH, CTACK, HCC-1, CD14, ErbB3, E-Selectin, Trappin-2, Cathepsin S and IL-18). The dataset was then clustered, according to the analytes that remained after feature selection, using unsupervised machine learning approaches. k-means analysis produced a distinct result in terms of separability of two clusters that associated only in SLE (**Figure 1)**, and was chosen as the final clustering algorithm. We analysed clinical parameters in patients categorised by these biomarker clusters, and found the clusters differed in clinical characteristics including organ damage (P = 0.04), proportion of patients with high ESR (P = 0.03), and SLEDAI2K (P = 0.08). Using multivariable linear regression models, cross-sectional associations with patient clinical characteristics were found for 8/10 analytes. We next assessed associations of baseline analytes with longitudinal disease outcomes, using multivariable logistic regression models. Trappin-2 and IL-18 were significantly associated with damage accrual. IL-18 and CTACK had positive and negative associations respectively with lupus low disease activity state (LLDAS) attainment, and converse associations with indices of active disease over time.

Conclusion: Unsupervised analytics of wide-angle serum cytokine profiles in SLE yielded a tractable reduced analyte set, which in turn revealed two biologically distinct clusters of patients who had significant differences in clinical profile, individual analytes from which were associated with longitudinal outcomes. These findings indicate the potential for biological subsets of SLE to be based on serum cytokine profiling.

Disclosure: F. Vincent, None; **J. Ong**, None; **A. Hoi**, None; **S. Boyd**, None; **H. Nim**, None; **E. Morand**, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, 5, Merck Serono, 2, 5, Neovacs, 5, Sandoz, 5, Novartis, 8, AbbVie, 5, Amgen, 5, Biogen, 5.

Abstract Number: 1810

Complement Activation in Systemic Lupus Erythematosus Patients with Low Disease Activity Is Not Inhibited by Hydroxychloroquine

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
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Background/Purpose: Mortality in patients with systemic lupus erythematosus (SLE) is significantly higher than in the general population. Treatment of SLE patients has improved, however, a majority of patients still experience symptoms like fatigue, pain and cognitive deficits even when they are clinically evaluated to have low disease activity (LDA) or being in remission. Immunosuppressants are tapered after clinical remission and patients are typically continued on hydroxychloroquine (HCQ).

Activation of the complement system is evident in most SLE patients with active disease. This is usually assessed by low C3 or C4 as a proxy for complement activation (CA). When levels normalize or stabilize, we assume CA has been controlled.

The aim of this project is to examine if SLE patients in remission or with LDA have ongoing CA. This is investigated by measuring the C3 breakdown product C3dg. In addition, we show that *in vitro* HCQ does not inhibit any of the CA pathways.

Methods: In 166 SLE patients and 145 age and gender-matched controls we measured the C3 breakdown product C3dg (37 kDa fragment), which is only present after activation of C3. Disease activity was assessed using SLEDAI-2K, LLDAS, PGA and remission criteria (SLEDAI-2K=0, corticosteroid-free and immunosuppressant-free, HCQ allowed). The association between CA measured by C3dg and disease activity was estimated. Further, we examined the inhibitory effect of HCQ on CA *in vitro* in erythrocyte cell lysis assays and by measuring deposition of activation fragments of C3 and C4 on relevant surfaces in microtiter wells, i.e. examining activation through the lectin, the classical and the alternative pathway.

Results: In this cross-sectional cohort of SLE patients the median SLEDAI-score was 4 (range 0-14), median PGA was 1 (range 0-3), 61.4 % of patients were in LLDAS (102/166) and 7.8% were in complete remission (13/166).

C3dg was significantly higher in SLE patients than in controls ($p< 0.0001$), whereas no significant difference was observed for C3 ($p=0.67$). Ongoing CA was seen in all SLE patients independently of disease activity assessment (SLEDAI-2K, PGA, LLDAS and PGA). No difference was observed between patients treated or not treated with HCQ ($p=0.07$). Physiological and supraphysiological concentrations of HCQ did not inhibit CA through any of the complement pathways (fig.1) or in erythrocyte cell lysis assays.

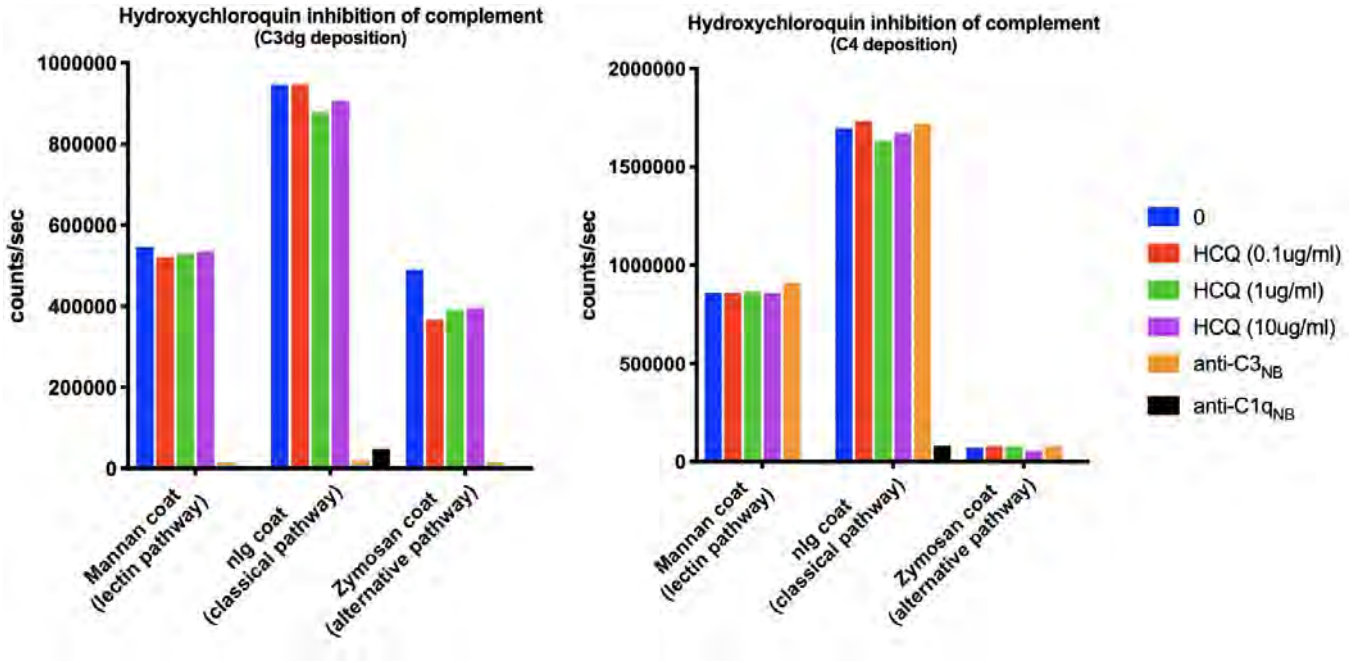

Figure 1. No inhibition of complement activation by hydroxychloroquine in vitro (HCQ).

Conclusion: SLE patients have ongoing CA even when our disease assessments scores show remission or LDA.

CA is not affected by HCQ treatment in patients, which in most cases is the drug-of-choice for SLE patients in remission. This is supported by our in *vitro* studies demonstrating that HCQ does not inhibit CA.

Our current disease activity scores do not include the best measures of biochemically active disease like CA measures. Ongoing CA is not captured by validated clinical disease activity scores and could be an explanation for persistent symptoms reported by many patients and potentially one of the pathogenic mechanisms leading to increased mortality in SLE.

Disclosure: A. Troldborg, None; **A. Hansen**, None; **K. Stengaard-Pedersen**, None; **S. Thiel**, None.

Abstract Number: 1811

Distinctive Molecular Signatures Among Monocytes from Childhood- and Adult-onset Systemic Lupus Erythematosus: Clinical Involvement and Relevance of Sustained Anti-dsDNA Positivity

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SESSION INFORMATION
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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: By using integrative transcriptomic and protein analyses, this study aimed at identifying and characterize distinctive molecular signatures between childhood-onset (cSLE) and adult-onset Lupus (aSLE) patients, along with their involvement in immunological and clinical features, and to analyze the relevance of the sustained positivity for anti-dsDNA antibodies.

Methods: Ninety-four subjects were enrolled, comprising two main combined study groups: 1) eleven consecutive children with pediatric-onset SLE (cSLE) and 11 age and sex matched healthy children (cHD); 2) sixty aSLE patients and 20 healthy adults (aHD). Total RNA was extracted from purified monocytes and pools from 5 subjects of each study group were obtained. Then, a nanostring autoimmune profiling array was used for mRNA expression data generation.

Results: Gene expression array identified 279 altered genes in monocytes from cSLE vs cHD. Comparatively, less than a half of genes (130) were found altered in monocytes from aSLE vs aHD. The analysis of common altered genes between the two study groups revealed 19 genes as upregulated in both patients' cohorts. Interestingly, Gene Ontology enrichment analysis identified as main biological processes integrated by these genes the interferon signature (IFNs). Moreover, cSLE displayed at least a double fold change in the levels of these genes *vs* cHD than aSLE *vs* aHD.

Correlation and association studies demonstrated that in the cSLE cohort the altered expression of a number of genes integrating the IFNs was linked to several clinical features. Specifically, increased levels of IFI27 were associated to the occurrence of lupus nephropathy (LN) and positivity for anti-dsDNA, and correlated positively with the activity of the disease (SLEDAI), CV-risk factors (atherogenic index and ApoB/ApoA ratio) and plasma levels of proteins of the IFN family such as IP-10.

Accordingly, in aSLE, altered expression of IFNs was associated to the presence of LN and low levels of complement factors C3 and C4, as well as to increased plasma levels of IFNγ. Interestingly, most of them were further associated with the positivity for anti-dsDNA. A deeper study in this cohort demonstrated that a third of the aSLE patients' displayed a sustained positivity for anti-dsDNA for more than 7 years. Moreover, these patients showed altered expression of several IFN genes, and presented LN along with a pathologic increase in the Carotid Intimae Media Thickness, and impaired microvascular endothelial function, thus supporting the potential role of the IFNs in the severity of the disease and the development of cardiovascular disease.

Conclusion: 1. Gene expression profile allowed the identification of distinctive molecular pathways among monocytes of cSLE and aSLE 2. An interferon signature, more strongly deranged in cSLE than in aSLE patients, is closely related to the activity of the disease and the renal involvement. 3. The sustained positivity for anti-dsDNA in aSLE, further linked to that deranged IFNs and to the development of lupus nephritis, might fosters the establishment of an atherothrombotic status in these autoimmune patients.

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Vilchez, None; **P. Segui**, None; **M. Espinosa**, None; **N. Barbarroja**, None; **E. Collantes**, Abbvie Inc, 5, 8, Amgen, 5, 8, Eli Lilly and Company, 5, 8, Janssen Pharmaceutical, 5, 8, MSD, 5, 8, Novartis, 5, 8, Pfizer Inc, 5, 8, UCB, 5, 8; **M. Aguirre-Zamorano**, None; **C. Lopez-Pedrera**, None.

Abstract Number: 1812

Longitudinal Blood DNA Methylation in a Multi-ethnic Cohort of SLE Patients

Cristina Lanata[1], Joanne Nititham[2], Kim Taylor[2], Sharon Chung[2], Laura Trupin[1], Patricia Katz[3], Maria Dall'Era[4], Jinoos Yazdany[1], Marina Sirota[1], Lisa Barcellos[5] and Lindsey Criswell[6], [1]UCSF, San Francisco, CA, [2]University of California, San Francisco, San Francisco, CA, [3]University of California, San Francisco, Novato, CA, [4]Division of Rheumatology, University of California, San Francisco, CA, [5]UC Berkeley, Berkeley, CA, [6]Rosalind Russell/Ephraim P. Engleman Rheumatology Research Center, University of California San Francisco, San Francisco, CA

SESSION INFORMATION
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Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Cross-sectional studies have shown associations between DNA methylation differences in whole blood with Systemic Lupus Erythematosus (SLE) status and outcomes such as lupus nephritis. However, DNA methylation is not static and a proportion of DNA methylation changes in response to environmental cues and with the effects of time. To study the trajectory of DNA methylation in whole blood in SLE we examined 101 participants at two time points in a well-characterized SLE cohort.

Methods: 101 participants from the California Lupus Epidemiology Study (CLUES), a longitudinal cohort of individuals with rheumatologist-confirmed SLE were studied. Participants are followed every 2 years through in-person research visits. DNA extracted from blood at cohort enrollment and after 2 years was analyzed on the illumina EPIC Beadchip. Single nucleotide polymorphism (SNP) genotype data was generated on the Affymetrix LAT1 World Array. First we performed a paired t-test between methylation at cohort enrollment and 2 years after, after adjusting for cell composition and methylation plate. We then applied a mixed linear model on methylation values adjusting for age, sex, population stratification and cell proportions. We previously reported 256 differentially methylated CpGs

Table 1. Top 10 results CpGs with significant changes in methylation between Time 1 and Time 2 adjusted for age, sex, population stratification and cell proportions

			Mean methylation Time 1	Mean methylation Time 2		P-value for cell proportion effects in the model				
	Gene	P value			Effect Size	CD8	CD4	NK cells	B cells	Monocytes
cg13452062	*IFI44L*	6.45E-25	0.39	0.23	0.213	0.276	0.461	0.308	0.023	0.262
cg21549285	*MX1*	6.14E-22	0.43	0.31	0.166	0.021	0.306	0.26	0.258	0.186
cg23570810	*IFITM1*	1.50E-21	0.49	0.42	0.089	0.426	0.187	0.182	0.125	0.018
cg10959651	*RDAD2*	4.43E-21	0.16	0.12	0.049	0.008	0.713	0.467	0.936	0.001
cg05671566	*IFI44L*	1.22E-20	0.35	0.24	0.158	0.007	0.054	0.156	0.22	0.02
cg07285983	*RAPGAP1L*	3.54E-20	0.42	0.34	0.116	7.90E-05	0.227	0.403	0.055	0.023
cg13100600	*AGRN*	3.16E-18	0.67	0.61	0.073	0.763	0.633	0.902	0.65	0.052
cg07815522	*PARP9*	3.48E-18	0.50	0.54	-0.037	0.66	0.83	0.133	0.24	0.02
cg12439472	*EPSTI1*	6.45E-18	0.46	0.37	0.126	0.983	0.267	0.121	0.095	0.008
cg20062691	*ISG15*	2.22E-17	0.36	0.27	0.125	0.114	0.178	0.272	0.12	0.101

Top 10 results CpGs with significant changes in methylation between Time 1 and Time 2 adjusted for age, sex, population stratification and cell proportions

according to disease severity at cohort enrollment.[1] We performed focused analysis on these 256 CpGs as well as exploratory genome-wide analysis.

[1]Lanata et al, Nat Comm **10**, 3902 (2019)

Results: After quality control 806,000 CpGs were analyzed. Of the 256 CpGs previously associated with disease severity, 55 CpGs (21.4%) had a significant change in methylation between the 2 time points ($p < 2E-04$, effect size > 0.03, paired t-test), 52 with a decrease and 3 with an increase in methylation. The largest effect size was observed for cg13452062 in *IFI44L* with a mean decrease of 0.16 (p=6.4e-25) and the most represented genes were *IFI44L*, *IFITM1, PARP9* with 4 CpGs each. In the mixed linear model, the 55 CpGs remained significant ($p < 2E-04$) although we found a significant effect of cell proportions with changes in methylation. As representative examples, we find a significant effect of CD8 proportions with cg07285983 in *RAPGAP1L,* B cell proportions with cg13452062 in *IFI44L* and monocyte proportions with cg10959651 in *RDAD2* (Table 1). Disease activity ((SLE Disease Activity Index score) did not vary significantly between time 1 and time 2 (p=1.0, paired t-test). Exploratory genome-wide analyses found 151 CpGs (0.02%) with a significant change in methylation between the 2 time points ($p < 6.2E-08$, effect size > 0.03 paired t-test). Of these, 55 (33%) were in the previously described 256 CpGs. Of the remaining CpGs, top associations included CpGs in *TLR6, RSAD2, MSRA and COPS8*.

Conclusion: In this study, a small proportion of DNA methylation signatures in blood previously associated with SLE phenotypes fluctuated over time. These changes in methylation associate with circulating cell proportion in SLE patients. Additional longitudinal studies will be needed to further describe and validate candidate CpGs that represent stable biomarkers of disease state as well as CpGs that change in relationship to cell proportions and other unmeasured factors.

Disclosure: C. Lanata, None; **J. Nititham**, None; **K. Taylor**, None; **S. Chung**, None; **L. Trupin**, None; **P. Katz**, None; **M. Dall'Era**, Janssen, 5, AstraZeneca, 5; **J. Yazdany**, Eli Lilly, 5, Astra Zeneca, 5; **M. Sirota**, None; **L. Barcellos**, None; **L. Criswell**, None.

Abstract Number: 1813

A Comprehensive Method to Study Environmental Chemicals in Serum in Patients with SLE

Cristina Lanata[1], Kim Taylor[2], James Hurst-Hopf[1], Laura Trupin[1], Patricia Katz[3], Jinoos Yazdany[1], Maria Dall'Era[4], Dimitri Abrahamsson[1], Lindsey Criswell[5] and Roy Gerona[1], [1]UCSF, San Francisco, CA, [2]University of California, San Francisco, San Francisco, CA, [3]University of California, San Francisco, Novato, CA, [4]Division of Rheumatology, University of California, San Francisco, CA, [5]Rosalind Russell/Ephraim P. Engleman Rheumatology Research Center, University of California San Francisco, San Francisco, CA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Time: 9:00AM–11:00AM

Background/Purpose: Environmental exposures may play a substantial role in the pathogenesis of Systemic Lupus Erythematosus (SLE), however it has been challenging to measure and capture relevant exposures in a comprehensive manner. The goal of this study is to develop a novel method to characterize the serum levels of circulating environmental chemicals and metabolites in a well-characterized cohort of SLE patients and controls.

Methods: Participants from the California Lupus Epidemiology Study (CLUES), a longitudinal cohort of individuals with rheumatologist-confirmed SLE were included (n=332). A cohort of healthy individuals matched by age, ethnicity and sex was recruited (n=100). Serum was analyzed by liquid chromatography quadruple time-of-flight Mass Spectrometry (**LC-QTOF/MS**). Feature detection, peak alignment, and abundance normalization using internal standards was performed using Agilent Mass Profiler and adjusted for batch effects using ComBat[1].Principal Components Analysis was used to assess batch adjustment and correct for residual batch effects. Compounds detected in at least 25% of participants were selected for association testing between chemical abundances and SLE status. We analyzed differences between cases and controls using linear models of feature abundances, adjusting for censoring below the detection limit, residual batch effects, and covariates age, sex, and ethnicity. Results of potential detected environmental chemicals were matched into a curated database of hazardous environmental chemicals.

[1]Johnson et al, Biostatistics. 2007; 8(1):118–27

Results: We detected 66,861 features in our cohort; with 3,192 present in at least 25% of samples and analyzed for association with case status. Out of the 3192 features, 70 were significantly different, including 4-Hexyloxyphenol and 39 additional formula-matched compounds.

Conclusion: LC-QTOF/MS can identify a wider range of potential chemical exposures in SLE, and may aid in prioritizing chemicals for further research and intervention. We found that patients with SLE had different chemicals and endogenous metabolites compared to healthy controls.

Disclosure: C. Lanata, None; **K. Taylor**, None; **J. Hurst-Hopf**, None; **L. Trupin**, None; **P. Katz**, None; **J. Yazdany**, Eli Lilly, 5, Astra Zeneca, 5; **M. Dall'Era**, Janssen, 5, AstraZeneca, 5; **D. Abrahamsson**, None; **L. Criswell**, None; **R. Gerona**, None.

Abstract Number: 1814

The Association of Urinary Membrane Attack Complex (C5b-9) with Proteinuria and Glomerular Activity in Lupus Nephritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Background/Purpose: Complement activation is known to play a major role in lupus nephritis (LN). Urinary membrane attack complex (C5b-9) has been shown to correlate with proteinuria and renal injury in other diseases such as diabetic nephropathy, IgA nephropathy and ANCA vasculitis, but its role is unclear in LN. This study aims to determine whether urine C5b-9 is associated with proteinuria and markers of glomerular or tubular disease activity in LN.

Methods: Urine samples from 42 adult and pediatric lupus patients with clinically indicated renal biopsies performed between 2010 and 2019, and 3 normal controls were collected. The urine C5b-9 levels were measured using specific enzyme linked immunosorbent assay kit (Quidel Corporation) and normalized by urine creatinine excretion. The urine

Table 1: Urine C5b-9 levels normalized by creatinine (ng/mg), by demographics and laboratory parameters at time of urine sample collection, N= 42

	N (%)	Urine C5b-9 level, median (IQR), ng/mg	P-value
Demographics			
Age			
<32 years old	20 (49%)	16.0 (10.7, 40.0)	0.08
= 32 years old	21 (51%)	8.1 (1.8, 18.6)	
Sex			
Women	37 (88.1%)	12.3 (2.0, 21.6)	0.40
Men	5 (11.9%)	39.1 (2.6, 90.3)	
Ethnicity			
Hispanic/Latino	19 (45.2%)	14.3 (3.5, 39.1)	0.20
Non-Hispanic	23 (54.8%)	9.5 (0.7, 18.6)	
Hydroxychloroquine Use			
Yes	37 (88.1%)	13.4 (3.0, 37.2)	0.19
No	5 (11.9%)	1.8 (0, 16.9)	
Prednisone dose, mg/kg			
= 40	21 (50%)	13.7 (1.6, 37.2)	0.90
<40	21 (50%)	11.2 (3.0, 21.6)	
Systolic Blood Pressure, mmHg			
> 120	25 (61.0%)	10.2 (2.0, 21.6)	0.41
=120	16 (39.0%)	17.7 (3.1, 38.1)	
Laboratory parameters			
eGFR, mL/min/1.73m^2			
>60	31 (75.6%)	13.4 (1.8, 27.3)	
30-59	5 (12.2%)	8.1 (2.6, 12.3)	0.82
<30	5 (12.2%)	22.8 (0.3, 40.8)	
Serum albumin, g/dL			
= 3.5	16 (47.1%)	5.8 (0.3, 16.9)	**0.02**
< 3.5	18 (52.9%)	18.9 (8.1, 60.3)	
Urine protein creatinine, mg/g			
= 1000	10 (26.3%)	1.8 (0.3, 8.2)	**0.004**
>1000	28 (73.7%)	14.8 (8.1, 46.8)	
Serum C3, mg/dl			
<80	19 (50%)	13.7 (2.6, 40.8)	0.85
= 80	19 (50%)	12.3 (1.6, 27.3)	
Serum C4, mg/dl			
<20	22 (57.9%)	14.4 (3.0, 37.2)	0.32
=20	20 (42.1%)	10.3 (1.0, 25.1)	
Serum Anti-dsDNA			
= 70	16 (45.7%)	10.2 (1.6, 52.7)	0.48
>70	19 (54.3%)	16.8 (6.1, 32.2)	

samples were ran immediately after thawing in duplicate and analyzed on a standard curve. Urine C5b-9 levels were correlated with demographic and laboratory parameters at time of urine collection (Table 1) and with renal pathology 0 to180 days prior to time of renal biopsy (Table 2).

Results: Patient with LN (n=42) had higher median (IQR) urine C5b-9 of 12.8 ng/mg (2.0, 27.3) as compared to 0 ng/mg (0, 2.4) among normal controls (n=3), p=0.03. Of the 42 LN patients, the median age (IQR) is 32 years (19, 41), 37 (88.1%) females and 19 (45.2%) Hispanic. Patients with low serum albumin (< 3.5 g/dL) had higher median (IQR) urine C5b-9 as compared to those with normal albumin: 18.9 ng/mg (8.1, 60.3) vs. 5.8 ng/mg (0.3, 16.9), p=0.02. Similarly, patients with elevated urine protein creatinine (>1000mg/g) had significantly higher median (IQR) urine C5b-9: 14.8ng/mg (8.1, 46.8) vs. 1.8ng/mg (0.3, 8.2), p=0.004. There was no significant association in eGFR, serum C3, C4, dsDNA and urine C5b-9 levels. 19 of the 42 LN patients had urine sample collected 0 to180 days prior to time of renal biopsy, of which 10 had urine sample collected on the day of renal biopsy. Of the 19 LN patients, 9 (47.4%) had proliferative/mixed class. LN patients with proliferative/mixed class had higher median (IQR) urine C5b-9 compared with membranous class: 21.6 ng/mg (10.2, 90.3) vs. 7.3 ng/mg (1.8, 18.5). However, tubular interstitial fibrosis and inflammation was found not to be associated with urine C5b-9 levels.

Table 2: Urine C5b-9 levels normalized by creatinine (ng/mg), by renal pathology 0 to 180 days prior to time of renal biopsy, N=19

	N (%)	Urine C5b-9, median (IQR), mg/ng	p-value
Glomerular Activity			
LN Class			
Proliferative/Mixed (4, 4+5, 3+5)	9 (47.4%)	21.6 (10.2, 90.3)	0.05
Membranous (5)	10 (52.6%)	7.3 (1.8, 18.5)	
Presence of Crescents			
Yes	3 (15.8%)	90.3 (10.2, 190.1)	0.14
No	16 84.2%)	12.3 (3.1, 20.1)	
Chronicity of lesions			
Active (A, or A/C)	5 (55.6%)	90.3 (10.2, 173.6)	0.55
Chronic (C)	4 (44.4%)	17.5 (10.8, 29.4)	
Tubular Activity			
Interstitial Fibrosis/Tubular Atrophy			
None	7 (36.8%)	13.4 (3.5, 39.1)	0.97
Present (mild to severe)	12 (63.2%)	14.3 (4.7, 29.4)	
Tubulointerstitial Inflammation			
None	8 (42.1%)	17.7 (10.0, 38.1)	0.27
Present (mild to severe)	11 (57.9%)	10.2 (1.8, 21.5)	

Conclusion: Although limited by sample size, this pilot study suggested that urine C5b-9 is associated with low serum albumin and proteinuria in LN. In addition, urine C5b-9 levels checked before or at time of biopsy may be a potential marker of glomerular activity in LN. More studies are needed to investigate urine C5b-9 as a biomarker of glomerular or tubular activity.

Disclosure: S. Wang, None; **E. Moore**, None; **B. Lally**, None; **B. Goilav**, None; **C. Putterman**, Equillium, 1, 2; **A. Broder**, None.

Abstract Number: 1815

Dynamic Changes in Microbiota Representation of a Gut Pathobiont and Clinical Disease Activity in Patients with Lupus Nephritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: From a cross-sectional cohort, we have recently identified a candidate human gut pathobiont, Ruminococcus gnavus (RG) of the Lachnospiraceae family and Blautia genus that was linked to active Lupus nephritis (LN)(1). LN patients often displayed gut blooms of RG, concordant with serum IgG anti-RG antibody responses that appeared intertwined with anti-dsDNA responses implicated in renal pathogenesis. The dynamics of

RG representation within SLE microbiota ecosystems have not been investigated. The genomic sequences of few RG strains have been reported, and these vary greatly in genome structure, gene representation and sequence.

Methods: A total of 53 fecal samples from 16 SLE patients and 63 samples from 11 CTL, at 2-12 time-points were studied, and patients were characterized for demographics, and clinical disease activity. High-throughput 16S rRNA amplicon libraries from fecal samples were analyzed using QIIME 2 and DADA2 (1). Hundreds of individual fecal RG colonies from two active LN patients were isolated and subjected to whole genome sequencing (WGS), with phylogenetic assignments in part based on inter-strain average nucleotide identity, multi-locus sequence typing and reference-guided genomic assemblies.

Results: Our analysis confirmed highly conserved patterns of gut community representation in SLE patients that displayed reduced microbiota richness, which was most pronounced in patients with high SLEDAI (p= 0.0023) and LN (p=0.002), confirming earlier reported findings [1]. Beta diversity analysis showed significant heterogeneity in SLE microbiome compared to CTL (p= 0.001). Similarly, RG abundance was greater in patients with high SLEDAI (p= 0.0021) and LN compared to CTL (p= 0.003). Tracking of the dynamic representation of RG at different time points within individual subjects, in CTL and many Lupus patients showed little or no detectable perturbations. Strikingly, in LN patients examined, there was a direct correlation between representation of RG and the SLEDAI score of overall disease activity in 53% of LN patients overtime. WGS analysis of the RG isolated colonies discovered four distinct RG strains with large genomic variations, which differ from previously reported RG strains from other diseases and healthy donors.

Conclusion: Our findings suggest that intestinal blooms of the RG candidate pathobiont correlate with serious increases in Lupus disease activity, and especially LN. In pilot studies we have isolated and characterized the genomes of the first RG strains from active SLE patients. Our findings suggest that both dynamic representation and colonization by specific RG strains identified by their genomic composition, may have implications for the host-pathobiont relationship and the immune activation that is integral to Lupus pathogenesis.

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Abstract Number: 1816

Urine Biomarkers of Tubulointersitital Damage in Lupus Nephritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Tubulointerstitial disease (TID), defined as tubulointerstitial inflammation (TII) or interstitial fibrosis/tubular atrophy (IFTA), is associated with progression to end stage renal disease (ESRD) in lupus nephritis. Early detection of TID via non-invasive methods is crucial to identifying those at highest risk for renal failure. A set of

Table 1. BioRad Biomarker Panel Location of Action

	Proximal tubules	Distal tubules	Collecting duct	Loop of Henle
KIM-1	x			
IL-18	x			
Clusterin	x	x		
Calbindin		x	x	
GST-π		x		
Bonventre JV, Vaidya VS, Schmouder R, Feig P, Dieterle F. Next-generation biomarkers for detecting kidney toxicity. Nature biotechnology. 2010;28(5):436-40. doi:10.1038/nbt0510-436				

Table 2. Baseline characteristics of IFTA patients at time of biopsy.

	IFTA- (n=11)	**IFTA+ (n=18)**	**p-value**
Age, years, median (IQR)	20 (14, 59)	36 (27, 50)	0.25
Women, n (%)	9 (82)	17 (89)	0.55
Race, n (%): White Black/African American Multiracial/Other	 2 (18) 4 (36) 5 (45)	 1 (5) 13 (68) 5 (26)	0.20
Hispanic/Latino, n (%)	7 (64)	6 (32)	0.09
LN class, n (%) Proliferative Membranous Mixed	 4 (36) 6 (55) 1 (9)	 6 (33) 6 (33) 6 (33)	0.30
Immunosuppression, n (%) None Cyclophosphamide Mycophenolate Other*	 6 (55) 2 (18) 1 (9) 2 (18)	 7 (37) 1 (5) 6 (32) 5 (26)	0.34
Hydroxychloroquine, n (%)	10 (91)	14 (74)	0.26
Pulse steroids within two weeks prior to date of biopsy, n (%)	1 (9)	4 (21)	0.40
Prednisone dose, mg/kg, median (IQR)	1 (0, 1)	0 (0, 1)	0.35
NSAID use, n (%)	0	2 (11)	0.27
ACE inhibitor use, n (%)	6 (55)	8 (42)	0.51
Serum creatinine, mg/dl, median (IQR)	1 (1, 1)	1 (1, 2)	0.008
eGFR > 60, n (%)	10 (91)	10 (53)	0.032
Urine protein creatinine, mg/g, median (IQR)	1.4 (1.0, 2.5)	2.9 (1.5, 5.8)	0.045
Anti-dsDNA, median (IQR; reference range < 70)	170 (160, 175)	61 (11, 194)	0.48
C3, median (IQR; reference range 80-300 mg/dl)	75 (42, 103)	63 (43, 90)	0.50
C4, median (IQR; reference range 20-60 mg/dl)	9 (4, 22)	11 (6.5, 17)	0.90
Diabetes, n (%)	0	4 (21)	0.10
Cigarette smoking, n (%) Never Past Current	 10 (90) 1 (9) 0	 14 (74) 4 (21) 1 (5)	0.49
BMI, kg/m^2, median (IQR)	23 (20, 26)	30 (24, 36)	0.002
Systolic blood pressure before biopsy, mmHg, median (IQR)	115 (113, 116)	128 (118, 144)	0.016
Diastolic blood pressure before biopsy, mmHg, median (IQR)	62 (59, 68)	83 (73, 94)	<0.001
*Including azathioprine, IVIG, methotrexate, ustekinumab, belimumab; combination therapies AZA + abatacept or mycophenolate + cyclophosphamide/tacrolimus/belimumab			

urine biomarkers of tubular damage has recently been developed to detect acute kidney injury.[1] This study sought to determine whether these biomarkers of tubular injury collected around the time of clinically indicated biopsies for lupus nephritis were associated with the presence of IFTA/TII.

Methods: Urine samples from 29 adult and pediatric lupus patients with clinically indicated renal biopsies performed between 2010 and 2019 were included. Samples were evaluated for tubular injury markers KIM-1, interleukin-18 (IL-18), clusterin, calbindin, and glutathione S-transferase-π (GST- π) using the Bio-Plex Pro™ kidney assay. Biomarkers (Table 1) were correlated with presence or absence of IFTA/TII on biopsies performed within 180 days prior to and 21 days after sampling. These biomarkers were normalized to urine creatinine excretion.

Table 3. Association between IFTA and biomarkers of tubular injury (ng/mg; median [IQR])

Biomarker	IFTA- n=11	IFTA+ n=18	p-value
KIM-1	0 (0, 0)	0.5 (0, 2)	0.06 2-sided; 0.04 one-sided
IL-18	0 (0, 0)	0 (0, 0)	0.42
Clusterin	83 (55, 384)	94 (25, 383)	0.89
Calbindin	54 (31, 128)	149 (26, 265)	0.54
GST-π	94 (26, 196)	68 (34, 141)	0.96

Results: Of 29 patients, 18 (62%) had evidence of IFTA on renal biopsy (Table 2). IFTA+ patients had a median age (IQR) of 36 (27, 50) vs. 20 (14, 59) in the IFTA group, p = 0.25. BMI was significantly higher in IFTA+ patients (median (IQR) 30 (24, 36) kg/m^2 vs. 23 (20, 26) kg/m^2, p < 0.001), as was blood pressure on day of biopsy. KIM-1 levels were higher when IFTA was present, median (IQR) 0.5 (0, 2) ng/mg vs. 0 (0, 0) ng/mg for IFTA+ and IFTA-, respectively, one sided p-value 0.04. KIM-1 was detectable (> 0) in 9 (50%) of IFTA+ and in 2 (18%) IFTA-, p = 0.09. No association between KIM-1 and TII was observed. There was no association between the other 4 biomarkers and IFTA or TII (Table 3). KIM-1 levels did not differ by age, sex, race, ethnicity, or lupus nephritis class, and were not associated with serum C3, C4, or dsDNA at time of sample collection. KIM-1, calbindin, GST-π and clusterin were associated with proteinuria.

Conclusion: Though limited by sample size, these pilot results suggest that urinary KIM-1, a kidney injury marker secreted by the proximal tubules, in samples collected around the time of biopsies may serve as a non-invasive biomarker for the presence of IFTA in lupus nephritis.

Reference

1. Stephen L, et al. Profiling of Human, Canine, and Rat Urine Samples Using Bio-Plex Pro™ RBM Kidney Toxicity Assays. Available from: http://www.bio-rad.com/webroot/web/pdf/lsr/literature/Bulletin_6400.pdf

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Abstract Number: 1817

Changes in Macular Capillary Network Measured with Optical Coherence Tomography-angiography in Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Eye involvement in systemic lupus erythematosus (SLE) occurs in approximately one-third of patients, usually related to disease activity. An early diagnosis and treatment could prevent structural eye damage and visual acuity worsening in these cases. The purpose of the present study was t o describe macular vascular

findings by optical coherence tomography angiography (OCT-A) in SLE patients related to the duration of disease and SLE activity/damage scores.

Methods: A cross-sectional, single-center study was carried out in 78 patients with SLE followed at Autoimmune Diseases and Ophthalmology Departments of the Hospital Clínic, Barcelona. As a control group, 80 sex and age-matched individuals were also analyzed. Clinical and immunological data, SLE activity and damage scores, and macular vascular parameters by OCT-A (CIRRUS ™ HD-OCT model 5000, Carl Zeiss Meditec, Inc., USA) were collected.

Results: Perifoveal vessel density in SLE patients was reduced compared to the control group (median 10.3 mm^{-1}[range 9.6-11.4] versus median 12.5 mm^{-1} [range 11,7-13,7]) (p=0.001) as well as vascular perfusion proportion compared to controls (0.35 [0.34-0.37] versus 0.38 [0.37-0.39]) (p=0.001). Likewise, SLE patients with >10 years of disease showed lower figures of vessel density (19.1 [18.2-20.2] versus 20.2 [19.7-20.9]) (p=0.04) and perfusion (0.34 [0.32-0.37] versus 0.36 [0.35-0.37]) (p=0.0017) compared to those with < 10 years of disease, respectively.

Patients with SLE damage index score >0 had worse values in area (median 0.18 mm^2 [range 0.15-0.21] versus 0.27 mm^2 [range 0.23-0.31]) (p=0.002) and perimeter foveal avascular zone (FAZ) (median 1.84 mm^2[range 1.70-2.12] versus 2.19 mm^2 [range 2.07-2.37]) (p=0.003). Likewise, patients with a clinical SLE disease activity index >4 showed a decrease in vessel density (14.6 mm^{-1} [11.7-18.3] versus 17.6 mm^{-1} [17.1-18.1])(p=0.02) and vascular perfusion (0.33 mm^{-1} [0.23-0.44] versus 0.43 mm^{-1} [0.42-0.45])(p=0.012).

Conclusion: The macular capillary network of SLE patients shows lower vessel density and perfusion proportion than healthy controls. In addition, retinal vascular findings in SLE patients could be associated with the duration of disease, SLE activity, and damage index. Retinal vascular imaging explorations based on OCT-A could be of great interest in future studies in SLE in order to further clarify systemic implications of such characteristics.

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Abstract Number: 1818

IgG and IgA Autoantibodies Against L1 ORF1p Expressed in Granulocytes Correlate with Granulocyte Consumption and Disease Activity in Pediatric Systemic Lupus Erythematosus

Kennedy Ukadike[1], Kathryn Ni[1], Victoria Carter[1], Martin Taylor[2], John LaCava[3], Lauren Pachman[4], Xiaoxing Wang[1], Mary Eckert[5], Anne Stevens[1], Christian Lood[1] and Tomas Mustelin[1], [1]University of Washington, Seattle, WA, [2]Massachusetts General Hospital, Boston, MA, [3]Rockefeller University, New York, NY, [4]Department of Pediatrics, Northwestern University Feinberg School of Medicine; The Ann and Robert H. Lurie Children's Hospital of Chicago, Division of Pediatric Rheumatology; The CureJM Center of Excellence in Juvenile Myositis Research and Care, The Stanley Manne Children's Research Center of Chicago, Lake Forest, IL, [5]Seattle Children's Hospital, Seattle, WA

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside

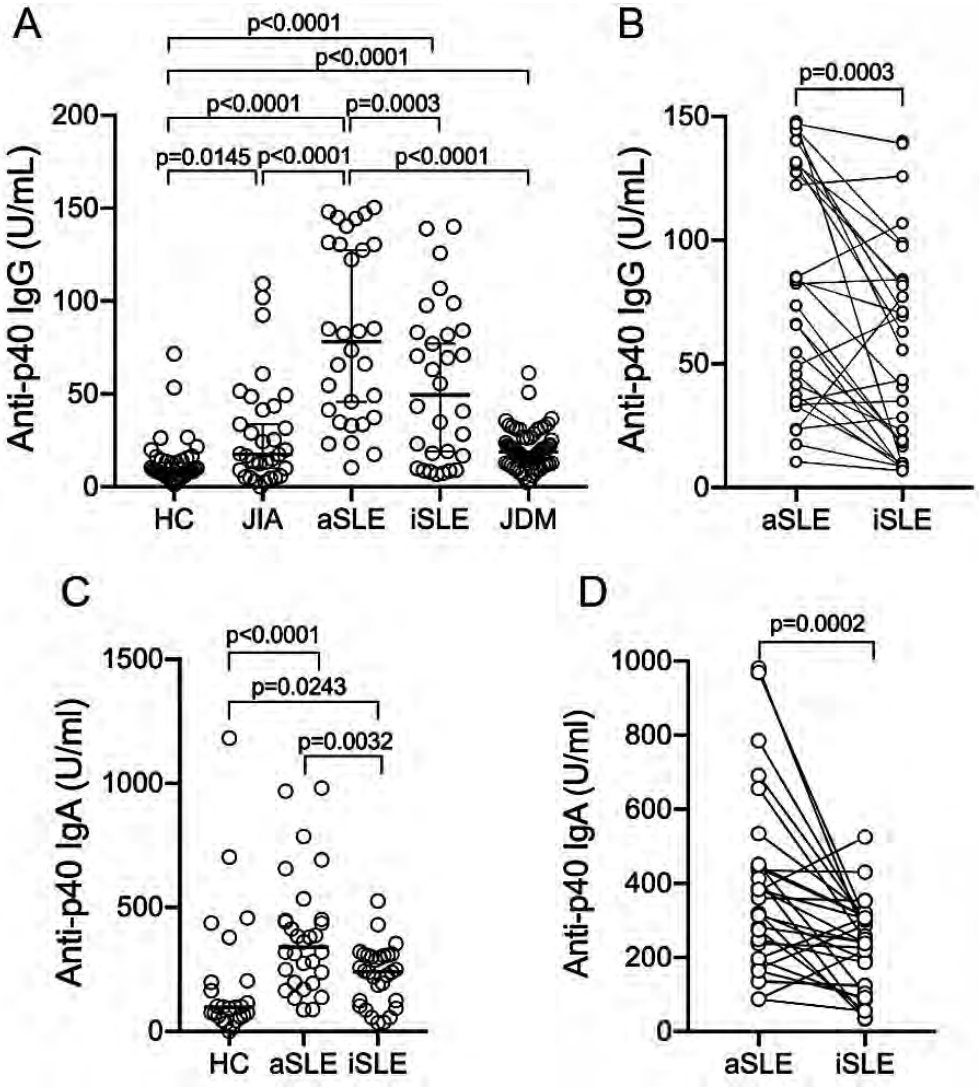
Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

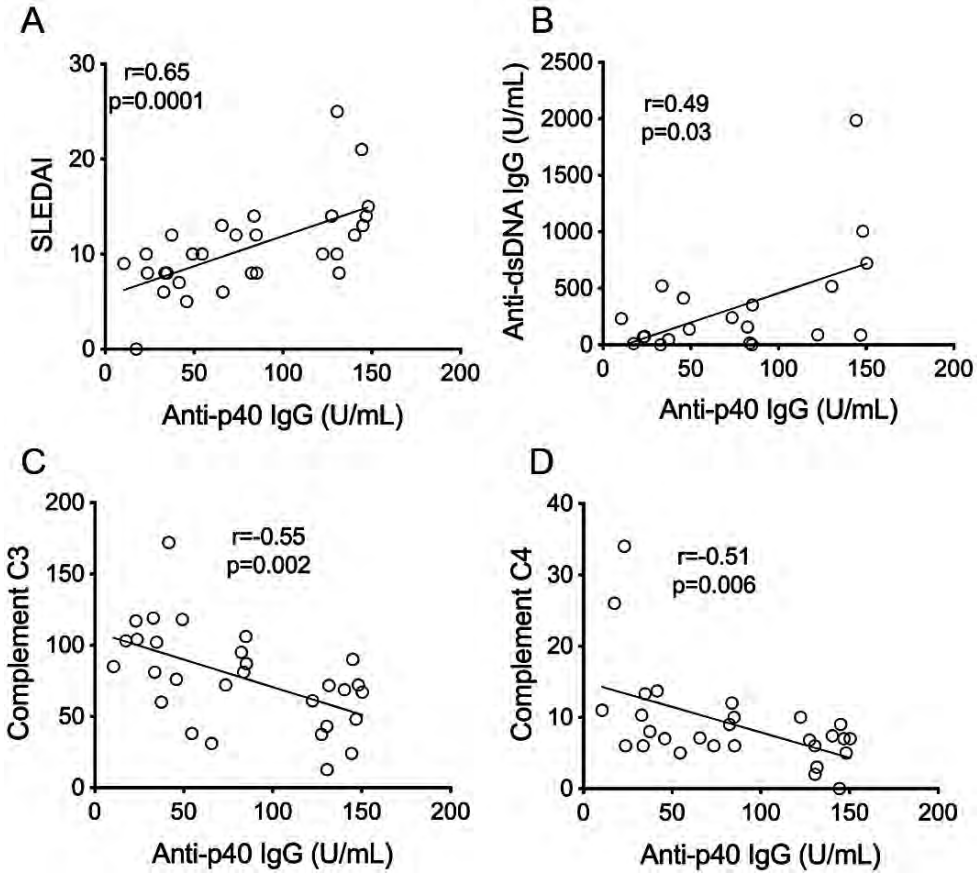
Background/Purpose: To quantitate autoantibodies against the RNA-binding p40 (ORF1p) protein encoded by the L1 retroelement, expression of p40 itself, and markers of neutrophil death in patients with pediatric systemic lupus erythematosus (pSLE), and to determine if correlations exist between these and disease activity.

Methods: Autoantibodies in the plasma of pSLE patients (n=30), healthy children (n=37), and disease controls juvenile idiopathic arthritis (JIA) (n=32) and juvenile dermatomyositis (JDM) (n=60), were measured by ELISA. Expression of p40 in immune cells was assessed by immunoblotting and flow cytometry. Markers of neutrophil activation were quantitated by ELISA.

Results: IgG and IgA autoantibodies reactive with p40 were detected in the pSLE patients, but were low in healthy controls and in JIA or JDM. pSLE patients with active disease (13 of them newly diagnosed) had higher titers than the same patients after effective therapy (p=0.0003). IgG titers correlated with SLEDAI (r=0.65, p=0.0001), ESR (r=0.43, p=0.02), and anti-dsDNA antibodies (r=0.49, p< 0.03), and inversely with complement C3 (p=0.002) and C4 (p=0.006). p40 protein was detected in a subpopulation of $CD66b^{+}$ granulocytes in pSLE, as well as in adult SLE patients. My-



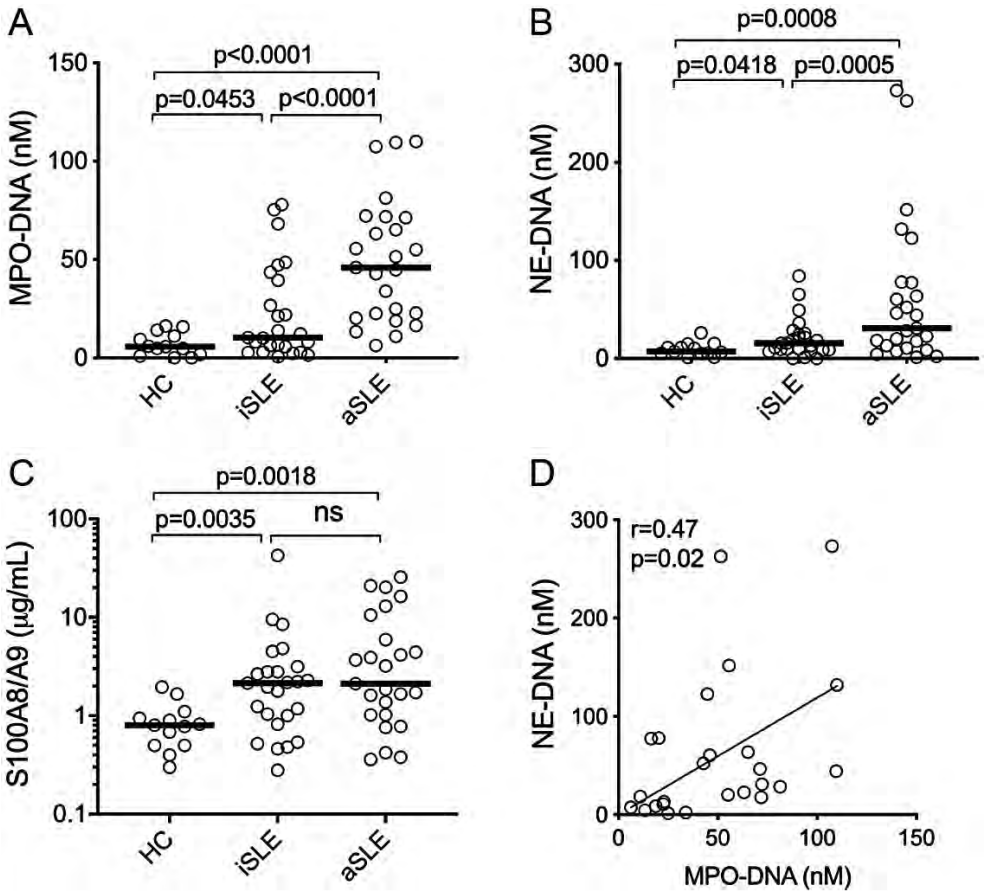
Anti-p40 and disease state correlations



Anti-p40 and disease activity correlations

eloperoxidase and neutrophil elastase complexed with DNA and the neutrophil-derived S100A8/A9 were elevated in plasma from pSLE patients with active disease and correlated with anti-p40 autoantibodies and disease activity.

Conclusion: Children with active SLE have elevated IgG and IgA autoantibodies against L1 p40, a protein found in circulating granulocytes. P40 expression and autoantibody levels correlate with disease activity and suggest that neutrophils are a source of retroelement expression.



Neutrophil activation and disease state correlations

Disclosure: K. Ukadike, None; **K. Ni**, None; **V. Carter**, None; **M. Taylor**, None; **J. LaCava**, None; **L. Pachman**, Reveragen, 2; **X. Wang**, None; **M. Eckert**, None; **A. Stevens**, None; **C. Lood**, None; **T. Mustelin**, None.

Abstract Number: 1819

Altered Brain Functional Connectivity in Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Table 1: Baseline characteristics

Variable		SLE-F (n=19)	SLE-S (n=23)	HC (n=30)	*p*-value	Post hoc
		Mean (S.D.), Median (LQ, UQ) or n (%)				
Demographic and clinical	Age (years)	37 (23, 48)	39 (33, 50)	32 (27, 46)	0.154	n/a
	Disease duration (years from diagnosis)	9.7 (8.0)	12 (7.4)	n/a	0.405	n/a
	BILAG global score	12 (10, 16)	1 (0, 2)	n/a	**<0.001**	n/a
	Current oral corticosteroids (n %)	12 (63)	7 (30)	n/a	**0.034**	n/a
	Current immunosuppressant use	14 (74)	8 (35)	n/a	**0.012**	n/a
	Current antimalarial use	13 (68)	15 (68)	n/a	0.987	n/a
	Biologic medication	4 (21)	2 (9)	n/a	0.255	n/a
Depression & anxiety	MADRS	11 (5, 14)	4 (0, 7)	1 (0, 3)	**<0.001**	HC vs SLE-F* HC vs SLE-S SLE-F vs SLE-S*
	HADS-D	7 (3.5, 10.25)	2 (1, 9)	1 (0, 2)	**<0.001**	HC vs SLE-F* HC vs SLE-S* SLE-F vs SLE-S
	HADS – A	8.4 (4.5)	5.7 (3.4)	5.1 (4.2)	**0.019**	HC vs SLE-F*

***Abbreviations: BILAG** – British Isles Lupus Assessment Group index, **MADRS** – Montgomery Asberg Depression Rating Scale, **HADS** - Hospital Anxiety and Depression Scale (D) Depression, (A) Anxiety.*
**Post-hoc Bonferroni corrected*

Background/Purpose: Cognitive dysfunction (CD) is very prevalent in SLE and significantly affects quality of life. Altered functional brain mechanisms are associated with CD in SLE. We previously used functional magnetic resonance imaging (fMRI) to show altered mechanisms in the Default Mode Network (DMN), a network involved in self-reflection and is acquiescent during cognitive tasks. In this study, we examined the effects of disease activity on functional connectivity (FC) within the DMN using resting state (rs) fMRI. We hypothesised that those with SLE, and specifically those with active disease, would have reduced FC within the DMN compared to healthy controls.

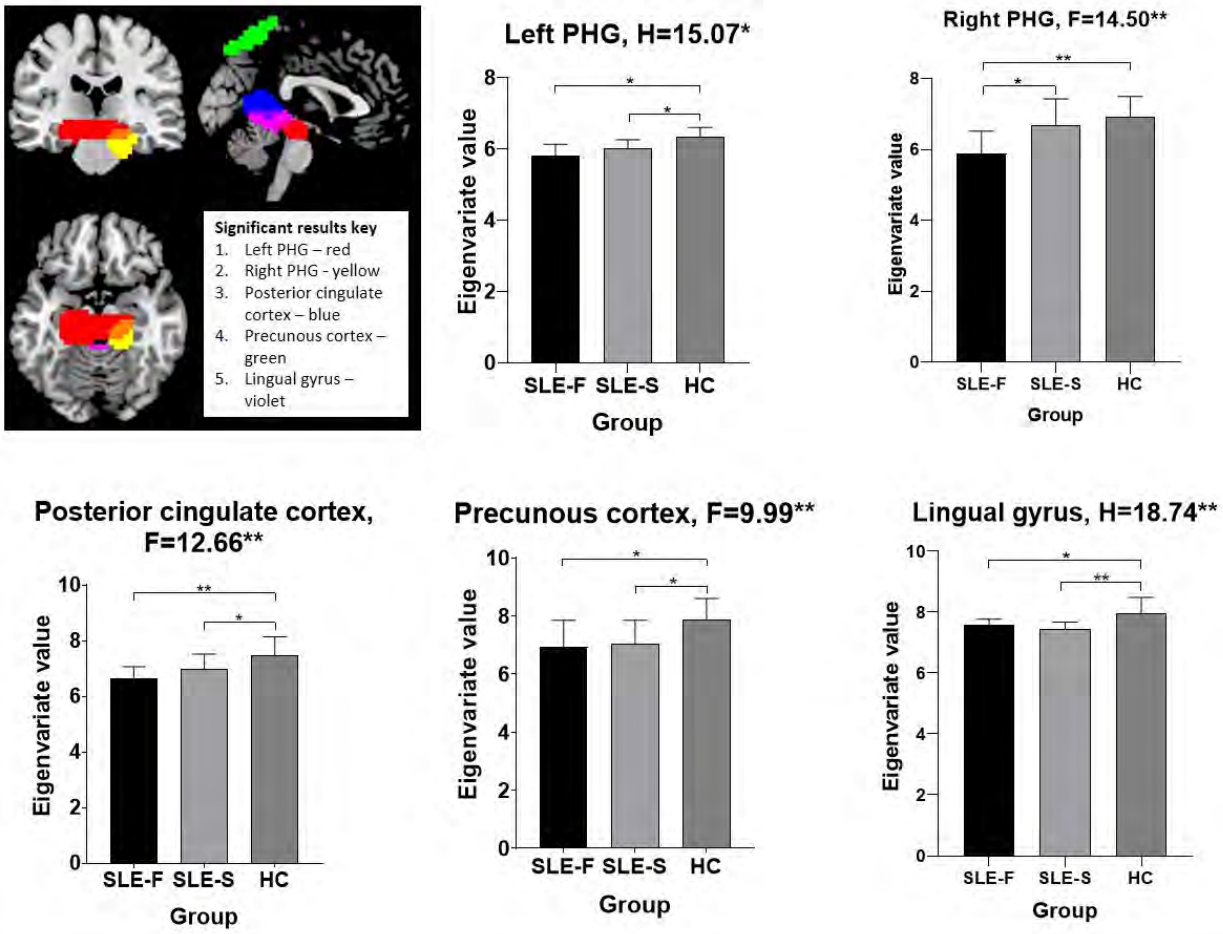
Methods: 19 SLE-active (SLE-F) and 23 SLE-stable (SLE-S) all meeting 1997 ACR or SLICC criteria and 30 healthy controls (HC) were recruited. In the SLE participants, active disease was defined as BILAG A or B with a change in treatment. Stable disease was defined as SLEDAI-2K ≤4. Demographic, clinical and psychiatric data were collected for all participants. A T2-weighted scan was undertaken and reviewed by a neuroradiologist to provide a Scheltens score for brain abnormalities. A T2*-weighted rsfMR scan was acquired. These images, after preprocessing, were analysed using independent component analysis (ICA). Fischer's z-scores were extracted from those temporospatial nodes associated with the DMN and entered into ANOVAs or Kruskal-Wallis tests.

Results: Participants were well matched on key demographics. Significant differences were found between the SLE groups on factors associated with disease activity and psychological factors (Table 1).

14 DMN nodes were defined using ICA. Significant group differences ($p< 0.001$) were found in five of the nodes: precunous cortex, right parahippocampal gyrus (PHG), posterior cingulate cortex, lingual gyrus and left PHG. In all regions, except the right PHG, the SLE groups had reduced FC compared to the HC group. In the right PHG the SLE-F group had reduced FC compared to the other two groups (Figure 1).

Correlations comparing the significant nodes with Scheltens score and depression and anxiety measures for the SLE groups combined were undertaken. Depression score (MADRS) was negatively correlated with FC in both the left and right PHG (r_s=-0.476, p=0.001 and r_s=-0.494, p=0.001, respectively).

Figure 1: Default mode network (DMN) regions with significant group differences



*p<0.01, **p<0.001
PHG = Parahippocampal gyrus

Conclusion: Altered FC was evident in DMN nodes for SLE groups irrespective of disease activity. Reduced FC in these areas could be indicative of fatigue. The inability to "switch off" the DMN during cognitive tasks may impact the FC of the DMN in SLE. The DMN is involved in self-reflective processes and altered FC is associated with major depression. Our SLE groups had higher, but not clinically significant, depression scores compared to HC and our correlations found altered FC associated with depression scores. When considering rsfMRI as a potential marker for CD in SLE other contributing factors, such as depression, must also be considered.

Disclosure: M. Barraclough, Sanofi Genzyme, 2; **S. McKie**, None; **B. Parker**, Fresenius-Kabi, 5, Lilly, 8, AbbVie, 8, GSK, 2; **A. Jackson**, None; **R. Elliott**, None; **I. Bruce**, Genzyme/Sanofi, 2, GlaxoSmithKline, 2, 5, 8, Roche, 2, UCB, 2, 5, 8, Eli Lilly, 5, Merck Serono, 5, ILTOO, 5, AstraZeneca, 8.

Abstract Number: 1820

Serum α-Klotho Is Decreased in Older Systemic Lupus Erythematosus Patients and Correlate with Markers of Disease Activity

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic, debilitating autoimmune disease characterized by heterogeneous, multiorgan involvement with female predominance. Lupus nephritis is one of the key complications of SLE with 10% of patients developing end-stage renal failure, and major risk for overall morbidity and mortality in SLE. The Klotho gene plays an important role in the process of aging, inflammation, and autoimmunity. Diminished levels of a-Klotho (Kl) were reported in age related diseases such as cancer, hypertension, and kidney disease. Significantly low a-Klotho levels were associated with an increased risk of progressive decline in renal function. The aim of our study was to evaluate the serum concentration of a-Klotho in patients with SLE only [Group I] ; SLE with hypertension (HTN)[Group II]; and SLE with lupus nephritis (LN) and HTN [Group III], and compare to that of healthy control and/or control with HTN to determine associations with disease and disease activity.

Methods: We used banked serum samples from patients and controls enrolled in a prospective longitudinal cohort study. Our study consisted of 20 paired serum samples from patients with SLE and/or LN and/or HTN (5 in each group) and 15 controls with or without HTN. SLE patients had serum collected during paired visits (first and second visit) with lower and higher disease activity determined through clinical and laboratory elements of the SLEDAI (SLE Disease Activity Index).The serum samples were analyzed through an enzyme-linked immunosorbent assay (ELISA) development system for the determination of human soluble a-Kl (R&D Systems).

Results: The serum concentration of Kl was 0.84 ± 0.599 ng/ml and 0.86 ± 0.449 ng/ml in SLE patients during inactive and active disease, respectively. Serum Kl averaged 0.82 ± 0.667 ng/ml in No HTN controls and 1.21 ± 1.252 ng/ml in HTN controls. Serum Kl negatively correlated with age among female SLE patients from all groups during active disease ($r = -0.524$, $p = 0.032$). Interestingly, serum Kl concentration positively correlated with anti-dsDNA antibody levels in all females with active disease ($r = 0.525$, $p = 0.046$). Moreover, the serum Klotho concentration positively correlated with protein/creatinine ratio in females with active disease and LN ($r = 0.974$, $p = 0.004$). There was no association between Kl concentration and C3, C4 levels in SLE patients.

Conclusion: This is the first study measuring Kl levels in serum from the inactive and active stage of SLE with hypertension as a covariable. Klotho levels negatively correlated with age of SLE patients, which is similar to the diminished concentration of Kl seen with chronological aging. We initially postulated that Kl levels would decrease in SLE patients since serum Kl acts as an anti-inflammatory molecule, but did not see this in our study. Surprisingly, we found an association between Kl levels and the positivity of dsDNA titers and protein/creatinine ratio. The positive correlation between elevated levels of Kl and laboratory measures of disease activity may be a compensatory response to inflammation, while decreases with age may reflect accelerated immune senescence.

Disclosure: M. Markiewicz, None; **D. Russell**, None; **J. Oates**, None.

Abstract Number: 1821

Early Assessment of Left Ventricular Assessment Using Speckle Tracking Echocardiography and It´s Relationship with Insulin Resistance in Women with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Diagnosis, Manifestations, & Outcomes Poster III: Bench to Bedside
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus patients (SLE) have increased cardiovascular risk. Patients with SLE are associated with significant alterations in cardiac structure and function as demonstrated by echocardiography. Insulin resistance (IR), which is higher in SLE patients than controls, adversely impacts left ventricular (LV) remodeling and function at middle age. Although IR may not play as marked role in determining LV dysfunction as is hypertension, the impact of IR on ventricular dysfunction is unknown in SLE patients.

The aim of this research were: 1) to determine the role of speckle tracking echocardiography in early detection of LV dysfunction in SLE and 2) to examine the influence of IR measured by Quantose score on subclinical LV dysfunction using speckle tracking echocardiography in normotensive SLE patients.

Methods: This cross-sectional study included SLE adult women without diabetes mellitus (DM), hypertension or obesity. All participants underwent detailed two- dimensional Doppler and two-dimensional speckle tracking echocardiography. Global longitudinal strain (GLS%) and global circumferential strain (GCS%) were determined from three standard apical views, using a combination of speckle tracking and tissue Doppler imaging to track regions of interest. The lower limits of normality for the strain components were < 18.5% for the longitudinal strain, and –15.4% for the circumferential. Left ventricular diastolic dysfunction (LVDD) was verified according to current guidelines. Blood sample were drawn to estimate the Quantose score for IR, which is derived from fasting measurements of insulin, α-hydroxybutyrate, linoleoyl-glycerophosphocholine, and oleate, three nonglucose metabolites shown to correlate with insulin-stimulated glucose disposal.

Results: Seventy female patients were included (mean age: 39.0 ± 9.9 years, mean disease duration 11.6 ± 4.9 years, mean disease activity: 1.8 ± 1.4). The frequency of IR was high (65%). Despite a normal ejection fraction in all participants, eleven (15.7%) patients had abnormal LV systolic GLS. Twenty-three (32.8%) patients had LVDD. The GLS% and GCS% did not differ in patients with and without IR (-20.8 ± 3.1 vs. -20.5 ± 2.1; p= 0.61 and -27.9 ± 4.4 vs. -27.4 ± 3.7; p= 0.57, respectively). The prevalence of LVDD was 38.1% in patients with IR vs. 25.0% in patients without IR (p= 0.30). E/E' and E/A ratios did not differ significantly between groups (6.6 ± 1.9 vs. 6.6 ± 1.5; p= 0.98 and 1.3 ± 0.3 vs. 1.3 ± 0.2; p= 0.27).

Conclusion: Although IR was high in our patients with SLE, IR was not associated with either left ventricular systolic dysfunction or LVDD in SLE patients without DM or hypertension.

Disclosure: P. Munguía-Realpozo, None; **C. Mendoza-Pinto**, None; **S. Méndez-Martínez**, None; **L. Pérez-Aquino**, None; **I. Etchegaray-Morales**, None; **M. Garcia-Carrasco**, None.

Abstract Number: 1822

Serum Proteomics from a Phase III, Randomized, Placebo-Controlled Study of Patients with Active Lupus Nephritis: Correlation with Baseline Disease Characteristics and Response to Therapy

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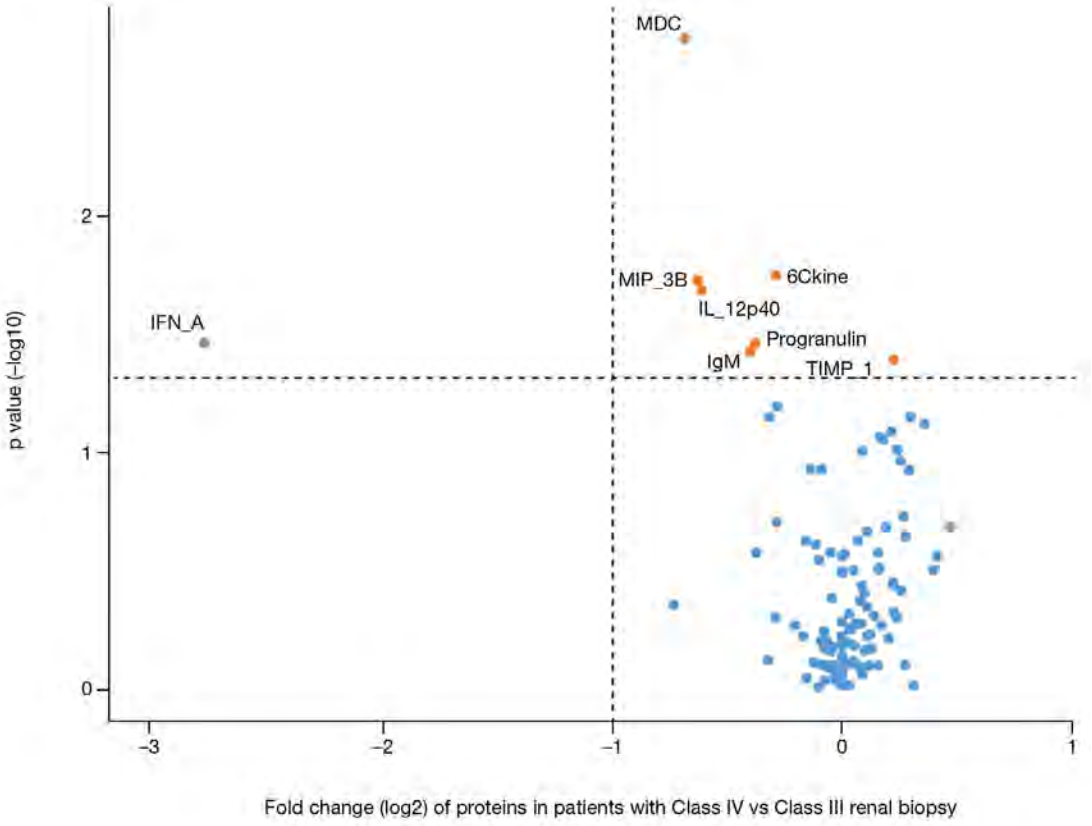
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The ALLURE study compared efficacy and safety of abatacept (ABA) vs placebo (PBO) on background MMF and CS for the treatment of active proliferative LN.[1] The primary endpoint of improvement in complete response (CR) rate at 1 year (ABA 35.1%, PBO 33.5%; p=0.73) was not met; however, the ABA-treated patient (pt) group had an earlier, more pronounced improvement in urine protein/creatinine ratio (UPCR; ABA –2.95, PBO –2.68) and estimated glomerular filtration rate (eGFR; ABA 109, PBO 105 mL/min/1.73 m^2) and a higher rate of sustained CR (sCR; ABA 48%, PBO 38%; hazard ratio estimate [95% CI] 1.41 [0.9942, 2.0068]) at 1 year. In this serum proteomic analysis, correlations between protein biomarkers, baseline (BL) disease characteristics and treatment outcomes were studied to better understand disease pathogenesis and treatment effects.

Methods: Serum samples from pts with SLE (ACR 1982 criteria)[2] and biopsy-proven LN (122 ABA, 119 PBO) in ALLURE (NCT01714817) were analyzed for 122 protein biomarkers. Associations between biomarkers, categorical disease measurements and clinical responses were assessed by Wilcoxon-Mann-Whitney test, and between biomarkers and continuous disease activity measurements by Spearman's rank correlation.

Results: Serum proteins at BL were comparable in both treatment groups. At BL, 17 serum proteins significantly correlated with UPCR, 33 with eGFR and 26 with BILAG score (adjusted $p< 0.01$); these included albumin, CD40, TNFR2, SCF and CD27. Several protein biomarkers were differentially expressed between pts with International Society of Nephrology and the Renal Pathology Society Class III and IV LN (**Figure 1**). Class IV LN was associated with lower levels of IFN-α, MDC, MIP-3B and IL12p14 than Class III LN, suggesting differential cytokine regulation. Some proteins (eg, TNFR1, SCF) correlated with changes from BL in eGFR and UPCR over time. Thirteen biomarkers, including MCP2, IGFBP2, AXL, SCF and MMP-2, correlated with early (Day 85) UPCR improvement in the ABA, but not PBO, group. Pts with lower BL CD40, B2M and MMP7 levels had better treatment outcomes for eGFR (achieving normal eGFR or >85% of the BL value) at Day 365 in both treatment groups. BL levels of myoglobin, CD27, APRIL, SCF, IGFBP7 and EGFR were associated with favorable eGFR outcomes in the ABA group, while TNFR1, Fib-1C,

Figure 1. Differential expression of serum proteomics at baseline between patients with Class III or IV LN



IL_12p40=interleukin-12 subunit p40; MDC=macrophage-derived chemokine; MIP_3B=macrophage inflammatory protein 3 beta; TIMP_1=tissue inhibitor of metalloproteinases 1.

Medical writing: Rachel Rankin (Caudex)

6CKine, HCC4 and FGF23 were associated with favorable eGFR outcomes in the PBO group. Similar patterns were observed for categorical improvement of UPCR (< 0.5, or >50% decrease from BL) at Day 365 with different serum protein biomarkers. A panel of BL protein biomarkers was identified including CD40, CD27, TNFR2 and FAS that strongly correlated with the achievement of sCR by Day 365 in the ABA, but not PBO, group.

Conclusion: Pts with active LN had distinct serum proteomic profiles that correlated with features of LN and treatment outcomes. Specific associations with abatacept are consistent with its immunomodulatory mechanistic effects. Clinical trials should endeavor to apply precision medicine approaches to improve understanding of LN and treatment strategies.

References

1. Furie R, et al. EULAR 2018. Oral OP0253.
2. Tan EM, et al. *Arthritis Rheum* 1982;25:1271–1277.

Disclosure: S. Wang, None; **R. Furie**, AstraZeneca/MedImmune, 2, 5; **M. Dooley**, Bristol-Myers Squibb Company, 5, GlaxoSmithKline, 5, Aurinia, 5; **D. Wofsy**, Novartis, 5, GlaxoSmithKline, 5, Principia, 5; **T. Takeuchi**, Astellas Pharma Inc., 2, 5, 8, Daiichi Sankyo Company, Limited, 2, 5, 8, Takeda Pharmaceutical Company Limited, 2, 5, 8, AbbVie GK., 2, 5, 8, Asahi Kasei Pharma Corporation, 2, 5, 8, Mitsubishi Tanabe Pharma Corporation, 2, 5, 8, Eisai Co., Ltd., 2, 5, 8, Nippon Kayaku Co., Ltd., 2, 5, 8, Chugai Pharmaceutical Co., Ltd., 2, 5, 8, Eli Lily Japan K.K, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Pfizer Japan, Inc., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, AYUMI Pharmaceutical Corporation, 2, 5, 8, Novartis Pharma K.K., 2, 5, 8, UCB, 2, 5, 8, Dainippon Sumitomo Co., 2, 5, 8, Shionogi & Co., Ltd., 2, 5, 8; **A. Malvar**, None; **A. Doria**, GlaxoSmithKline, 5, 8, Eli Lilly, 5, 8, Roche, 5, 8, Janssen, 5, 8, Pfizer, 5, 8; **J. Romero-Díaz**, Biogen, 5; **T. Chan**, None; **G. Appel**, Sanofi-Genzyme, 2, 5, 8, Achillion, 2, 5, Bristol-Myers Squibb Company, 2, 5, EMD Serono, 2, 5, Retrophin, 2, Aurinia, 2, Calliditas, 2, ChemoCentryx, 2, Zyversa, 2, Mallinkrodt, 2, 5, Genentech, 2, 5, 8, NIH, 2, Alexion, 5, Ionis, 5, Pfizer, 5, Merck, 5, Roche, 5, Up-to-Date, 5, Omeros, 5, Regulus, 5, Zyversa, 5; **D. Jayne**, Chemocentryx, 1, 2, 5, GlaxoSmithKline, 1, 2, 5, AstraZeneca, 1, 2, 5, Aurinia, 1, 2, 5, Bristol-Myers Squibb Company, 1, 2, 5, Boehringer Ingelheim, 1, 2, 5; **S. Hu**, Bristol-Myers Squibb Company, 1, 3, 4; **S. Gao**, Bristol-Myers Squibb Company, 1; **M. Maldonado**, Bristol-Myers Squibb Company, 1, 3.

Abstract Number: 1823

Mycophenolate Mofetil for Systemic Lupus Erythematosus: Our 20-year Experience

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Mycophenolate Mofetil (MMF) has been long used in the treatment of systemic lupus Erythematosus (SLE). Despite its proven effectiveness, particularly in the treatment of lupus nephritis, further studies are warranted to investigate its role in long-term maintenance therapy. The purpose of this study was to describe our 20 years of practice experience using MMF with regards to its indications, safety, tolerability and treatment efficacy. Among patients on long-term maintenance therapy, we sought to identify rates of renal flare and of progression to end-stage renal disease (ESRD).

Methods: In this retrospective chart review, we identified all patients with SLE who were treated with MMF between 1999 and 2019. We recorded data about indications, duration of treatment, reason for discontinuation, and side effects. Treatment efficacy for lupus nephritis was evaluated by occurrence of remission, occurrence of renal flare, and of progression to ESRD.

Results: Six hundred and sixty patients with SLE were evaluated; among them, 101 were treated with MMF. The indications for starting MMF were lupus nephritis (89%), interstitial lung disease (7%), and use as a steroid-sparing agent (4%). The mean duration of treatment was 69 months. Treatment was discontinued due to inefficacy in 9% of patients, and due to side effects in 8% of patients. The most common side effects were Leukopenia (9%), nausea (7%) and diarrhea (6%). Among patients with lupus nephritis, 60% achieved complete remission and 16% achieved partial remission at 1-year follow-up. Of those who did not achieve remission after one year, 7/14 (50%) did by second year. Among the 25 patients treated for at least 5 years, 1 developed a flare between the 5 and 10-year follow-up

period. Among the 15 patients treated for at least 10 years, no patients developed any flare at subsequent follow-up. Among patients on maintenance therapy, 3 progressed to ESRD.

Conclusion: Maintenance treatment with MMF constitutes an effective long-term treatment for lupus nephritis. Our practice demonstrates its tolerability over many years with few adverse effects, prevention of renal flares, and a low progression rate to ESRD.

Disclosure: M. Trevisonno, None; **A. Hall**, None; **C. Sorrento**, None; **E. Ginzler**, Aurinia Pharmaceuticals, Inc., 2.

Abstract Number: 1824

Selective Expansion of Regulatory T Cells in Patients with Systemic Lupus Erythematosus by a Novel IL-2 Conjugate, NKTR-358

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Treg dysfunction and impaired IL-2 production have been implicated as key immunological defects in the breakdown of immune self-tolerance in SLE. Low-dose IL-2 can expand Tregs, but this therapy has a narrow therapeutic window for stimulation of Tregs versus conventional T cells (Tcons), and a short half-life. NKTR-358, a polyethylene glycol (PEG) conjugate of recombinant human IL-2 (aldesleukin sequence), has altered IL-2 receptor binding and prolonged biological activity compared with native IL-2. In healthy volunteers, single SC administration led to a dose-dependent increase in Tregs with no elevation of Tcons.

Methods: In this double-blind, multiple ascending dose, Phase 1b study (NCT03556007), 48 patients with mild to moderate SLE activity (per ACR criteria) received 3 SC doses q2w of NKTR-358 in 4 cohorts ranging from 3 to 24 μg/kg (9 active: 3 placebo per cohort) and were followed for 50 days after the last dose. The time course and extent of activation and proliferation of peripheral blood Tregs, Tcons, and NK cells were assessed. Changes in gene expression and epigenetic markers were also investigated.

Results: There were no dose-limiting toxicities, deaths, or clinically significant abnormalities in vital signs or electrocardiograms. Adverse events attributed to NKTR-358 were primarily limited to mild (grade 1 or 2) injection site reactions. Dosing was stopped in 1 subject due to elevated eosinophil levels, without clinical sequelae. NKTR-358 demonstrated dose-dependent numerical improvements in the Cutaneous Lupus Erythematosus Disease Area and Severity Index score; however, the small number of patients per dose, low entry disease activity, and short treatment duration limited comprehensive assessment of disease activity.

The primary effect of NKTR-358 was seen on Tregs. In the 3 to 24 μg/kg cohorts, dose-dependent, sustained increases in absolute number, percentage, and proliferation (Ki67+) of circulating FoxP3+CD25^{bright} Tregs were observed, with levels remaining elevated throughout the dosing period. At 24 μg/kg, the maximum mean peak increase in number of CD25^{bright} Tregs was 12-fold above baseline and the maximum mean percentage of Ki67+ CD25^{bright} Tregs was

5-fold above baseline, not returning to predose levels until 20–30 days after the last dose. No increases in CD4+ or CD8+ Tcon numbers were detected, and low-level increases in the percentage of NK cells were noted at the highest dose tested. Induction of Tregs was further supported by a correlation of number of Tregs identified by flow cytometry and extent of demethylated FoxP3 at ≥12 μg/kg. Expression of Treg activation markers CD25, Helios, and CTLA4 were induced at ≥12 μg/kg, and NKTR-358 also led to dose-dependent induction of genes associated with Treg regulation, such as IDO1.

Conclusion: These results extend findings previously reported in healthy volunteers. In the current study in patients with SLE, NKTR-358 was safe and well tolerated, and led to a sustained and selective dose-dependent increase in $CD25^{bright}$ Tregs. Induced Tregs displayed increased levels of activation markers. Together, these data provide strong support for continued development of NKTR-358 in patients with SLE as well as in other inflammatory diseases.

Disclosure: C. Fanton, Nektar Therapeutics, 1, 3; **R. Furie**, Nektar Therapeutics, 2, 5; **N. Dixit**, Nektar Therapeutics, 1, 3; **C. Haglund**, Nektar Therapeutics, 1, 3; **L. Lu**, Nektar Therapeutics, 1, 3; **S. Siddhanti**, Nektar Therapeutics, 1, 3; **V. Chindalore**, GlaxoSmithKline, 2, Pfizer, 1, Amgen Inc, 1, Genentech, 1, Novartis, 1, Eli Lilly, 1, Nektar, 1, Boston Pharmaceuticals, 1, AbbVie, 1, Boehringer Ingelheim, 2, EMD Serono, 1, Roche, 1, Merck, 1; **R. Levin**, Industry-sponsored clinical trials, 1, Gilead, 1, Exagen, 1, Myriad Rheumatology, 1, Sanofi/Genzyme, 1, Regeneron, 1, Bristol Myers Squibb, 1, AbbVie, 1; **I. Diab**, None; **B. Kotzin**, Nektar Therapeutics, 1, 2; **J. Zalevsky**, Nektar Therapeutics, 1, 2.

Abstract Number: 1825

Risk Factors for Antimalarial-Induced Retinal Toxicity in Systemic Lupus Erythematosus and Other Rheumatic Diseases

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) and chloroquine (CQ) are antimalarial (AM) medications prescribed for a variety of rheumatic diseases, including systemic lupus erythematosus (SLE). Many patients will remain on these medications for years, and possibly lifelong. HCQ and CQ are associated with irreversible vision loss secondary to retinal toxicity. The prevalence of AM-induced retinopathy varies between studies and few studies have compared prevalence rates between rheumatologic conditions. The purpose of this study was to describe the pattern and risk factors for AM-associated retinopathy.

Methods: A retrospective chart review was conducted at an urban academic Canadian centre after obtaining ethics approval. Each patient was classified as SLE, based on ACR criteria, or non-SLE. The minimum duration of AM therapy was three months. AM-induced retinopathy was classified as possible or definite, which was determined based on characteristic visual field loss, abnormal retinal imaging and eye specialist's opinion. Univariate and multivariate regression analyses were performed to determine factors associated with definite AM-induced retinopathy. Sensitivity analyses included stratification of analysis by diagnosis and by HCQ versus CQ.

Results: A total of 680 patient charts were reviewed of whom 282 patients had SLE and the remaining had rheumatoid arthritis (N=224), cutaneous lupus (N=41) or other connective tissue diseases (N=133). Ninety percent of patients had a baseline eye examination within the first five years of AM treatment, and 74% had regular follow up exams beyond five years. Definite AM-induced retinal toxicity was observed in 12 patients, 11 of whom had SLE and 7 had been prescribed CQ (Figure 1). The earliest diagnosis of toxicity occurred after 5.4 years of AM therapy, and the prevalence beyond five years was 2.7% but increased over time. In univariate analysis (Table 1), a diagnosis of SLE (P=0.008; OR=16.1; 95% CI=[2.1, 125]), the daily weight-based dose of HCQ (P=0.035; OR=1.5; 95% CI=[1.0,

Figure 1: Distribution of duration of antimalarial use and onset of retinopathy

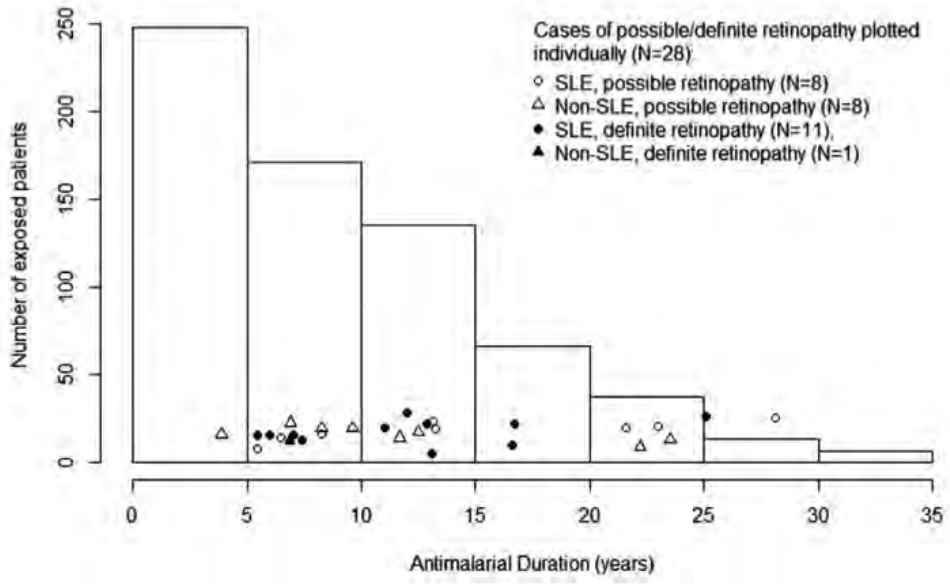
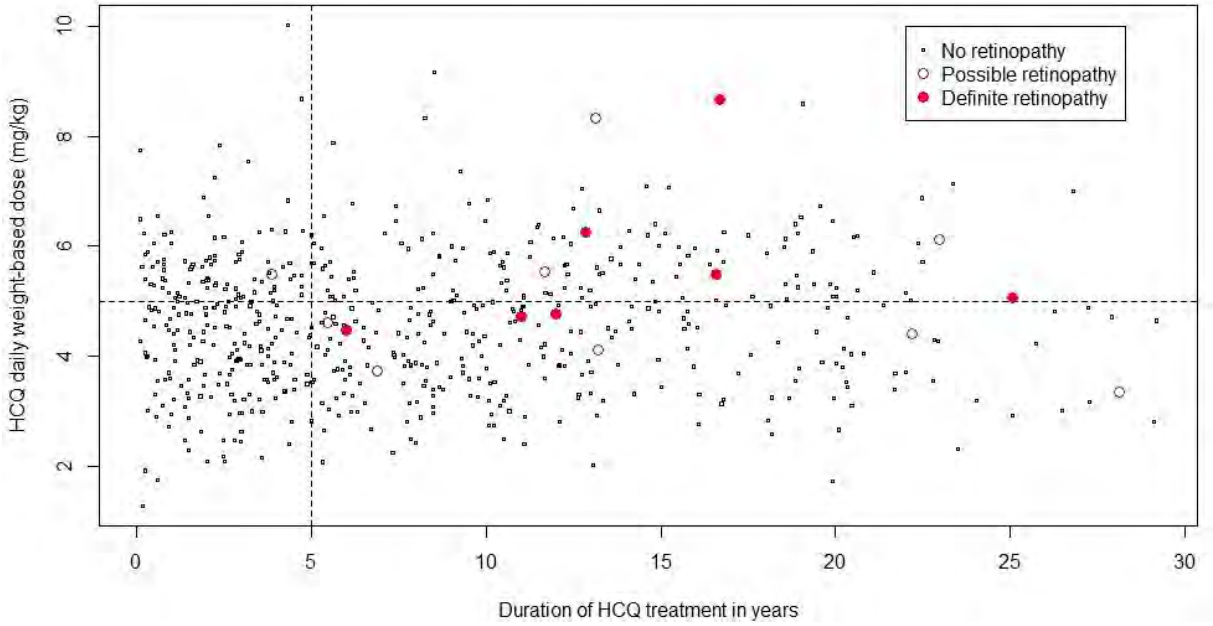


Table 1: Univariate logistic regression for risk of AM-induced retinopathy. Data represented as N (%) or mean ± SD

	Definite retinopathy			Possible or definite retinopathy		
	No retinopathy N=668	Retinopathy N=12	P	No retinopathy N=652	Retinopathy N=28	P
Age	46.5 ± 15.3	43.2 ± 14.3	0.452	46.4 ± 15.4	47.1 ± 12.4	0.832
Female	580 (87%)	11 (92%)	0.626	567 (87%)	24 (86%)	0.848
Weight (kg)	76.7 ± 19.3	67.3 ± 12.8	0.096	76.6 ± 19.3	73.5 ± 17.8	0.402
SLE Diagnosis	271 (41%)	11 (92%)	**0.008**	263 (40%)	19 (68%)	**0.006**
AM duration (years)	9 ± 7.4	11.7 ± 5.8	0.215	8.9 ± 7.3	12.8 ± 6.8	**0.007**
AM> 5 years	417 (63%)	12 (100%)	-	250 (40%)	1 (3%)	**0.006**
HCQ daily dose (mg/kg)	4.6 ± 1.3	5.4 ± 2.2	**0.035**	4.6 ± 1.3	4.9 ± 2.0	0.159
HCQ total dose (g)	1042 ± 914	1235 ± 1032	0.471	1040 ± 914	1187 ± 955	0.404
CQ daily dose (mg/kg)	0.3 ± 0.9	1.6 ± 2.1	**4.73×10^{-5}**	0.2 ± 0.9	1.4 ± 1.8	**1.52×10^{-7}**
CQ total dose (g)	46 ± 205.1	225± 291	**0.011**	37.6 ± 174	318 ± 529	**6.16×10^{-7}**
Renal Impairment	100 (15%)	2 (17%)	0.883	99 (15%)	3 (11%)	0.506
Hypertension	298 (45%)	5 (42%)	0.832	285 (44%)	18 (64%)	**0.038**
Diabetes	61 (9%)	1 (8%)	0.924	59 (9%)	3 (11%)	0.765

Figure 2: Hydroxychloroquine daily weight-based dose and retinopathy



2.3]), daily weight-based dose of CQ (P< 0.001; OR=1.9; 95% CI=[1.4, 2.6]), and cumulative CQ dosage (P=0.011; OR=5.0; 95% CI=[1.4, 17.3]) were significantly associated with definite AM-induced retinopathy. In multivariate analysis, diagnosis of SLE (P=0.015; OR=13.2; 95% CI=[1.6, 111.3]) and CQ daily weight-based dose (P=0.004; OR=2.0; 95% CI=[1.2, 2.3]) were significantly associated with ocular toxicity after adjusting for CQ/HCQ dosages, age, sex, weight, and renal impairment. When possible retinopathy was included in the univariate analysis, SLE and CQ dosages remained significant (Table 1). Total AM duration and hypertension also had significant associations. Patients prescribed HCQ doses less than the recommended maximum of 5mg/kg/day did develop retinopathy (Figure 2).

Conclusion: The risk of AM-induced retinal toxicity increases after five years of therapy. There may be higher rates of AM-induced retinopathy in SLE patients due to longer duration of treatment, more chloroquine use in this population, and SLE may be an independent risk factor.

Disclosure: G. Cramarossa, None; **H. Liu**, None; **J. Pope**, AbbVie, 2, 5, Amgen, 5, 8, Lilly, 2, 5, 8, UCB, 2, 5, 8, Sanofi, 5, 8, Sandoz, 5, 8, Roche, 2, 5, 8, Pfizer, 5, 8, Novartis, 5, 8, Merck, 2, 5, 8, Janssen, 5, 8, Gilead Sciences, Inc., 2, 5, BMS, 2, 5, 8, Abbott, 5, Actelion, 5, AstraZeneca, 5, Bayer, 5, Boehringer Ingelheim, 5, EICOS, 5, Emerald, 5, GlaxoSmithKline, 5, Medexus, 5, Seattle Genetics, 2.

Abstract Number: 1826

Maintenance of Efficacy and Safety and Reduction of BILAG Flares with Ustekinumab, an Interleukin-12/23 Inhibitor, in Patients with Active Systemic Lupus Erythematosus: 2-Year Results of a Phase 2, Randomized Placebo-Controlled, Crossover Study

Ronald van Vollenhoven[1], Bevra Hahn[2], George Tsokos[3], Peter Lipsky[4], Robert Gordon[5], Kaiyin Fei[6], Kim Hung Lo[7], Marc Chevrier[8], Qing Zuraw[9], Pamela Berry[10], Chetan Karyekar[10] and Shawn Rose[11], [1]Department of Rheumatology, Amsterdam Rheumatology and Immunology Center, Amsterdam, Netherlands, [2]University of California Los Angeles, Encino, CA, [3]Division of Rheumatology & Clinical Immunology/Beth Israel Deaconess Medical Center/Harvard Medical School, Boston, MA, [4]RILITE Foundation, Charlottesville, VA, [5]Janssen Research & Development, LLC, Chester Springs, PA, [6]Janssen Research & Development, LLC, Spring House, PA, [7]Janssen Research & Development, LLC, Spring House, [8]Janssen Research & Development, LLC, Collegeville, PA, [9]Janssen Research & Development, LLC, Wayne, PA, [10]Janssen Global Services, LLC, Horsham, PA, [11]Janssen Research & Development, LLC, Princeton Junction, NJ

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: SLE – Treatment Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Both IL-12 and IL-23 have been implicated in the pathogenesis of SLE. In a phase 2 study, treatment with the anti-IL-12/23 p40 monoclonal antibody ustekinumab (UST) resulted in greater improvement in several SLE disease measures through week (wk) 24 compared with placebo (PBO)[1], and efficacy was maintained through 1 year.[2] Here we report long-term safety and efficacy of ustekinumab through 2 years in patients (pts) with active SLE.

Methods: This was a PBO-controlled phase 2 study in 102 pts with seropositive active SLE (defined by SLICC criteria; SLEDAI score ≥6; ≥1 BILAG A and/or ≥2 BILAG B scores). Pts were randomized (3:2) to UST (~ 6 mg/kg single IV infusion, then 90 mg SC q8w at wk8) or PBO, both added to standard background therapy. Patients receiving PBO crossed over to UST (90 mg SC q8w) at wk24. The majority of pts were eligible to enter a voluntary open-label study extension after wk40; the final UST administration was at wk104. The primary endpoint was SLE Responder Index (SRI)-4 response at wk24. Treatment failure rules and nonresponder imputation were used through wks 24 & 48;[1,2] observed data are reported from week 48 - week 112. Disease flare was defined as ≥1 new BILAG A or ≥2 new BILAG B scores. Safety was assessed through wk120.

Results: 102 pts were randomized at wk0 (UST, n=60; PBO, n=42). The primary endpoint (SRI-4 response rate at wk24) was met,[1] and efficacy was sustained at 1 year.[2] 46 pts entered the extension (UST, n=29; PBO → UST, n=17), 26 pts at wk48, and 20 pts at wk56. SRI-4 response rates were maintained during the extension and were 79% in the UST group and 92% in the PBO → UST group at wk112. In both groups, response rates in joint and skin measures were maintained from wk48 through wk112 (Figures). At wk112, 92% in both the UST and PBO → UST groups had ≥4-point improvement from baseline in SLEDAI-2K score, 79% and 93% had ≥30% improvement from baseline in PGA, 86% and 91% had ≥50% improvement in active joint (pain and inflammation) count, and 79% and 100% had ≥50% improvement in CLASI score. During the extension period, the incidence per 100 pt-years of a BILAG 1A/2B flare was 0 in the PBO → UST group and 1.95 in the UST group. Improvements ≥2.5 points (Minimal Clinically Important Difference [MCID]) in SF-36 PCS scores were observed and maintained from baseline through wk72 (UST group) and at most timepoints from wk40 to wk112 (PBO → UST). No deaths, malignancies, opportunistic infections,

Table. Efficacy at week 112 and adverse events through week 120.

Clinical Efficacy and Health-Related Quality of Life at Week 112		
	PBO → UST	UST
Patients entering study extension, n	17	29
SRI-4	12/13 (92.3)	19/24 (79.2)
SRI-5	11/13 (84.6)	13/24 (54.2)
SRI-6	11/13 (84.6)	13/24 (54.2)
SLEDAI-2K Response	12/13 (92.3)	22/24 (91.7)
BICLA Response	12 (70.6)	16 (55.2)
PGA Response	13/14 (92.9)	19/24 (79.2)
CLASI Response	5/5 (100)	11/14 (78.6)
≥50% improvement in active joint count	10/11 (90.9)	12/14 (85.7)
Mean ± SD change from baseline in SF-36 PCS	4.7 ± 9.2	1.2 ± 6.7

Adverse events Through Week 120				
	PBO (Wk 0-24)	PBO → UST	UST	All UST
Patients, n	42	33	60	93
Mean follow-up, weeks	23.8	59.8	81.1	73.6
Patients with ≥ 1 AE	29 (69.0)	25 (75.8)	55 (91.7)	80 (86.0)
Infections	20 (47.6)	18 (54.5)	44 (73.3)	62 (66.7)
Opportunistic infections	0	0	0	0
Patients with ≥ 1 SAE	4 (9.5)	5 (15.2)	12 (20.0)	17 (18.3)
Serious infections	0	2 (6.1)	7 (11.7)	9 (9.7)
Deaths	0	0	0	0

Data presented as n/N (%) or n (%) unless otherwise noted.
AE = adverse event; CLASI = Cutaneous Lupus Erythematosus Disease Area and Severity Index (response defined as ≥ 50% improvement from baseline in patients with a baseline CLASI activity score ≥4); PGA = Physician's Global Assessment (response defined as ≥ 30% improvement from baseline); SAE = serious adverse event; SF-36 PCS = 36-item short-form survey physical component summary; SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000 (response defined as ≥ 4-point improvement from baseline); SRI-4/5/6 = SLE responder index, defined as ≥ 4/5/6-point reduction in SLEDAI-2K total score, no new BILAG A and no more than 1 new BILAG B domain score and no worsening (<10% increase) from baseline in the PGA. Joint response (defined as ≥ 50% improvement from baseline in the number of active joints in patients with ≥4 active joints at baseline).

or tuberculosis cases occurred through week 120. Of 93 pts who received ≥1 dose of UST through wk120, 17 (18%) had a serious AE. Safety events were consistent with the known UST safety profile.

Conclusion: UST provided sustained clinical benefit in global and organ-specific SLE-activity measures through 2 years with safety results consistent with the established profile.

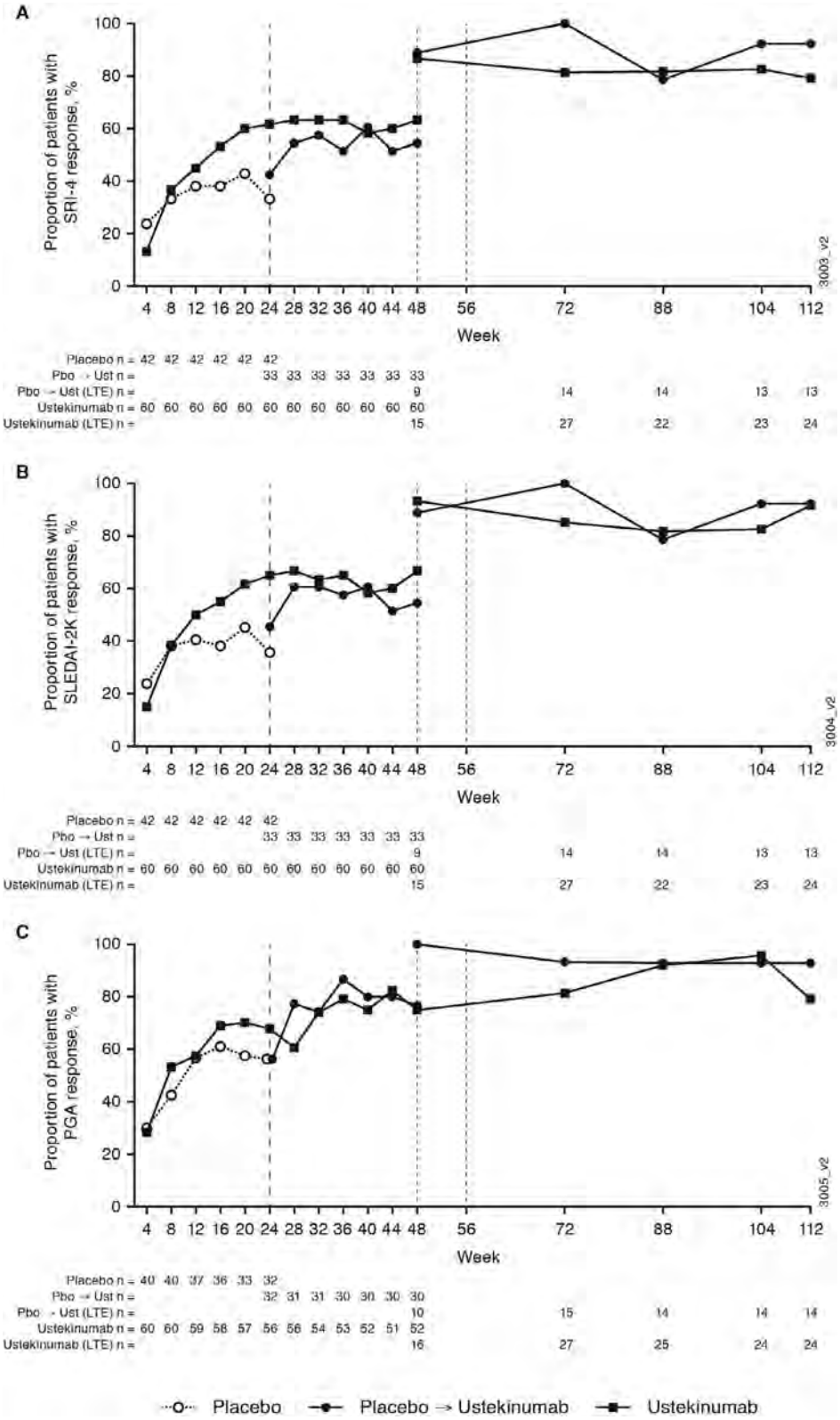


Figure 1. Proportions of patients with SRI-4 (A), SLEDAI-2K (B), and PGA (C) responses through week 112. SRI-4 = SLEDAI-2K responder index, defined as ≥ 4-point reduction in SLEDAI-2K total score, no new BILAG A and no more than 1 new BILAG B domain score and no worsening (<10% increase) from baseline in the PGA. SLEDAI-2K = Systemic Lupus Erythematosus Disease Activity Index 2000 (response defined as ≥ 4-point improvement from baseline). PGA = Physician's Global Assessment (response defined as ≥ 30% improvement from baseline). The study protocol was amended to add the extension period after the interim analysis, and some patients had already completed or discontinued from the main study. Patients participating in the study extension entered either at Week 48 or Week 56.

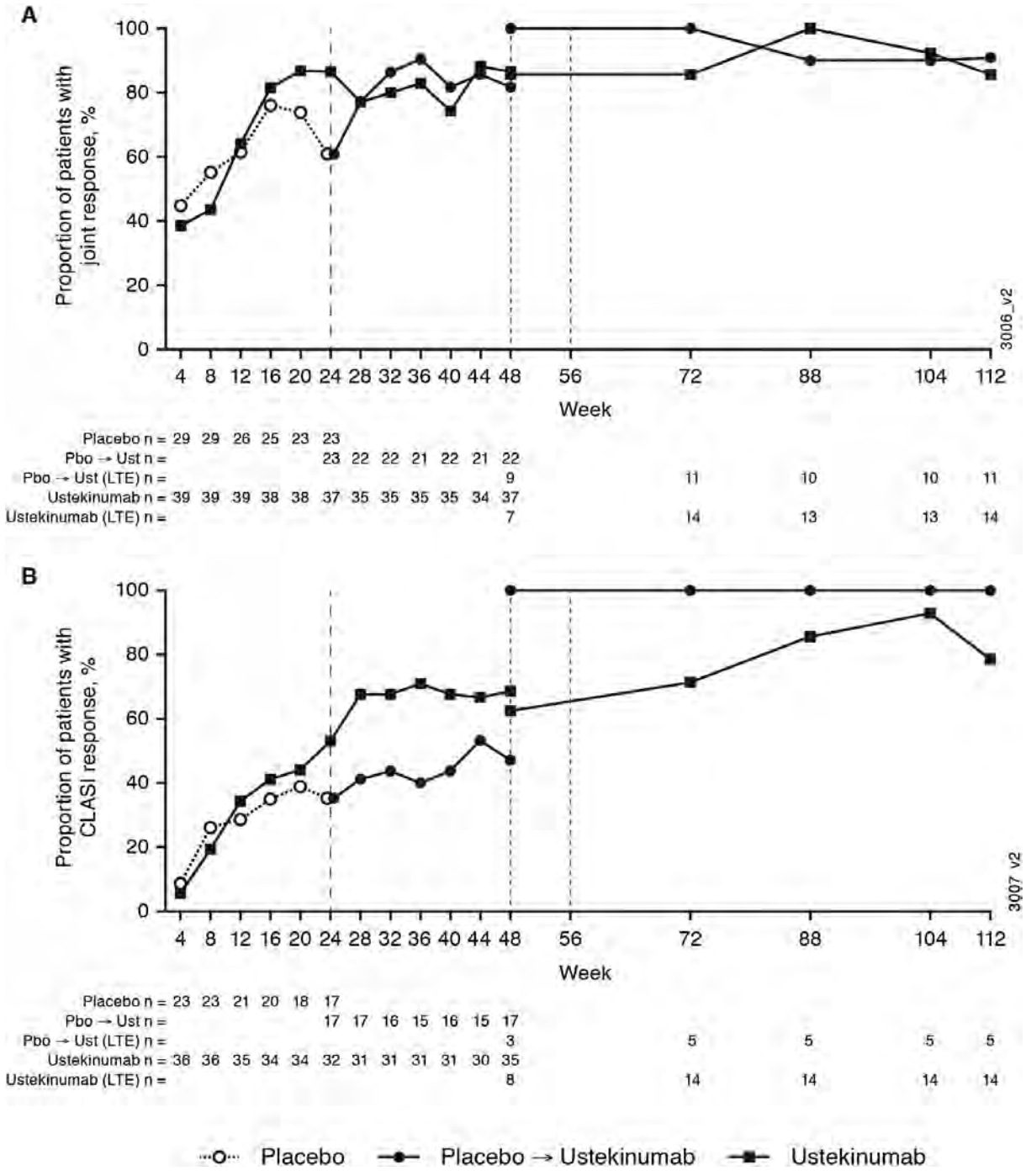


Figure 2. Proportions of patients with joint (A) and CLASI (B) responses. The study protocol was amended to add the extension period after the interim analysis, and some patients had already completed or discontinued from the main study. Patients participating in the study extension entered either at Week 48 or Week 56. Joint response (defined as ≥ 50% improvement from baseline in the number of joints with pain and inflammation [active joints] in patients with ≥4 active joints at baseline). CLASI response (defined as ≥ 50% improvement from baseline in patients with a baseline CLASI activity score ≥4).

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2. Arthritis Rheumatol. 2019 Nov 25. https://doi.org/10.1002/art.41179

Disclosure: R. van Vollenhoven, AbbVie, 2, 5, Bristol-Meyers Squibb, 2, 5, GlaxoSmithKline, 2, 5, Lilly, 2, 5, Pfizer, 2, 5, UCB, 2, 5, 8, AstraZeneca, 5, 8, Biotest, 2, 5, Celgene, 5, Janssen, 5, 8, Roche, 5, Biogen, 5, Galapagos, 5, 8, Gilead, 5, Servier, 5; **B. Hahn**, Janssen, 9; **G. Tsokos**, None; **P. Lipsky**, Janssen Research & Development, LLC, 1; **R. Gordon**, Janssen Research & Development, LLC, 1, 3; **K. Fei**, Janssen Research & Development, LLC, 1, 3; **K. Lo**, Janssen Research & Development, LLC, 1, 3; **M. Chevrier**, Janssen Research & Development, LLC, 1, 3; **Q. Zuraw**, Janssen Research & Development, LLC, 1, 3; **P. Berry**, Janssen Global Services, LLC, 1, 3; **C. Karyekar**, Janssen Global Services, LLC, 3, Johnson & Johnson, 1, Janssen, 5; **S. Rose**, Janssen Research & Development, LLC, 1, 3.

Abstract Number: 1827

Flare Reduction and Oral Corticosteroid Taper in Patients with Active SLE Treated with Anifrolumab in 2 Phase 3 Trials

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Objectives of long-term SLE management are not only to reduce disease activity, but also to prevent flares and minimize exposure to oral corticosteroids (OCS), which are associated with organ damage accrual.[1,2] As tapering OCS increases flare risk, a therapy that both prevents flares and permits safe reductions of OCS is desirable. Flare rates were lower in patients with SLE who received anifrolumab vs placebo, and greater numbers of patients were able to taper OCS with anifrolumab vs placebo in the phase 3 trials, TULIP-1 and TULIP-2.[3,4] We evaluated pooled TULIP trial data to further assess the capacity of anifrolumab to simultaneously prevent flares and permit OCS dosage reduction.

Methods: TULIP-1 and TULIP-2 were 52-week trials that evaluated the efficacy and safety of anifrolumab (300 mg IV Q4W for 48 weeks) or placebo in patients with moderately to severely active SLE despite standard-of-care treatment. Flares were defined as ≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B domain scores vs the prior visit. Patients receiving OCS ≥10 mg/day at baseline were required to attempt tapering to ≤7.5 mg/day between Weeks 8 and 40; this reduction had to be sustained through Week 52. TULIP-1 and TULIP-2 were analyzed using restricted medication rules per the TULIP-2 protocol, and data from both trials were pooled. We analyzed flare occurrence in all patients, area under the curve (AUC) of OCS dosage among patients on OCS ≥10 mg/day at baseline, and flare rates among patients on OCS ≥10 mg/day at baseline who were able to sustain OCS dosage reduction to ≤7.5 mg/day from Week 40 to Week 52.

Results: Overall, 360 patients received anifrolumab and 366 received placebo. In total, fewer patients had ≥1 flare with anifrolumab vs placebo (33.6% vs 42.9%) (**Table 1**). In pooled TULIP data, 375/726 (51.7%) patients were taking OCS ≥10 mg/day at baseline; among these patients, OCS cumulative dosage through Week 52 was reduced with anifrolumab vs placebo (mean [SD] AUC 3947.1 mg [3655.5] vs 4275.8 mg [1859.0]). Among patients who were able to sustain OCS taper to ≤7.5 mg/day, fewer experienced ≥1 flare through Week 52 with anifrolumab vs placebo in

Patients with flare, n (%)	Placebo (n=366)	Anifrolumab 300 mg (n=360)
0	209 (57.1)	239 (66.4)
≥1	157 (42.9)	121 (33.6)
1	89 (24.3)	74 (20.6)
2	49 (13.4)	28 (7.8)
≥3	19 (5.2)	19 (5.3)

A flare was defined as ≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B items compared with the prior visit.

Table 1. Number of Flares Through Week 52 in Pooled Data From the TULIP-1 and TULIP-2 Trials

Trial and treatment group (n=patients with OCS ≥10 mg/day at baseline)	Flares through Week 52	Sustained OCS dosage reduction from Weeks 40 to 52	
		Yes	No
TULIP-1			
Placebo (n=102)	No flares, n (%)	20 (58.8)	31 (45.6)
	≥1 flare, n (%)	14 (41.2)	37 (54.4)
	Total, n	34	68
Anifrolumab (n=103)	No flares, n (%)	41 (80.4)	24 (46.2)
	≥1 flare, n (%)	10 (19.6)	28 (53.8)
	Total, n	51	52
TULIP-2			
Placebo (n=83)	No flares, n (%)	12 (48.0)	30 (51.7)
	≥1 flare, n (%)	13 (52.0)	28 (48.3)
	Total, n	25	58
Anifrolumab (n=87)	No flares, n (%)	35 (77.8)	23 (54.8)
	≥1 flare, n (%)	10 (22.2)	19 (45.2)
	Total, n	45	42
Pooled TULIP			
Placebo (n=185)	No flares, n (%)	32 (54.2)	61 (48.4)
	≥1 flare, n (%)	27 (45.8)	65 (51.6)
	Total, n	59	126
Anifrolumab (n=190)	No flares, n (%)	76 (79.2)	47 (50.0)
	≥1 flare, n (%)	20 (20.8)	47 (50.0)
	Total, n	96	94

OCS, oral corticosteroid.
Sustained OCS dosage reduction was defined as OCS dosage of ≤7.5 mg/day achieved by Week 40 and sustained to Week 52. OCS are described as "prednisone or equivalent." OCS administered when necessary are not considered in the calculation of the daily dose. Flares were defined as ≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B domain scores vs the prior visit. Overall patient n values, TULIP-1: anifrolumab, n=180; placebo, n=184; TULIP-2: anifrolumab, n=180; placebo, n=182. Randomization in TULIP-1 and TULIP-2 was stratified by OCS dosage (<10 vs ≥10 mg/day), SLEDAI-2K score (<10 vs ≥10), and type I interferon gene signature (high vs low).

Table 2. Flares and Sustained OCS Dosage Reduction at Week 52 in Patients With OCS ≥10 mg/day at Baseline in TULIP-1, TULIP-2, and Pooled Data

pooled data (20.8% vs 45.8%) (**Table 2**). In contrast, in patients who were not able to taper OCS, there was no difference in the flare rates between anifrolumab and placebo (50.0% vs 51.6%). Overall, with anifrolumab, 76/190 (40.0%) patients were able to taper OCS without experiencing a flare through 52 weeks, compared with only 32/185 (17.3%) with placebo in pooled data.

Conclusion: In the phase 3 TULIP-1 and TULIP-2 trials, compared with placebo, anifrolumab was associated with reduced OCS cumulative dosage and, among patients who were able to taper and sustain OCS dosage to ≤7.5 mg/

day to Week 52, a >2-fold reduction in flares. TULIP data support the capacity of anifrolumab to reduce flares while permitting the tapering of OCS, an important management goal for patients with SLE.

References

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3. Furie RA. *Lancet Rheumatol*. 2019;1:e208–19.
4. Morand EF. *N Engl J Med*. 2020;382:211–21.

Writing assistance by Rosie Butler, PhD (JK Associates Inc., a Fishawack Health Company).
This study was sponsored by AstraZeneca.

Disclosure: R. Furie, AstraZeneca/Medimmune, 2, 5; **E. Morand**, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, 5, Merck Serono, 2, 5, Neovacs, 5, Sandoz, 5, Novartis, 8, AbbVie, 5, Amgen, 5, Biogen, 5; **A. Askanase**, GSK, 2, 6, AstraZeneca, 2, 6, Abbvie, 6, BMS, 6, Jannssen, 2, Lilly, 2, Pfizer, 2, LuCIN, 2; **E. Vital**, GSK, 8, AstraZeneca, 2, 5, 8, Genentech, 5, ILTOO, 5, Modus, 5, UCB, 5, Lilly, 5, Aurinia, 5, Hexal, 2; **J. Merrill**, Bristol Myers Squibb, 2, 5, GlaxoSmithKline, 2, 5, AstraZeneca, 5, AbbVie, 5, Amgen, 5, Aurinia, 5, EMD Serono, 5, Remegen, 5, Janssen, 5, Provention, 5, UCB, 5; **R. Kalyani**, AstraZeneca, 1, 3, 4; **G. Abreu**, AstraZeneca, 3; **L. Pineda**, AstraZeneca, 3; **R. Tummala**, AstraZeneca, 3.

Abstract Number: 1828

Comprehensive Efficacy of Anifrolumab Across Organ Domains in Patients with Active SLE: Pooled Data from 2 Phase 3 Trials

Eric Morand[1], Richard Furie[2], Ian Bruce[3], Ed Vital[4], Maria Dall'Era[5], Emmanuelle Maho[6], Lilia Pineda[7] and Raj Tummala[7], [1]Monash University, Melbourne, Australia, [2]Zucker School of Medicine at Hofstra/Northwell, Great Neck, [3]Centre for Epidemiology Versus Arthritis, The University of Manchester and NIHR Manchester Biomedical Research Centre, Manchester University Hospitals NHS Foundation Trust, Manchester Academic Health Science Centre, Manchester, United Kingdom, [4]University of Leeds; NIHR Leeds Biomedical Research Centre, Leeds Teaching Hospitals NHS Trust, Leeds, United Kingdom, [5]Division of Rheumatology, University of California, San Francisco, CA, [6]BioPharmaceuticals R&D, AstraZeneca, Cambridge, United Kingdom, [7]BioPharmaceuticals R&D, AstraZeneca, Gaithersburg

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: SLE is a heterogeneous autoimmune disease with clinical manifestations across multiple organ systems. In the phase 3 TULIP-1 and TULIP-2 trials, anifrolumab treatment resulted in greater percentages of patients with SLE achieving a BILAG-based Composite Lupus Assessment (BICLA) response vs placebo at Week 52.[1,2] We further evaluated the effects of anifrolumab on organ domain–specific SLE disease activity using pooled data from TULIP-1 and TULIP-2.

Methods: TULIP-1 and TULIP-2 were 52-week, randomized, double-blind, placebo-controlled trials that evaluated the efficacy and safety of anifrolumab (300 mg IV every 4 weeks for 48 weeks) in patients with moderately to severely active SLE despite standard-of-care treatment. Using pooled data, we compared BILAG-2004 and SLEDAI-2K responses across individual organ domains in patients receiving anifrolumab vs placebo. Organ improvement was

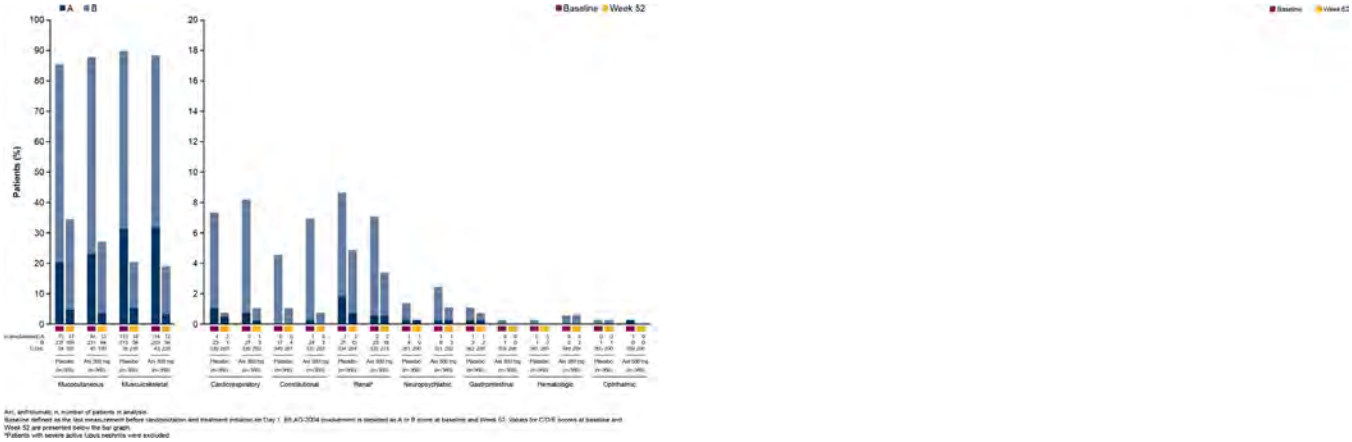

Figure 1. BILAG-2004 Organ Involvement at Baseline and Week 52 for Patients With SLE Receiving Anifrolumab or Placebo in Pooled Data From the TULIP-1 and TULIP-2 Trials

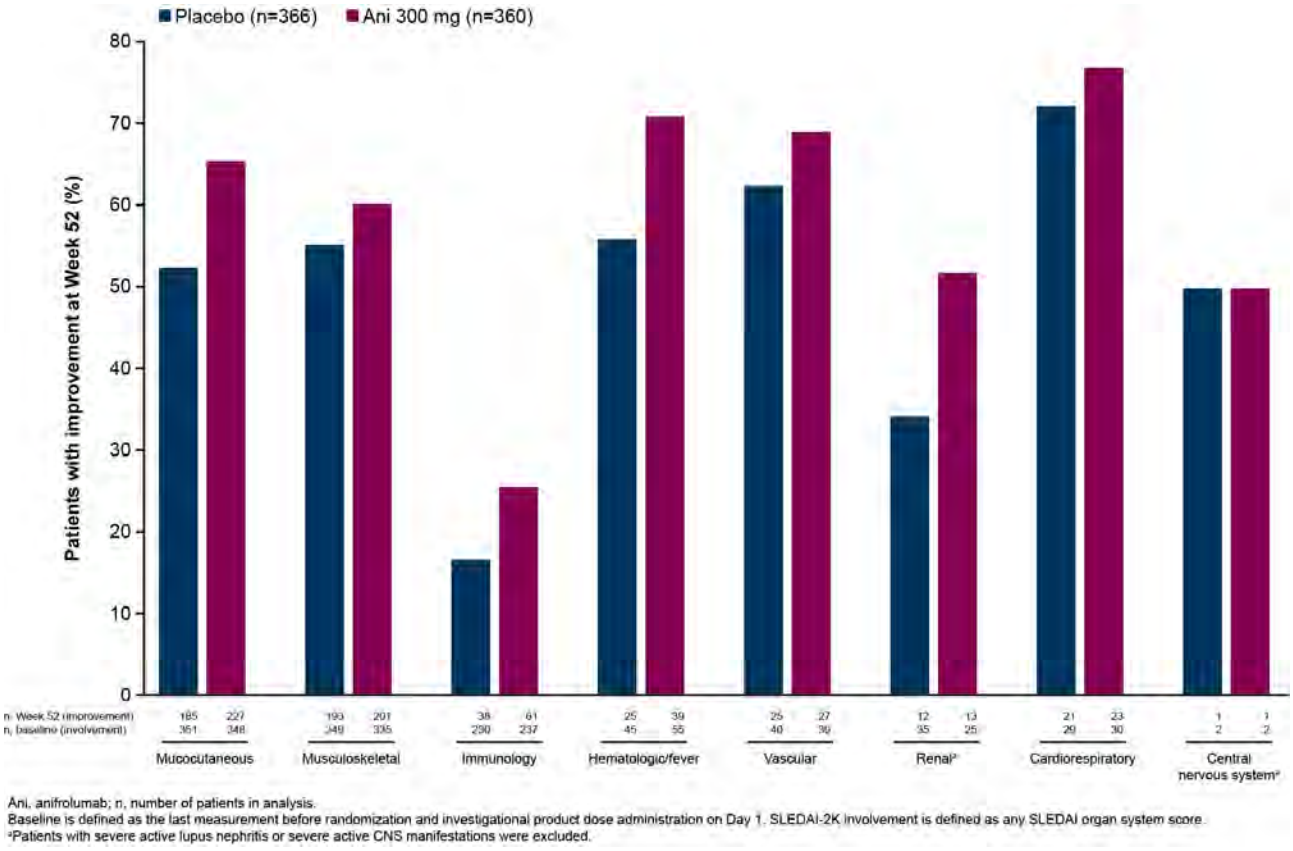

Figure 2. SLEDAI-2K Organ Improvement at Week 52 for Patients With SLE Receiving Anifrolumab or Placebo in Pooled Data From the TULIP-1 and TULIP-2 Trials

defined as a reduction in baseline BILAG-2004 or SLEDAI-2K organ domain scores and was assessed at Week 52. Tender and swollen joint counts were recorded, and an improvement was defined as a reduction of ≥50% from baseline in counts of both tender and swollen joints.

Results: In total, 360 patients received anifrolumab and 366 received placebo. The percentages of patients with BILAG-2004 A or B and SLEDAI-2K organ domain scores at baseline were generally similar between treatment groups across all organ domains. The most frequently affected organ domains at baseline were mucocutaneous and

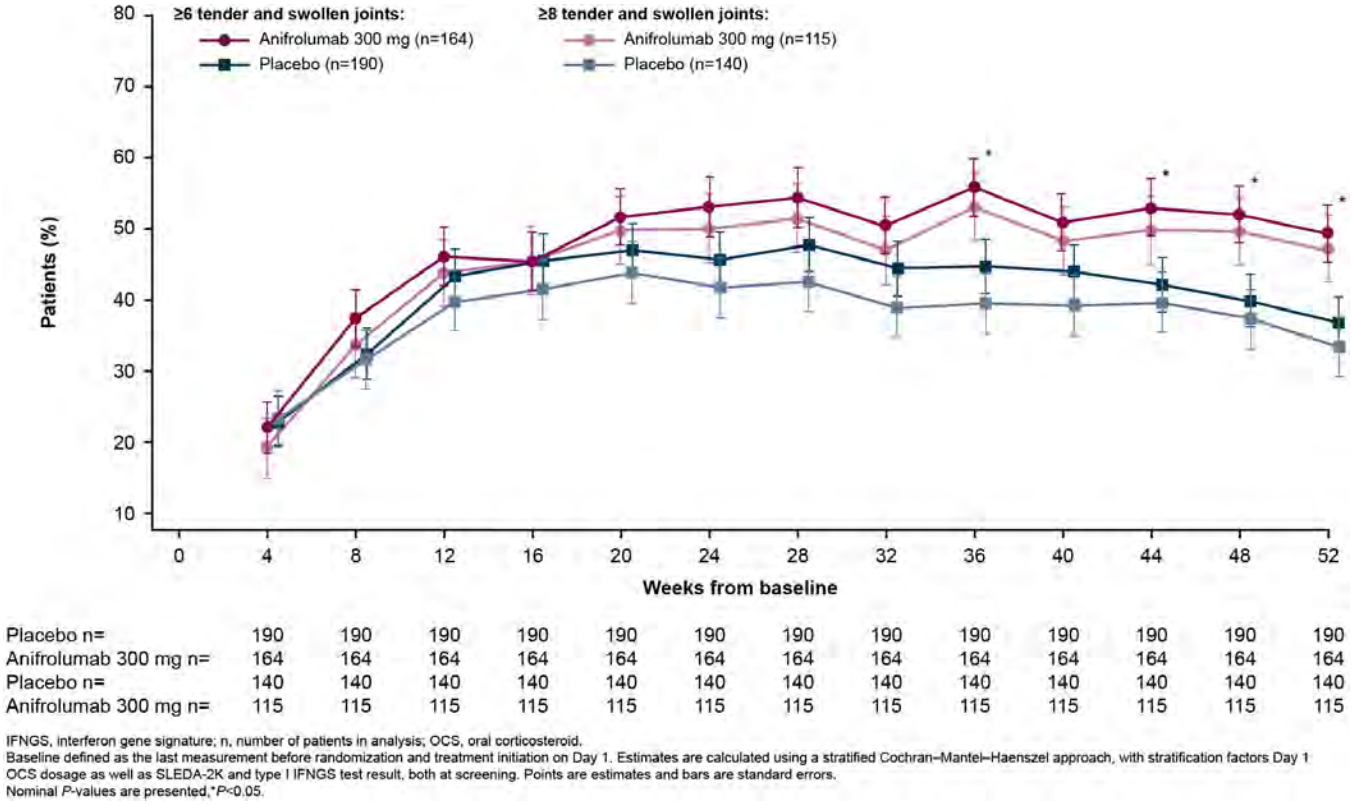

Figure 3. Percentage of Patients Who Achieved ≥50% Reductions in Baseline Tender and Swollen Joint Counts Over Time in Patients With ≥6 and ≥8 Tender and Swollen Joints at Baseline in Pooled Data From the TULIP-1 and TULIP-2 Trials

musculoskeletal by both BILAG-2004 and SLEDAI-2K, and immunology by SLEDAI-2K. Baseline BILAG-2004 A or B scores occurred less frequently in the cardiorespiratory, constitutional, renal, neuropsychiatric, gastrointestinal, hematologic, and ophthalmic domains, and baseline SLEDAI-2K activity was less frequent in the hematologic, fever, vascular, renal, cardiorespiratory, and central nervous system domains. At Week 52, a greater number of patients treated with anifrolumab vs placebo had improvements in the mucocutaneous and musculoskeletal domains by both BILAG-2004 and SLEDAI-2K (**Figures 1** and **2**). Improvements were also observed in the majority of less frequently affected domains (**Figures 1** and **2**). Higher percentages of patients treated with anifrolumab vs placebo achieved ≥50% reductions in baseline tender and swollen joint counts at Weeks 36, 44, 48, and 52 in those with baseline tender and swollen joint counts of ≥6 and ≥8 (**Figure 3**).

Conclusion: Higher percentages of patients treated with anifrolumab compared with placebo had improved BILAG-2004 and SLEDAI-2K domain scores at Week 52 in the 2 most frequently affected domains (mucocutaneous and musculoskeletal) and in less frequently affected domains, as well as reductions in arthritis scores. These data provide evidence of the benefit of anifrolumab across multiple organ domains in patients with active SLE.

References

1. Furie RA. *Lancet Rheumatol*. 2019;1:e208–19.
2. Morand EF. *N Engl J Med.* 2020;382:211–21.
Writing assistance by Rebecca Jones, PhD (JK Associates, Inc., a Fishawack Health Company).
This study was sponsored by AstraZeneca.

Disclosure: E. Morand, AstraZeneca, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Janssen, 2, 5, Merck Serono, 2, 5, Biogen, 5, Neovacs, 5, Sandoz, 5, Novartis, 8; **R. Furie**, AstraZeneca/Medimmune, 2,

5; **I. Bruce**, Genzyme/Sanofi, 2, GlaxoSmithKline, 2, 5, 8, Roche, 2, UCB, 2, 5, 8, Eli Lilly, 5, Merck Serono, 5, ILTOO, 5, AstraZeneca, 8; **E. Vital**, GSK, 8, AstraZeneca, 2, 5, 8, Genentech, 5, ILTOO, 5, Modus, 5, UCB, 5, Lilly, 5, Aurinia, 5, Hexal, 2; **M. Dall'Era**, Janssen, 5, AstraZeneca, 5; **E. Maho**, AstraZeneca, 3; **L. Pineda**, AstraZeneca, 3; **R. Tummala**, AstraZeneca, 3.

Abstract Number: 1829

Lupus Disease Activity After Cessation of Anifrolumab Treatment During the Phase 2b MUSE Trial Follow-up Period

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
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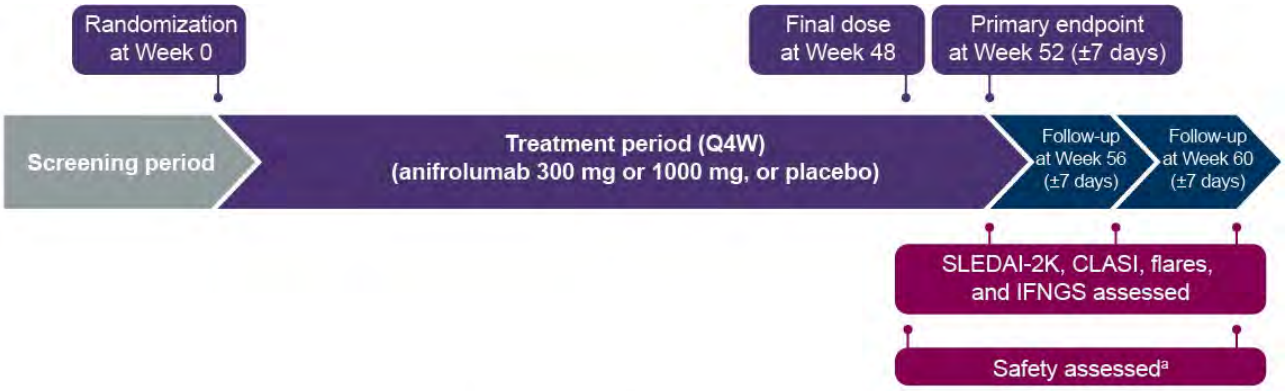
Background/Purpose: In the randomized, double-blind, phase 2b MUSE trial, anifrolumab reduced disease activity vs placebo across multiple endpoints in patients with moderately to severely active SLE.[1] Here, we assess changes in disease activity and safety in patients after cessation of anifrolumab treatment during the follow-up period in MUSE.

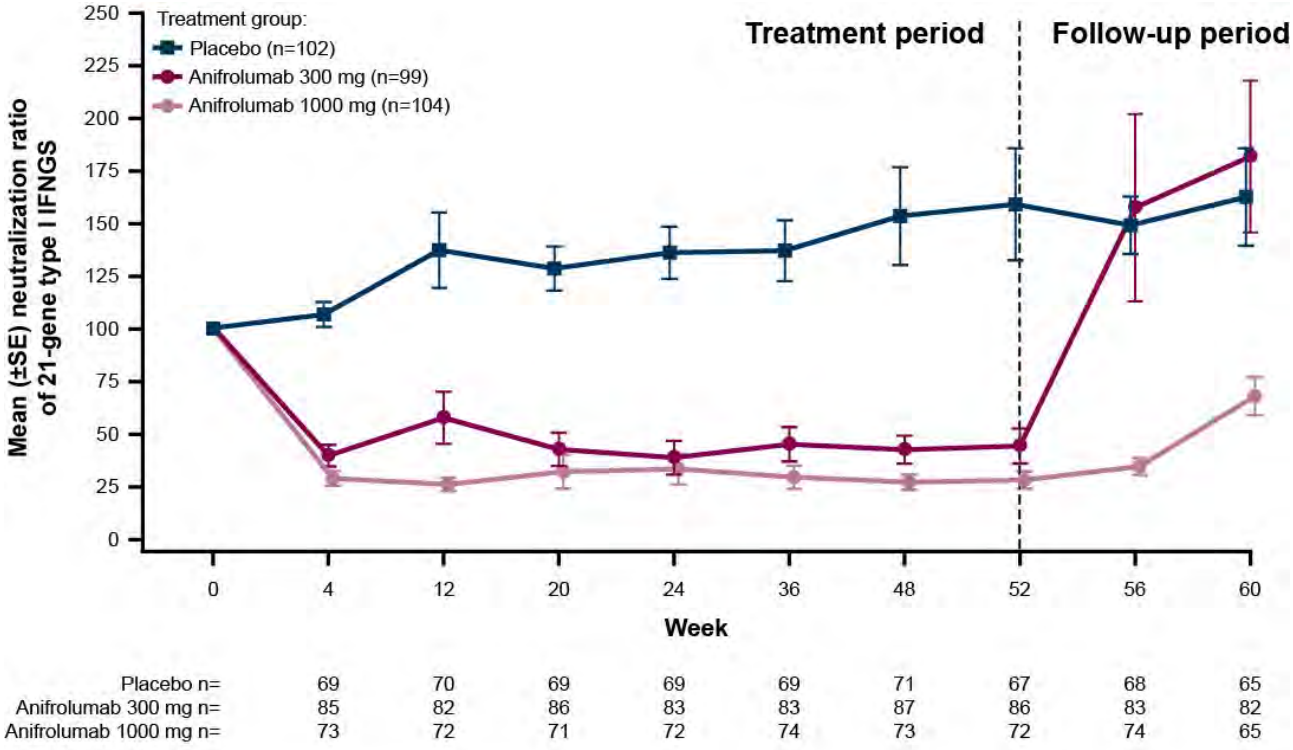
Methods: Patients were randomized 1:1:1 to receive placebo or anifrolumab 300 or 1000 mg IV every 4 weeks (wks). The final study dose was at Wk 48, and key efficacy endpoints were assessed at Wk 52. After receiving the final dose of study medication, patients were required to complete a follow-up period during which visits were conducted every 4 wks (±7 days) (**Figure 1**). Disease activity (measured with SLEDAI-2K and BILAG-2004 global scores, and Cutaneous Lupus Erythematosus Disease Area and Severity Index [CLASI] activity score), flares (defined as either ≥1 new BILAG-2004 A or ≥2 new BILAG-2004 B domain scores), adverse events (AEs), and 21-gene type I IFN gene signatures (IFNGS) were assessed. Disease activity scores, flares, and IFNGS were assessed over 8 wks from Wk 52 through Wk 60, and safety was evaluated over 12 wks from Wk 48 through Wk 60 or upon study discontinuation.

Results: Of 305 patients randomized in MUSE, 229 completed the last study visit (Wk 52): 86, 75, and 68 in the anifrolumab 300-mg, 1000-mg, and placebo groups, respectively. From Wk 52 to the end of the follow-up period (Wk 60), mean SLEDAI-2K global scores increased in patients ceasing treatment of anifrolumab 300 mg (mean change: 0.7) and 1000 mg (0.3), but not placebo (–0.1) (**Table 1**). A numeric worsening was also observed in mean BILAG-2004 global scores in patients ceasing anifrolumab 300-mg treatment (mean change: 2.4) vs placebo (0.8); in the 1000-mg group, mean change was 0.7. Of the various domains, worsening activity scores were most frequently observed in the mucocutaneous and musculoskeletal domains. Overall, 15.2% and 6.7% of patients ceasing treatment of anifrolumab 300 or 1000 mg, respectively, had ≥1 BILAG flare from Wk 52 through Wk 60 vs 2.0% with placebo. Mean CLASI activity scores increased slightly from Wk 52 to Wk 60 across the anifrolumab 300-mg (mean change: 0.4), 1000-mg (0.4), and placebo groups (0.5). From Wk 52 to Wk 60, IFNGS expression increased more rapidly in the anifrolumab 300-mg group vs the 1000-mg group, with negligible changes in the placebo group (**Figure 2**). AEs during the 12-wk safety follow-up period were similar between the anifrolumab 300-mg and 1000-mg vs placebo groups (≥1 AE: 29.3% and 26.7% vs 24.8%; ≥1 serious AE: 3.0% and 3.8% vs 5.0%).



CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; IFNGS, type I interferon gene signature; Q4W, every 4 weeks.
[a]Safety also assessed after final dose upon study discontinuation.

Figure 1. Trial Design for MUSE



IFNGS, type I interferon gene signature; n, number of nonmissing values; SE, standard error.

Figure 2. Change in Neutralization Ratio of the 21-Gene Type I IFNGS From Start of the MUSE Trial to End of Follow-up (Week 60)

Conclusion: No new or unexpected safety findings were observed in the MUSE follow-up period. There was a larger numeric worsening of disease activity in patients ceasing anifrolumab compared with placebo. A rebound in IFNGS was observed in patients previously treated with anifrolumab; this effect was more apparent with 300 vs 1000 mg. An analysis is underway evaluating the relationship between changes in IFNGS and disease activity.

Disease activity measure		Placebo (n=66)	Anifrolumab 300 mg (n=84)	Anifrolumab 1000 mg (n=73)
SLEDAI-2K score	Week 52, mean	5.9	4.3	3.8
	Week 60, mean	5.8	5.0	4.1
	Mean (SD) change[a]	−0.1 (2.4)	0.7 (3.5)	0.3 (2.3)
BILAG-2004 score	Week 52, mean	8.3	6.0	5.9
	Week 60, mean	9.1	8.5	6.6
	Mean (SD) change[a]	0.8 (3.8)	2.4 (6.7)	0.7 (5.3)
CLASI activity score	Week 52, mean	3.5[b]	1.9	1.8
	Week 60, mean	4.0[b]	2.4	2.2
	Mean (SD) change[a]	0.5 (2.3)[b]	0.4 (1.9)	0.4 (2.0)

CLASI, Cutaneous Lupus Erythematosus Disease Area and Severity Index; SD, standard deviation.
Values rounded to 1 decimal place; n varied between analyses depending on available data.
[a]Mean change may not equal difference between Week 52 and 60 owing to rounding; [b]n=65.

Table 1. Mean Change in SLEDAI-2K, BILAG-2004, and CLASI Activity Scores From MUSE Trial Efficacy Endpoint (Week 52) to End of Follow-up (Week 60)

References

1. Furie RA. *Arthritis Rheumatol*. 2017;69:376–86.
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Abstract Number: 1830

Adverse Drug Reactions to Trimethoprim-sulfamethoxazole as a Prophylactic Agent Against Pneumocystis Pneumonia in Patients with Systemic Lupus Erythematosus: anti-Sm Antibody as a Possible Risk Factor

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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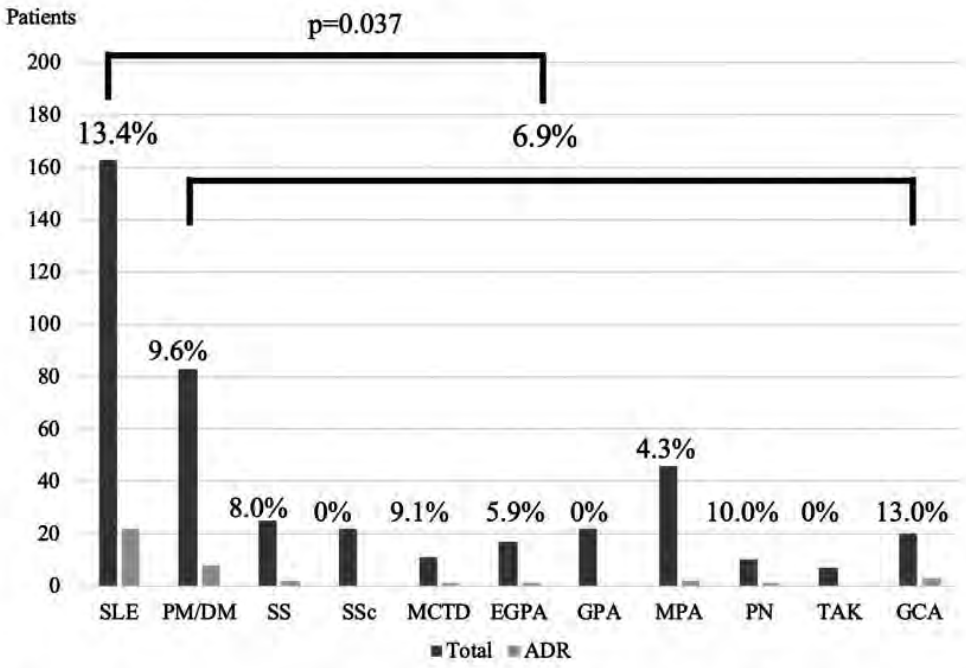
Session Time: 9:00AM–11:00AM

Background/Purpose: Pneumocystis pneumonia (PCP) is a life-threatening infection in immunocompromised patients, including those with connective tissue diseases (CTDs), treated with corticosteroids or immunosuppressive

Figure: Prevalence of ADRs caused by TMP-SMX.



ADR; adverse drug reaction, SLE; systemic lupus erythematosus, PM; polymyositis, DM; dermatomyositis, SS; Sjögren syndrome, SSc; systemic sclerosis, MCTD; mixed connective tissue disease, GPA; granulomatosis with polyangiitis, EGPA; eosinophilic granulomatosis with polyangiitis, MPA; microscopic polyangiitis, PN; polyarteritis nodosa, TAK; Takayasu arteritis, GCA; giant cell arteritis.

agents. Trimethoprim-sulfamethoxazole (TMP-STX) is widely used as a prophylactic agent against PCP. Although its efficacy is well-established, TMP-STX may cause adverse drug reactions (ADRs) among patients with CTDs. Previous studies showed that patients with systemic lupus erythematosus (SLE) are at high-risk of ADRs to TMP-SMX, but the prevalence varies among studies and the difference in risks between patients with SLE versus other CTDs is unclear. We examined the prevalence of ADRs to TMP-STX among patients with SLE and other CTDs, and identified specific risk factors for ADRs in SLE.

Methods: The in-patient database of our hospital was examined, and the records of CTD patients administered TMP-STX as a prophylactic agent against PCP between January 2009 and April 2020 were reviewed retrospectively. Baseline data were obtained at the time of TMP-STX initiation. Patients with human immunodeficiency virus, and those who did not suffer ADRs but who received TMP-SMX within 1 month, were excluded. ADR prevalence was compared between SLE patients and those with other CTDs. Univariate and multivariate analyses were conducted to identify the risk factors for ADRs in SLE patients.

Results: Among 427 patients with CTDs (SLE, n = 164; polymyositis or dermatomyositis, n = 83; Sjögren syndrome, n = 25; systemic sclerosis, n = 22; mixed connective tissue disease, n = 11; eosinophilic granulomatosis with polyangiitis, n = 17; granulomatosis with polyangiitis, n = 22; microscopic polyangiitis, n = 46; polyarteritis nodosa, n = 10; Takayasu arteritis, n = 7; giant cell arteritis, n = 20), 40 patients (9.4%) developed ADRs (thrombocytopenia, n = 10; skin rash, n = 9; liver function test abnormality, n = 7; fever, n = 7; others, n = 12). The prevalence of ADRs in SLE patients was 13.4% and 6.9% in control group. The odds ratio (OR) of an ADR for SLE patients was 2.12 (95% con-

Table. Risk factors for ADRs due to TMP-SMX in SLE patients

	ADRs (n = 22)	Non-ADRs (n = 142)	p value
Age, years [IQR]	39.5[27-50]	40.5[30-62]	0.35
Sex, Female (%)	19(86.3)	99(79.2)	0.13
Specific antibody			
anti-dsDNA (%)	15/22 (68.2)	79/139 (56.8)	0.36
anti-Sm (%)	13/22 (59.1)	28/125 (20.7)	<0.001
anti-RNP (%)	14/21 (66.7)	48/125 (38.4)	0.018
anti-Ro/SS-A (%)	16/22 (72.8)	66/137 (48.2)	0.039

fidence interval (CI) 1.05–4.35, p=0.037). By contrast, the ORs of ADRs for all other CTDs did not differ significantly. Univariate analyses of SLE patients revealed that positivity for anti-Sm antibody (OR 5.44, 95% CI 1.93–16.06, p< 0.001), anti-RNP antibody (OR 3.19, 95% CI 1.11–10.02, p = 0.018) and anti-Ro/SS-A antibody (OR 2.87, 95% CI 1.06–7.77, p = 0.039) was significantly associated with ADRs. In the multivariate analyses, only anti-Sm antibody was significantly associated with ADRs in SLE patients (OR 3.34, 95% CI 1.10–11.10, p = 0.048).

Conclusion: SLE patients prophylactically administered TMP-STX are at high risk of ADRs. In particular, anti-Sm antibody positivity was significantly associated with ADR. SLE patients showing anti-Sm antibody, anti-RNP antibody, or anti-Ro/SS-A antibody positivity who receive prophylactic TMP-SMX should be especially carefully monitored for ADRs.

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Abstract Number: 1831

Biomarkers Linked to Anti-IFN-I and Ustekinumab Suggest Distinct Mechanism of Action in Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Time: 9:00AM–11:00AM

Background/Purpose: Clinical and biological heterogeneity pose a significant hurdle in SLE, making biomarkers that define patient subsets crucial for developing tailored therapies. Interventional SLE trials using inhibitors of the IL-12/ IL-23 and type I interferon (IFN-I) pathways revealed gene signatures linked with each mechanism. We reported that response to the IL-12/IL-23 p40 inhibitor (Ustekinumab, UST) associates with baseline expression of a cytotoxic-cell associated gene signature (CTS). IFN-I gene signature (IGS) may serve as a patient selection tool and pharmacodynamic biomarker for IFN-I inhibitors. Here, we examined the expression of IGS and CTS signatures in two SLE trials:

UST Ph2 (NCT02349061) and JNJ-839, anti-IFN-α/ω antagonist, Ph1B (NCT02609789) to test whether the CTS association with response was specific to the mechanism of action of UST.

Methods: We conducted Gene Set Variation Analysis (GSVA) of CTS and IGS on whole blood transcriptomes from moderate-to-severe SLE patient samples collected in two distinct randomized, double-blind, placebo (PBO)-controlled trials (UST Ph2 [N=102] and JNJ-839 Ph1B [N=28]). In UST Ph2, patients were randomized (3:2) to receive UST IV ~6 mg/kg or PBO at Week 0, then UST SC ~90 mg or PBO every 8 weeks. In JNJ-839 Ph1B, IFN positive patients were randomized (3:1) to receive JNJ-839 IV 10 mg/kg or PBO every 2 weeks. Clinical response was defined by SLE Responder Index (SRI)-4 at Week 24 and Day 100, respectively.

Results: Unlike in UST Ph2, where CTS was lower at baseline in UST-nonresponders (NR) compared to UST-responders (R) (p=0.0087), CTS expression did not correlate with response to, nor was it modulated by JNJ-839. UST did not modulate IGS, and the treatment effect (difference in response rate UST vs. PBO) was similar between IFN-I high and IFN-I low patients. IGS expression was comparable in JNJ-839-R and JNJ-839-NR at baseline and rapidly decreased after JNJ-839 treatment and throughout the dosing period (Day 1-71). After the last dose, JNJ-839-R exhibited durable IGS suppression through Day 86 before returning to baseline levels and was comparable to levels observed in patients receiving PBO at Day 130. In contrast, JNJ-839-NR IGS levels rapidly reached PBO levels by Day 79.

Conclusion: Biomarkers linked to UST response did not associate with anti-IFN-α/ω response in SLE. Likewise, IFN-I pathway biomarkers did not specifically associate with UST response. These data support a distinct mechanism of action between UST and agents targeting IFN-I and provide a foundation for future biomarker response-based studies using additional therapies in SLE.

Disclosure: T. Dörner, Eli Lilly and Company, 2, 5, Roche, 2, 5, Sanofi, 2, 5, Novartis, 2, 5, Abbvie, 2, 5, Celgene, 5, Pfizer Corporation, 2; **G. Tsokos**, None; **K. Kalunian**, Roche, 5, Biogen, 5, Janssen, 5, AstraZeneca, 5, Lupus Research Alliance, 2, Pfizer, 2, Sanford Consortium, 2, Eli Lilly, 5, Genetech, 5, Gilead, 5, ILTOO, 5, Nektar, 5, Viela, 5, Equillium, 5, Bristol-Meyers Squibb, 5; **R. van Vollenhoven**, AbbVie, 2, 5, Bristol-Meyers Squibb, 2, 5, GlaxoSmith-Kline, 2, 5, Lilly, 2, 5, Pfizer, 2, 5, UCB, 2, 5, 8, AstraZeneca, 5, 8, Biotest, 2, 5, Celgene, 5, Janssen, 5, 8, Roche, 5, Biogen, 5, Galapagos, 5, 8, Gilead, 5, Servier, 5; **A. Orillion**, Janssen Research & Development, LLC, 1, 3; **M. Cesaroni**, Janssen Research & Development, LLC, 1, 3; **J. Benson**, Janssen Research & Development, LLC, 1, 3; **M. Chevrier**, Janssen Research & Development, LLC, 1, 3; **S. Rose**, Janssen Research & Development, LLC, 1, 3; **S. Marciniak**, Janssen Research & Development, LLC, 1, 3; **Z. Yao**, Janssen Research & Development, LLC, 1, 3; **B. Srivastava**, Janssen Research & Development, LLC, 1, 3; **J. Schreiter**, Janssen Research & Development, LLC, 1, 3; **F. Baribaud**, Janssen Research & Development, LLC, 1, 3; **T. Ort**, Janssen Research & Development, LLC, 1, 3; **J. Jordan**, Janssen Research & Development, LLC, 1, 3; **L. Seridi**, Janssen Research & Development, LLC, 1, 3.

Abstract Number: 1832

Barriers to Medication Adherence and Degree of Nonadherence in a Systemic Lupus Erythematosus Outpatient Population

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
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Background/Purpose: It has been reported that 50% to 75% of patients with SLE do not adhere to their medications. However, the reasons for nonadherence are not clear. We aimed to estimate the level of medication adherence and barriers to adherence among patients attending the Lupus Clinic.

Methods: Patients taking at least one medication to treat SLE including antimalarials, immunosuppressives, or steroids were included. All patients satisfied the ACR classification criteria for SLE. Adherence was measured using the Medication Adherence Self-Report Inventory (MASRI). Patients were defined as nonadherent with adherence rates < 80% or sufficiently adherent with adherence rates ≥ 80%, based on the MASRI visual analog scale (VAS). Pill counts

Table 1. Patient and Disease Characteristics

Characteristics	Value	Non-adherent (n = 10)	Sufficiently adherent (n = 84)	All patients (n = 94)	Between groups (p-value)
Age (years)	Mean ± SD	40.7 ± 8.0	47.3 ± 15.1	46.6 ± 14.6	0.181
Sex	F (%)	90	90.5	90.4	0.961
	M (%)	10	9.5	9.6	
SLE disease duration (years)	Mean ± SD	19.9 ± 10.4	17.8 ± 12.6	18.0 ± 12.4	0.607
Ethnicity	Black (%)	20	19	19.1	0.455
	Caucasian (%)	70	47.6	50	
	Chinese (%)	0	9.5	8.5	
	Others (%)	10	23.8	22.3	
SLEDAI score	Mean ± SD	3.4 ± 1.4	3.0 ± 3.1	3.1 ± 2.9	0.714
SLICC score	Mean ± SD	0.8 ± 1.0	1.7 ± 2.2	1.6 ± 2.1	0.232
SLE medication classes	Steroid (%)	40	46.4	45.7	0.7
	Antimalarial (%)	90	76.2	77.7	0.322
	Azathioprine (%)	20	19	19.1	0.942
	Methotrexate (%)	0	9.5	8.5	0.308
	Mycophenolate (%)	20	28.6	27.7	0.567
	Immunosuppressive (%)	40	57.1	55.3	0.303
	Biologic (%)	0	8.3	7.4	0.343
Non-SLE medications	Hypertension (%)	30	39.3	38.3	0.568
	Dyslipidemia (%)	0	20.2	18.1	0.116
	Diabetes insulin (%)	0	1.2	1.1	0.729
	Osteoporosis (%)	60	79.8	77.7	0.156
	Anticoagulant / Antiplatelet (%)	10	26.2	24.5	0.26
	Seizure disorder (%)	0	3.6	3.2	0.544
	Raynaud's (%)	0	3.6	3.2	0.544
	Any non-SLE disease (%)	60	91.7	88.3	0.003

Table 1. Patient and Disease Characteristics

Table 2. Barriers to Adherence

Barriers	Non-adherent (n = 10) (%)*	Sufficiently adherent (n = 84) (%)*	All patients (n = 94) (%)*	Between groups (p-value) **
Knowing how to take medications	0	1.2	1.1	0.729
Being physically able to take medications	0	0	0	n/a
Remembering to take medications	40	1.2	5.3	<0.001
Trusting doctors with healthcare decisions	10	0	1.1	0.012
Easily collecting medications from pharmacy	0	4.8	4.3	0.638
Negative emotions about taking medications	44.4	19	21.5	0.053
Motivation to take medications	20	3.6	5.3	0.034
Medication cost	10	0	1.1	0.015
Confidence in managing medications	10	1.2	2.1	0.171
Worry about harmful side effects of medications	50	66.7	64.9	0.574
Sufficient knowledge about medications	10	14.3	13.8	0.291
System(s) in place to order, collect and take medications	30	1.2	4.3	<0.001
Easily distracted from taking medications	50	7.4	12.1	<0.001
Available support from others	0	11	9.8	0.542
Changes to daily routine interfering with taking medications	30	19.8	20.9	0.695
Medications being an unwanted reminder of their condition	20	24.4	23.9	0.677
Prioritizing medications	10	0	1.1	<0.001
Fitting medications into daily routine	30	2.4	5.4	<0.001
Confidence in ability to solve difficulties in taking medications	10	2.5	3.3	0.01
Unsure or disagree that condition will worsen without medications	50	19.3	22.6	0.072
Having information to order and collect medications	0	0	0	0.072
Telling medications apart	30	11	13	0.136
Remembering to order and collect medications on time	0	2.4	2.2	<0.001
Stigma about taking medications	0	16.9	15.1	0.237
Pharmacy providing efficient service	10	0	1.1	0.012
Burden of taking medications	10	10.8	10.8	0.091
Intention to take medications	0	0	0	<0.001
Life getting in the way of taking medications	50	11	15.2	0.001
Ability to cope with changing medication regime	0	11	9.8	0.542
Having personal reasons for not taking medications	50	6.1	10.9	<0.001
IMABQ-30 total score (Mean ± SD)	67.2 ± 12.3	51.5 ± 11.4	53.2 ± 12.4	<0.001
MASRI VAS (Mean ± SD)	44.50 ± 23.39	96.2 ± 5.5	90.7 ± 18.4	<0.001

*Percentage of patients who indicated experiencing or strongly experiencing specified barrier
**P-value represents differences between groups from all five categories of responses (strongly agree, agree, neither agree nor disagree, disagree, strongly disagree)

Table 2. Barriers to Adherence

were conducted in a proportion of participants. Barriers to medication adherence were identified using the Identification of Medication Adherence Barriers Questionnaire (IMAB-Q).

Descriptive statistics were used.

Results: A total of 94 patients were recruited to the study and 28 pill counts were conducted. Ten patients were classified as nonadherent and 84 patients as sufficiently adherent. There were no statistically significant differences between groups in terms of demographics. The mean age of participants was 46.6 years, female: male ratio was approximately 9:1, mean disease duration was 18.0 years, mean SLEDAI score was 3.1, and mean SLICC score was 1.6. Forty-five percent of patients were taking steroid, 77.7% antimalarial, and 55.3% immunosuppressive medications. Eighty-eight percent of patients were taking at least one medication for non-SLE conditions (Table 1).

The mean medication adherence rate for the SLE patients was 90.7%, based on the MASRI VAS. Adherence rates were corroborated by pill counts. Important barriers to medication adherence reported by nonadherent patients were: concern about harmful medication side effects (50%), being easily distracted from taking medications as prescribed (50%), life getting in the way of taking medications as prescribed (50%), being unsure or disagreeing that their condition will worsen without taking medications as prescribed (50%), and having personal reasons for not taking medications as prescribed (50%). Patients defined as nonadherent reported significantly more barriers to medication adherence than patients defined as sufficiently adherent, based on IMAB-Q total scores ($p < 0.001$). Specific barriers to medication adherence that were experienced by nonadherent participants significantly more often ($p < 0.001$), included: being easily distracted from taking medications as prescribed, remembering to take medications as prescribed, having system(s) in place to help manage medications, taking medications as prescribed not fitting in their daily routine, not prioritizing or having the intention to take medications as prescribed, and having personal reasons for not taking medications as prescribed (Table 2).

Conclusion: The adherence rate in our population was higher than expected, reaching 90% on the MASRI, confirmed by pill count. A number of barriers to medication adherence were identified. These barriers to medication adherence need to be addressed on an individualized basis to improve patient outcomes.

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Abstract Number: 1833

Hydroxychloroquine and Vitamin D Both Reduce Proteinuria in SLE

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
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Background/Purpose: Hydroxychloroquine (HCQ) and vitamin D are both immunomodulators in SLE, but work through different mechanisms. Hydroxychloroquine has been proven to triple renal response to mycophenolate in membranous nephritis (Lupus 2006;15: 366–70) and may reduce end stage renal disease (Arthritis Rheum

	Proteinuria		Persistent renal insufficiency		Proteinuria or persistent renal insufficiency	
	OR (95% CI)	p-value	OR (95% CI)	p-value	OR (95% CI)	p-value
HCQ blood level						
<250 (n=435)	1.00 (ref)		1.00 (ref)		1.00 (ref)	
250-<500 (n=352)	0.86 (0.57, 1.3)	0.486	0.99 (0.69, 1.42)	0.9551	0.9 (0.67, 1.2)	0.4669
500-<750 (n=548)	0.66 (0.45, 0.97)	0.0348	0.83 (0.64, 1.07)	0.1524	0.75 (0.58, 0.97)	0.0272
750-<1000 (n=559)	0.81 (0.55, 1.2)	0.2979	0.89 (0.69, 1.15)	0.391	0.85 (0.66, 1.11)	0.2363
1000-<1250 (n=502)	0.7 (0.47, 1.04)	0.0766	0.85 (0.62, 1.15)	0.2911	0.73 (0.56, 0.96)	0.0262
1250-<1500 (n=396)	0.46 (0.28, 0.73)	0.0012	0.85 (0.6, 1.21)	0.373	0.63 (0.45, 0.87)	0.0055
>=1500 (n=652)	0.62 (0.41, 0.94)	0.0247	0.99 (0.73, 1.36)	0.9697	0.81 (0.6, 1.09)	0.1707

Adjusted associations between renal outcomes and HCQ Levels, adjusting for covariates.

HCQ blood level	Odds Ratio	P-value	Adjusted OR (95% CI)	Adjusted p-value
Per 100 ng/ml increase with respect to patient's mean HCQ blood levels	0.97 (0.95, 0.99)	0.0220	0.97 (0.94, 0.99)	0.0192

Within-person analysis of the relationship between proteinuria and HCQ blood levels: unadjusted and adjusted (adjusted for age, BMI, Cellcept, Imuran, ACE-inhibitor or ARB use, and implicitly for all time-invariant characteristics within a person)

	OR (95% CI)	p-value	OR (95% CI): age, sex, race adjusted	p-value: age, sex, race, adjusted
HCQ blood levels (per 100 unit difference)	0.98 (0.96, 1)	0.0486	0.98 (0.96, 1.002)	0.0814
Vitamin D (per 10 unit difference)	0.74 (0.67, 0.82)	<0.0001	0.77 (0.7, 0.85)	<0.0001
age at the visit (per 1 year difference)	-	-	0.99 (0.97, 1.002)	0.0863
Ethnicity (B vs. W)	-	-	2.14 (1.43, 3.21)	0.0002
Ethnicity (O vs. W)	-	-	2.92 (1.86, 4.6)	<0.0001
Sex (F vs .M)	-	-	0.63 (0.42, 0.94)	0.0244

Effect of vitamin D and hydroxychloroquine on proteinuria, within person analysis using GEE.

2009;61:830–39). Vitamin D reduces proteinuria in SLE (Arthritis Rheum 2013;65:1865–71) and in other renal diseases as well. We asked whether these effects were synergistic or additive.

Methods: SLE patients met revised ACR or SLICC classification criteria: 332 patients with biopsy-proven lupus nephritis (89% female, 54% African-American, 28% Caucasian) also had subsequent measurements of HCQ blood levels (method of Füzéry et al. Clin Chim Acta 2013;421:79–84) at the visits. After removing visits that had a large gap of more than 1 year, there were 324 patients with 3,444 visits. The number of HCQ blood level measures per patient ranged from 1 to 34 with a median of 11 measures. Generalized estimating equations (GEE) were used to look at the relationship between proteinuria (by urine pr/cr) and HCQ blood levels at the same visit, accounting for repeated measures in the same person. A conditional logistic regression was used to perform a "within-person" analysis to

look at the renal outcomes more closely. In this analysis, each person served as his/her own control, by comparing visits with increased proteinuria to visits with less proteinuria with respect to mean HCQ blood level.

Results: There were no significant differences between mean HCQ blood levels and sex (p=0.7166), ethnicity (p=0.5402), or mean body mass index (r=-0.02, p=0.6970), but significant results were observed for age (r=0.19, p=0.006). Using GEE models which account for repeated measures from the same person, the effects of vitamin D and of HCQ blood level on proteinuria were still significant after adjusting for each other (Table 3). However, the effect of HCQ blood level diminished (borderline significance) after further adjustment for sex, age, and race. Vitamin D appeared to be the stronger predictor of proteinuria. Because the probability of proteinuria changed for HCQ levels when vitamin D level was below or above approximately 20 ng/ml, we looked at the effects of HCQ blood levels on proteinuria stratifying by vitamin D levels. Results were adjusted for repeated measures in patients. There was no evidence of an association between HCQ blood levels and proteinuria if vitamin D was below 20 (OR 1.02, 95% CI 0.98, 1.07). When vitamin D levels were >=20, there was a reduced risk of proteinuria with higher HCQ blood levels (OR 0.97, 95% CI 0.95, 0.99, p=0.009).

Conclusion: Although both HCQ and vitamin D reduce proteinuria, in multivariate GEE models, vitamin D had the more important benefit. When vitamin D levels were >= 20 ng/mL, there was reduced proteinuria with higher HCQ blood levels. In clinical practice and in randomized clinical trials, prescribed HCQ and vitamin D (as well as adherence to them) will benefit proteinuria and thus improve renal response.

Disclosure: M. Petri, Astrazeneca, 2, 5, Exagen, 2, 5, GlaxoSmithKline (GSK), 2, 5, Eli Lilly and Company, 2, 5, AbbVie Inc., 5, Aleon Pharma International, Inc, 5, Amgen, 5, Annenberg Center for Health Sciences,, 5, Blackrock Pharma, 5, Bristol Myers Squibb, 5, Decision Resources, 5, Glenmark Pharmaceuticals, 5, INOVA, 5, IQVIA, 5, Janssen Pharmaceutical, 5, Merck EMD Serono, 5, Novartis, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5; **J. Li**, None; **D. Goldman**, None.

Abstract Number: 1834

Biomarker Analysis of IFN-I Modulation in JNJ-839: First-in-Human Study for Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: JNJ-839 is a fully human neutralizing antibody selective to human IFN-ω and IFN-α subtypes. Here we report the exploratory biomarker analyses of a Phase 1 study in mild to moderate SLE participants with elevated baseline IFN-I scores.

Methods: A screening strategy was implemented to enroll participants exhibiting elevated IFN-I scores using a whole blood qPCR 10 gene signature. The signature was calculated based on the following genes: *DHX58*, *EIF2AK2*, *HERC5*, *IFI44*, *IFI44L*, *IFI6*, *IRF7*, *PARP9*, *PLSCR1*, and *SAMD9L*. Patients with a score below the pre-defined signature cutoff were excluded, resulting in 28 SLE participants randomized (3:1) to receive six bi-weekly IV treatments of JNJ-839 (10 mg/kg) or placebo (PBO), response was defined as a ≥4-point improvement of SRI-4 at Day 100. The IFN-I gene signature was measured longitudinally using RNAseq analysis of PAXgene blood samples to assess the pharmacodynamic (PD) effect of treatment vs. PBO. A novel precision medicine tool, *in vitro* perturbation assay, was developed to assess *ex vivo* exposure as a means to potentially predict clinical response. Participant blood was collected directly into a tube resulting in a final concentration of 200 μg/mL JNJ-839 or null tubes prior to dosing patients with PBO or JNJ-839 and incubated *in vitro* for 24h, followed by transcriptome profiling using microarray.

Results: At baseline, *in vivo* IFN-I signature levels were not significantly different between treatment groups, irrespective of response status. IFN-I signature suppression was observed in treated participants vs. PBO. IFN-I suppression was similar in JNJ-839 non-responders (NR) and responders (R) throughout the dosing period. After the final dose of JNJ-839 at Day 71, R exhibited a sustained suppression through Day 86, reaching PBO levels only at Day 130, while the NR promptly returned to PBO levels at Day 79. In the *in vitro* perturbation assay, using blood from participants prior to *in vivo* dosing, the magnitude of IFN-I signature suppression between JNJ-839 treated vs. untreated samples was statistically significant (p=0.032) using blood from R. In contrast, IFN-I signature suppression was not statistically significant between JNJ-839 treated vs. untreated samples in NR blood.

Conclusion: A sustained PD effect on the IFN-I signature was noted in JNJ-839 treated participants relative to PBO. Transient longitudinal PD differences were observed between R and NR only after the final dose. Differential expression analyses using samples from the *in vitro* perturbation assay indicated downmodulation of IFN-inducible transcripts in treated samples relative to untreated, suggesting that the IFN-I signature is perpetuated under these *in vitro* conditions. Further, *in vitro* exposure revealed a significant change between treated and untreated blood in R, indicating that this assay may have utility for future use to identify R to anti-IFN-I agents without exposing patients to these immunomodulatory agents. Despite the limitations of sample size, these results support further testing with inhibitors of the IFN-I pathway in SLE.

Disclosure: A. Orillion, Janssen Research & Development, LLC, 1, 3; **L. Seridi**, Janssen Research & Development, LLC, 1, 3; **M. Cesaroni**, Janssen Research & Development, LLC, 1, 3; **J. Schreiter**, Janssen Research & Development, LLC, 1, 3; **J. Benson**, Janssen Research & Development, LLC, 1, 3; **W. Stohl**, Gilead Sciences, Inc., 2, GlaxoSmithKline, 2, Janssen Research & Development, 5; **W. Chatham**, Janssen, 9; **R. Furie**, Janssen, 5; **T. Migone**, None; **S. Marciniak**, Janssen Research & Development, LLC, 1, 3; **Z. Yao**, Janssen Research & Development, LLC, 1, 3; **B. Srivastava**, Janssen Research & Development, LLC, 1, 3; **M. Chevrier**, Janssen Research & Development, LLC, 1, 3; **J. Jordan**, Janssen Research & Development, LLC, 1, 3.

Abstract Number: 1835

Evaluation of Low Dose Glucocorticoid Effects on Infection Occurrence in Systemic Lupus Erythematosus Patients

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SESSION INFORMATION

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Session Title: SLE – Treatment Poster II

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Background/Purpose: Infection is major cause of morbidity and mortality in systemic lupus erythematosus (SLE) patient. The past exploratory study suggested various infection risk in SLE patients, such as administration of higher than 7.5mg prednisolone daily or equivalent, high disease activity of SLE, therapy of intravenous administration of cyclophosphamide and leukocytopenia. High dose glucocorticoids (GCs) administration is known to increase the risk of infection in SLE patients; however, the risk of infection in SLE patients receiving low-dose GCs remains unclear. In this study, we evaluated the risk of severe infection requiring hospitalization in SLE patients receiving low-dose GCs as remission maintenance therapy.

Methods: Study design was prospective cohort study. We enrolled SLE patients who fulfilled standardized SLE criteria and could follow up more than a year using the database from multicenter registries of SLE patients in Japan (Lupus registry of nationwide institutions: LUNA). We exclude the patients who are in the induction remission therapy phase (PSL >15mg or equivalent). We extracted data on the patient's sex, age, daily GC doses, and comorbidities that could potentially affect the infection occurrence. Our main exposure was the daily GC doses at the onset of infection. We divided the daily GC doses into four categories; 0-2.5mg of PSL or equivalent doses, 2.6-5.0mg, 5.1-7.5mg, and 7.6-15mg. Outcome measurement was infection occurrence that needed hospitalization. We used logistic regression model to analyze the correlation between GC doses and infection occurrence with adjustment for age, sex, immunosuppressants.

Results: Two hundred ninety patients were enrolled, and the mean age of patients was 47.3 years. The female rates were 88%, immunosuppressants were used in 44% of patients, the mean SLE disease activity index was 5.8 and diabetes mellitus patients were 4%. The overall infection occurrence was 57 events. In each group, 3 of 68 patients in PSL 0-2.5mg group, 28 of 111 patients in PSL 2.6-5.0mg group, 9 of 51 patients in PSL 5.1-7.5mg group, 17 of 60 patients in PSL 7.6-15mg group developed an infection. Compared with PSL 0-2.5mg group, the odds ratio for the development of infection was 8.0 (95% confidence interval (CI), 2.29-28.0) in PSL 2.6-5.0mg group, 5.3 (95% CI, 1.29-21.8) in PSL 5.1-7.5mg group, and 11.2 (95% CI, 2.92-43.0) in PSL 7.6-15mg group.

Conclusion: Even when relatively low doses of PSL are administered to patients with SLE in the maintenance phase, the risk of infection may remain.

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Abstract Number: 1836

Alternative Renal Response Definitions in a Randomized, Controlled Trial of Obinutuzumab for Proliferative Lupus Nephritis

Zahir Amoura[1], Philippe Remy[2], Luis Fernando Quintana Porras[3], Laurent Chiche[4], Dominique Chauveau[5], Dario Roccatello[6], Richard Furie[7], Thomas Schindler[8], Jay Garg[9], Matthew Cascino[9], Brad Rovin[10] and Andrea Doria[11], [1]Hôpital Pitié-Salpêtrière, Paris, [2]APHP Groupe Hospitalier Henri-Mondor, Creteil, France, [3]Hospital Clinic de Barcelona, Barcelona, Catalonia, Spain, [4]Hôpital Européen, Marseille, France, [5]Hôpital Rangueil, Centre Hospitalier Univ de Toulouse, Toulouse, France, [6]S Giovanni Hospital, Univ of Turin, Turin, Italy, [7]Zucker School of Medicine at Hofstra/Northwell, Great Neck, NY, [8]F. Hoffmann-La Roche Ltd., Basel, Switzerland, [9]Genentech, Inc., South San Francisco, CA, [10]The Ohio State University, Columbus, [11]University of Padua, Padua, Italy

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: SLE – Treatment Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

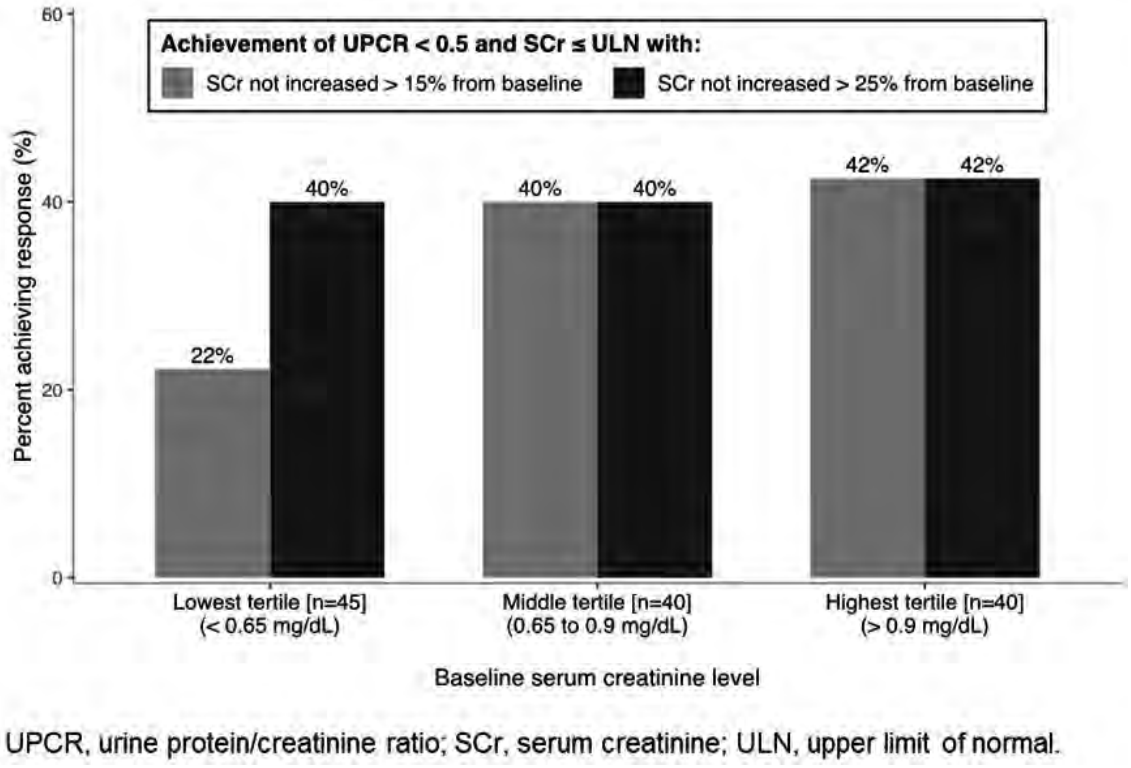

Figure. Week 76 response in NOBILITY by baseline serum creatinine level

Definition of response	Week 52			Week 76		
	OBI (n = 63)	PBO (n = 62)	Diff.	OBI (n = 63)	PBO (n = 62)	Diff.
NOBILITY complete response UPCR < 0.5, SCr ≤ ULN and not increased > 15% from baseline SCr, and < 10 RBC/hpf without casts	35%	23%	12%*	40%	18%	22%**
REGENCY complete response UPCR < 0.5, SCr ≤ ULN and not increased > 25% from baseline SCr	43%	29%	14%*	54%	31%	23%**
UPCR < 0.8 only	64%	48%	15%*	64%	47%	17%*
UPCR < 0.8 with SCr requirement UPCR < 0.8 and SCr ≤ ULN or not increased > 15% from baseline SCr	60%	48%	12%*	64%	45%	18%**
NOBILITY overall response CRR or ≥ 50% reduction in UPCR[a] with SCr not increased > 15% from baseline and urinary RBCs not increased > 50% from baseline	56%	36%	20%**	51%	29%	22%**
REGENCY overall response CRR or ≥ 50% reduction in UPCR[a] with SCr not increased > 25% from baseline	68%	45%	23%**	67%	50%	17%**

OBI, obinutuzumab; PBO, placebo.
* P < 0.2 vs. placebo group.
** P < 0.05 vs. placebo group.
[a] ≥ 50% reduction in UPCR to a value < 1 (< 3 if the baseline UPCR was ≥ 3).
All response definitions required no use of rescue medications or early withdrawal.

Table. Data from NOBILITY at weeks 52 and 76 using several response definitions

Background/Purpose: Obinutuzumab, a type II anti-CD20 mAb, resulted in rapid and complete B-cell depletion and improved renal responses in proliferative lupus nephritis (LN) in the Phase 2 NOBILITY trial and will be further evaluated in the Phase 3 REGENCY trial. Recent analyses suggest alternative urinary sediment, serum creatinine (SCr), and urine protein/creatinine ratio (UPCR) requirements may be better measures of response in LN than those used in NOBILITY [1,2]. The objective of this analysis was to evaluate the NOBILITY response definitions and to report the results of NOBILITY using alternative definitions of renal response.

Methods: 126 patients with active Class III/IV LN were randomized to obinutuzumab or placebo in combination with mycophenolate and glucocorticoids. NOBILITY complete renal response (CRR) required UPCR < 0.5, SCr ≤ the upper limit of normal (ULN) of the reference laboratory and not increased > 15% from baseline SCr, and inactive urinary sediment. Exploratory analyses were conducted, and alternative response definitions were evaluated post hoc.

Results: NOBILITY CRR was increased with obinutuzumab over placebo at Week 52 (35% vs. 23%, P = 0.11) and Week 76 (40% vs. 18%, P = 0.007). Response rates were low among patients with baseline SCr < 0.65 mg/dL (n = 45) due to the requirement that SCr not increase > 15% from baseline; increasing this threshold to 25% increased the response rate to a level similar to other groups (Figure). Alternative response definitions demonstrated increased rates of response in both treatment groups and similar benefits of obinutuzumab over placebo at Weeks 52 and 76 (Table).

Conclusion: Obinutuzumab resulted in consistent treatment benefits across a range of renal response definitions in NOBILITY and will be further evaluated in REGENCY. A requirement that SCr not increase > 15% from baseline may be overly restrictive in patients with low baseline SCr (< 0.65 mg/dL), where a change of 15% represents < 0.1 mg/dL and is of questionable clinical relevance. These findings may inform LN clinical trial design and more accurately reflect clinical practice.

References

1. Dall'era M et al. *Arthritis Rheumatol*. 2015;67:1305-13.
2. Almaani S et al. *J Am Soc Nephrol*. 2019;30:669 [abstract].

Disclosure: Z. Amoura, Roche, 2; **P. Remy**, None; **L. Quintana Porras**, None; **L. Chiche**, None; **D. Chauveau**, None; **D. Roccatello**, None; **R. Furie**, AstraZeneca/MedImmune, 2, 5; **T. Schindler**, Roche, 1, 3; **J. Garg**, Genentech, 1, 3; **M. Cascino**, Genentech, 1, 3; **B. Rovin**, GSK, 1, Aurinia, 5, AstraZeneca, 5, Novartis, 5, Alexion, 5, Bristol-Myers Squibb, 5; **A. Doria**, GlaxoSmithKline, 5, 8, Eli Lilly, 5, 8, Roche, 5, 8, Janssen, 5, 8, Pfizer, 5, 8.

Abstract Number: 1837

Clinical Outcomes in Lupus Nephritis by Renal Response Status: A Retrospective Analysis of the Hopkins Lupus Cohort

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SESSION INFORMATION
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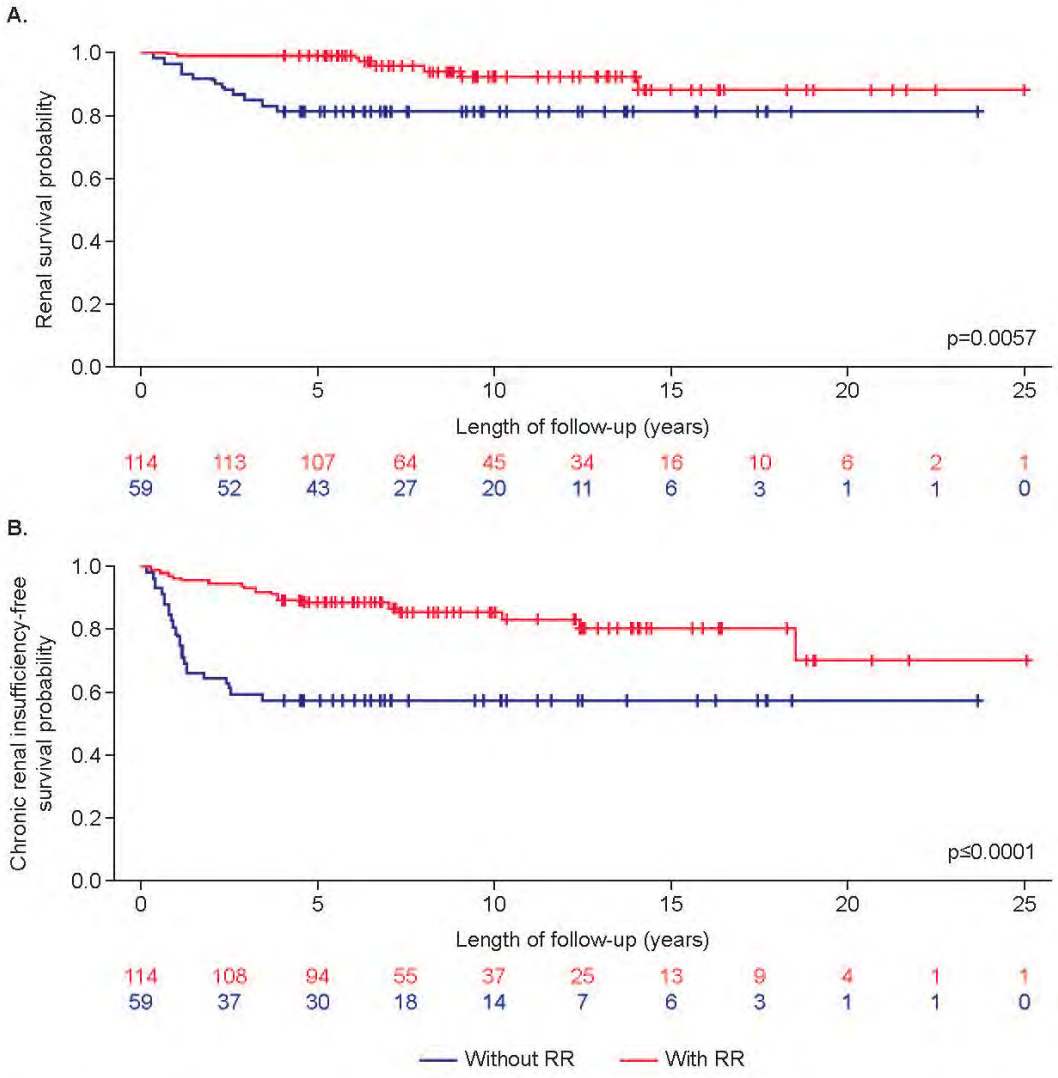
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: A retrospective analysis of the Hopkins Lupus Cohort (a prospective, longitudinal study of patients [pts] with systemic lupus erythematosus) reported that renal response (complete/partial/none) at 24 months post-diagnosis of lupus nephritis (LN) predicts long-term renal survival.[1] Here, we compare long-term renal survival and chronic renal insufficiency-free survival in pts with and without a renal response (RR) to standard LN therapy, as defined by primary endpoint in the Phase 3 BLISS-LN study (GSK Study BEL114054; NCT01639339).

Methods: This retrospective analysis (GSK Study 213039) of the Hopkins Lupus Cohort included pts with biopsy-proven class III, IV, or V LN. Endpoints were: long-term renal survival (no end-stage renal disease [ESRD] and/or mortality) and long-term chronic renal insufficiency-free survival by RR status at 24 months post-biopsy, both assessed by Kaplan–Meier plots with log-rank test and Cox proportional hazards regression.

Results: 173 pts with LN were included; 91.3% were female and mean (SD) age at biopsy was 36.2 (11.8) years. At 24 months post-biopsy, 114 (65.9%) pts achieved RR. Pts with RR at 24 months were less likely to experience an ESRD/mortality event and chronic renal insufficiency (**Figure**), even after adjusting for covariates (HR [95% CI] 0.33 [0.13, 0.87], p=0.0255; and HR [95% CI] 0.26 [0.14, 0.47], p< 0.0001, respectively).

Figure. Renal survival (A) and chronic renal insufficiency–free survival* (B) by RR status at 24 months



*New kidney damage OR new occurrence of glomerular filtration rate <60 ml/min/1.73m^2 on ≥2 consecutive occasions ≥3 months apart

Conclusion: Achieving BLISS-LN primary endpoint defined RR at 24 months post-biopsy is associated with long-term renal survival and chronic renal insufficiency-free survival in pts with LN.

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Reference

1. Davidson JE, et al. *J Rheumatol* 2018;45(5):671–7.

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Abstract Number: 1838

Aerobic Exercise Improves Fatigue and Quality of Life in Women with Systemic Lupus Erythematosus (Preliminary Analysis)

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SESSION INFORMATION

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Session Title: SLE – Treatment Poster II

Session Type: Poster Session D

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Background/Purpose: Systemic lupus erythematosus (SLE) is a chronic systemic autoimmune disease of female predominance. One of the most debilitating symptoms experienced by SLE-patients is persistent fatigue. Prior research from our group suggests that fatigue, as measured by the Fatigue Severity Scale (FSS), is independent of SLE disease activity, as measured by Safety of Estrogen in Lupus Erythematosus National Assessment Group-Systemic Lupus Erythematosus Disease Activity Index (SELENA-SLEDAI) scores. Mitochondrial dysfunction and the type I Interferon pathway may contribute to fatigue in SLE. The purpose of this study is to characterize the responses and adaptations to a program of aerobic exercise in SLE patients with significant fatigue and minimal disease activity. Here we present preliminary analysis of our study.

Table-1-Demographics and SELENA-SLEDAI score of patients enrolled in Exercise Study

Variables	*N=16*
Age (Years)	
Mean ±SD	**42.0 ± 10.3**
Disease Duration (years)	
Mean ±SD	**9.1 ± 6.5**
BMI	
Mean ±SD	**28.2 ± 5.2**
Race/Ethnicity, N (%)	
African American	**3 (18.8 %)**
Asian	**3 (18.8 %)**
Caucasian	**2 (12.5 %)**
Hispanic	**8 (50.0 %)**
Gender, N (%)	
Female	**16 (100.0%)**
SELENA-SLEDAI	
Mean ±SD	**1.4 ± 1.9**

Table-2- Pre and post exercise Fatigue Severity Scale (FSS) measures.			
Fatigue Severity Scale Parameters	**Pre-Exercise Median (Q1- Q3)**	**Post-Exercise Median (Q1-Q3)**	***p-value***
FSS LOW MOTIVATION	6 (3--7)	4 (1--7)	**0.0342**
FSS EXERCISE BRINGS	5 (2--6)	2 (1--5)	**0.0002**
FSS EASILY FATIGUE	4 (3--6)	3 (1--6)	**0.0293**
FSS INTERFERES PHYS FNCTN	5 (1--7)	3 (1--6)	**0.0005**
FSS CAUSE FREQ PROB	5 (1--7)	2 (1--7)	**0.0002**
FSS PREVNTS SUSTND PHYS FXN	4 (1--7)	2 (1--6)	**0.0205**
FSS INTERFERES DUTIES	5 (1--7)	2 (1--6)	**0.0022**
FSS AMONG 3 DISABLNG SX	6 (2--7)	2.5 (1--7)	**0.0088**
FSS INTERFERES WORK	5 (1--7)	3 (1--7)	**0.0234**
FSS AVERAGE	4.6 (3--6.3)	2.9 (1.2--5.9)	**<0.0001**

Table-3- Pre and post exercise Patient-Reported Outcomes Measurement Information System (PROMIS) measures.			
PROMIS Parameters	**Pre-Exercise Median (Q1--Q3)**	**Post-Exercise Median (Q1--Q3)**	***p-value***
PHYSICAL FUNCTION	4.6(3.9--4.8)	4.8(4.1--5)	**0.0342**
ANXIETY	1.8(1.1--2.8)	1.6(1--2.5)	**0.0391**
DEPRESSION	1.5(1.2--1.9)	1.1(1--1.6)	**0.0469**
FATIGUE	2.3(1.9--3.1)	1.9(1.5--2.1)	**0.0002**
SLEEP DISTURBANCE	2.6(2.2--2.8)	2.3(1.7--2.6)	**0.0161**
SATISFACTION WITH SOCIAL ROLES	1.6(1.2--2.5)	1.7(1.1--2.2)	0.6003
PAIN INTERFERENCE	1.9(1--2.2)	1.1(1--1.9)	0.1343
PAIN INTENSITY	2(1--3.5)	1.5(1--2.5)	0.0847

Methods: A cohort of 20 SLE patients with minimal disease activity (SELENA-SLEDAI < 4) and self-reported presence of fatigue (FSS ≥ 3) are being enrolled in an open label monitored, aerobic exercise intervention program. The exercise program consists of treadmill exercise for 30 minutes, three times a week for 12 weeks. Vascular endothelial dysfunction and arterial stiffness are measured by performing non-invasive vascular studies. The primary outcome measure of this study is the time it takes the subjects to reach their anaerobic threshold during a cardiopulmonary exercise test (CPET), which is performed before and after the exercise program. Secondary outcome measures such as the FSS, SELENA-SLEDAI scores and the Patient-Reported Outcomes Measurement Information System (PROMIS) survey assesses disease activity and fatigue. Other outcomes such as distance walked during a 10-minute walk test and peak O_2 consumption during a CPET assesses changes in physical capacity and function. Furthermore, mechanistic studies are planned to measure mitochondrial dysfunction and interferon gene signature.

Results: To date, 16 SLE patients have completed the protocol. The average age of recruited SLE patients was 42 ± 10.3 years and the average disease duration was 9.1 ± 6.5 years (Table 1). 50% of the patients were Hispanic, 18.8% were African- American and Asian, and 12.5% were Caucasian. The average SLEDAI score at baseline was 1.4 ± 1.9, which remained constant throughout the study. The median FSS score at baseline was 4.6 (3--6.3), which decreased to 2.9 (1.2--5.9) by the end of the study ($p < 0.0001$) (Table 2). The PROMIS survey demonstrated an improvement across most of the parameters at the end of the study, when compared to baseline (Table 3).

Conclusion: In this preliminary analysis, patients reported a significant improvement in their fatigue and overall health following participation in an exercise program. There was no increase of SLE disease activity. The data produced from this study will provide an understanding of the mechanisms leading to fatigue in SLE patients, and the potential role of exercise in mediating these improvements. These findings will be utilized in the planning of a larger randomized controlled study to address pathophysiology of fatigue in SLE patients and recommendations for exercise interventions to modulate this disease manifestation

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Abstract Number: 1839

Medication Adherence Barriers and Opportunities to Overcome Them Among Patients with SLE

Lena Eder[1], Megan Clowse[2], Amanda Eudy[3], Jennifer Rogers[4], Rebecca Sadun[3], Lisa Criscione-Schreiber[5], Jayanth Doss[3], Mithu Maheswaranathan[6], Amy Corneli[7], Hayden Bosworth[6] and Kai Sun[6], [1]Duke University Hospital, Chapel Hill, NC, [2]Duke University, Chapel Hill, NC, [3]Duke University, Durham, NC, [4]Duke University Hospital, Durham, DE, [5]Division of Rheumatology and Clinical Immunology, Department of Medicine, Duke University Medical Center, Durham, NC, [6]Duke University Hospital, Durham, [7]Duke University, Durham

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Medication non-adherence in SLE is as high as 80%, yet little is known about adherence barriers faced by patients or interventions that improve adherence in SLE. We developed an intervention based on our prior study results in collaboration with lupus clinic stakeholders and pilot-tested it in a tertiary care lupus clinic. As part of the intervention, providers shared objective pharmacy refill data with patients during the encounter to elicit adherence barriers and discussed approaches to overcoming barriers. These were then documented in the clinic note via a dropdown menu with multiple choice options (Table 1). Here we describe adherence barriers elicited and approaches suggested to overcome them as noted by lupus providers during this pilot intervention.

Methods: We conducted the pilot intervention during regular clinic visits over 12 weeks on consecutive follow-up SLE patients who were prescribed ≥1 SLE medication. Adherence was assessed by medication possession ration (MPR) based on Surescripts refill data available in the EMR supplemented by phone calls to patients' pharmacies. Adherence was assessed for the 3-month periods before and after the intervention visit, using MPR ≥80% as a cutoff for being adherent. Approaches to overcome barriers documented by providers were collected via chart review.

Results: Among 134 SLE patients seen during the intervention period, 70 (median age 40, 96% female, 66% African-American) were inconsistent at refilling at least one SLE medication (MPR < 80%). Lupus clinic providers identified and documented adherence barriers for 39 (56%) of the 70 patients with low refills. The most common barriers were busyness or forgetting (51%), cost or insurance issues (28%), side effects (15%), pill burden (8%), and lack of motivation (8%). Three months following the intervention visit, 33 (47%) of 70 patients with low refill rates now are considered adherent. There was no significant difference in the distribution of barriers between those with and without improved adherence after the intervention visit. Approaches to overcoming barriers documented by providers

Table 1. Dropdown menu choices for adherence barriers used in the clinic note template and distribution of adherence barriers among 39 patients who were non-adherent 3 months prior to the intervention visit and 33 patients who had improved adherence 3 months after the intervention visit.

Adherence Barriers	Non-adherent patients with barriers documented at intervention visit (n=39)*	Patients with improved adherence 3 months after the intervention visit (n=33)*
Cost, n (%)	7 (18%)	3 (9%)
Insurance, n (%)	4 (10%)	2 (6%)
Pharmacy issues, n (%)	2 (5%)	1 (3%)
Busyness or forgetting, n (%)	20 (51%)	9 (27%)
Pill Burden, n (%)	3 (8%)	2 (6%)
Side effects, n (%)	6 (15%)	4 (12%)
Concerns about side effects, n (%)	1 (3%)	0 (0%)
Believing medicines are not needed if feeling well, n (%)	0 (0%)	0 (0%)
Lack of knowledge, n (%)	1 (3%)	0 (0%)
Lack of motivation, n (%)	3 (8%)	1 (3%)
Depression, n (%)	1 (3%)	1 (3%)
Other, n (%)	6 (15%)	2 (6%)
*Among 70 patients who were non-adherent prior to the intervention visit based on refill data, 39 patients had adherence barriers documented by providers, and 33 patients had improved adherence 3 months after the intervention visit.		

included: strategies to help with remembering, for example, using a reminder, app, or pill box, moving pills to a more visible area, or involving a family member to remind the patient (n=10); modifying the medication schedule or prescription (n=7); eliciting help from the pharmacist and/or social worker for cost and insurance issues (n=5); providing education or clearer instructions (n=5); treating side effects (n=2); and addressing depression (n=1).

Conclusion: We found that the most frequent medication adherence barriers faced by SLE patients related to the logistics of taking medications, financial burden, and side effects. The most common approach to address barriers suggested by providers were strategies to help with logistics of taking medications. The similar distribution of adherence barriers between those who did and did not have improved adherence after the intervention visit suggests that most of the barriers are modifiable.

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Abstract Number: 1840

A Novel Biomarker Identifies Systemic Lupus Erythematous (SLE) Patients Who Benefit from Obexelimab (XmAb®5871) Treatment

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: We previously reported Phase 2 SLE trial results for obexelimab, a CD19-targeted FcγRIIb engager that suppresses B-cell activation [1]. The primary endpoint, which measured loss of baseline response to steroids, was not met, but a strong trend in favor of obexelimab and statistically significant efficacy in secondary endpoints supported further analysis. Here, we describe a novel whole blood gene expression biomarker that characterized patients with improved outcomes on obexelimab therapy.

Methods: Expression of individual genes and gene pathway scores were evaluated for 68 patients who either completed the study or terminated early for loss of response using a five-fold cross validation framework. The relevance

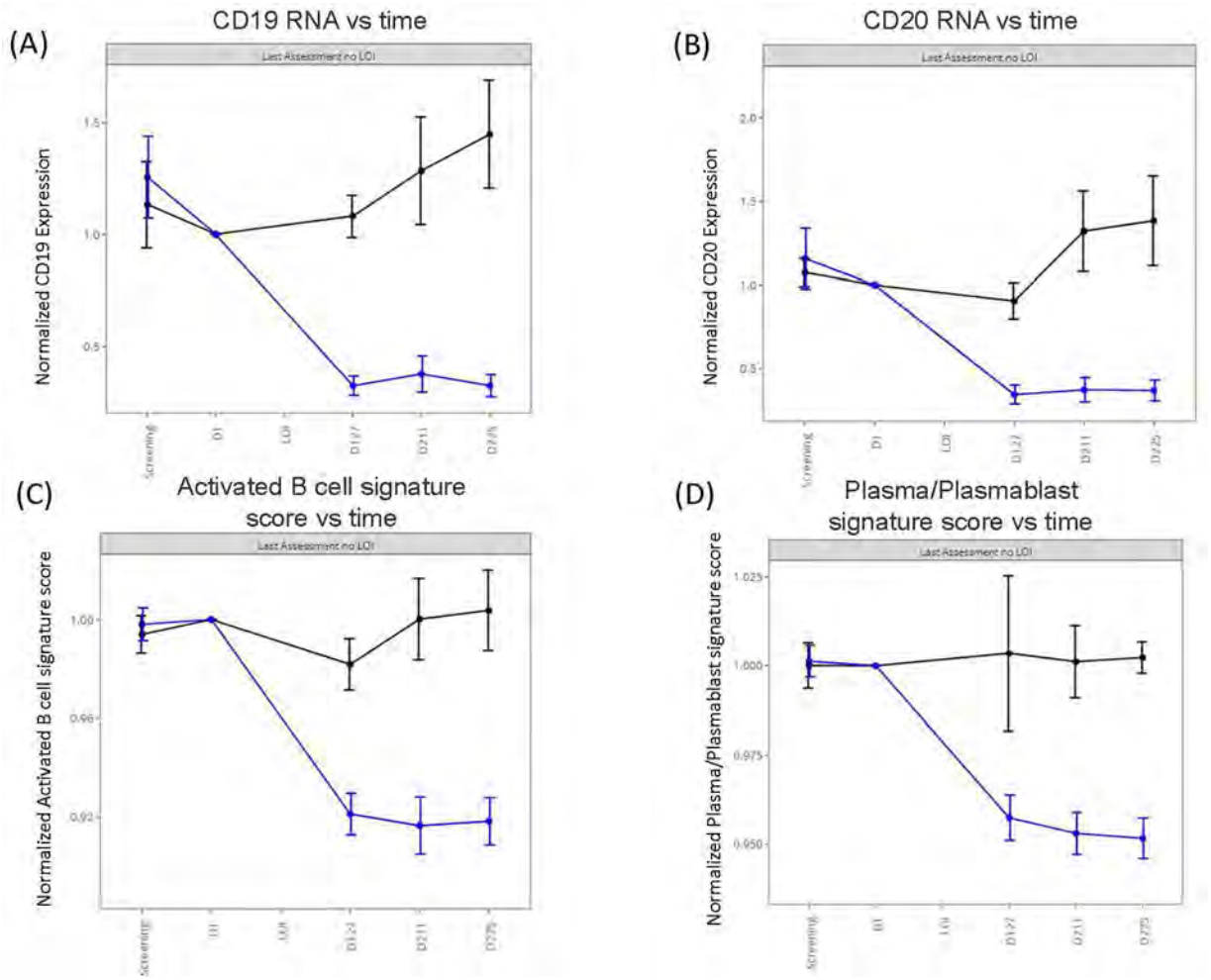

Figure 1. Pharmacodynamic effects of obexelimab (blue curve) compared with placebo (black curve) in patients with systemic lupus erythematosus (SLE) who had evaluable baseline whole blood transcriptomic (RNA-seq) data and either completed the study without a flare or experienced a flare on study. The RNA expression and signature scores are relative to baseline. Signature scores are based on immune cell signatures described in [3] and generated by the Singscore method[4] (A) B-cell marker gene CD19 gene expression over time (B) B-cell marker gene CD20 (transcript MS4A1) gene expression over time. (C) Activated B-cell signature score over time (D) Plasma/plasmablast signature score over time. [3] Arazi, A. et al. Nat. Immunol. 2019. 20;902-914. [4] Foroutan M, et al. . BMC Bioinformatics, 2018 19; 404.

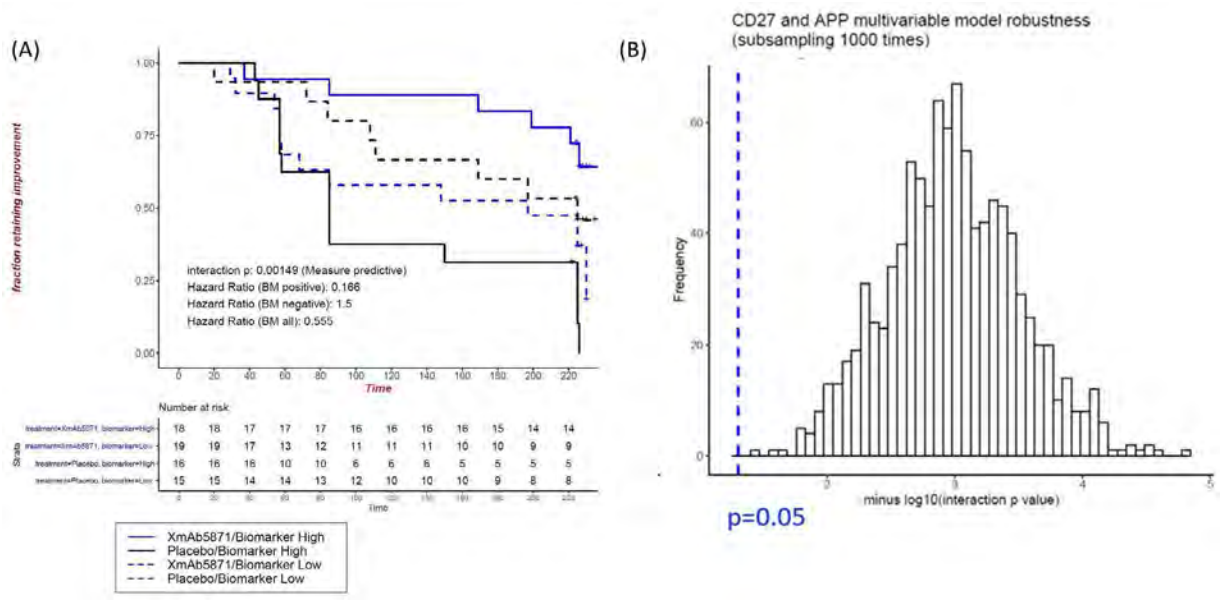

Figure 2. Two-gene predictive model (CD27 and APP). A five-fold cross validation framework was developed to ensure the generalizability of the results and to determine the number of genes needed and what fraction of patients to assign as cDx+. Classifications are based on a simple threshold for the sum of gene expression levels that have been normalized by the training sample mean and standard deviation. (A) Normalized expression levels of two genes classify patients as cDX+ or cDx-, with an estimated 50% of patients assigned to each group. The benefit from obexelimab over placebo in the cDx+ group (solid blue and solid black curves) was significantly greater than the benefit in the cDx- group (dashed blue and dashed black curves) (p=0.000149, HR cDx+ = 0.166 vs HR cDx- =1.5). (B) Robustness of the two-gene predictive model as shown by the distribution of the interaction p-value based on subsampling 80% of the datasets 1000 times.

of each gene to a potential biomarker predictive model was measured by the degree to which high or low expression identified a patient subgroup (cDx+) with greater reduction in risk of flare by obexelimab than in cDX- patients.

Results: Obexelimab treatment was associated with reduction of B-cell genes and gene-sets reflective of activated B-cells and plasma cells/plasmablasts (Figure 1), as previously reported [2]. Importantly, our cross-validated analyses determined that the baseline expression levels of 2 predictive genes, CD27 and APP, identified a cDx+ group (50% of all patients) with greatly reduced risk of flare on obexelimab (cross-validated HR=0.262, full data set HR=0.166) (Figure 2). Conversely, in the placebo group, the CDx+ subjects had higher flare risk, thus cDX+ also identifies poor-prognosis patients who might particularly benefit from obexelimab. The cDx+ group demonstrated increased obexelimab effects compared to cDx- patients over a range of clinical endpoints (SRI-4: 56% cDx+ vs 14% cDx-, SRI-6: 33% vs 6.2%, LLDAS: 50% vs 6.2%, BICLA: 33% vs 12.5%) (Figure 3). CD27, the top predictive biomarker, is highly expressed by T-naïve and memory cells. Consistent with the notion that CD27 expression is important within the T-cell lineage, increased expression of other T-cell genes was also associated with reduced flare risk, including CD28 (p=0.04), TCF7(p=0.03) and FOXP3 (p=0.05). Taken together with the reduction of B cell signatures seen on treatment, this new identification of CD27 as a potential T-cell associated predictive biomarker suggests an important therapeutic role of obexelimab in suppression of B-cell and T-cell interactions.

Conclusion: A novel two-gene classifier developed from whole blood transcriptomic data by RNA-sequencing identifies a biomarker positive group of patients with a high baseline resting and stem-like T-cell (CD27+, CD28+ and TCF7+) signature. These cDx+ patients had superior response rates compared to placebo across multiple clinical endpoints, suggesting that adaptive immune responses such as B-cell antigen presentation and/or T-cell costimulation may be key components of obexelimab effects. This exploratory biomarker analysis supports further assessment of the two gene signature as a patient stratification/companion diagnostic strategy in obexelimab clinical development for SLE and other autoimmune conditions.

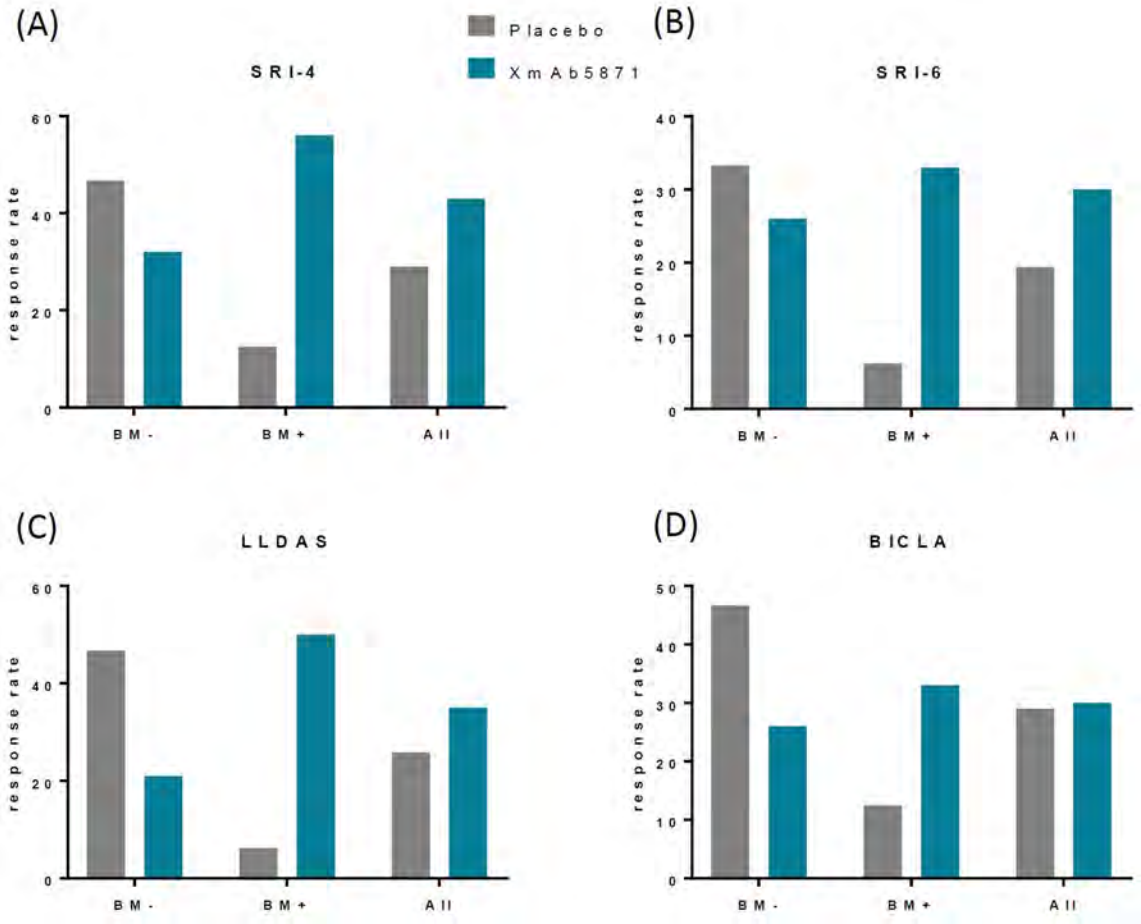

Figure 3. Response rates are enriched among cDX+ (50%) patients' four landmark endpoints at 32 weeks. (A) SRI-4 (B) SRI-6 (C) LLDAS (D) BICLA.

[1] Merrill JT, et al Arth Rheum 2018;70 Abs S10.
[2] Merrill JT, et al EULAR 2020; Abs SAT0187

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Abstract Number: 1841

Outcomes After Hydroxychloroquine Reduction or Discontinuation in a Multinational Inception Cohort of Systemic Lupus

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: SLE – Treatment Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is a cornerstone treatment for several autoimmune diseases including Systemic Lupus Erythematosus (SLE). Recently, concerns arose regarding HCQ shortages for SLE patients, due to its use as a potential COVID-19 treatment. Although some patients may remain well after reducing or stopping therapy, others will have potentially life-threatening complications related to SLE flares. We evaluated if HCQ reduction or discontinuation is associated with increased risk of poor outcomes.

Methods: We analyzed prospective data from the Systemic Lupus International Collaborating Clinics (SLICC) cohort, which includes SLE patients from 33 sites in Europe, Asia, and North America, enrolled within 15 months of diagnosis and followed annually, from 1999 to 2019. In patients receiving HCQ, we identified two sub-cohorts, one who reduced HCQ and one who stopped HCQ. We did not require patients to be in disease remission at the time of HCQ reduction/discontinuation for these analyses. Time zero for these sub-cohorts was the date of the first HCQ reduction/discontinuation. For comparison, we identified a third group of patients remaining on HCQ. A poor outcome was defined as either subsequent need for SLE therapy augmentation (steroids or other immunosuppressives), increase of ≥4 points in the SLE Disease Activity Index-2000 (SLEDAI-2K) or hospitalization for SLE. We estimated adjusted hazard ratios (HRs) and 95% confidence intervals (CIs) for poor outcomes among the three HCQ exposure groups. Models were adjusted for demographics and baseline clinical characteristics.

Table 1. Hazard ratios (HRs), and 95% confidence intervals (CIs) for poor outcomes in HCQ-exposed SLE patients

Characteristics*	HR (95% CI)	aHR (95% CI)
HCQ Group		
Maintenance	Reference	-
Taper	**1.35 (1.19, 1.53)**	**1.40 (1.22, 1.59)**
Discontinuation	**1.36 (1.17, 1.56)**	**1.48 (1.27, 1.73)**
Male sex	1.01 (0.85, 1.21)	0.96 (0.79, 1.15)
Race/ethnicity		
Caucasian	Reference	-
Asian	**1.26 (1.09, 1.46)**	0.91 (0.77, 1.07)
Black	**1.22 (1.03, 1.44)**	0.94 (0.78, 1.13)
Others	**1.49 (1.28, 1.74)**	1.07 (0.91, 1.27)
Age at SLE diagnosis in years	0.99 (0.99, 1.00)	1.00 (0.99, 1.00)
No college/university education	**1.17 (1.04, 1.31)**	1.03 (0.92, 1.16)
Active disease (SLEDAI-2K ≥ 4)	**1.36 (1.22, 1.52)**	**1.13 (1.01, 1.27)**
Renal damage	**1.25 (1.01, 1.55)**	0.89 (0.71, 1.13)
Body mass index	0.99 (0.98, 1.00)	1.00 (0.99, 1.02)
Smoker	0.93 (0.82, 1.05)	0.98 (0.86, 1.11)
Prednisone use	**2.19 (1.95, 2.47)**	**1.73 (1.50, 1.99)**
Immunosuppressive use	**2.27 (2.04, 2.54)**	**1.77 (1.56, 2.01)**
Biologic use	0.98 (0.68, 1.40)	0.74 (0.51, 1.07)
Time on HCQ	1.01 (0.98, 1.03)	0.97 (0.94, 1.00)

*At baseline, except for age. Other race/ethnicity includes Hispanic, Mixed and First-Nations. Immunosuppressives included azathioprine, mycophenolate, and methotrexate. Biologics included belimumab, rituximab and abatacept.

Hazard ratios (HRs), and 95% confidence intervals (CIs) for poor outcomes in HCQ-exposed SLE patients

Results: A total of 1460 patients were included (89% female, 52% Caucasian). Patients in the HCQ reduction group contributed 1087 person-years, those discontinuing HCQ contributed 677 person-years, and those maintaining HCQ contributed 1649 person-years. HCQ dose reduction or discontinuation occurred in many patients (40%) with a SLEDAI-2K >4. The crude poor outcome rate was significantly lower in the HCQ maintenance group (31.6 events per 100 person-years, 95% CI 29.0, 34.5) than in the reduction (43.0, 95% CI 39.3, 47.1) and in the discontinuation (43.0, 95% CI 38.3, 48.2) groups. Patients reducing or discontinuing HCQ had higher adjusted HRs for poor outcomes versus those maintaining HCQ (Table 1). Other factors independently associated with poor outcomes included active SLE and use of prednisone or immunosuppressive drugs, all measured at time zero.

Conclusion: Patients reducing or discontinuing HCQ are at greater risk of having a poor outcome versus those maintaining the drug. These analyses do not account for reasons HCQ was reduced/discontinued. Regardless, baseline disease activity, prednisone and immunosuppressive drugs were associated with the risk of poor outcomes in SLE patients reducing, discontinuing, or maintain HCQ.

Disclosure: C. Almeida-Brasil, None; **J. Hanly**, None; **M. Urowitz**, None; **A. Clarke**, AstraZenca, 5, Exagen Diagnostics, 5; **R. Ramsey-Goldman**, None; **C. Gordon**, UCB, 1, 2, 3, 4, CDC, 1, MGP, 1; **M. Petri**, AbbVie, 5, Amgen, 5, AstraZeneca, 2, 5, BMS, 5, Decision Resources, 5, GSK, 2, 5, INOVA, 5, IQVIA, 5, Janssen, 5, Eli Lilly, 2, 5, Merck EMD Serono, 5, Sanofi Japan, 5, Thermofisher, 5, UCB, 5, Exagen, 2; **E. Ginzler**, Aurinia Pharmaceuticals, Inc., 2; **D. Wallace**, Exagen, 1, 2, Exagen, 1, 2; **S. Bae**, None; **J. Romero-Diaz**, None; **M. Dooley**, None; **C. A. Peschken**, None; **D. Isenberg**, None; **A. Rahman**, None; **S. Manzi**, None; **S. Jacobsen**, BMS, 2; **S. Lim**, None; **R. Van Vollenhoven**, None; **O. Nived**, None; **A. Jönsen**, None; **D. Kamen**, None; **C. Aranow**, None; **G. Ruiz-Irastorza**, None; **J. Sanchez-Guerrero**, None; **D. Gladman**, AbbVie, 2, 5, Amgen, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2,

5, Bristol-Myers Squibb, 5, Gilead, 5, Galapagos, 5, Celgene, 2, 5, Eli Lilly, 2, 5; **P. Fortin**, None; **G. Alarcón**, None; **J. Merrill**, None; **K. Kalunian**, Roche, 5, Biogen, 5, Janssen, 5, AstraZeneca, 5, Lupus Research Alliance, 2, Pfizer, 2, Sanford Consortium, 2, Eli Lilly, 5, Genetech, 5, Gilead, 5, ILTOO, 5, Nektar, 5, Viela, 5, Equillium, 5, Bristol-Meyers Squibb, 5; **M. Ramos-Casals**, None; **K. Steinsson**, None; **A. Zoma**, None; **A. Askanase**, Glaxo Smith Kline, 2, Astra Zeneca, 2, Janssen, 2, Eli Lilly and Company, 2, Abbvie, 5, Mallinckrodt, 2, Regeneron, 9, Pfizer, 2, Bristol Myers Squibb, 9; **M. Khamashta**, None; **I. Bruce**, None; **M. Inanc**, None; **S. Bernatsky**, None.

Abstract Number: 1842

Repository Corticotropin Injection (Acthar® Gel) for Persistently Active Systemic Lupus Erythematosus: Post Hoc Analyses of Patient-Reported Outcomes from a Phase 4, Multicenter, Randomized, Double-blind, Placebo-Controlled Trial

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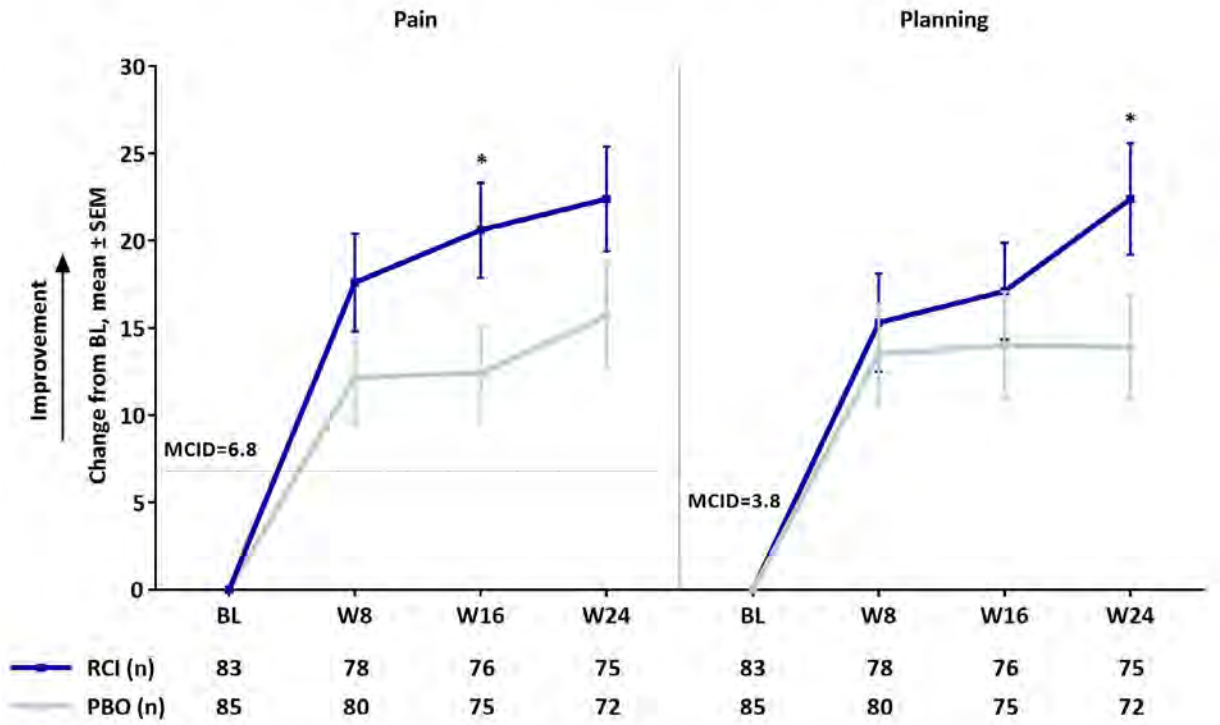
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Repository corticotropin injection (RCI, Mallinckrodt Pharmaceuticals) is a naturally sourced complex mixture of adrenocorticotropic hormone analogs and other pituitary peptides approved for the treatment of SLE flares and as maintenance therapy. This post hoc analysis of patient-reported outcomes (PROs) from a multicenter, double-blind, randomized, placebo (PBO)-controlled study of RCI in patients with persistently active SLE despite use of moderate-dose glucocorticoids (GCs) was conducted to assess RCI-dependent quality of life (QOL) improvements (NCT02953821).

Methods: Patients were ≥18 years old with active SLE (≥4 of 11 ACR criteria; SLEDAI-2000 [SLEDAI-2K] ≥6) and moderate-severe rash and/or arthritis by BILAG despite stable GC doses (7.5-30 mg/d prednisone equivalent), antimalarials, NSAIDs for ≥4 weeks (Ws), and/or immunosuppressants for ≥8 Ws before screening. Patients were randomized to 80 U RCI subcutaneously or PBO every other day to W4 followed by twice-weekly dosing to W24. Stable GC doses were required through W16 with optional taper from W16 to W24. Primary analyses evaluated the change from baseline (BL) in the LupusQOL and Work Productivity and Activity Impairment (WPAI)-Lupus questionnaires through W24. Post hoc analyses stratified these results by BL SLEDAI-2K (< 10 vs ≥10), Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity [CLASI-A (< 11 vs ≥11)], and BILAG (< 20 vs ≥20) scores and by BILAG-based Combined Lupus Assessment (BICLA) response (patients with BICLA responses at both W20 and W24). Analyses were performed in the modified intention-to-treat population (mITT-P; patients who received ≥1 dose of study drug and contributed any post-BL efficacy data).

Results: The mITT-P (RCI, n=84; PBO, n=85) was predominantly female (91.7%) with a mean age of 39.7 years, mean BL GC dose of 11.1 mg, and mean BL SLEDAI-2K score of 9.9. RCI treatment resulted in significantly greater improvement in the LupusQOL *pain* domain at W16 and *planning* domain at W24 compared with PBO (Figure 1) and exceeded the minimal clinically important difference at all time points. Post hoc analyses demonstrated significant improvements in the *pain*, *planning*, and *fatigue* domains at multiple time points in RCI-treated patients with higher

Figure 1. Change From BL in LupusQOL Domains in the Primary Analysis, mITT-P[a]



[a]Patients who received ≥1 dose of study drug and contributed any post-BL efficacy data.

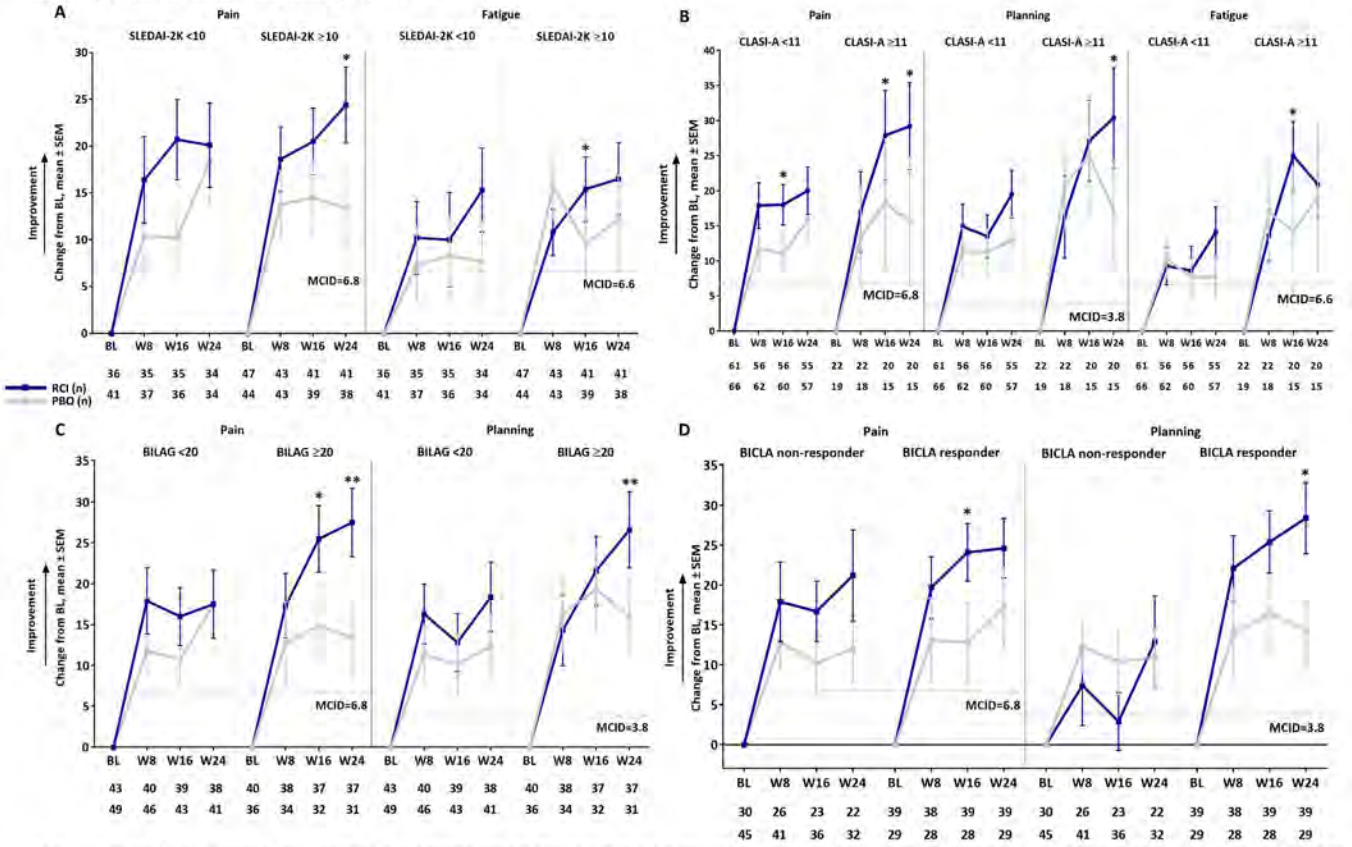
*$p<0.05$ for the LS mean difference using ANCOVA models with the change from BL as the dependent variable, treatments as the factor, and BL values of corresponding endpoints as the covariate, with stratification for location (US and outside the US) and BL GC dose (≤20 and >20 mg/d).

Abbreviations: ANCOVA, analysis of covariance; BL, baseline; GC, glucocorticoid; LS, least square; LupusQOL, Lupus Quality of Life; MCID, minimal clinically important difference; mITT-P, modified intention-to-treat population; PBO, placebo; RCI, repository corticotropin injection; SEM, standard error of the mean; W, week.

disease activity by BL SLEDAI-2K, CLASI-A, and BILAG and in BICLA responders (Figure 2). No significant differences between treatment groups were observed for any WPAI-Lupus parameter through W24 in the primary analysis or with higher disease activity in post hoc SLEDAI-2K, BILAG, or CLASI-A subgroups. However, RCI treatment resulted in significant improvements in *percent work time missed* at W24 in patients with BL CLASI-A < 11 (RCI mean change –8.4 [standard deviation (SD) 25.1]; PBO mean change 7.8 [SD 21.9]; p=0.0182 for least square mean difference) and in *percent impairment while working* at W16 in BICLA responders compared with PBO (Figure 3).

Conclusion: RCI treatment resulted in greater improvements in several PROs compared with PBO. These results suggest that treatment with RCI may improve QOL and *work productivity* in patients who have persistently active SLE despite treatment with standard SLE therapy, particularly in those with higher disease activity.

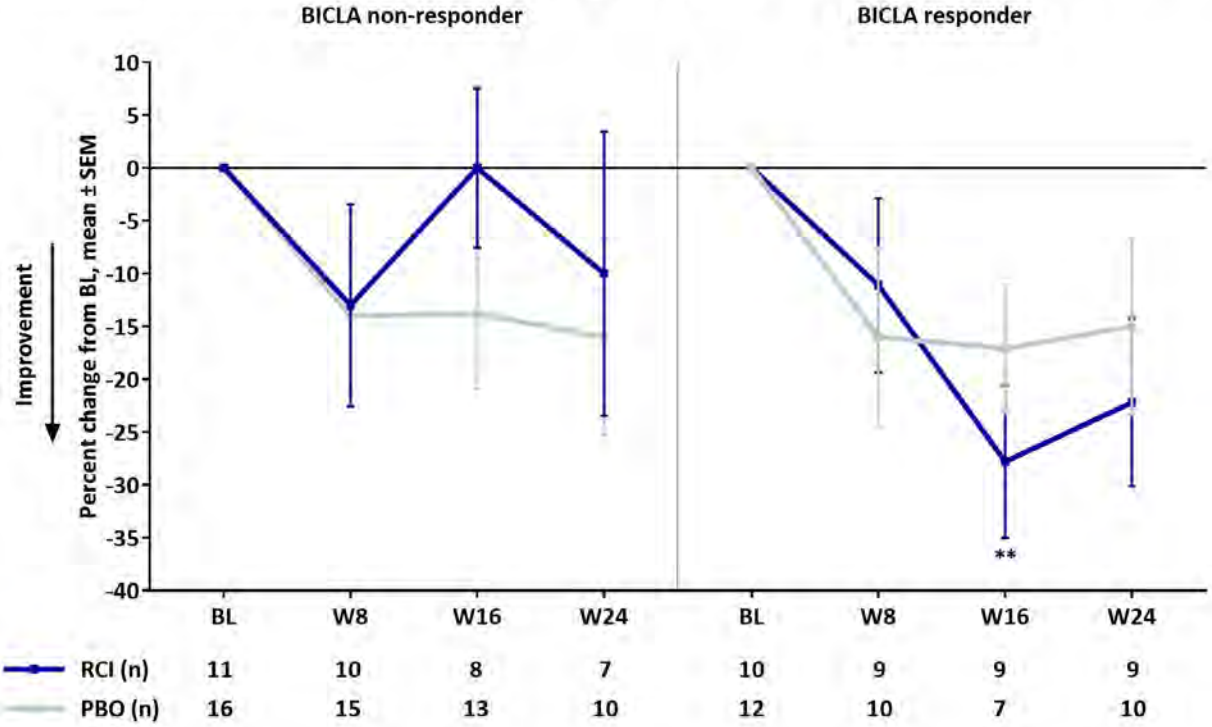
Figure 2. Change From BL in LupusQOL Domains in the Post Hoc Subgroups on the Basis of BL SLEDAI-2K (A), CLASI-A (B), and BILAG (C) and on BICLA Response (D), mITT-P[a]



*p<0.05; **p<0.01 for the LS mean difference using ANCOVA models with the change from BL as the dependent variable, treatments as the factor, and BL values of corresponding endpoints as the covariate, with stratification for location (US and outside the US) and BL GC dose (≤20 and >20 mg/d).

Abbreviations: ANCOVA, analysis of covariance; BICLA, BILAG-based Combined Lupus Assessment; BL, baseline; CLASI-A, Cutaneous Lupus Erythematosus Disease Area and Severity Index-Activity; GC, glucocorticoid; LS, least square; LupusQOL, Lupus Quality of Life; MCID, minimal clinically important difference; mITT-P, modified intention-to-treat population; PBO, placebo; RCI, repository corticotropin injection; SEM, standard error of the mean; SLEDAI-2K, SLEDAI-2000; W, week.

Figure 3. Percent Change From BL in WPAI-Lupus Percent Impairment While Working in the Post Hoc BICLA Responder Status Subgroups, mITT-P[a]



[a]Patients who received ≥1 dose of study drug and contributed any post-BL efficacy data.

***p*<0.01 for the LS mean difference using ANCOVA models with the change from BL as the dependent variable, treatments as the factor, and BL values of corresponding endpoints as the covariate, with stratification for location (US and outside the US) and BL GC dose (≤20 and >20 mg/d).

Abbreviations: ANCOVA, analysis of covariance; BICLA, BILAG-based Combined Lupus Assessment; BL, baseline; GC, glucocorticoid; LS, least square; mITT-P, modified intention-to-treat population; PBO, placebo; RCI, repository corticotropin injection; SEM, standard error of the mean; W, week; WPAI-Lupus, Work Productivity and Activity Impairment-Lupus.

Disclosure: A. Askanase, GlaxoSmithKline, 2, 5, AstraZeneca, 2, 5, AbbVie, 5, Bristol Myers Squibb, 5, Janssen, 2, Eli Lilly, 2, Pfizer, 2, LuCIN, 2, Mallinckrodt Pharmaceuticals, 2; **G. Wan**, Mallinckrodt Pharmaceuticals, 3; **M. Panaccio**, Mallinckrodt Pharmaceuticals, 3; **E. Zhao**, Mallinckrodt Pharmaceuticals, 3; **J. Zhu**, Mallinckrodt Pharmaceuticals, 3; **R. Bilyk**, Mallinckrodt Pharmaceuticals, 3; **R. Furie**, AstraZeneca/MedImmune, 2, 5.

Abstract Number: 1843

Integrated Efficacy of the AURORA 1 and AURA-LV Trials Confirms Voclosporin Rapid Proteinurea Reduction in the Presence of Low-Dose Steroids

Ellen M Ginzler[1], Joshua Kaplan[2], Laura Lisk[3], Ray Federico[4], Neil Solomons[5] and Robert Huizinga[5], [1]SUNY Downstate Health Sciences University, Brooklyn, [2]Rutgers University, New Brunswick, NJ, [3]Aurinia Pharmaceuticals Inc., Victoria, BC, Canada, [4]Aurinia Pharmaceuticals, Inc., Victoria, Canada, [5]Aurinia Pharmaceuticals, Victoria, BC, Canada

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Voclosporin (VCS) is a novel calcineurin inhibitor (CNI) with a favorable metabolic profile and a consistent predictable dose response potentially eliminating the need for therapeutic drug monitoring.

Voclosporin has been evaluated for the treatment of lupus nephritis (LN) in two double blind RCTs, the Phase 2 AURA-LV and Phase 3 AURORA 1 trials representing the largest successful LN program to date. Previously reported results from these studies demonstrated that the addition of VCS to MMF and low-dose steroids resulted in statistically superior renal response at 24 weeks and at one year (AURA-LV 48 weeks, AURORA 1 52 weeks).

Methods: The AURORA 1 and AURA-LV studies were of similar design and conducted in comparable patient populations. The results of the efficacy and safety analyses from AURORA 1 were consistent with and confirmed the conclusions from the AURA-LV study. The data from both studies for subjects treated with the recommended VCS dose of 23.7 mg BID(AURORA 1; n=179, AURA-LV; n=89) or with matching placebo (AURORA 1; n= 178, AURA-LV; n=88) were therefore pooled for an integrated analysis of efficacy.

The primary endpoint in both studies was renal response (RR), defined as UPCR of ≤ 0.5 mg/mg, eGFR ≥ 60 mL/min, or no confirmed decrease from baseline in eGFR of > 20%, ≤ 10 mg/d prednisone for at least 8 weeks prior to endpoint assessmentand no administration of rescue medication.

Results: In the integrated analysis, treatment with VCS resulted in a clinically meaningful and statistically significant higher renal response (RR) rate (43.7%) compared to placebo (23.3%) at 1 year (OR 2.76, 95% CI: 1.88, 4.05; $p < 0.0001$) and at 6 months (VCS 31.7%; placebo 20.3%), [OR: 2.01; 95% CI: 1.34, 3.01; p=0.0008].

Furthermore, a 50% reduction in UPCR from baseline at any time was achieved by 93.7% of subjects treated with VCS compared with 75.2% of subjects receiving placebo, with a median time to 50% reduction in UPCR of 29 days versus 58 days, respectively. The time taken to reach a 50% reduction in UPCR was significantly shorter for the voclosporin group than the placebo group (HR 1.96; 95% CI: 1.61, 2.38; p< 0.0001). At one year 160 (75.8%) patients in the VCS arm and 150 (73.9%) patients in the placebo arm were on oral prednisone ≤ 2.5 mg/d.

Conclusion: Integrated efficacy analysis further supports efficacy results from the AURORA 1 and AURA-LV trials. Adult patients with LN treated with VCS on top of MMF and steroids achieve meaningful reductions in proteinuria and achieve that reduction faster compared to patients on MMF and steroids alone.

Disclosure: E. Ginzler, Aurinia Pharmaceuticals, Inc., 2; **J. Kaplan**, Aurinia Pharmaceuticals, Inc., 1; **L. Lisk**, Aurinia Pharmaceuticals, 1, 3; **R. Federico**, Aurinia Pharmaceuticals, Inc., 1, 3; **N. Solomons**, Aurinia Pharmaceuticals, 1, 3; **R. Huizinga**, Aurinia Pharmaceuticals Inc., 1, 3.

Abstract Number: 1844

Hydroxychloroquine and QTc Prolongation in a Cohort of SLE Patients

Mayce Haj-Ali[1] and H. Michael Belmont[2], [1]NYU Langone Health, new york, [2]NYU School of Medicine, New York, NY

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Hydroxychloroquine (HCQ) is an antimalarial drug used in the treatment of systemic lupus erythematous (SLE). Cardiac toxicity is very rare in SLE, but has been reported in patients with ESRD. The normal corrected QT (QTc) interval is defined as 450 ms in males and 470 ms in females. Severe prolongation of QTc is defined as > 500 ms and is associated with higher risk of developing life threatening arrhythmias such as Torsades de pointes (Tdp). The purpose of this study was to compare QTc intervals in a cohort of SLE patients based on HCQ exposure and with and without chronic kidney disease (CKD).

Methods: Retrospective Epic EMR review of 194 SLE patients fulfilling criteria in a faculty practice at NYU Langone Health between 3/12/12 – 5/1/20. Data was collected on EKG, QTc of first and last EKG (QTc prolongation defined as: > 450 ms in males or > 470 ms in females. Severe QTc prolongation defined as > 500 ms), creatinine and demographics. CKD defined as eGFR < 60 ml/min.

Results: 90 of the 194 patient had at least one EKG. Of these 90 patients, 91% were female, 32.2% African Americans, 6.6% Asian, 38.8% Caucasian, 20% Hispanic, 2.2% other and 75 on HCQ and 15 not on HCQ. QTC was prolonged in 8/75 HCQ and 1/15 without HCQ (table 1). There was no significant difference in mean QTc interval based on HCQ use (p= 0.586). In the 23 patients with CKD, QTC was prolonged in 4/19 on HCQ and 0/4 without. In patients with CKD there was no significant difference in mean QTc interval based on HCQ use (p= 0.784). No patients had documented tachyarrthymia or Tdp.

Conclusion: In a cohort of SLE patients, at least one EKG was available in 46%. There was no significant difference in mean QTc based on HCQ use. Patients with CKD were more likely to have prolonged QTc when compared to those without CKD, but there was no significant difference in mean QTc based on HCQ use as well in this subset. Severe prolongation of QTc was rare in all groups and no episodes of serious tachyarrhythmia or Tdp were observed. A role for more severe stages of CKD, underlying heart disease, or concurrent use of drugs that also affect QTc was not studied. The data supports current standard of care which does not require monitoring with baseline and serial EKGs in the routine management of SLE patients on HCQ. It remains uncertain if the effect of HCQ on the conducting system is limited to a physiological result yet is clinically inconsequential absent other risk factors.

Total (n= 90)	HCQ (n= 75)	No HCQ (n= 15)	P-value
Prolonged QTc, (n, %)	8 (10.6%)	1 (6.6%)	
Severely prolonged QTc, (n, %)	3 (4%)	1 (6.6%)	
QTc, ms (mean, +/- SD)	437.91 ± 20.02	434.6 ± 27.49	p = 0.5859
CKD (n = 23)	**HCQ (n= 19)**	**No HCQ (n=4)**	**P-value**
Prolonged QTc, (n, %)	4 (21%)	0 (0%)	
Severely prolonged QTc, (n, %)	3 (15.8%)	1 (25%)	
QTc, ms (mean, +/- SD)	448.11 ± 23.37	444.5 ± 24.61	p = 0.7844

Table 1. Effect of HCQ on QTc interval

Disclosure: M. Haj-Ali, None; **H. Belmont**, Exagen, 5.

Abstract Number: 1845

Long-Term Clinical Outcomes of Patients with Lupus Nephritis Treated with an Intensified B-Cell Depletion Protocol: A Matched Case-Control Study

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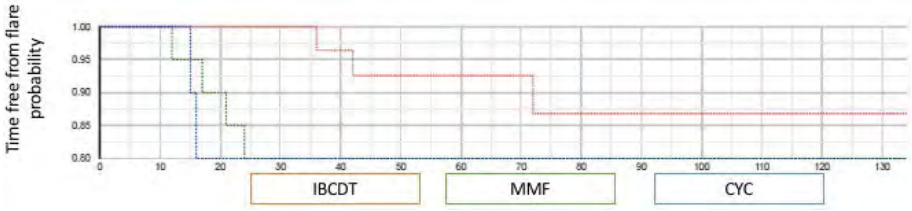
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Targeting B-cells remains an attractive option in Lupus Nephritis (LN) despite the negative results of RCTs.

Methods: Sixty patients with active LN were included in the present study. Thirty patients were administered an intensified B-cell depletion therapy (IBCDT; 4 weekly Rituximab 375mg/sm and 2more doses after 1and2 months;2 infusions of 10 mg/kg cyclophosphamide (CYC),3 methylprednisolone pulses), followed by oral prednisone (rapidly tapered to 5mg/day by the end of the 3rd month). No further immunosuppressive maintenance therapy was given. Thirty patients matched for LN class and age were selected as controls: 20 received 3 methylprednisolone pulses days followed by oral prednisone and mycophenolate mofetil (MMF) 2-3 g/day, while 10 were given the Euro Lupus CYC.

Results: At 12 months, complete renal remission was observed in 93% of patients on IBCDT, in 62.7% on MMF, and in 75% on CYC. When assessed at 12 months, the dose of oral prednisone was lower in the IBCDT group (mean±SD 2.9±5.0mg/dl) than in those on MMF (10.5±8.0 mg/day, p< 0.01) or in the CYC group (7.5±9.0mg/day,p< 0.01). Mean follow-up after treatment was 44.5 months (ICQ36–120months), 48.6 months (ICQ36–120months), and 45.3 (ICQ36–120months) for IBCDT, MMF and CYC, respectively. At their last follow-up visit, we observed no significant differences in terms of proteinuria, serum creatinine, nor in the frequency of new flares among the three groups.

Conclusion: When compared to conventional regimens with MMF and CYC, sustained clinical remission even without maintenance immunosuppressive therapy was obtained by the IBCDT. Moreover, IBCDT had a significant steroid-sparing effect and a lower rate of flares compared to either MMF- or CYC- based conventional protocols.



Disclosure: D. Roccatello, None; **S. Sciascia**, None; **R. Fenoglio**, None; **R. Daniela**, None.

Abstract Number: 1846

Evaluating the Risk of QT-prolongation Associated with Hydroxychloroquine Use with and Without Antidepressants in SLE Patients with Fibromyalgia

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic lupus erythematosus (SLE) is a complex systemic autoimmune disease predominantly affecting woman of child-bearing age. Concurrent fibromyalgia syndrome (FMS) has been reported in up to 40% of patients with SLE, which markedly affects their daily functionality and life satisfaction. Anti-depressants are used for the pharmacological therapy of FMS in both the general population and patients with connective tissue diseases. These agents include selective serotonin reuptake inhibitors (SSRIs), serotonin and norepinephrine reuptake inhibitors (SNRIs), tricyclic antidepressants (TCAs) and atypical antidepressants. Hydroxychloroquine (HCQ) is widely used in patients with SLE due to its immunomodulatory action on reducing lupus disease activity and good overall tolerance and safety profiles. However, both antidepressants and HCQ are reported to cause QT interval prolongation, a cardiac measure that serves as a surrogate indicator for increased risk of torsade de pointes, a potential lethal ventricular arrhythmia that can result in sudden death. A recent study of hospitalized COVID-19 patients being treated with combination HCQ and azithromycin observed prolonged QT intervals and events of torsade de pointes, raising concern of additive risk for arrhythmic mortality when HCQ is used concomitantly with other QT-prolonging medications including antidepressants. Our objective is to investigate the risk of QT prolongation associated with hydroxychloroquine use with and without concurrent use of antidepressants in SLE patients with fibromyalgia.

Methods: This is a retrospective analysis using electronic medical records sampling SLE patients who participated in Yale Lupus Wellness Program from 2016 to 2019. All patients included met 2012 SLICC classification criteria for SLE. 97 patients in the program had 12-lead ECG with QTc interval measures. 52 patients used HCQ alone, while 45 patients concomitantly used both HCQ and antidepressants including SSRI, SNRI, TCA, or tramadol. QTc intervals were compared in groups taking HCQ alone versus those taking HCQ and antidepressants.

Results: The average QTc interval was found to be 430 milliseconds at baseline, which was increased to 441 milliseconds after HCQ usage for 3 months or greater ($p < 0.05$). The average QTc interval was 436 milliseconds in total HCQ dose less than 720 g versus 447 milliseconds in total HCQ dose greater than 720 g ($p > 0.05$). However, QTc interval was found to be similar with and without concurrent use of antidepressants (451 milliseconds in patient on HCQ alone vs. 447 milliseconds in patients on HCQ with antidepressants) in this cohort study.

Conclusion: Our study indicates that chronic use of HCQ is associated with QTc interval prolongation in patients with SLE. However, concurrent use antidepressants for fibromyalgia did not appear to further increase QTc interval.

Disclosure: J. Renaldi, None; **F. Koumpouras**, Exagen, 5, celgene, 2, 8, abbvie, 2, NIH, 2, GSK, 8, Lupus Research Alliance, 5, Janssen, 2, BMS, 2; **M. Dong**, None.

Abstract Number: 1847

Delayed and Immediate Release Prednisone Decrease Fatigue Comparably in Patients with Systemic Lupus Erythematosus

Hope Rainey[1], Kristy Bell[1], Violeta Rus[2], Daniel Wallace[3], Claire Dykas[1], Mary Mora[1], Maggy Comberg[1] and Peter Lipsky[1], [1]AMPEL BioSolutions LLC., Charlottesville, VA, [2]University of Maryland School of Medicine, Baltimore, MD, [3]Cedars-Sinai Medical Center/UCLA, Los Angeles, CA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: SLE – Treatment Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Morning stiffness and fatigue are common symptoms in patients with SLE. Increased cytokines and disturbed sleep patterns may contribute to morning symptoms and fatigue in SLE. We, therefore, hypothesized that delayed release (DR) prednisone given in the evening might suppress morning symptoms of stiffness and fatigue better than standard immediate release (IR) prednisone given in the morning.

Methods: This was a multicenter randomized double-blind active comparator double baseline crossover study designed to compare the impact of morning IR prednisone to the same dose of evening DR prednisone in SLE patients with increased fatigue (NCT03098823). Eligible patients met ACR classification of SLE, had a Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-F) score ≤30 and were prescribed oral IR prednisone at 5-15 mg/day. Patients were randomized in a 1:1 ratio to receive either daily active DR prednisone (RAYOS) at 10pm and daily morning placebo or daily active morning IR prednisone and daily placebo capsules at 10pm at the same total dose they had previously been prescribed. After 3 months, the treatment regimens were reversed, and the patients continued for another 3 months. The primary endpoint was change in fatigue assessed by FACIT-F.

Results: 62 patients were enrolled and randomized and 60 were evaluable for treatment response. At 3 months, there was significant improvement in fatigue measure by FACIT-F, as well as by the Fatigue Severity Score (FSS) and the vitality questions of the SF-36. The mean degree of improvement in fatigue exceeded the minimal clinically important difference (MCID) (see Figures 1 and 2). However, there was no significant difference between the groups in the degree of improvement in fatigue. Following the crossover there was persistent improvement in fatigue compared to

Figure 1. FACIT-F results over study duration (mean ± SEM).

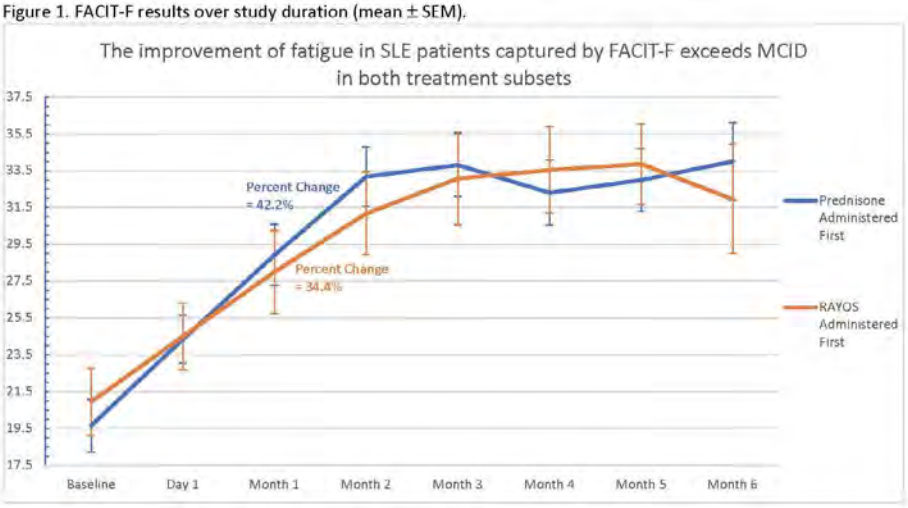
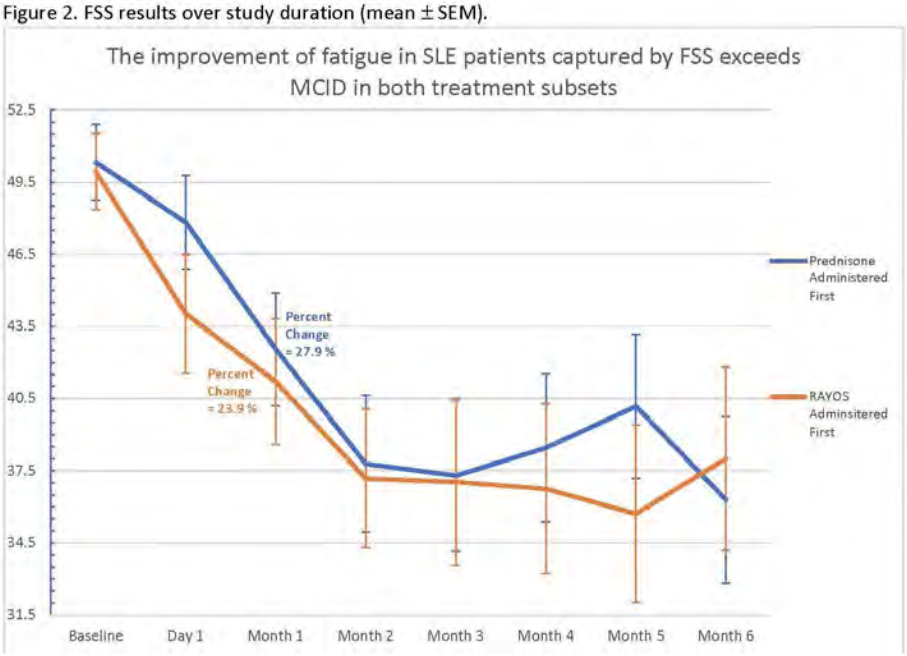


Figure 2. FSS results over study duration (mean ± SEM).



baseline, but again no significant difference between the groups. Daily estimates of morning stiffness assessed with a mobile app did not differ between the groups. The frequency of adverse events did not differ between the groups.

Conclusion: DR and IR prednisone were comparable in improving fatigue in patients with SLE. Despite no change in daily prednisone dosage from prescribed doses at entry, fatigue significantly improved, implying that one contributor to fatigue in SLE may be differences between prescribed and actual administered doses of prednisone.

Disclosure: H. Rainey, None; **K. Bell**, None; **V. Rus**, None; **D. Wallace**, None; **C. Dykas**, None; **M. Mora**, None; **M. Comberg**, None; **P. Lipsky**, Horizon Therapeutics, 3.

Abstract Number: 1848

Identification of Native and Citrullinated Autoantibodies to Psoriasis Related-antigen PsoP27 in Synovial Fluids of Patients with Psoriatic Arthritis

Marina Slobodkin[1], Smadar Gertel[1], Ari Polachek[2], Victoria Furer[3] and Ori Elkayam[4], [1]Tel-Aviv Sourasky Medical Center, Tel-Aviv, Israel, [2]Tel Aviv Sourasky Medical Center, Petah-Tikva, Israel, [3]Tel Aviv Sourasky Medical Center, Tel Aviv, Israel, [4]Tel Aviv Sourasky Medical Center,, Tel aviv, Israel

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriatic arthritis (PsA) is an inflammatory joint disease with no serological biomarkers, hence diagnosis is based on clinical evaluation alone. PsA is closely associated with Psoriasis (PsO), with up to 1/3 of psoriatic patients developing PsA via unknown mechanism.

PsoP27 -SF			
	PsA	RA	OA
Median	0.640	0.855	0.283
SD	0.298	0.286	0.28
P value (comp. to OA)	0.02	0.001	-
P value (comp. to RA)	0.165	-	0.001
Cit-PsoP27- SF			
Median	0.766	0.982	0.378
SD	0.373	0.348	0.279
P value (comp. to OA)	0.008	0.001	-
P value (comp. to RA)	0.33	-	0.001

Table 1. PsoP27 Ab level (Optical Density, OD) in SF of PsA, RA and OA patients.

PsoP27- Serum			
	PsA	RA	HC
Median	0.184	0.235	0.219
SD	0.137	0.097	0.141
P value (comp. to HC)	0.265	0.734	-
P value (comp. to RA)	0.686	-	0.734
Cit-PsoP27- Serum			
Median	0.317	0.232	0.321
SD	0.298	0.143	0.160
P value (comp. to HC)	0.49	0.507	-
P value (comp. to RA)	0.065	-	0.507

PsoP27 Ab level (OD) in sera of patients with psoriatic arthritis (PsA), rheumatoid arthritis (RA), and healthy controls (HC).

PsoP27 is an autoantigen found in skin lesions of PsO patients (1) and its levels correlate with psoriasis activity (2). PsoP27 is speculated to be involved in other inflammatory processes, yet it was not investigated in regard to PsA or RA.

The most common autoantigens in RA are citrullinated autoantigens which are formed by PAD (peptidylarginine deiminase enzymes) and can drive the autoimmune response (3). Although known to be present in other diseases, citrullination is commonly associated with RA.

Our aim was to characterize native and citrullinated PsoP27 antibodies (Ab) in synovial fluids (SF) and sera of PsA and RA as compared to osteoarthritis (OA) patients and healthy controls, respectively.

Methods: SF of PsA (*n=35*), RA (*n=11*) and OA (*n=13*) patients and sera of PsA (n=32), RA (n=32) patients and healthy controls (*n=31*) were analyzed by ELISA for native and citrullinated PsoP27 Ab.

Results: In SF, both native and citrullinated PsoP27 Ab were significantly higher in PsA and RA compared to OA patients (Table 1). Significant correlation was observed between both forms of PsoP27 Ab in SF and swollen joints count (Native: *p=0.029, r=0.39*, Cit: *p=0.041, r=0.369*), psoriasis area and severity index (PASI) score (Native: *p=0.011, r=0.56*, Cit: *p=0.008, r=0.369*), and CRP levels (Native: *p=0.017, r=0.446*, Cit: *p=0.03, r=0.408*). In contrast, in RA patients there was no correlation between levels of PsoP27 Ab in SF and swollen joint count or CRP levels. No difference in PsoP27 Ab were detected in sera of all groups (Table 2).

Conclusion: We determined for the first time the presence of antibodies to psoriatic-related autoantigen PsoP27, in SF of PsA and RA patients. Furthermore, we showed a positive correlation between levels of PsoP27 Ab and disease activity in

PsA, but not in RA. Also, we demonstrated the presence of citrullinated antibodies in PsA, commonly thought to be specific to RA. Our results suggest that PsoP27 Ab in SF may be utilized for diagnosis and disease assessment in PsA.

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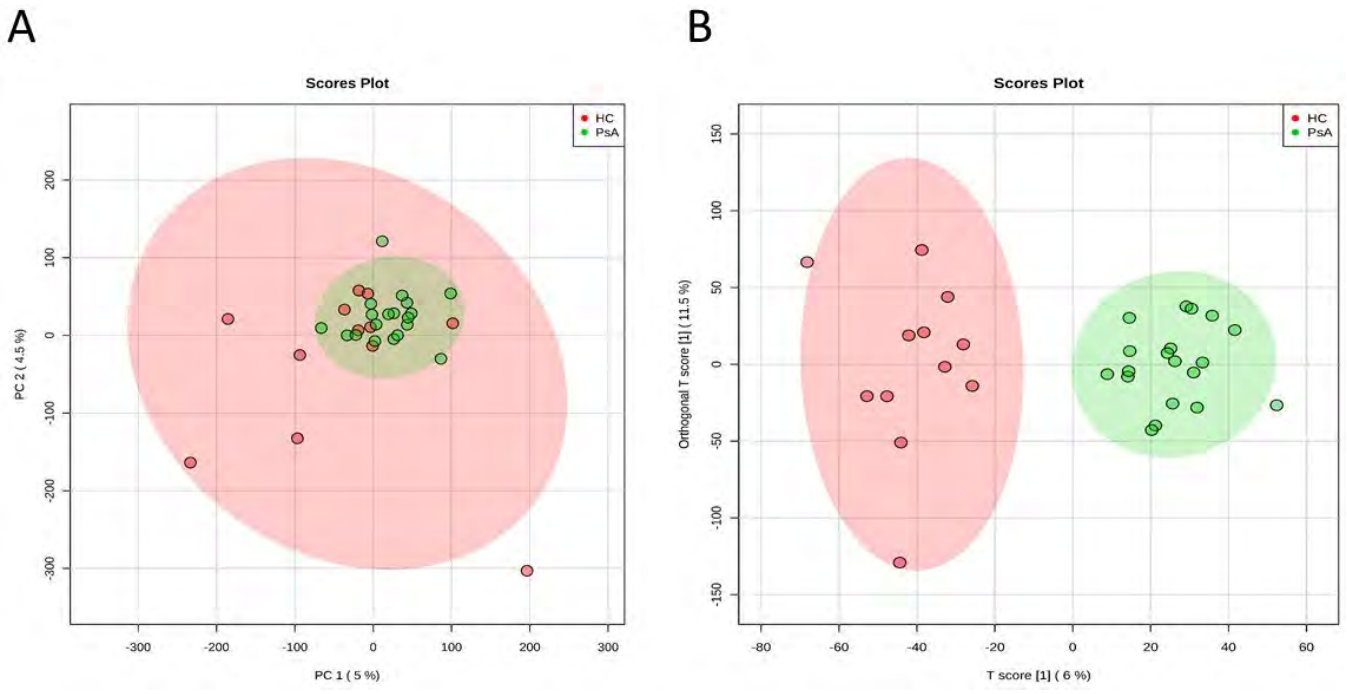
Disclosure: M. Slobodkin, None; **S. Gertel**, None; **A. Polachek**, None; **V. Furer**, None; **O. Elkayam**, None.

Abstract Number: 1849

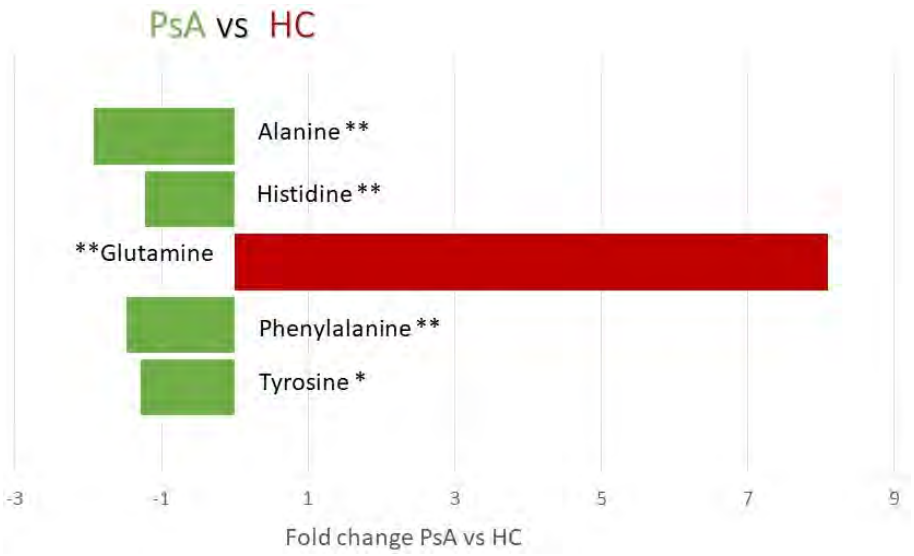
Identification of New Associations Between Psoriatic Arthritis and the Gut Microbiota. the Mi-PART, a Phenomic Study

Jesus Miguens Blanco[1], Uma Selvarajah[1], Zhigang Lui[1], Benjamin Mullish[1], James Alexander[1], Julie McDonald[2], Sonya Abraham[1] and Julian Marchesi[1], [1]Imperial College London, London, United Kingdom, [2]Imperial College London, London

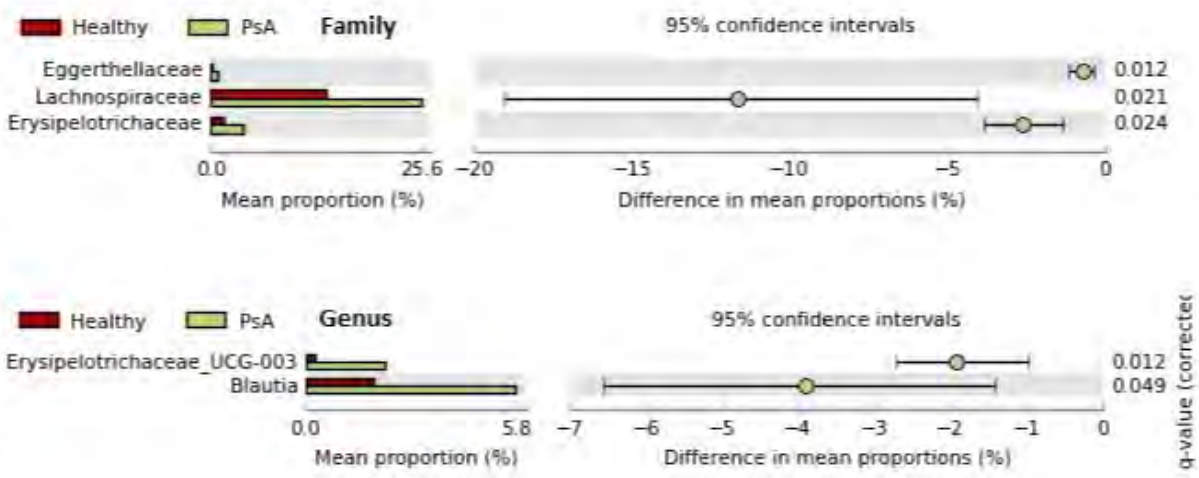
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM



Serum multivariate analysis techniques (A) Serum - PCA (B) Serum O-PLS after 1000 permutations (p-value = 0.0250)



Changes in the two groups of participants in the study (19 PsA ; 12 HC). * **p-value <0.005** ** **p-value < 0.005. Quantification of small molecules was performed with a simplex approach based algorithm developed in-house and implemented in MatLab**



16s rRNA gene sequencing. Illumina MiSeq Regions V1-V2

Background/Purpose: Perturbations of the gut microbiota have been associated with Psoriatic Arthritis (PsA), a chronic inflammatory disease. We aim to test the microbiome-metabolic interface of patients with PsA when compared to healthy controls (HC), this phenomic approach study the microorganism composition of the gut and specific gut-microbial-related metabolites

Methods: This was an observational study conducted in two centres at the United Kingdom. Stool, urine and serum samples from 19 PsA patients and 12 HC were collected. Stool microbial profiles were generated using 16S rRNA gene sequencing (using Illumina MiSeq and Oxford Nanopore Sequence). Fecal, serum and urine supernatants were analysed using a Bruker Avance IIII 600 MHz spectrometer. In-house scripts were used to process NMR spectra (Figure 1).

Results: Quantification of small molecules in serum samples; Tyrosine (*p-value < 0.05*), Phenylalanine (*p-value < 0.05),* Histidine (*p-value < 0.05*) and Alanine (*p-value < 0.005*) were increased in PsA participants and Glutamine (*p< 0.005)* was increased in the HC (Figure 2). The 16s rRNA gene sequencing reported an increase in the relative abundance of the family, *Lachnospiraceae* (*p-value < 0.005*) and one of its genus, *Blautia (p-value < 0.005*), taxa that have been positively associated with serum alanine levels in the literature (Figure 3).

Conclusion: While there are confounders in this pilot study which may contribute to findings, we found significant changes in the amino acids related to the gut microbiome in PsA patients. New associations were made for PsA when compare with previous studies of chronic inflammatory diseases. Further work will validate these results and disclose further links between PsA and the gut microbiota.

Disclosure: J. Miguens Blanco, None; **U. Selvarajah**, None; **Z. Lui**, None; **B. Mullish**, None; **J. Alexander**, None; **J. McDonald**, None; **S. Abraham**, None; **J. Marchesi**, None.

Abstract Number: 1850

The Association Between Imaging Sub-phenotypes of Psoriatic Arthritis and Gene Expression Profiles

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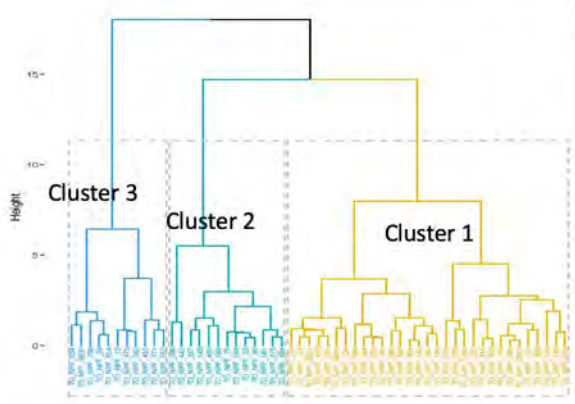
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Heterogeneity is a hallmark of psoriatic arthritis (PsA), which is reflected in diverse clinical, imaging and molecular features, various disease courses and treatment responses. We hypothesized that specific molecular markers underlie the various imaging manifestations of PsA. The study objective was to identify imaging sub-phenotypes in patients with PsA and determine their association with whole blood mRNA expression markers.

Methods: 55 patients with PsA ready to initiate treatment for active disease were prospectively recruited. An ultrasound assessment of the extent of musculoskeletal inflammation in 64 joints, 34 tendons and 16 entheses was performed. Sonographic inflammation (in greyscale and Doppler) of the following domains was graded for: a) synovitis; b) peritenonitis; c) tenosynovitis; and d) enthesitis. A global inflammatory score was calculated for each tissue domain. Peripheral blood was profiled with RNAseq, and gene expression data were obtained. Analyses were performed in two stages: 1) Unsupervised cluster analysis was performed to define imaging sub-phenotypes in PsA that reflected the predominant tissue involved; 2) Principal component analysis was used to determine the association between imaging-defined clusters and peripheral blood gene expression profile. Pathway enrichment analysis was performed to identify underlying mechanisms that characterize individual imaging clusters.

Results: The patients could be divided into 3 groups based on unsupervised hierarchical clustering of images indicating the predominant involved tissue (Figure 1): 1) Synovitis predominant (N=31 [56%]); 2) Enthesitis predominant (N=13 [24%]); 3) Peritenonitis predominant (N=11 [20%]). There were no significant differences in the demograph-

Figure 1 – Hierarchical clustering of imaging data based on tissue-level inflammation



Standardized Ultrasound Scores by Imaging Cluster (median and IQR)

	Cluster 1 Synovitis predominant (N=31)	Cluster 2 Enthesitis predominant (N=13)	Cluster 3 Peritenonitis predominant (N=11)	P value
Synovitis score	1.86 (0.64)	1.15 (0.34)	1.59 (1.40)	0.004
Enthesitis score	0.24 (0.34)	0.83 (0.19)	0.50 (0.45)	<0.001
Peritenonitis score	0.29 (0.70)	0.13 (0.27)	1.13 (0.22)	<0.001
Tenosynovitis score	0 (0.39)	0 (0.27)	0.27 (0.43)	0.59

*Standardized scores= total sonographic score in the domain divided by the total number of affected articular/tendon/entheseal sites

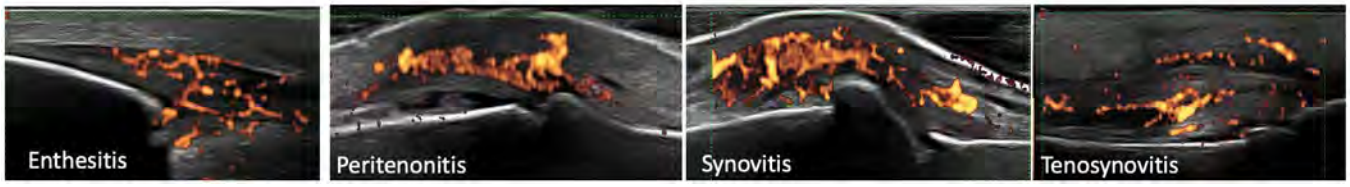


Figure 1. Hierarchical clustering of imaging data based on tissue-level inflammation

Figure 2 – Gene Expression Data by Imaging Clusters

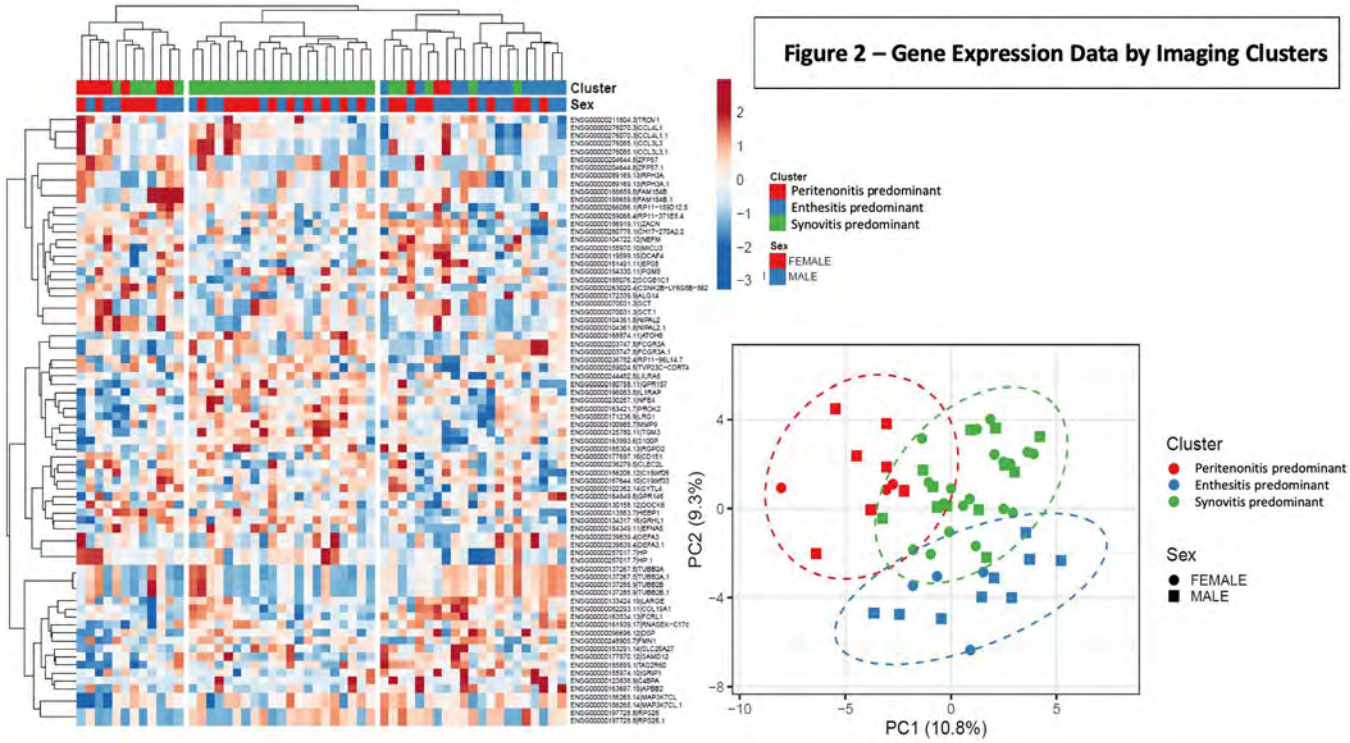
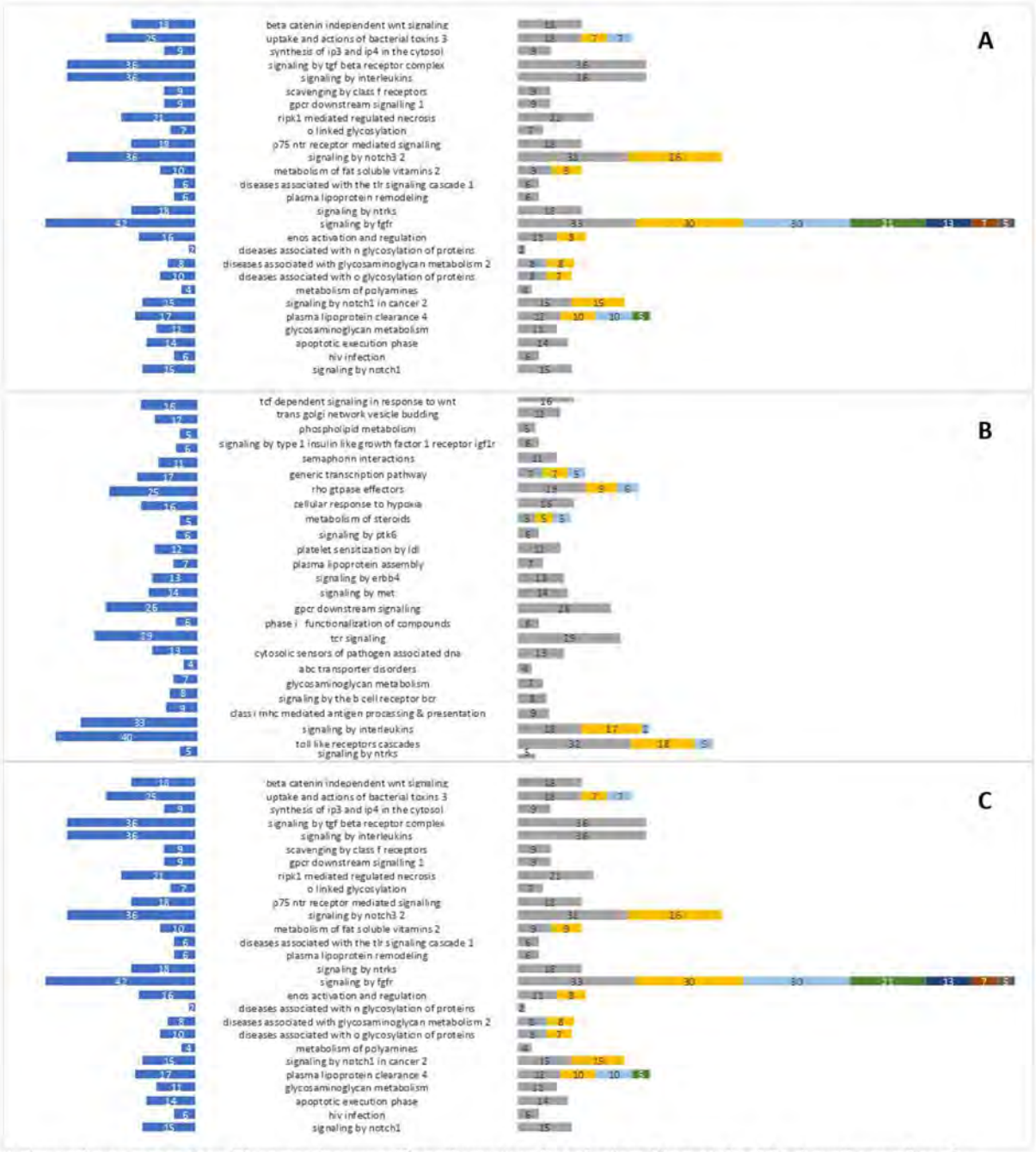


Figure 2. Gene Expression Data by Imaging Clusters

Figure 3 – Differentially Expressed Pathways Across the Imaging Clusters



Major pathway categories with comparison-specific pathway. Number of colored bars at the right show the number of comparison-specific pathway in each category and numbers on the bars show counts of genes in each pathway. Bars at the left show union of all genes whose breakdown across pathways is shown at the right.

A. Enthesitis vs. Peritenonitis predominant clusters; **B.** Synovitis vs. Enthesitis predominant clusters, **C.** Synovitis vs. Peritenonitis clusters

The three comparisons show low overlap: only one pathway category is shared in these figures. Pairwise overlap of categories across figures have sizes 3, 3, and 5.

Figure 3 . Differentially Expressed Pathways Across the Imaging Clusters

ics, duration of PsA and psoriasis characteristics between the clusters (Figure 1). The primary differences between the clusters were related to the severity of clinical joint ad entheseal involvement. Unsupervised clustering of gene expression data identified three clusters that partially overlapped with the imaging clusters (Figure 2). Overall, 344 genes were differentially expressed ($p< 0.05$) in two of the three comparisons between the imaging clusters. Enriched differential pathways included: toll-like receptor cascade, cytokine (TNF, IL-23, TGF-b) signaling, VEGF signaling, complement cascade and integrin signaling (Figure 3).

Conclusion: We identified three different imaging clusters based on the predominant tissue involved in patients with active PsA. Distinct biologic pathways may underlie these imaging clusters seen in PsA.

Disclosure: L. Eder, AbbVie, 2, 5, 8, Eli Lilly, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5, 8, Celgene, 5, Novartis, 5; **L. Quan**, None; **S. Rahmati**, None; **I. Eshed**, None; **P. Rahman**, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5; **I. Jurisica**, None; **V. Chandran**, Abbvie, 2, 5, Amgen, 2, 5, Celgene, 2, 5, Eli Lilly, 5, Eli Lilly, 3, Janssen, 8, Novartis, 5, Pfizer, 5, UCB, 5.

Abstract Number: 1851

Different Disease Activity Trajectories in Early Axial Spondyloarthritis Lead to Significantly Different Long-term Outcomes : A Cluster-based Analysis of the DESIR Cohort

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: AxSpA is a heterogeneous disease, leading to different treatment and follow-up modalities depending on the presentation, along with other elements (socio-economic, gender, etc..). In a previous work, we identified some disease activity trajectories in early axSpa[1], but we did not evaluate the long-term impact for patients in terms of outcomes such as function, work impairment or structural progression.

Objectives: To identify and describe different trajectories of activity over 5 years in patients with early axSpA and to determine the impact of each on long-term outcomes.

Methods: Prospective, multi-centre study (DESIR cohort) of patients with early inflammatory back pain suggestive of axSpA.

Disease activity trajectories were identified using the k-means method, which provides longitudinal clusters. Baseline characteristics were described and the probability to be associated with one Trajectory assessed by a multinomial regression.

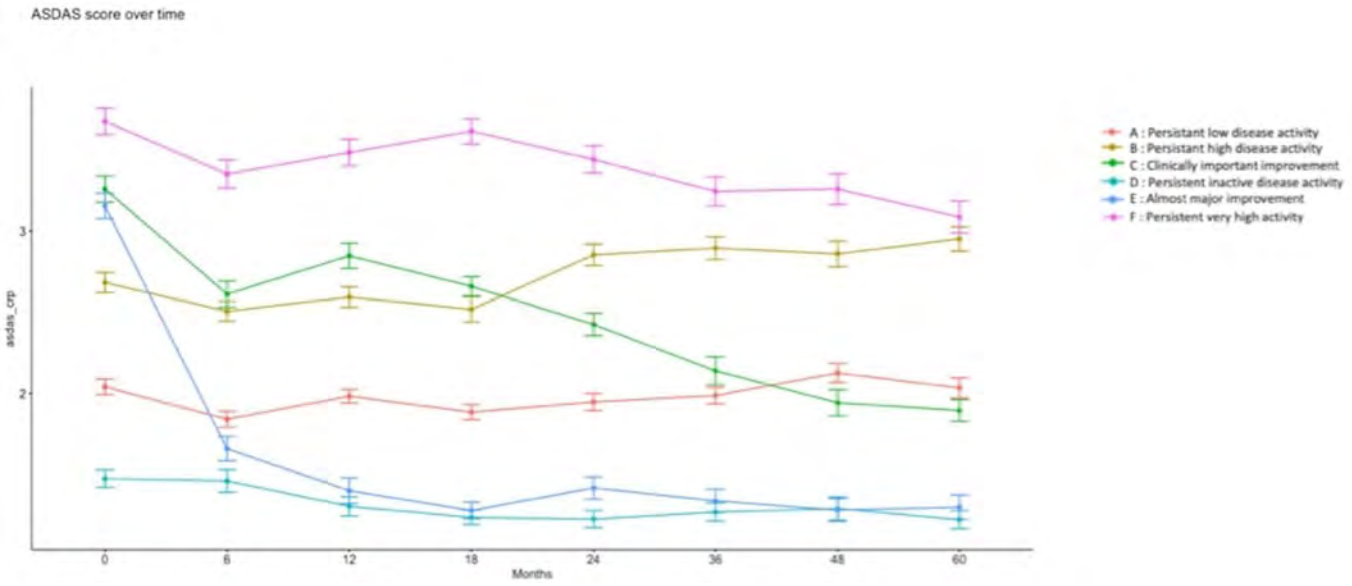

Figure. Trajectories of disease activity in early axial spondyloarthritis according to k-means technique. ASDAS, Ankylosing Spondylitis Disease Activity Score.

	Trajectory B (N = 94) Persistent high disease activity	Trajectory C (N = 94) Clinically important improvement	Trajectory D (N = 79) Persistent inactive disease	Trajectory E (N = 78) Almost major improvement	Trajectory F (N = 66) Persistent very high disease activity
	OR (95%IC)	**OR (95%IC)**	**OR (95%IC)**	**OR (95%IC)**	**OR (95%IC)**
TNFi prescription at 5 years	**2.72 (1.21 to 4.26)**	**2.66 (1.45 to 4.89)**	**0.40 (0.18 to 0.90)**	**2.51 (1.32 to 4.78)**	**7.94 (3.52 to 17.84)**
Structural progression at 5 years	1.58 (0.65 to 3.79)	1.32 (0.51 to 3.37)	1.32 (0.52 to 3.37)	1.60 (0.64 to 4.02)	1.44 (0.52 to 3.99)
					NC
Cardiovascular events over 5 years	NC	NC	NC	NC	NC
	B-Coefficient	**B-Coefficient**	**B-Coefficient**	**B-Coefficient**	**B-Coefficient**
BASMI (mean over 5 years (0-10))	**0.24**	**0.21**	**-0.42**	-0.03	**0.50**
BASFI (mean over 5 years (0-100))	**18.39**	**11.83**	**-11.24**	**-5.77**	**32.41**
SF-36 mental scale (mean over 5 years)	**-7.28**	**-3.36**	**2.7**	**1.9**	**-9.96**
SF-36 physical scale over 5 years (mean over 5 years)	**- 4.96**	**-4.55**	**6.58**	**3.82**	**-9.84**
Days of sick leave (accumulation over 5 years)	**95.70**	56.90	-47.04	-44.76	**189.41**

Table. Outcomes associated with distinct disease activity trajectories in early axial spondyloarthritis (mixed model)

Long term outcomes such as TNFi prescription, function (BASFI), work impairment, quality of life (SF36 scale) and structural progression, associated with each trajectory were identified using mixed models.

Results: 633 patients were included. Six trajectories of disease activity were identified: Trajectory A (n=140 patients, 25.4% of all patients): 'Moderate disease activity'; B (n=94, 17.1%) : 'Persistent high disease activity'; C (n=94,

17.1%) :'Clinically important improvement' (improvement of 1.36 points on the ASDAS between baseline and year 5) ; D (n=79, 14.3%) :'Persistent inactive disease activity'; E (n=78, 14.2%) :'Almost major improvement' (improvement of 1.8 points) ; F (n=66 (12%) : 'Persistent very high activity'.

The 'Persistent low disease activity' Trajectory was set as the reference trajectory: a university level of education was found to be predictive of belonging to the 'Inactive disease' trajectory (OR=3.04, 95% confidence interval [1.46 to 6.78]). Male gender (OR=2.99 [1.56 to 5.92]), and a history of articular peripheral involvement (OR=4.34 [2.14 to 9.10]) were predictive of belonging to the 'Almost major improvement' trajectory, whereas a low degree of education (OR=0.27 [0.14 to 0.52]), and female gender (OR=2.01 [1.03 to 4.34])were associated with the 'Persistent very high disease activity' trajectory.

All trajectories were associated with a higher TNFi prescription. Higher activity trajectories were associated to other poorer outcomes : the 'Persistent very high disease activity' and 'Persistent high disease activity' Trajectories presented respectively a mean of 189 and 95 more days of sick leave over 5 years than the reference Trajectory, but also significantly lower SF-36 scores, poorer BASFI and BASMI. However, no higher likelihood of structural progression was observed in high disease activity groups.

Conclusion: We identified 6 trajectories of ASDAS-CRP. Gender, a university level of education, and peripheral joint involvement were the main factors differentiating trajectories at baseline. Higher disease activity trajectories were significantly associated with poorer function, more days of sick leave, and poorer quality of life. Interestingly, no Trajectories were found to be predictive of structural progression.

Disclosure: B. Leslie, None; **A. Molto**, ABBVIE, 5, BMS, 5, 8, LILLY, 5, NOVARTIS, 5, 8, UCB, 5, 8, GILEAD, 5; **L. Gossec**, None; **R. Matthieu**, None.

Abstract Number: 1852

Intestinal Permeability in the Adjuvant Induced Arthritis Model: Preliminary Study and Impact of NSAIDs

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The gut is no longer considered as a simple element associated with spondyloarthritis but as a real actor of the disease. In patients with spondyloarthritis, the presence of intestinal inflammation and an increase in digestive permeability responsible for bacterial translocation has been described. No data are available on the effect of non-steroidal anti-inflammatory drugs (NSAIDs) on this bacterial translocation in patients with spondyloarthritis. Zonulin and lipopolysaccharide (LPS) have been described as good biomarkers of intestinal permeability and bacterial translocation, respectively. Adjuvant-induced arthritis (AIA) is a model of recent arthritis characterized by ossification and ankylosis in the post arthritis period. This model can be considered as a model of reactive arthritis in which our previous work has reported a clear efficacy of NSAIDs with differences between molecules at the structural

and vascular levels.To test the hypothesis that there is an increase in digestive permeability and bacterial translocation in the AIA model and to show the influence of different NSAIDs on these two parameters.

Methods: Adjuvant-induced arthritis (AIA) was induced in 6-week-old male Lewis rats by an injection at the base of the tail of Mycobacterium butyricum in incomplete Freund's adjuvant. A group of non-AIA (control) rats received saline. At the first signs of arthritis, the AIA-rats were evaluated (arthritis score 0-6) and treated daily intraperitoneally with naproxen (10 mg/kg/day), diclofenac (5mg/kg twice daily), celecoxib (3 mg/kg/day) or saline solution (AIA-vehicle group). After 21 days of treatment, the rats were sacrificed and serum levels of zonulin and LPS were evaluated by ELISA and liquid chromatography-mass spectrometry, respectively. Circulating levels of TNF-α and IL1-β were measured as well as the hind paw radiographic score.

Results: Compared to the control group, there was a significant increase in zonulin concentration ($p < 0.001$) in the AIA group. There was no significant difference in the concentration of LPS between the two groups. The levels of zonulin were correlated with the TNF-α levels (R= -0.42; p=0.032) and the arthritis score (R=0.45; p=0.013) but not with the level of IL1-β (R=; p-0.018; p=0.39). Treatment with NSAIDs significantly and equivalently decreased the arthritis score in each group. Compared to the vehicle group, treatment with naproxen significantly decreased the radiographic score ($p< 0.001$), TNF-α, IL1-β ($p < 0.01$), zonulin ($p< 0.001$) and LPS ($p < 0.05$). Celecoxib decreased radiographic score ($p < 0.001$), IL1-β ($p < 0.01$), TNF-α ($p < 0.01$) but increased zonulin levels ($p < 0.05$) without effect on LPS. Diclofenac also decreased radiographic score ($p < 0.001$), TNF-α ($p < 0.01$), and IL1-β ($p < 0.01$) but increased both zonulin ($p < 0.01$) and LPS ($p < 0.001$).

Conclusion: We have demonstrated an increase in serum zonulin levels in the AIA model and a beneficial effect of naproxen on intestinal permeability and bacterial translocation in contrast to celecoxib and diclofenac. Moreover, the plasmatic zonulin levels were correlated with TNF-α but not with IL1-β supporting a pivotal role of TNF-α on the tight junctions in this model.

Disclosure: S. Hecquet, None; **R. Bordy**, None; **C. Prati**, None; **D. Wendling**, None; **C. Demougeot**, None; **F. Verhoeven**, None.

Abstract Number: 1853

Association of Gut Dysbiosis with Radiographic and Enthesis Involvement, Disease Activity and Duration in Axial Spondyloarthritis. Data from CASTRO Registry

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The etiopathogenesis of axial spondyloarthritis (AxSpA) is multifactorial. The possible role of alteration in gut microbiome (dysbiosis) has been recently suggested. However, the association of dysbiosis with structural damage is still unknown and further studies are needed to assess its association with disease activity. Objectives: To determine the alterations in the gut microbiota in AxSpA patients. To evaluate whether changes in the gut microbiota in AxSpA patients are associated with radiographic and enthesis involvement or disease activity.

Methods: Cross-sectional study of 33 patients with AxSpA (according to ASAS criteria) and 7 sex-age matched healthy donors (HDs) was studied. Disease activity variables such as C-reactive protein and ESR were measured. The enthesis affectation was evaluated using ultrasound to obtain the Madrid Sonographic Enthesitis Index (MASEI). Gut microbiota was evaluated using the Ion Torrent S5 platform and the sequences were processed using the QIIME2 analysis platform. Chi-square and Mann-Whitney tests were used for qualitative and quantitative variables, respectively, correlations between quantitative variables were determined using the Spearman Rho test and univariate analysis with a simple linear regression. Significant differences were considered $p < 0.05$.

Results: α and β diversity data showed non-significant differences between AxSpA patients and HDs. The analysis demonstrated a significant increase in *Coprococcus comes* in AxSpA patients compared to HDs. Also, we observed

	AxSpA patients (n=33)	Healthy donors (n=7)	p
S_Coprococcus comes	0.0040 (0.0057)	0.00045 (0.00067)	0.003
F_Bacteroidaceae	0.22 (0.14)	0.36 (0.18)	0.069
F_Bifidobacteriaceae	0.015 (0.26)	0.0031 (0.0057)	0.088
G_Bacteroides	0.29 (0.17)	0.42 (0.18)	0.081
G_Bifidobacterium	0.021 (0.038)	0.0038 (0.0069)	0.075
G_Dialister	0.0048 (0.013)	0.00 (0.00)	0.063

Table 1. Microbial composition between AxSpA and HD. Values are expressed as relative abundance (sqrt/arcsin).

	Active (n=18)	Inactive (n=14)	p
F_Brucellaceae	0.00044 (0.0015)	0.0014 (0.0029)	0.037
F_Peptostreptococcaceae	0.0057 (0.011)	0.012 (0.0025)	0.002
S_Alistipes finegoldii	0.00055 (0.0011)	0.0018 (0.0025)	0.018
S_Alistiper putredins	0.015 (0.018)	0.034 (0.027)	0.034
S_Paraprevotella clara	0.00057 (0.0014)	0.0019 (0.0022)	0.034
	Radiographic (n=26)	**Non-Radiographic (n=7)**	**p**
F_Erysipelotrichaceae	0.010 (0.020)	0.00040 (0.00054)	0.048
G_Ruminococcus	0.030 (0.019)	0.017 (0.014)	0.024
S_Ruminococcus gnavus	0.013 (0.010)	0.0047 (0.0024)	0.010
	Pathological enthesis (n=7)	**Normal enthesis (n=18)**	**p**
F_Peptostreptococcaceae	0.010 (0.017)	0.0016 (0.0026)	0.025
F_Streptococcaceae	0.0060 (0.010)	0.00032 (0.00056)	0.029

Table 2. Microbial composition according to disease activity, radiographic and enthesis affectation. Values are expressed as relative abundance (sqrt/arcsin).

	Spearman Rho test		Univariate analysis	
	r	p	R^2	p
G_Roseburia	0.509	0.005	0.166	0.016
S_Roseburia faecis	0.481	0.008	0.162	0.017

Table 3. Correlation studies and univariate analysis between gut microbiota an disease duration.

that patients tend to differ from HDs in the families *Bacteroidaceae* and *Bifidobacteriaceae* and the genera *Bacteroides*, *Bifidobacterium* and *Dialister*.

AxSpA patients were divided in two groups: patients with active and patients with inactive disease. We observed that α-diversity indicator such as Shannon index was significantly decrease in patients with active disease (ASDAS >2.1). Family *Brucellaceae* was significantly decreased and family *Peptostreptococcaceae* was significantly increased in active group compared to inactive group. Moreover, species such as *Alistipes finegoldii*, *Alistiper putredins* and *Paraprevotella clara* were significantly decreased in active group.

Moreover, families *Peptostreptococcaceae* and *Streptococcaceae* were significantly increased in patients with pathological enthesis ultrasonography (MASEI >17) compared with patients with normal enthesis.

Finally, AxSpA patients were divided in other two groups: patients with a radiographic AxSpA and non-radiographic AxSpA. We observed that patients with radiographic AxSpA had an increase in family *Erysipelotrichaceae*, genus *Ruminococcus* and species *Ruminococcus gnavus versus* non-radiographic AxSpA. Further, positive correlation was observed between genus *Roseburia* and species *Roseburia faecis* with disease duration.

Conclusion: 1) AxSpA patients had a significant alteration of the gut microbiota. 2) These alterations are associated with disease activity and duration, and enthesis and radiographic involvement.

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Disclosure: I. Gómez-García, None; **I. Moreno-Indias**, None; **M. Abalos-Aguilera**, None; **C. Lopez-Medina**, None; **L. Ladehesa-Pineda**, None; **C. Aranda-Valera**, None; **C. Gutierrez-Repiso**, None; **Y. Jimenez-Gomez**, None; **N. Barbarroja**, None; **C. Lopez-Pedrera**, None; **F. Tinahones**, None; **E. Collantes-Estévez**, None; **A. Escudero-Contreras**, None; **P. Ruiz-Limon**, None.

Abstract Number: 1854

NGF/TrkA System Regulates Pain and the Pannus Formation: Targeting NGF-TrkA in Psoriatic Arthritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
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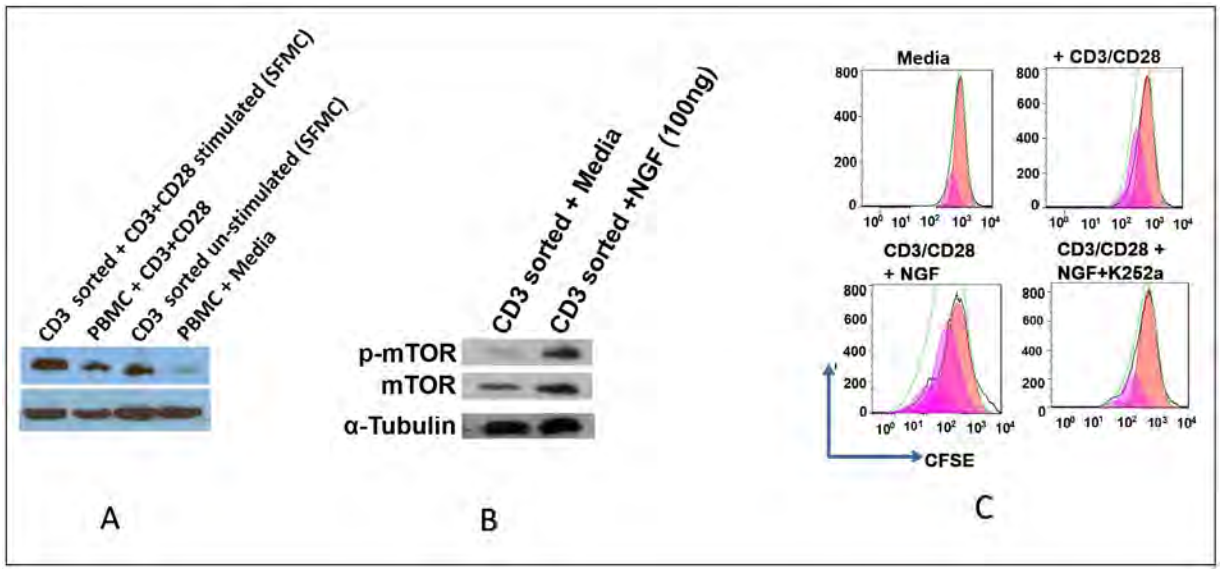

Figure 1. Here we are briefly providing our observations in the Fig 1 that in Psoriatic Arthritis (PsA) - (i) Synovial fluid (SFMC) T cells have higher levels of TrkA compared to the PBMC T cells (ii) NGF induces progrowth/survival mTOR kinase signaling in T cells (iii) NGF/TrkA regulates human T cell function such as T cell proliferation. A. Expression of TrKA on CD3/CD28 stimulated and unstimulated T cells derived from the synovial fluid (SFMC) and PBMC of a PsA patients. Western-blot assay was performed in 5 PsA patients. Expression of Trk-A was found to be significantly high in CD3/CD28 stimulated T cells ($p<0.05$) compared to the unstimulated T cells. B. NGF regulates mTOR signalling kinases in T cells: Enriched T cells from peripheral blood mononuclear cells (PBMC) were cultured in serum free media for 24hrs and then exposed to NGF (100ng/ml) for 2 hrs. Cells stimulated with NGF were found to have increased p-mTOR in comparison to the unstimulated T cells. Data was obtained from n=5 individual set of experiments and was compared at significance level p=0.05. C. NGF induces significant proliferation of T cells. CD3+ T cells were magnetically sorted from peripheral blood followed by staining with CFSE. Then cells were seeded in CD3/CD28 precoated 24 well plates with respective treatment (NGF: 100 ng/ml; K252a: 100 ng/ml) and cultured for 5 days at 370C with 5% CO2. Cells were collected and data acquired in flow cytometer followed by analysis in FlowJo software. This is a representative profile of CFSE dilution assay of CD3+ T lymphocytes from one subject (n=10). NGF (100 ng/ml) induced T cell proliferation (as shown by more generation as well as more number of cells in each generation) than CD3/CD28 stimulated alone ($p<0.01$). TrkA inhibitor, K252a (100 ng/ml) effectively inhibited the NGF induced T cell proliferation which in turn prove the relevance of NGF in T cell proliferation through its functional receptor TrkA.

Background/Purpose: Function of Nerve Growth Factor (NGF) in the nervous system and its regulatory role in pain is well defined. We have shown earlier that NGF levels are increased in synovial fluid (SF) from psoriatic arthritis (PsA) and rheumatoid arthritis (RA) patients (Raychaudhuri SP, eta al. Arthritis Rheum. 2011;63:3243-52) Here we are providing defined mechanism(s) through which NGF acts on human T cells, and provide a model which substantiates a key role of NGF in the pathogenesis of PsA

Methods: We investigated whether NGF and its high affinity receptor (TrkA) is upregulated at the disease site, the cellular source of NGF and the regulatory role of NGF in the inflammatory cascades of PsA. Untreated psoriatic arthritis (n=15) and osteoarthritis (OA, n=15) patients were recruited after proper IRB approval. PBMC/SFMC T cells and FLS were cultured as per our earlier studies (Raychaudhuri SP, eta al. Arthritis Rheum. 2011;63:3243-52; Saxena A, et al. Arthritis Rheum. 2011; 63:1465-6). We used ELISA, western blot and FACS analysis to determine NGF, TrkA and cellular phenotypes. Student t test and ANOVA were used for statistical analyses.

Results: In unstimulated T lymphocytes low level expression of TrkA was detected; whereas physiologically activated CD3+ T lymphocytes showed distinct upregulation of TrkA. SF collected from PsA was enriched with HLA-DR+CD3+ TrkA+ T lymphocytes. NGF significantly stimulated the proliferation of T lymphocytes. We have further noticed NGF induced phosphorylation of mTOR and this could be the possible mechanism for the pro-survival effect of NGF on T lymphocytes. Finally we showed that T cell activation could be inhibited by TrkA inhibitors such as K252a (Fig 1).

FLSs from patients with PsA produced significantly higher levels (< .001) of NGF (200±22 pg/ml) compared to FLS of patients with OA (42±15 pg/ml). Furthermore, we observed that NGF significantly stimulated the proliferation of FLS derived from PsA synovial tissue

Conclusion: Our observations suggest: (i) NGF is produced by FLS at the disease site in PsA (ii) NGF acts as a T cell growth factor, promotes survival of the pathologic effector T cells and thus, help to escape them from peripheral immuno-tolerance mechanisms. We show here enrichment of TrkA+ activated memory T cells in PsA and, we identified synovial cells (FLS) as the prime source for NGF. We propose that NGF as a T cell growth factor promotes survival of the pathologic effector T cells, contributes in sustaining the chronic inflammatory cascades of autoimmune diseases; and NGF/TrkA targeted therapies as a novel approach for PsA.

Disclosure: S. Raychaudhuri, None; **S. Raychaudhuri**, None.

Abstract Number: 1855

Elevated Calprotectin Levels Reveal Loss of Vascular Pattern and Atrophy of Villi in Ileum Using Digital Chromo-endoscopy and Magnification Colonoscopy in Patients with Spondyloarthritis Without Inflammatory Bowel Disease

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SESSION INFORMATION
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Background/Purpose: Fecal calprotectin (FC) is a well bio-marker related to mucosal inflammation. Digital chromo-endoscopy (DCE) with magnification is a technique to identify microscopic inflammation. The objective of the study is to establish the association between FC levels and DCE/histology for the detection of early bowel lesions related to structural inflammatory changes in patients with SpA without IBD (inflammatory bowel disease)

Methods: In total, 180 patients with SpA fulfilling ASAS classification criteria were assessed by rheumatologist. Of them, 42.2% met the selection criteria and 48.7 % had an indication by a gastroenterologist to perform DCE for co-

lon e ileum plus histological analysis. FC, CRP, and HLA-B*27 were performed. The association between FC levels and CDE/histological and clinical parameters were evaluated using Chi-square or Fisher's exact test with multivariate evaluation by principal components analysis (PCA)

Results: The average age of the patients included for DCE was 45,1±10.3 years, 56.8% were men, 40.9% were HLA-B*27:05 positive and 89.2% had axial involvement and 91.9% inflammatory back pain. Positive levels of FC (PFC >120ng/mL) and high levels (HFC) >250ng/Ml, were observed in 27% and 16% respectively. BASDAI >4 was found in 54.1% of patients and ASDAS-PCR >2.1 in 78.4%. High levels of PFC were associated with BASFI >4 (p = 0.036), BASDAI >4 (p = 0.047). More than 70% of these patients a loss of the vascular pattern in the ileum (LVPI) was observed (p = 0.005). Moreover, 77% of the patients having PFC with abdominal bloating, simultaneously had LVPI (p = 0.020) in addition to villous atrophy and microscopic inflammation in 66.7% (p = 0.012). In those patient having PFC plus abdominal pain the presence of LVPI was observed in 75% (p= 0.007). The HFC associated with alterations at the level of the ileum mucosa (p= 0.009), with LVPI (p= 0.001). At microscopic analysis, the HFC levels were associated with inflammation (p= 0.046) and a chronic pattern (p = 0.014) in 83.3%. Overall, 27.3% of patients had HFC and diarrhea, associated with LVPI and presence of erosions in ileum (p=0.026) and (p=0.031), respectively. Microscopically, ileum chronic inflammation was observed in 25% (p=0.037). All patients having increased HFC levels and ASDAS-CRP >2.1,the following findings were observed: alteration of ileum mucosa (p = 0.09), request for vascular pattern (p = 0.001) and villous atrophy reflected microscopically as a chronic pattern (p=0.014) in 66.7%. The PCA with Kaiser normalization of 0.642 and Bartlett test (p=0.0001), showed three factors:1) Micro and macroscopic changes of chronic inflammation and HFC (CC = 0.837, 2),increased CRP and microscopic acute inflammation (CC = 0.792) and 3) clinical activity scores ASDAS-PCR and BASDAI (CC = 0.914)

Conclusion: FC levels were significantly higher in patients with SpA group in which CDE showed LVPI as main finding with associations with disease activity score.FC levels may be used to guide patient management in SpA and further investigation is required. The presence of villi atrophy may suggest a shared immune pathway related to chronic damage in the intestinal tissue when the joint manifestations are active

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Abstract Number: 1856

Abnormal DNA Methylation in CD4$^+$T Cells Is Associated with Cardiovascular Risk in Psoriatic Arthritis

Iván Arias de la Rosa[1], Maria Dolores Lopez-Montilla[2], Carlos Pérez-Sánchez[1], Javier Rodriguez-Ubreva[3], Esteban Ballestar[3], Carmen Torres-Granados[1], María-Carmen Abalos-Aguilera[1], Ignacio Gómez-García[1], Alejandra Maria Patiño-Trives[1], Maria Luque-Tevar[1], Eduardo Collantes-Estévez[4], Chary Lopez-Pedrera[5], Alejandro Escudero-Contreras[4], Clementina Lopez-Medina[6] and **Nuria Barbarroja**[1], [1]Rheumatology Department, Reina Sofia University Hospital/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba, Cordoba, Spain, Cordoba, Spain, [2]IMIBIC/University of Cordoba/Reina Sofia Hospital, Cordoba, Spain, [3]Josep Carreras Institute (IJC), Badalona, Spain, [4]Rheumatology Department, Reina Sofia University Hospital/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba, Cordoba, Spain, Córdoba, Spain, [5]IMIBIC/Reina Sofia Hospital/University of Cordoba, Cordoba, Spain, [6]Rheumatology Department, Cochin Hospital, Paris, Paris, France

SESSION INFORMATION
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Background/Purpose: Cardiovascular risk factors are increased in Psoriatic Arthritis (PsA). Latest studies suggested that inflammatory and metabolic disorders may be under epigenetic control, including DNA methylation. DNA methylation is an unexplored area in the field of PsA.

Objective: To study the alterations in the genome-wide DNA methylation profile of CD4+T cells from PsA patients and its relationship with its pathology and the risk of cardiovascular comorbidity.

Methods: Twenty healthy controls (HC) and 20 PsA patients were included in the study. PsA patients were classified into insulin resistant and non-insulin resistant according to HOMA-IR index. CD4+ T lymphocytes were isolated from peripheral blood by positive immunomagnetic selection. The Illumina Infinium MethylationEPIC Beadchip was used to obtain DNA methylation profiles across approximately 850,000 CpGs (TSS1500, TSS200, 5UTR, 3UTR, first exon, gene body). Beta values (β) estimating methylation levels were obtained at each CpG site, and differentially methylated genes (DMG) between PsA and HC were identified. Functional classification of these genes was carried out through gene ontology analysis (PANTHER database). Gene expression analysis of the selected genes was also evaluated by RT-PCR. Vascular parameters including carotid intima-media thickness (cIMT) and endothelial function was analyzed by ecodoppler and periflux respectively.

Results: The genome-wide methylation analysis identified 112 DMGs including 41 hypomethylated and 71 hypermethylated. These differentially methylated genes were enriched with several signaling pathways and disease categories including immune response, metabolic processes, oxidative stress, vascular and inflammatory pathways. The altered gene expression of selected genes with altered methylation levels in PsA was also validated. Correlation and association analysis of these DMGs with clinical and analytical variables, cardiovascular risk factors and endothelial microvascular function revealed that the degree of methylation of these genes was significantly associated with cIMT (IGF1R, NDRG3, SMYD3, HLA-DRB1, WDR70), arterial pressure (METT5D1, NRDG3, ADAM17, SMYD3, WNK1, CBX1), insulin resistance (AKAP13, SEMA6D, PLCB1), altered lipid profile and atherogenic index (MYBL1, METT5D1, MAN2A1, SLC1A7, SEMA6D, PLCB1, TLK1, SDK1, CBX1), inflammation (MYBL1, NDUFA5, METT5D1, SEMA6D, PLCB1, TLK1), and endothelial dysfunction (ADAMST10, GPCPD1,

CCDC88A). In addition, this analysis also identified 435 DMGs including 280 hypomethylated and 155 hypermethylated in CD4+ T cells from IR-PsA vs non IR-PsA patients. Between these two groups of PsA patients, CHUK, SERINC1, RUNX1, TTYH2, TXNDC11, FAF1, BICD1, SCD5, PDE5A, FAS, NFIA and GRP75 displayed the most significantly altered methylation, suggesting the role of these genes in the metabolic complications associated with PsA.

Conclusion: These findings help our understanding of the pathogenesis of PsA and advance epigenetic studies in regards to this disease and the cardiometabolic comorbidities associated. Funded by ISCIII (PI17/01316 and RIER RD16/0012/0015) co-funded with FEDER and FAR.

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Abstract Number: 1857

KIR3DL2 Is Not Overexpressed on CD4+ T Cells and NK Cells in Patients with Axial Spondyloarthritis csDMARD and bDMARD Naive

Guillaume Larid[1], Sophie Trijau[1], Clothilde Barral[1], Pierre Lafforgue[1] and Thao Pham[2], [1]Aix Marseille Univ, APHM, Rheumatology department, Marseille, France, [2]Aix Marseille Univ, APHM, department of rheumatology, Marseille, France

SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Overexpression of KIR3DL2 on CD4+ T-cells and NK-cells has been reported in patients with ankylosing spondylitis (AS) HLAB27+. We aimed to 1) analyse KIR3DL2 expression in patients with active axial spondyloarthritis, radiographic (AS) and non radiographic (nr-axSpA), HLA B27+ and HLA B27 – and 2) to assess the impact of pharmacological stimulation on CD4+ T-cells of those patients.

Methods: We analysed by flow cytometry whole blood and PBMC samples from those patients using fluorescent antibodies against CD45, CD14, CD3, CD19, CD4, CD8, TCR GD, CD56, CD16, CD45RA, CXCR3, CCR6, KIR3DL1, KIR3DL2, IL17A, IL22, IL2, and IFN g. Positivity thresholds were set using control isotypes. Overnight pharmacological stimulation was performed with PMA/Ionomycin. All statistical analyses were performed using Graph Pad Prism

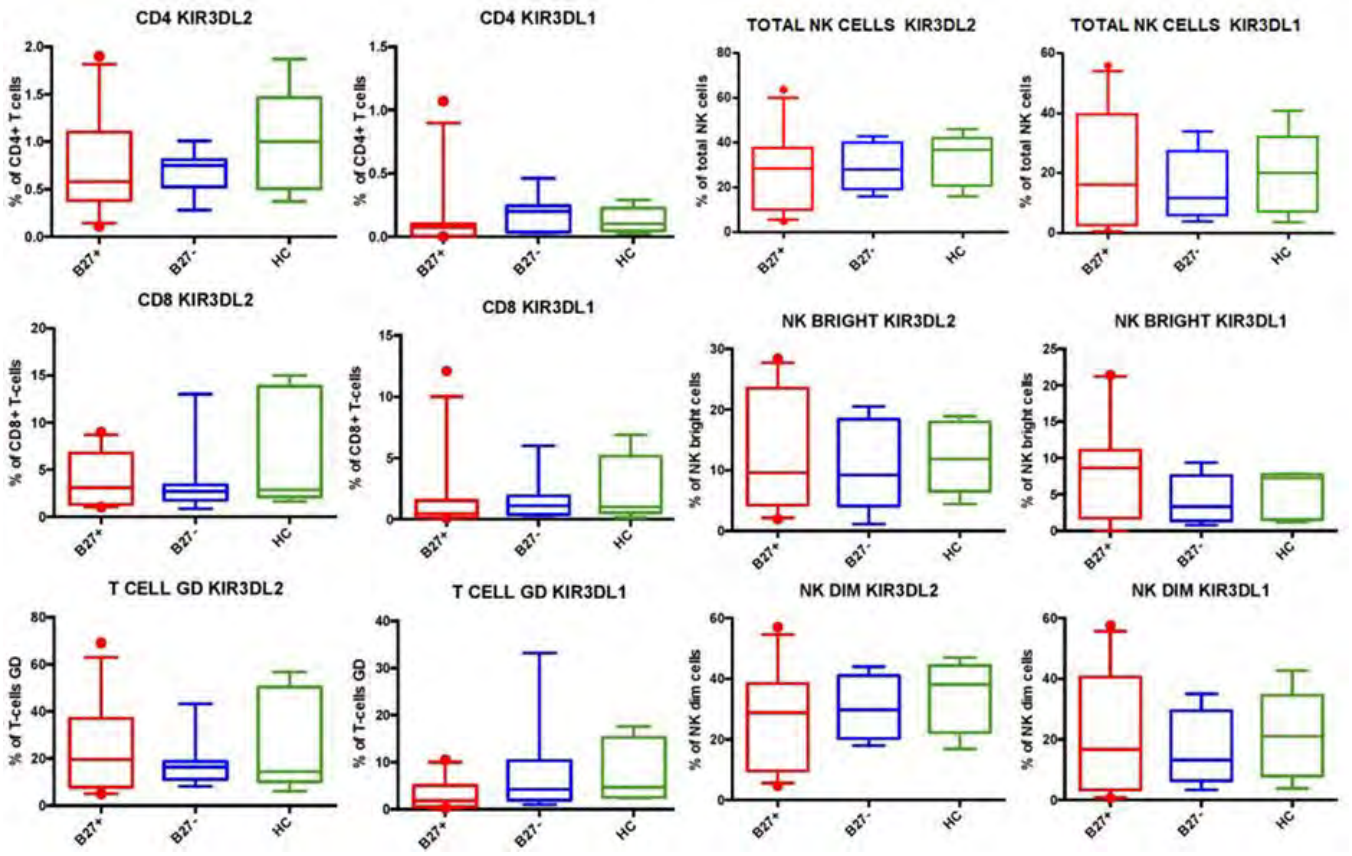

Figure 1. Expression of KIR3DL1 and KIR3DL2 on T-cells and NK cells.

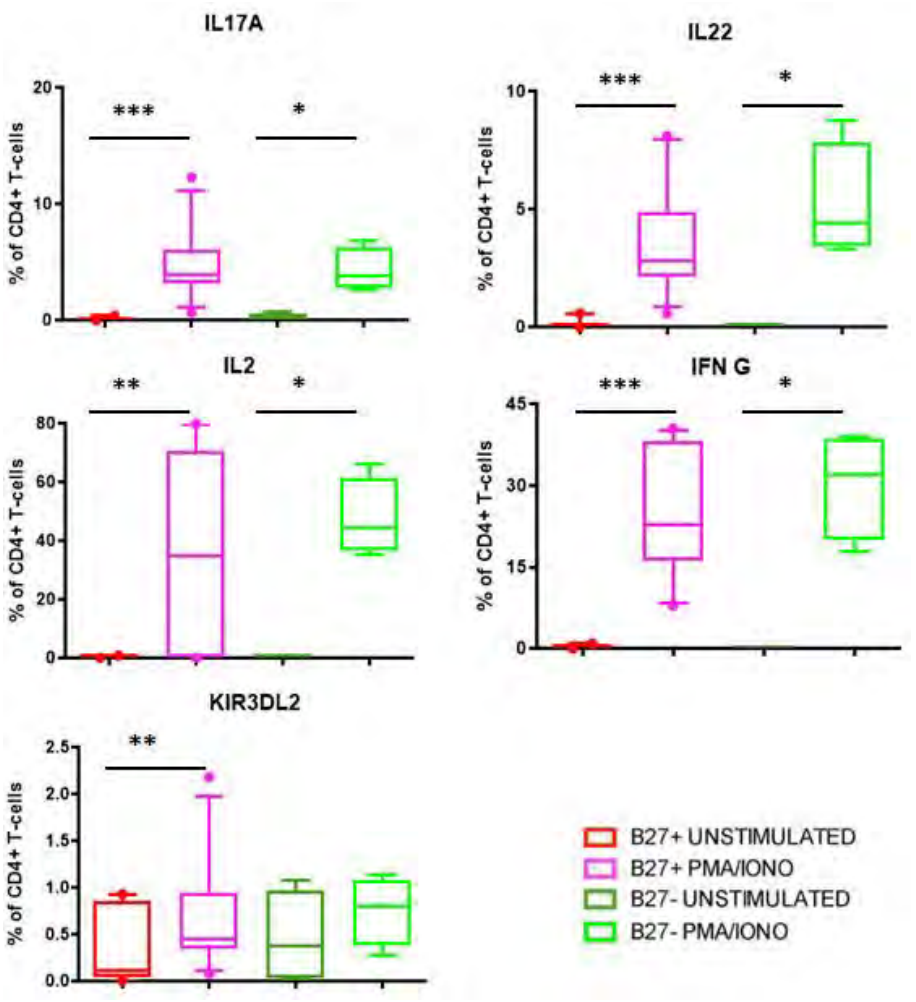

Figure 2. Cytokine production and KIR3DL2 expression on CD4+ T-cells upon PMA/Ionomycin stimulation

(GraphPad Software, San Diego, CA). Paired data were analysed with Wilcoxon test, and unpaired data with Mann Whitney test. P values < 0.05 were considered to be significant.

Results: We included 16 AS, 4 nr-axSpA patients, all fulfilling the 2009 ASAS criteria and 5 healthy controls. Their main characteristics were: 11 HLA B27+, 9 HLA B27-, 14 males, mean disease duration of 15.23 years, mean BASDAI of 4.56/10, all csDMARD and bDMARD naive. Analysis of CD4+ T-cells and NK cells of our patients shows similar expression of KIR3DL2 both in HLA B27+, HLA B27- patients and healthy controls (Fig. 1). PMA/Ionomycin stimulation induced a significant increase of IL17A, IL22, IL2, and IFN gamma in CD4+ T cells of both HLA B27+ ($p< 0.001$, $p< 0.001$, $p< 0.01$, and $p< 0.001$ respectively) and HLA B27- patients ($p < 0.05$ for all) as well as an increased KIR3DL2 expression in both groups but only significant in the HLA B27+ one ($p < 0.01$) (Fig. 2). Concerning KIR3DL2+ CD4+ T-cells (Fig. 3A), significantly increased production of IL17A was observed in HLA B27+ patients ($p < 0.01$), while increase of IL2 and IL22 production was observed in both HLA B27+ ($p < 0.01$) and HLA B27- group ($p < 0.05$). Concerning activated CD4+ Th17 cells (Fig. 3B), significantly increased production of IL17A, IL2, and IFN gamma was observed in both HLA B27+ ($p< 0.001$, $p< 0.01$, and $p< 0.001$ respectively) and HLA B27- patients ($p < 0.05$ for all) as well as significantly increased production of IL22 in the HLA B27+ one only ($p < 0.001$). No significant overexpression of KIR3DL2 was observed in this cell subtype after stimulation. Furthermore, no statistically significant difference between HLAB27+ and HLAB27- patients was observed for all previously cited analysis, as well as between AS and nr-axSpA patients.

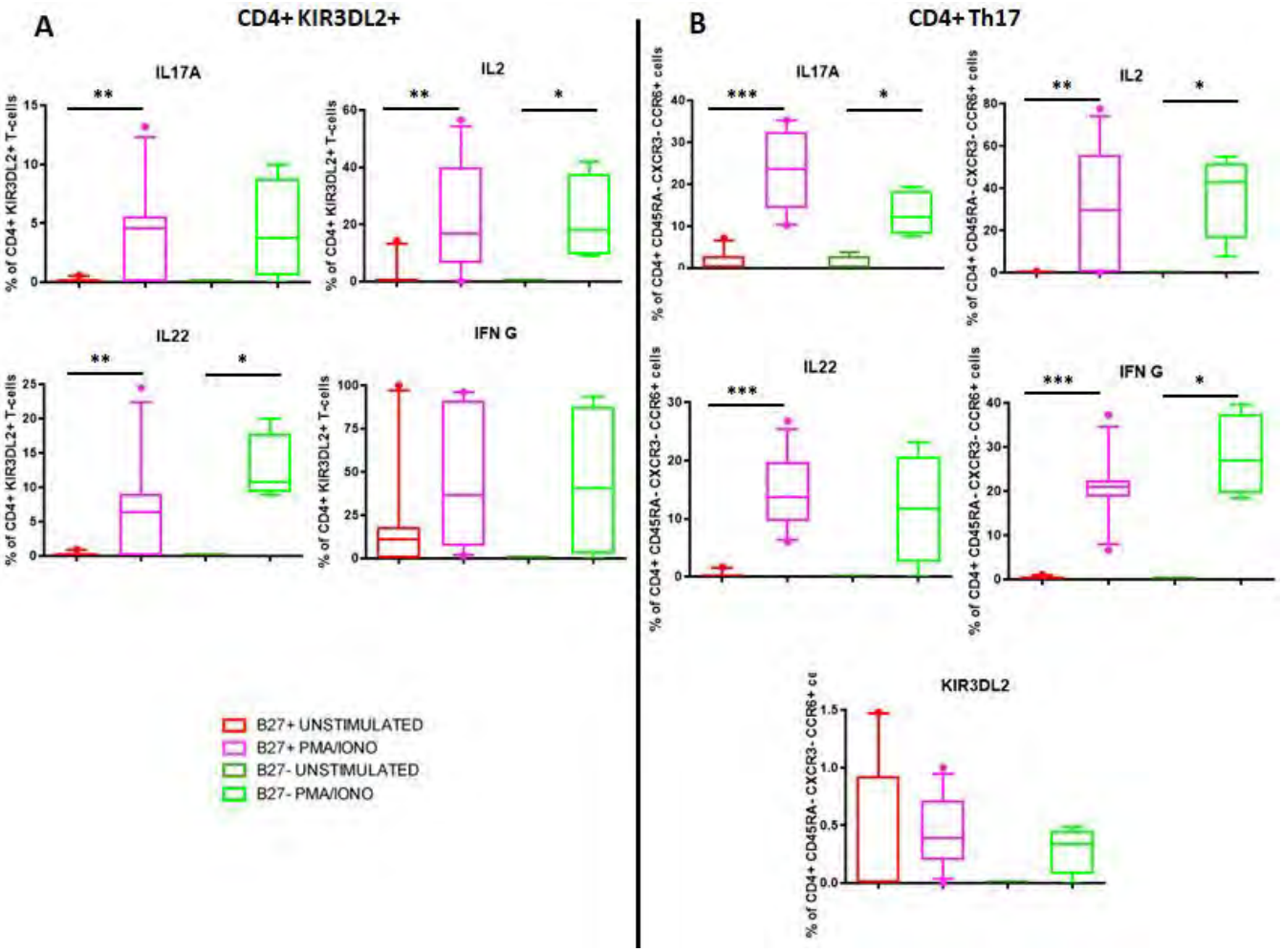

Figure 3. A. Cytokine production by KIR3DL2+ CD4+ T-cells upon PMA/Ionomycin stimulation B. Cytokine production and KIR3DL2 expression on Th17 CD4+ T-cells upon PMA/Ionomycin stimulation

Conclusion: No overexpression of KIR3DL2 on CD4+ T-cells and NK cells was observed in patients with active axial spondyloarthritis whatever their phenotype (AS vs nr-axSpA) and their HLA B27 status.

Disclosure: G. Larid, None; **S. Trijau**, UCB, 5, BMS, 5, Abbvie, 5, Amgen, 5, MSD, 5; **C. Barral**, None; **P. Lafforgue**, Chugai, 5, Amgen, 5, BMS, 5, Lilly, 5, Abbvie, 5, Pfizer, 5, Biogaran, 5, Mylan, 5, UCB, 5, MSD, 5, Expanscience, 5; **T. Pham**, Abbvie, 5, Amgen, 5, Biogen, 5, BMS, 5, Celgene, 5, Fresenius-Kabi, 5, Janssen, 5, Lilly, 5, Medac, 5, MSD, 5, Novartis, 5, Pfizer, 5, Roche-Chugai, 5, Sandoz, 5, Sanofi, 5, UCB, 5.

Abstract Number: 1858

Increased Proportion of TH17, TH22 and TC17 Cells and the Correlation to IL-22 and Clinical Parameters in Patients with Ankylosing Spondylitis from Northern Sweden

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SESSION INFORMATION
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Background/Purpose: Increased levels of TH17 and TH22 as well as TC17 and TC22 cells have previously been associated with ankylosing spondylitis (AS). The correlation between these inflammatory T cell subsets and clinically relevant parameters as well as cytokines has also been reported. However, the status of these inflammatory cells in a well characterized AS cohort from northern Sweden has not been studied. The purpose of this study was to confirm the increased presence of inflammatory T cell subsets in peripheral blood of patients with AS from northern Sweden in relation to age and sex-matched controls. In addition, associations of clinically relevant parameters with the level of the inflammatory T cell subset(s) and cytokines of interest were performed.

Methods: Peripheral blood mononuclear cells (PBMCs) from a cohort of 50 patients with AS from Region Västerbotten (Modif NY, mean age 52±9.1 years, 33 (66 %) men, 50 (100 %) HLAB27) and 50 pair wise matched blood donor controls (mean age 54±8.8 years, 33 (66 %) men) were stained with a combination of antibodies allowing for the detection of surface expressed CD45, CD3, CD4, CD8, intracellular IL-17 and IL-22 and analyzed by flow cytometry. In addition, levels of IL-17 and IL-22 in plasma were determined by the Meso Scale Discovery platform. The patient with AS were examined with spinal x-ray for radiographic alterations assessed with mSASSS. CRP and ESR were measured and physical function and disease activity were registered with BASMI and BASFI respectively ASDAS-CRP and BASDAI.

Results: Pair wise comparison of AS patients and controls showed a 1,5 to 2-fold increase of TH17, TH22 and TC22 cells among CD45+CD3+ lymphocytes in PBMCs of male patients (p=0,013, p=0,003 and p=0,024 respectively). Levels of IL-22 in plasma and proportion of TC17 correlated in male patients (R_s=0,499 p=0,003) and plasma levels of IL10 showed an inverse correlation in relation to TC17 in all patients (R_s=-0,276 p=0,05). In female AS patients there was a negative correlation between TC22 and CRP (R_s = -0,573, p=0,016). In addition, after splitting the group of female into pre- and postmenopausal correlation between TC17 and mSASSS (R_s = 0,845, p=0,034), TC22 and BASFI (R_s = 0,986, p=0,0003) (premenopausal) and TC22 and BASMI (R_s = 0,764, p=0,006) (postmenopausal) was observed.

Conclusion: We confirm an increased proportion of TH17, TH22 and TC17 cells in blood in AS male patients from northern Sweden. In addition, positive correlation of the proinflammatory cytokine IL-22 and negative correlation of anti-inflammatory cytokine IL-10 in relation to TC17 corroborate the influence of these cells in the disease process. Interestingly, in female AS patients there was a correlation between clinical relevant parameters to particular inflammatory T cell subset dependent on the menopausal status, suggesting a role of female sex hormones in AS pathogenesis.

Disclosure: K. Lejon, None; **U. Hellman**, None; **L. Do**, None; **A. Kumar**, None; **H. Forsblad-d'Elia**, None.

Abstract Number: 1859

Curdlan-induced Villous Permeability, Luminal Pathobiont Translocation to the Ileal Crypts, Ileitis and Arthritis Are Mitigated by Clostridia in Colonised Germ-free SKG Mice

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Background/Purpose: IL-23 dependent spondylitis, arthritis and inflammatory bowel disease (IBD) recapitulate human spondyloarthropathy (SpA) in 1,3 beta glucan (curdlan)-treated SKG mice. Human SpA and SKG mice have fecal dysbiosis, with increased *Bacteroidaceae* and *Porphyromonadaceae*. In SKG mice, anti-IL-23 supports homeostatic bacteria, including *Clostridiaceae*, which produce the short chain fatty acid (SCFA) butyrate. Similarly, the butyrate-producing Clostridium *F. prausnitzii* is beneficial in IBD. To study how pathobionts and commensals impact SpA, we colonised Germ-Free (GF) SKG mice with a single pathobiont or a mix of pathobionts and commensals.

Methods: GF SKG mice were gavaged with *Parabacteroides* sp., *Lactobacillus murinus*, or altered Schaedler flora (ASF), comprising Parabacteroides, *L. murinus*, *Mucispirullum* and *Clostridium* spp. for 4 weeks, then given i.p. curdlan. Some groups received anti-IL-23p19 or isotype before curdlan. *Parabacteroides*-colonised SKG mice received sodium butyrate in the drinking water, or were gavaged with *F. prausnitzii* for 4 weeks. Ileal cytokines were measured by Q-PCR, bacterial translocation was analysed in ileal sections by FISH, and goblet cells were enumerated after Alcian blue staining. Ileitis and arthritis were monitored by weight loss, visual and histological scoring.

Results: SKG mice monolonised with either *Parabacteroides*, *L. murinus*, or both bacteria, but not GF mice, developed IL-23-dependent ileitis and arthritis within 5 weeks of curdlan. At week 1 post curdlan, expression of *Il23a*, *Grp78* and *sXbp1* (ER stress genes), antimicrobial peptide *Reg3b* and *Reg3a* mRNA (released by Paneth cells) was significantly increased and goblet cells decreased in the ileum of SKG mice colonised with either *Parabacteroides* or *L. murinus*, relative to GF SKG, or colonised BALB/c ileum. Concomitantly, within 1 week of curdlan, *Parabacteroides* or *L. murinus* translocated from the ileal lumen to the crypts. In contrast, SKG mice colonised with ASF, containing *Clostridia*, were protected from ileitis. SKG mice receiving sodium butyrate in the drinking water or gavaged with *F. prausnitzii* developed less weight loss and arthritis, with reduced ileal disruption.

Conclusion: *Lactobacillus* or *Parabacteroides* monocolonisation is sufficient for IL-23-dependent arthritis and ileitis progression after curdlan-mediated systemic inflammation. Pathobiont colonisation is required for curdlan to trigger ER stress, IL-23, goblet cell loss and villous permeability, permitting luminal bacterial translocation to the lamina propria. Supplementation with *Clostridia* or sodium butyrate reduces the ileal damage caused by pathobionts and mitigates arthritis severity.

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Abstract Number: 1860

An Integrative Approach to Identify Heritable and De Novo Genomic Variations in Psoriatic Arthritis Mutilans and Understand Its Systems Biology

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Basic Science Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Psoriasis is a chronic autoimmune skin disease that burdens ~3% of North Americans. ~24% of psoriatic patients develop psoriasis arthritis (PsA), an inflammatory disease which is often progressive and in its extreme form, PsA mutilans, causes permanent joint damage and functional disability. PsA is highly heritable; ~40% of patients with PsA have at least one close relative with psoriasis or PsA. Characterizing heritable and de novo genomic variations and cellular processes behind extreme cases of PsA is a promising approach for understanding molecular mechanisms behind PsA and identifying patients at high-risk of PsA mutilans early.

Methods: We conducted Whole Exome Sequences (WES) of 7 trios with PsA mutilans trios (probands with PsA satisfying CASPAR criteria and with arthritis mutilans and their parents), using NovSeq 6000 (Illumina) at depth 100X. We developed a bioinformatics pipeline to identify genes and pathways involved in PsA mutilans with three modules: 1) characterization of genetic variants using WES of PsA mutilans trios; 2) their integration using network-based methods to highlight pathways relevant to identified variants; 3) network analysis to identify genes and pathways to cellular mechanisms involved in PsA mutilans.

We used three available algorithms for detection of genomic variations. To discover systems level dependencies among genes and proteins to perform cellular tasks we integrated these variations with physical protein interaction networks. Next, we applied a graph-mining technique to detect network modules and several novel genes involved in PsA mutilans. Finally, we performed pathway enrichment analysis and characterized several statistically significant pathways involved in PsA mutilans.

Results: We found a subnetwork of 44 proteins [Figure 1A-B] having physical interactions with protein products of the genes identified by three variation detection methods [Table 1] suggesting implication of these 44 genes in triggered pathways in PsA mutilans. Pathway enrichment analysis highlighted WNT, NOTCH, NOTCH1, Adherens, Autophagy, and Apoptosis, suggesting their disruption in PsA mutilans [Figure 1C]. These pathways have been previously studied in psoriasis, PsA, and autoimmunity supporting relevance of identified genes and pathways to PsA mutilans. *NTRK1* has the highest rank in the identified subnetwork. NTRK1, its interaction with NGF, and its mutations have previously been linked to autoimmune diseases, inflammatory arthritis, and psoriasis, and some groups are working on developing novel NGF/NTRK1-targeted therapies for these diseases. EED is another highly ranked gene in our list. Mutations in EED have been reported in several cases of over-growth disorders such as Cohen-Gibson and Weaver Syndromes.

Method	Gene set
Varscan	*ABHD5, ALOXE3, CDC27, GOLGA3, MSH3, PDE4D, PLXNA2, RBM14, RXFP4, SHARPIN, TTC28, ZNF492*
Tridenovo	*DSPP, FAM30A, GGTLC2, IFRD1, IRF2BPL, KRT6C, KRTAP10-4, KRTAP9-4, LINC01225, LSS, MUC20, MUC4, NAV2, PKD1L2. SFTPD, TBX19*
DNAcopy	*CDSN, GHR, KRT77, OR2T11, OR2T10, CFHR1, CFHR3, RHD, CHAC1, GBP3, OR52N5, COL11A2, OR52N5, GBP3, LILRA3, CYB561D1, SPAG11B, C18orf56, PRDX4, SPAG11B, MRGPRX1, TBCK, PPIG, PSMA8, ZNF43, KPNA4, C9orf24, JAK2, SYCP2, SYCP1, PGAP1, TTK, ZNF638, SYCP1, CENPE, ADAM2, PROS1, STX19, GNGT1, BET1, CXorf59, HECTD2, USP25, STAG2, LIPF, RIF1, TBK1*

Table 1. List of genes with variants based on different methods.

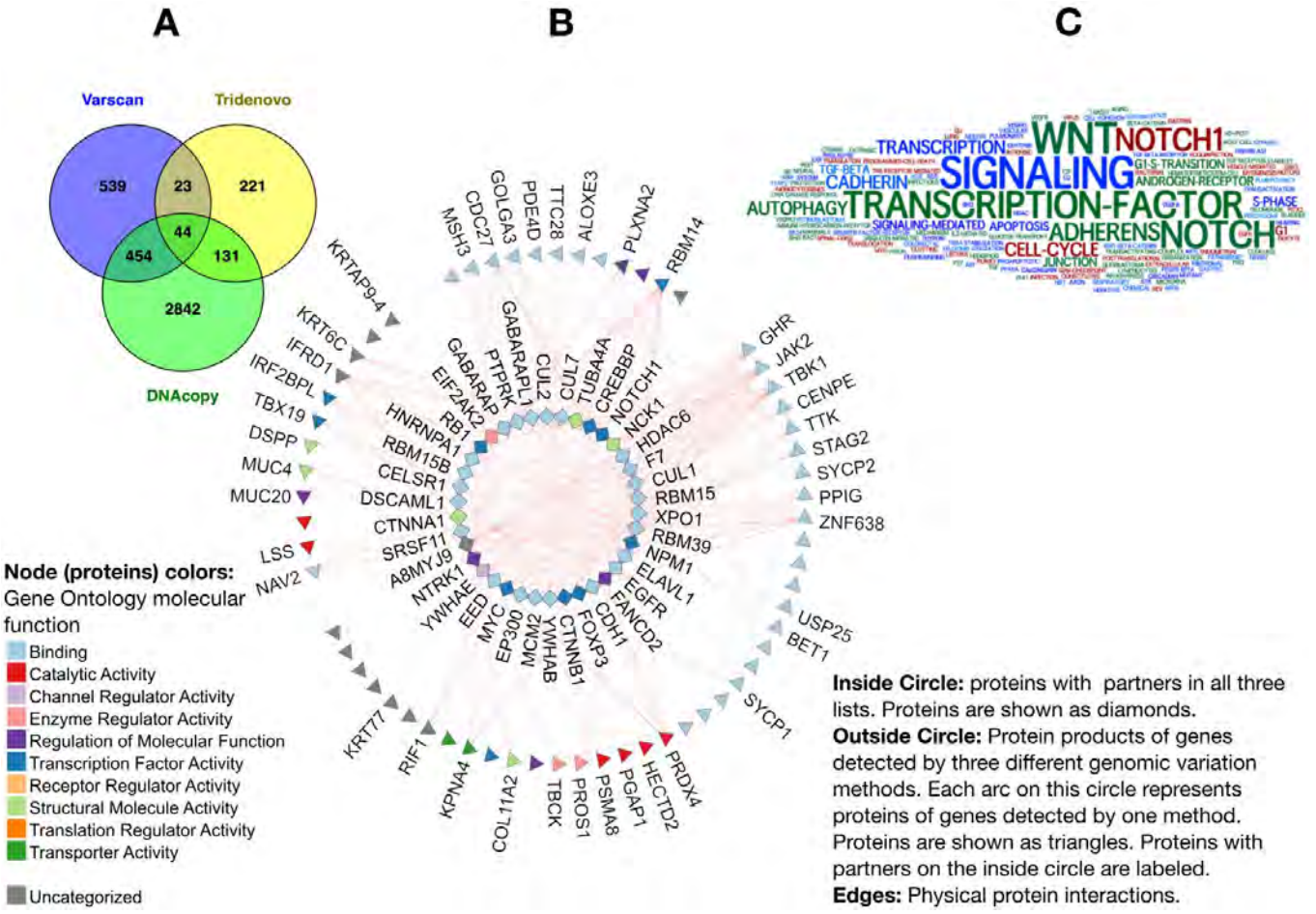

Figure 1 A. Venn diagram summarizing overlapping protein partners of genes detected through different methods (listed in Table 1). B. Protein interaction network of genes in the three lists. For details see legend. C. Results of pathways and term enrichment analysis of the 44 genes in the center of Venn diagram (ordered on the central circle in the network).

Its interaction with EZH2 (present in the list- not shown in Figure 1) has been reported to be important in psoriasis. EED mediates repression of gene activity through histone modifications.

Conclusion: Detecting heritable and de novo genomic variations by WES of PsA mutilans trios and application of network analysis has identified novel genes and pathways associated with PsA mutilans.

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Abstract Number: 1861

T Cells with IL-17A+ Signature in Psoriatic Arthritis Are of Different Subpopulations and Are Polyfuntional

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SESSION INFORMATION
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Background/Purpose: A variety of T cells such as Th1, Th2, Th9, Th17, NKT, MAIT, etc have been attributed to multiple autoimmune diseases. In psoriatic arthritis (PsA) contributing role of the Th17 cells have been observed and lately success of IL17/IL-23 targeted therapies has further substantiated this. Here we will share our cumulative data on Th17 cells in PsA collected over last 2 decades.

Methods: PBMCs and synovial fluid mononuclear cells (SFMCs) were collected from age/sex matched with active untreated PsA, rheumatoid arthritis (RA) and osteoarthritis patients (OA, n=50, each). Patients were recruited after proper IRB approval. Magnetically sorted $CD3^+$ T cells were isolated from PBMCs and SFMCs; were activated (10^6 cells/ml) with anti-human CD3/CD28 antibody cocktail and cultured in RPMI medium for 5 days. Hi-D FACS studies were performed; lymphocytes were gated first based on FSC and SSC, then $CD3^+CD11a^+CD45RO^+17A^+$ cells were gated. In these gated population MAIT cells were identified as $CD3^+CD161^+V\alpha7.2TCR^+$ cells, γδ-T cells as $CD3^+$ $\gamma\delta TCR^+$, NKT cells as $CD3^+CD161^+$ and αβ-T cells as $\alpha\beta TCR^+$. NKT cells ($CD3^+CD161^+$) were further gated for *TCR* Vα24-Jα18 (iNKT cell) ab positivity.

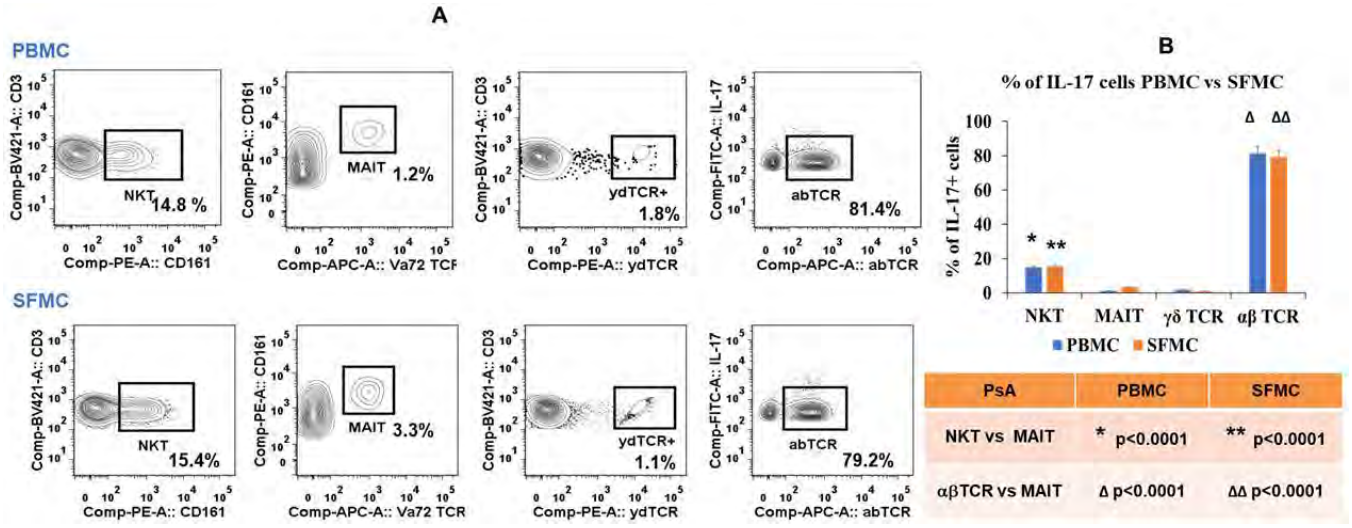

Figure 1. IL-17A+ cells in peripheral blood and synovial fluid of PsA patients. Peripheral blood mononuclear cells (PBMC) and synovial fluid mononuclear cells (SFMC) were isolated from PsA (n=15) and stimulated with with anti-human CD3/CD28 antibody cocktail. Lymphocytes were gated first based on FSC and SSC, then CD3+CD11a+CD45RO+17A+ T cells were gated. **αβ** TCR+, **γδ** TCR+ T cells, iNKT and MAIT cells were identified in these gated CD3+CD11a+CD45RO+17A+. (A) Representative FACS plots showing the frequencies of different IL-17A+ immune cells in PsA. (B) Bar diagram (n=15) showing the frequencies of IL-17A producing **αβ**, NKT, **γδ** T cells and MAIT cells in PBMC and SFMC of PsA patients.

Results: In OA activated Effector Memory T Cells (TEM cells) were < 1%. We noticed a marked polyfunctionality in PBMC/SFMC T cells both in PsA and RA. In PsA SFMC, memory T cells (CD3+CD4+CD45RO+) had IL-17A+ (18±0.5%), IL-22+(7±0.3%) and IL-23R+ (8.5±0.5%) T cells compared to SFMC memory T cells of RA (6.8±0.3%, 2.5±0.5%, 2.1±0.7%, respectively; p< 0.001). TEM cells in PsA and RA at single cell level also produced IL-9 and TNF-α.

IL-17A$^+$ TEM phenotypes in SFMC of PsA demonstrated both invariant and conventional αβT cell Immune response (Fig 1): αβTCR$^+$ (79.8±0.9%), γδ TCR$^+$ (1.5±0.2%), iNKT (15.5±1.1%) and MAIT (4.5±0.8%) cells. Majority of the αβTCR$^+$ T cells were CD4+ (>85%) whereas MAIT were predominantly CD8$^+$ (~ 90%).

Conclusion: In PsA TEM cells were polyfunctional in respect to their cytokines (IL-9, IL-17A,IL-22, TNF-α) however more skewed towards conventional activated memory αβTh17 cells. Our finding clearly suggests that TEM cells of adaptive as well as innate immune response produce IL-17A in PsA, but the major amount of IL-17A comes from the conventional CD4$^+$ (αβTCR$^+$) cells (~80%). The fact that synovial T cells of innate immune response also express IL-17A (~20%), suggest a bridge between adaptive and innate immune response.

Disclosure: S. Raychaudhuri, AbbVie, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sun Pharmaceutical Industries, Inc., 2, Amgen, 5, Eli Lilly, 5; **S. Raychaudhuri**, None.

Abstract Number: 1862

Genetic Influences on Occurrence of Axial Spondyloarthritis (axSpA) in First-degree Relatives During a Prospective Study Lasting 35 Years

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate the recurrence rate (RR) of ankylosing spondylitis (AS) over a lifespan, probands with clinically diagnosed AS and their first-degree relatives (FDRs) were studied in a Swiss cohort during 35 years of follow-up.

Methods: In 1985 members of the Swiss AS Patient Society who had been diagnosed as having AS by their own physicians, as well as their FDRs, were invited to participate in the current study. After obtaining ethical approval and informed consent, 363 probands and 715 first-degree relatives were recruited to the study. Participants completed questionnaires on disease manifestations, underwent rheumatological examination of axial and peripheral joints, and were genotyped for HLA-B27. 360 probands and all 713 relatives aged ≥ 18 year underwent pelvic radiography unless pregnant, which were then scored according to the modified New York AS (mNYAS) criteria. Participants with a

clinical diagnosis of AS with or without radiographic evidence of disease were deemed to have 'axial spondyloarthritis' (axSpA), those meeting the mNYAS criteria were said to have AS, and those with a clinical diagnosis of AS but not meeting the mNYAS criteria nr-axSpA. Following further ethics review and approval, a follow-up study was performed in 2019. A total of 462 surviving consenting original participants completed a 157 item disease related questionnaire, with diagnosis of AS determined by self-report. RR of axSpA amongst siblings and children of probands were analysed.

Results: The overall RR for FDRs was 41/411 (10%), the parent-child RR being 24/193 (12.4%) and sibling RR 17/218 (7.8%). Considering FDRs of mNYAS probands, the RR was even higher (41/351, 11.7%), with the parent-child RR being 24/154 (15.6%) and sibling RR 17/197 (8.6%). Amongst FDRs of probands with nr-axSpA, lower RRs were observed: overall FDR RR was 6/98 (6.1%), parent-child RR 2/39 (5.1%), sibling RR 4/59 (6.8%). AS occurred in only one HLA-B27(-) relative, with nr-axSpA, and no case of HLA-B27(-) mNYAS was observed amongst FDRs. Considering HLA-B27(+) FDRs of mNYAS probands, the RR was very high (overall 41/288, 14.2%; mNYAS probands 24/142, 16.9%). Mother-child RR was substantially higher than father-child RR, particularly amongst children of parents with mNYAS (11/27 vs 13/127 respectively, odds ratio = 6.0, $P=3.8x10^{-4}$, Fisher's exact test). No difference in risk of transmission from affected parents to daughters compared with sons was observed (parent-daughter 15/105 (14.3%), parent-son 9/88 (10.2%), P=0.40), including if the parent was a mother or father.

Conclusion: This study demonstrates that particularly amongst axSpA patients with mNYAS, the RR of axSpA in both siblings and children is very high, particularly amongst HLA-B27 positive relatives (16.9%). The relatively higher prevalence of mother to child transmission compared to father to child transmission suggests that female AS patients appear to be genetically "enriched" regarding transmission of the disease predisposing genes to their offspring. This is consistent with polygenic models of AS, in which women with AS require a higher genetic load to develop disease, and are thus more likely to have affected children.

Disclosure: M. Khan, None; **S. van der Linden**, None; **P. Villiger**, None; **Z. Li**, None; **M. Khan**, None; **H. Baumberger**, None; **H. Zandwijk**, None; **M. Brown**, None.

Abstract Number: 1863

Clinical History as Tool for Diagnosis and Classification of Patients with Ankylosing Spondylitis (Axial Spondyloarthritis): Evidence from a 35-Year Follow-up Family Study of a Swiss Cohort

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Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Table 1. Questions that have sensitivity and/or specificity > 70% and LR > 2 by anatomical region

Question	Sensitivity (number/total)	Sensitivity (percent)	Specificity (number/total)	Specificity (percent)	LR+	LR-	*p*-value
Chronic inflammatory backpain (CIBP)	64/87	73.6%	109/130	83.8%	4.55	3.17	< 0.00001
Lumbar Spine region							
insidious onset of back pain	72/86	83.7%	74/130	56.9%	1.94	3.50	< 0.00001
more than 3 months duration	67/86	77.9%	95/130	73.1%	2.89	3.31	< 0.00001
associated with morning stiffness > 30 min	66/86	76.7%	95/130	73.1%	2.85	3.14	< 0.00001
back pain starting before age 40	84/86	97.7%	82/130	63.1%	2.65	27.12	< 0.00001
pain & stiffness	68/87	78.2%	98/130	75.4%	3.18	3.45	< 0.00001
worsening at early morning	56/86	65.1%	118/129	91.5%	7.64	2.62	< 0.00001
waking up during the night because of complaints	56/86	65.1%	114/130	87.7%	5.29	2.51	< 0.00001
leaving bed and walking around during the night	50/84	59.5%	123/128	96.1%	15.24	2.37	< 0.00001
pain radiating into gluteal region	64/82	78.0%	85/130	65.4%	2.25	2.98	< 0.00001
usage of analgesics	82/86	95.3%	79/130	60.8%	2.43	13.07	< 0.00001
relief of symptoms due to analgesics	73/88	83.0%	81/129	62.8%	2.23	3.68	< 0.00001
Thoracic region							
complaints at thoracic region *ever*	67/84	79.8%	100/126	79.4%	3.87	3.92	< 0.00001
pain and stiffness	47/88	53.4%	123/130	94.6%	9.92	2.03	< 0.00001
complaints at early morning	54/86	62.8%	110/130	84.6%	4.08	2.27	< 0.00001
morning stiffness at thoracic spine region	45/84	53.6%	125/129	96.9%	17.28	2.09	< 0.00001
complaints if body position does not change	52/83	62.7%	113/129	87.6%	5.05	2.35	< 0.00001
usage of analgesics	48/85	56.5%	122/129	94.6%	10.41	2.17	< 0.00001
relief of symptoms due to analgesics	46/87	52.9%	123/130	94.6%	9.82	2.01	< 0.00001
Ventral chest wall region							
complaints at ventral chest wall region *ever*	62/86	72.1%	105/128	82.0%	4.01	2.94	< 0.00001

Table 2. Three Region (3R) Clinical History Tool for Diagnosis or Classification of Ankylosing Spondylitis (Axial Spondyloarthritis)

Chest	Have you *ever* had pain or discomfort at the ventral (anterior) chest wall region?
Thoracic spine	Have you *ever* had pain or discomfort at the thoracic spine region?
Lumbar spine	Have you *ever* had chronic inflammatory back pain (≥ 4 items should be present) - insidious onset - duration > 3 months - morning stiffness > 30 minutes - back pain started < age 40 - persistent complaints

Any 2 of 3 fulfilled: sensitivity 83.1% - specificity 86.4%
All 3 items fulfilled: sensitivity 47.0% - specificity 97.6%

Background/Purpose: Lack of sensitivity or specificity of symptoms may induce uncertainty in diagnosis and classification of AS/axSpA. We investigated if balanced sensitivity and specificity of tools from the patient's clinical history may help better define the 'Gestalt' of AS/axSpA

Methods: In 1985 members of the Swiss AS Patient Society who had been diagnosed as having AS by their own physicians, as well as their first degree relatives (FDRs) were invited to participate in the current study. After obtaining ethical approval and informed consent, 1178 subjects, 363 of them probands, formed our study cohort; they completed questionnaires on disease manifestations, underwent rheumatological examination of axial and peripheral

joints, and provided blood samples for genetic studies, including HLA-B27. Probands also provided a recent pelvic radiograph to document presence of sacroiliitis. If their pelvic radiograph was not available, it was performed on-site. Relatives aged ≥18 years underwent pelvic radiography, unless pregnant. Pelvic radiographs were available for 360 probands and 713 relatives. Radiographs were blindly assessed twice by each of 4 readers. The assessment could only be performed once for 164 (46%) of the 360 radiographs of the probands (available only for a few hours). The sacroiliitis score for each sacroiliac (SI) joint ranged from 0 (normal) to 4 (ankylosis). Scores were added and then divided by the number of assessments. Scores below bilateral grade 2.0 or grade 3.0 unilaterally were considered not meeting New York radiographic criteria (NYRC).

In 2018 the ethical committee of the Swiss Kanton of Bern approved the follow-up study. Many Swiss city and village administrations provided current addresses of former participants. By December 2019, 123 probands and 39 FDRs had died, and 462 consenting participants completed a 157 item postal disease related questionnaire dealing with symptoms at lumbar and gluteal region, thoracic spine, and front part of the chest.

The gold standard for sensitivity was AS patients meeting NYRC for AS. The gold standard for specificity was the HLA-B27(-) relatives of HLA-B27(+) probands, as this group have a near zero chance of developing axSpA. Statistical analysis was performed by chi-square test.

Results: Sensitivity was assessed in 88 (85 of them HLA-B27(+)) AS patients (mean age 72.1 ± 7.5 years) meeting the NYRC, and specificity in the group of 130 HLA-B27(-) relatives (mean age 62.8 ± 9.2 years). Table 1 shows by anatomical region the questionnaire items that have sensitivity or specificity > 70% and likelihood ratio (LR) values ≥ 2. None of the criteria individually demonstrate sensitivity and specificity values that both surpass 80%. But a 3-item 3-region index of ”chronic inflammatory back pain” and two one-question items (Table 2) show 83.1% sensitivity and 86.4% specificity with likelihood ratios >5, if any 2 of 3 index items are met.

Conclusion: We propose a simple 3-item index assessing complaints at 3 regions that might be a useful tool to better define and classify the “Gestalt” of AS/axSpA, and also to improve the specificity of the current classification criteria. Validation of our results is needed in other data sets.

Disclosure: S. van der Linden, None; **Z. Li**, None; **M. Brown**, None; **P. Villiger**, None; **H. Baumberger**, None; **H. Zandwijk**, None; **M. Khan**, None.

Abstract Number: 1864

How to Diagnose Axial Spondyloarthritis in 2020? A Data-Driven Estimation of the Disease Probability in Patients with *a priori* Different Likelihoods of the Diagnosis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Table 1 Sensitivity, specificity, positive and negative likelihood ratio, and post-test probabilities of spondyloarthritis features in patients referred via an online screening tool (pre-test probability of axial SpA = 20%, n = 180).

	Sensitivity	Specificity	Positive LR	Negative LR	Pre-test prob.	Post-test prob., test positive	Post-test prob., test negative
Inflammatory back pain, current	0.83	0.50	1.67	0.34	0.20	0.29	0.08
Good response of back pain to NSAIDs	0.85	0.31	1.23	0.49	0.20	0.24	0.11
Anterior uveitis, ever	0.17	0.98	8.29	0.85	0.20	0.67	0.17
Psoriasis, ever	0.17	0.90	1.66	0.92	0.20	0.29	0.19
Inflammatory bowel disease, ever	0.06	0.99	4.14	0.96	0.20	0.51	0.19
Arthritis, ever	0.14	0.82	0.80	1.04	0.20	0.17	0.21
Peripheral arthritis, current	0.03	0.98	1.38	0.99	0.20	0.26	0.20
Enthesitis, ever	0.17	0.83	0.99	1.00	0.20	0.20	0.20
Enthesitis, current	0.06	0.92	0.75	1.02	0.20	0.16	0.20
Dactylitis, ever	0.03	0.99	4.14	0.98	0.20	0.51	0.20
Dactylitis, current	0.00	0.99	0.00	1.01	0.20	0.00	0.20
Family history of SpA and related disorders*	0.44	0.70	1.49	0.79	0.20	0.27	0.17
HLA-B27 positivity	0.61	0.88	4.92	0.45	0.20	0.55	0.10
CRP elevation	0.31	0.95	6.38	0.72	0.20	0.61	0.15
Active sacroiliitis on MRI	0.83	0.92	10.63	0.18	0.20	0.73	0.04
Structural changes in the sacroiliac joints on MRI	0.44	0.88	3.70	0.63	0.20	0.48	0.14
Definite radiographic sacroiliitis**	0.44	1.00	n.a.	0.56	0.20	1.00	0.12

* Psoriasis, uveitis, inflammatory bowel disease. **Bilateral ≥grade II or unilateral ≥grade III according to the grading system of the modified New York criteria. CRP: C-reactive protein; LR: Likelihood ratio; MRI: magnetic resonance imaging; n.a.: not applicable; NSAIDs: non-steroidal anti-inflammatory drugs; prob.: probability; SpA: spondyloarthritis.

Table 2 Sensitivity, specificity, positive and negative likelihood ratio, and post-test probabilities of spondyloarthritis features in patients referred via a physician-based referral tool (pre-test probability of axial SpA = 40%, n = 181).

	Sensitivity	Specificity	Positive LR	Negative LR	Pre-test prob.	Post-test prob., test positive	Post-test prob., test negative
Inflammatory back pain, current	0.85	0.61	2.16	0.25	0.40	0.59	0.14
Good response of back pain to NSAIDs	0.83	0.40	1.39	0.42	0.40	0.48	0.22
Anterior uveitis, ever	0.17	0.96	4.65	0.86	0.40	0.76	0.37
Psoriasis, ever	0.07	0.92	0.86	1.01	0.40	0.36	0.40
Inflammatory bowel disease, ever	0.01	0.99	1.55	0.99	0.40	0.51	0.40
Arthritis, ever	0.17	0.95	3.10	0.88	0.40	0.67	0.37
Peripheral arthritis, current	0.06	0.97	2.07	0.97	0.40	0.58	0.39
Enthesitis, ever	0.13	0.90	1.27	0.97	0.40	0.46	0.39
Enthesitis, current	0.06	0.93	0.77	1.02	0.40	0.34	0.40
Dactylitis, ever	0.00	1.00	n.a.	1.00	0.40	n.a.	0.40
Dactylitis, current	0.00	1.00	n.a.	1.00	0.40	n.a.	0.40
Family history of SpA and related disorders*	0.22	0.80	1.12	0.97	0.40	0.43	0.39
HLA-B27 positivity	0.94	0.62	2.49	0.09	0.40	0.62	0.06
CRP elevation	0.32	0.88	2.62	0.78	0.40	0.64	0.34
Active sacroiliitis on MRI	0.88	0.85	5.81	0.14	0.40	0.79	0.09
Structural changes in the sacroiliac joints on MRI	0.52	0.90	5.41	0.53	0.40	0.78	0.26
Definite radiographic sacroiliitis**	0.63	0.98	31.58	0.38	0.40	0.95	0.20

* Psoriasis, uveitis, inflammatory bowel disease ** Bilateral ≥grade II or unilateral ≥grade III according to the grading system of the modified New York criteria. CRP: C-reactive protein; LR: Likelihood ratio; MRI: magnetic resonance imaging; n.a.: not applicable; NSAIDs: non-steroidal anti-inflammatory drugs; prob.: probability; SpA: spondyloarthritis.

Background/Purpose: The diagnosis of axial spondyloarthritis (axSpA) is often delayed by several years and reducing that gap between symptom onset and diagnosis poses a major challenge in rheumatology. The objective of this study was to evaluate the diagnostic value of SpA parameters and their combination for the diagnosis of axSpA in patient populations with different a priori probabilities of this disease.

Methods: For the aim of the present analysis we used data from the Optimal Referral Strategy for Early Diagnosis of Axial Spondyloarthritis (OptiRef) study comprising a total of 361 patients who presented to a rheumatologist because of chronic back pain and suspicion of axSpA. Of those, 181 were referred by primary care physicians or orthopaedists and 180 patients were recruited via an online screening tool. All patients received a structured rheumatologic examination which included the evaluation of SpA features and resulted into a diagnosis of axSpA/no axSpA. Sensitivities, specificities, and likelihood ratios (LRs) for SpA features were determined in the entire group and in both subgroups with different referral pathways. The respective post-test probabilities of axSpA were calculated.

Results: The prevalence of axSpA was 30% in the entire group, 20% in the online screening subgroup and 40% in the physician-referred subgroup. These frequencies were used as pre-test probabilities in the calculation of the post-test probabilities among the respective groups. It could be shown that differences in the pre-test probability affect not only the post-test probability of the disease, but also the relative diagnostic value of single SpA features. For instance, the presence of inflammatory back pain increased the probability of the presence of axSpA from the background 20% to 29% in the online screening group (positive LR of 1.67) (Table 1) and from the background 40% to 59% in the physician-referred group (positive LR of 2.16) (Table 2), whereas its absence decreased the respective probabilities to 8% and 14%, respectively.

Furthermore, combinations of parameters performed differently in the studied groups. For instance, combining IBP with anterior uveitis did not increase the post-test probability for axSpA in the online screening group (it remained 67%), but in the physician-referred group (from 76% to 93%). Using HLA-B27 positivity and active sacroiliitis on

Table 3 Post-test probabilities of spondyloarthritis features in patients referred via an online screening tool and/or a physician-based referral tool.

SpA feature 1	SpA feature 2	SpA feature 3	Post-test probability			Post-test probability†		
			Online screening group*	Physician-referred group**	Total ***	Online screening group*	Physician-referred group**	Total ***
IBP, current (+)	Uveitis, ever (+)		0.67	0.93	0.85	0.78	0.87	0.83
IBP, current (+)	Arthritis, ever (+)		0.21	0.81	0.51	0.25	0.82	0.50
IBP, current (+)	Good response of back pain to NSAIDs (+)		0.30	0.61	0.46	0.34	0.67	0.51
IBP, current (+)	Good response of back pain to NSAIDs (-)		0.22	0.38	0.29	0.17	0.38	0.27
IBP, current (+)	CRP elevation (+)		0.85	0.79	0.81	0.73	0.79	0.76
IBP, current (+)	HLA-B27 positive (+)		0.66	0.75	0.73	0.67	0.78	0.74
IBP, current (-)	HLA-B27 positive (+)		0.37	0.33	0.34	0.30	0.30	0.31
IBP, current (+)	Arthritis, ever (+)	Good response of back pain to NSAIDs (+)	0.21	0.90	0.57	0.29	0.86	0.57
IBP, current (+)	HLA-B27 positive (+)	Active sacroiliitis on MRI (+)	1.00	0.96	0.97	0.96	0.95	0.96
IBP, current (+)	HLA-B27 positive (-)	Active sacroiliitis on MRI (+)	0.69	0.41	0.57	0.67	0.44	0.57

† Calculated under the assumption that diagnostic tests are independent. *Pre-test probability = 20%. **Pre-test probability = 40%. ***Pre-test probability = 30%. CRP: C-reactive protein; IBP: inflammatory back pain; MRI: magnetic resonance imaging; NSAIDs: non-steroidal anti-inflammatory drugs; SpA: spondyloarthritis.

MRI in combination with IBP resulted in a surge in the post-test probability of the presence of axSpA to over 95% in all groups (Table 3). Using a simplified formula to calculate the post-test probabilities for axSpA for combinations of parameters, which is based on the product of the respective LRs and holds if the diagnostic tests are independent, could lead to differences of more than 10% (Table 3).

Conclusion: The diagnostic value of SpA features is not fixed and may vary substantially depending on the characteristics of the patient group including their referral pathway and their pre-test probability of axSpA. This should be taken into account in the diagnostic approach of axSpA.

Disclosure: D. Poddubnyy, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8; **F. Proft**, Novartis, 2, 8, AbbVie, 8, AMGEN, 8, BMS, 8, Hexal, 8, Celgene, 8, Lilly, 8, MSD, 8, Pfizer, 8, Roche, 8, UCB, 8; **J. Sieper**, AbbVie, 5, Novartis, 5, 8, Lilly, 8, Janssen, 5, Merck, 5, 8; **I. Redeker**, None.

Abstract Number: 1865

Identification of Parameters Associated with a Diagnostic Delay in Axial Spondyloarthritis:Results from the European Map of Axial Spondyloarthritis (EMAS)

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Early diagnosis of Axial Spondyloarthritis (axSpA) is crucial for timely access to specialist care and effective treatment. The aim is to assess the current diagnostic delay in axSpA and identify the parameters associated with increased diagnostic delay in a European sample.

Methods: Data from unselected patients participating in the European Map of Axial Spondyloarthritis (EMAS) study through an online survey (2017- 2018) across 13 countries were analysed. Mean differences in diagnostic delay were analysed using Mann-Whitney and Kruskal-Wallis tests, among sociodemographic and disease-related factors. A multivariate linear regression analysis was carried out to identify the relative weight of the associated parameters in determining diagnostic delay.

Results: 2,846 patients participated in EMAS. Mean age was 43.9 years, 61.3% were female, 48.1% had a university degree, and 53.9% were employed. Of the 2846 participants, 2652 provided information for calculating diagnostic delay. Mean age at symptom onset was 26.6 ± 11.1, mean age at diagnosis was 33.7 ± 11.5, and mean diagnostic delay was 7.4 ± 8.4 (Fig. 1). The following variables were associated with longer diagnostic delay in the bivariate anal-

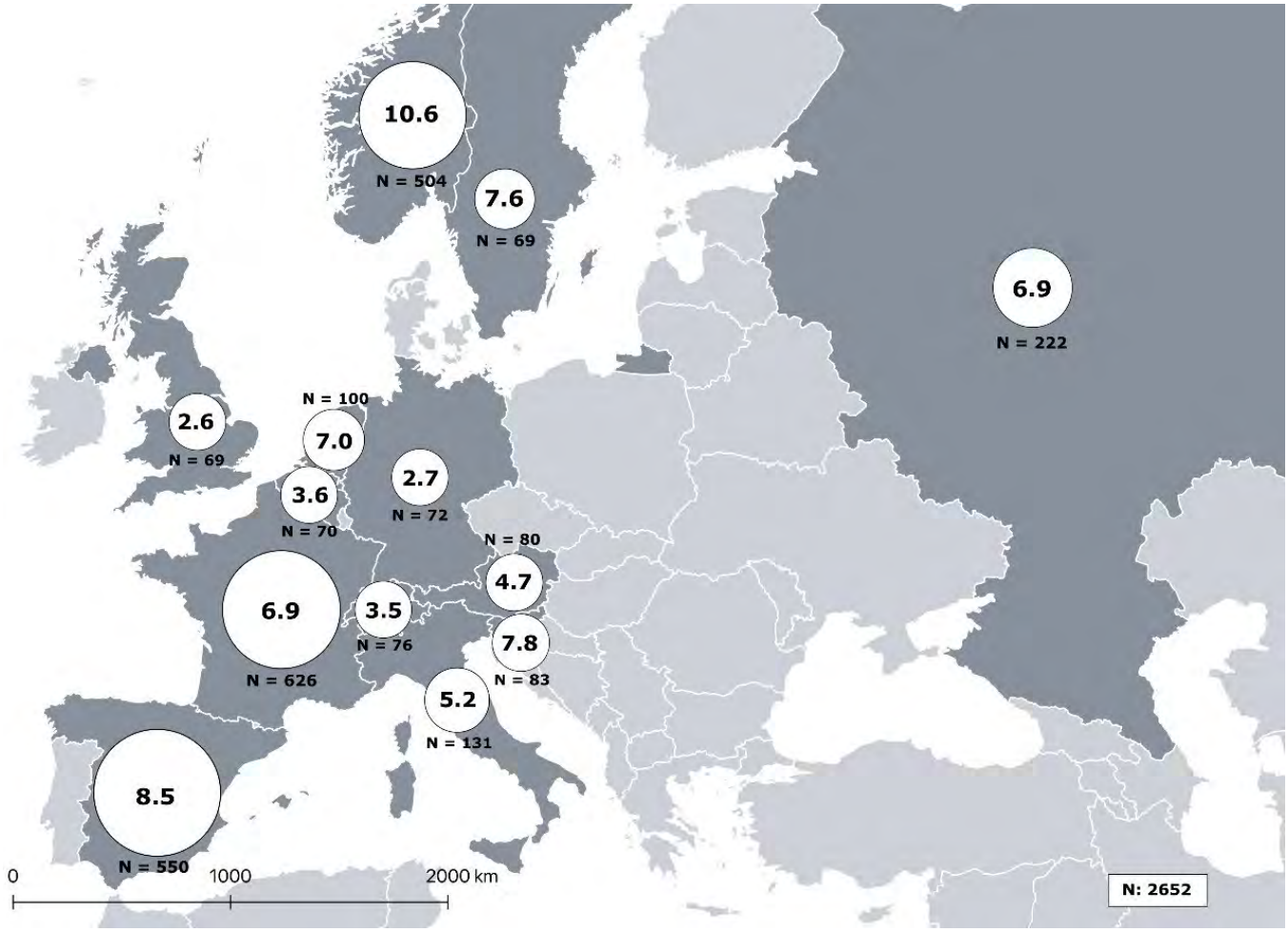

Figure 1. Average years of diagnostic delay across EMAS countries (N: 2,652)

ysis: older age, female gender, being diagnosed by a rheumatologist (Table 1). In the multivariate regression analysis younger age at symptom onset, number of HCPs seen before were associated with diagnostic delay (Table 2).

Conclusion: In this large sample of axSpA patients from 13 different European countries, the average diagnostic delay was more than seven years. The fact that one of the most strongly associated parameters to diagnostic delay was number of HCPs seen before diagnosis suggests the need for urgent action to reduce incorrect referrals to shorten the patient journey to diagnosis across Europe.

Variable		Diagnostic Delay, Mean ± SD	P-value
Age categories	18-34	4.4 ± 5.5	<0.001
	35-51	7.9 ± 8.2	
	52-68	9.5 ± 10.2	
	>68	7.3 ± 9.7	
Gender	Male	6.1 ± 7.4	<0.001
	Female	8.2 ± 8.9	
Education level	No school completed	8.0 ± 10.7	0.397
	Primary school	7.6 ± 8.9	
	High school	7.6 ± 8.4	
	University	7.3 ± 8.3	
Occupation	Manual worker	6.7 ± 8.3	0.163
	Non-manual worker	7.3 ± 8.4	
Diagnosed by rheumatologist	Yes	7.9 ± 8.7	<0.001
	No	5.7 ± 7.3	
HLA-B27	Positive	8.3 ± 8.3	0.775
	Negative	8.7 ± 9.0	
Uveitis (ever)	Yes	8.0 ± 8.3	0.098
	No	7.6 ± 8.4	
IBD (ever)	Yes	7.7 ± 8.7	0.944
	No	7.5 ± 8.5	

Table 1. Associations between sociodemographic and disease-related variables and diagnostic delay (N: 2,652)

Disclosure: M. Garrido-Cumbrera, None; **V. Navarro-Compán**, Novartis Pharma, 1, 5, 8, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, UCB, 5, 8; **C. Bundy**, Abbvie, 8, Celgene, 8, Janssen, 8, Lilly, 8, Novartis, 8, Pfizer, 8; **R. Mahapatra**, None; **S. Makri**, None; **J. Correa-Fernández**, None; **L. Christen**, Novartis Pharma AG, 3; **C. Delgado-Domínguez**, None; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8.

Abstract Number: 1866

Patient-reported Impact of Axial Spondyloarthritis on Working Life. Results from the Spanish Atlas 2017

Marco Garrido-Cumbrera[1], Eduardo Collantes-Estévez[2], Victoria Navarro-Compán[3], Pedro Zarco[4], Carlos Sastre[5], Sergio Sanz-Gomez[6], José Correa-Fernández[7] and Jordi Gratacós[8], [1]Health & Territory Research (HTR), Universidad de Sevilla / Spanish Federation of Spondyloarthritis Associations, Sevilla, Spain, [2]Rheumatology Department, Reina Sofia University Hospital/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba, Cordoba, Spain, Córdoba, Spain, [3]Hospital Universitario La Paz IdiPaz, Madrid, Pais Vasco, Spain, [4]Novartis Farmacéutica Spain, Alcorcon, Madrid, Spain, [5]Novartis Pharma AG, Basel, Switzerland, [6]Health & Territory Research, Seville, Spain, [7]Health & Territory Research (HTR), Universidad de Sevilla, Sevilla, Spain, [8]University Hospital Parc Tauli Sabadell, Barcelona, Spain

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (axSpA) impacts negatively on multiple dimensions of patient's life, including their working life. The present study aims to evaluate working status, work-related issues and their associated factors in a Spanish sample of patients with axSpA.

Methods: The Atlas 2017 based its results on an extensive cross-sectional patient survey conducted in Spain (2016), validated by a multidisciplinary group of experts on spondyloarthritis. Participants were recruited through an on-line panel and patient organizations. Participants were classified as active (employed, unemployed between 15-64 years) and inactive (retirees, on sick leave, students and homemakers). Those employed were asked to report work-related issues due to axSpA (sick-leave, difficulty fulfilling work hours, missing work for doctors' appointments, reducing working hours or taking days off) in the past 12 months. Diagnostic delay, disease activity (BASDAI), spinal stiffness (3-12), functional limitation (0-54) and psychological distress (General Health Questionnaire, GHQ-12 [0-12]) were compared between employed patients with or without work-related issues using a Mann-Whitney and Kruskal-Wallis test. Regression analysis was conducted to determine explicative disease outcome related factors (enter method for BASDAI, self-reported spinal stiffness, functional limitation and GHQ-12) over work-related issues.

Population	N	%	Employment status	N	%
Active population*	415	63.6	Employed	325	78.3
			Unemployed	90	21.6
			Total	415	100.0
Inactive population	238	36.4	Temporary sick leave	63	26.5
			Permanent sick leave	64	26.9
			Retired	63	26.5
			Homemakers	29	12.2
			Students	9	3.8
			Early retirement	10	4.2
			Total	238	100.0
Total	653	100.0			

*According to the ILO, the active population or labor force is the sum of persons between 15 and 64 years

Table 1. Employment status of survey respondents

Variable	N (%)
Employed participants (n = 325)	
Any work-related issue, n = 313	170 (54.3)
Work-related issues due to axSpA, (n = 170)	
Difficulty fulfilling working hours	75 (44.1)
I missed work only for the time my doctor appointment took	73 (42.9)
I took sick leave	63 (37.1)
My professional life has suffered	31 (18.2)
I asked for some days off	21 (12.3)
Changed shift sometimes	21 (12.3)
I had to give up my previous job	13 (7.6)

Table 2. Frequencies of work-related issues surveyed among employed respondents

Reference group	Employed			Active Population		
Subgroup	Any work-related issue	With no work-related issues		Employed	Unemployed	
N size	n: 170	n: 143	p-value	n: 325	n: 90	p-value
Sociodemographic characteritics						
Age (years)	41.9 ± 7.9	44.2 ± 9.4	0.513	42.9 ± 8.6	42.0 ± 9.1	**0.030***
Gender (Male)	79 (46.5)	75 (52.4)	0.133	159 (48.9)	36 (40.0)	0.292
Education level (University)	80 (47.1)	68 (47.6)	**0.001***	153 (47.1)	21 (23.3)	0.764
Marital status (Married)	110 (64.7)	109 (76.2)	0.051	231 (71.1)	54 (60.0)	0.062
Patient-reported outcomes						
BASDAI (0-10)	5.7 ± 1.8	4.5 ± 1.9	**<0.001***	5.2 ± 1.9	6.3 ±1.9	**<0.001***
Spinal Stiffness (3-12)	6.7 ± 2.7	6.1 ± 2.4	**<0.001***	6.5 ± 2.6	7.8 ± 2.3	**<0.001***
Functional Limitation (0-54)	43.9 ± 8.8	36.9 ± 10.3	**<0.001***	40.6 ± 10.1	45.0 ± 8.4	**<0.001***
GHQ-12 (0-12)	6.6 ± 4.2	3.0 ± 3.5	**<0.001***	4.9 ± 4.3	7.6 ± 4.2	**<0.001***
Anxiety	35 (20.6)	16 (11.2)	**0.011***	52 (16.0)	25 (27.8)	**0.025***
Depression	29 (17.1)	4 (2.8)	**0.001***	33 (10.2)	21 (23.3)	**<0.001***

Table 3. Differences between employees with/without work-related issues and between employed/unemployed participants in relation to sociodemographic characteristics and patient-reported outcomes

Results: Data from 680 patients were collected: mean age was 47±11 years, 52.5% were female and 36.9% were university educated. Mean disease duration and diagnostic delay were 20.9±12.2 and 8.5±7.7 years, respectively, and mean BASDAI was 5.5±2.2. A total of 63.6% (n=415) were considered active population, of which 49.8% (n=325) were employed (Table 1). Of those employed, 54.3% reported a work-related issue, specifically 37.1% took sick leave, 44.1% had difficulties in fulfilling the working hours and 42.9% missed work due to doctor's appointments (Table 2). Among all patients, 95.5% faced (or believed they would) difficulties finding a job due to axSpA. Experiencing work-related issues due to axSpA was significantly associated with higher disease activity, self-reported spinal stiffness, longer diagnostic delay, higher functional limitation and higher level of psychological distress ($p< 0.001$). However, the highest levels of disease burden were reported by unemployed participants (Table 3).

Conclusion: Results reveal a relevant impact of axSpA in patient working life. Approximately two out of three patients employed experienced work-related issues due to axSpA, being associated to worse disease outcomes and poorer psychological health. However, those who were unemployed faced a harsher situation reporting even poorer disease-related and psychological health outcomes. As psychological health appears impaired severely in axSpA patients regardless of their employment status it should be key for a holistic approach to patient care.

Disclosure: M. Garrido-Cumbrera, None; **E. Collantes-Estévez**, None; **V. Navarro-Compán**, Novartis Pharma, 1, 5, 8, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, UCB, 5, 8; **P. Zarco**, None; **C. Sastre**, Novartis, 3; **S. Sanz-Gomez**, None; **J. Correa-Fernández**, None; **J. Gratacós**, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, 8, MSD, 5, 8, UCB, 5, 8, Novartis, 5, 8, Janssen Pharmaceutical, 5, 8, Amgen, 5, 8, BMS, 2, 5, 8, Celgene, 2, 5, 8.

Abstract Number: 1867

Two-Year Diagnostic Consistency in Patients with Chronic Back Pain Suspected of Axial Spondyloarthritis in Protocolised Follow-up: Data from the Spondyloarthritis Caught Early Cohort

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: A diagnosis of (early) axial spondyloarthritis (axSpA) is based on pattern recognition, which can be challenging and may change over time. The aim of this study was to investigate consistency of diagnosis over two years in patients with chronic back pain (less than two years symptoms) suspected of axSpA.

Methods: In the SPACE cohort, patients over 16 years of age referred to the rheumatology outpatient clinic with chronic back pain (≥3 months and < 2 years) starting before the age of 45, suspected of axSpA were included. Follow-up was performed only in patients with at least two SpA features or one SpA feature with a positive likelihood ratio ≥6.4 (Rudwaleit, van der Heijde, Khan, Braun, & Sieper, 2004).

According to protocol, all SpA features as well as MRI and radiographs of the sacroiliac joints were performed at baseline and two years. Physicians were asked to report whether the diagnosis was axSpA or no axSpA at both timepoints, for which they had information available on all SpA features and locally read imaging.

Only patients with complete data on diagnosis and imaging at baseline and 2 years were included.

Patients were labelled with a consistent axSpA diagnosis if they had a diagnosis of axSpA at baseline and at two-year follow-up. Those patients whose diagnosis switched from axSpA to no axSpA; or from no axSpA to axSpA were labelled inconsistent axSpA diagnosis.

Results: Over two years the diagnostic consistency rate was 84%. The rate of change from axSpA to no axSpA was 9% and from no axSpA to axSpA 7% (table 1).

The patients who only had an axSpA diagnosis at baseline were more often female and less often HLA-B27 positive compared to the other two groups (table 2).

Furthermore, both groups with an inconsistent diagnosis had fewer SpA features and a lower level of confidence of the diagnosis (LoC) compared to the group with a consistent diagnosis of axSpA, especially at baseline.

Table 1 Consistency of diagnosis over 2 years

	Diagnosis axSpA at 2 years	Diagnosis no axSpA at 2 years
Diagnosis axSpA at baseline	184 (62%)	26 (9%)
Diagnosis no axSpA at baseline	19 (7%)	66 (22%)

Table 2 Characteristics at baseline and 2-year follow-up of the group with a consistent axSpA diagnosis over 2 years and the groups whose diagnosis (axSpA/no axSpA) changed between baseline and 2-year follow-up

Characteristic	Consistent diagnosis axSpA AxSpA at baseline and 2yrs (N=184)		Inconsistent diagnosis AxSpA at baseline only (N=26)		Inconsistent diagnosis AxSpA at 2yrs only (N=19)	
	Baseline	2-year visit	Baseline	2-year visit	Baseline	2-year visit
Male, n(%)	82 (45)		4 (15)		8 (42)	
Age at baseline (years), mean (SD)	30 (8)		33 (6)		33 (8)	
Symptom duration (months), mean (SD)	13 (7)		13 (7)		12 (6)	
IBP, n(%)	127 (69)	137 (74)	18 (69)	20 (77)	13 (68)	16 (84)
Good response to NSAIDs, n(%)	82 (45)	155 (84)	6 (23)	18 (69)	5 (26)	10 (53)
Positive family history of SpA, n(%)	89 (48)	97 (53)	13 (50)	14 (54)	10 (53)	13 (68)
Past history or current symptoms						
Peripheral arthritis, n(%)	46 (25)	54 (29)	1 (4)	3 (12)	0 (0)	1 (5)
Dactylitis, n(%)	24 (13)	37 (20)	0 (0)	0 (0)	0 (0)	1 (5)
Enthesitis, n(%)	58 (32)	74 (40)	6 (23)	9 (35)	2 (1)	2 (11)
Acute anterior uveitis, n(%)	25 (14)	35 (19)	2 (8)	2 (8)	1 (5)	2 (11)
IBD, n(%)	6 (3)	7 (4)	3 (12)	6 (23)	1 (5)	2 (11)
Psoriasis, n(%)	27 (15)	35 (19)	3 (12)	3 (12)	1 (5)	1 (5)
Elevated CRP/ESR, n(%)	66 (36)	92 (50)	12 (46)	8 (31)	4 (21)	10 (53)
HLA-B27 positive, n(%)	138 (75)	138 (75)	7 (27)	7 (27)	13 (68)	13 (68)
Sacroiliitis radiographs*, n(%)	49 (27)	70 (38)	0 (0)	0 (0)	1 (5)	1 (5)
Sacroiliitis MRI*, n(%)	127 (69)	149 (81)	6 (23)	7 (27)	1 (5)	4 (21)
Use of bDMARDs, n(%)	6 (3)	38 (21)	0 (0)	1 (4)	0 (0)	1 (5)
Use of NSAIDs, n (%)	139 (76)	125 (68)	17 (65)	12 (46)	9 (47)	6 (32)
Number of SpA features, mean (SD)	5 (2)	7 (2)	3 (1)	5 (2)	3 (1)	5 (1)
LoC diagnosis axSpA/no axSpA, mean (SD)	8.1 (2.0)	8.6 (1.8)	5.8 (1.7)	7.5 (1.9)	5.6 (2.2)	6.1 (2.3)

* Based on local reading

axSpA, axial Spondyloarthritis; bDMARD, biological Disease Modifying Anti-Rheumatic Drug; CRP, C-reactive protein; ESR, Erythrocyte Sedimentation Rate; HLA-B27, Human Leucocyte Antigen B27; IBD, Inflammatory Bowel Disease; IBP, Inflammatory Back Pain; LoC, Level of Confidence regarding diagnosis (either axSpA or no axSpA); MRI, Magnetic Resonance Imaging; NSAIDs, Non-Steroidal Anti Inflammatory Drugs; SpA, Spondyloarthritis.

Table 2 Characteristics at baseline and 2-year follow up of the group with a consistent diagnosis over 2 years and the groups whose diagnosis changed between baseline and 2-year follow up

At two-year follow-up the LoC in the group with an axSpA diagnosis at 2 years only was much lower than in the other two groups. In the group that only had an axSpA diagnosis at baseline, the LoC regarding the diagnosis increased most compared to baseline: physicians were more certain of the diagnosis no axSpA at two-year follow-up than they were of the diagnosis axSpA at baseline.

The number of patients with sacroiliitis on radiographs and MRI was much higher in the group with a consistent diagnosis of axSpA. Although the percentage of patients with sacroiliitis on MRI increased in the group with a diagnosis of axSpA at two-year follow-up only, this was still much lower (21%) as compared to the patients with a consistent diagnosis (81%). This was in line with a low LoC in this group.

Conclusion: In a cohort of patients with chronic back pain suspected of axSpA the diagnostic consistency rate was high. Interestingly, in the group that only had a diagnosis axSpA at baseline, rheumatologists were more certain about the absence of axSpA at two years than the presence of axSpA at baseline.Table 1 Consistency of diagnosis over 2 years

Disclosure: A. Boel, None; **M. van Lunteren**, None; **K. Fagerli**, None; **U. Lindström**, None; **R. Ramonda**, None; **M. van de Sande**, Boehringer Ingelheim, 2, AbbVie, 5, Eli Lilly, 2, 5, MSD, 5, 8, Janssen, 2, Novartis, 2, 5, 8; **D. van der**

Heijde, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5; **F. van Gaalen**, Reuma Nederland, 1, Stichting vrienden van Sole Mio, 1, MSD, 1, Abbvie, 1, Novartis, 1.

Abstract Number: 1868

Comparison of Quality of Life Between Chronic Back Pain Patients with and Without a Diagnosis of Axial Spondyloarthritis After 2-Year Protocolised Follow-up: Data from the Spondyloarthritis Caught Early Cohort

Anne Boel[1], Miranda van Lunteren[2], Karen Fagerli[3], Sofia Exarchou[4], Roberta Ramonda[5], Marleen van de Sande[6], Désirée van der Heijde[7] and Floris van Gaalen[8], [1]Leiden University Medical Centre, Hooge Zwaluwe, Netherlands, [2]Leiden University Medical Centre, Weesp, Netherlands, [3]Diakonhjemmet Hospital, Oslo, Norway, [4]Rheumatology, Department of Clinical Sciences Malmö, Lund University, Malmö, Sweden, Malmo, Sweden, [5]University of Padova, Padova, Italy, [6]Amsterdam UMC, AMC/University of Amsterdam, Department of Rheumatology and Clinical Immunology, Amsterdam Infection & Immunity Institute and Amsterdam Rheumatology and Immunology Center (ARC), Amsterdam, Netherlands, [7]Leiden University Medical Center, Leiden, Netherlands, [8]Leiden University Medical Center (LUMC), Leiden, Netherlands

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study was to compare quality of life (QoL) between chronic back pain (CBP) patients with and without a diagnosis of axial spondyloarthritis (axSpA), after two-years of protocolised follow-up.

Methods: Patients over 16 years of age referred to the rheumatology outpatient clinic with chronic back pain (≥ 3 months and < 2 years) starting before the age of 45, suspected of axSpA were included in the SPACE cohort. Follow-up was performed only in patients with at least two SpA features or one SpA feature with a positive likelihood ratio ≥6.4 (Rudwaleit, van der Heijde, Khan, Braun, & Sieper, 2004).

QoL was assessed using the Medical Outcomes Study 36-Item Short-Form Health Survey (SF-36). Age, sex and country weighted scale scores were calculated for each of the 8 subscales. Numeric scales ranged from 0 (worst health) to 100 (best health), after recoding and recalibration. The physical (PCS) and mental component summary (MCS) scores were calculated from the adjusted scores; and transformed to enable comparison to the general population mean of 50.

Additionally, the proportion of patients with an improvement or worsening of the PCS and MCS above the minimal clinically important difference (MCID) were assessed. We applied the commonly used MCID in clinical trials with bDMARDs in axSpA of 3 points for the PCS and MCS.

In this study we included patients with a diagnosis axSpA or no axSpA (CBP group), all with a level of confidence ≥7 (on a 0-10 scale) after locally read imaging, who had data available on the PCS and MCS at both timepoints.

Table 1 Baseline characteristics of patients with an axSpA diagnosis and those with CBP

Characteristic	Diagnosis axSpA (N=183)	CBP (N=74)
Male, n(%)	105 (57)	20 (27)
Age (years), mean (SD)	30 (8)	31 (8)
Symptom duration (months), mean (SD)	13 (7)	13 (7)
HLA-B27 positive, n(%)	137 (75)	23 (31)
Number of SpA features, mean (SD)	5 (2)	3 (1)
Use of NSAIDs, n(%)	139 (76)	52 (70)

axSpA, axial Spondyloarthritis; CBP, Chronic Back Pain; HLA-B27, Human Leucocyte Antigen B27; NSAIDs, Non-Steroidal Anti Inflammatory Drugs; SpA, Spondyloarthritis

Table 1. Baseline characteristics of patients with an axSpA diagnosis and those with CBP.

Table 2 PCS and MCS scores at baseline and 2-year follow-up for the group with an axSpA diagnosis and those with CBP

Characteristic	Diagnosis axSpA (N=186)		CBP (N=74)		
	Baseline	2 years	Baseline	2 years	p-values
SF-36 PCS, mean (SD) %	28.0 (14.8)	40.5 (12.3)†	26.4 (13.6)	34.7 (15.6)†	P<0.001*
Improvement >MCID, n(%)		143 (78)		49 (66)	
Worsening >MCID, n(%)		22 (12)		12 (16)	
SF-36 MCS, mean (SD) %	47.3 (13.7)	47.9 (11.8)	46.5 (11.2)	48.9 (10.6)	p=0.364
Improvement >MCID, n(%)		76 (42)		35 (47)	
Worsening >MCID, n(%)		69 (38)		26 (35)	

*Significant difference between groups at two years; after correction for baseline PCS scores and NSAID use over time (p<0.05); †Significant improvement within group over time

axSpA, axial Spondyloarthritis; CBP, Chronic Back Pain; MCID, Minimal Clinically Important Difference; MCS, Mental Component Summary; PCS, Physical Component Summary; SF-36, Medical Outcomes Study 36-Item Short-Form Health Survey

Table 2. PCS and MCS scores at baseline and 2-year follow-up for the group with an axSpA diagnosis and those with CBP

Linear regression models were used to test the difference between groups at two-year follow-up for PCS and MCS scores. Baseline PCS and MCS scores and NSAID-use over time were tested as confounders.

Results: Patients with a diagnosis of axSpA were more frequently male and HLA-B27 positive and had more SpA features at baseline compared to the patients with CBP (Table 1). Age, symptom duration and NSAID-use were similar between groups.

In both groups the PCS significantly improved over two years. However, the PCS was significantly better in the group with an axSpA diagnosis compared to the CBP group at two-year follow-up, after correction for baseline PCS scores and NSAID-use over time (table 2). Despite the improvements over time, PCS scores were still well below the general population mean of 50 in both groups at two-year follow-up. MCS scores were not significantly different between groups at follow-up, and they were close to the general population mean.

In these regression models with baseline values and NSAID-use over time as covariates, axSpA was an independent predictor of better PCS scores (data not shown).

The majority of patients in both groups improved their PCS scores with more than the MCID over two-years of protocolised follow-up. In contrast, the proportion of patients who improved or worsened more than the MCID in MCS scores are similar. Also the percentage of patients with an improvement or worsening larger than the MCID for either PCS or MCS is similar in axSpA and CBP patients.

Conclusion: After two years of protocolised follow-up the physical functioning as assessed by the SF-36 PCS was better in patients with an axSpA diagnosis compared to patients with CBP.

Disclosure: A. Boel, None; **M. van Lunteren**, None; **K. Fagerli**, None; **S. Exarchou**, Novartis, 1; **R. Ramonda**, None; **M. van de Sande**, Boehringer Ingelheim, 2, AbbVie, 5, Eli Lilly, 2, 5, MSD, 5, 8, Janssen, 2, Novartis, 2, 5, 8; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmith-Kline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5; **F. van Gaalen**, Reuma Nederland, 1, Stichting vrienden van Sole Mio, 1, MSD, 1, Abbvie, 1, Novartis, 1.

Abstract Number: 1869

"Rheum to Diagnosis": Uncovering Impediments to Accurate Diagnosis of Non-radiographic Axial Spondylarthritis (nr-axSpA)

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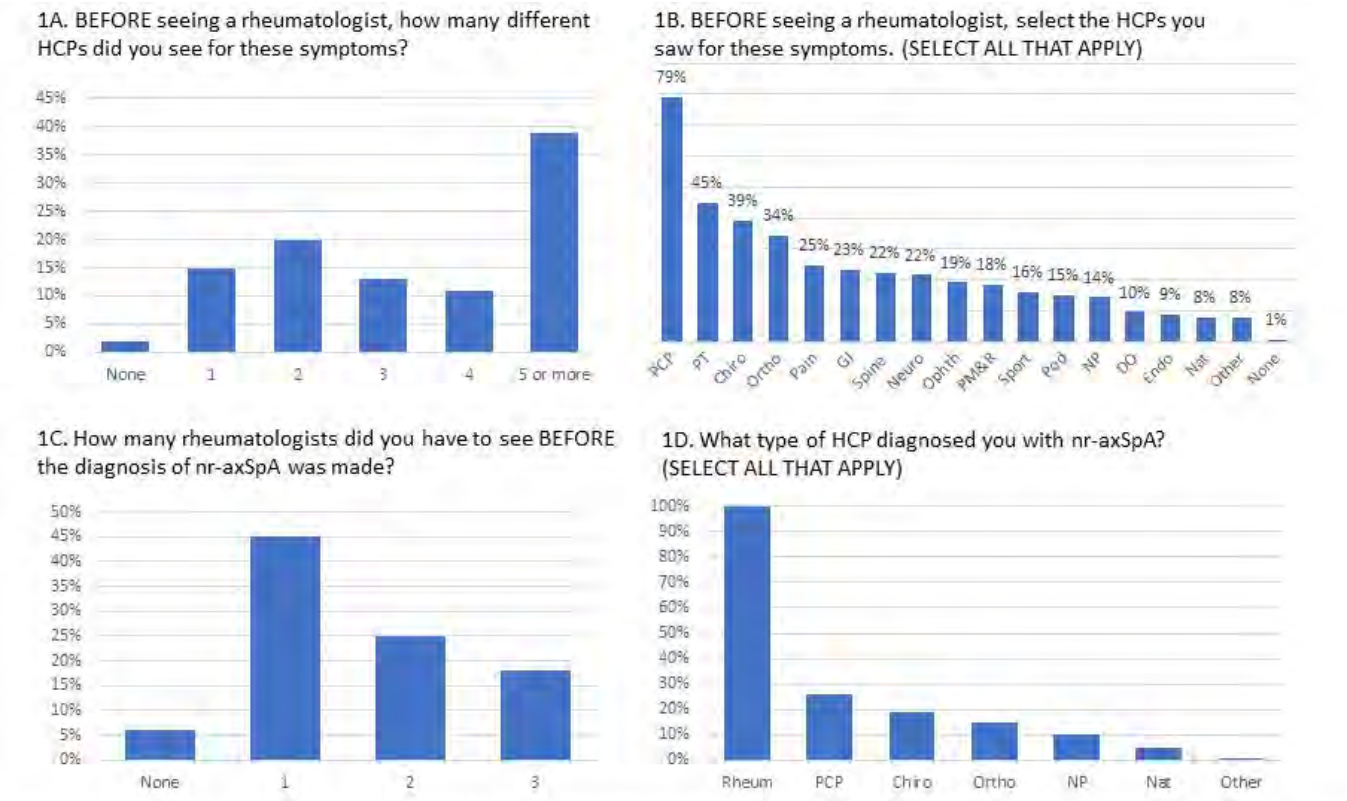
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: In the US, there is up to a 14-year delay in axSpA diagnosis, which is likely greater for nr-axSpA.[1] Impediments to timely diagnosis of nr-axSpA are unknown. This two-phased study used a grounded theory analytical approach to understand the healthcare journey leading to nr-axSpA diagnosis and factors contributing to diagnostic delay.

Methods: Adults with nr-axSpA fulfilling the eligibility criteria of rheumatologist-confirmed diagnosis of nr-axSpA, chronic back pain for ≥3 months starting before age 45, and presence of characteristic SpA symptoms were recruited from February-May 2020 via the Spondylitis Association of America newsletter, social media channels, and from back pain patient databases. In the qualitative component of the study, semi-structured telephone interviews with 25 patients and 15 rheumatologists were conducted to identify barriers and overarching themes. For the quantitative component, patients completed a detailed online questionnaire.

Results: Quantitative analysis was conducted on 125 patients (mean age, 43.5 years [range: 18-73 years]; female 74%; white 84%, LatinX 3%, and black 2%; bachelor's or advanced degree in 72%). Half of patients had seen ≥4 different healthcare providers (HCPs) before seeing a rheumatologist (Figure 1) and 50% saw ≥2 rheumatologists before receiving the nr-axSpA diagnosis. The interval from symptom onset to nr-axSpA diagnosis ranged between ≤2 years in 40% to ≥11 years in 25% (Figure 2). Both qualitative interviews and quantitative survey responses found that patients often perceived their symptoms as a typical consequence of activity or their age (Table 1). When patients did seek medical care, clinicians frequently minimized, overlooked, or misinterpreted signs and symptoms of inflammatory disease, particularly in young and female patients. Survey participants perceived these issues as leading barriers to timely diagnosis.



Abbreviations: Chiro, chiropractor; DO, osteopath; Endo, endocrinologist; GI, gastroenterologist; HCP, healthcare provider; Nat, naturopath; Neuro, neurologist; NP, nurse practitioner; nr-axSpA, non-radiograph axial spondyloarthritis; Ophth, ophthalmologist; Ortho, orthopedist; Pain, pain specialist; Pod, podiatrist; PCP, primary care physician; PM&R, physical medicine and rehabilitation; PT, physical therapist; Spine, spine specialist; Sport, sports medicine;

Figure 1. Health Encounters Leading to nr-axSpA Diagnosis

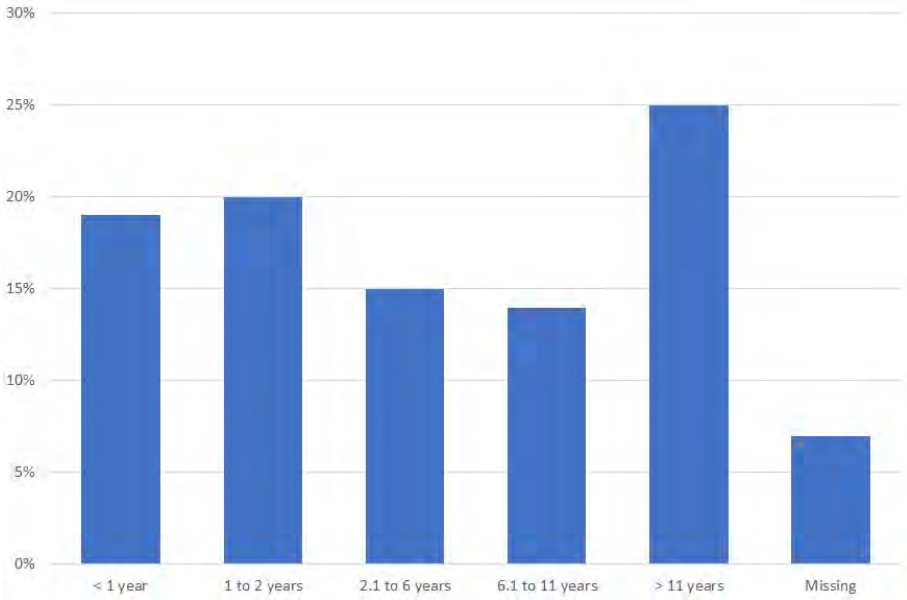


Figure 2. Duration of nr-axSpA Symptoms Before Diagnosis Established (N = 125)

Themes from Qualitative Interviews Patients (n = 25) and Rheumatologists (n = 15)	Quantitative Survey Findings Patients (N = 125)
Patients initially attribute back pain to normal wear and tear or age-related processes that do not require prompt medical care	58% initially thought their joint pains were due to activity or injury 26% thought their back pain was due to aging 20% thought their symptoms were growing pains due to their young age
Clinicians often minimize persistent symptoms, especially if they occur in young and/or female patients	34% reported their healthcare providers thought my symptoms were "in my head" 23% reported being told nr-axSpA is a "man's disease" (and so they couldn't have it). [female respondents only]
Physicians, including rheumatologists, do not know enough about nr-axSpA or inflammatory back disease	47% thought their HCPs attributed symptoms to activity or injury 28% reported that they were initially misdiagnosed
Specific biomarkers to facilitate diagnosis are currently lacking	38% thought that their normal x-rays or MRI were a barrier to timely diagnosis 13% felt that their negative HLA-B27 status contributed to delayed diagnosis
Delayed referral to rheumatologist	34% think medical professionals did not know to refer them to a rheumatologist 19% reported limited access to rheumatologists 12% requested a referral to a rheumatologist, but were denied
Seeing a rheumatologist does not necessarily lead to a prompt diagnosis	48% saw ≥2 rheumatologists before the diagnosis of nr-axSpA was made 25% reported receiving conflicting diagnoses from the rheumatologists they saw 13% reported that the rheumatologists they saw were unaware of nr-axSpA

Table 1. Barriers to nr-axSpA Diagnosis - Comparison of Qualitative and Quantitative Findings

Conclusion: Patients with nr-axSpA often see multiple HCPs before arriving at the diagnosis. While rheumatologists play a critical role in diagnosis, disease recognition by clinicians in other specialties is key for early referral. Findings suggest that both patients and clinicians may be unfamiliar with inflammatory back pain, and nr-axSpA—particularly in young, or female patients, or in those with normal x-rays. Education on the cardinal features, epidemiology, burden, and benefits of timely diagnosis of nr-axSpA is warranted for providers who commonly manage back pain.

1. Deodhar A, et al. Arthritis Rheum 2016;68:1669-1676.

Disclosure: S. Kiwalkar, None; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **R. Howard**, Novartis, 1, 5, AbbVie, 1, Amgen, 1, Bristol-Myers Squibb, 1, GSK, 1, Johnson & Johnson, 1, Lilly, 1, Merck, 1, Pfizer, 1, Teva, 1.

Abstract Number: 1870

Development of Candidate Criteria for Axial Disease in Juvenile Spondyloarthritis: An International Collaboration

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The lack of pediatric classification criteria for axial disease is a major impediment to the conduct of clinical trials for juvenile spondyloarthritis (SpA). Classification criteria for axial disease in children with SpA are being developed. The objective of this study was to identify and grade a set of items that maximizes the likelihood of accurate classification of children and adolescents with axial disease.

Methods: First, we conducted an item-generation exercise with an international group of pediatric rheumatologists to generate a comprehensive list of clinical, laboratory, and imaging features used to decide whether or not a child/adolescent has clinical evidence of axial involvement. Second, we performed a literature review to formulate a list of features used in juvenile and adult SpA clinical study inclusion criteria and adult axial SpA classification criteria. Next, we completed a grading exercise in which respondents in the item generation survey rated the features generated from the first 2 steps for specificity (-3 to +3), with anchors "much less likely to have axial disease" and "much more likely to have axial disease", respectively. Items with a mean score of zero or close to zero and redundant items were removed. The final list of items was reviewed by a panel of juvenile SpA experts and split into "entry criteria", which would be required for classification applicability, potential "additive criteria", and potential "exclusion" or "negatively weighted criteria". Additive and negatively weighted criteria were grouped into domains by an iterative process.

Results: One hundred and ninety-nine physicians from 45 countries proposed 108 items useful in the determination of axial involvement or not. Responses showed broad coverage but also high consistency. Responses were grouped into 15 domains with a range of 38-141 unique respondents noting ≥1 item in a domain. Most items were related to imaging, location of pain or stiffness, pattern of pain, genetics, range of motion, laboratory markers, and comorbidities. Literature review did not identify any additional clinical features to include in the item reduction exercise. In the grading exercise, 87 items had a mean score of ≥1.5 and 5 items ≤1.5. The expert panel reviewed the candidate items, grouped them into 6 independent domains, and identified 2 entry criteria, 2 exclusion criteria, 23 potential additive criteria, and 4 negatively weighted criteria (Table). The expert panel also voted to align criteria within the imaging domains with definitions provided by the OMERACT Juvenile Arthritis MRI Score (JAMRIS) international Working Group (1) when possible and to exclude radiographs and spinal MRI. Final additive and negatively-weighted criteria

Table. Inclusion, exclusion, additive, and negatively-weighted criteria

Eligibility criteria	Items
Inclusion criteria	PRINTO provisional revised updated criteria for enthesitis/spondylitis-related JIA (2):
	• Peripheral arthritis* and enthesitis OR
	• Arthritis* or enthesitis, plus ≥3 months of inflammatory back pain^ and sacroiliitis on imaging #, OR
	• Arthritis* or enthesitis plus ≥2 of the following:
	○ Sacroiliac tenderness
	○ Inflammatory back pain^
	○ Presence of HLA-B27
	○ Acute (symptomatic) anterior uveitis
	○ History of SpA in a 1st degree relative
	OR
	Physician diagnosis of spondyloarthritis
Exclusion criteria	High fevers
	Presence of rheumatoid factor or anti-cyclic citrullinated peptide
Domains	
Additive features	
Pain	Lumbar or sacroiliac or buttock daily pain for ≥6 weeks
	Hip or groin daily pain for ≥6 weeks
	Sacroiliac pain elicited on exam with deep palpation or by FABER/Mennell/Gaensien's maneuvers
Stiffness	Lumbar or sacroiliac or buttock stiffness
	Hip or groin stiffness
	Duration of stiffness
	Frequency of stiffness
	Improvement with exercise
	Improvement with rest
	Occurrence at night
Genetics	Family history of HLA-B27-associated disease in a 1st degree relative
	Presence of HLA-B27
Imaging: Active Inflammation	Subchondral inflammation/bone marrow edema
	Capsulitis
	Joint space enhancement
	Inflammation at the site of erosion
	Joint space fluid
	Enthesitis
Imaging: Chronic Inflammation/damage	Erosion
	Fat lesion/ fat metaplasia
	Fat metaplasia in an erosion cavity (Backfill)
	Sclerosis
	Ankylosis
Negatively-weighted features	Acute onset of pain
	Accompanying neurologic/radicular symptoms
	Total body pain
	Extreme tenderness to light touch (allodynia)

*Peripheral arthritis should be present for ≥6 weeks. ^≥4 of the following: improvement with exercise, pain at night, insidious onset, age at onset <40 years, and no improvement with rest (3). # modified NY criteria for radiographs(4) and ASAS MRI working group definitions of active sacroiliitis (5).

Acknowledgements: Volunteers for the initial Delphi exercise were solicited from the memberships of the Australian and New Zealand Paediatric Rheumatology groups, Canadian Rheumatology Association, the Childhood Arthritis and Rheumatology Research Alliance (CARRA), the international pediatric electronic bulletin board, Paediatric Rheumatology International Trials Organization (PRINTO), Pediatric Rheumatology Society of India, Pediatric section of the Brazilian Rheumatology Society, and the Society for Pediatric Rheumatology in Germany, Austria and Switzerland.

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2. Martini A, Ravelli A, Avcin T, Beresford MW, Burgos-Vargas R, Cuttica R, et al. Toward New Classification Criteria for Juvenile Idiopathic Arthritis: First Steps, Pediatric Rheumatology International Trials Organization International Consensus. J Rheumatol. 2019;46(2):190-7.
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5. Lambert RG, Bakker PA, van der Heijde D, Weber U, Rudwaleit M, Hermann KG, et al. Defining active sacroiliitis on MRI for classification of axial spondyloarthritis: update by the ASAS MRI working group. Ann Rheum Dis. 2016;75(11):1958-63.

will be determined after evaluation of the sensitivity and specificity of potential criteria in a development cohort of juvenile SpA cases.

Conclusion: The item-generation exercise, grading exercise, and expert panel's iterative work resulted in inclusion, exclusion, candidate additive and negatively weighted criteria. Refinement and weighting of criteria as well as determination of threshold for classification will be ascertained in the next phase.

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Abstract Number: 1871

Comparison of Work Productivity Outcomes Between Chronic Back Pain Patients with and Without a Diagnosis of Axial Spondyloarthritis After 2-Year Protocolised Follow-Up: Data from the Spondyloarthritis Caught Early Cohort

Anne Boel[1], Miranda van Lunteren[2], Karen Fagerli[3], Roberta Ramonda[4], Sofia Exarchou[5], Marleen van de Sande[6], Floris van Gaalen[7] and Désirée van der Heijde[8], [1]Leiden University Medical Centre, Hooge Zwaluwe, Netherlands, [2]Leiden University Medical Centre, Weesp, Netherlands, [3]Diakonhjemmet Hospital, Oslo, Norway, [4]University of Padova, Padova, Italy, [5]Rheumatology, Department of Clinical Sciences Malmö, Lund University, Malmö, Sweden, Malmo, Sweden, [6]Amsterdam UMC, AMC/University of Amsterdam, Department of Rheumatology and Clinical Immunology, Amsterdam Infection & Immunity Institute and Amsterdam Rheumatology and Immunology Center (ARC), Amsterdam, Netherlands, [7]Leiden University Medical Center (LUMC), Leiden, Netherlands, [8]Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The aim of this study was to compare work-productivity and activity impairment outcomes after two-year follow-up between chronic back pain (CBP) patients with and without an axSpA diagnosis

Methods: Patients over 16 years of age referred to the rheumatology outpatient clinic with chronic back pain (≥ 3 months < 2 years) starting before the age of 45, suspected of axSpA were included in the SPACE cohort. Follow-up was performed only in patients with at least two SpA features or one SpA feature with a positive likelihood ratio ≥6.4 (Rudwaleit, van der Heijde, Khan, Braun, & Sieper, 2004).

Work productivity was assessed using the Work Productivity and Activity Impairment (WPAI) general health version 1.0 questionnaire. Presenteeism was defined as a reduction in performance while at work due to disease; absenteeism was time missed from work due to disease; work productivity loss (WPL) was a combined measure of presenteeism and absenteeism; and activity impairment was impairment due to disease in all non-work related activities. All WPAI outcomes were presented as percentages between 0-100; higher scores implying greater impairment. Additionally, the proportion of patients with any (>0%) absenteeism, presenteeism, WPL and activity impairment were given.

Assessment of presenteeism, absenteeism and WPL was restricted to the working population, defined as having paid work at baseline and 2-year follow-up. Activity impairment was assessed for the entire study population. The employable population was defined as everyone of working age (>16), who was not a fulltime student.

In this study we included patients with a diagnosis axSpA or no axSpA (CBP group) all with a level of confidence ≥7 (on a 0-10 scale) after locally read imaging. Additionally, data had to be available on the WPAI questionnaire at both timepoints.

Regression models were used to test the difference between groups at two-year follow-up for each of the WPAI variables. Baseline WPAI values and NSAID-use over time were tested as confounders.

Table 1 Baseline characteristics of patients with a diagnosis of axSpA and those with CBP.

Characteristic	Diagnosis axSpA (N=181)	CBP (N=74)
Male, n(%)	101 (56)	22 (30)
Age (years), mean (SD)	30 (8)	31 (8)
Symptom duration (months), mean (SD)	13 (7)	13 (7)
HLA-B27 positive, n(%)	133 (73)	23 (31)
Number of SpA features, mean (SD)	5 (2)	3 (1)
Use of NSAIDs, n(%)	137 (76)	52 (70)
Employable population	*163 (90)*	*68 (92)*
Paid work, n(%)*	140 (86)	58 (85)

* Paid work at baseline, calculated based on the employable population.

axSpA, axial Spondyloarthritis; CBP, Chronic Back Pain; HLA-B27, Human Leucocyte Antigen B27; NSAIDs, Non-Steroidal Anti Inflammatory Drugs; SpA, Spondyloarthritis

Table 1. Baseline characteristics of patients with a diagnosis of axSpA and those with CBP.

Table 2 Work-productivity outcomes at baseline and two-year follow-up for the group with a diagnosis of axSpA and the group without a diagnosis.

Characteristic	Diagnosis axSpA		CBP		
	Baseline	2 years	Baseline	2 years	p-values
Working population	*N=124*		*N=52*		
Presenteeism, mean (SD) %	31 (28)	18 (24)†	40 (29)	30 (30)†	p=0.003*
Presenteeism present, %	73	52	87	67	
Absenteeism, mean (SD) %	7 (18)	4 (14)†	12 (25)	6 (21)†	p=0.334
Absenteeism present, %	22	7	27	12	
Overall work impairment, mean (SD) %	33 (29)	22 (27)†	43 (30)	35 (33)	p=0.005*
Overall work impairment present, %	72	46	87	65	
Total population	*N=181*		*N=74*		
Activity impairment, mean (SD) %	38 (28)	22 (24)†	50 (29)	33 (29)†	p=0.001*
Activity impairment, n(%)	86	64	93	70	

* Significant difference between groups at two years; after correction for baseline values and NSAID use over time ($p<0.05$).
†Significant improvement within group over time

Table 2. Work-productivity outcomes at baseline and two-year follow-up for the group with a diagnosis of axSpA and the group without a diagnosis.

Results: Patients with a diagnosis of axSpA were more frequently male and HLA-B27 positive and had more SpA features at baseline compared to the patients with CBP (Table 1). Age, symptom duration, NSAID-use and the percentage of patients with paid work at baseline were similar between groups.

The population having paid work at baseline and 2 years consisted of 124 patients (69%) in the axSpA group and 52 patients (70%) in the CBP group. In both groups the proportion of patients with any as well as the mean WPL reduces. This reduction was apparent in both presenteeism and absenteeism. Nevertheless, presenteeism, WPL and activity impairment were significantly higher at two-year follow-up in the group with CBP (Table 2). In these regression models with baseline values and NSAID-use over time as covariates, axSpA was an independent predictor of lower presenteeism, overall work impairment and activity impairment at two-year follow-up (data not shown).

Conclusion: Despite significant improvements in both groups, patients with a diagnosis of axSpA have significantly better work-related outcomes after two years of protocolised follow-up compared to patients with CBP.

Disclosure: A. Boel, None; **M. van Lunteren**, None; **K. Fagerli**, None; **R. Ramonda**, None; **S. Exarchou**, Novartis, 1; **M. van de Sande**, Boehringer Ingelheim, 2, AbbVie, 5, Eli Lilly, 2, 5, MSD, 5, 8, Janssen, 2, Novartis, 2, 5, 8; **F. van Gaalen**, Reuma Nederland, 1, Stichting vrienden van Sole Mio, 1, MSD, 1, Abbvie, 1, Novartis, 1; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5.

Abstract Number: 1872

Relative Associations of Sociodemographic, Clinical and HLA-B Alleles with Enthesitis and Peripheral Arthritis in Patients with Ankylosing Spondylitis

Benjamin Naovarat[1], Lianne Gensler[2], Michael Ward[3], Mark Hwang[4], Matthew Brown[5], Amirali Tahanan[6], Mohammad Rahbar[6], Mariko Ishimori[7], Michael Weisman[8] and John Reveille[9], [1]The University of Texas McGovern Medical School, Houston, TX, [2]University of California San Francisco, San Francisco, CA, [3]National Institutes of Health, Bethesda, MD, [4]McGovern Medical School at the University of Texas Health Science Center at Houston, Houston, TX, [5]Guy's and St Thomas, NHS Foundation Trust and King's College London NIHR Biomedical Research Centre, King's College London, London, United Kingdom, London, United Kingdom, [6]McGovern Medical School at UTHealth, Houston, [7]Cedars-Sinai Medical Center, Los Angeles, CA, [8]Cedars Sinai Medical Center, David Geffen School of Medicine at UCLA, Los Angeles, CA, [9]Department of Internal Medicine, University of Texas, Houston, TX

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Previous studies from Latin America have shown an association with peripheral arthritis in patients with spondyloarthritis with HLA-B*15 (as opposed to HLA-B27). We aimed to examine sociodemographic and clinical associations along with HLA-B alleles with peripheral arthritis and enthesitis in a longitudinal cohort of AS patients.

Methods: AS patients were derived from the Prospective Study of Outcomes in Ankylosing Spondylitis (PSOAS)/ Australo-Anglo-American Spondyloarthritis (TASC) Cohort. All patients met the modified New York Criteria for AS. In addition to a baseline visit (where a history of peripheral arthritis, heel pain and other comorbidities was ascer-

Factor	Achilles Tendonitis or Plantar Fasciitis N=314	No Achilles Tendonitis or Plantar Fasciitis N=459	P value	OR (CI)
Male, %	65.6	78.0	0.0001	0.54 (0.39, 0.74)
White, %	78.0	78.4	0.96	0.98 (0.69, 1.38)
Joint Swelling, %	20.1	12.0	0.003	1.84 (1.24, 2.74)
Smoking, %	15.9	19.3	0.37	0.79 (0.51, 1.24)
BASFI>40, %	43.7	30.9	0.0005	1.73 (1.28, 2.35)
Exercise >120 minutes/week, %	42.5	46.5	0.34	0.85 (0.63, 1.16)
NSAID use, %	65.0	66.2	0.77	0.95 (0.70, 1.28)
Anti-TNF Use, %	54.3	41.5	0.0006	1.68 (1.25, 2.24)
Sulfasalazine Use, %	9.3	5.7	0.08	1.69 (0.97, 2.93)
Methotrexate Use, %	10.9	5.3	0.006	2.19 (1.27, 3.78)
Sulfasalazine or Methotrexate Use, %	19.6	10.4	0.0004	2.11 (1.40, 3.18)
ESR > 20, %	27.9	27.2	0.91	1.04 (0.74, 1.45)
CRP >0.8 mg/dL, %	31.4	34.4	0.44	0.87 (0.63, 1.20)

Table 1. Associations of Achilles Tendonitis or Plantar Fasciitis on Clinical Evaluation at any Study Visit

Factor	Joint Swelling N=113	No Joint Swelling or h/o peripheral arthritis N=345	P value	OR (CI)
Male versus Female	66.4	81.5	0.001	0.45 (0.28,0.72)
White vs Non White	80.5	80.6	1.0	1.0 (0.58, 1.70)
Smoking	18.5	15.7	0.68	1.22 (0.63, 2.36)
BASFI>40	50.0	19.9	$<1x10^{-9}$	4.02 (2.51, 6.44)
Exercise >120 minutes/week, %	25.2	51.8	5.3×10^{-7}	0.31 (0.20, 0.49)
NSAID use, %	28.5	34.5	0.30	0.76 (0.48, 1.21)
Anti-TNF Use, %	54.5	38.7	0.007	1.90 (1.21, 2.97)
Sulfasalazine Use, %	9.82	3.52	0.027	3.00 (1.20, 7.43)
Methotrexate Use, %	16.1	4.30	0.003	4.27 (1.94, 9.37)
Sulfasalazine or Methotrexate Use, %	25.0	7.81	1×10^{-5}	3.93 (2.10, 7.35)
ESR > 20, %	37.0	26.8	0.08	1.61 (0.97, 2.65)
CRP >0.8 mg/dL, %	18.5	15.7	0.68	1.22 (0.63, 2.36)

Table 2. Associations of Joint Swelling by Physical Exam At Any Study Visit

Factor	Enthesitis N=668	No Enthesitis N=587	P value	OR (CI)
Male, %	65.6	78.0	0.75	0.95 (0.72, 1.27)
White, %	70.4	79.2	0.0004	0.98 (0.48, 0.81)
Joint Swelling, %	19.5	9.20	0.0003	2.39 (1.49, 3.82)
Smoking, %	15.9	19.3	0.14	1.32 (0.93, 1.86)
BASFI>40, %	41.0	35.5	0.067	1.26 (0.99, 1.61)
Exercise >120 minutes/week, %	43.3	51.0	0.046	0.73 (0.55, 0.98)
NSAID use, %	67.6	68.4	0.86	0.96 (0.72, 1.29)
Anti-TNF Use, %	46.5	38.9	0.03	1.36 (1.03, 1.80)
Sulfasalazine Use, %	8.90	5.61	0.10	1.64 (0.93, 2.87)
Methotrexate Use, %	7.2	7.3	1.00	1.00 (0.59, 1.68)
Sulfasalazine or Methotrexate Use, %	15.7	11.6	0.11	1.42 (0.94, 2.14)
ESR > 20, %	29.0	23.6	0.12	1.33 (0.95, 1.86)
CRP >0.8 mg/dL, %	34.2	32.6	0.71	1.07 (0.79, 1.46)

Table 3. Associations of Enthesitis by Physical Exam at any Study Visit

tained), study visits were conducted every 4 to 6 months consisting of an evaluation of spinal mobility, joint swelling/tenderness count, examination of enthesitis (using the UCSF Enthesitis Index) and disease activity (BASDAI, C-reactive protein [CRP], erythrocyte sedimentation rate [ESR]) and functional measures (Bath Ankylosing Spondylitis Functional Index [BASFI], exercise history) and medication use (NSAIDs, anti-TNF blockers, sulfasalazine (SSZ) and methotrexate (MTX). Relative predispositional effects analysis (RPE) was used to adjust for the effect of HLA-B*27 at the HLA-B locus to mask the alleles and analyze the other alleles for associations. Statistics were done using univariable and multivariable analyses for peripheral arthritis and enthesitis in association with clinical, sociodemographic factors, medications and HLA-B alleles.

Results: There were 1076 white AS patients with HLA-B typing included in this analysis. In the case of heel pain by history, at baseline visit affected AS patients were less likely to be taking NSAIDs, but more likely to be exercising >120 minutes a week and to have elevated ESR or CRP at baseline visit, even on multivariable analysis. For those found to have Achilles tendonitis or plantar fasciitis on physical exam, affected individuals were more likely to be female, to have concomitant joint swelling, to be functionally impaired (BASDAI > 40 mm), to be using anti-TNF agents and either MTX or SSZ (Table 1). For those with arthritis on physical exam (defined as joint swelling), again, associations were found with female gender, functional impairment (BASFI) >40 mm), to be exercising < 120 minutes/week, and to be using anti-TNF agents as well as MTX or SSZ (Table 2). Enthesitis at any point in the UCSF Enthesitis Index at any visit was associated with nonwhite ethnicity, concomitant joint swelling, a lower likelihood of regular exercise, and anti TNF use, as well as (marginally) with functioning less well (Table 3). No HLA-B association was found with heel pain, Achilles tendonitis or plantar fasciitis or enthesitis elsewhere, though the association with HLA-B15 persisted with peripheral arthritis.

Conclusion: This association study in a large prospective AS cohort shows a higher prevalence of peripheral musculoskeletal manifestations of AS in women, and the impact on physical function and activity and the concomitant use biologic and nonbiologic DMARDS. Further work is underway examining modifiable factors that might actually predict the future presence of arthritis and enthesitis in these patients.

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Abstract Number: 1873

The Changing Profile of Ankylosing Spondylitis in the Biologic Era

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: To compare disease characteristics, comorbidities, and medication utilization of 573 patients with ankylosing spondylitis (AS) with short (< 20 years) disease duration (from symptom onset) and 568 patients with long disease duration (≥ 20 years) enrolled in the Prospective Study of Outcomes in AS (PSOAS)/Australo-Anglo-American (TASC) study over three different periods of time (2003-2006, 2007-2015, 2015-2019) and followed longitudinally.

Table 1. Demographic/Clinical Characteristics and Medication Utilization of Patients across time periods with Baseline Disease Duration <20 years At Latest Interval Visit

Variable	Patients Enrolled 2002-2006*	All Patients Seen 2007-2014**	All Patients Seen 2015-2019**	p-value [a]
	N=220	N=433	N=267	
BASDAI, median (IQR)	3.5 (1.7, 5.7)	2.7 (1.2, 4.8)	2.0 (1.0, 3.9)	<0.0001
BASFI, median (IQR)	22.0 (9.1, 43.6)	17.6 (5.0, 39.8)	15.0 (4.0, 32.0)	0.004
HLA-B27 positive, %	87.0	80.1	81.9	0.02
NSAID use overall, %	82.8	58.9	53.6	<0.0001
TNFI use overall, %	27.1	55.9	60.7	<0.0001
Non-biologic DMARD use overall [c], %	23.7	11.8	10.1	0.002
Methotrexate, %	10.8	4.4	2.3	0.003
Prednisone use, %	7.4	3.5	3.8	0.02
Opioid use, %	11.8	14.6	10.9	0.03

* first visit; ** most recent visit; IQR: Inter-quartile range

a: overall p-values for all three groups based on regression models after adjusting for sites (logistic regressions for categorical variables; linear regressions for normally distributed continuous variables (age at enrollment, age at disease onset); Poisson regressions for non-negative continuous variables that are highly skewed)

Table 1. Demographic/Clinical Characteristics and Medication Utilization of Patients Across Time Periods with Baseline Disease Duration <20 years At Latest Interval Visit

Table 2. Clinical Features of 218 Patients Followed At Least Eight years Comparing Baseline and Most Recent Visit

	Long Term Patients (>8 years) Enrolled 2002-2010* Baseline Visit	Long Term Patients (>8 years) Enrolled 2002-2010 Most recent visit 2010-2019**	p-value [a]
BASDAI, median (IQR)	2.9 (1.5, 4.8)	2.6 (1.2, 4.5)	0.04
ESR mm/hr, median (IQR)	9.0 (4.0, 20.0)	6.0 (2.0, 14.0)	<0.001
CESD, median (IQR)	9.0 (4.0, 16.0)	8.0 (3.0, 14.0)	0.02
Patient global assessment of pain, median (IQR)	27.5 (13.0, 51.0)	20.0 (10.0, 50.0)	0.02
Hypertension (self-reported), %	22.5	32.9	0.001
NSAID use overall, %	68.8	51.8	<0.0001
TNFi use overall, %	44.5	54.1	0.01
mSASSS, median (IQR)	10.0 (0, 36.0)	16.0 (0, 46.0)	<0.0001

* first visit; ** most recent visit; IQR: Inter-quartile range

a: overall p-values for all three groups based on regression models using generalized estimating equation (GEE) to account for within-patient correlations (logistic regressions for categorical variables; linear regressions for normally distributed continuous variables (age, age at disease onset, disease duration); Poisson regressions

Table 2. Clinical Features of 218 Patients Followed At Least Eight years Comparing Baseline and Most Recent Visit

Table 3. Characteristics of Australian Patients Compared to US Patients

Variable	All AUS Patients* N=91	US Patients Enrolled 2007-2014* N=490	p-value[a]	All AUS patients seen 2015-17** N=73	All US Patients Seen 2015-2018** N=466	p-value[a]
Greater than 12th grade education, %	33.0	84.4	<.0001	30.1	88.6	<.0001
Exercise >120 minutes /week, %	62.6	47.2	0.03	56.2	54.1	0.24
Ever smoke tobacco, %	56.0	41.0	0.02	53.4	32.0	0.02
BASDAI (0-10 cm VAS), median (IQR)	2.2 (1.1, 3.9)	4.3 (2.1, 6.2)	<0.001	1.8 (1.0, 2.6)	2.40 (1.2, 4.7)	<0.001
BASFI (0-100 cm VAS), median (IQR)	17.40 (8.6, 36.6)	28.2 (11.4, 55.0)	<0.001	16.00 (9.0, 30.0)	22.0 (8.6, 36.5)	<0.001
ESR mm/hr, median (IQR)	9.00 (7.0, 18.0)	11.0(4.0, 24.0)	0.002	11.0 (7.0, 16.0)	7.0 (2.0, 16.0)	<0.001
CRP mg/dL, median (IQR)	0.2 (0.2, 0.8)	0.5 (0.2, 1.3)	0.09	0.2 (0.2, 0.4)	0.3(0.1, 0.7)	0.008
CESD, median (IQR)	8.0 (4.0, 12.0)	12.0 (6.0,20.0)	<0.001	8.0 (3.0, 13.0)	8.0 (3.0, 15.0)	0.02
Patient global assessment of pain, median (IQR)	18.0 (10.0, 35.0)	38.0(18.0, 70.0)	<0.001	10.0 (10.0, 30.0)	20.0 (10.0, 50.0)	<0.001
NSAID use overall, %	58.2	69.1	0.01	39.7	50.9	0.003
TNFi use overall, %	76.9	41.7	<.0001	89.0	56.7	<.0001

*Parameters recorded from first available visit; **Parameters recorded from most recent visit IQR: Inter-quartile range
a: p-values for the comparison between two groups based on regression models (logistic regressions for categorical variables; linear regressions for normally distributed continuous variables (age, age at disease onset, disease duration); Poisson regressions for non-negative continuous variables that are highly skewed) after adjusting for sites and early-adherence (4.4%, 28.6%, 0%, 11.2% for each of four groups, respectively)

Table 3. Characteristics of Australian Patients Compared to US Patients

Methods: Study visits were carried out every 6 months examining disease activity (Bath AS Disease Activity Index (BASDAI), C-reactive protein, erythrocyte sedimentation rate), functional impairment, depression, and medication utilization as well as clinical assessments of joint and entheseal involvement as well as spinal mobility and radiographic severity. Groups were compared with regression models using generalized estimating equation, linear and Poisson regressions after adjusting for sites and for patients withdrawing from the study at less than two years follow-up.

Results: Looking at those 573 U.S. patients with short disease duration (< 20 years), NSAID and non-biologic DMARD (particularly methotrexate) and prednisone use decreased over time and TNFi use rose between the initial period of enrollment (2002-2006) and the last period (2015-2019) (Table 1). During the middle period of the study (2007-2014) there was a slightly higher frequency of cardiovascular disease and opioid use that fell in the latest period of the study. No differences were seen over time in marital status, education level, frequency of exercising or either comorbidities associated with AS such as uveitis or psoriasis or comorbidities not directly disease related such as diabetes or osteoporosis (data not shown). Looking at those 568 U.S. patients with longer disease duration (≥20 years), there was a fall in functional impairment, current smoking rates and NSAID use comparing the initial study visits as well as the most recent study visits over the three phases of the study (data not shown). Disease activity, depression scores and NSAID use decreased and anti-TNF use increased between baseline and last followup visits in those followed > 8 years despite an increase in mSASSS scores over time (Table 2). The 91 Australian patients enrolled were more likely to be white (100% versus 74.3% of US patients, p< 0.00001), had lower disease activity (BASDAI, ESR, CRP), functional impairment and depression scores, and less NSAID and much more TNF inhibitor usage (Table 3) and secukinumab usage (4.1% vs 2.2% of US patients), despite having lower educational levels and a higher frequency of smoking.

Conclusion: Patients with AS enrolling in this multicenter longitudinal cohort have improved disease profiles and different medication utilization over time, including gr perhaps reflecting innovations in treatment and increasing disease awareness. The improved disease parameters seen in the Australian patients may be due to the much higher use of TNF blockers provided from their National Health Care Service compensating for other bad prognostic factors in this cohort (smoking, lower educational status).

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Abstract Number: 1874

Differences Between Men and Women in the Patient Pathways to Diagnosis of Ankylosing Spondylitis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Healthcare claims databases can be used to identify patients with ankylosing spondylitis (AS) prior to diagnosis. This study explores differences in pathways to AS diagnosis between men and women by examining the coding of health events over the 2 years prior to AS diagnosis.

Methods: This retrospective cohort study collected administrative claims data from patients in the Truven Health MarketScan® Commercial and Medicare Supplemental Databases from January 2006 to April 2019. The AS population included all patients aged ≥ 18 years with ≥ 2 diagnoses of AS (ICD-9-CM/ICD-10-CM) ≥ 30 days apart who had ≥ 2 years of continuous enrollment prior to first AS diagnosis. Male patients with AS were matched 1:1 to female patients with AS by age, date of AS diagnosis, insurance type, and enrollment duration. Diagnosis codes and physician types were examined over the 2 years prior to AS diagnosis and stratified by men vs women. A set of 1906 AS-related codes in men and women was examined using univariate χ^2 tests.

Results: A total of 7744 patients met the inclusion criteria for diagnosis of AS. The mean (SD) age for men and women, respectively, was 45.1 (14.4) and 45.3 (14.1) years; women were less likely than men to be working full time (41.2% vs 47.1%) (**Table 1**). Of 1906 codes examined for differences between men and women, 281 codes showed significant differences, some of which are highlighted in **Tables 2** and **3**. In general, women had more overall coding than men across diagnoses and providers. The greatest difference between men and women in categorized disease features was observed for peripheral symptom coding (57.7% of women vs 43.9% of men) (**Table 2**). Compared with men, women also showed much greater levels of other MSK coding (52.8% vs 40.0%), unspecified coding (59.6% vs 46.9%, and depression (21.2% vs 9.8%). Only gout was significantly more common in men vs women (6.5% vs 2.2%). These differences were observed throughout the 2 years prior to AS diagnosis. However, coding for backache

Table 1. Baseline Demographics of Men and Women Diagnosed With AS

Characteristic	Men (N = 3872)	Women (N = 3872)
Age, mean (SD), years	45.1 (14.4)	45.3 (14.1)
Work status, %		
Active full time	47.1	41.2
Active part time	0.5	1.3
Early retiree	6.1	5.0
Medicare-eligible retiree	6.2	6.7
Insurance type, %		
Commercial	90.2	90.2
Medicaid	1.2	1.2
Medicare	8.6	8.6
US geographical region, %		
Northeast	18.2	18.3
North central	18.0	14.2
South	43.4	46.8
West	18.8	18.9
Unknown	1.7	1.8

AS, ankylosing spondylitis.

gradually increased in men starting at 12 months before AS diagnosis, whereas axial and sacroiliitis coding increased sharply in men immediately before AS diagnosis, suggesting differences between men and women in pathways to AS or in presentation of disease. When looking at physician types visited in the 2 years prior to AS diagnosis, the greatest difference was observed for rheumatologists (64.2% of women vs 45.1% of men; difference = 19.1%) (**Table 3**).

Conclusion: This analysis revealed differences between men and women in the time leading up to diagnosis of AS, with the greatest variations observed for peripheral vs axial coding, unspecified coding, MSK symptoms, and depression. These findings, over a range of codes, are consistent with differences in disease phenotype between men and women that result in divergent pathways to diagnosis of AS. Women showed greater levels of coding regardless of the code being examined. A greater number of visits to community rheumatologists for women vs men support the hypothesis that there is a greater challenge in diagnosing the AS disease spectrum in women vs men by clinicians, which merits further investigation. These differences potentially contribute to a delayed, burdened journey to diagnosis of AS in women compared to men.

Table 2. Differences in the Proportion of Men and Women Who Had Different Categorized Diagnosis Features in the 2 Years Prior to AS Diagnosis

Grouped Diagnoses	Men, %	Women, %	Difference, %
Peripheral*	43.9	57.7	−13.7†
mSK NOS	40.0	52.8	−12.8†
Unspecified	46.9	59.6	−12.7†
Depression	9.8	21.2	−11.4†
Other malaise and fatigue	18.1	28.2	−10.1†
Skin	26.9	36.4	−9.4†
Rheumatoid arthritis	12.0	20.9	−8.9†
Inflammatory polyarthropathy‡	11.9	20.7	−8.8†
Osteoarthritis	25.5	34.0	−8.5†
GERD	13.1	21.0	−8.0†
Spondylopathy	17.6	24.0	−6.4†
Enthesitis	11.7	17.5	−5.8†
Axial§	50.0	54.6	−4.7
Fibromyalgia	0.7	4.3	−3.6†
Obesity	5.3	8.8	−3.4†
Sacroiliitis	8.8	12.1	−3.4†
Backache	20.1	22.9	−2.8
Inflammatory bowel disease	5.6	5.4	0.1
Psoriasis	4.0	3.4	0.6
Psoriatic arthritis	5.3	4.6	0.8
Gout	6.5	2.2	4.3†

AS, ankylosing spondylitis; GERD, gastroesophageal reflux disease; mSK NOS, musculoskeletal not otherwise specified.

* "Peripheral" comprises > 150 codes relating to pain or arthritis in hands/wrists, elbows, arms, feet/ankles, knees, and legs, and includes coding for rheumatoid arthritis, osteoarthritis, and enthesitis.

† *P* value < Bonferroni-corrected threshold of 0.05/1906.

‡ "Inflammatory polyarthropathy" includes codes for inflammatory polyarthropathy (ICD-10-CM, M064), unspecified inflammatory polyarthropathy (ICD-9-CM, 714.9), and other specified inflammatory polyarthropathies (ICD-9-CM, 714.89).

§ "Axial" comprises > 50 codes relating to axial disorders and syndromes, and includes coding for spondylopathy, sacroiliitis, and backache.

Table 3. Differences in the Proportion of Men and Women Who Visited Different Specialties During the 2 Years Prior to AS Diagnosis

Specialty	Men, %	Women, %	Difference, %
Rheumatology	45.1	64.2	−19.1*
Pathology	30.8	49.4	−18.6*
Radiology	67.1	82.3	−15.2*
Acute care hospital	68.1	81.6	−13.5*
Anesthesiology	24.1	37.1	−13.0*
Laboratory	58.6	69.8	−11.2*
Gastroenterology	18.8	27.0	−8.3*
Neurology	11.0	19.2	−8.2*
Imaging center	10.1	15.5	−5.4*
Ambulatory surgery centers	11.9	16.8	−4.9*
Psychiatry/psychology	7.4	12.0	−4.6*
Cardiovascular disease/cardiology	20.1	24.6	−4.5*
Therapy (physical)	19.7	24.2	−4.5*
Orthopedic surgery	32.9	37.2	−4.3
General practitioner	86.1	89.5	−3.4

AS, ankylosing spondylitis.
* *P* value < Bonferroni-corrected threshold of 0.05/1906.

Disclosure: M. Hwang, Novartis, 5, University of Texas Health Science Center at Houston (UTHealth) Center of Clinical and Translational Sciences KL2 program, 2; **M. Rozycki**, HVH Precision Analytics, 3; **T. Arndt**, HVH Precision Analytics, 3; **E. Yi**, Novartis Pharmaceuticals Corporation, 3; **M. Weisman**, Novartis, 5, GSK, 5, UCB, 5, Lilly, 5.

Abstract Number: 1875

Heterogeneity Amongst Men and Women with Ankylosing Spondylitis and Non-Radiographic Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (axSpA) includes both ankylosing spondylitis (AS) and non-radiographic axial disease (nr-axSpA). Our purpose was to investigate genetic heterogeneity of clinically diagnosed axSpA.

Table 1:

Affection Status	Gender	HLA-B27+	HLA-B27-	PRS (SE)
Unaffected	Male	69 (37.9%)	113 (62.1%)	0.0754 (0.023)
	Female	94 (43.5%)	122 (56.5%)	0.0376 (0.023)
	Total	163	235	
nr-axSpA	Male	19 (79.2%)	5 (20.8%)	0.104 (0.067)
	Female	17 (53.1%)	15 (46.9%)	0.322 (0.068)
	Total	36	20	
mNYAS	Male	115 (91.3%)	11 (8.7%)	0.418 (0.020)
	Female	40 (95.2%)	2 (4.8%)	0.377 (0.019)
	Total	155	13	
Clinical AS	Male	134 (89.3%)	16 (10.7%)	
	Female	57 (77%)	17 (23.0%)	
	Total	191 (85.3%)	33 (14.7%)	

1. Li Z, de Guzman E, Harris J, et al. Genetic Risk Score Prediction in Ankylosing Spondylitis. Arthritis Rheum 2018;70:1-3553.

Methods: In 1985 members of the Swiss AS Patient Society who had been diagnosed as having AS by their own physicians, and also their first-degree relatives whether or not they had any rheumatic disease, were invited to participate in this study. 1178 subjects, 355 of them probands, formed our study cohort. Participants completed questionnaires on disease manifestations, underwent rheumatological examination of axial and peripheral joints, and radiography of the sacroiliac joints. Further, they provided blood samples for genetic studies, including HLA-B27. Radiographs were graded according to the modified New York (mNYAS) criteria for AS. Patients diagnosed clinically with AS but with negative radiographs were considered to have nr-axSpA, whereas those with negative clinical diagnoses and radiographs were considered healthy. DNA from 702 participants was genotyped using Illumina CoreExome arrays, and a polygenic risk score (PRS) calculated from this genotype data, as previously reported[1]. Discriminatory capacity of the PRS between diagnostic groups, and comparing males and females was examined by receiver operator characteristic area under the curve (AUC) analysis.

Results: HLA-B27 was present in 191/224 (85.3%) probands, with HLA-B27 carriage being more common in men than women (odds ratio (OR)= 2.50, p=0.015). The lower HLA-B27 carriage amongst women clinically diagnosed with AS was due to a higher proportion of women with nr-axSpA than with AS being HLA-B27 negative (OR=3.35, P=0.044), with no difference in the HLA-B27 carriage rates of men and women with mNYAS (P=0.41). Considering PRS, both men and women with mNYAS, but only men with nr-axSpA, had higher PRS than healthy subjects ($P< 5x10^{-4}$ all comparisons). The PRS was higher in men than women with nr-axSpA (0.32 vs 0.10, P=0.029), whereas no difference in PRS was observed comparing men and women with mNYAS (0.80 vs 0.78, P=0.60). Whilst the PRS clearly distinguished males with nr-axSpA from healthy subjects (AUC=0.73, $P=1.9x10^{-4}$), it was not able to distinguish females with nr-axSpA from healthy subjects (AUC=0.51, P=0.90). The PRS was not able to distinguish men with mNYAS from those with nr-axSpA (AUC=0.50), whereas it clearly distinguished women with mNYAS from those with nr-axSpA (AUC=0.73, $P=6.4x10^{-4}$).

Conclusion: Whilst men and women with mNYAS have disease that is genetically similar, and men with nr-axSpA had PRS that was similar to mNYAS and distinct from healthy subjects, women with nr-axSpA had similar PRS to healthy subjects and distinct from women with mNYAS. This indicates that women clinical diagnosed with AS, but who are x-ray negative, as a group have a disease that is distinct from mNYAS overall, and from nr-axSpA in men. This study also demonstrates that PRS have good discriminatory performance for nr-axSpA in men.

Disclosure: Z. Li, None; **M. Khan**, None; **M. Khan**, None; **P. Villiger**, None; **H. Baumberger**, None; **H. Zandwijk**, None; **S. van der Linden**, None; **M. Brown**, None.

Abstract Number: 1876

The Role of HLA B27 in Axial Spondyloarthritis: Prevalence and Performance as a Marker in an Argentinian Cohort

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: HLA B27 prevalence in Latin America are heterogeneous and timeless, we propose to estimate the prevalence of HLA B27 in an Argentinian cohort of axial spondyloarthritis (SpA) and to evaluate the differences between positive and negative patients and to analyze its performance as a diagnostic biomarker.

Methods: An observational study included patients older than 18, with axial SpA diagnosis performed in a fast track evaluation program (Reuma-check SpA) between 2017-19. In this circuit, all patients underwent: blood tests, HLA B27, sacroiliac Rx, sacroiliac MRI and enthesitis ultrasound. Sociodemographic data and education level were also collected. SpA symptoms: Age of onset and characteristic of low back pain, SpA features, NSAIDs use and response, VAS: pain and night pain, time of morning stiffness. BASDAI, BASFI, MASES, HAQ was consigned. The clinical assessor was blinded to the complementary studies. For the sensitivity and specificity analysis, a group of patients with chronic low back pain who performed the same circuit in the same period of time were used as a control, paired 1:1 (gender and age).

Statistical analysis: descriptive statistics, Chi2 test or Fisher's exact and Student or Mann Whitney test were performed. Binomial logistic regression was performed, and sensitivity, specificity, PPV, NPV and LR were calculated.

Results: 150 patients were included, 75 with axial SpA and 75 controls, the characteristics are showed in Table 1. The prevalence of HLA B27 in SpA patients was 43% (CI95: 30-53). The differences between positive and negative patients are shown in table 2. In the logistic regression analysis, BASFI values and the SpA features showed independent differences. When this prevalence was compared with those of the control group the difference was 43% vs 9% OR: 7.7 (IC95: 2.8-24), HLA B27 had a sensitivity: 43%, specificity: 91 %, PPV: 85%, NPV: 58% and LR: 4.9 (IC95: 3-8).

Table 1: Characteristics of SpA Patients vs. non-SpA controls.

Varables	SpA axial(N: 75)	Cronic back pain (N:75)
Age (SD)	46 (12)	43 (10)
Male (%)	43	44
Low back pain onset age (SD)	39 (11,5)	39 (11,6)
Low back pain time (months)	37,2 (13-121)	33 (12-75)
Smoking (%)	42	48
SpA features (%)	41	24
SpA family history (%)	29	23
NSAIDs good response (%)	59	42
SI x-ray + (%)	52	17
SI MRI + (%)	63	15
Entesitys untrasound + (%)	46	17
VAS pain (SD)	7,1 (1,3)	6,1 (2,1)
VAS night pain (SD)	5,8 (2,5)	4,9 (2,6)
Morning stiffness (mint)	30 (15-40)	15 (7,5-30)
BASFI (SD)	4,4 (1,8)	3,3 (1,5)
BASDAI (SD)	5,5 (1,4)	3,6 (2,69)
MASES (SD)	1,9 (3)	0,73 (1,4)
HAQ (IQR)	0,75 (0,5-1)	0,5 (0,3-1)
CRP mg/L (IQR)	2 (1-6)	1 (1-3)
GSV 1 hr (IQR)	17 (10-25)	11 (6-20)

Conclusion: The prevalence of HLA B27 in axial SpA was 43%, positive patients had an earlier age of onset (36 years) and negative BASFI higher and more SpA features. For the diagnosis of SpA, HLA B27 had a good specificity but low sensitivity (91% vs 43).

Table 2. Difference between HLA B27 positive and negative.

	HLA B27 positive (32)	HLA B27 negative (43)	p
Male (%)	54	36	0,2
Low back pain onset age (SD)	**36 (28,5-41,7)**	**43 (33,5-49)**	**0,009**
Educationla level (IQR)	13 (11,5-15)	14 (10-16)	0,7
Inflamatory LBP (%)	86	87	0,8
Low back pain time (months)	37 (13,4-121)	37 (12,8-121)	0,8
Smoking (%)	43	41	0,8
SpA featuring(%)	**29**	**50**	**0,07**
SpA family history (%)	36	25	0,3
NSAIDs good response (%)	61	61	0,8
Sacroiliac test+(%)	58	62	0,7
Anterior chest pain (%)	36	23	0,2
Enthesitis (%)	36	52	0,1
Peripheral involment (%)	18	30	0,2
SI x-ray + (%)	54	51	0,8
SI MRI + (%)	50	72	0,08
Entesitys untrasound + (%)	58	39	0,09
Pain VAS (IQR)	7 (6-8)	7 (7-8)	0,9
Night painVAS (IQR)	6,5 (5-8)	7 (4-7)	0,8
Morning stiffness (mint-IQR)	30 (15-45)	30 (15-40)	0,7
BASFI (IQR)	**4 (2,5-6)**	**5,1 (4-6)**	**0,05**
BASDAI (IQR)	5 (2,7-6)	4 (3,2-5,3)	0,3
MASES (IQR)	0 (0-2)	1 (0-2)	0,2
HAQ (IQR)	0,63 (0,5-0,8)	0,8 (0,6-1)	0,2
CRP mg/L (IQR)	3 (1-7,5)	2 (1-6)	0,4
GSV 1 hr (IQR)	18 (8,5-35)	17 (11,2-25)	0,8

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Abstract Number: 1877

Diagnosis of Axial Spondyloarthritis: A Primary Unmet Educational Need for Rheumatologists Is Interpretation of MRI

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Assessors	Mean % Concordance (range) for diagnosis of axSpA		
	Stage 1	Stage 2	Stage 3
Experts in axSpA	64.2 (45-80)	75.8 (65-85)	84.2 (70-95)
Local rheumatologist vs Experts in axSpA	73.8 (70-80)	83.8 (80-85)	83.8 (80-90)
pF rheumatologist 1 vs Experts consensus	78.9	94.4	94.7
pF rheumatologist 2 vs Experts consensus	89.5	61.1	68.4
pF rheumatologist 3 vs Experts consensus	63.2	72.2	84.2
pF rheumatologist 4 vs Experts consensus	89.5	66.7	68.4

Background/Purpose: Diagnosis of axial spondyloarthritis (axSpA) is challenging because of absent physical findings in early disease and the limited diagnostic performance of laboratory markers. Considerable reliance is placed on imaging of the sacroiliac joints (SIJ). We aimed to identify what might be the primary unmet educational needs of rheumatologists completing fellowship training within the past 6 years (post-F) by using clinical and imaging data from an inception cohort of consecutive patients presenting with undiagnosed back pain. We hypothesized that concordance between post-F rheumatologists and axSpA experts would increase after imaging data is reviewed following the clinical data.

Methods: The diagnosis of axSpA was compared between local site rheumatologists recruiting patients for the cohort, axSpA experts who reviewed the diagnostic ascertainments, and post-F rheumatologists who assessed clinical and imaging data from the multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study. In this inception cohort, consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain undergo routine diagnostic evaluation by a local SASPIC rheumatologist, including imaging of the SIJ, who then records a global evaluation of presence/absence of axial SpA. This is done at 3 consecutive stages: 1.After the clinical evaluation. 2.After the results of labs (HLA B27, CRP) and radiography. 3.After review of the local MRI report. In this exercise, 20 cases were selected from the SASPIC cohort with an equal distribution of axSpA and non-axSpA cases. Four experts in axSpA reviewed the clinical and imaging data in each eCRF in a sequential manner and provided their global diagnostic evaluations blinded to the assessments of local site rheumatologists for stages 1, 2, and 3 of these 20 cases. Subsequently, 4 post-F rheumatologists conducted the same exercise blinded to the assessments of the local site rheumatologist and experts in axSpA. Concordance (% agreement) between the assessors was analyzed.

Results: Diagnosis of axSpA by the local SASPIC rheumatologist was made in 90%, 65%, and 75% of cases after stages 1, 2, and 3, respectively. Majority diagnosis of axSpA by experts was made in 84.2% (16/19), 57.9% (11/19), and 63.2% (12/19), after stages 1,2, and 3, respectively. Majority diagnosis of axSpA by post-F rheumatologists was made in 94.4% (17/18), 100% (16/16), and 93.8% (15/16). Concordance among experts and between experts and local SASPIC rheumatologists increased after review of imaging data. For post-F rheumatologists concordance with experts increased after review of imaging for 2 assessors and decreased for the other 2 assessors. For the latter, the primary reason for decrease in concordance with experts was false positive diagnosis of axSpA in 35% and 30% of the cases after review of the imaging.

Conclusion: A structured case-based and sequential evaluation of clinical and imaging data suggests a gap in the training of recently graduated rheumatologists, with over-interpretation of imaging leading to false positive diagnosis of axSpA.

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Abstract Number: 1878

Consensus Definitions for MRI Lesions in the Spine of Patients with Axial Spondyloarthritis: First Analysis from the Assessments in SpondyloArthritis International Society Classification Cohort

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SESSION INFORMATION

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Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: A broad spectrum of MRI lesions has been described in the spine of patients with axial spondyloarthritis (axSpA) and a recent consensus from the ASAS MRI group has culminated in updated spine lesion definitions (ASAS_MRI_def^{n})[1]. There has been no central reader evaluation of MRI spine scans from the ASAS Classification Cohort (ASAS-CC)[2]. We aimed to determine the spectrum and compare the frequencies of active and structural lesions on MRI images of the spine from the ASAS-CC according to the consensus ASAS_MRI_def^{n} update, the diagnosis of axSpA, and the presence of radiographic sacroiliitis.

Methods: ASAS_MRI_def^{n} were recorded by 9 central readers in an eCRF that comprises global assessment (MRI indicative of axSpA yes/no) and detailed scoring of each discovertebral unit as well as lateral and posterior structures. Detailed scoring is based on slices viewed in sagittal orientation and for the thoracic and lumbar spine is subdivided into assessment of central and lateral slices that include or do not include the spinal canal, respectively. Vertebral

Table 1. Spinal corner lesions stratification according to rheumatologist diagnosis of axial spondyloarthritis data.

Vertebral Corner MRI lesions	majority of readers (>=5)			≥2 readers		
	axSpA=Yes (n=44)	axSpA=No (n=20)	p-value	axSpA=Yes (n=44)	axSpA=No (n=20)	p-value
Corner Fat ≥1	12 (27.3%)	2 (10%)	0.19	17 (38.6%)	7 (35%)	0.78
Corner Fat ≥2	10 (22.7%)	2 (10%)	0.31	13 (29.5%)	4 (20%)	0.64
Corner Fat ≥3	8 (18.2%)	1 (5%)	0.25	10 (22.7%)	3 (15%)	0.74
Corner Fat ≥4	7 (15.9%)	1 (5%)	0.42	9 (20.5%)	2 (10%)	0.48
Corner Fat≥ 5	6 (13.6%)	0 (0%)	0.17	7 (15.9%)	1 (5%)	0.42
Corner BME ≥1	17 (38.6%)	1 (5%)	0.006	25 (54.5%)	6 (30%)	0.047
Corner BME ≥2	15 (34.1%)	1 (5%)	0.013	19 (43.2%)	2 (10%)	0.009
Corner BME ≥3	11 (25%)	0 (0%)	0.013	16 (36.4%)	1 (5%)	0.008
Corner BME ≥4	8 (18.2%)	0 (0%)	0.094	12 (27.3%)	1 (5%)	0.048
Corner BME ≥5	7 (15.9%)	0 (0%)	0.088	8 (18.2%)	0 (0%)	0.049

Table 2. Spinal corner lesions stratification according to radiographic sacroiliitis data.						
Vertebral Corner MRI lesions	majority of readers (>=5)			≥2 readers		
	mNY=Yes (n=10)	mNY=No (n=49)	p-value	mNY=Yes (n=10)	mNY=No (n=49)	p-value
Corner Fat ≥1	5 (50%)	9 (18.4%)	0.047	5 (50%)	17 (34.7%)	0.48
Corner Fat ≥2	5 (50%)	7 (14.3%)	0.022	5 (50%)	11 (22.4%)	0.12
Corner Fat ≥3	4 (40%)	5 (10.2%)	0.036	4 (40%)	9 (18.4%)	0.20
Corner Fat ≥4	4 (40%)	4 (8.2%)	0.022	4 (40%)	7 (14.3%)	0.079
Corner Fat≥ 5	4 (40%)	2 (4.1%)	0.006	4 (40%)	4 (8.2%)	0.022
Corner BME ≥1	5 (50%)	11 (22.4%)	0.116	7 (70%)	22 (44.9%)	0.18
Corner BME ≥2	5 (50%)	9 (18.4%)	0.047	5 (50%)	14 (28.6%)	0.27
Corner BME ≥3	5 (50%)	6 (12.2%)	0.014	5 (50%)	11 (22.4%)	0.12
Corner BME ≥4	5 (50%)	3 (6.1%)	0.002	5 (50%)	7 (14.3%)	0.022
Corner BME ≥5	5 (50%)	2 (4.1%)	0.001	5 (50%)	3 (6.1%)	0.002

corner bone marrow edema (VCBME) and corner fat (VCFAT) lesions were recorded if present on 2 slices; facet joint, lateral slice, and posterior element inflammatory lesions were recorded if present on a single slice. Vertebral corner erosion, bone spurs, and ankylosis (intervertebral, facet) were each scored on a single slice. Comparison of active and structural lesion frequencies according to local rheumatologist diagnosis of axSpA and the presence of radiographic sacroiliitis was assessed descriptively according to individual, ≥2, and majority reader (≥5/9) concordant data.

Results: MRI scans of the entire spine were available from 69 cases and rheumatologist diagnosis in 64. AxSpA was diagnosed in 44 (68.8%). VCBME was most frequent, ≥1 lesion being recorded in 32(46.4%) and 19 (27.5%) by ≥2 and majority of readers, respectively. VCFAT was the most frequent structural lesion, ≥1 lesion being recorded in 24 (34.8%) and 14 (20.3%) by ≥2 and majority of readers, respectively. There were significantly more VCBME lesions in axSpA patients (mean(SD):1.8 (2.7)) than non-axSpA (mean(SD):0.3 (0.5)) ($p< 0.001$) while differences in VCFAT were not significant (Table 1). The presence of ≥2 VCBME lesions had 90-95% specificity for axSpA. Significantly more VCBME and VCFAT were observed in the setting of radiographic sacroiliitis (modified New York criteria (mNY)) (Table 2).

Conclusion: Spine lesions on MRI are relatively frequent in patients with undiagnosed back pain presenting to the rheumatologist. The presence of at least 2 VCBME lesions (each on 2 consecutive sagittal slices and without degenerative disc disease), but not VCFAT, may have some diagnostic utility.

1. Maksymowych WP, et al. Arthritis Rheumatol 70 (suppl 10): 654, 2018
2. Rudwaleit et al. Ann Rheum Dis 2009;68: 777-83

Disclosure: W. Maksymowych, AbbVie, 2, 5, Janssen, 5, Lilly, 5, Pfizer, 2, 5, Novartis, 2, 5, Gilead, 5, UCB Pharma, 5, Boehringer Ingelheim, 5, Galapagos, 5; **I. Eshed**, None; **P. Machado**, Abbvie, 5, 8, Eli Lilly, 5, Novartis, 5, 8, UCB, 5, 8, Pfizer, 8; **S. Pedersen**, None; **U. Weber**, None; **M. de Hooge**, None; **J. Sieper**, AbbVie, 5, Novartis, 5, 8, Lilly, 8, Janssen, 5, Merck, 5, 8; **S. Wichuk**, None; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8; **M. Rudwaleit**, Bristol-Myers Squibb, 5, 8, Chugai Pharmaceutical Co., Ltd., 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Novartis, 5, 8, UCB Pharma, 5, 8, AbbVie, 5, 8, Pfizer, 5, 8, Celgene, 8, Roche, 5, 8, Merck Sharp & Dohme, 5, 8; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5; **R. Landewé**, AbbVie, 2, 5, 8, AstraZeneca, 5, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, Galapagos, 5, Novartis, 5, Pfizer Inc, 2, 5, 8, UCB, 2, 5, 8, GlaxoSmithKline, 5, Janssen, 2, 5, 8, Merck, 5, 8, Rheumatology Consultancy BV, 1, Ablynx,

5, Amgen, 2, 5, 8, Celgene, 5, Gilead, 5, Novo Nordisk, 5, Roche, 2, 5, 8, Schering, 2, 5, 8, TiGenix, 5; **R. Lambert**, None; **M. Østergaard**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Hospira, 5, 8, Janssen, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Novo Nordisk, 5, Orion, 5, 8, Regeneron, 5, Roche, 5, 8, UCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, Boehringer Ingelheim, 5, 8, Sandoz, 5, 8, Sanofi, 5, 8; **X. Baraliakos**, AbbVie, 2, 5, 8, Novartis, 2, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Pfizer, 5, 8, UCB, 5, 8, BMS, 5, 8, Merck, 5, 8, Galapagos, 5.

Abstract Number: 1879

Development of a Deep Learning Algorithm to Predict Positive MRI of the Sacroiliac Joints According to the ASAS Definition in Patients with Recent Axial Spondyloarthritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The magnetic resonance imaging (MRI) of the sacroiliac joints (MRI-SIJ) represents an essential tool in the evaluation of patients with spondyloarthritis (SpA). However, despite a clear definition of positive and negative MRI-SIJ formulated by the ASAS/OMERACT working group, the inter-reader agreement between readers is never perfect. Moreover, in daily practice, the radiologists in charge of the evaluation of the SIJ-MRI images are rarely experts in musculoskeletal radiology. The aim of this pilot study is to predict a positive or negative MRI-SIJ according to the ASAS definition in patients with in recent axial SpA (axSpA) applying Artificial Intelligence (AI) and machine learning.

Methods: Patients from the DESIR cohort with MRI-SIJ available at baseline and in full agreement for positive or negative MRI-SIJ according to the three central readers were included.

We first segmented the iliac and sacrum bones in each MRI-SIJ slice. Then, we extracted the right and left joint on each slice of MRI. Finally, we reported the presence of inflammatory lesions on each joint of the MRI-SIJ. Once all the inflammatory lesions of the joints have been reported, we defined the positiveness of the MRI-SIJ based on a decision rule. All of these steps were conducted without human intervention.

We solved two tasks in this work:

Task 1: Segmentation of iliac and sacrum bones in semi-coronal axis MRIs.

Task 2: Detection of inflammation in the MRI-SIJ.

For task 1, we manually segmented 51 MRIs. We found that using two independent U-Net [1] for each bone performed better than using a single one that predicts the two bones.

For task 2, we use a ResNet-18 [2] to determine if each half-slice presents inflammation or not.

Metric \ Bones	Iliac	Sacrum
IOU	0.73	0.56
DICE	0.84	0.67

Table 1. Segmentation results on 14 patients.

Readers	2	3	ResNet18 (k = 10)
1	87	84	62.96 +- 1.92
2	-	83	66.08 +- 1.41
3	-	-	56.99 +- 1.43

Table 2. Results of presence of inflammation in a selected region. Matthews Correlation Coefficient (multiplied by 100 for clarity).

Readers	2	3	ResNet18 (k = 10)
1	100	100	77.75 +- 4.50
2	-	100	77.75 +- 4.50
3	-	-	77.75 +- 4.50

Table 3. Results of positive MRI-SIJ. Matthews Correlation Coefficient (multiplied by 100 for clarity). Decision rule: each MRI must have at least 3 regions with inflammation.

Results: Task 1: We trained two U-Net, one for each bone. We split 51 patients in 31 train, 6 validation, 14 evaluation. The results on the evaluation set are presented on table 1. We segmented successfully 104 new patients out of the 114 tested.

Task 2: We had a total of 155 segmented patients (51 manually and 104 automatically). We extract 1790 joints regions of T1 and STIR sequence. We trained a ResNet-18 classifier to determine the presence or absence of inflammatory lesions. We split the 155 patients (1790 regions) into 105 (1220 regions) train, 14 (164 regions) validation and 36 (406 regions) evaluation. We trained k = 10 identical networks. The results are shown on table 2. We compared the opinion of the three readers for each region. The positiveness for an MRI-SIJ is presented on table 3 (decision rule: #inflammation >= 3).

Conclusion: We propose a novel method to determine the presence of positive MRI-SIJ in SpA patients. We successfully segmented the iliac and sacrum bones and extracted the regions of interest. We achieved good results on the classification of inflammation for each joint region. While the results are still not on a par with the performance of a radiologist, we are optimistic that future work bill be able to reach it.

References

[1] U-Net: Convolutional Networks for Biomedical Image Segmentation. https://arxiv.org/abs/1505.04597 [2]Deep Residual Learning for Image Recognition. https://arxiv.org/abs/1512.03385Table 1. Segmentation results on 14 patients.

Table 2. Results of presence of inflammation in a selected region. Matthews Correlation Coefficient (multiplied by 100 for clarity).

Table 3. Results of positive MRI-SIJ. Matthews Correlation Coefficient (multiplied by 100 for clarity). Decision rule: each MRI must have at least 3 regions with inflammation.

Disclosure: T. Aouad, None; **C. Lopez-Medina**, None; **A. Molto**, ABBVIE, 5, BMS, 5, 8, LILLY, 5, NOVARTIS, 5, 8, UCB, 5, GILEAD, 5; **A. Feydy**, None; **C. Martin-Peltier**, None; **H. Talbot**, None; **M. Dougados**, Pfizer, 1, 2, Abbvie, 1, 2, UCB, 1, 2, Merck, 1, 2, Lilly, 1, 2, BMS, 1, 2, Roche, 1, 2, Novartis, 1, 2.

Abstract Number: 1880

Association of Healthcare Utilization and Costs with Patient-Reported Outcomes in Patients with Ankylosing Spondylitis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Treatments for ankylosing spondylitis (AS) have been shown to improve patient-reported outcome (PRO) measures in clinical studies; however, healthcare decision makers have limited ability to translate these improvements to healthcare resource utilization (HCRU) or cost savings. Few studies have assessed the economic impact of functional status and patient-reported disease burden in US patients with AS. The purpose of this study was to evaluate the association of PRO measures with HCRU and medical costs in patients with AS from a national US registry.

Methods: FORWARD is a longitudinal observational databank for rheumatic diseases that collects patient-reported data through questionnaires administered every 6 months. Data collected include demographics, clinical characteristics, symptoms, health and functional status, health-related quality of life, and HCRU. This cohort study included adult participants with a diagnosis of AS enrolled in FORWARD between July 2009 and June 2019 who completed ≥ 1 questionnaire between January 2010 and December 2019 and had completed the Health Assessment Questionnaire Disability Index (HAQ-DI) and/or Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; added in 2018). Patient demographics, clinical characteristics, and PRO data were collected from the most recent questionnaire. HCRU and medical costs (USD 2019) for all hospitalizations, emergency department (ED) visits, outpatient visits, diagnostic tests, and procedures were assessed for the 6 months prior to survey completion. The relationships between HAQ-DI or BASDAI and HCRU and cost outcomes were assessed using negative binomial regression models for HCRU outcomes and generalized linear models with gamma distribution and log-link function for cost outcomes adjusted for confounders.

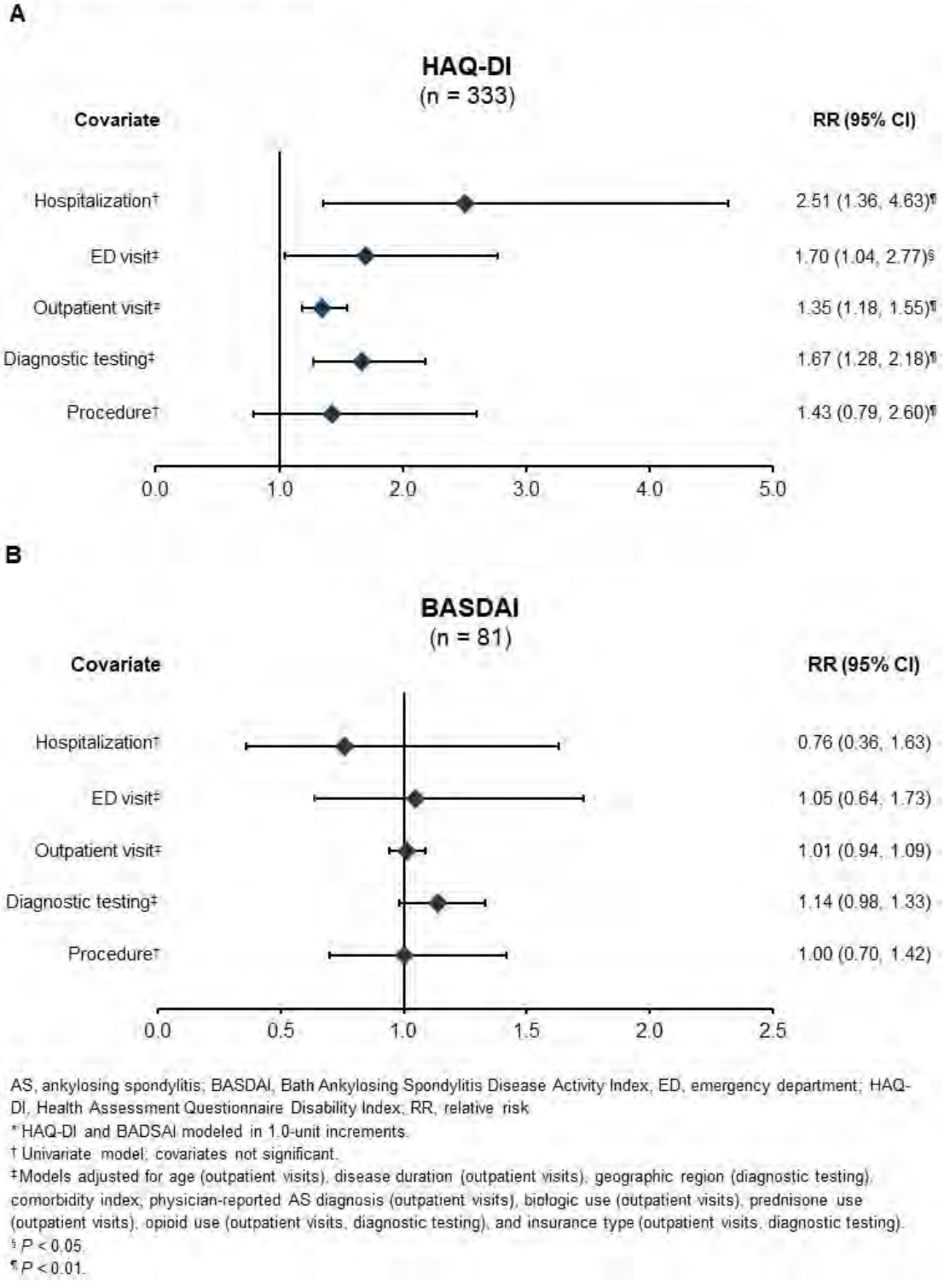
Table 1. Demographics, Clinical Characteristics, and Disease Activity Measures in Patients With AS Who Responded to HAQ-DI and/or BASDAI

Characteristic	Patients With AS (n = 334)
Age, mean (SD), years	54.4 (14.3)
Female, n (%)	206 (61.7)
White, n (%)	282 (94.6)
Insurance status, n (%)	n = 334
Private	114 (34.1)
Medicare	135 (40.4)
Medicaid	30 (9.0)
Other	43 (12.9)
None	12 (3.6)
Geographic location, n (%)	n = 323
Urban	229 (70.9)
Rural	94 (29.1)
Rheumatic disease comorbidity index, n (%)	n = 334
0	54 (16.2)
1	93 (27.8)
2	62 (18.6)
≥ 3	125 (37.4)
Disease duration, mean (SD), years [n]	17.5 (12.4) [303]
AS treatment history (current and past use), n (%) [n]	
DMARDs	114 (35.5) [321]
Biologics	141 (43.9) [321]
Prednisone	33 (11.3) [291]
NSAIDs	160 (49.8) [321]
Opioids	101 (30.2) [334]
AS disease activity, mean (SD) [n]	
HAQ-DI	0.9 (0.7) [333]
PROMIS-29 categories	
Physical function	42.6 (9.2) [169]
Anxiety	51.2 (14.3) [13]
Depression	50.8 (12.9) [13]
Fatigue	54.4 (11.5) [158]
Pain interference	57.8 (9.7) [94]
Sleep disturbance	52.4 (8.6) [158]
Satisfaction with social roles	48.5 (10.0) [158]
BASDAI	3.7 (2.3) [81]
Current work status, n (%)	n = 325
Unemployed	15 (4.6)
Employed	140 (43.1)
Retired	76 (23.4)
Disabled	69 (21.2)
Other	25 (7.7)
% Missed work time, mean (SD) [n]	14.7 (72.4) [132]

AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; DMARD, disease-modifying antirheumatic drug; HAQ-DI, Health Assessment Questionnaire Disability Index; NSAID, nonsteroidal anti-inflammatory drug; PROMIS-29, Patient-Reported Outcomes Measurement Information System 29-item form.

Results: A total of 334 patients with AS who completed the HAQ-DI and/or BASDAI questionnaires were included. The mean (SD) age and disease duration were 54.4 (14.3) and 17.5 (12.4) years, respectively. Overall, 61.7% of patients were female and 94.6% were white. The mean (SD) HAQ-DI and BASDAI at time of patients' most recent survey were 0.9 (0.7) and 3.7 (2.3), respectively (**Table 1**). HAQ-DI was positively associated with number of hospitalizations,

Figure 1. Association of Annualized Healthcare Resource Utilization With **(A)** HAQ-DI and **(B)** BASDAI Among Patients With AS Who Responded to HAQ-DI and/or BASDAI Questionnaires*



AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; ED, emergency department; HAQ-DI, Health Assessment Questionnaire Disability Index; RR, relative risk.

*HAQ-DI and BADSAI modeled in 1.0-unit increments.

†Univariate model; covariates not significant.

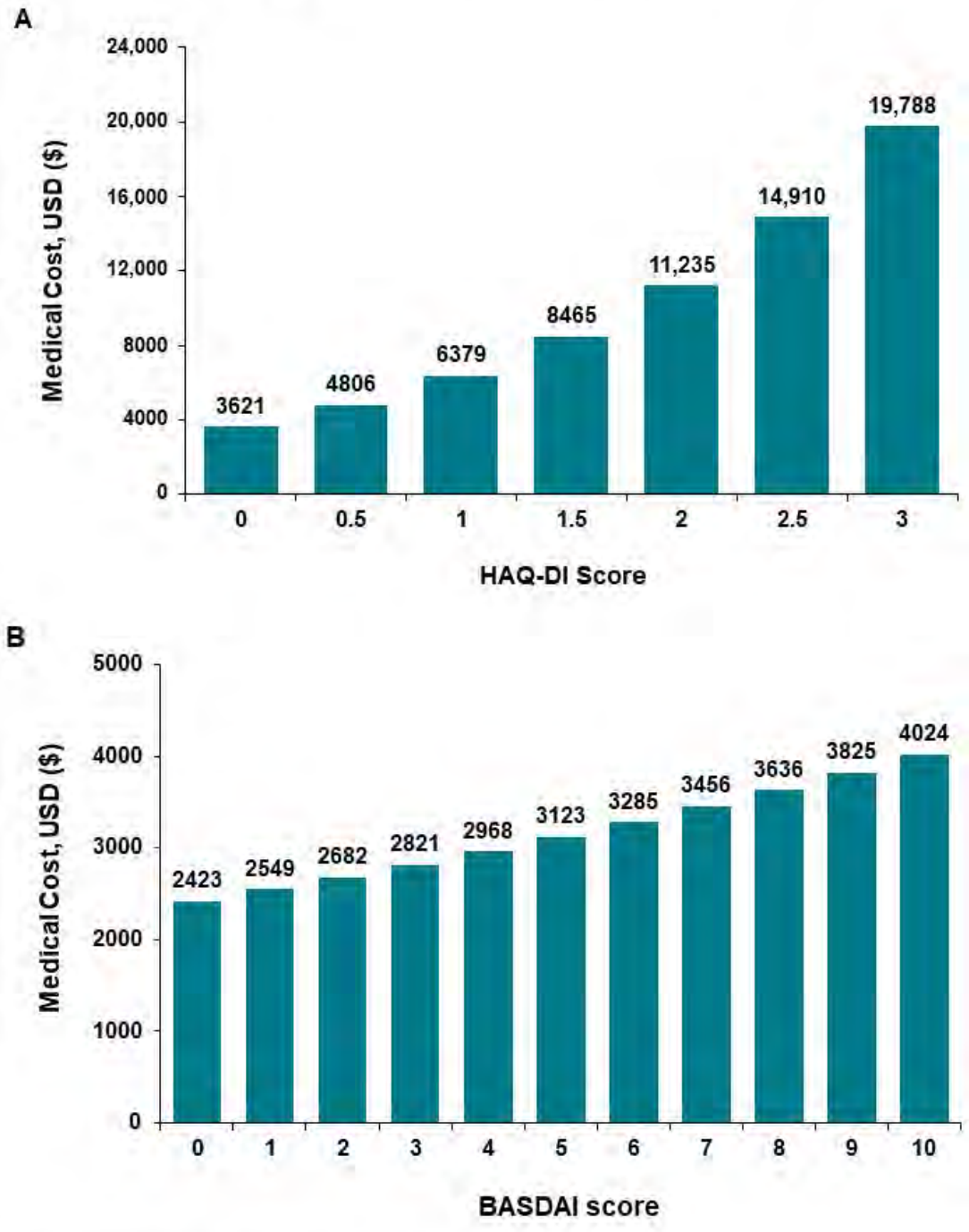
‡Models adjusted for age (outpatient visits), disease duration (outpatient visits), geographic region (diagnostic testing), comorbidity index, physician-reported AS diagnosis (outpatient visits), biologic use (outpatient visits), prednisone use (outpatient visits), opioid use (outpatient visits, diagnostic testing), and insurance type (outpatient visits, diagnostic testing).

§ $P < 0.05$.

¶ $P < 0.01$.

ED visits, outpatient visits, diagnostic tests, and procedures, whereas BASDAI was not associated with HCRU outcomes (**Figure 1**). Overall mean (SD) direct medical costs for patients with AS were $6520.50 ($12,732.90). There was a significant positive association (coefficient [95% CI]) between medical costs and HAQ-DI (1.76 [1.22-2.55]; *P*

Figure 2. Average Annualized Patient Medical Costs Across **(A)** HAQ-DI and **(B)** BASDAI Scores Among Patients With AS*



AS, ankylosing spondylitis; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; HAQ-DI, Health Assessment Questionnaire Disability Index.
* Adjusted for geographic region, rheumatic disease comorbidity index, and opioid use.

< 0.01), but not with BASDAI (1.05 [0.91-1.22]). Adjusted average medical costs increased with increasing HAQ-DI and BASDAI scores (**Figure 2**).

Conclusion: Higher HAQ-DI scores were associated with greater HCRU and higher medical costs among patients with AS included in FORWARD, but BASDAI scores were not. These findings indicate that greater functional impair-

ment may impose an increased economic burden compared with other patient-reported aspects of AS throughout the course of the disease. Therapies that effectively improve functional impairment may reduce costs for patients and the healthcare system.

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Abstract Number: 1881

In Radiographic Axial Spondyloarthritis, Bridging Syndesmophytes Increase Risk of Facet Joint Ankylosis Development on the Same Vertebral Level While Facet Joint Ankylosis Does Not Increase Risk of Same Level Syndesmophytes Development

Rosalinde Stal[1], Alexandre Sepriano[2], Floris van Gaalen[3], Xenofon Baraliakos[4], Rosaline van den Berg[1], Monique Reijnierse[1], Juergen Braun[5], Robert Landewé[6] and Désirée van der Heijde[1], [1]Leiden University Medical Center, Leiden, Netherlands, [2]Leiden University Medical Center, Portela Loures, Portugal, [3]Leiden University Medical Center (LUMC), Leiden, Netherlands, [4]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Bochum, Germany, [5]Rheumazentrum Ruhrgebiet and Ruhr-University, 44649 Herne, Germany, [6]Amsterdam University Medical Center & Zuyderland Hospital, Amsterdam, Netherlands

SESSION INFORMATION

Session Date: Monday, November 9, 2020

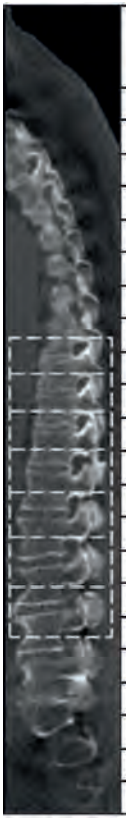
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: In radiographic axial spondyloarthritis (r-axSpA), spinal damage manifests as syndesmophytes and facet joint ankylosis (FJA). Whether there is an order in which lesion develops first is unknown.

Methods: Data were used from the Sensitive Imaging in Ankylosing Spondylitis (SIAS) cohort from Leiden and Herne. Inclusion criteria were: clinical r-axSpA diagnosis, ≥1 inflammatory lesion on spinal Magnetic Resonance Imaging (MRI), ≥1 and ≤18 syndesmophytes on conventional radiography of lateral cervical and lumbar spine, and fulfillment of the modified New York criteria. Patients underwent low-dose Computed Tomography (ldCT) at baseline and two-years. LdCT images were scored independently by two trained readers. Vertebrae were scored according to the Computed Tomography Syndesmophyte Score (CTSS) for presence and size of syndesmophytes; facet joints were scored as not-ankylosed and ankylosed. Analyses were performed on the vertebral unit (VU) level and using individual-reader data (Figure). Two hypotheses were tested: 1) presence of bridging syndesmophyte(s) is associated with FJA on the same VU two years later, and 2) presence of FJA is associated with syndesmophyte(s) on the same VU two years later. Generalized Estimating Equations (GEE) models were used to take into account the correlations between VUs from the same patient and adjusting for reader to account for individual reader scores. Two models were tested per hypothesis using different outcomes. Model 1 uses the presence of syndesmophytes or FJA as outcome adjusting for the outcome at baseline. Model 2 uses development of new syndesmophytes or FJA at two years plus an increase in the number of syndesmophytes or FJA.



VU	Segment	≥1 bridging synd at BL reader 1	≥1 bridging synd at BL reader 2	≥1 FJA at BL reader 1	≥1 FJA at BL reader 2
1	Cervical	22%	26%	12%	35%
2		28%	28%	14%	21%
3		26%	30%	23%	20%
4		32%	33%	28%	27%
5		22%	27%	27%	27%
6		26%	21%	32%	30%
7	Thoracic	26%	28%	29%	25%
8		32%	36%	22%	27%
9		50%	48%	26%	31%
10		56%	56%	24%	36%
11		46%	54%	22%	36%
12		48%	46%	24%	26%
13		56%	54%	28%	26%
14		52%	54%	22%	28%
15		52%	56%	22%	32%
16		58%	60%	24%	34%
17		54%	52%	26%	28%
18		47%	47%	27%	33%
19	Lumbar	24%	27%	14%	20%
20		27%	22%	10%	20%
21		20%	20%	10%	12%
22		18%	20%	8%	18%

Figure. Percentage of occurrence of syndesmophytes and facet joint ankylosis per vertebral unit and per reader at baseline. Figure displaying percentages of patients with a bridging syndesmophyte and with facet joint ankylosis at baseline, per reader. The image on the left illustrates the vertebral unit level (VU) at which analyses were performed. Seven VUs are illustrated in dashed boxes as example. Synd, syndesmophyte; FJA, facet joint ankylosis; BL, baseline.

	Model 1: development of new FJA/syndesmophytes at FU OR (95% CI)	**Model 2**: development and/or increase FJA/syndesmophytes at FU OR (95% CI)
Hypothesis 1 Presence bridging syndesmophytes at BL on development of FJA at FU	**3.35 (2.18-5.14)**	**2.23 (1.19-4.16)**
Hypothesis 2 Presence FJA at BL on development of syndesmophytes at FU	1.60 (0.88-2.91)	1.12 (0.76-1.66)

Table: Results of the GEE analyses of the two hypotheses Model 1 was adjusted for the outcome at baseline and both models were adjusted for the reader level, not shown in the table. Statistically significant odds ratios are presented in bold. FJA, facet joint ankylosis; BL, baseline; FU, follow-up

Results: In total, 50 patients were included (mean age 49, 84% male, 82% HLA-B27+). At baseline, there was a higher percentage of bridging syndesmophytes (range: 10-60%) than FJA (range: 8-36%) considering all VUs and both readers (Figure). In both models, presence of bridging syndesmophytes was associated with development of FJA two years later (OR (95%CI) Model 1: 3.35 (2.18-5.14); Model 2: 2.23 (1.19-4.16)) while presence of FJA at baseline did not have a statistically significant association with development of syndesmophytes two years later (Table).

Conclusion: The data showed a higher occurrence of bridging syndesmophytes than FJA at baseline and showed significantly increased odds to develop FJA when bridging syndesmophyte(s) are present on the same VU two years

prior. This mechanism did not hold true for the other direction. These results cautiously imply that in our study population with advanced r-axSpA bridging syndesmophytes precede FJA, rather than FJA preceding syndesmophytes.

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Abstract Number: 1882

Are There Any Clues to Predict Bamboo Spine in Axial Spondyloarthritis?

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Complete ankylosis of the entire spinal column is a severe condition seen in spondyloarthritis. This study aims to investigate the possible risk factors associated with the bamboo spine in axial Spondyloarthritis (axSpA) patients treated with biological DMARDs.

Methods: *TReasure*; is a multicentre database, started in December 2017, in which clinical and demographic data of inflammatory arthritis patients using biological and synthetic DMARDs are recorded (1). This database contains 4911 SpA patients using bDMARD therapy. axSpA patients fulfilling the ASAS classification criteria (Sacroiliitis defined either according to the mNY- or ASAS positive MRI criteria) were analyzed. Patients with complete cervical and lumbar x-rays were divided into three groups. Group-1 consists of patients with a bamboo spine, Group-2 consists of patients with bridging (advanced radiographic involvement) bridging of two vertebrae in a row, Group-3 consists of patients with syndesmophytes in at least one vertebra, and Group-4 consists of patients with no syndesmophytes. The demographic and clinical features of these patients were recorded. One hundred and ten patients were selected as a matched control group based on the disease duration of patients with a bamboo spine.

Results: Out of the 4911 patients in the TReasure database, sacroiliac joint MRI and/or cervical and lumbar lateral radiographs were available for 1381 patients. AS (1071, 77.6%), psoriatic arthritis (102, 7.4%), non-radiographic (144, 10.4%), peripheral SpA (128, 9.3%), enteropathic arthritis (39, 2.8%) in 1381 patient. The bamboo spine was seen in 111 (8.0%), bridging of two vertebrae in a row in 125 (9.0%), syndesmophytes in at least one vertebra in 329 (23.8%), and 816 (59.2%) had no syndesmophytes.

The comparison between the patients with a bamboo spine to those with no syndesmophytes revealed that; male gender (85.6% vs 61.8%, $p < 0.001$), age (51 (45-61) vs 43 (36-50), $p < 0.001$), BMI (27.9 (25.9-31.2) vs 25.9 (22.9-29.3) , $p < 0.001$), smoking as package/year (12.2 (1-30) vs 3 (0-11), $p < 0.001$), delay in diagnosis of SpA (61 (19-134) vs 12 (5-47), $p < 0.001$), hip involvement (53.7% vs 17.8%, $p < 0.001$), family history of SpA (40.8% vs 24.8%, $p = 0.014$), and uveitis (25.6% vs 13.6%, $p = 0.030$) were associated with bamboo spine.

Bamboo spine was less common in patients with peripheral arthritis (9.6% vs 21.3%, $p = 0.019$) and psoriasis (4.5% vs 12.7% , $p = 0.031$).

Disease activity (BASDAI) and functional status (BASFI) of both patient groups were similar before bDMARD treatment.

Table 1. Demographic and clinical parameters of study patients

	Group-1 N=111	Group-2 N=125	Group-3 N=329	Group-4 N=110
Age (Q1-Q3)	52 (45-61)	49 (43-57)	47 (41-55)	43 (36-50)
Male n (%)	95 (85.6)	103 (82.4)	216 (65.7)	68 (61.8)
Disease duration (month)	217 (124-290)	143 (83-229)	131 (81-180)	185 (119-241)
Delay in diagnosis (month)	61 (19-134)	49 (24-119)	37 (5-110)	12 (5-47)
BMI	27.9 (25.9-31.2)	27.6 (24.7-31.2)	27.3 (24.4-30.1)	25.9 (22.9-29.3)
Smoking (ever)	81/105	103/119	201/320	66/106
BASFI	5.5 (3.0-7.7)	4.4 (3.4-6.0)	4.3 (2.7-6.2)	5.0 (4.0-6.2)
Peripheral arthritis	10 (9.6)	5 (4.0)	45 (14.0)	108 (21.3)
Enthesitis	25 (29.1)	26 (28.6)	57 (26.4)	10 (16.7)
Psoriasis	5 (4.5)	6 (4.8)	37 (11.3)	14 (12.7)
Uveitis	28 (25.2)	29 (23.2)	60 (18.2)	15 (13.6)
IBH	3 (2.8)	6 (4.8)	14 (4.3)	7 (6.4)
Family history of SpA	42 (40.8)	41 (36.9)	103 (33.8)	26 (24.8)
HLA-B27	40/57 (70.2)	55/74 (74.3)	123/204 (60.3)	36/61 (63.9)
Hip involvement	58 (53.7)	51 (42.9)	66 (21.4)	19 (17.8)
MTX* (ever)	37 (33.3)	29 (23.2)	106 (32.2)	40 (36.4)
SSZ** (ever)	79 (71.2)	88 (70.4)	235 (71.4)	71 (64.5)

* MTX: Methotrexate

** SSZ: Sulfasalazine

In multivariate analysis, male gender OR 9.3 (95% CI 3.2-26.9), hip involvement OR 4.2 (1.8-9.5), family history for SpA OR 2.9 (1.3-6.6), delay in diagnosis 1.013 (1.005-1.021), age 1.11 (1.06 -1.116) as a risk factor.

Conclusion: Male gender, delay in diagnosis, family history of SpA, and hip involvement is the most important risk factors associated with a bamboo spine in axSpA patients, after a disease duration of more than 15 years. Interestingly, the presence of peripheral arthritis and psoriasis were protective.

References

1) Kalyoncu U, Taşcılar EK, Ertenli Aİ et al. Methodology of a new inflammatory arthritis registry: TReasure. Turk J Med Sci. 2018 Aug 16;48(4):856-861.

Disclosure: P. Atagündüz, None; **S. Kiraz**, Abbvie, 8, Amgen, 8, Johnson and Johnson, 8, MSD, 8, Novartis, 8, Pfizer, 8, Roche, 8, UCB, 8; **S. Akar**, None; **O. Küçükşahin**, Amgen, 8, Johnson and Johnson, 8, MSD, 8, Novartis, 8, Pfizer, 8, Roche, 8, UCB, 8; **A. Erden**, Amgen, 8, Novartis, 8, Roche, 8, UCB, 8; **N. Coşkun**, None; **B. Yağız**, None; **C. Bes**, None; **L. Kılıç**, Abbvie, 8, Amgen, 8, MSD, 8, Novartis, 8, Pfizer, 8, Roche, 8, UCB, 8; **Ö. Karadağ**, Amgen, 8, Johnson and Johnson, 8, MSD, 8, Novartis, 8, Pfizer, 8, Roche, 8, UCB, 8; **T. Kaşifoğlu**, Abbvie, 8, Amgen, 8, MSD, 8, Novartis, 8, Pfizer, 8, Roche, 8, UCB, 8; **H. Emmungil**, Novartis, 8, Roche, 8; **M. Çınar**, Abbvie, 8, Amgen, 8, MSD, 8, Novartis, 8, Pfizer, 8, Roche, 8, UCB, 8; **G. Kimyon**, Abbvie, 8, Amgen, 8, Novartis, 8, Pfizer, 8, UCB, 8; **V. Yazısız**, Abbvie, 8, Actelion, 8, Amgen, 8, MSD, 8, Novartis, 8, Pfizer, 8, Roche, 8, UCB, 8; **A. Ates**, None; **E. Ersozlu**, Celltrion, 8, MSD, 8, Novartis, 8, Pfizer Inc, 8, Roche, 8, UCB, 8; **E. Gönüllü**, None; **R. Mercan**, Abbvie, 8, Amgen, 8, MSD, 8, Novartis, 8, Pfizer, 8, Roche, 8, UCB, 8; **İ. Ertenli**, Abbvie, 8, Amgen, 8, Johnson and Johnson, 8, MSD, 8, Novartis, 8, Pfizer, 8, Roche, 8, UCB, 8; **U. Kalyoncu**, Abbvie, 1, Amgen, 1, Jannsenn, 1, Lilly, 1, Novartis, 1, UCB, 1.

Abstract Number: 1883

Exercise Partially Explains the Impact of Body Mass Index on Disease Activity in Ankylosing Spondylitis

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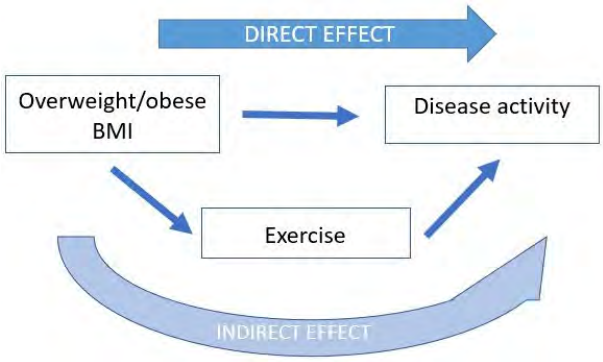
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) patients have elevated cardiovascular (CV) morbidity and mortality compared to general population comparators of the same age and sex. Although obesity is an important and modifiable CV risk factor, there are few prospective studies addressing the impact of higher body mass index (BMI) on clinical outcomes in AS. The aim of this study is to assess the relationship of BMI with disease activity in AS patients, and the extent to which the effect is mediated through exercise.

Methods: Data were available for 283 adults with AS meeting the 1984 modified New York criteria from a prospective cohort, who were followed at a single site at visits every 6 months with a median follow-up of 7 years. BMI (kg/m^2) and disease activity as measured by the Ankylosing Spondylitis Disease Activity Score (ASDAS) represented the exposure and outcome, respectively. In the main analysis, we included 183 subjects who had at least one available BMI and



Directed acyclic graph demonstrating the direct effect of an overweight/obese BMI on disease activity, and the indirect effect of overweight/obese BMI on disease activity through exercise.

one available ASDAS measure during any study visit; missing values were imputed using multiple imputation with chained equations. To determine the association of BMI and disease activity, we used generalized estimating equations to account for repeated measures per subject. We adjusted for age, sex, race, current smoking, nonsteroidal anti-inflammatory drug (NSAID) use, tumor necrosis factor inhibitor (TNFi) use, and follow-up time, and for interactions between BMI and sex and BMI and time. We then performed a causal mediation analysis to estimate the direct effect of BMI on disease activity, and the indirect effect through exercise.

Results: Among 183 subjects, 77% were male, 70% were white, and the mean±standard deviation age was 40.8±13.3 years. In adjusted analyses, higher BMI was significantly associated with higher disease activity over time; on average, for a 1 kg/m^2 higher BMI, the ASDAS was 0.06 units higher (95% CI 0.02-0.09). This association did not differ by sex (p=0.89) but did differ over time (p=0.03). The direct effect of an overweight/obese BMI accounted for most of the total effect on disease activity, with a much smaller indirect effect mediated by exercise (9%).

Conclusion: Higher BMI was associated with higher disease activity in a prospective AS cohort. We found that being overweight/obese largely influences disease activity directly, rather than indirectly through exercise. This suggests that other mechanisms such as increased inflammation may better explain the obesity-disease activity association. Interventions targeting obesity may improve both disease activity and CV risk in this population.

Disclosure: J. Liew, None; **M. Gianfrancesco**, None; **S. Heckbert**, None; **L. Gensler**, AbbVie, 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB Pharma, 2, 5.

Abstract Number: 1884

Disease Activity in an Axial Spondyloarthritis Cohort During the COVID-19 Pandemic

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Table 1. Baseline characteristics for survey respondents (n=203) stratified by Perceived Stress Scale score

	Overall N=203	Low stress N=94	High stress N=109
Demographics			
Age, years	46.4 (12.5)	47.6 (12.3)	45.4 (12.6)
Male gender	133 (66%)	74 (79%)	59 (54%)
Race/ethnicity			
White	157 (77%)	77 (82%)	80 (73%)
Asian	27 (13%)	9 (10%)	18 (17%)
Hispanic	6 (3%)	1 (1%)	5 (5%)
African-American	1 (2%)	1 (1%)	0 (0%)
Other	12 (3%)	6 (6%)	6 (6%)
Residence in California	178 (88%)	81 (86%)	97 (89%)
Any exercise	180 (89%)	87 (93%)	94 (86%)
Disease characteristics			
Classification			
Nonradiographic	51 (25%)	21 (22%)	30 (28%)
Radiographic/AS	147 (72%)	71 (76%)	76 (70%)
Not classified	5 (2%)	2 (2%)	3 (3%)
HLA-B27 positive	177 (88%)	79 (86%)	98 (90%)
Symptom duration, years	22.9 (12.4)	24.8 (12.7)	21.3 (12.0)
Abnormal CRP	29 (15%)	14 (15%)	15 (14%)
History of acute anterior uveitis	96 (47%)	38 (40%)	58 (53%)
History of inflammatory bowel disease	36 (18%)	16 (17%)	20 (18%)
History of psoriasis	26 (13%)	13 (14%)	13 (12%)
On NSAID	106 (52%)	49 (52%)	54 (50%)
On biologic	83 (41%)	83 (41%)	120 (59%)
BASDAI (0-10)	2.3 (1.8)	2.0 (1.7)	2.7 (1.9)
Comorbidities			
Hypertension	53 (26%)	31 (33%)	22 (20%)
Diabetes	10 (5%)	4 (4%)	6 (6%)
Cardiovascular disease	7 (3%)	4 (4%)	3 (3%)
Other cardiac disease	15 (7%)	11 (12%)	4 (4%)
BMI, kg/m^2	25.5 (4.8)	25.3 (4.33)	25.7 (5.2)
Smoking			
Current	4 (2%)	0 (0%)	4 (4%)
Ever	63 (31%)	31 (33%)	32 (29%)
Asthma	33 (16%)	12 (12%)	21 (19%)
Cancer	18 (9%)	8 (9%)	10 (9%)
Depression	66 (33%)	16 (17%)	50 (46%)
Anxiety	15 (7%)	6 (6%)	9 (8%)

Abbreviations: AS, ankylosing spondylitis; CRP, C-reactive protein; NSAID, nonsteroidal anti-inflammatory drug; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index.

Continuous variables are reported as mean (SD) and categorical variables as n (%).

Data were missing for 43 respondents for BASDAI.

Biologic use includes infliximab, etanercept, adalimumab, golimumab, certolizumab pegol, secukinumab, and ixekizumab. Cardiovascular disease is defined as history of myocardial infarction, stroke, or cardiovascular revascularization in the electronic medical record. Other cardiac disease includes heart failure, valvulopathy, arrhythmia, and angina. Cancer includes all but non-melanoma skin cancers. Hypertension, diabetes, depression, and anxiety are defined by the presence of either problem listed in the problem list, and/or medication use in the electronic medical record.

Table 1. Baseline characteristics for survey respondents (n=203) stratified by Perceived Stress Scale score

Background/Purpose: Response to the global coronavirus disease (COVID-19) pandemic has resulted in shelter-in-place orders and major changes to how people go about their daily lives. The impact of such stressors on disease activity in individuals with axial spondyloarthritis (axSpA) is unclear. The primary aim of this study is to examine whether stress and anxiety are associated with disease activity, after accounting for important factors.

Methods: We administered a survey to an axSpA cohort from a single center with well-defined demographic and disease characteristics. The survey included questions about changes in job status, exercise, medication use, disease activity (by the Bath Ankylosing Spondylitis Disease Activity Index [BASDAI]), and psychological factors (stress, depressive symptoms, and anxiety). Two separate multivariable linear models examined the associations between perceived stress with BASDAI, and anxiety with BASDAI.

Results: After adjustment for potential confounders, those with higher levels of stress had a statistically significant 0.54-point higher BASDAI, on average, compared to those with lower levels of stress (95% confidence interval [CI] 0.11, 0.97). Those with higher levels of anxiety also had a statistically significant higher BASDAI, on average, compared to those with lower levels of anxiety (β 0.95, 95% CI 0.18, 0.99). We did not find differences in these associations among subgroups of age, job status, or county of residence.

Conclusion: Individuals with axSpA with higher levels of stress and anxiety had significantly higher disease activity levels. Further studies are needed to evaluate the trajectory of disease activity as the pandemic continues to evolve.

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Abstract Number: 1885

Performance of SASDAS (Simplified Axial Spondyloarthritis Disease Activity Score) versus ASDAS in a Post Hoc Analysis of a Randomized Controlled Clinical Trial

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The Ankylosing Spondylitis Disease Activity Score (ASDAS) assesses axial spondyloarthritis (axSpA) with good internal consistency and discriminative capacity. However, a scientific calculator or electronic application is required for its calculation. SASDAS (simplified ASDAS) is the sum of the ASDAS´s components, which includes C-reactive protein (CRP), and is easy to perform in daily practice. The objective of this analysis was to compare the SASDAS index against the standard ASDAS index (CRP version) at baseline and post-baseline in a randomized controlled trial (EMBARK).

Methods: EMBARK assessed etanercept (ETN) 50 mg/week in early active NSAID-refractory non-radiographic axSpA patients receiving background NSAID. Subjects received ETN or placebo (PBO) for 12 weeks (double-blind) followed by ETN only (open-label). Continuous ASDAS and SASDAS were evaluated by Spearman's Correlations, and agreement in ASDAS vs SASDAS disease categories (minimal, low, high, very high disease activity) by Cohen's weighted kappa for individual and pooled treatments. The capacity to discriminate between treatments was evalu-

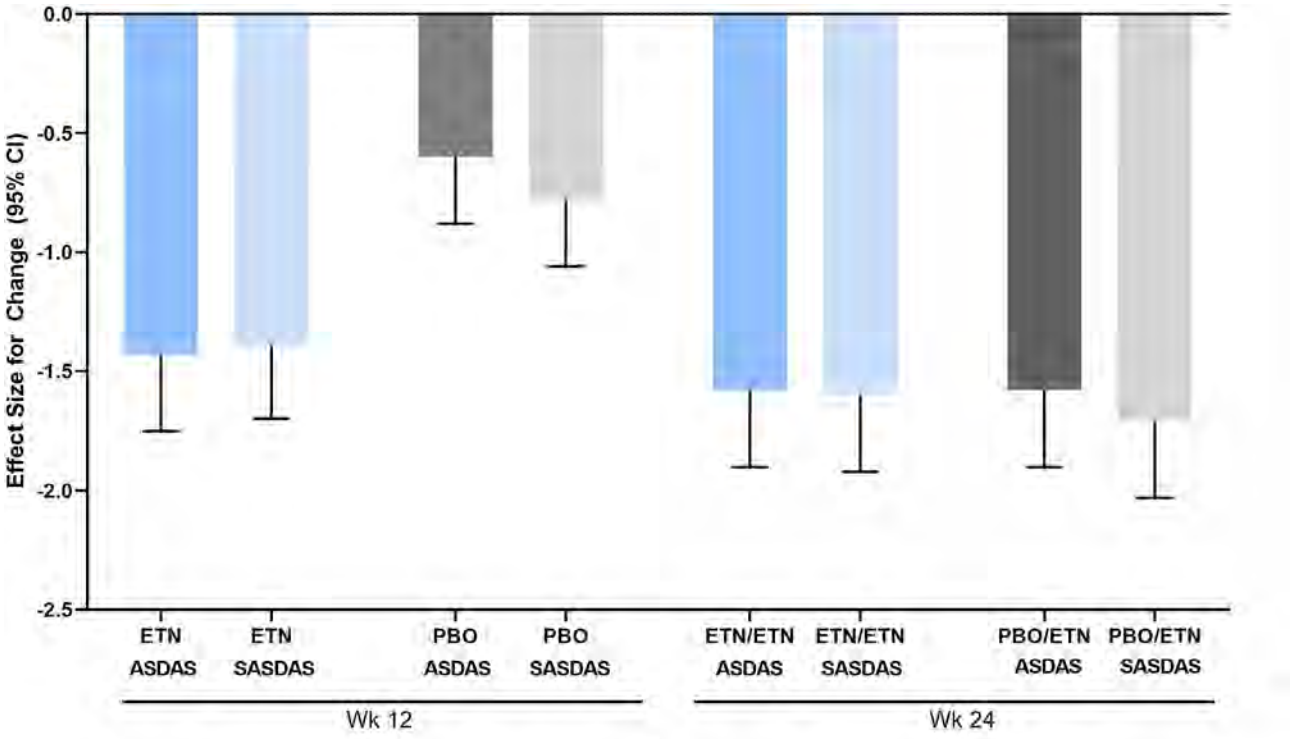

Figure 1: Responsiveness to change between ASDAS and SASDAS by treatment and time point

Table 1: ASDAS by SASDAS Categories at Baseline (mITT and observed cases; pooled treatments)

		SASDAS				
	Disease categories	Inactive	Moderate	High	Very high	Cohen's weighted kappa*
ASDAS	Inactive	2/213 (0.9%)	0/213 (0.0%)	0/213 (0.0%)	0/213 (0.0%)	0.58 (0.49, 0.67)
	Moderate	**3/213 (1.4%)**	13/213 (6.1%)	**20/213 (9.4%)**	0/213 (0.0%)	
	High	0/213 (0.0%)	**4/213 (1.9%)**	83/213 (39.0)	**18/213 (8.5%)**	
	Very high	0/213 (0.0%)	0/213 (0.0%)	**19/213 (8.9%)**	51/213 (23.9%)	

* Cohen's weighted kappa (95% CI)
CI, confidence interval

ated by treatment effect size (ES) for ETN vs PBO at Week 12, and the sensitivity to change from baseline at Weeks 12 and 24 by ES for change.

Results: Of 215 patients in the modified intention-to-treat (mITT) population (ETN, n=106; PBO, n=109), 208 entered the open-label phase (ETN/ETN, n=102; PBO/ETN, n=106). The mean age was 32 years, 64% (ETN) and 58% (PBO) were male, and average disease duration was 2.4 (ETN) and 2.5 years (PBO). There was a strong correlation between

continuous ASDAS and SASDAS. At baseline, Spearman's correlation was 0.82 (ETN) and 0.87 (PBO); at Weeks 12 and 24 it was 0.89 (ETN), 0.90 (PBO), and 0.88 (both treatments), respectively. The evaluation of categorical SASDAS placed more patients in high or very high disease activity compared with categorical ASDAS; for example, at baseline, in the whole population, 38/213 patients (17.8%) with moderate and high disease activity by ASDAS were categorized with higher disease activity by SASDAS (20/213 moderate, 18/213 high), and 26/213 patients (12.2%) categorized with lower disease activity (3/213 moderate, 4/213 high, 19/213 very high) (Table 1). A similar pattern was seen post-baseline. Cohen's weighted kappa statistics range from 0.54 – 0.73 for all individual/pooled treatments and time points, reflecting moderate-to-substantial agreement. The discriminant capacity evaluated by the treatment ES was higher with ASDAS compared with SASDAS (ES [95% CI], ASDAS: -0.74 [-1.03,-0.46]; SASDAS: -0.51 (-0.79, -0.23), but the sensitivity to change was similar (Figure 1).

Conclusion: Despite the simplicity of SASDAS, these data suggest a moderate-to-substantial agreement with ASDAS for classifying patients with active disease and a lower treatment discriminant capacity. Further evaluation of this composite index is required before implementation in daily practice and/or clinical trials.

Disclosure: E. Schneeberger, Abbvie, 1, 2, 3, Amgen, 1, 2, 3, BMS, 1, 2, 3, Genzyme, 1, 2, 3, Janssen, 1, 2, 3, Eli Lilly, 1, 2, 3, Novartis, 1, 2, 3, Pfizer, 1, 2, 3; **G. Citera**, AbbVie, 5, 8, Eli Lilly, 5, 8, Bristol-Myers Squibb Company, 5, 8, Gema, 5, 8, Pfizer, 5, 8, Janssen, 5, 8; **D. Ponce de Leon**, Pfizer, 1; **A. Szumski**, Syneos Health, 1; **K. Kwok**, Pfizer, 1, 2; **M. Cutri**, Pfizer, 1; **M. Dougados**, Pfizer, 1, 2, Abbvie, 1, 2, UCB, 1, 2, Merck, 1, 2, Lilly, 1, 2, BMS, 1, 2, Roche, 1, 2, Novartis, 1, 2.

Abstract Number: 1886

Measuring Physical Activity in AxSpA:Content Validity and Measurement Properties of the New AxSpA-SQUASH

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SESSION INFORMATION
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Background/Purpose: The ASAS-EULAR recommendations for management of axial Spondyloarthritis (axSpA) includes that patients should be encouraged to exercise. There is no validated instrument for measuring physical activity in axSpA. Our previous study recommends to adapt the Short QUestionnaire to Assess Health-enhancing physical activity (SQUASH) to improve the validity in axSpA patients. Our goal was to mak an AxSpA-disease specific adaptation of the physical activity questionnaire SQUASH to improve content validity and measurement properties.

Methods: This study was conducted according to the OMERACT-filter within the Groningen Leeuwarden AxSpA (GLAS) cohort and was performed in two parts. Part 1: adaptation and evaluation of content validity using a qualitative stepwise approach with in-depth interviews with different healthcare professionals (n=9) and patients (n=8), field testing in patients (n=10), and consensus meeting for final adaptations. Thereafter, content validity (n=45) was tested by filling out axSpA-SQUASH and SQUASH in random order two weeks apart. Part 2: measurement properties were tested using the International Physical Activity Questionnaire (IPAQ) as comparator. Criterion validity (n=40): Spear-

	SRM	95% CI	BASDAI T1	BASDAI T2
Improved (n=12)	-0.36	-0.99 to 0.28	5.01 (2.10)	3.93 (1.60)
Stable (n=21)	0.28	-0.18 to 0.73	3.76 (2.05)	3.76 (2.05)
Decreased (n=14)	0.75	0.18 to 1.33	4.71 (1.96)	5.79 (2.42)

Table 1. Responsiveness of the axSpA-SQUASH versus change in BASDAI

man's correlation with accelerometer as golden standard and classification accuracy of intensity. Construct validity (n=106): Spearman's correlation with disease activity, physical functioning and quality of life as clinical outcome with expected fair to moderated associations. Test-retest reliability (n=45): intraclass correlation coefficients (ICC) after 2 weeks. Responsiveness (n=47): standardized response mean (SRM) after 3 months stratified by Ancor method.

Results: In total 156 patients were included: mean age 48±13 years, 56% males, 72% HLA-B27 positive, symptom duration 21±13.3 years and ASDAS 2.0±1.0. Part 1: main adaptations were better explanation of intensities, adding answer option "not applicable", examples were modernized, physiotherapy and activity "shopping" were added. Compared to the original SQUASH, the adapted axSpA-SQUASH measured a systematically higher activity count and had less missing values (8% vs. 32%). Part 2: criterion validity: axSpA-SQUASH correlated better with accelerometer compared to IPAQ (ρ=0.51 vs. ρ=0.35). Classification accuracy: accelerometer defined most activity as light (97%), whereas axSpA-SQUASH and IPAQ defined most activity as moderate intensity (55% and 62% resp.). Construct validity: correlations were low to moderate and strongest for axSpA-SQUASH compared to IPAQ. Construct validity: correlations were low to moderate and stronger for axSpA-SQUASH compared to IPAQ (BASDAI -0.27 vs -0.15, BASDAI –0.27 vs. -0.15, ASDAS -0.24 vs -0.09, BASFI -0.39vs. -0.21, ASQoL -0.39 vs. -0.35). Test-retest reliability: ICC axSpA-SQUASH: 0.80. Responsiveness: axSpA-SQUASH changed over time in the corresponding direction (Table 1). Feasibility: considered comprehensible and average completion time was 7 minutes.

Conclusion: The new axSpA-SQUASH resulted in improved content validity and measurement properties. It seems the most appropriate questionnaire and can be used to assess daily physical activity in patients with axSpA.

Disclosure: M. Carbo, None; **D. Paap**, None; **F. Maas**, None; **M. Siderius**, None; **H. Bootsma**, Bristol-Myers Squibb, 2, 5, 8, Roche, 2, 5, Novartis, 5, 8, Medimmune, 5, Union Chimique Belge, 5; **F. Wink**, Abbvie, 5, Janssen, 5; **S. Arends**, Pfizer, 2; **A. Spoorenberg**, Pfizer, 1, 2, Novartis, 1, 2, Abbvie pharmaceuticals, 1, 2, MSD, 1, UCB, 1.

Abstract Number: 1887

Spinal Mobility and Function: How Closely Do They Associate in Axial Spondyloarthropathy?

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthropathy (axSpA) is a form of inflammatory arthritis affecting the axial skeleton. Persistent disease activity can result in restricted spinal mobility over time, and is presumed to lead to functional impairment although evidence to date on this subject has been limited. The Ankylosing Spondylitis Registry of Ireland (ASRI) is a source of epidemiological data on patients with axSpA in Ireland. The aim of this study was to examine the relationship between degree of spinal mobility (as assessed by BASMI score) and effect on functional ability (as assessed by BASFI score).

Methods: IBM SPSS version 24 was used to run the analysis of the patient population registered in the ASRI to date. Patients with both BASFI and BASMI scores were included in the analysis. Both variables were assessed with a Shapiro-Wilk's test for normal distribution. Variables were also assessed for presence of a monotonic relationship by visual inspection of a scatterplot of the two variables. Once a monotonic relationship was established a Spearman's rank-order correlation between BASMI and BASFI was analyzed. Further analysis with a Pearson's partial correlation was preformed to control for gender. Records were then split by gender and a Spearman's rank-order correlation was undertaken to assess strength of correlation of scores within each gender.

Results: In total 847 patients were assessed for inclusion. Data on both BASMI and BASMI scores were available on 647 of these patients, which were included in the analysis. Variables were not normally distributed as assessed by Shapiro-Wilk's test ($p < 0.01$). Preliminary analysis showed the relationship between these measures to be monotonic (as the BASFI score increases, so too does the BASMI score), as determined by visual inspection of the scatterplot. There was a statistically significant, strong positive correlation between BASMI and BASFI scores in axSpA patients, $r_s(645) = 0.509$, $p = 0.001$(figure 1) based on calculations by Spearman's rank-order correlation. A Pearson's partial

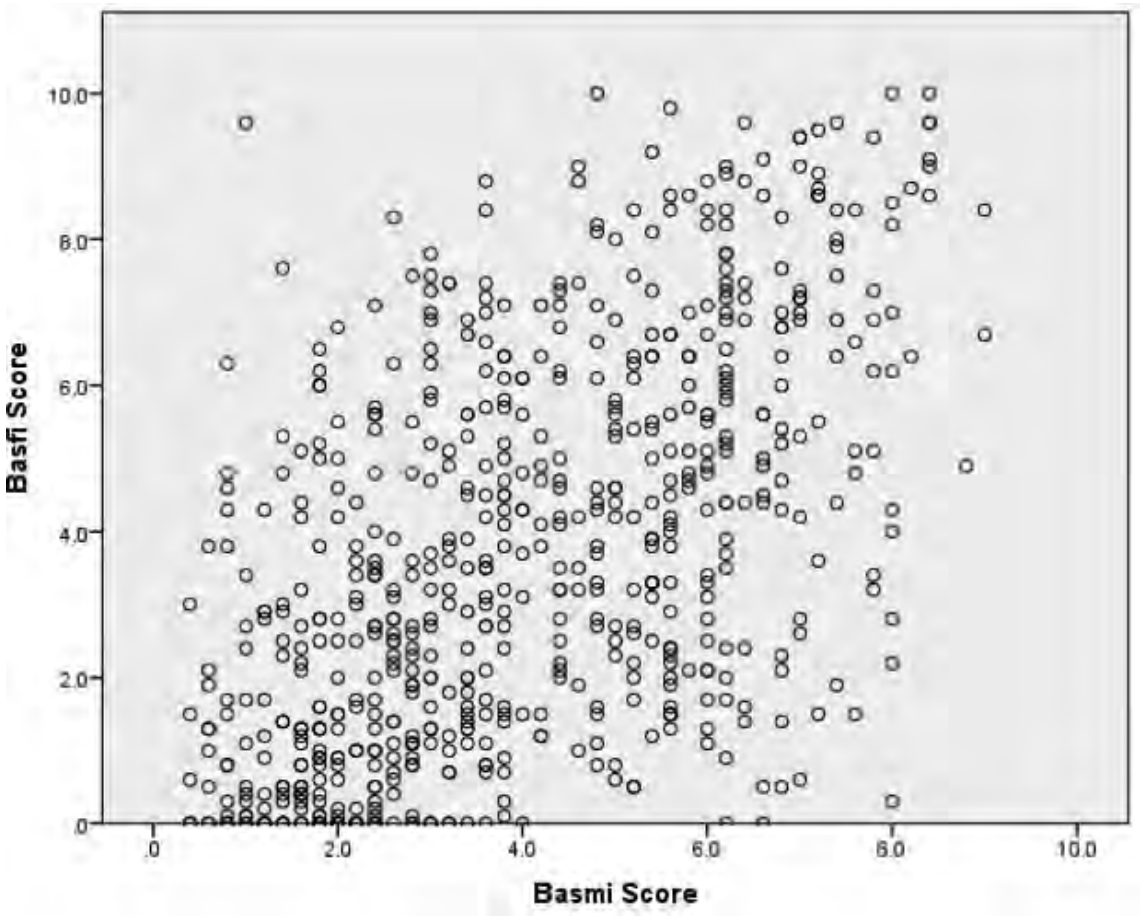

Figure 1. Correlation between BASFI and BASMI in the ASRI population

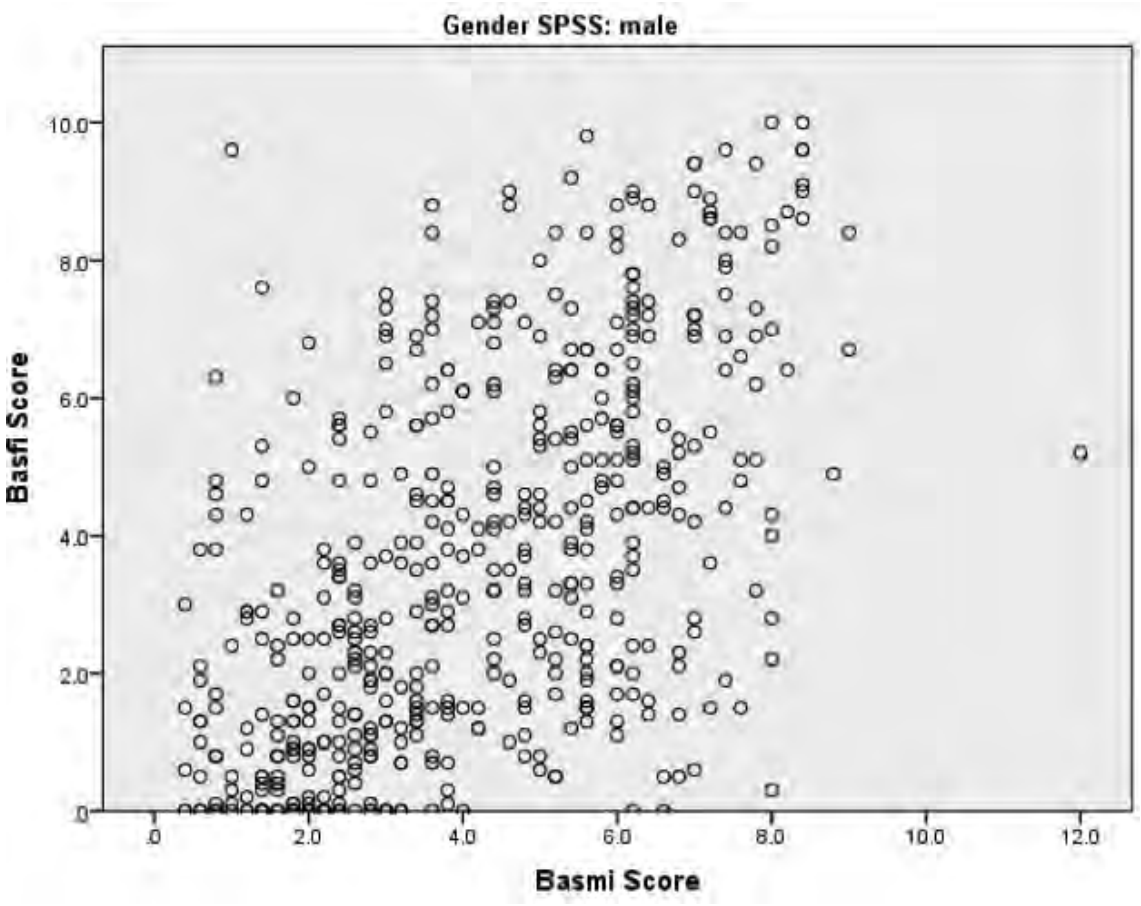

Figure 2a. Correlation between BASMI and BASFI in Males

correlation showed that the strength of this correlation was stronger when controlled for gender, rpartial(645) =0.521, and remained statistically significant p< 0.001. A Spearman's rank-order correlation analysis following splitting of records by gender showed the correlation becomes stronger if assessed within each gender (Females rs(144)= 0.577, p< 0.01; Males rs(509) =0.576, p< 0.01) and has a slightly stronger association with in females(figure 2).

Conclusion: BASFI scores have a strong positive correlation with BASMI scores in patients with axSpA. In clinical terms, patients with worse limitation of spinal mobility are likely to have greater level of functional impairment and vice versa. Analysis by gender shows this correlation is more significant if compared within each gender, and is slightly stronger in females with axSpA.

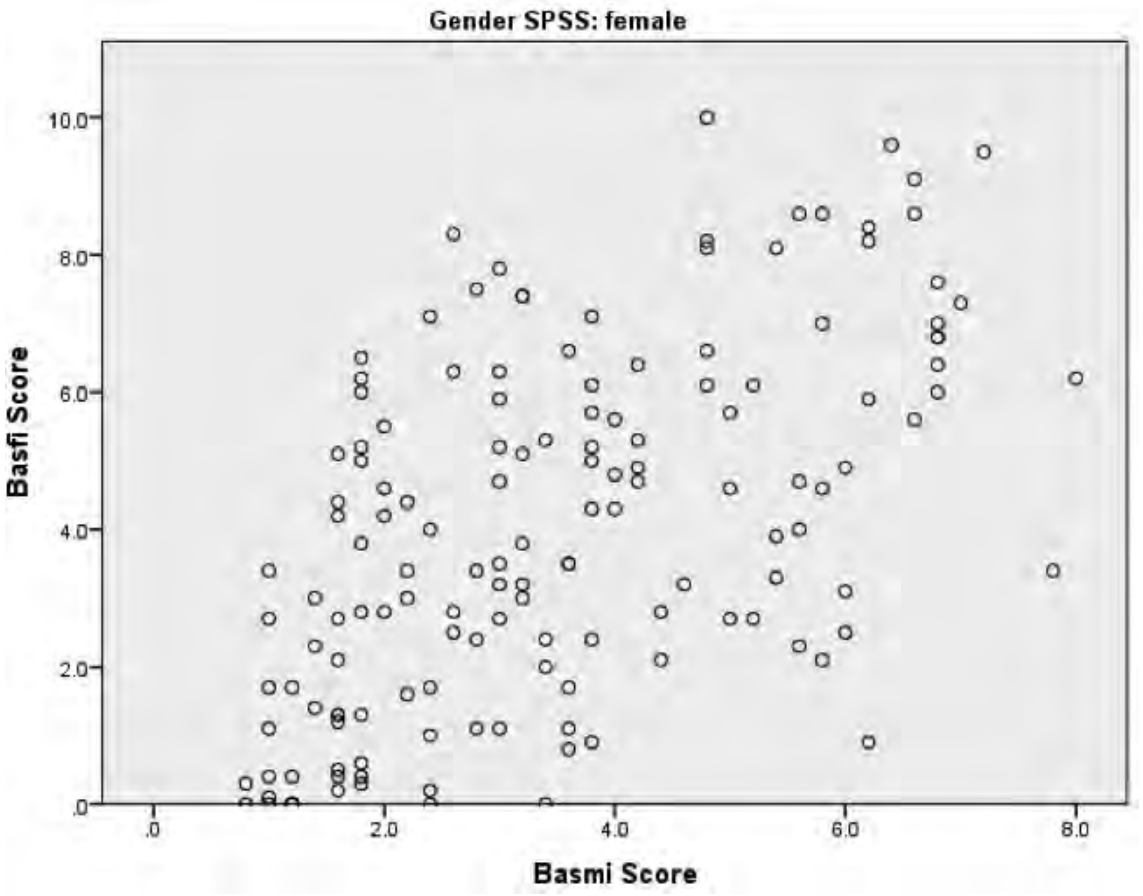

Figure 2b. Correlation between BASMI and BASFI in Females

Disclosure: S. Maguire, None; **P. Gallagher**, None; **F. O'Shea**, None.

Abstract Number: 1888

Successful Evaluation of Spinal Mobility Measurements with the Epionics SPINE Device in Patients with Axial Spondyloarthritis Compared to Controls

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Variable	Mean Difference	95%-LCL	95%-UCL	Pr > |t|
Flexion (RoK) (tr)	-2.53	-3.13	-1.93	**<.001**
Flexion (RoM)	-13.88	-18.68	-9.08	**<.001**
Extension (RoK) (tr)	-2.31	-3.19	-1.43	**<.001**
Extension (RoM)	-10.05	-15.73	-4.37	**0.001**
Rotation (RoK) (tr)	-6.09	-7.66	-4.52	**<.001**
Rotation (RoM)	-24.52	-31.48	-17.55	**<.001**
lateral Flexion (RoK) (tr)	-4.99	-6.49	-3.48	**<.001**
lateral Flexion (RoM)	-21.91	-29.29	-14.53	**<.001**

Table 1. Differences between axSpA and HC for ES scores (unadjusted analyses) axSpA: axial spondyloarthritis, ES: Epionics SPINE,HC: healthy controls RoM: Range of Motion, RoK: Range of Kinematics, (tr): log-transformed

Variable	AUC	LCL	UCL	Spec ≥80%	Sens
Rotation (RoM)	0.841	0.772	0.910	82.5 (33/40)	71.6 (63/88)
Rotation (RoK)	0.795	0.711	0.879	82.5 (33/40)	68.2 (60/88)
Extension (RoM)	0.819	0.746	0.891	82.5 (33/40)	67.0 (61/91)
Lateral Flexion (RoK)	0.783	0.697	0.870	82.5 (33/40)	65.9 (58/88)
Flexion (RoK)	0.780	0.692	0.868	82.5 (33/40)	63.8 (60/94)
Extension (RoK)	0.790	0.709	0.870	82.5 (33/40)	62.6 (57/91)
Lateral Flexion (RoM)	0.805	0.727	0.883	82.5 (33/40)	59.1 (52/88)
Flexion (RoM)	0.801	0.723	0.880	82.5 (33/40)	54.3 (51/94)
BASMI	0.748	0.664	0.831	82.5 (33/40)	62.8 (59/94)
BASFI	0.689	0.590	0.788	80.6 (29/36)	51.7 (46/89)
PCS	0.639	0.533	0.745	80.6 (29/36)	45.2 (38/84)
MCS	0.512	0.404	0.620	80.6 (29/36)	27.4 (23/84)
ASAS	0.593	0.484	0.702	84.2 (32/38)	26.7 (24/90)
ASDAS	0.531	0.413	0.650	81.8 (27/33)	22.8 (18/79)
BASG	0.538	0.429	0.647	84.2 (32/38)	22.2 (20/90)
BASDAI	0.503	0.392	0.615	81.6 (31/38)	16.7 (15/90)
Comprehensive model (based on Rotation (RoM))	0.854	0.787	0.921	82.5 (33/40)	70.1 (61/87)
Enlarged comprehensive model incl. BASFI	0.857	0.783	0.931	80.6 (29/36)	80.5 (66/82)

Table 2. Results of ROC curves for modeling r-axSpA of covariable-adjusted models of single derived ES variables, standardized questionnaires, the comprehensive model, and the enlarged comprehensive model incl. BASFI axSpA: axial spondyloarthritis, ES: Epionics SPINE, RoM: Range of Motion, RoK: Range of Kinematics, BASDAI: Bath ankylosing spondylitis (AS) disease activity score, BASFI: Bath AS functional index, BASMI, Bath AS metrology index, BAS-G: Bath patient global score, ASDAS: AS disease activity score, AS-HI: AS health index, PCS: physical component score of SF-12, MCS: mental component score of SF-12. AUC: area under the curve; LCL: lower confidence limit; UCL: upper confidence limit

Background/Purpose: Axial spondyloarthritis (axSpA) comprising radiographic (r-) and non-radiographic (nr)-axSpA is often associated with loss of mobility and impaired physical function. Established assessments of spinal mobility based on physical examination (BASMI) were shown to have limited reliability, whereas questionnaires (BASFI) are largely based on subjective perception of physical functioning. Epionics SPINE (ES) is a novel device that uses electronic sensors to measure spinal movements including range (RoM) and speed (RoK) of motion, it has already been validated in healthy individuals and in patients with mechanic back pain. The objective of this study was to evaluate the ES device for of the assessment of spinal mobility in patients with axSpA.

Methods: Spinal mobility was assessed in 153 individuals (40 nr- and 94 r-axSpA and 19 healthy controls (HC) using ES, BASMI, BASFI and other questionnaires. Mean scores were calculated to compare groups and modeling was performed using multivariable logistic regression.

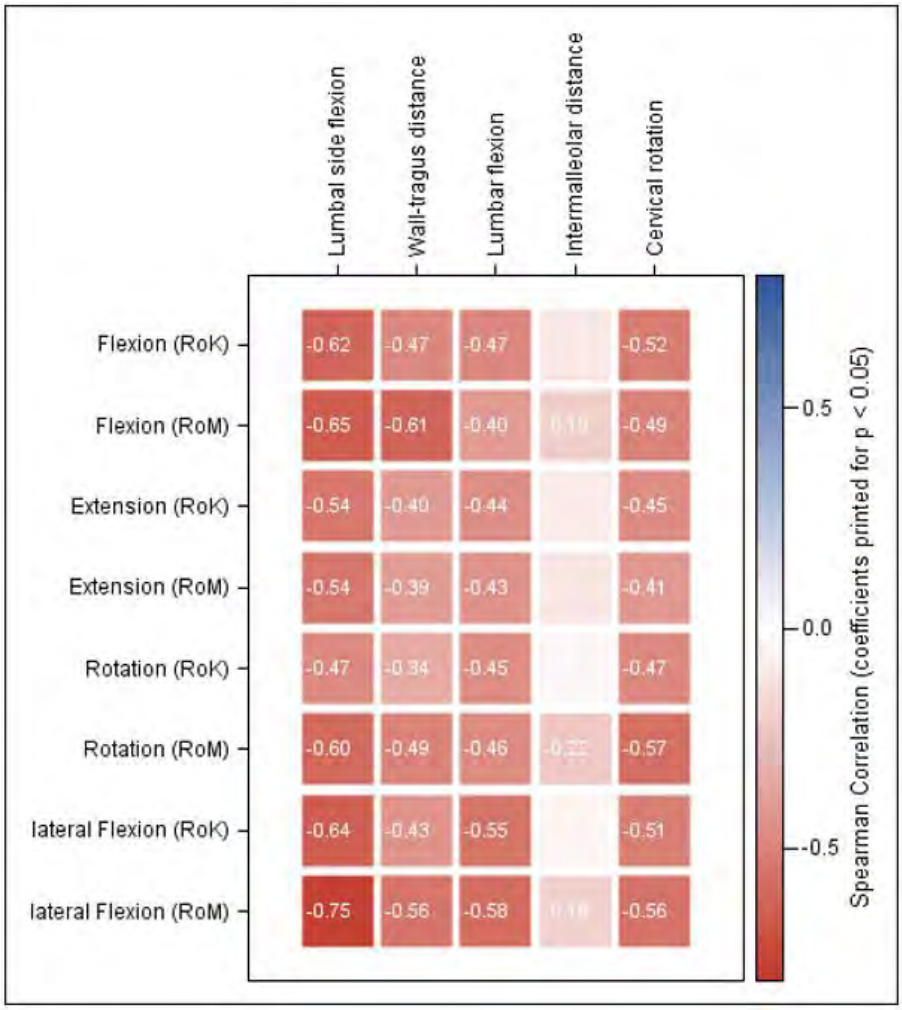

Figure 1. Heatmap of results of Spearman correlation analyses between Epionics SPINE variables and BASMI sub-scores for axSpA patients axSpA: axial spondyloarthritis, BASMI: Bath ankylosing spondylitis metrology index Correlation coefficient (r) values are only depicted in case of significance.

Results: ES scores showed meaningful differences between axSpA patients and HC (all p< 0.001) and between r- and nr-axSpA (p< 0.01) (Table 1 and 2). In axSpA patients, ES results correlated negatively with BASMI (Fig.1) and patients with r-axSpA had worse spinal mobility than those with nr-axSpA. RoK and RoM decreased significantly with age. ES scores showed only a weak negative correlation with BASFI (r >-0.39) and almost no correlation with other patient reported outcomes (BAS-G, ASAS-HI, PCS, MCS all r between -0,26 and 0,28).

Conclusion: ES measurements are a valid and objective measure to assess spinal mobility in patients with axSpA. Since rotation and time are new elements of assessment novel information is also provided. The exact measurement of spinal mobility in different planes with ES may improve our understanding of the functional status of patients with axSpA. It is likely that this will be more useful than standardized questionnaires only.

Disclosure: D. Kiefer, AbbVie, 1, Chugai, 1, Janssen, 1, MSD, 1, Novartis, 1, 2, Pfizer, 1, Roche, 1, UCB, 1; **X. Baraliakos**, AbbVie, 2, 5, 8, Novartis, 2, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Pfizer, 5, 8, UCB, 5, 8, BMS, 5, 8, Merck, 5, 8, Galapagos, 5; **D. Adolf**, None; **V. Chatzistefanidi**, None; **I. Schwarze**, None; **U. Lange**, None; **J. Brandt-Jürgens**, Abbvie, 5, 8, Pfizer, 5, 8, Roche, 5, 8, Sanofi-Aventis, 5, 8, Novartis, 5, 8, Lilly, 5, 8, MSD, 5, 8, UCB, 5, 8, BMS, 5, 8, Janssen, 5, 8, Medac, 5, 8; **E. Stemmler**, None; **S. Sartingen**, None; **J. Braun**, AbbVie (Abbott), 1, Amgen, 1, 2, 3, BMS, 1, 2, 3, Boehringer Ingelheim, 1, 2, 3, Celgene, 1, 2, 3, Celltrion, 1, 2, 3, Centocor, 1, 2, 3, Chugai, 1, 2, 3,

Medac, 1, 2, 3, MSD (Schering-Plough), 1, 2, 3, Mundipharma, 1, 2, 3, Novartis, 1, 2, 3, Pfizer (Wyeth), 1, 2, 3, Roche, 2, Sanofi-Aventis, 1, 2, 3, UCB, 1, 2, 3, Eli Lilly, 1, 2, 3, EBEWE Pharma, 5, 8.

Abstract Number: 1889

Reliability and Validity of the PROMIS-29 Health Profile in Ankylosing Spondylitis Patients

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: The Patient Reported Outcomes Measurement Information System 29-Item Profile Measure (PROMIS-29) is a generic measure of health-related quality of life (HRQOL) that has seven health domains: Physical Function, Anxiety, Depression, Fatigue, Sleep Disturbance, Ability to Participate in Social Roles/Activities and Pain Interference. We hypothesized that the physical aspects of Ankylosing Spondylitis (AS) may have more impact on sleep disturbance than mental factors, which are more impactful in the general population.

Methods: Participants from the Prospective Study of Outcomes in Ankylosing Spondylitis (PSOAS) cohort completed the PROMIS-29 from 2017-2019(2). Test-retest reliability and internal consistency was assessed using intraclass correlation coefficients (ICC) and Cronbach's alpha, respectively, of all PROMIS-29 domains. We conducted confirmatory factor analysis (CFA) using our hypothesized model (Figure 1a) as well as the general population model as described by *Hays et al* (Figure 1b) to study structural validity. The practical fit of the models was evaluated using the chi-squared goodness-of-test ($\chi 2$), comparative fit index (CFI) and the root mean square error of approximation (RMSEA). Good model fit was defined by a $\chi 2$ p-value >0.5, CFI > 0.95 and RMSEA < 0.06. Anxiety and Depression domains were combined into an 'Emotion' domain as studied in the *Hays* model(1). Construct validity of the PROMIS-29

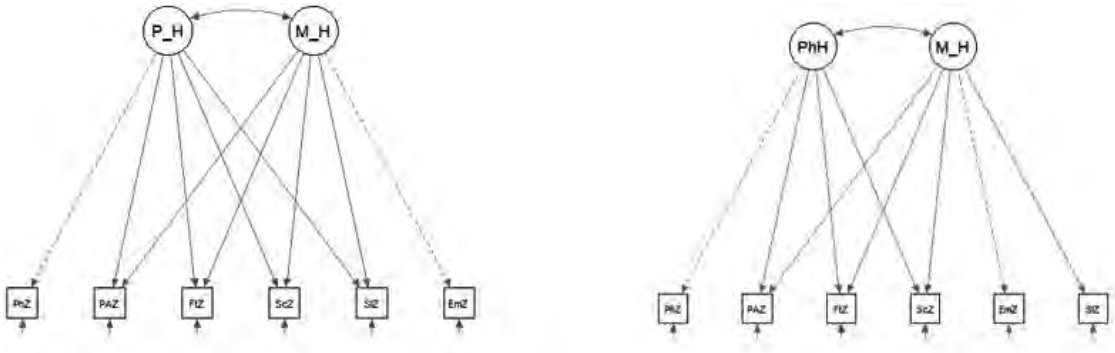

Figure 1. Schema of the Factor Structures of the PROMIS-20 v 2.0 Health Profile Literature 2-factor model of the PROMIS-29 v 2.0 Health Profile a) Hypothesized AS Model b) General Population Literature Model. The Hypothesized model has Sleep Disturbances (SlZ) related to Physical Health (P_H) and Mental Health (M_H) Factor.

Table 1. Participant characteristics (N=119)

Characteristic	N	Value (%)
Age (Mean SD; years)	119	50.85 ± 14.77
Male Gender	119	82 (69%)
Race	119	
White		96 (81%)
Other		23 (19%)
Education	119	
High School		16 (13%)
College		103 (87%)
Employment status	119	
Full time		76 (64%)
Not Working		32 (27%)
Disabled		11 (9%)
Self-Reported Depression	119	16 (13%)
AS Symptom Duration (Mean SD; years)	119	25.47 ± 13.32
ASDAS *	90	
Inactive		25 (31%)
Moderate		30 (33%)
High-Very High		35 (36%)
Biologic DMARD usage †	110	66 (56%)
Last mSASSS (Median [IQR])‡	85	4 (0-34)

* Missing = 29 due to lack of CRP labs.
† Missing = 9 due to incomplete medication list
‡ Missing = 34 due to incomplete radiographs

Table 2. Correlation of AS Legacy Measures with the 2-factor PROMIS-29 model

	Physical Health	Mental Health
BASDAI	.802**	.280**
BASFI	.767**	.311**
CRP	.282**	0.118
Pain NRS	.704**	.217*
Global NRS	.843**	.420**

**. Correlation is significant at the 0.01 level (2-tailed).
*. Correlation is significant at the 0.05 level (2-tailed).

were studied by studying Spearman's correlation coefficients of the factors with C-reactive protein and AS legacy measures: BASDAI, BASFI, Pain Numeric Rating Scale (NRS), and Global NRS.

Results: A total of 119 patients were enrolled (Table 1). All domains of the PROMIS-29 showed good test-retest reliability (ICC > 0.8) and excellent internal consistency with Cronbach's alpha ranging from 0.91(Physical Function) to 0.98(Sleep). In CFA of the hypothesized 2-factor model, we found a $\chi 2$ goodness-of-fit p-value of 0.081, a CFI of 0.988 and RMSEA of 0.095. In the general population, we found a similar $\chi 2$ goodness of fit (p-value of 0.081) and CFI (0.988), and a RMSEA of 0.090. In both CFAs, a 2-factor model was found with the physical function domain and emotional domain, respectively, having the highest loadings on Factor 1 and Factor 2. We thus named Factor 1 'Physical Health' Factor and Factor 2 'Mental Health' Factor in both analyses. Using Spearman's correlation coefficient, all AS legacy measures showed strong correlation, rho >0.7, with the 'Physical Health' factor (Table 2). C-reactive protein was weakly correlated (rho 0.28) with the Physical Health factor.

Conclusion: PROMIS-29 is reliable in AS and the physical component of PROMIS-29 has construct validity with AS legacy measures. The general population two-factor model showed a better fit than our hypothesized model in CFA of our patient sample but did not meet predetermined cutoffs of good fit. Thus while our results may provide guarded support for the validity of the PROMIS-29 health profile in AS, future study of this HRQOL instrument is needed to elucidate the clinical utility in AS patients.

Disclosure: Y. Farran, None; **A. Ogdie**, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1; **J. Reveille**, Eli Lilly, 2, UCB, 5, Janssen, 2; **M. Hwang**, Novartis, 5, University of Texas Health Science Center at Houston (UTHealth) Center of Clinical and Translational Sciences KL2 program, 2.

Abstract Number: 1890

Daily Management of Patients with Axial Spondyloarthritis: Self-monitoring of Disease Activity with a Smartphone App Is Feasible – a Proof of Concept Study

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SESSION INFORMATION
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Background/Purpose: Assessment and monitoring of disease activity and functioning is of major importance for the course of axial spondyloarthritis (axSpA). This is equally important for patient monitoring in daily routine as also for tight control strategies. Even though there is evidence that a closer monitoring of patients is better than routine care, more intensive treatment schedules are often not realized in daily practice for several reasons including shortage of time and personal resources. Using application software devices (apps) in clinical routine for the recording of disease-specific patient reported outcomes (PRO) may facilitate monitoring and improve clinical decision processes but there is a lack of data on the use of apps.To investigate the use of such App technology in respect to usability, feasibility and equivalence of data in daily care of patients with axSpA. In more detail, it will be first determined how many patients are capable and ready to use the technology in a routine setting. Furthermore, the usage and behavior of patients using the app will be studied, the usability of the app and the equivalence of the collected parameters as well as the adherence to the documentation of disease activity over time

Methods: Patients diagnosed with axSpA were consecutively included in this ongoing monocentric prospective cohort study. In addition to patient and disease characteristics, information on previous experience with digital health apps was collected. Patients were asked to submit BASDAI and BASFI scores regularly every 2 weeks. The free to use AxSpA Live App is available for Android and iOS as a Class I certified medical device.

Results: Out of 103 axSpA patients asked, 69 patients with axSpA (mean age 41.5 ± 11.3, 58% male, 76.8% use of bDMARDs, BASDAI 4.3 ± 2.0, BASFI 3.8 ± 2.5) out of 103 patients (67%) agreed to use participate, while 5 did not have a smartphone, 1 was unable to download the app for technical reasons, 28 reported other personal reasons). Of the 69, 62 patients (89.9%) reported using electronic media frequently and had used digital health apps (mean apps used 1.0 ± 1.3) in everyday life before. There were no systematic differences between pain levels documented on paper or by app at baseline (ICC 0.9 (95%CI 0.82 – 0.93). Out of 55 patients who completed week 2, only 33 patients (60%) used the App regularly to transmit their BASDAI/BASFI responses within the first two weeks (60%). Patients who started a new drug treatment because of high disease activity, reported BASDAI values more often than patients without a treatment change within a follow-up period of 5.5± 2.4 weeks (Table).

	Patients without change in their medication (n=53)	Patients with change in their medication (n=16)
Age, years	42.0 (11.9)	39.8 (9.3)
Sex, male (%)	62.3	43.8
BASDAI, baseline	4.1 (2.1)	4.9 (1.7)
BASFI, baseline	3.8 (2.6)	3.8 (2.3)
Time of follow-up, in weeks	5.4 (2.4)	5.6 (2.5)
Number of transmitted BASDAI values at week 2	22 (41%)	11 (69%)
Median number of transmitted BASDAI values during follow up	1.0 (3.6)	1.5 (1.4)

Conclusion: The majority of patients with axSpA were able to use the AxSpA Live App. Most patients report scores regularly. The current disease activity seems to influence the adherence to reporting.

Disclosure: U. Kiltz, Abbvie, 2, 5, Biocad, 2, 5, Biogen, 2, 5, Chugai, 2, 5, Eli Lilly, 2, 5, Grünenthal, 2, 5, Janssen, 2, 5, MSD, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Roche, 2, 5, UCB, 2, 5; **R. Kempin**, None; **J. Richter**, None; **A. Schlegel**, None; **X. Baraliakos**, None; **S. Tsiami**, None; **I. Andreica**, None; **B. Buehring**, GE/Lunar, 1, 2, Kinemed, 1, Gilead, 1, AbbVie, 1, 2, Lilly, 1, Janssen, 1, Amgen, 1, 2, UCB, 1, 2, 3, MSD, 1; **D. Kiefer**, AbbVie, 1, Chugai, 1, Janssen, 1, MSD, 1, Novartis, 1, 2, Pfizer, 1, Roche, 1, UCB, 1; **J. Braun**, None.

Abstract Number: 1891

Impact of Utilising Smart Phone Application in Ankylosing Spondylitis: SMART- as Study

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SESSION INFORMATION
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Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) is a chronic inflammatory disease that primarily affects the axial skeleton and characterized by inflammatory back pain, leading to decreased mobility, function, and quality of life. Management of the disease includes the use of DMARDs, physical therapy, and other lifestyle remedies. There is a global challenge in meeting patients' needs and discrepancies in access to AS care, highlighting the urgent need to implement cost-effective disease management programs and deliver equal access to care. In modern era, most people having access to smart phones create opportunities for patient care in chronic diseases. This study aims to investigate the impact of smart phone application (HealthCius) on inflammatory disease activity and quality of life in AS patients over a period of one year.

Methods: A total of 80 patients were recruited in this observational study fulfilling the Modified New York Criteria, 1984 for AS. These patients were allocated to two groups: Intervention group (n=50) and Control group (n=30). The ones having facility of smart phones as well as patients who accepted to use the HealthCius application were assigned to the Intervention group and patients who did not have the facility of smart phones were grouped as Control. The patients in the two groups received standard treatment of AS. The application was designed after obtaining feedback from health care providers, patient counselors and AS patients using a questionnaire. To the patients, the app was their individual treatment plan. It helped them comply with the plan by providing an easy to refer checklist, reminders, alerts and a visual dashboard of their progress through the day. The app served as the doctor's virtual

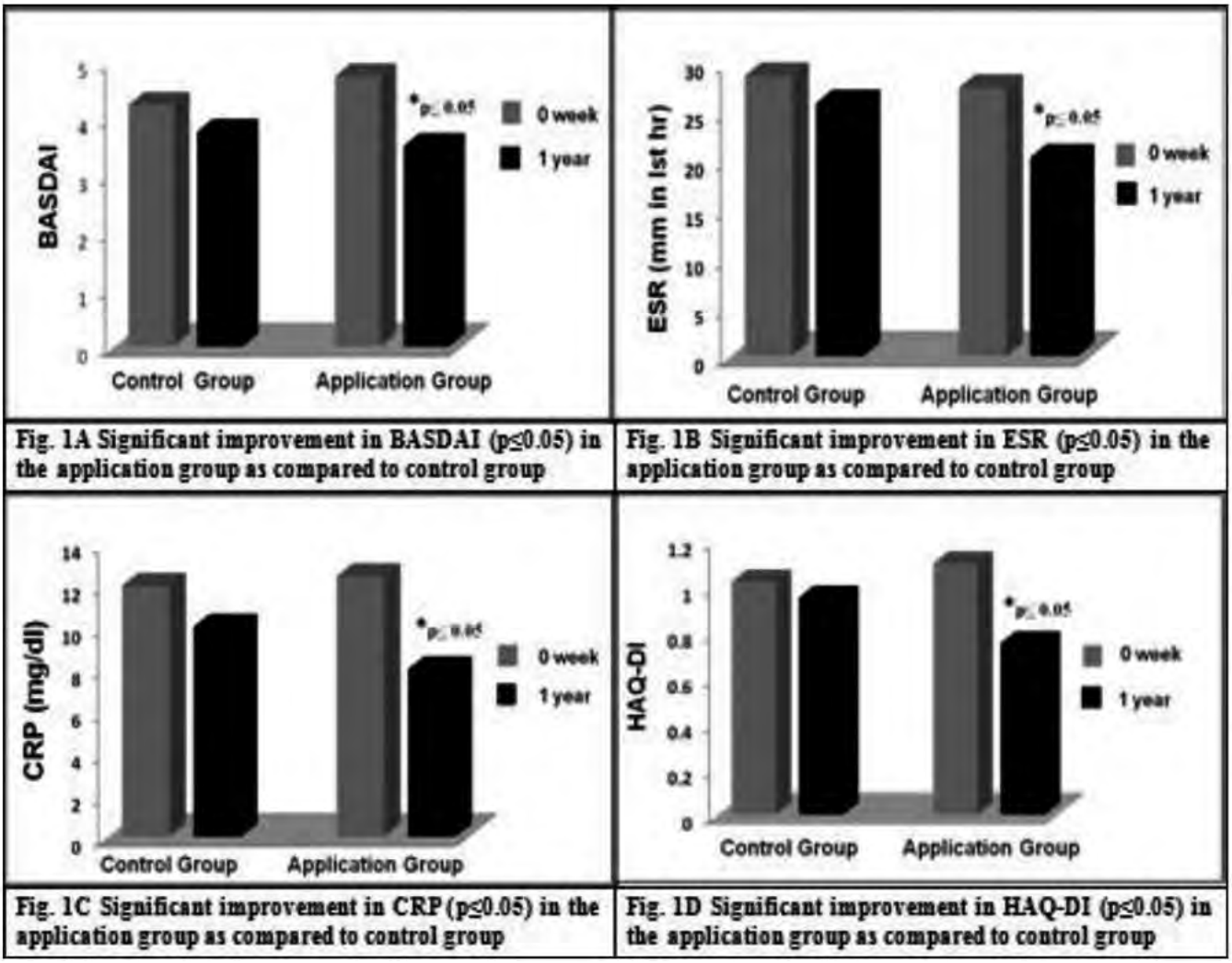


Fig. 1A Significant improvement in BASDAI (p≤0.05) in the application group as compared to control group

Fig. 1B Significant improvement in ESR (p≤0.05) in the application group as compared to control group

Fig. 1C Significant improvement in CRP (p≤0.05) in the application group as compared to control group

Fig. 1D Significant improvement in HAQ-DI (p≤0.05) in the application group as compared to control group

assistant inside the patient's smart phone. For the doctor, it was a live dashboard of all patients and their real time compliance levels. The data reported by the patients was available to the doctor in the form of time sliced charts and trend lines. Therefore, this app is designed to leverage technology to shift the patients' focus every day on to their treatment plan thereby driving up compliance and better health outcomes. Outcome measures included ESR, CRP, BASDAI, BASFI and health assessment questionnaire disability index (HAQ-DI) at baseline and after 1 year.

Results: Baseline characteristics were similar between groups with no significant difference. There was a significant difference between the control and intervention group for BASDAI (p ≤0.05), BASFI (p≤0.05), ESR (p≤0.05), CRP (p≤0.05) and HAQ-DI (p≤0.05) after 1 year in favor of smart phone application. Analysis within the groups revealed significant improvement in BASDAI (p≤0.05) (Fig.1A), ESR (p=0.02) (Fig.1B), CRP (p=0.01) (Fig.1C) and HAQ-DI (p=0.01) (Fig.1D) in the application group as compared to control group. Impact of DMARDs usage was also evaluated at the end of the study and it was found that the average drug usage of DMARDs was more in control group than the intervention group.

Conclusion: The study suggested that there was greater improvement in inflammatory disease activity and quality of life in smart phone application assisted AS patients suggesting that smart phone technology can be used to leverage health benefits in AS.

Disclosure: A. Syngle, None; **N. Garg**, None; **K. Chauhan**, None.

Abstract Number: 1892

Pattern and Influential Factors in Promoting Treat-to-Target (T2T) for F Ankylosing Spondylitis (AS) Patients with the App of Smart System of Disease Management (SSDM): A Cohort Study from China

Jing Xue[1], Hongzhi Wang[2], Hongbin Li[3], Hui Song[4], Yasong Li[5], Xiaofei Shi[6], Hongjun Zhao[7], Feng Wei[8], Bing Wu[9], Hui Xiao[10], Yuhua Jia[9], Fei Xiao[9] and Huaxiang Wu[1], [1]The Second Affiliated Hospital of Zhejiang University school of Medicine, Hangzhou, China (People's Republic), [2]The First Hospital of Jiaxing, Jiaxing, China (People's Republic), [3]The Affiliated Hospital of Inner Mongolia Medical University, Hohhot, China (People's Republic), [4]Beijing Jishuitan Hospital, Beijing, China (People's Republic), [5]Zhejiang Provincial People's Hospital, Hangzhou, China (People's Republic), [6]The First Affiliated Hospital of Henan University of science and technology, Luoyang, China (People's Republic), [7]Xiangya Hospital of Central South University, Changsha, China (People's Republic), [8]Jiangmen Central Hospital Affiliated Jiangmen Hospital of Sun Yat-Sen University, Jiangmen, China (People's Republic), [9]Shanghai Gothic Internet Technology Co., Ltd., Shanghai, China (People's Republic), [10]Shanghai Gothic Internet Technology Co., Ltd., Shanghai, Shanghai, China (People's Republic)

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

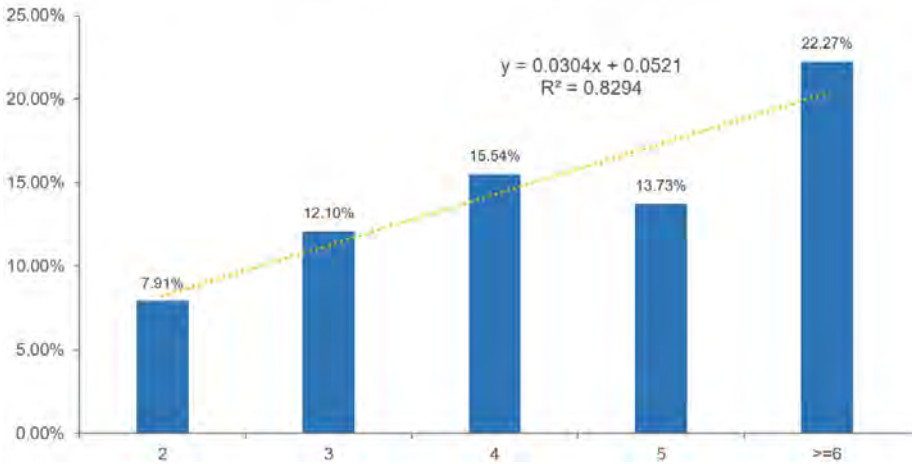
Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Table 1. The T2T results at baseline and in final follow up.

Baseline\Final follow-up	n	%	x <= 1.3	%	1.3 < x <= 2.1	%	2.1 < x <= 3.5	%	3.5 < x	%
x <= 1.3	315	27.95%	206	65.40%	74	23.49%	26	8.25%	9	2.86%
1.3 < x <= 2.1	340	30.17%	138	40.59%	114	33.53%	75	22.06%	13	3.82%
2.1 < x <= 3.5	363	32.21%	95	26.17%	106	29.20%	133	36.64%	29	7.99%
3.5 < x	109	9.67%	24	22.02%	25	22.94%	42	38.53%	18	16.51%
Total	1,127	100%	463	41.08%	319	28.31%	276	24.49%	69	6.12%

Figur1. The correlation between the improvement of T2T rate(y) and the times of self-assessment for ASDAS(x)



Background/Purpose: Ankylosing Spondylitis Disease Activity Score (ASDAS) is adopted to evaluate the degree of disease activity and the inflammatory response in AS patients. ASDAS score < = 1.3 represents inactive disease status and achievement of T2T. SSDM is a mobile application for disease management.

The purpose of this study is to evaluate the patterns of T2T and related influential factors among AS patients after applying SSDM in the real world.

Methods: AS Patients were trained to master SSDM by healthcare professionals (HCPs) and to conduct ASDAS self-assessments. Patients were also required for repeating self-assessments after leaving the hospital. After entry by patients, data can be synchronized to the SSDM terminal of authorized rheumatologists. Based on these data, the patients can apply for consultation to their physicians and rheumatologists can provide medical advices to their patients.

Results: From Jan 2015 to Jan 2020, 17,870 AS patients enrolled in SSDM with the mean age of 34.62±10.98 years old and the median disease duration of 3.58 years. Among them, 1,127 AS patients from 150 hospitals were followed up for more than 6 months through SSDM. The results at baseline and in final follow up were summarized in Table 1.

The rate of T2T achievers were 27.95% (315/1,127) at baseline, and improved significantly to 41.08% (463/1,127) after 6 months follow up, $p< 0.01$. Among T2T achievers at baseline, 65.40% (206/315) maintained T2T, 34.60% (109/315) relapsed. Of patients who didn't achieve T2T at baseline, only 31.65% (257/812) achieved T2T after 6 months follow up.

The impact of the online interaction between patients and physicians and the frequency of self-assessment for ASDAS on T2T has been analyzed. Compared with 544 patients who didn't interact online with their physicians and self-assessed less than 3times, 104 patients with online interaction and monthly assessments achieved significant higher improvement rate of T2T (9.19% vs 23.08%, $p< 0.01$). The more frequent of the self-assessments being performed by patients, the higher improvement of T2T rate will be. The improvement of T2T rate(y) was positively correlated with times of self-assessment for ASDAS(x) independently. The regression equation as "$y = 0.0304x + 0.0521$", $r = 0.9107$, $p< 0.01$ (Figure 1).

Conclusion: Significant improvement was observed under applying SSDM through empowering AS patients. After proactive disease management via SSDM for more than 6 months, patients with ASDAS< =1.3 score at baseline had a significantly higher retention rate of inactive disease activity. The patients who performed more frequent self-assessments had lower probability of relapse and higher rate of T2T. Online interaction between patients and physicians contributed to promote the improvement rate of T2T. SSDM is a valuable tool for long term follow-up through empowering patients.

Disclosure: J. Xue, None; **H. Wang**, None; **H. Li**, None; **H. Song**, None; **Y. Li**, None; **X. Shi**, None; **H. Zhao**, None; **F. Wei**, None; **B. Wu**, None; **H. Xiao**, None; **Y. Jia**, None; **F. Xiao**, None; **H. Wu**, None.

Abstract Number: 1893

Predictors of Response in Secukinumab-treated Patients with Ankylosing Spondylitis: Logistic Regression and Machine Learning Analyses

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Predicting outcomes early in the disease course in patients (pts) with ankylosing spondylitis (AS) is challenging, owing to heterogeneity of symptoms, varying disease severity, and the various outcome measures being mainly patient-reported, apart from radiographic progression. Using logistic regression analyses and machine learning (ML) techniques to predict the response to therapy may result in improved patient selection for optimized treatment regimens and setting the right expectations for individual patients[1,2]. We explored whether baseline (BL) disease characteristics could predict the response of secukinumab (SEC) therapy in AS pts, using logistic regression and ML analyses.

Methods: This post hoc analysis was performed on a pooled data of pts treated with SEC 300/150 mg from four phase 3 MEASURE studies (MEASURE 1–4)[3-5] in AS (N=860). SEC 300 mg (n=113) group included 76 pts originally randomized to 300 mg and 37 pts initially randomized to placebo and then switched to 300 mg. In SEC 150 mg (n=747) group, 504 pts initially randomized to 150 mg and 243 pts initially randomized to placebo and then switched to 150 mg. A univariate logistic regression analysis was applied to search for potential BL predictors ($P < 0.2$) commonly collected in the MEASURE trials as demographics, disease activity parameters, prior medications etc. Various BL factors including sex, TNF status (treatment naïve vs inadequate responder), HLA-B27 status, current smoking status, concomitant NSAID use, BMI (< 30 kg/m^2 vs ≥30 kg/m^2), and hsCRP (elevated ≥5 mg/L vs normal < 5 mg/L) [binary variables], as well as age, MASES score, patient global assessment(PGA), and BASMI parameters [continuous variables] were assessed. Potential predictors identified in the univariate analyses were subsequently included in multivariate logistic regression models for further selection to assess their association with the response to SEC in AS pts on the following outcomes measures: ASAS40, ASDAS-Inactive Disease(ASDAS-ID), and BASDAI50. Additionally, ML Random Forest methods were applied and optimized using a grid search to find the best set of predictors.

Results: The BL factors with a significant ($P < 0.05$) association with the assessed outcomes of ASAS40, ASDAS-ID and BASDAI50 in multivariate logistic regression at Week 52 are presented in the **Table**. Age, hsCRP, occiput-to-wall distance score and MASES score were associated with ASAS40 and BASDAI50 responses. BMI, TNF status, occiput-to-wall distance score and PGA were associated with ASAS40 and ASDAS-ID responses. Additional modeling attempts using ML tree-based classification models showed similar results, without demonstrating sufficient predictive power.

Predictors*	Odds Ratio (95% CI)		
	ASAS40	ASDAS-ID	BASDAI50
Age (years)	0.98 (0.97, 0.99)	_	0.98 (0.96, 0.99)
Sex (Male vs Female)	_	1.67 (1.07, 2.41)	_
BMI (<30 kg/m^2 vs ≥30 kg/m^2)	1.44 (1.04, 2.01)	2.35 (1.42, 3.89)	_
Current Smoker (No vs Yes)	1.41 (1.04, 1.92)	_	_
TNF status (Treatment Naïve vs Inadequate Responder)	1.58 (1.15, 2.18)	2.30 (1.42, 3.73)	_
hsCRP (Elevated ≥5 mg/L vs Normal <5 mg/L)	1.67 (1.24, 2.26)	_	1.59 (1.16, 2.18)
BL Occiput-to-wall distance	0.96 (0.94, 0.99)	0.89 (0.84, 0.93)	0.97 (0.94, 1.00)
BL PGA (every 10 unit increment on VAS 100 scale)	1.16 (1.06, 1.26)	0.82 (0.74, 0.91)	_
BL MASES Score	0.96 (0.92, 1.00)	_	0.92 (0.88, 0.96)

* Only predictors with P <0.05 are kept in the final multivariate model
AS, ankylosing spondylitis; ASAS, Assessment of SpondyloArthritis international Society; ASDAS-ID, AS Disease Activity Score-Inactive Disease; BASDAI, Bath AS Disease Activity Index; BASMI, Bath AS Metrology Index; BL, baseline; BMI, body mass index; CI, confidence intervals; hsCRP, high sensitivity C-reactive protein; MASES, Maastricht AS Enthesitis Score; PGA, patient global assessment

Table. Multivariate Logistic Regression analysis for baseline predictors of ASAS40, ASDAS-ID and BASDAI50 at Week 52: Significant Associations

Conclusion: The current analysis identified younger age, higher hsCRP, lower BMI, TNF naïve status, lower occiput-to-wall distance score and lower MASES score as factors associated with greater response that could potentially predict outcomes in AS pts treated with SEC.

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Disclosure: C. Miceli-Richard, AbbVie, 2, 5, Bristol-Myers Squibb, 2, 8, Novartis, 2, 5, MSD, 2, Pfizer, 2, 5, 8, UCB, 2, 5, Biogen, 2, Wyeth, 2, 8, Schering-Plough, 8, Roche, 5, 8, Merck, 2, 5, 8, Abbott, 8; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **W. Bao**, Novartis, 1, 3; **C. Parman**, Novartis, 3, IQVIA, 3; **B. Porter**, Novartis, 1, 3; **E. Pournara**, Novartis, 1, 3.

Abstract Number: 1894

Use of Facebook and Electronic Patient Portal to Identify Axial Spondyloarthritis in Patients with Chronic Back Pain

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Delay in diagnosis of Axial Spondyloarthritis (axSpA) remains a significant unmet need and can be partially attributed to lack of timely rheumatology referral. Current referral strategies advocate formal patient referral by non-rheumatologists, and this may be difficult given busy primary care practices and lack of awareness among non-rheumatologists of axSpA. In the ongoing Finding Axial Spondyloarthritis Study (FaxSpA), we are reaching out directly to patients by distributing online screening tool (A-tool) that we developed via electronic patient portal and Facebook. With increasing use of social media and patient participation in electronic medical record (EMR), we believe this may be a feasible approach for screening.

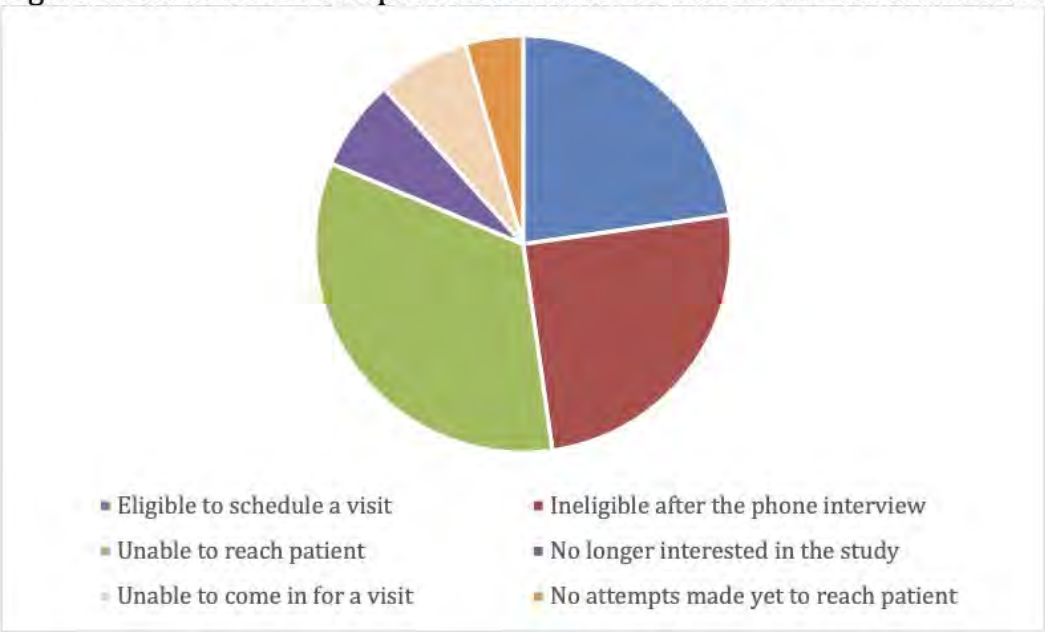
Methods: FaxSpA is a prospective study to evaluate the effectiveness of A-tool in identification of axSpA. A-tool contains 3 item prescreen followed by a clinical questionnaire that includes high yield axSpA features with good sensitivity and specificity. A-tool is distributed via Facebook to individuals in our geographic area and via MyChart to patients ages 18 to 65 with chronic back pain in EMR problem list. MyChart is the patient communication portal in EPIC EMR. Patients fulfilling pre-specified criteria on A-tool are contacted over the phone to confirm eligibility and then invited for clinical evaluation, labs (CRP, HLA B27) and imaging (x-ray and MRI of SI joints). Patients with diagnosed axSpA, spine surgery and age > 65 are excluded. We also collect and store blood samples for future translational biomarker research. SPSS v25 software was used for descriptive statistics and independent t-tests.

Results: Between 4/2019 and 4/2020, 634 subjects completed the survey. Average age (44.3±13.4) was not different for MyChart vs. Facebook groups. Persistent back pain for more than 3 months was reported by 593 (94%); 495 (78%) had gradual onset back pain and 547 (86%) had back pain that started before age 45. Of 634 subjects, 428 passed pre-screen (62% vs. 74% in MyChart vs. Facebook, p=0.002). A-tool was positive in 268 (40% vs. 45% in MyChart vs. Facebook, p=0.20). Out of 268 subjects, an attempt was made to reach 256 by phone and email to confirm their eligibility and schedule a research visit. We were unable to reach 90 subjects (35%), despite multiple attempts. Sixty seven subjects (26%) were deemed ineligible after a telephone interview (15 due to history of previous surgery, 20 due to alternative explanation for their back pain, 18 due to no longer meeting criteria for pre-screen

Table 1. Survey Results of Pre-screen and A-tool

	Total	MyChart	Facebook	p-value
Total number of survey responses	634	332	302	-
Mean age (years)	44.3±13.4	44.2±13.7	44.5±12.9	0.73
Positive pre-screen (out of total survey responses)	428	206 (62%)	222 (74%)	0.002
Positive A-tool (out of total survey responses)	268	132 (40%)	136 (45%)	0.20

Figure 1. Outcomes of Telephone Screen in Patients with a Positive A-Tool



or A-tool, 14 for other reason). Another 38 subjects (15%) were either unable to come or no longer interested in the study when contacted over the phone. So far, 50 patients have been seen in the study.

Conclusion: Using electronic patient portal and social media is a feasible and efficient strategy to screen for patients with suspected axSpA. The gap between the number of patients found eligible on A-tool and those who actually came for a visit may convey that there is need to improve awareness and education about axSpA among patients. It will be interesting to evaluate the effectiveness of A-tool based referral strategy in identifying axSpA.

Disclosure: Y. Afinogenova, None; **S. Alexander**, None; **A. Haims**, pfizer, 9; **A. Danve**, Novartis, 1, 2, Abbvie, 5, Medscape, 5, Peerview, 8.

Abstract Number: 1895

Radiographic Progression in Patients with Axial Spondyloarthritis Under Treatment with TNF Inhibitors. Data from REGISPONSERBIO (Spanish Register of Biological Therapy in Spondyloarthritides)

Maria Llop[1], Mireia Moreno[2], Jordi Gratacós[3], Victoria Navarro-Compán[4], Eugenio De Miguel[5], Pilar Font[6], Teresa Clavaguera[7], Luis Francisco Linares[8], Beatriz Joven[9] and Xavier Juanola[10], [1]Hospital Universitari Parc Taulí I3PT, Sabadell, Catalonia, Spain, [2]Hospital Universitari Parc Taulí I3PT, Sabadell, Spain, [3]University Hospital Parc Tauli Sabadell, Barcelona, Spain, [4]Hospital Universitario La Paz IdiPaz, Madrid, Pais Vasco, Spain, [5]Rheumatology Department, Hospital Universitario La Paz, Madrid, Spain, [6]Rheumatology Department, Reina Sofia University Hospital/ Maimonides Institute for Research in Biomedicine of Cordoba (IMIBIC)/ University of Cordoba, Cordoba, Spain, Córdoba, Spain, [7]Hospital Universitari Trueta, Girona, Spain, [8]Hospital de la Arrixaca, Murcia, [9]Hospital Universitario 12 de Octubre, Madrid, Spain, [10]Rheumatology Service, University Hospital Bellvitge, IDIBELL, Barcelona, Spain, Barcelona, Spain

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Table 1. Baseline characteristics at first radiograph of 101 patients

		N	
Age, years		101	46.68 ± 11.92
Male, sex %		101	82 (81.2%)
HLA-B27 positive, %		99	86 (85.1%)
AS, %		101	86 (85.1%)
BMI		95	26.38 ± 3.74
BMI > 30%		95	11 (10.9%)
Current smokers, %		101	31 (30.7%)
Symptom duration, years		97	17.76 (12.81%)
CRP (mg/L)		94	8.18 ± 13.25
Elevated CRP, %		94	41 (40.6%)
BASDAI		97	3.67 ± 2.28
ASDAS-PCR		96	1.98 ± 1.10
Inactive disease (ASDAS <1.3)		96	31 (23.5%
Low disease (ASDAS < 2.1)		96	62 (47%)
BASFI		98	3.93 ± 2.70
BASMI		82	3.09 ± 1.68
mSASSS		101	16.46 ± 20.92
Syndesmophytes present, %		101	51 (50.5%)
On NSAID treatment, %		99	57 (56.4%)
On TNFi treatment, %		101	75 (74.35)
Number of previous TNFi	0	101	75 (74.3%)
	1	101	20 (19.8%)
	2	101	6 (5.9%)
Months of TNFi treatment in treated patients		101	43.48 ± 39.8
At least 4 years of TNFi use		101	49 (48.5%)
Uveitis		101	22 (21.8%)
Psoriasis		99	7 (6.9%)
IBD		99	7 (6.9%)

ASDAS, Anklyosing Spondylitis Disease Activity Score; AS, Ankylosing spondylitis; HLA-B27, human leucocyte antigen B27; NSAID, non-steroidal anti-inflammatory drug; BMI, body mass index; CRP, c-reactive protein, TNFi, tumor necrosis factor inhibitor: IBD, inflammatory bowel disease; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BASFI, Bath Ankylosing Spondylitis Functional Index; BASMI, Bath Ankylosing Spondylitis Metrology Index; mSASSS, modified Stoke Ankylosing Spondylitis

Background/Purpose: Clinical efficacy of TNF inhibitors (TNFi) in axial spondyloarthritis (axSpA) has been widely probed in randomized control trials. In clinical practice, some studies suggested that long-term treatment with TNFi (more than 4 years) could slow down radiographic progression in axSpA. Furthermore, it is thought that the effect of TNFi on radiographic progression may be mediated by reducing disease activity.

To evaluate the effect of maintenance of low disease activity on radiographic progression in axSpA patients treated with TNFi.

Methods: Of the initial 204 patients a total of 101 patients with axSpA, 31 starting TNFi and 75 previously treated with TNFi, from the Spanish Register of Biological Therapy in Spondyloarthritides (REGISPONSERBIO) were included in the analysis based on the availability spinal radiographs (cervical and lumbar spine lateral views) at two time points and clinical data. Paired cervical and lumbar spine radiographs were available on all patients at a minimum interval of 2 years (mean 3.45±0.978 years; range 2 to 5 years). Two trained readers, independently and with known chron-

Table 2. Impact of persistent low disease activity on spinal radiographic progression

Variable	OR	95% CI	p value
Persistent low disease activity (ASDAS <2.1)	0.21	0.05-0.91	0.04
Duration of radiographic interval	0.87	0.48-1.60	0.67
Presence of syndesmophytes at baseline	5.82	1.26-26.8	0.02
Male	1.46	0.23-9.21	0.69
Current smoking	0.58	0.14-2.44	0.46
AS	0	0	0.99
HLA-B27	0.84	0.42-1.72	0.65
TNFi use during at least 4 years before radiographic interval yes/no	0.39	0.10-1.49	0.17
Disease duration (years)	0.99	0.93-1.04	0.65

Multivariable analysis of 93 patients with radiographic spinal progression defined as development of new syndemosphytes. ASDAS, Anklyosing Spondylitis Disease Activity Score; AS, Ankylosing spondylitis; HLA-B27, human leucocyte antigen B27; TNFi, tumor necrosis factor inhibitor

ological order, scored lateral cervical and lumbar spine images according to the mSASSS system (0-72). Following definitions for progression were used: change of the absolute scores, change of ≥2 points, development of new syndesmophytes, and development of new syndesmophytes or growth of the existing syndesmophytes. Disease activity was reported with ASDAS-PCR every 6 months in a 3-year period.

Results: Baseline characteristics of patients at first radiograph are presented in Table 1. Reliability of both readers was excellent with intraclass correlation coefficients (ICCs) of 0.986 (0.979-0.990) at inclusion and 0.981 (0.972-0.987) at follow-up. The mean±SD score at inclusion was 16.46±20.92, the change score between inclusion and follow-up was 1.98±0.83 and the smallest detectable change of progression was of 2.26 mSASSS units. Development of new syndesmophytes was present in 20 patients (15.2%) and growth of the existing syndesmophytes or new syndesmosphytes was present in 22 (21.8%). Data on disease activity in at least 3 time point in a 3-year period was available in 93 patients, of those 25 (26.9%) patients remain with persistent inactive disease and 65 (69.9%) with persistent low disease activity. In the multivariate analysis, adjusted for multiple baseline clinical and demographic characteristic, only the maintenance of low disease activity was significantly associated with a lower development of new syndesmophytes, OR 0.21 (95% CI 0.05-0.91) p=0.04 (Table 2).

Conclusion: Persistence of low disease activity in patients under TNFi seems to be the most important factor to slow down spinal radiographic progression in axSpA.

Disclosure: M. Llop, None; **M. Moreno**, Abvie, 8, Janssen, 8, Pfizer, 8, Novartis, 8, Celgene, 8; **J. Gratacós**, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, 8, MSD, 5, 8, UCB, 5, 8, Novartis, 5, 8, Janssen Pharmaceutical, 5, 8, Amgen, 5, 8, BMS, 2, 5, 8, Celgene, 2, 5, 8; **V. Navarro-Compán**, Novartis Pharma, 1, 5, 8, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, UCB, 5, 8; **E. De Miguel**, AbbVie, 2, 5, 8, BMS, 8, MSD, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 8, UCB, 8; **P. Font**, None; **T. Clavaguera**, None; **L. Linares**, None; **B. Joven**, None; **X. Juanola**, None.

Abstract Number: 1896

No Relationship Between Lumbar Bone Mineral Density and Syndesmophyte Formation at the Same Level - A Multilevel Analysis in Patients with Radiographic Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: In radiographic axial spondyloarthritis (r-axSpA) it has been hypothesized that inflammation-driven bone loss triggers bone repair but at anatomically distinct sites of the same vertebra (i.e. bone loss occurring in the trabecular bone and bone repair in the periosteum)[1]. However, the possible association between bone loss and new bone formation at the same individual vertebra has never been studied. The purpose of this study was to investigate if in r-axSpA low vertebral bone mineral density (BMD) is associated with development of new syndesmophytes at the same vertebral level.

Methods: In a post-hoc analysis from the ASSERT trial (infliximab vs placebo) dual-energy X-ray absorptiometry was used to measure baseline BMD (g/cm^2) of the lumbar spine L1 to L4. Syndesmophyte formation was assessed in the same vertebrae on conventional radiographs defined as an increase in modified Stoke Ankylosing Spondylitis Spine Score from 0 or 1 to 2 or 3 after 2 years. Radiographs were scored by two readers. Generalized estimating equations (GEE) adjusted for within-patient correlation across multiple vertebrae, taking potential confounders into account (Table 1).

Table 1. Relationship between baseline BMD and 2-year syndesmophyte formation as reported by both readers and at least one of the readers - multivariable analysis (adjOR (95% CI))

Independent variables	New radiographic syndesmophyte formation according to both reader 1 and reader 2	New radiographic syndesmophyte formation according to reader 1 or reader 2
BMD (g/cm^2)	0.56 (0.01, 44.45)	0.26 (0.03, 2.63)
Age (years)	1.03 (0.95, 1.11)	1.04 (1.00, 1.09)*
Gender (male)	0.82 (0.10, 6.85)	1.42 (0.50, 4.01)
Disease duration (years)	1.05 (0.97, 1.14)	1.00 (0.96, 1.05)
ASDAS-CRP	1.79 (0.66, 4.86)	1.09 (0.63, 1.87)
HLA-B27	0.13 (0.02, 0.89)	0.54 (0.15, 1.89)
Treatment with NSAIDs	0.41 (0.07, 2.47)	0.82 (0.21, 3.13)
Treatment with infliximab	1.82 (0.22, 15.31)	1.11 (0.45, 2.69)
Presence of MRI VCI at baseline	4.00 (0.99, 16.13)	4.32 (1.95, 9.60)*
Presence of MRI VCFD at baseline	0.69 (0.16, 3.01)	1.23 (0.60, 2.54)
Presence of syndesmophytes at baseline	20.20 (0.96, 424.63)	3.14 (1.14, 8.66)*

BMD, bone mineral density; **VCI,** vertebral corner inflammation; **VCFD,** vertebral corner fat deposition. *p<0.05

Results: We analyzed 599 vertebrae in 165 r-axSpA patients (78% male, mean (SD) age 38 (10) years, 67% with at least one syndesmophyte anywhere in the spine). In total, 24 to 74 new syndesmophytes developed in 9 (5%) to 30 (18%) patients and 13 (2%) to 39 (7%) vertebrae, if either a syndesmophyte was seen by both or only one of the readers (i.e. specific and sensitive definitions) respectively. Analyses with both definitions, and both uni- and multivariable, showed no significant association between baseline local vertebral BMD and new syndesmophyte formation after two years in the same vertebra (multivariable analysis adjOR (95%CI): 0.56 (0.01, 44.45) (specific definition) and 0.26 (0.03, 2.63) (sensitive definition)) (Table 1).

Conclusion: In patients with active and established r-axSpA, with an observed low incidence of lumbar spine syndesmophyte formation over two years, no relationship was found between baseline BMD and new radiographic syndesmophyte formation in the same vertebra.

[1] Lories RJ. Best Pract Res Clin Rheumatol. 2018 Jun;32(3):331–41.

This study, carried out under YODA Project #2018-2761, used data obtained from the Yale University Open Data Access Project, which has an agreement with JANSSEN RESEARCH & DEVELOPMENT, L.L.C.. The interpretation and reporting of research using this data are solely the responsibility of the authors and does not necessarily represent the official views of the Yale University Open Data Access Project or JANSSEN RESEARCH & DEVELOPMENT, L.L.C..

Disclosure: M. Marques, None; **S. Ramiro**, Abbvie, 8, Eli Lilly, 8, Novartis, 8, MSD, 8, UCB, 8, Sanofi, 8; **P. Machado**, Abbvie, 5, 8, Eli Lilly, 5, Novartis, 5, 8, UCB, 5, 8, Pfizer, 8; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5; **F. van Gaalen**, Reuma Nederland, 1, Stichting vrienden van Sole Mio, 1, MSD, 1, Abbvie, 1, Novartis, 1.

Abstract Number: 1897

Trends in Hospitalizations for Vertebral Compression Fractures in Ankylosing Spondylitis: Data from the National Inpatient Sample 2001-2014

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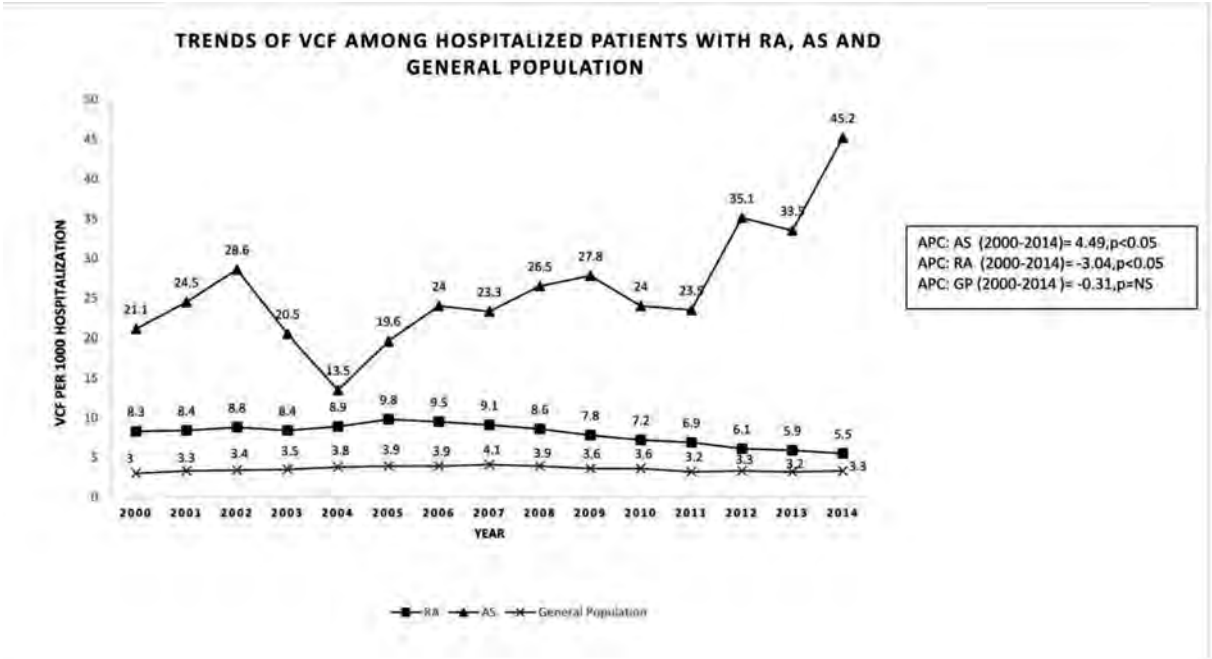
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Ankylosing spondylitis (AS) is a chronic inflammatory disease predominantly affecting the spine, leading to syndesmophyte formation, ankylosis, and osteoporosis. These factors have been associated with an increased risk of vertebral fractures after minor trauma. Whether improved recognition of AS and more effective management including biologics have impacted the risk of vertebral fractures is unclear. The aim of our study was to assess the yearly trends of vertebral compression fractures (VCF) among hospitalized patients with AS compared to RA and the general population.



Trends in Hospitalizations for Vertebral Compression Fractures in Ankylosing Spondylitis compared to Rheumatoid Arthritis and General Population

Methods: National Inpatient Sample (NIS) database from the years 2000-2014 was used to identify adult (≥18 years age) hospitalizations. NIS is the largest all-payer inpatient database in the US and represents 20% stratified sample of all hospital discharges. Previously validated ICD-9 diagnosis codes at secondary diagnosis positions were used to identify hospitalizations with AS (720.0) and RA (714.0, 714.1, 714.2). We created 3 mutually exclusive groups of cohorts: AS, RA and a third group from the general population without diagnoses of AS or RA as controls. VCF hospitalizations were identified in these 3 groups using validated ICD-9 codes (805.2, 805.4, 805.8, 733.13) at the primary diagnosis position. ICD-9 codes for malignant neoplasms, bone and plasma cell neoplasms, or non-specific hemangiomas (140.xx-208.xx, 228.09, 238.0, 238.6, 239.2) were used to exclude patients with malignancies and pathologic bone processes except osteoporosis. STATA version 16 and Joinpoint regression were used to analyze trends in VCF hospitalizations.

Results: In the years 2000-2014, there were a total of 4,364 (2.70%), 45,218 (0.77%), and 1,432,232 (0.35%) VCF hospitalizations in AS, RA and in the general population controls, respectively. Females accounted for 28.1%, 84.6%, and 67.3% VCF hospitalizations in AS, RA, and general population controls, respectively. Mean ages for VCF hospitalization were 71.4, 75.1, 71.6 years for AS, RA, and general population controls, respectively.

From the year 2000 to 2014, an overall increasing trend of VCF hospitalizations in AS (APC= 4.49, $p < 0.05$) was seen, in contrast to a decreasing trend in RA (APC= - 3.04, $p < 0.05$). The trend of VCF in the general population was stable over the years studied (APC = -0.31, p= NS) (**Fig 1**).

Conclusion: The trend of VCF hospitalizations in AS was noted to be increasing compared to a declining trend in RA and a stable trend in the general population. Early diagnosis and improved management of RA might have led to lower VCF hospitalizations in RA over time. While the trends in RA are encouraging, findings in AS suggest the need to improve screening and prevention of osteoporosis and VCF in patients with AS.

Disclosure: A. Paudel, None; **R. Dhital**, None; **D. Poudel**, None; **A. Donato**, None; **P. Karmacharya**, National Center for Advancing Translational Science, 2, SPARTAN (Spondyloarthritis Research and Treatment Network), 2.

Abstract Number: 1898

Comparative Effectiveness of Secukinumab, Adalimumab and Other Tumor Necrosis Factor Inhibitors in the Treatment of Axial Spondyloarthritis

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SESSION INFORMATION

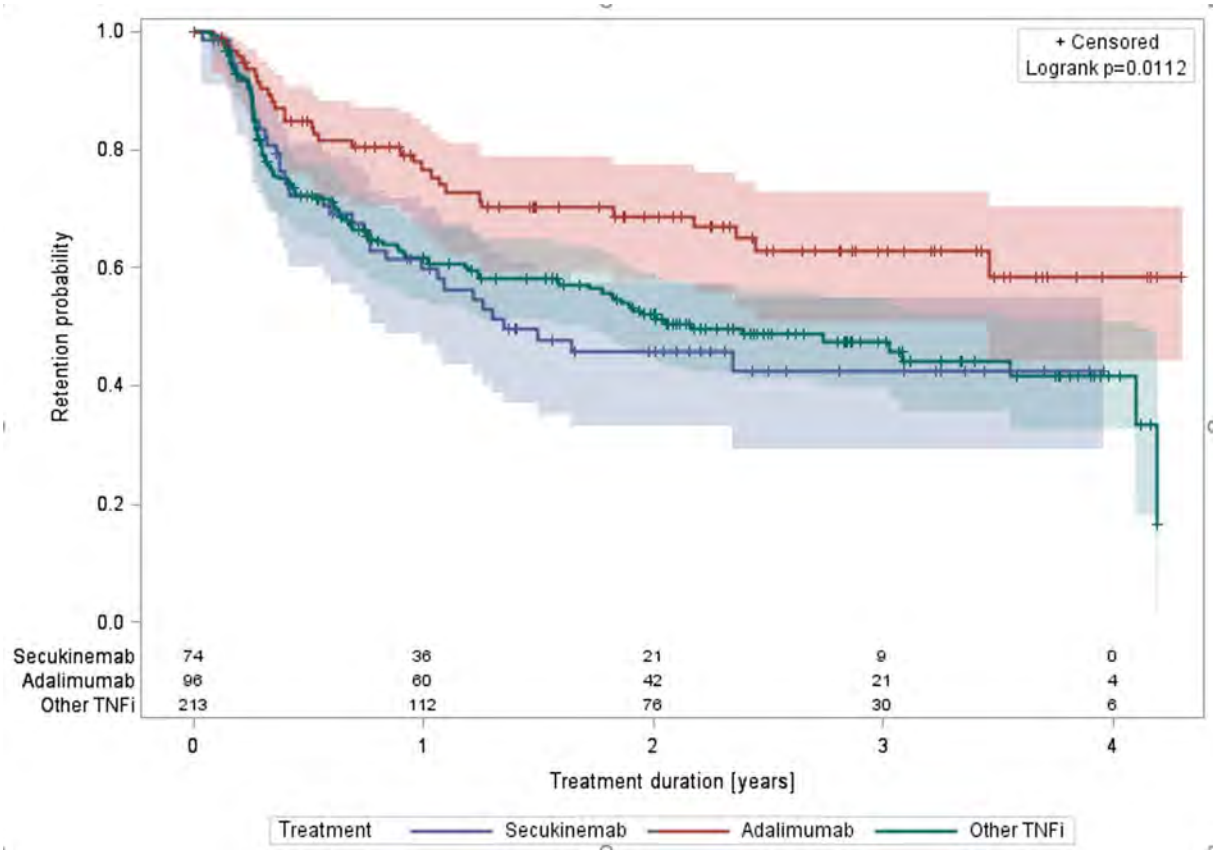
Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Studies comparing the effectiveness of biologics in the treatment of axial spondyloarthritis (axSpA) are sparse [1]. One study comparing secukinumab and adalimumab biosimilar is ongoing. Secukinumab is an agent targetting Il-17. The aim of our analysis is to compare the effectiveness of the most frequently used biologic

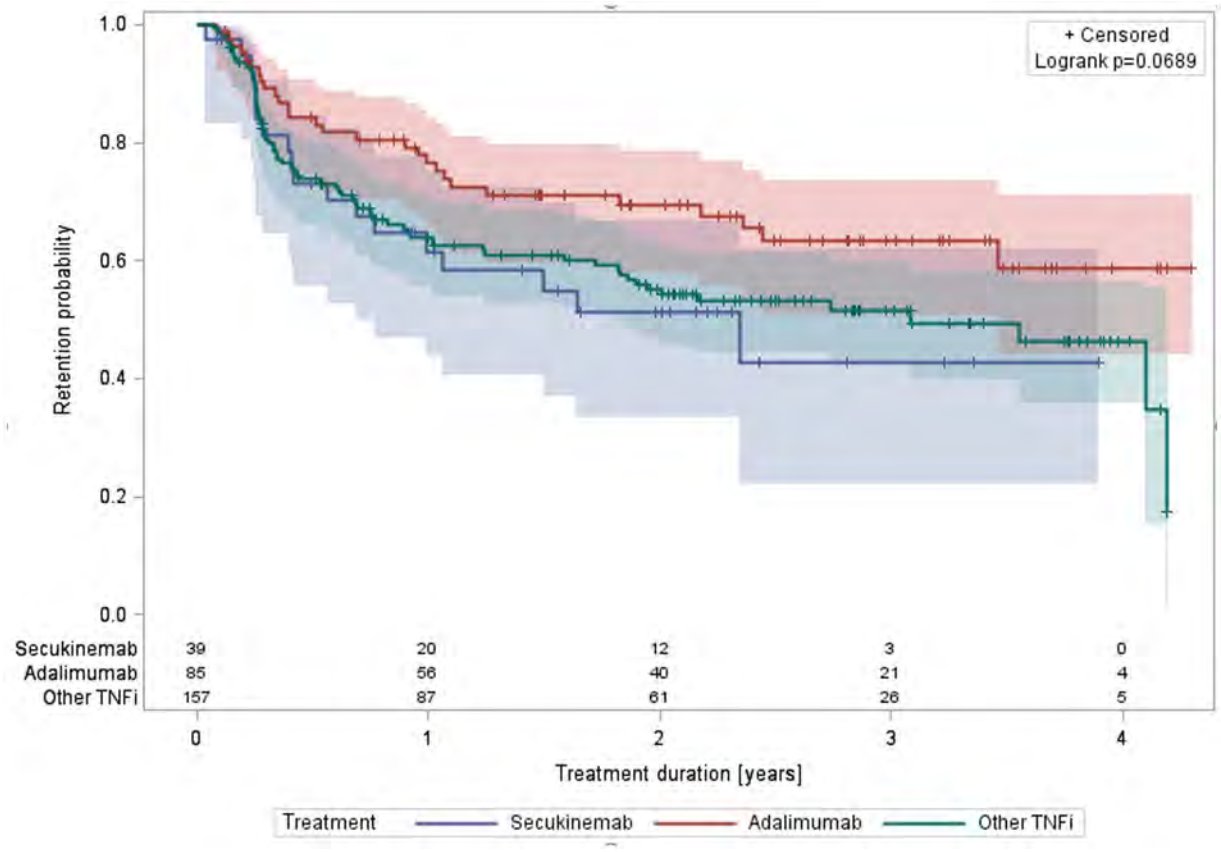


Retention of ADA, SEC and TNFi - all intentions

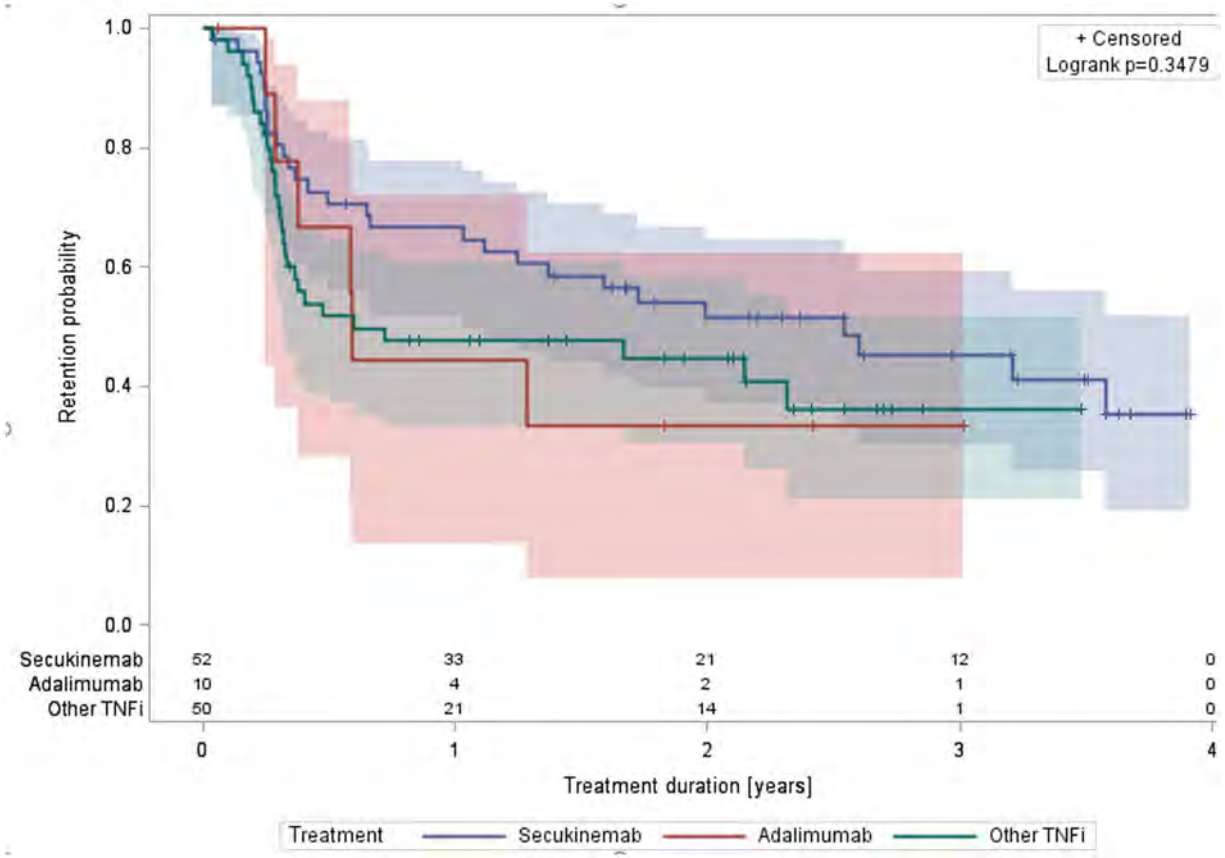
in axSpA since the marketing of secukinumab in all, first and second and third intention or more. Results are presented here.

Methods: Patients diagnosed with axSpA enrolled in RHUMADATA® giving informed consent and treated with secukinumab (SEC), adalimumab (ADA) or other TNF inhibitors (TNFi) on or after January 1, 2016 were extracted from the RHUMADATA® clinical database and registry. RHUMADATA® provides socio-demographics, comorbidities, patient-reported outcomes, disease activity indices, laboratory variables, rheumatologist exam report data, use of concomitant medications and axSpA treatment and reasons for treatment cessation. Kaplan-Meier survival curves and proportional hazard models were used to analyze time to treatment cessation.

Results: A total of 383 patients with axSpA were extracted from the RHUMADATA® registry. Seventy-four were treated with SEC, 96 with ADA and 213 with other TNFi (certolizumab, etanercept, golimumab or infliximab). Overall, 47.3% were women, the average age and disease duration at treatment initiation were respectively 44.8 (±standard deviation (STD)=13.3) and 6.0 (8.4) years. The overall age adjusted Charlson Comorbidity Index (aCCI) was 1.3 (2.1). The proportion of patients diagnosed and/or treated for diabetes and hypertension respectively were 14.9 and 40.5% (SEC), 5.2 and 25.0% (ADA) and 12.7 and 30.5% (TNFi). Overall BASDAI and BASFI scores were 6.0 (2.3) and 5.0 (2.6). SEC, ADA and TNFi were used in first intention in 18.9, 61.5 and 41.3% of patients respectively. Kaplan-Meier logrank p-values were 0.0112, 0.0689, and 0.3479 when comparing the three groups in all, first and second and third or more intentions. Pairwise comparisons showed better retention for ADA treated patients in all and first and second intentions (early treatments). A Cox proportional hazard model adjusting for age at diagnosis, disease duration at treatment initiation, aCCI, the number of prior advanced treatments and concomitant use of methotrexate at treatment initiation demonstrated a statistically better retention of ADA over TNFi.



Retention of ADA, SEC and TNFi - first and second intentions



Retention of ADA, SEC and TNFi - third + intentions

Conclusion: Based on our real-world datasets, ADA had better retention than SEC in treating early axSpA.

References

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Disclosure: L. Choquette Sauvageau, None; **D. Choquette**, AbbVie Canada, 5, 8, Amgen Canada, 5, 8, Bristol-Myers-Squibb Canada, 5, 8, Eli Lilly Canada, 5, 8, Merk Canada, 5, 8, Novartis Canada, 5, 8, UCB Canada, 5, Janssen Canada, 5, Sandoz Canada, 5, 8, Pfizer Canada, 5, 8, Roche Canada, 5, Sanofi-Genzyme Canada, 5, 8; **L. Bessette**, AbbVie Canada, 5, 8, Amgen Canada, 5, 8, Bristol-Myers-Squibb Canada, 5, 8, Merk Canada, 5, 8, Novartis Canada, 5, 8, Pfizer Canada, 5, 8, Sanofi-Genzyme Canada, 5, 8, Celgene Canada, 5, 8, Roche Canada, 5, 8, UCB Canada, 5, 8, Janssen Canada, 5, 8; **I. Ferdinand**, Pfizer Canada, 5, 8, AbbVie Canada, 5, Amgen Canada, 5, 8, Novartis Canada, 5; **B. Haraoui**, Pfizer Canada, 5, 8, UCB Canada, 5, 8, AbbVie Canada, 5, 8, Amgen Canada, 5, Bristol-Myers-Squibb Canada, 5, Eli Lilly Canada, 5, Merck, 5, Roche Canada, 5, Sanofi-Genzyme Canada, 5, Sandoz Canada, 5, Janssen Canada, 8, Celgene Canada, 8; **F. Massicotte**, AbbVie Canada, 8, Celgene Canada, 5, Janssen Canada, 8, Pfizer Canada, 5; **J. Pelletier**, Bioiberica, 8, Bayer Canada, 5, Pierre-Fabre, 5, IBSA, 8, TEVA, 5, Sanofi-Genzyme Canada, 8, Zodiac Laboratory, 5; **J. Raynauld**, AbbVie Canada, 8, Amgen Canada, 5, 8, Bristol-Myers-Squibb Canada, 8, Celgene Canada, 8, Eli Lilly Canada, 8, Novartis Canada, 8, Pfizer Canada, 8, Roche Canada, 8, Sanofi-Genzyme Canada, 5, 8, UCB Canada, 8, Janssen Canada, 8; **M. Rémillard**, AbbVie Canada, 5, 8, Amgen Canada, 5, 8, Eli Lilly Canada, 5, 8, Novartis Canada, 5, 8, Pfizer Canada, 5, 8, Sandoz Canada, 5, 8; **D. Sauvageau**, None; **É. Villeneuve**,

AbbVie Canada, 5, 8, Amgen Canada, 5, 8, Bristol-Myers-Squibb Canada, 8, Celgene Canada, 5, Merk Canada, 8, Novartis Canada, 8, Pfizer Canada, 5, 8, Roche Canada, 5, 8, UCB Canada, 5, 8; **L. Coupal**, None.

Abstract Number: 1899

Life Expectancy a Swiss Cohort of Patients with Ankylosing Spondylitis: A 35-Year Follow-up Study

Zhixiu Li[1], Mohammad Khan[2], Sjef van der Linden[3], Peter Villiger[4], Heinz Baumberger[5], Hermine Zandwijk[6], Matthew Brown[7] and Muhammad Khan[8], [1]Queensland University of Technology (QUT), Translational Genomics Group, School of Biomedical Sciences, Institute of Health and Biomedical Innovation, Translational Research Institute, Princess Alexandra Hospital, Brisbane, Qld, Australia, Brisbane, Queensland, Australia, [2]Kent State University, Kent, OH, [3]Department of Rheumatology, Immunology and Allergology, University of Bern, Inselspital, Bern, Switzerland, Mortroux, Belgium, [4]Department of Rheumatology, Immunology and Allergology, University of Bern, Inselspital, Switzerland, Bern, Switzerland, [5]Retired, Flims, Tajikistan, [6]Retired, Mortroux, Belgium, [7]Guy's and St Thomas, NHS Foundation Trust and King's College London NIHR Biomedical Research Centre, King's College London, London, United Kingdom, London, United Kingdom, [8]Case Western Reserve University, Cleveland OH, Westlake, OH

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate life expectancy of a Swiss cohort of patients with ankylosing spondylitis (AS) versus general population during 35 years of longitudinal follow up, and to study the association of HLA-B27 with mortality in the general population.

Methods: In 1985 AS-affected members of the Swiss Ankylosing Spondylitis Patient Society were contacted to participate in this study, together with their first-degree relatives (FDRs). After ethical approvals and informed written consent, 1178 subjects completed questionnaires on disease manifestations, underwent rheumatological examination of axial and peripheral joins, and provided blood samples for genetic studies. Pelvic radiographs of 363 probands and 713 relatives were assessed blindly for presence of sacroiliitis according to the modified New York (mNY) radiographic criteria. Patients previously clinically diagnosed with AS irrespective of the findings of their pelvic radiographic studies were deemed to have axial spondyloarthritis (axSpA), those meeting the mNY criteria mNYAS, and those with axSpA but not meeting the mNY criteria, non-radiographic axial spondyloarthritis (nr-axSpA).

Approval of a follow-up study was obtained in 2019 from the ethical committee of the Swiss Kanton of Bern. City and village administrations provided current addresses of former participants, and also the deceased persons' year of death, but not its cause. Among the 411 AS patients from the 1985 study, 182 were alive and 123 had died by December 31, 2019. For the remaining 106 patients who were lost to follow up, the year they moved away was taken as their year of last follow-up. Life expectancy was analysed in comparison with age- and gender-matched Swiss general population data, using Cesaro averaging methods and Kaplan-Meier analyses.

Survival in relation to HLA-B27 individuals in the general population was studied in the UK Biobank cohort (n=485,545, with 13,782 deaths).

Results: Patients meeting the mNYAS criteria have an increased standardized mortality rate (SMR) compared with the general population (1.21, 95% confidence interval 0.97-1.51, P=0.049). This was restricted to HLA-B27(+) mNYAS (SMR HLA-B27(+)=1.241, P=0.034, Figure 1; HLA-B27(-)=1.038, P=0.92). Mortality was increased amongst

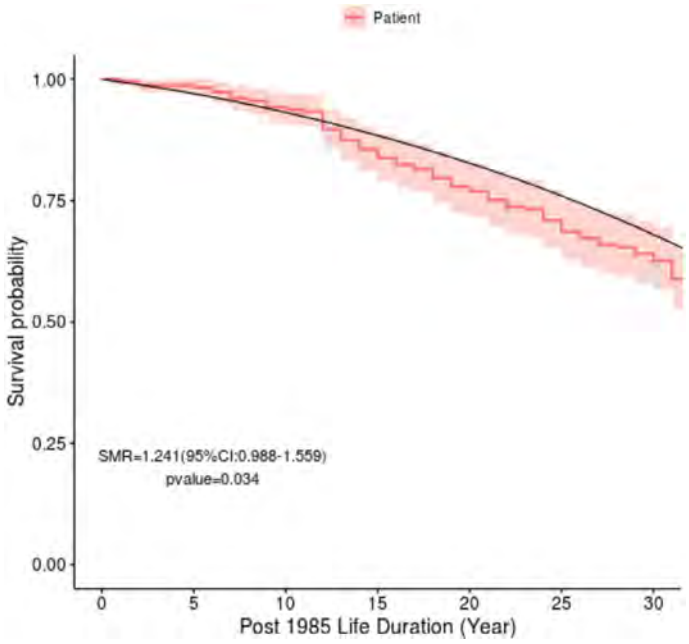


Figure 1. Kaplan-Meier survival probability plot for HLA-B27(+) AS patients.

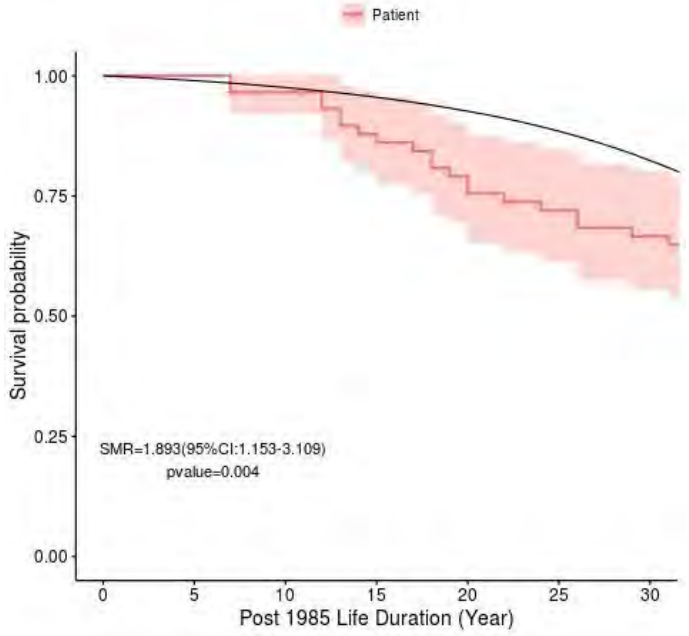


Figure 2. Kaplan-Meier survival probability plot for female HLA-B27(+) AS patients.

HLA-B27(+)mNYAS(+) women (SMR=1.89, P=0.004, Figure 2) but not men (SMR=1.14, p=0.26). No difference in survival was noted amongst HLA-B27(-)mNYAS(+) patients (SMR=1.04, p=0.92). Patients with nr-axSpA had reduced SMR compared with the general population (SMR=0.372, P=0.001). In the UK Biobank general population cohort, HLA-B27 carriage was not associated with mortality (hazard ratio (HR)=0.97, P=0.28), in either males (HR=1, P=0.96) or females (HR0.91, P=0.09).

Conclusion: We report in this 35 year longitudinal study that mNYAS patients, but not nr-axSpA patients, have a significantly shortened life expectancy. Increased mortality was particularly significant amongst women with HLA-B27(+)

mNYAS, perhaps a reflection of their more severe disease. It also provides additional clinical evidence indicating heterogeneity of AS. HLA-B27 carriage in the general population does not influence survival.

Disclosure: Z. Li, None; **M. Khan**, None; **S. van der Linden**, None; **P. Villiger**, None; **H. Baumberger**, None; **H. Zandwijk**, None; **M. Brown**, None; **M. Khan**, None.

Abstract Number: 1900

The Clinical and the Functional Impact of Central Sensitization on Patients with Axial Spondyloarthritis

Feyza Nur Yücel[1] and **Mehmet Tuncay Duruöz**[2], [1]Marmara University School of Medicine PMR Department, Istanbul, Turkey, [2]Marmara University School of Medicine, PMR Department, Rheumatology Division, Istanbul, Turkey

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: To evaluate the impact of central sensitization (CS) on axial spondyloarthritis (AxSpA) patients' clinical and functional situation and quality of life.

Methods: Subjects with axSpA according to ASAS criteria and healthy controls were recruited. The central sensitization (CS) was evaluated by the central sensitization inventory (CSI). Quantitative sensory testing, which consists of pressure pain threshold (PPT), temporal summation (TS), and conditioned pain modulation (CPM), were applied. The algometer was used in all kinds of pain parameters' assessment. The spinal hyperalgesia was evaluated from C3 and C7; T6 and T2; L3 and L5 levels. The sacroiliac PPT scores were obtained from 4 points. Trapezius muscle was

			AxSPA (n:100)			Healthy controls (n: 50) Mean (SD)	*Diff. Sig. between AxSPA and controls p-value*
			CS positive (n: 60) Mean (SD)	CS negative (n: 40) Mean (SD)	*Diff. Sig. between CS+ and CS- p value*		
PPT score (kg/cm^2)	Spinal	Cervical	21,52(5,93)	24,04(7,34)	0,062	26,55(6,94)	0,001*
		Thoracal	26,60(6,94)	28,05(7,77)	0,333	34,27(9,07)	<0,001*
		Lumbar	26,17(6,86)	28,36(7,98)	0,147	32,74(8,18)	<0,001*
	Sacroiliac	R	15,98(4,11)	18,43(5,80)	0,015*	20,73(5,49)	<0,001*
		L	16,35(4,18)	18,39(5,88)	0,045*	20,78(5,41)	<0,001*
	Trapezius		3,23 (1,06)	3,77 (1,19)	0,021*	4,14 (1,14)	0,001*
TS score (VAS_Δ)	Spinal	Cervical	11,12 (5,55)	10,03 (5,65)	0,341	10,54(4,65)	0,879
		Thoracal	9,31 (4,77)	9,77 (6,02)	0,673	8,90 (3,65)	0,472
		Lumbar	9,56 (4,67)	8,80 (5,41)	0,452	9,42 (5,50)	0,858
	Sacroiliac		7,45 (3,81)	7,27 (3,49)	0,817	7,82 (3,46)	0,482
	Trapezius		3,76 (2,12)	3,40 (1,89)	0,379	3,70 (1,86)	0,816
CPM			147,14(81,93)	183,09(96,21)	0,048*		
BASDAI			6,49 (1,69)	4,07 (1,85)	<0,001*		
ASQOL			11,45 (4,81)	5,63 (4,69)	<0,001*		
BDI			17,72 (10,13)	9,33 (9,44)	<0,001*		
ILBPDI			30,20(15,72)	16,05 (18,07)	<0,001*		
PSQI			8,15 (3,36)	5,52 (3,15)	<0,001*		
FSS			5,76 (1,33)	3,48 (1,80)	<0,001*		
FIRST			4,75 (1,16)	2,43 (1,96)	<0,001*		

used to evaluate distant control point. TS scores were evaluated over the trapezius muscle, sacroiliac joints, C7, T6, and L3 spine. In the evaluation of TS, a pressure as much the PPT value of each point was applied with pain pressure algometer ten times with a 1-second interstimulus interval. TS was calculated was by subtracting the rating at 0 seconds from the rating at 10 seconds. For the assessment of conditioned pain modulation (CPM), the first stimulus was applied to trapezius with the pressure that induced a pain intensity of 4/10 points on a VAS. After that, the right hand of the patient was immersed in 7 ^{0}C water for 20 seconds to create a conditioning stimulus. The second stimulus was applied to the trapezius. The ratio between the first and second VAS values was defined as CPM. Disease activity (BASDAI), disability (Istanbul Low Back Pain Disability Index: ILBPDI), quality of life (Ankylosing Spondylitis Quality of Life Questionnaires: ASQoL), sleep quality (Pittsburg Sleep Quality Index: PSQI), VASpain, depression (Beck Depression Inventory: BDI) and fatigue (Fatigue Severity Scale: FSS) were assessed. Comorbidities, fibromyalgia (Fibromyalgia Rapid Screening Tool: FIRST) were noted.

Results: One hundred patients (64 female) and 50 controls (32 female) were recruited. The mean age of patients and healthy controls were 42.31 (SS: 1.0) and 43.64 (SS:1.5), respectively. Central sensitization was detected in 60 of 100 AxSpA patients. When QST results were compared between the patient and control groups, all PPT scores were found lower ($p< 0.05$) in patients, but there was no significant difference between TS values. Regarding the comparison of the patients with and without CS, sacroiliac, and trapezius PPT scores were found lower in the patients with CS ($p< 0.05$). On the other hand, there was no significant difference between the groups in the mean measures of the other PPT and TS scores ($p >0.05$). CPM scores were significantly lower ($p=0.048$) and BASDAI, ASQoL, BDI, ILBPDI, PSQI, FSS, and FIRST scores were significantly higher ($p< 0.001$) in the patients with CS (Table). In regression analysis, female gender, morning stiffness duration, CPM, BDI, and FSS scores were detected as related parameters with CSI scores.

Conclusion: Central sensitization is an essential entity in axSpA patients, which affects their clinical and functional situation and quality of daily life negatively. The central sensitization assessment should be taken into consideration to determine the treatment strategy in axSpA patients.

Disclosure: F. Yücel, None; **M. Duruöz**, None.

Abstract Number: 1901

Clinical Characteristics of Importance to Outcome in Patients with Axial Spondyloarthritis: *A Prospective Cohort Study*

Rikke Asmussen Andreasen[1], Xenofon Baraliakos[2], Lars Erik Kristensen[3], Kenneth Egstrup[4], Vibeke Strand[5], Hans Christian Horn[6], Jimmi Wied[6], Berit Schiøttz-Christensen[7], Claus Aalykke[1], Inger Marie Hansen[1], Torkell Juulsgaard Ellingsen[8] and Robin Christensen[9], [1]Odense University Hospital, Svendborg, Svendborg, Denmark, [2]Rheumazentrum Ruhrgebiet-Ruhr-University Bochum, Herne, Germany, [3]The Parker Institute Copenhagen Denmark, Copenhagen, Denmark, Bispebjerg and Frederiksberg, Denmark, [4]Odense University Hospital Svendborg, Svendborg, Denmark, [5]Division of Immunology/Rheumatology, Stanford University, Palo Alto, CA, [6]Odense University Hospital, Odense, Denmark, [7]Spine Centre of Southern Denmark. Hospital lillebaelt, Middelfart, Denmark, [8]Rheumatology Research Unit, Dept of Rheumatology Odense University Hospital, Odense C, Denmark, [9]Musculoskeletal Statistics Unit, The Parker Institute/Odense University Hospital, Copenhagen F, Denmark

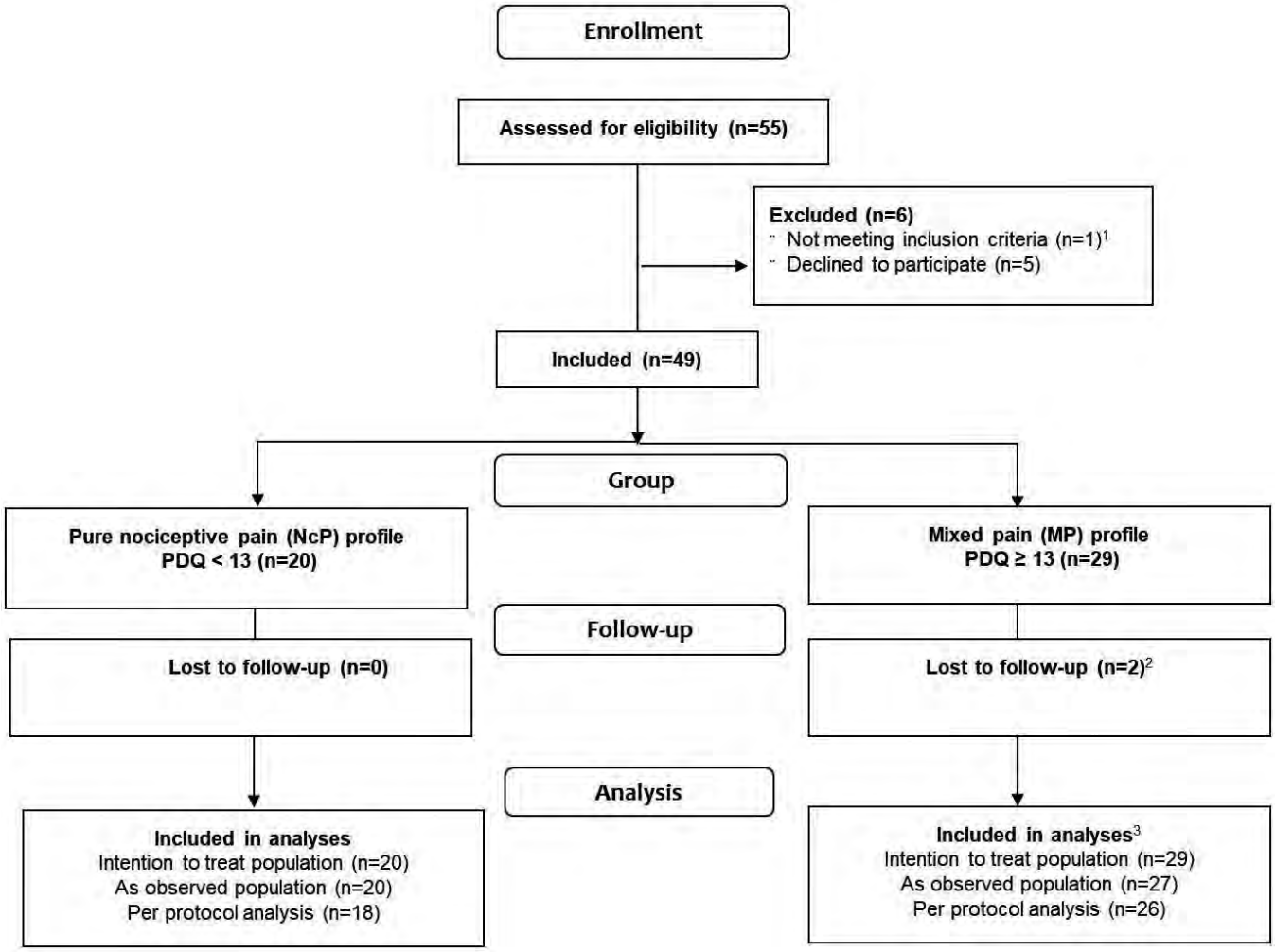
SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

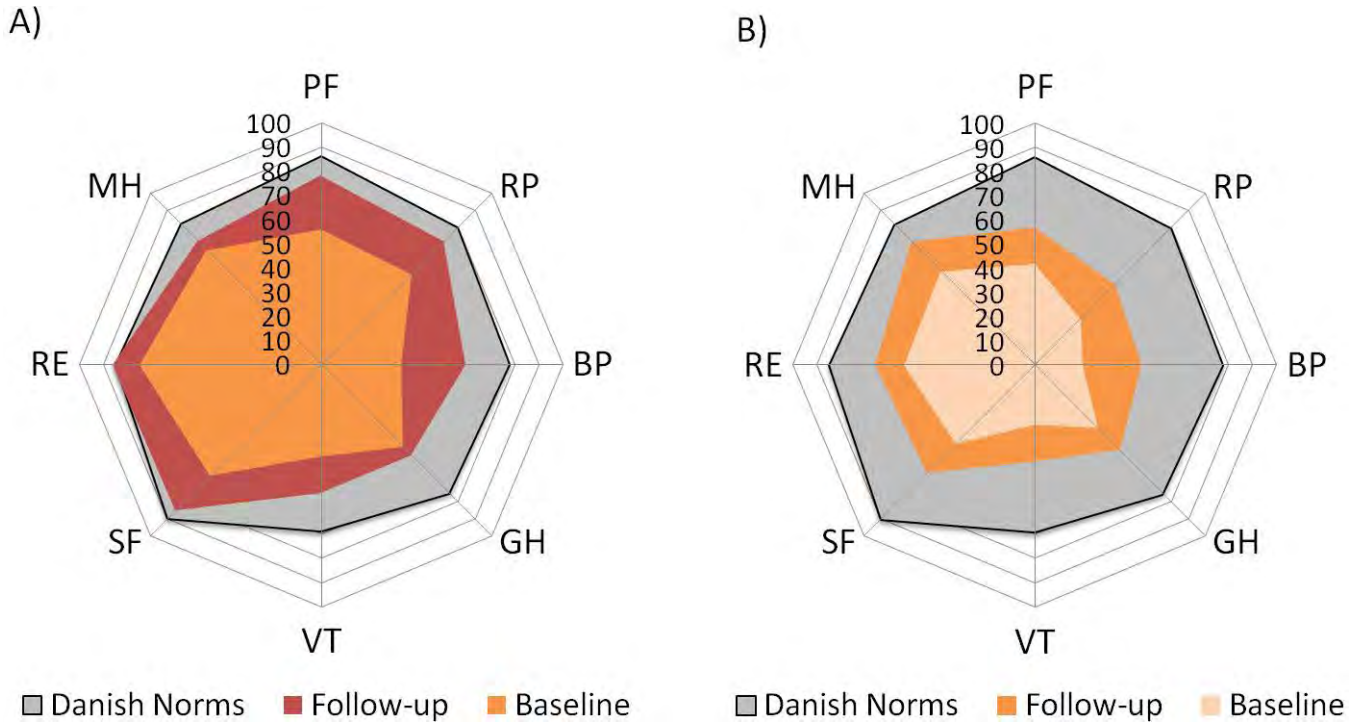


Flow chart 1Did not fulfill axSpA classification criteria. 2Resons for drop out: One participant moved to another hospital and one participant was hospitalized. 3As observed refers to participants with available data for analyses, and per protocol to participants with available data for analyses and adherence to the pre-specified protocol.

Background/Purpose: Despite better control of inflammation, many patients with axial spondyloarthritis (axSpA) still report pain, although they could be in remission. This suggests that in these patients chronic pain may prompt central sensitization. Our objective was to explore the prognostic value of the painDETECT questionnaire (PDQ) in relation to treatment outcomes in axSpA

Methods: AxSpA patients with high disease activity as an indication to initiate or switch a bDMARD were eligible. The PDQ score was used to distinguish participants with nociceptive pain (NcP) mechanisms from participants with mixed pain (MP); NcP was defined by a PDQ score < 13 vs. ≥13. The primary outcome was BASDAI50 responses at 12 weeks; logistic regression analysis models were used to determine the prognostic value of the NcP. Changes in continuous outcomes such were analyzed using analysis of covariance. Health related quality of life (HR-QoL) was addressed using SF-36.

Results: 49 axSpA patients were included; twenty (41%) had an NcP phenotype according to the PDQ score. BASDAI50 responses were reported by 40% (8/20) and 28% (8/29) NcP and MP groups, respectively. However, a prognostic value was not found in relation to the primary outcome (crude odds ratio [95% confidence interval] 1.75 [0.52



Mean SF-36 scores for Danish axSpA patients stratified by pain profiles. (A) axSpA patients classified as pure nociceptive pain (NcP) profile at baseline (B) axSpA patients classified as mixed pain (MP) profile. Mean SF-36 scores for Danish norms are also shown. PF, physical function; RP, role physical; BP, bodily pain; GH, general health; VT, vitality; SF, social functioning; RE, role emotional; MH, mental health.

to 5.87]. Across most of the secondary outcomes, axSpA NcP phenotype patients reported to have the most improvements in the HR-QoL measures.

Conclusion: These data indicate influence of personalized management strategies according to patients' pain phenotypes for stratification of axSpA patients in RCTs.

Disclosure: R. Andreasen, None; **X. Baraliakos**, AbbVie, 2, 5, Celgene, 2, 5, Galapagos, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 2, 5, Chugai, 2, 5, MSD, 2, 5, Sandoz, 2, 5, Hexal, 2, 5; **L. Kristensen**, AbbVie, 2, 8, Amgen Inc., 2, 8, Biogen, 2, 8, BMS, 2, 8, Eli Lilly, 2, 8, Janssen, 2, 8, Novartis, 2, 8, Pfizer, 2, 8, UCB Pharma, 2, 8, Sanofi, 2, 5, 8; **K. Egstrup**, None; **V. Strand**, AbbVie, 5, Amgen, 5, Celltrion, 5, Janssen, 5, Merck, 5, Novartis, 5, Regeneron, 5, Sanofi, 5, UCB, 5, Genentech/Roche, 5, GSK, 5, Pfizer, 5, Bayer, 5, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, Galapagos, 5, Lilly, 5, Gilead, 5, Samsung, 5, Servier, 5, Setpoint, 5, Arena, 5, AstraZeneca, 5, Horizon, 5, Ichnos, 5, Inmedix, 5, Sandoz, 5; **H. Horn**, None; **J. Wied**, None; **B. Schiøttz-Christensen**, None; **C. Aalykke**, None; **I. Hansen**, None; **T. Ellingsen**, None; **R. Christensen**, None.

Abstract Number: 1902

Determinants of Physician Global Assessment and Influence of Contextual Factors in Early Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes Poster III: Axial SpA

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: In rheumatic and musculoskeletal diseases, physician global assessment (PhGA) is a major factor of treatment decision. However, it is not well-known which disease manifestations contribute to PhGA in early axSpA and if contextual factors have an impact. The objective of this study is to investigate determinants of PhGA and the influence of contextual factors on this relationship in patients with early axSpA.

Methods: Five-year data from DESIR, a cohort of early axSpA, were analysed. Clinical data were collected every 6 months up to 2 years and annually thereafter. The primary analysis included all patients, and the subgroup analysis patients with follow-up MRI at 2 and/or 5 years. PhGA over 5 years was the outcome of interest. Univariable generalized estimating equation (GEE) models were used to investigate relationships between potential determinants and PhGA. Longitudinal relationships were investigated in autoregressive models. Effect modification by contextual factors (educational level, gender and age) was tested and, if significant, models were stratified. Univariable analyses were chosen to better assess the contributory explanatory effects of each of the determinants in each of the strata.

Results: A total of 708 patients were included, mean age 33.7 (SD 8.6) years, 46% male, 41% lower educated. The subgroup consisted of 220 patients with similar characteristics. Higher BASDAI questions 1-6, SJC28, TJC53, Maas-

	Female/Younger (n=181) Coefficient (95% CI)	Female/Older (n=200) Coefficient (95% CI)	Male/Younger (n=173) Coefficient (95% CI)	Male/Older (n=154) Coefficient (95% CI)
BASDAI Q1 (fatigue, 0-10)	0.39 (0.34, 0.44)	0.39 (0.34, 0.44)	0.46 (0.41, 0.51)	0.41 (0.35, 0.46)
BASDAI Q2 (back pain, 0-10)	0.53 (0.49, 0.57)	0.49 (0.45, 0.54)	0.58 (0.54, 0.63)	0.48 (0.43, 0.53)
BASDAI Q3 (peripheral joint pain, 0-10)	0.36 (0.31, 0.41)	0.31 (0.27, 0.36)	0.43 (0.37, 0.48)	0.32 (0.27, 0.37)
BASDAI Q4 (enthesitis, 0-10)	0.42 (0.37, 0.46)	0.37 (0.33, 0.41)	0.52 (0.47, 0.56)	0.36 (0.31, 0.41)
BASDAI Q5 (severity of morning stiffness, 0-10)	0.45 (0.40, 0.49)	0.42 (0.37, 0.46)	0.58 (0.54, 0.63)	0.44 (0.40, 0.49)
BASDAI Q6 (duration of morning stiffness, 0-10)	0.35 (0.30, 0.39)	0.30 (0.25, 0.35)	0.50 (0.45, 0.56)	0.36 (0.31, 0.41)
BASMI linear (0-10)	0.67 (0.48, 0.86)	0.61 (0.45, 0.78)	0.95 (0.75, 1.15)	0.49 (0.30, 0.68)
SJC28 (0-28)	**0.52 (0.31, 0.73)**	**0.13 (0.04, 0.22)**	**1.07 (0.71, 1.43)**	**0.58 (0.40, 0.76)**
TJC53 (0-159)ǂ	0.13 (0.11, 0.16)	0.05 (0.04, 0.06)	0.15 (0.13, 0.18)	0.13 (0.11, 0.16)
MASES (0-39)	0.15 (0.12, 0.17)	0.10 (0.08, 0.12)	0.30 (0.25, 0.35)	0.18 (0.14, 0.23)
CRP (mg/L)	0.03 (0.01, 0.05)	0.02 (0.01, 0.04)	0.04 (0.03, 0.05)	0.06 (0.04, 0.07)
Any extra-musculoskeletal manifestations (presence vs absence)	-0.20 (-0.58, 0.19)	-0.13 (-0.49, 0.23)	-0.28 (-0.69, 0.14)	-0.26 (-0.68, 0.17)
SPARCC-spine (0-414)§	0.05 (-0.11, 0.20)	0.06 (-0.11, 0.22)	0.05 (-0.04, 0.14)	0.02 (-0.03, 0.06)
SPARCC-SIJ (0-72)§	0.01 (-0.08, 0.10)	-0.02 (-0.13, 0.09)	0.01 (-0.04, 0.06)	0.05 (-0.01, 0.11)

ǂ Each joint graded 0-3. § Coefficients were estimated in the subgroup.

Table 1. Factors associated with PhGA over time in gender/age-stratified groups in univariable analysis

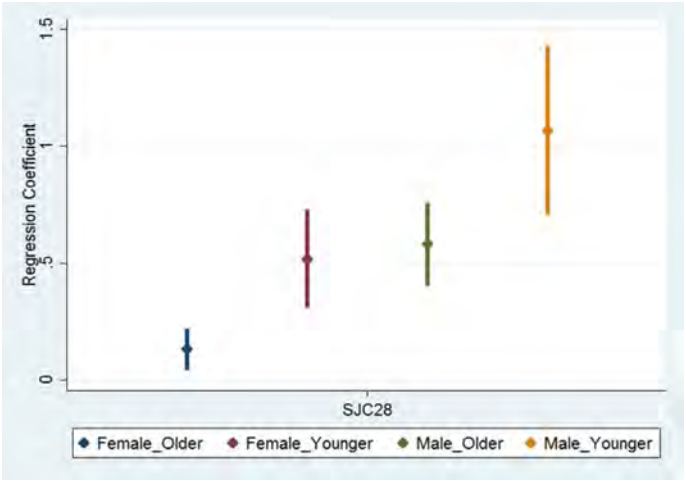

Figure 1. Impact of swollen joint count on physician global assessment across gender and age groups. Regression coefficients (95% CI) of the effect of SJC28 on PhGA in the univariable GEE analyses across gender/age-stratified groups (in an ascending order).

tricht Ankylosing Spondylitis Enthesitis Score (MASES), CRP and BASMI were associated with a higher PhGA (Table 1). Gender and age were effect modifiers of SJC28; the effect was largest in the younger male stratum (β [95% CI]; 1.07 [0.71, 1.43]), and smallest in the older female stratum (0.13 [0.04, 0.22]) (Figure 1). Autoregressive GEE models revealed the same determinants of PhGA and the same pattern of effect by gender and age.

Conclusion: Patient's subjective symptoms, peripheral arthritis, enthesitis, higher CRP and impaired spinal mobility contribute to explain PhGA in patients with early axSpA irrespective of gender and age. But physicians consider the presence of swollen joints as more important in males than in females.

Disclosure: F. Hirano, None; **R. Landewé**, AbbVie, 2, 5, 8, AstraZeneca, 5, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, Galapagos, 5, Novartis, 5, Pfizer Inc, 2, 5, 8, UCB, 2, 5, 8, GlaxoSmithKline, 5, Janssen, 2, 5, 8, Merck, 5, 8, Rheumatology Consultancy BV, 1, Ablynx, 5, Amgen, 2, 5, 8, Celgene, 5, Gilead, 5, Novo Nordisk, 5, Roche, 2, 5, 8, Schering, 2, 5, 8, TiGenix, 5; **F. van Gaalen**, Reuma Nederland, 1, Stichting vrienden van Sole Mio, 1, MSD, 1, Abbvie, 1, Novartis, 1; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5; **C. Gaujoux-Viala**, AbbVie, 5, Amgen, 5, 8, Bristol-Myers Squibb, 5, Celgene, 5, 8, Eli Lilly, 5, Gilead Sciences, Inc., 5, Janssen, 5, 8, Medac, 5, Merck-Serono, 5, Mylan, 5, 8, Nordic Pharma, 5, Novartis, 5, 8, Pfizer, 5, Roche, 5, Sandoz, 5, 8, Sanofi, 5, UCB, 5; **S. Ramiro**, Abbvie, 8, Eli Lilly, 8, Novartis, 8, MSD, 8, UCB, 8, Sanofi, 8.

Abstract Number: 1903

Assessment of Global DNA Methylation in Peripheral Blood Cell Subpopulations of Patients with Axial Spondyloarthritis : Preliminary Results

Eric Toussirot[1], Sebastien Pasquereau[2], Charline Vauchy[3], Zeina Nehme[4], Daniel Wendling[5], Jean Charles Balbalnc[6], Caroline Laheurte[7], Marc Puyraveau[8] and Georges Herbein[2], [1]CIC biotherapies, Besançon University Hospital, Besançon, France, [2]Pathogens & Inflammation/EPILAB Laboratory, UPRES EA 4266, Besancon, France, [3]INSERM CIC-1431, Besancon, France, [4]Pathogens & Inflammation/EPILAB Laboratory, UPRES EA 4266, Besancon, [5]CHU Besançon, department of rheumatology, Besancon, France, [6]Rhumatologie, Trevenans, France, [7]Plateforme de biomonitring, Besancon, France, [8]uMETh & INSERM CIC 1431, Besancon, France

SESSION INFORMATION

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Session Type: Poster Session D

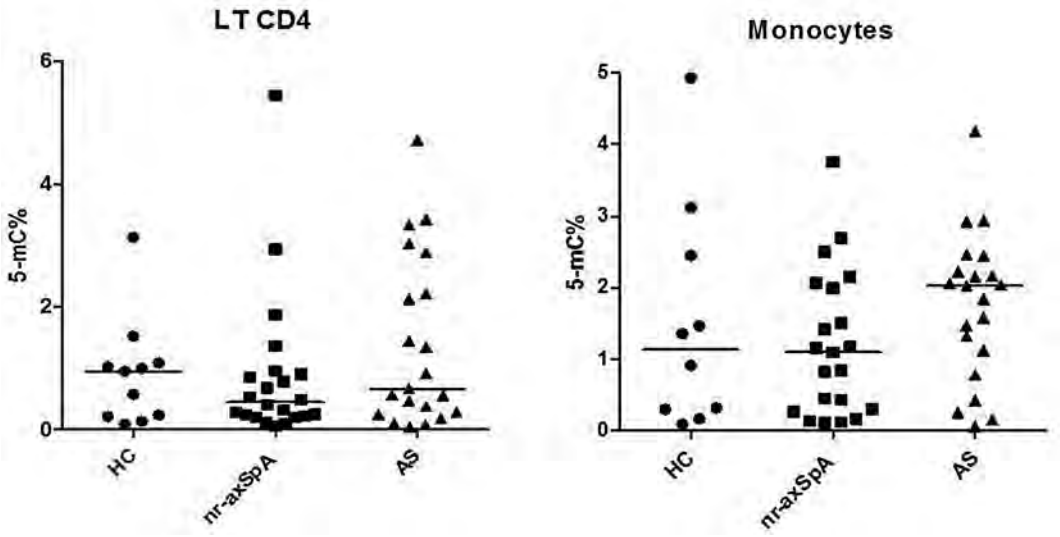
Session Time: 9:00AM–11:00AM

Background/Purpose: Axial spondyloarthritis (ax-SpA) corresponds to a group of chronic inflammatory disease mainly affecting the axial skeleton. TNFα and IL-17A have been identified as key inflammatory mediators driving the inflammatory process of ax-SpA. Epigenetics refers to different mechanisms that alter gene expression without involving changes in DNA sequence. The mechanisms of epigenetics include microRNA, histone modifications or DNA methylation. DNA methylation is associated with a repressed chromatin state and inhibition of gene expression. It is recognized that aberrant DNA methylation can result in immune cell autoreactivity. Epigenetics have been rarely evaluated in ax-SpA. We previoulsy reported that patients with ankylosing spondylitis (AS) had an imbalance between HAT and HDAC activities (Toussirot E et al, PlosOne 2013). In this study, we aimed to evaluate the global DNA methylation of patients with ax-SpA.

Methods: Case-control study (NCT03092583). Patients with radiographic (AS) or non radiographic (nr) ax-SpA (ASAS criteria) and healthy controls (HC) were evaluated. All the patients were biologic naïve and under NSAIDs. Disease activity was evaluated by BASDAI and ASDAS. CD4+T cells and CD14+ monocytes were isolated form peripheral blood and then DNA was extracted (E.Z.N.A. Blood DNA kit, Omega Bio-Tek). Global DNA methylation (5-mC) was determined using MethylAmp global DNA methylation quantification kit (Epigentek) using 150ng of total DNA.

Results: 25 patients with AS (18 M; mean age ± SEM: 48.9 ± 3.5 y; mean disease duration: 14.9 ± 2.2 y; B27+: 84%), 21 with nr-axSpA (11 M; age: 42 ± 3.3 y; disease duration: 7.9 ± 2.3 y; B27+: 68%) and 11 HC (7 M; age: 48.4 ± 3.9 y) were evaluated. Patients had active disease (BASDAI and ASDAS in AS and nr-axSpA: 5.1 ± 0.4 and 5.4 ± 0.5; 4.7 ± 0.4 and 5 ± 0.4, respectively). In CD4+ T lymphocytes, global DNA methylation was lower in the whole group of patients (AS and nr-ax-SpA) compared to HC (0.91 ± 0.26 *vs* 1.08 ± 0.19 % of 5-mC) (NS). Conversely, DNA methylation was higher in monocytes from patients compared to HC (1.43 ± 0.16 *vs* 1.15 ± 0.5 % of 5-mC) (NS). When analysing the results between ax-SpA subgroups, an hypomethylation was more evident in the CD4+T lymphocytes from patients with nr-axSpA compared to AS and HC, a result that was not observed in the monocyte subpopulation (Figure).

Figure: global DNA methylation of CD4+ T lymphocytes and monocyctes from patients with ankylosing spondylitis (AS), non radiographic axial spondyloarthritis (nr-ax-SpA) and healthy controls (HC)



Conclusion: A global DNA hypomethylation is observed in patients with ax-SpA, especially in the nr-axSpA subgroup. These results were more evident in T CD4+ lymphocytes. Additional analysis on a larger series of patients is required to confirm these preliminary results. In addition, we aim to examine the specific DNA methylation status of the TNF promoter gene.

Disclosure: E. Toussirot, None; **S. Pasquereau**, None; **C. Vauchy**, None; **Z. Nehme**, None; **D. Wendling**, None; **J. Balbalnc**, None; **C. Laheurte**, None; **M. Puyraveau**, None; **G. Herbein**, None.

Abstract Number: 1904

Clinical Features of Patients with Active Ankylosing Spondylitis Who Did Not Respond to Adalimumab but Responded to Ixekizumab: A Post-hoc Analysis

Xenofon Baraliakos[1], Rebecca Bolce[2], David Sandoval[2], Soyi Liu-Leage[3], Vladimir Geneus[3], David Adams[3], Atul Deodhar[4], Jessica Walsh[5] and Joachim Sieper[6], [1]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Bochum, Germany, [2]Eli Lilly and Company, Indianapolis, [3]Eli Lilly and Company, Indianapolis, IN, [4]Oregon Health & Science University, Portland, OR, [5]University of Utah School of Medicine, George E. Wahlen Veteran Affairs Medical Center, Salt Lake City, UT, [6]Charité Universitätsmedizin Berlin, Berlin, Germany

SESSION INFORMATION

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Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Table 1. Baseline demographics and clinical characteristics of patients in COAST-V study grouped according to response to adalimumab and/or ixekizumab at week 16/week 52.

Baseline Variable Mean (SD)[1]	ADA Resp/IXE Resp (N=25, 30.9%)	ADA Non-Resp/IXE Resp (N=19, 23.5%)	IXE Resp/IXE Resp (N=67, 45.9%)	IXE Non-Resp/IXE Resp (N=18 12.3%)
Age, years	37.3 (8.9)	38.5 (9.28)	37.5 (9.6)	42.6 (13.4)
Sex male, n (%) female, n (%)	 23 (92.0) 2 (8.0)	 12 (63.0) 7 (36.8)	 60 (89.6) 7 (10.4)	 12 (66.7) 6 (33.3)
Duration of Symptoms since axSpA onset, years	13.6 (5.3)	14.2 (8.2)	13.4 (8.3)	13.8 (11.0)
ASDAS, score	4.0 (0.70)	3.7 (0.85)	3.9 (0.76)	3.5 (0.74)
BASDAI, score	6.9 (1.3)	6.6 (1.6)	6.9 (1.4)	6.7 (1.9)
CRP, mg/L	16.0 (17.1)	11.2 (11.2)	15.9 (15.7)	8.7 (9.0)
MRI Spine SPARCC, score	24.6 (32.6)	11.6 (12.1)	15.0 (20.3)	3.6 (5.5)
MRI SIJ SPARCC, score	5.5 (9.8)	1.1 (2.2)	6.0 (9.0)	7.1 (11.7)

Notes: [1] Unless otherwise noted variables are mean (SD)

Abbreviations: ADA, adalimumab; ASDAS, assessment of disease activity; axSpA, Axial spondyloarthritis; BASDAI, bath ankylosing spondylitis disease activity index; CRP, C-reactive protein; IXE, ixekizumab; MRI, magnetic resonance imagining; N, number of patients with non-missing ASAS40 assessment; n, number of patients in variable; Non-Resp, ASAS40 non responsive; Resp, ASAS40 responsive; SD, standard deviation; SIJ, sacroiliac joints; SPARCC, Spondyloarthritis Research Consortium of Canada

Background/Purpose: Biologic therapy is recommended in patients with active ankylosing spondylitis (AS) despite adequate trial of NSAIDs. Biologic treatment in AS are currently limited to TNF and IL-17A inhibitors (IL-17Ai). It is unknown whether there are predictors of AS patients who only respond to 1 of these mechanisms of action or respond to switching from TNF-blocker to IL-17Ai. This post-hoc analysis evaluated whether patients who did not respond to TNF inhibitor adalimumab (ADA) but did subsequently respond to IL-17Ai ixekizumab (IXE) differed from those that responded to both ADA and subsequent IXE.

Methods: The analysis included patients from the phase-3 COAST-V trial in bio-naive patients with active AS (BASDAI ≥4 and back pain ≥4 on VAS of 0-10). There were 341 patients randomized 1/1/1/1 to IXE 80 mg/2 weeks (wks) (Q2W), IXE 80 mg/4 wks (Q4W), ADA 40 mg Q2W (reference arm), and placebo (PBO) for the 16-week blinded-treatment period. Of these, 329 entered the dose double-blind extended treatment period (wks 16 to 52). Those who received PBO or ADA were re-randomized to receive IXE 80 mg Q4W or Q2W. Patients were stratified as responders or non-responders based on their Assessment of Spondyloarthritis International Society (ASAS) 40 response at wks 16 and 52. Data for the 2 IXE dose groups were pooled.

Results: Overall, more patients responded to IXE than ADA at wk 16.[1] Based on ASAS40 response at wks 16 and at wk 52, 30.9% of patients responded to both initial ADA and subsequent IXE, 23.5% of patients did not respond to initial ADA but did respond to subsequent IXE, 45.9% of patients responded to IXE at both time points, and 12.3% of patients did not respond to IXE at wk 16 but did so at wk 52. Across the groups, patients were of similar age and predominantly males, though there were proportionally more women among those who did not respond to either ADA or IXE at wk 16. No meaningful differences were observed in disease duration or baseline clinical disease activity. However, ADA non-responders at wk 16/IXE responders at wk 52 had numerically lower baseline (mean[SD]) C-reactive protein (11.2 [11.2]), lower magnetic resonance imaging (MRI) Spondyloarthritis Research Consortium of Canada (SPARCC) scores of the spine (11.6 [12.1]), and lower MRI SPARCC score of the sacroiliac joints (1.1 [2.2]) than ADA responders at wk16/IXE responders at wk 52 patients (16.0 [17.1], 24.6 [32.6], and 5.5 [9.8]), respectively (Table 1).

Conclusion: In this analysis, patients who did not respond to ADA but subsequently responded to IXE exhibited overall lower levels of inflammation, as measured by CRP and MRI of the spine or sacroiliac joints, compared with patients who responded on ADA and also after switching to IXE. Along with comparative findings in patients who continuously received IXE and responded at both wks 16 and 52 or wk 52 only, these data indicate that IXE is efficacious in patients with active AS irrespective of inflammation level, assessed by CRP and MRI. Alternatively, lower baseline inflammation may be a predictor of delayed response.

Reference

1. van der Heijde et. al. Lancet 2018

Disclosure: X. Baraliakos, AbbVie, 2, 5, 8, Novartis, 2, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Pfizer, 5, 8, UCB, 5, 8, BMS, 5, 8, Merck, 5, 8, Galapagos, 5; **R. Bolce**, Eli Lilly and Company, 1, 3; **D. Sandoval**, Eli Lilly and Company, 3; **S. Liu-Leage**, Eli Lilly and Company, 3, 4; **V. Geneus**, Eli Lilly, 1, 3; **D. Adams**, Eli Lilly and Company, 1, 3; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **J. Walsh**, Pfizer, 2, AbbVie, 2, 5, Eli Lilly, 5, UCB, 5, Janssen, 5, Novartis, 5, Amgen, 5; **J. Sieper**, AbbVie, 5, Novartis, 5, 8, Lilly, 8, Janssen, 5, Merck, 5, 8.

Abstract Number: 1905

Soluble Guanylate Cyclase Reduced the Gastrointestinal Fibrosis in Bleomycin-induced Mouse Model of Systemic Sclerosis

Yuzuru Yamamoto[1], Takaichi Okano[2], Takumi Nagamoto[2], Yoshikazu Fujikawa[3], Yoshihide Ichise[2], Hirotaka Yamada[2], Ikuko Naka[2], Yo Ueda[4], Kengo Akashi[5], Sho Sendo[6], Akira Onishi[5], Jun Saegusa[7] and Akio Morinobu[5], [1]Kobe University, Kobe-city, Japan, [2]Kobe University, Kobe, Japan, [3]Kobe University, Kobe city, Japan, [4]Kobe UniversityRheumatology and Clinical Immunology, Kobe University Hospital, Kobe, Japan, [5]Rheumatology and Clinical Immunology, Kobe University Hospital, Kobe, Japan, [6]Kobe University, Kobe, [7]Department of Clinical Laboratory, Kobe University Hospital, Kobe, Japan

SESSION INFORMATION

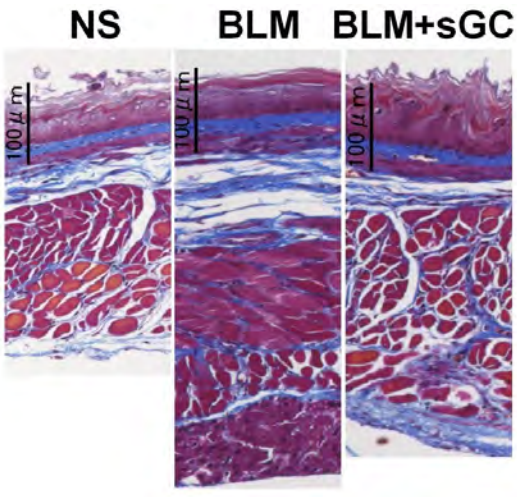
Session Date: Monday, November 9, 2020

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

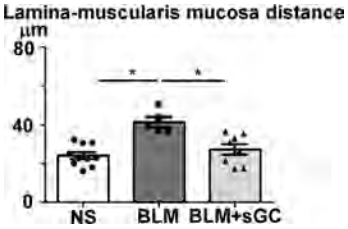
Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

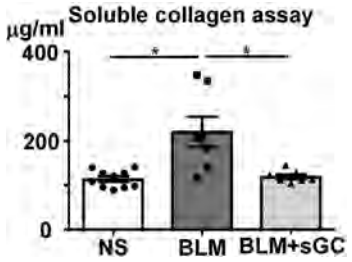
Background/Purpose: Systemic sclerosis (SSc) is a chronic autoimmune-mediated connective tissue disorder. Although the etiology of the disease remains undermined, SSc is characterized by fibrosis and proliferative vascular lesions of the skin and internal organs. SSc involves the gastrointestinal tract in more than 90% of patients. Soluble guanylate cyclase stimulator (sGC) is used to treat pulmonary artery hypertension (PAH), and has been shown to inhibit experimental skin fibrosis. The aim of this study is to investigate whether bleomycin (BLM) -treated mice show gastrointestinal fibrosis, and find a therapeutic strategy to the lesion.



Blomycin caused gastrointestinal fibrosis



Bleomycin induced mice reduced ITR%



The treatment of sGC improved gastrointestinal fibrosis

Methods: Female C57BL/6J mice were treated with BLM or normal saline by subcutaneous implantation of osmotic minipump. These mice were sacrificed on day 28 or day 42. Gastrointestinal pathologies were examined by Masson Trichrome staining. The expression of fibrosis-related genes in gastrointestinal tract were analyzed by real-time PCR, and the levels of collagen in the tissue was measured by Sircol collagen assay. To evaluate peristaltic movement, the small intestinal transport (ITR%) was calculated as [Dyeing distance×(Duodenum- Appendix)] -1 ×100 (%). We treated BLM-treated mice with soluble guanylate cyclase (sGC) or DMSO orally and analyzed them on day 42.

Results: Histological examination revealed that fibrosis from lamina propria to muscularis mucosa in the esophagus was significantly increased in BLM-treated mice, suggesting that BLM induces esophageal fibrosis in C57BL/6J mice. In addition, the levels of Col3a1 and CTGF were significantly increased in BLM-treated mice. More severe fibrosis was observed in the mice sacrificed on day 42 than the mice sacrificed on day 28. The ITR% was found to be significantly lower in BLM-treated mice, suggesting that gastrointestinal peristaltic movement was reduced in BLM-treated mice. Furthermore, we demonstrated that sGC treatment significantly reduced fibrosis of esophagus and intestine in BLM-treated mice, by histological examination and Sircol collagen assay.

Conclusion: These findings suggest that BLM induces gastrointestinal fibrosis in C57BL/6J mice, and treatment with sGC improves the BLM-induced gastrointestinal lesion.

Disclosure: Y. Yamamoto, None; **T. Okano**, None; **T. Nagamoto**, None; **Y. Fujikawa**, None; **Y. Ichise**, None; **H. Yamada**, None; **I. Naka**, None; **Y. Ueda**, None; **K. Akashi**, None; **S. Sendo**, None; **A. Onishi**, None; **J. Saegusa**, None; **A. Morinobu**, None.

Abstract Number: 1906

Hsp90 Inhibition Effectively Prevents Progression of Dermal Fibrosis and Induces Regression of Established Bleomycin-Induced Dermal Fibrosis

Hana Storkanova[1], Lenka Storkanova[2], Sabina Oreska[3], Maja Spiritovic[4], Barbora Hermankova[5], Radim Becvar[1], Karel Pavelka[6], Jiří Vencovský[6], Jörg HW Distler[7], Ladislav Šenolt[6] and Michal Tomcik[1], [1]Institute of Rheumatology, Prague, Czech Republic. Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Prague, Czech Republic, [2]Institute of Rheumatology, Prague, Czech Republic, [3]Institute of Rheumatology, Prague, Czech Republic. Department of Rheumatology, 1st Faculty of Medicine, Charles University, Prague, Czech Republic, Praha 2, Czech Republic, [4]Faculty of Physical Education and Sport, Charles University, Prague, Czech Republic, Prague, Czech Republic, [5]Faculty of Physical Education and Sport, Department of Physiotherapy, Charles University, Prague, Czech Republic,, Prague, Czech Republic, [6]Institute of Rheumatology and Department of Rheumatology, First Faculty of Medicine, Charles University, Prague, Czech Republic, [7]University of Erlangen-Nuremberg, Erlangen, Germany, Erlangen, Germany

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Our previous study demonstrated that Heat shock protein 90 (Hsp90) is overexpressed in the skin of patients with systemic sclerosis (SSc), in cultured SSc fibroblasts and preclinical models of SSc. HSP90 is a new regulator of canonical TGF-β signalling and its inhibition prevents the stimulatory effects of TGF-β on collagen synthesis and dermal fibrosis in three preclinical models of SSc. Herein, we aimed to evaluate the efficacy of Hsp90 inhibitor (17-DMAG) in the treatment of established experimental dermal fibrosis induced by bleomycin.

Methods: Design consisted of three control groups, I (NaCl-s.c./6 weeks), II (bleomycin-s.c./3w and NaCl-s.c./3w), III (bleomycin-s.c./6w), and 2 treatment groups (bleomycin-s.c./6w). During the last 3 weeks, one group was treated with 17-DMAG 0.5mg/kg-i.p. every third day, whereas one group (with nintedanib 50mg/kg-p.o. twice daily) served as a comparator with already published efficacy in this setting. Total of 40 BL6 mice were examined weekly for weight, activity and fur texture. The effects of 17-DMAG were determined by assessment of dermal thickness (HE-staining), collagen content (hydroxyproline assay), myofibroblast counts (α-SMA staining) and of 23 serum inflammatory cytokines/chemokines (Mouse-Cytokine-23-plex, Bio-Rad-Laboratories).

Results: 17-DMAG decreased dermal thickening by 53±3% ($p< 0.001$) (nintedanib by 46±2%,$p< 0.001$), collagen content by 48±5% ($p=0.004$) (nintedanib by 50±4%,$p=0.003$), myofibroblast counts by 42±9% ($p< 0.001$) (nintedanib by 44±7%,$p< 0.001$), and the count of CD3+ cells in the dermis by 46±7% ($p< 0.001$) and serum levels of IL-1a, IL-6, IL-12(p40), CXCL1, MCP-1, MIP-1a/b, RANTES (in all: $p< 0.05$) compared to vehicle-treated mice injected with bleomycin for 6w. Moreover, 17-DMAG also induced regression of pre-established fibrosis to below the levels of vehicle-treated mice injected with bleomycin for 3w and NaCl for 3w, i.e. the pre-treatment levels, (dermal thickness by 14±3%, collagen content by 20±5%, myofibroblast counts by 13±9%; whereas in nintedanib by 10±3%, 21±4%, 17±7%, respectively; in all: $p< 0.05$), and the count of CD3+ cells in the dermis by 22±7% ($p=0.006$) and levels of IL-12(p40), CXCL1, MCP-1, MIP-1b, RANTES (in all: $p< 0.05$). No significant weight loss, decrease in activity or changes in fur texture were observed upon 17-DMAG treatment.

Conclusion: This is the first study on effects of Hsp90 inhibitor 17-DMAG in the treatment of established dermal fibrosis. We demonstrate that 17-DMAG effectively prevents the progression and induces regression of established bleomycin-induced dermal fibrosis, in an extent that was comparable to nintedanib in this study (which was recently FDA approved for slowing the rate of decline in lung function in adults with SSc-ILD). 17-DMAG also reduced the T-cell infiltrate in the dermis and the systemic levels of inflammatory cytokines/chemokines. 17-DMAG was well tolerated without obvious clinical signs of toxicity. These data suggest that Hsp90 could be a novel potential target in the treatment of SSc dermal fibrosis.

Acknowledgement: Supported by AZV-16-33542A, MHCR00023728, SVV260373, Boehringer Ingelheim.

Disclosure: H. Storkanova, None; **L. Storkanova**, None; **S. Oreska**, None; **M. Spiritovic**, None; **B. Hermankova**, None; **R. Becvar**, None; **K. Pavelka**, AbbVie, 8, Merck Sharp & Dohme, 8, Bristol-Myers Squibb Company, 8, Roche, 8, Amgen, 8, Pfizer, 8, Novartis, 8, Egis, 8, Biogen, 8, UCB, 8; **J. Vencovský**, Eli Lilly, 5, 8, Abbvie, 5, 8, Boehringer, 5, Octapharma, 5, Sanofi, 8, Merck, 8, Biogen, 8, UCB Biopharma, 8, Roche, 8, Pfizer, 8; **J. Distler**, Actelion, 5, Active Biotech, 2, 5, AnaMar, 2, 5, UCB, 2, 5, Boehringer Ingelheim, 2, 5, Novartis, 2, GlaxoSmithKline, 2, 5, RuiYi, 5, Galapagos, 2, 5, Medac, 5, Celgene, 2, 5, Inventiva, 2, 5, Redx Pharma, 2, Bayer, 2, 5, JB Therapeutics, 5, Bristol-Myers Squibb, 2, Array BioPharma, 2, Pfizer, 5, Sanofi-Aventis, 2, Arxx Therapeutics, 2, 5, 4D Science, 1, aTyr Pharma, 2; **L.**

Šenolt, AbbVie, 2, 5, 8, Amgen, 5, 8, BMS, 5, 8, Celgene, 5, 8, Eli Lilly, 8, Merck Sharp and Dohme, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, Roche, 5, 8, UCB, 5, 8, Takeda, 8; **M. Tomcik**, None.

Abstract Number: 1907

DNASE1L3 R206C Polymorphism, a Systemic Sclerosis Risk Factor, Causes Impaired Digestion of Genomic DNA in Apoptosis-derived Extracellular Vesicles

Brian Skaug[1], Julio Charles[1], Jacob Couturier[2], Dorothy Lewis[2], Maureen Mayes[3] and Shervin Assassi[3], [1]University of Texas Houston, McGovern Medical School, Division of Rheumatology and Clinical Immunogenetics, Houston, TX, [2]University of Texas Houston McGovern Medical School, Division of Infectious Diseases, Houston, TX, [3]University of Texas Houston McGovern Medical School, Division of Rheumatology and Clinical Immunogenetics, Houston, TX

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Two independent studies on genetic risk factors for systemic sclerosis (SSc) identified a polymorphism of Deoxyribonuclease 1-like 3 (*DNASE1L3)* associated with increased SSc risk. This polymorphism is located in a coding region and results in an amino acid substitution of Arg 206 to Cys (R206C). The mechanisms by which *DNASE1L3* R206C polymorphism increase SSc risk are unknown. Based on prior studies indicating that DNASE1L3 is secreted into the circulation and digests DNA in apoptosis-derived extracellular vesicles (EVs), we sought to determine the effect of *DNASE1L3* R206C polymorphism on this activity. We tested plasma samples from SSc patients and healthy controls (HCs) with vs. without *DNASE1L3* R206C polymorphism for their ability to digest genomic DNA in apoptosis-derived EVs.

Methods: Plasma from SSc patients and HCs were previously collected as part of the Scleroderma Family Registry and DNA Repository based in Houston. Groups of SSc patients and HCs homozygous for the major allele (*DNASE1L3* R206 wild-type, or WT), heterozygous, or homozygous for *DNASE1L3* R206C were identified and matched for age and sex (with the exception of HCs homozygous for *DNASE1L3* R206C, since there were only two HCs with this genotype in the Registry). SSc patients were also matched for disease duration, limited vs diffuse cutaneous subtypes, and SSc-associated autoantibodies (Table 1). DNA-containing EVs were prepared by inducing apoptosis of cultured Jurkat cells with staurosporine, followed by isolation of the apoptosis-derived EVs by centrifugation. EVs were added to plasma samples and incubated for one hour, followed by extraction of the DNA. Each plasma sample was tested in triplicate. The extracted genomic DNA was quantified by qPCR (Figure 1), and the percent of genomic DNA digested in each sample was compared to that of a reference HC with *DNASE1L3* R206 WT. The relative DNA digestion in each group was compared by one-way ANOVA.

Results: Plasma from SSc patients and HCs heterozygous for *DNASE1L3* R206C polymorphism had less digestion of EV-associated DNA on average than plasma from *DNASE1L3* R206 WT SSc patients and HCs. Minimal to no digestion of EV-associated DNA was observed in plasma from individuals homozygous for *DNASE1L3* R206C (Figure 2).

Conclusion: Plasma from SSc patients and HCs harboring *DNASE1L3* R206C polymorphism has impaired ability to digest EV-associated genomic DNA. These findings solidify the hypotheses that circulating DNASE1L3 is a major determinant for digestion of DNA in apoptosis-derived EVs and that the R206C polymorphism reduces this activity.

Table 1

Demographics and disease characteristics of healthy controls and systemic sclerosis patients whose plasma was assayed

	Healthy control (n = 22)			Systemic sclerosis (n = 29)		
***DNASE1L3* genotype**	R206 WT (n = 10)	R206C heterozygous (n = 10)	R206C homozygous (n = 2)	R206 WT (n = 10)	R206C heterozygous (n = 10)	R206C homozygous (n = 9)
Age (years), mean (SD)	57.1 (8.4)	57.4 (11.9)	35.5 (13.4)	57.7 (8.1)	57.4 (7.7)	58.2 (6.8)
Female, n (%)	9 (90)	9 (90)	2 (100)	9 (90)	9 (90)	8 (88.9)
Disease duration in years, mean (SD)				9.3 (7.8)	8.8 (5.7)	9.4 (7.8)
Diffuse skin involvement, n (%)				4 (40%)	4 (40%)	4 (44.4%)
SSc-associated autoantibody, n (%)						
anti-Topoisomerase I				2 (20%)	2 (20%)	2 (22.2%)
anti-RNA Polymerase III				2 (20%)	3 (30%)	2 (22.2%)
anti-Centromere				4 (40%)	5 (50%)	3 (33.3%)

WT: wild type (homozygous for the major allele encoding Arg 206, R206C: Arg-->Cys at amino acid 206, SD: standard deviation, SSc: systemic sclerosis

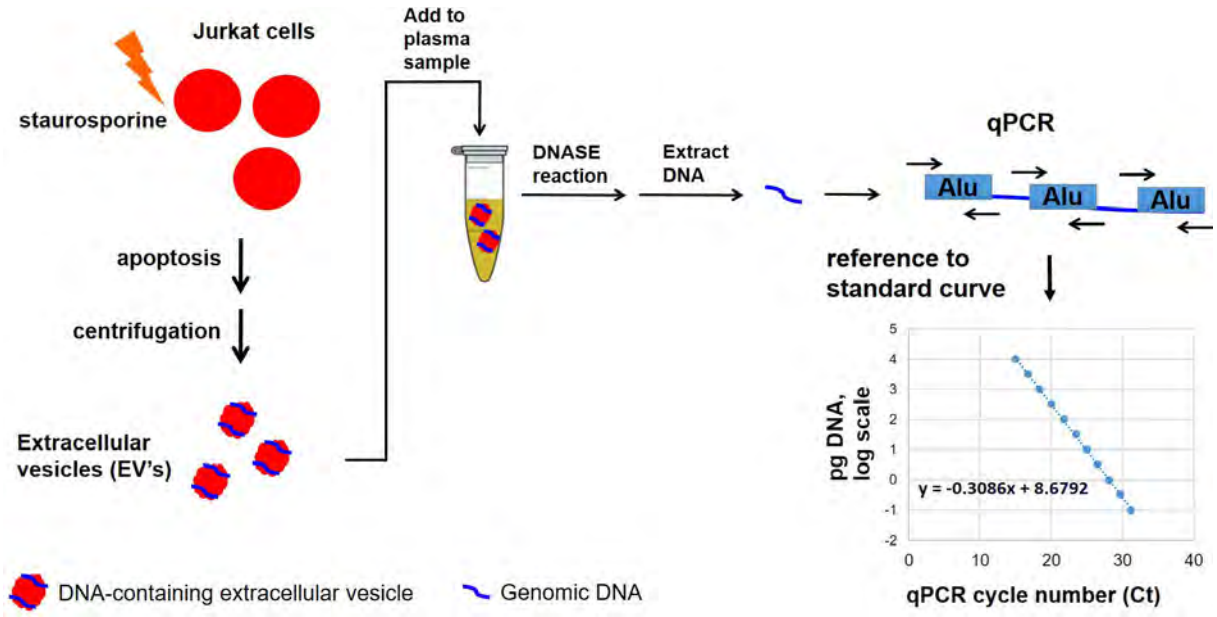


Figure 1. Schematic of assay to measure digestion of genomic DNA in apoptosis-derived extracellular vesicles (EVs) by plasma samples

Given that the *DNASE1L3* R206C polymorphism is a robustly-replicated risk factor for SSc, these results suggest that excess DNA in apoptosis-derived EVs may have a pathogenic role in SSc.

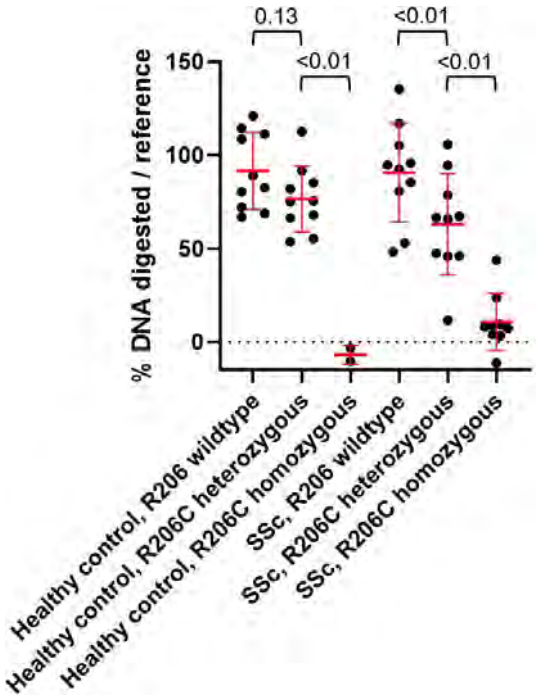


Figure 2. Impaired digestion of EV-associated genomic DNA in plasma from DNASE1L3 R206C SSc patients and healthy controls. Relative percentage of genomic DNA digested in each sample is plotted for each individual based on the mean of triplicates for each plasma sample. Each sample was compared to a reference healthy control with DNASE1L3 R206 WT. Red midlines and error bars indicate the mean and standard deviation for each group, respectively. Groups were compared by one-way ANOVA, with p values shown at top. SSc: systemic sclerosis

Disclosure: B. Skaug, None; **J. Charles**, None; **J. Couturier**, None; **D. Lewis**, None; **M. Mayes**, Actelion Pharmaceuticals, 1, Boehringer Ingelheim, 1, 2, Corbus, 1, Eicos Sciences, 1, Galapagos, 1; **S. Assassi**, Momenta, 1, corbus, 1, Integrity Continuing Education, 1, Boehringer Ingelheim, 1, 2, 3.

Abstract Number: 1908

Establishment of iPSc and Differentiated Endothelial Cells of Systemic Sclerosis Associated Pulmonary Arterial Hypertension ; Functional and Molecular Analysis

Yuki Kudo[1], Masaru Kato[2], Yuhei Shibata[1], Michihito Kono[2], Yuichiro Fujieda[2], Olga Amengual[2], Kenji Oku[2] and Tatsuya Atsumi[3], [1]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Japan, [2]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine and Graduate School of Medicine, Hokkaido University, Sapporo, Hokkaido, Japan, [3]Department of Rheumatology, Endocrinology and Nephrology, Faculty of Medicine, Hokkaido University, Sapparo, Hokkaido, Japan

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Pulmonary arterial hypertension (PAH) occurs either primarily or in association with other diseases such as connective tissue diseases. PAH associated with systemic sclerosis (SSc-PAH) is of particularly clinical significance since its outcomes remain unfavorable despite modern PAH therapies, suggesting its distinctive

pathogenesis. Previous studies have indicated the abnormality of endothelial cells (ECs) in the lung of SSc-PAH, but its details have yet to be clarified owing to the poor accessibility to lung samples from those patients. To overcome the problem and to elucidate the pathogenesis of SSc-PAH, we established SSc-PAH specific ECs differentiated from induced pluripotent stem cells (iPSc) and performed their functional and molecular analysis.

Methods: Peripheral blood mononuclear cells were obtained from a patient with SSc-PAH and a healthy donor. Yamanaka factors, including OCT3/4, SOX2, KLF4 and L-MYC, were transfected into peripheral blood mononuclear cells using sendai virus vector to establish iPSc. Following more than five passages of iPSc, ECs were differentiated with the culture system containing BMP-4, Activin, bFGF, CHIR99021, Y-27632, VEGF and SB431542. Differentiated ECs were confirmed by immunocytochemistry with specific markers, including VE-cadherin, KDR and CD34. The vasculogenesis and cell proliferative capacity of ECs were evaluated by the tube formation assay and the BrdU assay, respectively. RNA-sequencing was performed to evaluate differentially expressed genes between SSc-PAH ECs and healthy ECs.

Results: SSc-PAH ECs and healthy ECs equally VE-cadherin, KDR and CD34 with similar morphologies, but were functionally distinct. The cellular uptake of BrdU was higher (0.49±0.05(abs) vs 0.30±0.01(abs), $p< 0.05$, n=3) while the tube formation was impaired (31.2±2.0(mm) vs 47.0±1.3(mm), $p< 0.01$, n=3) in SSc-PAH ECs compared to healthy ECs, indicating disproportionately reduced vasculogenesis despite accelerated proliferation of SSc-PAH ECs. RNA-sequencing revealed some differentially expressed genes (DEGs) and significantly enriched Gene Ontology terms, including blood vessel development, vascular endothelial growth factor-activated receptor activity, regulation of cell proliferation and cell adhesion. From these terms, we detected some important DEGs, geneX, Y and Z, which have a potential to be involved in the pathogenesis of SSc-PAH.

Conclusion: We detected, at a cellular level, the alterations of ECs in patients with SSc-PAH, such as impaired vasculogenesis, facilitated cell proliferation, differentially expressed genes, enriched Gene Ontology terms. The current findings might be related to the pathogenesis of SSc-PAH.

Disclosure: Y. Kudo, None; **M. Kato**, None; **Y. Shibata**, None; **M. Kono**, GlaxoSmithKline K.K., 2; **Y. Fujieda**, None; **O. Amengual**, None; **K. Oku**, None; **T. Atsumi**, AbbVie Inc., 5, 8, 9, UCB Japan Co.,Ltd., 5, 8, Eisai Co., Ltd., 8, Gilead Sciences, Inc., 5, 8, Bristol Myers Squibb Co., 2, 8, Chugai Pharmaceutical Co., Ltd., 2, 8, 9, Mitsubishi Tanabe Pharma Corporation, 8, 9, Eli Lilly Japan K.K., 2, 5, 8, Astellas Pharma Inc., 8, 9, Pfizer Inc., 2, 8, 9, Daiichi Sankyo Company, Limited, 5, 8, 9.

Abstract Number: 1909

High-density Proteomic Analysis of Skin Blister Fluid and Plasma in Systemic Sclerosis Identifies Local and Systemic Differences for Key Proteins

Kristina Clark[1], Corrado Campochiaro[2], Eszter Csomor[3], Adam Taylor[3], Katherine Nevin[3], Mary Morse[3], Voon Ong[4], Emma Derrett-Smith[5], Nicolas Wisniacki[3], Shaun Flint[3] and Christopher Denton[1], [1]University College London, London, United Kingdom, [2]Royal Free Hospital NHS trust, London, United Kingdom, [3]GlaxoSmithKline, Stevenage, United Kingdom, [4]UCL, London, United Kingdom, [5]University College London Division of Medicine, London, United Kingdom

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Simultaneous analysis of multiple proteins in biological fluids offers insight into the pathogenesis of SSc. Here, we report a proteomic analysis of plasma and dermal interstitial fluid in SSc compared with healthy controls (HC).

Methods: The prospectively collected BIOPSY cohort recruited 52 SSc patients (21 early dcSSc, 15 established dcSSc, 16 lcSSc) and 16 matched HC. 36 (69%) of the SSc patients are female. Mean baseline skin score (MRSS) for early dcSSc was 21 (sd 11.2). This analysis utilised forearm skin blister fluid obtained using the dermal suction blister method and paired simultaneous plasma samples from early dcSSc and HC at baseline. These were assayed using the Olink antibody platform with proximity extension assay (www.olink.com) and reported as normalized protein expression (NPX), corresponding to log2 (expression). T-test with FDR correction ($p< 0.05$) assessed statistical significance. Pathway analysis was conducted by STRING consortium 2020.

Results: 1196 proteins were analysed in paired blister/plasma samples from 14 early dcSSc patients and 16 HC. 447 proteins were significantly different in the blister fluid of early dcSSc patients compared with HC (see Table 1), whereas in plasma this was only 183 proteins. Of these, 130 proteins were simultaneously different in both blister fluid and plasma of early dcSSc including key cytokines associated with fibrosis and vasculopathy such as IL-6, VEGF-1, MCP-1, COL4A1, COMP, Thy1 and THBS4. No correlation was seen between any of these proteins and MRSS.

There were 310 proteins significantly elevated in blister fluid alone in early dcSSc patients compared to HC. These included cytokines (IL7, IL18, OSM), chemokines (CCL7, CCL18, CCL3), matricellular proteins (CYR61 and osteopontin). Pathway analysis using all significantly elevated proteins in blister fluid in early dcSSc compared to HV identified the top GO biological processes as immune system, response to stimulus, immune response and cell communication (FDR< 0.01). KEGG pathway analysis highlighted cytokine-cytokine receptor interaction, cell adhesion molecules, MAPK signalling pathway and the PI3K-AKT signalling pathway (FDR< 0.01).

Protein symbol	Raw NPX	Fold Change		Details of protein
	HC	dcSSc	Adjusted p value	
KLK4	2.698	15.926	0.004	Kallikrein-related peptidase 4
IL6	16.138	15.107	0.008	Interleukin 6
NT-proBNP	33.607	12.857	0.018	N-terminal pro-brain natriuretic peptide
AREG	12.747	11.978	0.017	Amphiregulin
LTBP2	4.593	11.799	0.015	Latent-TGF beta-binding protein 2
SFRP1	81.107	10.404	0.025	Secreted Frizzled Related Protein 1
TNC	18.012	8.728	0.010	Tenascin C
CPXM1	2.147	7.465	0.002	Probable carboxypeptidase X1
CYR61	10.493	6.106	0.011	Cysteine-rich angiogenic inducer 61 (CCN1)
PAPPA	10.267	5.480	0.008	Pregnancy-associated plasma protein A
EDA2R	11.479	5.407	0.008	Ectodysplasin-A2 rceptor
NOV	61.638	5.119	0.003	Nephroblastoma overexpressed protein (CCN3)
GDF-15	20.807	4.540	0.002	growth/differentiation factor 15
SCARF2	11.868	4.377	0.008	Scavenger Receptor Class F Member 2
CXCL10	71.620	4.196	0.028	interferon-γ inducible protein 10
THBS4	110.682	4.163	0.008	Thrombospondin 4
CXCL13	24.256	4.047	0.011	C-X-C Motif Chemokine Ligand 13
MAPT	1.661	4.041	0.015	Microtubule-associated protein tau
COL4A1	16.705	4.009	0.003	Collagen type IV alpha 1
MCP-1	1128.94	3.651	0.016	Monocyte chemoattractant protein-1

Table 1. Top 20 most upregulated proteins in skin blister fluid for early dcSSc (n=14) compared with healthy control (HC, n=16)

Conclusion: Numerous dysregulated proteins were identified in dermal blister fluid and plasma of early dcSSc patients. Substantially more were identified in dermal blister fluid, highlighting the potential of this technique for providing detailed information on local pathologic processes. A subset of proteins were dysregulated in both plasma and blister fluid, suggesting these may reflect systemic abnormalities. Further work will utilise this cohort to integrate gene and protein expression across the full spectrum of early dcSSc, established dcSSc and lcSSc.

Disclosure: K. Clark, None; **C. Campochiaro**, None; **E. Csomor**, GlaxoSmithKline, 3; **A. Taylor**, GlaxoSmithKline, 3; **K. Nevin**, GlaxoSmithKline, 3; **M. Morse**, GlaxoSmithKline, 3; **V. Ong**, None; **E. Derrett-Smith**, None; **N. Wisniacki**, GlaxoSmithKline, 3; **S. Flint**, GlaxoSmithKline, 3; **C. Denton**, Janssen, 1, GlaxoSmithKline, 1, 2, Bayer, 1, Sanofi, 1, Inventiva, 1, 2, Boehringer Ingelheim, 1, Roche, 1, Bristol-Myers Squibb, 1, CSL Behring, 1, 2, UCB, 1, Leadiant Biosciences, 1, Corbus Pharmaceuticals, 1, Acceleron Pharma, 1, Horizon Therapeutics, 1, Forbius, 1, Servier, 1.

Abstract Number: 1910

Integrated Molecular Analysis of Systemic Sclerosis Skin and Blood Highlights Significant Differences Between Major Autoantibody Subgroups

Kristina Clark[1], Corrado Campochiaro[2], Eszter Csomor[3], Adam Taylor[3], Katherine Nevin[3], Nicholas Galwey[3], Mary Morse[3], Voon Ong[4], Emma Derrett-Smith[5], Shaun Flint[3] and Christopher Denton[1], [1]University College London, London, United Kingdom, [2]Royal Free Hospital NHS trust, London, United Kingdom, [3]GlaxoSmithKline, Stevenage, United Kingdom, [4]UCL, London, United Kingdom, [5]University College London Division of Medicine, London, United Kingdom

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster
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Background/Purpose: The major antinuclear autoantibodies of systemic sclerosis (SSc) associate with different skin score trajectories and risk of internal organ manifestations. To elucidate molecular differences between ANA-defined subgroups, we utilised the prospective BIOPSY cohort of well-characterised SSc patients.

Methods: The prospectively collected BIOPSY cohort recruited 52 SSc patients (21 early dcSSc, 15 established dcSSc, 16 lcSSc) and 16 matched HC. 36 (69%) of the SSc patients are female. Mean disease duration in the early dcSSc cohort was 24 months (sd 12 months). ANA frequency in BIOPSY reflected the overall dcSSc population: anti-topoisomerase-1 (ATA) n= 14 (27%), anti-RNA pol III (ARA) n= 12 (23%) and other n=26 (50%). Mean baseline skin score (MRSS) for early dcSSc was 21 (sd 11.2).At a group level mRSS peak was 21.9 (11.8) at 3 months and fell to 19.1(10.5) at 12 months. For comparison, the BIOPSY cohort also included cases of established dcSSc (n=15, mean disease duration 11.3 years), lcSSc (n=16) and matched health controls (HC) (n=16). Serum biomarkers of ECM turnover and fibrosis were measured every three monthly and genome-wide transcriptomic profiling of whole skin and whole blood performed by RNA-Seq. Statistical analysis used RStudio with ANOVA, and Tukey post-hoc test. Differential gene expression used the Bioconductor limma software, with standard thresholds for significance.

Results: We found clear differences when early dcSSc patients were analysed by major ANA subset for longitudinal change in serum markers of fibrosis and in whole skin gene expression, suggesting a mechanistic basis for the distinct clinical phenotypes associated with hallmark ANAs. At baseline, there was no significant difference in soluble markers by major ANA subset. During follow-up, significant differences were observed in HA, TIMP1, and PIIINP at 6

Upregulated Genes				Downregulated genes			
	Raw value in HC	Fold Change	Adj P value		Raw value in HC	Fold Change	Adj P value
HP	10.88	14.559	0.002	SPAG17	86.38	0.255	<0.001
COMP	1503.12	6.371	0.000	MATN4	239.64	0.264	<0.001
SFRP4	355.91	5.208	0.000	WIF1	1302.24	0.286	<0.001
TNFSF18	9.37	5.178	0.000	IL12A-AS1	17.57	0.324	0.029
ADAM12	125.24	5.119	0.000	SERTM1	9.85	0.327	<0.001
COL11A1	151.94	5.107	0.000	ZNF725P	13.35	0.335	0.027
LTF	174.66	5.045	0.002	ANGPTL5	187.35	0.409	<0.001
CXCL9	68.38	4.961	0.000	LGR5	386.86	0.413	<0.001
COL10A1	25.43	4.536	0.000	ELANE	67.11	0.419	<0.001
TGM2	103.94	4.533	0.000	LRFN5	105.35	0.419	<0.001
SCG2	25.2	4.519	0.000	LEPR	727.76	0.436	<0.001
COL4A4	78.71	4.485	0.000	USP6	40.27	0.438	<0.001
THBS4	430.74	4.481	0.000	SCARA5	5490.32	0.440	<0.001
CHRDL2	6.68	4.470	0.000	LINC02169	13.32	0.443	0.046
ADAMDEC1	22.65	4.237	0.000	TSPAN8	434.02	0.444	<0.001
SULF1	513.56	3.947	0.000	LVRN	134.89	0.444	<0.001
FCGR3A	73.51	3.896	0.000	PNLIPRP3	438.84	0.452	<0.001
CPXM1	246.02	3.798	0.000	SEMA3E	129.29	0.456	<0.001
PLA2G2D	5.9	3.673	0.001	C1QTNF7	354.52	0.471	<0.001
LAMP5	42.48	3.579	0.000	MCOLN3	317.64	0.474	<0.001
CXCL13	4.83	3.547	0.011	FGFBP2	424.05	0.478	<0.001
SPRR2F	4.36	3.505	0.039	ASIP	36.60	0.479	<0.001
CCL18	128.6	3.467	0.000	ANKRD20A19P	28.73	0.479	<0.001
CXCL10	20.6	3.439	0.001	SLC44A5	228.05	0.481	0.019
SPRR2B	23.98	3.439	0.043	HS6ST3	32.42	0.489	<0.001
TNFSF4	28.49	3.433	0.000	CDH10	18.18	0.489	<0.001
TIMD4	14.69	3.368	0.000	CNKSR2	139.75	0.489	<0.001
HAPLN1	15.22	3.330	0.003	PIP	1699.17	0.490	0.012
MZB1	13.72	3.313	0.002	LINC02345	30.79	0.491	<0.001
SERPINE1	239.95	3.296	0.000	PRKG2	126.66	0.494	<0.001

Table 1. Sample genes (60 of 854) with the greatest differential expression in skin of early dcSSc compared to healthy controls with adjusted p value.

and 12 months ($p< 0.05$), revealed by Tukey post-hoc analysis to reflect stable levels in ATA+ patients compared to progressively increased levels in the other subgroups.

There were 854 significantly differentially expressed genes in skin between early dcSSc and HC (Table 1) and unsupervised clustering also differentiated ARA and ATA patients with early dcSSc. 68 genes were significantly differentially expressed in skin between ATA and ARA patients (Table 2). Whilst 206 genes were differentially expressed in PBMC between early dcSSc compared with HC, only 2 genes were significantly different between ATA and ARA PBMCs (CACNG6; PLXNA2). Functional analysis suggested key biological processes distinguishing ARA and ATA skin included lipid metabolic process (PDE3B, ADIPOQ, GPAM), PPAR signaling pathway process (CD36, FABP4, PLIN1), and response to endogenous stimuli (FGF2, GPD1, FGF10)

Overexpressed genes in ARA compared to ATA			
	Mean raw value ATA	Fold change	Adj p value
HORMAD1	16.37	3.546	0.044
HRK	9.45	2.732	0.039
FABP4	798.61	2.625	0.039
TRARG1	232.19	2.571	0.039
PPP1R1A	193.09	2.525	0.039
GPAM	626.2	2.475	0.048
PDE3B	78.64	2.475	0.028
RBP4	371.05	2.475	0.044
PLIN1	1640.85	2.427	0.044
ADIPOQ	796.07	2.404	0.044

Overexpressed genes in ATA compared to ARA			
	Mean raw value ARA	Fold change	Adj p value
SERPINB9P1	16.9	1.864	0.044
LRRC38	8.58	1.678	0.048
PCSK9	46.16	1.662	0.039
HOTAIR	93.13	1.615	0.044
SERPINB10	11.91	1.592	0.048
PSG5	5.99	1.586	0.040
AGAP10P	5.54	1.524	0.044
OVOL1	577	1.523	0.044
TEX101	8.2	1.506	0.044

Table 2. Sample genes (n=19 of 68) differentiating ARA and ATA subtypes in early dcSSc skin

Conclusion: We have found significant differences in skin gene expression and longitudinal change in serum markers by autoantibody specificity in dcSSc. Our findings have implications for SSc pathogenesis and support stratification by ANA subgroup in clinical studies.

Disclosure: K. Clark, None; **C. Campochiaro**, None; **E. Csomor**, GlaxoSmithKline, 3; **A. Taylor**, GlaxoSmithKline, 3; **K. Nevin**, GlaxoSmithKline, 3; **N. Galwey**, GlaxoSmithKline, 3; **M. Morse**, GlaxoSmithKline, 3; **V. Ong**, None; **E. Derrett-Smith**, None; **S. Flint**, GlaxoSmithKline, 3; **C. Denton**, Janssen, 1, GlaxoSmithKline, 1, 2, Bayer, 1, Sanofi, 1, Inventiva, 1, 2, Boehringer Ingelheim, 1, Roche, 1, Bristol-Myers Squibb, 1, CSL Behring, 1, 2, UCB, 1, Leadiant Biosciences, 1, Corbus Pharmaceuticals, 1, Acceleron Pharma, 1, Horizon Therapeutics, 1, Forbius, 1, Servier, 1.

Abstract Number: 1911

IL-11 Expression in Systemic Sclerosis Pulmonary Fibroblasts Is Mediated by Caspase-1

Caya McFalls[1] and Carol Artlett[1], [1]Drexel University College of Medicine, Philadelphia

SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Type: Poster Session D
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Background/Purpose: Interleukin-11 (IL-11) has been shown to be associated with idiopathic pulmonary fibrosis, cardiac and kidney fibrosis. However, conflicting data shows IL-11 can be either pro- or anti-fibrotic. Scleroderma (SSc) is a fatal fibrotic disease of the vasculature, skin, and internal organs. Patients die of scarring and dysfunction of organs due to uncontrolled deposition of collagen and other extracellular matrix proteins. Our laboratory has been studying the signaling cascade mediated by caspase-1 in fibrosis. Caspase-1 activates downstream profibrotic cytokines including IL-1β, IL-18, and IL-33. We hypothesize that IL-11 may be linked to the fibrotic process in SSc through activation of caspase-1. Our purpose is to investigate the expression of IL-11 in SSc pulmonary fibroblasts and to determine the role for caspase-1 in this expression.

Methods: Fibroblasts were derived from fibrotic lung from 8 female patients with SSc with diffuse disease who developed pulmonary fibrosis. SSc patients were classified according to the ACR classification criteria for their disease. Pulmonary fibroblasts were also derived from 12 normal individuals who had died of acute events without pulmonary disease. Fibroblasts were cultured at low passage and treated with the caspase-1 inhibitor (Z-YVAD-FMK) or IL-1 receptor antagonist (IL-1RA). RNA was extracted and gene expression for IL-11, IL-11Rα1, and COL1A1 was analyzed using RT-PCR normalized to β-actin.

Results: SSc fibroblasts display a statistical trend for higher basal expression of IL-11 compared to normal fibroblasts ($p=0.07$) with a significantly increased expression of the IL-11 receptor, IL-11Rα1 ($p=0.0002$). When caspase-1 activity is inhibited with Z-YVAD-FMK, IL-11 expression is reduced ($p< 0.0001$), whereas receptor expression is not altered. We further show that IL-11 expression is mediated by IL-1β, as blockade of the IL-1 receptor with IL-1RA significantly reduces IL-11 ($p=0.03$). It did not alter IL-11Rα1 expression. Further studies show that bleomycin induces IL-11 expression in normal lung fibroblasts, and this is inhibited with either Z-YVAD-FMK ($p=0.008$) or IL-1RA ($p=0.02$). However, in our studies, we were unable to induce COL1A1 expression with IL-11 alone.

Conclusion: Our experiments show IL-11 and its receptor, IL-11Rα1, are elevated in SSc. We observed IL-11 expression is dependent on the inflammasome activation of caspase-1 as inhibition of this protein abrogates IL-11 expression. Furthermore, we identify the role for IL-1β in IL-11 expression. Further studies are warranted to determine the role for IL-11 in SSc fibrosis.

Disclosure: C. McFalls, None; **C. Artlett**, None.

Abstract Number: 1912

Novel Role of Thy-1 (CD90) in the Pathogenesis of Skin Fibrosis

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SESSION INFORMATION
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Background/Purpose: Thy-1 (CD90) is a GPI-anchored cell surface protein that is highly expressed in subsets of fibroblasts. Previous work has shown that Thy-1 deficiency exacerbates lung fibrosis. In inflammatory arthritis, Thy-1 marks a subset of pathogenic fibroblasts. Thy-1 is overexpressed in skin of patients with systemic sclerosis (SSc), and we previously showed that Thy-1 can serve as an *in vivo* marker of cutaneous fibrosis progression, but its role in pathogenesis remains unclear. This study focuses on the effect of Thy-1's modulation of cutaneous fibrosis.

Methods: To induce fibrosis, Thy-1 deficient mice were treated with subcutaneous bleomycin or crossed with TSK1 mice. Mice were fed chow or high fat diet for 12 weeks before starting bleomycin injections. Bleomycin time-course experiments were performed and skin was harvested at days 5, 12, 21, 35 and 52 and was processed for histology, qPCR and immunohistochemical staining. RNA sequencing was performed on affected skin from both wildtype and Thy-1 null mice treated either with bleomycin or PBS (n=12). Differential gene expression analysis was performed using deSeq2, and pathway analysis was performed using Enrichr. To assess Thy-1's role in SSc severity, Thy-1 expression was correlated to modified Rodnan skin score (MRSS) in publicly available datasets.

Results: Skin biopsies from SSc patients have elevated expression of Thy-1 compared to healthy controls ($p< 0.0001$). Patients with diffuse cutaneous and early disease have increased Thy-1 expression ($p< 0.001$), and this is associated with severity of skin involvement (Spearman 0.63, $p< 0.0001$). Mice lacking Thy-1 show protection from chemically-induced and genetically-mediated cutaneous fibrosis at both the histologic and biochemical levels. Fibrosis was attenuated in the Thy-1 null mice with a ~65% reduction in dermal thickness. While wildtype mice demonstrated resolution of fibrosis by later time-points, Thy-1 null mice showed a defective resolution response implicating different mechanisms of Thy-1 in early and late stages of fibrosis. RNA-seq clustering analysis differentiated control and bleomycin-treated Thy-1 null from wildtype mice. Bleomycin upregulated leukocyte chemotaxis, inflammatory response, and muscle contraction pathways regardless of genotype. In Thy-1 null mice, bleomycin specifically upregulated IL-17 and TNF pathways. Fatty acid metabolism pathways were the main feature that distinguished Thy-1 null from control mice treated with bleomycin. However, feeding Thy-1 null mice a high fat diet did not alter their anti-fibrotic phenotype.

Conclusion: Thy-1 expression is increased in SSc and associated with severity of skin involvement. In complementary murine models of cutaneous fibrosis, Thy-1 deficiency has an anti-fibrotic effect which appears to be mediated by TNF, IL-17 and fatty acid metabolism. Thy-1 appears to have different effects on the temporal stages of fibrosis indicating that targeting Thy-1 early in disease may be a rational approach.

Disclosure: R. Goncalves Marangoni, None; **S. Duemmel**, None; **M. Nuzzo**, None; **A. Paine**, None; **C. Ritchlin**, None; **B. Korman**, None.

Abstract Number: 1913

Investigation of the Cellular Mechanism for Estradiol-Induced Dermal Fibrosis

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SESSION INFORMATION
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Background/Purpose: Estradiol (E2), one of the three forms of estrogen, is pro-fibrotic in the skin because it positively influences ECM production in the dermis. In addition to the direct influence that E2 has on ECM production, E2 also induces pro-fibrotic mediators such as TGFβ1 in a wound healing model[1,2]. Yet, few experiments discuss E2-induced pro-fibrotic mediator production or the transcriptional regulation of these protein(s). Since TGFβ1 is central in the development of organ fibrosis, especially in systemic sclerosis (SSc), delineating the regulation of TGFβ isoforms is important in understanding disease pathogenesis and developing potential therapeutics. Therefore, we investigated which ECM components are directly stimulated by E2-induced TGFβ signaling and the important regulatory proteins for TGFβ transcription and translation.

Methods: We received skin samples from healthy donors of various ages who underwent skin-resection procedures in the Division of Plastic Surgery at the Medical University of South Carolina under an approved IRB protocol. The *ex-vivo* human skin model organ culture was used as previously described[3]. Human primary dermal fibroblasts were isolated from human dermal tissue using the outgrowth method[4]. For experimentation, we used 6-well tissue cul-

ture dishes with 4-3mm punches/well or fibroblasts plated at 1.5-2.0 x 10^5 cells/well in serum-free, phenol red-free DMEM. Steady-state mRNA levels were measured using quantitative PCR (qPCR) and signals normalized to *B2M* and G*APDH* levels. Primary dermal fibroblasts were transfected with siRNA targeted to early growth response 1 (*EGR1*) or control prior to vehicle or E2 treatment.

Results: We report that the transcription of TGFβ1, TGFβ2 and collagen 22A1 (Col22A1), the TGFβ responsive gene, are induced in response to E2 stimulation *in vitro* and *ex vivo*. Mechanistically, Col22A1 induction is blocked by the TGFβ receptor inhibitor SB-431542 despite E2 stimulation. Additionally, blocking E2-induced MAPK activation and *EGR1* transcription inhibit TGFβ1, TGFβ2 and Col22A1 transcription.

Conclusion: We conclude that E2-induced dermal fibrosis occurs in part through induction of TGFβ1, TGFβ2 and Col22A1 which is regulated though EGR1 and the MAPK pathway. Dermal fibrosis is a feature of pro-fibrotic diseases, such as SSc, emphasizing the necessity to understand the underlying mechanism of fibrosis. Here, we suggest a cell signaling mechanism for E2-induced fibrosis and TGFβ regulation. Based on the realization that E2-induced TGFβ1 and TGFβ2 directly increase Col22A1 and contribute to ECM accumulation, therapies that inhibit E2 signaling may reduce dermal fibrosis and present a novel therapeutic alternative in pro-fibrotic diseases.

Disclosure: D. Baker Frost, None; **A. Savchenko**, None; **A. Ogunleye**, None; **M. Armstrong**, None; **C. Feghali-Bostwick**, None.

Abstract Number: 1914

Long Non-coding RNA HOTAIR Induces GLI2 Expression Through Notch Signalling in Systemic Sclerosis Dermal Fibroblasts

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Background/Purpose: Systemic sclerosis (SSc) is characterised by tissue fibrosis of the major organs of the body including the skin, lungs and heart. We have previously reported that the lncRNA HOTAIR plays a central role in the activation of SSc myofibroblasts, the key cellular elements of fibrosis. HOTAIR induces fibroblast activation though H3K27me3 mediated activation of the Notch signalling pathway. Here we aimed to identify the signalling events downstream of Notch that drive SSc myofibroblast activation.

Methods: Patient fibroblasts were obtained from full thickness forearm skin biopsies of 3 adult patients with SSc of recent onset. The lncRNA HOTAIR was expressed in healthy dermal fibroblasts by lentiviral transduction. Hedgehog signalling pathway was inhibited with GANT61 and GLI2 siRNA. Gamma secretase inhibitors RO4929097 and DAPT were used to block Notch signalling. GSK126/503 were used to inhibit Enhancer of Zeste 2 (EZH2).

Results: Overexpression of HOTAIR in dermal fibroblasts induced the expression of the Hedgehog pathway transcription factor GLI2. This is mediated by activation of Notch signalling following epigenetic downregulation of miRNA-34a expression. Inhibition of H3K27 methylation and Notch signalling reduced expression of GLI2 in HOTAIR expressing fibroblasts as well as in SSc dermal fibroblasts. Importantly, the inhibition of GLI2 function using GANT61 or siRNA mitigates the pro-fibrotic phenotype induced by HOTAIR.

Conclusion: Our data indicates that GLI2 expression is stably upregulated in SSc myofibroblasts through HOTAIR and that GLI2 mediates expression of pro-fibrotic markers downstream of Notch.

Disclosure: C. Wasson, None; **R. Ross**, None; **R. Wells**, None; **C. Corinaldesi**, None; **I. Georgiou**, None; **N. Riobo-Del Galdo**, None; **F. Del Galdo**, None.

Abstract Number: 1915

Leptin Plays a Critical Role in Modulating Dermal Adipose Tissue, Inflammation and Skin Fibrosis

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Background/Purpose: We previously demonstrated that systemic sclerosis (SSc) patients have substantial reduction in dermal white adipose tissue (dWAT) which correlates with skin fibrosis. In animal models the loss of dWAT precedes dermal fibrosis indicating that this process may be a primary event. Leptin is a major adipokine involved in glucose homeostasis and known to be profibrotic in models of cardiac and lung fibrosis. We previously reported increased serum levels of leptin in patients with SSc. Given the important role of dWAT in SSc and skin fibrosis, we sought to investigate the role of leptin in *in vivo* fibrosis by comparing mice deficient in leptin (*ob*/*ob*) which have a substantially expanded dWAT with mice on diet-induced obesity which is known to increase levels of leptin.

Methods: *ob*/*ob* mice which lack functional leptin and littermate controls were treated with subcutaneous bleomycin or PBS. Wildtype mice were fed chow or high fat diet (60% kcal fat) for 12 weeks at libitum, and then treated with bleomycin or PBS injections. Skin was harvested and processed for histology, qPCR and immunohistochemical analysis. To assess the relevance of this pathway in disease, leptin expression in SSc was evaluated in publicly available gene expression datasets.

Results: *ob*/*ob mice* demonstrated significant protection from bleomycin-induced dermal fibrosis and loss of dermal white adipose tissue at both histological and gene expression level as compared to littermate mice. Conversely, although wildtype mice fed a high-fat diet showed significant expanded dWAT, bleomycin led to a complete loss of dWAT and fibrosis was comparable to mice fed a chow diet. Whereas *ob*/*ob* mice demonstrated a relative lack of inflammatory cellular infiltrate in response to fibrotic stimuli, the diet-induced obesity model showed an exuberant macrophage-rich inflammatory response. Interrogating skin biopsy transcriptome data, we found increased leptin pathway activation ($p< 0.0001$) in patients with SSc and mice treated with bleomycin ($p=0002$).

Conclusion: Our results implicate leptin as a profibrogenic mediator in skin fibrosis. Moreover, while these results continue to implicate the role of dWAT in skin fibrosis, they indicate that the quality rather than the quantity of dermal adipocytes is a key determining factor. A complex interplay between fibroblasts, adipocytes and macrophages define cutaneous fibrogenic potential.

Disclosure: R. Goncalves Marangoni, None; **S. Duemmel**, None; **M. Nuzzo**, None; **C. Ritchlin**, None; **B. Korman**, None.

Abstract Number: 1916

KZR-616, a First-in-class Selective Inhibitor of the Immunoproteasome, Ameliorates Polymyositis in a Murine Model

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Background/Purpose: Polymyositis (PM) is a chronic autoimmune inflammatory myopathy affecting striated muscles and resulting in muscle weakness. PM is a rare disease, and there are limited approved therapies available. High-dose corticosteroids or IV immunoglobulin are commonly used to treat PM, however response is poor and both treatments contribute to comorbidity. Here we have investigated KZR-616, a first-in-class selective inhibitor of the immunoproteasome in C protein-induced myositis (CIM), a mouse model of PM that closely resembles the human disease. Positive results from this study support the rationale for PRESIDIO (KZR-616-003, NCT: NCT04033926), an ongoing Phase 2 clinical trial of KZR-616 in patients with PM and dermatomyositis (DM).

Methods: CIM was induced in female C57BL/6 mice (5/treatment group) immunized subcutaneously (SC) with 200 µg of fragment 2 (amino acids 284-580) of recombinant skeletal muscle fast-type C protein in complete Freund's adjuvant combined with intraperitoneal (IP) administration of 2 µg of pertussis toxin. Diseased mice (Day 13 post immunization) were treated with 10 mg/kg KZR-616 or ONX 0914 (a structural analog of KZR-616) or vehicle three times per week until Day 28. Endpoints included muscle strength assessed by a grip strength meter, serum creatine kinase activity and immunohistology and immunohistochemistry of the triceps brachii muscle.

Results: Treatment with KZR-616 or ONX 0914 completely blocked the loss of grip strength in mice after vaccination for CIM induction while vehicle treated animals displayed progressive muscle weakness. Compared to vehicle, immunoproteasome inhibition resulted in lowered PM-associated leukocyte infiltration of the triceps brachii muscle, including $CD8^+$ T-cells and $F4\text{-}80^+$ macrophages, and prevented an increase in serum creatine kinase.

Conclusion: Selective immunoproteasome inhibition shows therapeutic efficacy in a preclinical mouse model of PM with suppression of muscle inflammation and prevention of muscle weakness. These results strengthen the hypothesis that KZR-616, currently under evaluation in PRESIDIO (KZR-616-003, NCT: NCT04033926), a Phase 2 placebo-controlled, cross-over study of KZR-616 for patients with PM and DM evaluating safety, tolerability, and exploratory efficacy such as muscle function and disease activity over a 32 week treatment period, will elicit similar results.

Disclosure: M. Del Rio Oliva, None; **M. Basler**, None; **D. Bomba**, Kezar Life Sciences, 1, 3; **D. Lam**, Kezar Life Sciences, Inc, 1, 3; **J. Brandl**, Kezar Life Sciences, 1, 3; **C. Kirk**, Kezar Life Sciences, 1, 3, 4, 6, Kezar Life Sciences, 1, 3, 4, 6; **M. Groettrup**, Kezar Life Sciences, 2.

Abstract Number: 1917

In Myositis Patients, Sjögren's Syndrome Is Associated with Inclusion Body Myositis and with anti-cN1A Antibody Independently of the Myositis Subgroups

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Systemic Sclerosis & Related Disorders – Basic Science Poster

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Myositis are characterized by weakness and muscle inflammation. They encompass heterogeneous conditions, which include dermatomyositis (DM), inclusion body myositis (IBM) and polymyositis (PM) according to the EULAR/ACR 2017 criteria. We recently recorded a high prevalence of IBM in a cohort of primary Sjögren's syndrome (SS). Our objective was to refine the signification of SS in the setting of myositis.

Methods: Among a monocentric myositis cohort (according to the EULAR/ACR 2017 criteria), SS patients (according to the ACR/EULAR 2016 criteria) were identified (myositis/SS+ group) and compared to myositis patients without SS (myositis/SS- group).

Results: Among 417 myositis patients, SS criteria were available for 99 patients. Thirty-four (34%) presented SS. Patients with SS tended to be more frequently women (F/M ratio 10.3 vs 3.1, p = 0.058). Age at diagnosis of myositis was similar in both groups (53 years [range 21-74] vs 53 years [range 16-77], p = 0.45).

Myositis subtypes repartition (as defined by EULAR/ACR 2017 criteria) was different in myositis/SS+ and myositis/SS- groups (p = 0.020), IBM being four-fold more prevalent in myositis/SS+ group (24% vs 6%, p = 0.020). Accordingly, the delay between the first muscle symptoms and myositis diagnosis was longer in myositis/SS+ group (6 months [0-336] vs 4 months [0-122], p = 0.057). Moreover, aside anti-cN1A antibodies, myositis-specific antibodies were less frequently found in myositis/SS+ patients than in myositis/SS- ones (53% vs 72%, p = 0.054).

Anti-cN1A antibodies were more prevalent in myositis/SS+ patients (38% vs 6%, p = 0.0005). However, in myositis/SS+ group, anti-cN1A were frequent in each of the EULAR/ACR 2017 myositis subtypes and the association between SS and anti-cN1A positivity was maintained in a multivariate analysis taking into account the diagnosis of IBM (p = 0.020).

Specificity of anti-cN1A for IBM was 0.96 [95% CI, 0.87 – 0.99] in the myositis/SS- group but dropped to 0.70 [95% CI, 0.48 – 0.85] in the myositis/SS+ group.

9 (26%) of the myositis/SS+ patients had systemic involvement typical of SS (vs 5 [7%] of the myositis/SS- patients, p = 0.11) including polyneuropathy (8 [24%] vs 5 [8%]) and type 2 cryoglobulinaemic vasculitis (1 [3%] vs none). In addition, 2 (6%) myositis/SS+ patients developed a lymphoma (one B diffuse large cell lymphoma of the parotid and one non-Hodgkin lymphoma), vs none of the myositis/SS- patients (p = 0.11). 2 (6%) of the myositis/SS+ patients developed myositis-associated cancer (diagnosed within 3 years of myositis diagnosis) versus 6 (8%) of the myositis/SS- patients.

Aside hydroxychloroquine, more frequently used in myositis/SS+ group (38% vs 16%, p = 0.012), no significant difference was found in the management of the patients (taking into account the myositis subtype).

Conclusion: Myositis patients with SS have more frequently IBM (without response to immunomodulatory drugs) than myositis patients without SS. They also have more frequently anti-cN1A antibody, independently of IBM diagnosis.

Disclosure: D. Lévy, None; **B. Nespola**, None; **M. Giannini**, None; **R. Felten**, Abbvie, 8, Biogen, 8, BMS, 8, Janssen, 8, Lilly, 8, Nordic Pharma, 8, Novartis, 8, MSD, 8, Pfizer, 8, UCB, 8, Abbvie, 6, Novartis, 6, Sanofi, 8; **F. Severac**, None; **C. Varoquier**, None; **M. Rinagel**, None; **A. Korganow**, None; **V. Poindron**, None; **T. Martin**, None; **J. Campagne**, None; **H. Chereih**, None; **B. Bouldoires**, None; **B. Hervier**, None; **C. Lenormand**, None; **E. Chatelus**, None; **L. Arnaud**, Alexion, 8, Amgen, 8, Astra-Zeneca, 8, GSK, 8, Janssen-Cilag, 8, LFB, 8, Lilly, 8, Menarini France, 8, Novartis, 8, Pfizer, 8, Roche-Chugaï, 8, UCB, 8; **B. Gény**, None; **J. Sibilia**, Roche-Chugaï, 8, BMS, 8, UCB, 8, GSK, 8, LFB, 8, Actelion, 8, Pfizer, 8, MSD, 8, Novartis, 8, Amgen, 8, Abbvie, 8, Sandoz, 8, Gilead, 8, Lilly, 8, Sanofi, 8, Janssen, 8, Mylan, 8; **J. Gottenberg**, Bristol-Myers Squibb, 2, 8, Pfizer, 2, 5, UCB, 5, 8, Eli Lilly, 2, 8, AbbVie, 2, 8, Roche, 2, 8, Sanofi-Genzyme, 5, 8; **A. Meyer**, None.

Abstract Number: 1918

Efficacy and Safety of Methotrexate in Giant Cell Arteritis: Results from a Bicentric Portuguese Cohort Study

Sofia Barreira[1], Ana Rita Cruz-Machado[2], Eduardo Dourado[3], Joana Martinho[2], Diana Raimundo[4], Luísa Brites[5], Helena Assunção[5], Vítor Teixeira[6], Nikita Khmelinskii[2], Carla Macieira[2], José A. P. da Silva[7], João Eurico Fonseca[8] and Cristina Ponte[2], [1]Rheumatology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal, [2]Rheumatology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal, [3]Rheumatology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Lisboa, Portugal, [4]Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, [5]Rheumatology Department, Centro Hospitalar Universitário Coimbra, Coimbra, Portugal, [6]Rheumatology Department, Centro Hospitalar Universitário do Algarve, Faro, Portugal, [7]9.Centro Hospitalar e Universitário Coimbra (Rheumatology Department), Coimbra, Portugal, Coimbra, Portugal, [8]Instituto de Medicina Molecular, Faculdade Medicina Universidade de Lisboa and Centro Hospitalar Universitário Lisboa Norte., Lisboa, Portugal

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Giant Cell Arteritis (GCA) is a large- and medium-sized vessel vasculitis affecting patients >50 years-old. High-doses of glucocorticoids (GCs) should be initiated promptly to induce remission in active GCA.

Adjunctive therapy with methotrexate (MTX) was tested in four randomized-controlled trials but only one met its primary endpoint. Our aim was to evaluate the effectiveness and safety of MTX in clinical practice, using data from a cohort of Portuguese patients with GCA.

Methods: Bicentric observational study using data from the Rheumatic Diseases Portuguese Register (Reuma.pt). We included patients with biopsy- or ultrasound-proven GCA treated with GCs with/without MTX. Clinical features of patients treated with GCs alone or GCs+MTX were compared using exact Fisher and Mann-Whitney U tests, as adequate. Association between continuous variables was assessed with Spearman's correlation coefficient. For pa-

Characteristics	GCs alone N=64	GCs+MTX N=66	p-value
Age at diagnosis, years	75.5 (13.0)	74.8 (10.6)	0.117
Female sex, n (%)	42 (65.6)	45 (68.2)	0.853
Body mass index, Kg/m^2	25.1 (7.9)	27.1 (6.3)	0.106
Diabetes, n (%)	16 (25.0)	27 (40.9)	0.064
Hypertension, n (%)	41 (64.1)	49 (74.2)	0.255
Delay in diagnosis, months	1.0 (2)	1.5 (4.0)	**0.046**
Ischemic event, n (%)	28 (43.8)	38 (57.6)	0.16
PMR features, n (%)	26 (40.6)	33 (50.0)	0.378
GC starting dose, mg	60.0 (20.0)	60.0 (20.0)	0.706
GC dose at index date, mg	15.0 (12.5)	20.0 (32.5)	**0.022**
GC cumulative dose at index date, mg	5335.0 (2677.2)	5515.0 (6662.5)	0.780
GC cumulative dose 6 months after index date, mg	6265.0 (2545.7)	9091.3 (6868.1)	0.069
GC cumulative dose 12 months after index date, mg	8050.0 (3751.6)	10395.0 (6160.0)	0.164
Total GC cumulative dose, mg	7327.5 (6470.0)	13710.0 (7767.5)	**<0.001**
ESR at diagnosis, mm/hour	85.0 (46.0)	80.0 (44.0)	0.466
CRP at diagnosis, mg/dL	4.6 (6.2)	4.9 (5.9)	0.777
ESR at index time, mm/hour	25 (23.0)	27 (28)	0.520
CRP at index time, mg/dL	0.5 (1.2)	0.5 (1.0)	0.791
ESR at 6-months after index date, mm/hour	20.5 (28.0)	17.0 (21.0)	0.211
CRP at 6-months after index date, mg/dL	0.6 (1.0)	0.4 (0.9)	0.828
ESR at 12-months after index date, mm/hour	17.5 (22.0)	17 (22.0)	0.863
CRP at 12-months after index date, mg/dL	0.3 (0.8)	0.3 (1.0)	0.960
Active disease 6-months after index date, n (%)	6 (9.4)	7 (10.6)	0.334
Active disease 12-months after index date, n (%)	3 (4.7)	6 (9.1)	0.916

Data for continuous variables are presented as median (IQR), and for categorical variables as absolute number (%). Index date relates to the time of MTX initiation in the GCs+MTX group and correspondent date in the GCs alone group.
CRP – C-reactive protein; GCs – glucocorticoids (prednisolone equivalent); ESR – erythrocyte sedimentation rate; MTX – methotrexate; PMR – polymyalgia rheumatica.

Table 1. Characteristics of the patients with GCA treated with GCs alone compared with patients treated with GCs+MTX

tients on the GCs alone group, an index date, correspondent to the median time to MTX start in the GCs+MTX group, was established for comparison of disease activity and total GCs dose at 6- and 12-months. Active disease was defined according to the presence of GCA-related symptoms and/or increased inflammatory markers. Relapse rate was defined as the number of events per patient-years (p-y) of follow-up, and relapse rates with or without exposure to MTX were compared using mid p-value test.

Results: We included 130 patients, with a median age at diagnosis of 74.9 years (IQR 11.8), 66.9% female. Sixty-six (50.8%) patients received MTX with a median time to start of 174 days (IQR 314), a median starting dose of 10 mg/week (range 5-15) and a median maximum dose of 15 mg (range 5-25). Characteristics of patients in the two treatment groups are summarized in Table 1. Inflammatory markers and proportion of patients with active disease at 6- and 12-months were not reduced in patients receiving MTX. Patients on the GCs+MTX group had a significantly higher median GC dose at index date and total GC cumulative dose, but a longer time to start MTX positively correlated with total GC cumulative dose (r=0.32, p=0.01). Relapses occurred in 28 patients, in a median of 13.5 (IQR 43.0) months from diagnosis: relapse rate in patients exposed to MTX was 2.75/100 p-y vs. 6.72/100 p-y in patients not exposed to MTX, with a rate ratio reduction of 0.41 (95%CI: 0.17-0.91). In subgroup analysis, comparing patients with or without relapses, neither demographic, baseline disease features or cumulative GC dose were different between groups. Twenty-one patients (31.8%) stopped MTX: 2 due to disease remission and 19 due to adverse events (AEs) - 10 mild, 7 moderate, and 2 severe AEs (pneumonitis and Kaposi sarcoma).

Conclusion: Treatment with MTX in GCA was associated with a reduced relapse rate during follow-up. Cumulative GC dose was higher in patients in the GCs+MTX group. In subgroup analysis, GC dose was not different in patients with or without relapses. The proportion of severe AEs was similar to previous studies. This is not a randomized study: the results may have been affected by confounding by indication, co-medication and other sources of bias. They suggest, however, that MTX provides a safe and effective contribution to prevent relapse in GCA.

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Abstract Number: 1919

Efficacy & Safety of Tocilizumab in Giant Cell Arteritis: A Single Centre NHS Experience Using Imaging (Ultrasound and PET CT) as a Diagnostic and Monitoring Tool

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Tocilizumab (TCZ), an IL-6 receptor blocker is approved to treat relapsing, refractory Giant cell arteritis (GCA) We here report our real-life clinical experience with the the efficacy and safety of TCZ in GCA. Furthermore, we assessed the effect of TCZ on imaging, i.e. ultrasound (US) and FDG-PET/CT, during the first year of treatment.

Methods: We included 22 consecutive patients with GCA, who were treated with TCZ. EULAR core data set was collected since July 2018. Data on disease activity, quality of life and treatment-related complications were collected. Pre-TCZ ultrasound and FDG-PET/CT findings were available for 21 patients and 4 patients, respectively. The effect of TCZ on the following parameters was determined: US halo thickness (n=21), US Temporal Artery Halo Score (n=5), US Axillary Artery Halo Score (n=8) and Total Vascular Score on FDG-PET/CT (n=4)

Results: The 22 patients with GCA (10 cranial GCA, 10 large vessel GCA, 2 cranial/large vessel GCA) had a median disease duration of 58.5 weeks (range 1-370) prior to initiation of TCZ. Half of patient had used prior csDMARD treatment. TCZ was indicated due to refractory (50%), ischemic (36%) or relapsing (14%) disease. Median follow up was 43 weeks (IQR 12-52). TCZ was discontinued due to SAEs in ?? patients. Upon treatment with TCZ, 13 patients went into remission with a median daily dose of ≤ 5mg prednisolone (equivalent), whereas 20 patients only required a median dose of 2.5 mg. Four patients were able to fully discontinue prednisolone treatment. Almost 50% of the patients claimed their QoL improved on TCZ. Overall, the US halo thickness decreased in 23 of arterial segments evaluated. The median Temporal Artery Halo Score decreased from 11 to 0. The median Axillary Artery Halo Score remains 6. The median Total Vascular Score on FDG-PET/CT showed a reduction of 11.5 to 6.5.

Conclusion: In our real-life clinical experience, TCZ showed an excellent response with acceptable safety in GCA. TCZ treatment was also associated with improvement on US and FDG-PET/CT imaging.

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Abstract Number: 1920

Efficacy and Safety of Tocilizumab in Patients with Giant Cell Arteritis and Visual Impairment

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Time: 9:00AM–11:00AM

Background/Purpose: Tocilizumab (TCZ) represents a potent new therapeutic principle for patients with GCA, however, data on efficacy and safety in patients who present with visual affection is still limited. We sought to study the outcome of patients with GCA and visual affection treated with TCZ.

Methods: This retrospective analysis was performed on all patients with GCA and visual disturbances consecutively recruited between April 2013 and May 2020 who underwent treatment with tocilizumab in addition to corticosteroids.

Results: 19 GCA patients (14 women, 5 male) with a mean age of 73.4 ± 10 yrs at GCA diagnosis and 28 affected eyes were treated with tocilizumab in addition to corticosteroids.

4/19 patients presented with visual disturbances on oral prednisone and 2/19 patients were on csDMARDs (leflunomide, MTX) for polymyalgia. 2 patients experienced unilateral blindness while receiving iv pulse corticosteroids. AAION was diagnosed in 23/28 eyes, PION in 1/28 eyes and occlusion of the central retinal artery in 4/28 eyes. Loss of vision below 0.1 BCVA occurred in 12/28 eyes. Non patients had bilateral blindness at baseline. 5/28 eyes were affected by sectorial anopsia, impaired vision was reported in 11/28 eyes. 17 patients were treated with TCZ iv 8mg/kg every 4 weeks, 2 patients received TCZ sc at 162mg every 2 weeks.

All patients with visual symptoms received intravenous steroid boluses, followed by predni-sone 1mg/kg/day with subsequent tapering.

Mean disease duration before initiation of tocilizumab was 1.8 $\pm$ 1.7 months. 11/19 patients started with TCZ within 6 weeks after diagnosis of GCA, in 3 patients TCZ was started because of refractory and/or relapsed disease.

Mean duration of TCZ therapy was 18.9 ± 11.5 months. 14/19 patients were able to stop steroids (GC) after a mean duration of 16.7 ± 14.8 months and have been steroid-free for an average time of 15 ± 10.4 months. In addition to cessation of GC, 8 patients have discon-tinued TCZ, 2 patients relapsed after 11 and 14 months. At present, 6 patients remain drug-free for 3 to 28 months (16 ± 11 months). None of the 12 eyes with vision < 0.1 BCVA recovered, but no new vision disturbances occurred during TCZ or after cessation of either TCZ or GC.

Two patients died during follow-up for reasons unrelated to GCA or TCZ. Overall tolerability of TCZ was good, complications were predominantly vascular (2 patients with VTE, one NSTEMI, one stroke and the development of an aortic aneurysm).

Conclusion: Inhibition of IL-6 with TCZ represents a valuable treatment option to prevent deterioration of visual complications in GCA patients with initial visual impairment.

Disclosure: A. Rubbert Roth, AbbVie, 1, Bristol-Myers Squibb, 1, Chugai Pharma, 1, 2, Eli Lilly, 1, 2, Hexal, 1, Novartis, 1, Sanofi, 1, 2, Roche, 1, 2, Pfizer, 1, Merck Sharp & Dohme (MSD), 1, Janssen, 1; **S. Tschuppert**, None; **T. Neumann**, None; **U. Benecke**, None; **I. Pirker**, None; **J. von Kempis**, None.

Abstract Number: 1921

Ongoing Vascular ^{18}F-FDG Uptake Despite Clinical Remission in Patients Receiving Tocilizumab for Large Vessel Vasculitis-Giant Cell Arteritis: Single Universitary Center Experience of 30 Patients

Lara Sanchez-Bilbao[1], Diana Prieto-Peña[2], Inigo Gonzalez-Mazon[3], David Martinez-Lopez[4], Monica Calderon-Goercke[5], Isabel Martínez-Rodríguez[5], Ignacio Banzo[5], Miguel Ángel González-Gay[6] and Ricardo Blanco[1], [1]Hospital Universitario Marques de Valdecilla, Santander, Spain, [2]Research group on genetic epidemiology and atherosclerosis in systemic diseases and in metabolic bone diseases of the musculoskeletal system, IDIVAL; and Department of Rheumatology, Hospital Universitario Marqués de Valdecilla, Santander, Spain, [3]Hospital Universitario Marques de Valdecilla, Bezana, Spain, [4]Hospital Universitario Marques de Valdecilla, Santander (SPAIN), Spain, [5]Hospital Universitario Marqués de Valdecilla, Santander, Cantabria, Spain, [6]Hospital Universitario Marques de Valdecilla, Santander, Cantabria, Spain

SESSION INFORMATION

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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

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Session Time: 9:00AM–11:00AM

Background/Purpose: Tocilizumab (TCZ) has shown efficacy in large vessel vasculitis (LVV)-giant cell arteritis (LVV-GCA). Disease activity in LVV assessed by laboratory parameters (ESR, CRP) may be of less value with TCZ. Imaging assessment by ^{18}F-fluodeoxyglucose positron emission tomography (^{18}F-FDG PET/CT) may be useful to monitor LVV disease activity.

Our aim was to determine if clinical improvement correlated with decrease of vascular uptake in follow-up PET/CT scans.

Methods: Single center study of patients with refractory LVV-GCA treated with TCZ who had a baseline and follow-up PET/CT scan. For the visual analysis, FDG uptake at the thoracic aorta wall was visually grading compared to the liver uptake (0: no uptake, 1: less than liver, 2: equal to liver, 3: uptake greater than liver uptake). We defined a total vascular score (TVS) which included 5 vascular regions (supra aortic trunks, thoracic aorta, abdominal aorta, iliac arteries, femorotibial arteries) ranging from 0 to 15. Besides, a semiquantitative analysis was performed as a target to background ratio (TBR)= SUVmax thoracic aorta wall/SUVmax aortic vascular pool. The baseline and follow-up TVS and TBR were compared. Clinical and analytical improvement and and reduction of prednisone dose (mg/day) were also assessed.

Results: We included 30 patients (24 women/6 men); mean age 65.7± 9.8 years. Baseline PET/CT scans were performed due to active disease at a median [interquartile range-IQR] of 1.5 [0.0-4.0] months before TCZ onset. Follow-

TABLE.

	Baseline (n=30)	Follow-up (n=30)	p
Clinical improvement			
Remission, n (%)		25 (83.3)	
Laboratory markers			
ESR (mm/1st hour), median [IQR]	24.0 [10.0-53.0]	2.0 [2.0-3.0]	< 0.001
CRP (mg/dL), median [IQR]	1.0 [0.5-2.4]	0.1 [0.1-0.1]	< 0.001
Glucocorticoid therapy			
Prednisone dose (mg/day), median [IQR]	7.5 [5.0-10.0]	2.0 [0.0-5.0]	< 0.001
18F-FDG vascular uptake			
Thoracic TBR, mean ± SD	1.70 ± 0.52	1.48 ± 0.25	0.005
Total vascular score, mean ± SD	4.97 ± 2.62	3.13 ± 1.89	< 0.001
Normalization of TBR*, n (%)		9 (30)	
Normalization of TVS**, n (%)		3 (10)	

CRP: C-reactive protein; ESR: erythrocyte sedimentation rate; TBR: target-to-background ratio. * Normalization of TBR was considered when TBR < 1.34. ** Normalization of TVS was considered when TVS=0.

ing TCZ therapy, 25 (83.33%) patients achieved clinical remission and reduction of FDG vascular uptake was also observed after a mean of 10.8±3.7 months. TBR decreased from 1.70 ± 0.52 to 1.48 ± 0.25 (p=0.005) and TVS from 4.97±2.62 to 3.13±1.89 (p< 0.001). However, only 9 (30%) patients showed complete normalization of TBR and only 3 (10%) normalization of TVS (**TABLE**).

Conclusion: Most of patients with LVV under TCZ therapy experienced a rapid and effective clinical and analytical improvement. However, less than one-third show normalization of 18F-FDG vascular uptake.

Disclosure: L. Sanchez-Bilbao, None; **D. Prieto-Peña**, None; **I. Gonzalez-Mazon**, None; **D. Martinez-Lopez**, Lilly, 2; **M. Calderon-Goercke**, None; **I. Martínez-Rodríguez**, None; **I. Banzo**, None; **M. González-Gay**, None; **R. Blanco**, None.

Abstract Number: 1922

Association of Leukocyte Populations in Peripheral Blood and Arterial Wall Inflammation Assessed by FDG-PET in Takayasu's Arteritis and Giant Cell Arteritis

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SESSION INFORMATION
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Background/Purpose: Positron emission tomography (PET) is useful to demonstrate fluorodeoxyglucose (FDG) uptake in the large arteries in both Takayasu's arteritis (TAK) and giant cell arteritis (GCA). Delayed FDG-PET imaging at 2 hours rather than 1 hour after FDG injection has greater sensitivity to detect vascular wall inflammation as measured by FDG uptake. The specific cell populations responsible for FDG uptake within the large arteries are not well defined. The objective of this study was to assess whether vascular PET activity is associated with specific leukocyte subsets in peripheral blood at 1- and 2-hour post-FDG injection timepoints in patients with TAK and GCA.

Methods: Patients with TAK and GCA were recruited into a prospective, observational cohort. All patients received PET imaging 2 hours after FDG injection, and a random subset of these patients had additional PET imaging 1 hour after FDG injection. PETVAS, a qualitative summary score of arterial uptake in 9 arterial territories, was used to quantify vascular PET activity. Absolute neutrophil, monocyte, and lymphocyte counts were determined by complete blood counts. CD8+ and CD4+ T lymphocytes, and CD19+ B lymphocytes were quantified by flow cytometry. CRP and ESR were measured. All laboratory tests were performed within 24 hours of PET imaging. Mixed model linear regression was used to identify associations between PETVAS and leukocyte populations, ESR, and CRP at both timepoints, adjusting for daily prednisone dose.

Results: 91 patients (TAK = 38, GCA = 53) contributed 201 visits for the 2-hour imaging timepoint. A subset of 75 patients (TAK = 31, GCA = 44) contributed 158 visits for the 1-hour imaging timepoint. Baseline characteristics were as follows: female gender (TAK: 79%, GCA: 75%), average age (TAK: 36.1±11 years, GCA: 70±8 years), average

prednisone dose (TAK: 3.8±6 mg/day, GCA: 14.3±19 mg/day), ESR (TAK: 20.8±11 mm/hr, GCA: 25.3±24 mm/hr), and CRP (TAK: 10.6±12 mg/L, GCA: 10.2±21 mg/L).

At the 2-hour time point, PET activity was associated with absolute monocyte count in TAK (β estimate: 1.47, 95%CI: 1.04-2.08) and GCA (β estimate: 1.20, 95%CI: 1.02-1.42). PET activity at the 2-hour timepoint was not associated with other leukocyte populations. At the 1-hour timepoint, CD8+ T lymphocyte count was weakly associated with PET activity in patients with TAK (β estimate: $1+4.6e^{-4}$, 95%CI: $1+3.1e^{-6}$ - $1+9.0e^{-4}$) but not in patients with GCA (β estimate: 1.00, 95%CI: 0.99-1.02). Other leukocyte populations, including absolute monocyte count, were not associated with PET activity at the 1-hour timepoint. There was no association between CRP or ESR with PET activity in TAK or GCA at either timepoint.

Conclusion: In both TAK and GCA, delayed FDG-PET imaging is associated with a patient's absolute monocyte count. The monocyte/macrophage lineage likely contributes to FDG uptake in large-vessel vasculitis and could be an important cell population to target therapeutically in these diseases. Circulating biomarkers related to monocytes may constitute novel biomarkers for vascular PET activity. Future studies that compare circulating biomarkers to vascular PET activity should employ delayed imaging approaches.

Disclosure: K. Gribbons, None; **K. Quinn**, None; **M. Ahlman**, None; **P. Merkel**, AbbVie, 5, Biogen, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Insmed, 5, Jannsen, 5, Kiniksa, 5, Magenta, 5, Novartis, 5, Pfizer, 5, Sparrow, 5, Talaris, 5, AstraZeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, UpToDate, 7; **P. Grayson**, None.

Abstract Number: 1923

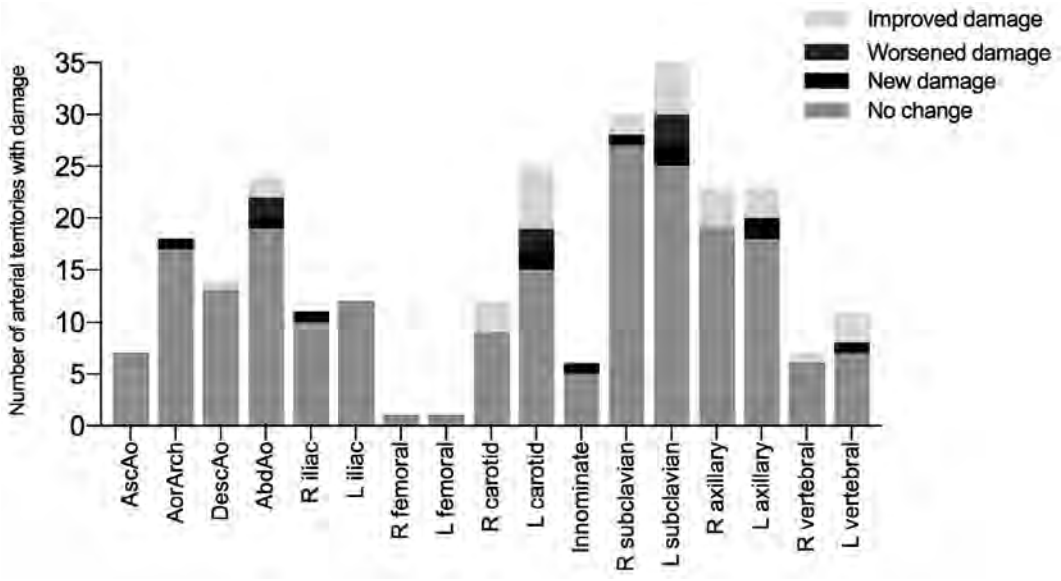
Angiographic Progression of Disease in Large-Vessel Vasculitis

Kaitlin Quinn[1], Himanshu Dashora[2], Mark Ahlman[3], Elaine Novakovich[2] and Peter C. Grayson[2], [1]Systemic Autoimmunity Branch, National Institutes of Health, NIAMS, Washington, DC, [2]Systemic Autoimmunity Branch, National Institutes of Health, NIAMS, Bethesda, MD, [3]National Institutes of Health, Clinical Center, Radiology and Imaging Sciences, Bethesda, MD

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Angiography is essential to detect vascular disease in patients with large-vessel vasculitis (LVV). Guidelines differ on the role of periodic angiography to monitor patients with LVV, in part due to limited prospective data regarding the natural history of angiographic disease. The objective of this study was to characterize angiographic progression of disease over time in Takayasu's arteritis (TAK) and giant cell arteritis (GCA).

Methods: Patients with GCA or TAK were recruited into a prospective, observational cohort. All patients underwent baseline magnetic resonance (MR) or computed tomography (CT) angiography and a follow-up study (same modality) at least one year after baseline per a standardized imaging protocol. Angiographic lesions, defined as stenosis, occlusion, or aneurysm, were evaluated by visual inspection in 4 segments of the aorta and 13 branch arteries by a single reader blinded to clinical status. On follow up angiography, the development of new lesions was recorded and existing lesions were characterized as improved, worsened, or unchanged. Change over time was evaluated at the patient level and within each individual arterial territory.



Results: 1162 arterial territories were evaluated from 70 patients with LVV (TAK=38; GCA=32). Baseline characteristics were as follows: Age [TAK=29.5 years (18.4-39.5), GCA=69.6 years (60.7-75.5)], Female gender [TAK=30 patients (79%), GCA=23 patients (72%)], Disease duration [TAK=2.2 years (0.6-5.5), GCA=0.7 years (0.1-2.6)], Active clinical disease [TAK=17 patients (45%), GCA=20 patients (63%)]. The median time from initial study to follow up study was 1.6 years (1.0-2.7).

At the patient level, there were 12 new arterial territories that developed in 9 (13%) patients and occurred more frequently in patients with TAK=8 than GCA=1; p=0.03. Sixty patients (86%) had ≥1 territory affected at baseline (TAK=33, GCA=27). Angiographic lesions improved in 17 (28.3%) patients, with greater frequency in TAK=13 than GCA=4; p=0.05. Lesions worsened in 6 (10%) patients with no differences between diseases (TAK=4, GCA=2). In 7 (11.7%) patients (TAK=6, GCA=1), specific arterial territories improved while other territories worsened over follow up within the same patient.

At the arterial territory level, 248 territories were affected at the baseline visit (TAK=145 territories, GCA=103 territories). At follow up, existing arterial lesions improved in 30 (12.1%) territories, worsened in 7 (2.8%) territories, and stayed the same in 211 (85.1%) territories. There were no significant differences in angiographic progression of disease at the territory level between GCA and TAK. Change in the branch arteries was more dynamic than change in the aorta (Figure).

Conclusion: Dynamic change in arterial lesions is observed in patients with TAK and GCA. Development of new angiographic lesions is infrequent and occurs more often in patients with TAK. Arterial lesions do not necessarily represent permanent damage, as a substantial number of lesions can improve. Discordant areas of improvement and worsening can occur within the same patient. These data may inform guideline recommendations for imaging monitoring in LVV.

Disclosure: K. Quinn, None; **H. Dashora**, None; **M. Ahlman**, None; **E. Novakovich**, None; **P. Grayson**, None.

Abstract Number: 1924

Low Immunogenicity in Patients with Giant Cell Arteritis Treated with Tocilizumab: 3-Year Results from the Randomized Controlled Portion and the Open-Label Follow-Up of a Phase 3 Trial

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Tocilizumab (TCZ) has low immunogenicity in patients with rheumatoid arthritis (RA).[1] The risk for TCZ immunogenicity remains to be determined in patients with giant cell arteritis (GCA). TCZ administered subcutaneously every week (QW) or every other week (Q2W) plus 26-week prednisone tapering was superior to placebo (PBO) plus 26-week (PBO+26) or 52-week (PBO+52) prednisone tapering for achievement of sustained remission in patients with GCA in the 52-week, double-blind part (part 1) of the GiACTA trial.[2] Part 2 was a 2-year, open-label, long-term, follow-up in which patients were treated at the investigators' discretion; part 2 treatment could include initiation/termination of TCZ QW with or without glucocorticoids or methotrexate. The objective of this analysis was to investigate immunogenicity of TCZ QW and Q2W regimens over the course of parts 1 and 2 of GiACTA.

Methods: In parts 1 and 2 combined, anti–TCZ antibodies (ADA) and corresponding pharmacokinetic (PK) parameters were assessed in serum samples at weeks 0, 8, 24, 36, 52, 76, 100, 136, and 156 or at early withdrawal, with additional assessments in patients who interrupted blinded TCZ for ≥4 weeks in part 1 and patients who withdrew because of anaphylaxis/hypersensitivity at any time. All samples were tested sequentially by screening assay and confirmation assay to verify specificity. If the confirmation assay was positive, 2 additional tests were performed to

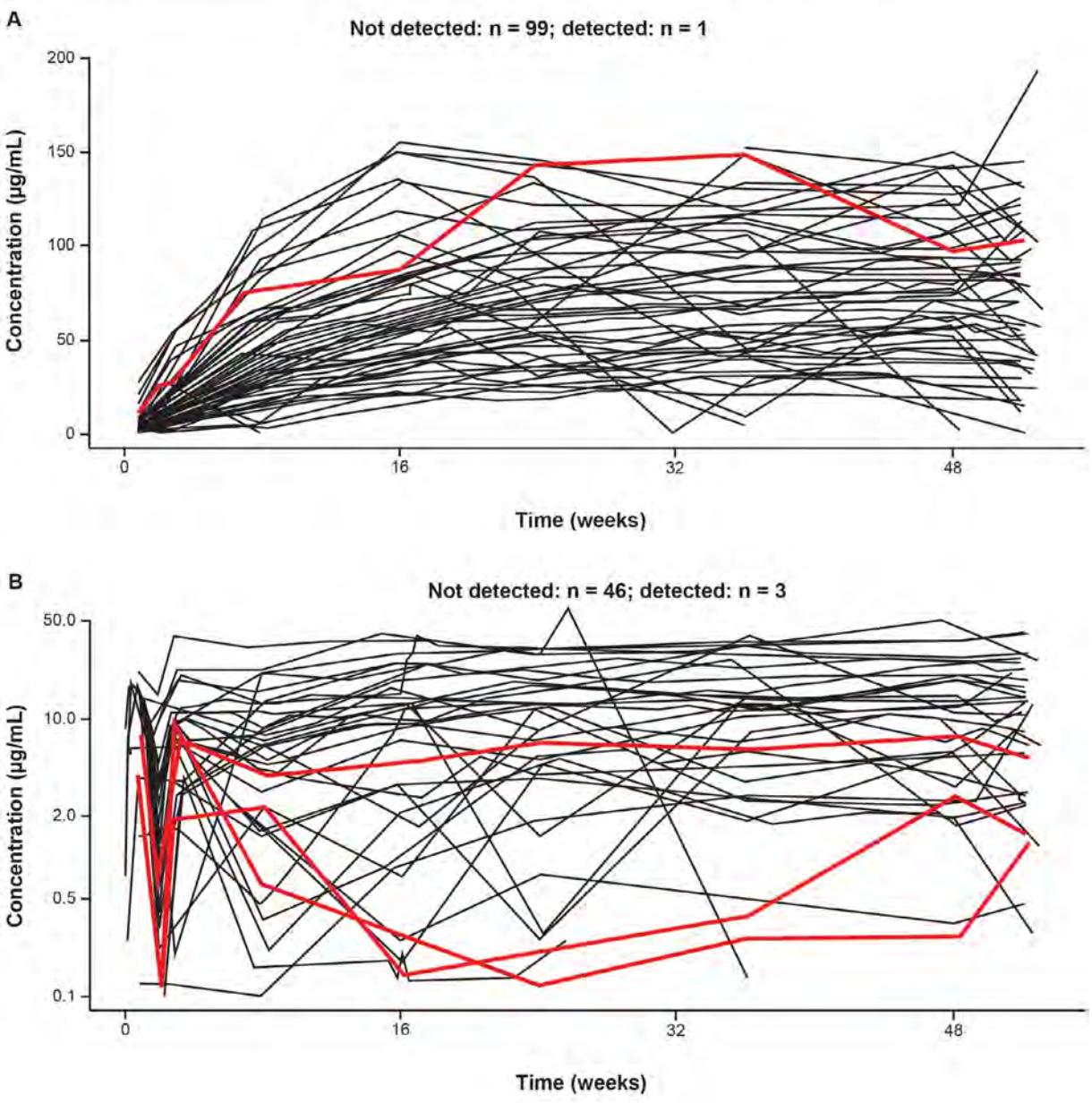
Table 1. Immunogenicity in Patients Who Received TCZ (part 1 + part 2)

	Patients Who Received TCZ N = 199
Baseline	
Evaluable patients	194 (97.5)
Positive screening assay	12 (6.0)
Positive confirmation assay	6 (3.0)
Postbaseline	
Evaluable patients	193 (97.0)
Treatment-induced ADA	13 (6.7)
Characterizaton of ADA	
Neutralizing potential	8 (4.1)
IgE	1 (0.5)

Data are number (%) of patients based on N at baseline and on number of evaluable patients postbaseline.

Table 1

Figure. Time-Concentration Profiles of TCZ in Part 1 by TCZ Dosing Regimen. (A) QW. (B) Q2W.



Patients in whom TCZ-induced ADA developed in part 1 are shown in red.

Figure 1

characterize the detected ADA: a neutralizing assay to test the neutralizing potential of ADAs and an assay to determine whether the ADAs were of the IgE isotype. Proportions of patients in whom ADA developed were summarized for the safety population. ACR GCA classification criteria were fulfilled by 78% of enrolled patients. The study was conducted in accordance with the principles of the Declaration of Helsinki and received IRB approval.

Results: Among evaluable patients (had baseline and ≥1 postbaseline ADA assessments and received ≥1 dose of study treatment) in part 1, ADA developed in 1 of 95 (1.1%) and 3 of 46 (6.5%) patients after TCZ QW and Q2W dosing, respectively. One of 49 (2.0%) and 1 of 47 (2.1%) patients in the PBO+26 and PBO+52 groups, respectively, tested positive for ADA but had not received TCZ and were considered false positives. In parts 1 and 2 combined,

among 199 patients who received ≥1 dose of TCZ, 193 (97%) were evaluable (Table 1); TCZ-induced ADA developed in 13 patients (6.7%) postbaseline (4 during part 1, 9 during part 2). Of these 13 patients, 8 (4.1%) had ADA with neutralizing potential and 1 (0.5%) had IgE ADA. Most TCZ-induced ADA were transient. There was no clear impact of TCZ-induced ADA on TCZ PK (Figure 1). No patients with TCZ-induced ADA experienced anaphylaxis, hypersensitivity reactions, or injection site reactions, and none withdrew because of lack of efficacy.

Conclusion: In patients with GCA, treatment-induced ADA developed in a minority of patients and had no clear impact on TCZ PK, efficacy, or safety. The immunogenicity of subcutaneous TCZ treatment was low, consistent with that observed in patients with RA.

References

1. Burmester GR et al. *Ann Rheum Dis* 2017;76:1078-85; 2. Stone JH et al. *N Engl J Med* 2017;377:317-28.

Disclosure: J. Stone, Roche, 2, 5, Genentech, 2, 5; **N. Mallalieu**, Roche, 4; **M. Bao**, Roche, 3, Roche, 4.

Abstract Number: 1925

Ultrasound Follow-up Examination of Intima-Media-Thickness of the Temporal and Axillary Artery over Six Months in Patients with Newly Diagnosed Giant Cell Arteritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Ultrasound (US) plays an important role in diagnosis of giant cell arteritis (GCA). To date it is unknown how intima-media-thickness (IMT) of affected arteries changes under therapy and time.

Methods: Prospective US examination of the common superficial temporal artery and the axillary artery in patients with newly diagnosed GCA, at time of diagnosis, three and six months later. All patients fulfilled ACR criteria for GCA and showed IMT values above published cut-off values of the respective artery [1]. On each visit US-examination with IMT measurement of the arteries mentioned above was performed. Glucocorticoid dose and c-reactive protein (CRP) values were recorded.

Patients were divided into four subgroups: Group 1, GCA and affection of large and intermediate vessels, group 2, GCA with affection of intermediate vessels only, group 3, GCA and polymyalgia rheumatica (PMR) and affection of large and intermediate vessels and group 4, GCA and PMR and affection of intermediate vessels only.

Group	Visit	Intima-media-thickness (mm)			
		Right axillary artery	Left axillary artery	Right common temporal artery	Left common temporal artery
1 (n=14)	1	1.2 (±0.3)	1.0 (±0.2)	0.5 (±0.1)	0.5 (±0.1)
	2	0.9 (±0.2)	0.9 (±0.2)	0.4 (±0.1)	0.4 (±0.1)
	3	0.9 (±0.2)	1.0 (±0.2)	0.4 (±0.1)	0.4 (±0.1)
2 (n=6)	1	0.8 (±0.1)	0.6 (±0.1)	0.6 (±0.1)	0.5 (±0.1)
	2	0.7 (±0.1)	0.6 (±0.1)	0.4 (±0.1)	0.4 (±0.1)
	3	0.8 (±0.1)	0.8 (±0.1)	0.4 (±0.1)	0.4 (±0.1)
3 (n=7)	1	1.2 (±0.3)	1.0 (±0.4)	0.6 (±0.3)	0.5(±0.2)
	2	1.0 (±0.3)	1.0(±0.1)	0.5 (±0.1)	0.5 (±0.1)
	3	0.8 (±0.2)	0.9(±0.2)	0.4 (±0.1)	0.5 (±0.2)
4 (n=3)	1	0.8(±0.3)	0.7(±0.3)	0.5 (±0.1)	0.5 (±0.2)
	2	0.8(± n.d.)	0.6 (±n.d.)	0.4 (±n.d.)	0.4 (±n.d.)
	3	0.8(±0.0)	0.7 (±0.0)	0.5 (±0.1)	0.4 (±0.0)
Visit 1: time of diagnosis Visit 2: after 3 months Visit 3: after 6 months n: number of patients in each group at time of diagnosis			Group 1: GCA, affection of large and intermediate vessels Group 2: GCA, affection of intermediate vessels only Group 3: GCA+PMR, affection of large and intermediate vessels Group 4: GCA+PMR, affection of intermediate vessels only		

Table 1. Reduction of intima-media-thickness of the axillary and common superficial temporal artery for each group over an observation time of 6 months.

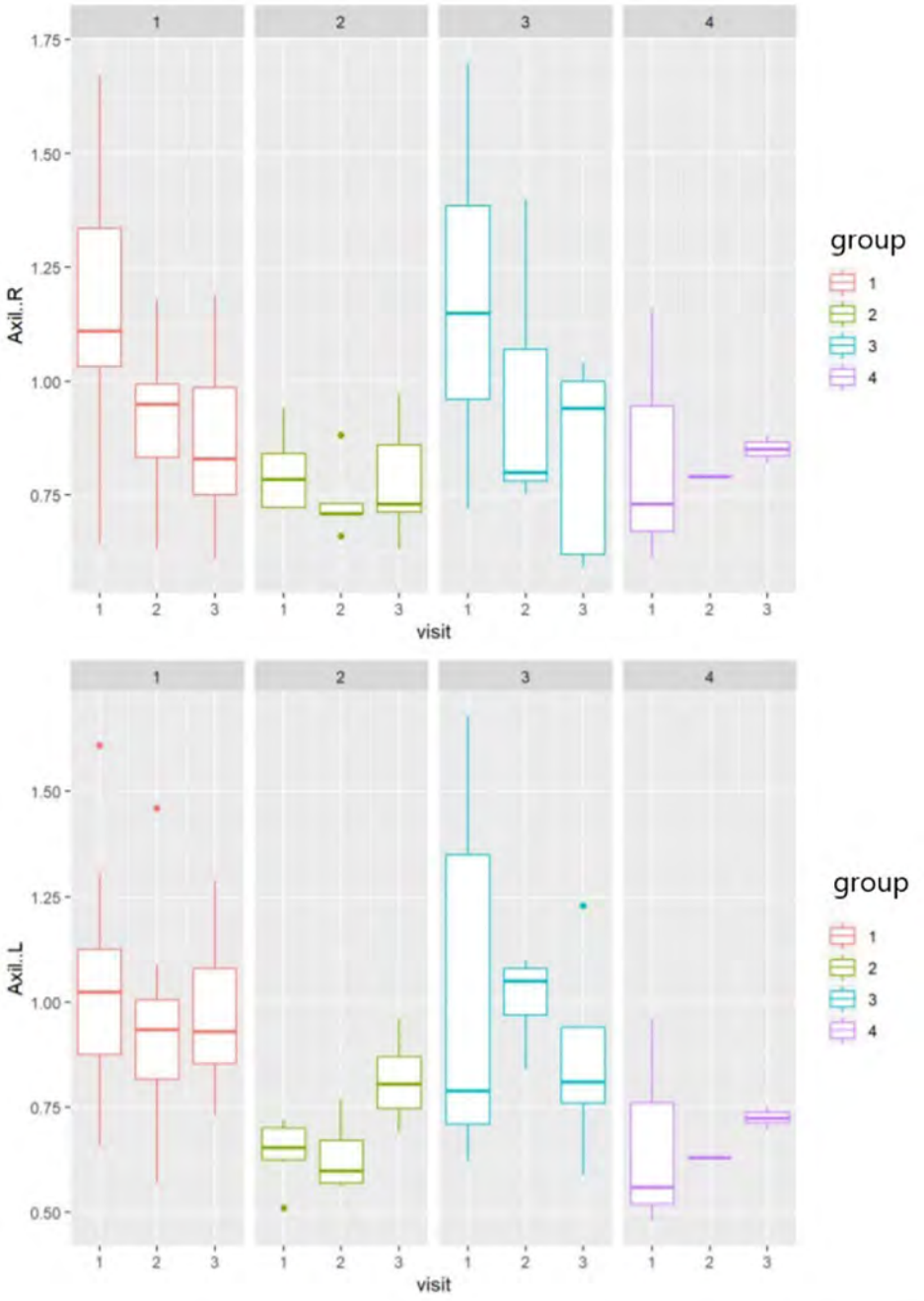
Results: We included a total of 30 patients, 18 (60 %) females. Mean age was 74 years (SD±10). At time of diagnosis, mean CRP-values were 59.9 mg/L (SD±58.8) and mean glucocorticoid dose was 171.3 mg (SD±312.5) per day. After three months, mean CRP was 8.2 mg/L (SD±16.4) and mean glucocorticoid dose was 10.7 mg (SD±4.4) per day while after six months mean CRP was 1.8 mg/L (SD±2.1) and mean glucocorticoid dose was 3.5 mg (SD±2.9) per day.

Overall a decrease of IMT values over three and six months could be observed. Exact values of each group are depicted in Table 1. Figure 1 and 2 show the decrease of IMT-values with the use of boxplots.

Conclusion: A relevant decrease of IMT-values over 6 months of therapy was observed in axillary and common superficial temporal arteries. During the first 3 months, IMT decrease was greatest. Mean CRP-values and glucocorticoid doses decreased over time and therapy. Further research in other arteries typically affected in GCA and a longer observation time in a larger cohort is obligate.

References

1. Schäfer VS, Juche A, Ramiro S, Krause A, Schmidt WA. Ultrasound cut-off values for intima-media thickness of temporal, facial and axillary arteries in giant cell arteritis. Rheumatology (Oxford) 2017;56:1479–83.



group 1: GCA, large and intermediate vessels affected

group 2: GCA, affection of intermediate vessels only

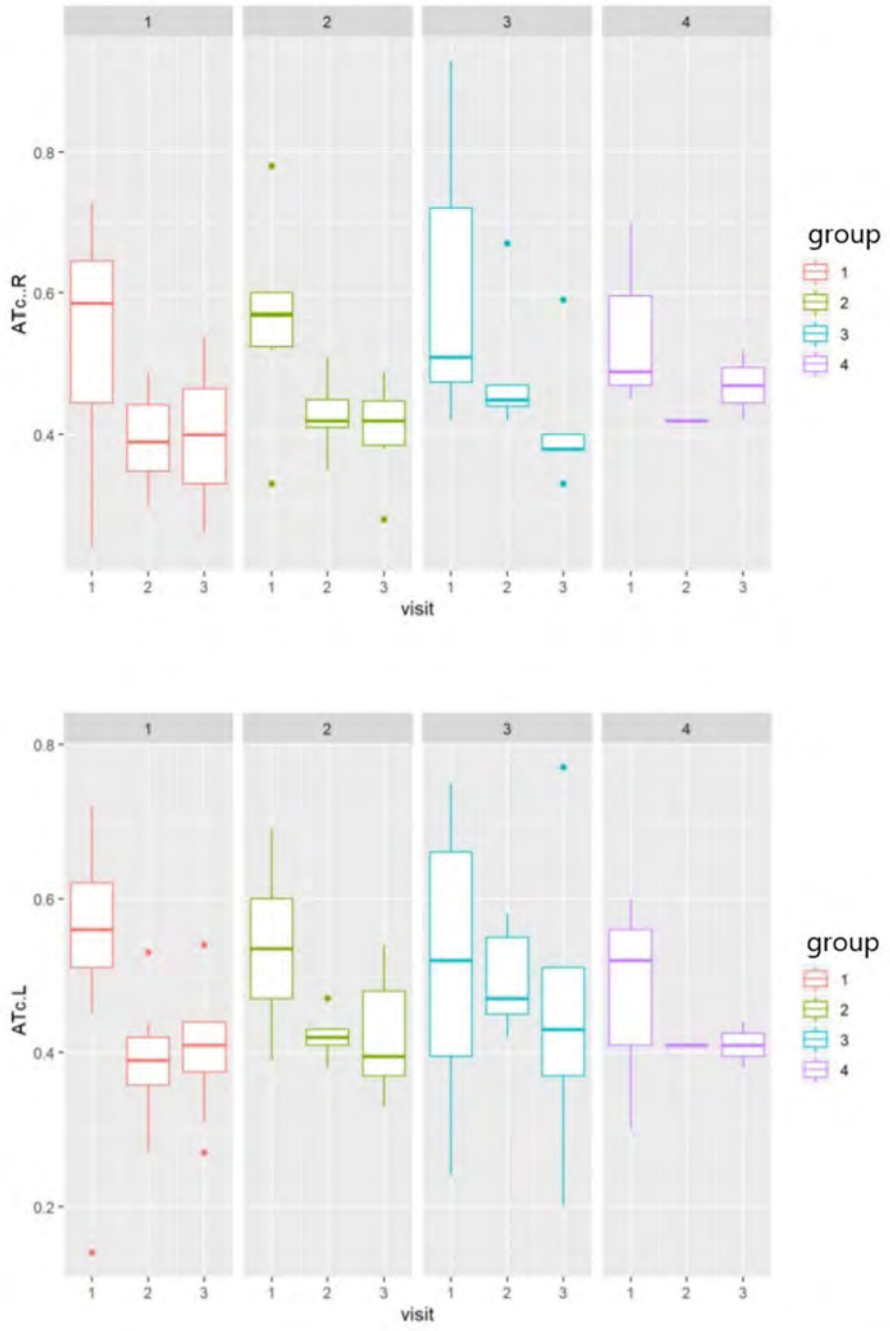
group 3: GCA and PMR, large and intermediate vessels affected

group 4: GCA and PMR, affection of intermediate vessels only

Axil. R: right axillary artery

Axil. L: left axillary artery

Figure 1 Boxplot showing decrease of intima-media-thickness of right and left axillary artery over 6 months between groups.



group 1: GCA, large and intermediate vessels affected

group 2: GCA, affection of intermediate vessels only

group 3: GCA and PMR, large and intermediate vessels affected

group 4: GCA and PMR, affection of intermediate vessels only

ATc. R: Right common superficial temporal artery

ATc. L: Left common superficial temporal artery

Figure 2 Boxplot showing decrease of intima-media-thickness of right and left common superficial temporal artery over 6 months between groups.

Disclosure: L. Burg, None; **P. Brossart**, None; **C. Behning**, None; **V. Schaefer**, None.

Abstract Number: 1926

Efficacy of Adjunctive Methotrexate in Patients with Giant Cell Arteritis Treated with Tocilizumab Plus Prednisone Tapering: Subanalysis of a Phase 3 Trial

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: There is conflicting evidence for methotrexate (MTX) efficacy in giant cell arteritis (GCA).[1,2] Subanalysis of data from the 52-week, double-blind, randomized controlled GiACTA trial in patients with GCA who received tocilizumab (TCZ) or placebo (PBO) with prednisone tapering was performed to assess efficacy and safety in patients who received adjunctive MTX.

Methods: In GiACTA, patients were randomly assigned to receive subcutaneous TCZ every week or every other week plus 26-week prednisone tapering or PBO every week plus 26-week or 52-week prednisone tapering for 52 weeks.[3] The two TCZ groups and the two PBO groups were pooled for this analysis. Stable doses of MTX could be initiated at screening, continued in the double-blind period, and reduced/discontinued at the investigator's discretion. Efficacy was defined as sustained remission (absence of GCA flare and C-reactive protein < 1 mg/dL from weeks 12 to 52 and adherence to the prednisone taper).[3] ACR GCA classification criteria were fulfilled by 78% of enrolled patients. The study was conducted in accordance with the principles of the Declaration of Helsinki and received IRB approval.

Results: Overall, 30 of 250 (12%) treated patients received adjunctive MTX for a median duration of 52.1 weeks: 15 of 149 (10%) TCZ-treated patients received MTX for a median of 52.1 weeks and 15 of 101 (15%) PBO-treated patients received MTX for a median of 52.0 weeks. Baseline characteristics (Table 1) were balanced, except for longer disease duration, higher proportion of patients with relapsing GCA, and lower baseline prednisone doses among patients who received MTX. The median cumulative glucocorticoid dose over 52 weeks was similar between patients who received MTX and those who did not in the PBO groups (2730 mg and 3694 mg, respectively) and the TCZ groups (1385 mg and 1862 mg, respectively). Sustained remission was achieved by 7 of 15 (47%) patients treated with MTX and 75 of 134 (56%) patients without MTX in the TCZ groups and by 1 of 15 (7%) patients treated MTX and 15 of 86 (17%) patients without MTX in the PBO groups (Figure 1). In the primary analysis,[3] 82 of 149 (55%) patients in the TCZ groups and 16 of 101 (16%) patients in the PBO groups achieved sustained remission. The mean annualized relapse rate at 52 weeks was not different between MTX-treated and MTX-untreated patients for the TCZ (0.71 with MTX vs 0.47 without MTX; $p = 0.3305$) or PBO (1.77 vs 1.48; $p = 0.6019$) groups. Adverse event rates per 100 patient-years were numerically higher in MTX-treated than MTX-untreated patients: 1207 and 862, respectively, in the TCZ groups and 1270 and 957, respectively, in the PBO groups.

Conclusion: Preliminary data from a small subgroup of patients suggest that adjunctive MTX does not increase the likelihood of sustained remission, reduce disease relapse rate, or improve steroid sparing in patients with GCA. Re-

Table 1. Baseline Demographics and Disease Characteristics

	PBO+Pred		TCZ+Pred	
	MTX n = 15	No MTX n = 86	MTX n = 15	No MTX n = 134
Age, median, years	71	68	63	71
Female, %	93	71	67	76
White, %	100	98	100	96
Body mass index, median, kg/m^2	27.0	24.8	25.4	25.6
GCA duration, median, days	273	42	199	42
Relapsing GCA, %	87	49	73	49
Pred dose ≤30 mg/day, %	73	49	80	48
CRP, median, mg/L	5.8	3.4	4.5	4.1
ESR, median, mm/h	21	20	15	18

Pred, prednisone.

Table 1

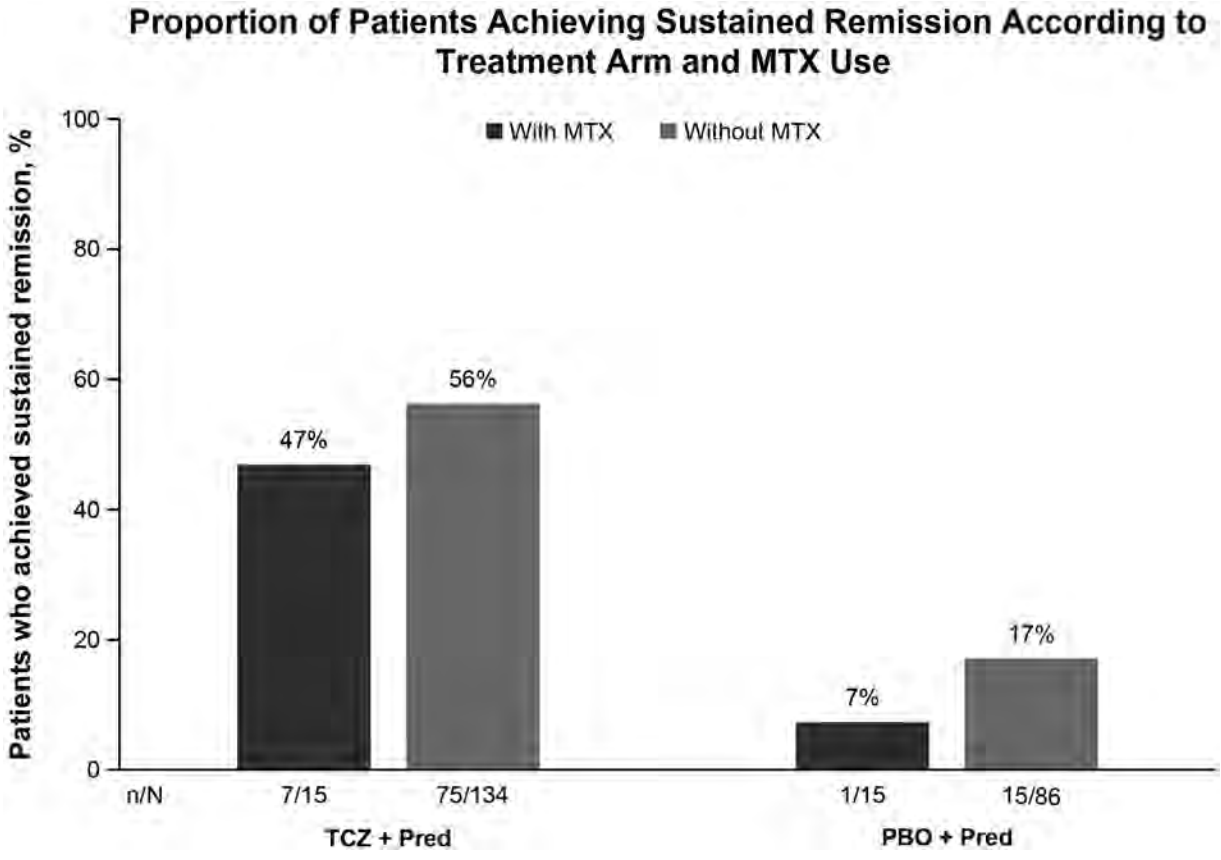


Figure 1

sponse rates in TCZ-treated patients appear to be independent of treatment with MTX. Results from this post hoc analysis should be confirmed in larger studies.

References

1. Hoffman GS et al. *Arthritis Rheum* 2002;46:1309-18; 2. Mahr AD et al. *Arthritis Rheum* 2007;56:2789-97; 3. Stone JH et al. *N Engl J Med* 2017;377:317-28.

Disclosure: J. Stone, Roche, 2, 5, Genentech, 2, 5; **J. Han**, Genentech, Inc., 1, 2; **S. Mohan**, Genentech, Inc., 1, 2.

Abstract Number: 1927

Ultrasonographic Halo Score as a Marker for Diagnosis and Monitoring of Disease Activity in GCA

Alwin Sebastian[1], Abdul Kayani[1], Sue Innes[2], Jo Jackson[2], Kornelis S. M. van der Geest[3] and Bhaskar Dasgupta[1], [1]Rheumatology, Mid and South Essex University Hospital NHS Foundation Trust, Southend University Hospital, United Kingdom, Westcliff on sea, England, United Kingdom, [2]School of Sport, Rehabilitation and Exercise science, Colchester Campus, University of Essex, United Kingdom, Colchester, England, United Kingdom, [3]Rheumatology and Clinical Immunology, University Medical Center Groningen, Netherlands, Groningen, Netherlands

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: EULAR recommendations highlights ultrasound (US) as the first line imaging investigation for giant cell arteritis (GCA). Traditionally, the halo sign and compression sign have been used to discriminate between GCA and non GCA patients. We propose a novel Halo Score (HS) as a potential marker to diagnose and assess disease activity in follow up GCA patients.

Methods: Preliminary data was collected from the ongoing prospective multicentre HAS GCA study (IRAS# 264294) from referrals of suspected GCA to UK fast track clinics with GCA follow up at months 1,3,6 and 12. Based on the GCA clinical pre-test probability score (PTPS)[1], patients were stratified in to Low , Intermediate and High risk categories[2]. US Halo Score was calculated from the halo thickness and extent in bilateral temporal arteries and branches (TA Halo Score) and bilateral axillary arteries (AA Halo Score) summed up to a Total Halo Score. GCA was diagnosed based on the clinical symptoms and signs, positive US or additional test results with CRP >5 mg/dl. The objective is to recruit 270 patients including 68 patients with GCA.

Mann Whitney U test was used to compare controls and baseline GCA

Wilcoxon signed rank test was used to compared baseline GCA and 1m GCA (only patients that had two measurements)

Results: Total of 47 patients have been recruited so far into HAS GCA with 1 month follow up assessments. Demographics, clinical features and US results are shown (Table 1).

Twelve (26%) were confirmed GCA (9 cranial, 2 large vessel and 1 cranial plus large vessel) and 35 (74%) confirmed non-GCA. Median age 72 years in GCA and 71.5 years in controls (42% females in GCA and 77% non GCA). GCA patients stratified by PTPS to Low risk (0%), Intermediate risk (33%) and High risk (66%) whereas the 35 non GCA were categorised by PTPS as Low risk 51%. Intermediate risk 37% and High risk 11%.

Table 1: Demographics, Clinical feature, US results and Laboratory data

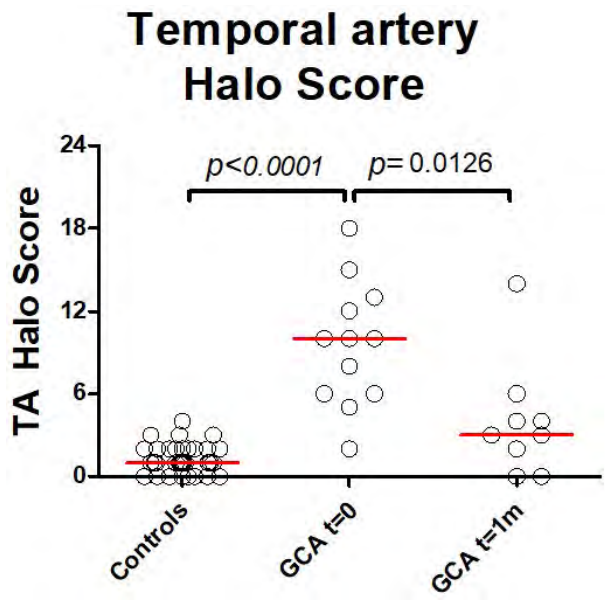
	GCA (12)	Controls (35)
GCA Type, n, (%)	Cranial 9 (75) Large vessel 2 (17) Both 1 (8)	
Age, median (IQR)	72 (65-76)	71.5 (64.75 – 75)
Females, n, (%)	5 (42)	27 (77)
PTPS category, n (%)		
Low Risk	0 (0)	18 (51)
Intermediate Risk	4 (33)	13 (37)
High Risk	8 (67)	4 (11)
Halo Score (HS) at baseline – median, (range)		
Temporal artery (TA Halo Score)	10 (2-18)	1 (0-4)
Axillary artery (AA Halo Score)	6 (0-18)	3 (0-18)
Total halo score	20 (2-28)	4 (0-19)
Clinical symptoms n, (%)		
Temporal headache	8 (67)	20 (57)
General Headache	4 (33)	14 (40)
Scalp Tenderness	6 (50)	17 (49)
Jaw claudication	5 (42)	2 (6)
PMR symptoms	4 (33)	4 (1)
Constitutional symptoms	6 (50)	9 (26)
Visual disturbance	6 (50)	16 (46)
Vision loss	4 (33)	3 (9)
History of PMR	3 (25)	3 (9)
Inflammatory markers, median, (IQR)		
C-Reactive Protein (mg/dl)	15 (8-38)	14 (7-40)
ESR (mm/hr)	24 (12.5 – 41)	20 (12-41)
Glucocorticoid use (GC)		
GC at presentation, n (%)	12 (100)	15 (43)
GC dose (mg), Median, (range)	40 (20 – 60)	40 (0-60)
GC stopped at 1st assessment, n, (%)	0 (0)	35 (100)
Cumulative GC (mg), Median, (range)	40 (40 – 5310)	40 (0 – 3750)

In High risk 1 LV GCA patient had negative US and FDG PET/CT confirmed bilateral vertebral arteritis. Another patient with axillary artery US positive LV-GCA had a negative FDG PET/CT without other pathologies. In the Intermediate risk, one patient had negative US and negative MRA.

Jaw claudication (42%) and polymyalgic symptoms (33%) were the dominant features in GCA patients contrast to controls. 4 had permanent visual loss prior to the assessment. a Median Total Halo Score in GCA was 20 and control group was 4 (p=0.0001). 9/12 patients with GCA have completed at least 1 month follow up (Table 2). Median TA Halo Score and Total Halo Score was reduced from 8 to 3 and 16 to 11 respectively (Image). AA Halo Score increased from 6 to 9 in 1 month. All the GCA patients were on glucocorticoids (GC) (prednisolone 40-60 mg daily) at presentation compare to 43% (15) in control group (in all GC discontinued after the assessment).

GCA – 9 out of 12 patients completed 1 month follow up

Number	ID	Age	Gender	GCA type	PTPS	Probability category	TA Halo Score-Baseline	TA Halo Score-1M	AA Halo Score-Baseline	AA Halo Score-1M	Total Halo Score-Baseline	Total Hal Score-1M
1	**1**	77	Female	Cranial	15	High	6	3	0	0	6	3
2	**4**	75	Male	Cranial	12	Intermediate	10	6	9	9	19	15
3	**9**	72	Female	Both	13	High	6	2	15	9	21	11
4	**15**	70	Male	Cranial	12	Intermediate	13	14	12	6	25	20
5	**19**	71	Male	Cranial	13	High	5	3	3	3	8	6
6	**20**	75	Female	LVV	17	High	2	0	0	9	2	9
7	**24**	92	Male	Cranial	12	Intermediate	10	4	6	9	16	13
8	**25**	80	Male	Cranial	10	Intermediate	12	4	9	12	21	16
9	**34**	64	Female	Cranial	14	High	8	0	6	3	14	3
Median HS							**8**	**3**	**6**	**9**	**16**	**11**



Conclusion: Along with GCA clinical PTPS, US Halo Score successfully discriminates GCA from non GCA mimics. TA Halo Score and Total Halo Score is effective in showing 4-week response and may be a useful marker to monitor GCA disease activity. The ongoing viral pandemic may have an effect on protocol-based US assessments.

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Abstract Number: 1928

Quantitative Ultrasound of Temporal, Axillary and Subclavian Arteries to Monitor Tocilizumab Treatment in Patients with Newly Diagnosed Giant Cell Arteritis: A 24 Week Analysis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

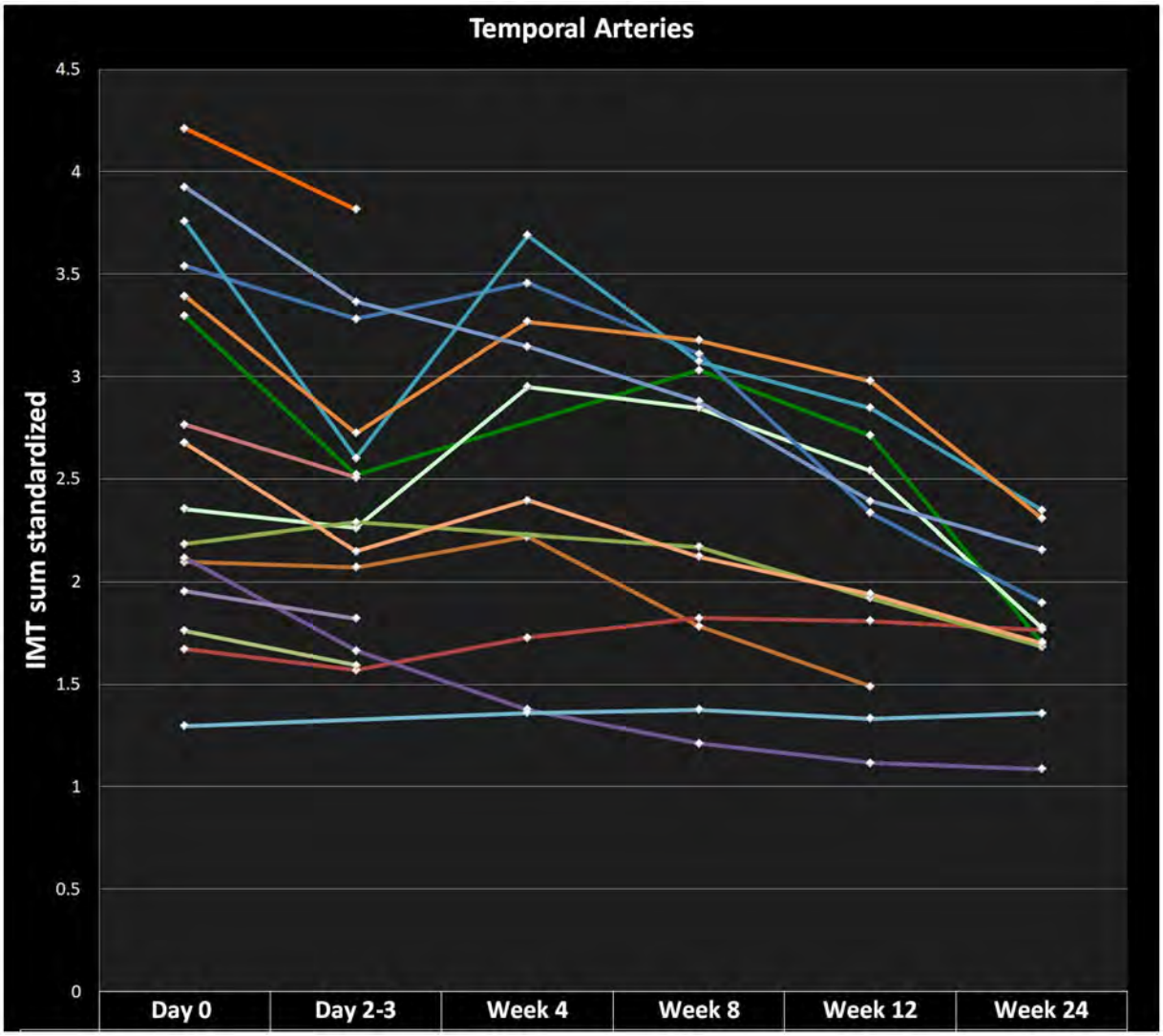
Background/Purpose: Tocilizumab (TCZ) suppresses CRP. Thus, CRP cannot be used as a marker for disease activity in GCA patients treated with TCZ and monitoring of disease activity is based on clinical signs and symptoms only. Novel methods to monitor disease activity in GCA under IL-6 blocking therapies are needed.

The **G**iant Cell Arteritis treated with **U**ltra-**S**hort Glucocorticoids and **TO**cilizumab (GUSTO) study (NCT03745586) offered a unique opportunity to test monitoring of the intima-media thickness (IMT) of arterial vessel walls with ultrasound (US) as a surrogate for disease activity.

Methods: In this single-arm, single-center, open-label clinical trial, 18 patients with newly diagnosed GCA were enrolled. They received 500 mg methylprednisolone intravenously for three consecutive days. Thereafter, glucocorticoids were discontinued and TCZ (8mg/kg body weight) was administered intravenously, followed by weekly subcutaneous TCZ injections (162 mg) from day 10 to week 52. Change of IMT was an exploratory secondary outcome.

US of temporal (TA), axillary (AA) and subclavian (SA) arteries was performed at baseline, on day 2-3, at week 4, 8, 12 and 24. The sonographer was not blinded. The maximum IMT of the compressed TA (mainstem, frontal/parietal branch) and single wall IMT at landmarks of AA/SA were measured with an 18-22 or 9-11 MHz probe in B-mode. Biopsied branches and incompressible TA mainstems were excluded from follow-up. Diagnostic cut-offs and mean normal values for IMT of TA and AA were taken from Schäfer et al. (Rheumatology 2017;56(9):1479-1483). For the SA, the diagnostic cut-off and mean normal IMT of the AA were used. For each examination, the IMT of each TA segment was standardized by dividing it by (2 x (mean normal IMT)), the sum of these values was then divided by the number of segments. The same was done for the AA/SA separately.

Results: According to diagnostic IMT cut-offs for GCA, at baseline 16/18 (89%) patients had involvement of the TA and 3/18 (17%) of the AA/SA. At week 12, the IMT was above the cut-off in 11/14 (79%) in the TA (1 missing value (MV)) and in 6/14 (43%) in the AA/SA (1 MV). At week 24, the IMT was above the cut-off in 10/13 (77%) in the TA and in 6/13 (46%) in the AA/SA. Of the individual segments of the TA at baseline, 66/92 (72%) were above the diagnostic cut-off, at week 12 and 24 the proportions fell to 34/50 (68%) and 27/50 (54%) respectively. Of the individual segments of the AA/SA at baseline, 10/70 (14%) were above the diagnostic cut-off, at week 12 and 24 the proportions rose to 19/52 (37%) and 20/52 (38%) respectively. At week 4, in 7/14 (50%) patients (5 MV), IMT values of TA were higher compared to day 2/3 and in three patients, new onset AA or SA involvement was seen. Figure 1 shows the sum of standardized IMT of the TA from baseline to week 24.



Conclusion: A three day glucocorticoid pulse, followed by TCZ monotherapy leads to a gradual reduction of IMT of the TA until week 24.

This is the first study to document the usefulness and feasibility of IMT monitoring with US in GCA patients treated with TCZ.

Disclosure: L. Seitz, None; **L. Christ**, None; **G. Scholz**, None; **F. Lötscher**, None; **J. Amsler**, None; **F. Kollert**, None; **S. Reichenbach**, None; **P. Villiger**, None.

Abstract Number: 1929

Visual Ischemia During Relapse and Follow-up of Giant Cell Arteritis: A Systematic Review

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The purpose of this study was to characterize the frequency of visual ischemia (VI) as a manifestation of relapse or during follow-up in patients with GCA through performance of a systematic literature review.

Methods: Potentially eligible studies were identified from Medline and EMBASE databases from inception to November 31, 2019 using a search strategy that comprised of terms for "giant cell arteritis," "temporal arteritis," or "Horton's disease," with "relapse," "recurrence," "flare," "outcome," "follow-up," or "prognosis." VI was defined as transient or permanent, full or partial, monocular or binocular visual field loss. VI occurring within 4 weeks of GCA diagnosis was considered due to active disease and not included as a relapse event. Inclusion criteria used: (1) original research reported in English, (2) GCA definition provided, (3) VI outcome described as one of the following: (a) relapse rate/frequency denoting the presence or absence of VI, or (b) absolute number of VI events (> 4 weeks after GCA diagnosis) even if total cohort relapse rate/frequency was not provided. In order to reduce bias from under-reporting of negative results, studies that reported relapse rates/frequencies with accompanying relapse characteristics but did not provide initial detail regarding the presence/absence of VI were also identified. In such circumstances, the pri-

Table 1A: Characteristics of included studies with visual ischemia as relapse or outcome in giant cell arteritis

Author (year)	Country	Design	GCA definition	Cohort Size	TAB (+) #/(%)	Female # (%)	Mean Age Dx	Mean ESR at Dx or study entry	Baseline VI # (%)	Relapse Definition	Average F/U (yrs)	# (%) Patients with 1+ Relapse	# (%) VI among relapsers	# (%) VI after Dx among entire cohort
Beevers (1973)	UK	Pro/Obs	TAB (+)	36	36 (100)	21 (58)	69.6	87	TVL 2 (6) PVL 3 (8)	Sx recur	2.5	16 (44)	2/16 (13)	2/36 (6)
Huston (1978)	USA	Retro	TAB(+) or consistent Sx	42	38 (90)	33 (79)	75	96	TVL 5 (12) PVL 7 (17)	Sx + ↑ESR	5	11 (26)	0/11 (0)	0/42 (0)
Jonasson (1979)	UK	Retro	TAB (+)	124	124 (100)	94 (76)	73	87	PVL 62 (50)	ND	4.2	ND	ND	2/124 (2)
Bengtsson (1981)	Sweden	Retro	TAB(+) or consistent Sx	73	50 (68)	53 (73)	71	ND	ND	Sx + ↑Tx	5.2	53 (73)	0/53 (0)	0/73 (0)
Graham (1981)	UK	Retro	TAB (+)	90	90 (100)	64 (71)	ND*	81	PVL 44 (49)	Sx + ↑ESR	5	18/58 (31)*	0/18 (0)	0/90 (0)
Spiera (1982)	USA	Retro	TAB (+)	51	51 (100)	38 (75)	ND	ND	PVL 8 (16)	ND	ND	ND	ND	1/51 (2)
Behn (1983)	UK	Pro/Obs	TAB (+) or consistent Sx	68	25 (37)	ND*	69	66	TVL 2 (3) PVL 3 (4)	Sx ± ↑ESR	3.2	11 (16)	0/11 (0)	0/68 (0)
Norborg (1991)	Sweden	Pro/Obs	TAB or consistent Sx	60	22 (35)	51 (81)	71.3	78	ND	Sx + ↑Tx	1.5	27 (45)	2/27 (7)	2/60 (3)
Myles (1992)	UK	Retro	TAB or consistent Sx	96	48 (50)	ND	ND	76	ND	ND	ND	ND	ND	9/96 (9.4)
Aiello (1993)	USA	Retro	1990 ACR	245	204 (83)	185 (76)	72	79	TVL 16 (7) PVL 32 (13)	ND	7.2	ND	ND	2/245 (1)
Kyle (1993)	UK	Pro/Obs	Jones and Hazelman	35	ND	ND	71.4	ND	ND	Sx + ↑Tx	1.2	19 (54)	1/19 (5)	1/35 (3)
Nesher (1997)	Israel	Retro	1990 ACR	96	86 (90)	50 (52)	73	ND	ND	Sx + ↑ESR	3	29 (30)	3/29 (10)	3/96 (3)
Narvaez (1999)	Spain	Retro	1990 ACR	35	27 (77)	20 (57)	71.8	93.6	TVL 9 (26)	Sx + ↑ESR	3	10 (29)	0/29 (0)	0/35 (0)
Jover (2001)	Spain	RCT	TAB (+)	42	42 (100)	29 (69)	78	96	TVL 1 (2) PVL 14 (33)	Sx + ↑Tx	2	25 (60)	0/25 (0)	0/42 (0)
Spiera (2001)	USA	RCT	TAB (+) or 1990 ACR	21	17 (81)	13 (62)	73	71	PVL 6 (29)	Sx + ↑Tx	2	9 (43)	0/9 (0)	0/21 (0)
Hachulla (2001)	France	Retro	TAB (+) or 1990 ACR	133	82 (62)	95 (71)	72	89	TVL 2 (2) PVL 11 (8)	↑APR ± Sx + ↑Tx	5.6	83 (63)	0/83 (0)	0/133 (0)
Hoffman (2002)	Multiple	RCT	Trial Criteria	98	79 (81)	70 (71)	74	ND	PVL 17 (17)	↑ESR + Sx	1	62 (63)	8/62 (13)	8/98 (8)
Hayreh (2003)	USA	Retro	TAB (+)	145	145 (100)	108 (74)	75.7	87	PVL 96 (66)	↑Tx	2.4	ND	ND	0/145 (0)
Hamidou (2005)	France	Retro	TAB (+)	50	50 (100)	37 (74)	74.6	ND	TVL 5 (10)	Sx + ↑ESR + ↑Tx	4.5	15 (30)	0/15 (0)	0/50 (0)
Salvarani (2005)	Italy	Retro	TAB (+)	136	136 (100)	102 (75)	73.6	98.5	PVL 25 (18)	ND	1.8	ND	ND	1/136 (0)
Mazlumzadeh (2006)	USA	RCT	TAB (+) and 1990 ACR	27	27 (100)	19 (70)	74	67	VL excluded	Sx or ↑ESR + ↑Tx	1.5	22 (81)	0/22 (0)	0/27 (0)
Hoffman (2007)	Multiple	RCT	1990 ACR	44	34 (77)	35 (80)	70	77	VL 7 (16)	Sx + ↑ESR	0.4	24 (55)	7/24 (29)	7/44 (16)
Nesher (2008)	Israel	Retro	TAB (+) or 1990 ACR	130	116 (89)	84 (64)	73	ND	ND	Sx + ↑Tx	3	55 (42)	5/55 (9)	5/130 (4)

Table 1B: Characteristics of included studies with visual ischemia as relapse or outcome in giant cell arteritis, continued

Author (year)	Country	Design	GCA definition	Cohort Size	TAB (+) #/(%)	Female # (%)	Mean Age Dx	Mean ESR at Dx or Study entry	Baseline VI # (%)	Relapse Definition	Average F/U (yrs)	# (%) Patients with 1+ Relapse	# (%) VI among relapsers	# (%) VI after Dx among entire cohort
Bley (2008)	Germany	Pro/Open Imaging	TAB (+) or 1990 ACR	17	11 (65)	10 (59)	68.5	88.8	ND	Sx	ND	ND	ND	0/17 (0)
Martinez-Taboada (2008)	Spain	RCT	TAB (+)	17	17 (100)	14 (82)	74.5	16	ND	Sx+↑APR	1.25	11 (65)	0/11	0/17 (0)
Martinez-Lado (2011)	Spain	Retro	TAB (+) or 1990 ACR	174	174 (100)	94 (54)	75	90	TVL 27 (16) PVL 15 (9)	Sx+↑ESR	8.7	71 (41)	0/71 (0)	0/174 (0)
Espitia (2012)	France	Pro/Obs	TAB (+) or 1990 ACR	22	22 (100)	17 (77)	74	80	PVL 3 (14)	↑CRP + Sx	7.8	9 (41)	0/9 (0)	0/22 (0)
Loock (2012)	Germany	Retro	1990 ACR or LVV imaging	35	13 (37)	27 (77)	65.3	ND	ND	Sx ± ESR + ↑Tx	4.2	12/28 (43)	0/12 (0)	0/35
Alba (2014)	Spain	Retro	TAB (+)	106	106 (100)	77 (73)	75	90	TVL 15 (14) PVL 12 (11)	Sx ± ESR + ↑Tx	7.8	68 (64)	1/68 (1.5)	1/106 (1)
Furuta (2015)	UK	Retro	1990 ACR or LVV imaging	22	1 (5)	19 (86)	65.8	77	VL 0	Sx ± ↑APR ±Imaging	4.3	8 (36)	0/8 (0)	0/22 (0)
Singh (2015)	USA	Retro	1990 ACR	204	177 (87)	163 (890)	76	78	TVL 7 (3) PVL 18 (9)	ND	5	ND	ND	0/204
Fukui (2016)	Japan	Retro	TAB (+) or 1990 ACR	29	28 (97)	12 (41)	76	111	0	Sx + ↑APR	2.3	6 (21)	0/6 (0)	0/29 (0)
Labarca (2016)	USA	Retro	TAB (+)	286	286 (100)	213 (75)	75	66	TVL 20 (7) PVL 16 (6)	Sx or ↑APR + ↑Tx	5.1	213 (75)	0/213 (0)	0/286 (0)
Restuccia (2016)	Italy	Retro	TAB (+)	157	157 (100)	123 (78)	74	87	TVL 17 (11) PVL 28 (18)	Sx + ↑APR + ↑Tx	6.7	57 (37)	1/57 (2)	1/157 (0.6)
Hocevar (2016)	Slovenia	Pro/Obs	1990 ACR or TAB(+) ± U/s	68	45 (66)	49 (72)	73.2	82	TVL 3 (4) PVL 4 (6)	Sx	2	31 (46)	1/31 (3)	1/68 (1.4)
Langford (2017)	USA and Canada	RCT	Modified ACR	41	25 (61)	37 (90)	66	ND	PVL 2 (5)	Sx + ↑ ESR	1.2	24 (59)	1/24 (4)	2/41 (5)*
Stone (2017)	Multiple	RCT	Modified ACR	251	156 (62)	188 (75)	69.5	25	VL 25 (10)	Sx and/or ↑ESR	1	95 (38)	2/95 (2)	2/251 (0.8)
Conway (2018)	Ireland	Pro/Open Drug	1990 ACR and/or TAB or LVV imaging	25	19 (76)	20 (80)	70	29	ND	Sx ± ↑APR	1	0/25	0	0/25 (0)
De Boysson (2018)	France	Retro	TAB(+) and/or LVV imaging	61	47 (77)	45 (74)	72	102	ND	Sx and/or ↑APR +↑Tx	4.2	31 (51)	1/31 (3)	1/61 (1.6)
Leon (2018)	Spain	Retro	1990 ACR	168	77 (46)	135 (80)	76	83	VI 26 (15)	Sx + ↑ESR + ↑Tx	4	52 (31)	1/52 (2)	1/168 (0.6)
Samson (2018)	France	Pro/Open Drug	1990 ACR	20	17 (85)	15 (75)	72	82.5	PVL 2 (10)	Sx and/or ↑APR	1	10 (50)	1/10 (10)	1/20 (5)
Matsumoto (2019)	Japan	Retro	1990 ACR	30	20 (67)	14 (47)	72.4	120	TVL 4 (13) PVL 1 (3)	Sx + ↑APR + ↑Tx	2	8 (27)	0/8 (0)	0/30 (0)
Berger (2019)	Switzerland	Pro/Open Drug	ACR or LVV imaging	22	12 (52)	12 (59)	70	78	TVL 4 (18) PVL 4 (18)	Sx or ↑APR + ↑Tx	0.9	12 (55)	0/12 (0)	0/22 (0)
Adler† (2019)	Switzerland	Pro/Obs	1990 ACR	17	11 (65)	13 (76)	70	ND	ND	Sx+↑APR	2.3	8 (47)	0/8 (0)	0/17 (0)

ACR, American College Rheumatology; APR, acute phase reactants (ESR/CRP); Dx, diagnosis; GCA, giant cell arteritis; ND, not defined; PVL, permanent vision loss; Sx, symptoms; TAB, temporal artery biopsy; TVL, transient vision loss (includes amarousis fugax, double vision); UK, United Kingdom, USA, United States of America; VI (visual ischemia). *Graham 1982, total cohort 90 but relapse calculated based on patients alive at end of follow up period; **Langford 2017, 1 patient had VL as relapse during study and 1 additional patient in post-treatment follow-up after study completion; †Initial RCT data not included as VI data not available

mary authors were directly contacted for patient-level data regarding VI and these studies were included in the final analysis if such data were available and provided.

Results: A total of 913 unique articles were identified and underwent screening (K.B. and M.J.K). Among these, 148 articles underwent independent full-text review by two physicians (K.B. and M.J.K). 33 articles met full inclusion criteria and an additional 21 articles included data on relapse but did not report VI patient data in the publication. Responses were received from authors of 11 of these 21 studies allowing for inclusion. 44 studies accounting for 3,649 patients with GCA were identified (Table 1). Average percentage of baseline VI was 19% (range 0-66%). The average length of follow-up was 3.4 years (range 0.4 to 8.7). VI developing > 4 weeks after GCA diagnosis was recorded in a total of 53 patients (1.5%).

Study-defined relapses were reported in 36 studies. A total of 1,215 patients with at least one or more relapses were recorded among 2,592 patients under observation (47%). Among these 36 studies, VI occurred in 37 patients (3.0%) with at least one study defined relapse event.

Comparing trial design, retrospective studies (n=25) reported 27 of 2,718 (1%) patients developed VI during follow-up whereas 19 of 541 (3.5%) patients in randomized controlled trials (n=8) developed VI during the trial or post-trial follow-up (Table 2).

Table 2: Randomized clinical trial design and reported visual ischemia outcomes

Author (Year)	Drug under study	Trial arms: (# patients)	Prednisone taper	Visual ischemia
Jover 2001	Methotrexate 10 mg/wk	SD: N=20 PBO: N=19	20 mg TID x 1wk, 60 mg/d x 1wk; ↓ 10 mg/wk to 40 mg; then down by 5 mg/wk to 20mg; then down by 2.5 mg/wk until off	SD: None PBO: None
Spiera 2001	Methotrexate 7.5 mg / wk	SD: N=12 PBO: N=9	Suggested (not-required) taper: 1mg/kg/day then ↓ 10mg/wk to 40mg/d then ↓ 5mg/wk to 20mg then ↓2.5 mg/wk until off	SD: None PBO: None
Hoffman (2002)	Methotrexate 0.15 mg/kg/wk rounded to nearest 2.5 mg dose	SD: N=51 PBO: N=47	1mg/kg/day (max 60) x 4wks, then ↓ 5mg every 4 days according to an alternate-day schedule [target 60mg every other day at 3 months] then ↓5mg/wk until off [total target duration 6 months]	SD: 4 patients PBO: 4 patients
Mazlumzadeh (2006)	Intravenous methylprednisolone 1000mg daily x 3 days	SD: N=14 PBO: N=13	40mg/d x2wks, 30mg/d x2wks, 25mg/d x2wks, 20mg/d x2wks, 17.5mg/d x2wks, 15mg/d x2wks, 12.5mg/d x2wks, 10mg/d x2wks, then ↓1mg every 2wks to off	SD: None PBO: None
Hoffman (2007)	Infliximab 5mg/kg week 0, 2, 6 then Q8wks	SD: N=28 PBO: N=16	Standardized taper: ↓10mg each wk to 20mg/d then ↓2.5mg every 2wks, to 10mg then ↓ 1mg every week until off	SD: 6 patients PBO: 1 patient
Martinez-Taboada (2008)	Etanercept 25 mg SubQ twice weekly	SD: N=8 PBO: N=9	↓10mg/wk to 30mg/d, then ↓5mg/wk to 15 mg/d; then ↓ 2.5mg/wk until off	SD: None PBO: None
Langford (2017)	Abatacept 10mg/kg every 4 wks	SD: N=22 PBO: N=21	Initial dose 40-60 mg with standard taper to week 12 (20mg/d), following which tapered off by week 28	SD: 2 patients* PBO: None
Stone (2017)	Tocilizumab (TCZ) 162mg SubQ weekly 162mg SubQ every other week	SD1: TCZ QW N=100 SD2: TCZ QOW N=50 PBO1: 26wk pred N=50 PBO2: 52wk pred N=51	Baseline prednisone 20-60mg/d, then tapered to off by Wk 26	SD1: None SD2: 1 patient (A-AION) PBO1: 1 patient (AF) PBO2: None
A-AION, arteritic anterior ischemic optic neuropathy; AF, amaurosis fugax; PBO, placebo arm; SD, study drug arm; SubQ, subcutaneous; QW, every week; QOW, every other week; *Langford 2017 – 1 patient with VI during treatment portion, 1 patient in post-treatment follow-up				

Conclusion: This report outlines the first systematic review evaluating VI as a manifestation of relapse and during follow-up in GCA. Overall, VI > 4 weeks after GCA diagnosis is uncommon (1.5%) but is noted in up to 3% of patients with at least one relapse event. Frequencies of reported VI were 3.5 times higher in randomized controlled trials compared to retrospective studies.

Disclosure: K. Bugdayli, None; **P. Ungprasert**, None; **K. Warrington**, Lilly, 2, Kiniksa, 2; **M. Koster**, None.

Abstract Number: 1930

Thirty-Day Readmission Rate in Patients Who Were Initially Admitted for Active Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is a large vessel vasculitis with high potential for morbidity leading to frequent hospitalizations and significant economic burden to the healthcare system. The goal of this study is to use

Table 1. Most common principal diagnoses on readmissions

Diagnosis	Patients readmitted
Giant Cell Arteritis	52
Acute Kidney Failure	33
Sepsis, unspecified organism	30
Paroxysmal Atrial Fibrillation	18
Type 2 Diabetes Mellitus with Hyperglycemia	14
Headache	13
Pneumonia, unspecified organism	10
Cerebral Infarction, unspecified	10
Syncope and Collapse	9
Gastrointestinal Hemorrhage, unspecified	9

Nationwide Readmissions Database (NRD) to determine the 30-day readmission rate of patients that were initially admitted for active GCA, to identify the reasons and predictors for readmission.

Methods: This is a retrospective cohort study using the NRD from 2016 and 2017. The International Classification of Diseases, Tenth Revision, Clinical Modification (ICD-10-CM) was used to identify diagnoses. The primary outcome was rate of all-cause readmission within 30 days of discharge for all patients with principle diagnoses of GCA on index admission. Secondary outcomes were principle diagnoses for readmission, predictive factors and resource use. We compared baseline demographics and calculated all-cause 30-day readmission rates in patients who survived their index hospitalization. Proportions were compared using the Fisher exact test, and continuous variables were compared using the Student t-test. Logistic regressions were used for binary outcomes and linear regressions were used for continuous outcomes. Multivariate logistic regression was conducted using Stata, version 16.0 to determine the predictors for readmission. All p-values were two-sided, with 0.05 as the threshold for statistical significance.

Results: There were 4,841 patients admitted for active GCA flares in the NRD from 2016 to 2017, of which 68.7% were female. The mean age was 72.4±11.9 years. The all cause 30-day readmission rate was 13.1%. The 30-day mortality rate was 0.7%. The five most common reasons for readmissions were GCA, acute kidney failure, sepsis, paroxysmal atrial fibrillation, type 2 diabetes mellitus with hyperglycemia. The adjusted odds ratios (aOR) and p-values were calculated and independent predictors of GCA readmission were identified: Coexisting heart failure (aOR 1.63, 95% CI 1.14- 2.34, p= 0.007) and higher Charlson comorbidity score (aOR 1.16, 95% CI 1.08- 1.23, p< 0.001). Discharge from teaching hospitals was associated with lower odds of being readmitted (aOR 0.72, 95% CI 0.55-0.95, p=0.019). The total hospital days associated with readmission were 3,894 days, with a total healthcare cost of $8.54 million.

Conclusion: This study showed 13.1% of the patients who were initially admitted for active GCA were readmitted within 30 days, creating a significant economic burden. Patients with coexisting heart failure and higher Charlson comorbidity core were significantly more likely to be readmitted.

We should be more cognizant of the poor outcomes and high disease burden of active GCA and its treatment complications which may lead to unnecessary readmission including infection, hyperglycemia and renal failure. More study on preventing GCA readmission is warranted.

Disclosure: S. Cao, None; **C. Bresnan**, None; **S. Li**, None; **Y. Wang**, None; **Y. Lin**, None.

Abstract Number: 1931

Effect of Cumulative Glucocorticoid Dose and Inflammation on Weight Change During Treatment of Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is a form of large vessel vasculitis that requires treatment with high-dose, long-term glucocorticoids (GC). Weight gain, among other side-effects of GC therapy, is a major concern for patients and is associated with increased morbidity and mortality. Prior studies have shown varying results regarding the independent association of GC dose and weight gain. Weight changes in GCA patients being treated with GC or in GCA patients receiving tocilizumab are poorly understood.

Methods: We analyzed GCA patients enrolled in the GiACTA (Tocilizumab in Giant Cell Arteritis) trial. Cumulative GC dose and weight were obtained at weeks 0, 12, 24, and 52. We used multivariable mixed-effects modeling to examine the effects of age, gender, cumulative GC dose, baseline GC exposure, disease status (newly-diagnosed versus relapsing), randomization to tocilizumab, and flares over 52 weeks on changes in weight. We used Student's unpaired t-test to evaluate weight change from 0 to 52 weeks and the Wilcoxon rank test to evaluate the cumulative prednisone from 0 to 52 weeks.

Results: 250 patients were included; 187 (75%) were female and the mean age ± SD was 69 ± 8 years. The mean baseline weight ± SD was 70.8 ± 14.9 kg, and the mean ± SD weight gain among all subjects was 3.2 ± 5.4 kg. Cumulative prednisone dose at 52 weeks was associated with weight change over this time (0.63kg per 1000mg of prednisone; p< 0.001) (**Table 1**). Furthermore, relapsing disease at baseline and flares over 52 weeks were significant-

Table 1. Multivariable mixed-effects modeling evaluating weight change (kg) according to glucocorticoid exposure

Variable	Estimate	p-value
Cumulative prednisone exposure during weeks 0-52 (/1,000mg)	0.63	< 0.001
Relapsing disease	-1.15	0.002
Randomized to tocilizumab	0.37	0.33
Baseline weight (/kg)	0.98	< 0.001
Male	-0.30	0.52
Age (/year)	-0.02	0.32
Baseline prednisone greater than 30mg daily	-0.08	0.83
Flares (/flare)	-0.39	0.04

Table 1. Multivariable mixed-effects modeling evaluating weight change (kg) according to glucocorticoid exposure

Table 2. Cumulative prednisone exposure and weight change per treatment group, stratified by primary endpoint of sustained, glucocorticoid-free remission at 52 weeks

	Tocilizumab groups			Prednisone groups		
	Did not meet primary endpoint (n=68)	Met primary endpoint (n=81)	p-value	Did not meet primary endpoint (n=85)	Met primary endpoint (n=16)	p-value
Cumulative prednisone over 52 weeks, mg, median (IQR)	3017.3 (2527.8, 4180.8)	1356.0 (952.0, 1604.5)	<0.0001	4284.8 (2813.8, 5818.0)	2150.8 (1862.0, 2397.5)	<0.0001
Weight change from 0-52 weeks, kg, mean (sd)	4.0 (5.2)	3.0 (5.0)	0.31	2.8 (6.2)	3.7 (4.1)	0.59

IQR: interquartile range

Table 2. Cumulative prednisone exposure and weight change per treatment group, stratified by primary endpoint of sustained, glucocorticoid-free remission at 52 weeks

ly associated with less weight gain. Among patients who received tocilizumab, those who met the primary endpoint of sustained, glucocorticoid-free remission at 52 weeks received less prednisone than did those who failed (median 1356 vs. 3017mg; p< 0.0001), but these subgroups experienced similar changes in weight (mean 3.0 vs. 4.0kg; p=0.31) (**Table 2**). Among patients who received prednisone alone, those who met the primary endpoint received less prednisone (median 2150 vs. 4284mg; p< 0.0001), yet those patients experienced numerically higher gains in weight compared with those who did not meet the primary endpoint (mean 3.7 vs. 2.8kg; p=0.59).

Conclusion: GC use and weight gain are linked tightly in the minds of providers and patients, but the relationship is actually complex. We found that cumulative GC exposure over 52 weeks is significantly associated with weight gain. However, the degree to which disease activity is controlled also contributes to weight gain, and modest weight gain may be an indicator of effective disease control. Additional research is required to better elucidate this relationship and to understand other determinants of excessive weight gain in this patient population.

Disclosure: N. Serling-Boyd, None; **X. Fu**, None; **Y. Zhang**, None; **S. Unizony**, Genentech, 2, Janssen, 2, 5, Sanofi, 5, Kiniksa, 5; **Z. Wallace**, Bristol-Myers Squibb, 2; **H. Choi**, AstraZeneca, 2, Takeda, 5, Selecta, 5, GlaxoSmithKline, 5, Horizon, 5; **J. Stone**, Roche, 2, 5, Genentech, 2, 5.

Abstract Number: 1932

Giant Cell Arteritis – the Relationship Between the Extensiveness of Vasculitis and the Clinical Presentation

Alojzija Hocevar[1], Rok Jese[1], Matija Tomsic[1] and Ziga Rotar[1], [1]University Medical Center Ljubljana, LJUBLJANA, Slovenia

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Recent data show that the extensiveness of inflammation observed on colour Doppler ultrasonography (CDS) may indicate the risk for ocular ischaemia giant cell arteritis (GCA) patients. [1]

The aim of our prospective study was to evaluate potential correlation between the clinical presentation of GCA and the extensiveness of vascular involvement assessed by CDS in preselected cranial and aortic arch arteries.

Methods: We performed CDS in incipient GCA patients between October 2013 and May 2020, using a Philips IU22 with 5–17.5 MHz linear probe or Philips Epiq 7 with 5–18.5 MHz linear probe. A total of 14 arteries were examined: bilateral temporal (main, frontal and parietal branch were considered as one vessel territory), facial, occipital, thyroid, carotid, vertebral, subclavian, and axillary arteries. A halo with positive compression sign was considered a positive finding. We explored correlations were explored between GCA clinical features and the number of involved vessels using Spearman test.

Results: During the 80-month observation period we diagnosed GCA in 267 patients (66.3% females, median (IQR) age 74.9 (67.0–80.4) years), median (IQR) symptom duration time 30 (21; 60) days). The CDS was positive in 263/267 (98.5%) patients in at least one of the examined arteries (range from 1 to 12). Table 1 shows the number of patients by number of involved vessels.

We observed a very weak positive correlation between symptom duration and the number of affected vessels (0.14 (95%CI 0.02; 0.25), p=0.024), and very weak inverse correlation between headache and the number of affected vessels (-0.14 (95%CI -0.24;-0.02), p=0.023). There was no significant correlation between patient age, sex, the presence of constitutional symptoms, polymyalgia rheumatica, vision manifestations (including severe manifestations), jaw claudication, ESR, CRP, haemoglobin level, platelet count, and the extensiveness of vascular involvement in GCA.

Conclusion: In our incipient GCA cohort, we found no strong correlation between the extent of vascular involvement, assessed by CDS of cranial and aortic arch arteries, and clinical symptoms, but there was a trend for patients with longer symptom duration to have more extensive vessel involvement.

No. of vessels	No. of GCA	No. of vessels	No. of GCA
0	4 (1.5%)	8	8 (3.0%)
1	26 (9.7%)	9	5 (1.9%)
2	51 (19.1%)	10	3 (1.1%)
3	29 (10.9%)	11	-
4	61 (22.8%)	12	2 (0.7)
5	32 (12.0%)	13	-
6	36 (13.5%)	14	-
7	10 (3.7%)		

Table 1. Patients by the number of vessels involved on CDS examination

Reference

1. van der Geest KSM, et al. ARD 2020;79:393–9. https://doi.org/10.1136/annrheumdis-2019-216343.

Disclosure: A. Hocevar, None; **R. Jese**, None; **M. Tomsic**, None; **Z. Rotar**, None.

Abstract Number: 1933

Small Vessel Vasculitis Surrounding a Preserved Temporal Artery: Search for Tissue Biomarkers with Potential Diagnostic Value

Georgina Espígol-Frigolé[1], Roser Alba-Rovira[2], Salvador Naranjo-Suárez[3], Magda Terenas[4], Sergio Prieto-González[1], Marc Corbera-Bellalta[3], Javier Marco-Hernández[4], Marco A. Alba[1], Farah Kamberovic[3], Roberto Ríos-Garcés[1], Jose Hernández-Rodríguez[1] and Maria C. Cid[1], [1]Vasculitis Research Unit, Department of Systemic Autoimmune Diseases, Hospital Clínic de Barcelona, IDIBAPS, University of Barcelona, Barcelona, Spain., Barcelona, Catalonia, Spain, [2]Vasculitis Research Unit, Department of Autoimmune Diseases, Hospital Clínic, University of Barcelona, IRB-CELLEX. Institut d'Investigacions Biomèdiques August Pi Sunyer (IDIBAPS), Barcelona, Spain, Barcelona, [3]IDIBAPS, Barcelona, Spain, [4]Hospital Clinic Barcelona, Barcelona, Spain

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Systemic vasculitides are complex and heterogeneous diseases with overlapping features that frequently pose a diagnostic challenge to clinicians. The temporal artery biopsy (TAB) is the gold standard for the diagnosis of giant cell arteritis (GCA) with cranial involvement. Occasionally, the TAB shows small vessel vasculitis (SVV) surrounding a normal temporal artery as the only pathological finding. Ultimate diagnosis and, consequently, optimal treatment remain uncertain in these patients.

The aim of this project is to characterize biomarkers with diagnostic potential in TAB disclosing SVV surrounding a spared temporal artery.

Methods: 51 Patients with TAB showing SVV surrounding a normal temporal artery were subjected to a pre-established diagnostic algorithm combining clinical, imaging and serological data (Fig 1). The algorithm led to the following classification: 19 GCA; 20 systemic vasculitis (ANCA-associated vasculitis (AAV) and other vasculitis); and 12 could not be classified. TAB samples from 15 SVV patients (8 classified as GCA[SVV-GCA] and 7 systemic vasculitis [SVV-SV]: 4 AAV and 3 other vasculitis) and 16 controls with negative temporal artery biopsies, were used for RNA isolation and microarray hybridization (Human Clariom S, Affymetrix). Genes differentially expressed were identified by a multivariate permutation t test using the BRB ArrayTools 4.6 software package (Biometric Research Branch, NCI). We set parameters in the univariate 2-sample t test permutation with a random variance model. Permutation P values for significant genes ($P < 0.001$) were computed based on 10,000 random permutations that result in an estimated false discovery rate below 1%.

Results: We compared gene expression in normal temporal arteries and the different subgroups of SVV. The expression level of 42 genes was found to be significantly different between normal arteries and SVV-GCA, whereas the expression level of 65 genes was significantly different between normal arteries and SVV-SV. Interestingly, an unsupervised hierarchical clustering based on this subset of 107 genes was able to cluster subgroups of SVV: SVV-GCA and SVV-SV (Fig 2). In addition, a hierarchical clustering analysis yielded a subset of 8 genes with significant different

Fig 1 51 patients with TAB showing SVV surrounding a normal temporal artery were subjected to the following algorithm.

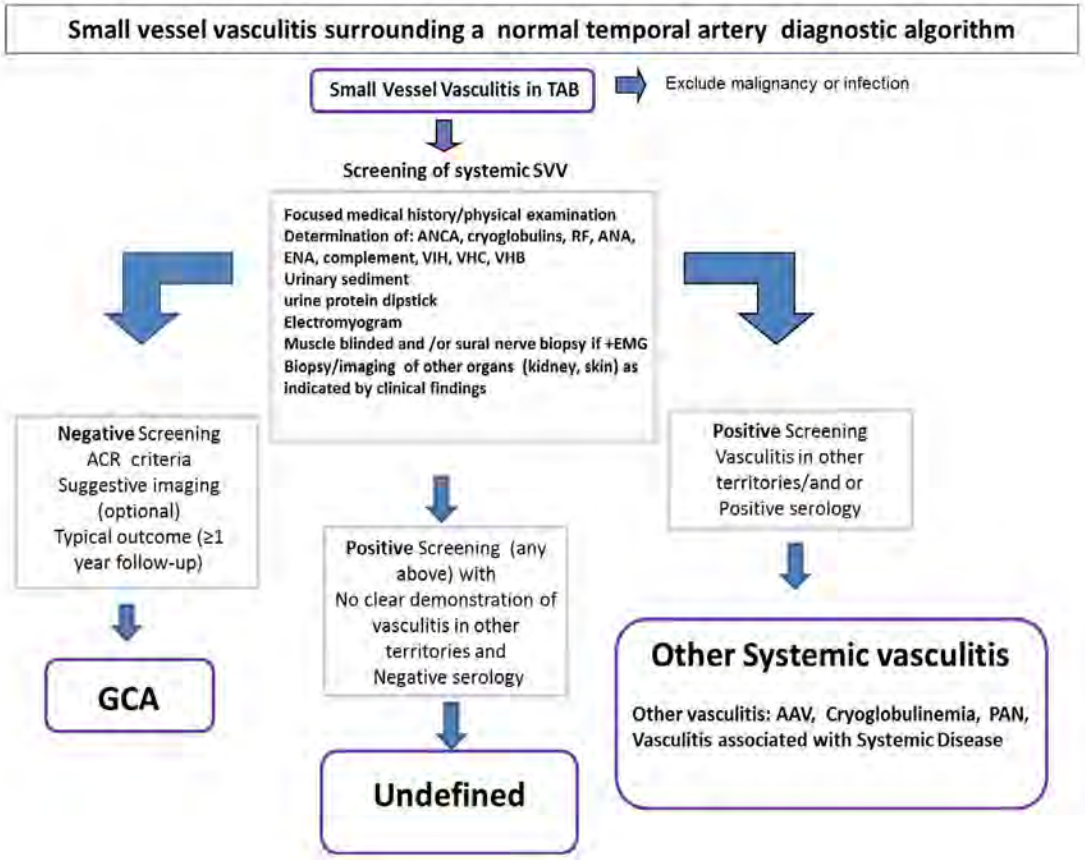


Fig 2 An unsupervised clustering annalysis based on 107 genes with different expression level between Controls and SVV, identified two major clusters of SVV: SVV-GCA and SVV-SV

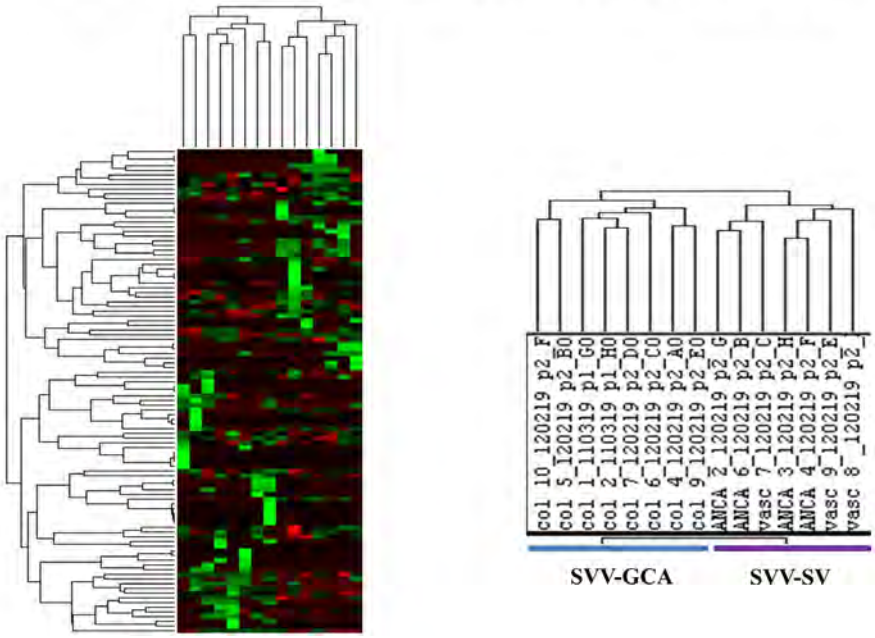
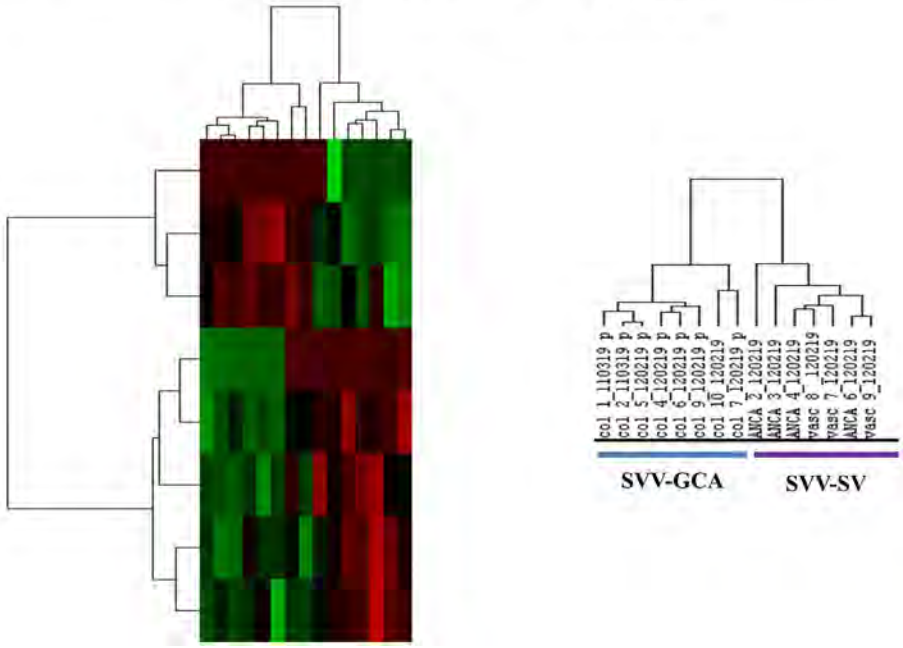


Fig 3 A hierarchical clustering analysis yielded a subset of 8 genes with significant different expression between SVV-GCA and SVV-SV



expression between SVV-GCA and SVV-SV (Fig 3). Sub-analysis between SVV-GCA and SVV-AAV and SVV-GCA and SVV-other vasculitis, showed significant differences in expression level of 17 and 23 genes respectively.

Conclusion: SVV surrounding a spared TA is a relevant but equivocal finding. After a detailed diagnostic work-up most patients can be diagnosed with GCA or other systemic vasculitis although diagnosis remains uncertain in some cases. Cluster analysis of the gene expression profile differentiates diagnostic subgroups of SVV. Further studies are needed to validate differentially expressed genes.

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Abstract Number: 1934

What Is the Significance of Periarterial Temporal Small Vessel Inflammation (SVI) on Temporal Artery Biopsy (TAB) in the Diagnosis of Vasculitis? A Systematic Review and Meta-analysis

Elise Belilos[1], Steven Carsons[2] and **Sonya Mehta**[1], [1]NYU Winthrop Hospital, Mineola, NY, [2]NYU Long Island School of Medicine, Mineola, NY

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Isolated inflammation of small vessels including capillaries, venules and arterioles surrounding a normal temporal artery (SVI) in patients suspected of having giant cell arteritis (GCA) has been described in the literature. However, the significance of this finding remains controversial. Authors have described SVI as highly suggestive of vasculitis while others consider it to be a non-specific finding associated with aging, infection and malignant disease. We performed a systematic review of the literature in order to characterize the diagnoses, clinical, and laboratory manifestations of patients with periarterial temporal small vessel inflammation as a sole finding on TAB

Methods: A search of the English language literature from 1990-2019 was performed using the following search terms: temporal artery, giant cell arteritis, vasculitis, small vessel, inflammation, vasa vasorum, and periarteritis. Data was extracted for cases that displayed isolated inflammation of small blood vessels external to a spared temporal artery on TAB. Clinical diagnosis, clinical and laboratory manifestations and treatment were recorded and included age, sex, presence of headache, polymyalgia rheumatica (PMR), temporal artery (TA) abnormality, fever, visual symptoms, and corticosteroid therapy. Data was extracted from individual studies and pooled odds ratios were calculated.

Results: Eleven studies were identified that provided data on 324 TAB demonstrating inflammation of small blood vessels external to the temporal artery. One hundred and fifteen (35.5%) were classified as definite or probable GCA and 80 of these (69.6%) had PMR symptoms. Fifty (15.4%) had isolated PMR. Twenty (6.2%), especially those having neutrophilic infiltrates had other forms of vasculitis. The remainder (42.9%) had other illnesses including infection, malignancy or undiagnosed conditions. Five studies reported clinical data on patients with SVI classified as GCA. The mean age was 73.2 years, 65.8% were male, 43.8% had headache, 9.8% had jaw claudication 23.7% had abnormal TA, 22.3% had fever and 30.5% had visual symptoms. Corticosteroid (CS) was administered to 79.4% (range- 39-100); 79% (range 59.6-100) responded. When SVI was compared to classical GCA, three studies reported significantly fewer SVI patients with jaw claudication whereas 2 studies reported a significant increase in PMR in SVI. Meta-analysis of 4 studies reporting jaw claudication and PMR revealed a significant increase of PMR in SVI (pooled OR 5.92; CI 3.32-10.55; P< 0.001) and less jaw claudication in SVI (pooled OR 0.248; CI 0.13-0.50; P< 0.0001).

Conclusion: Inflammation of capillaries, venules and arterioles surrounding a normal temporal artery on TAB in patients suspected of having giant cell arteritis (GCA) should not be ignored. While the clinical phenotype differs from classical GCA, the high prevalence of PMR, and response to CS suggests that this finding is associated with the PMR-GCA spectrum in a significant proportion of patients.

Disclosure: E. Belilos, None; **S. Carsons**, None; **S. Mehta**, None.

Abstract Number: 1935

Predictors of Early Mortality for Giant Cell Arteritis at the Time of Diagnosis

Eduardo Dourado[1], Sofia Barreira[2], Ana Rita Cruz-Machado[3], Joana Martinho[3], Diana Raimundo[4], Luísa Brites[5], Helena Assunção[5], Vítor Teixeira[6], Nikita Khmelinskii[3], Carla Macieira[3], José A. P. da Silva[7], João Eurico Fonseca[8] and Cristina Ponte[3], [1]Rheumatology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Lisboa, Portugal, [2]Rheumatology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisbon, Portugal, [3]Rheumatology Department, Hospital de Santa Maria, Centro Hospitalar Universitário Lisboa Norte, Lisboa, Portugal, [4]Faculdade de Medicina da Universidade de Lisboa, Lisboa, Portugal, [5]Rheumatology Department, Centro Hospitalar Universitário Coimbra, Coimbra, Portugal, [6]Rheumatology Department, Centro Hospitalar Universitário do Algarve, Faro, Portugal, [7]9.Centro Hospitalar e Universitário Coimbra (Rheumatology Department), Coimbra, Portugal, Coimbra, Portugal, [8]Instituto de Medicina Molecular, Faculdade Medicina Universidade de Lisboa and Centro Hospitalar Universitário Lisboa Norte., Lisboa, Portugal

SESSION INFORMATION
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Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
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Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is the most common form of primary systemic vasculitis, typically affecting patients aged > 50 years. If left untreated, GCA can lead to permanent visual loss and other ischaemic complications. During the first two years of diagnosis, mortality is significantly higher in GCA than in the general population, with a significant contribution of infections to mortality in the first year of treatment. Identifying patients with a higher risk of mortality at the time of diagnosis could be crucial for prevention and tailored treatment; however, independent predictors of early mortality have never been reported in the literature.

Methods: Bicentric observational study using data from the Portuguese Register of Rheumatic Diseases (Reuma.pt). Patients with biopsy- or ultrasound-proven GCA were included. Early mortality was defined as death occurring in the first two years after diagnosis. Univariate analysis was performed using Chi-Square, Fischer's Exact Test and Mann-Whitney Test, as appropriate. Multivariate analysis was

performed using binary logistic regression modelling. The linearity of the continuous variables with respect to the logit of the dependent variable was assessed via the Box-Tidwell procedure.

Results: The study included 133 patients with 85 (66.4%) females and a median age at diagnosis of 75.0 (interquartile range [IQR] 12.0) years. Fourteen (10.5%) deaths occurred during the first two years after diagnosis. Early mortality was significantly associated with: (i) cranial ischaemic event, anterior ischaemic optic neuropathy, permanent loss of vision and tongue claudication at disease presentation; (ii) older age, atrial fibrillation, chronic kidney disease, creatinine level and treatment with bisphosphonates at diagnosis; and (iii) treatment with anticoagulants before disease onset (Table 1).

The multivariate analysis included 124 patients (5 patients had missing information, 4 patients were outliers) with 81 (65.3%) females, a median age at diagnosis of 75.0 (IQR 12.0) years, and 10 (8.1%) deaths in the first two years of diagnosis. The logistic regression model was statistically significant, $\chi 2$ (7) = 42.0, p< 0.001. The model explained 66.9% (Nagelkerke R2) of the variance in early mortality and correctly classified 96.0% of all cases. Older age at diagnosis (OR 1.3/year, 95%CI: 1.0-1.6, p=0.032), tongue claudication at disease presentation (OR 2106.8, 95%CI: 4.2-1057334.5, p=0.016), previous treatment with anticoagulants (OR 42.1, 95%CI: 2.6-682.0, p=0.009) and treatment with bisphosphonates at diagnosis (OR 0.0, 95%CI: 0.0-0.4, p=0.019) were identified as independent predictors of early mortality and survival, respectively (Table 2).

Conclusion: In our cohort, older age at diagnosis, tongue claudication at disease presentation and previous treatment with anticoagulants were independent predictors of early mortality. On the other hand, treatment with bisphosphonates at diagnosis was an independent predictor of early survival. These findings are novel and require replication. However, they highlight the need for a disease management not only focused on clinical manifestations but also drug adverse effects and comorbidities.

Table 1 - Results of the univariate analysis testing the association between the outcome variable (early mortality) and predictor variables

Variables	Early mortality (n=14)	Early survival (n=119)	p-value
Demographic and anthropometric data at diagnosis			
Age, median (IQR) in years	**83 (10)**	**74 (13)**	**0.001**
Female sex, n/mN (%)	7/14 (50)	81/117 (69)	0.226
Weigh, median (IQR) in kg	58 (13)	61 (13)	0.253
Height, median (IQR) in cm	157 (12)	153 (13)	0.486
Body mass index, median (IQR) in kg/m^2	24 (9)	26 (6)	0.426
Diagnostic delay, median (IQR) in days	38 (99)	34 (110)	0.456
Patient habits at diagnosis, n/mN (%)			
Smoking habits (current or previous smoker)	1/11 (9)	19/95 (20)	0.623
Drinking habits (current or previous drinking habits)	1/12 (8)	12/88 (14)	0.490
Disease manifestations at diagnosis, n/mN (%)			
Large vessel involvement documented by imaging	0/14 (0)	13/104 (13)	0.359
New-onset headache	11/14 (79)	100/117 (85)	0.449
Pain or altered pulse at the temporal arteries	8/11 (73)	59/93 (63)	0.742
Scalp hypersensitivity	2/14 (14)	25/117 (21)	0.733
Jaw claudication	9/14 (64)	50/117 (43)	0.126
Tongue claudication	**3/14 (21)**	**5/117 (4)**	**0.040**
PMR-like symptoms	6/14 (43)	54/117 (46)	0.851
Fever	1/14 (7)	13/117 (11)	1.000
Weigh loss	7/14 (50)	46/117 (39)	0.441
Fatigue	7/14 (59)	54/117 (46)	0.785
Cranial ischaemic event	**11/14 (79)**	**54/117 (46)**	**0.022**
Anterior ischaemic optic neuropathy	**9/14 (64)**	**33/117 (28)**	**0.012**
Central retinal artery thrombosis	1/14 (7)	7/117 (6)	1.000
Permanent loss of vision	**11/14 (79)**	**30/117 (26)**	**<0.001**
Transient loss of vision	0/14 (0)	14/117 (12)	0.361
Diplopia	1/14 (7)	6/117 (5)	0.568
Ischaemic transient attack	1/14 (7)	3/117 (3)	0.367
Cerebral vascular accident	2/14 (14)	7/117 (6)	0.247
Laboratory findings at diagnosis, median (IQR)			
Erythrocyte sedimentation rate, mm/h	85 (51)	82 (43)	0.552
C-reactive protein, mg/dL	4.2 (4.8)	5.0 (6.6)	0.738
Haemoglobin, mg/dL	10.4 (1.8)	11.7 (2.3)	0.080
Leucocyte count, $x10^9$	9.4 (4.3)	9.8 (3.8)	0.739
Creatinine level, mg/dL	**1.1 (0.6)**	**0.8 (0.3)**	**0.002**
Imaging and biopsy findings at diagnosis, n/mN (%)			
Positive temporal artery biopsy	4/6 (67)	37/58 (64)	1.000
Positive ultrasound	13/13 (100)	90/106 (85)	0.211
Comorbidities at diagnosis, n/mN (%)			
At least one comorbidity	14/14 (100)	115/117 (98)	1.000
Obesity	0/10 (0)	20/107 (17)	0.208
Arterial hypertension	11/14 (79)	79/116 (68)	0.548
Hypercholesterolemia	9/14 (64)	43/116 (37)	0.080
Hypertriglyceridemia	1/14 (7)	9/116 (8)	1.000
Hyperuricemia	3/14 (21)	12/115 (10)	0.209
Diabetes mellitus	5/14 (36)	39/116 (34)	1.000
Ischaemic heart disease	2/14 (14)	15/115 (13)	1.000
Cerebrovascular disease	3/14 (21)	14/115 (12)	0.396
Atrial fibrillation	**6/14 (43)**	**9/115 (8)**	**0.002**

Table 1. Results of the univariate analysis testing the association between the outcome variable (early mortality) and predictor variables

Table 2 - Logistic regression predicting the likelihood of early mortality for GCA, based on age, sex, cranial ischaemic event, tongue claudication, chronic kidney disease and treatment with anticoagulants and bisphosphonates (at the time of diagnosis).

Variables							95% CI for OR	
	B	SE	Wald	*df*	*p*	OR	Inferior	Superior
Age at diagnosis	0.257	0.120	4.583	1	**0.032**	1.293	1.022	1.636
Sex	3.155	1.867	2.856	1	0.091	23.456	0.604	910.522
Anticoagulant	3.739	1.422	6.918	1	**0.009**	42.051	2.593	681.981
Bisphosphonate	-5.915	2.518	5.520	1	**0.019**	0.003	0.000	0.375
Cranial ischaemic event	0.286	1.283	0.050	1	0.824	1.331	0.108	16.463
Tongue claudication	7.653	3.173	5.818	1	**0.016**	2106.788	4.198	1057334.541
Chronic kidney disease	0.015	1.121	0.000	1	0.989	1.015	0.113	9.131
Constant	-26.049	11.337	5.279	1	0.022	0.000		

B – coefficients in log-odds units; CI – confidence interval; *df* – degrees of freedom; OR – odds ratio, *p* - Wald 2-tailed p-value; SE – standard errors associated with the coefficients; Wald – Wald chi-square value.

Table 2. Logistic regression predicting the likelihood of early mortality for GCA, based on age, sex, cranial ischaemic event, tongue claudication, chronic kidney disease and treatment with anticoagulants and bisphosphonates (at the time of diagnosis)

Disclosure: E. Dourado, None; **S. Barreira**, None; **A. Cruz-Machado**, None; **J. Martinho**, None; **D. Raimundo**, None; **L. Brites**, None; **H. Assunção**, None; **V. Teixeira**, None; **N. Khmelinskii**, None; **C. Macieira**, None; **J. da Silva**, MyFibromyalgia®, a webcompany delivering services to patients with Fibromyalgia, 9; **J. Fonseca**, None; **C. Ponte**, None.

Abstract Number: 1936

Prospective Analysis of Flow Velocity of the Central Retinal Artery in Newly Diagnosed Patients with Giant Cell Arteritis with Visual Symptoms and Controls

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is the most common form of systemic vasculitis in patients aged 50 years and older.[1] Visual symptoms as amaurosis and temporary or permanent loss of visual field secondary to optic

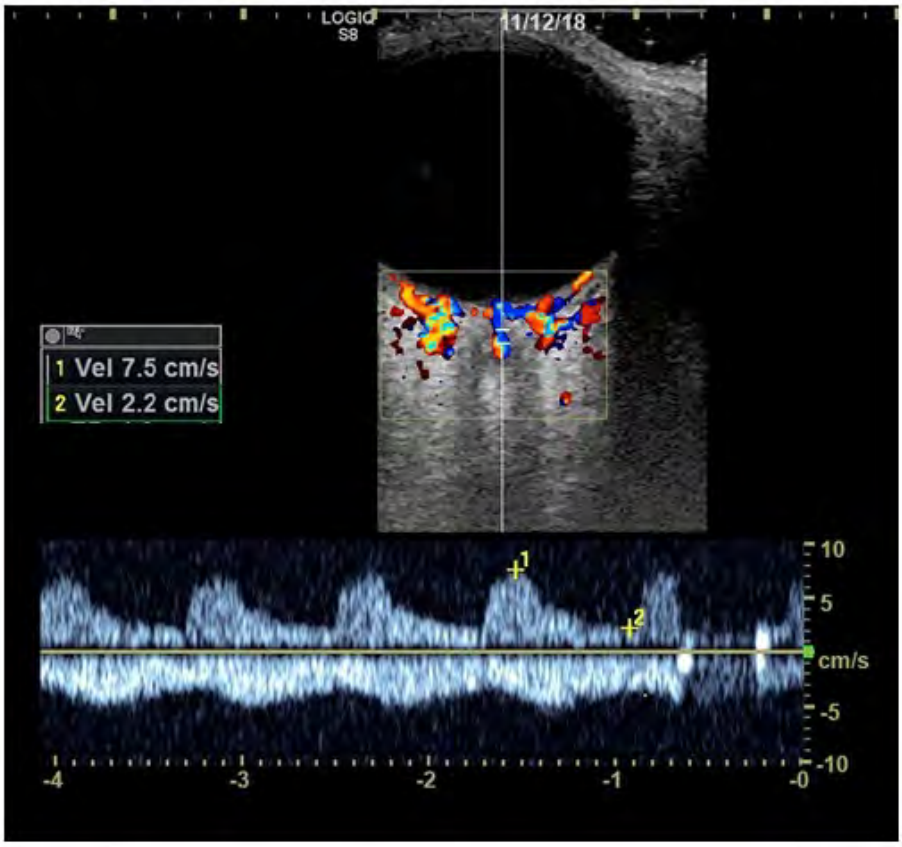

Figure 1. Transocular ultrasound of an affected eye in giant cell arteritis with reduced flow velocities.

nerve ischemia are common manifestations.[2] The role of ultrasound in diagnosis of GCA is known.[3] Transocular ultrasound of the central retinal artery in GCA patients with visual symptoms has not yet been examined.

Methods: Prospective analysis of flow velocities of the central retinal artery in newly diagnosed GCA patients with visual symptoms and eye-healthy controls. Visual symptoms were defined as amaurosis and temporary or permanent loss of visual field. For each eye, peak systolic values (PS) and end-diastolic values (ED) were recorded.

Results: We included 27 newly diagnosed consecutive GCA patients with visual symptoms (GCA-group) and 25 eye-healthy controls. Thirty of 54 eyes (55%) of 27 GCA patients were symptomatic. The control group consisted of 50 central retinal arteries of 25 eye-healthy individuals. Mean age and gender distribution was 75 years (SD± 8.1) with 17 females (63 %) in the GCA group and 67 years (SD± 8.9) with twelve females (48%) in the control group, respectively. Mean flow velocity of the central retinal artery was in 10.9 cm/s (SD± 4.6) in PS and 3.5 cm/s (SD± 1.5) in ED in the GCA group, while values of 14.4 cm/s (SD± 3.2) in PS and 5.1 cm/s (SD± 1.6) in ED were observed in the control group. Mean reduction in flow velocity in the GCA-group was 3.5 cm/s (p-value 0.001) in PS and 1.6 cm/s (p-value 0.000099) in ED, therefore highly significant. Figure 1 shows an ultrasound image of a pathological flow velocity of the central retinal artery in GCA. Figure 2 displays differences in flow velocities between the two groups.

Conclusion: In GCA patients with visual symptoms, a significant reduction of flow velocities of the central retinal artery compared to the eye-healthy control group was observed. Longitudinal data will show, if the flow velocities normalized under treatment.

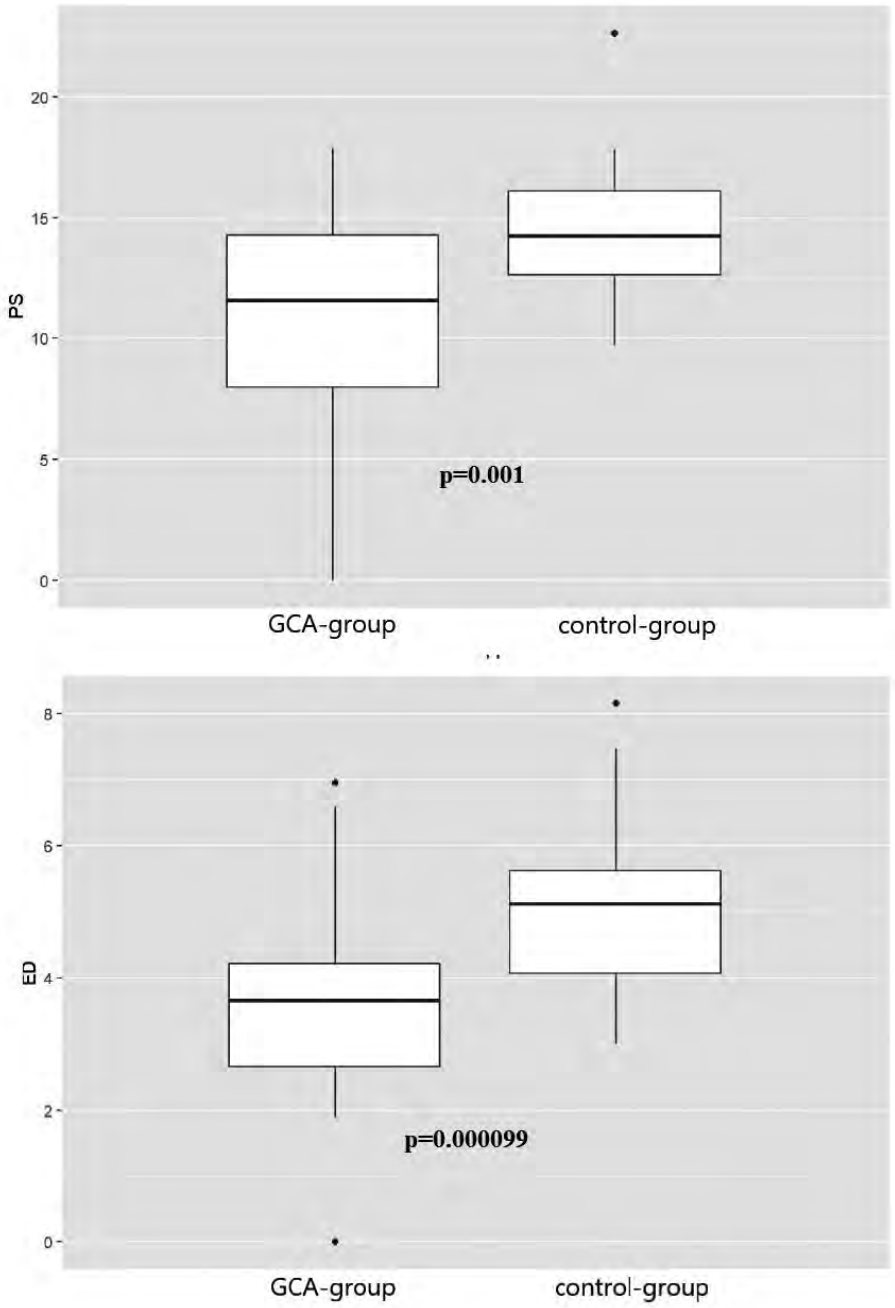

Figure 2. Differences in peak systolic (PS) and end-diastolic (ED) flow between the two groups. GCA-group: Patients with GCA and visual symptoms Control-group: eye-healthy control patients

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Abstract Number: 1937

Aortic Aneurysm in Giant Cell Arteritis: A Nationwide Analysis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is an inflammatory vasculopathy affecting primarily medium and large sized arteries. Previous studies have demonstrated a higher prevalence of aortic aneurysm in patients with GCA. The current study was conducted to better describe the characteristics as well as predictors of aortic aneurysm in patients with GCA in US population using data from a large national database.

Methods: This is a retrospective cross-sectional study using data from National Inpatient Sample (NIS) spanning the period from January 2006 to December 2010. Diagnoses were identified using the International Classification of Diseases, Ninth Revision, Clinical Modification (ICD-9-CM) codes. STATA/MP Version 15 and R 4.0.0 were used for statistical analyses. Categorical variables were calculated using chi-square tests and continuous variables were compared using Student's t-test or Wilcoxon rank-sum test based on the distribution of data. We also performed a multivariate logistic regression analysis to identify the potential risk factors and protective factors of aortic aneurysm in patients with GCA.

Results: We identified 263,384 records with a diagnosis of aortic aneurysm, 21,698 records with a diagnosis of GCA, and 387 records with concurrent GCA and aortic aneurysm. Among patients with aortic aneurysms, those with GCA were more likely to be older (mean age 78.6 vs 74.7, $p < 0.01$), to be female (33% vs 64%, $p < 0.001$), and to develop ruptured aortic aneurysms (9.3% vs 5.8%, $p < 0.01$). Patients with GCA were more likely to have thoracic aortic aneurysms (31.3% vs 16.0%, $p < 0.001$), whereas those without GCA were prone to abdominal aortic aneurysms (62% vs 79%, $p< 0.001$). In patients with thoracic aorta involvement, those with GCA had a longer hospital stay (8.2 vs 7.0 days, $p < 0.01$, Wilcoxon rank-sum test), but the mortality rates between the two groups were similar ($p = 0.8$). The multivariate logistic regression analysis showed that in patients with GCA, the presence of other aneurysms (OR 13.7, 95% CI: 6.1 – 27.3), aortic valve disorders (OR 3.02, 95% CI: 2.22 – 4.02), current or previous tobacco use (OR 2.03, 95% CI: 1.55 – 2.64), and hyperlipidemia (OR 1.29, 95% CI: 1.03 – 1.59) were possibly linked to the development of aortic aneurysm, while female gender (OR 0.65, 95% CI: 0.53 – 0.81) and diabetes mellitus (OR 0.46, 95% CI: 0.35 – 0.61) were potential protective factors.

Conclusion: Consistent with previous studies, GCA is more common in females, and it has a predilection to affect the thoracic aorta. Our study also suggests that GCA could be associated with the rupture of aortic aneurysms. The presence of other aneurysms, aortic valve disorders, tobacco use and hyperlipidemia are possible risk factors for the development of aortic aneurysm in patients with GCA, while female gender and diabetes mellitus are potential protective factors.

Disclosure: J. Zheng, None; **R. Ni**, None; **Y. Tang**, None; **L. Lu**, None.

Abstract Number: 1938

Risk for Vision Loss and Relapse in Patients with Giant Cell Arteritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) involves both the cranial and large vessels. Studies have shown that while the vision loss rates are higher, the relapse rates may be lower in patients with cranial arteritis without large vessel involvement (pure cranial arteritis). However, in many studies, the definition of pure cranial arteritis has not been accurate, as the supraaortic tree has not been thoroughly examined and they are based mainly on retrospectively collected data. This study aimed to investigate the rates of vision loss and relapse in patients with pure cranial GCA in a Norwegian prospective cohort of GCA patients.

Methods: Patients with new-onset GCA referred to the Department of Rheumatology, Martina Hansens Hospital in Bærum, Norway are prospectively included and followed-up. The diagnosis is based on typical for GCA clinical manifestations and ultrasound findings. All the patients are scanned by ultrasound using the anteromedial approach for the supraaortic vessels (carotid, vertebral, subclavian, axillary proximally, and distally) and cranial vessels (temporal, facial) as well. The examination utilizes a General Electric S8 ultrasound machine with a 9-12 MHz linear probe for the large vessels and an 18 MHz hockey stick probe for the cranial arteries and a Canon Aplio 700 with an 11 MHZ and 22 MHz probes for the large and cranial vessels respectively. The age, gender, CRP, Prednisolone dose, distribution of vasculitis in the vessels, vision loss, and relapse rates are recorded and relative risks (RR) are calculated.

Results: Seventy-nine patients, 58 (73%) females, and 21 (27%) males were diagnosed with GCA until May 2020. The mean age was 72 years. Mean CRP was 96 mg/dl (95% CI (63-96)). Of the 79 GCA patients, 20 had involvement of the cranial vessels only (pure cranial CGA), 19 patients have involvement of the large supraaortic vessels only, and 50 of both cranial and large supraaortic vessels. Seven patients suffered from vision loss (9%) and all these patients had a concomitant cranial disease. The GCA patients with pure cranial disease had a RR for visual loss of 1.14 (95% CI (0.3-3.9)) while GCA patients with both cranial and large vessel disease had a RR of 1.35 (95% CI (1.2-1.5)). No patients with pure large vessel GCA suffered from vision loss. The median Prednisolone dose at the first relapse was 10 mg (IQR 8). Of the 20 GCA patients with cranial arteritis, only 3 (4%) relapsed during the study period, while 33 (25 %) patients of the 59 GCA patients with concomitant large supraaortic vessels involvement relapsed. The Relative Risk for relapse in patients with pure cranial arteritis was 0.3 (95%CI 0.1-0.8).

Conclusion: In a prospective cohort of GCA patients, pure cranial disease appears to have a 14 % higher risk of vision loss and a 70% lower risk of relapse. It seems that concomitant large supraaortic vessel involvement does not reduce the risk of vision loss. We continue to recruit GCA patients in our prospective cohort and examine the RR of the vision loss and relapse in larger numbers of patients.

Disclosure: A. Bull Haaversen, None; **A. Diamantopoulos**, Sanofi, 5, Roche, 8.

Abstract Number: 1939

Definitions and Reliability Assessment of Chronic Ultrasound Lesions of the Axillary Artery in Giant Cell Arteritis: A Study from the OMERACT Large Vessel Vasculitis Ultrasound Working Group

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The OMERACT Ultrasound (US) large vessel vasculitis task force has recently defined the US appearance of normal axillary arteries (AA) and the key elementary US lesions in acute giant cell arteritis (GCA) of the AA (i.e.:“non-compressible halo sign”). The aim of the present study was to assess the reliability of a new OMERACT definition for the US appearance of chronic GCA lesions of the AA in a web-based reliability exercise (Table 1)

Methods: The reliability exercise was performed using a REDCap. One-hundred-fifty anonymized still images from AA, were assessed (50 each from chronic and acute GCA, and 50 from healthy individuals). Chronic GCA patients had a disease duration of more than one year and were in remission. Acute GCA patients had new-onset disease with glucocorticoid treatment duration ≤1 week. The members of the OMERACT Large Vessel Vasculitis Ultrasound Working Group (n=23, all ultrasound experts in GCA) were asked to assign all images to the categories of normal, acute GCA or chronic GCA applying the definitions agreed in previous Delphi exercises. In order to assess the intra-observer reliability, all task force members were asked to repeat the reliability exercise in a time range of at least two weeks later and using the same images presented in a different order. Light’s κ were used for evaluating intra- and inter-reader reliability, respectively. κ values of 0–0.2 were considered slight, 0.2–0.4 fair, 0.4–0.6 moderate, 0.6–0.8 substantial and 0.8–1 excellent.

Table 1 – Ultrasound definitions of normal, acute and chronic GCA of the axillary artery

	Definition of US appearance of normal axillary artery	Definition of US appearance of vasculitis- "Halo Sign"	Definition of US appearance of chronic GCA changes
Axillary artery	Pulsating, hardly compressible artery with anechoic lumen; the intima-media complex presents as a homogenous, hypoechoic or anechoic echostructure delineated by two parallel hyperechoic margins ('double line pattern'), which is surrounded by mid-echoic to hyperechoic tissue.	Homogenous, hypoechoic wall thickening, well delineated towards the luminal side, visible both in longitudinal and transverse planes, most commonly concentric in transverse scans.	Mostly homogenous, mid- to hyperechoic long-segmental thickening of the intima-media complex (IMC) > 0.9 mm, displaying several visible lines with loss of the typical double line pattern, well delineated towards the luminal side, visible both in longitudinal and transverse planes, most commonly concentric in transverse scans. Doppler sonography can be of help depicting stenosis, collaterals and occlusion. Atherosclerotic changes may coexist.

Table 2 – Results of the web exercise on still images of acute and chronic GCA of the axillary artery and normal axillary arteries

Section	Inter observer agreement round 1	Inter observer agreement round 2	Intra observer agreement
Normal vessels mean prevalence, %	34.5	34.5	34.5
Vessels with acute changes mean prevalence, %	33.5	31.5	32.4
Vessels with chronic changes mean prevalence, %	31.9	34.0	33.1
Agreement,mean, %	87	86	92
Agreement,range	66-99	63-99	75-99
Light's κ, mean	0.8	0.79	0.88
Light's κ, range	0.5-0.99	0.49-0.98	0.75-0.99

Results: The response rate for both rounds was 100%. The reliability of the new OMERACT definition for the US appearance of chronic GCA of the AA was substantial to excellent with Light's kappa values of 0.79-0.80 for inter-reader reliability and mean Cohen-kappa values of 0.88. The mean inter-rater agreements were 86-87%. The mean intra-reader agreements were 92% (Table 2).

Conclusion: Inter- and intra-observer agreement on the evaluation of US still images from normal, acute and chronic GCA AA was substantial to excellent when applying the new OMERACT definitions for key elementary US lesions in GCA of the AA. Further exercises are planned in order to test the reliability in patients with chronic GCA US changes of the AA.

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Abstract Number: 1940

In Newly Diagnosed Giant Cell Arteritis in a Real Life Setting Relapses Are Seen in More Than a Third of Patients – and Despite Faster Early Reduction High Cumulative Glucocorticoid Doses Are Reached

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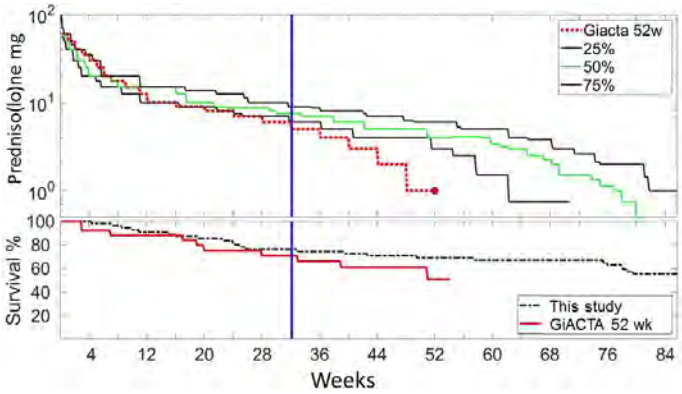
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: To investigate real life glucocorticoid (GC) dosing and relapse rates in patients with new onset giant cell arteritis (GCA) in a single center.

Methods: Complete clinical data taken from the inpatient and outpatient records of consecutive GCA patients followed beyond stopping GC were retrospectively analyzed for GC doses, other immunomodulatory agents and relapses. We excluded patients with incomplete follow-up, in interventional trials and on tocilizumab treatment. All patients consented to anonymous workup of their data, which was approved by the local ethics committee.

Results: 55 patients with GCA (71% female, age 71.4±10.2 (mean±SD) years), diagnosed by biopsy or FDG-PET were included. Of these, 24 (42%) patients relapsed. Methotrexate treatment was not significantly associated with fewer relapses. Of the 31 patients without relapse, one had additional GCs because of another condition. From the prednisolone equivalent data of the remaining 30 patients we calculated 25%, 50% and 75% quartiles. Patients were grouped according to prednisolone start doses of ≤100 mg (standard dose, n=17) and >100 mg (pulse, n=13). In the 25% percentile, patients reached a dose of 15 mg or lower at days 40 (standard) and 49 (pulse), of 7.5 mg prednisolone or lower on day 169 (after 24 weeks) in either arm, and were off prednisolone on days 496 (70 weeks) and 546 (78 weeks) for low dose and high dose start, respectively. Four of the 24 patients with relapses had relapsed after stopping prednisolone clearly (17 to 58 weeks) earlier than the 25% quartile. Of the 20 other patients with relapses, only one was distinctly (>10%) below the 25% glucocorticoid percentile, 13/20 (65%) were on GC doses between the 25% and 75% percentiles. The 50% quartile was largely overlapping the medium recommended doses of the British Society of Rheumatology (BSR) and the GiACTA 52-week GC taper (Stone et al, N Engl J Med 2017), but with shorter time spans on doses of 20 mg and above (Figure). On the other hand, the duration on low doses (< 5 mg q.d.) exceeded those of the minimum dose recommendations of the BSR and of the GiACTA 52-week arm (Figure). The respective cumulative prednisolone doses reached in this real-life cohort were 3.74 g for the 25% quartile and 6.22



Prednisolone doses and survival without flares of this cohort as compared to the GiACTA 52 week arm. 50% (green), 25% and 75% quartile of the GC doses in the standard dose group of this cohort vs the 52 weeks GC only (pacebo) arm with higher starting dose in the GiACTA trial.

g for the 75% quartile in the standard dose, and even higher (6.30 g and 8.98 g, respectively) for those starting with high dose GC pulses.

Conclusion: Despite a long-term GC regimen with slow rates of reduction in the low dose range, 44% of the patients relapsed. Only five of these relapses may have been prevented by adhering to the recommended GC regimen, for a still resulting rate of 35% of relapses. Typical cumulative prednisolone doses were slightly lower than those according to the BSR recommendations, because of a probably safe earlier reduction, but still ranged from 3.74 to 8.98 g. These data suggest that GC monotherapy for GCA may be suboptimal.

Disclosure: L. Felten, None; **N. Leuchten**, Roche, 5, 8; **M. Aringer**, Boehringer Ingelheim, 1, 2, Roche, 1, 2, Bristol Myers Squibb, 1, 2, Chugai, 1, 2, Sanofi, 1, 2, AbbVie, 1, 2, AstraZeneca, 1, 2, Lilly, 1, 2, MSD, 1, 2, Novartis, 1, Pfizer, 1, UCB, 1.

Abstract Number: 1941

Outcome of Giant Cell Arteritis Patients Who Were Primarily Admitted for Venous Thromboembolism Events

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
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Background/Purpose: Giant cell arteritis (GCA) has been shown to have an increased risk of developing deep venous thrombosis (DVT), pulmonary embolism (PE) and combined thromboembolism (VTE) events in many studies. However, the impact of GCA on hospital stay outcomes in these patients with VTE including mortality, length of stay (LOS) and hospitalization cost is unknown. The aim of this study is to assess whether patients with GCA are experiencing more negative outcomes when compared with the general population during their in-hospital stay for VTE events utilizing the National Inpatient Sample (NIS) database.

Table 1. Characteristics of adult patients admitted with VTE

Patient characteristics (%)	Without GCA	With GCA	P value
Female	52.2	81.2	<0.001
Chronic kidney disease	13.2	21.8	<0.001
Hypertension	58.7	70.8	<0.001
Coronary artery disease	17.8	17.3	0.8484
Congestive heart failure	12.7	13.8	0.6244
Diabetes mellitus	23.0	22.3	0.8121
Peripheral vascular disease	4.7	6.9	0.1272
Hyperlipidemia	33.0	42.1	0.0065
Obesity	18.7	13.4	0.0513
Race			0.0607
White	72.1	80.4	
Black	17.9	11.9	
Hispanic	6.3	2.7	
Asian or Pacific Islander	0.9	1.6	
Native American	0.4	0.5	
Other	2.3	2.7	
Charlson Comorbidity Index score			0.1129
0	38.6	30.7	
1	22.4	24.7	
2	15.3	17.3	
3	8.7	12.4	
≥4	15.0	14.8	
Insurance provider			<0.001
Medicare	54.4	91.0	
Medicaid	10.9	0.5	
Private	29.3	8.4	
Other	5.3	0	

Abbreviations: GCA, giant cell arteritis; VTE, venous thromboembolism

Methods: We conducted a retrospective study on the association between GCA and VTE. Adult patients admitted with a principal diagnosis of DVT or PE were included. GCA patients were identified among these patients if they also carry a diagnosis of GCA on admission. We used data from the NIS database between the period of 2012 to 2014. We used the International Classification of Diseases, Ninth Revision, Clinical Modification/Procedure Coding System (ICD-9-CM) to identify co-morbid conditions and in-hospital complications. Multivariate regression analysis via STATA 16.0 was used to examine the association of in-hospital mortality, LOS and cost between GCA and non-GCA patients during their VTE admissions. A p-value of 0.05 was selected as the statistical significance threshold.

Results: We identified 897,180 admissions with VTE, among which 1,010 had GCA. Patients with GCA were older (mean age 78.5 vs. 62.5), more likely to be female (81.2% vs. 52.2%), have Medicare insurance (91.0% vs. 54.4%), chronic kidney disease (21.8% vs. 13.2%), hypertension (70.8% vs. 58.7%) and hyperlipidemia (42.1% vs. 33.0%). After adjustment of possible confounding variables within the patient and hospital level, there was no statistically

significant difference in the in-hospital mortality, LOS, and cost of hospitalization when comparing GCA and non-GCA in VTE admissions (p = 0.752, 0.640, and 0.392, respectively).

Conclusion: GCA patients who were primarily hospitalized for VTE events do not have worse outcomes as compared to non-GCA patients in terms of mortality, LOS or cost of hospitalization. Future research will be warranted to investigate and confirm this finding.

Disclosure: S. Cao, None; **C. Bresnan**, None; **S. Li**, None; **Y. Wang**, None; **Y. Lin**, None.

Abstract Number: 1942

Analysis of Vasculitis Patterns in Patients with Giant Cell Arteritis Compared to Patients with Giant Cell Arteritis and Polymyalgia Rheumatica

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) and polymyalgia rheumatica (PMR) often coexist.[1] The role of modern ultrasound (US) in diagnosis of GCA as well as PMR is well known.[2]

To date it is unknown, whether patients with GCA and PMR have different vasculitis patterns in US examination of the vessels commonly affected than patients with GCA only.

Affected artery	Group					
	PMR-GCA-group (n=27)			GCA-group (n=18)		
	Unilateral	Bilateral	None	Unilateral	Bilateral	none
Axillary artery	9 (33%)	12 (45%)	6 (22%)	5 (28%)	7 (39%)	6 (33%)
Common superficial temporal artery	3 (11%)	21 (78%)	3 (11%)	5 (28%)	13 (72%)	0 (0%)
Frontal branch	6 (22%)	17 (63%)	4 (15%)	3 (17%)	11 (61%)	4 (22%)
Parietal branch	5 (18%)	21 (78%)	1 (4%)	3 (17%)	13 (72%)	2 (11%)
Facial artery	7 (26%)	17 (63%)	3 (11%)	4 (22%)	11 (61%)	3 (17%)

PMR-GCA-group: patients with diagnosis of giant cell arteritis and polymyalgia rheumatica
GCA-group: patients with diagnosis of giant cell arteritis only.

Table 1. Prevalence of vasculitis in patients with giant cell arteritis and polymyalgia rheumatica and patients with giant cell arteritis only.

Methods: Prospective analysis of newly diagnosed consecutive patients with GCA and PMR (GCA/PMR group) as well as GCA only (GCA group), who met ACR and ACR/EULAR criteria for GCA and PMR. US examination was performed of the arteries commonly affected in GCA, such as axillary arteries, vertebral arteries, superficial temporal arteries with both frontal and parietal branches and facial arteries.

Arteries were defined as pathological, if measured intima-media-thickness by US was above published cut-off values.[3]

Results: The GCA-PMR-group consisted of 27 patients, the GCA-group of 18 patients. In the GCA-PMR-group, a total of 206 arteries were affected, while in the GCA-group 131 arteries were affected.

Mean age and gender distribution of the GCA-PMR-group was 74 years (SD± 9) with 10 (37%) females in the GCA-PMR-group, and 76 years (SD± 9) with 10 (55%) females in the GCA-group, respectively. Median values of C-reactive protein (CRP) were 57.2 (IQR 31.7-75.7) in the GCA-group and 48.3 (IQR 17.5- 79.9) in the GCA-PMR-group, respectively. CRP values did not differ significantly between the two groups (p= 0.3577). Mean number of affected arteries per patient was 7.63 in the GCA-PMR-group and 7.28 in the GCA-group. Altogether we did not detect a significant difference in vascular pattern between the two groups. Exact numbers, distribution and IMT-values for all measured arteries are depicted in table 1.

Conclusion: We did not observe a significant difference in vascular patterns between GCA and PMR patients and GCA only patients.

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Disclosure: L. Burg, None; **P. Brossart**, None; **C. Behning**, None; **V. Schaefer**, None.

Abstract Number: 1943

The Prevalence of Anxiety and Depression in Patients with Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is the most common primary vasculitis of the elderly causing blindness if left untreated. However, its hallmark treatment with glucocorticoids (GCs) can lead to significant toxicity including psychiatric manifestations. Few studies have investigated the association between these symptoms and

	Patients (N=72)	Controls (N=288)	p-value
Demographics			
Mean age, years±SD	78.3±7.7	77.4±8.4	*p=0.186*
Female sex, n (%)	52 (72.2)	208 (72.2)	*p=1.000*
Comorbidities, n (%)			
Arterial hypertension	49 (68.0)	171 (60.0)	*p=0.209*
Diabetes mellitus	21 (29.2)	63 (22.2)	*p=0.213*
Hiperuricemia/gout	2 (2.8)	30 (10.8)	***p=0.036***
Neoplasic disease	13 (18.1)	19 (6.6)	***p=0.002***
Thyroid disease	5 (6.9)	28 (9.9)	*p=0.442*
Previous history of mental disease	4 (5.6)	47 (16.4)	***p=0.018***
Anxiety and depression (HADS) scores			
HADS-A, median (IQR)	7 (7)	5 (5)	***p<0.001***
HADS-A ≥8, n (%)	35 (48.6)	76 (26.4)	***p<0.001***
HADS-A ≥ 11, n (%)	22 (30.6)	35 (12.2)	***p<0.001***
HADS-D, median (IQR)	7 (7)	5 (5)	***p=0.013***
HADS-D≥8, n (%)	35 (48.6)	107 (37.2)	*p=0.075*
HADS-D≥11, n (%)	24 (33.3)	52 (18.1)	***p=0.004***

In bold statistically significant differences (p<0.05); HADS – Hospital Anxiety (A) and Depression (D) Scale; IQR – interquartile range; SD – standard deviation.

Table 1. Clinical features of patients with giant cell arteritis and matched controls.

	HADS-A						HADS-D					
	HADS-A <8 (N=37)	HADS-A ≥8 (N=35)	p-value	HADS-A <11 (N=37)	HADS-A≥11 (N=35)	p-value	HADS-D <8 (N=37)	HADS-D ≥8 (N=35)	p-value	HADS-D <11 (N=48)	HADS-D ≥11 (N=24)	p-value
Short-Form 36 components, median (IQR)												
SF-36 Physical function	55.0 (52.5)	25.0 (55.0)	**p=0.003**	55.0 (46.3)	20.0 (51.3)	**p=0.003**	70.0 (50.0)	20.0 (50.0)	**p<0.001**	55.0 (48.8)	10.0 (53.8)	**p<0.001**
SF-36 Role limitation (physical)	50.0 (75.0)	25.0 (50.0)	p=0.103	40.6 (64.1)	9.4 (32.8)	**p=0.018**	50.0 (59.4)	18.8 (31.2)	**p=0.001**	50.0 (62.5)	9.4 (25.0)	**p=0.001**
SF-36 Role limitation (emotional)	58.3 (75.0)	25.0 (66.7)	**p=0.006**	50.0 (75.0)	20.8 (66.7)	**p=0.012**	66.7 (66.7)	25.0 (41.7)	**p<0.001**	58.3 (72.9)	16.7 (25.0)	**p<0.001**
SF-36 Social function	87.5 (50.0)	50.0 (37.5)	**p<0.001**	75.0 (50.0)	37.5 (22.0)	**p<0.001**	87.5 (37.5)	50.0 (25.0)	**p<0.001**	75.0 (50.0)	43.8 (34.4)	**p<0.001**
SF-36 Pain	62.0 (43.0)	31.0 (29.0)	**p<0.001**	51.0 (40.0)	31.0 (42.5)	**p=0.017**	62.0 (43.0)	31.0 (40.0)	**p<0.001**	51.0 (39.0)	26.5 (47.3)	**p=0.006**
SF-36 Vitality	56.3 (42.5)	25.0 (33.8)	**p<0.001**	50.0 (38.8)	18.8 (25.0)	**p<0.001**	56.2 (32.5)	25.0 (27.5)	**p<0.001**	50.0 (38.4)	16.9 (25.0)	**p<0.001**
SF-36 Mental Health	80.0 (26.5)	40.0 (26.4)	**p<0.001**	69.0 (32.6)	30.0 (27.8)	**p<0.001**	76.0 (32.4)	40.0 (32.0)	**p<0.001**	69.0 (35.2)	30.0 (30.2)	**p<0.001**
SF-36 General Heath	50.0 (27.5)	30.0 (20.0)	**p<0.001**	47.5 (25.0)	30.0 (26.3)	**p<0.001**	50.0 (30.0)	30.0 (20.0)	**p<0.001**	45.0 (25.0)	30.0 (23.8)	**p<0.001**

In bold statistically significant differences (p<0.05); HADS – Hospital Anxiety (A) and Depression (D) Scale; IQR –interquartile range; SF-36 – Short Form-36

Table 2. Differences between the values of SF-36 in patients with HADS ≥8 and <8 and HADS ≥ 11 and <11.

GCA, mainly using Short Form 36 (SF-36), a generic patient-reported outcome (PRO) with a mental health component. Hospital Anxiety and Depression Scale (HADS) is a validated PRO to assess depression and anxiety and to the best of our knowledge has never been evaluated in patients with GCA. We aimed to assess the prevalence of anxiety and depression in patients with GCA using HADS and compare its results to SF-36.

Methods: HADS and SF-36 questionnaires were prospectively collected from patients with biopsy- or imaging-proven GCA evaluated from July 2018 to January 2020 in a tertiary centre. An age- and gender-matched control group was retrieved from a population-based dataset - the EpiReumaPT (the largest Portuguese epidemiologic study on rheumatic diseases). HADS-A and -D ≥8 defined possible and HADS-A and -D ≥11 defined probable anxiety and depression, respectively. Univariate analysis was performed using Chi-Square, Mann-Whitney and Fischer's exact tests, as appropriate. Multivariate analysis was performed using binary logistic regression. Association between values of HADS and SF-36 was assessed using Spearman's correlation coefficient.

Results: We included 72 patients diagnosed with GCA, 52 (72.2%) females, with a mean ± SD age of 78.3 ± 7.7 years. The control group consisted of 288 individuals. **Table 1** shows the comparison between groups. Patients with GCA had higher median [IQR] HADS-A than controls (7 [7] vs. 5 [5], p< 0.001), as well as a higher prevalence of HADS-A ≥8 and ≥11 (48.6% vs. 26.4%, p< 0.001; 30.6% vs. 12.2%, p< 0.001; respectively). Patients with GCA had higher median [IQR] HADS-D (7 [7] vs. 5 [5], p=0.013) and prevalence of HADS-D ≥11 (33.3% vs. 18.1%, p=0.004) than controls, but prevalence of HADS-D ≥8 did not differ between groups (48.6% vs. 37.2%, p=0.075). Multivariate analyses adjusted for neoplastic disease, hyperuricemia/gout, GCA and history of mental disease showed that GCA and history of mental disease were independent predictors of HADS-A ≥8 (OR 2.0 95%CI: 1.1-3.5, OR 4.4 95%CI: 2.3-8.7; respectively) and HADS-A ≥11 (OR 3.8 95%CI: 2.0-7.4, OR 2.5 CI95%: 1.1-5.5; respectively), but only GCA was an independent predictor of HADS-D ≥11 (OR 2.6 95%CI: 1.4-4.7). Patients with HADS-A or -D ≥8 or ≥11 had inferior levels of SF-36 in all categories except for physical role limitation in HADS-A ≥8 (Table 2). Moreover, values of

HADS and mental health component of SF-36 showed significant correlation (HADS-A: r=-0.780, HADS-D: r=-0.742; both p< 0.001).

Conclusion: Patients with GCA showed a higher prevalence of anxiety and depression when compared to the general population. HADS appeared to be an efficient screening tool for these psychiatric manifestations in GCA, correlating well with SF-36. Future replication of these results in independent cohorts are warranted; however, they currently raise awareness for the fact that mental health should not be overlooked when managing GCA.

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Abstract Number: 1944

Predictors of Visual Loss and Cerebrovascular Accidents in Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is the most common primary vasculitis in patients (pts) aged over 50 years. It is a medical emergency due to the potential occurrence of severe ischaemic events (SIEs), namely vision loss (VL) and cerebrovascular accidents (CVAs), largely responsible for the high burden of this disease. Identifying patients at a higher risk of developing VL and CVAs is clinically relevant to determine prognosis and tailor treatment.

Methods: Bicentric observational retrospective study using data from the Rheumatic Diseases Portuguese Registry (Reuma.pt). Pts with biopsy or ultrasound-proven GCA were included. VL and CVAs (stroke or transient ischaemic attacks) were considered the SIEs of interest. Clinical features of patients with or without SIEs were compared using Chi-square and Mann-Whitney U tests, as appropriate; multivariate logistic regression was used to identify predictors of SIEs.

Results: A total of 134 pts diagnosed with GCA between 1998 and 2019 were included. Median (IQR) age at diagnosis was 76.4 (70.2-82.4) years and 66% of pts were females. At least one SIE was reported in 65 (48.5%) pts; 8 pts had more than one SIE. A total of 73 SIEs were recorded: 44 cases of ischaemic optic neuropathy (29 anterior, 2 posterior, 13 not specified), 61% with unilateral involvement and 74% leading to permanent visual loss (PVL); 6 cases of central retinal artery occlusion with 100% PVL; 16 ocular events of non-specified cause (6 transient visual

	SIEs (N=65)	Non-SIEs (N=69)	p value
Age at diagnosis	79.2 (73.7-84.4)	74.2 (67.6-78.4)	**<0.001**
Time to diagnosis since first symptoms, days	37 (6-97)	36 (10-120)	0.65
Female sex, n/mN (%)	39/65 (60)	50/69 (72)	0.13
Comorbidities, n/mN (%)			
Hypertension	51/65 (78)	38/69 (55)	**0.005**
Dyslipidaemia	27/65 (42)	18/69 (26)	0.09
Diabetes mellitus	19/65 (29)	13/69 (19)	0.2
Hyperuricemia	6/62 (10)	7/61 (11)	0.75
Ischaemic heart disease	7/62 (11)	7/61 (11)	0.97
Cerebrovascular disease	8/62 (13)	6/61 (10)	0.59
Atrial fibrillation	10/62 (16)	5/61 (8)	0.18
Chronic kidney disease	10/62 (16)	8/61 (13)	0.64
Previous or current smoker	10/50 (20)	10/57 (18)	0.75
Baseline blood tests			
Erythrocyte sedimentation rate, mm/h	84 (65-109)	80 (61-103)	0.48
C-reactive protein, mg/dL	4.8 (3.0-8.6)	4.9 (2.6-9.4)	0.93
Leukocytes, x10^9cels	8.780 (6.810-10.900)	10.070 (7.600-11.600)	0.28
Haemoglobin, g/dL	11.5 (10.4-12.5)	11.9 (10.5-12.9)	0.38
Creatinine, mg/dL	0.9 (0.7-1.1)	0.8 (0.6-1.0)	**0.01**
Clinical features, n/mN (%)			
Constitutional symptoms *	30/65 (46)	38/69 (55)	0.26
Musculoskeletal manifestations	26/64 (41)	45/69 (65)	**0.005**
Arthralgia/myalgia/arthritis	24/64 (38)	39/69 (57)	**0.03**
PMR	21/64 (33)	29/69 (42)	0.27
New-onset headache	54/65 (83)	58/69 (84)	0.7
Jaw claudication	31/64 (48)	16/69 (23)	**0.002**
TA abnormalities on physical examination**	42/52 (81)	26/54 (48)	**0.001**
Medication before diagnosis, n/mN (%)			
Antiplatelet therapy	12/56 (21)	8/53 (15)	0.39
Statins or fibrates	12/54 (22)	3/39 (8)	0.06
Antihypertensive drugs	17/46 (37)	11/47 (23)	0.15

Table 1. Differences between GCA patients with and without severe ischaemic events. SIEs: severe ischaemic events; GCA: Giant cell arteritis; PMR: polymyalgia rheumatica; TA: temporal artery. Continuous variables are expressed as median (IQR). Categorical variables are expressed as n/modified(m)N (total N -missing data), %. * Fatigue, anorexia, weight-loss, fever, night sweats or lymphadenopathies. ** Thickness, tenderness, and reduced or absent pulse.

loss, 5 PVL, 5 diplopia); 6 ischeamic strokes; and 1 transient ischaemic attack. Table 1 presents the differences between pts with and without SIEs. On univariate analyses, pts with SIEs were older ($p< 0.001$), and more often had previous hypertension (OR: 3.0, 95%CI: 1.4-6.3), jaw claudication (OR 3.0, 95%CI: 1.5-6.5) and temporal artery (TA) abnormalities on clinical examination (OR 4.5, 95%CI: 1.8-10). By contrast, musculoskeletal (MSK) features including polymyalgia rheumatica (PMR) were negatively associated with the occurrence of SIEs (OR 0.37, 95%CI: 0.2-0.7). In terms of laboratory results, only creatinine levels at diagnosis were significantly higher ($p=0.014$) in pts with SIEs;

Table 2 - Multivariate logistic regression model for prediction of severe ischaemic events

	B	S.E.	Wald	df	p	OR	95% C.I. for OR	
							Inferior	Superior
Age at diagnosis	0.061	0.032	3.636	1	0.057	1.063	0.998	1.132
High blood pressure	1.353	0.562	5.788	1	0.016	3.869	1.285	11.652
Jaw claudication	1.251	0.609	4.226	1	0.040	3.496	1.060	11.527
Abnormalities on temporal artery palpation	1.465	0.606	5.842	1	0.016	4.328	1.319	14.199
Musculoskeletal features	-1.212	0.549	4.863	1	0.027	0.298	0.101	0.874
Baseline [creatinine]	1.082	0.896	1.459	1	0.227	2.950	0.510	17.072
Constant	-7.118	2.545	7.826	1	0.005	0.001		

B – coefficients in log-odds units; CI – confidence interval; df – degrees of freedom; OR – odds ratio, p - Wald 2-tailed p-value; SE – standard errors associated with the coefficients; Wald – Wald chi-square value.

no differences were seen between groups for baseline inflammatory markers or haemoglobin levels. Likewise, anti-platelet therapy started before GCA diagnosis did not seem to prevent severe SIEs. By multivariate logistic regression (Table 2), hypertension, jaw claudication and abnormalities of TA on palpation were independently associated with SIEs. The presence of MSK symptoms significantly decreased the risk of SIEs.

Conclusion: Almost half the pts in this cohort presented VL and/or CVAs, highlighting the need for an earlier recognition of symptoms and a fast-track approach to pts with suspected GCA to improve outcome. High blood pressure, jaw claudication and abnormalities of TA on palpation were associated with an increased risk of SIEs, while the presence of MSK symptoms including PMR had a protective role. The identification of pts with these high-risk features should prompt immediate treatment and tight follow-up. Future studies are warranted to determine the value of more aggressive immunosuppression in these cases.

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Characterization of Visual Manifestations and Identification of Risk Factors for Permanent Vision Loss in Patients with Giant Cell Arteritis

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SESSION INFORMATION
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Background/Purpose: Permanent vision loss (PVL) is a feared complication and a leading cause of morbidity in Giant Cell Arteritis (GCA). Multiple risk factors for ocular involvement have been identified with variable consistency, including older age, male sex, presence of cardio-vascular risk factors, transient ischemic symptoms, jaw claudica-

tion and thrombocytosis. The objective of this study is to describe visual manifestations and identify risk factors that predict ocular involvement in patients with GCA.

Methods: The retrospective database, CAPHECO-GCA (Characteristics, Phenotype, Evolution and Complications of patients with GCA at Hopital du Sacre-Coeur de Montreal) was used to collect data between January 1st, 2000 and December 31st, 2019. The presence of GCA was based on the treating physician's diagnosis and confirmed retrospectively by a separate GCA expert. Descriptive statistics comparing patients with and without visual symptoms and PVL were performed. Funding for the creation of the CAPHECO-GCA database was provided by CanVasc (Canadian Network for Research on Vasculitides).

Results: A total of 100 patients with GCA were included. Of these, 95 patients met the 1990 ACR classification criteria for GCA, and 53 patients had visual symptoms. Visual symptoms included blurred vision (30% of patients), diplopia (16% of patients), amaurosis fugax (14% of patients) and blindness (19% of patients). Out of the 19 patients with blindness, 16 did not recuperate and had PVL. Patients with PVL were older (79,2 ± 6,7 vs 74,2 ± 7,6 years; p = 0,008), more likely to have coronary artery disease (31% vs 10%; p = 0,018) and peripheral artery disease (19% vs 5%; p = 0,044) than patients without PVL. However, patients with PVL were less likely to have other cranial symptoms (81% vs 96%; p = 0,019), mainly headaches (64% vs 92%; p= 0,003). A total of 58 patients underwent ophthalmologic examination: 10 patients had anterior ischemic optic neuropathy, 3 patients had central retinal artery occlusion, 1 patient had branch retinal artery occlusion and 3 patients had cranial nerve palsy. Risk factors associated with an abnormal ophthalmologic examination were the same as for PVL, but patients were also more likely to have diabetes (29% vs 7%; p = 0,026) and less likely to have constitutional symptoms (53% vs 80%; p = 0,033). Presence of visual symptoms was associated with a lower mean C-reactive protein level (73,7 ± 59,3 vs 104,3 ± 80,3 mg/L; p = 0,035). There was no statistically significant difference for sex, prior eye disease, delay to presentation, polymyalgia rheumatica, abnormal temporal artery on physical examination, extra-cranial large vessel vasculitis and platelet count.

Conclusion: Patients with GCA and PVL and/or abnormal ophthalmologic examination were older and more likely to have baseline diabetes, coronary artery disease and peripheral artery disease. A predisposing vascular vulnerability might therefore increase the risk of ocular involvement in GCA.

Disclosure: H. Baalbaki, None; **D. Jalaledin**, None; **C. Lachance**, None; **J. Makhzoum**, None.

Abstract Number: 1946

Fast-Track Giant Cell Arteritis Clinic Experience in the United States

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Fast-track clinics incorporating ultrasound into the initial evaluation of patients suspected of having giant cell arteritis (GCA) have been implemented throughout Europe leading to reduced incidence of blindness and decreased overall cost of care. Ultrasound is now recommended as one of the initial diagnostic modalities for GCA, assuming availability and expertise per EULAR guidelines. In the United States, the use of ultrasound for GCA

diagnosis has been limited to date. Here we report our fast-track GCA clinic experience at Massachusetts General Hospital.

Methods: A fast-track GCA clinic was developed at our tertiary care academic medical center which serves as a referral center for GCA patients. A standardized algorithm was created for referred patients with suspected GCA. Clinical evaluation and a dedicated ultrasound exam of the bilateral temporal and axillary arteries were completed in a single clinic session within 48 hours of referral if the patient was able. Bilateral common superficial, parietal, and frontal branches of the temporal arteries were evaluated for both halo and compression signs, and bilateral axillary arteries for halo sign. Clinical evaluation and ultrasound exam were performed and interpreted by one rheumatologist (MAM). Ultrasound images were reviewed separately by a blinded rheumatologist (MJK), both with expertise in vasculitis ultrasound.

Results: Between September 2019 and March 2020, 18 patients were evaluated in the fast-track GCA clinic. Overall, 15 patients (83%) were seen within 48 hours, 11 patients (61%) within 24 hours and 2 patients within 1 hour of referral. Mean age was 72 years, 67% were female and 83% were Caucasian (17% Hispanic). Temporal headache was reported by 89% of patients. Mean ESR was 24.7 mm/h, mean CRP was 40.6 mg/L, and 6 patients had acute phase reactants within normal limits. Four patients (22%) had a positive temporal (n = 3) or axillary (n = 1) artery ultrasound confirmed by the blinded reviewer. Three of the 4 patients with a positive ultrasound also had a positive temporal artery biopsy (TAB). The remaining patient had relapsing GCA previously diagnosed with TAB, therefore a new biopsy was not pursued. In total, 10 patients underwent TAB after ultrasound. Mean time from fast-track evaluation to TAB was 6 days. There were no conflicting results between ultrasound and TAB. Four patients with negative results on both ultrasound and TAB and one additional patient who declined TAB went on to be treated for GCA given clinical suspicion. The remaining patients were diagnosed with headache (n = 5), infection (n = 2), cardioembolic transient vision loss (n = 1) and vasculitis not otherwise specified (n = 1). Of note, 1 patient with classic symptoms of GCA and a clearly positive ultrasound was found to have normal acute phase reactants and positive TAB. No patients developed vision loss attributed to GCA.

Conclusion: Ultrasound at the point of care is an effective diagnostic tool in GCA, assuming adequate training and availability. TAB can be obtained to confirm ultrasound findings particularly during the initial phase of a fast-track clinic. For a subset of patients with negative ultrasound and TAB, the diagnosis of GCA was made on clinical grounds.

Disclosure: M. Matza, None; **M. Kohler**, None; **J. Stone**, Roche, 2, 5, Genentech, 2, 5; **S. Unizony**, Genentech, 2, Janssen, 2, 5, Sanofi, 5, Kiniksa, 5.

Abstract Number: 1947

Risk Factors for Anxiety and Depression in Patients with Giant Cell Arteritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Vasculitis – Non-ANCA-Associated & Related Disorders Poster II

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Giant cell arteritis (GCA) is the most common primary vasculitis affecting patients aged above 50 years. Its clinical manifestations such as headache, jaw claudication and blindness, as well as its treatment with high doses of glucocorticoids (GCs) can have an impact on patients' mental health. Hospital Anxiety and Depression Scale (HADS) is a validated patient-reported outcome tool to assess anxiety and depression. We aimed to explore GCA-specific and non-specific contributive factors to mental status using HADS.

Methods: HADS questionnaires were prospectively collected from patients with biopsy- or imaging-proven GCA evaluated from July 2018 to January 2020 in the Vasculitis clinic of a tertiary centre. HADS-A and HADS-D ≥8 defined possible and HADS-A and HADS-D ≥11 defined probable anxiety and depression, respectively. A cross-sectional analysis comparing different clinical and demographic features of GCA patients with HADS scores ≥8 or < 8 and ≥11 or < 11 was performed. Univariate analysis was performed using T-student, Chi-Square, Mann-Whitney and Fischer's exact tests, as appropriate. Binary logistic regression was used to identify independent predictors of HADS ≥8 and HADS ≥11. Association between values of HADS and age was assessed using Spearman's correlation coefficient.

Results: We included 72 patients with GCA, 52 (72.2%) females, with a mean ± SD age of 78.3 ± 7.7 years. Patients presented a mean ± SD HADS-A of 8.2 ± 4.6 and mean ± SD HADS-D of 7.9 ± 5.0. Possible and probable anxiety was observed in 35 (48.6%) and 22 (30.6%) patients, respectively; possible and probable depression was observed in 35 (48.6%) and 24 (33.3%) patients, respectively. **Table 1** shows the differences between patients with HADS ≥8 and < 8, and HADS ≥11 and < 11. Patients with HADS ≥8 were more frequently under GC treatment and all patients

	HADS-A						HADS-D					
	HADS-A <8 (N=37)	HADS-A ≥8 (N=35)	p-value	HADS-A<11 (N=50)	HADS-A ≥11 (N=22)	p-value	HADS-D <8 (N=37)	HADS-D ≥8 (N=35)	p-value	HADS-D <11 (N=48)	HADS-D ≥11 (N=24)	p-value
Demographic data												
Mean age, mean ± SD	76.8 ± 7.3	79.9 ± 8.0	p=0.093	77.7 ± 7.5	79.6 ± 8.3	p=0.304	74.9 ± 7.4	81.9 ± 6.4	**p<0.001**	76.3 ± 7.5	82.3 ± 6.8	**p<0.001**
Female sex, n (%)	27 (73.0)	25 (71.4)	p=0.884	34 (68)	18 (81.8)	p=0.228	26 (70.3)	26 (74.3)	p=0.704	35 (72.9)	17 (70.8)	p=0.852
Clinical characteristics of the disease												
Permanent visual loss, n (%)	6 (16.2)	6 (17.1)	p=0.916	9 (18.0)	3 (13.6)	p=0.647	6 (16.2)	6 (17.1)	p=0.916	8 (16.7)	4 (16.7)	p=1.000
LV involvement by imaging, n (%)	11 (29.7)	10 (28.6)	p=0.914	15 (30.0)	6 (27.3)	p=0.815	12 (32.4)	9 (25.7)	p=0.531	14 (29.2)	7 (29.2)	p=1.000
Disease duration, median (IQR) years	1.0 (4.2)	2.9 (4.91)	p=0.383	2.1 (5.3)	3.1 (4.5)	p=0.334	1.0 (4.0)	3.1 (6.5)	p=0.481	2.5 (5.2)	2.8 (6.6)	p=0.282
Disease duration > 3 months, n (%)	28 (75.7)	29 (82.9)	p=0.453	38 (76.0)	19 (86.4)	p=0.529	29 (78.4)	28 (80.0)	p=0.866	36 (75.0)	21 (87.5)	p=0.218
Disease duration > 1 year, n (%)	22 (59.5)	25 (71.4)	p=0.286	24 (57.1)	16 (72.7)	p=0.221	22 (59.5)	25 (71.4)	p=0.286	23 (57.5)	17 (70.8)	p=0.286
Comorbidities, n (%)												
Atherosclerosis	0 (0)	3 (8.6)	p=0.110	2 (4)	1 (4.5)	p=1.000	1 (2.7)	2 (5.7)	p=0.609	2 (4.2)	1 (4.2)	p=1.000
Atrial fibrillation	1 (2.7)	1 (2.9)	p=1.000	1 (2)	1 (4.5)	p=0.521	0 (0.0)	2 (5.7)	p=0.233	0 (0)	2 (8.3)	p=0.108
Cerebrovascular disease	2 (5.4)	4 (11.4)	p=0.423	3 (6)	3 (13.6)	p=0.361	1 (2.7)	5 (14.3)	p=0.102	2 (4.2)	4 (16.7)	p=0.091
Chronic renal disease	3 (8.1)	1 (2.9)	p=0.615	3 (6.0)	1 (4.5)	p=1.000	3 (8.1)	1 (2.9)	p=0.615	3 (6.3)	1 (4.2)	p=1.000
Diabetes mellitus	15 (40.5)	6 (17.1)	**p=0.029**	18 (36.0)	3 (13.6)	p=0.054	12 (32.4)	9 (25.7)	p=0.531	15 (31.3)	6 (25)	p=0.582
Hypercholesterolemia	5 (13.5)	4 (11.4)	p=1.000	7 (14)	2 (9.1)	p=0.712	5 (13.5)	4 (11.4)	p=1.000	7 (14.6)	2 (8.3)	p=0.708
Hypertension	26 (70.3)	23 (65.7)	p=0.679	35 (70)	14 (63.6)	p=0.594	25 (67.6)	24 (68.6)	p=0.927	33 (68.8)	16 (66.7)	p=0.858
Hyperuricemia/ gout	2 (5.4)	0 (0)	p= 0.493	2 (4.0)	0 (0)	p=1.000	1 (2.7)	1 (2.9)	p= 1.000	1 (2.1)	1 (4.2)	p=1.000
Ischaemic cardiac disease	1 (2.7)	3 (8.6)	p=0.350	3 (6)	1 (84.5)	p=1.000	1 (2.7)	3 (8.6)	p=0.350	2 (4.2)	2 (8.3)	p=0.597
Mourning	1 (2.7)	5 (14.7)	p=0.088	2 (4.1)	4 (18.2)	p=0.070	2 (5.6)	4 (11.4)	p=0.429	3 (6.4)	3 (12.5)	p=0.399
Neoplastic disease	5 (13.5)	8 (22.9)	p=0.303	23 (7.6)	9 (15.8)	p=0.053	5 (13.5)	8 (22.9)	p=0.303	25 (8.8)	7 (9.2)	p=0.761
Obesity	0 (0)	1 (2.9)	p=0.486	0 (0)	1 (4.5)	p=0.306	0 (0.0)	1 (2.9)	p=0.486	0 (0)	1 (4.2)	p=0.333
Peripheral arterial disease	1 (2.7)	2 (5.7)	p=0.609	2 (4)	1 (4.5)	p=1.000	0 (0.0)	3 (8.6)	p=0.110	1 (2.1)	2 (8.3)	p=0.256
Previous history of mental disease	2 (5.4)	2 (5.7)	p=1.000	3 (6.0)	1 (4.5)	p=1.000	1 (2.7)	3 (8.6)	p=0.350	3 (6.3)	1 (4.2)	p=1.000
Thyroid disease	3 (8.1)	2 (5.7)	p=1.000	3 (6.0)	2 (9.1)	p=0.638	3 (8.1)	2 (5.7)	p=1.000	4 (8.3)	1 (4.2)	p=0.659
Laboratory results, median (IQR)												
C-reactive protein, mg/dL	0.35 (0.5)	0.46 (1.2)	p=0.556	0.41 (0.58)	0.38 (1.19)	p=0.959	0.40 (0.5)	0.36 (0.9)	p=0.581	0.42 (0.53)	0.29 (1.21)	p=0.311
Erythrocyte sedimentation rate, mm/h	25 (20.0)	36 (33.0)	**p=0.027**	28 (35)	35 (25)	p=0.530	25.5 (26.5)	35 (43.5)	p=0.318	28 (28)	35 (45)	p=0.985
GC treatment at the time of questionnaires												
Patients under GCs, n (%)	29 (78.4)	34 (97.1)	**p=0.028**	0 (0)	22 (100)	**p=0.049**	29 (78.4)	34 (97.1)	**p=0.028**	0 (0)	24 (100)	**p=0.023**
Current GC dose, median (IQR) mg *	10 (42.5)	7.5 (42.5)	p=0.994	10 (45)	7.5 (27.5)	p=0.459	18.8 (42.5)	7.5 (42.5)	p=0.827	12.5 (45)	7.5 (40)	p=0.631
Patients under GCs ≥30mg, n (%) *	11 (37.9)	10 (31.3)	p=0.583	15 (38.5)	15 (38.5)	p=0.377	11 (39.3)	10 (30.3)	p=0.462	14 (36.8)	7 (30.4)	p=0.610
Treatment with GCs ≥1year, n (%)	16 (53.3)	24 (70.6)	p=0.155	30 (60)	17 (77.3)	p=0.156	16 (55.2)	24 (68.6)	p=0.270	29 (60.4)	18 (75)	p=0.220

*In bold statistically significant differences (p<0.05) * Prednisolone equivalent. GCs – glucocorticoids; HADS – Hospital Anxiety (A) and Depression (D) Scale; IQR – interquartile range; LV – large vessel; SF-36 – Short Form-36*

Table 1. Results of univariate analysis comparing patients with HADS ≥8 and HADS <8 and HADS ≥11 and HADS <11.

with HADS ≥11 were on GCs. Patients with HADS-A ≥8 had higher levels of ESR and lower prevalence of diabetes mellitus, whereas HADS-D scores of ≥8 or ≥11 were associated with older age. Multivariate analyses adjusted for sex, age, disease duration > 1 year and treatment with GCs showed that only GC therapy was an independent predictor of HADS-A ≥8 (OR 10.40 95%CI: 1.15-94.23) and age was an independent predictor of HADS-D ≥8 (OR 1.20 95%CI: 1.08-1.34). Multivariate analysis adjusted for age, sex and treatment with GCs showed that older age was also an independent predictor of HADS-D ≥11 (OR 1.12 95%CI: 1.03-1.22); no independent predictors were identified for HADS-A ≥11. Moreover, age and scores of HADS-D and HADS-A showed correlation (r=0.53, p< 0.001 and r=0.26, p=0.03; respectively).

Conclusion: In our cohort, around half the patients with GCA showed possible anxiety and depression. Older patients had more depression and patients under GCs were more likely to present anxiety. Although these results require replication, they highlight the importance of including the evaluation of mental health as part of the disease management in GCA, particularly in the most elderly patients under GC treatment.

Disclosure: J. Martinho, None; **A. Ponte**, None; **E. Dourado**, None; **N. Khmelinskii**, None; **S. Dias**, None; **S. Barreira**, None; **A. Cruz-Machado**, None; **C. Macieira**, None; **V. Teixeira**, None; **A. Rodrigues**, None; **D. Telles-Correia**, None; **J. Fonseca**, None; **C. Ponte**, None.

Abstract Number: 1948

Identification of Small Molecules with Efficacy as Steroid Sparing Suppression of Chemokine and Cytokine Production by Rheumatoid Arthritis Fibroblast-like Synoviocytes

Tadashi Hosoya[1], Nikunj Shukla[2], Yuya Fujita[3], Shiyin Yao[4], Fitzgerald Lao[4], Hiroyuki Baba[1], Shinsuke Yasuda[5], Howard Cottam[4], Dennis Carson[4], Tomoko Hayashi[4] and Mary Corr[6], [1]Department of Rheumatology, Tokyo Medical and Dental University (TMDU), Tokyo, Tokyo, Japan, [2]Moores Cancer Center, University of California San Diego, San Diego, CA, [3]Department of Medicine, University of California San Diego, San Diego, CA, [4]Moores Cancer Center, University of California San Diego, San Diego, [5]Department of Rheumatology, Graduate School of Medical and Dental Sciences, Tokyo Medical and Dental University (TMDU), Tokyo, Tokyo, Japan, [6]Department of Medicine, University of California San Diego, San Diego

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Cytokines & Cell Trafficking
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Target-based drug discovery has expanded our therapeutic armamentarium in the treatment of inflammatory and autoimmune diseases. Despite these advances, glucocorticoids (GC) remain reliable agents that are used in many of these conditions. In this study we utilized a discovery based approach to identify small molecular weight synthetic compounds that reduced NF-κB signaling activity in cell-based assays. We assessed the potency of specific chemotypes in reducing pro-inflammatory cytokine production by stimulated RA fibroblast-like synoviocytes (RASF) and synergy with GC.

Methods: We re-analyzed existing data from two prior high throughput screens (HTS) which utilized a library from the Small Molecule *Discovery* Center (UCSF) and a Forster resonance energy transfer based NF-κB reporter assay in THP-1 cells. NF-κB activation resulted in beta-lactamase production, which shifted the fluorescence emission of the substrate from 530 nm to 460 nm. Hit compounds were rescreened with LPS (10ng/ml) stimulated NF-κB reporter

cells at 5 and 16 hours with an IκB kinase inhibitor (IKKI) and dexamethasone (DEX) as controls for variability. Compounds (5μM) were tested for toxicity by MTT. Selected lead compounds were commercially repurchased. CXCL8 production by THP-1 cells when stimulated with LPS (10ng/ml), TNFα (2ng/ml) or IL-1ß (2ng/ml) was measured by ELISA. Human synovial tissue derived RASF were treated with TNFα (1ng/ml) and graded amounts of lead compounds and DEX, and the levels of IL-6 and CXCL8 produced were measured by ELISA.

Results: Reanalyzing prior data we identified 1843 compounds that attenuated NF-κB activities in both HTS similar to the GCs included in the original 166,000 compound library. We performed confirmation screens with these hit compounds (5μM) for their effects on the kinetics of NF-κB activity in LPS stimulated reporter cells at peak (5 hours) and decay (16 hours) timepoints. There were 270 compounds that met the following criteria: NF-κB activity < 50 % max at 5 hours or < 25% max at 16 hours. Excluding compounds with < 90% viability by MTT, the remaining compounds were clustered into 15 chemotype families. Promising representatives from the largest chemotype families were commercially purchased for further testing. Amongst these index compounds two chemotypes: 1H-pyrazolo[3,4-*d*] pyrimidin-4-amine and bis-aryl urea, effectively suppressed CXCL8 production by THP-1 cells when stimulated with LPS, TNFα or IL-1ß ($p < 0.05$, by one-way ANOVA with Dunnett's post hoc tests). These lead compounds also reduced IL-6 and CXCL8 production by TNFα stimulated RASF ($p < 0.05$). Importantly a lead 1H-pyrazolo[3,4-*d*] pyrimidin-4-amine compound demonstrated a dose sparing effect for DEX when co-administered with TNFα stimulated THP-1 cells and had a synergistic effect with DEX in suppressing RASF chemokine production($p < 0.05$, and Bliss independence-based analysis).

Conclusion: In summary, using a broad cell-based HTS approach, lead compounds were identified that reduced NF-κB activity and chemokine/cytokine secretion induced by potent immunologic stimuli, and acted synergistically with glucocorticoids as anti-inflammatory agents.

Disclosure: T. Hosoya, GlaxoSmithKline Pharmaceuticals Ltd., 1; **N. Shukla**, None; **Y. Fujita**, None; **S. Yao**, None; **F. Lao**, None; **H. Baba**, None; **S. Yasuda**, Chugai Pharmaceutical Co., Ltd., 1, 2, GlaxoSmithKline Pharmaceuticals Ltd., 1, Mitsubishi Tanabe Pharma Co., 1, Astellas Pharma Inc., 1, Ono Pharmaceutical Co., Ltd., 1, Asahi Kasei Corporation, 1, 2, Bristol Myers Squibb, 1, 2; **H. Cottam**, None; **D. Carson**, None; **T. Hayashi**, None; **M. Corr**, None.

Abstract Number: 1949

CB2 Receptor Distribution and Effects of Lenabasum™ in Dermatomyositis *In Vitro*

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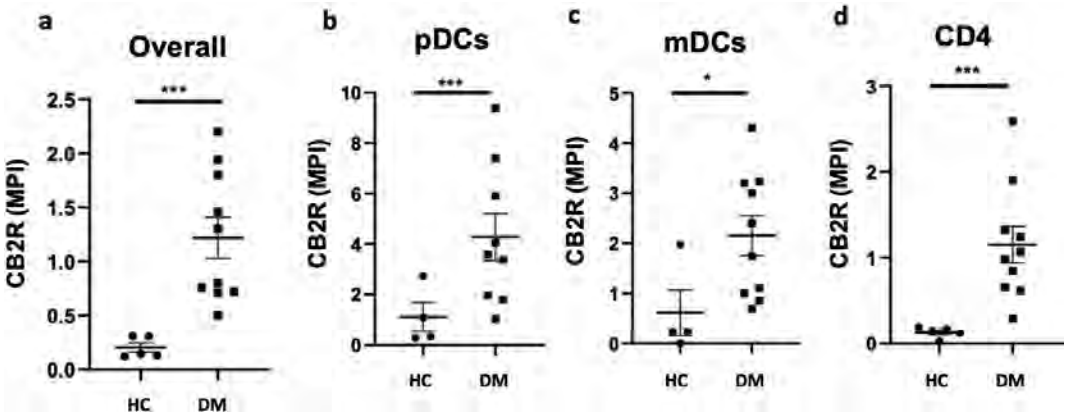
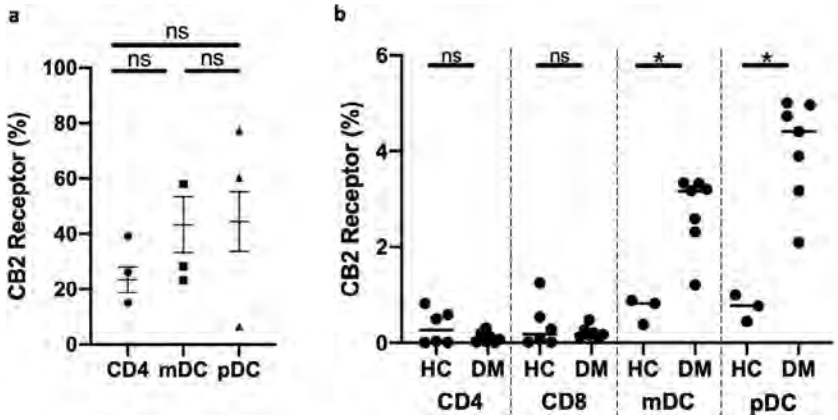
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Cytokines & Cell Trafficking
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Dermatomyositis (DM) patients report poor quality of life due to disease activity and persistent itch. Lenabasum is an oral non-immunosuppressive, non-psychoactive cannabinoid type 2 receptor (CB2R) reverse agonist being investigated for use in DM. Our previous studies showed increased IFNγ in DM compared to healthy controls (HC) and a decrease in IFNγ as a result of Lenabasum use. Literature also suggests upregulation of



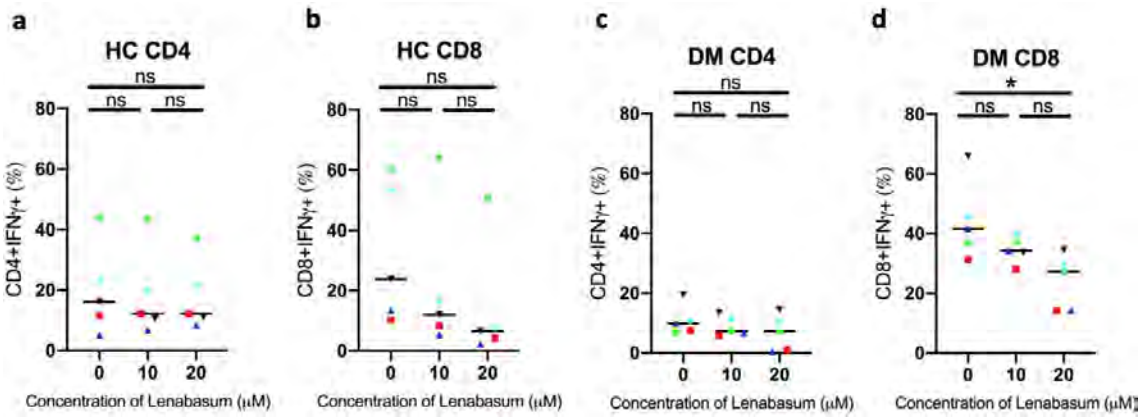
(a) Flow cytometry results from eluted DM skin cells show highest CB2R expression on pDCs (48.0% ± 21.4), followed by mDCs (36.4% ± 10.9) and CD4 T cells (26.7% ± 6.9). Skin CD8 T cells could not be analyzed because the population was too small. (b) Flow cytometry on HC and DM PBMCs shows significantly higher expression of CB2R in mDCs (p=0.0167) and pDCs (p=0.0167) in DM compared to HC. No significant difference in CB2R expression was noted in CD4 and CD8 T cells from PBMCs (b). Overall, CB2R expression is higher in eluted skin cells compared to PBMCs.



In vitro experiments in stimulated PBMCs treated with Lenabasum show no significant decreases in IFNg production in (a) HC CD4 T cells, (b) HC CD8 T cells, and (c) DM CD4 T cells. There was a significant decrease in IFNg production in (d) DM CD8 T cells treated with 20uM compared to 0uM (p=0.0207).

CB2R in the presence of IFNγ. The purpose of our study is to investigate the distribution of CB2R among immune cells in DM blood/skin and the *in vitro* effects of Lenabasum on these immune cells.

Methods: Image mass cytometry (IMC) was used on 5 HC and 10 DM patients; biopsies were stained with 37 cell markers and 1mmx2mm regions were ablated using the Hyperion Imaging System. Cells were segmented using a nuclear app-based algorithm in Visiopharm. Per cell mean pixel intensity analysis was done with histoCAT. The Phenograph algorithm was used to cluster cells based on expression of cell markers. FC was used on peripheral blood mononuclear cells (PBMCs) isolated from 6 HC and 7 DM patients and on eluted skin cells from 9 DM biopsies. Cells ($1x10^6$/mL) were stimulated with PMA/Ionomycin/Brefeldin A or Resiquimod/Brefeldin A if they were being stained for T cells or myeloid dendritic cells (mDCs) and plasmacytoid dendritic cells (pDC), respectively. For *in vitro* experiments, samples were treated with Lenabasum (0, 10, or 20μM) for 1 hour before stimulation. Samples were acquired on a BD FACS CANTO and analyzed with FlowJo.



(a) Image mass cytometry findings show that CB2R is significantly upregulated in lesional DM skin compared to HC skin. Mean pixel intensity of CB2R expression is highest on (b) pDCs. CB2R expression in lesional DM skin when compared to HC skin is greater on (b) pDCs, (c) mDCs, and (d) CD4 T cells. * $p<0.05$, ** $p<0.01$, *** $p<0.001$

Results: We found that CB2R expression is higher in DM lesional skin compared to HC skin ($p< 0.001$). CB2R expression is upregulated on pDCs ($p< 0.001$), mDCs ($p< 0.05$) and CD4 T cells ($p< 0.001$) in DM skin compared to HC skin. When evaluating CB2R distribution among lymphocytes, dendritic cells, monocytes, macrophages, NK cells, and endothelial cells, pDCs were found to be major expressors followed by mDCs. FC results from eluted skin cells corroborated these findings, showing a greater percentage of pDCs (48.0% ± 21.4) expressing CB2R compared to mDCs (36.4% ± 10.9) and CD4 T cells (26.7% ± 6.9). FC results revealed lower expression of CB2R on DM PBMCs (1.8% ± 0.3) than in cells eluted from DM skin (37.0% ± 7.8) ($p< 0.0001$). There was no significant difference in CB2R expression in PBMCs between HC and DM CD4 T cells. No difference was noted between HC and DM CD8 T cells as well. Significantly greater CB2R expression was noted in PBMC mDCs ($p=0.0167$) and pDCs ($p=0.0167$) in DM compared to HC, but CB2R expression on mDCs and pDCs in the periphery was about 12-fold and 18-fold lower than that of skin cells, respectively. Preliminary *in vitro* experiments examined Lenabasum's effects on T cells in the blood. A significant decrease in IFNγ production by lenabasum-treated DM CD8 T cells compared to lenabasum-untreated DM CD8 T cells was noted ($p=0.0207$). No significant decrease in IFNγ production was observed in DM CD4 T cells or HC CD4 or HC CD8 T cells.

Conclusion: We found that CB2R expression differs between the skin and blood of DM patients, with higher expression occurring in skin. pDCs were found to be major expressors of CB2R in DM skin through IMC and FC, suggesting that these cells may be most affected by Lenabasum in DM.

Disclosure: S. Maddukuri, None; **J. Patel**, None; **C. Bax**, None; **M. Wysocka**, None; **V. Werth**, Corbus Pharmaceuticals, 2, Biogen, 2, 5, Resolve, 2, CSL Behring, 5, Regeneron, 5, Argenx, 5, Viela Bio, 2, 5, Principia, 5, Lilly, 5, Abbvie, 5, AstraZeneca, 2, 5, Amgen, 5, Kyowa Kirin, 5, Glaxo Smith Kline, 5, Cugene, 5, Celgene, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Gilead, 2, 5, Genentech, 2, 5, Syntimmune, 2, MedImmune, 5, Idera, 5, BMS, 5, Medscape, 5, Nektar, 5, Incyte, 5, EMD Sorona, 5, Crisalis, 5, Octapharma, 5, University of Pennsylvania, 9.

Abstract Number: 1950

Elevated Serum Gasdermin D N-terminal Implicates Macrophage Pyroptosis in Adult-onset Still's Disease and Systemic Juvenile Idiopathic Arthritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Cytokines & Cell Trafficking
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Elevation of serum IL-18 in adult-onset Still's disease (AOSD) and systemic juvenile idiopathic arthritis (sJIA) suggests involvement of one or more inflammasome in these diseases, but their pathogenesis is still uncertain. We aimed to elucidate the auto-inflammatory mechanisms in AOSD and sJIA.

Methods: Patients with AOSD, sJIA, hemophagocytic lymphohistiocytsis (HLH), and Behçet's disease followed at Yokohama City University (YCU), or U.S. National Institutes of Health (NIH) were included in the study. Disease activity was evaluated by the modified Pouchot score. Ferritin and N-terminal gasdermin D (a pore-forming protein playing central roles in inflammasome-mediated inflammation) levels in serum and culture supernatant were measured by ELISA. Primary monocytes (Mo) were stimulated with GM-CSF or M-CSF and differentiated into M1 macrophages (Mφ) or M2Mφ, respectively. The number of Mo/Mφ and their viability were monitored over time.

Results: Patients with active AOSD and sJIA had increased levels of serum gasdermin D N-terminal, which correlated with serum ferritin and IL-18 levels. Mo-derived Mφ from active AOSD patients showed reduced cell viability and increased cell death. The number of cultured Mφ cells on day nine was negatively correlated with the serum ferritin and gasdermin D levels. Higher ferritin and gasdermin D levels were observed in the M1Mφ culture supernatant of active AOSD patients.

Conclusion: Elevation of serum gasdermin D N-terminal and increased Mφ cell death suggests that Mφ pyroptosis is associated with AOSD and sJIA.

Disclosure: H. Nagai, None; **Y. Kirino**, None; **H. Nakano**, None; **Y. Kunishita**, None; **M. Ombrello**, None.

Abstract Number: 1951

Possible Involvement of Fractalkine/CX3CR1 Axis in Peripheral $CD14^{++}CD16^{+}$ Monocytes in Disease Development of Patients with Systemic Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Cytokines & Cell Trafficking
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Fractalkine (FKN) binds its receptor, CX3CR1 and accelerates chemotaxis of immune cells by inducing cell surface molecules and mediating adhesion of the cells to vascular endothelial cells. Several lines of evidence suggest that the FKN/CX3CR1 axis plays a crucial role in local infiltration of inflammatory cells at the sites of injury, which may result in impairments of organs in systemic lupus erythematosus (SLE). Our previous data showed that the expression level of CX3CR1 in peripheral $CD14^{++}CD16^{+}$ monocytes was remarkably decreased in SLE active patients as compared with SLE inactive patients and healthy controls (HC). In this study, we investigated the possible involvement of FKN/CX3CR1axis in immunological abnormalities and clinical features of SLE.

Methods: Fifty-nine SLE patients (SLE_H; high disease activity, SLEDAI: >10, n = 32, $SLE_{M+L;}$ moderate and low disease activity, SLEDAI: < 10, n = 27) and 34 healthy controls (HC) were enrolled in this study. The expression level of CX3CR1 in peripheral $CD14^{++}CD16^{+}$ monocytes was analyzed by FACS using whole blood samples from patients and HC. The serum level of FKN was measured by a Slow Off-rate Modified DNA Aptamer (SOMAmer)-based capture array. Disease activities of SLE patients were quantified based on the SLEDAI scores. The serological data of the patients was collected by clinical records. Differences between the groups were examined for statistical significance by a *t*-test for single comparisons. Pearson's correlation analysis was employed to evaluate the relationship between two continuous variables.

Results: FACS analysis revealed that the proportion of CX3CR1 positive cells among $CD14^{++}CD16^{+}$ monocytes was significantly lower in SLE_H patients than in patients with SLE_{M+L} (p = 0.007) or HC (p = 0.007), whereas the difference was not significant between SLE_{M+L} and HC. Moreover, the $CX3CR1^{+}/CD14^{++}CD16^{+}$ ratio was negatively and positively correlated with the SLEDAI score (p = 0.031) and serum level of C3 (p = 0.045), respectively, of all SLE patients. In addition, serum level of FKN was significantly higher in SLE_H patients than those of SLE_{M+L} patients (p = 0.005) and HC (p = 0.001). Interestingly, the serum FKN level was positively and negatively correlated with SLEDAI score (p = 0.0004) and C3 (p = 0.0043), respectively, of all SLE patients. Notably, the $CX3CR1^{+}/CD14^{++}CD16^{+}$ ratio was negatively and significantly correlated with serum FKN level of the patients (p = 0.0078).

Conclusion: These results raised the possibility that reduced expression of CX3CR1 in peripheral $CD14^{++}CD16^{+}$ monocytes and the enhanced serum FKN level lead to acceleration of migration of FKN-stimulated $CD14^{++}CD16^{+}$ monocytes to organs.

Disclosure: K. Yoshimoto, None; **K. Suzuki**, None; **N. Seki**, Mitsubishi Tanabe Pharma Corporation, 3; **S. Saito**, Chugai Pharmaceutical Co. Ltd., 1, Eisai Co.,Ltd., 1, Pfizer Japan Inc., 1, Asahikasei Pharma Corp., 1, Bristol–Myers Squibb, 1, Mitsubishi Tanabe Pharma Co., 1; **J. Kikuchi**, None; **T. Takeuchi**, Astellas Pharma Inc., 2, 5, 8, Daiichi Sankyo Company, Limited, 2, 5, 8, Takeda Pharmaceutical Company Limited, 2, 5, 8, AbbVie GK., 2, 5, 8, Asahi Kasei Pharma Corporation, 2, 5, 8, Mitsubishi Tanabe Pharma Corporation, 2, 5, 8, Eisai Co., Ltd., 2, 5, 8, Nippon Kayaku Co., Ltd., 2, 5, 8, Chugai Pharmaceutical Co., Ltd., 2, 5, 8, Eli Lily Japan K.K, 2, 5, 8, Gilead Sciences, Inc., 2, 5, 8, Pfizer Japan, Inc., 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, AYUMI Pharmaceutical Corporation, 2, 5, 8, Novartis Pharma K.K., 2, 5, 8, UCB, 2, 5, 8, Dainippon Sumitomo Co., 2, 5, 8, Shionogi & Co., Ltd., 2, 5, 8.

Abstract Number: 1952

Activated Memory T Cells Produce Ligands That Cause NF-κB-dependent Inflammatory Activation of the Endothelium: Identification of Novel Therapeutic Targets

Kim Jeucken[1], Jan Piet van Hamburg[1], Lotte Kocken[1] and Sander Tas[2], [1]Amsterdam Rheumatology and Immunology Center (ARC), Department of Rheumatology and Clinical Immunology, Department of Experimental Immunology and Amsterdam Infection and Immunity Institute, Amsterdam UMC; location AMC, University of Amsterdam, Netherlands, Amsterdam, Netherlands, [2]Amsterdam Rheumatology and Immunology Center (ARC), Department of Rheumatology and Clinical Immunology, Department of Experimental Immunology and Amsterdam Infection and Immunity Institute, Amsterdam UMC; location AMC, University of Amsterdam, Netherlands, Utrecht, Netherlands

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Cytokines & Cell Trafficking
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Endothelial cells (EC) are important contributors to inflammation via expression of inflammatory mediators, including cytokines, chemokines and adhesion molecules. Production of these inflammatory mediators can be induced via canonical and NF-κB-inducing kinase (NIK)-dependent noncanonical NF-κB signalling. The ligands activating these pathways are well studied, but less is known about the cells producing ligands that can activate NF-κB signalling in EC. In this study, we investigated the effects of factors produced by activated memory T (T_m) cells on NF-κB dependent inflammatory activation of EC.

Methods: $CD4^+CD45RO^+$ memory T cells were isolated from healthy PBMC using MACS sorting and cultured in presence of anti-CD3 and anti-CD28 for 72h, after which supernatant was harvested. Endothelial cells were stimulated for 72h with 50% T_m supernatant (T_m sup) after which protein and RNA was harvested followed by analysis of NF-κB signalling and downstream expression of inflammatory mediators using qPCR and western blot. Culture supernatants were analysed by ELISA for various inflammatory mediators. To repress canonical NF-κB signalling an inhibitor of IKKβ (iIKKβ) was used and to repress NIK-dependent NF-κB signaling an inhibitor of NIK (iNIK) was used in the EC cultures.

Results: Stimulation with T_m sup led to activation of both canonical NF-κB signalling (increased levels of phosphorylated IκBα) and noncanonical NF-κB signalling (increased p100 to p52 processing). After stimulation with T_m sup EC had increased mRNA levels of all tested inflammatory mediators compared to non-treated cells. Gene expression of chemokines, cytokines, and growth factors (CXCL1, CXCL5, IL6, IL8 and GM-CSF) in T_m sup stimulated EC was significantly reduced after treatment with iIKKβ and to a lesser, but still significant, extent after treatment with iNIK. Treatment with iIKKβ also led to a reduction in mRNA levels of the adhesion molecules VCAM-1 and ICAM-1, while this effect was less pronounced after iNIK treatment. Of note, treatment with either IKKβ or iNIK led to a significant reduction of CXCL5 in the culture supernatant of T_m sup stimulated EC. Results of bioinformatic analysis of RNA-sequencing derived data are pending.

Conclusion: This study provides new insights into the cellular interactions leading to production of inflammatory mediators by EC. Our findings demonstrate that activated T_m cells produce factors that can cause NF-κB-dependent inflammatory activation of EC. Targeting canonical NF-κB signaling via IKKβ or NIK-dependent NF-κB signaling reduces inflammatory activation of the endothelium and may be a potential novel therapeutic target.

Disclosure: K. Jeucken, None; **J. van Hamburg**, None; **L. Kocken**, None; **S. Tas**, None.

Abstract Number: 1953

Somatic Mutations in a Single Residue of *UBA1* Cause VEXAS, a Severe Adult-Onset Rheumatic Disease Presenting as Relapsing Polychondritis, Polyarteritis Nodosa, or Giant Cell Arteritis

David Beck[1], Marcela Ferrada[2], Keith Sikora[3], Amanda Ombrello[4], Daniela Ospina Cardona[5], Nicholas Balanda[6], Wuhong Pei[6], Jason Collins[6], Robert Colbert[7], Mariana Kaplan[8], Massimo Gadina[9], Sinisa Savic[10], Helen Lachmann[11], Kyle Retterer[12], Shawn Burgess[13], William Gahl[6], Achim Werner[6], Ivona Aksentijevich[14], Neal S. Young[6], Katherine R. Calvo[6], Peter C. Grayson[15] and Daniel Kastner[16], [1]National Human Genome Research Institute, Bethesda, [2]Systemic Autoimmunity Branch, Vasculitis Translational Research Program, National Institute of Arthritis and Musculoskeletal and Skin Diseases, National Institutes of Health, Bethesda, MD, [3]National Institutes of Health Clinical Center, Bethesda, MD, [4]National Human Genome Research Institute/National Institutes of Health, Bethesda, MD, [5]National Institute of Health, Bethesda, [6]National Institutes of Health, Bethesda, [7]Pediatric Clinical Trials Unit and Office of Clinical Director, NIAMS, NIH, Bethesda, MD, [8]National Institute of Arthritis and Musculoskeletal and Skin Diseases, Bethesda, MD, [9]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), NIH, Bethesda, MD, [10]University of Leeds, England, United Kingdom, [11]National Amyloidosis Center\nRoyal Free Campus, Rowland Hill St, London, United Kingdom, [12]GeneDX, Gaithersburg, [13]National Institutes of Health, Bethesda, MD, [14]National Human Genome Research Institute, Bethesda, MD, [15]Systemic Autoimmunity Branch, National Institutes of Health, NIAMS, Bethesda, MD, [16]National Human Genome Research Institute (NHGRI), NIH, Bethesda, MD

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Genetics, Genomics & Proteomics

Session Type: Abstract Session

Session Time: 12:00PM–12:50PM

Background/Purpose: Identifying the causes of adult-onset rheumatic diseases remains a challenge, and limits diagnosis, prognosis, and targeted treatment. We hypothesized that mutations in genes regulating the post-translational modification ubiquitin, previously implicated in two autoinflammatory diseases, may define new rheumatic disorders.

Methods: We analyzed peripheral blood exome sequence data from 2,560 individuals with inflammation-related diagnoses for deleterious mutations in >800 ubiquitin-related genes. After discovering three patients with novel *UBA1* mutations, we identified additional cases based on clinical similarities. Sanger sequencing, digital droplet PCR, immunoblotting, immunohistochemistry, flow cytometry, and transcriptome/cytokine profiling were performed. CRISPR/Cas9 knockout zebrafish provided an *in vivo* model to assess *UBA1* gene function.

Results: Twenty-eight adult males were identified with somatic mutations at methionine 41 in *UBA1*, an X-linked gene, encoding the major E1 enzyme that initiates ubiquitylation. Methionine 41 is highly conserved in UBA1, and these somatic mutations were not observed in exome sequences from over 80,000 healthy controls. Among affected individuals, mutations were found in more than half of hematopoietic stem cells, exclusively in peripheral blood myeloid cells, and not in lymphocytes or fibroblasts. Patients developed an often-fatal, treatment-refractory inflammatory syndrome in late adulthood, with fevers, cytopenias, characteristic vacuoles in myeloid and erythroid precursors cells, dysplastic bone marrow, neutrophilic cutaneous and pulmonary inflammation, chondritis, and vasculitis. Patients fulfilled clinical criteria for inflammatory (relapsing polychondritis, Sweet syndrome, polyarteritis nodosa, giant cell arteritis) and hematologic (myelodysplastic syndrome or multiple myeloma) conditions. Mutations at p.Met41 resulted in loss of the cytoplasmic isoform of UBA1 and decreased ubiquitylation and, unexpectedly, the expression of a novel, catalytically inactive, toxic isoform, in mutant, but not wildtype, lineages. Mutant peripheral blood cells exhibited activated innate immune pathways and evidence for unfolded protein response (UPR). Knockout of the zebrafish UBA1 cytoplasmic isoform homologue caused systemic inflammation.

Conclusion: By querying exomes for mutations in ubiquitylation genes, we have defined a novel disorder, VEXAS (vacuoles, E1 enzyme, X-linked, autoinflammatory, somatic) syndrome, which connects seemingly unrelated adult-onset inflammatory syndromes and establishes a precedent for a new molecular taxonomy of rheumatic diseases. Our work also reveals somatic mutations as an underrecognized cause of adult-onset rheumatic diseases.

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Abstract Number: 1954

Genome-wide Association Study of Sjögren's Syndrome Identifies Ten New Risk Loci

Bhuwan Khatri[1], Tove Ragna Reksten[2], Kandice Tessneer[3], Astrid Rasmussen[1], R. Scofield[1], Simon Bowman[4], Joel Guthridge[1], Judith James[5], Lars Ronnblom[6], Blake Warner[7], Xavier Mariette[8], Roald Omdal[9], Javier Martin[10], Maria Teruel[10], Janicke Liaaen Jensen[11], Lara Aqrawi[11], Øyvind Palm[11], Marie Wahren-Herlenius[12], Torsten Witte[13], Roland Jonsson[14], Maureen Rischmueller[15], A Darise Farris[1], Marta Alarcon-Riquelme[10], Wan-Fai Ng[16], Kathy Sivils[1], Gunnel Nordmark[17] and **Christopher Lessard**[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]University of Bergen, Bergen, Norway, [3]Oklahoma Medical Research Foundation, Oklahoma City, [4]University Hospitals Birmingham, Birmingham, United Kingdom, [5]Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation;Department of Pathology, University of Oklahoma Health Sciences Center;Department of Medicine, University of Oklahoma Health Sciences Center, Edmond, OK, [6]Uppsala University, Uppsala, Sweden, [7]National Institute of Dental and Craniofacial Research, Bethesda, [8]Paris-Sud University, Rueil-Malmaison, France, [9]University of Oslo, Stavanger, Norway, [10]Center for Genomics and Oncological Research (GENYO), Granada, Spain, [11]University of Oslo, Oslo, Norway, [12]Karolinska Institute, Stockholm, Sweden, [13]Medizinische Hochschule Hannover, Klinik für Rheumatologie und Immunologie und Regionales Kooperatives Rheumazentrum Niedersachsen e.V., Hannover, Germany, [14]Haukeland University Hospital, Bergen, Norway, [15]The Queen Elizabeth Hospital and Univ of Adelaide, St Peters, South Australia, Australia, [16]Newcastle University, Gateshead, United Kingdom, [17]Uppsala University, Copenhagen S, Sweden

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Genetics, Genomics & Proteomics
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

Background/Purpose: Sjögren's syndrome (SS) is a complex autoimmune disease with exocrine gland dysfunction leading to substantial morbidity, and 10 published genetic susceptibility loci. Our genome-wide association study (GWAS) aimed to identify additional risk loci of genome-wide significance (GWS; p< 5E-08) in European-derived primary SS.

Methods: Study received IRB approval. All SS patients met 2002 AECG criteria for SS. A total of 3232 cases and 17481 controls genotyped on GWAS arrays and 619 cases and 6171 controls genotyped on ImmunoChip (IC) arrays were imputed after quality control. Logistic regression was calculated, adjusting for ancestry using the first 4 principal components to identify SS-associated SNPs. GWAS and IC results were meta-analyzed using weighted Z-scores. Bayesian statistics were used to assign posterior probabilities and define credible SNP sets for each locus. Bioinformatic analyses were used to predict functionality.

Results: Seven novel loci exceeded GWS in the GWAS analysis: *NAB1*, *MIR146A-PTTG1*, *XKR6*, *MAPT-CRHR1*, *RPTOR-CHMP6-BAIAP2*, *TYK2* and *SYNGR1*. Meta-analysis with IC data identified three more novel loci exceeding GWS: *CD247*, *PRDM1-ATG5* and *TNFAIP3*. Additional loci with suggestive association (p< 1E-05) were also identified: *ADAMTSL2*, *CGNL1* and *PHRF1*.

Several identified loci have reported functional implications in immune regulation and autoimmune disease. In lupus, rs2431697 correlated with rs2431098, which was shown to alter *MIR146A* expression, resulting in type I interferon pathway imbalance. Similarly, *TYK2* risk association reportedly drives interferon-g, IL10 and RET signaling pathways. *PRDM1* encodes Blimp-1, a master regulator of immune cell differentiation. *CD247* encodes the zeta subunit of the T cell receptor complex. *XKR6* is implicated in apoptotic cell ingestion. *ATG5* is also involved in apoptosis, as well as autophagy and antigen presentation.

Additional bioinformatics analyses (Haploreg, Regulome DB, ENCODE, etc.) revealed immune-relevant functional implications for each risk locus. The SS-associated credible set included variants downstream of *TNFAIP3* in a region reported to abolish looping between an enhancer and the*TNFAIP3* promoter in lupus and a coding variant that has been shown to alter NF-κB activity and neutrophil extracellular traps. The rs2293765 in the 5' UTR of *NAB1* showed evidence of enhancer/promoter activities. The rs2069235 in the *SYNGR1* locus showed enhancer and transcription start site activities in B and T cells. The rs7210219 in the *MAPT-CRHR1* locus showed enhancer/promotor activities in various tissues.

Conclusion: We have identified 10 novel genetic susceptibility loci associated with SS pathology. Our finding doubles the current number of GWS regions in SS patients of European origin from 10 to 20. Future work is needed to identify and characterize the functional variants in each locus.

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Abstract Number: 1955

High-throughput Identification of Functional Regulatory SNPs Associated with Systemic Lupus Erythematosus

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Genetics, Genomics & Proteomics

Session Type: Abstract Session

Session Time: 12:00PM–12:50PM

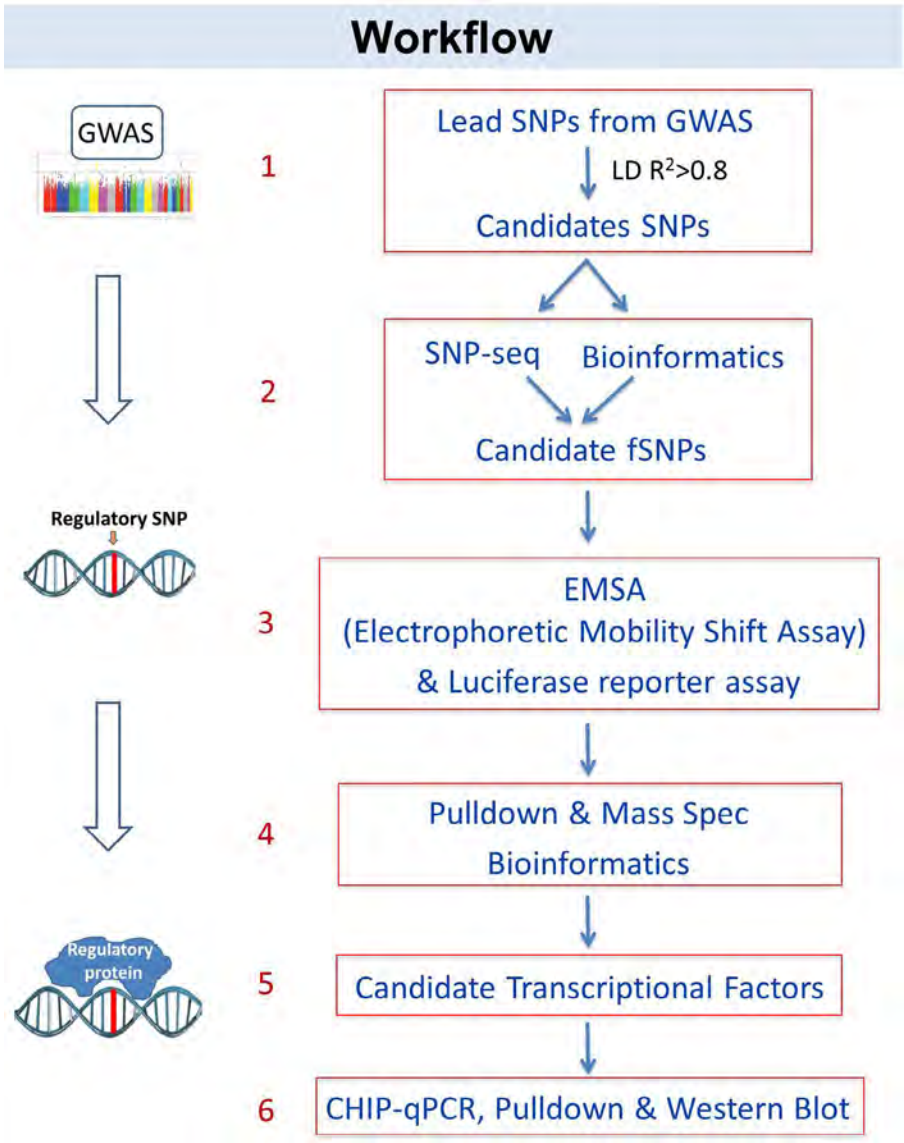


Figure 1. Workflow of identify variant-protein associations. 1-3: Identify novel regulatory variants that modulate SLE risk; 4-6: identify variant-protein associations in SLE.

Background/Purpose: Systemic lupus erythematosus (SLE) is a disease involves the complex interplay of many genes, reflected in more than one hundred loci linked with disease risk by genome-wide association studies (GWAS). Decoding GWAS is, therefore, a promising strategy to identify novel drug targets in SLE. However, most of the identified disease-associated hits are noncoding single-nucleotide polymorphisms (SNPs), and cannot be distinguished from others that reside incidentally within risk loci. To address this longstanding challenge of finding the real functional regulatory SNPs (fSNPs) from GWAS hits in SLE, we utilized an unbiased high-throughput screen method to investigate GWAS hits.

Methods: From 4 GWAS for SLE (Gateva, Sandling et al. 2009, Bentham, Morris et al. 2015, Morris, Sheng et al. 2016, Langefeld, Ainsworth et al. 2017, Zhang, Zhang et al. 2018), 87 disease-associated SNPs were chosen as lead SNPs and SNPs in linkage disequilibrium (LD)(R^2>0.8) with them are also included as the screening library. In a total of 2176 SNPs were screened by three different high-throughput methods, SNP-seq (Li, Martinez-Bonet et al. 2018), H3K4me3 epigenetic modification (Trynka, Sandor et al. 2013), and Combined Annotation Dependent Depletion (CADD) (Rentzsch, Witten et al. 2018). Top candidates from the screening were further tested for regulatory function

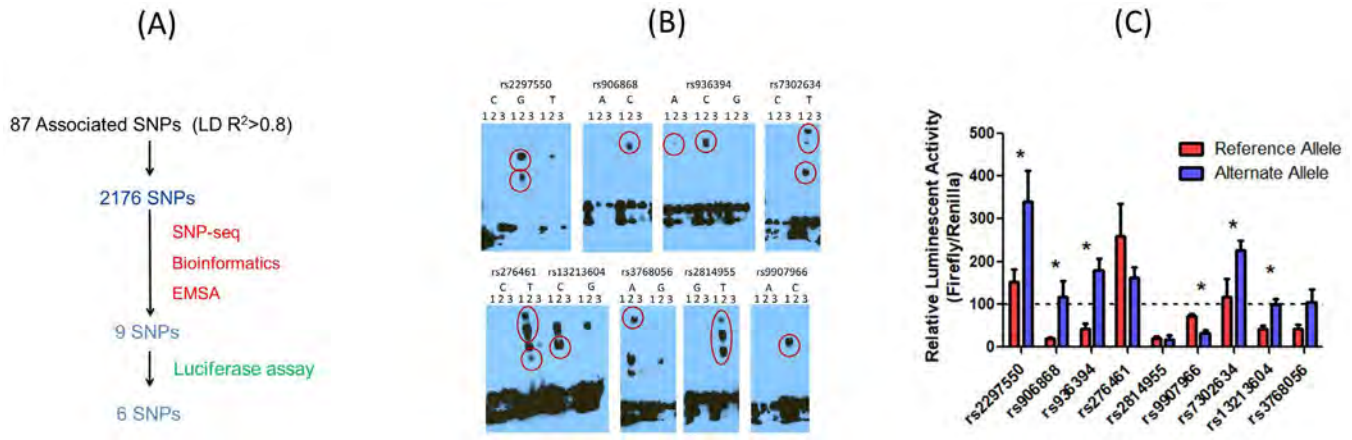


Figure 2. Identify Novel Regulatory Variants that Modulate SLE risk. (A): SNPs associated with SLE screening, 6 out of 2176 are found to be regulatory variants; (B): EMSA for 9 SNPs candidates that show allele-specific gel shift/binding (shown as red dots).1: biotinylated oligo alone; 2: biotinylated oligo with nuclear extract; 3: oligo with nuclear extract and non-biotinylated competitor. (n = 3 independent biological replicates with similar results). (C): Luciferase reporter assay shows allelic specific regulatory activity for 6 SNPs associated with SLE (* represents p<0.05).

(A)

SNPs ID	Associated gene (protein)	Candidate TF Binding Preference	EMSA Preferential binding	Luciferase assay
rs2297550	IKBKE(IKKε) Up in lupus	IKZF1 (G>C)	G>C	G>C>ctrl

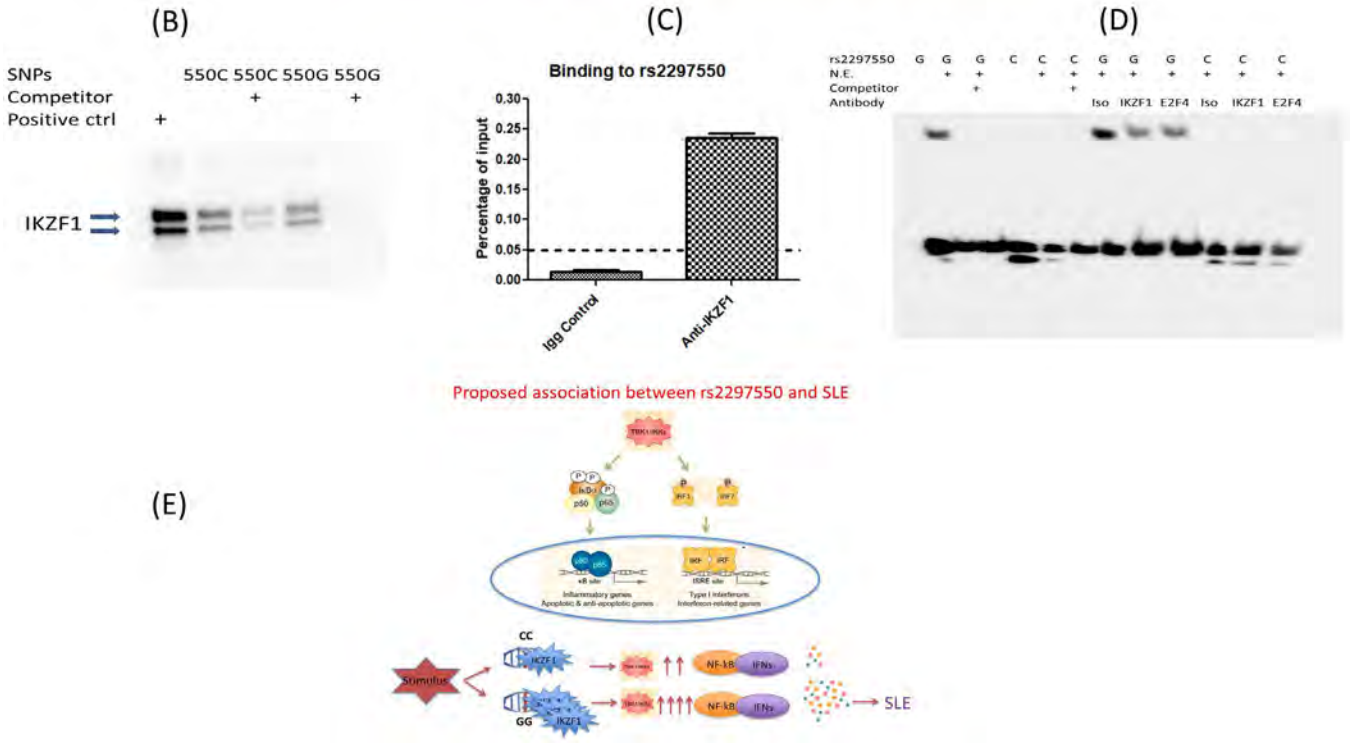


Figure 3. Identify Novel variant-protein association in SLE. (A): Table shows candidate TF (IKZF1) bound to variant rs2297550 after pulldown assay & MS and bioinformatics prediction. (B, C, D): Pulldown assay & WB and Chromatin Immunoprecipitation–qPCR and EMSA supershift assay show IKZF1 binds rs2297550, more specifically to G allele than C. (D): Proposed association between rs2297550 and SLE.

by electrophoretic mobility shift assay (EMSA) and luciferase reporter assay to get the final fSNPs candidates. Then through bioinformatics binding motif prediction and mass spectrometry for oligo pulldown assay, the transcriptional factor that might bind to the fSNPs was found and later validated by CHIP-qPCR, western blot for oligo pulldown assay as well as supershift assay.

Results: Fifty-four candidate fSNPs from 2176 SNPs after three screening methods were found to be possible regulatory variants and tested for regulatory function. After EMSA, 9 SNPs showed allelic specific binding to proteins from both BL2 cells (B cell line) and PBMC nuclear extract. Six out of these 9 SNPs showed allelic differential gene expression in luciferase reporter assay in a B cell line (Daudi). After bioinformatics predictions as well as mass spectrometry for oligo pulldown assay, two fSNPs (rs2297550 and rs9907966) were found to be able to bind to transcriptional factor IKZF1 and YBX1 in B cells respectively by allelic specific pulldown assay, CHIP-qPCR, and EMSA-supershift assay.

Conclusion: Our unbiased high-throughput screening for SLE GWAS hits, followed by a step-wise validation leads to the identification of real functional regulatory SNPs that are capable of binding to transcriptional factors and regulate gene expression, which establish a working model to bridge the gap between SLE GWAS and disease mechanism.

Disclosure: Q. Wang, None; **M. Martínez**, None; **M. Weirauch**, None; **P. Nigrovic**, Novartis, 2, 5, BMS, 2, 5, Pfizer, 2, 5, Sobi, 5, Miach Orthopedics, 5, Simcere, 5, XBiotech, 5, Quench Bio, 5, Siglion, 5, Cerecor, 5, UpToDate, 7, American Academy of Pediatrics, 7, CARRA, 9.

Abstract Number: 1956

Dysregulated Expression of the Long Non-coding RNA, *LINC01871*, Implicated in Sjögren's Syndrome Pathogenesis

Michelle Joachims[1], Bhuwan Khatri[1], Kandice Tessneer[2], Anna Stolarczyk[1], Graham Wiley[1], Astrid Rasmussen[1], Joel Guthridge[1], Judith James[3], R. Scofield[1], Kathy Sivils[1], Indra Adrianto[4] and **Christopher Lessard**[1], [1]Oklahoma Medical Research Foundation, Oklahoma City, OK, [2]Oklahoma Medical Research Foundation, Oklahoma City, [3]Arthritis and Clinical Immunology Research Program, Oklahoma Medical Research Foundation;Department of Pathology, University of Oklahoma Health Sciences Center;Department of Medicine, University of Oklahoma Health Sciences Center, Edmond, OK, [4]Henry Ford Health System, Detroit, MI

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Genetics, Genomics & Proteomics
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

Background/Purpose: Sjögren's syndrome (SS) is an autoimmune disease characterized by inflammatory destruction of the exocrine glands. Long non-coding RNAs (lncRNAs) are a functionally diverse class of non-protein coding RNA (ncRNA) with implications in immune cell regulation. The role of lncRNAs in SS pathogenesis is unknown.

Methods: Study received IRB approval. All SS cases met 2002 AECG criteria. RNA-seq was used on whole blood from SS patients (n=30 antibody negative (Ro^-); n=27 antibody positive (Ro^+)) and healthy controls (HC, n=27) to identify differentially expressed (DE) lncRNAs (log_2 fold change (FC) ≥ 2 or ≤ 0.5; $p_{adj} < 0.05$). Bioinformatic and pathway analyses were used to predict *LINC01871* function. CRISPR-targeted *LINC01871* deletion in the T lymphoblastic cell line HSB-2 was performed by RNP transfection and assessed by using an enrichment method that increases the sequencing reads across the region using Oxford Nanopore Minion sequencing. Transcripts of interest were measured by qRT-PCR. Protein expression was analyzed using flow cytometry and multiplex bead-based ELISAs.

Results: We identified 1054 unique DE ncRNAs between Ro^+, Ro^- and a combined analysis relative to HC. *LINC01871* (SS^{Ro-}: FC=2.85; $p_{adj}=1.1x10^{-4}$) was a previously uncharacterized lincRNA that was co-expressed in the SS^{Ro-} transcriptome with several protein coding RNAs involved in immune regulation (*TBX21*, *IL10RA*, *IL2RB,* etc.). DE of *LINC01871* was confirmed in an independent set of 35 SS cases and 21 HCs using qPCR. Bioinformatics analyses identified shared immune-related pathways including cytotoxic cell, cell migration, and T cell regulation. The Expression Atlas database showed DE of *LINC01871* in several published RNA-seq studies in cancer, autoimmune diseases (such as discoid lupus), and T cell states. CRISPR-targeting in HSB2 generated a single cell *LINC01871*$^{-/-}$ clone (one of ~100) with no RNA expression by qPCR. Using Nanopore Minion sequencing, the *LINC01871*$^{-/-}$ cell line was found to have a homozygous deletion encompassing the entire coding interval for *LINC01871* that was confirmed using PCR. RNA-seq analysis of *LINC01871*$^{-/-}$ compared to unmodified HSB-2 cells identified 1166 DE transcripts. Pathway analyses clustered the DE transcripts into SS^{Ro-}-similar immune regulatory, cytotoxic, and T cell pathways, with the addition of cancer/cellular growth and cell signaling. The *LINC01871*$^{-/-}$ clone displayed impaired growth at 4 days ($p< 0.05$) and exhibited significant modulation of many T cell regulatory transcripts (*CD8a*, *TBX21*, *IKZF3*, *CXCR3*, *PDCD1*, and *TIGIT*) and secreted growth factors (*IGFBP4*, *CSF1*, *CSF2*, *FGFPB2*). Changes were confirmed by protein analyses using flow cytometry and multiplex ELISA assays ($p< 0.05$), indicating loss of *LINC01871* resulted in widespread cellular changes affecting growth and immune regulatory pathways.

Conclusion: RNA-seq, bioinformatic data, and CRISPR technology identified and functionally characterized *LINC01871* as a potential mediator of the dysregulated T cell inflammatory response pathways implicated in SS pathogenesis.

Disclosure: M. Joachims, None; **B. Khatri**, None; **K. Tessneer**, None; **A. Stolarczyk**, None; **G. Wiley**, None; **A. Rasmussen**, None; **J. Guthridge**, None; **J. James**, Progentec Diagnostics, Inc., 9; **R. Scofield**, None; **K. Sivils**, None; **I. Adrianto**, None; **C. Lessard**, None.

Abstract Number: 1957

A Single Cell Stromal Atlas Identifies Conserved Fibroblast Phenotypes Expanded in the Inflamed Synovium, Lung, Intestine, and Salivary Gland

Ilya Korsunsky[1], Kevin Wei[2], Mathilde Pohin[3], Edy Kim[4], Jason Turner[5], Saba Nayar[6], Benjamin Fisher[7], Karim Raza[8], Matthias Friedrich[9], Jennifer Marshall[5], Adam Croft[5], Mark Coles[10], Andreas Frei[11], Andrew Filer[12], Francesca Barone[5], Kara Lassen[11], Fiona Powrie[10], Christopher Buckley[13], Michael Brenner[2] and Soumya Raychaudhuri[14], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [3]Kennedy Institute of Rheumatology, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Science, Oxford, United Kingdom, [4]Brigham and Women's Hospital, Division of Pulmonary and Critical Care Medicine, Boston, MA, [5]Rheumatology Research Group, Institute for Inflammation and Ageing, College of Medical and Dental Sciences, University of Birmingham, Queen Elizabeth Hospital, Birmingham, United Kingdom, [6]Institute for Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom, [7]University Hospitals Birmingham NHS Foundation Trust-Birmingham, Birmingham, United Kingdom, [8]Sandwell and West Birmingham Hospitals NHS Trust, Birmingham, United Kingdom, [9]Kennedy Institute of Rheumatology, Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Science, University of Oxford, Oxford, United Kingdom, [10]Kennedy Institute of Rheumatology, University of Oxford, Oxford, United Kingdom, [11]Roche Pharma Research and Early Development, Immunology, Infectious Diseases and Ophthalmology (I2O) Discovery and Translational Area, Roche Innovation Center Basel, Basel, Switzerland, [12]Institute of Inflammation and Ageing, University of Birmingham, Birmingham, United Kingdom, [13]University of Birmingham, Birmingham, United Kingdom, [14]Brigham and Women's Hospital and Harvard Medical School, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Genetics, Genomics & Proteomics
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

Background/Purpose: Pro-inflammatory fibroblasts have been independently implicated in the pathogenesis of rheumatoid arthritis (RA), inflammatory bowel disease (IBD), interstitial lung disease (ILD), and Sjogren's syndrome (pSS). While these fibroblasts are likely affected by disease modifying antirheumatic drugs that target broad cytokine pathways such as TNF, IL6, and GM-CFS, recent work suggests the possibility of *fibroblast-specific therapeutics*, such as Notch3 inhibition to disrupt $FAP^{+}THY1^{+}$ inflammatory fibroblasts in arthritis. The presence of common fibroblast phenotypes expanded in multiple inflamed tissues would suggest that one fibroblast therapeutic could be effective for multiple indications. Clinically, these common states would provide a molecular basis for rheumatology "basket" trials to select patients based on common disease etiology across diverse diagnoses. We therefore constructed a cross-tissue atlas to (1) identify shared inflammatory fibroblast states and (2) map new tissue samples to define the composition of their fibroblast phenotypes.

Methods: Inflamed and non-inflamed tissue samples were collected from 71 donors in the (1) synovium: RA and osteoarthritis; (2) intestine: IBD (inflamed and adjacent non-inflamed) and healthy; (3) salivary gland: pSS and Sicca syndrome; (4) lung: ILD and non-chronic inflammatory conditions. We constructed and analyzed an integrated reference of 73,260 single cell RNAseq (10X Genomics) fibroblast profiles using novel methods based on our published Harmony and MASC algorithms. We mapped external scRNAseq data from mouse disease models (serum transfer arthritis, DSS-colitis, and bleomycin lung fibrosis) onto our atlas using our novel Symphony algorithm and analyzed the distribution of inflammatory fibroblasts in each model.

Results:

1. Atlas of fibroblast phenotypes. We identified 9 conserved fibroblast states, including $THY1^{+}CD34^{+}$ interstitial, $NOTCH3^{+}$ perivascular, and $CCL19^{+}$ cytokine producing, and 3 tissue-specific states, including $CD55^{+}$ synovial lining and $MYH11^{+}$ myofibroblasts.
2. Phenotypes expanded in inflammation. Two fibroblast states were significantly expanded with inflammation in all four tissues. $CCL19^{+}$ fibroblasts, enriched in interferon-gamma signaling, may be involved in T cell recruitment. $NOTCH3^{+}$ fibroblasts, enriched in collagen production and proliferation, may orchestrate vascular remodeling.
3. Evaluation of mouse models. We mapped scRNAseq profiles from pre-clinical disease models to our fibroblast atlas. $CCL19^{+}$ cells were expanded with inflammation in all tissues, while $NOTCH3^{+}$ cells were expanded in lung and synovium but not in the intestine.

Conclusion: Our identification of two distinct inflammatory fibroblast states synthesize findings from multiple tissue-specific studies. Our comparison to mouse models predict that Notch3 based therapeutic approaches that are successful pre-clinical models of arthritis may also work on bleomyocin-induced pulmonary fibrosis but not in DSS-induced colitis. This study serves as a template for larger drug response studies to inform the feasibility of multi-tissue "basket" trials for Immune Mediated Inflammatory Diseases.

Disclosure: I. Korsunsky, Brilyant LLC, 5; **K. Wei**, Gilead, 5; **M. Pohin**, None; **E. Kim**, None; **J. Turner**, None; **S. Nayar**, None; **B. Fisher**, Novartis, 5, 8, Roche, 2, Servier, 5; **K. Raza**, Pfizer, 2; **M. Friedrich**, None; **J. Marshall**, None; **A. Croft**, None; **M. Coles**, None; **A. Frei**, F. Hoffmann-La Roche (Roche), 3; **A. Filer**, roche, 2, abbvie, 8; **F. Barone**, None; **K. Lassen**, Roche, 3; **F. Powrie**, None; **C. Buckley**, Mestag, 1, GSK, 5, Janssen, 5, Celsius, 2; **M. Brenner**, None; **S. Raychaudhuri**, None.

Abstract Number: 1958

Patterns and Impact of Long-term Glucocorticoid Use on RA Patients at Risk for Major Adverse Cardiac Events

Beth Wallace[1], Yuqing Gao[2], Punyasha Roul[3], Bryant England[3], Ted Mikuls[3], Shirley Cohen-Mekelburg[4], Daniel Clauw[5], Rodney Hayward[1] and Akbar Waljee[1], [1]Michigan Medicine, VA Ann Arbor Healthcare System Center for Clinical Management Research, Ann Arbor, MI, [2]VA Ann Arbor Healthcare System, Center for Clinical Management Research, Ann Arbor, MI, [3]University of Nebraska Medical Center, Omaha, NE, [4]Michigan Medicine/VA Ann Arbor Healthcare System Center for Clinical Management Research, Ann Arbor, MI, [5]Michigan Medicine, Ann Arbor, MI

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Health Services Research
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: One-quarter to one-third of RA patients use long-term glucocorticoids (GCs) despite their known, dose-dependent association with increased risk of major adverse cardiovascular (CV) events (MACE). Little is known about patterns of GC use among RA patients with MACE risk factors (e.g. diabetes, smoking), or how GC use may potentiate these risk factors.

Methods: In this retrospective cohort study, we used administrative data to identify 6,090 RA patients with ≥1 visit to Veterans Health Administration rheumatology clinic during 2013-2017. We excluded patients with no disease-modifying anti-rheumatic drug use (n = 686) and confounding disorders also treated with GCs (n = 2,520). In the resulting 2,884-patient cohort, we used logistic regression to evaluate associations between incident MACE during 2013-2018 (outcome), recent long-term GC use (predictor), and baseline MACE risk factors (covariates). We included 5 MACE risk factors: hypertension, diabetes, hyperlipidemia, tobacco use, and prior MACE. To examine how GC use influences the effects of MACE risk factors, we included two-way interaction terms between GC use and each of the five MACE risk factors defined above.

We used a validated claims-based algorithm to define MACE as any of acute myocardial infarction, ischemic stroke, transient ischemic attack, sudden death, or coronary revascularization, occurring between index date and December 31, 2018. Index date was defined as the patient's first rheumatology visit after meeting RA diagnostic criteria. We defined recent long-term GC use as ≥90 days' supply dispensed during the two years preceding index date.

Results: Among 2,884 RA patients, 1,553 (54%) had MACE risk factors, and 97 (3%) had prior MACE (Table 1). Overall, 16% of patients recently used long-term GC, compared to 17% of patients with MACE risk factors, and 22% of patients with prior MACE. Incident MACE occurred in 308 (11%) patients, 24% of whom had recent long-term GC use. Recent long-term GC use was independently associated with increased incident MACE (Table 2). While no interaction term was statistically significant overall, differences in odds of incident MACE were seen across levels of recent GC use for several risk factors, particularly diabetes (OR 2.10, 95% CI [0.93-4.77]), tobacco use (OR 2.88, 95% CI [1.16-7.14]) and prior MACE (OR 2.41, 95% CI [0.73-7.95]) (Table 3).

Conclusion: Long-term GC use is common among RA patients with MACE risk factors, including those with prior MACE. In this cohort, a quarter of patients with an incident MACE had recently used long-term GC. Long-term GC use may potentiate the effect of comorbidities like diabetes and tobacco use, disproportionately increasing MACE risk in certain patients. Further work is needed to evaluate the effect of persistent long-term GC use after MACE events, and to explore how GC use may amplify the effects of other CV risk factors.

	Overall cohort N = 2884	MACE risk factors N=1533	Prior MACE N=97	Incident MACE N=308
GC use, past 2 years				
Long-term GC use[1], N(%)	458 (16%)	265 (17%)	22 (23%)	76 (25%)
Demographics				
Age, mean (SD)	60.8 (12.7)	63.6 (10.5)	65.9 (8.3)	70.8 (9.6)
Male, N (%)	2373 (82%)	1345 (88%)	92 (95%)	292 (95%)
Elixhauser index, median (IQR)	2 (1-4)	3 (2-4)	4 (2-5)	3 (2-4)
Baseline MACE risk factors	1533 (53%)	1533 (100%)	82 (85%)	211 (69%)
Healthcare utilization, past year				
Office visits, median (IQR)	8 (4-15)	11 (6-18)	14 (8-21)	11 (6-18)
Prescriptions, median (IQR)	9 (5-15)	12 (8 –18)	16 (13-22)	12 (7-18)
RA status, past year				
Any biologic use, N (%)	777 (27%)	438 (29%)	36 (37%)	102 (33%)
≥2 biologics, N (%)	134 (5%)	83 (5%)	7 (7%)	14 (5%)
Rheumatologist visits, median (IQR)	1 (0-3)	1 (0-3)	2 (1-3)	2 (0-3)

[1]Long-term GC use = ≥90 days' supply dispensed during the 2 years prior to index date

Table 1. Baseline characteristics by risk of MACE, assessed at first VA rheumatologist visit during the study period.

	OR	95% CI	P value
Long-term GC use	**1.76**	**1.02-3.03**	**0.04**
Hypertension	1.17	0.85-1.61	0.32
Diabetes	**1.49**	**1.08-2.04**	**0.01**
Hyperlipidemia	**1.42**	**1.05-1.91**	**0.02**
Tobacco use	1.30	0.85-2.02	0.23
History of prior MACE	1.19	0.62-2.30	0.53
Age (per 1 year)	**1.10**	**1.08-1.12**	**<0.01**
Male Gender	**1.75**	**1.01-3.02**	**0.04**
Office visits (per 1 visit)	**1.02**	**1.00-1.03**	**0.01**
Biologic use	1.29	0.98-1.70	0.07

Table 2. Multivariable logistic regression model showing association between long-term GC use in the 2 years prior to index date and incident MACE.

	Overall Cohort			Risk factor + prior GC*		
	OR	95% CI	P value	OR	95% CI	P value
Hypertension	1.17	0.85-1.61	0.32	**1.98**	**0.99-3.93**	**0.05**
Diabetes	**1.49**	**1.08-2.04**	**0.01**	**2.10**	**0.93-4.77**	**0.07**
Hyperlipidemia	**1.42**	**1.05-1.91**	**0.02**	1.71	0.80-3.63	0.16
Tobacco use	1.30	0.85-2.02	0.23	**2.88**	**1.16-7.14**	**0.02**
History of prior MACE	1.19	0.62-2.30	0.53	2.41	0.73-7.95	0.15

*relative to risk factor without prior GC

Table 3. Odds ratios for two-way interactions between long-term GC use and five MACE risk factors.

Disclosure: B. Wallace, None; **Y. Gao**, None; **P. Roul**, None; **B. England**, None; **T. Mikuls**, Horizon Therapeutics, 2; **S. Cohen-Mekelburg**, None; **D. Clauw**, Pfizer, 1, 2, Tonix, 1, Aptinyx, 1, 2, Daiichi Sankyo, 1, Samumed, 1, Intec Pharma, 1, Eli Lilly, 1, Zynerba, 1, Williams & Connolly LLP, 1, Nix Patterson LLP, 1, Theravance, 1; **R. Hayward**, None; **A. Waljee**, None.

Abstract Number: 1959

Epidemiology of Hospitalizations and Associated Mortality in Vasculitis: A National Study

Jasvinder Singh[1] and John Cleveland[1], [1]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Health Services Research
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

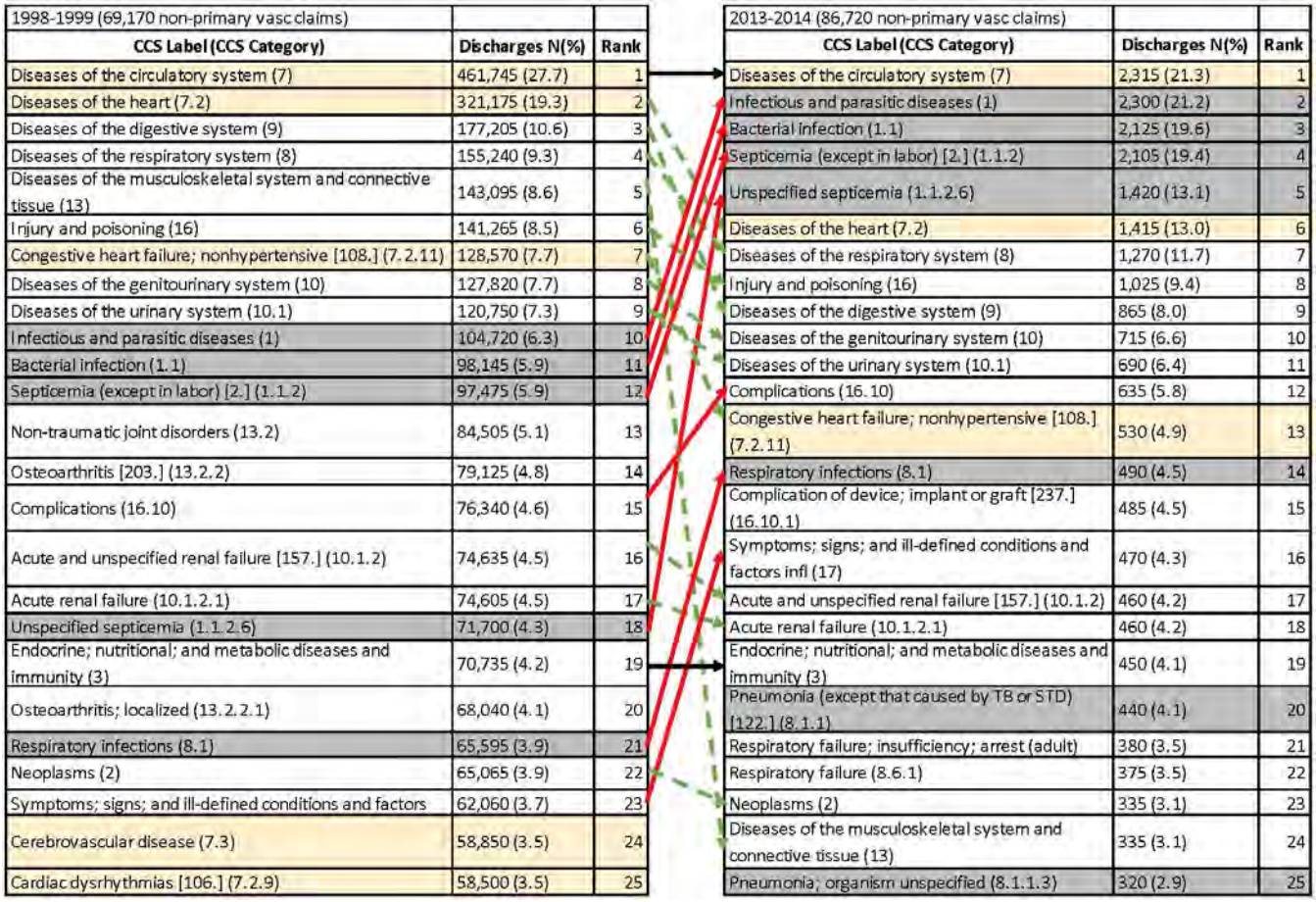
Background/Purpose: To assess whether comorbid diseases frequently associated with primary hospitalizations for non-vasculitis causes in people with vasculitis are changing over time in people with vasculitis in the U.S.

Methods: We identified people with vasculitis hospitalized with a non-primary/secondary diagnosis of vasculitis in the 1998-2014 U.S. National Inpatient Sample (NIS). We compared the rank (and percent) of top 25 Clinical Classification Software (CCS) categories (a standardized system for clustering diagnoses and procedures) associated with hospitalizations and in-hospital mortality in people with vasculitis, between 1998-99 versus 2013-14.

Results: In 1998-99, there were 69,170 non-primary vasculitis hospitalizations compared to 86,720 in 2013-14. The top 5 CCS categories associated with non-primary vasculitis hospitalizations in people with vasculitis in 1998-99 were circulatory system disease, heart disease, digestive system disease, respiratory disease, and musculoskeletal disease (Ranks 1-5 in order, respectively; **Figure 1**). In 2013-2014, the top 5 CCS (and change in rank from 1998-1999) categories were circulatory system disease (rank #1 to #1), infections/parasitic diseases (rank #10 to #2), bacterial infection (rank #11 to #3), septicemia (rank #12 to #4), and unspecified septicemia (rank #18 to #5; **Figure 1**). Compared to 27.7% non-primary vasculitis hospitalizations associated with circulatory system disease in 1998-99, 21.3% were associated in 2013-14.

In 1998-99, there were 817 deaths during non-primary vasculitis hospitalizations in people with vasculitis compared to 766 in 2013-14. The top 5 CCS categories associated with in-hospital death for non-primary vasculitis hospitalizations in 1998-99 were respiratory disease, circulatory system disease, heart disease, respiratory infection and pneumonia (Ranks 1-5 in order, respectively; **Figure 2**). In 2013-2014, these were infections/parasitic diseases (rank #6 to #1), bacterial infection (rank #7 to #2), septicemia (rank #9 to #3), unspecified septicemia (rank #22 to #4), and circulatory system disease (rank #1 to #5; **Figure 2**). In 1998-99, the top 3 CCS categories were all cardio-pulmonary diseases; in 2013-14, the top three CCS categories were all infections (**Figure 2**). Compared to 26.4% non-primary vasculitis hospitalization deaths associated with circulatory system disease in 1998-99, 20.5% were associated in 2013-14.

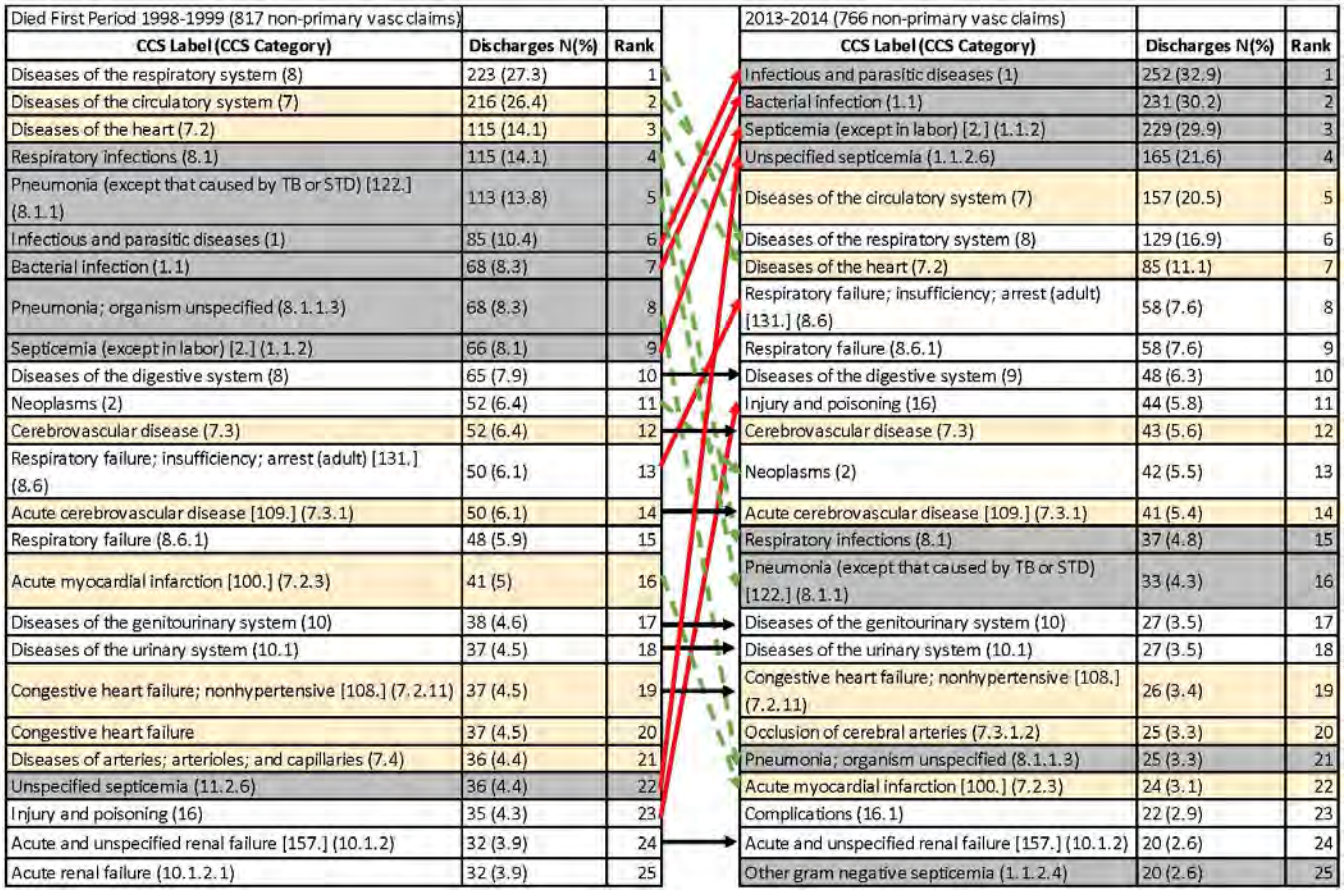
Conclusion: Infectious causes replaced cardio-pulmonary disease over time as the top causes of non-primary vasculitis hospitalizations and associated in-hospital mortality in people with vasculitis. Future studies should examine the modifiable factors associated with infection in vasculitis and design interventions to reduce this burden.



1998-1999 (69,170 non-primary vasc claims)		
CCS Label (CCS Category)	**Discharges N(%)**	**Rank**
Diseases of the circulatory system (7)	461,745 (27.7)	1
Diseases of the heart (7.2)	321,175 (19.3)	2
Diseases of the digestive system (9)	177,205 (10.6)	3
Diseases of the respiratory system (8)	155,240 (9.3)	4
Diseases of the musculoskeletal system and connective tissue (13)	143,095 (8.6)	5
Injury and poisoning (16)	141,265 (8.5)	6
Congestive heart failure; nonhypertensive [108.] (7.2.11)	128,570 (7.7)	7
Diseases of the genitourinary system (10)	127,820 (7.7)	8
Diseases of the urinary system (10.1)	120,750 (7.3)	9
Infectious and parasitic diseases (1)	104,720 (6.3)	10
Bacterial infection (1.1)	98,145 (5.9)	11
Septicemia (except in labor) [2.] (1.1.2)	97,475 (5.9)	12
Non-traumatic joint disorders (13.2)	84,505 (5.1)	13
Osteoarthritis [203.] (13.2.2)	79,125 (4.8)	14
Complications (16.10)	76,340 (4.6)	15
Acute and unspecified renal failure [157.] (10.1.2)	74,635 (4.5)	16
Acute renal failure (10.1.2.1)	74,605 (4.5)	17
Unspecified septicemia (1.1.2.6)	71,700 (4.3)	18
Endocrine; nutritional; and metabolic diseases and immunity (3)	70,735 (4.2)	19
Osteoarthritis; localized (13.2.2.1)	68,040 (4.1)	20
Respiratory infections (8.1)	65,595 (3.9)	21
Neoplasms (2)	65,065 (3.9)	22
Symptoms; signs; and ill-defined conditions and factors	62,060 (3.7)	23
Cerebrovascular disease (7.3)	58,850 (3.5)	24
Cardiac dysrhythmias [106.] (7.2.9)	58,500 (3.5)	25

2013-2014 (86,720 non-primary vasc claims)		
CCS Label (CCS Category)	**Discharges N(%)**	**Rank**
Diseases of the circulatory system (7)	2,315 (21.3)	1
Infectious and parasitic diseases (1)	2,300 (21.2)	2
Bacterial infection (1.1)	2,125 (19.6)	3
Septicemia (except in labor) [2.] (1.1.2)	2,105 (19.4)	4
Unspecified septicemia (1.1.2.6)	1,420 (13.1)	5
Diseases of the heart (7.2)	1,415 (13.0)	6
Diseases of the respiratory system (8)	1,270 (11.7)	7
Injury and poisoning (16)	1,025 (9.4)	8
Diseases of the digestive system (9)	865 (8.0)	9
Diseases of the genitourinary system (10)	715 (6.6)	10
Diseases of the urinary system (10.1)	690 (6.4)	11
Complications (16.10)	635 (5.8)	12
Congestive heart failure; nonhypertensive [108.] (7.2.11)	530 (4.9)	13
Respiratory infections (8.1)	490 (4.5)	14
Complication of device; implant or graft [237.] (16.10.1)	485 (4.5)	15
Symptoms; signs; and ill-defined conditions and factors infl (17)	470 (4.3)	16
Acute and unspecified renal failure [157.] (10.1.2)	460 (4.2)	17
Acute renal failure (10.1.2.1)	460 (4.2)	18
Endocrine; nutritional; and metabolic diseases and immunity (3)	450 (4.1)	19
Pneumonia (except that caused by TB or STD) [122.] (8.1.1)	440 (4.1)	20
Respiratory failure; insufficiency; arrest (adult)	380 (3.5)	21
Respiratory failure (8.6.1)	375 (3.5)	22
Neoplasms (2)	335 (3.1)	23
Diseases of the musculoskeletal system and connective tissue (13)	335 (3.1)	24
Pneumonia; organism unspecified (8.1.1.3)	320 (2.9)	25

Figure 1. Top 25 healthcare cost and utilization project (HCUP) Clinical Classifications Software (CCS) categories for hospitalizations in people with vasculitis, comparing 1998-1999 to 2013-2014, with respective ranks Figure 1 legend The figure shows the top 25 CCS categories for hospitalization for the first period, 1998-1999 (left) and the last study period, 2013-2014 (right). Each CCS category label and category are shown in the first column, followed by the number and percent of discharges of all hospitalizations in the next column, followed by the relative rank from 1-25. Square brackets show the single-level CCS categories and regular brackets show multi-level CCS categories. Red arrows indicate any category that went to a higher rank in 2013-2014 and green indicates those any category that descended to a lower rank in 2013-2014. Solid black arrows show the categories whose rank remained the same. Number of discharges (percent) for each CCS category and rank is shown next to each CCS category. CCS categories included diagnoses in primary or non-primary position with vasculitis in non-primary position for hospitalizations in people with vasculitis. CCS consists of two related classification systems, single-level and multi-level. Single-level CCS system classifies all diagnoses and procedures. The single-level diagnosis CCS aggregates illnesses and conditions into 285 mutually exclusive categories. Most of these categories are homogeneous; for example, CCS category #100 is “Acute myocardial infarction and #101 is “Coronary atherosclerosis and other heart disease”. Some CCS categories combine several less common, individual conditions, such as CCS category #3, which is "Other Bacterial Infections. Similarly, the single-level procedure CCS aggregates procedures into 231 mutually exclusive categories, most representing single types of procedures. For example, #43 is “Heart valve procedures”, #44 is “Coronary artery bypass graft (CABG)” and #45 is “Percutaneous transluminal coronary angioplasty (PTCA)”. The multi-level CCS expands the single-level CCS into a hierarchical system. The multi-level CCS groups single-level CCS categories into broader body systems or condition categories. It also splits single-level CCS categories to provide more detail. The multi-level system has four levels for diagnoses and three levels for procedures, which provide the opportunity to examine general groupings or to assess very specific conditions and procedures.



Died First Period 1998-1999 (817 non-primary vasc claims)			2013-2014 (766 non-primary vasc claims)		
CCS Label (CCS Category)	**Discharges N(%)**	**Rank**	**CCS Label (CCS Category)**	**Discharges N(%)**	**Rank**
Diseases of the respiratory system (8)	223 (27.3)	1	Infectious and parasitic diseases (1)	252 (32.9)	1
Diseases of the circulatory system (7)	216 (26.4)	2	Bacterial infection (1.1)	231 (30.2)	2
Diseases of the heart (7.2)	115 (14.1)	3	Septicemia (except in labor) [2.] (1.1.2)	229 (29.9)	3
Respiratory infections (8.1)	115 (14.1)	4	Unspecified septicemia (1.1.2.6)	165 (21.6)	4
Pneumonia (except that caused by TB or STD) [122.] (8.1.1)	113 (13.8)	5	Diseases of the circulatory system (7)	157 (20.5)	5
Infectious and parasitic diseases (1)	85 (10.4)	6	Diseases of the respiratory system (8)	129 (16.9)	6
Bacterial infection (1.1)	68 (8.3)	7	Diseases of the heart (7.2)	85 (11.1)	7
Pneumonia; organism unspecified (8.1.1.3)	68 (8.3)	8	Respiratory failure; insufficiency; arrest (adult) [131.] (8.6)	58 (7.6)	8
Septicemia (except in labor) [2.] (1.1.2)	66 (8.1)	9	Respiratory failure (8.6.1)	58 (7.6)	9
Diseases of the digestive system (8)	65 (7.9)	10	Diseases of the digestive system (9)	48 (6.3)	10
Neoplasms (2)	52 (6.4)	11	Injury and poisoning (16)	44 (5.8)	11
Cerebrovascular disease (7.3)	52 (6.4)	12	Cerebrovascular disease (7.3)	43 (5.6)	12
Respiratory failure; insufficiency; arrest (adult) [131.] (8.6)	50 (6.1)	13	Neoplasms (2)	42 (5.5)	13
Acute cerebrovascular disease [109.] (7.3.1)	50 (6.1)	14	Acute cerebrovascular disease [109.] (7.3.1)	41 (5.4)	14
Respiratory failure (8.6.1)	48 (5.9)	15	Respiratory infections (8.1)	37 (4.8)	15
Acute myocardial infarction [100.] (7.2.3)	41 (5)	16	Pneumonia (except that caused by TB or STD) [122.] (8.1.1)	33 (4.3)	16
Diseases of the genitourinary system (10)	38 (4.6)	17	Diseases of the genitourinary system (10)	27 (3.5)	17
Diseases of the urinary system (10.1)	37 (4.5)	18	Diseases of the urinary system (10.1)	27 (3.5)	18
Congestive heart failure; nonhypertensive [108.] (7.2.11)	37 (4.5)	19	Congestive heart failure; nonhypertensive [108.] (7.2.11)	26 (3.4)	19
Congestive heart failure	37 (4.5)	20	Occlusion of cerebral arteries (7.3.1.2)	25 (3.3)	20
Diseases of arteries; arterioles; and capillaries (7.4)	36 (4.4)	21	Pneumonia; organism unspecified (8.1.1.3)	25 (3.3)	21
Unspecified septicemia (11.2.6)	36 (4.4)	22	Acute myocardial infarction [100.] (7.2.3)	24 (3.1)	22
Injury and poisoning (16)	35 (4.3)	23	Complications (16.1)	22 (2.9)	23
Acute and unspecified renal failure [157.] (10.1.2)	32 (3.9)	24	Acute and unspecified renal failure [157.] (10.1.2)	20 (2.6)	24
Acute renal failure (10.1.2.1)	32 (3.9)	25	Other gram negative septicemia (1.1.2.4)	20 (2.6)	25

Figure 2. Top 25 healthcare cost and utilization project (HCUP) Clinical Classifications Software (CCS) categories for In-hospital death for hospitalizations in people with vasculitis, comparing 1998-1999 to 2013-2014 Figure 2 legend The figure shows the top 25 CCS categories for In-hospital death for hospitalizations for the first period, 1998-1999 (left) and the last study period, 2013-2014 (right). Each CCS category label and category are shown in the first column, followed by the number and percent of discharges of all hospitalizations in the next column, followed by the relative rank from 1-25. Square brackets show the single-level CCS categories and regular brackets show multi-level CCS categories. Red arrows indicate any category that went to a higher rank in 2013-2014 and green indicates those any category that descended to a lower rank in 2013-2014. Solid black arrows show the categories whose rank remained the same. Number of discharges (percent) for each CCS category and rank is shown next to each CCS category.

Disclosure: J. Singh, Crealta/Horizon, 1, Medisys, 1, Fidia, 1, UBM LLC, 1, Trio health, 1, Medscape, 1, WebMD, 1, Clinical Care options, 1, Clearview healthcare partners, 1, Putnam associates, 1, Focus forward, 1, Navigant consulting, 1, Spherix, 1, Practice Point communications, 1, the National Institutes of Health, 1, the American College of Rheumatology, 1, Amarin pharmaceuticals, 1, Viking therapeutics, 1, OMERACT, 1; **J. Cleveland**, None.

Abstract Number: 1960

Cost-effectiveness of Surgical and Non-Surgical Weight Loss Programs for Morbidly Obese Patients with Knee Osteoarthritis

Valia Leifer[1], Jeffrey Katz[2], Faith Selzer[3], Tuhina Neogi[4], Jamie Collins[5] and Elena Losina[2], [1]The Orthopaedic and Arthritis Center for Outcomes Research (OrACORe) at Brigham and Women's Hospital, Boston, [2]Harvard Medical School / The Orthopaedic and Arthritis Center for Outcomes Research (OrACORe) at Brigham and Women's Hospital, Boston, MA, [3]The Orthopaedic and Arthritis Center for Outcomes Research (OrACORe) at Brigham and Women's Hospital, Amesbury, MA, [4]Boston University School of Medicine, Boston, MA, [5]The Orthopaedic and Arthritis Center for Outcomes Research (OrACORe) at Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Health Services Research
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Growing numbers of knee osteoarthritis (KOA) patients are morbidly obese (BMI ≥ 35 kg/m^2). Evolving evidence suggests weight reduction may delay the structural progression of KOA, reduce knee pain, and improve total knee replacement (TKR) outcomes. The cost-effectiveness of surgical and non-surgical weight loss strategies among morbidly obese patients with KOA has not been assessed.

Table. Cost-effectiveness of weight reduction strategies* in morbidly obese (BMI ≥ 35 kg/m^2, obesity classes II and III) KOA patients

Strategy	QALE	Costs	ICER	%opioids	%TKR
SOC	13.58	$239,902	--	12.5%	65.1%
SOC + NSWL	13.61	$240,618	$24,384	12.4%	65.1%
SOC + NSWL + RYGB	15.01	$307,195	$47,523	8.9%	31.7%
SOC + RYGB	15.17	$316,236	$55,764	7.7%	26.6%

*For NSWL, subjects lost a maximum of 20% of their initial BMIs, and weight loss was not maintained beyond 3 years; for RYGB, weight loss ranged from 23-47% of initial BMI, and this weight loss was largely sustained.

Figure.

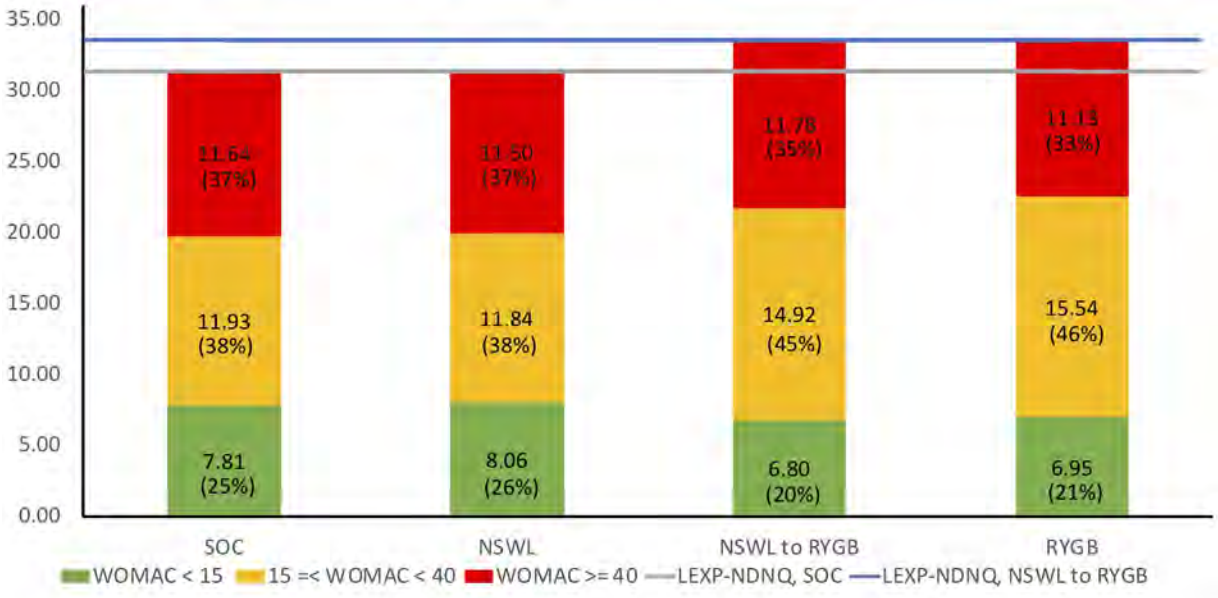


Figure. Number of non-discounted and non-quality adjusted (NDNQ) years spent by subjects in different WOMAC pain groups by treatment strategy. Solid lines indicate the NDNQ life expectancy (LEXP) of subjects from age 45 for the SOC (gray) and SOC+NSWL+RYGB (blue) strategies.

Table.

Methods: We used the Osteoarthritis Policy Model, a validated widely published microsimulation of KOA, to evaluate the cost-effectiveness of adding weight loss strategies to a KOA-related standard of care (SOC) in morbidly obese persons with KOA. The SOC includes physical therapy, NSAIDs, intra-articular injections, tramadol, oxycodone, TKR, and revision TKR. We considered 4 strategies: SOC only; SOC + a non-surgical weight loss (NSWL) program; SOC + Roux-en-Y Gastric Bypass (RYGB) surgery; and SOC + NSWL with RYGB after NSWL failure. For all strategies, we followed subjects until death, recording quality-adjusted life years (QALYs) accrued, lifetime medical costs, cumulative time in WOMAC pain states, and likelihoods of opioid and TKR use. We examined a KOA cohort with demographic and clinical characteristics consistent with those of patients enrolled in a long-term study of RYGB (mean age: 45, BMI: 46.6, WOMAC pain: 46.5). We used national databases and published data to estimate KOA structural progression, quality of life and background medical costs (stratified by pain, number of comorbidities, age, and BMI), treatment efficacy and costs ($14,819 for RYGB in year one and $251 in later years; $819 for NSWL in year one and $294 in later years), and costs and risks of complications. In sensitivity analyses we varied: the cost of health consequences of class III obesity (BMI ≥ 40) relative to class II (35 ≤ BMI < 40)($0 to $1,555 (base case = $1,555)), the likelihood of adverse events from RYGB (-50% to 50% relative to base case), and the maximum years weight loss from RYGB is maintained (5 to 20 (base case = 20)). We discounted costs and QALYs at 3%/year and conducted analysis from a healthcare perspective. We evaluated cost-effectiveness by calculating incremental cost-effectiveness ratios (ICERs) as the ratio of change in costs to change in QALYs for competing strategies in 2019 USD.

Results: Among morbidly obese patients with KOA, adding NSWL to the SOC added 0.3 QALYs and $716 in medical costs, resulting in an ICER of $24,384. Relative to the SOC + NSWL strategy, adding RYGB after NSWL added 1.4 QALYs and $66,577 in costs, leading to an ICER of $47,523. Relative to NSWL + RYGB, RYGB alone added 0.16 QALYs and $9,041 in costs with an ICER of $55,764. Relative to the SOC, the RYGB alone and NSWL + RYGB strategies reduced opioid use from 12.5% to 7.7-8.9%, and TKR use from 65.1% to 27-32% (Table). Number of years spent in different WOMAC pain groups are reported for each strategy (Figure). In sensitivity analyses, the additional cost of class III obesity was the most influential parameter affecting the cost-effectiveness of RYGB.

Conclusion: RYGB is cost-effective when preceded by NSWL at a willingness to pay (WTP) threshold of $50K/QALY. Proceeding directly to RYGB is cost-effective at a WTP threshold of $60K/QALY or higher.

Disclosure: V. Leifer, None; **J. Katz**, Samumed, 2, Flexion, 2; **F. Selzer**, None; **T. Neogi**, Lilly, 1, EMD Merck Serono, 1, Novartis, 1, Regeneron, 1, Pfizer/Lilly, 1; **J. Collins**, BICL, 9, OAC, 9; **E. Losina**, Pfizer, 9, Samumed, 2, JBJS, 9.

Abstract Number: 1961

Decreased Visits in RISE Practices Due to the SARS-CoV-2 Global Pandemic

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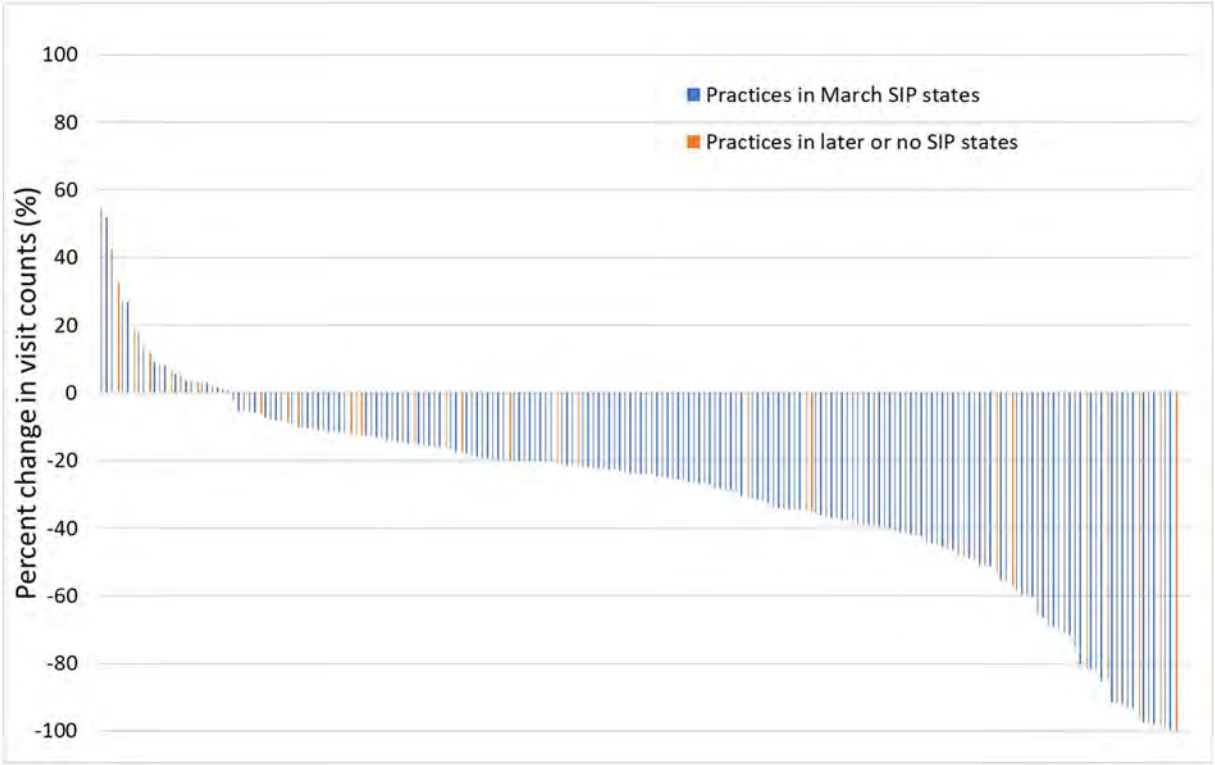
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Health Services Research
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM



Percent change in visit counts for RISE practices, March 2020 compared to March 2019 1: https://www.usatoday.com/story/news/nation/2020/03/30/coronavirus-stay-home-shelter-in-place-orders-by-state/5092413002/

Background/Purpose: The SARS-CoV-2 global pandemic has resulted in major disruptions to medical care, including rheumatology. We aimed to understand the changes in clinical visit counts from rheumatology practices across the U.S.

Methods: RISE is a national, EHR-enabled registry that passively collects data on all patients seen by participating practices, reducing the selection bias that may be present in more highly selected data sources. As of March 2020, RISE held data from 1,383 providers in 325 practices, representing ~39% of the U.S. clinical rheumatology workforce. Practices included in this study were required to have been participating in RISE from January 2019 through March 2020 and have visit data available (N=204). We obtained state-specific information on shelter-in-place (SIP) orders related to the pandemic and categorized each practice as being in a state where SIP was instituted in March 2020 vs. later or not at all.1 We analyzed visit counts (of all types – face-to-face and virtual visits combined) from RISE practices in the month of March 2020 and compared these to visit counts from March 2019. We also compared the change in visit counts according to the timing of SIP orders by state.

Results: 204 practices were included: 57% were single specialty group practices, with a median of 3 providers. Characteristics of patients seen at these practices were similar at the 2 time points (66% white, 75% female, mean (SD) age of 62 (15)). Overall, we found visit counts decreased by 34% (178,875 to 118,065) from March 2019 to March 2020 (see Figure). 168,126 unique patients were seen in March 2019 vs. 111,238 in March 2020, representing a 32.6% decrease. Almost 90% (179/204) of practices had reduced visit counts, regardless of the timing of the SIP order in their state. However, reductions were more dramatic in states where SIP orders were in place earlier: 64.4% (114/177) of March SIP practices had a > 20% decrease in visits vs. 44.4% (12/27) for those with later or no SIP orders (p=0.047)

Conclusion: We detected a significant decrease in rheumatology visits in March 2020 during the SARS-CoV-2 global pandemic compared to one year prior. The decrease in face-to-face visits may be underestimated because we were unable to distinguish between face-to-face and virtual (telemedicine) visits. Future work should address possible changes in patient outcomes due to decreased contact with clinicians. In addition, research using large observational datasets such as RISE will likely need to take this secular event into account.

Disclaimer: This data was supported by the ACR's RISE Registry. However, the views expressed represent those of the authors, not necessarily those of the ACR.

Disclosure: J. Li, None; **S. Ringold**, CARRA, 1, Up to Date, 1; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **K. Michaud**, Rheumatology Research Foundation, 2; **T. Johansson**, None; **J. Yazdany**, Eli Lilly, 5, Astra Zeneca, 5; **G. Schmajuk**, None.

Abstract Number: 1962

Utilization of Telehealth Among Patients with Rheumatic Diseases in the Early Months of the COVID-19 Pandemic

Kristin Wipfler[1], Yomei Shaw[2], Teresa Simon[3], Adam Cornish[1], Patricia Katz[4] and Kaleb Michaud[5], [1]FORWARD, The National Databank for Rheumatic Diseases, Omaha, NE, [2]FORWARD, The National Databank for Rheumatic Diseases, East Lansing, MI, [3]Bristol-Myers Squibb Company (at time of analysis), Princeton, NJ, [4]University of California, San Francisco, Novato, CA, [5]University of Nebraska Medical Center, Omaha, NE

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Health Services Research
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Many health care providers replaced in-person clinical visits with telehealth visits or expanded their telehealth offerings due to the COVID-19 pandemic. We sought to better understand the frequency of these changes and satisfaction with telehealth appointments among patients with rheumatic diseases during the first months of the COVID-19 pandemic in the US.

Methods: The study population included participants in FORWARD, The National Databank for Rheumatic Diseases who completed a supplemental COVID-19 questionnaire between May 20 and June 2, 2020. Respondents were asked about the number of telehealth appointments they had between March 1, 2020 and the date of questionnaire completion. If they had at least one telehealth appointment, they were asked to rate their satisfaction with the appointment(s) on a Likert scale. Logistic regression models were used to identify factors associated with having telehealth appointments and with telehealth satisfaction. Respondents' optional free text comments were qualitatively analyzed to assess reasons for satisfaction/dissatisfaction with telehealth.

Results: A total of 1,213 participants were included in this study, with 617 (51%) reporting at least one telehealth appointment between March 1, 2020 and questionnaire completion. Of those who had at least one telehealth appointment, 447 (72%) reported being "somewhat satisfied" or "very satisfied" with their appointment(s) (Table 1). Satisfaction appeared to decrease as the number of telehealth appointments increased (Table 2; X^2 p=0.01) but this was attenuated when considering demographic and clinical covariates. Younger age, higher Rheumatic Disease Comorbidity Index (RDCI), higher PAS-II, and prednisone use were associated with having at least one telehealth appoint-

	Telehealth n=617	No Telehealth n=596	Satisfied n=447	Not Satisfied n=170
Demographics				
Age, years	64.8 (11.0)	66.1 (10.6)	64.7 (11.4)	65.1 (10.0)
Female, %	85.5	86.9	84.9	86.9
Caucasian, %	92.2	93.8	92.0	92.8
Education, years	15.3 (2.1)	15.4 (2.1)	15.5 (1.9)	14.8 (2.5)
Married, %	67.1	67.6	66.1	69.8
Rural, %	20.7	24.8	20.6	21.2
History of smoking, %	38.1	35.1	38.7	36.5
BMI, kg/m2	28.8 (8.0)	27.8 (7.3)	28.8 (8.2)	28.9 (7.5)
RDCI, 0-9	2.6 (1.8)	2.2 (1.7)	2.6 (1.9)	2.6 (1.7)
Health insurance, %	100	98.5	100	100
PROMs				
Pain, 0-10	3.7 (2.6)	3.1 (2.6)	3.6 (2.5)	4.0 (2.7)
Global severity, 0-10	3.6 (2.4)	2.9 (2.4)	3.5 (2.4)	3.9 (2.5)
Fatigue, 0-10	4.1 (2.8)	3.3 (2.9)	4.1 (2.9)	4.2 (2.8)
PAS-II, 0-10	3.3 (2.0)	2.7 (2.0)	3.2 (2.0)	3.6 (2.1)
HAQ-II, 0-3	0.83 (0.59)	0.72 (0.59)	0.80 (0.58)	0.91 (0.64)
Primary Diagnosis				
Rheumatoid arthritis, %	64.8	61.4	62.7	70.2
Osteoarthritis, %	12.9	16.7	14.6	8.3
Lupus, %	5.2	5.2	4.5	7.1
Psoriatic arthritis, %	4.7	3.4	4.9	4.2
Fibromyalgia, %	4.2	4.9	4.0	4.8
Ankylosing spondylitis, %	2.6	1.0	3.4	0.6
Other, %	5.6	7.4	5.8	4.8
Medications				
csDMARD, %	50.6	54.5	48.8	55.3
bDMARD, %	45.1	39.2	44.4	47.0
JAKi, %	6.5	4.4	6.3	7.1
Prednisone, %	25.0	17.6	24.4	26.5
NSAID, %	39.5	40.9	38.7	41.6

Table 1. Demographics and clinical characteristics of participants who did and did not have telehealth appointments, and of those who were and were not satisfied with telehealth. Values are mean (SD) or %.

ment (Figure 1A). Lower education level and SLE diagnosis (with OA as the comparator) were associated with lower satisfaction with telehealth (Figure 1B). In the free text comments, respondents were satisfied with telehealth because it was safer, saved travel time, enabled continued access to services, and provided help with COVID-19 symptoms.

Number of Appointments	Very Unsatisfied	Somewhat Unsatisfied	Neutral	Somewhat Satisfied	Very Satisfied	Total
1-2	40 (8.1)	28 (5.7)	69 (14.0)	134 (27.2)	221 (44.9)	492
3-4	9 (9.6)	11 (11.7)	5 (5.3)	31 (33.0)	38 (40.4)	94
5+	5 (16.1)	2 (6.5)	1 (3.2)	14 (45.2)	9 (29.0)	31
Total	54 (8.8)	41 (6.6)	75 (12.2)	179 (29.0)	268 (43.4)	617

Table 2. Satisfaction with telehealth appointments by number of telehealth appointments reported. Values are n (%).

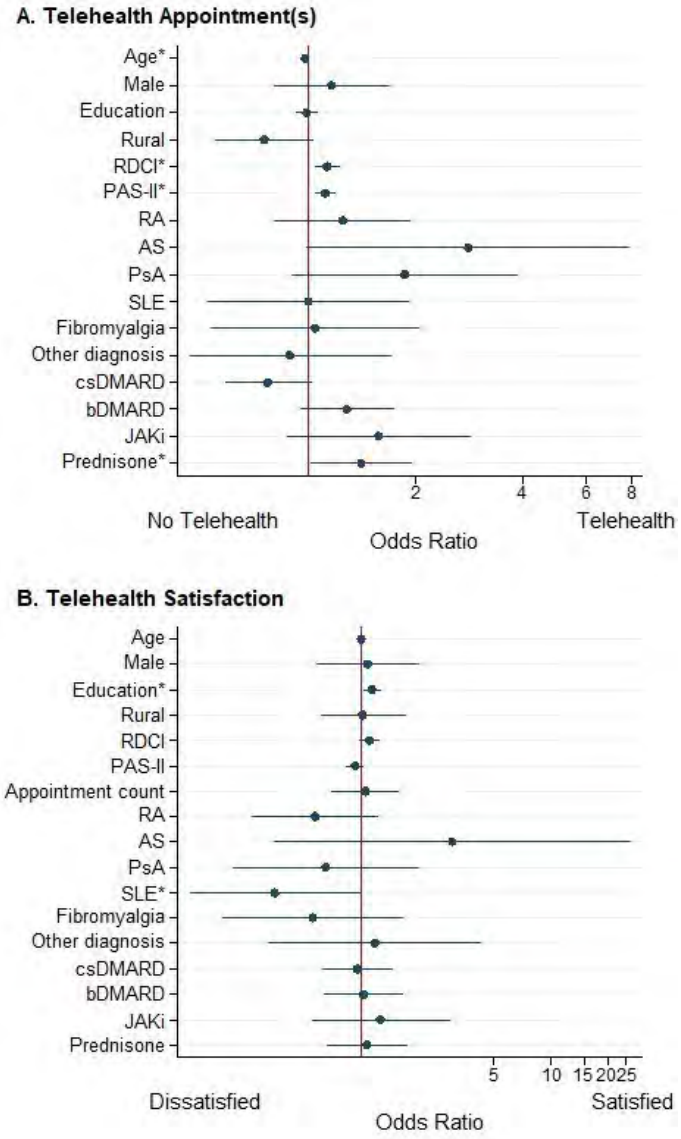


Figure 1. Factors associated with having one or more telehealth appointments (A) and with patient satisfaction with telehealth (B). OA was the comparator for diagnosis. Statistically significant covariates are labeled with an asterisk (*).

Respondents reported dissatisfaction with telehealth due to technical difficulties, perceptions that telehealth visits were less useful than in-person visits, and not being able to get needed services through telehealth.

Conclusion: About half of rheumatology patients in this cohort reported having one or more telehealth appointments during the first several months of the COVID-19 pandemic in the US, and most of them were satisfied with the ap-

pointment(s). Utilization of telehealth has expanded dramatically in a short period of time, with those with the greatest need (comorbidities and high disease activity) most likely to use these services. As clinics adapt to having more telehealth visits, it will be important to ensure quality of care and satisfaction is met for populations that are most at risk.

Disclosure: K. Wipfler, None; **Y. Shaw**, None; **T. Simon**, Bristol Myers Squibb, 5, Lexicon, 5; **A. Cornish**, None; **P. Katz**, None; **K. Michaud**, Rheumatology Research Foundation, 2.

Abstract Number: 1963

Variation in Quality of Care Among Patient Sociodemographic Groups in RISE Practices

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

Background/Purpose: Previous studies have shown that sociodemographic factors are associated with quality of care. Using the Rheumatology Informatics System for Effectiveness (RISE) registry, we assessed whether the area deprivation index (ADI) and/or race/ethnicity was associated with provider performance on quality measures among patients with rheumatoid arthritis (RA).

Methods: We analyzed data collected on all patients with a diagnosis of RA who had at least one clinic visit between January 2015 and December 2017. We examined performance on disease activity assessment, functional status assessment, tuberculosis (TB) screening prior biologic start and blood pressure (BP) control. Using mixed-effects regression, we assessed the effect of area deprivation (as measured by the ADI, above or below the median percentile, where higher scores reflect more deprivation) and race/ethnicity on measure performance and on change in performance over time. Since practice characteristics could mediate this effect, we controlled for practice type, number of providers, region, and eHR software. Analyses accounted for clustering by practice and by patient.

Results: Data from 58,432 patients from 54 practices was examined. Mean age was 63±14 years, 77% were female, and 69% were Caucasian. Over time, there were significant improvements in performance on functional status assessment (+13.5% per year) and disease activity assessment (+8.8%), smaller improvements in performance on TB screening (+2.9%) and no improvements in performance on BP control. Performance on disease activity assessment and functional status assessment was comparable across all subgroups (Table). Both measures improved faster over time among patients with higher ADI, but improvements were slower among African Americans and Hispanics than Caucasians. Performance on TB screening was higher among African Americans (59.0%) and Hispanics (58.0%) than Caucasians (54.7%) and improved faster over time among Hispanics (+7.7% points per year) than Caucasians (3.9%, $p< 0.05$) and among patients with higher ADI (+4.7%) than those with lower ADI (+2.7%, $p< 0.001$). Performance on BP control was lower among African Americans (59.6%) and patients with higher ADI (62.7%) than Caucasians (64.5%, $p< 0.001$) and patients with lower ADI (65.3%, $p< 0.001$), respectively.

Conclusion: Although performance on quality measures is improving overall, we found important differences across sociodemographic groups. Non-Caucasians and those with lower socioeconomic status (SES) had less improvement

Table: The association between area deprivation index and race/ethnicity and performance (%) and change in performance per year (% points) among rheumatoid arthritis patients in RISE

	Overall performance (%)	Change in performance per year (% points)
Disease Activity Assessment		
Area deprivation index (ADI)		
≤ Median ADI	59.4 (50.4, 68.3)	6.6 (6.4, 6.8)
> Median ADI	60.1 (51.2, 69.0)*	10.5 (10.3, 10.7)**
Race/ethnicity		
Non-Hispanic Caucasian	59.6 (50.7, 68.6)	9.1 (8.9, 9.3)
Black or African American	60.5 (51.6, 69.5)*	7.2 (6.7, 7.7)**
Hispanic or Latino	60.7 (51.7, 69.7)	4.8 (4.1, 5.5)**
Asian	56.3 (47.2, 65.5)*	8.9 (7.7, 10.1)
Other	59.9 (50.9, 68.9)	7.6 (7.1, 8.0)**
Functional Status Assessment		
Area deprivation index (ADI)		
≤ Median ADI	60.4 (51.4, 69.4)	10.9 (10.7, 11.1)
> Median ADI	61.5 (52.4, 70.5)**	16.0 (15.8, 16.2)**
Race/ethnicity		
Non-Hispanic Caucasian	60.9 (51.9, 69.9)	13.6 (13.5, 13.8)
Black or African American	62.1 (53.1, 71.1)*	10.3 (9.9, 10.8)**
Hispanic or Latino	61.1 (52.0, 70.1)	10.4 (9.7, 11.1)**
Asian	59.0 (49.9, 68.2)	9.9 (8.7, 11.1)**
Other	60.7 (51.7, 69.8)	16.8 (16.3, 17.2)**
Tuberculosis Screening		
Area deprivation index (ADI)		
≤ Median ADI	55.1 (46.9, 63.3)	2.7 (2.0, 3.4)
> Median ADI	55.7 (47.5, 64.0)	4.7 (4.0, 5.4)**
Race/ethnicity		
Non-Hispanic Caucasian	54.7 (46.4, 62.9)	3.9 (3.4, 4.5)
Black or African American	59.0 (50.5, 67.4)**	2.7 (1.2, 4.3)
Hispanic or Latino	58.0 (49.3, 66.7)*	7.7 (5.6, 9.7)*
Asian	55.4 (45.7, 65.1)	0.6 (-2.9, 4.1)
Other	56.1 (47.5, 64.7)	2.3 (1.1, 3.5)*
Blood Pressure Control		
Area deprivation index (ADI)		
≤ Median ADI	65.3 (61.8, 68.9)	0.8 (0.2, 1.5)
> Median ADI	62.7 (59.2, 66.2)**	-0.2 (-0.8, 0.4)
Race/ethnicity		
Non-Hispanic Caucasian	64.5 (61.0, 68.0)	-0.1 (-0.6, 0.5)
Black or African American	59.6 (55.8, 63.4)**	0.2 (-1.0, 1.4)
Hispanic or Latino	66.8 (61.9, 71.7)	0.9 (-1.7, 3.5)
Asian	70.5 (63.6, 77.4)	-1.0 (-5.4, 3.4)
Other	63.2 (58.6, 67.8)	5.0 (3.0, 7.0)**

Adjusted for time, practice characteristics, patient age, sex and insurance type; ** p <0.001; * p<0.05

compared to Caucasians and those with higher SES. TB screening seems to be improving more among higher risk groups. Consistent with studies in the general medical literature, BP control was lowest among African Americans. To address health disparities, future quality improvement initiatives should target patient groups with persistent gaps in quality of care.

Disclosure: Z. Izadi, None; **G. Schmajuk**, None; **J. Yazdany**, Eli Lilly, 1, Astra Zeneca, 1.

Abstract Number: 1964

Engaging Patients in the Development of a Quality Measure of Functional Status to Improve Care Among Patients with Rheumatoid Arthritis

Sarah Hopkins Gillespie[1], Liana Fraenkel[2], Lisa Suter[3], Gabriela Schmajuk[4], Patricia Katz[5], Alex Limanni[6] and Alexis Ogdie[1], [1]University of Pennsylvania, Philadelphia, PA, [2]Yale School of Medicine; West Haven VA; Berkshire Medical Center, Lenox, MA, [3]Yale School of Medicine, New Haven, CT, [4]University of California, San Francisco, Atherton, CA, [5]University of California, San Francisco, Novato, CA, [6]n/a, Dallas, TX

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

Background/Purpose: The ACR Quality of Care committee is working to develop a quality measure to reflect functional assessment in rheumatoid arthritis (RA). One proposed approach is to measure functional status over the course of one year. Scores on currently available functional status instruments may be affected by factors other than RA (e.g. comorbidities). The objective of this study was to identify factors associated with change in measures of functional status in RA. We used a mixed methods approach in which we performed a systematic literature review (SLR) followed by two focus groups to examine patients' perspectives.

Methods: In the SLR, we identified studies examining independent predictors of functional change as measured by the health assessment questionnaire (HAQ), multidimensional HAQ (MDHAQ), or PROMIS physical function in longitudinal studies. Next, we conducted two focus groups at different sites to elicit patients' views on what may affect scores and change in scores on functional status measures, using the MDAHQ as the example functional status instrument. Focus groups were audio-taped, transcribed, and analyzed via content analysis in NVivo, the code list was iteratively refined.

Results: In the SLR, all studies meeting inclusion criteria utilized the HAQ as the outcome of interest. Statistically significant factors associated with change in HAQ included disease activity, treatment of RA, disease duration, age, baseline activity level, adaptation, stress, mood, lifestyle factors (in particular smoking), education level, and comorbidities. Two focus groups with 3 and 5 patients with RA, respectively were conducted. Patients described factors that influenced functional status scores which included family responsibilities, types of activities participated in during the week (i.e., child care, cooking, cleaning, physical activity), seasonal variation, having a good relationship with the rheumatologist, having a responsive rheumatologist, and the patient's understanding of their disease (i.e., expectations about improvement, understanding what may be related to the disease, etc). While patients identified with some of the questions in the MDHAQ, they felt that many important activities/functions were missing and that function should be more broadly defined and incorporate facets of participation, in particular work and social participation. Patients also felt that stable function over a year was an acceptable performance measure, however, they also stressed the importance of incorporating individual patient goals (i.e., a newly diagnosed patient with early disease and moderate disease activity would be expected to improve over one year whereas an elderly patient with significant disease-related damage may be happy staying the same).

Conclusion: In RA, several external factors affect both static scores and change in measures of functional status. Patient focus groups provided additional factors to those identified in the literature. This study demonstrates the

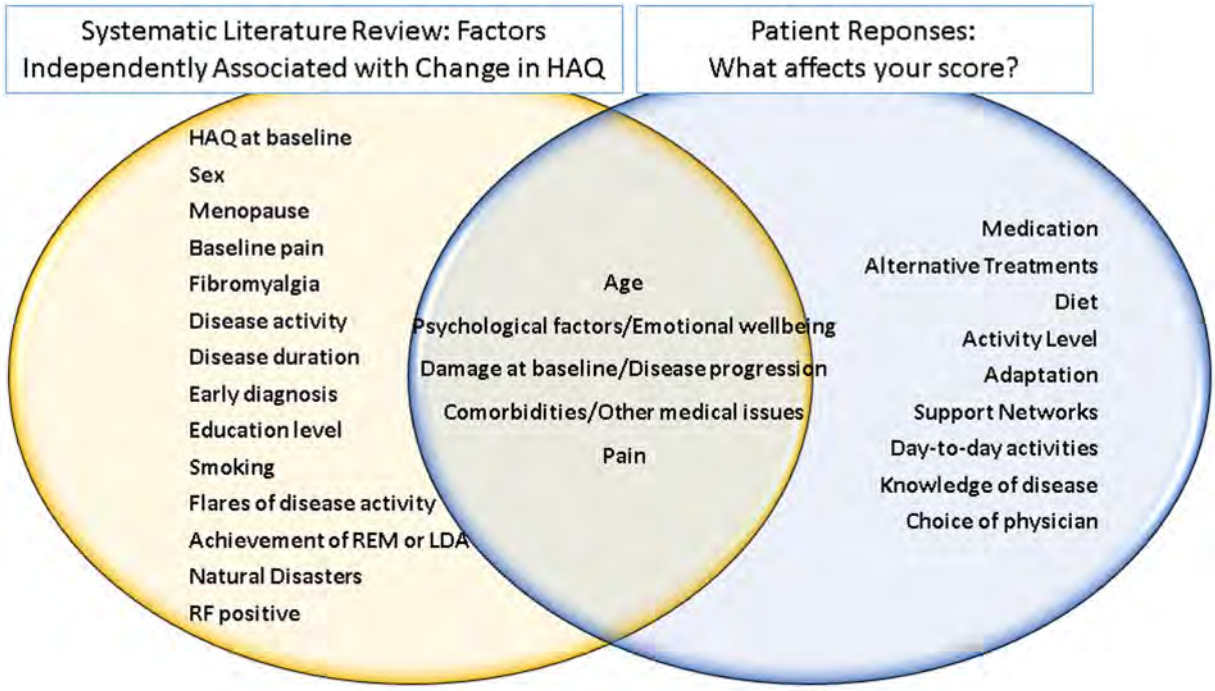

Figure 1. Factors that affect change in functional status measures: findings from a SLR and patient focus groups

importance of engaging patients in development of quality measures.Figure 1. Factors that affect change in functional status measures: findings from a SLR and patient focus groups

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Disclosure: S. Hopkins Gillespie, None; **L. Fraenkel**, None; **L. Suter**, None; **G. Schmajuk**, None; **P. Katz**, None; **A. Limanni**, None; **A. Ogdie**, abbvie, 1, amgen, 1, bms, 1, celgene, 1, corona, 1, lilly, 1, janssen, 1, novartis, 1, 2, novartis, 1, pfizer, 1.

Abstract Number: 1965

Reducing Delays for Biologic Medication Approval in Outpatient Rheumatology

Josh Waytz[1], Dahlia Sultan[1] and Veena Patel[2], [1]University of Chicago, Chicago, IL, [2]Dell Medical School - UT Health Austin, Austin, TX

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

Background/Purpose: Biologic medications are commonly used for numerous rheumatologic conditions. A significant proportion of these medications are denied for non-medical reasons by insurance companies causing delays in patients getting medication which can have negative downstream effects. The aim of this project was to develop an intervention to decrease delays and subsequent associated costs in the approval process of biologics denied for non-medical reasons in rheumatology clinic. Furthermore, we aim to have a 25% usage rate of our intervention by October 1st, 2020.

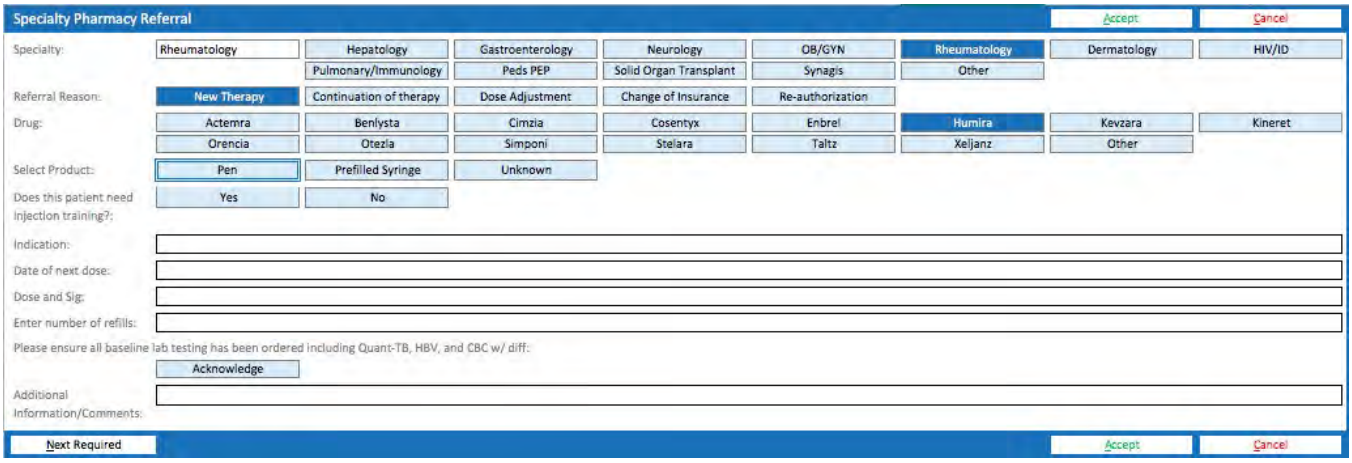


Figure 1a. Pre-Intervention Referral Shell. The previous order only allows providers to select a single medication without any alternatives in the event that the medication is denied.

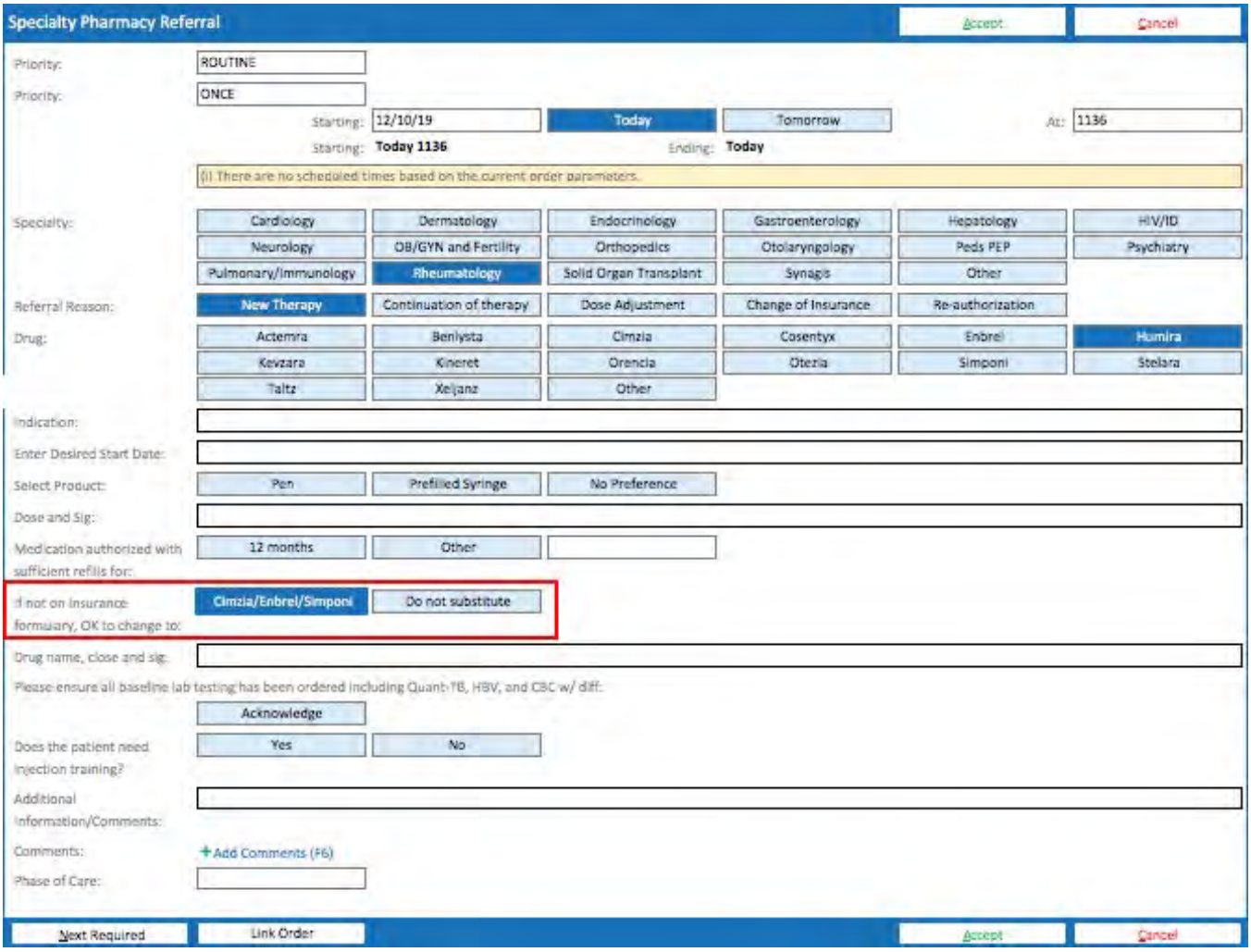


Figure 1b. Post-Intervention Referral Shell. The new order allows providers to select a replacement medication within the same class if the initial medication is not approved as shown by the red box.

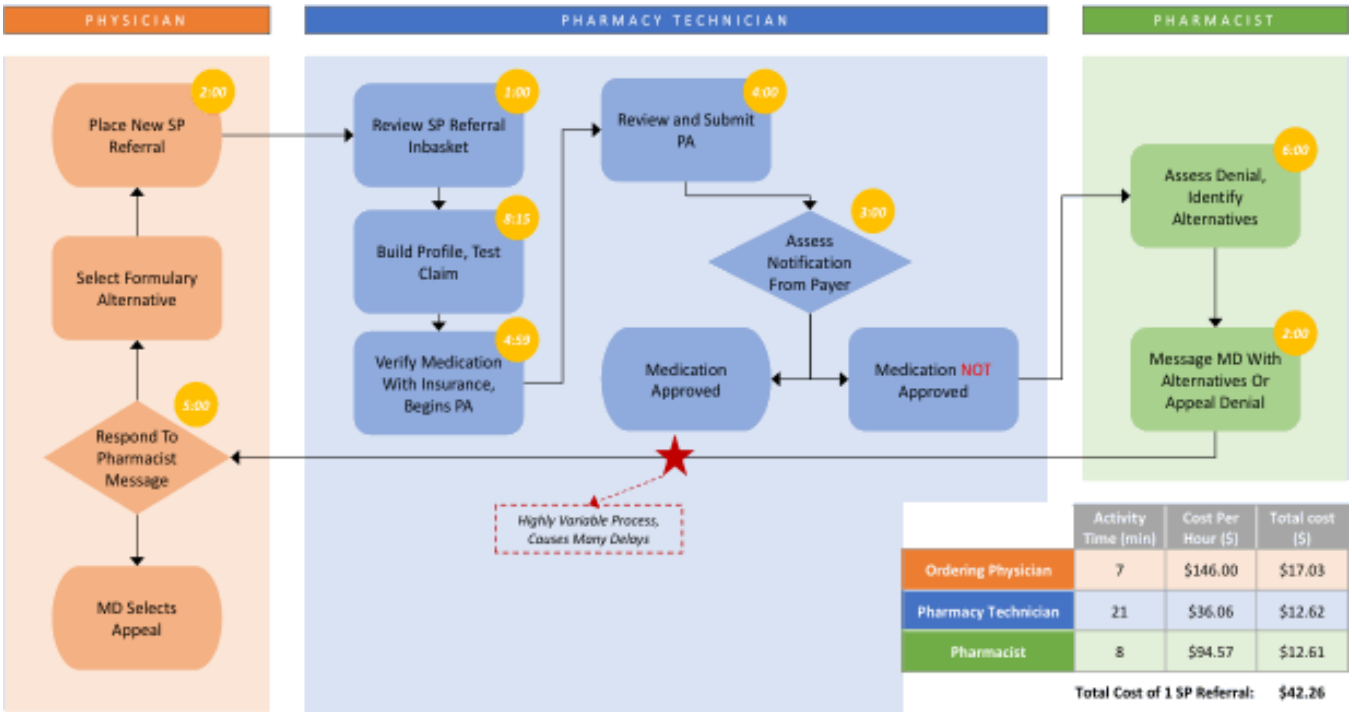


Figure 2. Specialty Pharmacy (SP) Referral Process Map. This map was created by our multidisciplinary group to identify all steps in our SP referral process and identify areas of delay within the process. Using time-driven activity-based costing (TDABC), a tool used to estimate the cost of processes in different sectors such as health care, we measured the amount of time (in minutes), noted in yellow circles, needed to complete each step in the process. This allowed us to generate an estimate for the cost of each SP referral.

Methods: To prescribe a biologic in rheumatology clinic, providers fill out a specialty pharmacy (SP) referral through our electronic medical record. They select which medication they would like to use and indication (Figure 1a). This is then sent to our pharmacy department for further review. We assembled a multidisciplinary team of pharmacy, medicine and rheumatology personnel and created a process map of the SP referral process and identified several causes of delay (Figure 2). The longest delay identified was waiting for provider approval of the subsequent, preferred, medication. We recorded the amount of time each step of the process took and their associated costs. We used Kaplan and Porter's time-driven activity-based costing (*Harv Bus Rev,* 2011*, 89(9), 46-52*) to estimate the resulting cost of this process.

Our intervention modified the SP referral to give the ordering physician the ability to allow the pharmacist to switch within the same class of biologic medication if the initial medication is denied (Figure 1b). This extra prompt was created for TNF-α, IL-6, IL-1 and IL-17A inhibitors.

Results: Pre-intervention, we found that 25% of rheumatologic SP referrals at our institution were denied by insurance. On 10/21/2019, our intervention was implemented. Subsequently, we analyzed all SP referrals between 10/21/2019-5/4/2020 and found 210 that were eligible for the ordering provider to use our intervention. The usage rate of our intervention was 15.7% (33/210 referrals). Of these 33 referrals, 21(64%), 7 (21%), and 5 (15%) were for TNF-α, IL-6 and IL-17A inhibitors, respectively. Four (12.1%) were denied by insurance and were appropriately switched to a same-class replacement. Three of these four referrals were for TNF-α inhibitors—the remaining referral was for an IL-17A inhibitor. Notably, the average time between initial referral—including insurance denial—and subsequent approval of the second, insurance-preferred medication, was 19 days post-intervention, compared to an average time of 64 days pre-intervention. Using time-driven activity-based costing, the amount saved each time the intervention was used was estimated to be $42.16.

Conclusion: There is significant time- and cost-related burden when medications are denied for non-medical reasons. Our early results show promise that our intervention will reduce cost and time delays and allow patients to start necessary treatment in a timely fashion. Though close, we have not yet met our desired usage rate but anticipate that we will be able to raise further awareness of the tool and also expand this intervention to other medications.

Disclosure: J. Waytz, None; **D. Sultan**, None; **V. Patel**, None.

Abstract Number: 1966

Improving Value Concordant Care Through Increased Use of Subcutaneous Methotrexate in Rheumatoid Arthritis

Jason Bankert[1], Jonida Cote[2], Joseph Chronowski[1] and Eric Newman[1], [1]Geisinger Medical Center, Danville, PA, [2]Geisinger Medical Center, Danvile, PA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

Background/Purpose: Rheumatoid Arthritis (RA) is an expensive disease which untreated can lead to disability and socioeconomic burden. This high cost of treatment impacts the use of limited medical resources. Subcutaneous (SC) methotrexate (MTX) has higher bioavailability, greater efficacy and better tolerability when compared with oral MTX. Furthermore, it is a less costly treatment prior to starting biologics. In our study, we aimed to provide Treat-to-Target and value concordant care by increasing the use of SC MTX.

Figure 1: Percent of methotrexate-treated Rheumatoid Arthritis patients using subcutaneous (SC) methotrexate (MTX)

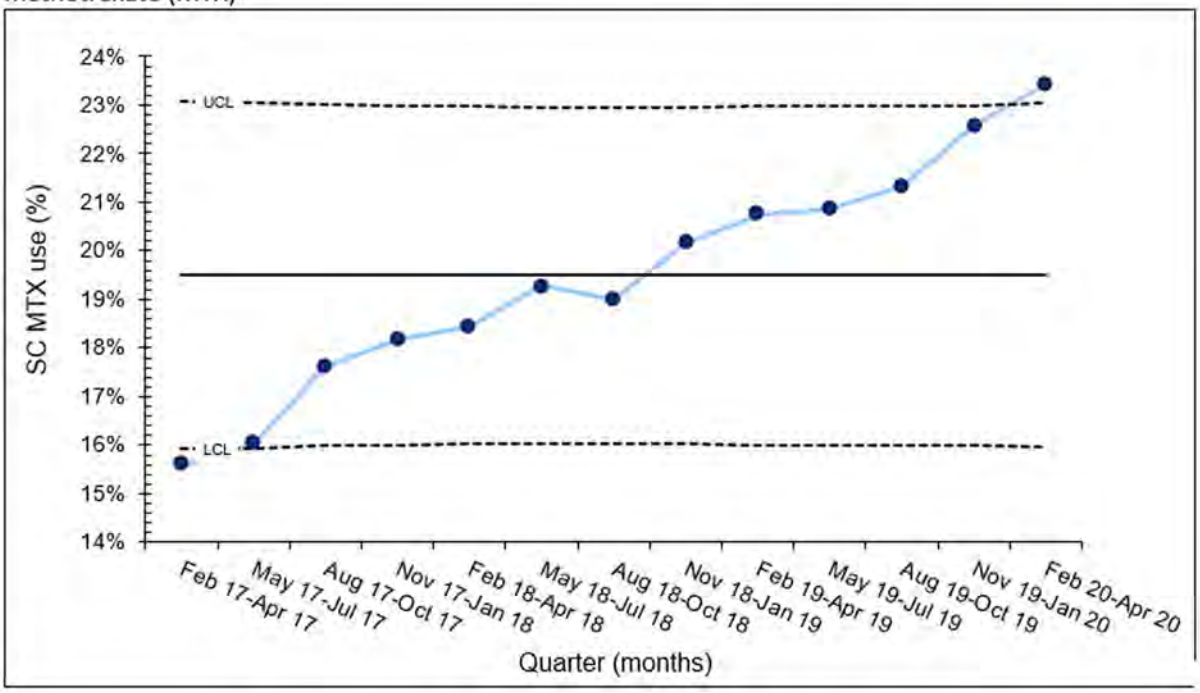
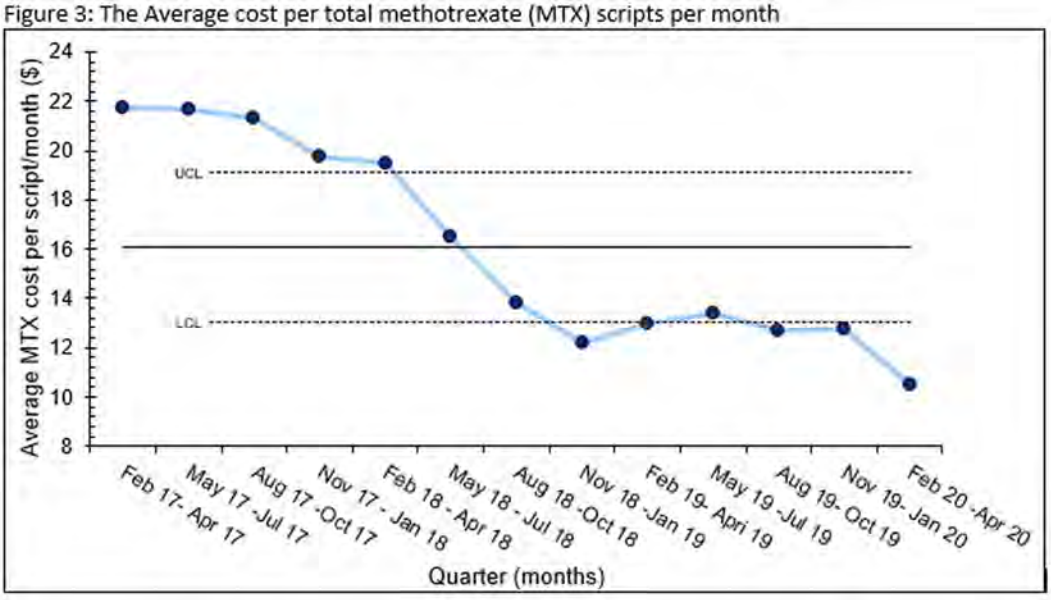


Figure 2. The relative increase of subcutaneous (SC) methotrexate (MTX) use per individual rheumatologist

Physicians	Baseline SC MTX use 2/28/2017 (%)	Post-intervention SC MTX use 4/30/2020 (%)	Relative increase of SC MTX use (%)
A	7.4	30.6	314
B	13.3	35.3	165
C	16.7	43.8	162
D	8.9	20.3	128
E	28.4	63.2	123
F	8.1	16.1	99
G	7.3	14.5	99
H	25.5	45.5	78
I	37.5	57.7	54
J	22.4	33.9	51
K	35.9	54.1	51
L	37.5	50	33
M	8.3	10.6	28
N	6.2	6.7	8
O	16.2	17.1	6
P	16.7	15.8	-5
Q	17.1	14	-18

Figure 3: The Average cost per total methotrexate (MTX) scripts per month



Methods: Baseline and prospective data on RA patients treated with MTX were obtained from the EHR (Epic) 2/1/2017 -4/2020 with intervention starting 11/2018. Prior to testing, a Treat-to-Target plan for increasing the use of SC MTX was discussed with the rheumatologists. A value concordant DMARD table was built and available in the EHR during each visit. Patients received medication education via the physician or rheumatology pharmacist. Data on value concordant MTX use, Clinical Disease Active Index (CDAI) and financial costs was collected and analyzed quarterly pre and post intervention. SC MTX was designated as value concordant while oral MTX was designated as non-value concordant. The percentage of value concordant MTX use was calculated by dividing SC MTX by total MTX use. The mean uncontrolled CDAI was calculated by dividing the number of RA patients with CDAI >10 by the total RA population with a CDAI. The MTX cost was determined by calculating the average cost per MTX script per

month (both oral and SC methotrexate). Shewhart charts were used to analyze data. The SC MTX use per individual physician pre and post intervention was determined by finding the absolute and relative increase for each.

Results: The use of total SC MTX among RA patients showed an absolute and relative increase of 8% and 50% respectively between 2/2017 at baseline to 4/30/2020 post intervention (Figure 1). The Shewhart P-Chart analysis met statistical significance for increased SC MTX use. 88% of individual physicians prescribing MTX had a relative increase of 93% SC use with high to low range varying between (+)315% to (-)18% (Figure 2). The % of RA patients with CDAI > 10 remained stable during the study. The average cost per MTX script per month within our health care plan steadily decreased from $21.73 (2/1/17- 4/30/17) pre intervention to $10.53 (2/1/20 - 4/30/20) post intervention for an absolute cost decrease of 49% meeting statistical significance per Shewhart I-chart (Figure 3).

Conclusion: The healthcare cost associated with RA treatment is substantial, and it creates a financial and economic burden. Patients and rheumatologists can work together to create individualized treatment plans to control the disease without causing excessive financial strain. Our study showed that the increased use of SC methotrexate provided a more cost-effective treatment plan for our RA population by reducing the average methotrexate cost per script per month by 49% without compromising the quality of care. It also suggested that the intervention we used was successful in modifying our rheumatologists' decision making to provide greater value concordant care.

Disclosure: J. Bankert, None; **J. Cote**, None; **J. Chronowski**, None; **E. Newman**, None.

Abstract Number: 1967

Combating Rheumatologist Burnout: Use of Protocol Driven Medication Refill by Pharmacists

Eva Rottmann[1], Jonida Cote[2], Swana Thomas[3], Dante Grassi[1], Joseph Chronowski[1], Lisa L. Schroeder[1], David Pugliese[4] and Eric Newman[1], [1]Geisinger Medical Center, Danville, PA, [2]Geisinger Medical Center, Danvile, PA, [3]Geisinger Medical Center, Wilkes-Barre, PA, [4]Geisinger Health System, Wilkes Barre, PA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Measures & Measurement of Healthcare Quality
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

Background/Purpose: Increased electronic health record (EHR) administrative workload is a great source of physician dissatisfaction. We embedded pharmacists into our Rheumatology team in 2019. This study explored the impact of pharmacist integration on reducing physician workload and burnout.

Methods: The monthly volume of medication refills by rheumatologists was measured as a baseline from 1/30/2019 to 9/30/2019 within our EHR (Epic). Protocol driven medication refill parameters for DMARDs and non-DMARDs were created per American College of Rheumatology guidelines. Using these refill parameters, physician time needed per refill was derived by averaging the time per message for 40 refills across 5 physicians. After implementation of pharmacists, the monthly volume of refills by pharmacists and physicians was measured from 10/1/2019 to 3/31/2020. Total physician time saved was calculated by multiplying the number of pharmacist refill encounters with average physician refill time. The time saved per month was divided by the number of clinical full-time equivalents to calculate the time saved per rheumatologist. Shewhart P-charts were used to measure significance for volume and time saved. Rheumatologists' satisfaction with EHR work was gauged via anonymous electronic survey pre- and post-pharmacist addition. Satisfaction was rated from 1 (not happy) to 5 (high satisfaction). Two additional questions were asked

Figure 1. Rheumatologists vs Rheumatology Pharmacists Monthly Refill Volume

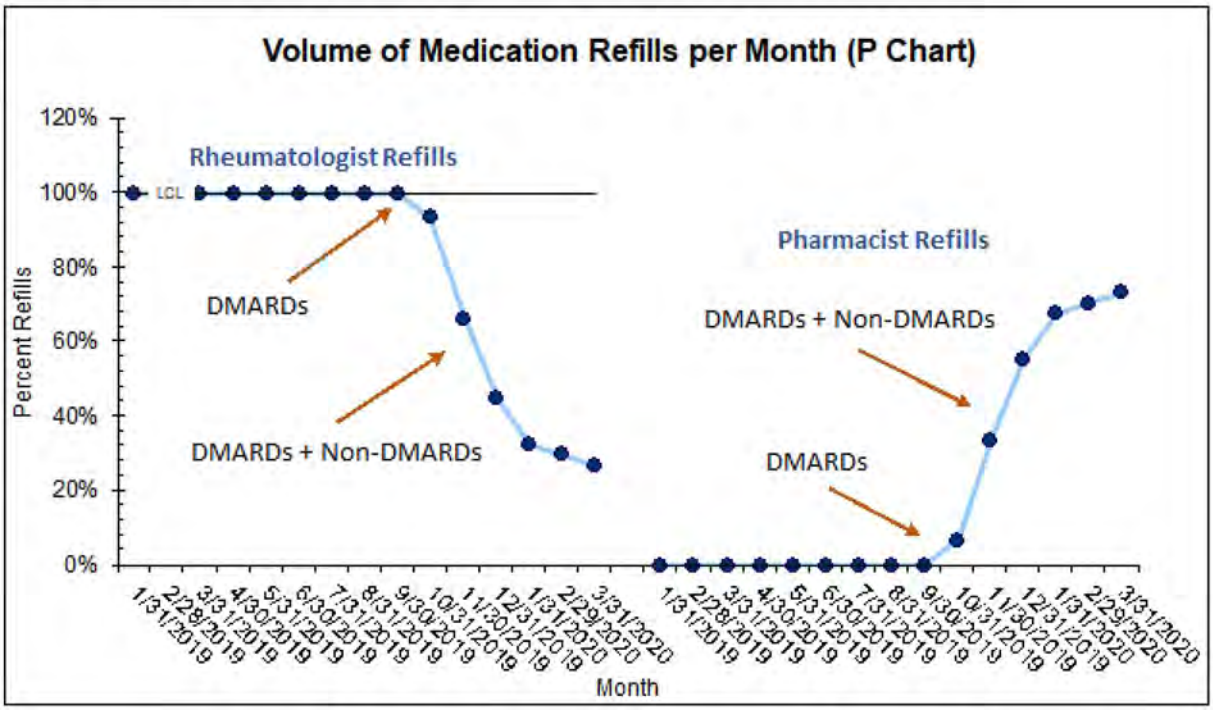
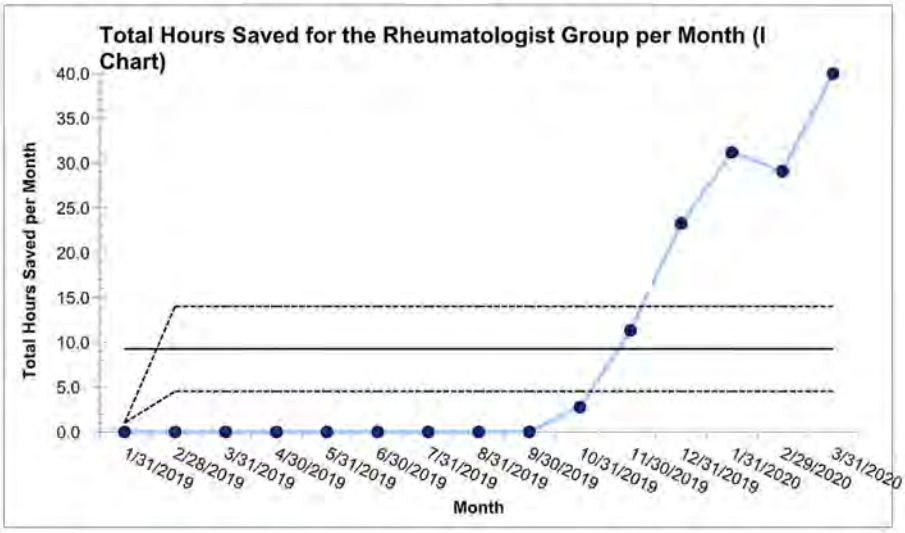


Figure 2. Time Saved for the Rheumatologist Group by the Introduction of Pharmacists



in the post pharmacist survey related to effect on work and burnout. 100% of physicians responded to the pre-survey and 93% of physicians responded to the post survey.

Results: The volume of medication refills by physicians decreased from about 1201 refills per month (or 100% of all refills) pre-pharmacist to 464 refills per month (or 27% of all refills) post-pharmacist integration (Figure1). The total time saved for all the rheumatologists (15 physicians, 7.75 FTEs) increased from 0 hours per month pre-pharmacist in September 2019 to 41.5 hours per month post-pharmacist in March 2020 (Fig.2). The time saved per physician FTE increased from 0 hours per month in September 2019 to 5.4 hours per month in March 2020 (Fig.3). Shewhart P

Figure. 3. Time Saved per Rheumatologist FTE by the Introduction of Pharmacists

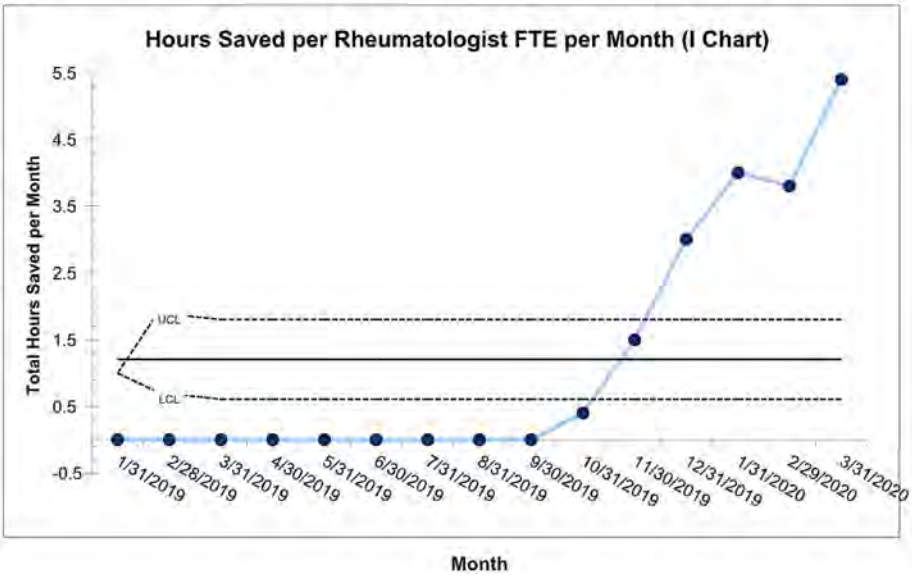


chart analysis met statistical significance for time saved per the individual and group of rheumatologists respectively with the implementation of pharmacists in our team. The surveys showed that the mean satisfaction with EHR refill work improved from 1.4 +/-0.2 at baseline to 4.3 +/-0.2 ($p< 0.001$) post pharmacist introduction. 100% of physicians reported that the pharmacist addition to their daily workflow helped them leave work on time and their workload interfered less with life outside of work (n=14), and 79% of physicians reported less burn out.

Conclusion: In early 2020, 51% of rheumatologists reported burnout in the workplace. This negatively impacts physician work effort, patient outcomes, and healthcare costs. Our study showed that pharmacists' medication refills alone have decreased physician EHR work and burnout. This shows great potential for other areas of improvement through pharmacist integration. Implementing a pharmacist into practice has brought us closer to achieving the 4th Aim of Quadruple Aim-improving the work life of the rheumatologist.

Disclosure: E. Rottmann, None; **J. Cote**, None; **S. Thomas**, None; **D. Grassi**, None; **J. Chronowski**, None; **L. Schroeder**, None; **D. Pugliese**, None; **E. Newman**, None.

Abstract Number: 1968

Cathepsin S Gene Expression Measured in the Peripheral Blood of Osteoarthritic Patients Prior to Surgery as a Biomarker of Post-operative Pain Development

Elena Tchetina[1], Kseniya Glemba[1], Galina Markova[1], Maksim Makarov[1] and Aleksandr Lila[1], [1]Nasonova Research Institute of Rheumatology, Moscow, Russia

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Osteoarthritis & Joint Biology – Basic Science

Session Type: Abstract Session

Session Time: 12:00PM–12:50PM

Background/Purpose: Osteoarthritis (OA) is a chronic rheumatic disease, which involves pain, limited inflammation, and local destruction of the knee joint. OA pain is a major clinical symptom, which limits working capacity and denotes an important indication for joint replacement in the end-stage OA. In spite of significant number of positive outcomes, chronic postoperative pain represents a major adverse consequence of surgery, which is observed in 10-40% of OA patients. Therefore, identification of patients potentially capable of developing chronic postoperative pain prior to surgery could significantly improve therapy outcome. Here we aimed to identify genes whose expression in the peripheral blood prior to surgery would indicate OA patients under risk of post-operative pain development.

Methods: We examined peripheral blood of 26 healthy volunteers (55±8.3 years) and 40 end-stage OA patients (56.5±8.9 years) undergoing knee joint replacement surgery. Patients were examined prior to surgery and 6 months' post-surgery. Nociceptive pain was assessed using VAS index whereas neuropathic pain, using DN4 and PainDETECT questionnaires prior to surgery. Functional activity was evaluated by WOMAC. Pain indices after surgery according to VAS of 30% and higher were considered. MMP-9 and caspase 3 protein levels were quantified by ELISA. Total RNA isolated from whole blood was used in expression studies for caspase 3; metalloproteinase (MMP)-9; cathepsins K and S genes. These were performed with quantitative real-time RT-PCR prior to surgery.

Results: Out of 40 patients pain complaints were obtained from 9 patients (22,5%) after 6 months' post-surgery. Prior to surgery all the examined genes were significantly upregulated in the patients who developed post-operative pain and those subjects who did not develop pain after surgery compared to healthy controls. However, no difference in the clinical levels of the pain-related and functional indices in the examined patients was observed before surgery. ROC curve analyses confirmed significant associations ($p< 0.05$) between expressions of the examined genes prior to surgery with the likelihood of pain development after surgery. The cut-off values for the examined gene expressions were 11.34 for cathepsin S, 10.11 for caspase 3, 10.09 for cathepsin K. Among the examined genes cathepsin S expression was the most appropriate predictor of post-operative pain development [AUC= 0.857, 95%CI (0.708-1.000)].

Conclusion: High cathepsin S gene expression in the peripheral blood of the end-stage OA patients measured prior to joint replacement surgery could serve an important biomarker of post-operative pain development.

Disclosure: E. Tchetina, None; **K. Glemba**, None; **G. Markova**, None; **M. Makarov**, None; **A. Lila**, None.

Abstract Number: 1969

The Dynamics of Macrophage Sub-Populations in the Inflammatory Phase Following Joint Trauma

Samuel Hamilton[1], Anna Montgomery[1], Niamh Fahy[2], Maximilian Mayr[1], Shang-Yang Chen[1], Gaurav Gadhvi[1], Yvonne Bastiaansen-Jenniskens[2] and **Deborah Winter**[3], [1]Northwestern University, Chicago, IL, [2]Erasmus MC, Rotterdam, Netherlands, [3]Northwestern University Division of Rheumatology, Chicago, IL

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis & Joint Biology – Basic Science
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

Background/Purpose: Macrophages fulfill critical functions in maintaining tissue homeostasis in steady-state, as well as in inflammation and immune response. In the joint synovium, we have previously shown using single-cell RNA-seq that four distinct populations of macrophage co-exist in steady state: synovial lining, interstitial, antigen-present-

ing, and infiltrating. Our goal is to understand the role of these different macrophages in the inflammatory phase that follows joint trauma. Synovial inflammation has been shown to key in the development of long term cartilage damage and osteoarthritis (OA): thus, macrophages may provide a therapeutic target for prevention and treatment.

Methods: We used a mouse model of post-traumatic OA (CIOA) where mice develop cartilage damage a few weeks after intra-articular injection of collagenase into the synovial space of the knee. We euthanized male mice (aged 8-12 weeks) at days 0, 3, 7, 11, and 28 post-CIOA. Knees were dissected, extraneous muscle tissue resected, and joints processed for Fluorescence-Activated Cell Sorting (FACS). Macrophages were identified as CD45+CD11B+Ly6G-Ly6C-CD64+ cells and further subdivided into four populations by expression of MHCII and CX3CR1. RNA was extracted from these cells and RNA-seq was performed using full-length SMART-seq v4 Ultra Low Input Kit. After sequencing on Illumina Nextseq, bcl files were demultiplexed and resulting fastq files were trimmed with Trimmomatic, aligned to mm10 with tophat, and mapped to genes with HTseq to generate a table of gene expression for analysis.

Results: All macrophage populations were increased in number during peak inflammation on day 3 post-CIOA and returned to approximately steady-state levels by day 28. We found that each macrophage sub-population exhibited distinct gene expression at day 0 but their transcriptional profiles appeared to converge on day 3. By resolution of inflammation on day 28, the transcriptional profile of each sub-population resembled steady-state. The transcriptional signatures over time suggested two dominant trends drove macrophage response: genes that were differentially expressed primarily in the synovial lining population and genes that were differentially expression in all four sub-populations in the same pattern. Synovial lining macrophages up-regulated of cell cycle and monocyte genes suggesting this population may expand through a combination of proliferation and differentiating monocytes. This population down-regulated genes associated with its specific synovial lining phenotype, which was confirmed by overlap with genes from human data. The expression patterns observed in all macrophages included the up-regulation of genes associated with IL-1B/IL-6 inflammation and down-regulation of homeostatic genes.

Conclusion: Understanding the function of macrophages following joint trauma is likely to provide insight into the resulting joint instability that leads to the development of cartilage damage and OA. By investigating the role of specific macrophage subsets, we may elucidate potential targets for the prevention or attenuation of OA-associated cartilage damage.

Disclosure: S. Hamilton, None; **A. Montgomery**, None; **N. Fahy**, None; **M. Mayr**, None; **S. Chen**, None; **G. Gadhvi**, None; **Y. Bastiaansen-Jenniskens**, None; **D. Winter**, None.

Abstract Number: 1970

Mimicking Cytokine-driven Key Features of Arthritis Using a Human *in Vitro* 3D Joint Model

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis & Joint Biology – Basic Science
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

Background/Purpose: Our ultimate goal is to study potential drug candidates in an experimental setting of arthritis. Therefore, we aim to develop a human *in vitro* 3D joint model mimicking key features of arthritis by applying inflammatory conditions namely immune cells and pro-inflammatory cytokines. Our i*n vitro* 3D joint model consists of different components: i) osteogenic and ii) chondrogenic part, iii) joint space with synovial fluid and iv) synovial membrane. Developed as an alternative *in vitro* approach to animal experiments, our 3D joint model will enable us to study efficiently the effects of potential drug candidates in a more translational setup.

Here, we aimed to demonstrate the suitability of our human *in vitro* 3D osteochondral tissue model (OTM) by analyzing the influence of the main cytokines involved in the pathogenesis of RA as well as the impact of approved drugs.

Methods: The OTM was engineered by co-cultivation of human mesenchymal stromal cell (hMSC)-derived bone and cartilage components in a 3D environment and comprehensively characterized (e.g. cell vitality, morphology, structural integrity) using histological, biochemical and molecular biological methods, µCT and scanning electron microscopy. In brief, to establish the osteogenic component, we populated β-tricalcium phosphate (TCP) – mimicking the mineral bony part – with hMSCs, while the scaffold-free cartilage component was generated by cellular self-assembly and intermittent mechanical stimulation (fzmb GmbH). To test the suitability of our OTM, we applied a cocktail of TNFα, IL-6 and MIF using concentrations reported from RA synovial fluid alone or in combination with approved therapeutic drugs and analyzed their impact by qPCR.

Results: We verified the osteogenic phenotype of our 3D bone component by demonstrating an increase in mineralized bone volume and the induction of bone-related gene expression (*RUNX2*, *SPP1*, *COL1A1, OC)* as compared to the corresponding control. Secondly, we verified the chondrogenic phenotype of our cartilage component by HE and Alcian Blue staining as well as by the reduced expression of *COL1A1* and an abundant expression of *COL2A1*. Interestingly, co-cultivation of both components for up to 3 weeks demonstrated colonization, connectivity and initial calcification implying a transitional bridging area. The exposure of OTM to TNFα, IL-6 and MIF caused cell- and matrix-related changes, such as the significant induced expression of the metabolic marker *LDHA,* the angiogenic marker *VEGF* and the inflammation markers *IL8* and *TNF* in both bone and cartilage, while *IL6* is downregulated in bone compared to the unstimulated control. Moreover, a cytokine-related significant upregulation of *MMP1* and *MMP3* expression was observed in cartilage compared to bone. Due to the specific drug treatment (adalimumab, tocilizumab, milatuzumab), the induction of inflammation and degradation could be prevented.

Conclusion: The results of our study showed that our human *in vitro* 3D OTM mimics cytokine-driven cell- and matrix-related changes - key features of RA. By combining the components in a 96-well format, we aim to provide a mid-throughput system for preclinical drug screening.

Disclosure: A. Damerau, None; **M. Pfeiffenberger**, None; **A. Lang**, None; **T. Gaber**, None; **F. Buttgereit**, AbbVie, 8, Eli Lilly, 8, Pfizer, 8, Roche, 8.

Abstract Number: 1971

Gut Microbiome Transplantation from MRL/MpJ Mice Prevents Post-Traumatic Osteoarthritis in C57BL6/J Mice

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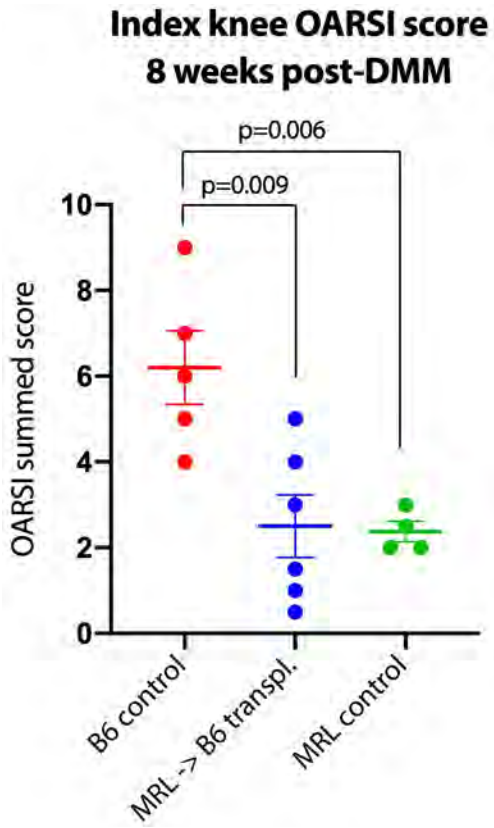
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis & Joint Biology – Basic Science
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

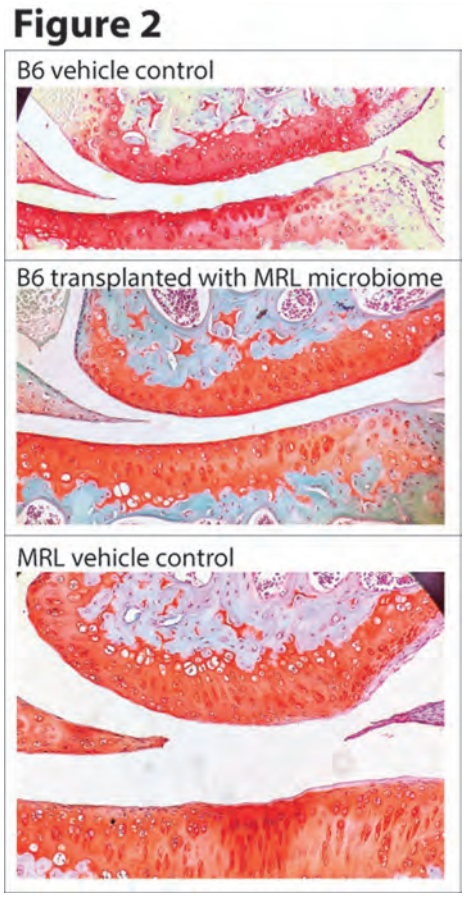
Background/Purpose: MRL/MpJ mice are substantially protected from developing post-traumatic osteoarthritis (OA), a trait with strong correlation to the ability to heal ear wounds. We have previously shown that this ear wound healing trait is partially determined by the gut microbiome, and that gut microbial transplantation into non-healer mice can confer the ear wound healing phenotype. In this study, we sought to examine whether microbiome-mediated cartilage regeneration extended to protection against post-traumatic osteoarthritis.

Methods: Twelve-week-old C57BL6/J mice were inoculated by oral gavage with diluted cecal contents from adult male MRL/MpJ mice (n=6). Separate groups of age-matched male C57BL6/J (n=5) and male MRL/MpJ mice (n=4) were gavaged with vehicle control. Destabilization of the medial meniscus (DMM) surgery was then performed unilaterally to induce OA. Eight weeks after DMM, mice were sacrificed, knee joints fixed in paraformaldehyde, decalcified, embedded in paraffin, stained with Safranin-O and histologically graded using the OARSI histopathology initiative recommendations by a blinded investigator. Differences in mean summed OARSI score per joint per group were determined by a Student t-test, $p \leq 0.05$ was considered significant.

Results: Adult male MRL/MpJ were protected against post-traumatic OA when compared to adult male C57BL/6J mice (mean summed OARSI score 2.4±0.2 vs. 6.2±1, p=0.006, Figure 1). MRL-transplanted adult male C57BL/6J mice were also protected against PTOA development (mean summed OARSI score 2.5±0.7, p=0.009 vs. B6 vehicle,



OARSI scoring of mouse knee following DMM surgery in microbiome transplanted and control animals.



Example histology images of mouse knee following DMM surgery in microbiome transplanted and control animals.

Figure 1) and were indistinguishable from MRL vehicle mice (p=0.90). Representative histologic sections are presented in Figure 2. Gut microbiome profiling and associations of specific gut microbial clades with OA susceptibility are forthcoming.

Conclusion: Gut microbiome transplantation from OA-protected MRL mice to OA-susceptible B6 mice is sufficient to confer protection against post-traumatic OA, consistent with previous data indicating microbiome transplantation-mediated transference of the MRL earhole healing phenotype. Future research should define the pathophysiological changes underlying this phenotype and may offer new insights into potential future therapies for articular cartilage regeneration.

Disclosure: M. Jeffries, None; **J. Martin**, None; **V. Izda**, None; **C. Garman**, None; **C. Velasco**, None; **C. Dunn**, None.

Abstract Number: 1972

NGF-Responsive Neurons Are Sensitized in Experimental Osteoarthritis

Rachel Miller[1], Shingo Ishihara[1], Alia Obeidat[1] and Anne-Marie Malfait[1], [1]Rush University, Chicago, IL

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoarthritis & Joint Biology – Basic Science
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

Background/Purpose: Nerve growth factor (NGF) is under investigation as a promising target for osteoarthritis (OA) pain. NGF exerts its potent pro-algesic effects through sensitization of nociceptors. Sensitization is a key process in chronic pain states, including OA, characterized by exaggerated responses to innocuous stimuli. However, the precise biological mechanisms underlying the pain-producing effects of NGF in OA are incompletely understood. Here, we tested whether nociceptors become sensitized to NGF in experimental OA.

Methods: DMM surgery was performed in the right knee of 10-week old male $Na_V1.8$ cre-GCaMP6s loxp mice. *In vivo* calcium imaging: $Na_V1.8$-GCaMP6s loxp mice 20 weeks after DMM (n=8) or age-matched naïve control (n=6) were used. These mice express the fluorescent calcium indicator, GCaMP6s, in nociceptors. *In vivo* calcium imaging of the L4-DRG was performed as described (Miller RE et al, Arthr Rheum 2018, PMID: 28992367). A series of compounds were injected IA into the right knee of anesthetized mice while imaging was performed: (1) Saline; (2) CCL2 (100 mg/mL); (3) 2.5S NGF (100 mg/mL); (4) Pam3CSK4 (1 mg/mL); (5) LPS (5 mg/mL); (6) capsaicin (10 mM). For each injection, a 30 G needle was inserted in the joint cavity, imaging was started, the compound was injected from frame 15-20, and imaging continued until frame 100. For each mouse, change in fluorescence over time was calculated using a custom ImageJ macro in order to identify responding sensory neurons. The area under the peak was calculated using GraphPad Prism. Knee hyperalgesia: 3 mL NGF (100 ng/mL, n=4 mice) or 3 mL of vehicle, n=4 mice) was injected IA in the right knee of 10-week old naïve mice. Knee hyperalgesia was assessed prior to injection and 30 mins, 2, 4, and 24 hours after injection using a Pressure Application Measurement device by a person blinded to treatment.

Results: Injection of NGF into the knee joints of anesthetized $Na_V1.8$-GCaMP6s mice elicited intracellular calcium increases in a similar number of neurons in naïve and DMM mice (mean±SEM; naïve: 1.7±1.0%; DMM: 2.6±0.7%; p=0.47), suggesting that the NGF receptor is expressed by a similar number of cells at this time point after DMM. As a comparison, we have previously shown that 15% of L4-DRG neurons innervate the knee joint in healthy mice.

Examining the intracellular calcium responses in each neuron, we found that responses were greater after DMM, as assessed by peak area under the curve (naïve: 0.9±0.2 peak AUC; DMM: 1.7±0.2 peak AUC; p=0.02), suggesting that neurons expressing the NGF receptor have become sensitized to NGF after DMM. Neurons that responded to NGF after DMM also responded more to CCL2 and LPS compared to NGF-responsive neurons in naïve mice (p=0.04 for both NGF-CCL2 and NGF-LPS), further suggesting that NGF-responsive neurons are sensitized in OA.

The neuronal response to NGF was reflected in the behavioral response, where IA administration of NGF, but not vehicle, induced knee hyperalgesia in naïve wild-type mice (NGF: 311±16 g; vehicle: 439±5 g; p=0.01).

Conclusion: These findings suggest that NGF directly binds to neuronal receptors in the IA space, and sensitizes neurons to mediators present in the OA joint.

Disclosure: R. Miller, None; **S. Ishihara**, None; **A. Obeidat**, None; **A. Malfait**, Pfizer, 5, Eli Lilly, 5.

Abstract Number: 1973

Treatment Sequences with Romosozumab Before or After Antiresorptive Medication

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Osteoporosis & Metabolic Bone Disease

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Prior studies of anabolic/antiresorptive treatment sequences indicate that using teriparatide first followed by an antiresorptive results in greater bone mineral density (BMD) gains, particularly at the total hip, vs using an antiresorptive first followed by teriparatide (Cosman JBMR 2017). Romosozumab (Romo) increases bone formation while decreasing bone resorption, significantly increasing BMD and reducing fracture risk within 1 year. Here we summarize BMD data with Romo prior to or following an antiresorptive (alendronate [Aln] or denosumab [DMAb]).

Methods: We evaluated percentage change from baseline in BMD at the total hip and lumbar spine from four trials where patients received Romo prior to an antiresorptive (Phase 3 ARCH [Saag NEJM, 2017] and Phase 3 FRAME [Cosman, NEJM 2016]) or Romo following antiresorptive therapy (Phase 3 STRUCTURE [Langdahl, Lancet 2017] and Phase 2 [Kendler, OI 2019]). Percentage change from baseline BMD was assessed by either an ANCOVA (FRAME) or repeated measures (ARCH, STRUCTURE) model adjusting for baseline covariates, or as summary statistics (Phase 2).

Results: Total hip BMD (Figure 1): In ARCH, BMD increased 6.2% with 1 year of Romo, and a total of 7.1% with the 2-year Romo/Aln sequence; and in FRAME, patients gained 6.8% with 1 year of Romo and a total of 8.8% with the 2-year Romo/DMAb sequence. Patients in STRUCTURE, who were previously treated for ≥1 year with Aln, gained 2.9% with 1 year of Romo. In a Phase 2 study, following 1 year of DMAb, 1 year of Romo increased BMD by 0.9%, for a total gain of 3.8% with the 2-year DMAb/Romo sequence.

Lumbar Spine BMD (Figure 2): In ARCH, BMD increased 13.7% with 1 year of Romo, and a total of 15.2% with the 2-year Romo/Aln sequence; and in FRAME, patients gained 13.3% with 1 year of Romo and a total of 17.6% with the 2-year Romo/DMAb sequence. Patients in STRUCTURE (previously on Aln for ≥1 year) gained 9.8% with 1 year of Romo. In the Phase 2 study (after 1 year of DMAb), 1 year of Romo increased BMD by 5.3%, for a total gain of 11.5% with the 2-year DMAb/Romo sequence.

Conclusion: These data demonstrate that treatment with Romo first produces substantial BMD gains at the total hip and lumbar spine within 1 year, and that subsequent transition to a potent antiresorptive can augment those gains. In patients treated with Aln or DMAb, transition to Romo can improve BMD, though gains are not as large as those seen when Romo is used first. Since BMD on treatment is a strong surrogate for bone strength, our findings support

Figure 1

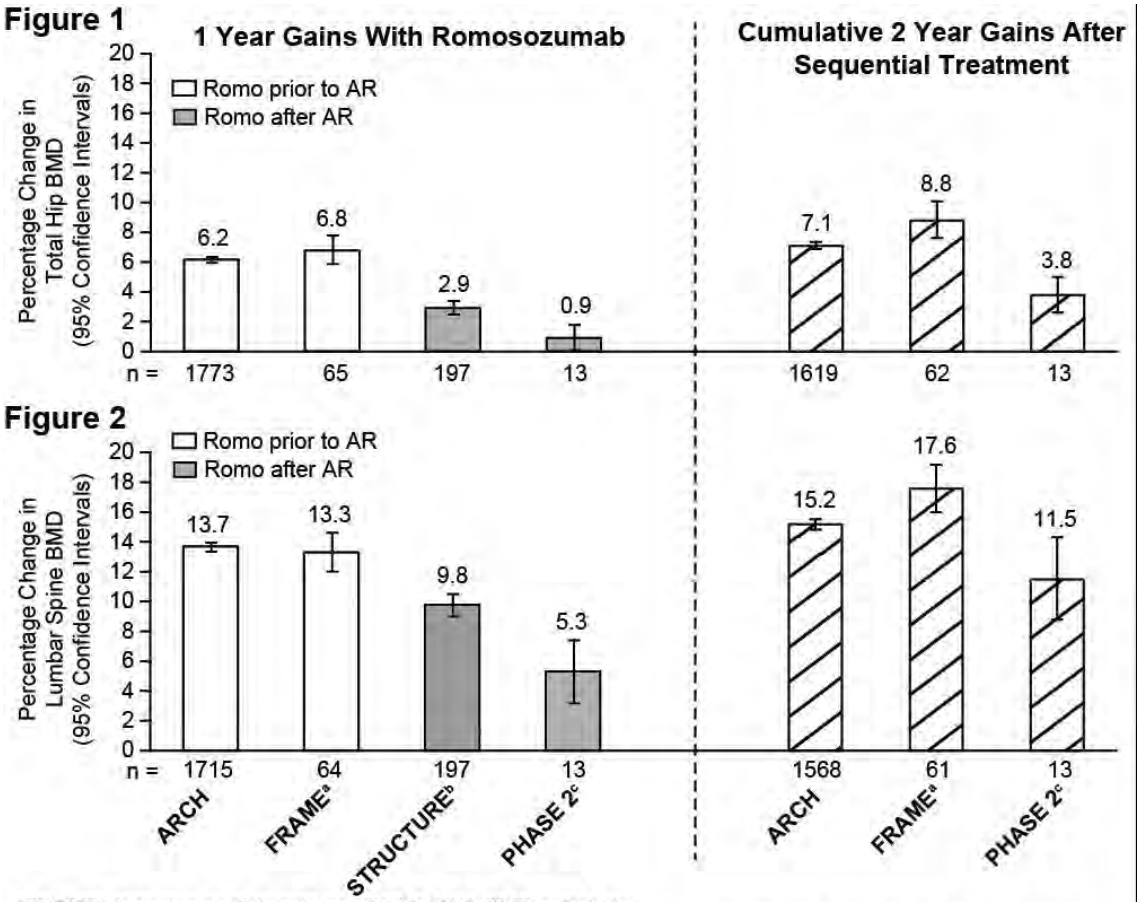

Figure 2

[a]FRAME: Includes participants enrolled in DXA BMD substudy.
[b]Participants had received oral bisphosphonate for ≥3 years before screening and alendronate (70 mg QW) ≥1 year immediately before screening; total study time was 1 year.
[c]A subset of participants in the Phase 2 study received placebo during months 0–24, denosumab during months 24–36 and romosozumab during months 36–48. Cumulative gains are relative to the month 24 baseline.
AR = antiresorptive, Romo = romosozumab.

the concept that high-risk patients should be offered treatment with Romo first, followed by transition to a potent antiresorptive

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Disclosure: F. Cosman, Amgen Inc., 1, 2, 3, Radius Health, 1, 2; **D. Kendler**, Radius, 1, Amgen Inc., 1, 2, 3, Eli Lilly, 1, 2, Pfizer, 1; **B. Langdahl**, Amgen Inc., 1, 2, 3, Novo Nordisk, 1, UCB, 1, 2, Eli Lilly, 1, Gedeon-Richter, 1, Gilead, 1; **B. Leder**, Amgen Inc., 1, 2, Radius, 1; **E. Lewiecki**, Radius, 1, 2, 3, Amgen Inc., 1, 2, Mereo, 1, Bindex, 1, Alexion, 1, 2, Sandoz, 1, Samsung, 1, Bioepis, 1, Sanifit, 1, University of New Mexico, 1, UpToDate, 1, National Osteoporosis Foundation, International Society for Clinical Densitometry, 1, National Osteoporosis Foundation, International Society for Clinical Densitometry, 1; **A. Miyauchi**, Amgen Inc., 1, Astellas BioPharma K.K., 1, Teijin Pharma, 1; **M. Rojeski**, Amgen Inc., 1, 2; **M. McDermott**, Amgen Inc., 1, 2; **M. Oates**, Amgen Inc., 1, 2; **C. Milmont**, Amgen Inc., 1, 2; **C. Libanati**, UCB Pharma, 1, 2; **S. Ferrari**, Amgen Inc., 1, 2, UCB, 1, 2, Agnovos, 1, 2, Alexion, 1, Radius, 1, Gideon Richter, 1, Galapagos, 1.

Abstract Number: 1974

Validation of a Deep Learning Based Algorithm to Diagnose Vertebral Compression Fractures

John Page[1], **Franklin Moser**[2], Marcel Maya[3], Ravi Prasad[3] and Barry Pressman[2], [1]Amgen, Inc, Thousand Oaks, CA, [2]Cedars-Sinai Medical Center, Los Angeles, CA, [3]Cedars-Sinai Medical Center, Los Angeles

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoporosis & Metabolic Bone Disease
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Vertebral Compression Fractures are common in patients above age 50, but are often undiagnosed. Patients with one VCF are at higher risk of other osteoporotic fractures. Zebra Medical Imaging developed a VCF detection algorithm, utilizing a combination of traditional machine vision segmentation and convolutional neural network (CNN) technology, to detect VCFs from evaluating CT images of the chest, and/or abdomen/pelvis.

Methods: We conducted an independent and blinded validation study to estimate the operating characteristics of the Zebra VCF detection algorithm in identifying VCFs on de-identified data from previously completed CT scans of chest and/or abdomen/pelvis from 1200 women and men aged 50 or older who had those scans (for multiple reasons) at the clinics and hospitals affiliated with the Cedars Sinai Medical Center. Each set of scans were independently read by two of three board certified, practicing neuroradiologists to identify and grade VCF at each evaluable vertebra (using the semiquantitative scale of Genant and colleagues). When there was disagreement between radiologists, the respective scans were reviewed by a senior neuroradiologist who provided a final evaluation. The final determination of presence and severity of VCF by the neuroradiologists was used as the reference standard. The Zebra VCF detection algorithm evaluated the CT scans in a separate workstream from that used by the neuroradiologists (The algorithm and neuroradiologists were blind to each other's evaluations).

		Combined Radiologist Diagnosis						
Zebra Detection Algorithm Diagnosis		Yes	No	Total N	Sensitivity (95%)	Specificity (95%)	Positive Likelihood Ratio (95%)	Negative Likelihood Ratio (95%)
Mild, Moderate or Severe versus No VCF	Yes	149	82	1087	0.66 (0.59, 0.72)	0.90 (0.88, 0.92)	6.88 (5.32, 8.44)	0.38 (0.31, 0.45)
	No	78	778					
Moderate or Severe versus Mild or No VCF*	Yes	107	124	1087	0.78 (0.70, 0.85)	0.87 (0.85, 0.89)	5.98 (4.87, 7.10)	0.25 (0.17, 0.33)
	No	30	826					
Severe versus No, Mild or Moderate VCF*	Yes	47	184	1087	0.84 (0.72, 0.92)	0.82 (0.80, 0.84)	4.70 (3.88, 5.52)	0.20 (0.08, 0.31)
	No	9	847					
³ 2 fractures versus none/one VCF*	Yes	90	141	1087	0.78 (0.70, 0.85)	0.85 (0.83, 0.88)	5.40 (4.42, 6.37)	0.25 (0.17, 0.34)
	No	25	831					

*Results include different cut-points for maximum VCF severity and number of fractures
95% confidence limits for the sensitivity and specificity were calculated using an exact binomial distribution.

Comparison of diagnoses by radiologists and Zebra VCF detection algorithm (Operating Characteristics)

Results: The Zebra VCF algorithm was not able to evaluate CT scans for 113 patients. Of the remaining 1087 CT patients, 588 (54%) were women. Median age was 73 (range 51, 102; interquartile range 66, 81). The four neuroradiologists who evaluated the CT scans each had over 10 years of experience in neuroradiology. For the 1087 Zebra evaluated patients, 227 had at least one VCF (90 with mild VCF, 81 with moderate VCF, and 56 with severe VCF; 115 of the 1087 Zebra evaluated patients (10.6%) presented with two or more VCFs). The sensitivity and specificity of the Zebra VCF algorithm in diagnosing any VCF were 0.66 (95% confidence interval 0.59, 0.72) and 0.90 (95% confidence interval 0.88, 0.92) respectively; and for diagnosing moderate/severe VCF were 0.78 (95% confidence interval 0.70, 0.85) and 0.87 (95% confidence interval 0.85, 0.89) respectively.

Conclusion: The Zebra VCF algorithm works to identify approximately three-quarters of moderate to severe VCF in patients, aged 50 and above, who receive CT scans for other reasons. Implementing the Zebra VCF algorithm within radiology systems may help to identify patients at increased fracture risk and could support the diagnosis of osteoporosis, and thus be a valuable adjunct for population health.

Disclosure: J. Page, Amgen, Inc, 1, 2; **F. Moser**, None; **M. Maya**, None; **R. Prasad**, None; **B. Pressman**, None.

Abstract Number: 1975

Predicting Bone Mineral Density of Lumbar Vertebrae by Assessing Plain Film with Deep Learning

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoporosis & Metabolic Bone Disease
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Osteoporosis is a silent disease characterized by a decrease in bone mineral density (BMD), causing bone fragility and increased risk of fracture. The most widely used screening tool for osteoporosis involves the use of dual-energy x-ray absorptiometry (DXA) to measure BMD. Vertebral plain films may serve as an opportunistic screening for osteoporosis to improve screening rates at no additional cost or radiation to patients. We describe a novel approach to assess vertebral BMD using plain film with deep learning and compare the performance with the DXA measurement.

Methods: In this study, we identified 2171 patients who underwent DXA and lateral plain film of lumbar vertebrae within six months. The dataset was split into a training set with 1796 patients and a testing set with 412 patients. First to fourth lumbar vertebrae images were detected automatically by using the Deep Adaptive Graph (a landmark detection technique based on graph convolutional network) and regions of interest (ROI) in each lumbar vertebra were segmented. The ROIs are processed using a regression neural network with a VGG11 backbone that was applied to each ROI to predict the BMD (Figure 1). During training, five-fold cross-validation is performed with an 8:2 split ratio of training/validation sets. The five models obtained from the cross-validation are all used to predict BMD on the input image of the testing set, and the predictions are averaged to produce the final output. Images with vertebral fractures were excluded from the analysis. Pearson's correlation coefficient was used to assess the correlation between predicted and reference BMD.

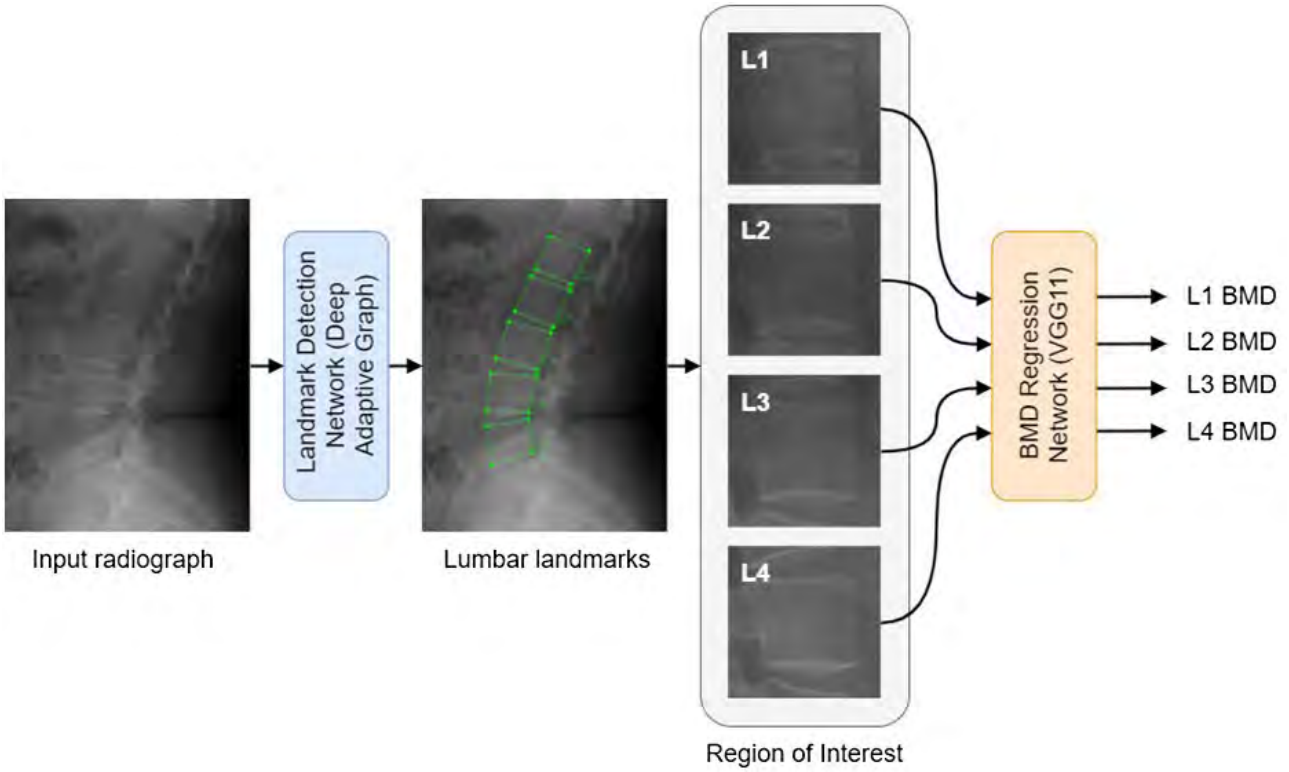

Figure 1. Schematic representation of deep learning models to extract image features for estimation of lumbar vertebral BMD.

Lumbar regions (n=412)	Mean BMD predicted by the model (g/cm^2)	Mean BMD measured by DXA (g/cm^2)	Absolute difference (g/cm^2)	Absolute difference percentage (%)	Pearson's correlation coefficient
L1 (n=347)	0.840±0.127	0.846±0.207	0.118±0.09	14.60%	0.68
L2 (n=371)	0.909±0.147	0.903±0.221	0.125±0.106	14.64%	0.67
L3 (n=367)	0.965±0.145	0.969±0.227	0.126±0.101	13.46%	0.71
L4 (n=358)	1.006±0.129	0.997±0.229	0.133±0.108	14.23%	0.67
Overall	0.930±0.123	0.926±0.206	0.126±0.084	14.23%	0.68

Table 1. Performance of prediction model for BMD using plain film compared with the measured BMD

Results: We included 395 women and 71 men in the testing dataset (female, 84.8%; mean age, 69.5 ± 10.7 years). The mean predicted BMD of first to fourth lumbar vertebrae was 0.930 g/cm^2 compared with that measured by DXA of 0.929 g/cm^2 (Student's t-test, p = 0.65). The mean absolute difference was 0.126±0.084 g/cm^2, with an absolute percentage difference of 14.6%. Pearson's correlation coefficient between predicted and true BMD was 0.68. The performance of the model to predict BMD and Pearson's correlation coefficient between predicted and measured BMD for each lumbar vertebra were shown in Table 1.

Conclusion: This study demonstrated that the deep learning model could predict vertebral BMD with reasonable precision, which might support automatic opportunistic bone density screening.\

Disclosure: C. Hsieh, None; **C. Kuo**, None; **S. Miao**, None; **K. Zheng**, None; **L. Lu**, None.

Abstract Number: 1976

High Disease Activity Is Associated with Incident Osteoporotic Fractures Among Veterans with Rheumatoid Arthritis

Katherine Wysham[1], Ted Mikuls[2], Bryant England[2], Dolores Shoback[3], Patricia Katz[4], Jose Garcia[1], Brian Sauer[5], Beth Wallace[6], John Richards[7], Paul Monach[8], Grant Cannon[9] and Joshua Baker[10], [1]VA Puget Sound/University of Washington, Seattle, WA, [2]University of Nebraska Medical Center, Omaha, NE, [3]San Francisco VA/University of California, San Francisco, San Francisco, CA, [4]University of California, San Francisco, Novato, CA, [5]University of Utah, Omaha, NE, [6]Michigan Medicine, VA Ann Arbor Healthcare System Center for Clinical Management Research, Ann Arbor, MI, [7]Veterans Affairs Pittsburgh Healthcare System, Pittsburgh, PA, [8]Brigham and Women's, Boston, [9]Salt Lake City VA Medical Center and University of Utah, Salt Lake City, [10]University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Osteoporosis & Metabolic Bone Disease

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Rheumatoid arthritis (RA) is a risk factor for osteoporosis and fractures yet the disease specific contributions to osteoporotic fractures (OFX) are not well understood. Chronic inflammation stimulates bone loss leading to low bone mineral density and also has negative effects on muscle mass and function, further amplifying the risk of falls and fractures. Our goal was to study whether RA disease activity, and its subcomponents, were independently associated with incident OFX.

Methods: We used the multicenter Veterans Affairs RA (VARA) registry, including participants with at least 1 DAS28-CRP measure in the analysis. Extremity, spine, and hip OFX were identified by ICD9/10 codes from inpatient and outpatient encounters and were confirmed by chart review. Cox proportional hazard models were used to assess the association between time-variant disease activity (averaged over all prior intervals) and incident OFX controlling for baseline sex, race, high ACPA (>60 units), rheumatic disease comorbidity index, osteoporosis status and time-variant age, BMI, smoking, prednisone use, conventional synthetic DMARDs (csDMARDs) and biologic use. Baseline osteoporosis diagnosis was defined by ICD9/10 code or prior fracture. We used DAS28-CRP in our primary analysis but also considered clinical disease activity index (CDAI) and individual RA disease activity components (Tender Joint Count (TJC), Swollen Joint Count (SJC), Patient Global Assessment (PatGA), Provider Global Assessment (PrGA), and CRP) in secondary analyses.

Results: Among 2,531 Veterans followed for 10,661 patient-years (including 25,694 unique observations), 145 incident OFX were identified at a rate of 1.4 per 100 person-years. Veterans were on average 71.2±10.5 years old, 11% were female, 79% were seropositive, and 10% had a diagnosis of osteoporosis at baseline (Table 1). High disease activity by average DAS28-CRP was associated with a significantly greater risk of incident OFX [HR 2.02 (1.22-3.33), p=0.006] (Table 2) compared to those in remission. In secondary analyses, high RA disease activity by CDAI was also associated with an increased risk of OFX [HR 3.56 (1.24-10.17), p=0.018]. All of the individual disease activity components were associated with a greater risk of OFX except TJC (Table 3). Female sex and high ACPA were significantly associated with higher and lower risks for OFX [HR 2.31 (1.44-3.71) and HR 0.69 (0.49-0.96), p< 0.05].

Conclusion: High RA disease activity is associated with twice the risk of OFX compared to those whose disease is in remission. All of the individual disease activity components were associated with a greater risk of OFX except TJC. The degree of control of RA disease activity may represent a modifiable risk factor for OFX. Studies evaluating the

Table 1. Descriptive table with baseline features as whole cohort and stratified by incident osteoporotic fracture (OFX). Numbers are mean±SD or N(%).

	Whole Cohort N=2531	Incident OFX N=144	No OFX N=2487
Age	71.2±10.5	71.6±8.3	71.2±10.6
Female	271 (11%)	26(18%)	245 (10%)
Black race	412 (16%)	20 (14%)	392 (16%)
Study visits (N)	12.8±11.3	15.8±13.2	12.6±11.1
High positive ACPA[a]	1421 (56%)	77 (53%)	1344 (56%)
RF positive	1754 (69%)	95 (66%)	1659 (70%)
RDCI score	0.30±0.75	0.35±0.98	0.30±0.74
Smoking category			
Never	519 (21%)	34 (24%)	485 (20%)
Current	633 (25%)	44 (31%)	589 (25%)
Former	1316 (52%)	65 (45%)	1251 (52%)
Prednisone use	901 (36%)	67 (47%)	834 (35%)
csDMARD use	1820 (72%)	100 (69%)	1720 (72%)
Biologic use	661 (26%)	38 (26%)	623 (26%)
OP medication	393 (16%)	35 (24%)	358 (15%)
OP diagnosis	243 (10%)	18 (13%)	225 (9%)
BMI category			
Underweight	72 (3%)	5 (3%)	67 (3%)
Normal weight	522 (21%)	30 (21%)	492 (21%)
Overweight	890 (35%)	60 (42%)	830 (35%)
Obese	542 (21%)	23 (16%)	519 (22%)
Morbidly obese	290 (11%)	17 (12%)	273 (11%)
DAS28-CRP[b]			
Remission	757 (30%)	33 (23%)	724 (30%)
Low	393 (16%)	21 (15%)	372 (16%)
Moderate	978 (39%)	58 (40%)	920 (39%)
High	403 (16%)	32 (22%)	371 (16%)
CDAI[c]			
Remission	164 (7%)	4 (3%)	160 (7%)
Low	485 (19%)	27 (19%)	458 (19%)
Moderate	471 (19%)	24 (17%)	447 (19%)
High	391 (15%)	29 (20%)	362 (15%)
Disease Activity Components			
TJC	4.8±6.6	5.2±6.7	4.8±6.6
SJC	3.9±5.3	5.1±6.3	3.8±5.2
PatGA	3.9±2.6	4.5±2.5	3.9±2.6
PrGA	3.3±2.3	3.7±2.4	3.3±2.3
CRP	1.5±2.6	2.2±3.5	1.5±2.5

-ACPA: anti-cyclic citrullinated peptide antibody; RF: rheumatoid factor; RDCI: rheumatic disease comorbidity index; conventional synthetic DMARDs; OP: osteoporosis; BMI: body mass index; DAS28-CRP: disease activity scale 28 joints with c-reactive protein; CDAI: clinical disease activity index; TJC: tender joint count; SJC: swollen joint count; PatGA: patient global assessment; PrGA: provider global assessment.

[a]-High positive ACPA defined as >60 units.

[b]-DAS28-CRP Categories: Remission <2.6, Low: 2.6-3.2, Moderate: 3.2-5.1, High: >5.1

[c]-CDAI Categories: Remission 0-2.8, Low: 2.9-10.0, Moderate: 10.1-22.0, High: 22.1-76.0

Table 2. Multivariable Cox proportional hazard model showing association between time-variant disease activity, measured DAS28-CRP averaged over all prior intervals, and incident osteoporotic fracture (OFX) in the VARA Registry.

	DAS28-CRP Model (N= 2531, OFX N= 144)		
	HR	**95% CI**	**p-value**
Age	1.01	0.99-1.03	0.162
Female	2.31	1.44-3.71	0.001
Black Race	0.78	0.48-1.27	0.326
RDCI Score	0.90	0.72-1.11	0.320
High Positive ACPA[a]	0.69	0.49-0.96	0.027
OP Diagnosis	1.33	0.80-2.22	0.271
Smoking category			
Never	ref	--	--
Current	1.25	0.78-2.02	0.359
Former	0.85	0.55-1.31	0.466
Prednisone use	1.35	0.96-1.88	0.084
csDMARD use	0.81	0.56-1.16	0.250
Biologic use	0.86	0.59-1.26	0.449
BMI category			
Underweight	1.02	0.39-2.64	0.972
Normal weight	ref	--	--
Overweight	1.22	0.78-1.89	0.386
Obese	0.82	0.47-1.43	0.486
Severely Obese	1.00	0.54-1.84	0.992
Disease Activity Category			
Remission	ref	--	--
Low	1.05	0.61-1.82	0.862
Moderate	1.28	0.83-1.98	0.264
High	2.02	1.23-3.33	0.006

-ACPA: anti-cyclic citrullinated peptide antibody; RF: rheumatoid factor; RDCI: rheumatic disease comorbidity index; csDMARD: conventional synthetic DMARDs; OP: osteoporosis; BMI: body mass index; DAS28-CRP: disease activity scale 28 joints with c-reactive protein; CDAI: clinical disease activity index.
[a]-High positive ACPA defined as >60 units.

specific mechanisms that drive the association between RA disease activity and OFX are needed to inform interventions focused on preventing this outcome.

Table 3. Multivariable Cox proportional hazard model comparing the individual components of rheumatoid arthritis disease activity measures (DAS28-CRP and CDAI) and their independent associations with incident osteoporotic fracture in the VARA registry. Each individual component modeled as time-variant value averaged over all prior intervals. Separate models were run for each individual component.

	HR	95% CI	p-value
Tender joint count (0-28)	1.01	0.99-1.04	0.319
Swollen joint count (0-28)	1.06	1.03-1.09	<0.0001
Patient global assessment (0-10)	1.10	1.03-1.18	0.006
Provider global assessment (0-10)	1.01	1.00-1.02	0.017
C-reactive protein	1.08	1.03-1.12	0.001

Controlled for: age, female sex, Black race, rheumatic disease comorbidity index, high positive ACPA level, osteoporosis diagnosis, smoking status, medication use (prednisone, csDMARD, biologics) and body mass index.
-DAS28-CRP: disease activity scale 28 joints with c-reactive protein; CDAI: clinical disease activity index.
-Missingness 7% for PrGA and 3% for CRP.

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Abstract Number: 1977

Delivering Fracture Prevention Through Telemedicine: A Process Evaluation

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Osteoporosis & Metabolic Bone Disease
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Guidelines recommend osteoporosis screening using dual-energy X-ray absorptiometry (DXA) in men and women at risk for osteoporosis, but screening remains low, especially in men and in rural populations. System level approaches to aid in identification of at-risk populations have been suggested to close this clinical gap. An informatics-driven population health clinic, the "Bone Health Team" (BHT) was implemented to identify and treat rural Veterans lacking evidence of bone health care. We report the results of our process evaluation conducted to understand BHT feasibility.

Methods: The primary outcome of the process evaluation was the number of at-risk Veterans screened with DXA; a secondary outcome was the number of eligible Veterans who initiated prescription therapy to reduce fracture risk. Outcomes were measured between 5/1/2017-9/30/2018 and analyzed descriptively. Qualitative data to understand successful implementation were collected concurrently by conducting in-person interviews with clinical personnel interacting with BHT, interviews with BHT staff, and observations of BHT processes at three site visits. Data analyses followed the Promoting Action on Research Implementation in Health Services (PARIHS) Framework to characterize context, evidence, and facilitation.

Bone Health Team Enrollment Table

	Overall		Women		Men	
	n	%	n	%	n	%
	4500	100.00	292	6.49	4208	93.51
Engagement with Screening						
Declined	531	11.80	60	20.55	471	11.19
No Response	2888	64.18	165	56.51	2723	64.71
Completed DXA	1081	24.02	67	22.95	1014	24.10
Diagnosis[a]						
Normal Bone Density	399	36.54	14	20.90	385	37.56
Osteopenia Low Risk	324	29.67	39	58.21	285	27.80
Osteopenia High Risk	203	18.59	3	4.48	200	19.51
Osteoporosis by DXA	132	12.09	11	16.42	121	11.80
Osteoporosis by Clinical Fracture History	34	3.11	0	0.00	34	3.32
Medication Indicated	338	31.27	14	20.90	324	31.95
Initiated or Maintained Medication	306	90.53	12	85.71	294	90.74
Refused Medication	32	9.47	2	14.29	30	9.26

[a] Veterans can be diagnosed with osteoporosis by DXA and osteoporosis by clinical fracture history

BHT Enrollment Table

Results: Of the 4500 rural Veterans identified for osteoporosis screening, 292 (6%) were women, and 1081 (24%) completed screening (Table). Among these Veterans, 399 (37%) were found to have normal bone density, 527 (48%) osteopenia, and 156 (14%) osteoporosis with 338 (31%) eligible for prescription therapy to reduce fracture risk (Table). Of the Veterans eligible for prescription therapy, 306 (90%) initiated pharmacotherapy. Qualitative analysis identified contextual factors of rural geography and population characteristics including rugged terrain, harsh seasons, long distances between services, and limited access to cellular, internet, and mail services as barriers to the potential for travel, communication, and care delivery. The primary evidence factor acting as an implementation barrier was implementation complexity due to the requirement of significant infrastructural resources to sustain BHT processes. Factors of facilitation and evidence such as data infrastructure, evidence base for care delivery, stakeholder buy-in, formal and informal facilitator engagement, and focus on teamwork facilitated BHT implementation and expansion success.

Conclusion: The population telehealth model employed by the BHT is a feasible approach to delivering preventative osteoporosis care to rural Veterans and identified 31% of at-risk rural Veterans as eligible for prescription therapy to reduce fracture risk with 90% of those eligible choosing to initiate prescription therapy. The identified barriers and facilitators to implementing this model in the VHA will inform future model refinement and efforts to improve bone health care delivery systems for the Veteran population. Further evaluation to understand why more Veterans do not engage when offered osteoporosis screening, as well as the clinical and sociodemographic factors that predict Veteran acceptance of osteoporosis care, is ongoing.

Disclosure: K. Miller, None; **M. Steffen**, None; **A. Seaman**, None; **Z. Anderson**, None; **J. Green**, None; **S. Patel**, None; **S. Wardyn**, None; **S. Solimeo**, None.

Abstract Number: 1978

Prevalence and Factors Associated with Patient-Physician Discordance Among RA Patients Initiating Advanced Therapy

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes II: Engagement, Perceptions, & Quality of Life

Session Type: Abstract Session

Session Time: 11:00AM–11:50AM

Background/Purpose: Some rheumatoid arthritis (RA) patients rate their disease activity worse than their physician does, but recent prevalence and factors associated with such discordance have not been reviewed in a large real-world database. This study describes discordance at biological initiation (index visit) and over time. We hypothesized that higher levels of pain, morning stiffness, fatigue, Health Assessment Questionnaire (HAQ) score, Clinical Disease Activity Index (CDAI), and depression are associated with discordance at the index visit.

Methods: We included patients enrolled in the Corrona RA Registry who initiated their first biological or Janus kinase inhibitor on or after 2/1/2015 with both 6- and 12-month (± 3 mo) follow-up visits. Patient global assessment (PtGA) - physician's global assessment (PhGA) (disease severity) ≥ 30 points on a 0-100 VAS scale was defined as positive discordance; > -30 to < 30 as concordance; and ≤ -30 as negative discordance. Patients with negative discordance were excluded based on prior studies. Positive discordance at all three (index, 6-, 12-mo) visits was classified as persistent discordance. Differences between discordant and concordant patients at index visit were quantified using effect sizes (standardized differences) based on Cohen's descriptions for continuous variables (|*d*|): ~0.2 small effect size, ~0.5 medium, ~0.8 large; for categorical variables (w): ~0.1 small, ~0.3 medium, ~0.5 large. Mixed-effects logistic regression was used to test our *a priori* hypothesis.

Results: Among 54,307 patients in the registry, 758 patients met the inclusion criteria for analysis at the index visit, and of these, 752 were included in the analysis of persistent discordance. A total of 80 patients with negative discordance at any visit were excluded. Discordance prevalence was similar at the index (27%), 6- (30%), and 12-mo (30%) visits; 10% (n=65) had persistent discordance.

At the index visit (Table 1), large differences for discordant vs concordant patients included RAPID3 score (mean 16 vs 7.3, |*d*| = 1.5), pain (mean 63 vs 32, |*d*| = 1.2), fatigue (mean 61 vs 35, |*d*| = 0.9), morning stiffness severity (61 vs 40, w = 0.9), and HAQ (0.7 vs 0.3, w = 0.9), and a medium effect size for DAS28-ESR (mean 4.3 vs 3.6, |*d*| = 0.5). Results were similar for patients with persistent discordance (Table 2).

In a logistic regression model regressed on age, CDAI, opioid (including tramadol) use, pain, morning stiffness, fatigue, HAQ, depression, academic site; discordance (vs concordance) was positively associated with pain (OR=1.04, p=0.001) and HAQ (OR=1.72, p=0.053), and inversely associated with CDAI (OR=0.94, p=0.001). Morning stiffness, fatigue, and depression were not associated with discordance (Table 3).

Conclusion: About 30% of RA patients who initiated DMARDs had patient-physician discordance at any visit, and one-third of these (10% total) persisted at all three visits. Greater patient-reported pain and functional impairment

Characteristics	Positive Discordance	Concordance	Effect size[1]
	n = 191	n = 487	
Age in years	N = 191	N = 486	
Mean (SD)	60.0 (11.4)	60.2 (13.1)	0.02
Gender, n (%)	N = 191	N = 486	
Female	147 (77%)	361 (74%)	0.03
Education, n (%)	N = 180	N = 474	
12th grade or less	4 (2.2%)	9 (1.9%)	0.12
High school graduate/GED	98 (54%)	196 (41%)	
Some college/associate degree	29 (16%)	110 (23%)	
College graduate or higher	49 (27%)	159 (34%)	
Work status, n (%)	N = 185	N = 479	
Full time	49 (26%)	190 (40%)	0.24
Part time	17 (9.2%)	37 (7.7%)	
At home	13 (7%)	31 (6.5%)	
Student	1 (.54%)	5 (1%)	
Retired	64 (35%)	184 (38%)	
Disabled	41 (22%)	32 (6.7%)	
BMI (kg/m^2) continuous	N = 189	N = 476	
Mean (SD)	30.9 (7.4)	30.2 (7.1)	0.10
History of comorbidities, n (%)	N = 191	N = 487	
Hyperlipidemia	38 (20%)	101 (21%)	0.01
Hypertension	75 (39%)	162 (33%)	0.06
Diabetes	28 (15%)	61 (13%)	0.03
Depression	43 (23%)	55 (11%)	0.14
RA duration (years)	N = 191	N = 487	
Mean (SD)	7.7 (10.0)	6.6 (8.6)	0.12
Erosive disease,[2] n (%)	N = 190	N = 486	
Yes	19 (10%)	74 (15%)	0.07
Clinical joint deformity, n (%)	N = 191	N = 485	
Yes	45 (24%)	144 (30%)	0.06
Clinical Disease Activity Index (CDAI)	N = 191	N = 487	
Mean (SD)	17.7 (11.9)	13.9 (13.2)	0.30
Simple Disease Activity Index (SDAI)	N = 118	N = 336	
Mean (SD)	17.5 (11.9)	13.9 (13.1)	0.28
RAPID3	N = 170	N = 425	
Mean (SD)	15.8 (5.2)	7.3 (5.7)	1.52
Disease Activity Score (DAS28 ESR)	N = 185	N = 458	
Mean (SD)	4.3 (1.3)	3.6 (1.5)	0.50
Swollen joint count (28)	N = 191	N = 487	
Mean (SD)	3.5 (4.8)	4.0 (5.1)	0.10
Tender joint count (28)	N = 191	N = 487	
Mean (SD)	5.4 (6.3)	4.6 (6.1)	0.13
Patient-reported opioid (including tramadol) use, n (%)	N = 191	N = 487	
Yes	67 (35%)	93 (19%)	0.17
Patient-reported anti-depressant use, n (%)	N = 191	N = 487	
Yes	54 (28%)	83 (17%)	0.13
HAQ	N = 185	N = 458	
Mean (SD)	0.7 (0.6)	0.3 (0.4)	0.86
Patient overall pain (VAS range 0-100)	N = 191	N = 487	
Mean (SD)	52.9 (24.7)	32.0 (26.3)	1.19
Patient overall fatigue (VAS range 0-100)	N = 190	N = 485	
Mean (SD)	61.2 (27.9)	35.1 (28.3)	0.92
Morning stiffness (presence), n (%)	N = 189	N = 486	
Yes	174 (92%)	366 (75%)	0.19
Duration of morning stiffness (hours)	N = 173	N = 366	
Mean (SD)	2.6 (4.7)	1.2 (2.0)	0.45
Severity of morning stiffness (VAS range 0-100)	N = 174	N = 363	
Mean (SD)	60.6 (23.8)	39.7 (23.9)	0.88
EQ-5D-3L dimensions, n (%)	N = 185	N = 478	
Walking: some problems or confined to bed	129 (70%)	207 (43%)	0.24
Self-care: some problems or unable to do	91 (49%)	111 (24%)	0.25
Usual activities: some problems or unable to do	151 (80%)	247 (52%)	0.26
Pain and discomfort: moderate or extreme	180 (96%)	366 (78%)	0.21
Anxiety and depression: moderate or extreme	99 (54%)	154 (33%)	0.19
Unable to do usual work over the past 3 months, n (%)	N = 186	N = 478	
Yes	107 (58%)	158 (33%)	0.22
Number of days of work missed	N = 84	N = 126	
Mean (SD)	30.2 (33.6)	20.4 (26.0)	0.33
Patient-reported history of depression, n (%)	N = 191	N = 487	
Yes	51 (27%)	54 (11%)	0.19
Patient-reported history of anxiety, n (%)	N = 191	N = 487	
Yes	56 (29%)	62 (13%)	0.20

[1] Effect sizes are Cohen's d for continuous variables, and Cohen's w for categorical variables. Guidelines for |d| are ~0.2 small effect size, ~0.5 medium, and ~0.8 large. For w, guidelines are ~0.1 small effect size, ~0.3 medium, and ~0.5 large

[2] The RA lab form collects information on erosive disease found via radiographs, MRI, and ultrasound

Table 1. Patient Demographics and Clinical Characteristics of Patients by Discordance Status at Index Visit

Characteristics	Persistently Discordant	Not Persistently Discordant	Effect size[1]
	N = 65	N = 607	
Age in years	N = 65	N = 606	
Mean (SD)	59.4 (11.5)	60.2 (12.8)	0.06
Gender, n (%)	N = 65	N = 606	
Female	57 (88%)	445 (73%)	0.10
Education, n (%)	N = 60	N = 588	
12th grade or less	1 (1.7%)	12 (2%)	0.06
High school graduate/GED	32 (53%)	258 (44%)	
Some college/associate degree	12 (20%)	125 (21%)	
College graduate or higher	15 (25%)	193 (33%)	
Work status, n (%)	N = 64	N = 595	
Full time	13 (20%)	225 (38%)	0.33
Part time	3 (4.7%)	49 (8.2%)	
At home	8 (13%)	36 (6.1%)	
Student	0 (0%)	6 (1%)	
Retired	14 (22%)	233 (39%)	
Disabled	26 (41%)	46 (7.7%)	
Lifestyle characteristics			
BMI (kg/m2) continuous	N = 65	N = 594	
Mean (SD)	31.0 (8.0)	30.4 (7.1)	0.09
History of comorbidities			
History of comorbidities, n (%)	N = 65	N = 607	
Hyperlipidemia	16 (25%)	121 (20%)	0.03
Hypertension	28 (43%)	206 (34%)	0.06
Diabetes	12 (18%)	77 (13%)	0.05
Depression	22 (34%)	74 (12%)	0.18
Disease characteristics			
RA duration (years)	N = 65	N = 607	
Mean (SD)	8.7 (11.6)	6.8 (8.7)	0.22
Erosive disease, n (%)	N = 65	N = 605	
Yes	8 (12%)	85 (14%)	0.01
Clinical joint deformity, n (%)	N = 65	N = 605	
Yes	15 (23%)	174 (29%)	0.04
Clinical Disease Activity Index (CDAI)	N = 65	N = 607	
Mean (SD)	17.6 (11.1)	14.6 (13.1)	0.23
Simple Disease Activity Index (SDAI)	N = 40	N = 409	
Mean (SD)	18.4 (11.4)	14.3 (12.9)	0.32
RAPID3	N = 56	N = 533	
Mean (SD)	17.4 (4.5)	8.9 (6.5)	1.34
Disease Activity Score (DAS28 ESR)	N = 64	N = 573	
Mean (SD)	4.5 (1.2)	3.7 (1.5)	0.49
Swollen joint count (28)	N = 65	N = 607	
Mean (SD)	3.1 (4.4)	3.9 (5.1)	0.17
Tender joint count (28)	N = 65	N = 607	
Mean (SD)	5.6 (6.1)	4.7 (6.2)	0.14
Medication use			
Patient reported opioid (including tramadol) use, n (%)	N = 65	N = 607	
Yes	29 (45%)	129 (21%)	0.16
Patient reported anti-depressant use, n (%)	N = 65	N = 607	
Yes	22 (34%)	112 (18%)	0.11
Patient-reported outcome measures			
HAQ	N = 64	N = 573	
Mean (SD)	0.9 (0.6)	0.4 (0.5)	0.97
Patient overall pain (VAS range 0-100)	N = 65	N = 607	
Mean (SD)	70.9 (20.0)	37.5 (28.4)	1.20
Median [p25, p75]	70 [65, 85]	35 [10, 60]	
Patient overall fatigue (VAS range 0-100)	N = 64	N = 605	
Mean (SD)	70.9 (23.6)	39.5 (29.6)	1.08
Median [p25, p75]	73 [60, 90]	40 [10, 65]	
Morning stiffness (presence), n (%)	N = 63	N = 606	
Yes	59 (94%)	476 (79%)	0.11
Duration of morning stiffness (hours)	N = 58	N = 476	
Mean (SD)	2.6 (4.4)	1.6 (3.0)	0.32
Severity of morning stiffness (VAS range 0-100)	N = 59	N = 473	
Mean (SD)	65.6 (20.1)	44.0 (25.5)	0.87
EQ-5D-3L dimensions, n (%)	N = 64	N = 593	
Walking: some problems or confined to bed	47 (73%)	285 (48%)	0.15
Self-care: some problems or unable to do	38 (60%)	163 (28%)	0.21
Usual activities: some problems or unable to do	57 (88%)	336 (56%)	0.19
Pain and discomfort: moderate or extreme	64 (98%)	477 (81%)	0.14
Anxiety and depression: moderate or extreme	36 (56%)	214 (37%)	0.12
Unable to do usual work over the past 3 months, n (%)	N = 64	N = 594	
Yes	43 (67%)	220 (37%)	0.18
Number of days of work missed	N = 33	N = 175	
Mean (SD)	41.9 (34.4)	20.6 (27.2)	0.75
Median [p25, p75]	30 [14, 90]	7 [4, 20]	
Patient-reported history of depression, n (%)	N = 65	N = 607	
Yes	22 (34%)	81 (13%)	0.17
Patient-reported history of anxiety, n (%)	N = 65	N = 607	
Yes	23 (35%)	92 (15%)	0.16

[1] Effect sizes are Cohen's d for continuous variables, and Cohen's w for categorical variables. Guidelines for |d| are ~0.2 small effect size, ~0.5 medium, and ~0.8 large. For w, guidelines are ~0.1 small effect size, ~0.3 medium, and ~0.5 large. * The RA lab form collects information on erosive disease found via radiographs, MRI, and ultrasound

Table 2 Patient Demographics and Clinical Characteristics of Patients by Persistent Discordance Status

Patient and Clinical Characteristics (n=493)[1]	Odds Ratio (CI)	Average Marginal Effect (CI)
Age in years	1.02 (1.00, 1.03)	0.00 (-0.00, 0.01)
Clinical Disease Activity Index (CDAI)	0.94 (0.92, 0.96)***	-0.01 (-0.01, -0.01)***
Patient reported opioid (including) tramadol use	0.97 (0.60, 1.58)	-0.00 (-0.08, 0.07)
Patient overall pain (VAS range 0–100)	1.04 (1.03, 1.06)***	0.01 (0.00, 0.01)***
HAQ	1.72 (0.99, 2.98)	0.09 (0.00, 0.17)*
Anxiety and depression:[2] moderate or extreme	1.08 (0.66, 1.77)	0.01 (-0.07, 0.09)
Severity of morning stiffness (VAS range 0–100)	1.01 (1.00, 1.02)	0.00 (-0.00, 0.00)
Patient overall fatigue (VAS range 0–100)	1.01 (1.00, 1.02)	0.00 (-0.00, 0.00)
Academic affiliation	1.74 (0.35, 8.55)	0.09 (-0.18, 0.37)
Baseline odds	0.02 (0.01, 0.08)***	
Results on logit scale		
Intercept	-5.49 (0.01, 0.08)***	
Random intercept S.D.[3]	0.00 (0.00, 3.11e+08)	

CI, Confidence Interval; VAS, visual analog scale; HAQ, Health Assessment Questionnaire; [1]Overall test for fixed portion of model $\chi^2(9) = 99.6$, $p < 0.001$; [2]Taken from the EQ-5D-3L where patients responded *not*, *moderately*, or *extremely* anxious or depressed; [3] Likelihood ratio test versus logit model $\chi^2(1) = .000059$, $p = 0.497$; * $p \leq 0.05$, ** $p \leq 0.01$, *** $p \leq 0.001$; Hypothesis tests were performed using a mixed-effects logistic regression model of positive patient-physician discordance at index visit regressed on age, CDAI, patient reported opioid (including tramadol) use, pain, HAQ, patient-reported anxiety and/or depression, severity of morning stiffness, fatigue, and academic affiliation of the treating site. Variables were selected based on review of the literature, on examination of the descriptive tables, and clinical judgement. Odds ratios (OR) provide information on the multiplicative change in odds, and average marginal effects (AME) provide information on the additive change in predicted probability.

Table 3. Mixed-Effects Logistic Regression of Factors Associated with Positive Discordance (Referent to Concordance)

were associated with discordance in adjusted models. Understanding factors associated with patient-physician discordance will help clinicians foster a more patient-centric discussion in treatment decisions.

Disclosure: J. Curtis, AbbVie, 1, 2, Amgen, 1, 2, Bristol-Myers Squibb, 1, 2, Corrona, 1, 2, Crescendo, 1, 2, Janssen, 1, 2, Pfizer, 1, 2, Sanofi, 1, 2, UCB, 1, 2; **R. Medeiros**, None; **I. Lee**, Gilead Sciences, 1, 2; **R. Mackey**, Corrona, LLC, 3; **R. Haubrich**, Gilead Sciences, 1, 2; **H. Hu**, Gilead Sciences, Inc., 1, 3; **J. Greenberg**, Corrona, LLC, 1, 3; **A. Wu**, None.

Abstract Number: 1979

Participant Engagement and Adherence in an ArthritisPower Real-World Study to Capture Smartwatch and Patient-Reported Outcome Data Among Rheumatoid Arthritis Patients

William Nowell[1], Jeffrey R Curtis[2], Hong Zhao[3], Fenglong Xie[3], Laura Stradford[4], David Curtis[5], Kelly Gavigan[4], Jessica Boles[4], Justin Owensby[3], Cassie Clinton[2], Ilya Lipkovich[6], Shilpa Venkatachalam[7], Sandra Nolot[6] and Virginia Haynes[6], [1]Global Healthy Living Foundation, New York City, NY, [2]Division of Clinical Immunology and Rheumatology, University of Alabama at Birmingham, Birmingham, AL, [3]University of Alabama at Birmingham, Birmingham, AL, [4]Global Healthy Living Foundation, Upper Nyack, NY, [5]Global Healthy Living Foundation, New York City, [6]Eli Lilly & Company, Indianapolis, IN, [7]Global Healthy Living Foundation, Upper Nyack

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes II: Engagement, Perceptions, & Quality of Life

Session Type: Abstract Session

Session Time: 11:00AM–11:50AM

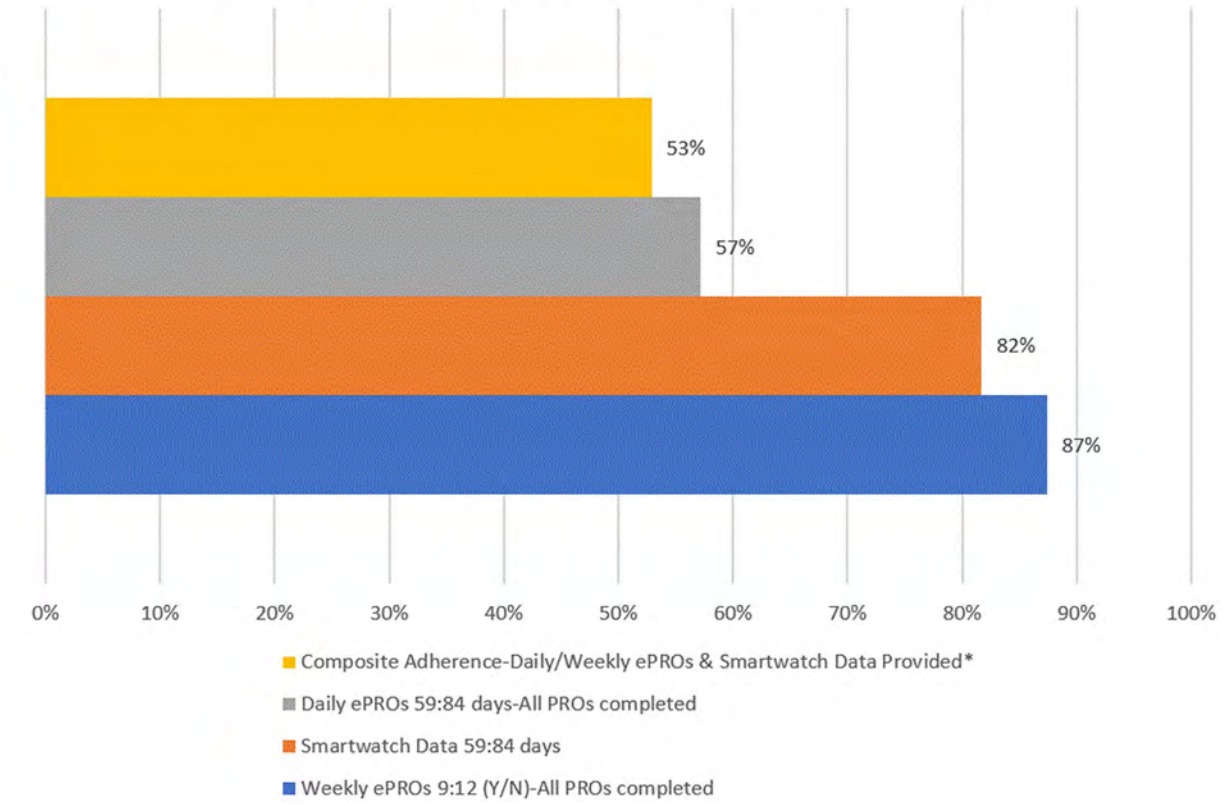
Table 1. Demographic and Clinical Characteristics of Participants at Baseline and During Lead-In Period, by Main Study Eligibility (N=470)

	Qualified for Main Study n=278		Did Not Qualify for Main Study, n=192		
	n (%) or mean (SD)	Range (q1, q3)	n (%) or mean (SD)	Range (q1,q3)	p-value
Age	50.20 (11.05)	(44, 58)	52.12 (12.09)	(44, 61)	0.08
Female	255 (91.7)	-	173 (90.1)	-	0.66
White	239 (86.0)	-	165 (85.9)	-	1
Osteoarthritis	124 (44.6)	-	69 (35.9)	-	0.07
Fibromyalgia	85 (30.6)	-	57 (29.7)	-	0.92
Other rheumatic or musculoskeletal condition	122 (43.9)	-	92 (47.9)	-	0.44
Years since RA diagnosis	9.40 (10.10)	(3, 12)	10.51 (10.26)	(3, 15)	0.25
Currently Employed	154 (55.4)	-	76 (39.6)	-	<0.01*
Regular daytime shift work schedule (i.e. 9-5) (among employed)	130 (46.8)	-	65 (33.9)	-	<0.01*
Current RA Treatment†					
Biologics +/- csDMARDs	176 (63.3)	-	95 (49.5)	-	<0.01*
tsDMARDS +/- csDMARDS	34 (12.2)	-	21 (10.9)	-	
csDMARDs w/o b/tsDMARDs	68 (24.5)	-	55 (28.6)	-	
None of the Above	0 (0.0)	-	21 (10.9)	-	
Daily/Weekly PROs					
Pain (daily, NRS)	4.9 (2.5)	(3.0, 7.0)	6.2 (2.5)	(4.5, 8.0)	<0.01*
Fatigue (daily, NRS)	5.4 (2.5)	(3.5, 7.0)	6.8 (2.5)	(5.5, 8.5)	<0.01*
PROMIS Pain Interference (weekly)	61.4 (6.6)	(57.3, 66.9)	64.5 (6.2)	(61.5, 66.9)	<0.01*
PROMIS Physical Function (weekly)	39.2 (6.6)	(34.7, 43.4)	35.8 (5.9)	(32.5, 38.6)	<0.01*
PROMIS Fatigue (weekly)	60.6 (7.7)	(55.5, 65.8)	64.4 (7.9)	(60.4, 68.1)	<0.01*
PROMIS Sleep Disturbance (weekly)	57.1 (7.3)	(53.1, 61.9)	57.4 (8.7)	(51.8, 63.0)	0.66
PROMIS Satisfaction with Participation in Discretionary Social Activities (weekly)	43.3 (6.7)	(39.7, 47.7)	41.1 (6.9)	(36.6, 46.2)	<0.01*
RA Flare (weekly)	27.8 (11.3)	(20.0, 36.0)	34.7 (10.3)	(29.0, 43.0)	<0.01*

*Statistical significance between groups of pts who qualified and did not qualify for Main Study, $p < 0.05$; t tests were performed for continuous variables and chi square tests for categorical variables; p values are nominal in nature and should be interpreted in an exploratory manner † DMARDs = disease modifying antirheumatic drugs csDMARDs = conventional synthetic DMARDs (e.g. methotrexate, sulfasalazine) bDMARDs = biologics or biologic DMARDs (e.g. TNFi, IL-6, IL-7) tsDMARDs = targeted synthetic DMARDs (e.g. JAKi) None of the above = on NSAIDs or corticosteroids, but no DMARD or cs/b/tsDMARD

Background/Purpose: Characterization of how different types of patient-generated data reflect patients' experience is needed to guide integration of electronically collected patient-reported outcome (ePRO) measures and passive biometrics into real-word evidence (RWE) platforms. Our objective was to characterize engagement, protocol adherence, and data completeness in an ongoing study in rheumatoid arthritis (RA) participants (pts) enrolled in the Digital Tracking of Arthritis Longitudinally (DIGITAL) study, an ancillary study of the ArthritisPower® registry.

Figure. Participant Adherence During Main Study Period by Data Collection Platform (N=278)



Methods: Pts were invited to join the app-based study which included a 2-week (14-day) Lead-In and 12-week (84-day) Main Study Period. Study-specific customization of the ArthritisPower mobile application collected ePROs. For at least 10 days of the Lead-In period, pts were required to electronically complete: a) two daily single-item Pain and Fatigue numeric rating scales and b) longer weekly sets of ePROs. Successful completers of the Lead-In were mailed a smartwatch (Fitbit® Versa™) and study materials. Main Study Period included automated and manual prompts to complete ePROs, wear the smartwatch and regularly sync it. Study coordinators monitored pt data and contacted pts via email, text and/or phone to resolve adherence issues per a priori rules triggering pt contact due to consecutive spans of missing data. Adherence to data collection during the Main Study was defined as providing requested data > 70% of 84 days (daily ePRO, smartwatch data), or ≥ 9 of 12 weeks.

Results: As of 4/2020, and referent to the 470 pts expressing initial interest, 278 (59.1%) completed the Lead-In and qualified for the Main Study. Of the 278 pts enrolled, 91.7% female, mean (SD) age 50.2 (11.1), 9.4 (10.1) years since RA diagnosis (Table 1). Those qualifying for the Main Study were more likely to be currently employed (55.4% vs. 39.6%, p< 0.01) and on biologic monotherapy (63.3% vs. 49.5%, p< 0.01). Over the 84-day Main Study period, the proportion of pts meeting the definition of adherence to protocol-specified data collection was lowest (57%) for daily ePRO data capture, highest for weekly ePRO data (87%), and intermediate (82%) for smartwatch data. A total of 147 (53%) of pts met composite adherence (Figure), while 27/278 met neither smartwatch/PRO adherence, 80/278 met smartwatch adherence but not PRO adherence, and 24/278 did not meet smartwatch adherence but met PRO adherence. Pts experiencing high levels of pain and low levels of physical function at Lead-In were more likely to complete ePROs but not adhere to smartwatch use when they advanced to the Main Study period (Table 2).

Conclusion: Compared to other digital health RA studies, a short lead-in period appears useful to identify pts likely to engage in a longitudinal digital health study collecting data on a mobile app and was associated with subsequent pt adherence, and this adherence may vary by data collection platform. RWE studies involving passive data collection

Table 2. Demographic and Clinical Characteristics of Main Study Participants at Baseline and During Lead-In Period, by Whether Composite Adherence Was Met During Main Study Period (N=278)

	Met Composite Adherence (n=147)	Did Not Meet Composite Adherence (n=131)	
	n (%) or mean (SD)	n (%) or mean (SD)	p-value
Age	51.93 (10.57)	48.27 (11.29)	<0.01*
Female	132 (89.8)	123 (93.9)	0.31
White	133 (90.5)	106 (80.9)	0.03*
Osteoarthritis	68 (46.3)	56 (42.7)	0.64
Fibromyalgia	41 (27.9)	44 (33.6)	0.37
Other rheumatic or musculoskeletal condition	65 (44.2)	57 (43.5)	1.00
Years since RA diagnosis	9.86 (11.03)	8.88 (8.97)	0.42
Currently Employed	76 (51.7)	78 (59.5)	0.23
Regular daytime shift work schedule (i.e. 9-5) (among employed)	64 (43.5)	66 (50.4)	0.31
Current RA Treatment†			
Biologics +/- csDMARDs	95 (64.6)	81 (61.8)	0.88
tsDMARDS +/- csDMARDS	35 (23.8)	33 (25.2)	
csDMARDs without b/tsDMARDs	17 (11.6)	17 (13.0)	
Lead-In Daily ePROs (mean)			
Pain	4.9 (2.4)	5.0 (2.6)	0.55
Fatigue	5.3 (2.4)	5.4 (2.6)	0.38
Lead-In Weekly ePROs (mean)			
PROMIS Pain Interference	61.1 (6.3)	61.8 (7.0)	0.30
PROMIS Physical Function	39.4 (6.8)	39.0 (6.4)	0.47
PROMIS Fatigue	60.2 (7.5)	61.0 (7.9)	0.30
PROMIS Sleep Disturbance	57.0 (6.9)	57.3 (7.9)	0.72
PROMIS Satisfaction with Participation in Discretionary Social Activities	43.6 (6.8)	42.9 (6.5)	0.21
RA Flare	27.1 (11.0)	28.7 (11.6)	0.12

*Statistical significance between groups of pts who met and did not meet composite adherence in Main Study, $p < 0.05$; t tests were performed for continuous variables and chi square tests for categorical variables; p values are nominal in nature and should be interpreted in an exploratory manner † DMARDs = disease modifying antirheumatic drugs csDMARDs = conventional synthetic DMARDs (e.g. methotrexate, sulfasalazine) bDMARDs = biologics or biologic DMARDs (e.g. TNFi, IL-6, IL-7) tsDMARDs = targeted synthetic DMARDs (e.g. JAKi)

in RA require pt-centric implementation and design to minimize pt burden, promote longitudinal engagement and maximize adherence.

Disclosure: W. Nowell, None; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **H. Zhao**, None; **F. Xie**, None; **L. Stradford**, None; **D. Curtis**, None; **K. Gavigan**, None; **J. Boles**, None; **J. Owensby**, None; **C. Clinton**, None; **I. Lipkovich**, Eli Lilly and Company, 1, 3; **S. Venkatachalam**, None; **S. Nolot**, Eli Lilly and Company, 1, 3; **V. Haynes**, Eli Lilly and Company, 1, 3.

Abstract Number: 1980

Understanding the Relationship Between Illness Perceptions and Self-Efficacy Among Latin Americans with SLE Through the *Hablemos De Lupus* Facebook Page

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes II: Engagement, Perceptions, & Quality of Life

Session Type: Abstract Session

Session Time: 11:00AM–11:50AM

Background/Purpose: SLE disproportionately strikes Latinos, who are also at high risk for poor outcomes. Self-efficacy (SE) to manage chronic disease correlates with outcomes through self-management behavior. Illness perceptions (IP) are modifiable mental representations that vary among populations and may impact SE. This study aimed to explore IP and SE in this population and determine if one IP domain, emotional distress, increases the odds of low SE to manage symptoms.

Methods: We collected self-reported measures through an anonymous survey posted on the *Hablemos de Lupus* (Let's Talk about Lupus) education Facebook page (followed by 74,000 Spanish-speakers). Participants were eligible if they were 18 or older, located in the American continent and self-reported a SLE diagnosis by a physician. The Brief Illness Perception Questionnaire (BIPQ) Likert scale was used to assess IP and the Patient Reported Outcomes Measurement Information System (PROMIS) to assess SE (to manage symptoms, treatment, emotions and social interactions). A higher BIPQ score (range 0-10) indicates more of the IP domain being measured, and a lower SE T-score indicates worse SE. We reported the mean score and SD of each BIPQ question; emotional distress IP was

Figure 1. Illness Perception Mean Scores* by Domain among 1401 Latino SLE Patients

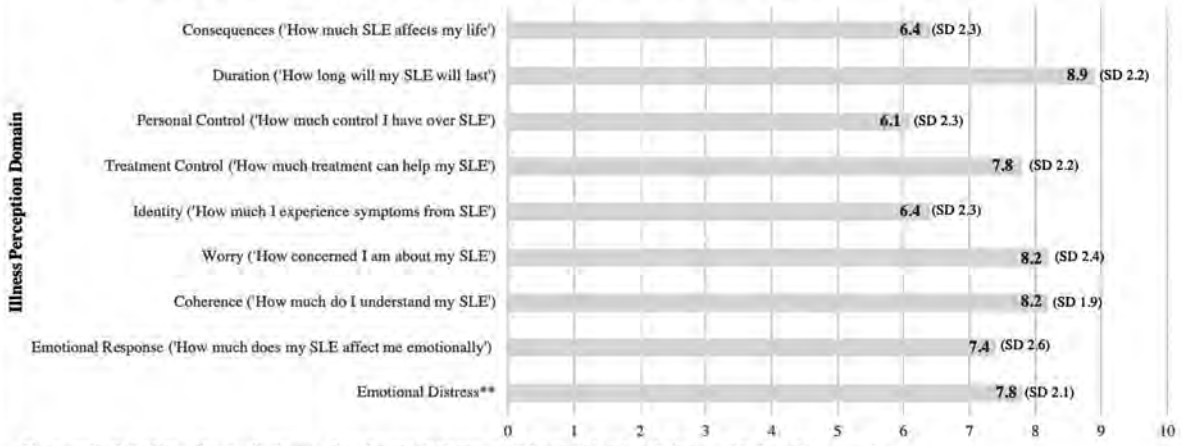
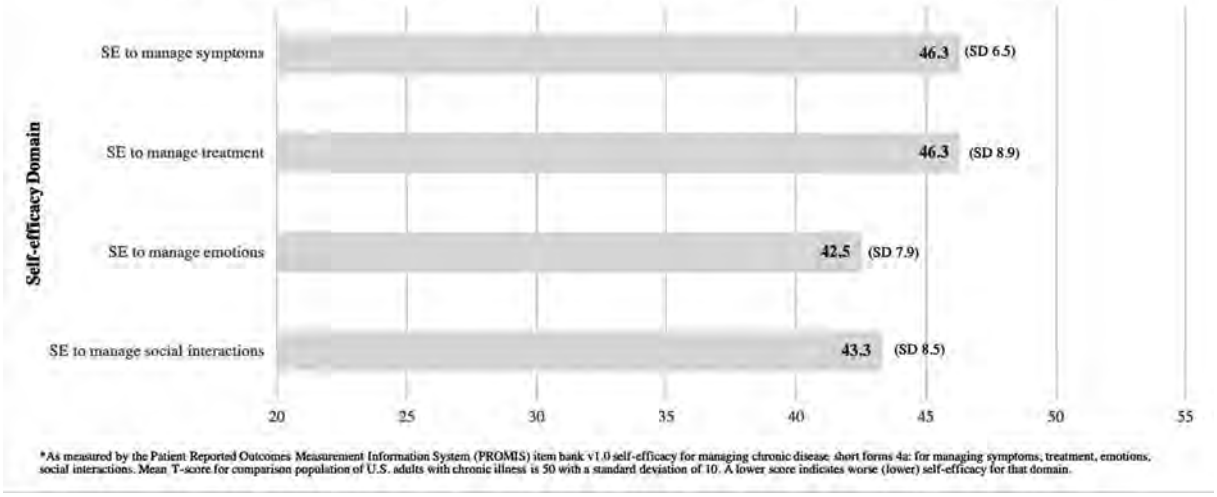


Figure 2. Self-efficacy Mean T-Scores* by Domain among 1401 Latinos with SLE



*As measured by the Patient Reported Outcomes Measurement Information System (PROMIS) item bank v1.0 self-efficacy for managing chronic disease short forms 4a: for managing symptoms, treatment, emotions, social interactions. Mean T-score for comparison population of U.S. adults with chronic illness is 50 with a standard deviation of 10. A lower score indicates worse (lower) self-efficacy for that domain.

Table. Association of Emotional Distress Illness Perception and Low Self-Efficacy* to Manage Symptoms among Latinos with SLE. Multivariate Logistic Regression

Variable	Odds Ratio	95% CI	P-value
Emotional distress (1-unit increase)**	**1.44**	**1.29 – 1.61**	**<.0001**
Female sex	1.21	0.58-2.51	0.61
Age (ref 36-55)			
18-35	1.22	0.88-1.69	0.24
56 and older	1.34	0.65-2.73	0.43
No college degree (ref college or higher)	1.26	0.93-1.73	0.14
Insurance (ref private)			
Uninsured or disabled	1.25	0.81-1.93	0.32
Public insurance	1.38	0.95-2.00	0.09
Monthly financial strain	1.58	1.01-2.47	0.04
Time since diagnosis (ref >5 years)			
≤1 year	2.03	1.26-3.27	0.004
1-5 years	1.31	0.93-1.85	0.12
Lack of social support∝	2.75	1.95-3.87	<.0001
Severe SLE^	0.92	0.67-1.27	0.61
Low *HdL* user (watched <5 *HdL* educational videos)	0.66	0.48-0.90	0.01

*Low self-efficacy was measured with PROMIS self-efficacy to manage symptoms; a T-score <= 40 indicates low SE. **Emotional distress score was measured with the Brief Illness Perception Questionnaire (BIPQ); BIPQ score ranges 0 to 10; a higher score indicates higher emotional distress. ∝Lack of social support defined as a 'no' response when a participant was asked if felt emotionally supported by family or friends. ^Severe SLE: endorsed central nervous system, renal, pulmonary, or vascular SLE manifestations. Abbreviations: CI= confidence interval, HdL=*Hablemos de Lupus* Facebook page.

calculated using the average score of 'worry' and 'emotional response' questions. SE domains were reported as mean T-scores and SD, with the U.S. population with chronic illnesses as reference. Logistic regression was used to examine the association of emotional distress IP and low SE to manage symptoms (defined as a T-score ≤40) after controlling for confounders.

Results: There were 1401 eligible participants who started the survey and 100% completed. Participants were from 19 countries; ages 18-80; 95% females; 33% diagnosed in past 3 years; 46% reported renal, neurologic, vascular or pulmonary SLE manifestations, and 79% were under the care of a rheumatologist. Figures 1 and 2 depict mean IP and SE scores, with perceived emotional distress of 7.8 (SD 2.1). SE mean T-scores were lower than the reference population (T-score=50), ranging between 42.5 for managing emotions to 46.3 for treatment and symptom manage-

ment (Figure 2). Per 1-unit increase of emotional distress the OR of low SE to manage symptoms was 1.44 [95% CI 1.29-1.61], after controlling for covariates (Table). Lack of social support and recent diagnosis were independently associated with low SE to manage symptoms in the multivariate model (Table).

Conclusion: Our findings underscore high illness-related emotional distress in Latinos with SLE, despite reporting relatively high understanding of SLE and its treatment. Moreover, SE levels in Latinos with SLE were below the average U.S. population across multiple domains. We found that those who perceive SLE as more emotionally distressing had lower SE to manage symptoms, suggesting that emotional illness perception may be a promising target for Latino SLE interventions. Our data also suggest that patients recently diagnosed or lacking social support may benefit from SE interventions. Education to modify perceived SLE emotional distress may improve SE to manage symptoms among Latino patients, potentially contributing to better patient-centered and clinical outcomes in this population.

Disclosure: E. Crosley, Lupus Foundation of America, 2; **C. Elera-Fitzcarrald**, None; **L. Ferreyra Garrot**, None; **Y. Fuentes-Silva**, None; **S. Ibañez**, None; **B. Pons-Estel**, None; **C. Reátegui-Sokolova**, Janssen, 2; **C. Drenkard**, None.

Abstract Number: 1981

Patients with Inflammatory Arthritis Who Are More Adherent to Treatment Do Not Perform More Physical Activity Collected by Smartphone Apps: A Cross-sectional Study of 101 Patients, the ImBAIA Study

Thomas Davergne[1], Rawdha Tekaya[2], Camille Deprouw[3], Anne Tournadre[4], Stéphane Mitrovic[5], Adeline Ruyssen-Witrand[6], Christophe Hudry[7], Sabrina Dadoun[8], Jérôme Avouac[9], Kate Betteridge[10], Bruno Fautrel[11] and Laure Gossec[12], [1]Sorbonne University, INSERM, IPLES, Paris, France, [2]Hôpital Charles Nicolle, Rheumatology department, Tunis, Tunisia, Tunis, Tunisia, [3]1. AP-HP, Hôpital Saint-Antoine, Service de Rhumatologie, Paris, 75012, France, Paris, France, [4]CHU Gabriel Montpied, Clermont-Ferrand, [5]Institut Mutualiste Montsouris, Rheumatology department, Paris, France, Paris, Ile-de-France, France, [6]Hôpital Purpan, CHU Toulouse, Toulouse, France, [7]CeSOA, MGEN, Paris, France, Paris, Ile-de-France, France, [8]Medical centre, Paris, France, paris, Ile-de-France, France, [9]Cochin hospital, Rheumatology department, Paris, France, Paris, Ile-de-France, France, [10]Patient research partner, UK, london, England, United Kingdom, [11]Sorbonne University, INSERM, IPLES; Pitié-Salpêtrière Hospital, Paris, Ile-de-France, France, [12]Sorbonne University, INSERM; Pitié-Salpêtrière Hospital, Paris, Ile-de-France, France

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Patient Outcomes, Preferences, & Attitudes II: Engagement, Perceptions, & Quality of Life

Session Type: Abstract Session

Session Time: 11:00AM–11:50AM

Background/Purpose: Adherence to both medications and physical activity is insufficient in patients with inflammatory arthritis (IA), such as spondyloarthritis (axSpA), rheumatoid arthritis (RA) or psoriatic arthritis (PsA). Are there patterns towards adherence to both of these aspects of management?

Objectives: to assess and compare adherence to medication and levels of physical activity collected through Apps, in patients with IA.

Methods: This was an international, multicentric, cross-sectional study performed between October 2019 and June 2020 (ClinicalTrial NCT04426747). Consecutive patients were included if they had definite axSpA, RA or PsA, were aged above 18 and able to walk, with smartphones compatible with Apps measuring steps. Adherence to medication

was assessed using the Medication Adherence Report Scale MARS-9 (ranging from 9 to 45 with higher scores indicating higher adherence). Physical activity was measured by steps per day over the past week, through the patient's smartphone apps. The link between the MARS-9 score and physical activity was assessed by linear and logistic regression. For the logistic regression, patients were considered less adherent for the lowest tertile of the MARS score. They were compared to more adherent patients by univariable and multivariable logistic regression. There was no imputation of missing data.

Results: Of 130 patients included, 101 had analyzable data (46 (46%) axSpA, 26 (26%) RA, 27 (27%) PsA). Mean age was 45.2 years (standard deviation 13.1), mean disease duration 10.0 (8.5) years and 47% were women. 67% were receiving a biologic, and disease activity was moderate. Adherence to medication was high: the mean MARS score was 38.9 (7.0) with a median of 41. Physical activity was moderate: the mean steps per day collected with apps was 5631 (4286), median 4244 with 29% walking over 7000 steps per day. The linear regression between adherence to medications and steps per day did not indicate a link (R=-0.04, p=0.72). Furthermore, patients with a lower adherence to medication (lowest tertile scores, ie, < =38) did not differ in terms of physical activity 5703 (4014) versus 5602 (4419) steps per day, p=0.80 in multivariable analysis.

Conclusion: In this population of long-standing IA, adherence to medication was high whereas physical activity was insufficient. Patients with IA who were more adherent to treatment were not more physically active than those less adherent. Adherence to medication and adherence to lifestyle changes may be linked to different coping mechanisms.

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Abstract Number: 1982

Quality of Life of Patients with Facial Cutaneous Lupus Erythematosus

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Type: Abstract Session
Session Time: 11:00AM–11:50AM

Background/Purpose: Cutaneous Lupus Erythematosus (CLE) is an autoimmune skin disease that may occur with or without systemic lupus erythematosus (SLE). Active CLE lesions present with erythema and scale on photoexposed areas that can lead to dyspigmentation and scarring. This study aims to compare the QoL of patients with CLE on the face versus patients without facial lesions, and to determine the impact of facial lesion activity (erythema, scale) and damage (pigmentation, scarring) on patient QoL.

Methods: This is a cross-sectional study of a prospectively collected database of CLE patients seen at the Autoimmune Skin Diseases Unit of the University of Pennsylvania from 2007 to 2019. Patients were included if a Cutaneous

	N	%
Gender		
Female	291	79
Male	75	21
Ethnicity		
White	231	63
Black	114	31
Asian	14	4
Other	7	2
Age at diagnosis	37 (mean)	
Predominant CLE subtype		
Acute	43	12
Subacute	101	28
Chronic	211	60
Facial CLE		
Activity only	124	33
Damage only	32	8
Both	99	27
No Facial Lesion	111	32

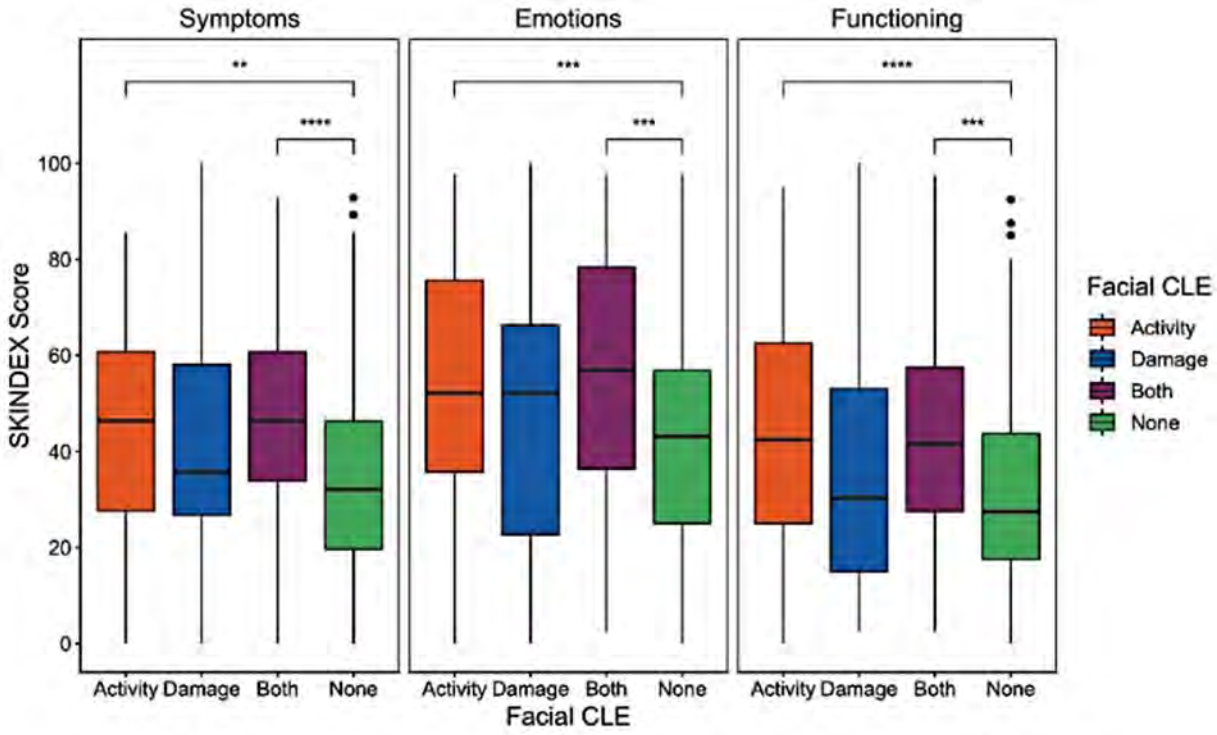
Table 1. Characteristics of CLE patients

Lupus Erythematosus Disease Area and Severity Index (CLASI) assessment and Skindex-29+3 questionnaire were completed on the initial visit. The CLASI is a validated instrument that quantifies CLE disease activity and damage in several exposed and covered areas of the body. Skindex-29+3 is a skin-specific QoL questionnaire that includes several domains such as symptoms, emotions, functioning and three additional lupus-specific questions on alopecia, photosensitivity and limitation of outdoor activities. A higher Skindex-29+3 domain score translates to poorer patient QoL. Based on clinical findings, patients were categorized into one of four groups, defined as those with: 1) active facial disease, 2) facial damage, 3) both facial activity and damage, or 4) no facial lesions. A one-way analysis of variance (ANOVA) and Bonferroni correction were used to compare QoL across the four groups. In addition, a multi-variable regression analysis was used to determine the relationship of facial disease and other pre-determined clinical variables to the QoL of CLE patients.

	Symptoms		Emotions		Functioning		Lupus-specific	
	β-Coefficient (95% CI)	p-value	β-Coefficient (95% CI)	p-value	β-Coefficient (95% CI)	p-value	β-Coefficient (95% CI)	p-value
FCLE with activity only (n=124)	7.91 (1.37 to 14.44)	**0.018**	8.41 (0.77 to 16.04)	**0.031**	7.79 (0.88 to 14.70)	**0.027**	2.97 (-5.64 to 11.57)	0.498
FCLE with damage only (n=32)	0.15 (-9.26 to 9.56)	0.975	-2.11 (-13.10 to 8.88)	0.706	-2.67 (-12.61 to 7.27)	0.597	-7.38 (-19.76 to 5.00)	0.242
FCLE with both activity and damage (n=99)	8.18 (2.01 to 14.36)	**0.010**	9.98 (2.78 to 17.20)	**0.007**	10.51 (3.98 to 17.03)	**0.002**	3.17 (-4.96 to 11.29)	0.444
Smoking status (current smokers vs. non-smokers) (current smokers n=102)	11.03 (5.79 to 16.28)	**<0.0001**	8.89 (2.76 to 15.01)	**0.005**	10.40 (4.86 to 15.94)	**<0.001**	8.71 (1.81 to 15.61)	**0.014**
Gender (females vs. males) (females n=291)	11.51 (5.79 to 16.28)	**<0.0001**	13.60 (6.84 to 20.37)	**<0.001**	12.22 (6.10 to 18.34)	**<0.001**	15.27 (7.64 to 22.89)	**<0.001**
*Race								
White (n=231)	2.93 (-10.23 to 16.08)	0.662	6.92 (-8.44 to 22.29)	0.376	5.88 (-8.02 to 19.78)	0.406	-5.75 (-23.06 to 11.56)	0.514
Black (n=114)	8.92 (-4.62 to 22.46)	0.196	9.48 (-6.32 to 25.30)	0.239	7.85 (-6.46 to 22.16)	0.281	-3.30 (-21.12 to 14.52)	0.716
Other (n=7)	7.11 (-17.49 to 31.70)	0.570	6.34 (-22.38 to 35.06)	0.664	0.59 (-25.40 to 26.58)	0.964	-15.09 (-47.46 to 17.28)	0.360
Predominant CLE subtype								
ACLE (n=43)	-10.56 (-28.00 to 6.88)	0.234	-10.60 (-30.97 to 9.76)	0.306	-9.23 (-27.66 to 9.20)	0.325	4.01 (-18.94 to 26.97)	0.731
SCLE (n=101)	-5.37 (-15.17 to 4.42)	0.281	-8.99 (-20.42 to 2.44)	0.123	-6.30 (-16.65 to 4.04)	0.231	4.63 (-8.26 to 17.52)	0.480
CCLE (n=211)	-1.53 (-8.48 to 5.42)	0.665	-2.56 (-10.68 to 5.56)	0.535	-4.73 (-12.07 to 2.62)	0.206	-7.12 (-16.27 to 2.03)	0.127

*"Asian" (n=14) was arbitrarily chosen to be dependent on "African-American", "Caucasian" and "Other" in this model
"No FCLE" (n=111) was the constant variable in the regression analysis.
Bold figures represent statistically significant values.

Table 2. SKINDEX-29+3 scores in patients with facial cutaneous lupus erythematosus – multivariable regression



Mean Skindex symptoms, emotions, and functioning scores of patients with facial disease who had both activity and damage, or activity alone, were higher and significantly different from those who had no facial lesions. Scores of patients who only have lesions of damage on the face did not significantly differ from those who have no facial lesions. (** = $p \leq 0.01$, *** = $p \leq 0.001$, **** = $p \leq 0.0001$)

Results: A total of 366 CLE patients were included in the study. Among them, 255 (68%) had facial CLE. Specifically, 99 (27%) patients had both activity and damage, 124 (33%) had activity only, and 32 (8%) had damage only (Table 1). The mean Skindex-29 Symptoms (S), Emotions (E) and Functioning (F) scores of facial CLE patients who had both activity and damage (S=47.34, E=55.06, F=43.45) or activity alone (S=43.55, E=53.72, F=43.91) were significantly higher compared to those who had no facial lesions (S=35.05, E=42.50, F=31.78) ($p < 0.05$) (Figure 1). Further, having both activity and damage on the face and having active facial CLE alone were significantly associated with poorer QoL across all three Skindex-29+3 indices, even after controlling for female gender and current smoking status, which are known to be associated with poor QoL scores in CLE patients (Table 2).

Conclusion: Patients with facial CLE have worse QoL compared with patients having no facial lesions. Facial CLE activity has a more significant effect on QoL than facial damage. A possible explanation for this finding is that patients with facial activity are concerned about potential systemic flares, while the damage is typically persistent but less worrisome to the patient. Clinicians should be aware that patients with facial activity are more affected in terms of quality of life and their fears of systemic disease should be addressed.

Disclosure: J. Concha, None; **D. Yan**, None; **C. Bax**, None; **A. Ravishankar**, None; **R. Borucki**, None; **R. Feng**, None; **V. Werth**, Corbus Pharmaceuticals, 2, Biogen, 2, 5, Resolve, 2, CSL Behring, 5, Regeneron, 5, Argenx, 5, Viela Bio, 2, 5, Principia, 5, Lilly, 5, Abbvie, 5, AstraZeneca, 2, 5, Amgen, 5, Kyowa Kirin, 5, Glaxo Smith Kline, 5, Cugene, 5, Celgene, 2, 5, Janssen, 2, 5, Pfizer, 2, 5, Gilead, 2, 5, Genentech, 2, 5, Syntimmune, 2, MedImmune, 5, Idera, 5, BMS, 5, Medscape, 5, Nektar, 5, Incyte, 5, EMD Sorona, 5, Crisalis, 5, Octapharma, 5, University of Pennsylvania, 9.

Abstract Number: 1983

Trajectories of Disease Activity in Patients with Newly Diagnosed Juvenile Idiopathic Arthritis in the Childhood Arthritis and Rheumatology Research Alliance Registry

Natalie Shiff[1], Peter Shrader[2], Colleen Correll[3], Anne Dennos[4], Thomas Phillips[2] and Timothy Beukelman[5], [1]Florida, Gainesville, FL, [2]Duke University, Durham, [3]University of Minnesota, Minneapolis, MN, [4]Duke University, Durham, NC, [5]University of Alabama at Birmingham, Birmingham, AL

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Pediatric Rheumatology – Clinical II: Outcomes & Care Delivery
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: To describe data-derived 2-year trajectories of disease activity in patients with recently diagnosed juvenile idiopathic arthritis (JIA) as measured by the clinical Juvenile Arthritis Disease Activity Score measured in 10 joints (cJADAS10), and to identify key baseline characteristics associated with disease trajectories.

Methods: The Childhood Arthritis and Rheumatology Research Alliance (CARRA) Registry includes a large cohort of children with JIA with clinical and medication data. JIA patients eligible for this study were enrolled between April 15, 2016 and December 6, 2019, within 3 months of JIA diagnosis, had at least 2 follow-up (FU) visits with cJADAS10 scores, and had 24 months of FU. Latent trajectory analysis of cJADAS10 using maximum likelihood estimation technique was performed. Model of best fit was selected by a combination of Bayesian information criterion (BIC), posterior probabilities, and clinical judgement. Select pairwise comparisons of baseline characteristics by trajectory were performed.

Table 1: Pairwise comparisons of baseline* characteristics between cJADAS10[β] trajectories with High, Rapidly Decreasing as the reference category.

Characteristic	High, Slowly Decreasing (N=154) OR (95% CI)	P	High, Increasing (N=39) OR (95% CI)	P
Age at diagnosis, per year	1.09 (1.04-1.14)	0.0003	1.08 (1.00-1.16)	0.05
Sacroilitis by clinical exam	2.13 (0.99-4.58)	0.05	1.20 (0.32-4.48)	0.79
ANA[€], yes vs. no	1.12 (0.72-1.75)	0.61	0.40 (0.18-0.89)	0.02
Abnormal ESR[¶]	0.54 (0.31-0.94)	0.03	0.53 (0.22-1.26)	0.15
Abnormal CRP[Φ]	0.36 (0.20-0.65)	0.0008	0.51 (0.19-1.33)	0.17
Taking any non-biologic DMARD[§] at baseline	0.92 (0.60-1.41)	0.69	0.48 (0.24-0.96)	0.04
Taking any biologic DMARD at baseline	0.65 (0.39-1.08)	0.10	0.69 (0.30-1.60)	0.39
Time from diagnosis until first biologic, per month	1.07 (1.02-1.12)	0.003	1.06 (1.01-1.12)	0.03
Physician global assessment	0.87 (0.78-0.97)	0.009	0.88 (0.74-1.05)	0.16

*baseline=within 3 months of diagnosis; [β]cJADAS10=clinical Juvenile Arthritis Disease Activity Score,10 joints; [€]ANA=antinuclear antigen [¶]ESR=erythrocyte sedimentation rate; [Φ]CRP=c-reactive protein; [§]DMARD=disease modifying anti-rheumatic drug. Only characteristics with p values ≤0.10 in one of the trajectories are shown.

Table 2: Pairwise comparisons of baseline* characteristics between cJADAS10[β] trajectories with Moderate, Decreasing as the reference category.

Characteristic	Moderate, Persistent OR (95% CI)	P
Age at diagnosis (per year)	1.08 (1.03-1.13)	0.0009
Time from onset to diagnosis (per month)	1.05 (1.01-1.10)	0.008
Number of joints with limited range of movement	1.33 (1.09-1.61)	0.004
Time from diagnosis until first biologic, per month	1.04 (1.00-1.08)	0.06
Physician global assessment	1.18 (1.03-1.35)	0.02
Taking any non-biologic DMARD at baseline	1.60 (1.02-2.49)	0.04
cJADAS10	1.18 (1.10-1.26)	<.0001
CHAQ	2.58 (1.51-4.40)	0.0005
Pain intensity in the past 7 days	1.31 (1.16-1.47)	<.0001
Pediatric global health survey T-score	0.90 (0.85-0.95)	<.0001

*baseline=within 3 months of diagnosis; [β]cJADAS10=clinical Juvenile Arthritis Disease Activity Score,10 joints; [Ψ]CHAQ=Childhood Health Assessment Questionnaire, Only characteristics with p values ≤0.10 in one of the trajectories are shown.

Results: There were 8,736 JIA patients in the Registry; 746 met study selection criteria. Clinician assigned JIA categories were: 32.6% rheumatoid factor (RF) negative polyarticular, 26.0% oligoarticular, 13% enthesitis related arthritis, 10.6% RF positive polyarticular, 8.7% systemic, 7.0% psoriatic, and 2.1% undifferentiated. Figure 1 shows the model of best fit, which identified 5 disease trajectories: High, Rapidly Decreasing (HRD) (n=199, 26.7%); High, Slowly Decreasing (HSD) (n=154, 20.6%); High, Increasing (HI) (n=39, 5.2%); Moderate, Persistent (MP) (n=218, 29.2%); and Moderate, Decreasing (MD) (n=136, 18.2%). When compared to the HRD trajectory, patients with a HSD trajectory were more likely to be older, have normal erythrocyte sedimentation rate and c-reactive protein, longer time from diagnosis to first biologic, and a lower baseline physician global assessment (PGA). Those with a HI trajectory were more likely to be ANA negative, have a longer time from diagnosis to first biologic, and less likely to be taking a non-biologic disease modifying anti-rheumatic drug (DMARD) at baseline (Table 1). Patients starting with moderate cJADAS10 scores with MP trajectory were more likely to be older, have a longer time from onset to diagnosis, more joints with restricted range, taking a non-biologic DMARD at baseline, have higher PGA, cJADAS10, CHAQ, and pain intensity, and lower pediatric global health survey scores at baseline (Table 2).

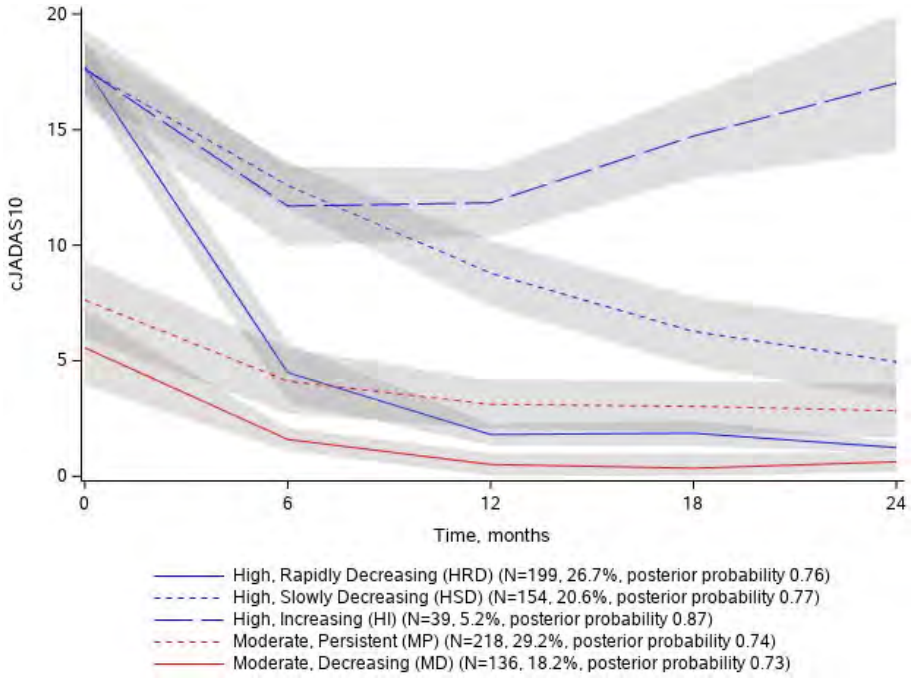


Figure 1. Trajectories of cJADAS10 with 95% CIs in patients with juvenile idiopathic arthritis (n=746)

Conclusion: This study identified 5 distinct data derived trajectories of JIA disease activity. Baseline variables associated with concerning trajectories are described, and could assist with targeting patients for more aggressive intervention shortly after diagnosis.

Disclosure: N. Shiff, None; **P. Shrader**, None; **C. Correll**, None; **A. Dennos**, None; **T. Phillips**, None; **T. Beukelman**, Novartis, 5, UCB, 5.

Abstract Number: 1984

Causal Pathways to Health-Related Quality of Life in Children with Juvenile Idiopathic Arthritis: Results from the ReACCh-Out Cohort

Kiem Oen[1], Jiahao Tian[2], Thomas Loughin[2], Roberta Berard[3], Mercedes Chan[4], Ciaran Duffy[5], Brian Feldman[6], Adam Huber[7], Deborah Levy[8], Dax G. Rumsey[9], Natalie Shiff[10], Shirley Tse[11], Lori Tucker[4], Karen Watanabe-Duffy[5] and **Jaime Guzman**[12], [1]University of Manitoba, Toronto, ON, Canada, [2]Simon Fraser University, Burnaby, BC, Canada, [3]London Health Sciences Centre, London, ON, Canada, [4]BC Children's Hospital, Vancouver, BC, Canada, [5]Children's Hospital of Eastern Ontario, Ottawa, ON, Canada, [6]The Hospital for Sick Children, Toronto, ON, Canada, [7]Dalhousie University, Halifax, NS, Canada, [8]Division of Rheumatology, The Hospital for Sick Children, Toronto, ON, Canada, [9]University of Alberta, Edmonton, AB, Canada, [10]Florida, Gainesville, FL, [11]SickKids, Toronto, ON, Canada, [12]University of British Columbia and BC Children's Hospital, Vancouver, BC, Canada

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical II: Outcomes & Care Delivery

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: The relative roles of disease activity and disability as determinants of health-related quality of life (HRQoL) in children with JIA have been controversial; sometimes their statistical significance disappears when pain is added to multivariate models. We explored whether structural equation modelling (SEM) may help clarify the causal pathways leading to decreased HRQoL in children with JIA. SEM estimates direct and indirect effects of candidate determinants along a causal pathway and uses multiple indicators to study determinants that are imperfectly quantified, such as disease activity and treatment intensity.

Methods: We used data from the Research in Arthritis in Canadian Children emphasizing Outcomes (ReACCh-Out) cohort. Based on published literature and clinical plausibility we proposed *a priori* models with explicit root causes (disease activity, treatment intensity) and mediators (pain, disease symptoms, function) leading to HRQoL measured with the Quality of my Life scale (QoML, 0=worst, 10=best) and the Juvenile Arthritis Quality of Life Questionnaire (JAQQ, 1=best, 7=worst), at five stages of disease: 1) diagnosis (within 28 days), 2) 3-9 months after diagnosis, 3) flare, 4) remission on medications, and 5) remission off medications. SEM was applied to the data and *a posteriori* models were selected based on fit statistics, parameter estimates, and plausibility. Here we focus on the models for QoML at diagnosis.

Results: We included 563 children with assessments of HRQoL within 28 days of diagnosis (Table 1). The *a priori* model is shown in Figure 1, where the direction and magnitude of hypothesized effects are depicted by the number of + or – signs. Figure 2 shows the *a posteriori* model with the best fit, where path coefficients estimated by SEM (numbers in Figure 2) quantify the observed direction and magnitude of effect. Comparison of the two figures shows that most hypothesized effects were supported, with a few modifications: 1) Drug categories and Discomforts and concerns were eliminated due to overlap or for lack of measures; 2) The paths from disease activity first to pain, functional deficit (CHAQ DI) and disease symptoms are supported; 3) Participation restrictions is a subsequent common intermediary, as proposed; 4) A direct path from treatment to QoML is the only one supported, whereas the path through side effects is not significant; 5) Pain, participation restrictions and effects of treatment not mediated by side effects are then the immediate determinants of QoML. In results not shown, models for 3-9 months after diagnosis

Characteristic	Median (IQR) or n (%)
Age at diagnosis, years	9.7 (4, 13) *
Female sex	361 (65)
Months from diagnosis to enrolment	0 (0, 0.1)
JIA category:	
Oligoarthritis	232 (41)
Polyarthritis RF negative	110 (20)
Enthesitis-related arthritis	84 (15)
Psoriatic	35 (6)
Systemic	25 (4)
Polyarthritis RF positive	19 (3)
Undifferentiated	58 (10)
Active joint count	2 (1,7)
Physician Global Assessment of Disease Activity	3.2 (1.9, 5.4)
Erythrocyte Sedimentation Rate, mm/h	18 (7, 38)
C-Reactive Protein, mg/L	2.8 (0.4, 13)
Pain intensity in a 10cm visual analogue scale	3.4 (0.9, 6.1)
Childhood Health Assessment Questionnaire score	0.5 (0.1, 1.1)
QoML scale	7.5 (5, 9.1)
JAQQ score	3 (2, 4.1)

Table 1. Baseline characteristics of 563 children with HRQoL assessments within 28 days of diagnosis in the ReACCh-Out cohort

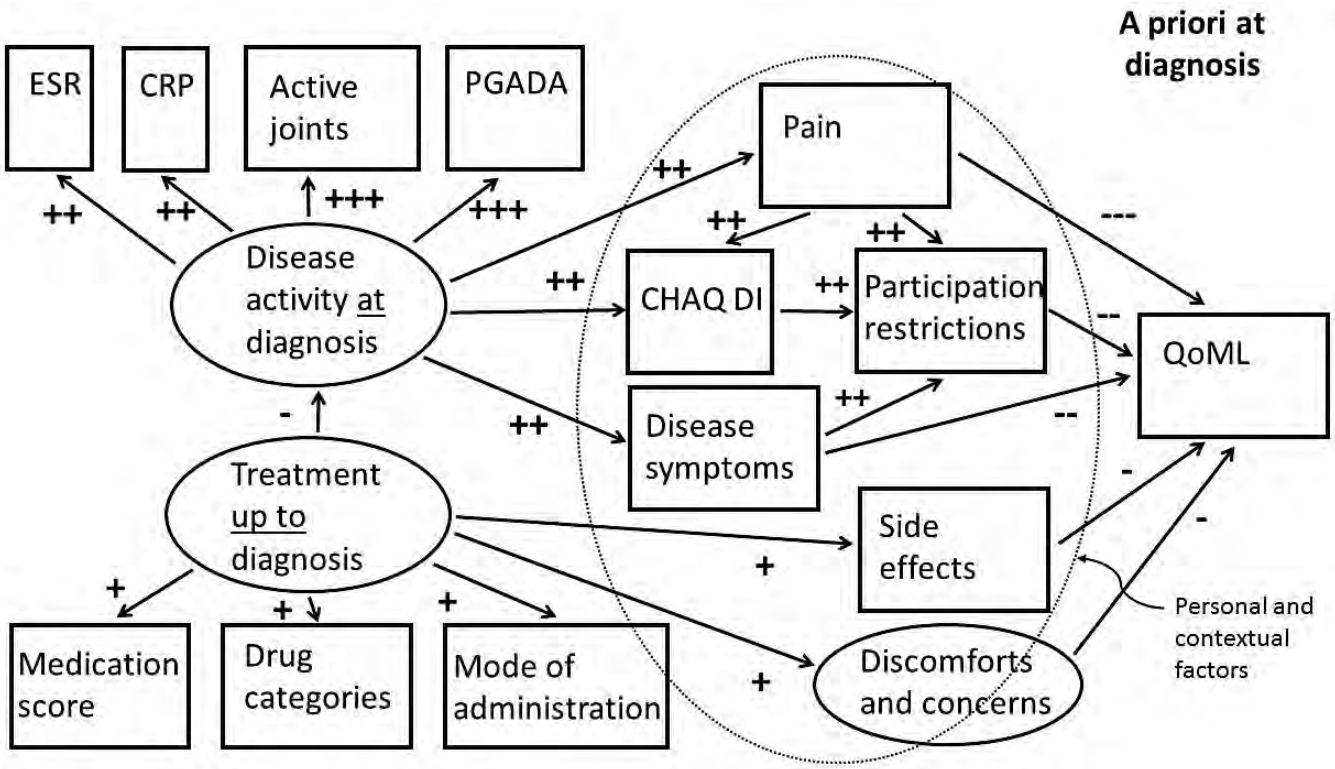


Figure 1. Hypothesized a priori model of the causal pathways leading to HRQoL at diagnosis as measured by QoML. ESR, CRP, active joint count and physician global assessment of disease activity (PGADA) are proposed as measures of disease activity; and medication score, drug categories and mode of administration as measures of treatment intensity. Disease activity and treatment intensity have proposed effects on mediators, such as pain, other symptoms and function which in turn impact HRQoL. Personal and contextual factors were not analysed.

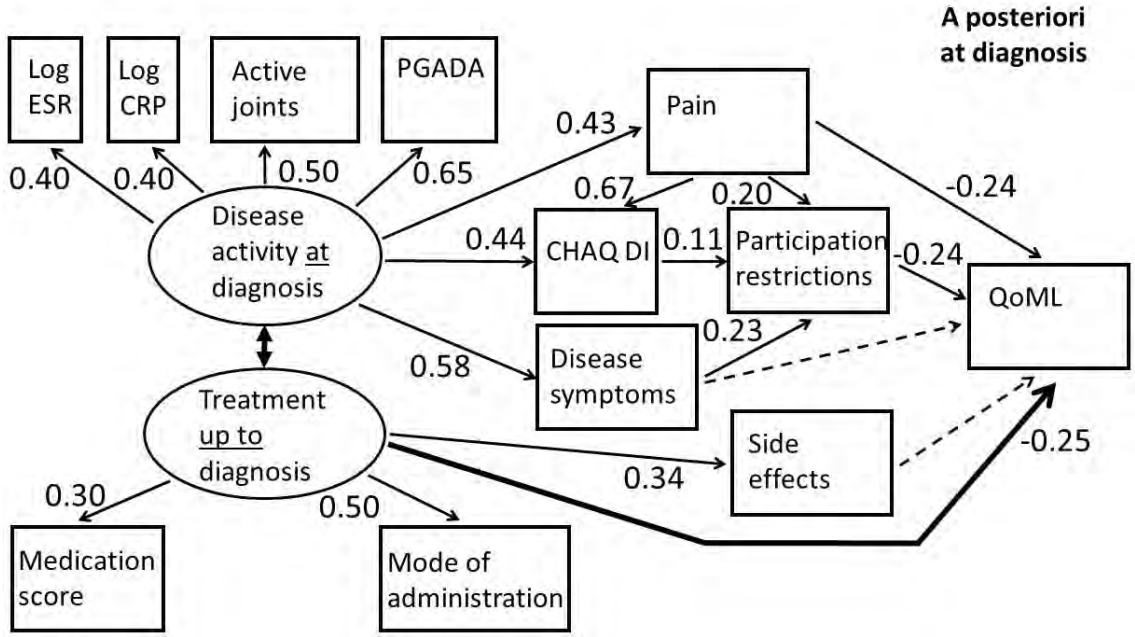


Figure 2. A posteriori model of best fit at diagnosis. Drug categories and Discomforts and concerns were removed due to overlap or lack of measures. Dashed lines represent postulated relationships not supported ($p>0.05$) and bold lines represent new paths that improve fit. Numbers signify path coefficients for the relationship between the variable at the arrow tail and the variable at the arrow head. A positive path coefficient of 0.5 means that a 1.0 standard deviation increase in the variable at the arrow tail corresponds to a 0.5 standard deviation increase in the variable at the arrow head. A negative path coefficient means an increase in the arrow tail variable corresponds to a decrease in the arrow head variable; and a path coefficient close to 0 reflects negligible impact.

and flare were similar to that at diagnosis and largely supported the hypothesized relationships (path coefficients 0.1 to 1.0 in the expected direction). Models for JAQQ provided greater specificity as to the domains of HRQoL affected. Models for remission stages were unsatisfactory.

Conclusion: Using SEM, we found support for disease activity and treatment intensity as root determinants of decreased HRQoL in children with JIA. Disease activity acts mainly via pain, functional impairments and participation restrictions. Treatment main effects at diagnosis were not mediated by side effects.

Disclosure: K. Oen, None; **J. Tian**, None; **T. Loughin**, None; **R. Berard**, None; **M. Chan**, None; **C. Duffy**, None; **B. Feldman**, Pfizer, 1, AB2-Bio, 1, Optum, 1, Novartis, 1; **A. Huber**, None; **D. Levy**, None; **D. Rumsey**, None; **N. Shiff**, None; **S. Tse**, None; **L. Tucker**, None; **K. Watanabe-Duffy**, None; **J. Guzman**, None.

Abstract Number: 1985

Validity and Reliability of Four Parent/Patient Reported Outcome Measures for Juvenile Idiopathic Arthritis

Chiara Trincianti[1], E. H. Pieter Van Dijkhuizen[2], Serena Calandra[3], Helga Sanner[4], Tamas Constantin[5], Troels Herlin[6], Marco Cattalini[7], Flavio Sztajnbok[8], Despoina Maritsi[9], Nicolino Ruperto[10], Angelo Ravelli[11] and **Alessandro Consolaro**[11], [1]Istituto Giannina Gaslini, Genova, Liguria, Italy, [2]Wilhelmina Children's Hospital, Utrecht, Netherlands, [3]IRCCS Istituto Giannina Gaslini, Genoa, Liguria, Italy, [4]Oslo University Hospital, Oslo, Norway, [5]Semmelweis University, Budapest, Hungary, [6]Aarhus University Hospital, Aarhus, Denmark, [7]Università di Brescia, Brescia, Italy, [8]Universidade do Estado do Rio de Janeiro, Rio de Janeiro, Brazil, [9]National and Kapodistrian University of Athens, Athens, Greece, [10]Istituto Giannina Gaslini, Genova, Italy, [11]Università degli Studi di Genova, Genoa, Italy

SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: In the last years, the interest in the assessment of parent- and child-reported outcomes (PCROs) in paediatric rheumatic diseases is gaining increasing importance. These measures reflect the parent and child perception of the disease course and effectiveness of therapeutic interventions and may facilitate concordance with physician's choices, improve treatment adherence, and participation in a shared decision -making strategy. Moreover, the availability of reliable PCROs could be crucial for remote monitoring of patients when in person clinical evaluation may be difficult or even not possible. Aim of this work is to provide further evidence of validity and reliability for four PCRO measures included in the OMERACT JIA core domain set: the evaluation of the child's pain and of the child's level of disease activity, the assessment of the morning stiffness (MS) duration, and an active joint count for parent/patient proxy or self-assessment.

Methods: Pain and disease activity were rated on a 21-numbered circle scale ranging from 0 (best result) to 10 (worst result). MS was measured with a 5-point Likert scale. The proxy- and self-assessment of active joints was obtained by rating the presence of pain or swelling in the following joints or joint groups: cervical spine, lumbo-sacral spine, shoulders, elbows, wrists, small hand joints, hips, knees, ankles, and small foot joints. To each joint or joint group, one point was given in case of monolateral involvement, two points in case of bilateral involvement. Patients were included in a multinational dataset of patients enrolled in the Epidemiology Treatment and Outcome of Childhood Arthritis study. Criterion validity was assessed by examining the correlation of the four tested measures with physician centered measures, ESR, and composite disease activity scores. Correlations of the measure with the cJADAS10 were also computed after grouping patients by ILAR category, by geographic area, and by education level. Reliability

was assessed in a subset of subjects with Spearman correlations and intraclass correlation coefficients (ICC), comparing two visits 7-14 days apart.

Results: A total of 8,848 parents and 6,204 patients had all the evaluations available. Correlations of tested measures were moderate (0.4–0-7) with physician centered measures and poor (< 0.4) with ESR. The level of correlation of the tested parent measures with the cJADAS10 remained stable after grouping patients by ILAR category. In the same analysis with patients grouped in eight geographic areas, correlation levels were similar, although, on average, they were higher in Latin America and slightly lower in North America. The levels of correlation with the cJADAS10 were similar in subjects in which the level of education of the parent filling the questionnaire was elementary or lower, high school, or degree, respectively. In 442 parents and 344 children, correlations between first and second assessment was > 0.7 for all measures; ICC ranged between 0.79 and 0.87 for parents and 0.81 and 0.88 for children.

Conclusion: The four tested PCROs showed good criterion validity and excellent reliability. These tools can be considered for remote patient assessment, when in person evaluation might not be possible.

Disclosure: C. Trincianti, None; **E. Van Dijkhuizen**, None; **S. Calandra**, None; **H. Sanner**, None; **T. Constantin**, None; **T. Herlin**, None; **M. Cattalini**, None; **F. Sztajnbok**, None; **D. Maritsi**, None; **N. Ruperto**, Ablynx, 5, 8, Astrazeneca-Medimmune, 5, 8, Biogen, 5, 8, Boehringer, 5, 8, Bristol Myers Squibb, 2, 5, 8, 9, Eli Lilly, 2, 5, 8, 9, EMD Serono, 5, 8, GlaxoSmithKline, 2, 5, 8, 9, F Hoffmann-La Roche, 2, 5, 8, 9, Janssen, 2, 5, 8, 9, Merck, 5, 8, Novartis, 2, 5, 8, 9, Pfizer, 2, 5, 8, 9, R-Pharma, 5, 8, Sanofi, 5, 8, Servier, 5, 8, Sinergie, 5, 8, Sobi, 2, 5, 8, 9, AbbVie, 5, 8, Takeda, 5, 8; **A. Ravelli**, AbbVie, BMS, Pfizer, Hoffman LaRoche, Novartis, Centocor, “Francesco Angelini” and Reckitt Benckiser., 1, 2; **A. Consolaro**, None.

Abstract Number: 1986

Determinants of Variation in Pediatric Systemic Lupus Erythematosus Care Delivery

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Patients with pediatric systemic lupus erythematosus (pSLE) receive only a fraction of recommended care. Moreover, variation in care delivery likely contributes to pervasive racial and ethnic disparities in pSLE outcomes. We aimed to begin improving pSLE and mixed connective tissue disease (MCTD) care delivery by defining and assessing variation in performance of a pediatric lupus care index (p-LuCI).

Methods: This was a cross-sectional study of pSLE quality measure performance in the context of an improvement project conducted in the Division of Rheumatology at a large tertiary-care pediatric hospital. Providers included nine attending pediatric rheumatologists and 4 fellow trainees. The project team identified four key drivers of high-quality pSLE care potentially linked to improved outcomes: 1) accurate tracking of pSLE characteristics and treatments, 2) point-of-care outcome assessment, 3) comorbidity assessment and prevention, and 4) timely follow up. To address key drivers, we defined 13 metrics that were bundled into the p-LuCI (**Table 1**). The p-LuCI was scored from 0-1

Table 1. Pediatric systemic lupus erythematosus care index component performance.						
Domain	**Metric**	**Specification**	**Performance**	**Index values above mean**	**Index values below mean**	**p-value**
Clinical / Outcome focus	SLEDAI score documented[a]	Yearly	62% (61/99)	75%	25%	<0.001
	SLICC-DI score documented	Yearly	31% (34/111)	48%	5%	<0.001
	PGA score score documented	Each visit	67% (74/111)	82%	43%	<0.001
	Target attestation[ad]	Each visit	61% (60/99)	69%	34%	<0.001
	Disease characteristics review[e]	Yearly	63% (70/111)	87%	27%	<0.001
Comorbidity care	Pneumococcal vaccination	Up to date	69% (77/111)	81%	52%	0.002
	Influenza vaccination[b]	Up to date	52% (49/95)	53%	50%	0.80
	Blood pressure assessment[f]	Each visit	53% (59/111)	69%	30%	<0.001
	Lipid testing	Every 2 years	76% (84/111)	87%	59%	0.001
	Vitamin D testing	Yearly	59% (66/111)	72%	41%	0.001
	Stress-dose steroid plan[acg]	Documented	62% (31/50)	68%	42%	0.10
	Steroid-sparing agent prescribed[ach]	Each visit	96% (48/50)	97%	92%	0.38
Population management	Visit scheduling[i]	Up to date	20% (22/111)	24%	14%	0.19

The p-value is based on a χ^2 test of metric completion comparing those with p-LuCI values above versus below the division mean.

SLEDAI: Systemic lupus erythematosus disease activity index 2000 version

SLICC-DI: Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index modified for pSLE

[a] SLEDAI and target attestation measures only used for patients with pSLE. Therefore, the p-LuCI denominator in MCTD patients was reduced by two for a maximum of 11.

[b] Influenza vaccination metric includes only patients with visits after August 1 of the flu year and do not refuse the influenza vaccine.

[c] Stress-dose steroid plan and steroid-sparing agent measures only assess among individuals with steroid prescriptions for greater than 14 consecutive days within the previous 18 months. Therefore, the p-LuCI denominator for patients not exposed to chronic steroids was reduced by two for a maximum of 11.

[d] Target attestation: Completion of visit note element indicating that patient's disease activity is at target – no clinical active disease, at target – minimal disease activity, not at target.

[e] Disease characteristics review: Clinician confirmation of up to date disease summary form in the electronic health record.

[f] Blood pressure assessment: Classification of age and sex-specific blood pressure status according to the National Institutes of Health National Heart Lung and Blood Institute guidelines.

[g] Stress-dose steroid plan: Documentation of secondary adrenal insufficiency in the electronic health record.

[h] Steroid-sparing agent prescribed: Steroid-sparing agents included cyclophosphamide, mycophenolate mofetil, mycophenolic acid, azathioprine, methotrexate, cyclosporin A, tacrolimus, sirolimus, rituximab, belimumab, abatacept, ustekinumab, or other biologic medication documented in a standard electronic health record note element.

[i] Visit scheduling: Appointment scheduled within 30 days after clinician-specified follow-up interval at last visit. If no follow-up interval was specified, 180 days was used as the recommended follow-up interval. Performance on the visit scheduling metric was lower because this sample was drawn during the SARS-CoV2 pandemic with altered patient scheduling procedures.

Table 1. Pediatric systemic lupus erythematosus care index component performance.

based on the number of metrics completed divided by the number of eligible metrics. We combined discrete data from a pSLE visit template along with prescribing and appointment data to capture index components in an automated pSLE report.

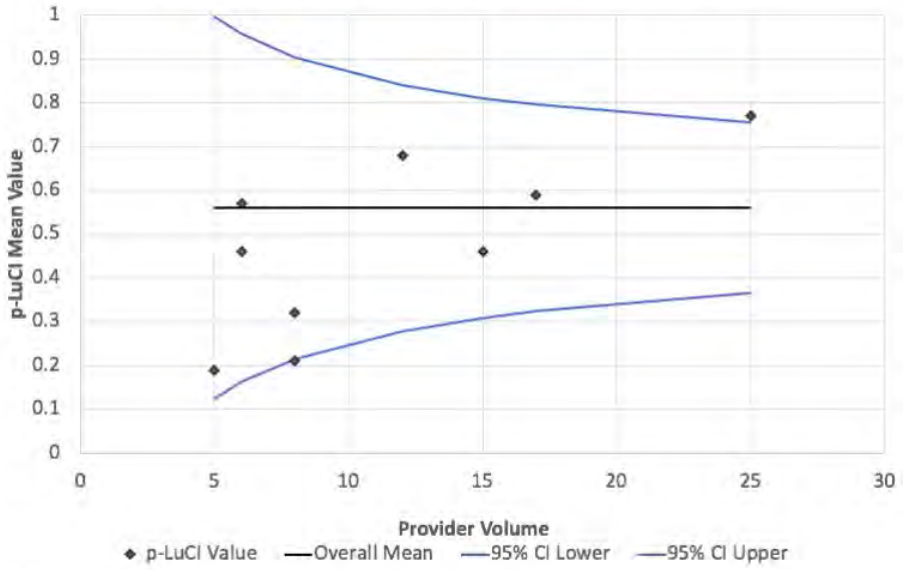
We included patients clinically diagnosed with pSLE and MCTD with at least one visit in the Division of Rheumatology within the prior 15 months. After bivariate analyses, independent p-LuCI predictors were identified using multivariable linear regression with clustering by provider. Provider-level variation was defined as +/- 2 SD from the p-LuCI mean.

Results: We included 111 patients (99 SLE, 12 MCTD) with a mean age of 16.9 ± 3.0 years. 88 (79%) were female, 39 (35%) were black, and 12 (11%) were Hispanic. 10 (9%) had families who were not English-speaking. Of 33 patients with nephritis, 16 (48%) had prior visits in a multi-disciplinary Rheumatology/Nephrology Clinic.

Table 2. Predictors of performance on the pediatric systemic lupus erythematosus care index.				
Variable	**Unadjusted**		**Adjusted**	
	β (95% CI)	**p-value**	**β (95% CI)**	**p-value**
Age (years)	-0.01 (-0.02, 0.01)	0.50		
Sex (Female)	-0.04 (-0.13, 0.05)	0.33		
Black race	0.05 (-0.04, 0.13)	0.26		
Hispanic ethnicity	0.20 (0.10, 0.30)	0.001	0.11 (0.04, 0.18)	0.005
Chronic steroid exposure	0.15 (0.05, 0.25)	0.006	0.08 (0.02, 0.15)	0.02
Nephritis	0.17 (0.04, 0.30)	0.01	0.09 (0.01, 0.03)	0.01
Provider volume (per patient)	0.01 (0.00, 0.03)	0.01	0.02 (0.01, 0.03)	0.001
Rheumatology fellow assigned	0.14 (-0.12, 0.41)	0.09	0.37 (0.03, 0.41)	0.01
Note: Linear regression with clustering according to provider was performed for all models.				

Table 2. Predictors of performance on the pediatric systemic lupus erythematosus care index.

Figure: Funnel plot demonstrating provider-level p-LuCI performance.



* Only providers with ≥ 5 pSLE patients are included.

Figure. Funnel plot demonstrating provider-level p-LuCI performance.

The mean p-LuCI was 0.56 ± 0.25. p-LuCI component performance is shown in **Table 1**. Patients with higher p-LuCI values were more likely to receive care across nine of 13 metrics. The predictors of p-LuCI performance are shown in **Table 2**. Independent predictors of higher p-LuCI values were Hispanic ethnicity, chronic steroid exposure, history of nephritis, higher provider pSLE/MCTD volume, and fellow provider assignment. Among providers with ≥ 5 patients under care, p-LuCI values ranged from 0.19 to 0.77. One provider each was significantly above and below the cohort mean (**Figure**).

Conclusion: We demonstrated that pSLE patients received 56% of p-LuCI measures with significant variation at the provider level. In addition, we identified demographic, disease-specific, and provider characteristics associated with

higher performance. Future p-LuCI components should include reproductive counseling, transition preparation, and mental health screening. Multicenter studies are needed to assess the impact of efforts to decrease p-LuCI variation and increase performance on disease activity and damage accrual, disparities in health care utilization, and patient/caregiver satisfaction.

Disclosure: J. Burnham, None; **R. Peterson**, None; **J. Ukaigwe**, None; **L. Cecere**, None; **A. Knight**, None; **J. Chang**, None.

Abstract Number: 1987

Predictors of Adverse Outcomes in Patients with Childhood-Onset Systemic Lupus Erythematosus Transitioning to Adult Care

Nicole Bitencourt[1], Una Makris[1], Elizabeth Solow[1], Tracey Wright[2] and Bonnie Bermas[3], [1]UT Southwestern Medical Center, Dallas, TX, [2]UT Southwestern, Plano, TX, [3]UTSouthwestern.edu, Dallas, TX

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Pediatric Rheumatology – Clinical II: Outcomes & Care Delivery
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: The transition from pediatric to adult care is a vulnerable period and is linked to increased healthcare utilization and poor outcomes. We sought to identify risk factors associated with an unsuccessful transfer to adult care in childhood-onset systemic lupus erythematosus (cSLE).

Methods: A retrospective analysis of patients with cSLE seen in adult public or private rheumatology clinics was performed. Outcomes of interest were development of end-stage renal disease (ESRD) or death and time to first hospitalization following the final pediatric rheumatology visit. Independent variables included sociodemographic and disease characteristics. Pediatric factors influencing ESRD or death were assessed using Chi-square, Fisher's test, or the Wilcoxon rank-sum test. A stepwise multivariable logistic regression model to predict ESRD or death was used. Pediatric factors influencing time to first hospitalization were assessed using the log-rank test. Stepwise multivariable Cox regression analysis was performed to define predictors of time to adult hospitalization.

Results: Of 190 patients with cSLE, 21 (11%) developed ESRD and 9 (5%) died following the final pediatric rheumatology visit. As seen in Figure 1, ESRD or death were more common among patients of Black race or Hispanic ethnicity, those with public insurance, a history of child protective services (CPS) involvement or abuse, an outpatient narcotic prescription for non-procedural pain management during pediatric care, a history of unscheduled hospitalization, emergency department (ED) visit, or at least one no-show visit during the final year in pediatric care, and prior cyclophosphamide therapy ($p < 0.03$). Gender, age at transfer, SLE disease duration, and income based on zip-code were not significantly related to development of ESRD or death. In logistic regression, public insurance, history of CPS involvement or abuse, and an unscheduled pediatric hospitalization were associated with development of ESRD or death (Table 1).

Of 114 patients for whom healthcare utilization data were available following final pediatric visit, 53% had a hospitalization in adult care. Time interval to first adult hospitalization was shorter for patients of Black race or Hispanic ethnicity, those with public insurance, a history of CPS involvement or abuse, an outpatient narcotic prescription for non-procedural pain management during pediatric care, a history of unscheduled hospitalization, ED visit, and no-

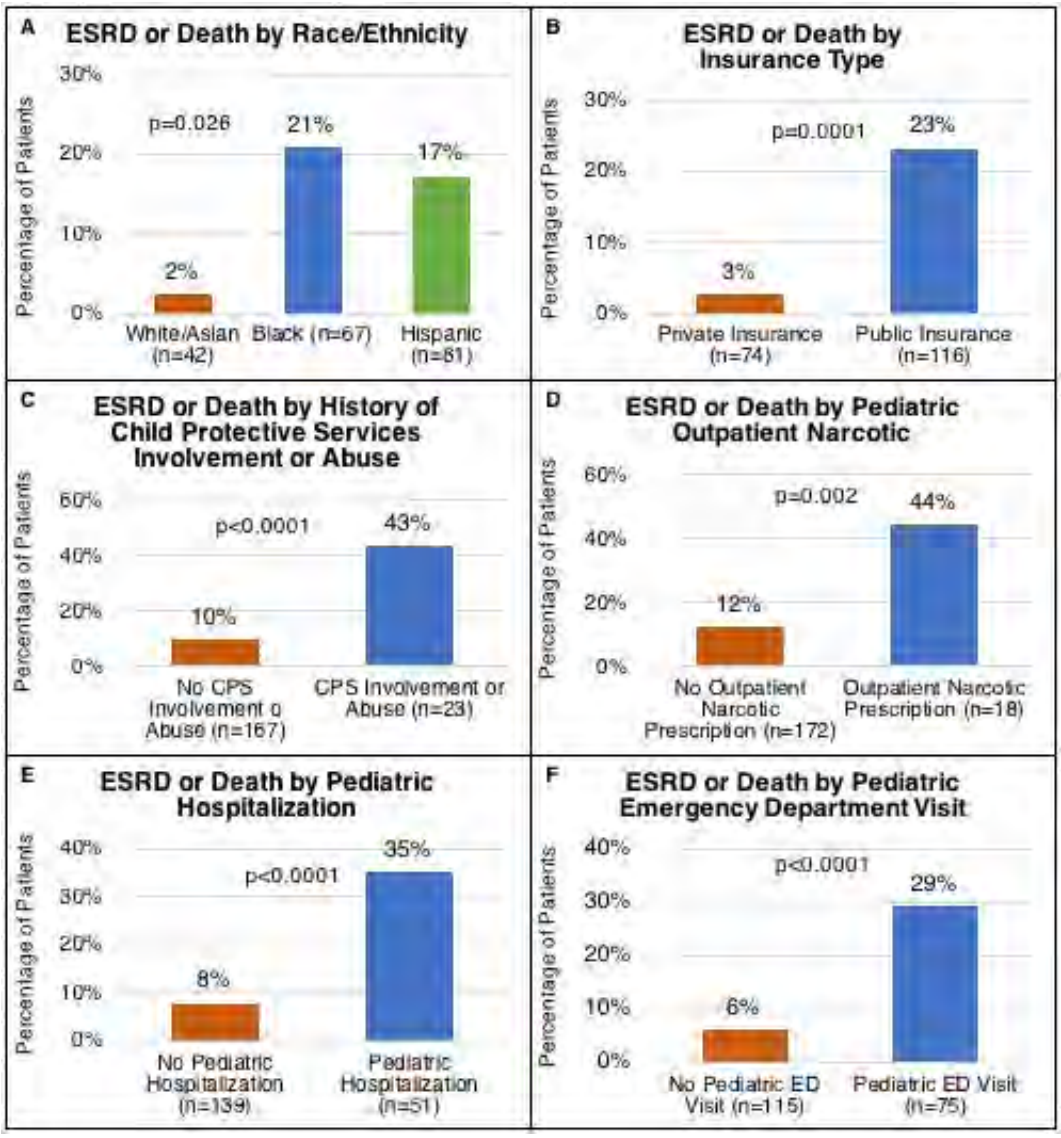


Figure 1. Pediatric Factors Associated with ESRD or Death after Transfer to Adult Care

show visit during the final year in pediatric care ($p< 0.03$) (Figure 2). In Cox regression analysis, a pediatric outpatient narcotic prescription was associated with shorter time to hospitalization while White or Asian race was associated with longer time to first hospitalization ($p< 0.007$).

Conclusion: Our findings indicate that efforts to improve transition outcomes among patients with cSLE should focus on high risk individuals in pediatric care, including those of Black race or Hispanic ethnicity, patients with public insurance, a history of CPS involvement or abuse, outpatient narcotic prescription for non-procedural pain management, and history of hospitalization, ED visit or no-show visit in the final year of pediatric care.

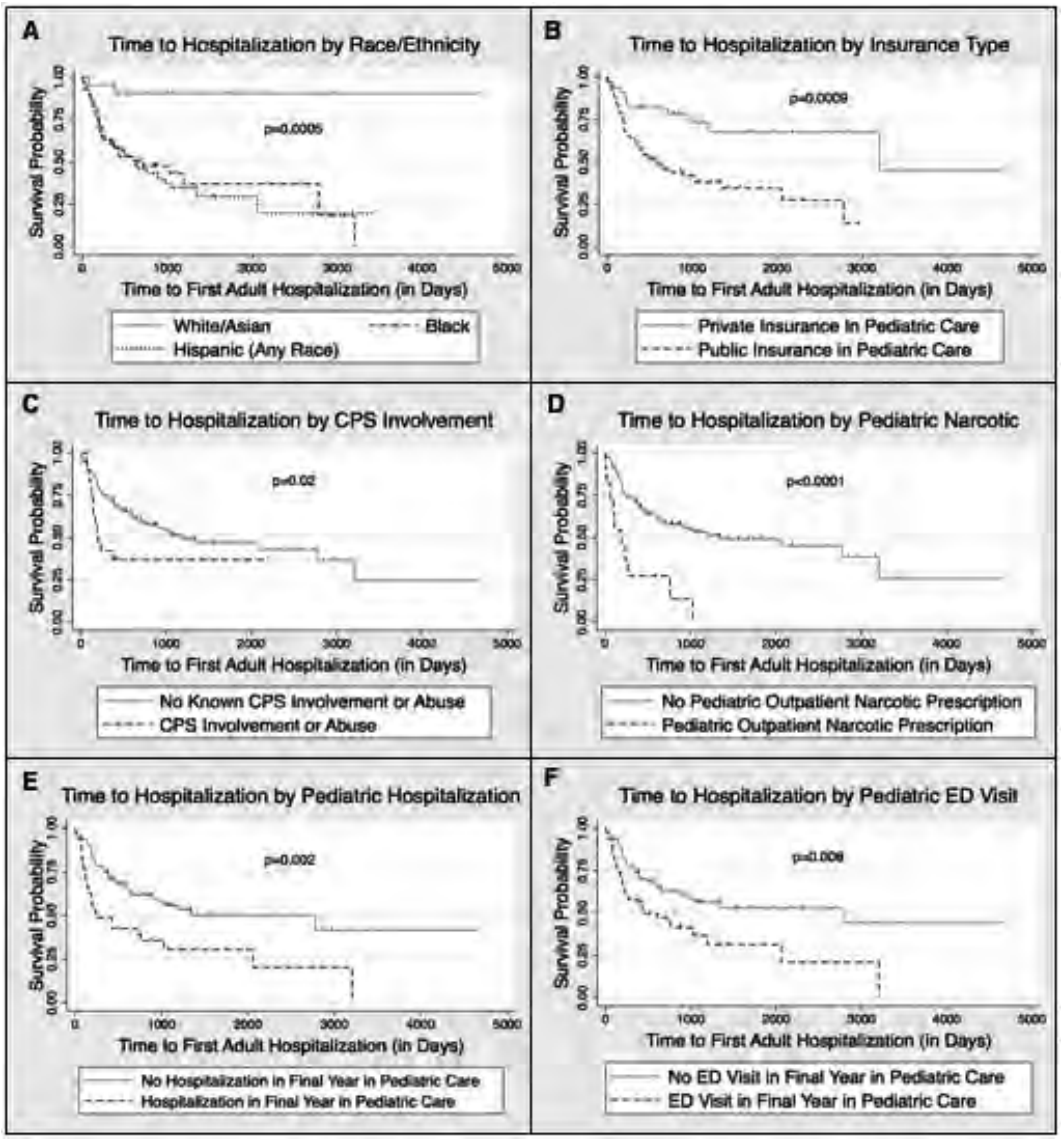


Figure 2. Time to Adult Hospitalization by Pediatric Factors

Table 1. Stepwise Regression Models of Pediatric Predictors of Adult Outcomes in SLE

Multivariable Logistic Regression of ESRD or Death in Adult Care

	Odds Ratio (CI)	p-value
Public Insurance in Pediatrics	6.7 (1.5-30.7)	0.002
CPS Involvement or Known Abuse	6.6 (2.3-19.1)	<0.0001
Hospitalization in Pediatric Care	3.2 (1.3-8.3)	0.01

Multivariable Cox Regression of Time to First Adult Hospitalization

	Hazard Ratio (CI)	p-value
Pediatric Outpatient Narcotic Prescription	3.3 (1.6-6.5)	0.001
White or Asian Race	0.14 (0.03-0.58)	0.007
Public Insurance in Pediatrics	2.0 (0.996-4.3)	0.051

SLE: Systemic Lupus Erythematosus; ESRD: End-Stage Renal Disease; CI: Confidence Interval; CPS: Child Protective Services

Table 1. Stepwise Regression Models of Pediatric Predictors of Outcomes in SLE

Disclosure: N. Bitencourt, None; **U. Makris**, None; **E. Solow**, None; **T. Wright**, None; **B. Bermas**, None.

Abstract Number: 1988

Skin Disease More Recalcitrant to Intervention Than Muscle Disease: A Long-Term Prospective Study of 184 Children with Juvenile Dermatomyositis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical III: Systemic Autoimmune Disease

Session Type: Abstract Session

Session Time: 11:00AM–11:50AM

Background/Purpose: Persistent skin manifestations, in particular calcinosis, contribute to significant morbidity in patients with JDM. The goal of this study was to compare the course of skin vs muscle symptoms and document the frequency of calcinosis in children with JDM.

Methods: Data were extracted from the Lurie Children's CureJM Center of Excellence's Juvenile Myositis Registry, a dataset that includes all children diagnosed with definite/probable JDM based on Bohan and Peter criteria (n=485). The duration of untreated disease (DUD), the interval between first symptom and start of therapy was calculated. The children were assessed for calcifications and for extent of disease, using the JDM Disease Activity Score (DAS) for skin (DAS-S), muscle (DAS-M) and total (DAS-T). Among this dataset were data on 184 untreated children with JDM, seen from July, 1971 to May, 2019. A paired t-test was used to analyze differences in mean DAS scores at baseline and 6, 12, 24, and 36 months on medication; as well as time to reach clinically inactive skin vs. muscle scores (DAS 0, ≤1, ≤2). Differences in time for abnormal vascular elements in DAS-S to resolve was calculated using a one-way ANOVA.

Results: 138 girls (75%) and 46 boys (25%) with untreated JDM and a mean age of 7.1±3.9 (mean±SD) years were enrolled and followed for 6.6±5.5 years. At baseline, the mean DAS-Muscle (DAS-M) score was 4.9±1.4 compared to DAS-Skin (DAS-S) score of 5.8±3.0 ($p< 0.01$). DAS-S was persistently higher than DAS-M at 6, 12, 24, and 36 months of treatment and reached 0/clear, ≤1/almost clear, and ≤2/mild later than DAS-M. The mean time to reach a DAS score of 0 was 18.4±20.4 months for skin compared to muscle of 9.5±9.9 months ($p< 0.001$). Altogether, 92% reached clinical inactivity for skin compared to 97% for muscle ($p< 0.05$). Of the vascular features in DAS-S, eyelid margin capillary dilatation was seen most frequently (54%) and persisted longest before clearance at a mean duration of 7.8±14.5 months. This was significantly longer than recovery time for periungual capillary telangiectasia (3.5±4.0 months) ($p< 0.05$) and palate vessel dilatation (3.3±3.2 months) ($p< 0.05$). 9 (5%) patients had calcifications at baseline and an additional 23 (15%) developed calcifications during the course of disease. The majority (83%) of calcifications were classified as mild. Calcifications developed after a mean of 64.7±71.5 months on medication and took an average of 6.1±7.0 months to resolve. 26% (6 out of 23) of patients had a recurrence of calcification at the same site; calcifications never resolved in 7 patients, 5 of whom (71%) had calcifications at first visit. These 7 children had a mean duration of untreated disease (DUD) at diagnosis of 60.2±44.5 months, in comparison to the children whose calcifications resolved, who had a mean DUD at diagnosis of 12.5±14.8 ($p< 0.001$).

Conclusion: Skin disease presents with greater activity and persists longer than muscle disease in children with JDM. Vascular features within skin, particularly eyelid margin capillary dilatation, tend to be most persistent. Early and aggressive treatment can limit the severity and persistence of calcifications that recur late in the disease course.

Disclosure: A. Wang, None; **G. Morgan**, None; **C. Huang**, None; **A. Paller**, None; **L. Pachman**, Reveragen, 2.

Abstract Number: 1989

NXP2 Autoantibodies Link to Interferon Signature in Juvenile Myositis Lesional Skin

Jessica Turnier[1], Lauren Pachman[2], Lori Lowe[3], Alex Tsoi[3], Sultan Elhaj[1], Rajasree Menon[1], Maria Amoruso[2], Gabrielle Morgan[4], Johann Gudjonsson[5], Celine Berthier[3] and J Michelle Kahlenberg[1], [1]University of Michigan, Ann Arbor, MI, [2]Northwestern University Feinberg School of Medicine, Chicago, IL, [3]University of Michigan, Ann Arbor, [4]Ann & Robert H. Lurie Children's Hospital of Chicago and Northwestern University Feinberg School of Medicine, Chicago, IL, [5]University of Michigan, Ann ArborUniversity of Michigan

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical III: Systemic Autoimmune Disease

Session Type: Abstract Session

Session Time: 11:00AM–11:50AM

Figure 1.

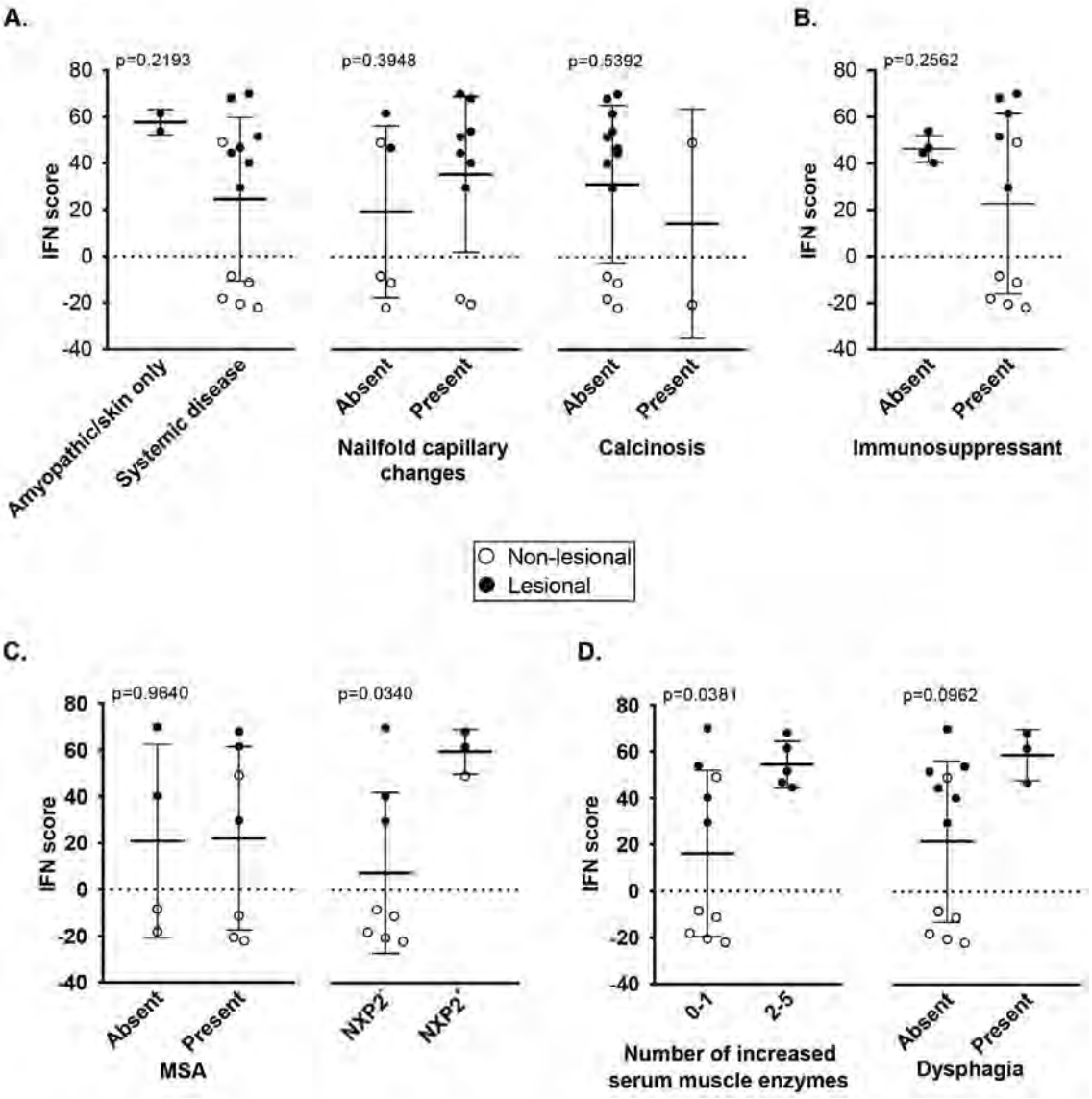


Figure 1. JM IFN score with clinical variables. A. The IFN score is not significantly modified by the presence of systemic disease, nailfold capillary changes or calcinosis. B. The IFN score is not significantly changed by treatment status. C. The presence alone of a myositis-specific autoantibody (MSA) does not significantly alter the IFN score; however, NXP2+ JM patients have a significantly higher IFN score (p-value=0.034). D. An increased overall number of serum muscle enzymes was associated with a higher IFN score (p-value=0.0381). A higher IFN score demonstrated a trend toward presence of dysphagia.

Background/Purpose: Skin inflammation can herald systemic disease in juvenile myositis (JM), yet we lack an understanding of pathogenic mechanisms driving skin inflammation in JM. The goals of this study were to 1) define JM cutaneous gene expression signatures in the context of patient data, and 2) identify key genes and pathways differentiating skin disease in JM from childhood-onset systemic lupus erythematosus (cSLE).

Methods: We utilized formalin-fixed paraffin-embedded (FFPE) skin biopsies from 15 JM (9 lesional, 6 non-lesional), 5 cSLE (all lesional), and 8 controls to perform transcriptomic analysis and identify significantly differentially expressed genes (DEGs; q-value ≤ 5%) between patient groups. Ingenuity Pathway Analysis (IPA) was used to highlight enriched biological pathways and Genomatix Pathway System (GePS) to characterize regulated genes within biological networks. We validated DEGs using immunohistochemistry and quantitative real-time PCR. Interferon (IFN) scores

Figure 2.

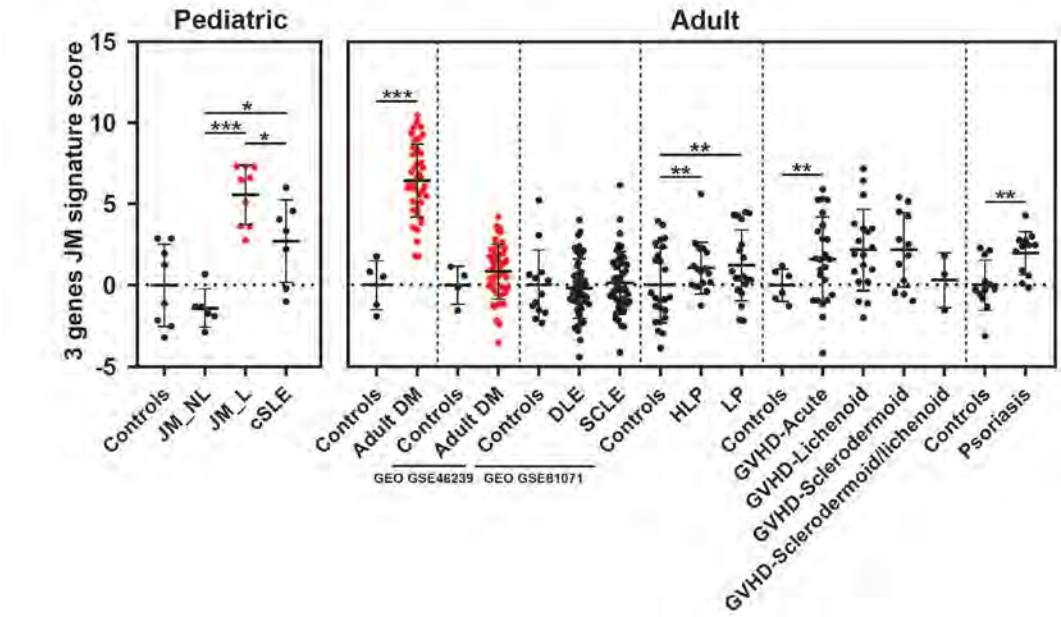


Figure 2. JM disease signature: comparison with transcriptomic datasets of skin lesions from adult DM and other inflammatory skin diseases. The 3-gene JM transcriptomic signature identified is the highest in juvenile and adult dermatomyositis compared to other skin disease lesions. Dermatomyositis lesional samples are represented in red. Vertical dashed lines separate the studied datasets. Each dataset had its control sample set. DLE: discoid lupus erythematosus, SCLE: subacute cutaneous lupus erythematosus, HLP: Hypertrophic lichen planus, LP: lichen planus, GVHD: graft versus host disease. * p-value<0.05; ** p-value<0.01; *** p-value<0.0001.

were calculated and compared amongst patient groups and between JM clinical features. A JM-specific signature was derived from comparison of cSLE and lesional JM (JM_L) skin transcriptomes relative to controls and compared to adult skin disease array datasets. Cell type enrichment analysis was then performed using the xCell webtool.

Results: Comparison of JM_L to control revealed 221 DEGs, with the majority of upregulated genes representing IFN-stimulated genes. *CXCL10*, *CXCL9* and *IFI44L* represented the top three DEGs (fold-change respectively = 23.2, 13.3, 13.0, q-value < 0.0001). While IFN scores in JM did not differ based on individual skin disease manifestations or treatment status, NXP2+ JM patients exhibited the strongest IFN signature (Figure 1) and also demonstrated the most extensive MX1 immunostaining, both in keratinocytes and perivascular regions. When compared to cSLE, JM_L skin showed no difference in IFN scores and shared a similar gene expression pattern, with only 28 unique DEGs. The top most significant unique DEGs in JM_L included *FBLN2*, *CHKA* and *SLURP1*, genes with diverse roles in extracellular matrix structure, keratinocyte proliferation and differentiation, calcium signaling and phospholipid metabolism. A 3-gene JM-specific skin signature derived using *FBLN2*, *CHKA* and *SLURP1* was higher in dermatomyositis (both pediatric and adult) as compared to other skin diseases, including cutaneous lupus (Figure 2). cSLE skin had 722 unique DEGs compared to JM_L, notably increased expression of IFNγ relative to control. Cell type enrichment analysis showed that cSLE skin exhibited an overall higher inflammatory cell signature compared to JM_L, with increased T-cells, B-cells, macrophages and plasmacytoid dendritic cells (Figure 3).

Conclusion: JM lesional skin demonstrates a prominent IFN signature, similar to cSLE. A candidate JM-specific skin signature was derived using *FBLN2*, *CHKA* and *SLURP1*, all genes not typically considered to have immunomodulatory roles but instead functions in cellular structure and metabolism. Further investigation into the association of a higher IFN score with NXP2 autoantibodies may lend insight into JM disease endotypes and pathogenesis.

Figure 3.

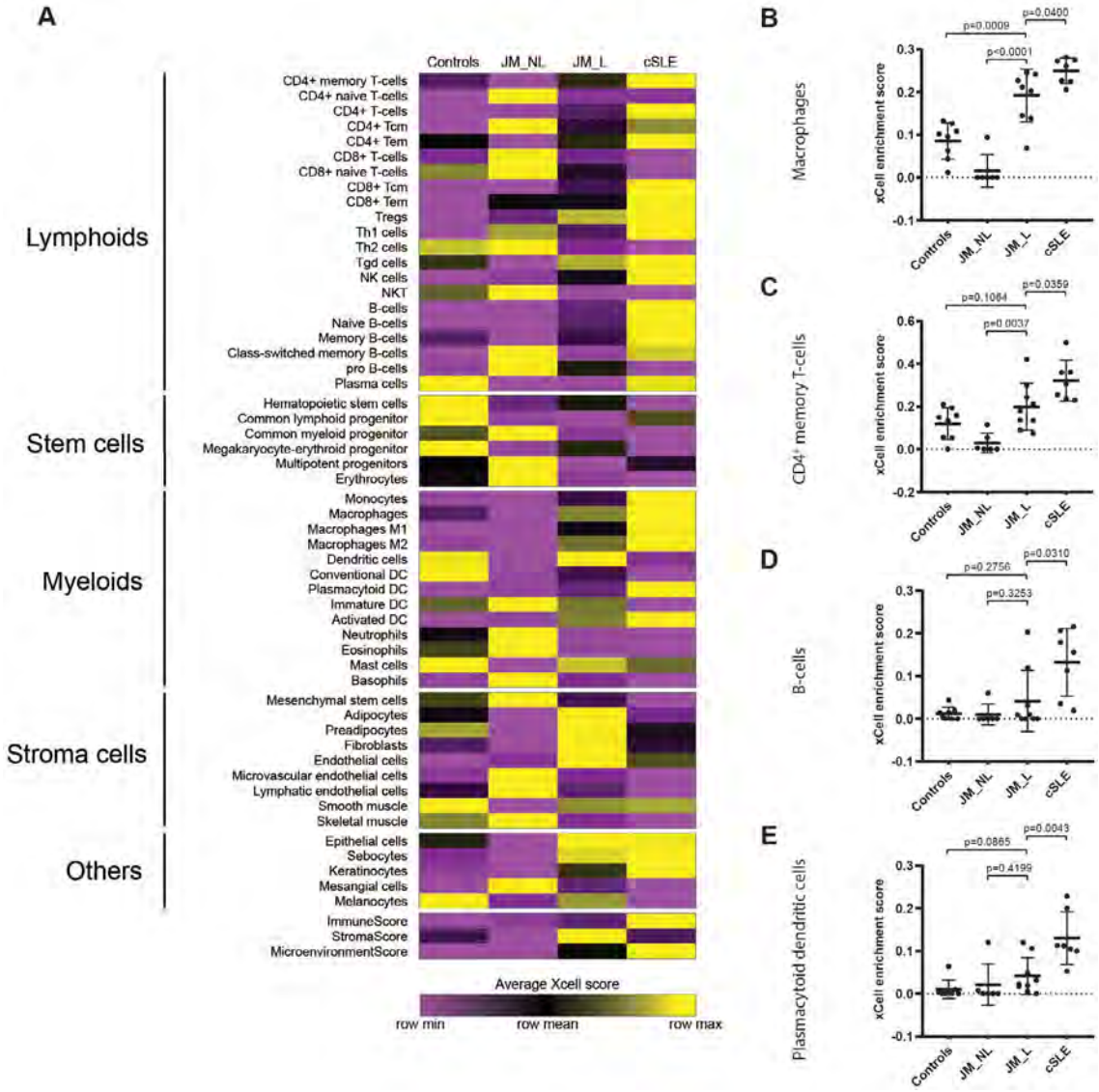


Figure 3. Cell type enrichment analysis using xCell webtool. A. Heatmap of relevant cell types representing average xCell enrichment score for controls, JM_NL, JM_L and cSLE. B. Graph of the macrophage xCell score, showing a significantly higher score in JM_L compared to JM_NL and controls and in cSLE compared to JM_L. C. Graph of the CD4+ memory T-cells xCell score, showing a significantly higher score in JM_L compared to JM_NL and in cSLE compared to JM_L. D. Graph of the B-cells xCell score showing a significantly higher score in cSLE compared to JM_L. E. Graph of the plasmacytoid dendritic cells xCell score, showing a significantly higher score in cSLE compared to JM_L. For (B-E) comparisons were made via unpaired Students' t-test.

Disclosure: J. Turnier, None; **L. Pachman**, None; **L. Lowe**, None; **A. Tsoi**, None; **S. Elhaj**, None; **R. Menon**, None; **M. Amoruso**, None; **G. Morgan**, None; **J. Gudjonsson**, Celgene, 2; **C. Berthier**, None; **J. Kahlenberg**, AstraZeneca, 5, Eli Lilly, 5, VielaBio, 5, Avion Pharmaceuticals, 5, Bristol Myers Squibb, 2, 5, Q32 Bio, 2, Boehringer Ingleheim, 5.

Abstract Number: 1990

Janus Kinase (JAK) Inhibition with Baricitinib in Refractory Juvenile Dermatomyositis

Hanna Kim[1], Lylan Bergeron[2], Samantha Dill[2], Michelle O'Brien[2], Laura Vian[3], Minal Jain[4], Manuk Manukyan[2], Xiaobai Li[5], Shajia Lu[3], Wanxia L. Tsai[3], Kalyani Mishra Thakur[6], Yinghui Shi[6], Massimo Gadina[7], April Brundidge[2], Michelle Millwood[2], Lisa G. Rider[8] and Robert Colbert[2], [1]Juvenile Myositis Pathogenesis and Therapeutics Unit / NIAMS / National Institutes of Health, Bethesda, MD, [2]Pediatric Clinical Trials Unit and Office of Clinical Director, NIAMS, NIH, Bethesda, MD, [3]Translational Immunology Section, NIAMS, NIH, Bethesda, MD, [4]Rehabilitation Medicine Department, Physical Therapy Section, Clinical Research Center, NIH, Bethesda, MD, [5]Biostatistics and Clinical Epidemiology Service, Clinical Center, NIH, Bethesda, MD, [6]Office of Clinical Director, NIAMS, NIH, Bethesda, MD, [7]National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS), NIH, Bethesda, MD, [8]Environmental Autoimmunity Group, Clinical Research Branch, NIEHS, NIH, Garrett Park, MD

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical III: Systemic Autoimmune Disease

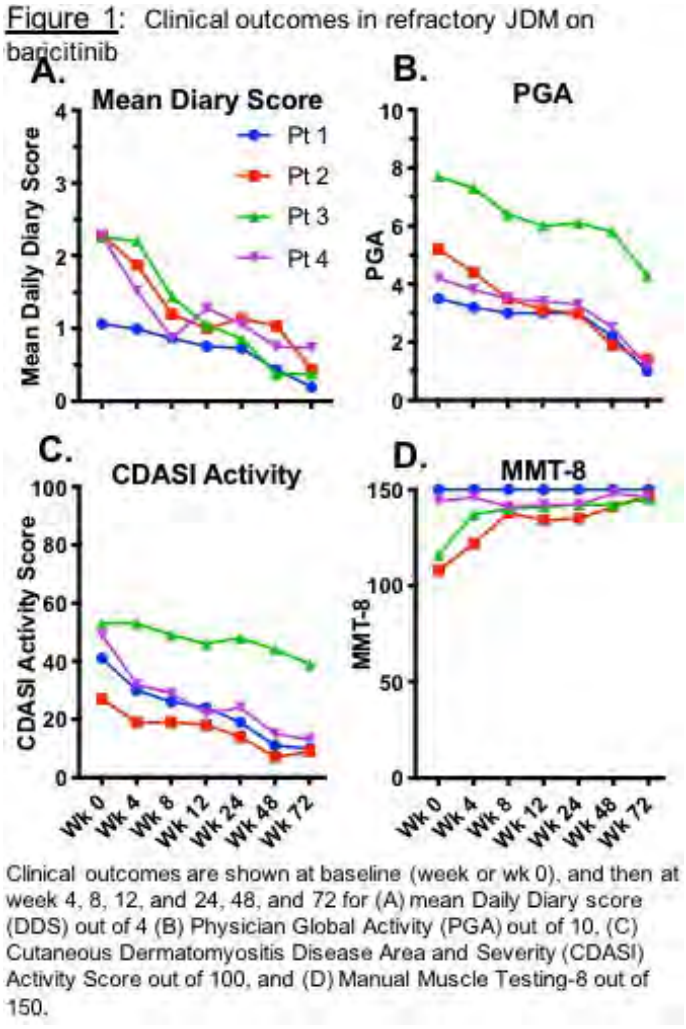
Session Type: Abstract Session

Session Time: 11:00AM–11:50AM

Background/Purpose: Juvenile dermatomyositis (JDM) is a systemic autoimmune disease with a prominent interferon (IFN) signature. Treatment often requires prolonged high-dose steroids and other immunosuppressive medications. In a compassionate use program, we assessed efficacy and safety of baricitinib (JAK 1/2 inhibitor) in active refractory JDM.

Methods: Active (based on ≥3 core set measures (CSM)) and refractory (use of high dose steroids and ≥2 other medications, including ≥1 biologic therapy) patients with JDM were enrolled after washing out biologic agents other than IVIG. Baricitinib was dosed based on weight and renal function. Primary outcome was reduction in symptom daily diary score (DDS) of weakness, fatigue, musculoskeletal pain, and rash. Other assessments included International Myositis Assessment and Clinical Studies (IMACS) disease activity CSMs and Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI). STAT-1 phosphorylation (pSTAT1) and peripheral IFN markers (IFN-regulated gene score, CXCL10/IP-10) were assessed. Linear mixed models were used to compare measures to baseline. Safety and tolerability were assessed.

Results: Four paitents with JDM (5.8-20.7 years old) were enrolled (NCT01724580). Patients received baricitinib 4-12 mg/day PO divided BID. There were clinically relevant improvements up to 72 weeks after baricitinib. DDS changed from a mean of 2.0 (range 1.1-2.3) to 0.4 (0.2-0.7; 68-83% decrease, $p< 0.01$) (Fig 1A). Physician Global Activity visual analog scale (VAS) decreased from a mean of 5.2 (3.5-7.7) to 2.0 (1.0-4.3; 44-73% decrease, $p< 0.01$) (Fig 1B). Extramuscular Global Activity VAS decreased from mean 5.1 (3.0-7.3) to 1.8 (0.5-4.5; 38-83% decrease, $p< 0.01$). CDASI activity score reduced from mean 43 (27-53) to 18 (9-39; 14-36 point decrease, $p< 0.01$) (Fig 1C). In 2/4 pts with baseline weakness, manual muscle testing (MMT8) increased from 108 to 147 and 116 to 145 (mean improvement 24%) (Fig 1D). By the ACR-EULAR JDM response criteria, the Total Improvement Score at 72 weeks was mean 60.6, range 42.5-80 (1 minimal, 1 moderate, 2 major improvement). Three patients reduced prednisone: mean 13.7 (range 10-21) to 4 (3.5-4.5) mg/day; 1 patient remained on 5mg/day. IFN-alpha stimulated pSTAT1 in different immune cell subsets negatively correlated with plasma baricitinib levels. All IFN markers decreased. Baricitinib was generally well tolerated. There were no serious adverse events (AEs). Infections were the most common AE. No AEs required holding/discontinuing baricitinib.



Clinical outcomes are shown at baseline (week or wk 0), and then at week 4, 8, 12, and 24, 48, and 72 for (A) mean Daily Diary score (DDS) out of 4 (B) Physician Global Activity (PGA) out of 10, (C) Cutaneous Dermatomyositis Disease Area and Severity (CDASI) Activity Score out of 100, and (D) Manual Muscle Testing-8 out of 150.

Conclusion: Preliminary data on the use of baricitinib (JAK 1/2 inhibitor) in four patients with refractory JDM are encouraging, showing steady and prolonged improvement in symptom DDS as well as in validated disease activity measures, including both skin and muscle. All patients met clinically significant improvement by the ACR-EULAR response criteria. A corresponding decrease in pSTAT1 and IFN markers was observed. Baricitinib was generally well tolerated and further evaluation in JDM should be considered.

Disclosures: Baricitinib provided by Eli Lilly and Company, expanded access program sponsor. Other support: IRP of NIH, NIAMS, NIEHS, CC.

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Abstract Number: 1991

Abatacept Treatment Reduces Cutaneous and Joint Activity in Juvenile Localized Scleroderma

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical III: Systemic Autoimmune Disease

Session Type: Abstract Session

Session Time: 11:00AM–11:50AM

Background/Purpose: Juvenile localized scleroderma (jLS) is an autoimmune disease commonly associated with damage. Damage includes dyspigmentation, tissue atrophy, arthropathy, hemiatrophy, vision loss, and seizures. To limit damage severity, methotrexate (MTX), with or without glucocorticoids (GC), is recommended to treat patients with active disease. This regimen is effective in ~70% of patients. Evidence on how to treat non-responders is limited, with some patients having persistently active disease for decades.

Many studies have identified T cells and their associated cytokines in patients with active disease, which suggests abatacept (ABA), a selective T cell co-stimulatory signal inhibitor, could be an effective treatment. A good response to ABA has been reported in small case series of adult onset patients who failed MTX. We report our experience using ABA to treat refractory jLS patients.

Methods: This was a multi-center retrospective cohort study of jLS patients that initiated ABA treatment prior to 7/1/18. Inclusion criteria included diagnosis of jLS, with onset < 16 years. Charts were reviewed to extract demographics, disease characteristics, medication history, and reasons for ABA use. Data was collected at start of ABA (baseline), and at 6 month intervals up to 24 months, or ABA discontinuation, whichever was sooner. Descriptive statistics analysis was performed.

Results: 18 patients were evaluated, median age 13.4 years, disease duration 3.7 years. Most had linear scleroderma (Table 1). All had been previously treated with glucocorticoids, and MTX (17) and/or mycophenolate mofetil (MMF, 16), each for a median duration of >1 year (Table 1). Reasons for ABA use included persistent disease or flare (14, 78%), intolerance of other medications (5, 28%), and GC dependence (4, 22%). ABA was dosed per JIA recommendations, with 16 treated intravenously. All patients concurrently received other treatment: MTX (12), MMF (10), hydroxychloroquine (1), and GC (14).

Median scores for physician global assessment of disease activity and skin activity measures all declined by 12 months, and then stabilized or further declined (Figure 1). At 12 months, 17 (94%) patients were rated as improved in activity status compared to baseline, and 9 of the 12 patients with joint involvement were rated as improved. At 24 months, 9 of 11 patients (82%) on ABA were rated as improved, and 7 with joint involvement were all rated as improved. During ABA treatment, 10 patients were able to discontinue GC (71% of patients on GC, Figure 2).

Eight patients had an adverse event (AE); 7 were on concomittant medications. AE included fatigue, moodiness, behavioral change, and one infection (upper respiratory infection). No laboratory abnormalities were attributed to ABA. Two patients discontinued ABA because of mood and/or behavioral issues.

Number of patients	18
Sex: Female, no (%)	12 (66.7)
Race White, no (%)	18 (100)
Age of onset, years (IQR)	8.7 (7.5, 10.3)
Age at start of ABA, years (IQR)	13.4 (11.4, 15.0)
Disease duration at start of ABA, years (IQR)	3.7 (2.8, 6.5)
Subtype, no (%)	
Circumscribed Deep Morphea	1 (5.6)
Linear Head	2 (11.1)
Linear Trunk/Limb	9 (50)
Generalized Morphea	1 (5.6)
Mixed Morphea	5 (27.8)
Pansclerotic Morphea	1 (5.6)
Eosinophilic fasciitis	2 (11.1)
Extracutaneous involvement, no (%)	13 (72.2)
Joint involvement (%)	12 (66.7)
Muscle involvement (%)	9 (50)
Elevated CK/aldolase (%)	7 (38.8)
ANA Positivity (% of 17 performed)	8 (47.1)
Family History of rheumatic disease, no (%)	6 (33.3)
Duration of other treatment prior to ABA	
GC, months (IQR)	15.9 (10.1, 29.2)
MTX, months (IQR)	20.4 (15.6, 45.8)
MMF, months (IQR)	12.3 (6.5, 16.8)
Duration of ABA treatment, months (IQR)	23.2 (15.1, 25.3)

Table. Characteristics of the 18 jLS patients who were treated with abatacept. All of the patients received other jLS treatment prior to being treated with abatacept: 17 were treated with methotrexate, 16 with mycophenolate mofetil, and 17 with glucocorticoids. The median duration of these treatments are listed. The median duration of abatacept treatment for the patients during their study follow-up is shown. ABA:abatacept; ANA: anti-nuclear antibody; CK: creatine kinase; GC: glucocorticoid; IQR: interquartile range; MMF: mycophenolate mofetil; MTX: methotrexate; no: number.

Conclusion: ABA was found to be a safe and effective treatment for jLS patients who previously failed MTX and/or MMF. There were no serious AE. Patients treated with ABA had a decrease in both skin and joint activity. Seventy percent of GC treated patients were able to discontinue GC. Prospective studies should be done to further evaluate ABA's efficacy, potentially as stand-alone therapy and/or in combination with DMARDs.

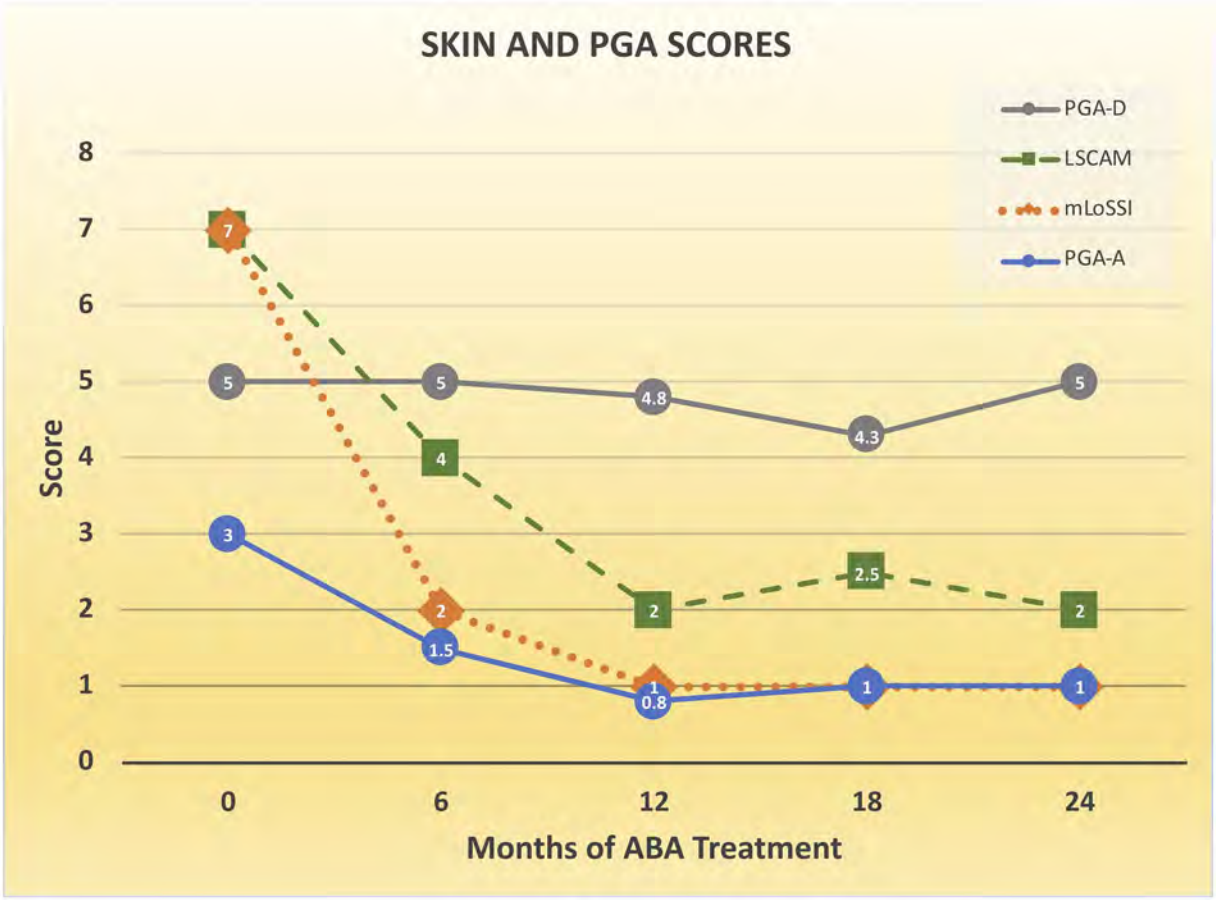


Figure 1. Change in skin activity and physician global assessment scores on ABA. Skin Activity measures were mLoSSI and LSCAM. Physician global assessment were of activity (PGA-A) and damage (PGA-D). mLoSSI sums 3*disease extension + erythema + skin thickening across affected sites, LSCAM sums same variables without weighting disease extension, and also includes scoring for violaceous color, waxy white/ yellow, and tactile warmth features. Number of patients that were scored at each time point: 18 at 0, 6 months; 17 at 12 months; 14 at 18 months, 11 at 24 months. Reasons for missing visits were: discontinuation of abatacept prior to 24 months (because of adverse event [2], pregnancy [1], persistent disease activity [1]), end of study collection period (2), and patient moved out of state (1). LSCAM: Localized scleroderma cutaneous activity measure mLoSSI: modified localized scleroderma severity index PGA-A = Physician global assessment of disease activity PGA-D = Physician global assessment of disease damage

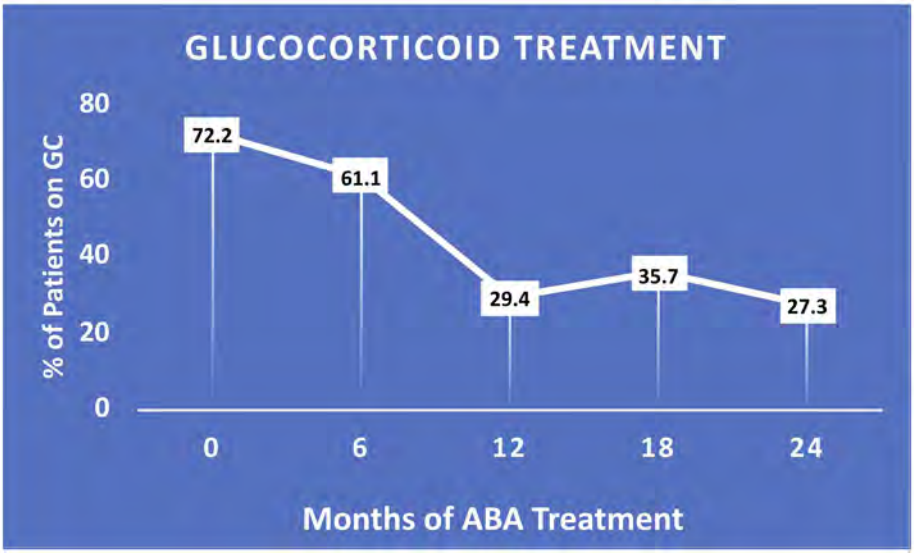


Figure 2. Concomitant glucocorticoid treatment with Abatacept treatment The percent of patients on glucocorticoid treatment at each study visit is shown. Overall, 14 patients were treated with glucocorticoids during the study, 13 begun at baseline and an additional 1 by 6 month visit. Percentages shown are based upon total number of patients at each study visit; 18 patients at 0 and 6 month, 17 at 12 month, 14 at 18 month, and 11 at 24 month visit. Ten patients discontinued glucocorticoids by their last study visit.

Disclosure: S. Li, Merck, 3, CARRA, 9, UpToDate, 7, Arthritis Foundation, 2, Scleroderma Foundation, 2; **S. Ishaq**, None; **M. Buckley**, None; **K. Torok**, None; **B. Edelheit**, None; **K. Ede**, None; **C. Liu**, None; **C. Rabinovich**, AbbVie, 2, CARRA, 2, UCB Pharma, 2, Janssen Research & Development, 2.

Abstract Number: 1992

Longitudinal Evaluation of Axonal Dysfunction, Neuronal Markers and Serum Cytokines in Childhood-onset Systemic Lupus Erythematosus

Renan Frittoli[1], Danilo Rodrigues[1], Aline Lapa[1], Mariana Postal[1], Roberto Marini[1], Gabriela Castellano[1], Fernando Cendes[1], Leticia Rittner[1] and **Simone Appenzeller**[1], [1]UNICAMP, Campinas, Brazil

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Pediatric Rheumatology – Clinical III: Systemic Autoimmune Disease

Session Type: Abstract Session

Session Time: 11:00AM–11:50AM

Background/Purpose: To analyze 1H-MRS brain metabolites in a longitudinal study and to determine clinical, laboratory and treatment features associated with its occurrence. To determine, additionally if sera Th1 (IL-12, TNF-α, IFN-γ), Th2 (IL-6 and IL-10), Th17 (IL-17) cytokines levels, neurofilament (NF-H) and S100β influence brain metabolite levels.

Methods: We included 123 consecutive cSLE patients [median age 16 years (range 7-31)] from the Pediatric Rheumatology outpatient unit and 76 healthy controls (HC) [median age 18 years (8-33)]. All patients underwent two magnetic resonance imaging (MRI) exams during a period of 13.5 ± 9.4 months. We performed multi voxel 1H-MRS using point resolved spectroscopy sequence over the superior–posterior region of the corpus callosum (3T Phillips®scanner) and signals from N-acetylaspartate compounds (NAA), choline-based compounds (Cho); creatine containing compounds

(Cr), glutamate (Glu), glutamine (Gln) and lactate (Lac) were measured and metabolites/Cr ratios were determined. A complete clinical, laboratory and neurological evaluation was performed in all subjects. Neurological manifestations were analyzed according to the ACR classification criteria. Mood and anxiety disorders were determined through Beck Depression and Beck Anxiety Inventory. SLE patients were further assessed for clinical and laboratory SLE manifestations, disease activity [SLE Disease Activity Index (SLEDAI)], damage [Systemic Lupus International Collaborating Clinics/American College of Rheumatology Damage Index (SDI)] and current drug exposures. Th1 (IL-12, TNF-α, IFN-γ), Th2 (IL-6 and IL-10), Th17 (IL-17) cytokines levels, S100β and NF-H levels were measured by ELISA using commercial kits. Data were compared by non-parametric tests.

Results: NAA/Cr ratio (p=0.021) and Lac/Cr ratio (p=0.009) levels were significantly decreased and Glu/Cr ratio (0.004) and Gln/Cr ratio levels (p=0.042) were increased in cSLE patients when compared to HC. During follow-up time, no significant fluctuation in metabolites was observed in both groups. We observed that persistent reduction of NAA/Cr ratio was associated with neuropsychiatric manifestations [symptoms of anxiety (p=0.04), symptoms of depression (p=0.006)], presence of autoantibodies [antiphospholipid antibodies (p=0.03)] and cytokine levels [TNF-α (r=-0.546; p=0.0023) and INF γ (r=-0.746; p=0.0002)]. Persistent increased Cho/Cr ratio was associated with cognitive dysfunction (0.003), anti-SM (0.005), and correlated with S100β (r=0.641; p=0.005) and NF-H (r=-0.225, p=0.05). Increased Glu/Cr ratio was associated with stroke (0.043) and symptoms of depression (p= 0.0007).

Conclusion: We observed significant persistent axonal dysfunction in cSLE associated with increased inflammatory markers, autoantibodies and neuropsychiatric manifestations. Persistent axonal dysfunction could be a marker of future structural damage and patients should be followed-up closely.

Disclosure: R. Frittoli, None; **D. Rodrigues**, None; **A. Lapa**, None; **M. Postal**, None; **R. Marini**, None; **G. Castellano**, None; **F. Cendes**, None; **L. Rittner**, None; **S. Appenzeller**, None.

Abstract Number: 1993

Cardiovascular Risk in Rheumatoid Arthritis Patients Treated with Methotrexate versus Hydroxychloroquine

Mengdong He[1], Ajinkya Pawar[1], Rishi Desai[1], Robert Glynn[1], Hemin Lee[1], Michael Weinblatt[1], Daniel H Solomon[1] and Seoyoung Kim[1], [1]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments I: Maximizing Health in RA
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Rheumatoid arthritis (RA) is a known risk factor for cardiovascular (CV) events. While most RA patients use conventional disease-modifying antirheumatic drugs (DMARDs) such as methotrexate (MTX) and hydroxychloroquine (HCQ) as the 1st line DMARD, little is known about the comparative cardiovascular safety of these DMARDs. The objective of this study was to compare the incidence rate of CV events in RA patients initiating MTX versus HCQ as their 1st line therapy.

Methods: We conducted a cohort study of RA patients who initiated MTX or HCQ using Medicare claims data (Parts A/B/D 2008-2016) linked with the National Death Index. All patients were required to be ≥65 years old and have ≥365 days of continuous insurance enrollment and no prior use of any DMARDs at the cohort entry (i.e. MTX or HCQ initi-

Table 1. Selected baseline characteristics in the 1:1 propensity score matched cohort

Patient characteristics	MTX (N = 22,923)	HCQ (N = 22,923)	Standardized Difference
Demographics			
Age in years, mean (SD)	74.12 (6.64)	74.11 (6.63)	0.003
Female	79.7%	79.7%	0.002
Comorbidities			
Heart failure	9.2%	9.1%	0.006
Atrial fibrillation	4.9%	5.0%	0.001
Coronary artery disease	20.6%	20.3%	0.007
Stroke or transient ischemic attack	5.2%	5.1%	0.003
CHADS2 score, mean (SD)	1.75 (1.06)	1.74 (1.05)	0.011
Hypertension	84.6%	84.3%	0.010
Hyperlipidemia	71.5%	71.0%	0.010
Diabetes	31.3%	30.8%	0.010
Renal dysfunction	13.2%	13.2%	0.000
Combined comorbidity index, mean (SD)	1.02 (1.93)	1.03 (1.95)	0.001
Medications			
Oral steroids	64.0%	64.3%	0.007
Cumulative steroids dose (365 days, prednisone equivalent), median (IQR)	110.00 (0.00, 545.00)	110.00 (0.00, 545.00)	0.000
NSAIDs/Coxibs	47.6%	48.0%	0.007
ARBs	22.7%	22.7%	0.001
ACEis	32.3%	31.9%	0.008
Beta blockers	38.0%	37.5%	0.010
Calcium channel blockers	29.9%	29.9%	0.001
Diuretics	47.0%	47.0%	0.000
Statin	48.8%	48.5%	0.005
Antiplatelets	8.9%	8.8%	0.004
Antiarrhythmic Drugs	1.1%	1.1%	0.002
Insulin	5.6%	5.6%	0.001
Procedures			
Coronary revascularization (including PTCA, stenting, and CABG)	0.6%	0.6%	0.008
Healthcare utilization			
Emergency room visits	30.1%	30.2%	0.002
Any hospitalization	14.5%	14.3%	0.004
Number of rheumatologist visits, median (IQR)	2.00 (0.00, 3.00)	2.00 (1.00, 3.00)	0.003
Number of cardiologist visits, median (IQR)	0.00 (0.00, 1.00)	0.00 (0.00, 1.00)	0.010

Abbreviations: SD- Standard deviation; IQR- Interquartile range; NSAIDs- Nonsteroidal anti-inflammatory drugs; Coxibs- Cyclooxygenase inhibitors; ARBs- Angiotensin II receptor blockers; ACEis- Angiotensin-converting enzyme inhibitors; PTCA- Percutaneous transluminal coronary angioplasty; CABG- Coronary artery bypass grafting.

ation date). Patients with a hospitalization for myocardial infarction (MI), unstable angina, stroke, transient ischemic attack, or heart failure (HF), or a procedure for coronary revascularization within 60 days prior to the cohort entry were excluded. The primary outcome was a composite endpoint of major adverse CV event (MACE) including MI, stroke, or CV mortality. Secondary outcomes included a modified definition of MACE (MI, stroke, or all-cause mortality), individual components of MACE, and hospitalized HF. To control for 59 baseline covariates, we used 1:1 propensity score (PS) matching. For the primary as-treated analysis, Cox proportional hazards models were used to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) of the primary and secondary outcomes.

Results: We included a total of 22,923 PS-matched pairs of MTX and HCQ initiators with a mean (standard deviation) age of 74 (7) years and 80% female. Even before PS matching, baseline characteristics were similar between the two groups except 6% higher steroids use among MTX initiators. After PS matching, all the patient characteristics were well balanced (**Table 1**). Over a median of 212 days (interquartile range 105-529 days) on treatment, 660 MACE occurred in MTX initiators and 610 in HCQ initiators. The incidence rate (per 1,000 person-years) of MACE was 23.38 (95% CI 21.63-25.23) in the MTX group and 24.32 (95% CI 22.43-26.33) in the HCQ group (**Table 2**). The HR for MACE associated with MTX versus HCQ initiation was 0.96 (95% CI 0.86-1.08). The two groups had no different

Table 2. Incidence rates and hazard ratios (95% CI) of primary and secondary outcomes in the 1:1 propensity score matched cohort

Outcome	Exposure group	Number of events	Total person-years	Incidence rate per 1,000 person-years (95% CI)	Hazard ratio (95% CI)
Primary outcome					
MACE (MI, stroke, or CV mortality)	MTX	660	28,234	23.38 (21.63-25.23)	0.96 (0.86-1.08)
	HCQ	610	25,080	24.32 (22.43-26.33)	Ref.
Secondary outcome					
Modified MACE (MI, stroke, or all-cause mortality)	MTX	1,173	28,221	41.56 (39.22-44.01)	0.95 (0.88-1.03)
	HCQ	1,092	25,074	43.55 (41.01-46.21)	Ref.
MI	MTX	241	28,403	8.49 (7.45-9.63)	0.80 (0.67-0.95)
	HCQ	269	25,197	10.68 (9.44-12.03)	Ref.
Stroke	MTX	226	28,471	7.94 (6.94-9.04)	1.33 (1.08-1.63)
	HCQ	152	25,278	6.01 (5.10-7.05)	Ref.
CV mortality	MTX	256	28,671	8.93 (7.87-10.09)	0.86 (0.72-1.02)
	HCQ	263	25,411	10.35 (9.14-11.68)	Ref.
All-cause mortality	MTX	821	28,656	28.65 (26.72-30.68)	0.91 (0.82-1.00)
	HCQ	795	25,404	31.29 (29.16-33.55)	Ref.
Hospitalized heart failure	MTX	244	28,484	8.57 (7.53-9.71)	0.60 (0.51-0.71)
	HCQ	358	25,141	14.24 (12.80-15.79)	Ref.

Abbreviations: CI- Confidence interval; MACE- Major adverse cardiovascular event; MI- Myocardial infarction; CV- Cardiovascular; Ref.- Reference.

risk for the modified MACE (HR 0.95, 95% CI 0.88-1.03), CV mortality (HR 0.86, 95% CI 0.72-1.02), and all-cause mortality (HR 0.91, 95% CI 0.82-1.00). However, comparing MTX with HCQ initiators, we observed an increased risk of stroke (HR 1.33, 95% CI 1.08-1.63), but a decreased risk of MI (HR 0.80, 95% CI 0.67-0.95) and hospitalized HF (HR 0.60, 95% CI 0.51-0.71) (**Table 2**).

Conclusion: In this large observational study of 45,846 older RA patients enrolled in Medicare, we found no difference in the risk of MACE between patients who newly received MTX versus HCQ. However, results from the secondary analyses were different with respect to individual endpoints – a greater stroke risk but a lower risk of MI and hospitalized HF in MTX than HCQ initiators.

Disclosure: M. He, None; **A. Pawar**, None; **R. Desai**, None; **R. Glynn**, AstraZeneca, 2, Kowa, 2, Pfizer, 2, Novartis, 2; **H. Lee**, None; **M. Weinblatt**, Crescendo Bioscience, 1, Bristol Myers Squibb, 1, Sanofi, 2, Lilly, 1, Amgen, 1, AbbVie, 5, Amgen, 2, 5, Arena, 5, Bristol Myers Squibb, 2, 5, Canfite, 1, 5, Corrona, 5, Crescendo, 2, 5, GlaxoSmithKline, 5, Gilead, 9, Horizon, 9, Johnson and Johnson, 9, Lilly, 2, 9, Pfizer, 9, Scipher, 1, 9, Set Point, 9, Roche, 9, Canfite, 1, Inmedix, 1, Lycera, 1, Vorso, 1, Scipher, 1; **D. Solomon**, AbbVie, 2, Amgen, 1, Genentech, 1, Janssen, 1, Corrona, 1; **S. Kim**, Pfizer, 1, Roche, 1, AbbVie, 1, Bristol-Myers Squibb, 1.

Abstract Number: 1994

Rheumatoid Arthritis Improvement After Exposure to an Anti-Inflammatory "ITIS" Diet Is Associated with Changes of Gut Microbiome and Systemic Metabolome

Roxana Coras[1], Cameron Martino[2], Julia Gauglitz[3], Anupriya Tripathi[3], Alan Jarmusch[4], Francesca Cedola[5], Marta Fernandez Bustamante[6], Meritxall Agustín-Perez[7], Maram Alharthi[8], Susan Lee[8], Abha Singh[8], Soo In Choi[8], Tania Rivera[8], Katherine Nguyen[8], Tatyana Shekhtman[9], Tiffany Holt[10], Shahrokh Golshan[11], Rob Knight[3], Pieter Dorrestein[12] and Monica Guma[13], [1]University of California San Diego, La Jolla, CA, [2]Bioinformatics and Systems Biology, University of California San Diego, San Diego, [3]University of California San Diego, San Diego, [4]Univesity of California San Diego, San Diego, [5]Hospital Policlinico Tor Vergata, Rome, Italy, [6]Departement of Medicine, Division of Rheumatology, University of California San Diego, San Diego, [7]Department of Medicine, University of California San Diego, San Diego, San Diego, [8]Department of Medicine, Division of Rheumatology, University of California San Diego, San Diego, [9]Department of Psychiatry, University of California, San Diego, San Diego, [10]Center for Integrative Nutrition, University of California San Diego, San Diego, [11]Department of Psychiatry, University of California San Diego, San Diego, CA, USA, San Diego, [12]Department of Pharmacology and Pediatrics, University of California San Deigo, San Diego, [13]Division of Rheumatology, University of California San Diego, Department of Medicine, Autonomous University of Barcelona, La Jolla, CA

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Treatments I: Maximizing Health in RA

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: A new dimension has been added to the link between diet and health, the gut microbiome. Of particular interest is the influence of diet on the microbiome and how this affects pain/inflammation by modifying circulating pro/anti-inflammatory metabolites. Microbiome-derived metabolites have been related to beneficial or deleterious effects on the host. Thus, changes in diet and microbiome might change the systemic metabolite profiling and influence pain and inflammation in rheumatoid arthritis (RA). We recently described that RA patients exposed to an anti-inflammatory ITIS diet had improvement of clinical outcomes. Here, we examine the effect of the ITIS diet on gut microbiome and fecal and plasma metabolome in RA patients.

Methods: We conducted an open-label pilot trial to evaluate feasibility and efficacy of a 2-week anti-inflammatory diet (ITIS) in RA patients. 17 patients with active RA (at least 3 tender and 3 swollen joints) participated. Physical examination and collection of fecal and plasma samples for microbiome and metabolomics were performed at each visit. Using a 50% pain improvement, patients were categorized as responders (R, N=11) or non-responders (NR, N=6). 16S rRNA gene amplicon profiling of the stools and untargeted mass spectrometry (MS)-based metabolomics in stool and plasma were performed. Dietary adherence was evaluated based on food logs and metabolomics readouts.

Results: Clinical outcomes showed significant improvements (pain: 3.9±2.3 before vs 2.45±2.4 after diet, $p< 0.01$; Clinical Disease Activity Index (CDAI): (29±11.7 before vs 12.7±11.3 after diet, $p< 0.001$). A diet score (up to 200) showed good adherence, with an average improvement of 148.18 (± 58.10). Changes due to diet intervention were captured by MS analysis and reflected the prescribed diet as well as the individual dietary diary entries (Figure 1A). Alpha diversity was higher at baseline in R (Figure 1B). Interestingly, R had a smaller change in alpha diversity after diet than NR suggesting that an already high alpha diversity with relatively limited capacity for further change may be necessary for response with this dietary intervention (Figure 1C). *Ruminococcaceae, Clostridium, Bacteroides and Lachnospira* genera negatively correlated with measures of disease activity at baseline, while *Enterobacteriaceae* positively correlated with the same measures. (Figure 1D). Baseline plasma metabolites profiles were different in R

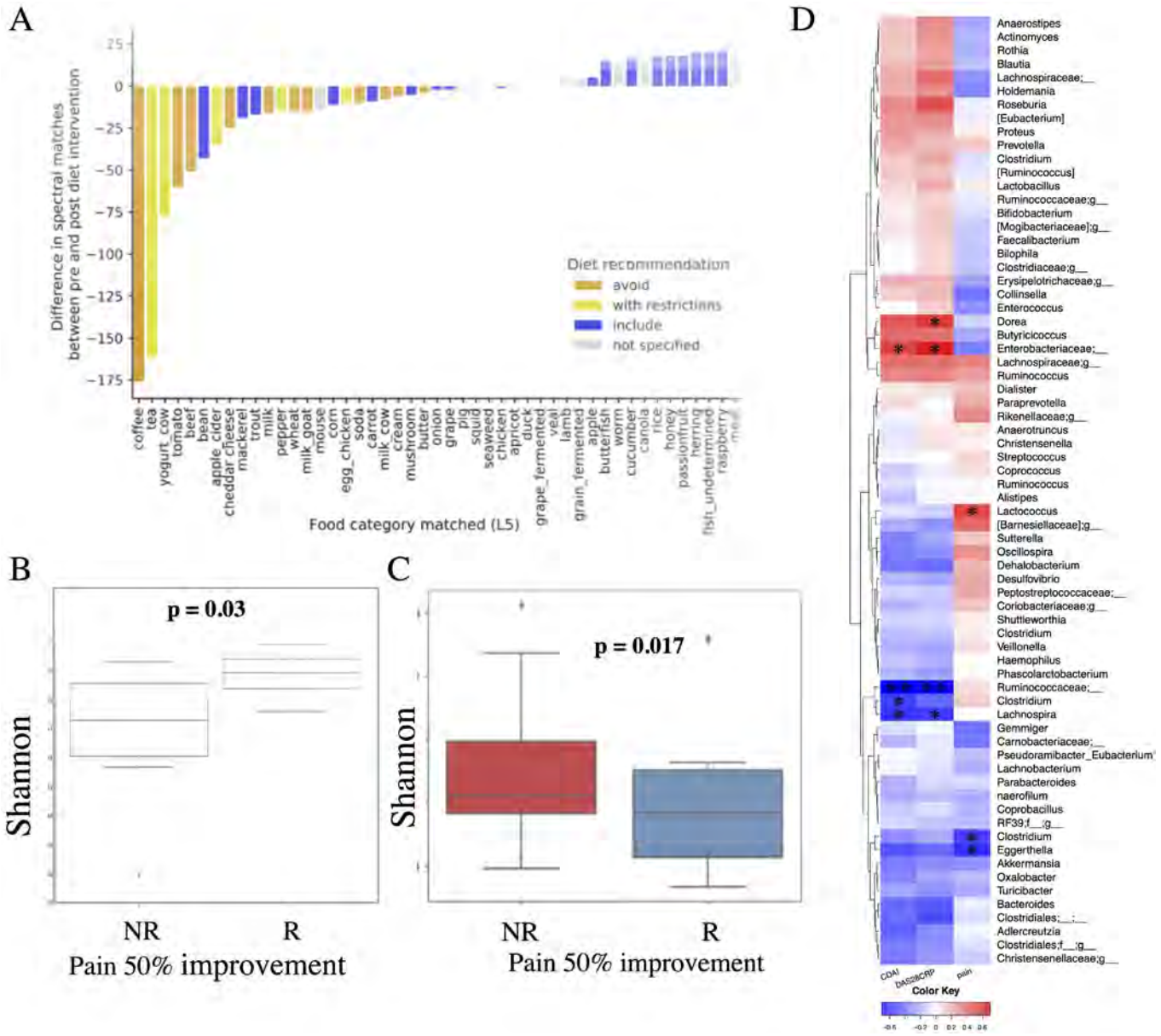


Figure 1. Adherence to diet and microbiome at baseline. A) Adherence to diet evaluated by the plasma metabolomics readout. B) Alpha diversity (Shannon) at baseline is significantly higher in patients with at least 50% pain improvement (R) compared to patients with a less than 50% improvement in pain (NR). C) Change in alpha diversity from day-14 (before diet) to day +14 (after diet) in R versus NR, assessed by at least 50% pain improvement. Boxes represent group means with standard deviations. D) Correlation (Spearman rank correlation) of bacterial genus with clinical outcomes at baseline (CDAI – clinical disease activity index, DAS28CRP – disease activity score using 28 joint count and C reactive protein). The significant correlations are marked with * ($p < 0.05$) or ** ($p < 0.01$).

compared to NR (Figure 2A). The differential analysis showed that responders of both Pain 50 and CDAI 70 were enriched for both conjugated linoleic acid (CLA) and Mollicutes or depleted in taurocholic acid, phosphocholines and Coriobacteriales (Figure 2B-C). Of interes, CLA is an anti-inflammatory metabolite previously associated with dietary changes in the number of types of plants eaten.

Conclusion: The "ITIS" diet induced changes in both metabolome and microbiome which correlate with clinical outcome measures. Further studies are needed to provide insight into specific long-term dietary interventions or supplements as a complementary treatment in RA, and to establish the scientific basis for using diet to adjust the gut microbiome to improve RA management.Figure 1. Adherence to diet and microbiome at baseline. A) Adherence to diet evaluated by

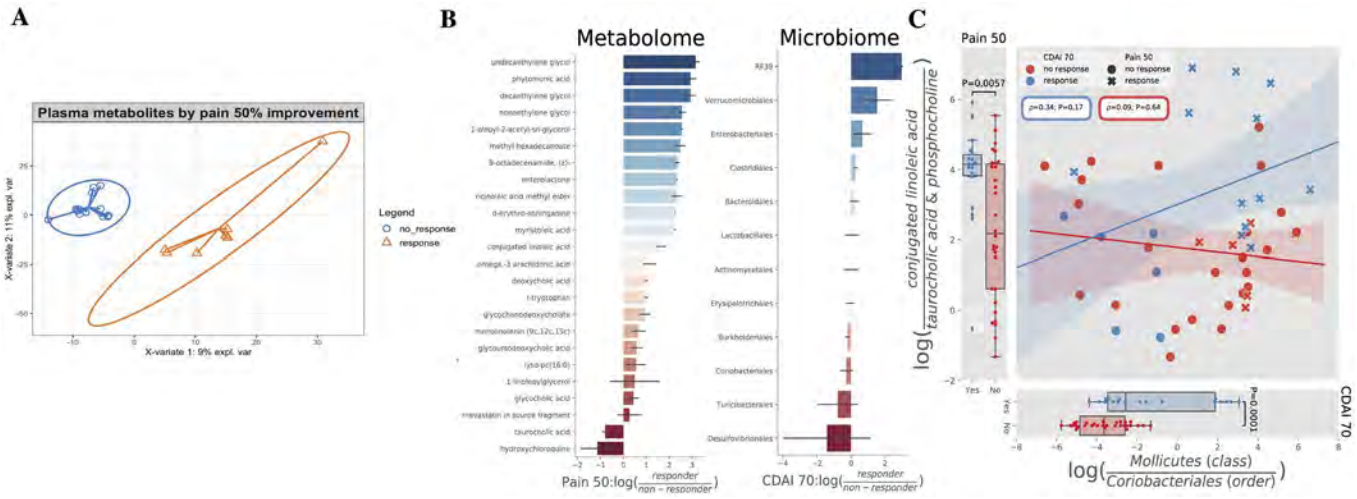


Figure 2. Plasma metabolome is different in R versus NR. A) Partial least square regression showing that plasma metabolome is different in R versus NR. B) Differential metabolites (left) and microbes (right) by chemical name and taxonomic order (y-axis) between responders and non-responders (x-axis). C) In the analysis of differential metabolomics Pain50 responders are enriched in conjugated linoleic acid (CLA) compared to non-responders (NR), while the Pain50 NR are enriched in the biliary metabolite taurocholic acid and phosphocholines compared to R (left). This trend was verified with a log-ratio between the two metabolite groups which is significant between R and NR (T=2.9, P=0.006). In the analysis of differential sub-operational taxonomic units by CDAI 70, Mollicutes were found to be enriched and Coriobacteriales depleted in R compared to NR (right). This trend was verified with a log-ratio between the two taxonomic orders which is significant between R and NR (T=4.22, P=0.0001). Error bars in all figures shaded by standard error. Correlation performed through spearman rank-order correlation. Log-ratio significance determined through two-sided T-test.

the plasma metabolomics readout. B) Alpha diversity (Shannon) at baseline is significantly higher in patients with at least 50% pain improvement (R) compared to patients with a less than 50% improvement in pain (NR). C) Change in alpha diversity from day-14 (before diet) to day +14 (after diet) in R versus NR, assessed by at least 50% pain improvement. Boxes represent group means with standard deviations. D) Correlation (Spearman rank correlation) of bacterial genus with clinical outcomes at baseline (CDAI – clinical disease activity index, DAS28CRP – disease activity score using 28 joint count and C reactive protein). The significant correlations are marked with * ($p < 0.05$) or ** ($p < 0.01$).

Disclosure: R. Coras, None; **C. Martino**, None; **J. Gauglitz**, None; **A. Tripathi**, None; **A. Jarmusch**, None; **F. Cedola**, None; **M. Fernandez Bustamante**, None; **M. Agustín-Perez**, None; **M. Alharthi**, None; **S. Lee**, Gilead Sciences, 3; **A. Singh**, Pfizer, 2, Novartis pharmaceuticals, 2; **S. Choi**, None; **T. Rivera**, None; **K. Nguyen**, None; **T. Shekhtman**, None; **T. Holt**, None; **S. Golshan**, None; **R. Knight**, None; **P. Dorrestein**, None; **M. Guma**, None.

Abstract Number: 1995

Non-invasive Vagus Nerve Stimulation Improves Signs and Symptoms of Rheumatoid Arthritis: Results of a Pilot Study

Sara Marsal[1], Hector Corominas[2], Juan Jose De Agustin De Oro[3], Carolina Perez Garcia[4], Maria Lopez Lasanta[3], Helena Borrell[3], Delia Reina[5], Raimon Sanmartí[6], Francisco Javier Narváez[7], Clara Franco-Jarava[8], Charles Peterfy[9], Jose Antonio Narvaez[10], Vivek Sharma[11], Konstantinos Alataris[11], Mark Genovese[12] and Matthew Baker[13], [1]Hospital Universitari Vall d'Hebron, Barcelona, Spain, [2]Institut Rec. Hospital de la Santa Creu I Sant Pau., Barcelona, Spain, [3]Hospital Universitari Vall d'Hebron, Barcelona, Spain, [4]Hospital Universitari Parc Salut Mar, Barcelona, Spain, [5]Hospital Moises Broggi, Barcelona, Spain, [6]Hospital Universitari Clínic de Barcelona, Barcelona, Catalonia, Spain, [7]Hospital Bellvitge, BARCELONA, Spain, [8]1Hospital Universitari Vall d'Hebron, Barcelona, Spain, [9]Spire Sciences, Inc., Boca Raton, FL, [10]Clinica Diagonal, Barcelona, Spain, [11]Vorso Corp, Redwood CIty, CA, [12]Stanford University Medical Center, Palo Alto, CA, [13]Stanford University, Menlo Park, CA

SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: RA – Treatments I: Maximizing Health in RA
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Vagus nerve stimulation (VNS) has been shown to improve rheumatoid arthritis (RA) disease severity in patients with refractory disease (1,2). A multi-center pilot study investigated the safety and efficacy of a wearable device to treat RA via electrical stimulation of the auricular branch of the vagus nerve.

Methods: Patients with active RA defined by ≥4 tender/swollen joints (28 jt count), DAS28-CRP >3.8, active synovitis detected on ultrasound and MRI, and who had inadequate response to conventional synthetic disease-modifying antirheumatic drugs (csDMARDs) were enrolled in the open-label pilot study. The primary endpoint was the change in the DAS28-CRP score at Week 12. Secondary endpoints included the mean change in HAQ-DI, the proportion of patients achieving ACR20/50/70, and the proportion of patients achieving a HAQ-DI of 0.22. Low disease activity (LDA) and remission were assessed based on DAS28-CRP (LDA if < 3.2; remission if < 2.6). MRI was performed at Weeks 0 and 12 and changes in synovitis, osteitis and bone erosion were assessed using the OMERACT-RAMRIS method. Safety and adverse events were assessed throughout the study.

Results: Thirty patients were enrolled and 27 completed the study. The mean age was 54 years, 90% were female, and the mean duration of disease was 7.3 years. The mean change in DAS28-CRP at Week 12 was -1.4 ($p < 0.001$) (Figure 1). Eleven patients (37%) attained LDA and 7 (23%) achieved remission. The mean percent change in the DAS28-CRP at Week 12 for patients with moderate and high disease activity was 24% and 27% respectively (Figure 2). ACR20/50/70 response rates were 53%, 33%, and 17% respectively. Individual components of DAS28-CRP and ACR scoring for all observed data appear in Table 1. The change in HAQ-DI from baseline was -0.47 ($p < 0.05$), and 57% of patients achieved an overall HAQ-DI reduction of 0.22 or more. The mean change in the OMERACT-RAMRIS synovitis, osteitis, and bone erosion scores at week 12 compared to baseline were -0.10 (p=0.16), -0.43 (p=0.46), and 0.047 (p=0.80), respectively. Four adverse events (AEs) were reported: 1 device-related AE due to a superficial skin abrasion where the earpiece contacts the ear and 3 non-device related AEs -- 2 accidental patient falls and one report of mucous build-up in the throat. All 4 AEs resolved without intervention or further sequelae.

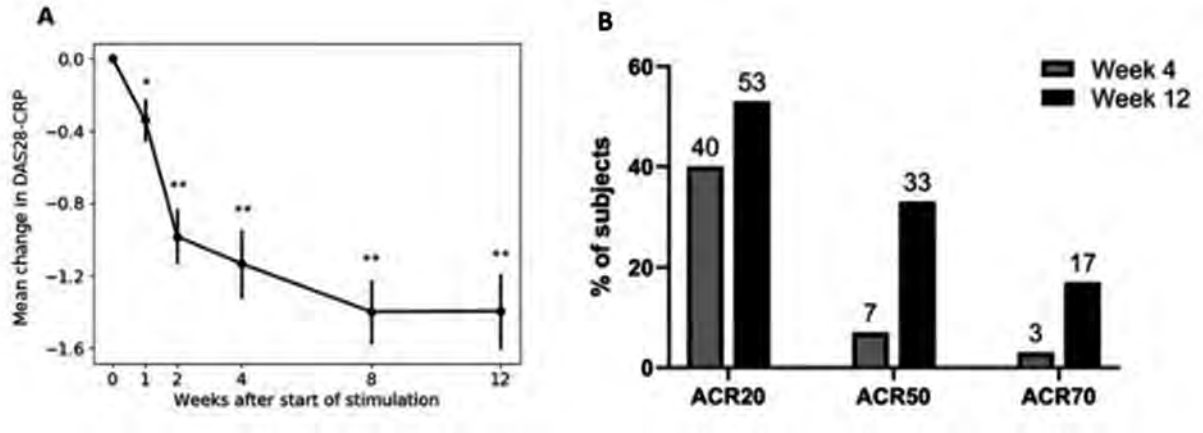


Figure 1. Primary and secondary endpoint. A) Mean change in DAS28-CRP score for each study visit. For the 27 patients who completed the study, there is a significant reduction in the DAS28-CRP after Week 1, and it continues to decrease through the end of the study. At Week 12, there is a mean reduction of 1.40 in the DAS28-CRP relative to Baseline. B) Percentage of all 30 patients that achieved ACR20/50/70 at Week 4 (grey) and Week 12 (black). The percentage of patients who met ACR20/50/70 is provided at the top of each bar. Patients who did not complete the study were deemed non-responders. One (*) asterisk indicates $p < 0.05$ and two (**) asterisks indicate $p < 0.01$. P-values were calculated using paired two-tail t-tests.

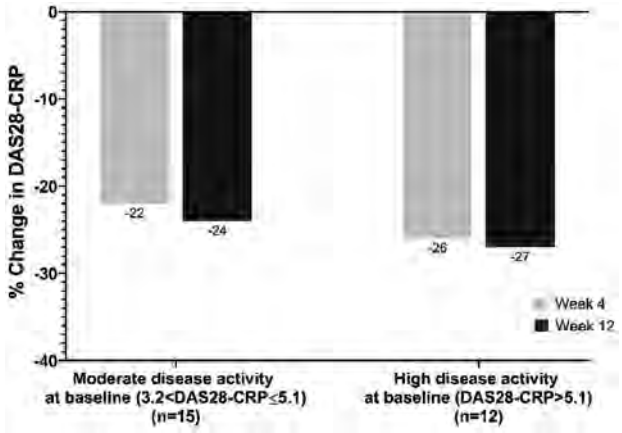


Figure 2 The mean change in DAS28-CRP score for patients with moderate or high disease activity at Baseline. The DAS28-CRP percentage change from Baseline is provided at the bottom of each bar.

Score or Component	Baseline (n=30), mean (SD)	Week 12 (n=27), mean (SD)	Change (n=27), mean (SD)	P-value
DAS28-CRP	5.30 (1.03)	3.76 (1.40)	-1.40 (1.16)	<0.0001
Tender joints	12.17 (3 – 28)	4.70 (5.83)	-6.74 (5.40)	<0.0001
Swollen joints	7.00 (2 – 16)	3.44 (3.90)	-3.15 (3.48)	<0.0001
HAQ-DI	1.59 (0.73)	1.05 (0.78)	-0.47 (0.61)	0.0004
Patient global health assessment	72.20 (19.97)	45.33 (31.60)	-24.89 (31.86)	0.0004
Physician global health assessment	56.17 (16.52)	29.62 (25.08)**	-27.16 (25.02)**	<0.0001
Pain score	75.23 (19.09)	43.30 (26.29)	-30.30 (28.67)	<0.0001
CRP (mg/L)	10.35 (11.63)	12.48 (21.27)	2.87 (16.05)	0.36

**Data only available for 25 patients
CRP = C-reactive protein; HAQ-DI = Heath activity questionnaire disability index

Table 1 Individual components of DAS28-CRP and ACR scoring for all observed data.

Conclusion: In this pilot study, transcutaneous stimulation of the auricular branch of the vagus nerve was well tolerated and improved signs and symptoms of RA. Further evaluation in larger controlled studies is needed to confirm whether this non-invasive vagus nerve stimulator might offer an alternative approach to the treatment of RA.

Disclosure: S. Marsal, None; **H. Corominas**, None; **J. De Agustin De Oro**, None; **C. Perez Garcia**, None; **M. Lopez Lasanta**, None; **H. Borrell**, None; **D. Reina**, None; **R. Sanmartí**, None; **F. Narváez**, None; **C. Franco-Jarava**, None; **C. Peterfy**, AbbVie, 1, Acerta, 1, Amgen, 1, 2, Astra Zeneca, 1, Bristol-Myers Squibb, 1, Centrexion, 1, Daiichi Sankyo, 1, Five Prime Therapeutics, 1, Genentech, 1, Gilead, 1, Hoffman-La Roche, 1, Janssen, 1, Lilly, 1, Medimmune, 1, Merck & Co, 1, Myriad, 1, Novartis, 1, Plexxikon, 1, Pfizer, 1, Sanofi, 1, Salix Santarus, 1, Samsung, 1, Samumed, 1, Setpoint, 1, Sorrento, 1, UCB, 1, Vorso, 1, Spire Sciences, 1, 2, 3; **J. Narvaez**, None; **V. Sharma**, None; **K. Alataris**, None; **M. Genovese**, Abbvie, 2, 5, Eli Lilly and Company, 2, 5, Galapagos, 2, 5, Gilead Sciences Inc., 2, 5, Pfizer, 2, 5, EMD Merck Serono, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, RPharm, 2, 5, Sanofi-Genzyme, 2, UCB, 5, Amgen, 5; **M. Baker**, Vorso Corp, 1, 5.

Abstract Number: 1996

Evaluation of Response to Pneumococcal Vaccination in Patients with Rheumatoid Arthritis Receiving Upadacitinib: Results from a Phase 2 Open-Label Extension Study

Kevin Winthrop[1], Juan Vargas[2], Edit Drescher[3], Conrado Garcia[4], Alan Friedman[5], Jeffrey Enejosa[5], Nasser Khan[5], Yihan Li[5], Justin Klaff[5] and Alan Kivitz[6], [1]Oregon Health & Science University, Portland, OR, [2]Quantum Research, Puerto Varas, Chile, [3]Veszprém Csolnoky Ferenc County Hospital, Veszprém, Hungary, [4]Hospital General de México "Dr. Eduardo Liceaga", Mexico, Mexico, [5]AbbVie Inc., North Chicago, IL, [6]Altoona Center for Clinical Research/Altoona Arthritis and Osteoporosis Center, Duncansville, PA

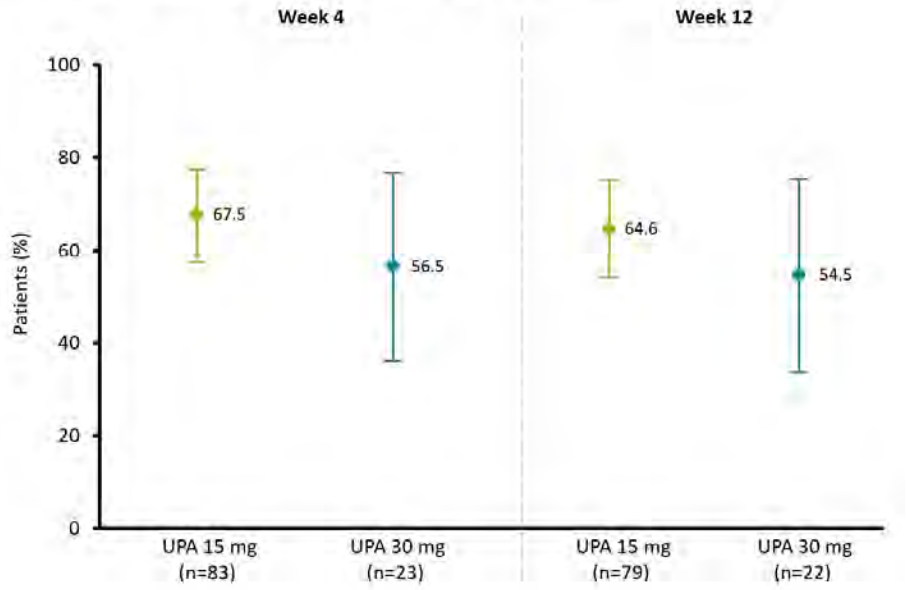
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments I: Maximizing Health in RA
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Pneumococcal vaccination is recommended in patients with RA who are receiving conventional synthetic/biologic DMARDs.[1] Upadacitinib (UPA) is an oral Janus kinase (JAK) inhibitor engineered to have a greater selectivity for JAK1 versus JAK2, JAK3, and tyrosine kinase 2, and is approved for the treatment of RA. The aim of this analysis was to assess the impact of long-term treatment with UPA + background MTX on immunologic responses to Prevnar 13® (Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM_{197} Protein]; PCV13) in patients with RA enrolled in the ongoing Phase 2 open-label extension study BALANCE-EXTEND.

Methods: Patients from BALANCE-EXTEND receiving PCV13 vaccination were required to be on UPA 15 mg once daily (QD) or 30 mg QD and background MTX for ≥4 weeks prior to, and after, PCV13 vaccination; MTX was not interrupted prior to vaccination. Vaccination antibody titers were collected pre-vaccination (Week 0) and post-vaccination (Weeks 4 and 12). The primary variable was the proportion of patients with satisfactory humoral response to PCV13 (≥2-fold increase in antibody concentration from pre-vaccination [Week 0] in ≥6/12 pneumococcal antigens [1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F]) at 4 weeks post-vaccination.

Results: Of 111 patients (UPA 15 mg, n=87; UPA 30 mg, n=24), 86% were female, most (98%) were white, and mean (standard deviation) age was 58.4 (12.0) years. Prior to vaccination, patients had a median (range) duration of RA of 9.3 (3.4–35.0) years and had been receiving UPA for a median (range) of 3.9 (3.0–4.9) years. All but 3 patients were taking concomitant MTX, and 44.1% were taking a CS (median daily dose, 5.0 mg). All 111 patients received PCV13, none discontinued UPA during the first 4 weeks, and blood samples were available from 83/23 and 79/22 patients in the UPA 15/30 mg groups at Weeks 4 and 12, respectively. At 4 weeks, satisfactory humoral response to PCV13 occurred in 67.5% (95% confidence interval [CI]: 57.4–77.5) and 56.5% (95% CI: 36.3–76.8) of patients receiving UPA 15 and 30 mg, respectively. At 12 weeks, satisfactory humoral response to PCV13 occurred in 64.6% (95% CI: 54.0–75.1) and 54.5% (95% CI: 33.7–75.4) of patients receiving UPA 15 and 30 mg, respectively (**Figure 1**). There was no clear difference in response between patients receiving and not receiving concomitant CS. Within 30 days post-vaccination, 2 adverse events (AEs) were considered as possibly related to UPA (1 case of diverticulitis, UPA 15 mg; 1 case of anemia, UPA 30 mg) and no serious AEs were reported (**Table 1**). Two patients experienced pyrexia and 1 subject each experienced vaccination-site pain and headache within 1 day post-vaccination (all in UPA 15 mg group).

Figure 1. Proportion (%, 95% CI) of UPA-treated patients with satisfactory humoral response[a] to PVC13 at Weeks 4 and 12 (full analysis set)[b]



[a]Satisfactory humoral response was defined as ≥2-fold increase in antibody concentration from the vaccination baseline in ≥6 out of 12 pneumococcal antigens (1, 3, 4, 5, 6B, 7F, 9V, 14, 18C, 19A, 19F, and 23F). [b]Number of patients based on availability of blood samples collected at Weeks 4 and 12. CI, confidence interval; PVC13, Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM_{197} Protein]; UPA, upadacitinib

Table 1. Safety through 30 days post-PVC13 vaccination in UPA-treated patients (safety analysis set)

Event, n (%)	UPA 15 mg QD (n=87)	UPA 30 mg QD (n=24)
Any AE	15 (17.2)	3 (12.5)
Serious AE	0	0
AE leading to discontinuation of study drug	0	0
AE with reasonable possibility of being related to UPA[a]	1 (1.1)[b]	1 (4.2)[c]
Death	0	0

[a]As assessed by the investigator. [b]Diverticulitis. [c]Anemia. AE, adverse event; PVC13, Pneumococcal 13-valent Conjugate Vaccine [Diphtheria CRM_{197} Protein]; QD, once daily; UPA, upadacitinib.

Conclusion: Satisfactory humoral response to PCV13 at 4 weeks occurred in ~two-thirds of patients with RA receiving long-term treatment with UPA 15 mg QD + background MTX. This is broadly consistent with pneumococcal vaccine humoral responses observed in patients with RA treated with other JAK inhibitors, biologics, or placebo.[2–4]

1. Singh JA, et al. Arthritis Care Res 2016;68:1–25.
2. Winthrop KL, et al. Arthritis Res Ther 2019;21:102.
3. Bingham CO, et al. Ann Rheum Dis 2015;74:818–22.
4. Winthrop KL, et al. Ann Rheum Dis 2016;75:687–95.

Disclosure: K. Winthrop, Pfizer, 2, 5, UCB, 2, 5, Abbvie, 2, 5, Galapagos, 2, 5, Gilead, 2, 5, Roche, 2, 5, Bristol-Myers Squibb, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 5; **J. Vargas**, AbbVie, 9; **E. Drescher**, None; **C. Garcia**, None; **A. Friedman**, AbbVie, 1, 2; **J. Enejosa**, AbbVie, 1, 3; **N. Khan**, AbbVie, 1, 2; **Y. Li**, AbbVie, 1, 2; **J. Klaff**, AbbVie, 1, 2; **A. Kivitz**, Sanofi, 1, 5, 8, Amgen, 1, Gilead, 1, AbbVie, 5, Genzyme, 5, 8, Janssen, 5, Novartis, 8, Regeneron, 5, 8, Boehringer Ingelheim, 5, Celgene, 8, Flexion, 8, Horizon, 8, Merck, 8, Pfizer, 1, 5, 8, Sun Pharma, 5, UCB, 5.

Abstract Number: 1997

Immunogenicity of Adjuvanted Herpes Zoster Subunit Vaccine in Rheumatoid Arthritis Patients Treated with Janus Kinase Inhibitors and Controls: Preliminary Results

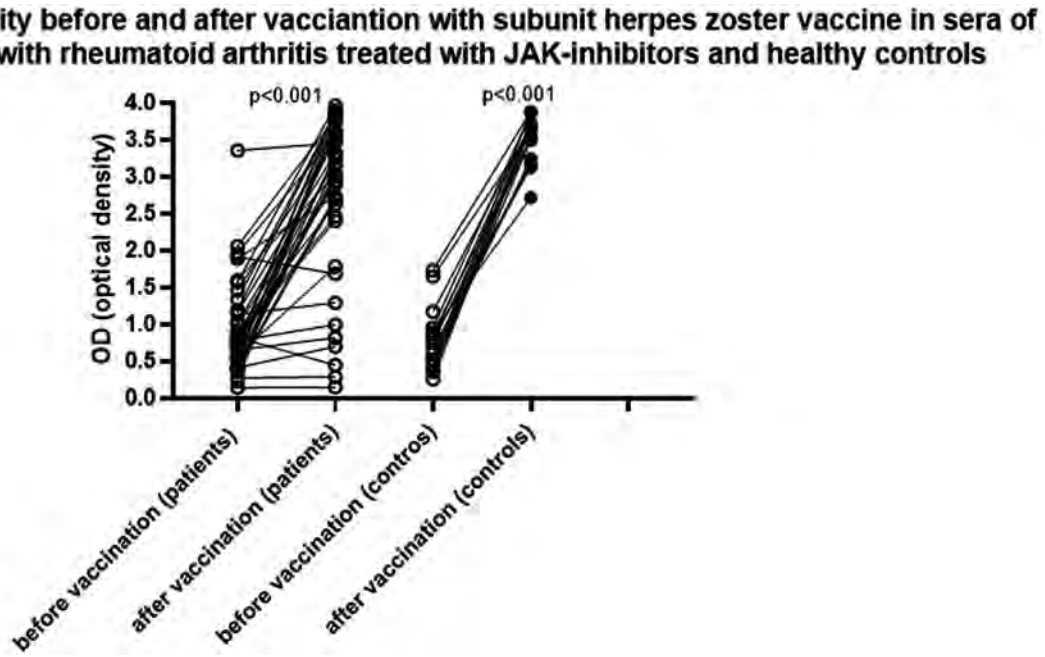
Hanna Källmark[1], Birgitta Gullstrand[2], Johanna Nagel[3], Jon Einarsson[1], Göran Jönsson[4], Fredrik Kahn[5], Robin Kahn[6], Anders Bangtsson[2], Tomas Bergström[7] and Meliha Kapetanovic[1], [1]Department of Clinical Sciences Lund, Section of Rheumatology, Lund University, Lund, Sweden and Skåne University Hospital Sweden., Lund, Sweden, [2]Department of Rheumatology, Clinical Sciences, Lund University Sweden, Lund, Sweden, [3]Lund University, Skåne University Hospital, Department of Clinical Sciences Lund, Rheumatology, Lund, Sweden, Lund, Sweden, [4]Lund University, Skåne University Hospital, Department of Clinical Sciences Lund, Infection Medicine, Lund, Sweden, Lund, Sweden, [5]Division of Infection Medicine, Department of Clinical Sciences, Lund University, Lund, Sweden, Lund, Sweden, [6]Department of Clinical Sciences Lund, Section of Pediatrics, Lund University, Lund, Sweden; Wallenberg Centre of Molecular Medicine, Lund University, Lund, Sweden, [7]Department of Infectious Diseases, Section for Clinical Virology, Institute of Biomedicine, University of Gothenburg, Sweden, Gothenburg, Sweden

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments I: Maximizing Health in RA
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Patients with rheumatoid arthritis (RA) are at increased risk of contracting herpes zoster (HZ) and treatment with JAnus Kinase inhibitors (JAKi) further adds on to that risk. A novel subunit vaccine against HZ (HZ/su; Shingrix) composed of VZV glycoprotein E (gE) and adjuvant system $AS01_B$ has recently been licensed. The HZ/su vaccine has been shown safe and effective in healthy elderly but data on patients with rheumatic disease are scarce. The objective of this study was to investigate the antibody responses to the HZ/su vaccine in RA patients treated with JAKi and controls.

Methods: RA patients at the rheumatology outpatient department, Skåne University Hospital, Lund, Sweden, fulfilling the ACR87 criteria and receiving JAKi as monotherapy or in combination with other disease modifying anti-rheumatic drugs (DMARDs) and individuals ^{3}18 years without known rheumatic disease and not receiving immunosuppressive treatment for other conditions served as controls. All participants were immunized with two intramuscular doses of 50 mg HZ/su vaccine administered at least two months apart. Blood was sampled prior to first and 4-6 weeks after the second vaccine dose. ELISA using varicella zoster virus (VZV) glycoprotein E (gE) as the antigen was employed to measure anti-gE levels (1). Results are presented as optical density (OD). A positive antibody response was defined as a difference of ^{3}1.2 in OD between the post- and pre-vaccination sera. The difference between ODs before and after vaccination among patients and controls separately were calculated using Wilcoxon signed-rank test. Chi2 test was used to compare % of individuals with positive antibody response between the two groups.

Results: Data from 40 RA patients (mean age 62.3 years; 77.5% female, mean disease duration 16 years) treated with JAKi and 20 controls (mean age 61.5 years and 70% female) were analysed. Compared to prevaccination sera, OD levels increased significantly in both patients and controls ($p< 0.001$). Mean changes in anti-gE antibody OD between



post- and prevaccination sera were +1.8 and +2.6 for patients and controls respectively (Figure1). Positive humoral responses (delta OD[3]1.2) were observed in 75% of patients and 100% of controls (p=0.014). The majority of patients reported mild to moderate vaccine related side effects (pain and redness at the injection site, headache, fever for a few days) which resolved without any treatment. In total, 3 patients and 0 controls withdrew from the study prior to the second vaccine dose, 2 of these due to adverse events (diarrhoea, joint and muscle pain) and are not included in these preliminary results. No patient experienced worsening or flare of RA. No case of HZ has been reported yet (up to 15 months after start of enrolment in the study).

Conclusion: These preliminary results show satisfactory serological responses and acceptable tolerability of two doses HZ/su vaccine in RA patients treated with JAKi known to be at a particularly increased risk of HZ.

Reference

1. Thomsson E, Persson L, Grahn A, et al. Recombinant glycoprotein E produced in mammalian cells in large-scale as an antigen for varicella-zoster-virus serology. J Virol Methods. 2011;175(1):53-59.

Disclosure: H. Källmark, None; **B. Gullstrand**, None; **J. Nagel**, None; **J. Einarsson**, None; **G. Jönsson**, None; **F. Kahn**, Hansa Biopharma, 1, Piereis Pharmaceuticals Inc, 1, Gilead Sciences Inc, 1, ChemoCentryx Inc, 1; **R. Kahn**, None; **A. Bangtsson**, None; **T. Bergström**, None; **M. Kapetanovic**, Pfizer, 2.

Abstract Number: 1998

Ten-year Analysis of the Risk of Severe Outcomes Related to Very Low-dose Glucocorticoids in Early Rheumatoid Arthritis

Camille Roubille[1], Amandine Coffy[2], Nathalie Rincheval[2], Jean Pierre Daures[2], René-Marc Flipo[3], Maxime Dougados[4] and **Bernard Combe**[5], [1]CHU LAPEYRONIE, Montpellier, France, [2]INSERM, Montpellier, France, [3]Univ-Lille, CHU Lille, department of rheumatology, Lille, France, [4]Department of Rheumatology, Hopital Cochin, Université de Paris, Paris, France, [5]University of Montpellier, Montpellier, France

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Treatments II: Potential Harms & Adverse Events

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Although glucocorticoids (GC) remain an essential part of the therapeutic strategy in Rheumatoid Arthritis (RA), the long-term risk of adverse events of low-dose GC treatment is still controversial.

Methods: We analysed data from the early arthritis (less than 6 months' disease duration) ESPOIR cohort. Patients were stratified in two groups, with or without GC treatment at least once during their follow-up (median 10 years IQR [9-10]). The primary outcome was a composite of death, cardiovascular diseases (CVD) (including myocardial ischemia, cerebrovascular accident and heart failure), severe infection and fracture. In order to reduce the impact of treatment selection bias and potential confounding factors, the weighted Cox time-dependent analysis model was used with inverse probability of treatment weighting (IPTW) propensity score method.

Results: Among the 608 RA patients (480 women, mean age of 47.5 ± 12.1 years), 397 patients (65%) received low-dose prednisone (mean 2.8 ±2.8 mg/d, median 1.9 mg/day [IQR 0.6-4.2], mean cumulative GC dose of 8468 mg ±8376), mainly during the first 6 months (70%). The mean duration of GC treatment was 44.6 months ± 40.1. Overall,

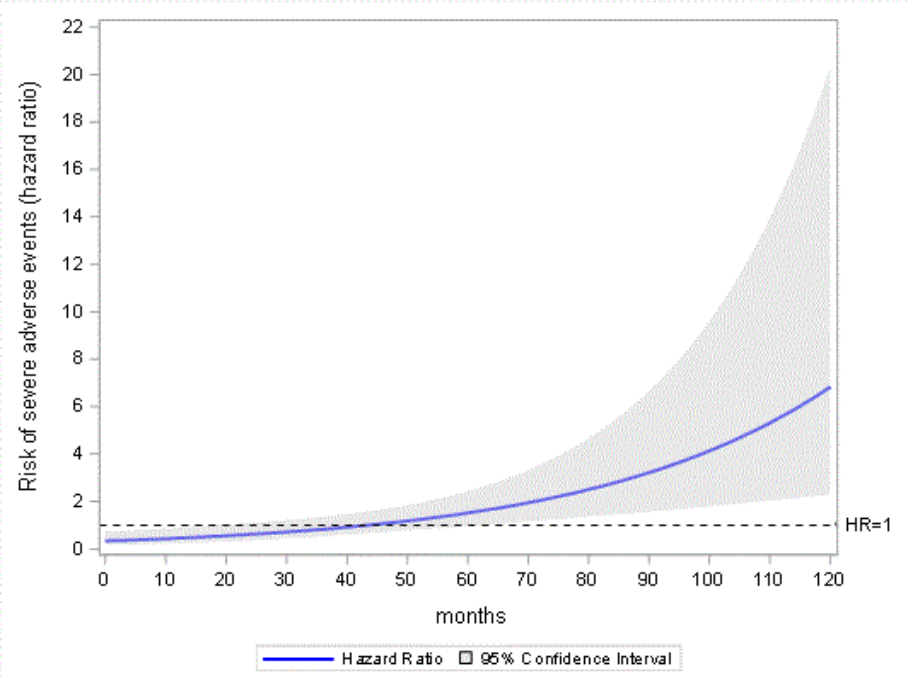
Table 1. Primary outcome at 10 years (death, cardiovascular disease, severe infection or fracture) in the total sample and with and without glucocorticoid (GC) (univariate analysis).

	Total study population (n=608)	Without GC	With GC	P Value
Primary outcome	95 (15.6%)	24 (11.4%)	71 (17.9%)	**0.035**
Death	10 (1.6%)	1 (0.5%)	9 (2.3%)	0.103
Cardiovascular diseases	18 (3%)	3 (1.4%)	15 (3.8%)	0.177
Severe infections	35 (5.8%)	5 (2.4%)	30 (7.6%)	**0.009**
Fractures	32 (5.3%)	15 (7.1%)	17 (4.3%)	0.137

Table 2: Time-dependent relationship between glucocorticoids treatment and risk of severe adverse events estimated by hazard ratio

Time (Years)	Hazard Ratio (95% CI)
1	0.46 (0.23 - 0.90)
2	0.62 (0.36 - 1.08)
3	0.83 (0.52 - 1.33)
4	1.12 (0.73 - 1.72)
5	1.52 (0.96 - 2.40)
6	2.05 (1.19 - 3.52)
7	2.77 (1.44 - 5.34)
8	3.74 (1.69 - 8.26)
9	5.05 (1.98 - 12.91)
10	6.83 (2.29 - 20.35)

Figure 1: Time-dependent relationship between glucocorticoids treatment and risk of severe adverse events estimated by hazard ratio (HR)



95 events were identified during the follow-up: 10 deaths, 18 CVD, 32 fractures and 35 severe infections. Based on univariate analysis at 10 years, patients taking GC experienced significantly more events (n=71) than those without GC (n=24) (p=0.035) (table1). Interestingly, we evidenced a significant cumulative dose-effect (p=0.007), particularly for the risk of severe infections (p=0.024) and CVD (p=0.001). On weighted Cox time-dependent analysis, using the IPTW propensity score method, the risk of events over time was significantly associated with GC treatment ($p < 0.001$), age, history of hypertension and erythrocyte sedimentation rate (figure1). The risk associated with GC treatment, estimated by the hazard ratio (HR), increased between the first follow-up visit (HR at 6 months = 0.39, 95% CI 0.19-0.82) and 10 years (HR=6.83, 95% CI 2.29-20.35) (table 2).

Conclusion: The 10-year analysis of this prospective early RA cohort supports a dose and time-dependent impact of very low-dose GC treatment, with a long-term high risk of severe outcomes.

Disclosure: C. Roubille, None; **A. Coffy**, None; **N. Rincheval**, None; **J. Daures**, None; **R. Flipo**, Abbvie, 1, 2, Biogen, 1, BMS, 1, Janssen, 1, 2, MSD, 1, Nordic, 1, Novartis, 1, 2, Pfizer, 1, 2, Roche-Chugai, 1, 2, Sanofi, 1; **M. Dougados**, Pfizer, 1, 2, Abbvie, 1, 2, UCB, 1, 2, Merck, 1, 2, Lilly, 1, 2, BMS, 1, 2, Roche, 1, 2, Novartis, 1, 2; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8.

Abstract Number: 1999

Hydroxychloroquine Is Not Cardiotoxic in Patients with Rheumatoid Arthritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments II: Potential Harms & Adverse Events
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Hydroxychloroquine (HCQ) has been proposed as a potential treatment for COVID-19, but early reports suggested that it could have cardiotoxic effects. Despite widespread and longstanding use to treat rheumatic diseases, cardiotoxicity was not on the risk radar of most rheumatologists prescribing HCQ. Our objective in the present analysis is to examine the risk of cardiotoxicity among members of a well-characterized RA cohort who were receiving HCQ.

Methods: We studied RA patients meeting the 1987 ACR criteria, recruited from public, private, military, and Veterans Administration rheumatology clinics. Patients were invited to participate in yearly follow up evaluations in which we ascertained clinical and laboratory features, including HCQ use. The assessment included an electrocardiogram and a detailed medical record review.

We ascertained cardiac events, including myocardial infarction (MI), cardiomyopathy, cardiac conduction disorders, or cardiac dysrhythmias in all patients. We also ascertained vital status in all participants, obtaining a certificate for all deaths. We compared the frequency of these events between patients who received HCQ and patients who did not receive it using generalized estimating equation (GEE) models, including all follow-up visits. We considered HCQ exposure in three categories: Those who did not receive HCQ during the study period, those who were receiving it during some of the visits, and those who were receiving it at all of the visits. We adjusted for the propensity to receive HCQ to control for potential bias for indication.

Results: We studied 1328 patients, 981 of whom were women (74%). These patients completed 5826 visits, for a total of 8336 patient-years (pt-yrs) of follow up. There were 114 patients who were receiving HCQ at every one of 338 visits, for 347 pt-yrs; 323 patients who were receiving HCQ during some of 1742 visits, for 2793 pt-yrs; and 891 patients who were not receiving HCQ at any of 3746 visits, for 5147 pt-yrs. We ascertained 120 cases of MI, 185 of cardiac dysrhytmias, 13 cardiomyopathies, and 21 cases with conduction disorders. The table below shows the number and incidence of these events per 100 pt-yrs for each of the HCQ exposure categories.

We did not find significant differences in the risk of cardiomyopathy, conduction disorders, or MI between the three HCQ exposure categories. Cardiac dysrhythmias were significantly less likely to occur in patients who were taking HCQ compared to patients who were not taking it (OR 0.61, 95% CI 0.37-0.96, p= 0.03). The GEE regression models according to HCQ exposure, adjusted by age and sex, did not uncover associations between HCQ and cardiac events use (Table), nor did adding a score for the propensity to receive HCQ to the models. Patients who were receiv-

	Visits Receiving Hydroxychloroquine		
Cardiac Events	**All**	**Some**	**None**
Myocardial Infarction	4, 1.1 (0.03, 2.9)	29, 1.0 (0.6, 3.7)	87, 1.6 (1.3,2.0)
Conduction Disorder	1, 0.2 (0.007, 1.6)	5, 0.1 (0.05, 0.4)	15, 0.2 (0.1, 0.4)
Cardiomyopathy	0	4, 0.1 (0.03, 0.3)	9, 0.1 (0.07, 0.3)
Cardiac Dysrhytmias	6, 1.7 (0.6, 3.7)	50, 1.7 (1.3, 2.3)	129, 2.5 (2.0, 2.9)
Total Cardiotoxicity	**11, 3.1 (1.5, 5.6)**	**88, 3.1 (2.5, 3.8)**	**240, 4.6 (4.0, 5.2)**
	Values represent the number of events observed, and incidence per 100 patient-years (95% confidence intervals)		

Table. Observed events and incidence of cardiotoxicity events according to HCQ exposure.

ing HCQ continuously had significantly lower mortality than those who were not receiving it at any of the visits (OR 0.55, 95% CI 0.40, 0.76, p < 0.0001).

Conclusion: Our findings suggest that HCQ is not associated with an increased risk of cardiotoxicity among RA patients. Moreover, HCQ exposure may be associated with a reduction in mortality among RA patients. HCQ appears to be safe among RA patients in terms of its cardiac effects.

Disclosure: J. Restrepo, None; **A. Escalante**, None; **D. Battafarano**, None; **C. Lorenzo**, None; **I. Del Rincon**, None.

Abstract Number: 2000

Risk of Venous Thromboembolism in Rheumatoid Arthritis Patients Treated with Methotrexate versus Hydroxychloroquine

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments II: Potential Harms & Adverse Events
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Prior studies suggest an increased risk of venous thromboembolism (VTE) among patients with rheumatoid arthritis (RA). However, little is known about the comparative risk of VTE associated with the 1st line conventional disease-modifying antirheumatic drugs (DMARDs), methotrexate (MTX) and hydroxychloroquine (HCQ). The objective of this study was to compare the incidence rate of VTE in RA patients who were newly treated with MTX versus HCQ.

Methods: Using Medicare claims data (Parts A/B/D 2008-2017), we identified RA patients who were new users of MTX and HCQ and had no prior use of any DMARDs. Patients were required to be ≥65 years old at the cohort entry (i.e. MTX or HCQ initiation date) and have ≥365 days of continuous insurance enrollment. Patients with a diagnosis of VTE, cancer (except non-melanoma skin cancer), or lupus, or use of anticoagulants or chloroquine at baseline were excluded. The primary outcome was VTE, defined as an inpatient primary diagnosis of pulmonary embolism (PE) or deep vein thrombosis (DVT). Secondary outcomes included VTE defined as an inpatient or outpatient diagnosis of PE or DVT plus a dispensing of anticoagulants within 30 days, and separate PE and DVT based on an inpatient primary diagnosis. Using as-treated analysis, the study participants were followed from one day after the cohort entry until the earliest event of the outcome, treatment discontinuation or switch, insurance disenrollment, death, or end of data. To control for confounding, MTX and HCQ new users were 1:1 matched on the propensity score (PS) that was estimated based on patient baseline demographics, comorbidities, medication use, medical procedures, and healthcare utilization. Hazard ratios (HRs) and 95% confidence intervals (CIs) were estimated using Cox proportional hazards models.

Results: We identified a total of 26,534 PS-matched pairs of MTX and HCQ initiators. Their mean (standard deviation) age was 74 (7) years and 79% were female. We observed a slightly higher proportion of steroids use in the MTX group before PS matching, but the patient baseline characteristics in the PS matched cohort were well balanced between the two treatment groups (**Table 1**). In the primary analysis, 208 MTX and 83 HCQ new users developed VTE during a median follow up of 190 days (interquartile range 93-452 days). The incidence rate (per 1,000 person-years) was 6.94 (95% CI 6.03-7.95) in the MTX group and 3.11 (95% CI 2.47-3.85) in the HCQ group (**Table 2**). The HR for incident VTE

Table 1. Selected baseline characteristics of MTX and HCQ new users in the propensity score matched cohort

Patient characteristics	MTX (N = 26,534)	HCQ (N = 26,534)	Standardized Difference
Demographics			
Age in years, mean (SD)	74.05 (6.59)	74.00 (6.59)	0.007
Female	79.2%	79.1%	0.002
Comorbidities			
Stroke or transient ischemic attack	5.3%	5.1%	0.009
Hyperlipidemia	71.6%	71.1%	0.011
Diabetes	30.1%	29.7%	0.008
Renal dysfunction	13.7%	13.5%	0.005
Extremity fracture	4.9%	4.8%	0.003
Varicose veins	3.1%	3.1%	0.002
Combined comorbidity index, mean (SD)	1.04 (1.91)	1.03 (1.93)	0.006
Medications			
Oral steroids	64.5%	64.4%	0.001
Cumulative steroids dose (365 days, prednisone equivalent), median (IQR)	115.00 (0.00, 550.00)	110.00 (0.00, 537.94)	0.009
Other hormonal agents (including hormone replacement therapy)	2.7%	2.8%	0.005
NSAIDs/Coxibs	47.7%	47.6%	0.002
Statin	49.1%	48.9%	0.004
Antiplatelets	8.7%	8.6%	0.005
Procedures			
Surgeries on the cardiovascular system	2.2%	2.2%	0.002
Surgeries on the digestive/gynecologic system	1.9%	1.9%	0.005
Surgeries on the musculoskeletal system	2.5%	2.5%	0.000
Healthcare utilization			
Any hospitalization	14.3%	14.1%	0.006

Abbreviations: SD- Standard deviation; IQR- Interquartile range; NSAIDs- Nonsteroidal anti-inflammatory drugs; Coxibs- Cyclooxygenase inhibitors.

Table 2. Incidence rates and hazard ratios (95% CI) of primary and secondary outcomes for MTX and HCQ new users in the propensity score matched cohort

Outcome	Exposure group	Number of events	Total person-years	Incidence rate per 1,000 person-years (95% CI)	Hazard ratio (95% CI)
VTE (Primary)*	MTX	208	29,963	6.94 (6.03-7.95)	2.26 (1.75-2.91)
	HCQ	83	26,723	3.11 (2.47-3.85)	Ref.
VTE (Secondary)**	MTX	371	29,780	12.46 (11.22-13.79)	1.64 (1.38-1.95)
	HCQ	203	26,605	7.63 (6.62-8.76)	Ref.
PE	MTX	132	30,045	4.39 (3.68-5.21)	3.30 (2.28-4.77)
	HCQ	36	26,752	1.35 (0.94-1.86)	Ref.
DVT	MTX	80	30,073	2.66 (2.11-3.31)	1.53 (1.07-2.19)
	HCQ	47	26,741	1.76 (1.29-2.34)	Ref.

Abbreviations: CI- Confidence interval; VTE- Venous thromboembolism; PE- Pulmonary embolism; DVT- Deep vein thrombosis; Ref.- Reference.

* The primary definition of VTE: ≥1 inpatient primary diagnosis of PE or DVT.

** The secondary definition of VTE: ≥1 inpatient or outpatient diagnosis of PE or DVT plus ≥1 dispensing of anticoagulants within 30 days.

comparing MTX with HCQ initiators was 2.26 (95% CI 1.75-2.91) using the primary definition and 1.64 (95% CI 1.38-1.95) using the more sensitive but less specific secondary definition. The results were consistent in the analyses of PE and DVT, separately (**Table 2**).

Conclusion: In this large cohort of older RA patients, we observed an approximately 2-fold increased risk of VTE among patients who were newly treated with MTX versus HCQ. The comparative thrombotic safety profile of MTX and HCQ should be considered when physicians treat newly diagnosed RA patients with known VTE risk factors.

Disclosure: M. He, None; **A. Pawar**, None; **R. Desai**, None; **R. Glynn**, AstraZeneca, 2, Kowa, 2, Pfizer, 2, Novartis, 2; **H. Lee**, None; **M. Weinblatt**, Crescendo Bioscience, 1, Bristol Myers Squibb, 1, Sanofi, 2, Lilly, 1, Amgen, 1, AbbVie, 5, Amgen, 2, 5, Arena, 5, Bristol Myers Squibb, 2, 5, Canfite, 1, 5, Corrona, 5, Crescendo, 2, 5, GlaxoSmithKline, 5, Gilead, 9, Horizon, 9, Johnson and Johnson, 9, Lilly, 2, 9, Pfizer, 9, Scipher, 1, 9, Set Point, 9, Roche, 9, Canfite, 1, Inmedix, 1, Lycera, 1, Vorso, 1, Scipher, 1; **D. Solomon**, AbbVie, 2, Amgen, 1, Genentech, 1, Janssen, 1, Corrona, 1; **S. Kim**, Pfizer, 1, Roche, 1, AbbVie, 1, Bristol-Myers Squibb, 1.

Abstract Number: 2001

Adverse Effects of Low Dose Methotrexate: Adjudicated Hematologic Outcomes in a Large Randomized Double-blind Placebo-controlled Trial

Kathleen Vanni[1], Nancy Berliner[1], Nina Paynter[2], Robert Glynn[2], Jean MacFadyen[1], Joshua Colls[1], Fengxin Lu[1], Chang Xu[2], Paul Ridker[1] and Daniel H Solomon[1], [1]Brigham and Women's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments II: Potential Harms & Adverse Events
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Low dose methotrexate (LD-MTX), a cornerstone in the treatment of rheumatoid arthritis, is associated with a moderately increased risk of anemia and leukopenia, but the risk of myelosuppression during LD-MTX use of up to 20mg/week remains incompletely described. We examined the hematologic outcomes among patients taking LD-MTX versus placebo in a large randomized controlled trial (RCT).

Methods: We pre-specified secondary analyses of a double-blind placebo-controlled RCT that included adults with known cardiovascular disease plus diabetes or metabolic syndrome in the US and Canada. Subjects with rheumatic disease were excluded. Subjects were randomly allocated to LD-MTX (20mg/week maximum) or placebo, and all subjects received folic acid 1mg daily for six days/week. Laboratory monitoring was performed every 1-2 months. Abnormal cell count definitions were pre-specified according to the Common Terminology Criteria for Adverse Events (CTCAE v.5.0). We assessed the frequency of blindly adjudicated hematologic adverse events (AEs) and laboratory abnormalities.

Results: 2,391 subjects were randomized to LD-MTX (mean dosage 14.9 mg/week) and 2,395 to placebo. Simultaneous two-line cytopenias were infrequent in both the LD-MTX arm (n=92, 3.9%) and the placebo arm (n=70, 2.9%) during follow-up. Pancytopenia was rare but numerically more common among patients randomized to LD-MTX (n=13, 0.5%) versus placebo (n=6, 0.3%). We examined the cases of LD-MTX-associated pancytopenia in detail (see **Table 1**). Pancytopenia developed as soon as 4 months and as late as 3.5 years after beginning LD-MTX, though the latter subject was diagnosed with multiple myeloma a week prior. The median age of subjects who developed pan-

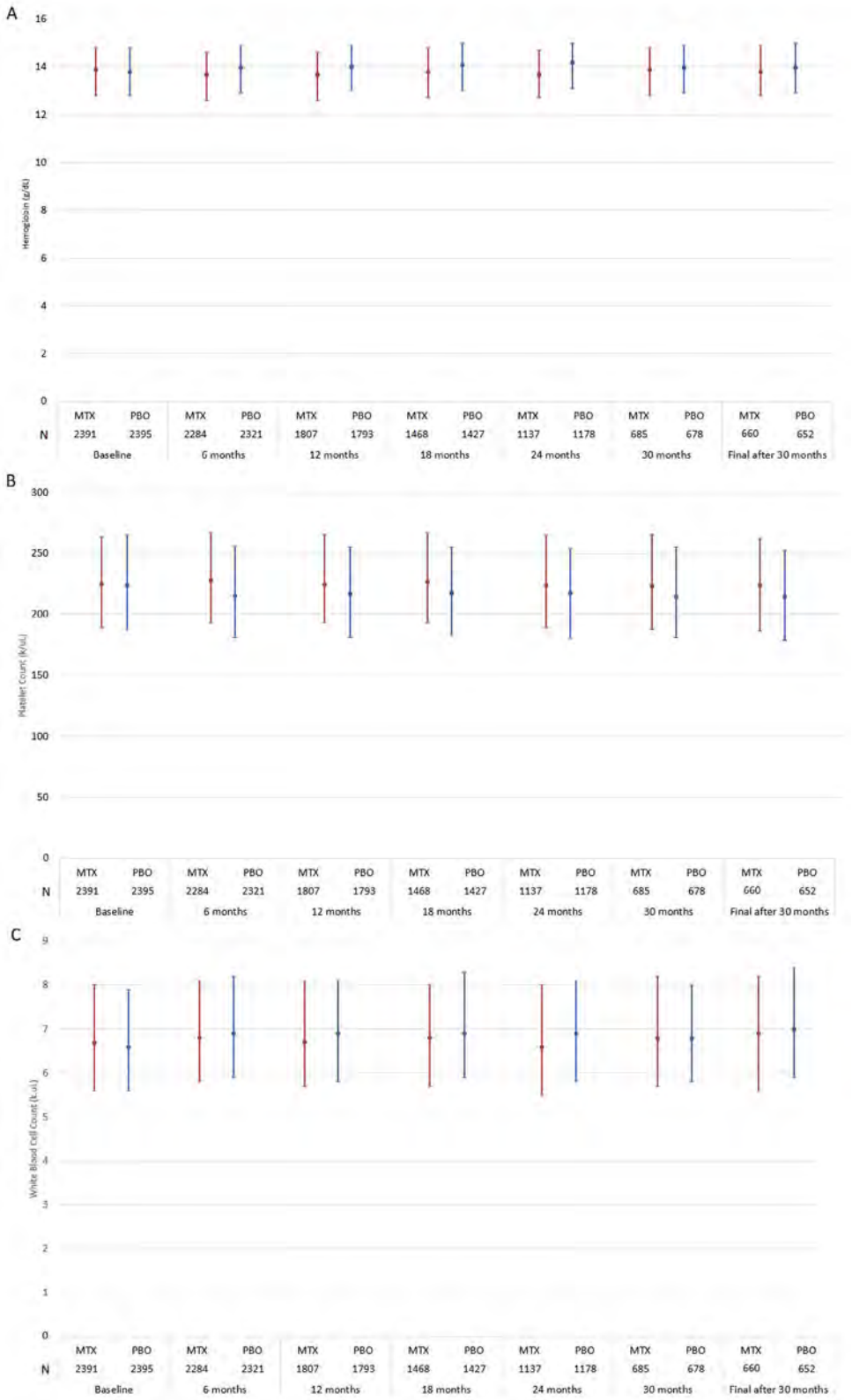
Case	Age (years)	Sex	LD-MTX Dose at time of event (mg/week)	Duration of LD-MTX use prior to event (months)	BMI (kg/m2)	Alcohol use at baseline	Tobacco use at baseline	Aspirin use at baseline	Other Anti-coagulant use at baseline	Hgb (g/dL)		WBC (k/μL)		PLT (k/μL)		Study Drug Change
										At baseline	At time of event	At baseline	At time of event	At baseline	At time of event	
1	74	M	20	31.4	30.5	Never or < 1/month	No	Yes	Yes, clopidogrel	13.8	13.4	4.7	3.9	160	142	Continued
2	71	M	20	6.0	27.4	2-3 times/week	No	Yes	No	14.2	13.2	5.9	3.9	150	144	Decreased to 15mg weekly
3	69	M	15	21.9	27.2	2-3 times/week	No	Yes	No	13.7	13.3	5.1	3.5	176	136	Decreased to 10mg weekly
4	69	F	20	8.0	27.1	Never or < 1/month	No	Yes	Yes, dipyridamole	10.7	9.6	5.1	2.8	222	123	Temporary stop; resumed after 10 weeks
5	68	M	20	41.4	31.6	Never or < 1/month	No	Yes	No	12.7	7.0	5.9	3.5	219	143	Permanent stop
6	67	F	15	4.0	19.4	Never or < 1/month	Yes	No	Yes, clopidogrel	12.6	11.1	4.5	3.4	164	138	Decreased to 10mg weekly
7	76	M	20	17.8	35.4	1-3 times/month	No	No	Yes, clopidogrel	13.9	12.3	4.7	3.6	170	137	Continued
8	75	M	20	29.8	34.6	Never or < 1/month	No	Yes	Yes, clopidogrel	14.3	13.4	5.9	3.4	158	133	Decreased to 15mg weekly
9	83	M	20	13.6	27.3	1-3 times/month	No	Yes	No	13.7	12.4	5.0	3.7	167	141	Continued
10	70	M	20	13.8	33.7	Never or < 1/month	No	Yes	Yes, clopidogrel	12.9	8.6	6.0	2.4	246	112	Permanent stop
11	69	F	20	24.7	40.2	Never or < 1/month	No	Yes	Yes, clopidogrel	12.0	9.5	4.8	2.3	203	124	Permanent stop
12	73	M	20	7.9	25.5	2-3 times/week	No	Yes	Yes, apixaban	13.5	13.4	4.3	3.1	151	138	Decreased to 15mg weekly
13	75	M	20	30.0	26.0	1/week	No	Yes	No	14.4	13.2	4.3	3.8	157	142	Continued

Hgb, hemoglobin; WBC, white blood cell count; PLT, platelet count; LD-MTX, low dose methotrexate

cytopenia was 70.5 years (interquartile range, IQR 69, 75), compared to a median age of 65.6 years (IQR 59.7, 71.8) in the entire LD-MTX arm. The platelet counts in all 13 cases showed only mild reductions.

Figure 1 presents median hemoglobin levels and platelet and leukocyte counts during follow-up. Baseline values represent the end of the active follow-up period immediately before randomization. Between baseline and final study visits, median hemoglobin decreased in both arms: by 0.40g/dL (IQR -0.90, 0.10) in the LD-MTX arm and by 0.10g/dL (IQR -0.60, 0.30) in the placebo arm. White blood cell counts did not change in the LD-MTX arm (median change 0.00k/uL; IQR -0.90, 0.80) and increased by 0.20k/uL in the placebo arm (IQR -0.70, 1,10). The median platelet count did not change in the LD-MTX arm (median change 0.00k/uL; IQR, -18, 16k/uL) but decreased by 9k/uL (IQR -26, 9) in the placebo arm.

Conclusion: Among subjects using LD-MTX, simultaneous two-line cytopenias and pancytopenia were uncommon. The absolute reductions in hemoglobin were small, white blood cell counts did not change between baseline and end of follow-up, and platelet counts decreased in the placebo arm but not in LD-MTX. These findings offer reassurance about the hematologic safety of LD-MTX.



This figure represents the median (filled circle) and interquartile range for (A) hemoglobin, (B) platelet count and (C) white blood cell (WBC) count during the CIRT trial. Compared to baseline, by the end of the study, the median hemoglobin value among patients randomized to LD-MTX decreased by 0.4 g/dL (IQR -0.90, 0.10) and decreased by 0.1 mg/dL (IQR -0.60, 0.30) among those randomized to placebo. The median platelet count did not change in the LD-MTX arm (IQR -18, 16 k/uL) and decreased by 9 k/uL (IQR -26, 9) among those randomized to placebo. The median WBC count did not change in the LD-MTX arm (IQR -0.90, 0.80) and increased by 0.2 k/uL (IQR -0.70, 1.10) in the placebo arm. LD-MTX, low dose methotrexate. PBO, placebo.

Disclosure: K. Vanni, None; **N. Berliner**, None; **N. Paynter**, None; **R. Glynn**, AstraZeneca, 1, Kowa, 1, Pfizer, 1, Novartis, 1; **J. MacFadyen**, None; **J. Colls**, None; **F. Lu**, None; **C. Xu**, None; **P. Ridker**, Kowa, 2, Novartis, 2, Amarin, 2, Corvidia, 5, Inflazome, 5, CiviBioPharm, 5; **D. Solomon**, AbbVie, 2, Amgen, 1, Genentech, 1, Janssen, 1, Corrona, 1.

Abstract Number: 2002

Incidence and Risk Factors for Herpes Zoster in Rheumatoid Arthritis Patients Receiving Upadacitinib

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Treatments II: Potential Harms & Adverse Events

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

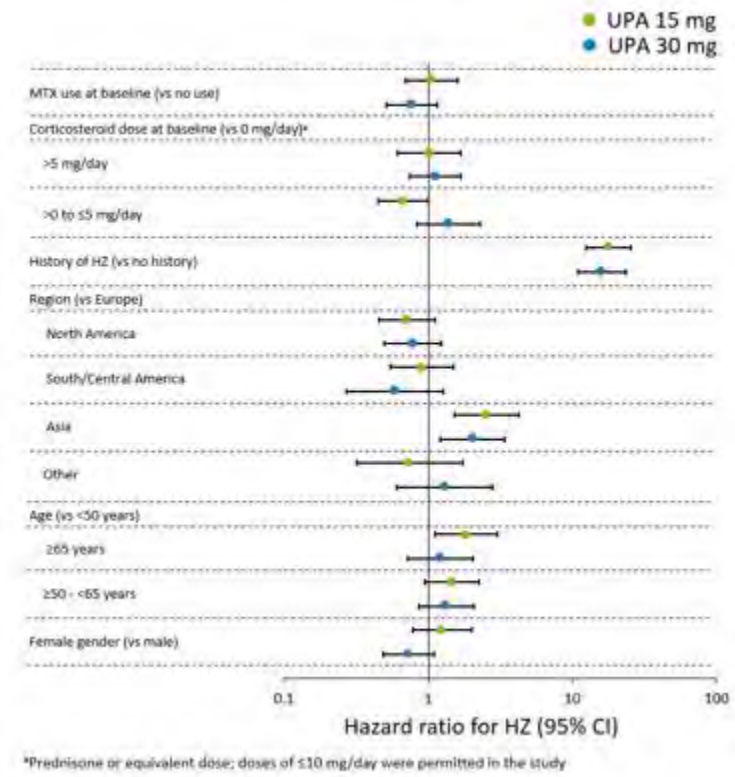
Background/Purpose: Upadacitinib (UPA) is an oral JAK inhibitor approved for the treatment of rheumatoid arthritis (RA). The background rate of herpes zoster (HZ) in patients (pts) with RA is around 0.98/100 person years (PY)[1]. Pts with RA receiving JAK inhibitors have been reported to have an increased risk of HZ. We evaluate the incidence and risk factors for HZ in pts with RA receiving UPA relative to active comparators in the Phase 3 clinical trial program.

Table. Summary of extent of involvement in pts with HZ

Categories, n (%)[a]	Any UPA 15 mg QD (N=2629)	Any UPA 30 mg QD (N=1204)
Total patients with ≥1 HZ event	142 (5.4)	126 (10.5)
Single dermatome	101 (71.1)	89 (70.6)
Ophthalmic involvement	6 (4.2)	3 (2.4)
HZ Oticus (Ramsay Hunt Syndrome)	2 (1.4)	1 (0.8)
Multidermatomal (unilateral)[b]	26 (18.3)	23 (18.3)
Disseminated, cutaneous only (no CNS involvement)[c]	7 (4.9)	8 (6.3)
Disseminated with CNS or visceral involvement	0	1 (0.8)[d]
Missing	8 (5.6)	5 (4.0)

[a]Pts may fall into >1 category; [b]≤2 adjacent dermatomes; [c]≥3 dermatomes, unilateral nonadjacent dermatomes, or bilateral dermatomes; [d]HZ meningitis

Figure: Multivariable-adjusted risk factors for HZ in pts receiving UPA



*Prednisone or equivalent dose; doses of ≤10 mg/day were permitted in the study

Methods: The incidence rate of HZ was determined in pts receiving UPA (as monotherapy [mono] or combination therapy) in five randomized Phase 3 trials (SELECT-EARLY, SELECT-MONOTHERAPY, SELECT-NEXT, SELECT-COMPARE, and SELECT-BEYOND), of which 4 evaluated both the UPA 15 and 30 mg once-daily (QD) doses and 1 trial (SELECT-COMPARE) evaluated only the 15 mg QD dose. Incidence of HZ was also determined in pts receiving adalimumab (ADA) + methotrexate (MTX) in SELECT-COMPARE and MTX mono in SELECT-EARLY. Risk factors for HZ were assessed using univariate and multivariate Cox regression models. Data cut-off was 30 June 2019.

Results: Overall, 2629 pts who received UPA 15 mg QD (4565.8 patient-years [PY]), 1204 pts who received UPA 30 mg QD (2309.7 PY), 579 pts who received ADA + MTX (768.6 PY), and 314 pts who received MTX mono (456.0 PY) were analyzed. Fewer than 5% of pts across the treatment groups reported prior HZ vaccination. HZ (n/100 PY [95% CI]) occurred in 142 pts (3.1 [2.6–3.7]) with UPA 15 mg, 126 pts (5.5 [4.5–6.5]) with UPA 30 mg, 8 pts (1.0 [0.4–2.1]) with ADA + MTX, and 5 pts (1.1 [0.4–2.6]) with MTX mono. Most of the HZ cases (~71%) with UPA (Table) and all cases with ADA + MTX and MTX mono involved a single dermatome. Ophthalmic involvement was seen in 6 (4.2%) and 3 (2.4%) cases in the UPA 15 and 30 mg groups, respectively, and unilateral involvement with multiple dermatomes was seen in 26 (18.3%) and 23 (18.3%) cases. There was a single case of HZ meningitis reported in a Japanese pt on UPA 30 mg. In multivariate analyses, prior history of HZ and Asian region were associated with an increased risk of HZ in both the UPA groups ($p \leq 0.01$; Figure). In addition, pts ≥65 years old had increased risk of HZ in the 15 mg group.

Conclusion: HZ events in pts with RA receiving UPA were more common in the 30 mg vs 15 mg group, and in both UPA groups compared with the ADA + MTX and MTX groups.

References

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Original abs: *Ann Rheum Dis.* 2020; 79(S1):331.

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Abstract Number: 2003

Individualized Prediction of Response to Methotrexate Treatment in Patients with Rheumatoid Arthritis: A Pharmacogenomics-driven Machine Learning Approach

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments III: Predictors of Treatment Response
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Methotrexate (MTX) is the most common anchor drug for rheumatoid arthritis (RA), but the risk of missing the opportunity for early effective treatment with alternative medications is substantial given the delayed onset of MTX action and 30-40% inadequate response rate. There is a compelling need to accurately predict MTX response before treatment initiation, in order to effectively identify patients at RA onset who are likely to respond to MTX. We aimed to test the ability of machine learning (ML) approaches with clinical and genomic biomarkers to predict MTX response in patients with RA.

Methods: Age, sex, clinical, serological and genome wide association study (GWAS) data on patients of European ancestry with early RA available through the PhArmacogenetics of Methotrexate in RA (PAMERA) consortium were used. A total of 647 patients were included: 336 recruited in the United Kingdom [UK]; 307 recruited across Europe (70% female; 72% rheumatoid factor [RF] positive; mean age 54 years; mean baseline Disease Activity Score with

28-joint count [DAS28] 5.65). The genomic data comprised 160 genome-wide significant single nucleotide polymorphisms (SNPs) with p< 1x10-5 that were associated with risk of RA and MTX metabolism. DAS28 scores were available at baseline and 3-month follow-up. Response to MTX monotherapy (>/=15 mg/week) was defined as good or moderate by the EULAR response criteria at 3-month follow-up. Supervised ML methods were trained with 5 repeats and 10-fold Cross validation using data from the UK patients. Class imbalance in training was accounted for by using simulated minority oversampling technique. Prediction performance was validated in the European patients (not used in training).

Results: Age, sex, RF positivity and baseline DASA28 data predicted response to MTX with area under the receiver operating curve (AUC) 0.54 in the UK subjects and 55% accuracy in European patients (p=0.98). However, supervised ML methods that combined demographics, RF status, baseline DAS28 and genomic SNPs predicted EULAR response at 3 months with AUC 0.84 (p=0.05) in UK patients, and achieved prediction accuracies of 76.2% (p=0.05) in the European patient's (sensitivity 72%, specificity 77%). The addition of genomic data improved the predictive accuracies of MTX response by 19% and achieved cross-site replication. Baseline DAS28 and SNPs in or near the CASC15 (rs12446816), B3GNT2 (rs13385025), PARK2 (rs113798271), and ATIC (rs2372536) genes were among the top predictors of MTX response.

Conclusion: Pharmacogenomic biomarkers including gene variants for cancer susceptibility genes (CASC15) and important MTX pathway enzymes (ATIC) combined with baseline DAS28 score predicted MTX response in patients with early RA more reliably than demographics and baseline DAS28 alone, with replication in an independent cohort. Using pharmacogenomic biomarkers for the identification of MTX responders in early RA may help to guide effective RA treatment choices, including timely escalation of RA therapies. Further studies of personalized prediction of response to MTX and other antirheumatic treatments are needed to optimize control of RA disease and improve outcomes in patients with RA.

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Abstract Number: 2004

Circulating Biomolecules as Potential Biomarkers of Early and Establishedresponse to TNFi Therapy in Rheumatoid Arthritis Patients

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments III: Predictors of Treatment Response
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: To evaluate changes produced in circulating inflammatory mediators and their regulatory miRNAs in RA patients after 3 and 6 months of treatment with TNF-α inhibitors (TNFi), in order to identify biomarkers of clinical efficacy and potential predictors of therapeutic response to TNFi therapies.

Methods: In a prospective RA cohort multicenter study, serum from125 RA patients with moderate/high disease activity was collected prior and after 3 and 6 months of TNFi treatment. Patients' response was determined according to EULAR response criteria. The inflammatory profile was analyzed by using a multiplex immunoassay and circulating levels of several microRNAs -whose potential targets were mRNAs encoding inflammatory proteins- were evaluated. Then, their discriminative ability was evaluated. To assess the added value of these biomolecules, logistic prediction models were created.

Results: Among RA patients, 79% (99/125) showed early response after 3 months of TNFi treatment, of which a 67% (66/99) showed clinical response after 6 months of therapy. Inflammatory mediators related to activation and proliferation (IL-6, IL-13), adhesion and migration (MIP-1a, RANTES, FGFb), chemotaxis (MIP1-b, IL8, IP-10) and angiogenesis (VEGF), showed a trend to reduction after 3 months, but were significantly downregulated only after 6 months of TNFi therapy. In addition, several molecules upregulated after 3 months of TNFi therapy -involved in cell activation and differentiation (IFNg, GM-CSF, IL-4, IL-5), immunoregulation (IL-1RA, IL-10) and migration (MCP-1, PDGFb)- were thereafter downregulated, consolidating the reduction in the inflammatory response. Moreover, a decline in 7 of these molecules correlated with DAS28 reduction.

In the search for predictors of response to this drug, clinical and molecular parameters were evaluated. High DAS28/SDAI scores or levels of auto-antibodies (RF or ACPA) at baseline were not predictive of response to the treatment. Instead, atherogenic index, smoking habit and hyperlipidemia at baseline were predictors of a worse response to TNFi therapy. Moreover, both, baseline microRNAs and inflammatory profiles clearly distinguished among patients with differential therapeutic response. High baseline levels of inflammatory mediators related to the leukocyte activation and proliferation, adhesion and migration, along with high baseline levels of several microRNAs (miR-106a-5p, miR-199a-5p, miR-346, miR-223-3p, and miR-143-5p) regulating their expression, were predictive of response to TNFi treatment both, at 3 and 6 months.

Receiver operating characteristic (ROC) analyses for those biomarkers allowed us to further identify specific signatures of circulating biomolecules that may serve as predictors of response to TNFi therapy with high sensitivity and specificity.

Conclusion: The extensive analysis of the serum inflammatory and microRNAs profiles allowed identifying specific and distinctive signatures of biomolecules that, in coordination with known clinical and serological profiles, might predict early and established response of RA patients to TNFi treatment.

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Abstract Number: 2005

Histo-pathological Cellular Markers of Treatment Response to Rituximab and Tocilizumab in Matched Pre- and Post-treatment Synovial Biopsies from the R4RA Randomised Clinical Trial in Rheumatoid Arthritis

Felice Rivellese[1], Frances Humby[2], Giovanni Giorli[2], Alessandra Nerviani[1], Rebecca Hands[2], Liliane Fossati-Jimack[2], Georgina Thorborn[2], Myles Lewis[1] and Costantino Pitzalis[2], [1]Centre for Experimental Medicine and Rheumatology, Queen Mary University of London, London, United Kingdom, [2]Queen Mary University of London, London, United Kingdom

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments III: Predictors of Treatment Response
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: The results of the R4RA trial, the first biopsy-based RCT in TNF-i inadequate responders patients with Rheumatoid Arthritis (RA), showed that molecular stratification of RA synovial tissue in B-cell poor/rich had stronger associations with clinical responses compared to histopathological classification at baseline demonstrating that, in patients with low/absent B-cell lineage signature in synovial-tissue, Tocilizumab (TCZ) is significantly superior to Rituximab (RTX). Here, we investigate the relationship of synovial immune cells in matched pre- and post-treatment synovial biopsies and treatment response.

Methods: 164 patients underwent pre-treatment US-guided or arthroscopic synovial biopsy prior to randomization 1:1 to RTX (83) or TCZ (81). 65 patients had a repeated biopsy at 16 weeks, primary end-point Clinical Disease Activity Index (CDAI) ≥50% improvement. A minimum of 6 synovial samples/patient were paraffin-embedded and sections stained by immunohistochemistry, followed by semi-quantitative scoring (0-4) for CD20+ total B-cells, CD79a+ B cells, CD3+ T cells, CD138+ plasma cells and CD68+ lining (L) and sub-lining (SL) macrophages, and classification into lympho-myeloid (LM), diffuse-myeloid (DS) and fibroid/pauci-immune (F/PI) pathotypes, as previously described (Humby et al Ann Rheum Dis. 2019 Jun;78(6):761-772).

Results: At baseline, no significant differences were observed in semi-quantitative synovial immune scores in patients classified as CDAI≥50% responders and non-responders, both for RTX and TCZ. Looking at pathotypes, TCZ-treated patients with a DM pathotype had a significantly higher CDAI≥50% response compared to LM and F/PI (81% vs 48%, p=0.024), while no differences were found in RTX treated patients. When analysing matched pre and post-treatment biopsies (Table 1) RTX-treated patients showed a significant reduction of synovial CD20+ total B cells [-1.53 (-81%), p< 0.001], CD79a+ B cells [-0.87 (-49%) p< 0.001] and CD138+ plasma cells [- 0.76 ‡ (-45%) p< 0.05]. TCZ treated patients, on the other hand, showed a significant reduction of CD68+ sub-lining macrophages [-1.04 (-54%) p< 0.05] but not B-lineage cells. Finally, while CD20 and CD79a showed a significant reduction in all RTX-treated patients, including both responders and non-responders, a significant reduction of CD138 was only observed in responders. On the other hand, a significant reduction of CD68SL macrophages was only observed in responders to TCZ (Table 2).

TABLE 1 Synovial histological analysis stratified according to treatment at baseline and 16 weeks

	Unpaired analysis (all patients)		Paired analysis						
	Baseline biopsy†		Rituximab (N=41)			Tocilizumab (N=24)			Treatment effect
	Rituximab N=82 mean(SD)	Tocilizumab N=79 mean(SD)	Baseline mean(SD)	Week 16 mean(SD)	Absolute Change (%)	Baseline mean(SD)	Week 16 Mean (SD)	Absolute Change (%)	Least Squares mean difference (95% CI)
CD20	1.62 (1.3)	1.5 (1.4)	1.88 (1.4)	0.35 (0.8)	-1.53 ‡‡ (-81%)	1.67 (1.3)	1.33 (1.3)	-0.34 (-20%)	1.02 (0.52 to 1.52) §
CD79a	1.54 (1.3)	1.6 (1.4)	1.77 (1.4)	0.9 (1.1)	-0.87 ‡‡ (-49%)	1.54 (1.3)	1.47 (1.2)	-0.07 (-5%)	0.55 (0.04 to 1.06) §
CD138	1.43 (1.3)	1.42 (1.4)	1.68 (1.3)	0.92 (1.1)	-0.76 ‡ (-45%)	1.58 (1.4)	1.25 (1.1)	-0.33 (-21%)	0.36 (-0.16 to 0.88)
CD3	1.43 (1.1)	1.47 (1.2)	1.63 (1.1)	1.52 (1.2)	-0.11 (-7%)	1.58 (1.1)	1.42 (1.2)	-0.16 (-10%)	-0.08 (-0.64 to 0.49)
CD68L	1.11 (1)	1.2 (1.1)	1.2 (1)	1.07 (0.9)	-0.13 (-11%)	1.46 (1.1)	1.38 (1.1)	-0.08 (-5%)	0.2 (-0.27 to 0.66)
CD68SL	1.67 (1)	1.75 (1.1)	1.88 (0.8)	1.3 (0.6)	-0.58 ‡ (-31%)	1.92 (1)	0.88 (0.7)	-1.04 ‡ (-54%)	-0.43 (-0.78 to -0.08) §
SYNOVIAL SCORE	3.99 (2.6)	3.88 (2.9)	4.63 (2.5)	3.23 (2)	-1.4 ‡‡ (-30%)	4.38 (2.8)	3.46 (2.4)	-0.92 (-21%)	0.32 (-0.69 to 1.32)

† No significant difference between treatments was observed for the presented values (tested through Mann-Whitney U test
‡ P<0.05 and ‡‡ P<0.001 for the within group change from baseline (paired Wilcoxon test comparing baseline values with values at 16 weeks within the same patients).
§ P<0.05 for the comparison with Non-Responders of the change from baseline (analysis of covariance testing the difference in the changes from baseline between treatments, with treatment as factor and baseline score as covariate)

TABLE 1. Synovial histological analysis stratified according to treatment at baseline and 16 weeks

TABLE 2 Change in synovial immune cell infiltrate between baseline and 16 weeks stratified according to CDAI≥50% response

	Rituximab							Tocilizumab						
	Non responders (N=26)			Responders (N=15)			Treatment effect	Non responders (N=14)			Responders (N=10)			Treatment effect
	Baseline mean(SD)	Week 16 mean(SD)	Absolute Change (%)	Baseline mean(SD)	Week 16 mean(SD)	Absolute Change (%)	Least Squares mean difference (95% CI)	Baseline mean(SD)	Week 16 mean(SD)	Absolute Change (%)	Baseline mean(SD)	Week 16 mean(SD)	Absolute Change (%)	Least Squares mean difference (95% CI)
CD20	1.88 (1.3)	0.52 (1)	-1.36 ‡ (-72%)	1.87 (1.5)	0.07 (0.3)	-1.8 ‡ (-96%)	-0.46 (-0.97 to 0.06)	1.71 (1.3)	1.21 (1.3)	-0.5 (-29%)	1.6 (1.3)	1.5 (1.3)	-0.1 (-6%)	0.34 (-0.64 to 1.33)
CD79a	1.54 (1.4)	0.88 (1.1)	-0.66 ‡ (-43%)	2.13 (1.4)	0.93 (1.1)	-1.2 ‡ (-56%)	-0.25 (-0.88 to 0.38)	1.64 (1.4)	1.31 (1.2)	-0.33 (-20%)	1.4 (1.3)	1.83 (1.2)	0.43 (31%)	0.4 (-0.57 to 1.36)
CD138	1.58 (1.4)	1.0 (1.3)	-0.58 (-37%)	1.87 (1.2)	0.8 (0.9)	-1.07 ‡ (-57%)	-0.31 (-1.01 to 0.38)	1.5 (1.4)	1.21 (1.1)	-0.29 (-19%)	1.7 (1.4)	1.3 (1.2)	-0.4 (-24%)	0.01 (-0.84 to 0.86)
CD3	1.58 (1.1)	1.4 (1.2)	-0.18 (-11%)	1.73 (1.1)	1.73 (1.3)	0 (0%)	0.27 (-0.45 to 0.98)	1.57 (1.2)	1.57 (1.1)	0 (0%)	1.6 (1.1)	1.2 (1.4)	-0.4 (-25%)	-0.38 (-1.38 to 0.61)
CD68L	1.08 (0.9)	1.08 (0.9)	0 (0%)	1.4 (1.2)	1.07 (1)	-0.33 (-24%)	-0.11 (-0.69 to 0.48)	1.5 (1.3)	1.71 (1.2)	0.21 (14%)	1.4 (0.8)	0.9 (0.9)	-0.5 (-36%)	-0.76 (-1.51 to 0)
CD68SL	1.85 (0.8)	1.28 (0.6)	-0.57 ‡ (-31%)	1.93 (1)	1.33 (0.7)	-0.6 (-31%)	0.04 (-0.39 to 0.47)	1.71 (1.1)	1.14 (0.8)	-0.57 (-33%)	2.2 (0.9)	0.5 (0.5)	-1.7 ‡ (-77%)	-0.7 (-1.31 to -0.09) §
SYNOVIAL SCORE	4.46 (2.2)	3.2 (2.1)	-1.26 ‡ (-28%)	4.93 (3)	3.27 (1.8)	-1.66 ‡ (-34%)	-0.16 (-1.29 to 0.98)	4.43 (3)	4.0 (2.5)	-0.43 (-10%)	4.3 (2.6)	2.7 (2.3)	-1.6 (-37%)	-1.26 (-3.26 to 0.74)

‡ P<0.05 for the within group change from baseline § P<0.05 for the comparison with Non-Responders of the change from baseline (analysis of covariance testing the difference in the changes from baseline between treatments, with treatment as factor and baseline score as covariate

Conclusion: Treatment of RA patients with RTX or TCZ has a different impact on synovial immune cells infiltration. In line with their mechanisms of action, RTX reduces synovial B cells, while TCZ affects sub-lining macrophages. Interestingly, the reduction of plasma cells and sub-lining macrophages identifies responders to RTX and TCZ, re-

spectively. These results indicate that the analysis of immune cell infiltration in synovia helps to define a biological response to immunomodulatory agents in RA.

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Abstract Number: 2006

Identification of a Rule to Predict Response to Sarilumab in Patients with Rheumatoid Arthritis Using Machine Learning and Clinical Trial Data

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments III: Predictors of Treatment Response
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Despite the existence of guidelines for DMARD treatment of RA, a more individualized approach to treatment is needed to maximize efficacy while minimizing risk of adverse events. In phase 3 trials, sarilumab, an IL-6 receptor (IL-6R) inhibitor approved for treatment of moderate to severe RA, has been shown to be superior to both placebo (clinical trials MOBILITY [NCT01061736] and TARGET [NCT01709578]) and the TNF-α inhibitor adalimumab (MONARCH [NCT02332590]). However, the characteristics of patients who are most likely to benefit from sarilumab treatment remain poorly understood. Here, we describe the application of machine learning to select from a predefined set of patient characteristics that could facilitate the choice between anti-IL-6R and anti-TNF-α treatment, using data from the sarilumab clinical development program.

Methods: A decision tree classification approach was used to build predictive models on ACR response criteria at Week 24 in patients from MOBILITY, using the Generalized, Unbiased, Interaction Detection and Estimation (GUIDE) algorithm (Version 27.9; available as free software). A total of 17 categorical and 25 continuous baseline variables were included as candidate predictors, chosen based on subject matter expertise. These included protein biomarkers, disease activity scoring, and demographic data (Table). The endpoints used were ACR20, ACR50, and ACR70 at Week 24. The resulting rule was validated through application on independent data sets from MOBILITY (N=1197; sarilumab [150 mg and 200 mg combined], 799; placebo, 398), TARGET (N=546; sarilumab [150 mg and 200 mg combined], 365; placebo, 181), and MONARCH (N=369; sarilumab, 184; adalimumab, 185), as well as on the tocilizumab-calibrator study ASCERTAIN (NCT01768572; N=202; sarilumab [150 mg and 200 mg combined], 100; tocilizumab, 102). The analysis focused on the 200 mg sarilumab dose.

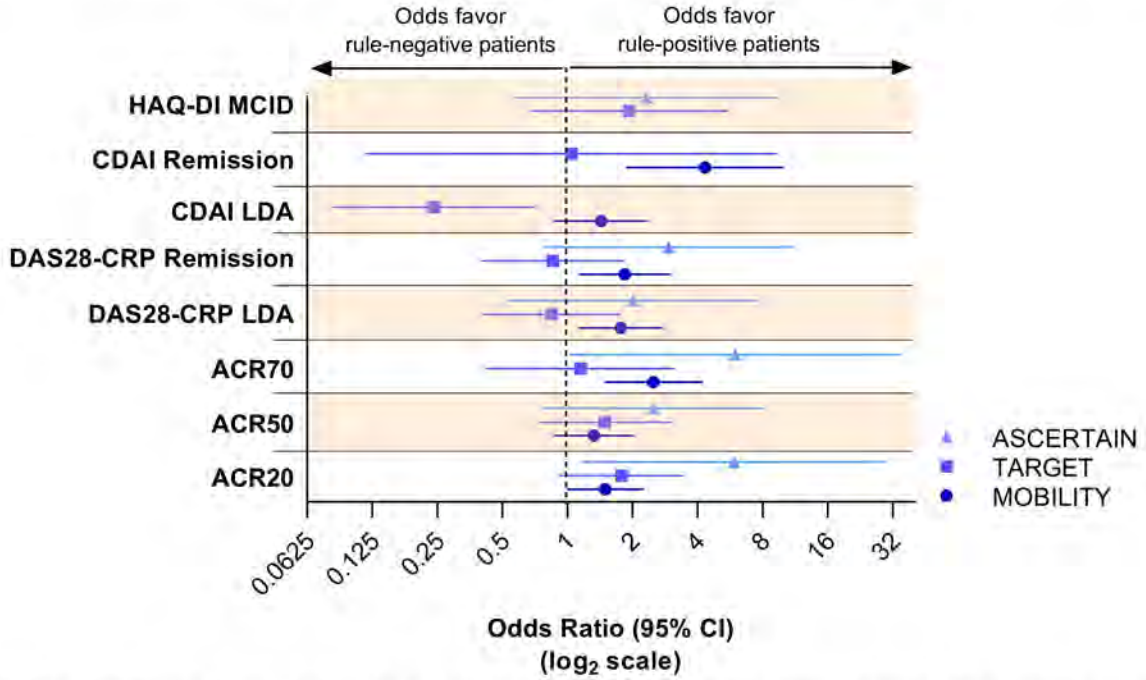
Table. Parameters used in the GUIDE algorithm		
Demographics	**Clinical characteristics**	**Biomarkers**
Continuous		
1. Age	1. ACR20 at Week 24 2. Duration of RA 3. DAS28 at Baseline 4. Joint erosion score 5. Joint space narrowing score 6. SJC (28 joints) 7. SJC (68 joints) 8. TJC (28 joints) 9. TJC (68 joints)	1. C x C motif chemokine ligand 13 2. CRP 3. IL-6 4. MMP3 5. MMP-degraded type 1 collagen 6. MMP-degraded type 3 collagen 7. OC 8. OPG 9. RANKL 10. RANKLF 11. RANKL : OPG ratio 12. RANKLF : OPG ratio 13. Soluble glycoprotein 130 14. Soluble intercellular adhesion molecule 15. Transmembrane IL-6 receptor
Categorical		
2. Alcohol use 3. Sex 4. BMI stratum 5. Race 6. Region 7. Smoking history	10. Prior DMARDs 11. Number of DMARDs 12. Number of Prior bDMARDs 13. Type of prior bDMARDs 14. Duration of RA (3-year strata) 15. Arm code (left or right)	16. ACPA 17. Persistent ADAbs 18. Rheumatoid factor 19. Transient ADAbs 20. Neutralizing anti-drug antibodies
ACPA=anti-citrullinated protein antibodies; ADAb=anti-drug antibody, BMI=body mass index; CRP=C-reactive protein; MMP=matrix metalloproteinase; OC=osteocalcin; OPG=osteoprotegerin; RANKL=receptor activator of NF-kappa B ligand; RANKLF=free RANKL; SJC=swollen joint count; TJC=tender joint count.		

Table 1

Results: The most successful GUIDE model was trained against the ACR20 response. Out of the 42 candidate variables, the combined presence of anti-citrullinated protein antibodies (ACPA) and CRP >12.3 mg/L was identified as a predictor (ie, rule) of better treatment outcomes with sarilumab. Rule-positive patients (34-51% in sarilumab groups across the 4 trials) had more severe disease and poorer prognostic factors at baseline. Rule-positive patients had a better outcome than rule-negative patients for most endpoints assessed, with the exceptions observed in patients with inadequate response to TNF inhibitors (TARGET; Figure 1). In addition, rule-positive patients had a better response to sarilumab but an inferior response to adalimumab, with the exception of HAQ-Disability Index minimal clinically important difference endpoint (Figure 2), equivalent to an approximately 5-fold difference in the chance of achieving ACR70 (34% versus 7%).

Conclusion: Machine learning ascertained a simple selection rule, ACPA positivity and CRP >12.3 mg/L, to identify patients with an increased chance of achieving clinical response with sarilumab. If verified in prospective studies, this rule could facilitate treatment decision-making for patients with RA.

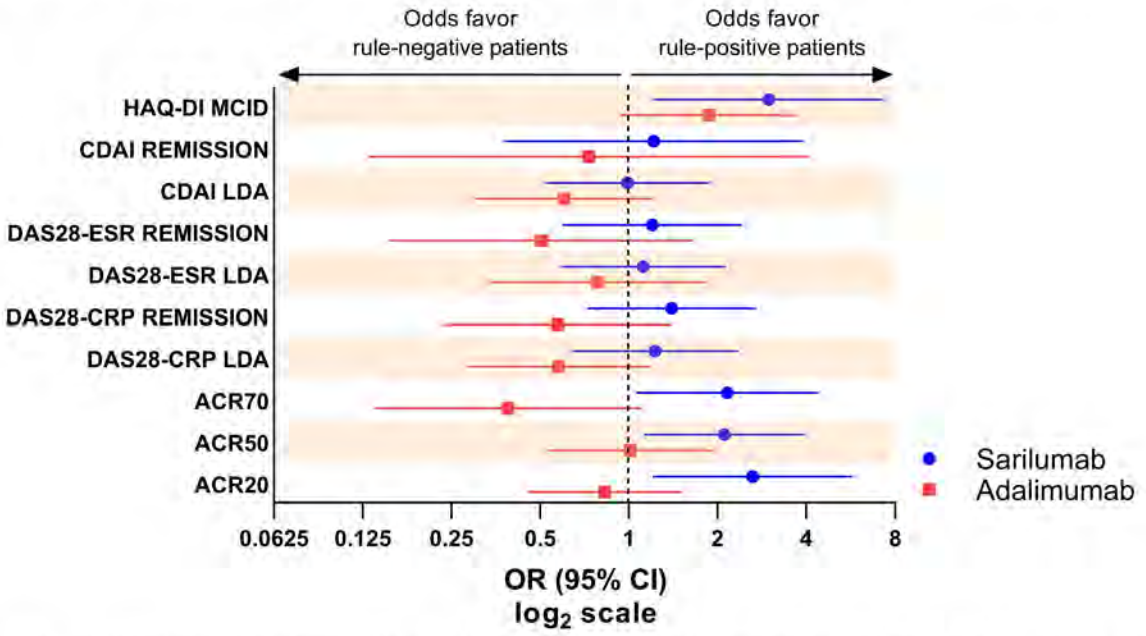
Figure 1. Odds ratios of achieving response at Week 24 in the placebo- (MOBILITY, TARGET) or active-controlled studies (ASCERTAIN): Rule-positive versus -negative patients



CDAI=Clinical Disease Activity Index; HAQDI=HAQ Disability Index; LDA=low disease activity; MCID=minimal clinically important difference

Figure 1

Figure 2. Odds ratios of attaining clinical response in rule-positive vs -negative patients for sarilumab and adalimumab treatment in the MONARCH study



CDAI=Clinical Disease Activity Index; HAQDI=HAQ Disability Index; LDA=low disease activity; MCID=minimal clinically important difference

Figure 2

Disclosure: M. Rehberg, Sanofi, 3, 4; **C. Giegerich**, Sanofi, 3, 4; **A. Praestgaard**, Sanofi, 3; **H. van Hoogstraten**, Sanofi, 1, 3, 4; **M. Iglesias-Rodriguez**, Sanofi, 3; **J. Curtis**, AbbVie, 2, 5, Amgen, 2, 5, Bristol-Myers Squibb, 2, 5, Corrona, 2, 5, Janssen, 2, 5, Lilly, 2, 5, Myriad, 2, 5, Pfizer, 2, 5, Regeneron, 2, 5, Roche, 2, 5, UCB, 2, 5, Gilead Sciences, Inc., 5, Sanofi, 5; **J. Gottenberg**, Bristol-Myers Squibb, 2, 8, Pfizer, 2, 5, UCB, 5, 8, Eli Lilly, 2, 8, AbbVie, 2, 8, Roche, 2, 8, Sanofi-Genzyme, 5, 8; **A. Schwarting**, Pfizer, 2, 8, GSK, 2, 5, 8, AbbVie, 2, 8, BMS, 2, 8, Novartis, 2, 5, 8, Roche, 2, 5, Astra Zeneca, 5, Lilly, 8, MSD, 8; **S. Castañeda**, Roche, 2; **A. Rubbert Roth**, AbbVie, 1, Bristol-Myers Squibb, 1, Chugai Pharma, 1, 2, Eli Lilly, 1, 2, Hexal, 1, Novartis, 1, Sanofi, 1, 2, Roche, 1, 2, Pfizer, 1, Merck Sharp & Dohme (MSD), 1, Janssen, 1; **E. Choy**, Abbvie, 2, 8, Amgen, 2, 8, AstraZeneca, 2, 8, Biogen, 2, 8, Bio-Cancer, 2, 8, Boehringer Ingelheim, 2, 8, Bristol-Myers Squibb, 2, 8, Celgene, 2, 8, Chugai Pharma, 2, 8, Eli Lilly, 2, 8, Ferring Pharmaceuticals, 2, 8, GlaxoSmithKline, 2, 8, Janssen, 2, 8, Novartis, 2, 8, Novimmune, 2, 8, ObsEva, 2, 8, Pfizer, 2, 8, R-Pharm, 2, 8, Roche, 2, 8, SynAct Pharma, 2, 8, Tonix, 2, 8, UCB, 2, 8, Synovate, 2, 8, Sanofi, 2, 8, Regeneron, 2, 8, Napp, 2, 8, Hospira, 2, 8, Merck Sharp & Dohme, 2, 8.

Abstract Number: 2007

Whole Blood Transcriptional Changes Following Selective Inhibition of Janus Kinase 1 (JAK1) by Filgotinib in Adults with Moderately-to-Severely Active Rheumatoid Arthritis with Prior Inadequate Response to Methotrexate

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Treatments III: Predictors of Treatment Response

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: Filgotinib (FIL), a selective, oral JAK1 inhibitor, has shown efficacy and safety in phase 3 studies in adults with moderately-to-severely active rheumatoid arthritis (RA). We have previously described the molecular response to FIL in large-scale RNA sequencing studies of gene expression in other RA populations[1-3] and herein conducted a similar study in RA patients (pts) with prior inadequate response to methotrexate (MTX-IR; FINCH1; ClinicalTrials.gov NCT02889796).

Methods: RA pts with MTX-IR were enrolled and randomized to receive either stable dose of MTX with placebo (PBO+MTX), adalimumab (ADA+MTX), or one of two doses of FIL (FIL 100mg+MTX, FIL 200mg+MTX) once daily. Whole blood samples were collected using PAXgene tubes at baseline, weeks 4, and 12. RNA were extracted and sequenced on Illumina HiSeq 2500 platform following globin RNA depletion. Correlations between baseline gene expression and disease measurements were performed using Spearman's rank partial correlation with covariates. Differentially expressed genes (DEGs) were identified using voom-limma. Pathway analysis was performed on v6.1 of the Molecular Signature Database using single sample gene set enrichment analysis (GSEA) with the focus on immune signaling pathways from the Kyoto Encyclopedia of Genes and Genomes (KEGG). A false-discovery rate of 5% was applied for all analyses.

Results: Differential gene expression analyses comparing baseline samples with after-treatment samples revealed more rapid transcriptional kinetics for FIL-treated pts compared to ADA+MTX-treated pts. No significant DEGs were observed in PBO-treated pts. More significant DEGs were observed in FIL 200mg+MTX arm compared to FIL 100mg+MTX arm, consistent with superior clinical efficacy of FIL 200mg dosage. As with other FIL clinical trial RNA-seq studies and consistent with the selective MoA of FIL, JAK-STAT pathway-induced genes *SOCS2* and *CISH* were significantly downregulated across both FIL arms and timepoints, but not in ADA+MTX arm. RA disease activity associated genes[2-3] *FAM20A* and *METTL7B* were significantly reduced at both 4 and 12 weeks only in the FIL 200mg+MTX arm. While no significant changes in KEGG immune signaling pathways were observed in the PBO+MTX arm, a dose-dependent effect on pathway modulation was observed in the FIL arms. The most prominently down-regulated KEGG pathways included JAK-STAT signaling and leukocyte transendothelial migration.

Conclusion: More rapid and sustained changes of transcriptional activity were observed in the whole blood transcriptional profile of RA pts following FIL 200mg+MTX compared to ADA+MTX treatment. Dose-dependent changes were observed in FIL-treated pts, most notably in the KEGG JAK-STAT signaling pathway. These observations confirm an inhibition of JAK-STAT signaling by FIL and are consistent with the observed clinical efficacy of FIL in these pts.

1. Taylor PC, *et al.* (EULAR 2018). http://dx.doi.org/10.1136/annrheumdis-2018-eular.3759
2. Taylor PC, *et al.* (ACR 2018). https://doi.org/10.1093/rheumatology/kez105.001
3. Taylor PC, *et al.* (EULAR 2019). http://dx.doi.org/10.1136/annrheumdis-2019-eular.2509

Disclosure: P. Taylor, Eli Lilly, 2, 5, 8, Celgene, 2, 5, 8, AbbVie, 2, 5, 8, Biogen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Celltrion, 2, 5, 8, Fresenius, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Janssen, 2, 5, 8, Nordic Pharma, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8, Pfizer, 2, 5, 8, Gilead, 2, 5, 8, Galapagos, 2, 5, 8; **B. Downie**, Gilead Sciences, Inc., 3, Gilead Sciences, Inc., 1; **E. Elboudwarej**, Gilead Sciences, Inc., 3, Gilead Sciences, Inc., 1; **S. Kim**, Gilead Sciences, Inc., 1, 3; **A. Hertz**, Gilead Sciences, Inc., 1, 3; **A. Mirza**, Gilead Sciences, Inc., 3, Gilead Sciences, Inc., 1; **J. Siegel**, Gilead Sciences, Inc., 1, 3, Gilead Sciences, Inc., 3, Roche, Inc., 1; **R. Hawtin**, Gilead Sciences, Inc., 3, Gilead Sciences, Inc., 1; **J. Liu**, Gilead Sciences, Inc., 3, Gilead Sciences, Inc., 1, Roche, 1.

Abstract Number: 2008

Should We Use Glucocorticoid in Early Rheumatoid Arthritis? : Results at 5 Years from the ERA Louvain Brussels Cohort

Emilie Sapart[1], Tatiana Sokolova[1], Stéphanie de Montjoye[1], Stéphanie Dierckx[2], Adrien Nzeusseu Toukap[3], Aleksandra Avramovska[1] and Patrick Durez[4], [1]Rheumatology, Cliniques Universitaires Saint-Luc – Université catholique de Louvain (UCL) – Institut de Recherche Expérimentale et Clinique (IREC), Brussels, Belgium, [2]Rheumatology, CHU Mont-Godinne, Mont Godinne, Belgium, [3]1Department of Rheumatology, Cliniques Universitaires Saint Luc, 2Institut de recherche expérimentale et clinique (IREC), Brussels, Belgium, [4]Division of Rheumatology, Cliniques Universitaires Saint-Luc, Bruxelles, Belgium

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments IV: New Therapies & Strategies
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: The EULAR recommendations, updated in 2016[1] and 2019[2], propose the initiation of glucocorticoid (GC) therapy in combination with cDMARDs background therapy for every patient with early rheumatoid arthritis (ERA).

The aim of this study is to evaluate the proportion of patients with ERA who have been treated with GC in daily practice, to analyse the baseline characteristics of these patients, and to assess the clinical benefit and side effects of GC during 5 years of follow-up.

Methods: We included patients with ERA from the UCLouvain Brussels cohort who met the ACR/EULAR 2010 classification criteria and were naïve to cDMARDs. Treatments were initiated based on the decision of a senior rheumatologist. We retrospectively collected patient characteristics prior to the introduction of cDMARDs with or without GC. Efficiency and serious adverse events were analysed at 6 months, 1 year, 3 years and 5 years.

Results: Data from 474 eligible ERA patients were collected. The average age of the population is 48.9 years. 70.5% of the patients are women. 27.3% are smokers and 68.8% are positive for anti-citrullinated protein antibody (ACPA).

178 patients (37.7 %) initiated GC compared to 294 patients (62.3%) who received only NSAIDs and/or analgesics in combination with cDMARDs.

At baseline, the elevation of CRP is the main factor that favors the initiation of GC (CRP 2.9 vs 2.0 mg/dl, p = 0.015) followed by smoking habits (34.2% vs 23.3%, p = 0.018), the absence of ACPA (37.2% vs 27.6%, p = 0.037), the prescription of methotrexate as a monotherapy (70.6% vs 50.5%, p < 0.001), and the age (50.6 vs 48.0, p = 0.050). Other parameters such as swollen joint count, tender joint count, DAS28-CRP, HAQ or baseline erosion were similar between groups.

5 years follow-up of DAS28-CRP, HAQ or VAS pain values did not differ between the two groups (Fig1A).

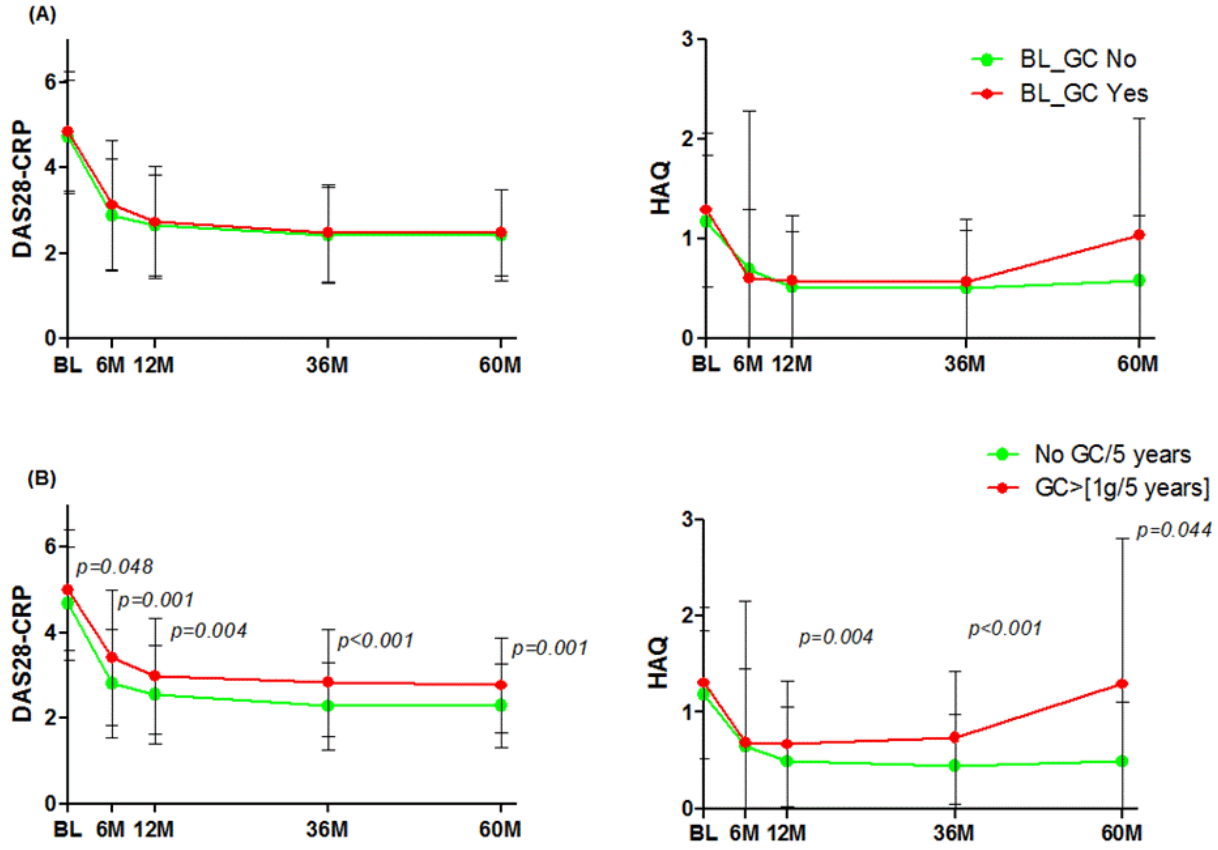


Figure 1. Comparison of DAS28-CRP and HAQ scores evolution. (A) in two groups of patients: treated with GC (BL-GC Yes) or without GC (BL_GC No) in combination with cDMARDs as first line treatment. (B) in two groups of patients: never treated with GC during 5 years follow-up (No GC/ 5 years) and those who received a high cumulative dose of GC ≥ 1 g/5years (GC>[1G/5years]).

Interestingly, patients not exposed at baseline to GC showed a higher remission rate (DAS28-CRP< 2.6) of 48.4% vs 44.3% at 6 months.

We also analysed a subgroup of patients (n=139) who received a cumulative dose of more than 1 g of prednisolone during the 5 years period. We confirmed the baseline differences for CRP, smoking habits, age and found in this subgroup more males (36.7% vs 28.2%, p=0.021) and higher DAS-28CRP values (5.0 vs 4.7, p=0.048). During the 5 years follow up, DAS-28CRP, VAS pain and HAQ remained significantly higher leading to a higher number of bi-oDMARDs prescribed in this group (Fig1B). More severe infections were reported in this subgroup (11.5% vs 4.2%). Bone densitometry values, number of fractures, and cardiovascular profiles were similar between groups.

Conclusion: In our ERA cohort, initiation of GC treatment does not add additional benefit for the short and long-term control of the disease.

GC were more prescribed in seronegative RA patients with higher level of inflammation and we confirm that patients exposed to higher cumulative doses of GC are at higher risk to develop severe infections.

Further studies are needed to support that GC induction therapy should not be offered to all ERA patients.Figure 1 Comparison of DAS28-CRP and HAQ scores evolution. (A) in two groups of patients: treated with GC (BL-GC Yes) or without GC (BL_GC No) in combination with cDMARDs as first line treatment. (B) in two groups of patients: never treated with GC during 5 years follow-up (No GC/ 5 years) and those who received a high cumulative dose of GC ≥ 1 g/5years (GC>[1G/5years]).

Disclosure: E. Sapart, None; **T. Sokolova**, None; **S. de Montjoye**, None; **S. Dierckx**, None; **A. Nzeusseu Toukap**, AbbVie, 1, 2, Eli Lilly, 1, 2, Janssen, 1, 2, UCB, 1, 2, Novartis, 1, Celgene Corporation, 1, Pfizer, 1; **A. Avramovska**, None; **P. Durez**, None.

Abstract Number: 2009

Treat-to Target for Early RA Patients in Usual Clinical Practice, a Randomized Study with a Favorable Effect of a Second Oral Pulse of Prednisolone. the Amsterdam COBRA Treat-to-target Study

Linda Hartman[1], Linda Rasch[2], Samina Turk[3], Marieke ter Wee[1], Pit Kerstens[4], Conny van der Laken[5], Mike Nurmohamed[6], Dirkjan van Schaardenburg[7], Lilian van Tuyl[8], Alexandre Voskuyl[1], Maarten Boers[7] and Willem Lems[1], [1]Amsterdam Rheumatology and Immunology Center, location Amsterdam UMC, VUmc, Amsterdam, Netherlands, [2]Amsterdam Rheumatology and Immunology Center, location Amsterdam UMC, VUmc, Amsterdam, [3]Amsterdam Rheumatology and Immunology Center, location Reade, Amsterdam, Netherlands, [4]Westfriesgasthuis, Hoorn, Netherlands, [5]Amsterdam Rheumatology and immunology Center, location Amsterdam UMC, VU medical center, Amsterdam, Netherlands, [6]Amsterdam Rheumatology and immunology Center, location Reade and Amsterdam UMC, VU medical center, Amsterdam, Netherlands, [7]Amsterdam Rheumatology and immunology Center | Reade and Amsterdam UMC, Amsterdam, Netherlands, [8]Nivel, Utrecht, Netherlands

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments IV: New Therapies & Strategies
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: EULAR guidelines advise to start with methotrexate (MTX) for early rheumatoid arthritis (RA), either alone or combined with prednisolone. Since this strategy is not effective in all patients after 13 weeks, we

performed a randomized controlled trial to compare the effect of the addition of a second oral pulse of prednisolone versus continuation of MTX and prednisolone.

Methods: Newly diagnosed RA patients with symptom duration < 2 years were classified into a low- and high-risk group. High-risk patients either had DAS44 >3.7, or presented with at least 2 out of 3 unfavorable prognostic factors: CRP >10 mg/l; IgM RF or antiCCP with high titer; at least 1 erosion. The remaining patients were classified as low-risk. The treatment target was response (DAS44 < 1.6) or EULAR good response. Nonresponders at 13 weeks were randomized to treatment intensification or continuation, and the primary endpoint was % responders at 26 weeks.

Results: In total 189 patients were included. High-risk patients (n=150; mean age 51 years, 63% female, baseline DAS44 3.50, RF+ 75%, antiCCP+ 77%) were treated with COBRA-light (1, 2) (30 mg/day oral prednisolone, tapered in 8 weeks to 7.5 mg/day, and MTX increasing to 25 mg/week): 112 (75%) patients reached the treatment target at 13 weeks and 2 patients dropped out. On continued treatment, 92% of the responders retained the target. The 36 incomplete responders were randomized to treatment intensification with 60 mg/day prednisolone, tapered in 6 weeks to 7.5 mg/day, and addition of sulfasalazine 2000 mg/day and hydroxychloroquine 400 mg/day (COBRA-plus, n=17) or continuation (n=19). After 26 weeks the treatment target was met in 14 patients (82%) of the intensified group vs 9 (47%) of the control group (difference: 35%, [95%CI 6;64]; p=0.01).

The low-risk group (n=39; mean age 56 years, 59% female, baseline DAS44 2.66, RF+ 21%, antiCCP+ 26%) was treated with MTX monotherapy increasing to 25 mg/week: only 19 (49%) reached the target at week 13 and 4 patients dropped out. On continued treatment, 95% of the responders retained the target after 26 weeks. The 16 incomplete responders were randomized to treatment intensification with a COBRA-light oral pulse of prednisolone (n=9) or continuation (n=7). After 26 weeks the treatment target was met in 5 patients (56%) of the intensified group vs 3 (43%) in the control group (difference: 13%, [95%CI –36;62]; p=0.28).
1 den Uyl D, et al. Ann Rheum Dis 2014; 1071-8.
2 ter Wee M, et al. Ann Rheum Dis 2015; 1233-40.

Conclusion: With the COBRA-light strategy, 75% of RA patients with moderate to high disease activity or poor prognostic factors met the treatment target after 13 weeks. Remarkably, intensification at week 13 with added DMARDs and a second oral pulse of prednisolone even further improved the initial high response rate suggesting that patients not reaching the target at 13 weeks benefit from COBRA-plus. In the small low-risk group, only 49% met the treatment target after 13 weeks. Here, no effect of treatment intensification was found, possibly related to the small number of individuals. More treat-to-target trials are needed, particularly in patients with mild RA.

Disclosure: L. Hartman, None; **L. Rasch**, None; **S. Turk**, None; **M. ter Wee**, None; **P. Kerstens**, None; **C. van der Laken**, None; **M. Nurmohamed**, None; **D. van Schaardenburg**, None; **L. van Tuyl**, None; **A. Voskuyl**, None; **M. Boers**, None; **W. Lems**, None.

Abstract Number: 2010

Stable versus Tapered and Withdrawn Treatment with Tumor Necrosis Factor Inhibitor in Rheumatoid Arthritis Remission: A Randomized, Open-Label, Phase 4, Non-Inferiority Trial

Siri Lillegraven[1], Nina Paulshus Sundlisæter[1], Anna-Birgitte Aga[1], Joseph Sexton[1], Inge C. Olsen[2], Åse Lexberg[3], Tor Magne Madland[4], Hallvard Fremstad[5], Christian Høili[6], Gunnstein Bakland[7], Cristina Spada[8], Hilde Haukeland[9], Inger Myrnes Hansen[10], Ellen Moholt[1], Till Uhlig[1], Daniel H. Solomon[11], Désirée van der Heijde[12], Tore K. Kvien[1] and Espen A. Haavardsholm[1], [1]Diakonhjemmet Hospital, Oslo, Norway, [2]Oslo University Hospital, Oslo, Norway, [3]Vestre Viken HF, Drammen, Norway, [4]Haukeland University Hospital, Bergen, Norway, [5]Ålesund Hospital, Ålesund, Norway, [6]Hospital Østftfold HF, Moss, Norway, [7]University Hospital of North Norway, Tromsø, Norway, [8]Revmatismesykehuset, Lillehammeer, Norway, [9]Martina Hansens Hospital, Bærum, Norway, [10]Helgelandssykehuset Mo i Rana, Mo i Rana, Norway, [11]Brigham & Women's Hospital and Harvard Medical School, Boston, MA, [12]Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: RA – Treatments IV: New Therapies & Strategies

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: Remission is the preferred treatment target in rheumatoid arthritis (RA), and many patients require biologic disease-modifying antirheumatic drugs (DMARDs) to reach this state. It is debated whether tapering of tumor necrosis factor inhibitor (TNFi) treatment to discontinuation should be considered in RA patients who sustain remission on treatment (1). The primary study objective was to assess the effect of tapering and withdrawal of TNFi on the risk of flares in RA patients in clinical remission.

Table: Baseline characteristics

	Stable, n=45	Tapering, n=47
Age, yrs	57 (11)	58 (13)
Female	30 (67%)	25 (53%)
ACPA+	35 (78%)	36 (77%)
Symptom duration, yrs	10 (7)	12 (7)
DAS	0.9 (0.4)	0.8 (0.3)
CRP mg/L, median (IQR)	1 (1 – 2)	1 (1 – 3)
No ultrasound power Doppler signal in any of 32 joints	42 (96%)	44 (94%)

Figure 1: Non-inferiority plot of stable vs tapered TNFi treatment in per protocol population, per protocol patients with csDMARD co-medication, and in the full analysis set. The broken vertical line represents the non-inferiority margin.

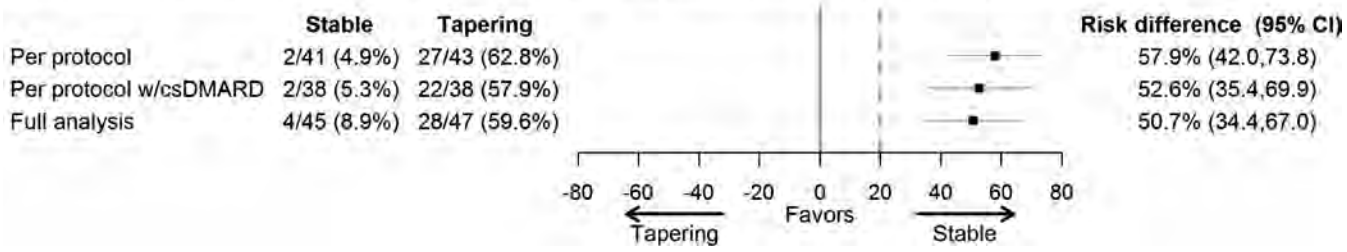
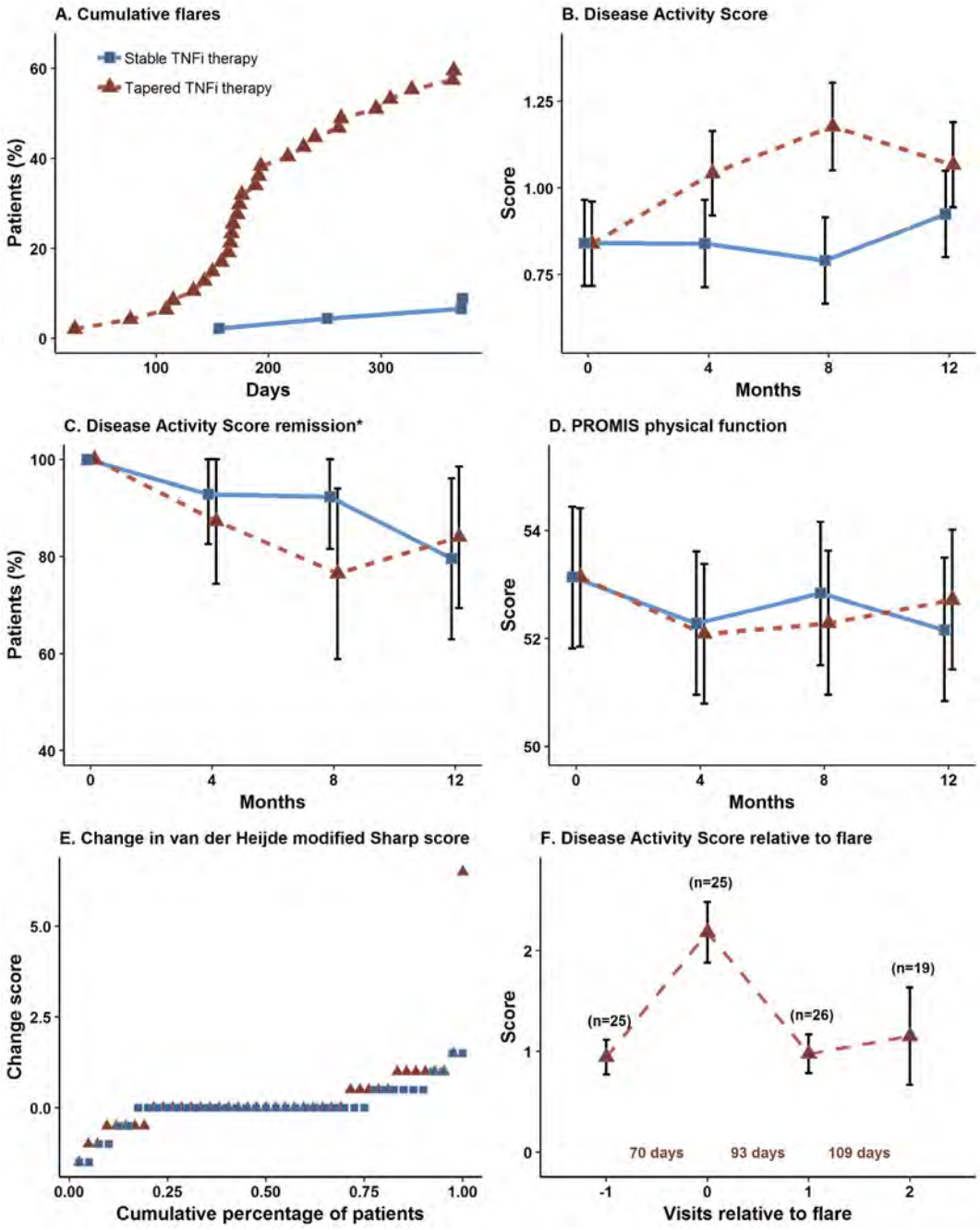


Figure 2: Secondary endpoints



Methods: In the non-inferiority ARCTIC REWIND trial, RA patients in remission for at least 12 months on stable TNFi therapy were randomly assigned to continued stable TNFi or tapering (half-dose TNFi for 4 months, thereafter withdrawal of TNFi), with visits every four months. csDMARD co-medication was kept stable in both arms. Patients had to be in DAS remission at inclusion with 0 swollen joints of 44 assessed. The primary endpoint was the proportion of patients with disease flare during the 12-month study period (defined as DAS >1.6, change in DAS >0.6 and 2 or more swollen joints, or the physician and patient agreed that a clinically significant flare had occurred). Full-dose TNFi was reinstated in case of flares in the tapering arm. The non-inferiority margin was 20%, with a predefined superiority test if non-inferiority was not shown. The inferiority null-hypothesis was tested in the per-protocol population by mixed ef-

fect logistic regression. Radiographs were scored by van der Heijde modified Sharp score (0 and 12 months, average of two readers, progression: ≥1 unit change). Clinicaltrials NCT01881308.

Results: We randomized 99 patients, 92 received the allocated treatment strategy, 84 were included in the per-protocol population. Baseline characteristics, clinical and ultrasound disease activity were balanced (Table). csDMARD co-medication was used by 93% in the stable and 88% in the tapering arm. In the primary analysis, 5% of patients in the stable TNFi arm experienced a flare during 12 months, compared to 63% in the tapering TNFi arm. The risk difference (95% CI) was 58% (42% to 74%, Fig 1), with stable treatment being deemed superior to tapering. 90% in the stable and 81% in the tapering arm did not show progression of radiographic joint damage, difference (95% CI) -9% (-24%, 6%). At 12 months, DAS scores, DAS remission and function were similar between groups (Fig 2). The numbers of adverse events (AE)/serious AE in the stable and tapering arm were 57/2 and 50/3, respectively, with 26 and 15 infections.

Conclusion: In a randomized clinical trial assessing patients in prolonged and deep RA remission, we observed a large increase in the flare rate in patients who tapered and discontinued TNFi. Patients responded well to reinstated treatment and remission rates in the two study arms were comparable at 12 months.

REFERENCES

[1] Smolen et al. EULAR recommendations for the management of rheumatoid arthritis with synthetic and biological disease-modifying antirheumatic drugs: 2019 update. ARD 2020

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Abstract Number: 2011

Olokizumab Improves Patient Reported Outcomes in Patients with Moderately to Severely Active Rheumatoid Arthritis Inadequately Controlled by Methotrexate: Results from the Double-Blind, Randomized Controlled Phase III Study

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: RA – Treatments IV: New Therapies & Strategies
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: We previously reported positive efficacy and safety results of olokizumab (OKZ), an interleukin-6-inhibitor, in patients with RA inadequately controlled by MTX (NCT02760368; CREDO-1) [Nasonov E.et al. Arthritis Rheumatol. 2019; 71 (suppl 10); E. Nasonov,et al. 2020; EULAR Abstracts THU0176]. Here we present the patient reported outcomes (PRO) of CREDO-1 study and assess the effect of OKZ treatment comparing to placebo (PBO) on quality of life, work productivity and fatigue in patients with moderate to severe RA who have previously failed MTX therapy.

Methods: We compared PRO between three groups 1) subcutaneous injections of OKZ 64 mg every 2 weeks (q2w), 2) OKZ 64 mg every 4 weeks (q4w) and 3) PBO every q2w.

PRO included change from baseline in: Health Assessment Questionnaire-Disability Index (HAQ-DI); Patient's Global Assessment of Disease Activity (PtGA), Patient's Assessment of Arthritis Pain (Pain), Short Form-36 (SF-36) Physical (PCS) and Mental (MCS) components; European Quality of Life- Five-Dimension Questionnaire (EQ-5D), Functional Assessment of Chronic Illness Therapy-Fatigue Scale (FACIT-F) and Work Productivity Survey-Rheumatoid Arthritis (WPS-RA).

Results: 428 patients were enrolled and 396 completed the study. All PRO baseline characteristics were comparable across treatment arms: mean (SD) PtGA was 69.5 (15.5); Pain was 68.6 (17.5); HAQ-DI was 1.7 (0.5); SF-36 PCS was 32.1 (6.5); SF-36 MCS was 42.3 (10.0); EQ-5D was 40.3 (20.0) and FACIT-F was 26.8 (8.7).

Treatment with OKZ 64 mg q2w and 64 mg q4w resulted in significant improvement in PRO measures (Table 1). Improvements in all PRO measures observed at week 12 were sustained over week 24.

Mean improvements in both OKZ groups for PtGA, Pain, HAQ-DI, SF-36 PCS and MCS, and FACIT-F surpassed defined MCIDs for these measures. There were clear differences between both OKZ treatment groups and placebo in all

Table 1. **Changes from baseline at months 3 (12 week) and 6 (24 week) for PRO**

LSM change from baseline (SE) Treatment comparison vs placebo LSM difference (SE) 97.5% CI for LSM difference	Week 12			Week 24		
	OKZ q2w (n=143)	OKZ q4w (n=142)	Placebo (n = 142)	OKZ q2w (n=143)	OKZ q4w (n=142)	Placebo (n = 142)
PtGA	**-30.6**(1.7) 17.5(2.5) -23.0,-12.0	**-31.0**(1.7) -17.9(2.5) -23.4,-12.4	**-13.1**(1.8)	**-32.1**(1.9) -12.7(2.7) -18.8,-6.6	**-36.3**(2.0) -16.8(2.8) -23.0,-10.6	**-19.4**(1.9)
Pain	**-31.6**(1.8) -18.7(2.6) -24.6,-12.9	**-31.8**(1.8) -19.0(2.6) -24.8,-13.1	**-12.8**(1.9)	**-34.5**(2.1) -13.0(2.9) -19.5,-6.5	**-37.1**(2.1) -15.7(2.9) -22.3,-9.1	**-21.4**(2.1)
HAQ-DI†	**-0.54**(0.04) -0.34(0.06)*** -0.47,-0.21	**-0.56**(0.04) -0.36(0.06)*** -0.49,-0.23	**-0.20**(0.04)	**-0.55**(0.05) -0.27(0.07) -0.43,-0.12	**-0.65**(0.05) -0.37(0.07) -0.53,-0.22	**-0.28**(0.05)
SF-36 PC	**6.7**(0.6) 4.5(0.8) 2.7,6.3	**6.0**(0.6) 3.8(0.8) 2.0,5.6	**2.2**(0.6)	**7.8**(0.7) 4.3(0.9) 2.2,6.4	**8.7**(0.7) 5.2(1.0) 3.1,7.4	**3.5**(0.7)
SF-36 MCS	**6.5**(0.7) 3.0(1.0) 0.7,5.3	**7.0**(0.7) 3.6(1.1) 1.2,5.9	**3.5**(0.8)	**6.2**(0.8) 3.7(1.1) 1.2,6.2	**8.9**(0.8) 6.4(1.1) 3.8,8.9	**2.5**(0.8)
EQ-5D Health Today Score	**19.7**(1.7) 12.2(2.4) 6.8,17.6	**18.7**(1.7) 11.2(2.4) 5.8,16.7	**7.4**(1.7)	**20.9**(2.0) 12.6(2.7) 6.5,18.7	**23.6**(2.0) 15.3(2.8) 8.9,21.7	**8.3**(2.0)
FACIT-F	**8.2**(0.7) 4.6(1.0) 2.4,6.8	**8.7**(0.7) 5.1(1.0) 2.9,7.3	**3.6**(0.7)	**8.5**(0.8) 4.8(1.1) 2.3,7.3	**10.6**(0.8) 6.9 (1.1) 4.3, 9.5	**3.7**(0.8)
WPS-RA Missed Work Days	**-11.14**(3.6) -10.3(5.2) -22.0,1.4	**-13.5**(3.3) -12.7(5.1) -24.0,-1.3	**-0.9**(3.7)	**-10.5**(3.0) -2.9(4.4) -12.8,6.9	**-12.8**(3.1) -5.2(4.5) -15.3,4.8	**-7.6**(3.3)
WPS-RA Missed Household Days	**-15.4**(1.7) -7.5(2.5) -13.0,-2.0	**-17.9**(1.7) -10.0(2.5) -15.5,-4.6	**-7.8**(1.8)	**-17.2**(2.0) -10.0(2.7) -16.1,-3.8	**-18.0**(1.9) -10.8(2.8) -17.0,-4.6	**-7.2**(1.9)
WPS-RA Work Impairment	**-21.5**(3.2) -12.9(4.6) -23.3,-2.6	**-23.8**(3.0) -15.2(4.4) -25.0,-5.3	**-8.6**(3.3)	**-22.5**(3.3) -12.8(4.8) -23.6, -2.0	**-30.1**(3.3) -20.4(4.8) -31.2, -9.6	**-9.7**(3.6)
WPS-RA Household Impairment	**-25.1**(1.9) -13.7(2.7) -19.8,-7.6	**-29.1**(1.9) -17.7(2.7) -23.8,-11.6	**-11.3**(1.9)	**-31.6**(2.2) -16.1(3.1) -23.0,-9.2	**-36.2**(2.2) -20.6(3.1) -27.6,-13.7	**-15.5**(2.2)
WPS-RA Work Day Productivity	**-16.7**(4.3) -8.3(62) -22.1,5.5	**-18.6**(3.9) -10.2(5.9) -23.4,3.0	**-8.4**(4.4)	**-14.7**(4.2) -7.3(6.0) -20.7,6.1	**-22.6**(4.1) -15.2(6.0) -28.6,-1.9	**-7.4**(4.4)
WPS-RA Household Day Productivity	**-17.5**(2.0) -8.4(2.8) -14.7,-2.0	**-19.6**(2.0) -10.4(2.8) -16.7,-4.1	**-9.2**(2.0)	**-19.2**(2.2) -11.2(3.0) -18.0,-4.4	**-22.2**(2.1) -14.2(3.1) -21.0,-7.4	**-8.0**(2.1)

PRO changes were analyzed using ANCOVA model adjusted for the baseline value of the corresponding parameter. Missing data resulted from study withdrawal imputed based on the return to baseline assumption;
†, secondary endpoint; ***P<0.0001

PtGA, Patient's Global Assessment of Disease Activity; Pain, Patient's Assessment of Arthritis Pain; PCS, HAQ-DI, Health Assessment Questionnaire-Disability Index; SF-36, Short Form-36; PSC, Physical Component Score; MCS, Mental Component Score; EQ-5, European Quality of Life-5 Dimensions; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue Scale; WPS-RA, Work Productivity Survey-Rheumatoid Arthritis.

PRO measures, with the exception of some WPS measures where differences between groups were variable. There were statistically significant changes between OKZ treatment groups and placebo for change from baseline in HAQ; however, no formal statistical testing was done for other PRO measures. No notable differences in PRO measures were observed between the two dose regimens of OKZ.

Conclusion:

1. Treatment with OKZ over a 24-week period was associated with significant improvements in PRO in patients with moderate to severe RA.
2. There were no discernible differences between the two regimens of OKZ from patient's perspective.

Disclosure: E. Nasonov, Eli Lilly, 5, 8, AbbVie, 8, Pfizer, 8, BIOCAD, 8, R-Pharm, 8; **S. Fatenejad**, JSC "R-Pharm", 5; **M. Ivanova**, JSC "R-Pharm", 2; **D. Krechikova**, Janssen, 8, Eli Lilly, 8, Celtrion, 8, R-Pharm, 8; **S. Kuzkina**, JSC "R-Pharm", 3; **A. Maslyanskiy**, R-Pharm, 5; **T. Plaksina**, R-Pharm, 2; **M. Samsonov**, JSC "R-Pharm", 3; **M. Stanislav**, R-Pharm, 5, Janssen, 2, Celtrion, 2, Sanofi Aventis, 2; **T. Tyabut**, KRKA, 8, Gedeon Richter, 8, R-Pharm, 2, MEDPACE, 2, ABBVE, 2; **I. Vinogradova**, R-Pharm, 2, Eli Lilly, 2, GSK, 2, MSD, 2, Yanssen, 2, Bayer, 2; **S. Yakushin**, R-Pharm, 2; **E. Zonova**, R-Pharm, 2, Pfizer, 8, Novartis, 8, AbbVie, 8, Bayer, 8; **M. Genovese**, Abbvie, 2, 5, Eli Lilly and Company, 2, 5, Galapagos, 2, 5, Gilead Sciences Inc., 2, 5, Pfizer, 2, 5, EMD Merck Serono, 2, 5, Genentech/Roche, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, RPharm, 2, 5, Sanofi-Genzyme, 2, UCB, 5, Amgen, 5.

Abstract Number: 2012

A Phase IIb, Randomized, Double-blind Study in Patients with Rheumatoid Arthritis Evaluating the Safety and Efficacy of Evobrutinib Compared with Placebo in Patients with an Inadequate Response to Methotrexate

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
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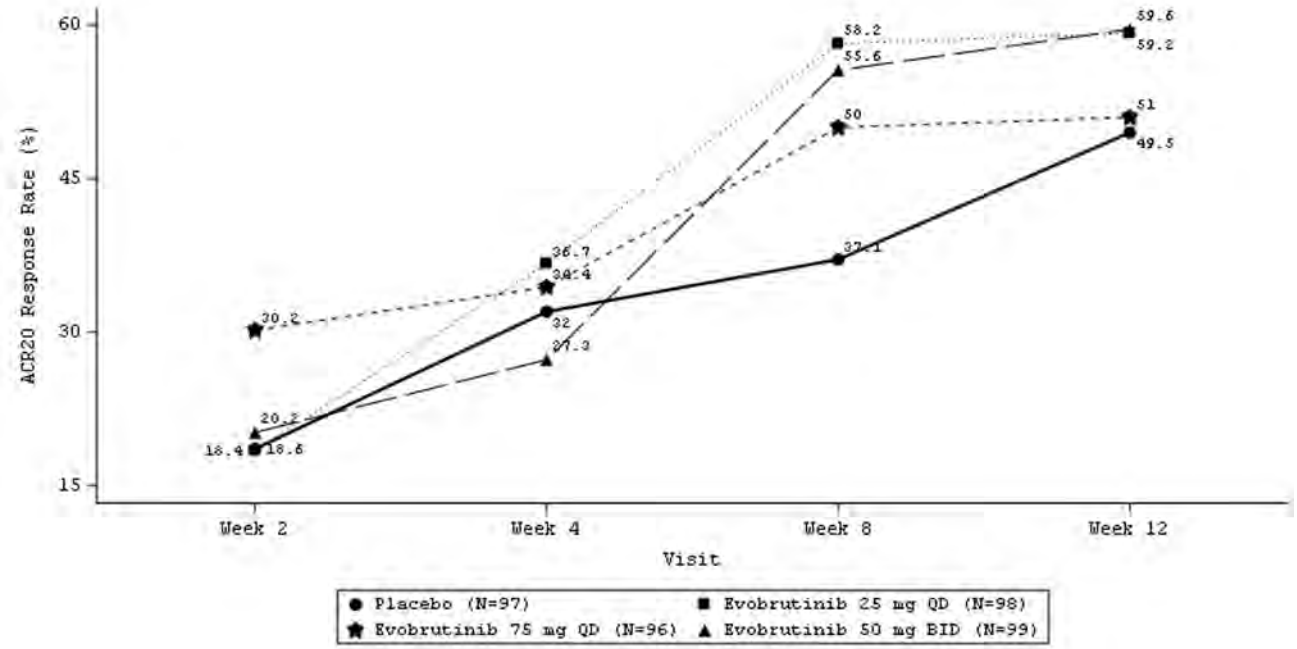
Background/Purpose: Bruton's tyrosine kinase (BTK) is involved in multiple signalling pathways potentially implicated in rheumatoid arthritis (RA). Evobrutinib is a highly selective, oral BTK inhibitor. This phase IIb, randomized, double-blind study evaluated efficacy, dose response, and safety to 12 weeks of treatment with evobrutinib versus placebo in RA patients with inadequate response to methotrexate (MTX).

Methods: Patients enrolled were 18–75 years of age, with confirmed diagnosis of RA ≥ 6 months duration (EULAR/American College of Rheumatology [ACR] criteria), with active disease at screening and randomization, defined by ≥ 6 swollen and ≥ 6 tender joints, and with high-sensitivity CRP (hsCRP) ≥ 5.0 mg/L. Participants had received MTX treatment 7.5–25 mg/week for ≥ 16 weeks at stable dose for ≥ 8 weeks, and had not received prior treatment with a biologic DMARD. They were randomized 1:1:1:1 to oral evobrutinib 25 mg once-daily (QD), 75 mg QD, 50 mg twice-daily (BID), or placebo. Stable use of NSAIDs and/or glucocorticoids (≤10 mg daily) was allowed. The primary endpoint was ACR 20% response (ACR20), assessed at Week 12, using hsCRP. Key secondary endpoints

Figure 1. Primary Endpoint: ACR20 Response Rate over Time



were ACR50 and ACR70 and disease activity scores (DAS28) CRP, DAS28CRP < 3.2 and DAS28CRP < 2.6. Safety endpoints included adverse events (AEs), serious AEs (SAEs), and laboratory studies. Other secondary endpoints included change from baseline in OMERACT RAMRIS scores and RAMRIQ scores for synovitis, osteitis and erosion for patients in an MRI substudy.

Results: 390 patients were randomized. Baseline age was 52.7±12.2 years (mean±SD), 80.0% were female, hsCRP 21.77mg/L ±24.1 (mean±SD), and time since diagnosis 6.9±6.7 years (mean±SD). The treatment groups were balanced for sex, race, age, time since diagnosis, joint counts, and other baseline disease characteristics. The primary endpoint of ACR20 response was not met (Figure 1). ACR20 response in the placebo group (49.5%) was higher than other trials in RA. Evobrutinib at all doses was nominally significant versus placebo on DAS28CRP < 3.2, and DAS-28CRP < 2.6. HsCRP decreased in all evobrutinib arms (Table 1). No dose response was observed. There were no significant differences in MRI scores between placebo and evobrutinib by either RAMRIS (Table 1) or RAMRIQ (data not shown). Evobrutinib was well tolerated at all doses (Table 2). Three patients showed Grade 3 elevations in ALT, all in the 75 mg QD arm. LFT elevations were reported across all groups. Very few patients experienced Grade 3 events, and only one patient experienced a Grade 4 event (unrelated to treatment).

Conclusion: This phase IIb study of evobrutinib in patients with RA with inadequate response to MTX did not meet its primary efficacy endpoint of ACR20 response. MRI endpoints did not show differences between evobrutinib and placebo. However, MRI placebo scores were not consistent with other studies, showing greater improvements in synovitis and osteitis, and less progression of erosions than typically reported. Evobrutinib was well tolerated at all doses. No dose effect was identified.

Table 1. Primary and Key Secondary Endpoints

Primary Endpoint	**Placebo N=97 (100%)**	**Evobrutinib 25 mg QD N=98 (100%)**	**Evobrutinib 75 mg QD N=96 (100%)**	**Evobrutinib 50 mg BID N=99 (100%)**
ACR20 Response Rate, n (%)	48 (49.5)	58 (59.2)	49 (51.0)	59 (59.6)
ACR20 Response Rate difference (compared to placebo) [95% CI]		0.10 [-0.04, 0.23]	0.02 [-0.12, 0.16]	0.11 [-0.03, 0.24]
Odds-ratio (model-based, compared to placebo) [95% CI]		1.48 [0.84, 2.61]	1.06 [0.61, 1.87]	1.55 [0.88, 2.74]
P-value		0.1746	0.8283	0.1298
P-value adjusted with Hochberg procedure		0.3491	0.8283	0.3491
Key Secondary Endpoints	**Placebo N=97 (100%)**	**Evobrutinib 25 mg QD N=98 (100%)**	**Evobrutinib 75 mg QD N=96 (100%)**	**Evobrutinib 50 mg BID N=99 (100%)**
DAS28-hsCRP < 3.2 (LDA) at Week 12, n (%) Response rate difference, stratified (compared to placebo) [95% CI] P-value	7 (7.2)	20 (20.4) 0.13 [0.04, 0.23] 0.0077	23 (24.0) 0.17 [0.07, 0.27] 0.0013	20 (20.2) 0.13 [0.04, 0.23] 0.0080
DAS28-hsCRP < 2.6 (Remission) at Week 12, n (%) Response rate difference, stratified (compared to placebo) [95% CI] P-value	1 (1.0)	10 (10.2) 0.09 [0.03, 0.17] 0.0056	10 (10.4) 0.09 [0.03, 0.17] 0.0050	10 (10.1) 0.09 [0.03, 0.17] 0.0053
ACR50 Response Rate at Week 12, n (%) Response rate difference, stratified (compared to placebo) [95% CI] P-value	19 (19.6)	28 (28.6) 0.09 [-0.03, 0.21] 0.1419	26 (27.1) 0.07[-0.05, 0.19] 0.2202	26 (26.3) 0.07[-0.05, 0.19] 0.2328
ACR70 Response Rate at Week 12, n (%) Response rate difference, stratified (compared to placebo) [95% CI] P-value	5 (5.2)	11 (11.2) 0.06 [-0.02, 0.15] 0.1232	10 (10.4) 0.05 [-0.03, 0.13] 0.1725	10 (10.1) 0.05 [-0.03, 0.13] 0.1795
hsCRP % Change from Baseline at Week 12, median [Q1, Q3]	0.232 [-41.05; 66.63]	-38.537 [-65.83; 15.25]	-39.290 [-70.26; 10.92]	-38.974 [-72.54; 1.01]
MRI (RAMRIS Week 12 Change from Baseline)	**Placebo N=54 (100%)**	**Evobrutinib 25 mg QD N=56 (100%)**	**Evobrutinib 75 mg QD N=55 (100%)**	**Evobrutinib 50 mg BID N=56 (100%)**
Osteitis Score, n (%)	44 (81.5)	49 (87.5)	47 (85.5)	51 (91.1)
Osteitis Score, Least-squares Mean	-3.44	-3.17	-3.10	-3.29
Osteitis Score, Difference in LS Means from Placebo [95% CI]		0.27 [-1.73, 2.28]	0.34 [-1.68, 2.36]	0.15 [-1.84, 2.15]
Synovitis Score, n (%)	44 (81.5)	49 (87.5)	47 (85.5)	51 (91.1)
Synovitis Score, Least-squares Means	-1.09	-1.30	-1.61	-1.61
Synovitis Score, Difference in LS Means from Placebo [95% CI]		-0.21 [-1.22, 0.80]	-0.52 [-1.53, 0.49]	-0.52 [-1.51, 0.48]
Erosion Score, n (%)	44 (81.5)	49 (87.5)	47 (85.5)	51 (91.1)
Erosion Score, Least-squares Means	0.46	-0.18	0.38	-0.57
Erosion Score, Difference in LS Means from Placebo [95% CI]		-0.64 [-1.75, 0.47]	-0.07 [-1.19, 1.04]	-1.03 [-2.13, 0.07]

Table 2. Overview of TEAEs ≥5%

Preferred Term n (%)	Placebo N=97 (100%)	Evobrutinib 25 mg QD N=98 (100%)	Evobrutinib 75 mg QD N=96 (100%)	Evobrutinib 50 mg BID N=99 (100%)
Patients with at least one event	44 (45.4)	48 (49.0)	48 (50.0)	50 (50.5)
Anemia	6 (6.2)	2 (2.0)	3 (3.1)	7 (7.1)
Dyslipidemia	0 (0.0)	5 (5.1)	0 (0.0)	2 (2.0)
Headache	5 (5.2)	6 (6.1)	5 (5.2)	8 (8.1)

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Abstract Number: 2013

Substantial Lifetime Risk of Developing Ankylosing Spondylitis (Axial Spondyloarthritis) for Relatives. Evidence from a 35-Year Follow-up Family Study of a Swiss Cohort

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SESSION INFORMATION

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Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II

Session Type: Abstract Session

Session Time: 12:00PM–12:50PM

Background/Purpose: Familial occurrence of ankylosing spondylitis (AS) is well known. Our follow-up study aimed at assessing the incidence of clinically defined AS among first degree relatives (FDR) and to explore 'hidden' manifestations of axial spondyloarthritis (axSpA) among 'healthy' FDR.

Methods: Our cohort study started in 1985 when the Swiss Ankylosing Spondylitis Patient Society member patients clinically diagnosed with AS were contacted to participate in this study, together with their FDR, irrespective of whether they were known to have any disease. After ethical approval and Informed consent, 1178 subjects completed questionnaires on disease manifestations, underwent rheumatological examination of axial and peripheral joints, and provided blood samples for genetic studies, including HLA-B27. Pelvic radiographs of 363 probands and 713 FDR were assessed blindly for presence of sacroiliitis according to the New York (NY) radiographic criteria.

In 2018 the ethical committee of the Swiss Kanton of Bern approved the follow up study. City and village administrations provided current addresses of former participants. 124 Probands and 338 FDR were available for follow-up and were screened by questionnaire.

Results: First study (1985): 308 of 358 HLA-tested AS probands were HLA-B27(+) (86.0%). The mean age of the 672 FDR (311 males) was 26.9± 8.2 years. At that time 14 (7 males) of the 308 HLA-B27(+) FDR (4.5%) had sacroiliitis and met the mNY criteria for AS (mean age 33.5 ± 4.1 years). In contrast, none of the 278 HLA-B27(-) FDR of HLA-B27(+) probands showed sacroiliitis (p=0.00032), nor did anyone of the 83 HLA-B27(-) FDR of 50 HLA- B27(-) probands (p= 0.048). Considering FDR of probands with a clinical diagnosis of AS in the absence of sacroiliitis (now called non-radi-

Table 1. Prevalence of symptoms suggesting 'hidden' AS or axial SpA in healthy HLA-B27 positive relatives of HLA-B27 positive probands with AS compared with their HLA-B27 negative counterparts

Question	*Relatives HLA-B27* (n=111) # positive/total and percentage		*Relatives HLA-B27* (n=130) # positive/total and percentage		LR+	LR-	*p*-value
Chronic inflammatory backpain (CIBP)	24/111	21.6%	21/130	16.2%	1.34	1.07	0.277
Pain or discomfort at thoracic spine	23/108	21.3%	26/126	20.6%	1.03	1.01	0.90
Pain or discomfort at ventral chest wall	25/108	23.1%	23/128	18.0%	1.29	1.07	0.32
Worsening of back pain during early morning before getting up	26/106	24.5%	11/129	8.5%	2.88	1.21	0.0008
Persisting back pain after getting up	19/111	17.1%	10/129	7.8%	2.21	1.11	0.0264
Waking up regularly after 4:00 AM because of pain or discomfort at the thoracic spine	6/110	5.5%	1/129	0.8%	7.04	1.05	0.0324
*Morning stiffness at thoracic spinal region	11/111	9.9%	4/129	3.1%	3.20	1.08	0.0298
*Morning stiffness at the thoracic spinal region for at least 15 – 60 minutes	8/111	7.2%	2/130	1.5%	4.68	1.06	0.0278
*Improvement of stiffness at the thoracic spinal region through exercises	12/107	11.2%	4/126	3.2%	3.53	1.09	0.0155
*Improvement by exercises of complaints due to persistent body position through exercises	17/110	15.5%	7/128	5.5%	2.83	1.12	0.0107
Change of body position causes exacerbation of complaints at the ventral chest wall	6/109	5.5%	1/130	0.8%	7.16	1.05	0.0305

ographic axSpA (nr-axSpA)), two of the 59 HLA-B27(+) FDR (3.4%) of 58 HLA-B27(+) nr-axSpA probands themselves had AS, compared with none of 47 HLA-B27(-) FDR of 28 HLA-B27(-) nr-axSpA probands (p=0.50).

In 2019, 36 of 152 (23.7%) HLA-B27(+) FDR reported themselves to have AS, including 6 of the 14 FDR who already met mNY criteria in 1985. In contrast, amongst HLA-B27(-) FDR only 3 of 173 HLA-B27(-) (1.7%) FDR reported themselves to have AS (odds ratio 18, p=1.2x10^{-9}). The current mean age of the 39 FDR is 58.4 ± 8.7 years.

Considering 'inflammatory' spinal arthritis symptoms assessed by questionnaire, eight of these were reported significantly more often by HLA-B27(+) than HLA-B27(-) FDR, in the absence of any rheumatic disease diagnosis (Table 1). These items individually have low sensitivity with low negative likelihood ratios, but are highly specific with high positive likelihood ratios. Interestingly, 8 of 111 (7.2%) HLA-B27(+) FDR share 4(*) items compared with 2 of 130 HLA-B27(-) FDR (1.5%) (odds ratio=5.0, p= 0.028). This points to 'hidden' AS/axSpA manifestations among HLA-B27(+) FDR.

Conclusion: For HLA-B27(+) FDR the risk of developing AS/axSpA over a period of more than 35 years is substantial (23.7%). This confirms our previous finding of a 21% risk figure in a Dutch family study (Arthritis Rheum 1984; 27:241). It is unlikely that the life-time incidence will increase further given the age of the cohort.

Disclosure: S. van der Linden, None; **P. Villiger**, None; **Z. Li**, None; **M. Brown**, None; **H. Baumberger**, None; **H. Zandwijk**, None; **M. Khan**, None.

Abstract Number: 2014

The Relative Diagnostic Utility of Inflammatory Back Pain Criteria in an Inception Cohort of Patients with Psoriasis, Iritis, and Colitis Presenting with Undiagnosed Back Pain

Georg Kröber[1], Ulrich Weber[2], Raj Carmona[3], James Yeung[4], Jon Chan[5], Sibel Aydin[6], Liam Martin[7], Ariel Masetto[8], Stephanie Keeling[9], Olga Ziouzina[7], Sherry Rohekar[10], Rana Dadashova[11], Joel Paschke[11], Amanda Carapellucci[11], Robert G Lambert[12] and Walter Maksymowych[9], [1]University of Southern Denmark, Sønderborg, Denmark, [2]University of South Denmark, Odense, Denmark, [3]St. Joseph's Healthcare, Hamilton, ON, Canada, [4]James Yeung Rheumatology, Vancouver, BC, Canada, [5]Artus Health Clinic, Vancouver, BC, Canada, [6]University of Ottawa Faculty of Medicine, Rheumatology, Ottawa, ON, CANADA; The Ottawa Hospital Research Institute, Ottawa, ON, CANADA, Ottawa, ON, Canada, [7]University of Calgary, Calgary, AB, Canada, [8]University of Sherbrooke, Sherbrooke, QC, Canada, [9]University of Alberta, Edmonton, AB, Canada, [10]Lawson Health Research Institute, London, ON, Canada, [11]CARE Arthritis, Edmonton, AB, Canada, [12]University of Alberta and CARE Arthritis, Edmonton, AB, Canada

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II
Session Type: Abstract Session
Session Time: 12:00PM–12:50PM

Background/Purpose: Patients with psoriasis, iritis, or colitis and back pain represent a high-risk population for the presence of axial spondyloarthritis (axSpA). Clinicians rely on the elicitation of features of inflammatory back pain (IBP) to discriminate between more common non-specific back pain and inflammatory conditions. Different criteria have been developed for classification purposes, but these have been developed and validated in patients with established idiopathic ankylosing spondylitis. It is unknown how these criteria, namely ASAS, Berlin and Calin criteria, perform in patients presenting with back pain and extra-articular features of axSpA. To address the circularity between elicitation of IBP and clinical diagnosis, we used not only rheumatologist diagnosis as benchmark, but also

Table 1. Rheumatologist diagnosis as external reference.				
	Sensitivity	**Specificity**	**LR+**	**LR-**
Psoriasis				
ASAS IBP	65.0%	52.0%	1.4	0.7
Berlin IBP	80.0%	36.0%	1.3	0.6
Calin IBP	80.0%	28.0%	1.1	0.7
All 3 criteria sets	60.0%	56.0%	1.4	0.7
IBP global >5	85.0%	36.0%	1.3	0.4
AAU				
ASAS IBP	84.4%	42.9%	1.5	0.4
Berlin IBP	80.0%	57.1%	1.9	0.4
Calin IBP	93.3%	17.9%	1.1	0.4
All 3 criteria sets	77.8%	60.7%	2.0	0.4
IBP global >5	86.7%	57.1%	2.0	0.2
IBD				
ASAS IBP	78.4%	45.0%	1.4	0.5
Berlin IBP	82.4%	52.1%	1.7	0.3
Calin IBP	84.3%	19.7%	1.0	0.8
All 3 criteria sets	70.6%	57.8%	1.7	0.5
IBP global >5	80.4%	66.2%	2.4	0.3

imaging. We aimed to assess the diagnostic utility of all available criteria for IBP in an inception cohort of patients with psoriasis, iritis, or inflammatory bowel disease (IBD) referred to a rheumatologist with undiagnosed back pain, using the final rheumatologist diagnosis and imaging as the benchmarks.

Methods: The multicenter Screening for Axial Spondyloarthritis in Psoriasis, Iritis, and Colitis (SASPIC) Study is aimed at early detection of axial SpA in consecutive patients presenting with undiagnosed back pain to the rheumatologist. Consecutive patients ≤45 years of age with ≥3 months undiagnosed back pain with any one of psoriasis, acute anterior uveitis (AAU), or IBD diagnosed by the relevant specialist undergo routine clinical evaluation by a rheumatologist for axial SpA. The rheumatologist determines the presence or absence of axial SpA at 3 consecutive stages: 1. After the clinical examination; 2. After the results of labs (B27, CRP) and radiography; 3. After the results of

Table 2. Central MRI assessment that MRI is indicative of axSpA as external reference.				
	Sensitivity	**Specificity**	**LR+**	**LR-**
Psoriasis				
ASAS IBP	28.6%	38.5%	0.5	1.9
Berlin IBP	42.9%	15.4%	0.5	3.7
Calin IBP	71.4%	23.1%	0.9	1.2
All 3 criteria sets	14.3%	42.3%	0.3	2.0
IBP global >5	85.7%	23.1%	1.1	0.6
AAU				
ASAS IBP	75.0%	26.9%	1.0	0.9
Berlin IBP	70.0%	38.5%	1.1	0.8
Calin IBP	90.0%	15.4%	1.1	0.7
All 3 criteria sets	65.0%	38.5%	1.1	0.9
IBP global >5	75.0%	38.5%	1.2	0.7
IBD				
ASAS IBP	92.3%	37.7%	1.5	0.2
Berlin IBP	76.9%	39.6%	1.3	0.6
Calin IBP	92.3%	17.0%	1.1	0.5
All 3 criteria sets	76.9%	45.3%	1.4	0.5
IBP global >5	92.3%	47.2%	1.8	0.2

local MRI evaluation. Imaging was also assessed centrally by 3 expert readers. Majority central reader evaluation of presence/absence of MRI indicative of axSpA and final diagnosis by the rheumatologist were used as external standards to test the performance (sensitivity, specificity, positive and negative likelihood ratios (LR+/LR-)) of the following criteria for IBP: ASAS, Berlin, Calin, rheumatologist global for likelihood of IBP >5 (0-10 scale).

Results: 246 patients were included, of whom 47.6% were diagnosed with axSpA by the local rheumatologist. The diagnosis of axSpA was confirmed in 45.7%, 61.6% and 40.2 % of patients with undiagnosed back pain and psoriasis, iritis, and IBD. The diagnostic utility for all IBP criteria was equally poor, especially showing a lack of specificity (Table 1). MRI was considered indicative of axSpA by central readers in 21.2%, 43.5% and 19.7% of patients with psoriasis, iritis, and IBD. When using MRI as external reference (Table 2), all IBP criteria performed even worse.

Conclusion: All IBP criteria, as well as rheumatologist global assessment, have poor diagnostic utility for diagnosis of axSpA in patients with undiagnosed back pain and extra-articular features. This should be a reminder to not rely only on the concept of IBP in daily routine, and also reinforces the desirability of less subjective assessment tools, especially imaging.

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Abstract Number: 2015

Prevalence and Distribution of Peripheral Musculoskeletal Manifestations in Axial Spondyloarthritis, Peripheral Spondyloarthritis and Psoriatic Arthritis: Results of the International, Cross-sectional ASAS-PerSpA Study

Clementina Lopez-Medina[1], Anna Molto[1], Joachim Sieper[2], Mehmet Tuncay Duruöz[3], Uta Kiltz[4], Bassel El-Zorkany[5], Najia Hajjaj-Hassouni[6], Ruben Burgos-Vargas[7], Jose Maldonado-Cocco[8], Nelly Ziade[9], Meghna Gavali[10], Victoria Navarro-Compán[11], Shue Fen Luo[12], Sara Monti[13], Tae-Jong Kim[14], Mitsumasa Kishimoto[15], Fernando Pimentel-Santos[16], Jieruo Gu[17], Ruxandra Schiotis[18], Floris van Gaalen[19], Pál Géher[20], Marina Magrey[21], Sebastian Ibanez[22], Wilson Bautista-Molano[23], Walter Maksymowych[24], Pedro M Machado[25], Robert Landewé[26], Désirée van der Heijde[27] and Maxime Dougados[28], [1]Rheumatology Department, Cochin Hospital, Paris, Paris, France, [2]Charité Universitätsmedizin Berlin, Berlin, Germany, [3]Marmara University School of Medicine, PMR Department, Rheumatology Division, Istanbul, Turkey, [4]Rheumazentrum Ruhrgebiet, Ruhr-University Bochum, Herne, Germany, [5]Cairo University, Cairo, Egypt, [6]Health Sciences College, International University of Rabat (UIR), Rabat, Morocco, [7]Department of Rheumatology, General Hospital of Mexico, Ciudad de Mexico, Mexico, [8]Buenos Aires School of Medicine, Buenos Aires, Argentina, [9]Saint-Joseph University, Beirut, Lebanon, Beirut, Lebanon, [10]Nizam's Institute of Medical Sciences, Hyderabad, India, [11]Hospital Universitario La Paz IdiPaz, Madrid, Pais Vasco, Spain, [12]Chang Gung Memorial Hospital-Linkou, Taoyuan, Taipei, Taiwan (Republic of China), [13]Fondazione IRCCS Policlinico S Matteo, University of Pavia, Pavia, Italy, [14]Department of Rheumatology, Chonnam National University Medical School and Hospital, Gwangju, Republic of Korea, [15]Department Nephrology and Rheumatology, Kyorin University School of Medicine, Tokyo, Japan, [16]3.CEDOC, NOVA Medical School, Faculdade de Ciências Médicas da Universidade NOVA de Lisboa, Lisboa, Portugal; 7.Hospital Egas Moniz (CHLO) (Rheumatology Department), Lisboa, Portugal, Lisbon, Portugal, [17]Third Affiliated Hospital of Sun Yat-Sen University, Guangzhou, guangzhou, China (People's Republic), [18]Pharmacology Department Department, Iuliu Hatieganu University of Medicine and Pharmacy, SCBI-Rheumatology Department, Cluj-Napoca, Romania, [19]Leiden University Medical Center (LUMC), Leiden, Netherlands, [20]Semmelweis University, Budapest, Hungary, [21]Case Western Reserve University School of Medicine, Cleveland, OH, [22]Facultad de Medicina Clínica Alemana – Universidad del Desarrollo, Santiago, Region Metropolitana, Chile, [23]University Hospital Fundación Santa Fé de Bogotá and Universidad El Bosque, Bogotá, Colombia, [24]University of Alberta, Edmonton, AB, Canada, [25]University College London, London, United Kingdom, [26]Amsterdam University Medical Center & Zuyderland Hospital, Amsterdam, Netherlands, [27]Leiden University Medical Center, Leiden, Netherlands, [28]Department of Rheumatology, Hopital Cochin, Université de Paris, Paris, France

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II

Session Type: Abstract Session

Session Time: 12:00PM–12:50PM

Background/Purpose: Peripheral musculoskeletal manifestations in patients with Psoriatic Arthritis (PsA) have been widely studied. However, there is a lack of knowledge on the distribution of such manifestations in the whole group

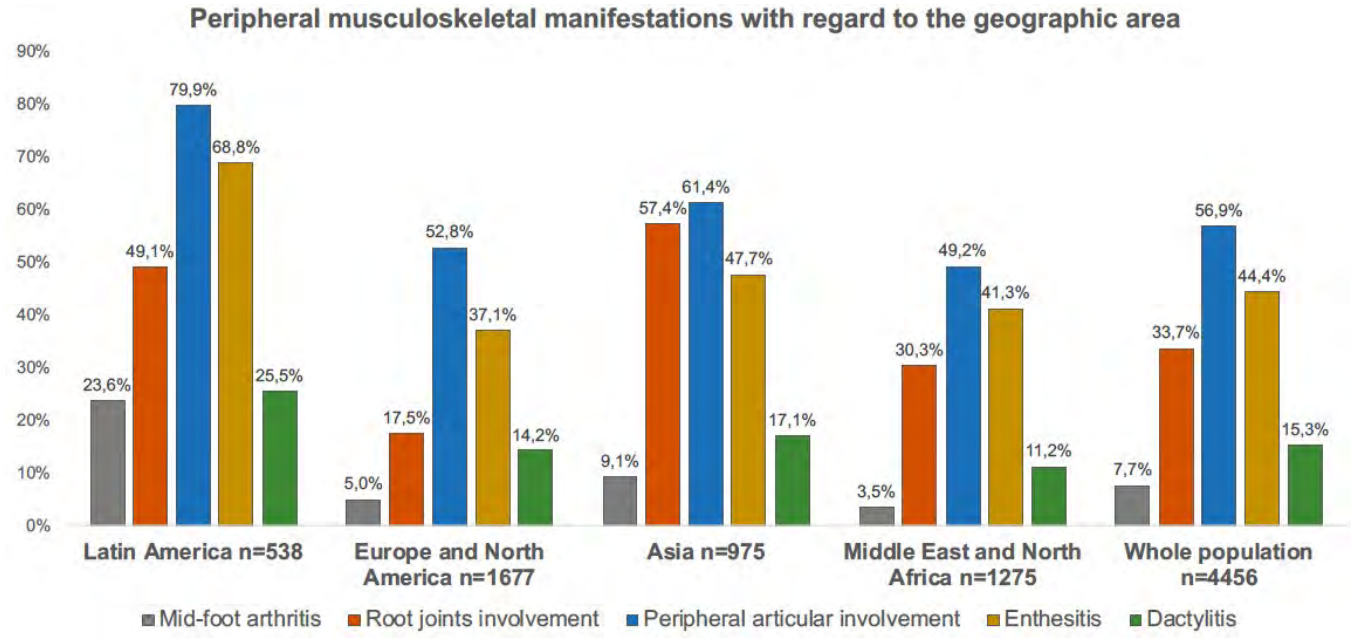

Figure 1. Peripheral musculoskeletal manifestations with regard to the geographic area.

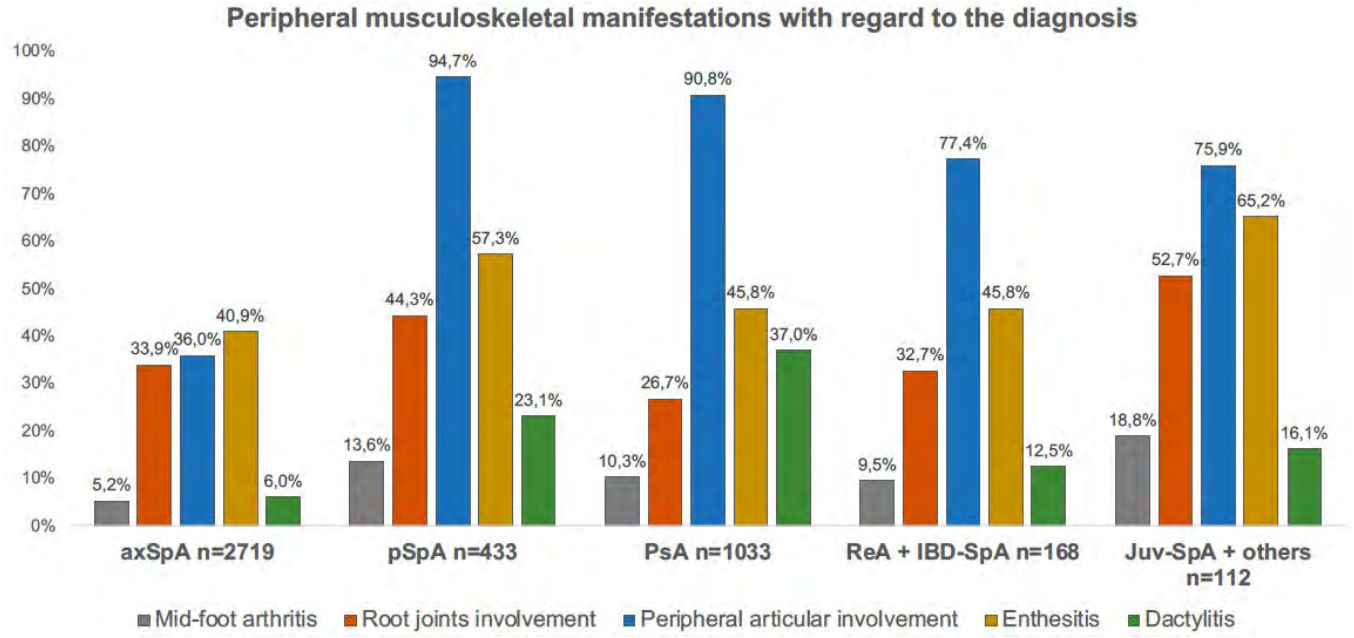

Figure 2. Peripheral musculoskeletal manifestations with regard to the diagnosis.

of spondyloarthritis (SpA) and specifically in axial SpA (axSpA), even though an important overlap exists between SpA subtypes and PsA. The ASAS-PerSpA study aimed to evaluate the prevalence, characteristics and treatment of peripheral musculoskeletal manifestations in patients with axSpA and peripheral SpA (pSpA) as well as in PsA across regions of the world.

Methods: Data was collected cross-sectionally in an international multicentre study with 24 participating countries. Consecutive patients diagnosed as having axSpA, pSpA, PsA, inflammatory bowel disease-associated SpA (SpA-IBD), reactive arthritis (ReA), juvenile SpA (JuvSpA) or other form of SpA were eligible for the study. Data concerning the presence of peripheral musculoskeletal manifestations, their localization and specific treatments were collected.

Results: A total of 4465 patients were included (61% men, mean (SD) age of 45 (14) years). Patients came from four geographic areas: Latin America (12.0%), Europe and North America (37.6%), Asia (21.8%) and Middle East and North Africa (28.6%). The most prevalent clinical diagnosis was axSpA (60.9%), followed by PsA (23.1%), pSpA (9.7%), SpA-IBD (2.5%), ReA (1.3%), JuvSpA (1.2%) and others (1.3%).

The prevalence of musculoskeletal manifestations were plotted against geographic area and diagnosis in Figures 1 and 2. The most prevalent peripheral manifestation was peripheral articular involvement (excluding root joints) (56.9%) (Figure 1, whole population), with polyarticular involvement more often found in PsA (58.9%) and monoarticular involvement in axSpA (20.1%) (Fig.2). Predominantly upper limb- and small joint involvement were found more often in PsA (52.0%). Predominantly lower limb- and large joint involvement were found more often in ReA and IBD-SpA (55.9%) and in pSpA (51.2%) (Figure 2). Root joint (i.e., hip or shoulder) involvement was found in 33.7% and, of these, 21.8% had both hip and shoulder involvement. Among the total patients with root joint disease, hip involvement alone was found in 57.1%, being most frequent in axSpA (65.0%). Enthesitis in the different groups ranged between 40.9% and 65.9%, with the lowest prevalence found for axSpA; PsA showed the highest mean number of locations of all episodes of enthesitis (4.3 (4.6)). Finally, the prevalence of dactylitis was 15.3%. Dactylitis of the fingers was more prevalent in the group of ReA and IBD-SpA (75.0%), but a higher prevalence of toe-involvement was found in Juv-SpA (66.7%). Only 8.1%, 12.1% and 14.3% of patients had received local injections of corticosteroids for peripheral enthesitis, dactylitis and root joint involvement, respectively.

Conclusion: Although all types of peripheral manifestations are present in the different subtypes of SpA, this study suggests a high inter-region and inter-diagnosis variability of the prevalence of the various peripheral musculoskeletal manifestations in patients with either SpA or PsA.

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Abstract Number: 2016

Baseline Serum Biomarker Levels Predict Spinal Radiographic Progression in Ankylosing Spondylitis Patients on TNF Inhibitor Therapy

Judith Rademacher[1], Mark Siderius[2], Laura Gellert[1], Freke Wink[3], Maryna Verba[1], Fiona Maas[4], Lorraine M Tietz[1], Denis Poddubnyy[5], Anneke Spoorenberg[3] and Suzanne Arends[3], [1]Charité Universitätsmedizin Berlin, Berlin, Germany, [2]Department of Rheumatology and Clinical Immunology, University of Groningen, University Medical Center Groningen, Groningen, Netherlands, [3]University Medical Centre Groningen and Medical centre Leeuwarden, Groningen, Netherlands, [4]University medical Centre Groningen, Groningen, Netherlands, [5]Charité – Universitätsmedizin Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Monday, November 9, 2020

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Session Type: Abstract Session

Session Time: 12:00PM–12:50PM

Biomarker	Unit	Baseline	3 months		2 years	
		Serum level	Serum level	p value#	Serum level	p value#
Markers of inflammation						
Calprotectin	µg/ml	5.17 [4.61]	3.61 [3.28]	0.000	3.99 [4.23]	0.000
MMP-3	ng/ml	18.63 [13.25]	17.91 [12.00]	0.000	17.42 [12.90]	0.000
SAA	mg/l	74.43 [243.79]	18.50 [26.65]	0.000	21.71 [37.33]	0.000
VEGF	pg/ml	368.43 [298.95]	284.54 [222.45]	0.000	289.10 [277.44]	0.000
Markers of bone formation						
PIINP	ng/ml	32.56 [14.19]	29.70 [14.61]	0.014	33.14 [13.59]	0.687
Osteoprotegerin	pmol/l	4.25 [1.82]	4.04 [1.73]	0.036	4.17 [1.45]	0.101
Sclerostin	pg/ml	109.40 [94.55]	108.96 [107.29]	0.808	139.37 [110.50]	0.000
Adipokines						
HMW-adiponectin	µg/ml	4.20 [3.54]	4.38 [3.57]	0.904	4.61 [3.28]	0.684
Leptin	ng/ml	8.40 [11.89]	9.07 [15.04]	0.142	9.26 [11.78]	0.060
Visfatin	ng/ml	1.38 [3.26]	1.36 [2.21]	0.110	2.03 [2.25]	0.288

Table 1. Serum biomarker levels at baseline (before start of TNFi), after 3 months and 2 years. Values presented as medians [interquartile range (IQR)]. # Wilcoxon signed-rank test compared to baseline. HMW high molecular weight. MMP-3 matrix metalloproteinase-3. PIINP procollagen type II N-terminal propeptide. SAA serum amyloid A. VEGF vascular endothelial growth factor.

Background/Purpose: Radiographic spinal progression determinates functional status and mobility in ankylosing spondylitis (AS) (Poddubnyy et al, 2018). Our objective was to analyze whether biomarker levels at baseline or their change after 3 months or 2 years can predict spinal radiographic progression in AS patients treated with TNF-α inhibitors (TNFi).

Methods: Consecutive AS patients from the Groningen Leeuwarden Axial Spondyloarthritis (GLAS) cohort (Maas et al, 2019) starting TNFi between 2004 and 2012 were included. The following serum biomarkers were measured at baseline, 3 months and 2 years of follow-up with commercially available ELISA: calprotectin, matrix metalloproteinase-3 (MMP-3), serum amyloid A (SAA), vascular endothelial growth factor (VEGF), osteoprotegerin (OPG), procollagen type II N-terminal propeptide (PIINP), sclerostin, high molecular weight adiponectin, leptin and visfatin. Two independent readers assessed spinal radiographs according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS).

Logistic regression was performed to examine the association between biomarker values at baseline, their change after 3 months and 2 years and radiographic spinal progression (defined as mSASSS change ≥2 units or the formation of ≥1 new syndesmophyte over 2 years). Multivariable models for each biomarker were adjusted for mSASSS or syndesmophytes at baseline, elevated CRP (≥5mg/l), smoking status, male gender, symptom duration, BMI, and baseline biomarker level (the latter only in models with biomarker change).

Results: Of the 137 included AS patients, 72% were male, 79% HLAb27+, mean age was 42 years (SD 10.8) and baseline ASDAScrp 3.8 (SD 0.8). Serum levels of calprotectin, MMP-3, SAA and VEGF showed a significant reduction after 3 months and 2 years of TNFi therapy. OPG and PIINP decreased significantly after 3 months, but did not differ from baseline after 2 years. Sclerostin increased after 2 years.

Univariable logistic regression revealed a significant association of baseline visfatin (odds ratio (OR) [95% confidence interval] 1.106 [1.007-1.215]) and sclerostin serum levels (OR 1.006 [1.001-1.011]) with radiographic progression defined as mSASSS change ≥2 units after 2 years. In multivariable logistic analysis, only baseline visfatin level remained significantly associated (OR 1.337 [1.088-1.642]). Furthermore, baseline calprotectin showed a positive association (OR 1.146 [1,011-1,299]) when adjusting for known risk factors for radiographic spinal progression. Interestingly, the change of visfatin level after 2 years was associated with both measures of radiographic progression after 2 years – mSASSS progression (OR 1.108 [1.004-1.224]) and syndesmophyte formation (OR 1.115; [1.002-1.24]). However, those associations were lost in multivariate analysis.

Conclusion: While serum levels of biomarkers of inflammation (calprotectin, MMP-3, SAA, VEGF) and bone formation (OPG, PIINP, sclerostin) showed significant changes under TNFi therapy, adipokine levels (HMW-adiponektin, leptin, visfatin) were not altered. Independent of known risk factors, baseline calprotectin and visfatin levels were associated with radiographic spinal progression after 2 years of TNFi.

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Abstract Number: 2017

Machine Learning Identifies an Association Between Pre-existing Radiographic Damage and Long-term Clinical Outcomes with Secukinumab Therapy in Patients with Psoriatic Arthritis

Philip Mease[1], Désirée van der Heijde[2], Bruce Kirkham[3], Georg Schett[4], Ana-Maria Orbai[5], Christopher Ritchlin[6], Joseph Merola[7], Luminita Pricop[8], Xuan Zhu[9], DavidA James[9] and Gregory Ligozio[9], [1]Seattle Rheumatology Associates, P.L.L.C., Seattle, WA, [2]Leiden University Medical Center, Leiden, Netherlands, [3]Guy's & St Thomas' NHS Foundation Trust, London, United Kingdom, [4]Friedrich-Alexander-Universität Erlangen- Nuremberg, Erlangen, Germany, [5]Division of Rheumatology, Johns Hopkins University School of Medicine, Baltimore, MD, [6]Department of Medicine, University of Rochester Medical Center, Rochester, NY, [7]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [8]Novartis Pharmaceuticals Corporation, East Hanover, [9]Novartis Pharmaceuticals Corporation, East Hanover, NJ

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes II

Session Type: Abstract Session

Session Time: 12:00PM–12:50PM

Background/Purpose: Assessment of radiographic joint damage extent and progression is important in clinical trials evaluating treatments for psoriatic arthritis (PsA). Joint damage in patients with PsA has substantial impact on

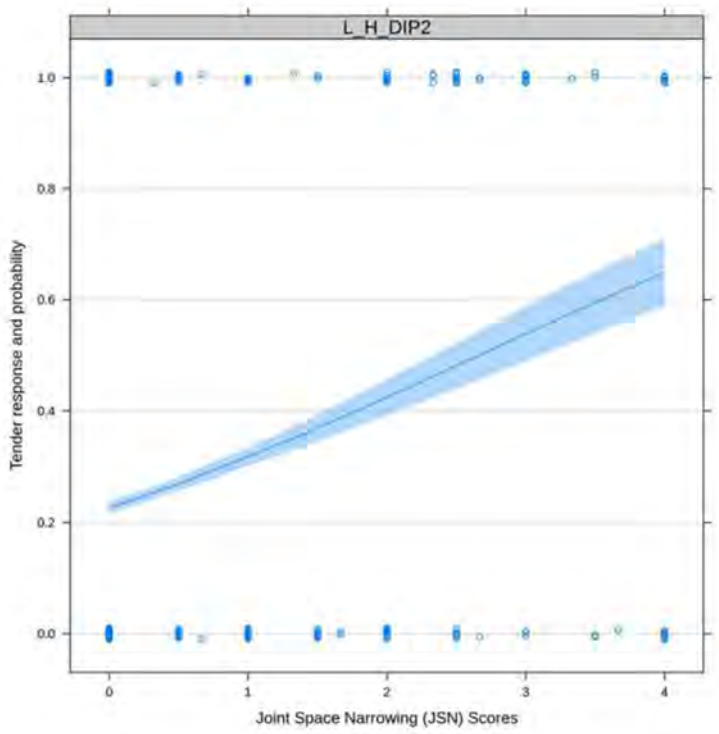
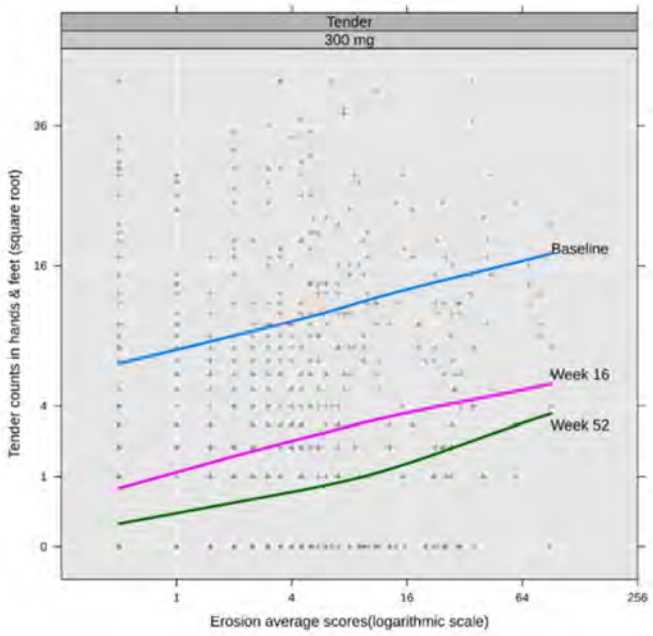


Figure shows one of the 42 joints on the hands and feet (i.e. left hand DIP2). The dots at y=0 and 1 (vertically jittered to reduce over-plotting) depict the assessed tenderness (no/yes) and JSN (x-axis) for each patient. The curves and associated standard error bands depict the (mostly increasing) probability of joint tenderness as a function of JSN.

Association between tenderness and joint space narrowing on individual joints assessed radiographically across patients at baseline



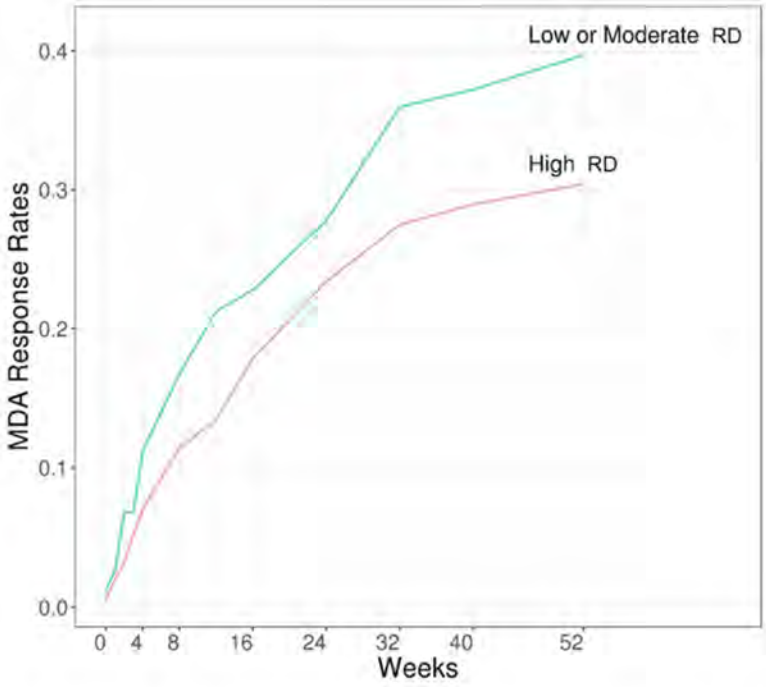
The lines depict average trend at baseline, Weeks 16, and 52. The roughly parallel decrease of the curves illustrates the effect of secukinumab on joint counts approximately uniformly across all values of erosion, although patients with very high levels of erosion would have lower probability of complete remission (counts=0).

Number of tender joint counts versus erosion scores for every patient at baseline, Week 16, and Week 52
MDA response rate through Week 52

physical function, quality of life and survival, therefore, inhibiting radiographic progression is one of the main goals of therapy.[1,2] Here we present results from a machine learning analysis of pooled data from two phase 3 secukinumab trials in PsA aimed to identify prevalence and magnitude of pre-existing radiographic damage at baseline and its association with clinical swollen and tender joint count; and investigate the extent to which radiographic damage at baseline could influence the response to secukinumab therapy.

Methods: Mixed-effects linear regression models were applied to data from FUTURE 1 and FUTURE 5 studies to investigate the association at baseline between overall radiographic damage and swollen / tender joint counts on a patient level and on a joint-within-patient / individual joint level; random effects were used to account for variability at both the levels. Visualization was used to explore joint activity progression patterns as functions of time and secukinumab dosing, and to estimate the probability of joint activity as a function of radiographic damage at each joint. Two additional mixed-effects models (one at overall patient level and another at joint segment level) were implemented to estimate the impact of radiographic damage, treatments and baseline patient characteristics on joint activity over time. Response to secukinumab therapy was assessed using swollen/tender joint count and proportion of patients achieving minimal disease activity (MDA) over time.

Results: Data for 1554 patients from FUTURE 1 and FUTURE 5 studies were pooled. At baseline, 69.4% and 50.1% of patients, respectively, showed detectable erosions and joint space narrowing (JSN; defined as patients with radiographic scores >1). Patients with early PsA diagnosis (≤2 years) showed strong prevalence of erosions and JSN, which progressively worsened over time. At an individual joint level, the probability of tenderness and swelling was strongly and significantly associated with the extent of radiographic damage **(Figure 1)**. At a patient level, significant reductions of swollen/tender joint count were observed in all secukinumab dose regimens regardless of the levels of



MDA response rates over time for high radiographic damage patients ($n_1 = 342$) compared with low or moderate radiographic damage patients ($n_2 = 645$). The response rates are 17.8%/22.8% at Week 16 and 30.4%/39.7% at Week 52 for high radiographic damage patients (defined as patients with mTSS≥8) and low or moderate radiographic damage patients (defined as patients with mTSS<8), respectively. The high radiographic damage patients at baseline tend to have around 10% lower response rate than low or moderate radiographic damage patients on an average at Week 52

MDA response rate Through Week 52

radiographic damage. However, patients with higher radiographic damage showed a lower proportion of complete remission of joint symptoms (swollen joint count and tender joint count = 0; **Figure 2**). The MDA response showed a similar pattern to the tender/swollen joint count responses corresponding to low and high levels of radiographic damage **(Figure 3)**.

Conclusion: A strong and significant association was demonstrated between disease activity and baseline radiographic damage at the individual joint level, whereas the analysis at patient level showed a weaker association. High radiographic damage at baseline was associated with a lower rate of achieving remission.

References

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2. Gossec L, et al. *Ann Rheum Dis.* 2016;75:499–510.

Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheu-

matology bv, 3, Eisai, 5; **B. Kirkham**, AbbVie, 9, Eli Lilly & Co, 2, 9, Novartis, 2, 9, Janssen, 9, Gilead, 9, UCB, 2, 9; **G. Schett**, None; **A. Orbai**, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 5, UCB, 5, AbbVie, 2, Celgene, 2, Horizon, 2; **C. Ritchlin**, None; **J. Merola**, AbbVie, 1, Arena, 1, Avotres, 1, Biogen, 1, Celgene, 1, Dermavant, 1, Eli Lilly, 1, EMD Serono, 1, Janssen, 1, LEO Pharma, 5, Merck, 1, Novartis, 1, Pfizer Inc, 5, Sanofi, 1, Regeneron, 1, Sun Pharma, 1, UCB Pharma, 5; **L. Pricop**, Novartis, 1, 3; **X. Zhu**, Novartis, 1, 3; **D. James**, Novartis, 1, 3; **G. Ligozio**, Novartis, 1, 3.

Abstract Number: 2018

Development and Validation of an Artificial Intelligence Approach for the Detection of Radiographic Sacroiliitis

Keno-Kyrill Bressem[1], Janis Vahldiek[1], Lisa Adams[1], Stefan Niehues[1], Hildrun Haibel[1], Valeria Rios Rodriguez[1], Murat Torgutalp[1], Mikhail Protopopov[1], Fabian Proft[1], Judith Rademacher[1], Joachim Sieper[1], Martin Rudwaleit[2], Bernd Hamm[1], Markus Makowski[1], Kay-Geert Hermann[1] and **Denis Poddubnyy**[3], [1]Charité Universitätsmedizin Berlin, Berlin, Germany, [2]Department of Internal Medicine and Rheumatology, Klinikum Bielefeld, Germany, [3]Charité – Universitätsmedizin Berlin, Berlin, Germany

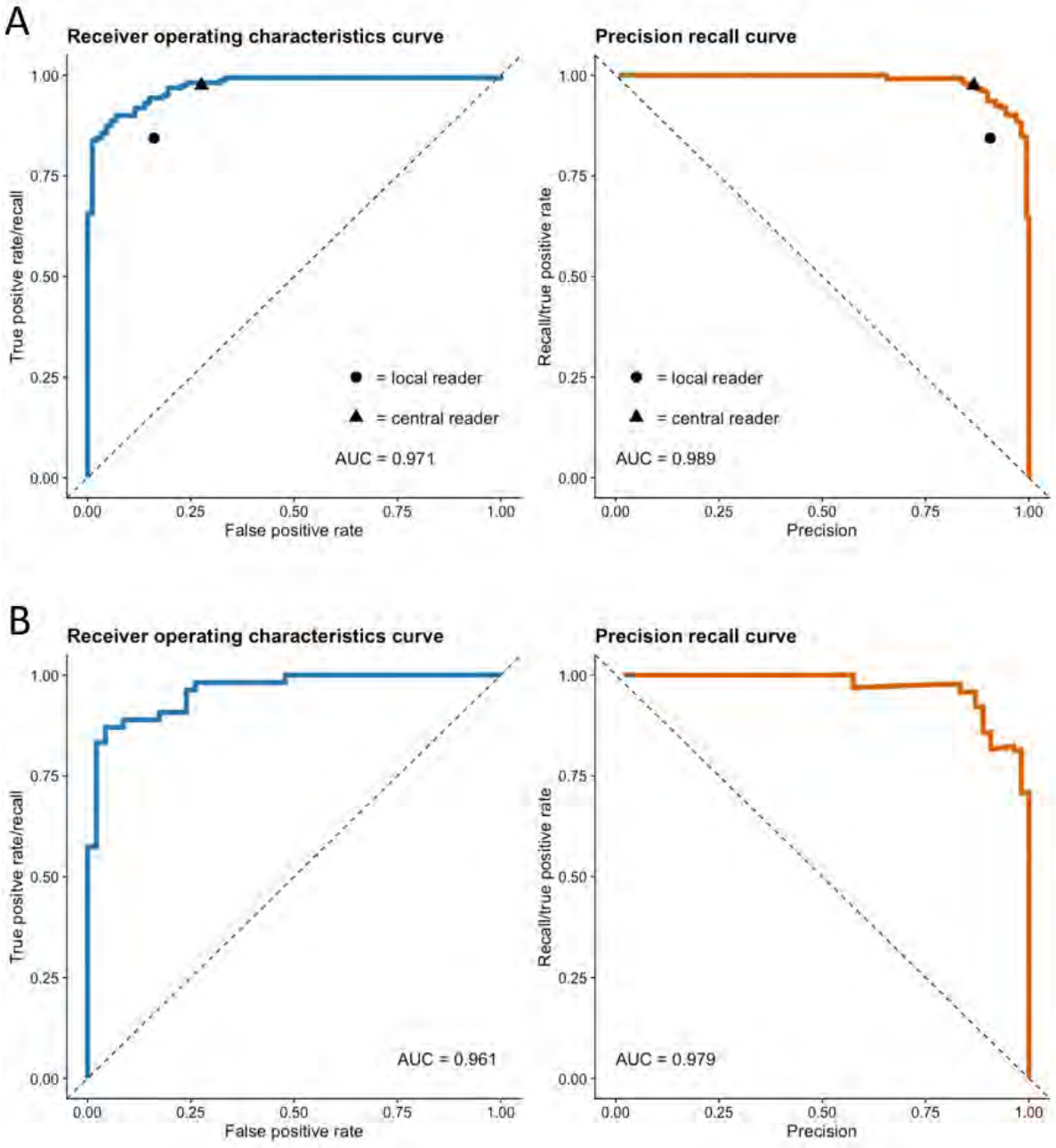
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes III: Imaging in SpA
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: Conventional radiography of the sacroiliac joints is still recommended as the first imaging method if axial spondyloarthritis (axSpA) is suspected. Furthermore, radiographic sacroiliitis is included – together with sacroiliitis on magnetic resonance imaging – in the Assessment of Spondyloarthritis International Society (ASAS) classification criteria for axSpA. Depending on the presence or absence of definite radiographic sacroiliitis, axSpA can be classified either as radiographic axSpA (r-axSpA, synonymous to ankylosing spondylitis) or non-radiographic axSpA (nr-axSpA). Although conventional radiography of sacroiliac joints still plays an important role in clinical practice and for clinical trials, the reliability of radiographic sacroiliitis assessment has been reported in a number of studies as mostly poor, even if performed by expert readers. Furthermore, it was shown that untrained local readers perform worse than expert readers specialised in SpA. One possible solution to achieve a comparable high accuracy as an expert on detection of radiographic sacroiliitis, even in non-specialised clinics, could be development of an artificial intelligence-based model for analysis of radiographs.

The aim of this study was to develop and validate an artificial neural network for the detection of definite radiographic sacroiliitis as a manifestation of axial spondyloarthritis.

Methods: Conventional radiographs of sacroiliac joints from two independent cohorts of patients with axSpA were used. The first cohort (PROOF) consisted of 1669 radiographs and was used for training and validation of a neural network. The second cohort consisted of 100 randomly selected radiographs from GESPIC, which were used as an independent test dataset. In both cohorts all radiographs underwent central reading; the final decision on the presence or absence of definite radiographic sacroiliitis according to the radiographic criterion of the modified New York criteria was used as a reference. For performance evaluation of the neural network, areas under the receiver operating characteristic curves (AUROC) were calculated. Sensitivity and specificity for the prediction cut-offs were calculated. Cohen's Kappa and the absolute agreement were used to assess the agreement between the neural network and the human readers.

Figure 1. Receiver operating characteristic and precision recall curves for the validation (A) and independent test (B) data sets.



Results: The neural network achieved an excellent performance in recognition of definite radiographic sacroiliitis with AUROC of 0.97 and 0.96 for the validation and test datasets, respectively (Figure 1). Sensitivity and specificity for the cut-off weighting both measurements equally were 0.90 and 0.93 for the validation and 0.87 and 0.97 for the test set. The Cohen's kappa between the neural network and the reference judgements were 0.80 for both validation and test sets, and the absolute agreement on the classification yielded 91% and 90%, respectively (Table). Examples of the activation maps of the neural network are presented in Figure 2.

Table. Confusion matrices on the presence or absence of definite radiographic sacroiliitis for the validation and independent test data for the prediction cut-off with an optimal relationship between sensitivity and specificity.

Validation data set

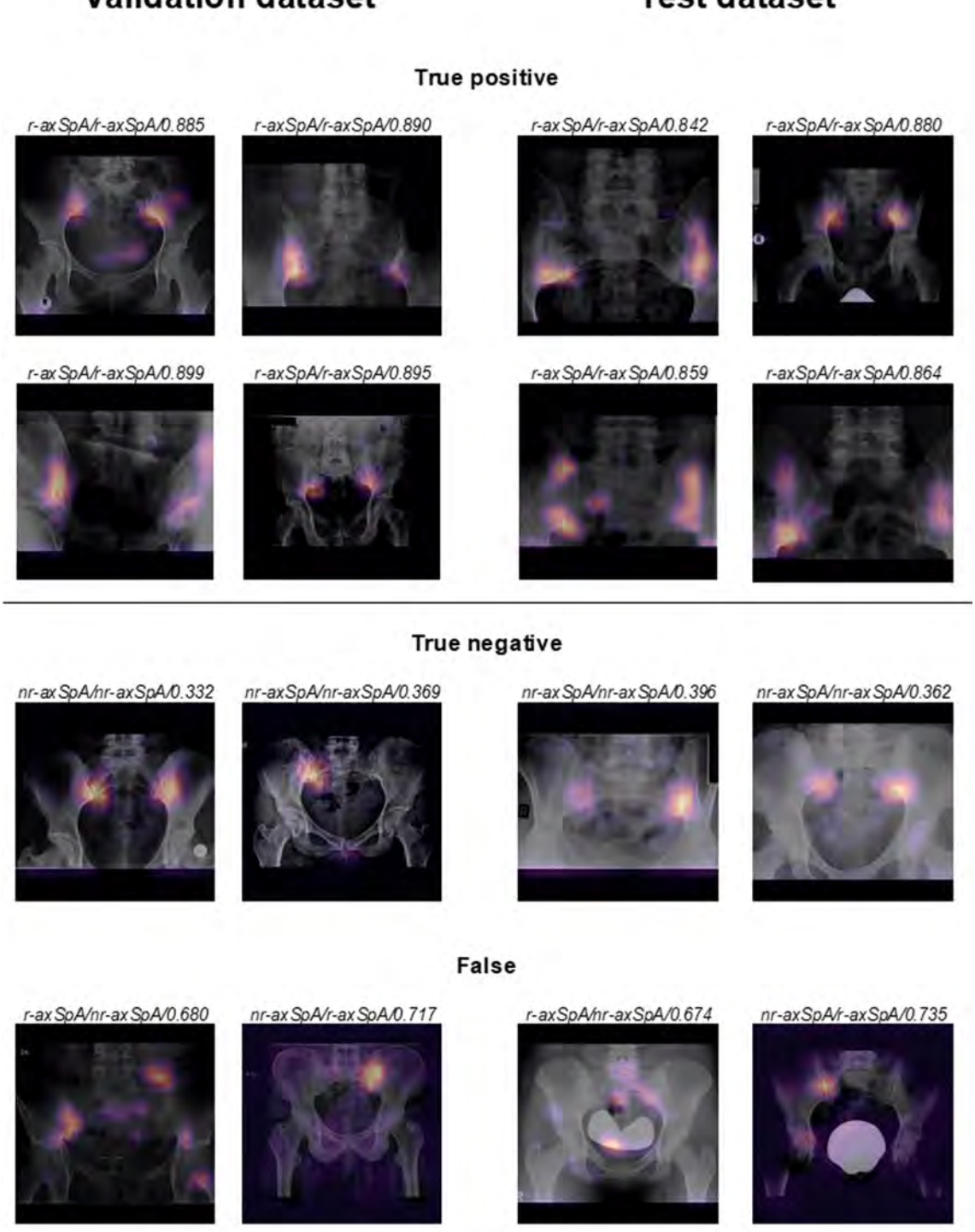
	Reference negative	Reference positive	
Model negative	81	17	98
Model positive	6	143	149
	87	160	247
Cohen's Kappa:	0.802 (95% CI 0.731 to 0.875)	Absolute agreement:	n=224 (90.7%)

Independent test data set

	Reference negative	Reference positive	
Model negative	44	8	52
Model positive	2	46	48
	46	54	100
Cohen's Kappa:	0.801 (95% CI 0.688-0.919)	Absolute agreement:	n=90 (90%)

Conclusion: Artificial neural networks enable the accurate detection of definite radiographic sacroiliitis relevant for the diagnosis and classification of axSpA.

Figure 2. Example activation maps of the neural network in the validation and test data sets.



Actual class, predicted class and the probabilities are shown

Disclosure: K. Bressem, None; **J. Vahldiek**, None; **L. Adams**, None; **S. Niehues**, None; **H. Haibel**, None; **V. Rios Rodriguez**, None; **M. Torgutalp**, None; **M. Protopopov**, None; **F. Proft**, Novartis, 2, 8, AbbVie, 8, AMGEN, 8, BMS, 8, Hexal, 8, Celgene, 8, Lilly, 8, MSD, 8, Pfizer, 8, Roche, 8, UCB, 8; **J. Rademacher**, None; **J. Sieper**, AbbVie, 5, Novartis, 5, 8, Lilly, 8, Janssen, 5, Merck, 5, 8; **M. Rudwaleit**, Bristol-Myers Squibb, 5, 8, Chugai Pharmaceutical Co., Ltd., 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Novartis, 5, 8, UCB Pharma, 5, 8, AbbVie, 5, 8, Pfizer, 5, 8, Celgene, 8, Roche, 5, 8, Merck Sharp & Dohme, 5, 8; **B. Hamm**, None; **M. Makowski**, None; **K. Hermann**, None; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8.

Abstract Number: 2019

Preliminary Definition of a Positive MRI for Active Lesions in the Sacroiliac Joints Typical of Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes III: Imaging in SpA

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: The ASAS definition of a positive MRI for inflammation (ASAS-MRI+) is intended for classification of patients as having axSpA but is often misused for diagnostic purposes. This is problematic because bone marrow edema (BME) in the sacroiliac joints (SIJ) may occur in 20-40% of both healthy individuals and those with mechanical back disorders when only the quantitative aspect of the definition is applied (presence of BME in ≥2 locations on one slice or one location in ≥2 slices). The definition also requires that BME is considered "highly suggestive" of SpA but interpretation of this qualitative component may vary according to expertise. Revised definitions of MRI lesions in the SIJ have been validated by 7 readers from the ASAS-MRI group on images from the ASAS Classification Cohort[1-3]. We aimed to identify quantitative cut-offs based on numbers of slices and SIJ quadrants that define a positive MRI for active lesions typical of axSpA, the gold standard being majority central reader decision as to the presence of a definite active lesion typical of axSpA with high confidence.

Methods: MRI active lesions meeting ASAS definitions from 160 cases were recorded by 7 ASAS-MRI readers in an eCRF that comprises global assessment (Is there an active lesion typical of axSpA (yes/no) and degree of confidence (-4 (lesion absent) to +4 (lesion present)), and detailed scoring of lesions per SIJ quadrant and per slice. Detailed scoring was based only on assessment of DICOM images. We calculated sensitivity and specificity for numbers of SIJ quadrants and consecutive slices with BME where a majority of readers (≥4/7) agreed as to the presence of an active lesion typical of axSpA with high confidence (≥ +3). We selected cut-offs with ≥95% specificity. These cut-offs were analyzed for their predictive utility for rheumatologist diagnosis of axSpA at follow up (average of 4.4 years) by calculating positive and negative predictive values (PPV, NPV) and selecting those cut-offs with PPV of ≥95% and

Table 1. Majority readers agree active lesion indicative of axSpA is present with confidence ≥3/4 is the gold-standard external reference		
MRI cut-offs	**Sensitivity (95%CI)**	**Specificity (95%CI)**
Majority (≥4/7) reader agreement for definite active lesion		
BME in ≥1 SIJ quadrant	100.0 (86.8-100.0)	71.6 (63.2-79.1)
BME in ≥2 SIJ quadrants	100.0 (86.8-100.0)	85.8 (78.7-91.2)
BME in ≥3 SIJ quadrants	100.0 (86.8-100.0)	91.8 (85.8-95.8)
BME in ≥4 SIJ quadrants	**100.0 (86.8-100.0)**	**96.3 (91.5-98.8)**
BME in ≥2 consecutive slices	100.0 (86.8-100.0)	88.1 (81.3-93.0)
BME in ≥3 consecutive slices	**100.0 (86.8-100.0)**	**94.8 (89.5-97.9)**
BME in ≥4 consecutive slices	96.2 (80.4-99.9)	98.5 (94.7-99.8)
Majority (≥4/7) reader agreement for definite ASAS positive MRI		
BME in ≥1 SIJ quadrant	100.0 (86.8-100.0)	71.6 (63.2-79.1)
BME in ≥2 SIJ quadrants	100.0 (86.8-100.0)	85.8 (78.7-91.2)
BME in ≥3 SIJ quadrants	100.0 (86.8-100.0)	91.8 (85.8-95.8)
BME in ≥4 SIJ quadrants	**100.0 (86.8-100.0)**	**96.3 (91.5-98.8)**
BME in ≥2 consecutive slices	100.0 (86.8-100.0)	88.1 (81.3-93.0)
BME in ≥3 consecutive slices	**100.0 (86.8-100.0)**	**94.8 (89.5-97.9)**
BME in ≥4 consecutive slices	96.2 (80.4-99.9)	98.5 (94.7-99.8)

Table 2. Predictive values of cut-offs for baseline MRI SIJ lesion scores and slices according to the diagnostic ascertainment of the rheumatologist at follow-up after 4.4 years				
MRI cut-offs	**Sensitivity (95%CI)**	**Specificity (95%CI)**	**PPV**	**NPV**
BME in ≥2 SIJ quadrants	47.8 (35.6-60.2)	82.4 (56.6-96.2)	91.7 (79.3-96.9)	28.0 (22.1-34.8)
BME in ≥3 SIJ quadrants	34.8 (23.7-47.2)	88.2 (63.6-98.5)	92.3 (75.8-97.9)	25.0 (20.7-29.9)
BME in ≥4 SIJ quadrants	**31.9 (21.2-44.2)**	**94.1 (71.3-99.9)**	**95.7 (76.1-99.3)**	**25.4 (21.8-29.4)**
BME in ≥2 consecutive slices	43.5 (31.6-56.0)	82.4 (56.6-96.2)	90.9 (77.6-96.7)	26.4 (21.0-32.7)
BME in ≥3 consecutive slices	**30.4 (19.9-42.7)**	**100 (80.5-100.0)**	**100**	**26.2 (23.3-29.3)**
BME in ≥4 consecutive slices	26.1 (16.3-38.1)	100 (80.5-100.0)	100	25.0 (22.5-27.7)

comparable predictive utility with global MRI assessment. Both specificity of ≥95% for a definite lesion as well as a PPV of ≥95% were considered requirements for preliminary designation of MRI lesion cut-offs defining a positive MRI for active lesions.

Results: Active lesions typical of axSpA were observed by majority read in 39 (35.8%) of 109 cases diagnosed with axSpA, and 1 (2.0%) of 49 cases without axSpA and 26 cases were assigned a high degree of confidence (≥ +3) by a majority of readers. Cut-offs achieving specificity of ≥95% for a definite active lesion were BME at the same location in ≥3 consecutive slices (sensitivity 100%) and BME at any location in ≥4 SIJ quadrants (sensitivity 100%) (Table 1). Both of these cut-offs had very high positive predictive values (≥95%) for diagnosis of axSpA in cases diagnosed by the rheumatologist after 4.4 years follow up (Table 2).

Conclusion: ASAS-defined BME at the same location in ≥3 consecutive slices or in ≥4 SIJ quadrants at any location, are high priority candidates for defining an MRI active lesion typical of axSpA. This will require similar assessment in additional axSpA cohorts.

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2. Rudwaleit et al. Ann Rheum Dis 2009;68: 777-83
3. Maksymowych et al. Ann Rheum Dis May 05 2020

Disclosure: W. Maksymowych, AbbVie, 2, 5, Janssen, 5, Lilly, 5, Pfizer, 2, 5, Novartis, 2, 5, Gilead, 5, UCB Pharma, 5, Boehringer Ingelheim, 5, Galapagos, 5; **X. Baraliakos**, AbbVie, 2, 5, 8, Novartis, 2, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Pfizer, 5, 8, UCB, 5, 8, BMS, 5, 8, Merck, 5, 8, Galapagos, 5; **U. Weber**, None; **P. Machado**, Abbvie, 5, 8, Eli Lilly, 5, Novartis, 5, 8, UCB, 5, 8, Pfizer, 8; **S. Pedersen**, None; **J. Sieper**, AbbVie, 5, Novartis, 5, 8, Lilly, 8, Janssen, 5, Merck, 5, 8; **S. Wichuk**, None; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8; **M. Rudwaleit**, Bristol-Myers Squibb, 5, 8, Chugai Pharmaceutical Co., Ltd., 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Novartis, 5, 8, UCB Pharma, 5, 8, AbbVie, 5, 8, Pfizer, 5, 8, Celgene, 8, Roche, 5, 8, Merck Sharp & Dohme, 5, 8; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5; **R. Landewé**, AbbVie, 2, 5, 8, AstraZeneca, 5, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, Galapagos, 5, Novartis, 5, Pfizer Inc, 2, 5, 8, UCB, 2, 5, 8, GlaxoSmithKline, 5, Janssen, 2, 5, 8, Merck, 5, 8, Rheumatology Consultancy BV, 1, Ablynx, 5, Amgen, 2, 5, 8, Celgene, 5, Gilead, 5, Novo Nordisk, 5, Roche, 2, 5, 8, Schering, 2, 5, 8, TiGenix, 5; **J. Paschke**, None; **M. Østergaard**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Hospira, 5, 8, Janssen, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Novo Nordisk, 5, Orion, 5, 8, Regeneron, 5, Roche, 5, 8, UCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, Boehringer Ingelheim, 5, 8, Sandoz, 5, 8, Sanofi, 5, 8; **R. Lambert**, None.

Abstract Number: 2020

Preliminary Definition of a Positive MRI for Structural Lesions in the Sacroiliac Joints in Axial Spondyloarthritis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes III: Imaging in SpA

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Background/Purpose: There is lack of international consensus as to what defines a structural lesion on MRI of the sacroiliac joints (SIJ) typical of axial spondyloarthritis (axSpA). The ASAS MRI group has generated updated consensus lesion definitions that describe each of the MRI lesions in the SIJ[1] which have been validated by 8 readers from the ASAS-MRI group on MRI images from the ASAS Classification Cohort[2,3]. We aimed to identify quantitative cut-offs based on numbers of slices and SIJ quadrants that define a positive MRI for structural lesions typical of axSpA,

Table 1. Majority readers agree structural lesion indicative of axSpA is present with confidence ≥3/4 is the gold-standard external reference

MRI cut-offs	Sensitivity (95%CI)	Specificity (95%CI)
Erosion in ≥1 SIJ quadrant	93.1 (77.2-99.2)	80.6 (72.4-87.3)
Erosion in ≥2 SIJ quadrants	93.1 (77.2-99.2)	90.8 (84.1-95.3)
Erosion in ≥3 SIJ quadrants	**89.7 (72.6-97.8)**	**95.8 (90.5-98.6)**
Erosion in 2 consecutive slices	**82.8 (64.2-94.2)**	**95.0 (89.3-98.1)**
Fat lesion in ≥1 SIJ quadrant	82.8 (64.2-94.2)	81.5 (73.4-88.0)
Fat lesion in ≥2 SIJ quadrants	69.0 (49.2-84.7)	86.6 (79.1-92.1)
Fat lesion in ≥3 SIJ quadrants	62.1 (42.3-79.3)	91.6 (85.1-95.9)
Fat lesion in ≥4 SIJ quadrants	62.1 (42.3-79.3)	94.1 (88.3-97.6)
Fat lesion in ≥5 SIJ quadrants	**62.1 (42.3-79.3)**	**97.5 (92.8-99.5)**
Fat lesion in ≥2 consecutive slices	55.2 (35.7-73.6)	93.3 (87.2-97.1)
Fat lesion in ≥3 consecutive slices	**51.7 (32.5-70.6)**	**97.5 (92.8-99.5)**
Fat lesion (>1cm extent) ≥1 SIJ quadrant	58.6 (38.9-76.5)	95.0 (89.3-98.1)
Fat lesion (>1cm extent) ≥2 SIJ quadrants	**55.2 (35.7-73.6)**	**95.8 (90.5-98.6)**

Table 2. Predictive values of cut-offs for baseline MRI SIJ lesion scores and slices according to the diagnostic ascertainment of the rheumatologist at follow-up after 4.4 years

MRI cut-offs	Sensitivity (95%CI)	Specificity (95%CI)	PPV	NPV
Erosion in ≥3 SIJ quadrants	38.1 (26.1-51.2)	93.8 (69.8-99.8)	96.0 (77.8-99.4)	27.8 (23.4-32.6)
Erosion in ≥2 consecutive slices	38.1 (26.1-51.2)	93.8 (69.8-99.8)	96.0 (77.8-99.4)	27.8 (23.4-32.6)
Fat lesion in ≥5 SIJ quadrants	31.8 (20.6-44.7)	93.8 (69.8-99.8)	95.2 (74.3-99.3)	25.9 (22.0-30.1)
Fat lesion in ≥3 consecutive slices	30.2 (19.2-43.0)	93.8 (69.8-99.8)	95.0 (73.3-99.2)	25.4 (21.7-29.5)
Fat lesion (>1cm extent) in ≥2 SIJ quadrants	25.4 (15.3-37.9)	100 (79.4-100)	100	25.4 (22.8-28.2)

the gold standard being majority central reader decision as to the presence of a definite structural lesion typical of axSpA with high confidence.

Methods: MRI structural lesions meeting ASAS definitions from 148 cases were recorded in an eCRF that comprises global assessment (Is there a structural lesion typical of axSpA (yes/no) and degree of confidence (-4 (lesion absent) to +4 (lesion present)), and detailed scoring of lesions per SIJ quadrant and per slice. We calculated sensitivity and specificity for numbers of SIJ quadrants and consecutive slices with erosion, sclerosis, and fat lesions where a majority of readers (≥4/7) agreed as to the presence of a structural lesion typical of axSpA with high confidence (≥ +3). We selected cut-offs with ≥95% specificity. These cut-offs were analyzed for their predictive utility for rheumatologist diagnosis of axSpA at follow up (average of 4.4 years) by calculating positive and negative predictive values (PPV, NPV) and selecting those cut-offs with PPV of ≥95% and comparable predictive utility with global MRI assessment. Both specificity of ≥95% for a definite lesion as well as a PPV of ≥95% were considered requirements for preliminary designation of MRI lesion cut-offs defining a positive MRI for structural lesions.

Results: Structural lesions typical of axSpA were observed by majority read in 33 (32.4%) of 102 cases diagnosed with axSpA, and 3 (6.8%) of 44 cases without axSpA and 29 cases were assigned a high degree of confidence (≥ +3) by a majority of readers. Cut-offs achieving specificity of ≥95% for a definite structural lesion were erosion at the same location in ≥2 consecutive slices (sensitivity 83%), erosion at any location in ≥3 SIJ quadrants (sensitivity 90%), fat lesion at any location in ≥5 SIJ quadrants (sensitivity 62%), fat lesion at the same location in ≥3 consecutive slices (sensitivity 52%), and 'deep' fat lesion (≥1cm extent) in ≥2 SIJ quadrant (sensitivity 55.2%) (Table 1). All of these had very high positive predictive values (≥95%) for diagnosis of axSpA in cases diagnosed by the rheumatologist after 4.4 years follow up (Table 2). Combinations of cut-offs for different structural lesions were not superior to single lesion cut-offs.

Conclusion: ASAS-defined erosion in ≥2 consecutive slices or in ≥3 SIJ quadrants, and ASAS-defined fat lesion in ≥3 consecutive slices or in ≥5 SIJ quadrants or 'deep' fat lesion (≥1cm extent) in ≥2 SIJ quadrants are high priority candidates for defining an MRI structural lesion typical of axSpA. This will require similar assessment in additional axSpA cohorts.

1. Maksymowych et al. Ann Rheum Dis 2019; 78:1550-8.
2. Rudwaleit et al. Ann Rheum Dis 2009;68: 777-83
3. Maksymowych et al. Ann Rheum Dis May 05 2020

Disclosure: W. Maksymowych, AbbVie, 2, 5, Janssen, 5, Lilly, 5, Pfizer, 2, 5, Novartis, 2, 5, Gilead, 5, UCB Pharma, 5, Boehringer Ingelheim, 5, Galapagos, 5; **X. Baraliakos**, AbbVie, 2, 5, 8, Novartis, 2, 5, 8, Celgene, 5, 8, Chugai, 5, 8, Pfizer, 5, 8, UCB, 5, 8, BMS, 5, 8, Merck, 5, 8, Galapagos, 5; **U. Weber**, None; **P. Machado**, Abbvie, 5, 8, Eli Lilly, 5, Novartis, 5, 8, UCB, 5, 8, Pfizer, 8; **S. Pedersen**, None; **J. Sieper**, AbbVie, 5, Novartis, 5, 8, Lilly, 8, Janssen, 5, Merck, 5, 8; **S. Wichuk**, None; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8; **M. Rudwaleit**, Bristol-Myers Squibb, 5, 8, Chugai Pharmaceutical Co., Ltd., 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Novartis, 5, 8, UCB Pharma, 5, 8, AbbVie, 5, 8, Pfizer, 5, 8, Celgene, 8, Roche, 5, 8, Merck Sharp & Dohme, 5, 8; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5; **R. Landewé**, AbbVie, 2, 5, 8, AstraZeneca, 5, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, Galapagos, 5, Novartis, 5, Pfizer Inc, 2, 5, 8, UCB, 2, 5, 8, GlaxoSmithKline, 5, Janssen, 2, 5, 8, Merck, 5, 8, Rheumatology Consultancy BV, 1, Ablynx, 5, Amgen, 2, 5, 8, Celgene, 5, Gilead, 5, Novo Nordisk, 5, Roche, 2, 5, 8, Schering, 2, 5, 8, TiGenix, 5; **J. Paschke**, None; **R. Lambert**, None; **M. Østergaard**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Hospira, 5, 8, Janssen, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8,

Novo Nordisk, 5, Orion, 5, 8, Regeneron, 5, Roche, 5, 8, UCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, Boehringer Ingelheim, 5, 8, Sandoz, 5, 8, Sanofi, 5, 8.

Abstract Number: 2021

The Reliability of Scoring Sonographic Entheseal Abnormalities – the Diagnostic Ultrasound Enthesitis Tool (DUET) Study

Lihi Eder[1], Sibel Aydin[2] and Gurjit Kaeley[3], [1]Women's College Research Institute, University of Toronto, Toronto, ON, Canada, [2]University of Ottawa Faculty of Medicine, Rheumatology, Ottawa, ON, CANADA; The Ottawa Hospital Research Institute, Ottawa, ON, CANADA, Ottawa, ON, Canada, [3]University of Florida College of Medicine - Jacksonville, Jacksonville, FL

SESSION INFORMATION

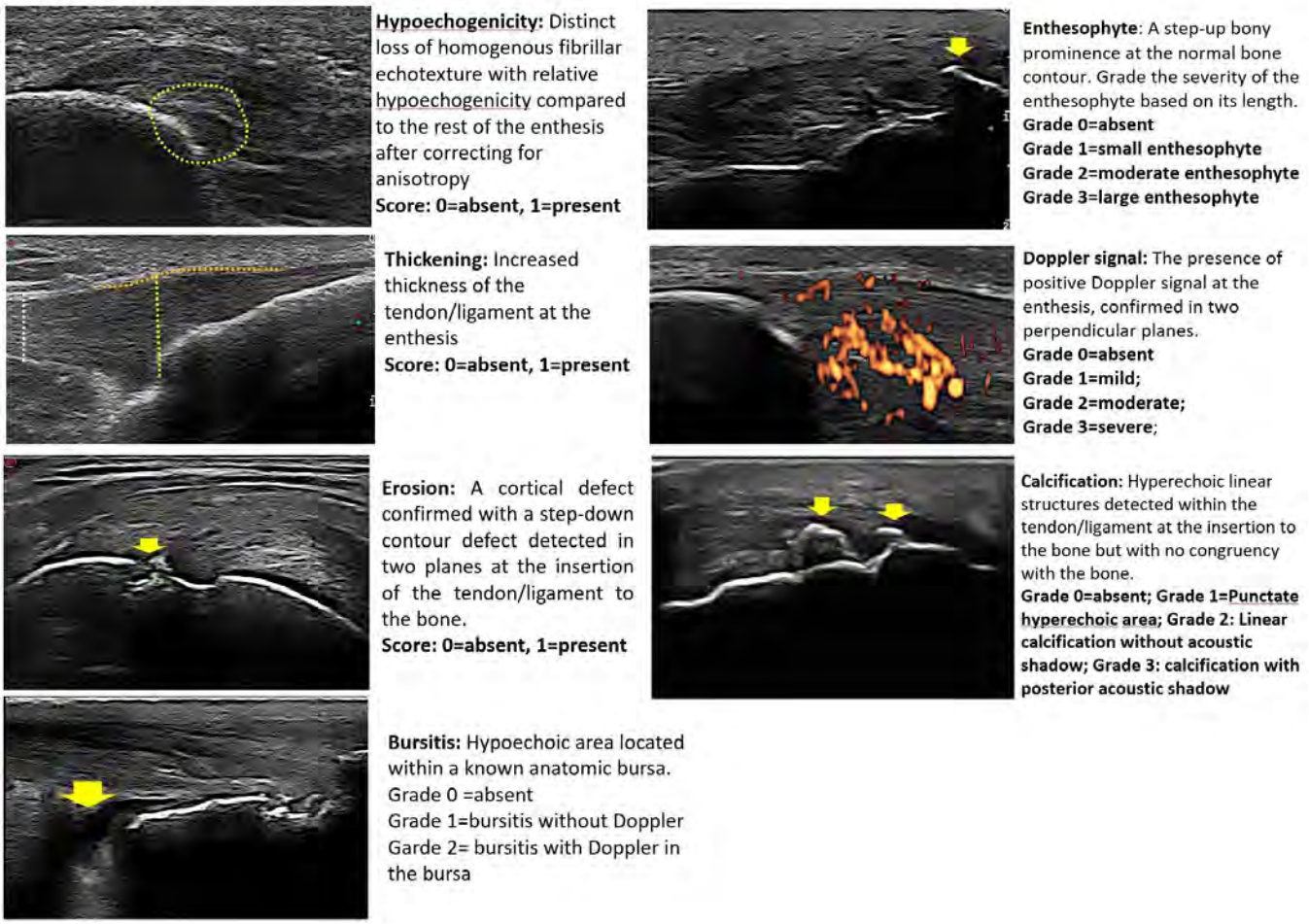
Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes III: Imaging in SpA

Session Type: Abstract Session

Session Time: 5:00PM–5:50PM

Figure 1: Scoring of Sonographic Elementary Lesion – The DUET study



Scoring of Sonographic Elementary Lesion - The DUET Study

Table 1 – Inter-Rater Agreement for Scoring of Entheseal Lesions (N=262 entheseal sites, 18 patients)				
	Rate 1 – Rate 2	Rater 1 – Rater 3	Rater 2 – Rater 3	All Raters
Hypoechogenicity (0-1)	0.49	0.41	0.54	0.47
Thickening (0-1)	0.42	0.46	0.56	0.47
Thickness (mm)*	0.78	0.78	0.79	0.78
Erosions (0-1)	0.79	0.70	0.71	0.73
Enthesophytes (0-3)**	0.69	0.78	0.77	0.75
Calcifications (0-3)**	0.40	0.07	0.18	0.22
Doppler (grade)**	0.84	0.86	0.91	0.87
Bursitis (grade)**	0.55	0.55	0.70	0.60
Total score*	0.79	0.81	0.85	0.82
*ICC **Weighted Kappa				

Inter-Rater Agreement for Scoring of Entheseal Lesions (N=262 entheseal Sites, 18 patients)

Background/Purpose: DUET is a study supported by the Group for Assessment for Psoriasis and Psoriatic Arthritis (GRAPPA) that aims to develop a novel sonographic scoring system for enthesitis to assist with PsA diagnosis. The objectives of the present study are to define the elementary lesions of enthesitis for the DUET study and to assess the inter-rater reliability of the central readers in scoring these lesions.

Methods: The DUET study steering committee, that included three experienced sonographers, reached a consensus regarding the definitions and grading of the sonographic elementary lesions for enthesitis that will be used in the study. The following elementary lesions were considered: hypoechogenicity (yes/no), thickening (yes/no and quantitative), enthesophyte (graded 0-3), erosion (yes/no), calcification (graded 0-3), bursitis (graded 0-2) and Power Doppler (graded 0-3). An atlas with images depicting each elementary lesion was created (Figure 1). For the inter-rater reliability assessment the three readers were asked to score 18 sets of short video clips of ultrasound scans from patients with active PsA. Each set included B-mode and Doppler scans that followed the DUET scanning protocol and included 16 entheseal sites around the knee, ankle, elbow and shoulder. The readers were blinded to the clinical data. Inter-rater reliability was calculated using Kappa statistics (K) for categorical variables and intraclass correlation coefficient (ICC) for continuous variables.

Results: A total of 262 entheseal sites were scored. The prevalence of the elementary lesions (range by reader) were: hypoechogenicity (53.4-54.8%), thickening (26-43.2%), erosion (7.7-10.9%), enthesophyte (48.2-61.3%), calcification (3.4-11.5%), Doppler signal (27.1-42.2%) and bursitis (12-22.5%). The inter-rater agreement ranged from excellent to fair as follows (Table 1): Doppler (K=0.87), enthesophyte (K=0.75), erosion (K=0.73), bursitis (K=0.60), hypoechogenicity (K=0.47), thickening (K=0.47), calcification (K=0.22). Thickness measurement and the total score per entheseal site showed very good inter-rater agreement (ICC of 0.78 and 0.82, respectively). The agreement for hypoechogenicity and thickening varied by site being lowest for the plantar fascia, supraspinatus, quadriceps and lateral epicondyle.

Conclusion: Good agreement was found between expert sonographers for scoring the majority of the entheseal sonographic lesions for the DUET study.

Disclosure: L. Eder, AbbVie, 2, 5, 8, Eli Lilly, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5, 8, Celgene, 5, Novartis, 5; **S. Aydin**, None; **G. Kaeley**, Novartis Pharmaceuticals Corporation, 5.

Abstract Number: 2022

Effects of Anti-TNF-therapy on Osteoblastic Activity in Ankylosing Spondylitis – Results from a Prospective Study Using PET-MRI of SIJ and Spine

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Diagnosis, Manifestations, & Outcomes III: Imaging in SpA
Session Type: Abstract Session
Session Time: 5:00PM–5:50PM

Background/Purpose: The clinical efficacy of TNFi in patients with axSpA is well established but its effect on new bone formation is still unclear. Positron emission tomography (PET) using bone-seeking ^{18}F-Fluoride [18F]F in combination with magnetic resonance imaging ([18F]F/MRI) can depict bone marrow edema (BME) but also shows the quantity of tracer uptake in the late phase of perfusion suggestive of remodeling and osteoblastic activity. We assessed the effect of TNFi on bone remodeling processes in the axial skeleton of r-axSpA patients using [18F]F/MRI prior (baseline, BL) and 4 months after (follow-up, FU) treatment.

Methods: Patients (11 male, 5 female, mean age 38.6±12.0 years) with clinically active AS (BASDAI >4, failure of NSAIDs, no previous biologics) prospectively underwent 3-Tesla and [18F]F PET/MRI (40 minutes after injection of a mean activity of 157 MBq [18F]F). Images of the SIJ (n=16 patients) and the whole spine (n=10 patients) were performed at BL and FU. Three readers (1 for [18F]F/MRI and 2 for conventional MRI) evaluated all images independently and blinded to timepoint allocation. Only lesions on which all readers agreed on were used for further analyses. Inflammation (bone marrow edema, BME), structural lesions (fat deposition (FD), sclerosis, erosions and ankylosis) and focal [18F]F uptake were recorded on the level of SIJ (SIJ-Q) and vertebral quadrants (V-Q), with each SIJ or vertebral body consisting of 4 VQs (superior and inferior sacral and iliac for the SIJ, and superior and inferior, anterior and posterior for the vertebral bodies).

Results: A total of 128 SIJ-Q and 920 VQs were analyzed at both BL and FU. In the SIJs, 75 (58.6%), 120 (93.8%), 69 (53.9%), 99 (77.3%) and 16 (12.5%) SIJ-Q showed BME, FD, sclerosis, erosions and ankylosis, while 111 (86.7%) SIJ-Q showed focal [18F]F-uptake at BL. Association with increased [18F]F-uptake was found most frequently in SIJ-Q with BME (70/75 SIJ-Q, 93.3%), sclerosis (65/69 SIJ-Q, 94.2%) and FD (105/120 SIJ-Q, 87.5%). At FU, 37 SIJ-Q still showed BME (improvement by 50.7%), while almost no changes were observed in chronic lesions. In comparison, improvement of focal [18F]F-uptake was found in all lesion combinations, with improvement of focal [18F]F-lesions associated with BME by 62.9%, with sclerosis by 33.8% and with FD by 22.9% of SIJ-Q.

In the spine, only 41 (4.5%), 61 (6.6%), 14 (1.5%) V-Q showed BME, FD and sclerosis, respectively, while 77 V-Q (8.4%) showed focal [18F]F-uptake. An association to increased [18F]F-uptake was found most frequently with sclerosis (7/14 V-Q, 50%) and FD (25/61 V-Q, 41%). At FU, 12 V-Q still showed BME (improvement by 70.7%), almost no changes were observed for chronic lesions. The largest improvement was found in focal [18F]F-lesions associated with BME 81.8% and with FD by 22.9% of V-Q.

Conclusion: In this first prospective study on whole spine and SIJ [18F]F/MRI in patients with AS, a significant decrease of osteoblastic activity was observed over 4 months of continuous anti-TNF treatment. These data support a short-term effect of anti-TNF treatment on osteoblastic activity, while the long-term effects need to be further studied

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Disclosure: X. Baraliakos, AbbVie, 2, 5, Celgene, 2, 5, Galapagos, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 2, 5, Chugai, 2, 5, MSD, 2, 5, Sandoz, 2, 5, Hexal, 2, 5; **S. Tsiami**, None; **C. Rischpler**, None; **N. Bruckmann**, None; **W. Fendler**, None; **J. Kirchner**, None; **K. Herrmann**, None; **L. Sawicki**, None; **J. Braun**, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, BMS, 2, 5, 8, Boehringer, 2, 5, 8, Celgene, 2, 5, 8, Celltrion, 2, 5, 8, Centocor, 2, 5, 8, Chugai, 2, 5, 8, EBEWE Pharma, 5, 8, Medac, 2, 5, 8, MSD, 2, 5, 8, Mundipharma, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 2023

Efficacy and Safety of Upadacitinib in Patients with Active Ankylosing Spondylitis: 1-Year Results from a Randomized, Double-Blind, Placebo-Controlled Study with Open-Label Extension

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: Emerging Therapies

Session Type: Abstract Session

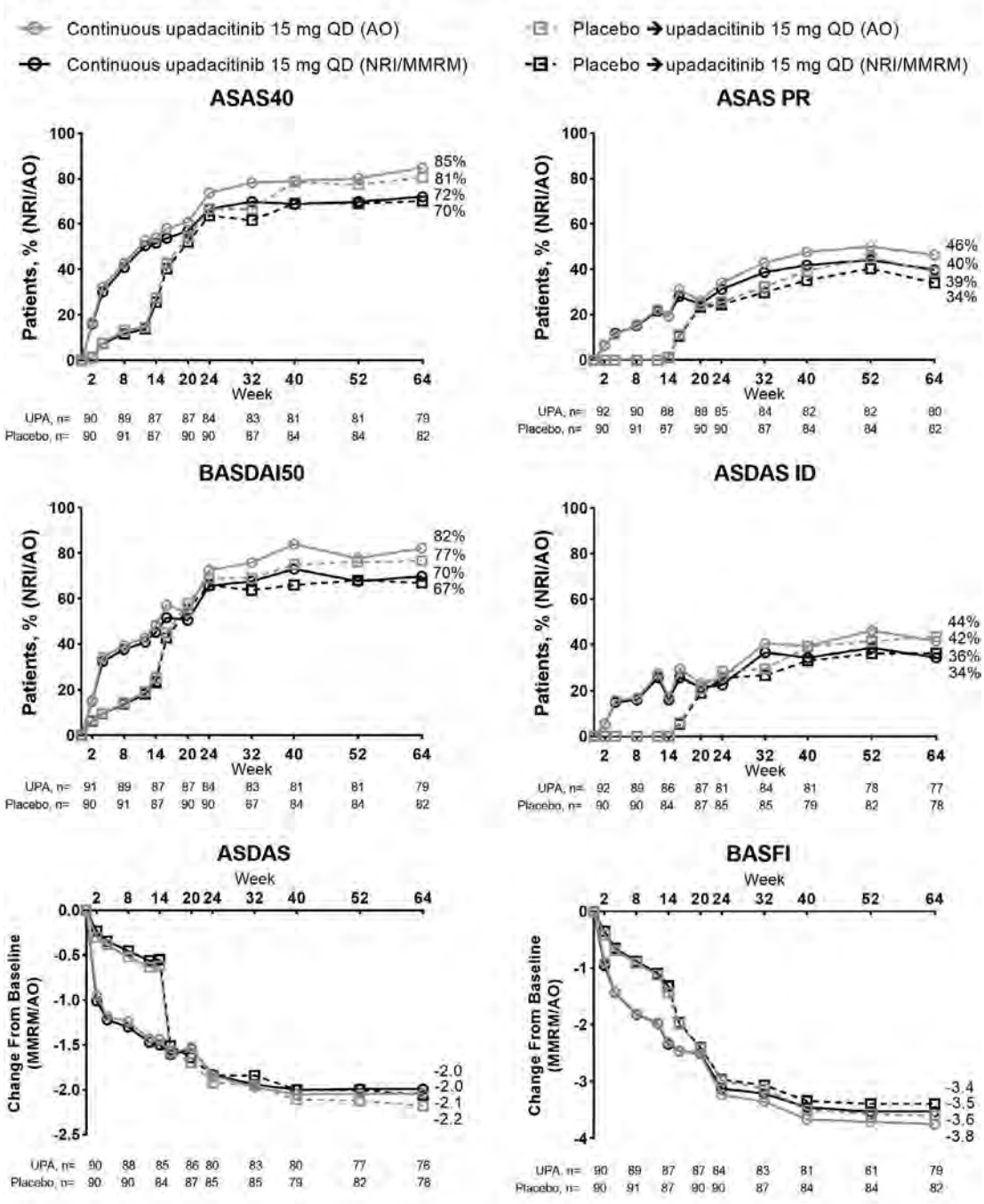
Session Time: 11:00AM–11:50AM

Background/Purpose: Upadacitinib (UPA), a Janus kinase (JAK) inhibitor, was efficacious and well tolerated vs placebo (PBO) during the first 14 weeks (wks) of the phase 2/3 SELECT-AXIS 1 study in patients (pts) with active ankylosing spondylitis (AS) who had an inadequate response to NSAIDs.[1] The objective of this interim analysis was to report efficacy and safety of UPA through 1 year in the SELECT-AXIS 1 study.

Methods: SELECT-AXIS 1 (NCT03178487) included a randomized, placebo-controlled, 14-wk period followed by 90-wk open-label extension; reported here are data up to wk 64. The study enrolled pts (≥18 y) with active AS (defined as BASDAI ≥4 and pt assessment of back pain ≥4 [numeric rating scale, 0–10] at screening and baseline [BL]) who had an inadequate response to ≥2 NSAIDs or intolerance to or contraindication for NSAIDs and were biologic DMARD naive. At BL, pts were randomized 1:1 to UPA 15 mg once daily (QD) or PBO; at wk 14, pts continued in the open-label extension and received UPA 15 mg QD. Efficacy assessments included the percentage of pts with Assessment of SpondyloArthritis international Society (ASAS) 20/40 response, ASAS partial remission, BASDAI50, and AS Disease Activity Score (ASDAS) responses over time and as change from BL in ASDAS and BASFI. Data are reported both as observed and by using non-responder imputation (NRI) for binary or mixed-effect model repeated measures for continuous efficacy endpoints for missing data. Treatment-emergent adverse events (TEAEs) were monitored throughout the study and reported as events per 100 patient-years (PY) up to January 31, 2020.

Results: Of 187 pts, 178 pts (each n=89 for UPA and PBO arms) completed wk 14 on study drug and entered the open-label extension; 160 pts completed wk 64. Efficacy was maintained or continued to improve throughout the study in the continuous UPA group: 85% (95% CI, 77%–93%) of pts achieved ASAS40 at week 64 in the as-ob-

Figure. Efficacy Endpoints Over Time



AO, as observed; ASAS, Assessment of SpondyloArthritis international Society; ASDAS, Ankylosing Spondylitis Disease Activity Score; ID, inactive disease; MMRM, mixed-effect model repeated measures; NRI, non-responder imputation; PR, partial remission; QD, once daily; UPA, upadacitinib.
Dashed line: all patients randomized to placebo received open-label UPA starting from week 14.
N's below the graphs are for as observed analysis. N's for NRI analysis were 94 for placebo to upadacitinib and 93 for continuous upadacitinib.
160 patients completed week 64; lack of efficacy (n=10) and adverse events (n=4) were the most common reasons for discontinuation between weeks 14 and 64.

Figure. Efficacy Endpoints Over Time

Table 1. TEAEs per 100 PYs

Events/(E/100 PY)	UPA 15 mg QD N=182 (237.6 PY)
Any AE	618 (260.1)
Serious AE	14 (5.9)
AE leading to discontinuation	15 (6.3)
Infections	205 (86.3)
Opportunistic infection*	2 (0.8)
Herpes zoster†	5 (2.1)
Creatine phosphokinase elevation‡	28 (11.8)
Hepatic disorder§	24 (10.1)
Neutropenia‖	7 (2.9)
Anemia‖	3 (1.3)
Lymphopenia‖	2 (0.8)
Malignancy¶	1 (0.4)
Death	0

AE, adverse event; PY, patient-year; QD, once daily; TEAE, treatment-emergent AE; UPA, upadacitinib.
*Two non-serious events of esophageal candidiasis in the same patient.
†Five events in 4 patients; all non-serious and limited to 1 dermatome.
‡All events were non-serious and none led to study drug discontinuation; majority were asymptomatic.
§Majority based on asymptomatic alanine aminotransferase/aspartate aminotransferase elevations; all were non-serious and none led to study drug discontinuation.
‖All events were non-serious and none led to study drug discontinuation.
¶Squamous cell carcinoma of tongue in 61-year-old male former smoker; no reasonable possibility to be study drug related per investigator.

Table 1. TEAEs per 100 PYs

served analysis and 72% (63%–81%) in the NRI analysis (**Figure**). Pts who switched from PBO to UPA at wk 14 showed a similar speed of onset and magnitude of response compared with pts who were initially randomized to UPA: 81% (95% CI, 72%–89%) of pts in the as-observed analysis and 70% (61%–80%) of pts in the NRI analysis achieved ASAS40 at wk 64 (**Figure**). Similar results were observed for other efficacy endpoints (**Figure**). Among all 182 pts receiving UPA (237.6 PY), 618 AEs (260.1/100 PY) were reported. AEs leading to discontinuation (15 events [6.3/100 PY]) and serious AEs (14 events [5.9/100 PY]) were low (**Table 1**). No serious infections, active tuberculosis, venous thromboembolic events, gastrointestinal perforation, major adverse cardiovascular events, renal dysfunction, or deaths were reported.

Conclusion: UPA 15 mg QD showed sustained and consistent efficacy over 1 year. Pts who switched from placebo to UPA at wk 14 showed a similar efficacy response compared with those who received continuous UPA. No new safety findings were observed compared with safety data from the UPA clinical development program in other indications.[2]

1. van der Heijde D, et al. *Lancet*. 2019;394(10214):2108-2117.
2. Cohen, et al. *Arthritis Rheumatol*. 2019;71(suppl 10).

Disclosure: A. Deodhar, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmith-Kline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5; **J. Sieper**, AbbVie, 5, Novartis, 5, 8, Lilly, 8, Janssen, 5, Merck, 5, 8; **F. Van den Bosch**, AbbVie, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Gilead, 5, Merck, 5, 8; **W. Maksymowych**, AbbVie, 2, 5, Janssen, 5, Lilly, 5, Pfizer, 2, 5, Novartis, 2, 5, Gilead, 5, UCB Pharma, 5, Boehringer Ingelheim, 5, Galapagos, 5; **T. Kim**, AbbVie, 1, Celltrion, 1, Kirin, 1, Lilly, 1, Novartis, 1; **M. Kishimoto**, AbbVie, 1, 2, Amgen-Astellas BioPharma, 1, 2, Asahi-Kasei Pharma, 1, 2, Astellas, 1, 2, Ayumi Pharma, 1, 2, BMS, 1,

2, Chugai, 1, 2, Daiichi-Sankyo, 1, 2, Eisai, 1, 2, Eli Lilly, 1, 2, Gilead, 1, 2, Janssen, 1, 2, Kyowa Kirin, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, Tanabe-Mitsubishi, 1, 2, Teijin Pharma, 1, 2, UCB Pharma, 1, 2, Celgene, 5, 8; **A. Östör**, AbbVie, 5, Roche, 5, Janssen, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, Gilead, 5, Paradigm, 5, UCB Pharma, 5, Bristol-Myers Squibb, 5; **B. Combe**, AbbVie, 5, 8, Janssen, 5, Eli Lilly, 2, 5, 8, Novartis, 2, Gilead Sciences, Inc., 5, 8, Roche-Chugai, 5, 8, Sanofi, 5, Pfizer, 2, 8, MSD, 8, Bristol-Myers Squibb, 8; **Y. Sui**, AbbVie Inc, 1; **X. Wang**, AbbVie Inc., 1; **A. Chu**, AbbVie Inc., 1, 3, 4; **I. Song**, AbbVie, 1, 3.

Abstract Number: 2024

Effects of Filgotinib on Spinal Lesions in Patients with Ankylosing Spondylitis: Magnetic Resonance Imaging Data from the Placebo-Controlled, Double-Blind, Randomized TORTUGA Trial

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: Emerging Therapies
Session Type: Abstract Session
Session Time: 11:00AM–11:50AM

Background/Purpose: The oral, selective Janus kinase 1 inhibitor filgotinib (FIL) significantly improved Spondyloarthritis Research Consortium of Canada (SPARCC) MRI inflammation scores (bone marrow edema) in the spine and sacroiliac joints vs placebo (PBO) in the Phase 2 TORTUGA trial (NCT03117270) in patients with active ankylosing spondylitis (AS; van der Heijde D, et al. *Lancet* 2018;392:2378–87). The current post hoc analysis evaluated the effects of FIL on Canada-Denmark (CANDEN) MRI measures of spinal inflammation and structural lesions in patients from the TORTUGA trial.

Methods: TORTUGA was a PBO-controlled, multicenter, double-blind, randomized trial in which 116 patients with active AS (as per modified New York classification criteria, with sacroiliitis confirmed by central reading) were treated with FIL 200 mg (n=58) or PBO (n=58) once daily for 12 weeks. MRIs of the total spine were conducted at baseline and at the end of treatment. Scans were re-evaluated post hoc by 2 independent experts (blinded to time point and assigned treatment) according to the detailed anatomy-based CANDEN method (Krabbe S, et al. *RMD Open* 2019;5:e001057); inter-reader discrepancies were resolved by an independent adjudicator. Observed changes from baseline were evaluated using analysis of covariance with factors for treatment, baseline value, and randomization stratification by prior TNF inhibitor use. Least-squares mean changes from baseline and between-group differences with 95% confidence intervals were calculated; p-values are nominal.

Results: MRI scans from 88 patients (47 FIL, 41 PBO) with an evaluable MRI at baseline and Week 12 (or early termination visit) were re-evaluated. Baseline characteristics were generally similar between subjects with and without an MRI scan. Of those with MRI scans, mean total spine inflammation score (which ranges from 0 to 614) was higher in the FIL vs PBO group and mean ankylosis score (which ranges from 0 to 460) was lower in the FIL group vs PBO at baseline (Table 1). Total spine inflammation scores decreased from baseline in the FIL group but not in the PBO group (Figure; Table 2; p=0.0003 for between-group difference). Cumulative probability plots favored FIL over PBO

Characteristic	Filgotinib (n=47)	Placebo (n=41)	All (N=88)
Age, years	40.4 (11.40)	42.0 (9.09)	41.1 (10.36)
Male sex, % of patients	76.6	73.2	75.0
Time since diagnosis, years	5.3 (5.38)	7.8 (8.44)	6.5 (7.04)
HLA-B27 positivity, % of patients	95.3	92.1	93.8
ASDAS	4.3 (0.53)	4.2 (0.71)	4.2 (0.62)
MRI SPARCC spine	20.6 (20.54)	15.6 (21.33)	18.2 (20.94)
MRI SPARCC SIJ	7.9 (11.58)	4.9 (6.28)	6.5 (9.56)
MASES	4.9 (2.74)	4.4 (3.01)	4.7 (2.86)
CANDEN ankylosis score, % of patients			
0–100	95.7	85.4	90.9
>100–200	2.1	12.2	6.8
>200	2.1	2.4	2.3
Total CANDEN spine inflammation score	18.0 (21.35)	11.8 (17.05)	15.1 (19.61)
Total CANDEN spine fat score	15.4 (27.63)	11.9 (16.33)	13.8 (23.01)
Total CANDEN spine bone erosion score	0.5 (1.13)	0.3 (0.57)	0.4 (0.91)
Total CANDEN ankylosis score	15.4 (42.11)	31.1 (54.99)	22.7 (48.89)
Previous TNF inhibitor therapy, % of patients	8.5	12.2	10.2

Table 1. Demographics and baseline characteristics for patients with an MRI scan. Data are mean (SD) unless otherwise indicated. ASDAS, Ankylosing Spondylitis Disease Activity Score; CANDEN, Canada-Denmark; HLA, human leukocyte antigen; MASES, Maastricht Ankylosing Spondylitis Enthesitis Score; MRI, magnetic resonance imaging; SD, standard deviation; SIJ, sacroiliac joint; SPARCC, Spondyloarthritis Research Consortium of Canada; TNF, tumor necrosis factor

for change from baseline in subregion inflammation scores, including postero-lateral elements (i.e. sum of lesions in ribs, transverse processes, spinous processes, soft tissue inflammation and posterolateral vertebral body), facet joint (Figure), and vertebral body. Total spine fat lesion scores numerically increased from baseline in the FIL group but decreased in the PBO group (p=0.0878 for between-group difference; Table 2). There were no statistically significant differences between groups for changes in erosion (p=0.1956) or ankylosis (p=0.2203) scores (Table 2).

Conclusion: Compared with PBO, FIL decreased inflammation, including in the postero-lateral elements of the spine and facet joints, which has not been demonstrated previously in a PBO-controlled trial. As expected in a 12-week study period, no changes in erosion or ankylosis were seen. Due to the imbalance in MRI measures at baseline and post hoc nature of the analysis, our findings need to be confirmed in a large trial.

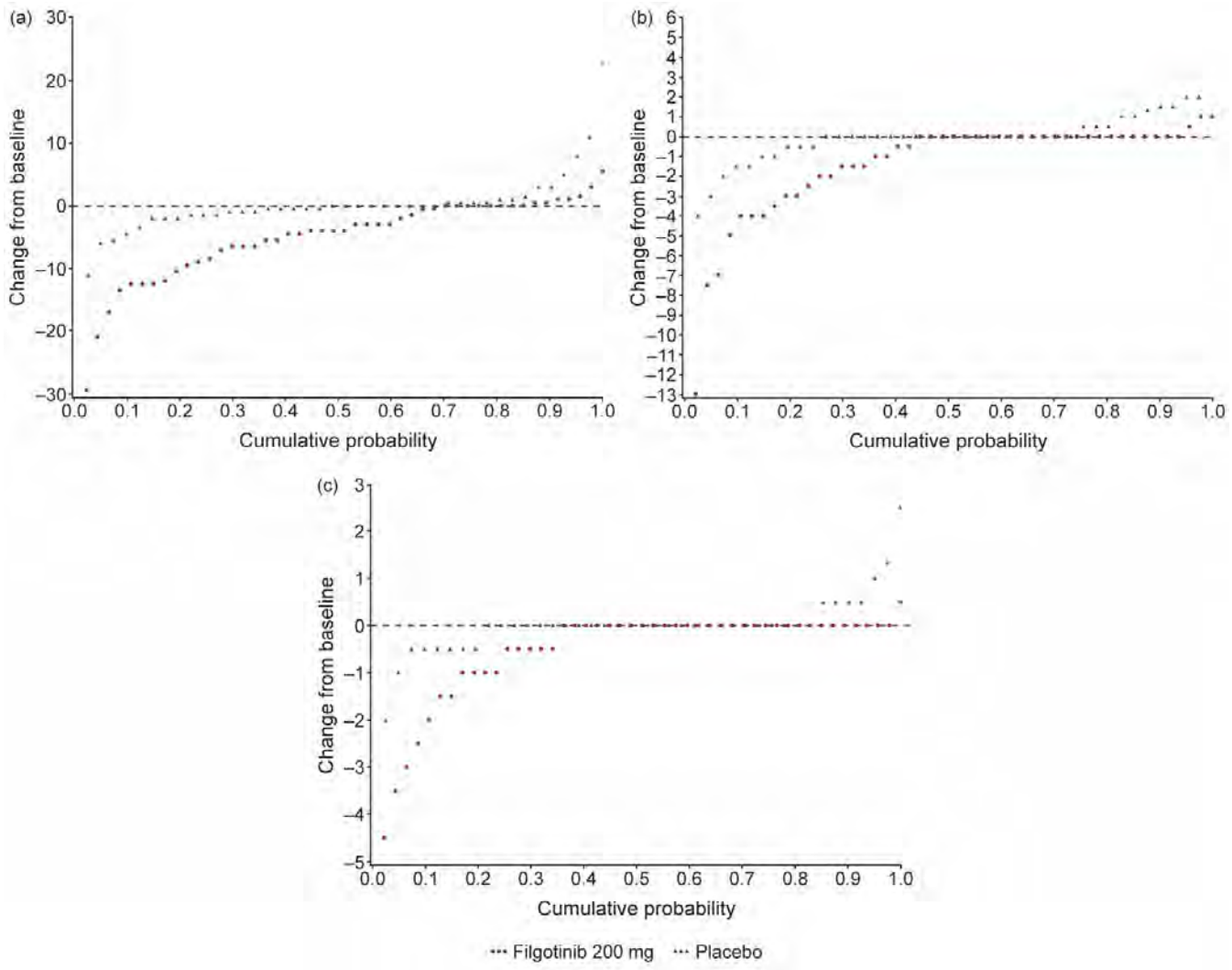

Figure 1. Change from baseline in (a) total CANDEN spine inflammation score, (b) posterior elements inflammation subregion score, and (c) facet joint inflammation subregion score. CANDEN, Canada-Denmark

	Treatment group	N	Sample mean (SE)	LS mean (SE)	95% CI of treatment mean	LS mean of group difference (SE)	95% CI of group difference	Between-group p-value
Total spine inflammation score	Filgotinib	47	–4.98 (0.96)	–4.40 (1.13)	–6.65, –2.15	–4.49 (1.21)	–6.85, –2.12	0.0003
	Placebo	41	0.29 (0.78)	0.09 (1.13)	–2.17, 2.34			
Total spine fat score	Filgotinib	47	1.01 (0.62)	1.09 (0.66)	–0.22, 2.40	1.18 (0.69)	–0.18, 2.55	0.0878
	Placebo	41	–0.25 (0.19)	–0.09 (0.66)	–1.40, 1.21			
Total spine bone erosion score	Filgotinib	47	0.01 (0.02)	0.07 (0.03)	0.00, 0.14	0.05 (0.04)	–0.02, 0.12	0.1956
	Placebo	41	–0.02 (0.03)	0.02 (0.03)	–0.04, 0.09			
Ankylosis score	Filgotinib	47	0.11 (0.08)	0.08 (0.08)	–0.07, 0.24	0.10 (0.08)	–0.06, 0.27	0.2203
	Placebo	41	0.00 (0.00)	–0.02 (0.08)	–0.18, 0.14			

Table 2. Change from baseline at Week 12 in CANDEN total spine inflammation, total spine fat, total spine bone erosion, and ankyloses scores. CANDEN, Canada-Denmark; CI, confidence interval; LS, least squares; SE, standard error

Disclosure: W. Maksymowych, CARE Arthritis Limited, 9, AbbVie, 2, 5, 8, Boehringer Ingelheim, 5, Celgene, 5, Eli Lilly, 5, Galapagos, 5, Janssen, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, UCB, 2, 5, 8; **M. Østergaard**, AbbVie, 2, 5, 8, Celgene, 2, 5, 8, Hospira, 5, 8, Janssen, 5, 8, Merck, 2, 5, 8, Novartis, 2, 5, 8, Novo Nordisk, 5, Orion, 5, 8, Regeneron, 5, Roche, 5, 8, UCB, 5, 8, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 5, 8, Pfizer, 5, 8, Boehringer Ingelheim, 5, 8, Sandoz, 5, 8, Sanofi, 5, 8; **R. Landewé**, AbbVie, 2, 5, 8, AstraZeneca, 5, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, Galapagos, 5, Novartis, 5, Pfizer Inc, 2, 5, 8, UCB, 2, 5, 8, GlaxoSmithKline, 5, Janssen, 2, 5, 8, Merck, 5, 8, Rheumatology Consultancy BV, 1, Ablynx, 5, Amgen, 2, 5, 8, Celgene, 5, Gilead, 5, Novo Nordisk, 5, Roche, 2, 5, 8, Schering, 2, 5, 8, TiGenix, 5; **W. Barchuk**, Gilead Sciences, 1, 3, AbbVie, 9, Eli Lilly, 9, Johnson & Johnson, 9; **K. Liu**, Gilead Sciences, 1, 3; **C. Tasset**, Galapagos, 1, 3; **L. Gilles**, Galapagos, 3; **T. Hendrikx**, Galapagos, 1, 3; **R. Besuyen**, Galapagos, 1, 3; **X. Baraliakos**, AbbVie, 2, 5, Celgene, 2, 5, Galapagos, 2, 5, Janssen, 2, 5, Eli Lilly, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, UCB, 2, 5, Bristol-Myers Squibb, 2, 5, Chugai, 2, 5, MSD, 2, 5, Sandoz, 2, 5, Hexal, 2, 5.

Abstract Number: 2025

Efficacy of Guselkumab, a Monoclonal Antibody That Specifically Binds to the p19 Subunit of IL-23, on Axial-Related Endpoints in Patients with Active PsA with Imaging-Confirmed Sacroiliitis: Week-52 Results from Two Phase 3, Randomized, Double-blind, Placebo-controlled Studies

Philip Mease[1], Philip Helliwell[2], Dafna Gladman[3], Denis Poddubnyy[4], Xenofon Baraliakos[5], Soumya Chakravarty[6], Alexa Kollmeier[7], Elizabeth Hsia[8], Xie Xu[9], Shihong Sheng[10], Prasheen Agarwal[10], Bei Zhou[10], May Shawi[11], Chetan Karyekar[12], Kristen Sweet[10], Atul Deodhar[13] and Désirée van der Heijde[14], [1]Seattle Rheumatology Associates, P.L.L.C., Seattle, WA, [2]Leeds Institute of Rheumatic and Musculoskeletal Medicine, University of Leeds, Leeds, United Kingdom, [3]Krembil Research Institute, Toronto Western Hospital, Toronto, ON, Canada, [4]Charité – Universitätsmedizin Berlin, Berlin, Germany, [5]Rheumazentrum Ruhrgebiet Herne, Ruhr-University Bochum, Bochum, Germany, [6]Janssen Scientific Affairs, LLC, Horsham, PA, USA and Drexel University College of Medicine, Horsham, PA, [7]Janssen Research & Development, LLC, La Jolla, CA, [8]Janssen Research & Development, LLC and University of Pennsylvania Medical Center, Spring House, PA, [9]Janssen Research & Development, LLC, San Marcos, CA, [10]Janssen Research & Development, LLC, Spring House, PA, [11]Janssen Global Services, LLC, Toronto, ON, Canada, [12]Janssen Global Services, LLC, Horsham, PA, [13]Oregon Health & Science University, Portland, OR, [14]Leiden University Medical Center, Leiden, Netherlands

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: Emerging Therapies

Session Type: Abstract Session

Session Time: 11:00AM–11:50AM

Background/Purpose: Guselkumab (GUS), an interleukin-23 inhibitor, improved axial symptoms of active psoriatic arthritis (PsA) through week 24 in a pooled analysis from two phase 3 trials (DISCOVER-1 and DISCOVER-2).[1] We now report the efficacy of GUS through 1 year in PsA patients (pts) with imaging-confirmed sacroiliitis in DISCOVER-1&2.

Methods: In DISCOVER-1, 381 pts with active PsA (≥ 3 swollen joints, ≥ 3 tender joints; C-reactive protein ≥ 0.3mg/dL despite standard therapies) and in DISCOVER-2, 739 pts with active PsA (≥ 5 swollen joints, ≥ 5 tender joints, CRP ≥ 0.6mg/dL despite standard therapies) were randomized 1:1:1 to GUS 100mg q4w, GUS 100mg q8w (wk0, wk4, then q8w), or placebo (PBO). PBO pts crossed over to GUS 100mg q4w at wk24. Only pts with sacroiliitis at baseline who had either documented imaging confirmation of sacroiliitis in the past or pelvic radiograph confirmation of sacroiliitis at screening (based on investigators' judgment) were included in this analysis (pooled data from DISCOVER

Table. Efficacy results of GUS at weeks 24 and 52 in PsA patients with axial involvement.[a]

	GUS100 mg every 4 weeks (n=103)	GUS 100 mg every 8 weeks (n=91)	PBO →GUS 100 mg every 4 weeks (n=118)
Week 24			
LS Mean change in BASDAI (0-10)	-2.7*	-2.7*	-1.3
LS Mean change in spinal pain[b]	-2.5*	-2.7*	-1.2
LS Mean change in modified BASDAI[d]	-2.6*	-2.7*	-1.4
BASDAI50[c], %	(38%) 36/95**	(40%) 34/84 **	(19%) 21/110
LS Mean change in ASDAS	-1.4*	-1.4*	-0.7
Week 52			
LS Mean change in BASDAI (0-10)	-3.1	-2.8	-2.8
LS Mean change in spinal pain[b]	-3.0	-2.7	-2.7
LS Mean change in modified BASDAI[d]	-3.1	-2.7	-2.8
BASDAI50[c], %	48% (46/95)	43% (36/84)	49% (54/110)
LS Mean change in ASDAS	-1.7	-1.6	-1.6

[a]Pts with axial involvement consistent with sacroiliitis at baseline and either a history of imaging confirmation or pelvic radiograph at screening (pooled data from DISCOVER-1 & 2)
[b]Question 2 of the BASDAI.
[c] Excludes question 3 of the BASDAI.
[d]Pts with BASDAI > 0 at baseline.
Unadjusted p-values as noted: *$p < 0.001$, ** $p < 0.01$. No statistical comparisons were performed at week 52.

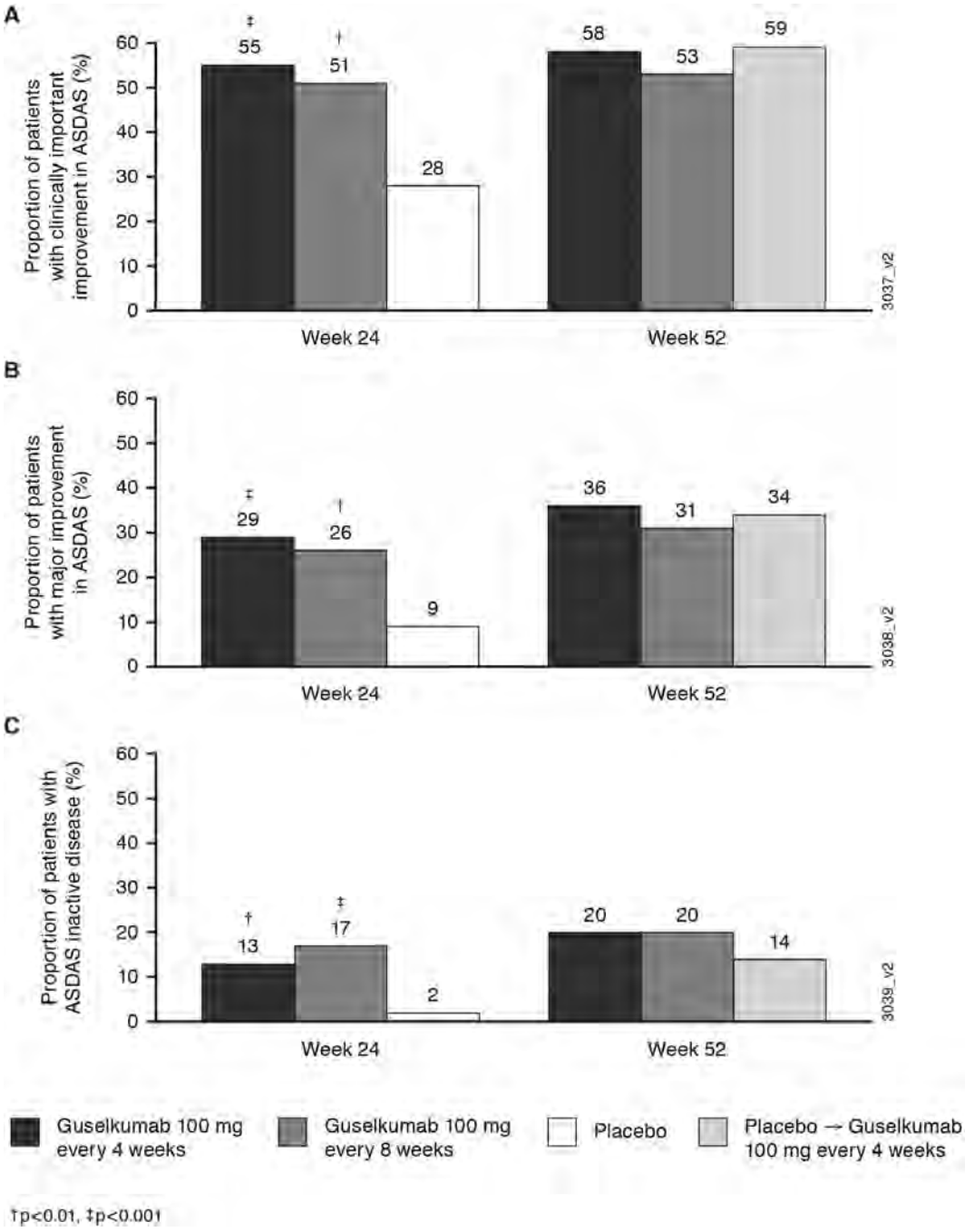

Figure. Proportion of patients with ASDAS clinically important improvement, major improvement, and inactive disease

1&2). Efficacy was assessed by BASDAI score, BASDAI50, modified BASDAI (mBASDAI; excludes Q#3), spinal pain (BASDAI Q#2), ASDAS(-CRP) score, and ASDAS responses of inactive disease (< 1.3), major improvement (decrease ≥2.0), and clinically important improvement (decrease ≥1.1) through week 52. For response endpoints, pts who met treatment failure rules or had missing data were counted as nonresponders through week 24; pts with missing data were counted as nonresponders from weeks 24-52. For changes in scores, a change of 0 was assigned for treatment failures through week 24, and pts who discontinued or had missing data were set to 0 for weeks 24-52. HLA-B27 was assayed in a subset of 190 of these pts.

Results: 312 pts across both studies presented with imaging confirmed sacroiliitis (PBO, n = 118; GUS q8w, n = 91; GUS q4w, n = 103). At baseline, mean BASDAI and ASDAS scores ranged from 6.5 - 6.6 and 3.9 - 4.0, respectively;

57/190 (30%) pts were HLA-B27+, and 133/190 (70%) were HLA-B27-. Improvements in axial symptoms of PsA were greater in the GUS q4w and q8w groups vs PBO through week 24. The LS mean changes from baseline in BASDAI, spinal pain, mBASDAI, and ASDAS were maintained from week 24 to week 52 in the GUS groups (Table); improvements from baseline to week 52 in the PBO pts who crossed over to GUS were similar to those in the GUS groups. Similar trends were observed for the proportions of pts achieving BASDAI50 (Table) and ASDAS responses of inactive disease, major improvement, and clinically important improvement (Figure) at week 52. Efficacy at week 52 trended similarly between HLA-B27+ and HLA-B27- pts.

Conclusion: Improvements in axial symptoms were maintained through week 52 in GUS-treated pts with active PsA who had imaging-confirmed sacroiliitis.

Reference

1. Helliwell P, Gladman D, Poddubnyy D, et al. Efficacy of Guselkumab, a Monoclonal Antibody that Specifically Binds to the p19 Subunit of IL-23, on Endpoints Related to Axial Involvement in Patients with Active PsA with Imaging-Confirmed Sacroiliitis: Week-24 Results from Two Phase 3, Randomized, Double-blind, Placebo-controlled Studies. EULAR 2020.

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Abstract Number: 2026

Efficacy and Safety of Upadacitinib versus Placebo and Adalimumab in Patients with Active Psoriatic Arthritis and Inadequate Response to Non-Biologic Disease-Modifying Anti-Rheumatic Drugs: A Double-Blind, Randomized Controlled Phase 3 Trial

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: Emerging Therapies

Session Type: Abstract Session

Session Time: 11:00AM–11:50AM

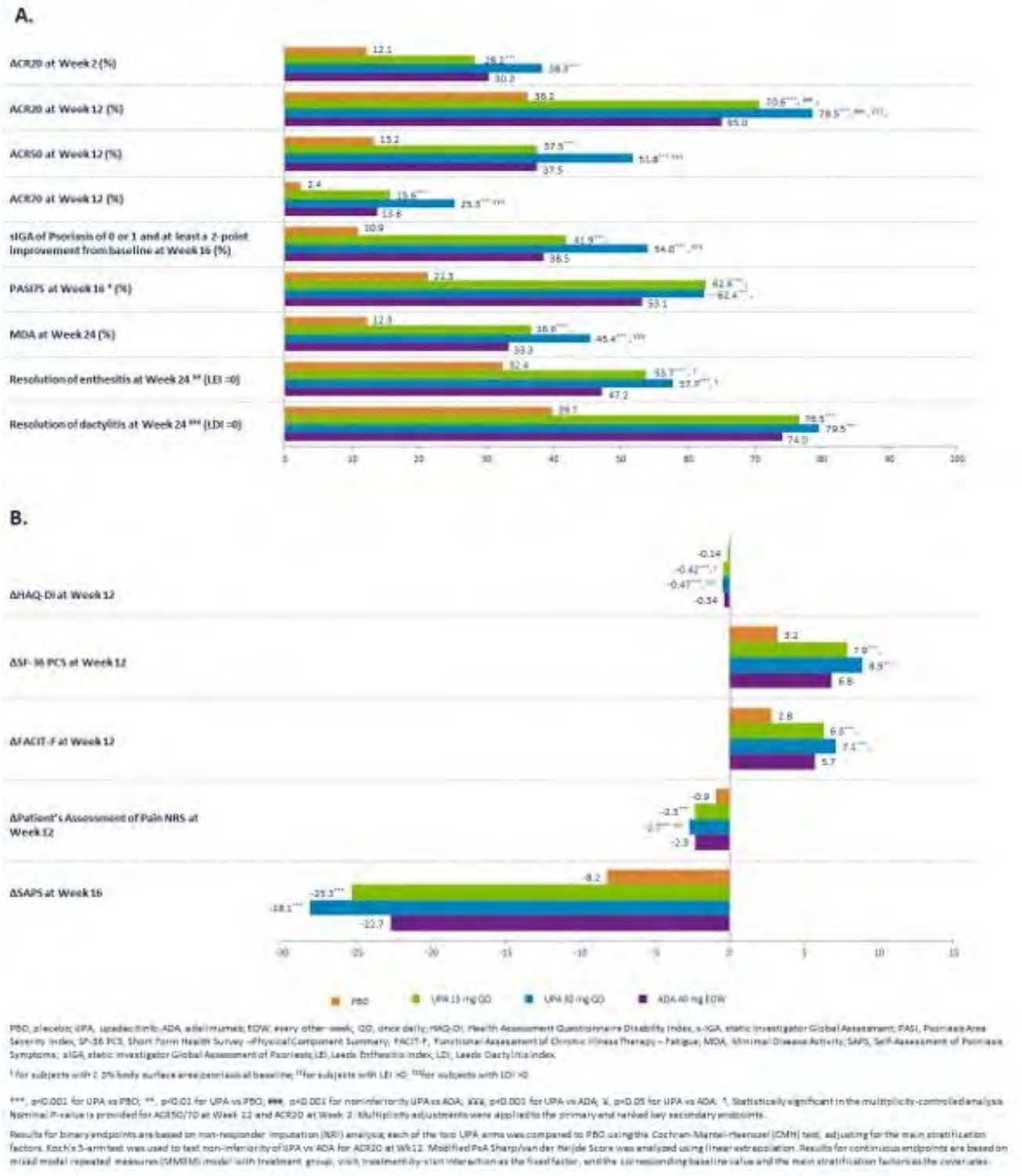
Background/Purpose: Upadacitinib (UPA), an oral, reversible, JAK inhibitor approved to treat rheumatoid arthritis (RA), is under evaluation for psoriatic arthritis (PsA). We assess efficacy and safety of UPA vs placebo (PBO) and adalimumab (ADA) in patients (pts) with PsA and prior IR or intolerance to ≥1 non-biologic DMARD (non-bDMARD).

Methods: Pts with active PsA (≥3 swollen and ≥3 tender joints), active or historical psoriasis, and on ≤2 non-bDMARDs were randomized 1:1:1:1 to once daily UPA 15 mg (UPA15), UPA 30 mg (UPA30), ADA 40 mg every other week, or PBO. Primary endpoint was proportion of pts achieving ACR20 for UPA vs PBO at Wk 12. Multiplicity controlled secondary endpoints for each dose of UPA vs PBO included change in HAQ-DI, FACIT-F, and SF-36 PCS (Wk 12); static Investigator Global Assessment of Psoriasis of 0 or 1, PASI75, and change in Self-Assessment of Psoriasis Symptoms (Wk 16); change in modified Sharp/van der Heijde Score (mTSS), proportion of pts achieving MDA, and resolution of enthesitis (LEI=0) and dactylitis (LDI=0) (Wk 24). For each dose of UPA, the multiplicity-controlled analysis also included non-inferiority and superiority vs ADA for ACR20 and superiority for HAQ-DI and pt's assessment of pain NRS (Wk 12). ACR50/70 at Wk 12 and ACR20 at Wk 2 were additional secondary endpoints. Adverse events (AEs) through 24 wks are reported for pts who received ≥1 dose of study drug.

Results: 1705 pts were randomized; 1704 received study drug (53.2% female, mean age 50.8 yrs, mean duration of PsA diagnosis 6.1 yrs). 82% were on ≥1 concomitant non-bDMARD, of whom 84% received MTX +/- another non-bDMARD.

At Wk 12, ACR20 rates were 70.6% with UPA15 and 78.5% with UPA30 vs 36.2% with PBO ($p < .001$ for UPA15/30 vs PBO) and 65.0% with ADA (non-inferiority, $p < .001$ for UPA15/30 vs ADA; superiority, $p < .001$ for UPA30 vs ADA). A greater proportion of pts achieved ACR50/70 with UPA15/30 vs PBO and UPA30 vs ADA. Improvements were observed with UPA15/30 vs PBO for all multiplicity controlled secondary endpoints and for UPA 15/30 vs ADA for HAQ-DI and UPA 30 vs ADA for improvement in pain (**Figure 1A and 1B**). At Wk 24, change in mTSS was 0.25 for PBO, -0.04 for UPA15, 0.03 for UPA30, and 0.01 for ADA ($p < 0.001$ for UPA15/30 vs PBO). AE/SAE rates, including serious infections, were similar in PBO, UPA15, and ADA arms and higher with UPA30 (**Figure 2**). Herpes zoster rates

Figure 1. Efficacy Outcomes



PBO, placebo; UPA, upadacitinib; ADA, adalimumab; EOW, every other week; QD, once daily; HAQ-DI, Health Assessment Questionnaire Disability Index; s-IGA, static Investigator Global Assessment; PASI, Psoriasis Area Severity Index; SF-36 PCS, Short Form Health Survey –Physical Component Summary; FACIT-F, Functional Assessment of Chronic Illness Therapy – Fatigue; MDA, Minimal Disease Activity; SAPS, Self-Assessment of Psoriasis Symptoms; sIGA, static Investigator Global Assessment of Psoriasis; LEI, Leeds Enthesitis Index; LDI, Leeds Dactylitis Index.

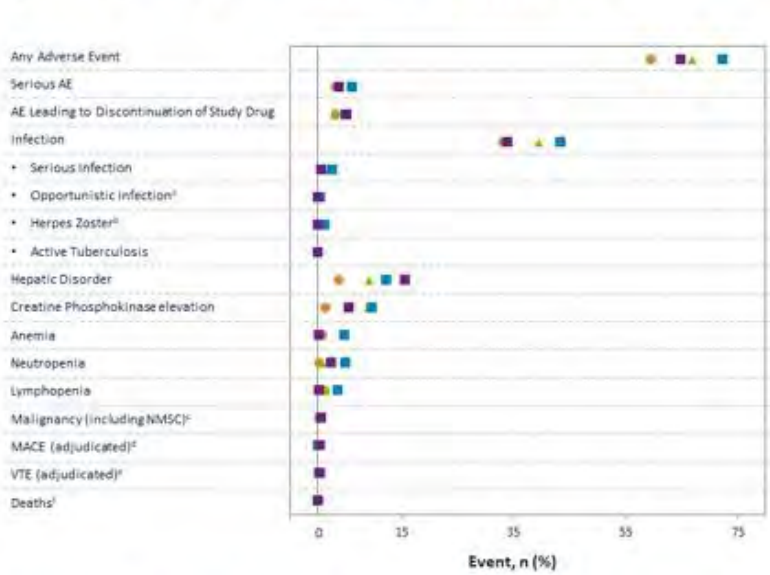
† for subjects with ≥ 3% body surface area psoriasis at baseline; ‡‡for subjects with LEI >0; ‡‡‡for subjects with LDI >0

***, p<0.001 for UPA vs PBO; **, p<0.01 for UPA vs PBO; ###, p<0.001 for non-inferiority UPA vs ADA; ¥¥¥, p<0.001 for UPA vs ADA; ¥, p<0.05 for UPA vs ADA; ↑, Statistically significant in the multiplicity-controlled analysis. Nominal P-value is provided for ACR50/70 at Week 12 and ACR20 at Week 2. Multiplicity adjustments were applied to the primary and ranked key secondary endpoints.

Results for binary endpoints are based on non-responder imputation (NRI) analysis; each of the two UPA arms was compared to PBO using the Cochran-Mantel-Haenszel (CMH) test, adjusting for the main stratification factors. Koch's 5-arm test was used to test non-inferiority of UPA vs ADA for ACR20 at Wk12. Modified PsA Sharp/van der Heijde Score was analyzed using linear extrapolation. Results for continuous endpoints are based on mixed model repeated measures (MMRM) model with treatment group, visit, treatment-by-visit interaction as the fixed factor, and the corresponding baseline value and the main stratification factors as the covariates.

were similar for PBO and UPA15/30. No MACE was reported with UPA. One malignancy occurred in each PBO and UPA15 arms, and 3 malignancies occurred in each UPA30 and ADA arms. VTE were reported in 1 pt on PBO, 1 pt on UPA30, and 2 pts on ADA. One death occurred in the PBO arm.

Figure 2. Safety Summary Through Week 24



	PBO N=423; n (%)	UPA 15 mg QD N=429; n (%)	UPA 30 mg QD N=423; n (%)	ADA 40 MG EOW N=429; n (%)
Any Adverse Event	252 (59.6)	287 (66.9)	306 (72.3)	278 (64.8)
Serious AE	13 (3.1)	14 (3.3)	26 (6.1)	16 (3.7)
AE Leading to Discontinuation of Study Drug	13 (3.1)	13 (3.0)	21 (5.0)	22 (5.1)
Infection	140 (33.1)	169 (39.4)	183 (43.3)	146 (34.0)
• Serious Infection	4 (0.9)	5 (1.2)	11 (2.6)	3 (0.7)
• Opportunistic infection[a]	0	1 (0.2)	2 (0.5)	0
• Herpes Zoster[b]	3 (0.7)	4 (0.9)	5 (1.2)	0
• Active Tuberculosis	0	0	0	0
Hepatic Disorder	16 (3.8)	39 (9.1)	52 (12.3)	67 (15.6)
Creatine Phosphokinase elevation	6 (1.4)	38 (8.9)	41 (9.7)	24 (5.6)
Anemia	4 (0.9)	3 (0.7)	20 (4.7)	1 (0.2)
Neutropenia	1 (0.2)	4 (0.9)	21 (5.0)	10 (2.3)
Lymphopenia	5 (1.2)	6 (1.4)	15 (3.5)	1 (0.2)
Malignancy (including NMSC)[c]	1 (0.2)	1 (0.2)	3 (0.7)	3 (0.7)
MACE (adjudicated)[d]	1 (0.2)	0	0	2 (0.5)
VTE (adjudicated)[e]	1 (0.2)	0	1 (0.2)	2 (0.5)
Deaths[f]	1 (0.2)	0	0	0

PBO, placebo; UPA, upadacitinib; ADA, adalimumab; QD, once daily; EOW, every other week; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular event; VTE, venous thromboembolic events

[a]Opportunistic infections: UPA15, candida urethritis; UPA30, 1 pneumocystis jirovecii pneumonia, 1 cytomegalovirus infection. [b]Herpes zoster: All events of herpes zoster were mild or moderate in severity involving 1-2 dermatomes. [c]Malignancies: PBO, basal cell carcinoma; UPA15, 1 neuroendocrine carcinoma; UPA30, 2 basal cell carcinoma, 1 lung neoplasm malignant; ADA, 1 colon cancer, 1 ovarian cancer, 1 uterine cancer. [d]MACE (includes CV death, non-fatal myocardial infarction, non-fatal stroke): PBO, 1 non-fatal myocardial infarction; ADA, 1 non-fatal myocardial infarction, 1 cerebrovascular accident. [e]VTE: PBO, 1 deep vein thrombosis; UPA30, 1 pulmonary embolism; ADA: 2 deep vein thrombosis. [f]Deaths: PBO, 1 cardiac arrest (death adjudicated to unknown cause)

Conclusion: In this non-bDMARD-IR PsA population, treatment with UPA15/30 demonstrated improvement in musculoskeletal symptoms, psoriasis, physical function, pain, and fatigue and inhibited radiographic progression; improvements were observed by Wk 2. At Wk 12, UPA15/30 were non-inferior to ADA for ACR20, with superiority demonstrated for UPA30. Greater percentages of UPA vs PBO pts achieved stringent measures of disease control (MDA, ACR50/70, sIGA 0/1). No new safety signals were identified compared with the safety profile observed in RA.

Disclosure: I. McInnes, Novartis, 9, AbbVie, 9, Celgene, 9, Janssen, 2, 9, UCB, 2, 9, Bristol Myers Squibb, 2, 9, AstraZeneca, 2, Boehringer Ingelheim, 2, Lilly, 9, LEO, 9; **J. Anderson**, AbbVie Inc., 1, 3, 4; **M. Magrey**, Novartis, 5, Eli Lilly, 5, AbbVie, 2, UCB, 2, Amgen, 2, Pfizer, 5, Janssen, 5; **J. Merola**, AbbVie, 1, Arena, 1, Avotres, 1, Biogen, 1, Celgene, 1, Dermavant, 1, Eli Lilly, 1, EMD Serono, 1, Janssen, 1, LEO Pharma, 5, Merck, 1, Novartis, 1, Pfizer Inc, 5, Sanofi, 1, Regeneron, 1, Sun Pharma, 1, UCB Pharma, 5; **Y. Liu**, None; **M. Kishimoto**, AbbVie, 1, 2, Amgen-Astellas BioPharma, 1, 2, Asahi-Kasei Pharma, 1, 2, Astellas, 1, 2, Ayumi Pharma, 1, 2, BMS, 1, 2, Chugai, 1, 2, Daiichi-Sankyo, 1, 2, Eisai, 1, 2, Eli Lilly, 1, 2, Gilead, 1, 2, Janssen, 1, 2, Kyowa Kirin, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, Tanabe-Mitsubishi, 1, 2, Teijin Pharma, 1, 2, UCB Pharma, 1, 2, Celgene, 5, 8; **S. Jeka**, Pfizer, 2, 8, Novartis, 2, 8, Abbvie, 2, 8, UCB, 2, 8, MSD, 2, 8, Roche, 2, 8, Sandoz, 2, 8, Egis, 2, 8, Lilly, 2, 8, Celgene, 2, 8; **C. Pacheco Tena**, None; **X. Wang**, AbbVie Inc., 1; **L. Chen**, AbbVie, 1, 3; **P. Zueger**, AbbVie Inc., 1, 3; **A. Pangan**, AbbVie, 1, 3; **F. Behrens**, Pfizer, 2, 5, 8, Janssen, 2, 5, 8, Chugai, 2, 5, 8, Celgene, 2, 5, 8, Bionorica, 2, Roche, 2, 5, 8, Abbvie, 5, 8, Sanofi, 5, 8, Lilly, 5, 8, Novartis, 5, 8, Genzyme, 5, 8, Boehringer, 5, 8, MSD, 5, 8, Amgen, 5, 8, UCB, 5, 8, Gilead, 5, 8, Sandoz, 5, 8.

Abstract Number: 2027

Efficacy and Safety of Tildrakizumab, a High-Affinity Anti–Interleukin-23p19 Monoclonal Antibody, in Patients with Active Psoriatic Arthritis in a Randomized, Double-Blind, Placebo-Controlled, Multiple-Dose, Phase 2b Study

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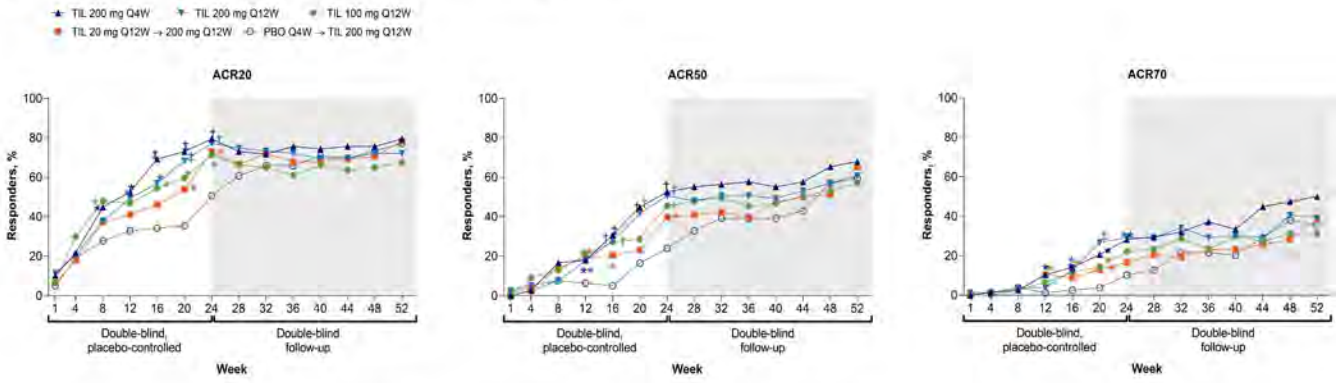
SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment II: Emerging Therapies
Session Type: Abstract Session
Session Time: 11:00AM–11:50AM

Background/Purpose: Tildrakizumab (TIL), a high-affinity anti–interleukin-23p19 monoclonal antibody, is approved to treat moderate to severe plaque psoriasis.[1] The efficacy and safety of TIL up to week (W)52 in patients with psoriatic arthritis (PsA) was evaluated in a randomized, double-blind, placebo-controlled, multiple-dose, phase 2b study (NCT02980692).

Methods: Patients (pts) ≥18 years with active PsA[2] were randomized 1:1:1:1:1 to TIL 200 mg every 4 weeks (Q4W) to W52, TIL 200 mg Q12W to W52, TIL 100 mg Q12W to W52, TIL 20 mg Q12W until W24 then TIL 200 mg Q12W to W52, or placebo Q4W until W24 then TIL 200 mg Q12W to W52. Efficacy assessments included ACR20/50/70, 75%/90%/100% improvement in Psoriasis Area and Severity Index, proportion of pts with residual minimal disease

Figure 1. Response rates for (**A**) ACR20, (**B**) ACR50, and (**C**) ACR70 through week 52



Missing responses were imputed as nonresponses. Shown for randomized patients who received ≥1 dose of study drug.

*P <0.05; †P <0.001; ‡P <0.0001 vs PBO. P-values were not analyzed beyond week 24.

ACR, American College of Rheumatology; PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; TIL, tildrakizumab.

Table 1. Baseline patient characteristics and demographics

	TIL 200 mg Q4W (N = 78)	TIL 200 mg Q12W (N = 79)	TIL 100 mg Q12W (N = 77)	TIL 20→200 mg Q12W (N = 78)	PBO→TIL 200 mg Q12W (N = 79)
Age, years, mean ± SD	50.1 ± 13.3	49.3 ± 11.2	49.2 ± 11.9	47.2 ± 13.4	48.1 ± 13.3
Female, n (%)	46 (59.0)	37 (46.8)	47 (61.0)	41 (52.6)	44 (55.7)
Race, n (%)					
White	76 (97.4)	78 (98.7)	75 (97.4)	75 (96.2)	74 (93.7)
Black or African American	0	0	1 (1.3)	1 (1.3)	3 (3.8)
Other	2 (2.6)	1 (1.3)	1 (1.3)	2 (2.6)	2 (2.5)
Weight, kg, mean ± SD	85.1 ± 19.7	87.2 ± 19.5	83.7 ± 18.9	85.2 ± 18.1	85.3 ± 20.2
BMI, kg/m^2, mean ± SD	30.1 ± 6.5	30.2 ± 6.5	29.5 ± 6.8	29.4 ± 5.2	29.5 ± 6.0
Duration of PsA, years, mean ± SD	7.5 ± 8.5	6.2 ± 7.2	7.0 ± 6.6	6.6 ± 6.7	6.3 ± 6.1
Prior anti–TNF-α therapy, n (%)*	18 (22.8)	17 (21.8)	19 (23.8)	19 (24.4)	18 (23.7)

*For prior anti–TNF-α therapy, total patients analyzed (N) = 79, 78, 80, 78, and 76 for TIL 200 mg Q4W, TIL 200 mg Q12W, TIL 100 mg, TIL 20 mg, and PBO.

Shown for randomized patients who received ≥1 dose of study drug.

PBO, placebo; Q4W, every 4 weeks; Q12W, every 12 weeks; SD, standard deviation; TIL, tildrakizumab.

activity response; and mean change from baseline (BL) in HAQ-Disability Index, Leeds Dactylitis Index (LDI, pts with BL LDI ≥1), and Leeds Enthesitis Index (LEI, pts with BL LEI ≥1) to W52. Treatment-emergent adverse events (TEAEs) were recorded.

Results: Of 500 pts screened, 391 were randomized and received ≥1 dose of drug. Demographics and baseline disease characteristics were generally consistent across treatment arms (**Table 1**). Proportions of ACR20/50/70 responders were superior with TIL vs PBO through W24; after W24 rates of responses further increased for TIL 20→200 mg Q12W and PBO→200 mg Q12W through W52 (**Figure**). Other efficacy results are shown in **Table 2**. Overall, 252 (64.5%) patients had a TEAE, the most common being nasopharyngitis (8.4%) and upper respiratory tract infection (6.4%). Most TEAEs, including infections, were mild. One (0.3%) malignancy (intraductal proliferative breast lesion) occurred in the TIL 20→200 mg Q12W arm. Serious TEAEs were observed in 13 (3.3%) patients. One serious infection (chronic tonsillitis) was reported in the TIL 20 mg Q12W arm during the first 24 weeks. One case each of pyelonephritis and urinary tract infection were reported as TEAEs of special interest (both in the same patient in the TIL 100 mg Q12W arm). No deaths or major adverse cardiac events occurred.

Conclusion: TIL was well tolerated and improved musculoskeletal and skin manifestations of PsA through W52.

References

1. Reich, et al. *Lancet* 2017;390:276–88.
2. Taylor, et al. *Arthritis Rheum* 2006;54:2665–73.

Table 2. Week 52 clinical efficacy

	TIL 200 mg Q4W (N = 78)	TIL 200 mg Q12W (N = 79)	TIL 100 mg Q12W (N = 77)	TIL 20→ 200 mg Q12W (N = 78)	PBO→ TIL 200 mg Q12W (N = 79)
HAQ-DI					
BL mean ± SD	1.0 ± 0.6	1.0 ±0.6	1.0 ± 0.7	1.1 ± 0.6	1.2 ± 0.6
W52 mean ± SD[a]	−0.4 ± 0.5	−0.4 ± 0.6	−0.4 ± 0.5	−0.4 ± 0.5	−0.4 ± 0.5
LEI					
BL mean ± SD[b]	3.1 ± 1.7	2.8 ± 1.7	3.2 ± 1.8	3.1 ± 1.7	2.8 ± 1.8
W52 mean ± SD[a,b]	−1.7 ± 2.0	−1.6 ± 1.6	−2.0 ± 2.1	−1.7 ± 1.8	−2.1 ± 1.9
BL median (IQR)[b]	3.0 (2.0)	2.0 (2.0)	3.0 (3.0)	3.0 (2.0)	2.0 (2.0)
W52 median (IQR)[b]	0 (2.50)	0 (2.0)	0 (2.0)	0 (2.0)	0 (1.0)
LDI					
BL mean ± SD[c]	32.8 ± 32.9	61.3 ± 73.5	93.8 ± 146.5	71.4 ± 118.5	99.6 ± 170.7
W52 mean ± SD[a,c]	−21.4 ± 37.1	−42.1 ± 76.7	−41.6 ± 89.3	−56.5 ± 123.4	−81.5 ± 173.0
BL median (IQR)[c]	21.8 (27.0)	28.3 (55.0)	32.1 (72.5)	28.6 (48.9)	34.0 (133.5)
W52 median (IQR)[c]	7.4 (17.1)	3.2 (22.4)	20.0 (30.4)	0 (27.5)	5.6 (17.6)
MDA[e], %	47.4	48.1	35.1	41.0	36.7
PASI 100[e], %	50.9	36.4	32.7	46.3	33.3
PASI 90[e], %	67.9	65.9	43.6	53.7	47.6
PASI 75[e], %	77.4	77.3	61.8	73.2	64.3

[a]Mean change from BL ± SD.

[b]Pts with BL LEI ≥1 using nonresponder imputation (n = 48, 43, 51, 55, 43).

[c]Pts with BL LDI ≥1 (n = 27, 21, 21, 19, 25) using nonresponder imputation. [e]% at W52

Missing data imputed as nonresponses.

BL, baseline; HAQ-DI, Health Assessment Questionnaire-Disability Index; IQR, interquartile range; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; PASI, Psoriasis Area and Severity Index; PBO, placebo; Pts, patients; Q4W, every 4 weeks; Q12W, every 12 weeks; SD, standard deviation; TIL, tildrakizumab; W52, week 52.

Disclosure: P. Mease, Amgen, 2, 5, 8, Bristol-Myers Squibb, 2, 5, Novartis, 2, 5, 8, Pfizer Inc, 2, 5, 8, Sun, 2, 5, UCB, 2, 5, 8, AbbVie, 2, 5, 8, Gilead, 2, 5, Janssen, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 5, GlaxoSmithKline, 5; **S. Chohan**, Arizona Arthritis and Rheumatology Associates, 9; **F. García Fructuoso**, AbbVie, 2, 5, 8, Eli Lilly, 2, 5, 8, Gedeon Richter, 2, 5, 8, MedImmune, 2, 5, 8, Nichi-Iko, 2, 5, 8, Pfizer, 2, 5, 8, Sanofi-Aventis, 2, 5, 8, Takeda, 2, 5, 8, UCB, 2, 5, 8; **A. Gottlieb**, Janssen, 2, 5, Incyte, 2, 5, Novartis, 2, 5, 8, Xbiotech, 2, 9, Boehringer Ingelheim, 2, 5, UCB Pharma, 2, 5, 8, Beiersdorf, 5, Bristol-Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, Sun Pharma, 2, 5, Leo Pharma, 5, Avotres Therapeutics, 5; **M. Luggen**, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Genentech, 2, 5, 8, Eli Lilly, 2, 5, 8, Nichi-Iko, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, R-Pharm, 2, 5, 8, Sun Pharmaceutical Industries, Inc, 2, 5, 8; **P. Rahman**, AbbVie, 5, 8, Amgen, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Abbott, 8, Centacor, 8, Merck, 8, Bristol Myers Squibb, 5, 8, Roche, 5; **S. Raychaudhuri**, AbbVie, 2, Janssen, 2, 5, Novartis, 2, 5, Pfizer, 2, 5, Sun Pharmaceutical Industries, Inc., 2, Amgen, 5, Eli Lilly, 5; **R. Chou**, Sun Pharmaceutical Industries, Inc, 5; **A. Mendelsohn**, Sun Pharmaceutical Industries, Inc., 3, Johnson and Johnson, 1, 9; **S. Rozzo**, Sun Pharmaceutical Industries, Inc., 3; **A. Orbai**, Eli Lilly, 2, 5, Janssen, 2, 5, Novartis, 2, 5, Pfizer Inc, 5, UCB, 5, AbbVie, 2, Celgene, 2, Horizon, 2.

Abstract Number: 2028

Predictors of Maintaining Inactive Disease After Etanercept Withdrawal, and Regaining Inactive Disease Status After Flare and Retreatment, in Adults with Non-radiographic Axial Spondyloarthritis: Results from RE-EMBARK

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment III: Axial Spondyloarthritis

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: RE-EMBARK was a phase 4, multicenter, open-label, 3-period study that evaluated etanercept (ETN) withdrawal and retreatment in adult patients with non-radiographic axial spondyloarthritis (nr-axSpA) and an adequate response to initial ETN treatment. The aim of the current analyses was to explore baseline predictors of the maintenance and regain of inactive disease during Period 2 and Period 3 of RE-EMBARK, respectively.

Table 1. Baseline predictors of the maintenance of inactive disease following etanercept withdrawal during Period 2 of RE-EMBARK

Univariate analyses (N=115[a])			
Patient characteristic[b]	**Inactive disease n/N (%)**	**Odds ratio (95% CI)**	**p value**
hs-CRP			
>3 mg/L	7/74 (9)		
≤3 mg/L	10/39 (26)	3.30 (1.14, 9.52)	0.027
Positive MRI and hs-CRP >3 mg/L			
Yes	2/47 (4)		
No	15/66 (23)	6.62 (1.43, 30.53)	0.015

Multivariate analysis (N=115[a])		
Baseline characteristic[b]	**Odds ratio (95% CI)**	**p value**
Positive MRI and hs-CRP >3 mg/L (No vs Yes)	6.58 (1.42, 30.43)	0.016

[a]Of the 119 patients who entered Period 2 and had etanercept withdrawn, 4 did not have ≥1 efficacy evaluation during Period 2 and were excluded from the analysis.

[b]Baseline characteristics investigated as potential predictors were: Age (<40 years vs ≥40 years); Body mass index (<25 vs ≥25); Disease duration (<2 years vs ≥2 years); Enthesitis (No vs Yes); HLA-B27 status (Negative vs Positive); hs-CRP (≤3 mg/L vs >3 mg/L); MRI sacroiliitis classification at screening (Negative vs Positive); MRI SIJ SPARCC score (≤2 vs >2); Positive MRI and hs-CRP >3 mg/L (No vs Yes); Race (Non-white vs White); Sex (Female vs Male); Weight (<70 kg vs ≥70 kg).

CI: confidence interval; hs-CRP: high-sensitivity C-reactive protein; MRI: magnetic resonance imaging; SIJ: sacroiliac joints; SPARCC: Spondyloarthritis Research Consortium of Canada.

Table 2. Baseline predictors of the regain of inactive disease following a flare and retreatment with etanercept during Period 3 of RE-EMBARK

Univariate analyses (N=87)

Baseline characteristic[a]	Inactive disease n/N (%)	Odds ratio (95% CI)	p value
Sex			
Female	16/32 (50)		
Male	48/55 (87)	6.86 (2.39, 19.65)	<0.001
Age			
≥40 years	8/20 (40)		
<40 years	56/67 (84)	7.64 (2.53, 23.03)	<0.001
Enthesitis			
Yes	19/32 (59)		
No	44/54 (81)	3.01 (1.12, 8.06)	0.028

Multivariate analysis (N=87)

Baseline characteristic[a]	Odds ratio (95% CI)	p value
Sex (Male vs Female)	5.46 (1.68, 17.72)	0.005
Age (<40 vs ≥40 years)	8.10 (2.10, 31.20)	0.002

[a] Baseline characteristics investigated as potential predictors were: Age (<40 years vs ≥40 years); Body mass index (<25 vs ≥25); Disease duration (<2 years vs ≥2 years); Enthesitis (No vs Yes); HLA-B27 status (Negative vs Positive); hs-CRP (≤3 mg/L vs >3 mg/L); MRI sacroiliitis classification at screening (Negative vs Positive); MRI SIJ SPARCC score (≤2 vs >2); Positive MRI and hs-CRP >3 mg/L (No vs Yes); Race (Non-white vs White); Sex (Male vs Female); Weight (<70 kg vs ≥70 kg).

CI: confidence interval; hs-CRP: high-sensitivity C-reactive protein; MRI: magnetic resonance imaging; SIJ: sacroiliac joints; SPARCC: Spondyloarthritis Research Consortium of Canada.

Methods: RE-EMBARK enrolled patients aged 18 to < 50 years with active nr-axSpA, an inadequate response to ≥2 non-steroidal anti-inflammatory drugs (NSAIDs), and on a stable dose of 1 NSAID for ≥2 weeks prior to first study dose of ETN. Active nr-axSpA was defined as the combination of meeting Assessment in SpondyloArthritis international Society (ASAS) criteria, having active symptoms of nr-axSpA, and having an Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS-CRP) ≥2.1. In Period 1, all patients received ETN (50 mg once weekly) and background NSAID for 24 weeks. Patients who achieved inactive disease (ASDAS-CRP < 1.3) at Week 24 were eligible to enter Period 2. In Period 2, ETN was withdrawn (without downward tapering) for up to 40 weeks while background NSAID was maintained. Patients who experienced a flare (ASDAS with erythrocyte sedimentation rate ≥2.1) during Period 2 were eligible to immediately enter Period 3 in which they were retreated with ETN (50 mg once weekly) for 12 weeks. Baseline characteristics of the patients who entered Period 2 and Period 3 (2 separate baselines) were analyzed post hoc as categorical predictors of the maintenance of inactive disease and the regain of inactive disease, respectively, using univariate logistic regression models and stepwise multivariate logistic regression models. Analyses were based on observed cases.

Results: A total of 209 patients were treated during Period 1 and 119 (57%) achieved inactive disease at Week 24 and had ETN withdrawn after entering Period 2. Univariate analyses showed that high-sensitivity CRP (hs-CRP) ≤3 mg/L and the absence of a combination of positive MRI and hs-CRP >3 mg/L were associated with the maintenance of inactive disease following ETN withdrawal (**Table 1**). Multivariate analysis showed that the absence of a combination of positive MRI and hs-CRP >3 mg/L was a significant predictor of maintaining inactive disease following ETN

withdrawal. There were 87 (73%) of the 119 patients in Period 2 who experienced a flare following ETN withdrawal and were retreated during Period 3. Univariate analyses showed that male sex, age < 40 years, and the absence of enthesitis were associated with the regain of inactive disease following retreatment, with multivariate analysis showing that male sex and age < 40 years were significant predictors (**Table 2**).

Conclusion: The absence of a combination of positive MRI and hs-CRP >3mg/L at baseline was a significant predictor of adult patients with nr-axSpA maintaining inactive disease following withdrawal of ETN over 40 weeks. Male sex and age < 40 years were significant predictors of a patient regaining inactive disease after a flare and subsequent 12-week retreatment with ETN.

Disclosure: F. Van den Bosch, AbbVie, 5, 8, Celgene, 5, 8, Eli Lilly, 5, 8, Galapagos, 5, 8, Novartis, 5, 8, Pfizer, 5, 8, UCB, 5, 8, Gilead, 5, Merck, 5, 8; **J. Wei**, AbbVie, 1, 2, Bristol-Myers Squibb, 1, 2, Celgene, 1, 2, Chugai, 1, Janssen, 1, 2, Novartis, 1, 2, Pfizer, 1, 2, Sanofi, 1, UCB, 1, 2, Eli Lilly, 1, MSD, 5, 8, Abbott, 5, 8, GSK, 5, 8, Roche, 5, 8; **F. Blanco**, AbbVie, 1, Pfizer, 1, UCB, 1, Bristol-Myers Squibb, 1, Roche, 1, Servier, 1, Bioiberica, 1, Sanofi, 1, Grünenthal, 1, GSK, 1, Eli Lilly, 1, Janssen, 1, Regeneron, 1, Amgen, 1, TRB Chemedica, 1; **P. Selema**, Pfizer, 1, 2; **D. Graham**, Pfizer, 1, 2; **E. Arthur**, Pfizer, 1, 2; **V. Tsekouras**, Pfizer, 1, 2; **B. Vlahos**, Pfizer, 1, 2; **C. Zang**, Pfizer, 1, 2; **A. Deodhar**, AbbVie, 2, 5, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Janssen, 5, Pfizer, 2, 5, Boehringer Ingelheim, 5, UCB Pharma, 2, 5, Amgen Inc., 5, Celgene, 5, Galapagos, 5, Bristol-Myers Squibb, 2; **P. Nash**, AbbVie, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Celgene, 2, 5, 8, Eli Lilly, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, Roche, 2, 5, 8, Sanofi, 2, 5, 8, UCB, 2, 5, 8.

Abstract Number: 2029

Therapeutic Drug Monitoring Compared to Standard Treatment of Patients Starting Infliximab: Results from a Multicenter Randomized Controlled Trial of 400 Patients

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment III: Axial Spondyloarthritis
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: A lack or loss of response to TNFα inhibitors (TNFi) has been associated with low serum drug levels and formation of anti-drug antibodies (ADAb). Therapeutic drug monitoring (TDM), an individualized treatment strategy based on regular assessments of serum drug levels, has been suggested to optimize efficacy of TNFi. It is still unclear if TDM improves clinical outcomes, and the value of TDM has recently been included in the research agenda across different specialties. This first randomized controlled trial on the effectiveness of TDM in a range of immune mediated inflammatory diseases including rheumatic diseases, the NORwegian DRUg Monitoring trial part A (NOR-DRUM (A)) focus on the induction period of infliximab (INX) treatment and aim to assess if TDM is superior to standard treatment in order to achieve remission.

Methods: In the investigator-initiated, randomized, open-label, multicenter NOR-DRUM (A) study, adult patients with rheumatoid arthritis (RA), psoriatic arthritis (PsA), spondyloarthritis (SpA), ulcerative colitis (UC), Crohn's disease

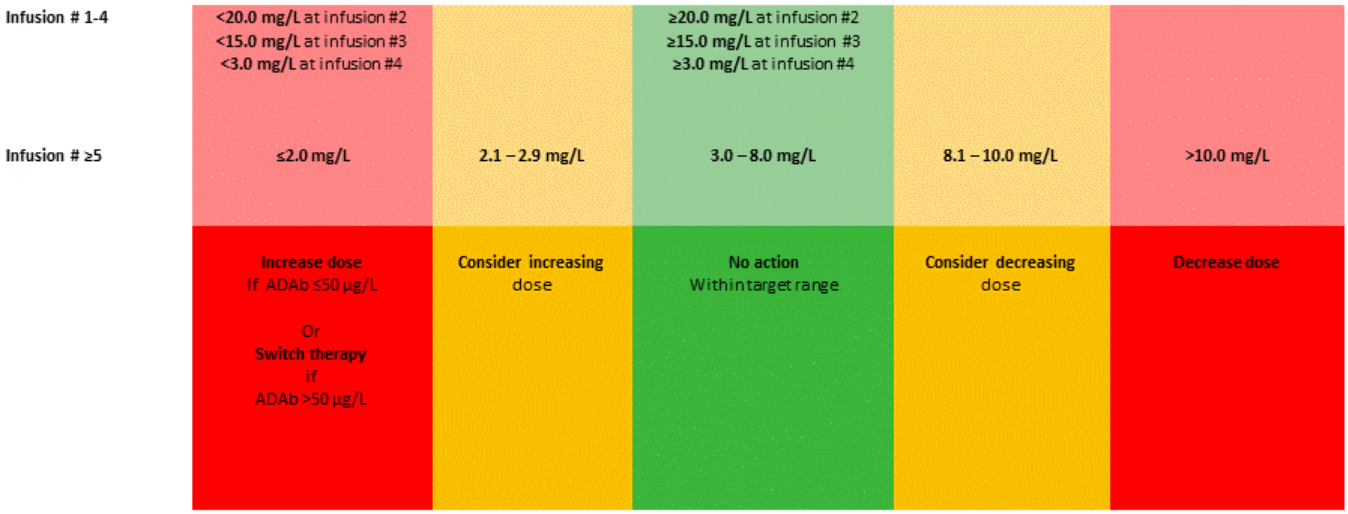


Figure 1. Treatment algorithm in the therapeutic drug monitoring group

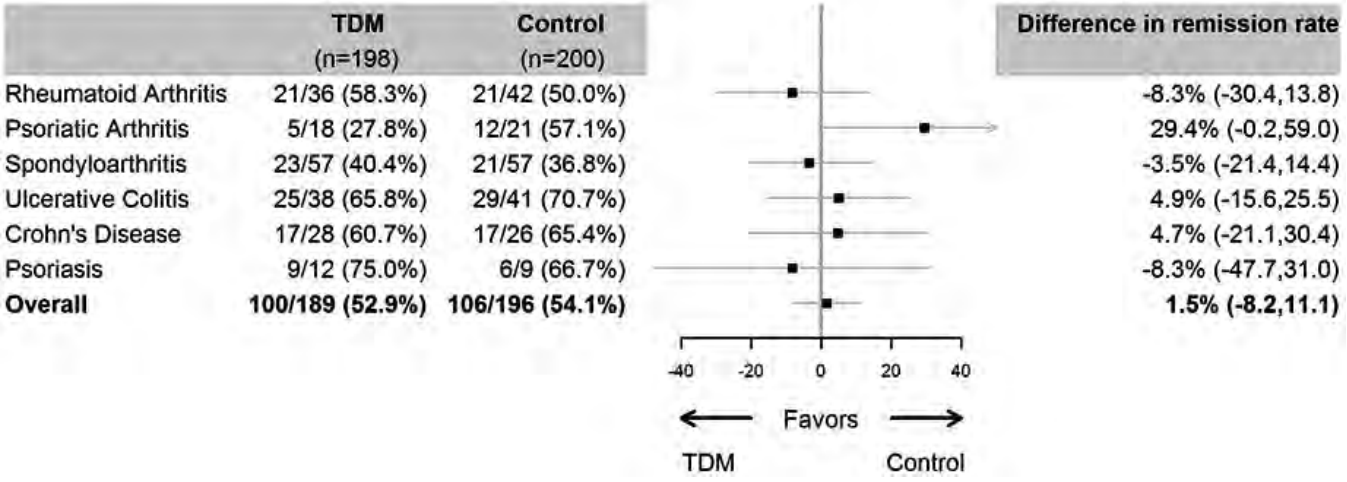


Figure 2. Forest plot of difference in clinical remission rates, overall results and according to disease Figure shows results of the main analysis (primary outcome) conducted in the full-analysis set TDM= therapeutic drug monitoring

(CD) and psoriasis (Ps) starting INX therapy were randomly assigned administration of INX according to a treatment strategy based on TDM (TDM arm) or to standard administration of INX without TDM (control arm). Study visits were conducted at each infusion. The primary endpoint was remission at week 30. In the TDM arm, the dose and interval were adjusted according to INX trough levels to reach the therapeutic range (Figure 1). If the patient developed significant levels of ADAb, INX was terminated. To guide the investigators, the TDM strategy was integrated in an interactive eCRF. The primary endpoint was analysed by mixed effect logistic regression in the full analyses set (FAS), adjusting for diagnoses. Infections and infusion reactions were specified as adverse events (AEs) of special interest.

Results: We enrolled 411 patients at 21 study centers between January 2017 and December 2018. 398 patients (RA 80, PsA 42, SpA 117, UC 80, CD 57, Ps 22) received the allocated strategy and were included in the FAS population. Demographic and baseline characteristics were comparable in both arms. TDM was not found to be superior to standard treatment with regard to the primary outcome. Remission at week 30 was reached in 100 (53%) and 106 (54%) of the patients in the TDM and control arm, respectively (adjusted difference, 1.5%; 95% confidence interval (CI), -8.2 to 11.1, p=0.78) (Figure 2). Consistent results were shown for all the secondary endpoints (Figure 3) and in the sensitivity analyses. Twenty patients (10%) in the TDM arm and 30 patients (15%) in the control arm developed

Figure 3. Generic (A-F) and disease specific (G-L) composite measures over study period.

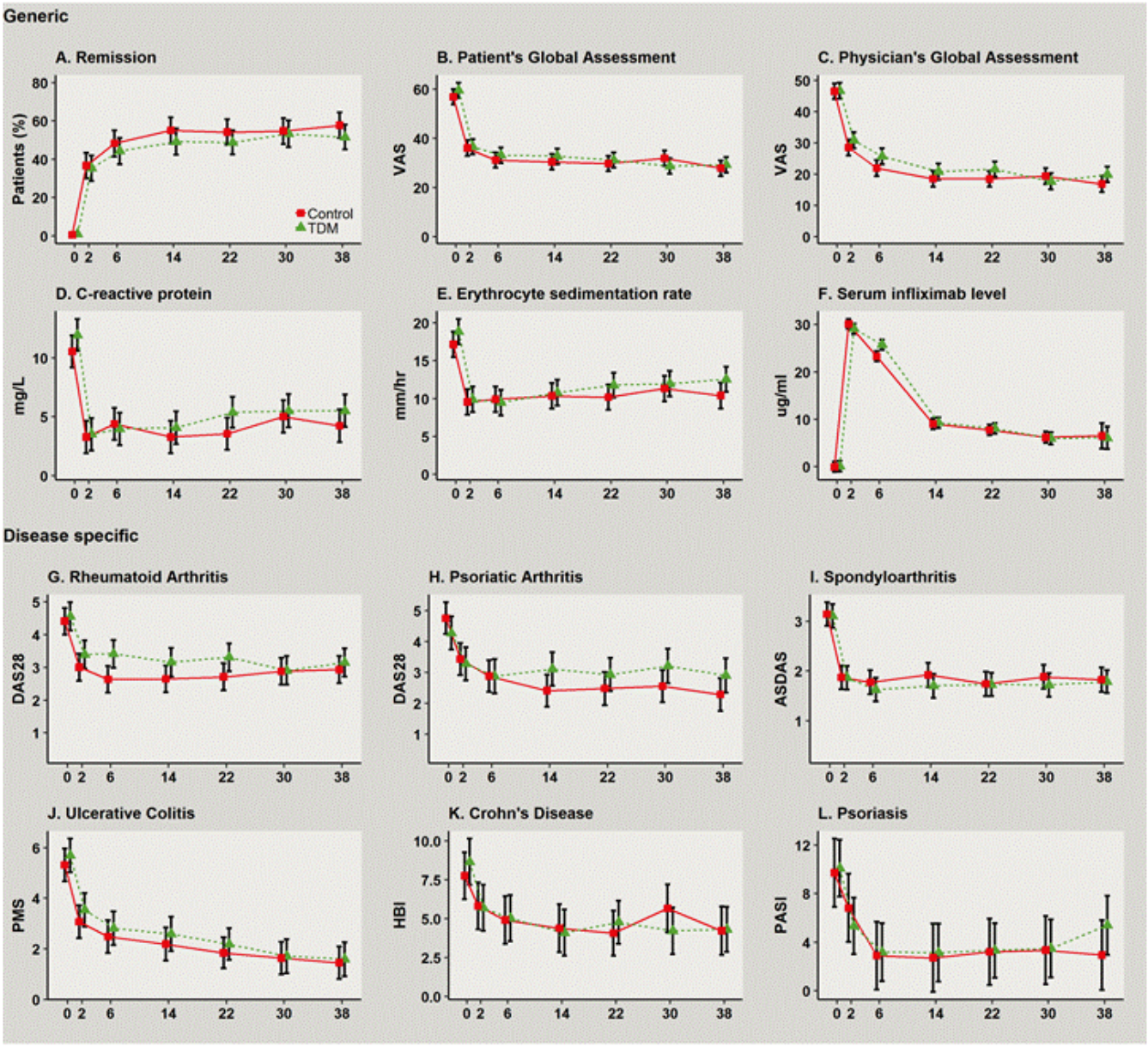


Figure 3 Main secondary outcomes A-F: Generic outcomes; A Proportion of patients in clinical remission, B Patient's Global Assessment Visual analogue scale 0-100 mm, C Physician's Global Assessment Visual analogue scale 0-100 mm, D C-reactive protein mg/L, E Erythrocyte sedimentation rate mm/hour, F Serum infliximab level mg/L. G-L: Disease specific activity measures; G: Rheumatoid Arthritis, Disease Activity Score 28 joints, H: Psoriatic Arthritis, Disease Activity Score 28 joints, I: Spondyloarthritis, Ankylosing Spondylitis Disease Activity Score, J: Ulcerative Colitis, Partial Mayo Score, K: Crohn's Disease, Harvey Bradshaw Index, L: Psoriasis, Psoriasis Area and Severity Index. All data except for serum infliximab levels (patients still on medication) are from the full-analysis set. Values are adjusted means with 95% CI.

significant levels of ADAb. The number of adverse events (AE) was similar in both groups, however infusion reactions were less frequent (5 patients (2.5%) vs 16 patients (8.0%)) in the TDM arm (difference 5.5% (95% CI 1.1, 9.8%))

Conclusion: NOR-DRUM (A) is the first randomized trial to address effectiveness of TDM in rheumatic diseases. In this study, TDM was not superior to standard treatment in order to achieve remission. Although improved safety is

indicated by a reduction in infusion reactions, implementation of TDM as a general strategy in the induction period of INX is not supported by the NOR-DRUM (A) study.

Disclosure: S. Syversen, roche, 8, Thermo Fisher, 8, Hospira/Pfizer, 8; **G. Goll**, Novartis, 8, Pfizer, 8, Abbvie, 8, Biogen, 8, Boehringer Ingelheim, 8, Orion Pharma, 8, Eli Lilly, 8, MSD, 8, Roche, 8, UCB, 8; **K. Jørgensen**, AOP Orphan, 5, Celltrion, 5, Norgine, 8; **Ø. Sandanger**, None; **J. Sexton**, None; **I. Olsen**, None; **J. Gehin**, Roche, 8; **M. Brun**, None; **C. Mørk**, Abbot, 5, 8, Novartis, 5, 8, AbbVie, 5, 8, Celagene, 5, 8, Almiral, 5, 8, LEO, 5, 8, ACO, 5, 8; **T. Kvien**, AbbVie, 2, 5, 8, Hospira/Pfizer, 2, 5, 8, 9, MSD, 2, 5, 8, 9, Roche, 2, 5, 8, 9, Biogen, 5, 8, BMS, 5, 8, Celltrion, 5, 8, Eli Lilly, 5, 8, Novartis, 5, 8, Orion Pharma, 5, 8, Sanofi and Mylan, 5, 8, Sandoz, 5, 8, UCB, 5, 8; **J. Jahnsen**, None; **N. Bolstad**, Pfizer, 5, Janssen, 5, Orion Pharma, 8, Napp Pharmaceuticals, 8, Takeda, 8, Roche, 8, Novartis, 8; **E. Haavardsholm**, AbbVie, 2, 5, 8, UCB, 2, 5, 8, Pfizer, 2, 5, 8, MSD, 2, Roche, 2, 8, Janssen-Cilag, 2, Gilead, 5, Celegene, 5, 8, Lilly, 5, 8.

Abstract Number: 2030

Treatment with Selective Cyclooxygenase-2 Inhibitors Is Associated with Inhibition of Radiographic Spinal Progression in Patients with Axial Spondyloarthritis: Long-term Results from the German Spondyloarthritis Inception Cohort

Denis Poddubnyy[1], Valeria Rios Rodriguez[2], Murat Torgutalp[2], Ani Dilbaryan[2], Maryna Verba[2], Mikhail Protopopov[2], Fabian Proft[2], Judith Rademacher[2], Hildrun Haibel[2], Martin Rudwaleit[3] and Joachim Sieper[2], [1]Charité – Universitätsmedizin Berlin, Berlin, Germany, [2]Charité Universitätsmedizin Berlin, Berlin, Germany, [3]Department of Internal Medicine and Rheumatology, Klinikum Bielefeld, Germany

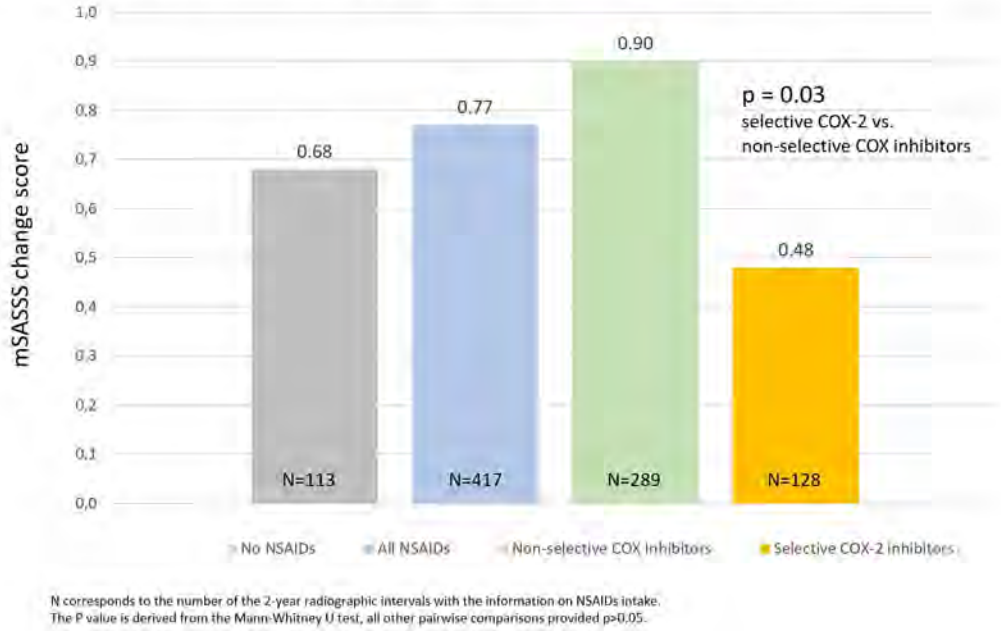
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment III: Axial Spondyloarthritis
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: There are conflicting data on the effect of non-steroidal anti-inflammatory drugs (NSAIDs) on radiographic spinal progression in axial spondyloarthritis (axSpA). One randomized controlled trial could show that continuous treatment with NSAIDs (mostly with a cyclooxygenase -2 – COX-2 – selective inhibitor celecoxib) was associated with inhibition of radiographic spinal progression, while another study showed no effect of continuous intake of the non-selective COX-inhibitor diclofenac on progression. In the analysis of the first 2 years of the German Spondyloarthritis Inception Cohort (GESPIC), higher NSAIDs intake was associated with retardation of radiographic progression, although it remained uncertain, whether COX-2-selective inhibitors have a stronger effect than non-selective ones.

The aim of the current analysis was to evaluate the effect of NSAIDs including non-selective and selective COX-2 inhibitors on radiographic spinal progression in patients with early axSpA in a long-term inception cohort.

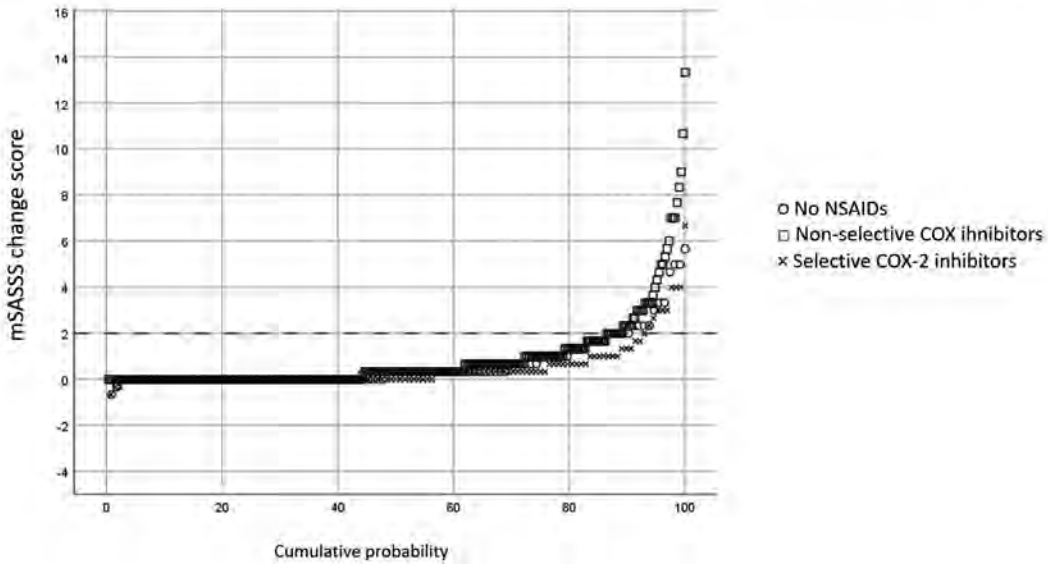
Methods: A total of 266 patients with early axSpA (with r-axSpA with symptom duration ≤10 years and nr-axSpA with symptom duration ≤5 years) from the German Spondyloarthritis Inception Cohort (GESPIC) with at least two sets of spinal radiographs obtained at least 2 years apart during a 10-year follow-up were included. These patients contributed with a total of 542 2-year radiographic intervals. Spinal radiographs were evaluated by three trained and calibrated readers according to the modified Stoke Ankylosing Spondylitis Spine Score (mSASSS). The final mSASSS was calculated as a mean of three reader scores. NSAIDs intake (NSAIDs type, daily dosage and frequency of intake) was

Figure 1. The mSASSS change scores over 2 years in patients with in patients with axial spondyloarthritis receiving no NSAIDs, non-selective COX inhibitors or selective COX-2 inhibitors.



N corresponds to the number of the 2-year radiographic intervals with the information on NSAIDs intake.
The P value is derived from the Mann-Whitney U test, all other pairwise comparisons provided p>0.05.

Figure 2. Cumulative probability plots depicting mSASSS change scores over 2 years in patients with axial spondyloarthritis receiving no NSAIDs, non-selective COX inhibitors or selective COX-2 inhibitors.



recorded at every visit. Coxibs (i.e., celecoxib, etoricoxib and rofecoxib) were considered selective COX-2 inhibitors, all other NSAIDs – as non-selective ones. The Assessment of Spondyloarthritis International Society (ASAS) NSAIDs intake score (0 – no NSAID intake, 100 – daily intake in the maximal anti-inflammatory dose dose) was calculated for 2-year intervals. The association between NSAIDs intake (NSAIDs type and NSAIDs score) and radiographic spinal progression defined as the absolute mSASSS change score over 2 years was analyzed using longitudinal generalized estimating equations (GEE) analysis.

Table. The association between the NSAIDs intake and radiographic spinal progression defined as mSASSS change score over two years in the longitudinal generalized estimation equation analysis.

Parameter	Reference	Model 1 β (95% CI)*	Model 2 β (95% CI)*	Model 3 β (95% CI)*	Model 4 β (95% CI)*
NSAIDs intake	No NSAIDs	0.25 (-0.19 to 0.70)	-	-	-
COX-2-selective inhibitors	Non-selective inhibitors	-	**-0.42 (-0.64 to -0.20)**	-	-
COX-2-selective inhibitors	No NSAIDs	-	-	0.21 (-0.70 to 1.12)	-
Non-selective inhibitors	No NSAIDs	-	-	-	-0.43 (-1.09 to 0.23)
NSAIDs intake score (0-100)	Per point of the score	**-0.007 (-0.012 to -0.001)**	-0.002 (-0.007 to 0.003)	-0.005 (-0.020 to 0.011)	-0.004 (-0.009 to 0.002)

*Parameter estimates from the multivariable models adjusted for sex, symptom duration at the beginning of the current 2-year interval, treatment with TNFi in the currents 2-year interval, time-averaged ASDAS in the current 2-year interval, smoking in the current 2-year interval and performing exercises in the current 2- year interval.

Results: At baseline, 67% of the patients received NSAIDs. A total of 289 2-year radiographic intervals were covered by non-selective NSAIDs, 128 intervals with COX-2 selective ones, while 113 intervals were not covered by NSAIDs. Overall, the intake of COX-2 selective inhibitors was associated with lower radiographic spinal progression across all 2-year intervals as compared to non-selective NSAIDs (figure 1 and 2). In the longitudinal multivariable GEE analysis, intake of COX-2 selective inhibitors was associated with a lower mSASSS progression (as opposed to the treatment with non-selective NSAIDs) after adjustment for the NSAIDs intake score, treatment with tumor necrosis factor inhibitors and disease activity (table).

Conclusion: An inhibitory effect of NSAIDs on radiographic spinal progression in this axSpA cohort was attributable to the COX-2 selective inhibitors.

Disclosure: D. Poddubnyy, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8; **V. Rios Rodriguez**, None; **M. Torgutalp**, None; **A. Dilbaryan**, None; **M. Verba**, None; **M. Protopopov**, None; **F. Proft**, Novartis, 2, 8, AbbVie, 8, AMGEN, 8, BMS, 8, Hexal, 8, Celgene, 8, Lilly, 8, MSD, 8, Pfizer, 8, Roche, 8, UCB, 8; **J. Rademacher**, None; **H. Haibel**, None; **M. Rudwaleit**, Bristol-Myers Squibb, 5, 8, Chugai Pharmaceutical Co., Ltd., 5, 8, Eli Lilly and Company, 5, 8, Janssen, 5, 8, Novartis, 5, 8, UCB Pharma, 5, 8, AbbVie, 5, 8, Pfizer, 5, 8, Celgene, 8, Roche, 5, 8, Merck Sharp & Dohme, 5, 8; **J. Sieper**, AbbVie, 5, Novartis, 5, 8, Lilly, 8, Janssen, 5, Merck, 5, 8.

Abstract Number: 2031

Which Disease Activity Outcome Measure Discriminates Best in Axial Spondyloarthritis? A Systematic Literature Review and Meta-analysis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment III: Axial Spondyloarthritis

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: Several disease activity response and status criteria are used to assess treatment efficacy in RCTs in axial spondyloarthritis (axSpA). Response criteria include: the Assessment of SpondyloArthritis international Society (ASAS)-based ASAS 20, ASAS 40, and ASAS 5/6; the Bath Ankylosing Spondylitis Disease Activity Index BASDAI 50; the Ankylosing Spondylitis Disease Activity Score (ASDAS)-based clinically important improvement (ASDAS-CII) and major improvement (ASDAS-MI). Additionally, the following disease activity status are used: ASAS partial remission (ASAS-PR), ASDAS-low DA (ASDAS-LDA) and ASDAS-inactive disease (ASDAS-ID). All these 9 are variably used in RCTs, but it remains unknown which one is the most discriminative. Our aim was to compare the ability of different criteria to discriminate the response in treatment and placebo arm in axSpA.

Methods: A systematic literature review was performed in Medline and Embase to identify RCTs of biological and targeted synthetic DMARDs (b- and tsDMARDs). Placebo-controlled RCTs meeting the primary endpoint have been included provided they reported ≥2 response/status criteria. Outcomes were collected at the timepoint of primary endpoint assessment. Risk of bias was evaluated by The Cochrane tool. Meta-analysis with the Mantel-Haenszel method was conducted to calculate the Chi-square between percentages of patients fulfilling each criterion in the treatment arm versus the placebo arm (higher Chi-square, better discrimination). Per meta-analysis, we pooled RCTs presenting the same sets of outcomes.

Results: Eleven articles fulfilling inclusion criteria were retrieved from a preceding SLR about RCTs in axSpA (2001-2013), and 12 from another SLR (2009-2016) [3,4]. The search update resulted in 6 additional articles out of 130 hits. Thus, 29 RCTs in total were eligible. Meta-analysis included 23/29 RCTs with primary endpoint at 12-16 weeks, all at a low risk of bias. Other 6 RCTs had later (e.g. 24 weeks) or earlier (e.g. 6 weeks) primary endpoint, thus could not be meta-analyzed due to heterogeneity. Out of the 23 RCTs, 2 studies reported 2 outcomes, 2 reported 3 outcomes and 19 RCTs reported ≥4 outcomes. The most frequently reported outcomes were ASAS 20, ASAS 40, ASAS-PR and BASDAI 50 (Set 1). Sixteen RCTs presented all outcomes from Set 1 (Table 1): the discriminative performances were, in descending order, ASAS 40 – ASAS 20 – BASDAI 50 - ASAS-PR. In 11/16 RCTs ASAS 5/6 was additionally included (Table 1, Set 2): this outcome showed the best performances among ASAS-based response criteria. 8/16 RCTs additionally included some ASDAS-based outcomes (Table 1, Set 3). Here, ASDAS-CII and -MI showed a much higher discrimination than the ASAS-based criteria. In only 3 trials all outcomes could be compared, with again the ASDAS-CII and -MI as the most discriminative criteria, followed by ASAS 5/6 (Table 1, Set 4).

Conclusion: ASDAS-based response criteria showed better discrimination than ASAS-based response criteria. ASDAS-CII and ASDAS-MI should be the preferred primary outcomes for future RCTs comparing a bDMARD or tsD-

Table 1. Discriminative performances of response and status criteria in RCTs of biological and targeted synthetic DMARDs in axial spondyloarthritis

Minimum set of outcomes	Set 1: ASAS 20,-40,-PR, BASDAI 50		Set 2: ASAS 20,-40,-5/6, -PR BASDAI 50		Set 3: ASAS 20,-40, -5/6, -PR, BASDAI 50 ASDAS-CII, -MI, -ID		Set 4: All	
N° of RCTs Total=16*	16		11		8		3	
N° of patients	3465		2468		1845		562	
Descending X^2 order		X^2		X^2		X^2		X^2
1	ASAS 40	300	ASAS 5/6	335	ASDAS-CII	273	ASDAS-CII	86
2	ASAS 20	276	ASAS 40	225	ASDAS-MI	187	ASDAS-MI	65
3	BASDAI 50	243	ASAS 20	218	ASAS 40	131	ASAS 5/6	56
4	ASAS-PR	132	BASDAI 50	190	ASAS 20	115	ASDAS-LDA	55
5			ASAS-PR	105	BASDAI 50	114	BASDAI50	37
6					ASDAS-ID	113	ASAS 40	35
7					ASAS-PR	66	ASAS 20	32
8							ASDAS-ID	28
9							-PR	22

Legend. *Total of 16 RCTs analysed, with different sets of RCTs within the 16 analysed based on the availability of response criteria; X^2=Chi-square; RCTs=randomized controlled trials; BASDAI= Bath Ankylosing Spondylitis Disease Activity Index; ASAS= Assessment in SpondyloArthritis International Society; PR= partial remission; CII= clinically important improvement; MI= major improvement; LDA= low disease activity; ID= inactive disease

Discriminative performances of response and status criteria in RCTs of biological and targeted synthetic DMARDs in axial spondyloarthritis

MARD with placebo, as a smaller sample size can be used with the same statistical power, in comparison to the currently most frequently used ASAS 40.

Disclosure: A. Ortolan, None; **V. Navarro-Compán**, Novartis Pharma, 1, 5, 8, AbbVie Inc., 5, 8, Eli Lilly and Company, 5, 8, Pfizer Inc., 5, UCB, 5, 8; **A. Sepriano**, NOVARTIS, 1, UCB, 1; **R. Landewé**, AbbVie, 2, 5, 8, AstraZeneca, 5, Bristol-Myers Squibb, 5, 8, Eli Lilly, 5, Galapagos, 5, Novartis, 5, Pfizer Inc, 2, 5, 8, UCB, 2, 5, 8, GlaxoSmithKline, 5, Janssen, 2, 5, 8, Merck, 5, 8, Rheumatology Consultancy BV, 1, Ablynx, 5, Amgen, 2, 5, 8, Celgene, 5, Gilead, 5, Novo Nordisk, 5, Roche, 2, 5, 8, Schering, 2, 5, 8, TiGenix, 5; **D. van der Heijde**, AbbVie, 5, Bristol-Myers Squibb, 5, Cyxone, 5, Galapagos NV, 5, Gilead Sciences, Inc., 5, GlaxoSmithKline, 5, Eli Lilly, 5, Novartis, 5, Pfizer, 5, UCB Pharma, 5, Amgen Inc., 5, Astellas, 5, AstraZeneca, 5, Boehringer Ingelheim, 5, Celgene, 5, Daiichi-Sankyo, 5, Janssen, 5, Merck, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, Imaging Rheumatology bv, 3, Eisai, 5; **S. Ramiro**, Abbvie, 8, Eli Lilly, 8, Novartis, 8, MSD, 8, UCB, 8, Sanofi, 8.

Abstract Number: 2032

Treatment Response to Biological Disease-modifying Anti-rheumatic Drugs Is Associated with Favorable Changes of the Body Composition in Patients with Ankylosing Spondylitis

Valeria Rios Rodriguez[1], Mikhail Protopopov[1], Fabian Proft[1], Judith Rademacher[1], Burkhard Muche[1], Anne-Katrin Weber[1], Susanne Lüders[1], Hildrun Haibel[1], Maryna Verba[1], Joachim Sieper[1] and Denis Poddubnyy[2], [1]Charité Universitätsmedizin Berlin, Berlin, Germany, [2]Charité – Universitätsmedizin Berlin, Berlin, Germany

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Spondyloarthritis Including Psoriatic Arthritis – Treatment III: Axial Spondyloarthritis

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: There is few data available regarding differences in body composition and its possible changes in patients with ankylosing spondylitis (AS) treated with biological disease-modifying anti-rheumatic drugs (bDMARDs). An increase of body weight and lean mass in patients receiving TNF inhibitors, as well as a possible muscle wasting by high disease activity have been previously described. Bioelectrical impedance analysis (BIA) is a valid method to assess body composition and allows to distinguish between fat, fat-free mass and skeletal muscle mass.

The aim of this study is to evaluate changes in body composition in patients with AS after 6 months of treatment with bDMARDs.

Methods: Patients with a diagnosis of AS, fulfilling the modified New York criteria and starting a bDMARD therapy were included in the extension of the prospective German Spondyloarthritis Inception Cohort (GESPIC). All patients had high disease activity (BASDAI >=4 and/or ASDAS >=2.1) despite previous treatment with nonsteroidal anti-inflammatory drugs. Disease activity and body composition were assessed at baseline and after 6 months of bDMARD treatment. Body composition was assessed by the BIA with the seca© mBCA 515 device (SECA Deutschland GmbH, Hamburg/Germany) and included the following parameters: weight, body mass index (BMI), fat mass index (FMI), fat

	Mean±SD	Difference, mean±SD	95% CI		P*
			Lower	Upper	
Weight at baseline, kg	77.19±15.71	0.75±3.80	0.04	1.47	0.04
Weight at 6 months, kg	77.94±16.25				
BMI at baseline, kg/m^2	25.03±4.32	0.30±1.29	0.06	0.55	0.02
BMI at 6 months, kg/m^2	25.33±4.43				
FMI at baseline, kg/m^2	6.74±3.39	0.31±0.97	0.07	0.54	0.01
FMI at 6 months, kg/m^2	7.05±3.42				
FFMI at baseline, kg/m^2	18.27±2.18	0.15±0.48	0.04	0.27	0.01
FFMI at 6 months, kg/m^2	18.42±2.27				
SMM at baseline, kg	27.40±5.85	0.32±1.11	0.05	0.59	0.02
SMM at 6 months, kg	27.73±5.90				
VAT at baseline, liters	1.94±1.62	-0.12±0.63	-0.27	0.04	0.14
VAT at 6 months, liters	1.82±1.56				

BMI: Body Mass Index; FMI: Fat Mass Index; FFMI: Free Fat Mass Index; SMM: Skeletal Muscle mass; VAT: Visceral Adipose Tissue.
*Wilcoxon test

TABLE 1. Body composition parameter at baseline and after 6 months of treatment with a bDMARDs in patients with AS (n=77)

free mass index (FFMI), skeletal muscle mass value (SMM), and visceral adipose tissue value (VAT). Response to a bDMARD therapy was defined as achievement of clinically important improvement of ASDAS (>=1.1).

Results: A total of 129 patients (66.7% male) with AS were recruited in this cohort extension between 2015 and 2019. The mean (mean ± SD) age was 36.2 ± 10.3 years, and symptom duration was 10.7 ± 9.1 years. HLA-B27 test was positive in 89.1% patients. BIA was assessed in 77 patients; the baseline characteristics of these patients were similar to those of the whole cohort. Of these, 75 patients were treated with TNF inhibitors and 2 patients were treated with an IL-17A inhibitor.

After 6 months of a bDMARD treatment, body composition changed significantly with an increase of weight and BMI due to the gain of FMI but also of FFMI and SMM, while there was no increase of the visceral fat – table. In responders (improvement of ASDAS >=1.1 after 6 months) the results were similar to the whole group with a significantly gain (mean±SD) on BMI, FMI, FFMI and SMM (0.3 ± 1.4 kg/m^2, 0.3 ± 1.0 kg/m^2, 0.2 ±0.5 kg/m^2, 0.5 ± 1.2 kg, p< 0.05, respectively). In non-responders, there were no significant changes on the body composition after 6 months of treatment.

Conclusion: Treatment with bDMARDs is associated with favorable changes of the body composition with increase of the muscle mass but not of the visceral fat. These changes were evident in treatment responders only.TABLE 1. Body composition parameter at baseline and after 6 months of treatment with a bDMARDs in patients with AS (n=77)

Disclosure: V. Rios Rodriguez, None; **M. Protopopov**, None; **F. Proft**, Novartis, 2, 8, AbbVie, 8, AMGEN, 8, BMS, 8, Hexal, 8, Celgene, 8, Lilly, 8, MSD, 8, Pfizer, 8, Roche, 8, UCB, 8; **J. Rademacher**, None; **B. Muche**, None; **A. Weber**, None; **S. Lüders**, None; **H. Haibel**, None; **M. Verba**, None; **J. Sieper**, AbbVie, 5, Novartis, 5, 8, Lilly, 8, Janssen, 5, Merck, 5, 8; **D. Poddubnyy**, Eli Lilly and Company, 2, 5, 8, MSD, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, BioCad, 5, Gilead, 5, GSK, 5, UCB, 5, 8, BMS, 8.

Abstract Number: 2033

Large-scale Examination of Longitudinal Skin Gene Expression and Its Associations with Skin Thickness in Systemic Sclerosis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical I: Stratification Strategies for Clinical Trials
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Numerous studies have revealed dysregulated gene expression in the skin of systemic sclerosis (SSc) patients, with varying degrees of inflammatory/immune and fibroblast upregulation. However, the progression of skin gene expression over time and the relationships between skin gene expression and clinical manifestations are incompletely understood. We sought to address these questions through transcriptomic profiling of skin biopsies from a large, diverse group of well-characterized SSc patients, the majority of whom underwent longitudinally-collected biopsies.

Methods: 339 total skin biopsies were obtained from the forearm of 113 SSc patients and 44 matched healthy controls. Disease duration was less than six years at initial biopsy (mean of 2.6 years), and 59.3% of patients had diffuse cutaneous involvement. 105 SSc patients underwent a second biopsy, and 77 underwent a third biopsy (mean of 0.8 years and 1.9 years after baseline biopsy, respectively). Biopsy samples were analyzed by microarray, and normalized transcript levels were analyzed for cell type-specific gene expression signatures comprising 15 cell types. Each SSc patient's cell type signatures were compared to the average amongst healthy controls.

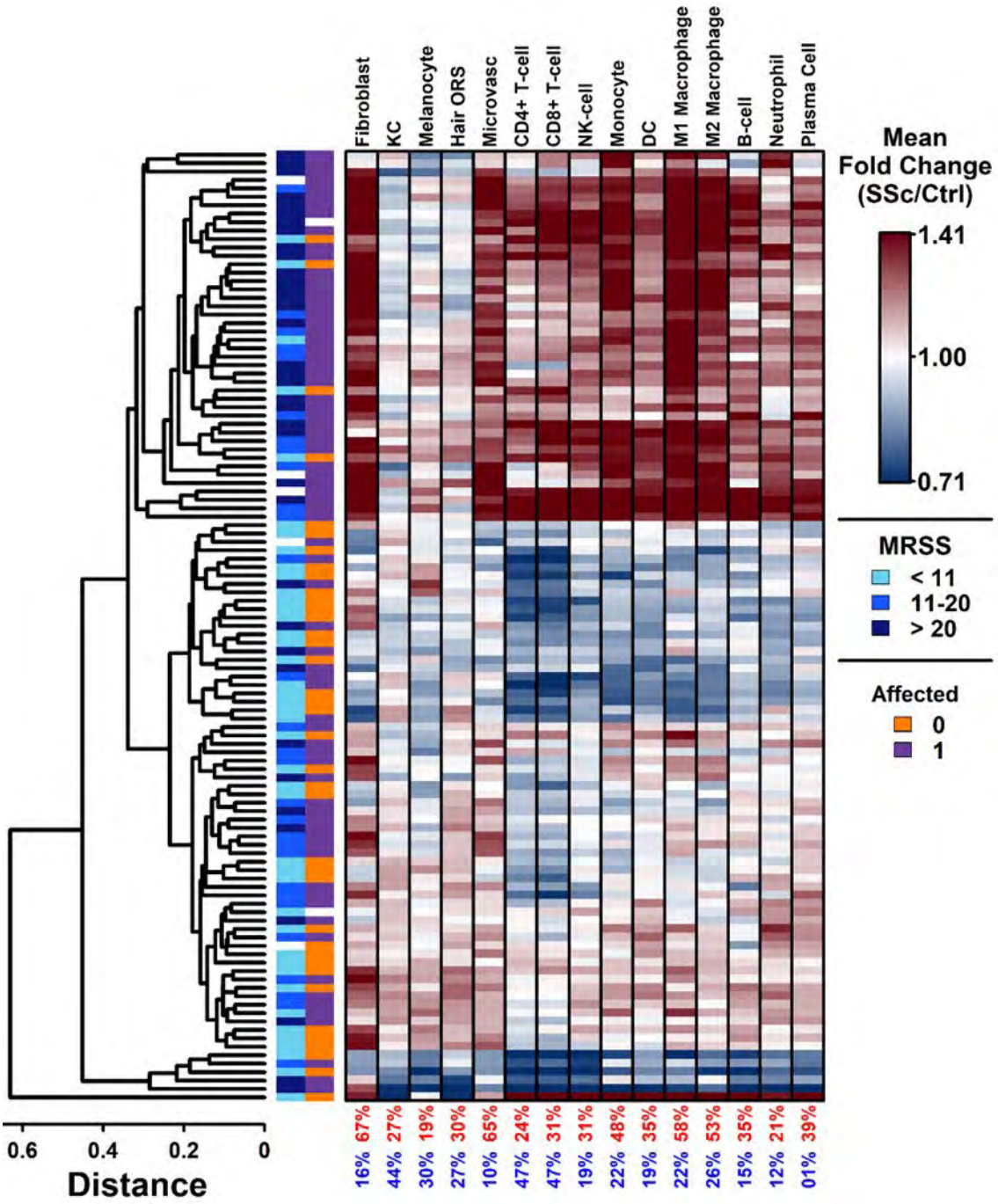

Figure 1. Cell type signatures in baseline skin biopsies of systemic sclerosis patients. Each row represents an SSc patient. Each patient's cell type signature scores were compared to the average amongst the 44 healthy controls. mRSS: modified Rodnan skin score, SSc: systemic sclerosis, Ctrl: healthy control, KC: keratinocyte, NK cell: natural killer cell, DC: dendritic cell

Table 1

Skin immune cell and fibroblast signatures correlated with earlier disease duration

	Disease duration	
	all SSc (n = 113)	diffuse SSc (n = 67)
M1 macrophage	-0.17 (0.07)	-0.32 (<0.01)
M2 macrophage	-0.18 (0.05)	-0.31 (<0.01)
CD4 cell	-0.08 (0.43)	-0.11 (0.36)
CD8 cell	-0.10 (0.30)	-0.15 (0.24)
B cell	-0.15 (0.11)	-0.19 (0.12)
NK cell	-0.13 (0.16)	-0.19 (0.13)
Fibroblast	-0.22 (0.02)	-0.41 (<0.01)

Spearman's rank order correlation coefficients between disease duration and cell type signatures are shown, with p values in parentheses. Red indicates p <0.05. Disease duration was defined as the time from the first non-Raynaud's symptom.

Results: 67% of baseline SSc biopsies had upregulation of the fibroblast signature, 58% and 53% had upregulation of M1 and M2 macrophage signatures, respectively, and 24%, 31%, 35%, and 31% had upregulation of CD4 T cell,

Table 2

Skin immune cell and fibroblast signatures predicted longitudinal mRSS, but were not independently predictive after adjustment for baseline mRSS

	Without adjustment			With adjustment for baseline mRSS		
	Coef.	95% CI	p value	Coef.	95% CI	p value
M1 macrophage	10.5	6.7, 14.3	<0.01	0.1	-1.9, 2.1	0.92
M2 macrophage	13.3	8.0, 18.5	<0.01	0.1	-2.6, 2.8	0.94
CD4 cell	11.6	5.4, 17.7	<0.01	0.8	-2.0, 3.6	0.58
CD8 cell	9.0	4.2, 13.9	<0.01	0.2	-2.0, 2.4	0.86
B cell	12.6	5.9, 19.4	<0.01	0.8	-2.3, 3.9	0.60
NK cell	12.0	5.6, 18.4	<0.01	0.2	-2.8, 3.1	0.91
Fibroblast	13.1	8.4, 17.8	<0.01	1.1	-1.4, 3.7	0.39

Mixed effects linear regression models of longitudinal mRSS as a function of baseline cell type signature scores, without vs. with adjustment for baseline mRSS. mRSS: modified Rodnan skin score

CD8 T cell, B cell, and NK cell signatures, respectively (Figure 1). Fibroblast and immune cell signatures correlated with local skin score and total modified Rodnan skin score (mRSS), with the strongest correlations observed for fibroblast, M1 macrophage, and M2 macrophage signatures. At baseline biopsy, fibroblast and immune cell signatures correlated with shorter disease duration, particularly amongst diffuse cutaneous SSc patients (Table 1). Longitudinal biopsies revealed that immune cell signatures tended to decline over time, particularly in diffuse cutaneous SSc. Immune cell and fibroblast signatures at baseline biopsy predicted subsequent skin fibrosis course, measured as longitudinal mRSS, based on mixed effects linear regression modeling. However, the predictive values were not statistically significant after adjustment for baseline mRSS (Table 2).

Conclusion: Immune cell and fibroblast signatures in the skin of SSc patients were associated with skin thickness and tended to decline over time. Baseline immune cell and fibroblast signatures did not provide predictive significance for the course of skin thickness beyond the information provided by the baseline mRSS.

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Abstract Number: 2034

Resolving Phenotypic and Prognostic Differences in Interstitial Lung Disease Related to Systemic Sclerosis by Computed Tomography-based Radiomics

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical I: Stratification Strategies for Clinical Trials

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Radiomics describes the in-depth analysis of tissue phenotypes by computational retrieval of high-dimensional quantitative imaging features including tissue intensity, texture, and wavelet characteristics. Here, we aimed to evaluate high-resolution computed tomography (HRCT)-based radiomics for disease phenotyping and risk stratification in interstitial lung disease related to systemic sclerosis (SSc-ILD).

Methods: In this study, we investigated two independent, prospectively followed SSc-ILD cohorts including 90 patients (76.7% female, median age 57.5 years) from the University Hospital Zurich and 66 patients (75.8% female, median age 61.0 years) from the Oslo University Hospital. For every subject, we defined and extracted 1,386 radiomic features from semi-automated segmented HRCT images including 17 intensity, 137 texture, and 1,232 wavelet features using our in-house developed radiomics software Z-Rad. After filtering of robust radiomic features, we performed unsupervised k-Means clustering and supervised prediction modelling to 1) identify homogeneous imaging-based groups without any a priori assumptions, and 2) to derive a quantitative radiomic risk score for progression-free survival (PFS) in SSc-ILD. PFS was defined as the time to a relative decline in FVC% predicted ≥ 15%. Associations with clinical characteristics at baseline and PFS among the obtained clusters and risk score groups were assessed by Fisher's Exact and Mann-Whitney U test, or univariable Cox regression, respectively.

Results: Unsupervised cluster analysis of 1,355 robust radiomic features revealed two distinct patient clusters based on their radiomic profiles. The two patient clusters exhibited significant differences in their lung disease-specif-

ic baseline parameters, but not in serological or demographic characteristics. Cluster 2 presented a more severe ILD phenotype than cluster 1, and was significantly associated ($p< 0.05$) with a worse restrictive ventilation defect, pulmonary hypertension, a fibrosis extent on HRCT of ≥ 20%, and certain visual HRCT ILD patterns, including UIP radiological subtype and honeycombing. The clusters further significantly differed in their outcome with cluster 2 showing a decreased PFS and thus a higher risk of faster disease progression ($p=0.001$). We next derived a quantitative radiomic risk score (qRISSc) composed of the sum of 26 equally weighted radiomic features that accurately predicted PFS and showed prognostic power in both study cohorts (C-index = 0.67 for Zurich, 0.71 for Oslo). We also compared the prognostic potential of qRISSc to existing SSc-ILD stratification tools, including subgrouping of patients based on HRCT (< 20% or ≥20% fibrosis) or the FVC% predicted threshold of < 70%, respectively. In both cohorts, neither HRCT- nor FVC%-based risk stratification was prognostic for future lung function decline, overall indicating the superiority of qRISSc over current prognostic measures.

Conclusion: Our data suggests that radiomic features and radiomics-derived scores can capture important phenotypic and prognostic information thus showing great potential for risk stratification in SSc-ILD.

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Abstract Number: 2035

Exploring Stratification Strategies for Early Diffuse Systemic Sclerosis Clinical Trial Design

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical I: Stratification Strategies for Clinical Trials

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Clinical trials in early diffuse systemic sclerosis (SSc) using the modified Rodnan skin score (mRSS) as the primary outcome have been largely negative. This may reflect limitations of clinical trial design or outcome measures, as opposed to therapeutic failures. Our objective was to assess if stratification could enhance early diffuse SSc clinical trial design and analysis. Our primary hypothesis was that given the predominance of RNA poly-

merase III (RNAP3) in recent clinical trials and its association with severe skin involvement, stratification by RNAP3 or other factors could improve trial design.

Methods: We used a large, observational Scleroderma Center cohort from a US tertiary care referral site. We identified early diffuse SSc patients first seen between 1980 and 2015. We included those with < 36 months from first non-Raynaud manifestation and ≥3 recorded mRSS scores in the analysis. Our modeling strategy reflected typical disease duration inclusion criteria for ongoing clinical trials: < 18 months and < 36 months of disease. We used descriptive, time to event, group-based trajectory modeling to determine mRSS trajectory groups, multivariable regression modeling as well as classification tree analyses (CTA) to assess contributing factors to predict mRSS trajectory groupings. We analyzed the following variables: age, gender, race, antibody, skin thickness progression rate (STPR), tendon friction rubs (TFR), elevated ESR and medication use.

Results: We found 514 patients who met criteria with < 36 months of disease, of which 403 had < 18 months of disease at first visit (Table 1). The median disease duration was 0.90 (IQR 0.59, 1.39) years at first visit, median follow-up 10.2 (4.5, 16.3) years with 14 (8, 23) SSc clinic visits. The majority, 273 (53%) were RNAP3 positive, and 137 (27%) were Scl-70 positive.

Initial time-to event analysis demonstrated a significant difference between time to peak mRSS for those positive for Scl-70 (p=0.04) or RNA3 positive (p=0.02). Trajectory modeling showed distinctly different mRSS trajectory patterns over 5 years by autoantibody regardless of disease duration (Figure 1). Regression analysis confirmed that STPR (p< 0.0001), TFR (p=0.002) and RNAP3 (p=0.01) were predictors of trajectory groupings. CTA analysis (Figure 3) demonstrated that measured characteristics performed better in predicting trajectory grouping for < 18 months than

	Disease duration <18 months (n=403)	Disease duration <36 months (n=514)
Mean age at first visit (±SD)	50.0 ± 13.8	49.4 ± 13.8
Female	205 (76%)	382 (74%)
Caucasian	370 (92%)	468 (91%)
Median disease duration (years) from first non-Raynaud manifestation (IQR)	0.76 (0.55, 1.04)	0.90 (0.59, 1.39)
Median follow-up time in years (IQR)	10.2 (4.6, 16.3)	10.2 (4.5, 16.3)
Median number of clinic visits (IQR)	16 (9, 24)	14 (8, 23)
SKIN CHARACTERISTICS		
Mean mRSS (±SD) at 1st visit	25 ± 11	25 ± 11
Maximum mRSS during follow-up (mean ±SD)	32 ± 11	31 ± 11
STPR rapid	141 (35%)	194 (38%)
intermediate	146 (37%)	163 (32%)
slow	113 (28%)	154 (30%)
NON-CUTANEOUS DISEASE CHARACTERISTICS		
Tendon friction rubs present	182 (45%)	231 (45%)
Gastrointestinal involvement	173 (43%)	235 (46%)
Fibrosis on chest imaging	77 (23%)	103/440 (23%)
Renal crisis	37 (9%)	50 (10%)
Pulmonary Hypertension		9 (2%)
AUTOANTIBODIES		
RNA polymerase III	228 (57%)	273 (53%)
Scl-70	106 (27%)	137 (27%)

Table 1. First Visit Demographic and Systemic Sclerosis Charcteristics

Figure 1: Pictorial comparison of 5-year skin score trajectory plots from the first visit by autoantibody

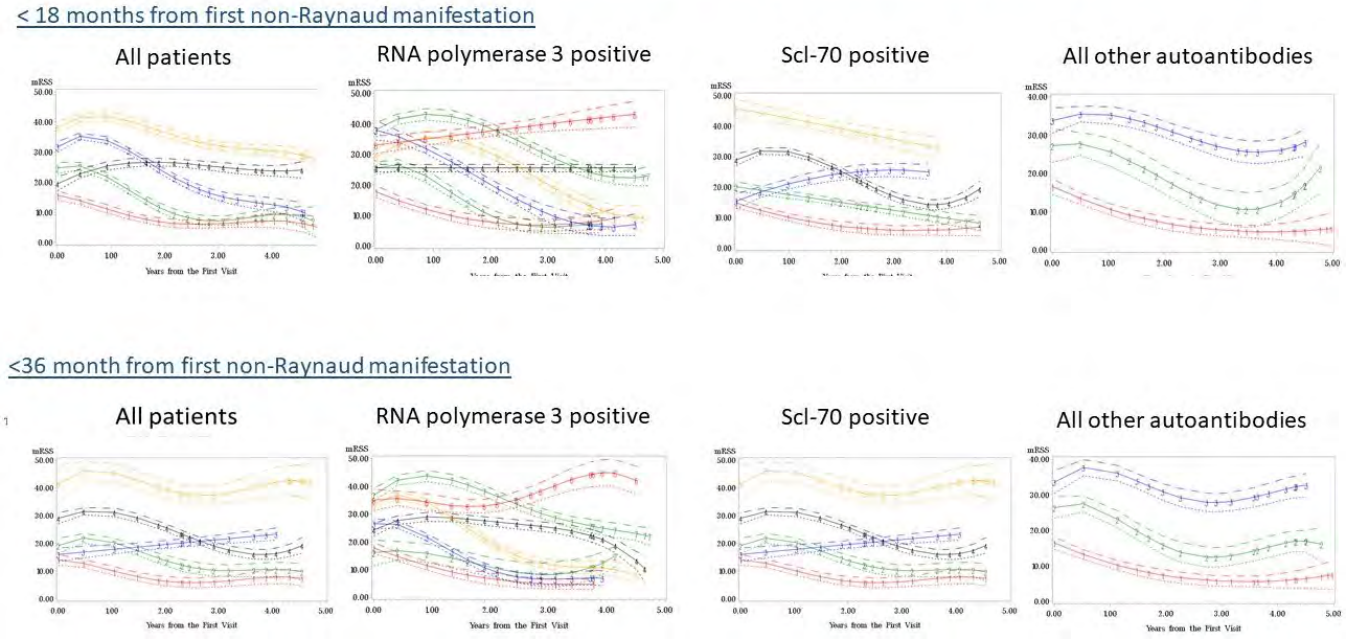
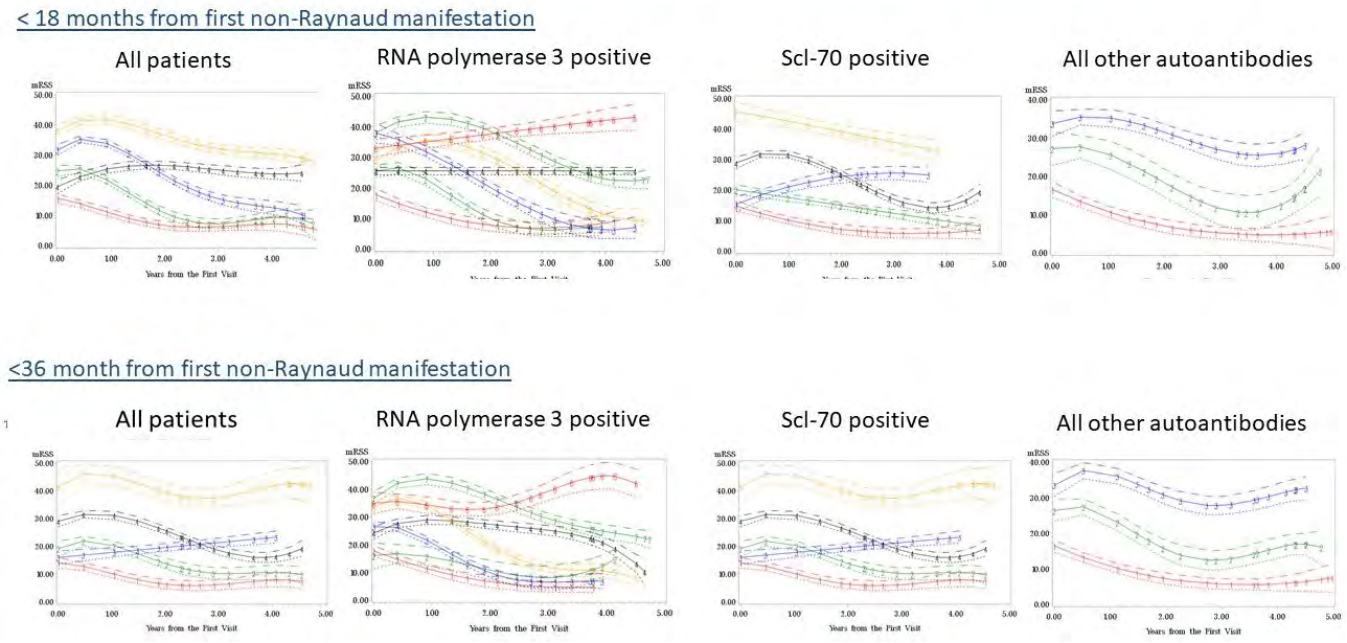


Figure 1: Pictorial comparison of 5-year skin score trajectory plots from the first visit by autoantibody



predicting trajectory groups for < 36 months of disease. STPR and presence of TFR were suggested as predictive factors for trajectory grouping for both < 18 months and < 36 months disease duration.

Conclusion: STPR, presence of TFR and RNAP3 antibody are consistently associated with mRSS trajectory patterns over time using multiple analysis methods. STPR and TFR are early nodal breaks in CTA analysis, suggesting they may be preferred stratification strategies over RNAP3 status. As STPR is intended to be used at the initial SSc clinic visit, TFR presence is the more feasible data-supported stratification strategy for early diffuse clinical trials.

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Abstract Number: 2036

Damage Trajectories in Systemic Sclerosis Using Group-Based Trajectory Modeling

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical I: Stratification Strategies for Clinical Trials

Session Type: Abstract Session

Session Time: 3:00PM–3:50PM

Background/Purpose: Systemic sclerosis (SSc) is a rare systemic autoimmune disease associated with a high mortality and characterized by the accrual of organ damage over time. The Scleroderma Clinical Trials Consortium Damage Index (SCTC-DI) is a recently validated tool to measure this damage (Ferdowsi et al., 2019). Identifying predictors of future damage is of utmost importance for prognostication and guiding research. This study aimed to identify if there are distinct trajectories of damage accrual from early in the disease and to determine which variables are associated with different trajectories, which could help guide when to initiate aggressive therapy early.

Figure - Group-based Trajectory Model of Scleroderma Clinical Trials Consortium - Damage Index at Yearly Visits

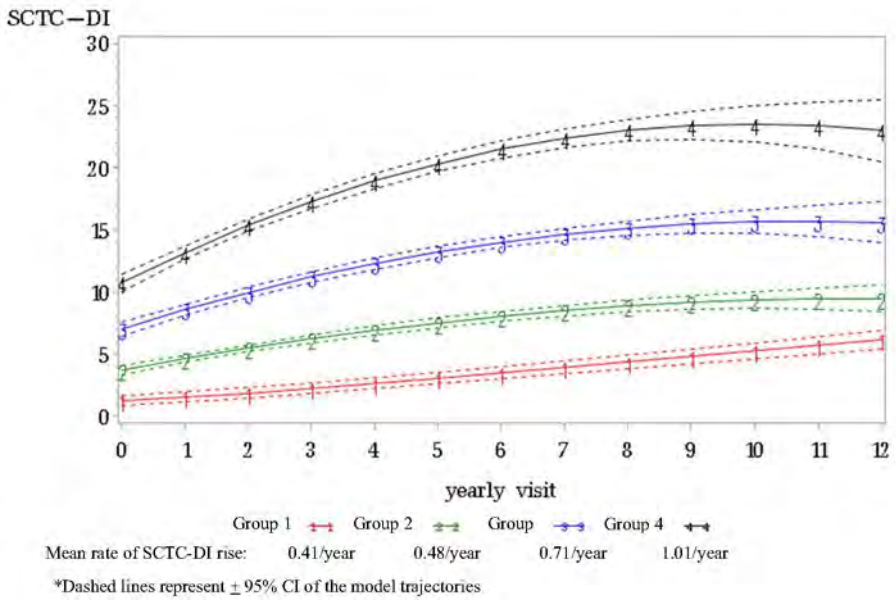

Table – Baseline Characteristics of Trajectory Groups

	Group 1 (n=101)	Group 2 (n=190)	Group 3 (n=86)	Group 4 (n=32)	P values**
Age, mean ± sd	52.3 ± 12.9	53.2 ± 12.8	53.5 ± 13.0	59.1 ± 11.7	0.074
Female, n (%)	89 (88.1%)	154 (81.1%)	65 (75.6%)	21 (65.6%)	**0.022**
Caucasian, n (%)	85 (87.6%)	164 (86.8%)	68 (80.9%)	25 (78.1%)	0.352
Postsecondary education, n (%)	48 (49.5%)	88 (49.2%)	30 (36.1%)	13 (44.8%)	0.217
Employed, n (%)	34 (38.2%)	61 (35.7%)	23 (29.1%)	8 (25.8%)	0.444
Ever smoking, n (%)	47 (56.5%)	99 (52.4%)	56 (65.1%)	21 (65.6%)	**0.038**
Disease duration since onset of NR, mean ± sd	1.1 ± 0.5	1.1 ± 0.5	1.0 ± 0.5	1.0 ± 0.6	0.708
Diffuse subset, n (%)	23 (24.0%)	82 (43.9%)	66 (76.7%)	21 (65.6%)	**<.001**
Antibodies, n (%)					
ACA	41 (41.8%)	52 (29.4%)	11 (14.5%)	7 (21.9%)	**<.001**
ATA	23 (23.5%)	41 (23.0%)	15 (20.3%)	5 (15.6%)	0.772
ARNAP	11 (12.1%)	38 (22.9%)	26 (37.7%)	10 (32.3%)	**0.001**
C-reactive protein, median [IQR]	3.2 [1.4, 5.6]	4.0 [2.1, 8.7]	6.1 [3.3, 15.1]	8.7 [4.2, 18.1]	**<.001**
Erythrocyte Sedimentation Rate, median [IQR]	13 [7, 22]	14 [7, 29]	18.5 [10, 38]	29.5 [11.5, 55.5]	**<.001**
Tendon friction rubs, n (%)	5 (5.0%)	21 (11.2%)	21 (24.4%)	12 (37.5%)	**<.001**
Synovitis, n (%)	32 (32.3%)	60 (32.4%)	27 (32.5%)	12 (38.7%)	0.916
Silica and other environment exposure*, n (%)	10 (10.5%)	27 (14.6%)	14 (17.1%)	6 (19.4%)	0.525
Nailfold capillaroscopy abnormalities, n (%)	78 (78.0%)	140 (74.9%)	60 (70.6%)	25 (78.1%)	0.675
Other comorbidities, n (%)					
Diabetes	2 (2.0%)	16 (8.5%)	8 (9.3%)	3 (9.4%)	0.142
Atherosclerotic disease	4 (4.0%)	10 (5.3%)	7 (8.1%)	5 (15.6%)	0.095
Lung disease	11 (11.0%)	23 (12.2%)	13 (15.1%)	7 (21.9%)	0.389
eGFR, n (%)					**0.006**
>60	88 (90.7%)	170 (91.4%)	70 (84.3%)	22 (71.0%)	
30-60	9 (9.3%)	12 (6.5%)	10 (12.1%)	5 (16.1%)	
0-30	0	4 (2.1%)	3 (3.6%)	4 (12.9%)	

* Other environment exposure includes organic solvents, vinyl chloride & epoxy resins

** One-way analysis of variance (ANOVA) and Kruskal-Wallis Test were used to compare continuous variables. Chi-square test and Fisher's exact test were used for categorical variables.

Methods: Using a prospective cohort design, incident adult cases of SSc (disease onset < 2 years) were identified in two large databases. Patients from these databases are enrolled consecutively and followed with yearly standardized assessments. Patients who met the ACR-EULAR classification criteria for systemic sclerosis with at least two cohort visits and two SCTC-DI values were included. Due to missing data, three elements of the SCTC-DI were removed from the scoring (small joint contractures, pericardial effusion, GAVE). Group-based trajectory modelling (GBTM) was used to identify clusters of patients with similar DI trajectories. Their baseline characteristics were then compared for statistical significance using a one way-analysis of variance (ANOVA) and Kruskal-Wallis Test for continuous variables and chi-square test and Fisher's exact test for categorical variables.

Results: 409 patients were included in this study. Four trajectories (Figure) of damage accrual were identified, with increasing damage over time and a plateauing effect observed in the three groups with higher damage scores. The average of posterior probabilities of group membership assigned to each group was 0.92, suggesting our trajectory

model fits well. The groups were distinct at baseline, with patients who had the fastest damage accrual also having a higher baseline SCTC-DI. Clinical factors that were more prevalent in the worst damage trajectories were older age, male sex, current or previous smoking history, diffuse disease, tendon friction rubs, renal impairment, anti-RNA polymerase positivity and higher baseline inflammatory markers (Table). Anti-centromere antibody positivity was more prevalent in the lower disease damage groups.

Conclusion: We have identified four distinct trajectories of disease damage in a combined incident cohort of patients with SSc. Several clinical and serological characteristics were more prevalent in those with worse damage trajectories. These findings may be helpful in recognizing patients in whom early aggressive treatment is necessary.

Disclosure: A. Barbacki, None; **M. Baron**, None; **M. Wang**, None; **Y. Zhang**, None; **M. Nikpour**, Actelion, 2, 5, 8, GSK, 2, 5, 8, Boehringer Ingelheim, 5; **A. Man**, Boehringer Ingelheim Canada, 5.

Abstract Number: 2037

Geographic Distribution and Environmental Triggers of Systemic Sclerosis in Massachusetts

Anastasiya Muntyanu[1], Bina Kassamali[2], Ruth Ann Vleugels[3] and Avery LaChance[3], [1]McGill University, Montreal, QC, Canada, [2]Harvard Medical School, Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical I: Stratification Strategies for Clinical Trials
Session Type: Abstract Session
Session Time: 3:00PM–3:50PM

Background/Purpose: Systemic sclerosis (SSc) is a chronic autoimmune sclerosing disease with a 10-year survival rate of less than 65%. This rate has remained unchanged for over 40 years. Although the exact pathogenesis remains unclear, it has been hypothesized that an environmental trigger leads to disease development in a genetically predisposed host. Assessment of high incidence geographic disease clusters can be an initial step in cause identification. ArcGIS is a geospatial processing program used to create and analyze geographic distribution and has recently been utilized to determine high incidence clusters for several cancers and autoimmune diseases. The objectives of this study are to analyze the geographic distribution of SSc in Massachusetts between 1989-2019, determine incidence rates, and evaluate potential environmental exposures.

Methods: Demographic and geographic patient data for SSc cases was obtained from two large, academic tertiary centers in Massachusetts. Incidence rates were calculated per year and per geographic area, based on zip code. Maps were created using ArcMap 10.7.1 to identify case clusters across the state. The SSc incidence maps were compared to maps of environmental exposures to determine potential contribution of pollutants to disease development.

Results: 4,579 patients diagnosed with SSc between 1989-2019 were identified. The crude incidence rate was 24.2 cases per million individuals per year. Geographic analysis revealed increased incidence in specific geographic regions in Massachusetts including Boston, Lynn, Revere, Chelsea, Newton Upper Falls, and Charlestown (Figure 1). The density of industry presence and waste sites was found to be significantly higher in the areas with elevated incidence of SSc compared to low incidence areas (8.5-fold increase; p=0.0087) (Figure 2). Particulate pollution ($PM_{2.5}$)

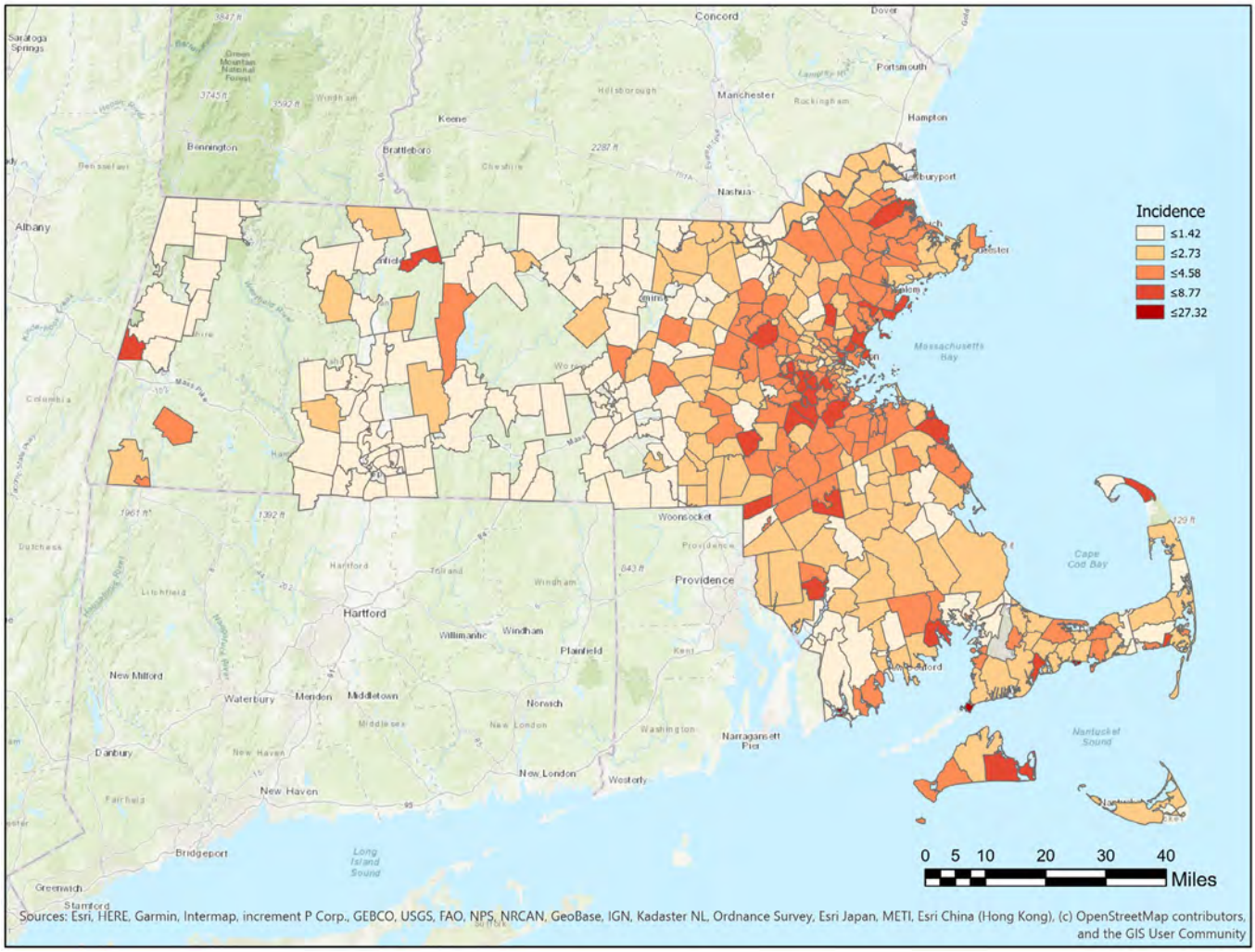

Figure 1. Incidence rates per zip code of SSc in Massachusetts

levels were increased in high incidence areas (Figure 3), and airborne benzene levels correlated well with incidence rates of SSc in the Boston area.

Conclusion: To our knowledge, this is the first study to explore geographic distribution of SSc and evaluate possible triggers for disease development in the United States. The presence of regional clustering and increased density of industry and waste sites in those areas suggests that multiple environmental factors may play a critical role in the development of SSc. Further investigation is warranted to explore these findings.

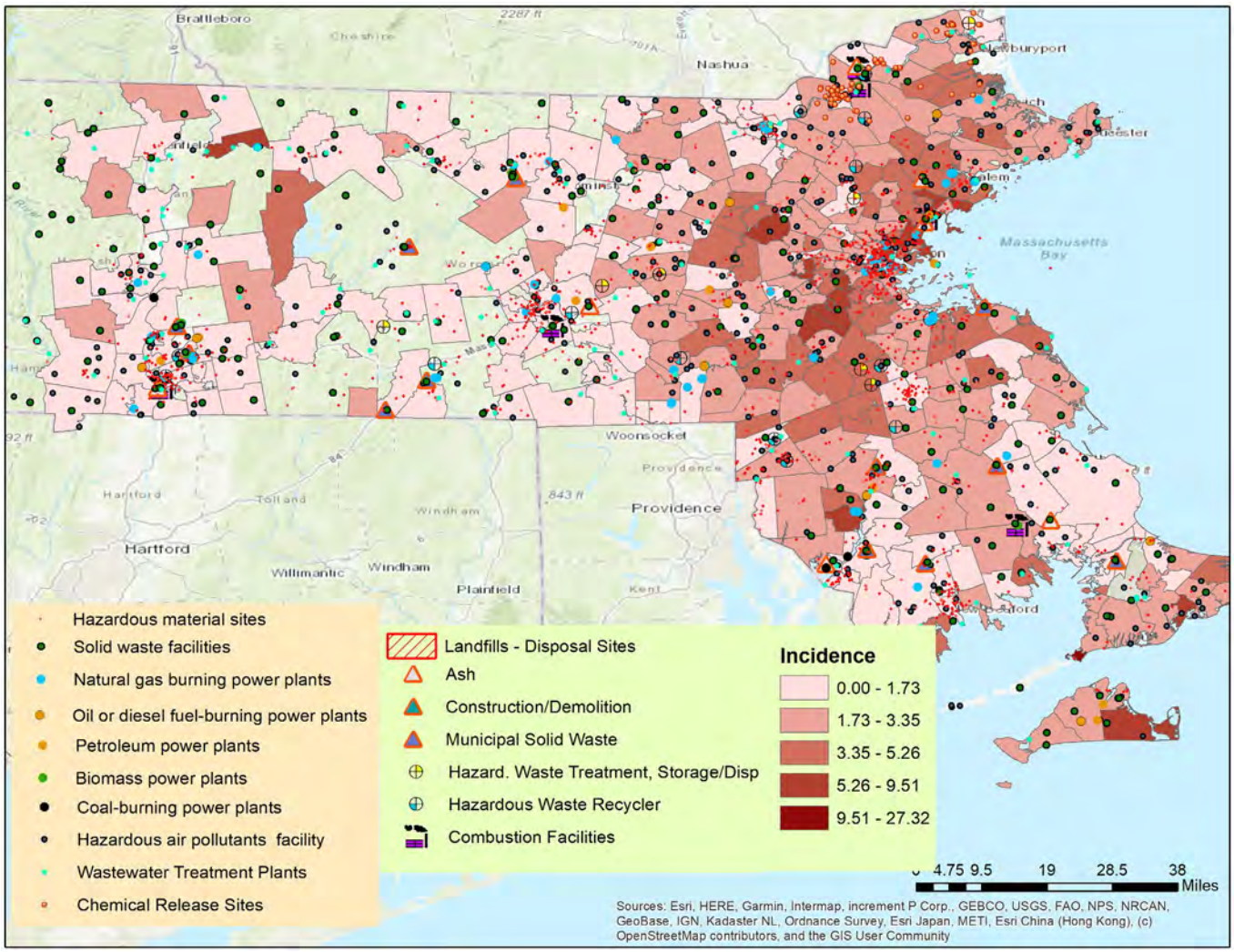

Figure 2. Industries and waste facilities in Massachusetts

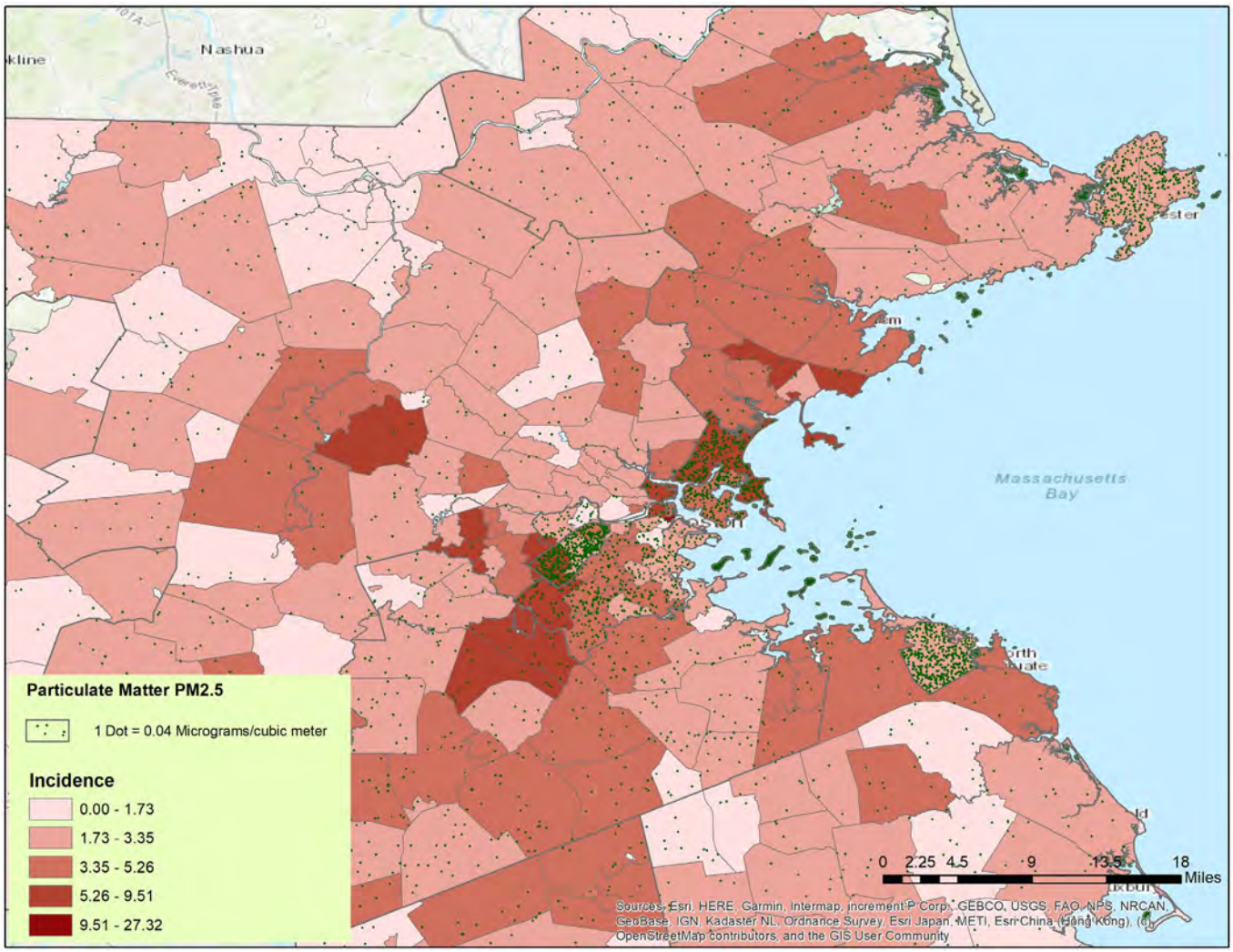

Figure 3. Particulate pollution levels in relation to SSc incidence in Massachusetts

Disclosure: A. Muntyanu, None; **B. Kassamali**, None; **R. Vleugels**, None; **A. LaChance**, None.

Abstract Number: 2038

Characterizing Morphea Subsets Using a Multi-center, Prospective, Cross-sectional Analysis

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical II: Lessons Learned from Clinical Trials & Cohorts

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: Morphea, or localized scleroderma, is an inflammatory condition of the skin and soft tissue that results in excessive collagen deposition, often producing permanent functional and cosmetic impairment.

Table 1: Demographic and clinical characteristics of morphea by age at onset

Characteristic	All patients (n=944)	Linear Morphea (N=500)*	Generalized Morphea (N=222)	P Value
Age (y), median (IQR)	16 (8-44)	11 (6-18)	55 (40-64)	<0.001[a]
Sex, n (%)				
Male	203 (22%)	121 (25%)	36 (16%)	0.001[b]
Female	741 (78%)	372 (75%)	186 (84%)	
Race, n (%)				0.001[b]
White	723 (77%)	371 (75%)	173 (78%)	
Non-White	221 (23%)	122 (25%)	49 (22%)	
LoSCAT component score, median (IQR)				
mLoSSI	4 (0-10)	3 (1-7)	14 (5-29)	<0.001[a]
LoSDI	9 (5-19)	9 (5-16)	19 (12-30)	<0.001[a]
PGA-A	20 (0-40)	19 (0-40)	30 (15-60)	<0.001[a]
PGA-D	30 (15-41)	30 (20-50)	20 (10-40)	<0.001[a]
Patient Reported Outcomes: DLQI and cDLQI, n (%)^				<0.001[b]
Mild	511 (64%)	358 (73%)	104 (47%)	
Moderate	155 (19%)	27 (5%)	49 (22%)	
Severe	135 (17%)	42 (9%)	48 (22%)	
Clinical features and disease modifiers, n (%)				
Deep Involvement	367 (39%)	224 (45%)	76 (34%)	0.005[b]
Superficial Involvement	116 (12%)	34 (7%)	64 (29%)	<0.001[b]
Pansclerotic	16 (2%)	0 (0%)	16 (7%)	<0.001[c]
Erythema in Lesion	122 (13%)	81 (16%)	2 (1%)	<0.001[b]
Dermal Involvement	245 (32%)	111 23%)	75 (34%)	0.001[b]
Hair Loss in Lesion	122 (16%)	88 (18%)	27 (12%)	0.055[b]
Limited Range of Motion	202 (21%)	128 (26%)	47 (21%)	0.168[b]
Joint Deformity	57(6%)	46 (9%)	0 (0%)	<0.001[c]
Functional Abnormality – by location, n (%)				
Face/Head/Neck	19 (2%)	12 (2%)	5 (2%)	0.882[b]
Trunk	29 (3%)	18 (4%)	5 (2%)	0.962[b]
Lower Extremity	147 (16%)	87 (18%)	39 (18%)	0.979[b]
Upper Extremity	92 (10%)	47 (10%)	32 (14%)	0.054[b]

Abbreviations: *IQR,* Interquartile range; *ECDS,* en Coup de Sabre; *PRS,* Parry-Romberg Syndrome; *LoSCAT,* Localized Scleroderma Cutaneous Assessment Tool; *mLoSSI,* modified Localized Scleroderma Skin Severity Index; *LoSDI,* Localized Scleroderma Skin Damage Index; *PGA-A,* Physician Global Assessment of Disease Activity; *PGA-D,* Physician Global Assessment of Disease Damage; *DLQI,* Dermatology Life Quality Index; *cDLQI,* Child Dermatology Life Quality Index

[a] Values computed with Mann-Whitney U Test

[b] Values computed with chi-square test

[c] Values computed with Fisher's exact test

^ Severity stratification: Mild = 0-5, Moderate = 6-10, Severe =11-30

Table 1. Demographic and clinical characteristics of morphea by subtype

Morphea affects both adults and children, with approximately 50% of patients having childhood onset disease[1,2]. Numerous classification schemes for morphea exist, but none have been evaluated for accuracy in categorizing large patient cohorts. We aimed to determine which existing morphea classifications (i.e. Padua criteria, Peterson criteria, and European Classification scheme) best characterized and identified clinically relevant morphea patient subsets using cross sectional analysis of two large patient cohorts.

Methods: We conducted a cross-sectional study of adults and children from two prospective cohorts - The Morphea in Adults and Children (MAC) at UT Southwestern Medical Center (Dallas, Texas) and the National Registry for Childhood-Onset Scleroderma (NRCOS) at University of Pittsburgh (Pittsburgh, PA). Patient demographics, morphea subtype, quality of life measures, disease activity as measured by the Localized Scleroderma Cutaneous Assessment Tool scores during their initial visits were examined.

Results: A total of 944 adults and children were included in this study. The mean (IQR) age of patients was 16 (8-44) years, and 741 of 944 were female. Majority were white individuals and had the linear or generalized subtype. Utilizing the previously published Padua criteria, the majority of the patients were classified to have linear morphea (n=492, 52%), followed by generalized (n=222, 24%), plaque (n=95, 10%), and then mixed (n=3). Overall, the Padua criteria failed to classify 14% of patients that were found to be "indeterminate" in comparison to the Peterson criteria and European classification schemes which failed to classify 39% and 47% of patients, respectively.

Conclusion: The Padua criteria is widely used by clinicians to categorize morphea patients and performed best in classifying patients into groups with cohesive demographic and clinical features. However, it has ambiguities that might lead to misclassification particularly in terms of generalized and pansclerotic morphea and descriptors such as morphea profunda. Consensus based approaches are needed to address these ambiguities in order to develop a unified classification scheme.

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2. Marzano AV, Menni S, Parodi A, et al. Localized scleroderma in adults and children. Clinical and laboratory investigations on 239 cases. *Eur J Dermatol.* 2003;13(2):171-176.

Disclosure: J. Zhu, None; **S. Prasad**, None; **K. Schollaert-Fitch**, None; **R. Haley**, None; **K. Torok**, None; **H. Jacobe**, None.

Abstract Number: 2039

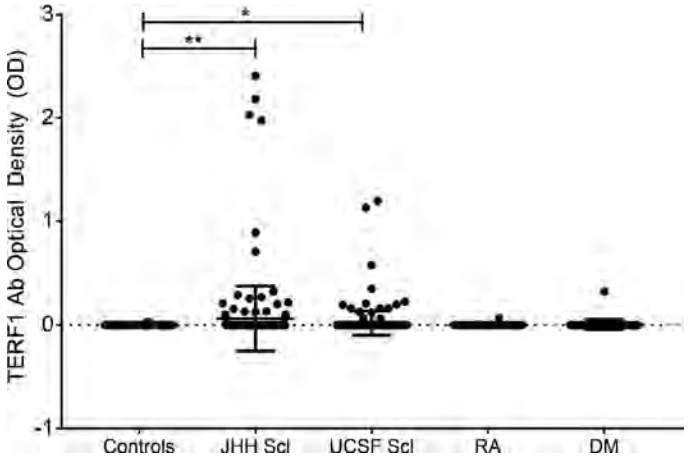
Short Telomeres and Autoantibodies Targeting Telomere-Associated Proteins in Scleroderma

Britany Adler[1], Ami Shah[2], Francesco Boin[3], Paul Wolters[3], Livia Casciola-Rosen[4] and Antony Rosen[1], [1]Johns Hopkins University, baltimore, MD, [2]Johns Hopkins University School of Medicine, Ellicott City, MD, [3]University of California, San Francisco, San Francisco, CA, [4]Johns Hopkins University, Johns Hopkins University, MD

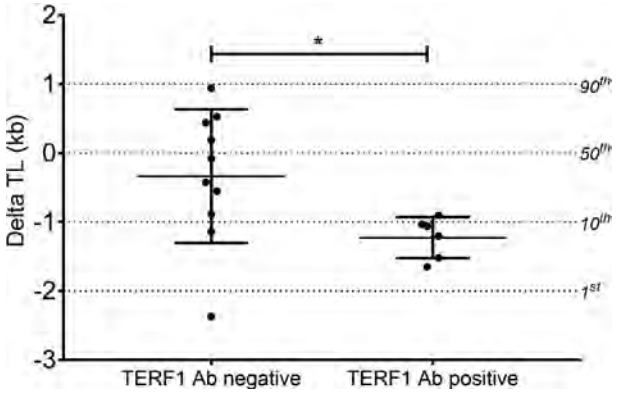
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical II: Lessons Learned from Clinical Trials & Cohorts
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Scleroderma is a systemic fibrosing disease of unknown etiology that often manifests with interstitial lung disease (ILD). Prior studies have found an association between telomere shortening in lymphocytes and scleroderma-ILD, but the mechanisms underlying this association are unclear. Because autoantibodies strongly predict clinical phenotype in scleroderma, we investigated whether patients with scleroderma and short telomeres have autoantibodies targeting telomerase (hTERT) and the shelterin complex which protects telomeres.

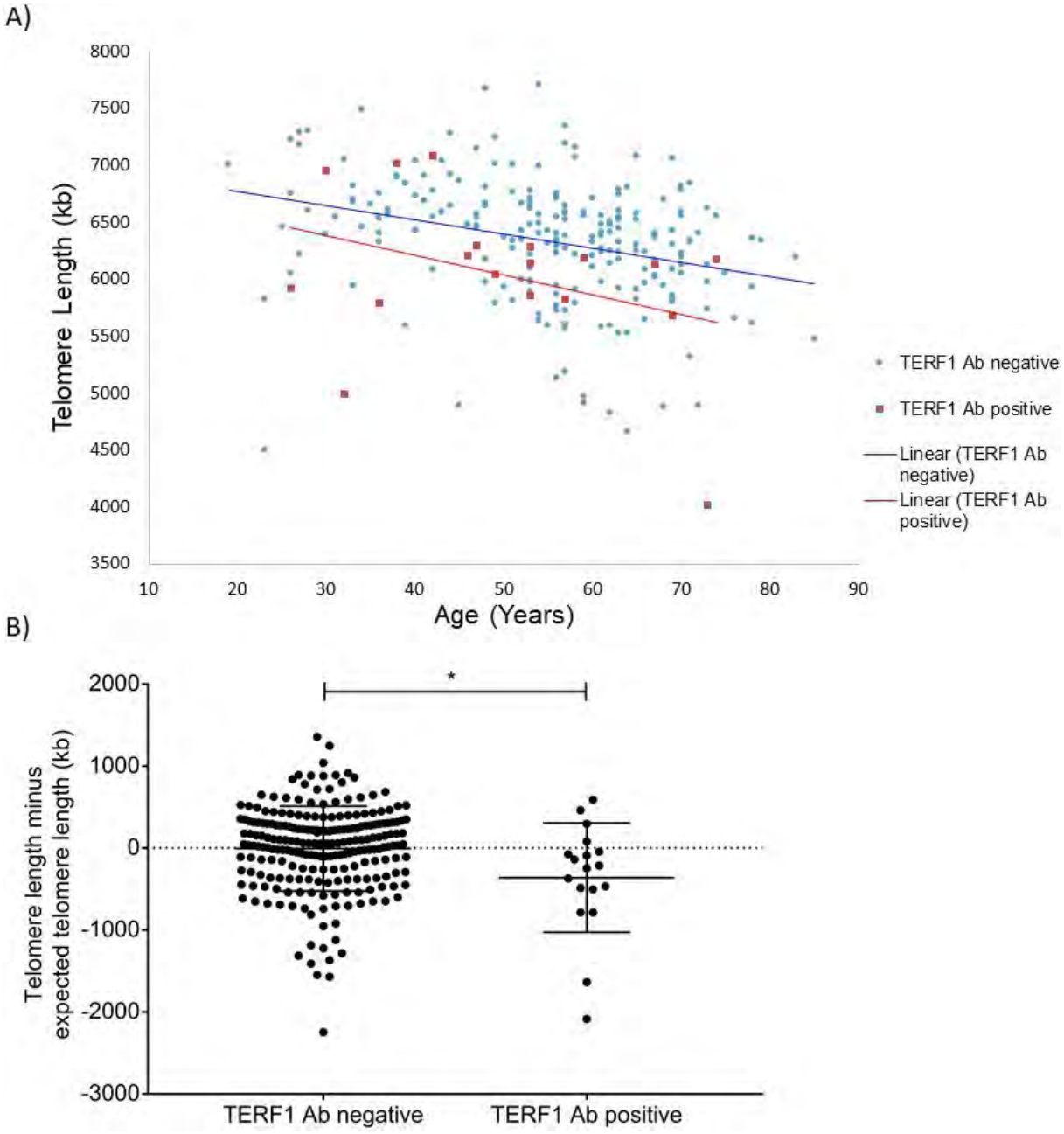
Methods: We screened patient sera from two separate longitudinal scleroderma cohorts from Johns Hopkins (JH, n=200) and the University of California, San Francisco (UCSF, n=242) for autoantibodies targeting hTERT and the six shelterin proteins TERF1, TERF2, POT1, TPP1, TIN2L, and RAP1. ELISA and immunoprecipitation assays were used for autoantibody detection. Peripheral leukocyte telomere length was measured in all patients from the UCSF Cohort using qPCR, and telomere length was measured in lymphocytes and granulocytes from a subset of the JH Cohort (n=16) using Flow Cytometry and Fluorescent in-situ Hybridization (Flow-FISH). To determine if telomere-associated



Telomere length measured by FlowFISH in lymphocytes of 6 TERF1 autoantibody positive scleroderma patients and 10 TERF1 autoantibody negative scleroderma patients. Patients with TERF1 autoantibodies have shorter telomere lengths in lymphocytes compared to TERF1 autoantibody negative patients. Delta TL is the difference between the patient telomere length and the median telomere length of a healthy control population. Statistics were done with the Wilcoxon rank sum, * $p < 0.05$.



Peripheral blood leukocyte telomere length measured by qtPCR in 242 scleroderma patients from the University of California, San Francisco Scleroderma Center. A) Relationship between leukocyte telomere length and age for TERF1 autoantibody positive (n=18) and negative (n=224) patients. B) Patients with TERF1 autoantibodies have a greater difference between the expected age-adjusted telomere length and their actual telomere length compared to TERF1 autoantibody-negative patients. Statistics done using Wilcoxon Rank Sum, * $p< 0.05$.



TERF1 autoantibodies detected by ELISA in healthy controls (n=78), the Hopkins Scleroderma cohort (n=200), the University of California, San Francisco Scleroderma Cohort (n=242), rheumatoid arthritis (n=50), and dermatomyositis (n=50). Chi-square test was used for to compare the frequency of TERF1 autoantibodies between different cohorts. * p< 0.05, **p<0.01.

autoantibodies are present in other diseases for which telomere dysfunction and lung fibrosis are prominent features, we screened a cohort of 153 UCSF patients with idiopathic pulmonary fibrosis (IPF) for autoantibodies targeting telomere-associated proteins.

Results: We identified a subset of scleroderma patients with multiple autoantibodies targeting hTERT and the six shelterin proteins, of which TERF1 autoantibodies were the most common. TERF1 autoantibodies were detected by ELISA in 22/200 (11%) of the JH Cohort and 18/242 (7%) of the UCSF Cohort, and were rarely present in patients with rheumatoid arthritis (1/50) or dermatomyositis (1/50). TERF1 autoantibodies were associated with shorter telomere lengths in both the JH and UCSF Cohorts. Compared to scleroderma patients without TERF1 autoantibodies,

a greater frequency of UCSF scleroderma patients with TERF1 autoantibodies had a shorter telomere length in leukocytes than the expected age-adjusted telomere length (78% vs 43%, Fisher's exact test, p=0.006). Similarly, JH scleroderma patients with TERF1 autoantibodies had a shorter age-adjusted telomere length in lymphocytes (-1.2 ± 0.3 vs -0.3 ± 1.0 kb, p=0.02, student's t-test). When the JH and UCSF Scleroderma Cohorts were combined, TERF1 autoantibodies were associated with a history of severe lung disease (OR 2.0, p=0.03, chi-square) and the presence of Ku (OR 5.4, p=0.02, chi-square) and U1RNP autoantibodies (OR 4.8, p=0.0006, chi-square). We further identified TERF1 autoantibodies in 12/153 (8%) of patients with IPF.

Conclusion: We have identified novel autoantibodies targeting multiple telomere-associated proteins in scleroderma and IPF, which are associated with short telomere length in peripheral lymphocytes and severe lung disease. Autoantibodies targeting telomere-associated proteins may have utility in the diagnosis and subtyping of scleroderma and may provide novel insights into the role of telomere dysfunction in scleroderma and other fibrotic lung diseases.

Disclosure: B. Adler, None; **A. Shah**, None; **F. Boin**, None; **P. Wolters**, Boehringer Ingelheim, 2, Roche/Genentech, 2; **L. Casciola-Rosen**, None; **A. Rosen**, Inova, 7, Celgene, 7.

Abstract Number: 2040

Continued Treatment with Nintedanib in Patients with Systemic Sclerosis-Associated Interstitial Lung Disease (SSc-ILD): Interim Analysis of SENSCIS-ON

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical II: Lessons Learned from Clinical Trials & Cohorts

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: In the SENSCIS trial in patients with SSc-ILD, nintedanib reduced the rate of decline in forced vital capacity (FVC) (mL/year) over 52 weeks by 44% compared with placebo, with adverse events that were manageable for most patients. The SENSCIS trial (NCT02597933) was followed by an open-label extension trial, SENSCIS-ON (NCT03313180), to provide safety data, including data on decline in FVC and adverse events, in patients treated with nintedanib over the longer term.

Methods: Patients who completed the SENSCIS trial on treatment (nintedanib or placebo) and attended a follow-up visit 28 days later were eligible to participate in SENSCIS-ON. Female patients with SSc-ILD who completed an open-label, drug–drug interaction study of nintedanib plus oral contraceptive (ethinylestradiol and levonorgestrel), in which patients received nintedanib for up to 28 days (NCT03675581), were also eligible to enter SENSCIS-ON to enable treatment continuation. In an interim analysis, we analyzed the change from baseline in FVC (mL) and adverse events over 52 weeks in SENSCIS-ON, a) in patients who had received nintedanib in the SENSCIS trial and contin-

Figure. Change from baseline in FVC (mL) over time in SENSCIS-ON

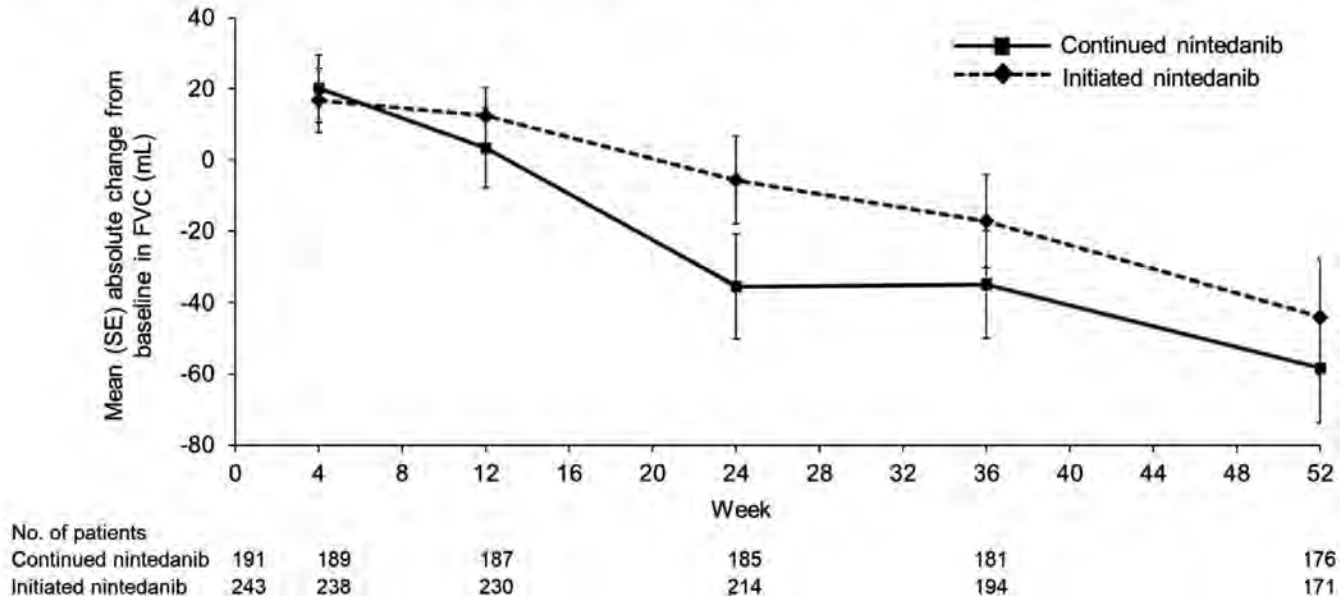

Table. Adverse events (reported irrespective of causality) over 52 weeks in SENSCIS-ON

	Continued nintedanib (n=197)	Initiated nintedanib (n=247)
Any adverse event(s)	191 (97.0)	243 (98.4)
Most frequent adverse events*		
Diarrhea	134 (68.0)	170 (68.8)
Nausea	32 (16.2)	60 (24.3)
Vomiting	27 (13.7)	53 (21.5)
Skin ulcer	36 (18.3)	43 (17.4)
Nasopharyngitis	28 (14.2)	33 (13.4)
Upper respiratory tract infection	27 (13.7)	26 (10.5)
Cough	24 (12.2)	21 (8.5)
Weight decreased	14 (7.1)	26 (10.5)
Abdominal pain	6 (3.0)	33 (13.4)
Serious adverse event(s)†	42 (21.3)	60 (24.3)
Adverse event(s) leading to treatment discontinuation	9 (4.6)	53 (21.5)

Adverse events were coded according to preferred terms in the Medical Dictionary for Regulatory Activities (MedDRA). Data are n (%) of patients with ≥1 such event reported over 52 weeks (or until 7 days after last trial drug intake for patients who discontinued trial drug before week 52). *Events reported in >10% of patients in either treatment group are shown. †Adverse events that resulted in death, were life-threatening, resulted in hospitalization or prolongation of hospitalization, resulted in persistent or clinically significant disability or incapacity, were a congenital anomaly or birth defect, or were deemed to be serious for any other reason.

ued nintedanib in SENSCIS-ON ("continued nintedanib" group), and b) in patients who had received placebo in the SENSCIS trial and initiated nintedanib in SENSCIS-ON or who had received nintedanib in the drug-drug interaction study ("initiated nintedanib" group). Analyses were pre-specified and descriptive.

Results: In SENSCIS-ON, there were 197 patients in the "continued nintedanib" group and 247 patients (231 from SENSCIS, 16 from the drug-drug interaction study) in the "initiated nintedanib" group. In these groups, respectively, mean (SD) FVC at inclusion in SENSCIS-ON was 2379 (754) mL and 70.4 (18.1) % predicted and 2443 (814) mL and 70.8 (17.9) % predicted. Mean (SE) changes in FVC from baseline to week 52 of SENSCIS-ON were –58.3 (15.5) mL in patients who continued nintedanib in SENSCIS-ON, –44.0 (16.2) mL in patients who initiated nintedanib in SENSCIS-ON (Figure), and –51.3 (11.2) mL in all patients treated in SENSCIS-ON, similar to the change from baseline to week 52 in the SENSCIS trial (–42.7 [14.2] mL). Diarrhea was the most frequently reported adverse event (Table). Adverse events led to discontinuation of nintedanib in 9 patients (4.6%) who continued nintedanib in SENSCIS-ON and 53 patients (21.5%) who initiated nintedanib in SENSCIS-ON. Elevations in alanine aminotransferase and/or aspartate aminotransferase to ≥3 times the upper limit of the normal range were reported in 3 patients (1.5%) who continued nintedanib in SENSCIS-ON and 20 patients (8.1%) who initiated nintedanib in SENSCIS-ON.

Conclusion: The change in FVC in patients who received nintedanib over 52 weeks of SENSCIS-ON was similar to the change in FVC in patients who received nintedanib over 52 weeks of the SENSCIS trial. The adverse event profile of nintedanib over longer-term use was consistent with that reported over 52 weeks in the SENSCIS trial. These findings support a clinically meaningful benefit of nintedanib in slowing the progression of SSc-ILD.

Disclosure: Y. Allanore, Sandoz, 1, Bayer, 1, Boehringer Ingelheim, 1, 2, Curzion, 1, Medsenic, 1, Sanofi, 1, 2, Roche, 1; **M. Vonk**, Actelion Pharmaceuticals, 1, 2, 3, Boehringer Ingelheim, 1, 2, Roche, 1, 2, GlaxoSmithKline, 1, 2, Ferrer, 1; **A. Azuma**, Boehringer Ingelheim, 6, 8, Shionogi & Co., Ltd, 1, Taiho Pharmaceutical Co., Ltd, 1, Asahikasei Pharma Co., 1; **M. Mayes**, Actelion Pharmaceuticals, 1, Boehringer Ingelheim, 1, 2, Corbus, 1, Eicos Sciences, 1, Galapagos, 1; **M. Gahlemann**, Boehringer Ingelheim, 1; **A. James**, Boehringer Ingelheim, 3; **V. Kohlbrenner**, Boehringer Ingelheim, 1; **S. Stowasser**, Boehringer Ingelheim, 1; **K. Highland**, Actelion Pharmaceuticals, 1, 2, 3, Bayer, 1, 2, Boehringer Ingelheim, 1, 2, 3, Eiger BioPharmaceuticals, 1, Genentech, 1, Gilead Sciences, 1, Gossamer Bio, 1, Reata Pharmaceuticals, 1, United Therapeutics, 1, 2, 3, Viela Bio, 1.

Abstract Number: 2041

Disease Features of Systemic Sclerosis Are Associated with Alterations in Gastrointestinal Microbial Composition in Two Independent Cohorts

Kristofer Andréasson[1], Sungeun Lee[2], Venu Lagishetty[2], Meifang Wu[2], Natalie Howlett[2], James English[2], Roger Hesselstrand[1], Jonathan Jacobs[2] and **Elizabeth Volkmann**[3], [1]Lund University, Lund, Sweden, [2]University of California, Los Angeles, Los Angeles, [3]University of California, Los Angeles, Los Angeles, CA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Systemic Sclerosis & Related Disorders – Clinical II: Lessons Learned from Clinical Trials & Cohorts
Session Type: Abstract Session
Session Time: 4:00PM–4:50PM

Background/Purpose: Previous studies have demonstrated alterations in GI microbiota of patients with systemic sclerosis (SSc) compared with healthy controls [1]. However, these prior studies did not adequately examine the impact of disease features and patient characteristics on microbial composition. The purpose of the present study was to examine associations between specific SSc disease features/patient characteristics and GI microbial composition using two independent SSc cohorts and compare GI microbiota between cohorts.

Methods: Patients fulfilling the 2013 ACR/EULAR Classification Criteria for SSc were recruited from the rheumatology clinics at Lund University, Sweden and the University of California, Los Angeles (UCLA). Unaffected controls

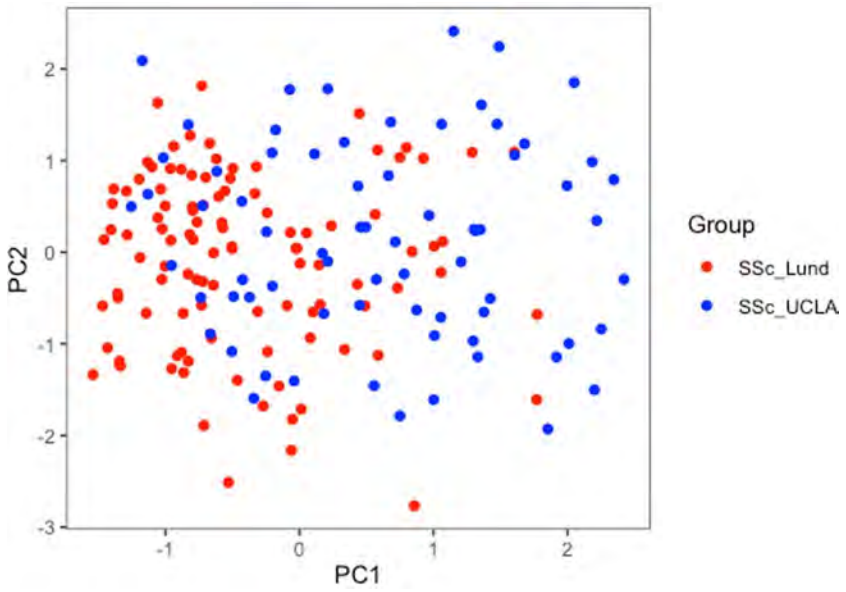

Figure 1. Significant differences in the beta diversity of the Lund-SSc (Red) and UCLA-SSc (blue) patients as demonstrated by principal coordinate analysis plots of the robust Aitchison distance. Each dot represents a patient sample. The P-value (0.0001) was calculated by analysis of variance using distance matrices.

were also recruited at Lund University. All participants provided stool specimens for 16S rRNA sequencing. Extensive clinical data were collected to evaluate the effects of specific disease features on lower GI microbiota. Alpha diversity was assessed by metrics of richness, evenness, and phylogenetic diversity. Beta diversity analysis was performed with DEICODE in QIIME2. Multivariate negative binomial models were used to identify differentially abundant bacterial genera associated with SSc disease features and cohort (UCLA SSc vs. Lund SSc; Lund SSc vs. Controls).

Results: Compared with the Lund SSc patients (N=106), UCLA SSc patients (N=71) had increased disease duration (median 7.1 vs. 2.0 years) and a higher prevalence of diffuse cutaneous disease (44% vs. 19%), interstitial lung disease (87% vs. 33%), Scl-70 antibody positivity (31% vs. 18%), and small intestine bacterial overgrowth [SIBO] (22% vs. 5%). However, both groups had a similar age, %female, and BMI. UCLA SSc patients had decreased alpha diversity ($P< 0.0001$ for all alpha diversity metrics) and altered beta diversity ($P=0.0001$; Figure 1) compared with Lund SSc patients. Factors significantly associated with alpha and/or beta diversity included age, sex, diffuse disease, disease duration, smoking history, and SIBO. After adjusting for the aforementioned factors, the Lund cohort had increased abundance of commensal genera (e.g. *Bifidobacterium*) and decreased abundance of potentially pathobiont genera (e.g. *Streptococcus*) compared with the UCLA cohort (Figure 2). Compared with unaffected controls from Lund (N=85), Lund SSc patients had increased abundance of pathobiont genera (e.g. *Desulfovibrio*) (Figure 3), consistent with our prior studies.

Conclusion: In the first study to examine the associations between specific disease features and GI microbial composition in two independent SSc cohorts, we found that both disease duration and SSc subtype independently affect microbial composition and should be considered in future SSc microbiome analyses. Even after controlling for potential confounders, genus level differences were observed between the two cohorts, suggesting that external factors, such as diet, geography and genetic factors, may affect GI microbial composition and should be taken into account in future studies.

References

1. Volkmann ER, et al. *Arthritis Rheum* 2016..

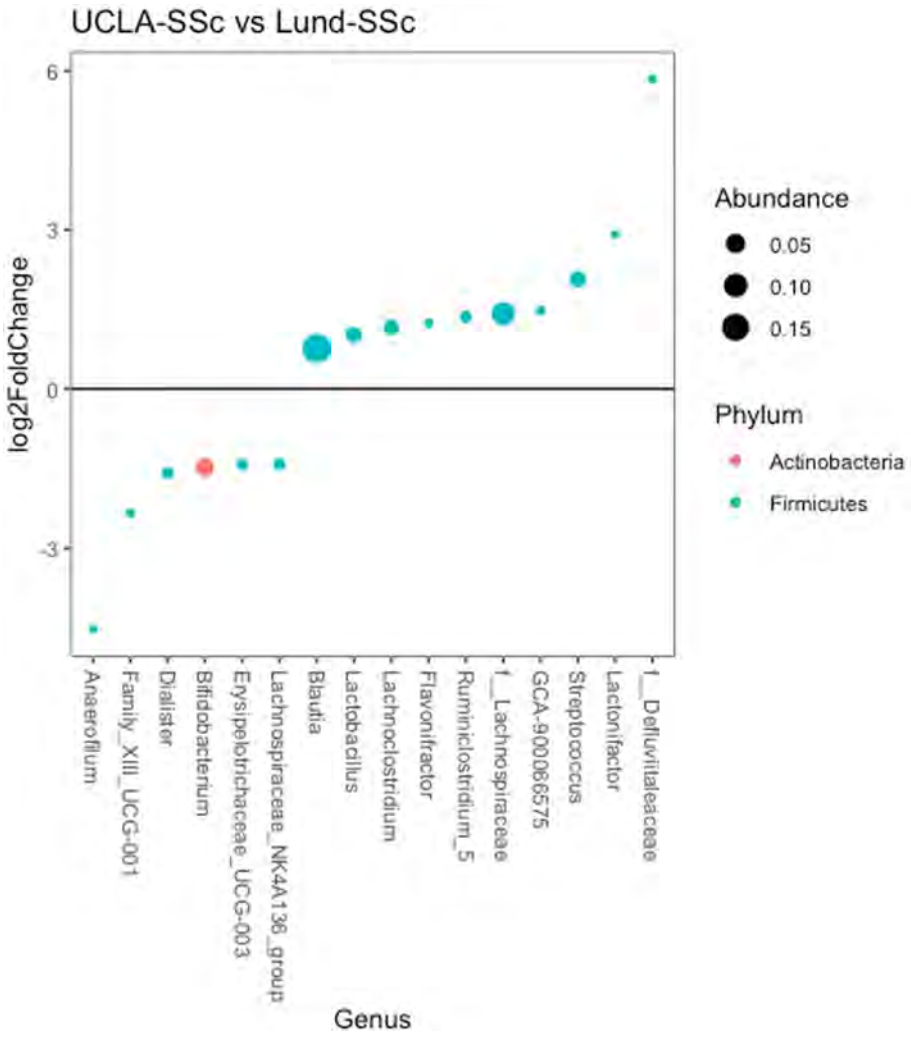

Figure 2. Genus level taxa with significant (q<0.1) differential abundance in SSc patients from Lund, Sweden, and UCLA. Circles with a positive fold change score represent genera with increased abundance in the UCLA-SSc group and those with a negative fold change score represent genera with increased abundance in the Lund-SSc group. The color of the circle signifies the phylum level of the genera with differential abundance. The size of the circle indicates the relative abundance of the specific genus.

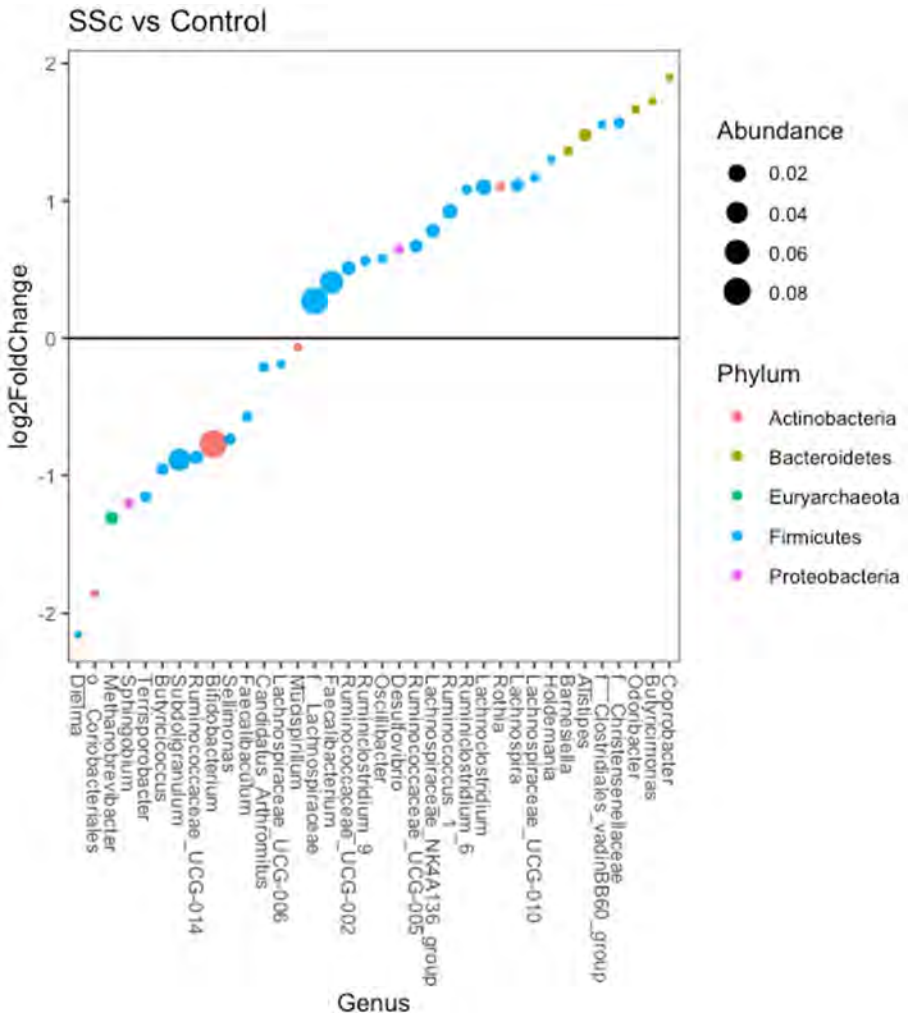

Figure 3. Genus level taxa with significant (q<0.1) differential abundance in SSc patients and unaffected controls from Lund, Sweden, after adjusting for sex and age. Circles with a positive fold change score represent genera with increased abundance in the Lund-SSc group and those with a negative fold change score represent genera with increased abundance in the Lund-Control group. The color of the circle signifies the phylum level of the genera with differential abundance. The size of the circle indicates the relative abundance of the specific genus.

Disclosure: K. Andréasson, None; **S. Lee**, None; **V. Lagishetty**, None; **M. Wu**, None; **N. Howlett**, None; **J. English**, None; **R. Hesselstrand**, None; **J. Jacobs**, None; **E. Volkmann**, Boehringer Ingelheim, 2, 5, Forbius, 2, 5, Corbus, 2.

Abstract Number: 2042

A Low FODMAP Diet Is Not Associated with Decreased GI Symptoms or Changes in GI Microbial Composition in Patients with Systemic Sclerosis

Natalie Howlett[1], Sungeun Lee[1], Venu Lagishetty[1], Zsuzsanna McMahan[2], Meifang Wu[1], Jonathan Jacobs[1] and Elizabeth Volkmann[3], [1]University of California, Los Angeles, Los Angeles, [2]Johns Hopkins University, Baltimore, [3]University of California, Los Angeles, Los Angeles, CA

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Systemic Sclerosis & Related Disorders – Clinical II: Lessons Learned from Clinical Trials & Cohorts

Session Type: Abstract Session

Session Time: 4:00PM–4:50PM

Background/Purpose: Dietary restriction of short-chain fermentable oligosaccharides, disaccharides, monosaccharides and polyols (low FODMAP) has been found to reduce GI symptoms in patients with IBS and is often recommended to patients with SSc. However, no studies have evaluated whether a low FODMAP diet leads to a meaningful improvement in GI symptoms in patients with SSc. The purpose of this study was to (1) compare GI symptoms in SSc patients adhering to a low versus high FODMAP diet, and (2) determine whether GI microbial composition is altered in SSc patients adhering to a low FODMAP diet.

Table 1. Demographics, Clinical Characteristics and GIT 2.0 Scores of SSc Patients.

Characteristic	FODMAP High (N=16)	FODMAP Low (N=19)	P-value
Age, years, Mean +/- SD	54.7 +/- 12.8	59.5 +/- 10.4	0.232
Female, N (%)	15/16 (93.8%)	14/19 (73.7%)	0.187
Race, N (%) White AA Asian American Indian/Alaskan Native Native Hawaiian/Pacific Islander More than one race Unknown	 15/16 (93.8%) 0/16 (0%) 0/16 (0%) 0/16 (0%) 0/16 (0%) 1/16 (6.2%) 0/16 (0%)	 12/19 (63.2%) 1/19 (5.3%) 2/19 (10.5%) 1/19 (5.3%) 1/19 (5.3%) 1/19 (5.3%) 1/19 (5.3%)	0.047*
Hispanic, N (%)	5/16 (31.3%)	5/19 (26.3%)	1.0
Diffuse disease, N (%)	7/16 (43.8%)	8/19 (42.1%)	1.0
Disease duration, years (N=32) Median (IQR) Mean +/- SD	 8.7 (6.2) 11.6 +/- 9.9	 5.0 (8.1) 7.0 +/- 5.3	 0.210
SIBO, N (%)	3/16 (18.8%)	3/19 (15.8%)	1.0
Pseudo-obstruction, N (%)	0/16 (0%)	1/19 (5.3%)	1.0
Fecal incontinence, N (%)	3/16 (18.8%)	1/19 (5.3%)	0.312
BMI, kg/m2, Mean +/- SD	25.4 +/- 4.1	26.9 +/- 4.4	0.297
HRCT-defined ILD, N(%)	14/16 (87.5%)	16/18 (88.9%)	1.0
mRSS(0-51), Mean +/- SD (N=27)	6.4 +/- 4.3	7.2 +/- 8.8	0.771
Any immunosuppression use ever, N (%)	14/16 (87.5%)	17/19 (89.5%)	1.0
Smoking, N (%)	4/16 (25%)	5/19 (26.3%)	1.0
Vegetarianism, N (%)	1/16 (6.3%)	1/19 (5.3%)	1.0
PPI Use, N (%)	13/16 (81.3%)	13/19 (68.4%)	0.461
Scl-70 antibody, N (%)	7/15 (46.7%)	4/14 (28.6%)	0.450
Anti-centromere antibody, N (%)	5/15 (33.3%)	2/14 (14.3%)	0.390
RNA polymerase III antibody, N (%)	0/7 (0%)	1/8 (12.5%)	1.0
GIT 2.0 Scores			
Total, Mean +/- SD Median (IQR)	0.49 +/- 0.35 0.37 (0.33)	0.37 +/- 0.40 0.23 (0.40)	0.349
Reflux, Mean +/- SD Median (IQR)	0.67 +/- 0.47 0.5 (0.53)	0.5 +/- 0.38 0.44 (0.56)	0.245
Distension, Mean +/- SD Median (IQR)	0.89 +/- 0.56 0.75 (0.75)	0.65 +/- 0.84 0.25 (0.94)	0.343
Fecal Soilage, Mean +/- SD Median (IQR)	0.19 +/- 0.54 0 (0)	0.22 +/- 0.55 0 (0)	0.854
Diarrhea, Mean +/- SD Median (IQR)	0.5 +/- 0.61 0.5 (0.63)	0.36 +/- 0.45 0 (0.88)	0.449
Social Functioning, Mean +/- SD Median (IQR)	0.33 +/- 0.52 0.17 +/- 0.38	0.19 +/- 0.41 0 +/- 0.17	0.363
Emotional Well-being, Mean +/- SD Median (IQR)	0.35 +/- 0.59 0.06 +/- 0.5	0.28 +/- 0.47 0 (0.31)	0.679
Constipation, Mean +/- SD Median (IQR)	0.44 +/- 0.65 0.13 (0.56)	0.42 +/- 0.51 0.25 (0.75)	0.917

Table 1. Demographics, clinical characteristics and GIT 2.0 scores of SSc patients.

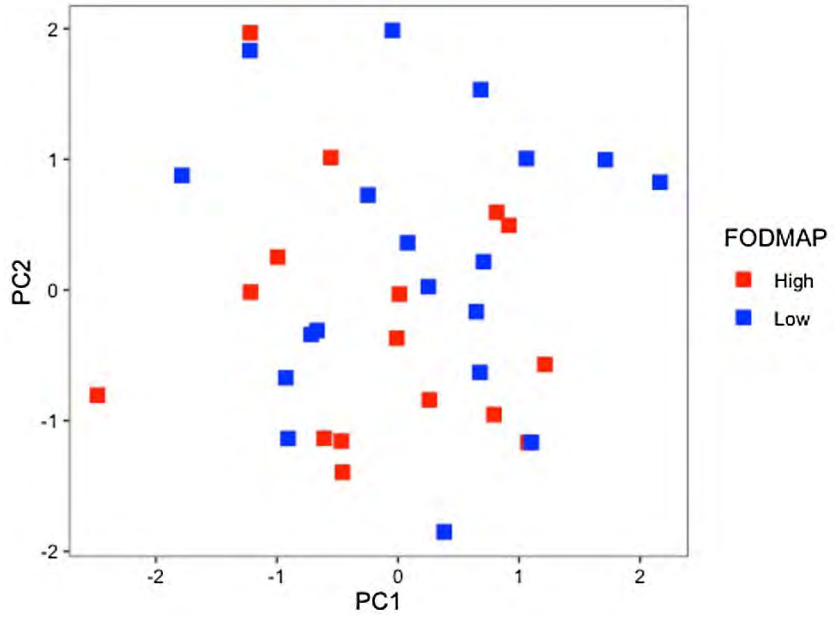

Figure 1. Beta diversity of the High (Red) and Low (blue) FODMAP group patients as demonstrated by principal coordinate analysis plots of the robust Aitchison distance. Each dot represents a patient sample. The P-value (0.264) was calculated by analysis of variance using distance matrices.

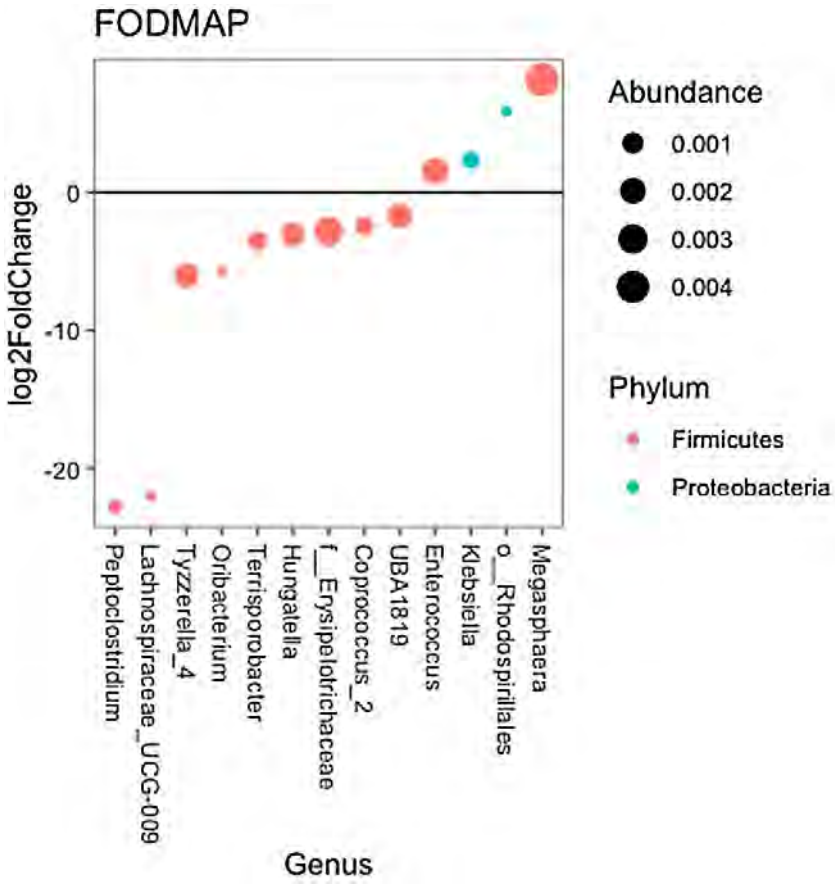

Figure 2. Genus level taxa with significant (q<0.1) differential abundance between low versus high FODMAP groups. Circles with a positive fold change represent genera with increased abundance in the high FODMAP group, and circles with a negative fold change represent genera with increased abundance in the low FODMAP group. The color of the circle signifies the phylum level of the genera with differential abundance. The size of the circle indicates the relative abundance of the specific genus.

Methods: Adult patients satisfying the 2013 ACR/EULAR Classification Criteria for SSc provided stool samples for 16S rRNA sequencing. Participants completed the Diet History Questionnaire (DHQ) II, a valid, 153-item food frequency questionnaire that assesses dietary recall in the past month. Forty DHQ II items were characterized as high FODMAP items using the Monash University FODMAP food database. Patients were dichotomized into low versus high FODMAP groups, and GI symptoms, as measured by the UCLA GIT 2.0, were compared between the two groups. Microbial community differences between the low and high FODMAP groups were assessed using 3 metrics of alpha diversity (richness, evenness, phylogenetic diversity), as well as beta diversity. Multivariate negative binomial models were used to identify differentially abundant bacterial genera in the high versus low FODMAP groups.

Results: Patients in the low (N=19) and high (N=16) FODMAP groups were similar in terms of age, %female, BMI, disease duration, %diffuse disease, smoking history and %small intestine bacterial overgrowth [SIBO] (Table 1). There were no significant differences in GIT 2.0 scores between the low and high FODMAP groups, although the scores for some of the domains (e.g., Reflux, Distension, Diarrhea) were numerically higher in the high FODMAP group; whereas scores for the constipation domain were similar for both groups. There were no significant differences in alpha diversity between the two groups on both univariate and multivariate analysis controlling for age, sex, SSc subtype, smoking, SIBO and disease duration. There was no significant difference in beta diversity between the two groups on univariate and multivariate analysis (Figure 1). Compared with the low FODMAP group, the high FODMAP group had increased abundance of *Enterococcus,* a genus considered in a number of studies to be pathobiont (Figure 2); however, in the multivariate analysis, there was no significant genus level differences between the two groups with the exception of *Parvimonas* enrichment in the low FODMAP group.

Conclusion: Evidenced-based dietary recommendations for SSc are lacking. This is the first study to examine the relationship between diet, GI symptoms, and GI microbial composition in patients with SSc. Although this was a small study, the results demonstrate that consuming a low FODMAP diet is not associated with significant alterations GI microbial composition, nor significant improvements in SSc-GI symptoms. Larger, prospective SSc-GI studies are needed to help guide the clinical management of this troubling and understudied dimension of SSc.

Disclosure: N. Howlett, None; **S. Lee**, None; **V. Lagishetty**, None; **Z. McMahan**, None; **M. Wu**, None; **J. Jacobs**, None; **E. Volkmann**, Boehringer Ingelheim, 2, 5, Forbius, 2, 5, Corbus, 2.

Abstract Number: 2043

Identification and Validation of Citrulline Specific TCRs in CD4+T Cells in Rheumatoid Arthritis

Ravi Kumar[1], Niyaz Yoosuf[2], Sanjay Boddul[2], Christina Gerstner[3], Sara Turcinov[4], Anatoly Dubnovitsky[5], Fredrik Wermeling[2], Karine Chemin[6] and Vivianne Malmström[7], [1]Division of Rheumatology, Department of Medicine, Stickholm, Stockholms Lan, Sweden, [2]Division of Rheumatology, Department of Medicine, Stockholm, Sweden, [3]Division of Rheumatology, Department of Medicine,Center for Molecular Medicine, Karolinska Institutet, Stockholm, Sweden, [4]Division of Rheumatology, Department of Medicine,Center for Molecular Medicine, Institutet, Stockholm, Sweden, [5]Karolinska Institutet, Stockholm, [6]Division of Rheumatology, Department of Medicine, Stockholm, Stockholms Lan, Sweden, [7]Karolinska Institutet, Stockholm, Stockholms Lan, Sweden

SESSION INFORMATION

Session Date: Monday, November 9, 2020

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

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: Citrulline (cit) autoimmunity is central in rheumatoid arthritis (RA), including both anti-citrulline protein antibodies (ACPA) and autoreactive CD4+ T cells. While the ACPA are abundant, studies of cit-reactive T cells have been hampered by their scarcity. Still, cit-reactive T cells have been reported in the RA joint and in peripheral blood by peptide-HLA tetramer technology. We have set up an *in-vitro* antigen(ag)-specific expansion method [1] for generating TCR sequences to dissect the diversity of the autoreactive T cell repertoire. Hereby we can look for dominant T cell clones amongst different patients sharing the same HLA genes.

Methods: We subjected synovial fluid-derived cells (SFMC) from HLA-DRB1*04:04 RA patients (n=4) and peripheral blood (PBMC) from HLA-DRB1*04:04 healthy controls (n=4) to our ag-specific expansion method [1]. A cit-peptide from cartilage intermediate layer protein (cit-CILP2) was used to query autoimmunity whereas an influenza matrix protein derived peptide (MP54) was used as positive control. *In-vitro* expanded tetramer positive cells were single sorted and processed for PCR based TCR amplification, followed by barcoding and TCR sequencing using miSeq. The data was demultiplexed by our in-house script and clones identified by comparison of both CDR3α and β amino acid sequences. TCRs were further validated for specificity by transient re-expression into HEK293 cells, followed by staining with the same tetramers initially used for sorting.

Results: Cit-CILP2+ T cells could be expanded *in vitro* in all samples and clonal TCR expansions were prominent. Collectively, we could get 27 cit-CILP2 specific (PB n=6 and SF n=21) and 56 MP54 specific (PB n=37 and SF n=19) expanded T-cell clones. We also captured another 101 cit-CILP2 specific and 190 MP54-specific unique TCRs. The proportion of unique and expanded clones for cit-CILP2 and MP54 was similar in the joint-derived samples. The CDR3 length distribution for cit-CILP2 specific clones was different from MP54 specific clones for both the TCR α and β chain. Longer CDR3 length were more common in cit-CILP2 specific clones and there were differences in distribution of amino acids at specific positions. Clones derived from same patient showed shared usage of V and J genes for both α and β chains. HEK cell Re-expression of TCRs validated their target specificity.

Conclusion: This method provides a rapid tool for generation and validation of ag-specific TCRs. So far, the gene usage and CDR3 profiles appear subject-driven with limited sharing among subjects. Today, many studies are generating transcriptomic data (including TCR) from sites of inflammation and generating orphan TCRs, i.e. without known ag-specificity. We are accumulating cit-peptide ag-specific TCR sequences, which may in the future be used to identify ag-specific TCR signatures among “orphan” TCRs in such public big data sets. Until then, cit-reactive TCRs will be used in functional *in vitro* studies as well as in establishing relevant mice models for RA. Finally, we will also evaluate longitudinal changes in the autoreactive TCR repertoire during disease progression and after therapeutic intervention.

Reference

Kumar R et. al. DOI: 1136/annrheumdis-2020-eular.1093

Disclosure: R. Kumar, None; **N. Yoosuf**, None; **S. Boddul**, None; **C. Gerstner**, None; **S. Turcinov**, None; **A. Dubnovitsky**, None; **F. Wermeling**, Pfizer, 2; **K. Chemin**, None; **V. Malmström**, Pfizer, 2.

Abstract Number: 2044

Complex, Dynamic Attributes of Antigen-specific T Cells in Rheumatoid Arthritis

Eddie James[1], Virginia Muir[2], Cliff Rims[1], Hannes Uchtenhagen[3], Anne Hocking[3], Sylvia Posso[3], Heather Bukiri[4], Jeffrey Carlin[4], Bernard Ng[5], Peter Linsley[3] and Jane Buckner[1], [1]Center for Translational Immunology, Benaroya Research Institute at Virginia Mason, Seattle, WA, [2]Center for Systems Immunology, Benaroya Research Institute at Virginia Mason, Seattle, WA, [3]Benaroya Research Institute at Virginia Mason, Seattle, WA, [4]Virginia Mason Medical Center, Seattle, WA, [5]VA Puget Sound Health Care System, Seattle, WA

SESSION INFORMATION

Session Date: Monday, November 9, 2020

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

Session Type: Abstract Session

Session Time: 10:00AM–10:50AM

Background/Purpose: CD4$^+$ T cells are implicated in the pathogenesis of rheumatoid arthritis (RA) due to strong genetic association with HLA class II alleles, the presence of CD4$^+$ T cells in the rheumatoid joint and the efficacy of T cell directed therapies. In addition, CD4$^+$ T cells specific to citrullinated epitopes are increased in RA and their frequency is influenced by disease duration and by biologic therapy. However, technical challenges due to the rarity of citrulline (cit)-specific T cells have limited our understanding of how T cell phenotype and specificity can vary within and between individuals. To address this gap in knowledge, we characterized the frequency and phenotype of cit-specific CD4$^+$ T cells in a cross-sectional cohort of RA subjects using multiplex HLA class II tetramer staining combined with our new computational approach for phenotyping rare cell populations.

Methods: The cohort consisted of 77 seropositive RA subjects and 30 healthy control subjects matched for age, sex and race. All RA subjects met the 2010 American College of Rheumatology criteria, and had at least one HLA-DRB1*04:01 allele, and were ACPA positive. The multiplex HLA class II tetramer assay stained six distinct groups of epitope specificities: alpha-enolase, aggrecan, cartilage intermediate layer protein, a combined vimentin and fibrinogen peptide pool with influenza included as a reference for comparison to a known vaccine response. To facilitate unbiased assessment of the phenotypic distribution of rare, autoreactive T cells within and across subjects, we first clustered total CD4$^+$ T cells from each individual using Phenograph, and then performed hierarchical metaclustering

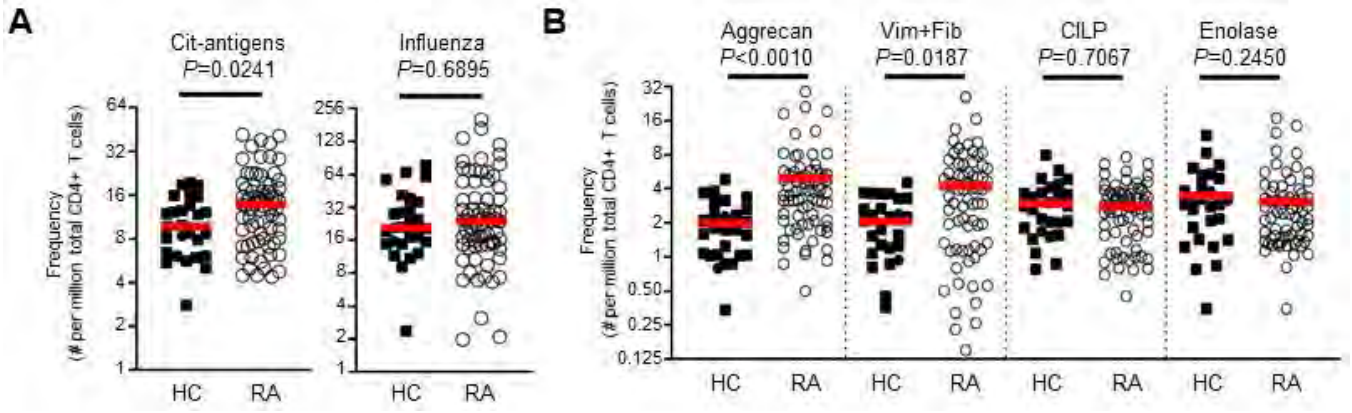

Figure 1. ncreased frequency of citrulline specific CD4 T cells in individuals with rheumatoid arthritis (RA) compared to healthy control (HC) subjects. (A) Ex vivo frequencies of T cells for all cit-antigens combined, and for influenza antigen. (B) Ex vivo frequencies of T cells specific for each cit-antigen specificity individually. For A and B, symbols represent individual subjects (n=30 for HC; n=77 for RA), and horizontal bars show the median. P-values were calculated with an unpaired non-parametric Mann-Whitney test.

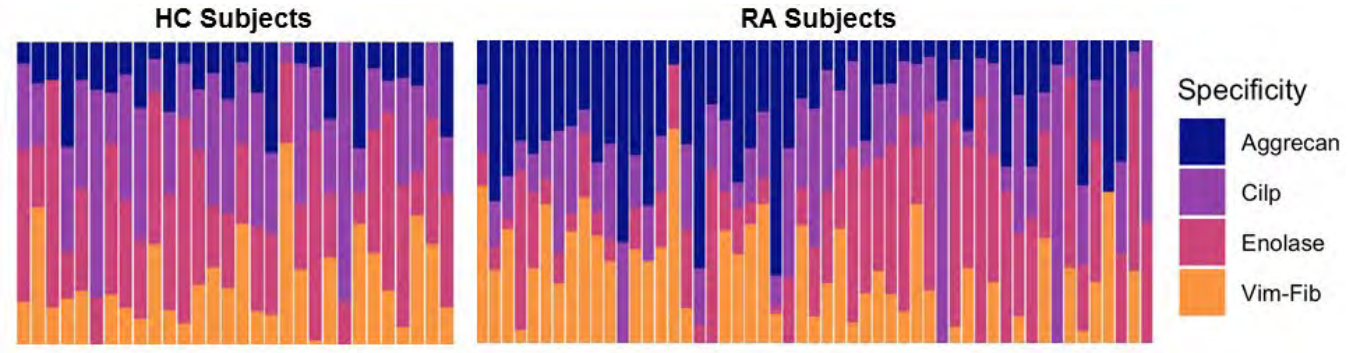

Figure 2. The dominant specificities of citrulline-specific CD4 T cells in rheumatoid arthritis differ between individual subjects. Stacked bar plot showing distribution of antigen specificity for each individual HC subject (n=30) and each individual RA subject (n=52) with >8 Tmr positive cells of any specificity.

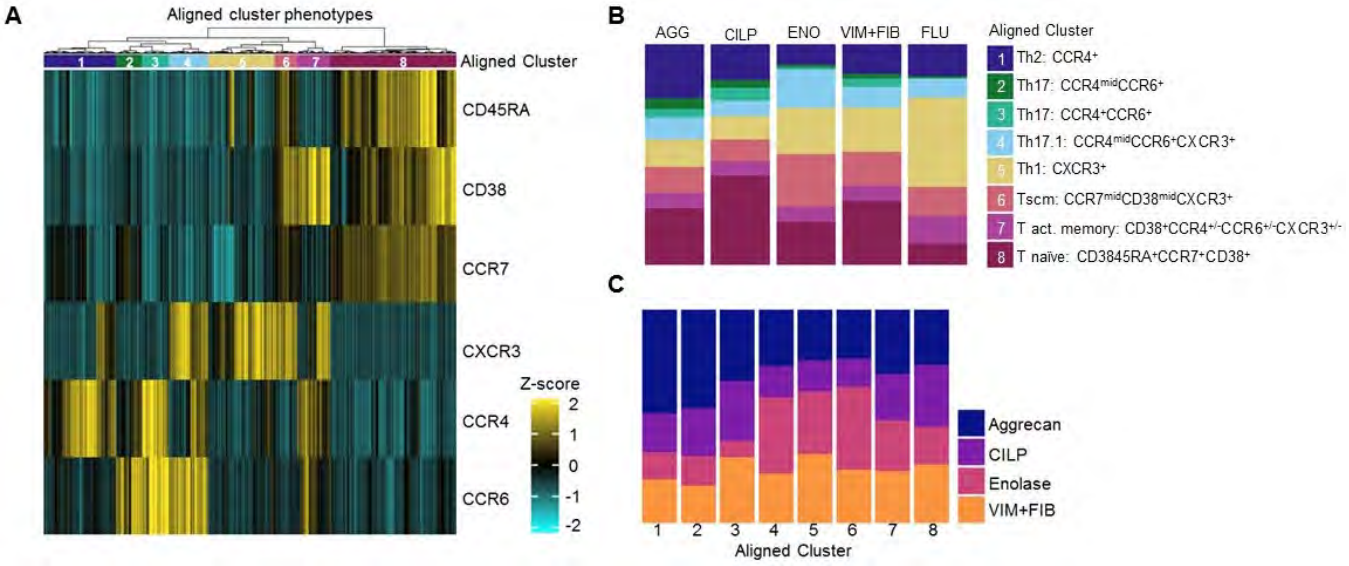

Figure 3. Cell phenotype is linked to specificity. To facilitate direct comparisons of complex surface phenotypes and unbiased assessment of the phenotypic distribution of rare, autoreactive T cells within and across subjects, we used our recently developed computational strategy DISCOV-R (DIStribution analysis across Clusters of a parent population OVerlaid with a Rare subpopulation). In brief, we first cluster total CD4+ T cells from each individual using Phenograph, and then perform hierarchical metaclustering to align clusters between individuals thereby generating a common CD4T cell landscape across all subjects. (A) Heat map showing all CD4+ T cell clusters from 66 RA subjects and 30 HC subjects hierarchically clustered (Euclidean distance, Ward's minimum variance linkage) by expression of six phenotyping markers as a z-score comparing mean cluster intensity to total CD4 T cell intensity for each subject. The resulting dendrogram is sliced into eight aligned clusters with color bar across top indicating aligned cluster assignment. (B) Stacked bar plot showing aligned clusters for each antigen specificity for 93 subjects (RA n=63, HC n=30) with >8 Tmr+ cells. Suggested lineage of aligned clusters representing CD4+ T cell landscape defined by the heatmap in A. (C) Distribution of antigen-specific T cells pooled from RA subjects across aligned clusters colored by specificity.

to align clusters between individuals. The relationship between clinical variables and cell frequencies was modeled using quasibinomial generalized linear models with age and sex as covariates.

Results: Consistent with our previous study analyzing single antigen specificities, the frequency of cit-specific $CD4^+$ T cells was significantly increased in RA subjects. Notably, individual RA subjects had $CD4^+$ T cells specific for multiple cit-specific antigens, yet the predominant specificities varied between individuals. Furthermore, the predominant immunophenotype of cit-specific CD4+ T cells varied based on antigen specificity. Importantly, we also observed

significant associations between immunophenotype and disease duration and disease activity for individual antigen specificities.

Conclusion: Here, we show that there is not a single dominant specificity or cellular phenotype present in individuals with RA. Instead, the immune response to cit-antigens targets multiple antigens with a broad range of phenotypes and these features are dynamic, which parallels reported characteristics of ACPA responses during development of RA. Serologic studies have demonstrated an expansion of frequency and targets of ACPA prior to RA development. Our findings suggest that a similar process may occur for cit-specific $CD4^+$ T cells, perhaps initiated by failed tolerance to a single initiating cit-antigen years prior to disease onset, followed by an expansion of the T cell response to multiple cit-antigens.

Disclosure: E. James, Pfizer, 2, Janssen, 2, Sanofi, 2, Novartis, 2; **V. Muir**, Janssen, 3; **C. Rims**, None; **H. Uchtenhagen**, Anocca, 3; **A. Hocking**, None; **S. Posso**, None; **H. Bukiri**, None; **J. Carlin**, None; **B. Ng**, None; **P. Linsley**, Bristol Myers Squibb, 2, 5, Eos Biosciences, 5, Lumen Biosciences, 5, Celgene, 2; **J. Buckner**, Bristol-Myers Squibb, 2, 5, Janssen, 2.

Abstract Number: 2045

Resident Memory T Cells in Synovial Tissue Mediate Arthritis Flares

Margaret Chang[1], Anais Levescot[2], Nathan Nelson-Maney[2], Rachel Blaustein[2], Kellen Winden[1], Allyn Morris[3], Spoorthi Balu[3], Alexandra Wactor[2], Ricardo Grieshaber-Bouyer[4], Kevin Wei[5], Lauren Henderson[6], Rachael Clark[3], Deepak Rao[2], Robert Fuhlbrigge[7] and Peter Nigrovic[8], [1]Boston Children's Hospital, Boston, MA, [2]Brigham and Women's Hospital, Boston, MA, [3]Brigham and Women's Hospital, Boston, [4]Department of Medicine V, Hematology, Oncology and Rheumatology, Heidelberg University Hospital, Heidelberg, Germany; Division of Rheumatology, Inflammation and Immunity, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA, Heidelberg, Germany, [5]Brigham and Women's Hospital and Harvard Medical School, Boston, MA, [6]Boston Children's Hospital, Watertown, MA, [7]University of Colorado, Denver, CO, [8]Division of Rheumatology, Inflammation and Immunity, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, USA; Division of Immunology, Boston Children's Hospital, Harvard Medical School, Boston, MA, USA, Boston

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: Resident memory T cells (T_{RM}) are site-specific memory T cells that take up long-term residence in peripheral tissues and aid in local immune defense. T_{RM} have also been implicated in autoimmune diseases by driving localized recurrent inflammation. As chronic arthritis is characterized by recurrent site-specific joint inflammation, we sought to investigate the role of T_{RM} in joint-specific memory.

Methods: We performed 10x genomics droplet-based single cell RNA sequencing and immune repertoire profiling on memory T cells disaggregated from human rheumatoid arthritis synovium to evaluate transcriptomic signature. We also used Mantra multispectral immunofluorescence microscopy to evaluate T cells expressing common T_{RM} protein markers in human arthritic synovial tissue sections. To assess the functional contribution of T_{RM} cells in arthritis in vivo, we generated a novel murine model of joint-specific recurrent synovitis. We utilized adoptive transfer, in vitro metabolic and migration assays, in vivo cell labeling, and localized depletion strategies to characterize T_{RM} cells in the synovium and their functional role in arthritis flare.

Results: We identified cells with the phenotypic and transcriptomic signature of T_{RM} within human arthritic synovium. These cells were primarily CD8+ and exhibited restricted T cell receptor clonotypes as well as a pro-inflammatory gene expression profile. Adoptive transfer studies in our animal model of joint-specific recurrent inflammation confirmed that arthritis flares were mediated by antigen-specific CD8+ T cells that remained within previously inflamed joints during remission. These cells were bona fide T_{RM}, as confirmed through surface signature, failure to migrate in vivo or in vitro, preferential uptake of free fatty acids, and long-term residency. Site-specific depletion of synovial T cells during remission markedly ameliorated disease recurrence, establishing a role of synovial T_{RM} in arthritis flares.

Conclusion: Here, we demonstrate that synovial T_{RM} present in human inflamed synovium are a targetable mediator of joint-specific memory in arthritis.

Disclosure: M. Chang, None; **A. Levescot**, None; **N. Nelson-Maney**, None; **R. Blaustein**, None; **K. Winden**, None; **A. Morris**, None; **S. Balu**, None; **A. Wactor**, None; **R. Grieshaber-Bouyer**, None; **K. Wei**, Gilead, 5; **L. Henderson**, Adaptive Biotechnologies, 5, Sobi, 5, CARRA, 9; **R. Clark**, None; **D. Rao**, None; **R. Fuhlbrigge**, None; **P. Nigrovic**, Novartis, 2, 5, BMS, 2, 5, Pfizer, 2, 5, Sobi, 5, Miach Orthopedics, 5, Simcere, 5, XBiotech, 5, Quench Bio, 5, Siglion, 5, Cerecor, 5, UpToDate, 7, American Academy of Pediatrics, 7, CARRA, 9.

Abstract Number: 2046

Alterations in Circulating CD4+ T Cell Phenotypes in CCP+ Early RA and CCP+ At-risk Individuals by Mass Cytometry

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: The cyclic citrullinated peptide (CCP) autoantibody is a highly specific and predictive marker for the clinical diagnosis of RA. Elevation in CCP titers can be detected several years before patients develop clinical arthritis and is also a predictive biomarker for RA risk. CCP+ RA is associated with increased levels of distinct synovial and circulating T cell immunophenotypes, including the expansion of PD-1^{hi} CXCR5- T peripheral helper (Tph) cells. However, whether these and other immune cell populations are altered in the peripheral blood of CCP+ individuals without RA is unknown.

Methods: We employed time of flight mass cytometry (CyTOF) with a panel of 39 surface markers to characterize T cells in cryopreserved peripheral blood mononuclear cells from a cohort of CCP- controls (n=23), CCP- first-degree relatives (FDRs) of patients with classified RA (n=27), CCP+ individuals at-risk of future RA (n=30), and active CCP+

Figure 1. Tph cells and Tfh cells were expanded in CCP+ early RA cohort.
Biaxial gated the frequencies of PD-1^{hi} CXCR5+, PD-1^{hi} CXCR5- CD4+ memory T cells. * p<0.05, ** p<0.01 by Mann-Whitney U test.

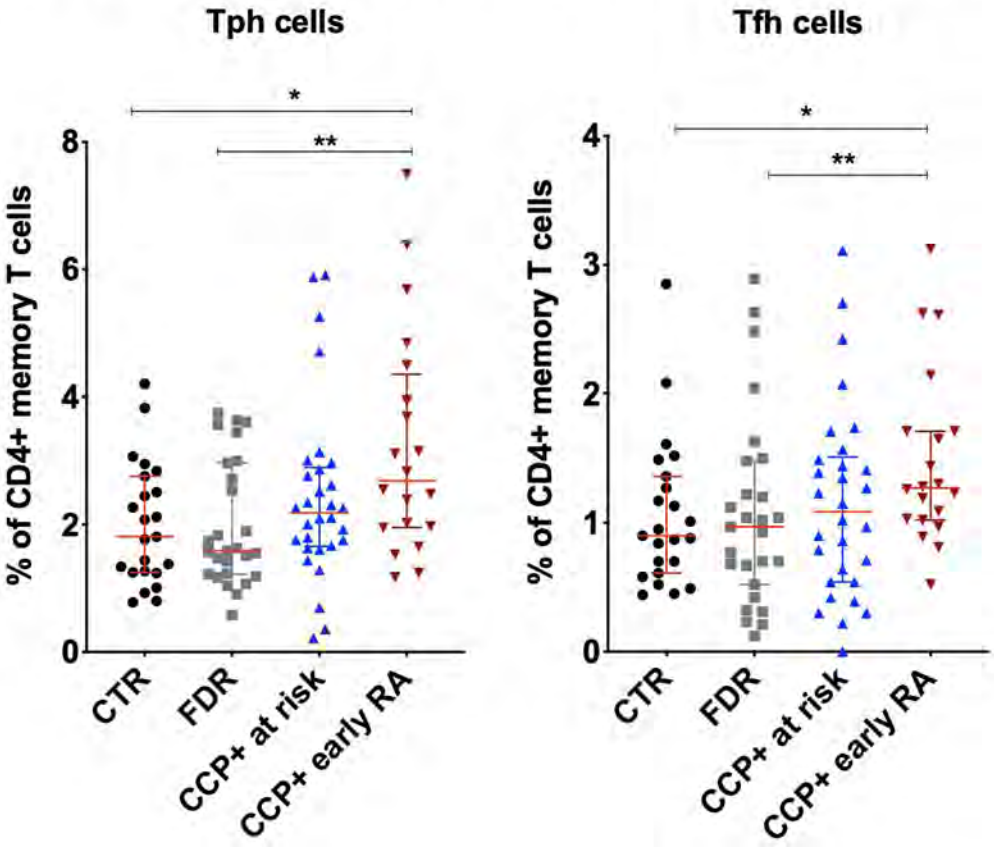

Figure 1. Tph cells and Tfh cells were expanded in CCP+ early RA cohort.

Figure 2. Expanded PD-1^{hi} CD39^{hi} cells in the blood of CCP+ early RA patients.
A. CITRUS analysis of PD-1^{hi} cells shows an increased abundance of two CD39^{hi} clusters in CCP+ donors.
B. Quantification of CD3+CD4+CD45RO+PD-1^{hi}CD39^{hi} cells. * p<0.05, ** p<0.01, *** p<0.001 by Mann-Whitney U test

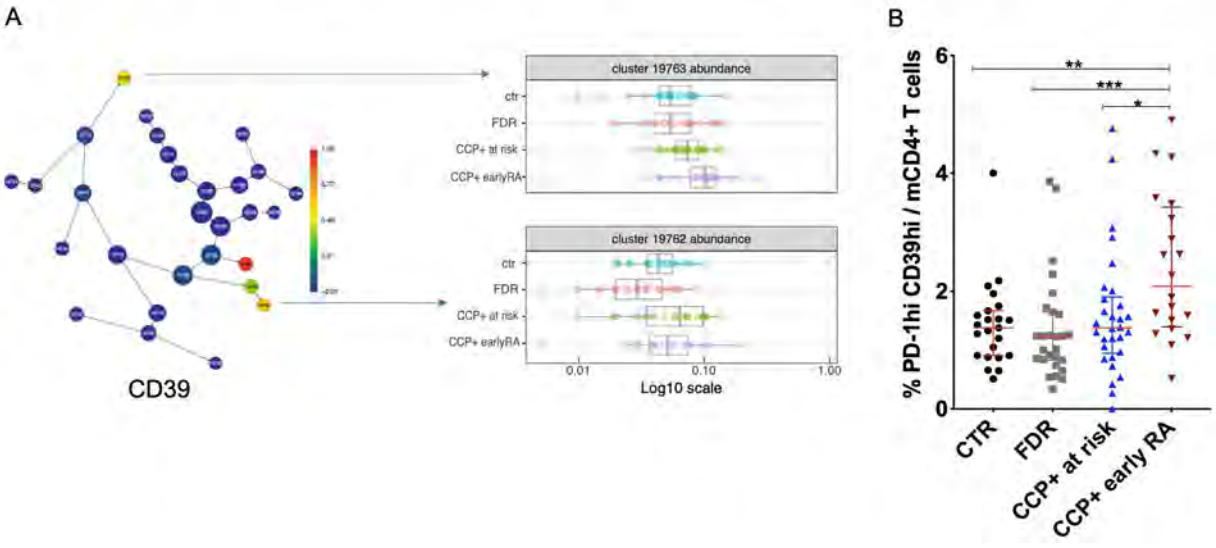

Figure 2. Expanded PD-1hi CD39hi cells in the blood of CCP+ early RA patients.

Figure 3. Increased PD-1 expression of CD39^{hi} Tph cells in CCP+ at-risk individuals.
Mean fluorescence intensity (MFI) of PD-1 in gated populations.
* p<0.05, ** p<0.01, *** p<0.001 by Mann-Whitney U test.

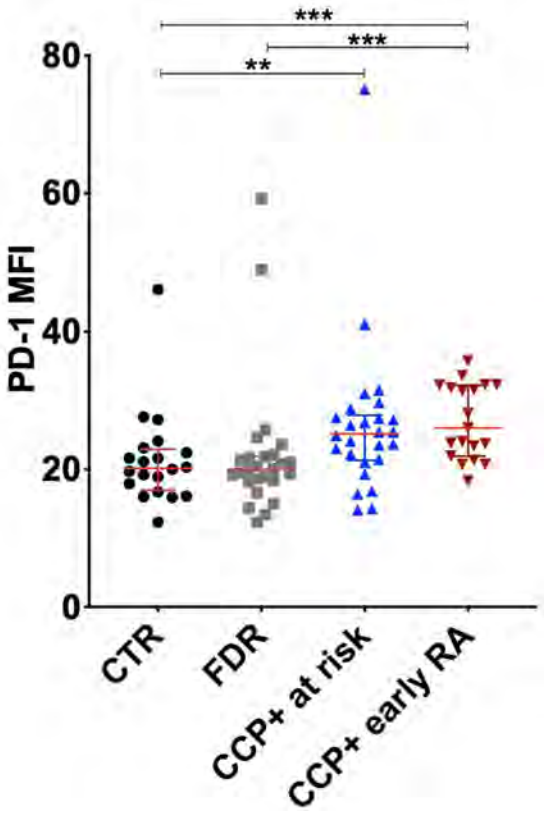

Figure 3. Increased PD-1 expression of CD39hi Tph cells in CCP+ at-risk individuals.

early RA patients (diagnosis within 1 year, n=20). RA patients fulfilled the 2010 ACR/EULAR criteria. We used CITRUS to define and quantify the clusters of PD-1^{hi} cells based on their multi-dimensional features. Expanded cell populations were confirmed by biaxial gating, and the statistical significance was determined by Mann-Whitney U test.

Results: Global T cell phenotypes were generally similar in CCP- groups, CCP+ at risk, and CCP+ early RA, including frequencies of naïve and memory CD4 and CD8 T cells and Tregs. By biaxial gating, both Tph cells and Tfh cells (PD-1^{hi} CXCR5+) were increased in this CCP+ early RA cohort (Figure 1). The number of Tph cells in CCP+ at-risk individuals was increased compared to CCP- controls, although not statistically significant. For a broader assessment of PD-1^{hi} T cells, we used CITRUS to cluster gated PD-1^{hi} cells, including both CD4 and CD8 T cells. Among PD-1^{hi} T cells, 2 specific subpopulations were identified as significantly expanded in CCP+ early RA patients (Figure 2A). Phenotypic assessment highlighted increased CD39 expression on the expanded subclusters. Biaxial gating confirmed the significant expansion of PD-1^{hi} CD39^{hi} CD4 memory T cells in CCP+ early RA patients compared to all the other groups (Figure 2B). In addition, the CD39^{hi} subset of Tfh or Tph cells, but not total Tph and Tfh cells, were significantly higher in CCP+ RA compared to CCP+ at-risk group. The frequency of CD39^{hi} Tph cells was not increased in CCP+ at-risk individuals compared to CCP- controls; however, the expression of PD-1 on these cells was increased in CCP+ at-risk compared to controls (p=0.003, 1.25-fold change), a finding also seen in CCP+ early RA patients (Figure 3). The mean expression intensity of PD-1 on CD39^{hi} Tph cells was significantly correlated with CCP titer across all donors (r=0.376, p< 0.0001).

Conclusion: Detailed immunophenotyping analyses highlighted a robust expansion of CD39^{hi} Tph cells in CCP+ early RA patients. In CCP+ individuals at risk of future RA, CD39^{hi} Tph cells were not clearly increased in frequency, but expressed higher levels of PD-1 compared to CCP- controls and PD-1 levels were correlated with CCP titer. These results suggest that alterations in T cell phenotypes may be detectable not only early in RA but even preceding clinical onset after CCP elevation.

Disclosure: Y. Cao, None; **J. Keegan**, None; **A. Zaccardelli**, None; **G. Keras**, None; **J. Seifert**, None; **E. Bemis**, None; **M. Feser**, None; **M. Demoruelle**, Pfizer Inc., 2; **K. D. Deane**, None; **J. Norris**, None; **M. Brenner**, None; **J. Lederer**, None; **V. Holers**, None; **J. Sparks**, Optum, 1, Janssen, 1, Inova, 1, Gilead, 1, Amgen, 1, Bristol-Myers Squibb, 1, 2; **D. Rao**, None.

Abstract Number: 2047

Synovial CD8 T Cells in Rheumatoid Arthritis Exhibit High Antigen-independent Cytokine Production and Low Cytotoxic Potential

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: T Cell Biology & Targets in Autoimmune & Inflammatory Disease
Session Type: Abstract Session
Session Time: 10:00AM–10:50AM

Background/Purpose: T cell-derived pro-inflammatory cytokines are major drivers of RA pathogenesis, and these cytokines have traditionally been attributed to CD4 T cells. However, single-cell RNA-sequencing (RNA-seq) of RA synovial tissue has revealed that CD8 T cells, which represent nearly half of T cells in inflamed RA synovium, are the predominant expressors of IFNγ and TNF transcripts[1]. Here, we present data indicating that synovial CD8 T cells are major cytokine producers in response to both TCR-mediated and cytokine-mediated stimulation and have low cytotoxic potential.

Methods: Blood, synovial fluid, and synovial tissue were obtained from RA patients meeting the 2010 ACR criteria for RA. Single-cell RNA-seq data sets were generated by integrating new and publicly available data from synovial tissue and fluid from patients with RA and from blood from healthy controls. For stimulation assays, peripheral blood mononuclear cells or synovial fluid mononuclear cells were stimulated with IL-12 and IL-15 for 20 hours or with anti-CD3/CD28 antibody-coated beads for 4 hours, with brefeldin A and monensin included during the last 4 hours of culture. Cytokine production was assessed by intracellular cytokine staining and flow cytometry. Additional flow cytometry experiments were performed on unstimulated cells.

Results: The majority of CD8 T cells in synovial tissue and fluid from patients with seropositive RA express granzyme K (GzmK), either alone or together with granzyme B (GzmB), a marked enrichment compared to blood (Fig. 1A). These cells express lower levels of GzmB and perforin compared to classical GzmB^{+} CD8 cytotoxic T lymphocytes (CTLs) in blood (Fig. 1B), and they do not express high levels of CD57 or CX3CR1, two surface markers associated with cytotoxicity. GzmK itself does not cleave caspases to activate apoptotic cell death pathways but instead signals synovial

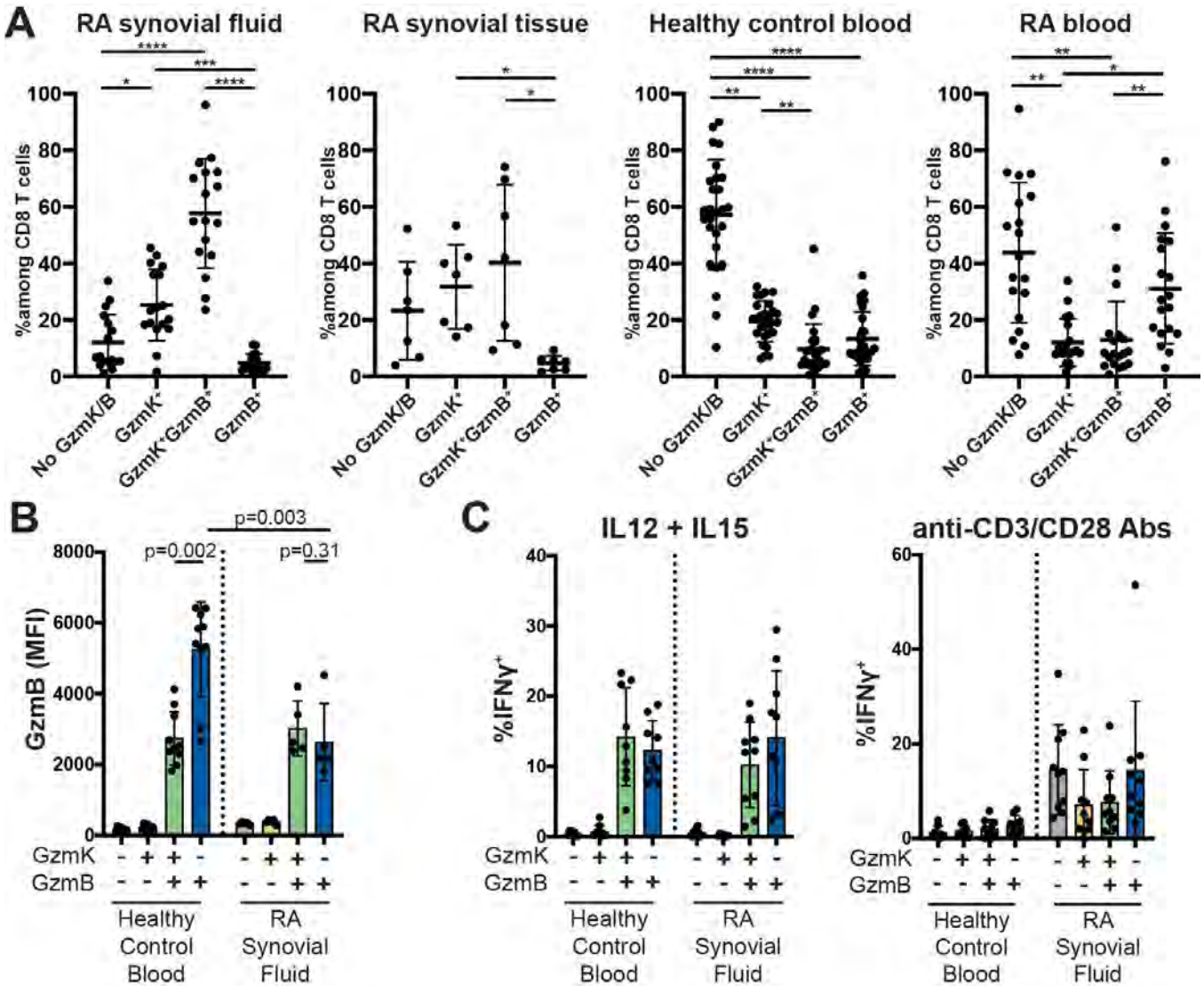


Figure 1. GzmK+ GzmB+ CD8 T cells, the predominant CD8 T cell population in RA synovial fluid and tissue, have low cytotoxic potential but can respond to antigen-independent stimulation. (A) Frequency of intracellular GzmK and GzmB expression among unstimulated CD8 T cells. (B) Mean fluorescence intensity of GzmB staining of unstimulated CD8 T cells categorized by GzmK and GzmB expression. (C) Intracellular cytokine staining after stimulation with IL-12 and IL-15 or anti-CD3/CD28-coated beads. Statistics by Friedman test (A) and Mann-Whitney and Wilcoxon signed rank tests (B). *p<0.05, **p<0.01, ***p<0.001, ****p<0.0001.

fibroblasts to produce IL-6 and other inflammatory factors. Together, these results indicate that GzmK$^+$ GzmB$^+$ CD8 T cells have low cytotoxic potential.

In stimulation assays, GzmK$^+$ GzmB$^+$ CD8 T cells responded to stimulation with IL-12 and IL-15 as well as anti-CD3/CD28 antibody-mediated stimulation. CD8 T cells represented half or more of IFNγ-producing T cells in both conditions, matching or out-producing CD4 T cells. Antigen-independent stimuli are likely the predominant activation pathway for GzmK$^+$ GzmB$^+$ CD8 T cells *in vivo*, since they express low levels of Nur77, a marker of TCR-mediated stimulation, compared to the rare GzmB$^+$ CD8 T cells.

Conclusion: GzmK$^+$ GzmB$^+$ CD8 T cells are the largest CD8 T cell population in synovial fluid and tissue from patients with RA. These cells have low cytotoxic potential but produce cytokines such as IFNγ in response to antigen-independent stimulation. These findings argue that the dominant CD8 T cell population in RA synovium amplifies inflammation by producing IFNγ and other inflammatory mediators (including GzmK itself) in response to cytokines found

in inflamed RA tissue. This antigen-independent activation of CD8 T cells may represent a major mechanism for breaking self-tolerance in RA and other autoimmune diseases.

1. Zhang, F. *et al. Nat Immunol* **20**, 928-942 (2019).

Disclosure: A. Jonsson, None; **F. Zhang**, None; **E. Gomez-Rivas**, None; **K. Rupani**, None; **G. Watts**, None; **K. Wei**, Gilead, 5; **R. Wang**, None; **D. Rao**, None; **A. Partnership (AMP) - RA/SLE**, None; **S. Raychaudhuri**, None; **M. Brenner**, None.

Abstract Number: 2048

Comparison of Two Rituximab Regimens for Induction of Remission in Antineutrophil Cytoplasm Antibody-associated Vasculitis: Systematic Review and Meta-analysis

Valerie Benard[1], Cynthia Farhat[2], Melissa Zarandi-Nowroozi[2], Madeleine Durand[3], Christian Pagnoux[4], Pierre Charles[5], Xavier Puechal[6], Loïc Guillevin[7] and Jean-Paul Makhzoum[1], [1]Vasculitis Clinic, Canadian Network for Research on Vasculitides (CanVasc), Department of Internal Medicine, Hopital du Sacre-Coeur de Montreal, University of Montreal, Montreal, QC, Canada, [2]Department of Medecine, University of Montreal, Montreal, QC, Canada, [3]Department of Internal Medicine, Centre Hospitalier de l'Universite de Montreal (CHUM) and Centre de Recherche du Centre Hospitalier de l'Universite de Montreal (CRCHUM), Montreal, QC, Canada, [4]Vasculitis Clinic, Canadian Network for Research on Vasculitides (CanVasc), Department of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, [5]Department of Internal Medicine, Institut Mutualiste Montsouris, Paris, France, [6]National Referral Center for Rare Systemic Autoimmune Diseases, Cochin Hospital, Paris-Descartes University, Paris, France, [7]Department of Internal Medecine, National Referral Center for Rare Systemic Autoimmune Diseases, Cochin Hospital, Paris-Descartes University, Paris, France

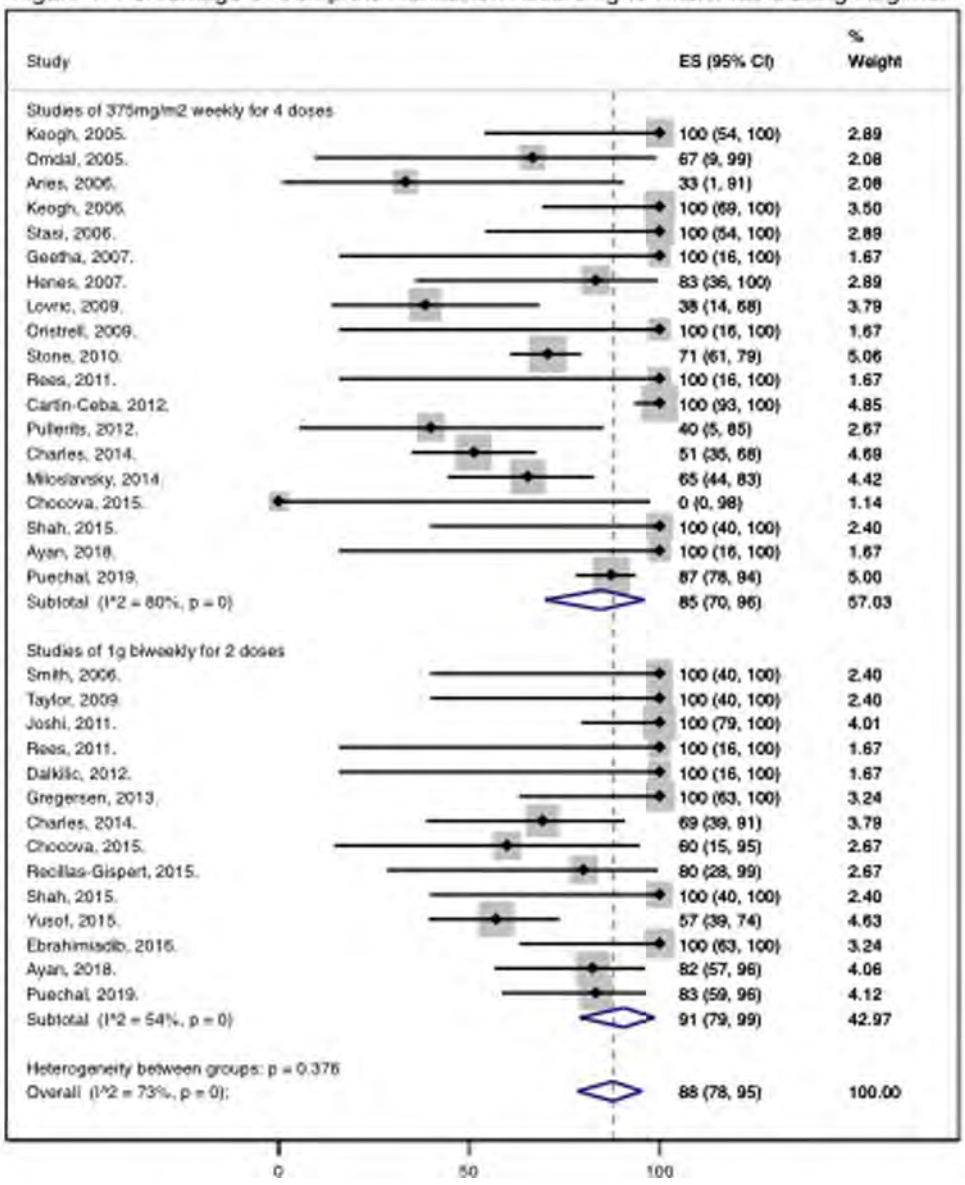
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Vasculitis – ANCA-Associated
Session Type: Abstract Session
Session Time: 11:00AM–11:50AM

Background/Purpose: Organ or life-threatening granulomatosis with polyangiitis (GPA) and microscopic polyangiitis (MPA), two of the antineutrophil cytoplasm antibody-associated vasculitis (AAV), are treated with cyclophosphamide or rituximab (RTX) in combination with glucocorticoids. Different RTX regimens for induction of remission are available: the 4-dose AAV regimen at doses of 375 mg/m^2 I.V. weekly, and the 2-dose rheumatoid arthritis (RA) regimen at doses of 1000 mg I.V. on day 1 and 15. Although the 4-dose regimen has been most extensively studied for induction therapy in AAV, many clinicians choose to use the 2-dose RA regimen to reduce infusion frequency, total dose, and cost. Head-to-head comparative studies of these two regimens have not yet been conducted. Thus, strong evidence is lacking to demonstrate if they are equivalent for the treatment of severe AAV.

The objective of this meta-analysis was to compare the efficacy and safety of these two RTX regimens for the induction of remission in severe AAV.

Methods: A systematic review was performed (PubMed, Cochrane, Google scholar, ClinicalTrials.gov, MEDLINE, and CENTRAL) to identify studies using the 4-dose AAV and/or 2-dose RA rituximab regimens for induction of remission in severe AAV. Availability of disease status 6 months after RTX induction therapy was required for inclusion. Patients were excluded if they received concomitant cyclophosphamide or plasma exchange. The primary endpoint was the proportion of patients in complete remission, which was defined as a BVAS of 0 and/or as the absence of disease

Figure 1. Percentage of Complete Remission According to Rituximab Dosing Regimen



activity on clinical assessment. The pooled estimate was obtained using meta-analysis methods for proportions with random effects. Other secondary endpoints at 6 months included ANCA status, number of patients with B cell depletion, mean prednisone dose, infections, and death.

Results: Out of the 3619 studies identified, 27 met inclusion criteria, including 1 RCT, 4 prospective cohorts, 9 retrospective cohorts and 13 case series. A total of 506 patients with GPA or MPA were included for analysis: 361 patients were treated with the 4-dose AAV regimen and 145 patients with the 2-dose RA regimen. Mean age was 50 years, 52% were women, and 86% were ANCA-positive. Relapsing disease at inclusion accounted for 83% and 92% of patients in the 4-dose AAV and the 2-dose RA regimen group, respectively. Overall, complete remission at 6 months was achieved in 88 % (95% CI: 78–95) of patients. There was no significant difference between the 4-dose AAV and 2-dose RA regimens, complete remission reaching respectively 85% (95% CI: 70-96) and 91% (95% CI: 79-99) (fig 1). Results remained consistent after the exclusion of low-quality studies. At 6 months, the mean daily dose of prednisone was 8.1 mg and was comparable in both groups. Both regimens led to a similar proportion of patients with infections (12% in both) and death (1% vs. 0%), respectively, at 6 months, with insufficient data to conclude on other secondary endpoints.

Conclusion: No difference was found in terms of efficacy and safety between the 4-dose AAV and the 2-dose RA rituximab regimens for induction of remission in severe AAV.

Disclosure: V. Benard, None; **C. Farhat**, None; **M. Zarandi-Nowroozi**, None; **M. Durand**, None; **C. Pagnoux**, chemocentryx, 1, roche, 1, 2, GSK, 1, 2, Janssen, 1, Sanofi, 5; **P. Charles**, Roche Pharma, 2; **X. Puechal**, Roche Pharma, 2; **L. Guillevin**, None; **J. Makhzoum**, Hoffman-La Roche ltd, 5, 8.

Abstract Number: 2049

Nasal Bacteria Associated with Disease Activity and ANCA Levels in Granulomatosis with Polyangiitis

Rennie Rhee[1], Jiarui Lu[1], Kyle Bittinger[2], Antoine Sreih[1], Jung-Jin Lee[3], Lisa Mattei[3], Brendan Kelly[4], Peter C. Grayson[5], Hongzhe Lee[4], Ronald Collman[4] and Peter Merkel[1], [1]University of Pennsylvania, Philadelphia, PA, [2]Children's Hospital of Philadelphia, Philadelphia, PA, [3]Children's Hospital of Philadelphia, Philadelphia, [4]University of Pennsylvania, Philadelphia, [5]Systemic Autoimmunity Branch, National Institutes of Health, NIAMS, Bethesda, MD

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Vasculitis – ANCA-Associated
Session Type: Abstract Session
Session Time: 11:00AM–11:50AM

Background/Purpose: Nasal bacteria have been linked to disease activity in granulomatosis with polyangiitis (GPA) with most studies focused on *Staphylococcus aureus*. Our previous study identified dynamic changes in the ratio of nasal *Corynebacterium* to *Staphylococcus* (at the genus level) prior to and during a relapse. Corynebacteria are a common commensal that inhabits the skin and nose and is known to directly interact with *S. aureus*. The objective of this study was to evaluate species-level identity of nasal bacteria and their association with disease activity and ANCA levels in GPA.

Methods: Nasal bacterial composition was examined using 16S rRNA gene sequencing of nasal swabs of 19 patients with GPA followed longitudinally approximately every 3 months (N = 76 visits, median time between visits 4 months). Nine patients had at least 1 visit with active disease and 10 patients remained in remission during follow-up. Disease activity was determined by BVAS/WG. Only PR3-ANCA results obtained by ELISA at the study site were included for ANCA analyses (11 patients with 29 visits). We evaluated the relative abundance of the 10 most abundant bacterial species across all visits as well as the ratios between these 10 species. Generalized estimating equations evaluated the association between bacteria and i) visit type (stable remission [n=41], pre-pre-relapse [n=4], pre-relapse [n=10], relapse [n=10], post-relapse [n=9]), and ii) ANCA levels, accounting for repeated measures within an individual. Test for trend examined linear trends in bacterial abundance across visit types. Models were adjusted for use of antibiotics, immunosuppressive medications, nasal irrigation, and, when analyzing Corynebacteria, presence of *S. aureus*.

Results: *Corynebacterium tuberculostearicum* featured prominently in our analyses. Specifically, we found the abundance of *C. tuberculostearicum* significantly increased across visit types in GPA when evaluating any relapse (adjusted P = 0.04; **Figure 1**) and relapse involving the sinonasal area (adjusted P < 0.01). The presence of *S. aureus* (32/76 visits [42%]) was independently associated with a higher *C. tuberculostearicum* abundance (adjusted P = 0.02). *C. tuberculostearicum* abundance was associated with higher levels of PR3-ANCA (adjusted P = 0.02; **Figure 2**). Analysis of bacterial ratios identified significantly increasing ratios of *C. tuberculostearicum* to *S. caprae* abundance and *C. pseudodiphtheriticum* to *S. caprae* abundance across visit types (both adjusted P < 0.01; **Figure 3**).

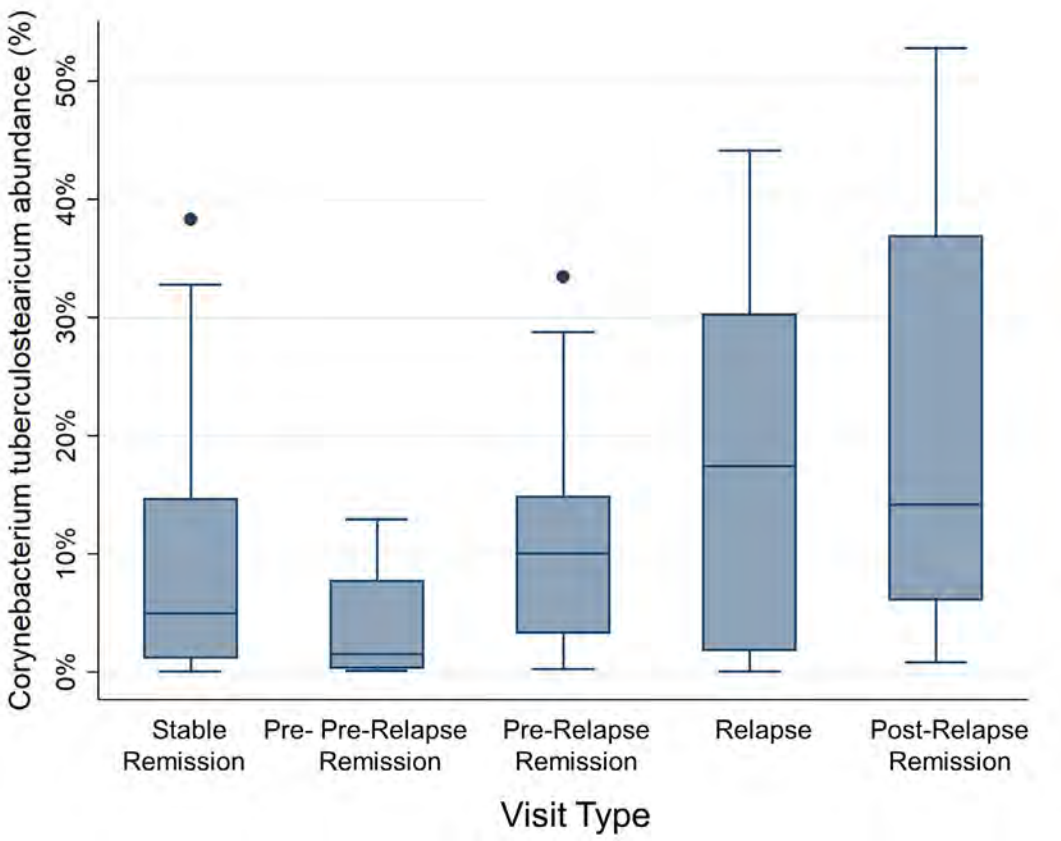


Figure 1. Increasing abundance of nasal Corynebacterium tuberculostearicum is associated with relapse in granulomatosis with polyangiitis (GPA). Longitudinal study visits categorized by visit type: stable remission (n=41), pre-pre-relapse remission (n=4), pre-relapse remission (n=10), relapse (n=12), and post-relapse remission (n=9). Test for trend detected a significant linear increase in nasal C. tuberculostearicum abundance across visits even after adjusting for antibiotics, immunosuppressives, nasal irrigation, and presence of S. aureus (adjusted P = 0.04). Similar results found when analyzing only relapses involving sinonasal area.

Conclusion: Our species-level analysis has uncovered a novel finding between *C. tuberculostearicum* and both disease relapse and ANCA levels in GPA. Our results also detected associations between *C. tuberculostearicum* and *Staphylococcus* species, including *S. aureus*. Prior studies demonstrated a pathogenic role for *C. tuberculostearicum* in chronic rhinosinusitis and direct interactions between *Corynebacterium* spp. and *S. aureus*. We propose that competitive interactions between Corynebacteria and Staphylococci induce nasal mucosal immune responses which, in susceptible hosts predisposed to autoimmunity and ANCA formation, lead to systemic relapse in GPA.

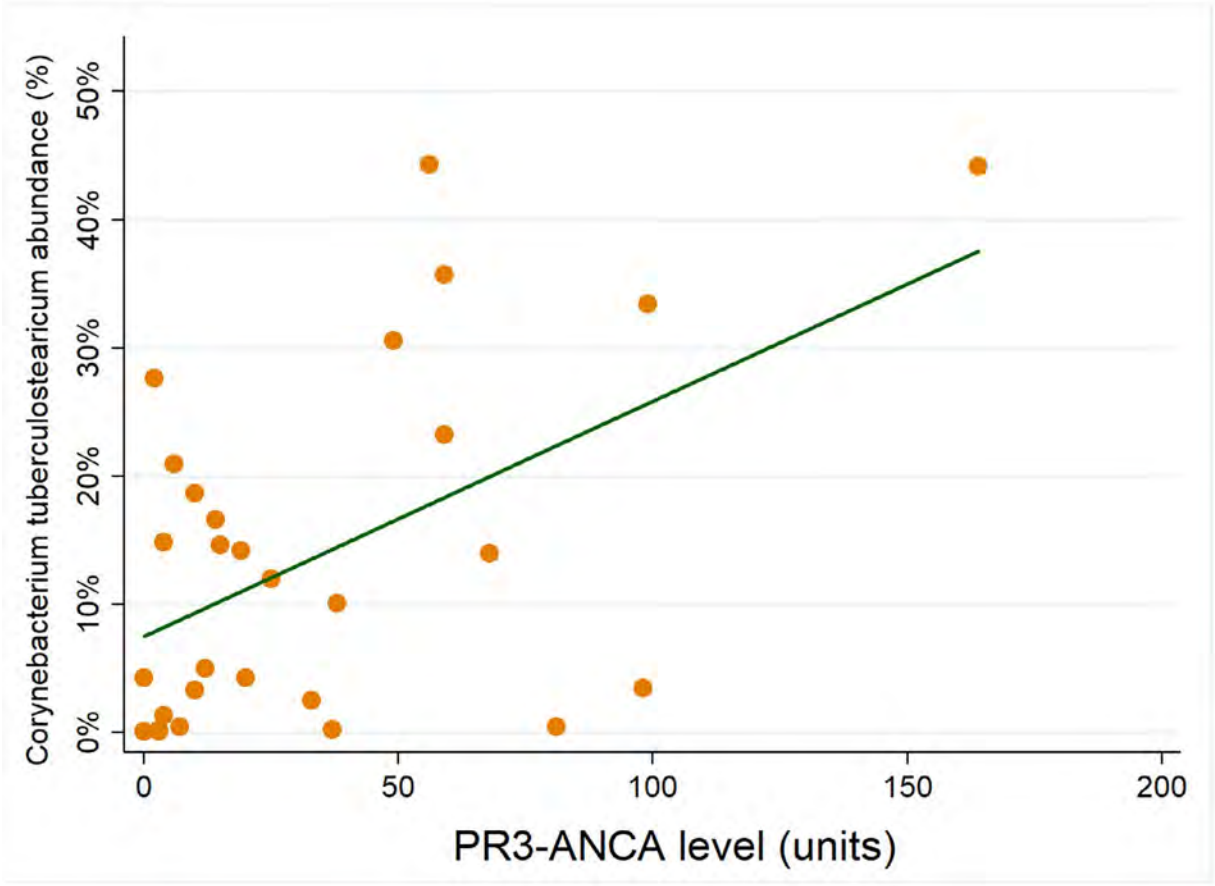


Figure 2. Relative abundance of nasal Corynebacterium tuberculostearicum is associated with PR3-ANCA level in granulomatosis with polyangiitis (GPA). Scatterplot demonstrates association between abundance of nasal C. tuberculostearicum and serum PR3-ANCA levels in 11 patients with total of 29 visits (unadjusted $P < 0.01$). Association remained significant even after adjusting for use of antibiotics, immunosuppressives, and nasal irrigation (adjusted $P = 0.02$). Reference range for normal PR3-ANCA < 20 units.

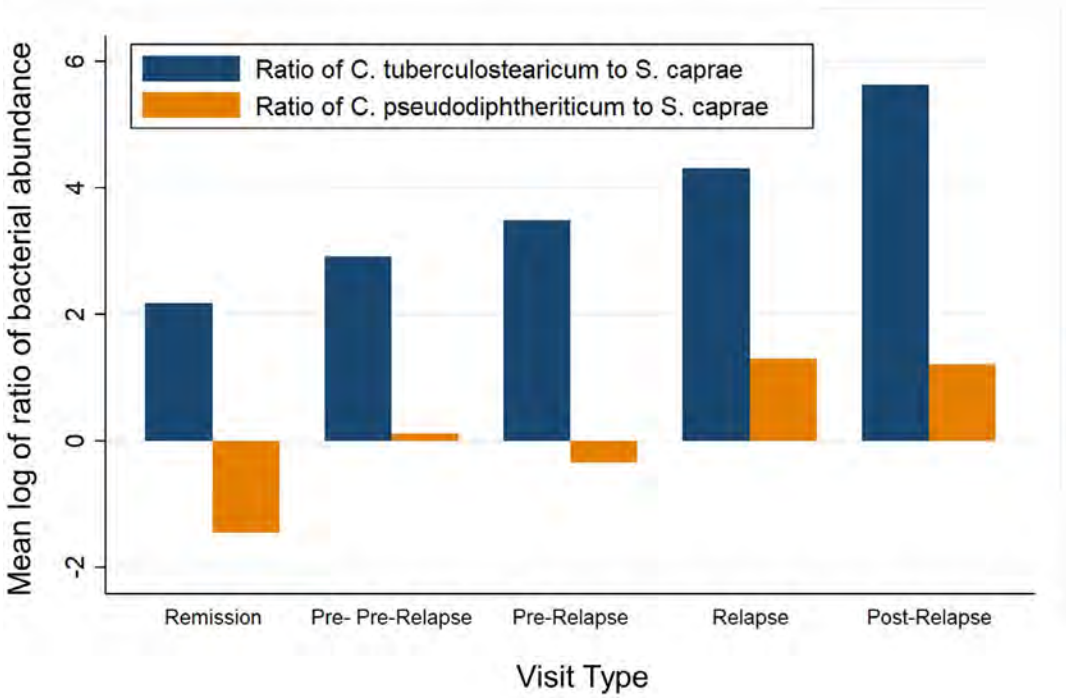


Figure 3. Ratio of bacteria associated with relapse in granulomatosis with polyangiitis (GPA). Ratio of bacterial abundance were log-transformed and test for trend evaluated for changes across visit types. An increasing ratio of Corynebacterium tuberculostearicum to Staphylococcus caprae and C. pseudodiphtheriticum to S. caprae were both associated with visit type, even after adjusting for antibiotics, immunosuppressives, and nasal irrigation (both adjusted $P < 0.01$).

Disclosure: R. Rhee, None; **J. Lu**, None; **K. Bittinger**, None; **A. Sreih**, Bristol-Myers Squibb, 3, Alexion, 1; **J. Lee**, None; **L. Mattei**, None; **B. Kelly**, None; **P. Grayson**, None; **H. Lee**, None; **R. Collman**, None; **P. Merkel**, AbbVie, 5, Biogen, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Insmed, 5, Jannsen, 5, Kiniksa, 5, Magenta, 5, Novartis, 5, Pfizer, 5, Sparrow, 5, Talaris, 5, AstraZeneca, 2, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, UpToDate, 7.

Abstract Number: 2050

Autoantibodies Targeting Complement Receptors C3aR and C5aR1 Are Decreased in ANCA-associated Vasculitis and Correlate with a Higher Relapse Rate

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SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Vasculitis – ANCA-Associated
Session Type: Abstract Session
Session Time: 11:00AM–11:50AM

Background/Purpose: Activation of the alternative and common terminal complement pathways has been shown in ANCA-associated vasculitis (AAV). Circulating titers of the anaphylatoxin C5a are increased and correlate with disease activity in AAV. Binding to the corresponding G protein-coupled receptor (C5aR1/CD88) enhances the influx of neutrophils and their activation, leading to ROS generation and endothelial damage. Blocking of the receptor C5aR1 was protective in a murine model of NCGN in AAV (4). In humans, the oral C5aR1 inhibitor avacopan showed promis-

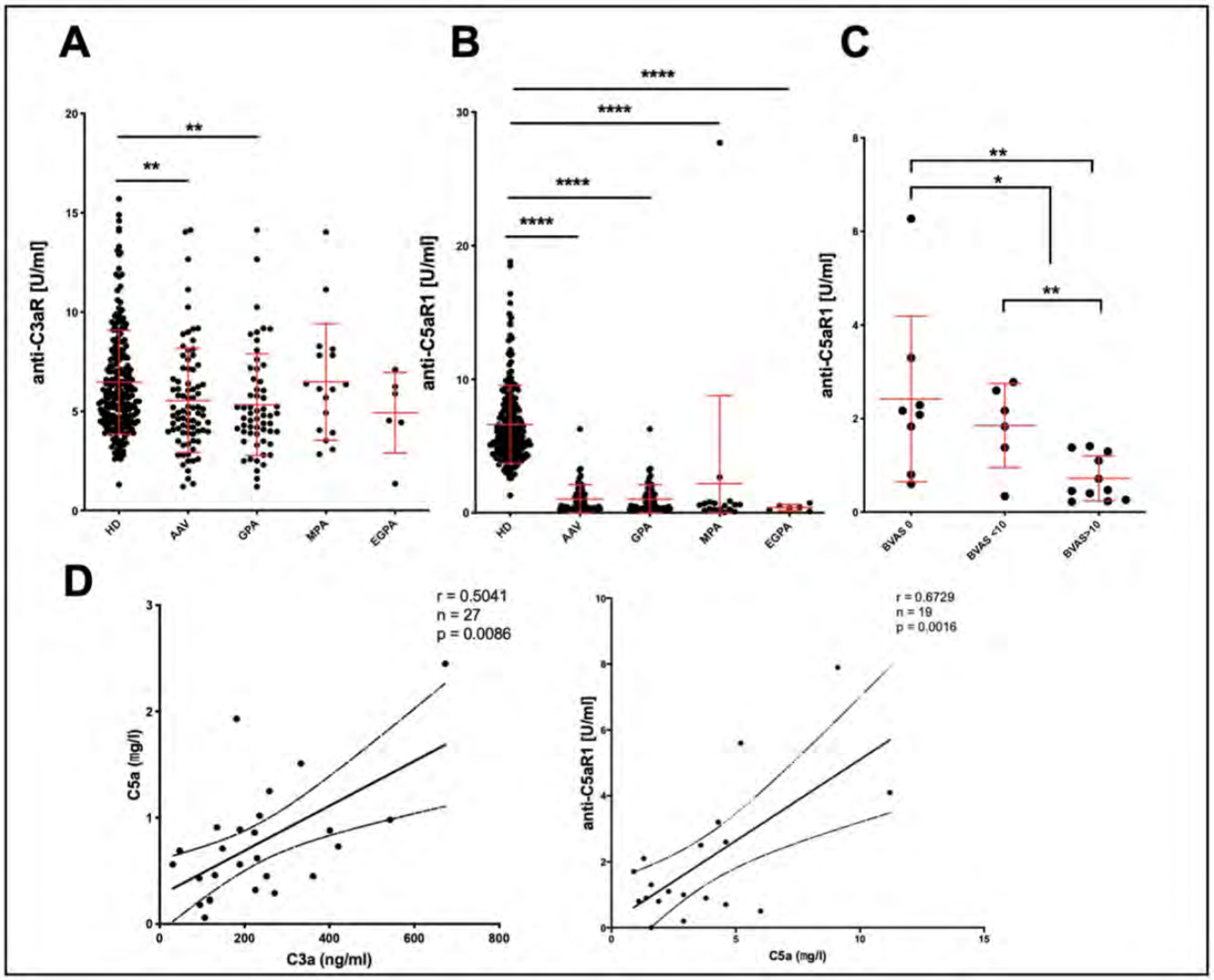

Figure 1. Anti-C3aR and anti-C5aR1 autoantibodies in AAV. A: GPA patients displayed significantly lower titers of circulating anti-C3aR aab in comparison to MPA, EGPA and HD. B: concentrations of anti-C5aR1 aab were decreased in AAV with the lowest titers in GPA compared to HD. C: GPA patients with a BVAS >10 showed the lowest levels of anti-C5aR1 aabs. D: Plasma levels of C3a and C5a correlated positively in GPA, whereas only C5a and anti-C5aR1 correlated positively in GPA patients performing the spearman's rank correlation coefficient. Data are presented as mean±SD; p values were determined using one-way ANOVA with Tuckey's multiple comparison post hoc test (A,B) or two-tailed Mann-Whitney U-test if two groups were compared (C,D) or Spearman's rho (E); *p≤0.05, **p≤0.01, and ****p≤0.0001; HD, healthy donors; AAV, ANCA-associated vasculitis; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; EGPA, eosinophilic granulomatosis with polyangiitis; aab, autoantibody; BVAS, Birmingham Vasculitis Activity Score

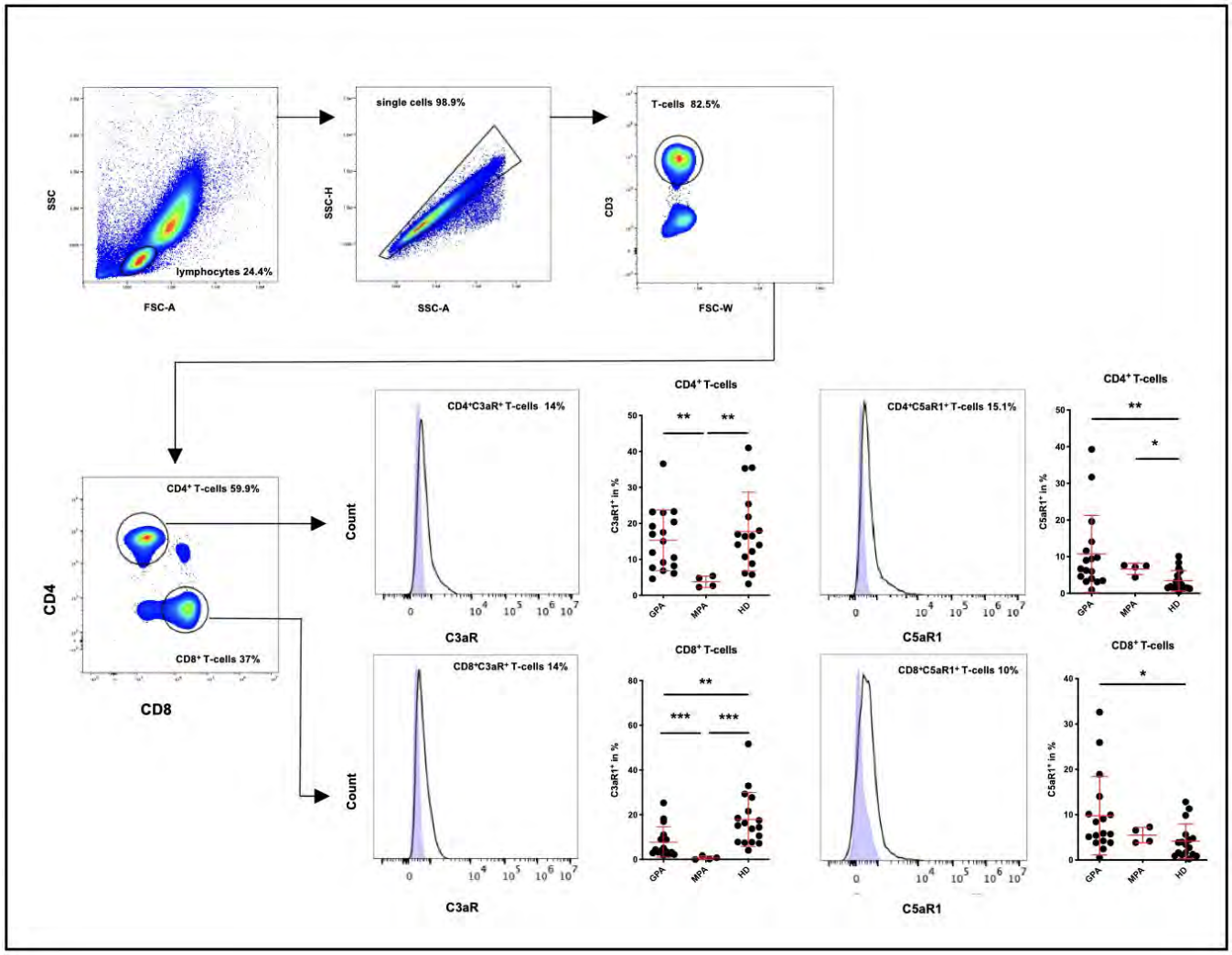

Figure 2. C5aR1 is overexpressed on CD4+ and CD8+ T-cells in GPA. Gating strategy of circulating CD4+ and CD8+ T-cells focused on the surface expression of C3aR and C5aR1 (Histogram: for comparison, shade blue area presented the isotype control). Data are presented as mean±SD; Mann-Whitney U-tests were used to determine significance *p≤0.05, **p≤0.01 and ***p≤0.001; HD, healthy donors; GPA, granulomatosis with polyangiitis; MPA, microscopic polyangiitis; FSC, forward scatter; SSC, side scatter

ing results as glucocorticoid-sparing agent in two randomized phase 2 trials. The phase 3 trial was reported to have met its primary endpoints (NCT02994927). Notably, disease-specific anti-G protein-coupled receptor autoantibody (aab) signatures have been found in different autoimmune diseases, but have not been evaluated in AAV so far.

The aim of the present study was to examine whether circulating anti-C3aR and anti-C5aR1 autoantibodies (aabs) correlate with clinical findings in AAV and are linked to the clinical outcome. Values of anti-C3aR and anti-C5aR1 aabs AAV were analyzed and correlated with the clinical course.

Methods: Sera and plasma of AAV patients [granulomatosis with polyangiitis (GPA), n=64; microscopic polyangiitis (MPA), n=26; eosinophilic granulomatosis with polyangiitis (EGPA), n=11] were measured in a cross-sectional analysis by enzyme-linked immunosorbent assay (ELISA) for circulating autoantibodies against anti-C3aR and anti-C5aR1 aabs and plasma levels of C3a and C5a. Expression of C3aR and C5aR1 on T-cells and neutrophils was determined using flow cytometry. Clinical data including Birmingham vasculitis activity score (BVAS V3.0) were assessed at the time of serum sampling and during follow-up for 48 months.

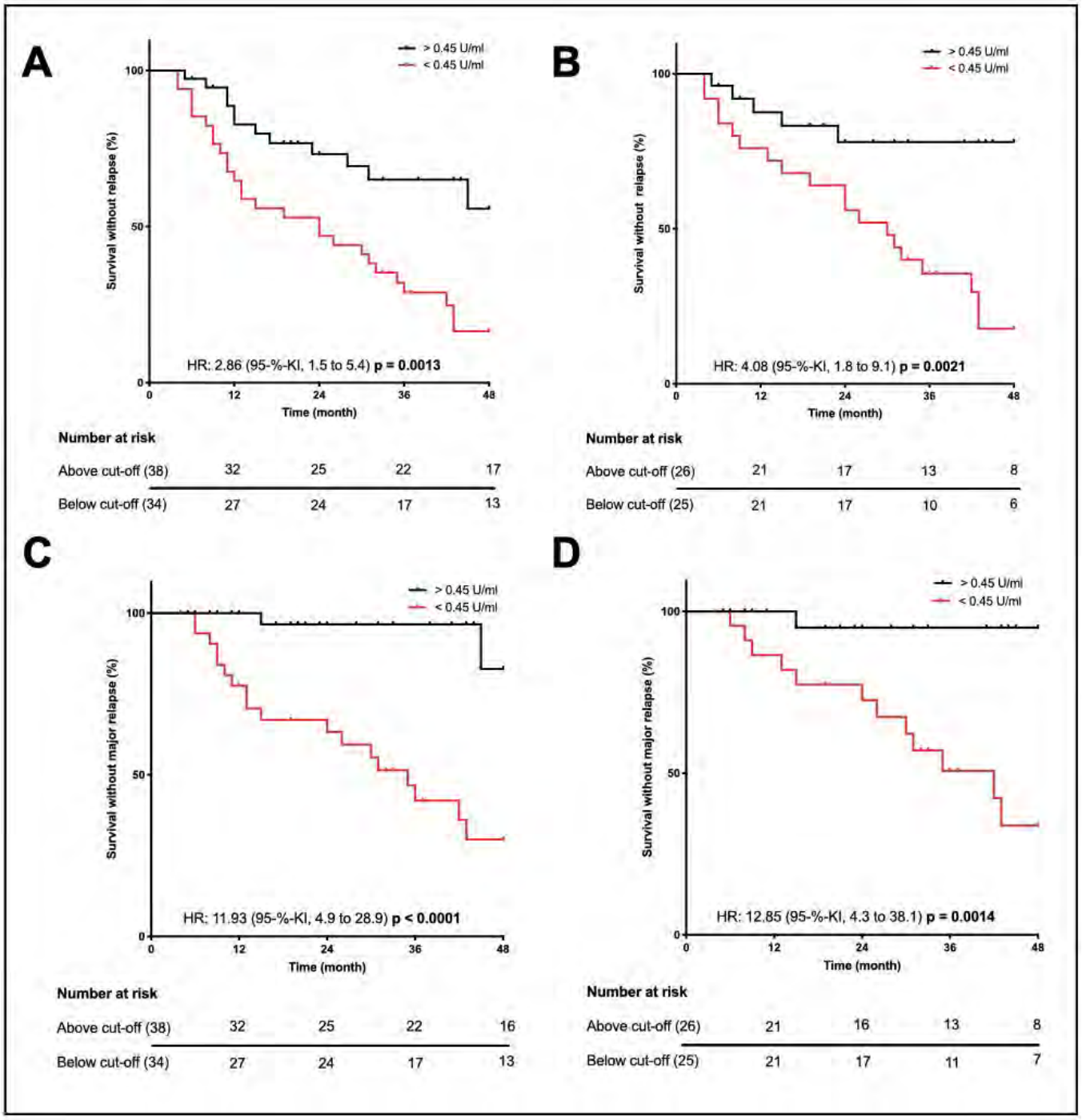

Figure 3. Anti-C5aR1 aab levels below 0.45 U/l were associated with higher relapse rates in AAV, especially in GPA A: AAV patients with reduced titers of anti-C5aR1 aab <0.45U/ml displayed an increased relapse risk, especially in GPA (B). C: Risk of major relapse for in AAV and GPA (D) (AAV: HR: 11.93, p<0.0001; GPA: HR: 12.85, p=0.0014); AAV, ANCA-associated vasculitis; GPA, granulomatosis with polyangiitis

Results: Patients with GPA displayed low titers of anti-C3aR aabs (Fig. 1a, p≤0.05). Anti-C5aR1 aabs were decreased in AAV, especially in GPA (Fig.1b, p≤0.0001). GPA patients with a high BVAS had the lowest levels of anti-C5aR1 aabs Fig. 1c, p≤0.01). Plasma levels of C3a and C5a correlated positively in GPA. C5a and anti-C5aR1 levels correlated positively in GPA (Fig.1d). C5aR1 expression was increased on T-cells in GPA (Fig. 2). Titers of anti-C5aR1 aabs < 0.45U/ml correlated with an increased relapse risk for major relapse in GPA (Fig. 3; HR 12.85, P=0.0014).

Conclusion: Anti-C5aR1 aabs reflect complement activation and disease activity in GPA. Moreover, Anti-C5aR1 aabs may be useful to monitor disease activity. C5aR1 expression on T-cells may also play a role in AAV-pathogenesis.

Disclosure: S. Klapa, None; **A. Müller**, None; **A. Koch**, None; **A. Kerstein-Staehle**, None; **W. Kaehler**, None; **H. Heidecke**, None; **S. Schinke**, None; **M. Huber-Lang**, None; **M. Nitschke**, None; **S. Pitann**, None; **C. Karsten**, None; **G. Riemekasten**, None; **P. Lamprecht**, None.

Abstract Number: 2051

Localized versus Systemic Granulomatosis with Polyangiitis: Data from the French Vasculitis Study Group Database

Michele Iudici[1], Christian Pagnoux[2], Delphine Courvoisier[3], Pascal Cohen[4], Mohamed Hamidou[5], Achille Aouba[6], François Lifermann[7], Marc Ruivard[8], Olivier Aumaitre[9], Bernard Bonnotte[10], Julien Campagne[11], Olivier Decaux[12], Eric Hachulla[13], Alexandre Karras[14], Chahéra Khouatra[15], Noémie Jourde-Chiche[16], Jean-François Viallard[17], Pascal Godmer[18], Claire Blanchard-Delaunay[19], Alain Le Quellec[20], Thomas Quéméneur[21], Claire de Moreuil[22], Alexis Regent[4], Benjamin Terrier[4], Luc Mouthon[4], Loïc Guillevin[4] and Xavier Puechal[4], [1]National Referral Center for Rare Systemic Autoimmune Diseases, Cochin Hospital, Paris-Descartes University and Geneva University Hospitals, Geneva, Switzerland, [2]Division of Rheumatology, Mount Sinai Hospital, University of Toronto, Toronto, ON, Canada, [3]Division of rheumatology, Geneva University Hospitals, Geneva, Switzerland, [4]National Referral Center for Rare Systemic Autoimmune Diseases, Cochin Hospital, Paris-Descartes University, Paris, France, [5]Department of Internal Medicine, Hôtel-Dieu, CHU Nantes, Nantes, France, [6]Department of Internal Medicine, CHU Côte de Nacre, Caen, France, [7]Department of Internal Medicine, CH Côte d'Argent, Dax, France, [8]Department of Internal Medicine, CHU Estaing, Clermont Ferrand, France, [9]Department of Internal Medicine, CHU Gabriel Montpied, Clermont Ferrand, France, [10]CHU Dijon, Dijon, France, [11]Department of Internal Medicine, Hôpitaux Privés de Metz, Metz, France, [12]CHU Rennes, Rennes, France, [13]Department of Internal Medicine, CHRU, Lille Cedex, France, [14]Department of Nephrology, Hôpital Européen Georges Pompidou, Paris, France, [15]Department of Respiratory Medicine, CHU Louis Pradel, Lyon, France, [16]Department of Nephrology, CHU de la Conception, Marseille, France, [17]Department of Internal Medicine, CHU Haut-Lévêque, Bordeaux, France, [18]Department of Internal Medicine, CH Bretagne Atlantique, Vannes, France, [19]Department of Internal Medicine, CH, Niort, France, [20]Department of Internal Medicine, CHU Saint Eloi, Montpellier, France, [21]Department of Internal Medicine, CH, Valenciennes, France, [22]Department of Internal Medicine, CHU Cavale Blanche, Brest, France

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Vasculitis – ANCA-Associated
Session Type: Abstract Session
Session Time: 11:00AM–11:50AM

Background/Purpose: The clinical picture at onset and evolution of localized forms of granulomatosis with polyangiitis (L-GPA) have already been investigated but, to our knowledge, have not been directly compared to those of patients with initial systemic disease (S-GPA); nor have the risk factors for L-GPA progression to systemic disease (LS-GPA) or its main characteristics been examined in large samples. We undertook this study to describe the main L-GPA features at diagnosis and their evolution over time, with comparisons of L- vs S-GPA patients.

Methods: French Vasculitis Study Group Registry patients had an isolated orbital mass and/or met EULAR recommendations[1] for L-GPA, ie upper and/or lower respiratory tract, and, for S-GPA, categorizing them as early systemic, generalized or severe subset. All patients' demographics, disease manifestations at diagnosis and long-term clinical outcomes were extracted from the database for analyses and L-GPA vs S-GPA comparisons.

Results: Among the 795 FVSG-Registry GPA patients, 87 (10.9%) had L-GPA (M/F ratio 1; mean±SD age 45.8±18.0 years) involving upper and lower airways in 56 (64.4%). Most L-GPA patients were positive for anti-proteinase-3

(PR3) (56.3%) or anti-myeloperoxidase (MPO) (21.8%) ANCA. Their main clinical manifestations were rhinitis (54.0%), lung nodules (50.6%), sinusitis (42.5%) and otitis (26.4%), with 5.7% each having subglottic stenosis or saddle nose. Comparing L-GPA vs. S-GPA patients at diagnosis, respectively, they were younger (mean±SD 45.8±18.0 vs. 54.1±15.9 years; P< 0.001), more frequently had saddle nose (5.7% vs. 0.7%; P=0.001) or subglottic stenosis (5.7% vs. 1.1%; P=0.006), were less often PR3-ANCA–positive (56.3% vs. 76.6%;< 0.001) and had lower BVAS (7.2 vs. 18.6; P< 0.001). L-GPA induction therapy less frequently included intravenous cyclophosphamide (46.0% vs. 79.4%; P< 0.001) or glucocorticoids (90.8% vs. 97.9%; P< 0.001; mean dose 48.7 vs. 58.0 mg; P< 0.001) but more often methotrexate (14.9% vs. 3.2%; P< 0.001). L- and S-GPA patients' relapse-free–survival probability estimates (P=0.97), relapse rates (P=0.927) and refractory disease rates at each visit (P=0.543) were comparable, but the L-GPA overall survival rate from diagnosis was significantly higher (P< 0.0001). During follow-up (median 42 (range 6–241) months), 21 (24.1%) L-GPA progressed to LS-GPA after a median of 21 (range 3–93) months with peripheral/central neuropathy (n=8), ocular (n=8), renal (n=6), severe pulmonary (n=1), cardiovascular (n=1) and/or skin (n=1) relapses. No patient evolved into a severe renal subset. None of the evaluated demographic, clinical or serological factors predicted progression to LS-GPA.

Conclusion: The risk of L-GPA relapse was similar to that of S-GPA but L-GPA patients' overall survival rate was higher. About a quarter of L-GPA patients developed clinical S-GPA manifestations, but never life-threatening end-stage organ disease.

Reference

[1]Hellmich B, et al. Ann Rheum Dis. 2007;66:605-17.

Disclosure: M. Iudici, None; **C. Pagnoux**, Chemocentryx, 1, GlaxoSmithKline, 1, 2, 3, Sanofi, 1, Hoffman-LaRoche, 1, 2, 3; **D. Courvoisier**, None; **P. Cohen**, None; **M. Hamidou**, None; **A. Aouba**, None; **F. Lifermann**, None; **M. Ruivard**, None; **O. Aumaitre**, None; **B. Bonnotte**, None; **J. Campagne**, None; **O. Decaux**, None; **E. Hachulla**, None; **A. Karras**, None; **C. Khouatra**, None; **N. Jourde-Chiche**, None; **J. Viallard**, None; **P. Godmer**, None; **C. Blanchard-Delaunay**, None; **A. Le Quellec**, None; **T. Quéméneur**, None; **C. de Moreuil**, None; **A. Regent**, None; **B. Terrier**, None; **L. Mouthon**, None; **L. Guillevin**, None; **X. Puechal**, Roche Pharma, 2.

Abstract Number: 2052

Extended Follow-Up of Patients Recruited to a Randomized, Controlled Trial of Rituximab versus Azathioprine After Induction of Remission with Rituximab for Patients with ANCA-Associated Vasculitis and Relapsing Disease

Rona Smith[1], David Jayne[2] and Peter A. Merkel[3], [1]University of Cambridge, Cambridge, United Kingdom, [2]Department of Medicine, Vasculitis and Lupus Research Group, University of Cambridge, Cambridge, UK, Cambridge, United Kingdom, [3]Division of Rheumatology University of Pennsylvania, Philadelphia, PA

SESSION INFORMATION

Session Date: Monday, November 9, 2020
Session Title: Vasculitis – ANCA-Associated
Session Type: Abstract Session
Session Time: 11:00AM–11:50AM

	Rituximab (N=85)	Azathioprine (N=85)	Total (N=170)
Age, years: median (range)	57 (18-89)	61 (27-83)	59 (18-89)
Female, number (%)	42 (49.4%)	44 (51.8%)	86 (50.6%)
Disease duration, years, median; (range)	5.8 (0.4-38.5)	4.9 (0.4-25.8)	5.3 (0.4-38.5)
Prior cyclophosphamide therapy			
Number of patients (%)	67/85 (78.8%)	66/85 (77.6%)	133/170 (78.2%)
Cumulative dose, grams (g): median (range)	7.1 g (0.2-301)	12 g (1.0-146)	10 g (0.2-301)
Prior rituximab therapy			
Number (%) patients	33/85 (38.8%)	27/85 (31.8%)	60/170 (35.3%)
Cumulative dose, grams (g, median); (range)	3.2 g (2.0-16.0)	5.4 g (1.5-14.0)	3.9 g (1.5-16.0)
Glucocorticoid induction regimen			
1 mg/kg/day starting dose	24/85 (28.2%)	24/85 (28.2%)	48/170 (28.2%)
0.5 mg/kg/day starting dose	61/85 (71.8%)	61/85 (71.8%)	122/170 (71.8%)
ANCA type			
Anti-proteinase 3	61/85 (71.8%)	62/85 (72.9%)	123/170 (72.4%)
Anti-myeloperoxidase	24/85 (28.2%)	23/85 (27.1%)	47/170 (27.6%)
Relapse type upon entry into trial			
Severe	52/85 (61.2%)	52/85 (61.2%)	104/170 (61.2%)
Non-severe	33/85 (38.8%)	33/85 (38.8%)	66/170 (38.8%)

Table 1. Baseline characteristics of patients enrolled in RITAZAREM trial

Background/Purpose: Rituximab is an effective therapy for induction of remission in ANCA-associated vasculitis (AAV). However, the effect of rituximab is not sustained, and subsequent relapse rates are high, especially in patients with a history of relapse. The RITAZAREM trial (ClinicalTrials.gov identifier: NCT01697267) was an international, multi-center, open-labelled, randomized, controlled trial of patients with AAV with relapsing disease comparing the efficacy, after induction of remission with rituximab, of two relapse-prevention strategies: repeat dosing of rituximab or daily oral azathioprine. The extended follow-up phase of the trial provides a unique opportunity to ask important questions about durability of effects of therapies, safety of extended courses of azathioprine and rituximab, and clinical and laboratory biomarkers of remission and relapse in AAV.

Methods: Patients with AAV were recruited at the time of relapse and received induction therapy with rituximab and glucocorticoids. If remission was achieved by month 4, patients were randomized in a 1:1 ratio to receive either rituximab (1000 mg every 4 months for 5 doses) or azathioprine (2 mg/kg/day) as maintenance therapy. Patients were followed for a minimum of 36 months, with most patients followed for 48 months. The primary outcome of the trial was time to disease relapse. The trial was completed in November 2019.

Results: 188 patients were enrolled and 170 randomized at 4 months (85 to rituximab; 85 to azathioprine). Median age was 59 years (range 19-89), with a prior disease duration of 5.3 years (0.4-38.5). 123/170 (72%) patients had a history of testing positive for anti-proteinase 3-ANCA; 47/170 (28%) for myeloperoxidase-ANCA. 104/170 (61%) were enrolled having suffered a major relapse, and 48/170 (28%) received a pre-specified higher dose glucocorticoid induction regimen (**Table 1**). 114 (67%) patients had prior renal involvement. Previously presented data demonstrated the superiority of rituximab over azathioprine during the maintenance treatment period. Results of the follow-up phase of the study after discontinuation of maintenance therapy will be presented at the meeting and include analyses of clinical courses and the utility of biomarkers to predict relapse and/or sustained remission, including ANCA titers, B cell counts, and immunoglobin levels.

Conclusion: The results of RITAZAREM through month 48 will demonstrate whether rituximab leads to sustained remission beyond the treatment period in patients with AAV with a prior history of relapse following induction of remission with rituximab. These data will also inform clinicians and patients about the longer-term safety of azathioprine and rituximab and provide important insight into the pathophysiology of relapse and remission in AAV.

Disclosure: R. Smith, None; **D. Jayne**, Chemocentryx, 1, 2, 5, GlaxoSmithKline, 1, 2, 5, AstraZeneca, 1, 2, 5, Aurinia, 1, 2, 5, Bristol-Myers Squibb Company, 1, 2, 5, Boehringer Ingelheim, 1, 2, 5; **P. Merkel**, AbbVie, 5, AstraZeneca, 2, 5, Biogen, 5, Boeringher-Ingelheim, 2, 5, Bristol-Myers Squibb, 2, 5, Celgene, 2, 5, ChemoCentryx, 2, 5, CSL Behring, 5, Forbius, 2, 5, Genentech/Roche, 2, 5, Genzyme/Sanofi, 2, 5, GlaxoSmithKline, 2, 5, InflaRx, 2, 5, Insmed, 5, Jannsen, 5, Magenta, 5, Pfizer, 5, Sparrow, 5, Talaris, 5, UpToDate, 7.

Abstract Number: L01

Outcomes of COVID-19 Infection in Patients with Rheumatic Diseases in a Multicenter Healthcare System: A Comparative Cohort Study

Naomi Serling-Boyd[1], Kristin D'Silva[1], Tiffany Hsu[2], Xiaoqing Fu[3], Rachel Wallwork[4], April Jorge[1], Yuqing Zhang[1], Ellen Gravallese[5], Hyon K. Choi[6], Jeffrey Sparks[7] and Zachary Wallace[8], [1]Massachusetts General Hospital, Boston, MA, [2]Brigham and Women's Hospital, Jamaica Plain, MA, [3]Mass General Hospital, Boston, MA, [4]Johns Hopkins Hospital, Baltimore, MA, [5]Brigham and Women's Hospital, Harvard Medical School, Boston, MA, [6]MASSACHUSETTS GENERAL HOSPITAL, Lexington, MA, [7]Brigham and Women's Hospital, Boston, MA, [8]Massachusetts General Hospital, Newton, MA

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Late-Breaking Posters

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: The risk of poor outcomes from COVID-19 among rheumatic disease patients compared to the general population remains poorly understood. Filling this knowledge gap is a high priority for patients and providers. We previously observed a higher risk of mechanical ventilation in patients with rheumatic diseases compared to the general population in a small cohort study early in the pandemic.

Table 1. Clinical characteristics of patients with systemic rheumatic disease with COVID-19 infection (N=143) and matched comparators (N=688) at the time of COVID-19 infection diagnosis.

Characteristic	Rheumatic Disease (N=143)	No Rheumatic Disease (N=688)	p-value
Age, years (mean ± SD)	59.5 ± 16.0	59.0 ± 16.1	0.75
Female (N, %)	108 (76)	520 (76)	1.00
Race (N, %)			0.19
White	68 (48)	342 (50)	
Black/African American	35 (25)	117 (17)	
Asian	5 (4)	26 (4)	
Other	35 (25)	203 (30)	
Hispanic ethnicity (N, %)	11 (8)	81 (12)	0.16
Body mass index, kg/m^2 (mean ± SD)	30.2 ± 6.7	29.5 ± 7.0	0.33
Smoking status (N, %)			0.0003
Never	75 (52)	341 (50)	
Former	47 (33)	146 (21)	
Current	5 (4)	20 (3)	
Unknown	16 (11)	181 (26)	
Comorbidities (N, %)			
Hypertension	77 (54)	241 (35)	<0.0001
Diabetes	30 (21)	123 (18)	0.38
Coronary artery disease	25 (17)	40 (6)	<0.0001
Heart failure	16 (11)	42 (6)	0.03
Asthma	20 (14)	52 (8)	0.01
Chronic obstructive pulmonary disease	11 (8)	29 (4)	0.08
Obstructive sleep apnea	17 (12)	36 (5)	0.003
Interstitial lung disease	10 (7)	7 (1)	<0.0001
Chronic kidney disease	26 (18)	53 (8)	0.0001
Any neoplasm	41 (29)	162 (24)	0.19
Charlson comorbidity index (median, IQR)	2.0 (1.0, 4.0)	0.0 (0.0, 2.0)	<0.0001

COVID-19: coronavirus disease 2019; SD: standard deviation; IQR: interquartile range. Statistically significant findings are in bold.

Table 1. Clinical characteristics of patients with systemic rheumatic disease with COVID-19 infection (N=143) and matched comparators (N=688) at the time of COVID-19 infection diagnosis.

Methods: We conducted a cohort study of COVID-19 patients (confirmed by polymerase chain reaction [PCR]) between January 30 and July 16, 2020, at a multicenter healthcare system including academic and community hospitals and longitudinal clinics. We compared each patient with systemic rheumatic disease to up to 5 matched (by age, sex, and date of COVID-19 PCR) comparators without rheumatic disease. In our primary analysis, we used multivariable Cox proportional hazard regression to estimate hazard ratios (HR) and 95% confidence intervals (CI) for COVID-19 outcomes, comparing patients with and without rheumatic disease and adjusting for potential confounders. Outcomes were evaluated through end of follow-up in the system or August 18, 2020. To further evaluate temporal trends in mechanical ventilation among rheumatic disease patients, we compared risk of this outcome in an early vs. recent cohort (PCR testing before vs. after the midpoint among rheumatic disease patients) using similar methods.

Results: We identified 143 rheumatic disease patients (mean age 60 years, 76% female) and 688 matched comparators (mean age 59 years, 76% female) out of 16,211 patients who had confirmed COVID-19 (**Table 1**). Median Charlson Comorbidity Index (CCI) scores and interquartile range (IQRs) were higher among patients with rheumatic disease (2 [IQR: 1, 4]) vs. comparators (0 [IQR: 0, 2]). The most common rheumatic diseases were rheumatoid arthritis

Table 2. Details of rheumatic disease diagnosis and management at the time of COVID-19 diagnosis (N=143).

Characteristic	N (%)
Rheumatic disease diagnosis	
Rheumatoid arthritis	44 (31)
Systemic lupus erythematosus	27 (19)
Other inflammatory arthritis	10 (7)
Psoriatic arthritis	10 (7)
Polymyalgia rheumatica	8 (6)
ANCA-associated vasculitis	6 (4)
Other vasculitis	6 (4)
Axial spondyloarthritis	5 (4)
Multiple diagnoses*	5 (4)
Inflammatory myositis	4 (3)
Systemic sclerosis	3 (2)
Undifferentiated connective tissue disease	3 (2)
Sarcoidosis	2 (1)
Mixed connective tissue disease	2 (1)
Juvenile idiopathic arthritis	2 (1)
Kikuchi disease	2 (1)
Giant cell arteritis	2 (1)
Antiphospholipid syndrome	1 (1)
Sjögren's syndrome	1 (1)
Rheumatic disease duration (median, IQR, years)	12 (6, 18)
Active disease	90 (63)
Baseline rheumatic disease medications	
Biologic DMARDs†	41 (29)
TNF inhibitor	17 (12)
CD20 inhibitor	11 (8)
CTLA-4 immunoglobulin	4 (3)
IL-17 inhibitor	3 (2)
IL-6 receptor inhibitor	3 (2)
B-cell activating factor inhibitor	2 (1)
IL-12/IL-23 inhibitor	1 (1)
C5 inhibitor	1 (1)
Targeted synthetic DMARDs (JAK inhibitors)	4 (3)
Conventional synthetic DMARDs‡	44 (31)
Methotrexate	18 (13)
Mycophenolate	10 (7)
Leflunomide	9 (7)
Azathioprine	6 (4)
Tacrolimus	2 (1)
Sulfasalazine	1 (1)
Cyclophosphamide	1 (1)
Hydroxychloroquine	30 (21)
Oral glucocorticoid	51 (36)
Prednisone-equivalent daily dose (median, IQR, mg)	5 (5, 10)

ANCA: antineutrophil cytoplasmic antibody; DMARD: disease-modifying anti-rheumatic drug; TNF: tumor necrosis factor; IL: interleukin; CTLA-4: cytotoxic T-lymphocyte-associated protein 4; C5: complement factor 5; JAK: Janus kinase; IQR: interquartile range
*Multiple diagnoses category includes patients with overlap features of multiple primary rheumatic diseases
†One patient was on two biologic DMARDs (rituximab and eculizumab).
‡Three patients were on multiple conventional synthetic DMARDs.

Table 2. Details of rheumatic disease diagnosis and management at the time of COVID-19 diagnosis (N=143).

Table 3. COVID-19 outcomes in patients with systemic rheumatic disease vs. matched comparators.

	Rheumatic Disease (N=143)	No Rheumatic Disease (N=688)
Hospitalization (N, %)	58 (41)	295 (43)
Total follow-up time (Person-days)	5847	21671
Incidence rate/1000 days (95% CI)	9.90 (7.40, 12.50)	13.60 (12.10, 15.20)
Unadjusted HR (95% CI)	0.95 (0.75, 1.21)	1.0 (Ref)
Adjusted HR (95% CI)*	0.87 (0.68, 1.11)	1.0 (Ref)
Intensive care unit admission (N, %)	28 (20)	96 (14)
Total follow-up time (Person-days)	7502	29746
Incidence rate/1000 days (95% CI)	3.70 (2.30, 5.10)	3.20 (2.60, 3.90)
Unadjusted HR (95% CI)	1.38 (0.95, 2.00)	1.0 (Ref)
Adjusted HR (95% CI)	1.27 (0.86, 1.86)	1.0 (Ref)
Mechanical ventilation (N, %)	22 (15)	63 (9)
Total follow-up time (Person-days)	7812	31042
Incidence rate/1000 days (95% CI)	2.80 (1.60, 4.00)	2.00 (1.50, 2.50)
Unadjusted HR (95% CI)	1.75 (1.12, 2.74)	1.0 (Ref)
Adjusted HR (95% CI)	1.51 (0.93, 2.44)	1.0 (Ref)
Death (N, %)	12 (8)	48 (7)
Total Follow-up Time (Person-days)	8790	33428
Incidence rate/1000 days (95% CI)	1.40 (0.60, 2.10)	1.40 (1.00, 1.80)
Unadjusted HR (95% CI)	1.16 (0.63, 2.13)	1.0 (Ref)
Adjusted HR (95% CI)	1.02 (0.53, 1.95)	1.0 (Ref)

HR = hazard ratio; CI = confidence interval.
*Adjusted for race, smoking, and Charlson Comorbidity Index (dichotomized as ≤2 or >2).

Table 3. COVID-19 outcomes in patients with systemic rheumatic disease (N=143) versus matched comparators (N=688).

(44, 31%) and systemic lupus erythematosus (27, 19%) (**Table 2**). Fifty-one (36%) rheumatic disease patients were on glucocorticoids, 30 (21%) were on hydroxychloroquine, 41 (29%) were on at least 1 biologic disease-modifying antirheumatic drug (DMARD), and 44 (31%) were on at least 1 conventional synthetic DMARD. Patients with rheumatic disease had higher unadjusted risk of mechanical ventilation than comparators (unadjusted HR 1.75, 95% CI: 1.12 to 2.74) (**Table 3**). After adjustment for race, smoking, and CCI, there were no significantly higher risks of hospitalization (HR 0.87, 95% CI: 0.68 to 1.11), intensive care unit admission (HR 1.27, 95% CI: 0.86 to 1.86), mechanical ventilation (HR 1.51, 95% CI: 0.93 to 2.44), or death (HR 1.02, 95% CI: 0.53 to 1.95) in rheumatic disease patients vs. comparators. We observed a trend toward improvement in the risk of mechanical ventilation in the recent vs. early rheumatic disease cohorts (10% vs. 19%, adjusted HR 0.44, 95% CI: 0.17 to 1.12).

Conclusion: Patients with rheumatic disease had similar risk of severe COVID-19 outcomes vs. comparators. There was a temporal trend toward improvement in risk of mechanical ventilation for rheumatic disease patients. These findings provide reassurance for rheumatic disease patients but close monitoring of rheumatic disease patients with other comorbidities is warranted.

Disclosure: N. Serling-Boyd, None; **K. D'Silva**, None; **T. Hsu**, None; **X. Fu**, None; **R. Wallwork**, None; **A. Jorge**, None; **Y. Zhang**, None; **E. Gravallese**, Rheumatology Textbook, 7; **H. Choi**, AstraZeneca, 2, Takeda, 5, Selecta, 5, GlaxoSmithKline, 5, Horizon, 5; **J. Sparks**, Amgen, 2, Bristol-Myers Squibb, 2, 5, Gilead, 5, Inova, 5, Janssen, 5, Optum, 5; **Z. Wallace**, Viela Bio, 5, Bristol-Myers Squibb, 2.

Abstract Number: L02

Risk Mitigating Behavior in People with Rheumatic Diseases or Psoriasis During the COVID-19 Pandemic Differ by Immunosuppressant Treatment Type: A Patient survey Study

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Late-Breaking Posters
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Clinician-reported registry data suggest that use of biologics in people with immune-mediated inflammatory diseases (IMIDs) is associated with a lower risk of adverse COVID-19 outcomes compared with no treatment. However, the role of potentially confounding risk-mitigating behaviors is unclear. Given the variation in public health messaging between countries, it is possible that risk mitigating behavior in people with IMIDs will also vary, but this has not been explored to date. We sought to explore risk mitigating behavior using global patient survey data by: (1) determining associations with immunosuppressant treatment type, and (2) characterizing international variation.

Methods: Online surveys were completed by individuals with rheumatic diseases (UK only) and psoriasis (global) between 20th May and 7th September 2020. Data were collected on diagnosis, treatment types, demographics and risk mitigating behaviors. Multiple logistic regression assessed the association between treatment type and the most stringent risk mitigating behavior ('shielding', defined as quarantine/staying home/distancing within the home), adjusting for clinical and demographic characteristics. Incomplete covariates were accounted for using multiple imputation in sensitivity analyses. International variations in shielding were assessed in a mixed effects model, adjusted for clinical and demographic differences between nations and accounting for varying sample sizes. Observed and estimated findings were visualized using a caterpillar plot.

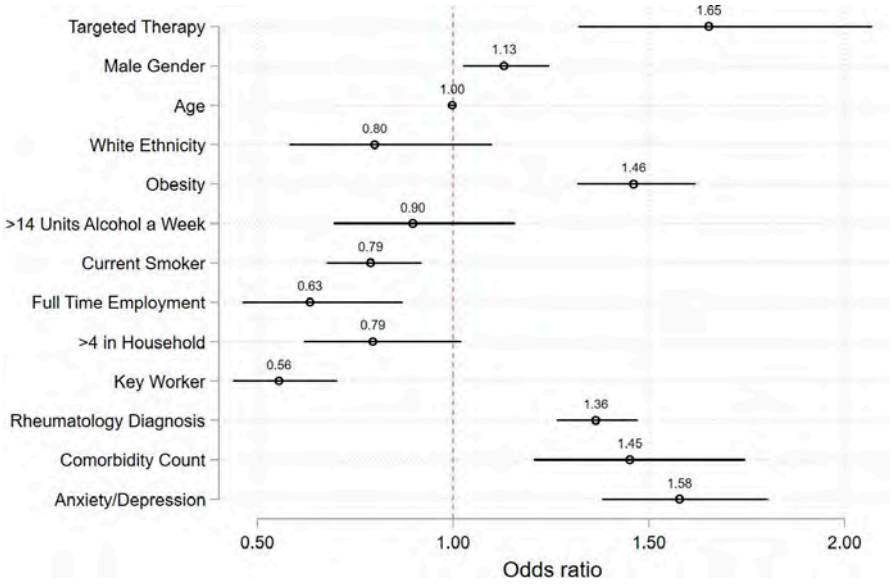

Figure 1. Multiple logistic regression effect estimates for risk mitigating behavior.

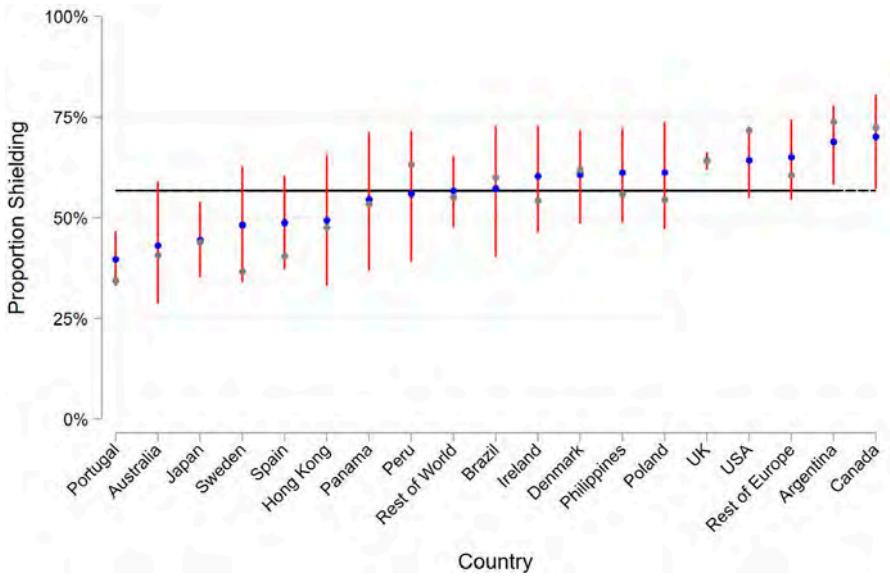

Figure 2. Caterpillar plot of observed and estimated risk mitigating behavior, by nation. The grey markers are the observed national proportions of survey respondents who shielded. The blue markers are the predicted random national effect on shielding from a mixed effects model, with 95% confidence intervals in red. The black horizontal line represents the overall mean.

Results: Of 3,714 participants from 74 countries, 2,259 (60.8%) reported the most stringent risk mitigating behavior (i.e. shielding). Use of biologics was associated with higher shielding rates compared to no systemic therapy (odds ratio [OR] 1.65, 95% CI 1.32-2.07) and standard systemic therapy (OR 1.37, 95% CI 1.23-1.52). No differences in shielding was found between standard systemic therapies and no therapy. Shielding was also associated with established risk factors for severe COVID-19 (male sex [OR 1.13, 95% CI 1.02-1.25], obesity [OR 1.46, 95% CI 1.32-1.62], comorbidity burden [OR 1.45, 95% CI 1.21-1.75]), rheumatic disease (OR 1.36, 95% CI 1.26 to 1.47) and a positive screen for anxiety or depression (OR 1.58, 95% CI 1.38-1.80). Findings were unchanged following multiple imputation. After accounting for sample size and clinical/demographic differences, modest differences in the mean proportion of patients shielding were observed across different nations.

Conclusion: Higher rates of shielding among people with IMIDs receiving biologics may contribute to the reported lower risk of adverse COVID-19 outcomes. The observed variation in shielding among treatment groups reinforces the need for clear patient communication on risk mitigation strategies. The findings help inform how clinicians discuss COVID-19 risks with vulnerable patients and will inform public health guidelines as the global COVID-19 pandemic continues to unfold.

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Abstract Number: L03

Efficacy and Safety of Deucravacitinib (BMS-986165), an Oral, Selective Tyrosine Kinase 2 Inhibitor, in Patients with Active Psoriatic Arthritis: Results from a Phase 2, Randomized, Double-Blind, Placebo-Controlled Trial

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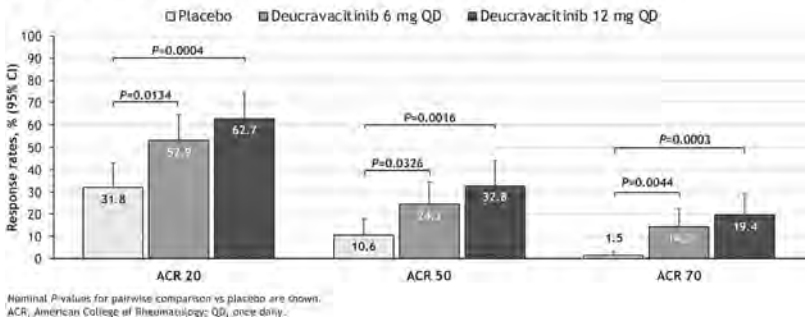
SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Late-Breaking Posters
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: Tyrosine kinase 2 (TYK2) is an intracellular kinase that mediates signaling by key cytokines involved in psoriatic arthritis (PsA) pathophysiology. Deucravacitinib (BMS-986165) is a novel oral agent that selectively inhibits TYK2 through an allosteric mechanism by binding to the regulatory domain of TYK2 in contrast to inhibitors of the closely related Janus kinases (JAK1–3) that bind to the active site in the kinase domain.[1] In a previous Phase 2 trial in plaque psoriasis (PsO), 67%–75% of patients who received deucravacitinib ≥3 mg twice daily achieved PASI 75 at 12 weeks versus 7% for placebo (PBO; $P< 0.001$).[2] No deucravacitinib-related serious adverse events (AEs) were observed.[2] The current trial evaluated the efficacy and safety of deucravacitinib in PsA.

Methods: This is an ongoing, 1-year, randomized, double-blind, PBO-controlled (initial 16 weeks), multicenter, Phase 2 trial (NCT03881059). Eligible patients had a PsA diagnosis for ≥6 months, met CASPAR criteria, and had active disease (≥3 tender and ≥3 swollen joints), C-reactive protein ≥3 mg/L (ULN, 5 mg/L), and ≥1 psoriatic lesion (≥2 cm). Patients had failed or were intolerant (IR) to ≥1 nonsteroidal anti-inflammatory drug, corticosteroid, and/or conventional synthetic disease-modifying antirheumatic drug (csDMARD), or 1 TNF inhibitor (TNFi; ≤30%). Patients were randomized 1:1:1 to deucravacitinib 6 mg once daily (QD) or 12 mg QD, or PBO. The primary endpoint was ACR

Figure 1. ACR 20/50/70 responses at Week 16

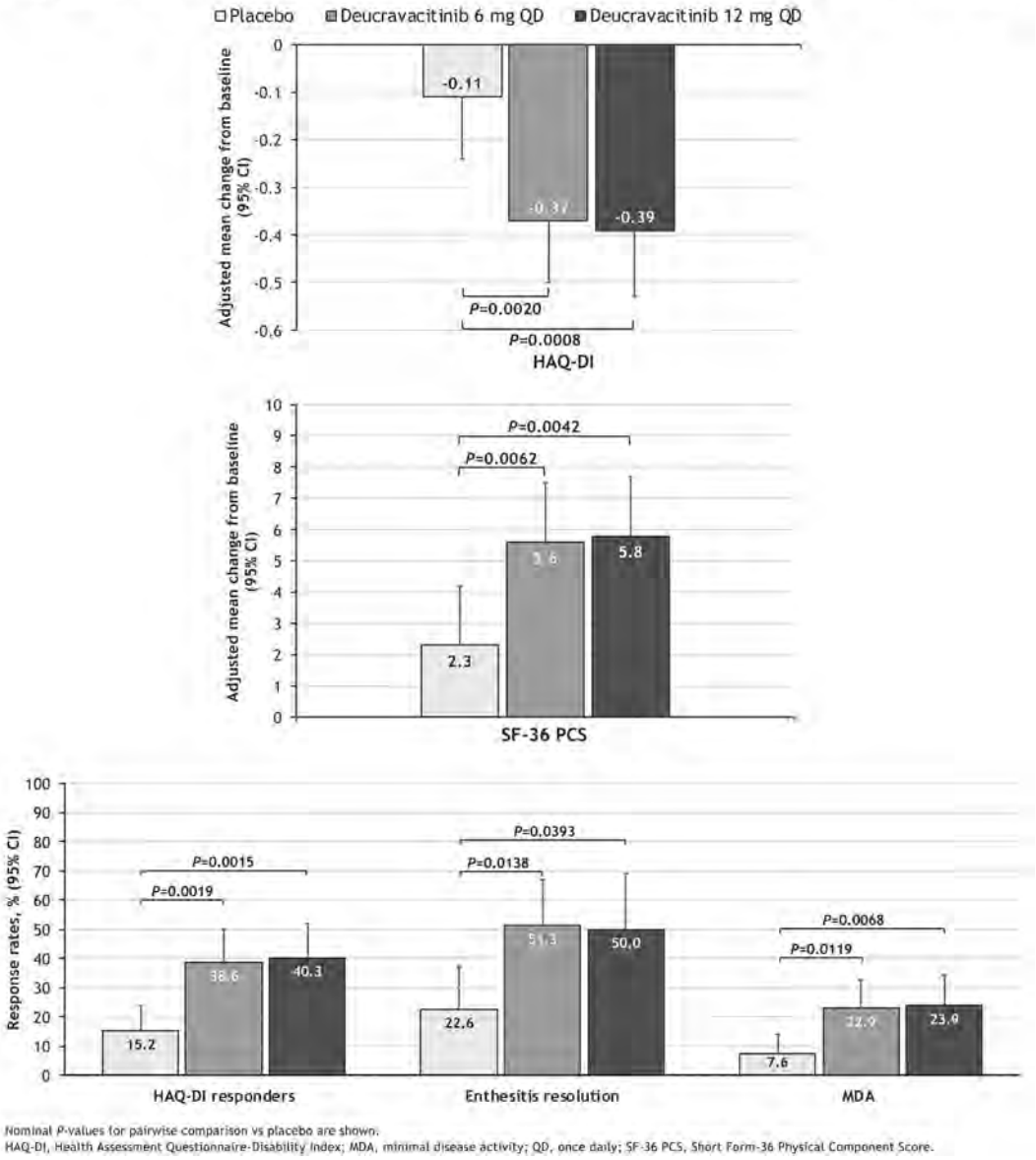


Nominal P-values for pairwise comparison vs placebo are shown.
ACR, American College of Rheumatology; QD, once daily.

20 response at Week 16. Key secondary endpoints included improvement from baseline in the Health Assessment Questionnaire–Disability Index (HAQ-DI) and Short Form-36 Physical Component Score (SF-36 PCS). Additional endpoints included the proportion of patients achieving ACR 50/70, HAQ-DI response (≥0.35 improvement from baseline), minimal disease activity, enthesitis resolution (Leeds Index), and AEs.

Results: Of 203 patients randomized, 180 (89%) completed 16 weeks of treatment. Demographic and baseline disease characteristics were similar across the 3 groups. Mean age was 49.8 years, median PsA duration was 4.5 years, 66% of patients were using csDMARDs at baseline, and 15% were TNFi-IR. The study met its primary objective of showing a dose-response relationship ($P< 0.001$), with both deucravacitinib 6 mg (n=70) and 12 mg QD (n=67) demonstrating significantly greater ACR 20 responses versus PBO (n=66) at Week 16 (52.9% and 62.7% versus 31.8%, respectively; **Figure 1**). Key secondary objectives were achieved with significant and generally similar improvements in secondary endpoints for both deucravacitinib doses versus PBO (**Figure 2**). Nasopharyngitis, sinusitis, headache, and rash were the most common AEs in deucravacitinib-treated patients (**Table**). Most AEs were mild or

Figure 2. Summary of other efficacy endpoints at Week 16



Nominal P-values for pairwise comparison vs placebo are shown.
HAQ-DI, Health Assessment Questionnaire-Disability Index; MDA, minimal disease activity; QD, once daily; SF-36 PCS, Short Form-36 Physical Component Score.

Table. Adverse events occurring in ≥5% of patients

Adverse event, n (%)	Placebo (N=66)	Deucravacitinib 6 mg QD (N=70)	Deucravacitinib 12 mg QD (N=67)
Total	28 (42.4)	46 (65.7)	44 (65.7)
Nasopharyngitis	5 (7.6)	4 (5.7)	12 (17.9)
Sinusitis	0	0	5 (7.5)
Headache	3 (4.5)	5 (7.1)	1 (1.5)
Rash	0	3 (4.3)	4 (6.0)
Upper respiratory tract infection	0	4 (5.7)	1 (1.5)
Bronchitis	1 (1.5)	4 (5.7)	0
Diarrhea	0	4 (5.7)	0

QD, once daily.

moderate. No serious AEs were reported in deucravacitinib-treated patients, including no serious infections, herpes zoster, opportunistic infections, or thrombotic events.

Conclusion: Deucravacitinib was efficacious versus PBO over 16 weeks of treatment in patients with active PsA. Treatment was well tolerated and the safety profile was consistent with that observed in the Phase 2 PsO trial.[2]

References

1. Burke JR et al. *Sci Transl Med.* 2019;11:1-16.
2. Papp K et al. *N Engl J Med.* 2018;379:1313-21.

Disclosure: P. Mease, AbbVie, 2, 5, 8, Amgen, 2, 5, 8, Boehringer Ingelheim, 2, 5, 8, Bristol Myers Squibb, 2, 5, 8, Eli Lilly, 2, 5, 8, Galapagos, 2, 5, 8, Gilead, 2, 5, 8, GlaxoSmithKline, 2, 5, 8, Janssen, 2, 5, 8, Novartis, 2, 5, 8, Pfizer, 2, 5, 8, SUN Pharma, 2, 5, 8, UCB, 2, 5, 8; **A. Deodhar**, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5, AbbVie, 2, 5, Amgen, 5, Boehringer Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Janssen, 5, Galapagos, 5, Gilead, 2, 5; **D. van der Heijde**, AbbVie, 5, Amgen, 5, Astellas, 5, AstraZeneca, 5, Bayer, 5, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, Celgene, 5, Cyxone, 5, Daiichi, 5, Eli Lilly, 5, Galapagos, 5, Gilead, 5, GlaxoSmithKline, 5, Janssen, 5, Merck, 5, Novartis, 5, Pfizer Inc, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, UCB, 5, Imaging Rheumatology BV, 3; **F. Behrens**, Pfizer, 2, 5, 8, Janssen, 2, 5, 8, Chugai, 2, 5, 8, Celgene, 2, 5, 8, Roche, 2, 5, 8, AbbVie, 5, 8, Sanofi, 5, 8, Lilly, 5, 8, Novartis, 5, 8, Genzyme, 5, 8, Boehringer, 5, 8, Bristol Myers Squibb, 5, 8, MSD, 5, 8, UCB Pharma, 5, 8; **A. Kivitz**, Pfizer, 1, 5, 8, Sanofi, 1, 5, 8, GlaxoSmithKline, 1, Gilead Sciences, Inc, 1, 5, Novartis, 1, 8, AbbVie, 5, 8, Boehringer Ingelheim, 5, Flexion, 5, 8, Janssen, 5, Regeneron, 5, SUN Pharma Advanced Research, 5, Celgene, 8, Merck, 8, Lilly, 8, Genzyme, 8; **J. Kim**, Bristol Myers Squibb, 1; **S. Singhal**, Bristol Myers Squibb, 1; **M. Nowak**, Bristol Myers Squibb, 1; **S. Banerjee**, Bristol Myers Squibb, 1.

Abstract Number: L04

Influenza Adverse Events in Patients with Rheumatoid Arthritis in the Tofacitinib Clinical Program

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Late-Breaking Posters

Session Type: Poster Session D

Session Time: 9:00AM–11:00AM

Background/Purpose: Patients (pts) with RA have increased susceptibility to seasonal influenza and its complications.[1] The COVID-19 pandemic highlights the need to understand acute respiratory RNA viral infections in pts receiving tofacitinib. We present data on influenza adverse events (AEs) in the tofacitinib RA clinical program.

Methods: Influenza AEs were evaluated in pts with RA from 21 Phase (P)1–3b/4 trials and two open-label, long-term extension (LTE) studies from 2005–2019. These were analyzed as two cohorts: P2–3b/4 cohort (pts who received tofacitinib 5 or 10 mg twice daily [BID] as monotherapy or with background conventional synthetic [cs]DMARDs, adalimumab [ADA], MTX, or placebo in P2–3b/4 controlled studies) and Overall cohort (pts who received ≥ 1 dose of tofacitinib, as monotherapy or with background csDMARDs, in P1–3b/4 and LTE studies; data were summarized by average tofacitinib dose [average tofacitinib 5 or 10 mg BID based on average total daily dose of < 15 or ≥ 15 mg, respectively]). Incidence rates (IRs; unique pts with events/100 pt-years of exposure; censored at day of first worst event or up to last dose +28 days) were evaluated for influenza AEs (a composite of several MedDRA preferred terms). In the Overall cohort, the time to resolution of influenza AEs by action taken was summarized descriptively.

Results: In total, 7,964 pts were included; 496 (6.2%) reported influenza AEs, three of which occurred outside the risk period. In the P2–3b/4 cohort (N=6,690), IRs for influenza AEs generally appeared similar across treatment arms (Table 1). In the Overall cohort, IRs for influenza AEs were also similar across average tofacitinib doses and pt age groups (Table 2). Mild, moderate, and severe influenza AEs were reported in 311 (62.7%), 170 (34.3%), and 15 (3.0%) pts, respectively. Nine (1.8%) pts had serious influenza AEs (average tofacitinib 5 mg BID, n=6; average tofacitinib 10 mg BID, n=3); eight (1.6%) of these were hospitalized (average tofacitinib 5 mg BID, n=6; average tofacitinib 10 mg BID, n=2), and two (0.4%) died (at time of death, one pt each was receiving tofacitinib 5 and 10 mg BID; both had H1N1 and risk factors for mortality due to influenza). In the majority of pts with influenza AEs, no change to tofacitinib treatment was made (69.6%, n=345) or tofacitinib was stopped temporarily (28.8%, n=143) for a mean duration of

Table 1. Summary of influenza AEs in pts with RA in the P2–3b/4 cohort

	Tofacitinib 5 mg BID (N=2,664) [PY=2,476.66][a]	Tofacitinib 10 mg BID (N=2,024) [PY=1,952.13][a]	ADA (N=643) [PY=518.62][a]	MTX (N=223) [PY=293.39][a]	Placebo (N=1,136) [PY=295.47][a]
Influenza AEs (overall)[b]					
n (%)	53 (2.0)	66 (3.3)	11 (1.7)	5 (2.2)	10 (0.9)
IR [95% CI]	2.07 [1.55, 2.71]	3.37 [2.61, 4.29]	2.00 [1.00, 3.58]	1.68 [0.55, 3.93]	3.23 [1.55, 5.94]
Influenza (PT)					
n (%)	47 (1.8)	59 (2.9)	10 (1.6)	3 (1.3)	9 (0.8)
IR [95% CI]	1.84 [1.35, 2.44]	3.01 [2.29, 3.88]	1.82 [0.87, 3.34]	1.01 [0.21, 2.94]	2.90 [1.33, 5.51]
Influenza-like illness (PT)					
n (%)	3 (0.1)	5 (0.2)	1 (0.2)	2 (0.9)	1 (0.1)
IR [95% CI]	0.12 [0.02, 0.34]	0.25 [0.08, 0.58]	0.18 [0.00, 1.01]	0.67 [0.08, 2.40]	0.32 [0.01, 1.79]
H1N1 (PT)					
n (%)	3 (0.1)	2 (0.1)	0 (0)	0 (0)	0 (0)
IR [95% CI]	0.12 [0.02, 0.34]	0.10 [0.01, 0.36]	0.00 [0.00, 0.67]	0.00 [0.00, 1.22]	0.00 [0.00, 1.19]
Avian, encephalitis, H2N2, H3N2, and pneumonia influenza (PTs)					
n (%)	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)
IR [95% CI]	0.00 [0.00, 0.14]	0.00 [0.00, 0.18]	0.00 [0.00, 0.67]	0.00 [0.00, 1.22]	0.00 [0.00, 0.19]

IRs were calculated as the number of unique pts (per 100 PY) with events during the time between the first and last dose plus 28 days, divided by the pt time accrued during the first and last dose plus 28 days, or up to the first event, whichever occurred earlier. If there were multiple events per pt, the worst event was selected according to the level of seriousness (yes/no) and the level of severity (in the order of 'severe', 'moderate', or 'mild'). 95% CI is based on the Exact Poisson method adjusted for exposure time.
The P2–3b/4 cohort included data from 9 P2, 6 P3, and 1 P3b/4 completed studies, which span influenza seasons 2004/2005–2015/2016.
[a]Total PY of study drug exposure for all pts in treatment group
[b]Includes all PTs (MedDRA v22.0) under the high-level term 'influenza viral infections', and includes PT 'influenza-like illness' during the Winter seasons, per geographic area
ADA, adalimumab; AE, adverse event; BID, twice daily; CI, confidence interval; IR, incidence rate (unique pts with events/100 PY of exposure); N, number of pts in the treatment group; n, number of unique pts with a particular AE PT; MedDRA, Medical Dictionary for Regulatory Activities; MTX, methotrexate; P, Phase; PT, preferred term; pt, patient; PY, pt-yrs; RA, rheumatoid arthritis; yrs, years

11.1 days; the mean number of days to resolution of influenza AEs was numerically similar irrespective of these actions (Table 3).

Conclusion: This post hoc analysis of influenza AEs across the RA clinical program, over 14–15 seasons, showed generally similar rates between tofacitinib, ADA, MTX, and placebo, and between tofacitinib doses and pt age groups. Limitations include varying exposure across treatment arms in the P2–3b/4 cohort. The majority of pts reported mild to moderate influenza AEs.

1. Blumentals WA et al. BMC Musculoskelet Disord 2012; 13: 158.

Acknowledgments: Study sponsored by Pfizer Inc. Medical writing support was provided by Kirsten Woollcott, CMC Connect, and funded by Pfizer Inc.

Table 2. Summary of influenza AEs in pts with RA in the Overall cohort shown for a) all tofacitinib-treated pts and b) all tofacitinib-treated pts, stratified by age group (<65 years and ≥65 years)

	Average tofacitinib 5 mg BID (N=3,969) [PY=8,759.64][b]	Average tofacitinib 10 mg BID (N=3,995) [PY=14,737.08][b]	All tofacitinib[a] (N=7,964) [PY=23,496.73][b]
a) All tofacitinib-treated pts			
Influenza AEs (overall)[c]			
n (%)	197 (5.0)	296 (7.4)	493 (6.2)
IR [95% CI]	2.30 [1.99, 2.64]	2.07 [1.84, 2.32]	2.16 [1.97, 2.36]
Influenza (PT)			
n (%)	186 (4.7)	270 (6.8)	456 (5.7)
IR [95% CI]	2.16 [1.86, 2.50]	1.88 [1.66, 2.12]	1.99 [1.81, 2.18]
Influenza-like illness (PT)			
n (%)	9 (0.2)	20 (0.5)	29 (0.4)
IR [95% CI]	0.10 [0.05, 0.19]	0.13 [0.08, 0.21]	0.12 [0.08, 0.17]
H1N1 (PT)			
n (%)	2 (0.1)	6 (0.2)	8 (0.1)
IR [95% CI]	0.02 [0.00, 0.08]	0.04 [0.01, 0.09]	0.03 [0.01, 0.07]
Avian, encephalitis, H2N2, H3N2, and pneumonia influenza (PTs)			
n (%)	0 (0)	0 (0)	0 (0)
IR [95% CI]	0.00 [0.00, 0.04]	0.00 [0.00, 0.02]	0.00 [0.00, 0.02]
b) All tofacitinib-treated pts, stratified by age group			
Influenza AEs (overall)[c] in pts <65 yrs			
n/N (%)[d]	169/3,247 (5.2)	257/3,447 (7.5)	426/6,694 (6.4)
IR [95% CI]	2.33 [1.99, 2.71]	2.04 [1.80, 2.30]	2.14 [1.94, 2.36]
Influenza AEs (overall)[c] in pts ≥65 yrs			
n/N (%)	28/722 (3.9)	39/548 (7.1)	67/1,270 (5.3)
IR [95% CI]	2.14 [1.42, 3.09]	2.36 [1.68, 3.23]	2.26 [1.75, 2.87]

IRs were calculated as the number of unique pts (per 100 PY) with events during the time between the first and last dose plus 28 days, divided by the pt time accrued during the first and last dose plus 28 days, or up to the first event, whichever occurred earlier. If there were multiple events per pt, the worst event was selected according to the level of seriousness (yes/no) and the level of severity (in the order of 'severe', 'moderate', or 'mild'). 95% CI is based on the Exact Poisson method adjusted for exposure time
Pts were categorized based on the average tofacitinib dose (average tofacitinib 5 or 10 mg BID, based on average total daily dose <15 or ≥15 mg, respectively)
The Overall cohort included data from 2 P1, 10 P2, 7 P3, 2 P3b/4 index, and 2 LTE completed studies, which span influenza seasons 2004/2005–2018/2019
[a]Pts who received ≥1 dose of tofacitinib, as monotherapy or with background conventional synthetic disease-modifying antirheumatic drugs
[b]Total PY of tofacitinib exposure for all pts in treatment group
[c]Includes all PTs (MedDRA v22.0) under the high-level term 'influenza viral infections', and includes PT 'influenza-like illness' during the Winter seasons, per geographic area
AE, adverse event; BID, twice daily; CI, confidence interval; IR, incidence rate (unique pts with events/100 PY of exposure); LTE, long-term extension; N, number of pts in the treatment group; n, number of unique pts with a particular AE PT; MedDRA, Medical Dictionary for Regulatory Activities; P, Phase; PT, preferred term; pt, patient; PY, pt-yrs; RA, rheumatoid arthritis; yrs, years

Table 3. Summary of the number of days to resolution of influenza AEs by action taken with tofacitinib in pts with influenza AEs in the Overall cohort

	Average tofacitinib 5 mg BID		Average tofacitinib 10 mg BID		All tofacitinib[a]	
Action taken[b]	N	No. days, mean (SD)	N	No. days, mean (SD)	N	No. days, mean (SD)
No change to tofacitinib treatment	133	11.23 (16.47)	212[c]	10.45 (8.95)	345[c]	10.75 (12.38)
Tofacitinib treatment reduced	2	5.50 (2.12)	3	12.33 (4.62)	5	9.60 (5.08)
Tofacitinib stopped temporarily	62[c]	10.34 (6.29)	81	11.83 (9.93)	143[c]	11.18 (8.55)
Tofacitinib stopped permanently	1	26.00 (0.00)	1	15.00 (0.00)	2	20.50 (7.78)

The Overall cohort included data from 2 P1, 10 P2, 7 P3, 2 P3b/4 index, and 2 LTE completed studies, which span influenza seasons 2004/2005–2018/2019
Influenza AE includes all PTs (MedDRA v22.0) under the high-level term 'influenza viral infections', and includes PT 'influenza-like illness' during the Winter season, per geographic area
[a]Pts who received ≥1 dose of tofacitinib, as monotherapy or with background conventional synthetic disease-modifying antirheumatic drugs
[b]If there are multiple events per pts, worst event is selected according to the level of action taken: stopped permanently, stopped temporarily, reduced, no action taken. In case of multiple events with the same level of action taken, first occurred event is selected. Pts were categorized based on the average tofacitinib dose (tofacitinib 5 or 10 mg BID, based on average total daily dose <15 or ≥15 mg, respectively)
[c]Includes 1 fatality due to H1N1 influenza
AE, adverse event; BID, twice daily; LTE, long-term extension; N, number of pts with non-missing data; MedDRA, Medical Dictionary for Regulatory Activities; P, Phase; PT, preferred term; pt, patient; SD, standard deviation

Disclosure: K. Winthrop, AbbVie, 2, Bristol-Myers Squibb, 2, Eli Lilly, 2, Galapagos, 2, Gilead, 2, Pfizer Inc, 2, Roche, 2, UCB, 2; **A. Yndestad**, Pfizer Inc, 1, 3; **D. Henrohn**, Pfizer Inc, 1, 3; **H. Jo**, Syneos Health, 3; **S. Marsal**, IMIDomics, 1, AbbVie, 2, 5, Bristol-Myers Squibb, 2, Pfizer Inc, 2, 5, Roche, 2, UCB Pharma, 2, Sandoz, 2, 5, Novartis, 2, Jansen-Cilag, 2, Celgene, 2, 5, Sanofi, 2, 5, MSD, 2, Gilead, 5, Galapagos, 5; **M. Galindo**, AbbVie, 2, Eli Lilly, 2, GlaxoSmithKline, 2, Janssen-Cilag, 2; **A. Diehl**, Pfizer Inc, 1, 3; **A. Shapiro**, Pfizer Inc, 1, 3; **S. Cohen**, AbbVie, 2, 5, Eli Lilly, 2, 5, Genentech, 2, 5, Gilead, 2, 5, Pfizer Inc, 2, 5.

Abstract Number: L05

DMARD Changes for Patients with Rheumatoid Arthritis in the US During the First Three Months of the COVID-19 Pandemic

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Late-Breaking Posters
Session Type: Poster Session D
Session Time: 9:00AM–11:00AM

Background/Purpose: To understand medication and clinical care changes by patients with RA during the first 3 months (March through May 2020) of the COVID-19 pandemic in the US.

Methods: Data were provided by adults with RA participating in the FORWARD observational registry who answered COVID-19 web-based surveys in May/June 2020 and who previously provided baseline characteristics and medication use for 2019. We compared medication changes by pre-COVID DMARD exposure in logistic models first without adjustment and then adjusting for age, sex, comorbidities including pulmonary and cardiovascular diseases, educa-

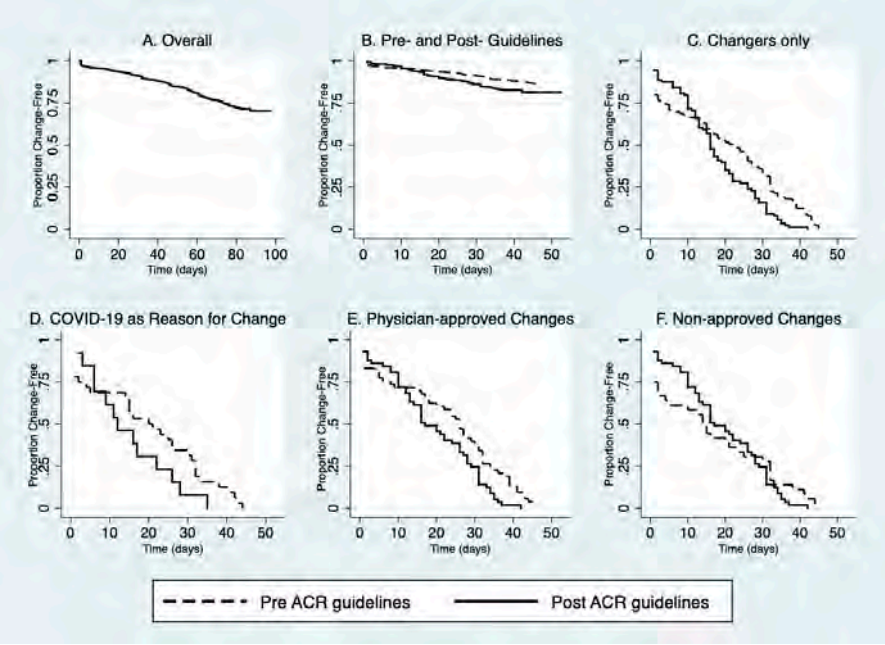
tion, health insurance, RA activity (PAS-II), fatigue, and polysymptomatic distress (PSD). We also examined rates of medication change before and after the first COVID-19 ACR treatment guidelines in April.

Results: Of the 734 respondents, 221 (30%) reported medication changes. Changers were more likely to use glucocorticoids (GCs, 33% vs 18%) and less likely to use non-hydroxychloroquine (HCQ) csDMARDs (49% vs 62%) pre-COVID. While JAKi use was associated (OR 1.9 [95% CI 1.0, 3.4]) with change in bivariate analyses, only GCs remained as a strong factor (OR 3.0 [1.9, 4.9]) in multivariable models. Change in care was most associated with pulmonary disease (OR 2.9 [1.3, 6.5]) and GC use (OR 1.6 [1.0, 2.5]). While the incidence of medication change before and after April 15 was the same, patient-initiated changes due to COVID-19 were twice as likely before April 15, and physician-guided changes were more likely after.

Conclusion: Our findings confirm US patients with RA made substantial changes to their medication use during the first 3 months of the COVID-19 pandemic. Almost half of DMARD decrease or discontinuations were made without physician guidance, and all types of medication changes after ACR recommendations were made with increased physician guidance. While no direct causation was measured, our findings provide evidence of possible implementation of these recommendations.

Mean (SD) baseline characteristics of RA patients who changed their medications vs. those who did not.

n (%) =	Non- Changer 513 (70)	Changer 221 (30)	p
Demographics			
Age, yrs	65.9 (10.4)	61.9 (11.7)	<0.001
Male, %	15.8	10.5	0.06
White, %	93.7	92.7	0.63
Education, yrs	15.3 (2.0)	15.3 (2.2)	0.91
Economic hardship from COVID-19, %	14.6	22.6	0.01
Comorbid conditions			
RD Comorbidity Index	2.3 (1.9)	2.4 (1.7)	0.77
Heart disease, %	7.2	8.8	0.47
Pulmonary disease, %	7.0	8.8	0.41
Diabetes, %	6.6	5.4	0.54
Pre-COVID Medications			
HCQ, %	20.7	21.3	0.85
Other csDMARD, %	62.0	49.2	<0.001
TNFi bDMARD, %	35.3	34.4	0.82
non-TNFi bDMARD, %	26.7	28.1	0.71
JAKi, %	8.4	12.2	0.11
GCs, %	18.1	32.6	<0.001
NSAID, %	38.6	35.8	0.47
Number of DMARDs	3.9 (2.1)	4.3 (2.0)	0.03
Other med changes non-RA, %	9.8	14.9	0.04
Pre-COVID Patient-reported outcomes			
Disease activity, self-reported			
Low	51.1	35.8	
Moderate	42.8	47.5	<0.001
Severe	6.1	16.7	
Pain	3.1 (2.5)	3.4 (2.5)	0.09
Global Assessment	2.9 (2.3)	3.5 (2.4)	0.003
Fatigue	3.3 (2.8)	4.2 (2.9)	<0.001
HAQ-II	0.7 (0.6)	0.9 (0.6)	0.02
PAS-II	2.7 (1.9)	3.1 (2.0)	0.02
Polysymptomatic distress	7.2 (5.5)	8.7 (6.1)	0.01



Kaplan-Meier time to medication change by reason for change and physician approval status before and after April 15, 2020, ACR guidelines

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Disclosure: K. Michaud, None; **S. Pedro**, None; **K. Wipfler**, None; **E. Agarwal**, Pfizer, 3; **P. Katz**, None.

Abstract Number: L06

Mavrilimumab (anti GM-CSF Receptor α Monoclonal Antibody) Reduces Time to Flare and Increases Sustained Remission in a Phase 2 Trial of Patients with Giant Cell Arteritis

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: T helper (Th)1 and Th17 lymphocytes play a role in the pathogenesis of giant cell arteritis (GCA). Current treatments (e.g., corticosteroids and tocilizumab) target primarily the Th17 axis, leaving substantial residual Th1 activity. Preclinical research in human GCA models implicate granulocyte macrophage colony stimulating factor (GM-CSF), an upstream mediator of both Th1 and Th17 cells, as a pathogenic factor for GCA. We evaluated the efficacy and safety of mavrilimumab (anti GM-CSF receptor α monoclonal antibody) for maintaining disease remission in patients with GCA.

Methods: Patients with active new onset (N/O) or relapsing refractory (R/R) GCA were enrolled in a randomized, double-blind, placebo-controlled phase 2 trial. GCA was confirmed by temporal artery biopsy or vascular imaging. Active disease was defined as presence of GCA symptoms and erythrocyte sedimentation rate (ESR) (≥30 mm/hr) and/or

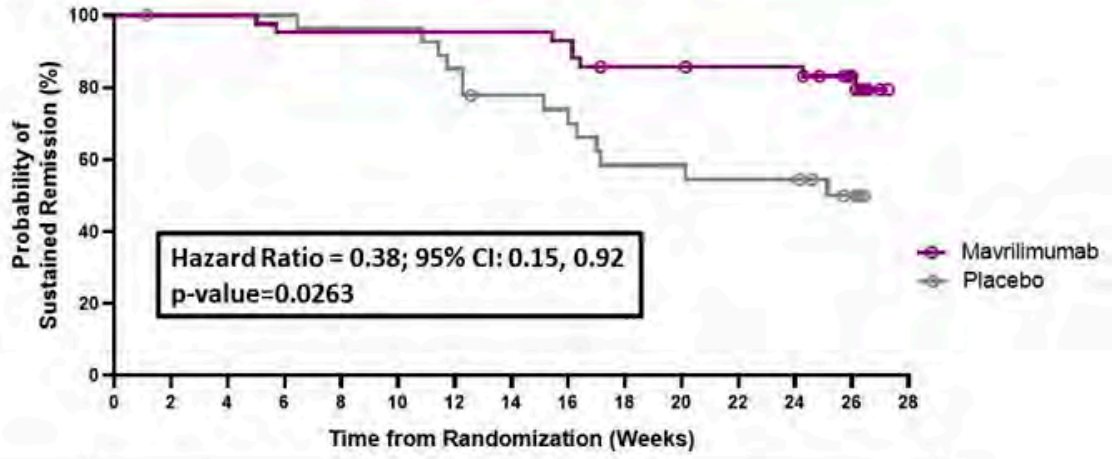
C-reactive protein (CRP) (≥1 mg/dL) elevation within 6 weeks from randomization. Corticosteroid-induced remission (resolution of GCA symptoms and CRP < 1 mg/dL or ESR < 20 mm/hr) was required by baseline. Patients were randomized 3:2 to receive mavrilimumab 150 mg or placebo subcutaneously every two weeks in addition to a protocol-defined 26-week prednisone taper starting at 20-60 mg/day. Stratification by disease type (N/O vs. R/R) was applied.

The primary efficacy endpoint was time to first flare by Week 26 in all treated patients (modified intention-to-treat population). Flare, confirmed by an independent adjudication committee, was defined as ESR ≥30 mm/hr and/or CRP ≥1 mg/dL and re-appearance of GCA symptoms or new/worsening vasculitis determined by imaging. Sustained remission through Week 26 was a key secondary endpoint. Safety up to Week 30 was assessed.

Results: 70 patients (35 N/O, 35 R/R) were randomized to mavrilimumab (N=42) or placebo (N=28). Mean (SD) age was 69.7 (7.48) years and 71.4% were female. Disease flare by Week 26 occurred in 8 (19%) and 13 (46.4%) patients receiving mavrilimumab and placebo, respectively (27.4% reduction). Median time to flare by Week 26 could not be estimated in the mavrilimumab group due to too few events (Not Estimable [NE]) and was 25.1 weeks [95% CI: (16.0, NE)] in the placebo group (HR [95% CI] 0.38 [0.15, 0.92]; p=0.0263) (Figure). Sustained remission at Week 26 occurred in 83.2% of the patients receiving mavrilimumab and in 49.9% of those receiving placebo (33.4% increase; p=0.0038). Results were consistent across disease type subgroups (HR for flare: N/O patients 0.29 [95% CI: 0.06, 1.31; nominal p= 0.0873]; R/R patients 0.43 [95% CI: 0.14, 1.30]; nominal p=0.1231) (Table 1). Adverse events (AEs), mostly mild to moderate in severity, were comparable between groups. There were 5 serious AEs (mavrilimumab 2 [4.8%], placebo 3 [10.7%]), none drug-related (Table 2). No deaths or vision loss occurred.

Conclusion: Mavrilimumab was superior to placebo on the primary and secondary efficacy endpoints of time to flare and sustained remission at Week 26 in patients with GCA. Mavrilimumab was well tolerated, and no new safety signals were observed. Results with this novel treatment are encouraging for the management of GCA.

Figure. Time to Flare by Week 26 after randomization in All Patients.



	Patients at Risk, n														
Week	0	2	4	6	8	10	12	14	16	18	20	22	24	26	28
Mavrilimumab	42	42	42	40	40	40	40	40	39	35	35	34	34	28	0
Placebo	28	27	27	27	26	26	23	20	19	15	15	14	14	10	0

Table 2. Treatment-Emergent Adverse Events over 30 Weeks.

Category	Mavrilimumab 150mg (N=42) n (%)	Placebo (N=28) n (%)
Treatment Emergent Adverse Events	33 (78.6)	25 (89.3)
By Maximum Severity [1]		
Mild	18 (42.9)	13 (46.4)
Moderate	14 (33.3)	11 (39.3)
Severe	1 (2.4)	1 (3.6)
Related to Mavrilimumab or Placebo [2]	10 (23.8)	7 (25.0)
Related to Prednisone [2]	11 (26.2)	11 (39.3)
Serious Treatment Emergent Adverse Events	2 (4.8)	3 (10.7)
Related to Mavrilimumab or Placebo [2]	0	0
Related to Prednisone [2]	0	0
Non-serious Treatment Emergent Adverse Events	33 (78.6)	25 (89.3)
Treatment Emergent Adverse Events Resulting in Death	0	0
Treatment Emergent Adverse Events Leading to Dose Interruption	1 (2.4)	2 (7.1)
Treatment Emergent Adverse Events Leading to Withdrawal of Treatment	1 (2.4)	1 (3.6)
Treatment Emergent Adverse Events of Special Interest	0	1 (3.6)

Subjects with multiple events in the same category are counted only once in the category. Subjects with events in more than one category are counted once in each of those categories.
Treatment emergent AEs (TEAEs) are defined as AEs that begin after the first administration of investigational products or existing AEs that worsen after the first dose of study medication through the 90 days after the last dose date.
[1] Each subject has only been represented with the maximum severity.
[2] Possibly or probably related, as assessed by the investigator.
TEAE of Special Interest include: Hepatic function abnormality, Acute hypersensitivity reaction, Delayed hypersensitivity reaction, Clinically significant pulmonary abnormality, Neutropenia, and Serious infection.

Median time to flare by Week 26 could not be estimated in the mavrilimumab group due to too few events (Not Estimable [NE]) and was 25.1 weeks [95% CI: (16.0, NE)] in the placebo group (HR [95% CI] 0.38 [0.15, 0.92]; p=0.0263).

Median time to flare by Week 26 could not be estimated in the mavrilimumab group due to too few events (Not Estimable [NE]) and was 25.1 weeks [95% CI: (16.0, NE)] in the placebo group (HR [95% CI] 0.38 [0.15, 0.92]; p=0.0263). Sustained remission at Week 26 occurred in 83.2% of the patients receiving mavrilimumab and in 49.9% of those receiving placebo (33.4% increase; p=0.0038).

Adverse events, mostly mild to moderate in severity, were comparable between groups. There were 5 serious AEs (mavrilimumab 2 [4.8%], placebo 3 [10.7%]), none drug-related. No deaths or vision loss occurred.

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Related to Mavrilimumab or Placebo [2]	0	0
Related to Prednisone [2]	0	0
Non-serious Treatment Emergent Adverse Events	33 (78.6)	25 (89.3)
Treatment Emergent Adverse Events Resulting in Death	0	0
Treatment Emergent Adverse Events Leading to Dose Interruption	1 (2.4)	2 (7.1)
Treatment Emergent Adverse Events Leading to Withdrawal of Treatment	1 (2.4)	1 (3.6)
Treatment Emergent Adverse Events of Special Interest	0	1 (3.6)

Subjects with multiple events in the same category are counted only once in the category. Subjects with events in more than one category are counted once in each of those categories.
Treatment emergent AEs (TEAEs) are defined as AEs that begin after the first administration of investigational products or existing AEs that worsen after the first dose of study medication through the 90 days after the last dose date.
[1] Each subject has only been represented with the maximum severity.
[2] Possibly or probably related, as assessed by the investigator.
TEAE of Special Interest include: Hepatic function abnormality, Acute hypersensitivity reaction, Delayed hypersensitivity reaction, Clinically significant pulmonary abnormality, Neutropenia, and Serious infection.

Disclosure: M. Cid, Kiniksa Pharmaceuticals, 5, Janssen, 5, AbbVie, 5; **S. Unizony**, Kiniksa Pharmaceuticals, 5, Sanofi, 5, Janssen, 5, Genentech, 2; **L. Pupim**, Kiniksa Pharmaceuticals, 3; **F. Fang**, Kiniksa Pharmaceuticals, 3; **J. Pirrello**, Kiniksa Pharmaceuticals, 3; **A. Ren**, Kiniksa Pharmaceuticals, 3; **M. Samant**, Kiniksa Pharmaceuticals, 3; **T. Zhou**, Kiniksa Pharmaceuticals, 3; **J. Paolini**, Kiniksa Pharmaceuticals, 3.

Abstract Number: L07

Tocilizumab for COVID-19 Infection: A Randomized, Double-Blind, Placebo-Controlled Trial

John Stone[1], [1]Massachusetts General Hospital, Boston, MA

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 11:30AM–1:00PM

Characteristic	Placebo (n=82)	Tocilizumab (n=161)	All (n=243)
Age, yrs, median (IQR)	56.5 (44.7-67.8)	61.6 (46.4-69.7)	59.8 (45.3-69.4)
Age > 65 yrs, n (%)	22 (27)	60 (37)	82 (34)
Male sex	45 (55)	96 (60)	141 (58)
Race			
American Indian/Alaska Native	0 (0)	1 (1)	1 (<1)
Asian	2 (2)	7 (4)	9 (4)
Black or African American	16 (20)	24 (15)	40 (16)
Native Hawaiian or Pacific Islander	1 (1)	0 (0)	1 (0)
White	33 (40)	71 (44)	104 (43)
Other	15 (18)	35 (22)	50 (21)
Unknown	15 (18)	23 (14)	38 (16)
Hispanic ethnicity			
Hispanic or Latino	39 (48)	70 (43)	109 (45)
Not Hispanic or Latino	35 (43)	84 (52)	119 (49)
Unknown	8 (10)	7 (4)	15 (6)
BMI, kg/m2, median (IQR)	30.2 (25.7-33.8)	29.9 (26.0-34.2)	30.1 (25.9-34.2)
BMI ≥ 30 kg/m2, n (%)	42 (51)	80 (50)	122 (50)
Days from symptom onset to randomization, median (IQR)	10.0 (7.0-13.0)	9.0 (6.0-13.0)	9.0 (6.0-13.0)
Hypertension, n (%)	38 (46)	80 (50)	118 (49)
Heart failure, n (%)	7 (9)	17 (11)	24 (10)
History of myocardial infarction, n (%)	6 (7)	15 (9)	21 (9)
Chronic obstructive pulmonary disorder, n (%)	7 (9)	15 (9)	22 (9)
Asthma, n (%)	7 (9)	15 (9)	22 (9)
Smoking history, n (%)			
Current	0 (0)	7 (4)	7 (3)
Former	26 (32)	46 (29)	72 (30)
Never	48 (59)	99 (61)	147 (60)
Unknown	8 (10)	9 (6)	17 (7)
Diabetes, n (%)	30 (37)	45 (28)	75 (31)
Chronic kidney disease, n (%)	13 (16)	29 (18)	42 (17)
History of malignancy, n (%)	8 (10)	22 (14)	30 (12)
Absolute lymphocyte count, cells/mm3, median (IQR) (n=241)	1.03 (0.68-1.36)	1.04 (0.70-1.40)	1.03 (0.70-1.40)
C-reactive protein, mg/l, median (IQR) (n=241)	94.3 (58.4-142.0)	116.0 (67.1-190.6)	110.0 (64.9-175.3)
Ferritin, ng/ml, median (IQR) (n=242)	686 (382-1228)	723 (413-1212)	708 (411-1225)
D-dimer, ng/ml, median (IQR) (n=241)	980 (500-1739)	857 (536-1695)	884 (527-1730)
Lactate dehydrogenase, U/l (n=240)	324 (290-395)	351 (287-420)	340 (289-413)
Serum IL-6, pg/ml (n=234)	25.4 (14.6-40.3)	23.6 (14.0-49.9)	24.4 (14.1-45.5)
Erythrocyte sedimentation rate, mm/hr (n=219)	63 (42-87)	61 (42-90)	61 (42-88)
Troponin, ng/l (n=234)	9 (6-24)	8 (6-22)	9 (6-22)
NT-proBNP, pg/ml (n=224)	93 (33-431)	110 (50-438)	108 (38-437)
Procalcitonin, ng/ml (n=227)	0.2 (0.1-0.3)	0.2 (0.1-0.4)	0.2 (0.1-0.4)

Table 1. Baseline Demographic and Clinical Features of the Trial Cohort, by Group.

Background/Purpose: The efficacy of interleukin-6 receptor blockade in hospitalized COVID-19 patients not on mechanical ventilation is unclear.

Methods: We performed a randomized, double-blind, placebo-controlled trial in patients with patients confirmed SARS-CoV-2 infection, elevated serum inflammatory markers, and at least two of: 1) pulmonary infiltrate; 2) supplemental oxygen requirement to maintain oxygen saturation >92%; or, 3) fever >38°C. Patients were randomized 2:1 to standard care plus intravenous tocilizumab 8mg/kg or placebo. The primary outcome was time to mechanical ventilation or death during the 28-day study period. The two secondary efficacy outcomes were time to clinical worsening and time to resolution of supplemental oxygen requirement.

Results: Two-hundred forty-three patients were enrolled. One-hundred forty-one (58%) were men, 102 (42%) women. Median age was 58.8 years (range 21.7-85.4 years). Forty-five percent self-identified as Hispanic/Latino. The hazard ratio (HR) for progression to intubation or death in the tocilizumab group was 0.83 (95% confidence interval [CI] 0.38, 1.81; P=0.64). The HR for disease worsening was 1.11 (95% CI 0.59, 2.10; P=0.73) in the tocilizumab group. At 14 days, 18.0% versus 14.9% (tocilizumab versus placebo) had experienced disease worsening. The median time to oxygen discontinuation was 5.0 days (3.8, 7.6 days) in the tocilizumab group and 4.9 days (3.8, 7.8 days) with placebo (P=0.69). At 14 days, 24.6% of tocilizumab-treated patients still required oxygen, compared with 21.2% in the placebo group. Tocilizumab-treated patients had fewer serious infections.

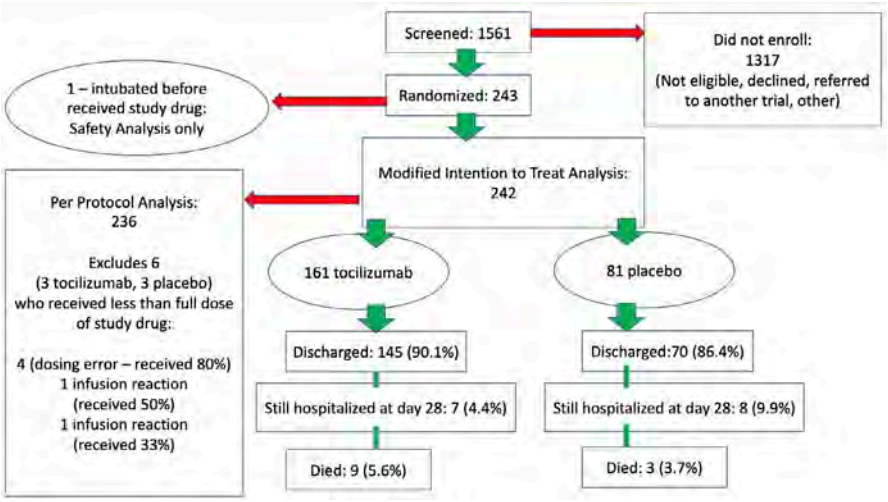

Figure 1. CONSORT Diagram

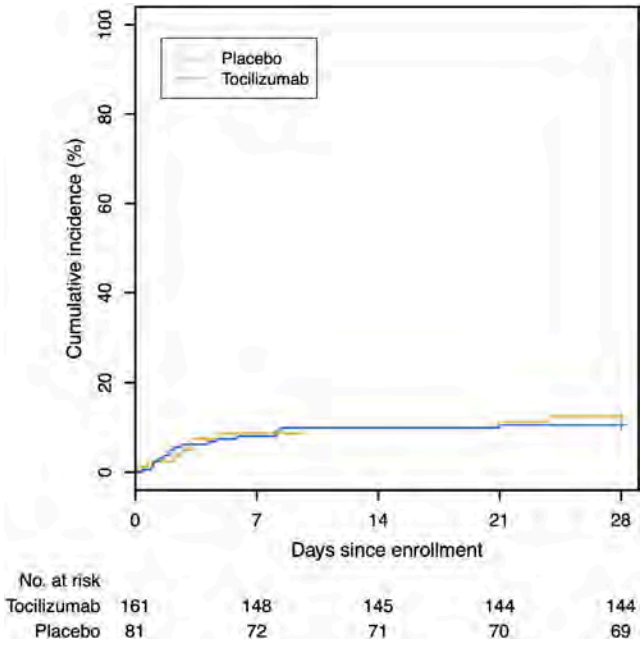

Figure 2. Time to Intubation or Death

Conclusion: Interleukin-6 receptor blockade is not effective for preventing mechanical ventilation or death among moderately ill patients with COVID-19 infection.

Disclosure: J. Stone, Genentech/Roche, 2.

Abstract Number: L08

Long Term Cardiovascular Safety of Febuxostat and Allopurinol in Patients with Chronic Gout: The Febuxostat versus Allopurinol Streamlined Trial (on Behalf of the FAST Investigators)

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SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Febuxostat and allopurinol are uric acid lowering agents. Following concerns about the cardiovascular safety of febuxostat, the European Medicines Agency (EMA) recommended a post-authorization study comparing the cardiovascular (CV) safety of febuxostat versus allopurinol.

Methods: We did a prospective, randomized, open-label, blinded endpoint (PROBE) trial of febuxostat versus allopurinol in patients with chronic symptomatic hyperuricaemia (gout) in the UK, Denmark, and Sweden. Eligible patients were 60 years or older, were currently treated with allopurinol, and had at least one additional cardiovascular risk factor. After increasing allopurinol dose if necessary to achieve serum uric acid (SUA) levels < 0·357 mmol/L (< 6 mg/dL), patients were randomly assigned to continue allopurinol (at optimised dose) or start febuxostat at a dose of 80mg daily, increasing to 120mg, if necessary, to achieve serum uric acid level < 0·357 mmol/L. A short washout period (7-21 days) was included before randomized therapy was started. The primary outcome was the composite of hospitalisation for non-fatal myocardial infarction/biomarker positive acute coronary syndrome, non-fatal stroke or cardiovascular death. The hazard ratio (febuxostat versus allopurinol) in a Cox proportional hazards model was assessed for non-inferiority (limit of 1·3) in an on-treatment (OT) analysis and then by intention to treat (ITT). This study is registered with the EU Clinical Trials Register (EudraCT 2011-001883-23) and ISRCTN (ISRCTN72443728).

Results: 6128 patients (mean age 71, 85·3% male, 33·4% prior established CV disease) were randomised to receive allopurinol (n=3065) or febuxostat (n=3063) and were followed up for a median of 4 years during which 5·5% and 6·2% respectively withdrew from all follow up. In both the on-treatment and intention-to-treat analyses, febuxostat was non-inferior to allopurinol for incidence of the primary endpoint (OT analysis: febuxostat 172 patients [1·72 events per 100 patient years]; allopurinol 241 patients [2·05 events per 100 patient years]; hazard ratio 0·85 [95% CI 0·70-1·03], p< 0·001; ITT analysis: febuxostat 256 patients [2·05 events per 100 patient years], allopurinol 285 patients [2·29 events per 100 patient years]; hazard ratio 0·89 [95% CI 0·75-1·06], p< 0·001). 222 (7·2%) patients died in the febuxostat group compared to 263 deaths (8·6%) in the allopurinol group.

Conclusion: Febuxostat was non-inferior to allopurinol therapy for the primary cardiovascular outcome. Long-term use of febuxostat was not associated with an increased risk of death compared with allopurinol.

Funding: Menarini provided funding. The University of Dundee was the sponsor and Menarini had no involvement in the running of the study.

Disclosure: T. MacDonald, Pfizer, 2, GSK, 2, Amgen, 2, Menarini, 2, 8, Takeda, 8, Astellus, 8, Servier, 8, Shire, 8, AstraZeneca, 8; **I. Mackenzie**, Sanofi, 2, Menarini, 2, AstraZeneca, 5; **G. Nuki**, Research funding from Menarini to the University of Edinburgh for conducting this study, 2; **I. Ford**, Servier, 2, 5, GSK, 2, 5, Adaptimmune, 2, 5, Pharmacosmos, 2.

Abstract Number: L09

A Phase 2a Randomized, Double-blind, Placebo-controlled Study of Ziritaxestat in Early Diffuse Cutaneous Systemic Sclerosis (NOVESA)

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UCLA, Los Angeles, CA, [4]University of Texas Health Science Center at Houston, Houston, TX, [5]Università degli Studi di Firenze, Firenze, Italy, [6]Ghent University Hospital, Ghent, Belgium, [7]Galapagos BV, Leiden, Netherlands, [8]Galapagos NV, Mechelen, Belgium, [9]Ahmed Science Medicine, Basel, Switzerland

SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Late-Breaking Abstracts

Session Type: Late-Breaking Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: There is a high unmet need for systemic sclerosis (SSc) treatments. Ziritaxestat (ziri; GLPG1690) is an autotaxin inhibitor with a novel mechanism of action. NOVESA (NCT03798366) is a phase 2a randomized, double-blind, placebo (PBO)-controlled trial evaluating the efficacy, safety, and tolerability of ziri for diffuse cutaneous (dc) SSc.

	Ziritaxestat 600 mg (n=21)	Placebo (n=12)	Total (N=33)
Age (yrs), mean (SD)	50.4 (13.6)	47.3 (18.0)	49.3 (15.1)
Sex, n (%)			
Female	15 (71.4)	8 (66.7)	23 (69.7)
Male	6 (28.6)	4 (33.3)	10 (30.3)
Duration of disease (yrs)			
Mean (SD)	1.5 (1.0)	2.6 (2.0)	1.9 (1.5)
Range	(0.3–4.2)	(0.4–5.1)	(0.3–5.1)
<2 yrs	16 (76.2)	6 (50.0)	22 (66.7)
≥2 yrs	5 (23.8)	6 (50.0)	11 (33.3)
Baseline total mRSS			
Mean (SD)	27.0 (8.8)	22.5 (6.2)	25.3 (8.2)
Range	(11.0–46.0)	(12.0–29.0)	(11.0–46.0)
Baseline percent predicted FVC (%)			
Mean (SD)	94.0 (14.8)	87.6 (18.4)	92.0 (15.9)
Range	(70.0–125.0)	(57.0–111.0)	(57.0–125.0)
Medical history of interstitial lung disease, n (%)	10 (47.6)	5 (41.7)	15 (45.5)
Baseline HAQ-DI			
Mean (SD)	1.24 (0.70)	0.84 (0.89)	1.10 (0.78)
Range	(0.00–2.38)	(0.00–2.75)	(0.00–2.75)
Receiving background immunosuppressive therapy*, n (%)	20 (95.2)	10 (83.3)	29 (87.9)
MTX	2 (9.5)	2 (16.7)	4 (12.1)
MTX + Pred	4 (19.0)	2 (16.7)	6 (18.2)
MYC	9 (42.9)	2 (16.7)	11 (33.3)
MYC + Pred	4 (19.0)	4 (33.3)	8 (24.2)
Pred	1 (4.8)	0	1 (3.0)

Table 1. Demographics and baseline patient characteristics. *Includes MTC, MYC, and Pred FVC, forced vital capacity; HAQ-DI, Health Assessment Questionnaire Disability Index; mRSS, modified Rodnan skin score; MTX, methotrexate; MYC, mycophenolate; Pred, prednisone; SD, standard deviation; yr, year

Methods: Patients with dcSSc were randomized (2:1) to receive oral ziri 600 mg once daily or matching PBO for 24 weeks. Protocol-defined immunosuppressive background therapies were allowed to continue unchanged if doses were stable for ≥3 months prior to ziri treatment. Eligible patients were adults with a confirmed diagnosis of dcSSc (by ACR/EULAR/Van den Hoogen/LeRoy 2013 criteria) and a modified Rodnan skin score (mRSS) >10 at screening. The primary endpoint was change from baseline mRSS at 24 weeks. Secondary endpoints were incidence of treatment-emergent adverse events (TEAEs), serious AEs and tolerability of ziri. Additional endpoints included changes in forced vital capacity (FVC), Health Assessment Questionnaire Disability Index (HAQ-DI) and Combined Response Index for Systemic Sclerosis (ACR CRISS) score. Analyses used a mixed-effects model for repeated measures. Least square (LS) mean (95% confidence interval [CI]) was calculated for the primary endpoint, descriptive statistics for other endpoints. Covariates included baseline mRSS and country.

Results: Thirty-three patients with active dcSSc were randomized: 21 to ziri; 12 to PBO. The majority of patients were female (69.7%); mean (standard deviation [SD]) age was 49.3 (15.1) yrs (Table 1). In the ziri and PBO groups, respectively, mean (SD) disease duration was 1.5 (1.0) and 2.6 (2.0) yrs; mean (SD) mRSS was 27.0 (8.8) and 22.5 (6.2). 95.2% and 83.3% of patients in the ziri and PBO groups were on background immunosuppressive therapy. A statistically significant difference was observed between groups for mRSS at Wk 24: LS mean difference (95% CI) was –2.8 (–5.6, –0.1) for ziri vs PBO (p=0.0411; Figure 1). Median CRISS score was 0.97 for ziri and 0.83 for PBO at Wk 24 (0.69 in the PBO group excluding a single outlier patient with implausible Wk 24 FVC change [+1381 mL]). ACR CRISS showed likelihood of improvement (score ≥0.60 on a 0.0–1.0 scale) in 64.7% and 62.5% of patients at Wk 24 in ziri and PBO groups, respectively (57.1% of PBO patients at Wk 24 with exclusion of the FVC outlier). No changes in FVC (mL) or HAQ-DI were observed. Ziri was well tolerated; most AEs were mild or moderate; no TEAEs led to study drug discontinuation. Serious TEAEs occurred in 2 patients in the ziri group (pharyngitis and sepsis; device-related infection and sepsis) and 1 patient in the PBO group (foreign body ingestion); these were considered unrelated or unlikely related to study drug. No deaths occurred. Preliminary data show target inhibition reflected by an average reduction in circulating lysophosphatidic acid of ~80%.

Conclusion: In the small NOVESA study, ziri significantly improved mRSS vs PBO at Wk 24 and was well tolerated when administered with standard-of-care immunosuppressive therapy. Results support a possible role for the autotaxin pathway in the pathogenesis of SSc skin disease and warrant further clinical research.

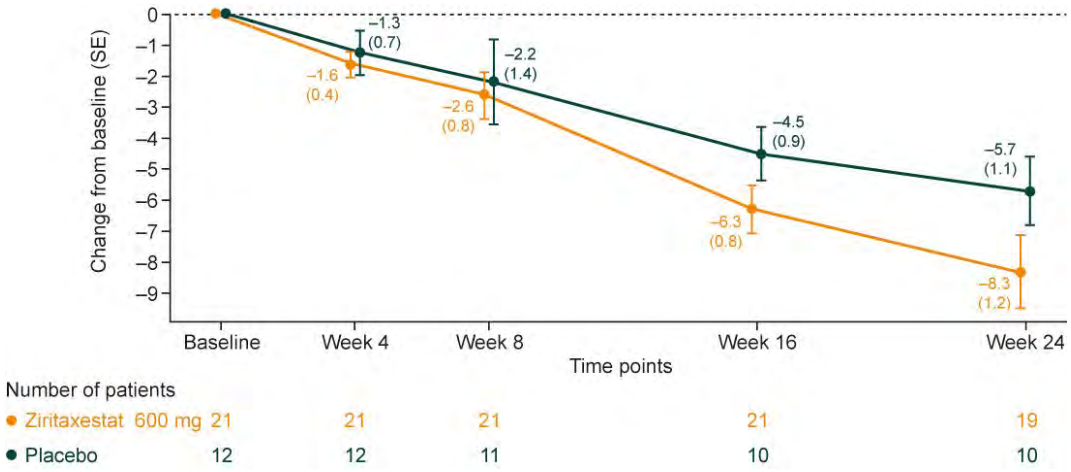

Figure 1. Change in mRSS from baseline. Changes in N are due to 1 patient being lost to follow-up and patients having the mRSS assessment outside the allowable window, due to COVID-19 restrictions limiting onsite visits COVID-19, coronavirus disease 2019; mRSS, modified Rodnan skin score; SE, standard error

Disclosure: D. Khanna, Pfizer, 2, AbbVie, 5, Acceleron, 5, Actelion, 5, Amgen, 5, Boehringer Ingelheim, 5, CSL Behring, 5, Corbus, 5, Galapagos, 5, Genentech/Roche, 5, Gilead, 5, GlaxoSmithKline, 5, Merck, 5, Mitsubishi Tanabe Pharma, 5, Sanofi-Aventis, 5, United Therapeutics, 5, Eicos Sciences, Inc, 9, CiviBioPharma/Eicos Sciences, Inc, 9, Bayer, 2, 5, Bristol-Myers Squibb, 2, Horizon, 2, 5, Immune Tolerance Network, 2, National Institutes of Health, 2; **C. Denton**, Acceleron, 2, 9, Actelion, 2, 9, Arxx Therapeutics, 2, 9, Bayer, 2, 9, Boehringer Ingelheim, 2, 9, Bristol-Myers Squibb, 2, 9, Corbus, 2, 9, CSL Behring, 2, 9, Galapagos, 2, 9, GlaxoSmithKline, 2, 9, Horizon, 2, 9, Inventiva, 2, 9, Leadiant Biosciences, 2, 9, Roche, 2, 9, Sanofi, 2, 9; **D. Furst**, Actelion, 2, Amgen, 2, 9, Bristol Myers Squibb, 2, 9, Galapagos, 2, 9, Novartis, 2, 9, Pfizer, 2, 9, Sanofi, 2, Roche/Genentech, 2, Corbus, 2, 9, GlaxoSmithKline, 2; **M. Mayes**, Galapagos, 2, 9, Actelion Pharma, 9, Astellas, 9, Medtelligence, 9, Mitsubishi-Tanabe, 9, Bayer, 2, Corbus, 2, GlaxoSmithKline, 2, Reata, 2, Sanofi, 2, Boehringer Ingelheim, 2, 9, EICOS, 2, 9; **M. Matucci-Cerinic**, Acceleron, 5, Actelion, 5, Bayer, 5, Boehringer Ingelheim, 5, Chemomab, 5, CSL Behring, 5, Corbus, 5, Galapagos, 5, Janssen, 5, Inventiva, 5, Lilly, 5, Mitsubishi, 5, MSD, 5, Pfizer, 5, Regeneron, 5, Roche, 5, Samsung, 5, Biogen, 5; **V. Smith**, Actelion, 2, 5, 8, Bayer, 2, 5, 8, Boehringer Ingelheim, 2, 5, 8; **D. de Vries**, Galapagos, 3, 9; **L. Deberdt**, Galapagos, 3, 9; **P. Stiers**, Galapagos, 3, 9; **N. Prasad**, Galapagos, 3, 9; **S. Ahmed**, Galapagos, 3, 9.

Abstract Number: L10

Targeting Plasmacytoid Dendritic Cells Improves Cutaneous Lupus Erythematosus Skin Lesions and Reduces Type I Interferon Levels: Results of a Phase 1 Study of VIB7734

Victoria Werth[1], Jodi Karnell[2], William Rees[2], Nanette Mittereder[3], Li Yan[2], Yanping Wu[3], Jorn Drappa[2], Gabor Illei[2] and John Ratchford[2], [1]University of Pennsylvania, Philadelphia, PA, [2]Viela Bio, Gaithersburg, MD, [3]Viela Bio, Gaithersburg

SESSION INFORMATION
Session Date: Monday, November 9, 2020
Session Title: Late-Breaking Abstracts
Session Type: Late-Breaking Abstract Session
Session Time: 11:30AM–1:00PM

Background/Purpose: Plasmacytoid dendritic cells (pDCs) secrete large amounts of type I interferon (IFN) and other cytokines upon activation. pDCs migrate to sites of active disease in lupus. VIB7734 is a monoclonal antibody that selectively targets pDCs for antibody-dependent cellular cytolysis.

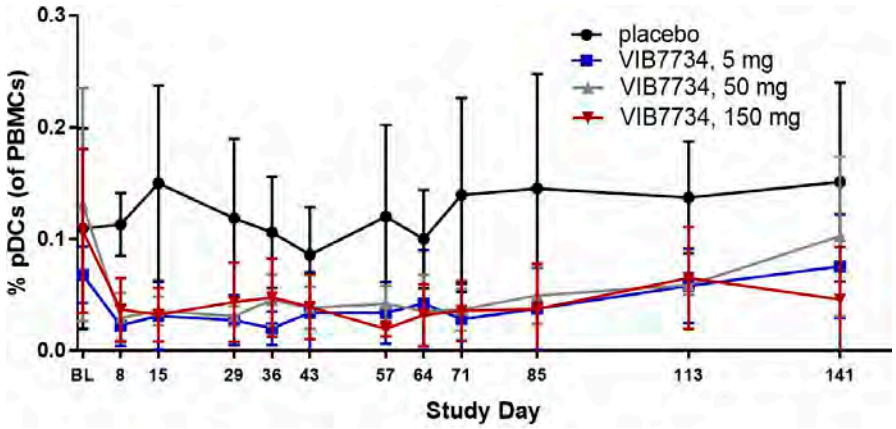

Figure 1: Mean Circulating pDC levels by treatment arm and time. Vertical bars represent standard deviation. PBMCs = peripheral blood mononuclear cells.

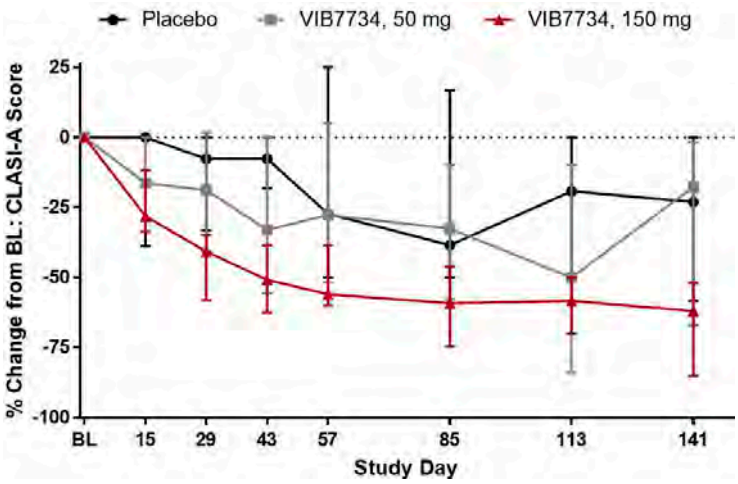

Figure 2: % change from baseline (BL) in median CLASI-A score by treatment arm and time. Vertical bars represent the interquartile range.

Methods: VIB7734 was tested in a phase 1, randomized, double-blind, placebo-controlled, multiple ascending dose clinical trial (NCT03817424). Adult subjects were enrolled in 3 sequential cohorts and received placebo (n=9) or 5 mg (n=6, cohort 1), 50 mg (n=8, cohort 2), or 150 mg (n=8, cohort 3) of VIB7734. Cohort 1 enrolled subjects with SLE or Sjogren's syndrome with no minimum disease activity requirement. Cohorts 2 & 3 included subjects with SLE or cutaneous lupus erythematosus (CLE) with a CLE Disease Area and Severity Index Activity score (CLASI-A) of ≥ 8. Subjects received VIB7734 or placebo subcutaneously every 4 weeks for 3 doses as an add-on to standard of care. In cohorts 2 and 3, a biopsy of affected skin was performed at baseline and Month 3. pDC levels were quantified in the blood and skin. The type I IFN signature was measured in blood. As a marker of IFN activity, myxovirus resistance protein A (MxA) was quantified within the epidermis as the percent of area reaching the positive staining threshold.

Results: 31 subjects were randomized and treated; all completed the study. Reductions in circulating pDCs were evident at Week 1 and persisted through the 3-month treatment period (Figure 1). A high type I IFN signature was present at baseline in 18 of 23 subjects (78%) in cohorts 2 and 3. The median change in IFN signature at Month 3 was -54% in the VIB7734 50 mg group, -83% in the VIB7734 150 mg group, and +8% in the placebo group. On the Month 3 biopsy the median change in pDC density was -87% for the 50 mg group, -99% for the 150 mg group, and -14% for the placebo group. The median area of MxA staining decreased with VIB7734 treatment (50 mg group: 50% to 1.7% affected area; 150 mg group: 90% to 1.1% affected area; placebo group: 5.5% to 18% affected area). The median change in CLASI-A from baseline to Month 3 was -5 in the 50 mg group, -9.5 in the 150 mg group, and -5 in the placebo group (Figure 2). At Month 3, a ≥50% improvement in CLASI-A was observed in 9 of 16 (56%) VIB7734-treated subjects and 2 of 7 (29%) placebo-treated subjects. No serious adverse events occurred in VIB7734-treated subjects. The proportion of subjects with an adverse event was similar in the VIB7734 and placebo groups (73% vs. 67%).

Conclusion: VIB7734 reduced blood and skin pDCs, thereby reducing type I IFN levels in blood and inflamed skin. More CLE subjects treated with VIB7734 than placebo had a clinically significant improvement in CLASI-A scores, and VIB7734 had an acceptable safety profile. Additional studies of VIB7734 in lupus are planned.

Disclosure: V. Werth, Vielabio, 5, Vielabio, 2; **J. Karnell**, Viela Bio, 1, 3; **W. Rees**, Viela Bio, 1, 3; **N. Mittereder**, None; **L. Yan**, None; **Y. Wu**, Viela Bio, 1, 3; **J. Drappa**, Viela Bio, 1, 3; **G. Illei**, Viela Bio, 1, 3; **J. Ratchford**, Viela Bio, 1, 3.

Abstract Number: L11

Tofacitinib for the Treatment of Adult Patients with Ankylosing Spondylitis: Primary Analysis of a Phase 3, Randomized, Double-blind, Placebo-controlled Study

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SESSION INFORMATION

Session Date: Monday, November 9, 2020

Session Title: Late-Breaking Abstracts

Session Type: Late-Breaking Abstract Session

Session Time: 11:30AM–1:00PM

Background/Purpose: Tofacitinib is an oral JAK inhibitor that is being investigated for the treatment of adult patients (pts) with AS.

Table 1. Demographics and baseline disease characteristics

	Tofacitinib 5 mg BID (N=133)	PBO (N=136)
Male, n (%)	116 (87.2)	108 (79.4)
Age (years), mean (SD)	42.2 (11.9)	40.0 (11.1)
Race, n (%)		
White	107 (80.5)	106 (77.9)
Asian	25 (18.8)	30 (22.1)
Not reported	1 (0.8)	0
Region, n (%)		
North America (US and Canada)	16 (12.0)	11 (8.1)
European Union	51 (38.3)	55 (40.4)
Asia	23 (17.3)	30 (22.1)
Rest of World	43 (32.3)	40 (29.4)
Duration since AS symptoms (years), mean (SD)	14.2 (9.8)	12.9 (9.5)
Duration since AS diagnosis (years), mean (SD)	8.9 (9.1)	6.8 (6.9)
HLA-B27 positive, n (%)	111 (83.5)	116 (85.3)
hsCRP (mg/dL), mean (SD)	1.64 (1.73)	1.80 (1.97)
ASDAS(CRP), mean (SD)	3.8 (0.9)	3.9 (0.8)
ASQoL, mean (SD)	11.6 (4.7)	11.3 (4.2)
SF-36v2 PCS score, mean (SD)	33.5 (7.3)	33.1 (7.0)
FACIT-F total score, mean (SD)	27.2 (10.7)	27.4 (9.3)
BASMI–linear method, mean (SD)	4.5 (1.7)	4.4 (1.8)
BASFI (NRS 0–10), mean (SD)	5.8 (2.3)	5.9 (2.1)
BASDAI (NRS 0–10), mean (SD)	6.4 (1.5)	6.5 (1.4)
Inflammation (morning stiffness; NRS 0–10),[a] mean (SD)	6.6 (1.9)	6.8 (1.9)
PtGA (NRS 0–10), mean (SD)	6.9 (1.8)	7.0 (1.7)
Total back pain (NRS 0–10), mean (SD)	6.9 (1.5)	6.9 (1.6)
Prior bDMARD use, n (%)		
bDMARD-naive	102 (76.7)	105 (77.2)
TNFi-IR[b] or bDMARD use (non-IR)	31 (23.3)	31 (22.8)
Concomitant medication use on Day 1, n (%)		
NSAIDs	105 (78.9)	108 (79.4)
Oral corticosteroids	13 (9.8)	7 (5.1)
Methotrexate	5 (3.8)	13 (9.6)
Sulfasalazine	24 (18.0)	31 (22.8)

Data cut-off Dec 19, 2019; data snapshot Jan 29, 2020; database was not locked, study was ongoing and data are subject to change in the final analysis
[a]Inflammation (morning stiffness) assessed as mean of questions 5 and 6 of the BASDAI
[b]Patients designated as TNFi-IR must have had an inadequate response and/or intolerance to at least one, but not more than two, approved TNFi
AS, ankylosing spondylitis; ASDAS(CRP), AS Disease Activity Score using C-reactive protein; ASQoL, AS Quality of Life; BASDAI, Bath AS Disease Activity Index; BASFI, Bath AS Functional Index; BASMI, Bath AS Metrology Index; BID, twice daily; bDMARD, biologic disease-modifying antirheumatic drug; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; hsCRP, high-sensitivity C-reactive protein; HLA-B27, human leukocyte antigen-B27; IR, inadequate responder; N, number of patients in full analysis set; n, number of patients with characteristic; NRS, numerical rating scale; NSAID, non-steroidal anti-inflammatory drug; PBO, placebo; PtGA, Patient Global Assessment of disease; SD, standard deviation; SF-36v2 PCS, Short Form-36 Health Survey Version 2 Physical Component Summary; TNFi, tumor necrosis factor inhibitor

Methods: This Phase 3, randomized, double-blind (DB), placebo (PBO)-controlled study (NCT03502616) enrolled pts aged ≥ 18 years with a diagnosis of active AS documented with centrally read radiographs, who met modified New York Criteria, and had an inadequate response or intolerance to ≥ 2 NSAIDs. In the 16-week DB phase, pts were randomized 1:1 to receive tofacitinib 5 mg BID or PBO. After Week (W)16, all pts received open-label tofacitinib until W48. We report the primary analysis of the study. Four separate families of efficacy endpoints were tested in hierarchical sequences to control for type I error: 1) ASAS20 response at W16 (primary endpoint), ASAS40 response at W16 (key secondary endpoint), change from baseline (Δ) to W16 in ASDAS(CRP), hsCRP, ASQoL, SF-36v2 PCS, BASMI–linear method, and FACIT-F total score; 2) Δ to W16 in ASAS components: PtGA, total back pain, BASFI, and Inflammation (morning stiffness); 3) ASAS20 response over time; 4) ASAS40 response over time. Statistical tests were conducted at the 2-sided 5% significance level. Safety data up to W16 and up to W48 are presented (data cut-off Dec 19, 2019; database was not locked and study was ongoing).

Results: 269 pts were randomized and treated (tofacitinib, n=133; PBO, n=136); 77.0% were bDMARD-naïve (Table 1). Efficacy results are shown in Table 2. At W16, the % of ASAS20 responders was significantly greater with tofacitinib (56.4%) vs PBO (29.4%) ($p < 0.0001$). The % of ASAS40 responders at W16 was significantly greater with tofacitinib (40.6%) vs PBO (12.5%) ($p < 0.0001$), and significant improvements with tofacitinib vs PBO were seen for Δ to W16 in ASDAS(CRP), hsCRP, ASQoL, SF-36v2 PCS, BASMI–linear method, and FACIT-F total score. Improvements in ASAS components were significantly greater with tofacitinib vs PBO. Significant improvements with tofacitinib vs

Table 2. Efficacy of tofacitinib 5 mg BID vs PBO up to W16: type I error-controlled primary and secondary endpoints[a]

	Tofacitinib 5 mg BID (N=133)	PBO (N=136)	p value
Global type I error-controlled endpoints at W16, tested in the sequence below			
ASAS20 response,[b] n (%)	75 (56.4)	40 (29.4)	< 0.0001
ASAS40 response,[b] n (%)	54 (40.6)	17 (12.5)	< 0.0001
ΔASDAS(CRP),[c] LSM (SE) [N1]	-1.46 (0.08) [129]	-0.37 (0.08) [131]	< 0.0001
ΔhsCRP (mg/dL),[c] LSM (SE) [N1]	-1.05 (0.10) [129]	-0.09 (0.10) [131]	< 0.0001
ΔASQoL,[d] LSM (SE) [N1]	-4.03 (0.40) [129]	-2.01 (0.41) [130]	0.0001
ΔSF-36v2 PCS score,[d] LSM (SE) [N1]	6.69 (0.59) [129]	3.14 (0.59) [130]	< 0.0001
ΔBASMI–linear method,[c] LSM (SE) [N1]	-0.63 (0.06) [129]	-0.11 (0.06) [131]	< 0.0001
ΔFACIT-F total score,[c] LSM (SE) [N1]	6.54 (0.80) [129]	3.12 (0.79) [131]	0.0008
Type I error-controlled ΔASAS components at W16,[c,e] tested in the sequence below			
ΔPtGA (NRS 0–10), LSM (SE) [N1]	-2.47 (0.20) [129]	-0.91 (0.20) [131]	< 0.0001
ΔTotal back pain (NRS 0–10), LSM (SE) [N1]	-2.57 (0.19) [129]	-0.96 (0.19) [131]	< 0.0001
ΔBASFI (NRS 0–10), LSM (SE) [N1]	-2.05 (0.17) [129]	-0.82 (0.17) [131]	< 0.0001
ΔInflammation (morning stiffness, NRS 0-10),[f] LSM (SE) [N1]	-2.69 (0.19) [129]	-0.97 (0.19) [131]	< 0.0001
Type I error-controlled ASAS20 response over time,[b,e] tested in the sequence below			
W12, n (%)	85 (63.9)	40 (29.4)	< 0.0001
W8, n (%)	76 (57.1)	34 (25.0)	< 0.0001
W4, n (%)	68 (51.1)	27 (19.9)	< 0.0001
W2, n (%)	38 (28.6)	14 (10.3)	0.0001
Type I error-controlled ASAS40 response over time,[b,g] tested in the sequence below			
W12, n (%)	57 (42.9)	16 (11.8)	< 0.0001
W8, n (%)	46 (34.6)	8 (5.9)	< 0.0001
W4, n (%)	36 (27.1)	5 (3.7)	< 0.0001
W2, n (%)	14 (10.5)	6 (4.4)	0.0548

Data cut-off Dec 19, 2019; data snapshot Jan 29, 2020. Efficacy assessments used only on-drug data up to W16; efficacy data final

[a]In each group of type I error-controlled endpoints, statistical significance could be declared only if the prior endpoint (or time points) in the sequence met the requirements for significance ($p \leq 0.05$)

[b]ASAS20 response was defined as ≥ 20% and ≥ 1 unit improvement in ≥ 3 components on a scale of 0–10 and no worsening of ≥ 20% and ≥1 unit in the remaining component. ASAS40 response was defined as ≥ 40% and ≥ 2 units improvement in ≥ 3 components on a scale of 0–10 and no worsening at all in the remaining component. Normal approximation adjusting for the stratification factor (prior treatment history: bDMARD-naïve vs TNFi-IR or bDMARD use (non-IR)) derived from clinical database via Cochran–Mantel–Haenszel approach was used. Missing response was considered as non-response

[c]Mixed model for repeated measures included fixed effects of treatment group, visit, and treatment-group by visit interaction, stratification factor derived from clinical database, stratification-factor by visit interaction, baseline value, and baseline-value by visit interaction; an unstructured covariance matrix was used. Missing values were not imputed

[d]Analysis of covariance model included fixed effects of treatment group, stratification factor derived from clinical database, and baseline value. Missing values were not imputed

[e]Statistical significance could be declared only if ASAS20 response at W16 (and all other prior timepoints, per footnote [a]) met the requirement for significance ($p \leq 0.05$); ASAS20 response at W16 data presented in the global type I error-controlled endpoints section

[f]Inflammation (morning stiffness) assessed as mean of questions 5 and 6 of the BASDAI

[g]Statistical significance could be declared only if ASAS40 response at W16 (and all other prior timepoints, per footnote [a]) met the requirement for significance ($p \leq 0.05$); ASAS40 response at W16 data presented in the global type I error-controlled endpoints section

Δ, change from baseline; AS, ankylosing spondylitis; ASAS20/40, Assessment in AS ≥ 20/40% improvement; ASDAS(CRP), AS Disease Activity Score using C-reactive protein; ASQoL, AS Quality of Life; BASDAI, Bath AS Disease Activity Index; BASFI, Bath AS Functional Index; BASMI, Bath AS Metrology Index; bDMARD, biologic disease-modifying antirheumatic drug; BID, twice daily; FACIT-F, Functional Assessment of Chronic Illness Therapy-Fatigue; hsCRP, high-sensitivity C-reactive protein; IR, inadequate responder; LSM, least squares mean; N, number of patients in full analysis set; N1, number of patients with observation at visit; n, number of patients with response; NRS, numerical rating scale; PBO, placebo; PtGA, Patient Global Assessment of disease; SE, standard error; SF-36v2 PCS, Short Form-36 Health Survey Version 2 Physical Component Summary; TNFi, tumor necrosis factor inhibitor; W, week

PBO were seen from W2 (first post-baseline visit) in ASAS20 response and W4 in ASAS40 response. Up to W16, adverse events (AEs) were reported in 72 pts (54.1%) receiving tofacitinib and 70 pts (51.5%) receiving PBO; serious and severe AEs were each reported in 2 pts (1.5%) receiving tofacitinib and no pts receiving PBO; 3 pts (2.3%) receiving tofacitinib and 1 pt (0.7%) receiving PBO discontinued study drug due to AEs. Safety trends were similar up to W48 (Table 3). With tofacitinib: there were no deaths, DVT, PE, ATE, GI perforation, ILD, MACE, malignancies, or opportunistic infections up to W48; adjudicated hepatic events were reported in 1 pt (0.8%) up to W16 and 2 pts (1.5%) up to W48; 1 pt (0.8%) had a serious infection (meningitis) up to W16; 3 pts (2.3%) had non-serious HZ up to W48. With PBO: there were no deaths or AEs of special interest up to W16; 1 pt (0.7%) in the PBO → tofacitinib group had non-serious HZ up to W48.

Conclusion: Pts with active AS had a rapid clinical response to tofacitinib. Efficacy was significantly greater with tofacitinib vs PBO for primary and secondary endpoints. AEs were more frequent with tofacitinib vs PBO; there were no new safety risks.

Acknowledgments: Study sponsored by Pfizer Inc. Medical writing support was provided by Sarah Piggott, CMC Connect, and funded by Pfizer Inc.

Table 3. Summary of safety up to W16 and up to W48

	Up to W16 (DB phase)		Up to W48 (DB and OL phases)	
Patients with events, n (%)	**Tofacitinib 5 mg BID (N=133)**	**PBO (N=136)**	**Tofacitinib 5 mg BID (N=133)**	**PBO → Tofacitinib 5 mg BID (N=136)**
AEs	72 (54.1)	70 (51.5)	99 (74.4)	91 (66.9)
SAEs	2 (1.5)	0	6 (4.5)	1 (0.7)
Severe AEs	2 (1.5)	0	6 (4.5)	0
Discontinued study drug due to AEs	3 (2.3)	1 (0.7)	7 (5.3)	1 (0.7)
Deaths	0	0	0	0
Most common AEs (> 5% of any treatment group)				
Upper respiratory tract infection	14 (10.5)	10 (7.4)	20 (15.0)	14 (10.3)
Nasopharyngitis	9 (6.8)	10 (7.4)	11 (8.3)	18 (13.2)
Diarrhea	6 (4.5)	5 (3.7)	9 (6.8)	7 (5.1)
ALT increased	4 (3.0)	1 (0.7)	8 (6.0)	2 (1.5)
Arthralgia	1 (0.8)	9 (6.6)	2 (1.5)	10 (7.4)
Headache	2 (1.5)	3 (2.2)	5 (3.8)	7 (5.1)
AEs of special interest				
Malignancies (including NMSC)[a]	0	0	0	0
DVT, PE, or ATE[a]	0	0	0	0
MACE[a]	0	0	0	0
GI perforation[a]	0	0	0	0
Hepatic events[a]	1 (0.8)	0	2 (1.5)	0
HZ (serious and non-serious)	0	0	3 (2.3)[b]	1 (0.7)[b]
Opportunistic infections[a]	0	0	0	0
Serious infections	1 (0.8)[c]	0	1 (0.8)[c]	0
ILD[a]	0	0	0	0
Laboratory abnormalities[d]				
Hemoglobin				
< 0.8 × LLN	0	1 (0.7)	1 (0.8)	1 (0.7)
Lymphocytes				
< 0.8 × LLN	0	1 (0.7)	1 (0.8)	1 (0.7)
> 1.2 × ULN	0	1 (0.7)	0	1 (0.7)
Neutrophils				
< 0.8 × LLN	1 (0.8)	1 (0.7)	2 (1.5)	1 (0.7)
> 1.2 × ULN	4 (3.0)	12 (9.0)	10 (7.6)	17 (12.7)
AST				
> 3 × ULN	1 (0.8)	0	3 (2.3)	0
ALT				
> 3 × ULN	3 (2.3)	0	5 (3.8)	0
Cholesterol				
> 1.3 × ULN	0	1 (0.7)	0	1 (0.7)
Creatine kinase				
> 2 × ULN	2 (1.5)	4 (3.0)	7 (5.3)	8 (6.0)

Data cut-off Dec 19, 2019; data snapshot Jan 29, 2020; database was not locked; study was ongoing and safety data are subject to change in the final analysis
[a]Adjudicated events
[b]Non-serious; did not meet opportunistic infection adjudication criteria
[c]Meningitis; did not meet opportunistic infection adjudication criteria
[d]For tofacitinib 5 mg BID, N=132; for PBO → tofacitinib 5 mg BID, N=134
AE, adverse event; ALT, alanine aminotransferase; AST, aspartate aminotransferase; ATE, arterial thromboembolism; BID, twice daily; DB, double-blind; DVT, deep vein thrombosis; GI, gastrointestinal; HZ, herpes zoster; ILD, interstitial lung disease; LLN, lower limit of normal; N, number of patients in safety analysis set; n, number of patients with event; NMSC, non-melanoma skin cancer; MACE, major adverse cardiovascular events; OL, open-label; PBO, placebo; PE, pulmonary embolism; SAE, serious AE; ULN, upper limit of normal; W, week

Disclosure: A. Deodhar, Eli Lilly, 2, 5, GlaxoSmithKline, 2, 5, Novartis, 2, 5, Pfizer Inc, 2, 5, UCB, 2, 5, AbbVie, 2, 5, Amgen, 5, Boehringer Ingelheim, 5, Bristol-Myers Squibb, 5, Celgene, 5, Janssen, 5, Galapagos, 5, Gilead, 2, 5; **P. Sliwinska-Stanczyk**, None; **H. Xu**, None; **X. Baraliakos**, AbbVie, 5, Amgen, 5, Bristol-Myers Squibb, 5, Celgene, 5, Eli Lilly, 5, Gilead, 5, Janssen, 5, Novartis, 5, Pfizer Inc, 5, UCB, 5, MSD, 5; **L. Gensler**, Pfizer Inc, 2, AbbVie, 5, Eli Lilly, 5, Gilead, 5, GlaxoSmithKline, 5, Novartis, 2, 5, UCB, 2, 5; **D. Fleishaker**, Pfizer Inc, 1, 3; **L. Wang**, Pfizer Inc, 1, 3; **J. Wu**, Pfizer Inc, 1, 3; **S. Menon**, Pfizer Inc, 1, 3; **C. Wang**, Pfizer Inc, 1, 3; **O. Dina**, Pfizer Inc, 1, 3; **L. Fallon**, Pfizer Inc, 1, 3; **K. Kanik**, Pfizer Inc, 1, 3; **D. van der Heijde**, AbbVie, 5, Amgen, 5, Astellas, 5, AstraZeneca, 5, Bayer, 5, Bristol-Myers Squibb, 5, Boehringer Ingelheim, 5, Celgene, 5, Cyxone, 5, Daiichi, 5, Eli Lilly, 5, Galapagos, 5, Gilead, 5, GlaxoSmithKline, 5, Janssen, 5, Merck, 5, Novartis, 5, Pfizer Inc, 5, Regeneron, 5, Roche, 5, Sanofi, 5, Takeda, 5, UCB, 5, Imaging Rheumatology BV, 3.

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Abstract Number: PP01

Impacting Change Through Facilitation and Advocacy for Lupus

Monica Watson[1], [1]Lupus Foundation of America, Darby, PA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Perspectives Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: My story started as one of disbelief in 2009 with my Lupus diagnosis. How could a woman in the prime of her career be diagnosed with a disease with no cure? Being a female in a technical field, when I heard my diagnosis, I thought fix it. When I heard there was no fix, I was taken off guard. This disbelief had to quickly turn to how can I live well with this disease. It has been a journey, but a grateful one of self -discovery. Although this disease has caused me to be unable to work in my profession, brought about a myriad of other conditions and co-morbidities, I have discovered that I am resilient, persistent and a warrior.

Intervention: Navigating such a complex illness that drastically changes your life is no easy feat. One must adjust and accommodate to a "new you" in the process. Managing and adhering to treatment plans in coordination with my rheumatologist and other specialists is a way of life. A part of this new life led me to adding additional tools to my toolbelt in order to live well**.** One of which was attending a lupus support group. This opened up a whole new world of meeting people like me. They understood and connected over everyone's journey. My involvement led to becoming a support group facilitator. This group has developed into the largest lupus support group of the chapter. In this role, I continually serve as a conduit to bring information to attendees to encourage them to be empowered, engaged, educated and enlightened on their journey with Lupus. Facilitation has developed into advocacy. My voice as a patient to raise awareness, educate others and advocate for policies has been monumental. I have seen on a national and local level, the results of advocacy efforts and the ability to effect change.

Maintenance: My role as a support group facilitator and advocate has spawned continued education and learning. The sustained need to be engaged in your healthcare and total wellness are paramount. Doctor patient relationships have evolved into partnerships. Raising my voice through advocacy has served as a catalyst for others to raise their voices as well. Support group efforts have enlightened me and other patients on their road to self- discovery with Lupus. Promoting awareness for Lupus remains a key focus on this path. Advocating through sponsored events and meeting with both local and national political representatives still provides the ability to foster change.

Quality of Life: The people, experiences and knowledge I have gained on this path with Lupus have been invaluable. My service to others through my support group facilitator and advocacy roles has not only improved my quality of life but helped other patients as well. The expansion of my network through various engagements and forums has fostered additional relationships with other advocates, industry experts and increased doctor patient relationships. All this has led to providing not only valuable information for myself but serving as a gateway to share and impact the lives of patients. I always get inspired and invigorated by the synergy of those of us living with Lupus who come together to provide compassion, insights and determination to continue to fight on this journey. It has been a gratifying feeling to know that my voice along with others can make a difference.

Disclosure: M. Watson, None.

Abstract Number: PP02

Low- and Hi-Tech Tools for Enhancing Patient-Hospital Care Team Communication in the Context of Rare Disease

Ida Hakkarinen[1], [1]Vasculitis Patient-Powered Research Network (VPPRN) / Member, Vasculitis Foundation, Greenbelt, MD

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Perspectives Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: For over two years, I experienced a variety of disparate symptoms including: joint aches, sinus congestion, shortness of breath and chronic cough. An episode of hemoptysis led to laryngoscopy in December 2011 and a diagnosis of subglottic stenosis (SGS). Test results showed a high ANCA titer. Referral to a rheumatologist resulted in a diagnosis of Granulomatosis with Polyangiitis (GPA). Eight years later, a recurrence of SGS required another laryngoscopy. My hospital experience the second time allowed the use of a high-tech tool for communication with the health care team.

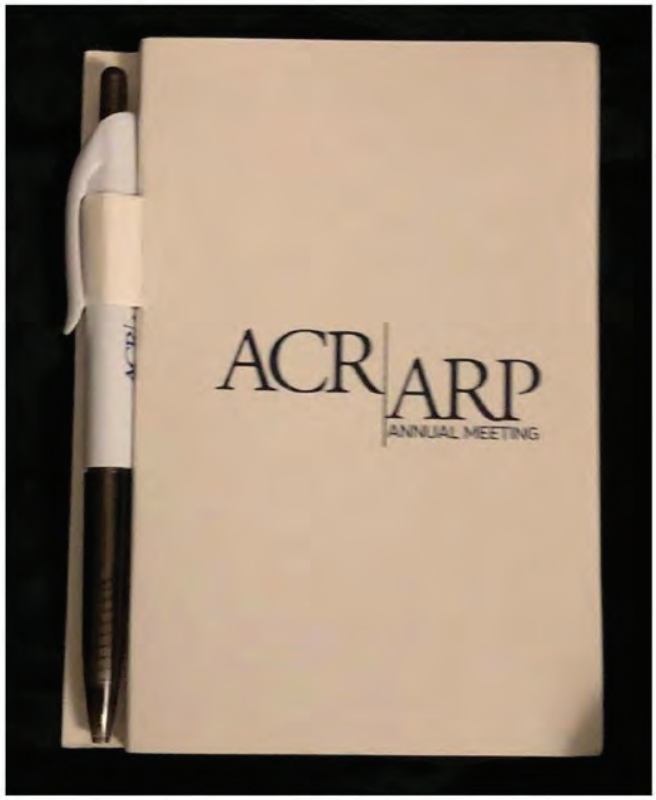

Fig. 1 – Notebook for observations and questions

Figure 1. Notebook for Observations and Questions

Date: MM/DD/YY

PENELOPE PROACTIVE PATIENT
DOB: MM/DD/YYYY

ABOUT ME
I'm a 58-year-old widow with one son. I work as a self-employed graphic artist. At my congregation, Grace Evangelical Lutheran Church in Anytown, MD, I'm on the board of directors, sing in the choir, and serve as an assisting minister.

MY SIX-WORD MEMOIR
Thanks to research, living with vasculitis.

TREATMENT PHILOSOPHY
Want to be an active participant in shared decision-making w/my medical team. My values: 1) use the least amount of medication to address the problem, and 2) reduce cost impact to health care system. My Risk/benefit view: Dr. Ruth Chang (Prof. of Jurisprudence, Oxford) says when choices are on par with each other, any of them is appropriate: "It's...in the space of hard choices that we get to exercise our normative power."

CONTACT INFORMATION
Cell: 123-456-7890
Home: 345-678-9102
E-mail: XXX Patient Portal or
firstname.lastname@mailprovider.com

My son Jacob graduated from college in June and will be joining the U.S. Army in December. This is his graduation photo.

REASON FOR HOSPITALIZATION
Recurrence of symptomatic subglottic stenosis. Dr. Jodie Gargle, my otolaryngologist, will be performing the laryngoscopy and keeping me overnight for observation. She anticipates the stenosis is a result of scar tissue rather than active inflammation.

UPCOMING MEDICAL APPOINTMENTS
16 Oct 2020 – 3-mo check up with Dr. Michaela Joints, my rheumatologist
18 Nov 2020 – consultation with Dr. Julia Driller, my oral surgeon, regarding potential for second dental implant

MEDICAL CONDITIONS
GRANULOMATOSIS WITH POLYANGIITIS (GPA) Dx Jan 2012, **OSTEOPEROSIS** Dx Feb 2010, **HYPOTHYRODISM** Dx June 2000

MEDICATIONS
Rx: levothyroxine 200 mcg daily, dapsone 100 mg daily (prophylaxis for pneumocystis pneumonia)
OTC: aspirin 81 mg daily, calcium citrate (slow release) 1200 mg daily, vitamin D 1000 mg daily, olopadtadine ophthalmic solution 0.2% PRN

SURGICAL HISTORY
March 2017 – dental implant
Dec 2011 - laryngoscopy for subglottic stenosis (inflammation was due to GPA)

VACCINATIONS
15 Nov 2019 – high-dose influenza trivalent
16 Jun 2019 – Shingrix (1st dose), 16 October 2019 – Shingrix (2nd dose)
19 Jan 2018 - PPSV23 booster (initial shot 08 Jun 2012)
20 Apr 2014 - PCV 13
04 Jan 2014 - Hep-B (2nd booster 25 Feb 2014, 3rd booster 26 Jul 2014)
02 Jun 2012 - Hep-A - booster 15 Jan 2013 // 12 Apr 2011 - Tdap

TESTS
Mammogram – 16 May 2019
DXA – 08 Nov 2018, previous scans 11 Oct 2016, 07 Mar 2014, and 21 Feb 2012

ALLERGIES TO MEDICATIONS
Sulfa drugs, adhesive tape

SOCIAL HISTORY
Never smoked. Drink one glass of red wine 2-3 times per week.

FAMILY HISTORY
Mother - Dx hypertension @ age 35, Dx w/breast cancer @ 60, died @ 65 of cancer.
Father – Dx cardiovascular disease @ age 44, died @ 70 of heart attack.
Paternal grandmother - senility in elderly years, macular degeneration, died @ 81.
Paternal grandfather - profound hearing loss in elderly years, died @ 99.
Maternal grandmother - pernicious anemia, cataracts, died @ 80 of liver cancer.
Maternal grandfather - hypertension, heart attack, died @ 60 of stroke.

Figure 2. Health Resume Template

Intervention: I've used both low-tech and high-tech tools to enhance communications with my hospital care teams. For both my 2011 and 2019 surgeries, I used a small notebook with attached pen (Fig. 1) to document my observations and questions. Following my 2011 surgery, I was told to rest my voice. After I pressed the call button in my

hospital room, a disembodied voice asked “What do you need?”, and I squeaked out a response. In 2019, however, I sent multiple text messages to myself on my mobile phone the night before surgery. The next day in my hospital room after surgery, I used the text-to-speech capability of the phone to “read aloud” a text through the built-in speaker, e.g., “I would like an orange popsicle, please.”

Writer and mother Shannon Dingle shared on her twitter feed in June 2019 a picture of a “health resume” she uses to help remember important information to share with her doctors. Physicians responded favorably, and said they wished more patients used such resumes. Borrowing her idea, I’ve started to provide a resume to each new health care team member I see (template in Fig. 2), whether at a clinic, ER, or hospital visit.

Maintenance: Being hospitalized with a rare disease at an academic medical center often results in many visitors for rounds. Once, when hospitalized for a relapse, there were 14 people across the room at the foot of my bed. I gave a medical student a copy of the ACR patient education brochure on GPA (Fig. 3) as a way to share information about my rare disease. Use of low- and high-tech tools has fostered improved communication in my interactions with my health care team in both clinical and hospital settings.

Quality of Life: I’m deeply grateful to the team of medical professionals who work in partnership with me to monitor, manage, and treat my GPA. Fortunately, my disease has not flared since September 2013. I’m a lifetime member of the Vasculitis Foundation, a patient advocacy group. In 2014, I joined a natural history study in the Vasculitis Translational Research Program at the National Institutes of Health. My six-word memoir is: “Thanks to research, living with vasculitis.”

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Granulomatosis with Polyangiitis (Wegener's)

Fast Facts

- Granulomatosis with polyangiitis (Wegener's) - GPA - is serious but treatable. To prevent complications, prompt diagnosis and treatment are essential.
- The cause of GPA is unknown.
- GPA often affects the sinuses, lungs, and kidneys. It can lead to kidney failure if not treated.
- Recurrences of disease is common.
- Significant side effects of medications used to treat GPA can be minimized with preventive strategies.

Granulomatosis with polyangiitis (Wegener's), also known as GPA, is a rare blood vessel disease. It can cause symptoms in the sinuses, lungs, and kidneys as well as other organs. It is a potentially serious disease. However, with prompt diagnosis, granulomatosis with polyangiitis can be treated effectively.

What is Granulomatosis with Polyangiitis (Wegener's)?

GPA is abnormal inflammation of the blood vessels, which is also called a vasculitis. GPA involves the small and medium-sized blood vessels throughout the body. The inflammation in the blood vessel does not allow blood to flow properly, so the cells do not get the oxygen they need. This causes tissue injury called granulomatous inflammation. A granuloma is a type of cellular inflammation that can usually be seen on biopsies of affected organs. The cause of GPA is not known.

Most commonly, GPA affects the sinuses, lungs, and kidneys, but also can affect the eyes, ears, skin, nerves, joints, and other organs. Symptoms can develop over days to months. The first symptoms generally appear in the respiratory tract (e.g., nose, sinuses, and lungs). The symptoms include nasal congestion, frequent nosebleeds, shortness of breath, and cough that may produce bloody phlegm. Other early symptoms can include joint pain, decreased hearing, skin rashes, eye redness and/or vision changes, fatigue, fever, appetite and weight loss, night sweats, and numbness or loss of movement in the fingers, toes, or limbs.

Updated March 2019 by Vaneet Sandhu, MD, and reviewed by the American College of Rheumatology Committee on Communications and Marketing.

https://www.rheumatology.org/I-Am-A/Patient-Caregiver/Diseases-Conditions/Granulomatosis-with-Polyangitis-Wegners (accessed June 15, 2020.)

Figure 3. ACR Patient Education Brochure for GPA (page 1 of 3 pages shown)

Reference

Naftulin, Julia (2019, June 21). Woman's 'health resume' is a hit with doctors. *Microsoft News (msn) lifestyle*. Retrieved from: https://www.msn.com/en-us/health/medical/womans-health-resume-is-a-hit-with-doctors/ar-AADelc4 (accessed June 15, 2020)

Disclosure: I. Hakkarinen, None.

Abstract Number: PP03

Connecting with Rheumatology Professionals and Thought Leaders Inspired the Creation of a New Program Focused on Relapsing Polychondritis ("RP"), a Rare Rheumatic Disease: Participating at ACR Annual Meetings Has Provided Exceptional Opportunities to Learn and Build Relationships

Nancy Linn[1], Catherine Bammert[2], David Bammert[3] and Michael Linn[4], [1]Relapsing Polychondritis Foundation, Palos Verdes Estates, CA, [2]MD Anderson, Houston, TX, [3]Relapsing Polychondritis Foundation, Houston, TX, [4]Relapsing Polychondritis Foundation, New York, NY

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Perspectives Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In 2011, I was diagnosed with relapsing polychondritis ("RP"), a debilitating and sometimes fatal rheumatic disease that is characterized by inflammation of cartilage and other tissues. The disease affects multiple organs, particularly cartilaginous structures such as the ears, nose, airways, and joints as well as the eyes, skin, heart valves and brain. The cause of RP is unknown and there currently is no cure for the disease.

After diagnosis, I realized that I could focus on my specific case – or, I could combat RP more broadly and help others. I decided to live my life with the purpose of helping others.

Intervention: As a patient, I had the opportunity to be evaluated by an incredible team of multidisciplinary expert medical professionals. While interacting with these experts, it was evident that there were tremendous unmet needs in the areas of diagnosis and treatments. As a retired Registered Nurse, it was clear that targeted research initiatives would be required to combat RP.

Maintenance: While fighting RP, I met many highly skilled, collaborative research scientists, especially at ACR Annual Meetings.

In 2017 in San Diego, I participated in an RP study group that received a tremendous response from participating clinicians, clinical and basic scientist researchers, patients, and patient advocacy groups.

In 2018 in Chicago, I helped organize the RP Foundation's reception, co-hosted an event with the University of Michigan Division of Rheumatology, participated on a podcast of a news source dedicated to the field of rheumatology, and facilitated two ACR exhibitor booths.

In 2019 in Atlanta, I participated in an RP investigators meeting, which provided an update on a classification criteria project, introduced a new project to modify the disease activity index, and summarized RP-related projects.

With knowledge gleaned at ACR Annual Meetings, my husband and I collaborated with the RP Foundation to provide a substantial gift in 2020 to establish the Penn RP Fund, which will support a unique partnership between the University of Pennsylvania and the National Institutes of Health sponsored Vasculitis Clinical Research Consortium.

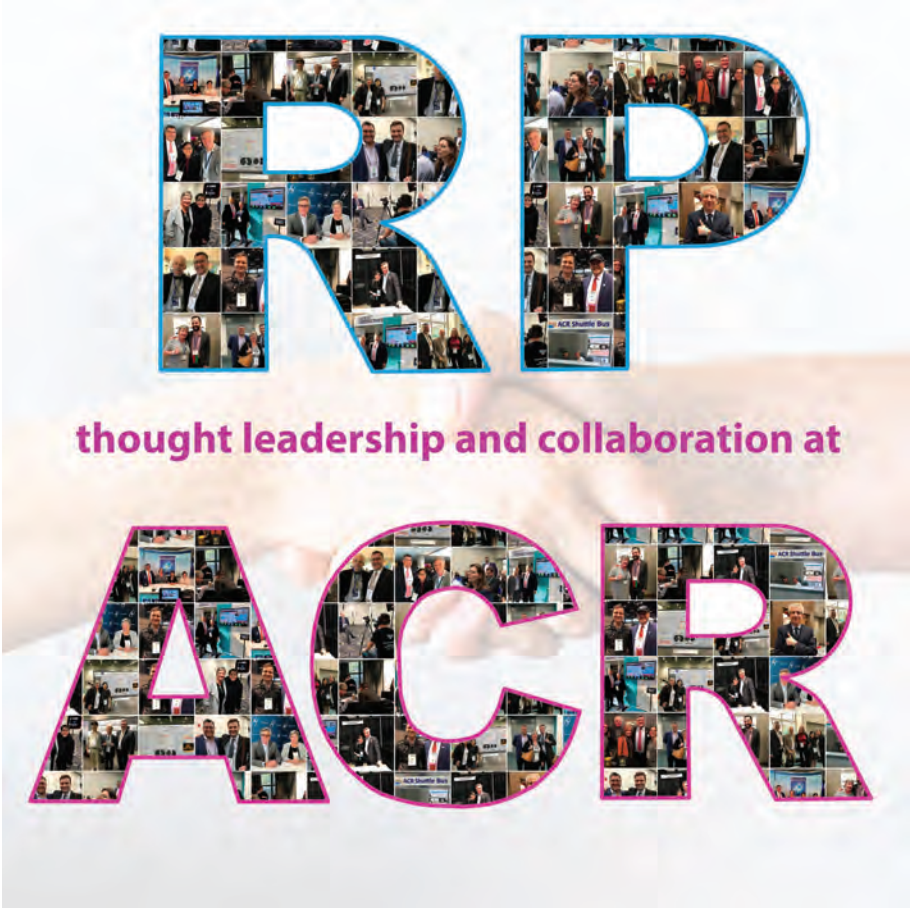
Quality of Life: Living with the purpose of helping other patients continues to improve the quality of my life. It affords me the opportunity to be excited about the extraordinary advances in patient care and cutting-edge research.

Participating at ACR Annual Meetings has provided exceptional opportunities to learn and collaborate with highly skilled research scientists. Further, I was able to build relationships with these scientists, which played a key role in the launch of the Penn RP program.

This program will allow researchers to pursue important projects, including the development of a world-class referral center to examine the impact of the microbiome on RP disease activity. Additionally, patients with RP will have the opportunity to be evaluated by multiple subspecialties in a coordinated patient-centered manner.

I am confident that the Penn RP program will significantly improve the quality of my life and other RP patients for years to come.

Photo collage of highly skilled, collaborative research scientists and relapsing polychondritis advocates



Relapsing polychondritis (RP) thought leadership at the American College of Rheumatology (ACR) meetings

The Relapsing Polychondritis Foundation formed a powerhouse healthcare coalition with the University of Pennsylvania and the NIH sponsored Vasculitis Clinical Research Consortium

Disclosure: N. Linn, None; **C. Bammert**, None; **D. Bammert**, None; **M. Linn**, None.

Abstract Number: PP04

My Multidisciplinary Healthcare Team and Patient Advocacy Groups Saved My Life

Tedi LaMere[1], Michael Linn[2] and David Bammert[3], [1]Relapsing Polychondritis Foundation, Kalispell, MT, [2]Relapsing Polychondritis Foundation, New York, NY, [3]Relapsing Polychondritis Foundation, Houston, TX

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Perspectives Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: I enjoyed being physically active my entire life – climbing mountains, hunting, and hiking. This drastically changed around 2012, when I noticed that I was increasingly experiencing shortness of breath and fatigue, despite being physically fit. I developed a nagging cough and my heart function decreased dramatically. I was tested for numerous conditions, but a diagnosis eluded me, and my health continued to deteriorate. Ironically, at the time, I was working as a respiratory therapist and was helping patients breathe, yet I could not breathe! I had to leave the career I was passionate about because my health became so poor. Eventually, my doctors ran out of potential diagnoses and began to discount my symptoms and brush me off. Meanwhile, my joints and tendons began to swell and become painful, my airways were collapsing, and I had to endure chemotherapeutic infusions to save my life.

Eventually, I was diagnosed with a rare autoimmune disease called relapsing polychondritis ("RP"), which is characterized by recurrent inflammation of cartilage in the body. RP is difficult to diagnose, challenging to treat and currently is not curable.

Intervention: After trying to schedule an appointment at the National Institutes of Health (NIH) for quite some time, I had to postpone my visit because I became too sick to travel. Living in Montana, traveling to Bethesda, Maryland was overwhelming and simply not feasible – both physically and financially.

Thankfully, the RP Foundation and Race for RP established a fund to support the Friends of Patients at the NIH program ("Friends of Patients") to offset travel costs and assist with providing for essential needs. The fund directly benefits RP patients and their families and advances RP research. Fortunately, I received assistance with transportation and made it to my appointments at the NIH! The clinicians and research scientists at the NIH identified several serious health conditions that could easily have cost me my life had they not been addressed, including cardiac amyloidosis, multiple pulmonary embolisms, and airways collapsing nearly 100%.

Maintenance: Currently, my medications are addressing the severe inflammation and heart condition caused by RP. High-dose corticosteroids have undoubtedly saved my life but have also resulted in significant damage to my body as well. Chimeric monoclonal antibody infusions also seem to manage my symptoms, and anticoagulant therapy reduces the risk of abnormal blood clot formation.

Quality of Life: I am grateful for the medical treatments that saved my life, yet I continue to have numerous daily struggles that I have learned to live with. I experience brain fog and joint pain all the time, and my heart and lung functions are greatly impaired. I have compression fractures in my back. I developed Cushing's disease and diabetes and

gained eighty pounds due to high-dose corticosteroids. However, my health is not declining at the rapid pace that it was prior to visiting NIH. Despite the severity of my symptoms, I remain hopeful that researcher scientists will unlock the mysteries of my disease and prolong my life – and the lives of others. I cannot thank NIH, Friends of Patients, RP Foundation, and Race for RP enough!

Tedi LaMere, a Registered Respiratory Therapist (RRT) with a Neonatal/Pediatric Specialist (NPS) certification, pictured outdoors prior to being diagnosed with relapsing polychondritis

Tedi LaMere, RRT-NPS and research advocate, pictured after being diagnosed with relapsing polychondritis

Tedi LaMere's patient advocacy groups (Relapsing Polychondritis Foundation, Friends of Patients at NIH, and Race for RP) worked together to facilitate her healthcare.

Disclosure: T. LaMere, None; **M. Linn**, None; **D. Bammert**, None.

Abstract Number: PP05

Coping Through Advocacy - My Story Living with Relapsing Polychondritis

Allegonda Imeson[1], [1]The Canadian Society for Relapsing Polychondritis, Stony Plain, AB, Canada

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Perspectives Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: Becoming a mother was the most pivotal moment of my life. From early on, I instilled the importance of a physical, healthy lifestyle for my two boys. I encouraged adventure and exploration with biking, walking and swimming in our picturesque Canadian backdrop.

In 2011, I started to experience painful swelling of the cartilaginous portions of my ears - which was so intense, I could not function. I was treated consistently and unsuccessfully with antibiotics. I was weak, tired, and in a constant state of cloudiness - I could no longer keep up with my children. As time moved forward, the episodes increased in intensity and frequency, and I started experiencing debilitating joint pain. Everyday was a struggle.

After finally being referred to a rheumatologist in 2015, I was diagnosed with the rare and sometimes fatal disease Relapsing Polychondritis (RP). Although relieved to finally have an answer, I was distraught with the lack of resources and information available for RP.

Intervention: The complexities of RP require a multidisciplinary team. Although treatment was started swiftly, the doctors I met with admittedly knew little of the disease. I decided to do whatever I could to educate myself about the illness. In late 2015, I reached out to the Relapsing Polychondritis Foundation and became the first international advocate for the U.S based group - eventually meeting a fellow patient in person at the 2016 LA autoimmune walk.

After this inspiring encounter, I decided to expand my international mission of awareness for RP. In 2017, I spearheaded the creation of the Canadian Society for Relapsing Polychondritis (CSRP) and successfully established the first Canadian RP non-profit organization focused on awareness, education, and patient support.

Maintenance: As Chair of the CSRP, I lead in the organization of annual awareness campaigns in Canada. Our inaugural event featured medical professionals speaking about the illness to a crowd of 100, which was only a dream

a few years previous. Each subsequent CSRP event has seen an increase in attendees - promoting awareness and encouraging patient wellness while focusing on what those with RP **CAN** do.

I proudly represent the CSRP in partnerships with the RP Foundation and Race for RP, attending the past three American College of Rheumatology (ACR) conferences alongside these organizations. I have had the honor of meeting experts in the field of rheumatology and the privilege of attending the 2019 RP investigators meeting - an international collaboration of professionals and advocates interested in the advancement of research for RP.

Quality of Life: RP will forever be synonymous with who I am. Although I am plagued with the effects of the disease everyday, I am grateful for my ability to increase awareness.

Supporting those who feel like I did 5 years ago when I was first diagnosed has been the most rewarding aspect for me living with a rare autoimmune disease. I have solace in knowing that that my efforts, and the efforts of our international team, are helping others with RP.

Although it is difficult to be exactly who I was before RP, I am now instilling the power of knowledge and advocacy in my children. Teaching them that when life throws you obstacles, it is important to face them head on as there is strength in knowledge.

Allegonda Imeson and the Canadian Society for Relapsing Polychondritis (CSRP).

Allegonda Imeson and her family.

THE CANADIAN SOCIETY FOR
RELAPSING
POLYCHONDRITIS

The Canadian Society for Relapsing Polychondritis (CSRP) logo.

Disclosure: A. Imeson, None.

Abstract Number: PP06

Only in My Dreams Can I Do the Things I Used to Do: Where There Is Research, There Is Hope

Dan Smith[1], Robert Smith[1] and Jillian Covault[1], [1]Canton, MI

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Perspectives Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In Mach 2020, I was diagnosed with relapsing polychondritis ("RP"), a multisystem, rheumatologic disease characterized by inflammation of cartilaginous structures including the ear, nose, joints, and airways. The cause of RP is unknown and there is no cure.

After my diagnosis, my family members contacted the RP Foundation to learn about this rare, debilitating disease. The RP Foundation was a tremendous resource and provided educational material and contact information for RP experts at the National Institute of Arthritis Musculoskeletal and Skin Diseases (NIAMS) at the National Institutes of Health (NIH). The RP Foundation also introduced me to an online RP support group.

Intervention: To share perspective and learn how to better manage my disease, I joined the support group. I learned the importance of lending hope to my peers and borrowing it from them, when needed. I am also learning new activities that provide a sense of well-being without requiring physical activity and robust breathing. One new hobby that I find personally rewarding is writing. I wrote the poem below:

Only in my dreams
Can I do the things I used to do
To take long walks in the woods
Go for bike rides with my love

Only in my dreams
Is my soul set free
To roam where it wants
To take the grandkids putt-putt
Or play yard games with them
On nice summer days

Only in my dreams
Can I work in my yard
Fiddle with landscaping
To putz in my man cave
Without gasping for air

Only in my dreams
Can I enjoy doing all the things
That made me “ME”
I guess you would say
You see I’m not a sitter or idle person

I will continue to fight and battle
That is what I know,
That’s what I was taught
But excuse me
If I turn to be early tonight
Because I can be me
Only in my dreams.

Maintenance: Recently, I was in the hospital fighting for my life after being infected with COVID-19. Thanks to my wife and family, a talented and dedicated medical team, the members of the RP Foundation, and the support group, my spirits were lifted, and I mustered the strength to fight my way back home. My family and team made a positive difference in my recovery.

I have been a life-long fan of professional hockey and was overjoyed when the local team won four Stanley Cup championships. While I was recently in the hospital, my peers posted videos with inspiring messages from professional hockey athletes. These athletes encouraged me (specifically) to keep fighting RP and the coronavirus. This support was fantastic, especially because hockey is an important part of our family.

For generations, hockey has provided great times together at ice rinks during tournament weekends with my children and grandchildren. One of the most difficult and frustrating things about RP is that I have had to stop attending family hockey games. My absence has been difficult for my family too. (One of my sons and one of my grandchildren are goalies on hockey teams.)

Quality of Life: The expertise of my medical team and the kindness of my wife, family, RP Foundation, and the RP support group helped me survive and has inspired me to help others. I will be forever grateful for the care and support that I received. I am also committed to advancing RP research. As one of my fantastic doctor says, “Where there is research, there is hope.” She is correct!

Dan & Debbie Smith and family

RELAPSING POLYCHONDRITIS FOUNDATION

polychondritis.org

Relapsing Polychondrtis Foundation logo

Disclosure: D. Smith, None; **R. Smith,** None; **J. Covault,** None.

Abstract Number: PP07

Improving Communication with My Physician Drastically Improved My Health

Whitney Carter[1], [1]Lupus and Allied Diseases Association, Inc., Pleasanton, CA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Perspectives Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: In 2011, at the age of 14, I was sent to the emergency room with a platelet count of 19. The hematologist diagnosed me with idiopathic thrombocytopenic purpura (ITP). After further testing, I was diagnosed with systemic lupus erythematosus (SLE). After a severe reaction to intravenous immunoglobulin (IVIG), the doctors put me on hydroxychloroquine (HCQ), prednisone, and azathioprine (AZA). Three years later, at the age of 17, I was diagnosed with central nervous system lupus (CNS lupus) after a lumbar puncture. After the diagnosis of CNS lupus, I was switched from AZA to mycophenolate mofetil, cyclophosphamide (CYC), and IV steroids. After six months, I was put on rituximab. Three months later, I did nine courses of plasmapheresis followed by both rituximab and CYC with IV steroids.

Intervention: After years of trial and error with intensive and time consuming treatments, the solution I kept coming back to was communication. If my physician didn't understand what was going on, he/she couldn't diagnose or treat me appropriately. Research is an important component in finding new treatments and potentially cures, but there is a lot to be said about effectively using the resources and tools that we already have. A huge communication block that affected me getting proper treatment for over a year was simply the description of one of my symptoms—dizziness. There are so many different kinds of dizziness, and many of them indicate different causes and treatments. I lacked the ability to describe it more specifically, and my physician never asked or helped by giving examples. The understanding that I felt lightheaded sometimes and other times like the room was spinning was a key factor in determining one, vertigo, as part of CNS lupus and the other as autonomic dysfunction from CNS lupus—orthostatic hypotension. Until both were treated, I continued to feel "dizzy," so we believed that the treatment wasn't working even though it was in many ways. This is just one example in my medical story, and many, if not all, patients have also had a delay in medical care for the same reason.

Maintenance: Individually treating both kinds of dizziness has helped me to be more functional. The vertigo improved with the CNS lupus treatments, but the lightheadedness didn't improve until I was put on the blood pressure increasing medications midodrine and droxidopa in addition. Communicating effectively with my doctors has also helped in finding and treating new conditions—dizziness was just the tip of the iceberg in my healthcare communication. Proper communication is the reason why I could get out of my wheelchair and walk, return to school, and even play volleyball again.

Quality of Life: I have a very high quality of life, being able to attend school, be involved in my community, and maintain friendships. Going to social events and being able to leave the house at all were things I took for granted before, but thankfully, I can do them again.

Disclosure: W. Carter, None.

Abstract Number: PP08

Patient Participation in the COVID-19 Global Rheumatology Alliance as a Model for Involving Patients from the Ground Up

Carly Harrison[1], Rashmi Sinha[2], Emily Sirotich[3], Naira Ikram[4], Kristen Young[5], Christele Felix[1], Karen Durrant[6], Richard Beesley[7], Serena Mingolla[8], Ana Isabel Martín Mancheño[9], Dawn Richards[10], Evelyn Olmedo[11], Wendy Costello[12], Monique Gore-Massy[13], Laurie Proulx[14], Maria Marino[15] and Richard Howard[16], [1]LupusChat, New York, NY, [2]Systemic JIA Foundation, Cincinnati, OH, [3]LA Lupus Lady, Hamilton, ON, Canada, [4]Duke University, Austin, TX, [5]Phoenix, AR, [6]Autoinflammatory Alliance, San Francisco, CA, [7]Juvenile Arthritis Research, United Kingdom, [8]Associazione Nazionale Persone con Malattie Reumatolgiche e Rare APMARR APS, Brindisi, Italy, [9]CEADE, Madrid, Spain, [10]Canadian Arthritis Patient Alliance, Toronto, ON, Canada, [11]Buenos Aires, El Salvador, [12]iCAN, Bansha, Tipperary, Ireland, [13]Lupus Foundation of America, Brooklyn, NY, [14]Canadian Arthritis Patient Alliance, Ottawa, ON, Canada, [15]Arthritis Foundation; Vectra, Athens, GA, [16]Spondylitis Association of America, Van Nuys, CA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Perspectives Poster
Session Type: Poster Session C
Session Time: 9:00AM–11:00AM

Background/Purpose: The COVID-19 Global Rheumatology Alliance (GRA) is a volunteer-driven organization that originated in response to the global pandemic. It was created to improve patient care, by collecting and disseminating information about the impact of COVID-19 on rheumatic disease. From the very beginning GRA involved patients in its activities.

Intervention: GRA was conceptualized in Twitter discussions between rheumatologists and patient representatives. More were invited to join through social media and patient organizations. A diverse group of patients from across the world, representing many rheumatic diseases, both adult and pediatric ended up joining the effort.

GRA involves patients at all levels of the organization, while Slack channels promote open communication between patients and researchers.

Maintenance:

Collecting and Disseminating Data

A key way that GRA collects information is through its Patient Experience Survey. The goal of this anonymous survey is to understand patients' experiences managing their care during COVID-19. Representatives actively collaborated with researchers to create the survey, translate it into 9 languages, and distribute to patient groups and promote on social media.

Accessible Scientific Information

Every GRA publication is summarized into lay summaries written in non-technical language. Patients help in creating and then disseminating these summaries back to their patient groups and broader networks on social media.

Figure 1: Patient involvement in GRA in numbers

GRA Patient Engagement Structures	Number of Individuals/Units
Patient Experience Survey Responses	12,499
Survey Language Translations	9
Patient Organizations	100
Patient Board	6
Patient Slack Channel	81
Subcommittees	
Steering Committee Patient Engagement Co-Leads	2
Research	23
Communications	10
Resources	13

Figure 1. Patient involvement in GRA in numbers

Patient Representation in Organizational Structure

Patient representation is reflected in several ways: (a) two patient representatives on the steering committee, (b) a patient board that serves as a conduit between the broader patient community and GRA steering committee, and (c) three teams led by patients. The research team coordinates and develops research initiatives, the resources team compiles and shares resources, and the communications team disseminates relevant information to the broader community.

Open Communication Channels

Global communication within GRA is facilitated by the use of open, asynchronous Slack channels enabling collaborationbetween the teams, researchers, and patient representatives.

Quality of Life: The collective impact of these patient engagement efforts has been positive. Considering GRA was founded in March 2020, there are many areas for growth, and as needs are identified, GRA tries to quickly address them by creating new patient roles. While many organizations are either centered around researchers or patients, GRA uniquely facilitates collaboration and conversation between both sides, serving as a model to involve patients from the ground up.

Disclosure: C. Harrison, Aurinia Pharmaceuticals Inc, 5, Astra Zeneca Pharmaceuticals, 5; **R. Sinha**, None; **E. Sirotich**, None; **N. Ikram**, None; **K. Young**, None; **C. Felix**, CISCRP, 9, Lupus Therapeutics, 9, Astrazeneca, 5, Aurinia, 5; **K. Durrant**, None; **R. Beesley**, None; **S. Mingolla**, None; **A. Martín Mancheño**, None; **D. Richards**, Eli Lilly Canada, 8, Various companies, 9; **E. Olmedo**, None; **W. Costello**, None; **M. Gore-Massy**, Aurinia Pharmaceuticals, 5; **L. Proulx**, None; **M. Marino**, Vectra, 5; **R. Howard**, Novartis, 5, AbbVie, 1, Amgen, 1, Bristol-Myers Squibb, 1, GSK, 1, Johnson & Johnson, 1, Eli Lilly, 1, Merck, 1, Novartis, 1, Pfizer, 1, Teva, 1.

Abstract Number: PP09

An Integrative Approach to Managing Rheumatoid Arthritis (RA): Healing the Body, Mind & Spirit

Elisabeth Abeson[1], [1]Westport, CT

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Perspectives
Session Type: Patient Perspectives
Session Time: 12:00PM–1:00PM

Background/Purpose: Diagnosed with RA in 2012, rheumatologists prescribed methotrexate or a biologic. As I was profoundly impacted by my mom's 30-year battle with RA, I wanted to explore natural healing modalities as well. In partnership with my rheumatologist, I took hydroxychloroquine while specialists addressed inflammation in different parts of my body. Despite expert care, I was intuitively drawn to treating my systemic condition more holistically.

Intervention: Two elements symbiotically restored me to health: Ayurveda & a hospital-based RA Support & Education Group. 1. Ayurveda is a traditional Indian system of medicine that equates good health with a balanced body, mind & spirit - treating them collectively through diet, lifestyle & herbal remedies. A pilot study presented at the ACR found Ayurveda equivalent in efficacy as methotrexate with fewer adverse events[1]. I became a patient of the allopathic & ayurvedic authors & followed an integrative protocol ever since. 2. My RA group made allopathic (conventional western) medicine accessible by explaining RA in a patient-centric manner & addressing it on the level of body, mind & spirit. Co-facilitated by a clinical social worker & rheumatology nurse, multi-disciplinary experts led lectures & discussions that made me feel whole, heard & valued. Together, we have built an empowered community.

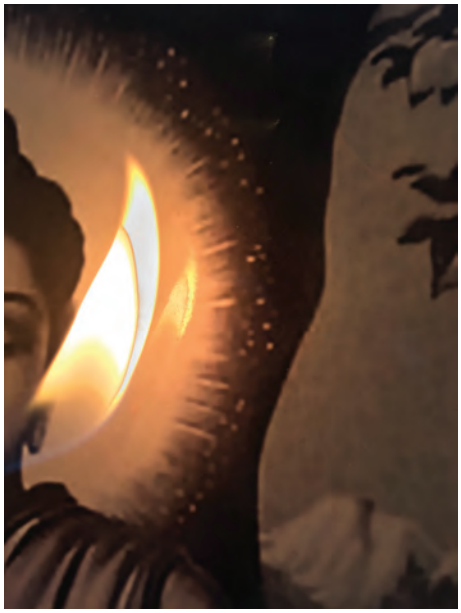
[1] __,__Double-blind, Randomized, Controlled, Pilot Study Comparing Classic Ayurvedic Medicine, Methotrexate, and Their Combination in Rheumatoid Arthritis. *J Clin Rheumatol*. 2011;17(4):185–192

Maintenance: 1. Ayurveda After 4 years on this integrative regimen, my rheumatologist shared significant improvement on several validated measures. Psychologically, Ayurveda helped heal childhood trauma, & spiritually, I reconnected with art after 25 years. At first, I processed treatment discomfort through art therapy. IMAGE 1. Later, I shared my healing journey through art to comfort others & inspire hope. 2. My RA group gifted an arsenal of clinical knowledge that made me the most valuable member of my wellness team. Emotionally, the safe environment enabled me to share my depression, deepen self-compassion & bond with peers sharing the same co-morbidity. Spiritually, our art therapy project helped me come to terms with my RA & see it as an opportunity for growth. IMAGE 2

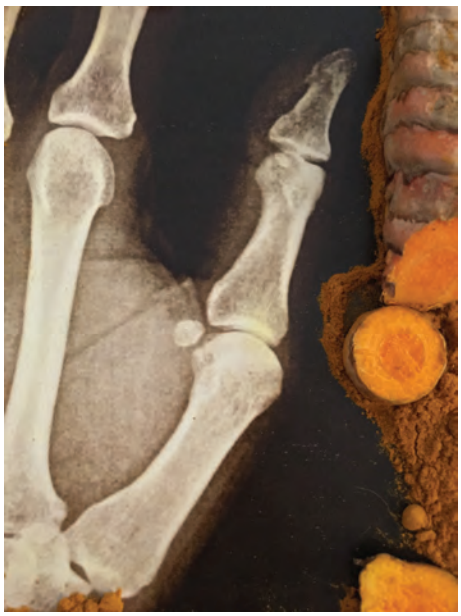
[1] DAS, HAQ, x-rays, ultrasounds, MRIs, blood markers, ophthalmic & dental values

Quality of Life: I yearned to return to work, collaborate with kindred spirits & contribute to society. Being ill taught me I linked my identity & self-worth to professional status, so I vowed to rejoin the workforce with this awareness & value myself regardless of 'output'. I also chose to re-frame my healing journey as an asset rather than a liability. Leveraging my background in international development, I am building a practice that makes it easier for others (than it has been for me) to treat RA with ayurveda & allopathy's collective strength. Why settle on a geographic or culture-specific healing modality when battling an illness that knows no boundaries? IMAGE 3

RESTORATION TO FLIGHT © Elisabeth Abeson — IMAGE 1 OF 3 This illustration depicts a limping bird that is restored to flight – thanks to an expanded wingspan. Elisabeth created this mixed-media collage as a form of art therapy while undergoing medical treatment for her RA at an Ayurvedic Hospital in _____. The piece is composed of an x-ray of her left hand, a bird she cut out of a local newspaper, gouache, pencil & prayer beads from the Hospital's temple that honors the God of Healing. She was under the care of her long-time Ayurvedic Physician (Vaidya),_____,Chief Medical Director at___,in ___,___. Elisabeth became his patient based on his work as the Lead Investigator of the ayurvedic component of the previously-cited pilot study that was presented at ACR in 2011. She is also grateful to _____, the Lead Investigator of the allopathic component who became her Rheumatologist and supported her integrative treatment plan.



TOWARDS THE LIGHT © Elisabeth Abeson — IMAGE 2 of 3 TOWARDS THE LIGHT Depression and RA often fester together. RA has forced me to try to seek comfort and hope outside of myself. So, I have become more spiritual and faith-filled. For this I am grateful.



INTEGRATIVE MEDICINE © Elisabeth Abeson — IMAGE 3 of 3 This photo-installation is composed of organic Turmeric on an x-ray of Elisabeth's left hand. It celebrates the powerful fusion of Ayurveda, (symbolized by Turmeric, Curcuma longa, known for its anti-inflammatory properties), and Allopathic medicine, which is represented by a high-resolution radiograph. Using two different medical systems with their own distinct improvement markers & outcome measures, both Elisabeth's Rheumatologist & Vaidya (Ayurvedic Doctor) agree that a combination of the two healing modalities have improved her health.

Disclosure: E. Abeson, None.

Abstract Number: PP10

Patients with Relapsing Polychondritis ("RP") and an Advocate Manufactured Custom Cloth Masks to Combat COVID-19: This Mask Project Provided a Sense of Purpose, Created Unity, Increased Awareness of RP, Facilitated Research, and Generated Hope

Isabel Bautista[1] and Michael Linn[2], [1]Relapsing Polychondritis Foundation, Wilmington, CA, [2]Relapsing Polychondritis Foundation, New York, NY

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Perspectives
Session Type: Patient Perspectives
Session Time: 12:00PM–1:00PM

Background/Purpose: In 2013, I was diagnosed with Relapsing Polychondritis ("RP"), a systemic inflammatory disease of unknown etiology that can be fatal. The disease affects multiple organs, particularly cartilaginous structures such as the ears, nose, airway, and joints as well as eyes, skin, vasculature, heart valves, and brain.

After my diagnosis, I joined a private online support group (the "RP Support Group") to connect with other RP patients and gain a sense of empowerment and hope regarding this rare, debilitating disease.

Intervention: In April 2020, a member of the RP Support Group posted an inquiry asking her peers if the group could have masks created to protect our community from COVID-19. Soon after, the inquirer and five other members volunteered to donate their time and materials to make cloth masks and ear savers for RP patients, and together, became known as the "RP Mask Team."

The RP Mask Team received outstanding support from its community. Initially, we planned to work with the materials we had on hand. However, when the RP Foundation (polychondritis.org) and Race for RP (RaceForRP.org) donated custom fabric, the scope of the project grew and became an international disease awareness campaign. With funding from individual donors, the RP Mask Team was able to provide high-quality, handmade cloth masks "free of charge" to each RP patient who requested one, regardless of their geographical location.

Maintenance: With individual and institutional support, the RP Mask Team produced and shipped well over 300 masks and ear savers to patients throughout the United States, Canada, United Kingdom, France, Austria, Romania, Germany, Netherlands, Australia, and New Zealand.

Our "one of a kind" masks positively impacted international RP communities by combating the spread of COVID-19, while uniting patients, raising morale, increasing awareness of RP, and demonstrating success through collaboration.

The mask project also facilitated research. When posting information about the project, the RP Mask Team encouraged participation in the National Institutes of Health Patient Reported Symptoms Survey and a COVID-19 Patient Research Project being conducted with support from the Vasculitis Foundation, Vasculitis Clinical Research Consortium, and the RP Foundation.

Quality of Life: Having a rare disease is often extremely difficult and disheartening. Prior to the RP mask project, I was extremely stressed and had a sense of hopelessness because of COVID-19. I was especially concerned about how the pandemic would impact people with an autoimmune disease, like myself.

The RP mask project changed my perspective. It gave me a sense of purpose, created unity among the international RP communities, increased awareness about my disease, gave me an opportunity to help advance research, and perhaps most importantly, created hope. When I follow the #RPmaskteam, I see photos of other patients proudly wearing their custom RP masks increasing awareness, and this fills me with joy. When I wear my RP mask, I feel proud, strong, heard, and noticed. I believe that our custom masks give the RP community one voice that says, “we are strong, and we will triumph over relapsing polychondritis.”

Relapsing Polychondritis Mask Makers worked together to produce cloth masks to protect RP patients from COV-ID-19

Relapsing Polychondritis Ear Saver Makers worked together to protect RP patients from pain and combat COVID-19

Relapsing polychondritis patients often experience burning or throbbing ear pain, so the RP Mask Team manufactured ear savers to secure handmade cloth masks

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Disclosure: I. Bautista, None; **M. Linn**, None.

Abstract Number: PP11

"Knitting a Community of Hope"- Supporting, Empowering and Educating Those Living with Lupus, and Overlapping Conditions and Their Loved Ones via in Person and Virtual Support Groups That Include Art Therapy, and Wellness Techniques Is Key; Mental Health Is as Important as Physical Health

Juana Mata[1] and Ma. Estela Mata-Carcamo[2], [1]Looms for Lupus, La Puente, CA, [2]Looms for Lupus, Baldwin Park, CA

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Perspectives
Session Type: Patient Perspectives
Session Time: 12:00PM–1:00PM

Background/Purpose: Juana was Diagnosed with Rheumatoid Arthritis in April 2009. In May 2009 she ended up in the hospital with a variety of symptoms and was sent home with a diagnosis of Anxiety because she insisted that something was wrong. She refused to go home unless she had testing done, after the testing was completed, She was admitted to ICU with platelet count of 2,000 (normal is 150,000-450,000), she was diagnosed with Thrombocytopenia and Lupus SLE. If she would have gone home that day she would have died. She was scared and knew very little about Lupus, she wanted to learn, and empower others about self advocacy.

Intervention: Learning about Lupus, treatments, tracking symptoms and becoming a better self advocate while working together with her care team was something that Juana and her support system had to do. Loom knitting was a great way for Juana to relieve her stress and every weekend all her family would gather to learn, support and loom knit together. Supporting each other and learning more about Lupus helped Juana and her family. Loom knitting had given Juana a stress relieving technique, it helped her fight depression and together with her family, they were knitting hope.

Maintenance: In 2011 the Mata Sisters co-founded Looms for Lupus, non profit organization that provides support, resources and awareness to minority families, those living with Lupus, overlapping conditions and their caregivers\loved ones. Juana and Estela, (caregiver\loved one) facilitate in person support group in Baldwin Park, CA and a virtual Facebook live Spanish Support Group every second Saturday of the month, where they include Art therapy such as loom knitting, painting, rock art, vision boards, other forms of art therapy and wellness techniques such as yoga, mindfulness and meditation. Living with an autoimmune and chronic condition can be hard not only physically but mentally, incorporating these modalities help in the overall health; Mental Health is as important as Physical Health.

Quality of Life: Juana and Estela are patients, advocates; together they support, empower, and educate others, helping others helps them. Educating others on different modalities to relief stress can help prevent flares and also help with their quality of life.

Empowering and supporting the caregivers by providing them with education and tools to be supportive and to also practice self care is essential for both the caregiver and the patient.

Empowering the patient on how to advocate for themselves and providing tools and resources to track their symptoms, prepare for their visits and work closely with their provider helps both the patient and the care team provide better treatments and have better patient outcomes. Educating them on insurance plans/authorizations and Maintaining copies of their medical record helps them keep track and be proactive with their care.

Art Therapy- incorporating Art Therapy can alleviate symptoms of depression, reduce stress, improve self esteem and improve mental health.

Social Media Platforms- Provide support\educate and connect via Twitter, Instagram and Facebook in English and Spanish. This helps bring up to date information and connect with others and ensure they are not alone.

Knitting a Community of Hope

Disclosure: J. Mata, None; **M. Mata-Carcamo**, None.

Abstract Number: PP12

COVID-19, Racism, and Gender Discrimination: The Function of Stress in Widening the Gap in Health Disparities

Carly Harrison[1] and Christele Felix[2], [1]LupusChat, Richmond, VA, [2]LupusChat, Rosedale, NY

SESSION INFORMATION
Session Date: Sunday, November 8, 2020
Session Title: Patient Perspectives
Session Type: Patient Perspectives
Session Time: 12:00PM–1:00PM

Background/Purpose: Populations experiencing rheumatic diseases are often at higher risk of increased levels of stress. This may result in disease complications and can potentially lead to escalation and development of new diseases as well. Because of the heterogeneity of many rheumatic diseases, it is difficult to understand which forms of stress could exacerbate one's condition. What is known however, is that stress intensifies mental health issues.The COVID-19 global pandemic and the national protest movement sparked by the latest round of police violence, both predominantly affect Black people. The events have caused immense stress on people with rheumatic conditions, a large percentage of which are Black, with 6.1 million Black people diagnosed with Rheumatoid Arthritis, and as many as 1 in 250 Black women diagnosed with and being treated for Lupus, according to the latest statistics for the United States.

Intervention: Because of the added danger, patients are often advised to avoid stress and/or reduce any stressful activities in their lives. We are reminded very often of the necessity of living a stress-free life as part of our care regimen for our rheumatic diseases. As is well known, mental health directly affects physical health. Added stress in patients' lives leads to increased consultations with rheumatologists and other specialists, because of the increased physical symptoms caused by stress. Additionally, psychological consults and support groups are recommended for mental and emotional support. Formal and informal support group settings are very beneficial to patients as a space to unpack their feelings and emotions.

Maintenance: The goal is to decrease stress, as stress negatively impacts patient health. To that effect, issues of health disparities as well as extrajudicial violence must be addressed. To protect the overall health of the patient, racism and gender discrimination must be highlighted and eradicated. Women, specifically Black cis women like ourselves and espcially Black women of trans experience, are dying at a disproportionate rate due to societal violence and negligence within the healthcare system. We must remember that when we protect the most vulnerable and marginalized among us, we ensure protections and a better quality of life for all.

Quality of Life: International Rheumatology organizations (and the medical community at large) should be invested in dismantling these inhumane systems that overwhelmingly affect the physical and mental health of their patients. Stress is defined as physiological disturbance or damage caused to an organism by adverse circumstances. Patients deserve a life free of such a burden as we work together with our care teams to manage our rheumatic diseases.

Disclosure: C. Harrison, Aurinia, 5, Astrazeneca, 5, US Department of Defense CDMRP, 5; **C. Felix**, Aurinia, 5, Astrazeneca, 5, Lupus Therapeutics, 9, CISCRP, 9, US Department of Defense CDMRP, 5.

Author Index

B

E

F

G

H

K

M

N

O

P

Z

Keyword Index

S

W

X